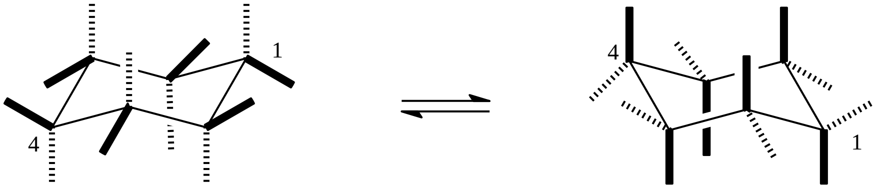
CONFORMATIONAL ANALYSIS OF CYCLOHEXANOLS

Background Information

You may remember from first semester organic chemistry that the lowest energy conformation of cyclohexane is the *chair*. There are two equivalent chair conformations. When one chair conformation "flips" into the other, the *axial* and *equatorial* hydrogens interconvert.



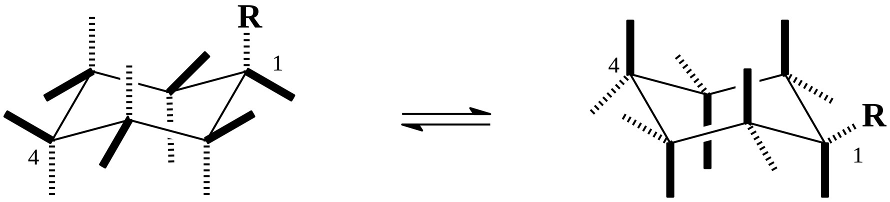
In the illustration above, the two chair conformations are in equilibrium. In the left-hand cyclohexane chair, carbon atoms 1,3 and 5 are above an imaginary horizontal plane and carbon atoms 2,4 and 6 are below the plane. When the chair flips to the right-hand conformation, the carbon atoms that were below the plane are now above it, and the carbon atoms that were above the plane are now below it.

On the left-hand chair, the hydrogen atoms shown with a dashed line are all *axial*. The hydrogens are axial and *up* when they are attached to a carbon atom that is "up", or above the plane. The hydrogens are axial and *down* when they are attached to a carbon atom that is "down", or below the plane. The hydrogen atoms shown with a solid line are all equatorial. The hydrogens are equatorial and *down* when they are attached to a carbon atom that is "up", or above the plane. The hydrogens are equatorial and *up* when they are attached to a carbon atom that is "down", or below the plane. Each carbon atom is attached to one hydrogen that is up (either ax. or eq.) and one that is down (either eq. or ax.).

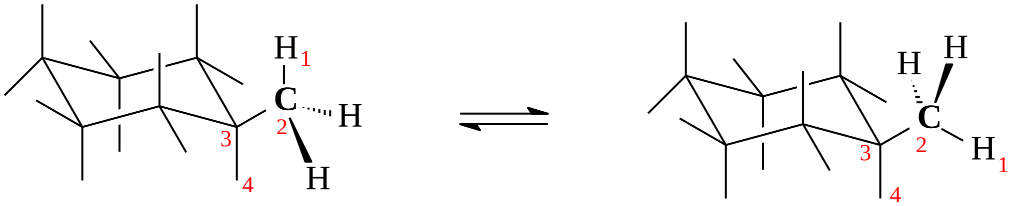
When the chair flips, the hydrogens that were down are still down, and the hydrogens that were up are still up. However, the hydrogens that were axial are now equatorial and the hydrogens that were equatorial are now axial.

Hydrocarbon Substituents

When a hydrocarbon substituent is bonded to the cyclohexane, replacing a hydrogen, it affects the relative stabilities of the two chair conformations since now the substituent can be either axial or equatorial. As you learned in organic chemistry, the equatorial position is favored. As the size of the alkyl substituent increases, the percent of the equatorial conformation increases.



In addition to the axial/equatorial placement of the alkyl group, the orientation of the atoms within the alkyl group will affect the energy.



In the left-hand conformer, the C-H bonds in the methyl group are all staggered with the ring carbons and axial hydrogen; in the right-hand conformer, the methyl hydrogens eclipse the C-C and C-H bonds of the ring, a higher energy conformation (e.g. H1 and H4).

Exercise

You can calculate the steric energies of these two conformations of the methyl group in CHEM3D to see the differences.

Build a methylcyclohexane in either ChemSketch or Chem3D. Don't worry about the conformation of the methyl group itself. Make sure the methyl group is in the equatorial position by moving it if necessary.

In Chem3D, *minimize the energy* of methylcyclohexane. Rotate the model so the chair conformation is oriented as you see it above. Now rotate the methyl group around its bond to the ring carbon so it is approximately in the left-hand conformation as you see it above. Show the dihedral angle Measurements in the measurements window.

To ensure that the bonds are perfectly staggered, select the atoms 1-4 shown in red, and change the Actual dihedral angle in the measurements window to 180 deg. Now calculate a *single point energy* for the conformation. Copy the messages to Excel.

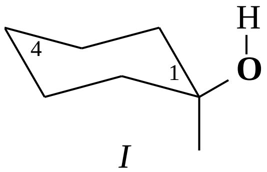
Rotate the methyl group so it is approximately in the right-hand conformation as you see it above. To ensure that the bonds are perfectly eclipsed, select the atoms 1-4 shown in red, and change the Actual dihedral angle in the measurements window to 0 deg. Now calculate a *single point energy* for the conformation. Copy the messages to Excel.

Compare the various energy terms as was done for the *cis*- and *trans*-butene isomers in a previous exercise.

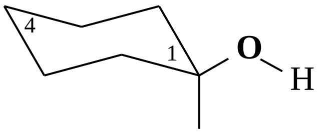
Other Substituents

The situation is not quite as simple when non-hydrocarbon groups are substituted on the ring. Solvent and other factors influence the conformer population.

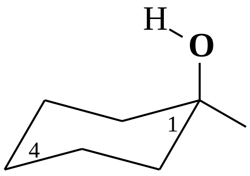
For cyclohexanol, the hydroxyl group can be either axial or equatorial, and the hydrogen can point either into or away from the ring.



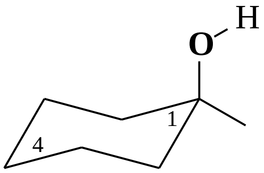
I



II



III

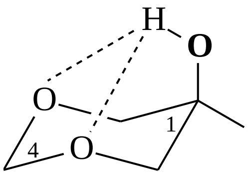


IV

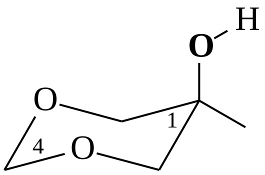
Exercise

Calculate the steric energies of the four cyclohexanol conformations. Compare the two equatorial conformations with the similar conformations of methylcyclohexane, above.

There is an additional interaction when there are oxygens within the ring. Consider the 5-hydroxy-1,3-dioxacyclohexane conformers below:



V



VI

Calculate the steric energy of these conformations. Where is the biggest energy difference: between III and V or between IV and VI? (The steric energy difference between either of these pairs (III and V or IV and VI) is meaningless, but a comparison of their differences is valid.)