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PHARMACEUTICAL ORGANIC CHEMISTRY – I

UNIT 5

TOPIC :

- **Aliphatic amines*–** Basicity, effect of substituent on Basicity. Qualitative test, Structure and uses of Ethanolamine, Ethylenediamine, Amphetamine

Aliphatic Amines

→ Amines are organic compounds derived from ammonia (NH_3) by replacing one or more hydrogen atoms with alkyl or aryl groups.

→ Aliphatic amines contain only alkyl groups attached to the nitrogen atom.

General Formula

- Primary (1°) amine: $R–NH_2$
- Secondary (2°) amine: $R_2–NH$
- Tertiary (3°) amine: $R_3–N$
  (where R = alkyl group)

Examples

- Methylamine: CH_3NH_2 (1°)
- Dimethylamine: $(CH_3)_2NH$ (2°)
- Trimethylamine: $(CH_3)_3N$ (3°)

Basicity of Aliphatic Amines

Basicity

Basicity is the ability of a compound to **accept a proton (H^+).**

- In amines, the nitrogen atom has a **lone pair of electrons,** which can accept a proton.
- Thus, amines act as **Lewis bases.**

Aliphatic Amines

- The **lone pair on nitrogen** is readily available for protonation.
- In aqueous solution, they form **alkylammonium ions:**

$$R\text{–}NH_2 + H_2O \rightleftharpoons R\text{–}NH_3^+ + OH^-$$

Effect of Substituents on Basicity

→ Substituents can affect basicity through inductive and solvation effects.

1. Inductive Effect (–I and +I effects)

- **Electron-donating groups (EDG)** like alkyl groups push electrons toward nitrogen via **+I effect**, increasing electron density and **increasing basicity**.
- More alkyl groups → greater +I effect → stronger base.

Order in gas phase:
3°amine>2°amine>1°amine>NH_3

2. Solvation Effect in Aqueous Solution

- In water, **hydrogen bonding** stabilizes the protonated amine.
- Primary amines are better solvated than tertiary, so:

Order in water (aqueous phase):
2°amine>1°amine>3°amine>NH_3

Qualitative Tests for Aliphatic Amines

1. Litmus Test

- **Test**: Add a few drops of the amine to moist **red litmus paper**.
- **Observation**: The red litmus turns **blue.**
- **Inference**: Confirms **basic nature** of the amine.

2. Carbylamine Test **(for** Primary Amines **only)**

Also called Isocyanide Test

- **Reagents**: Chloroform ($CHCl_3$) + alcoholic KOH
- **Procedure**: Heat the primary amine with $CHCl_3$ and alcoholic KOH.
- **Reaction**:

$$R\text{-}NH_2 + CHCl_3 + 3KOH \rightarrow R\text{-}NC + 3KCl + 3H_2O$$

Observation: Formation of foul-smelling isocyanide (R–NC).

Inference: Positive test indicates presence of a primary aliphatic amine.

3. Reaction with Acyl Chlorides

Used for 1° and 2° amines

- **Reagent**: Acid chloride (e.g., acetyl chloride)
- **Reaction with 1° Amine**:

$$R\text{–}NH_2 + CH_3COCl \rightarrow R\text{–}NHCOCH_3 + HCl$$

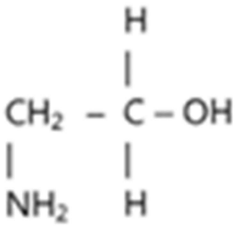
Observation: Formation of white precipitate of amide.

Inference: Confirms presence of primary or secondary amine

Ethanolamine

→ Chemical Formula: C_2H_7NO
→ IUPAC Name: 2-Aminoethanol
→ Common Name: Ethanolamine
→ Other Names: Monoethanolamine (MEA)
→ Functional Groups:
- Hydroxyl group (–OH)
- Amino group ($–NH_2$)

Structure of Ethanolamine



- It is a simple alkanolamine.
- Contains both:
  - Alcohol group (–OH)
  - Primary amine group ($–NH_2$)

Uses of Ethanolamine:

✓ In Pharmaceutical Industry:
- Used as an alkalizing agent in creams, lotions, and ointments.
- Acts as a buffering agent in topical formulations.
- Used in the preparation of emulsifiers and soap bases.
- Found in some cough syrups and eye drops.

✓ As a Surfactant and Emulsifier:
- Common ingredient in:
  - Shampoos

- Conditioners
- Cleansers

- Helps to stabilize emulsions and acts as a foam booster.

✓ In Gas Treatment:

- Used in scrubbing acidic gases like CO_2 and H_2S from natural gas and refinery streams.
- Forms water-soluble salts with acidic gases.

✓ In Detergents and Soaps:

- Improves cleaning power, solubility, and foam stability.
- Used in industrial degreasers, floor cleaners, and surface disinfectants.

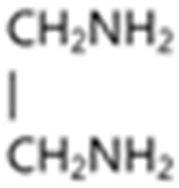
✓ In the Production of Other Chemicals:

- Intermediate in the synthesis of:
  - Detergents
  - Textile additives
  - Cosmetics
  - Corrosion inhibitors
  - Herbicides (e.g., glyphosate)

Ethylenediamine

→ Chemical Formula: $C_2H_8N_2$
→ IUPAC Name: 1,2-Diaminoethane
→ Common Name: Ethylenediamine (EDA)
→ Functional Group:
- Two primary amine groups ($-NH_2$) on adjacent carbon atoms

Structure of Ethylenediamine



- Contains a two-carbon ethylene backbone with a $-NH_2$ group at each end.

Uses of Ethylenediamine:

✓ In Pharmaceutical Industry:
- Used as an intermediate in the manufacture of:
  - Antihistamines (e.g., Tripelennamine)
  - Chelating agents like EDTA (Ethylenediaminetetraacetic acid)
- Used to stabilize some vaccine and injection solutions.

As a Chelating Agent:
- Binds to metal ions via both nitrogen atoms to form chelates.
- Forms stable complexes with:
  - Nickel (Ni^{2+})
  - Copper (Cu^{2+})

- Cobalt (Co^{2+})
- Important in analytical and coordination chemistry.

✓ In Polymer and Resin Industry:

- Used in the production of:
  - Polyamides
  - Epoxy resins
  - Urethane foams
- Acts as a curing agent and hardener.

✓ In Detergents and Fabric Softeners:

- Used to produce cationic surfactants and fabric softener bases.
- Provides alkalinity and helps in dirt removal.

✓ In Agrochemical Industry:

- Used in the synthesis of:
  - Herbicides
  - Fungicides
  - Pesticides

✓ In Corrosion Inhibitors and Coolants:

- Acts as a corrosion inhibitor in boiler water treatments.
- Added to coolants and antifreeze formulations.

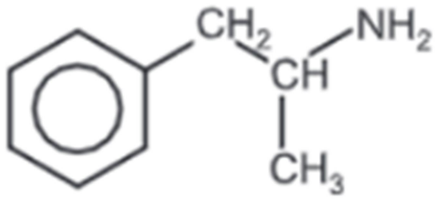
✓ In Research and Coordination Chemistry:

- Used as a ligand in inorganic synthesis.
- Part of Werner complexes and coordination compound studies.

Amphetamine

→ Chemical Formula: $C_9H_{13}N$
→ IUPAC Name: 1-Phenylpropan-2-amine
→ Common Name: Amphetamine
→ Drug Class: CNS stimulant, sympathomimetic amine

Structure of Amphetamine



- Structure contains:
  - A phenyl ring (C_6H_5–)
  - A propyl chain with a methyl group (–CH_3) and a primary amine group (–NH_2)

Uses of Amphetamine:

✓ Treatment of ADHD (Attention Deficit Hyperactivity Disorder):
- One of the primary drugs used for treating ADHD.
- Improves attention span, concentration, and behavior control.

✓ Treatment of Narcolepsy:
- Used to promote wakefulness in patients with narcolepsy (a sleep disorder).
- Reduces excessive daytime sleepiness.

✓ Appetite Suppressant:

- Historically used in the treatment of obesity (now limited due to abuse potential).
- Suppresses appetite by stimulating the hypothalamus.

✓ CNS Stimulant:

- Increases the release of dopamine and norepinephrine in the brain.
- Enhances alertness, focus, mood, and physical performance.

✓ Military and Aviation Use:

- Sometimes issued in military/aviation settings as "go pills" to maintain alertness during long missions (under strict supervision).

✓ For Depression (historical use):

- Used in the past to treat treatment-resistant depression, but replaced by safer drugs today.