

Subject
Pharmaceutical Organic
Chemistry II

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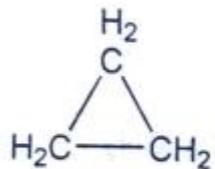
Cycloalkanes

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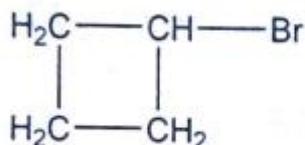


Alicyclic Compounds

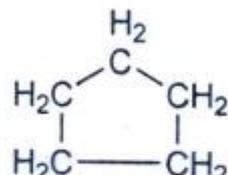
- Cycloalkanes or cycloparaffins are saturated hydrocarbons in which the carbon atoms are joined by single covalent bonds to form a ring. They are also called **Alicyclic Compounds**.



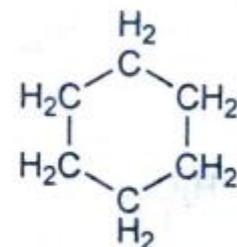
Cyclopropane



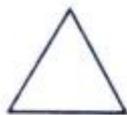
Bromocyclobutane



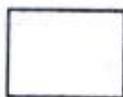
Cyclopentane



Cyclohexane



Cyclopropane



Cyclobutane



Cyclopentane

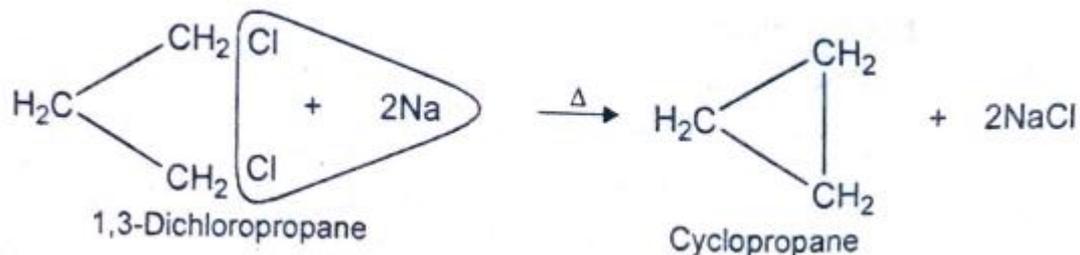


Cyclohexane

Method of Preparation of Cycloalkanes

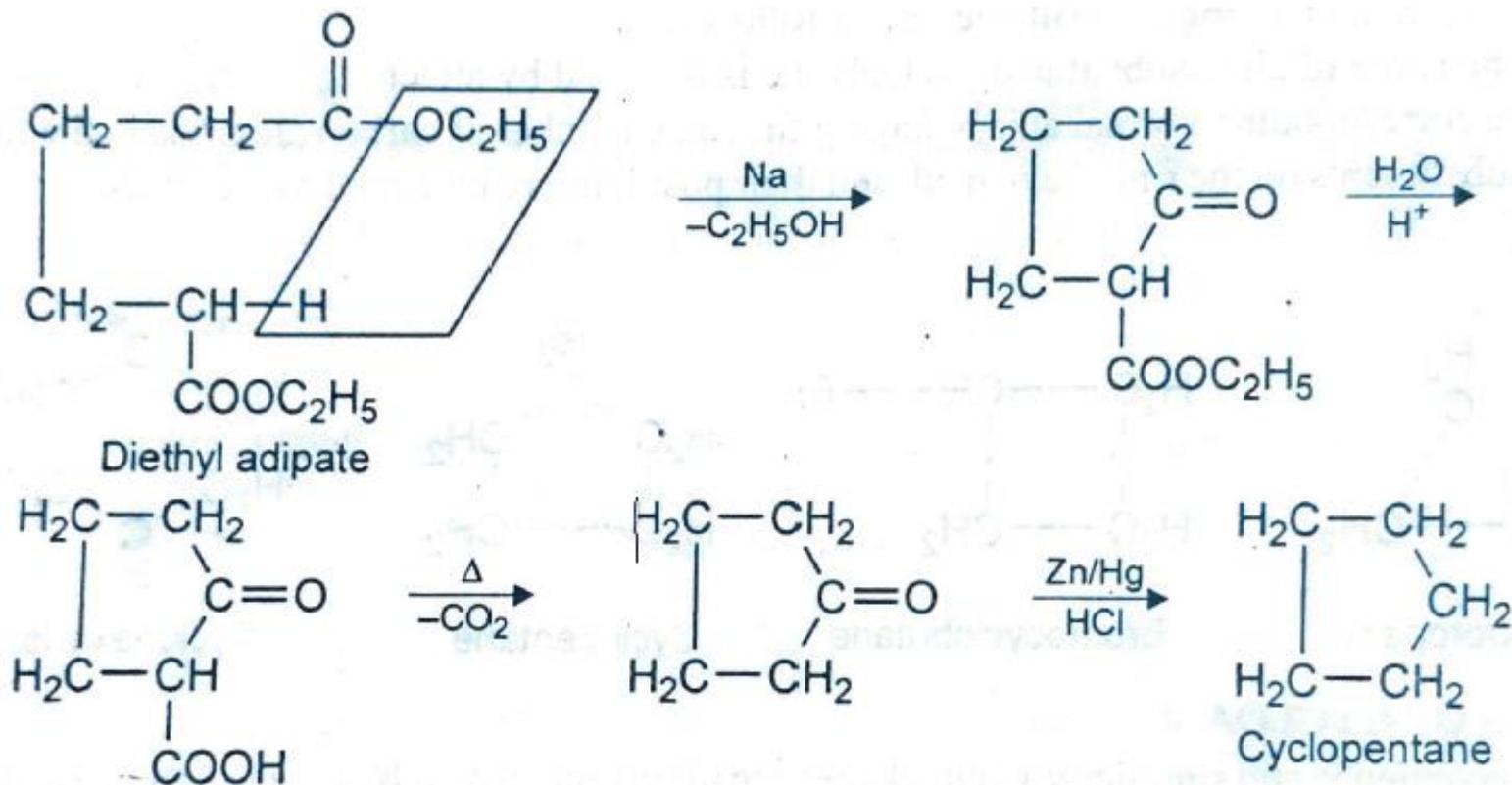
Cycloalkanes are obtained

1) From Dihalides: Terminal dihalides when treated with sodium or zinc form cycloalkanes. This reaction is an extension of Wurtz reaction and is useful for the preparation of 3-to 6-membered rings.



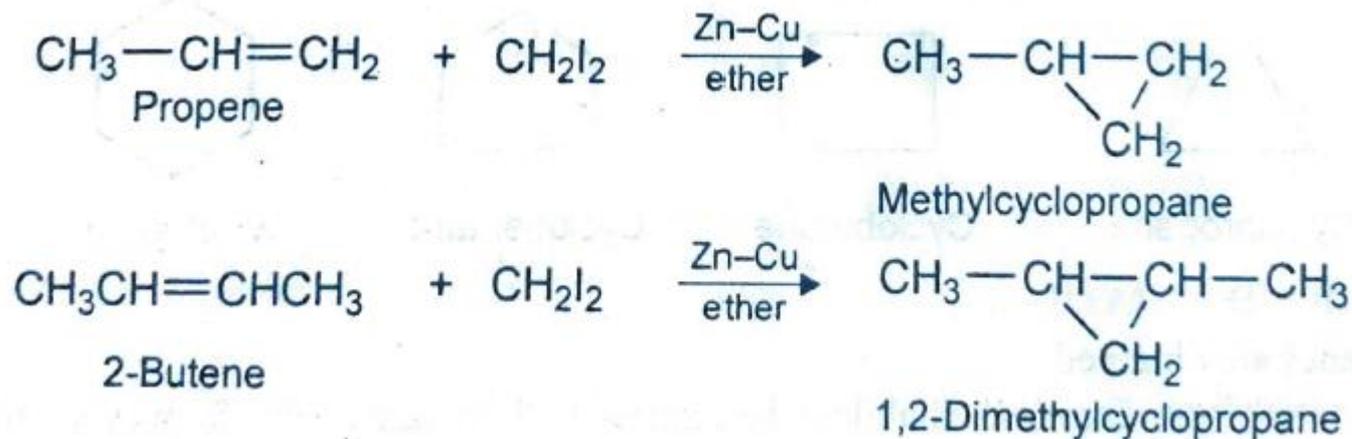
2) From Calcium Salts of Dicarboxylic Acids:

When the calcium or barium salts of dicarboxylic acids are heated, cyclic ketones are formed. The cyclic ketones can be readily converted into the corresponding cycloalkanes by Clemmensen reduction.



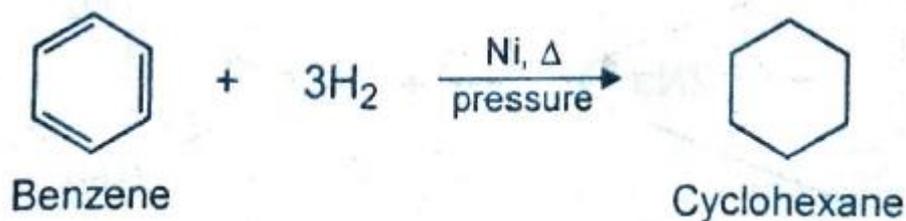
3) From Alkenes (Simmons-Smith Reaction):

When alkenes are treated with methylene iodide (CH_2I_2) in the presence of a zinc copper couple, cyclopropane derivatives are formed.



4) From Aromatic Hydrocarbons:

Six-membered cycloalkanes can be prepared by the catalytic reduction of benzene and its derivatives.



STABILITY OF CYCLOALKANES

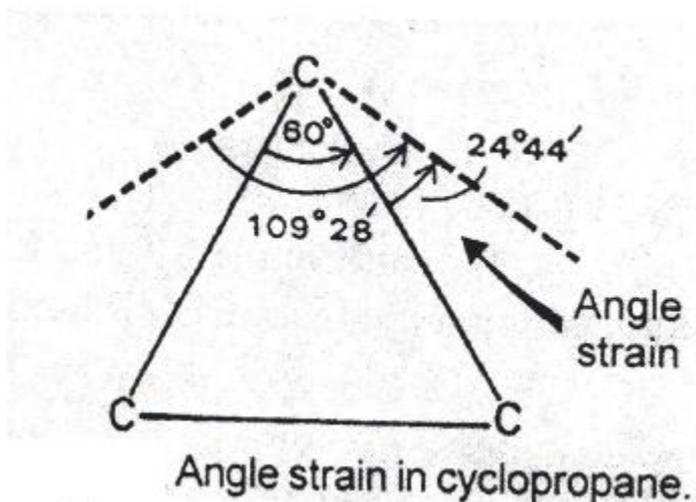
BAEYER STRAIN THEORY

In 1885 Adolf Baeyer proposed a theory to explain the relative stability of the first few cycloalkanes.

He based his theory on the fact that the normal angle between any pair of bonds of a carbon atom is $109^{\circ}28'$.

Baeyer postulated that any deviation of bond angles from the normal tetrahedral value would impose a condition of internal strain on the ring.

He also assumed that all cycloalkanes were planar.



Cyclopropane

In cyclopropane, the three carbon atoms occupy the corners of an equilateral triangle.

Thus cyclopropane has C-C bond angles of 60° . This implies that the normal tetrahedral angle of $109^\circ 28'$ between any two bonds is compressed to 60° , and that each of the two bonds involved is pulled in by $(109^\circ 28' - 60^\circ) = \mathbf{24^\circ 44'}$

$$\text{Calculation} = \frac{1}{2}(109^\circ 28' - 60^\circ)$$

$$= \frac{1}{2}(49^\circ 28')$$

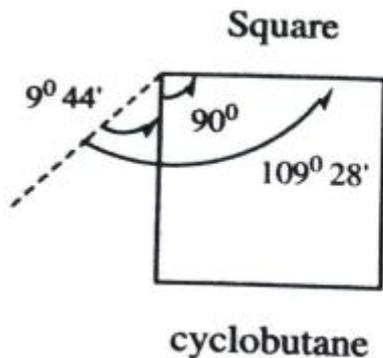
$$= \frac{1}{2}(48^\circ 28' + 60')$$

$$= \frac{1}{2}(48^\circ 88')$$

$$\text{Note: } 1^\circ = 60'$$

Cyclobutane:

In cyclobutane four carbon atoms occupy the corners of square, it has C-C-C bond angles of 90° . This shows deviation from the normal tetrahedral angle



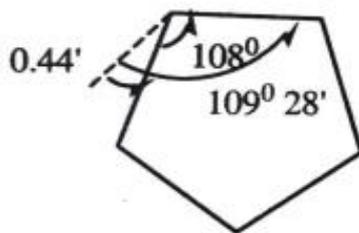
$$\begin{aligned} & \frac{1}{2} (109^\circ 28' - 90^\circ) && 60' = 1^\circ \\ & = 19^\circ 28' / 2 \\ & = +9^\circ 44' \end{aligned}$$

The value of $+9^\circ 44'$ represent its deviated from the normal tetrahedral value and compressed to satisfy the geometry of the ring

Cyclopentane

In cyclopentane five carbon atoms occupy the corners of regular pentagon, it has C-C-C bond angles of 108° . This shows each bond deviated from the normal tetrahedral angle.

Pentagon



cyclopentane

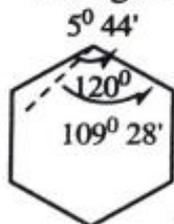
$$\begin{aligned} & \frac{1}{2} (109^\circ 28' - 108^\circ) \quad 60' = 1^\circ \\ & = 1^\circ 28' / 2 \text{ (or) } 0.88' / 2 \\ & = +0.44' \end{aligned}$$

The value of $+0^\circ.44'$ represents its deviation from the normal tetrahedral value and is compressed to satisfy the geometry of the ring.

Cyclohexane

In cyclohexane six carbon atoms occupy the corners of a regular hexagon, it has C-C-C bond angles of 120° . This shows each bond deviated from the normal tetrahedral angle.

Hexagon



cyclohexane

$$\begin{aligned} & = 11^\circ 28' / 2 \text{ (or) } 10^\circ 88' / 2 \\ & = -5^\circ 44' \end{aligned}$$

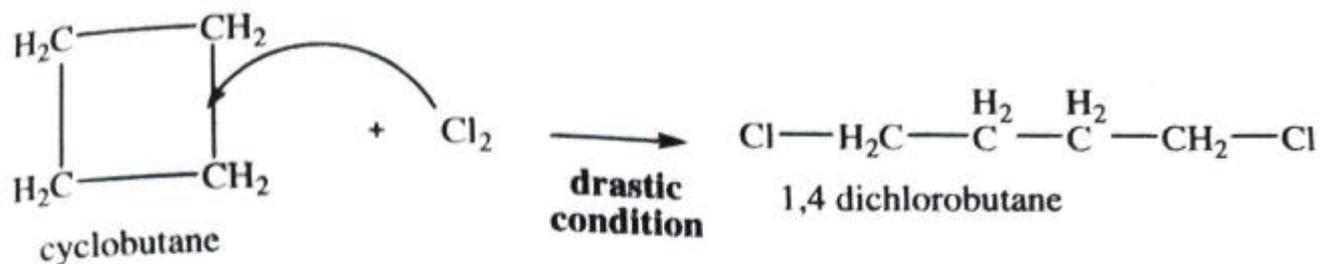
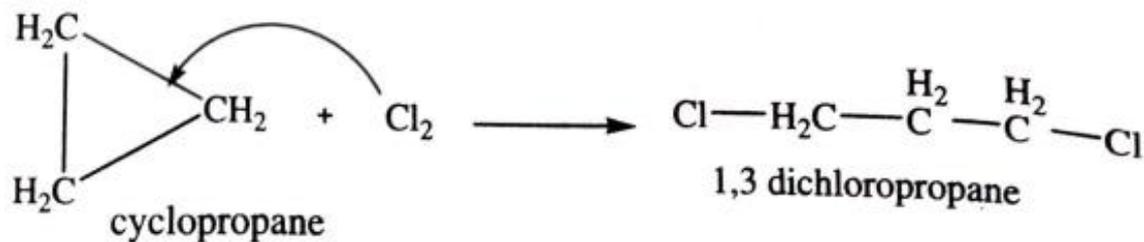
The value of $-5^\circ 44'$ represents its deviation from the normal tetrahedral value and is broadened to satisfy the geometry of the ring.

According to the Bayer strain theory,

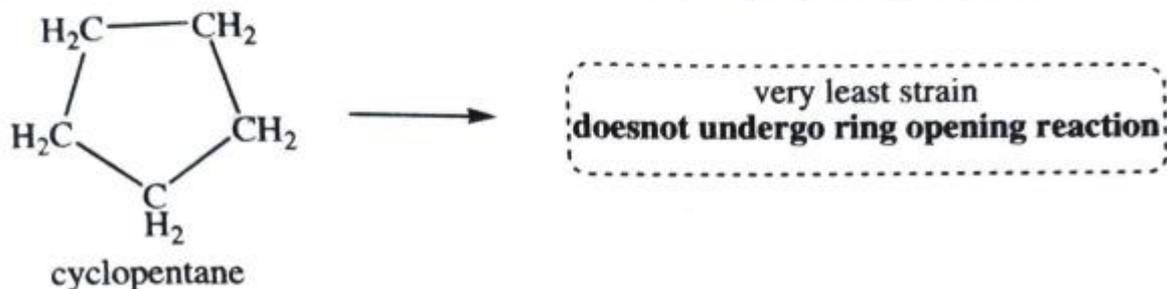
The angle strain is maximum in cyclopropane, due to this cyclopropane is highly strained molecule and also unstable, so it's easily undergoes the ring opening reaction because of bond angle was compressed than normal tetrahedral value.

Cyclopropane is react with Cl_2 , Br_2 , HBr , H_2 (Ni) to give open- addition product.

Example,



The cyclopentane angle strain is minimum, this shows the cyclopentane is under very least strain and most stable, due to this it doesnot undergo ring opening reaction.



Limitations of Baeyer Theory

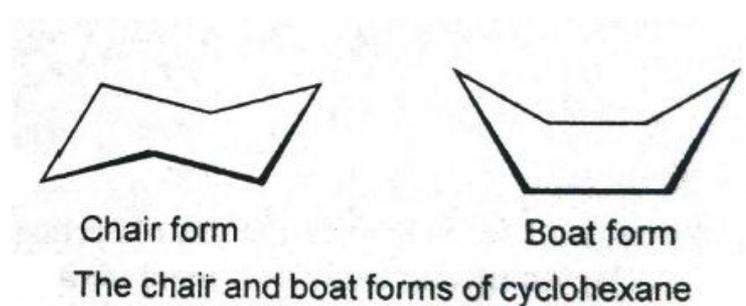
1. The Baeyer was not able to describe the impact of an angle pressure in the larger structures.
2. According to him, cyclohexane is less stable than cyclopentane, but the reality is the opposite of this.
3. He stated that due to negative pressure, larger ring structures are not possible, but they do exist and are highly stable.
4. For the removal of angle pressure, larger ring structures are wrinkled (puckered) instead of being planar (flat).

SACHSE MOHR THEORY (THEORY OF STRAINLESS RINGS)

In order to account for the stability of cyclohexane and higher members, Sache and Mohr (1918) proposed that such rings can become free from strain if all the ring carbons are not forced into one plane.

If the ring assumed a 'folded' or puckered' condition, the normal tetrahedral angles of $109^{\circ}28'$ are retained and as a result, the strain within the ring is relieved.

For example, cyclohexane can exist in two non-planar puckered conformations both of which are completely free from strain. These are called the chair form and the boat form because of their shape.



Such non-planar strain-free rings in which the ring carbons can have normal tetrahedral angles are also possible for higher cycloalkanes

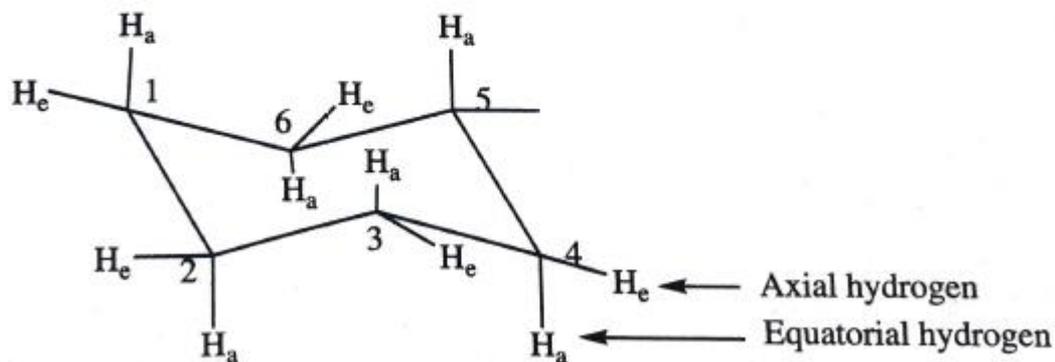
The chair form of cyclohexane is more stable than the boat form.

Under ordinary conditions, cyclohexane molecules will mostly exist in the chair form.

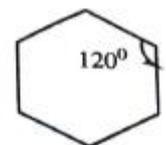
Examination of the chair form of cyclohexane reveals that the hydrogen atoms can be divided into two categories. Six of the bonds to hydrogen atoms point straight up or down almost perpendicular to the plane of the molecule. These are called **Axial Hydrogens**. The other six hydrogens lie slightly above or slightly below the plane of the cyclohexane ring, and are called **Equatorial Hydrogens**.

Hydrogen atoms in cyclohexane can be called as two categories

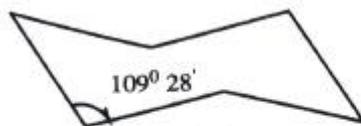
- Axial hydrogen (H_a) - Perpendicular to the plane
- Equatorial hydrogen (H_e) - Parallel to the plane



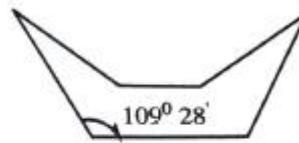
This chair form & boat form creates strain less rings in which the ring carbon can normal tetrahedral angles so this forms are possible for all higher cycloalkanes (rings larger than 5 members). In case of cyclohexane chair form is more stable than boat form.



cyclohexane



chair form



boat form



Staggered conformation

No crowding of hydrogens
Free from strain



Eclipsed conformation

Crowding of hydrogens
Torsional strain

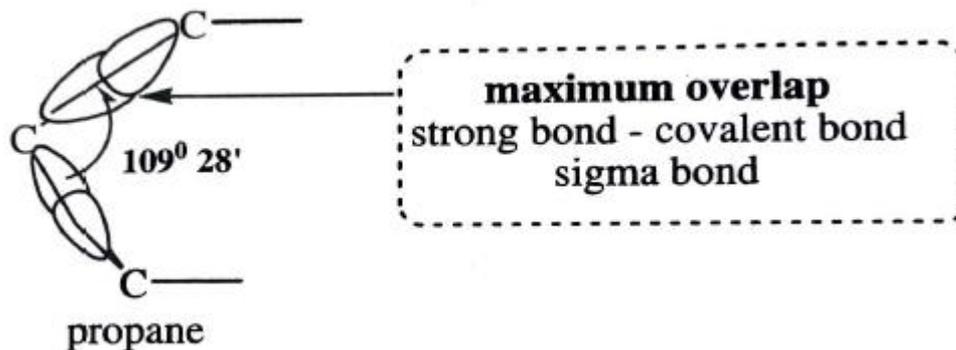
Orbital Picture of Angle Strain (Coulson and Moffitt's Modification)

(or) Relative stability of cycloalkane according to molecular orbital theory)

1. The overlap of orbital of the atoms is involved in the formation of bond.
2. The maximum extent of overlap creates strong bond formation.

The carbon is bonded to 4 other atoms, its bonding orbital (sp^3 orbital) are directed to the corner of a regular tetrahedral atom.

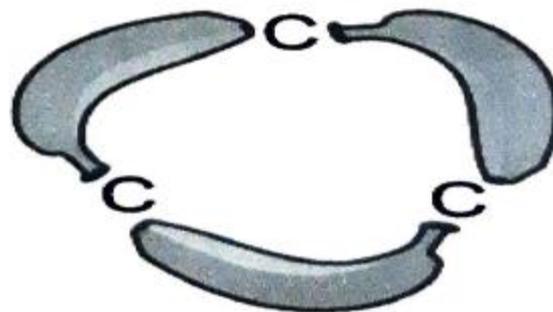
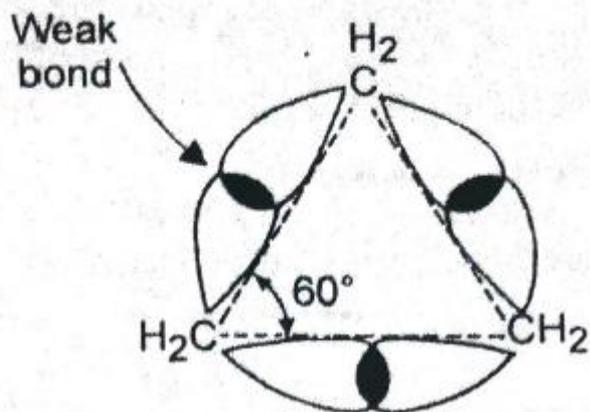
The C-C bond will be strongest when an sp^3 orbital of one carbon maximum overlap with sp^3 orbital of another carbon. This will takes place only bond angle should be $109^\circ 28'$ and sp^3 orbitals overlap along their axis.



Cyclopropane:

According to the quantum mechanical calculation and x-ray studies Coulson and Moffitt's proposed bent bonds between carbon atoms of cyclopropane rings.

Bent bonds or banana bonds are found in strained organic compounds such as cyclopropane. In cyclopropane, the maximum electron density between two carbon atoms does not correspond to the internuclear axis, hence the name bent bond. In cyclopropane, the interorbital angle is 104° .



The C-C bond orbitals provide a site for the attack by acids that are the first step of ring opening.

Ring opening is due to weakness of the carbon-carbon bonds.