



M.Sc SEM- 2 CHNN : 502 UNIT:

AROMATIC ELECTROPHILIC SUBSTITUTION
REACTIONS

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Learning Outcomes

Introduction: Electrophilic Aromatic Substitution

Arenium Ion Mechanism

**Some Aromatic Electrophilic Substitution Reactions Viz. Nitration,
Sulphonation, Halogenation, Friedel- Crafts Reaction**

Orientation & Reactivity in Mono Substituted Benzene

***IPSO* Attack**

Vilsmeier Haack Reaction

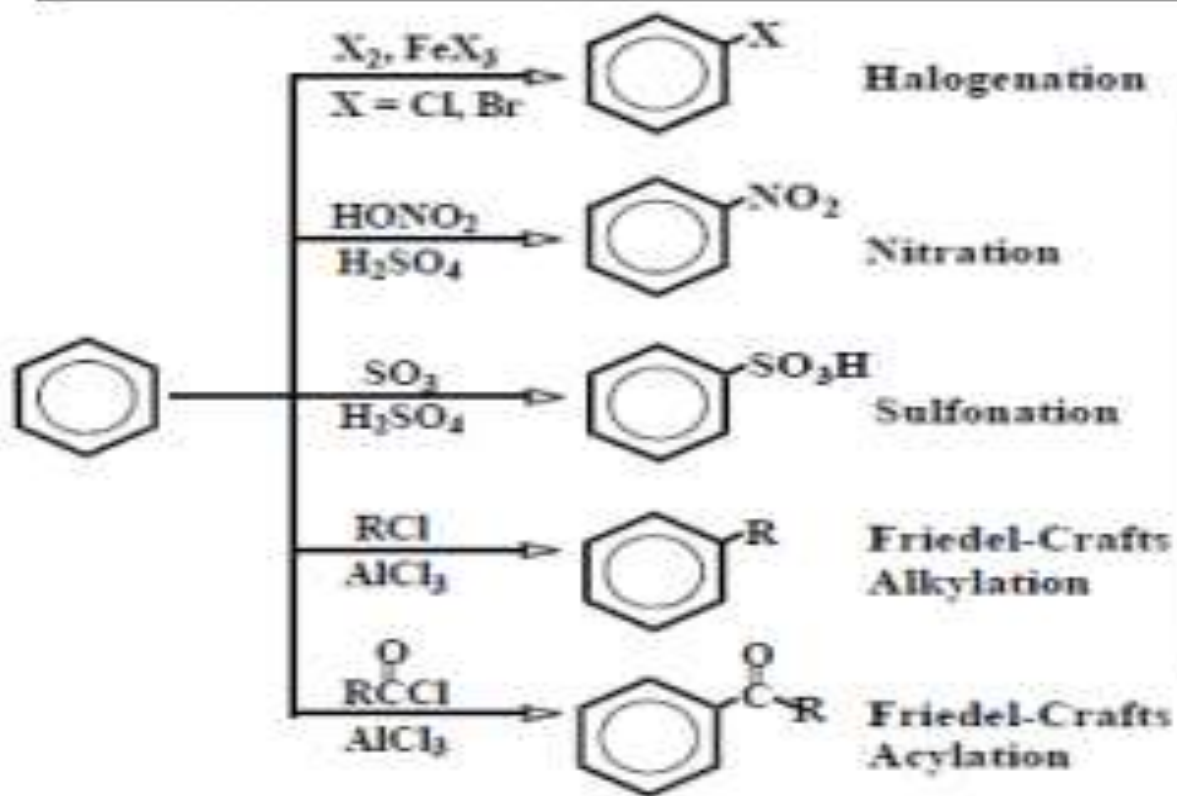
Gattermann Koch Reaction

Diazonium Coupling Reaction

Reference from e-PG Pathshala, Wikipedia, Vedantu e-learning

Electrophilic Aromatic Substitution : Electrophilic aromatic substitution is an [organic reaction](#) in which an atom that is attached to an [aromatic system](#) (usually hydrogen) is replaced by an [electrophile](#). e.g. [aromatic nitration](#), [aromatic halogenation](#), [aromatic sulfonation](#), and alkylation and acylation ([Friedel–Crafts reaction](#)).

Examples of Electrophilic Aromatic Substitution Reactions



These reactions are commonly used synthetic procedures for modifying arenes. They proceed by a general mechanism initiated by addition of an electrophile E^+ to the aromatic π -system, forming a nonaromatic carbocation intermediate called an arenium ion.

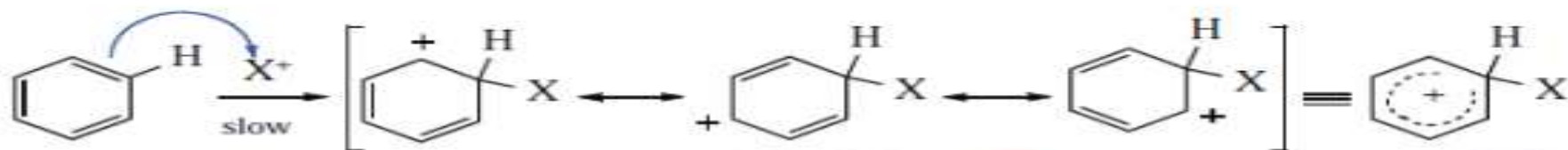
ARENIUM ION MECHANISM :

The mechanism aromatic electrophilic substitution is known as the *arenium ion mechanism* and has two main steps.

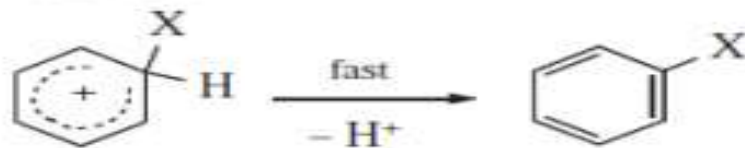
Step 1: The initial step is the attack of an electrophile creating a resonance stabilized carbocation/intermediate called *arenium ion*, which is also known as the *Wheland Intermediate*.

Although the *Wheland intermediate* or σ -complex or now popularly known as *arenium ion* is stabilized by resonance (with charge dispersal over the carbons *ortho* and *para* to the site of attachment of the electrophile), this step is accompanied by loss of aromaticity, so the energy of activation is high.

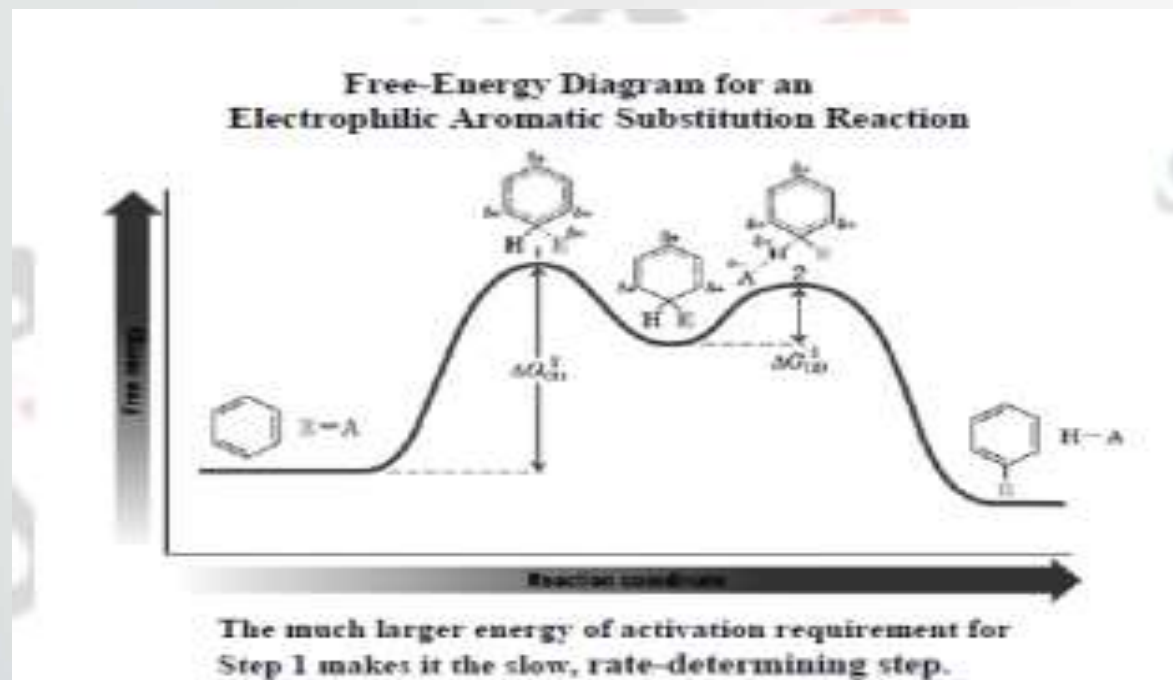
This is also the rate-determining step of the reaction because of the disruption of aromaticity.



Step 2: In the second step the leaving group departs. This leads to regeneration of aromatic stabilization. The second step is nearly always faster than the first, making the first rate determining, and the reaction is second order.



Energy Profile Diagram of the Arenium Ion Mechanism of Electrophilic Aromatic Substitution

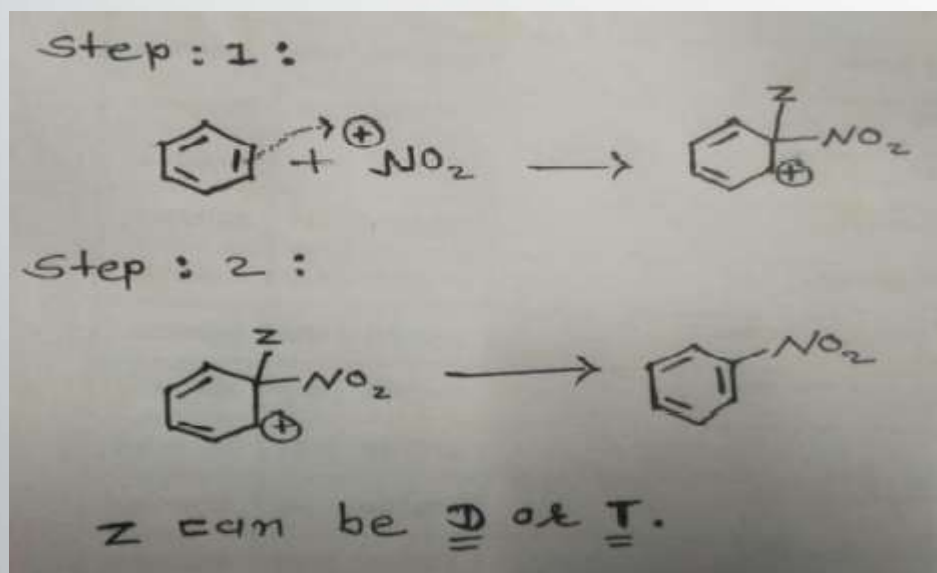


<https://youtu.be/mY8o-Ew-GZg>

The energy diagram of this reaction shows that step 1 is highly endothermic and has a large $\Delta G^\ddagger(1)$. The first step requires the loss of aromaticity of the very stable benzene ring, which is highly unfavorable. The first step being a slow step, is rate-determining. Step 2 is highly exothermic and has a small $\Delta G^\ddagger(2)$. The ring regains its aromatic stabilization, which is a highly favorable process.

1. Isotope Effects : • “A difference in the rate of a reaction due to a difference in the isotope present in the reaction system is called Isotope Effect.” • If the proton is lost before the arrival of the Electrophile (SE1 mechanism) then there should be a substantial isotope effect. • In This effect, Each Case the C—H bond broken in the Rate determining step but In Arenium Ion mechanism, the C—H bond not broken in the rate determining step, Hence No isotope effect should be found.

As expected , isotope effect has not observed in most aromatic Electrophilic Substitution.

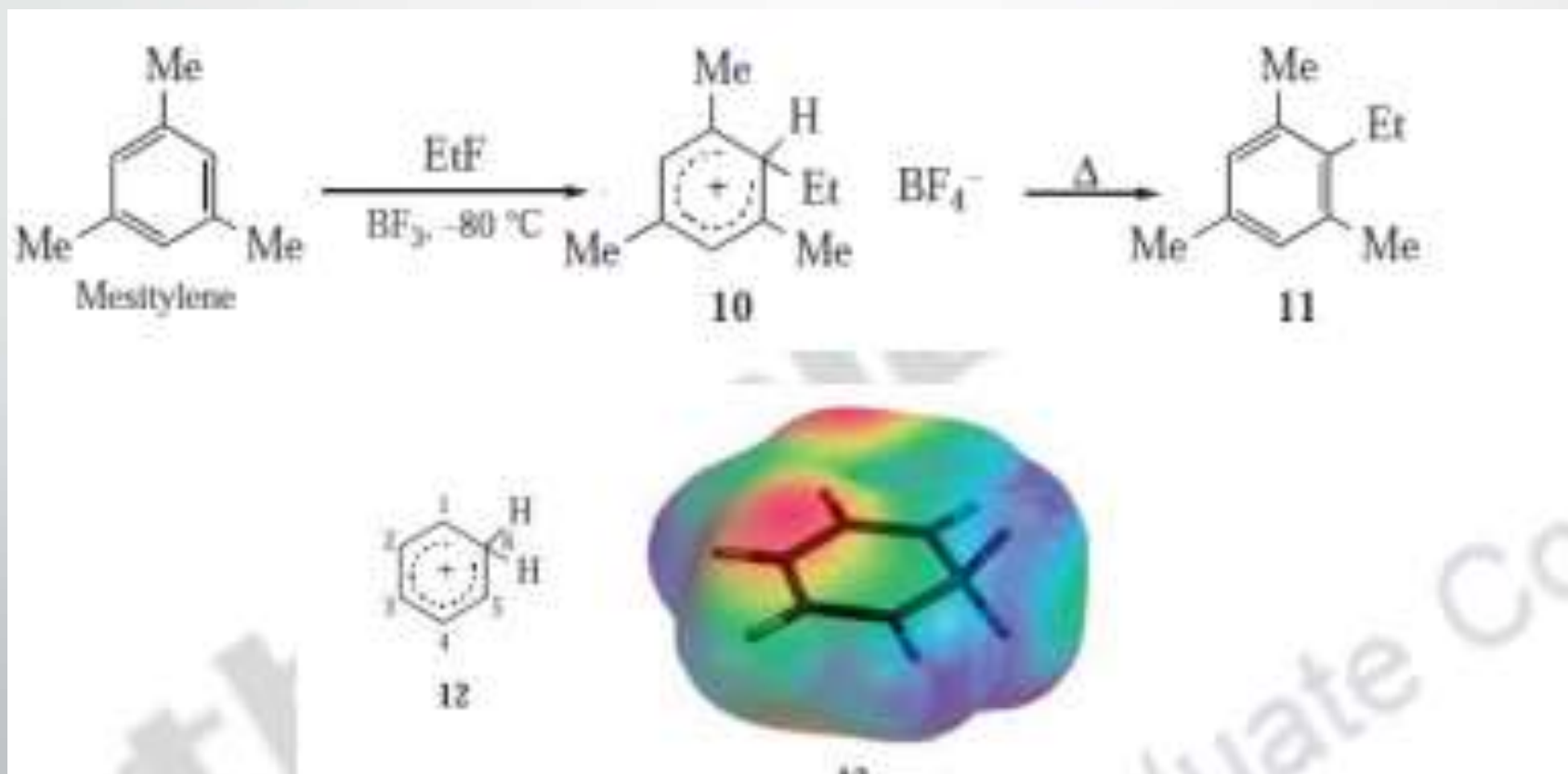


Rates of Nitration of deuterio- and tritobenzenes are the same as the rate of benzene. • This Clearly shows that aromatic electrophilic substitution involves two steps and that the loss of proton is not the rate-determining step.☆☆☆☆.....

<https://youtu.be/DuuyEbxWCkw>

2. Isolation of Arenium Ion Intermediates: The isolation of Arenium ions in many cases provides for a very strong evidence for the Arenium ion mechanism. When 10 was heated, the normal substitution product (11) was obtained. Even the simplest such ion, the benzenonium ion (12) has been prepared in HF-SbF₅-SO₂ClF-SO₂F₂ at -134 °C, where it could be studied spectrally. Fig. 8:

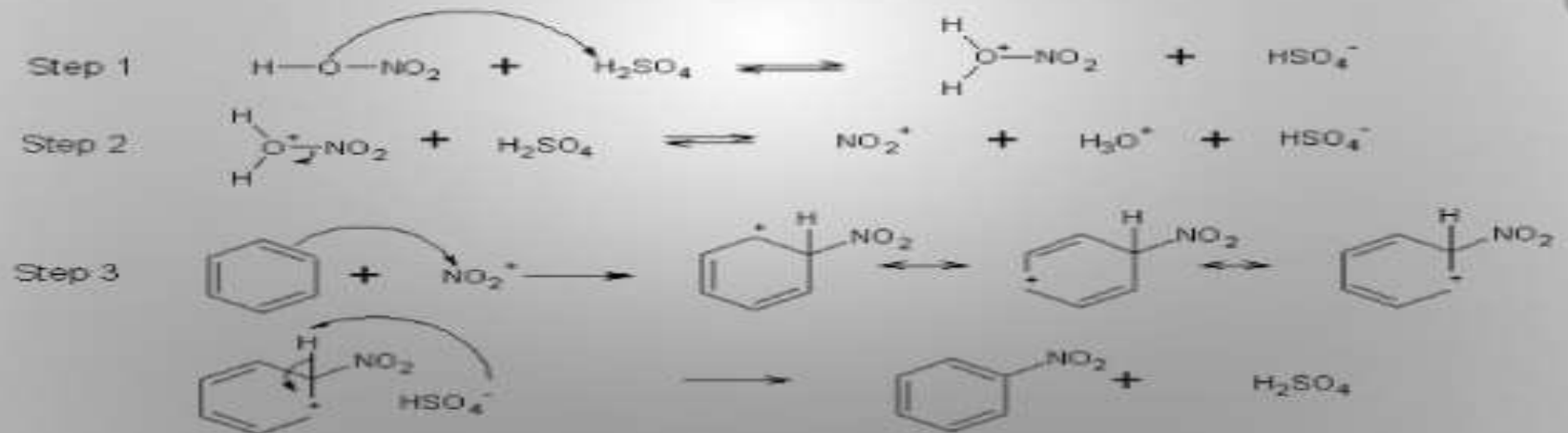
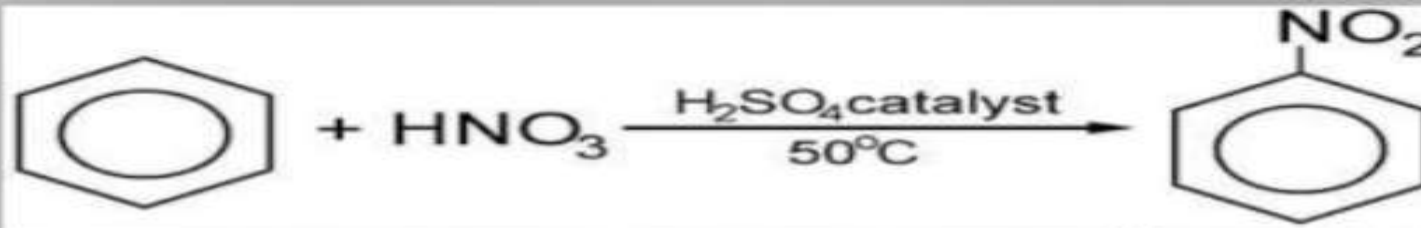
Isolation of Arenium ion intermediate



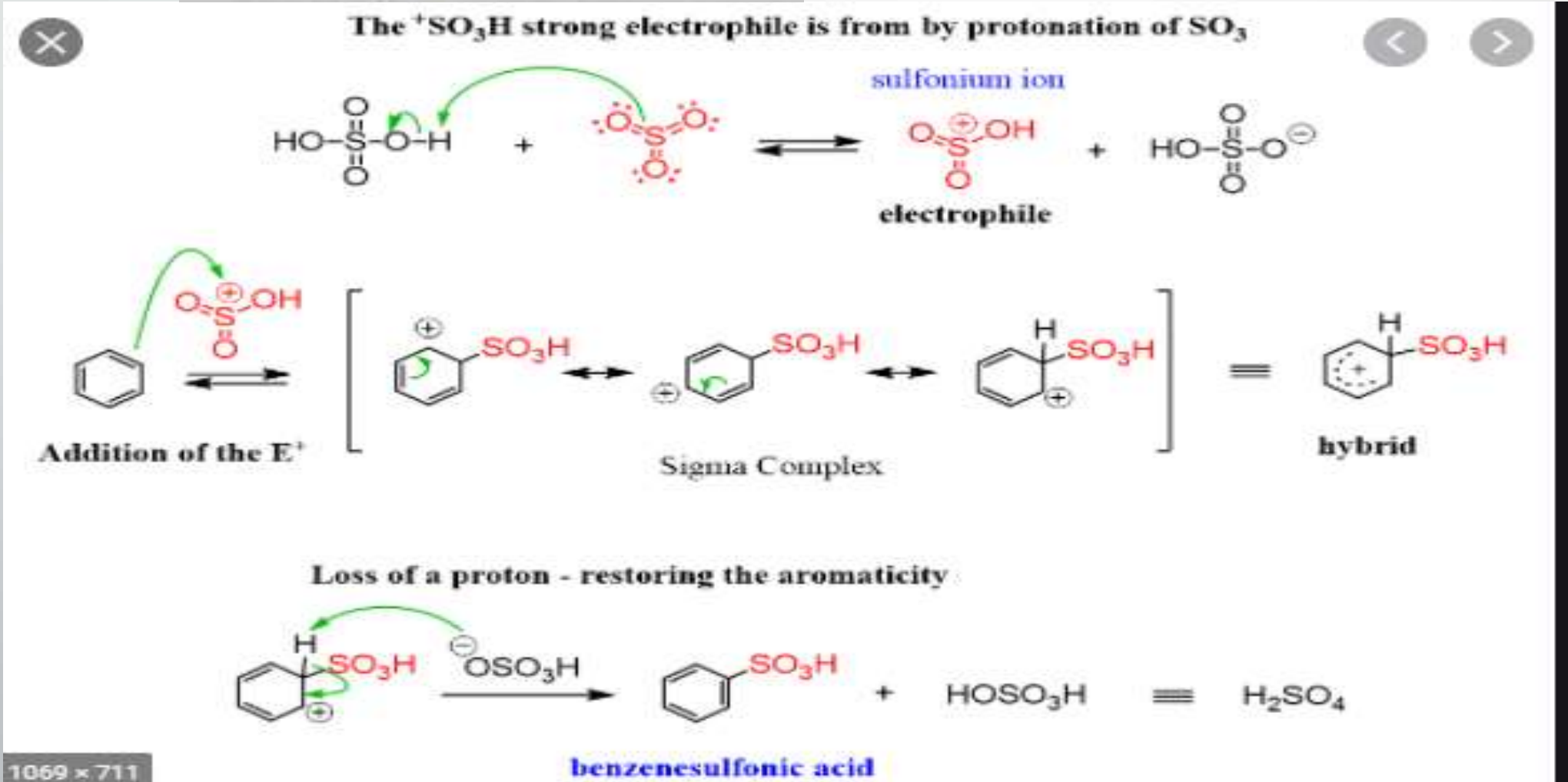
REACTION

Nitration of Benzene

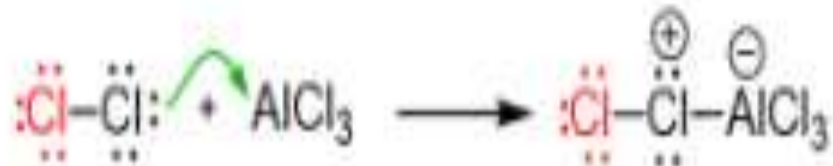
- The nitric acid reacts with benzene in the presence of conc. H_2SO_4 at 50°C temperature and produces Nitrobenzene with the



Sulfonation

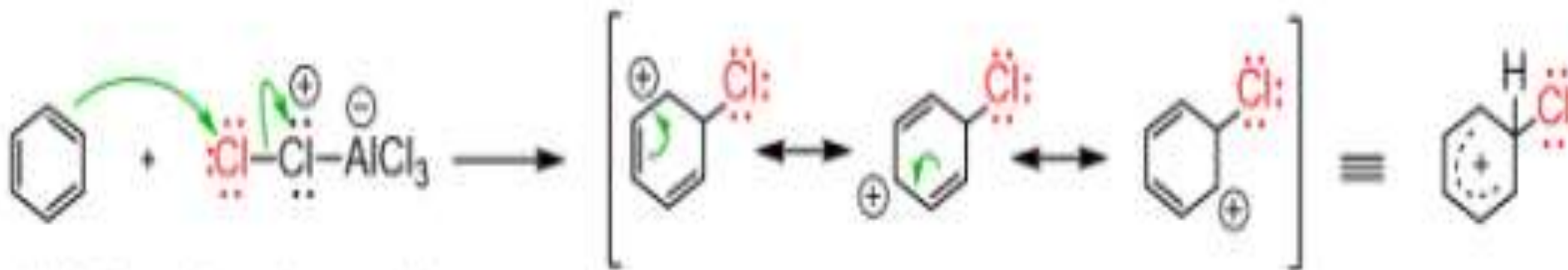


Chlorination of Benzene



Lewis base Lewis acid

electrophile - E⁺
the source of Cl⁺

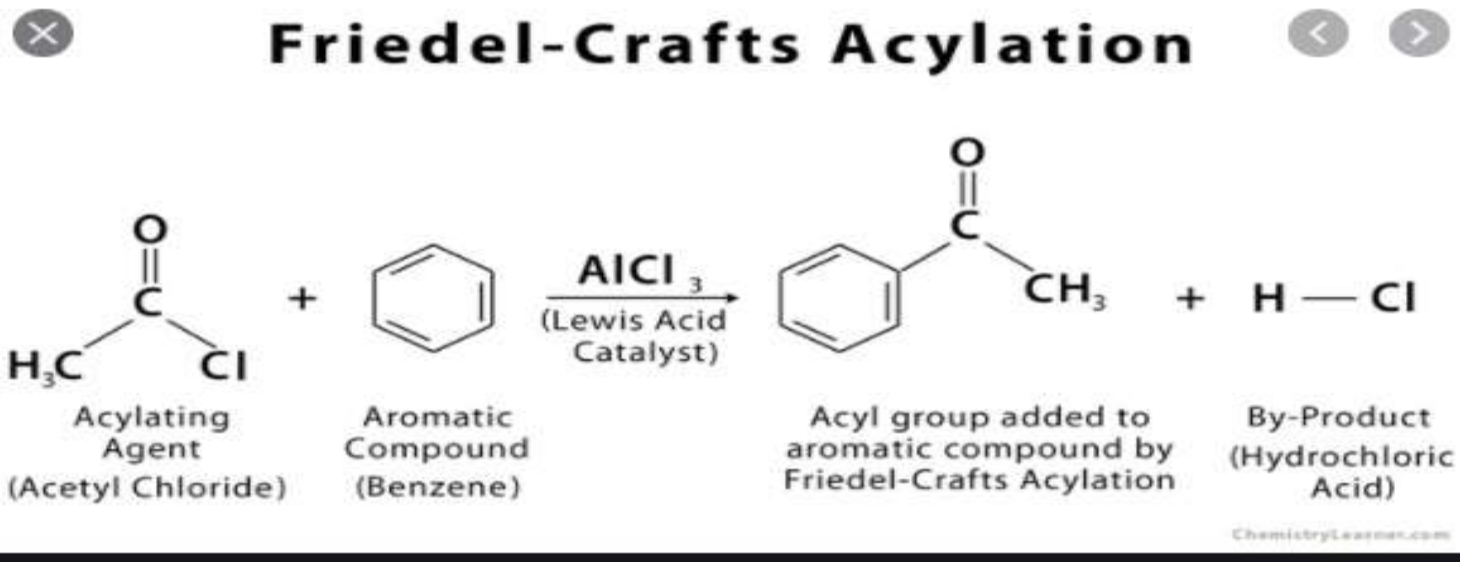
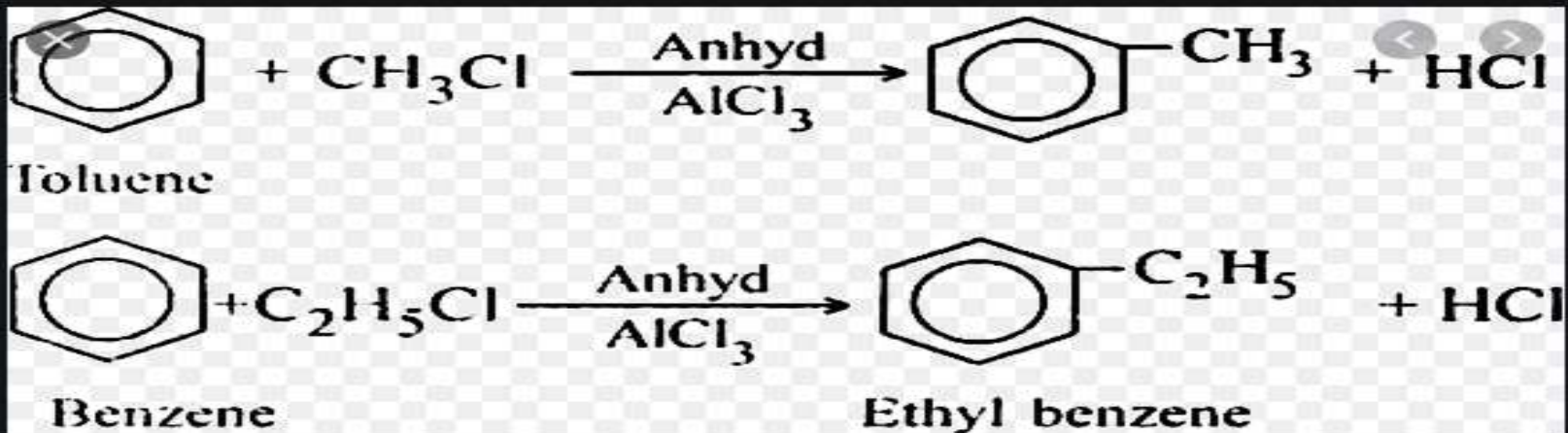


Addition of the electrophile

Sigma Complex

hybrid

Friedel Crafts Alkylation and Acylation of Benzene



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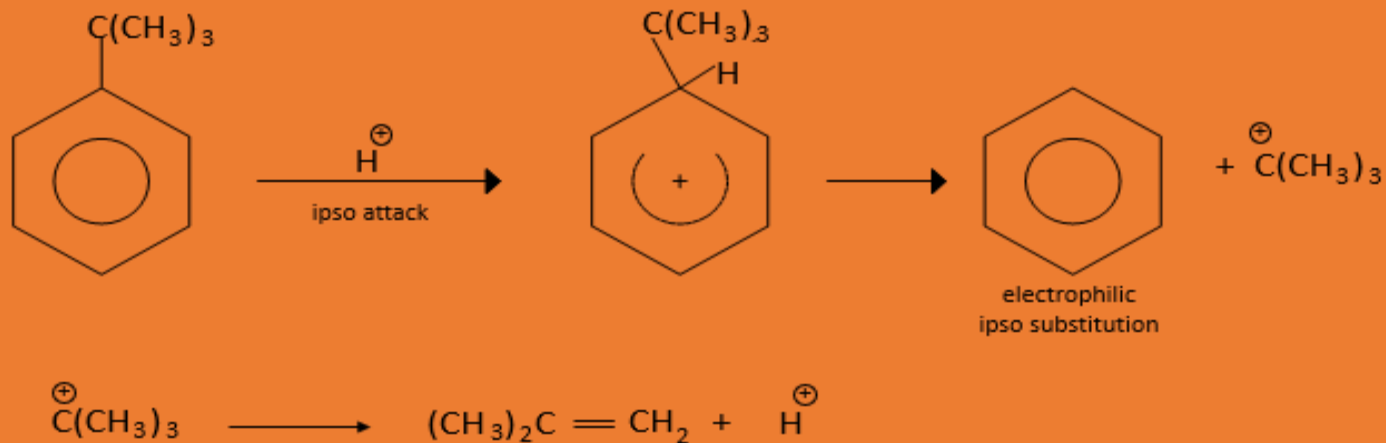
IPSO ATTACK

- ▶ A Position which is already occupied by a non-hydrogen substituent in an aromatic ring is called “IPSO Position”.
- ▶ The attack on this position is called “IPSO ATTACK”(or IPSO Addition)
- ▶ The Aromatic substitution in which a substituent already present is replaced is called “IPSO Substitution”



- ▶ For Example: Protodealkylation of an alkylbenzene (reverse of Friedel-Crafts alkylation)
- ▶ In this reaction tertiary alkyl groups are most easily removed, since they depart as stabler carbocations.
- ▶ Thus, t-butyl groups is used to protect the most reactive position in a compound to effect reaction elsewhere.

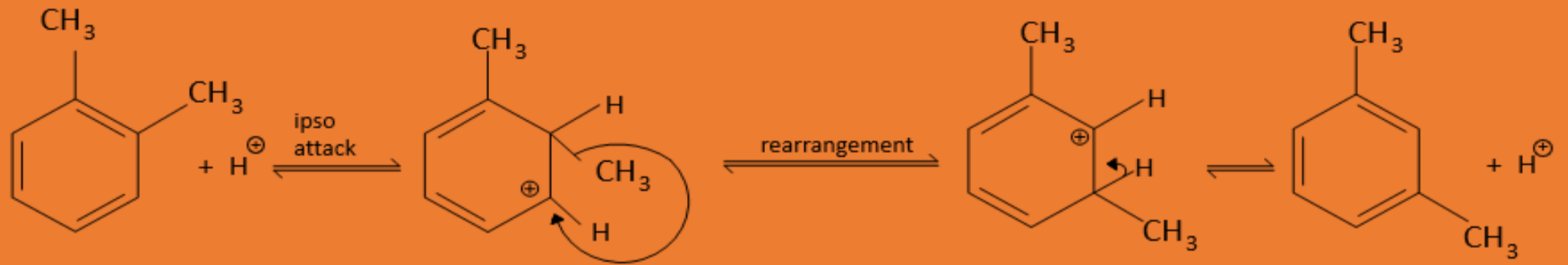
The mechanism is as follows:





▶ The Rearrangement of alkylbenzenes leading to their isomerisation also involves ipso attack.

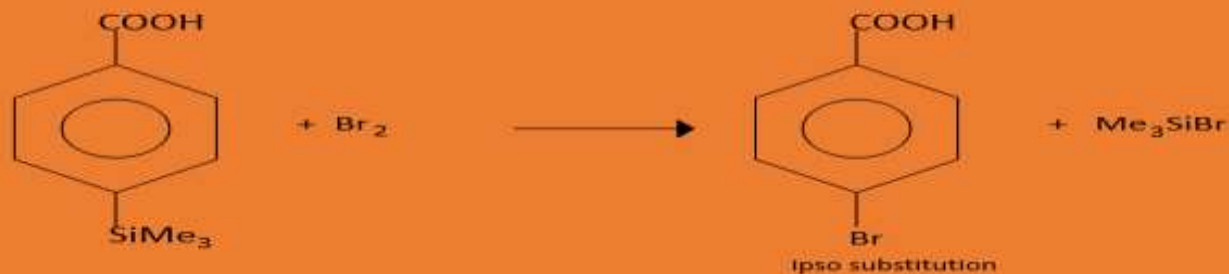
For Example, o-xylene isomerises to m-xylene as follows:





- ▶ Silyl group has a strong tendency to direct the entering electrophile to the position occupied by it ,i.e,ipso position.
- ▶ This is due to the strong stabilisation of cationic centre β to the silicon.

Bromodesilylation:



▶ PROTODESILYLATION



<https://youtu.be/w0CFe8Fg1o8>

VILSMEIER – HAACK REACTION

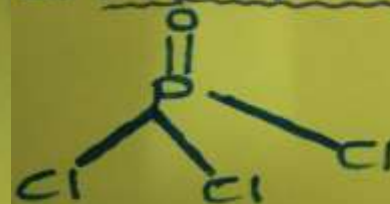
- The vilsmeier – haack reaction (also called the vilsmeier reaction) is the chemical reaction of a substituted amide (1) with phosphorus oxychloride and an electron-rich arene (3) to produce an aryle aldehyde or ketone (5) the reaction is named after anton vilsmeier and albrecht haack. The reaction of a substitute amide with phosphorus oxychloride gives gives a substituted chloroiminium ion (2) also called the vilsmeier reagent . The intital product is an iminium ion(4b), which is hydrolyzed to the corresponding aromatic ketone or aldyhyde during workup.

(1) substituted amide:-



N,N dimethyl
Formamide

2) Phosphorus oxychloride:-



Phosphoryl
trichloride

aromatic hydrocarbon:-



benzen

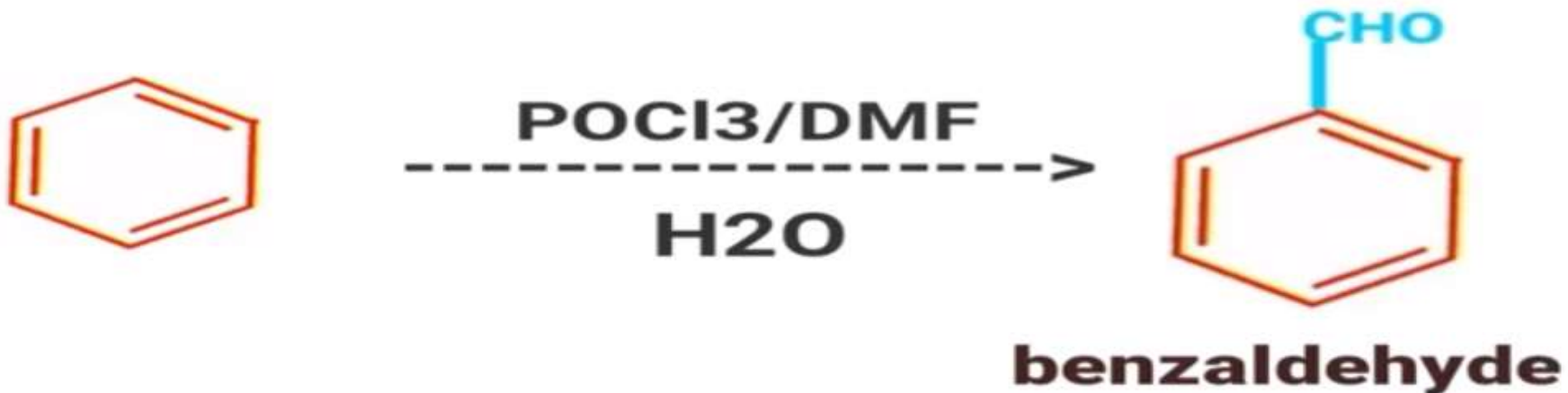


anisole



resorcinol

Overview of Vilsmeier Haack formylation



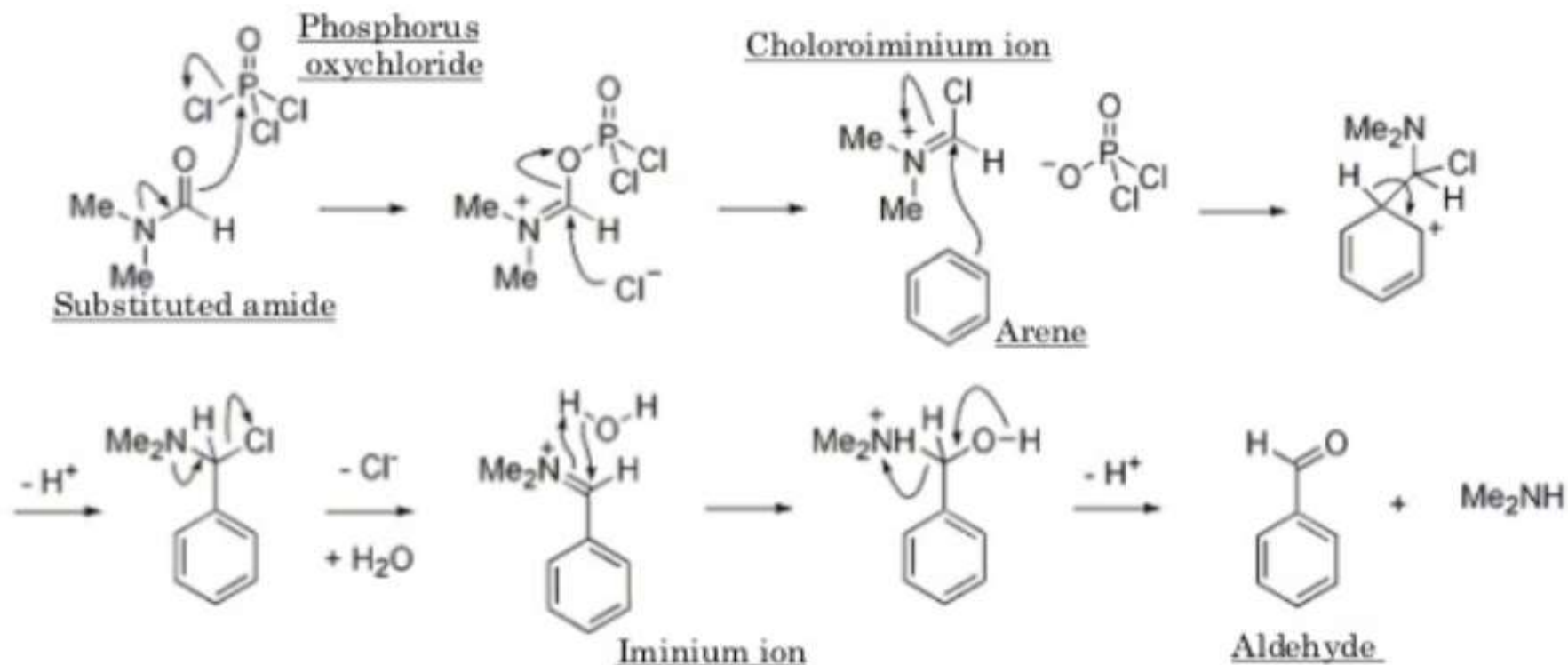
Vilsmeier Haack Formylation Reaction

Application of Vilsmeier Haack formylation



REACTION MECHANISM

- The reaction of the amide with phosphorus oxychloride produces an electrophilic iminium cation. The subsequent electrophilic aromatic substitution produces an iminium ion intermediate, which is hydrolyzed to give the desired aryl ketone or aryl aldehyde



Gattermann Koch Reaction

Gattermann – Koch reaction is used for industrial production of benzaldehyde. It is one of the very important name reactions for students. Chemists generally give names to reactions associated to either products of reactions or discoverers of the reactions. Gattermann – Koch reaction was given by Ludwig Gattermann and Julius Arnold Koch.

Gattermann – Koch Reaction

In Gattermann – Koch reaction, benzene is treated with carbon monoxide in acidic medium in presence of anhydrous aluminum chloride to give benzaldehyde. In this reaction anhydrous aluminum chloride works as catalyst. It is an electrophilic substitution reaction.

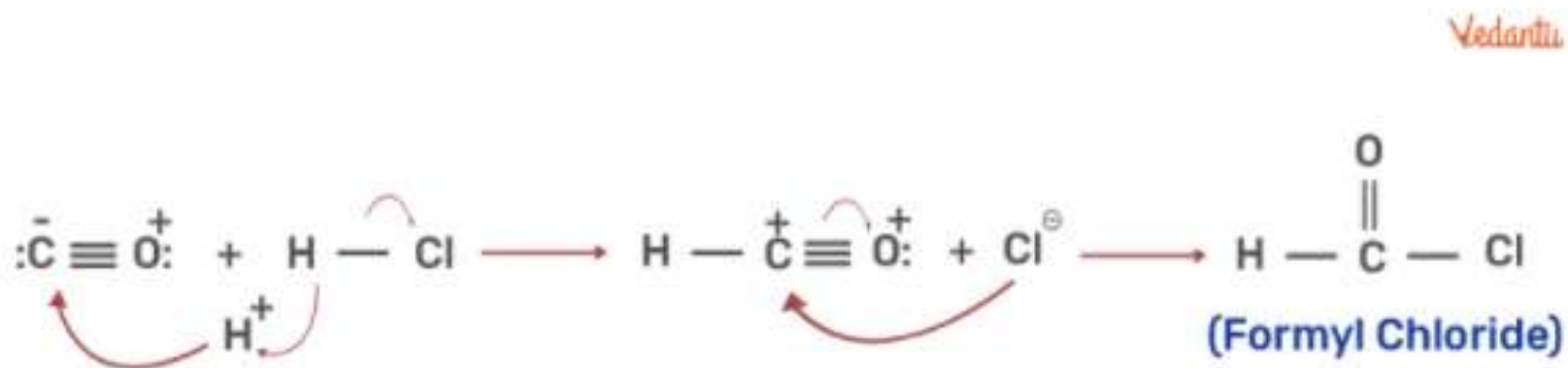
Gattermann – Koch Reaction can be written as follows –



Phenol and phenol ether substrates are not applicable for Gattermann – Koch Reaction.

Step 1. Formation of Formyl chloride

In this step carbon monoxide reacts with HCl and forms formyl chloride. Reaction can be written as follows -



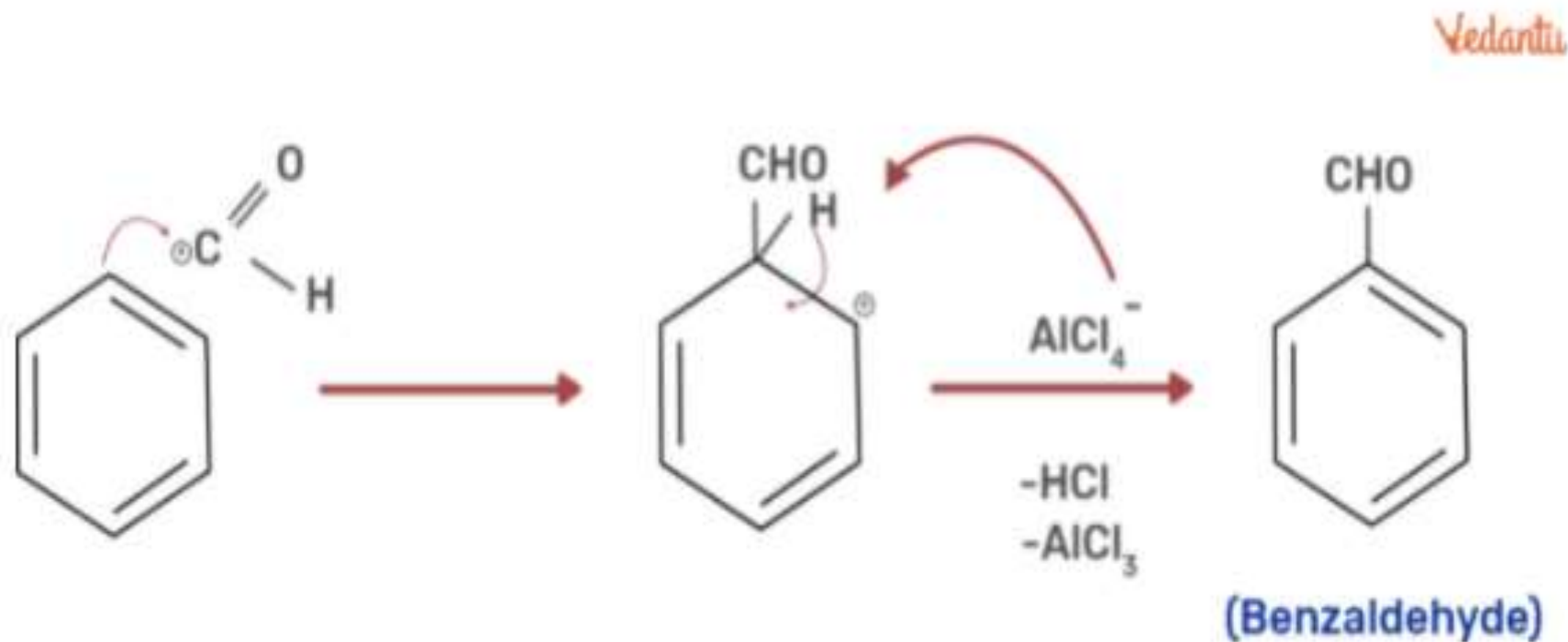
Step 2. Formation of Electrophile: H-C+=O

In this step formyl chloride reacts with anhydrous aluminum chloride and forms an electrophile (H-C+=O). Reaction can be written as follows -



Step 3. Formation of benzaldehyde

In this step $\text{H-C}^+=\text{O}$ (electrophile) reacts with benzene and forms benzaldehyde. During the reaction in this step AlCl_3 and HCl is removed. Reaction can be written as follows -



<https://youtu.be/fZyBY6VzAXE>