

## Lab 5B • 05/01/12

The Fischer projection is named after that same person that we have for the Fischer esterification and this Fischer stereochemistry proof. This Fischer projection came about not long after the idea of tetrahedral carbon came into existence. To give us some context, it was only in the [1870s] that the idea of tetrahedral carbon came about. Stereochemistry, stereoisomerization has a couple of different forms. If you think of an alkene, at one carbon or another of the alkene, if you were to switch the position of the two substituents on one carbon or another, potentially you produce a different molecule, even though you have all the same atoms all connected to each other in the same way, but just arranged differently in three-dimensional space. We're going to focus on something called an asymmetric carbon, something that has tetrahedral geometry.

If have tetrahedral geometry, what's the quickie rule we use to say it's going to be a stereocenter, something that could generate different molecules with different 3D arrangements. An asymmetric center, a stereocenter is created if we have four different substituents attached to that position. Let's review how we assign what's known as an absolute configuration to that position. [I'll use a halogenated methane for our example.] Notice the way that I've drawn this: the two bonds that are in the plane of the board, they are making an angle pointing down and to the left; notice that the dash and the wedge are written in that same kind of direction. Two of the bonds come into that center, two of the bonds come out of that center. If I was to write either the dash or the wedge on the other side, where the two plain lines are, then in that case you could interpret this structure incorrectly [or is it more just that it's inappropriately written]. Sometimes those kinds of structures will be drawn if you're trying to achieve a very specific viewpoint of the molecule, a very specific representation, but by convention, the dash and the wedge should both point one direction, and the two plain lines should point the other direction.

If we did want to assign an absolute configuration, we have these Cahn-Ingold-Prelog rules that we use to assign first a priority to each one of these substituents and then somehow we determine what the arrangement of those substituents is. What's the first rule as far as figuring out what's important? Atomic number. There's two places on the periodic table where increasing atomic number occurs with decreasing average atomic mass, so atomic mass is not an ideal factor to use in determining priority]. It's highest atomic number first, so what would be the highest-priority substituent on this molecule? Bromine, highest atomic number; second, chlorine; fluorine, three. If you didn't assign a viewpoint, if you just tried to look at the molecule as-is, as written, what stereochemistry does this appear to have? R, because if I just look at the raw position of those substituents, it looks like bromine's there, wrap around here's chlorine, wrap around here's fluorine, but that's the incorrect answer. Why? Because you have to visualize the molecule in such a way that the least-important group is explicitly oriented away from you. Right now, it's in the plane of the board; that means I really have to be looking at the molecule this direction. If I'm looking this direction, bromine is in the plane of the board and it's up above me, so here's position one from my perspective. Chlorine is priority number 2, but it's in the plane of the board, which means it's to my left from my viewpoint; then, the fluorine is on my right. When we're just looking at it from this flat paper perspective, it looks like the fluorine's on the left, the chlorine's on the right. But that's the incorrect way to view the molecule. Remember that you always have to establish a perspective. My symbol for that perspective is a little eye, then there's a line on top of it which represents the eyebrow; it really does matter where you put that eyebrow position.

Right now, the way I've drawn it, it means I'm looking down upon the molecule like this, instead of looking at the molecule like that. As I'm looking down, bromine is up top here, chlorine's to my left because it's in the plane of the board, and fluorine's to my right. If I were to precess around those priorities and then turn in such a way that you were also looking at that hydrogen, now we can see that this is counterclockwise, so this is the S configuration. The apparent configuration of this is R, if all we do is look at the orientation in this 2D plane. But, that's incorrect, because we didn't use the correct viewpoint, correctly putting the hydrogen in the back of the plane. What we've done in the past in this situation, besides visualization, is to try to rewrite the structure. Some people visualize very well in 3D; engineers, in particular, tend to be people who see almost anything in three dimensions. But in an exam situation, you might not want to take the risk that you can somehow magically see this structure. [hand motions and popping sounds of the model sets]

What can we do to rewrite this structure? Think about this: if these three colored groups that are on here are the three halogens; I'll orient [the] hydrogen in the plane of the board. I'll put one of these groups in the plane of the board as well. Then, we've got the other two halogens pointed towards you and away from you. What we want to do, then, is somehow get the hydrogen pointed away. If I hold on to the halogen that is on top, I can simply spin the molecule around to get the hydrogen in the right position. That's easy to do in 3D space, that's easy for us to view in 3D space – the problem is how do we translate that into this two-dimensional representation.

I wanted you to consider something else: we could just take the hydrogen and put it in back and swap it's position with another substituent. For example, we could take the hydrogen and the chlorine and swap their places. If we do that, what's going to happen to the configuration of the molecule? It's going to be inverted. That's the whole point of these asymmetric carbons - if you swap two substituents, it's as if you've taken its mirror image, because two of the positions will be parallel to the mirror itself, so they won't be reflected, so they won't change. Automatically, two other positions will be reflected, so two groups, if you exchange, you've inverted the stereocenter. I want you to consider another subtle detail of that.

Which one of these two is correct? We said that the above stereocenter the S configuration. [?] Hydrogen's in the back, the way it's supposed to be. We have bromine, priority one, chlorine, priority two, fluorine, priority three. It really is clockwise, so yes, it really is R. Let's look that the first molecule. Same thing: the hydrogen's in back, bromine position one, chlorine position two, fluorine position three, it's still correct in terms of its orientation. That means both of these ways are correct ways to represent this molecule. What's the difference? If you look at me observing this molecule, I'm going to put the hydrogen away from me, and I've got a fluorine pointed out towards me. It depends on whether I'm looking at the molecule like this, where now that fluorine looks above and the hydrogen looks below, or whether I'm peering over the bond in this way, where the hydrogen now looks above, the fluorine looks below. It's simply a matter of perspective, but it's the same molecule that I'm drawing. This is why it's best to have that least important group in the back, cause effectively what we're doing is ignoring the position of the dash, and if we ignore the position of the dash, then it doesn't matter where you draw the wedge.

In a molecule that has multiple stereocenters, whatever way you do draw it, whichever one you happen to draw more to the right or more to the left, the dash or the wedge, you want to repeat that same perspective for the whole molecule; otherwise, it could become confusing to the reader. Both of these are a perfectly correct interpretation or representation of the structure, but we have inverted the stereocenter. What we really wanted to do originally, if we were trying to better visualize that, is to not change the stereocenter – just get the hydrogen into the correct position. What if we now, though, switched another pair of substituents? Since I want the hydrogen in back, this time I'm not going to mess with it. What if I flipped the chlorine and the fluorine around, for example? Then I'm going to again invert the stereocenter. In this case, a double negative is a positive – you invert it, you've taken its mirror image, you invert it again, you're taking the mirror image of the mirror image, which means you get the same thing back again. If two groups on a tetrahedron are exchanged, the configuration is inverted. If I've exchanged again, I've inverted again – which better means we end up with the S configuration (we'll confirm that momentarily). We have bromine priority 1, chlorine priority 2, fluorine priority 3. Hydrogen's in the back, the way it needs to be to correctly visualize this. We have the groups in a counterclockwise fashion, so it really is S.

Let me write next to it the original molecule over again. Notice that, from that original molecule, if we had put hydrogen in the back the way we wanted, but as response allowed chlorine to continue rotating around to where fluorine is, and then fluorine rotate around to where they hydrogen is, that's exactly what I was doing with the model set originally. I had the hydrogen on the side that I wanted to rotate in back, so when I rotated it, three of the groups turned around. But, because of the type of geometry that a tetrahedron is, that same operation of rotation around this three-fold axis is exactly the same as reflecting two groups twice – it can't be the same group, because if you took the same group and reflected and reflected again, then you haven't changed anything. But if you take one pair of substituents, exchange it, another pair of substituents and exchange it, there are only three positions on that wheel as it is, so by doing that double exchange, effectively, you have rotated it – which means there's just a rotamer difference, but otherwise they're the same stereocenter. The whole point here is that swapping the positions of two substituents twice has the same effect on tetrahedral geometry as rotation.

Let's move on to the Fisher projection. To get to the Fischer projection, though, I'm going to tell you a little side story about carbohydrates, because that's where we're normally going to use these Fischer projections. As the carbohydrate might imply, the general formula for a simple carbohydrate is carbon and water, that whole thing multiplied by x. I say simple – [monosaccharide, disaccharide, trisaccharides] there are these smaller sugar units which, in their linear form, each have one carbonyl in them [and have a continuous, unbroken carbon chain]. Those structures, though, can combine with each other and form, essentially, an organic polymer. If just two units combine, that's a disaccharide; three units, trisaccharide; a few, oligosaccharide; a whole bunch, polysaccharide. What's an example of one of these simple carbohydrates? I'll show you the simplest one, which is d-glyceraldehyde. Let me tell you a few side stories about this. Glyceraldehyde is related to the molecule glycerol [endurance sports, fats – tricycleride]. What is a triglyceride? Three esters. If we take a carboxylic acid – a long chain carboxylic acid – and put it on each one of those -OH groups, that's a triglyceride – that fat, that's what the simplest form of a fat molecule is. If we change the structure of that a little bit from, for example, instead of just an oxygen we make one of those some kind of phosphorus containing group, the we get the structures that lead to phospholipid bilayers.

From glycerol, we oxidize either the top or the bottom position – it's symmetric, so it doesn't matter which one – we get glyceraldehyde. There's this designation d. There is an interesting side story to this. That d designation does have to do with stereochemistry, and it does have to do with optical rotation. Back in the 1860's/70's, the idea of tetrahedral carbon was just coming about. It was about the same time that polarized light microscopy showed that there is this unusual interaction that could occur between matter and light, where you get a twisting in just one direction of light. Very soon after this idea of tetrahedral carbon, they realized that's going to cause asymmetry in molecules which would cause optical rotation. We're familiar with optical rotation, because we know that one enantiomer's going to turn light one direction, the other enantiomer is going to turn light the other direction. What are enantiomers? Molecules that are mirror images of each other. What are the differences or the similarities in physical properties between enantiomers? They're similar in all properties – except optical rotation [and some kind of polarized spectroscopy].

If they were inventing the idea of optical rotation, if it had never been measured before, and if I gave you a solution of some compound and said: here, measure its optical rotation and you did, how would you then determine whether that compound, if it had just one stereocenter, was R or S?

It's arbitrary, but what that really means is you can't determine it, because there is no connection between positive rotation or negative rotation and R or S. Glyceraldehyde, they determined, had optical rotation, but they didn't know whether it was the R or S form, for that particular version that they measured. So Fischer guessed – he said: here's this d form that has this particular configuration of the stereocenter. As we're going to learn, we can synthesize many of the naturally-occurring sugars from glyceraldehyde. Since they came from this d-glyceraldehyde form – which it turns out that this is the form that is biologically active – then those other molecules that are also biologically active get that same d label. Glyceraldehyde, since it is an aldehyde, can be converted into other functional groups, and so there are other molecules that also, therefore, carry this d designation. From the time that stereochemistry was invented, you could say, until the 1950's, they still didn't know the right answer, which meant this: if they ever did figure out what the correct orientation was – which we did – if it was correct, then all the molecules across the literature would have the correct orientation ascribed to them. If, in '50s when they determined the real configuration, they determined that they'd been wrong, that every molecule in every textbook everywhere would have to be reversed. Everybody knew that was the case. He just happened to make a really, really, really good guess, because he got it right – but he had, literally, just a 50/50 chance. The way that they eventually solved it was similar to the way that we figured out the structure of DNA – x-ray crystallography: you get a crystal of a material, you shine x-ray light through it, you get reflections or diffraction in all different directions. You can take that pattern of dots that's produced [and] backwards figure out where the positions of the atoms would have been that caused those different patterns. There was a salt of a carboxylic acid derivative that they eventually figured out the configuration of. It was related to glyceraldehyde, and from there they figured out all those other configurations were correct. That's where the d in glyceraldehyde comes from.

The first step of the Fischer proof is: he guessed, and he got it right.

What is this thing we're looking at? There's a specific way that Fischer projections are defined. By definition, any group written on the backbone of a Fischer projection – the vertical part of it – is oriented away from the viewer, while any group on the arms – the horizontal part, left or right – anything on that position is oriented towards the viewer. As we will see in a moment, this is not a normal kind of space – we cannot, for example, rotate things around in this definition of space. You always have to remember: anything up and down is really pointed away from you; anything left or right is really pointed towards you. First, let's just deal with Fischer projection itself for a moment, explore this idea of the Fischer projection space. I'll rewrite it the way I just said it: that those groups that are vertical are really positioned away from you; those groups that are horizontal are really oriented towards us.

Let's see if we can do the more difficult operation first. Let's see if we can take a regular dash-wedge stereocenter and take these groups and put [them] on it. I'll just draw a typical dash-wedge stereocenter. The first thing that I've got to do is establish a viewpoint. Here's my recommendation: since a dash always means into the back of the paper, since a wedge always means towards the viewer, I like to keep my viewpoint so that I'm looking down on the plain lines as if its part of the backbone. In other words, as we make a longer Fischer projection, it's going to have more rungs on this ladder. Those will correspond to all of these different stereocenters; it's usually easier to deal with this if you take the center line itself and make it the plane of the paper. I can, for example, look down on this stereocenter and see that one plain line is there in front of me, pointed away; if I look down, the groups are going to be away from me. One of these other plane lines is going to be away but behind me. That means I need to choose where my eyebrow's going to. Which way do we want it in this case: do we want the top of the molecule, this carbonyl, to be over on the left, or do we want it to be on the right? Left, ok. I've established my viewpoint there. I'll put the carbonyl, then, on that left position, and I'll put the  $\text{CH}_2\text{OH}$  group on the right. If I'm looking down on the molecule from this angle – standing over here on the right looking down on it – the wedge is the group that pointed, from my perspective, to the left; that would be a hydrogen on the Fischer projection. From that viewpoint, I'm looking down and the dash and the wedge are pointed up at me – they need to be, if we're properly making the Fischer projection. The hydrogen is on the left which, from my perspective, is going to match up with the wedge, and the  $-\text{OH}$  group is on my right, which means it's going to mash up with the dash.

I'm going to look at this model in such a way where two of the groups are like the way I'm holding it in my fingers, and from my perspective they're pointed away from me. Automatically, that's going to make these other two groups pointed towards me. The suggestion is: it's easier to deal with these molecules if the vertical part is the plain-line part, the part that's in the plane of the paper. I'm going to take this molecule and I'm going to take the two groups that I'm holding on to and make them parallel with the plane of the paper. I've got one group pointed toward you, one group pointed away. When I look at the molecule, one of these is on the left, one of these is on the right. The one on the left, from the Fischer projection, is hydrogen; the one on the right, from the Fischer projection, is the  $-\text{OH}$  group. I just turn the molecule around, and we can see that the one that was on the left is pointed towards, cause that's the way I was visualizing it. The one on the left is that hydrogen; I put the hydrogen on a wedge. Then, the  $-\text{OH}$  group, which was on my right, is going to be the dash. We can confirm whether we've done this correctly or not by trying to figure out if it's R or S. Let's start with the dash-wedge structure first, cause that's where we're used to determining R or S. Right now, the hydrogen's pointed towards us, and that's the incorrect perspective; we're supposed to have the least important group pointed away from us. But, there is this little trick we could do where we view whatever we've got and, if we know it's wrong, just invert the answer. If we put the hydrogen in the back, where it's supposed to be, and took the  $-\text{OH}$  group in back and moved it to the front, that would invert the stereocenter. [rewrite versus visualize]

In order to do that trick, we need to figure out the priorities for each of the substituents. Hydrogen is the least-important substituent. What is the most-important substituent: the carbonyl, the CH<sub>2</sub>OH, or the alcohol group? The alcohol group – highest atomic number (at the point of attachment). So what if it's a carbonyl; it's a carbon first at the point where the stereocenter is; same thing with the CH<sub>2</sub>OH, it's carbon first and then an -OH group. The one up top is an oxygen first, so it's priority one. How do we deal with the carbonyl? We use what are called phantom or virtual atoms; we duplicate. On the carbon, we add an oxygen, cause that's what carbon is double bonded to. On the oxygen, we add a carbon, because that's why oxygen is double-bonded to. So we rewrite the molecule. We have the single-bond carbon and oxygen that's the real bond, you could say. On the carbon, you duplicate what it's connected to; on the oxygen, we duplicate what it's connected to. If we had a triple bond you would do that process twice – put two nitrogens (they say we have a nitrile) on carbon and two carbons on the nitrogen. Now we can do a comparison, because it's the first point of difference. We look at what's immediately attached to the stereocenter and see if we can make a determination there. The righthand group, we have attached to that carbon [oxygen, hydrogen, hydrogen]. On the left, we have attached to it [O, O, H]. We don't have to look at what's attached to the oxygens, because at this first point, there's a difference, and that's all that matters. At this point, we have that oxygen is more important than hydrogen, which means the group on the left is the more important substituent. The carbonyl is priority 2, the CH<sub>2</sub>OH group is priority 3. This has the appearance of being S, but because the hydrogen is actually pointed towards us, it's really R. Although groups appear to be in the S configuration, the least important group is oriented towards the viewer, so that apparent configuration must be inverted.

If you knew ahead of time that you were going to run into this problem and put the hydrogen in the front, why didn't you visualize the molecule to start with with the hydrogen in the back – in other words, stand here, look at the molecule this way, have the carbonyl up here, which would make the hydrogen in back. You could and you should if you saw that enough ahead of time. What I'm going to do next is if you did it the wrong way how, just like you can turn groups around in the dash-wedge structure, you can turn them around in a Fischer projection as well. To get to that, notice what we did here with this dash-wedge structure – we said: oh, the hydrogen's in front, whatever we see, we reverse. Notice that the hydrogen on a Fischer projection, if it's on a side arm, is similarly also in front, automatically. That means we should get the same result if we look at the substituents and we were to reverse their order, just like we did with the stereocenter. As you'll see in a moment, once we get the hydrogen oriented to be explicitly away from us, the way we would do with a dash-wedge structure, we'll again see we can read the remaining pattern or configuration and figure out if it's R or S. We take the same determination of priority order: the alcohol is 1, the carbonyl is 2, the CH<sub>2</sub>OH group is 3. This is counterclockwise; that means that, because the hydrogen is pointed towards us, this really is R.

What if we wanted to rewrite the Fischer projection, put the hydrogen pointed away from us, the way it's supposed to be. Let me rewrite the Fischer projection the way it normally is, with plain lines. Let's say that I rotate 90°. It doesn't matter which way we rotate, because now the hydrogen is vertical. By definition, hydrogens that are vertical are pointed away from us. What is the configuration of the stereocenter in this rewritten molecule? It is S. We had an R molecule and all we did is turn 90° on the paper, and now we've made it S. That's cause we didn't just turn it 90° on paper, because in regular space, we don't have this silly thing that says horizontal is towards us, vertical is away from us. In regular 2D space, it's left, right, up, down, period, there's no dimensionality to it. But, in Fischer space, there is this hitch to it: it's an asymmetric scape, so in normal space, if I rotate something, I just rotate it by 90°. That's not what's going on in the Fischer projection, because whatever is oriented here must always be pointed towards us, whatever's here must be away from us. This used to be towards us, then when I turned it 90°, it's actually flipping over at the same time, so every time you rotate, you get inversion like that. It's called improper rotation; that's the definition of a Fischer projection. If I'm inverting like this, when I keep the positions of the substituents relatively to each other on the paper the same way, I've inverted the stereocenter. You cannot rotate a Fischer projection 90°; it's simply not allowed. Improper rotation of a Fischer projection by 90° will cause inversion of configuration. It's because of the definition of Fischer space: horizontal towards you, vertical away from you.

But, if we exchange the position of two groups twice, that is just the same thing as rotation. Instead of just flipping two groups twice, we simply precess, we take the three groups and exchange their position in a circle. The really trippy thing about a Fischer projection is it doesn't matter which one of the bonds you keep still – either in real space or in the Fischer projection – the other three groups may be rotated and it won't change the configuration – again because if you flip two groups, that's reflection, do it twice, it's simple rotation. It's a crazy coincidence of taking a tetrahedron that has four things to it and making a simple cross out of it that has four things to it. If I want to get the hydrogen in the back, we will exchange three of these substituents. If I rewrite it, it'll look like this with the carbonyl still in the same place; now we have the CH<sub>2</sub>OH group on the arm, we have the hydrogen below, we have the -OH group on the other arm. The hydrogen, by definition, is now pointed away; we have the alcohol, priority 1, the carbonyl, priority 2, last group, priority 3; it is clockwise in orientation, so it really is R. Since the hydrogen is pointing away from us, we can look at this can get the stereocenter's correct configuration. [those who know about coffee mug do not talk about coffee mug]

Now we get to play with multiple stereocenters. [can leave lone pairs out] This the molecule d-glucose, that which is blood sugar. Notice the way I've written the Fischer projection, similar to the one I did for glyceraldehyde, where I put the carbonyl up top. That's the standard convention for Fischer projections of carbohydrates. In this case, we have an aldehyde; some sugars can be ketones. Whether it's an aldehyde or a ketone, the carbonyl is still written at the top.

Instead of it being referred to as the carbonyl, you might see it referred to as the anomeric position. [subset of diastereomers called epimers; subset of epimers called anomers, which only forms when a sugar like this cyclizes]. Look at all of these -OH groups: what if one of them was to react with the carbonyl and add into it, forming a hemiacetal? Normally, that's not a favorable process; for sugars in water, it is. Most of these sugars exist in cyclic form in solution. A carbonyl, which is planar, if you suddenly attack it and turn it tetrahedral, you've just made a new stereocenter. Everything else can stay the same, but depending on the way you close it, you make one stereocenter or another – that's an epimer, that's specifically an anomer.

d-Glucose: this is an aldohexose, meaning it is an aldehyde that contains six carbons. There are seven other [aldo]hexoses that are unique, so there are eight total six-carbon [aldehyde] sugars; there's four five-carbon [aldehyde] sugars; there's two three-carbon [aldehyde] sugars; and glyceraldehyde is the one three-carbon [aldehyde] sugar. If you were thinking quickly, you'd say: wait, four stereocenters, there's 16 molecules, not 8. It turns out, they're just enantiomers of each other, which means they're the same, other than its mirror plane, so they're given the same name. [couple of ketones to be learned] If you write it in standard Fischer projection, from top to bottom the -OH groups are [right, [[left, right]], right]. Let's draw the dash-wedge version of this. Remember what's the definition of a Fischer projection: every group is pointed away from you [in the backbon]. But wait a minute: if you've got this many carbons, how can each one be away from the other if, as you go from one carbon to the next, it really is away from each other, which means you're going to be going around in a circle. In other words, the proper way to write the molecule, in this case, is as follows. Our perspective for this ring is right up above. I always recommend that you put the backbone in the plane of the paper. If I'm looking [from] up above here, this carbonyl is pointed away from me; if I'm looking here, this is pointed away. Think of it this way: here's a Fischer projection on a piece of paper [rolled up into a tube]. If each position's supposed to be away from the next, then what you end up with is that. As you look along the compound and you rotate this ring, the top and the bottom are always away from you.

As we crawl along the molecule and observe it, each time the wedges and the dashes are pointed towards us, the way it's supposed to be. Notice that I've put the carbonyl on the righthand side of the paper. That means my viewpoint has to have the eyebrow on the right; no choice. When I do that, everything that's a wedge is on my right; everything that's a dash, is on my left. All these groups, I just put straight away onto each of the wedges [-OH, -H, -OH, -OH]. But this is not the way that we normally write molecules. We normally do it like this. Where do we need to fix our viewpoint when we're trying to write it this way? It's a trick question, because the first stereocenter, the arms are pointed down. My carbonyl's here, that means my viewpoint needs to be like this. My eyebrow needs to be up, so I'm looking at the carbonyl, and I have to have the arms coming pointed down at me. The first stereocenter, the first -OH group which is on my right, the hydrogen is on my left, looking at this perspective, which means that the -OH group is going to be pointed down into the plane of the board, which is a dash, the hydrogen's going to be pointed down this way towards my left, which is a wedge. The next group, I have to look from the opposite direction, because the arms are pointed in the opposite direction, so now I have to look down, with my eyebrow in front here. If I just reversed and looked like this, I'm looking at the tail end; if I'm looking down this way, the carbonyl has to be in front of me. It's over there, so I have to look this way at it. -OH on the [left], which means it's [still] a dash, hydrogen on the [right], which means it's [still] a wedge, so it's [the same as] we did for the first one – our perspective is backwards. The next group, I have to reverse again and look [from] down below, because the arms are pointed down to me like this. Now, the -OH group is on my right, which means it's coming down this way, so the -OH group is a [dash], just like it on the previous stereocenter, but notice it's on the other side of the Fischer projection, again because I'm looking from below. That means the hydrogen's going to be a [wedge], cause it's on my [left]. These arms are pointed down at me, so for these two stereocenters, I have to be down below the molecule with these arms pointed towards me; that's why I was doing this – one arm's coming this way at me, one arm's coming this way at me. Then, for the top two stereocenters, it's reversed – I need to be here with those groups coming at me like this. I can convert this structure into this one by making the double rotomer. This third stereocenter, I'm looking up, -OH group here, hydrogen here. Last stereocenter, I again look down. -OH group here, so it's [now] a wedge; hydrogen in back, so it's [now] a dash.

If I stayed down here, then for the second stereocenter, the groups are pointed away from me. But the definition of a Fischer projection is that, whatever is left and right, has to be pointed towards me, so I'm not allowed to view it from underneath for that one or that one; I'm not allowed to view it from the top for that one or that one. It's simply not the definition. If I wrote my molecule like this, in a circle, there's never a problem; all I do is start at the top and roll around with the molecule and see where the groups are. But we don't normally write the molecules like this, we write in zigzag, because every time you zig and zag, you're going the opposite way, you have to flip your viewpoint around.

What might help is to show you this: this is [l-allose]. I want to convert this a dash-wedge structure. I'm doing this structure because all the -OH groups are on one side. There are four answers. We could put the carbonyl on the left, or we could put the carbonyl on the right. When we put it on either place, it could be pointed up or it could be pointed down. Which way do you want me to do it: do you want the carbonyl on the left or the right? Right. Do you want it up or down? Up. Let's start with the second stereocenter, because I could fix my viewpoint up here. Since we're used to looking down on things, maybe this would be the more intuitive stereocenter to start with. Looking down with my eyebrow at the carbonyl, cause the carbonyl, by definition's, on the top of the Fischer projection, we see that all of the -OH groups are on my righthand side, which since my righthand side is out towards you, that means everything is going to be a wedge, so I can automatically, for both of those stereocenters, put the -OH group on the wedge.

You've got two choices, the other two stereocenters, I could crawl under the molecule and look up at it; or, I do this realization that, if those other two stereocenters are pointed away from me, I just need to flip what I see, so if they're on the right, then when they're pointed away, they're on the left. Think of this: of that group is pointed down and to my left, and if I did take it, and me, and turn the way I'm supposed to visualize it, then it now ends up over here, which is exactly matching these stereocenters. If you didn't want to flip it around like that, then you need to mentally or physically crawl under the molecule, look up at it. The -OH groups need to be on the right, which from this perspective, the right is here, which is in the plane of the board. I have to keep my top oriented the same way [as] I invert my perspective; my head needs to swivel this way each time.

I'm going to show you one last example. Make a Fischer projection [from this dash-wedge structure][dentists should never say oops]. From top to bottom, give me the lefts or rights for -OH groups: [left, left, right, right] – d-mannose. First stereocenter, I look down with my head towards the carbonyl – the -OH group is out, which is on my left. Next stereocenter: I look up, but still with my head towards the carbonyl; from that perspective, it's a dash, which means it's still on my left. Third stereocenter, again I look this way, down, at the carbonyl; group's on the right. Fourth stereocenter, I look up towards the carbonyl, the group's still on the right.

[lab directions]

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Fischer projection

– The apparent configuration of this stereocenter is R, when viewing (improperly) the structure in the 2D plane of the page. Instead, the molecule must explicitly be viewed so that the least important group is oriented away from the viewer.

If two groups on a tetrahedron are exchanged, the configuration is inverted

\*Swapping the positions of two substituents twice has the same effect on tetrahedral geometry as rotation.

Carbohydrates – (CH<sub>2</sub>O)<sub>x</sub>

By definition, any group written on the “backbone” (vertically) is oriented away from the viewer, while any group on the “arms” (horizontal) is oriented towards the viewer.

Although the groups appear to be in the S configuration, the least important group is oriented towards the viewer, so that apparent configuration must be inverted (it's really R).

Improper rotation of a Fischer projection by 90° will cause inversion of configuration, due to the spatial definition of a Fischer projection.

For carbohydrates, C=O is drawn @ top.

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Structures (remaining structures identical to lab 4A)

05/01/12 lab • 1

