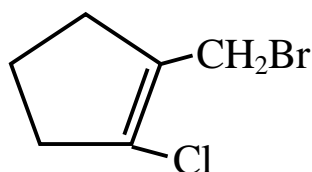
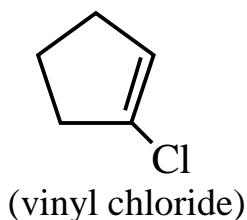


Alkyl Halides

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,



(vinyl chloride and allyl bromide)

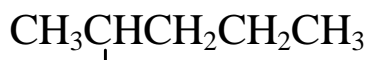
Alkyl halides are classified as primary (1°), secondary (2°) or tertiary (3°), depending upon the type of carbon to which X is bonded. When X is bonded to a carbon, which is bonded to one more carbon is called 1° halide and their general representation is RCH_2X . When X is linked to a carbon, which 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 halogen 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,



1-Chloropentane



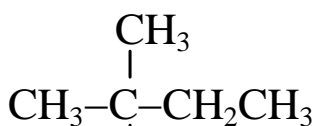
2-Chloropentane



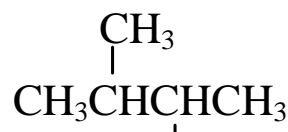
3-Chloropentane



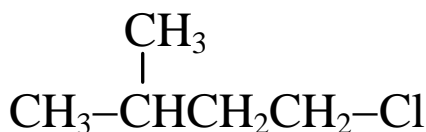
1-chloro-2-methyl butane



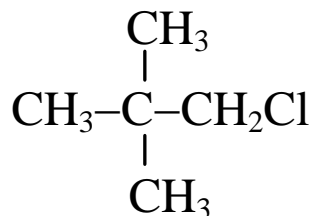
2-chloro-2-methyl butane



2-chloro-3-methyl butane



1-chloro-3-methyl butane



1-chloro-2, 2-dimethyl propane



1,1-Difluorobutane

(Geminal)



2,2-Difluorobutane

(Geminal)



1,2-Difluorobutane

(Vicinal)



1,3-Difluorobutane



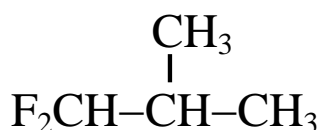
1,4-Difluorobutane



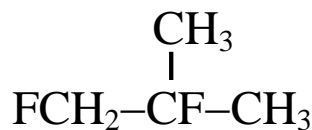
2,3-Difluorobutane

(Vicinal)

ALKYL HALIDES AND ARYL HALIDES



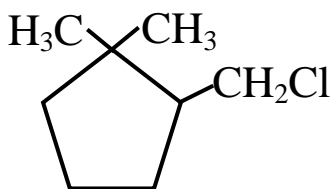
1,1-difluoro-2-methyl propane
(gem)



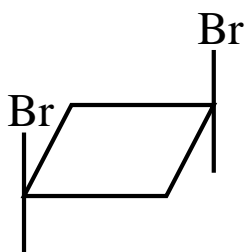
1,2-difluoro-2-methyl propane
(vic)



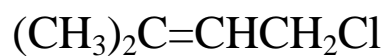
3-bromo-1, 1, 2-trichloropropane



2-chloromethyl-1,
1-dimethyl cyclopentane



cis-1,
3-dibromocyclobutane

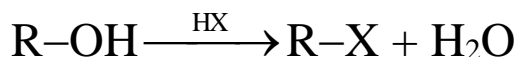


1-chloro-3-methyl-2-butene.

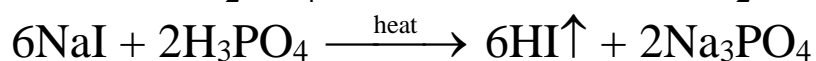
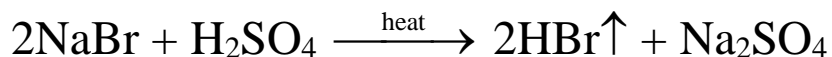
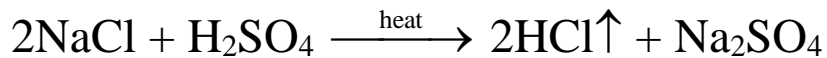
2. Methods of Preparation of Alkyl Halides

2.1 From Alcohols

2.1.1 By Using Hydrogen Halides



It must be noted that the HX used should be dry, which is produced, in situ, as follows

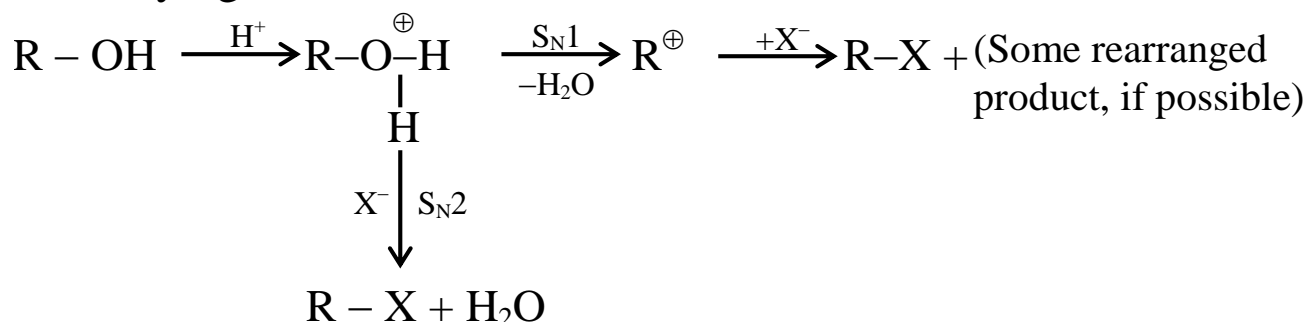


It may be noted that H_3PO_4 is used in place of H_2SO_4 to prepare HI. This is because HI is a reducing agent and H_2SO_4 being an oxidising agent can oxidize it.

The above conversion of alcohol to alkyl halides proceeds via $\text{S}_\text{N}1$ or $\text{S}_\text{N}2$ mechanism. Both the mechanisms are operative during the reaction, having competition between them. The type of mechanism followed by an

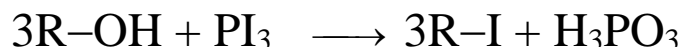
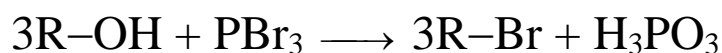
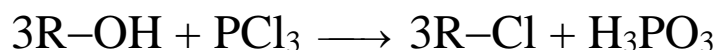
ALKYL HALIDES AND ARYL HALIDES

alcohol depends on the structure of alcohol and the type of solvent used for carrying out reaction.



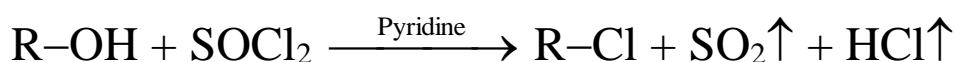
Details about S_N1 and S_N2 mechanism will be discussed later in this topic.

2.1.1 By Using Phosphorous Halides



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.

2.1.1 By Using SOCl₂ (Thionyl Chloride)



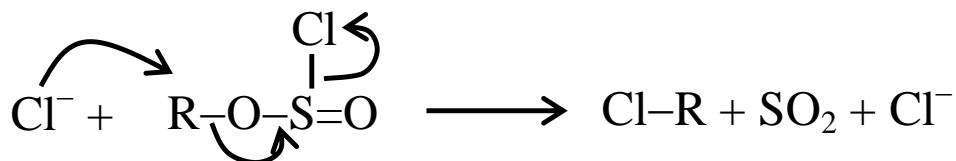
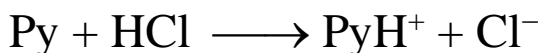
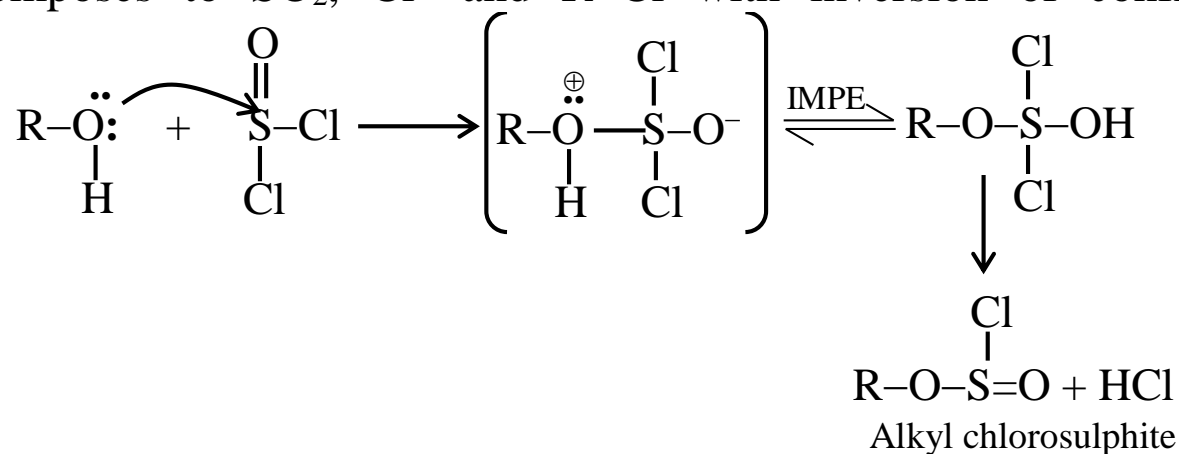
The usefulness of this method is that there is no side product, which has to be separated. The side products are gaseous SO₂, which escape from the reaction mixture and HCl, which forms a salt with the base (pyridine), named pyridinium chloride (C₅H₅N⁺Cl⁻). The product alkyl chloride has a configuration 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:

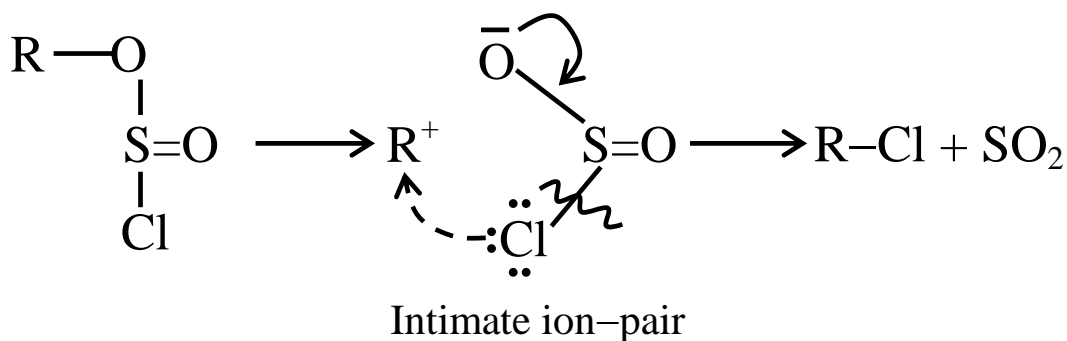
Alcohol first reacts with SOCl₂ to form an intermediate chlorosulphite ester, which gives alkyl chlorosulphite and HCl. In presence of pyridine,

ALKYL HALIDES AND ARYL HALIDES

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.

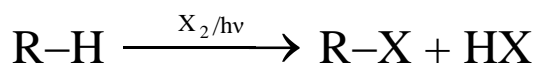


In the absence of a base and polar solvent, the chlorosulphite ester dissociates into an intimate ion-pair. The Cl of the anion of ion-pair attacks from the front side of R^+ to give retention of configuration. The retention is observed because Cl cannot reach the rear of the R^+ group but is close to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



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



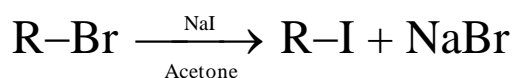
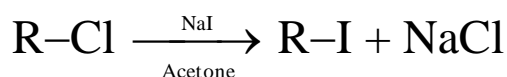
Reactivity of above reaction with respect to type of hydrogen to be replaced follows following order

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.



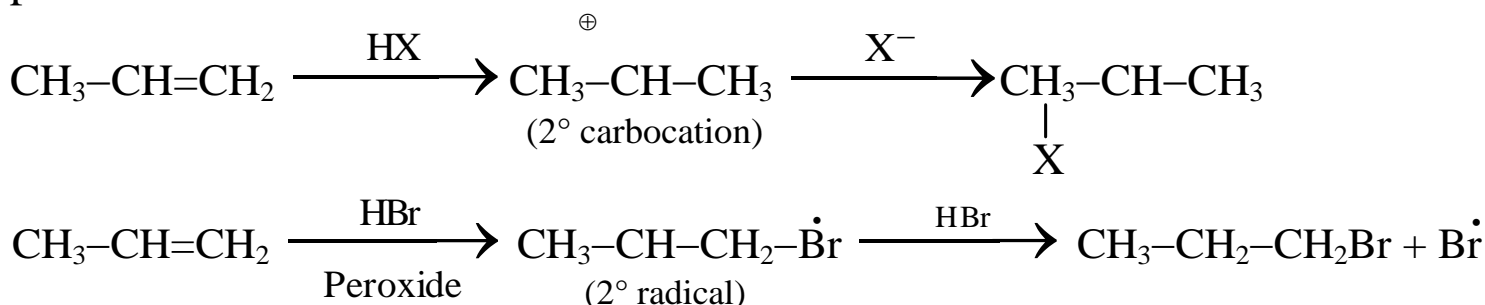
The reaction proceeds by $\text{S}_{\text{N}}2$ mechanism and is possible because NaCl and NaBr are precipitated in the reaction, as they are not soluble in weakly polar aprotic solvent.

2.4 By Addition of H-X to Alkenes

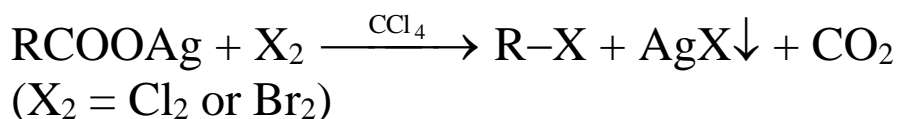
Alkyl chlorides, bromides and iodides can be prepared by treating an alkene with corresponding hydrogen halide (HCl , HBr or HI). The addition of these compounds to alkene takes place according to Markownikov's rule. The reaction proceeds by electrophilic addition of H^+ to give more stable carbocation followed by attack of X^- . Anti-Markownikov addition of HBr can be achieved, if the reaction is

ALKYL HALIDES AND ARYL HALIDES

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.



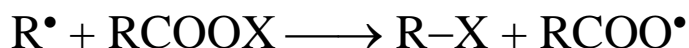
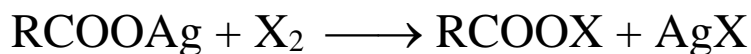
2.5 From Silver Salt of Carboxylic Acid



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.



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.

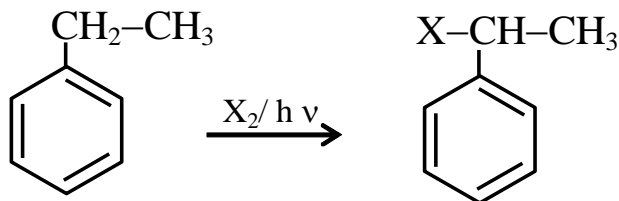
In Hunsdieker reaction, the yield of R-Br is better than R-Cl because O-Br bond is weaker than O-Cl bond as well AgBr is less soluble than AgCl .

The yield and ease of formation of R-X is



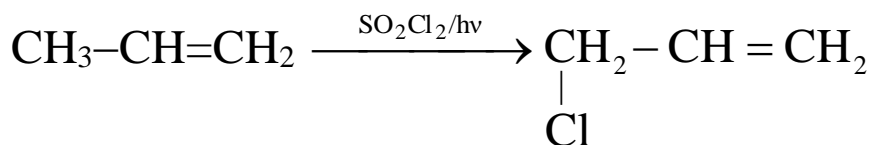
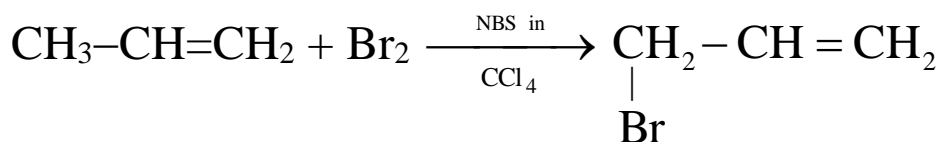
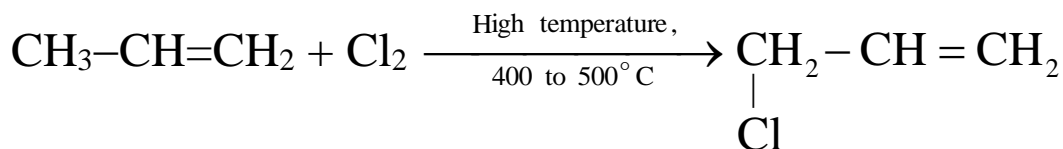
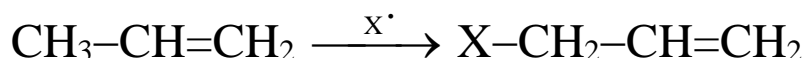
2.6 Preparation of Allylic or Benzylic Halides

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



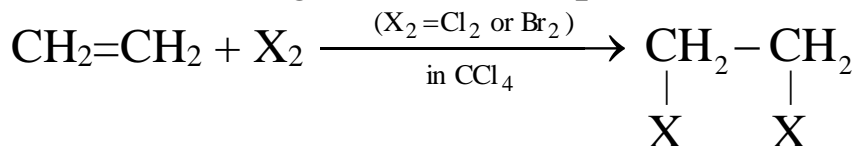
The reaction follows free radical mechanism.

(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.

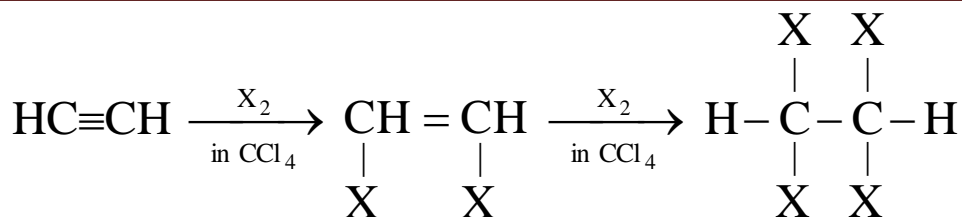


2.7 Preparation of Polyhalides

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

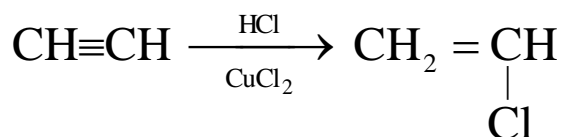


(ii) Addition of halogen (Cl_2 or Br_2) to alkynes produces tetrahaloalkanes.

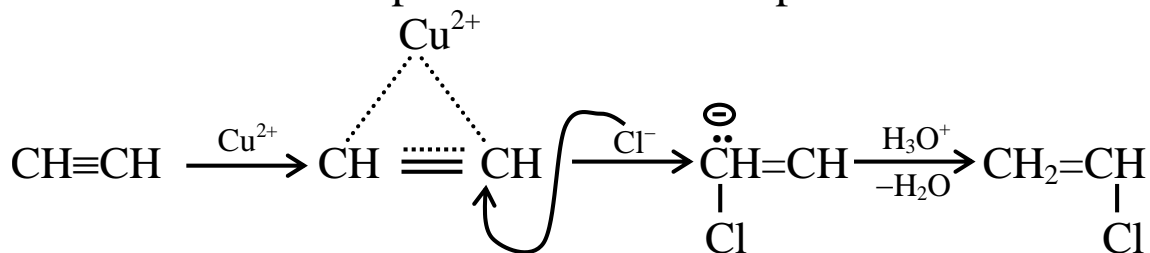


Mechanism of addition of halogen to alkenes and alkynes has been discussed in the lesson “alkenes”.

2.8 Preparation of Vinyl Halides

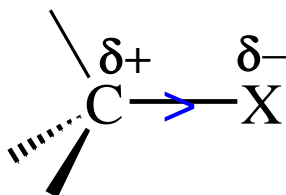


The above reaction proceeds via electrophilic addition as follows



3. General Physical Properties of Alkyl Halides

1. Polarity of C–X bond:



- (1) The carbon-halogen bond of alkyl halides is **polarized**.
- (2) The **carbon** atom bears a partial **positive** charge, the **halogen** atom a partial **negative** charge.

2. The bond length of C–X bond:

Carbon-Halogen Bond Lengths, Bond Strength and Dipole Moment

Bond	Bond Length (Å)	Bond Strength (Kcal/mol)	Dipole Moment (D)
CH ₃ –F	1.39	109	1.82
CH ₃ –Cl	1.78	84	1.94
CH ₃ –Br	1.93	70	1.79
CH ₃ –I	2.14	56	1.64

(1) The size of the halogen atom increases going down the periodic table \Rightarrow the C–X bond length increases going down the periodic table.

3. Solubility:

- (1) Many alkyl and aryl halides have very low solubilities in water, but they are miscible with each other and with other relatively nonpolar solvents.
- (2) Dichloromethane (CH₂Cl₂, *methylene chloride*), trichloromethane (CHCl₃, *chloroform*), and tetrachloromethane (CCl₄, *carbon tetrachloride*) are often used as solvents for nonpolar and moderately polar compounds.

4. Densities:

The densities of alkyl iodides and bromides is more than that of H₂O that the densities of alkyl chlorides and fluorides in less than that of H₂O. The order of densities of alkyl halides and H₂O is RI > RBr > H₂O > RCl > RF and the densities of polychloro methane varies as CCl₄ > CHCl₃ > CH₂Cl₂ > H₂O > CH₃Cl. The alkyl halides are in general insoluble in water.

5. Carcinogenic Nature:

Many chloroalkanes, including CHCl_3 and CCl_4 , have a **cumulative toxicity** and are **carcinogenic**.

6. Boiling points:

- (1) Methyl iodide (bp 42°C) is the only monohalomethane that is a liquid at room temperature and 1 atm pressure.
- (2) Ethyl bromide (bp 38°C) and ethyl iodide (bp 72°C) are both liquids, but ethyl chloride (bp 13°C) is a gas.
- (3) The propyl chlorides, propyl bromides, and propyl iodides are all liquids.
- (4) In general, higher alkyl chlorides, bromides, and iodides are all liquids and tend to have boiling points near those of alkanes of similar molecular weights.
- (5) **Polyfluoroalkanes** tend to have **unusually low boiling points**. Hexafluoroethane boils at -79°C , even though its molecular weight (MW = 138) is near that of decane (MW = 144; bp 174°C).

ALKYL HALIDES AND ARYL HALIDES

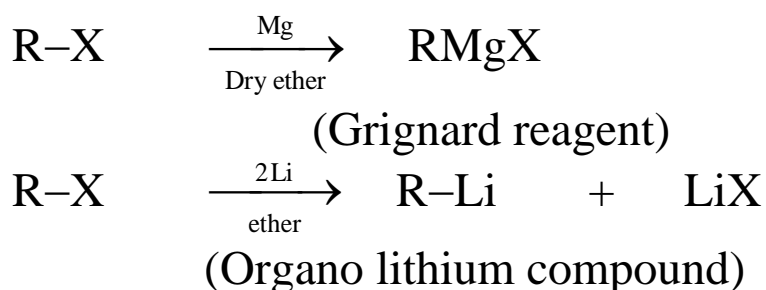
Physical Properties of Organic Halides

Group	Fluoride		Chloride		Bromide		Iodide	
	BP (°C)	Density (g mL ⁻¹)	BP (°C)	Density (g mL ⁻¹)	BP (°C)	Density (g mL ⁻¹)	BP (°C)	Density (g mL ⁻¹)
Methyl	-78.4	0.84	-23.8	0.92	3.6	1.73	42.5	2.28
Ethyl	-37.7	0.72	13.1	0.91	38.4	1.46	72	1.95
Propyl	-2.5	0.78	46.6	0.89	70.8	1.35	102	1.74
Isopropyl	-9.4	0.72	34	0.86	59.4	1.31	89.4	1.70
Butyl	32	0.78	78.4	0.89	101	1.27	130	1.61
<i>sec</i> -Butyl			68	0.87	91.2	1.26	120	1.60
Isobutyl			69	0.87	91	1.26	119	1.60
<i>tert</i> -Butyl	12	0.75	51	0.84	73.3	1.22	100	1.57
Pentyl	62	0.79	108.2	0.88	129.6	1.22	155	1.52
Neopentyl			84.4	0.87	105	1.20	127	1.53
CH ₂ =CH-	-72	0.68	-13.9	0.91	16	1.52	56	2.04
CH ₂ =CHCH ₂ -	-3		45	0.94	70	1.40	102-103	1.84
C ₆ H ₅ -	85	1.02	132	1.10	155	1.52	189	1.82
C ₆ H ₅ CH ₂ -	140	1.02	179	1.10	201	1.44	93	1.73

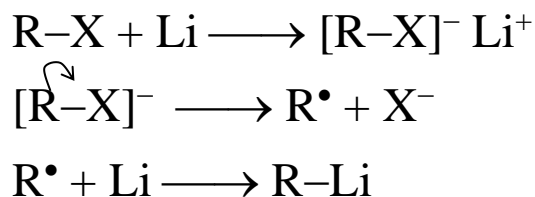
4. General Chemical Properties of Alkyl Halides

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



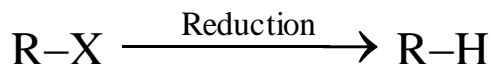
Mechanism:



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 iodides. 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.

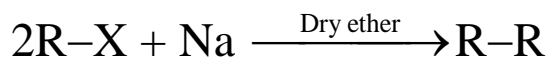
Alkyl organometallic compounds are good source of carbanions (as carbon is more electronegative than the metals) and are very useful in organic synthesis.

4.2 Reduction of Alkyl Halides



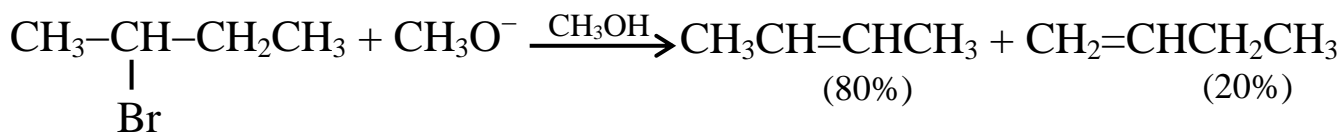
The reagents used for the reduction of alkyl halides to alkanes are Zn and CH_3COOH , Zn and HCl, Zn and NaOH, Zn – Cu couple and alcohol, aluminium amalgam and alcohol etc.

4.3 Wurtz Reaction

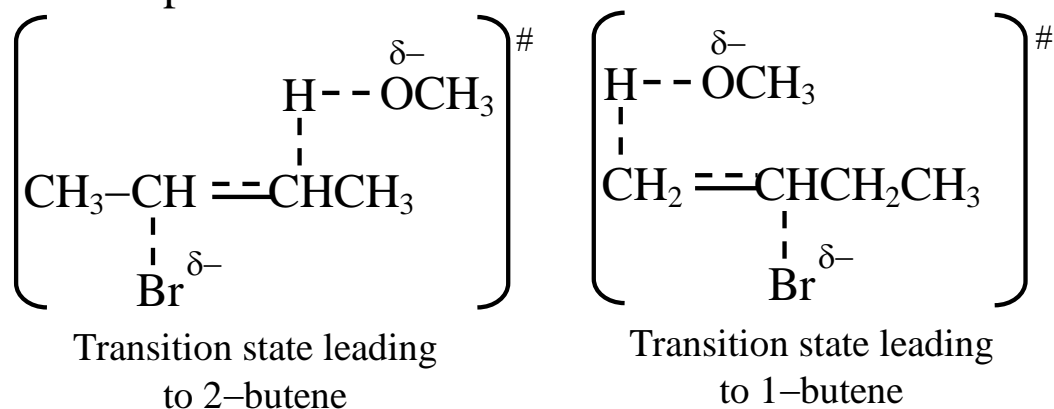


4.4 Elimination Reactions of Alkyl Halide

E₂ Elimination:



2-bromopentane 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

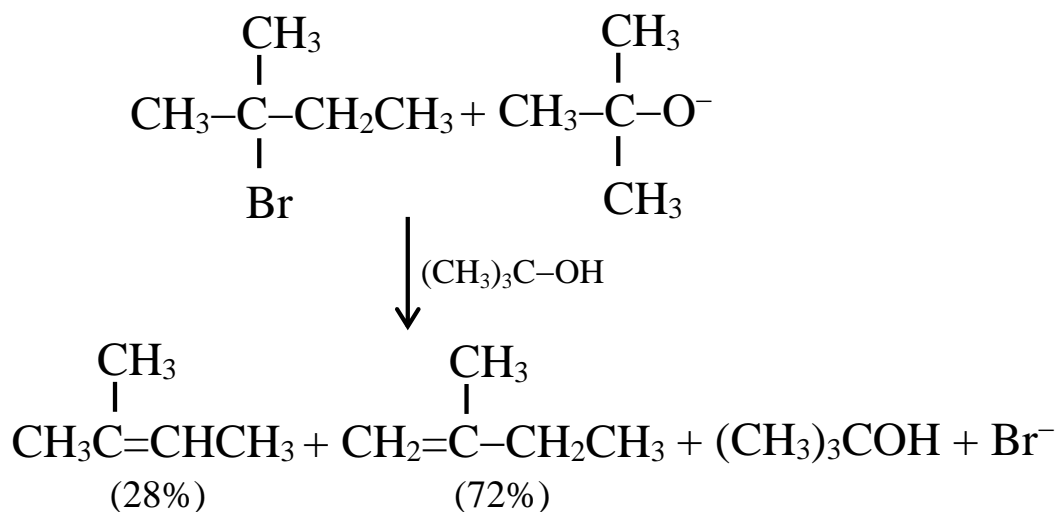


The transition state leading to 2-butene is more stable than that leading to the formation of 1-butene, as this transition state has more hyperconjugable hydrogens. Thus, 2-butene is a more stable product than 1-butene and is formed in greater quantity than 1-butene. The stability of

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the product is governed by Saytzeff's rule (according to which more substituted alkene is the major product).

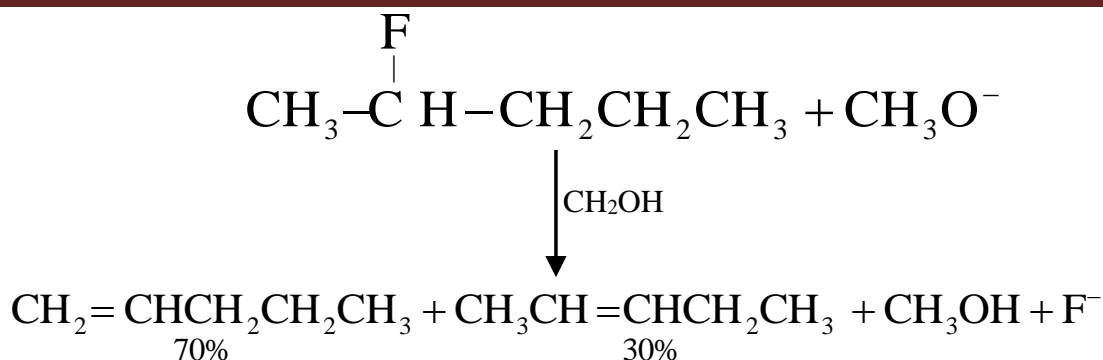
If the base in an E₂ reaction is sterically bulky and hindered, it will preferentially remove the most accessible hydrogen. For example, when 2-bromo-2-methyl butane is treated with bulky t-butoxide ion, base removes one of the more exposed terminal hydrogens, which leads to the less substituted alkene.



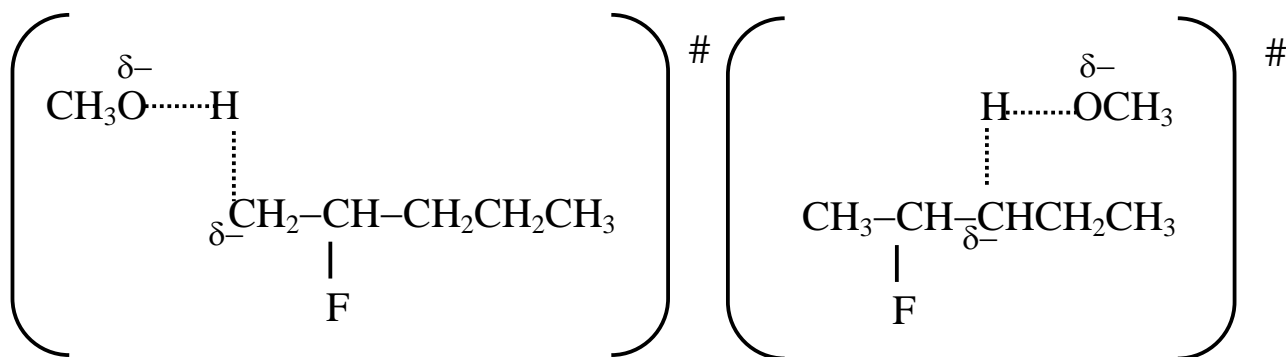
The less substituted product is called Hoffmann's product and is governed by Hoffmann's rule (according to which less substituted alkene is the major product).

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.

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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 fluoride, 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 $\text{E}_{1\text{CB}}$ mechanism. The carbanionic transition state is stabilized by strongly electron-withdrawing fluorine.

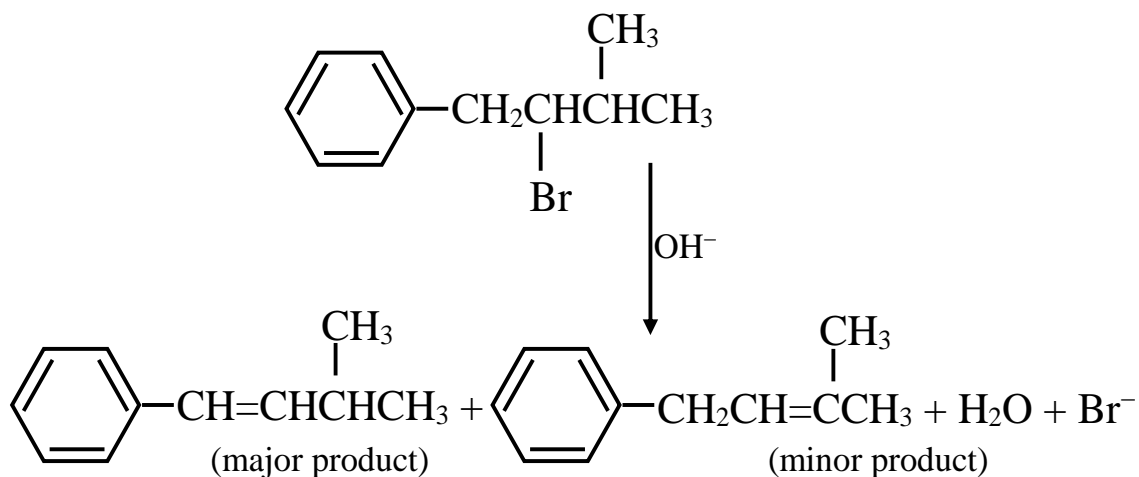
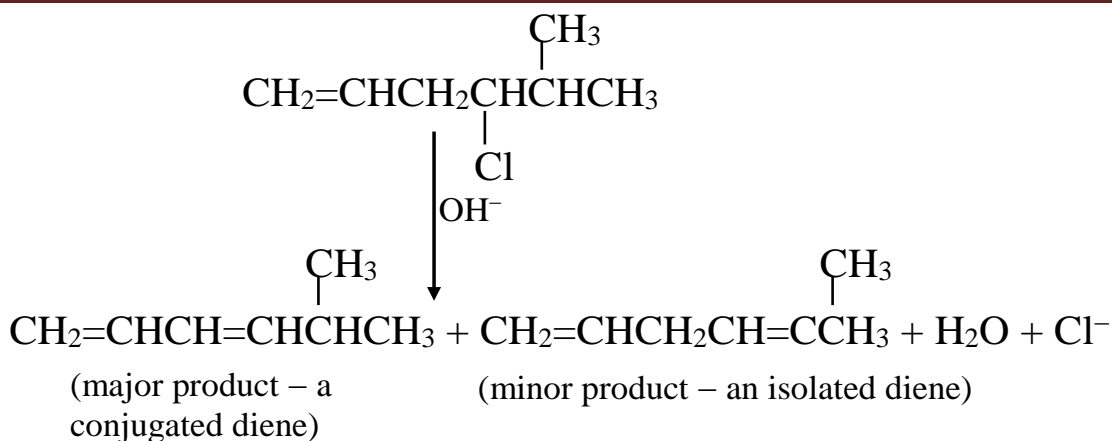


Transition state leading to 1-pentene

Transition state leading to 2-pentene

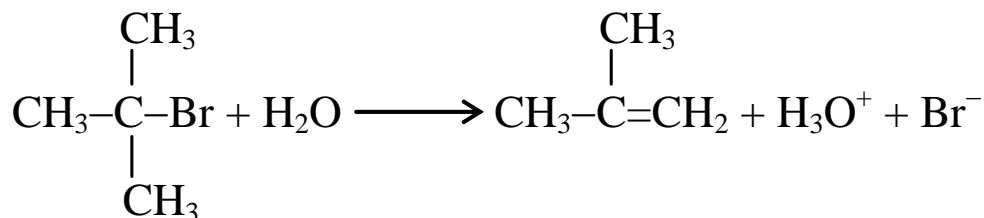
The transition state leading to 1-pentene has the developing negative charge on a primary carbon. This is more stable than the transition state leading to 2-pentene, which has the developing negative charge on a secondary carbon. Because the transition state leading to the formation of 1-pentene is more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

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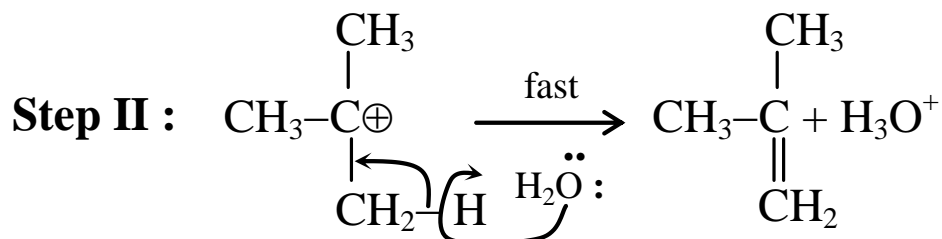
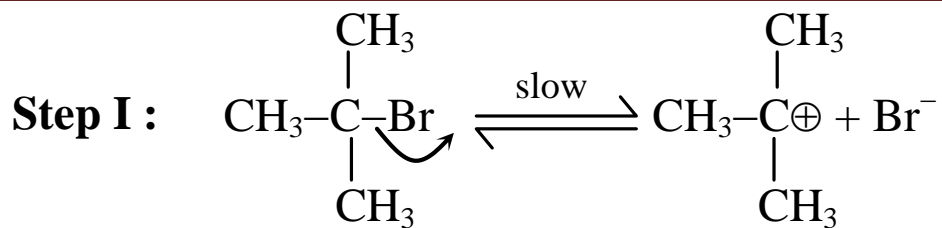
In the given reactions, Saytzeff's rule is not followed, although the substrates are alkyl chlorides/bromides and bases are also small, because the rule does not take into account the fact that conjugated double bonds are more stable than isolated double bonds.

E₁ Elimination:

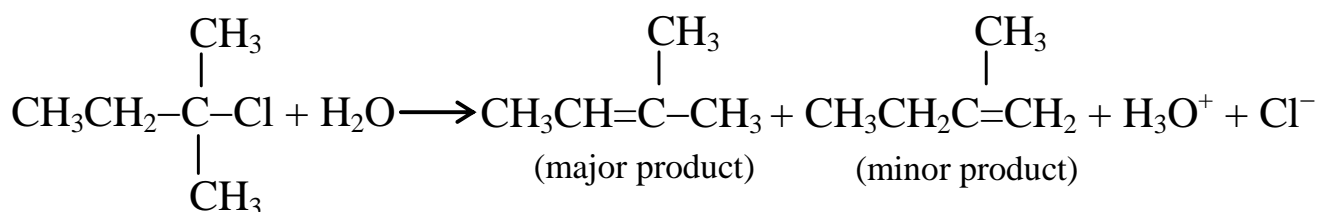


t-Butyl bromide undergoes hydrolysis in two steps. In the first rate-limiting step, the alkyl halide dissociates heterolytically. In the second step, the base forms an elimination product by removing a proton from a carbon adjacent to the positively charged carbon. Increasing the concentration of base has no effect on the rate of the reaction.

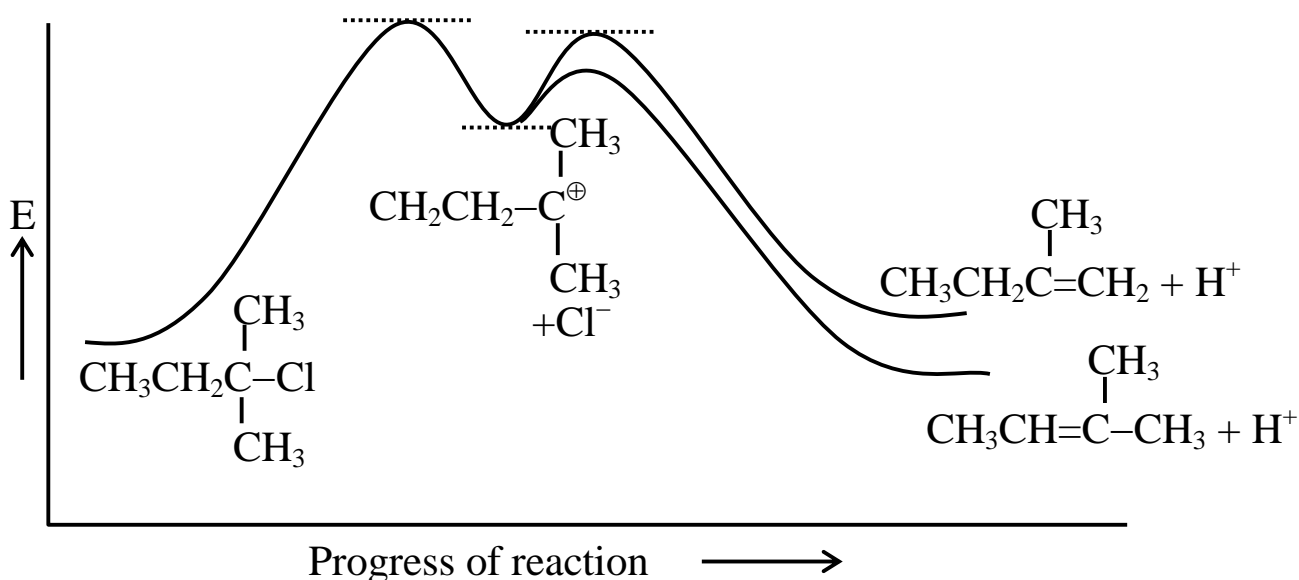
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When two elimination products can be formed, the major product is generally the one obtained by following Saytzeff's rules.



The energy profile diagram for this reaction is



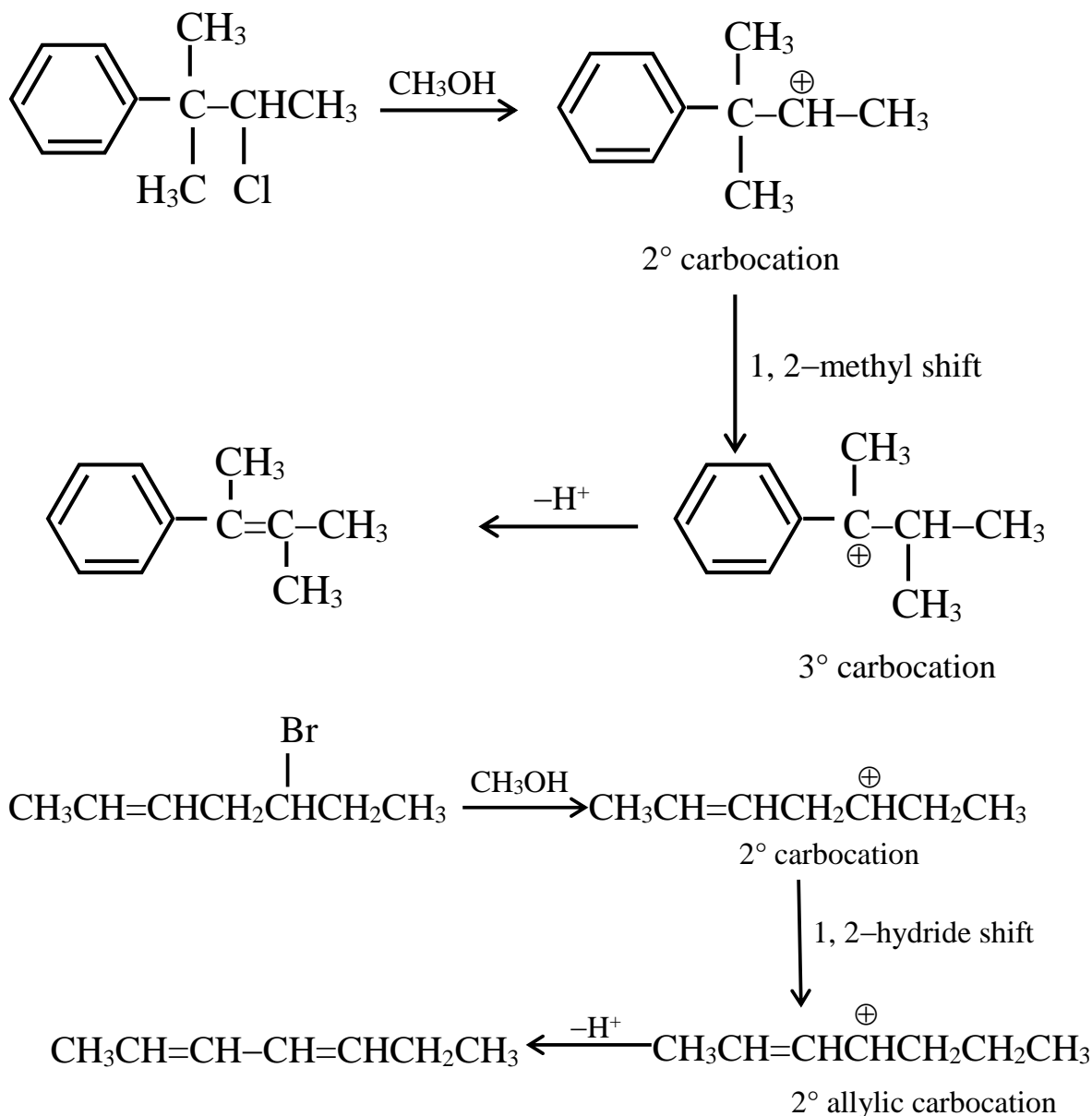
Rate of E_1 reaction depends on the ease with which the leaving group leaves and the stability of the carbocation formed. Thus, the relative reactivities of a series of alkyl halides with the same leaving group

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parallels the relative stabilities of carbocations and the order is represented as

3° benzylic $\approx 3^\circ$ allylic $> 2^\circ$ benzylic $\approx 2^\circ$ allylic $\approx 3^\circ$ alkyl $> 1^\circ$ benzylic $\approx 1^\circ$ allylic $\approx 2^\circ > 1^\circ > \text{vinyl}$

Because E_1 reaction involves formation of carbocation as intermediate, so rearrangement of the carbon skeleton is also frequently observed. For example,



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:

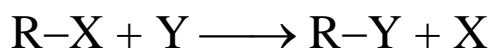
Primary alkyl halides undergo only E₂ elimination reactions. They cannot undergo E₁ reactions because of the difficulty encountered in forming primary carbocations. Secondary and tertiary alkyl halides can undergo either E₁ or E₂ reactions.

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.

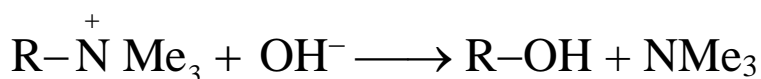
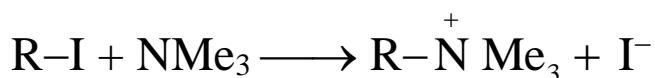
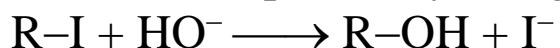
An important reaction of alkyl halides i.e. aliphatic nucleophilic substitution is dealt as a separate heading.

5. Aliphatic Nucleophilic Substitution

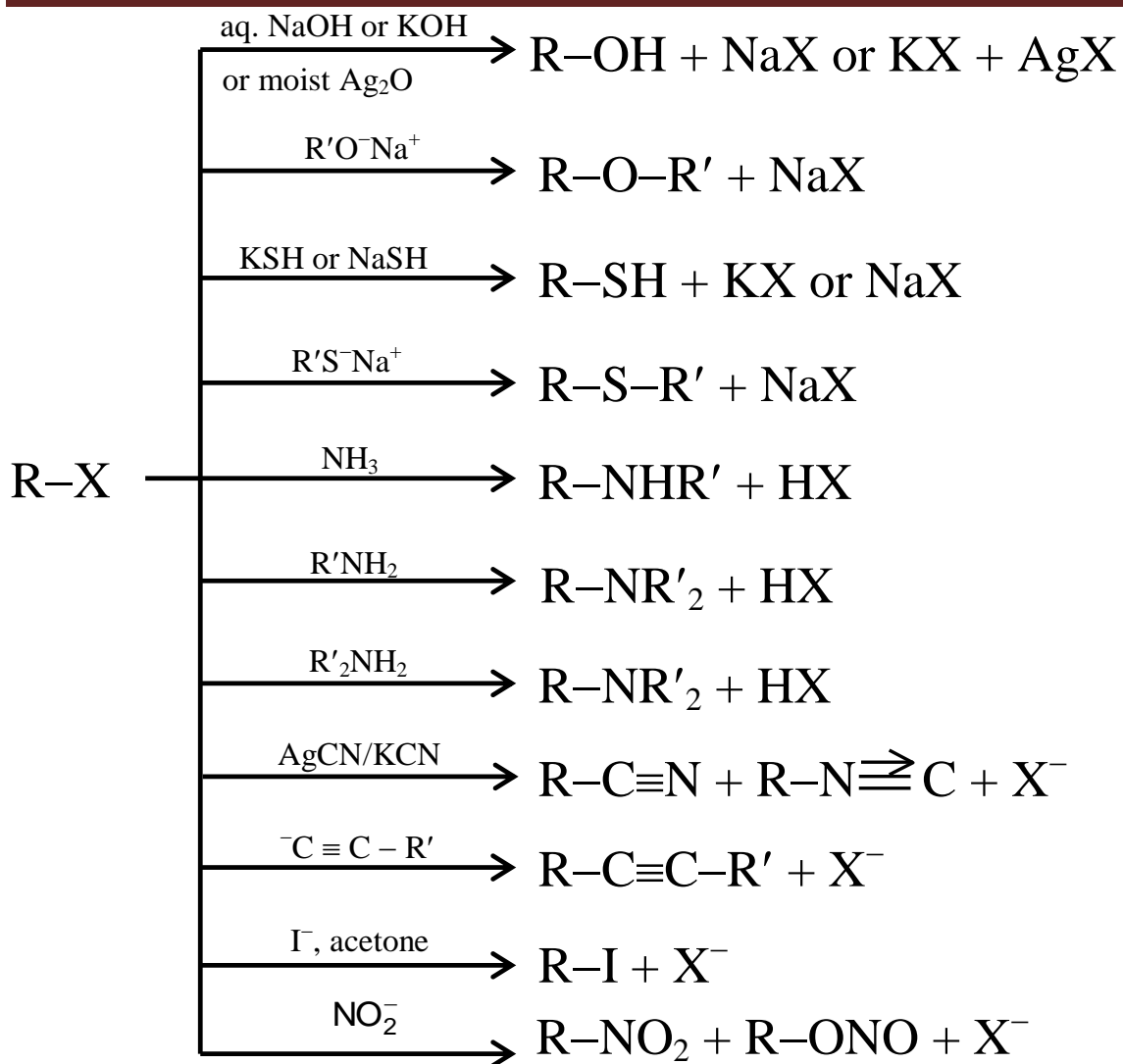
In nucleophilic substitutions, the attacking reagent (nucleophile) brings an electron pair to the substrate, which uses this pair to form a new bond and the leaving group goes away with an electron pair. When nucleophile is a solvent, the reaction is called *solvolysis*.



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



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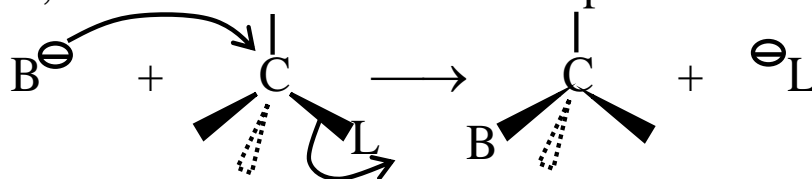
Before embarking on the mechanism of nucleophilic substitution reactions in alkyl halides, we must know certain basic terms.

5.1 HSAB (Hard and Soft Acid–Base) Principle

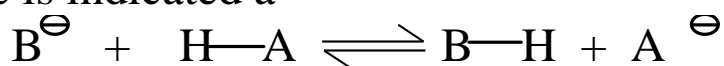
According to hard and soft acid–base principle, hard acids are those species, which have less tendency to attract an electron pair (like H⁺, Li⁺, Mg²⁺, Cr³⁺, Al³⁺ etc.) and hard bases are those species, which have more tendency to hold electron pair (like F⁻, O²⁻ etc.). A hard base prefers a hard acid 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



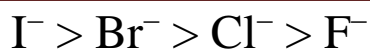
The nucleophilicity is determined by the kinetics of the reaction, which is reflected by its rate constant (k) while basicity is determined by the equilibrium constant, which is reflected by its K_b .

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.

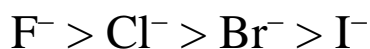
In non-polar and weakly polar aprotic solvents, all the salts will exist as ion-pairs. The ion-pairing will be strongest with the smallest anion (F^-) and weakest with the largest anion (I^-), thus the reactivity of X^- decreases with decreasing size. Thus, the nucleophilicity order of X^- in such solvents would be

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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. Therefore, the nucleophilicity order of X^- in polar protic solvent would be $\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$.

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



On this basis, certain nucleophilicity orders are

(i) In polar protic solvents, $\text{HS}^- > \text{HO}^-$

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

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



(iv) In non–polar solvents, ${}^-\text{CH}_3 > {}^-\text{NH}_2 > {}^-\text{OH} > {}^-\text{F}$

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



(vi) When the atom bonded to nucleophilic site also has an unshared pair of electrons, nucleophilicity of species increases. For example,



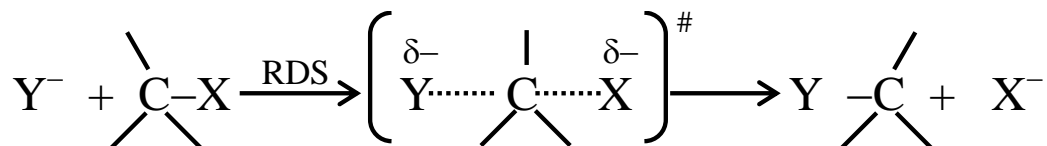
Edwards and Pearson gave following order of nucleophilicity for $\text{S}_{\text{N}}2$ reactions in protic solvents.

$\text{RS}^- > \text{ArS}^- > \text{I}^- > \text{CN}^- > \text{OH}^- > \text{N}_3^- > \text{Br}^- > \text{ArO}^- > \text{Cl}^- > \text{pyridine} > \text{AcO}^- > \text{H}_2\text{O}$.

Several distinct mechanisms are possible for aliphatic nucleophilic substitution reactions. By far the most common are $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ mechanisms.

6. $\text{S}_{\text{N}}2$ Reaction

$\text{S}_{\text{N}}2$ 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.



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

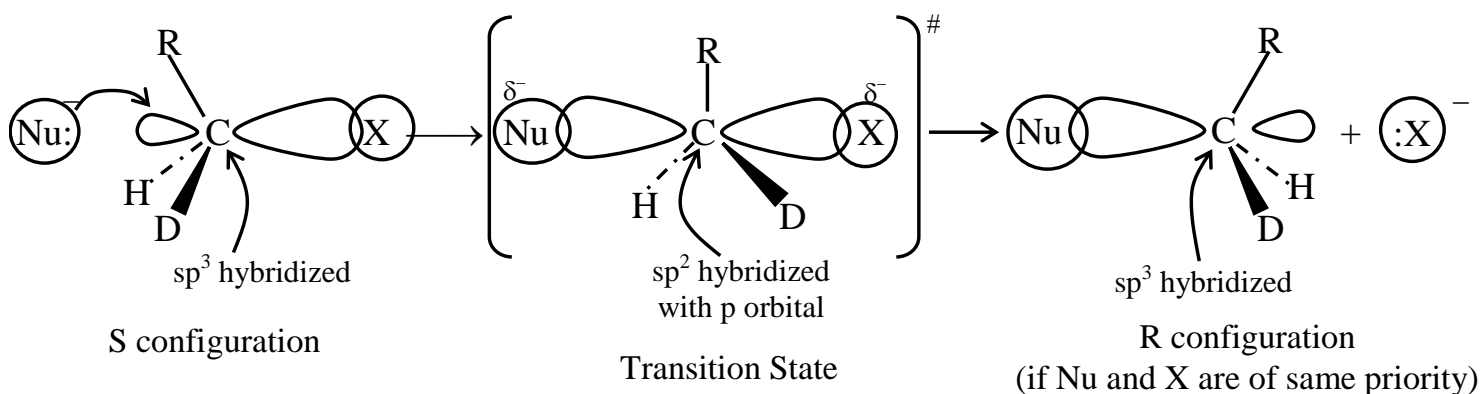
In the transition state, the carbon is sp^2 hybridized with a p-orbital available for overlapping of its lobes with an orbital of the incoming: Nu^- while the other lobe overlaps with an orbital of the leaving group X^- . The reaction is initiated by: Nu^- beginning to overlap with the small lobe (tail) 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

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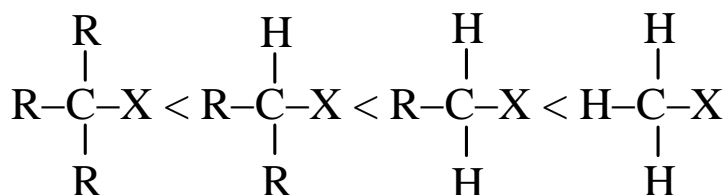
(-) to (+). This inversion in configuration would be observed only when the leaving group and incoming nucleophile have same priority relative to other atoms or group of atoms.

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 $\text{S}_{\text{N}}2$ 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.



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 $\text{S}_{\text{N}}2$ mechanism. Thus, the reactivity of alkyl halides towards $\text{S}_{\text{N}}2$ reaction is as follows,



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The rate law for the S_N2 reaction is

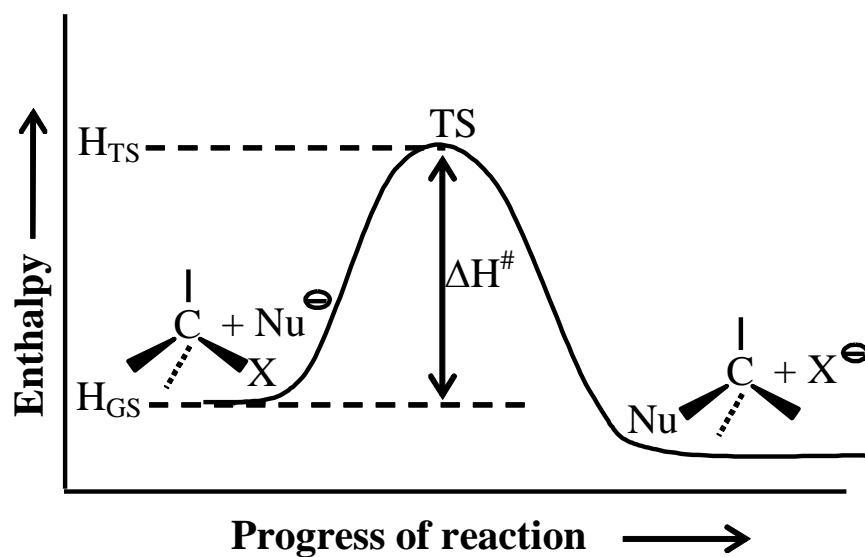
$$\text{Rate} = k [\text{R-X}] [\text{Nu}^-]$$

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.

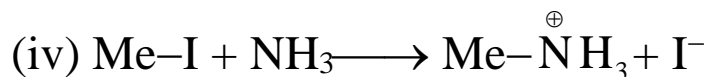
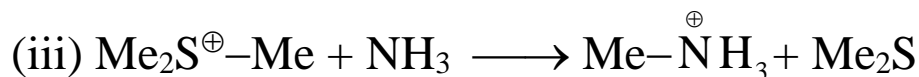
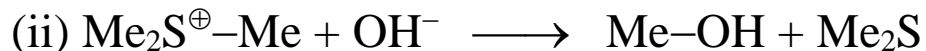
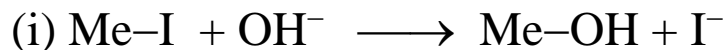
We know that successful S_N2 displacements are exothermic in nature and its energy profile can be shown as



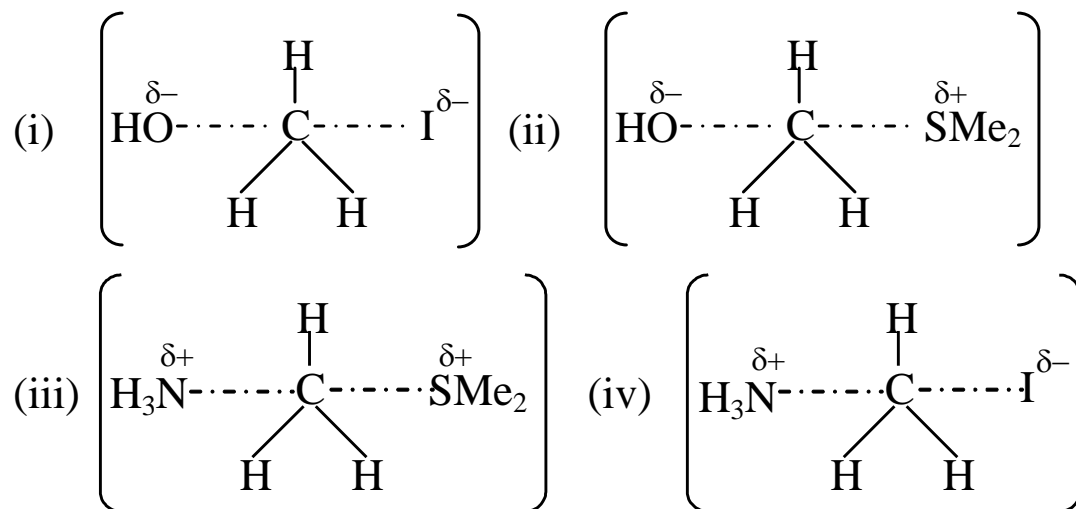
In general, if we change solvent that increases ΔH^\ddagger would decrease the rate of S_N2 reaction. ΔH^\ddagger can be increased by decreasing H_{GS} or by increasing H_{TS} or by doing both. Conversely, any change in solvent that decreases ΔH^\ddagger will increase the S_N2 rate and the decrease in ΔH^\ddagger can be achieved by increasing H_{GS} or by decreasing H_{TS} or by doing both.

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



Their respective transition states are shown as



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.

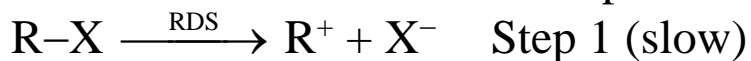
But in reaction (iv), the reactants are uncharged while the transition state has diffused charge. Thus, increasing solvent polarity lowers H_{TS} but

not H_{GS} . So, ΔH^\ddagger 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

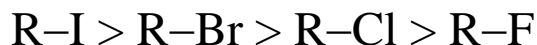
S_N1 stands for substitution nucleophilic unimolecular. The ideal version of S_N1 consists of two steps. The first step is the slow ionization of the substrate and is rate limiting step. The second step is the rapid reaction between the carbocation and nucleophile.



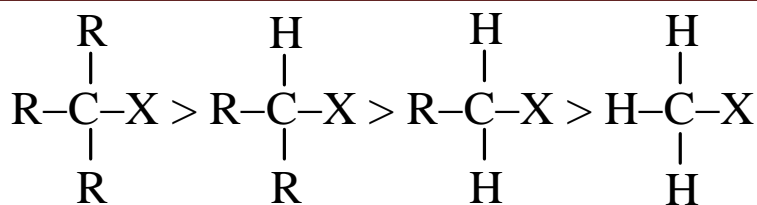
Solvent assists the ionization process, since the energy of activation required for breaking of the bond is largely recovered from solvation of ions produced. In pure S_N1 reactions, solvent molecules assist the departure of leaving group from the front side.

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,



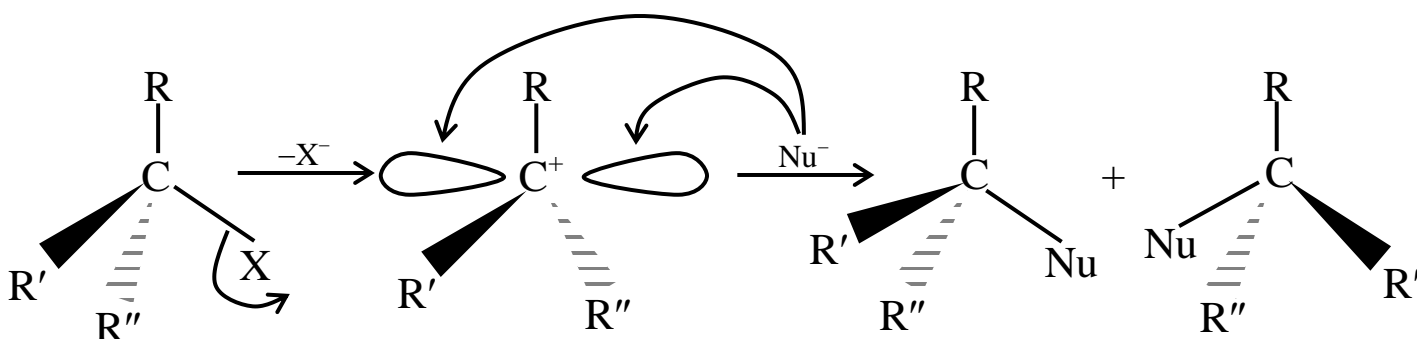
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The rate law for the $\text{S}_{\text{N}}1$ reaction is

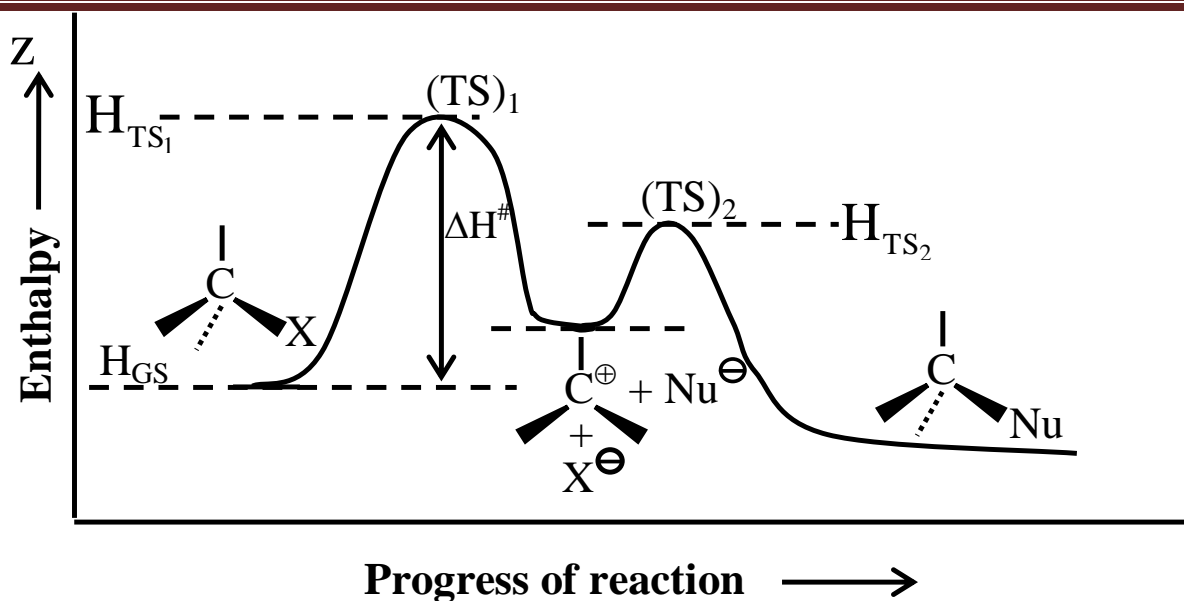
$$\text{Rate} = k [\text{R}-\text{X}]$$

The rate of $\text{S}_{\text{N}}1$ 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.

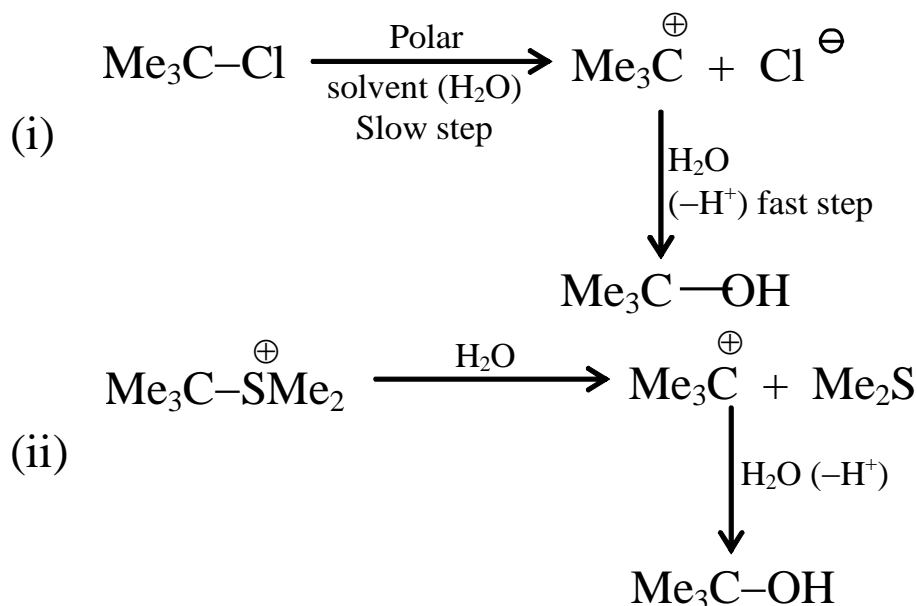


Now, let us observe the effect of solvent polarity on the rate of $\text{S}_{\text{N}}1$ reaction. It is generally said that the rate of $\text{S}_{\text{N}}1$ reactions is favoured in polar solvents than in non-polar solvents. Successful $\text{S}_{\text{N}}1$ reactions are exothermic in nature and their general energy profile can be shown as

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Let us consider the rate of solvolysis of $t\text{-BuCl}$ and $\text{Me}_3\text{C}-\overset{\oplus}{\text{S}}\text{Me}_2$. The solvolysis reaction of $t\text{-BuCl}$ and $\text{Me}_3\text{C}-\overset{\oplus}{\text{S}}\text{Me}_2$ can be represented as



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



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 ΔH^\ddagger and thereby increasing the rate of reaction.

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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 ΔH^\ddagger . Hence, such reactions proceed with faster rate in solvents with high polarity.

8. COMPARISON OF S_N1 AND S_N2 REACTIONS

	S_N1	S_N2
Number of steps	2 steps : (i) $R : L \xrightarrow{\text{slow}} R^+ + :L^-$ (ii) $R^+ + :NuH \xrightarrow{\text{fast}} R:Nu + H^+$	1 step : $R : L + :Nu^- \rightarrow R:Nu + :L^-$ Or $R : L + :NuH \rightarrow R : N^+uH + :L^-$
Reaction rate & order	Rate = $k_1[RL]$; first order	Rate = $k_1[RL] [:Nu^-]$; second order
Molecularity	Unimolecular	Bimolecular
TS of slow step	$\overset{\delta+}{R} \cdots \cdots \overset{\delta-}{L} \cdots \cdots HNu:$	$\overset{\delta-}{Nu} \cdots \cdots C \cdots \cdots L^{\delta-}$ (with Nu^-) $\overset{\delta+}{H}Nu \cdots \cdots C \cdots \cdots L^{\delta-}$ (with HNu)
Stereochemistry	Inversion and retention (Partial racemization)	Inversion of configuration (backside attack)
Reacting nucleophile	Nucleophilic solvent; stable R^+ may react with added nucleophile	Added nucleophile
Structure of R	$3^\circ > 2^\circ > 1^\circ > Me$	$Me > 1^\circ > 2^\circ > 3^\circ$
Nature of Leaving group	Weakest base is best leaving group, i.e. $I^- > Br^- > Cl^- > F^-$	Weakest base is best leaving group, i.e. $I^- > Br^- > Cl^- > F^-$
Nature of nucleophile	For HNu : (solvent), rate \propto basicity of HNu :	In protic solvents, (i) Within a periodic table group, rate \propto polarizability of Nu (ii) For same nucleophilic site,

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		rate \propto basicity of Nu In polar aprotic solvents, rate \propto basicity of Nu
Solvent effect	Rate \propto H-bonding ability and dielectric constant	Depends on charge type. Polar aprotic solvents leave “freest” most reactive Nu.
Determining factor	Stability of R ⁺	Steric hindrance
Rearrangement	Observed	Not observed, except for allylic
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:)

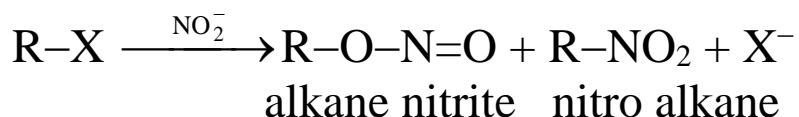


In CN⁻, carbon (negatively charged) will be a soft base as compared to nitrogen. So, if the reaction proceeds via S_N1 mechanism, which produces a free carbocation (a hard acid), then attack through nitrogen (hard base) will take place. But if the reaction proceeds via S_N2 mechanism (small positively charged carbon is soft acid) then attack

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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 favoured due to more favourable S_N1 substitution in tertiary alkyl halide. But the exception is that tertiary alkyl halides undergo elimination and the yield decreases. This is because CN^- is a strong base, which can also cause elimination reaction.

9.2 Attack By NO_2^- Nucleophile ($-O-N=O$)



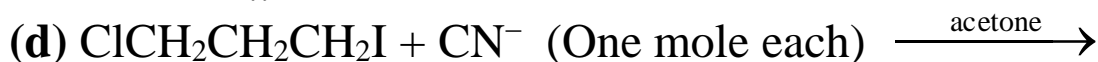
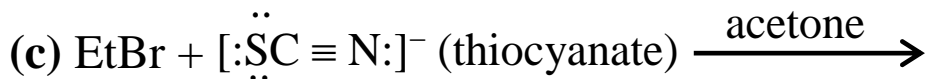
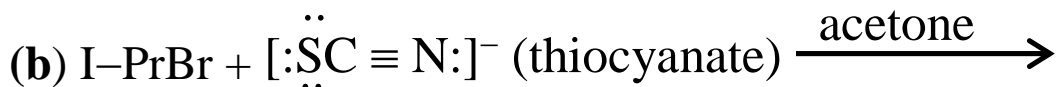
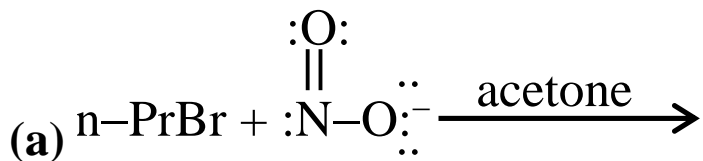
In NO_2^- , oxygen (negatively charged) will be a hard base as compared to nitrogen. So, if the reaction proceeds via S_N1 mechanism, then attack through oxygen (hard base) will take place to produce alkane nitrite. But if the reaction takes place via S_N2 mechanism then attack through nitrogen (soft base) takes place to give nitro alkane.

If we want to increase the yield of nitro alkane, 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 nitrite 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 nitrite as the major product.

Illustration

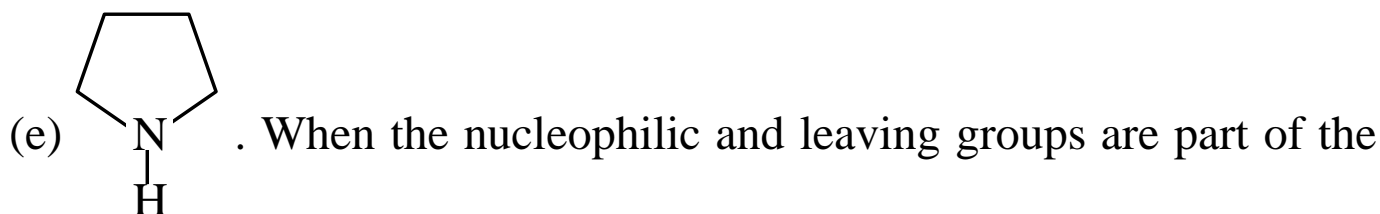
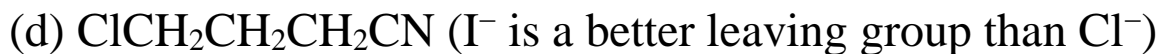
ALKYL HALIDES AND ARYL HALIDES

Give the organic products of the following reactions.



Solution:

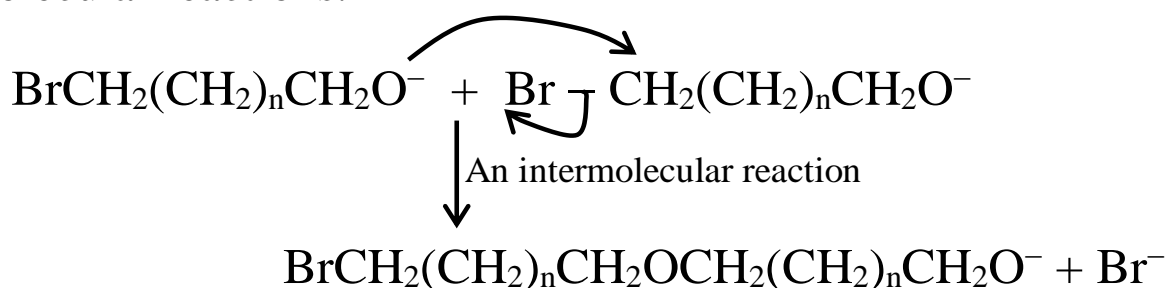
The nucleophiles in (a), (b) and (c) are ambident since they each have more than one reactive site. In each case, the more nucleophilic atom reacts even though the other atom may bear a more negative charge.



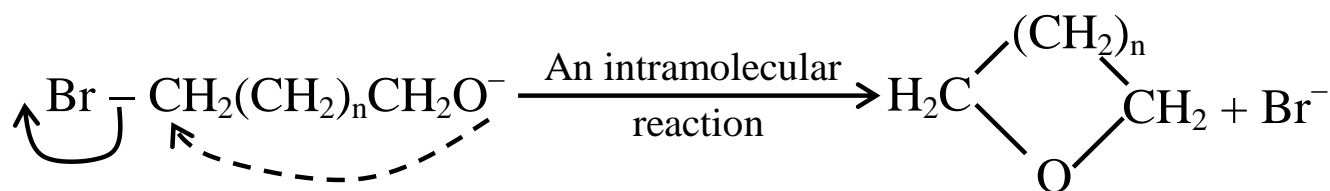
same molecule, an intramolecular displacement occurs if a three-, a five- or a six-membered ring can form.

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.



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.



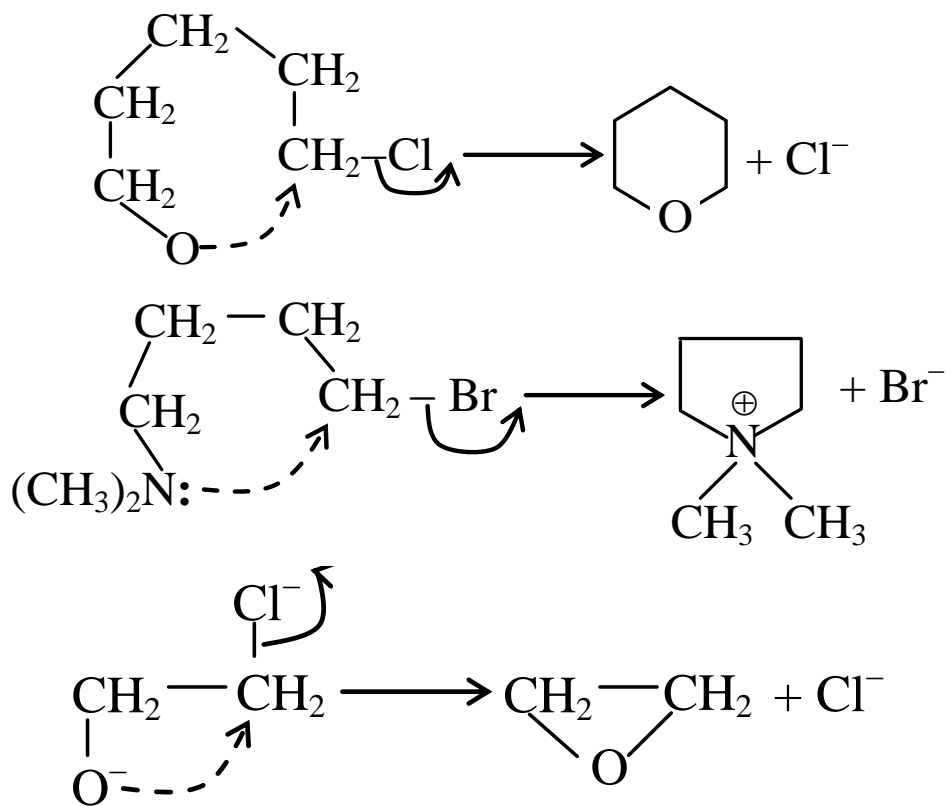
In such cases, when the nucleophile and the leaving group are part of the same molecule, inter as well as intramolecular reactions, both can take place. Which reaction is more likely to occur, can be determined by the concentration of the bifunctional molecule and by the size of the ring that will be 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

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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.



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 $E1/S_N1$ 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:

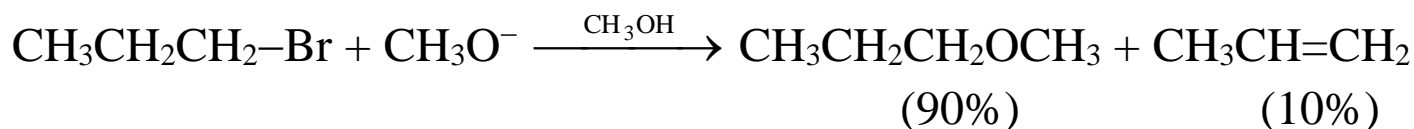
In an S_N2 reaction: $1^\circ > 2^\circ > 3^\circ$

In an $E2$ reaction: $3^\circ > 2^\circ > 1^\circ$

In an S_N1 reaction: $3^\circ > 2^\circ > 1^\circ$

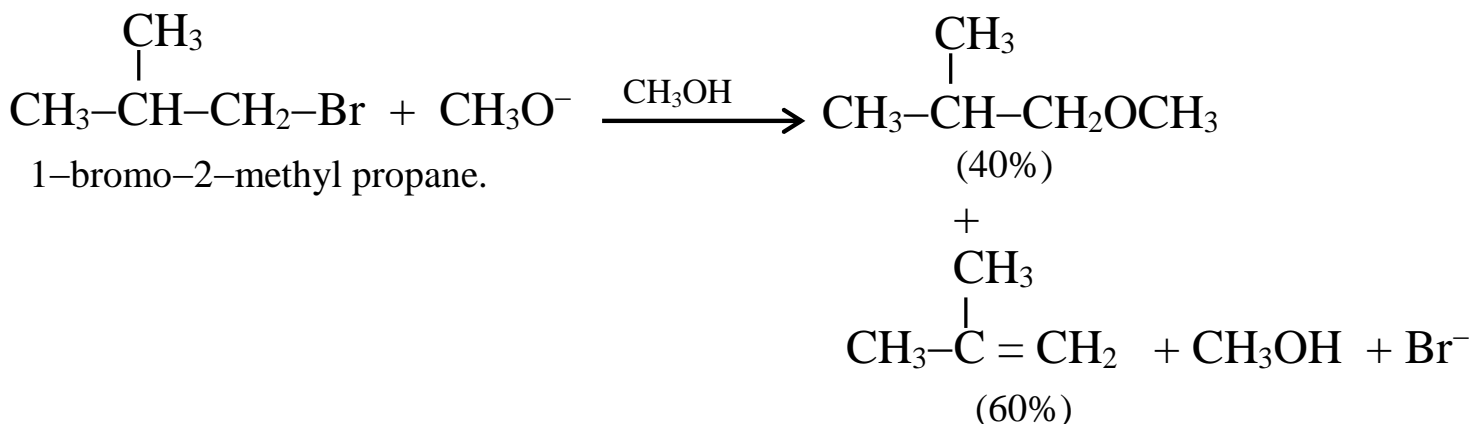
In an $E1$ reaction: $3^\circ > 2^\circ > 1^\circ$

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.

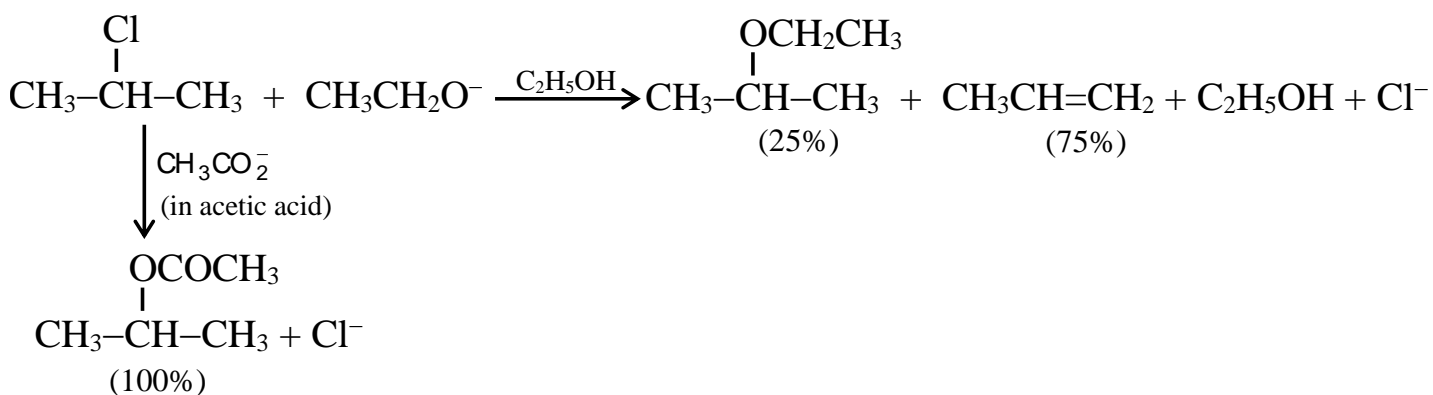


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But when the primary alkyl halide or the nucleophile / base is sterically hindered, the nucleophile will have difficulty getting to the back of α -carbon and thus, elimination product will predominate. For example,



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.



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.

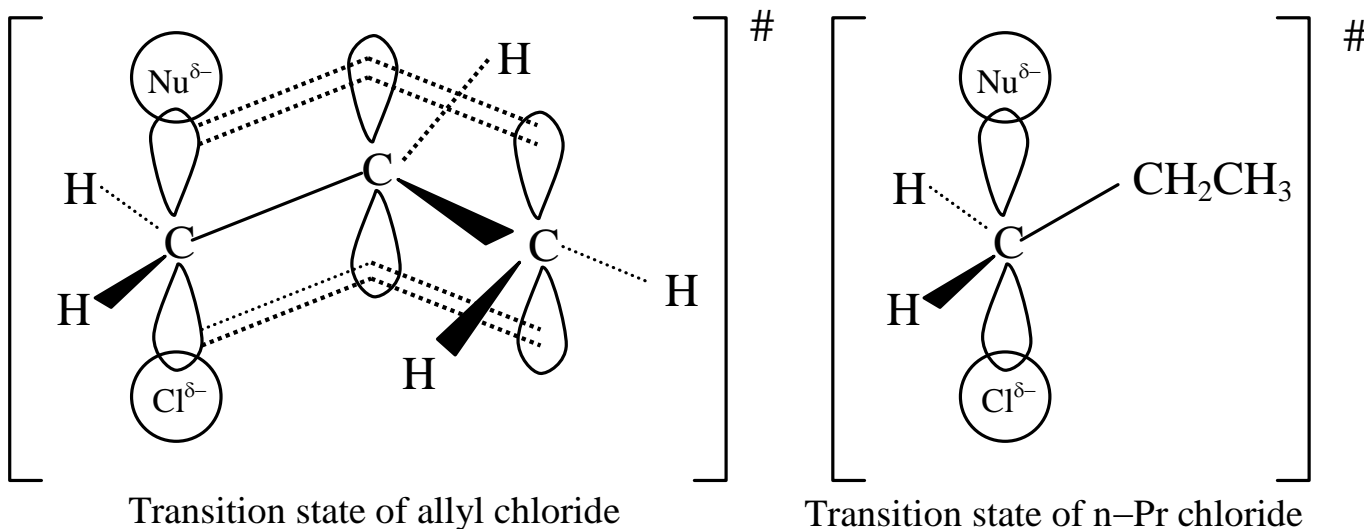
A tertiary alkyl halide is least reactive towards $\text{S}_{\text{N}}2$ reaction but most reactive towards E_2 reaction. Thus, only elimination product is formed.

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When the nucleophile is poor or base is weak, E_1/S_N1 reactions will be preferred. Both E_1/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 E_1 and S_N1 reaction because they have the same rate-determining step. Thus, all alkyl halides that react by E_1/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 E_1/S_N1 reactions because primary carbocations are not too stable.

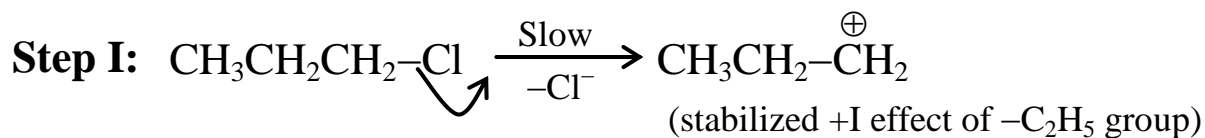
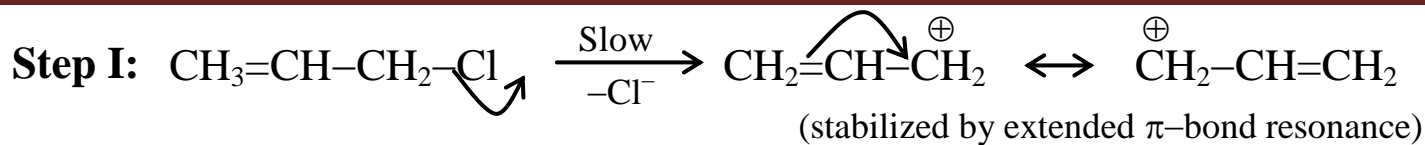
12. Nucleophilic substitution in allyl & vinyl halides

Let us compare the S_N1 and S_N2 rates of allyl chloride and n-Pr chloride. Both allyl chloride ($\text{CH}_2=\text{CHCH}_2\text{Cl}$) 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.



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.

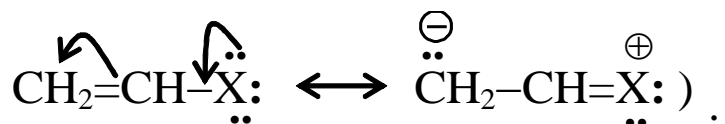
ALKYL HALIDES AND ARYL HALIDES



The rate of $\text{S}_{\text{N}}1$ reaction for allyl chloride is faster than the $\text{S}_{\text{N}}2$ rate while for n-propyl chloride, $\text{S}_{\text{N}}2$ rate is faster than $\text{S}_{\text{N}}1$ rate.

Now let us see the $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ 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,



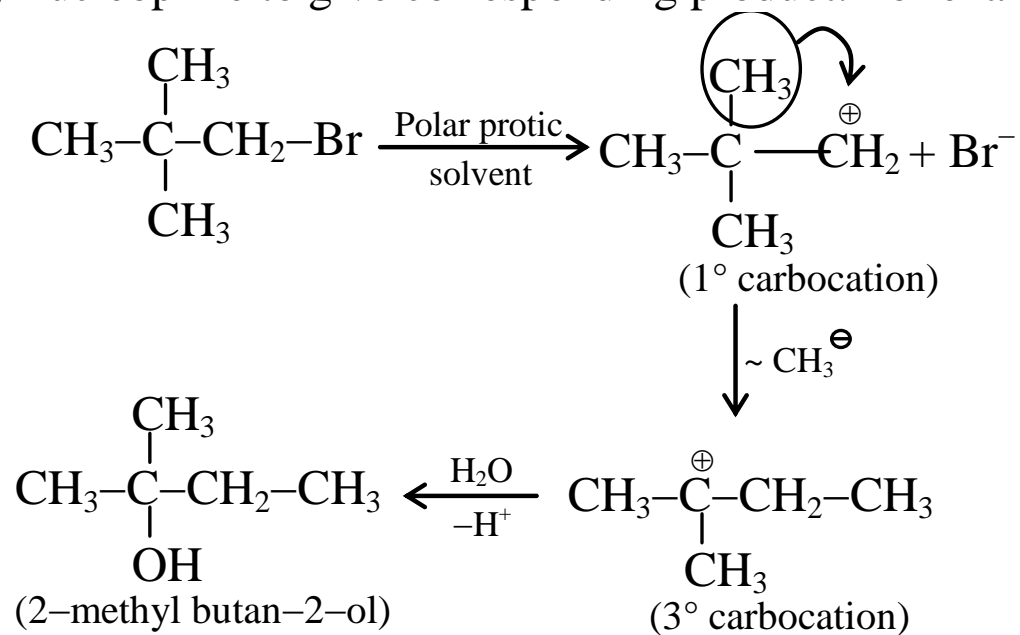
Therefore, they are inert towards displacement reactions.

When they show $\text{S}_{\text{N}}1$ 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 $\text{S}_{\text{N}}2$ 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 $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ 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,

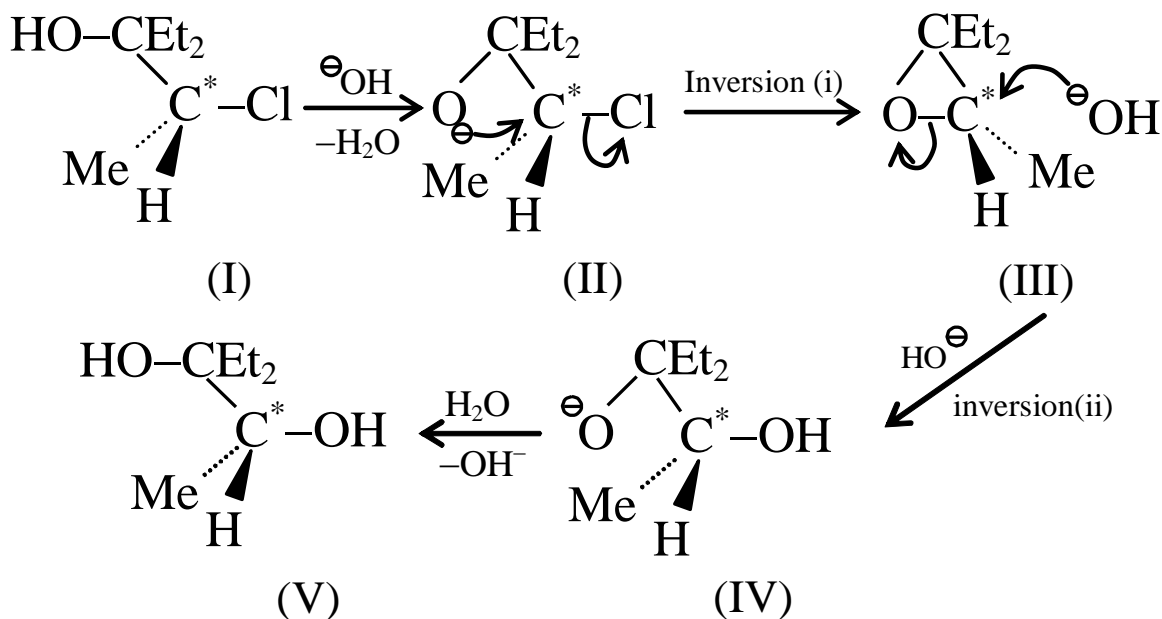


14. Neighbouring Group Participation: Retention

There are some examples of retention of configuration in nucleophilic displacement reactions. The common feature for such nucleophilic displacements is an atom or group—close to the carbon undergoing attack—which has at least one electron pair available on it. This neighbouring group can use its electron pair to interact with the ‘backside’ of the carbon atom undergoing substitution, thus preventing attack by the external nucleophilic reagent. Attack can thus take place only ‘from the front side’, leading to retention of configuration.

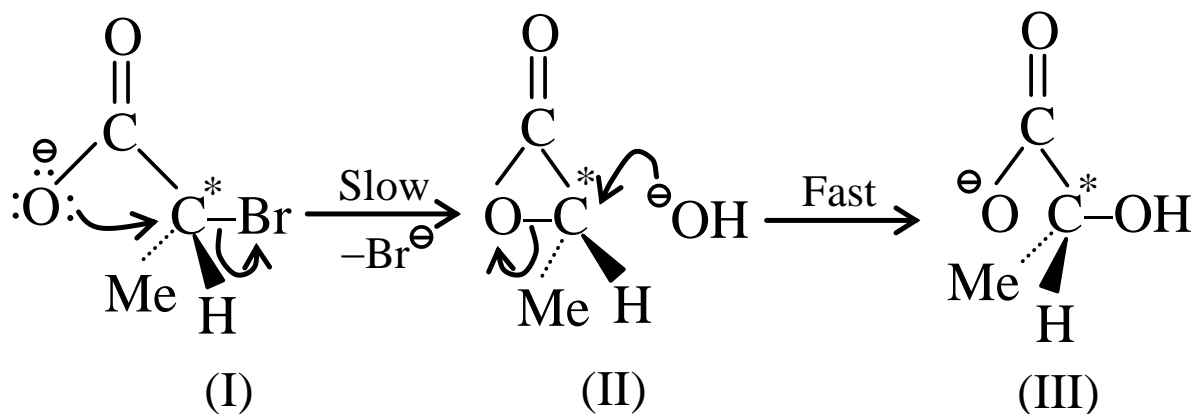
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Base hydrolysis of the 1, 2–chlorohydrin is found to yield 1,2–diol with the same configuration (retention).



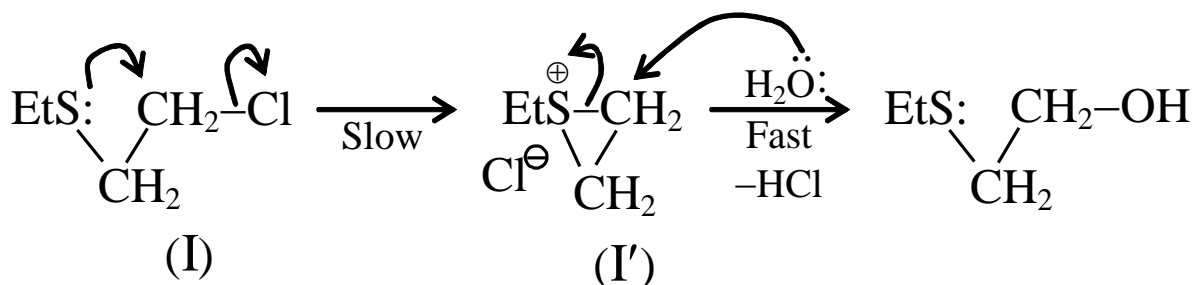
Initial attack by base on (I) yields the alkoxide anion (II). This alkoxide anion then acts as nucleophile (internal) and yield the epoxide (III) with inversion of configuration at C^* . This carbon atom, in turn, undergoes ordinary S_N2 attack by ^-OH (external nucleophile), with a second inversion of configuration at C^* . Finally, this second alkoxide anion (IV) abstracts a proton from the solvent to yield the product 1,2–diol (V) with the same configuration as that of the starting material (I). This apparent retention of configuration has been brought about by two successive inversions.

Another example of oxygen as a neighbouring group occurs in the hydrolysis of the 2–bromopropanoate anion (I) at low $[^-OH]$, which is also found to proceed with retention of configuration (III). The rate is found to be independent of $[^-OH]$ and the reaction is believed to proceed as follows:



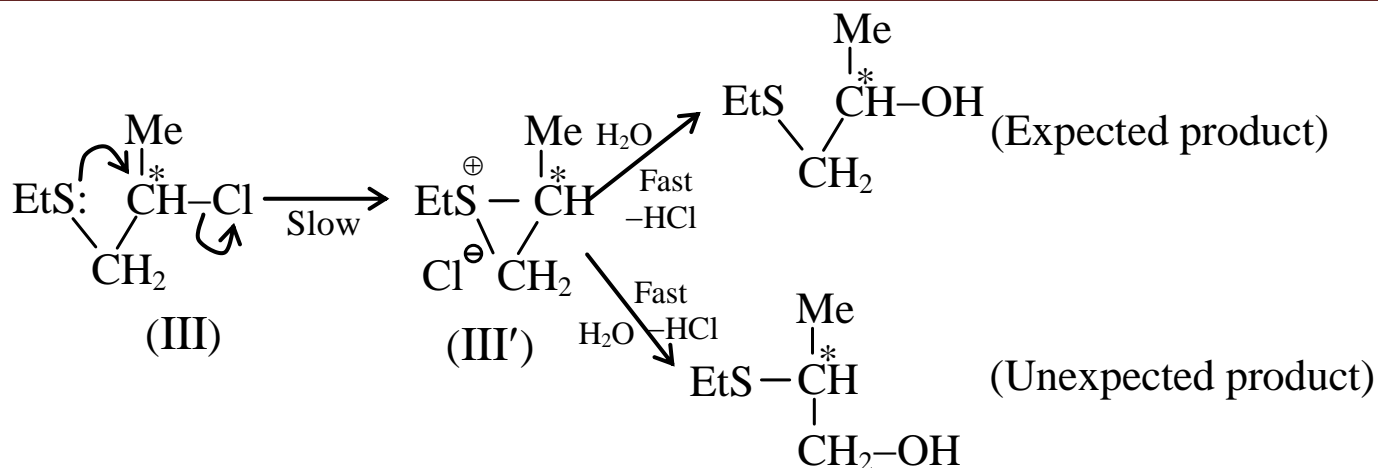
But with a higher concentration of nucleophile, $[\text{OH}^-]$ an increasing proportion of normal $\text{S}_{\text{N}}2$ 'attack from the back' takes place and leads to product with inversion of configuration.

Neighbouring group effect also occurs with atoms other than oxygen, e.g. sulphur and nitrogen where unexpectedly rapid rates suggest a change in reaction pathway. Thus, $\text{EtSCH}_2\text{CH}_2\text{Cl}$ (I) is found to undergo hydrolysis 10^4 times faster than $\text{EtOCH}_2\text{CH}_2\text{Cl}$ (II) under comparable conditions. This can be explained on the basis of involvement of S acting as a neighbouring group participant.



By contrast, O in (II) is sufficiently electronegative not to donate an electron pair (unlike O^- in RO^- and RCO_2^- above) and hydrolysis of (II) thus proceeds via ordinary $\text{S}_{\text{N}}2$ attack by an external nucleophile, which is very much slower than the internal nucleophilic attack in (I). A cyclic sulphonium salt such as (I') is involved is demonstrated by the hydrolysis of the analogous compound (III), which yields two alcohols (the unexpected one in greater yield) indicating the participation of the unsymmetrical intermediate (III').

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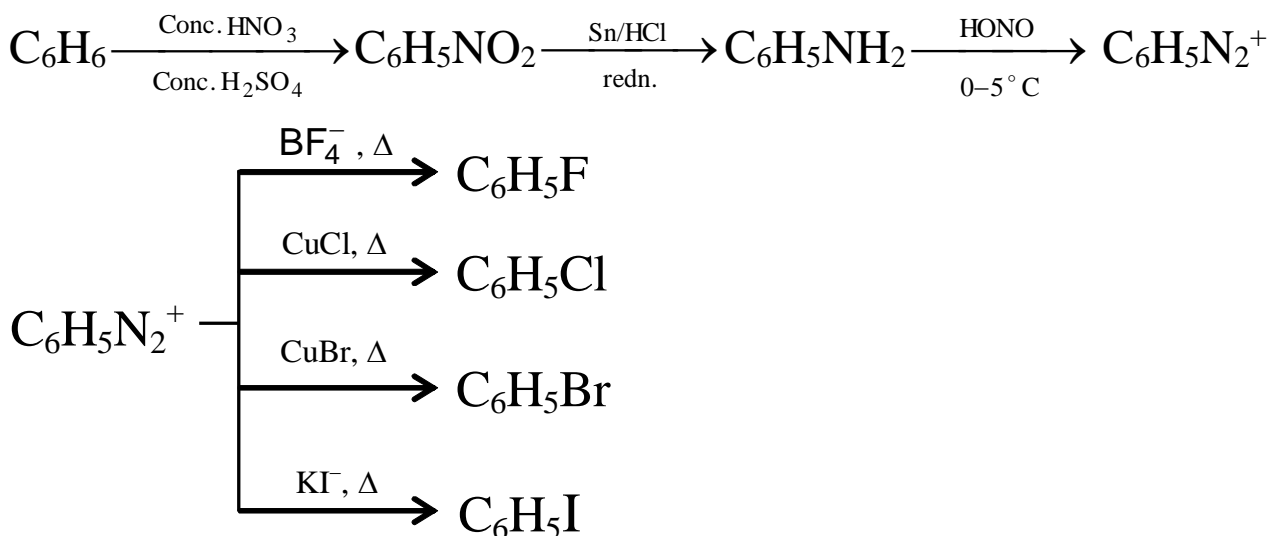
N: can also act as a neighbouring group participant in similar circumstances, e.g. the hydrolysis of $\text{Me}_2\text{NCH}_2\text{CH}_2\text{Cl}$, but the rate is markedly slower under comparable conditions than that for (I).

Aryl Halides

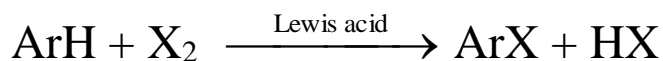
Aryl halides are the compounds in which the halogen atom (F, Cl, Br and I) is directly attached to benzene. They are less reactive compounds than alkyl halides.

15. Preparation of Aryl Halides

15.1 From Diazonium Salts



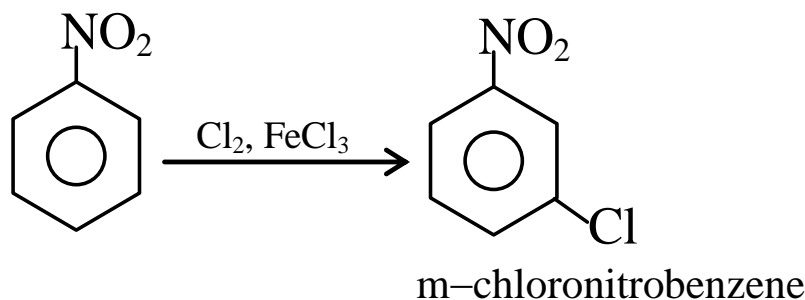
15.2 By Halogenation of Arenes or Substituted Arenes

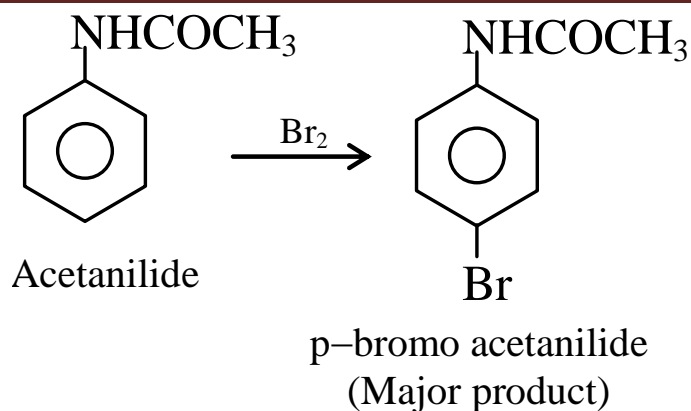


where $\text{X}_2 = \text{Cl}_2$ or Br_2

Lewis acid = FeCl_3 , AlCl_3 etc.

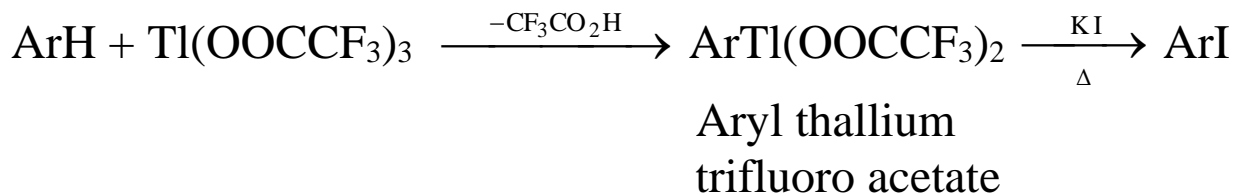
For example,



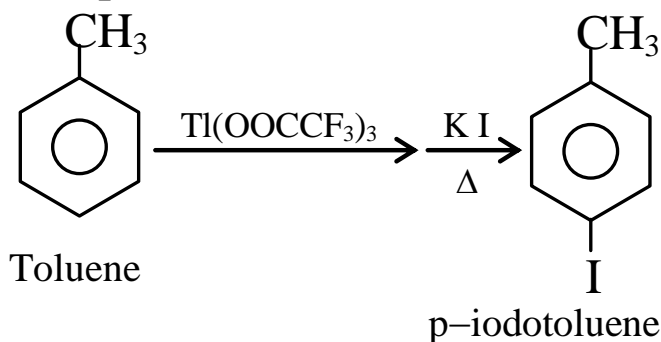


(Note: Acetanilide group is majorly p-director)

15.3 From Arylthallium Compounds



This method is applicable for the preparation of aryl iodides only because I^- is a better nucleophile than other halide ions in $\text{S}_{\text{N}}2$ displacements. For example,

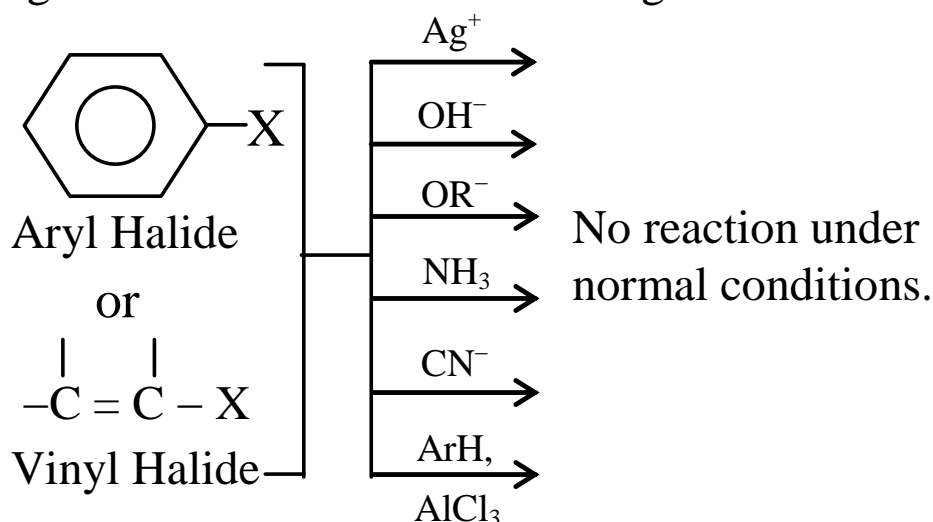


The preparation of aryl halides from diazonium salts is more useful than direct halogenation for many reasons. First of all, fluorides and iodides, which can seldom be prepared by direct halogenation, can be obtained through diazonium salts. Secondly, where direct halogenation yields a mixture of ortho and para isomers, the ortho isomer, atleast, is difficult to obtain pure.

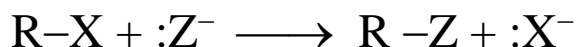
16. General Chemical Properties of The Aryl Halides

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.



where $\text{Z} = \text{OH}^-$, 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

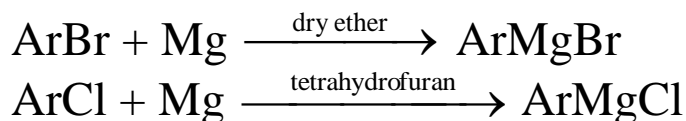
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substitution. The presence of electron withdrawing groups like $-\text{NO}_2$, $-\text{CF}_3$ at ortho or para position to the halogen atom makes the aryl halides more susceptible to nucleophilic attack.

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.

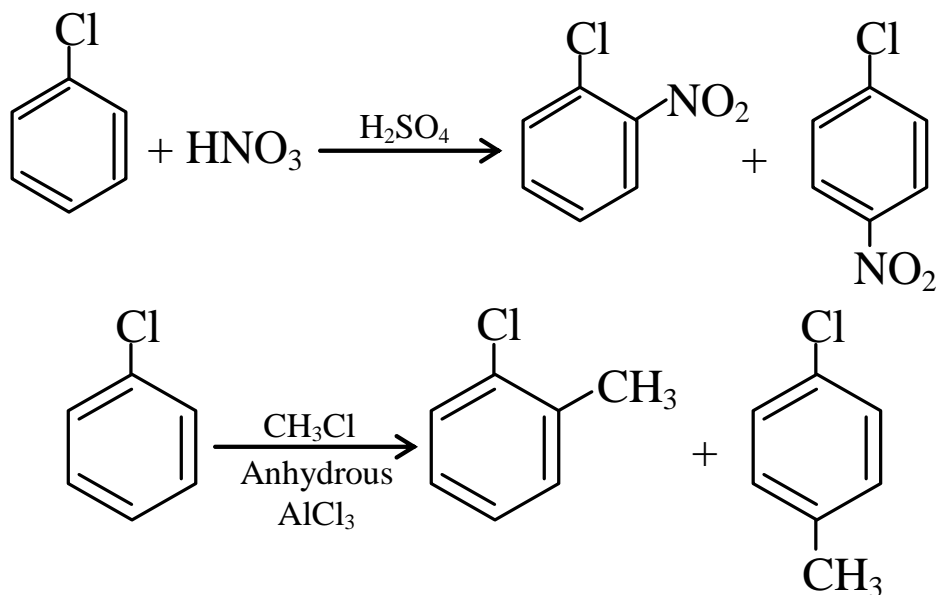
16.2 Formation of Grignard Reagent

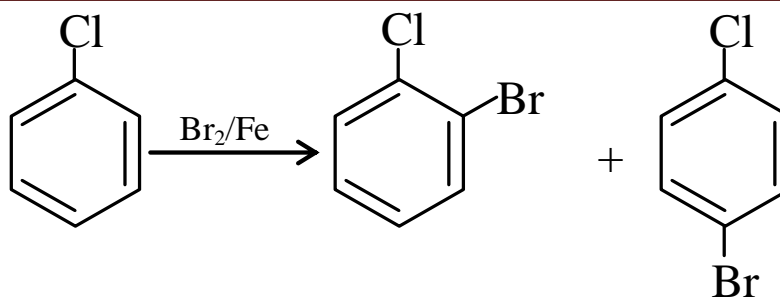


16.3 Electrophilic Aromatic Substitution

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

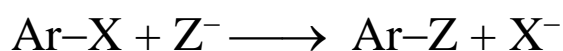
For example,



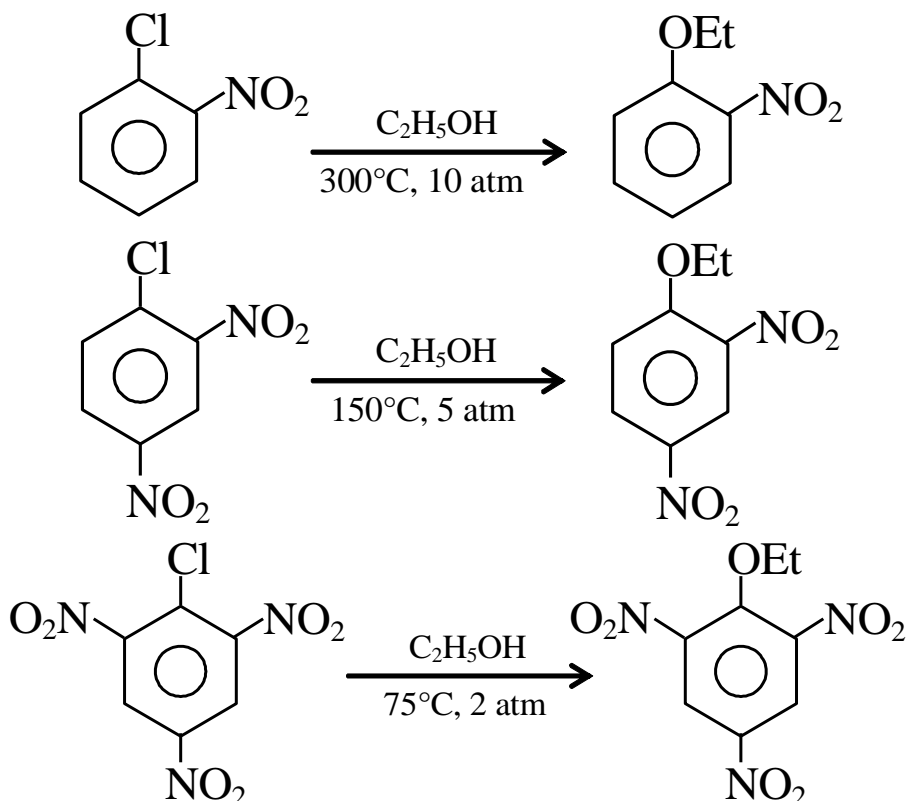


17. Nucleophilic Aromatic Substitution

17.1 S_NAr Mechanism



For facile reaction, Ar must contain strongly electron withdrawing groups at ortho and/or para position to the halogen atom. The reaction involves formation of carbanion as intermediate.

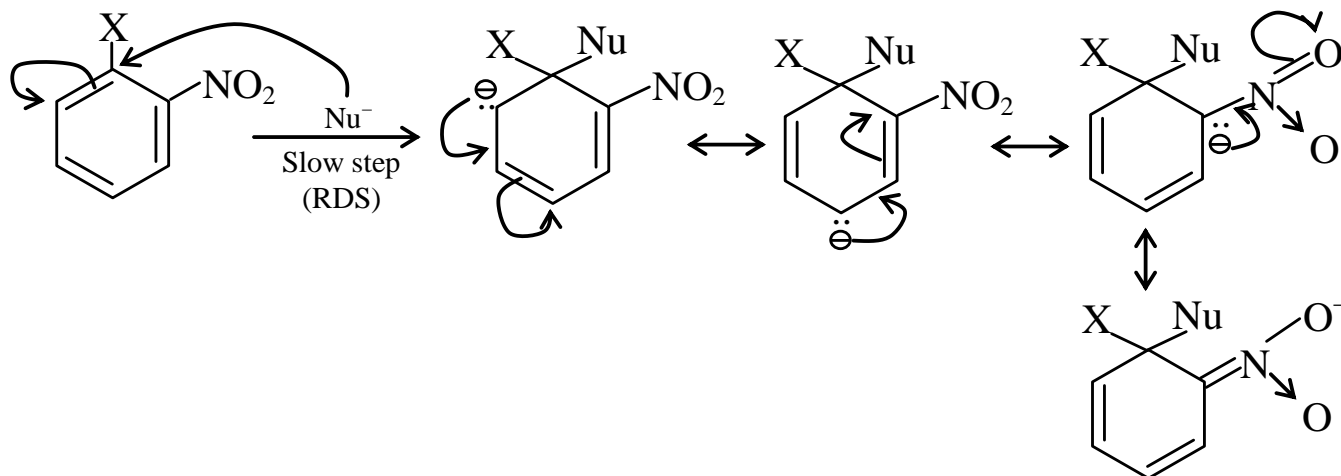


Reaction proceeds through carbanion formation as intermediate. The rate of the reaction increases with the increase in the number of electron withdrawing groups at ortho and para positions, since the carbanion

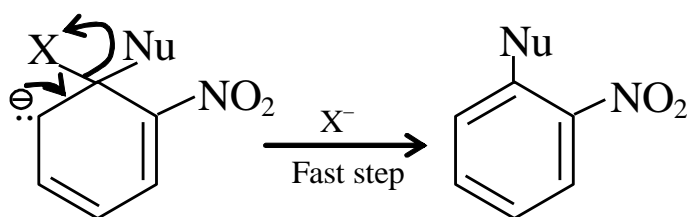
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formed would be readily stabilized. The mechanism of the reaction is addition in the first step and elimination in the second step.

Step: 1

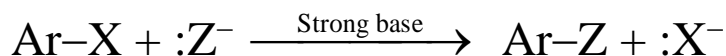


Step: 2

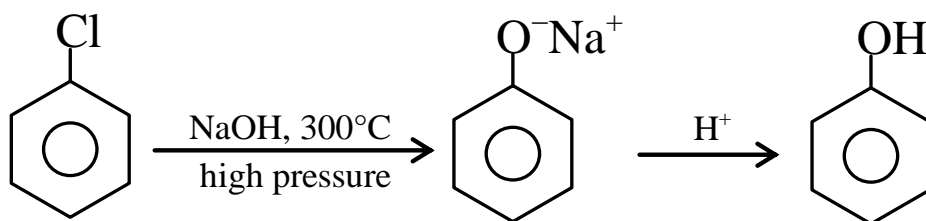


It can be seen that the presence of -NO₂ group at ortho or para position would facilitate to disperse the negative charge of the carbanion, thus stabilizing it and allowing the reaction to occur fast.

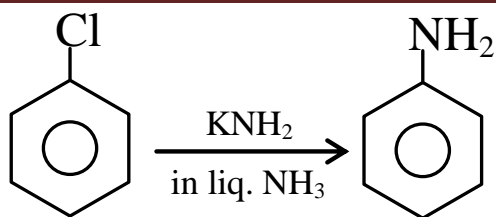
17.2 Benzyne Mechanism



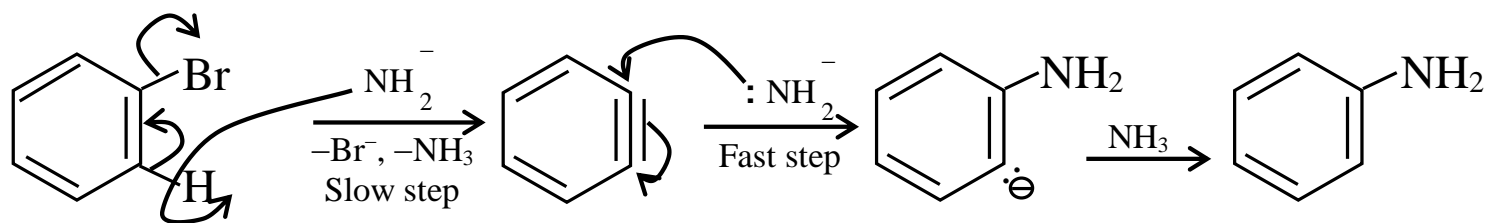
Those rings, which are not activated towards bimolecular displacement, undergo substitution by benzyne mechanism.



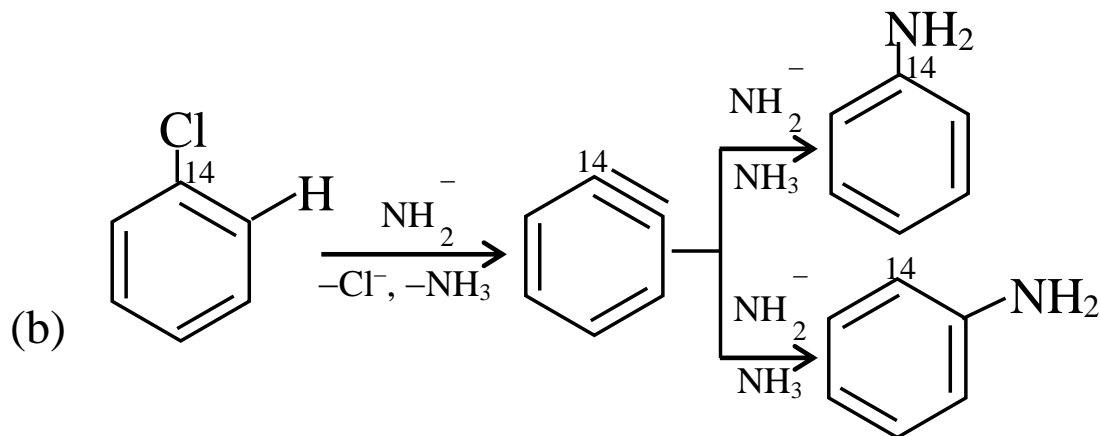
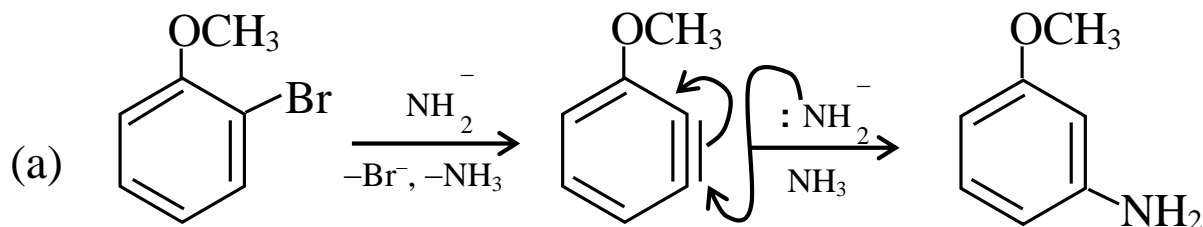
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Unactivated and deactivated aryl halides undergo nucleophilic substitution by benzyne mechanism. In benzyne mechanism, first step involves elimination while second step involves addition of nucleophile. Unactivated aryl halide means either no substituent is present or the presence of electron withdrawing group at meta position. Deactivated aryl halides imply the presence of electron donating groups at any position. Rate determining step of the reaction is the formation of benzyne / aryne intermediate.

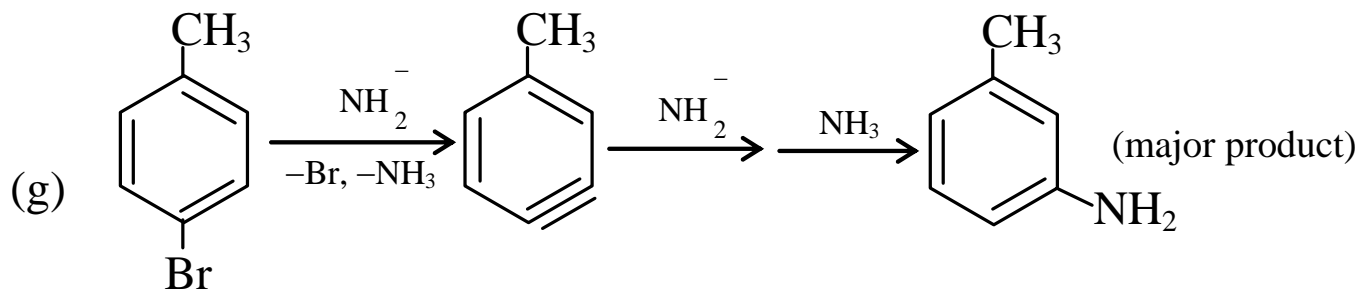
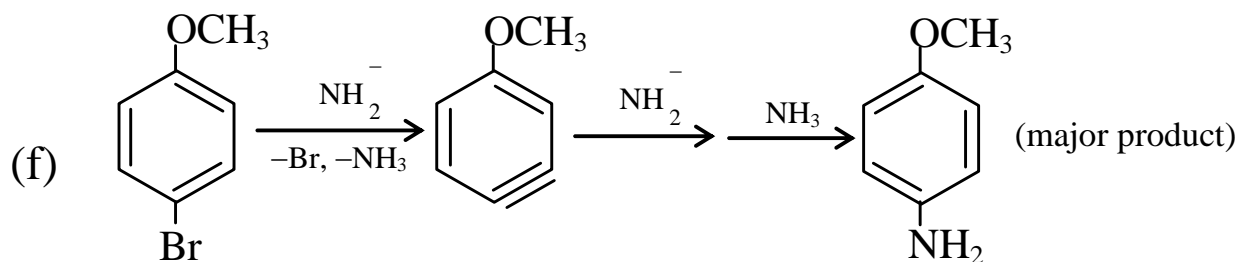
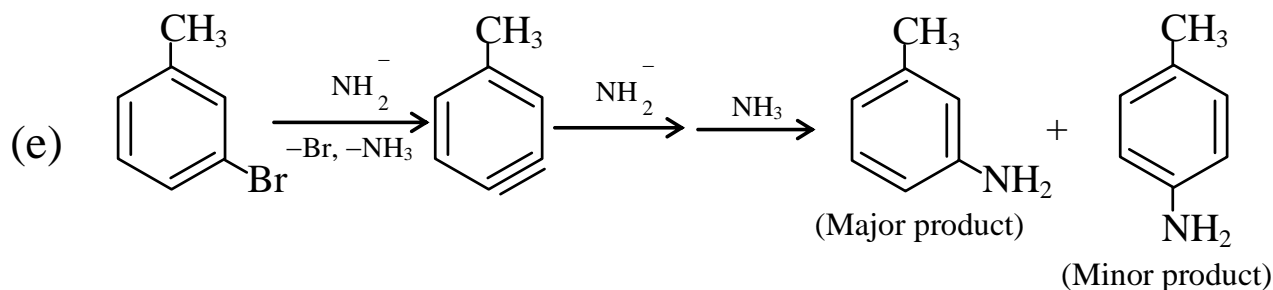
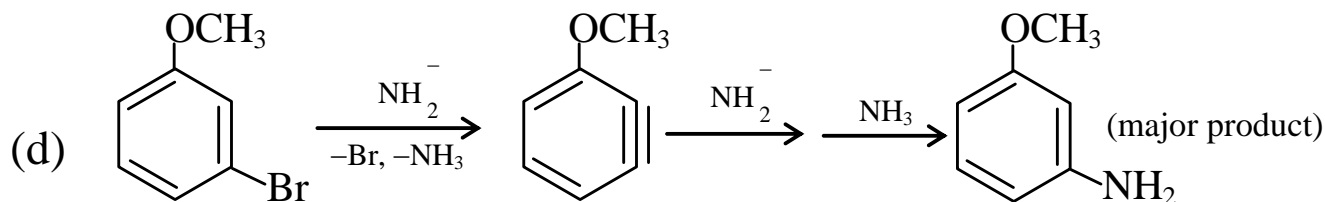
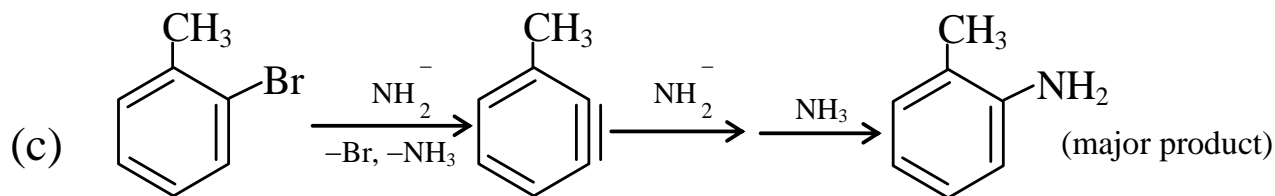


For example,



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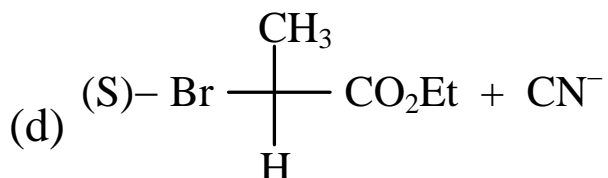
Chlorobenzene with chlorine bonded to ^{14}C gives almost 50% aniline having NH_2 bonded to ^{14}C and 50% aniline with NH_2 bonded to normal ^{12}C atom.



Solved Fundamental Examples

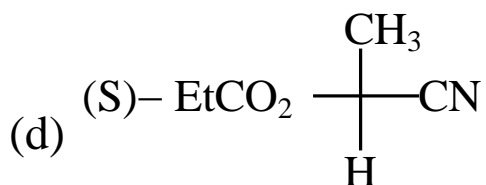
Example 1.

Give the products of the following displacement reactions.



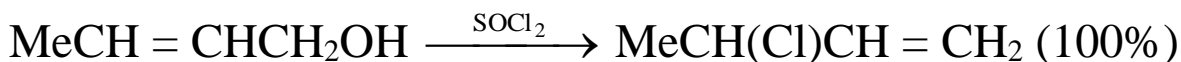
Solution

These are S_N2 reactions involving inversion of configuration. change in configuration from (R) to (S) or (S) to (R) is observed only when the nucleophile and nucleofuge have same priorities.

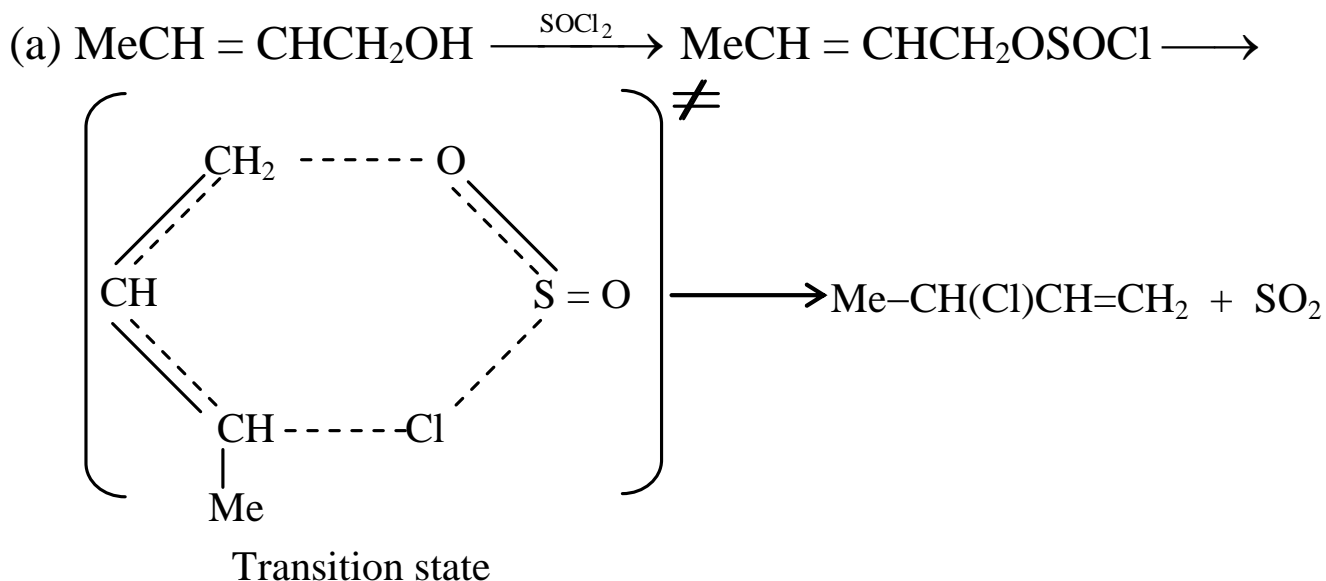


Example 2.

Give plausible mechanism of the following reaction.



Solution



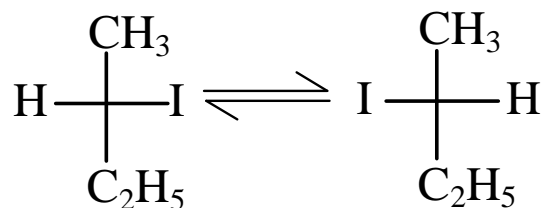
the intermediate $\text{MeCH}=\text{CHCH}_2\text{OSOCl}$ dissociates to an intimate ion pair whose ClSO_2^- loses SO_2 and Cl^- attacks at C_3 with movement of π e^- 's to give a double bond between C_1 and C_2 .

Example 3.

Optically active 2-iodobutane on treatment with NaI in acetone gives a product, which does not show optical activity. explain why?

Solution

In this reaction $\text{C}-\text{I}$ bond is broken and reformed to give a racemic mixture of 2-iodobutane and thus remains optically inactive. the presence of I^- provides opportunity for the remaking of the $\text{C}-\text{I}$ bond.



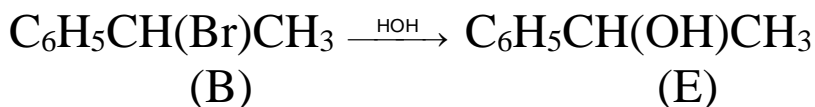
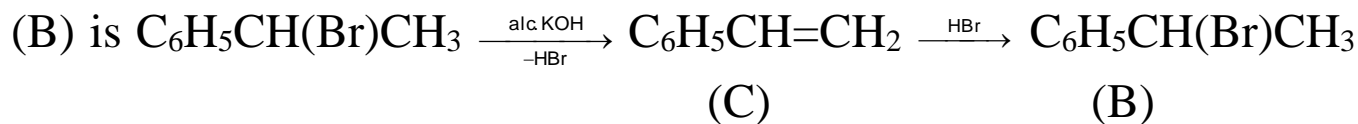
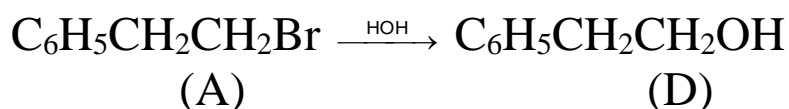
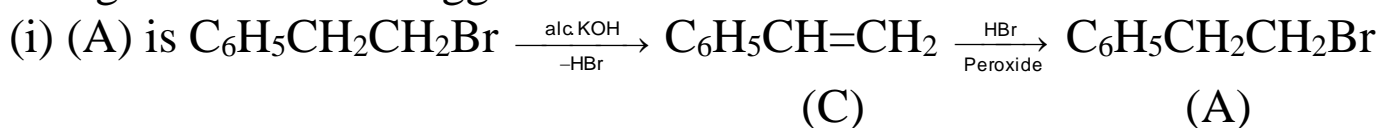
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Example 4.

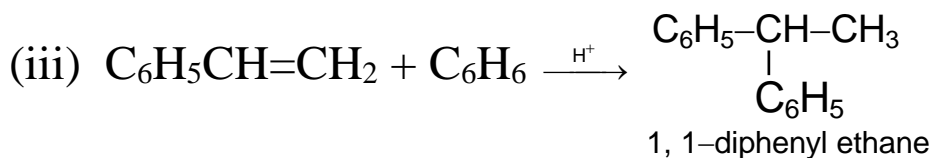
Dehydrobromination of compounds (A) and (B) yield the same alkene (C). Alkene (C) can regenerate (A) and (B) by the addition of HBr in the presence and absence of peroxide respectively. Hydrolysis of (A) and (B) give isomeric products, (D) and (E) respectively. 1,1-diphenylethane is obtained on reaction of (C) with benzene in the presence of H^+ . Give structures of (A) to (E) with reasons.

Solution

The given reactions suggest that



(ii) (D) and (E) are isomeric alcohols.



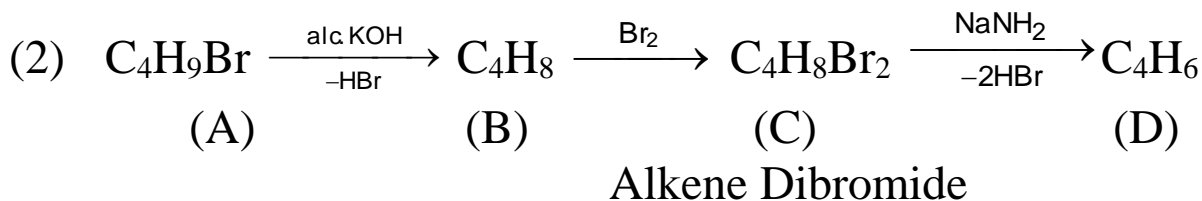
Example 5.

The alkyl halide C_4H_9Br (A) reacts with alcoholic KOH and gives an alkene (B), which reacts with bromine to give dibromide (C). (C) is transformed with sodamide to a gas (D) which forms a precipitate when passed through an ammonical silver nitrate solution. Give the structural formulae of the compounds (A), (B), (C) and (D) and explain the reactions involved.

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Solution

(1) (D) is a terminal alkyne since it forms precipitate with ammonical AgNO_3 , i.e. $\text{R}-\text{C}\equiv\text{CH}$.

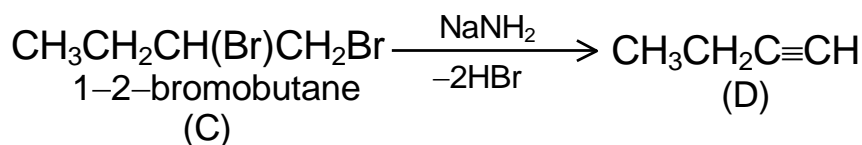
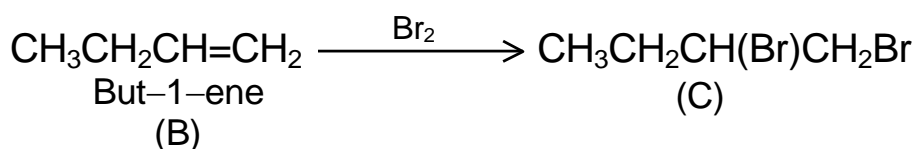
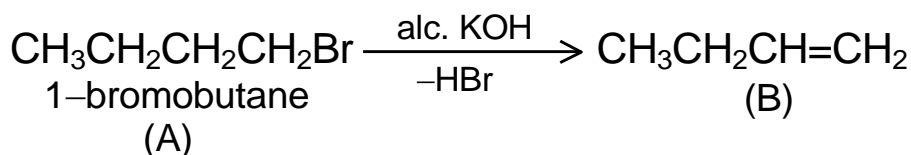


(3) Thus, if (D) is $\text{R}-\text{C}\equiv\text{CH}$, then (C) should be $\begin{array}{c} \text{R}-\text{CH}-\text{CH}_2 \\ | \quad | \\ \text{Br} \quad \text{Br} \end{array}$ because it is

formed by the action of Br_2 on (B). Thus, (B) should be $\text{R}-\text{CH}=\text{CH}_2$.

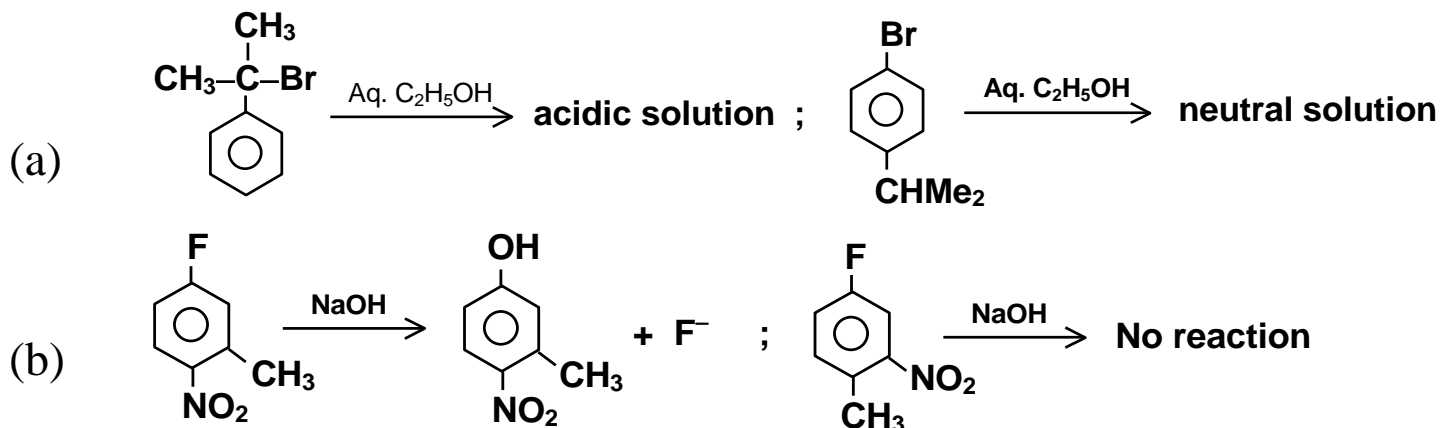
(4) Since (B) is obtained by dehydrobromination of (A) and thus, (A) should be $\text{R}-\text{CH}_2\text{CH}_2\text{Br}$. (A) is of 4 carbon atoms and therefore, (A) is $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br}$.

Reactions:



Example 6.

Give reasons for the following observations.



Solution

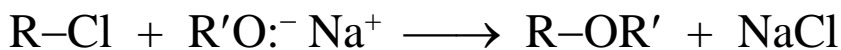
(a) In aqueous solution, the given alkyl bromide ionizes to give corresponding resonance stabilised tertiary benzylic carbocation and Br^- . This carbocation is attacked by ethanol followed by abstraction of proton by Br^- to produce corresponding ether and HBr . Due to HBr , the resultant solution becomes acidic.

But the aryl bromide cannot ionise even in aqueous solution due to partial double bond between carbon and bromine as a result of resonance. Therefore, no reaction will take place.

(b) In the first aryl fluoride, attack of nucleophile (OH^-) is favoured by the presence of a strong electron withdrawing group ($-\text{NO}_2$) at para position. On the other hand, in second aryl fluoride, attack of nucleophile (OH^-) is opposed by the presence of an electron donating methyl group at para position.

Example 7.

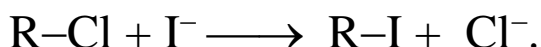
Explain the fact that a small amount of NaI catalyzes the general reaction:



Solution

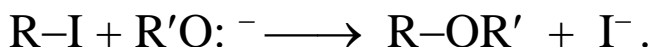
With I^- ion, the overall reaction occurs in two steps, each of which is faster than the uncatalyzed reaction.

Step 1:



This step is faster because I^- , a soft base has more nucleophilicity than OR^- , a hard base.

Step 2:



This step is faster because I^- is a better leaving group than Cl^- .

Example 8.

Account for the following observations:

- (a) t-BuF is solvolyzed only in very acidic solutions.
- (b) t-BuCl is solvolyzed more slowly than 2-chloro-2,3,3-trimethylbutane (A).
- (c) t-BuCl is solvolyzed much faster than 2-chloro-1,1,1-trifluoro-2-methylpropane (B).
- (d) t-BuCl is solvolyzed more slowly in 90% D_2O –10% dioxane than in 90% H_2O –10% dioxane solution.

Solution

- (a) F^- is a poor leaving group but H-bonding with a strong acid encourages its departure. This is an example of electrophilic catalysis.

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- (b) Formation of $\text{Me}_3\text{C}-\overset{\text{Me}}{\underset{\text{Me}}{\text{C}^+}}$ alleviates some of the steric crowding in (A) induced by the two Me's and the t-Bu on the α -carbon. This is an example of steric acceleration.
- (c) $\text{F}_3\text{C}-\overset{\text{Me}}{\text{CH}^+}$ is destabilized by the strongly electron-withdrawing $-\text{CF}_3$ group, making the solvolysis of (B) slower.
- (d) D-bonds are not as stabilizing as H-bonds.

Example 9.

Compare the rates of $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ reactions of

- (a) cyclopropyl and cyclopentyl chloride and
(b) 1-chlorobicyclo[2.2.2]octane and 9-chlorodecalin (A).

Solution

- (a) Cyclopropyl chloride is much less reactive than cyclopentyl chloride in each type of reaction because the sp^2 hybridised carbon (120° bond angle) created in each transition state augments the ring strain.
- (b) The bridgehead halide is inert by both reaction types. A flat R^+ cannot be formed at the bridgehead carbon, making $\text{S}_{\text{N}}1$ reaction impossible and the three bridges prevent the backside attack necessary for $\text{S}_{\text{N}}2$ reaction. Furthermore, inversion is impossible. (A) is a typical 3° halide and reacts rapidly via $\text{S}_{\text{N}}1$ reaction, but poorly via $\text{S}_{\text{N}}2$ reaction.

Example 10.

Provide the products of the reactions of the following substrates with NaNO_2 in EtOH:

- (i) n-BuCl and (ii) $\text{ClCH}_2\text{OCH}_2\text{CH}_3$.

Solution

- (i) n-Bu- NO_2 and (ii) $\text{ONO}-\text{CH}_2\text{OCH}_2\text{CH}_3 + \text{EtO}-\text{CH}_2\text{OCH}_2\text{CH}_3$.

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The less the positive charge on the attacked carbon, the more likely it will bond to the less electronegative nucleophilic site of the ambident ion (N). This happens in the S_N2 reaction in (i), where a C–N bond forms. The greater the positive charge on the attacked carbon, the more likely it will bond to the more electronegative nucleophilic site of the ambident ion (O). This happens in the S_N1 reaction in (ii), where a C–O bond forms. Since the R^+ in (ii) is so stable, it has a long enough half-life to react with any added nucleophile as well as nucleophilic solvent.