

1. Introduction

Alicyclic compounds (*aliphatic cyclic* compounds) are organic compounds that resemble both aliphatic and cyclic compounds in their properties. The saturated alicyclic compounds have the general formula C_nH_{2n} (same as that of the alkene and are isomers of alkene); they do not have double bond but possess a ring structure.

When the molecular formula of the saturated hydrocarbon corresponds to the general formula C_nH_{2n} , then the compound has one ring; if the general formula is C_nH_{2n-2} , then the compound have two rings; if C_nH_{2n-4} , then the compound have three rings and so on.

Classification of monocyclic compounds: Monocyclic compounds have been classified on the basis of number of carbon atoms in the ring in the following way:

Small rings: 3-4 carbon atoms Common/normal rings: 5-7 carbon atoms Medium rings: 8-11 carbon atoms

Large rings: >12 carbon atoms

Many chemical properties depend upon the class of the cycloalkane, and these differences in behaviour were explained by the Baeyer's Angle Strain Theory. Baeyer observed different bond angles for different cycloalkanes and also observed some different properties and stability. Baeyer proposed that the optimum overlap of atomic orbitals is achieved for bond angle of $109^\circ 28'$ for carbon atom in tetrahedral geometry (like methane molecule). In short, it is ideal bond angle for alkane compounds. Effective and optimum overlap of atomic orbitals produces maximum bond strength and stable molecule. If bond angles deviate from the ideal value then the ring produces strain. Higher the strain in the ring, higher would be the instability. Also, higher strain produce increased reactivity and increases heat of combustion. On this basis, Baeyer proposed angle strain theory, which explains reactivity and stability of cycloalkanes. Baeyer proposed 'any deviation of bond angle from ideal bond angle value ($109^\circ 28'$) produces a strain in molecule. The Baeyer's theory is based upon some assumptions, which are helpful in understanding the instability of cycloalkane ring systems. These assumptions are:

- All ring systems are planar. Deviation from normal tetrahedral angles leads to unstable cycloalkanes,
- The large ring systems involve negative strain hence do not exist ,
- The bond angles in cyclohexane and higher cycloalkanes (cycloheptane, cyclooctane, cyclononane.....) are not larger than $109^\circ 28'$ (or 109.5°) because the carbon rings of those compounds are not planar (flat) but they are puckered (wrinkled).

The distortion for each ring size assuming cycloalkanes rings to be planar,

(i) Cycloalkane: The ring of cyclopropane is triangle. All the three angles are of 60° in place of 109.5° (normal bond angle for carbon atom) to adjust them into triangle ring system.

Thus, Deviation = (Normal tetrahedral bond angle) – (Actual bond angle) = $109.5^\circ - 60^\circ = 49.5^\circ$.

(ii) Cyclobutane: The ring of cyclobutane is square and the bond angles are of 90° in place of 109.5° (normal bond angle for carbon atom) to adjust them into square ring system.

Thus, Deviation = (Normal tetrahedral bond angle) – (Actual bond angle) = $109^\circ 5' - 90^\circ = 19.5^\circ$.

Since deviation from the normal bond angle is higher for cyclopropane (49.5°) than cyclobutane (19.5°) therefore

cyclopropane has higher strain which make it less stable in comparison to cyclobutane. As a result, cyclopropane is more prone to undergo ring opening reactions as compare to cyclobutane.

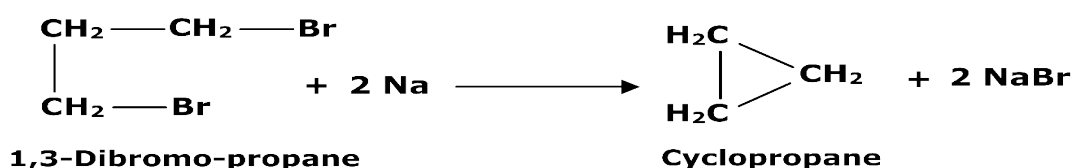
According to Baeyer, the relative order of stability for some common cycloalkanes is as follows: Cyclopentane > Cyclohexane > Cyclobutane > Cyclopropane

But the actual observed order of stability for these cycloalkanes is as follows: Cyclohexane > Cyclopentane > Cyclobutane > Cyclopropane

2. Synthesis of small ring compounds

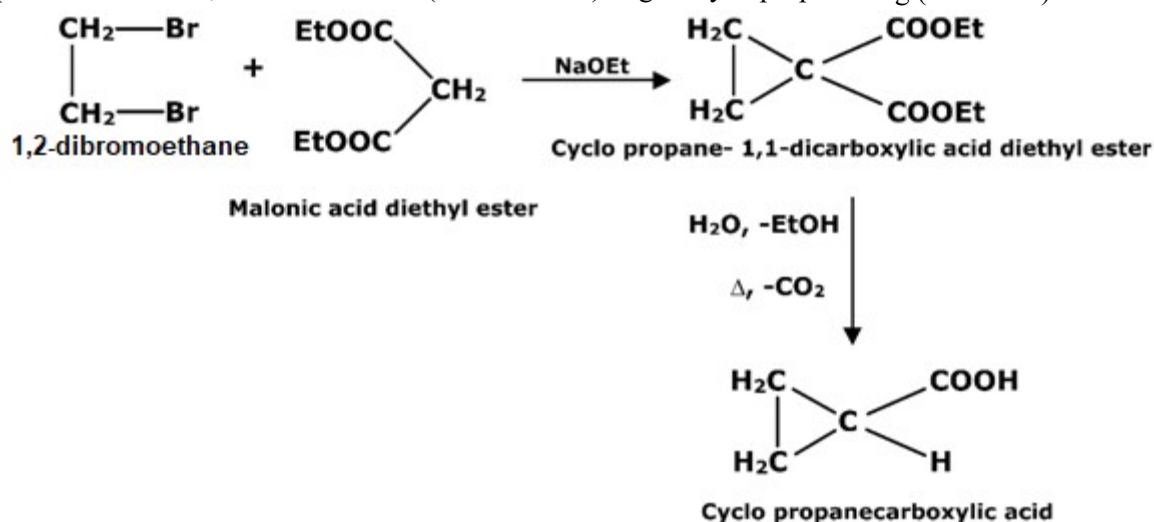
Few important methods for the synthesis of cyclopropane ring are discussed below:

- (i) **From 1, 3-dibromopropane:** The cyclization of 1,3-Dibromopropane using sodium metal under anhydrous conditions gives cyclopropane. The reaction follows the pathway of Wurtz coupling as shown in scheme 1. The yield of this reaction can be improved by using zinc metal.



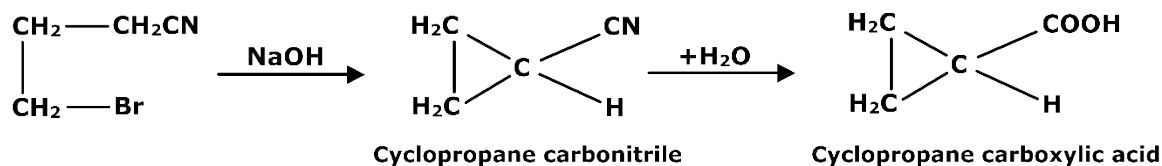
Scheme 1. Synthesis of cyclopropane ring using Wurtz coupling

- (ii) **From 1,2-dibromoethane:** 1,2-Dibromoethane can be cyclized on reaction with malonic acid diethyl ester in the presence of a base, sodium ethoxide ($\text{NaOCH}_2\text{CH}_3$) to give cyclopropane ring (Scheme 2).



- (iii) **Scheme 3. Synthesis of cyclopropane ring from From 1-bromo-3-cyanopropane:**

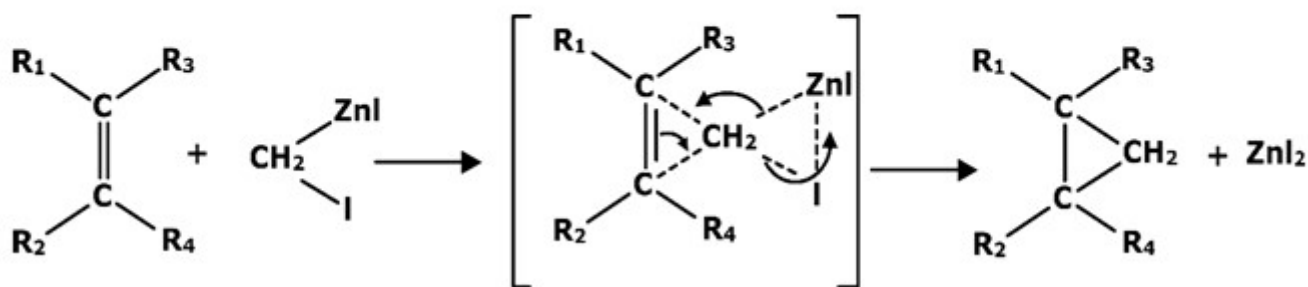
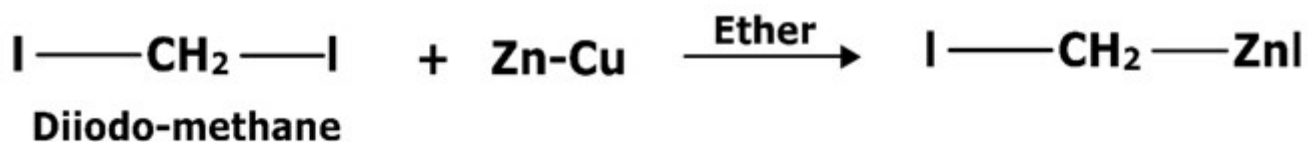
1-bromo-3-cyanopropane in the presence of a base (NaOH) cyclized to form cyclopropanecarbonitrile, which on hydrolysis form cyclopropanecarboxylic acid s shown in scheme 3.



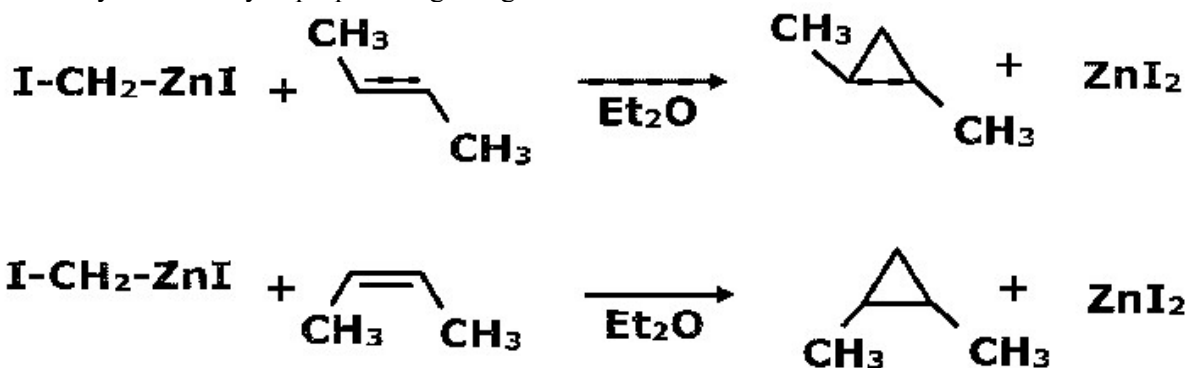
Scheme 3. Synthesis of cyclopropane ring from 1-bromo-3-cyanopropane

(iv) **From alkenes using Simmons-Smith reaction:** In this reaction, iodomethylzinc iodide (ICH_2ZnI) is the reactive carbenoid intermediate formed by the reaction between diiodomethane and a zinc-copper couple. Alkenes on reaction with iodomethylzinc iodide form cyclopropane derivative *via* a concerted reaction. Here the nucleophilic carbon-carbon double bond ($\text{C}=\text{C}$) causes the loss of the iodide ion (I^-) as the leaving group and the electrons from the nucleophilic carbon- zinc bond ($\text{C}-\text{Zn}$) are being used to form the other carbon-carbon single bond ($\text{C}-\text{C}$). Thus, both the new carbon-carbon single bonds ($\text{C}-\text{C}$) are formed simultaneously as shown in scheme 4. Major drawback of this reaction is the high cost of diiodomethane.

(v) Substituents that are trans in the alkene remain trans in the cyclopropane, while substituents that are cis in the alkene remain cis in the cyclopropane (Scheme 5).

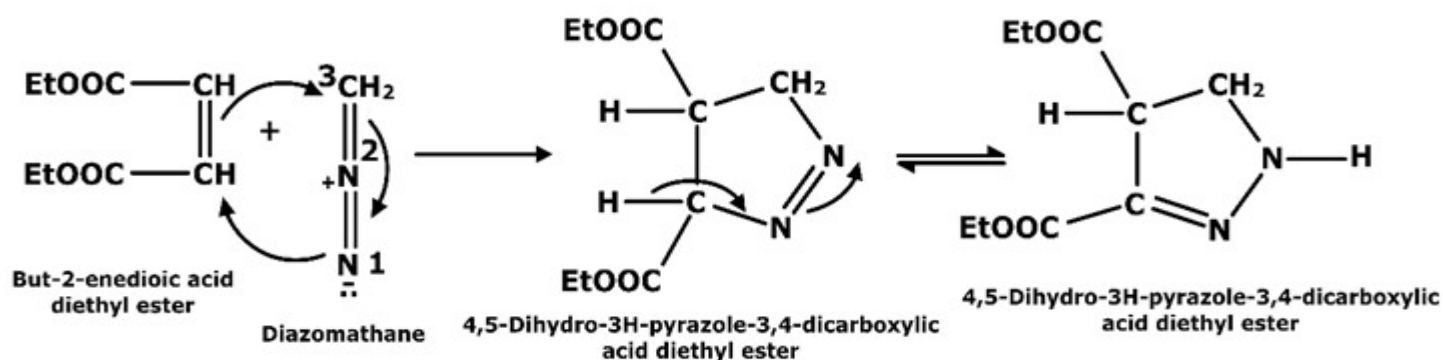


Scheme 4. Synthesis of cyclopropane ring using Simmons-Smith reaction



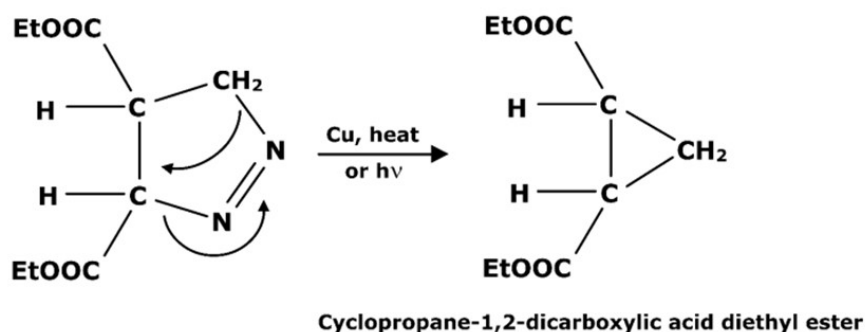
Scheme 5. Stereochemistry of cyclopropane ring using Simmons-Smith reaction

(vi) **From diazo compounds:** Diazo compounds like diazomethane reacts with alkenes and form cyclopropanes (Scheme 6). The reaction takes place in two steps:



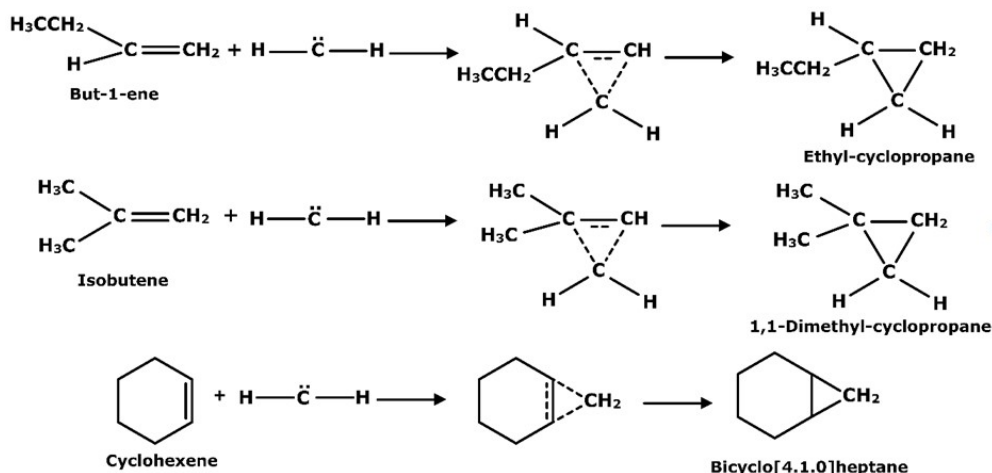
Step 1: 1, 3-Dipolar cycloaddition: Activated alkene like but-2-enedioic acid diethyl ester reacts with diazomethane at 1 and 3-position forming the corresponding pyrazole derivative 4,5-dihydro- 3H-pyrazole-3,4-dicarboxylic acid diethyl ester.

Step 2: Nitrogen removal: Pyrazole derivative 4,5-dihydro-3H-pyrazole-3,4-dicarboxylic acid diethyl ester on either photochemical or thermal decomposition loses one molecule of nitrogen and forms cyclopropane.



Scheme 6. Synthesis of cyclopropane ring using diazo compounds

(vii) If the above reaction is done using potassium hydroxide (KOH) and platinum as catalyst *via* thermal route, it is known as Kishner cyclopropane synthesis.



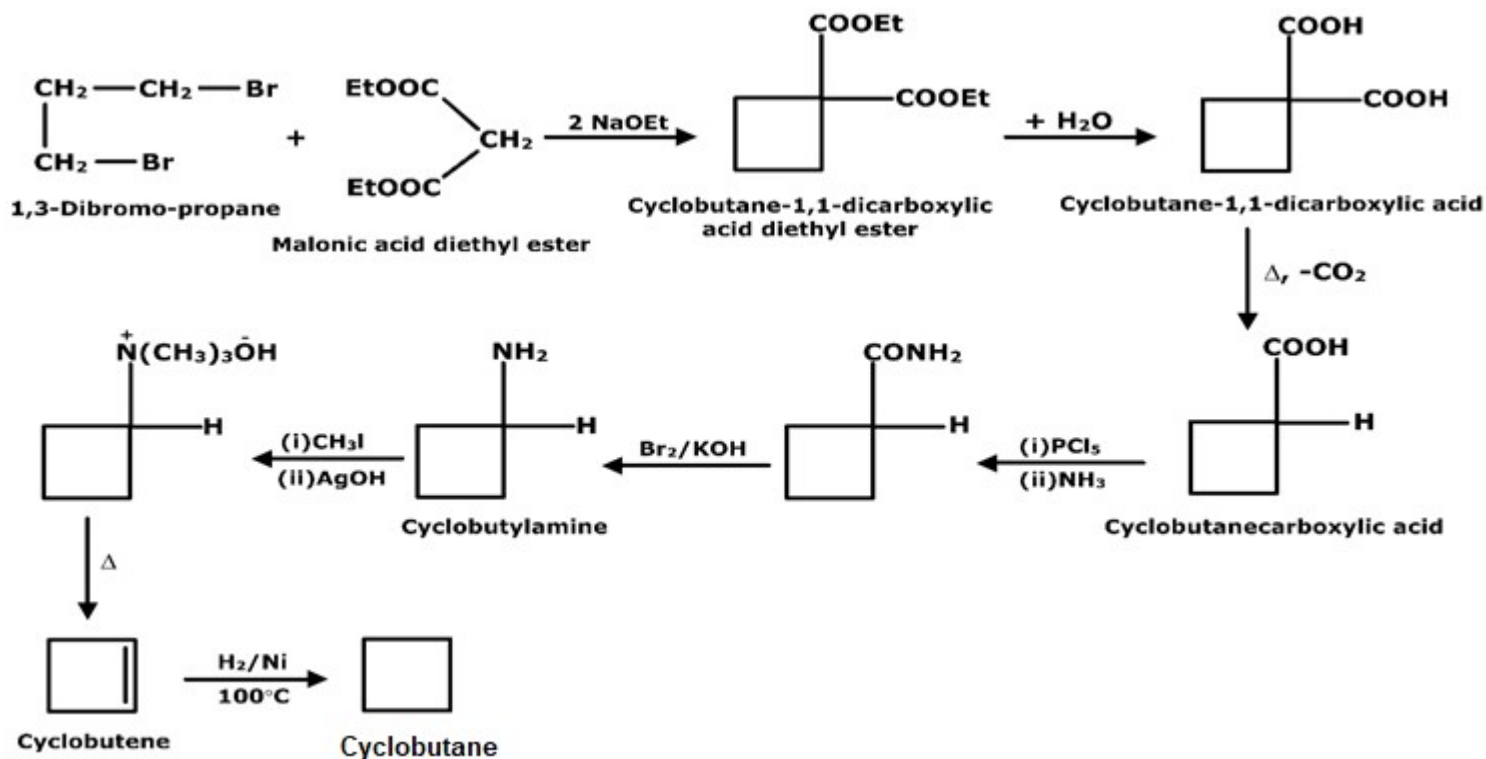
Scheme 7. Synthesis of cyclopropane ring from (a) but-1-ene; (b) isobutene; and (c) cyclohexene

(viii) **From alkenes:** Alkenes on reaction with carbene like methylene form cyclopropane *via* cyclic transition state to form cyclopropane ring. The reaction of but-1-ene with methylene gives ethyl cyclopropane (Scheme 7a). The reaction of isobutene with methylene gives 1,1- dimethylcyclopropane (Scheme 7b) whereas reaction of cyclohexene with methylene gives bicyclo[4.1.0]heptane (Scheme 7c).

Synthesis of cyclobutane ring:

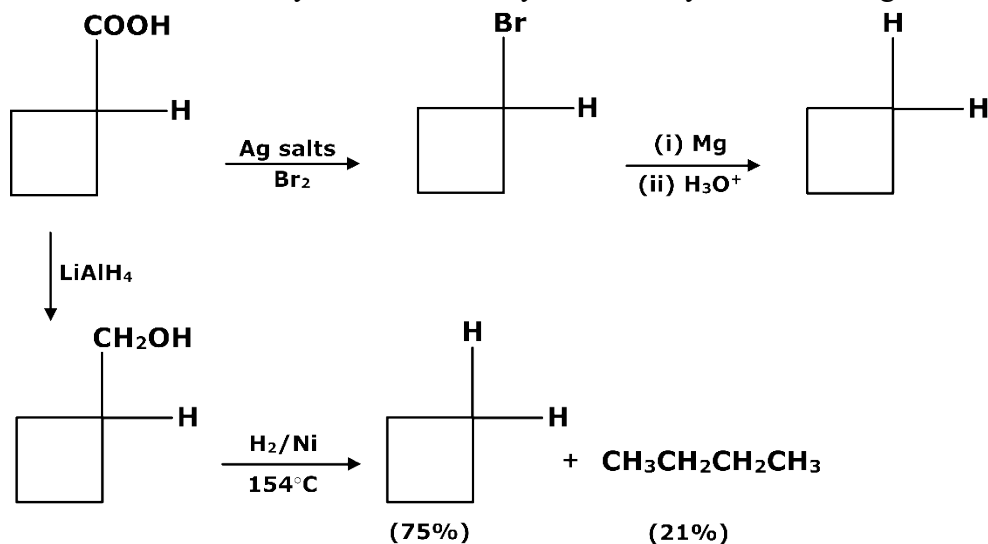
Few important methods for the synthesis of cyclobutane ring are discussed below:

(i) **From 1,3-dibromopropane:** The reaction of 1,3-dibromopropane with malonic acid diethyl ester in the presence of a base, sodium acetate (NaOEt) gives a cyclized product, cyclobutane-1,1-dicarboxylic acid diethyl ester which on hydrolysis gives cyclobutane-1,1-dicarboxylic acid (Scheme 8).

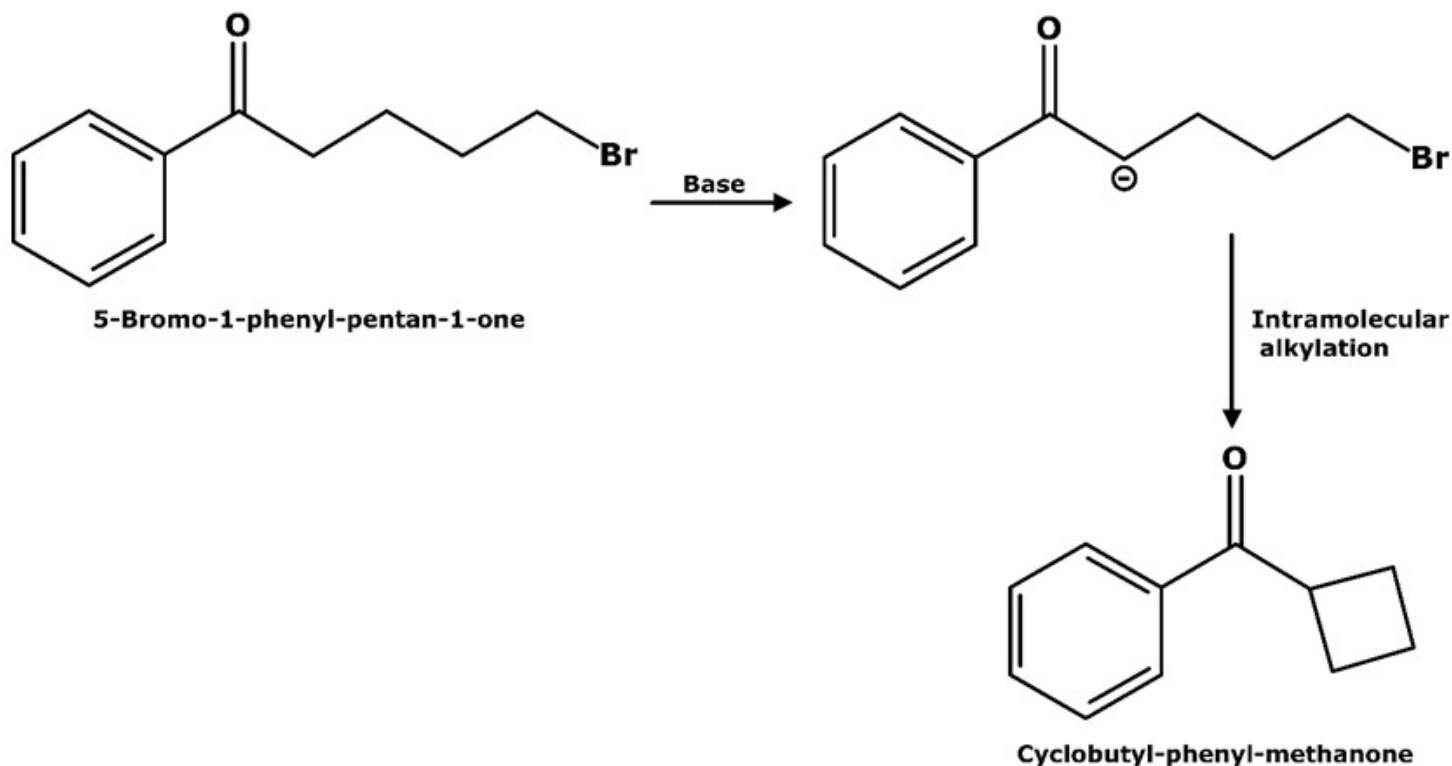


Scheme 8. Synthesis of cyclobutane ring from 1,3-dibromopropane

Other methods used to convert cyclobutanecarboxylic acid to cyclobutane are given below:

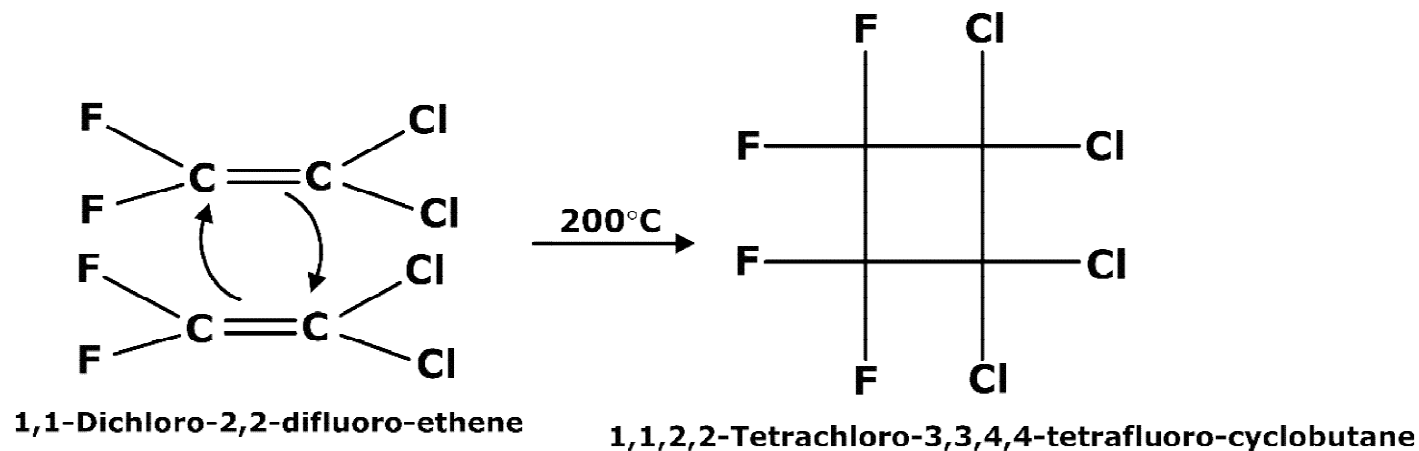


(ii) **By non-reversible cyclization:** The reaction of 5-bromo-1-phenyl-pentan-1-one with suitable base leads to the cyclization and formation of cyclobutane derivatives (Scheme 9).



Scheme 9: Synthesis of cyclobutane by intramolecular alkylation

(iii) **From difluorodichloroethene:** Difluorodichloroethene on heating at 200°C dimerizes to form 1,1,2,2-tetrachloro-3,3,4,4-tetrafluorocyclobutane (Scheme 10). This is also called [2+2] cycloaddition reaction.



Scheme 10. Synthesis of cyclobutane by [2+2] cycloaddition reaction

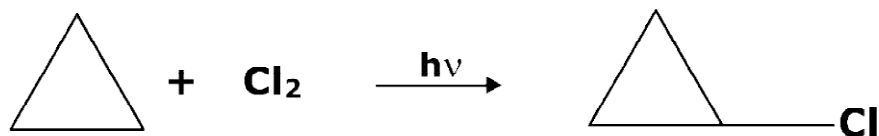
3. Reactions of small ring compounds

4.1 Reactions of cyclopropane

Cyclopropane having boiling point -33°C is one of the best anaesthetics known.

The cyclopropane ring undergoes ring substitution and ring opening reactions. Some reactions are discussed below.

(i) **Halogenation:** Cyclopropane undergoes halogenations in the presence of sunlight *via* free radical substitution reaction. For example, cyclopropane undergoes chlorination in the presence of sunlight to form chlorocyclopropane.

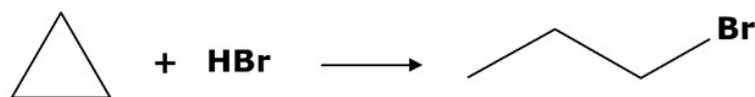


Cyclopropane

Chloro-cyclopropane

(ii) **Addition reactions:** Due to the increased π -character in carbon-carbon (C-C) bonds of cyclopropane, it reacts like an alkene in certain cases. For example,

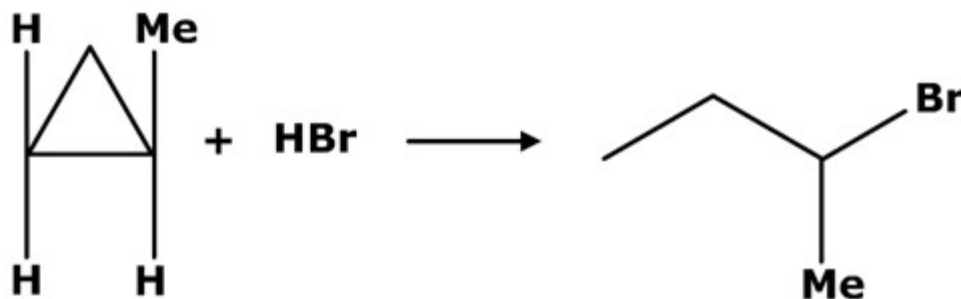
(a) **Hydrohalogenation:** Cyclopropane undergoes hydrohalogenation with mineral acids to form linear alkyl halides.



Cyclopropane

1-Bromo-propane

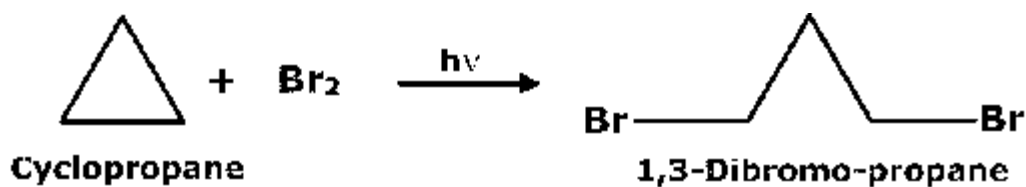
(b) Substituted cyclopropanes follow Markovnikov's rule in their addition to HBr.



Methyl-cyclopropane

2-Bromo-butane

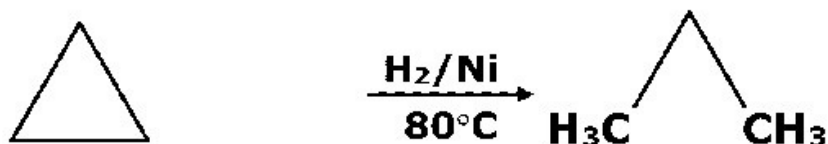
(b) **Bromination:** Cyclopropane undergoes bromination in the presence of Lewis acid catalyst like FeBr_3 and form 1,3-dibromoalkane.



Cyclopropane

1,3-Dibromo-propane

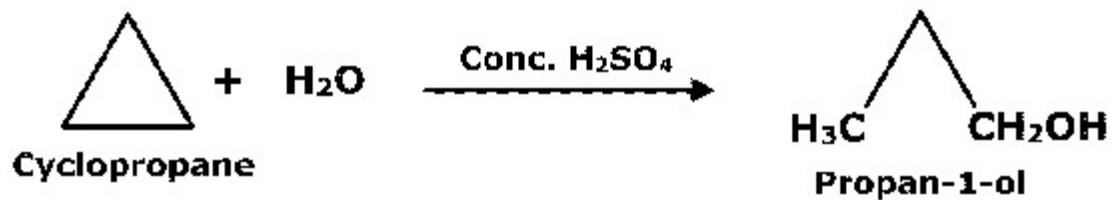
(c) **Hydrogenation:** Cyclopropane undergoes hydrogenation in the presence of raney nickel at 80°C and form propane.



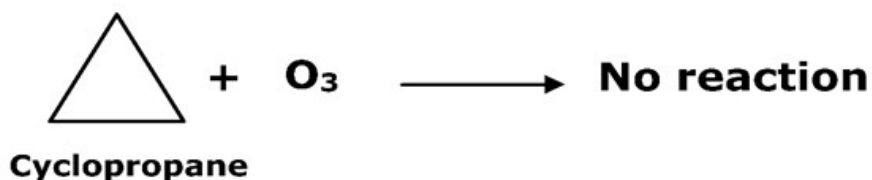
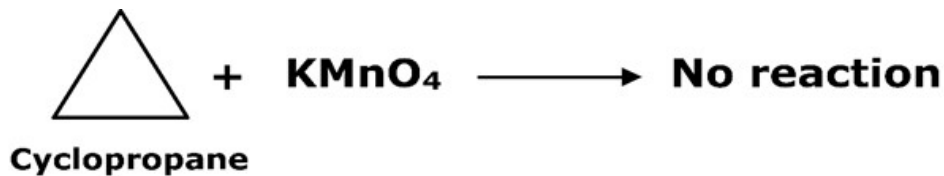
Cyclopropane

Propane

(d) **Hydration:** Cyclopropane undergoes water addition in the presence of conc. sulphuric acid used as catalyst and form propanol.



- But like alkenes cyclopropane does not get hydroxylated and shows no oxidation reaction with ozone:



4.2 Reactions of cyclobutane

