Lecture 8B • 10/13/11

Cyclic compounds

Let me start out with a demonstration of model sets. {encouragement to use model sets; demonstration of forming a single carbon} Let's say you take three of them and try to bend them into a ring. I'm not going to do so because I've already slightly damaged this set from doing the demonstration yesterday, but you can see that if I tried to connect these together to make a bond, then there's a huge amount of strain you'd be putting on the model set. This is something that your textbook refers to as angle strain. Can you imagine why this would cause the potential energy of a molecule to increase? What's going on when you strain a molecule in this way? It's like you're trying to break a bond. When you have direct overlap of orbitals, when they are directly overlapping with each other, that makes a stronger bond – stronger bond means that more energy is released, there's more interaction of the negative charge between the nuclei with the nuclei. In a case like this, the bonds end up getting distorted, so there's not a good overlap there. If there's not as good an overlap there, that means the bond is not as strong, so not as much energy has been released, which means the molecule is in a higher potential energy state. Another way we can think about it is: what is the geometry of a normal tetrahedral center? What is the bond angle that you'll normally find on a tetrahedral center? 109.5°. But, in this kind of molecule, what would be bond angle have to be, in cyclopropane? In an equilateral triangle, what is the angle? 60°. So 60° versus 109.5° – that's a huge deviation of bond angle, and that's the origin of the strain.

What if we put in one more carbon, to make cyclobutane? You can see that for cyclobutane, I am able to make the model, but even once I do so, you can see how it's still puckering out a little bit at the sides. So, this would have roughly a 90° bond angle; in real life, there's an ever so slight bit of puckering that occurs, so the two ends will naturally end up being a little bit different, a little bit out of plane, with the other two carbons, so the angle will end up being more like 88° – but near 90°, still not 109.5° the molecule would like to be in. But then add one more carbon to it, and we'll find that we quite easily [can form the ring]. There's only a very small amount of strain energy per carbon. We'll find out that a reaction that causes ring closure, that causes a ring to form, it's favorable because it's easy for the two ends to find each other.

Even easier is a six-member ring. What should the angle be in a perfect pentagon? 108°. If we had a hexagon, what would the angle between any two sides in a hexagon be? 120°. But it doesn't end up being 120° in real life, because this is not just going to exist in a plane; it's going to exist as a three-dimensional structure. That's the chair form. This is the lowest-energy conformation of a six-member ring. As I wrap this around, it has a sort of a zigzag pattern to it. As a consequence of having tetrahedral geometry, when you link one tetrahedron to the next, you can see that we generate this kind of zigzag pattern, which is why we're been writing line structures in that way.

First, cyclopropane. It would have to have 60° between bonds, but that's highly unfavorable, and we call that angle strain, which could be defined a higher potential energy caused by distortion of bonds caused by deviation of molecular geometry from ideal angles. Roughly 88° in cyclobutane. These two structures are highly strained. Highly strained does not mean they can't exist, though, so cyclopropane is a perfectly isolatable molecule; cyclobutane and relatives of cyclobutane can be synthesized. There's one super-important molecule that has a four-member ring in it: penicillin. Once we get to a five-member ring, since the angle is approximately 108° (if the molecule was planar), much more closely matches that 109.5° the tetrahedral carbon would rather have. Then, we get to cyclohexane. It is not planar, and the bond angle ends up being 109.5°. So, there's little or no angle strain in those molecules.

If you go beyond six carbons, you'll initially end up causing just a little bit of strain in the molecule. It's carbons 7 through 11 where you'll have a little bit of angle strain. They can be formed, but then it becomes a real-life problem in forming those rings, because the longer the chain that you make, if you start out with a linear compound, the more difficult it is for the two ends of those compounds to find each other and form a ring. There are ways to make them; they're not unstable if you make them, but they're less-frequently encountered than the five- and six-member rings. Rings with 7 through 11 carbons have a very small amount of strain. Past 11 carbons, rings again have not strain. {commentary of focus on six-member rings}

Let's focus on cyclohexane. The first thing we've got to learn is how to draw cyclohexane – not in the flat form that I have up here. This molecule I've written in the chair conformation. We'll find out in a minute why that chair conformation is the lowest-energy conformation of a cyclohexane ring. Chemists, sometimes, can be rather creative, especially in the way that they name or visualize things. I don't know exactly how this came about – again, maybe a little creativity, maybe a little too much time spent smelling the solvents in o-chem or something – but if you look at this zig-zag form, somewhere along the way imagined: what if you were sit on this molecule? If one raised part of it was like the back of a chair, this was like the legs of an easy chair. This called the chair conformation; how to write it on paper? Start with two parallel lines; the general convention is to have them tilted to the right like this. It would not be wrong to do it the other, this is the convention used. Once you have the two parallel lines, you draw Vs at the top and the bottom. That will generate this chair shape.

In the chair shape, there are two different kinds of substituents; let me write those separately. First, if you notice the model, I've got it resting on me at three positions that are pointed straight down from three of the carbons, and then I've got three substituents that are pointed straight up from three of the carbons. Notice that the carbon that's closest to you, from your left and your right, the ring seems to be pointed in the up direction, and the group that is oriented vertically is also pointed straight up. We can do the same thing on paper. On every point on the ring, where the ring is going up itself, then that substituent is pointed up. On the positions on the ring where the ring itself is pointed down, then the substituents on the ring are pointed down. Since these are parallel to an axis that, you could imagine, goes through the cyclohexane ring, imagine that you spun the cyclohexane ring about that axis, these are therefore called axial substituents.

The tricker ones to draw are the other substituents. If you were to look at a model or think about it on paper, think about the way that I went about writing tetrahedral carbons before. When we were using the dash-wedge system, any time that we had two plain lines coming together, the wedge and the dash had to continue pointing in that same direction. We can use that same logic here. When you have the two lines coming from the ring and then one substituent pointing out away from the ring, the other substituent is going to have to point out and away from the ring. If we look at the model, we can see that where the vertical substituent is pointed up, it's only slightly so, but the other substituent on that position is pointed ever so slightly down. Wherever an axial substituent is pointed down, the other substituent will be pointed up. You write it parallel to one of the other bonds that's in the ring. Let me write in those six positions. These are known as equatorial substituents – why, cause it's like they're sticking out on their equator. {need to practice drawing chair structures}

Let's look at how we can translate a flat drawing into one of these chair structures. A little terminology. Vicinal. Is anyone good with languages and knows what vicinal means? Close by; very similar to "neighbor" in Spanish. Two substituents that are right next door on neighboring carbons, so it refers to neighboring positions. Another common term – geminal. Twin. The constellation Gemini. This refers to two substituents that are on the same position. I'm going to write a vicinal dihalide. I'm going to make it a relatively simple compound. Put one bromine and one chlorine on it. Let's say we wanted to translate this now to a chair form. Should I put the bromine at an axial or equatorial position? Later on, I'll ask: which position would be be energetically more favorable for it to be on. But at the moment, if all I'm worried about is writing the structure, it's arbitrary how you do it. I'm going to choose, for convenience sake, to put the bromine at one of the axis positions, just cause it's rather easy to draw. I'll put bromine on an axial position? Where does that mean I'm going to have to put the chlorine? If I put it at another axial position, then that will actually be pointing down. My viewpoint, my visibility point right now is from in front of the paper and I'm looking down on the cyclohexane ring. Both the bromine and the chlorine need to point back up, so if I put the bromine in axial position, which means it's pointed p to mn, then since, since I go clockwise around the molecule to get to chlorine, I'll go clockwise around the molecule to get to the next carbon. The position that's actually pointing up, it's the equatorial one. This is one way of correctly representing the molecule that I have on paper. {red – bromine, green – chlorine} The bromine I put in the axial position, and the chlorine has to go at an equatorial position.

If I have both of the substituents pointed the same direction, what kind of term can I use to describe that relative geometry? Cis, as in cis and trans. When we have two things on the same face of a double bond we also call that cis; when we have them on opposite faces, we call that trans. That same relative terminology can be used here. We can call this cis because they're both pointed the same way. For vicinal cis-substituted cyclohexane rings, one substituent must always be axial, the other must be equatorial.

This is just one way to represent the molecule. Let me now introduce one of the trickiest topics of this whole section: the fact that rings can invert. If I were to take the lefthand carbon and rotate it around. Notice that we now have two groups that are pointed kinda towards each other. Sterically, that wouldn't be good, so this is a higher-energy form of the molecule (a rotomer argument can also be made why this molecule is higher in energy). This is called the boat form of cyclohexane – which I won't write down, because we'll never use it; you just need to be familiar that inversion is possible [and this is one of the distinct forms that appears during that inversion]. If I continue and take the righthand carbon and twist it around, you can see that I'm able to make another chair form. Notice that the bromine used to be axial, but now in this ring flip, it's gone equatorial. Notice that the chlorine that used to be equatorial has now gone axial. So the two have "switched" position. The ring flip is a conformer of cyclohexane, where the substituents change their positions. A ring flip is an inversion of a cyclohexane ring, in which the axial substituents become equatorial and vise versa.

But, you have to be extraordinarily careful how you write a ring flip structure. I'll show you an example that will be one of the most difficult to follow. Here's what you need to watch out for. Let's say that I take this definition and blindly operate on it. If I take my original structure and just move the bromine from being the axial to the equatorial position, move the chlorine from being the equatorial to the axial position. There is a problem, though, with the way that I've written this molecule – this is the mirror image. What we had originally was a molecule in which both substituents were pointed up at me. If you flip the molecule upside down, think of it this way: if I flip it upside down, chlorine would occupy the position in back, bromine would occupy the position in front. But that's not what I've got; I've still got bromine in the back position, and chlorine in the front position. Here is the molecular model to show what it should like when I do a ring flip. Bromine is in the equatorial position, but it's pointing up. If I flip the molecule 180° around, notice that I'm going to have to go counterclockwise to get to where the chlorine is now located. But in this structure, I had to go clockwise.

It's just like the left and the right hands: they're very similar, they're mirror images, but they're distinct geometry. So this is an incorrect way to draw the structure. Why? Because the way that I got here was done incorrectly. When I flipped the axial and equatorial substituents, I didn't ring flip, I literally pulled the bromine off and stuck it on the other position. Same thing with the chlorine – I just pulled the chlorine and stuck it on the other position. That means I broke bonds – that means I made a different molecule. You cannot just simply swap the two; you've got to keep perspective in mind. So this is an improper ring flip, because the axial and equatorial positions were simply exchanged, producing a mirror-image molecule.

How could we write this correctly? Don't worry about how the molecule originally started; don't worry about the original structure. Refer back to that flat cyclohexane ring. We still want bromine and chlorine to both be pointed up, and we still want the chlorine to be, from this perspective, clockwise from the bromine. Let's draw a chair form, and then choose one of the positions to put the bromine in. There are three equatorial positions on this molecule that are pointed up. Doesn't matter which one we use, as long as we're consistent in the way that we draw the structure. Let me choose the back carbon – it's equatorial and pointed up. Now the chlorine, since it's to the right, since it's clockwise, I'm going to write on this carbon. I want it pointed up, so this time it has to be in an axial position. But look at our structure: here's bromine in the back, it's in an equatorial position, it's pointed up; that matches what we just drew. Here's the chlorine, it's pointed straight up in an axial position, which is the way we just drew it. The confusion might come in this: the appearance that bromine and chlorine changed carbons, because in the top structure, the top-right corner had the bromine, while on this bottom structure, that same carbon has the chlorine. But what if you did this – just rotate? That's all that's going on on paper; you've shifted your perspective. If you labeled your carbons, you'd find out that the relative positions are still the same.

Referring to nomenclature and numbering compounds, let's talk briefly about how do we number this. We've got a few options. Let's say that I assign number one to bromine. Why do you think I might be assigning the number one to bromine? Because B comes before C – bromo, bromine would come alphabetically before chlorine. The reason we have to worry about that is if I make chlorine the number one, I might then number this way to the bromine. If I started here at number one and labeled to the chlorine, I'd get the same sets of numbers: 1 and 2. Since we've got two equal possibilities, remember that one of our rules is you go with the lower one alphabetically. So bromine would get number one. Then there are two ways I could number around the ring. If I were numbering this direction, then it would be 1, 2, 3, 4, 5, 6, gives a big number for chlorine, but if I labeled this direction, 1, 2, then that gives a smaller number for chlorine. Numbering in this fashion is the correct way to do it. If I numbered the bottom compound, I would still make bromine position one, cause nothing has changed, just the way I've drawn it has changed. Chlorine would still be at number 2. This is a correct or proper ring flip because the relative geometry has been maintained.

To show you that this is not the only possible ring flipped form, let's draw one more example. Let's say that I had made this front position the bromine. This is done correctly, because it's pointed up. The chlorine is clockwise relative to it, so I'd have to draw it at this next carbon that's in front. You can see that at that position, pointing up is axial, exactly the way that we want it. This is yet another correct structure.

Let's move to the next example, which is if bromine and chlorine started out pointing in opposite directions. If cis was the label when the two were pointed the same way, what would we call this one? Trans – substituents are pointed opposite ways. For vicinal trans-substituted cyclohexane, both substituents must either be axial or equatorial. Let's see how that would be the case. I'll again start with the bromine and put it where I want to. Since it's pointing up, why not I again take the easier-to-visualize position and put it on one of the axial positions. Then, relative to that, the chlorine is clockwise in front, so I have to move one position around this way. Now the chlorine is pointed straight down. On that next carbon, the one that's pointed straight down is another axial position. When you've got a trans and they're vicinal, one must point one way and one must point the other.

Let's translate that to a 2D structure – bromine pointed up, and chlorine pointed down. Let's do a ring flip. This curly arrow is not a reaction arrow, it just means that I'm redrawing something. I'm going to draw the ring flipped form. If both of the substituents started out axial, then when we do the ring flip, we're going to find they have to become equatorial. Now you can see that bromine is in the back, it's pointed up, but it's in an equatorial position. We can see the chlorine is pointed down, but it's also in an equatorial position. THe bromine back, chlorine in front, we've got the right positions. Let's translate this to the flat drawing. I'll take the back carbon and show it as an up-pointing equatorial position. If bromine to chlorine is clockwise in orientation, then I'm going to go clockwise around the molecule, and chlorine will therefore be pointed down.

Here's a question that we haven't addressed yet: which of thee two structures that I just drew do you think would be the most energetically favored structure? The one on the left, or the one on the right? Why would you say it's the right? Repulsive forces. What do we call that kind of repulsive force of groups bumping into each other? Steric hindrance is the general term. This specific cause is known as diaxial strain. The groups are going to bump into each other because the electron clouds are bumping into each other. The same thing happens in a cyclohexane ring. This model is very deceptive because it has everything represented as little sticks. Realize that there are these clouds of electrons around then. These two carbons are close enough – one side of the ring to the other – that you put anything except a hydrogen on there, there's going to be some of that steric hindrance. Since these are both axial positions, this is called a diaxial interaction.

In cyclohexane rings, diaxial interactions experience steric hinderance. In cyclohexane rings, substitution at an axial position produces steric hinderance due to diaxial interactions. Thus, when possible, a substituent would prefer to be at the equatorial position. At room temperature, there's enough energy generally for that ring flip to continually occur. This is the energetically most favored, because both substituents are equatorial.

It isn't the case where you can just take the substituents and throw all of them at equatorial positions automatically. If we have vicinal cis substitution, one has to be axial, one has to be equatorial. How can we figure out which one want to be where? There are energy factors associated with each substituent, so we could look at a table to see, for example, chlorine would have a smaller repulsive factor than bromine. Sometime it is related just to size, but not always. Bromine would "win" over chlorine: if bromine has more repulsive force energetically than chlorine, bromine would want to be in the equatorial position, so this is lower energy.

I want to discuss one reason why is it that these chair forms of cyclohexane are energetically more favorable. One reason is, of course, that you achieve that 109.5° angle that you want for a tetrahedral carbon. Here's another trick. What if I took the molecule, and looked along one of the carbon-carbon bonds of the ring. If I visualize it this way, that means I'm looking at a rotomer of that molecule. If I did visualize from the front of the cyclohexane ring, what would I see? Just to keep it generic, I'll label these as A, B, C, D, and I'll visualize along the left-hand bond. What would I get? Writing a rotomer diagram – remember the things in the front join through to the center of the projection, the things in the back do not connect through, and, notice the shorthand that I'm using – I connected two of the positions, because that's the rest of the ring. What kind of conformation is this? It's a staggered conformation. If I had to choose between eclipsed and staggered, staggered's the better conformation. If you look at the ring, if all of these were just hydrogens, what form of staggered is this? It's a gauche conformations, because it's one of those local minima of energy. A cyclohexane ring can't be anti, it can never be that conformations, so of the possible conformations it could form, this is the lowest energy. On top of the fact that it's going 109.5°, all of the bonds are oriented so that they're staggered.

If we could look along one bond, then realize that if I'm looking along a ring this way that there's two of these bonds that are parallel to each other. So what if I simultaneously made two rotomer projections? Then it would look like this. Here is the front of the ring then the back of the ring, then all of the other groups are arranged in a staggered conformation.

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

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 – refers to neighboring positions; geminal – refers to two substituents on the same position

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

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

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

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.

Every bonds in a chair structure has a staggered – not eclipsed – geometry.

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Structures

Identical to those from lec 8A (10/12/12)