GE CHEMISTRY SEMESTER-III

Section-B: Organic Chemistry II

AROMATIC HYDROCARBON

Lecture-2

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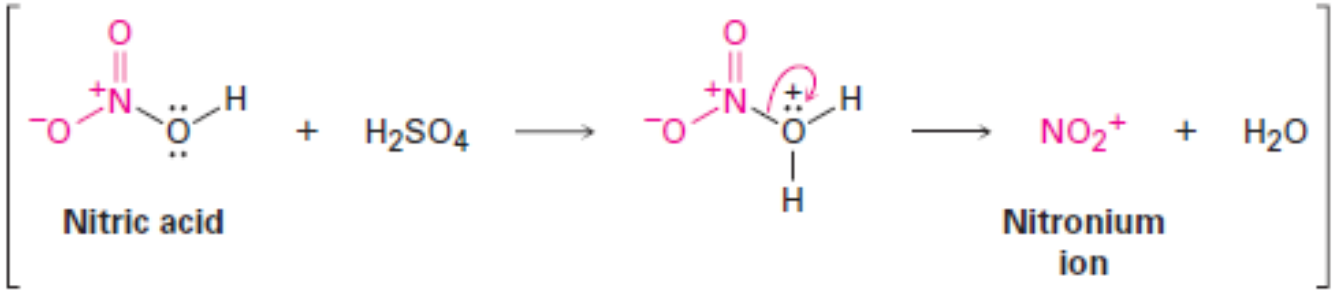
OVERVIEW

- Nitration to Benzene Ring
- Sulphonation to Benzene Ring
- Halogenation to Benzene Ring
  1. BROMINATION OF BENZENE
  2. CHLORINATION OF BENZENE
- Friedel-Craft Alkylation to Benzene Ring (In 1877)
- Friedel-Craft Acylation to Benzene Ring
- Substituent Effects in Electrophilic Aromatic Substitution
- Side Chain Oxidation in Alkylbenzenes

Nitration to Benzene Ring

Aromatic rings are nitrated by reaction with a mixture of concentrated nitric and sulfuric acids. The electrophile is the nitronium ion, NO_2^+, which is formed from HNO_3 by protonation and loss of water.



On the other hand in more dilute nitric acid solution , nitracidium ion (less reactive than NO_2^+) is the probable electrophile for nitration.

$$2HNO_3 \rightleftharpoons H_2NO_3^+ + NO_3^-$$

Nitronium salts can be effective nitrating agents where NO_2^+ is active electrophile

e.g. **(NO_2^+) (BF_4^-)**

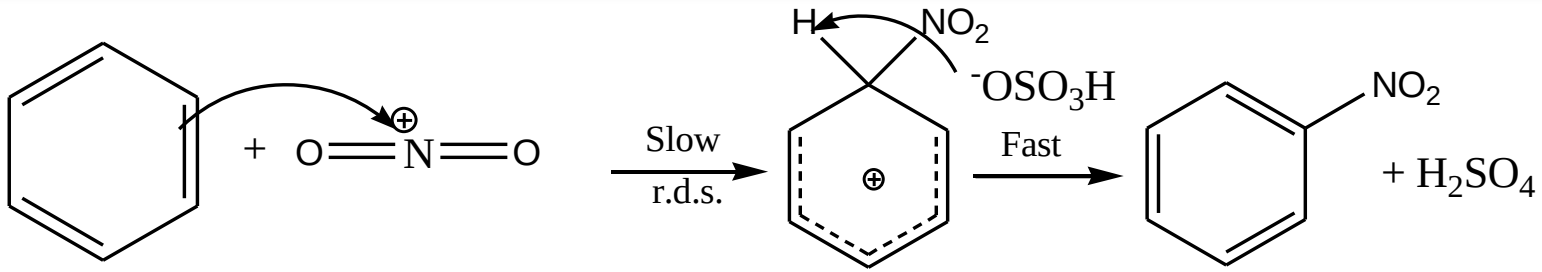
Mechanism of reaction

Reaction follow 2nd order kinetics, Rate= k[substrate][NO_2^+]

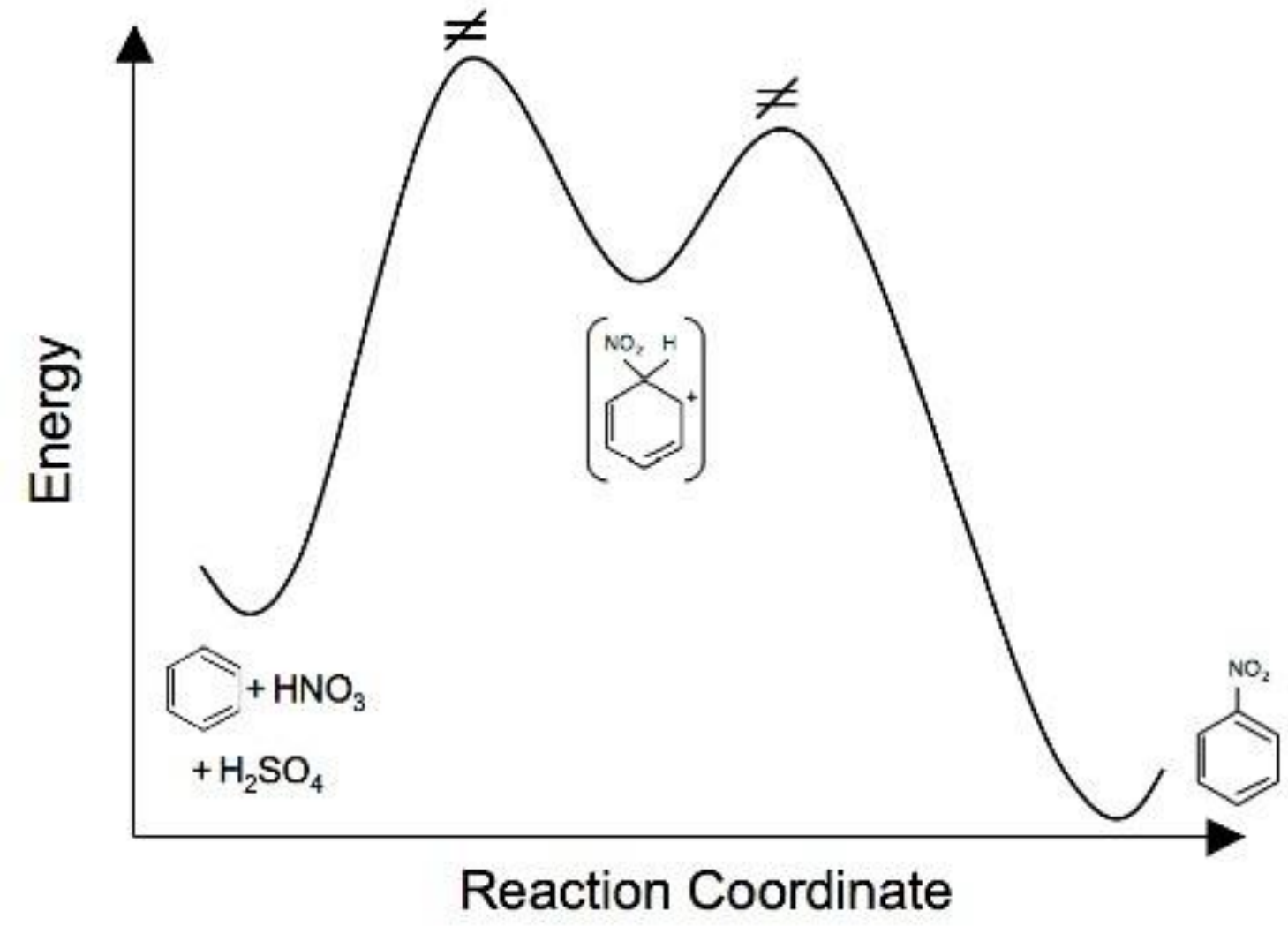
There is two possible mechanism which can follow 2nd order kinetics

1) Simultaneous formation of C-N bond and breaking of C-H bond i.e. single step process.
2) Two step process, a) addition of nitronium ion and b) removal of proton, where, either a) or b) will be rate determining step (r.d.s.)

To find out the exact mechanistic pathway Melander examined the nitration with toluene having tritium (isotope of H) at 2-position. The product is 2,4-dinitrotoluene with 50% of the original tritium content. This means rate of substitution 2-H & 2-T are equal. So there is no kinetic isotope effect. So the exact mechanism is a two step process where addition of electrophile is r.d.s.



ENERGY PROFILE DIAGRAM FOR AROMATIC NITRATION REACTION



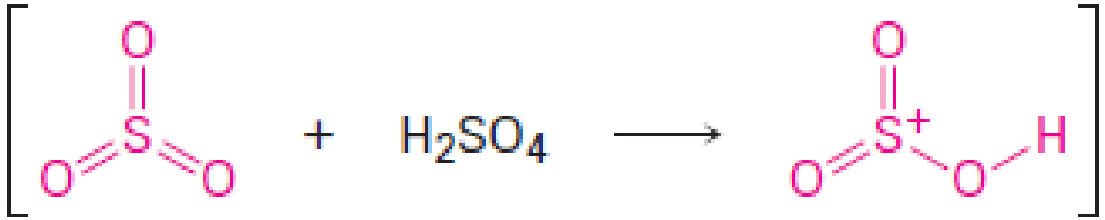
Sulphonation to Benzene Ring

A. Benzene rings are sulfonated with fuming sulfuric acid (oleum), a mixture of SO_3 and concentrated H_2SO_4 at 40°C or concentrated H_2SO_4 at 80°C. The reactive electrophile is HSO_3^+ or SO_3

$$C_6H_6 + H_2SO_4 \xrightleftharpoons{80^0C} C_6H_5SO_3H + H_2O$$

B. This method is used to synthesize compounds of the sulfa drug family of antibiotics.

Formation of electrophile with (1) fuming sulfuric acid

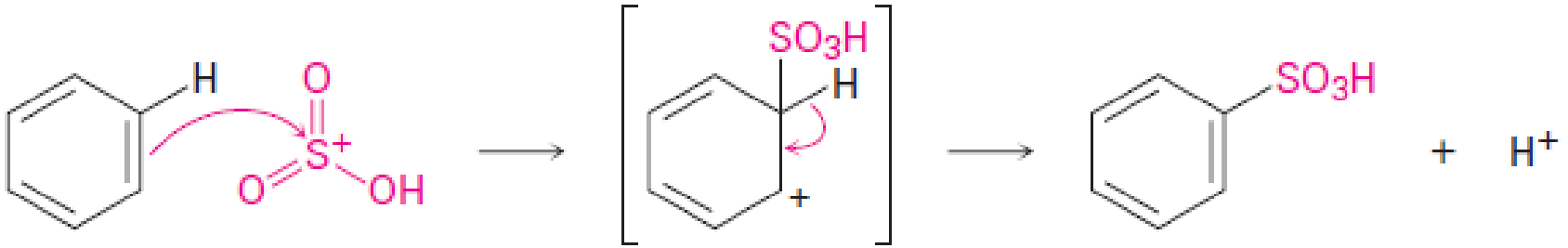


(2) With concentrated sulfuric acid

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

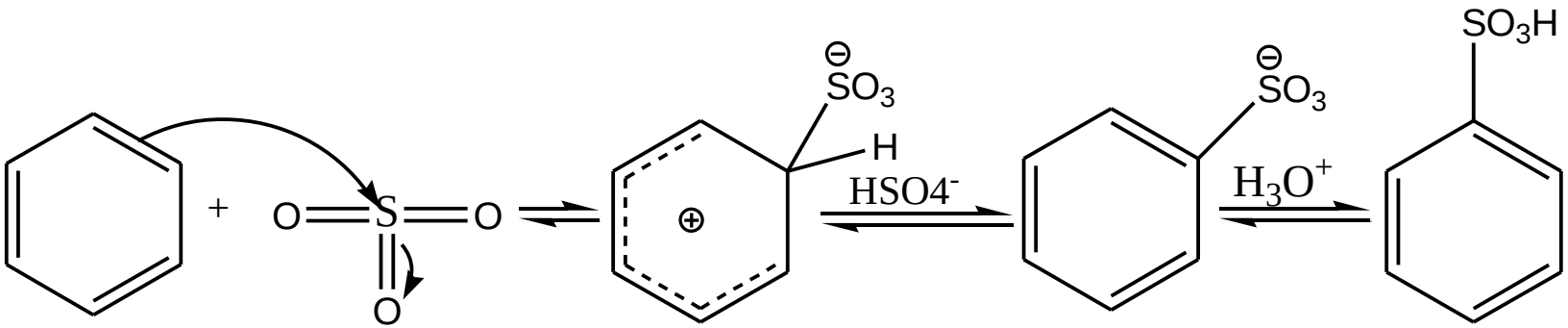
Mechanism of reaction

At first attack by electrophile HSO_3^+ or SO_3 to the benzene ring to give the resonance stabilized benzenium ion and finally removal of proton to give the substituted product

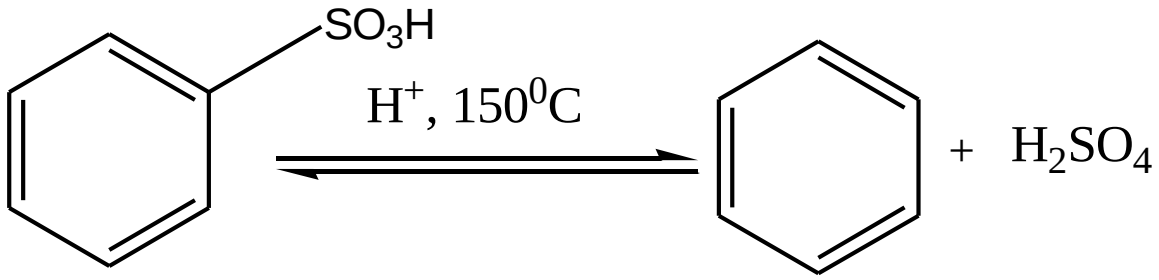


Carbocation intermediate

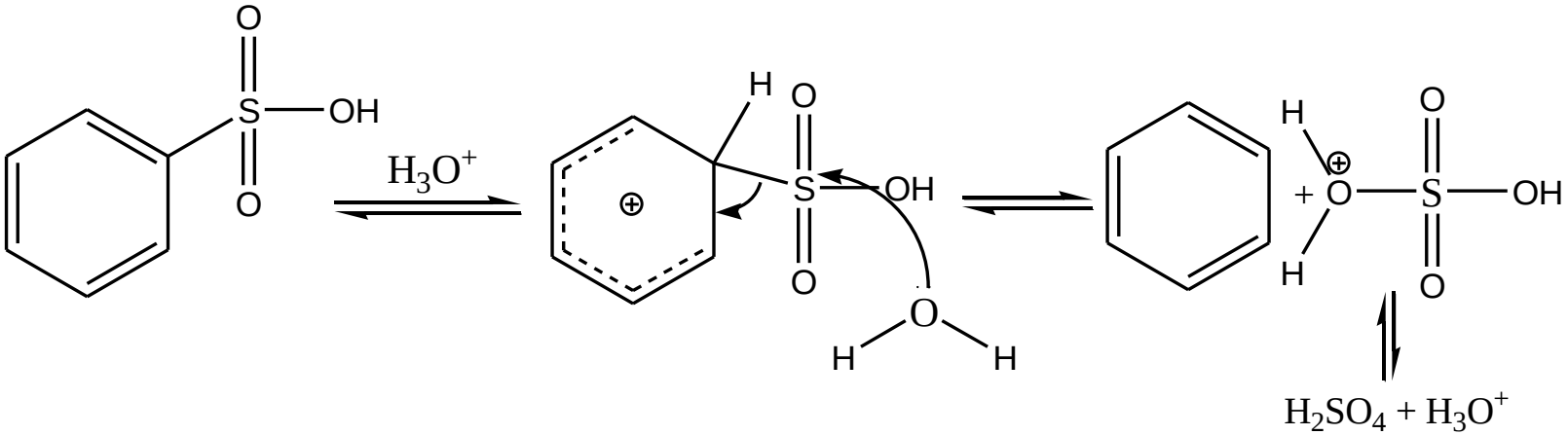
[OR]



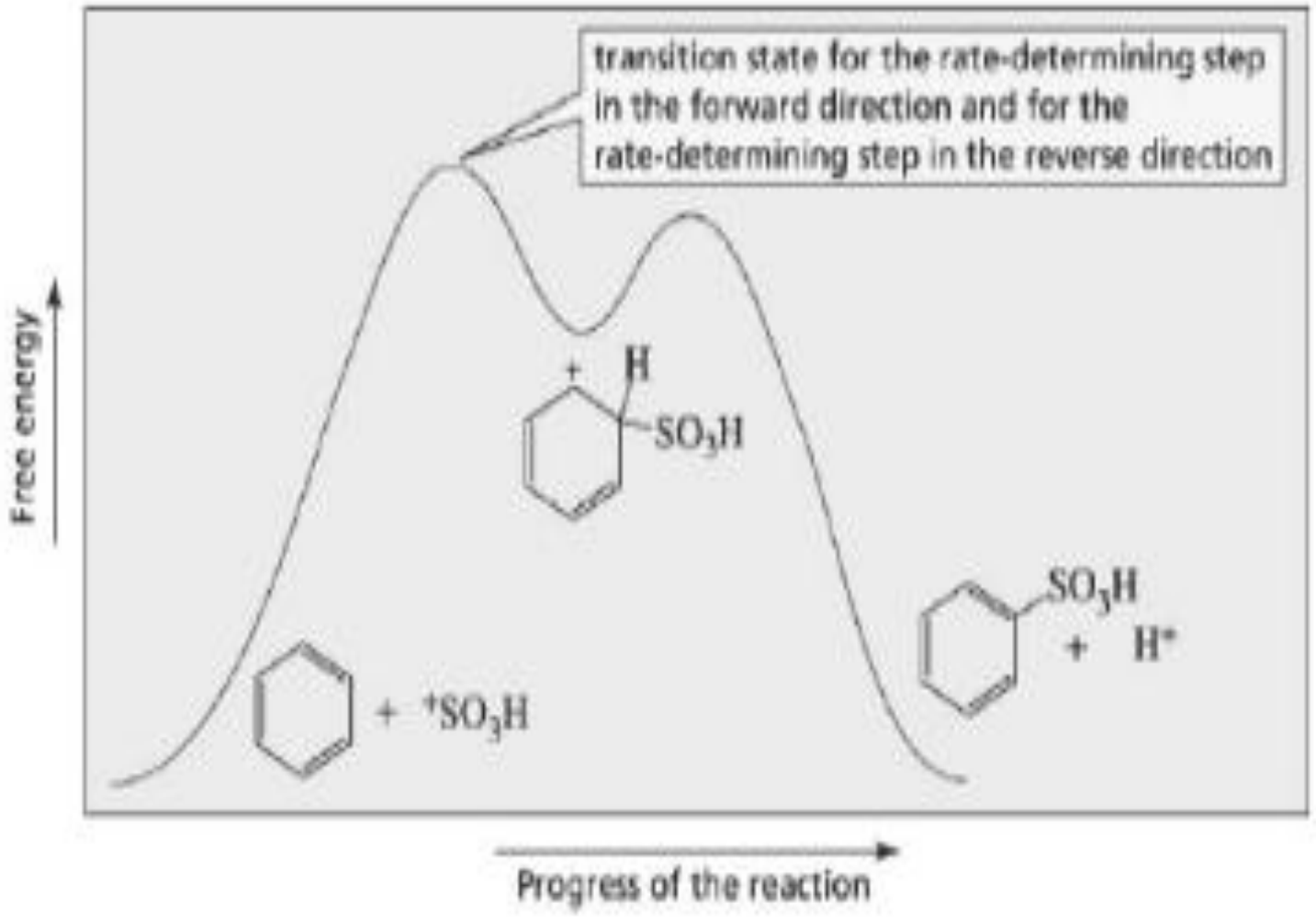
Sulphonation is reversible reaction, at high temperature when benzenesulphonic acid is treated with dilute aqueous acid, benzene is regenerated



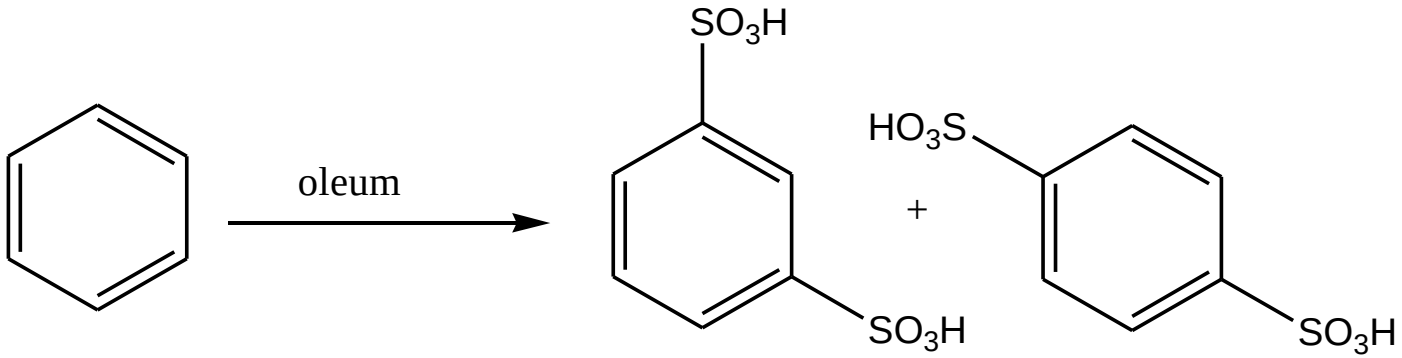
Mechanism of reaction



ENERGY PROFILE DIAGRAM FOR SULPHONATION REACTION

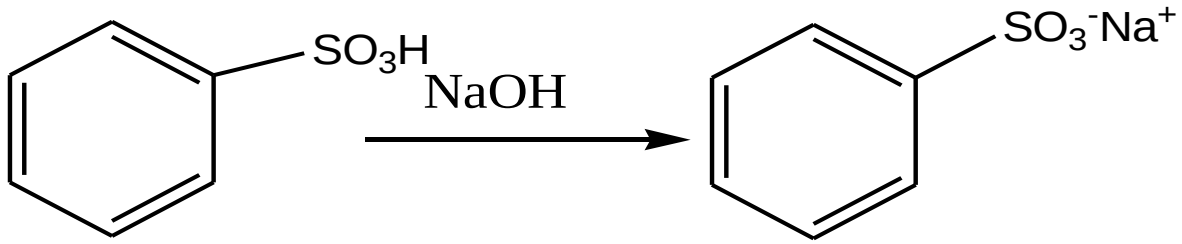


When benzene is heated with excess of fuming sulphuric acid at 200^0C, benzene forms benzene-m-disulphonic acid as the main product and the p-isomer in a small amount



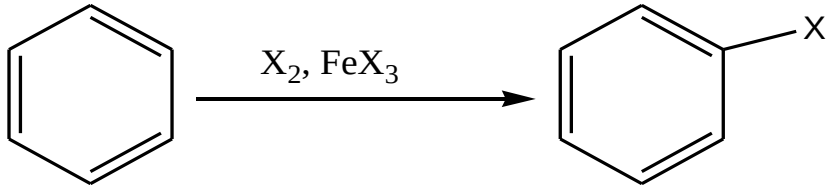
Use of benzenesulphonic acid

A. Sodium salts of benzenesulphonic acid can be used as detergents
B. In the manufacture of certain dyes.



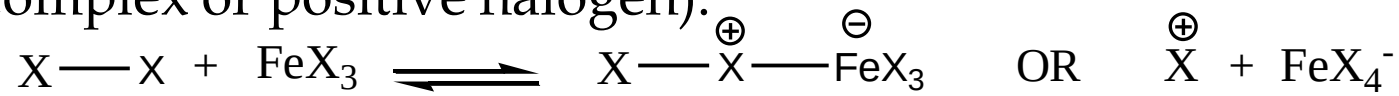
Halogenation to Benzene Ring

Benzene can be halogenated by halogen (Br_2, Cl_2) with the help of a Lewis acid catalyst. Bromine/Chlorine is non polar so is not a good electrophile. The halogen carrier (Lewis acid) is required to polarise the halogen.



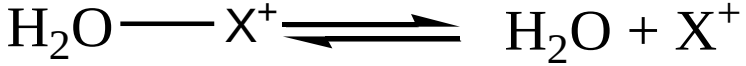
The rate law is; Rate=k[Benzene][X_2] [Lewis acid]

1. Hence, The active electrophile is either the halogen-Lewis acid complex or positive halogen).



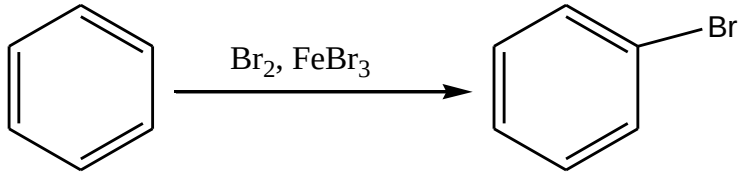
Where, X=Cl, Br

2. Fe is most commonly used as it can be converted to FeX_3 by X_2.
3. Hypochlorous (HOCl) or Hypobromous (HOBr) acid can be used for halogenation, where acid is used as catalyst. Active species is H_2OX^+ or X^+

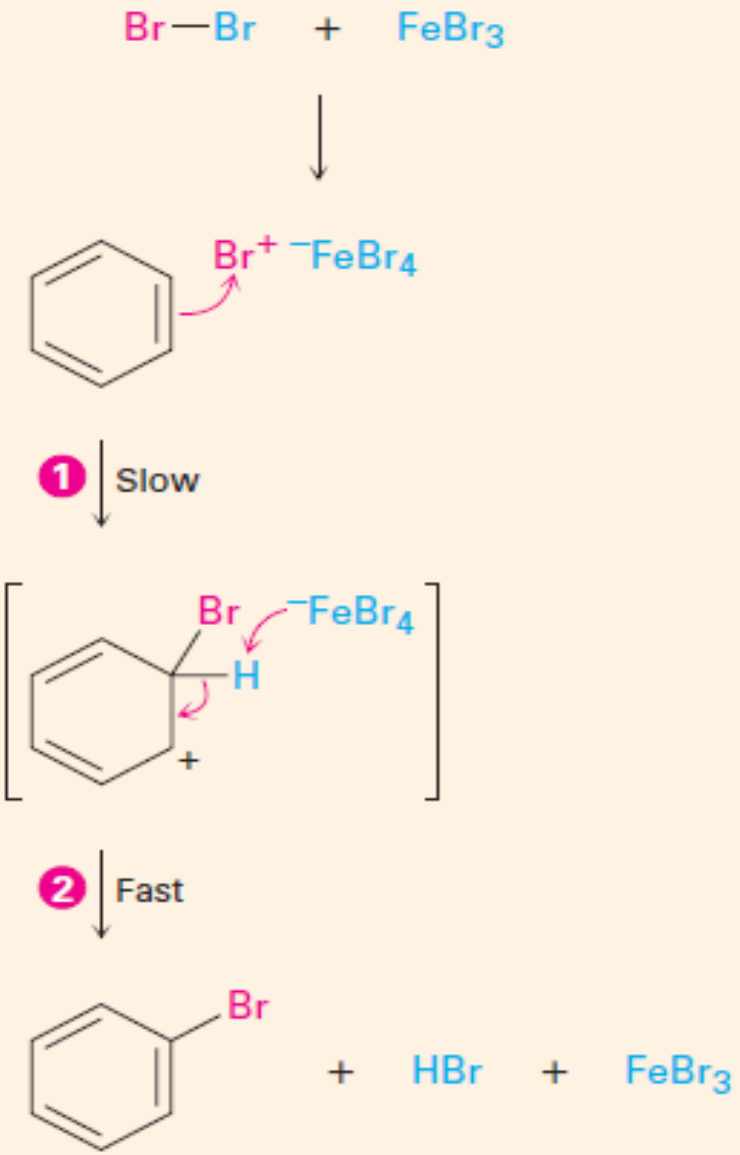


BROMINATION OF BENZENE

1. For bromination of benzene to take place, a catalyst such as $FeBr_3$ is needed along with Br_2.
2. The catalyst makes the Br_2 molecule more electrophilic form Br^+.
3. The electrophilic Br^+ then reacts with the electron-rich (nucleophilic) benzene ring to yield a nonaromatic carbocation intermediate.
4. This carbocation is doubly allylic and is a hybrid of three resonance forms but it is less stable than benzene.
5. Thus, reaction of an electrophile with a benzene ring has a relatively high activation energy and is rather slow.
6. The carbocation intermediate loses H^+ from the bromine-bearing carbon to give a substitution product (Regain aromaticity/stability).



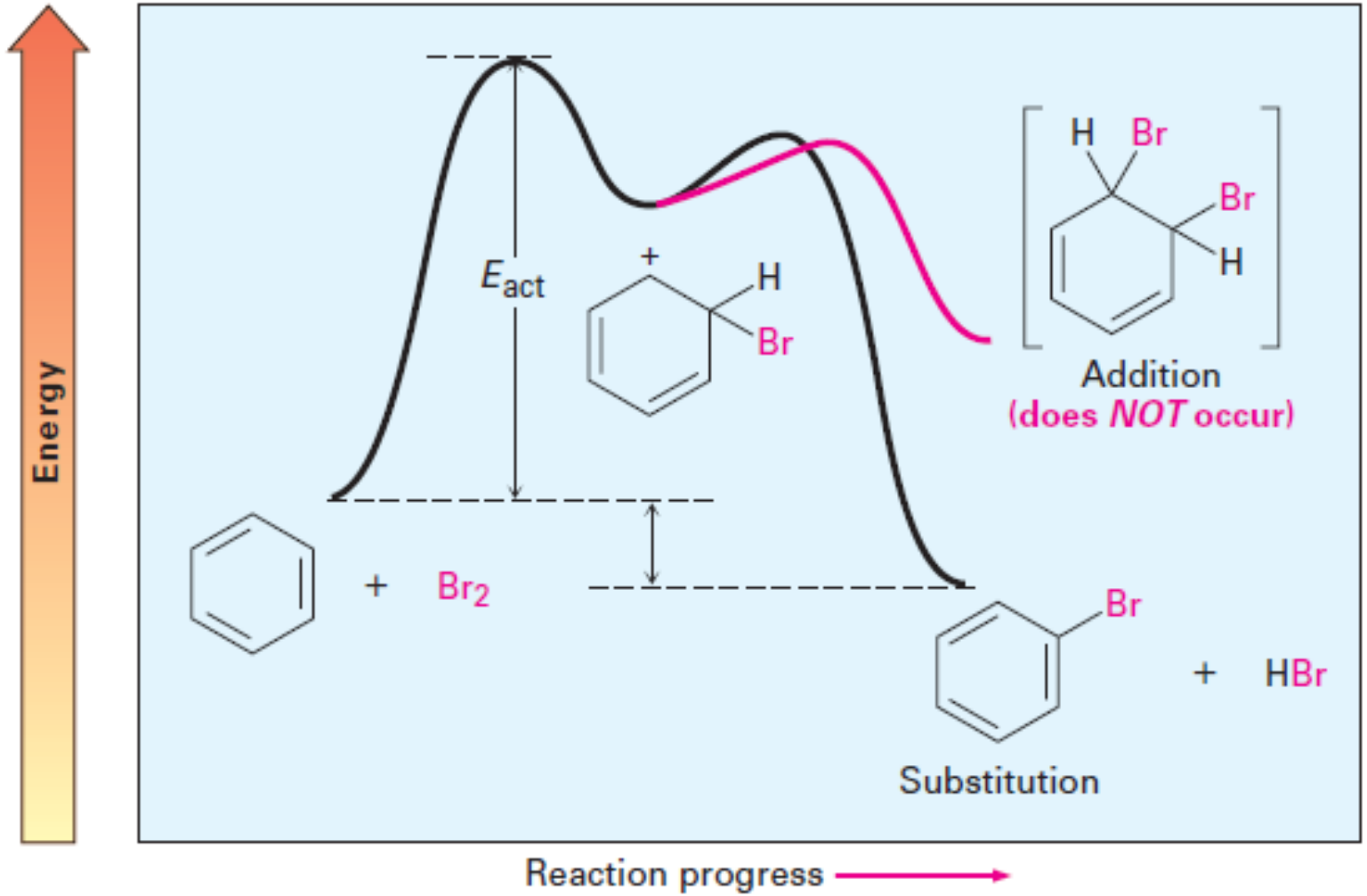
MECHANISM OF REACTION



1. An electron pair from the benzene ring attacks the positively polarized bromine, forming a new C–Br bond and leaving a nonaromatic carbocation intermediate.

2. A base removes H^+ from the carbocation intermediate, and the neutral substitution product forms as two electrons from the C–H bond move to re-form the aromatic ring.

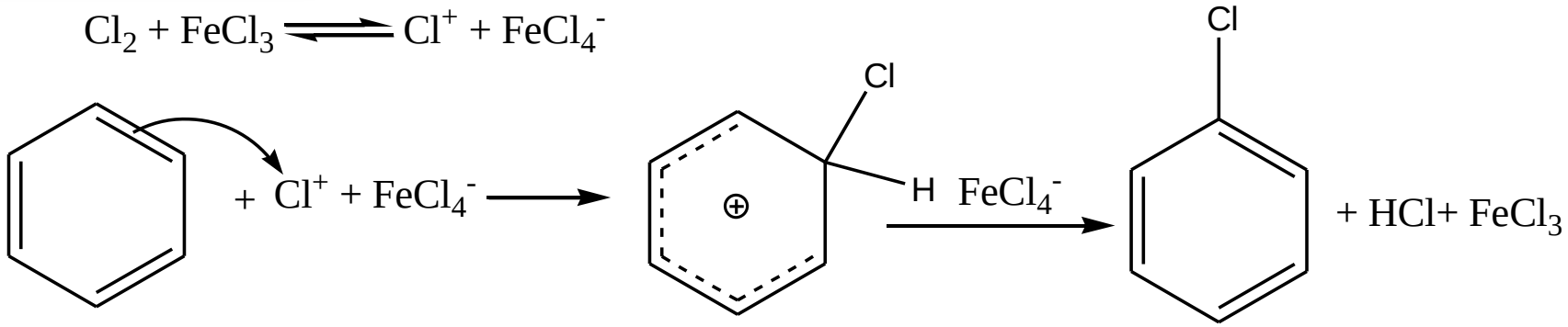
ENERGY PROFILE DIAGRAM FOR BROMINATION REACTION



CHLORINATION OF BENZENE

1. For bromination of benzene to take place, a catalyst such as Fe or $FeCl_3$ is needed along with Cl_2.
2. The catalyst makes the Cl_2 molecule more electrophilic form Cl^+.
3. The electrophilic Cl^+ then reacts with the electron-rich (nucleophilic) benzene ring to yield a nonaromatic carbocation intermediate.
4. The carbocation intermediate loses H^+ from the bromine-bearing carbon to give a substitution product (Regain aromaticity/stability).

MECHANISM



Friedel-Craft Alkylation to Benzene Ring (In 1877)

One of the most useful electrophilic aromatic substitution reactions is alkylation—the introduction of an alkyl group onto the benzene ring. Called the Friedel–Crafts alkylation reaction. It involves generation of carbocation or related electrophilic species which was generated by reaction between alkyl halide and Lewis acid.

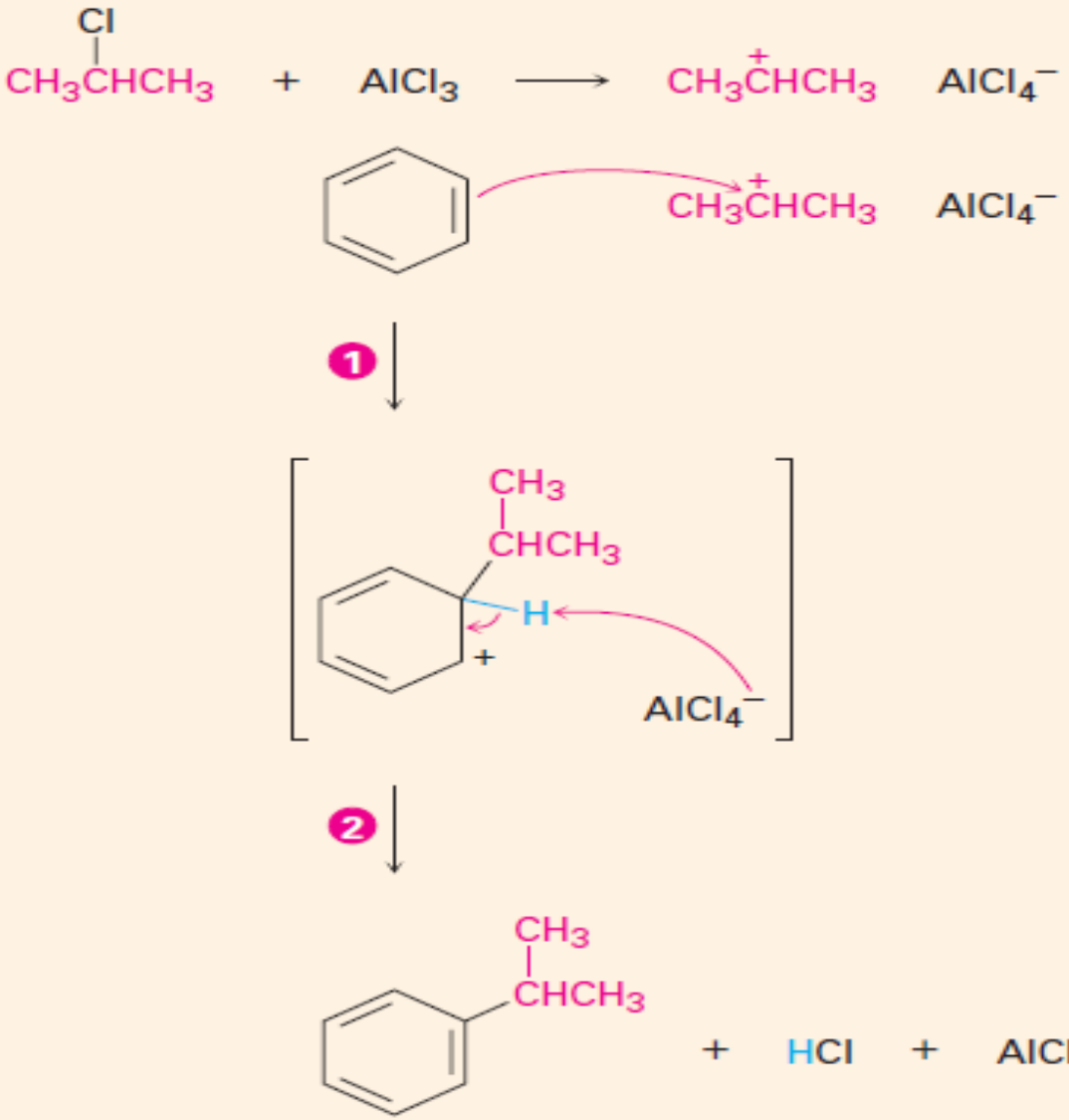
1. $AlCl_3$ is the most commonly used Lewis acid, other L.A. such as SbF_5, $TiCl_4$, BF_3 etc. can promote the reaction.

Note: Carbocation can also be generated by the reaction between alkene with proton (H_2SO_4 acid) and alcohol with proton (H_2SO_4 acid) . So, these are the alternative reagents for alkylation.

2. Aromatic (aryl) halides such as chlorobenzene don't react.
3. In addition, Friedel–Crafts reactions don't succeed on aromatic rings that are already substituted by the groups -NO_2, -CN, -SO_3H, or -COR. Such aromatic rings are much less reactive than benzene. So one can used nitrobenzene as a solvent for F-C reaction.

4. L.A. catalyst: $AlCl_3 > BF_3 > SbCl_5 > FeCl_3 > SnCl_4 > ZnCl_2$
5. Proton Acid catalyst: HF, H_2SO_4, H_3PO_4
6. Order of alkylation of alkyl halide (with same halide):
   t-R-X> s-R-X >p-R-X (Where X=halogen, Cl, Br, I)
4. For alcohol the order is also remain same, where X=-OH
5. The reactivity of haloalkanes increases as you move up the periodic table and increase polarity. So for the same R the order will be: R-F>R-Cl>R-Br>R-I
6. Dry $AlCl_3$ is used, otherwise water will react with $AlCl_3$ and convert it into $Al(OH)_3$.

MECHANISM OF REACTION

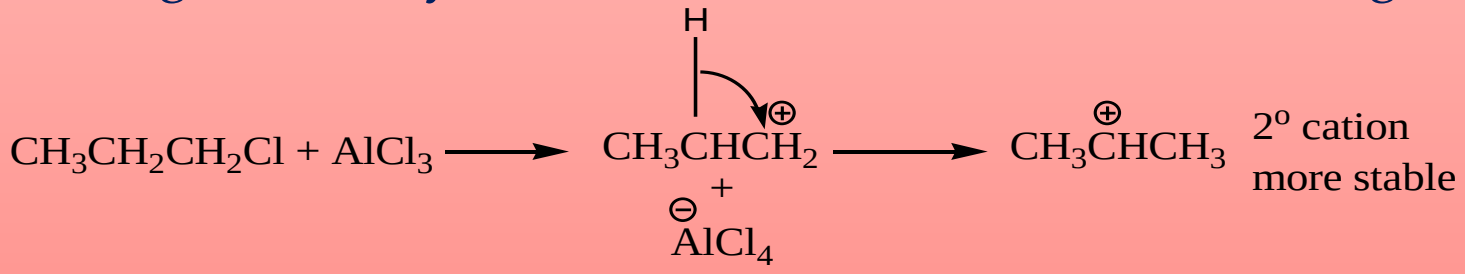


1. An electron pair from the aromatic ring attacks the carbocation, forming a C–C bond and yielding a new carbocation intermediate.

2. Loss of a proton then gives the neutral alkylated substitution product.

The three key limitations of Friedel-Crafts alkylation are:

1. **Carbocation Rearrangement** - Only certain alkylbenzenes can be made due to the tendency of cations to rearrange.
2. So, it is easy to introduce methyl, ethyl or iso-propyl group, but usually difficult to introduce n-propyl or n-butyl or higher homologues of alkyl halides, since these tends to rearrange.



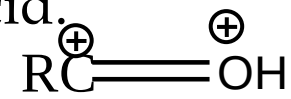
3. **Compound Limitations** - Friedel-Crafts fails when used with compounds such as nitrobenzene and other strong deactivating systems.
4. **Polyalkylation** - Products of Friedel-Crafts are even more reactive than starting material. Alkyl groups produced in Friedel-Crafts Alkylation are electron-donating substituents meaning that the products are more susceptible to electrophilic attack than what we began with.

Friedel-Craft Acylation to Benzene Ring

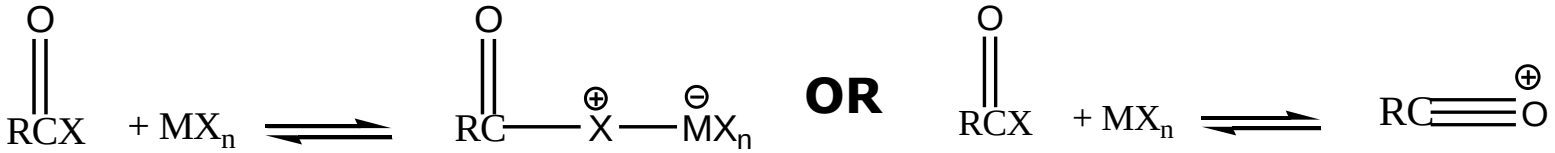
Friedel–Crafts acylation reaction is closely related to the Friedel–Crafts alkylation reaction**.** When an aromatic compound is treated with a carboxylic acid chloride or acyl chloride (RCOCl) in the presence of Lewis acid for e.g. $AlCl_3$, an **acyl group** (R-C=O) is introduced onto the ring i.e. synthesis of aromatic ketone.

REACTIVE ELECTROPHILE

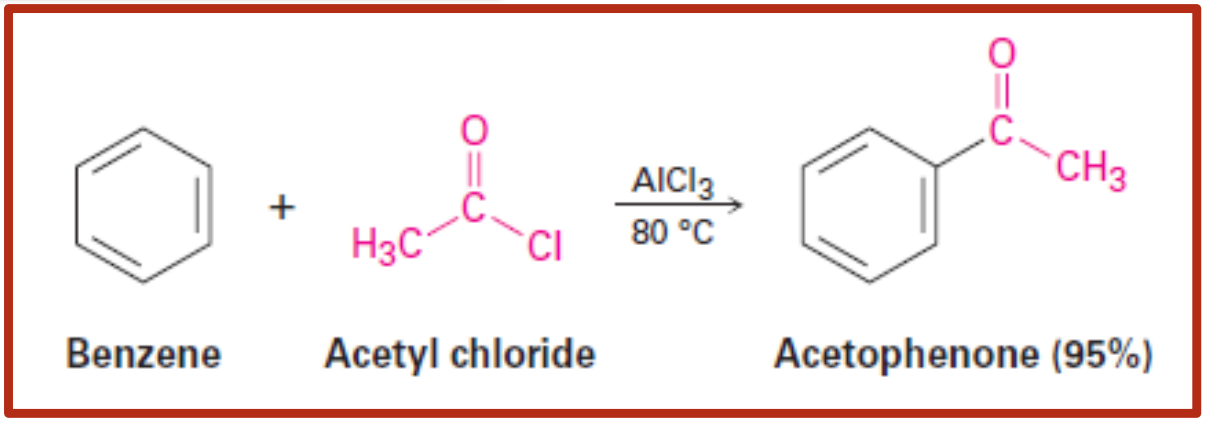
1. For benzene or less reactive aromatic compounds, the active electrophile is a protonated acylium ion or an acylium ion complexed by a Lewis acid.

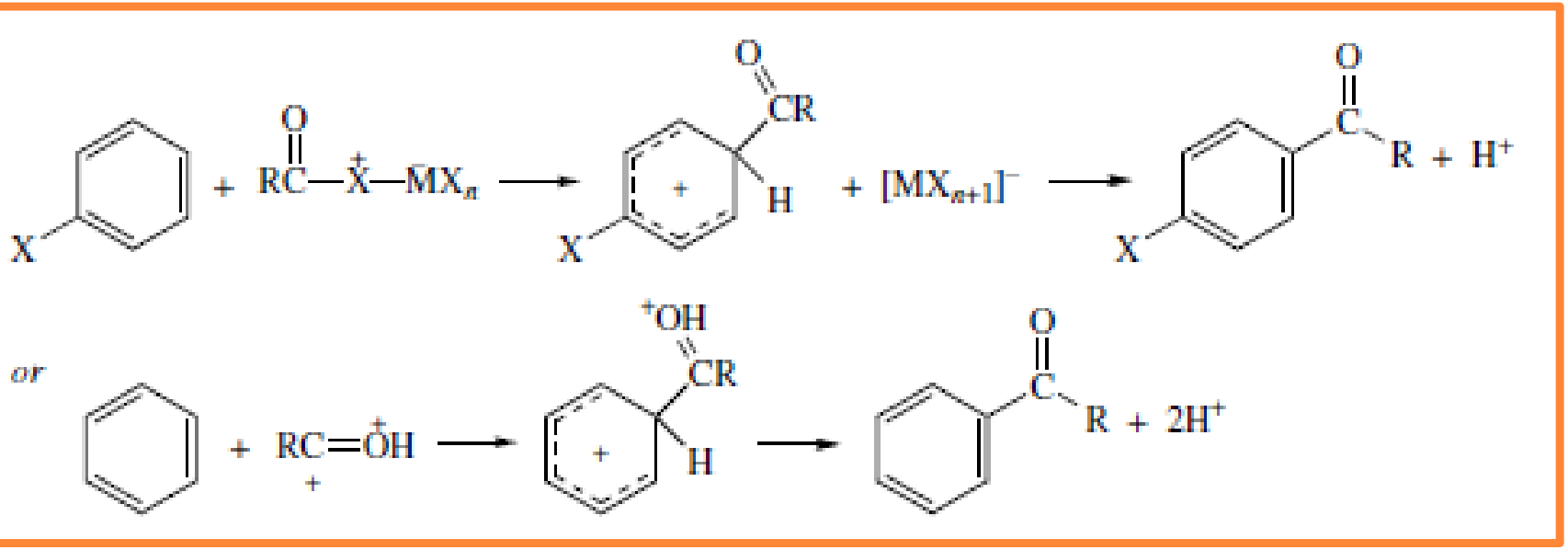


2. For activated aromatic compounds, the active electrophile is a discrete positively charged acylium ion or an acyl chloride complexed by a Lewis acid



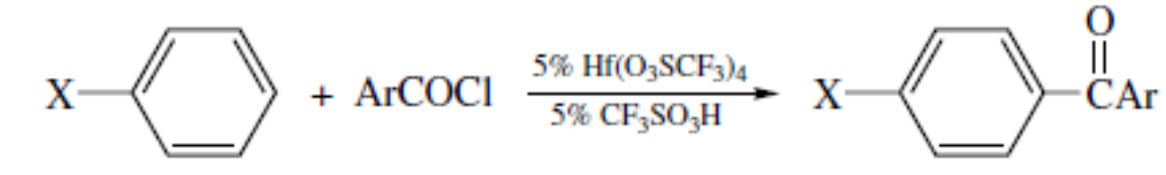
MECHANISM OF REACTION



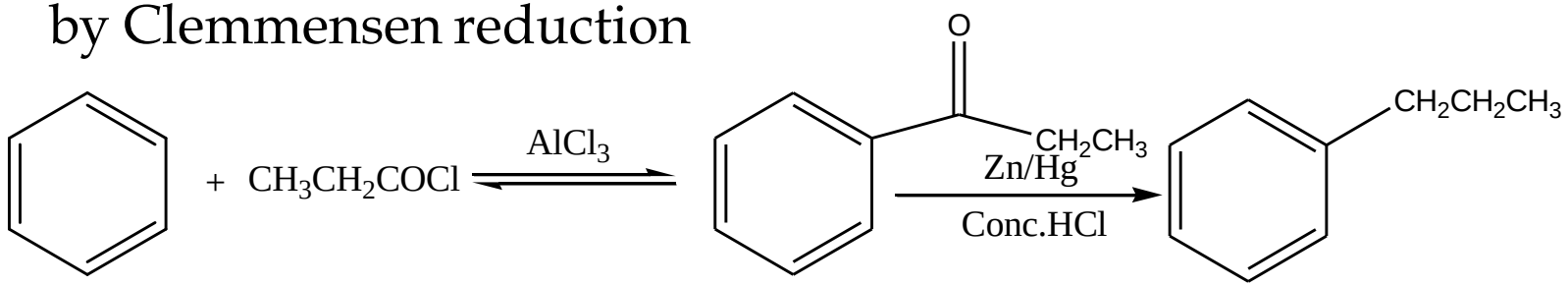


NOTE:

1. In F-C acylation reaction Lewis acid can't be used as catalyst because it is consumed by acid (HCl) with the progress of the reaction. Lanthanide triflate can be used as a catalyst for this reaction. The reaction is presumed to occur through aroyl triflate intermediate which dissociates to aryl acylium ions. Lithium perchlorate and scandium triflate also promote acylation.

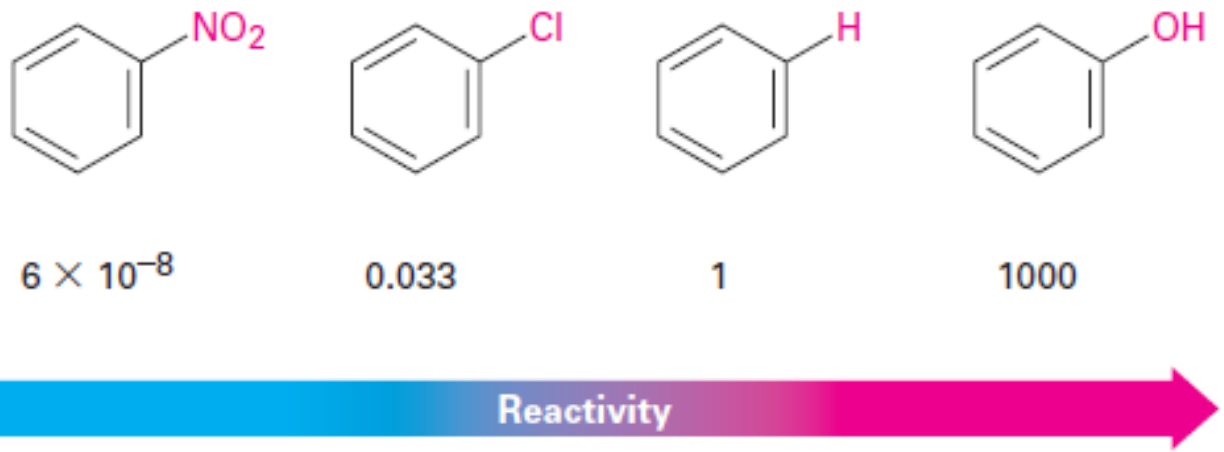


2. Propyl group can be inserted by F-C acylation reaction followed by Clemmensen reduction

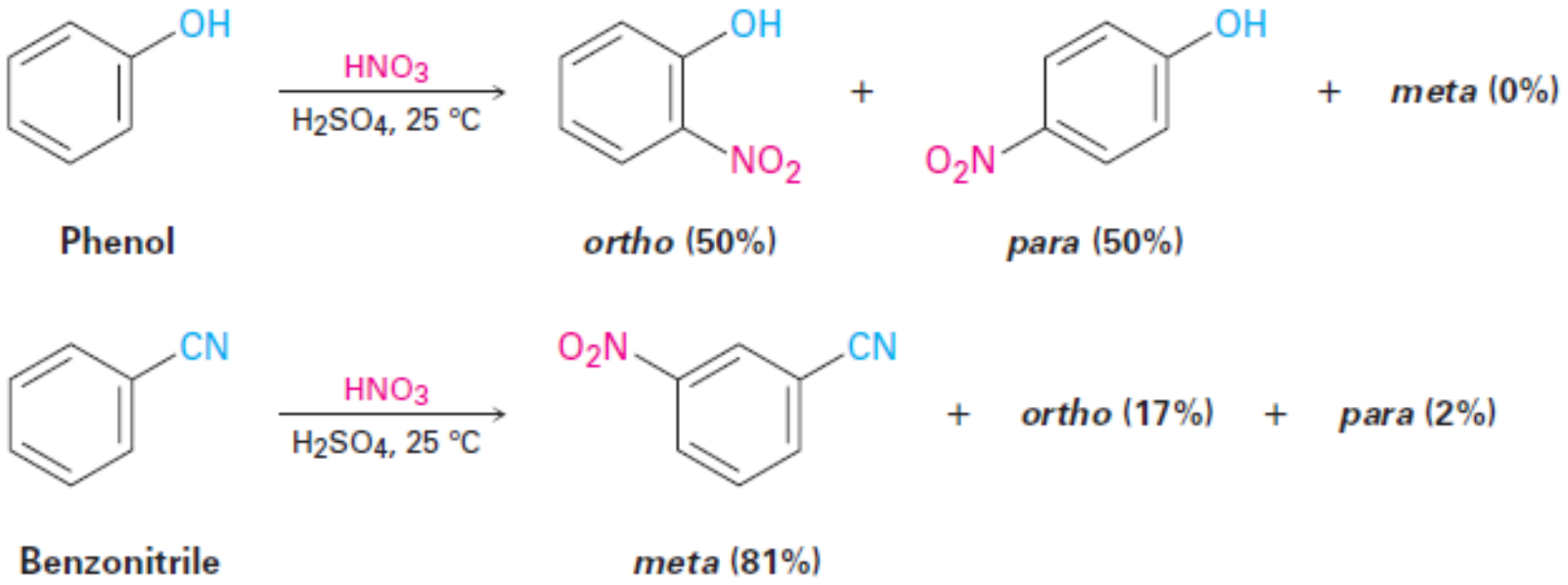


Substituent Effects in Electrophilic Aromatic Substitution

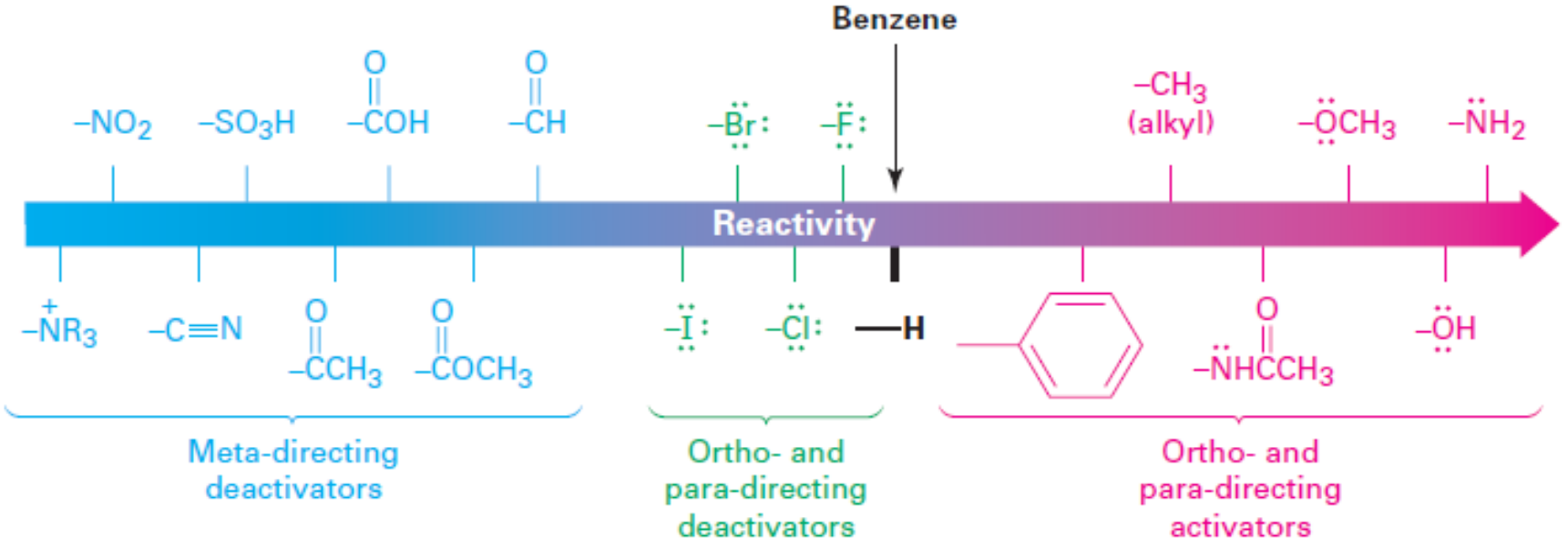
Substituents affect the *reactivity of an aromatic ring*. Some substituents activate a ring, making it more reactive than benzene, and some deactivate a ring, making it less reactive than benzene. In aromatic nitration, for instance, the presence of an OH substituent makes the ring 1000 times more reactive than benzene, while an NO_2 substituent makes the ring more than 10 million times less reactive.



Substituents affect the orientation of a reaction. The three possible disubstituted products—ortho, meta, and para—are usually not formed in equal amounts. Instead, the nature of the substituent already present on the ring determines the position of the second substitution. An OH group directs further substitution toward the ortho and para positions, for instance, while a CN directs further substitution primarily toward the meta position.



Substituents can be classified into three groups, as shown in Fig. 1 meta-directing deactivators, ortho- and para-directing deactivators, and ortho and para-directing activators. There are no meta-directing activators. Note how the directing effect of a group correlates with its reactivity. All meta directing groups are deactivating, and all ortho- and para-directing groups other than halogen are activating. The halogens are unique in being ortho and para-directing but deactivating.



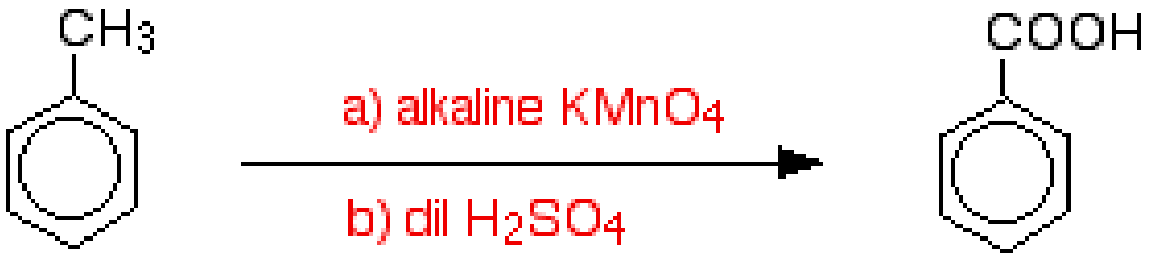
Side Chain Oxidation in Alkylbenzenes

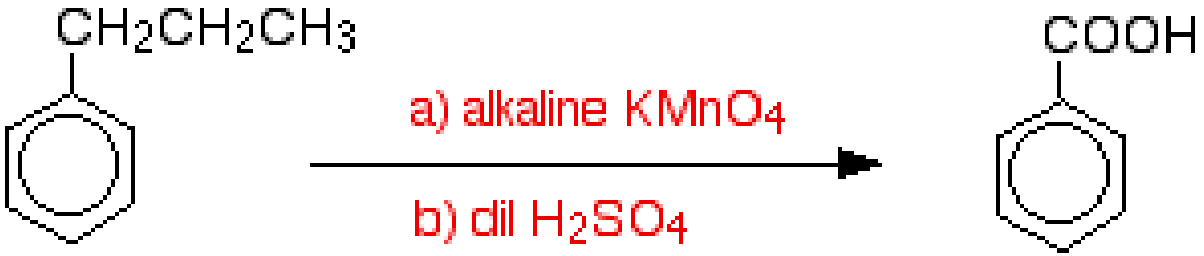
A. An alkylbenzene is simply a benzene ring with an alkyl group attached to it. Methylbenzene is the simplest alkylbenzene.

B. Alkyl groups are usually fairly resistant to oxidation. However, when they are attached to a benzene ring, they are easily oxidised by an alkaline solution of potassium manganate(VII) (potassium permanganate).

C. Methylbenzene is heated under reflux with a solution of **potassium manganate(VII)** made alkaline with sodium carbonate. The purple colour of the potassium manganate(VII) is eventually replaced by a dark brown precipitate of manganese(IV) oxide. The mixture is finally acidified with dilute sulphuric acid. **Overall, the methylbenzene is oxidised to benzoic acid.**

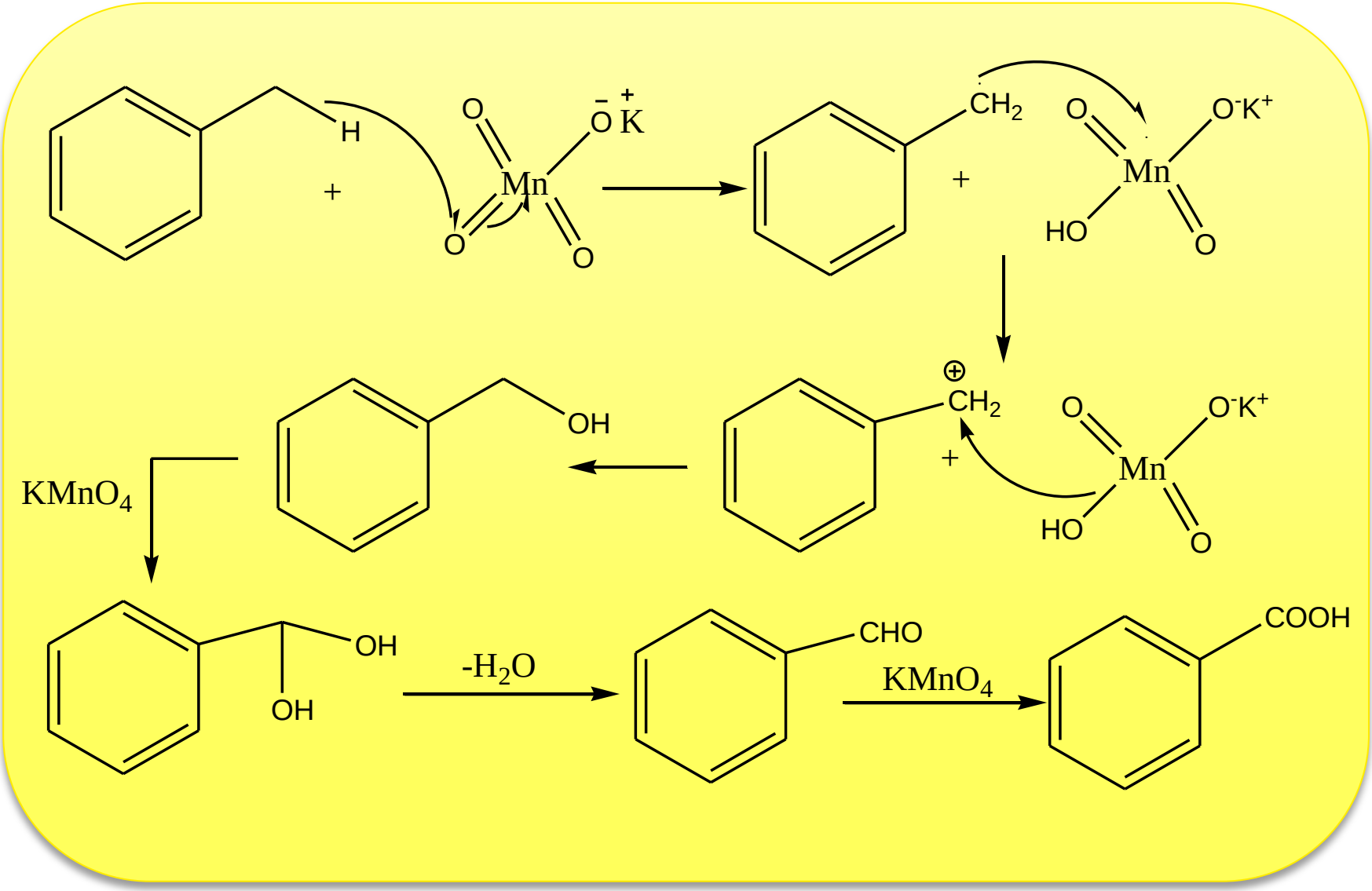
Interestingly, any alkyl group is oxidised back to a -COOH group on the ring under these conditions. So, for example, propylbenzene is also oxidised to benzoic acid.





KEY POINT: Benzylic hydrogen is required for oxidation. Hence,1º alkyl group and 2º alkyl group will give benzoic acid in oxidation but 3º alkyl group is non-reactive.

MECHANISM OF REACTION



THANK YOU