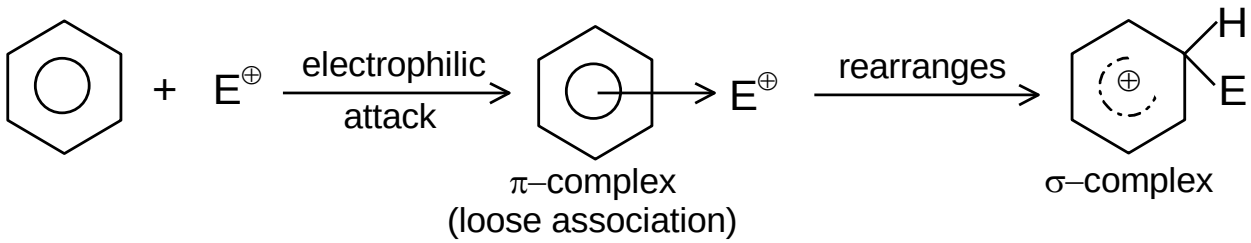
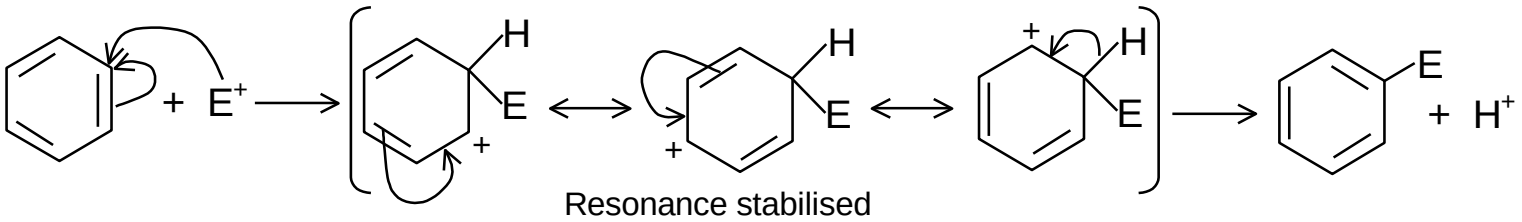
1. ELECTROPHILIC SUBSTITUTION

Benzene nucleus is composed of six sp^2 hybridized carbon atoms linked together to form a hexagonal planar structure with one H atom bonded to each carbon. All the carbon atoms have one unhybridized p-orbital with one electron, which forms a sextet cloud of electrons above and below the plane of the benzene ring. It means that there is high density of electronic charge in benzene. Hence, a strong electrophile (electron deficient group) can now attack this electron cloud i.e. benzene readily undergoes electrophilic substitution. Electrophilic substitution in benzene ring is believed to be a bimolecular (S_E2) reaction, which involves the following pathways. As the electrophile comes closer to the benzene nucleus, a π-complex is formed. π-complex rearranges to give σ-complex.



σ-complex formation results in the loss of aromaticity (breaking of the sextet) which is compensated to some extent by resonance.



In the last step, intermediate carbonium ion, in the presence of a proton acceptor, loses a proton to give the substituted product with complete sextet.

Above E^+ is an electrophile and may be X^+ (Cl^+, Br^+, I^+) in halogenation, NO_2^+ in nitration, SO_3 in sulphonation and R^+ or RCO^+ in Friedel Craft's reaction.

2. Examples of Electrophilic Aromatic Substitution Reactions

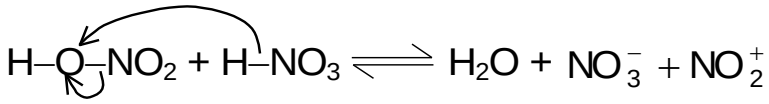
Substitution reactions like halogenation, nitration, sulphonation, Friedel Craft's reactions are common examples of electrophilic aromatic substitution reactions. The mechanism of these reactions is described as below.

2.1. Nitration

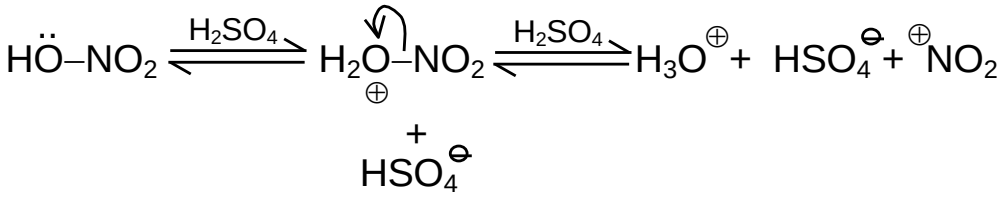
Nitration is brought about by the action of concentrated nitric acid or a mixture of concentrated nitric acid and sulphuric acid often called nitrating mixture. HNO_3 alone is a weak nitrating agent whereas the mixture is strong nitrating mixture.

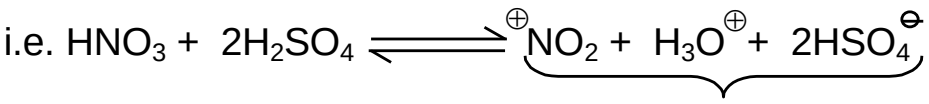
The reaction involves electrophilic attack by the nitronium ion, $NO_2^{\oplus}$ which is produced under the conditions of reaction.

When HNO_3 alone is the nitrating agent:



When concentrated HNO_3 and concentrated H_2SO_4 is the nitrating mixture, NO_2^+ (Nitronium ion) is produced as follows:

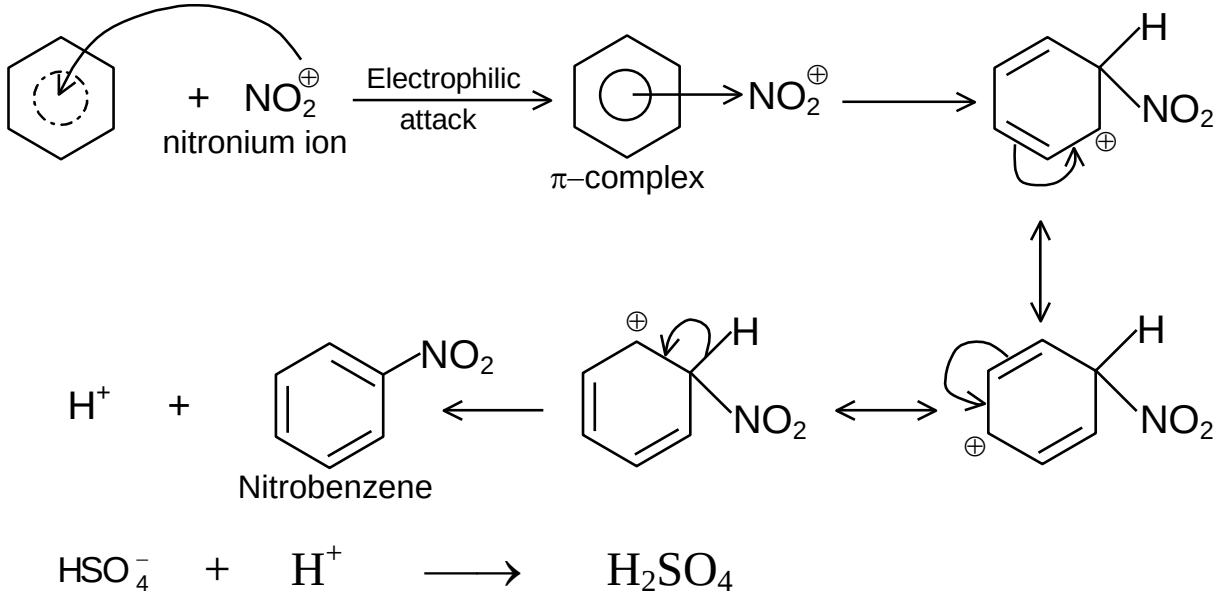




When HNO_3 alone is the nitrating agent, generation of water dilutes the acid and generation of NO_2^+ ion is slowed down. Hence it is a mild nitrating agent.

But when mixture of concentrated HNO_3 and concentrated H_2SO_4 is the nitrating agent, concentrated sulphuric acid helps to speed up the generation of nitronium ion by absorbing water molecule and producing H_3O^+ in the medium.

Now, the NO_2^+ ion attacks the benzene nucleus and forms an intermediate cation,
a benzenonium ion, which loses a proton to yield the nitro derivative.

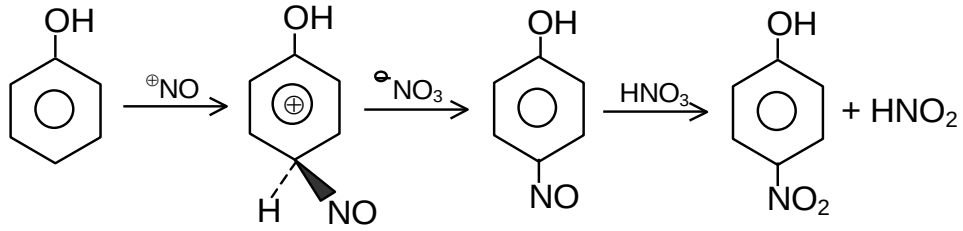


$$HSO_4^- + H^+ \longrightarrow H_2SO_4$$

The reaction by which nitronium ion is produced is simply an acid base equilibrium in which sulphuric acid serves as the acid and the much weaker nitric acid serves as a base. The very strong acid, sulphuric acid causes nitric acid to ionise in the sense, $HO^-\cdots\cdots NO_2^+$, rather than in the usual way, $H^+\cdots\cdots\bar{O}NO_2$. The nitronium ion is well known existing in salts such as $NO_2^+ClO_4^-$ and $NO_2^+BF_4^-$ which smoothly nitrate benzene at room temperature. It supports the mechanism, in which the electrophile species attacking the aromatic compound is nitronium ion, NO_2^+.

Highly reactive aromatic compounds, such as phenol, are found to undergo ready nitration even in dilute nitric acid and at a far more rapid rate that can be explained on the basis of the concentration of $^{\oplus}NO_2$ that is present in the mixture. This has been shown to be due to the presence of nitrous acid in the system which nitrosates the reactive nucleus via the nitrosonium ion, $^{\oplus}NO$.

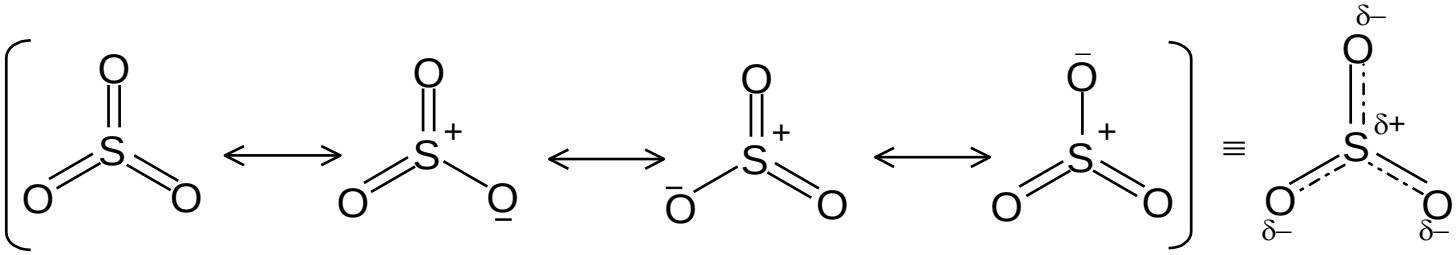
$$HNO_2 + 2HNO_3 \rightleftharpoons H_3O^{\oplus} + 2\overset{\ominus}{N}O_3 + {}^{\oplus}NO$$



2.2 Sulphonation

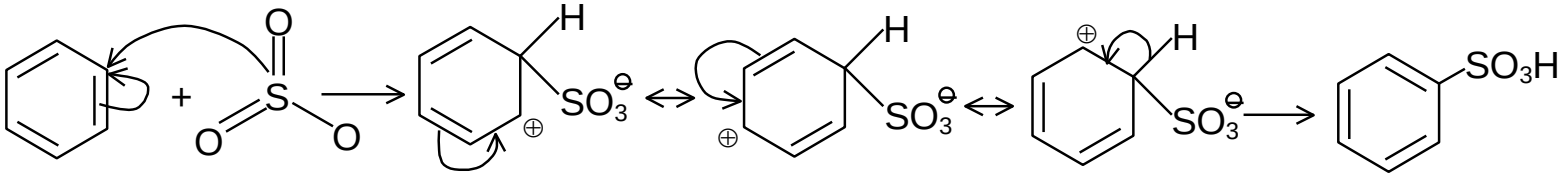
Sulphonation is done by heating the substrate with conc. sulphuric acid or fuming sulphuric acid containing varying proportions of sulphur trioxide.

Experimental work based on kinetic studies in concentrated sulphuric acid and in oleum (H_2SO_4, SO_3) strongly favours the theory that sulphur trioxide is the active species. SO_3 is bonded to three more electronegativity oxygen atoms. Hence S is electron deficient centre acting as electrophile.

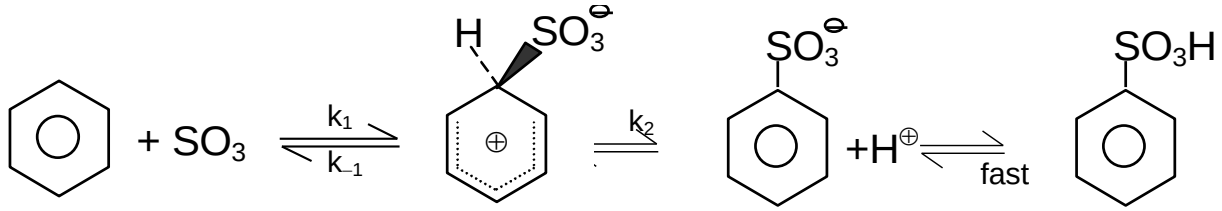


Now the electrophilic reagent, SO_3, attacks the benzene ring to form the intermediate carbocation.

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



Sulphonation, like iodination, is reversible and is believed to take place in concentrated sulphuric acid via the pathway,



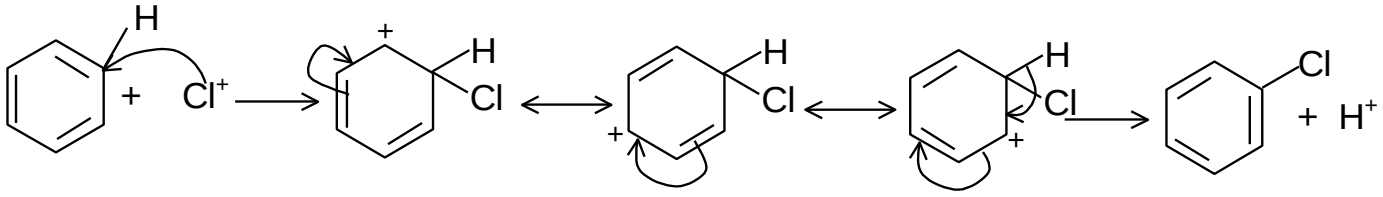
In oleum, the σ complex is believed to undergo protonation of the SO_3 before undergoing C–H fission to yield the SO_3H analogue. Like iodination, sulphonation exhibits a kinetic isotope effect, indicating that C–H bond breaking is involved in the rate determining step of the reaction, i.e. that $k_{-1} \gtrsim k_2$.

2.3 Halogenation

In halogenation, electrophiles are Cl^+, Br^+ and I^+. As halogens are neutral (non-polar) covalent molecules, so to generate polarity these react with halogen carriers i.e. Lewis acids (transition metal halides). The Lewis acid polarizes the halogen molecule forming complexes with negative ion, leaving positively charged halonium ion to react with benzene nucleus. The positively charged or electrophile species then attacks the nucleophilic aromatic substrate to give an intermediate carbonium ion which is resonance stabilized. It abstracts a proton and electron pair binding the hydrogen to the ring moves to restore the highly stable benzene ring system.

(i) $FeCl_3 + Cl_2 \longrightarrow Cl^{\delta+}\!\!-\!\!Cl^{\delta-}\cdots FeCl_3 \longrightarrow Cl^+ + FeCl_4^-$

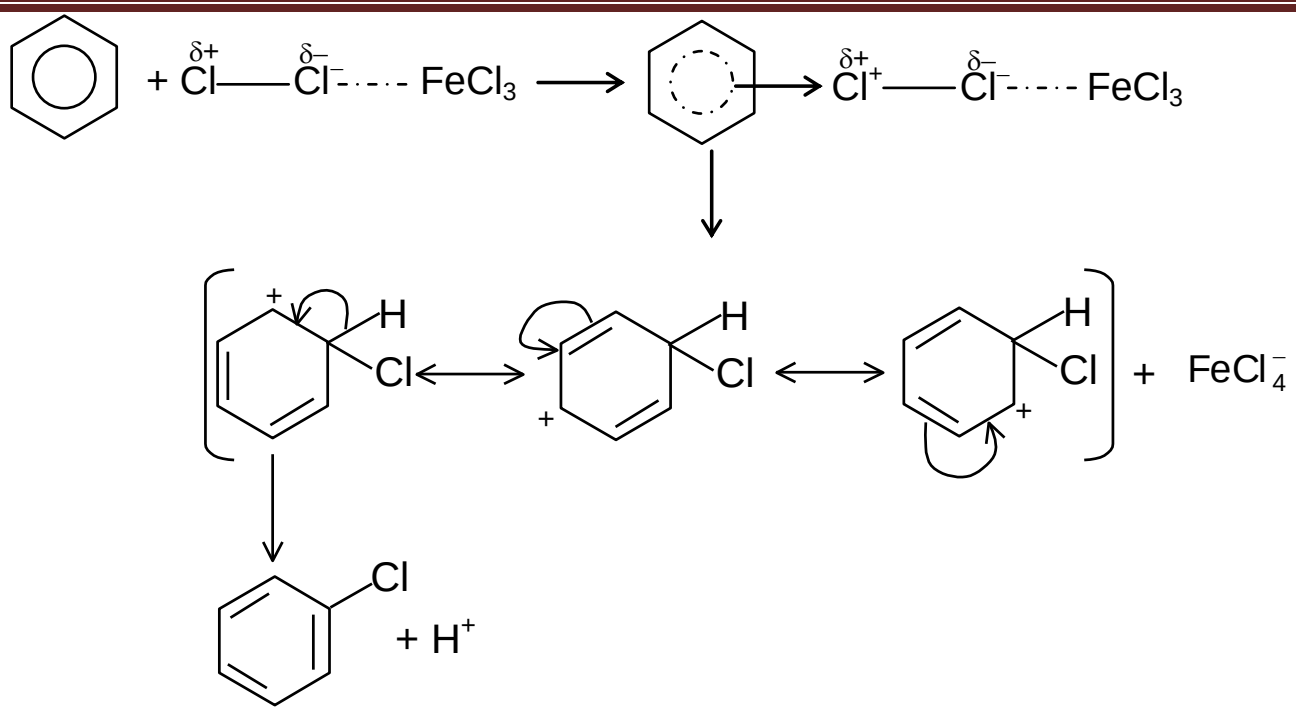
(ii)



(iii) $FeCl_4^- + H^+ \longrightarrow FeCl_3 + HCl$

Or

$FeCl_3 + Cl_2 \longrightarrow Cl^{\delta+}\!\!-\!\!Cl^{\delta-}\cdots FeCl_3$



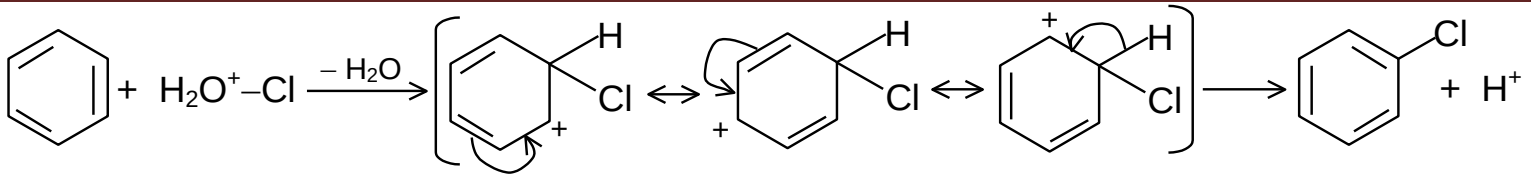
$$FeCl_4^- + H^+ \longrightarrow FeCl_3 + HCl$$

Role of Lewis acid

The loosely held π electrons of the double bond in alkenes polarize the halogen molecule even in the absence of a Lewis acid catalyst. The π electrons cloud in benzene is relatively less available and consequently the presence of a Lewis acid catalyst is necessary to polarize the halogen molecule, at least in the case of less reactive aromatic compounds (benzene, chlorobenzene etc.). The fact that halogenation of more reactive aromatic compounds (phenol, aniline etc.) where π electrons are more available proceeds smoothly even in the absence of Lewis acid catalyst establishes the role of Lewis acid in the above mechanism for halogenation of aromatic compounds.

Note: A similar dual mechanism can also operate when halogenation is carried out with hypochlorous or hypobromous acid. This reaction is acid catalysed.

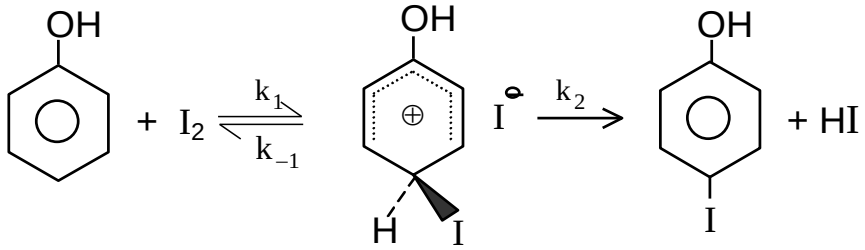
$$H–O–Cl + H^+ \longrightarrow H_2O^+–Cl$$



Instead of a protonated hypohalous acid, the attacking reagent can be a positive halogen cation, without affecting the course of reaction.

$$H_2O^+Cl \rightleftharpoons H_2O + Cl^+$$

Kinetic isotope effects have not been observed for chlorination and only rarely for bromination, i.e. the reactions normally follow pathway like nitration. In iodination, which only takes place with iodine itself on activated species, kinetic isotope effects are the rule. This presumably arises because the reaction is readily reversible (unlike other halogenations), loss of I^+ occurring more often from the σ complex than the loss of H^+, i.e. $k_{-1} \gtrsim k_2$.

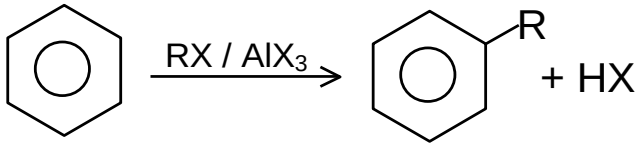


Thus k_H/k_D for the iodination of phenol and 2,4,6-Trideuteriophenol is found to be ≈ 4. Iodination is often assisted by the presence of bases or of oxidising agents, which remove HI and thus displace the above equilibrium to the right. Oxidising agents also tend to produce $I^{\oplus}$, or a complex containing positively polarized iodine, from I_2, thus providing a more effective electrophile. Halogenation may also be carried out by use of interhalogen compounds $\overset{\delta+}{Br}–\overset{\delta-}{Cl}$, $\overset{\delta+}{I}–\overset{\delta-}{Cl}$,etc., attack occurring through the less electronegative halogen as this will constitute the 'electrophilic' end of the molecule.

2.4 Friedel Craft's Reaction

Alkylation or acylation of aromatic ring with alkyl halides or acyl halides in presence of a Lewis acid, generally anhydrous $AlCl_3$ (Friedel craft catalyst) is called Friedel crafts reaction.

The aromatic ring, to which the side chain is attached, may be that of benzene itself, certain substituted benzenes or more complicated aromatic ring systems like naphthalene and anthracene. e.g.



where X = Cl, Br, I, but the most effective catalyst is anhydrous $AlCl_3$:

R = CH_3- , CH_3-CH_2- , $C_6H_5CH_2-$ substituted alkyl groups, or acyl group $CH_3-\overset{\overset{O}{\|}}{C}-$ or $C_6H_5-\overset{\overset{O}{\|}}{C}-$ etc. Because of low reactivity of halogen attached to an aromatic ring, aryl halides cannot be used, in place of alkyl halides. Also, vinyl halides cannot be used instead of alkyl halides.

MECHANISM

It has been observed that rate of reaction $\propto$ [substrate] [RX] [AlX_3]. It means the reaction is 3rd order, which suggests that AlX_3 is involved in the formation of transition complex.

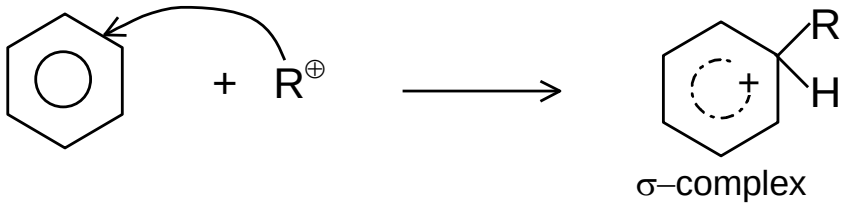
4.1 ALKYLATION

The carbon atom of alkyl halides, $\overset{\delta^+}{R}—\overset{\delta^-}{X}$, is electrophile, but rarely is it sufficiently effective so, to affect the substitution of aromatic species. So, the presence of a Lewis acid catalyst is also required. Anhydrous aluminium chloride, $AlCl_3$, being a Lewis acid, accepts a lone pair of electrons from halogen (Chlorine atom) of $R-\ddot{\underset{\cdot\cdot}{Cl}}:$. This makes R (alkyl) group to be sufficiently polar so as to act as an electrophile. Now, two mechanisms are possible for

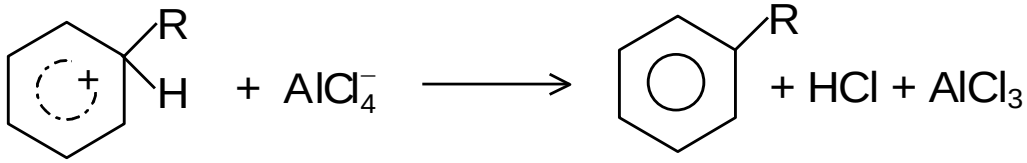
Friedel Craft's alkylation. Both involve electrophilic substitution, but they differ as to the nature of the electrophile. One of the mechanism for Friedel Craft's reaction involves the following steps.

(i) $R-\ddot{\underset{\ddot{}}{Cl}}: + AlCl_3 \longrightarrow R^{\oplus}\!-\!\overset{\delta+}{Cl}\!-\!\overset{\delta-}{AlCl_3} \longrightarrow R^+ + AlCl_4^-$

Carbocation

(ii) 

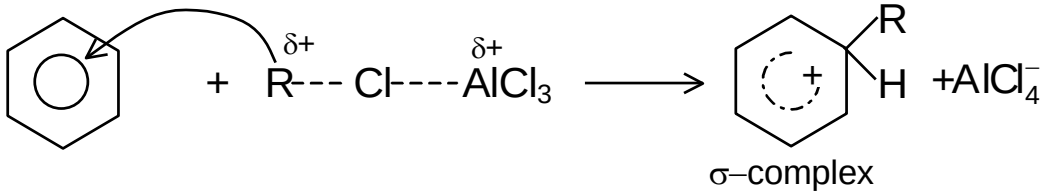
σ–complex

(iii) 

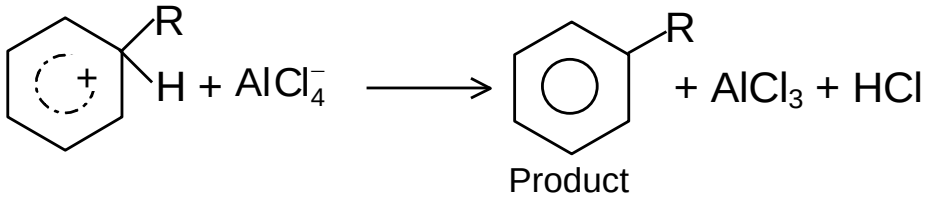
In the above mechanism, the electrophile is a carbocation. The function of the aluminium chloride is to generate this carbocation by abstracting the halogen from alkyl halide.

On the other hand, another mechanism is carried out by the electrophile which is an acid base complex of alkyl halide and Lewis acid, from which the alkyl group is transferred in one step from halogen to the aromatic ring.

(i) $R-\ddot{\underset{\ddot{}}{Cl}}: + AlCl_3 \longrightarrow \overset{\delta+}{R}\cdots Cl\cdots\overset{\delta-}{AlCl_3}$.

(ii) 

σ–complex

(iii) 

Product

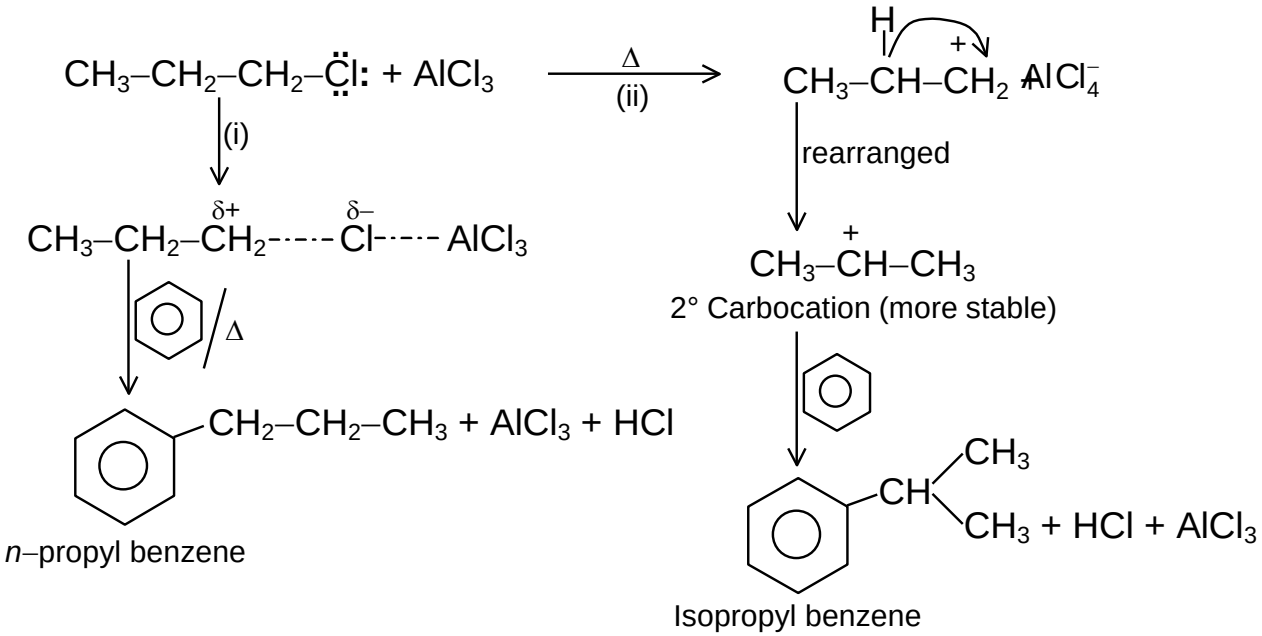
(i) Nature of alkyl groups

If the alkyl group is simple CH_3- or CH_3CH_2-, then a complex between alkyl halide and Lewis acid is the electrophile as shown in second mechanism. But because of the relative stability of s- and t-carbonium ions, the adducts with s- and t-alkyl halides ionise and it is now the carbonium ion that is predominantly the active species. e.g.

$$Me_3C{-}Cl + AlCl_3 \longrightarrow Me_3C^{\oplus} + AlCl_4^{-}$$

(ii) Temperature

Not only nature of the alkyl group, but also temperature determines the nature of electrophile. e.g. n-alkyl group can be introduced to a fair extent without rearrangement at low temperatures, because ionisation of the adduct is retarded. But at higher temperatures, carbonium ion is formed which rearranges and the product is rearranged alkyl benzene. Thus n-propylchloride gives isopropyl benzene.



In the same way, isobutyl chloride gives t–butyl benzene.

(iii) Nature of Lewis acid as catalyst

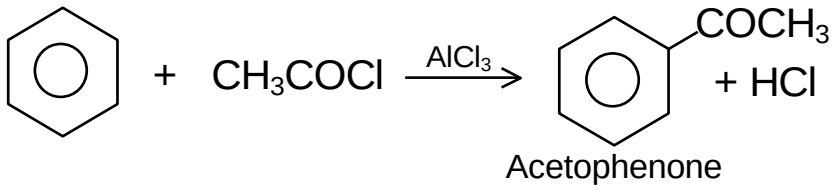
The order of effectiveness of Lewis acid catalysts has been shown to be

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

The action of $Me_3CCH_2Cl/AlCl_3$ on benzene is found to yield almost completely the rearranged product, $PhCMe_2CH_2Me$, which can be explained on the basis of the initial electrophilic complex being polarized enough to allow the rearrangement of $[Me_3CCH_2]^{\delta+}---Cl--AlCl_3^{\delta-}$ to more stable $[Me_2CCH_2Me]^{\delta+}---Cl---AlCl_3^{\delta-}$. By contrast $Me_3CCH_2Cl/FeCl_3$ on benzene is found to yield almost completely the unrearranged product, Me_3CCH_2Ph. This is due to the fact that the complex with the weaker Lewis acid, $FeCl_3$, is not now polarized enough to allow of rearrangement.

4.2 ACYLATION

Acylation of benzene may be brought about with acid chlorides or anhydrides in presence of Lewis acids. e.g.



Mechanism:

Friedel crafts acylation is found to follow the same general rate law as alkylation

Rate $\propto$ [Substrate] [RCOCl] [AlX_3]

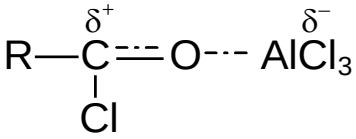
In case of acylation, the nature of electrophile will be as follows:

(i) $R-\overset{\overset{O}{\|}}{C}-\ddot{\underset{\ddot{}}{Cl}}: + AlCl_3 \longrightarrow R-C\equiv O^{\oplus} + AlCl_4^-$

(ii) $R-\overset{\overset{O}{\|}}{C}-Cl + AlCl_3 \longrightarrow R-\underset{\delta+}{\overset{O^{\delta-}\cdots AlCl_3}{\overset{\|}{C}}}-Cl$

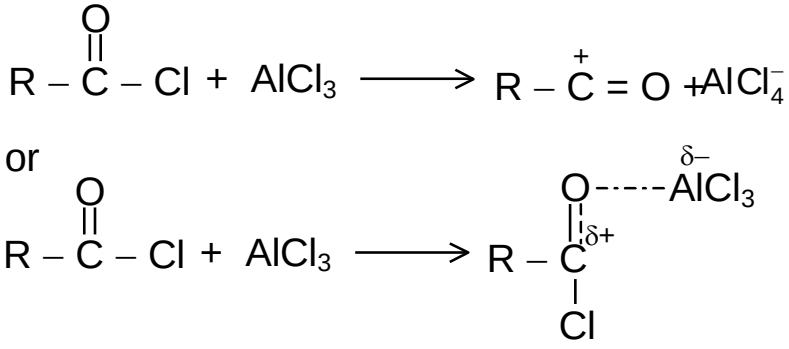
(iii) $R-\overset{\overset{O}{\|}}{C}-\ddot{\underset{\ddot{}}{Cl}}: + AlCl_3 \longrightarrow R-\underset{\delta+}{\overset{O}{\overset{\|}{C}}}-Cl^{\delta-}\cdots AlCl_3$

Due to the presence of lone pair of electron on both chlorine and oxygen two intermediates are possible and both are capable of electrophilic attack on benzene.

Acylium ions have been detected in a number of solid complexes, in the liquid complex between CH_3COCl and $AlCl_3$ (by spectroscopy), in solution in polar solvents and in a number of cases where R is very bulky. In less polar solvents the polarized complex  has been detected to act as the electrophile. Direct chemical evidence clearly indicates that both can be involved depending upon the circumstances.

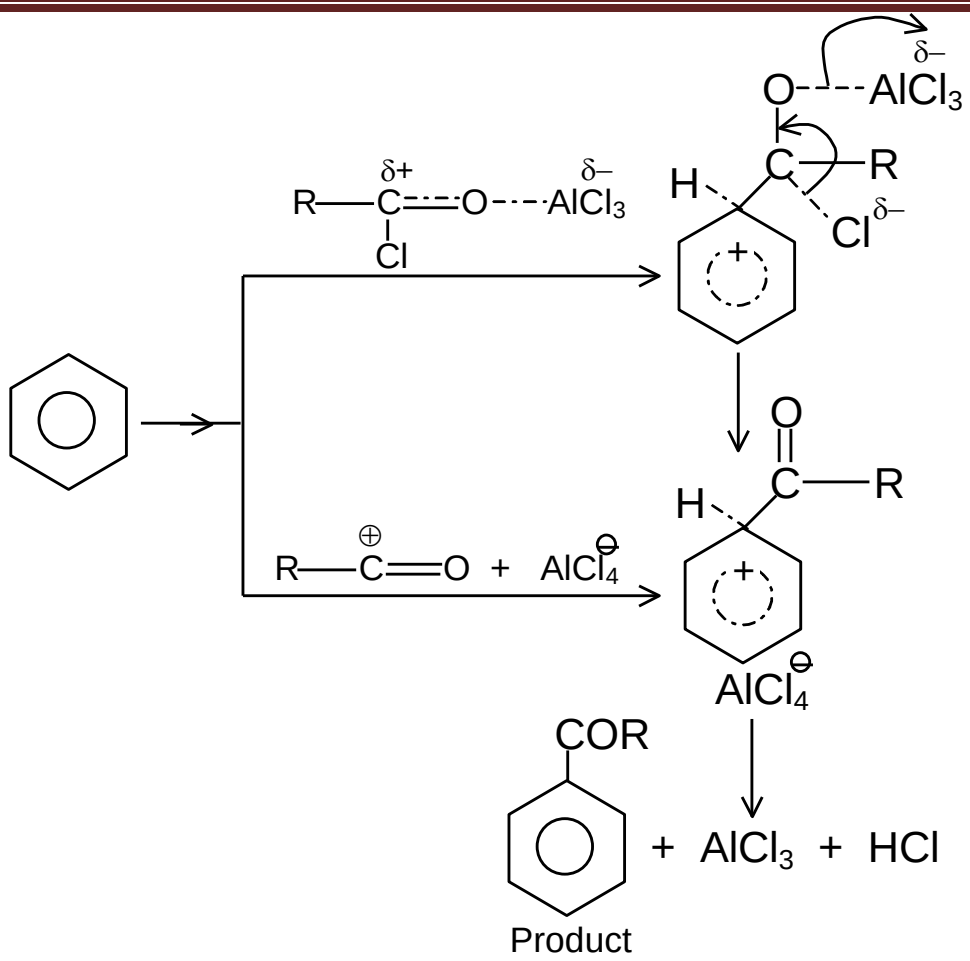
Mechanism may be represented as follows:

(i)



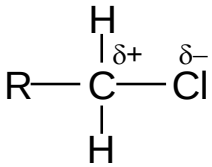
or

(ii)

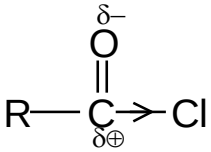


Comparison between alkylation and acylation

(i) A comparison of the electrophilic nature of both alkyl and acyl group indicates that acyl group is a better electrophile on account of two electron withdrawing atoms attached to C.

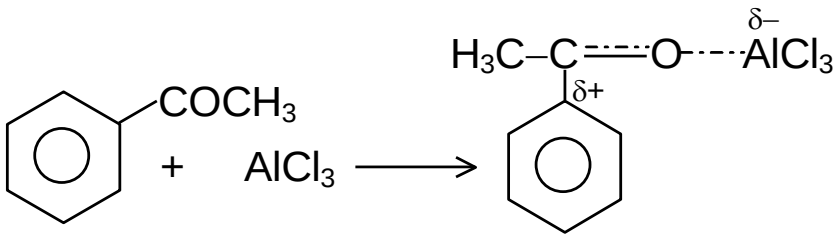


alkyl halide



Effective +ve charge density on carbonyl carbon is greater.

(ii) Acylation requires more catalyst than alkylation because much of the catalyst is removed by the formation of a complex with the product (ketone)

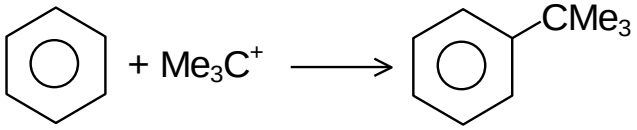


and is removed from further participation in the reaction.

(iii) Unlike polyalkylation, polyacylation does not take place as the product ketone is much less reactive than the original hydrocarbon.

(iv) Rearrangement of R does not take place, as in alkylation, but decarbonylation can take place, especially where R would form a stable carbonium ion, so that the end result is then alkylation rather than the expected acylation.

$$Me_3C - C^{\oplus} = O \xrightarrow{\Delta} CO + Me_3C^{\oplus}$$



3. Directive Influence of Sustituents in Benzene

The first substituent may occupy any position in benzene ring i.e. one and only one monosubstituted benzene is obtained. The next group may go to ortho, meta or para position. It is the group already present in the benzene nucleus that determines how readily the attack occurs and at what position of the ring it occurs. In other words, the group attached to the ring not only affects the reactivity but also determines the orientation of substitution. This is called directive influence of substituents in benzene nucleus. The substituent group is able to activate or deactivate the ring due to a number of factors like inductive effect, electromeric effect, resonance effect and hyperconjugative effect. Depending on their directive influence the substituent groups, except halogens, are divided into two different classes:

Class I :

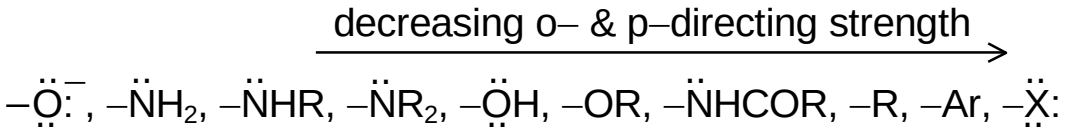
R, OH, OR, NH_2, NHR, NR_2, $NHCOCH_3$, $OCOCH_3$, Cl, Br, I, F, CH_2Cl, SH, Ph, etc. These groups direct the incoming electrophile mainly to the o/p–positions.

Class II :

NO_2, CHO, CO_2H, COCl, $CONH_2$, CO_2R, SO_3H, SO_2Cl, $COCH_3$, CN, CCl_3, $\overset{\oplus}{N}H_3$, $\overset{\oplus}{N}R_3$, $\overset{\oplus}{O}R_2$ etc. These groups direct the incoming electrophile mainly to the meta position.

3.1 Activating Groups OR Electron Releasing Groups

All groups having one or more lone pair of electrons are activating groups because they release electrons towards the nucleus increasing electron density and hence energy of the system. Reaction rate is increased due to low energy of activation. Examples:



Activating groups make the π electrons more readily available to an attacking electrophile by increasing the electron density at o- & p-positions and the product is always a mixture of o- & p-isomers.

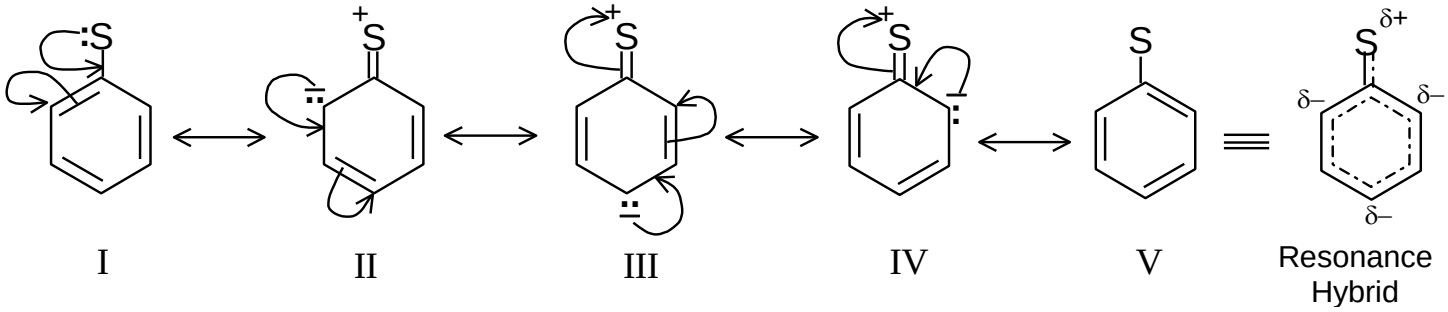
From an examination of the electronic structure and polar characteristics of o- and p- directing groups, it is evident that with the exception of alkyl groups all of them possess at least one lone pair of electrons at the atom adjacent to the benzene ring known as key atom. Also that their polar characteristics are –I effect and + R types, except alkyl group which is +I type and halogens which have strong + E effect in addition.

This lone pair of electrons is in conjugation with the π electrons of the ring and exhibits a strong +R effect, thus increasing the overall electron density in the benzene ring. Although the –I effect opposes the +R effect but latter predominates. Such groups e.g. –OH, –OR, $–NH_2$, –NHR, $–NR_2$ etc. activate

the benzene ring towards electrophilic substitution. However the relative increase of electron density is great at o- & p- position and due to the nature of conjugation and hence the substitution occurs at these positions. Let us consider monosubstituted benzene, C_6H_5S where S is a substituent.

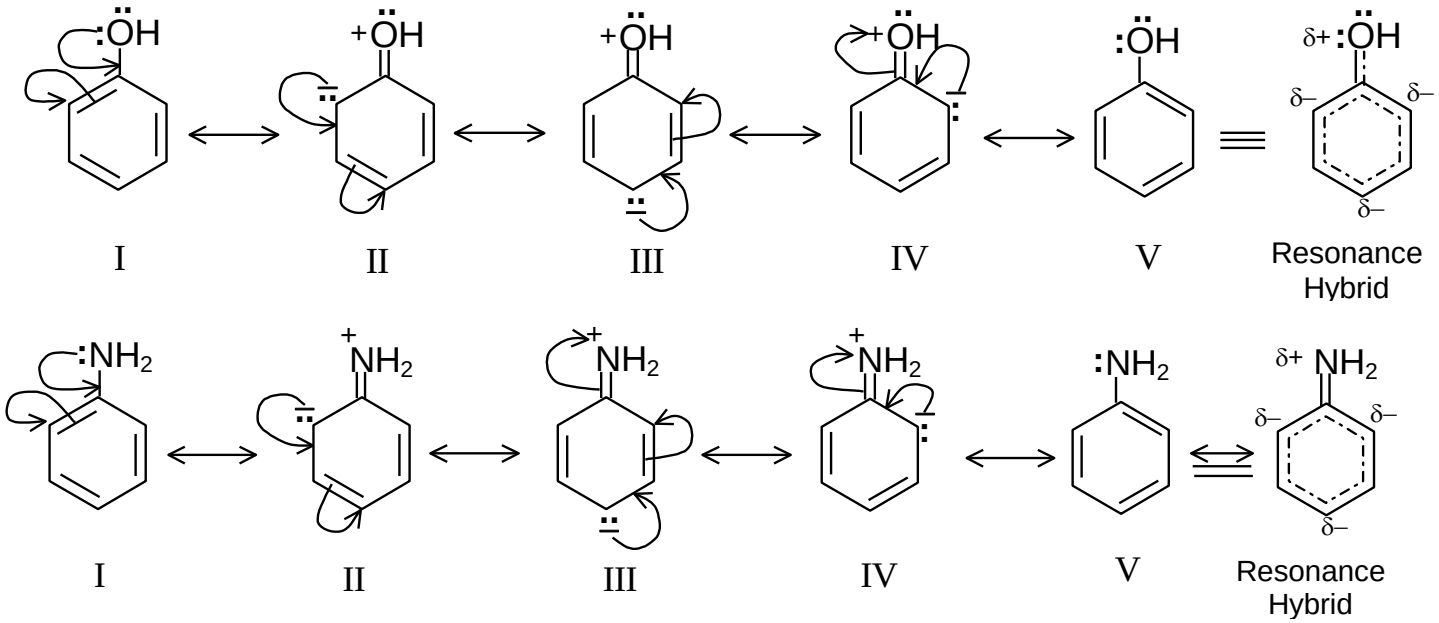
When The Substituent(s) is Electron-Donating

When the substituent –S present in the ring, has one or more lone pairs of electrons on the atom adjacent to the ring, it interacts with π electron system of the ring. This gives rise to the following five resonance forms.



The structure of the monosubstituted benzene, $C_6H_5-\ddot{S}$, is in fact represented by the resonance hybrid. In the hybrid structure the overall electron density of the benzene ring is enhanced compared to unsubstituted benzene ring and more so at the o- & p- positions of the ring. Therefore the presence of an electron donating group such as $-\ddot{S}$ causes further electrophilic substitution in o- & p- positions and also activates the ring to electrophilic attack.

Let us take the example of phenol, $C_6H_5-\ddot{O}-H$, and aniline $C_6H_5-\ddot{N}H_2$, which have available electron pair on the key atoms of the substituents. Thus phenol and aniline exhibit resonance and can be represented as hybrid of the fine canonical forms.



The overall electron density of the ring in each hybrid is increased and the benzene ring system as a whole is activated to electrophilic attack. Of course, the electrophile (E^+] would attack the ring preferentially at o- and p- positions where the electron density is relatively greater as compared to the meta positions.

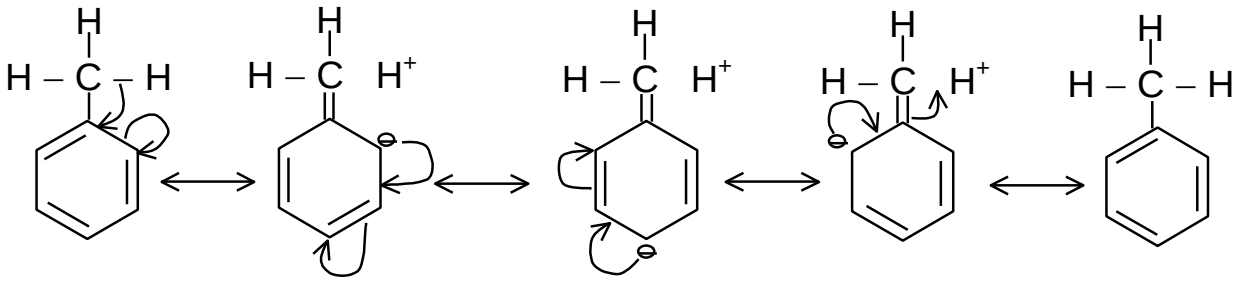
Thus, all the groups which are electron donating $-\ddot{O}H$, $-\ddot{O}R$, $-\ddot{N}H_2$, –NHR, $–NR_2$, $–NR_3$, etc. are ortho-para directing and facilitate electrophilic substitution in the benzene ring.

Effect of Alkyl Group as A Substituent

Since alkyl group has no lone pair of electrons on key atom i.e. carbon atom, yet it is o- & p- directing. First it is because of the fact, that alkyl group releases electron due to its +I (inductive) effect and hence tends to stabilise the carbocation by dispersal of its positive charge.

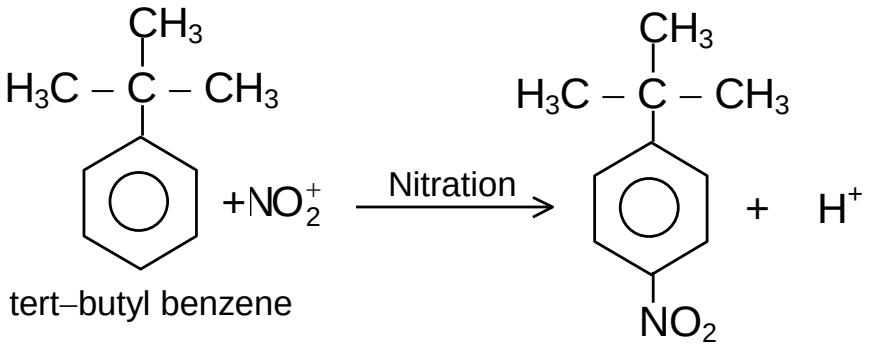
Secondly it is because the group electronegativity of methyl group is less than that of phenol group. At the same time, c of methyl group is sp^3– hybridized whereas that of phenyl group is sp^2– hybridized. So due to greater s–character of carbon atom of phenyl group, electron is withdrawn towards

benzene ring. Third, methyl group repels electrons towards the ring by hyperconjugation.



All the nine hyperconjugative resonating structures reveal that electron density is enhanced (i.e. –ve charge is developed) at o- & p- positions simultaneously. Therefore, further electrophilic substitution occurs at these positions.

The electrophilic substitution of tert-butyl benzene yields almost exclusively the para isomer. This is so because the electrophile approach to the ortho position is impossible on account of the steric influence of the substituent $-C(CH_3)_3$.

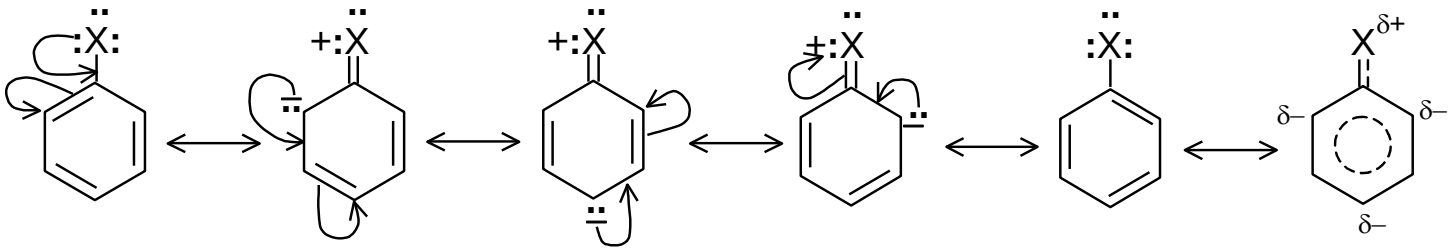


It has been observed that the larger the size of the alkyl group already present, the smaller is the amount of the o- isomer formed in an aromatic electrophilic substitution reaction. In other words, the bulky alkyl groups lead to steric hindrance to the introduction of new substituents in o- positions.

Effect of Halogens

Halogens are unusual in their effect on electrophilic aromatic substitution. They are deactivating yet ortho, para directing.

A halogen substituted benzene (C_6H_5–X) by virtue of the presence of unshared electron pair on the halogen, exhibits resonance. Thus it can be represented by the resonance hybrid of the following canonical forms:



Halogens withdraw electrons through its inductive effect (–I) and releases electrons through it resonance or mesomeric effect (+M). Thus for halogen, the two effects are more evenly balanced and we observe the operation of both.

Through its inductive effect halogen tends to withdraw electrons and thus destabilise the intermediate carbocation. This effect is felt for attack at all positions, but particularly for attack at the positions ortho and para to the halogen.

Through its resonance effect halogen, tends to release electrons. This electron release is effective only for attack at the positions ortho and para to the halogen. The combination of the two effects makes the halogenated benzene deactivated. This is so because the inductive effect is stronger than the resonance effect. Thus halogen, though, o- and p- directing, yet deactivates the benzene ring.

3.2 Deactivating Group or Electron Withdrawing Group or Meta Directors

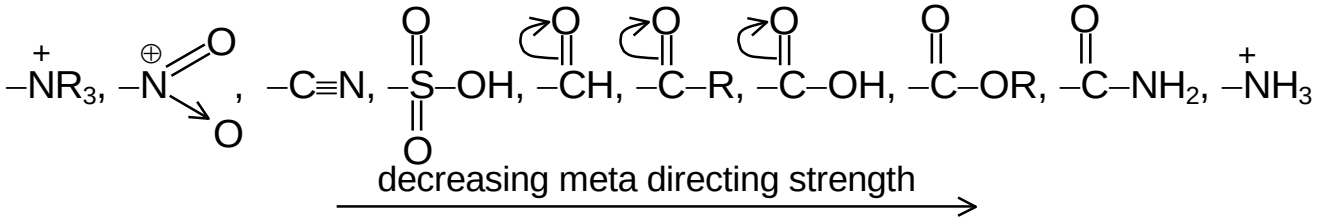
Such groups have tendency to withdraw π electrons from the benzene nucleus and thus decreasing its electron density are known as deactivating groups.

Due to decrease in electron density of the ring, the rate of electrophilic substitution is retarded. That's why these group are called deactivating group.

A look on the resonating structure reveal that these groups develop positive charge at ortho and para positions leaving the meta positions as the point of

relatively high electron density and hence the electrophilic substitution occurs at m position, not at ortho and para positions. Deactivating groups have π bonds with one more electronegative atom.

Examples:



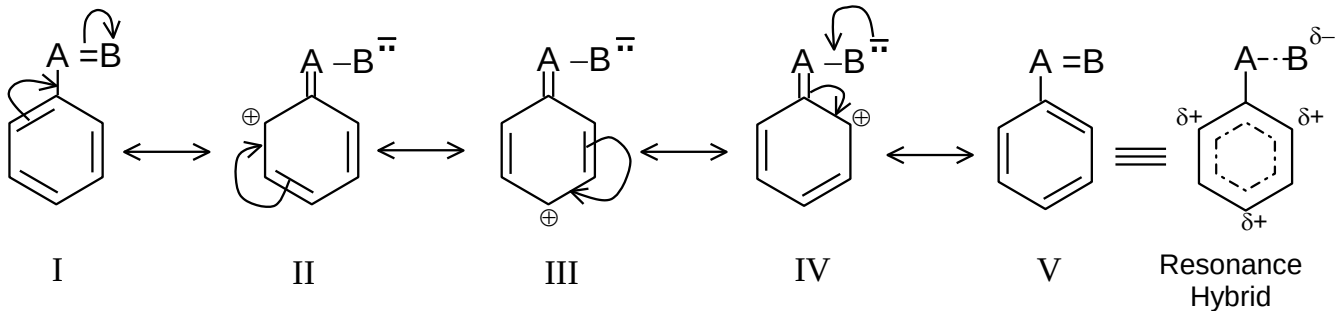
Electronic Explanation of Meta Directive Influence:

The polar characteristic of these groups is –I and –R with the exception of $-NR_3^+$ and $-CCl_3$ groups which exhibit only –I effect. Hence $-\overset{+}{N}R_3$ and $-CCl_3$ groups deactivate the benzene ring in general by decreasing electron density due to –I effect. However, the withdrawal of electron from ortho and para positions is as compared to meta position. Thus, meta position remains the point of comparatively high electron density and electrophilic substitution occurs preferentially at meta position.

Examples:

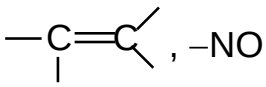
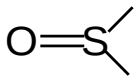
When the substituent has at least one strongly electronegative atom and a multiple bond in conjugation with benzene ring:

Let –A = B represents the group in which B is more electronegative than A. The highly electronegative atom pulls the electron pair of the multiple bond which in turn withdraws electrons from benzene ring (– M effect) giving rise to the following five canonical forms:



The structure of the benzene derivative $C_6H_5–A=B$ is, in fact, represented by the resonance hybrid shown above. Evidently electrons are withdrawn by the substituent group from the ring and more so from the o– p– positions where the electron density declines. Also, the meta positions have relatively more electron density and therefore electrophile substitution take place at the meta positions.

The nitro and sulphonic acid groups offer examples of the type of electron withdrawing substituents which are characterized by the presence of a strongly electronegative atom attached to another more electronegative atom by a multiple bond.

ortho, para				***meta***	
VSA	SA	A	D	SD	VSD
–OH, $–NH_2$,	–NHCOR,	–R, –Ar	–I, –Br, –Cl,	$–SO_3H$, –CN, –CHO	$–NO_2$, $–CF_3$,
–NHR, $–NR_2$	–OCOR, –OR		$–CH_2X$	–CHO	$–\overset{+}{N}R_3$
				–COOH, –COOR, –COCl	

4. Orientation in Benzene Ring With Two Substituents

The position taken up by a third electrophile entering the ring depends on the nature of the two groups already present. Coming electrophile mainly reacts at the position where the directive influence of both already present groups is satisfied. However, if the directive influence of both already present groups is not synergic, major product depends on dominating

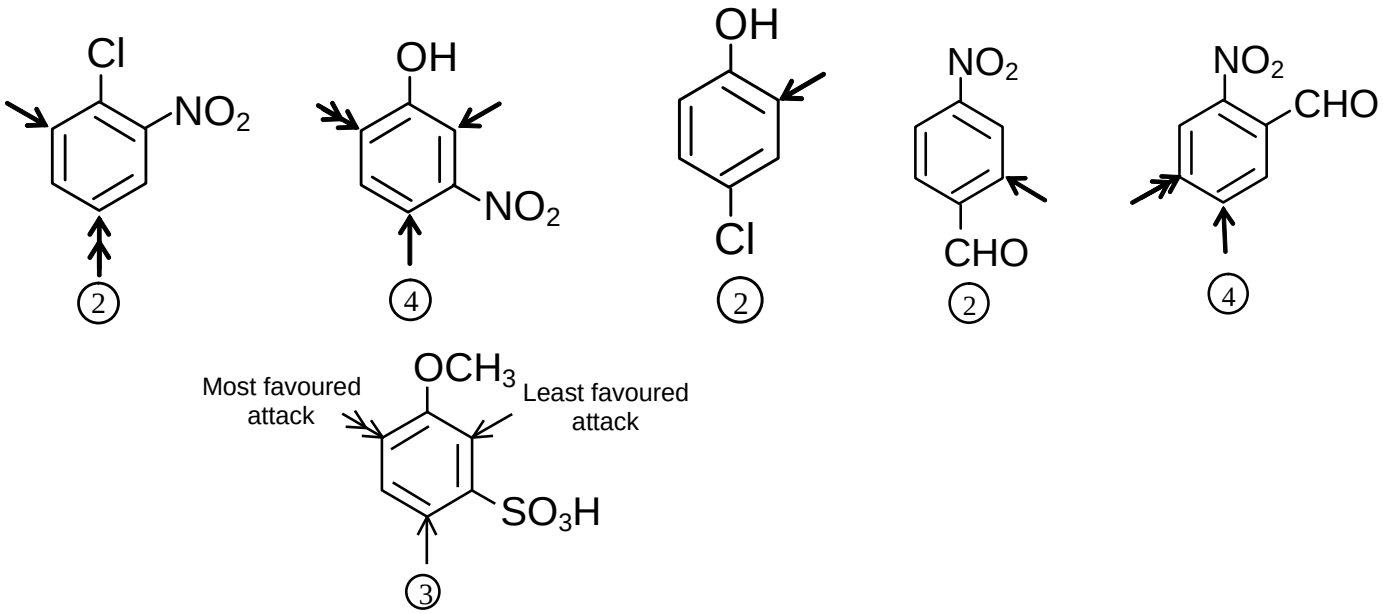
directive influence. Dominating directive influence can be predicted based on following generalizations:

1. When both the groups are different ortho, para directing, directive influence of more activating group will dominate.
2. When one group is ortho, para-directing and the other is meta-directing, directive influence of ortho, para-directing group will dominate.
3. When both the groups are different meta-directing groups, directive influence of more deactivating group will dominate i.e. coming electrophile will mainly attack the meta position of more deactivating group.

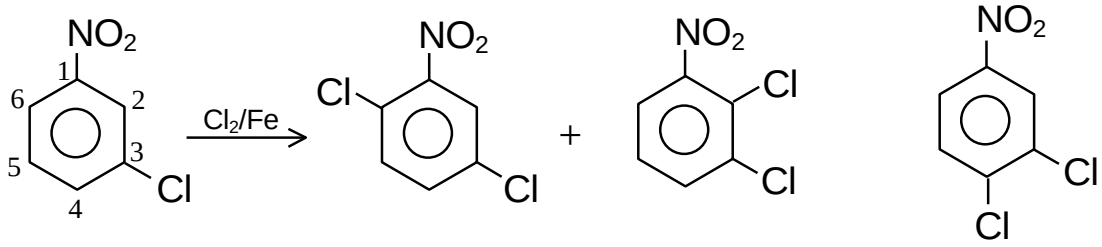
Note: If dominating directive influence suggests more than one isomeric product, major amongst them is decided by considering the steric hindrance i.e. least crowded position amongst them is generally attacked by electrophile. Moreover, electrophilic attack at a position is generally neglected if directive influence of none of the already present groups favours its formation.

In the following examples, the number of arrowheads indicates (qualitatively) the amount of substitution and the encircled number below indicates the number of isomers formed after neglecting the negligible products.

For example,



5. When a meta directing group is meta to an ortho/para directing group, the incoming group primarily goes ortho to the meta directing group rather than para. For example, chlorination of m–chloronitrobenzene (I) mostly gives (II) and small amounts of (III) but (IV) is not formed at all.

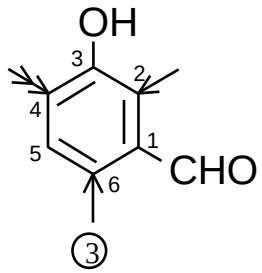


(I) (II) (III) (IV)

It is interesting that chlorination of (I) illustrates three rules. Of the four positions available to electrophile, the position–5 violates rule 1, position–2 violates rule 4 and position–4 disregards rule 5. Thus, principal attack of $Cl^{\oplus}$ is taking place at position–6 giving (II) as the major product.

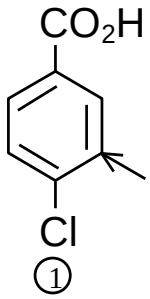
Now, using these generalizations, we can predict the preferable attack by the incoming group in disubstituted benzene. We can have following possibilities:

(a) When the two groups present are such that they belong to different categories and oppose each other. For example, in m–hydroxy benzaldehyde, the incoming electrophile is oriented by –OH group (and not by –CHO group). As –OH group is o/p–directing, thus attack of the electrophile can take place at three sites. Attack at position–2 is least favoured according to rule 3, but attack at position–4 is the most preferred.

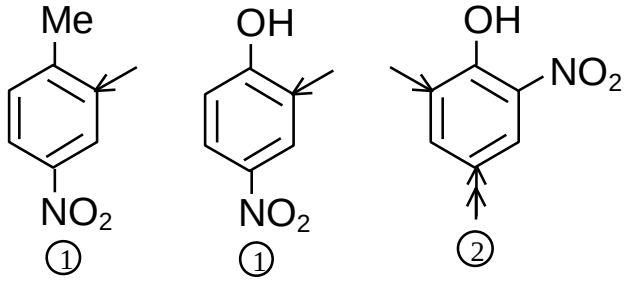


(b) When the two groups present are such that they belong to different categories but they reinforce each other, then the third group enters almost

entirely at one position. For example, the incoming group in p–chlorobenzoic acid goes to the position ortho to the chloro group and meta to the carboxyl group.

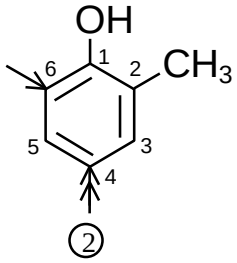


Some other examples are:



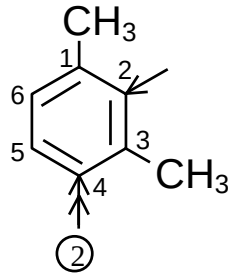
(c) When the two groups belongs to category I (having large difference in their activating ability) and are placed such that they oppose each other, then the third group enters in accordance with the group having higher activating ability.

For example, in o–cresol (o–methyl phenol), the incoming electrophile could go at position–4 and 6 but attack at position–4 is greatly favoured due to less steric repulsion.

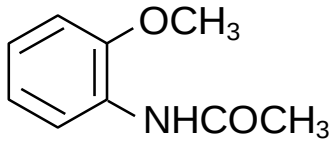


(d) When the two groups belong to category I and are placed such that they reinforce each other, the incoming electrophile enters almost entirely at one position. For example, 1,3-Dimethylbenzene is substituted at the position–4

(ortho to one CH_3 group and para to the other CH_3 group), but not at the position–5 (meta to both) because of rule 4.

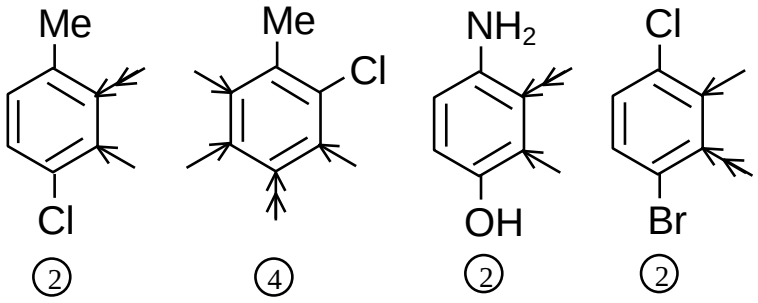


(e) When the groups are such that they belong to category I with almost identical directing abilities and oppose each other, then predictions are more difficult. In a case such as,



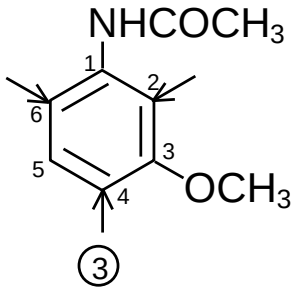
where two groups of about equal directing ability are in competing positions, all four products can be expected and it is not easy to predict the proportions, except that steric hindrance should probably reduce the yield of substitution ortho to the acetamido group, especially for large electrophiles. Mixtures of about equal proportions are obtained in such cases.

Few other examples are



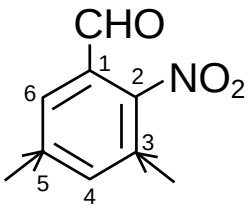
(f) When the groups are such that they belong to category I with almost identical directing ability and they reinforce each other, then also the predictions are difficult.

For example, in m–Methoxyacetamide, the attack at position–2 is least favoured according to rule 4 but attack at position–4 and at 6 is equally feasible.



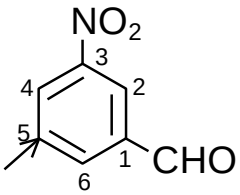
③

(g) When both the groups belong to class II and are present such that they oppose each other, then the less deactivating group decides the orientation of incoming electrophile. For example, in o–nitro benzaldehyde, the incoming group attacks at position–3 and at position–5, of which position–5 is more favoured because of lesser steric repulsion.



②

(h) When both the groups belong to class II and are present such that they reinforce each other, then attack takes place entirely at one position. For example, 3-nitro benzaldehyde is substituted at position–5 as it is meta to both the groups.



①

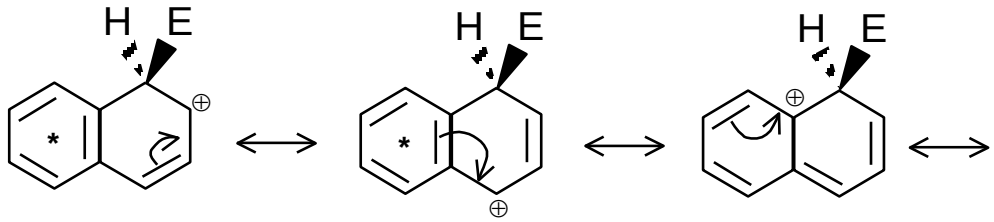
5. Substitution in Other Aromatic Systems

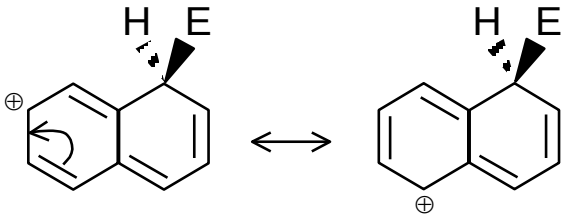
5.1 Naphthalene And Anthracene Rings

The delocalization of the positive charge in the transition states of electrophilic substitutions is increased by the fusion of two or more benzene rings and the polycyclic hydrocarbons are therefore all more reactive than benzene.

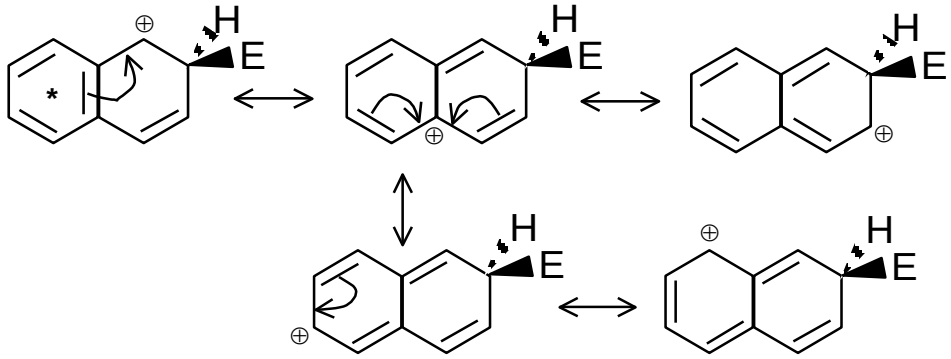
Substitution in naphthalene is illustrative. The transition states for the reaction at 1– and 2–positions may be represented as follows:

1–substitution:



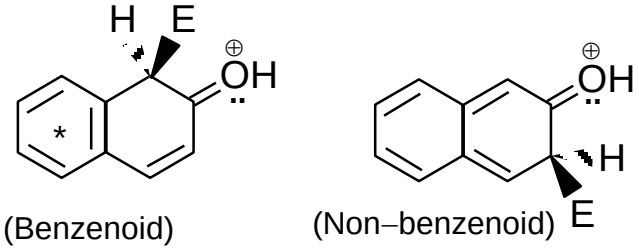


2–substitution:



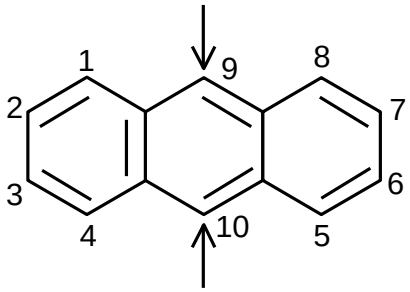
In each of the two transition states, the positive charge is more extensively delocalized than in reaction with benzene, leading to lower activation energies. Further, the three starred structures are of benzenoid type and therefore of lower energy content than the remainder in which the benzenoid nature of the second ring has been destroyed. Since there are two such low–energy contributors for 1–substitution as compared with one for 2–substitution, it is understandable that the 1–position should be the more reactive than 2–position.

The presence of an electron–attracting group in naphthalene reduces the reactivity and causes substitution to occur in the unsubstituted ring, mainly at the 5– and 8–positions (i.e. the two 1–positions of that ring). An electron–releasing group activates the molecule further and reaction occurs in the substituted ring. If the group is in the 1–position, substitution occurs at the 2– and 4–positions (i.e. ortho and para to the electron–releasing group), but a 2–substituent directs almost entirely to the 1–position, although the 3–position is also an ortho position. The reason is that the stabilization of the transition state which is provided by the substituent is more effective when the appropriate resonance structure is benzenoid (1–substitution) than when it is not (3–substitution). For instance,



(Benzenoid) (Non–benzenoid)

In anthracene, the electrophile attacks preferentially at the 9 or 10–positions since the arenium ion formed by the electrophilic attack at any of these positions can have two intact benzene rings in its canonical forms, while attack of electrophile at any other position (1 or 2) would give arenium ion having a naphthalene ring in its canonical forms. The resonance energy of 2 benzene rings is more than the resonance energy of a naphthalene ring.



(Position 1,4,5 and 8 are identical, positions 2,3,6 and 7 are also identical and positions 9 and 10 are same)

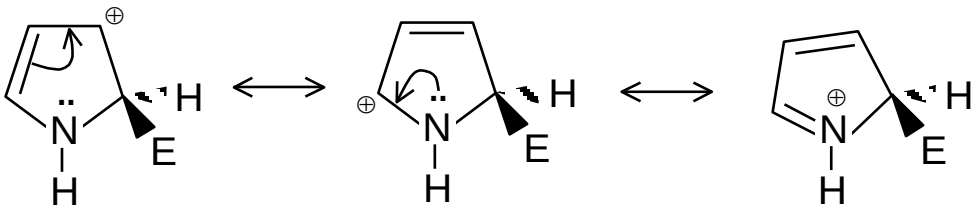
5.2 Five Membered Heterocyclic Rings

The principles that govern the electrophilic substitutions of this group of heteroaromatic compounds will be illustrated by reference to pyrrole.

Pyrrole is highly reactive at both the 2– and 3–positions. The reason is that the transition state for substitution at each position is strongly stabilized by the accommodation of the positive charge by nitrogen, in just the way that aniline owes its reactivity to the exocyclic nitrogen. 2–substitution predominates because the positive charge in the transition state is delocalized over a total of three atoms, compared with two for 3–substitution.

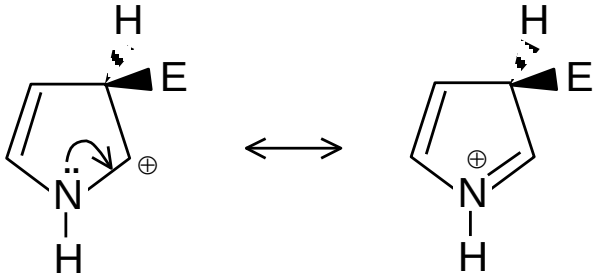
The similarity of pyrrole and aniline is particularly apparent in their reactions with bromine: each reacts at all its activated carbon atoms, pyrrole giving tetrabromopyrrole and aniline giving 2,4,6–tribromoaniline. In fact, pyrrole is even more strongly activated than aniline and should perhaps be compared with the phenoxide ion: each undergoes the Reimer–Tiemann reaction, unlike other benzenoid compounds. In addition, pyrrole undergoes Friedel–Crafts acylation in the absence of a catalyst.

2–substitution:



(Stable contributor–octet of every atom is complete)

3–substitution:



(Stable contributor–octet of every atom is complete)

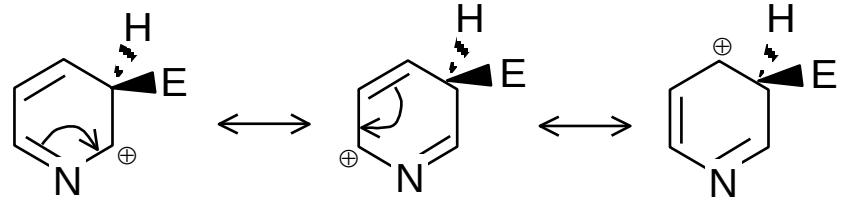
Furan and thiophen are also activated towards electrophiles and react predominantly at the 2–position. The underlying theory is similar to that for pyrrole, namely, that the heteroatom is able to delocalize the positive charge on the transition state. Since oxygen accommodates a positive charge less readily than nitrogen, furan is less reactive than pyrrole, just as phenol is less reactive than aniline. The +M effect of sulphur is smaller than that of oxygen because the overlap of the differently sized p–orbitals of carbon and sulphur is less than in the case of carbon and oxygen so that, understandably, thiophen is less reactive than furan. Thus, the reactivity order of 5–membered heterocyclics towards electrophilic substitution would be

pyrrole > furan > thiophene.

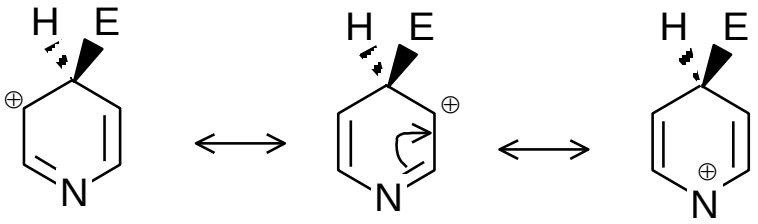
5.3 Six Membered Heterocyclic Rings

The principles governing the reactivity of these compounds are illustrated by reference to pyridine. The transition states for substitution at the 3– and 4–positions can be represented as the hybrids.

3–substitution:



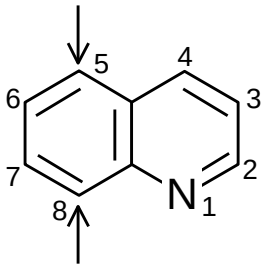
4–substitution:



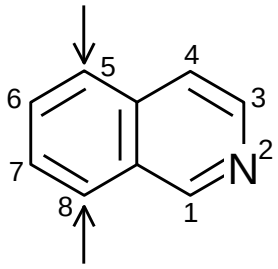
In each case, the positive charge is less well accommodated than in reactions on benzene because nitrogen is more electronegative than carbon. Hence, both the 3– and 4–positions are deactivated, the latter more strongly because of the high energy of the contributing structure which contains

divalent positive nitrogen. The 2–position resembles the 4–position, as reference to the appropriate resonance structures will show.

Quinoline and isoquinoline are also deactivated, though less so than pyridine and reaction normally occurs in the homocyclic ring at the 5– and 8–positions.



Quinoline



Isoquinoline

Illustration 1.

Compare the products of the reactions of $PhCH_2CH_3$ with Br_2 and Cl_2 in light and explain any differences.

Solution:

Bromination gives α–bromoethylbenzene exclusively. The 2° benzylic position is only slightly favored over the 1° alkyl position in chlorination, the products being $PhCHClCH_3$ (56%) and $PhCH_2CH_2Cl$ (44%). The less reactive $Br^{\bullet}$ is more selective than the $Cl^{\bullet}$, which abstracts an $H^{\bullet}$ in a more random fashion (Reactivity–Selectivity principle).

Illustration 2.

Irradiation of an equimolar mixture of cyclohexane and $PhCH_3$ gives mostly cyclohexyl chloride with Cl_2 and $PhCH_2Br$ with Br_2. Explain.

Solution:

In these competitive reactions the reactivities of cyclohexane and toluene are compared, $Cl^{\bullet}$, being more reactive and less selective than $Br^{\bullet}$, reacts with the kind of H present in greatest number, which in this case is one of the twelve equivalent H's of cyclohexane. The less reactive and more

selective $Br^{\bullet}$ reacts with the most reactive H, in this case one of the three alkyl H's of $PhCH_3$.

Illustration 3.

Deduce the structure of compound A, C_9H_8, from the following experimental data: A decolorizes Br_2 in CCl_4 and adds one eq. of H_2 under mild conditions, forming B, C_9H_{10}. At high temperature and pressure, A adds four eq. of H_2. Vigorous oxidation of A yields phthalic acid, 1, 2–$C_6H_4(COOH)_2$.

Solution:

A has 6° of unsaturation, four of which often signal the presence of a benzene ring, as confirmed by isolation of phthalic acid on vigorous oxidation. Reaction with Br_2 and one eq. of H_2 indicate there is a C=C. Addition of three more eq. of H_2 further indicates the presence of a benzene ring. So far 5° of unsaturation have been accounted for –the sixth degree resists reduction and must be a ring with C=C. Oxidation to the ortho–dicarboxylic acid indicates the ring is fused to the benzene ring. The structure is indene.

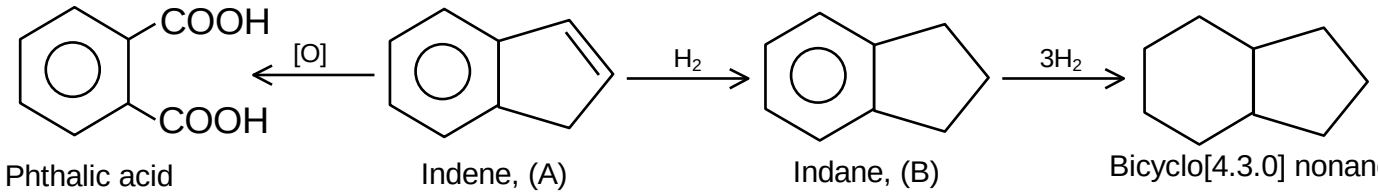


Illustration 4.

Identify (a) the chiral compound C, $C_{10}H_{14}$, that is oxidized with alkaline $KMnO_4$ to PhCOOH and (b) the achiral compound D, $C_{10}H_{14}$, inert to oxidation under the same conditions.

Solution:

(a) C is a monoalkyl substituted benzene with four C's in the side chain. The only R with four C's, one of which is a chiral center, is $–CH(CH_3)CH_2CH_3$; C is sec–butylbenzene, $PhCH(CH_3)CH_2CH_3$.

(b) Any R attached to the benzene ring cannot have a benzylic H (no oxidation); D is tert–butylbenzene, $PhCMe_3$

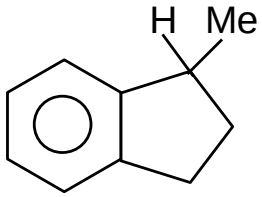
Illustration 5.

(a) Give the structures for all possible chiral compounds, $C_{10}H_{12}$, that do not decolorize Br_2 and that can be oxidized to phthalic acid.

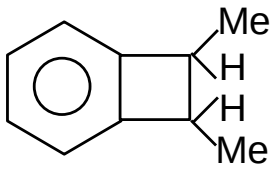
(b) Identify E, also chiral, with the same formula, but which is oxidized to PhCOOH.

Solution:

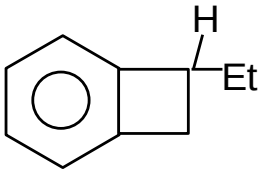
(a) The formula reveals a fifth degree of unsaturation in addition to the four of the benzene ring. This fifth degree of unsaturation must be a ring, not C=C, because the Br_2 test is negative. Production of phthalic acid means the ring is fused to the benzene ring. This fused ring has the chiral carbon and must be a mono–R–substituted five–membered or di–R–substituted four–membered ring. Only in this way can we account for the additional four C's of the formula.



1–Methylindane



trans–1, 2–Dimethylbenzcyclobutane



1–Ethylbenzcyclobutane

(b) The extra unsaturation is in the single side chain. E is 3-Phenyl-1-butene, $CH_3–\underset{\displaystyle Ph}{\underset{|}{C}}HCH=CH_2$.