Lecture 16A • 05/18/12

Disaccharide – when you have two smaller sugar units that are put together. We've studied two disaccharides so far: one of them is maltose – what are the sugar units that are part of maltose? Glucose, and glucose – it's two units of glucose put together. What about lactose – that's the other sugar we've done so far – glucose and galactose. If we want to think of going from left to right, the way that we've been drawing the structures, where we can, we've been trying to write the anomer positions on the righthand side. When I drew lactose, the part of the molecule that can actually open and close, the glucose portion, because it's only a hemiacetal, that we tend to write on the right. In the middle of the molecule, we have a full acetal, because galactose has made what kind of sugar derivative? What is the link that we call between the two sugars? Anomer is the carbon through which it's connected. The type of linkage is referred to as a glycosidic linkage – in other words, we've made a glycoside, a derivative of a sugar.

The next sugar that we're going to tackle is sucrose, which is a glycoside as well, but it's a slightly different type of structure, because both anomeric positions end up being "trapped", you could say. Sucrose's scary-looking formal name is 2-O-(alpha-d-glucopyranosyl)-beta-d-fructofuranoside. Notice it does not end with the -ose ending, because as we're going to see, it is not a free sugar; it's bound up in a full acetal, both sugars. This is our first furanose structure that we're going to be drawing. When we do it for fructose, it's not such a bad thing to do.

Let's just, for practice sake, do a furanose of an aldose and see what that entails. Since we need to do alpha-d-glucose, let's do alpha-d-glucofuranose for practice, and then we'll come back and do sucrose. Instead of trying to jump straight to the ring, let's go ahead and do this in linear form, since this is our first furanose that we're drawing. d-Glucose, what's the configuration, -OH from top to the bottom, what are the positions? [right, left, right, right] It is the anomer position that's automatically going to be part of the ring; that's true whether it's an aldose or a ketose. Carbon 1, itself, is not necessarily part of the ring; it won't be if we have a ketose. If we take the oxygen off of carbon 4, that would be the fifth atom that could be part of the ring. The next thing that I'm going to do is make the five-membered ring. I create one more stereocenter; I have two stereocenters here that are the same. I've made a ring. There is on more stereocenter here, and then we have that bottom CH2OH group. In order to figure out whether I've got the alpha or beta form, I need to figure out whether the rest of this structure that's not in the ring – is it cis or trans to the -OH group that I'm about to make. We want it to end up being trans, therefore, like before with the furanoses, we're going to have to turn this structure. Turning a Fischer projection 90° is not allowed, so yes, we can turn this stereocenter in the fact that we exchange these three groups here to get the oxygen where we want it to be. I'm drawing one of these groups like a Fischer projection, so we're going to have to do this somewhat improperly, but we want to make sure we preserve the correct configuration of this stereocenter as we do it. Is this bottom stereocenter R or S? Oxygen is going to be priority #1, cause it's the highest atomic number. Then we have carbons attached – on one carbon, we have attached to it [O, C, H]; at the bottom carbon, all that is attached to it is [O, H, H]. Where we can compare first, carbon is more important that hydrogen, so the top substituent is #2, the bottom is #3, the hydrogen is #4. It appears to be counterclockwise, but the hydrogen is pointed towards us, so this is really R.

I'm going to twist the stereocenter where the ring comes in – I'm going to twist it to get the oxygen where I want it. That means I'll not longer be properly writing the bottom stereocenter, but I'm going to remember that it's R and ignore the way I'm drawing it for the moment. I'll say rotate carbon #3. For d-[aldohexopyranoses], alpha alway points down, beta always points up. That's because of which way that last stereocenter does point in the ring. If you start going up the chain to the next position up, there, you're not guaranteed any particular configuation. d sugars, the last stereocenter's on the right; for the other stereocenters, they can be anything potentially. In this case, since I'm using glucose with that third stereocenter's oxygen. [For glucose], yes, the next stereocenter up is still oriented towards the right, so I'm still going to twist it around the way that I normally would, but if this was a sugar was a sugar where this stereocenter was on the left instead, like galactose, if the oxygen's on the left, you're going to have to turn it the other way, which means alpha will be pointed the opposite direction that it would for something like the pyranose form of glucose.

The hydrogen that was here on the third carbon is now going to be rotated around onto the right; the ring itself is now going to be pointed down the way I want; I've got that new stereocenter; and I'm just for ease going to put R here to represent the rest of the chain. Notice that now I know which way the R is pointing; now I can figure out which way alpha would be, because I'm trying to do the alpha-d-glucofuranose. Alpha means trans. Now I've got my correct Fischer projection. Let's tip this into a Haworth projection. [A] Haworth projection would still work the same way as before. Sometimes, to make the structure a little bit more symmetric-looking, you might see if drawn more like this, where the oxygen's almost in the center of the molecule instead of one side. Main point is: we're going to have four rungs like this – imagine a ladder – instead of five, because we're now dealing with a furanose instead of a pyranose. Everything else, as far as transferring groups to this structure, is the same – what was on the right of the Fischer projection is now going to be on the bottom of the Haworth projection; what was on the left of the Fischer's going to be on the top of the Haworth. On the righthand side here, I've got [-OH, -OH, -H, -H]. I've got two more carbons coming off the side chain. Normally, there's only one kink in this part of the structure, because it's usually CH2OH. There's the CH2OH; that is the stereocenter that got rotated around - so do I draw a dash or a wedge to make that R (because it has to be R)?

If I view this like I'm peering down over the molecule like this, notice the two carbon-carbon bonds will be pointed away from me. Notice where my eyebrow is. That means the CH2OH group is that way, down below me. In the regular Fischer projection, isn't that same CH2OH group down below me? This -OH group is on the right, so if I'm looking down on the molecule like this, then if the -OH group is on the right, do I use a dash or a wedge? A wedge. [difficulty of writing furoses of aldohexoses – one stereocenter must be represented in similar dash or wedge form.

Started out with glucose. Oxygen on the 4th carbon is what I'm using to make the ring this time because I want a furanose, which is only a five-membered ring. [At first, don't know which way to put alpha] When the ring is not in the backbone, you can't tell which way it is [alpha or beta]. I've put the ring in the backbone, same type of thing I've done before. I took the whole bottom part of the molecule here and called that R, just to make this easier to drawn. That means that, once I did go into the cyclic form, I had to resolve what should be the correct way to draw that stereocenter. To make sure I've drawn it correctly, let's take a look at it here: we have the oxygen, which is priority 1; we have a carbon that has [O, C, H] on it, for priority 2; we have CH2OH, which means you have [O, H, H], [and] there is an implicit hydrogen in the back. This is clockwise precession of the substituents, so yes, it really is R.

Anything below that stereocenter I need to rotate; I'm calling it R [as in radical]. Once I'm here, it's easier to see that I moved the hydrogen where the oxygen is, the oxygen where the R group is, and the R group where the hydrogen is. If you swap rotationally three substituents on any point of a Fischer projection, it gives you back exactly the same stereoconfiguration again.

How did I get the five-membered ring? I chose the oxygen that was on carbon 4 [instead of taking] the bottom -OH group into the ring. The carbonyl has to be in the ring, cause that's where the closure occurs, the carbonyl center, so that's carbon 1; if I went to the [bottom stereocenter, that oxygen] would be the sixth atom in that line. But, I didn't go there; I went to the fourth carbon and went to that oxygen, which is just the fifth atom. That's the oxygen that attacks the carbonyl, which is why I ended up with a five-membered ring.

I didn't have to guess once I had the R group here, because alpha means that that R group and the -OH group are trans to each other. [previously called CH2OH cause previously just covered aldohexopyranoses][recap of interpreting stereocenter]

If I wrote this carbon-carbon bond and that carbon-carbon bond in the plane, like I have now, then the -OH group has to be either a dash or a wedge. Instead of trying to worry about priorities, I went back to the Fischer projection, cause the Fischer projection, if you have the two carbon-carbon bonds in a line, like I do here, and notice that by putting my viewpoint here, both of these are slanted away from the eye. When something is away, it means it's vertical in the Fischer projection. So why not take advantage of the Fischer projection I've already got, because when viewing down upon that center, the -OH group is on the right. The carbonyl, which is at the top of the Fischer projection, is somewhere in here, so from the perspective of the visualization point, it's up, the way it should be in the Fischer projection, the CH2OH is down, so that means the -OH group I want to be on the righthand side, which is towards you, which is why I made it a wedge.

Sucrose, when we take a ketose and make a furanose out of it, we don't have this stereocenter problem [for an hexose]. Let's see that. For sucrose, we want the beta-d form of fructofuranose. Let's try it by itself: beta-d-fructofuranose. What does the structure of fructose look like? It's a ketose, that means that the top is going to be CH2OH, and then you have the carbonyl. We've already seen a way that we can interconvert between aldoses and ketoses; [you can start] with glucose and make a double enol out of it, where [you] tautomerize, put a double bond between the top two carbons; that meant that one or the other carbon eventually could turn into a carbonyl. Of course, if we had this in a bottle, it's not going to do it on its own, but once we put it in solution, you could get a distribution of products. [4% mannose, 34% fructose, 6x% glucose; the spontaneous relative concentrations at room temperature in water][Tollens' test] Fructose is structurally related to both glucose and mannose; like arabinose, it has the same bottom three stereocenters. So, if glucose is [right, left, right, right], then we have [left, right, right][for d-fructose]. In terms of counting carbons, if I was going to name any kind of derivative of this, the carbonyl's actually at position 2 now. If I'm just counting carbons for the purpose of determining the ring, I'll label it [starting at the carbonyl]. Now, the fifth atom is the oxygen at that bottom stereocenter.

Let's now go ahead and try to turn this into b-d-fructofuranose, so we'll make the ring. I'm going to take this CH2OH group and call it R, for the moment. The bottom oxygen I'll connect up to the top of the ring; I have the two stereocenters above it which are not involved in the reaction, so they're exactly the same that they were. We're going to have the anomer position; I don't yet know where to put it. The oxygen in the ring is on the right, which means, like the [d-]aldohexopyranoses, I'm going to need to rotate that stereocenter clockwise to get the oxygen in the ring. Now that I have it on the left – more importantly, I have it on one side or the other, [and] I've got the oxygen in the ring [backbone] now – so because this has ended up on the left, and I want cis at the top because I want beta, now I can figure out where to put that last -OH group. Now, let's go into the Haworth projection. Standard Haworth, we put the anomer position on the righthand side. The things on the right end up on the bottom; the things on the left end up at the top [CH2OH, H, OH, last CH2OH is up; two CH2OH groups]

Let's join that now into sucrose. Sucrose has got alpha-glucopyranose as the substituent. Glucose is [down, up, down, twisted up]. Look at the two sugars: at the top, I've got beta-d-fructofuranose, and down at the bottom I have the alpha-d-glucopyranose. Notice that if I want to have both anomer positions on the right as I've got it, I've got to stack one molecule directly on top of the other and write a long bond in between them. But, I could do like what I did with galactose, which is to either flip one ring – in this case not upside down – but take it and just swivel it 180° this way. So, you could draw one ring pointed one way, and the other ring pointed the other way. I'm going to choose to take the fructofuranose and turn it 180° around, without flipping it or anything like that. Since I'm swinging it 180[°] in the plane, that's going to make the ring oxygen now pop towards us. Fructose is a double acetal. Which means what? Which means this is not in equilibrium with its ring-opened form.

If I took just this molecule [alpha-d-glucopyranose] and put it in water, what's going to happen to its optical rotation? Why? How? [rant] The ring opens and closes because its a hemiacetal – protonate-open-attack-deprotonate, protonate-open-attack-deprotonate – to open and close and open and close. Every time it opens, you make the carbonyl planar again, which means when it closes, both the alpha and beta forms become possible. It won't be 50/50, but they'll both be possible. The point is, the compound on the left, because it is a hemiacetal, is going to be able to open and close spontaneously. Acetals are tougher, so this acetal is not in equilibrium with its linear form. [clarifying why both furanose and pyranose drawn for glucose][clarifying swiveling with reflecting][build a model]

How do you take a 3-dimensional object on 2-dimensional paper and, in your brain, rotate it in 2 dimensions, even though it's 3-dimensional. [make sure context is in your notes as well]

Let's take this molecule and react it with silver oxide and methyl iodide. Let's say there's a massive excess of both of those; what's going to happen? Silver oxide in solution acts like hydroxide. What's going to happen to that molecule in hydroxide? What will happen to the acetal in hydroxide? Acetals plus base equals: nothing. [acetal protecting group used – DHP] This is an acetal, is it not? What happens to that when we throw a Grignard at it? Nothing; that's the point: it's base-stable. What is going to happen to the acetal [in the sugar] in these conditions? Nothing. If the acetal's not going to do anything, what is? What would happen – with enough time – to the -OH groups in hydroxide? Notice we don't have hydroxide here, because what would happen if I had a solution of sodium hydroxide and methyl iodide? It would make methanol; it would never react with anything else, so we can't put sodium hydroxide in solution. What if we were really sneaky? What if somehow [an alcohol] got deprotonated by oxide? Couldn't an Sn2 reaction happen, [since] you have such a great substrate? In other words, you're going to put CH3 groups everywhere there's an -OH group: it's called exhaustive alkylation – same exhaustive alkylation [as in] the Hofmann reaction.

I've got all these ether groups now – except where? Except where we had the acetal, because that -OH group is not available until you hydrolyze it. What does that mean? That means once we react this derivative with water and acid and force the rings to open back up again, whichever carbon bears a free -OH group on it was the -OH group that was part of the ring. In other words, if you have a sugar that you've never seen before, you could derivatize it like this, hydrolyze it, and then figure out what the ring size was.

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sucrose: 2-O-(alpha-d-glucopyranosyl)-beta-d-fructofuranoside

alpha-d-glucofuranose

beta-d-fructofuranose

exhaustive methylation

NaOH + CH3I –> CH3OH

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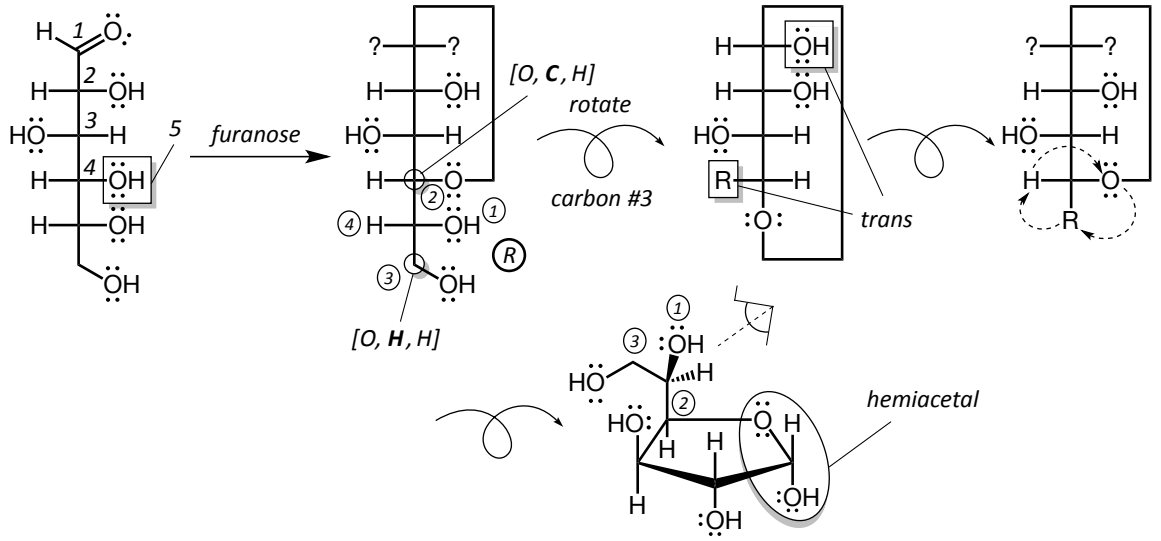
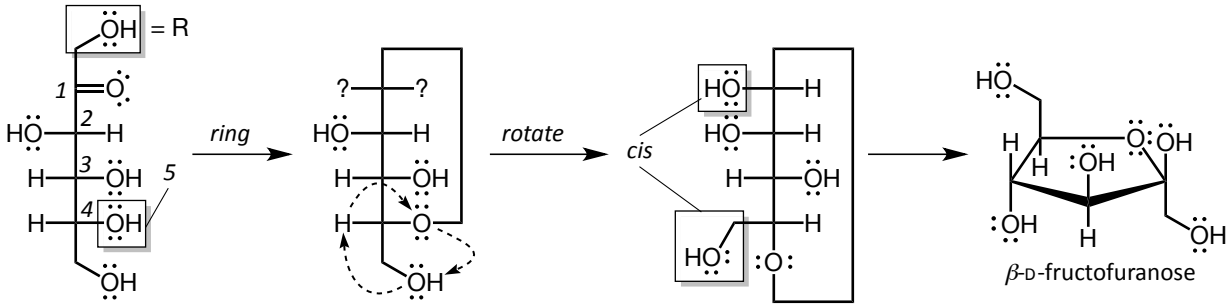


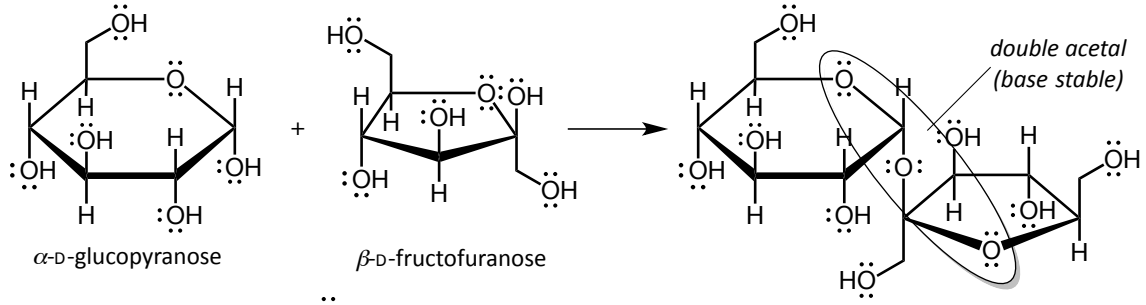
α-D-glucofuranose

05/18/12A lec • 2

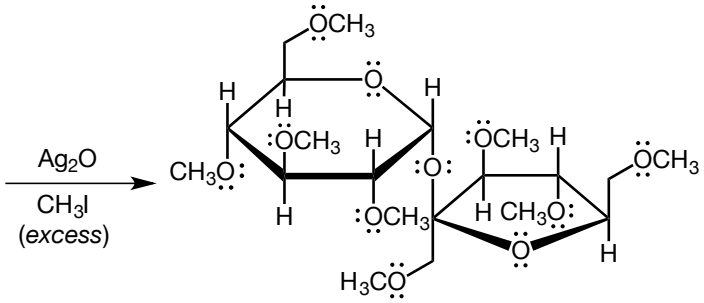


β-D-fructofuranose

05/18/12A lec • 3



α-D-glucopyranose + β-D-fructofuranose → sucrose



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