UNIT 1 REACTION MECHANISM — INTRODUCTION

Structure

1.1 INTRODUCTION

As mentioned in the Block Introduction, reaction mechanism involves an understanding of the detailed description of stepwise progress of a reaction as the reactants are converted into products. A knowledge of reaction mechanism is of utmost importance in devising synthesis of new molecules. These find applications in medicine, industry, textiles, household appliances, defence, space research, etc., in fact, practically in every sphere of modern life.

Study of reaction mechanism is very interesting as it gives us an opportunity to have a feel of the fantastic world of atoms and molecules, their nature and their reactions. If the fundamentals of reaction mechanism are clear, it is easy to understand the mechanism of any particular reaction. In this unit you will study the basic types of reaction mechanism, the types of reagents and types of reactions. Thermodynamic and kinetic aspects of reaction mechanism would be discussed in the next unit.

Objectives

After studying this unit you should be able to :

- explain the general types of reaction mechanism,
- define the terms, nucleophile, electrophile, free radical and radical ion with examples,
- differentiate a nucleophile from a base, nucleophilicity from basicity, and
- define and categorise a reaction as substitution, addition, elimination, rearrangement or oxidation-reduction.

1.2 TYPES OF MECHANISM

There are two features which, in general, characterise the reactions of organic compounds. One of these is the relative slowness of most organic reactions compared to many familiar inorganic reactions. For example, the reaction between hydrochloric acid and sodium hydroxide is instantaneous, whereas the esterification of acetic acid by ethyl alcohol takes hours and occurs only if the reaction mixture is heated with a catalyst such as sulphuric acid. Even then the reaction hardly ever goes to completion. The other characteristic feature of organic reactions is that, in general, the greater part of the reacting molecule remains relatively unchanged during the course of a reaction. Thus you may recall that most organic reactions

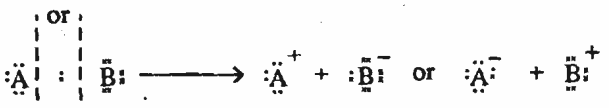
occur at the site of functional groups which leave the rest of the molecule intact. For example, in the reaction between bromoethane and aqueous sodium hydroxide,

$$CH_3CH_2—\boxed{Br} + NaOH \longrightarrow CH_3CH_2—\boxed{OH} + NaBr$$

the hydrocarbon part of the molecule, i.e., CH_3CH_2 is retained as such and the bromo functional group is replaced by the hydroxy one.

The slowness and the relative stability of the molecule in reactions are due to the type of bonding that exists in organic compounds. We know that atoms in organic compounds are covalently bonded. When reactions involving organic compounds take place one or more of these bonds may be broken and atoms (or groups) originally attached may be replaced by other atoms (or groups) or may be lost altogether. The type of mechanism followed by the reaction is determined by the way the bond breaks. The cleavage of a covalent bond may take place in one of the following ways :

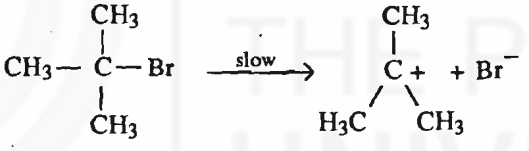
i) **Bond heterolysis** : When a bond breaks in an unsymmetrical way, such that both the bonding electrons remain with either of the fragments, then it is called bond heterolysis.



Bond heterolysis

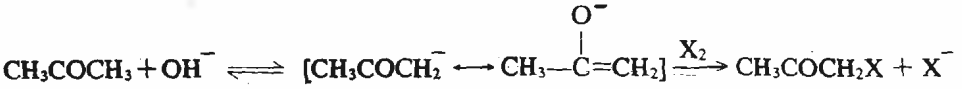
In heterolytic cleavage of a bond, the resulting species are charged. Depending upon the site of cleavage, either of the resulting species can be positively or negatively charged as shown above.

If the species resulting from heterolytic cleavage has a carbon atom bearing positive charge, then it is called a **carbocation** or **carbonium ion**. For example, the hydrolysis of 2-bromo-2-methylpropane to 2-methyl-2-propanol follows a two step mechanism, the first step being the slow heterolytic cleavage forming a carbocation.



2-bromo-2-methylpropane (carbocation)

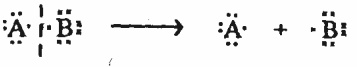
On the other hand, reaction of propanone with halogens in the presence of a base proceeds by a different mechanism :



We see that here we get a species having a carbon atom bearing a negative charge, such a species is called a **carbanion**.

In bond heterolysis, which fragment would carry the pair of bonding electrons is determined by the electronegativity of the constituent atoms of the bond in question. The more electronegative atom retains the electrons and gives rise to a negatively charged ion. Since carbon has very low electronegativity, very often, in the event of heterolytic cleavage, it loses its share in the bond and becomes a part of the positively charged fragment. Therefore, while carbocations are very common as intermediates, carbanions are rare. You would learn about these in later units when we talk about nucleophilic and electrophilic substitution reactions in detail. As these reactions involve charged species, these are said to follow **ionic** or **polar** mechanism.

ii) **Bond homolysis** : If a bond cleaves in a symmetrical way, such that either fragment of the molecule gets one electron, then it is referred to as bond homolysis.



Bond homolysis

For example, in photochlorination of methane,

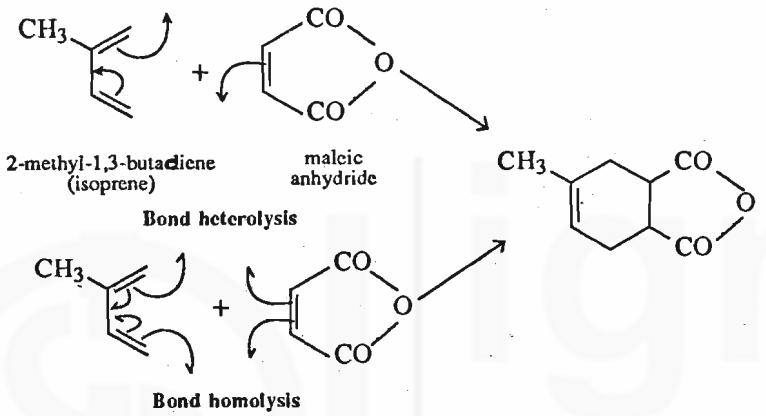
$$CH_4 + Cl_2 \xrightarrow{h\nu} CH_3Cl + HCl$$

which is a multistep reaction, the first step is homolysis of Cl_2 molecule as,

$$Cl : Cl \longrightarrow Cl\cdot + Cl\cdot$$

The resulting species have got an unpaired electron each and are referred to as **free radicals**. Chlorine free radical, same as chlorine atom, has got seven valence electrons. It means, therefore, that a chlorine radical is a neutral species. In fact, it is true of any free radical. Further, due to the presence of unpaired electrons, free radicals are very reactive. Reactions involving the formation of free radicals are said to follow **free radical mechanism.**

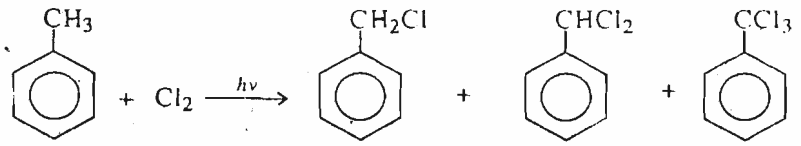
ii) **Pericyclic mechanism** : In certain cases it is difficult to ascertain whether the reaction involves bond homolysis or heterolysis. In such reactions both types of bond cleavages are possible and lead to the same product. For example, in the case of Diels-Alder reaction, the two possibilities are as shown below :



Here the reaction is said to proceed in a concerted manner, i.e., bond making and bond breaking is simultaneous. These reactions are said to follow pericyclic mechanism. Many photochemical reactions which you would study in detail in Unit 12 of this course follow this kind of a mechanism.

SAQ 1

Indicate the probable mechanism type-ionic or radical for the following reactions.

i) 

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ii) $CH_3Br + NaOH \longrightarrow CH_3OH + NaBr$

.....

iii) $CH_3CH_2Br + KCN \longrightarrow CH_3CH_2CN + KBr$

.....

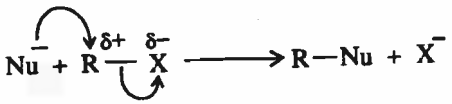
1.3 TYPES OF REAGENTS

In the previous section, we have tried to focus our attention only on a single molecule and attempted to visualise the process of bond breaking. You would have noticed that organic reactions often involve two reactants : one is the organic molecule which is referred to as the **substrate** and the other is called the **reagent**. You may recall in the reaction between bromoethane and sodium hydroxide, the former is a substrate and the latter is a reagent. Since these reagents are the ones which bring about changes in organic mole cules it is important to know more about their types and their nature.

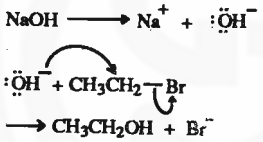
On the basis of their electronic structure, reagents can be broadly classified into the following types.

1.3.1 Nucleophiles

These are electron rich reagents possessing at least one nonbonded pair of electrons. These are attracted towards an electron deficient site in the substrate. Nucleophiles are thus "nucleus loving" and tend to donate electrons. Most of the nucleophiles are negatively charged or negatively polarised. However, a few of them are also neutral molecules with at least one lone pair. A reaction initiated by a nucleophile is called nucleophilic reaction. A nucleophilic reaction is represented in the following manner :



You would recall that as per convention, movement of an electron pair is depicted by the use of a curved **arrow**. For example, the reaction between bromoethane and sodium hydroxide can be represented as :



A list of nucleophiles with corresponding nucleophilic atoms is given in Table 1.1. A nucleophile with a negative charge is stronger than its conjugate acid. For example, OH^- is a stronger nucleophile than H_2O and NH_2^- than NH_3.

Table 1.1 : List of some common nucleophiles

Nucleophilic atom	Nucleophile
Halogen, X = F, Cl, Br, I	X^-
Oxygen	OH^-, RO^-, $R-\overset{\overset{O}{\|}}{C}-O^-$, H_2O, ROH, RCOOH
Sulphur	SH^-, RS^-, H_2S, RSH
Nitrogen	NH_3, RNH_2, R_2NH, R_3N
Carbon	$-CN^-$, $RC\equiv C^-$

The nonbonded pair of electrons in a nucleophile is provided by C, N, O, S or a halogen atom. The strength of a nucleophile depends upon a number of factors like the nature of the electron donating atom, its position in the periodic table, its polarisability, size and the nature of the solvent, etc. The relative strength of nucleophiles is measured in terms of their **nucleophilicities**. As nucleophiles donate electrons, these are bases according to Lewis definition. Different nucleophiles would have different basic strength, i.e., **basicity**. It is reasonable to expect that strong bases are good reagents for nucleophilic substitution reactions. This is generally true but there are some deviations also. For example, the iodide ion (I^-) is a good nucleophile but a very weak base. It is worthwhile to understand the difference between the two closely related terms, viz., nucleophilicity and basicity.

Basicity and Nucleophilicity

Basicity is a measure of a reagent's ability to accept a proton in an acid-base reaction. It pertains to the acid-base equilibrium,

$$Nu^- + H^+ \rightleftharpoons Nu-H$$

which is characterised by an equilibrium constant, K_b. It is customary to treat this as an acid dissociation equilibrium.

$$Nu-H \rightleftharpoons Nu^- + H^+$$

with an equilibrium constant, K_a which is characterised as pK_a. The magnitude of pK_a serves as an index of basicity. The basicities of two nucleophiles are compared in terms of the pK_a values of their respective conjugate acids. A higher value of pK_a indicates a weaker conjugate acid or a strong base, i.e., a strong nucleophile. A list of pK_a values of the conjugate acids of common nucleophiles is given in Table 1.2.

$pK_a = -\log K_a$

Table 1.2 : List of common nucleophiles with pK_a values of their conjugate acids

Nucleophile	Conjugate acid	pK_a
I^-	HI	−10
Br^-	HBr	−9
Cl^-	HCl	−7
CN^-	HCN	9.2
RS^-	RSH	10-11
R_3N	R_3NH^+	10-11
R_2NH	$R_2NH_2^+$	11
OH^-	H_2O	15.7
$CH_3CH_2O^-$	CH_3CH_2OH	16
$RCHCN^-$	RCH_2CN	25
$HC\equiv C^-$	$HC\equiv CH$	25
NH_2^-	NH_3	38
$CH_2=CH^-$	$CH_2=CH_2$	44
CH_3^-	CH_4	48
$(CH_3)_2CH^-$	$(CH_3)_2CH_2$	51

The increasing order of basicity of some reagents is,

$$I^- < Br^- < Cl^- < ROH < H_2O < C\equiv N^- < \underbrace{OH^- < OR^-}_{\text{strong bases}}$$

Let us recall here the two important structural features affecting the basicity of a molecule. These are :

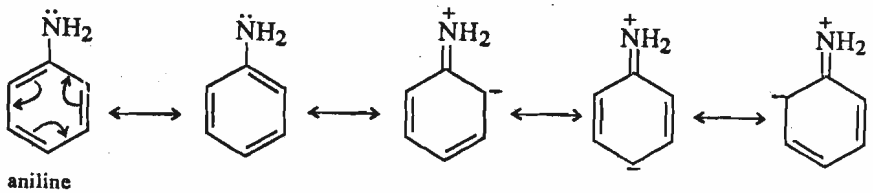
i) **Inductive effect** : In general, the substituents having + I effect, i.e., electron releasing effect increase basicity. For example, in the case of amines an alkyl group on nitrogen increases basicity by dispersing the positive charge in the cation which is stabilised relative to the free amine.

$$CH_3 \rightarrow \ddot{N}H_2 + H_2O \rightleftharpoons CH_3 \rightarrow \overset{+}{N}H_3 + OH^-$$

Therefore base strength increases in the series,

$$NH_3 < CH_3NH_2 < (CH_3)_2NH$$

ii) **Resonance** : Resonance effects the base strength of an amine. For example, cyclohexylamine is a far stronger base than is aniline. The reason is that the availability of lone pair in case of aniline will be reduced due to the delocalisation of the lone pair over the ring as shown in the resonance structures below.



aniline

In contrast to basicity, nucleophilicity is a measure of a reagent's ability to cause substitution at a carbon atom. The relative nucleophilicities of a series of reagents are determined by their relative rates of reaction in a substitution reaction, e.g., substitution reaction with bromoethane,

It is important to note here that while basicity is a thermodynamic property (measured by equilibrium constant) nucleophilicity is a kinetic phenomenon.

$$OH^- + CH_3CH_2{-}Br \longrightarrow CH_3CH_2{-}OH + Br^-$$

the increasing order of nucleophilicity of some reagents is,

$$H_2O < ROH < Cl^- < Br^- < \bar{O}H < \bar{O}R < I^- < C\equiv\bar{N}$$

The order of nucleophilicity can be rationalised in terms of polarisability and solvation of nucleophiles and the nature of the solvent. Steric considerations are also associated with

nucleophilicity. These aspects would be taken up later in Unit 3 when we talk about nucleophilic substitution reactions in detail.

1.3.2 Electrophiles

Electron deficient reagents which tend to accept electrons and are "electron loving" are called electrophiles. These reagents attack electron rich centres or nucleophiles and form a bond during the reaction.

$$Nu^- + E^+ \longrightarrow Nu - E$$

Since electrophiles can accept an electron pair or get attracted towards a negative centre, they also act as Lewis acids. Electrophiles are of two types, positively charged and neutral. A list of electrophiles is given in Table 1.3.

Table 1.3 : List of some electrophiles

Positively charged	Neutral
H^+	$I-Cl$, $\ddot{C}Cl_2$
M^+, MX^+	$RC(=O)-Cl$
Br^+, Cl^+	$R-C(=O)-O-C(=O)-R$
NO_2^+, NO^+, NH_4^+	CO_2, SO_3
H_3O^+	BF_3, $ZnCl_2$, $AlCl_3$, $FeCl_3$,
R_3C^+, $Ar-\overset{+}{N}\equiv N$, $R\overset{+}{C}O$	

1.3.3 Free Radicals

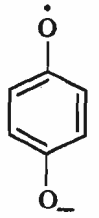
Two types of reagents that we discussed earlier, i.e., electrophiles and nucleophiles, need not necessarily be added reagents. They can be transient species formed during the course of a reaction. Free radicals, the third type, produced as a result of homolytic cleavage of a covalent bond, are essentially reaction intermediates. These are important because of their high reactivity. A free radical is any atom or group that possesses one or more unpaired electrons; because of this and an incomplete octet, it is highly reactive. You will read more about radical intermediates in Unit 9 of Block 3 of this course. Table 1.4 gives a list of some free radicals.

Table 1.4 : Some free radicals

hydrogen	$H\cdot$
chlorine	$Cl\cdot$
silver	$Ag\cdot$
sodium	$Na\cdot$
oxygen	$\dot{O}-\dot{O}$ (diradical)
carbon	$-C\cdot$
alkoxy	$-CO\cdot$
nitroxide	$-\dot{N}-O\cdot$

1.3.4 Radical Ions

We should also briefly refer to another type of reagents which are encountered during reactions as intermediates. These are the radicals ions. Radical ions possessing both an odd electron and charge are known. These may carry a positive or negative charge along with an odd electron and are correspondingly known as **radical cations** or **radical anions** respectively. The semiquinone anion (I) and the metal ketyls (II) produced by donation of an electron by a metal atom to a ketone are well known examples of radical anions. An example of a radical cation is aminium radical ion (III).



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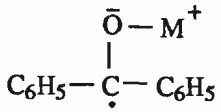


II

III

The relation between the structures of carbocation, carbanions, radical cations and radical anions can be best illustrated by considering the reaction of anthracene with different reagents. Under suitable reaction conditions, anthracene can produce any one of these four species, as it can,

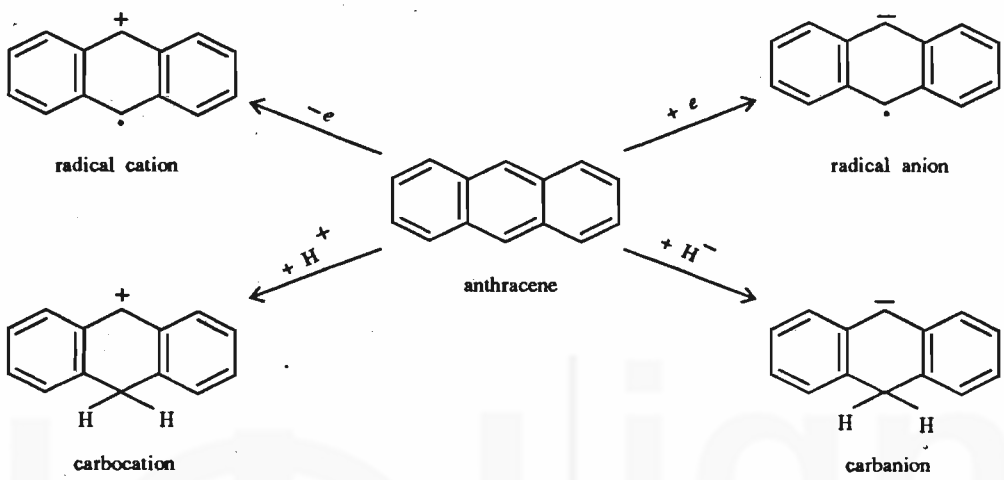
a) add an electron to produce a radical anion (sodium in liquid ammonia will accomplish this);

b) add hydride ion to produce a carbanion (lithium aluminium hydride is expected to do this but a very high temperature is required to reduce anthracene with this reagent);

c) remove an electron to form a radical cation (a good one-electron oxidising agent such as Mn^{3+} produces this species);

d) add a proton to form a carbocation (a nonoxidising acid such as HF can do this).

These reactions of anthracene are summarised in the following scheme :



In the case of the radical ions above, the charge and/or the odd electron can be distributed over the rings by resonance.

SAQ 2

i) Pick up the nucleophiles in the following reactions.

a) $CH_3CH_2Cl + KOH \longrightarrow CH_3CH_2OH + KCl$

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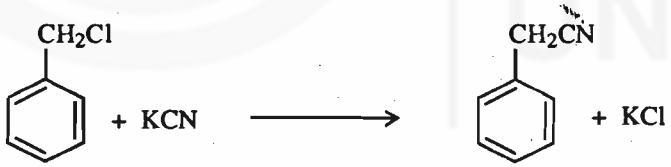
b) 

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c) $CH_3CH_2Cl + NaSCH_3 \longrightarrow CH_3CH_2SCH_3 + NaCl$

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d) $CH_3Cl + NaSH \longrightarrow CH_3SH + NaCl$

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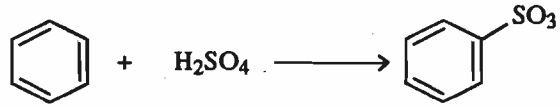
ii) Pick up the electrophiles in the following reactions.

a) 

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b) $CH_4 + H^+ \longrightarrow CH_3^+ + H_2$

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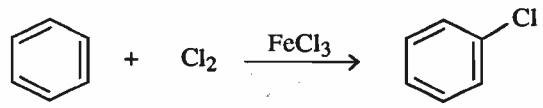
c) 

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d) $CH_3MgI + I_2 \longrightarrow CH_3I + MgI_2$

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Having understood what reaction mechanism is, the different ways in which the covalent bond of organic molecules can break leading to different kinds of mechanism, the different types of reagents bringing about organic reactions; we would now study the different types of organic reactions. Here you would learn to classify these reactions depending upon the kind of mechanism operating in them and the reagent used.

1.4 TYPES OF REACTIONS

In your previous course, you must have studied classification of organic compounds. You would have noticed that it becomes very easy to understand the nature of organic compounds by categorising them according to the structural types and functional groups. Similarly, it becomes very easy to understand organic reactions if these are categorised into different types which also helps to frame a series of rules pertaining to each type. However, you should remember that products obtained in a reaction depend upon conditions under which the reaction is carried out. Depending upon the substrate, reagent and reaction conditions, sometimes very different and unexpected products are formed.

Let us study the five main types of organic reactions which essentially involve bond making and bond breaking processes at carbon atoms of a substrate. Each of these types will be dealt with in detail in the following units.

1.4.1 Substitution Reactions

In a substitution reaction, the attacking species of one type (nucleophilic, electrophilic or radical) replaces a similar species.

When an atom or group provided by the reagent replaces an atom or group of the substrate molecule, the reaction is called a **substitution reaction.** It can take place in a number of ways.

Consider, for example, the following substitution reaction,

$Y + R—X \longrightarrow Y—R + X$

Where R—X and Y—R are both covalent molecules.

i) This reaction may involve a homolytic fission as shown below,

$R—X \longrightarrow R\cdot + X\cdot$

$Y\cdot + R\cdot \longrightarrow R—Y$

or $Y\cdot + R—X \longrightarrow Y—R + X\cdot$

where the free radicals are produced first and later they combine with other free radicals to give substitution products. This is called a **free radical substitution.**

Photochemical chlorination of methane is an example.

$Cl_2 \xrightarrow{h\nu} 2Cl\cdot$

$Cl\cdot + CH_4 \longrightarrow CH_3\cdot + HCl$

$CH_3\cdot + Cl_2 \longrightarrow CH_3Cl + Cl\cdot$ etc.

ii) Another way in which the above substitution reaction can take place is represented as :

$R—X \longrightarrow R^+ + X^-$

$Y^- + R^+ \longrightarrow Y—R$

or $Y^- + R—X \longrightarrow Y—R + X^-$

This occurs when the reaction involves heterolytic fission. The reagent Y is a nucleophile (nucleus-loving) and it seeks a centre of electron deficiency or an electrophilic (electron-loving) centre. The electron deficient centre here is a carbocation. Since the attacking reagent is a nucleophile, the substitution is called **nucleophilic substitution**. You are familiar with nucleophilic substitution reactions of alkyl halides, like, hydrolysis of 2-bromo-2-methylpropane,

$$(CH_3)_3CBr \longrightarrow (CH_3)_3C^+ + Br^-$$

$$(CH_3)_3C^+ + H_2O \longrightarrow (CH_3)_3COH + H^+$$

Nucleophilic substitution reactions can proceed by more than one type of mechanism. The mechanistic details of these would be dealt with in Unit 3 of this course.

iii) There is yet another way in which a substitution reaction can take place. Here also the heterolytic fission of the molecule R—X takes place.

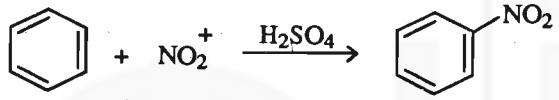
$$R—X \longrightarrow R^- + X^+$$

$$Y^+ + R^- \longrightarrow Y—R$$

or $Y^+ + R—X \longrightarrow Y—R + X^+$

The reagent Y^+ is an electrophile. It seeks a reaction centre which has a high electron density, a carbanion here. Attacking reagent being an electrophile in this case, the substitution is called **electrophilic substitution**. This type of substitution is most common in aromatic compounds, like, nitration of benzene.

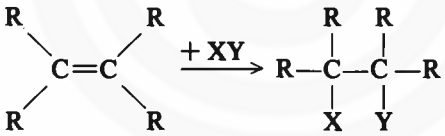
$$HNO_3 + H_2SO_4 \rightleftharpoons H_3O^+ + 2HSO_4^- + NO_2^+$$



You will study this type of substitution in detail in Unit 4 of this course.

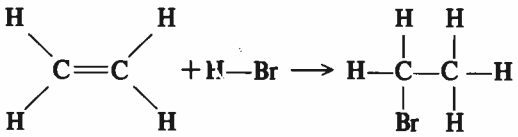
1.4.2 Addition Reactions

Addition is the most characteristic reaction of alkenes and alkynes. In addition reactions, two atoms or groups are added to a molecule containing a double or a triple bond.

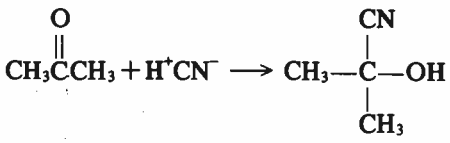


In most of these reactions, the addendum is an electrophile and the alkene, a nucleophile. The reactions are called **electrophilic addition reactions**. Free radicals being electron deficient species, even **free radical additions** can be classified as electrophilic attacks.

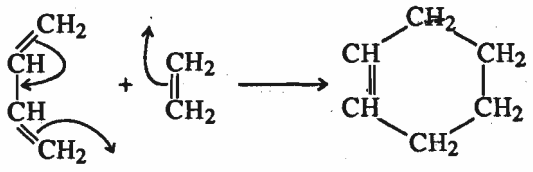
A simple example of an addition reaction is the addition of HBr to ethene to give bromoethane.



Electrophilic and free radical addition reactions are common with alkenes and alkynes while **nucleophilic addition reactions** are encountered in double bonds with hetero atoms, e.g., with carboxyl compounds. The formation of a cyanohydrin by the reaction between propanone and HCN is a common example.

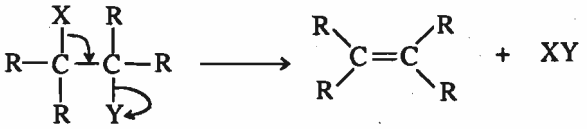


When bond breaking and addition to the double bond take place simultaneously as shown below, it is referred to as **pericyclic addition**.

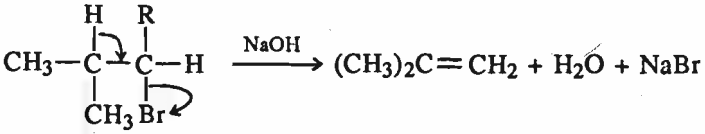


1.4.3 Elimination Reactions

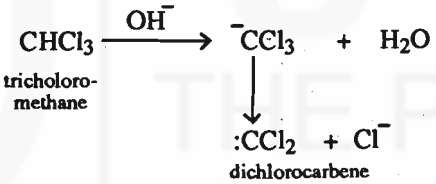
These are reactions that involve the loss of two groups or atoms, commonly from adjacent carbon atoms, introducing a double bond.



For example,



Since the above elimination involves two groups (or atoms) on adjacent carbon atoms, it is called a 1, 2 or β-elimination. When elimination involves loss of two atoms or groups from the same atom, it is called (1, 1) or α-elimination. For example,



The hypovalent neutral species $:CCl_2$ is called a **carbene**. It is an unstable intermediate about which you will study in detail in Unit 9.

SAQ 3

Write the products of the following reactions and categorise them as substitution, elimination or addition reactions.

i) $CH_4 + Cl_2 \longrightarrow$

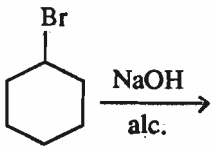
.....

ii) $CH_3CH_2OH + PCl_5 \longrightarrow$

.....

iii) $CH_2{=}CH_2 + HBr \longrightarrow$

.....

iv) 

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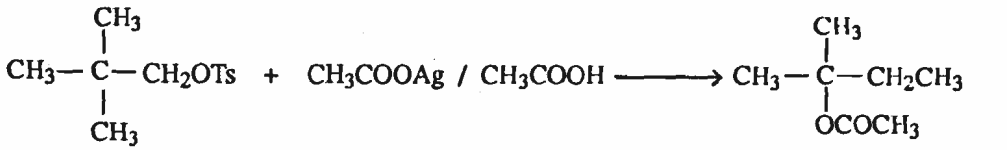
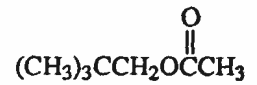
1.4.4 Rearrangements

As said before, most of the reactions of organic compounds take place at a functional group while the rest of the molecule does not undergo any change. There are some organic reactions wherein this "intact" part also takes part in the reaction. These are rearrangement reactions in which an atom or a group moves from one position to another within the molecule. In other words, if in a reaction, instead of getting the expected product, an isomerised product is obtained due to the migration of an atom or group it is called a rearrangement. For example, the rearrangement of 2, 2-dimethylpropyll-4′-methylbenzenesulphonate (neopentyl tosylate) to 1, 1-dimethylpropylethanoate (amyl acetate) is given below.



neopentyl tosylate

*tert*amylacetate
(observed or rearranged product)

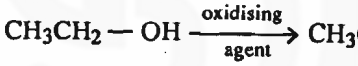


2,2-dimethylpropylethanoate
(neopentyl acetate)
(expected product)

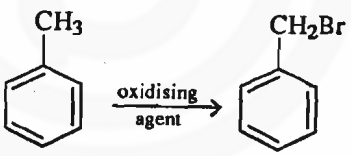
1.4.5 Oxidation and Reduction Reactions

It is difficult to define oxidation or reduction as applied to organic compounds. You might recollect that in Inorganic Chemistry, oxidation is defined as either loss of electrons or increase in **oxidation number**. Conversely reduction is defined as gain of electrons of decrease in oxidation number. Thumb rules to determine whether an organic compound has been oxidised or reduced are :

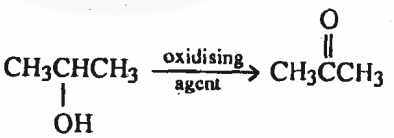
i) If a molecule gains an electronegative element (nitrogen, halogen or oxygen) or loses hydrogen it is oxidised, e.g.,



(gain of O)

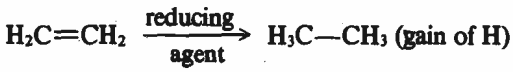


(gain of Br)



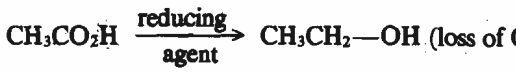
(loss of H)

ii) If a molecule loses an electronegative element (nitrogen, halogen or oxygen) or gains hydrogen it is reduced, e.g.,



(gain of H)

(loss of S, gain of H)



(loss of O, gain of H)

Another way to determine whether an organic molecule is oxidised or reduced is to arrange a series of functional groups in order of increasing oxidation state (Table 1.5) and define oxidation as the conversion of a functional group in a molecule from one category to a higher one. The opposite is true for reduction. You know that oxidation states or oxidation numbers enable us to follow the paths of electrons during a reaction and tell which substances were oxidised and which reduced. Oxidation numbers can be positive or negative. The oxidation

number of carbon in the series representing oxidation of methane to carbon dioxide is as follows:

$$\overset{-4}{CH_4} \longrightarrow \overset{-2}{CH_3OH} \dashrightarrow \overset{0}{HCHO} \longrightarrow \overset{+2}{HCOOH} \longrightarrow \overset{+4}{CO_2}$$

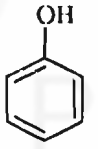
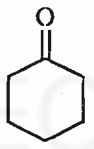
Table 1.5 : Functional groups arranged according to increasing oxidation state

Approximate Oxidation number	−4	−2	0	+2	+4
FUNCTIONAL GROUP	⟶		OXIDATION	⟶	
	*RH	$-C=C-$	$R-C\equiv C-R$	RCO_2H	CO_2
		ROH	$R-\overset{\overset{O}{\|\|}}{C}-R$	$RCNH_2$	CCl_4
		RCl	$>CCl_2$		
		RNH_2	$Cl-\overset{R}{\overset{\|}{C}}-\overset{R}{\overset{\|}{C}}-Cl$	$-CCl_3$	
			$R-\overset{\|}{\underset{OH}{C}}-\overset{\|}{\underset{OH}{C}}-R$		
	⟵		REDUCTION	⟵	

*R = alkyl group : where not indicated substituent is H.

SAQ 4

Arrange the following in order of increasing oxidation state.

CH_3COOH, $HO_2C(CH_2)_4CO_2H$,  ,  , C_2H_6

.....

.....

.....

1.5 SUMMARY

Let us summarise the important aspects of reaction mechanism we have studied in this unit.

- The detailed description of how a reaction occurs is called reaction mechanism. All reactions involve bond breaking and bond making. Depending upon the way a bond is broken, mechanism of organic reactions can be broadly classified into homolytic, heterolytic or pericyclic types.
- The reagents generally used in organic reactions are nucleophiles, attracted towards a positive centre; electrophiles, attracted towards a negative centre; free radicals with unpaired electrons on them and radical ions which are radicals with positive or negative charges.
- It becomes easy to understand the large number of organic reactions if categorised into different types. When a group or atom in an organic molecule is replaced by another group or atom, it is called a substitution reaction. Depending upon the reagent, substitution reactions can be nucleophilic, electrophilic or free radical type. When two atoms or groups are added to a double or a triple bond, it is called an addition reaction. This can also be classified into nucleophilic, electrophilic and free radical type. Elimination reactions are those in which two atoms or groups are removed from a molecule, usually from adjacent carbon atoms leading to unsaturation in the molecule.

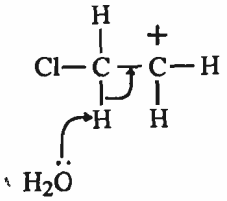
Rearrangement reactions are the ones where in an atom or group shifts to another position in the same molecule. Nucleophilic and electrophilic rearrangements are more common than the free radical types. Another type of organic reactions may involve any of the above four types. These are oxidations and reductions which again can take place in the presence of a number of reagents.

1.6 TERMINAL QUESTIONS

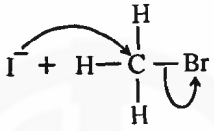
1) In the following reaction, reactants and arrows showing the flow of electrons are indicated. Write the products of the reactions.

i) $CH_3CH_2-\ddot{O}H + H-I$

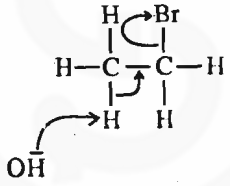
ii)



iii)



iv)



2) Why is iodide ion a good nucleophile but a weak base?

3) Categorise the following species into electrophiles and nucleophiles.

CH_3O^-, PH_3, H^+, $CH_3\overset{\overset{O}{\|}}{C}-Cl$, CH_3NH_2, H^-,

$AlCl_3$, $H_2C{=}O$, I^-, $CH_3CH_2S^-$, Hg^{2+}.

4) What type of reaction must be carried out to convert,
   i) an alcohol to a carboxylic acid.
   ii) an alkyl chloride to an alkyl bromide.
   iii) an alkene to an alkane.
   iv) a haloalkane to an alkene.

1.7 ANSWERS

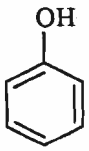
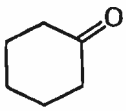
Self Assessment Questions

1) i) Radical mechanism
   ii) Ionic mechanism
   iii) Ionic mechanism

2) i) Nucleophiles — OH^-, CN^-, SCH_3^-, SH^-
   ii) Electrophiles — SO_3, H^+, Cl^+, I^+

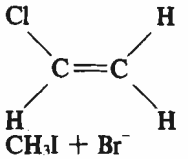
3) i) $CH_3Cl + HCl$ — substitution
ii) CH_3CH_2Cl — substitution
iii) CH_3CH_2Br — addition

iv)  + NaBr — elimination

4) C_2H_6 <  <  < CH_3COOH < $HOOC(CH_2)_4COOH$

Terminal Questions

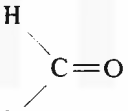
1) i) $CH_3CH_2—I + H_2O$

ii) 

iii) $CH_3I + Br^-$

iv) $H_2C=CH_2 + H_2O + Br^-$

2) Iodine has a large atom and the outer electrons in it being farther from the nucleus are less tightly held. The outer electrons are, therefore, more easily distorted by attraction to a positive centre and can attack a partially positive carbon atom readily. However, it does not easily accept a proton from an alkyl halide and thus act as a good nucleophile and a weak base.

3) Electrophiles : H^+, $CH_3\overset{O}{\overset{\|}{C}}—Cl$, $AlCl_3$ Hg^{2+}, 

Nucleophiles : CH_3O^-, PH_3, H^-, I^-, $CH_3CH_2S^-$, CH_3NH_2

4) i) oxidation reaction
ii) substitution reaction
iii) addition or reduction reaction
iv) elimination reaction

UNIT 2 KINETICS AND MECHANISM OF REACTIONS

Structure

2.1 INTRODUCTION

In the previous unit you learnt about the types of reaction mechanism, types of reagents and the types of reactions. You have learnt to classify the reactions, that is, in a reaction you can identify the reagent, the substrate and assign a type or category to it. You can also have some idea about its mechanism. But how do we ascertain whether a reaction would take place or not? If a reaction does take place, how long would it take for the reactant(s) to get converted into the product(s)? These questions of "possibility" and "time factor" are important from the point of actual practice. If for a reaction of practical utility, a good yield of the product is required in a reasonable time, then it is desirable that both the factors are favourable. These questions would be dealt with in this unit. We would study the factors that determine the feasibility of a reaction, the kind of information we get regarding the mechanism of reaction from kinetic measurements and also the kind of nonkinetic information required for delineating the mechanism of a chemical reaction. All this will form the fundamental basis of reaction mechanism which in fact would be dealt with in detail in the later units.

Objectives

After studying this unit you should be able to :

- explain thermodynamics of reactions,
- explain importance of kinetic parameters of a reaction in determining reaction mechanism,
- explain transition state theory of reaction rate,
- explain and differentiate thermodynamically and kinetically controlled reactions,
- describe nonkinetic methods for determination of reaction mechanism, and
- explain Hammett equation and its importance in predicting the equilibrium constant or rate of a reaction.

2.2 THERMODYNAMIC AND KINETIC CONSIDERATIONS

First of all we shall take up the question of the 'possibility' and the 'time factor' of a reaction, i.e., its thermodynamics and kinetics as mentioned in the introduction to this unit.

2.2.1 Thermodynamic Considerations

You would recall from your earlier studies that a reaction occurs spontaneously if the free energy change accompanying the reaction, ΔG, is negative, i.e., the free energy of the products is lower than that of the reactants. The free energy is related to two other thermodynamic functions, viz., enthalpy, H and entropy, S.

Free energy change = Free energy of the products − free energy of the reactants, i.e.,

$\Delta G = G_P - G_R$

At constant temperature we have the following expression for free energy change,

$$\Delta G = \Delta H - T\Delta S \quad \text{... (2.1)}$$

where ΔG, ΔH and ΔS are the changes in the free energy, enthalpy and entropy respectively, while T is the temperature on absolute scale. Before we analyse Eq. 2.1 it would be worthwhile to know a little about the two thermodynamic functions, H and S. Enthalpy, H, is a function which depends upon the state of a system. It is not possible to compute the enthalpy of any reactant or the product. What best can be done is to measure the enthalpy change of a given reaction, which is equal to the difference in enthalpies of the products and the reactants. A good empirical estimate of the enthalpy of a given reaction can be made in terms of the bond energies of the reactants and the products. This is calculated by totalling the bond energies of all the bonds broken, subtracting it from the total of bond energies of all the bonds formed, also accounting for any changes in resonance, strain or solvation energies. You can get details of this method from any standard book on thermodynamics.

Enthalpy change = Enthalpy of the products − enthalpy of the reactants, i.e.,

$\Delta H = H_P - H_R$

Entropy, S, like enthalpy is also a state function and it is not possible to compute or estimate the entropy of any given substance. Conceptually speaking, entropy is a measure of randomness or disorderliness of a given system. A more random system is said to possess a higher entropy. The entropy change, ΔS of a given reaction is positive if the reaction leads to higher randomness.

Water has a higher entropy than ice.

Entropy change = Entropy of the products − entropy of the reactants, i.e.,

$\Delta S = S_P - S_R$

Coming back to Eq. 2.1, it can be seen that the free energy change has got two components. One is coming from the enthalpy change (ΔH) and the other from entropy change ($-T\Delta S$). It is clear from the equation that to make ΔG negative it is best if ΔH is negative and ΔS positive, i.e., the enthalpy should decrease and enthalpy increase. If the entropy change is negative, i.e., the second term becomes positive, the free energy can still decrease if the first term (ΔH) is sufficiently negative to over-balance the second term. Similarly, an increase in enthalpy (ΔH positive) can be tolerated if ΔS is sufficiently positive such that the second term over-balances the first one.

Majority of the common chemical reactions are exothermic (ΔH, negative) in their natural direction, often so highly exothermic that the term $T\Delta S$ has little influence in determining the equilibrium position. The reactions for which spontaneity is determined mainly by the enthalpy term are called **'enthalpy driven'** reactions. On the other hand certain reactions, e.g., of the type $A \longrightarrow B + C$ are accompanied by a large gain in entropy and the reaction is thermodynamically favoured because of the entropy factor. Such reactions are called **'entropy driven'** reactions.

All that is discussed above has been with reference to reactions which go in one direction, namely, the forward direction, i.e., from reactants to products. In actual practice, reactions do not go in such a straight forward manner. Once the products are formed, they have a tendency to react and give back the reactants. Invariably at the end of a reaction we land up with a mixture of reactants and products. No reaction, as said, goes to 100% completion. The proportion of reactants and products in the mixture at the end of a reaction is determined by the equilibrium constant.

Equilibrium constant for a simple reaction like,

$aA + bB \longrightarrow cC + dD$

can be defined as,

$$K = \frac{[C]^c\,[D]^d}{[A]^a\,[B]^b}$$

where square brackets represent the concentration of the species enclosed in it.

The value (magnitude) of the equilibrium constant determines which way would the equilibrium lie—more towards the products or the reactants! Further ΔG and K are interrelated through the following equation,

$$\Delta G = -RT \ln K \quad \text{... (2.2)}$$

More negative value of ΔG corresponds to a greater value of K and hence, more of product formation.

This means that for a large positive value of ΔG, K would be far less than unity ($<<<1$). The equilibrium would be towards the side of reactants, the amount of the products would be very little. On the other hand, a good yield of the product(s) is obtained for $K >>> 1$ which corresponds to a negative ΔG value. For $\Delta G = 0$, K is equal to unity and one apparently gets an equimolar mixture of reactants and products. In such cases, a judicious adjustment of reaction conditions on the basis of Le Chatelier's principle can make the reaction go more to the right.

The discussion so far has apparently answered our first question, i.e., about the feasibility of a reaction. We have got an idea of the thermodynamic terms involved and their significance. All this does not seem enough to guarantee a reasonable yield of the product with a time frame. Let us take a few examples. Equilibrium constant for the reaction between chloromethane and NaOH,

$$CH_3Cl + NaOH \longrightarrow CH_3{-}OH + NaCl$$

has been estimated to be of the order of 10^6. The equilibrium is expected to lie far towards the right but it takes many weeks for an equeous solution of the reactants to give the products. Similarly, a mixture of H_2 and O_2 can be kept at room temperature for centuries without getting even a trace of water.

These examples suggest that a negative value of ΔG for a given reaction does not necessarily mean that it will proceed in a reasonable period of time. Besides the thermodynamic considerations discussed above we need to look into yet another aspect to ensure a reasonable course of reaction in terms of product formation. This is the 'time factor' or the 'kinetic' aspect which we will discuss in the next subsection. Before going ahead why don't you try the following SAQ.

Negative ΔG is a necessary but not a sufficient condition for spontaneity of a reaction.

SAQ 1

Thermodynamic data for a reaction is given below. Predict whether the reaction is spontaneous or not and if yes, is it enthalpy or entropy driven?

$T = 400$ K, $\Delta H = 5.2$ kJ mol^{-1}, $\Delta S = 150$ J mol^{-1}K^{-1}

.....

.....

.....

.....

2.2.2 Kinetic Considerations

Kinetics is concerned primarily with the measurements of rates of chemical reactions, i.e., 'how fast or slow' a reaction is. Let us review a few fundamental concepts of chemical kinetics. We will discuss different kinetic parameters which are experimentally determined. We will also see what kind of information, regarding the mechanism of a reaction, can be discerned from such data.

In kinetic measurements, the progress of reaction is followed by monitoring the appearance of the product(s) or the disappearance of any of the reactants as a function of time. These are measured either directly by suitable titrimetric method or indirectly by variation in some physical property like refractive index, optical density, etc. of the reacting system. The choice of technique also depends on the time frame of the reaction. Special instruments have to be used if a reaction is very fast (the half life is say < 1 second).

Half life of a reaction is the time taken by the reactants to get reduced to half their initial concentration.

The data obtained from rate measurements is incorporated into a mathematical expression called a **rate equation** or **rate law** which relates the rate of a reaction to the concentration of different reacting species. The rate law, e.g., for a reaction,

$$A + B \longrightarrow C$$

takes the following form,

$$\text{Rate} = -\frac{d[A]}{dt} = -\frac{d[B]}{dt} = \frac{d[C]}{dt} = k[A]^x[B]^y$$

We see that the rate of a reaction can be expressed in terms of more than one species. Negative sign indicates the disappearance while positive sign shows the appearance of a species.

In this expression the differential term refers to the incremental amount of product C formed or the reactants A or B consumed during an incremental time dt. Here k is the constant of proportionality called the **rate constant** and the terms in square brackets represent the concentration (more appropriately the activity) of the species contained in them. x and y represent the order of the reaction with respect to A and B respectively. The overall kinetic **order of the reaction** is the sum of the powers of concentration terms in the experimentally determined rate law expression. Order of a reaction is **unity** if the rate is directly proportional to the concentration of any one of the reactants and **two**, if it is proportional to its square or directly proportional to the concentration of two of the reactants and so on.

Another related concept is one of **molecularity** which is defined as the number of species (atoms, ions or molecules) that come together to form the activated complex or the transition state. In contrast to order, an experimentally determined overall characteristic of a reaction, molecularity is a theoretical concept which pertains to any elementary step of the many step mechanism. Order and molecularity of a reaction may or may not be the same. For example, for a S_N1 reaction, the rate depends only on the concentration of the substrate, as a result the order is one. Also it is only the substrate which gives rise to an intermediate carbocation. Therefore, molecularity of the reaction is also one. Whereas, for the photolysis of the CH_3CHO, the order is 3/2, we cannot have one and a half of a molecule reacting. So here order and molecularity are not same. Order of a reaction can be determined by a number of methods, the simplest one being the study of the effect of varying the concentration of reactant(s) of the rate of reaction. Such measurements lead to the determination of rate law which is the first step in deciphering the mechanism of a reaction. Let us study this aspect in detail.

For a single step reaction, order and molecularity are same.

A majority of organic reactions follow a complex mechanism consisting of a series of steps. Different steps have different rates, some being slower than the others. The slowest of all the steps is of interest from the point of view of reaction mechanism, because it is this step which determines the overall rate of a reaction. A reaction cannot proceed faster than its slowest step! This step is referred to as the **rate controlling, the rate determining** or **the rate limiting step**. The experimentally determined rate equation often (not always) permits us to determine the species involved in the rate determining step (rds) with a reasonable degree of confidence. This information is then exploited in suggesting the mechanism of a reaction.

There seems to be no general way of arriving at the mechanism from the rate equation. One is supposed to pick up different plausible mechanisms and then theoretically derive rate expression for each of them. The mechanism whose rate expression is closest to the experimentally obtained one is the most likely mechanism of the reaction.

Many a times we find that more than one mechanism can conform to the same rate expression. What does one do then? One needs to do some more experiments to obtain information regarding the intermediates formed, if any, or to see the effect of modifying the reactants or changing the solvent, etc. These aspects we shall take up at a later stage. Let us now see how do the energy changes take place during the course of a reaction and how do we describe this aspect of a chemical reaction. Before we go ahead try the following SAQ.

SAQ 2

What is the order of hypothetical reactions which have the following rate equations :

i) $\frac{dx}{dt} = k[A][B]$

ii) $\frac{dx}{dt} = k[A][B]^{1/2}$

iii) $\frac{dx}{dt} = k\frac{[A]^2[B]^{1/2}}{[C]^{1/2}}$

Can we find the molecularity of these reactions from the information given above?

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2.2.3 Transition State Theory

To compute the exact energies as the reaction progresses is a formidable job; rather an impossible one, because it involves several events — the rearrangement of atoms, change in hybridisation of atoms, change in bond angles, orientation of the molecule, its solvation

structure, etc. However, a qualitative picture can still be visualised with the help of the **transition state theory of reactions**. According to this theory, when the reactants change into products they pass through an unstable state of maximum free energy called the **transition state**. Energy of the transition state is higher than that of the reactants as well as the products. Therefore, it acts as an energy barrier required to be crossed by the reactants to get changed to the products and vice-versa. Energy changes in the course of a reaction are represented with the help of potential energy diagram like Fig. 2.1. Y-axis in the diagram is potential energy which is related to but is not identical with ΔH. We can take the reaction between CH_3I and NaOH as an example to understand this diagram. The reaction,

$$NaOH \longrightarrow Na^+ + OH^-$$

$$CH_3—I + OH^- \longrightarrow CH_3—OH + I^-$$

is found to follow the following rate expression,

$$\text{rate} = k[CH_3I][OH^-]$$

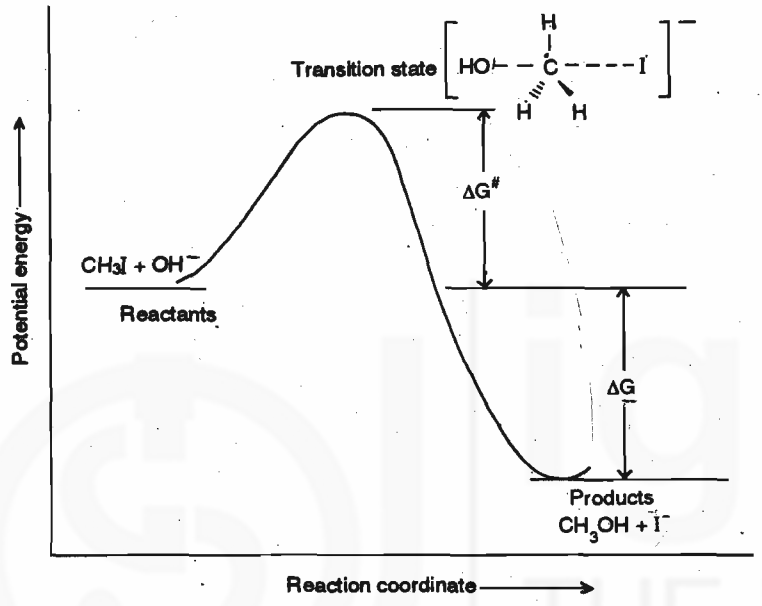

Fig. 2.1 : Potential energy diagram for the reaction, $CH_3I + OH^- \rightarrow CH_3—OH + I$

One way of visualising the course of this reaction is to visualise an energetic OH^- ion approaching the CH_3—I molecule from a direction opposite to that of the C—I bond. As the two come closer, the energy increases and continues to increase as the molecule "spreads out". The C—I bond weakens and the C—O bond begins to form as shown below. The energy becomes maximum when the C—I bond is "half broken" and C—O bond is "half formed".

$$OH^- + —\overset{|}{\underset{|}{C}}—I \longrightarrow \left[HO \cdots \overset{\diagdown\ \diagup}{C} \cdots I \right]^- \longrightarrow HO—\overset{|}{\underset{|}{C}}— + I^-$$

The high energy complex is called the transition state or the **activated** complex. Beyond this point further approach of the OH^- ion completes the breaking of C—I bond and the making of C—O bond; the energy decreases as shown in Fig. 2.1. Difference in the energy of the isolated reactants and the maximum energy at the transition state which the system passes through on path to the products, is the **free energy of activation**, $\Delta G^{\#}$. This equals the difference of free energies of the transition state (T.S.) and the reactants. The X-axis of the potential energy diagram is the reaction coordinate. It is a measure of the progress of reaction from the reactants to the products. In the above example, the reaction progress can be monitored in terms of say, C—I bond length. In the beginning the C—I bond has its equilibrium length. As the C—O interaction builds up, the C—I interaction diminishes and the C—I bond length increases. The increase in C—I bond length is a measure of the extent of reaction. The same may be perceived in terms of C—O bond length which is infinity before the reaction starts and goes on decreasing as the nucleophile approaches the carbon. The completion of reaction is indicated by the formation of C—O bond. The difference between the free energy levels of reactants and products represents the free energy of the reaction, ΔG, as indicated in Fig. 2.1.

According to the transition state theory, there exists an equilibrium between the reactants and the activated complex or the transition state. It is characterised by an equilibrium constant, $K^{\#}$.

$$A + B \rightleftharpoons \underset{(T.S.)}{\text{Transition state}} \longrightarrow \text{Products}$$

$$K^{\#} = \frac{[T.S.]}{[A][B]}$$

It is further assumed that all activated complexes get converted into products at the same rate and the rate constant of the reaction depends solely on the equilibrium constant, $K^{\#}$. Magnitude of $K^{\#}$ being governed by the free energy requirement for attaining the transition state; the two are related as,

$$\Delta G^{\#} = -RT \ln K^{*} \qquad \ldots (2.3)$$

It means that for a higher value of free energy of activation, $(\Delta G^{\#}), K^{\#}$ and hence the rate of reaction is small.

The rate of reaction is inversely proportional to the height of the energy barrier—higher the barrier the lower the rate.

The reactants having acquired sufficient energy to cross the activation barrier may still not give the product, instead there may be the formation of an intermediate which gives the products or a yet another intermediate which eventually gives the products. That is, the reaction involves two or three steps, respectively. The potential energy diagrams for two step reactions where the first and second step respectively are rds, are shown in Fig. 2.2. Here $\Delta G^{\#}_1$, and $\Delta G^{\#}_2$ are the free energies of activation for steps I and II respectively. Similar potential energy diagrams can be drawn for the reactions involving more than two steps.

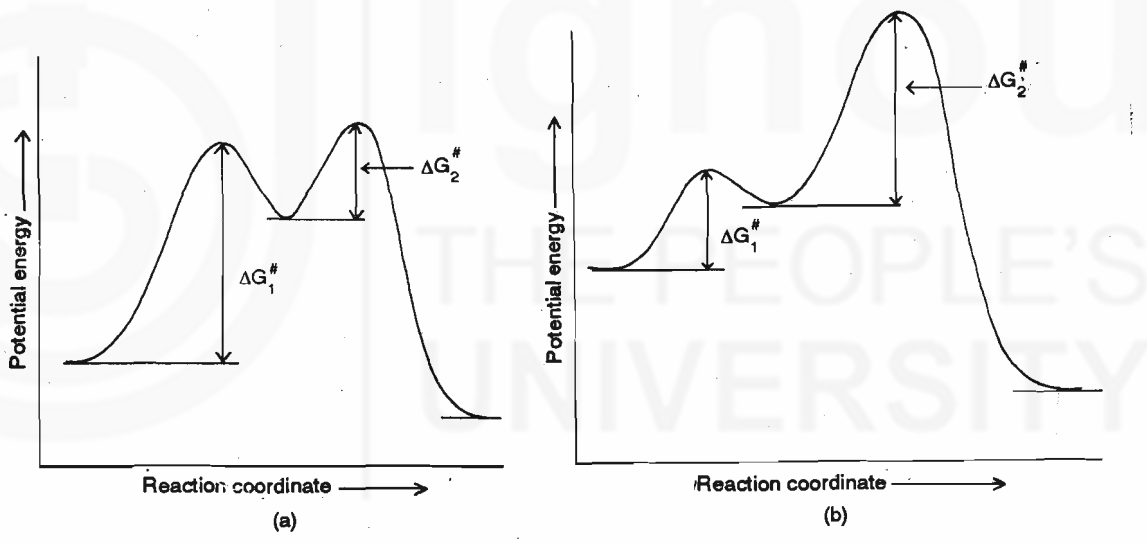

Fig. 2.2 : Potential energy diagram for two step reactions
a) first step rds
b) second step rds

Depressions or potential energy wells in the potential energy diagram correspond to intermediates. These are real species like carbocations, carbanions, free radicals, etc. Intermediates have a finite life time depending on the depth of the depression. A shallow depression implies a low activation energy for the subsequent step and, therefore, a short life time. The deeper the depression, the longer would be the life time of the intermediate, i.e., it would be fairly stable. The transition state on the other hand corresponds to an energy maximum and, therefore, has only a fleeting existence with almost a zero life time.

If a reaction has a number of pathways available to get converted into the same product, the path which involves the lowest potential energy maximum is followed. In a reversible reaction, the products formed have to traverse the same pathway to get transformed to the reactant. This is again the path of lowest energy maximum. This principle is called the **principle of microscopic reversibility**. It holds for the reactions involving intermediates also. If, in a reaction, A ⟶ C, B is an intermediate, then the conversion of C ⟶ A would also involve the same intermediate. B.

SAQ 3

Draw schematic potential energy diagram for a three step reaction A ⟶ B ⟶ C ⟶ D in which step 2 is rds.

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2.2.4 Thermodynamic and Kinetic Control

We have so far learnt that thermodynamically speaking, a reaction occurs if it is accompanied by a decrease in free energy (ΔG is negative), i.e., products have lower free energy than reactants. From transition state theory we saw that the rate of a reaction is governed by the free energy of activation ($\Delta G^{\#}$), i.e., the difference in free energies of reactants and the transition state, lower the $\Delta G^{\#}$, faster is the reaction. So, we have 'thermodynamic' and 'kinetic' factors which influence the progress of a reaction.

In the case of competitive reactions, i.e., the ones where more than one product can be formed from the same reactants, a question arises, which of the products would be formed? The one which is accompanied by greater free energy decrease (thermodynamically stable) or the one for which $\Delta G^{\#}$ is quite low (kinetically favoured)? The problem becomes slightly more complicated if the energy requirements of the two competing reactions are comparable. In such a case one has to analyse various factors which determine the actual course of the reaction under given experimental conditions.

Let us take an example where reactant A gives product B which can get converted into C. Which product would be obtained under a given set of reaction conditions? We can make an attempt to understand this by taking the potential energy diagram for the reaction as given in Fig. 2.3.

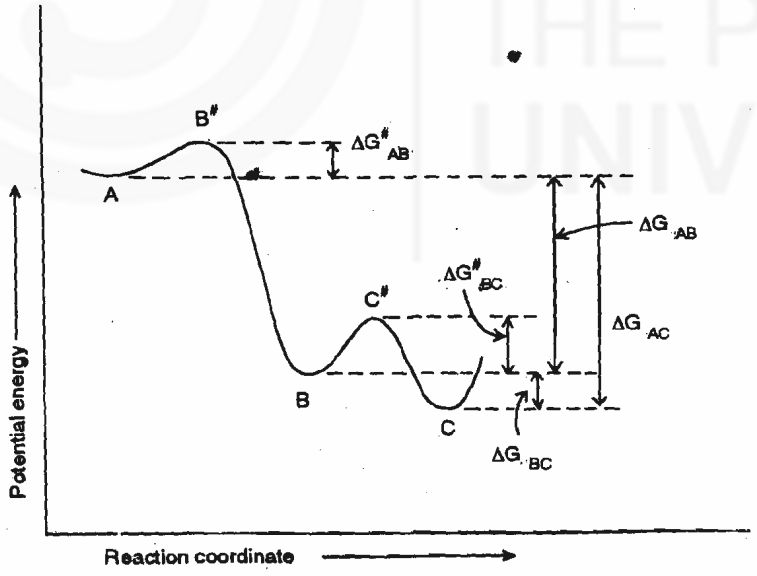
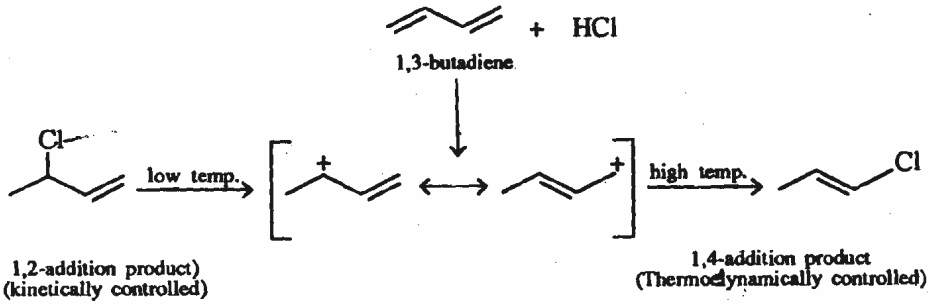


Fig. 2.3 : Potential energy diagram for a competitive reaction

As we can see from the potential energy diagram, $\Delta G^{\#}_{AB,}$ is quite low, so A very readily gets converted into B which does not go back to A ($\Delta G^{\#}_{BA}$ being high). Once B is formed, it has an intrinsic tendency to get converted into thermodynamically more stable C. Now, if the temperature of the reaction is sufficiently high, then B gets converted into C almost as soon as it is formed and one gets a mixture of B and C, thermodynamically stable C being predominant. The reaction is said to be **thermodynamically controlled**. On the other hand, if we keep the temperature low, the cross over of B → C can be checked and one gets

kinetically favoured B as the predominant product, though it is thermodynamically less favoured than C. Here B is said to be **kinetically controlled** product. The addition of HCl to 1, 3-butadiene is a good example of such a case. At high temperature, thermodynamically more stable 1, 4-addition product is predominant, whereas kinetically favoured 1, 2-addition product is obtained at low temperatures.



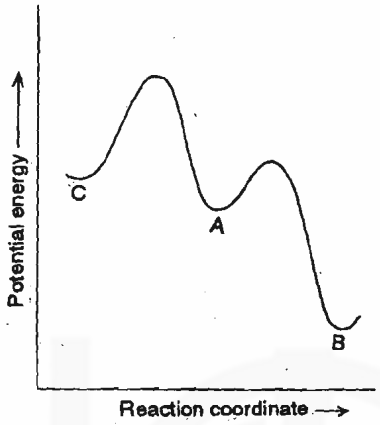


Fig. 2.4 : Potential energy diagram for the reaction, $A \nearrow^{B}_{C}$

SAQ 4

For a competitive reaction $A \nearrow^{B}_{C}$ the potential energy diagram is given in Fig. 2.4: Which product whould be formed at room temperature? Which type of control is operative in this case?

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2.3 DETERMINATION OF REACTION MECHANISM—NONKINETIC METHODS

As was pointed out earlier, kinetic data alone is not sufficient to decipher the mechanism of a chemical reaction. It can only provide some clues for the same and needs to be supplemented with some more data from other methods like isolation of products, isotope effect, stereochemical considerations, etc. We shall individually discuss these briefly. Information obtained from any or all of these methods is used along with kinetic data to arrive at a reasonably plausible mechanism for the reaction.

2.3.1 Product Identification

Identification of all the products, not only the major, is a must before even an attempt is made to suggest the mechanism of a reaction. Without this, the reaction in question cannot even be defined, as we can not be sure of which reaction we are talking about. The relative proportions of the products formed should also be known. This is important because any mechanism proposed should account for all the products with their relative proportions, at least qualitatively. For example, any plausible mechanism for photochlorination of methane has to account for the formation of a small amount of ethane, as along with other products, it is also formed in the reaction.

$Cl_2 + h\nu \longrightarrow 2Cl\cdot$

$Cl\cdot + CH_4 \longrightarrow \cdot CH_3 + HCl$

$CH_3 + Cl_2 \longrightarrow CH_3Cl + Cl\cdot$

$CH_3 + HCl \longrightarrow CH_4 + Cl\cdot$

$CH_3 + \cdot CH_3 \longrightarrow C_2H_6$

$Cl\cdot + Cl\cdot \longrightarrow Cl_2$

2.3.2 Evidence for an Intermediate

It was stated earlier that in a multistep reaction, the reactants pass through some kind of intermediates before getting converted into products. Intermediates are relatively stable species. Their stability being governed by the depth of potential energy well. If for a reaction, one suggests a mechanism involving the formation of an intermediate, it needs to be substantiated by a suitable experiment showing its presence and also its structure. The required experiment would depend upon the stability of the intermediate and the rates of its formation and

disappearance. It may involve its actual isolation and characterisation or its detection spectroscopically. Let us see the various possibilities.

• Isolation and Characterisation of Intermediates

If an intermediate is relatively stable and the rate of its formation is much faster than that of its consumption, then its concentration builds up after some time. At this stage the temperature of the reaction is suddenly decreased or a reagent is added which can stop the reaction. This is called **'arresting'** or **'quenching'** of the reaction. The intermediate isolated from a quenched reaction is characterised with the help of chemical or spectroscopic methods.

Is every species so isolated, an intermediate? The answer is 'NO'.

A species isolated by quenching a reaction is subjected again to the conditions that prevail during the course of the reaction. If the appropriate products are formed at a rate no slower than that from the starting reactants, then only can we say that we have a strong evidence for the given species to be an intermediate. Note that it is still not conclusive. For example, in case of Hoffman rearrangement reaction, i.e., conversion of an amide into an amine having one carbon atom less,

$$RCONH_2 + NaOBr \longrightarrow RCONHBr \longrightarrow RNH_2$$

the N-bromoamide (RCONHBr) can be isolated which gives the products at a desired rate. So, N-bromoamide is an intermediate in this reaction.

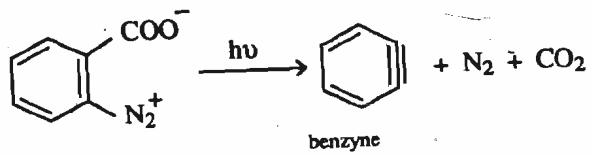
• Spectroscopic Identification of Intermediates

If the formation as well as consumption of an intermediate are very fast then it becomes quite difficult to isolate it. In such cases it is possible to get some meaningful information with the help of spectroscopic methods like ir (infra red), nmr (nuclear magnetic resonance), esr (electron spin resonance) or Raman spectroscopy. For example, detection of NO_2^+ (nitronium ion) by Raman spectroscopy in the nitrating mixture ($H_2SO_4 + HNO_3$) gave a strong evidence for its being an intermediate in the nitration reaction of aromatic hydrocarbons.

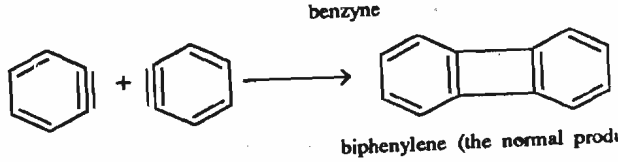
• Trapping the Intermediates

If the rates of formation and consumption of an intermediate are comparable and not very fast, then at a given instance in the course of a reaction, only a small amount of the intermediate is present. In such cases a compound that reacts specifically with the suspected intermediate can be used to **'trap'** it. In 'trapping', the said compound is added to the reaction mixture. The intermediate does not follow its normal course, instead it reacts with the added compound. If the structure of the product formed as a result of trapping is as expected, we say we have got evidence for the existence of the suspected intermediate.

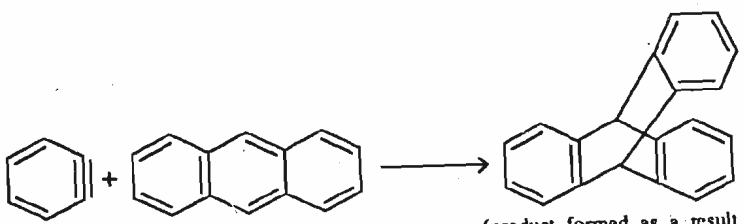
Formation of the intermediate 'benzyne', C_6H_4, in the photolysis reaction of *o*-carboxybenzene diazonium ion was established by trapping benzyne by adding anthracene to the system.



benzyne



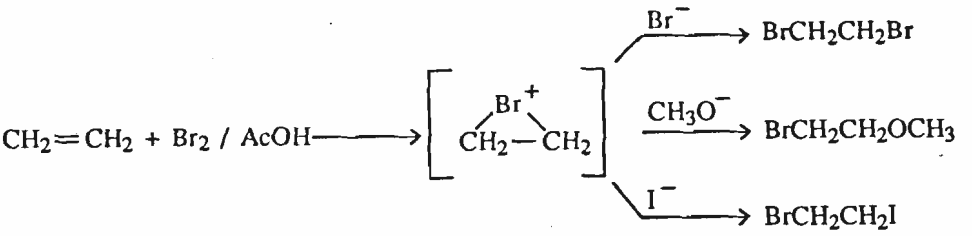
biphenylene (the normal product)



(product formed as a result of trapping with anthracene)

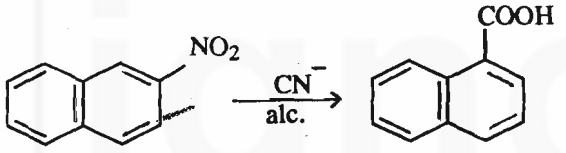
Benzyne, instead of dimerising to give biphenylene (the normal course) gives an addition product with anthracene. It can be isolated and characterised.

Nucleophiles are commonly used to trap carbocations. Direct evidence for the intermediacy of carbocations in the addition of a halogen to an alkene is provided by the observation that when the reaction is carried out in the presence of other nucleophiles a mixture of products is obtained.



• Addition of Suspected Intermediate

It is an interesting method which gives a conclusive negative evidence for a given intermediate in the reaction. In this approach, the likely intermediate is prepared separately by some other method and is subjected to conditions identical to those of the reaction. If the same products are obtained, then we say that the compound in question is the likely intermediate. On the other hand, if the desired products are not formed, we can conclusively say that the given compound is not an intermediate in the reaction in question. For example, in von Richter rearrangement of β-nitronaphthalene which gives α-naphthoic acid,



β-nitronapthalene α-naphthoic acid

the formation of α-naphthylcyanide as an intermediate is ruled out because it does not give α-naphthoic acid under the reaction conditions.

α-naphthylcyanide

2.3.3 Isotopic Studies

Isotopes have been used to study the reac[illegible] and mechanism in two distinct ways. These [illegible] latter actually being a kinetic effect. We shall study both [illegible]ere as tracer and as subst[illegible]head.

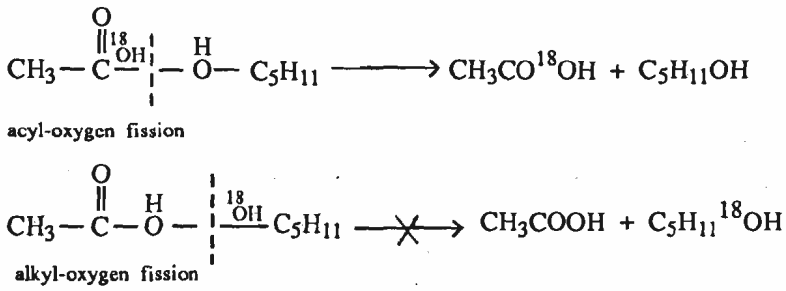
Isotopic Labelling

In this method the reaction is carried out using reactants which are isotopically labelled. In isotopic labelling certain atoms in the molecule are replaced by their isotopes. After the reaction is over, the products are analysed for the labelled species. Radioactive as well as stable isotopes can be made use of in this method. The commonly used isotopes are of hydrogen (^2D, deuterium or ^3T, tritium), carbon (^{13}C or ^{14}C) or oxygen (^{17}O or ^{18}O).

One of the first applications of isotopes in organic chemistry was the use of ^{18}O to probe the mechanism of ester hydrolysis. The hydrolysis of amyl acetate ($CH_3COOC_5H_{11}$) carried out in the presence of $H_2{}^{18}O$ gave unlabelled amyl alcohol and labelled acetic acid as,

$$CH_3COOC_5H_{11} + H_2{}^{18}O \longrightarrow CH_3CO^{18}OH + C_5H_{11}OH$$

This observations lead us to the conclusion that ester hydrolysis involves acyl-oxygen fission and not alkyl-oxygen fission.



Isotope Effect

Replacement of an atom by one of its isotopes, i.e., isotopic substitution, does not qualitatively effect the course of a reaction, however, rate of the reaction is altered. The difference in the masses of the isotopes is responsible for the effect. Rates of reactions for unsubstituted and substituted reactants are compared to get the information about the bonds being broken in the rate determining step. Besides, it may also provide some qualitative indication about the nature of the transition state.

Isotopic substitution can involve replacement of hydrogen (by ^2D or ^3T) or carbon (by ^{13}C or ^{14}C), etc. However, it is the replacement of hydrogen by deuterium which is used most often because it gives a substantial change in the rates. While isotopic substitution of ^{13}C for ^{12}C may change a reaction by only a few percentages, the calculated maximum for the isotopic effect K_H/K_D involving a C—H bond is about 7 at room temperature, i.e., the rate may be lowered by as much as 85 per cent. We shall confine our discussion to isotope effect involving hydrogen.

K_H/K_D is the ratio of the rates fc unsubstituted and substituted reactants.

If the magnitude of the kinetic isotope effect, K_H/K_D is 2 or more, it suggests that the bond involving isotopically substituted hydrogen atom is being broken in the rate determining step. The effect in this case is referred to as the primary isotope effect. For example, the isotope effect in the following reaction at 350 K is as high as 4.6.

$C_6H_5—CH_2—H^* + Br\cdot \longrightarrow C_6H_5—\dot{C}H_2 + H^*—Br$
(* indicates a hydrogen atom substituted by D).

If the isotope effects are relatively small, ($K_H/K_D = 0.7 - 1.5$), then they are called **secondary isotope effects**. These arise when the substituted hydrogen atom is not directly involved in the reaction. For example, in the solvolysis of isopropyl bromide, the kinetic isotope effect is found to be just 1.34.

$$(CH_3)_2CHBr + H_2O \longrightarrow (CH_3)_2\,CHOH;\quad \frac{K_H}{K_D} = 1.34$$

A comparison of nitration and sulphonation of benzene which you would study in detail in Unit 4 of this course also illustrates the isotope effect.

SAQ 5

D_2O and $H_2{}^{18}O$, both contain heavier isotopes and are almost equally heavy. Yet, while D_2O is extensively used to study kinetic isotope effect, $H_2{}^{18}O$ is rarely tried. Why?

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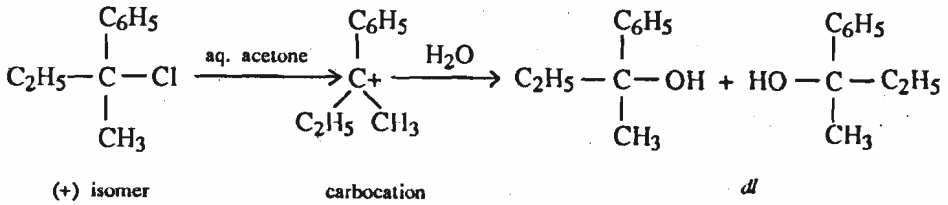
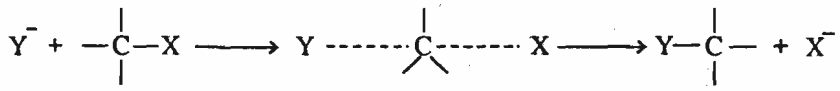
2.3.4 Stereochemical Studies

Study of the stereochemistry of reactants and products in many reactions can provide useful information regarding the mechanism. When an optically active compound undergoes reaction at the asymmetric centre, the product may or may not be optically active. The latter possibility is called racemisation. It usually arises in case of reactions where the reactant dissociates to give an intermediate. The intermediate then loses its symmetry before combining with the reagent to give the product. For example, the S_N1 solvolysis of optically active tertiary alkyl halide results in partial or complete racemisation.



The second possibility, i.e., the product being optically active can be achieved by either retention or inversion of configuration. This is the outcome of concerted processes in which free intermediates are absent. For example, direct S_N2 displacements at carbon proceed in all cases virtually by an attack of the nucleophile from the backside of the bond which is broken. This results in complete inversion of configuration.

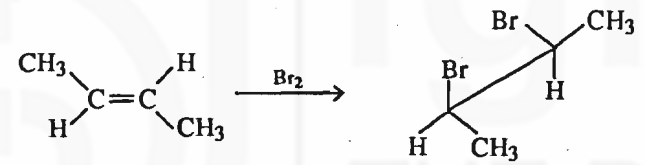


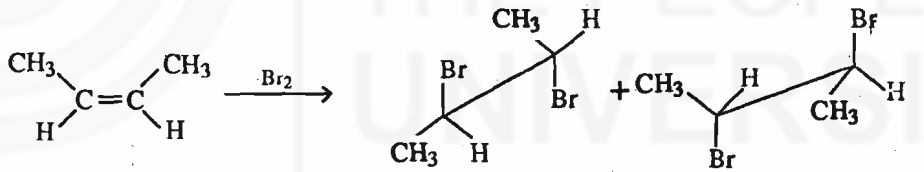
Stereochemical studies have shed considerable light in several other reactions like additions, eliminations and rearrangements.

Stereospecific and stereoselective reactions

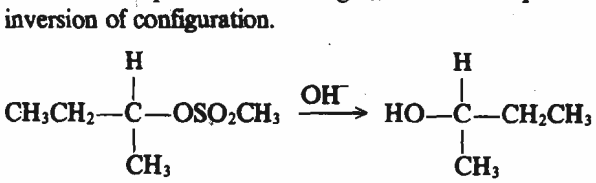
A reaction in which stereoisomeric starting materials afford stereoisomerically different products under the same reaction conditions is called a **stereospecific reaction**. Bromination of alkene in a polar medium is electrophilic and stereospecifically *trans*. For example, addition of bromine to *trans*-2-butene yields exclusively the *meso*-product, while only a *dl* pair is formed from *cis*-2-butene. The starting butenes are a stereoisomeric pair, and the products are also stereoisomeric with respect to each other. This can be shown as given below :

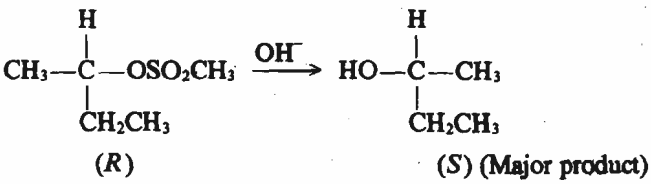
ompounds made up of the same oms bonded by the same sequence bonds but having different three mensional structures which are not terchangeable are called **ereoisomers.**





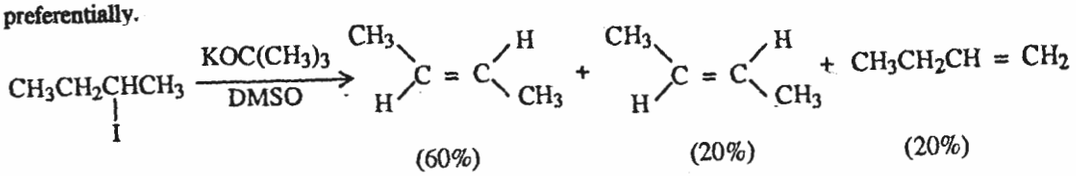
Another example is the following S_N2 reaction at sp^3 carbon which always proceeds with an inversion of configuration.





A **stereoselective reaction** is one in which a single reactant has the capacity of forming two or more stereoisomeric products in a particular reaction but one is formed preferentially. All stereospecific reactions are necessarily stereoselective, however, a stereoselective reaction need not be stereospecific. For example, in a moderately stereoselective elimination reaction like,

dehydrohalogenation of 2-iodobutane, the more stable of the two alkene isomers is formed preferentially.



(60%) (20%) (20%)

2.3.5 Substituent effect—Hammett Equation

Modification of a reactant by introducing a substituent (atom or group) effects a chemical reaction in two ways. Firstly, it alters the rate of the reaction and secondly, it influences the extent of the reaction, i.e., the equilibrium. We have seen earlier that an alteration in the rate (kinetics) or the equilibrium (thermodynamics) can provide useful inference regarding the mechanism of a reaction. It would be worthwhile if one could correlate the effect of a substituent on the reaction rate in a quantitative way.

A number of important correlations between a substituent group and chemical activity have been developed. Of these the most widely applied is the one developed by Hammett. This correlation is based on the relationship observed between the acid strength of substituted benzoic acids and the equilibrium and rates of many reactions of the compounds containing corresponding substituted phenyl groups.

The two forms of Hammett equation are given below :

$$\log \frac{K}{K_0} = \rho\sigma \qquad \ldots (2.4)$$

$$\log \frac{k}{k_0} = \rho\sigma \qquad \ldots (2.5)$$

While Eq. 2.4 pertains to the correlation between the equilibrium constants of substituted and unsubstituted species, Eq. 2.5 holds for the rate constants . K and K_0 are the equilibrium constants, k and k_0 are the rate constants for the substituted and unsubstituted substrates respectively. The two constants σ and ρ have the same meaning (given below) in either case.

The substituent constant, σ equals the difference in pK_a values of benzoic acid and the substituted benzoic acid. It is a measure of the extent to which the benzoic acid equilibrium is affected on introduction of a given substituent.

$$\sigma = pK_o - pK$$

In defining σ we have seen that a given substituent affects ionisation equilibrium of benzoic acid. Now, if we introduce the same substituent in the same position in phenol or say aniline or any other compound with different reaction centre, what will be the effect in such a case? Would it be identical to the one obtained in benzoic acid or would it be more or less? The susceptibility of a given reaction centre relative to benzoic acid on introducing a substituent is measured by the reaction constant, ρ.

Reaction constant for benzoic aci ion has been considered to be eq to 1.

To obtain ρ for a given reaction series, equilibrium constant for a number of compounds, each having a reaction centre under consideration and different substituents with known σ values are measured. log K/K_0 values are plotted against σ and the slope of the line gives the corresponding ρ value. Fig. 2.5 shows Hammett plots for ionisation of 2-phenylacetic acid ($X\text{-}C_6H_4CH_2COOH$). Effect of substituents on reaction rates can be treated in a similar way.

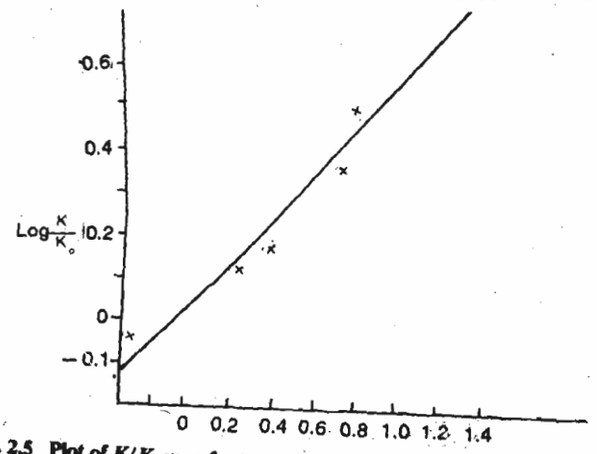


Fig. 2.5 Plot of K/K_0 vs. σ for ionisation of substituted phenylacetic acids

Let us see the utility of Hammett equation. Having known ρ and σ values for various reactions and substituents, we can use this data to predict the equilibrium constant or the rate of a reaction. For example, for ionisation of phenol, the reaction constant is 2.26 and for *p*-NO_2 group the σ value is 0.81. If the K_a of phenol is known (10^{-10}), that of *p*-nitrophenol can be calculated as,

$$\log \frac{K_{p\text{-}NO_2C_6H_4OH}}{K_{C_6H_5OH}} = \sigma \rho$$

substituting the values,

$$\log \frac{K_{p\text{-}NO_2C_6H_4OH}}{K_{C_6H_5OH}} = (2.26) \,.\, (0.81)$$

Taking antilog,

$$\frac{K_{p\text{-}NO_2C_6H_4OH}}{K_{C_6H_5OH}} = 67.70$$

$$\Rightarrow \quad \frac{K_{p\text{-}NO_2C_6H_4OH}}{10^{-10}}$$

$$= 67.70$$

$$K_{p\text{-}NO_2C_6H_4OH} = 67.70 \times 10^{-10}$$
$$= 6.77 \times 10^{-9}$$

The value shows that *p*-nitrophenol is ionised more than phenol, and is more acidic.

In other substituted aromatic compounds and in the reactions of alphatic series, Hammett equation does not hold. It is because of steric reasons. In such cases some other correlations like Taft equation have been developed. These are beyond the scope of this course.

SAQ 6

The pK_a values of benzoic acid and its *p*-bromo derivative are 4.19 and 3.93, respectively. Find the substituent constant for bromo group at *para* position.

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2.4 SUMMARY

Let us summarise the kinetic and thermodynamic aspects of reaction mechanism discussed in this unit.

According to thermodynamics, a spontaneous reaction is accompanied by a decrease in free energy, i.e., ΔG is negative. The sign of ΔG is determined by the sign of enthalpy change and the entropy change. A negative enthalpy change and positive entropy change are most favourable for the spontaneity of a reaction. Further, a reaction is said to be enthalpy or entropy driven depending on whether enthalpy or entropy contribution is more towards making ΔG negative.

Kinetics is concerned with time factor of a reaction. Rate of reaction measured by varying the concentration of various reactants is expressed in terms of a rate equation. Sum of the powe. of all the concentration terms involved in the experimentally determined rate equation is called

the order of the reaction. Order is an experimental characteristic for a reaction. Determination of rate equation for a reaction is important as it gives an idea about the number and nature of the species involved in the slowest or rate determining step of a many step reaction. Its knowledge helps in proposing a plausible mechanism for the reaction. According to transition state theory, on their way to products, the reaction molecules pass through a complex called the transition state. The complex has higher energy than any of the reactants or products. Energy of a system in the course of a reaction is represented by the potential energy diagram, which would depend on the nature of the reaction whether it is one, two or many step.

In case of competitive reactions, i.e., where more than one product can be obtained from a given reactant, the product formed under a given set of conditions may either be governed by its rate of fomation or its stability and is correspondingly known as kinetically or thermodynamically controlled product.

Besides kinetics and thermodynamics, other experiments like aiming at identification of all the products of a reaction, isolation of an intermediate or the stereochemistry of the products also provide important information regarding the mechanism. Experiments with heavy or radio isotopes are also helpful.

Relationship between the structure of a reactant and its activity can be expressed quantitatively in terms of linear free energy relationship. In the Hammett equation, the effect of introducing a substituent in benzoic acid is measured in terms of the change in pK_a and is known as substituent effect, σ. On the other hand, the susceptibility of a given reaction to such structural changes relative to the ionisation of benzoic acid is characterised by another constant known as reaction constant, ρ.

2.5 TERMINAL QUESTIONS

1) For the reaction $A + B \longrightarrow C$, the following two step mechanism has been proposed :

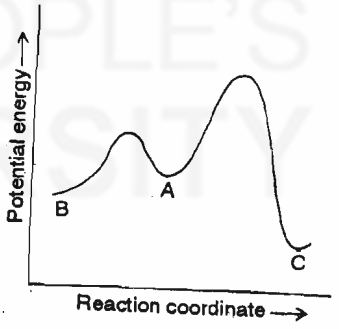
$$A + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} I$$

$$I + B \xrightarrow[\text{slow}]{k_2} C$$

i) derive the rate expression.
ii) what is the over all order of the reaction?

2) Draw schematic potential energy diagram for the reaction sequence $A \longrightarrow B \longrightarrow C \longrightarrow D$ if the thermodynamic stabilities of various species are in the order $A > D > B > C$ and step $C \longrightarrow D$ is rds.

3) A reactant A can give either B or C as the product. The potential energy diagram for the system is given in the margin. Which product would be obtained at (i) low temperature and (ii) high temperature? Also indicate the kind of control operative.



4) Photochemical monochlorination of α-d-methylbenzene ($C_6H_5CH_2D$) with Cl_2 at 353 K gave 0.0212 mol of DCl and 0.0868 mol of HCl. What is the value of the isotope effect, $\frac{K_H}{K_D}$ per H-atom.

5) The reaction constant for saponification of substituted ethyl benzoates is 2.61. If the rate constant for saponification of unsubstituted ethylbenzoate is $2 \times 10^{-4} mol^{-1} s^{-1}$, find the same for ethyl *p*-bromobenzoate : use data from SAQ 6 also.

2.6 Answers

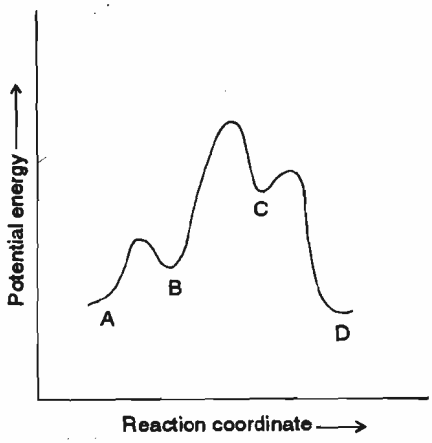
Self Assessment Questions

1) To predict spontaneity we have to calculate ΔG, we are given, $\Delta H = 5.2$ kJ mol^{-1}, $\Delta S = 150 \times 10^{-3}$ kJ K^{-1}mol^{-1} and $T = 400$ K.
$\Delta G = 5.2 - (400 \quad 150 \cdot 10^{-3})$kJ K^{-1} mol^{-1}.
$= 5.2 - 60.0 = -54.8$ kJ K^{-1} mol^{-1}.

(i) Since ΔG is negative, the reaction is spontaneous and (ii) Since $T\Delta S >>> \Delta H$; the reaction is entropy driven.

2) i) order = 1
ii) order = 3/2
iii) order = 2
The molecularity cannot be found out with the information given.

3)



4) B, it is the thermodynamically as well as kinetically controlled product at room temperature.

5) D_2O is preferred over $H_2{}^{18}O$ for studying kinetic isotope effect because the magnitude of the effect is much more pronounced in the former than the latter. The magnitude depends on the masses and m_D/m_H (2.0) is much larger than m_{18}/m_{16} (1.125).
O O

6) By definition $\sigma = \log \frac{K}{K_o}$

$\sigma_{p\text{-Br}} = \log \frac{K_{p\text{-Br}}}{K_o}$

$= pK_o - pK_{p\text{-Br}}$

We are given, $pK_o = 4.19$, $pK_{p\text{-Br}} = 3.93$
$= \sigma_{p\text{-Br}} = 4.19 - 3.93 = 0.26$

Terminal Questions

1) i) $\text{rate} = \frac{dc}{dt} = k_2[I]\,[B]$

from first step,

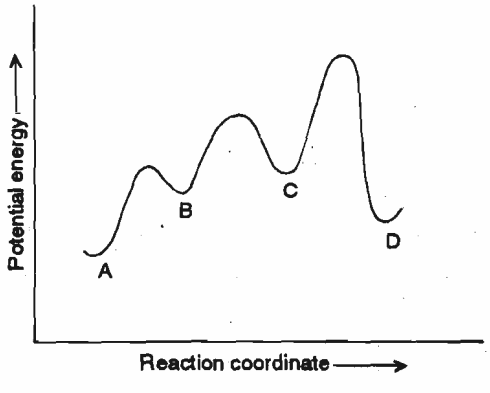
$\frac{[I]}{[A]\,[B]} = \frac{k_1}{k_{-1}} = k_{eq} \Longrightarrow I = \frac{k_1}{k_{-1}}\,[A]\,[B]$

Substituting in the rate equation,

$\text{rate} = \frac{dc}{dt} = \frac{k_1}{k_{-1}}\,[A]\,[B]^2$

ii) order = 3

2)



3) i) At low temperature, kinetically controlled product B is formed.

ii) At high temperature the thermodynamically controlled product C is obtained.

4) Amount of HCl obtained per H-atom $= \frac{0.0868}{2} = 0.0434$ (since either of the two H-atoms would give HCl). Amount of DCl obtained per D-atom $= 0.0212$. The rates (K_H and K_D) would be proportional to the amounts of HCl and DCl, respectively, and we have,

$$\frac{K_H}{K_D} = \frac{0.0434}{0.0212} = 2.05$$

5) From SAQ 6, the substituent constant for *p*-bromo group is 0.26.

According to Hammett equation $\log \frac{k}{k_o} = \rho\sigma$

Given, $\rho = 2.61$, $k_o = 2 \times 10^{-4}$ mol^{-1}s^{-1}

$\Rightarrow \log \frac{k}{k_o} = 2.61 \cdot 0.26 = 0.6786$

Taking antilog,

$\Rightarrow \log \frac{k}{k_o} = 4.77 \Rightarrow k = 4.77 \cdot 2 \cdot 10^{-4}$ mol^{-1} s^{-1}

$\Rightarrow 9.54 \cdot 10^{-4}$ mol^{-1} s^{-1}.

UNIT 3 ALIPHATIC NUCLEOPHILIC SUBSTITUTION

Structure

3.1 INTRODUCTION

In Unit 1 you learnt about different types of reactions and in Unit 2, you familiarised yourself with the general methods of determination of reaction mechanism. Now we would start with specific reaction types and study them in detail. In this unit we would discuss nucleophilic substitution in aliphatic compounds. We would study the currently accepted mechanisms of these reactions. We will also consider the relationship between structure and reactivity, the stereochemical course of these reactions and how a solvent can effect these reactions. In the next unit you will study the other type of substitution reactions, viz., the electrophilic substitution reactions which are common in aromatic compounds. Nucleophilic substitution is much less common in aromatic compounds.

Objectives

After studying this unit you should be able to :

- explain the S_N2 and S_N1 mechanisms of nucleophilic substitution reactions,
- explain the effect of the structure of an alkyl group, nucleophile, leaving group and the solvent on the reactivity in substitutions proceeding by S_N2 and S_N1 mechanisms,
- compare S_N2 and S_N1 mechanisms in all respects,
- explain the neighbouring group participation and formation of nonclassical carbocations, and
- explain the B_{AC} and A_{AC} mechanism of ester hydrolysis.

3.2 NUCLEOPHILIC SUBSTITUTION REACTIONS

You may recall the reaction given earlier in Unit 1.

$$\underset{\text{nucleophile}}{OH^-} + \underset{\text{substrate}}{CH_3CH_2Br} \longrightarrow \underset{\text{product}}{CH_3CH_2OH} + \underset{\text{leaving group}}{Br^-}$$

In the above reaction, nucleophile (hydroxide ion) attacks the saturated carbon substrate (bromoethane) giving ethanol and bromide ion as the products. You would notice that the reaction involves heterolysis of carbon-bromine bond such that the electron pair becomes associated with bromine which leaves as a bromide ion. A group like bromide ion which leaves the carbon substrate is called a **leaving group.**

The following examples of substitution at saturated carbon atom illustrate the various charge types of nucleophiles, substrates, products and leaving groups.

$$NH_3 + CH_3I \longrightarrow CH_3\overset{+}{N}H_3 + I^-$$

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

$$(CH_3)_3N + (CH_3)_3\overset{+}{S} \longrightarrow (CH_3)_4\overset{+}{N} + (CH_3)_2S$$

$$2\,H_2O + (CH_3)_3CCl \longrightarrow (CH_3)_3COH + Cl^- + H_3O^+$$

nucleophiles substrates products leaving groups

It would be clear from the above reactions that like nucleophiles, the leaving groups which are either negatively charged or neutral have unshared electron pair(s).

3.3 S_N2 REACTIONS

Let us take the case of the reaction of bromoethane with sodium hydroxide to give methanol,

$$CH_3Br + NaOH \longrightarrow CH_3OH + NaBr$$

How do we find out which pathway this reaction would take? Reaction kinetics can help us here. You would recall from the previous unit that the experimentally determined rate expression gives an idea of the number of species involved in the rate determining step of a multistep reaction.

Now the rate of the above reaction can be determined by following either the rate of disappearance of the base, OH^- or appearance of the bromide ion, Br^-. This rate is found to be proportional to the concentrations of both bromoethane and hydroxide ion. The experimental rate expression is,

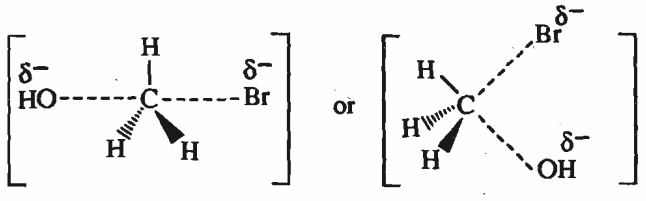
$$\text{rate} = k[CH_3Br]\,[OH^-]$$

This means that for this reaction both the reactants take part in the transition state. So it has to be a bimolecular mechanism. The mechanism is described by the symbol S_N2 meaning **substitution nucleophilic bimolecular**. The 2 in the symbol signifies bimolecularity of the reaction.

You would recall that the order of a reaction is an **experimental** quantity defining the relation of reaction rate with concentration of reactants, while molecularity refers to the number of species involved in the rate determining step of a particular **mechanism** being considered.

3.3.1 Mechanism of S_N2 Reactions

In S_N2 reactions, a transition state is supposed to be formed in which both the nucleophile and the substrate take part. This implies that S_N2 reaction is a concerted process which occurs in one step with only a single transition state, where carbon is partially bonded to both the incoming nucleophile and the departing/leaving group. Cleavage of the bond between carbon and the leaving group is accompanied by a synchronous formation of a bond between carbon and the nucleophile. In effect, the nucleophile "pushes off" the leaving group from its point of attachment to carbon. Therefore, S_N2 mechanism is sometimes referred to as a **direct displacement** process. Let us see how the transition state is formed taking hydrolysis of bromoethane as an example. Here, the nucleophile, OH^- may approach the substrate, CH_3Br, from the same or the opposite side of the leaving group and consequently the transition state may have either of the following two structures.



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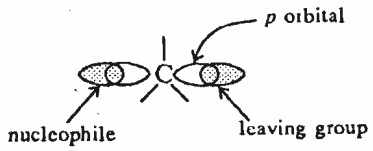
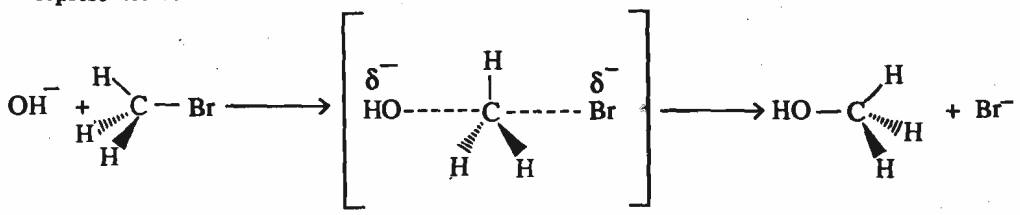
Apart from stereochemical evidence described later, the approach of the nucleophile from the side of the leaving group would be difficult due to electrostatic repulsion, both being negatively charged. The transition state would also be stabilised only when the nucleophile attacks the carbon from backside enabling a spread of negative charge. In the transition state, the hybridisation of the central carbon atom changes from sp^3 to sp^2. The weak bonds to the nucleophile and the leaving group can be considered being due to the overlap of their orbitals with the two lobes of a *p*-orbital. This is shown as :



It is, therefore, more plausible that in S_N2 mechanism, the attack of the nucleophile is from the side opposite to that of the leaving group. Therefore, structure I would represent the structure of transition state. The S_N2 mechanism for the hydrolysis of bromomethane may be represented as :



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The potential energy diagram of the above reaction is given in Fig. 3.1.

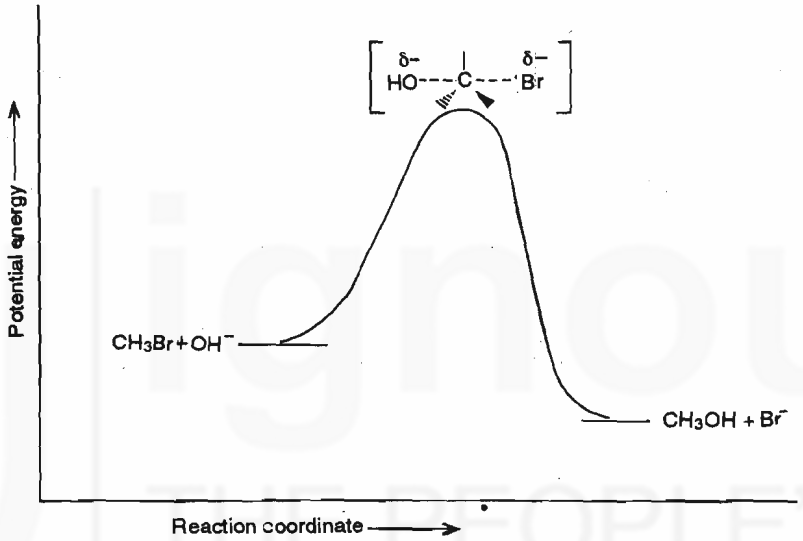
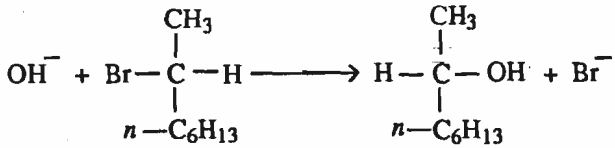


Fig. 3.1 : Potential energy diagram for the hydrolysis of bromomethane by S_N2 mechanism

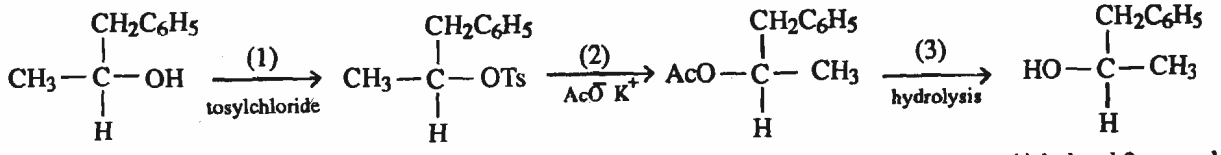
Stereochemical evidence

The stereochemistry of the reaction proceeding through a S_N2 mechanism also supports the backside attack of the nucleophile given above. The same side attack and displacement of leaving group would not alter the configuration of the substrate whereas the opposite side attack would lead to an inversion of configuration. Of course, this cannot be demonstrated in the case of the bromomethane-hydroxide reaction. However, if an optically active alkyl halide is used, an inversion of configuration can be demonstrated. For example, hydrolysis of optically active 2-bromooctane with sodium hydroxide gives optically active 2-octanol with inverted configuration,



R (-)-2-bromooctane — *S* (+) -2-octanol (major product)

An example which shows when exactly the inversion occurs in a sequence of reactions is the conversion of (+)-1-phenyl-2-propanol to its enantiomer by the following route.



(+)-1-phenyl-2-propanol — (-)-1-phenyl-2-propanol

As is seen from the sign of rotation of the final product, there is inversion of configuration at some step, but where? This can happen only in the step involving breaking of the C—O bond. Since, steps (1) and (3) do not involve breaking of the C—O bond, the configuration can not change here. This, therefore, happens only during step (2) where the C—O bond breaks. For a S_N2 reaction it would mean the step where carbon-leaving group bond breaks.

Thus, we see that the requirement for back-side attack of the entering nucleophile from a direction 180° away from the departing group causes the stereochemistry of the substrate to invert much like an umbrella turning inside out in the wind (Fig. 3.2). This inversion is called **Walden inversion** after Paul Walden who first reported it in 1896. Walden cycle interconverting (+)—and (−)—malic acids is given in the margin.

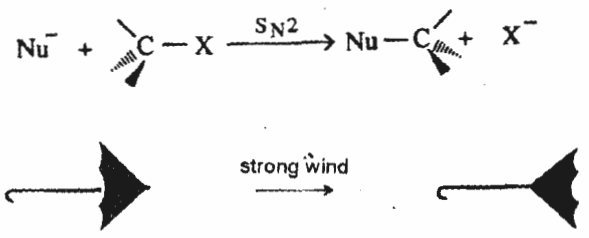
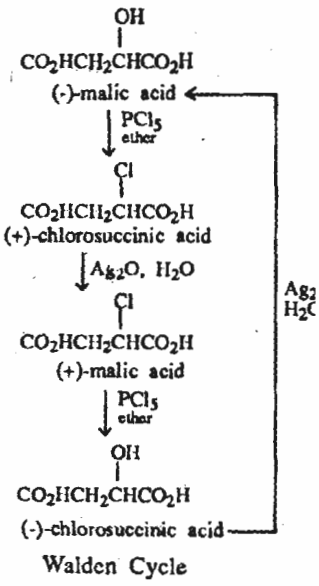
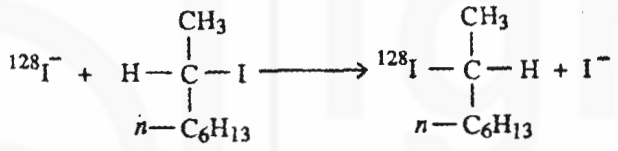


Fig. 3.2 : Inversion of configuration during S_N2 reaction



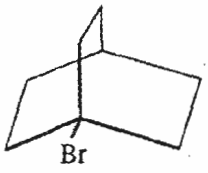
Another example supporting inversion in S_N2 reactions is the ^{128}I catalysed racemisation of 2-iodooctane,



In this case, it is observed that the rate of racemisation is twice the rate of exchange of radioactive iodine. Substitution (exchange) in one molecule of the substrate results in its inversion, the product being an enantiomer of the starting compound. This, therefore would result in racemisation of two molecules. Remember racemic product consists of a pair of enantiomeric molecule denoted by *dl* or ±.

SAQ 1

The following alkyl bromide does not undergo reaction with a nucleophile in S_N2 conditions. Can you suggest a reason for its total lack of reactivity?



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3.3.2 Reactivity of S_N2 Reactions

The rates of reactions proceeding by S_N2 mechanism are affected by the,

- nature of substrate
- nature of the nucleophile
- nature of the leaving group and
- nature of the solvent

Nature of substrate

Relative reactivity of a molecule in a S_N2 displacement depends on its structure. Table 3.1 gives the "average" relative rates of various alkyl substrate in S_N2 reactions.

Table 3.1 : Relative rates of some alkyl substrates in S_N2 reactions

Alkyl group	Relative rate
Methyl CH_3-	30
Ethyl CH_3CH_2-	1
2-Methylethyl (Isopropyl) $(CH_3)_2CH$-	0.025
1, 1-Dimethylethyl (*tert*-Butyl) $(CH_3)_3C$-	~ 0
Phenylmethyl (Benzyl)	120

Among the primary, secondary and tertiary halides, a typical sequence for S_N2 reactivity is thus,

$$CH_3X > C_2H_5X > (CH_3)_2CHX > (CH_3)_3CX$$

or

p-halide > *sec*-halide > *tert*-halide

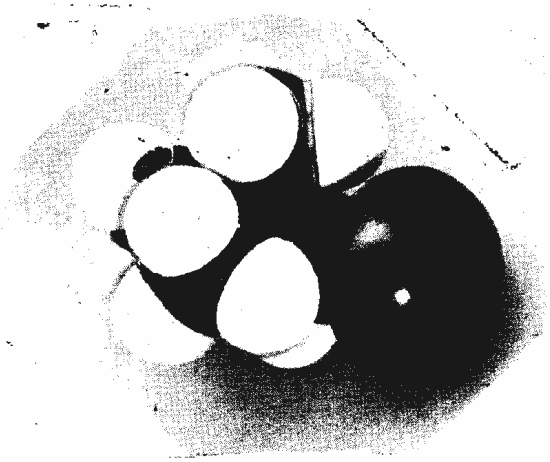
Similarly, among simple primary halides the reactivity is,

$$CH_3X > C_2H_5X > CH_3CH_2CH_2X > CH_3CH_2CH_2CH_2X$$

Primary halides which have an unsaturated group attached to the carbon react much faster than bromomethane. Thus,

$$C_6H_5CH_2Br > CH_2{=}CH{-}CH_2Br > CH_3Br$$

Two distinct effects appear to be responsible for the wide variations in the foregoing table. Electronic effects apparently are responsible, but steric effects also have a major role. As hydrogen atoms of methyl group are gradually replaced by bulkier alkyl groups, the nucleophile finds it more and more difficult to push in among the three carbon substituents in order to form the transition state. If the substituents are bulky, the transition state will be heavily crowded and the nonbonded interactions between various substituents would raise its energy and make it unstable. The steric effect is also noticed, when the carbon next to the reaction site is highly branched, there is a severe hinderance to the approach of the attacking group. This effect is responsbile for the very low reactivity of 1-bromo-2, 2-dimethylpropane (neopentyl) substrate inspite of its being primary in nature. The back-sided attack of the nucleophile is hindered by three β-methyl groups.



1-Bromo-2, 2-dimethylpropane

SAQ 2

Order each set of compounds with respect to S_N2 reactivity. Give reasons for your choice.

a) $CH_3CH_2CH_2Cl$, $CH_3CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3$, $CH_2{=}CHCH_2Cl$

.....

.....

b) $(CH_3)_2CHCH_2Br$, $(CH_3)_2CHBr$, $(CH_3)_3CCH_2Br$

.....

.....

.....

Nature of the nucleophile

We have seen that the rate of a S_N2 reaction depends upon the concentration of both, the substrate and the nucleophile. Therefore, nucleophilicity of the reagent is also important in S_N2 reactions. The order of nucleophilicity in some oxygen nucleophiles is,
$C_2H_5O^- > OH^- > C_6H_5O^- > CH_3COO^- > H_2O$ — and this you would recall is the order of decreasing basicity.

Nucleophiles with atoms of the same period in the periodic table show a decrease in nucleophilicities with an increase in electronegativity. For example, oxygen is less electronegative than fluorine and holds the electrons around it less firmly than flourine does. Therefore, in hydroxide ion it is better able to donate its electrons and consequently is more nucleophilic than F^- ion. The order of nucleophilicity is as follows :
$OH^- > F^-$
$NH_3 > H_2O > HF$
$R_3C^- > R_2N^- > RO^- > F^-$

A nucleophile with a charge is more powerful than its conjugate acid, thus,
$OH^- > H_2O$
$RO^- > ROH$
$NH_2^- > NH_3$

This is because in a neutral molecule, the electrons are held tightly by the atom, whereas the electrons on an atom bearing a negative charge are more loosely held, and therefore, can be easily donated to a positive centre.

In larger atoms, the outer electrons are less tightly bound to the nucleus and hence are more polarisable. This would lead to a certain amount of distortion of the outer electrons, and consequently equip them better to attack the carbon atom of the substrate. Thus, nucleophilicity is dependent on polarisability. For example, the increasing order of nucleophilicity in the following is as given :
$RS^- > RO^-$
$R_3P > R_3N$
$I^- > Br^- > Cl^- > F^-$

Nucleophilicity depends on the type of solvent used in a reaction. A solvent that can solvate and thus stabilise an anion reduces its nucleophilicity. Thus, chloride ion is a far better nucleophile in dimethyl formamide (DMF) or dimethyl sulphoxide (DMSO) where it is not solvated than in ethanol or water (protic solvents) in which it is solvated due to hydrogen bonding.

$CH_3CH_2OH\cdots Cl^-\cdots HOCH_2CH_3$

Ethanol can solvate a negative ion by H-bonding

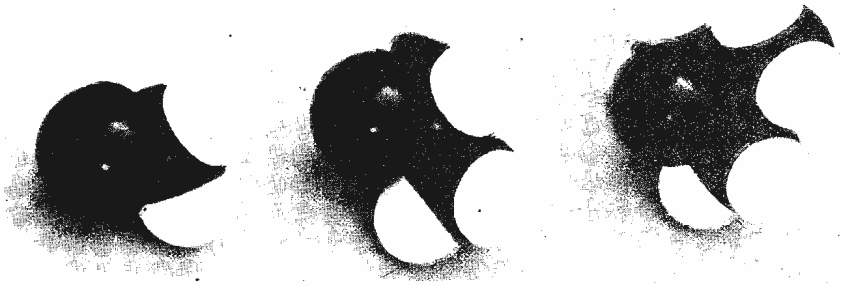
$HCN(CH_3)_2$ (DMF) $\quad CH_3SCH_3$ (DMSO)

No H capable of hydrogen bonding for solvation

As you can see, H-bonding will reduce the charge density on Cl^-, thus reducing its nucleophilicity.

The reactivity of uncharged nucleophiles is not much affected by the sovent.

Nucleophilicity also depends upon the size of a reagent. It is easier for a small nucleophile to attack the carbon atom in nucleophilic substitution. For example, methoxide anion is a small species which can easily approach a carbon atom, in contrast 1, 1- dimethyl ethoxide (*tert*-butoxide) is very bulky and consequently a poor nucleophile.



methoxide 2-methylethoxide 1, 1-dimethylethoxide

SAQ 3

Which of the following pairs is more nucleophilic and why?

$(CH_3)_2N^-$ or $(CH_3)_2NH$, $(CH_3)_3B$ or $(CH_3)_3N$, H_2O or H_2S, $(CH_3)_3P$ or $(CH_3)_3N$

.....

.....

.....

Water may be a leaving group if a hydroxyl group is protonated by an acid before displacement, e.g.,

$$CH_3CH_2OH + H_2SO_4 \rightleftharpoons CH_3CH_2\overset{+}{O}H_2 + HSO_4^-$$

$$CH_3CH_2\ddot{O}H + CH_3CH_2{-}\overset{+}{O}H_2 \longrightarrow CH_3CH_2OCH_2CH_3 + H_3O^+$$

Nature of the leaving group

The rate of a reaction is very often dependent on the type of leaving group. We would expect that weak bases would be good leaving groups. Good leaving groups are conjugate bases of acids with pK_a value below 3. Strong bases, such as OH^-, are never good leaving groups in substitution reactions. Other strong bases which are poor leaving groups are H^-, RO^-, H_2N^-, R_2N^-.

The order of reactivity, I^-, Br^-, Cl^-, F^- parallels the carbon-halogen bond strengths. The toluene-*p*-sulphonate group (tosylate, OTs) is a good leaving group and undergoes nucleophilic substitution reactions easily, for example,

$$K^+ CN^- + RCH_2{-}OSO_2{-}C_6H_4{-}CH_3 \longrightarrow RCH_2CN + K^+ {}^-OSO_2{-}C_6H_4{-}CH_3$$

Another good leaving group is *p*-bromobenzenesulphonate (brosylate, OBs),

$$-OSO_2{-}C_6H_4{-}Br$$

SAQ 4

Arrange $CH_3CH_2CH_2OCH_3$, $CH_3CH_2CH_2OTs$ and $CH_3CH_2CH_2Br$ in increasing order of S_N2 reactivity and justify your answer.

.....

.....

.....

Nature of the solvent

Solvent plays a dominant role in nucleophilic substitution reactions in two ways. One is **polarity** of the solvent expressed by its dielectric constant, $\in$ (Table 3.2). Dieletric constant is a measure of the ability of a solvent to disperse the force of attraction between oppositely charged particles. Polar solvents like water have high dielectric constants and a great ability to stabilise charge separated systems. Nonpolar solvents like pentane have low dielectric constants and limited ability to disperse the force of attraction. The other solvent effect is **solvation** in which both anions and cations are stabilised by the surrounding sheath of weakly bonded solvent molecules. Solvents are classified as; protic e.g., water, alcohols, carboxyllic acids and ammonia which have mobile protons such as those bonded to oxygen, nitrogen or sulphur capable of forming hydrogen bonds, and aprotic, e.g., dimethyl sulphoxide (DMSO), N, N —dimethylformamide (DMF), etc. The latter exhibit large effects on the rate of S_N2 reactions. Since the ability of DMSO and DMF to participate in hydrogen bonding is limited, both are poor at solvating anions.

Table 3.2 : **Dielectric constants of some common solvents**

Solvent	Dielectric constant (Debye) at 298 K	
H_2O	81	protic
HCO_2H	59	
CH_3OH	33	
CH_3CH_2OH	24	
$(CH_3)_2CHOH$	18	
$(CH_3)_3COH$	11	
CH_3CO_2H	6	
$(CH_3)_2SO$	45	aprotic
$HCON(CH_3)_2$	37	

An anion which is not solvated is a much more powerful nucleophile than a highly solvated one. Therefore, S_N2 reactions take place much faster in polar, aprotic solvents than in protic ones. For example, the reaction,

$$\underset{\text{halohexane}}{CH_3(CH_2)_4CH_2X} + NaCN \longrightarrow \underset{\text{cyanohexane}}{CH_3(CH_2)_4CH_2CN} + NaX$$

proceeds with 71% yield of cyanohexane in 20 hrs in aqueous methanol. Changing the solvent to DMSO brings about an increase in the reaction rate where the product yield is 91% and the reaction is completed in only 20 minutes.

In general, the effect of solvent polarity on S_N2 reactions can be summarised as follows :

i) If the substrate is neutral and the nucleophile is charged, dispersal of charge occurs in the transition state. Less polar solvents favour the reaction.

$$R{-}L + Nu^- \longrightarrow R{-}Nu + L^-$$
$$CH_3Cl + OH^- \longrightarrow [HO^{\delta-}\cdots CH_3\cdots X^{\delta-}] \longrightarrow CH_3OH + X^-$$

ii) When both the substrate and reactant are neutral, charge is formed in the transition state. A more polar solvent favours the reaction.

$$Nu + R{-}L \longrightarrow R{-}Nu^+ + L^-$$
$$R{-}I + N(CH_3)_3 \longrightarrow [(CH_3)_3N^{\delta+}\cdots R\cdots I^{\delta-}] \longrightarrow RN^+(CH_3)_3 + I^-$$

iii) When both the nucleophile and substrate possess formal charges, charge gets destroyed. A less polar solvent is favourable in such cases.

$$Nu^- + R{-}L^+ \longrightarrow R{-}Nu + L$$
$$OH^- + RN^+(CH_3)_3 \longrightarrow [HO\cdots R\cdots N(CH_3)_3] \longrightarrow ROH + N(CH_3)_3$$

SAQ 5

Complete the following reaction and suggest an appropriate solvent for it.

$$(CH_3)_2CHBr + CN^- \longrightarrow$$

.....

.....

.....

3.4 S_N1 REACTIONS

We saw in the previous section that *tert*-alkyl halides either have a very slow rate of reaction or do not undergo S_N2 reactions. Then the question is how do we get substitution products of such halides? The answer is that these halides undergo reaction by a different mechanism, viz., S_N1 (**substitution nucleophilic unimolecular**) mechanism.

3.4.1 Mechanism of S_N1 Reactions

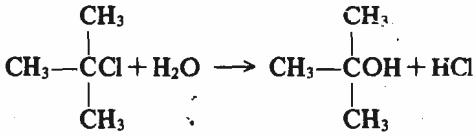
In S_N1 mechanism substitution occurs in two steps. First, the leaving group departs as a result of heterolytic cleavage leaving a carbocation, and then the nucleophile combines with the carbocation to give the product. Carbocations, being unstable and, therefore, very reactive species, react rapidly with the nucleophile. Thus, the first step is slow and the rate determining step. Accordingly, the kinetics should be first order, the rate depending on the concentration of the substrate but not on that of the nucleophile. The two steps of S_N1 mechanism can be shown as follows,

$$RX \overset{\text{slow}}{\rightleftharpoons} R^+ + X^-$$

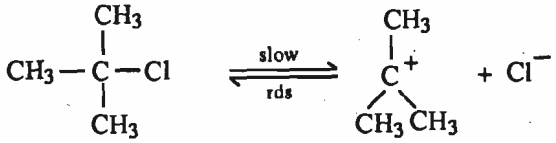
$$R^+ + Y^- \xrightarrow{\text{fast}} RY$$

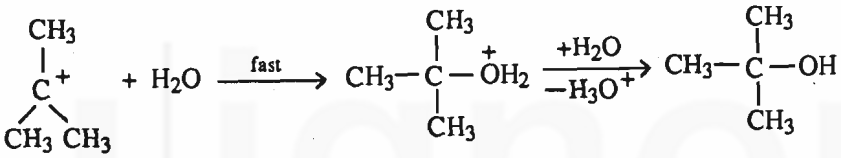
$$\text{Rate} = k[RX]$$

Concentration of the nucleophile has little effect on the overall rate of S_N1 reaction. For example, when hydrolysis of 2-methyl-2-chloropropane (*tert* butyl chloride) occurs in the presence of water, a very weak base,



the rate of the reaction depends only on the concentration of the alkyl chloride. Concentration of water has no effect. Since water is also used as solvent in the reaction, this type of substitution reaction is sometimes called a **solvolysis reaction**. The mechanism of the reaction is given below :





The potential energy diagram for a S_N1 reaction is given in Fig. 3.3. Step 1 has high energy of activation and is, therefore, the slow step. The carbocation is an intermediate in this reaction. Here we must appreciate the fact that an intermediate has a finite lifetime, whereas a transition state does not. Also potential energy of the transition state, where bond breaking and bond making actually occur, is a high point on the potential energy curve, e.g., I and II in Fig. 3.3. As shown in this figure, an intermediate has lower energy than the transition state. However, the intermediate has higher energy than the final products.

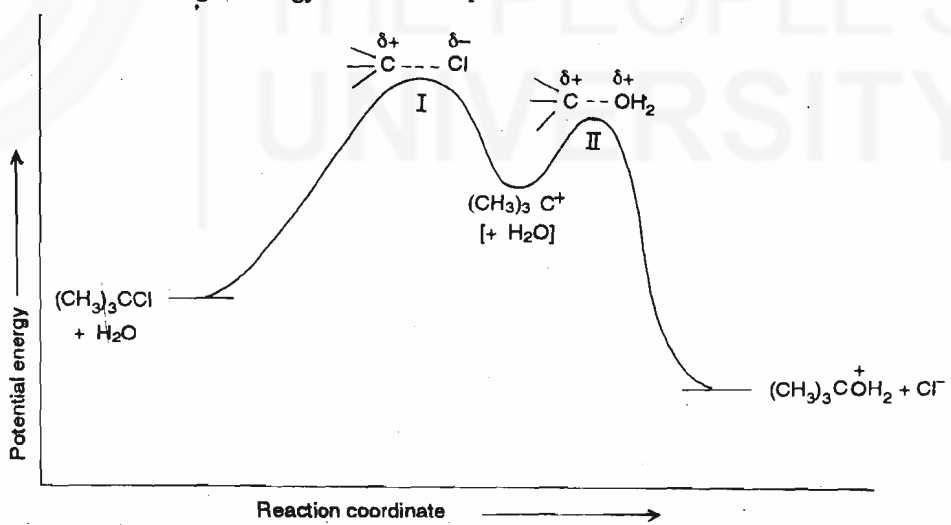


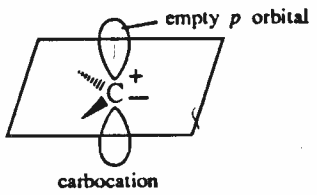
Fig. 3.3 : Potential energy diagram for solvation of *tert* butyl chloride by S_N1 mechanism

Perhaps the most convincing evidence for a S_N1 mechanism in a solvolysis reaction is the stereochemistry of the reaction. The experimental results obtained in S_N1 reactions are considerably different from those obtained in S_N2 reactions. As we have seen, S_N2 reactions proceed with inversion of configuration where as most S_N1 reactions lead to extensive racemisation at the reaction centre.

Stereochemistry of S_N1 reaction

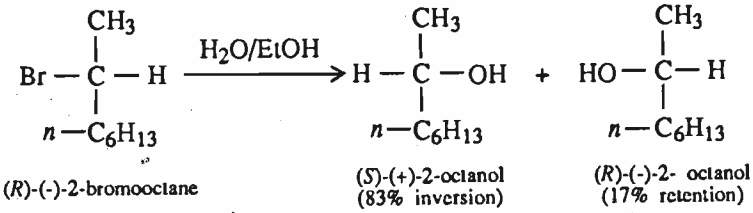
As said before, in a S_N1 reaction, the product is formed from a carbocation intermediate. The stereochemistry of the product would, therefore, depend on the stereochemistry of the

intermediate. Theory and experimental evidence both suggest that carbocations are planar. The carbon atom carrying the charge in sp^2 hybridised, so that the groups attached to it are in a plane and the bond angles between them are 120°. The cation possesses a plane of symmetry and attack by the solvent or nucleophilic reagent should occur with equal probability on either side of the plane. Regardless of whether the starting material is the (+) or the (−) enantiomer, the product should be a 50 : 50 mixture of (+) and (−) isomers, i.e., racemic.



carbocation

In practice, however, it is found that complete racemisation is not there and that inversion almost always exceeds retention. For example, the hydrolysis of 2-bromooctane forms the product 2-octanol with 66% net inversion and 34% racemisation of configuration which is equivalent to 83% inversion and 17% retention.



(*R*)-(-)-2-bromooctane (*S*)-(+)-2-octanol (83% inversion) (*R*)-(-)-2- octanol (17% retention)

There is reason for this deviation from the theoretical predictions. This happens when the nucleophile attacks the newly formed carbocation before the leaving group has completely left the substrate carbon. In such a situation, the leaving group would, to a certain extent, shield the carbocation from its side while the nucleophile captures the carbocation from the side opposite to the leaving group. As a result, more of the product with inverted configuration would be formed than that with retention of configuration.

This explanation was first proposed by Winstein. According to him, intermediates in S_N1 reactions are actually ion pairs. In these cases, the covalent carbon-halogen bond is no doubt broken, but the two fragments remain closely associated as R^+X^-. In some instances the ion pairs seem to react directly with the solvent to give the final product; in others they seem to dissociate to free ions first. Ion pairs are most often encountered in acetic acid and similar solvents that are sufficiently polar for promotion of ionisation but not polar enough for solvating free ions.

3.4.2 Reactivity in S_N1 reactions

We saw in the previous section that an S_N2 reaction is strongly influenced by variables such as the substrate, nucleophile, leaving group and the solvent. similar observations have been made for S_N1 reaction. Let us study them one by one.

Nature of the Substrate

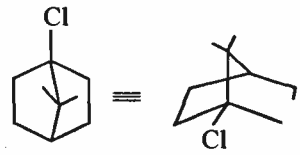
The rate of a reaction proceeding by S_N1 mechanism is fast when energy of activation is low i.e., the intermediate carbocation is stable. You may recall (Unit 5, Organic Chemistry course) that the carbocation is stabilised by inductive effect, resonance effect and hyperconjugation. Electron-donating effect of alkyl groups, i.e., their inductive effect (+ I) has been used to explain the relative stabilities of carbocation. The order of stability of carbocation is tertiary > secondary > primary. Hyperconjugation has also been used to explain the above order.

Carbocations are also stabilised by resonance by phenyl and allyl groups. The order of stability of cations as a result of resonance effect is as follows :

$$(C_6H_5)_3C^+ > (C_6H_5)_2\overset{+}{C}H > C_6H_5\overset{+}{C}H_2 \cong CH_2 = CH—\overset{+}{C}H_2$$

triphenyl methyl — benzhydryl — benzyl — allyl

Thus, the electronic effects; inductive and resonance play a major role in S_N1 mechanism whereas the steric effects are more important in S_N2 mechanism. However, sometimes the steric effects become important in S_N1 reaction also. For example, apocamphyl chloride does not undergo solvolysis readily. This is due to the failure to attain a planar structure of the carbocation due to the rigid bicyclic structure of the molecule. S_N2 reaction is also not possible as the nucleophile cannot attack from the backside which is protected by the bicyclic ring.



apocamphyl chloride

Effect of the solvent

S_N1 reaction is favoured by highly polar, protic solvents. Water is the most effective solvent for promoting ionisation, but many organic compounds are only very slightly soluble in it. Mixed solvents, such as methanol-water, acetone-water are more effective as their proportion in water is increased. Pure formic acid is also an effective ionising solvent. Non-hydroxylic solvents are almost all poor at promoting ionisation.

Nature of the nucleophile

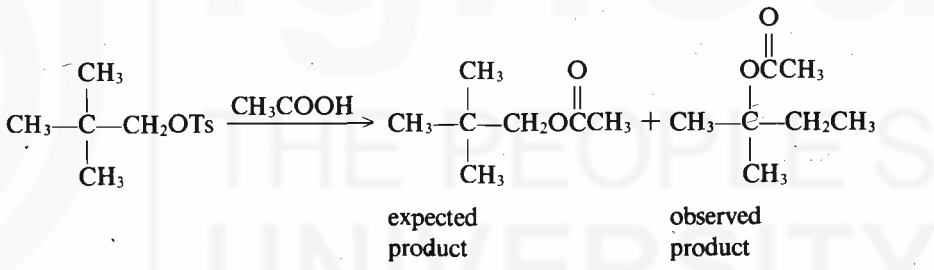
Since in an S_N1 reaction, the nucleophile attacks the carbocation after the rate determining step, it cannot affect the rate of the reaction. The second step will be fast for all nucleophiles. However, if the intermediate carbocation has a choice of several nucleophiles, then the nature of the product is determined by their relative nucleophilicities. The same general order of reactivity is found here as was discussed for S_N2 reactions.

Effects of the leaving group

Effect of the leaving group is relatively simple as in S_N2 reactions. The more easily the bond to the leaving group is broken, the more reactive the substance will be.

We have learned that an increase in solvent polarity increases the rate for most S_N1 reactions and lowers the rate for most S_N2 reactions. Addition of salts has a similar effect (salt effect). Addition of leaving group ion decreases the rate of the first step in S_N1 reaction which is reversible (common-ion effect). Sometimes the S_N1 rates are accelerated in the presence of metal ions, e.g., Ag^+, Hg_2^{++}. These help to remove the leaving group.

In some reactions proceeding by S_N1 mechanism, rearrangement occurs. An example has been given earlier in Unit 1 in the acetolysis of neopentyl tosylate



expected product

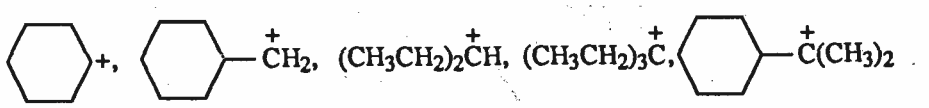
observed product

We have known that usually a primary halide, e.g., CH_3Br undergoes hydrolysis in a S_N2 fashion and a tertiary halide, e.g., $(CH_3)_3CCl$ generally follows a S_N1 mechanism. You would recall that the mechanism is not only dependent on the nature of the substrate but also on other conditions like the nucleophile, leaving group and the solvent. It is quite possible for a reaction to go by S_N1 mechanism in one solvent and by S_N2 in another. What would be the mechanism in the case of secondary halides? Some reactions proceed both by S_N1 and S_N2 mechanisms. These are borderline cases. Either both operate simultaneously or in some cases a common mechanism—an in between type can be given. These complications will be dealt with in an advanced course.

In many substitution reactions, the nucleophile can also act as a base. In these cases, elimination becomes a competitive reaction along with substitution. This aspect will be covered in Unit 7 of this course.

SAQ 6

a) List the following carbocations in increasing order of stability. Justify your answer.



b) Which in the following pairs would undergo a faster S_N1 reaction and why?

i) $(CH_3)_3Cl$ or $(CH_3CH_2)_2CHI$

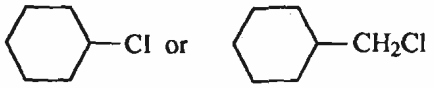
.....

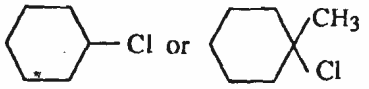
ii) $(CH_3)_2CHI$ or $(CH_3)_2CHCl$

.....

iii) CH_3Cl or CH_3OTs

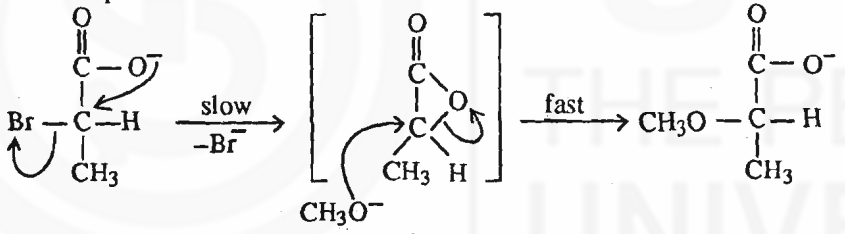
.....

iv) 

v) 

3.5 NEIGHBOURING GROUP PARTICIPATION

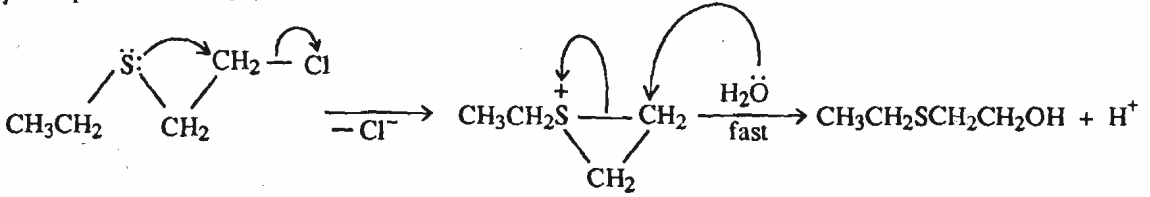
You know that the reactions of organic molecules are related to their structures; inductive, conjugative and steric effects play important roles to make molecules more reactive or otherwise. You may refresh your memory by reading up Unit 5 of Organic Chemistry Course. In such cases a group closer to the reaction site affects the reactivity without directly participating in the reaction. In this section, we will study some reactions in which a group lying near the reaction site; a neighbouring group, becomes bonded (either fully or partially) to the reaction centre in the substrate for sometime during a reaction. For example, in the substitution of bromine in (L) - 2 - bromopropionate by the methoxy group; a retention in configuration is observed, both the substrate and the product have the same configuration. This reaction takes place in dilute sodium methoxide in methanol.



(L)-2-bromopropionate — α-lactone (not isolated) — (L)-2-methoxypropionate

The above result cannot be explained by either a S_N2 mechanism (inversion in configuration) or a S_N1 mechanism (partial racemisation). We have to think in terms of a neighbouring group like carboxylate group participating in the reaction. In the first step (slow), the nucleophilic carboxylate ion displaces bromine attacking the asymmetric carbon atom from the backside leading to inversion. The methoxide ion attacks the carbon in the intermediate from the side opposite to the three-membered ring in the second step leading to a second inversion which nullifies the first. The net result is a retention of configuration of the substrate in the product. Thus, the observed stereochemistry supports the participation of a neighbouring group in this reaction.

Sometimes an enhanced rate of a reaction also called as anchimeric assistance, provides an evidence for the neighbouring group participation. It has been observed that 2-chloroethyl ethylsulphide is hydrolysed in aqueous acetone about 10,000 times faster than the corresponding ether. This rate difference cannot be explained by either electronic (inductive and conjugative) or steric effect. The larger sulphur atom provides an effective neighbouring participation as compared to an oxygen in the corresponding ether.

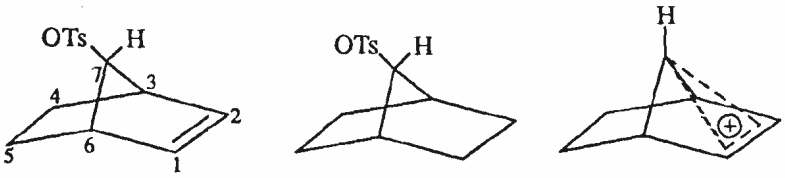


sulphonium ion (a strained ring)

Besides the carboxylate anion and sulphide given above, other groups such as alkoxy (ÖR), amino or substituted amino (NH_2, NHR, NR_2, NHCOR), halogens (I, Br and Cl), ester (COOR), aryl (C_6H_5 and C_6H_4R), etc. act as neighbouring groups in many reactions.

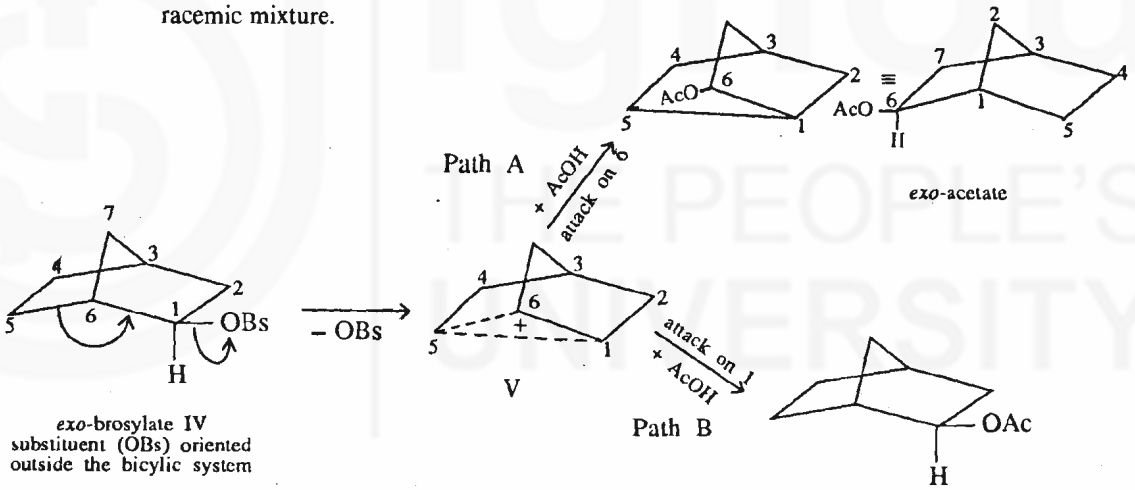
Sometimes a neighbouring π or a σ bond may also participate in a reaction. Stereochemical evidence or rate enhancement (anchimeric assistance) supports the participation of a neighbouring group or bond. Following are some selected examples from bicyclic system.

It was found that the rate of acetolysis of tosylate-I is 10^{11} times faster than that of tosylate-II and proceeds with retention of configuration. As you can see the only difference between the two being the $>C=C<$ bond at 1, 2 position. This double bond is situated on the backside of the leaving tosylate and can give anchimeric assistance. Evidence is available in the actual (though fleeting) existence of nonclassical intermediate-III which confirms the assistance of C = C group in departure of OTs group. Bridged cations containing pentavalent carbon with delocalised bonding electrons are known as **nonclassical ions,** e.g., III below :

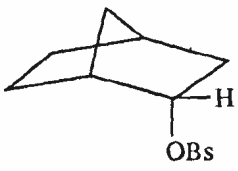


tosylate-I tosylate-II nonclassical intermediate-III

It is known that optically active *exo* - 2 - norbornyl brosylate undergoes acetolysis about 350 times faster than the corresponding *endo* - isomer. A racemic mixture of *exo* -2 - norbornyl acetate is the product. Anchimeric assistance by the $C_5 - C_6$ σ-bond (which is on the backside to the leaving group, brosylate) explains the faster rate of IV as compared to VI. Intervention of a non classical ion V as an intermediate accounts for the formation of a racemic mixture.



exo-brosylate IV substituent (OBs) oriented outside the bicylic system



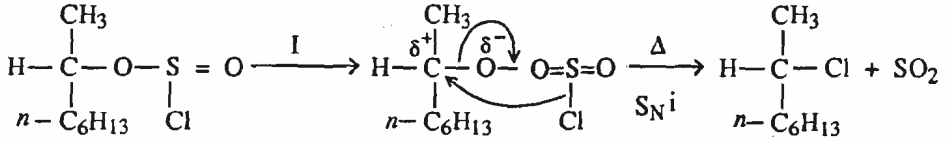
endo-brosylate VI substituent oriented inside the bicyclic system

3.6 S_Ni REACTIONS

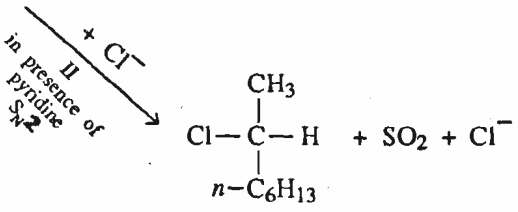
So far we have discussed substitution reactions which involve two reactants — a substrate and a nucleophile. In some substitution reactions, the nucleophile is a part of the substrate. Such intramolecular substitutions are more rapid than the corresponding intermolecular reactions.

These reactions are said to proceed by S_Ni mechanism meaning **substitution nucleophilic internal,** since both the nucleophile and the leaving group are part of a single molecule.

Stereochemistry of these reactions shows retention of configuration at the asymmetric carbon atom. The first step is like that an S_N1 reaction, i.e., formation of an ion pair. In the second step, a part of the leaving group attacks only from the front side leading to retention of configuration. This mechanism can be shown in case of (D -)- 2 - octylchlorosulphite as follows :



(D)-2-octylchlorosulphite ion-pair (D)-2-chlorooctane



(L)-2-chlorooctane

As you can see, in reaction I, chlorine from chlorosulphite attacks the asymmetric carbon from the same side (internal return) leading to a retention of configuration. If, however, an external chloride ion is available in the presence of an amine like pyridine (reaction II), a normal S_N2 reaction occurs with inversion of configuration.

SAQ 7

You know that substitution reaction can also occur intramolecularly. What product would you expect from the treatment of 4 - bromo - 1 - butanol with a base. Write the various steps involved.

.....

.....

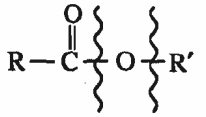
.....

3.7 HYDROLYSIS OF ESTERS AND ESTERIFICATION

The mechanisms of nucleophilic substitution at a saturated carbon substrate have been given above. Nucleophiles readily attack the electron-deficient carbon atom in compounds containing carbonyl function. These reactions will be described in detail in Unit 6 of this course. In this section, some mechanisms of the hydrolysis of esters and esterification of carboxylic acids are given.

3.7.1. Hydrolysis of Esters

Hydrolysis of esters is catalysed by either bases or acids. It can be either unimolecular or bimolecular. It can involve either acyl-oxygen or alkyl-oxygen cleavage. Thus several mechanisms of hydrolysis of esters are possible. We will discuss two of the most common ones.

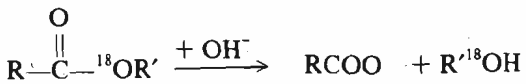


acyl-oxygen cleavage alkyl-oxygen cleavage

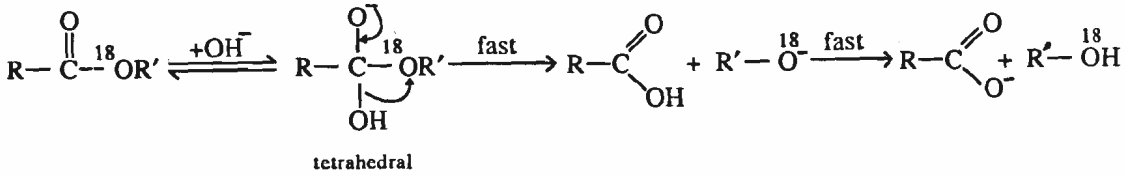
The alkaline hydrolysis of esters has been studied in great detail. This reaction has been shown to be bimolecular. The rate is dependent on the concentration of ester as well as of hydroxide ion.

$$\text{rate} = k\,[\text{ester}]\,[OH^-]$$

It is believed to occur via a tetrahedral intermediate (sp^2 hybridised carboxyl carbon is trigonal). Using labelled esters it has been shown that the acyl-oxygen cleavage takes place in the hydrolysis of many esters. The labelled oxygen is present in the alcohol part and not in carboxylate anion.



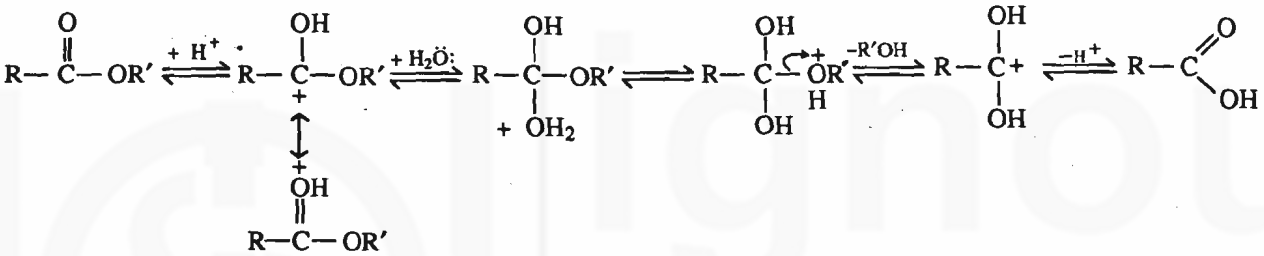
The accepted mechanism is :



tetrahedral

The above mechanism is called $B_{AC}2$, base-catalysed acyl-oxygen cleavage, bimolecular. All the steps in this case are not reversible. Thus esterification of carboxylic acids in basic medium is not observed. The acid is converted to carboxylate anion in this medium. The anion, being negatively charged is not attacked by nucleophiles (either $R'O^-$ or $R'OH$).

In acid medium, initial protonation of the carboxyl oxygen followed by attack of water (nucleophile), proton exchange, loss of alcohol (acyl-oxygen cleavage), and subsequent deprotonation gives the carboxylic acid. This is called $A_{AC}2$ mechanism; acid-catalysed, **acyl-oxygen cleavage, bimolecular.** In this mechanism each step is reversible. Hence esterification is carried out in the presence of an acid.



The common acid catalysts used in esterification of carboxylic acids with alcohols are either sulphuric acid or *p*-toluene sulphonic acid. Esterification is reverse of hydrolysis. The yield of ester can be increased by a shift of equilibria to the left. This can be achieved by,

i) using excess of alcohol,
ii) removal of ester by distillation (being more volatile), and
iii) removal of water by a dehydrating agent or molecular sieve.

SAQ 8

Write T for true and F for false in front of the statements given below :

a) acyl-oxygen fission is more common in ester hydrolysis.

b) esters undergo hydrolysis only by an S_N2 mechanism.

c) acid catalysed hydrolysis of esters follows a reversible pattern.

d) cleavage of acyl-oxygen bond is the rate determining step in alkaline ester hydrolysis.

e) esterification of carboxylic acids proceeds rapidly in basic medium.

3.8 SUMMARY

Now we will summarise what all has been discussed about nucleophilic substitution reactions in this unit.

Nucleophilic substitution reactions are very common in aliphatic compounds. The most common mechanisms followed in these reactions are the S_N2 and the S_N1. S_N2 is a bimolecular mechanism where the nucleophile attacks the substrate from the side opposite to

that of the leaving group. The rate of the reaction depends upon the concentration of both the nucleophile and the substrate. We observe an inversion of configuration in these reactions.

S_N1, in contrast to the S_N2 is a unimolecular mechanism where the first step is the formation of a carbocation followed by attack of the nucleophile in the second step. The rate determining step here is the formation of the carbocation and the rate depends only upon the concentration of the substrate. Both S_N2 and S_N1 reactions are affected by variables like the structure of the substrate, the nature of the nucleophile, the nature of the leaving group and the nature of the solvent.

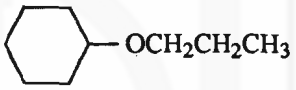
Nucleophilic substitution reactions go faster if neighbouring groups or π or σ bonds participate in stabilising the carbocation formed. This is called anchimeric assistance. It often results in the formation of nonclassical carbocations. Besides the mechanisms discussed above, aliphatic compounds undergo substitution by S_Ni type of mechanism also. Here we observe an intramolecular reaction in which the nucleophile is a part of the substrate.

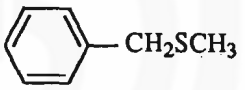
Nucleophilic substitution takes place at an unsaturated carbon also. One such example is the carbonyl carbon, like in esters. Hydrolysis of esters is an important reaction for studying the mechanism of nucleophilic substitution reactions of this type. Esters undergo both alkaline and acid hydrolysis by S_N2 or S_N1 mechanism. Isotope labelling studies show that in both cases, acyl-oxygen fission is more common than the alkyl-oxygen fission.

3.9 TERMINAL QUESTIONS

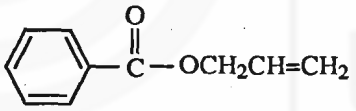
1) The S_N2 reaction of 1-bromo, 2-2-dimethylpropane (neopentylbromide) with NaOEt proceeds about 0.00001 times slower than the reaction of bromoethane. Explain.

2) Suggest reagents for the preparation of following compounds :

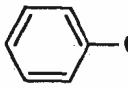
a) 

b) 

c) $CH_3CH_2OCH_2CH_2CH_3$

d) 

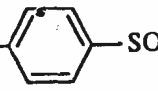
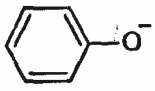
3) Arrange the following compounds with respect to increasing S_N1 reactivity. Justify your answer.

a) $(CH_3)_3C-Cl$,  $C(CH_3)_2Cl$, $CH_3CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3$

b) $(CH_3)_3C-F$, $(CH_3)_3C-Br$, $(CH_3)_3C-OH$

4) 1-chloro-1, 2-diphenylethane reacts with the nucleophiles F^- and $(C_2H_5)_3N$: at exactly the same rate. Why?

5) Arrange the following two sets of compounds in decreasing order as leaving groups in nucleophilic substitution :

a) H_2O, CH_3  SO_3^-,  O^-

b) CH_3^-, Cl^-, Br^-, $CH_3CO_2^-$, OH^-

3.10 ANSWERS

Self Assessment Questions

1) The back side approach of the incoming nucleophile is blocked by rigid carbon skeleton of the bicyclic substrate molecule.

2) a) $CH_2 = CHCH_2Cl > CH_3CH_2CH_2Cl > CH_3CH_2\underset{Cl}{\underset{|}{C}}HCH_3$

The allyl halide is most reactive because of unsaturation than the primary halide without an allyl group which, in turn is more reactive than the secondary halide because of steric reasons.

b) $(CH_3)_2CHCH_2Br > (CH_3)_2CHBr > (CH_3)_3CCH_2Br$

Most reactive halide being the primary than the secondary which is more reactive than a primary halide with too much of steric hinderance at a C atom next to the reaction centre.

3) $(CH_3)_2N^-$ (charged), $(CH_3)_2\ddot{N}$ (lone pair on nitrogen), H_2S (large atom and more polarisable), $(CH_3)_3P$ (higher atomic number).

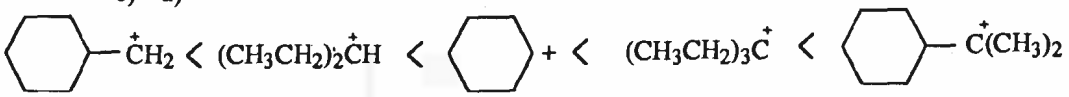
4) $CH_3CH_2CH_2OCH_3 < CH_3CH_2CH_2Br < CH_3CH_2CH_2OTs$

The reactivity is in this order because the order of reactivity of the leaving groups in these compounds is the same viz., $OCH_3^- < Br^- < OTs^-$

5) $(CH_3)_2CHBr + NO_2^- \longrightarrow (CH_3)_2CH - NO_2$

When reactions are carried out under conditions most favourable for the S_N2 mechanism, the nucleophile, NO_2^- will attack the substrate through the nitrogen atom to form nitro compound. Therefore, polar aprotic solvent incapable of dissociating the initial compound into ions should be used.

6) a)

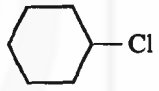


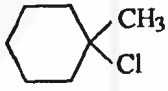
Inductive effect, steric effect and hyperconjugation are responsible for this stability order.

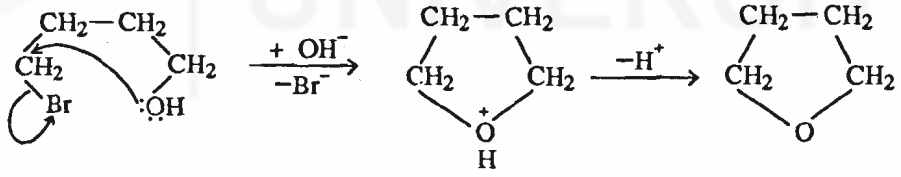
b) i) $(CH_3)_3Cl$ – because tertiary carbocation formed in the reaction would be more stable than the secondary.

ii) $(CH_3)_2CHI$ – because iodine is a better leaving group than chlorine.

iii) $CH_3 - OTs$ – because tosyl group is a better leaving group.

iv)  because the secondary carbocation formed during the reaction would be more stable.

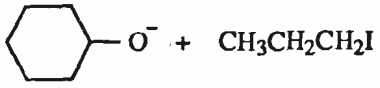
v)  because it again leads to the formation of a tertiary carbocation.

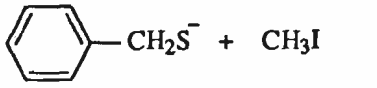
7) 

8) a) T b) F c) T d) F e) F

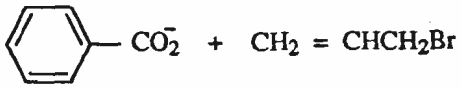
Terminal Questions

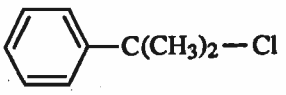
1) Although it is a primary alkyl halide, the alkyl group attached to the head carbon atom is very bulky. The steric hinderence in the transition state is considerable, therefore, the activation energy is high and the rate is slow.

2) a) 

b) 

c) $CH_3CH_2Br + CH_3CH_2CH_2O^-$

d) 

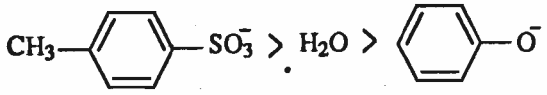
3) a) $CH_3CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3 < (CH_3)_3C-Cl <$  $-C(CH_3)_2-Cl$

the carbocations formed by these have the same order of stability, i.e., a secondary carbocation is less stable than a tertiary which in turn is less stable than the carbocation which is attached to phenyl ring.

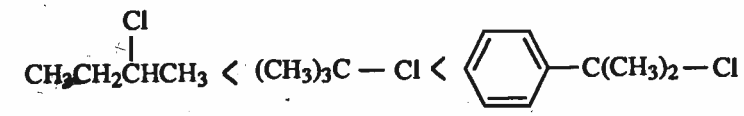
b) $(CH_3)_2C-OH < (CH_3)_3C-F < (CH_3)_3C-Br$

— These would no doubt lead to the same carbocations but the leaving groups have the increasing order of the ease with which they can be removed as given here, $OH^- < F^- < Br^-$

4) The compound reacts by an S_N1 mechanism. The rate of substitution is independent of the concentration of the nucleophile. Hence same rate in the two cases.

5) a) 

b) $Br > Cl^- > CH_3CO_2^- > OH^- > CH_3$

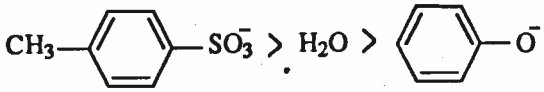
3) a) 

the carbocations formed by these have the same order of stability, i.e., a secondary carbocation is less stable than a tertiary which in turn is less stable than the carbocation which is attached to phenyl ring.

b) $(CH_3)_2C-OH < (CH_3)_3C-F < (CH_3)_3C-Br$

— These would no doubt lead to the same carbocations but the leaving groups have the increasing order of the ease with which they can be removed as given here, $OH^- < F^- < Br^-$

4) The compound reacts by an S_N1 mechanism. The rate of substitution is independent of the concentration of the nucleophile. Hence same rate in the two cases.

5) a) 

b) $Br > Cl^- > CH_3CO_2^- > OH^- > CH_3$

UNIT 4 AROMATIC ELECTROPHILIC SUBSTITUTION

Structure

4.1 INTRODUCTION

In Unit 1, you studied about various kinds of reactions and learnt that alkenes undergo addition reactions, e.g., ethene would add on a molecule of bromine and give a dibromo product. The reaction,

$CH_2 = CH_2 + Br_2 \longrightarrow BrCH_2CH_2Br$

is quite facile and is accompanied by a substantial decrease in enthalpy. On the other hand if we take benzene as our substrate and make it react with Br_2 as in the above case, we do not get the addition product so readily. The reaction is endothermic. The benzene-bromine reaction becomes quite favourable in the presence of a Lewis acid like $FeBr_3$ but here it chooses to undergo substitution rather than addition.

Further, aromatic compounds are comparatively unreactive towards nucleophilic substitution reactions which are so characteristic of aliphatic compounds. Aromatic compounds undergo nucleophilic substitution only under very severe conditions. The question arises as to why do benzene like compounds behave differently towards addition or nucleophilic substitution and opt for electrophilic substitution instead. In this unit, we would first make an attempt to look for the reasons for this different behaviour of aromatic compounds. Then we would study in detail the mechanism of electrophilic substitution reactions which the aromatic compounds undergo. We would also study the mechanism of aromatic nucleophilic substitution reactions where ever these can occur.

Objectives

After studying this unit you should be able to :

- explain aromaticity in terms of experimental and theoretical criteria and also ascertain the aromaticity of a given compound,
- describe the mechanism of various electrophilic substitution reactions of benzene, like, halogenation, nitration, sulphonation, alkylation and acylation,

- describe the mechanism of electrophilic substitution reactions in heteroaromatic compounds and compare it with that in benzene,
- explain orientation and reactivity in aromatic electrophilic substitution,
- describe the S_NAr2 and benzyne mechanisms of aromatic nucleophilic substitution, and
- compare the S_NAr2 mechanism of aromatic nucleophilic substitution with that of S_N2 mechanism of aliphalic nucleophilic substitution.

4.2 AROMATICITY

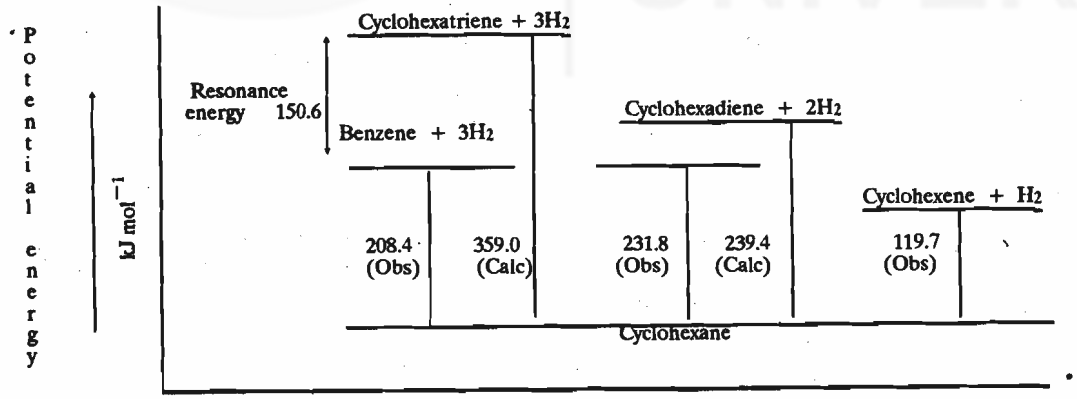
The relative inertness of benzene towards addition and nucleophilic substitution as highlighted above is attributed to its aromatic nature. Similar behaviour is observed for other aromatic compounds also. Let us try to understand the meaning of aromaticity.

You would have learnt that the term "aromatic" was derived from the Greek word 'aroma' meaning fragrance. Now a days this definition of aromatic compounds does not hold, though the name is still retained and is in wide use.

Originally aromaticity was associated with a certain stability inspite of a high degree of unsaturation. The unsaturated systems which underwent substitution in preference to addition were called aromatic. This property is a characteristic of benzene and its derivatives.

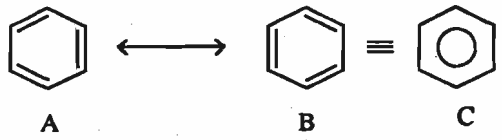
Besides undergoing electrophilic substitution reactions, benzene has low enthalpies of combustion and hydrogenation. The values are much lower than the ones expected from the degree of unsaturation corresponding to its molecular formula. The low values suggest an unusual degree of stabilisation of the molecule. This can be explained as follows. Experimental data for catalytic hydrogenation of cyclohexene shows a value of 119.7 kJ mol^{-1}. The value for 1, 3-cyclohexadiene is expected to be twice that for cyclohexene and, in fact, it is 231.8 kJ mol^{-1}. On the same analogy we might predict the heat of hydrogenation for cyclohexatriene to be approximately three times the cyclohexene value. The actual value as indicated by the energy released during hydrogenation of benzene is 208.4 kJ mol^{-1}. This, as you can see, is 150.6 kJ mol^{-1}. less than the expected value. In other words benzene has 150.6 kJ mol^{-1} "extra" stability. Heats of hydrogenation of benzene, cyclohexadiene and cyclohexene are schematically shown below.

Hydrogen deficiency index of benzene
$= C_6H_{14} - C_6H_6$
$= 8/2 = 4$



This stabilisation is explained on the basis of resonance concept. You would recall that Kekule, based on his intuition, proposed two forms of benzene molecule with alternate double bonds. This structure of benzene is unable to explain the unusual stability of benzene. Also it was found that according to the Kekule formula, benzene should have three single (154 pm) and three double (134 pm) bonds. But actual measurements have been shown that all the carbon-carbon bond lengths of benzene are equal (139 pm) which are intermediate between a single and a double bond. To explain this, it has been conceived that benzene is a resonance hybrid of two Kekule structures. A and B, and is represented by structure C. In structure C,

the ring is shown with a circle inside. Resonance explains the extra stability and equivalence of C—C bond lengths. The stabilisation energy discussed above is referred to as **resonance energy.** The unusual stabilisation due to resonance is yet another criterion for aromaticity.



Orbital picture of benzene

Benzene is visualised as a symmetrical, flat, planar molecule having a regular hexagonal shape. Each carbon atom is bonded to two other carbon atoms and one hydrogen atom by σ bonds using sp^2 hybrid orbitals, Fig. 4.1(a).

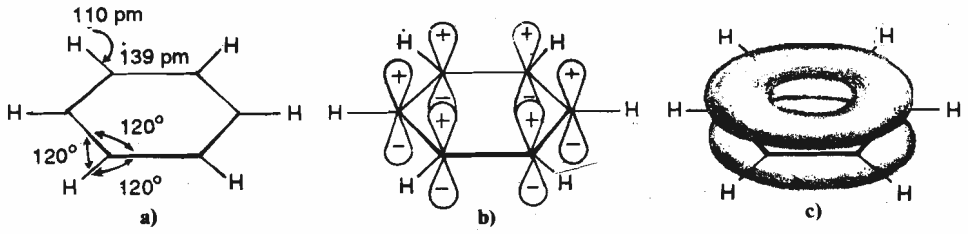
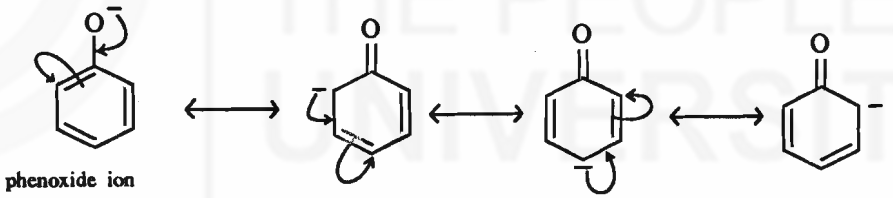
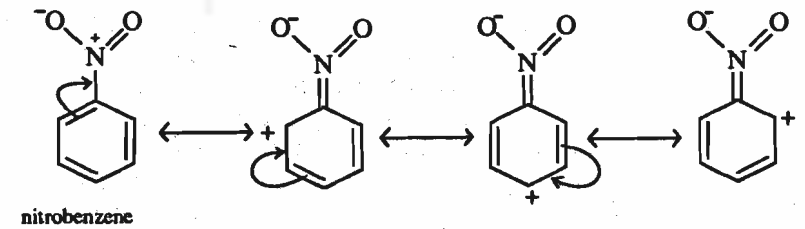


Fig. 4.1 : a) σ Skeleton of benzene
b) π Bond formation in benzene
c) π Cloud in benzene

Third p orbital of each C atom lies perpendicular to the plane of the molecule and has a lobe each, above and below the plane, Fig. 4.1(b). These p orbitals, have one electron each. The sideways overlap of these p orbitals accounts for the π bonding in benzene. The six electrons which form an electron cloud above and below the plane of the ring are called aromatic sextet, Fig. 4.1(c). An electrical disturbance at any carbon of the benzene ring is readily transmitted to the other parts of the molecule. This as you know is indicated in the resonance effect by placing + ve or − ve charge on alternate carbons of benzene ring as shown below for phenoxide ion and nitrobenzene.





The orbital picture accounts for the equivalence of six C—C bonds. The delocalisation of π electrons explains the extra stability of benzene. Other chemical and spectroscopic properties of benzene can also be explained by this structure.

Spectroscopy (pmr)

The delocalised π cloud above and below the flat molecule manifests itself in terms of a significant experimental observation. In PMR spectrum, the olefinic protons are expected to give a signal around 5.0 — 6.50 δ, but in the case of benzene, the signal is observed quite downfield, at 7.27 δ. In the presence of a magnetic field, a current is induced into the π electrons and as the electrons are delocalised over the whole ring, a ring current is generated. This ring current has a induced magnetic field that adds to the applied field at the protons. Fig. 4.2. As a consequence a smaller applied field is required, resulting in a downfield shift.

This experimental property, i.e, the sustenance of a ring current in pmr is yet another criterion for aromaticity.

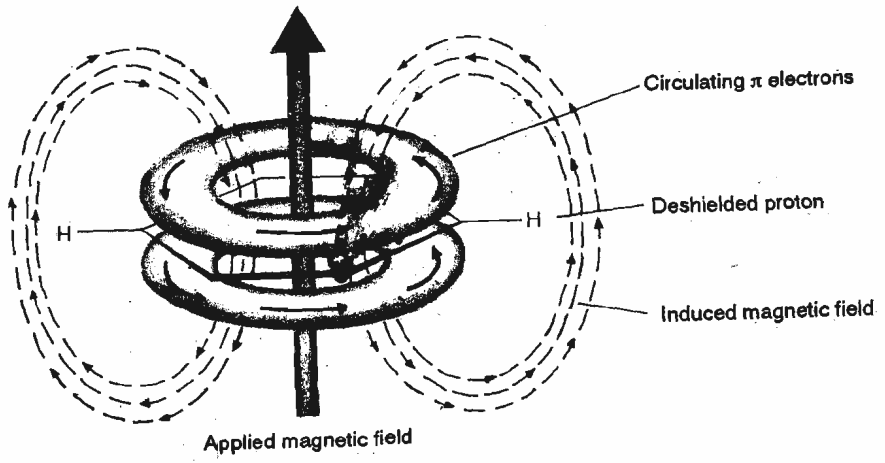


Fig. 4.2 : Ring current in benzene in presence of applied field.

Molecular orbital description of aromaticity

So far we have tried to define aromatic compounds in terms of some experimental property; electrophilic substitution instead of addition, unusual stability or sustenance of ring current, etc. Currently aromaticity is defined in terms of molecular orbital terminology—a theoretical approach. Aromatic compounds have particularly stable arrangement of π-molecular orbitals. This is given by Huckel molecular orbital (HMO) theory. According to this theory, planar, monocyclic, completely conjugated hydrocarbons will be aromatic, when the ring contains $(4n + 2)\pi$ electrons where n is an integer (that is 0, 1,2 ...). This is called 4n + 2 rule or **Hückel rule.**

In the case of conjugated, planar molecules, Huckel's approach treats the π electrons independent of σ framework. As stated above, in benzene the six overlapping *p* orbitals on six carbons constitute its π system. These give rise to six molecular orbitals as shown in Fig. 4.3. The orbitals below the dashed line are bonding while the ones above it are antibonding. If the electrons are placed in bonding molecular orbitals, the molecule is stabilised, while the presence of electrons in antibonding molecular orbitals destabilises the molecule. Since benzene has 6 electrons, all of these are accomodated into three bonding molecular orbitals. This leads to a considerable amount of stabilisation which accounts for the experimental facts. When the π bonding molecular orbitals are filled completely with electrons, it imparts extra stability. Addition or removal of one or more electrons decreases stability.

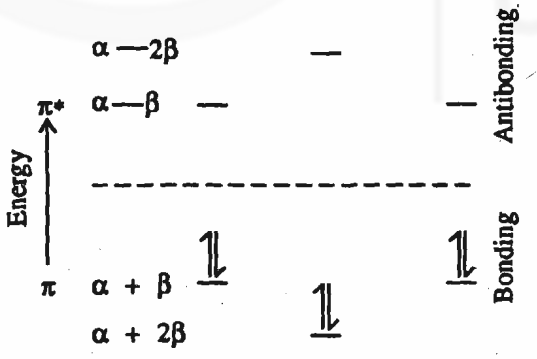
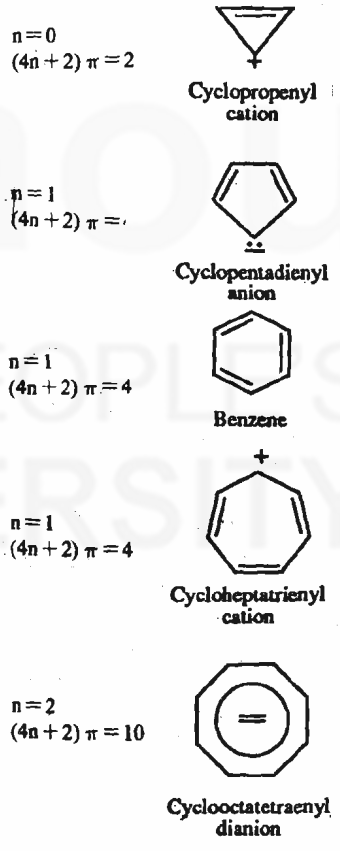


Fig. 4.3 : MO energy level diagram for benzene.

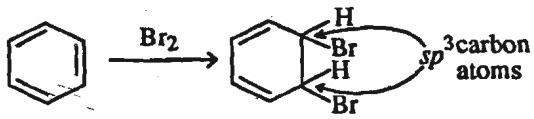
Similar molecular orbital analysis of various conjugated systems eventually led Hückel to propose his rule for aromaticity as enunciated above. Let us now briefly summarise various criteria which make a given unsaturated compound aromatic.

- Resistance to undergo addition or nucleophilic substitution and instead show electrophilic substitution.
- Unusual stabilisation due to delocalisation of π electrons suggested by low enthalpies of combustion and hydrogenation.
- Sustenance of ring current in pmr spectrum.
- Planar, conjugated system with $(4n + 2)$ π electrons.

Some aromatic Compounds



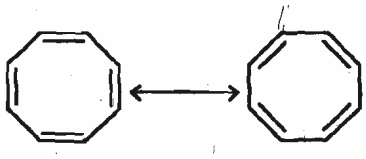
Having understood the characteristics of aromatic compounds, let us now see why benzene does not undergo addition reactions. Now, if benzene were to undergo an addition reaction, the product formed would have two carbon atoms in the ring which would be sp^3 hybridised. As a consequence, the ring becomes somewhat strained and nonplanar. Further the delocalisation of π electrons in the ring is also restricted to 4 carbon atoms destroying the complete conjugation in benzene.



As this π cloud is responsible for the extra stability of benzene, its disruption causes the energy of the product to increase and as such the reaction is not favoured.

SAQ 1

Cyclooctatetraene is a conjugated polyene and one can write two resonance structures of the Kekule type.



yet it is not an aromatic compound. Explain.

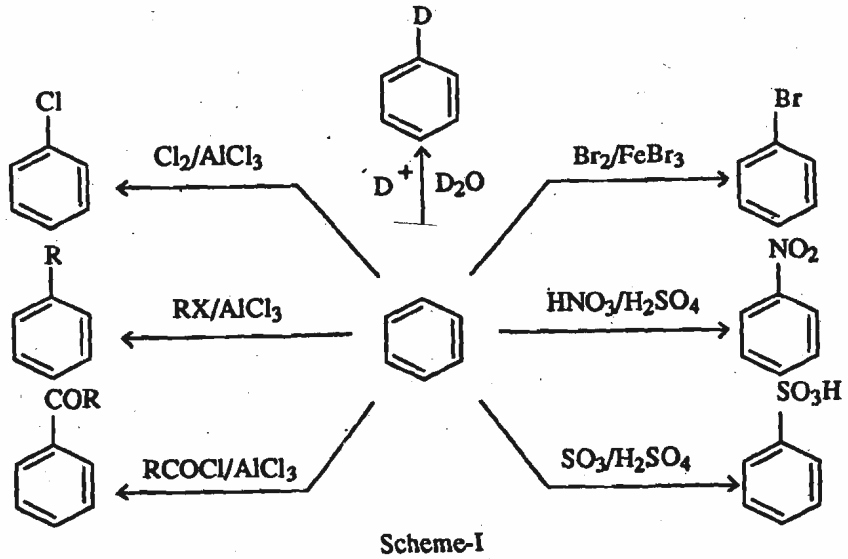
.....

.....

.....

4.3 AROMATIC ELECTROPHILIC SUBSTITUTION

We have so far seen why a given compound is aromatic. Now we will see the consequences of its being aromatic that is the mechanism of reactions generally undergone by aromatic compounds. You have studied that aromatic compounds have got a delocalised cloud of π electrons which is available for a reaction, i.e., aromatic compounds behave like Lewis bases. Reagents which are deficient in electrons and are seeking them, namely, the electrophiles, react easily with aromatic compounds and give the product. Here a hydrogen atom is replaced by the electrophile. Such a reaction is referred to as an **electrophilic substitution reaction.** These reactions are synthetically and mechanistically very important. A wide variety of reactions like halogenation, nitration, sulphonation, alkylation or arylation of benzene and other aromatic compounds as given in scheme I, fall under electrophilic substitutions. There are certain other electrophilic reactions like nitrosation and diazo coupling, etc., which can occur only in the case of strongly activated aromatic rings.



Scheme-I

Despite a wide range of electrophilic species and number of aromatic ring systems capable of undergoing electrophilic substitution, a generalised mechanism holds for a large majority of electrophilic aromatic substitution reactions. Generation of the electrophile, identity of the rate determining step and the shape of the potential energy diagram depends on the specific reaction involved. However, the series of steps and nature of the intermediate are quite similar in all these cases. We will first give the generalised mechanism of aromatic electrophilic substitution, thereafter, we would study the mechanism of specific reactions.

4.4 MECHANISM OF AROMATIC ELECTROPHILIC SUBSTITUTION REACTIONS (AESR)

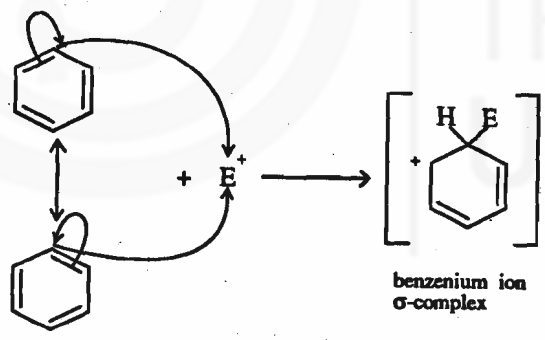
We will take up a general reaction between benzene as substrate and a reagent, EZ. The obvious first step in the reaction would be generation of the electrophile from the reagent. Generation of the electrophile in different electrophilic substitution reactions takes place by widely different ways. We will represent it as a simple dissociation of the reagent molecule, EZ.

$$EZ \rightleftharpoons E^+ + Z^-$$

Once the electrophile, E^+ is generated in the reaction, it enters into some kind of a weak interaction with the π cloud of benzene ring leading to the formation of a **π-complex.** This π-complex is a donor-acceptor type of a complex, benzene being the donor and electrophile, the acceptor. This is generally reversible and is not associated with any kind of positional selectivity. The complex may or may not be involved directly in the substitution mechanism. It is represented as follows :

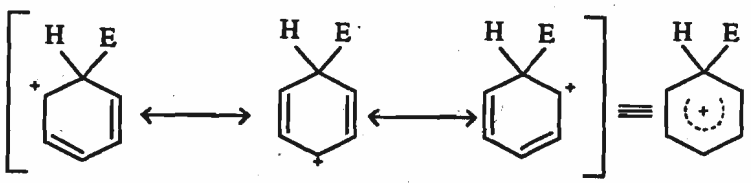
π - complex

Mechanistically important is the formation of a σ-complex in a slow step. The σ-complex is an intermediate in which carbon at the site of substitution is bonded to both the electrophile and the group to be displaced.

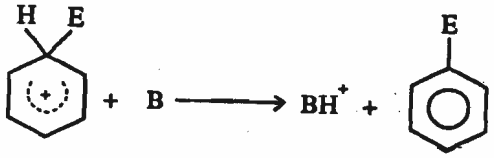


benzenium ion
σ-complex

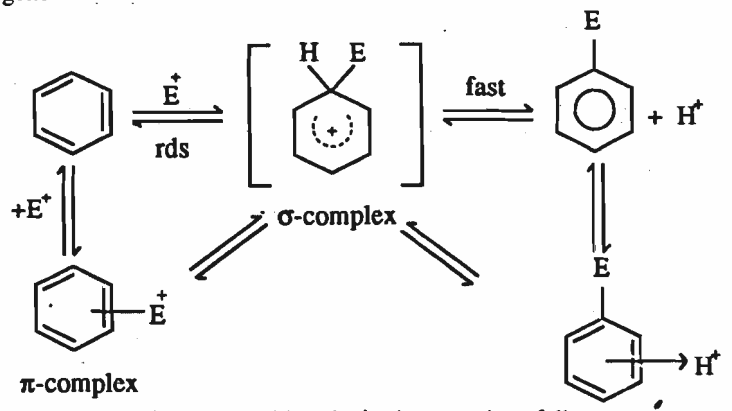
The intermediate is a cyclohexadienyl cation also called as benzenium ion (in general arenium ion) and is resonance stabilised. Here the positive charge is delocalised in the ring. The intermediate is represented with a broken circle inside the ring as shown below :



The reaction is completed by abstration of the proton or the group to be replaced with the help of a suitable base (fast step). The leaving group is also an electrophile.



Thus, the general mechanism of an aromatic electrophilic reaction can be summarised as below :



As given above, aromatic electrophilic substitution reactions follow a two step mechanism where the first step, viz., formation of a σ-complex is slow and rate determining while the second step is fast. It is assumed that generation of the electrophile before σ-complex formation is quite fast. Let us now consider some of the evidence for this generalised mechanism.

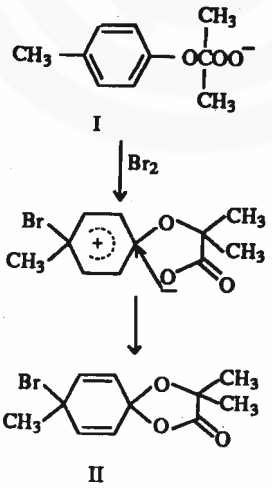
Evidence for mechanism of electrophilic substitution

Evidence for a two step mechanism of electrophilic substitution has been obtained from the study of mechanism of specific reactions. In the first instance, one would like to seek evidence for the very involvement of an electrophile in such reactions. To this effect nitration reaction has been studied in detail. On the basis of kinetic studies, it has been shown that the active electrophile in nitration reaction is nitronium ion, NO_2^+. The reaction is observed to be second order for relatively unreactive substrates, first order in the nitrating reagent and also first order in the aromatic substrate. Presence of NO_2^+ ion has also been detected spectroscopically in the nitrating mixture, H_2SO_4 + HNO_3. It has further been supported by freezing point depression data.

Isotope effects

The next question which comes up is how do we ascertain the presence of two discrete steps in the mechanism and also that the formation of σ -complex is the rate determining step. Answer to this question can be obtained from the study of kinetic isotope effect.

You would recall from Unit 2, that if the rate of a reaction depends on a step which involves breaking of a C—H bond, then a kinetic isotope effect (K_H/K_D) of 6-7 is expected. Absence of any significant isotope effect in aromatic electrophilic substitution (except sulphonation) suggests that the proton is lost in the fast step, subsequent to rds. We see that the isotope effect study has provided two pieces of important information regarding the mechanism. Firstly, it has shown that the reaction takes place in two steps and secondly, that the first step is slower than the second.



The most convincing evidence for the mechanism is the actual isolation of certain σ -complexes. These are trapped in some cases. For example, treatment of carboxylate anion, I, with bromine, gives the cyclohexadienyl lactone II. The intramolecular attack of the carboxylate group on the σ -complex occurs. The schematic potential energy diagram for generalised mechanism is given in Fig. 4.4.

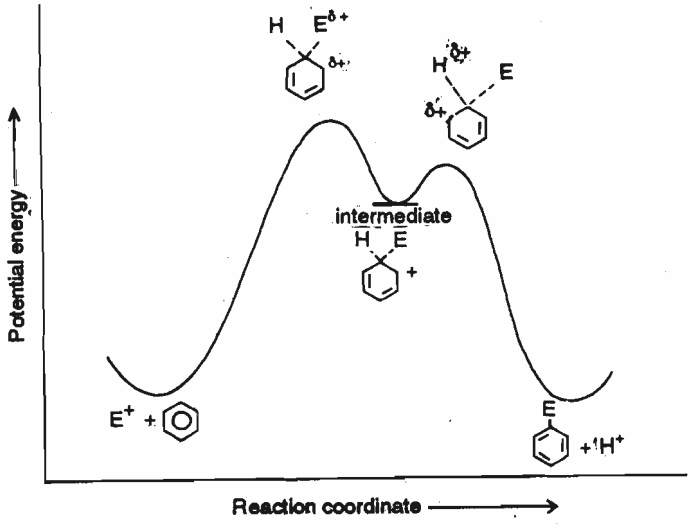


Fig. 4.4 : Schematic potential energy diagram for the generalised mechanism of AESR

Based on the above discussion try the following SAQ.

SAQ 2

Write down the mechanism for nitration of benzene. The electrophile is nitronium ion, NO_2^+.

.....

.....

.....

Having understood the generalised mechanism of aromatic electrophilic substitution reactions, let us now take up special features in specific reactions.

4.4.1 Halogenation

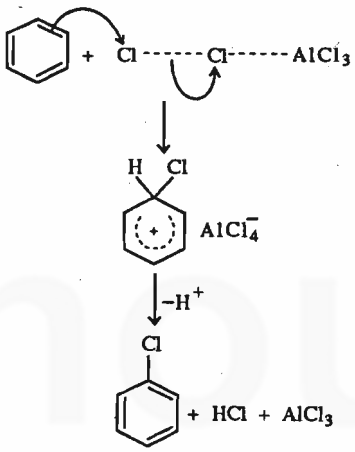
Halogenation of an aromatic ring is a synthetically important reaction. It takes place in the presence of varied reaction conditions depending on the reactivity of the aromatic ring. For very reactive aromatic compounds in polar solvents, the molecular halogens themselves may act as electrophiles. In the case of nonpolar solvents, halogenation is catalysed by a Lewis acid like $AlCl_3$ or $FeCl_3$. Reactivity of halogens has the following order,

$I_2 < Br_2 < Cl_2$

Let us take chlorination as a representative reaction to understand the mechanism of halogenation. Chlorine, in the presence of $AlCl_3$ or $FeCl_3$ forms a complex, $Cl_2 - AlCl_3$. This complex can itself be the reactive electrophile or it may dissociate to give Cl^+.

$$Cl_2 - AlCl_3 \rightleftharpoons Cl_2^+ + AlCl_4^-$$

However, there is no significant evidence for the involvement of Cl^+ as an electrophile and it is likely that the complex itself attacks the substrate. In the $Cl_2 - AlCl_3$ complex, role of the Lewis acid is to polarise the halogen molecule and weaken the Cl – Cl bond. This lowers the activation energy for the formation of σ -complex, Fig. 4.5.



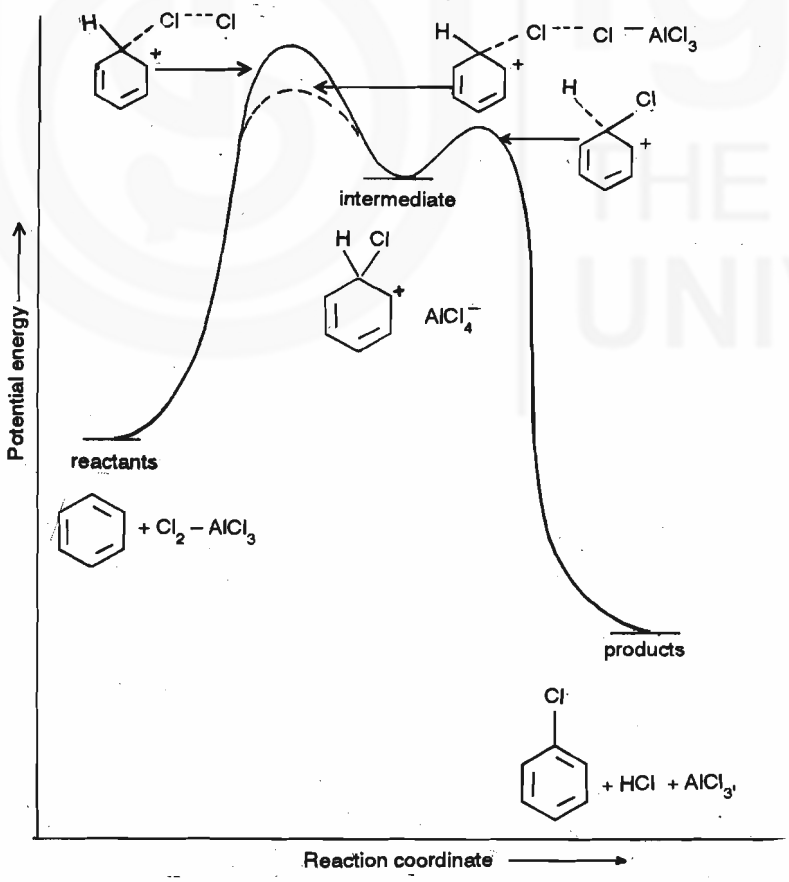


Fig. 4.5 : Schematic potential energy diagram for chlorination of benzene with Cl_2 (——) and Cl_2AlCl_3 (– – – –) as the electrophile

Bromination follows a similar mechanism. As said above, iodine is weakest of the three halogens and even in the presence of a Lewis acid, it can halogenate reactive aromatics only. Therefore, in most other cases iodine-monochloride is used in the presence of Lewis acid, $ZnCl_2$

4.4.2 Nitration

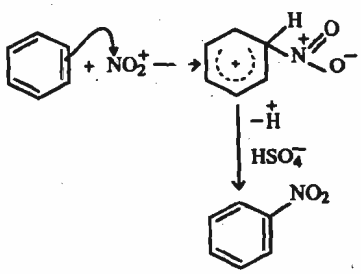
Mechanism of nitration reaction has been studied quite thoroughly. Nitration of an aromatic ring can be brought about by HNO_3, if the ring is very reactive. Otherwise a nitrating mixture containing nitric acid along with a much stronger acid like H_2SO_4 or $HClO_4$ is used. In either of the two cases, the active electrophile is the same, viz., nitronium ion, NO_2^+. Generation of the electrophile is given by the following equations,

Some nitrating mixtures
$NO_2^+BF_4^-$, $NO_2^+NO_3^-$
$NO_2^+ClO_4^-$, $NO_2^+CH_3COO^-$

$$2HNO_3 \rightleftharpoons NO_2^+ + NO_3^- + H_2O$$

or

$$HNO_3 + 2H_2SO_4 \rightleftharpoons NO_2^+ + 2HSO_4^- + H_3O^+$$



In the case of nitrating mixture, the sulphuric or perchloric acid force the weaker nitric acid to act as a base and produce nitronium ion. The nitronium ion has been detected spectroscopically in the nitrating mixture. Cryoscopic measurements show that the common nitrating mixture forms four particles in the solution, consistent with the equation given above

Nitronium ion can be converted into crystalline salts by anions like tetrafluoroborate. Solutions of these salts also nitrate aromatic compounds proving the involvement of nitronium ion.

SAQ 3

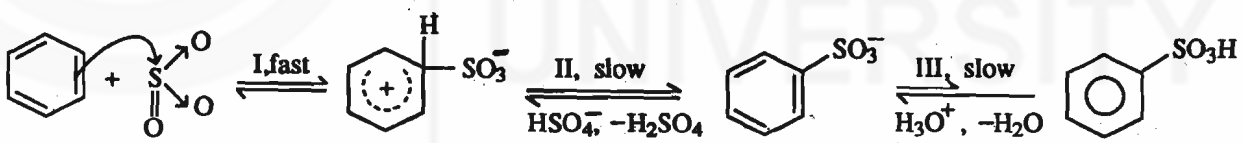
Represent nitration of benzene on a schematic potential energy diagram suitably indicating various species.

4.4.3 Sulphonation

Sulphur trioxide is generated from sulphuric acid as follows,
$2H_2SO_4 \rightleftharpoons HSO_4^- + H_3O^+ + SO_3$

Sulphonation is another synthetically important reaction. It is often accomplished with concentrated sulphuric acid or fuming sulphuric acid containing excess of SO_3 or chlorosulphonic acid, $ClSO_2OH$.

It is believed that the electrophile varies with the reagent, though in all cases SO_3 is involved either free or along with a carrier, like in $H_3SO_4^+(SO_3 + H_3O^+)$ or $H_2S_2O_7$. The mechanism of sulphonation of benzene is given below :



Sulphonation is different from other AESRs. Firstly, it is reversible and secondly, it shows some amount of isotope effect which is totally absent in other cases. Let us have a look at the potential energy diagram, Fig. 4.6, of sulphonation reaction to understand these anomalies.

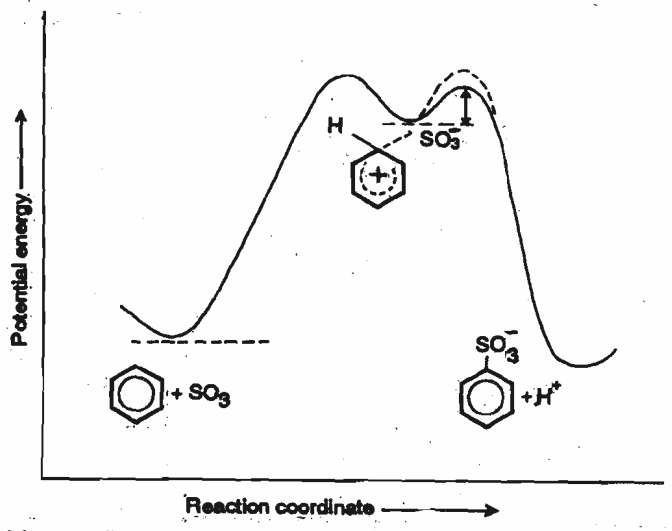


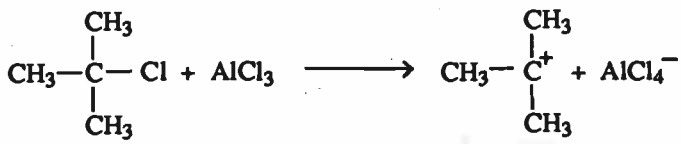
Fig. 4.6 : Potential energy diagram for sulphonation of benzene (———) and deutorobenzene (— — —)

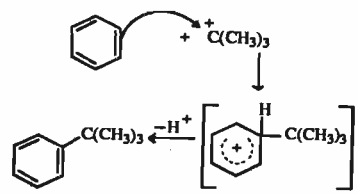
We see that once the σ -complexed benzenium intermediate is formed, the energy barriers on either side of the intermediate are roughly of the same magnitude. This means that the intermediate can cross over to the product and can also come back to the reactant. This accounts for a reversible nature. Now, if we have the deuterated substrate, then the potential energy diagram gets slightly modified (dotted curve). The barrier to step II becomes higher as it now involves the cleavage of C—D bond. The barrier for step I, on the other hand, remains the same as it pertains to σ -complex formation. The rate of its reverting back to reactants is higher than its crossover to the product. Therefore, there is a net decrease in the overall rate of sulphonation for deuterated substrate-it shows a kinetic isotope effect. The loss of proton (step II) is the slowest step (rds). The equilibrium in step III lies to the left as aryl sulphonic acids are strong acids.

In the case of other electrophilic substitutions, in constrast, energy barrier for the first step is much higher than that for the second step even for a deuterated substrate.

4.4.4 Alkylation

Introduction of an akyl group in an aromatic ring is called alkylation. Alkyl halides in the presence of Lewis acids like $AlCl_3$, $FeBr_3$, $GaCl_3$, etc. bring about alkylation in aromatic systems. This reaction is known as **Friedel—Crafts alkylation.** Lewis acid generates the electrophile from the alkyl halide by polarising the C—X bond. For example,



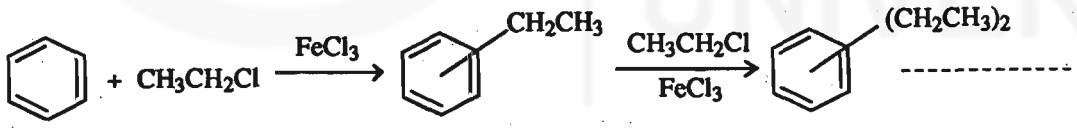


In the case of tertiary halides, as given above, the carbocation is reasonably stable and can act as an electrophile in free state. In primary and secondary alkyl halides, the alkyl halide-catalyst complex acts as the electrophile.

In the presence of strong acids and a catalyst, even alcohols or alkenes can provide suitable electrophiles for alkylation.

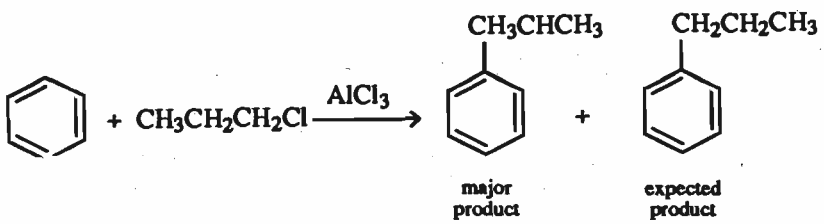
$$(CH_3)_2C = CH_2 + BF_3 + HF \rightleftharpoons (CH_3)_3C^+BF_4^-$$

The Friedel-Crafts alkylation reaction is a very useful and simple method of introducing alkyl substituents. One has to be cautious while using it because it has some limitations which restrict its usefulness. The first limitation is that, once an alkyl group is introduced into an aromatic ring, it becomes more reactive towards alkylation. As a consequence, one gets a mixture of mono-, di- and trisubstituted products instead of the required mono-substituted products.



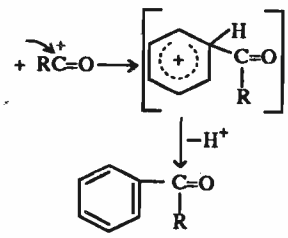
Benzene, being readily available and relatively inexpensive, may be used in large excess to avoid these additional reactions.

Another major drawback is that certain carbocations once generated can undergo some kind of rearrangement to the more stable isomeric carbocation. As a consequence one gets a mixture of alkyl-substituted products. For example, 1-chloropropane reacts with benzene in the presence of $AlCl_3$ to give 2-phenylpropane (isopropylbenzene) as the major product as against the expected 1-phenylpropane (*n*-propylbenzene).

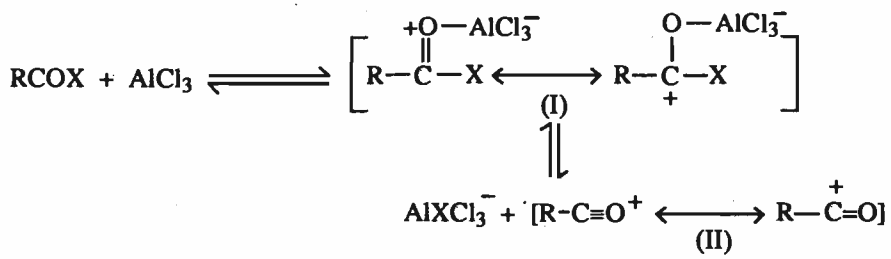


Alkylation reaction does not work in the presence of deactivating groups on the aromatic ring or a group like NH_2 which can form a complex with the catalyst and deactivate the ring.

4.4.5 Acylation

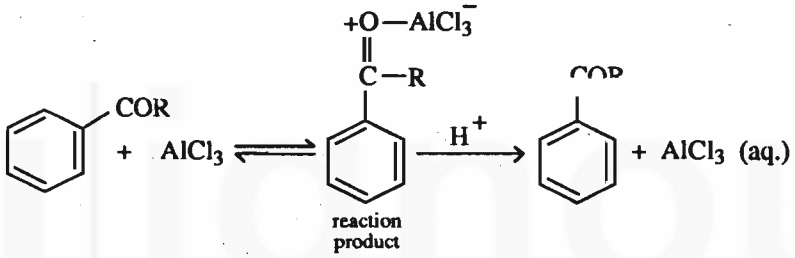


Another type of Friedel-Crafts reactions where carbocation is the electrophile are acylation reactions. Acylation is the introduction of a R—CO or Ar-CO group into an aromatic ring. Acyl electrophile is generated from an acyl halide or acid anhydride by the help of a strong Lewis acid like $AlCl_3$. In some acylation reactions, even proton acids, e.g., polyphosphoric acid, are used as catalysts.



In many cases the acyl halide-Lewis acid complex (I) is electrophilic enough to bring about the reaction and in other cases the acylium ion (II) does the job. The mechanism of acylation is similar to other AESRs.

The aromatic ketone which is a formed as the product gets complexed with the catalyst and the actual reaction product is the complex, which needs to be hydrolysed to obtain free ketone.



Acylation reactions are free from the limitations of alkylation reactions. Introduction of acyl group deactivates the ring whereby there is no polysubstitution. Secondly, the acylium ions do not undergo rearrangements.

SAQ 4

Complete the following giving equations.

i) Benzene $\xrightarrow{?}$ 2-phenylpropane

.....

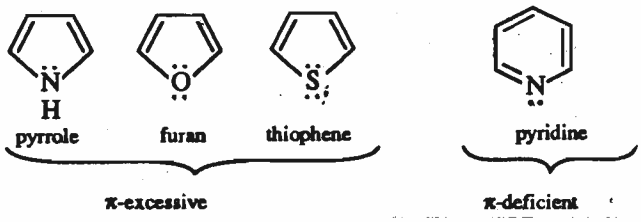
ii) Benzene + propene $\xrightarrow{HF/BF_3}$?

.....

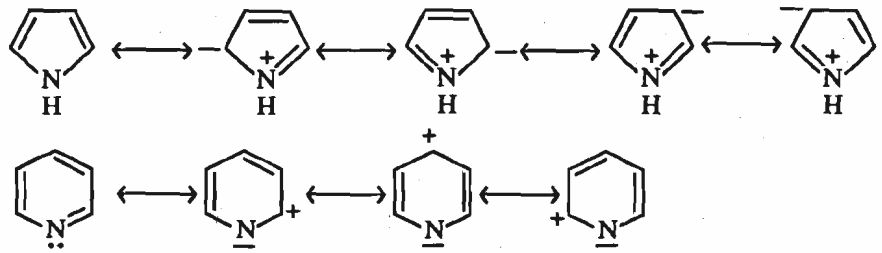
4.5 ELECTROPHILIC SUBSTITUTION IN HETEROAROMATIC COMPOUNDS

Cyclic compounds containing a heteroatom like O, N or S and $(4n + 2)$ π electrons are also aromatic. As these compounds are associated with special chemical stability like benzene, these also undergo substitution and not addition reactions.

Heteroaromatic compounds given below are called π-excessive or π-deficient depending on whether the heteroatom provides the ring with electrons or depletes it.



Five membered pyrrole is π-excessive while six membered pyridine is π-deficient though the heteroatom is same in both the cases. You can understand this by writing the various possible reasonating structures as given below :

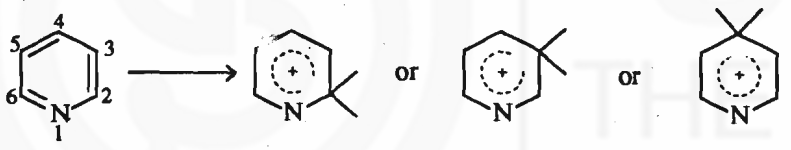


As you can see, while in the case of pyrrole, there is an excess of negative charge on the ring π-electron cloud is depleted in the case of pyridine. This variation in the density of the π-cloud affects their reactivity towards electrophilic substitution. The π-excessive heterocycles are more reactive than benzene and the π-deficient ones are deactivated with respect to benzene as, nitrobenzene. Let us try to compare benzene and these heterocycles.

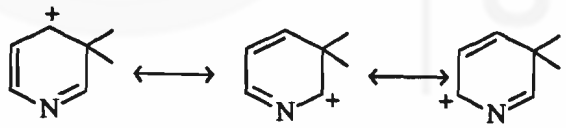
4.5.1 Comparison between Benzene and Pyridine

Pyridine is structurally similar to benzene but for the heteroatom. Due to its being π-deficient, it is a weak nucleophile as compared to benzene and as such it is much less reactive towards electrophilic substitution reactions. You know that a similar deactivation of the ring occurs in nitrobenzene (Unit 3, CHE-05). Besides the presence of positive charge over the ring in the resonating structures, there is yet another factor that makes pyridine deactivated towards electrophilic substitution reactions, that is the presence of a lone pair on nitrogen. Because of this, it can coordinate with a Lewis acid and acquire positive charge which further deactivates the ring.

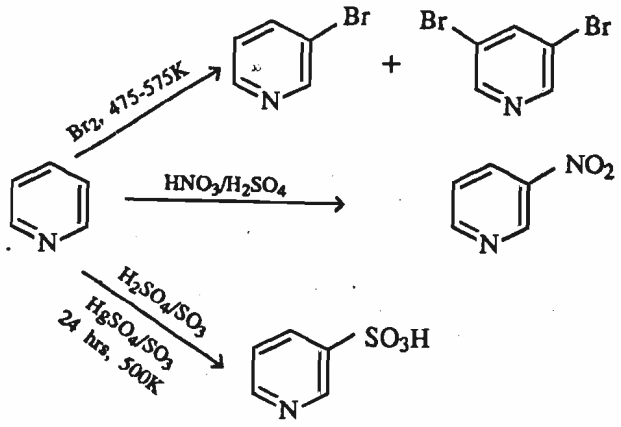
As against benzene, where all the six positions are alike for monosubstitution, in the case of pyridine, the reactivities of different positions are different. Electrophilic substitutions can take place at position 2,3 or 4.



Of the three σ-complexes possible, the 3-substituted σ-complex is more stable than the 2-or 4-substituted ones. The σ-complex in 3-substitution is stabilised by resonance as shown below :



Where as in the case of the 2-or 4-substituted complex, one of the canonical forms would have positive charge (sextet) on nitrogen atom which makes it relatively unstable. As a result electrophilic substitution takes place, in case of pyridine, with difficulty under rigorous conditions as given in scheme II.



Scheme-II

Another point of difference between benzene and pyridine is that pyridine does not undergo Friedel-Crafts alkylation or acylation. This is so because the Lewis acid catalyst added for the reaction gets attached to nitrogen through its lone pair. As a consequence, the aromatic ring gets further deactivated.

SAQ 5

Write canonical structures for the σ-complex of 2-and 4-substituted pyridine.

.....

.....

.....

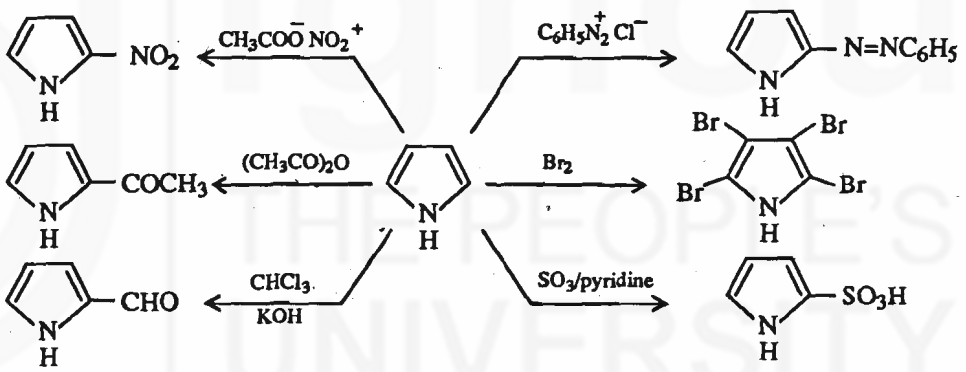
4.5.2 Comparison between Benzene and 5-Membered Heteroaromatics

After comparing benzene and pyridine, let us now try to see how do five membered heteroaromatic compounds behave, vis-a-vis benzene, towards electrophilic substitution reactions. As pointed out earlier these five membered heteroaromatics belong to π-excessive systems. All the three are more reactive than benzene. The reactivity order,

pyrrole > furan > thiophene

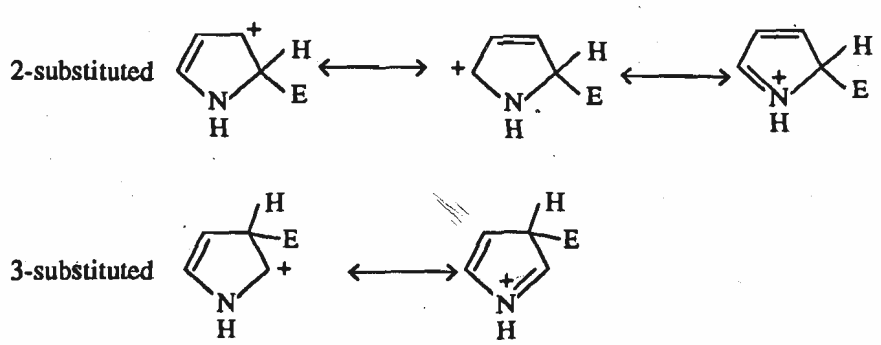
is parallel to the electron donating capacities of the heteroatoms, N > O > S, as expected from the electronegativity and size. We shall take pyrrole as a representative of the five membered heteroaromatics for our discussion here.

Due to its high reactivity and for the fact that pyrrole tends to polymerise in acidic solutions, conditions for electrophilic substitution reactions are much milder, similar to phenol or aniline and unusual as compared to benzene. Typical reactions of pyrrole are given in scheme III.



Scheme-III

As is evident from this scheme, substitution takes place at 2-position. Reason for this becomes clear if we write the reasonating structures for 2 and 3-substituted σ -complexes.



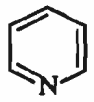
We see that the positive charge in the case of 2-substitution can be very effectively delocalised by the 4, 5 C = C bond, which is not the case in 3-substitution.

SAQ 6

Complete the following reactions. Give only the products.

i)  + $CH_3COO^-NO_2^+ \xrightarrow{Ac_2O}$?

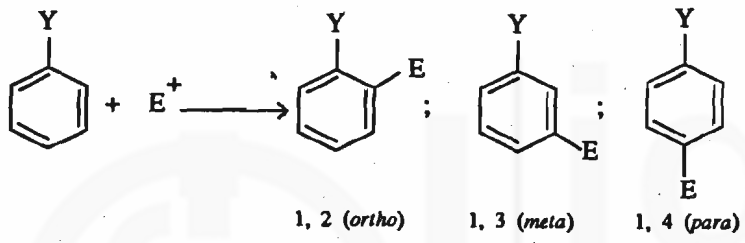
.....

ii)  + $HNO_3/H_2SO_4 \longrightarrow$?

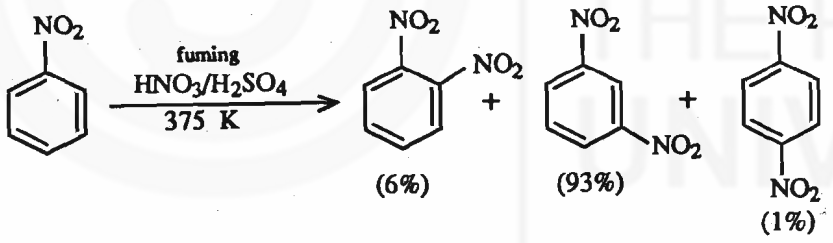
.....

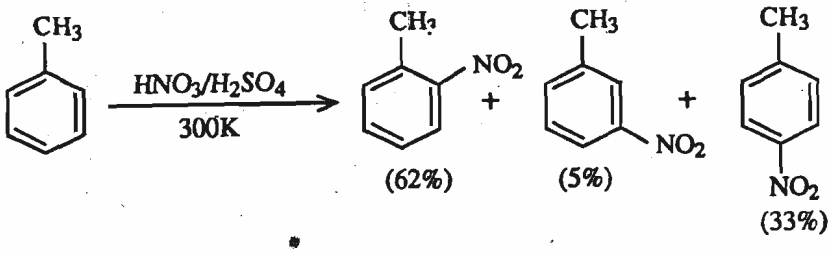
4.6 ORIENTATION AND REACTIVITY IN AROMATIC ELECTROPHILIC SUBSTITUTION

You know that in the case of benzene we get just one monosubstituted product in electrophilic substitution as all the positions are equivalent. However, for substitution in a compound which already has a group attached to the ring, three disubstituted products, (1, 2), (1, 3), (1, 4) commonly called *ortho, meta* and *para* meaning next to, between and opposite, respectively are possible. These are abbreviated as *o, m,* and *p.*



One may ask, are all the three products formed in equal amounts or is there some kind of preference? Let us take two examples.





We see that nitration of nitrobenzene and methylbenzene gives entirely different composition of the products. While *meta* product is predominant in the case of nitrobenzene, *ortho* and *para* products are favoured in methylbenzene. We see that a nitro substituent on benzene ring 'directs' the second substituent to the *meta* position. Such a substituent is called *meta* directing. Similarly, CH_3 group is an example of an *ortho/para* directing substituent.

Besides being different in their 'directing' tendencies, CH_3 and NO_2 groups differ in one more aspect and that is the rate of the reaction. If we compare the reactivities of benzene,

methylbenzene and nitrobenzene towards nitration reaction, we find that,

methylbenzene > benzene > > > nitrobenzene

24 1 10

i.e., as compared to benzene, methylbenzene is about 24 times more reactive while nitrobenzene is about ten million times less reactive. CH_3 group is called an activating group, while NO_2 is a deactivating group for electrophilic substitution of aromatic compounds. By and large, the *meta* directing groups are deactivating and the *o/p* directing groups are activating, with the exception of halogens. This is also reflected in the reaction conditions for the nitration of nitro- and methylbenzene. Table 4.1 gives a list of substituents with their directive influence and also whether they activate or deactivate the ring.

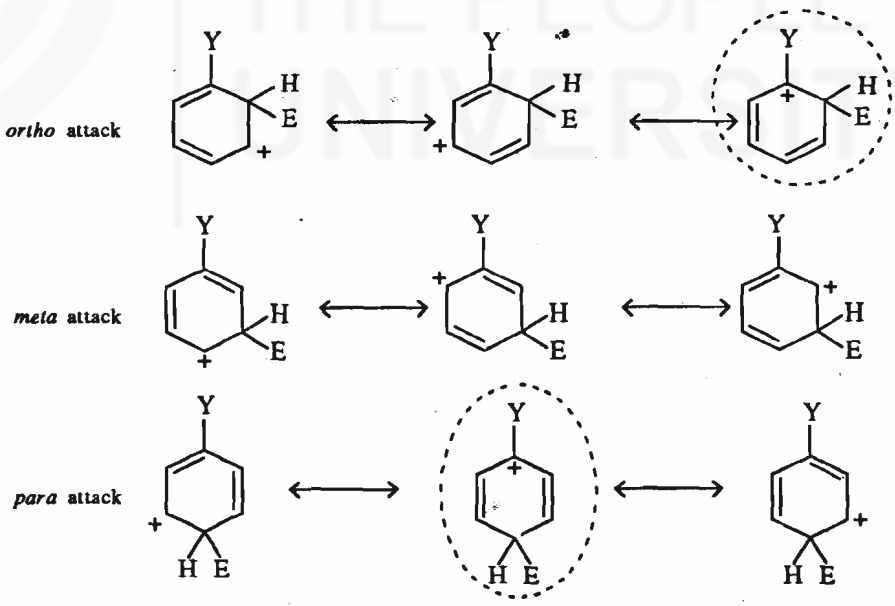
Table 4.1 : List of substituents—their reactivity effects and directive influence

ortho/para directing	*meta* directing
Activating	**Deactivating**
—OR	$—NO_2$
$—NR_2$	$—CF_3$
$—NHCOCH_3$	$—CCl_3$
—alkyl	—COOR
	$—CONR_2$
Deactivating	
—F	—COR
—Cl	$—\overset{+}{N}R_3$
—Br	$—\overset{+}{P}R_3$
—I	—C≡N
R=H, alkyl or aryl	

Theory of Orientation and Reactivity

You would recall that in AESR, the rate determining step is the formation of σ-complex, i.e., the rate of the reaction would be determined by the free energy of activation, $\Delta G^{\ddagger}$. Reactivity and orientation are both essentially kinetic effects and are due to the interplay of resonance and inductive effects. These can be rationalised in terms of the alteration in the $\Delta G^{\ddagger}$s. We would make an attempt to understand this correlation.

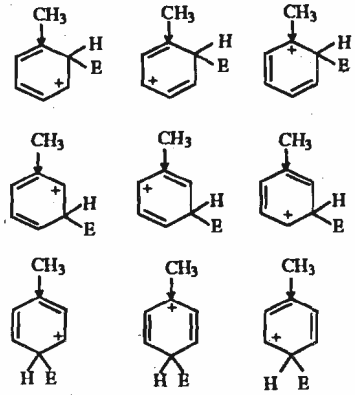
Let us take the general case again where we take monosubstituted benzene as the substrate an E as the electrophile. Resonating structures for the intermediates formed by *ortho, meta* and *para* attack of the electrophile are given below :



We see here that in the case of *ortho/para* attack, one of the resonating structures (encircled) has a positive charge on the carbon atom bearing the substituent. These are the structures which are responsible for the orientational effect and reactivity. If Y = H, the overall stability in case of *ortho, para* and *meta* attack is same and there is no preference which, in fact, is true since for Y = H, the substrate is benzene itself.

If the substituent Y happens to have a + I effect (e.g., CH_3 group), i.e., it is an electron releasing group, then it would be able to reduce the positive charge on the carbon bearing it.

As a consequence, this structure becomes more stable than the other two resonating structures. The overall stability of the intermediate in the case of *ortho/para* attack becomes more than that in *meta* attack and we say that CH_3 group is a *ortho/para* directing group.



In terms of potential energy diagrams the relative reactivities would depend on $\Delta G^{\ddagger}$, i.e., if we wish to assess the relative rates we need to estimate energies of the transition states. Such an estimate is difficult but since the transition state resembles the σ -complex in its structure and energy we can use the energy and stability of the σ -complex for argument.

The schematic potential energy diagram for the reaction on methylbenzene as compared with that on benzene is given in Fig. 4.7. For simplification it is assumed that the reactants in both the cases have equal energies.

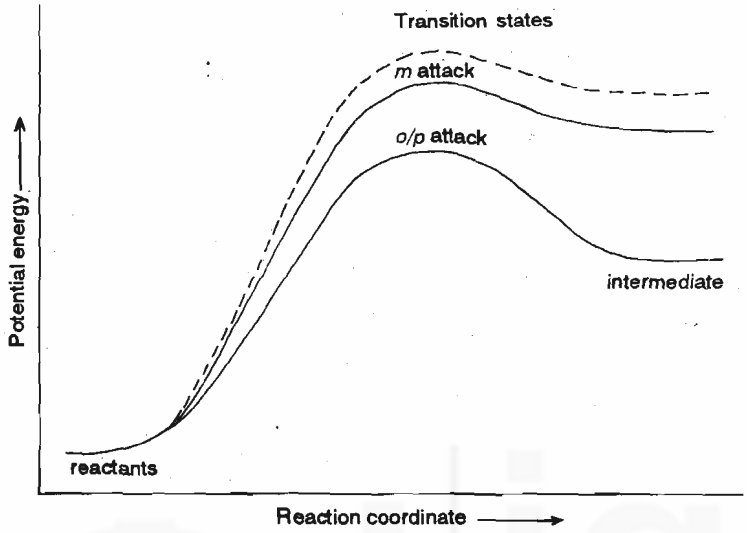
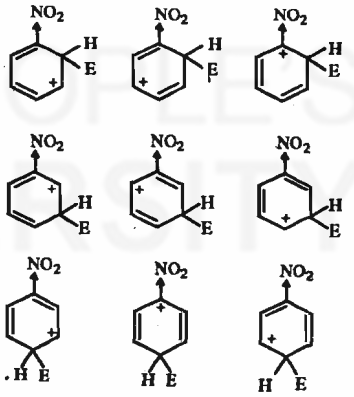


Fig. 4.7 : Schematic potential energy diagram for AESR in benzene (— — — —) and methylbenzene (————)

Since an electron releasing group like CH_3, in general, activates the ring towards electrophilic attack, the energy of the intermediate in the case of methylbenzene is lower than that in benzene. The transition state in the case of *ortho/para* attack has lower energy than that in the case of *meta* attack.



If the substituent is an electron withdrawing group (e.g., NO_2 group) then it would make the encircled structures especially unstable by increasing the positive charge on the carbon bearing this substituent. As a consequence the *ortho/para* attack is unfavourable as compared to the *meta* attack. The major product in such a case is *meta* and the group is called *meta* directing. As the electron withdrawing groups, in general, deactivate the ring towards electrophilic attack, the three possible intermediates would be of higher energy as compared to the intermediate in case of benzene. Further, the energy for the *ortho/para* case would be relatively higher than that of the *meta*. The potential energy diagram is shown in Fig. 4.8.

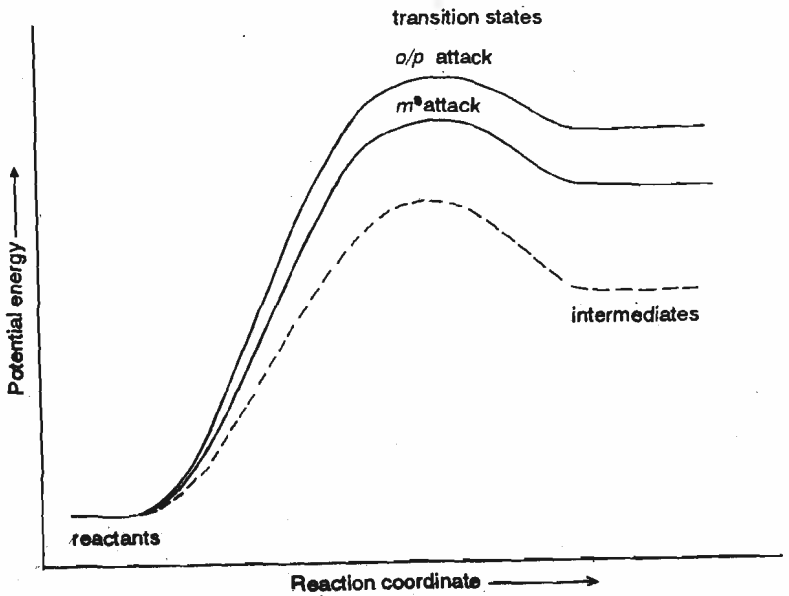
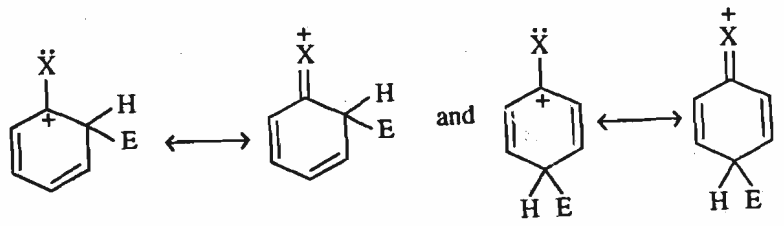


Fig. 4.8 : Schematic potential energy diagram for AESR in benzene (— — — —) and nitrobenzene (————)

Now if we take the case where the substituent is a halogen, the relative energies of the intermediates change. As halogens also have a —I effect, i.e., they withdraw electrons, they also deactivate the ring in general and the order of energies is expected to be similar to the ones given in Fig. 4.8. But in this case another effect comes into play whereby the halogen lone pair can enter into an interaction with the benzenium ion.

This gives additional resonating structures for *ortho* and *para* intermediates as shown below :



As a consequence the energies of *ortho/para* intermediates become lower than that of the *meta* intermediate. The potential energy diagram for such a case is given in Fig. 4.9. So, the halogens as you can see, inspite of being electron withdrawing (deactivating) would be *ortho/para* directing.

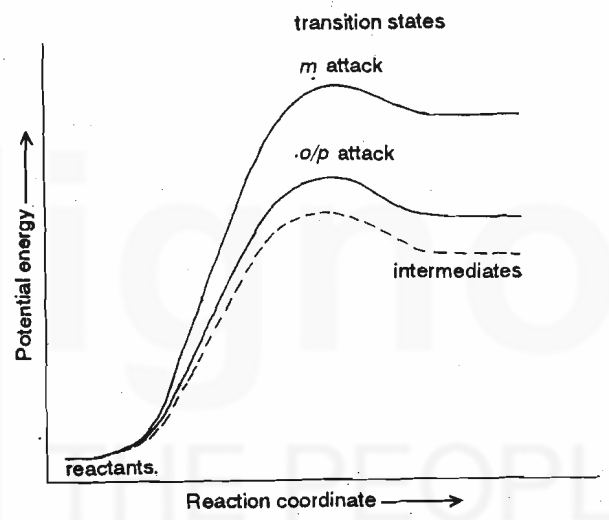
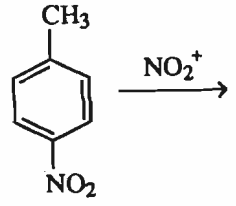


Fig. 4.9 : Schematic potential energy diagram for AESR in benzene (— — — —) and chlorobenzene (————)

SAQ 7

Predict the products of the following reactions.

i) 

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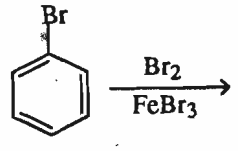
ii) 

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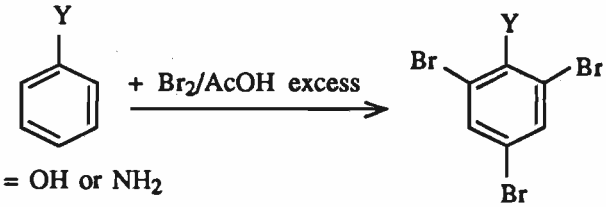
The nature of product in electrophilic aromatic substitution very often depends upon the conditions of the reaction such as the nature of substrate, nature of reagent, order of reagents and temperature. The following examples are illustrative :

- **Nature of substrate**

Highly activating group

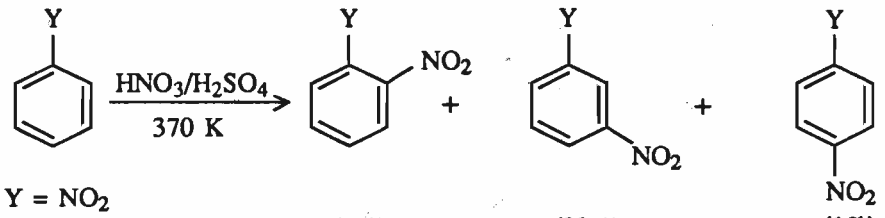


(reaction takes place at room temp., No Lewis acid is required.)

Y = OH or NH_2

tribromo derivative

Deactivating group

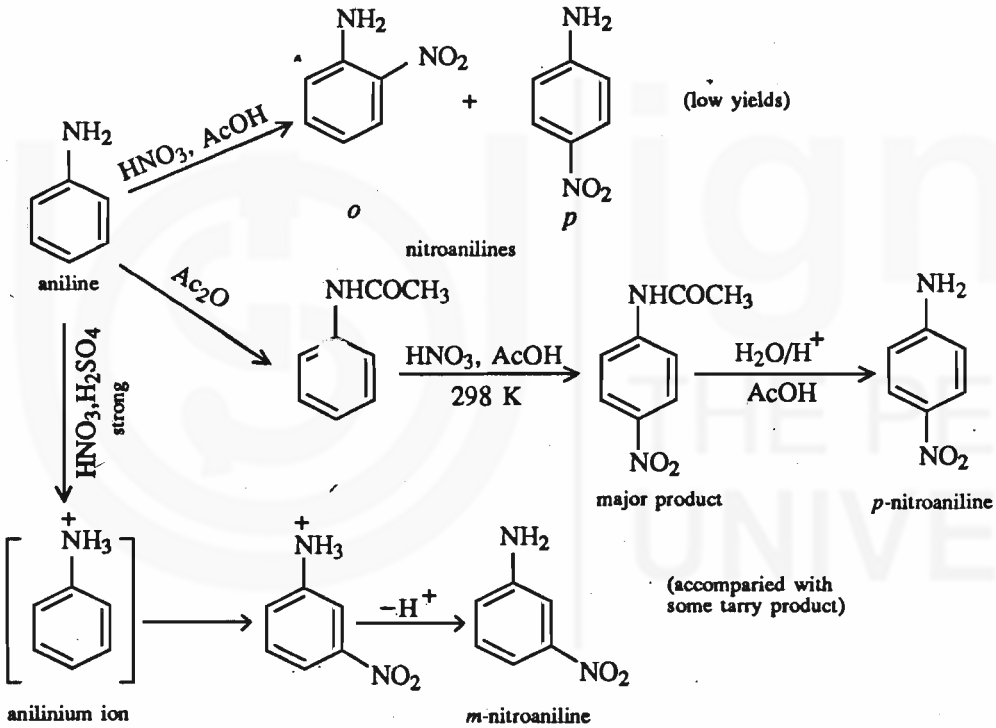


Y = NO_2

o (7%) *m* (88%) *p* (1%)

dinitrobenzenes

- **Nature of reagent**



(low yields)

o *p*

nitroanilines

major product

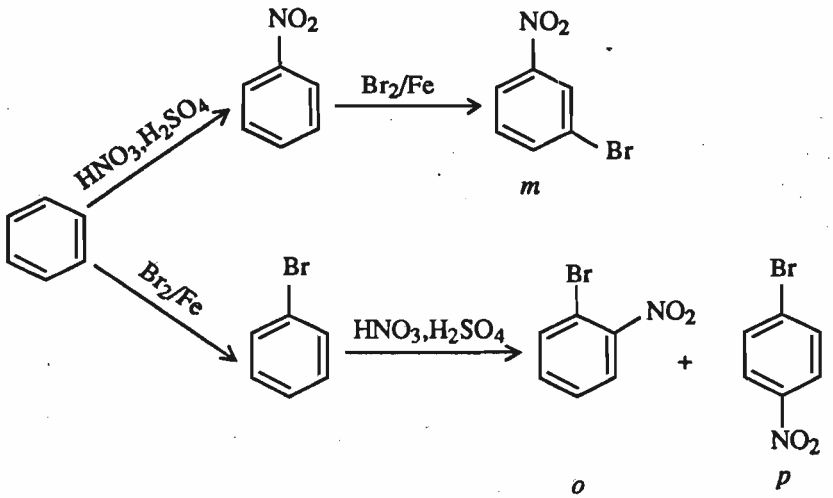
p-nitroaniline

(accomparied with some tarry product)

anilinium ion

m-nitroaniline

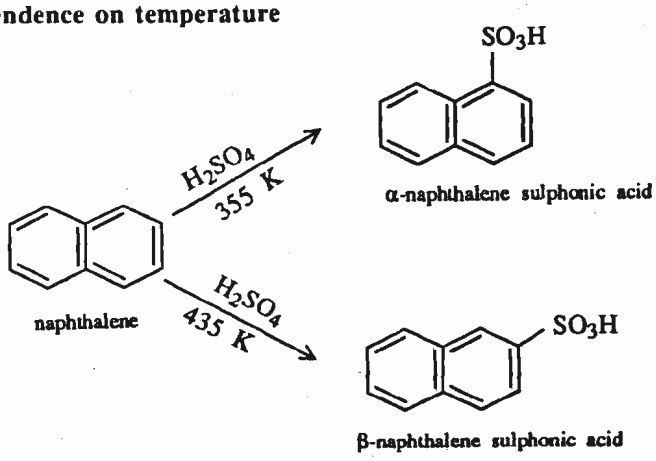
- **Order of reagents**



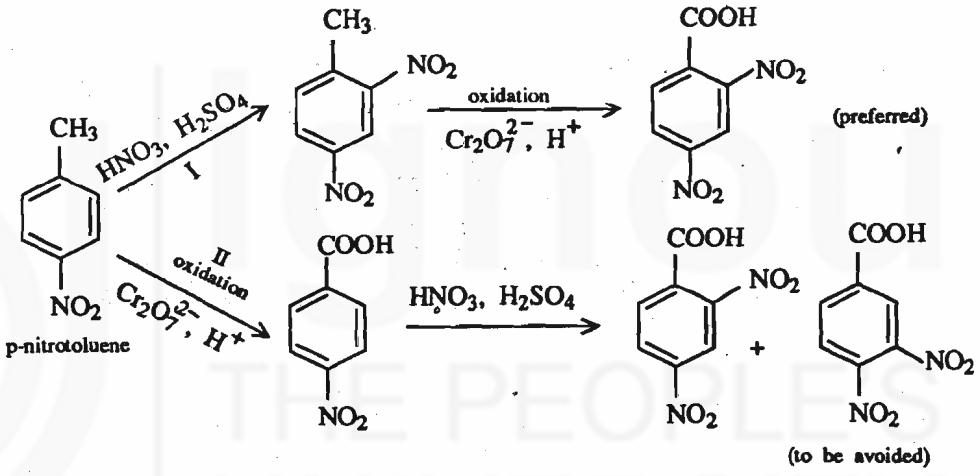
m

o *p*

● **Dependence on temperature**



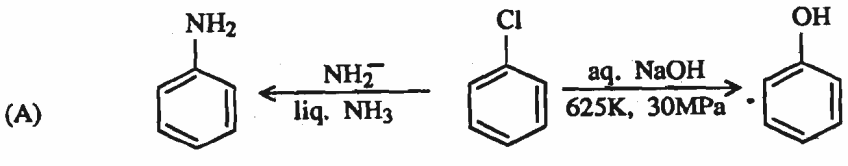
The aim in synthesis is to prepare one single compound. Reactions giving mixtures are to be avoided. For example, in order to prepare 2, 4-dinitrobenzoic acid, it is preferable to follow route I in which p-nitrotoluene is nitrated to give 2, 4-dinitrotoluene which is oxidised to give 2, 4-dinitrobenzoic acid as a single product. Route II, in which *p*-nitrotoluence is first oxidised to *p*-nitrobenzoic acid, on nitration gives a mixture of products and therefore should be avoided.

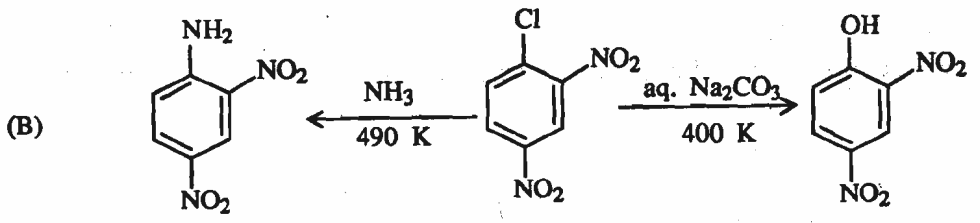


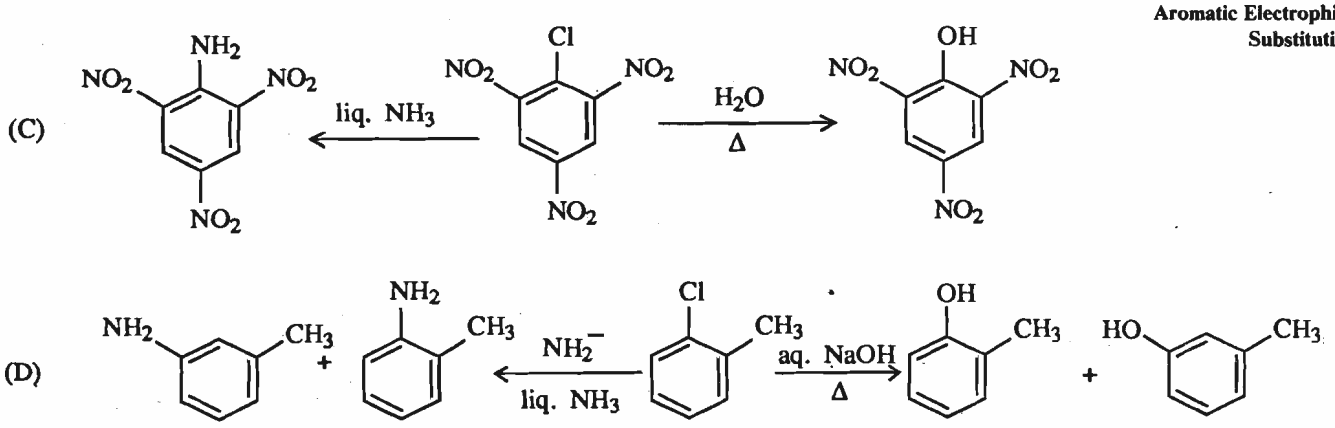
4.7 AROMATIC NUCLEOPHILIC SUBSTITUTION REACTIONS (ANSR)

We have seen in Unit 3 that aliphatic compounds readily undergo nucleophilic substitution while aromatic compounds do not.

Drastic conditions are required for aromatic nucleophilic substitution reactions (ANSR) as given in scheme IV.







Scheme-IV

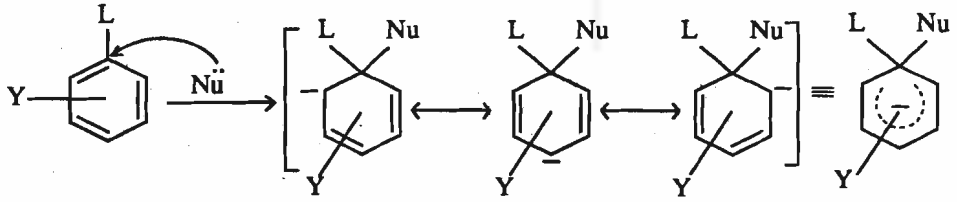
We can see that chlorobenzene needs very drastic conditions for nucleophilic substitution. The reaction condition requirements get milder with the introduction of electron withdrawing NO_2 groups (B&C) at ortho and para positions to the chloro substituent. The more the NO_2 groups, easier the substitution reaction. Interestingly introduction of the CH_3 group, which is electron donating, also makes the reaction conditions milder. In (D), we get two products of substitution as against one in other cases.

Two mechanisms are possible in aromatic nucleophilic substitution. These are **addition-elimination** or **S_NAr2** and **elimination-addition or benzyne** mechanism. In B and C types of scheme IV, addition-elimination mechanism with one product is predominant. While for A and D types, elimination-addition mechanism with two products is operative. However, two products in the case of chlorobenzene (A type) are identical. In a given reaction, both the mechanisms may be operative, albeit to different extent. Let us now try to understand their mechanisms in detail.

4.7.1 Addition-elimination or S_NAr2 Mechanism

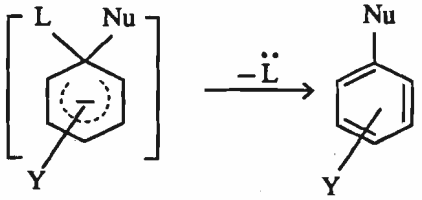
Aromatic compounds having electron attracting groups like NO_2 at *ortho* and *para* position to the leaving group undergo this kind of mechanism. It is a two step mechanism, addition in the first step is followed by elimination in the second step. In this mechanism, the nucleophile attacks the aromatic moiety and gets attached to it through one of the empty π orbitals at the substrate. This addition of the nucleophile to the aromatic ring generates an anion which is stabilised through resonance. In the scheme shown below,

Step I : Addition

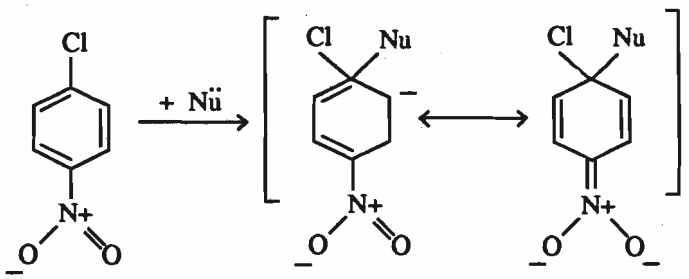


L is the leaving group, e.g., Cl in B and C and Y is some electron attracting group (NO_2) on the aromatic ring (Scheme IV). The addition intermediate is generally detected spectroscopically but sometimes it can be isolated also. It is called a **Meisenheimer complex.** After this addition step, the intermediate loses the leaving group which is eliminated also with its pair of electrons. The ring is rearomatised and we get the substituted product. This is shown as,

Step II : Elimination



In the attack of a nucleophile on *p*-nitrochlorobenzene, the intermediate can be stabilised as :



Evidence for the bimolecular nature of the mechanism comes from the fact that there is often very little difference in the reactivity of various aryl halides. Further, the fluoro derivative is the most reactive. The order being, Ar — F > Ar — Cl > Ar — Br > Ar — I. This is opposite to the trend observed in the case of aliphatic halides which is,

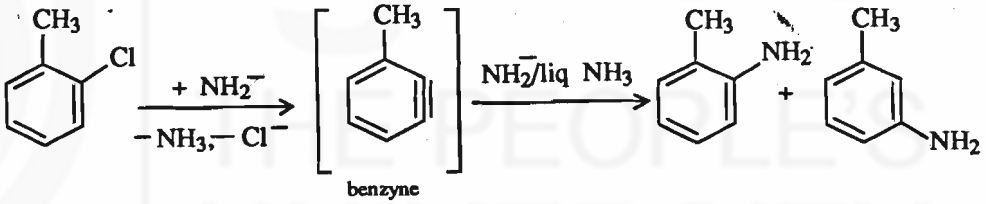
R — I > R — Br > R — Cl > R — F

Nondependence of reactivity on the C-halogen bond suggests that the reaction whose rate determining step is being measured does not involve breaking of the C — X bond.

The solvent effects in S_NAr2 are similar to the ones described for S_N2 reactions (Unit 3). Dipolar aprotic solvents increase the rate of the reaction.

4.7.2 Elimination-addition Mechanism

It has been shown that the compounds in A and D types (scheme IV) undergo nucleophilic substitution by a mechanism different from the one for the compounds belonging to C and D types. In type A we do not have any group which can activate the aromatic ring towards nucleophilic substitution. In type D we have, in fact, a deactivating group. In such cases drastic reaction conditions are required and the reaction proceeds by a mechanism entirely different from the addition-elimination mechanism. The mechanism here is **elimination-addition** or **benzyne.** You will read about this mechanism in detail in Unit 9 of this course.



4.7.3 Nucleophilic Substitution—Comparison between Aliphatic and Aromatic Compounds

The first and obvious observation is that while nucleophilic substitution is a characteristic reaction of aliphatic halides it is not so common in aromatic systems. Secondly, the benzyne mechanism is not possible in aliphatic compounds. The nucleophilic substitution of aliphatic compounds can be compared only with S_NAr2 mechanism of aromatic compounds. In S_N2 mechanism the substrate-nucleophile adduct is an unstable species with high energy and corresponds to the top of the energy barrier (Fig. 3.1 in Unit 3). On the other hand, In S_NAr2 mechanism, the intermediate is reasonably stabilised by reasonance and is actually a compound which, in some cases, can even be isolated.

The role of leaving group in determining the rate of a reaction is different in alkyl and aryl halides. In aliphatic halides the order of reactivity of the halogens is I > Br > Cl > F. The governing factor being the bond strength. In the case of aromatic nucleophilic substitution, formation of addition intermediate is the rds and C—X bond strength does not affect the rate. The order is F > Cl > Br > I. The governing factor here is the polarity of the C—X bond. A more polar C—F bond favours the addition of nucleophile and increases the rate.

4.8 Summary

Now we will summarise what all has been discussed about substitution reactions of aromatic compounds in this unit.

Inspite of being unsaturated species, the aromatic compounds are relatively inert towards addition. They undergo nucleophilic substitution with great difficulty and readily undergo electrophilic substitution reactions. The inactivity has been explained in terms of aromaticity for which various experimental and theoretical criteria are responsible. According to one of these difinitions of aromaticity, a planar, cyclic molecule with $(4n + 2)$ π electrons capable of delocalisation is aromatic.

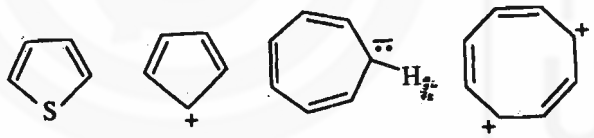
Different aromatic electrophilic substitution reactions proceed by more or less a similar mechanism and a general mechanism can be given for the same. In a two step mechanism, the first step involves the attack of an electrophile to give a benzenium ion intermediate. This slow step is followed by a fast step where a proton is lost to give the substituted product. Evidence for the mechanism is sought from kinetic isotope effect studies and other experiments. With the help of the general mechanism, mechanism for other AESRs like nitration, halogenation, sulphonation, alkylation and acylation can be explained. Five and six membered heteroaromatic compounds like pyrrole and pyridine, also undergo electrophilic substitution reactions. The mechanism in this case can be compared with that in benzene in terms of reactivity and orientation.

Electrophilic substitution in monosubstituted benzene depends upon the reactivity of the substrate and the directive influence of the substituent. The electron releasing groups activate while electron withdrawing groups deactivate the aromatic ring towards electrophilic substitution. Further, the substituent also directs the incoming electrophile to *ortho/para* or *meta* position. Ring activating groups are, by and large, *ortho/para* directing. While ring deactivating groups are *meta* directing. Halogens are an exception as they are deactivating as well as *ortho/para* directing.

Nucleophilic substitution, though not very common in aromatic compounds, does occur. The two types of mechanisms operative are addition-elimination (S_NAr2) and elimination-addition (benzyne mechanism). S_NAr2 and S_N2 mechanisms of the aromatic and aliphatic nucleophilic substitution reactions respectively can be compared.

4.9 TERMINAL QUESTIONS

1) Indicate whether the following planar species are aromatic or not. Give reasons for your answer.

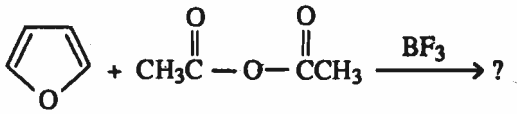


2) 1, 3, 5-cycloheptatrienyl cation is aromatic where as, 1, 3, 5-cycloheptatriene is not. Explain.

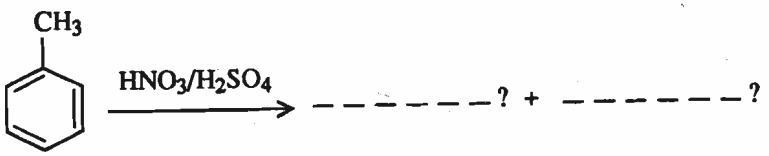
1, 3, 5-cycloheptatriene 1, 3, 5-cycloheptatrienyl cation

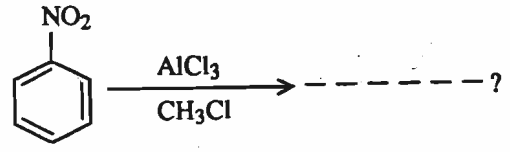
3) How would you explain the kinetic isotope effect observed for sulphonation of benzene?

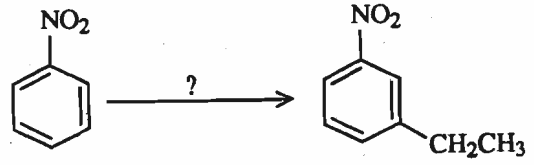
4) Complete the following reaction and give its mechanism.

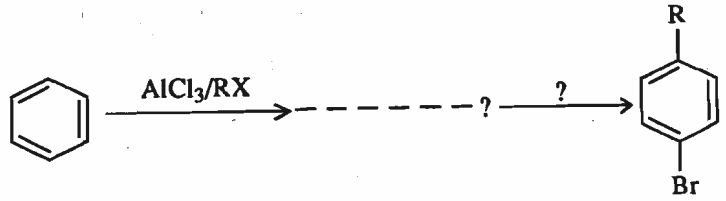


5) Complete the following reactions :

a) 

b) 

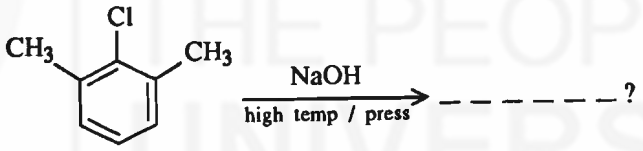
c) 

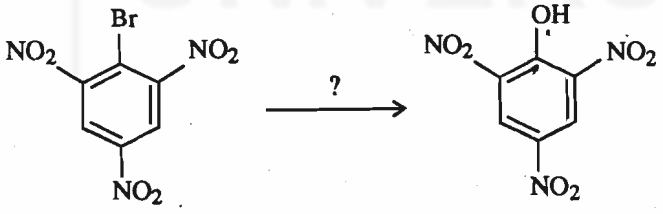
d) 

6) Methyl group is *ortho/para* directing while trichloromethyl group is *meta* directing. Explain.

7) Complete the following reactions :

a) 

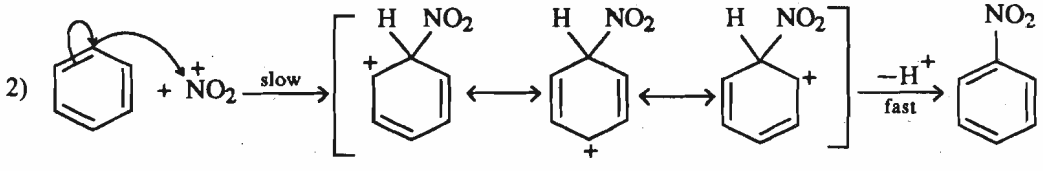
b) 

c) 

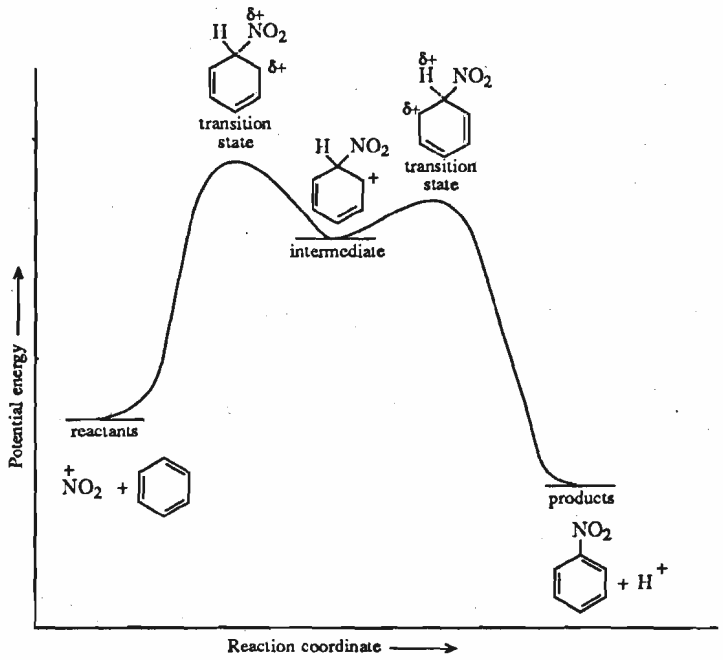
4.10 ANSWERS

Self Assessment Questions

1) It is not planar molecule hence the π electrons are not completely delocalised as in benzene.

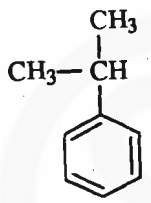
2) 

3)

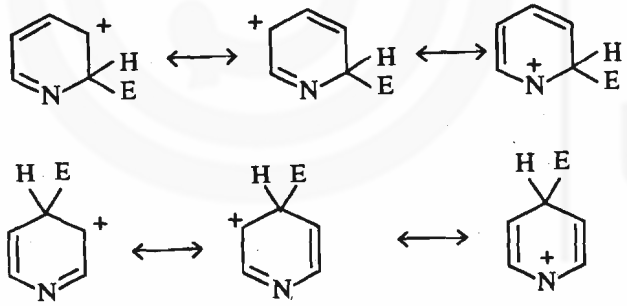


4) i) $CH_3CH_2CH_2Cl/AlCl_3$

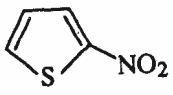
ii)



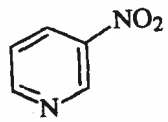
5)



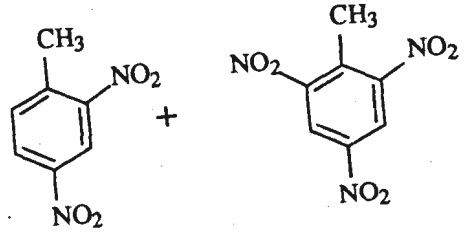
6) i)

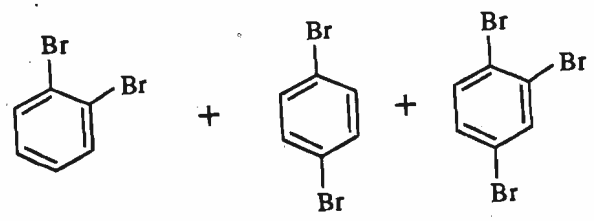


ii)



7) i)

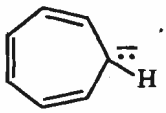


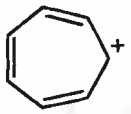
ii) 

Terminal Questions

1)  Aromatic; there are 2π electrons from C = C and two from an electron pair on S to make an aromatic sextet.

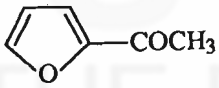
 Nonaromatic, has only 4 π electrons

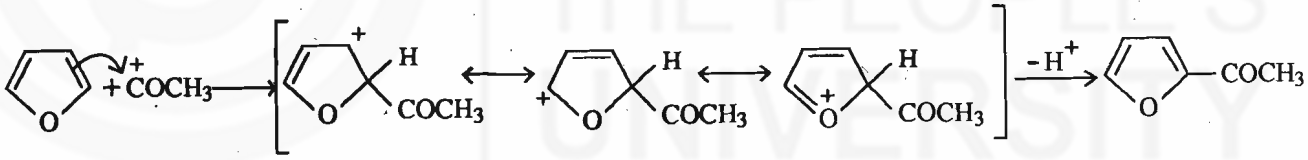
 Nonaromatic with 8π electrons

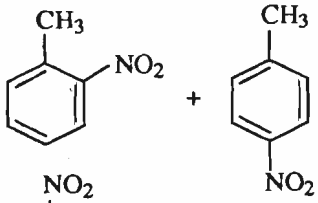
 Aromatic with 6π electrons.

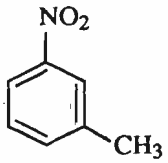
2) Cycloheptatriene has got three double bonds i.e. 6π electrons but because of the presence of sp^3 carbon atom, these π electrons cannot undergo cyclic overlapping. Generation of the cation removes the hinderance and the delocalised 6π electrons (Hückel rule) make the cation aromatic.

3) Hint—Consult Fig. 4.6 and its explanation in the text.

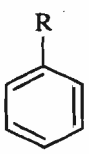
4) The product is  and the mechanism is as follows :



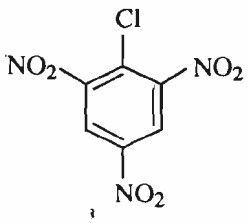
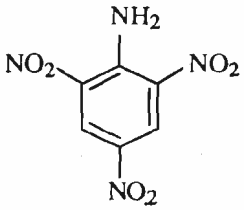
5) a) 

b) 

c) $CH_3CH_2Cl/AlCl_3$

d)  ; Br_2

6) The carbon atom in trichloromethyl group becomes positive due to the presence of three chlorine atoms and makes the group deactivating and hence *meta* directing.

7) a)  

b) No reaction, no hydrogen available at *ortho* position to halogen.

c) H_2O/Δ

Further Readings

1) *A Guidebook to Mechanism in Organic Chemistry;* Peter Sykes, Fifth edition; Longman, New York, 1981.

2) *Organic Chemistry;* R.T. Morrison and R.N. Boyd, 5th edition, Prentice-Hall of India Pvt. Ltd.

3) *Organic Chemistry;* Vol. I and II: S.M. Mukherji, S.P. Singh and R.P. Kapoor; Wiley Eastern Ltd.

NOTES