## Lab 9B • 05/17/12

Carbohydrate derivatives

Which sugar is this? Mannose. If we were to react mannose with sodium borohydride followed up by acidic work-up, what would we expect to get? You'll get an alcohol, because we have an aldehyde to start with. In other words, we end up with a molecule in which every carbon has an alcohol group on it. As a general term, these are called alditols. A lot of these derivatives, you take the same ending – this is ald-itol – you take that -itol ending and put it on another name, and that's how you could name these derivatives. If you have mannose, this is then called mannitol. [sorbitol is glucitol]

Which sugar is this? Talose, the last one. If you react that with an aqueous solution of bromine, it is able to selectively oxidize the aldehyde. [mechanism?] We get a monocarboxylic acid; this is called an aldonic acid – specifically, this would be d-talonic acid.

Last one is now the case where we do oxidize that primary alcohol and the aldehyde. Wich sugar is this? Altrose. It turns out that nitric acid is able to accomplish that selective oxidation – of course, not if you had a concentrated solution of nitric acid. This particular derivative we'll see extensively featured in the FIscher stereochemistry proof. This is called an aldaric acid – this would be d-altraric acid. [mechanism?]

Cyclic sugars

Let's look at the alpha-d-form of glucopyranose. What does the 'pyranose' part of that name mean? It's a six-membered ring. The d form's the regular form, so in linear glucose, what would be the configuration of -OH groups as we go from top to bottom? [right, left, right, right] Let's see if we can get to a Haworth projection without first writing that linear structure; there's a few observations – now that we've already seen Haowrth projections – that we could make. Let me draw linear d-glucose to point out that, when we do try to visualize this in a Haworth projection, we want to try to take whatever oxygen that becomes part of the ring and put it into the backbone of the projection. If we're making aldohexopyranoses – in other words, if we're always going to be taking this last stereocenter's -OH group in order to make that ring, then if we're trying to properly visualize, that means we're always going to turn it clockwise, which means the CH2OH group is always going to end up on the lefthand side – if we're making a six-membered ring sugar out of a d-sugar. If we wanted to jump to the Haworth projection, then, for this and all other d-sugars, the back CH2OH group will always be on top – that's if you're doing a standard Haworth projection where the anomer position goes on the right. If I want to make the alpha form, alpha means the anomeric -OH group is trans on the ring relative to this CH2OH group, which if that group is always up for d sugars, that means alpha's always going to be down for d sugars, when drawn in this standard configuration. Following the standard visualization, anything that's on the righthand side of the Fischer projection's going to be on the bottom of the ring; anything that's on the lefthand side of the Fischer projection's going to be on the top of the ring. I could look at this and say [right, left, right, right], or I could tilt myself sideways and look at the ring and say [bottom, top, bottom, bottom] (but remember we have to twist that last stereocenter). As far as these first three, though: [bottom, top, bottom]. This would be alpha-d-glucopyranose – which has a specific rotation of +112.2°.

Specific rotation is how much light is twisted as it passes a specific distance through a solution of a specific concentration. Enantiomers are going to have opposite rotations. This is +112.2°; it's enantiomer is going to have an optical rotation, specific rotation, of -112.2°. It's observed, though, that if we take the pure version of this and put it into solution, over time, we're going to end up with an optical rotation value of 52.7°. Why might we think that should be? What could be going on in solution that would cause that to change? If we had a reaction of two things, what kind of reaction would be going on, then? What kind of functional group is this, in the ring form? It comes from an aldehyde. It is a functional group that has two oxygens connected to a common carbon, which means it's one of four things: a hemiacetal, an acetal, a hemiacetal, or a ketal. We have a hydrogen present [on the carbon] and on one of the two oxygens, there's only a hydrogen. With the hydrogen present on that carbon, we know it's either an acetal or a hemiacetal; it's a hemiacetal, because only one of the oxygens has an R group on it. Why does that matter? Hemiacetals and hemiketals are generally not isolatable; they easily either form acetals, or they decompose back to their original aldehyde. This is a hemiacetal that turns out to be stable, because we have so many intramolecular interactions going on, all these -OH groups interacting with each other; in aqueous solution, this is extremely compatible with water, all these sugars are water soluble.

What is the ring was to open up? If the ring was to open up, it becomes planar agin, then if it were to try to re-close and re-form the ring, that means even though you started with the alpha form, there's a possibility that upon the re-closure of that ring, you're going to have the beta form instead. Here's beta-d-glucopyranose. What should its specific rotation value be? [it's a trap!] What's the relationship between these two compounds? They're not enantiomers; they're epimers, because there's only one stereocenter difference between the two. Enanitomers, yes, are mirror images, therefore if one has a + rotation, one has an equal but opposite rotation, its mirror image form. Epimers are not mirror images, they're distinct molecules that have nothing to do with each other, in terms of physical properties.

If we do know the optical rotation for the alpha form, we don't know anything about the beta form, because there is no relatioship between epimers. Knowing the optical rotation of the alpha anomer does not allow us to predict the optical rotation of the beta anomer; that's because the two compounds are epimers, which means there's no connection between their optical rotation. There is a real optical rotation; it turns out to be +18.7°. 52.7[°], which is the angle that both of these adopt, is not the average of the two compounds, which mean you don't necessarily have a 50/50 mixture of the two compounds in solution. But, whichever compound you start with, it's going to achieve equilibrium with its opposite, alpha and beta. Since we will achieve an equilibrium, that's why whichever one of these we put into solution, we get the same [optical] rotation after some time. This process of that specific form entering into equilibrium with its opposite form, that's known as mutarotation. The exact proportion of which one of these two is going to form depends on exactly the structure of the compound.

Whenever a pure sample of one anomer of an [cyclic sugar] is placed in solution – anything that's got an anomer position could technically open and close – that anomer will interconvert with its opposite form until an equilibrium between the two forms is established, resulting in an equilibrium optical rotation – not equal, but equilibrium. If you think about just the sugar itself, depending on whether the -OH groups are up or down, maybe they'll interact with each other across the ring, so for different sugars, maybe you might have more of the five-member ring for some reason, or less for a particular sugar, or the alpha versus beta forms ... if we made a chair structure out of this, we might wonder if the alpha form puts that -OH group on the axial versus equatorial position. Whether it ends up on the axial or equatorial position will depend on how the other groups interact to determine which of those two forms is more favorable. Maybe for one sugar, the alpha's more favorable; maybe for another sugar, maybe the beta's more favorable. The exact proportion of this and any of the forms that form in solution depends on the unique intramolecular interactions that happen for that particular sugar. It's not just there two forms that could form; glucose could form a five-membered ring, and when it form[s] that five-membered ring, you're going to form an alpha and a beta anomer. If you're given any form of d-glucose, when you put it in solution, you're going to get alpha-d-glucofuranose, beta-d-glucofuranose, alpha-d-glucopyranose, and beta-d-glucopyranose. The exact proportion of the cyclic forms of a sugar that will form in solution depend on the intramolecular interactions that will occur for that particular sugar.

Glycosides

Let's start with the alpha-d-pyranose form of glucose again. If I reacted this with acid and methanol, what do you think is going to happen? Let's say there's an excess of methanol. It is a protonate-open-attack-deprotonate sequence. We would take a hemiacetal and make an acetal; we would push it to completion. But, the mechanism's not quite what we've seen in the past. The reason that this hemiacetal formed is that there used to be a carbonyl here. Protonate. We're going to have an open step, but it turns out that this is a case where the resonance aspect really matters. I'm going to write the lone pair of the neighboring oxygen, the one that's in the ring, as having an active role in kicking this group off. Notice what we form: we have a planar intermediate, which means that, when methanol comes in to attack, it's got two different directions that it could attack from: above and below the ring. I've just used this split arrow to highlight that there's two attacks possible; I'm doing so because I've just said that two attacks are possible. [might have something written in the notes, but you need to know the context of what was being said at the time][reversibility][skipping showing H+] Here, we're getting the alpha and beta forms of this new acetal, the exact proportion of which, the alpha versus beta, forms [is influenced by] the anomeric effect. We just linked a sugar with an alcohol. A sugar is an alcohol, so the next step is to show one sugar linking with the next. It is exactly this connection from the anomer position to something else that makes it a glycoside [some define more narrowly].

There is one variation, which is we were to take something like glucose and react it with an amine, or just plain, old ammonia. It turns out that an amine can substitute at that anomeric position as well. [squiggly bond to represent both stereochemical possibilities] This is an N-glycoside, cause we have a nitrogen in there instead; since we have glucose that's been derivatized to have an amine functionality, this is glucosamine.

Complex sugars

Monosaccharide essentially means one sugar unit; what does that mean? We could observe that, in all of the sugars we've seen so far, there's not glycosidic linkages; there's only one carbonyl [in the linear form]. Each individual sugar unit has its own, individual carbonyl. Stick two of them together [the sugar units], and that is called a disaccharide; it is a complex sugar formed by joining two monosaccharides through a glycosidic link. [maltose, lactose, sucrose, cellubiose][Oligo – a few; poly – many, starch]

Let's start with maltose: 4-O-(alpha-d-glucopyranosyl)-alpha-d-glucopyranose. What does this mean? This is 4-[]-alpha-d-glucopyranose. The four means we substitute at the 4 position; the 'O' means we don't just substitute on the carbon; we leave the oxygen that's already there and substitute on instead. I'm showing you alpha-maltose, which has to do with the configuration of this last sugar. I'm going to link one sugar through its anomer to another sugar, which is going to make that linked sugar an acetal. Acetals don't open up as easily; it's like it traps the sugar. This, the end of the chain, that's just a hemiacetal, so that's much easier to open, so we could end up with alpha and beta forms of that end portion of this complex sugar. That's why its anomeric configuration is what we ascribed to the compound maltose itself. Here's the substituent; what is the substituent? alpha-d-glucopyranosyl.

The -yl ending comes from -ide. If we have alpha-d-glucopyranoside, that's one of these glycosides – in other words, close up the ring and connect through the anomeric position. I'm going to connect the anomer [position] to the oxygen of the next sugar over. If you're not entirely satisfied with having a curly bond in your molecule, then that's going to require taking one or the other of the Haworth projections and flipping them upside down. If we flip it 180°, realize there's two things we're going to do: from the way it's drawn now, it's going to appear that what's in front becomes what's in back, but at the same time, what's on the top is going to appear to exchange and end up with what's on bottom. If we only did one of those two things – if all I did was reverse what's pointing up and down – that's making the enantiomer, which means we'd have the l sugar instead. If all we did was to take the things in front and swap them with the back, that's again just reflection. But, a 180° turnover flip is just like a double reflection, and if we do reflection twice, that means we get the same molecule back again. I'm going to flip the ring on the right and rewrite it in more conjoined form. [malt]

Lactose: 4-O-(beta-d-galactopyranosyl)-alpha-d-glucopyranose. We're going to have one ring on the left – that's the galactose – that's in its beta form. It's going to be attached to a glucose that ... I'll make it its alpha form. For both of these sugars, just left of the ring oxygen, they'll both have that CH2OH group pointed up, cause these are d sugars. For galactose, in the linear form, we have the -OH groups [right, left, left, right], which means they're going to be [bottom, top, top, twisted top]. Glucose, we already know, is [right, left, right] to start with, so it's [bottom, top, bottom].

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Knowing the optical rotation of the alpha-anomer does not allow us to predict the optical rotation of the beta anomer since the two compounds are epimers – not enantiomers – so there is no connection between their optical rotations.

Mutarotation – Whenever a pure sample of on anomer or a cyclic sugar is placed in solution, that anomer will interconvert with its opposite form until an equilibrium between the two forms is established, resulting in an equilibrium optical rotation.

The exact proportions of the cyclic forms of a sugar that will be present in solution will depend on the unique intramolecular interactions that occur for that particular sugar upon cyclization.

Complex sugars

Monosaccharide – "one sugar unit" – no glycosidic linkages (only one "C=O")
Disaccharide – a complex sugar formed by joining two monosaccharides through a glycosidic link [sucrose; maltose; lactose; {sucrose}]
oligo – "several"
poly – "many"

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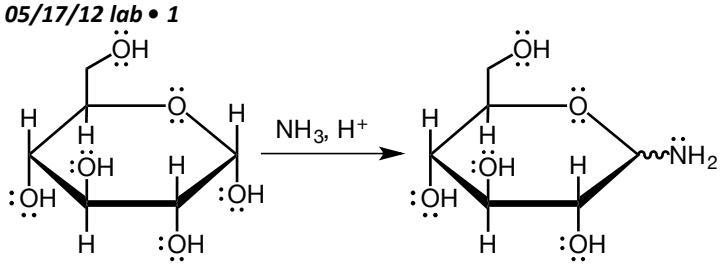
**Structures** *(remaining structures identical to lab 8A)*

***05/17/12 lab • 1***




$\alpha$-D-glucopyranose
*+112.2° specific rotation*

glucosamine
*an N-glycoside*