

4.4: Substituted Cyclohexanes

Monosubstituted cyclohexane

For the cyclohexane ring itself, the two conformers from the ring flipping are equivalent in terms of energy since there are always six hydrogens in *axial* position and six hydrogens in *equatorial* position. For substituted cyclohexane however, the two chair conformations are **not** equivalent any more. Let's see the example of methylcyclohexane.

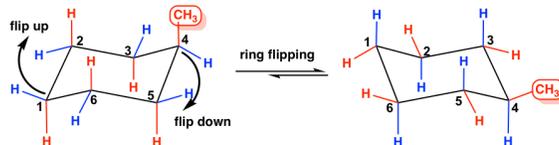


Figure 4.4a (Left one) I, less stable & (Right one) II, more stable

Methylcyclohexane has two chair conformations that are interconvertible through the ring flipping. In conformation **I** the methyl group occupies an *axial* position, and in conformation **II** the methyl group occupies an *equatorial* position. Studies indicate that the **conformer II** with the *equatorial*-methyl is more stable, with the energy of about 7.6 kJ/mol lower than the other conformer.

This difference is due to the “**1,3-diaxial interaction**”. In *axial*-methyl conformation, the methyl CH₃ group (regarded as #1 position) is very close to the *axial* hydrogens that is one carbon away (regarded as #3 position), and it causes the repulsion between each other that is called the 1,3-diaxial interaction. This type of repulsion is essentially the same as the *gauche* steric strain because the CH₃ group and the CH are in *gauche* position. While for *equatorial*-methyl conformer, no such strains applied because the CH₃ group and the CH are in *anti*-position. This interaction could be illustrated more clearly by Newman projection.

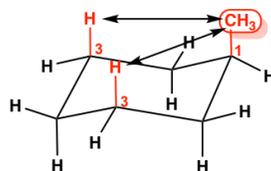
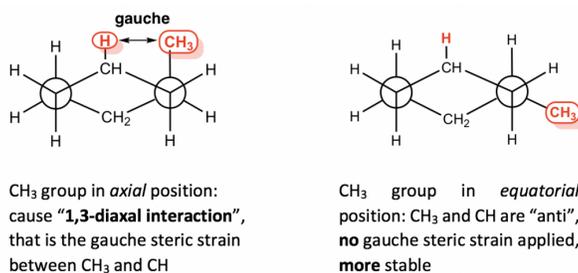


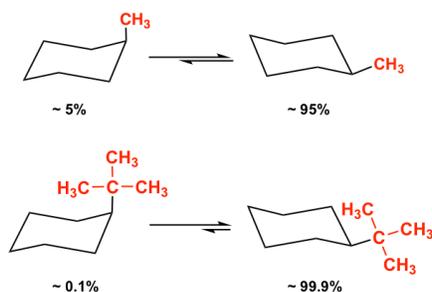
Figure 4.4b 1,3-diaxial interaction



For mono-substituted cyclohexane, the *equatorial*-conformer is more stable than the *axial*-conformer because of the 1,3-diaxial interaction.

Since 1,3-diaxial interaction is essentially the steric strain, so the larger the size of the substituent, the greater the interaction is. For *t*-butylcyclohexane, the conformation with the *t*-butyl group in the *equatorial* position is about 21 kJ/mol more stable than the *axial* conformation.

Because of the stability difference between the two chair conformers, the *equatorial*-conformation is always the predominant one in the equilibrium mixture. The larger the size of the substituent, the larger the energy difference and the equilibrium constant *K*, so the equilibrium lies more toward the “*equatorial*” side. For methylcyclohexane, there is about 95% of *equatorial*-conformer in the mixture, and the percentage is about 99.9% for *t*-butylcyclohexane.



Disubstituted cyclohexane

When there are two substituents on different carbons of a cycloalkane, there are two possible relative positions between the two groups, they can be either on the same side, or opposite side, of the ring, that are called **geometric isomers**, a type of **stereoisomers** (more discussions in **Chapter 5**). The isomer with two groups on the same side of the ring is the “*cis*” isomer, and the one with two groups on opposite side is called the “*trans*” isomer. Because the C-C bond can not rotate freely due to the restriction of the ring, the two geometric isomers can not be interconverted.

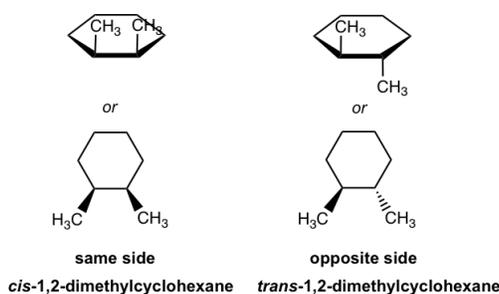
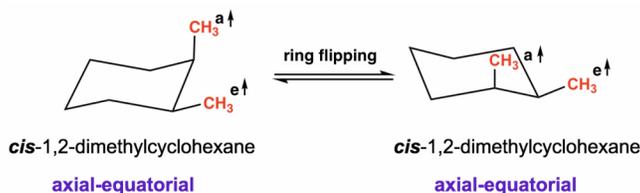


Figure 4.4c *cis*-1,2-dimethylcyclohexane (same side) & *trans*-1,2-dimethylcyclohexane (opposite side)

So now when considering about the conformational isomer, the stereoisomers should be taken into account as well. The general guideline for determining the relative stability of conformers for a certain isomer is:

- The steric effects of all substituents are *cumulative*, more substituents in *equatorial* positions, when possible, the more stable the conformation isomer will be.
- For different substituents, the conformer with *larger* substituent in *equatorial* position is more stable.

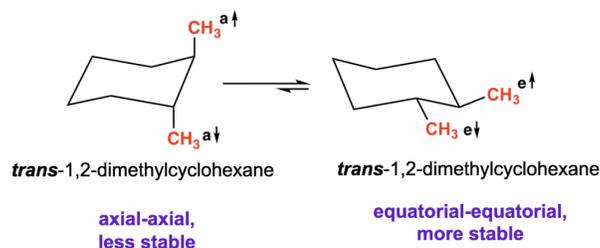
Let us start with *cis*-1,2-dimethylcyclohexane, and compare between the two possible chair conformations:



For both conformations, there is one methyl group in *equatorial* and the other methyl group in *axial*, so the two conformers are **equivalent**, have same energy and stability level.

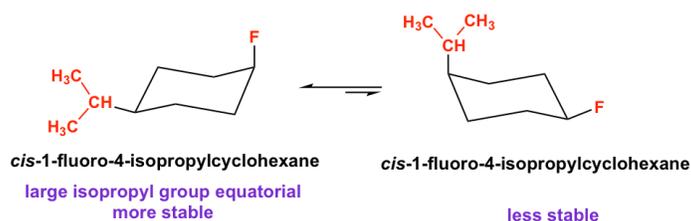
How to tell a isomer in chair conformation is *cis* or *trans*? A general way to recognize is to check that whether a group attached by the bond is above the ring (\uparrow , point up), or below the ring (\downarrow , point down). If both groups point to the same side, the compound is *cis* isomer; otherwise it is *trans* isomer.

How about the *trans*-1,2-dimethylcyclohexane? There are also two possible chair conformations:



In one conformation both methyl groups are *axial*, in the other conformation both methyl groups are *equatorial*. These two conformers are **not** equivalent, and the di-*equatorial* one is the more stable conformation as we would expect.

cis-1-fluoro-4-isopropylcyclohexane is the structure with two different substituents. Both chair conformations have one *axial* substituent, and one *equatorial* substituent. According to the guideline, the conformer with *larger* substituent in *equatorial* is more stable because if the large group is axial, stronger steric strain will be generated and it is less stable.



Exercises 4.3

Determine which is the more stable isomer, *cis* -1-ethyl-2-methylcyclohexane or *trans* -1-ethyl-2-methylcyclohexane?

Tips: draw all the chair conformers of each isomer, and decide which is the most stable one.

[Answers to Practice Questions Chapter 4](#)

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