Aromatic electrophilic Substitution Reaction

An electrophilic substitution reaction may be represented as —

$$R - L + E^{\oplus} \longrightarrow R - E + L^{(+)}$$

Here the leaving electrophile or better electrofuge is $L^{(+)}$ gets displaced by $E^{(+)}$ the incoming electrophile. The $E^{(+)}$ may be NO_2^+, NO^+, $Br^{(+)}$, $Cl^{(+)}$, $I^{(+)}$, $R^{(+)}$, RCO^+, i.e. positively charged species or electron deficient uncharged species like SO_3, BF_3 etc.

It has been stated that an aromatic ring has negetive charge cloud below and above its plane. Electrophiles being positively charged or electron deficient species, they are very prone to attack the negetive charge cloud of the delocalised π es.

Therefore, it might be expected that electrophilic reactions will occur on aromatic rings much readily; but an aromatic compound wants to preserve its aromatic character and hence its stability, and therefore it is to some extent reluctant to utilise its π es.

For this reason the electrophiles react with aromatic compounds but not readily, rather slowly. However, the most important type of reactions that the aromatic compounds undergo is bimolecular electrophilic substitutions which are designated as S_E^2 aromatic.

Aromatic S_E^2 reactions are supposed to occur in two discrete steps:

Step 1. In this step the electrophile, $E^{\oplus}$, is attacked by the aromatic substrate laterally i.e. perpendicular to the ring and forms

a sigma - complex or wheland complex (or hexadienyl cation in the case of benzene) in which a specific atom of the electrophile forms a covalent bond with a specific C atom of the ring; the involved sp^2 hybridised C atom of the ring then assumes sp^3 hybridised state. Let us represent the step taking benzene as an aromatic substrate.
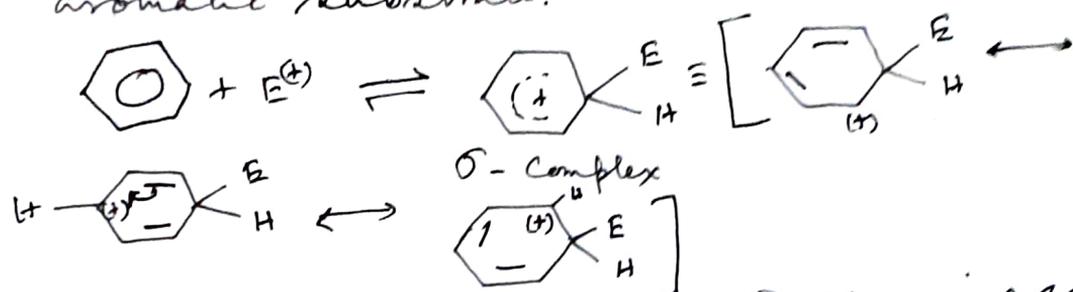

σ - Complex

The sigma - complex so formed remains as a salt which is formed by the union of the cationic σ - complex with an anion.

Step II. In this step, the σ- complex gives up a proton and gets converted into another aromatic compound, a derivative of the aromatic substrate; the proton is removed by the anionic part of the σ - complex salt.
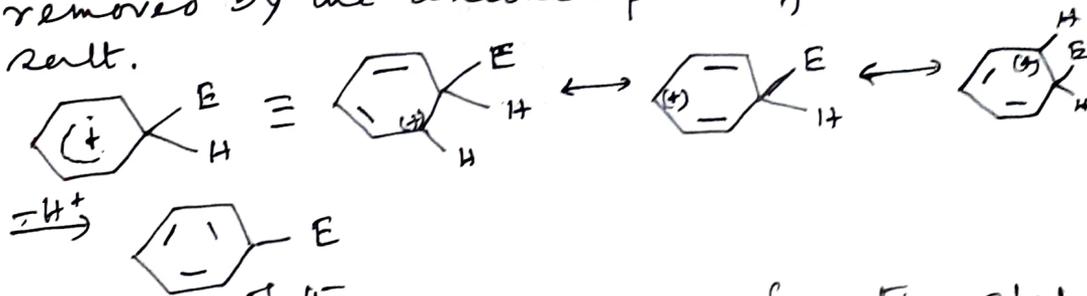
In most cases of the the σ - complex formation step is the slower step and hence it is the rate determining step. Since σ- complex consists of the electrophile and the substrate the transition of the reaction involves each of them; and hence aromatic electrophilic substitution are usually bimolecular reactions. The T.S of the step 1, the rate - determining step, and that of the step II may be represented as:


TS 1   TS II
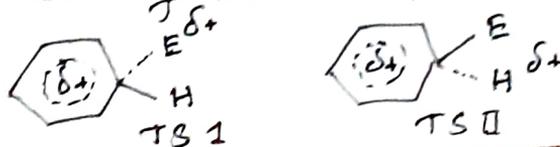
There fore the overall reaction may be written as:

TS I

σ - complex

TS II

−4 +

E
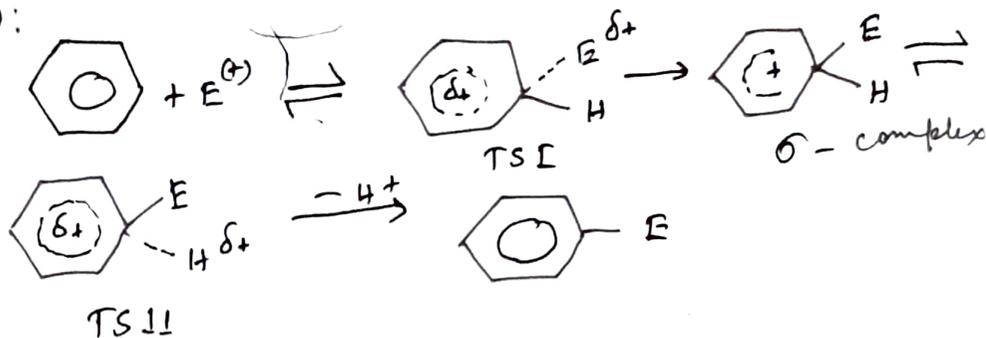
Since the TS of the rate-determining step of an aromatic S_E2 reaction involves two species, it is expected that the reaction will follow the 2nd order kinetics.
The energy profile for the reaction is shown below.

Progress of the reaction

I
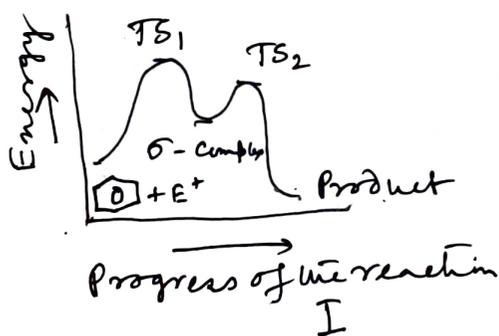
a) The energy profile of an exothermic aromatic SE2 reaction with out the formation of a π - complex

Of course, one may suppose that an aromatic SE2 reaction consists of four steps involving two π and one σ complexes as shown below.

Step 1: formation of a π complex (Pi complex)

+ E⁺ (electrophile) ⇌ slow
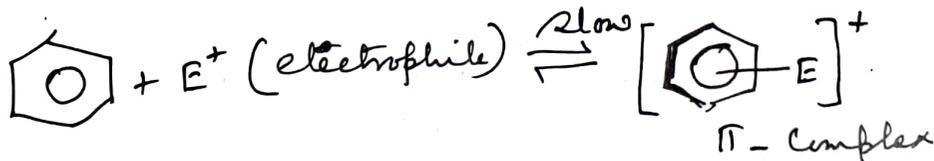
π - complex

Step 2: Conversion of a π complex into a σ com- plex
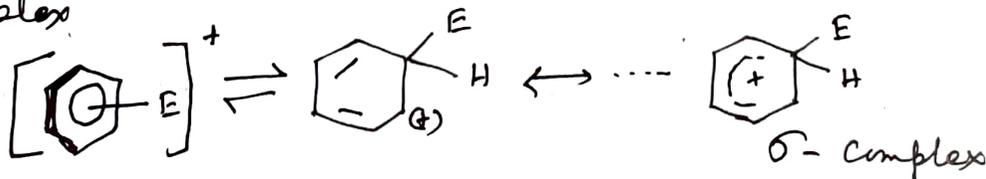
σ - complex

Step 3: Conversion of the σ-complex to a new π-co- plex
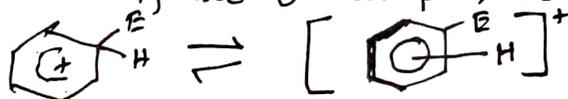
Step 4: Decomposition of π complex to produce

$$\left[\bigcirc\!\!\!\!\!\bigcirc\!-\!\overset{E}{\underset{H}{}}\right]^{+} \longrightarrow \bigcirc\!\!\!\!\!\bigcirc\!\overset{E}{} + H^{+}$$
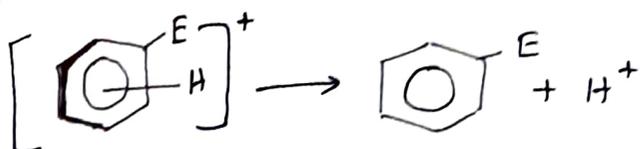
The energy profile of the 4-step rxⁿ is shown below.
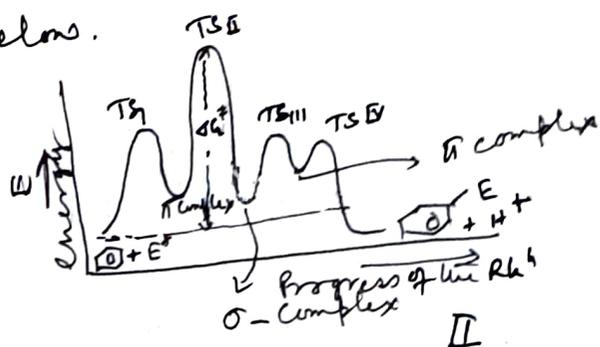
II

b) The energy profile of an exothermic aromatic SE2 reaction involving π-complex.

TS₁ - represents the transition state when in step 1 the electrophile is attracted by the electron cloud it is not formed easily as aromaticity is lost if goes through a transition state.

TS₂ - The transition step for the formation of sigma complex it has been shown earlier

TS₃ - It is also a transition state before formation of another π complex. H⁺ will not be removed easily it will also go through the transition state.

TS₄ - This transition is shown earlier in step 2 of the reaction.

The σ-complex contains the electrofuge (Here H) and electrophile both attached to a SP³ carbon atom, and there is a possibility that both may be eliminated at the aro- matisation step. Which group, i.e. either E or H will be eliminated depends on the following factors:

a) The polarisability of the bond attached to the electrofuge, and

b) The stability of electrofuge

Generally H atom attached to an SP^3 carbon atom of a σ-complex is acidic as the σ-complex being positively charged is electron attracting. As a result, C-H bond polarisability becomes more than the polarisability of C-E bond. Moreover the stability of $H^{(+)}$ is in general more than that of $E^{\oplus}$. As a result $H^{(+)}$ is eliminated quickly as soon as the σ-complex is formed.

Two situations may arise:

Case 1: Chlorination, Bromination or nitration reactions where

$$E^+ = Cl^+, Br^+, NO_2^+, etc.$$
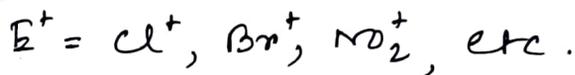
Cl^+, Br^+, NO_2^+ are poor electrofuges, so H^+ is eliminated fast as an electrofuge. As a result, chlorination, bromination and nitration reactions are irreversible in nature.
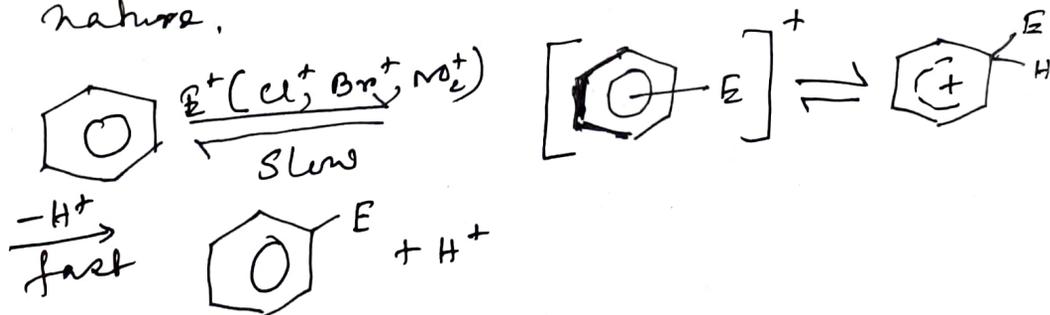
$\Delta G^{\ddagger}$ (activation energy) is too high for the reverse process due to poor electro fugacity of NO_2^+, Br^+, Cl^+ and thus, thus the reaction becomes irreversible in nature. The aromatisation step i.e. where H^+ is eliminated is a fast step, so we do not observe any PKIE (Primary kinetic isotope effect) for these type of reactions.

c) Fig II is the energy profile diagram of an irreversible $Ar\,S_E^2$ reaction

$$\Delta G^{\ddagger}_{-H^{(\oplus)}} \gg \Delta G^{\ddagger}_{-E}$$
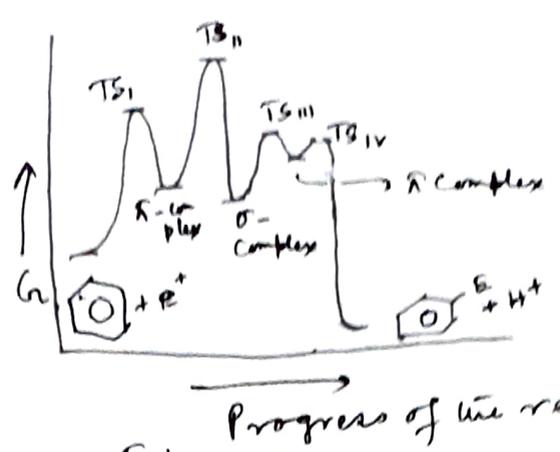
Fig – II

Case 2 — There are some electrophiles which take part in $Ar\,S_E^2$ reactions may eliminate as E^+ because these electrofuges are stable and $C-E$ bond has high polarisability. As a result, $\Delta G^{\ddagger}_{-E^+}$ becomes less than $\Delta G^{\ddagger}_{-H^+}$. Ultimately there is a competition between the two processes i.e. elimination of H^+ and elimination of E^+ both take place and the reaction becomes reversible in nature. This type of reaction includes alkylation, sulphonation, iodination etc of aromatic systems, where the active electrophiles are R^+, SO_3^+H, I^+ etc. These electrofuges are quite stable and bond polarisability of $C-E$ bond is quite high, even higher than $C-H$ bond. As a result $\Delta G^{\ddagger}_{-H^+}$ becomes some how higher than the $\Delta G^{\ddagger}_{-E^+}$. Expectedly $C-H$ bond breaking step becomes slow and it becomes the rate determining step. In other words alkylation, sulphonation and iodination in aromatic systems show primary kinetic isotopic effect (PKIE). For example the rate of sulphonation of

of hexa deuterobenzene is less than that of benzene ($k_H/k_D > 1$), but the rate of chlorination or nitration of benzene and hexa deuterobenzene shows the same rate. In the former case C–H bond breaking step is slow and reversible whereas in the latter it is a fast step

Naturally sulphonation reaction shows a prominent PKIE, whereas no PKIE is observed for nitration or chlorination reactions.

d)

$$\Delta G^{\ddagger}_{-H^+} > \Delta G^{\ddagger}_{-E^+}$$

Progress of the reaction
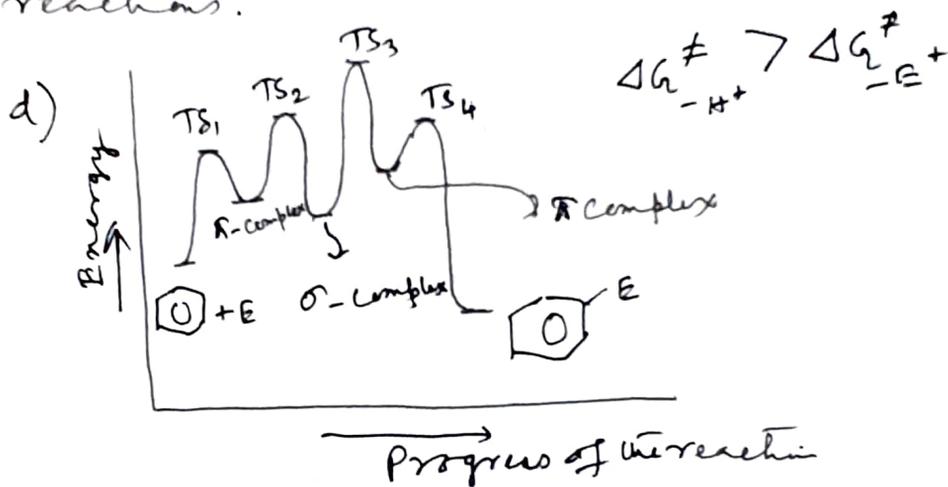
d) The energy profile diagram of a reversible for $S_E 2$ reaction.

Orientation of the Attacking Electrophile.

By orientation of the attacking electrophile in an aromatic electrophilic substitution reaction we mean the assigning of its position in the aromatic ring in which the attacking electrophile attaches itself.

when benzene undergoes electrophilic substitution only one mono substituted derivative of benzene is obtained since all the H atoms of benzene are equivalent. Here the question of orientation does not arise

In the cases of kinetically controlled reactions of mono and higher substituted benzenes and other aromatic rings (e.g

Pyrrole, Pyridine etc) all the ring H atoms are not equivalent and the attacking electrophile attaches it self to that C-atom where the electron density is relatively high.

Orientation in mono substituted benzenes: When a mono substituted benzene molecule under goes an electrophilic substitution reaction, the incoming electrophile (E^+) may have three orientations, ortho, meta and para with respect to the substituent already present in the ring.

ortho- isomer   Meta- isomer   Para-isomer
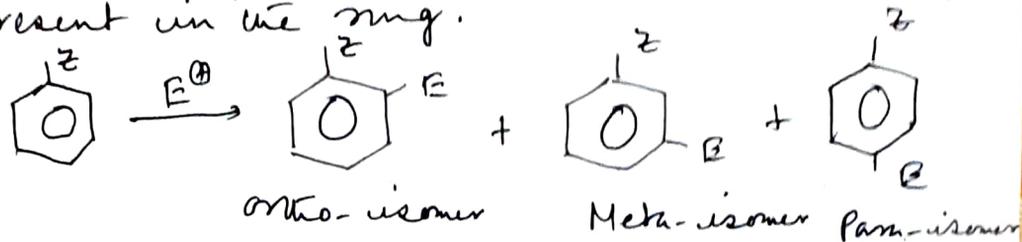
There are some groups which direct the incoming electrophile to take O and P - positions and the substituents are called activating or o/p directing groups. De activating substituents (excluding halogens) direct the incoming electrophile to acquire m- position and are known as m-directing group.

Here $-NO_2$, $-NO$, SO_3 group has $-I$ and $-R$ effect and are m-directing group.

where as $-CH_3$ group has $+I$ and hyper conjugative effect and is ortho, para orienting.

The o/p or m-directing nature of different groups may be explained by

a) Explanation on the basis of the stability of σ- Complex and

b) Explanation on the basis of charge distribution in the substrate.

Nitration of benzene - Substitution of a hydrogen atom in an aromatic nucleus by a nitro group ($-NO_2$) is known nitration of benzene

The nitration reaction may be carried out with several nitrating agents as given below.

1. Concentrated HNO_3 and glacial CH_3COOH
2. Dilute nitric acid (aqueous HNO_3)
3. 1:1 Concentrated HNO_3 in Concentrated H_2SO_4 (mixed acid)
4. Fuming HNO_3 in Concentrated H_2SO_4.
5. Fuming HNO_3 in Fuming H_2SO_4.
6. Acyl nitrates like acetyl and benzyl nitrate in organic solvent.
7. Nitrosonium salts like nitrosonium fluo borate ($NO_2^+ BF_4^-$)
8. Nitrogen pentoxide (N_2O_5) in carbon tetra Chloride in the presence of P_2O_5.
9. Fuming HNO_3 in acetic anhydride.

Among the available nitrating agents, the most common nitrating agent is mixed acid.

The nitrating agents and conditions for the reaction differ from substrate to substrate Benzene nucleus containing activating groups require mild nitrating agents and mild conditions; while aromatic compounds containing deactivating groups demand strong nitrating agents and vigorous conditions e.g. alkyl grs activate the benzene ring, so alkyl benzene require mild nitrating agent and mild conditions for nitration on the other hand, $-NO_2$ group is deactivating, so nitro benzene requires stronger nitrating agent and drastic - tic conditions for further nitration

Mechanism of nitration reaction :-
 With most of the nitrating agents, the attacking electrophile is nitronium

(NO_2^+) ion.

1. when conc HNO_3 is used NO_2^+ is produced through an acid-base reaction;

$$HNO_3 \rightleftharpoons H^+ + NO_3'$$
$$H^+ + HNO_3 \rightleftharpoons H_2O + NO_2^+$$
$$\overline{2HNO_3 \rightleftharpoons NO_3' + H_2O + NO_2^+}$$
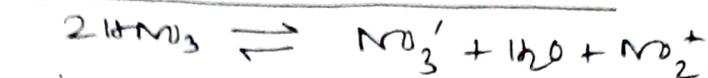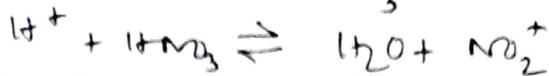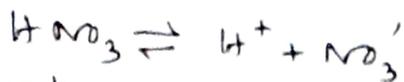
2. With mixed acid (1:1 conc HNO_3 and conc H_2SO_4) an acid-base reaction is found to occur. Here H_2SO_4 acts as an acid and HNO_3 as a base

$$H_2SO_4 \rightleftharpoons H^+ + HSO_4'$$
$$HNO_3 + H^+ \rightleftharpoons H_2O + NO_2^+$$
$$H_2O + H_2SO_4 \rightleftharpoons H_3O^+ + HSO_4'$$
$$\overline{HNO_3 + 2H_2SO_4 \rightleftharpoons H_3O^+ + NO_2^+ + 2HSO_4'}$$
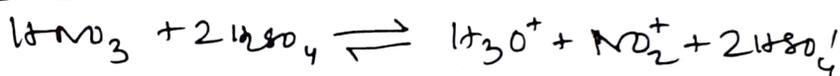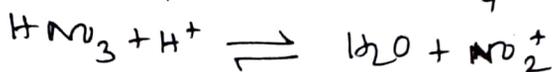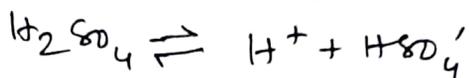
3. With N_2O_5 as nitrating agent nitronium ion (NO_2^+) is formed through spontaneous dissociation.

$$N_2O_5 \rightleftharpoons NO_2^+ NO_3' \rightleftharpoons NO_2^+ + NO_3'$$
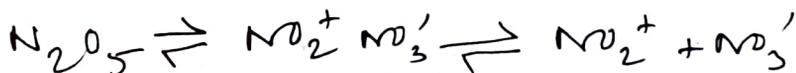
4. With nitronium salts like nitronium hydro fluoride $(NO_2^+ HBF_4')$, the salt it self contains NO_2^+ ion.

$$NO_2^+ HBF_4' \rightleftharpoons NO_2^+ + HBF_4'$$
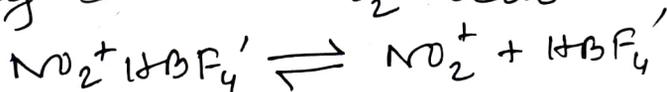
In this way different NO_2^+ ion will be produced.

Mechanistic steps of Nitration Reaction in Benzene.

Step 1 —

(Nitronium ion acts as an electrophile)

π- Complex

$$\left[\begin{array}{ccc} \text{(structure with } NO_2, H, (+)) & \leftrightarrow & \text{(structure with } NO_2, H, (+)) & \leftrightarrow & \text{(structure with } NO_2, H, (-)(+)) \end{array} \right] \equiv$$

(structure: NO_2, H, σ-complex with (+))

σ- Complex

Step 2 - (structure NO_2, H, (+)) $\xrightarrow{\quad -H^+/fast \quad}$ (benzene ring with NO_2)

expulsion of
proton rearomatisation
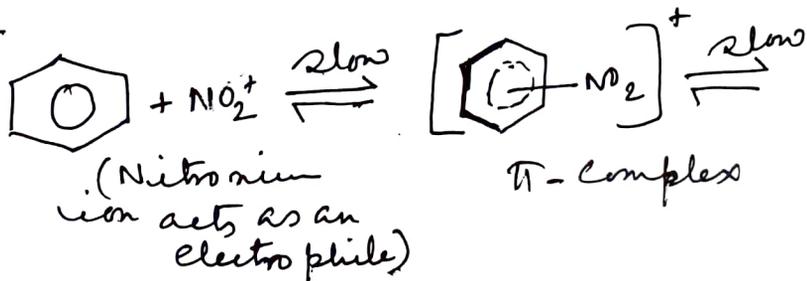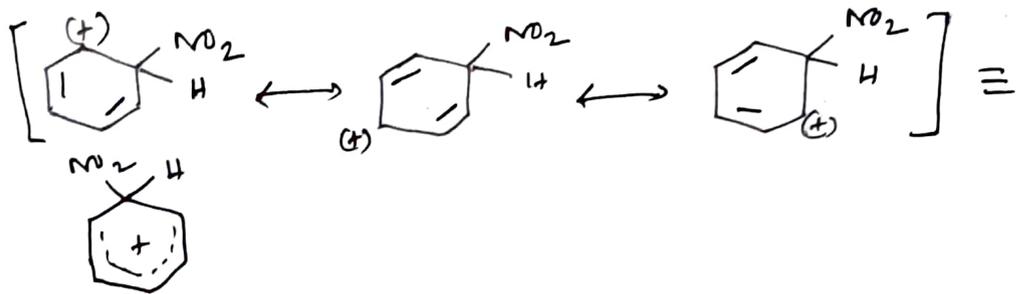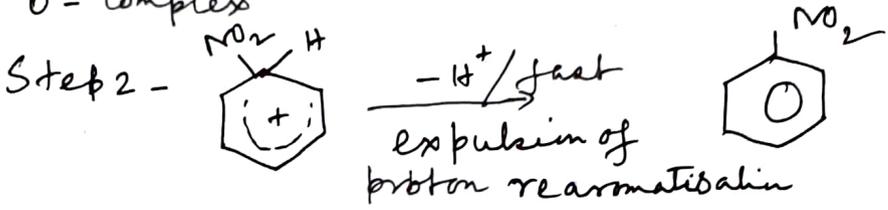
In aromatic electrophilic substitution re-
action as shown above, both the subs-
trate and the electrophile take part in
the slow step i.e. rate determining-
step and so is known as $ArSE^2$

Energy profile diagram of nitration of
benzene.
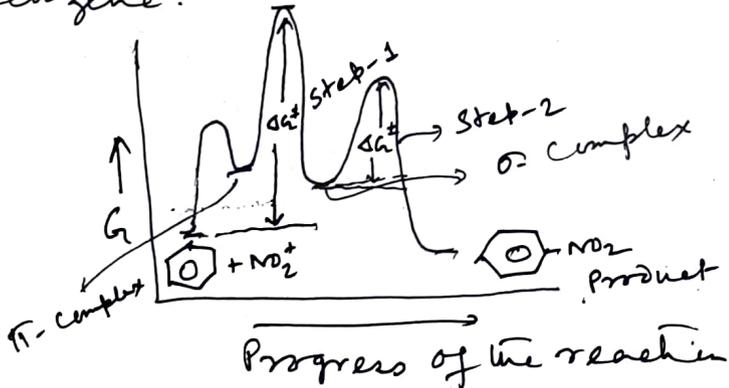
$\Delta G^{\ddagger}_{step-1} > \Delta G^{\ddagger}_{step2}$

So step-1 is slow and rate determining.