Subject	Chemistry
Paper No and Title	1: ORGANIC CHEMISTRY- I (Nature of Bonding and Stereochemistry)
Module No and Title	17: Conformational Analysis of decalins, decalones and decanols
Module Tag	CHE_P1_M17

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1. Learning Outcomes

After studying this module, you shall be able to

- Know about bicyclic molecules
- Learn about stereoisomers of decalin
- Understand the conformational analysis of cis and trans decalins, decanols and decalones
- Identify different types of strains in conformations of decalins
- Predict the most suitable and energetically favourable conformation of decalins in natural compounds

2. Introduction

Compounds with two rings fused together are known as bicycles. Bicyclic systems can be either fused or bridged bycyclic (fig 1). Fused rings share two adjacent carbon atoms while the bridged rings sharec two non-adjacent carbon atoms (called the bridgehead carbons) with one or more carbon atoms between them. In this module our focus will be on the former category of bicycles, mainly decalins and its derivatives.

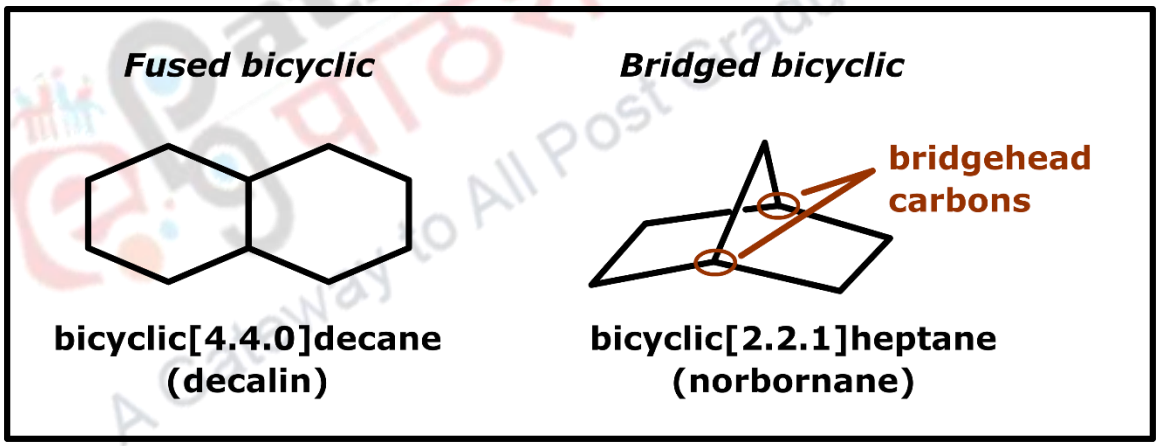

Figure 1. Fused and bridged bicyclic rings

The IUPAC name of decalin is bicyclo[4.4.0]decane (the numbers 4, 4, 0 represents the number of carbon atoms in each ring besides the bridgehead carbons). Decalin is also known as decahydronaphthalene as it is a saturated analog of naphthalene and can be prepared from it by hydrogenation in a fused state in the presence of a catalyst (fig 2). The synthesis lead to the formation of two stereoisomers of decalin. One, where both the hydrogens at the bridgehead carbons are ‘cis’ to each other and the other, where both the hydrgens are ‘trans’ to each other as shown in the figure.

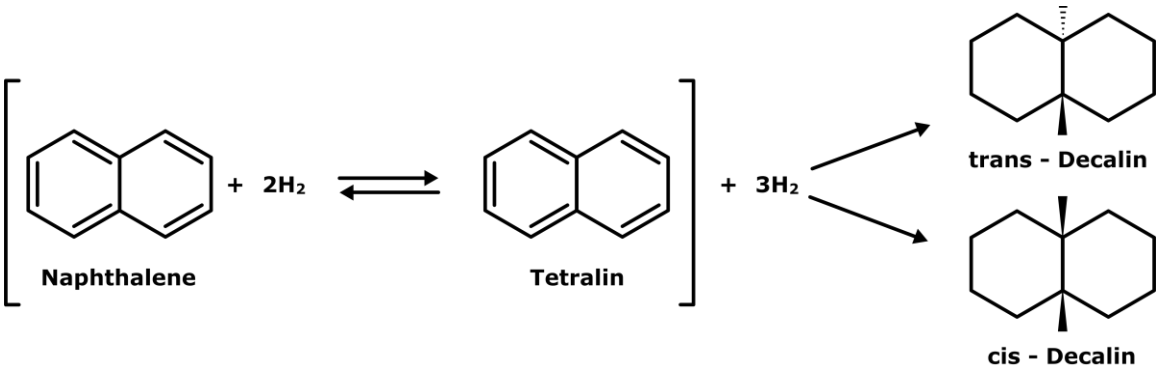

Figure 2. Synthesis of decalin by dehydrogenation of naphthalene

3. Conformations of Decalin

Decalin has two cyclohexane rings fused together which are most stable in their chair form. So it is expected that the two fused cyclohexane rings in decalin should exist in their chair form. Infact, Sachse and Mohr suggested decalin to be a strain-free puckered structure which exists in two isomeric forms that cannot be interconverted without breaking a bond, i.e. they are configurational isomers or diastereomers. Figure 3 shows the puckered structures of the two cis and trans isomers of decalin.

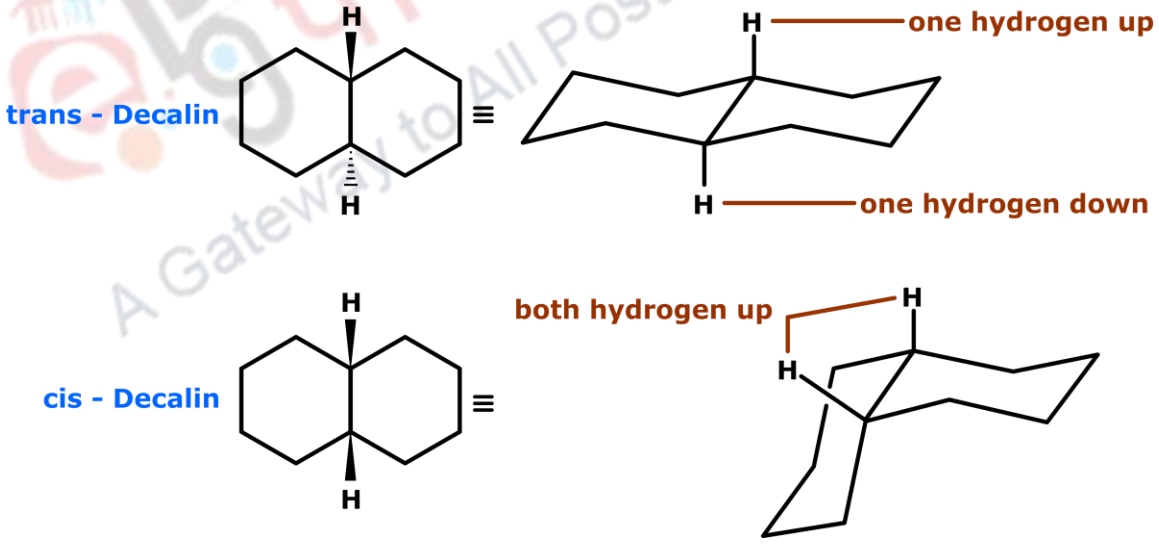

Figure 3. Planar and puckered structures of cis and trans isomers of decalin

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Since both the isomers have cyclohexane rings in chair conformation, there is no angle or torsional strain in decalins. It can be seen from the figure that in trans decalin, the two bridgehead hydrogens are pointing in opposite directions and are both axial hydrogens. On the other hand, in cis decalin the two bridgehead hydrogens are pointing in the same direction and one of them is axial while the other is equatorial.

Ring flipping in decalins

In trans decalin, the two cyclohexane rings are joined through the equatorial positions (Remember! The equatorial position in cyclohexane is less hindered and more stable than the axial position to place a substituent- learnt in last module). As we know, the ring flipping in cyclohexane, changes all the equatorial bonds to axial bonds and vice versa, likewise ring flipping in trans decalin would give a conformation where the two cyclohexane rings would be joined through axial bonds. However, this ring flipping is highly prohibited as it is not possible to have a six membered ring build with two of its bonds in diagonally opposite directions!! We would fail if we try to construct a model where the cyclohexane rings are joined through axial bonds! (fig 4)

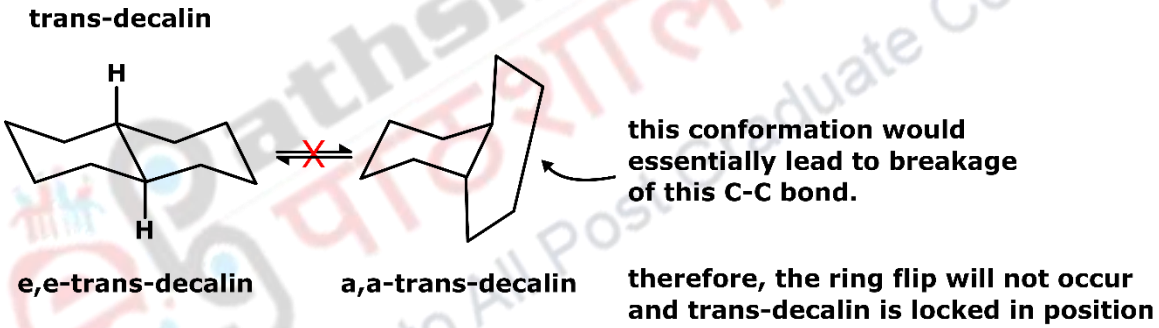

Figure 4. Ring flipping in trans decalin would lead to breakage of C-C bond

Thus, trans Decalin is '**conformationally locked**' as ring flipping cannot happen. It remains in the equatorial conformation with respect to both the rings (e,e conformation). The e,e-trans decalin has a centre of symmetry lying at the mid of C9 and C10 bond (fig 5) and hence it is an achiral or optically inactive molecule, i.e. its mirror image is superimposable on it. It also has two C2 axes of symmetry one passing through the equator and the other passing through the axis as shown in the figure 5.

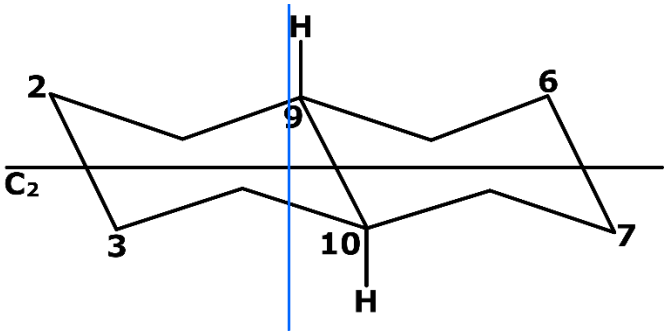

Figure 5. Trans decalin showing axes of symmetry

In contrast to trans decalin which is comparatively flat, the cis decalin is more like a tent shaped molecule with convex (less hindered) and concave (more hindered) sides (fig 6). Although in both the cases the cyclohexane rings are in their most stable chair conformations.

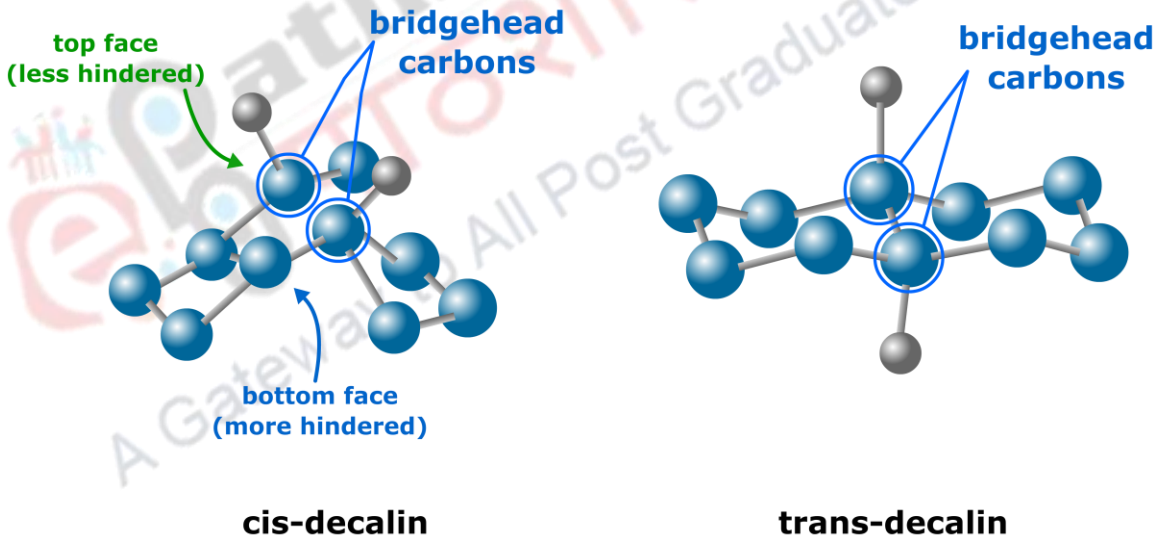

Figure 6. Shapes of cis and trans decalin

In cis decalin, the two cyclohexane rings are joined through an equatorial and an axial bond. The ring flipping is permissible in this case which converts one cis form into another and converts the equatorial bonds to axial and vice versa (i.e. The e,a-cis decalin on ring flipping will result in a,e-cis decalin) (fig 7).

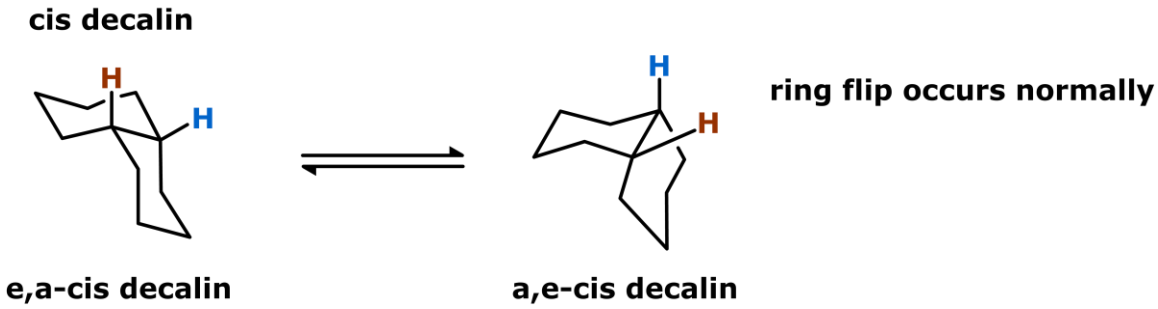

Figure 7. Ring flipping occurs normally in cis decalin

Conformational analysis of cis decalin shows that it is a chiral molecule though it has no chiral carbon. It has a non-superimposable mirror image. However, a rapid ring flipping cancels its chirality and converts it into its mirror image! Thus the two chiral forms are not resolvable (due to the rapid ring inversion) and exist as racemic mixture.

The ring flipping in cis decalin was also supported by its NMR spectra which shows only one proton peak in contrast to trans decalin which shows two proton peaks. The two proton peaks in trans decalin can be attributed to its rigidity. The axial and equatorial protons are held in different environments and thus show different chemical shifts. The cis isomer, on the other hand, is capable of rapid interconversion. Consequently it results in a single chemical shift for all the protons.

Energy considerations

A closer look at the trans decalin shows that all the carbon-carbon bonds are equatorial to each other (an arrangement which leads to flat shape of this isomer) and hence there are no gausche interactions. While in cis decalin there are three gausche interactions as shown in figure 8. Comparing it with the gausche interaction in n-butane which amounts to an increase of 3.35 kJ/mol, the total energy difference between the trans and cis decalins is therefore equal to 3 x 3.35 = 10.5 kJ/mol. **Thus, trans decalin is more stable than cis decalin by 10.5 kJ/mol**. There is also an argument which says that cis decalin is less stable because of weak non-bonded interactions in the concave side (fig 8).

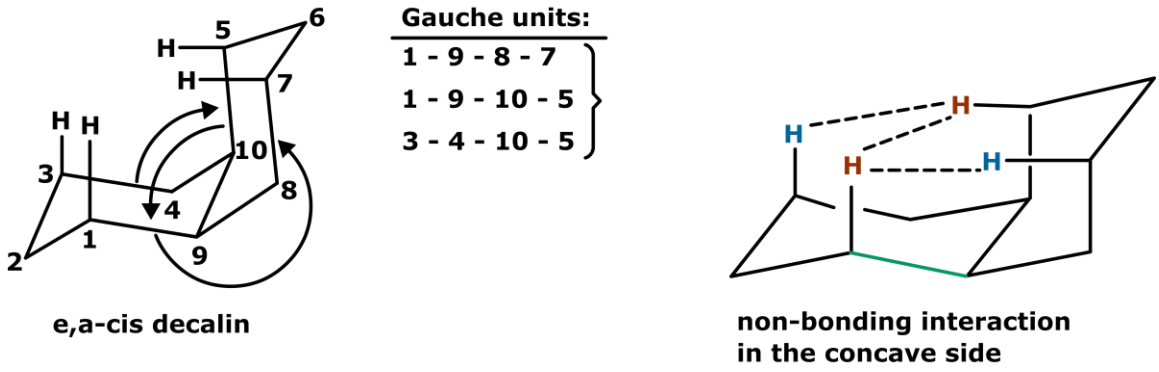

Figure 8. Gausche interactions and non-bonding interactions in cis decalin

The number of gausche interactions remains the same on ring flipping of cis decalin. So we can say that the two conformers of cis decalin are exactly equal in energy (a reason for rapid ring inversion).

Due to the concave-convex tent like shape of cis decalin, the two faces are sterically non-equivalent (fig 6). Hence an incoming substituent would prefer the less hindered convex face which is more accessible. For example, in cis-9-methyldecalin, the methyl group occupies the convex face over the concave. However, it is less stable than trans-9-methyldecalin due to larger amount of gausche interactions in the latter (fig 9). Introduction of a substituent on the bridgehead carbon imparts destabilization equivalent to four butane gausche interactions in trans decalin (two with each ring) as the substituent is axial to both the rings. On the other hand, in cis decaline, the substituent imparts destabilization equivalent to two butane gausche interactions as it is axial to only one ring. Thus, in all, there are four butane gausche interactions in trans decalin and five in cis decalin thereby reducing the energy gap between cis and trans decalins to only one butane gausche interaction.

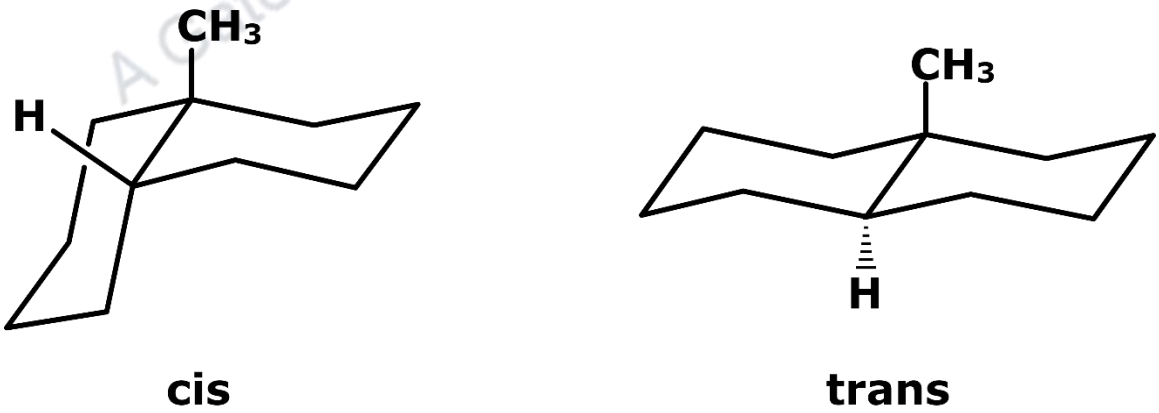

Figure 9. Methyl substituted cis and trans decalins

Similar analysis suggests that on introduction of a second substituent on the other bridgehead carbon would increase the energy of trans isomer (which would have eight butane gausche interactions) more than the cis isomer (which would have seven butane gausche interactions), consequently making cis isomer more stable than trans.

Examples of molecules containing decalin moiety and their conformations

The decalin moiety appears frequently in natural products like steroids, terpenes and alkaloids. Figure 10 shows some of the natural products having decalin moiety.

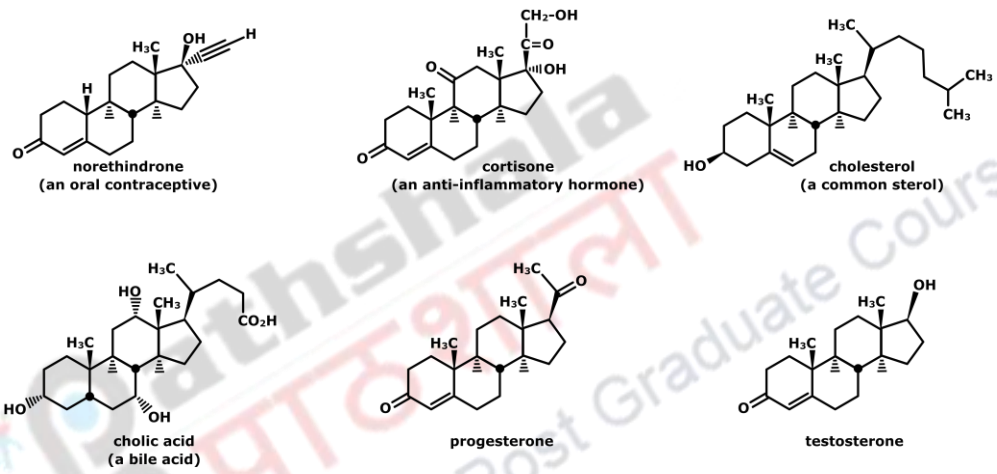

Figure 10. Examples of some steroids containing decalin moiety

However, the cis isomer exists in a particular conformation in these natural products especially in steroids. Thus the conformations of cis-decalin can be classified as steroidal and non-steroidal on the basis of its occurrence in these natural products (fig 11).

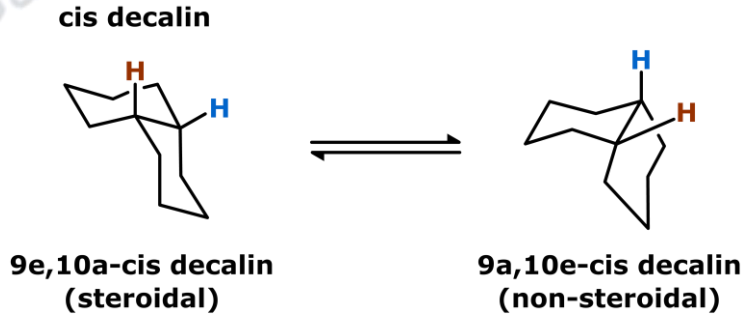

Figure 11. Classification of conformations of cis decalin as steroidal and non-steroidal

4. Configurations of Decalols and decalones

Introduction of a substituent other than on bridgehead carbons gives rise to a new chiral centre in the decalins and thus increases the number of stereoisomers. For monosubstitution in decalins, there are two equivalent positions (besides bridgehead positions) namely 1 and 2 as shown in the figure 12.

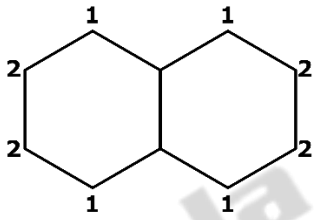

Figure 12. Equivalent positions for monosubstitution in decalin

So, there can be two structural isomers for decalol namely, 1-decalol and 2-decalol. Similarly, there can be two structural isomers for decalone, i.e., 1-decalone and 2-decalone.

The substituent not only generates the chiral centre at the point of substitution but also makes the bridgehead carbons chiral by disrupting the symmetry in decalin. Hence, decalols will have three chiral centres and decalones will have two chiral centres at the two bridgeheads (fig 13).

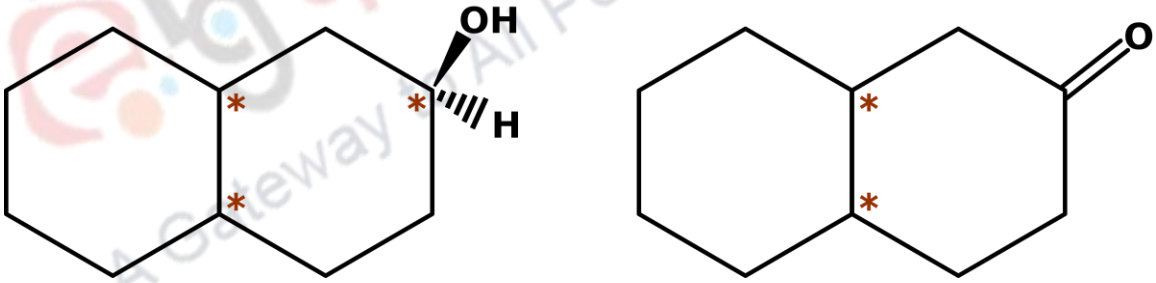

Figure 13. Chiral centres in decalols and decalones

The number of stereoisomers theoretically possible thus would be: for decalols, $2^3 = 8$ and for decalones, $2^2 = 4$. Let us identify the possible stereoisomers in each case.

In decalones, we would first have the two geometrical isomers cis and trans. And both of these isomers would have their mirror images that are non-superimposable, i.e. they would exist in resolvable enantiomeric pairs as shown for 1-decalone in figure 14.

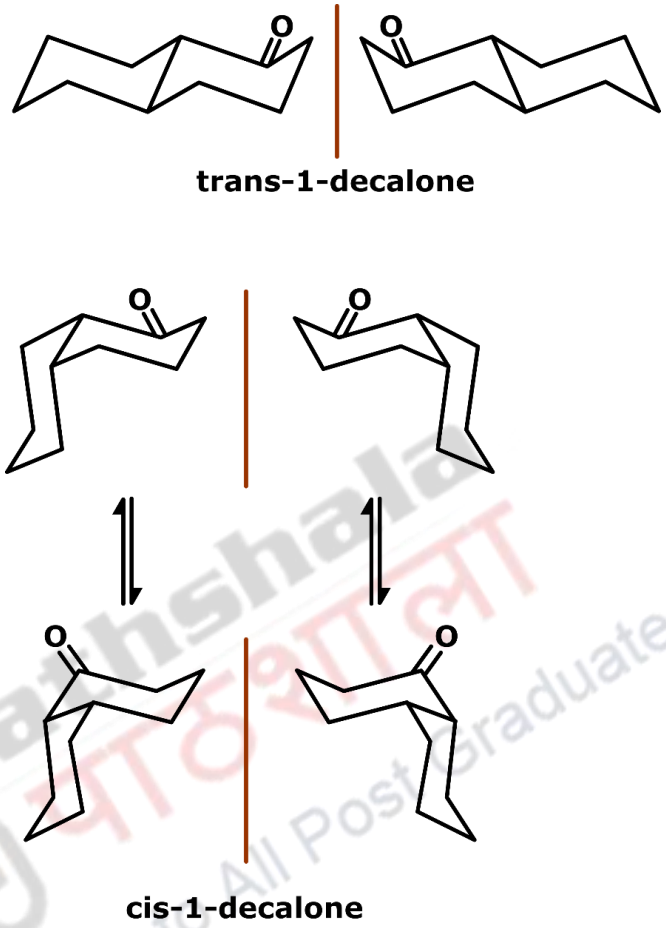

Figure 14. Theoretically possible stereoisomers of 1-decalone

Each resolvable pair in cis-1-decalone is in equilibrium with its conformer due to ring flipping. This doesn't happen in case of trans decalone as it is conformationally locked. So, in all, there are four stereoisomers in 1-decalone. Conformational analysis predicts trans decalone to be more stable than the cis isomer beacuase of the similar reasons as in decalins. The cis isomer has more butane gausche interactions than the trans isomer. 2-decalones shows similar stereochemistry as in 1-decalones.

Reduction of the carbonyl group to give a hydroxyl group introduces a new chiral centres and a corresponding increase in the number of stereoisomers. Let us now identify the stereoisomers in decalols and predict their relative energies.

Theoretically, eight stereoisomers (four pairs of enantiomers) are expected for decalols having three chiral centres. Actually all the eight forms have been isolated, however, their configurations

have not yet been established with certainty. Let us take 2-decalol as a representative example. It can exist as cis and trans decalol. And each isomer can have hydroxyl group either at axial or equatorial positions.

As we know, the trans decalol is conformationally locked (it cannot undergo ring flipping), it is not possible to interconvert the axially substituted hydroxyl to equatorially substituted hydroxyl. Consequently, both would exist as diastereomers. Further, these diastereomers would have non-superimposable mirror images. Thus, trans-2-decalol exists as two pairs of enantiomers as shown in figure 15. Conformational analysis predicts the equatorially substituted trans decalol to be more stable than the axial isomer (due to 1,3-diaxial interactions in the latter).

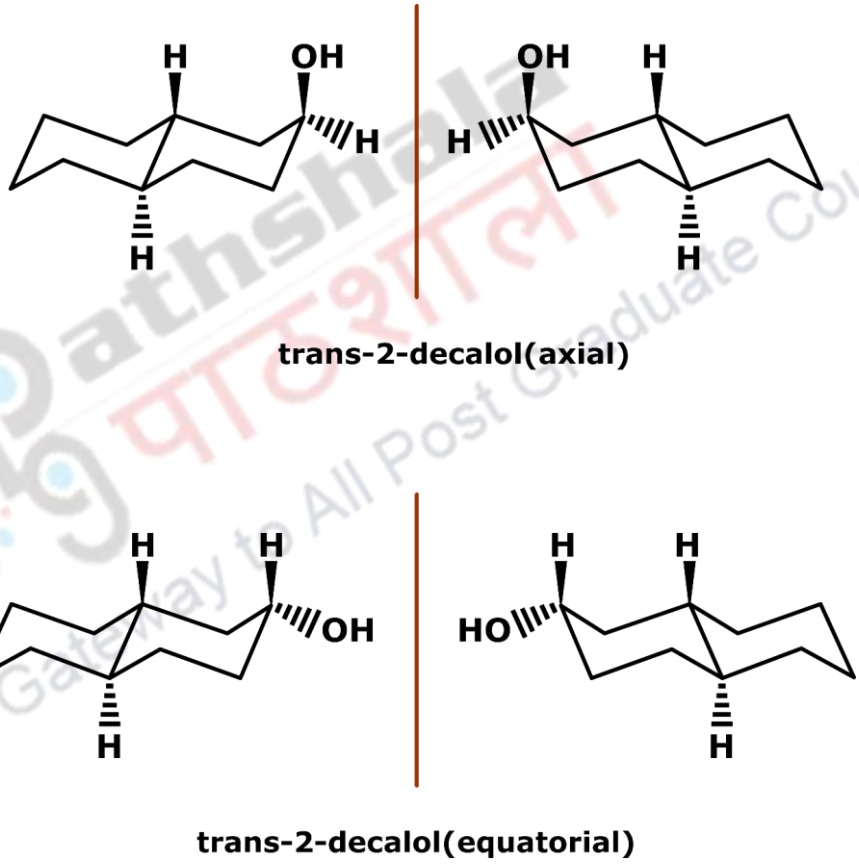

Figure 15. Stereoisomers of trans-2-decalol

The cis-isomer, on the hand, is more complicated owing to its flexibility and the possibility of ring flipping. Ring inversion would convert the axially substituted hydroxyl to equatorially substituted hydroxyl. However, due to the presence of two non-equivalent faces (concave and convex faces - as mentioned in case decalins), there are two different arrangements for axially

substituted hydroxyls and same is true for equatorially substituted hydroxyls as shown in figure 16. The equilibrium shown on the top has axial hydroxyl on the concave side while in the equilibrium shown on the bottom has axial hydroxyl on the convex side. Each of the isomers shown would have their non-superimposable mirror images to add on to the number of isomers!

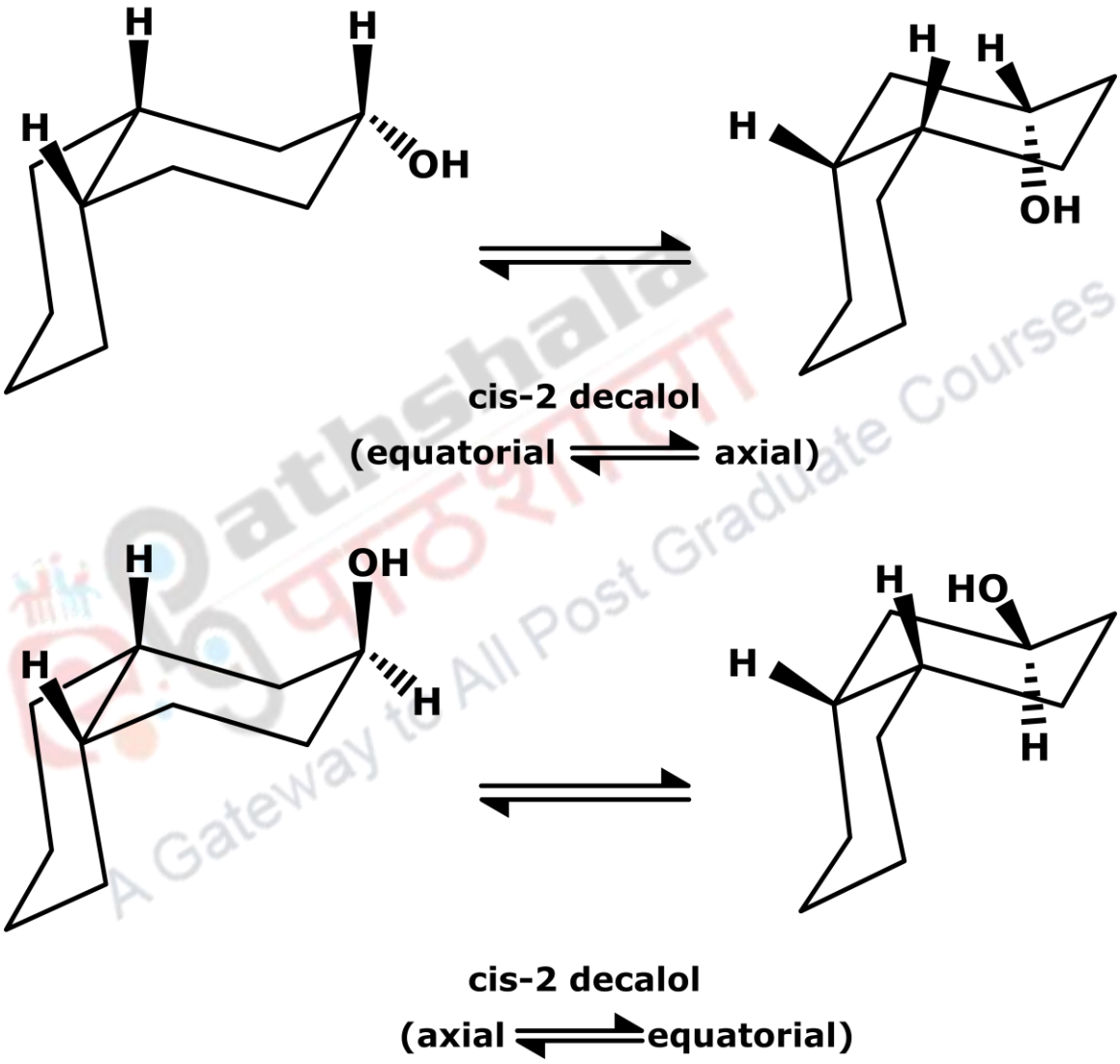

Figure 16. Stereoisomers of cis-2-decalol

Conformational analysis of cis-2-decalols suggests the bottom equilibrium to be more stable than the one shown on top due to the non-equivalence of the convex and concave sides. The axial hydroxyl group on the concave side would experience 1,3-diaxial interactions making it less

stable. The equatorially substituted hydroxyls in both the equilibriums have same energy as they do not face any steric repulsions. Both the equatorially substituted decalols are more stable than their axial counterparts and hence contribute more towards the actual state of the molecule.

5. Summary

- Decalin also known as bicycle[4,4,0]decane is a bicyclic molecule that has more interesting configurations and conformations over the regular cyclohexane. The fusion of two cyclohexane rings imparts special characteristics to this molecule.
- Decalin has two cyclohexane rings both in their most stable chair form and thus it is free from any torsional strain.
- Due to the rigidity imparted by the fusion of two rings, it exhibits geometrical isomerism and exists as two diastereomers, namely, cis and trans decalins.
- In cis decalin, the two bridgehead hydrogens point in the same direction and one of them is axial while the other is equatorial.
- In trans decalin, the two bridgehead hydrogens point in opposite directions and are both axial hydrogens.
- trans Decalin is '**conformationally locked**' in equatorial conformation and any attempt to invert the ring would lead to breaking of bond. (The two axial carbons would be too far apart to form a six membered ring). The same is supported by NMR studies.
- Cis decalin, on the other hand, exhibits a rapid ring inversion.
- The trans decalin is achiral as it has a centre of symmetry while the cis decalin is chiral. However, the chirality in cis isomer gets cancelled due to rapid ring inversion that results in a non-resolvable isomers (mixture of +/-).
- trans decalin is more stable than cis decalin by 10.5 kJ/mol owing to three gausche interactions in the latter.
- Cis decalin is more like a tent shape molecule with two non-equivalent faces (convex and concave sides) in contrast to trans isomer which is more or less flat.
- Substitution at the bridgehead carbons increases the number of butane gausche interactions in both the isomers (more in trans as it is an axial substitution) and thus alters the energy gap between the two isomers.
- The decalin moiety appears frequently in natural products like steroids, terpenes and alkaloids and in these natural compounds, the cis isomer exhibits a particular conformation termed as steroidal conformation.
- Introduction of a substituent other than on bridgehead carbons gives rise to a new chiral centre in the decalins and thus increases the number of stereoisomers.
- The substituent not only generates the chiral centre at the point of substitution but also makes the bridgehead carbons chiral by disrupting the symmetry in decalin. Hence, decalols will have three chiral centres and decalones will have two chiral centres at the two bridgeheads.
- The number of stereoisomers theoretically possible for decalones are, $2^2 = 4$. These exist as two enantiomeric pairs, one each for cis and trans decalone. The conformational flexibility in cis isomers, however, increases the possibility of more stereoisomers.

- The number of stereoisomers theoretically possible for decalols having three chiral centres are, $2^3 = 8$. These exists as four pairs of enantiomers, two each for cis and trans decalol.
- Trans decalol, being more conformationally rigid, exhibits two diastereomeric isomers, namely axial decalol and equatorial decalol. Each of these diastereomers further exhibits enantiomerism resulting in a total of four stereoisomers in trans decalols.
- The cis-isomer, on the hand, is more complicated owing to its flexibility and the possibility of ring flipping. There are two different spatial arrangements for axially as well as equatorially substituted decalols. However, they can interconvert through the equilibrium involving ring flipping.