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Name Rearrangements

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What is organic reaction?

- Organic compounds can be transformed into product and the process is termed as organic reaction. It is represented by stoichiometric equation. Most organic reactions belong to one of the five main classes.
    1) Substitution Reaction
    2) Addition Reaction
    3) Elimination Reaction
    4) Rearrangement
    5) Oxidation-Reduction

What is Reaction Mechanism?

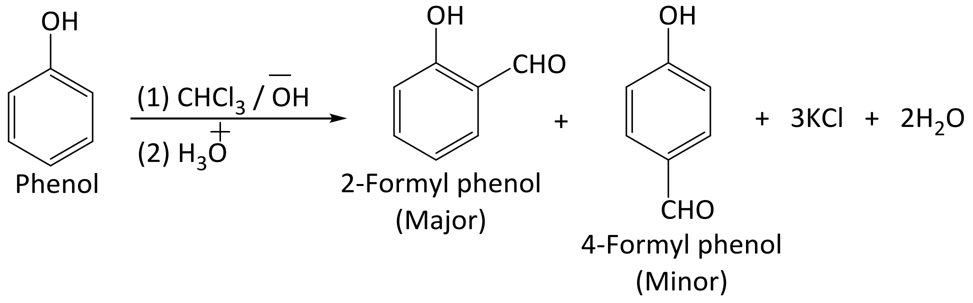
- A detailed study of the sequence of steps which are involved in the conversion of reactants into products is known as **reaction mechanism**.

Electron donating functional groups (*ortho-para* directing)	$-\ddot{N}H_2$, $-\underset{\cdot\cdot}{\ddot{O}}CH_3$, $-CH_3$, $-\underset{\cdot\cdot}{\ddot{O}}H$, $-\ddot{N}HCOCH_3$
Electron withdrawing functional groups (*meta* directing)	$-COOH$, $-COOR$, $-NO_2$, $CONH_2$, $-CN$

(1) Reimer Tiemann Reaction

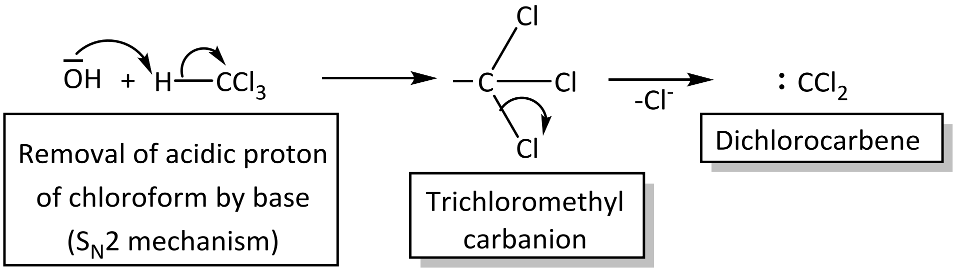
Defination: The reaction was discovered by Karl Reimer and Ferdinand Tiemann. Reaction of phenols with chloroform in presence of strong base followed by hydrolysis gives primarily 2-formyl phenols in very poor yield. This is known as Reimer Tiemann reaction.

Reaction:



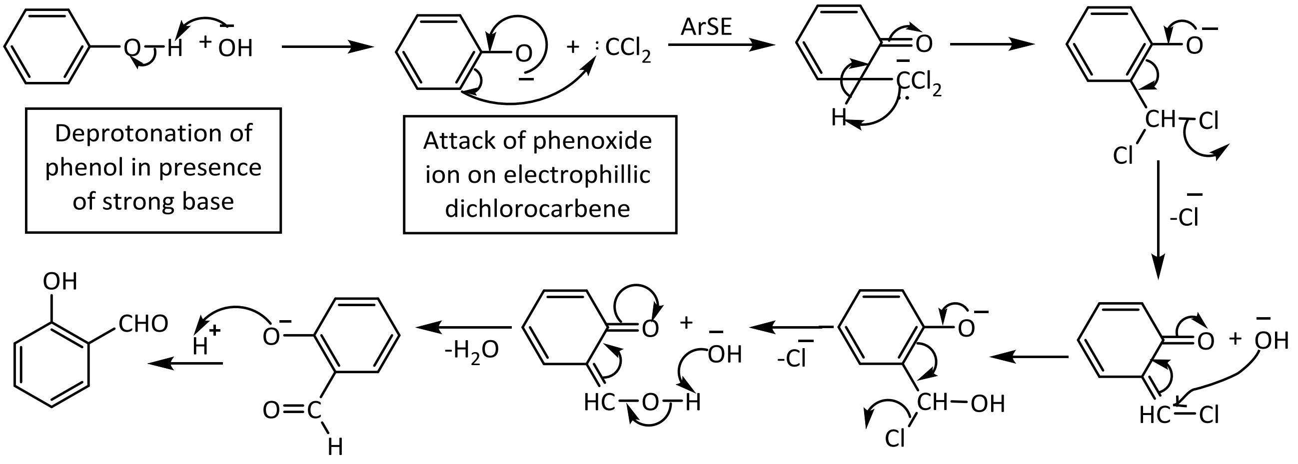
Mechanism:

Step-1: Formation of Dichlorocarbene: Due to presence of three strong electron withdrawing chlorine atoms, the hydrogen atom of chloroform is acidic. Thus, removal of proton by base would result in formation of trichloromethyl carbanion.



Step-2: Reaction of Dichlorocarbene with phenoxide ion: Reaction of phenolate ion with dichlorocarbene affords dichloromethyl derivative which undergoes a rapid hydrolysis to give the product.

The negative charge on phenoxide ion is delocalized into the aromatic ring. This increases the nucleophilicty of phenoxide ion.



Key Points

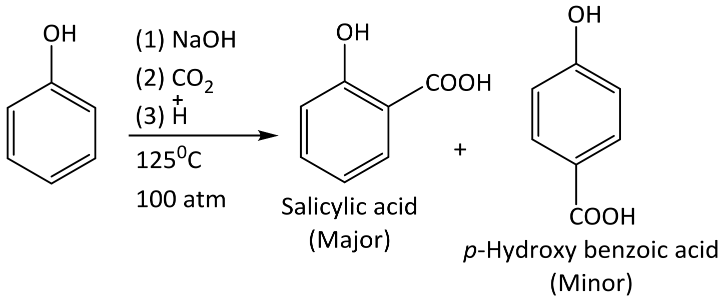
1. Reactive intermediate is dichlorocarbene (Strong Electrophile)
2. Reaction of dichlorocarbene with phenoxide ion is an example of aromatic electrophilic substitution reaction.
3. The yield of reaction is very poor.

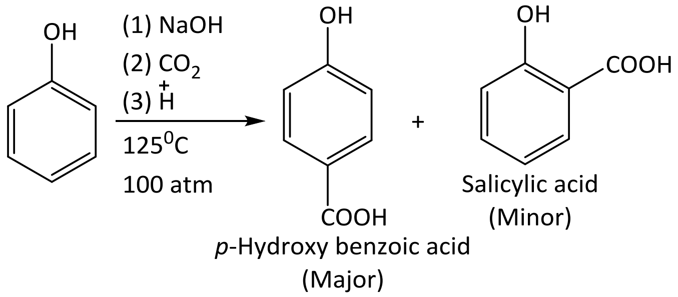
(2) Kolbe Schmitt Reaction (Carboxylation of Phenol)

Defination:

The Kolbe-Schmitt reaction is an organic reaction used to convert a phenol to a hydroxy benzoic acid using a base, carbon dioxide gas under high temperature and high pressure followed by treatment with acid. It is named after **Adolph Wilhelm Hermann Kolbe** and **Rudolf Schmitt**.

Reaction:

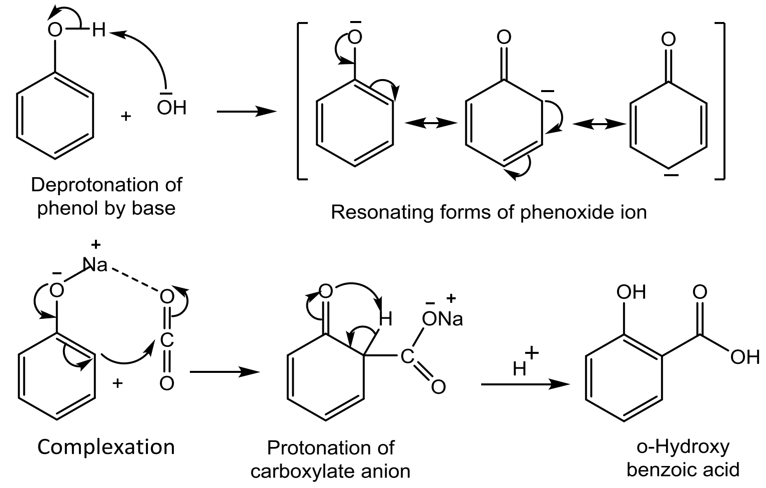


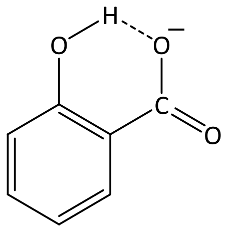


Mechanism:

Mechanism of reaction is not clearly understood, but some kind of a complex is formed between CO_2 and sodium phenoxide, making the carbon of CO_2 more electrophilic that undergoes intramolecular electrophilic aromatic substitution at elevated temperature.

Although a hydroxyl group strongly activates an aromatic ring towards electrophilic attack, phenoxide ion is even more reactive towards electrophilic attack than phenol. Electron delocalization in phenoxide ion leads to an increased electron density at the position *ortho* and *para* to oxygen. The increased nucleophilicity of the ring permits it to react even with such weak electrophiles as carbon dioxide.





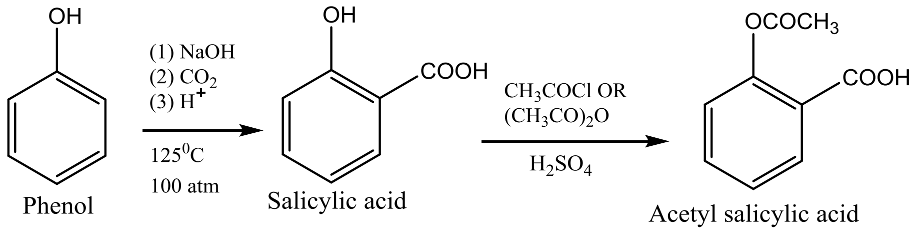
Intramolecular hydrogen bonding in salicylate anion

Key Points:

1) This reaction is used industrially to prepare salicylic acid, a precursor in making aspirin.
2) If KOH is used instead of NaOH, *para* isomer predominates.
3) Reaction is an example of aromatic electrophilic substitution reaction.
4) Reaction generates large amount of byproducts which subsequently have to be separated.
5) High reaction temperature and pressure have negative impact on environment.

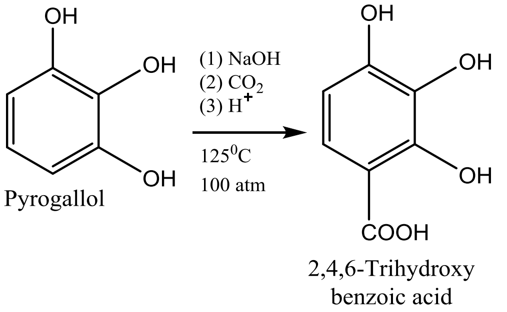
Applications:

(1)

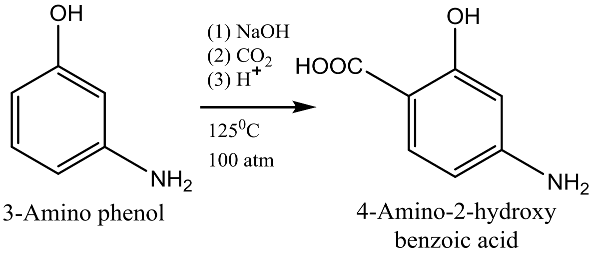


Salicylic acid is 2-hydroxybenzoic acid and is named after the willow trees (genus Salix) from which it was first isolated.

(2)



(3)



(3) Carbylamine Reaction (Hoffmann Isocyanide synthesis)

Defination:

Reaction of **1^0-amine** with chloroform in presence of alcoholic KOH/alkali to give isonitriles/ isocyanides/carbylamine is known as carbylamines reaction.

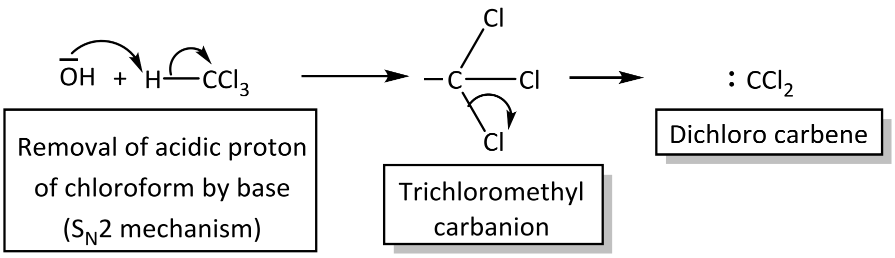
Reaction:

$$\underset{\text{Primary amine}}{R-NH_2} + CHCl_3 + 3KOH \longrightarrow \underset{\text{Isonitrile / Isocyanide / Carbylamine}}{R-\overset{+}{N}\equiv\overset{-}{C}} + 3KCl + 3H_2O$$

Mechanism:

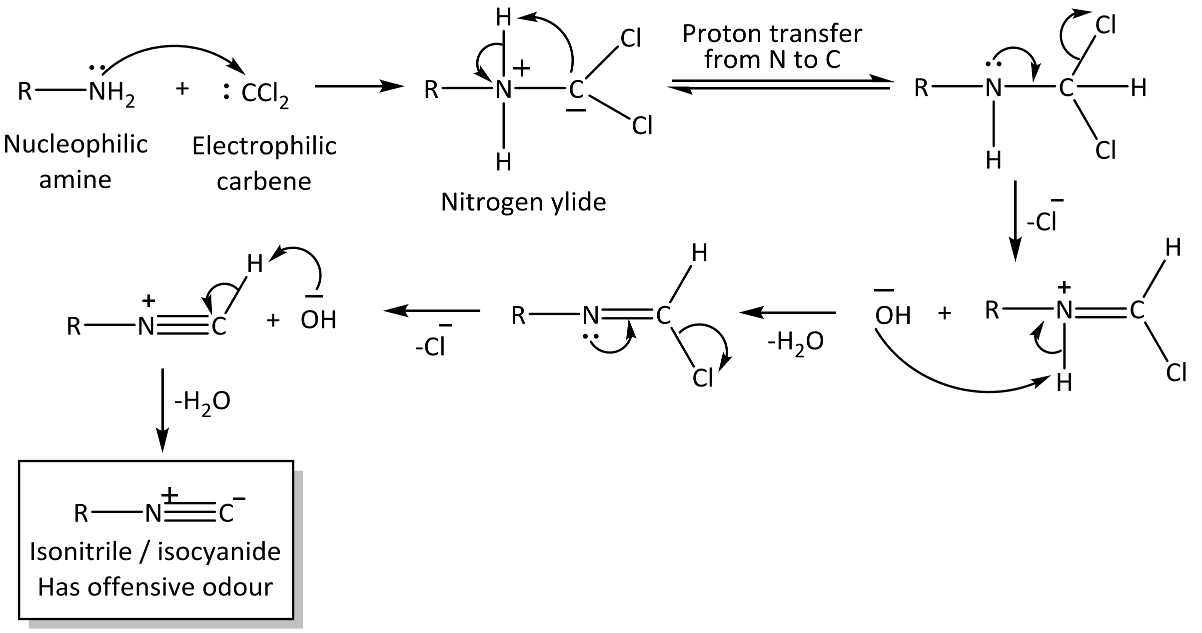
Step-1: Formation of Dichlorocarbene

Due to presence of three strong electron withdrawing chlorine atoms, the hydrogen atom of chloroform is acidic. Thus removal of proton by base would result in formation of trichloromethyl carbanion.



Step-2: Reaction of amine with dichlorocarbene

Interaction of 1^0-amine with $:CCl_2$ to produce nitrogen ylide* which subsequently eliminates two molecules of HCl to produce the carbylamine. The mechanistic scheme for this transformation may be written as follows:



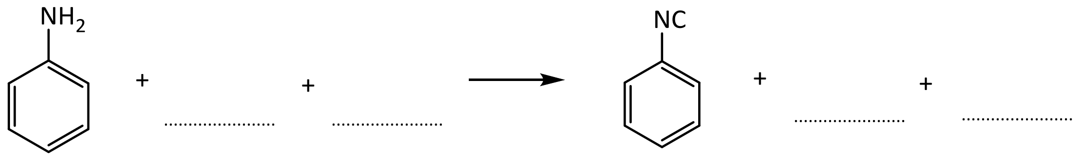
Key points

1) This reaction is also known as Hoffmann isocyanide test.
2) Only 1^0-amines give this reaction, 2^0 and 3^0-amines do not react.
3) As this reaction is not given by 2^0 and 3^0-amines, it is used as a test to distinguish 1^0-amines from 2^0 and 3^0-amines.
4) Both aromatic and aliphatic amines give this reaction.
5) Reaction intermediate is dichlorocarbene (strong electrophile).
6) Nitrogen ylide* is formed during the reaction.

(*Ylides are species having opposite charge on C and hetero atom directly linked to each other.)

Complete the following reactions

(1)



(2) $CH_3CH_2NH_2 + CHCl_3 + 3KOH \longrightarrow$ .... + ... + ...

(3) .... + $CHCl_3 + 3KOH \longrightarrow CH_3NC + 3KCl + 3H_2O$

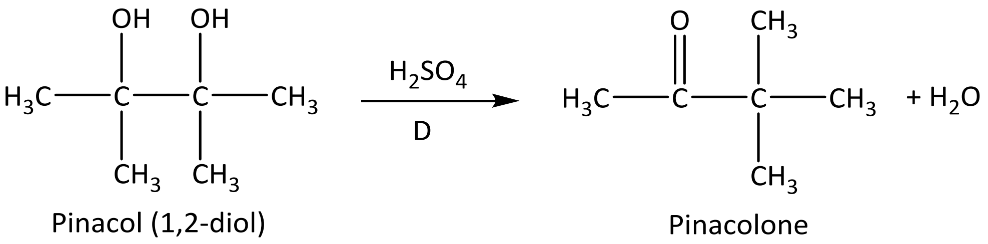
(1) Pinacole-Pinacolone Rearrangement

Defination:

The acid catalyzed rearrangement of diols (1,2-diols/vicinal diols*) to ketone or aldehyde with elimination of water is known as pinacol-pinacolone rearrangement.

The name is given from classical example of conversion of pinacol to pinacolone.

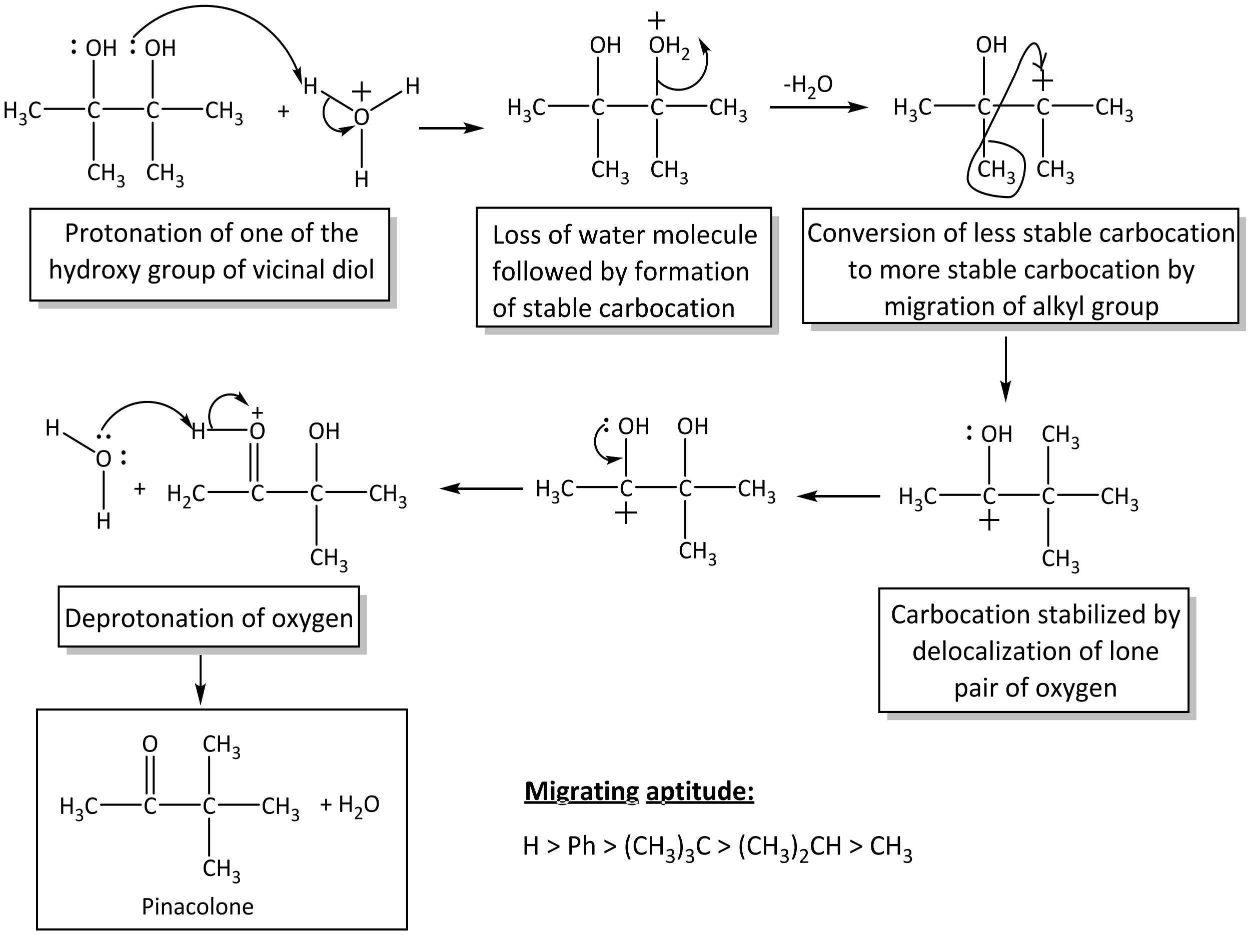
Reaction:



Pinacol (1,2-diol) Pinacolone

Mechanism:

Mechanism of this rearrangement involves the following steps.



Migrating aptitude:

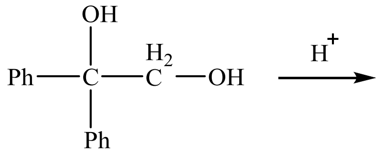
$H > Ph > (CH_3)_3C > (CH_3)_2CH > CH_3$

Key Points

1) In this mechanism protonation of one of the –OH groups occurs and a carbocation is formed.
2) If both the –OH groups are not same (i.e. in case of assymetric diol), then the one which gives a more stable carbocation participates in the reaction.
3) Subsequently, an alkyl group from the adjacent carbon migrates to the carbocation center.
4) The migration of alkyl groups in this reaction occurs in accordance with their usual migratory aptitude, i.e. hydride > Phenyl > tertiary carbocation (if formed by migration) > secondary carbocation (if formed by migration) > methyl cation.

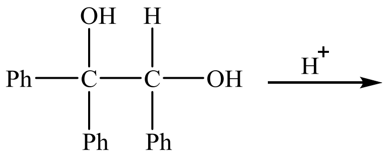
Practice problems:

(1)



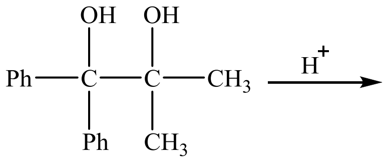
$$Ph-\overset{OH}{\underset{Ph}{C}}-\overset{H_2}{C}-OH \xrightarrow{H^+}$$

(2)



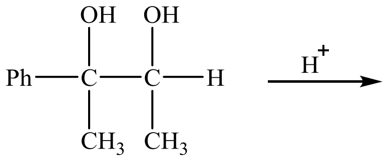
$$Ph-\overset{OH}{\underset{Ph}{C}}-\overset{H}{\underset{Ph}{C}}-OH \xrightarrow{H^+}$$

(3)



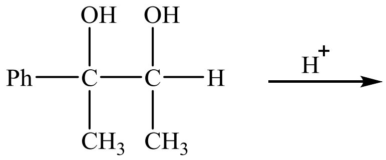
$$Ph-\overset{OH}{\underset{Ph}{C}}-\overset{OH}{\underset{CH_3}{C}}-CH_3 \xrightarrow{H^+}$$

(4)



$$Ph-\overset{OH}{\underset{CH_3}{C}}-\overset{OH}{\underset{CH_3}{C}}-H \xrightarrow{H^+}$$

(5)



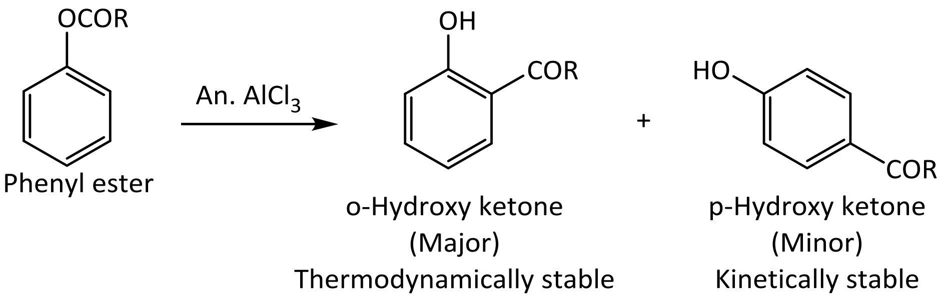
$$Ph-\overset{OH}{\underset{CH_3}{C}}-\overset{OH}{\underset{CH_3}{C}}-H \xrightarrow{H^+}$$

(2) Fries Rearrangement

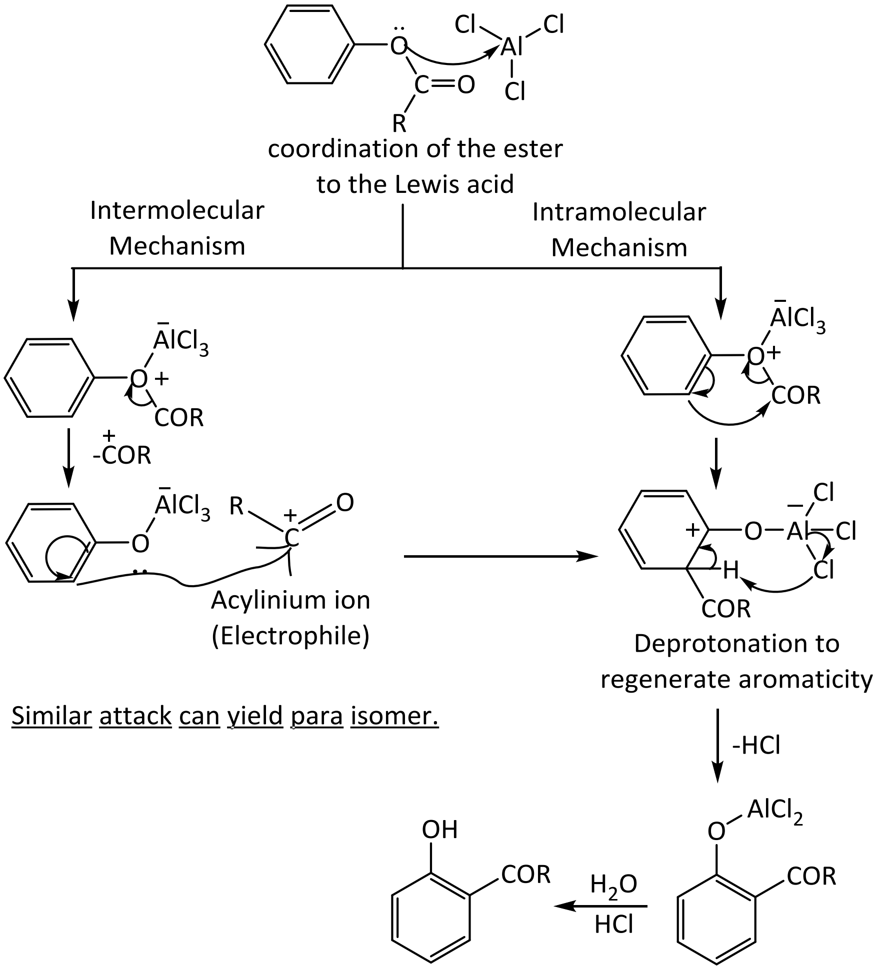
Defination:

Phenolic esters can be rearranged to *o*-hydroxy ketone (Major, thermodynamically stable) and/or *p*-hydroxy ketone (Minor, Kinetically stable) by heating with lewis acid catalyst. If the reaction is carried out at high temperature, *ortho* isomer predominates. If the *ortho* position is not vacant or reaction is carried out at low temperature, para product predominates.

Reaction:



Mechanism:



Several mechanisms have been proposed to explain the Fries Rearrangement but without any success. Sufficient evidence is available for Intermolecular and Intramolecular mechanism. Both the mechanisms are given below. Whatever might be the mechanism of Fries Rearrangement it generally gives mixture of *ortho* and *para* isomer.

Para isomer is formed more rapidly, it appears that the *ortho* isomer is more stable of the two. Greater stability of the *ortho* product may be due to the existence of intramolecular hydrogen bonding.

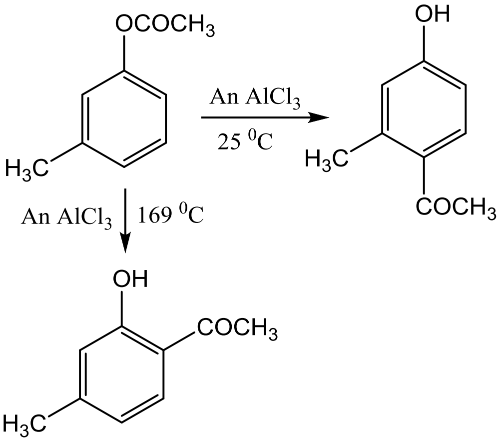
Key Points :

(1) This reaction is an example of electrophilic aromatic substitution.

(2) Higher temperature yields ortho isomer and lower temperature yield para isomer as major product. *Ortho* isomer is thermodynamically stable and para isomer is kinetically stable.

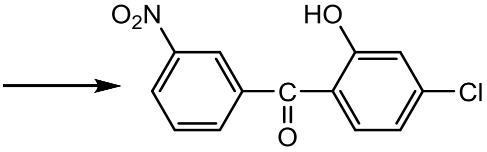
(3) Acylinium ion acts as electrophile and catalyst is lewis acid ($AlCl_3$, BF_3, $FeCl_3$ etc)

Applications:



Predict the starting material of following molecules obtained by Fries rearrangement.

(1)

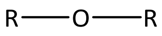


(3) Claisen Rearrangement

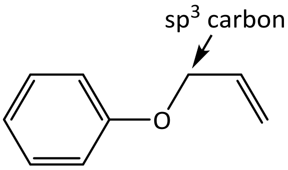
Defination:

The allyl phenyl ethers and allyl vinyl ethers on heating undergo thermal rearrangement to give 2-allyl phenol and an unsaturated carbonyl compounds respectively. This is known as Claisen rearrangement.

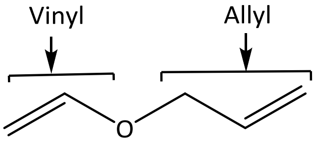
What is Allyl phenyl ether and allyl vinyl ether?



Ether



Allyl phenyl ether



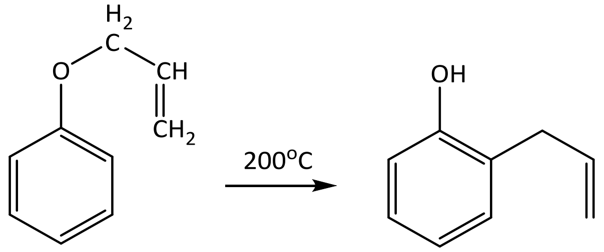
Allyl vinyl ether

Allyl: Oxygen and carbon of double bond are seperated by sp^3 carbon

Vinyl: Oxygen and carbon with double bond are directly connected

Reaction:

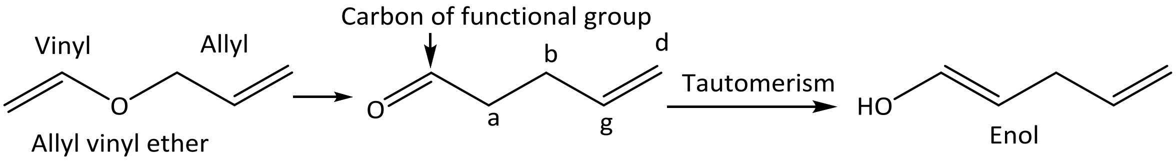
(1)



Allyl phenyl ether

2-Allyl phenol

(2)



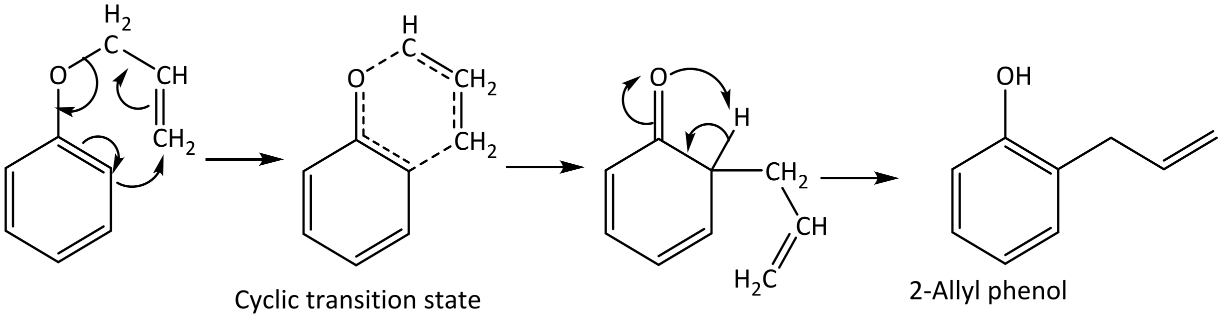
Allyl vinyl ether

γ,δ–Unsaturated carbonyl Compound

Enol

Mechanism:

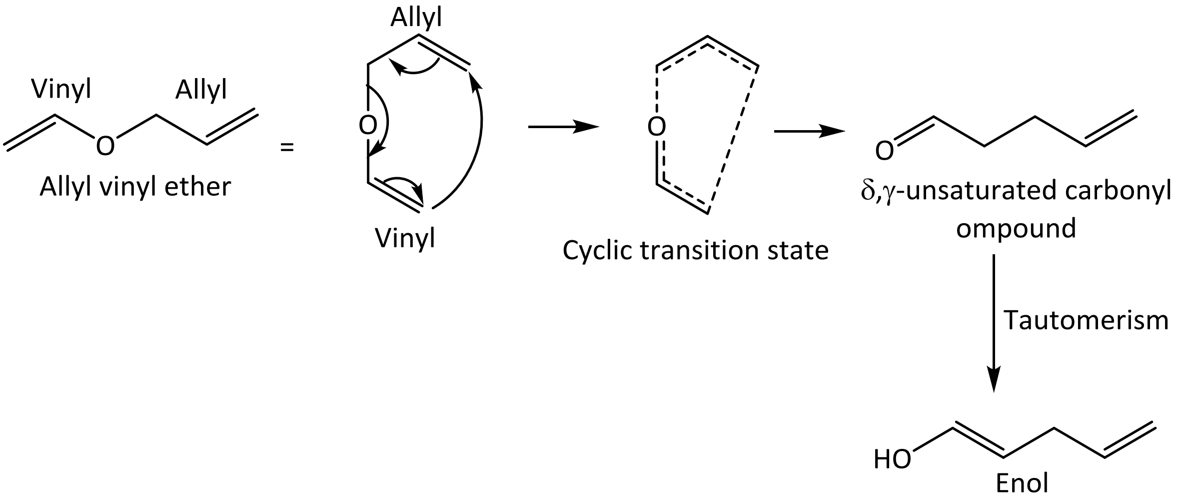
(1) Mechanism for allyl phenyl ethers



Cyclic transition state

2-Allyl phenol

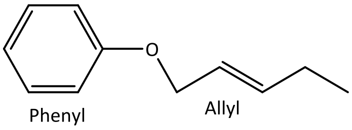
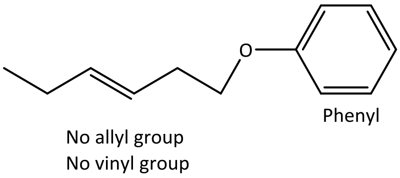
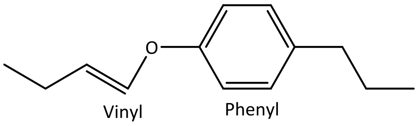
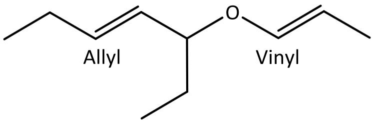
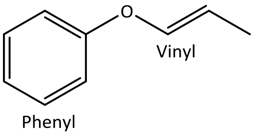
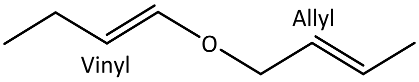
(2) Mechanism for allyl vinyl ethers



Key Points

1) This reaction belongs to a class of reactions termed as "sigmatropic rearrangement" and it is a concerted process where bonds are forming and breaking at the same time.
2) In this rearrangement allyl group gets migrated from ether oxygen atom to carbon atom of aromatic ring. The migrant allyl group goes preferentially to *ortho* position. But if both the *ortho* positions are block it goes to the *para* position. If both the *ortho* positions are block then migration to *meta* position has not been observed.
3) It follows first order kinetic and is exothermic rearrangement.
4) Its mechanism involves formation of cyclic transition state.

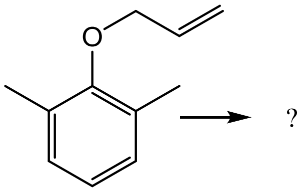
Identifying the Starting Material

Structure	YES / NO	Structure	YES / NO
			
			
			

Practice Problem

Predict the product in following reactions and draw the mechanism

(1)



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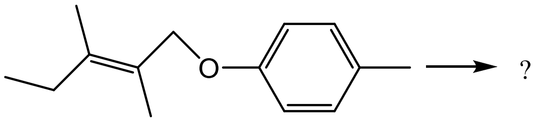

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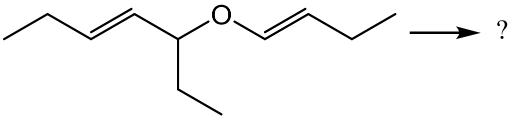

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