

Lecture 8A • 10/12/11

Cyclic compounds

{using models}

You can make a cyclic alkane with as few as three carbons. If you've only got two carbons, you've got ethane; two points can't make a circle. But if you had three carbons, you could make cyclopropane. This model would demonstrate to you what the difficulty in making cyclopropane would be. I don't want to ruin my models, so I won't actually do it, but if you tried to join these three carbons in a circle, it isn't going to go too terribly well. There's an awful lot of angle strain that's involved; already these are puckering, if I push too hard, they're gonna break. Why is it that you would expect that there would be a lot of stress in the system with only three carbons in a ring? Because for sp^3 -hybridized carbons, the ideal angle is 109.5° . If you had cyclopropane, then what would the angle between any two of the bonds be? Only 60° . This is called angle strain. It is higher potential energy caused by the distortion of bonds caused by deviation of molecular geometry from ideal bond angles. For something like cyclopropane, only 60° angles would be possible; that's way off from 109.5° . That means that the bonds won't overlap as efficiently, the orbitals. More orbital produces a stronger bond; if you then try to bend the bonds, where there's not as good an orbital overlap, that means the bonds are weaker. Weaker bonds means that not as much energy is released in making the bonds, so putting that the other way around, that means that, technically, you're raising the energy of the system as you're distorting and acting like you're going to break these bonds.

The situation gets a little bit better if you were to add one more carbon to it. If I put four carbons together, you can see I can almost make this model without bending it too extremely. Notice that you don't automatically make perfect 90° angles because this is a three-dimensional object, so it is going to pucker a little. But it's close enough to 90° that it's not going to be terribly favorable. By the time you get to cyclopentane, though, if we have five carbons, we can easily make a ring compound out of it, with very little stress at all. The molecule won't exist totally planar, it will pucker a bit, but it will be close to that 108° angle in a pentagon – awfully close to that 109.5° angle. Then we add one more carbon – in a hexagon, if it were flat, what would the bond angle be? 120° . But you're not going to have 120° in cyclohexane. Why? Because this is a three-dimensional structure, so it will try to adopt some kind of geometry where every carbon gets its 109.5° angle.

So, three-member rings, highly strained; four-member rings, strained, but you can form them – penicillin has a four-member ring as one of the major structural components of the compound; five-member ring, almost no strain; and six-member ring, technically zero strain. Five- and six-member rings are the easiest ones to form.

What do you think happens if you put a seventh carbon in? It actually becomes strained just a little bit again. From 7 through 11, there's a little bit of this ring strain that comes back; past that point, the molecules get so huge that atoms are no longer bumping into each other at all, and all of those rings would be stable in terms of thermodynamics, The large the ring that you're trying to make, if you're trying to close the ring, then the large number of carbons that you get, the harder it is to close that ring because the two ends are so far away from each other, the chain would flop around so much that it would be difficult for those two ends to come together to form a ring.

Angle strain is higher potential energy caused by bonds distorting cause by their bond angles being pulled away from ideal values. Cyclobutane – not totally planar, angle approximately 88° . These [cyclopropane and cyclobutane] are very strained. Cyclopentane we're going to have 108° angle, awfully close to that 109.5° . And then cyclohexane, even though on flat paper a hexagon should have 120° angles, it [cyclohexane] doesn't. It will adopt that 109.5° angle, because there is the room for it to do so. These [cyclopentane and cyclohexane] have little to no angle strain. Rings with 7 through 11 carbons have a very small amount of strain. Past 11, rings again have no strain.

{focus placed on geometry of six-member rings}

Cyclohexane has two principal lowest-energy forms; one of them is much lower energy than the other. If you arrange a cyclohexane ring so that, as you are going around the ring, you appear to have the same kind of zigzag shape that we expect in a straight-chain compound Let me show you that when you start to link carbon to carbon to carbon, because of the 109.5° angles, since each carbon is tetrahedral in geometry, you can see that you get this natural zigzag pattern, which is exactly why I've been writing these zigzags down for the structures that you've see so far. When you bring this around into a ring, you effectively are able to keep that zigzag pattern; as I turn this around, you can see it's got that kind of up, down, up, down geometry. Chemists are sometimes very imaginative. If I tilt this a little bit to the side and if you imagine that I'm sitting down like on a chair – this is called the chair form of cyclohexane. Chemists are either imaginative, or they spend too much time in lab smelling the ether; maybe a little bit of both.

How do you write the chair form of cyclohexane. The most common convention is to have two of the bonds – the ones on the left and right sides of the compound – slanting from lower-left to upper-right. Thus, start by writing two parallel lines like that.

Next, write two v's, like this. That is a rough version of the chair form of cyclohexane. Let me show you the other form that can be made, but let me show you how I'm going to do it. I'm holding on to this structure, and I'm going to twist one of the carbons. Notice what happens: the two carbons connected to it appear to pucker in the other direction. Now I have a structure where I have two substituent points up at the top that are now pointed towards each other. Hopefully it makes sense that when we have these two groups pointed to each other, we're going to potentially run into that steric hinderance, that steric strain seen in rotomers. We can look along the bonds and figure out that there's some strain in the rotomers that form by doing this. This is a less-favorable structure. Again being creative, this was named the boat form of cyclohexane. The reason I care about this is: if I start out with one form of cyclohexane with two substituents on here – you can see that the two substituents I've added to the ring are currently pointed straight up or down; the one on the right is pointed down, the one on the left is pointed up. These are all single bonds, so single bond can rotate. They'll rotate around. If I do this kind of double flip – I flip the carbon on the left, I flip the carbon on the right – I've made another chair form; but, the substituents that used to be pointed up and down are now pointed side-to-side instead. This process of going back and forth between the two possible forms of cyclohexane, this is called a ring flip.

In green, I'll write in all of the lines that are pointed straight up and down from the structure. How do you know which way to draw the line? How do you know whether to draw it up or draw it down? We're not using dashes and wedges at the moment; remember that when we saw dashes and wedges, where the two plain lines are pointed towards, the dash and wedge point away from that. You can use the same kind of reasoning here. For example, if you've got on the left of this compound two lines that are pointed down and making a point; the other two substituents have to point away from that position. One of them is going to point down, one of them is going to point up. Moving to another position on the molecule, back behind here; you have the two plain line of the ring that are pointing up, and so what other substituents you have must also be pointed in that up direction. So every other point, the substituent that's vertical is pointed up and then down then up and down. Since these positions are parallel to the axis through this – if you wanted to just rotate this compound around just like it was a circle – since they're parallel to that axis, these are known as axial substituents.

Let me write another separate ring. This is the trickier one, to write that other set of substituents. Now on the left here, I've have three substituents that I've drawn; two of them are pointing down this way, that means the other one has to come out this direction. You're going to make that same zigzag pattern. Coming from the right, I'm going up, down, and the next one is going to be up. If I'm coming around to this other carbon, I'm going up, down, up, so the next one's going to be down. Let me go ahead and write in all six of them. These are the equatorial substituents. Why? Cause it's like they're coming out on the equator.

We're going to learn how to rewrite structures in line structure form or going back and forth to this chair form of cyclohexane. Let's start with a simple example. Let's say I have a cyclohexane ring that has two bromines attached. Notice that I've written both of these with wedges. Right now we're visualizing the molecule like we're looking down on top of the cyclohexane ring. So, if I have two bromines on neighboring carbons like this, how can I make it so that both of them are pointed up, relative to my point of view? Am I going to start with an axial or an equatorial substituent? The answer is yes. Remember that this ring is really flipping back and forth, so no matter which on you start with, it's going to turn into the other one eventually; so you choose one to start one. I'm going to choose this axial substituent. I'm going to start out arbitrarily with one of the substituents being on the axial. You can see that the other axial position is pointed down, so another way of saying it is it's not the one pointed up. The one that's equatorial, it almost looks like it is just coming out straight at you, but it's not; it's really tilted up just a few degrees. This is straight down; 109.5° , that means this is 19.5° from horizontal, so it is pointing up just a little bitty bit. That means that putting the substituents on that equatorial position is going to give you the correct kind of geometry. This type of substituent pattern, where both the substituents are on the same face of the ring, that's called cis, just the same cis and trans terms we saw for double bonds.

Now let's going ahead and translate that to the chair form of cyclohexane. So draw chair cyclohexane. Because it's pretty easy to identify, I'll take this back carbon and make this axial positions where I place one of the bromines. Let's say I wanted to put the other bromine in the front here. The top bromine would now correspond to the bromine I just wrote; the bottom bromine would therefore have to go at the equatorial position. Vicinal means neighboring positions. This would be referred to as a vicinal dihalide. There another term that's very common – geminal, gemini, the twins. Geminal means double substitution at one position. If I had a geminal diol, –ol means alcohol, –diol means two alcohols, geminal would mean two alcohols at the same carbon. Whenever you have a vicinal cis substitution pattern on a cyclohexane ring, one substituent is always cis, and the other's always trans.

Let's do a ring flip, which is the following. if you take the molecule and you invert one side and then invert the other, you're going to go back to a chair form again. Observe what happens during the ring flip. So I have a substituent that's further in back in the axial position; I have the substituent that's closer to you in the equatorial position. Currently, the one that's in back is red, the one that's in front is green. Let me do a ring flip; I'll take one half of the molecule and invert it, I'll take the other half of the molecule and invert it. Notice that the one that's closer to you is now the axial position, and the one that's further away from you, it is now the equatorial position. That looks easy on the model, let's do it on paper.

Let me show you one answer that's often given. A ring flip is an inversion of a cyclohexane ring in which axial substituents become equatorial and vice versa. I'll start with the same type of example; I'll make one of them bromine, but I'll make the other one chlorine. Let's make the bromine red and the chlorine green, just for the models. I'm going to start out with bromine in the back in the axial position, then I'll move to the front and make chlorine in the equatorial position. Now if I draw this in ring flipped form, the answer that is often given If you take me literally and take the bromine and instead of the axial you put it now in the equatorial position, and I take the equatorial chlorine and now make it axial, this appears to be the ring flipped version, but there's a problem. Take the model, do the ring flip. So bromine was axial in the back, chlorine was equatorial and in front. You can see [after the ring flip], we have the chlorine axial now, the bromine equatorial. But wait, chlorine is pointed down in that molecule, and bromine is also pointed down in that molecule. If I tried to make that match with this model, I'll just turn it 180° upside down. But now look what we've got: we've got the chlorine axial, which would match this, but bromine's in front of me, here it's in back. This is related to stereoisomers. If I took the bromine and put it at this other position, in order to do it what I really did, I took the bromine off the molecule, I broke the bond, moved it to the other position, which means I didn't really do a ring flip, I just threw the bonds around. Same thing with the chlorine; in order to get it to the position with this ring being in the same place, the chlorine I'd have to pluck off and then put on the other position. I just made the mirror image. This is an improper ring flip. The axial and equatorial positions were exchanged, producing a mirror-image molecule. Why is it that switching the two positions around would change the molecule?

What would be the proper ring flip? Here's another way that may be simpler to explain it. I had this molecule before, the two groups were pointed up at me. So why do I think I can get away with a molecule where the groups are pointed away from me? Why not we just write it the way we want it? Starting out with that same cyclohexane, I need to keep the relative positions of everything the same. So, bromine, if we're going to do the alternate form, needs to be in the equatorial position, but needs to be pointed up. Well, now it is. Chlorine needs to go into the axial position, but be pointed up, which now it is. Notice how this appears on paper to be scooted one carbon back, but it isn't really. If we take the proper model and visualize it, that's exactly what we have – chlorine in front in the axial position, bromine in back in the equatorial position. This is just some of the difficulty of working with cyclic structures on two-dimensional paper. This is a correct inversion, a proper ring flip, because the relative geometry – up versus down – is maintained.

Another way that sometimes people show the ring flips: the drawing convention that I've been using so far is that the lefthand side is low, and the righthand side is high. When I ring flip, look what happens, the lefthand side goes high, the righthand side goes low. Another way to avoid this problem is to write the cyclohexane ring backwards. If I write it backwards, it's easy for me to make the bromine equatorial and the chlorine axial. Whichever way you do it is fine, as long as you maintain the proper orientation. In this case, translating back to the flat structure, the line structure, it would look like this for any of the correct representations.

It might help if I went back and numbered my carbon positions. I numbered the bromine as number 1 because if I'm trying to figure out what the most important substituent on a ring is, if I could number it from different directions, I give the lowest number to the lowest alphabetical substituent. Bromo versus chloro, bromo would therefore end up with position one. When numbering a ring compound, I wouldn't number this way, I wouldn't go this way, because it would give me substituent numbers of one and six. Instead, I would go this direction, because it gives me substituent numbers of 1 and 2. Let's do the same kind of numbering with the correctly ring-flipped structure. Where the carbons show up is at a different position, but it has to be, in order to maintain a correctly-drawn structure. The chlorines and bromines are still on the exactly the same carbons, but that doesn't mean they're on the same place on paper. That's the part that confuses people.

The other possibility for a vicinal disubstituted compound would be if one is pointed up and one is pointed down. This, when they're in opposite directions from each other, this is trans, which would be both substituents pointed opposite ways. For vicinal trans-substituent cyclohexane rings, both substituents are either axial or equatorial. Again, I will arbitrarily begin in my example showing both of them at the axial position. Why? Because it's easier to draw the axial positions. I need bromine pointed up towards me, that's the only reason I will put bromine here. The way I draw the ring, I could have put the bromine on this carbon, or I could have put it on this carbon, it doesn't matter, as long as it's pointed up. Once I've established that bromine's pointed up, then relative to it, chlorine is in the clockwise position, so I have to go clockwise around my structure to the next carbon over. That one has to be pointed down, and the only way we can have it down is if the chlorine is also in the axial position. For vicinally substituted cyclohexane rings, if it's trans, both with either will axial like this or they'll both be equatorial. Before I write it down, try to draw the ring-flipped version.

If you have a cyclohexane ring, this is not the axial position, because the two lines that are part of the ring are going up, so the axial position must be written up; there is no choice. The equatorial, make that slanted to the left because it would be parallel to the other lines already part of the structure.

Let's see one possible answer. I'm going to make my answer using the standard orientation of the cyclohexane ring, with the parallelogram lying to the right. I have to have bromine up and chlorine down, and I need bromine in back of where the chlorine is. I'm going to choose this back position for my bromine. Once I have chosen it, whatever else I write on the structure, I just write in such a way that it's correct.

I strongly urge you not to memorize where these positions are; try to rationalize your way through it. Bromine is pointed up; chlorine needs to be pointed down and it needs to be clockwise, so this would be one correct way to write the structure. Let's draw one other alternate. Let's say that I had chosen this for my position for bromine, because it is equatorial, which it should be if it's ring-flipped, and it's pointed up, which it needs to be. If I then continued on clockwise, that means chlorine would need to be here, in the very front of the molecule.

Which of the two forms of the compound would be the preferential one, which would be lower in energy? Why would one be different in energy than the other? Equatorial is the lower-energy form; why? Let's draw a general cyclohexane ring and imagine that we had two really big groups, and they were both attached at axial positions. If they were both really big groups, you can see they're not that far away from each other. Anything more than a hydrogen on there, you're potentially going to have steric hinderance – not one carbon next to the other, but the fact that one axial substituent can bump into another axial substituent. That is called diaxial steric strain. Two axial substituents are close enough together to experience steric hinderance. Therefore, when possible, the most sterically-strained substituent will adopt the equatorial position. In this trans case, that means that the one were both are equatorial is the lower-energy form. This one because they're both axial, this is higher energy. At equilibrium, you'll have both of these structures in solution, because any time you have an equilibrium, you automatically have a non-zero quantity, even if that non-zero quantity means one molecule out of a trillion. You'll have more of this diequatorial one.

Backing up to the previous problem, one of these substituents – the bromine or the chlorine – could be equatorial, but not both at the same time. Since bromine is bigger than chlorine, bromine's the one that's going to be equatorial. We have a table of energy values that we could use if we're comparing. Since bromine is bigger than chlorine, we'll say that this is the higher-energy, because of the bromine being axial, and this other one would be the lower-energy form.

Technically, the cyclohexane ring should be written with dashes and wedges, since all of the bonds are pointed towards you or away from you. You will see it done sometime, particularly when encountering carbohydrates.

As soon as you put one substituent on there, it'd rather be equatorial. Why equatorial? Because it doesn't bump into anything, it's pointed off in some other odd direction.

Why is the chair form the lowest energy, besides the fact that you have the correct bond angles? What if I set my viewpoint here and look along this bond? To jump to the answer, I'm going to see this. If I look along that bond, in back, I've got an axial position, so I'm going to have something pointed straight up. In front, I have an axial position pointed straight down. Then we have the ring, which would connect around. The important point is that every bond in a chair structure has a staggered, not eclipsed, geometry.

Angle strain; chair & boat forms of cyclohexane; cis & trans; axial vs equatorial; ring flips

Angle strain – higher potential [energy] caused by distortion of bonds caused by deviation of molecular geometry from ideal bond angles.

– Rings with 7-11 carbons have a very small amount of strain; past 11, rings again have no strain.

vicinal – neighboring positions; geminal – double substitution at one position

For vicinal cis-substituted cyclohexane rings, one substituent must always be axial, the other equatorial.

ring flip – an inversion of a cyclohexane ring in which the axial substituents become equatorial and vice versa.

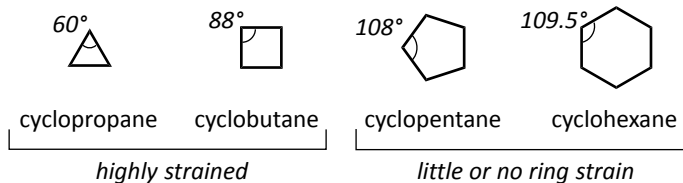
For vicinal trans-substituted cyclohexanes, both substituent must be axial or equatorial

In cyclohexane rings, substitution at an axial position causes steric hinderance due to diaxial interactions. Thus, when possible, a substituent would prefer to be at an equatorial position.

All bonds in a chair form of cyclohexane are staggered (gauche)

Structures

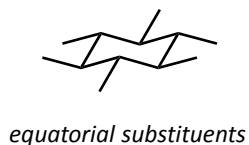
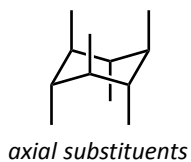
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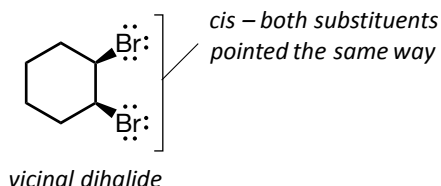
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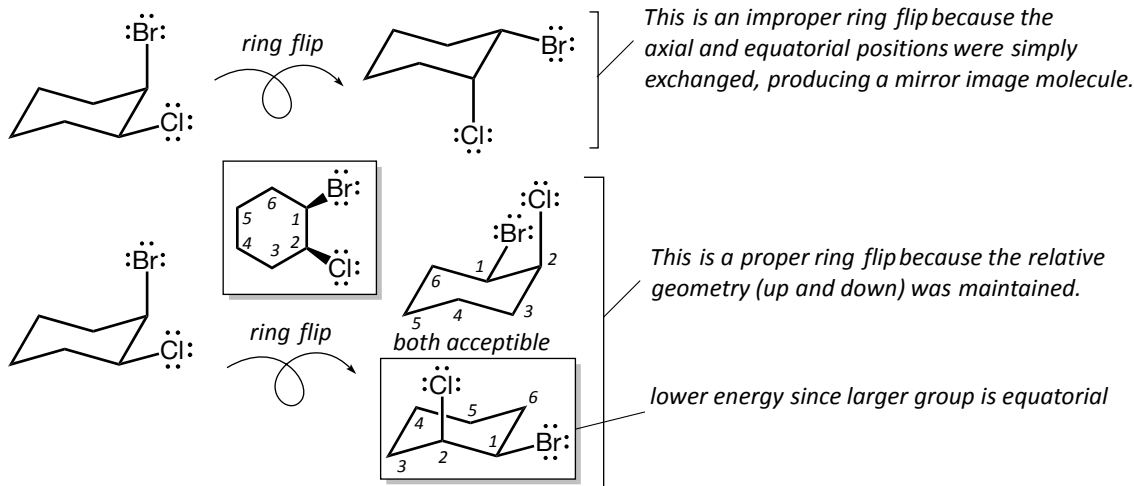
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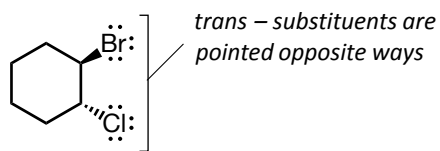
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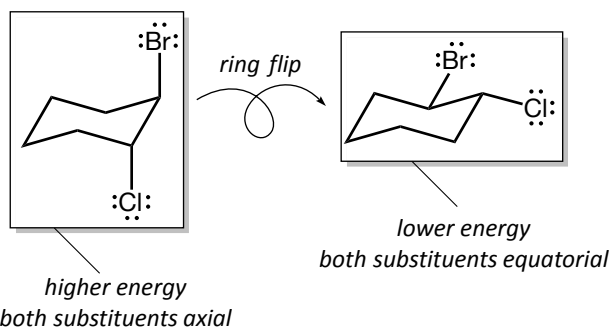
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