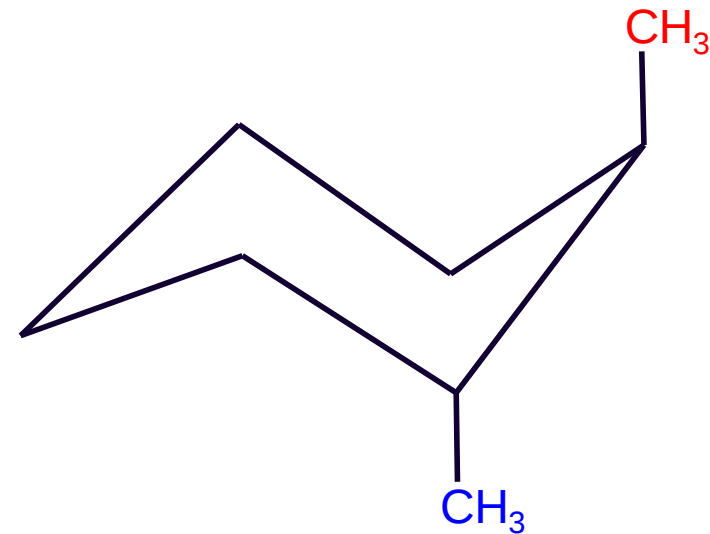
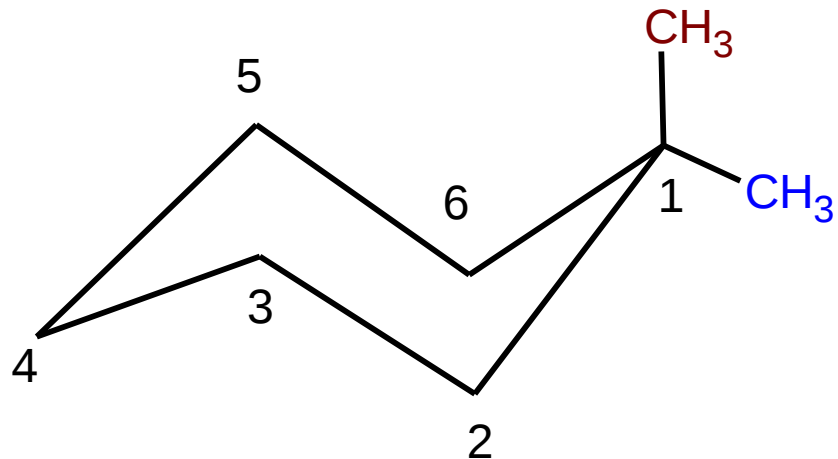
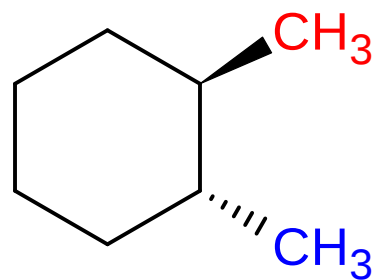
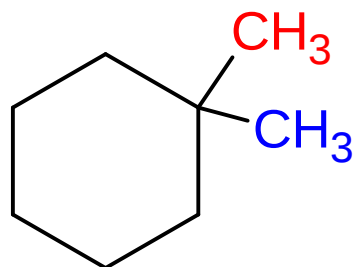


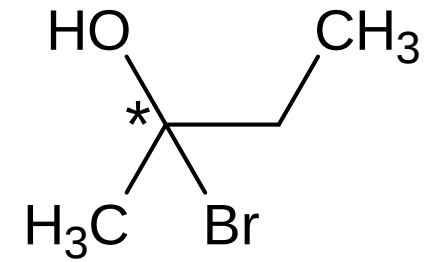
STEREOCHEMISTRY OF DISUBSTITUTED CYCLOHEXANE



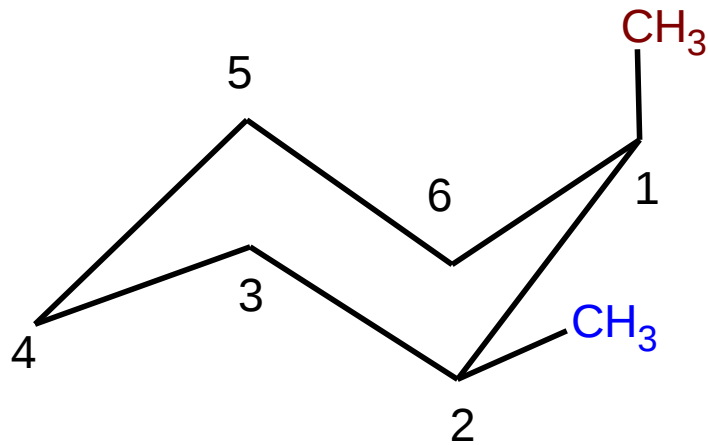
Stereochemistry

Stereochemistry is the branch of chemistry deals with study of three dimensional structures of organic compounds.

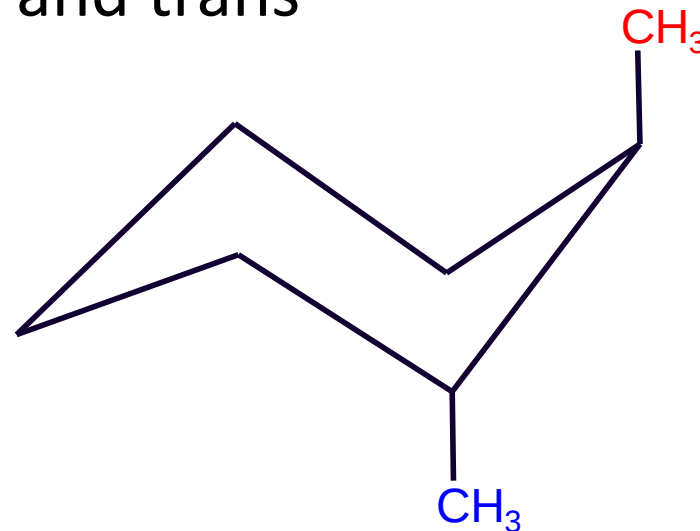
Chiral Carbon: Carbon atom to which four different atoms/ groups are attached.



Geometrical Isomerism: Cis and trans



Cis Isomer



Trans Isomer

Chiral carbon

Stereochemistry

Optical isomerism: Compound that rotates the plane of plane polarized light is said to be optically active compound.

Dextrorotatory (+) : Rotates the plane of plane polarized light in clockwise direction (d)

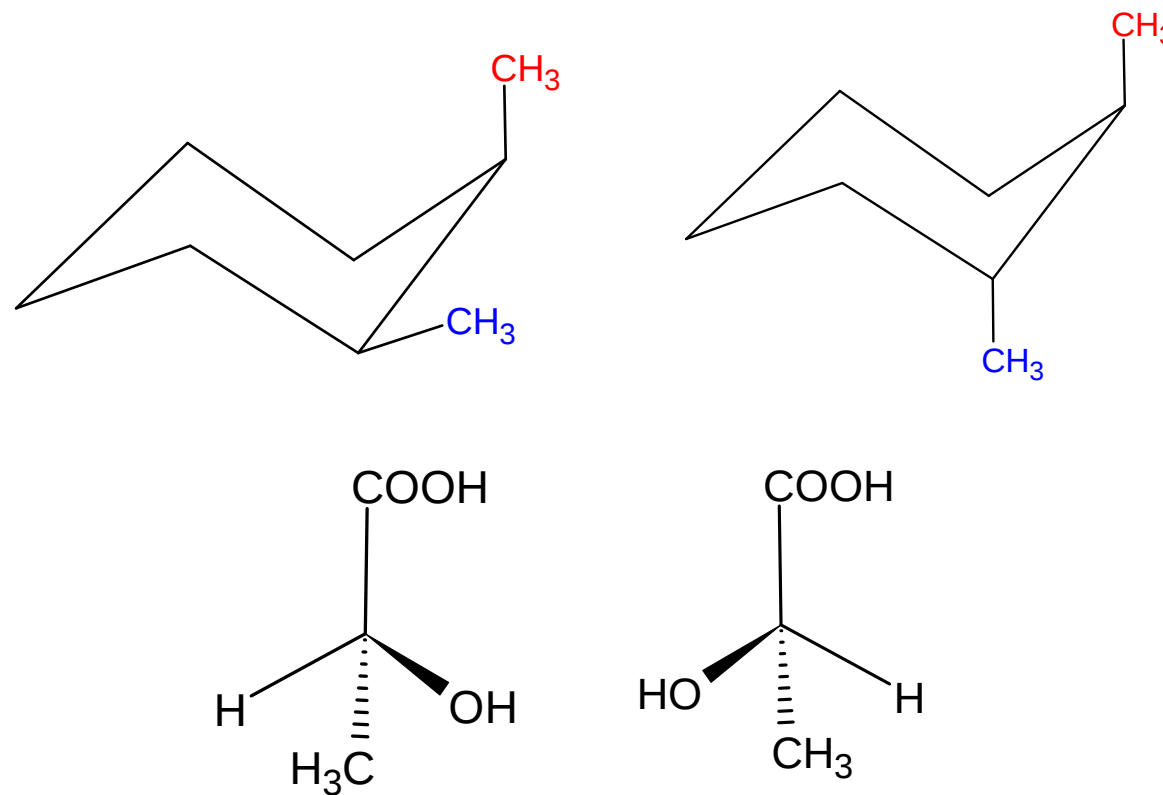
Levorotatory (-) : Rotates the plane of plane polarized light in anticlockwise direction (l)

Stereochemistry

Stereoisomers: They have same molecular formula, same bonding connectivity but different orientation of atoms/groups in space.

Enantiomers: A chiral molecule/object has a non superimposable mirror image.

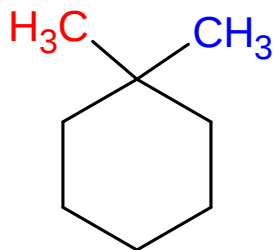
Diastereomers: Stereoisomers which are not enantiomers are called as diastereomers.



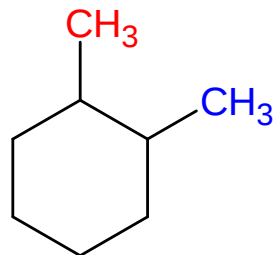
Disubstituted Cyclohexane

In disubstituted cyclohexane two hydrogen atoms of cyclohexane molecule are replaced by two other atoms or groups.

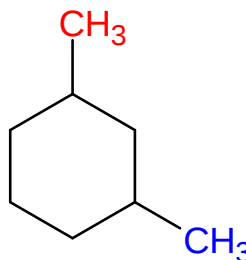
Depending upon relative position of two substituents following isomers are possible



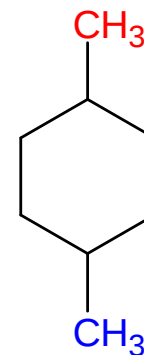
1,1
disubstituted



1,2
disubstituted



1,3
disubstituted

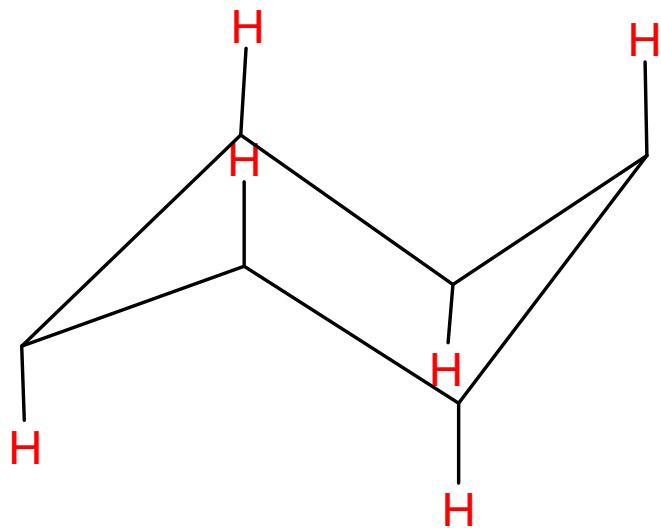


1,4
disubstituted

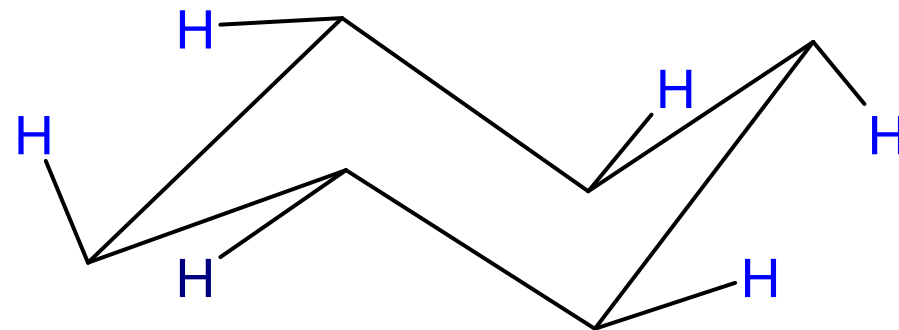
Axial and Equatorial Hydrogen

Axial Hydrogens: Hydrogen atoms perpendicular to the ring in the chair configuration.

Equatorial Hydrogens: Hydrogen atoms present in the general plane of the molecule, around the equator.



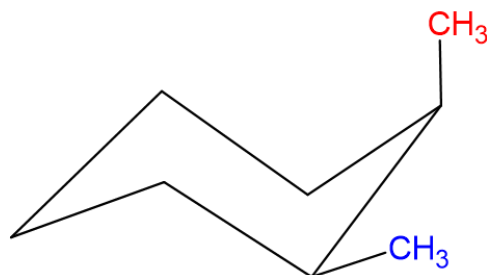
Axial Hydrogens



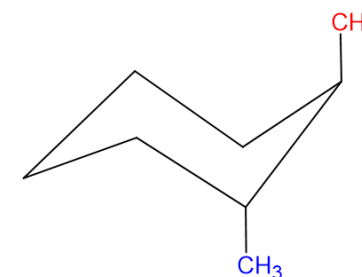
Equatorial Hydrogens

Cis and Trans Isomers of Cyclohexane

- **Cis Isomer:** In cis isomer both substituents are present on the same side of the general plane of molecule
- **Trans Isomer:** In trans isomer one substituent is present above the general plane of molecule while other substituent present below the plane.



Cis Isomer



Trans Isomer

Ring Flip: Conversion of one chair conformation of cyclohexane into another chair conformation by rotation around carbon-carbon single bond.

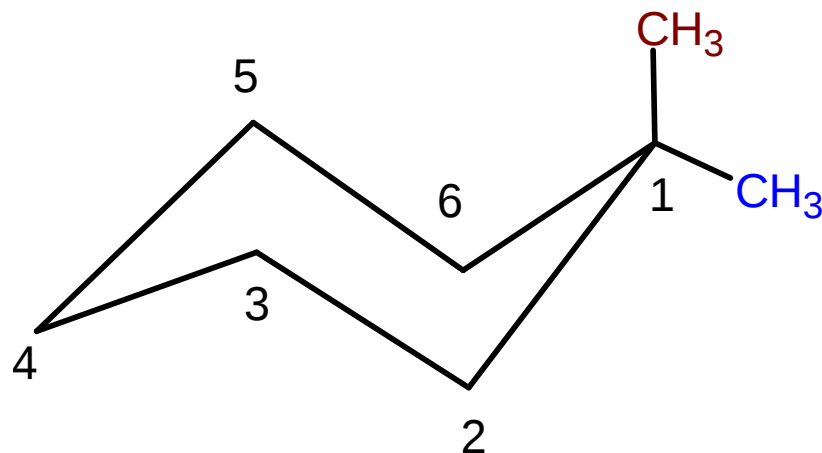
On ring flipping axial substituents become equatorial, and equatorial substituents become axial.

1,1-Disubstituted Cyclohexane

Both substituents are present on same carbon atom.

Optical Isomerism: 1,1-dimethyl cyclohexane posses plane of symmetry (passing through C1 and C4),hence optical isomerism is not possible

Geometrical isomerism: No geometrical isomerism as both substituents are present on same carbon atom.

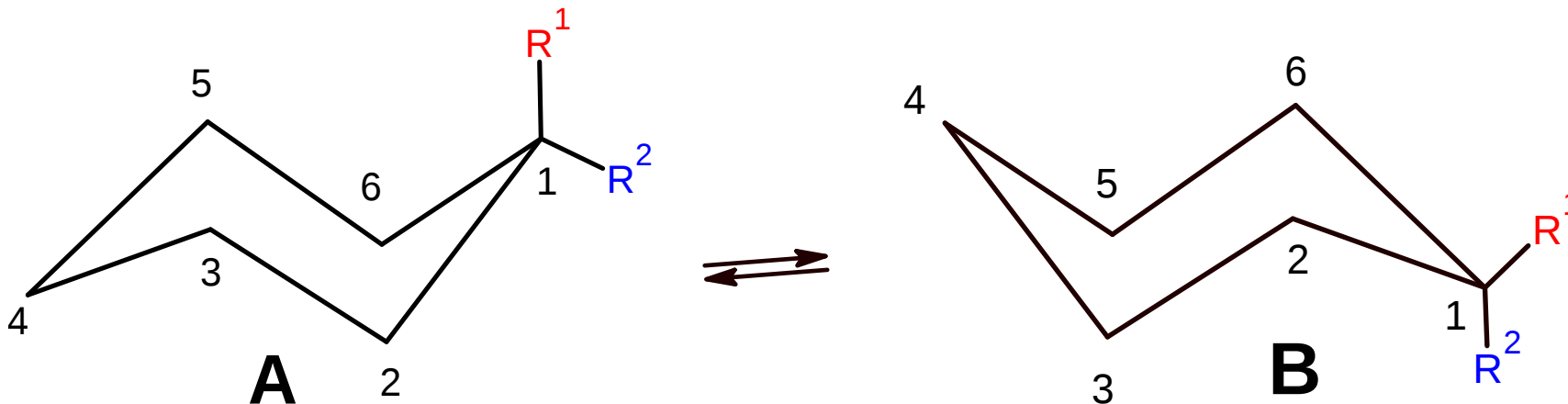


1,1-Disubstituted Cyclohexane

Conformational isomerism: Two distinct chair conformations are possible for 1,1-disubstituted cyclohexane.

Ring flipping of conformation **A** produce conformation **B**.

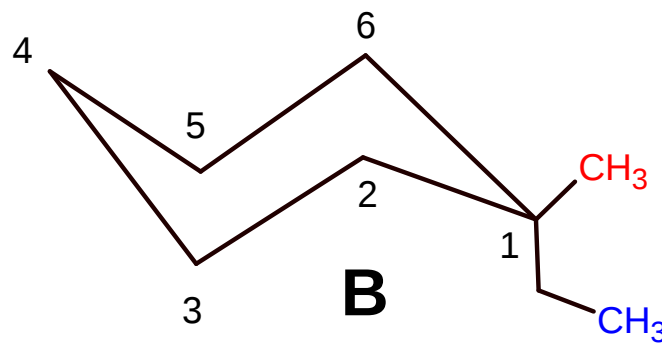
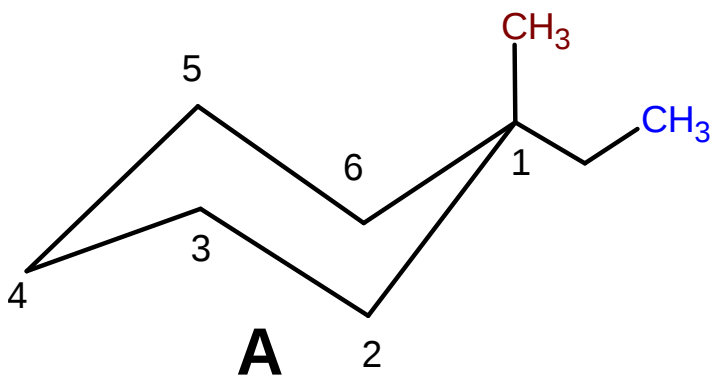
In conformation **A** substituent R^1 is axial while substituent R^2 is equatorial, On ring flipping axial substituent become equatorial and equatorial substituent become axial



When R^1 and R^2 are same , then A and B are also same

1,1-Disubstituted Cyclohexane

- **Relative Stability:** Stability of conformation is depends upon the size of the substituent.
- The conformation in which larger(bulkier) group is present at equatorial position is more stable.
- Example- 1-ethyl,1-methyl cyclohexane



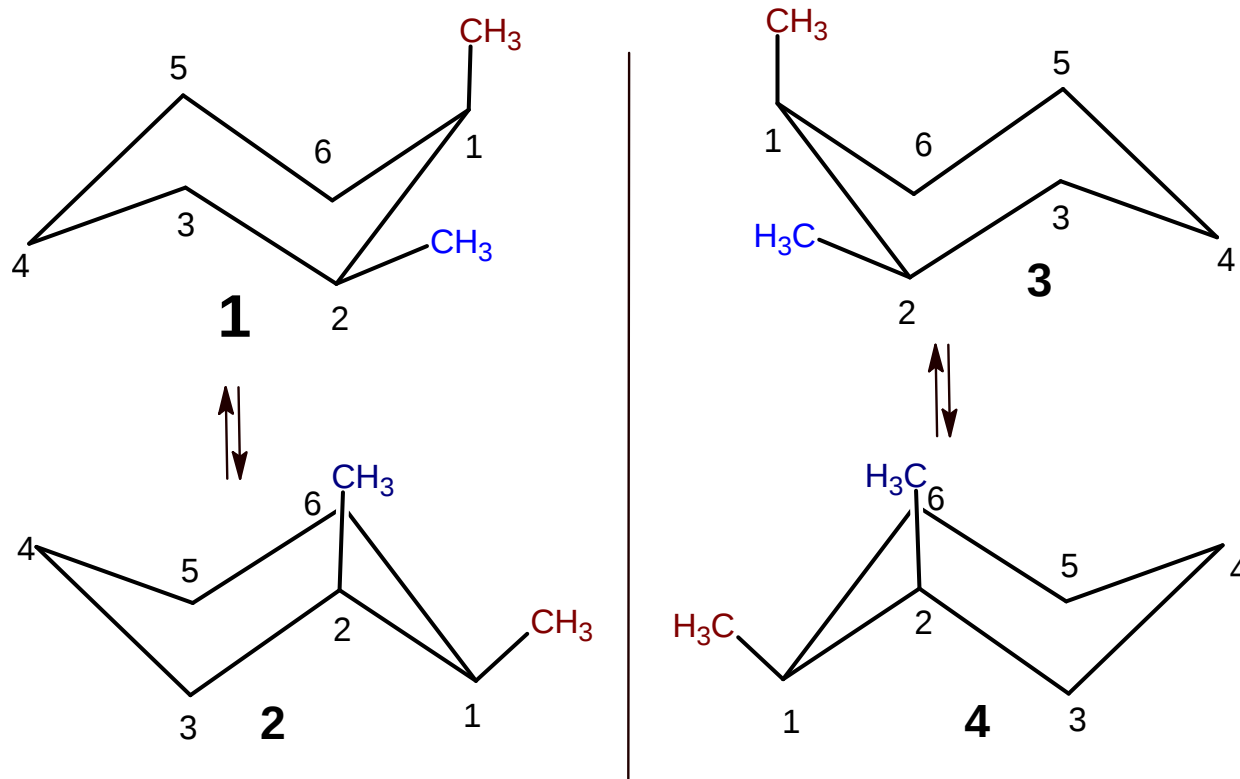
Conformation A is more stable than conformation B

1,2-Disubstituted Cyclohexane [Cis isomer (a, e form)]

Cis 1,2 dimethyl cyclohexane

Cis isomer: Both substituents are on the same side of general plane of the molecule.

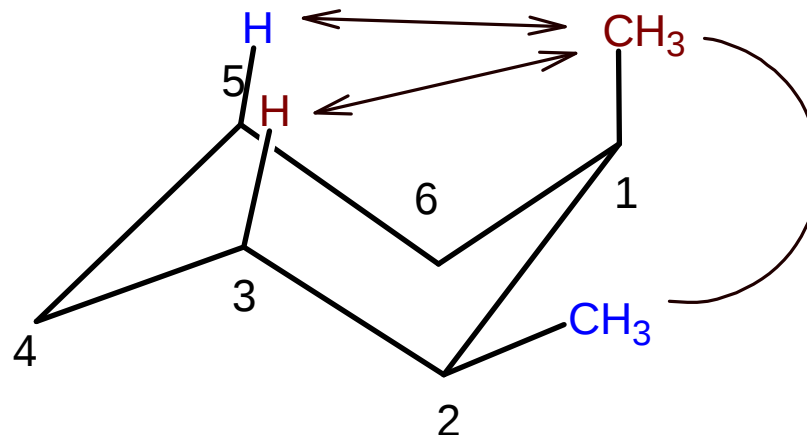
Optical Isomerism: There is no element of symmetry, thus molecule is expected to be optically active but it is optically inactive.



Conformation 1 and 3 are non superimposable mirror images of each other (Enantiomer). Similarly Conformation 2 and 4 are also enantiomer. Flipping of conformation 1 produce conformation 2 having equal stability, similarly flipping of 3 produce conformation 4 with same stability. Thus two conformations are interconverted rapidly to each other via ring flipping at normal temperatures and exist in equal proportions. Thus molecule exist as a racemic mixture.

Cis 1,2-Dimethyl Cyclohexane

Cis isomer (a,e form), Relative Stability



In Cis-1,2- Dimethyl cyclohexane, axial methyl group have two $\text{CH}_3\text{-H}$, 1,3- diaxial interactions and one butane gauche interaction between two methyl groups. Thus total strain is 2.7 kcal/mole

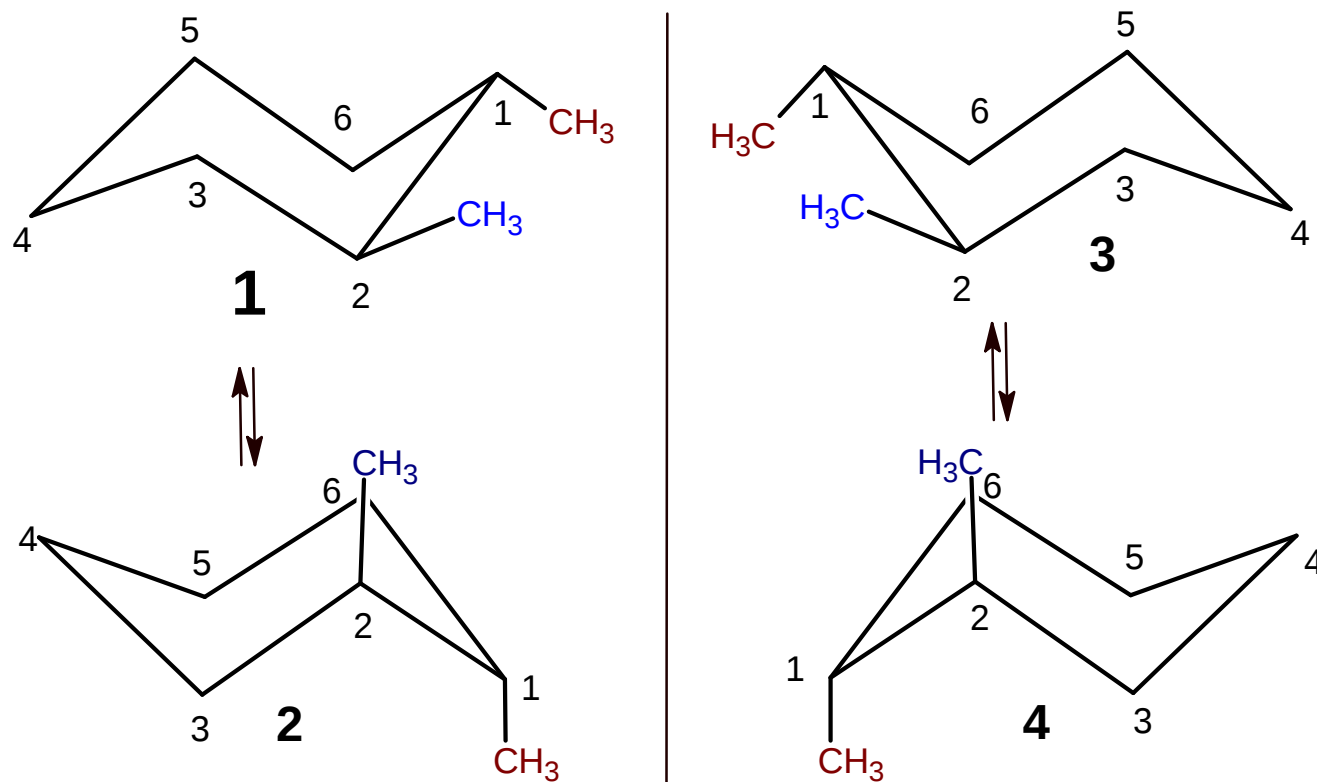
One gauche Interaction (0.9 kcal/mole) + Two $\text{CH}_3\text{-H}$ diaxial interaction (1.8 kcal/mole) = 2.7 kcal/mole

1,2-Disubstituted Cyclohexane

A) Trans 1,2 dimethyl cyclohexane (e, e or a, a form)

Trans isomer: Substituents are on the opposite side of general plane of molecule.

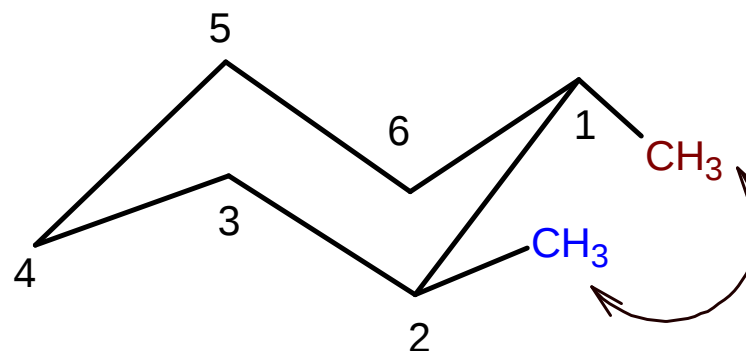
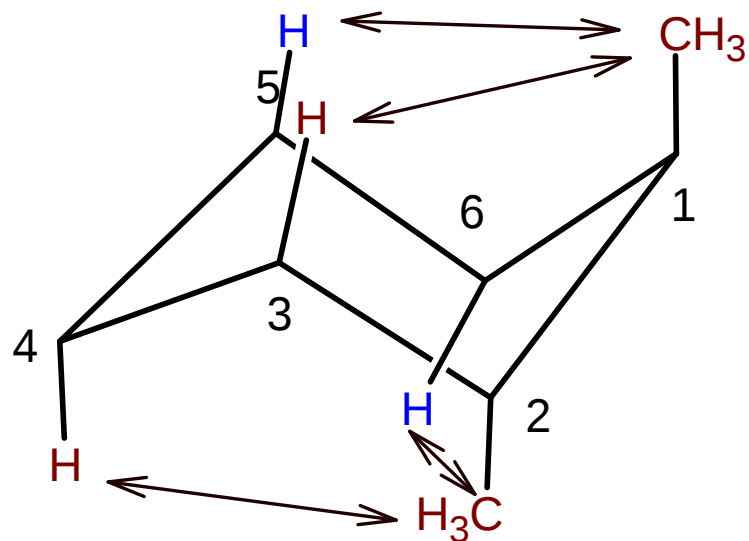
Optical Isomerism: There is no element of symmetry, thus as expected molecule is optically active.



As expected trans 1,2 dimethyl cyclohexane exist in pair of enantiomers 1 and 3 or 2 and 4. Conformation 1 on ring flipping produce less stable diaxial conformation 2. Conformation 1 and 2 or 3 and 4 are diastereomers of each other

1,2-Dimethyl Cyclohexane

Trans isomer, Relative stability

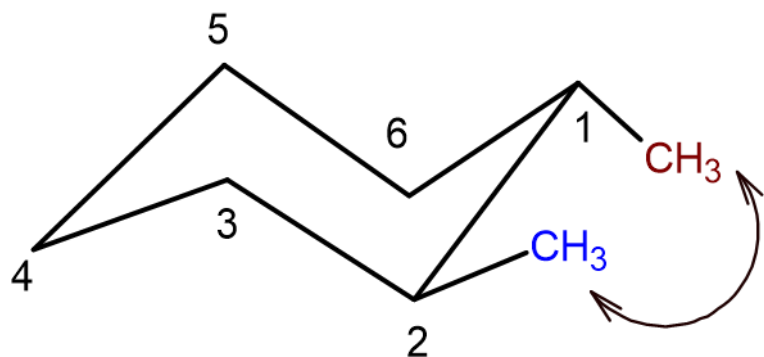


In trans 1,2- Dimethyl cyclohexane (diaxial form), each axial methyl groups have two CH₃-H, 1,3- diaxial interactions. Thus total 4 such interactions contribute $0.9 \times 4 = 3.6$ kcal/mole strain

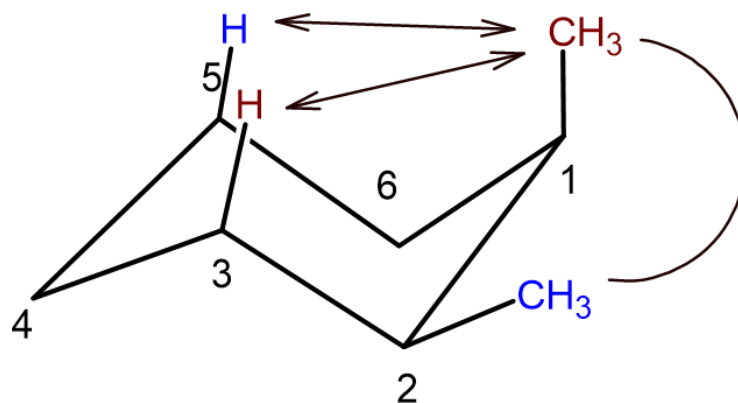
In trans 1,2- Dimethyl cyclohexane (diequatorial form), There is one butane gauche interaction between two methyl groups. Thus total energy of molecule is 0.9 kcal/mole

Stability order

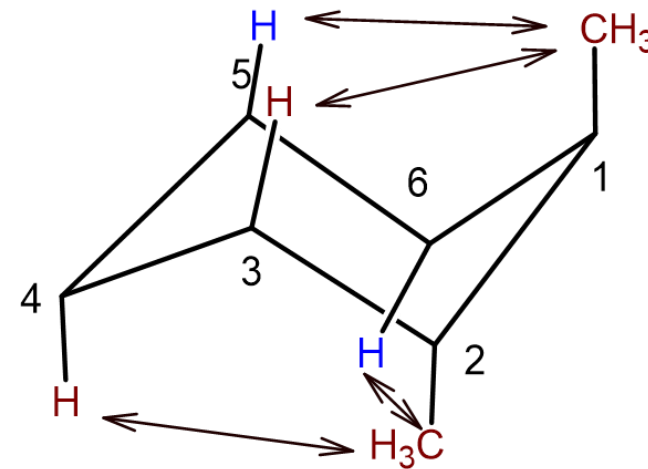
1,2-Disubstituted Cyclohexane



Trans (e, e)
0.9 kcal /mole



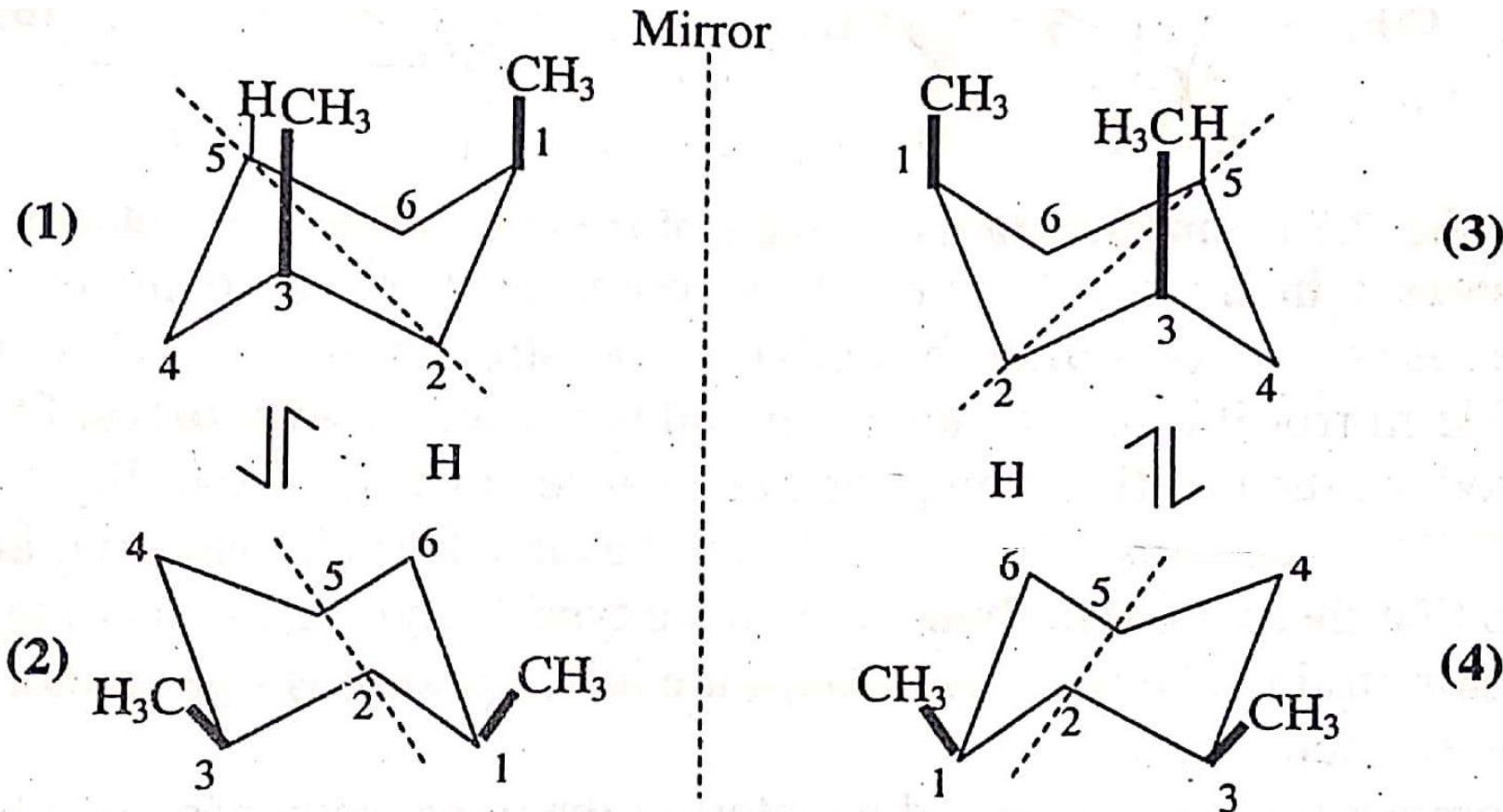
Cis (a, e)
2.7 kcal /mole



Trans (a, a)
3.6 kcal /mole

1,3-Disubstituted Cyclohexane

Cis 1,3 dimethyl cyclohexane (a, a or e, e form)

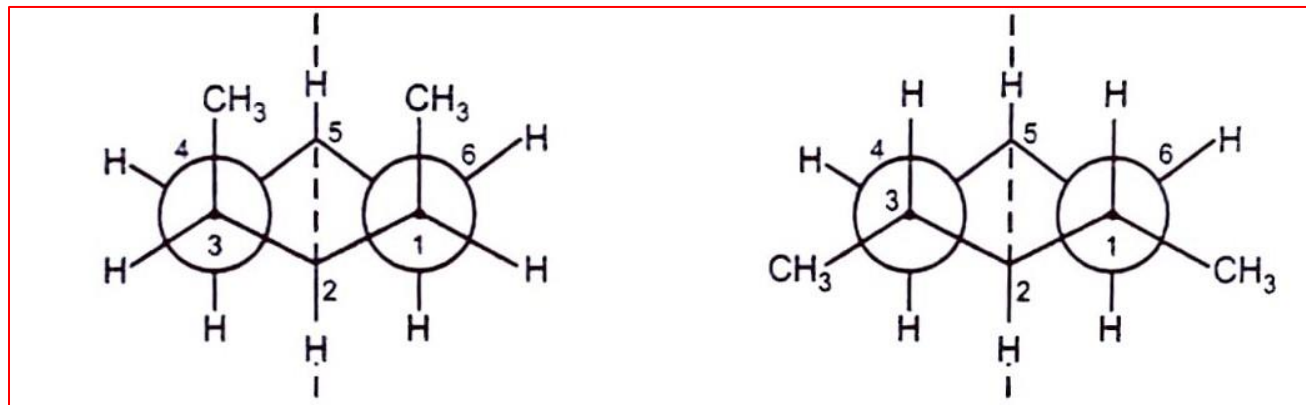
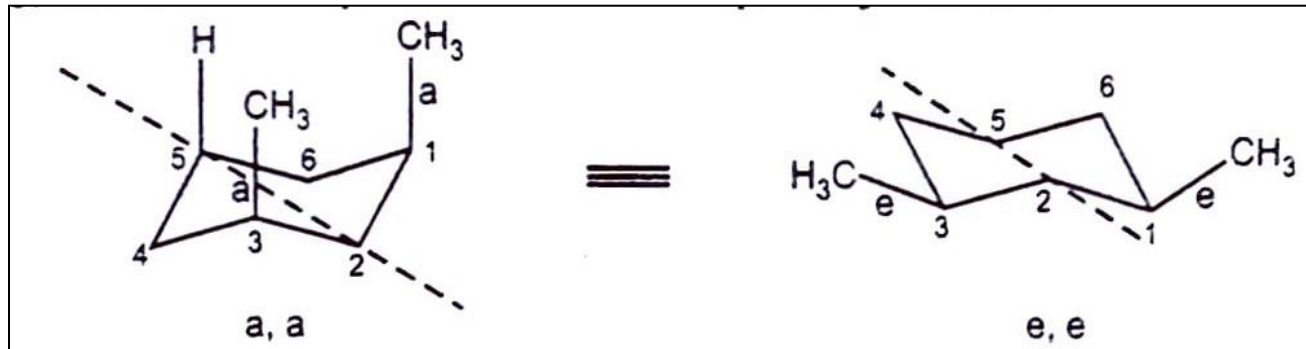


Conformation 1 and 3 as well as 2 and 4 are non super imposable mirror images of each other (enantiomers)

1,3-Disubstituted Cyclohexane

Cis 1,3 dimethyl cyclohexane (a, a or e, e form)

Optical Isomerism: Cis 1,3 dimethyl cyclohexane possess a plane of symmetry (Passing through C2 and C5) Hence it is meso compound and is optically inactive



Plane of Symmetry passing through C2 and C5 can easily seen in Newman's structure

1,3-Disubstituted Cyclohexane

Cis isomer, Relative stability

In cis 1,3- Dimethyl cyclohexane (diaxial form), each axial methyl groups have two butane gauche interactions.

(Methyl group at C1 is gauche to C3 and C5 carbon of the ring and methyl group at C3 is gauche to C1 and C5 carbon of the ring)

These four interactions contributes 3.6 kcal/mole energy.

In addition to this there is one interaction between two CH₃ groups which contribute 1.8 kcal/mole.

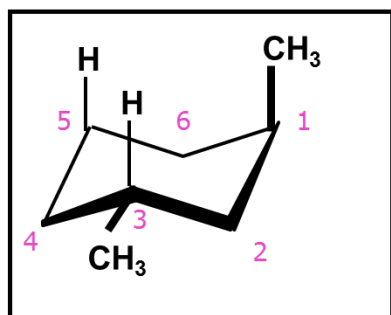
Thus total strain is $3.6 + 1.8 = 5.4$ kcal/mole.

In diequatorial form (e.e), there is no such interaction, hence strain is 0 kcal/mole

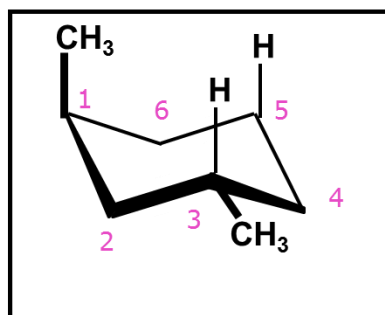
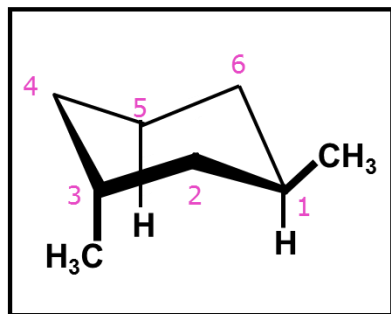
1,3-Disubstituted Cyclohexane

Trans isomer (a,e form)

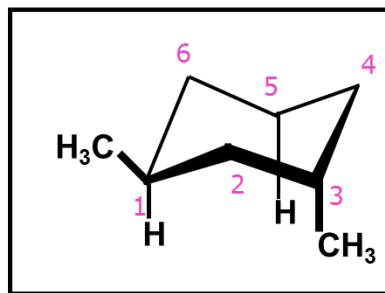
Optical Isomerism: In trans 1,3 dimethyl cyclohexane there is no plane of symmetry. Hence molecule is expected to be optically active.



(1) $\rightleftharpoons$



(3) $\rightleftharpoons$

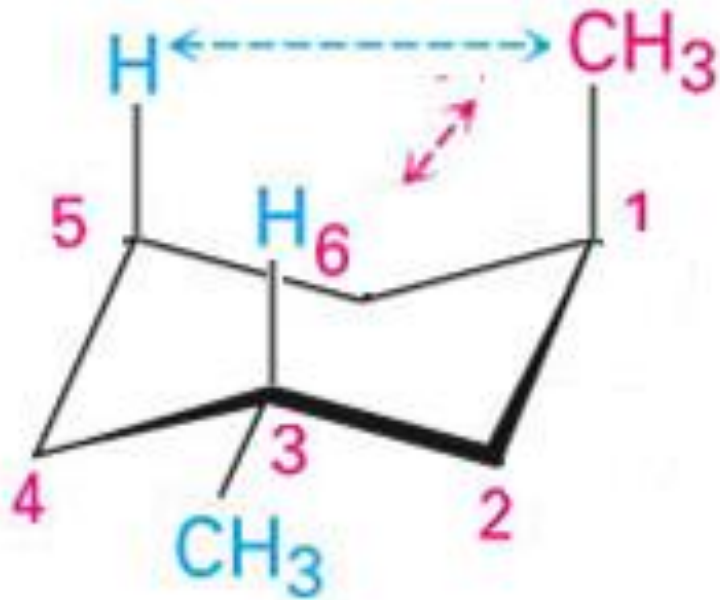


(4)

Conformation 1 and 3 as well as 3 and 4 are non super imposable mirror images of each other (enantiomers). Ring flipping produce identical compounds and have equal energy.

1,3-Disubstituted Cyclohexane

Trans isomer, Relative stability



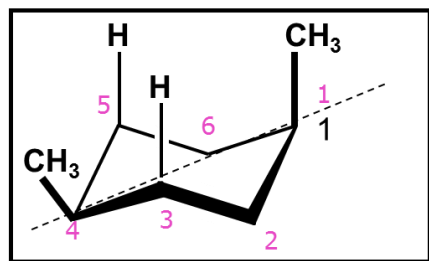
In trans 1,3- Dimethyl cyclohexane, axial methyl groups have two CH₃-H, 1,3 diaxial interaction. These two interactions contributes 1.8 kcal/mole energy. $0.9 + 0.9 = 1.8 \text{ kcal/mole}$.

Stability order Cis 1,3 (e, e) 0 kcal/mole > Trans 1,3 (a, e) 1.8 kcal/mole > Cis 1,3(a, a) 5.4kcal/mole

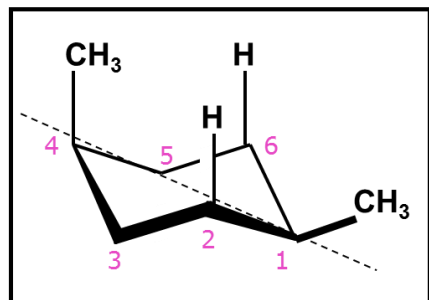
1,4-Disubstituted Cyclohexane

Cis isomer (a,e form)

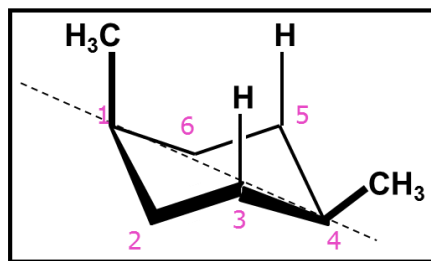
Optical Isomerism: Cis 1,4 dimethyl cyclohexane possess a plane of symmetry (Passing through C1 and C4) Hence it is optically inactive and exist in meso form.



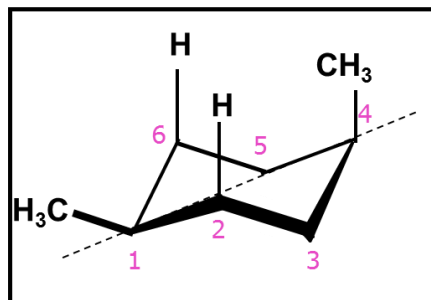
(1) ⇌



(2)



(3) ⇌

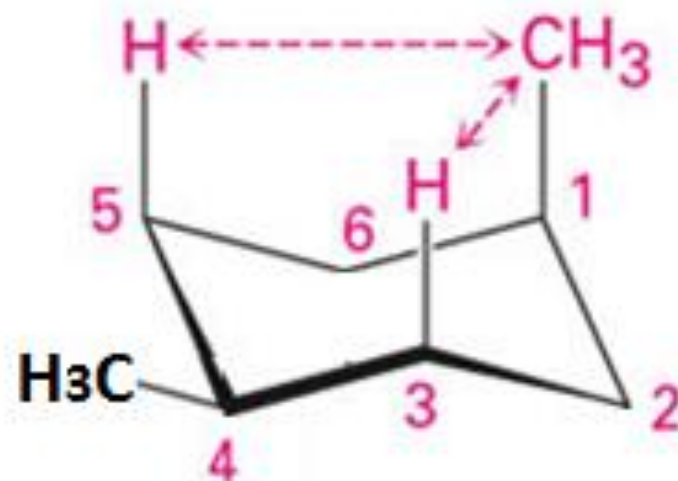


(4)

Conformation 1 and 2 as well as 3 and 4 are superimposable.

1,4-Disubstituted Cyclohexane

Cis isomer, Relative stability

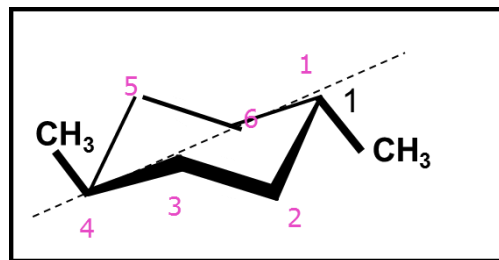


In Cis 1,4- Dimethyl cyclohexane, axial methyl group have two $\text{CH}_3\text{-H}$, 1,3 diaxial interaction. These two interactions contributes 1.8 kcal/mole energy. Other methyl group present at equatorial position have no interaction. Thus total strain is **0.9 + 0.9 = 1.8 kcal/mole**.

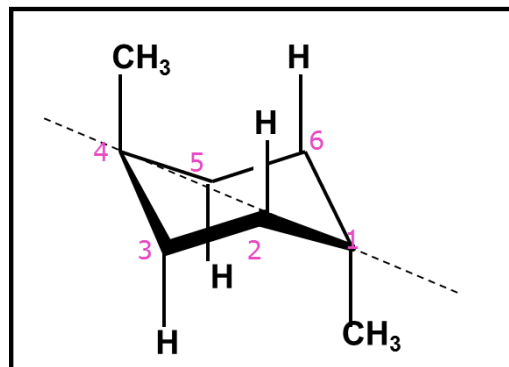
1,4-Disubstituted Cyclohexane

Trans isomer (a, a or e, e form)

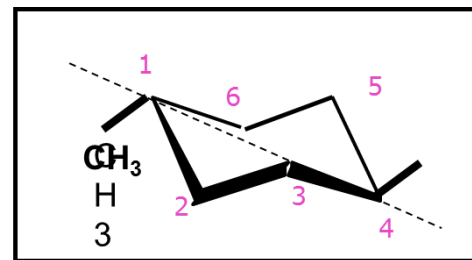
Optical Isomerism: Trans 1,4 dimethyl cyclohexane possess a plane of symmetry (Passing through C1 and C4) and also Centre of symmetry. Hence it is optically inactive.



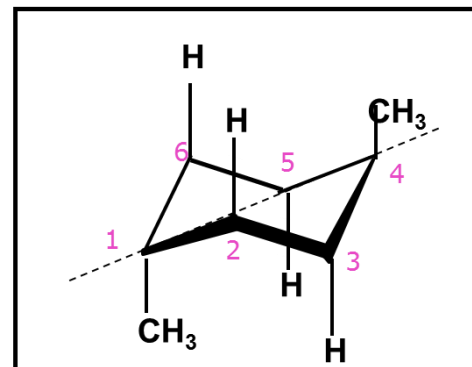
(1)



(2)



(3)

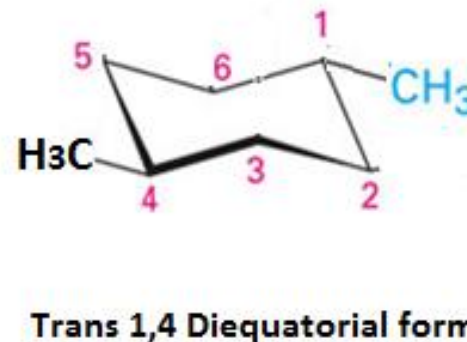
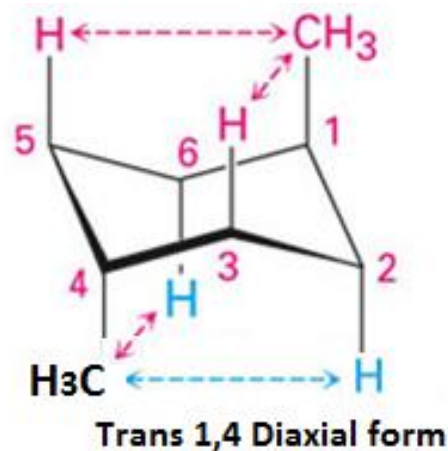


(4)

Ring flipping of diequatorial form produce less stable diaxial form

1,4-Disubstituted Cyclohexane

Trans isomer, Relative stability



In trans 1,4- Dimethyl cyclohexene diaxial form, Each axial methyl group have two $\text{CH}_3\text{-H}$, 1,3 diaxial interaction. These four interactions contributes 3.6 kcal/mole energy. Diequatorial form is more stable and have 0 kcal/mole strain

Stability order: Trans 1,4 (e, e) 0kcal/mole > Cis 1,4(a, e) 1.8kcal/mole > Trans 1,4 (a, a) 3.6 kcal/mole

Conformations and energies of dimethyl cyclohexane

Isomer	Conformation	No.of Gauche interaction	Relative energy Kcal/mol	Optical activity
a.cis,1,2	e,a or a,e	3	2.7	inactive
b.trans1,2	e,e	1	0.9	active
c.trans1,2	a,a	4	3.6	active
a.cis,1,3	a,a	4	5.4*	inactive
b.cis,1,3	e,e	0	0	inactive
c.trans1,3	e,a or a,e	2	1.8	active
a.cis,1,4	e,a or a,e	2	1.8	Inactive
b.trans,1,4	e,e	0	0	inactive
c.trans1,4	a,a	4	3.6	inactive

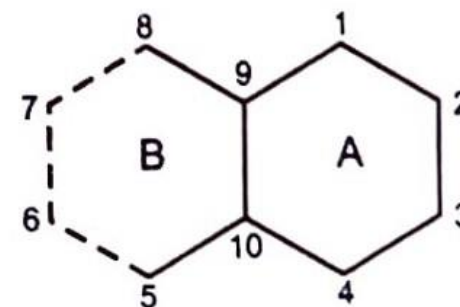
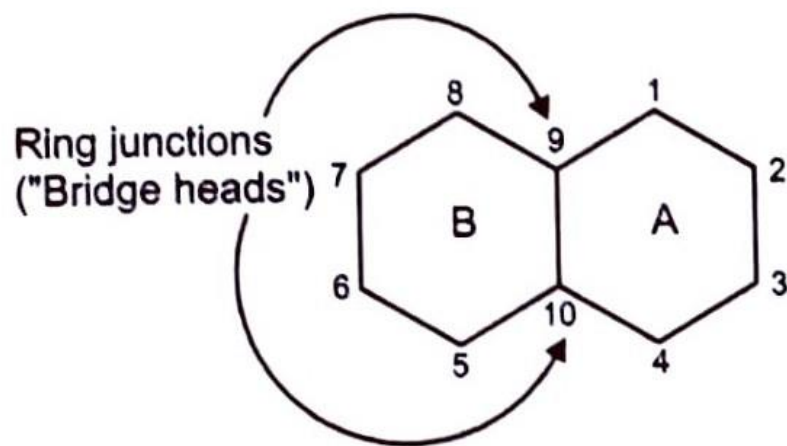
Conformations of Decalin and their stability

- Saturated analogue of naphthalene
- Can be prepared by catalytic hydrogenation of naphthalene in fused
- It is also known as bicyclo[4,4,0]decane



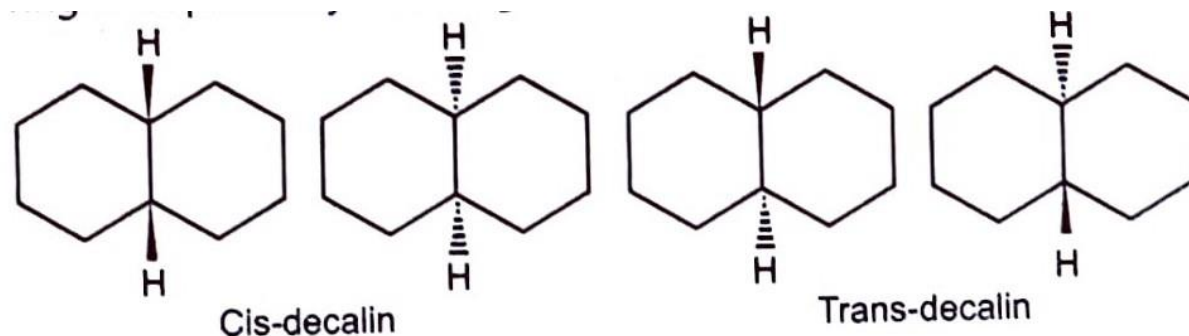
Conformations of Decalin and their stability

- Decalin is numbered like naphthalene where ring junction known as bridgehead and get number 9 and 10
- If one of the six membered ring of decalin is viewed as an independent cyclohexane ring then it appear like 1,2 disubstituted cyclohexane



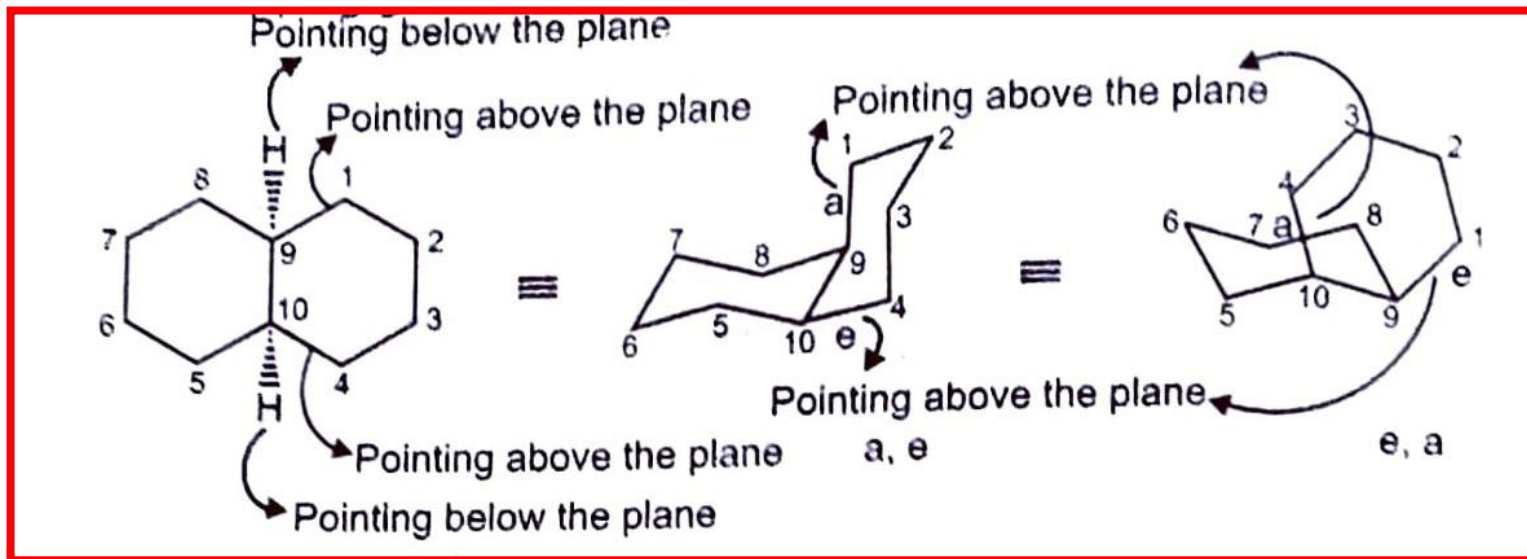
Conformations of Decalin and their stability

- Stereochemistry of decalin can be understood as similar to that of 1,2 disubstituted cyclohexane.

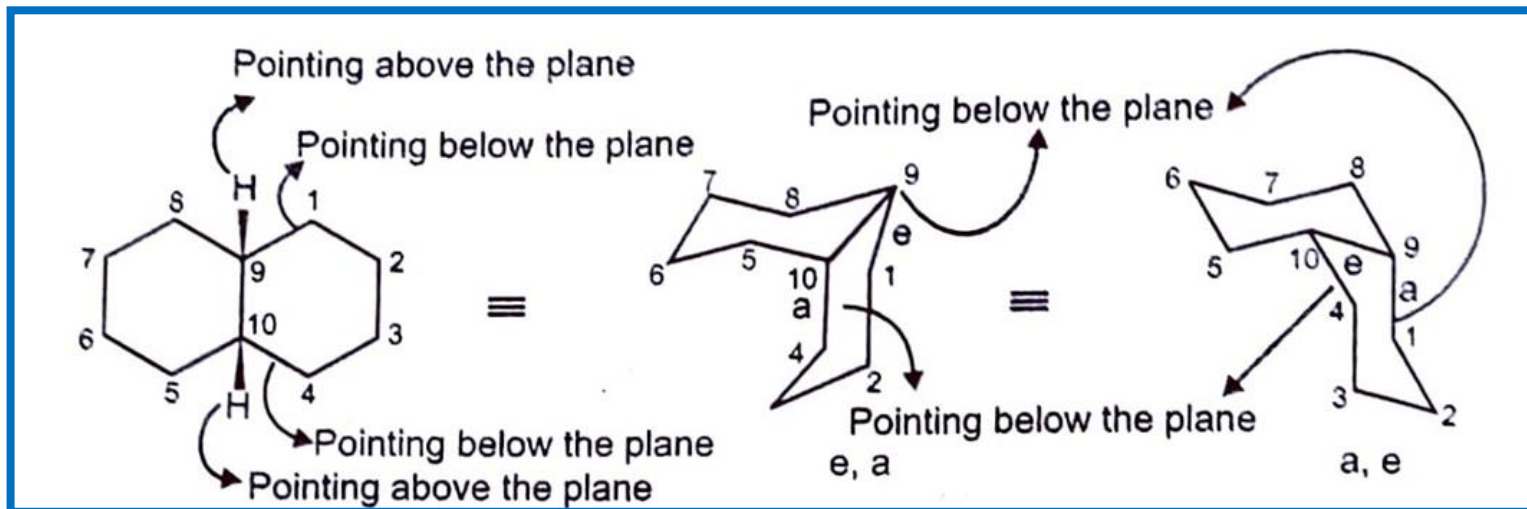


- In cis isomer both C9 and C10 hydrogens are present either upward or downward

Conformations of Decalin and their stability

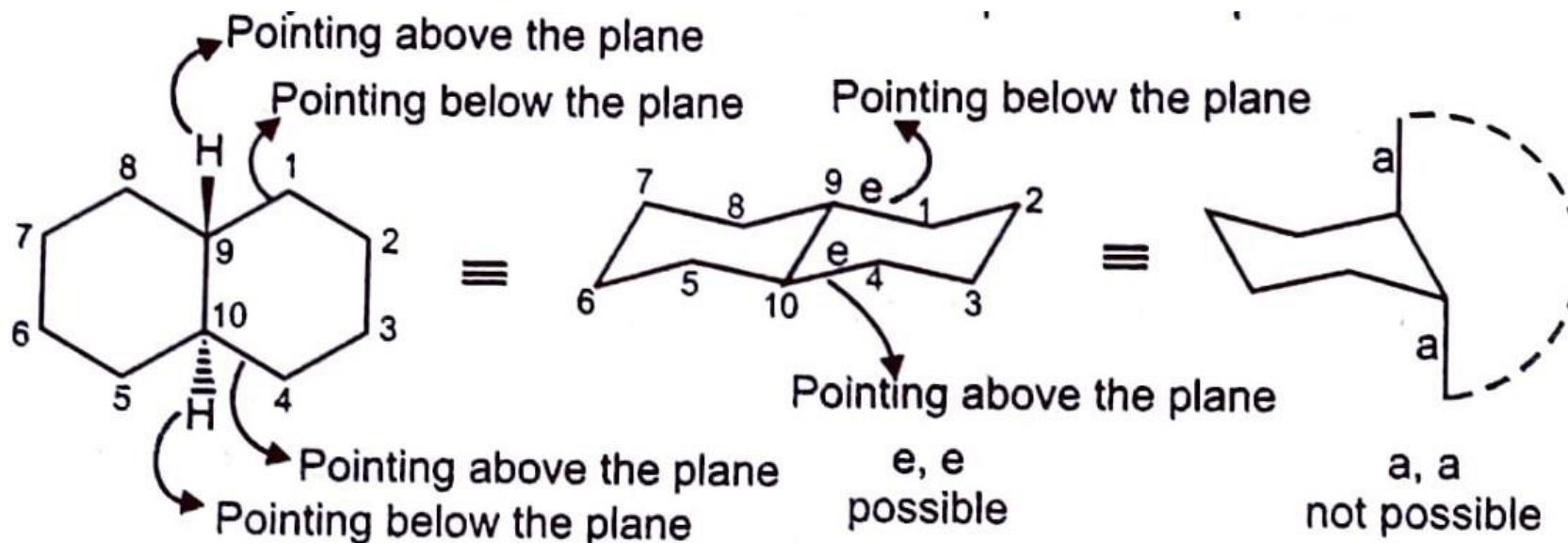


➤ In cis isomer both C9 and C10 hydrogens are present either upward or downward

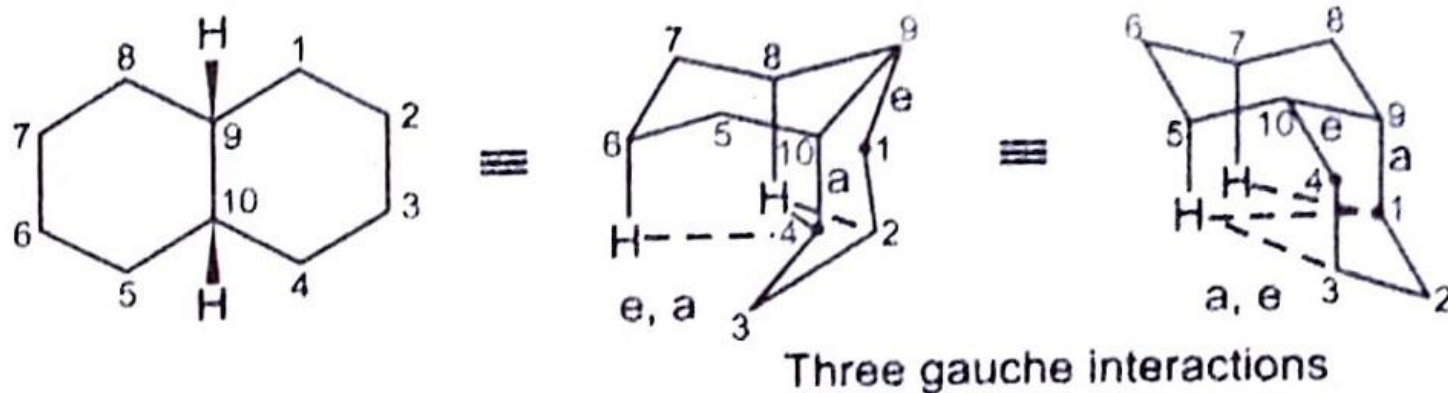


Conformations of Decalin and their stability

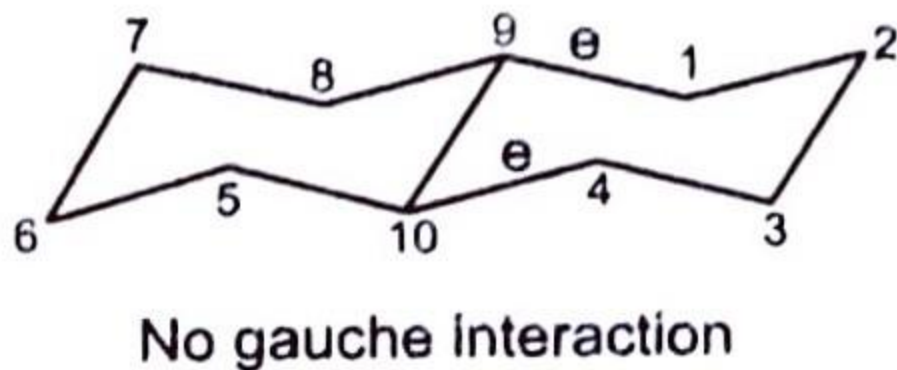
- In trans isomer one hydrogen (either C9 or C10) is present above the plane (upward) while other present below the plane (downward)
- Similar to trans 1,2 dimethyl cyclohexane, two orientation of methylene group of ring B are expected (i.e e, e and a ,a)
- Formation of ring B in diaxial form is not possible hence this conformation does not exist and trans decalin exist as diequatorial form



Conformations of Decalin and their stability



- In cis isomer there are three butane gauche interactions Hence total energy is $0.9 \times 3 = 2.7$ kcal/mole



- In trans isomer there is no butane gauche interaction. Hence total energy is 0 kcal/mole

THANK YOU