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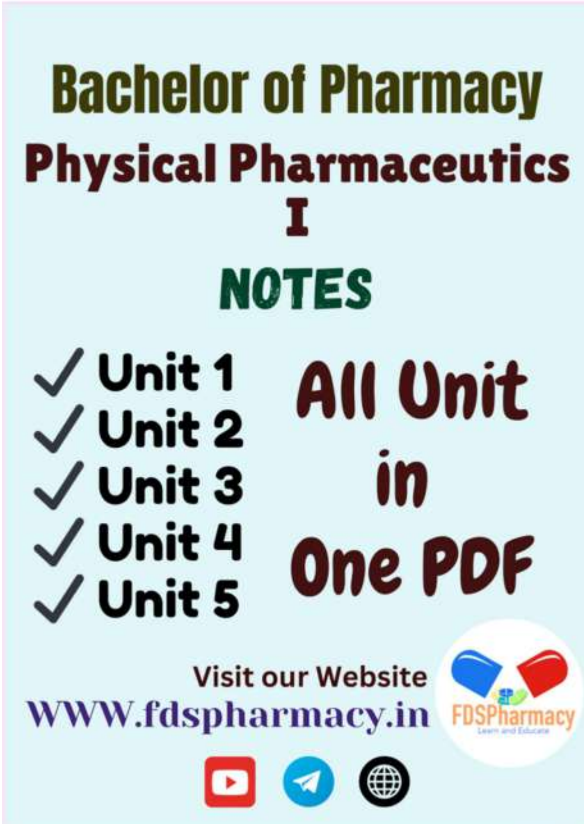
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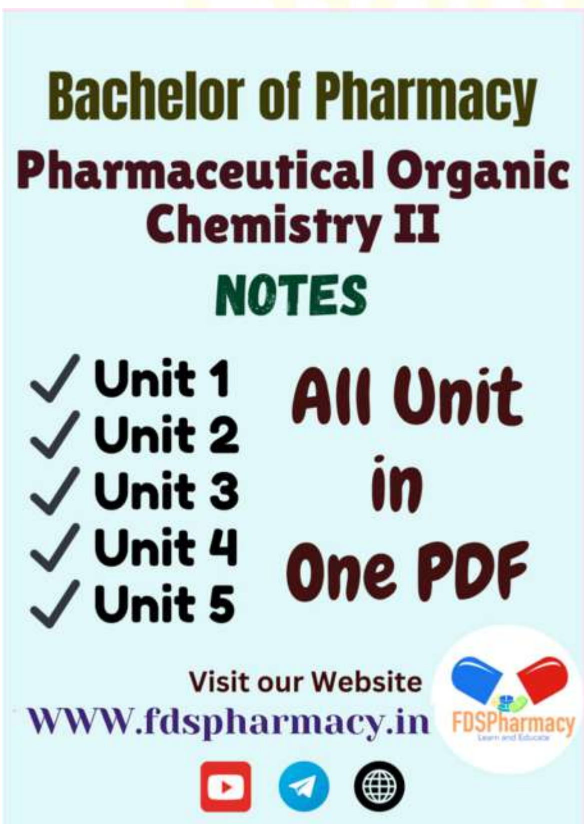
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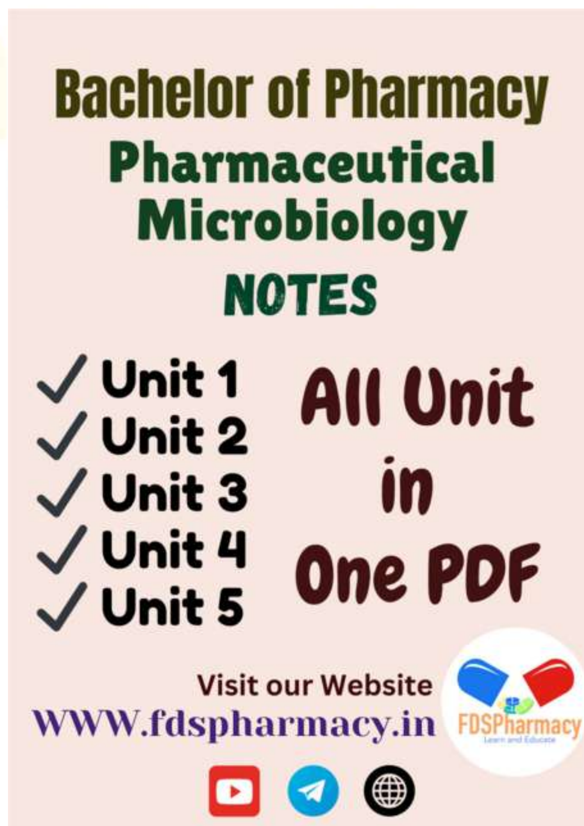
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PHARMACEUTICAL ORGANIC CHEMISTRY - II

UNIT 2

TOPIC :

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

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:

Ar–COOH

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 → Benzoic acid

$$C_6H_5CH_2Cl \xrightarrow{[O], KMnO_4/H^+} C_6H_5COOH$$

Other oxidizable compounds:

- Toluene ($C_6H_5CH_3$) → Benzoic acid
- Benzyl alcohol ($C_6H_5CH_2OH$) → Benzoic acid

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 $NaNO_2$ + HCl to form benzenediazonium chloride

$$C_6H_5NH_2 + HNO_2 + HCl \rightarrow C_6H_5N_2^+Cl^- + 2H_2O$$

Step 2: Benzenediazonium chloride reacts with CuCN to form benzonitrile

$$C_6H_5N_2^+Cl^- + CuCN \rightarrow C_6H_5CN + N_2 \uparrow$$

Step 3: Hydrolysis of benzonitrile gives benzoic acid

$$C_6H_5CN + 2H_2O \xrightarrow{H^+/Heat} C_6H_5COOH + NH_3$$

Acidity of Aromatic Acids

- Aromatic acids are organic acids in which the –COOH (carboxylic acid group) is directly attached to an aromatic ring, such as benzene.
- A common example is benzoic acid (C_6H_5–COOH).

Acidic Nature of Aromatic Acids

- Aromatic acids are acidic because the carboxyl group (–COOH) can release a proton (H^+) in aqueous solution:

$$C_6H_5COOH \rightleftharpoons C_6H_5COO^- + H^+$$

- The resulting ion is called the benzoate ion.

Resonance Stabilization of Benzoate Ion

- After loss of H^+, the negative charge on the benzoate ion ($C_6H_5COO^-$) 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 (–COOH), altering how easily the acid donates a proton (H^+).
- Substituents are generally classified into two types:

1. Electron-Withdrawing Groups (EWGs)

e.g., $–NO_2$, –CHO, –CN, –COOH, $–SO_3H$, –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., $–CH_3$, –OH, $–NH_2$, $–OCH_3$

- 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 –COOH group and on the aromatic ring.

I. Reactions at the –COOH group

1. Formation of Acid Chloride:

1. Reagent: **$SOCl_2$** or **PCl_5**
2. Reaction:
   $C_6H_5COOH + SOCl_2 \rightarrow C_6H_5COCl + SO_2 + HCl$
   (Benzoyl chloride)

2. Esterification:

- Reagents: Alcohol + acid catalyst (H_2SO_4)
- Reaction:
  $C_6H_5COOH + CH_3OH \rightarrow C_6H_5COOCH_3 + H_2O$
  (Methyl benzoate)

II. Reactions at the Aromatic Ring

Nitration:

- Reagents: $HNO_3 + H_2SO_4$
- Reaction:
  $C_6H_5COOH \rightarrow NO_2–C_6H_4–COOH$ (mainly *meta* product)

Halogenation:

- Reagent: $Br_2/FeBr_3$
- Reaction:
  $C_6H_5COOH \rightarrow Br–C_6H_4–COOH$ (meta-bromobenzoic acid)