

## Lab 9A • 05/16/12

### Derivatives of carbohydrates

Which sugar is this? d-Mannose. What do you think you're going to get if you reduce mannose with sodium borohydride? An alcohol. The aldehyde will be reduced down to an alcohol functionality, so every carbon on the molecule will just have an alcohol. As a functional group, this is called an alditol; this particular one would be d-mannitol. [sorbitol is glucose?]

Which sugar is this? Talose. If I oxidize with aqueous bromine, it is able to oxidize just the aldehyde but leave every other position on the molecule untouched. It's a carboxylic acid, but only at one end of the molecule – the end that used to be the anomer [position]. This is an aldonic acid – specifically, this would be d-talonic acid. Notice that a lot of the terms that we have that end in -ose in some way or another, or this ald- prefix that we've got, you can interchange different endings to express all these different functional groups. We had -pyranose, -furanose that we could tack on to the name of glucose and say things like glucopyranose, glucofuranose. Same thing's going on here: I've shown mannose going to mannitol; we could have glucitol, iditol – just add -itol to the name where -ose would go. Same thing here: just drop the -ose and add -onic acid – that's an aldonic acid.

Last derivative [is] if we did oxidize with nitric acid instead. What is this sugar? Gulose. Concentrated nitric acid for too long a time under heat is going to oxidize lots of stuff, but under more controlled conditions, lower temperatures, it's able to selectively oxidize primary alcohols and aldehydes – that's an aldaric acid; this would be d-gularic acid.

Next, we're going to work toward this thing called a glycoside.

### Cyclization

What is this sugar? Glucose. What are we going to get if we have that in acidic, aqueous solution? A hemiacetal. Let's draw the alpha-d-pyranose form of glucose, but let's not go through the process of drawing it in a linear structure and then cyclizing it and then turning the bottom stereocenter then flopping the structure sideways – let's make some realizations, some short cuts, that we could make. If I wanted to do a Haworth projection, for d-sugars, the CH<sub>2</sub>OH group is always going to be at the top of the ring, if you do the Haworth projection in the standard configuration. We do do this rotation of the bottom stereocenter when trying to go from the linear to the cyclic form of the sugar. For d-sugars, every single time, since the d means that the bottom stereocenter is on the right, that means every single time, we're going to turn that stereocenter clockwise when we're trying to do that visualization. That means the CH<sub>2</sub>OH group always goes to the lefthand position on this Fischer projection when you have it drawn correctly. Since when you tip it over things on the left end up on the top, on Haworth projections for d-aldohexoses, that CH<sub>2</sub>OH group's always going to be up. [practice long way]

Once we know the configuration of that CH<sub>2</sub>OH group, remember that the alpha form if it is such that the -OH group at the anomer position is trans to the CH<sub>2</sub>OH group. For d sugars, alpha is always going to be down. Then, what's the normal configuration of glucose? [right, left, right, right] Right always ends up on the bottom of Haworth projections; left always ends up on the top. If I can look at the line of the projection itself, the ring, and I can imagine [right, left, right], the first three stereocenters, then I can put them directly on the ring. The optical rotation – alpha-d-glucose has what's called a specific rotation of 112.2° – it means over a certain distance, length [1 cm?], light will rotate by 112.2°; a positive number means clockwise. If that is the optical rotation of the alpha version of this sugar, what would the rotation of the beta form be? Ah, you just fell into my trap. Why? What is the relationship between the alpha and the beta forms? They're stereoisomers; they have the same bonds, and alpha and beta [are] just whether that anomer position is pointed up or down. What do we call the relationship between the two compounds? Anomers. Alpha and beta are not enantiomers, they are epimers. d and l sugars are enantiomers of each other, which means everything's a mirror image. If you only have one stereocenter that's different, which is the only thing different between the alpha and beta forms, those are epimers. What is the relationship between enantiomers, in terms of optical rotation? They're opposite, because they're mirror images. What is the relationship between epimers; what's the optical rotation effect? None; there is no relationship, because they're different compounds, they're not mirror images, so their optical rotation's gonna depend on exactly where the atoms are located. Since they're different compounds, there's no comparison, there's no way to predict it. If I asked you what the optical rotation of alpha-l-glucopyranose, then the answer to that would have been -112[.2°]. But beta-d-glucopyranose, we'd have to look it up, because there's no way to predict it. This change in the optical rotation is a significant observation. Knowing the optical rotation of the alpha-d form of glucose does not help in determining the optical rotation of [the] beta-d form of glucose, since the two are epimers, not enantiomers, so there's no relationship between their optical activities.

Our next situation: if I take the alpha=d=pyranose form of glucose, which, as a pure compound, has an optical rotation in solution of 112.2°, and I put it back into solution and just leave it there, eventually, it's optical rotation is going to shift to 52.7°. Why? Why do you think that's going to happen? What's going to happen to this compound if you put it in acid and water? Hydration, but of what? What functional group is this, by the way? When we have a carbon with two oxygens on it, it's one of four functional groups: hemiacetal, acetal, hemiketal, or ketal. This is a hemiacetal; why is it an acetal?

Because we have the hydrogen. Why is it only a hemiacetal? Because one of the oxygens has a hydrogen. Are hemiacetals normally isolatable? No. What would happen to them in acidic solution? They would open back up again. If it opens up, doesn't it have another chance to close, and instead of making the alpha form making the beta form instead? What if I only had the beta form? The beta form has an optical rotation of  $+18.7^\circ$ . Notice that  $52[.7]$  is not the average of those two numbers, which means there's not necessarily a 50/50 proportion of these two epimers in solution. In fact, the exact equilibrium concentration of the two forms depends on exactly the unique types of intramolecular interactions you have, due to this being a molecule filled with -OH groups, so every sugar's going to have a different balance. The point is, in every aldohexose, when it cyclizes into its pyranose form, you get the alpha and beta forms that can interconvert very easily, very rapidly. You put either of the two pure forms in solution, over time they both attain the same equilibrium optical rotation, because they become a mixture of epimers; this process is known as mutarotation. Whenever a pure sample of an alpha- or beta-aldopyranose is placed in solution, the alpha & beta forms will interconvert, achieving an equilibrium between the two forms, with an equilibrium optical activity. That is mutarotation. The both have their individual optical activities; they reach this common one, which is what occurs at equilibrium.

Technically, if you take glucose and put it in solution, it forms alpha-d-glucopyranose, alpha-d-glucopyranose, beta-d-glucopyranose, and beta-d-glucopyranose. For several of the sugars, the six-member ring form may be more favorable than a five-member ring form. Due to intramolecular effects, the alpha versus the beta [configuration], one might be more favorable than the other. For example, depending on how many of the other alcohol groups are axial or equatorial, you might the alpha position go equatorial to avoid steric hinderance, or it might be forced axial depending on the remaining substituents [or intra affects trump sterics]. For each sugar, it's different as far as whether its alpha or beta for is more or less favorable, and whether its five- or six-membered ring form is more or less favorable. That percentage, for each sugar, is unique to the types of intramolecular interactions that occur once it cyclizes.

### Glycosides

Let's stick with glucose. What's going to happen when I take glucose and I put it in a solution of a little acid and methanol? What's going to happen mechanistically? Forget that it's a carbohydrate – it's a hemiacetal. What happens when a hemiacetal reacts with an excess of alcohol? Forms a full acetal, through some version of protonate-open-attack-deprotonate. What form of protonate-open-attack-deprotonate is going to happen here? Slightly different than what you're used to, because to decompose the ring, we would have the ring get protonated, open, and then another sequence of events occurs. But it not the mechanism; instead, it happens like this: yes, we protonate, but we protonate the anomeric position. All of the [oxygens] are going to get protonated at one point or another; what causes the formation of a glycoside is this particular attack. After protonate, we have open and attack. Look at what the attack is: that the oxygen that is part of the ring assists the departure of the water. Why does that matter? Because it means we formed a planar intermediate, so when methanol comes in, it's able to attack either from above or below. The attack is not going to be 50/50 in proportion; exactly what that proportion is [is influenced by something known as the anomeric effect]. All that matters is that we're going to get two production: and alpha and a beta form. When methanol attacks, we're going to end up with oxygen being positively charged on the methanol, and it has to deprotonate. [how to write two arrows to show two possibilities; forked arrow] Methanol attacks, pushes the double bond open, and then methanol needs to lose a proton. We could say that there are two products that form: an alpha form of the methoxy group is trans to the back CH<sub>2</sub>OH; the beta form, where it's cis, otherwise the molecules would be identical. Before, we had a hemiacetal; now, we have a true acetal, which is tougher to decompose. You would have to hydrolyze this in order to break it back into being just normal glucose, whereas if you have just the cyclic form of glucose, just a hint of water and acid will get that to pop open. There's a difference in stability in sugars with glycosidic linkages, verus just plain, old sugar. [-ide child of, son of] Chloride is the offspring of chlorine, for example; glucoside is the offspring of glucose, you've made a derivative of glucose. This is if we just took plain, old ethanol. What would happen if we took glucose and reacted it with glucose? [aha! argggg!]

We get maltose, on of the saccharides. What is a disaccharide? What's a monosaccharide? It literally means one sugar unit. All the sugars that we've studied so far have a carbonyl. Of course, when you cyclize you lose the carbonyl, but it's still buried in there. None of these sugars have been linked to other sugar units, yet; that's why they're all classified as monosaccharides. A disaccharide would be a complex sugar created by taking two individual sugars and joining them through a glycosidic link. [sucrose, maltose {malt}, lactose, cellulbiose] Maltose [is] nothing more than a dimer of glucose. [oligo – several; poly – many] An oligosaccharide would be a larger sugar with a few units, and a polysaccharide would be something like starch, which has an indefinite number of sugar units linked together. Some of these sugars cannot be found in isolated form [or may not be naturally-occurring]. Maltose is dimer of the alpha-d-pyranose form of glucose. One version of the proper name for maltose is 4-O-[alpha-d-glucopyranosyl]-alpha-d-glucopyranose. [say that ten times fast] What does this mean? It's two alpha-d-glucopyranoses that you're doing something with. Let me draw two of those sugar units. One sugar is a substituent to the other. The way that these are often written is to put the sugar that is the end, the one where the anomer position can open easily, put it on the right. As the name is: 4-O-something, alpha-d-glucopyranose. What does the O mean? It means we're substituting not at carbon #4, but the oxygen attached to carbon #4. Since the carbonyl is the top of the molecule, it's also where number from in a carbohydrate. That's position 4. There's an oxygen that's supposed to go there; on that oxygen, we have a substituent. What is that substituent?

Glucopyranose, in its alpha-d form, connected through its anomeric position, where we would have glucopyranoside; the substituent name, -ide goes to -yl, so we get glucopyranosyl, which means it looks like this.

If you're unsatisfied with that curved bond, in order to draw some of these disaccharides correctly or in a way that the bonds make sense, you have to draw them using Haworth projections that are not in standard configuration. That Haworth projections [normally take] those Fischer projections, tipping them to the side, the anomer goes on the right, and the anomer oxygen goes on the back. But if I want to make that bond not twisted, I have to flip the molecule 180° over on paper, which means that what was on top is now on the bottom, and what was in back is now in front. The common mistake made at this point is to do only one of those two things – to switch the top and bottoms. If I switch all the top and bottoms and the bond was pointed the correct way, that's the mirror image of that portion of the sugar; that's the enantiomer of that portion of the sugar, so it would be l-glucose if I did that. If I swapped the front and the back, that's again inverting the molecule, making a mirror image, which again means I'm making the l form of the sugar. But if I both swapped the front [and] back positions and swapped the top and the front, that is the same thing as 180° rotation. Since I did a double reflection, I made the mirror mirror image, which means I got the original compound back again. If I wanted to take this and turn it, just this portion, 180°, here's what I get.

Notice I circled the alpha and pointed to one particular -OH group. The back part of the molecule, the left-hand unit, that's trapped; it is a full acetal. The front part, where I've pointed at, is a hemiacetal. The hemiacetal opens more easily than a regular acetal. So, the front part of this molecule can easily open, close, open, close still, which means there's an alpha form of maltose and a beta form that depends of the configuration of that openable anomeric position.

### Lactose

What is lactose? It is 4-O-(beta-d-galactopyranosyl)-alpha-d-glucopyranose. What does that mean? We have a unit of galactose that is the back unit, and we have a unit of glucose that is the front unit. Again, the right-hand anomeric position could open more easily, so would potentially have alpha and a beta form of lactose.

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Knowing the optical rotation of the alpha-d form of glucose does not help in determining the optical rotation of beta-d-glucose since they are epimers – not enantiomers – so there is no relationship between their optical activities.

Mutarotation – Whenever a pure sample of an alpha or beta aldopyranose is placed in solution, the alpha & beta forms will interconvert, achieving an equilibrium between the two forms with an equilibrium optical activity.

The exact proportion of the various ring forms that will result from a particular sugar depends on the intramolecular interactions that occur upon cyclization that are unique to each sugar.

### Glycoside

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; cellulose]

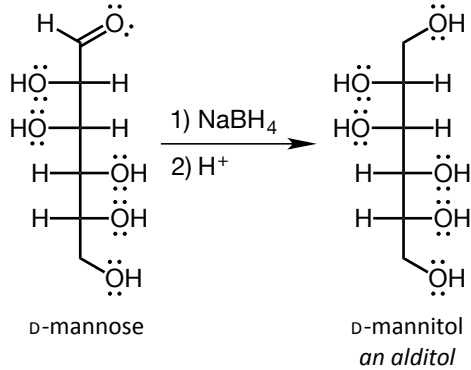
oligo – “several”

poly – “many”

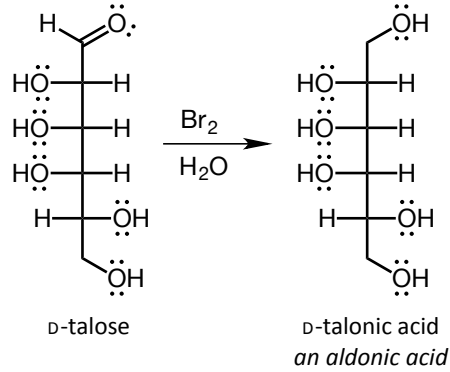
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Structures

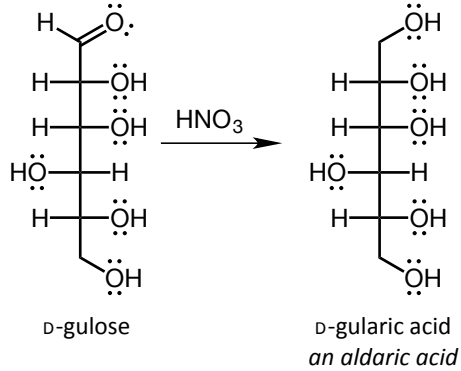
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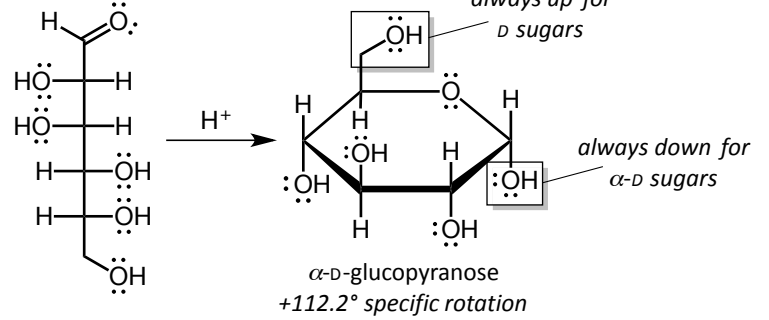
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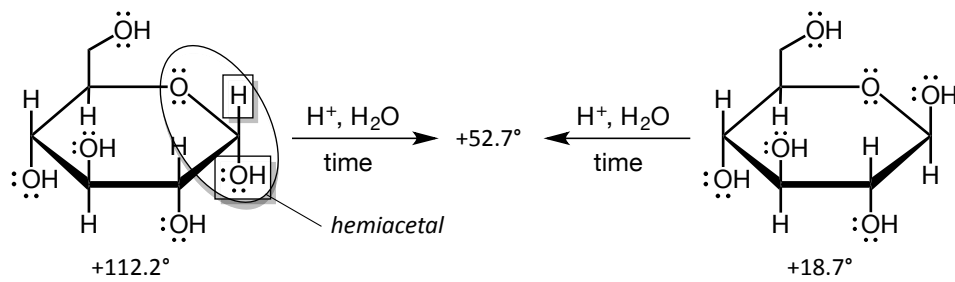
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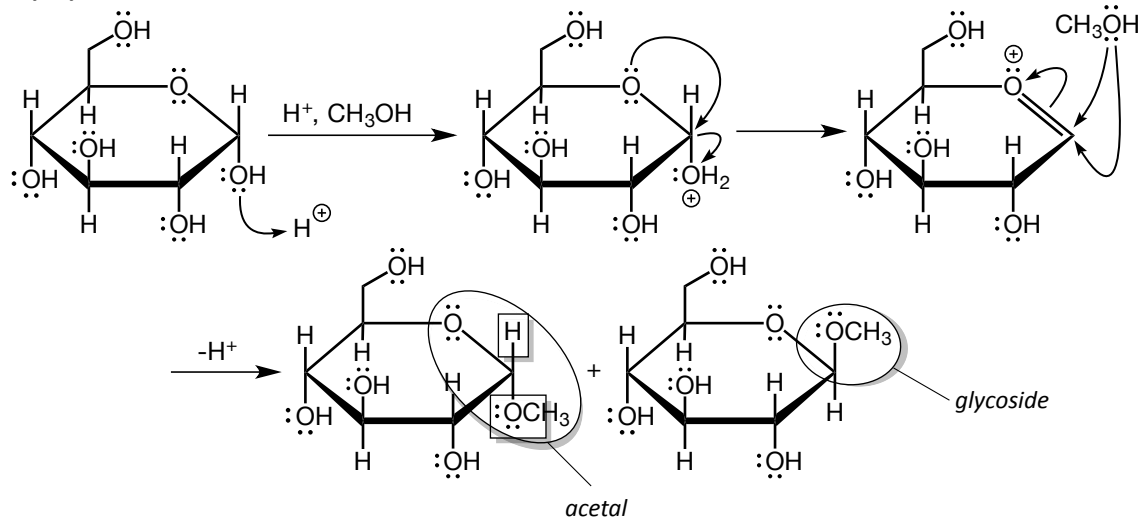
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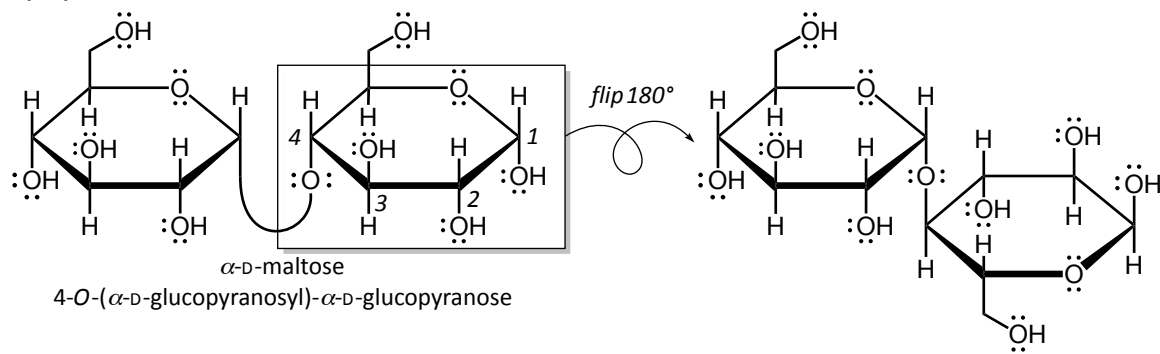
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05/16/12 lab • 8

