PHARM.D • YEAR 1

Pharmaceutical Organic Chemistry

CHAPTER 4

Alicyclic Compounds

PPT CHAPTER COVER



ALICYCLIC COMPOUNDS: CLASSIFICATION AND PROPERTIES

→ WHAT ARE ALICYCLIC COMPOUNDS?

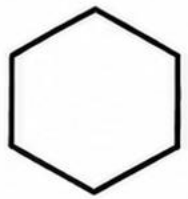
Alicyclic compounds are organic compounds that are both aliphatic (non-aromatic) and cyclic (contain one or more rings). The term "alicyclic" is a combination of "aliphatic" and "cyclic".

These compounds show properties that are intermediate between alkanes/alkenes and aromatic compounds.

STRUCTURE AND NATURE

- Alicyclic compounds contain one or more carbon rings, which may or may not have substituents.
- Unlike aromatic compounds, alicyclic rings do not have delocalized π electrons (as seen in benzene). Hence, they follow the typical rules of saturated or unsaturated hydrocarbons.
- They can be:
  - → Saturated (cycloalkanes): contain only single bonds.
  - → Unsaturated (cycloalkenes, cycloalkynes): contain double or triple bonds in the ring.
  - → Substituted alicyclic compounds: contain one or more substituents attached to the ring.

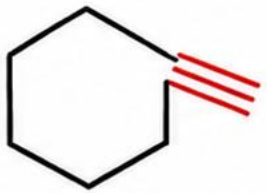
EXAMPLES:



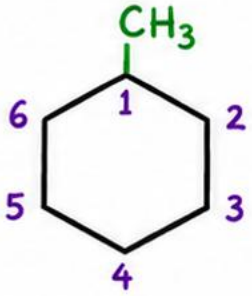
Cyclohexane
(Saturated)
(Cycloalkane)



Cyclopentene
(Unsaturated)
(Cycloalkene)



Cyclohex-1-yne
(Unsaturated)
(Cycloalkyne)



1-Methylcyclohexane
(Substituted alicyclic compound)

KEY TAKEAWAY

Alicyclic = Aliphatic + Cyclic

↓

No aromatic π delocalization; behave like open-chain saturated or unsaturated hydrocarbons.

Ring Size, Nomenclature and Ring Strain

Ring size matters: small rings store strain energy!

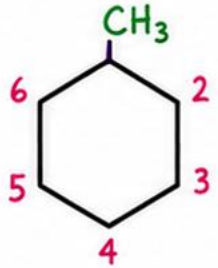
1) Ring Size

- Most stable rings have 5 or 6 members (near ideal geometry).
- Small rings (<5) are angle-strained.
- Large rings (>6) are transannularly tensed (atoms far apart crowd each other).

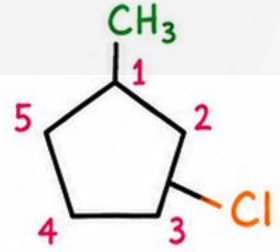


2) Nomenclature

- Alicyclic rings are named as cycloalkanes/alkenes/alkynes.
- Prefix "cyclo-" + parent hydrocarbon name.
- Number the ring to give substituents the lowest set of locants.
- For multiple substituents, list in alphabetical order.



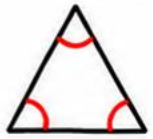
methylcyclohexane
(1-methylcyclohexane)



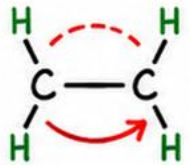
1-methyl-3-chlorocyclopentane

3) Ring Strain

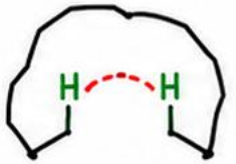
- Ring strain = extra energy of the ring compared to an open-chain form.
- Arises mainly due to:
  - → Angle strain (bond angles deviate from ideal).
  - → Torsional strain (eclipsing interactions).
- Strain decreases as ring size increases to 5–6; rises again in larger rings (transannular strain).



Angle strain
(60° << 109.5°)



Torsional strain
(eclipsing)

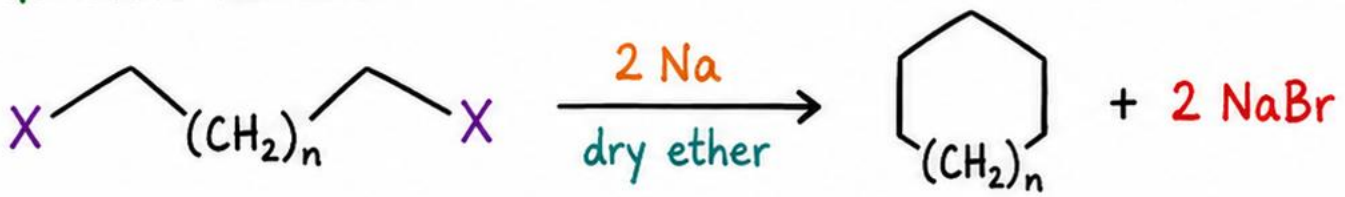


Transannular strain
(large rings)

Takeaway: Rings have optimum sizes! 5–6 membered rings are most stable; small rings are angle-strained and large rings are transannularly tensed.

CYCLIZATION BY INTRAMOLECULAR WURTZ REACTION

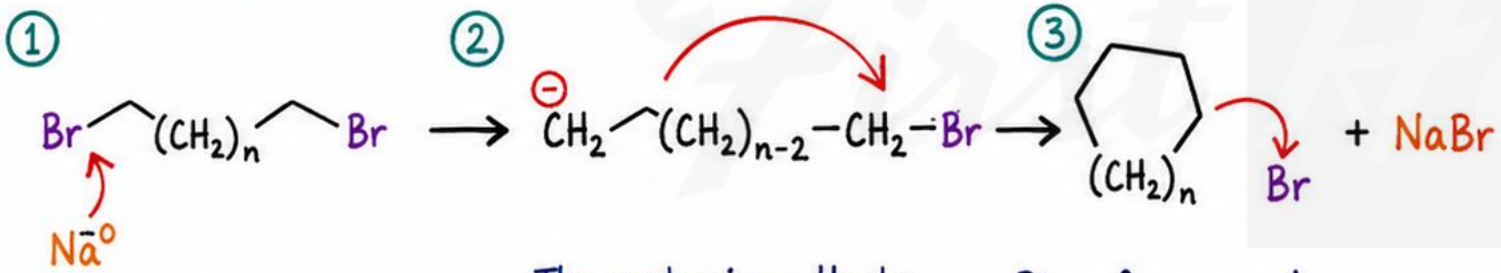
GENERAL REACTION



α,ω-DIHALOALKANE

CYCLOALKANE
(n = 1 to 4)

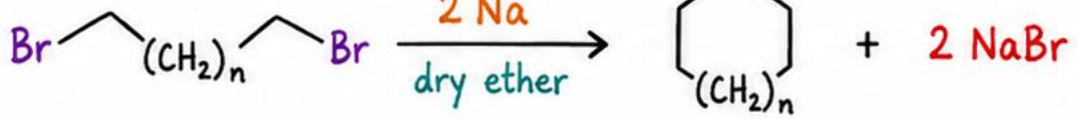
MECHANISM (INTRAMOLECULAR)



Sodium reduces one halogen to form a carbanion.

The carbanion attacks the other end in an intramolecular S_N2 manner.

Ring forms and bromide leaves.

OVERALL: 

CYCLOALKANE

- Cyclization of α,ω-dihaloalkanes with sodium metal in dry ether gives cycloalkanes. It is an intramolecular Wurtz reaction.
- Sodium first reduces one halogen to form a carbanion, which attacks the other end (S_N2) to form the ring and eliminate NaBr.
- Most suitable for three- to six-membered rings (n = 1 to 4). Larger rings often give low yields due to ring strain or side reactions.
- Example: $Br-(CH_2)_3-Br + 2\,Na \xrightarrow{\text{dry ether}}$ cyclopropane + 2 NaBr.

DICARBOXYLATE CYCLIZATION: CYCLIC KETONES

Ketonic decarboxylation occurs on dry distillation of a calcium or barium salt of a suitable dicarboxylic acid. The two carboxylate groups are within the same chain; intramolecular ketone formation occurs as one carboxylate is lost and the other forms the carbonyl, giving a cyclic ketone.

WORKED EXAMPLE:

$$Ca[-OOC-(CH_2)_4-COO^-] \xrightarrow[\text{dry distillation}]{\text{heat}} \text{cyclopentanone} + CaCO_3$$

calcium adipate

cyclopentanone

calcium carbonate

KEY POINTS:

- Intramolecular ketone formation occurs.
- The carbonyl carbon is part of the ring.
- Adipate gives cyclopentanone.
- Analogous salts can give other cyclic ketones.

CORRECTION:

Product is a CYCLIC KETONE—not cyclopentane. This is ketonic decarboxylation, not a Wurtz reaction.

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