Lab 14A • 06/18/12

[lab exam – DCC, BOC anhydride, Merrifield resin synthesis, phthalimidomalonic ester synthesis, Strecker synthesis]

[Exam 2]

Fischer projection of the aldaric acid of d-mannose, d-mannaric acid. Aldaric acids are ones in which both ends of the molecule have been oxidized to carboxylic acids. Mannose is [left, left, right, right], and it is d-mannose, so regular mannose. This is the structure of mannaric acid, and the reagent used to synthesize it: nitric acid.

Aldonic acid of d-xylose, d-xylonic acid. Aldonic acids are where only the aldehyde portion gets oxidized; top oxidized, bottom not. Since this is #3, and it's a d, it's going to be [right, left, right]. The reagent to make it: aqueous bromine.

Fischer projection of the alditol of l-threose, l-theritol. That's only going to have two streocenters. Erythrose is when they're on the same side, threose is oppose. This is an l sugar, so the bottom will be on the left; top will therefore be on the right. Alditol is where both the top and the bottom end with just an alcohol, so you've reduced, so the reagent there is sodium borohydride.

alpha-l-ribofuranose. d-ribose would be [right, right, right[; l-ribose, therefore, is [left, left, left]. Because I know we're going to make a cyclic compound, I'm going to go ahead and rotate the oxygen for the bottom stereocenter to be in the bottom position. Since it's an l-sugar, then we have the bottom stereocenter's CH2OH group on the right, which is what we always have for l sugars. The top two stereocenters remain unchanged. The reason I went ahead an wrote it in this form is because we need the alpha version of this, so when make the ring and make the new stereocenter, we want it trans from the CH2OH group, which it currently is in. We simply connect the ring around. That gives us a five-membered ring, which is what a furanose is – a five-membered ring. Showing that these are trans, that's alpha. Counting up the numbers of atoms demonstrates that it's a furanose.

Haworth projection. SInce it's d, we know that that back CH2OH group is going to be up, and pyranose – a six-membered ring. It's supposed to be beta-d-idopyranose. Beta means the -OH group should be on the same side as the CH2OH group. [Idose, number 6, binary 5: left, right, left].

Dash-wedge form of l-talose. Let's do it in Fischer projection form first. [d-talose: left, left, left, right; l-talose: right, right, right, left] To into dash-wedge form, I've drawn the main backbone of the molecule, following the convention that I normally use of putting the carbonyl on the right and pointed up. That means that the first stereocenter, you have to be a little careful of as you visualize, because you're going to be looking up at the molecule looking up towards the carbonyl, you have be looking up towards the molecule from below it, because the side groups have to be pointed at you, [according] to interpretation of the Fischer projection. If I'm looking up in this way, the wedge is what's going to correspond to what's on my lefthand side; since the -OH group is on the right on that first stereocenter, that means it's going to be a dash. Whatever is a dash on the first stereocenter would be a wedge on the second one, because now you're looking down from up above, so if I'm looking down from above and my carbonyl's in front of me, then on the righthand side, where that -OH group is, it's out towards you, which is why it's a wedge. The next one, for similar reasons as the first one, is going to be a dash, and the fourth one, because it flips sides, is going to also end up being a dash. This is one of several possible answers, because the carbonyl could be pointed down here instead of up, which, if you followed the standard dash-wedge pattern means all the wedges and dashes are inverted. We could have put the carbonyl on the left pointed up, which again would mean that the dashes and wedges are backwards, or you could put it on the left but put it down, which means you turn this 180° around on paper, which means everything stays the way it is.

You're given alpha-d-galactopyranose. [describing making structure] You're told that the specific rotation, which is how much it rotates plane-polarized light [given a certain concentration over a certain pathlength], is +150.7°. You asked can you predict what beta-d-galactopyranose's optical rotation is going to be? No, because alpha and beta forms of a sugar are epimers, and there's no relationship between the physical properties of epimers, because epimers are diastereomers, which don't have to have any relationship between physical properties because they're distinct structures. If you had enantiomers – enantiomers are mirror images. If you had one mirror image, then the opposite would be the same number, just the negative value. But alpha and beta are not enantiomers, because you're only changing the anomer's center; those are epimers, which are a subset of diastereomers, which aren't related.

Anomers are epimers, are diastereomers, are not related. Alpha and beta, those are anomers, are epimers, are diastereomers; they're not related, so you can't predict their physical properties. If I was talking about alpha-l-galactopyranose, that would be the enantiomer, that would have a -150.7[°} specific rotation. What about the other part of the question, which is, if you have either the alpha- or beta-d-galactopyranoses in solution, then over time they'll both end up with the same optical activity, the same specific rotation, which won't match either of the individual pure compounds You were asked to use an appropriate mechanism to explain why.

Appropriate does not mean complete; appropriate means: how much of the mechanism do you need to prove your point? Here's the appropriate amount. First step is for the ring to get protonate. Second step is for the ring to open. Notice that this is a different mechanism than the formation of a glycoside. It's a slightly different mechanism because we're protonating a different oxygen. This is the reverse of how the cyclic sugar formed in the first place; it's just that reverse mechanism.

Once you go through that much of the mechanism, then you end up with with an intermediate that's planar. We've protonated the ring oxygen, allowing it to open; it can come right back around and close again, but when it closes again, it's got a planar intermediate. Since it's planar, that means it can be attacked from both sides, which means you end up with a mixture of the alpha and beta formed. The opening of the ring, the closing the ring – both reversible, cationic processes, so that means that there's going to be an equilibrium that will be established, not matter which of those forms – alpha [or] beta – you start with, they're going to interconvert until they reach a common average value, that has one optical rotation associated with it, which is why both sugars end up with the same optical rotation. This is the process of mutarotation.

Problem 3. You're told that glucose, mannose, and fructose are related. In aqueous sodium hydroxide, they can all be converted into each other. Using an appropriate mechanism, explain this. I'll start with glucose. This process is tautomerization, where we form an enolate from a structure that can have an enediol. The fact that across a double bond you have two positions that are -OH groups, one or the other could be a carbonyl; that's the whole point of this conversion.

Starting with hydroxide as our base, we can deprotonate the alpha position relative to the carbonyl, which makes our enolate. Notice that the top stereocenter is affected: it's not planar. One possibility is for the enolate to collapse and attack water. Since the enolate became planar, once it reattacks water and makes a stereocenter again, you get a 50/50 chance of which way that stereocenter's going to be oriented. That's why you can end up with a mixture of both glucose and mannose. But that's just one possibility. If I take that same enolate intermediate and allow it to get protonated, but not through the alpha position, but from that negative charge directly attacking water [through oxygen], then I end up with an enol. Of course, to go backwards, the oxygen that just got protonated would get deprotonated. But if I didn't want to go backward, then the other oxygen on that ene position could get deprotonated instead, which means once it does re-turn int a carbonyl, it is now a ketone because it's moved one carbon in, which means we've now made fructose. We have d-glucose [which makes] d-mannose and d-fructose.

Lactose [description of drawing structure: beta-d-galactopyranosyl-beta-d-galactose] The beta designation in lactose is connected to the righthand side's anomeric position. That's the anomeric position that can open and close. Here we have an acetal connection; over here, we have a hemiacetal. Lactose is a disaccharide. You're asked to define the term disaccharide, which is: a larger sugar created by linking two smaller sugars through a glycoside. What is a glycoside? When you take the anomeric position's -OH group and connect it to something. Lactose is a glycoside of galactose stuck on to glucose. Unlike sucrose, lactose does form a silver mirror when it's reacted with the Tollens' reagent – why? Because lactose has a hemiacetal. In aqueous solution, hemiacetals, hemiketals easily open and close. When they open up, you make a carbonyl. Carbonyls that are part of aldehydes or carbonyls that are part of alpha-hydroxyketones, both get oxidized by the Tollens' reagent; that's because of the tautomerization that can happen with an alpha-hydroxyketone. If you can't make the carbonyl, then you don't get any form of reaction. In this sugar, the acetal – without actively protonating it, without actively hydrolyzing it – will not simple open and close. That carbonyl was always hidden, you could say, on the acetal portion. On the hemiacetal, it is hydrolyzeable, it does open up, which allows the Tollens' reagent to react with it, which is why the silver mirror does form. In sucrose, it's an acetal and a ketal, not a hemiacetal or a hemiketal on either side; both anomeric positions are joined to each other, so it does not exist in equilibrium with its open form in solution, so it never can get oxidized. That's why sucrose is not a reducing sugar.

Explain how the size of the ring or rings in lactose can be determined by exhaustive methylation. The lefthand ring, if we exhaustively methylated by using dimethyl sulfate and silver oxide, we do that first. Second, if we hydrolyze. When we do the methylation, we're going to make methyl ethers. Ethers do not easily hydrolyze. When we hydrolyze, we're going to destroy the disaccharide, we're going to destroy the glycoside. What are we going to end up with? As far as the galactose portion of this sugar, you're going to end up with most of the -OH groups instead being methyl esters – except for one -OH group. These methylations occur under basic conditions. Acetals and ketals are stable under basic conditions and don't open. If they don't open, their oxygens never are made available to be methylated, so any oxygen that fails to be methylated was part of either the glycose itself or, in this case, it was part of the ring. This is how we could tell the ring size, because the oxygen that would make a six-membered ring is the one not methylated. We know, therefore, that the galactose part of the sugar is galactopyranose, a six-membered ring.

Last problem was about the Kiliani-Fischer synthesis. You were asked to show the Kiliani-Fischer synthesis to make glucose, and you were supposed to write the sugar and name it that you would start with. That would be arabinose that you start with. This is exactly the KFC that we talked about in the Fischer [stereochemistry] proof that establishes the link between glucose, mannose, and arabinose. First, we use sodium cyanide [similar to early step in Strecker synthesis]. After reacting with sodium cyanide, we're going to end up with a nitrile that we partially hydrogenate. We use something like Lindlar's catalyst with hydrogenation to prevent the triple bond going down to a single bond. You want to stop at the double bond, because when we get to the double bond, that means we have an imine.

That imine, if we hydrolyze, we end up with two sugars, cause at the point where we make the nitrile, that generates a new stereocenter. Since in that process where' attacking a planar carbonyl, that's why we end up with two potential configurations.

The second part of that question is: explain why this provides evidence that there is a relationship between glucose, mannose, and arabinose. Because he could start with arabinose, he could make the products from this by doing the chain extension, he demonstrated that they weren't glucose and mannose. They knew that this chain extension only added one stereocenter, so he know that glucose and mannose had one more stereocenter than arabinose, and he knew that the bottom three stereocenters of all three compounds were the same. Last part of that question was about osazones. The reagent is phenylhydrazine, which make phenylhydrazones. If we only had one carbonyl, it'd be easy to remember the structure, cause a hydrozone versus a phenylhydrazone, just add a benzene. But, in this reaction, we use three equivalents because there is a redox reaction that occurs that causes two positions to turn into hydrazones. An osazone of glucose has the following structure. Both the first and second carbons turn into hydrazone derivatives. Why was this pivotal to carbohydrate research in general? Because it allowed us to make crystalline, isolatable derivatives. If melting point was such an important thing at that time, and previously you couldn't make crystalline products, how could you characterize them? This allows for the formation of crystalline products. How's this related to the structural determination of d-glucose? It's yet one more piece of evidence that glucose and mannose are related to each other, because they both make the same osazone, so they're both related just by the difference in this one stereocenter.

Exam 3

Why does glycine not have a d or l designation? Because glycine doesn't have any stereocenters; if it doesn't have a stereocenter, it can't be d or l, so you don't use the designations because it's not chiral. How do you determine what is the d or l configuration? If you said it's when the amino group is on the left, my answer to that is: left of what? If you said: of this Fischer projection, then I have this counter to make: I drew the amino group on the left of the Fischer projection. Is this correct? No, because it's when you have the Fischer projection written in its default form, where the carboxylic acid is on the top and the R group on the bottom, when you write it that way, then if the amino group is on the left, it's l, and if it's on the right, it's d. If all you said is it's on the left or the right, that's not complete enough.

Lysine. The four forms – not the six or eight or two – of lysine. [structures] What if I put the NH3 on the other position, on the alpha position, and left the side chain NH2, would that also be correct? No, why not? Different pKas. The side chain has a pKa of 10.79. What does that mean? That means that the side chain, once it's protonated, is less strong acid than the alpha position. That means as you're pulling the protons off, the proton comes off from the carboxylic acid first, pKa of 2; it comes off the alpha position second, pKa of 9; it comes off here last. If you're writing the zwitterionic form, if you put the hydrogen where I did, on the side chain, that's correct, because the side chain's more basic. If you put it here on the alpha position instead, it is zwitterionic, but it's not the one more likely to exist in solution. Take one more proton off, we get the anionic form. Put one more proton back on, allow both amino groups to be protonated, we get the cationic form, which mean put one more proton on back onto the carboxylic acid, and that gets us the double cationic form. [reviewing test questions] At [pH=]pKa1, you have half of it in its cationic and double cationic forms; at [pH=]pK2, half of it's cationic and [half] neutral; at [pH=]pK3 half is neutral and [half] anionic. pKa3 corresponds to the side chain.

Explain how pKas can be experimentally determined [in three sentences]. [sentence 1] The amino acid is titrated with a strong base. [sentence 2] A titration curve is drawn so that the equivalence point can be identified. [sentence 3] Using the equivalence point, the half-equivalence point is found, at which point th pH = pKa. In solution, what would be the net charge, regardless of which form of the amino acid you have? Neutral; the solution will never be anything except neutral, because if you're in the double cationic form, that's cause you've got two chlorides from the HCl you would have used to make it; if you have the anionic form, that's because you would have the sodium floating around from the sodium hydroxide it took to made it. Unless you could spectroscopically tell the difference between the double cationic, cationic, neutral, and anionic forms, no, you can't use those crossovers to determine pKa; the crossover points you establish by looking up the pKa values. To experimentally determine it, it's titration. By titrating to find the equivalence point, you can then find the half-equivalence point, which at that point, its pH is the pKa of each different functionality.

Construct a graph [of the forms of an amino acid versus pH]. There should be four different regions to this that correspond to the double cation, the cation, the neutral, and the anion forms. Notice the lefthand righthand side of the graph do not go back down to zero – how can you have a solution with o% amino acid if you have a solution of that amino acid? You can't. The minimum total value at any point on the graph is 100; the maximum total value anywhere on the graph is 100, because it's how much of the solution exists in these different forms. If pH really does start from 0 and increase, [the order that the forms would appear in is] double cationic, cationic, neutral, and anionic. The crossover points, those do correspond to the pKa values. The pKa values show where you cross from 50% one form to 50% the other form. The pI was right here.

Question 3. Explain what the pI of an amino acid stands for. It's the pH at which you have the maximum amount of the neutral form [must state pH]. How [can] you calculate it? If you look back at the pKa values, realize that if you looked at the percentage curve on either side of the pI point are pKa2 and pKa3 – the amino group pKa values.

So, the pI will be the average of those two, which [is] 9.87. Explain how and why the two amino acids can be separated by the technique of electrophoresis. The pI of alanine is 6.02; the pI of lysine [is] 9.87 [average of pKa2 and pKa3]. The pH given to you in this problem is lower than either of those, around 4, which meant that both amino acids existed in their cationic form. Are any of the amino acids in 100% either its cationic or anionic form? No. Look at the pH versus the pIs – the lysine is much further away from its pI than the environmental pH; the alanine is much closer. If I started out with a very basic solution, both of these amino acids would just be in their anionic form, because they only have one carboxylic acid on each one. If I start to make it a little more acidic, a little more acidic, then what these numbers means is when I reach pH 9.87, then that's when the lysine has moved to being in its neutral form, but alanine will still be anionic, because the pH is greater than the pI. When the pH is greater than pI, you're anionic; when the Ph is below the pI, you're cationic. Which means, if we get to pH 7, which at a certain temperature means neutral, then alanine will still be anionic, while lysine will already be cationic. You keep moving further away until you get down to pH 4.2; at that point both are cationic, but lysine is more cationic.

At pH 4.2 will be in a greater cationic form, proportionally, than alanine. When you put a mixture of the compounds on a paper which then has charges applied to it, the amino acids will migrate towards the appropriate charge. Since one is more cationic than the other, one will move more to the negative terminal than the other, which allows the amino acids to be separated.

Question 4. Ion-exchange chromatography. Describe the conditions used to prepare for chromatography and explain why these lead to the inability to determine the order. You first break the disulfide linkages [2-thioacetic acid]. Then, you cook up the polypeptide in an acid solution. That causes all the amino acids to become separated, which means you'll loose the order. You can't sequence them because it all becomes separate. Draw a simplified structure for what an ion-exchange resin would look like. Very simplified would look like this: a polymer chain, with every once in a while having a benzene, and then every once in a while instead of just plain benzene, you have a sulfonate, which is technically neutral because it's the conjugate of a strong acid, but it's charged. Explain how this resin is able to separate out amino acids. Depending on pH, different proportions of amino acid will be cationic versus anionic. Cationic amino acids will be attracted, due to charge, more preferentially than anionic amino acids. Therefore, as the material passes through, some amino acids are separated on the basis of charge. [Does size matter?] All of these amino acids will want to interact somewhat with this resin, but it's the ones that have more plus charge that get hung up on this sulfonate group; that is the ion exchange going on, that's what'll slow some of them down.

Explain the physical process of how amino acids are separated and identified. 1) A column is created and loaded with the separatory resin. 2) The amino acids are placed on the column and then eluted with a solvent. 3) Depending on the amount of interaction of the amino acid with the column, the amino acids will come off at different times. 4) The elution time can be used to identify the amino acid. 5) The presence of the amino acid can be confirmed by ninhydrin.

Aside from visualization, why is ninhydrin used, but not used to identify? Because we can use the absorbance to determine the concentration of the amino acid. One of the goals of this chromatography technique is to determine how many of each amino acid is around. You can't use it to identify because the structure of the amino acid is destroyed by ninhydrin. The complex formed by the ninhydrin is this; the only thing left of the amino acid is the nitrogen. All the amino acids end up the same, [so] this can't be used to identify the amino acids.

The Edman degradation, which uses phenylisothiocyanate, unlike the ninhydrin chromatography method, can be used to sequence; why? Because after many cycles of protonate-open-attack-deprotonate, we end up with a derivative that looks like this: a phenylthiohydantoin (PTH), the final, isolatable derivative that you end up with. The point here is that each R group gives a different PTH derivative. Since each of these derivatives is formed one at a time by taking it only off the amino portion of the polypeptide, then doing it one at a time, we sequence the polypeptide. This does not destroy the order all at once, but only one at a time, which means it'll work for us.

Lipids are naturally-occurring fat-soluble molecules. Hydrophilic/phobic – water-loving or -fearing; lipophobic/philic – fact-fearing or -loving [other than our natural fear of fat] Lipid is a more broad category; fat is a certain class of molecule. Lipids are more generally these non-polar materials that are found in fatty tissue. Hydrophilic is the same thing as lipophobic – if it likes being in water, it doesn't like being in the organic phase, and vice versa: if it's hydrophobic, which means it fears water, that means it should be fat-soluble, so it's going to be lipophilic.

The first class of compounds we're going to look at are fatty acids, of which there's many. There are the saturated fatty acids: lauric (12), myristic (14), palmitic (16), stearic (18), and arachidic (20). These are the types of carboxylic acids that are incorporated into fat molecules. [back of shampoo bottles] Let me show you just a subset of unsaturated fatty acids: oleic (18/9), linoleic acid (18/9,12), linolenic (18/9,12,15). You'll start out with one structural motif, one thing that shows up in one common plant source, and in lots of related plants, you have different proportions of very related compounds. If we numbered from the end of the chain, we can find that this has an unsaturation six from the end. If alpha is the term that we use to refer to the beginning, the position near the carboxylic acid group, omega is the symbol we use to say the end of a molecule, so this is also known as an omega-6 acid. Because if we number from the end of the chain we have an unsaturation at the 3 point, this is called an omega-3 acid. These bottom two compounds are what are known as essential fatty acids. Similar to essential amino acids, they're compounds that we can't biosynthesize; our only sources of them are food sources.

Why, biologically, would unsaturated fats possibly be more advantageous than saturated fats? Because they have alkenes, which could be used to break the molecules apart. Carbon-carbon single bonds – think of how many reactions that we've learned that operate on carbon-carbon single bonds: hardly any. But we've learned plenty of reactions that can operate on carbon-carbon double bonds [ozonolysis]. [Why are trans fats bad]? Two reasons: one, trans [is] more energetically favorable than cis. Cis, more energetic – easier, therefore, for something to react with it. Also, think about these big, huge molecules floating through your arteries: the cis, having a kink in it, it's going to have a different kind of crystallization possible than if you had the trans. Cis unsaturated fats are generally the healthier fats, than the trans unsaturated, then the saturated, you can't react as easily, so they're generally the less healthy ones – although for whatever reason they tend to be the tastier ones. These unsaturated fats, because oxygen can react with them, over time, these types of compounds can decompose; if we're talking about food, we talk about fats going rancid. One by-product that often appears in the decomposition of larger carboxylic acids is butyric acid. What do you think the word butyric is related to? Butter. This is the smell of butter gone bad. Butyric acid smells nasty, but it's a very simple compound.

One step up from this would be naturally-occurring waxes, such as beeswax. Beeswax does not have just one compound in it, but the major component of beeswax is an ester that [made from] a 26-carbon carboxylic acid and a 30-carbon alcohol. Huge, ginormous molecule. If you had a small carboxylic acid like butyric acid or acetic acid, those are liquids. Waxes are solids, but this is not a polar compound. Buried in the middle of the molecule, we have this slightly, slightly polar ester group. But, look at the huge carbon chain that we have on either side. This makes this molecule, for all purposes, totally non-polar – and yet, it's a solid at room temperature. Why? Remember what causes things to be solids or liquids in the first place – there's some kind of attraction between molecules. Whether something's a solid at room temperature depends on whether the forces between molecules are more powerful, or the thermal kinetic energy is more powerful. In other words, are molecules better able to stick together because they're attracted, or they're more likely to separate because they're shaking so much because of the temperature that they have? Generally, the better forces to keep molecules together are created by permanent dipoles or by charges – dipole-dipole interacts. This molecule doesn't really have any permanent dipoles that are strong. But, because the molecule's so huge, it's very susceptible to having dispersion forces – temporary dipoles that are formed by temporary deformations of the molecule. With the huge surface area, it gives plenty of room for one chain to be attracted to another in order to be held together as a solid. Waxes are solids not due to their charge or polarity, but due to extensive dispersion forces. [other waxes, carnauba]

Another form of ester is everybody's favorite – the fat molecule. What do fats look like, the simple fats? They are known as triglycerides or triacylglycerols – glyceride focuses on the carboxylic acid functionality, glycerol focuses on the fact that the core, all of these simple fats are glycerols. Glycerol, as a compound, is technically achiral, but if we functionalize this, there is a biological preference for one enantiomer versus another. We take three carboxylic acids and esterify them. A carbonyl with an alkyl group is referred to as an acyl group, so we put three acyl groups onto to glycerol, which is how we come up with this triacylglycerol. [-ide use to show glycerol became the alcohol that was esterified]

What's the difference between a fat and an oil? Fats are things that are solid at room temperature; oils are things that are liquid at room temperature. [proportion of fatty acids found in common fats and oils]

Phospholipids [role of phosphate in biological pathways]

If you take glycerol and you esterify it and at the same time throw in some carboxylic acids – so you have a phosphoester plus you have two regular esters on the same molecules – then this is a phoshpolipid. If you're in high pH, you could double-deprotonate; if you're in medium pH, it's singly deprotonated; or if you're in acidic conditions, this would be fully protonated. This form where I only have one negative charged is referred to as monobasic phosphate; if I took both of the [hydrogens] off, it would be the dibasic phosphate. This is the general structure of a phospholipid; the general name is phosphatidic acid, because it's like phosphoric acid, it's a derivative. If we now added a substitutent – I made an ester on one side of phosphorus; I could make an other ester on the other side of phosphorus. If I make an ester with the molecule choline – choline has this structure – [acetylcholine – metabolism] esterify one of these phosphatidic acids and you get phosphatidyl choline, which is a class of compounds, a type of compound of which is a leicithin, which in humans is a major component of phospholipid bilayers. This specific kind is known as a leicithin. [cephalin – more prominent in phospholipid bilayers of bacteria, lacks methyl groups on choline, just an amino group][structure of phospholipid bilayer] We can simplify the structures of amphiphiles such as this by just drawing the head group and the tail group. In biological systems, we're water-based, so water's going to be the predominant medium. You get these extended sheets where the surface is all these polar headgroups, and because water's on the outside here, then all the tails get pushed to the inside. These phospholipid bilayers often form the basis of cell membranes. [some cells more special – more specialized linings] Nerve cells have another kind of compound that their phospholipids are derived from. [sphingosine – unsaturated tail fused to glycerol-like platform, combined with carboxylic acid, phosphate, choline – sphingomyelin][myelin – sheath of nerve cells]

Terpenes

Terpenes are a class of compounds that have as their basis a structural unit that we refer to as isoprene, which is the common name for this five-carbon diene. [The isoprene, if you were supremely imaginative, you could pretend that this is the molecule standing on its legs, and it's got its head up in the air like that. We refer to the branch side of this as the tail of the isoprene unit, and we refer to this two-carbon portion sticking out as the head group. – backwards?] Biologically, there is a synthetic route to create this five-carbon template, and it uses as its leaving group this thing called pyrophosphate or triphosphate [found in ATP]; it is a phosphorus mini-polymer [oligomer]. We could take three of these, for example, and combine them into one compound [alpha-farnesene]. This is created out of three isoprene units, but when you take two isoprenes, that is called a monoterpene. What do we get when we put three isoprenes together? It's a "one-and-a-half" terpene, or sesquiterpene. [sesquicentennial] There are diterpenes, triterpenes, larger molecules. For example, cholesterol can be synthesized from a triterpene, which means put six of these [isoprenes] together.

What I've shown here that the head of one unit has joined with the tail of the next unit, the most frequent kind of joining that occurs. You can have head-to-head or tail-to-tail, especially once you get into having cyclic molecules. You'll notice that there are some key structural features that are found all across a related set of molecules. Let me point some of these structures out. [comparison of zingiberene (ginger, 3 isoprenes); geraniol (germanium, 2 isoprenes); menthol (peppermint, 2 isoprenes)] There's thousands of these compounds all created from the same type of platform. [lycopene, carotene, tetraterpenes – retinol]

If we take two farnesenyl pyrophosphates (a sesquiterpene) and effectively make a dimer, and you end up with squalene, which is a triterpene [used to make important molecules, steroids]. If you take squalene and rewrite it a little bit, and if we epoxidize to make squalene oxide [enzyme squalene epoxidase, named with -ase] Now imagine that we had acid-catalyzed epoxide opening. The epoxide is going to want to open at the tertiary position because that would more favor the potential formation of a carbocation. It turns out that you can have attack across the ring. Of course, that would make a carbocation at this position that could be attacked across the ring, which would form a carbocation that could be attacked, which forms a carbocation that could be attacked. You get simultaneous closure of four different rings [6,6,6,5] – that's an important ring structure that is common to all common steroids – steroids including cholesterol, lanosterol, estrogen, testosterone [important bioregulators]. We have this intermediate that's still a carbocation, which a base is able to attack to rip off a proton that can collapse due to this methyl group shifting to where this methyl group shifts to where this one shifts to where the hydrogen shifts. Once you've done that elimination, then you end up with lanosterol, which is 19 steps away from cholesterol.

_____

1a) d-mannaric acid b) d-xylonic acid c) l-threitol
d) alpha-l-ribofuranose e) beta-d-idopyranose f) l-talose
2) alpha-d-galactopyranose

Exam #3

pKa1 2.18; pKa2 8.95; pKa3 10.79

3) pIala = 6.02; pIlys = 9.87 (avg. pKa2 + pKa3); pH = 4.20 4) 5)

Lipids – naturally-occurring fat-soluble molecules
hydrophilic/phobic – "water-loving/fearing"
lipophopic/philic – "fat-fearing/loving"

Fatty acids – saturated; unsaturated

waxes – example: beeswax – waxes are very non-polar but are able to form solids due to extensive formation of temporary dipoles (dispersion forces)

fats – triglycerides/triacylglycerols
fat = solid @ RT
oil = liquid @ RT

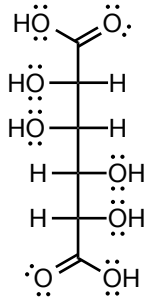
phospholipids – phospholipid bilayer

terpenes

_____

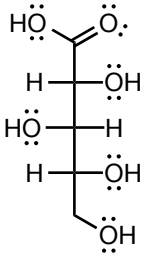
Structures *(remaining structures identical to lecture 13A)*

06/18/12 lab • 1



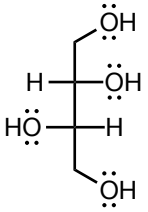
HNO_3

06/18/12 lab • 2



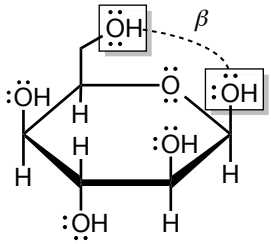
Br_2, H_2O

06/18/12 lab • 3

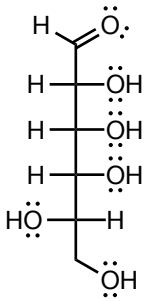


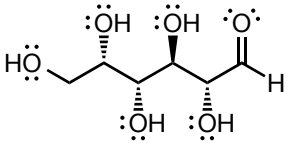
1) $NaBH_4$
2) H^+

06/18/12 lab • 5

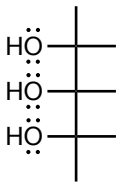


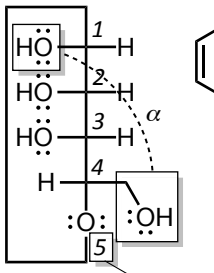
06/18/12 lab • 6





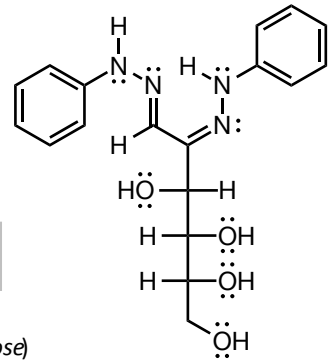
06/18/12 lab • 4





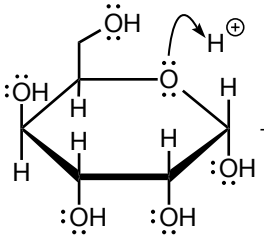
(*furanose*)

06/18/12 lab • 10

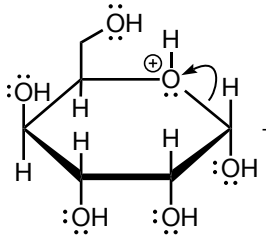


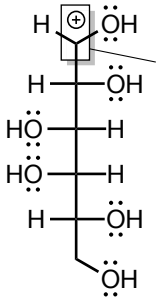
osazone

06/18/12 lab • 7



+150.7°





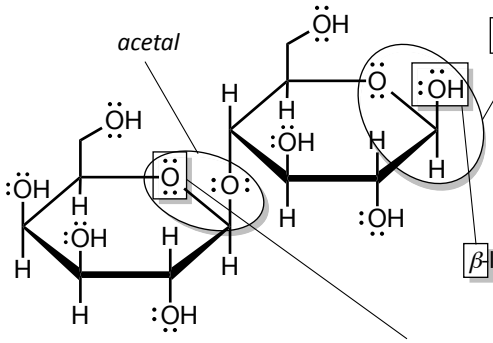
planar;
can be attacked
on either side

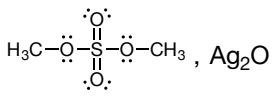
06/18/12 lab • 8

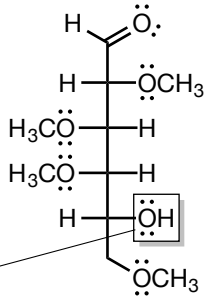
is in equilibrium with open form,
therefore can be oxidized

hemiacetal

acetal



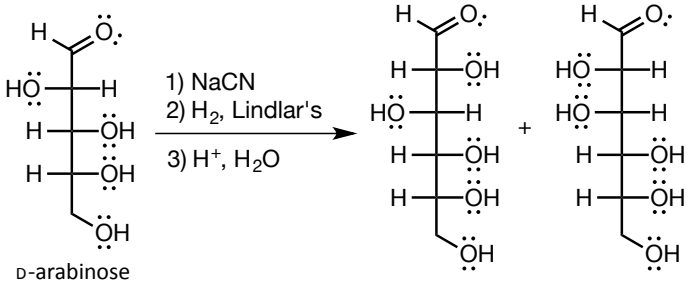
1) 
2) H_2O, H^+



β-lactose

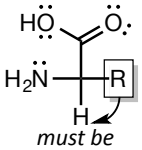
was part of ring, therefore not methylated

06/18/12 lab • 9

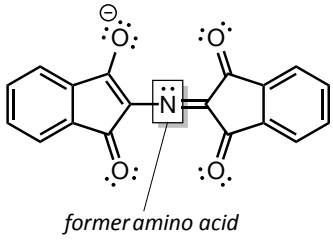


D-arabinose

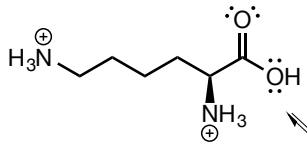
06/18/12 lab • 11



06/18/12 lab • 14

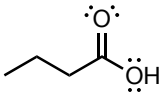


06/18/12 lab • 12

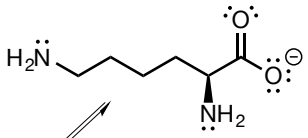


double cationic

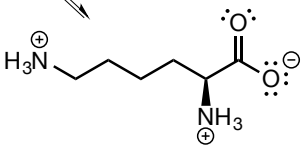
06/18/12 lab • 18



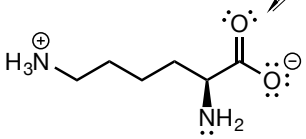
butyric acid



anionic

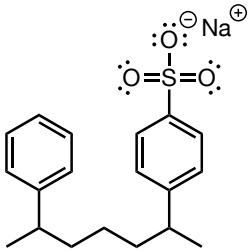


cationic

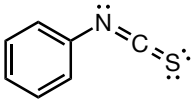


zwitterionic

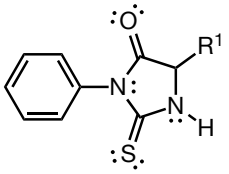
06/18/12 lab • 13



06/18/12 lab • 15

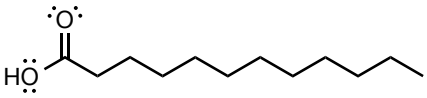


phenyl isothiocyanate

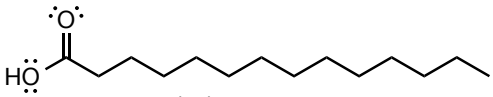


PTH

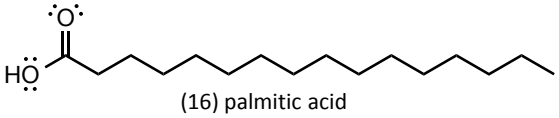
06/18/12 lab • 16



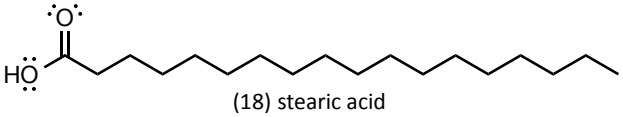
(12) lauric acid



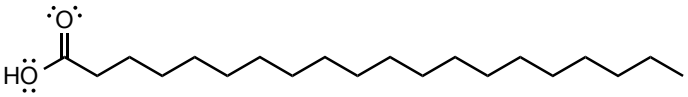
(14) myristic acid



(16) palmitic acid

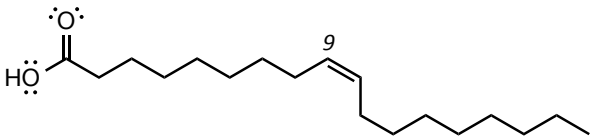


(18) stearic acid

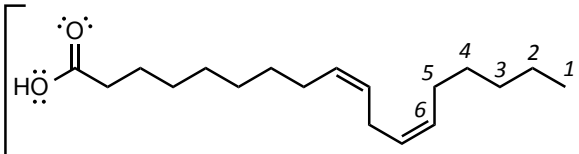


(20) arachidic acid

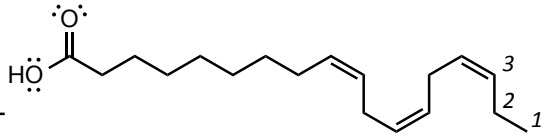
06/18/12 lab • 17



(18) oleic acid



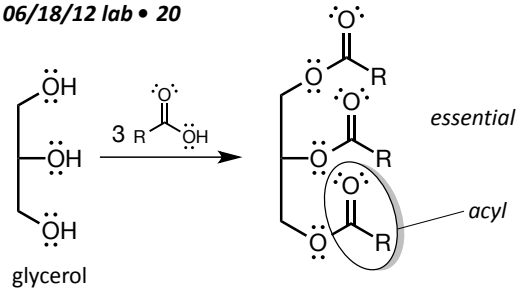
linoleic acid (ω-6)



linolenic acid (ω-3)

essential fatty acids

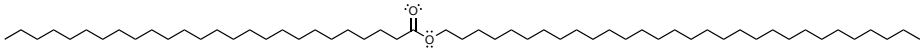
06/18/12 lab • 20



glycerol

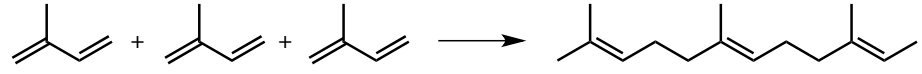
acyl

06/18/12 lab • 19



(26) (30)

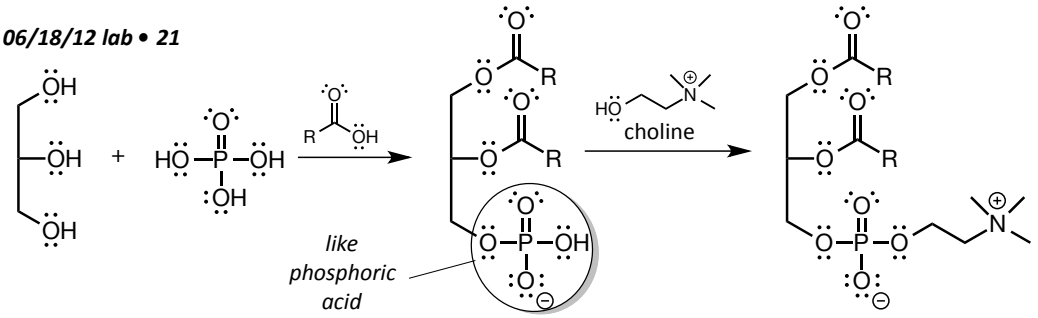
06/18/12 lab • 25



monoterpene
(2 isoprenes)

α-farnesene
sesquiterpene
(3 isoprenes)

06/18/12 lab • 21



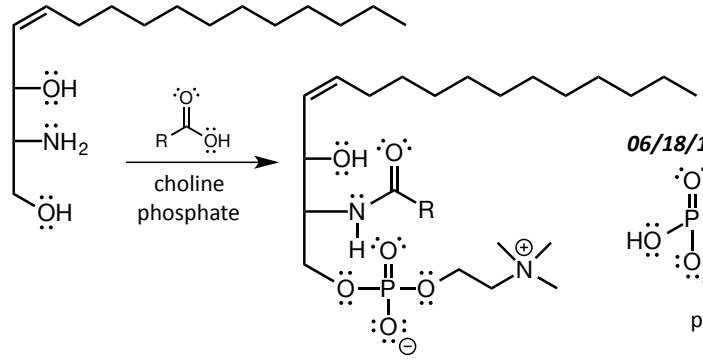
choline

like phosphoric acid

phospholipid
phosphatidic acid

a phosphatidylcholine (general)
a leicithin (more general)

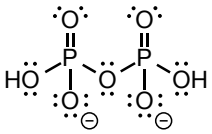
06/18/12 lab • 22



choline phosphate

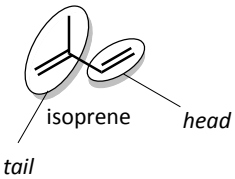
sphingomyelin

06/18/12 lab • 23



pyrophosphate

06/18/12 lab • 24

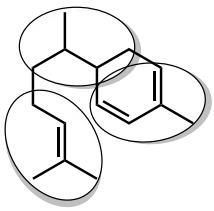


isoprene

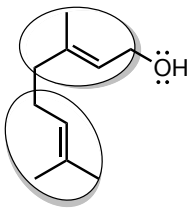
head

tail

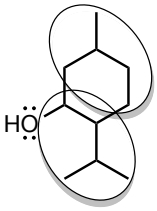
06/18/12 lab • 26



zingiberene
(ginger)
sesquiterpene

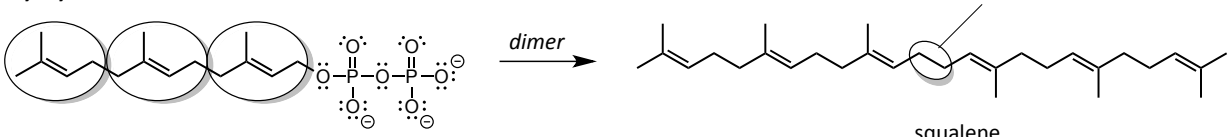


geraniol
(geranium)
monoterpene



menthol
(peppermint)
monoterpene

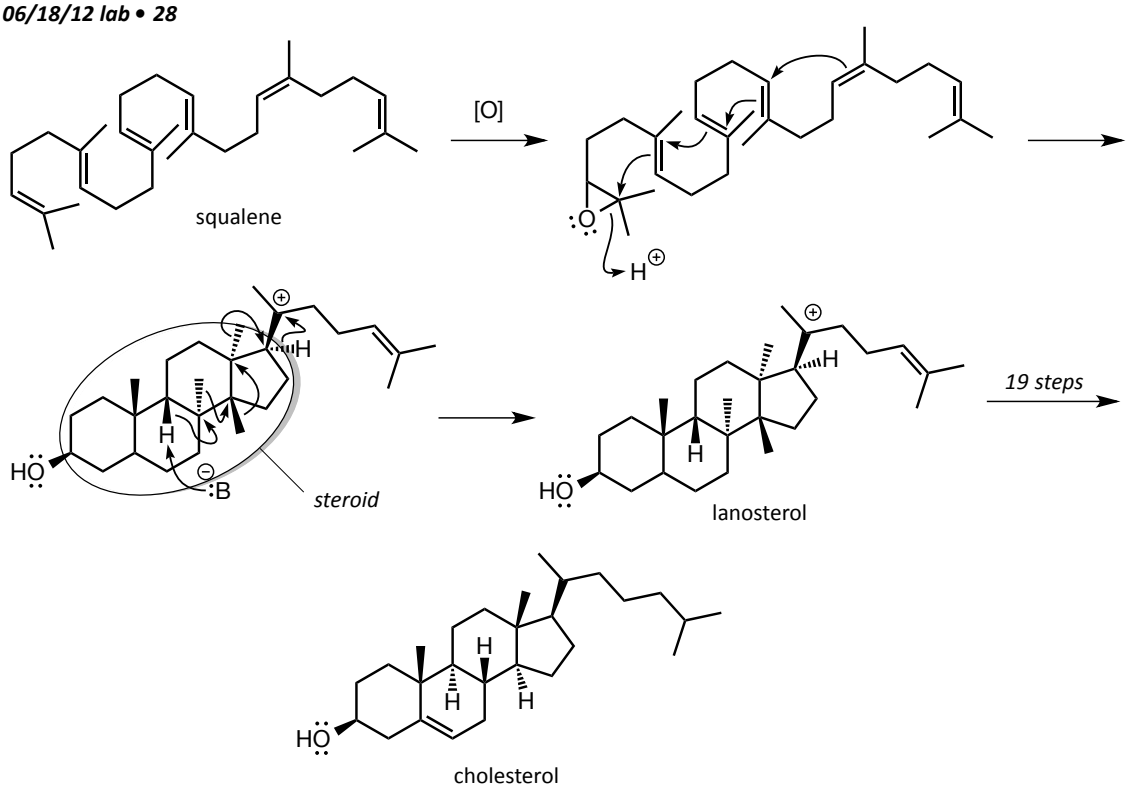
06/18/12 lab • 27



farnesyl pyrophosphate

squalene
triterpene

06/18/12 lab • 28



cholesterol