

# **SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES**

*Affiliated To The Tamil Nadu Dr. MGR Medical University, Chennai*

*Approved by Pharmacy Council of India, New Delhi.*

**Coimbatore -641035**

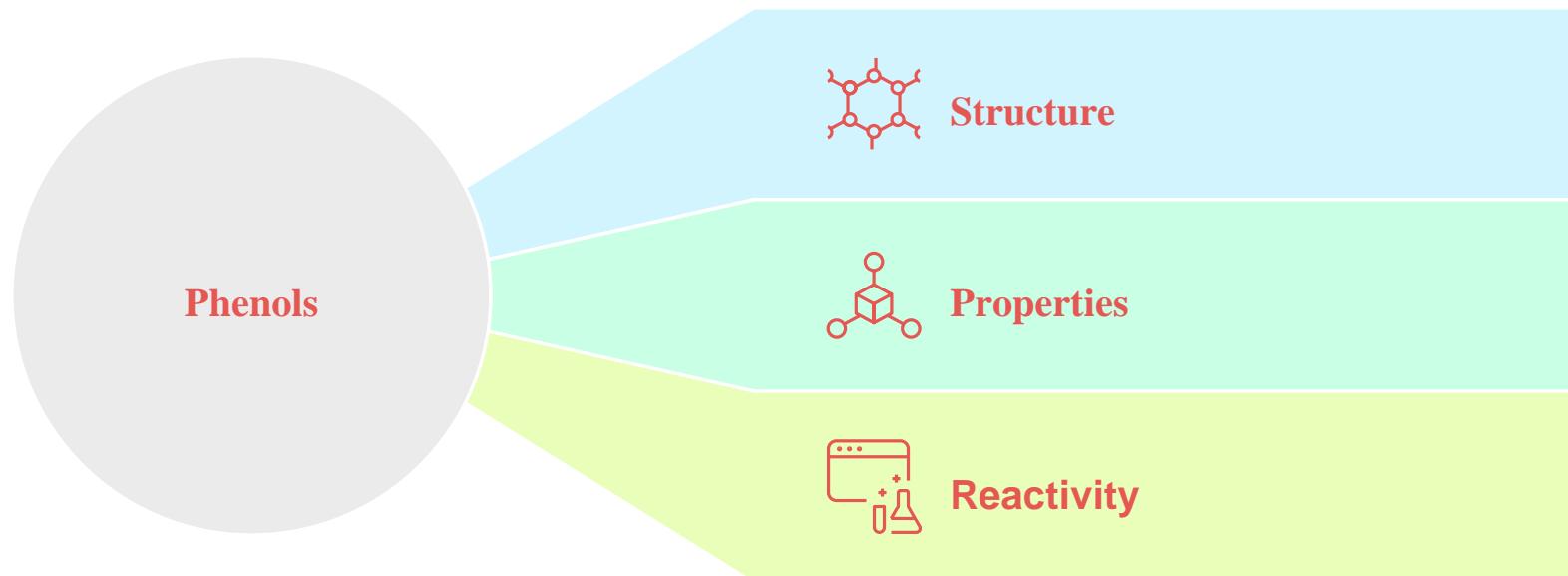


**COURSE NAME : PHARMACEUTICAL ORGANIC CHEMISTRY-II**

**III SEM / II YEAR**

**TOPIC 1 : PHENOLS -CHEMISTRY**

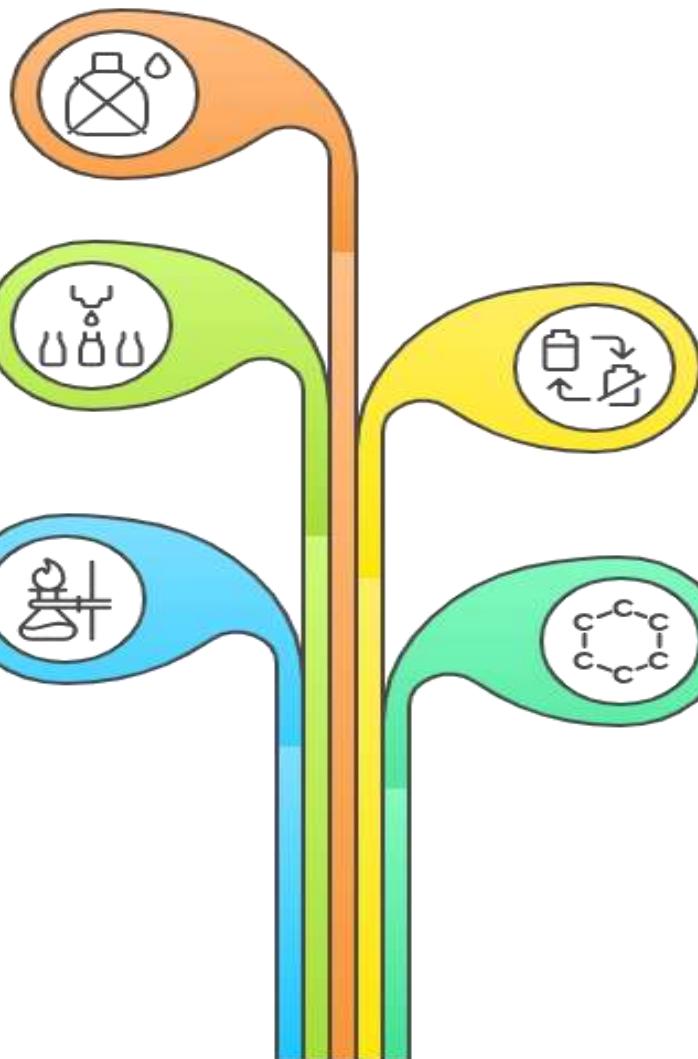
# Exploring the Dimensions of Phenols



# DOW'S PROCESS

## Phenol Purification

Phenol is purified for commercial applications.



## Cooling and Distillation

Reaction mixture is cooled and phenol is distilled.

## High-Pressure Steam and NaOH

Chlorobenzene reacts with high-pressure steam and NaOH.

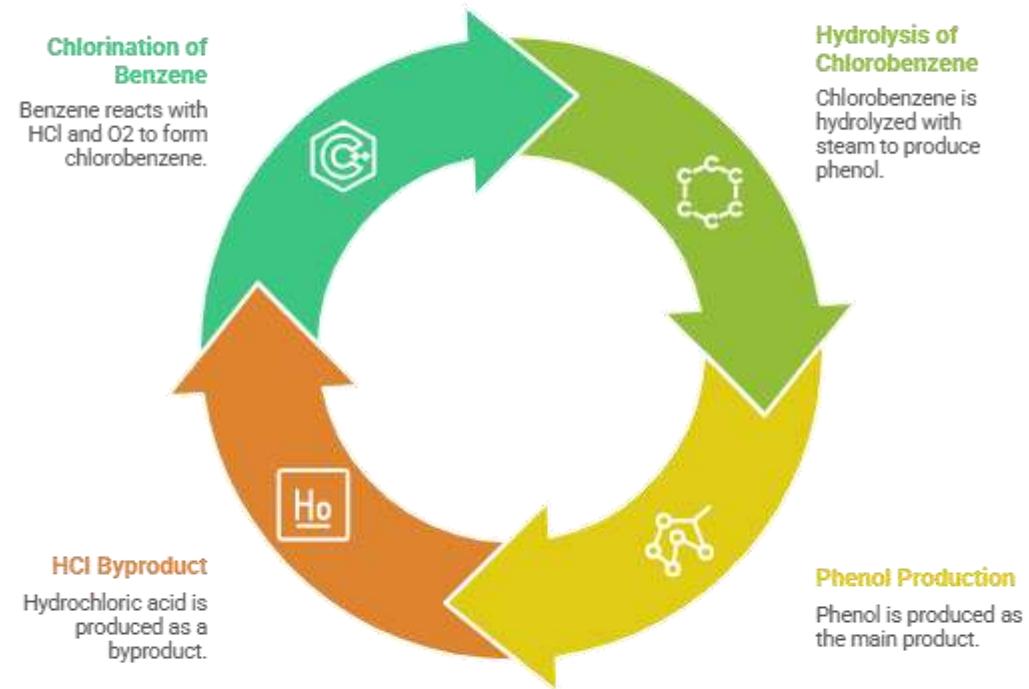
## By-Product Separation

By-products are separated from the phenol product.

## Phenol and NaCl Formation

Phenol and sodium chloride are formed in the reaction.

## Raschig-Hooker Process Cycle



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## Cumene Process Cycle

### Acetone Production

Acetone is produced as a valuable industrial chemical.

### Phenol Production

Phenol is produced as a valuable industrial chemical.



### Cumene Oxidation

Cumene is oxidized to form cumene hydroperoxide.

### Acid-Catalyzed Cleavage

Cumene hydroperoxide is cleaved into phenol and acetone.

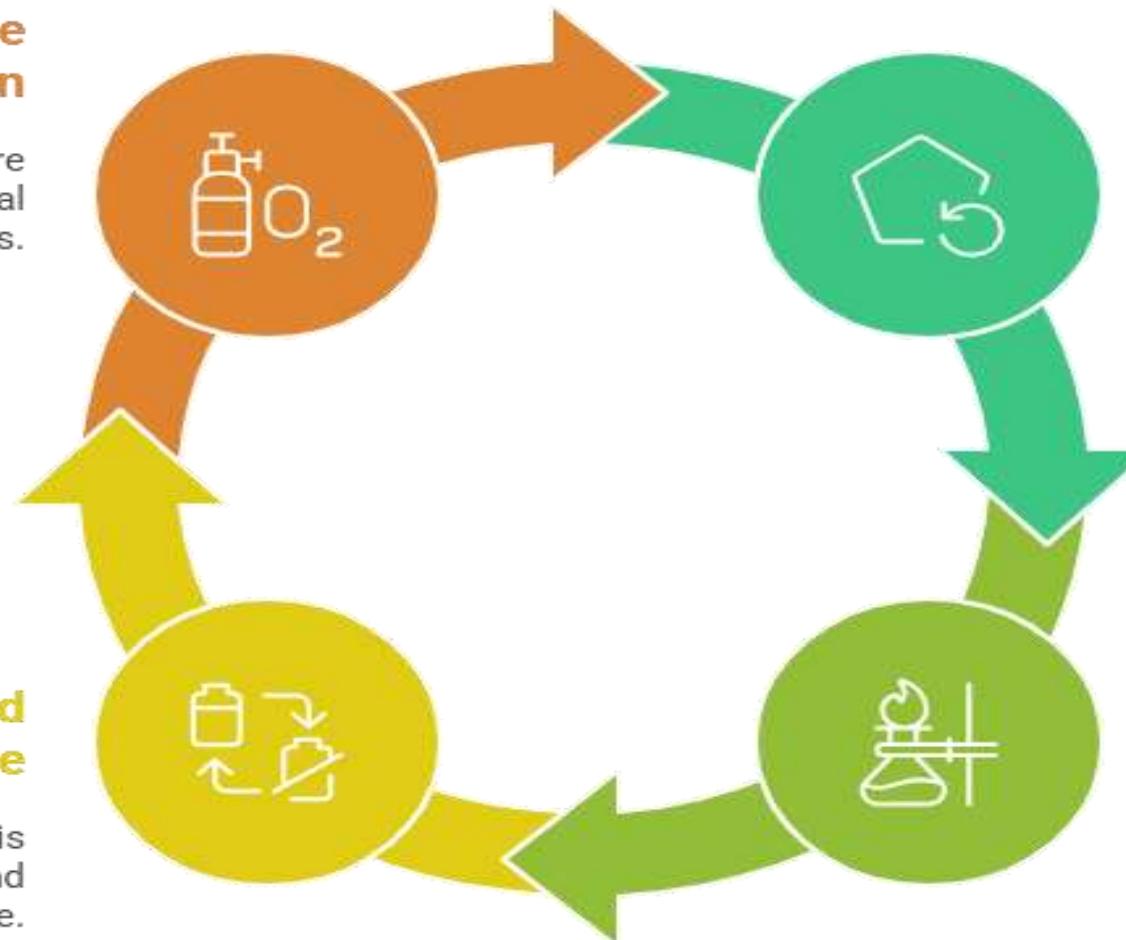
# Cumene Process Cycle

## Phenol and Acetone Production

Phenol and acetone are produced as final products.

## Acid-Catalyzed Cleavage

Cumene hydroperoxide is cleaved into phenol and acetone.



## Alkylation of Benzene

Benzene reacts with propene to form cumene.

## Oxidation of Cumene

Cumene is oxidized to form cumene hydroperoxide.

## Diazotization Process

### Aromatic Amine

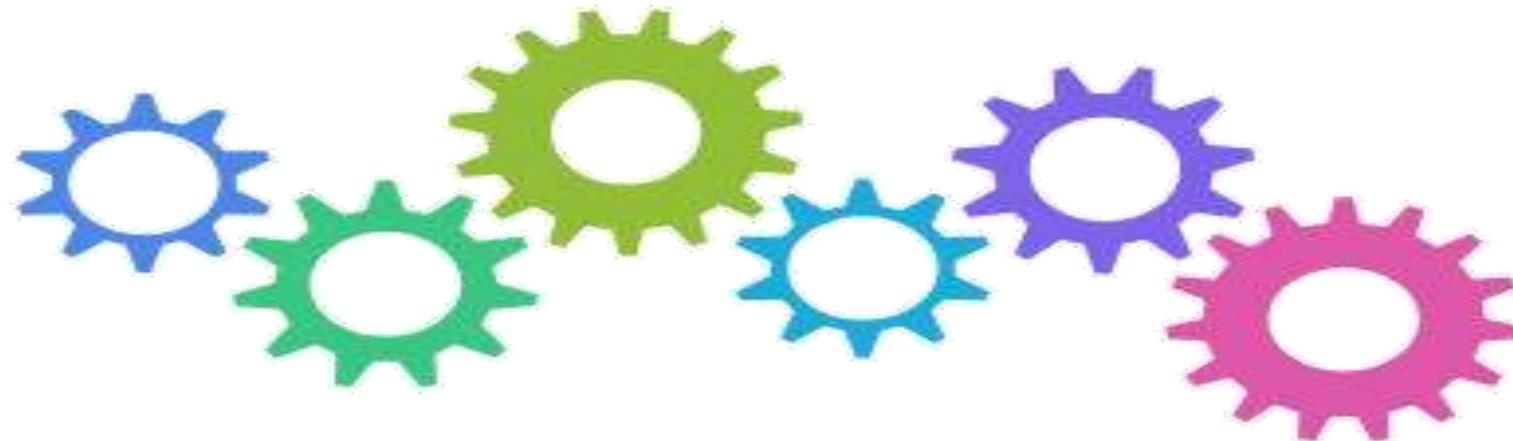
Aniline is the starting aromatic amine.

### Sodium Nitrite

$\text{NaNO}_2$  is used to produce  $\text{HNO}_2$ .

### Low Temperature

The reaction is conducted at  $0\text{--}5^\circ\text{C}$ .



### Nitrous Acid

$\text{HNO}_2$  is generated *in situ*.

### Mineral Acid

$\text{HCl}$  or  $\text{H}_2\text{SO}_4$  is used to produce  $\text{HNO}_2$ .

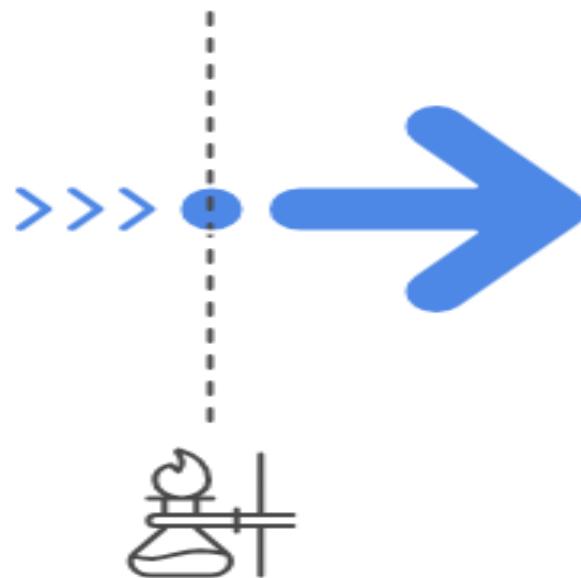
### Diazonium Salt

The final product is a diazonium salt.

# Phenol Synthesis from Diazonium Salts

## Diazotization

Aniline reacts with nitrous acid to form a diazonium salt.



## Phenol Formation

Phenol, nitrogen gas, and mineral acid are produced.



## Hydrolysis

The diazonium salt is heated with water or dilute acid.

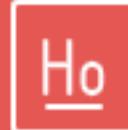
# Phenol Synthesis from Sulfonic Acids



Benzene reacts with  
oleum to form  
benzenesulfonic acid.



Benzenesulfonic acid  
is fused with NaOH at  
high temperatures.



The sulfonic acid  
group is converted to  
sodium phenoxide.



Sodium phenoxide is  
acidified to yield  
phenol.

# Grignard Reagent Reaction with Oxygen

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## Reaction with Oxygen

- Grignard reagents can react with oxygen to form a magnesium phenoxide.
- This reaction highlights the reactivity of Grignard reagents in the presence of atmospheric oxygen, leading to the formation of a stable intermediate.

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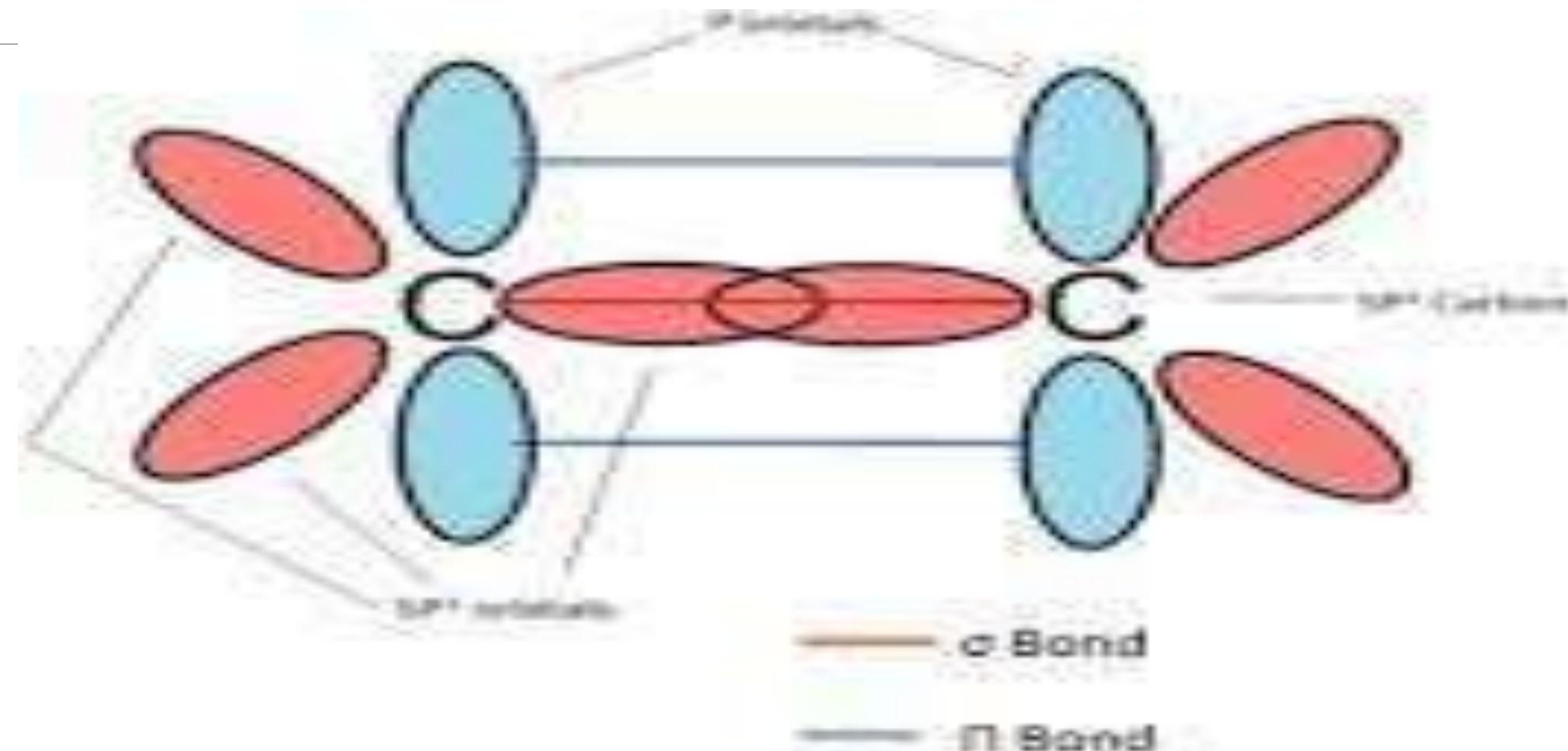
## Hydrolysis of Magnesium Phenoxide

- which can then be hydrolyzed to yield a phenol.
- The subsequent hydrolysis step is crucial as it transforms the magnesium phenoxide into a valuable phenolic compound, showcasing the versatility of Grignard reagents in organic synthesis.

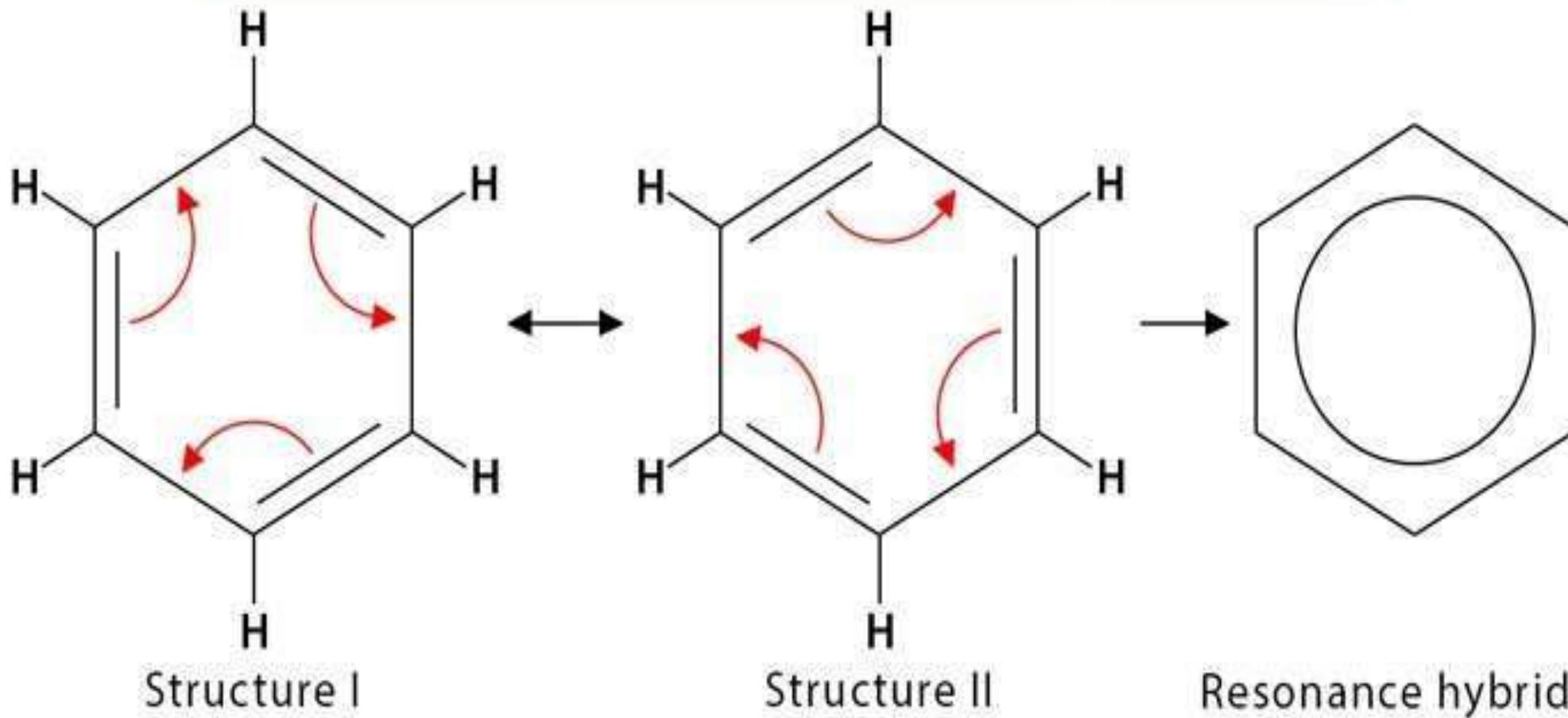
## Magnesium Phenoxide Hydrolysis

- The magnesium phenoxide that is produced undergoes hydrolysis with dilute acid
- resulting in the formation of phenol

# FORMATION OF THE $\Pi$ SYSTEM



## Delocalization of Pi Electrons in Benzene

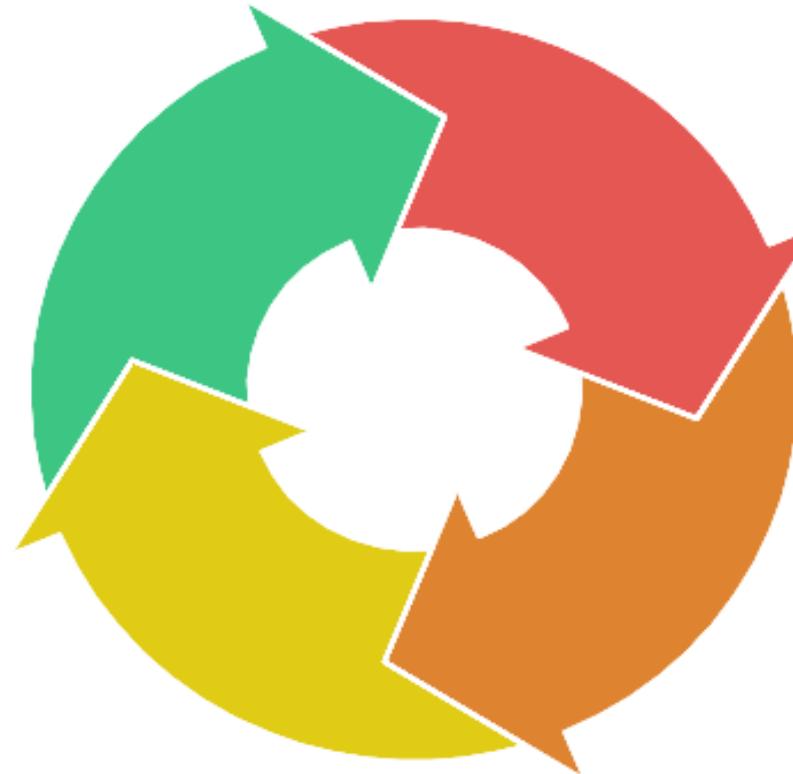


# Acidity Enhancement Cycle in Phenols

 **Acidity Increase**  
The phenol's acidity increases.



**Ion Stabilization**  
The phenoxide ion becomes more stable.



## EWG Attachment

Electron-withdrawing groups attach to the phenol ring.



## Charge Delocalization

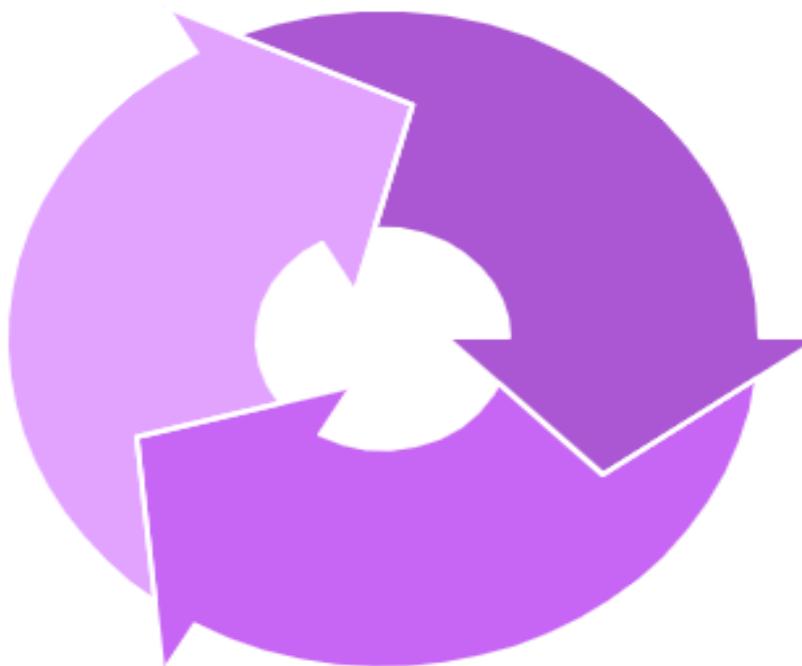
EWGs delocalize the negative charge in the phenoxide ion.

# Impact of Electron-Donating Groups on Phenol Acidity



## Acidity Decreases

Destabilization leads to lower acidity.



## EDGs Increase Electron Density

EDGs add electrons to the aromatic ring.



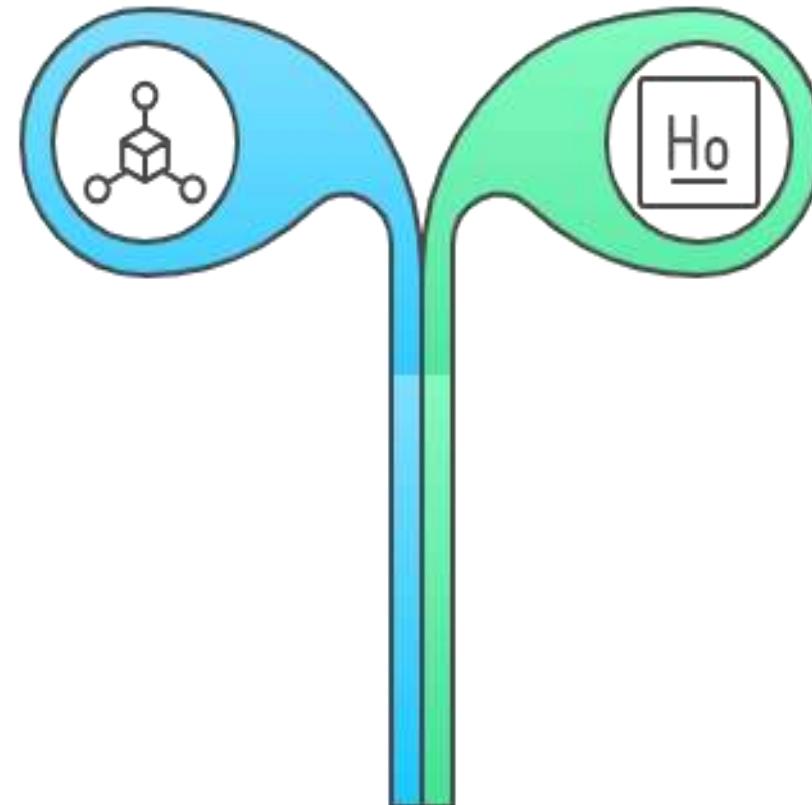
## Phenoxide Ion Destabilization

Increased electron density destabilizes the phenoxide ion.

# Unveiling the Impact of Solvent Effects on Phenol Acidity

## Polar Solvents

Polar solvents stabilize phenoxide ion, increasing acidity.

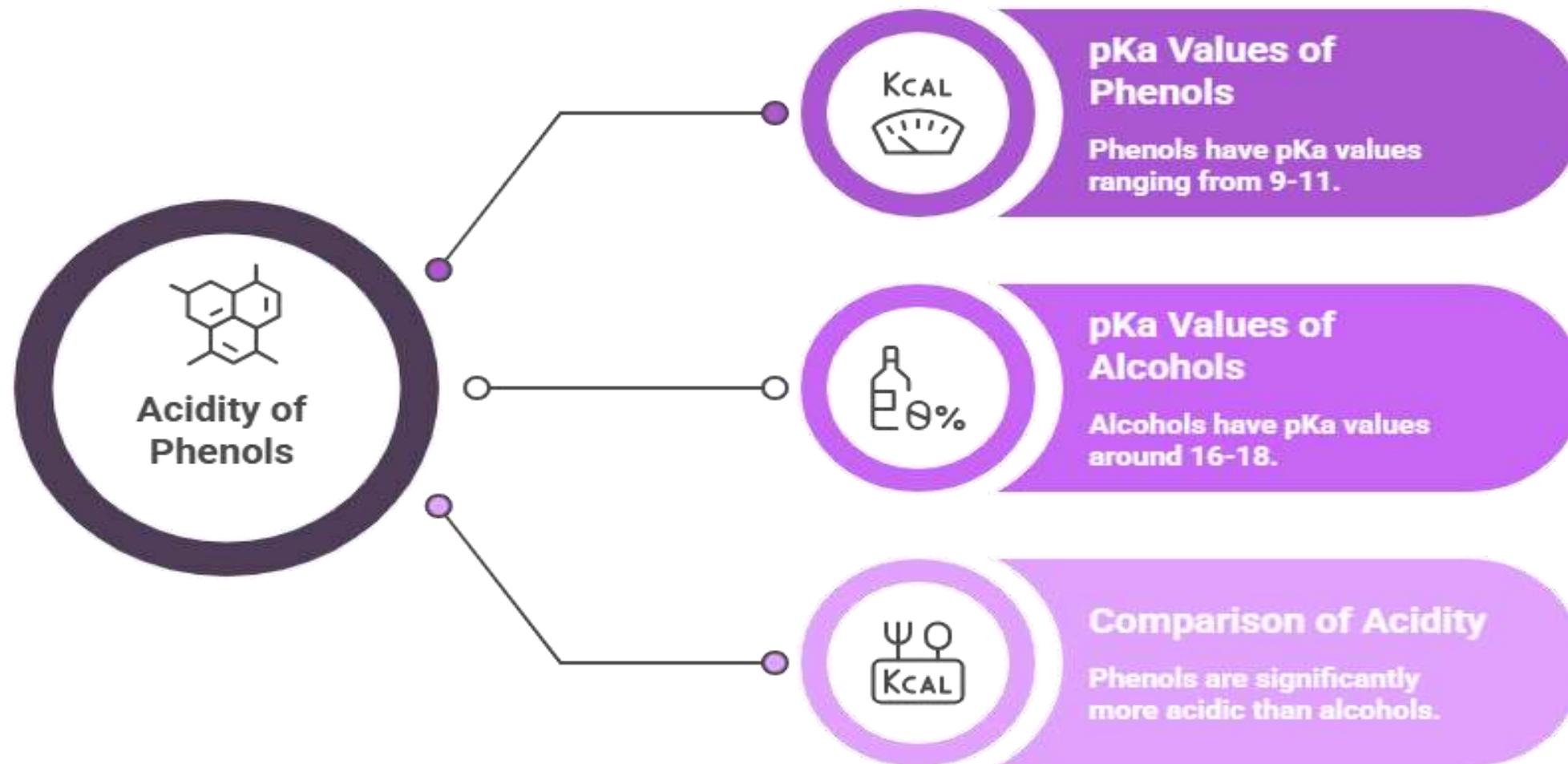


## Hydrogen Bonding

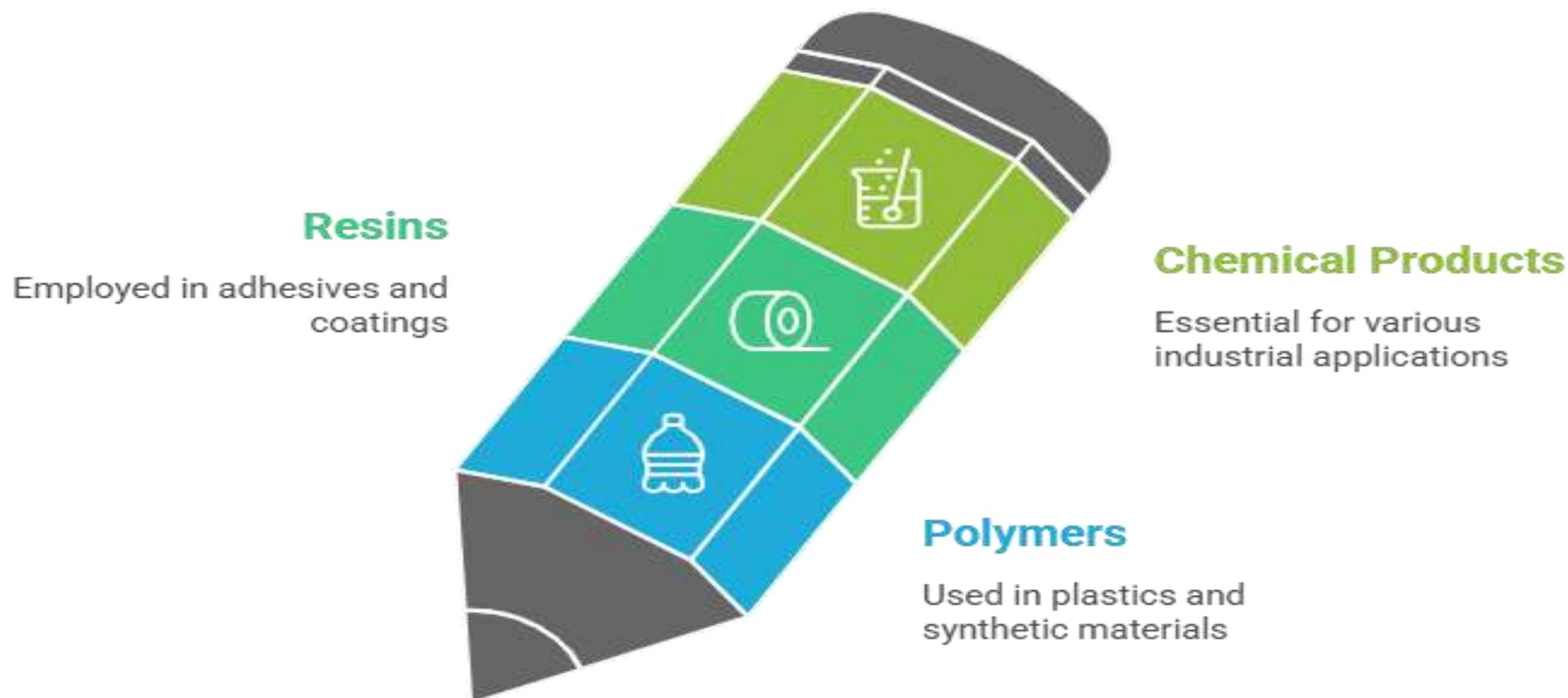
Hydrogen bonding enhances solvation, boosting phenol acidity.

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# Unveiling Phenol Acidity Through pKa Values

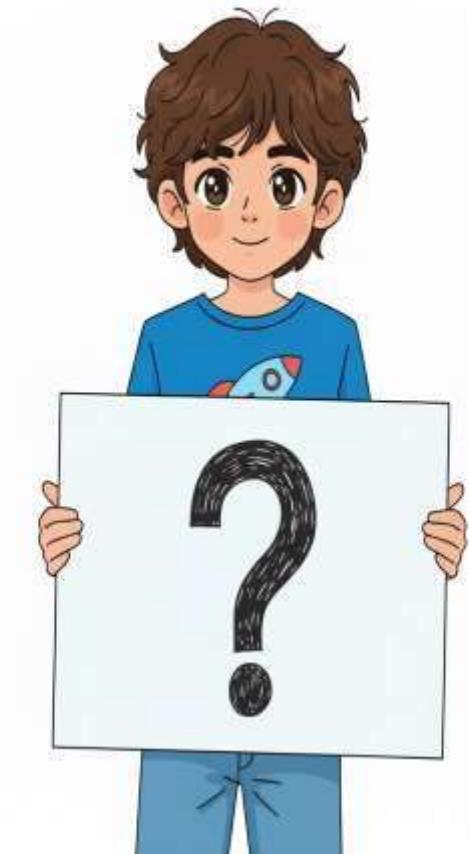
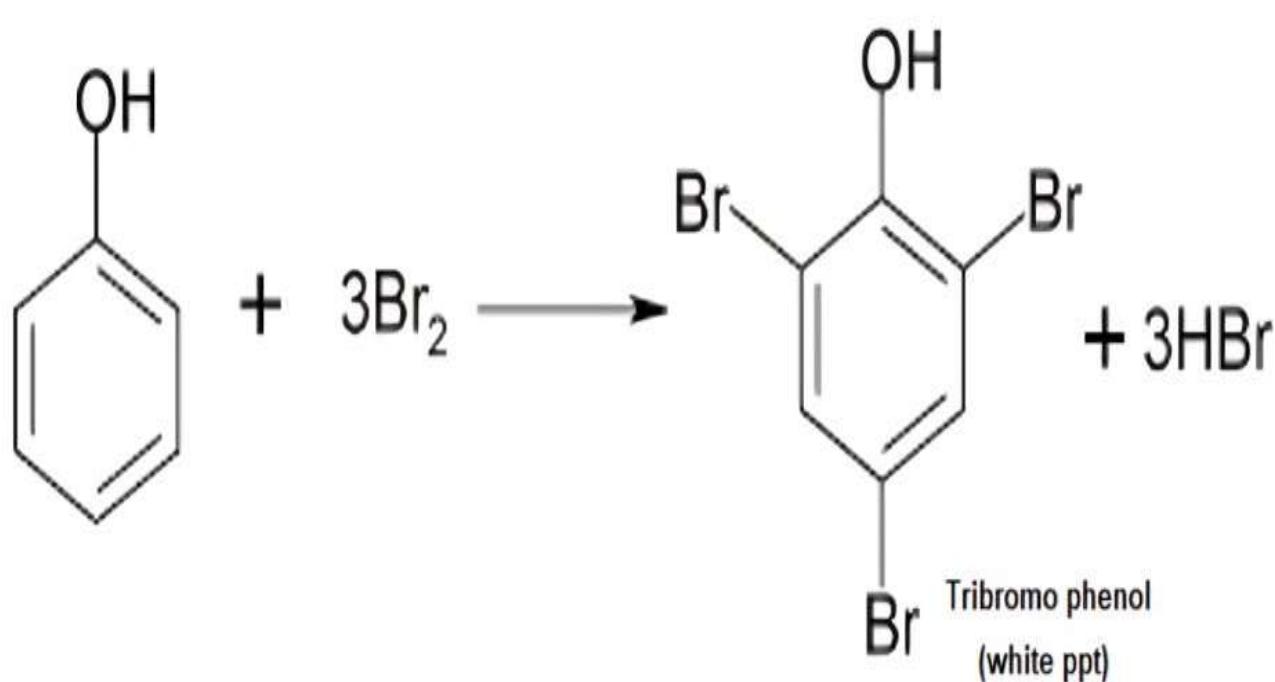


# Phenol's Industrial Significance



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## ASSESSMENTS



## Explain the molecular orbital picture of Benzene

