Lecture 18A • 05/25/12

[exam 2 – carbohydrates: hexose/pentose; furanose /ketose; aldose/ketose; alpha/beta; d/l][monosaccharides: aldotrioses, aldotetraoses, aldopentoses, aldohexoses][ketose: fructose][disaccharides: maltose, sucrose, lactose][enolate interconversion][Tollens' test][mutarotation][Kiliani-Fischer chain extension][exhaustive methylation][Fischer stereochemistry proof][osazone]

Exhaustive methylation

Lactose – glucose and galactose. Galactose is a substituent of glucose. Beta-d-galactopyranosyl-alpha/beta-d-glucopyranose. [galactose structure description; righthand position alpha or beta because it's openable] Let's say that we had methyl iodide and silver oxide. The silver oxide is a way, indirectly, of creating hydroxide, indirectly creating a base to deprotonate all these -OH groups. In base, what can you say about the stability of either an acetal or a ketal? They're not affected by base; that's why we use them as protecting groups when we used the THP protecting group. All that's going to happen is that all these -OH groups that are open are going to be converted into methyl groups – meaning that this oxygen will not me methylated, since the ring is not sensitive to base. That's true all three of these oxygens. On the righthand side, even though that's a hemiacetal, it is an available -OH group as written; there's no reason we couldn't deprotonated it, and so it's also going to get methylated, so we end up with this. What would happen is we totally hydrolyzed this? H+ and H2O. What is going to happen to the rings. They'll split, because this is acid-catalyzed ring opening of hemiacetals, hemiketals, acetals, ketals – they'll all go back to their carbonyl forms. In other words, we're going to end up with the linear forms of the sugars. We're going to lose the beta configuration for the galactose, because that beta configuration only exists in its beta form, so we go linear there's nothing left of it. That simply goes back to the carbonyl. Look at the methylated version, because yes, that carbonyl position is going to open up, splitting the glycoside, the connect to the next sugar. But, all of the -OCH3 groups, those are ethers. In order to cleave an ether successfully, you need a strong acid, something like HI, to protonate the oxygen and then have the iodide kick the ether open. [Since such strong conditions are not being used,] we'll presume that ethers persist. So we'll have what?

Notice that the oxygen that is in the ring is the oxygen here that ends up with just a plain -OH group, because when it was part of the ring, it didn't get methylated, because the ring is not subject to base conditions. But under acid conditions, once we open the ring up, we can see this exposed to show which oxygen had been connected as part of the ring, so by this method, we know the ring size of galactose in lactose. Since the indicated oxygen was part of the ring, during methylation, it did not get methylated, since the ring was resistant to base conditions. Once the sugar was hydrolyzed, the fact that the oxygen was not methylated is revealed. The fact that it's revealed can be used to show what the ring size had been in galactose. There's a way to somewhat carefully cleave the rings so you can first tell which oxygen from glycose was connected to galactose, then you could fully hydrolyze it to figure out what the ring size in glucose was.

Tollens' test

[sucrose structure – alpha-d-glucopyranosyl-beta-d-fructofuranoside, coul be beta-d-fructofuranosyl-alpha-d-glucopyranoside]

When I talk that diaminesilver complex, I get a mirror when I do it with lactose, but I don't have a mirror when I do it with sucrose. The result of this, we say lactose is a reducing sugar, but we say sucrose is not a reducing sugar. What's going on here? Why does either of these sugars reduce silver, because that's what the phrase 'reducing sugar' means; the sugar itself gets oxidized. What these behaviors mean is that lactose gets oxidized, but sucrose does not. Why? The end of the molecule is a hemiacetal. What kind of functional group do we have on sucrose instead? We have a full ketal – we have a full ketal here on one side; we also technically have a acetal on the other side here. It's not a hemiacetal or a hemiketal. The conditions under which this Tollens' reagent is used, the ring is able to open and close. If you're able to open and close, only the hemiacetal portion of it will then temporarily make that aldehyde. [Even though the amine is a substituent here, this is done under slightly acidic conditions.] With this reagent, the ring can open, so under the conditions of the Tollens' test, hemiacetals and hemiketals are able to be in equilibrium with their aldehyde or ketone forms, which can then be oxidized. Ketals and acetals, however, cannot ring open, so ketals and acetals are not in equilibrium with their carbonyl forms, and therefore do not get oxidized. Since lactose has a hemiacetal, it reacts with Tollens' reagent, but since sucrose only has full ketals or acetals, it does not react.

Since this is a hemiacetal, the ring could open; when it closes again, maybe it makes the beta form instead; that's how you get beta-lactose. Over here we have an acetal, which does not open, not unless you hydrolyze it, not unless you force it to react and hydrolyze. In terms of just being in equilibrium with its linear form, it's not. It's only the hemiacetal that's gonna open and close. [optical rotation – quoted in names; positive clockwise, negative counterclockwise][glucose could be produced by chain extension from a smaller sugar; or, Wohl degradation could have been done to get arabinose then erythrose then glyceraldehyde]

[four sugars have rotational symmetry, only one connected with glucose proof] Rotational symmetry does not show up in optical rotation; rotational symmetry is something on paper that he used as logic to eliminate possible structures, cause he knew out of those 16 sugars, glucose made he same sugar as some other sugar; mannose was the only one that could make what it makes. That's, by a geometric argument, how he established which is mannose, cause it's the only one that does have the rotationally symmetric stereocenters, or which one is glucose that did not have the rotational symmetric stereocenters. There's no physical piece of evidence that he used to determine, other than the fact that mannose was the only sugar that made what it ddi, but glucose made the same thing some other sugar did.

[old digitization box bit the dust][singing in the rain]

Amino acids

[This] amino acid has two pKa values. If we were in acidic conditions, then the amino group is going to be protonated; unless we are in wildly conditions, though, it's not likely that the carboxylic acid itself is going to be protonated. This is the cationic form of an amino acid. If it were to lose a proton and end up under more neutral conditions, then it would be possible to write the amino acid as I did originally – but, think about that. Amino – acid. An amine is a base; an acid is an acid. The two could self-neutralize; this is the other way an amino acid structure is often written. This is in its zwitterionic [twin, more like hermaphrodite]. If we were to continue making the conditions more and more basic, we could finally deprotonate – deprotonate the amino terminus – and ending up with out anionic form; it's under basic conditions.

There is a classic graph that is draw that shows the relative proportion of each one of these forms of the amino acid in solution. This is going to be a graph of pH; I tend to start from the acidic end and go basic, it makes sense to have lower numbers on the left since that the way that we normally do things. Percent in this case will be mole fraction. What is mole fraction? Moles of that one particular substance versus the total moles in solution. Since we have a 1:1:1 interconversion, we can assume that, if we, for example, started out with the pure cationic form, 100% it which means a mole fraction of 1, that if we were to make the solution sufficiently basic, all of it's going to be converted, so that we eventually end up with a mole fraction of 1 for the base form. [acid – red; neutral – green; basic – blue] We expect to have a mole fraction of 1, if we're in sufficiently acidic conditions, for the acid form, and we'd expect a mole fraction of one of the base form under sufficiently basic conditions. What's going to happen in between? There'll be some point where we have the maximum amount of the neutral form. That ends up also having, at that point, a mole fraction of one. For amino acids, the exact pKa values and the pHs that would generate these forms of amino acids shift. I'm just doing this as a general graph to get an idea of what it looks like, then we're going to talk about how would we establish where are those pH and pKa values, and how are they tied to each other.

Back to completing the graph. We start with only the acidic form, but as we get more and more and more and more basic, that is going to deprotonate. Notice how this kinda looks like a titration curve. It should, cause that's effectively what's going on. The only difference between this and a standard titration curve is that our scale is pH, which is itself a log scale, on our x axis, where normally we have pH on the y axis. If this is getting titrated, then its conjugate, which is the neutral form, is going to increase in value, until it reaches this maximum point where we have the optimum pH for it to be in its neutral form. If we then continue to increase in pH, we're going to decrease again, because we're going to deprotonate a second time, until we end up with none of the neutral form left once we're in sufficiently basic conditions. If that's occurring, then that means the proportion of the base form of the amino acid is increasing in solution. There is the look of the graph – forms of amino acids based on pH.

Come back to constructing this graph, I've just marked where the curves intersect each other. What is special about those intersection points? The point there seems to be drawn roughly at half mole fraction; that's not coincidence. If this is half mole fraction, then if this were a titration, it's the equivalence of the half equivalence point. Why is the half equivalence point in a titration a significant point? What does an acid dissociation constant mean? That we have a form of equation that looks like this. If we were to put exactly half a mole of the acid and the base, each one, into one liter of solution, so we had equal concentration of the two, what will happen? If I had, let's say, acetic acid that, not reaction-wise, just in terms of dissociation, make acetate and H plus. If a solution is prepared with exactly 0.500 moles of acetic and and 0.500 moles as well of sodium acetate, what will happen? The concentrations shift very slightly. Because if you throw a half mole of acetic acid and acetate together, they're not in equilibrium, because equilibrium says there's a balance between those two things and H+. You could argue back and say there's going to be H+ in solution, but not until you add those reagents. There is 10^-7 at [4 °C] that the Kw is exactly 1.00000 x 10^-14. Other than that residual concentration of H+, there's nothing there until you add the reagents, which at the moment you add the reagents, you're not at equilibrium.

First thing that happens when you add the two things together is they form an equilibrium. If it's a weak acid, but not too weak and not too strong, then that shift that occurs is minor; you can ignore it. Then, we go back to the acid dissociation equation and something special happens. In a solution prepared in this manner, in 1 L total volume, a small shift in concentrations will occur as the system attempts to reach equilibrium. However, for weak acids in dilute concentration, the shift is generally minor and is therefore often ignored. [manipulating Ka; Henderson-Hasslebach equation]

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Since the indicated oxygen was part of the ring during methylation, it di not get methylated, since the ring was resistant to base conditions. Once the sugar is hydrolyzed, the fact that the oxygen was not methylated can be used to establish that galactose was in its pyranose form when part of lactose.

Under the conditions ot he Tollens' test, hemiacetals & hemiketals are able to be in equilibrium with their aldehyde or ketone forms, which can then be oxidized. Ketals and acetals, however, are not in equilibrium with their carbonyl forms ad therefore do not get oxidized. Since lactose has a hemiacetal, it does react with Tollens' reagent, but since sucrose only has a full acetal & ketal, it does not react.

If a sol'n is prepared with exactly 0.500 mol of acetic acid & 0.500 [mol] of sodium acetate, (total volume 1.000 L H20), a small shift in concentrations will occur as the system attempt to reach equilibrium. However, for weak acids in dilute concentration, this shift is generally minor and is therefore often ignored.

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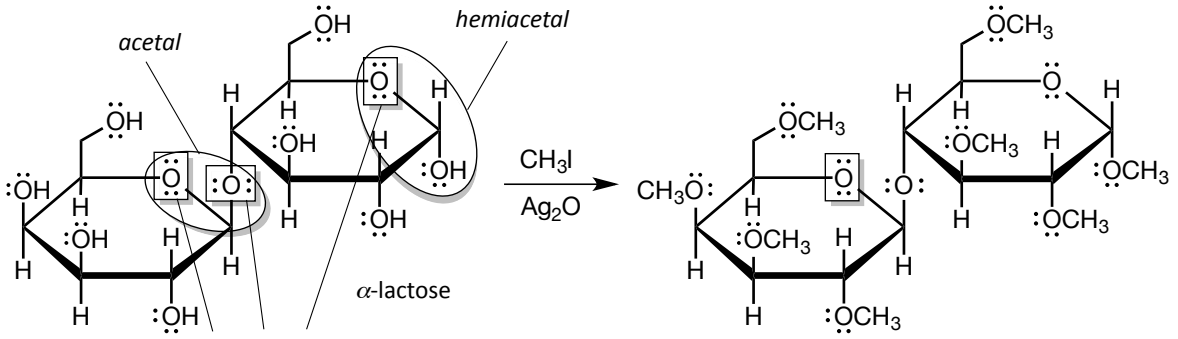
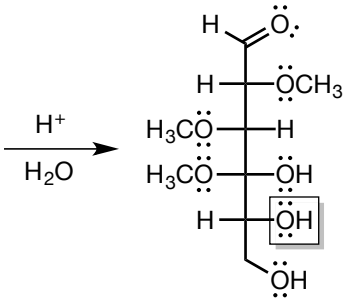
05/25A/12 lab • 1



will <u>not</u> be methylated since the ring is not sensitive to base



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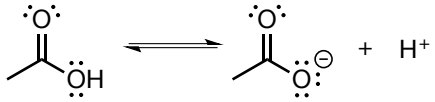

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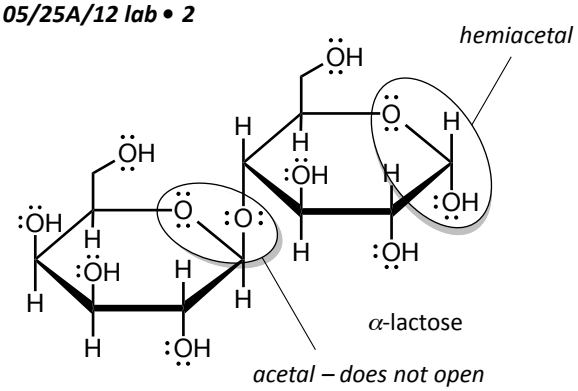
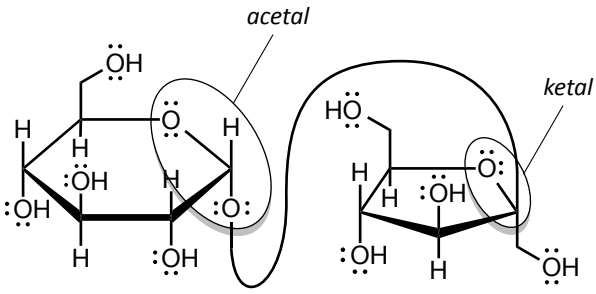
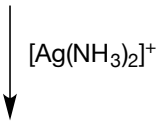


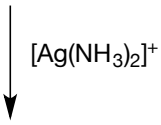
acetal – does not open



sucrose



mirror
lactose is a reducing sugar



no mirror
sucrose is not a reducing sugar

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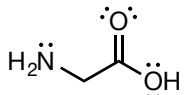

amino acid

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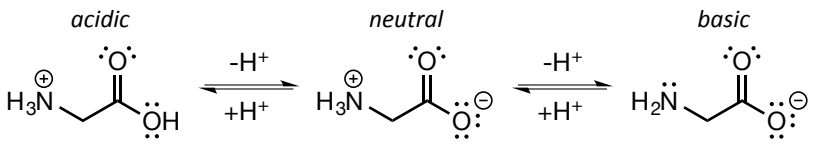

cationic *zwitterionic ("twin ion")* *anionic*