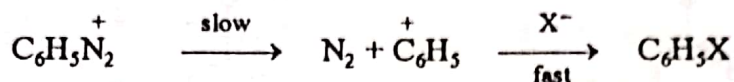# 15.20 Nucleophilic Aromatic Substitution

The replacement of hydrogen or a substituent by a nucleophilic reagent is known as nucleophilic aromatic substitution. It must be noted that the nucleophilic substitution does not take place with the benzene itself but with its some substituted derivatives and with naphthalene. The unreactivity of benzene itself towards nucleophilic reagents is partly due to the concentration of negative charge above and below the plane of the ring carbon atoms and partly due to the formation of less stable hydride ion.

$$C_6H_6 + X^- \longrightarrow C_6H_5X + H^-$$

There are three mechanisms under which all nucleophilic aromatic substitution reactions fall viz. unimolecular, bimolecular and benzyne type.

1. **Unimolecular substitution :** There is only one example of unimolecular nucleophilic aromatic substitution and that is the uncatalysed decomposition of aryl diazonium cation.
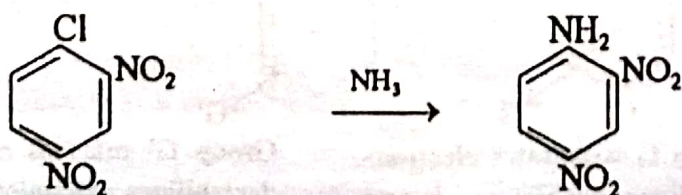
$$C_6H_5\overset{+}{N_2} \xrightarrow{slow} N_2 + \overset{+}{C_6H_5} \xrightarrow[fast]{X^-} C_6H_5X$$

where $\bar{X} = \bar{O}H, \bar{O}R, \bar{C}l, \bar{I}, \bar{C}N$ or $\bar{N}O_2$
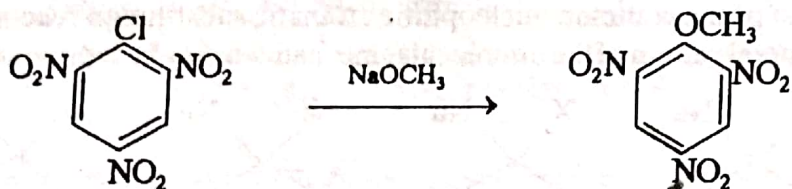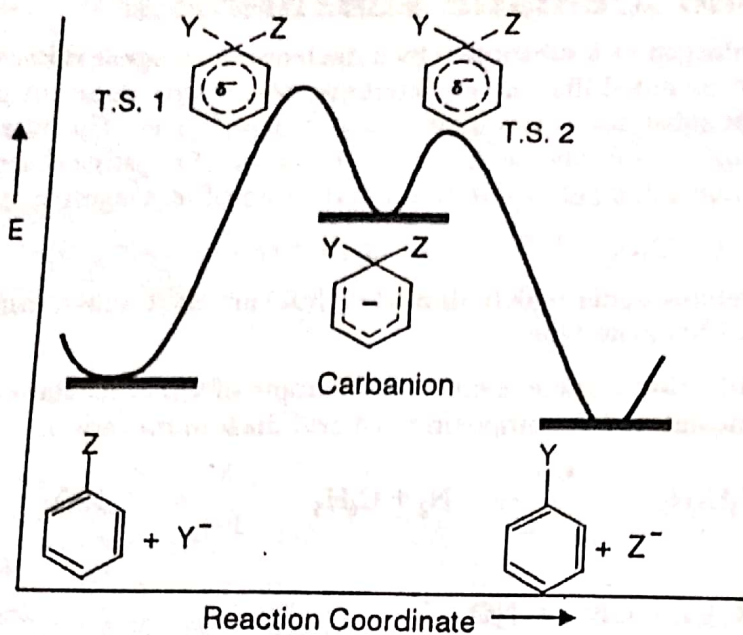
2. Bimolecular substitution : Most of the common nucleophilic aromatic substitution reactions proceed by bimolecular mechanism. The general pattern of the bimolecular mechanism may be represented as below.

Resonating structures of the
phenonium carbanion (cyclohexadienyl anion) intermediate
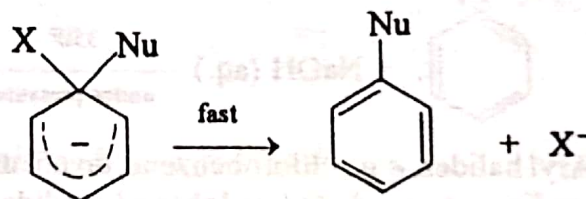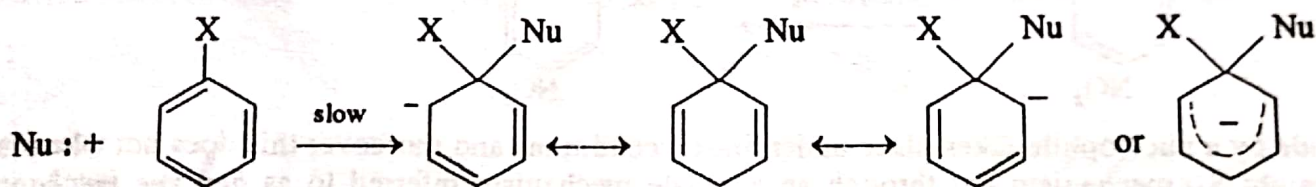
The formation of intermediate during bimolecular nucleophilic aromatic substitution and hence, two-step mechanism for such reaction is confirmed by energy diagram (Fig. 15.6 on the next page).

However, in nucleophilic substitution reactions the potential leaving group (usually halogen atom) has non-bonding pair of electrons which are in conjugation with the benzene ring, its displacement is a rather difficult process. But if the aryl halide is appropriately substituted by the electronegative group (e.g., —NO₂) in the o- or p- position the halogen atom can be easily displaced by the nucleophile, i.e., nucleophilic substitution becomes feasible. Thus, the chlorine atom of 2, 4-dinitrochlorobenzene and 2, 4, 6-trinitrochlorobenzene is easily substituted by the nucleophile. Replacement of halogen of an

Energy diagram: T.S. 1, T.S. 2, Carbanion intermediate, Reaction Coordinate, E

$$O_2N{-}C_6H_3(Cl)(NO_2){-}NO_2 \xrightarrow{\text{NaOCH}_3} O_2N{-}C_6H_3(OCH_3)(NO_2){-}NO_2$$

aryl halide by a nucleophile takes place under drastic conditions and moreover this does not take place by a straight S_N mechanism but through an alternate mechanism referred to as *benzyne mechanism* (discussed further).

$$C_6H_5Cl + NaOH\ (aq.) \xrightarrow[\text{under pressure}]{350°} C_6H_5OH$$
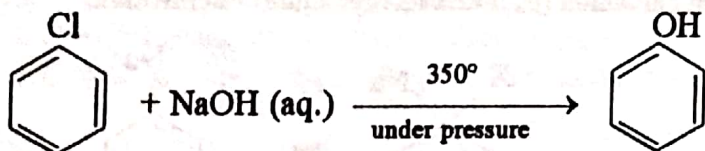
Aryl halides, *e.g.*, chlorobenzene, do not undergo nucleophilic bimolecular substitution because the corresponding intermediate (cyclohexadienylide ion) is not capable of being accommodating the negative charge present in the *ortho* and *para* positions. In case an electron-attracting group (*e.g.*, $-NO_2$) is present in *ortho* and/or *para* position to the halogen atom, it accommodates negative charge on the respective position with the result that particular resonating structure becomes more stable and hence such intermediate is liable to be formed, *i.e.*, the compound undergoes substitution easily. Thus, in short any group that withdraws electrons, stabilizes the carbanion and thus, increases nucleophilic substitution; on the other hand, the group that releases electrons will intensify the negative charge and thus, destabilises it and hence, slows down the substitution reaction.
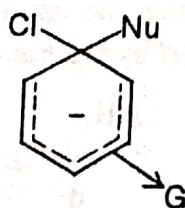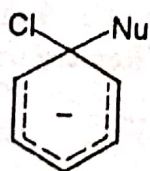
Group G withdraws electrons, stabilizes carbanion, hence, activates substitution
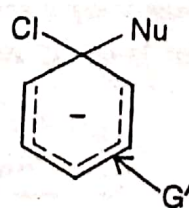
Group G′ releases electrons, destabilizes carbanion, hence, deactivates substitution

It is worth-noting that an electron withdawing group helps in dispersing the negative charge, thus, stabilizing the intermediate carbanion when it is present in the *ortho* or *para* position (not in *meta*). This can be realised by drawing and comparing the resonating structures of the intermediate carbanion obtained by the attack of nucleophile on *p*-, *o*- and *m*- nitrochlorobenzenes.
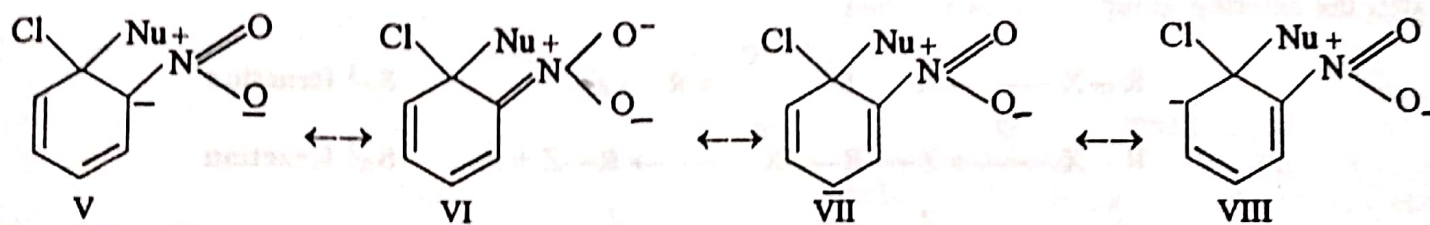
Possible resonating structures for the carbanion obtained during *p*-attack
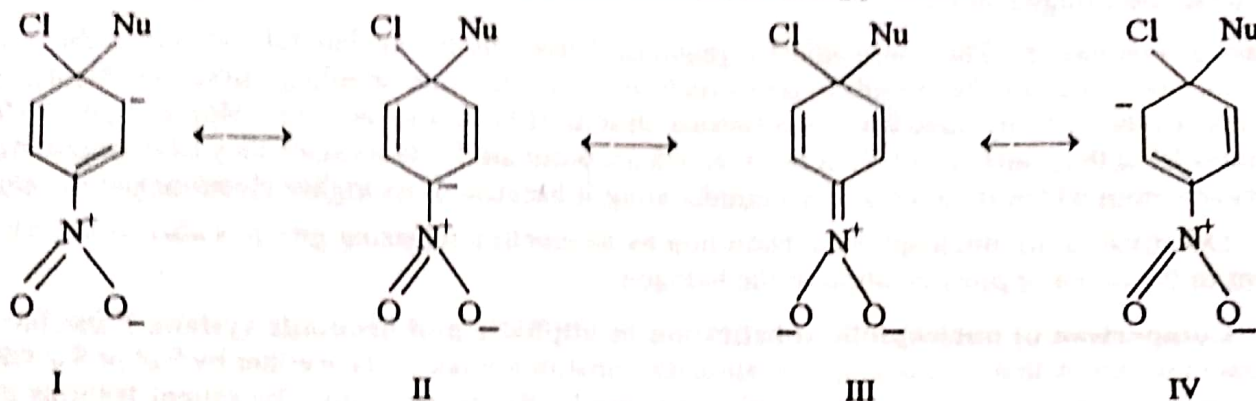
|	Especially stable since negative charge is present on C bearings —NO_2 group	Especially stable since negative charge is carried by oxygen of the —NO_2 group	
I	II	III	IV

Possible resonating structures for the carbanion obtained during *o*-attack.

V	VI	VII	VIII
Especially stable as negative charge is present on C having —NO_2 group	Especially stable as negative charge is present on oxygen		

Possible resonating structures for the carbanion obtained during *m*-attack.
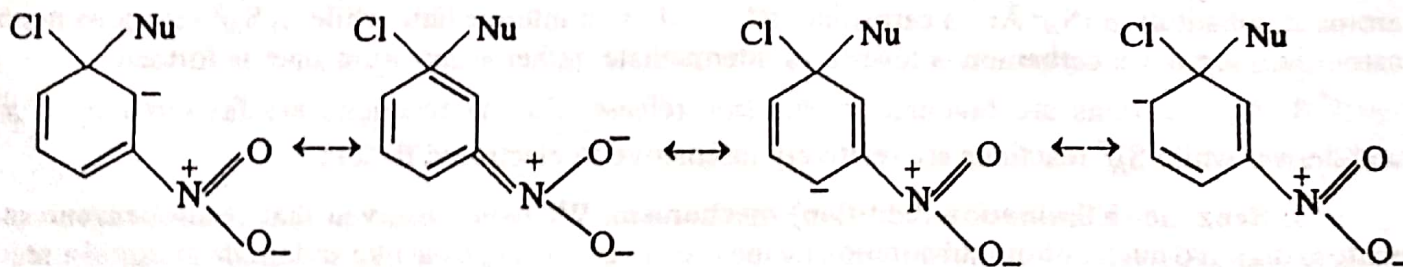
(Such structure not possible since one of the C atoms becomes pentavalent)

Let us compare the impacts of inductive effect and resonance on the intermediates of the *p*-, *o*- and *m*- attacks.

Impact of Inductive Effect

Although —NO_2 group, being electronegative, attracts electrons from all positions of the ring it does so most readily from the carbon atom nearest to it with the result a structure having negative charge on

the carbon atom bearing —NO_2 group is most liable to be formed. In other words, carbon atom having —NO_2 group is most capable of accommodating the negative charge and hence, it is more stable. Note that such structure is present in the *para* attack (structure II) as well as in *ortho* attack (structure V) but not in *m*-attack. Thus, we can say that the carbanions corresponding to the *p*- and *o*- attacks are more stable than that of the *m*- attack and hence, nucleophilic substitution occurs readily when the —NO_2 group is present *p*- or *o*- to the halogen atom.

Impact of resonance : The intermediate carbanions formed by the nucleophilic attack on the *o*- and *p*-chloronitrobenzenes are the hybrids of four structures, while the corresponding carbanion obtained during *m*-attack is hybrid of only three structures because structure like X is not possible. Moreover, the additional structures III in the *p*-attack and VI in the *o*- attack are particularly stable since they have negative charge on oxygen atom which is capable of accommodating it because of its highly electronegative nature.

Deactivation for nucleophilic substitution by an electron releasing group is also strong when it is present in the *ortho* or *para* position to the halogen.

Comparison of nucleophilic substitution in aliphatic and aromatic system. From the earlier discussion we know that the nucleophilic aliphatic substitution takes place either by S_N^1 or S_N^2 while the nucleophilic aromatic substitution takes place mainly by S_N^2 mechanism. The salient features of these mechanism are summarised below for comparing them.

1. **In S_N^1 reactions**, the departing group leaves the molecule before the entering group becomes attached ; in S_N^2 reactions the departing group leaves and the entering group attaches the substrate molecule at the same time; while in nucleophilic aromatic substitution reactions the leaving group leaves the molecule after the entering group becomes attached
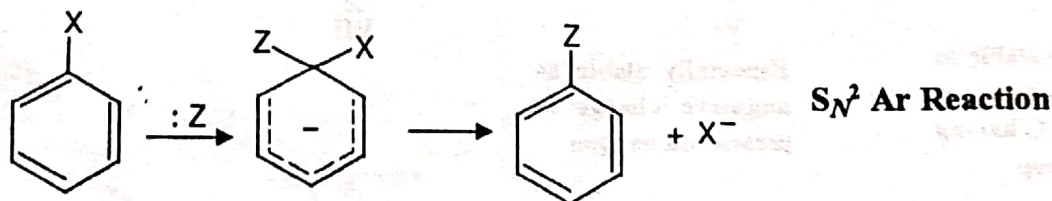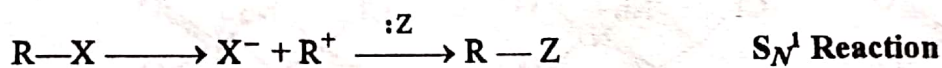
2. In S_N^1 reactions, a carbonium ion is formed as an intermediate, in bimolecular nucleophilic aromatic substitution (S_N^2 Ar), a carbanion is formed as an intermediate while in S_N^2 reactions neither a carbonium ion nor a carbanion is formed as intermediate, rather a transition state is formed.

3. S_N^1 reactions are favoured by electron release, S_N^2 Ar reactions are favoured by electron withdrawal while S_N^2 reactions are relatively insensitive to electronic factors.

3. **Benzyne (Elimination-Addition) mechanism.** We have observed that chlorobenzene can be made to undergo nucleophilic substitution by the use of very strong base like sodamide in liquid ammonia. However, in this case, substitution does not take place by the usual bimolecular mechanism but by an entirely different mechanism : the *benzyne* (or *elimination-addition*) *mechanism*.
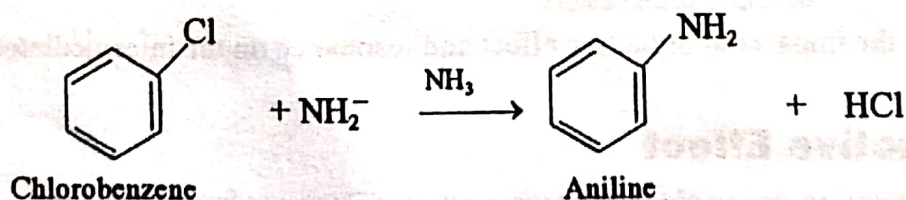
The reaction is not the simple displacement but involves two stages; elimination followed by addition.

(i) **Elimination stage :** This stage again involves two steps :

(a) abstraction of a hydrogen ion by the amide ion to form ammonia and carbanion I, and (b) the carbanion I loses halide ion to form benzyne.

(a)

Chlorobenzene $+ \overline{NH}_2 \longrightarrow$ I $+ NH_3$

(b)

I $\longrightarrow$ Benzyne $+ Cl^-$
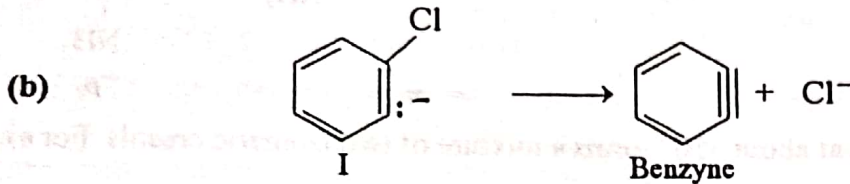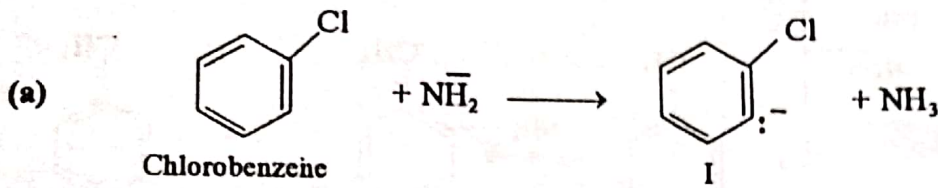
(ii) **Addition stage :** This stage again involves two steps : (a) attachment of amide ion on the benzyne intermediate to form carbanion II, and (b) in the second step the carbanion II abstracts a proton from ammonia (hence, note that here ammonia is acting as an acid) to form aniline.

(a)

Penzyne $+ NH_2^- \longrightarrow$ II

(b)

II $+ NH_3 \longrightarrow$ Aniline $+ NH_2^-$
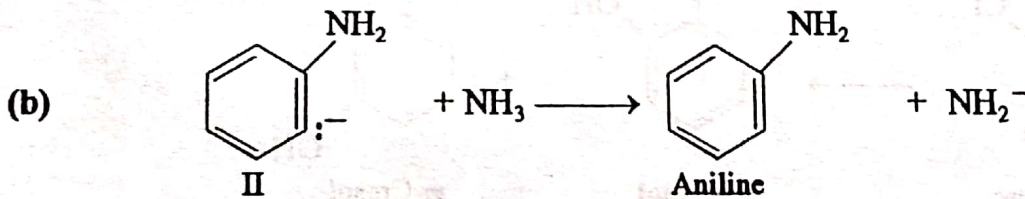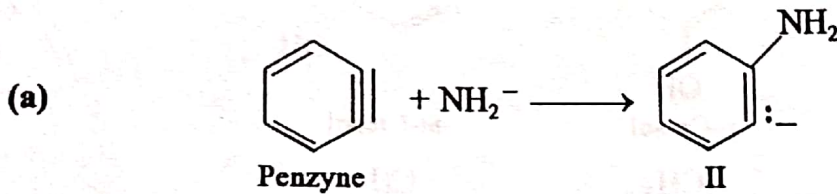
Evidences in favour of benzyne mechanism : (i) The formation of a benzyne intermediate has been proved by Professor J.D. Roberts (1953) from the following observation. When a chlorobenzene labelled at $C_1(CCl)$ is treated with potash amide, the product, aniline is found to contain labelled carbon on C_1 as well as on C_2 with respect to the amino group.

$\longrightarrow$

Aniline
having C^{14}—NH_2

$+$

Aniline
having C—NH_2
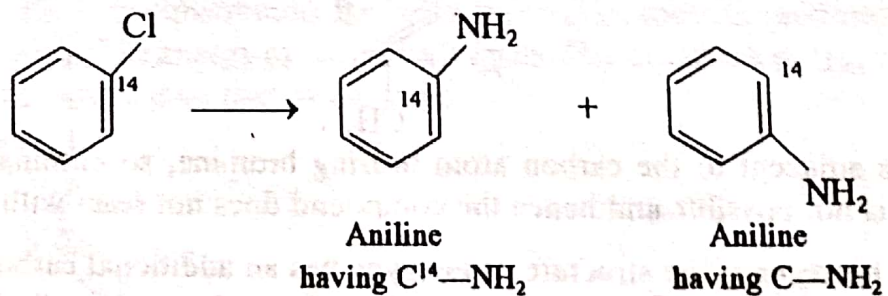
(ii) The formation of all the three toludines from *m*-chlorotoluene can be explained on the basis of the formation of benzyne as intermediate.
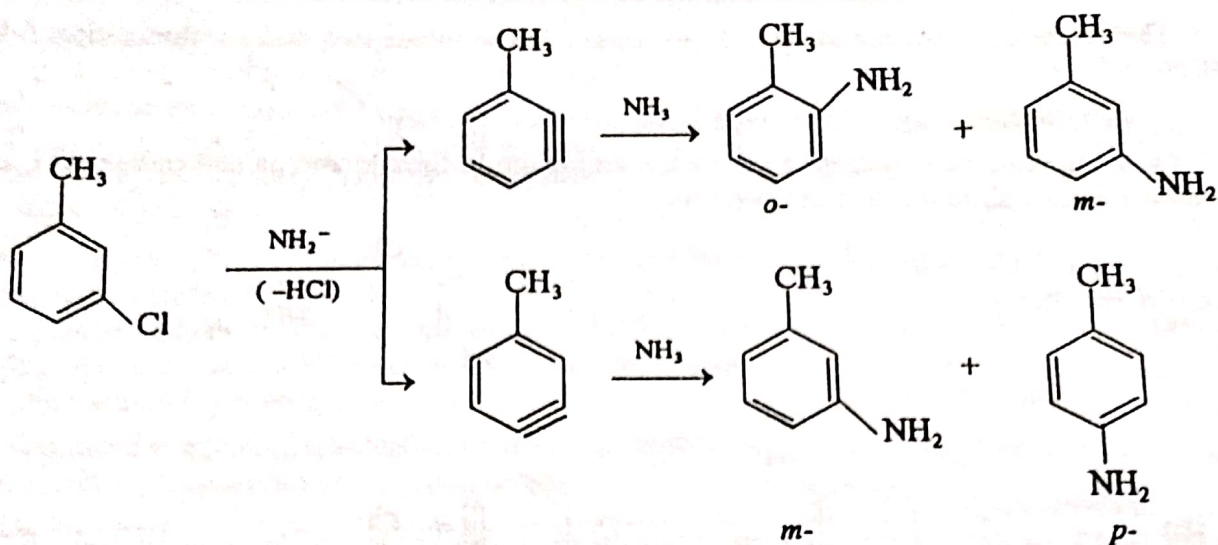
(iii) Hydrolysis of chlorotoluenes at about 350° forms a mixture of two isomeric cresols. For example,

| p-Chlorotoluene | p-Cresol | m-Cresol |

| o-Chlorotoluene | o-Cresol | m-Cresol |
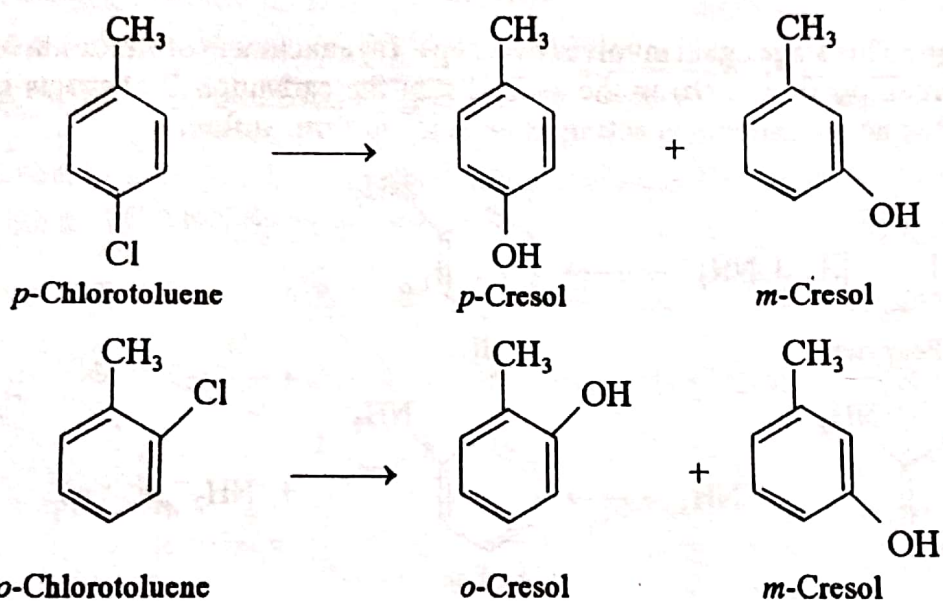
(iv) Lastly it must be noted that the bromomesitylene does not have any hydrogen atom on the
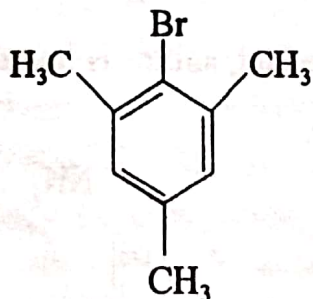
carbon atoms adjacent to the carbon atom bearing bromine, so elimination of HBr to form benzyne intermediate is not possible and hence the compound does not react with sodamide in liquid ammonia