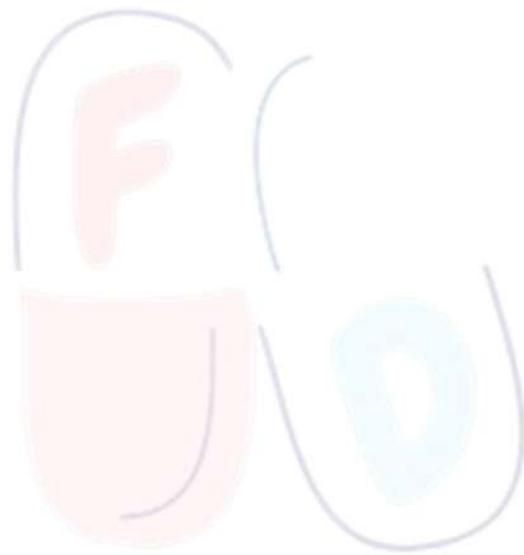


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PHARMACEUTICAL ORGANIC CHEMISTRY - II

UNIT 2

TOPIC :

- **Aromatic Acids*** - Acidity, effect of substituents on acidity and important reactions of benzoic acid.



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Aromatic Acids

- Aromatic acids are organic compounds that are derivatives of aromatic hydrocarbons in which one hydrogen atom of the aromatic ring is replaced by a carboxylic acid functional group (-COOH).
- These compounds contain both an aromatic ring and a carboxylic acid group.

General Structure:



Where Ar = Aromatic ring

Physical Properties of Benzoic Acid

- Physical State:
 - White crystalline solid
 - Colorless in pure form
- Melting Point:
 - Has a high melting point (around 122°C), due to strong intermolecular hydrogen bonding between carboxylic acid groups.
- Solubility:
 - Slightly soluble in cold water, but more soluble in hot water
 - Highly soluble in organic solvents like ethanol, ether, and benzene
- Polarity:
 - Despite containing a polar -COOH group, benzoic acid as a whole is considered non-polar due to the dominance of the aromatic ring in hydrophobic interactions.
- Odor:
 - Has a faint pleasant smell, somewhat similar to benzaldehyde
- Salt Formation:
 - Forms salts with bases like NaOH or KOH, which are used in medicine and industry (e.g., sodium benzoate as a preservative).

Methods of Preparation of Aromatic Acids

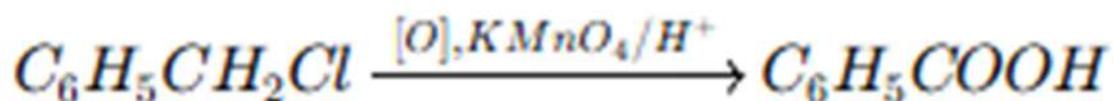
Aromatic acids like benzoic acid can be prepared using various methods:

1. Oxidation of Side Chain of Aromatic Compounds

- Aromatic acids are commonly prepared by oxidizing the side chain (especially methyl or methylene groups) of aromatic compounds.
- Oxidizing agents like acidic potassium permanganate (KMnO_4) or chromic acid (H_2CrO_4) are used.

Example:

Benzyl chloride \rightarrow Benzoic acid



Other oxidizable compounds:

- Toluene ($\text{C}_6\text{H}_5\text{CH}_3$) \rightarrow Benzoic acid
- Benzyl alcohol ($\text{C}_6\text{H}_5\text{CH}_2\text{OH}$) \rightarrow Benzoic acid

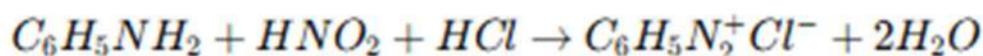
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2. From Aryl Diazonium Salts

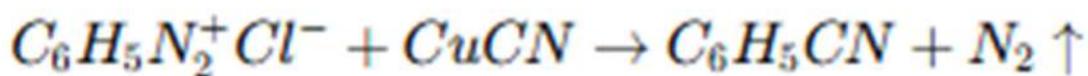
- Aryl diazonium salts can be used to synthesize benzoic acid via the Sandmeyer-type reaction followed by hydrolysis.

Steps:

Step 1: Aniline reacts with $\text{NaNO}_2 + \text{HCl}$ to form benzenediazonium chloride



Step 2: Benzenediazonium chloride reacts with CuCN to form benzonitrile



Step 3: Hydrolysis of benzonitrile gives benzoic acid



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Acidity of Aromatic Acids

- Aromatic acids are organic acids in which the $-\text{COOH}$ (carboxylic acid group) is directly attached to an aromatic ring, such as benzene.
- A common example is benzoic acid ($\text{C}_6\text{H}_5-\text{COOH}$).

Acidic Nature of Aromatic Acids

- Aromatic acids are acidic because the carboxyl group ($-\text{COOH}$) can release a proton (H^+) in aqueous solution:



- The resulting ion is called the benzoate ion.

Resonance Stabilization of Benzoate Ion

- ❖ After loss of H^+ , the negative charge on the benzoate ion ($\text{C}_6\text{H}_5\text{COO}^-$) is delocalized (shared) between the two oxygen atoms via resonance.
- ❖ This resonance stabilization increases the stability of the conjugate base, which in turn increases the acidity of benzoic acid.
- ❖ The aromatic ring also plays an inductive role (pulling electrons), which helps stabilize the negative charge on the ion further.

Effect of Substituents on Acidity of Aromatic Acids

- Substituents on the aromatic ring of aromatic acids (e.g., benzoic acid) can influence their acidity.
- These substituents affect the electron density around the carboxylic acid group ($-\text{COOH}$), altering how easily the acid donates a proton (H^+).
- Substituents are generally classified into two types:

1. Electron-Withdrawing Groups (EWGs)

e.g., $-\text{NO}_2$, $-\text{CHO}$, $-\text{CN}$, $-\text{COOH}$, $-\text{SO}_3\text{H}$, $-\text{Cl}$

- These groups pull electron density away from the aromatic ring via $-I$ (inductive) and/or $-M$ (mesomeric/resonance) effects.
- This decreases the electron density on the benzene ring and the carboxyl group.
- As a result, the negative charge on the conjugate base (benzoate ion) is better stabilized.
- Increased stability of the conjugate base = stronger acid.

Conclusion:

Electron-withdrawing groups increase the acidity of aromatic acids.

2. Electron-Releasing Groups (ERGs)

e.g., $-\text{CH}_3$, $-\text{OH}$, $-\text{NH}_2$, $-\text{OCH}_3$

- These groups donate electrons to the aromatic ring through $+I$ (inductive) or $+M$ (resonance) effects.
- This increases the electron density around the ring and the carboxyl group.
- The conjugate base becomes less stable due to the excess negative charge.
- Less stability of the conjugate base = weaker acid.

Conclusion:

Electron-releasing groups decrease the acidity of aromatic acids.

Important Reactions of Benzoic Acid

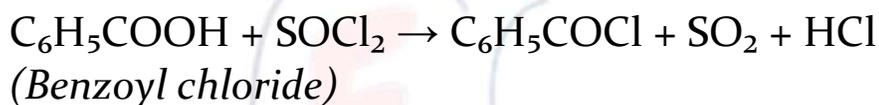
→ Benzoic acid is reactive both at the $-\text{COOH}$ group and on the aromatic ring.

I. Reactions at the $-\text{COOH}$ group

1. Formation of Acid Chloride:

1. Reagent: SOCl_2 or PCl_5

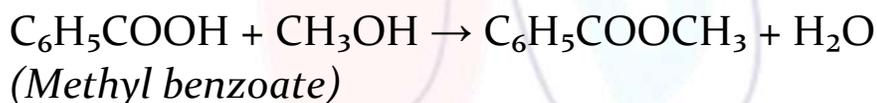
2. Reaction:



2. Esterification:

• Reagents: Alcohol + acid catalyst (H_2SO_4)

• Reaction:



II. Reactions at the Aromatic Ring

Nitration:

• Reagents: $\text{HNO}_3 + \text{H}_2\text{SO}_4$

• Reaction:



Halogenation:

• Reagent: $\text{Br}_2/\text{FeBr}_3$

• Reaction:

