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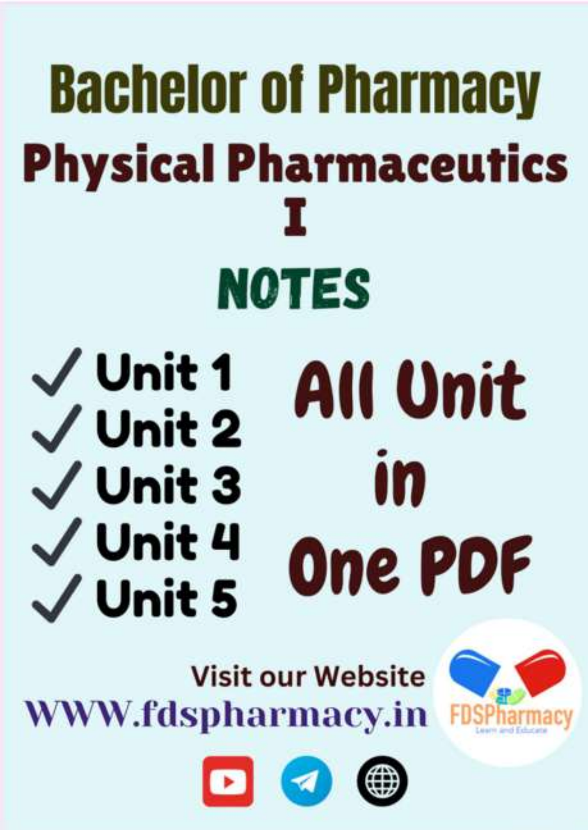

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PHARMACEUTICAL ORGANIC CHEMISTRY - II

UNIT 5

TOPIC :

- **Cyclo alkanes***

  Stabilities– Baeyer's strain theory, limitation of Baeyer's strain theory, Coulson and Moffitt's modification, Sachse Mohr's theory (Theory of strainless rings), reactions of cyclopropane and cyclobutane only

CYCLOALKANES

- Cycloalkanes are saturated, cyclic hydrocarbons containing only single covalent bonds between carbon atoms.
- All carbon-carbon bonds are sigma (σ) bonds.
- These compounds form closed ring structures.
- Also known as Cycloparaffins.
- They follow the general formula:

$$C_nH_{2n}$$

- Each carbon in the ring is bonded to two other carbon atoms and two hydrogen atoms.
- Exhibit sp^3 hybridization with bond angles depending on the ring size.
- Smaller rings like cyclopropane and cyclobutane are strained due to angle strain.
- Larger rings are more stable.

Examples of Cycloalkanes

Cycloalkane	Molecular Formula	Structure Type
Cyclopropane	C_3H_6	Triangle (3-membered)
Cyclobutane	C_4H_8	Square (4-membered)
Cyclopentane	C_5H_{10}	Pentagon
Cyclohexane	C_6H_{12}	Hexagon
Cycloheptane	C_7H_{14}	Heptagon
Cyclooctane	C_8H_{16}	Octagon
Cyclononane	C_9H_{18}	9-membered ring
Cyclodecane	$C_{10}H_{20}$	10-membered ring

Methods of Preparation of Cycloalkanes

Cycloalkanes can be synthesized by the following methods:

1. From Dihalogen Compounds (Internal Wurtz Reaction)

- Reagents: Sodium (Na) or Zinc (Zn) metal in dry ether
- Reaction Type: Dehalogenation followed by ring closure

Example:

1,3-Dibromopropane + Zinc → Cyclopropane

$$\mathrm{Br{-}CH_2{-}CH_2{-}CH_2{-}Br} + 2Zn \xrightarrow{\text{dry ether}} \text{Cyclopropane} + 2ZnBr_2$$

2. From Calcium Salts of Dicarboxylic Acids (Ketone Intermediate Method)

- Reagents: Calcium salt of a dicarboxylic acid, followed by Zn/HCl
- Step 1: Dry distillation forms cyclic ketone
- Step 2: Reduction of the cyclic ketone gives cycloalkane

Example:

Calcium adipate (from adipic acid) → Cyclopentanone → Cyclopentane

Step 1:

$$\mathrm{(CH_2{-}CH_2{-}COO)_2Ca} \xrightarrow{\Delta} \text{Cyclopentanone}$$

Step 2:

$$\text{Cyclopentanone} + Zn/HCl \rightarrow \text{Cyclopentane}$$

Chemical Reactions of Cycloalkanes

Cycloalkanes mainly undergo two types of chemical reactions:

1. Substitution Reactions

- Cycloalkanes can undergo **free radical substitution** reactions similar to open-chain alkanes.
- When treated with halogens (Cl_2 or Br_2) in the presence of UV light or at 298 K, a hydrogen atom from the ring is replaced by a halogen atom.
- This reaction proceeds via a free radical mechanism.

Example :

Cyclopropane + Cl_2 (UV light) → Chlorocyclopropane + HCl

$$C_3H_6 + Cl_2 \xrightarrow{h\nu} C_3H_5Cl + HCl$$

2. Addition Reactions (Ring Opening Reactions)

- Small ring cycloalkanes like cyclopropane and cyclobutane have high ring strain.
- They behave like alkenes and undergo electrophilic addition reactions.
- These reactions break the ring and form open-chain saturated or halogenated compounds.

Example :

Cyclopropane + HCl → 1-Chloropropane

$$C_3H_6 + HCl \rightarrow CH_3\text{–}CHCl\text{–}CH_3$$

Baeyer's Strain Theory

→ Proposed by: Adolf von Baeyer in 1885

→ Baeyer's strain theory explains the relative stabilities of cycloalkanes based on the deviation of bond angles from the ideal tetrahedral angle (109.5°) of sp^3-hybridized carbon atoms.

KeyPoints:

- A perfectly tetrahedral carbon has a bond angle of 109.5°.
- When the carbon atoms are forced into ring structures, the bond angles may deviate from 109.5°, creating angle strain (also known as Baeyer strain).
- The greater the deviation, the greater the strain and the lower the stability.

Predicted Strain in Cycloalkanes:

Cycloalkane	Number of Carbons	Ring Angle	Deviation from 109.5°	Predicted Strain	Stability
Cyclopropane	3	60°	Very large	Very high	Least stable
Cyclobutane	4	90°	Large	High	Less stable
Cyclopentane	5	108°	Small	Low	Fairly stable
Cyclohexane	6	120° (planar assumption)	Moderate	Moderate	Less stable (as per Baeyer)

Limitations of Baeyer's Strain Theory

Baeyer's theory was revolutionary but had several limitations, especially due to the assumption that all ring systems are planar:

✕Incorrect Planarity Assumption:

- Baeyer assumed all cycloalkanes are planar (flat), which is not true for rings with 5 or more carbon atoms.
- Cyclopentane and larger rings adopt non-planar (puckered) conformations to relieve strain (e.g., envelope form, chair form).

✕Ignored Torsional Strain:

- Theory only considered angle strain, not torsional strain (strain due to eclipsed bonds).
- For example, cyclopropane has severe torsional strain due to eclipsing of all C–H bonds.

✕Ignored Steric (Van der Waals) Strain:

- Baeyer's theory didn't account for non-bonded atom repulsion in large rings (transannular strain).
- Large rings (C8 and above) can have crowding inside the ring leading to instability.

✕Misjudged Cyclohexane Stability:

- Baeyer predicted cyclohexane to be moderately strained.
- In reality, cyclohexane in chair form has no angle or torsional strain, and is most stable.

✕Failed for Larger Rings:

- According to Baeyer, stability decreases with ring size, but experimental data shows that rings with 6–15 atoms are reasonably stable due to flexible conformations.

Coulson–Moffitt's Modification

→ (Also known as Banana Bond Theory or Bent Bond Theory)

→ Coulson and Moffitt proposed this theory as a modification of Baeyer's Strain Theory.

→ It was developed to explain the stability and bonding in small ring cycloalkanes, especially cyclopropane.

→ The theory is based on quantum mechanical principles and better explains the bonding in strained ring compounds.

Key Concept: Banana (Bent) Bonds

- In small rings like cyclopropane, the bond angle is around 60°, which is much less than the ideal 109°28′ for sp^3 hybridized carbon.
- This makes it impossible for the orbitals to overlap directly in a straight (axial) line.
- Instead, the bonds are bent outward, resulting in a banana-like shape—called Bent Bonds or Banana Bonds.

Types of Orbital Overlap

Bond Type	Overlap Type	Description
σ (Sigma)	Axial / Head-on	Strongest overlap (in alkanes)
π (Pi)	Sidewise / Parallel	Weaker (in alkenes)
Bent Bond	Intermediate (Bent/Curved)	Weaker than σ but stronger than π

Characteristics of Banana Bonds

- Formed by the bending of sp^3 orbitals due to angle compression.
- The C–C bond is not linear but curved, resembling a banana.
- These bonds are weaker than normal σ-bonds due to less effective overlap.
- Explains why cyclopropane is less stable and highly reactive.

Consequences in Cyclopropane

- Each carbon in cyclopropane forms two bent bonds with its neighboring carbons.
- The weaker bonds result in:
    - High strain energy
    - Low stability
    - High reactivity, especially towards ring-opening reactions

Cyclopropane behaves like an alkene in many reactions due to its strained, reactive structure.

Advantages Over Baeyer's Theory

- Baeyer assumed planar structures and angle strain only.
- Coulson–Moffitt’s theory explains:
    - Why cyclopropane exists despite the high angle strain
    - The nature of bonding in small rings
    - The instability of cyclopropane due to weakened bent bonds

Limitations

- Applies mainly to small-ring systems like cyclopropane and cyclobutane.
- Does not fully explain larger ring conformations, which are better described by conformational analysis (e.g., chair form of cyclohexane).

SACHSE–MOHR'S THEORY

(Theory of Strainless Rings)

- → Baeyer's Strain Theory assumed that all cycloalkanes are planar.
- → According to Baeyer, any deviation from the ideal bond angle of 109°28′ (tetrahedral angle) causes angle strain.
- → This explained the instability of small rings like cyclopropane and cyclobutane, but failed for larger cycloalkanes like cyclohexane, cycloheptane, and cyclooctane, which are actually stable.

Sachse–Mohr's Contribution

- ➢ In 1918, Sachse and Mohr proposed a new theory to explain the stability of higher cycloalkanes.
- ➢ They suggested that larger rings do not need to be planar; instead, they adopt non-planar (puckered or folded) conformations.
- ➢ These folded structures allow the bond angles to return close to the ideal tetrahedral angle (109°28′).
- ➢ As a result, angle strain is minimized, and the molecule becomes strainless and more stable.

Application to Cyclohexane

According to Sachse–Mohr's theory, **cyclohexane** can adopt **two main non-planar conformations**:

1. **Chair Form**
2. **Boat Form**

1. **Chair Conformation (Most Stable)**

- In this form:
  - Carbons 2, 3, 5, and 6 lie in the same plane.
  - Carbon 4 is above the plane.
  - Carbon 1 is below the plane.
- This conformation minimizes torsional strain and steric repulsion, making it the most stable.
- The bond angles are nearly 109.5°, close to ideal sp^3 geometry.

2. **Boat Conformation (Less Stable)**

- In this form:
  - Carbons 2, 3, 5, and 6 are in the same plane.
  - Carbons 1 and 4 are both above the plane, forming a boat-like shape.
- This form suffers from:
  - Torsional strain (due to eclipsed bonds)
  - Steric hindrance (from hydrogen atoms on carbons 1 and 4 clashing – called flagpole interactions)
- Therefore, the boat form is less stable than the chair form.

Importance of Sachse–Mohr's Theory

- Explained the stability of larger cycloalkanes like cyclohexane.
- Showed that planar structure is not always required.
- Introduced the idea of puckered conformations for strain relief.
- Served as a foundation for modern conformational analysis.

Reactions of Cyclopropane and Cyclobutane

- Cyclopropane (C_3H_6) and cyclobutane (C_4H_8) are small-ring cycloalkanes with significant angle strain and torsional strain due to their planar or nearly planar structures.
- As a result, they are more reactive than larger cycloalkanes and behave somewhat like alkenes in some reactions.

1. Ring-Opening Reactions

a. With Hydrogen (Hydrogenation):

→ Cyclopropane and cyclobutane undergo ring-opening hydrogenation in the presence of nickel or platinum catalyst to form alkanes.

Cyclopropane:

$$\mathrm{C_3H_6} + H_2 \xrightarrow{\text{Ni, heat}} \text{Propane}$$

Cyclobutane:

$$\mathrm{C_4H_8} + H_2 \xrightarrow{\text{Ni, heat}} \text{Butane}$$