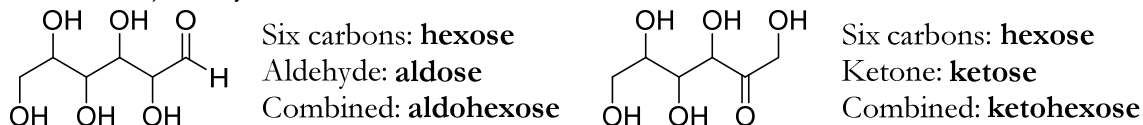


Loudon Chapter 24 Review: Carbohydrates

Jacque Richardson, CU Boulder – Last updated 4/26/2018

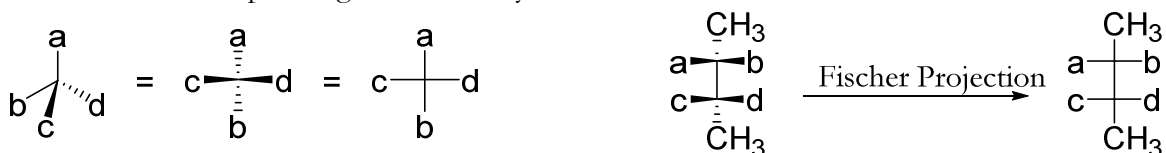
This chapter is about carbohydrates – molecules with the general formula of $C_n(H_2O)_n$, or in other words $C_nH_{2n}O_n$. This is a very common formula for sugars and many other natural products. The structure is usually laid out so that the carbons are in a line and every carbon has an OH group, except for one which has a carbonyl (required to get the right degree of unsaturation). Many of them look like this:



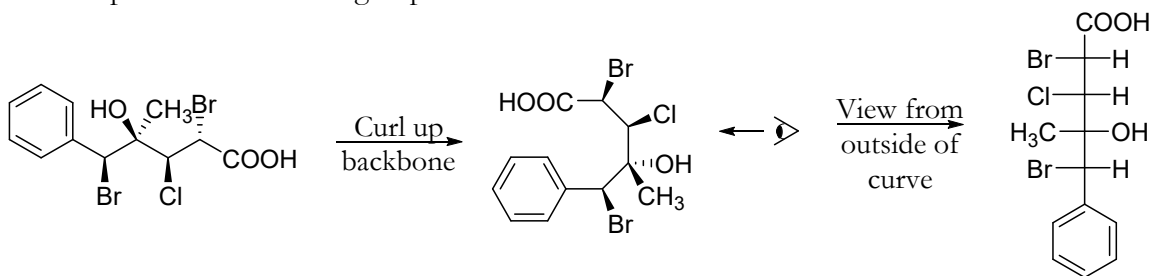
The naming is subdivided based on how many carbons they have, and whether the carbonyl is an aldehyde or a ketone. These simple molecules (monosaccharides) can be joined into long chains (polysaccharides), in ways we'll see later.

Fischer Projections

Since almost all the carbons in carbohydrates are stereocenters, there's a lot of chiral information that needs to be depicted. The standard way of doing this is with Fischer projections. This is done by putting the molecule's carbons into a vertical line, and having every junction follow the same pattern: the vertical lines are pointing into the page, and the horizontal lines are pointing out towards you.



This can get confusing with a long chain, but the easiest way to think of it is to push the entire molecule over to one side. When viewed in Fischer projection, the molecule shown above is arching out towards you like a bridge. But viewed from the side, every kink in the chain is bending in the same direction, rather than a zigzag formation like at the top of this page. The molecule itself doesn't necessarily bend into this shape in reality, but this is just a standardized way of showing it. There are standard ways of redrawing the molecule based on certain rules that are covered in the book. By convention, the carbonyl carbon is put as close to the top end of the drawing as possible.



Stereochemistry

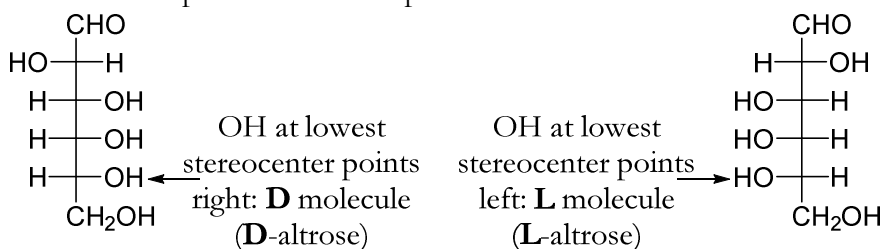
Every chiral center can be either R or S, and a molecule with n stereocenters has 2^n possible structures. For a molecule with three or four stereocenters, the number of possibilities gets pretty big.



Loudon Chapter 24 Review: Carbohydrates

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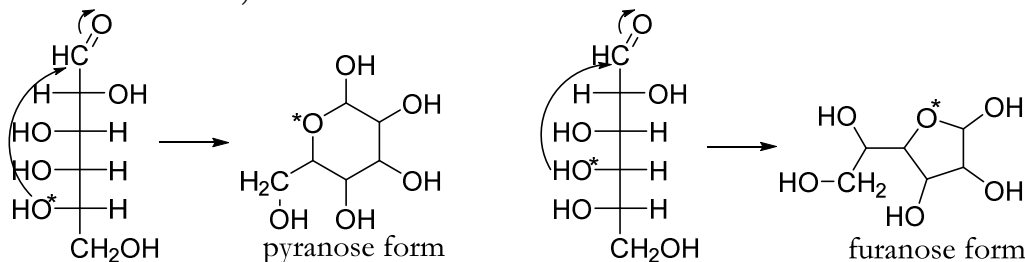
The possible structures come in pairs of enantiomers, where every stereocenter is flipped (R to S, or S to R) between the two molecules. The two enantiomers have the same common name, but are distinguished by having a **D** or **L** added to the name. This is based on the OH at the stereocenter furthest from the carbonyl, once all the carbons of the chain are placed in a vertical line for the Fischer projection (this may be something you need to arrange, if CH₂OH is hanging off to one side). If the OH at that stereocenter points left, it's an **L** molecule. If the OH points right, it's **D**. The two molecules below are enantiomers, so they have the same name except for the **D** or **L** part.



Any time you have two structures that are the same except for one stereocenter, they're called epimers, and converting between them is called epimerization.

Cyclization and Haworth Projections

Just because monosaccharides are drawn as Fischer projections doesn't mean that they are in this linear form all the time. Since they have an aldehyde or ketone at one end, and at least one alcohol group at the other, they usually react with themselves to form a cyclic hemiacetal. Ideally they make five-membered rings (called furanoses) or six-membered rings (called pyranoses). Often they can make both, depending on which OH group is involved in the hemiacetal. The OH group that does the attack always becomes the oxygen in the ring (marked with an asterisk).



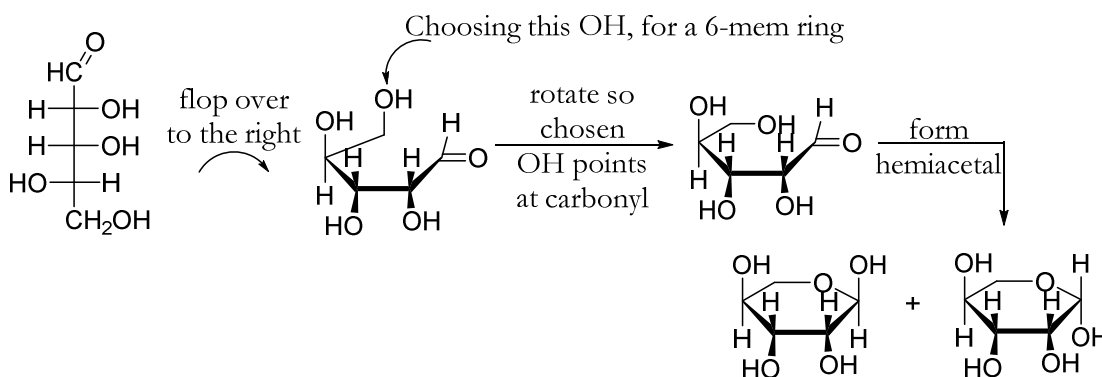
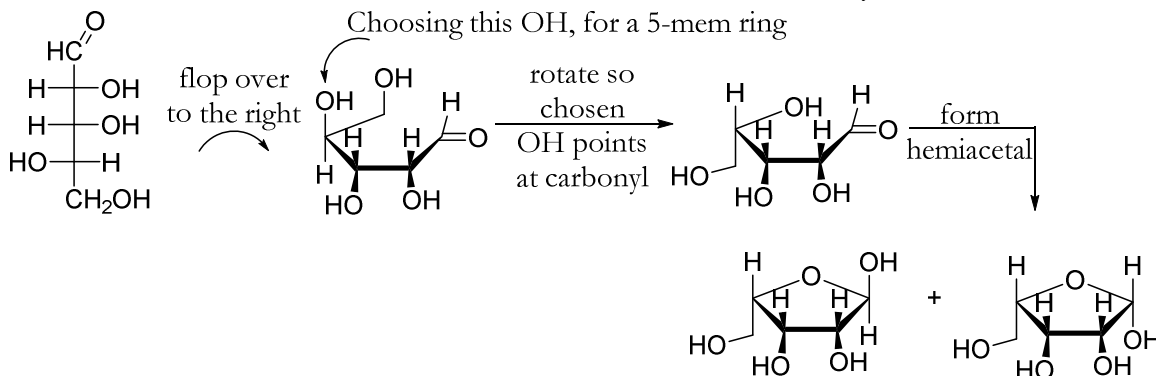
To help show what's going on with the stereocenters, Haworth projections are used. These show the cyclic form of the molecule in a flat ring, but viewed from the side rather than from above. To generate the Haworth projection, there are several steps to follow. See the example on the next page.

1. Take the Fischer projection and flop it over to the right, so that it's curled with the carbonyl at the right end and the terminal OH at the back. This means that any groups on the **left in the Fischer projection** are pointing **up in the Haworth projection** and anything on the right in the Fischer projection is down in the Haworth projection. The lowest carbon in the chain is usually achiral, so it doesn't matter which way its OH points.
2. Decide which OH group you're going to cyclize onto. For the five-membered ring, choose the OH on the third carbon after the carbonyl. For the six-membered ring choose the OH on the fourth carbon after the carbonyl.

Loudon Chapter 24 Review: Carbohydrates

Jacque Richardson, CU Boulder – Last updated 4/26/2018

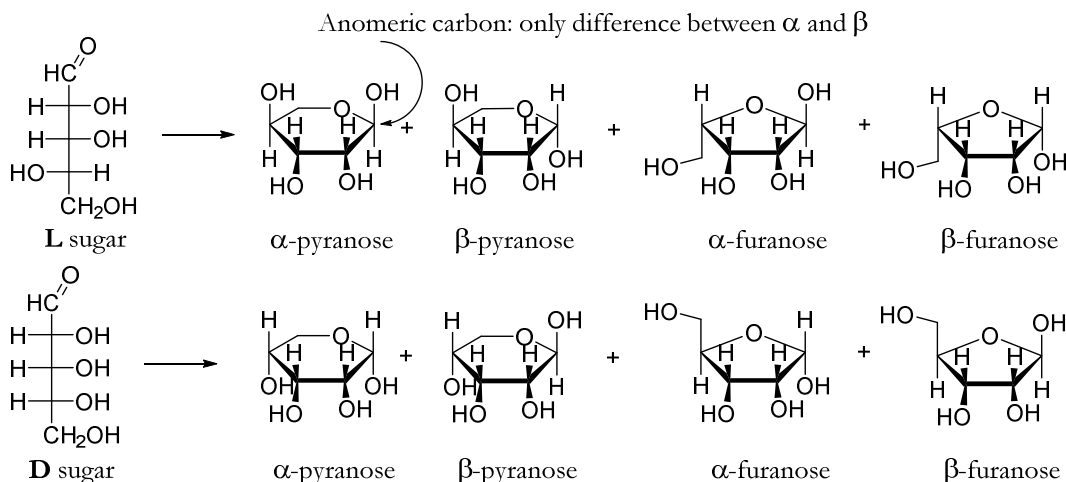
- If necessary, rotate the chosen OH into position so it's in the plane of the molecule, pointing towards the carbonyl. The rest of the chain after this gets rotated out to become an up or down substituent.
- Form the hemiacetal between the chosen OH and the carbonyl.



As a result of these steps, the OH group that used to be the carbonyl is one step clockwise from the O in the ring. It's identifiable because it's on the only carbon in the ring with two bonds to oxygen, which is now a new stereocenter. This carbon is called the anomeric carbon. Because this stereocenter has free choice of being R or S, there are two different forms of each ring which vary only at the anomeric carbon and are called anomers. In the α anomer, the anomeric OH is pointing the same direction as the OH that determines **D** or **L**. In the β anomer, it's pointing the opposite direction. In effect, this means that a **L** structure has the anomeric OH pointing up in the α form and down in the β form. The opposite is true for **D** structures. (If you make the six-membered ring, you may also have to draw out the chair cyclohexane conformation. Each product has two different chair forms, but one is usually more favored than the other.)

Loudon Chapter 24 Review: Carbohydrates

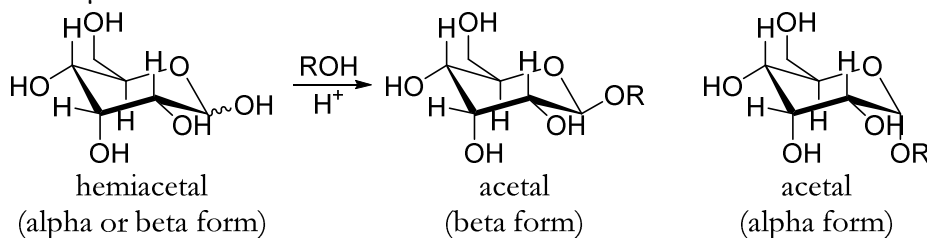
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Since the anomeric carbon isn't a permanent stereocenter (the hemiacetal formation can reverse itself at any time), these anomers do not count as epimers. All the possible cyclic forms of a molecule will interconvert if you give the hemiacetal a chance to reverse itself. This interconversion is called mutarotation. Just like hemiacetal formation, it's catalyzed by either acid or base, but it happens in neutral water too.

Glycosides

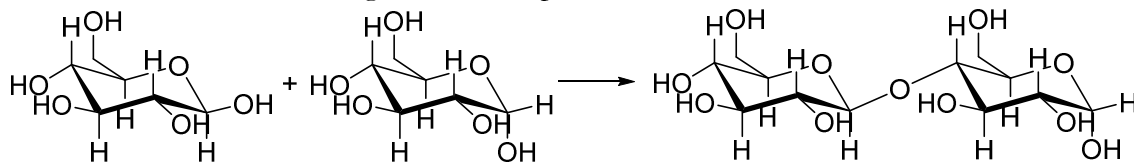
Since the cyclic forms of carbohydrates are hemiacetals, they can do things that other hemiacetals can do. For instance, they can convert to the full acetal if there's another molecule of alcohol (and an acid catalyst) for them to react with. Just like in the cyclic hemiacetal, there are α and β forms.



The overall effect of this reaction is to convert the anomeric OH group into some kind of OR group. The mechanism is exactly the same as the mechanism for hemiacetals going to acetals. Once the acetal is formed it's stable in base, but can be hydrolyzed back to the hemiacetal in H_3O^+ .

Disaccharides and Polysaccharides

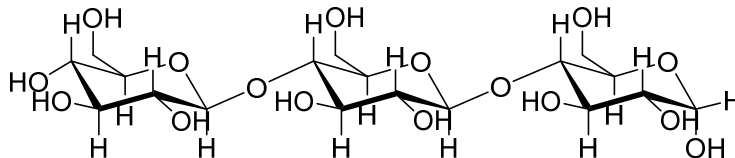
Simple alcohols aren't the only kind that you can attach at the anomeric carbon. You can also attach an entire second molecule of carbohydrate. This links two saccharides together to make a disaccharide. Table sugar is an example of this.



Loudon Chapter 24 Review: Carbohydrates

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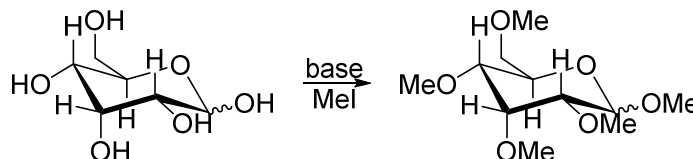
Again, these can be either alpha or beta linkages. The chain can continue to a polysaccharide if you keep linking chains together at the anomeric OH of each ring.



A huge number of natural products follow this pattern, such as starch, cellulose, chitin, etc. Not all of them use the same kinds of linkages – some of them have beta linkages, and many of them use attachments to different OHs around the ring to create a branch in the polysaccharide.

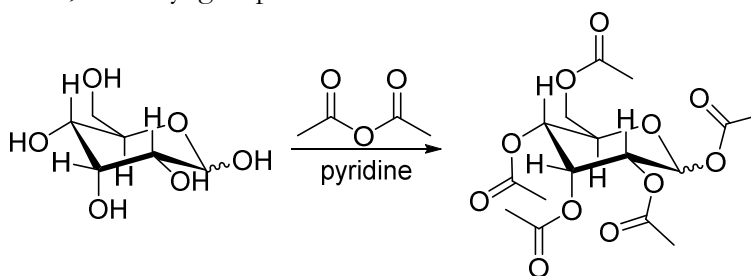
Ether and Ester Derivatives

The anomeric OH isn't the only group that can have other things added to it. Any of the OHs around the ring can be put through reactions that regular OHs can do, but ether and ester formation is particularly common. For ethers, Williamson is still the default reaction. You don't need NaH though – the OHs on a carbohydrate are slightly more acidic, thanks to other nearby OHs, so you can get away with using a weaker base like NaOH. Then you bring in an alkyl halide to do S_N2.



To remove these groups, you need to do ester hydrolysis: heat, water, and acid. The anomeric group comes off much more easily than the other groups.

To make esters, the most commonly used method is with either the acid chloride or the anhydride. Often, an acetyl group is attached to each OH.



Again, you need to hydrolyze these groups if you want them to come off. Heat, water, and either acid or base will do it.