

I MSc., CHEMISTRY
ORGANIC CHEMISTRY – I
SEMESTER – I
CODE: DCHII

UNIT – 4

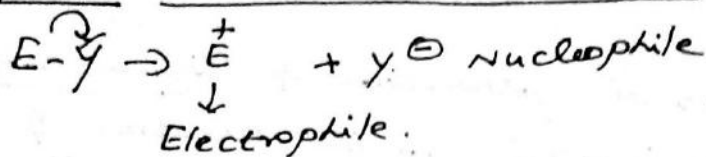
AROMATIC SUBSTITUTION REACTIONS

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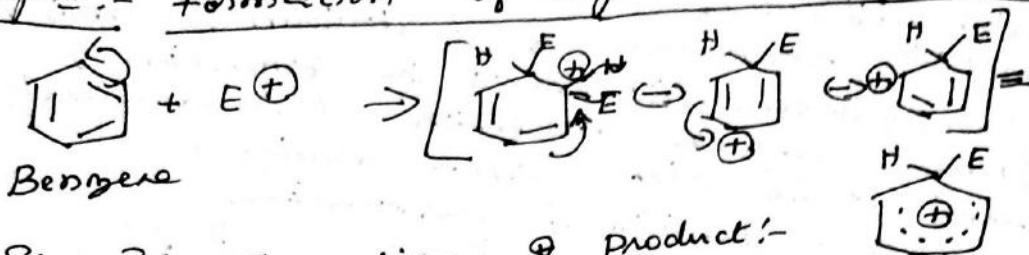
UNIT V ELECTROPHILIC AROMATIC SUBSTITUTION:-

Arenium ion mechanism:-

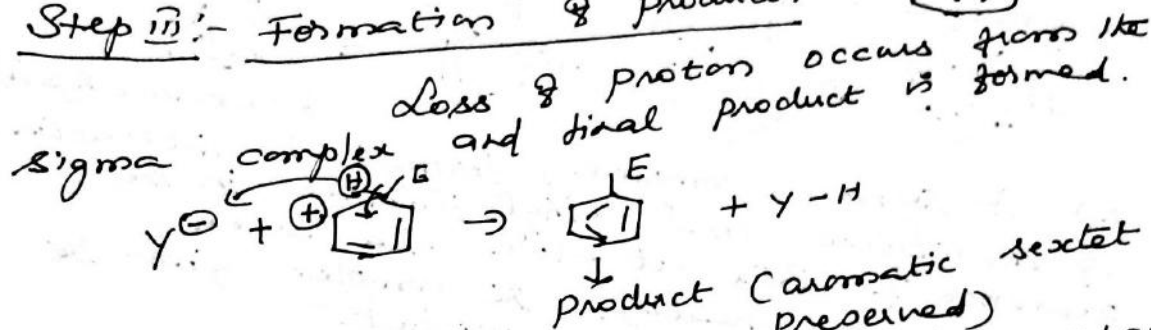
Step I:- Formation of electrophile:-



Step II:- Formation of sigma complex (Arenium ion):-



Step III:- Formation of product:-



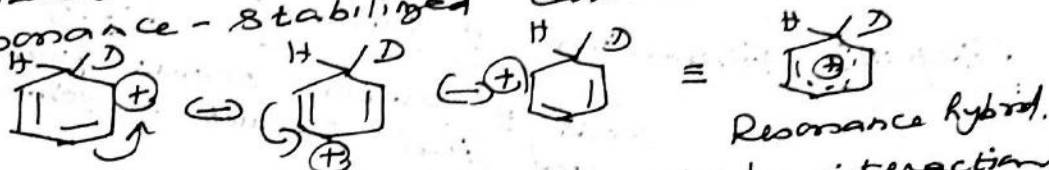
- (i) Benzene has clouds of π electrons, above and below its sigma framework.
- (ii) Although benzene's π electrons are a part of stable aromatic system, they are able to attack the electrophile E^+ to form a sigma complex / carbocation / arenium ion.
- (iii) The resonance stabilized carbocation is called sigma complex because the electrophile bonds with the benzene ring by a sigma bond.

- (iv) The sigma complex is not aromatic, because the sp^3 hybrid carbon atom interrupts the ring of p orbitals.
- (v) Since step II involves loss of aromaticity, it is highly endothermic. So the sigma complex regains aromaticity either by loss of proton on the tetrahedral carbon forming the substituted product. So electrophile is substituted for a ring proton in aromatic electrophilic substitution.

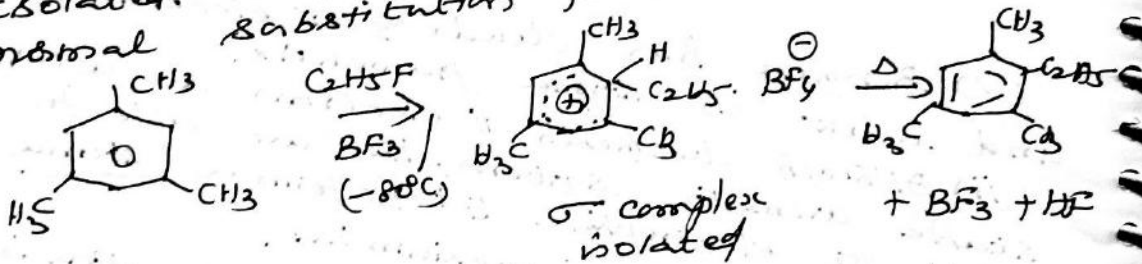
6. Various electrophiles are halogen cation (X^+) in halogenation, nitronium ion NO_2^+ in nitration reaction, alkyl carbocation R^+ in alkylation and RCO^+ (acylium ion) in acylation reaction.

Evidences for the formation of sigma complex:

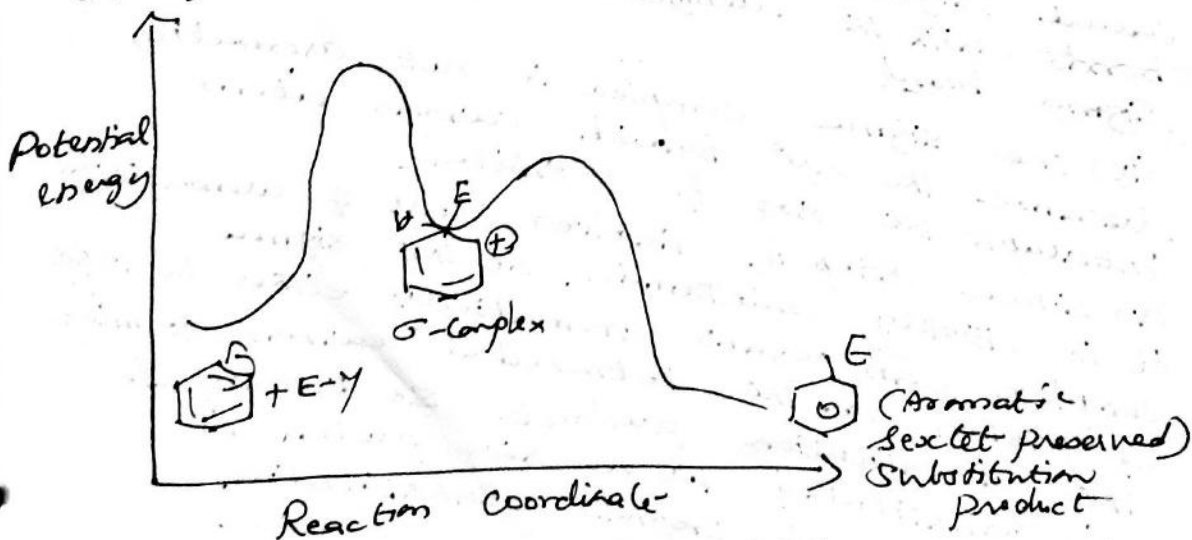
1) When DCl is used in the presence of Lewis acid $AlCl_3$ reacts with benzene, there is a rapid exchange of deuterium (D) with the ring hydrogen. This shows the formation of sigma complex in which D^+ is covalently bonded to the ring carbon forming a resonance-stabilized carbocation.



2) A sigma complex, formed by interaction of mesitylene and ethyl fluoride in the presence of BF_3 at $-80^\circ C$ has been isolated. On heating, the complex gives the normal substitution product.



Energy profile diagram of the reaction of benzene with electrophilic reagent



② State and explain the orientation and reactivity of aromatic electrophilic substitution reactions.

Reactivity and orientation:-

(i) Certain groups activate the benzene ring and direct the incoming substituents to ortho and para positions while some others deactivate the ring and direct the incoming substituents to meta position.

(ii) An activating group activates all positions of the benzene ring. Its ortho and para directing influence is due to the fact that it activates these positions much more as compared to meta position. These groups are known as o/p directing groups.

E.g. OH, OR, NH₂, NHR, NR₂, NHCO₂R

(iii) A deactivating group deactivates the aromatic ring towards electrophilic substitution reaction by strong electron withdrawing -I effect

(e.g.) NH₃⁺, \oplus (CH₃)₃ and also by -M mesomeric effect. (-M) effect is rendered by substituents contain atoms directly linked to the aromatic ring on one side and the electronegative atoms like nitrogen, oxygen and sulphur through multiple bonds on other side. (E.g.) NO₂, CN, COOH, COOR, ClO, CO₂R, SO₃H

(iii) The above facts can be explained by two factors.

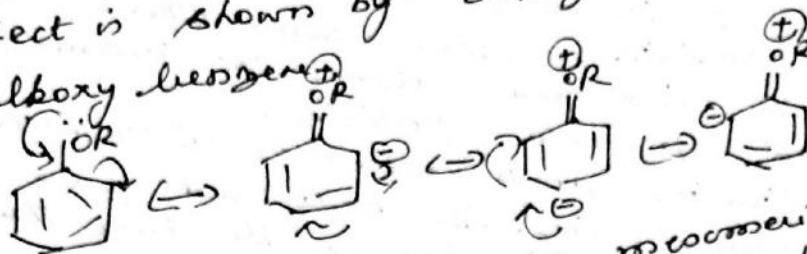
- (a) charge distribution.
- (b) stability of the intermediate carbocation (σ complex).

(iv) Charge distribution:-

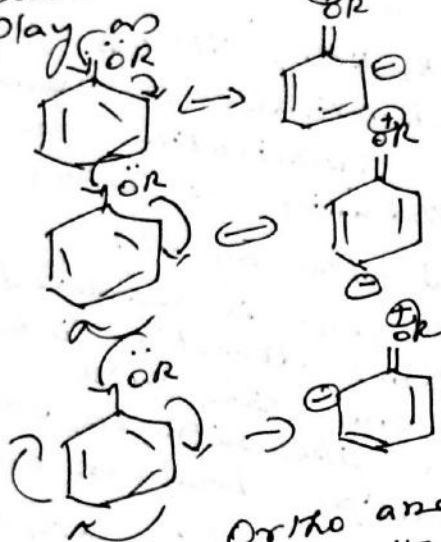
The polar effect (i.e.) inductive and resonance effect of the substituent Y already present in the benzene ring is charge comes these positions to become points of high electron density by inductive, group Y already

electromeric and mesomeric effects. Overall electron density of the ring also increases and therefore further substitution is facilitated.

(v) The atom adjacent to the nucleus has at least one lone-pair of electrons. Mesomeric effect is shown by taking example of alkoxy benzene.

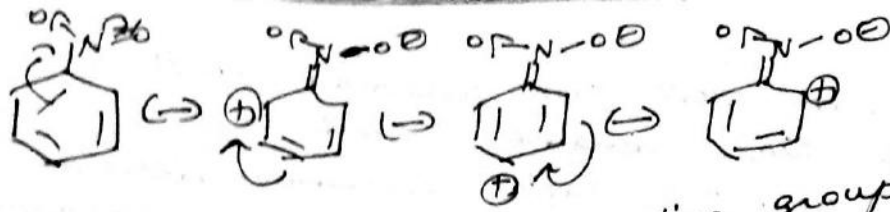


In addition to mesomeric effect, electromeric effect (±E) will be brought into play as



Ortho and para substitution takes place by the combined mesomeric and electromeric effect. This combined effect is known as tautomeric effect (±T).

(vi) In meta substitution, group Y comes with a point of relatively high electron density and further substitution by electrophilic groups occurs. Since overall electron density of the ring decreases, this is shown by taking an example of nitrobenzene.



So meta directing group contains at least one strong electron withdrawing atom. Due to inductive effect (-I) of this atom electrons are withdrawn from ortho and para positions.



Here mesomeric and inductive effect all assist one another and net result is (-M, -I).

③ Write short notes on o/p ratio?
In mono-substituted benzene, there are two ortho position and one para position. The ratio of these isomers is 67:33. But we couldn't get this ratio in the products. Ortho-para ratio will be affected by two factors.

(1) STERIC EFFECT:-

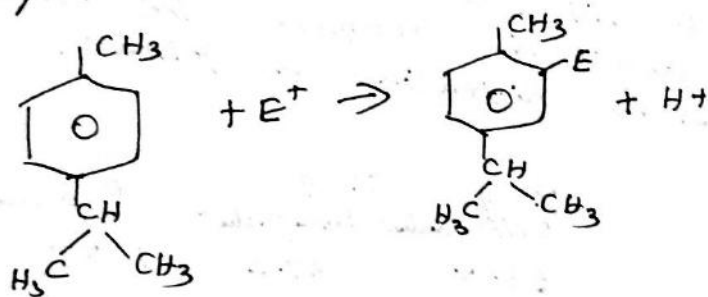
The group already present in benzene nucleus is large means, the % of ortho product will be decreased. Larger the substituent group is benzene, the ortho product ratio is lesser in nitration as follows.

Compound	% of ortho product	% of para product	O/p ratio
1. $C_6H_5CH_3$	58.5	37.2	1.57
2. $C_6H_5C_2H_5$	45	48.5	0.93
3. $C_6H_5CH(CH_3)_2$	30	62.3	0.48
4. $C_6H_5C(CH_3)_3$	15.8	72.7	0.22

When we move from compound ① to ④, since the size increases, steric effect increases and o/p ratio decreases. When the newly entered group approaches the benzene nucleus at ortho position, there will be interaction between this group and the group already present and so the energy of the intermediate increases and stability decreases. When the reaction occurs at high temperature, ortho isomer is formed in large amount. For eg) acetanilide on nitration at 0°C, p-nitroacetanilide is formed, but at high temperature, ortho isomer is formed.

Tert-butylbenzene on chlorination gives the product with higher o/p ratio, but on bromination lesser o/p ratio occurs. This is due to the larger size of bromine compared to chlorine.

In p-cumene, electrophile attacks ortho position to methyl and not ortho to isopropyl group even though on electronic grounds, substitution should occur ortho to isopropyl group only. Due to steric effect, substitution occurs ortho to methyl group.



(ii) INDUCTIVE EFFECT:-

The results of nitration of fluoro, chloro and bromobenzenes are as follows.

S.No	COMPOUND	% of ortho product	% of para product	o/p ratio
1.	C ₆ H ₅ F	12.6	87.14	0.4
2.	C ₆ H ₅ Cl	30.1	73.1	0.41
3.	C ₆ H ₅ Br	37.1	62.5	0.59.

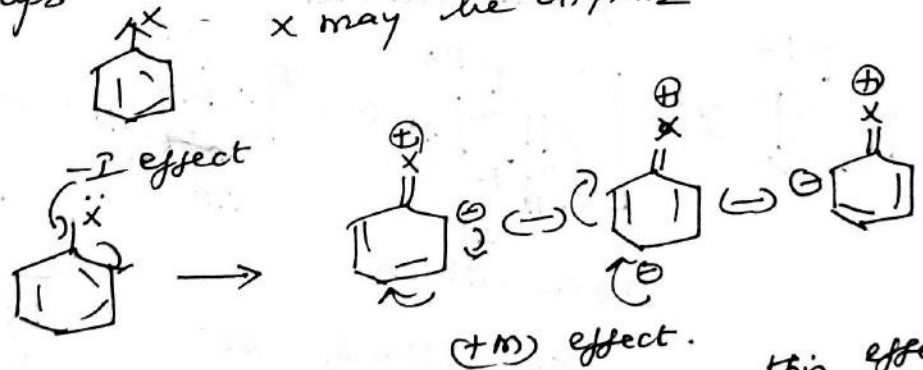
If steric effect is the only factor that decides o/p ratio, o/p ratio should be decreased, when one moves from (1) to (3). Since size of halogens increase. But actually o/p ratio increases from (1) to (3).

Electrophilic inductive effect (-I) is more in the ortho position since it is near to the ring and is less in para position since it is far away. Since electrophilic inductive effect decreases from F to Br, o/p ratio also increases from c1ccccc1F to c1ccccc1Br on nitration.

(4) o/p directing or m-directing nature of any substituent is not only decided by electron withdrawing power (-I), but also decided by mesomeric and electromeric effect.

Explanation:-

(-I) effect which tends to promote m-substitution. Mesomeric effect in this case is stronger than (-I) effect, due to favourable overlap of 2p orbital of oxygen. So these two groups are o/p directing. X may be OH/NH₂

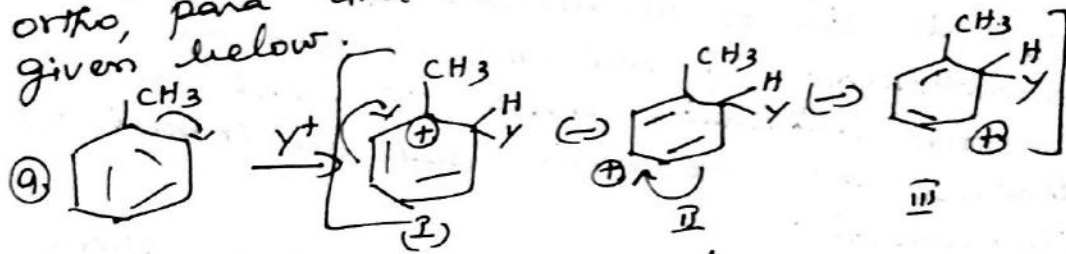


Since +M is stronger, this effect increases the electron density in o/p position. Chlorine atom in chlorobenzene has (-I) and (+M) effect. (-I) effect is greater than (+M) effect. (-I) effect deactivates the ring.

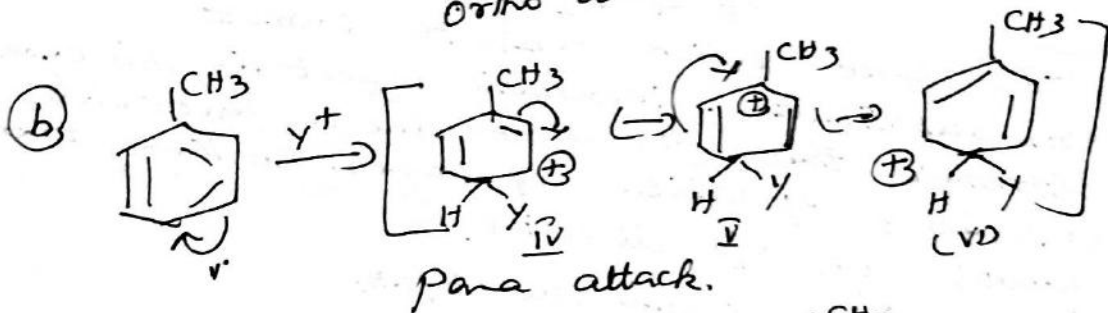
While (+R) is too small to be significant. However when the (+E) effect is brought into play at the requirement of the attacking reagent, the electron density at o and para positions become greater than at m-position itself. Chlorine atom is therefore ortho and para directing with deactivation.

⑤ Methyl group is o+p-directing whereas NO₂ group is meta-directing - explain.

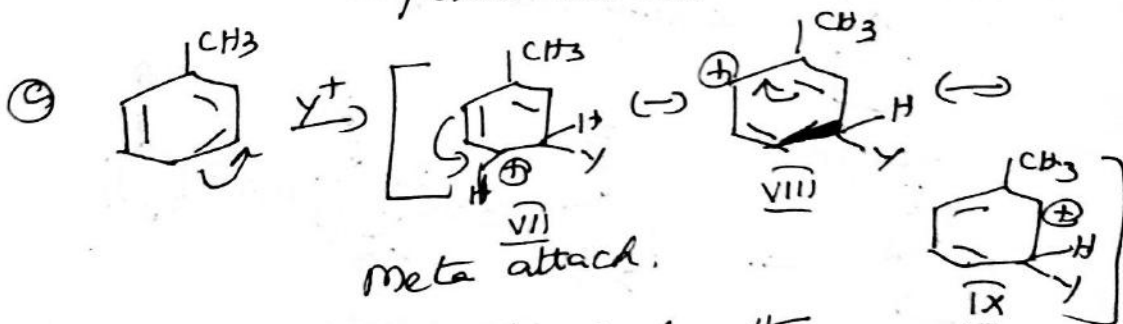
Resonance structures formed by (methyl group) toluene, when it undergoes ortho, para and meta attack by Y are given below.



Ortho attack.



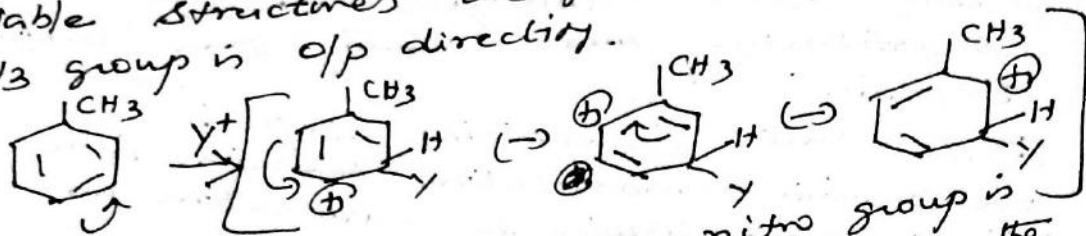
Para attack.



Meta attack.

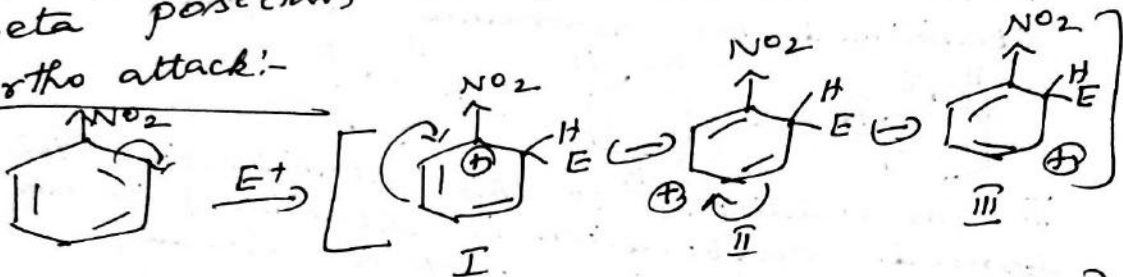
In ortho attack, the resonance hybrid (I) and in para attack the resonance hybrid (IV) are most stable, because (+ve) charge is the carbon containing electron releasing CH₃ group. It releases electrons to ortho and para position.

But in meta attack, no such stable structures are found and so CH_3 group is o/p directing.

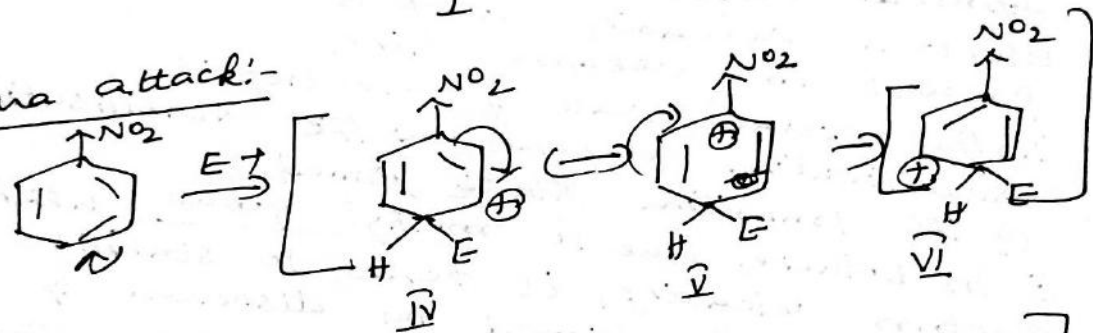


In nitro benzene, nitro group is electron withdrawing and deactivating the ring. Resonance structures formed when the electrophile E^+ attacks ortho, para + meta positions are given below.

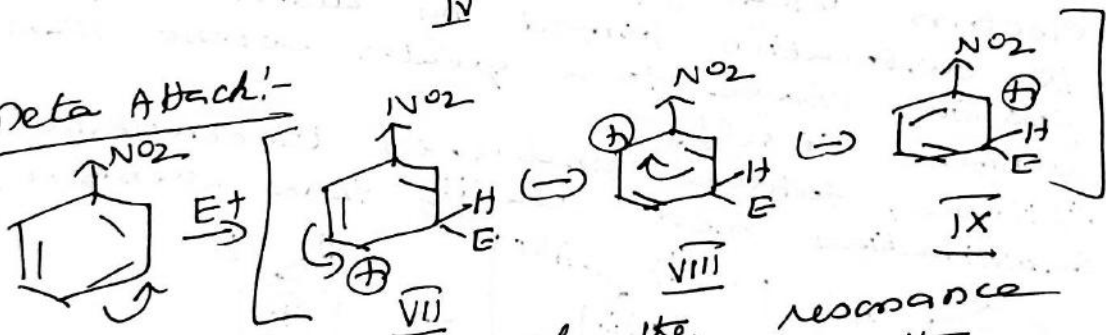
Ortho attack:-



Para attack:-



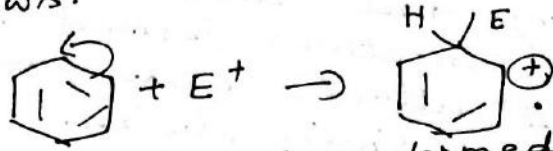
Meta Attack:-



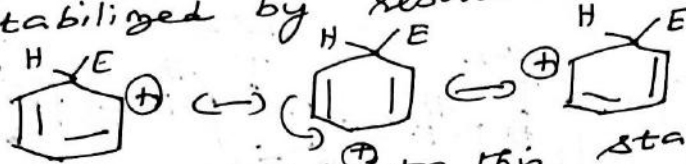
In ortho attack, the resonance hybrid (I) and in para attack, the resonance hybrids V and VI are unstable, because positive charge is on the carbon containing electron withdrawing group. But in meta attack, no such unstable hybrid isomer is found. So nitro group is meta director. It directs the incoming group to meta position.

⑥ Why toluene undergoes electrophilic substitution more readily than benzene. Explain.

(i) The rate determining step in electrophilic substitution reaction is a slow step forming the carbocation as follows.



(ii) The carbocation formed in benzene is stabilised by resonance as follows.

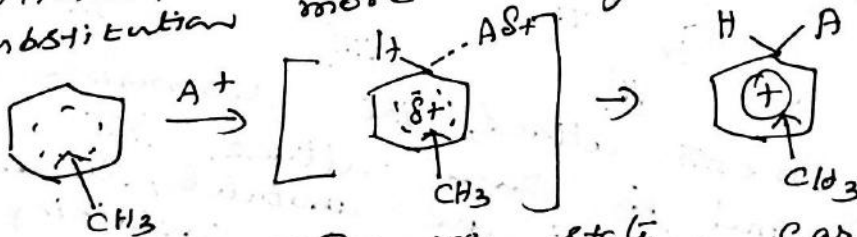


(iii) In addition to this stabilisation, the formed carbocation is stabilised, if an electron releasing group is already present in benzene ring.

(iv) The overall rate of electrophilic substitution depends on the stabilisation of the transition state formed.

(v) In toluene, due to methyl group, which is electron releasing, it tends to stabilise the carbocation formed by dispersal of positive charge to a greater extent than benzene itself.

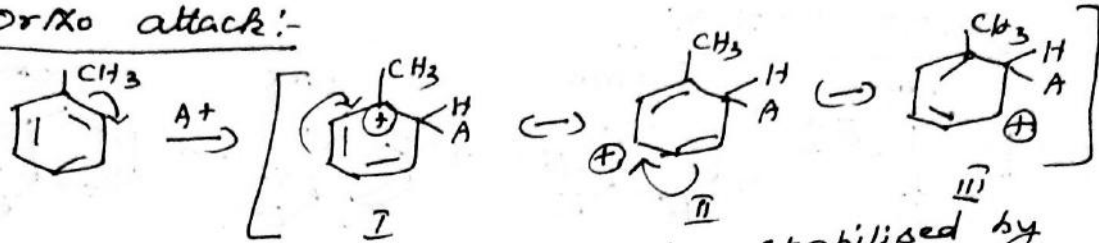
(vi) Hence, toluene undergoes electrophilic substitution more readily than benzene.



Transition state stabilised by dispersal of developing positive charge by CH₃ group

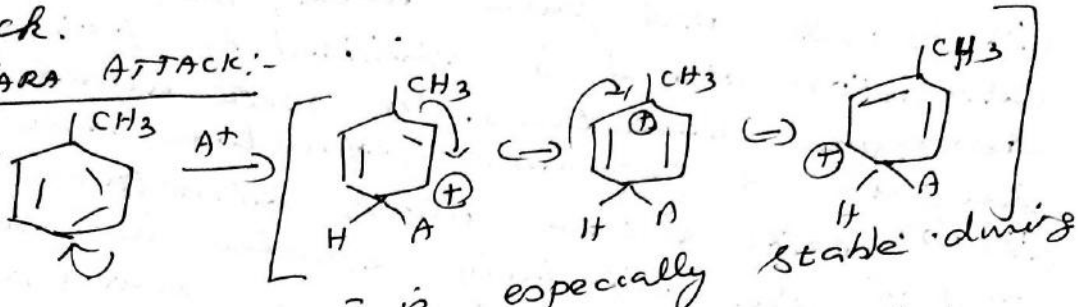
Carbocation stabilised by fully developed positive charge by electron releasing CH₃ group.

Ortho attack:-



Carbocation formed is stabilised by electron releasing CH₃ group. (+I). Structure (I) is especially stable during ortho attack.

Para Attack:-

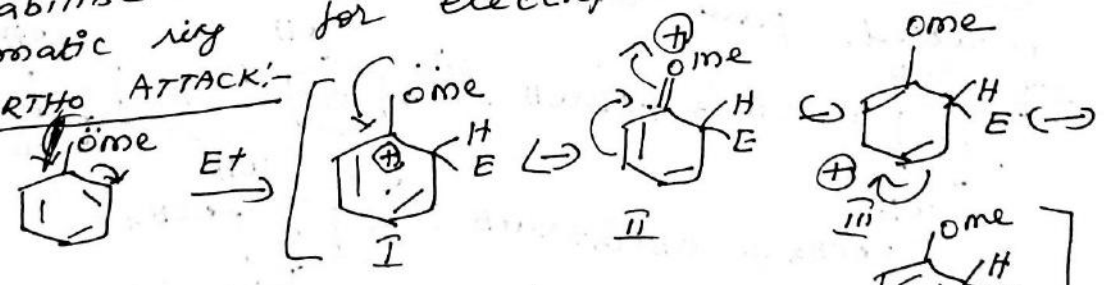


Structure I is especially stable during para attack.

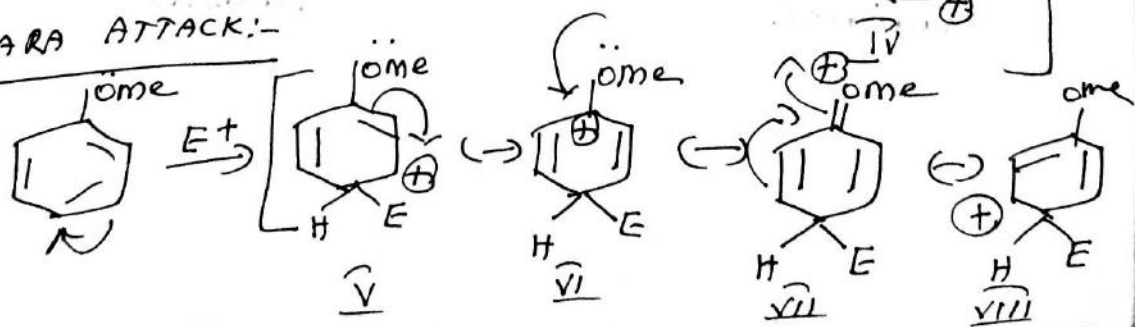
⑦ Why methoxy group in methoxy benzene is o/p directing?

- ① methoxy group (ome) contains lone pair of electrons on oxygen atom which is directly linked to benzene ring.
- ② ome group releases electrons to the ring by resonance or mesomeric effect.
- ③ This electron release by ome should stabilise the carbocation and activate the aromatic ring for electrophilic substitution.

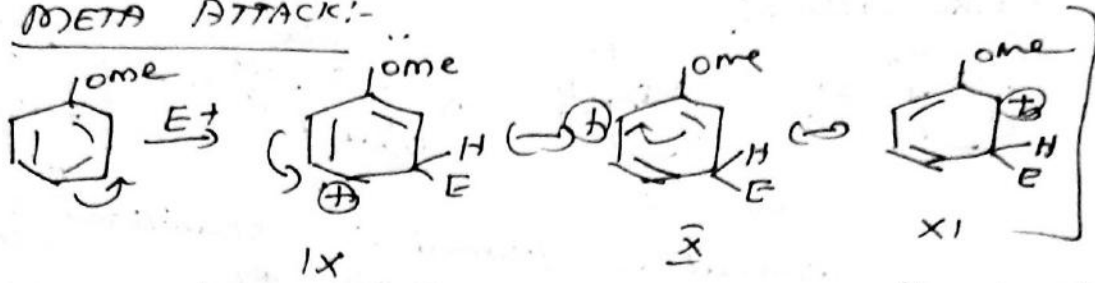
Ortho Attack:-



Para Attack:-



META ATTACK:-

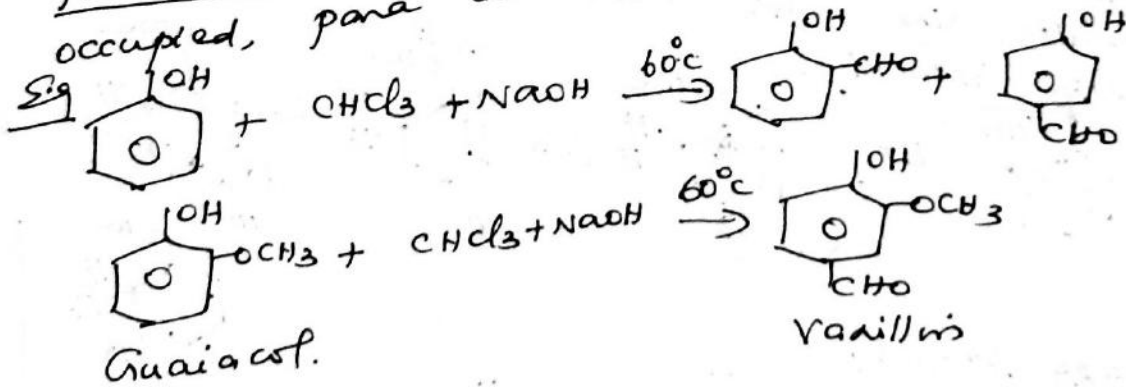


- Reasons for o/p directing nature of Ome group:-
- (i) In ortho and para attack, the carbocation formed is stabilised by four resonance structures. In meta attack, there are 3 resonance structures only.
 - (ii) In ortho & para attack, structures I & VI are especially stable because the carbon bearing the charge is nearer to the Ome group which is electron releasing.

REIMER-TIEMANN REACTION:-

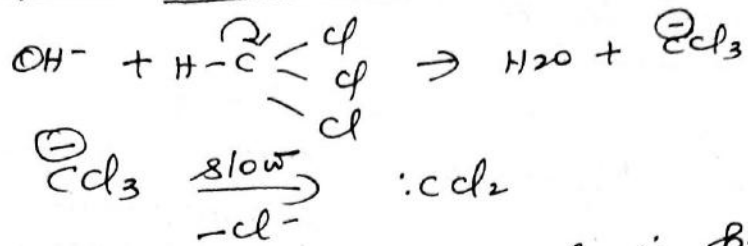
Definition:-

Formylation of phenols with chloroform in alkaline solution is known as Reimer-Tiemann reaction. This method is applicable to phenols and certain heterocyclic compounds. A mixture of ortho and para isomers is obtained but ortho isomer predominates. If one of the ortho positions is occupied, para isomer is the main product.



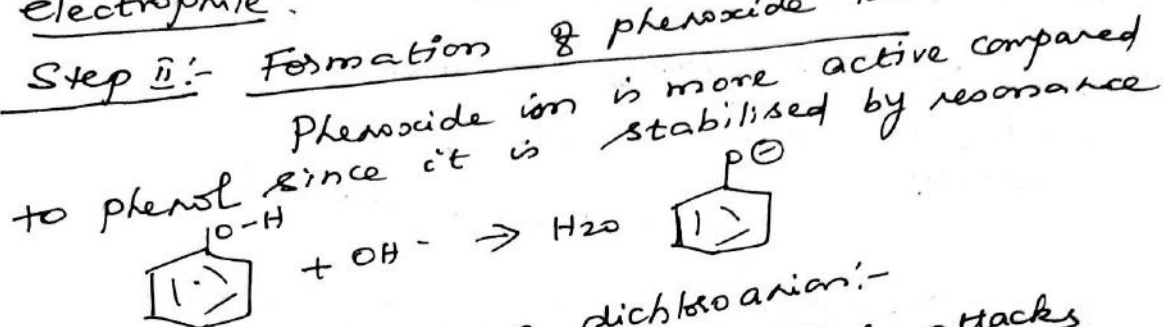
Mechanism:-

Step I:- Formation of electrophile:-



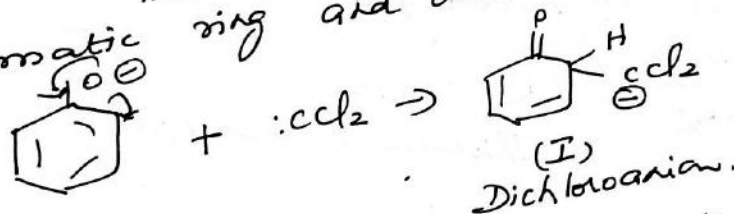
Dichlorocarbene :CCl_2 is highly electron deficient and it is a powerful electrophile.

Step II:- Formation of phenoxide ion:-



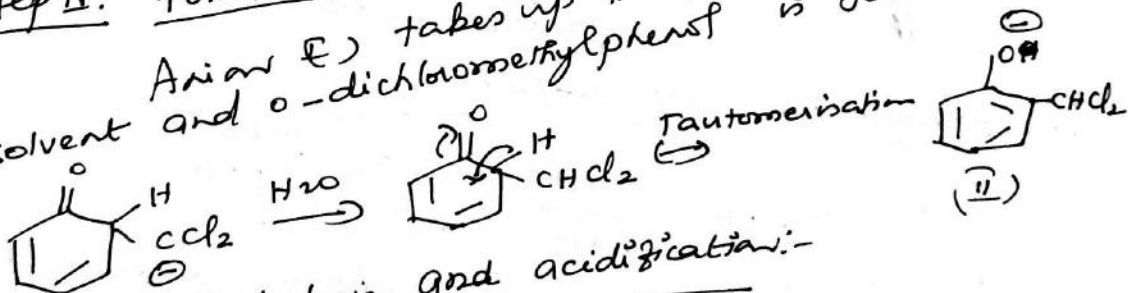
Step III:- Formation of dichloroanion:-

The formed electrophile :CCl_2 attacks aromatic ring and dichloroanion is formed.

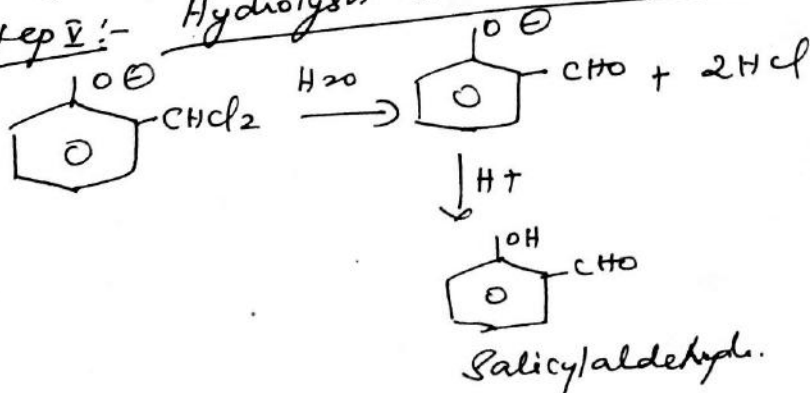


Step IV:- Formation of anion of o-dichloromethylphenol

Anion (I) takes up the proton from the solvent and o-dichloromethylphenol is formed.

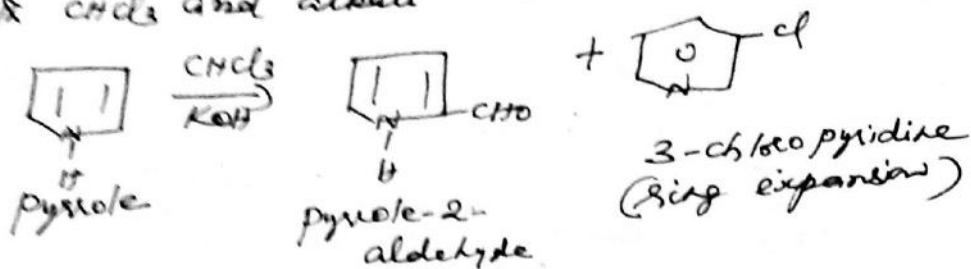


Step V:- Hydrolysis and acidification:-

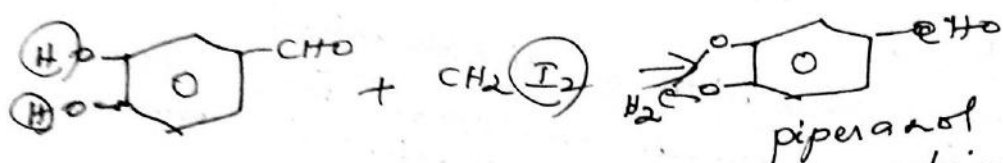
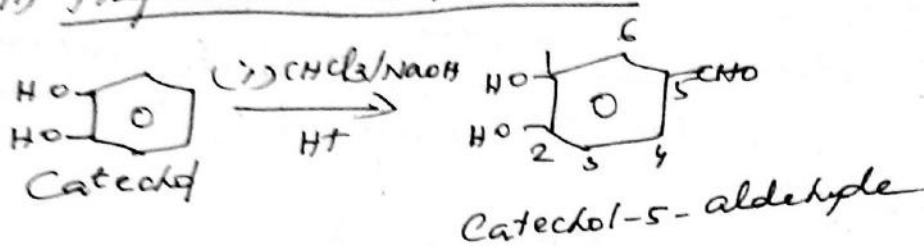


Applications:-

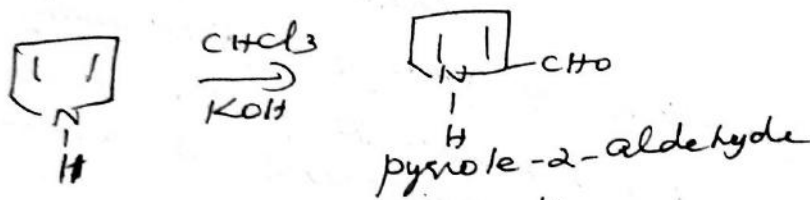
(i) Dichlorocarbene is used for ring expansion which is observed in the reaction of pyrrole with CHCl_3 and alkali



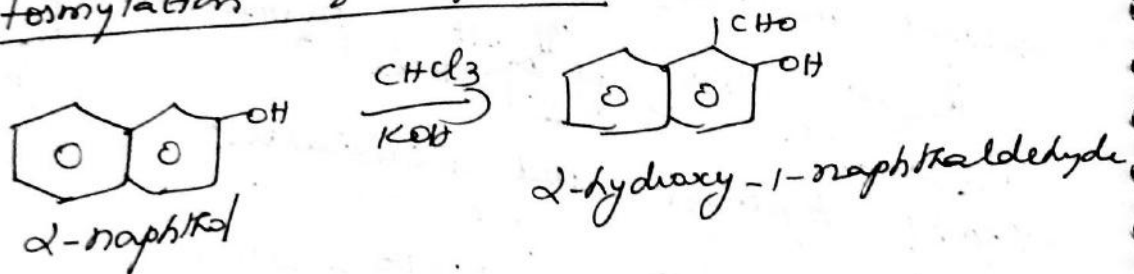
(ii) Preparation of piperonal:-



(iii) Formylation of heterocyclic compounds:-



(iv) Formylation of naphthal:-

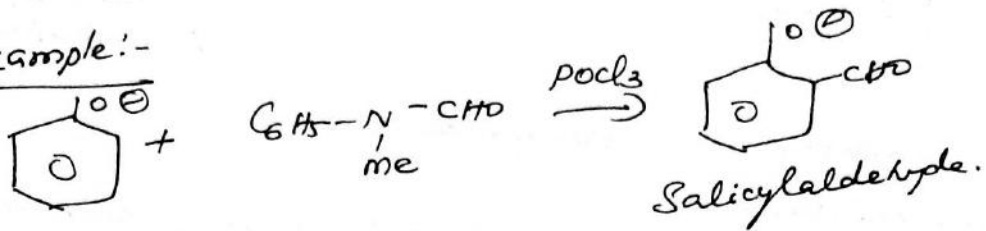


9. Vilsmeier-Haack Reaction:-

Definition:-

Formylation of aromatic rings by using N-phenyl-N-methyl formamide in the presence of POCl₃ is known as Vilsmeier-Haack reaction.

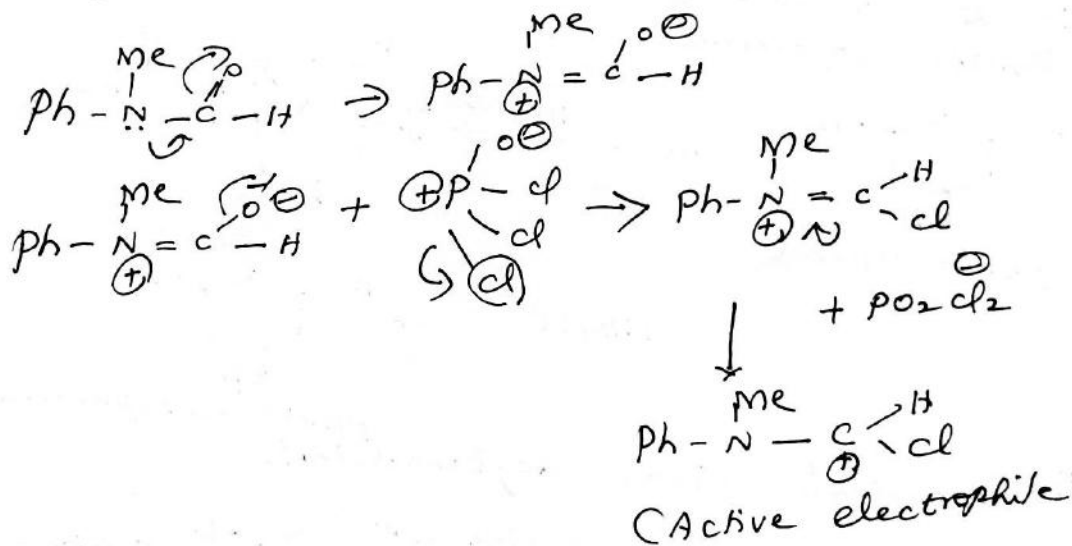
Example:-



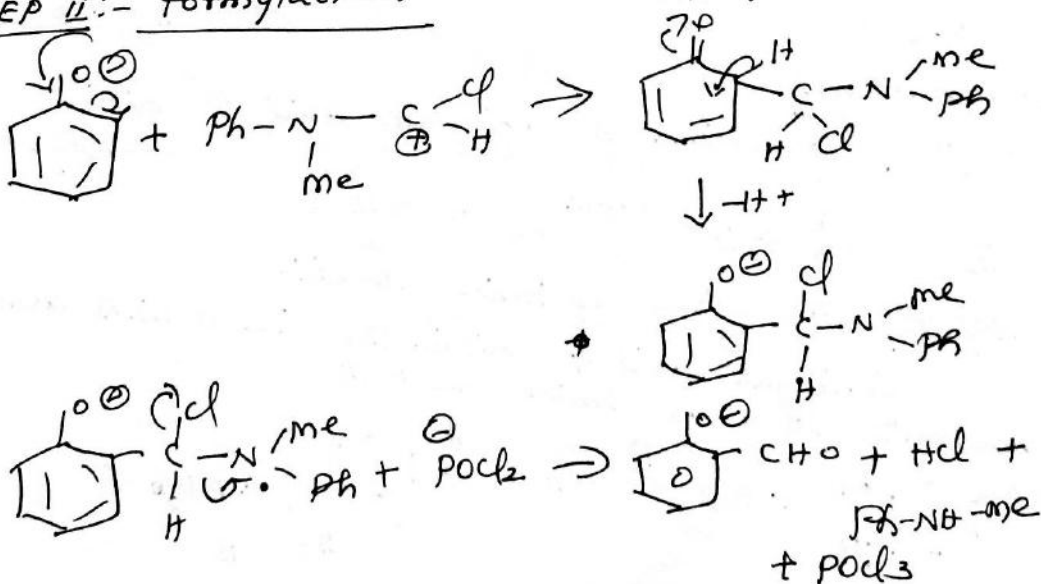
Mechanism:-

Step I:- Formation of electrophile:-

N-methylaniline reacts with HCOOH and N-phenyl-N-methyl formamide is formed as follows.



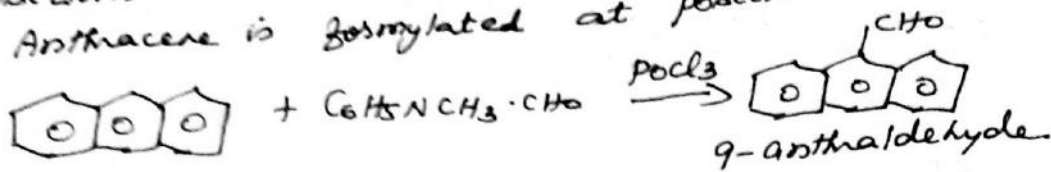
STEP II:- Formylation:-



Applications:-

(i) Phenolic ethers and dialkylamines are smoothly formylated at ortho and para positions.

(ii) Anthracene is formylated at position 9.

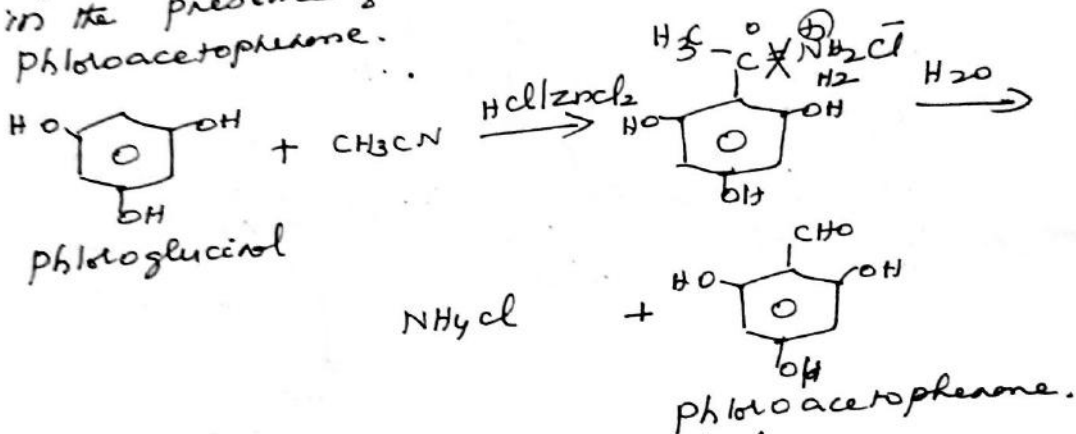


⑩ Gattermann formylation:-

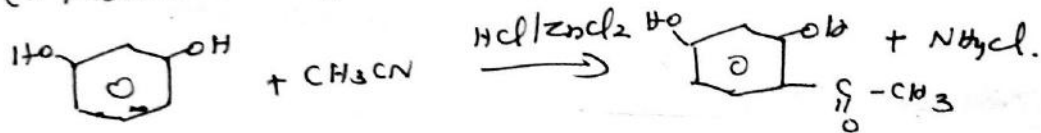
Definition:-

Highly activated phenols such as di and polyhydric phenols or their ethers undergo formylation with RCN (R may be alkyl/aryl) in the presence of ZnCl_2 and HCl is known as Gattermann formylation.

(E.g.) Phloroglucinol on reaction with acetonitrile in the presence of HCl/ZnCl_2 to give phloroacetophenone.

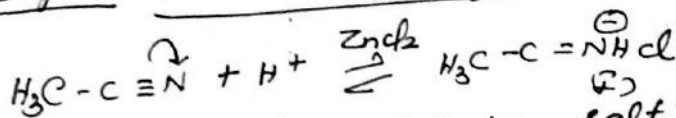


(i) Resorcinol gives acylresorcinol.

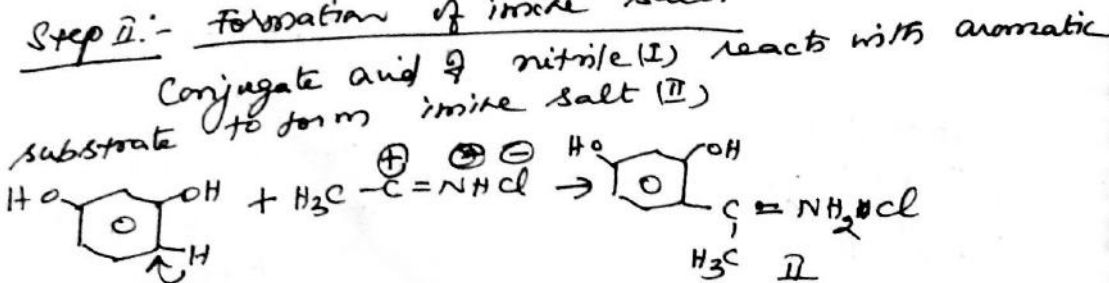


Mechanism:-

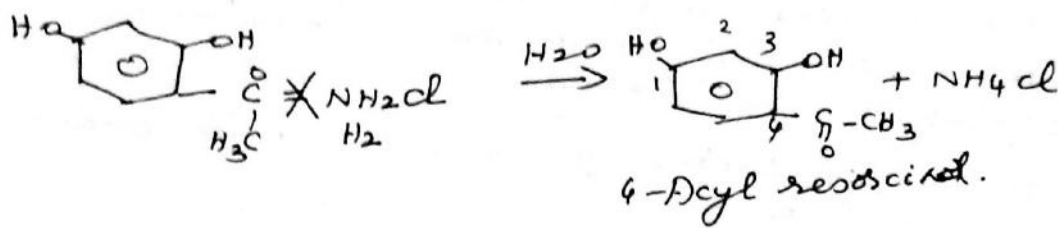
Step I:- Formation of conjugate acid of nitrile:- (I)



Step II:- Formation of imine salt:-



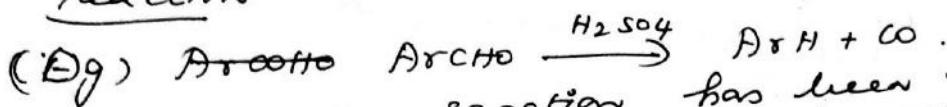
Step iii:- Hydrolysis and formation of product:-



II. GATTERMANN - KOCH REACTION:-

Definition:-

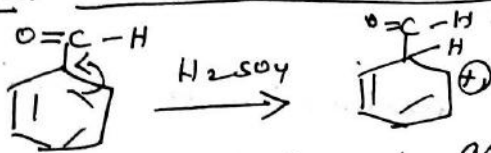
The decarbonylation of aromatic aldehydes with sulphuric acid, basic catalysts and decarbonylation of aromatic acids by Cu/quinoline is known as Gattermann-Koch reaction.



This reaction has been carried out with trialkyl and trialkoxy benzaldehydes.

① Mechanism:-

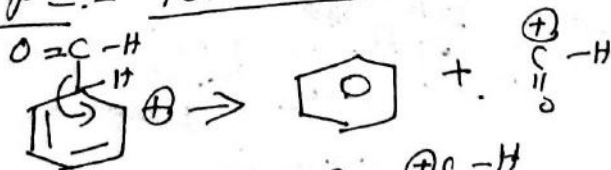
Step I:- Formation of arenium ion:-



The formed arenium ion is stabilised by resonance as follows-

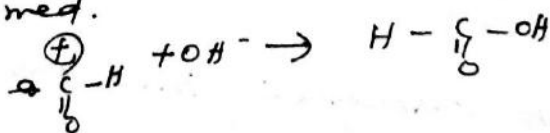


Step ii:- Formation of product:-



Step iii:- Fate of H-C+=O

H-C+=O can lose a proton & CO is formed or it reacts with OH⁻ to form water and formic acid is formed.



② Aromatic aldehydes can also be decarboxylated with basic catalysts. When basic catalyst is used the mechanism is similar to SEI process

③ Decarboxylation of aromatic acids takes place as follows.



④ This reaction can also be carried out by the following two ways.

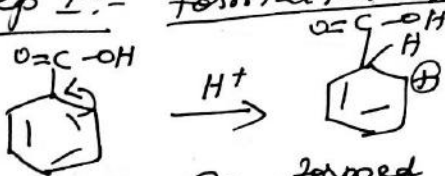
- (i) Salt of the acid ArCOO^- is heated
- (ii) Carboxylic acid is heated with a strong acid often with H_2SO_4 .

⑤ Method (ii) is accelerated by the presence of electron donating groups in ortho and para positions and steric effect of the groups in ortho positions.

⑥ Method (ii):-

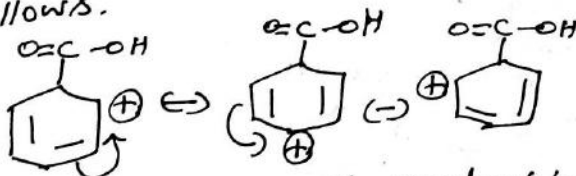
Mechanism:-

Step I:- Formation of arenium ion:-

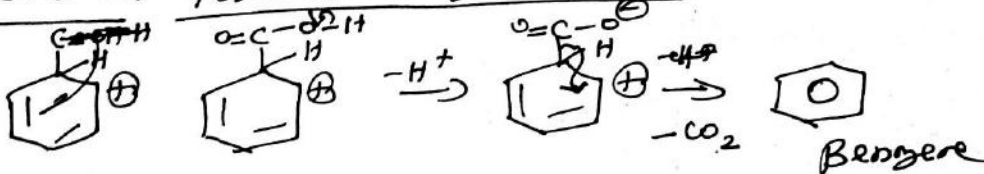


The formed arenium ion is stabilised

as follows.



STEP II:- Formation of product:-



⑦ The order of electrofugal ability is $\text{CO}_2 > \text{H}^+ > \text{COOH}$. So only in most cases, for COOH to leave, H^+ should leave.

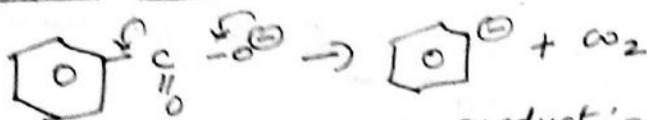
⑧ When salt of ArCOO^- is heated:-

Mechanism:-

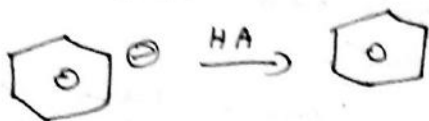
When carboxylate ions are decarboxylated,

The mechanism is entirely different (S_E, type). The reaction is first order and that electron withdrawing groups, which would stabilise a carbanion facilitate the reaction.

Step I:- Removal of CO₂:-



Step II:- Formation of product:-

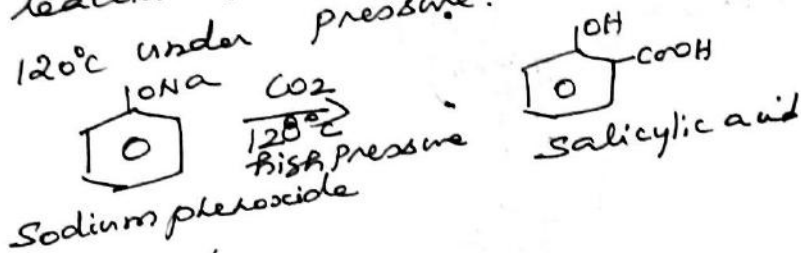


(12) KOLBE REACTION:-

Definition:-

The formation of aromatic hydroxy acids by carboxylation of phenolates, in ortho positions by CO₂ is known as Kolbe reaction.

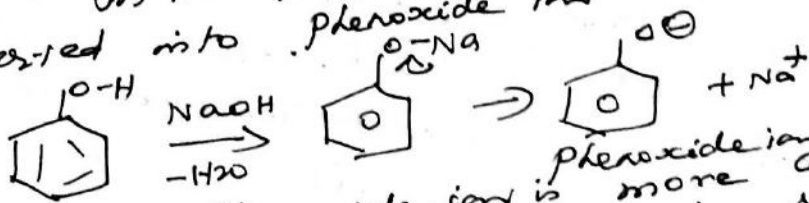
(E.g) Preparation of salicylic acid by the reaction of sodium phenoxide with CO₂ at 120°C under pressure.



Mechanism:-

Step I:- Formation of phenoxide ion:-

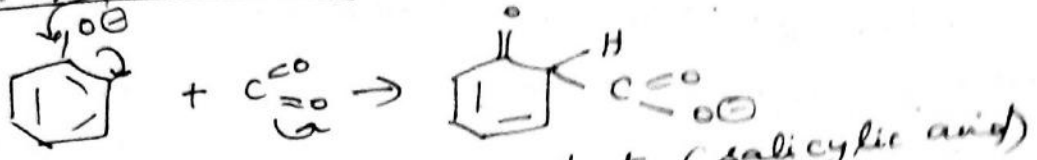
In the presence of CO₂ & NaOH, phenol is converted into phenoxide ion



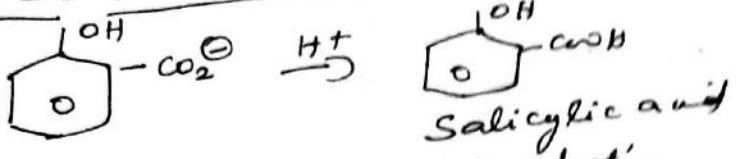
Phenoxide ion is more active than phenol since it is stabilised by resonance as follows.



Step II :- Attack of CO₂ on benzene nucleus of phenoxide ion:-



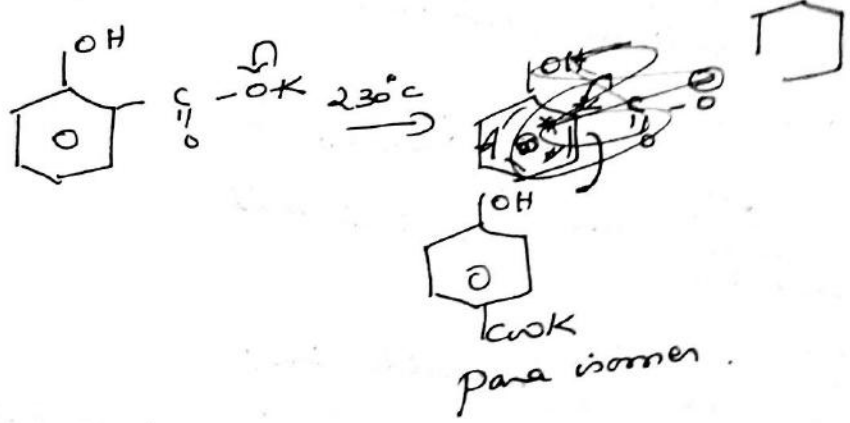
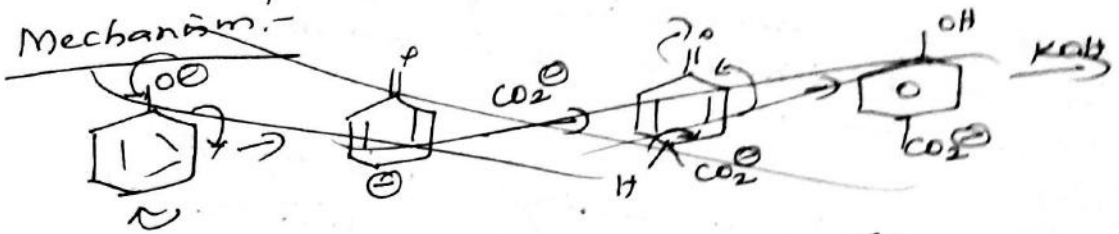
Step III :- Formation of product (salicylic acid)



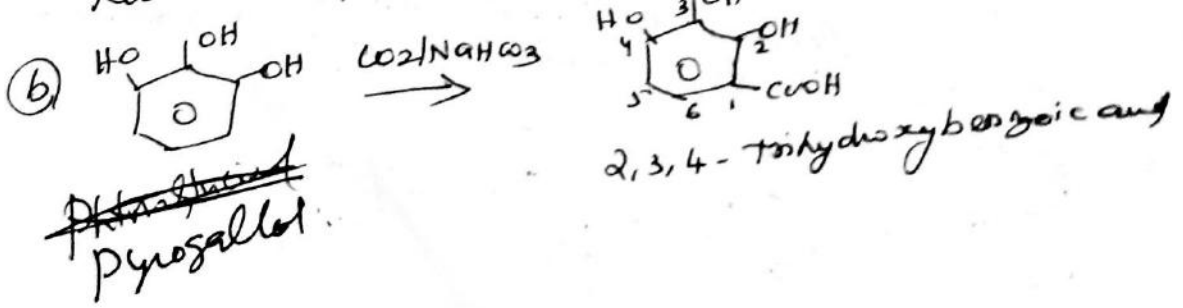
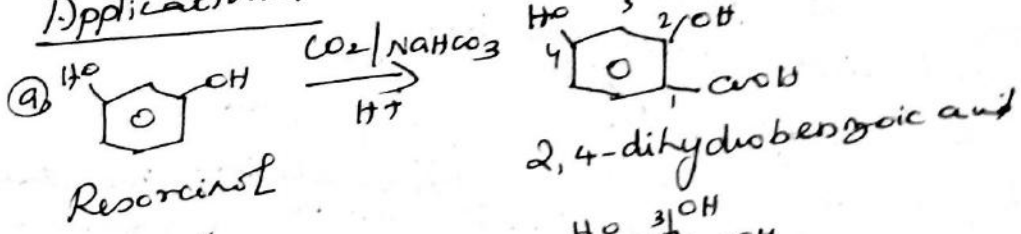
Formation of para product:-

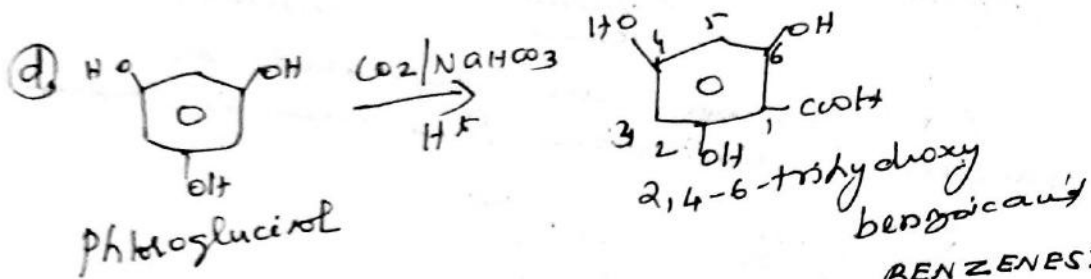
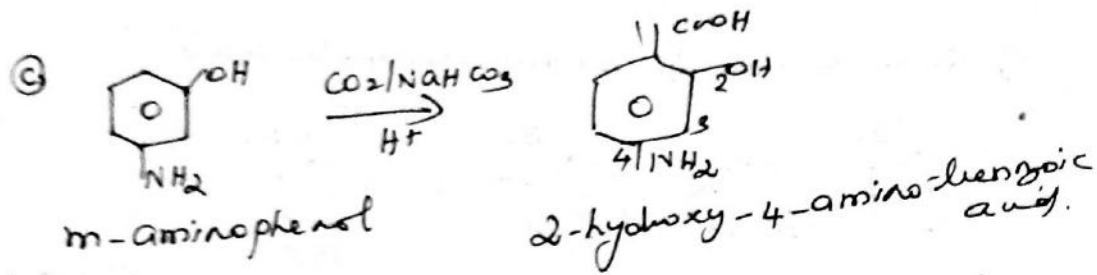
At 230°C, the more stable para-product predominates. The carbonyl group migrates to para position when potassium salicylate is heated at 230°C.

Mechanism:-



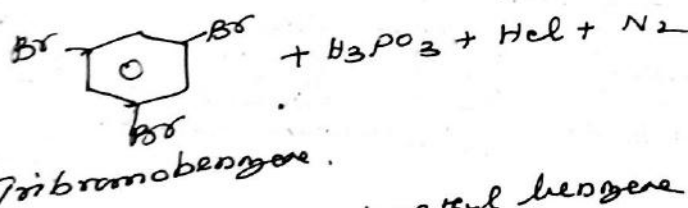
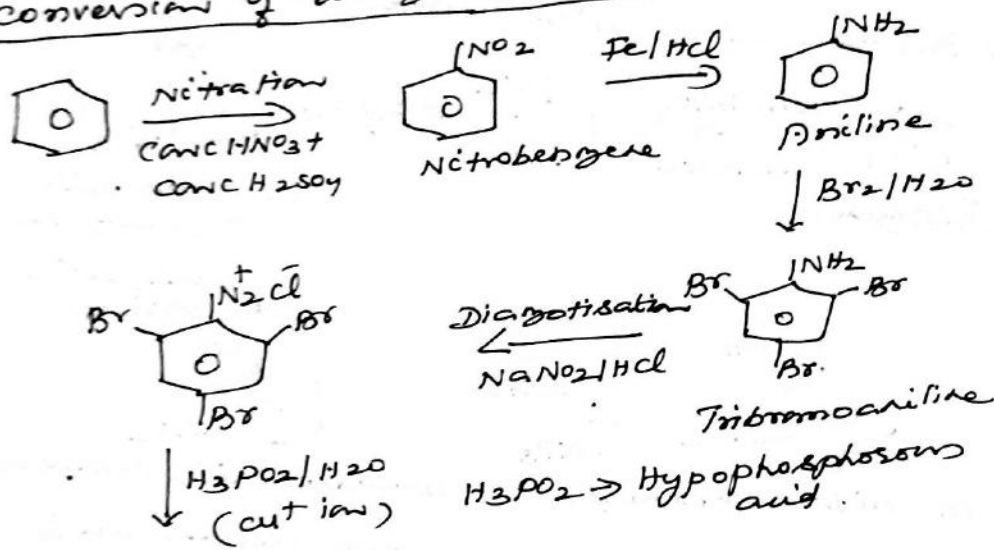
Applications:-



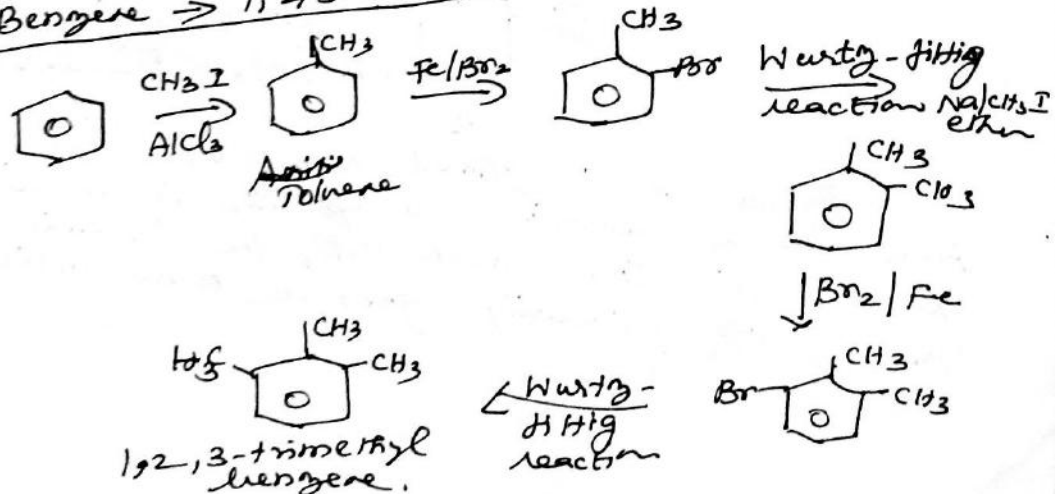


③ SYNTHESIS OF DI + TRI SUBSTITUTED BENZENES:-

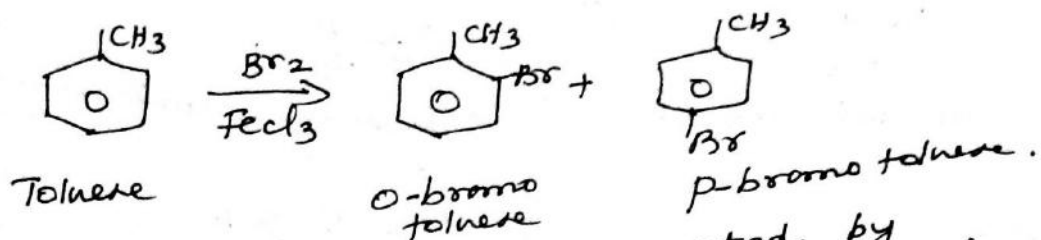
① Conversion of benzene into tribromobenzene:-



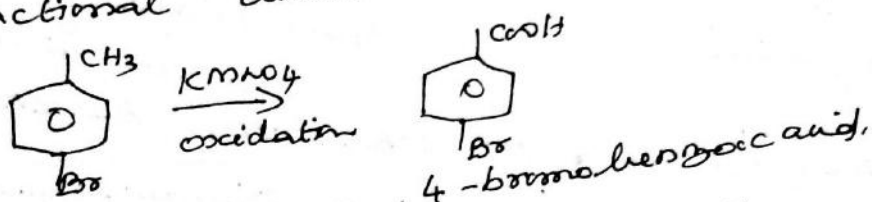
② Benzene \rightarrow 1,2,3-trimethyl benzene



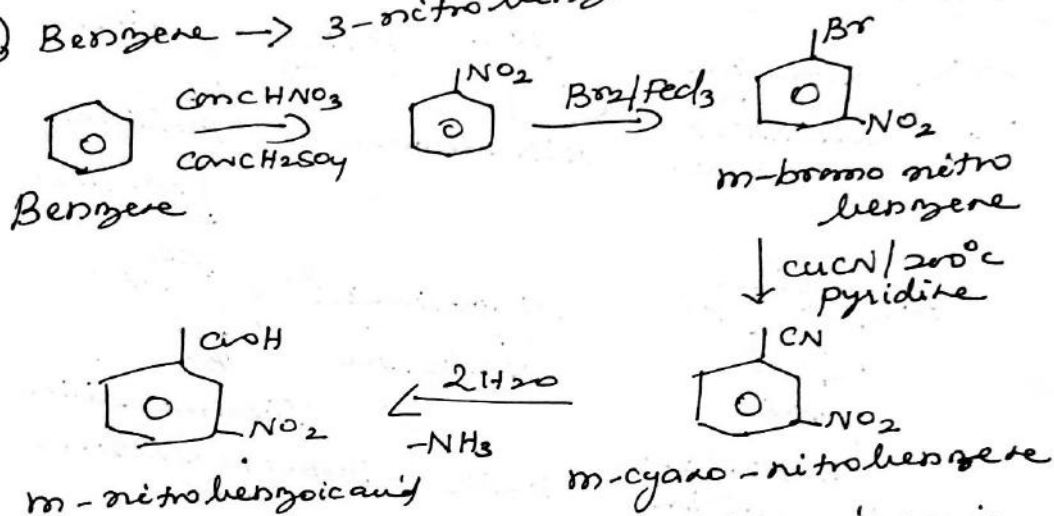
c) Toluene \rightarrow 4-bromobenzoic acid.



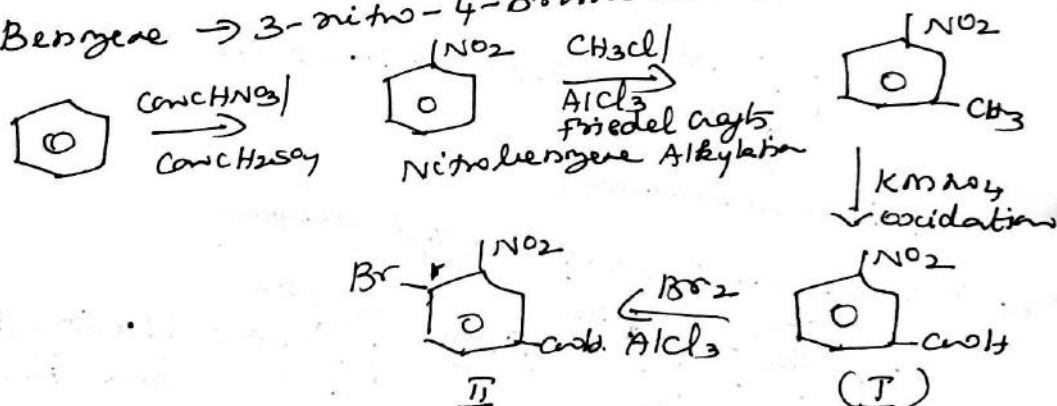
O & P-isomers are separated by fractional distillation. Para isomer is taken.



d) Benzene \rightarrow 3-nitrobenzoic acid.



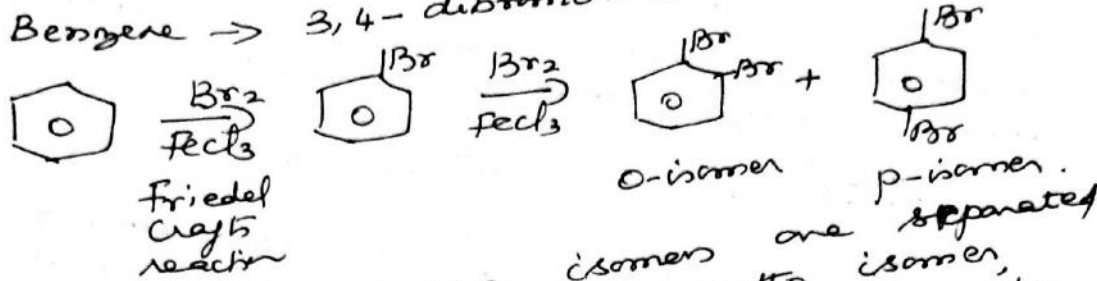
e) Benzene \rightarrow 3-nitro-4-bromo benzoic acid



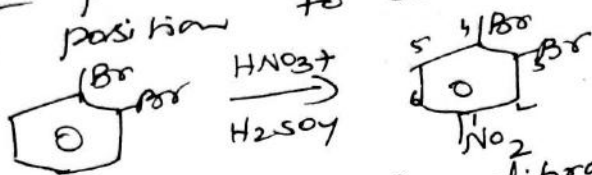
Product (II) is formed from product (I). Here meta directing group NO_2 is meta to the o/p directing group COOH , the incoming (Br) group primarily goes to ortho position.

to the meta directing group rather than to para position. This is called as ortho effect.

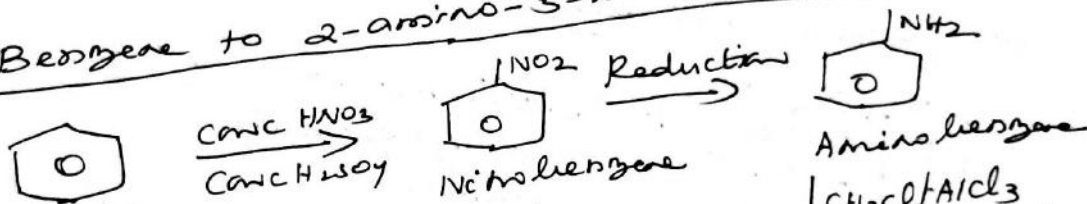
⑥ Benzene \rightarrow 3,4-dibromo-nitrobenzene.



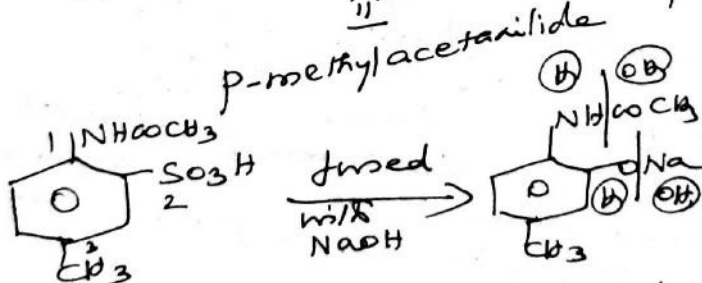
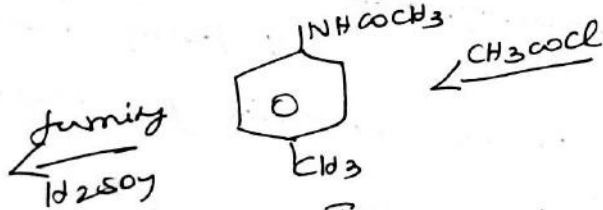
ortho and para isomers are separated by fractional distillation. Ortho isomer, when it is nitrated, nitro group enters to para position to bromine and not to ortho position to bromine due to steric effect.



⑦ Benzene to 2-amino-5-methyl phenol



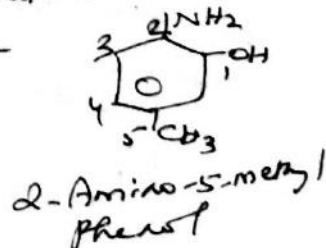
Friedel Crafts Alkylation



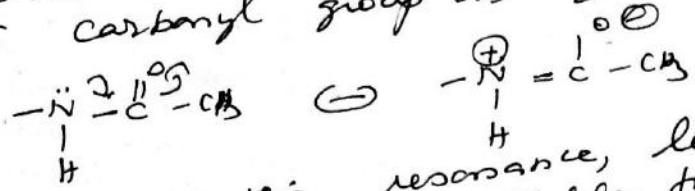
p-methylacetanilide-2-sulphonic acid

p-methylacetanilide-2-phenoxy

Hydrolysis

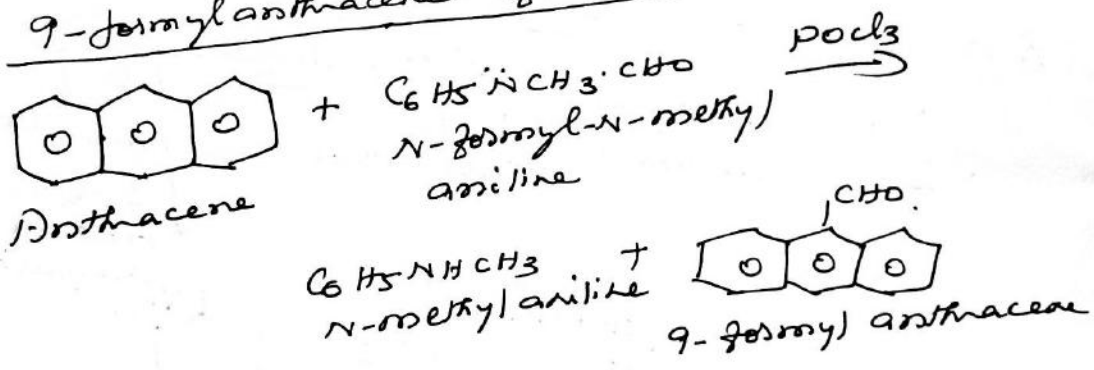


During the conversion of I to II, NH₂ group is converted into NHCOCH₃ (acetanilide) group since the lone pair of electrons on nitrogen undergoes resonance with carbonyl group as follows.

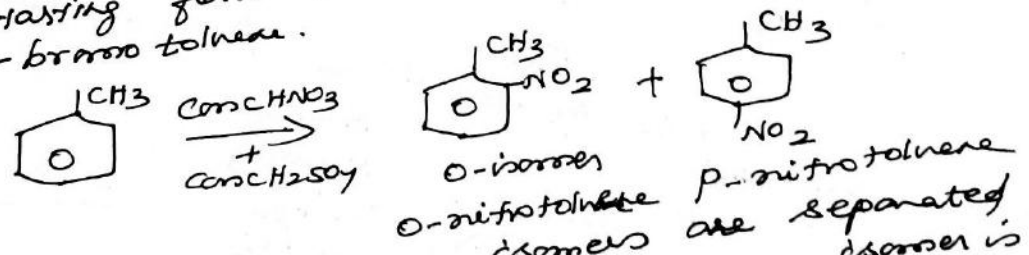


Due to this resonance, lone pair of electrons are not available for resonance with the ring. Due to the conversion of II to III, out of two ortho + para directing groups (C₆H₅ + NHCOCH₃) since NHCOCH₃ group is more activating, compared to methyl group, the entering new electrophile enters ortho to NHCOCH₃.

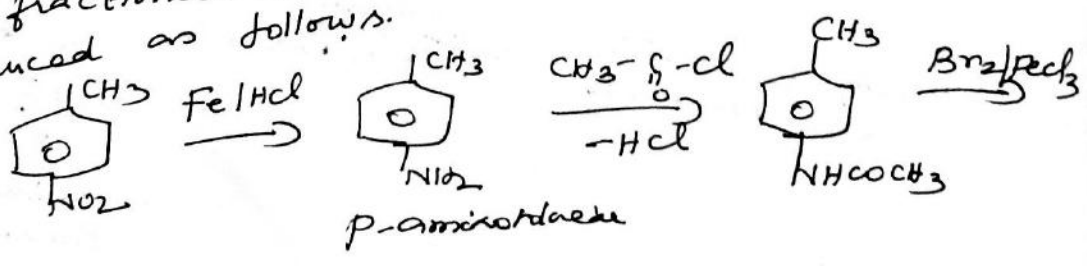
8) 9-formylanthracene from anthracene.

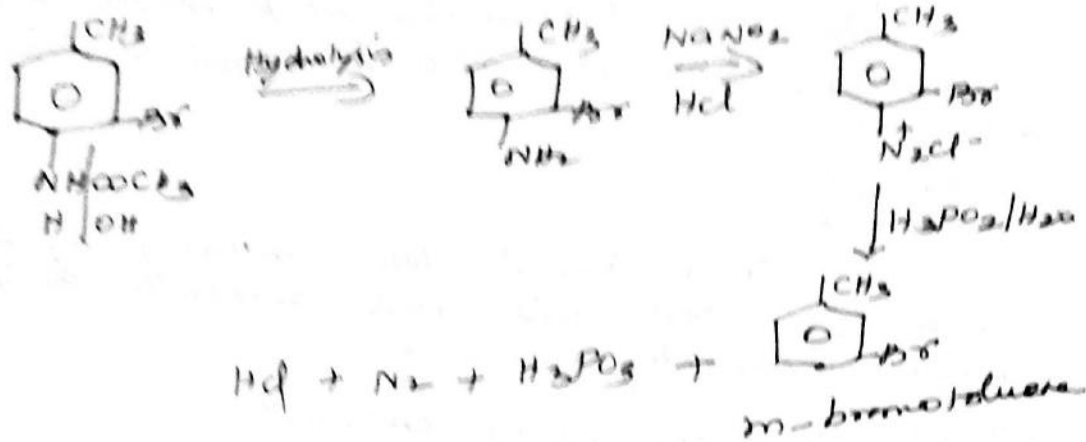


9) Starting from toluene, how will you prepare m-bromo toluene.



Ortho and para isomers are separated by fractional distillation and para isomer is reduced as follows.





④ Explain aromatic electrophilic substitution reaction of halogenation.

Step I:- Formation of electrophile:-

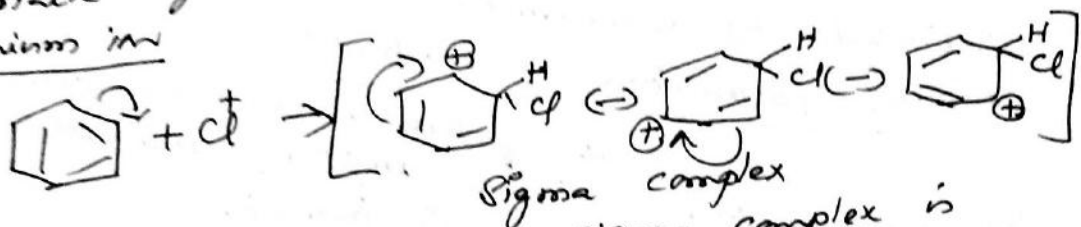
Chlorine molecule in the presence of FeCl_3 gives the electrophile Cl^+



π electron cloud of benzene is less available for polarization of Cl_2 and \therefore the presence of Lewis acid is necessary to polarize the halogen molecule.

Step II:- Formation of sigma complex:-

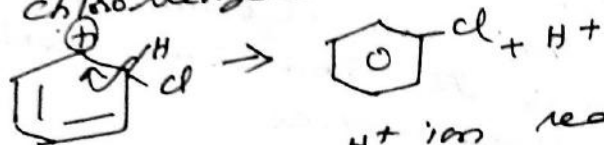
The formed electrophile attacks benzene aromatic system and forms sigma complex or arenium ion



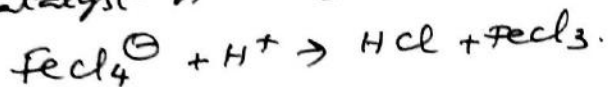
The formed sigma complex is stabilized by resonance.

Step III:- Formation of product:-

Loss of proton occurs and final product chlorobenzene is formed.

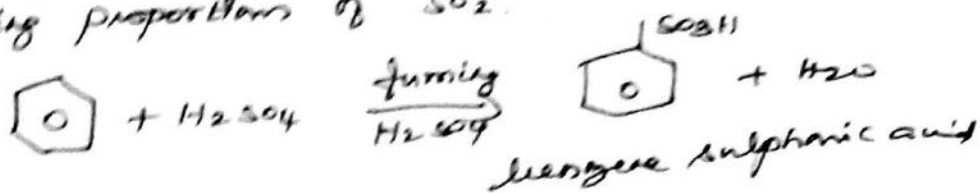


The formed H^+ ion reacts with FeCl_4^- and the catalyst is regenerated



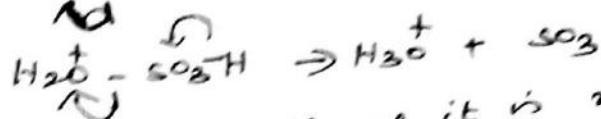
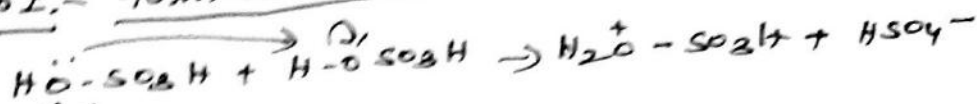
SULPHONATION:-

Sulphonation is accomplished by H_2SO_4 with the help of conc H_2SO_4 or fuming H_2SO_4 containing varying proportions of SO_2 .



Mechanism:-

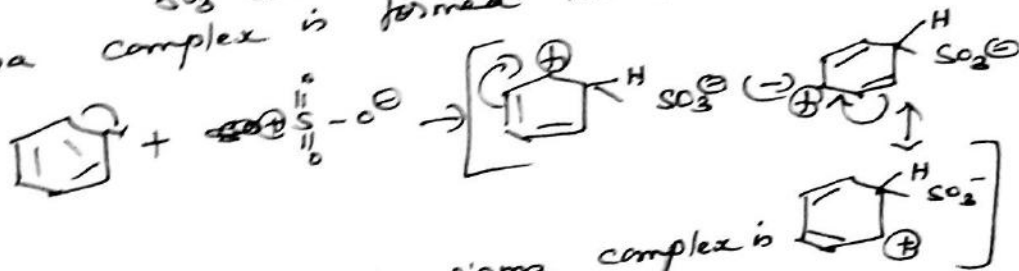
Step I:- Formation of electrophile:-



SO_3 , though it is neutral, it exists as SO_3^+ and acts as an electrophile.

Step II:- Formation of sigma complex:-

SO_3 attacks benzene nucleus and sigma complex is formed as follows.



The formed sigma complex is stabilised as follows by resonance.

Step III:- Formation of product:-

