UNIT – 5 📚 CARBOXYLIC ACIDS AND ALIPHATIC AMINES

POINTS TO BE COVERED IN THIS TOPIC 📋

- ➤ CARBOXYLIC ACIDS
- ➤ ACIDITY OF CARBOXYLIC ACIDS
- ➤ EFFECT OF SUBSTITUENTS ON ACIDITY
- ➤ INDUCTIVE EFFECT
- ➤ QUALITATIVE TESTS
- ➤ STRUCTURE AND USES OF IMPORTANT CARBOXYLIC ACIDS
- ➤ ALIPHATIC AMINES
- ➤ BASICITY OF ALIPHATIC AMINES

🧪 CARBOXYLIC ACIDS

Carboxylic acids are organic compounds containing the carboxyl functional group (-COOH). These compounds are characterized by their acidic properties and are widely used in pharmaceutical applications. The carboxyl group consists of a carbonyl group (C=O) attached to a hydroxyl group (-OH), making these compounds capable of donating protons (H+) in aqueous solutions.

🔬 ACIDITY OF CARBOXYLIC ACIDS

Carboxylic acids exhibit acidic behavior due to the presence of the carboxyl group. The acidity arises from the ability of these compounds to donate a proton (H+) from the hydroxyl group attached to the carbonyl carbon. The resulting carboxylate anion is stabilized through resonance, which makes the compound acidic.

Mechanism of Acidity:

- The hydrogen atom of the hydroxyl group is released as H+
- The remaining carboxylate ion (RCOO-) is stabilized by resonance
- The negative charge is delocalized between the two oxygen atoms
- This delocalization makes the conjugate base more stable
- Greater stability of the conjugate base increases the acidity

Factors Affecting Acidity:

- **Resonance stabilization** of the carboxylate anion
- **Inductive effects** of substituent groups
- **Hybridization** of the carbon atom
- **Solvation effects** in different solvents

⚡ EFFECT OF SUBSTITUENTS ON ACIDITY

The presence of different substituent groups attached to the carboxylic acid molecule significantly affects its acidic strength. These effects can be categorized based on the nature of the substituent groups.

Electron-Withdrawing Groups (EWG):

- **Increase acidity** by stabilizing the carboxylate anion

- Examples include halogens (F, Cl, Br, I), nitro groups ($-NO_2$), cyano groups (-CN)
- The closer the electron-withdrawing group to the carboxyl group, the stronger the effect
- Multiple electron-withdrawing groups have cumulative effects

Electron-Donating Groups (EDG):

- **Decrease acidity** by destabilizing the carboxylate anion
- Examples include alkyl groups ($-CH_3$, $-C_2H_5$), amino groups ($-NH_2$)
- These groups increase electron density, making proton removal more difficult
- The effect decreases with increasing distance from the carboxyl group

Substituent Type	Effect on Acidity	Examples	Mechanism
Electron-Withdrawing	Increases acidity	-F, -Cl, $-NO_2$, -CN	Stabilizes carboxylate anion
Electron-Donating	Decreases acidity	$-CH_3$, $-NH_2$, -OH	Destabilizes carboxylate anion
Aromatic Ring	Moderate effect	Phenyl group	Resonance and inductive effects

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🔄 INDUCTIVE EFFECT

The **inductive effect** is the permanent displacement of electrons along a sigma bond due to the electronegativity difference between atoms. In carboxylic acids, this effect plays a crucial role in determining acidity.

Types of Inductive Effects:

1. Negative Inductive Effect (-I Effect):

- Occurs when an atom or group withdraws electrons
- **Increases acidity** of carboxylic acids
- Groups showing -I effect: halogens, $-NO_2$, -CN, $-SO_3H$
- The effect decreases with increasing distance from the carboxyl group

2. Positive Inductive Effect (+I Effect):

- Occurs when an atom or group releases electrons
- **Decreases acidity** of carboxylic acids
- Groups showing +I effect: alkyl groups ($-CH_3$, $-C_2H_5$, $-C_3H_7$)
- Alkyl groups stabilize the neutral acid more than the carboxylate anion

Distance Effect:

- The inductive effect decreases rapidly with distance
- α-substituents have the strongest effect
- β-substituents have moderate effect
- γ-substituents and beyond have minimal effect

🧪 QUALITATIVE TESTS FOR CARBOXYLIC ACIDS

Several qualitative tests can identify the presence of carboxylic acids, amides, and esters. These tests are based on the characteristic chemical properties of these functional groups.

Tests for Carboxylic Acids:

1. Litmus Test:

- Carboxylic acids turn blue litmus paper red
- Indicates acidic nature of the compound
- Simple and quick preliminary test

2. Sodium Bicarbonate Test:

- Carboxylic acids react with $NaHCO_3$ to produce CO_2 gas
- Effervescence indicates presence of carboxylic acid
- Reaction: $RCOOH + NaHCO_3 \rightarrow RCOONa + H_2O + CO_2\uparrow$

3. Ester Test (Esterification):

- Carboxylic acid + alcohol + conc. H_2SO_4 → fruity smell
- Formation of ester produces characteristic odor
- Confirms presence of carboxylic acid group

Tests for Amides:

1. Hydrolysis Test:

- Amides undergo hydrolysis in acidic/basic conditions
- Produces carboxylic acid and amine
- NH_3 gas evolution indicates amide presence

2. Biuret Test:

- Specific for compounds with -CONH- linkage
- Purple color formation in alkaline copper sulfate solution

Tests for Esters:

1. Hydrolysis Test:

- Esters undergo saponification with NaOH
- Produces carboxylate salt and alcohol
- Sweet odor disappears upon hydrolysis

2. Hydroxamic Acid Test:

- Esters react with hydroxylamine to form hydroxamic acids
- Red color with ferric chloride confirms ester presence

💊 STRUCTURE AND USES OF IMPORTANT CARBOXYLIC ACIDS

🍋 ACETIC ACID

- **Molecular Formula:** CH_3COOH
- **Molecular Weight:** 60.05
- **Structure:** Simple aliphatic monocarboxylic acid

Properties:

- Colorless liquid with pungent odor

- Miscible with water and alcohol
- Weak acid (pKa = 4.76)
- Corrosive nature

Uses:

- Used as pharmaceutical solvent and preservative
- Important intermediate in drug synthesis
- Used in preparation of acetate salts
- Antiseptic and antimicrobial applications

LACTIC ACID

- **Molecular Formula:** $C_3H_6O_3$
- **Molecular Weight:** 90.08
- **Structure:** 2-hydroxypropanoic acid with chiral center

Properties:

- White crystalline solid or syrupy liquid
- Two enantiomers: L(+) and D(-) lactic acid
- Hygroscopic and water-soluble
- Mild acidic taste

Uses:

- Used in pharmaceutical formulations as pH adjuster
- Important in metabolic processes
- Used in preparation of lactate salts

- Antimicrobial and preservative applications
- Treatment of vaginal infections

🍇 TARTARIC ACID

- **Molecular Formula:** $C_4H_6O_6$
- **Molecular Weight:** 150.09
- **Structure:** Dihydroxybutanedioic acid with two chiral centers

Properties:

- White crystalline powder
- Four stereoisomers possible
- Highly water-soluble
- Strong complexing agent

Uses:

- Used as antioxidant in pharmaceutical formulations
- Chelating agent for metal ions
- Used in effervescent tablets and powders
- Important in analytical chemistry
- Food additive and preservative

🍊 CITRIC ACID

- **Molecular Formula:** $C_6H_8O_7$
- **Molecular Weight:** 192.12
- **Structure:** Tricarboxylic acid with hydroxyl group

Properties:

- White crystalline powder
- Highly water-soluble
- Triprotic acid
- Natural preservative properties

Uses:

- Used as preservative and antioxidant
- pH adjuster in pharmaceutical formulations
- Chelating agent for metal ions
- Used in effervescent formulations
- Important intermediate in cellular metabolism

⚡ SUCCINIC ACID

- **Molecular Formula:** $C_4H_6O_4$
- **Molecular Weight:** 118.09
- **Structure:** Butanedioic acid (dicarboxylic acid)

Properties:

- White crystalline solid
- Moderately water-soluble
- Diprotic acid
- Important metabolic intermediate

Uses:

- Used in pharmaceutical synthesis
- Intermediate in Krebs cycle
- Used as pH buffer
- Important in drug metabolism studies

☠️ OXALIC ACID

- **Molecular Formula:** $C_2H_2O_4$
- **Molecular Weight:** 90.03
- **Structure:** Ethanedioic acid (simplest dicarboxylic acid)

Properties:

- White crystalline solid
- Highly water-soluble
- Strong reducing agent
- Toxic in large quantities

Uses:

- Used as analytical reagent
- Reducing agent in chemical analysis
- Used in pharmaceutical synthesis
- Metal cleaning and rust removal

🌿 SALICYLIC ACID

- **Molecular Formula:** $C_7H_6O_3$
- **Molecular Weight:** 138.12
- **Structure:** 2-hydroxybenzoic acid

Properties:

- White crystalline powder
- Phenolic and carboxylic acid properties
- Anti-inflammatory properties
- Keratolytic action

Uses:

- Used as antiseptic and disinfectant
- Treatment of skin conditions
- Anti-inflammatory applications
- Precursor for aspirin synthesis
- Used in topical preparations

🧴 BENZOIC ACID

- **Molecular Formula:** $C_7H_6O_2$
- **Molecular Weight:** 122.12
- **Structure:** Simplest aromatic carboxylic acid

Properties:

- White crystalline solid
- Slightly water-soluble
- Antimicrobial properties
- Pleasant aromatic odor

Uses:

- Used as preservative in pharmaceutical formulations
- Antimicrobial and antifungal applications
- Used in topical preparations
- Important synthetic intermediate
- Food preservative

🌸 BENZYL BENZOATE

- **Molecular Formula:** $C_{14}H_{12}O_2$
- **Molecular Weight:** 212.25
- **Structure:** Ester of benzoic acid and benzyl alcohol

Properties:

- Colorless oily liquid
- Pleasant aromatic odor
- Water-insoluble but alcohol-soluble
- Non-volatile nature

Uses:

- Used as scabicide and pediculicide

- Treatment of parasitic skin infections
- Used as solvent in pharmaceutical preparations
- Topical antiseptic applications
- Treatment of lice and mites

🧪 DIMETHYL PHTHALATE

- **Molecular Formula:** $C_{10}H_{10}O_4$
- **Molecular Weight:** 194.18
- **Structure:** Diester of phthalic acid

Properties:

- Colorless oily liquid
- Low volatility
- Good solvent properties
- Plasticizer characteristics

Uses:

- Used as plasticizer in pharmaceutical coatings
- Solvent in topical preparations
- Used in sustained-release formulations
- Industrial applications as plasticizer

❄️ METHYL SALICYLATE

- **Molecular Formula:** $C_8H_8O_3$
- **Molecular Weight:** 152.15

- **Structure:** Ester of salicylic acid and methanol

Properties:

- Colorless liquid with wintergreen odor
- Slightly water-soluble
- Volatile nature
- Pleasant aromatic smell

Uses:

- Used as topical analgesic and anti-inflammatory
- Treatment of muscle and joint pain
- Used as flavoring agent
- Rubefacient and counterirritant applications
- Sports medicine applications

ACETYLSALICYLIC ACID (ASPIRIN)

- **Molecular Formula:** $C_9H_8O_4$
- **Molecular Weight:** 180.16
- **Structure:** Acetyl ester of salicylic acid

Properties:

- White crystalline powder
- Slightly water-soluble
- Hydrolyzed to salicylic acid in body
- Antiplatelet properties

Uses:

- Used as analgesic, antipyretic, and anti-inflammatory
- Cardiovascular protection (antiplatelet therapy)
- Prevention of stroke and heart attacks
- Treatment of rheumatic conditions
- Most widely used pharmaceutical compound

🔗 ALIPHATIC AMINES

Aliphatic amines are organic compounds derived from ammonia (NH_3) by replacement of one or more hydrogen atoms with alkyl groups. These compounds are characterized by their basic nature and nitrogen-containing structure.

Classification of Aliphatic Amines:

Type	Structure	Example	General Formula
Primary (1°)	$R-NH_2$	Methylamine	$R-NH_2$
Secondary (2°)	R_2-NH	Dimethylamine	R_2-NH
Tertiary (3°)	R_3-N	Trimethylamine	R_3-N

Structural Features:

- Nitrogen atom with lone pair of electrons
- Tetrahedral geometry around nitrogen
- Bond angles approximately 109.5°

- Presence of N-H bonds in primary and secondary amines

🧪 BASICITY OF ALIPHATIC AMINES

Aliphatic amines exhibit basic properties due to the presence of a lone pair of electrons on the nitrogen atom. This lone pair can accept protons (H+), making these compounds Lewis bases and Brønsted-Lowry bases.

Mechanism of Basicity:

- Lone pair of electrons on nitrogen accepts H+
- Formation of ammonium ion (R_3NH^+)
- Stabilization through solvation and hydrogen bonding
- The basicity depends on the availability of the lone pair

Factors Affecting Basicity:

1. Inductive Effect:

- Alkyl groups show +I effect, increasing electron density on nitrogen
- Greater electron density increases basicity
- More alkyl groups generally mean higher basicity

2. Steric Hindrance:

- Bulky alkyl groups hinder the approach of H+
- Reduces the effective basicity despite increased electron density
- Balance between electronic and steric effects

3. Solvation Effects:

- Smaller ammonium ions are better solvated
- Better solvation stabilizes the conjugate acid
- Affects the overall basicity in aqueous solutions

⚡ EFFECT OF SUBSTITUENTS ON BASICITY

The basicity of aliphatic amines is significantly influenced by the nature and number of substituents attached to the nitrogen atom.

Electronic Effects:

Electron-Donating Groups:

- **Increase basicity** by increasing electron density on nitrogen
- Alkyl groups show +I effect
- Order of basicity: $(C_2H_5)_2NH > C_2H_5NH_2 > NH_3$

Electron-Withdrawing Groups:

- **Decrease basicity** by reducing electron density on nitrogen
- Groups like $-NO_2$, -CN, halogens show -I effect
- Make the lone pair less available for proton acceptance

Steric Effects:

- Large substituents create **steric hindrance**
- Reduce the accessibility of the nitrogen lone pair
- Can override electronic effects in highly substituted amines

- Explains why tertiary amines are sometimes less basic than secondary amines

Order of Basicity in Different Media:

In Gas Phase: Tertiary > Secondary > Primary > Ammonia

In Aqueous Solution: Secondary > Primary > Tertiary > Ammonia

The difference arises due to solvation effects and steric hindrance in aqueous solutions.

🧪 QUALITATIVE TESTS FOR ALIPHATIC AMINES

Several qualitative tests can identify and differentiate between different types of aliphatic amines.

General Tests for Amines:

1. Litmus Test:

- Amines turn red litmus paper blue
- Indicates basic nature of amines
- Simple preliminary test

2. Carbylamine Test (Isocyanide Test):

- **Specific for primary amines**
- Amine + $CHCl_3$ + KOH → offensive smell
- Forms carbylamine (isocyanide) with characteristic odor

3. Hinsberg Test:

- Uses benzenesulfonyl chloride (Hinsberg reagent)
- **Differentiates between 1°, 2°, and 3° amines**
- Different solubility patterns in alkali

4. Nitrous Acid Test:

- **Different reactions for different types of amines**
- Primary: Evolution of N_2 gas
- Secondary: Formation of N-nitroso compound
- Tertiary: Salt formation only

Specific Differentiation Tests:

Amine Type	Carbylamine Test	Hinsberg Test	Nitrous Acid Test
Primary (1°)	Positive (offensive odor)	Soluble in alkali	N_2 gas evolution
Secondary (2°)	Negative	Insoluble in alkali	N-nitroso compound
Tertiary (3°)	Negative	No reaction	Salt formation

💊 STRUCTURE AND USES OF IMPORTANT ALIPHATIC AMINES

🧴 ETHANOLAMINE

- **Molecular Formula:** C_2H_7NO

- **Molecular Weight:** 61.08
- **Structure:** $HO-CH_2-CH_2-NH_2$ (Primary amine with hydroxyl group)

Properties:

- Colorless, viscous liquid
- Highly hygroscopic
- Strong ammonia-like odor
- Completely miscible with water
- Basic nature due to amino group

Uses:

- Used in pharmaceutical formulations as pH adjuster
- Important intermediate in drug synthesis
- Used in preparation of ethanolamine salts
- Emulsifying agent in cosmetic preparations
- Corrosion inhibitor in industrial applications
- Used as absorbent for acidic gases

🔗 ETHYLENEDIAMINE

- **Molecular Formula:** $C_2H_8N_2$
- **Molecular Weight:** 60.10
- **Structure:** $H_2N-CH_2-CH_2-NH_2$ (Primary diamine)

Properties:

- Colorless liquid with ammonia-like odor

- Hygroscopic nature
- Completely miscible with water
- Strong base (both nitrogen atoms are basic)
- Forms stable complexes with metal ions

Uses:

- Used as chelating agent in pharmaceutical applications
- Important intermediate in drug synthesis
- Used in preparation of EDTA
- Stabilizer in pharmaceutical formulations
- Used in treatment of heavy metal poisoning
- Important building block for various drugs
- Used as corrosion inhibitor

⚡ AMPHETAMINE

- **Molecular Formula:** $C_9H_{13}N$
- **Molecular Weight:** 135.21
- **Structure:** C_6H_5-CH_2-$CH(CH_3)$-NH_2 (Primary amine with benzyl group)

Properties:

- White crystalline powder or colorless liquid
- Characteristic amine odor
- Water-soluble salts
- Chiral compound with two enantiomers

- Strong central nervous system stimulant

Uses:

- Used in treatment of attention deficit hyperactivity disorder (ADHD)
- Treatment of narcolepsy
- Weight loss management (controlled use)
- Enhancement of alertness and concentration
- Treatment of certain depressive conditions
- **Note:** Highly regulated due to abuse potential
- Used in research for neurological studies

Pharmacological Properties:

- Increases dopamine and norepinephrine levels
- Crosses blood-brain barrier easily
- Long duration of action
- Potential for dependence and abuse
- Requires strict medical supervision

📊 COMPARATIVE TABLE: CARBOXYLIC ACIDS vs ALIPHATIC AMINES

Property	Carboxylic Acids	Aliphatic Amines
Functional Group	-COOH	$-NH_2$, -NHR, $-NR_2$
Chemical Nature	Acidic	Basic

Property	Carboxylic Acids	Aliphatic Amines
pH Behavior	Lower pH (acidic)	Higher pH (basic)
Litmus Test	Blue → Red	Red → Blue
Hydrogen Bonding	Strong (through OH and C=O)	Moderate (through N-H)
Solubility	Lower acids soluble	Lower amines soluble
Boiling Point	Generally higher	Generally lower
Biological Role	Metabolic intermediates	Neurotransmitters, hormones

This comprehensive study of carboxylic acids and aliphatic amines provides essential knowledge for understanding their pharmaceutical applications, chemical properties, and biological significance in drug development and therapeutic applications.