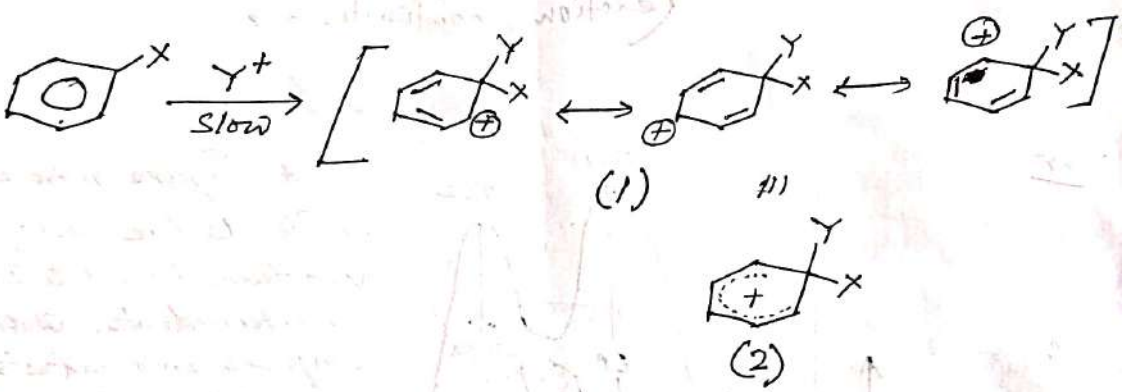
IV Aromatic electrophilic Substitution

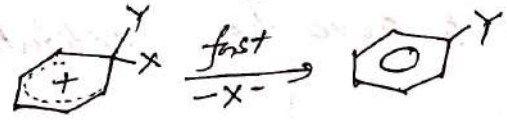
In the arenium ion mechanism the attacking species may be produced in various ways, but what happens to the aromatic ring is basically the same in all cases. For this reason most attention in the study of this mechanism centers around the identity of the attacking entity and how it is produced.

The electrophile may be a positive ion or a dipole. If it is a positive ion, it attacks the ring, removing a pair of electrons from the sextet to give a carbocation, which is a resonance hybrid, as shown in 1, and is frequently represented as in 2. Ions of this type are called Wheland intermediates, σ complexes or arenium ions.

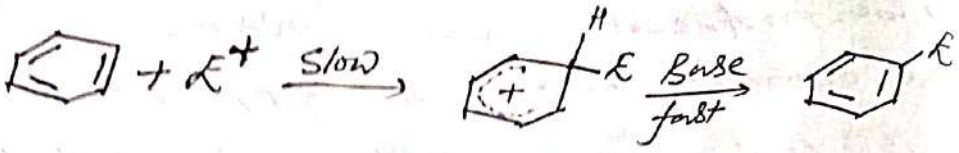


In the case of benzenoid systems they are cyclohexadienyl cations. It is easily seen that the great stability associated with an aromatic sextet is no longer present in (1), though the ion is stabilized by resonance of its own. The arenium ion is generally a highly reactive intermediate and must stabilize itself by a further reaction although it has been isolated.

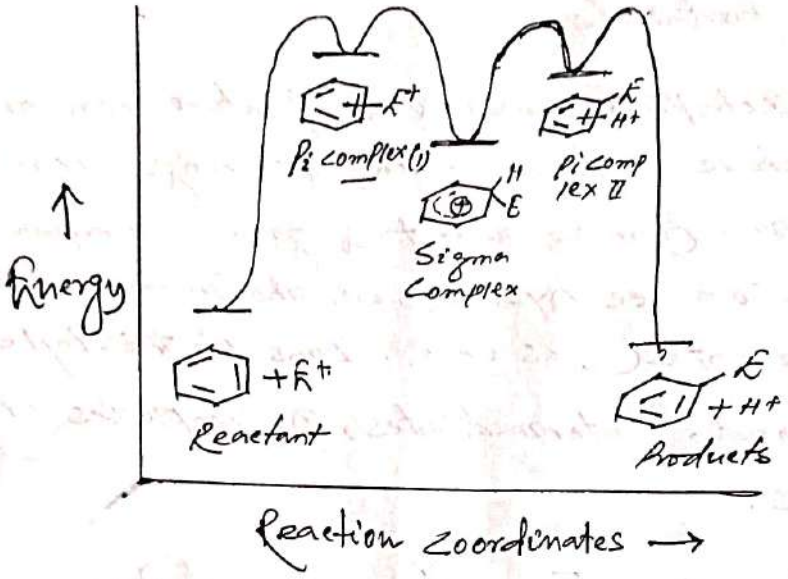
Carbocations can stabilize themselves in various ways but for this type of ion the most likely way is by loss of either X^- or Y^-. The aromatic sextet is then restored, and this is in fact second step of the mechanism.



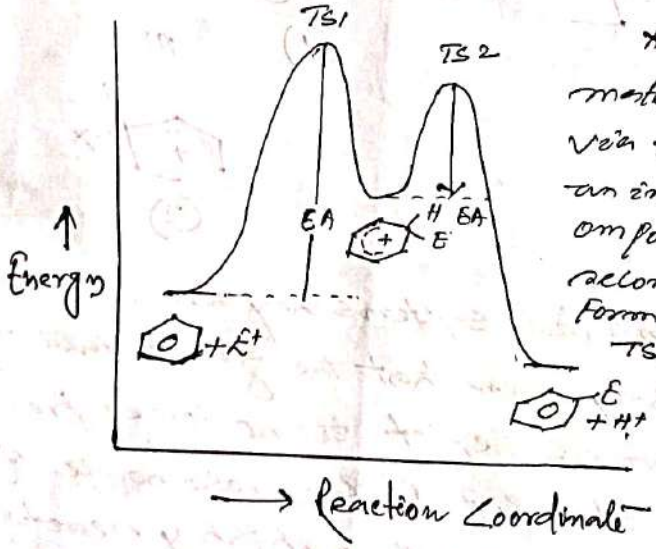
* Draw the Energy Profile diagram for the following reaction: (2)



Ans.



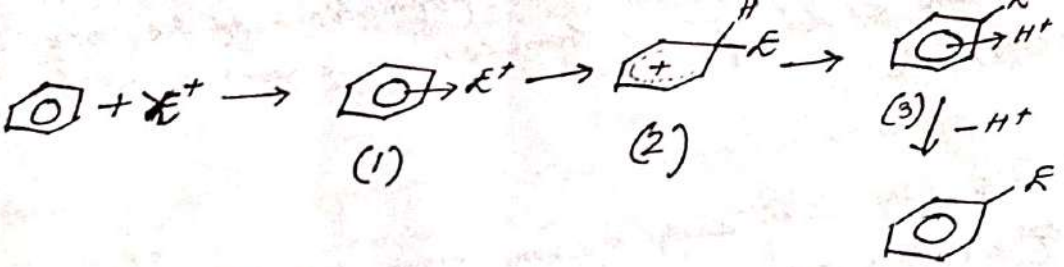
or



* figure represents stoic... materials are being convert... via transition state 1 (TS1) int... an intermediate, which then d... composes into products via a... second transition state (TS2). Formation of intermediate vi... TS1 is more energy-demand... of two step and hence... be slower. It is followed... a fast, non-rate-limi... conversion of the interm... diate into products.

* Explanation for first one:

Positive ion (E^+) can form addition... complexes with π system of benzene ring. Such comp... called a π complex (I), is formed first and then it is converted to arenium ion 2, which subsequently los... a hydrogen to give the substituted product.



(1) (2) (3)

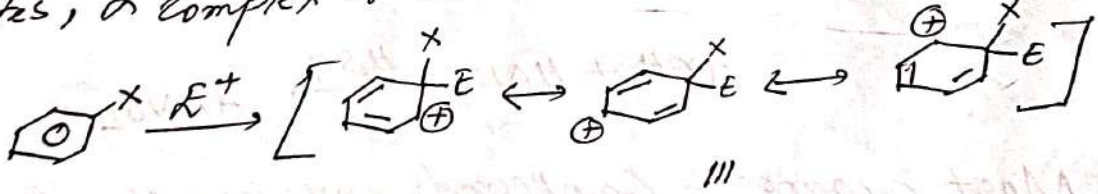
* What is meant by π and σ complex in aromatic electrophilic substitution? What are the differences between the two. (3)

Ans

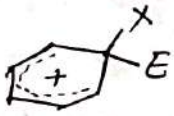
In aromatic electrophilic substitution reaction the first phase of reaction would be interaction between the approaching electrophile and the delocalised π-orbitals and the intermediate so formed is called π-complex.

π-complex

Attacks of electrophile, by removing a pair of electrons from the sextet to give a carbocation, which is a resonance hybrid, as shown below. Ions of this type is called wheland intermediates, σ complex or arenium ions.



III



σ-complex

In contrast to the sigma complex, the Pi complex does not involve actual bonding but the electrophile is held near the Pi electron cloud of the aromatic ring.

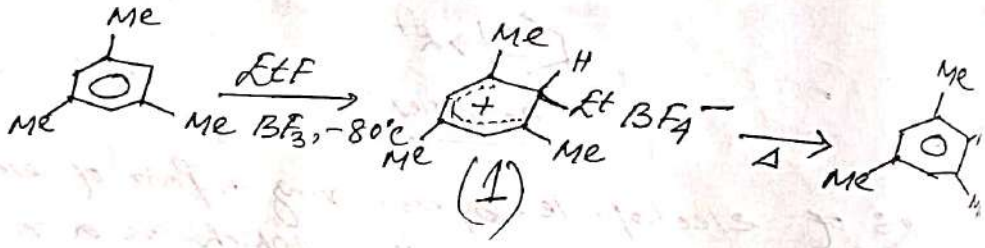
The electron transfer does not occour during the Pi complex formation. This induction type bonding is of higher energy and lesser stability than sigma complex and

thus eventually leads to the formation of the latter in order to attain stability by transferring charges (electrons) to the electrophile.

* Discuss critically the modern concept of the mechanism of electrophilic aromatic substitution giving evidence in support of it.

Ans: See in notes first part.

Evidence: Very strong evidence for the arenium ion-mechanism comes from the isolation of arenium ions in a number of instances. For examples, (1) was isolated as a solid with melting point −15°C from treatment of mesitylene with ethyl fluoride and the catalyst BF_3 at −80°C. When '1' was heated, the normal substitution product (2) is obtained.



Nitration rexn

$$ArH + HNO_3 \xrightarrow{H_2SO_4} ArNO_2$$

Most aromatic compounds, whether of high or low reactivity, can be nitrated, because a wide variety of nitrating agents is available. For benzene, the simple alkyl benzenes and less reactive compounds, the most common reagent is a mixture of concentrated nitric and sulfuric acids, but for active substrates, the reaction can be carried out with nitric acid alone, or in water, acetic acid, or Ac_2O. In fact, these milder conditions are necessary for active compounds such as amines, phenols and furans since reaction with mixed nitric and sulfuric acids would oxidise these substrates.

* What is the role of H_2SO_4 in nitration of aromatic compounds with mixed acids?

Ans

Nitration of aromatic compound apply mixed acid, a mixture H_2SO_4 and nitric acid. This mixture produce the nitronium ions, which is the active species in aromatic nitration. Mixed acid synthesis H_2SO_4 is not consumed and hence acts as catalyst as well as absorbent for water

$$\underset{\text{(base)}}{HNO_3} + 2H_2SO_4 \rightleftharpoons \overset{\oplus}{N}O_2 + H_3O^+ + 2HSO_4^-$$
$$\text{(acid)}$$

Although conc. HNO_3 produces $\overset{\oplus}{N}O_2$ ion by itself, the equilibrium is so far to the left the process is slow. Adding conc. H_2SO_4 to the rxn mixture increases the conc. of $\overset{+}{N}O_2$ ions, thereby increases the rate of reaction.

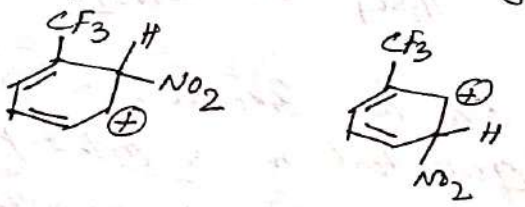
* In concentrated nitric acid alone, by a similar acid-base reaction in which one molecule of nitric acid acts as a acid and another as the base.

$$2HNO_3 \rightleftharpoons \overset{\oplus}{N}O_2 + NO_3^- + H_2O$$

* With N_2O_5 in CCl_4, there is spontaneous dissociation.

$$N_2O_5 \rightleftharpoons \overset{\oplus}{N}O_2 + NO_3^-$$

* Nitration of trifluoromethyl benzene may proceed through the formation of two following σ-complexes. Which one between them you expect to be formed faster and why

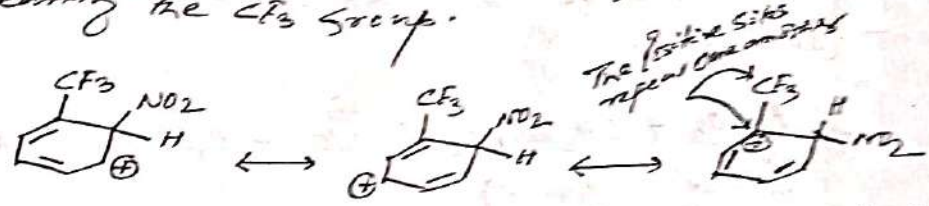


Ans:

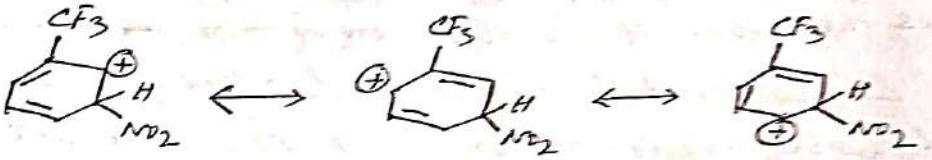
The CF_3- Group is strongly electron withdrawing. Because of the high electronegativity of the fluorines, the C-F bond is quite polar with the positive end of the dipole at the carbon.

When a resonance contributer from a CF_3- σ complex has the positive charge on the carbon bearing

the CF_3- Groups, the positive charge from the CF_3- dipole and positive charge from the resonance contributor repel each other. This repelling behavior destabilize that carbocation, and makes destabilizes the whole σ complex. Ortho σ complex has One resonance contributor with a positive charge on the carbon bearing the $-CF_3$ Group's where as none of the resonance contributors in the meta σ complex has a positive charge on the carbon bearing the CF_3 Group.



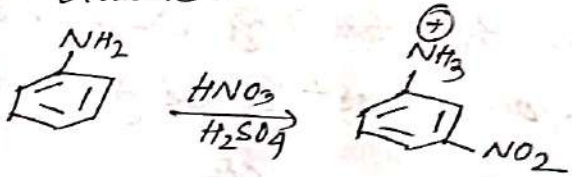
Sigma Complex (I) — most destabilized



Sigma Complex (II)

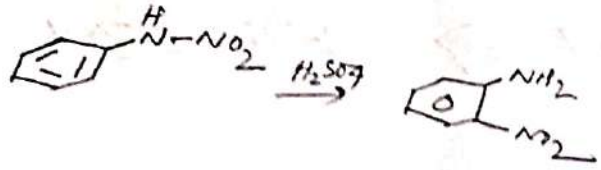
Since CF_3- Groups destabilize σ-complex (I) compared to σ-complex (II) therefore rate of formation of former is slower than the latter.

* When amines are nitrated under strong acid conditions meta Orientation is Generally Observed, because the Species Undergoing nitration is actually the Conjugate acid of the amine.



If the Conditions are less acidic, the free amine is nitrated and the Orientation is ortho-para. Although the free base may be present in much smaller amounts than the Conjugate acid, it is far more Susceptible to aromatic substitution. Because of these factors and because they are Vulnerable to Oxidation by nitric acid Primary aromatic amines are often Protected before nitration by acetyl chloride or acetic anhydride. There is evidence that when the reaction take place on the free amine, it is the nitrogen that is attacked

5 give an N-nitro compound $Ar-NH-NO_2$ which rapidly undergoes rearrangement to give the product.



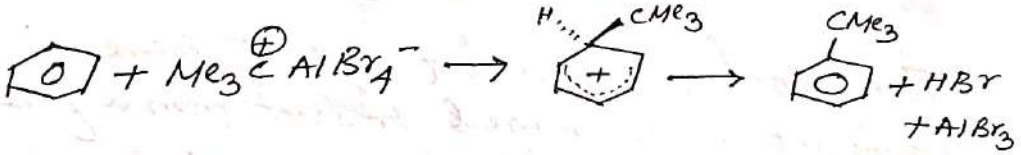
* Explain why nitration of aniline is so sluggish and it gives mostly meta-oriented product?

Ans Write yourself

Friedel-Crafts reactions:

The carbon atom of alkyl halide $\overset{\delta+}{R}-\overset{\delta-}{X}$, is electrophilic, but rarely is it sufficiently so to effect the substitution of aromatic species: the presence of a Lewis acid catalyst. e.g. AlX_3 is also required. That alkyl halides do react with Lewis acids has been demonstrated by the exchange of radioactive bromine into EtBr from $AlBr_3^*$ on mixing and re-isolation; also the actual isolation of solid 1:1 complexes e.g. $CH_3Br:AlBr_3$ at low temperature (-78°C).

Where 'R' is capable of forming a particularly stable carbocation e.g. with Me_3C-Br, it is probable that the attacking electrophile in alkylation is then the actual carbocation $Me_3C^{\oplus}$, as part of an ion pair:

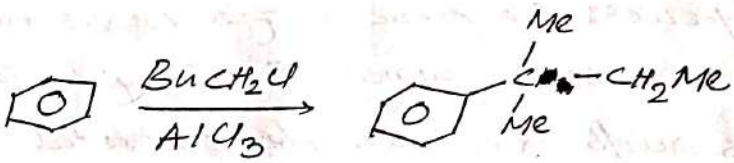


For other cases it seems more likely that the attacking electrophile is a polarised complex, the degree of polarisation for a particular case depending on R in R-X and the Lewis acid employed:

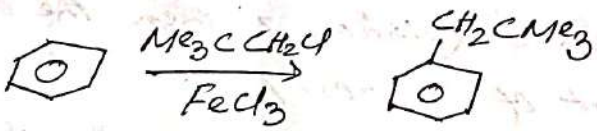
The order of effectiveness of Lewis acid catalysts has been shown to be:

$$AlCl_3 > FeCl_3 > BF_3 > TiCl_3 > ZnCl_2 > SnCl_4$$

In a number of cases of Friedel-Crafts alkylation the final product is found to contain a rearranged alkyl group. Thus the action of $Me_3CCH_2Cl/AlCl_3$ on benzene is found to yield almost wholly the rearranged product $PhCMe_2CHMe_2$ which would be explained on the basis of initial electrophilic complex being polarised enough to allow the rearrangement of $[Me_3CCH_2]^{\delta+}\cdots Cl\cdots AlCl_3^{\delta-}$ to the more stable — $[Me_2CCH_2Me]^{\delta+}\cdots Cl\cdots AlCl_3^{\delta-}$.



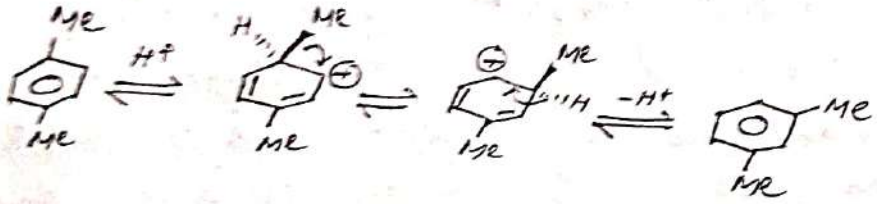
By contrast $Me_3CCH_2Cl/FeCl_3$ on benzene is found to yield almost wholly the unrearranged product $PhCH_2$ the presumption being that the complex with the weaker Lewis acid, $FeCl_3$, is not now polarised enough to allow of isomerisation taking place



Temperature is also found to have an effect, the amount of rearranged product from a given halide and Lewis acid being less at lower temperature

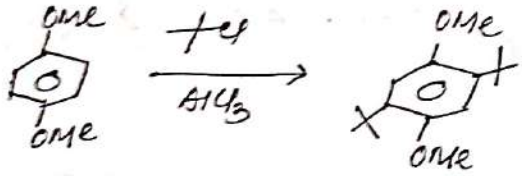
Heating p-dimethyl benzene (p-Xylene), with $AlCl_3$ and HCl results in the conversion of the major of it into more stable m-dimethyl benzene. The presence of HCl is essential, and the change is believed to involve migration of an 'Me' group in the initial

protonated species.



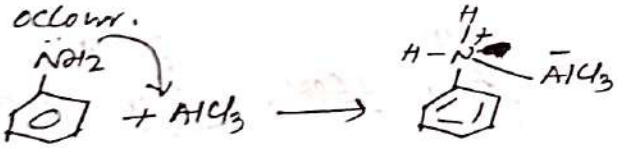
The presence of an electron withdrawing substituent is generally sufficient to inhibit Friedel-Craft alkylation; thus nitrobenzene is often used as a solvent for the reaction because $AlCl_3$ dissolves readily in it, thus avoiding a heterogeneous reaction.

Steric hindrance can be exploited to limit the number of alkylations, as in the t-butylation of 1,4-dimethoxybenzene.

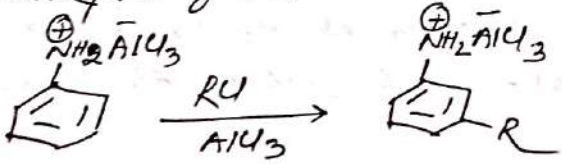


* OH, OR, NH_2 groups do not facilitate the reaction, since the catalyst coordinates with these basic groups. Although phenols give the usual Friedel-Crafts reactions, orienting ortho and para, the reaction is very poor for amines.

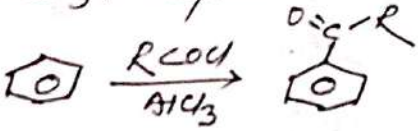
* The lone pair electrons of the amines react with lewis acid $AlCl_3$. This places a positive charge next to the benzene ring, which is so strongly deactivating that the Friedel-Craft reaction cannot occur.



However using excess of lewis acid may cause some amount of m-alkylating product.



* The most important method for the preparation of aryl ketones is known as Friedel-Craft acylation.



The reaction is of wide scope. Reagents used are not only acyl

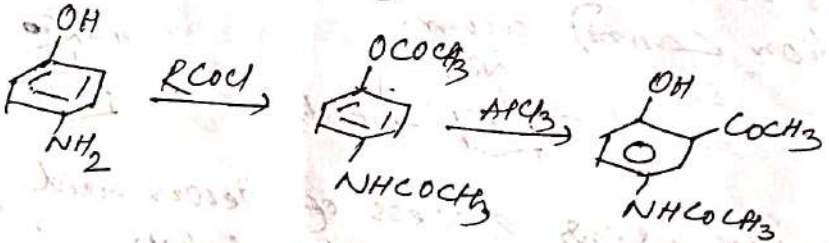
halides but also carboxylic acids, anhydrides, and ketenes may be aryl as well as alkyl. The major disadvantage of alkylation are not present here. Rearrangement of R never found, and because the RCO group is deactivating the reaction stops cleanly after one group is introduced. All four acyl halides can be used, though chloride are most commonly employed. The order of activity $I > Br > Cl$

* Catalyst are Lewis acid, similar to those used in alkylation but in acylation a little more than 1 mole of catalyst is required per mole of reagent, because the first mole coordinates with the oxygen of the reagent.

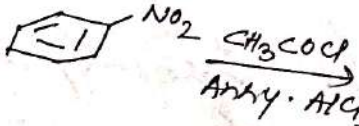
$$R-\underset{\underset{O}{\|}}{C}-Cl + AlCl_3 \longrightarrow R-\underset{\underset{\oplus O-\bar{A}lCl_3}{\|}}{C}-Cl$$

The reaction is quite successful for many types of substrate, including fused ring systems which give poor results with alkylation. Compound containing ortho-para-directing groups, including alkyl, hydroxy, alkoxy, halogen and acetamido groups, are easily acylated and give mainly or exclusively the para product because of large size of acyl group.

* With amines and phenols there may be competition from N- or O- acylation. However, O-acylated phenols can be converted to C-alkylated phenols by the Fries rearrangement.

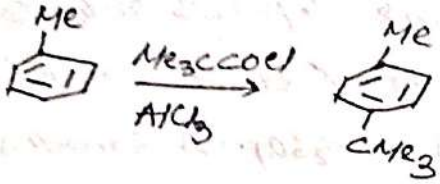


Friedel-Crafts acylation is usually prevented by meta-directing groups. Indeed, nitrobenzene is often used as a solvent for the reaction.

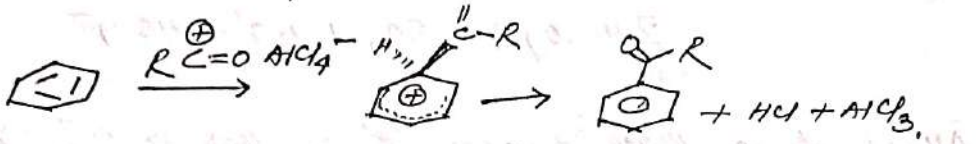


Rearrangement of R' does not take place, as in alkylation, but decarbonylation can take place, especially where R' would form a stable carbocation, so the end result is then alkylation rather than the expected acylation

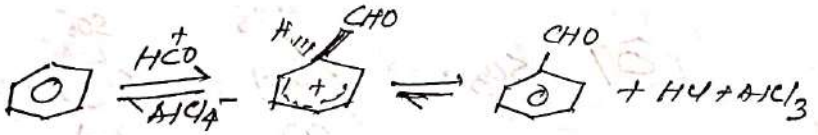
$$Me_3C-\overset{\oplus}{C}=O \longrightarrow CO + Me_3\overset{\oplus}{C} \xrightarrow{C_6H_6} PhCMe_3$$

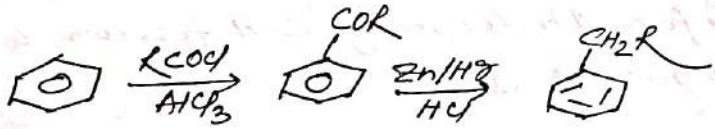
* 

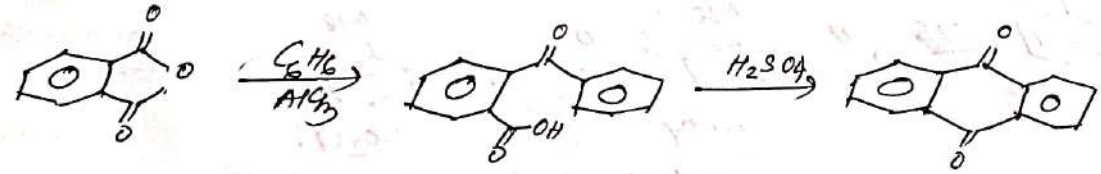
General mechanism of acylation:

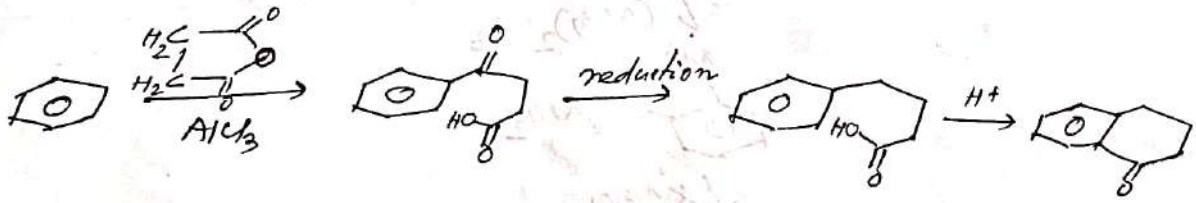


+ Formylation may be carried out by use of CO, HCl and $AlCl_3$ (the Gattermann–Koch reaction); it is doubtful whether HCOCl is ever formed, the most likely electrophile being the acyl cation $H\overset{\oplus}{C}=O$ (i.e. protonated CO) in the ion pair $H\overset{\oplus}{C}O\,AlCl_4^-$



* 



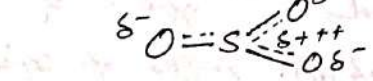


* **Sulphonation:**

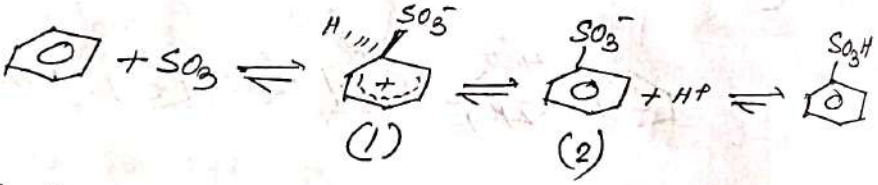
The mechanistic details of sulphonation have less closely explored than those of nitration or halog Benzene itself is sulphonated fairly slowly by H_2SO_4 H_2SO_4, but rapidly by oleum or by SO_3 in inert so The nature of the actual electrophile depends on the co but is probably always SO_3: either free or linked Lewis, e.g. $H_2SO_4 \cdot SO_3$ ($H_2S_2O_7$) in H_2SO_4. A small of SO_3 is developed in H_2SO_4 itself through the equili

$$2H_2SO_4 \rightleftharpoons SO_3 + H_3O^+ + HSO_4^-$$

Attack take place through 'S' as this is highly polari i.e. electron deficient.



Sulphonation, like iodination, is reversible and is to take place in conc. H_2SO_4 via the pathway:



(1) (2)

In oleum the σ complex (1) is believed to undergo protonation of SO_3^- before undergoing C–H fission to yield the SO_3H analogue of (2)

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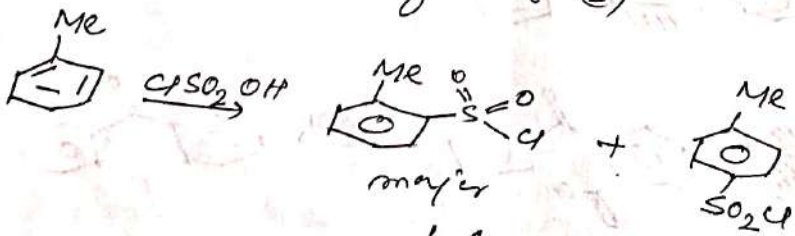
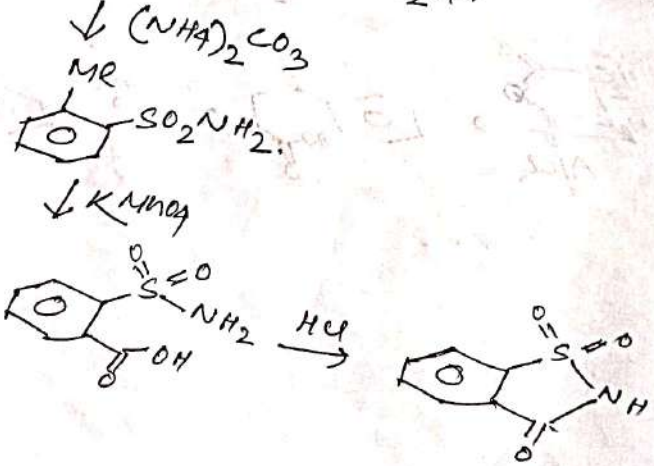
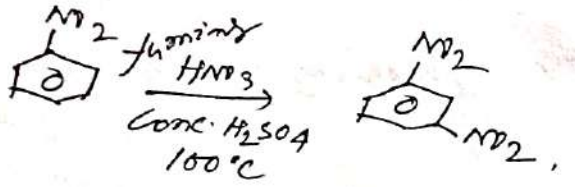
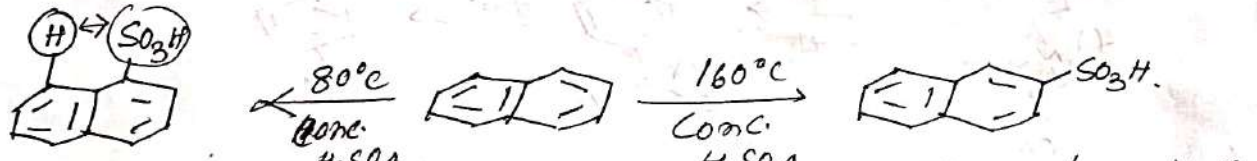






Sulphonation of Naphthalene : (Kinetic vs thermodynamic Controlled Product)

Sulphonation of naphthalene with conc. H_2SO_4 at 80°C is found to lead to complete 1-substitution, the rate of formation of the alternative 2-sulphonic acid being very slow at this temperature i.e. Kinetic control. Sulphonation at 160°C, however, leads to the formation of no less than 80% of the 2-sulphonic acid, the remainder being the 1-isomer. That we are now seeing thermodynamically control is confirmed by the observation that heating pure naphthalene 1- or 2-sulphonic acid with conc. H_2SO_4 at 160°C results in the formation of exactly the same equilibrium mixture as above, containing 80% of 2-, 20% of 1-sulphonic acids. The greater stability of 2-acid stems from the destabilising effect, in the 1-acid, of ~~Ea~~ steric - interaction between the very bulky SO_3H and the H-atom in the adjacent 8-position; the 1- and 3-H atoms, in the 2-acid are both further away.



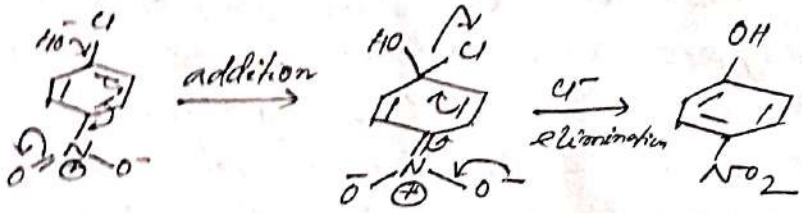
Kinetically Controlled

Peri-effect

Thermodynamically Controlled

* How would you carry out the following transformation? Give plausible mechanism: (2)

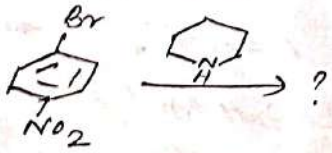
Ans:



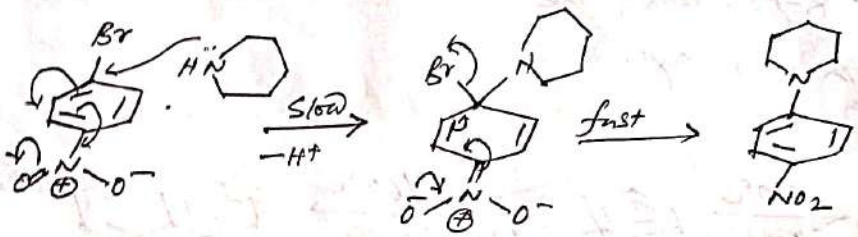
The nucleophile is a good one, the negative charge can be pushed through on to the oxygen atoms of the nitro group, and chloride is a better leaving group than OH.

[* The chlorine atom in p-nitro chloro benzene is more reactive than that in chlorobenzene towards nucleophilic substitution-ex

* Predict the product and mechanism:



Ans:



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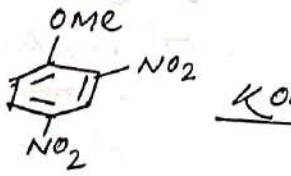
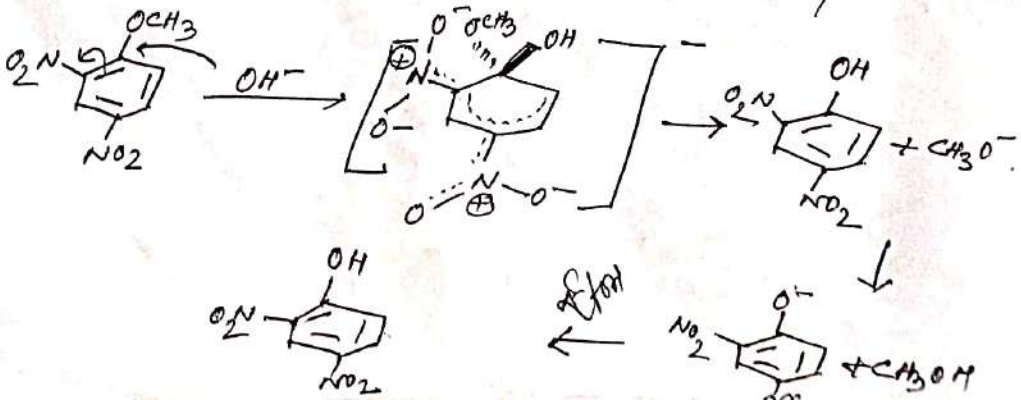
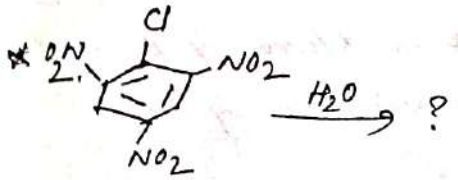


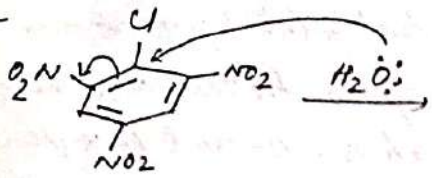
Ans:

2,4-dinitro anisole undergoes ready cleavage by alk... because two $-NO_2$ groups ortho and para to $-OCH_3$ activates the substrate towards nucleophilic substit...

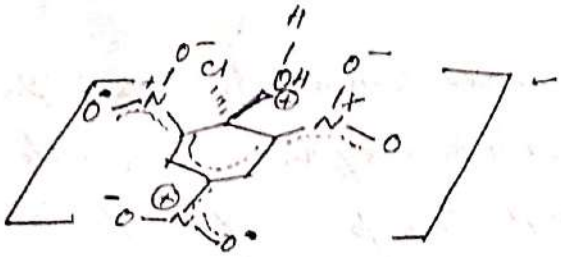


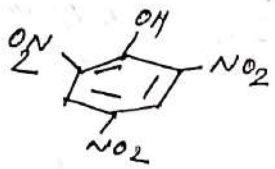


Ans

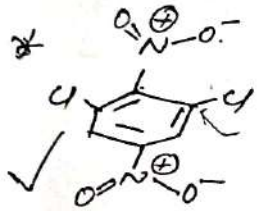


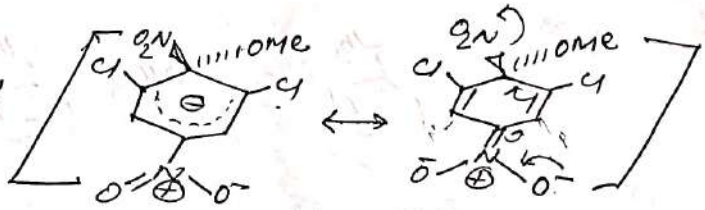
Picryl Chloride



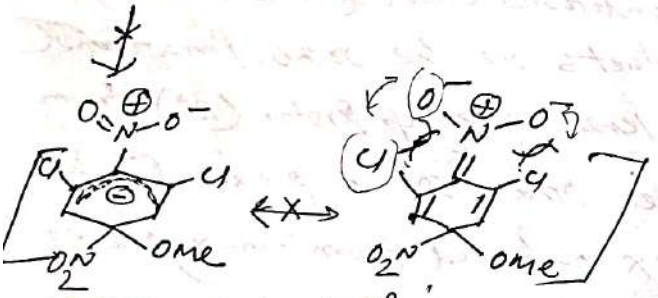


Picric acid



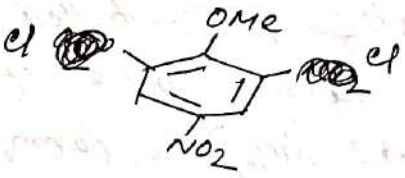


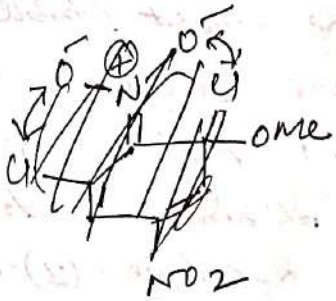
More Stable



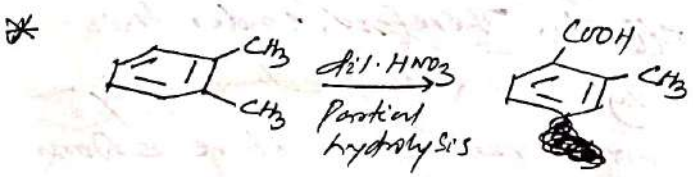
Not Possible

due to steric interaction





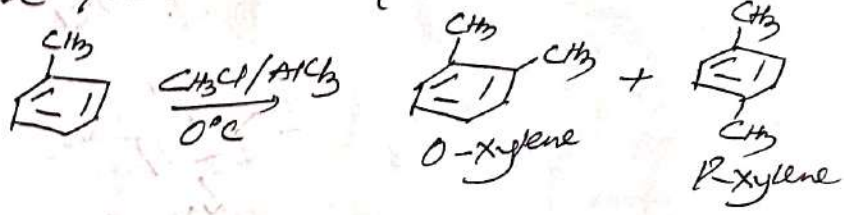
NO2



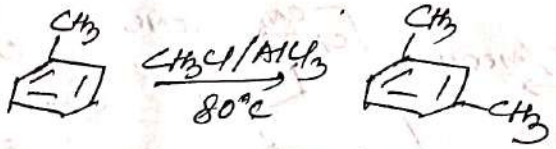
* Methylation of toluene at 0°C gives a mixture of o- & p-xylene while at 80°C it gives mainly m-xylene.

Ans:

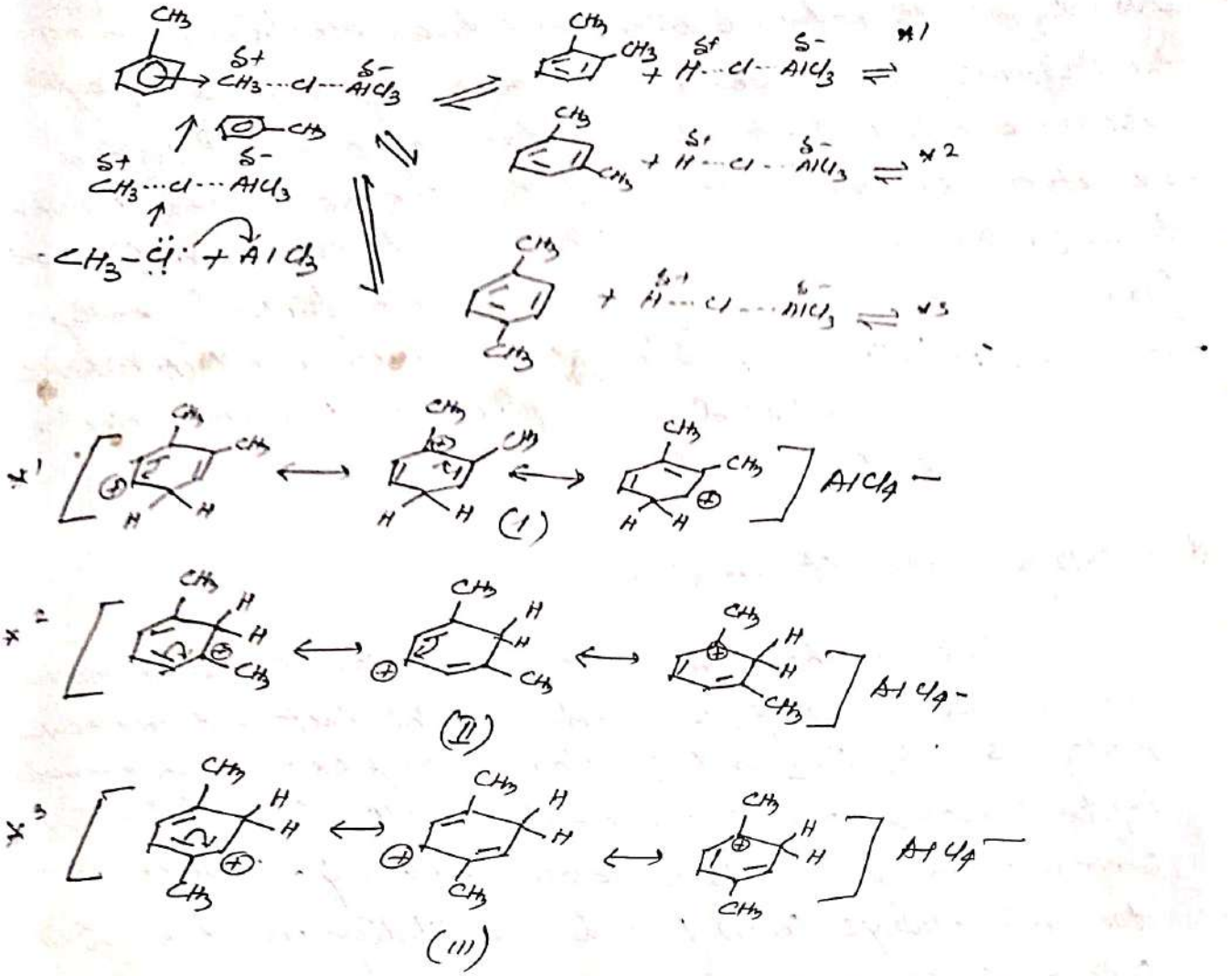
At lower temperature the product development is Friedel-Crafts alkylation is kinetically controlled and as the methyl group is o-, p- directing, o- and p-xylene are obtained predominantly.



At higher temperature, on the other hands the reaction is reversible and results in predominant formation of m-xylene



Under this equilibrium conditions each of the initially kinetically controlled products i.e. the ortho, para and the meta isomer of xylene take up proton (H^+) from ($H^{\delta+}\cdots Cl\cdots AlCl_3^{\delta-}$) to form three other σ complexes (I, II and III). The σ-complex obtained from m-xylene is the most stable one because both the $-CH_3$ groups are involved in stabilising the positive charge by and hyperconjugation effects. Therefore, under this equilibrium conditions m-xylene exists predominantly the σ-complex (II) and when the reaction mixture is work-up by addition of water, m-xylene is obtained predomin



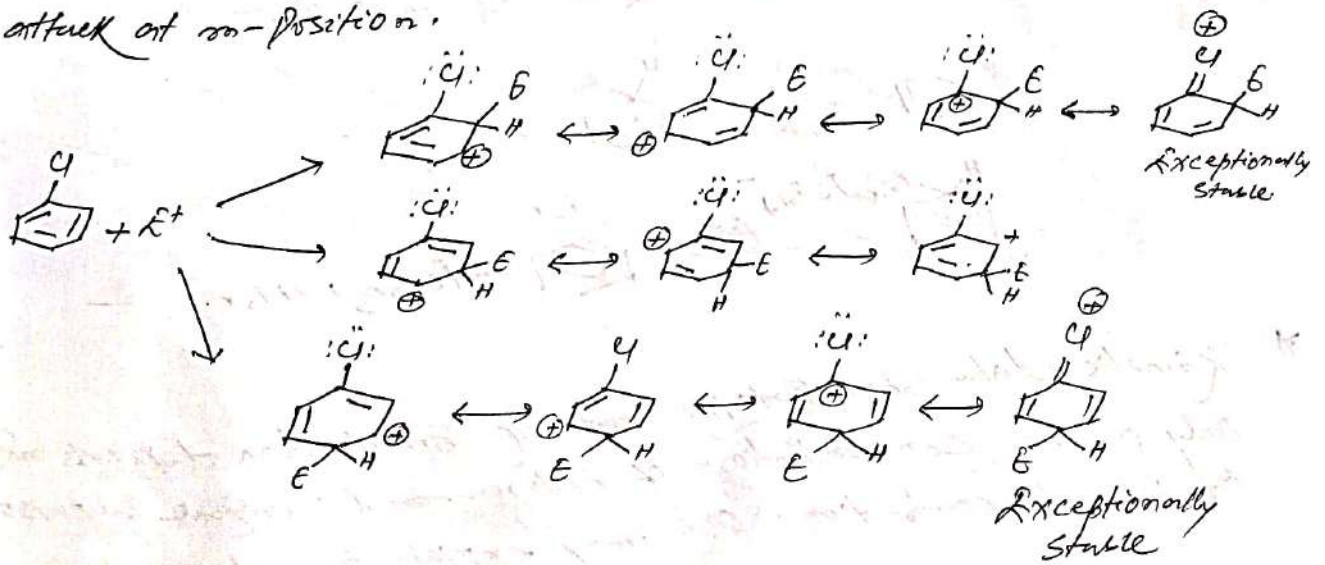
(I)

(II)

(III)

+ Inspite of its −I effect, Cl is ortho-para orienting group?

Ans The ortho and para orientation is favoured because of o & p-positions as compared to the σ-complex is more stable for electrophilic attack at m-position.



Exceptionally stable

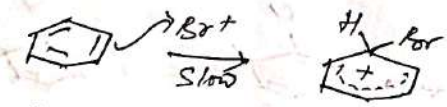
Exceptionally stable

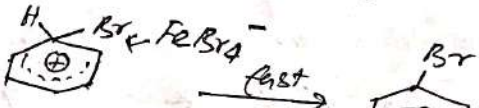
Chlorine by its inductive effect withdraws electrons from a the positions i.e., it deactivates all the positions and by resonance effect it donates electrons to O- and P- positions i.e. it makes the deactivation less for the O- and P- po than for the meta-position. The result is the predomi formation of O- and P-substitution products. Recently is thus controlled by stronger inductive effect whe Orientation is controlled by weaker but more selecti resonance effect.

* Halogenation of Benzene:

The mechanism of halogenation e.g. bromination is somewhat complicated due to the fact that molecu halogens, Cl_2, Br_2 and I_2, form complexes with aroma hydrocarbons. Complex formation helps substitution by bringing the reactants in close proximity; however, it does not always follow that a substitution reaction will occour. A catalyst is usually necessary. The catalysts us are metal halides which act as Lewis acids ($FeBr_3$, $AlCl_3$ and $ZnCl_2$). Their catalytic activity is attributed to the ability to polarize halogen-halogen bond and just like an usual aromatic ion mechanism the bromination of benzene may be thus represented below:

$$:\ddot{Br}-\ddot{Br}: + FeBr_3 \rightleftharpoons Br^+ + FeBr_4^-$$

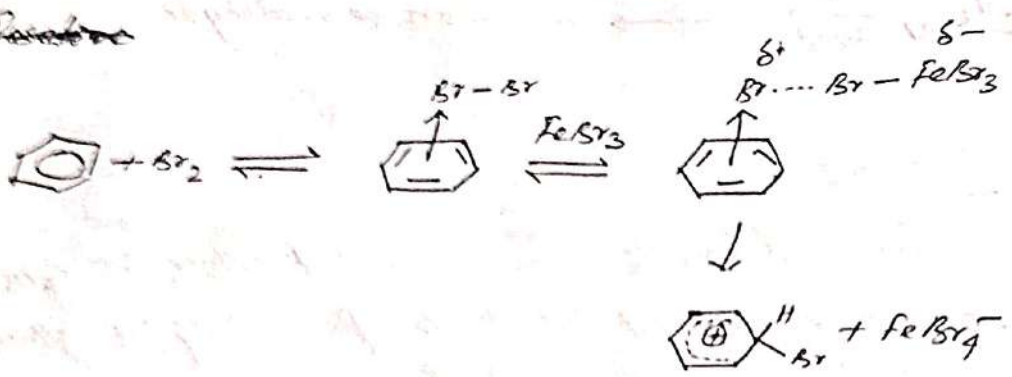


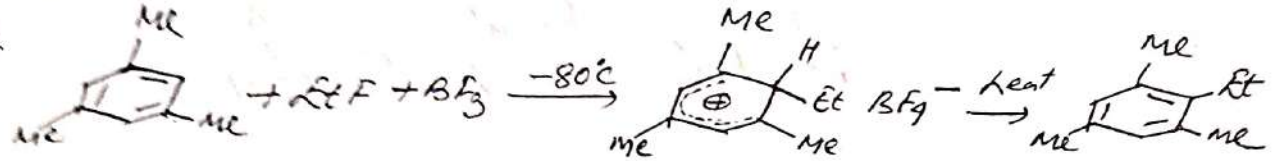


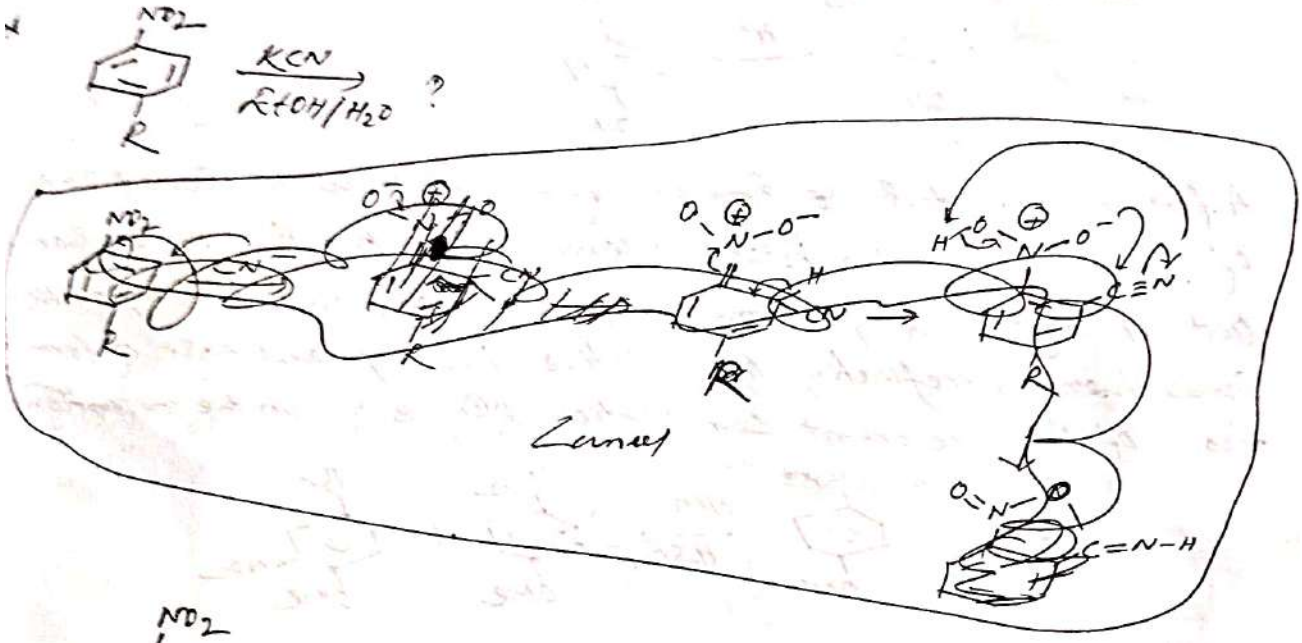
$+ FeBr_3 + HBr.$

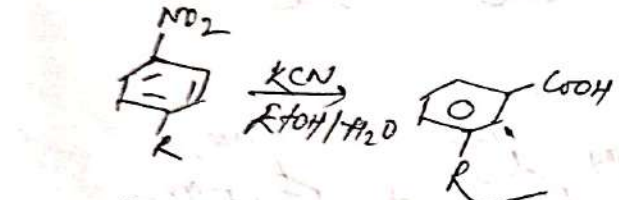
* Kinetic data show that the rate of bromination depends only on the concentration of halogen and benzene but on $FeBr_3$ concentration. One may explain this due to the

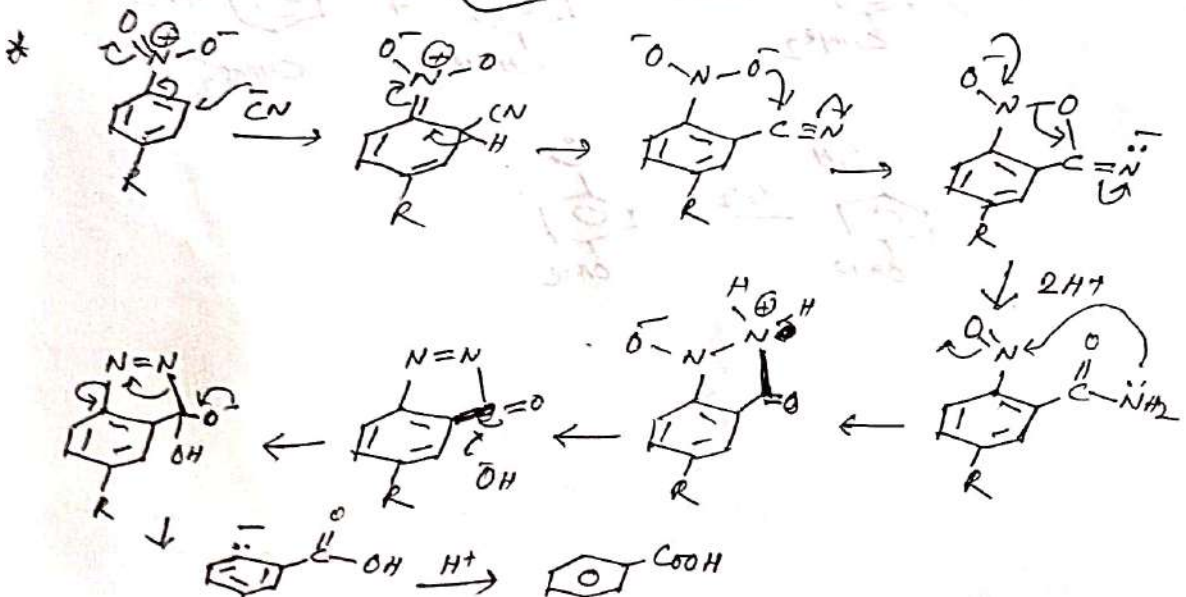
movement of a molecular complex with ionic character.

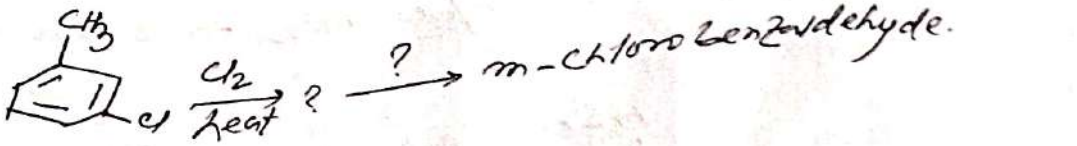






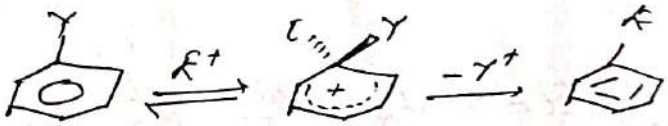




* 

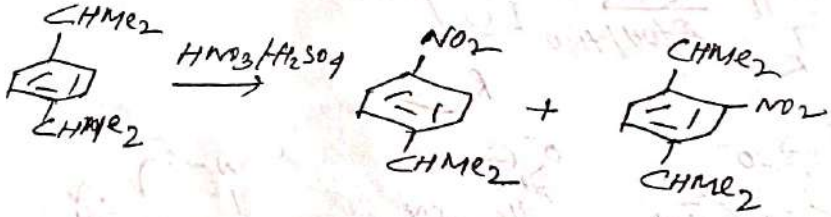
Ipso Substitution:

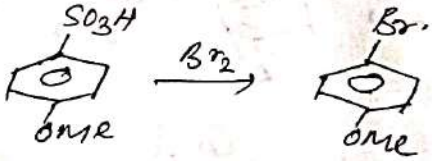
In addition to o-, m- and p- attack on C_6H_5 there is, in theory at least, the possibility of attack by an electrophile occurring on the ring carbon atom to which the substituent Y is already attached:

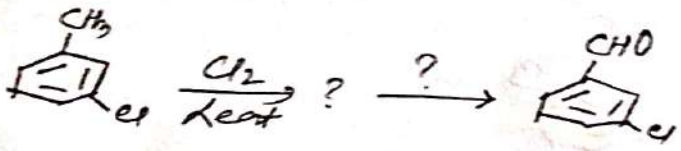


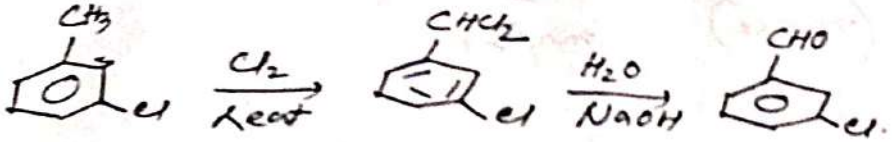
Examples

A factor expected to promote ipso substitution would be ease of formation of the potential leaving group $Y^{\oplus}$. This is borne out by known displacement of secondary and tertiary alkyl substituents, reflecting the relative stability and ease of formation of the relevant carbocation $R^{\oplus}$, e.g. in the nitration



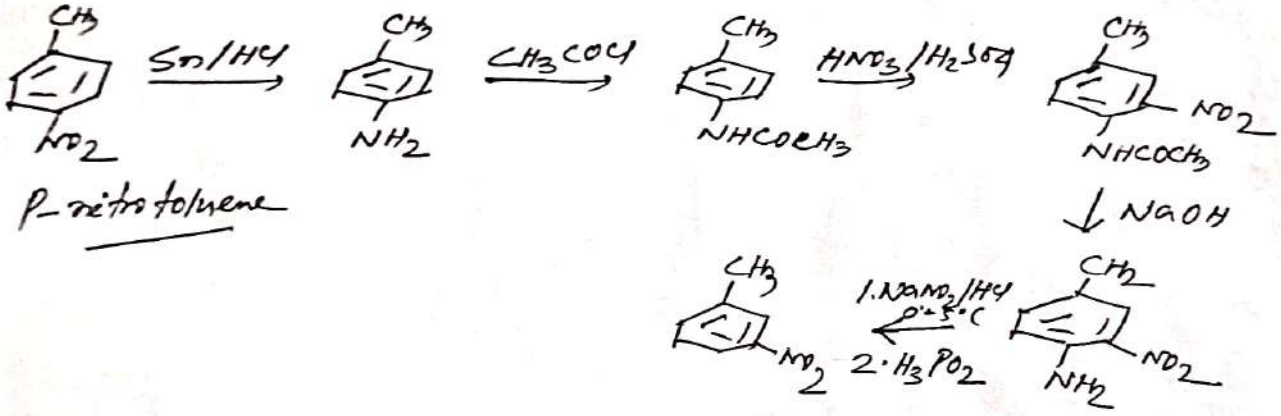


* 

Ans. 

* How would you prepare m-nitro toluene from p-NO_2-toulene?

Ans 



p-nitro toluene

m-nitrotoluene

*