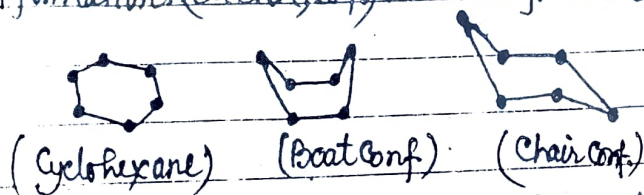
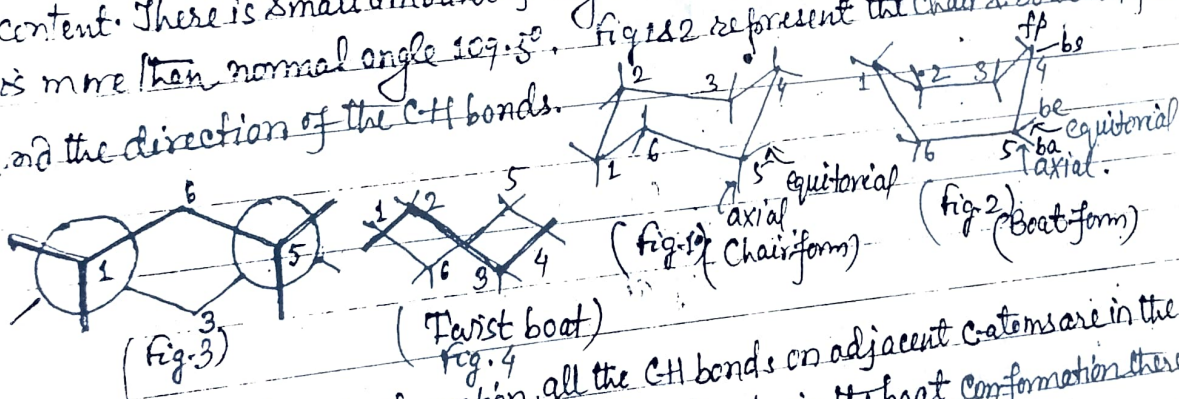


Conformation of Cyclohexane.

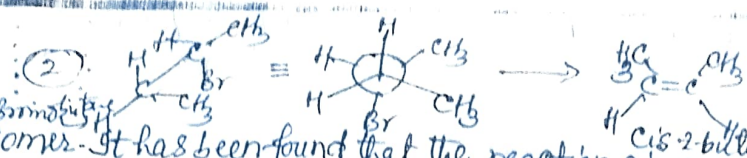
The stereochemistry of Cyclohexane and its derivatives presents a detailed example of conformational analysis. On the basis of the tetrahedral theory, two forms are possible for Cyclohexane, neither of which is planar. These two forms are known as boat & chair conformations (Sachs, 1890). Both the forms are stairless.



The chair form is rigid (since it resists distortion), and when it is transformed into the boat form some angular deformation is necessary. The energy barrier in this process has been determined by NMR and it is about $37.7-46 \text{ kJ mole}^{-1}$. This value is large enough for each conformation to retain its identity, but is not large enough to prevent their rapid interconversion at room temp. Thus, it is not possible to isolate each conformation. The chair & boat forms are both free from angle strain, but because of differences in steric strain and bond opposition strain, the two forms differ in energy content. There is small amount of angle strain, the ring angles being $\sim 111.5^\circ$ which is more than normal angle 109.5° and the direction of the C-H bonds. Fig 1 & 2 represent the chair & boat conformation.

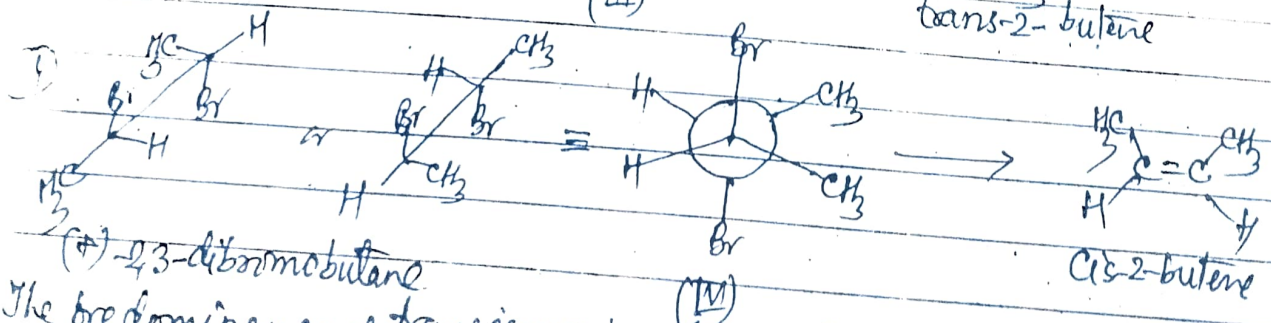
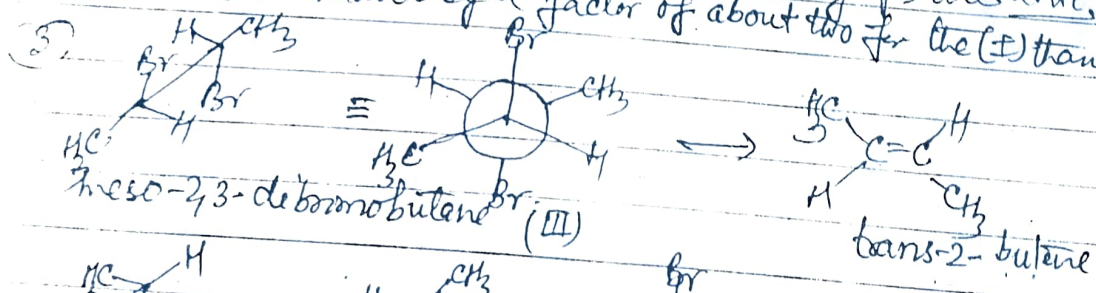


In the chair conformation, all the C-H bonds on adjacent carbons are in the skew positions (Fig 3) like n-butane. On the other hand, in the boat conformation there are four skew interactions (1,2; 3,4; 4,5 & 6,1) and two eclipsed interactions (2,3 & 5,6). At the same time, there will also be some bond opposition strain for these two pairs of eclipsed bonds, and also steric repulsion between the two flagpole hydrogens (at 1 & 4), which are 1.83 \AA apart. Hence, the total strain in the boat conformation is larger than that in the chair conformation, and consequently the former is less stable than the latter. The boat form, however, is flexible and can readily be distorted into many shapes, and



whereas (II) is its *cis* isomer. It has been found that the reaction gives mainly the *trans* alkene; this proves that the elimination, this proves that the elimination involving the conformation (I) proceeds more readily than through (II). This is because in the *trans* state of the *cis*-alkene the two bulky methyl groups are *gauche* to each other and exert repulsive force (van der Waals strain) which makes the transition state less stable than that in the case of *trans* alkene in which the two bulky methyl groups are staggered (*anti*). It should be noted that the reaction (i) is favoured because both the conformation (I) of the starting compound and the *trans* alkene formed are thermodynamically more stable as compared to their respective alternatives depicted in the reaction (i).

Similarly, the effect of conformations on reactivity may be demonstrated by taking the examples of debromination of 2,3-dibromobutane either with Zn or with a metal such as Zn . Elimination (B) can occur only through a conformation of the starting compound which places the two eliminating groups (bromine atoms) in an *anti*-periplanar arrangement, regardless of the fact if or not this is the most stable conformation. The *meso*-2,3-dibromobutane can eliminate bromine gainfully only from the conformation (III) to give *trans*-2-butene (reaction 3), whereas its reaction (4) (\pm)-2,3-dibromobutane (IV) reacts to give *cis*-2-butene. The reaction (4) isomer involves a less stable transition state (the two methyl groups are *gauche*) compared to the *meso* isomer (the two methyl groups are *anti*), thus the elimination with iodide ions is slower by a factor of about two for the (\pm) than for the *meso* isomer.

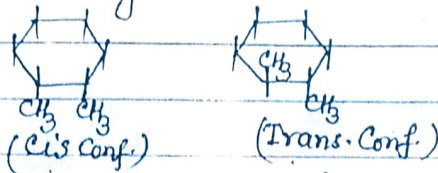


The predominance of *trans* isomer is explained by Curtin-Hammett principle, according to which it is only on the relative energy of the transition state of various processes that ground state conformations.
 Trans-Deccalin

Q. Discuss Conformations of disubstituted Cyclohexanes.

Ans. when two substituents are present on a cyclohexane ring, one has to consider whether they are 'cis' or 'trans' to each other, and whether they are 1,2; 1,3- or 1,4- with respect to each other. * In general, in disubstituted cyclohexanes the chair conformation containing both the substituents in equatorial positions will be the preferred conformation, or when this is not possible, the conformation with bulkier substituent in an equatorial position will be preferred conformation. * [Here we have a number of factors to consider (i) position isomerism (ii) stereoisomerism (iii) the relative size of the two substituents]

(1) 1,2-disubstituted compounds: Let us consider 1,2-dimethylcyclohexane. On the basis of the planar cyclohexane ring the disubstituted cyclohexane can exist in cis & trans configurations.

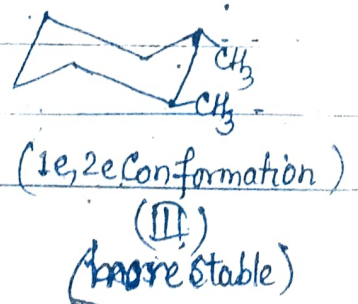
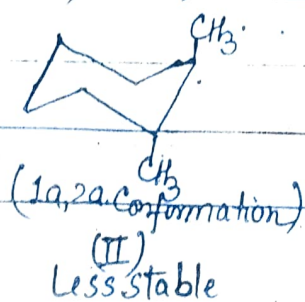
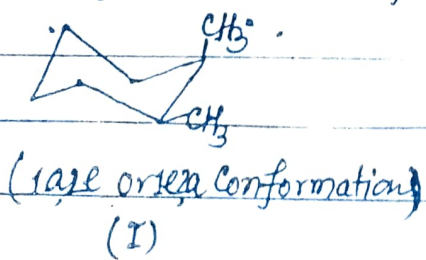


The Conformation of the cis configuration must have one axial and one equatorial substituents (i.e., 1a, 2e or 1e, 2a). The trans configuration can exist in two different conformations, either both axial or equatorial substituents i.e.

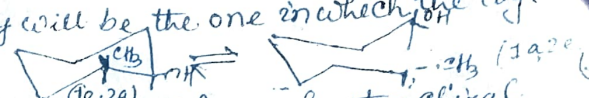
1a, 2a & 1e, 2e. In cis-1,2-dimethylcyclohexane there is one axial-CH₃g, which causes two 1,3 diaxial methyl-hydrogen interactions (Me/H 1,3 interactions).

In the diequatorial trans-1,2-dimethylcyclohexane, there is no axial methyl group, hence there is no 1,3-diaxial interaction causing strain. Thus, 1e, 2e-dimethylcyclohexane is more stable than 1e, 2a or 1a, 2e-dimethylcyclohexane. In the case of 1a, 2a dimethylcyclohexane, there are two axial methyl groups, which cause four Me/H 1,3-diaxial interactions resulting in greater strain and lesser stability than that of

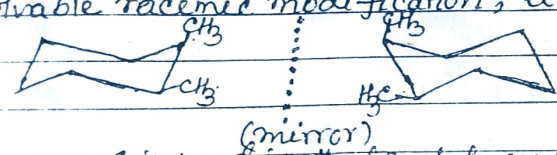
1a, 2e-dimethylcyclohexane. Thus the decreasing order of stability of different conformations of 1,2-dimethylcyclohexane is: ee > ae or ea > aa; and the preferred conformation (most stable conformation) is 1e, 2e-dimethylcyclohexane.



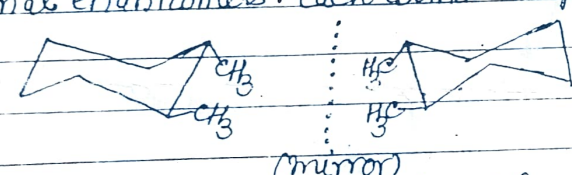
If the substituents differ in size, the 1,3 interactions will be most powerful when la_1 is axial. Thus, the conformer with lower energy will be the one in which the large group is equatorial i.e. this is the preferred form.



Enantiomerism in 1,2-dimethylcyclohexane: 1,2-dimethylcyclohexane has two chiral centres, hence can have no more than four stereoisomers ($2^2=4$), but actually it has only three. The cis-1,2-dimethylcyclohexane (ae or ea) molecule is not superimposable on its mirror image but the molecule and its mirror image are readily interconvertible ~~to one another~~ ^(at RT) by flipping one chair conformation into the other. Hence, these are called conformational enantiomers. Cis-1,2-dimethylcyclohexane constitutes a non-resolvable racemic modification; it is not the meso compound.



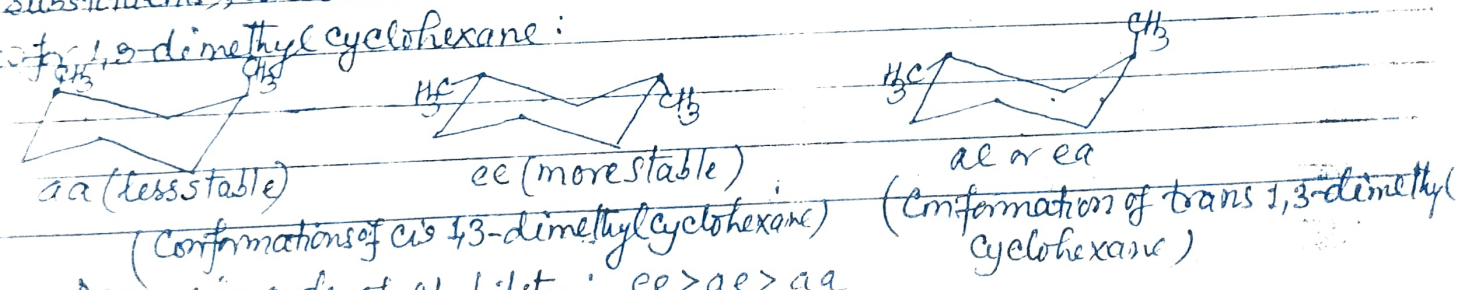
The trans-1,2-dimethylcyclohexane (ee) molecule, and its mirror image are not superimposable, hence constitute an enantiomeric pair. These are not interconvertible by flipping one chair conformation into the other. On flipping, the ee chair conformation is converted into an aa conformation. The two isomers are known as configurational isomers or configurational enantiomers. Each isomer is optically active and their mixture is resolvable.



Trans 1,2-dimethylcyclohexane (ee)

Thus, 1,2-dimethylcyclohexane exists as a pair of (Configurational) diastereomers, the cis and the trans isomers. The cis isomer exists as a pair of conformational enantiomers, whereas the trans isomer exists as a pair of configurational enantiomers, each of which in turn exists as two conformational diastereomers (aa & ee).

1,3-disubstituted cyclohexane: In the case of 1,3-disubstituted cyclohexanes (with identical substituents), two cis and one trans chair conformations are possible as shown below for 1,3-dimethylcyclohexane:



Decreasing order of stability: $ee > ae > aa$

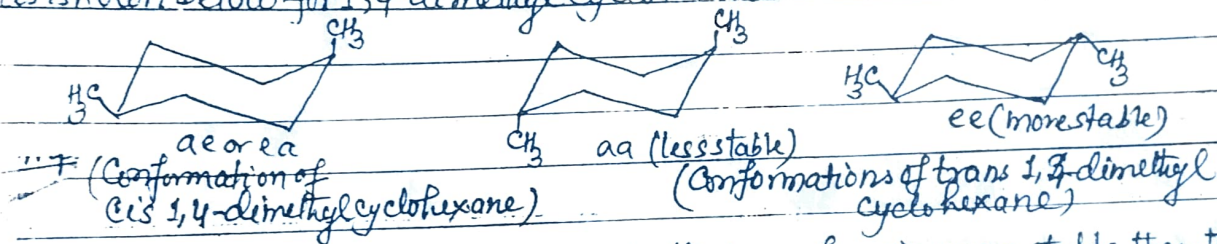
(5)

In the case of 1,3-disubstituted cyclohexanes, the cis isomer (e,e) is more stable than the trans isomer (a,e).
Cis (aa) isomer, more over the cis (e,e) isomer is more stable than the trans isomer (ae).

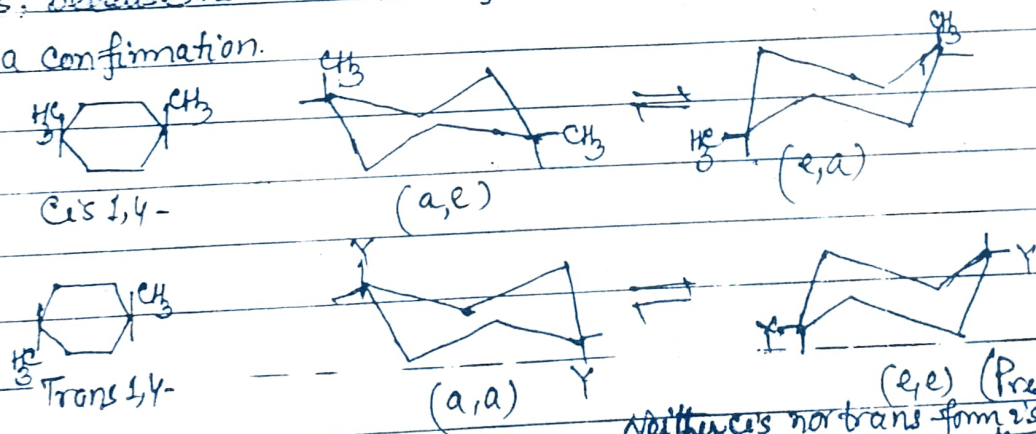
Thus most stable or preferred conformation of 1,3-disubstituted cyclohexane is cis (e,e) form.

1,3-Dimethyl cyclohexane has two chiral centres, and can have no more than four stereoisomers ($2^2=4$). Actually, there are only three. The cis 1,3-dimethyl cyclohexane has a plane of symmetry and is achiral. Thus, it is a meso compound. The trans 1,3-dimethyl cyclohexane does not have a plane of symmetry & exists as a pair of enantiomers.

1,4-disubstituted cyclohexane: In the case of 1,4-disubstituted cyclohexanes (with identical substituents), one cis & two trans conformations are possible as shown below for 1,4-dimethyl cyclohexane:



In 1,4-disubstituted cyclohexane again the trans form is more stable than the cis, because here the e,e conformation exists in the former, whereas the latter has e,a conformation.



Here cis & trans isomers possess a plane of symmetry & so they are optically inactive. Neither cis nor trans form is chiral. It exists as cis-trans diastereomers.

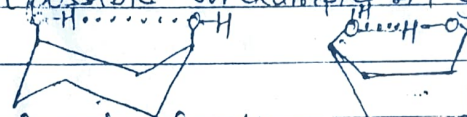
In general, the chair conformation with the maximum number of equatorial substituents will be preferred conformation provided that the other factors such as dipole interaction, hydrogen bonding etc. are absent. Bulky group always occupies equatorial position (e) & lighter or smaller group must be axial.

Decreasing order of stability

(6)

The 1,3 interactions will be most powerful when the larger group is axial, the preferred conformation will therefore, be the one in which the larger group is equatorial. Thus, since the methyl group is larger than hydroxyl, the preferred form of 2-methylcyclohexanol is aOH, e-Me.

Cis 1,3-cyclohexanediol has been shown to have the diaxial rather than the diequatorial orientation. This is because of stabilisation of the diaxial form by intramolecular hydrogen bonding which is not possible in the diequatorial form. The preferred conformation of the cyclohexane ring is the chair form, but when intramolecular hydrogen bonding is possible between groups in 1 & 4 position the molecule assumes a boat conformation rather than the chair in which the hydrogen bonding is not possible. For example, 1,4-cyclohexanediol exists in the boat conformation.

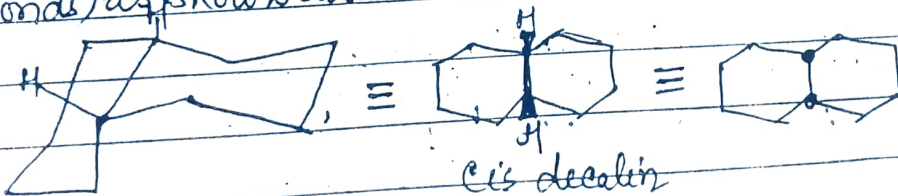


(Preferred Conformation of cis 1,3-Cyclohexanediol)

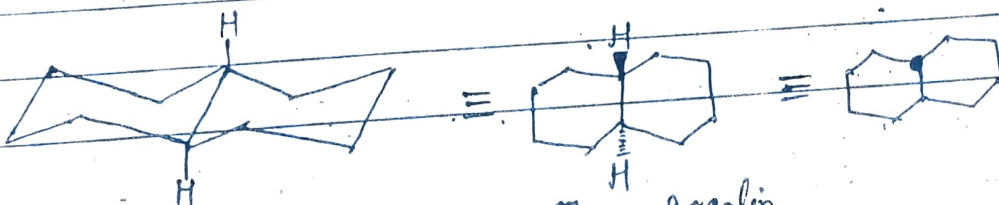
(Preferred Conformation of 1,4-Cyclohexanediol)

Q. Discuss Conformations of fused rings (Decalins).

Ans. Decalin (bicyclo[4.4.0]decane) exists in two diastereoisomeric forms cis & trans decalins, depending on the way in which the two cyclohexane rings are fused together. In both the diastereoisomers of decalin, the two cyclohexane rings are fused together in the chair conformation. Since the decalin is analogous to 1,2-disubstituted cyclohexane, in the cis isomer the two cyclohexane rings are fused together in ea form (i.e., the equatorial bond of one ring is fused with the axial bond of the other), while in the trans isomer the two rings are fused in ee form (i.e., each ring is fused with other ring by equatorial bonds) as shown below.



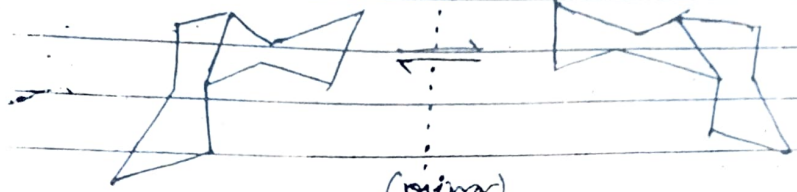
Cis-decalin



Trans-decalin

axial
equatorial
axial
equatorial

The trans decalin is more stable than the cis by 2.7 kcal/mole. Thus cis decalin can be smoothly pyrolysed to the trans isomer irreversibly. In cis decalin the ring fusion involves σ bonds, hence it is flexible & exists in two forms which are interconvertible as a result of conformational flipping similar to that of the chair conformations of monocyclic cyclohexane as shown below:

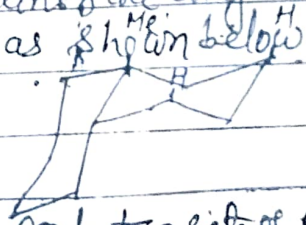
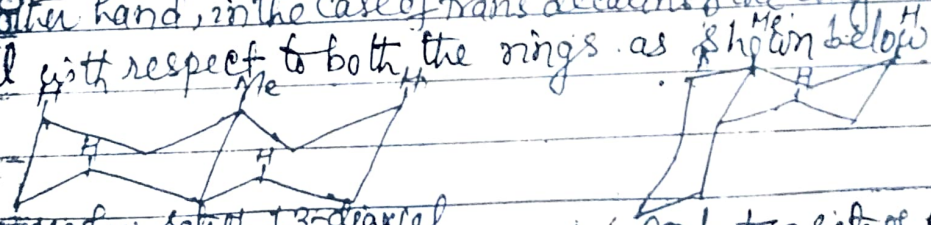


(mirror)
Cis decalin
(two enantiomeric conformations)

Since, trans decalin involves two equatorial bonds for the ring fusion, it is a rigid molecule & cannot undergo conformational flipping, i.e. it cannot be converted into cis conformation which also does not exist in decalin type of fused ring compounds.

Any substituent attached to the cis decalin system is free to adopt the equatorial orientation. Cis decalin is chiral in both the conformations which are non superimposable mirror images of each other. Because of rapid interconversions of the two cis conformations, cis decalin exists as a non resolvable enantiomeric pair. On the other hand, trans decalin has a plane of symmetry and is therefore, optically inactive.

In case of substituted decalins, substituents located at the fusion points of the two rings (angular positions) are axial with respect to one ring, while equatorial with respect to the other in cis decalins. On the other hand, in the case of trans decalins the angular substituents are axial with respect to both the rings as shown below:



There are four sets of 1,3-diaxial interactions involving the bulky Me gr. & H (Only two sets of 1,3-diaxial interaction with the methyl group.)

It should be noted that rotation about C-C bonds cannot bring about conversion of cis & trans decalins.