Cyclohexane Ring Stereochemistry   -   Chem 2100 Handout

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There has always been confusion regarding cyclohexane rings, their conformations and their stereochemistry. I have prepared this handout in hopes of reducing this confusion. This is the "gospel" according to Kevin and "thou shalt not believeth" something different.

Part I.   How do you draw the cyclohexane ring and position the substituents?

Start by drawing the ring as one of the following:

You may find it easier to keep your 3-D perspective if you darken the front pointing bonds using heavy bonds and wedges as follows:

Now you need to place the axial substituent bonds. These bonds will point upward towards the top of the page or downwards towards the bottom of the page (3 in each direction). The direction of the bonds alternate up-down-up-down-up-down as you go from one carbon to the next:

Now that the axial bonds are in place, the equatorial become much easier if you keep one thought in mind - "bond angles around C with 4 bonds are optimally ~109.5 degrees". Draw the equatorial bonds so that they form a 109.5 deg angle (i.e. >90 deg) with the axial bond draw above. Make sure they point a little up or a little down rather than pointing directly towards the left or right margin. This will be extremely helpful latter when we determine the _cis-trans_ relationship between substituents.

or
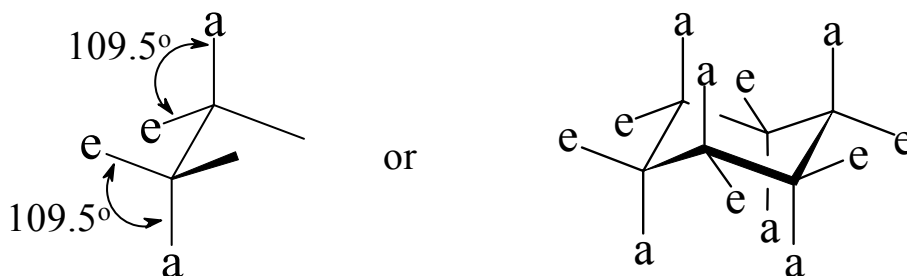
The next thing we need to do is to determine what happens to each substituent when we "flip" the cyclohexane ring. What you need to remember is that each axial substituent becomes equatorial and each equatorial becomes axial.
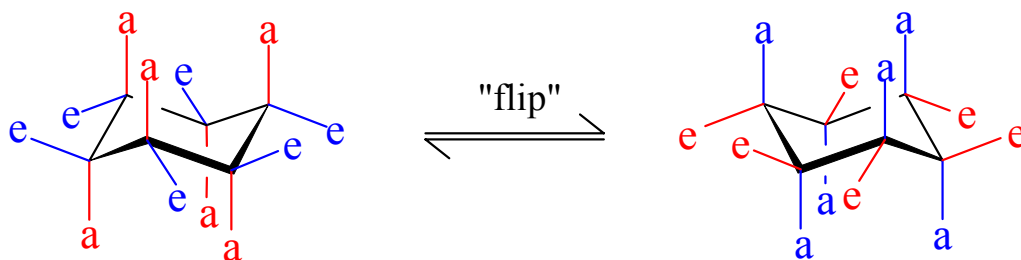

Part II. Determining the position of a substituent in the most stable conformer.

This is very easy if you remember a couple of points: 1) the electrons of the substituents repel one another and therefore, they prefer to be as far as possible from other substituents and 2) the axial positions above the ring point into the same space as is true for the axial positions below the ring (see figure) thereby putting the substituents very close together. However, the equatorial bonds point out away from the ring providing much more room for the substituents (compare below).
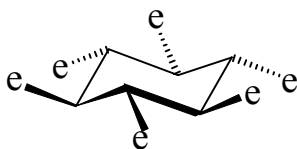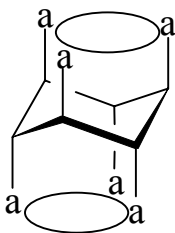
Therefore, if possible all substituents would prefer to be in equatorial positions. However, if one is in the equatorial and one is axial, preference would be given to the larger group being equatorial. Do you recall our example of a bulking substituent: t-butyl group better know as "the shrub!!"
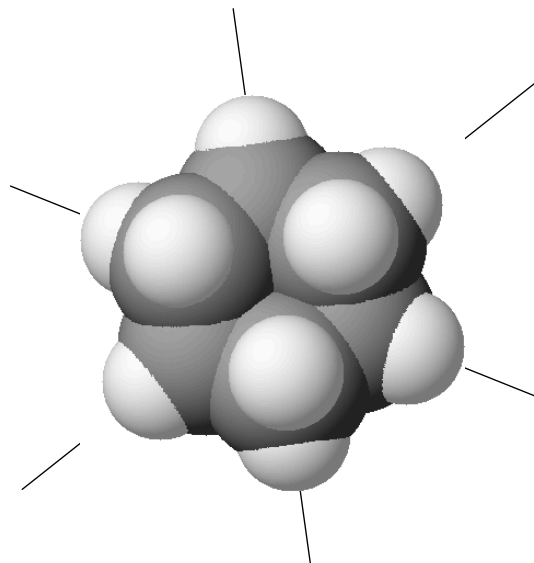
## Part III. *Cis-trans* relationship between cyclohexane substituents

Your first rule: **there is no rule to predict this**. If you walked out of the lab thinking there was a rule, congratulations!!!! You will be **WRONG 50% of the time**.

Example of what I mean: If two groups are AXIAL, then CIS - **WRONG 50% of the time**
                        If two groups are EQUATORIAL, then CIS - **WRONG 50% of the time**

In my mind, a 50% error rate "sucks" so DON'T USE A RULE. Let me show you the relationship.

First, we define:

        cis   - refers to two substituents being on the same side of the ring (or double bond)
        trans - refers to two substituents being on the opposite side of the ring (or double bond)
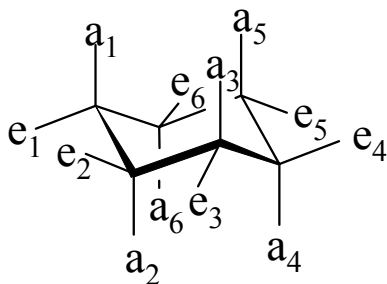
If you have drawn your cyclohexane substituents correctly as shown at left, this next bit should be straight forward.

Carbons 1 and 2:

The axial substituents (a_1 and a_2) are pointing 180 degrees apart (*ie.* on opposite sides of the ring) and therefore, they are _trans_ to one another. Then also, the equatorial substituents (e_1 and e_2) must be _trans_ to one another and each axial substituent must be _cis_ to the equatorial substituent on the other carbon (ie. a_1 is _cis_ to e_2 and a_2 is _cis_ to e_1). If your equatorial substituents point slightly down or up, then you can see this relationship.

Carbons 1 and 3:

The axial substituents (a_1 and a_3) are both pointing up (*ie.* on same side of the ring) and therefore, they are _cis_ to one another. Then also, the equatorial substituents (e_1 and e_3) must be _cis_ to one another and each axial substituent must be _trans_ to the equatorial substituent on the other carbon (ie. a_1 is _trans_ to e_3 and a_3 is _trans_ to e_1).

Carbons 1 and 4: *(as above with carbons 1 and 2)*

The relationship here is the same as we saw for carbon 1 and 2 above. The axial substituents (a_1 and a_4) are pointing 180 degrees apart (*ie.* on opposite sides of the ring) and therefore, they are _trans_ to one another. Then also, the equatorial substituents (e_1 and e_4) must be _trans_ to one another and each axial substituent must be _cis_ to the equatorial substituent on the other carbon (ie. a_1 is _cis_ to e_4 and a_4 is _cis_ to e_1).

This relationship continues to alternate as you go around the ring and therefore, one rule will not allow you to predict the relationship of any set of substituents. However, look at the following to see the pattern.

	Relationship between Substituents		
Carbons	Axial - Axial	Axial - Equatorial	Equatorial - Equatorial
1 and 2	Trans	Cis	Trans
1 and 3	Cis	Trans	Cis
1 and 4	Trans	Cis	Trans
1 and 5	Cis	Trans	Cis
1 and 6	Trans	Cis	Trans

I hope this will help your understanding of cyclohexane stereochemistry. Make sure you are very careful with a general rule here and you should be fine. If the is still problems, we need to try to take care of them during tutorials or in my office.

                                           Thanks, Kevin.