Lab 12B • 03/06/12

I have three compounds – fairly simple in terms of their structure, but each one's going to be useful for learning a particular trick. Let's just start with one of the simpler ones: a molecule with the formula C4H8O that has three absorbances in its spectrum – one at delta 2.449 that is a quartet that integrates to 2; another one that's at 2.34 that's a singlet that integrates to 3; then one last one that's 1.058 that is a triplet that integrates also to 3. [comment on whether formula given to solve problem] What if you've got an unknown compound? You do have some chance of being able to get the molecular formula. [You might recall a type of problem where you have] a compound that's 70% carbon, 18.2% hydrogen, and whatever percent oxygen; here's your molar mass; figure out the empirical and molecular formulas. That is something that really is done to try to give some information to solve the structure. Molar mass, there is a technique known as mass spectrometry, where you can try to determine what the molar mass of a compound is. If you have a well-isolated compound, you can send it out for elemental analysis – which will give you the composition; you can send it out or do mass spectrometry. The two of those together give you the molecular formula, [which] can help you solve for the structure of a compound. In fact, just on the basis of this formula, and not even looking at the splitting, just looking at one of the chemical shifts of this compound, we're going to solve the whole darn structure.

If I'm going to start with the formula, if the formula's going to be useful, you need to know how to use it. The place you always start is to figure out the degree of unsaturation. What does the term saturated mean in a rigorous sense? There's a way that we often use it when we're talking about fats, but there's a slightly different definition we use if we're talking about unsaturation. What's that more specific definition? Each carbon has to have four bonds, and maximum number of hydrogens possible, given the number of carbons, which means you're not going to have any double bonds, you're not going to have any triple bonds – that what people usually think of when you use term saturated. But what about rings? Because, if you take a linear compound and bring it around into a ring, you have to remove one hydrogen from each position in order to make that new carbon-carbon bond. Effectively, you're removing hydrogen, so that's a form of unsaturation. When we talk about saturated versus unsaturated fats, rings are kinda left out of that. We really are, in that case, talking about double and triple bonds [often excluding double bonds between a carbon an a heteroatom]. For the purpose of analysis, we have to remember that a ring counts as well.

We learned a formula for calculating degree of unsaturation. 2C+2 is normally that maximum number of hydrogens that a compound could have. If you think about some kind of straight chain compound like hexane, the middle carbons, the four carbons in the middle, each of those have two hydrogens on them. The ends have three hydrogens, but you could think of it as being yet another case of having two hydrogens, but they just happen to have one extra hydrogen on each end because they are the ends. If you look at the number of carbons, there are six; each of those has got two hydrogens at least, and then you add two extra for the ends. That's where the 2C + 2 comes from.

But there's a little more to it. We are going to compare to how many hydrogens are present, but before we make that comparison, there's certain situations in which we need to adjust this number. Do you remember that portion of it? There's two more things that get thrown in. Nitrogen can affect the count, because if we take a hydrocarbon – which means just carbon and hydrogen – and you put a nitrogen in it, the least you can do is put it in between a carbon-hydrogen bond. But, nitrogen is normally trivalent, meaning it wants to have three connections, so for that to be a valid structure, you have to throw one more hydrogen in from each nitrogen that you have. You take this count and you adjust it by adding for nitrogens. Phosphorus is in the same column as nitrogen, so that'll have the same effect. Oxygen is divalent, so you can take a carbon-hydrogen bond, put an oxygen in between, and not affect the hydrogen count, so things in that column – oxygen, sulfur, selenium – those you don't have to adjust the count. But move one more column on the periodic table over to the halogens – in order for a halogen to have a bond, you have to take a hydrogen off and put the halogen in its place. That means that we loose a hydrogen for each halogen present, so we need to adjust that count. It's 2C + 2 + N - X: that's the maximum number adjusted for what are called heteroatoms – hydrocarbon, something with just carbon and hydrogen, if any other atom is different, that's what the prefix hetero means, so a heteroatom is something besides carbon and hydrogen. This is a comparison, so you are going to then subtract the number of hydrogens to make that comparison, and then divide the whole thing by two.

For this first example compound, what would be the degree of unsaturation? One, because we only have oxygen as a heteroatom, and that, therefore, is not going to affect our hydrogen count. We have four carbons, so 4 * 2 is 8, plus 2 is 10; we only have eight hydrogens, so 10 - 8 is 2; then 2 /2 is one. So, this compound has one degree of unsaturation, which means it either has a ring, a carbon-carbon double bond, or, a carbon-oxygen double-bond. Let's guess – since this is our first problem, let's just start somewhere and see if we can work with the information we're given. What if it was a ring? There's only a certain number of compounds that could exist that could have a ring: three, four, five, and six-membered rings – we can't even have a six-membered ring in this case, we only have four carbons and one oxygen, put all of them in a ring and that's the largest ring compound that we can come up with. We could do one smaller – put just the four carbons together, that would get us an alcohol. There's a few more compounds I can think of. Is it really all that useful to draw all these different compounds? Yes, because we'll take the first two examples and show how they can't be this molecule, because we do have to compare back to the signal information that we're given. I'll show you why neither of the first two compounds can match that.

Starting with the first compound: what is its name? Tetrahydrofuran; remember that furan is a molecule that has two double bonds in it, THF, our solvent, is this molecule. There is a way to name the cycle: it's called oxacyclopentane; the oxa- prefix means the oxygen's actually in the ring. How many unique sets of hydrogens exist on this molecule if we don't worry about stereochemistry at all? Two. What does it means for two hydrogens to be chemically equivalent? There's two [or more] different hydrogens that have the same environment – if you look wherever they are in the molecule, the hydrogens that your comparing, and you look at what their neighbors are and then those neighbors and then those neighbors, all the way across the molecule, if the relative position's exactly the same, then they have the same environment, they act the same, they generate the same NMR signal. If we know how many different kinds of hydrogens we have, we know how many NMR signals are going to be generated. [How do arrive at two sets of hydrogens for this compound?] Identify for me what the two types of hydrogens are? One next to the oxygen – notice the molecule's completely symmetric, so it doesn't matter which side I go, they're the same, so we've got the two hydrogens next to the oxygen on the left, two oxygens next to the oxygen on the right. They're different from the other hydrogens, because the other hydrogens are two positions away from the oxygen, not one. We have two unique types of hydrogens – that means it can't be the compound, because we have three absorbances and this only has two.

What about the next compound: how many types of hydrogens does it have? Four; why? There's the hydrogen that's the furthest from the oxygen, then there's the hydrogen on either side that are equivalent, because they're the same distance from that oxygen – yes there's really two hydrogens at that position, but just to reduce the clutter on the structure, I'm only going to write one hydrogen each time. There is just the one hydrogen where the –OH group is attached, and then the hydrogen on the alcohol itself. That means the first compound's going to have two signals, the next one's going to have four signals; this next one's going to have five signals; next one, this one's only going to have three, but it's not the right answer. Let's declare that there's no ring.

If there is no ring, the compound must have a carbon-carbon or carbon-oxygen double bond. Let's wonder if there might be a carbon-carbon double bond. If we're trying to figure out different types of bonds, now we need to look at our correspondance chart. If you have an alkene, and you have a hydrogen on the alkene carbon, that has a chemical shift of 4.6 through 5.9. If we have a carbonyl, and it's an aldehyde, so that the hydrogen's directly on the carbonyl, then it has a chemical shift of between 9 and 10. Then, if we have a ketone, where you can have a hydrogen next to the carbonyl but not directly on it, that has a chemical shift of, on average, between 2 and 2.7. There's lots of factors that can affect these numbers. Generally, if you're at the end of a molecule, if it's a terminal position, it'll be on the low end of the chemical shift rangel; if it's on the inside, it's going to be on the high end of that range. If we look at the chemical shifts that we do have, does it look like we have any alkene hydrogens? What's the largest value chemical shift that we have? 2.5, isn't it? That's nowhere close to the 4.6 range, so does that mean automatically that we don't have an alkene? In this case, it does, but, it is possible to have an alkene without having alkene hydrogens if the alkene is fully substituted. An example of that would be 2,3-dimethylbut-2-ene – there are hydrogens of course, but they're not on the alkene; since they're near an alkene, they're going to be higher chemical shift than a plain alkane, but there's no alkene hydrogens themselves. In this case, though, we only have five main atoms – four carbons, one oxygen – so there's no way we could come up with a structure like this. Even if we tried to throw and oxygen in here, unless you make it an ether, you're just going to have tautomerization and the structure couldn't exist anyways. So in this case, due to the limited number of atoms and the fact there's no chemical shift greater than three, there is no alkene.

There is that one ring compound up above that does have three absorbances. We'll walk through why it's not the correct structure. An alcohol absorbance can show up as little as 2.5 on chemical shift, but what would the integration of that alcohol hydrogen be? One, because there's only one hydrogen. Look at this position: still the same problem, it's a hydrogen next to an ether, but there's only one hydrogen there, it still would only have an integral of one. It wouldn't match the signal information that we have. There is a methyl group that, yes, it would integrate to three, but then these other two positions are chemically equivalent, and so that integrates to four. Since the integrations don't match, it's not that compound. The last one is going to have four absorbances itself, so not a possible structure.

So if it has no ring and it doesn't have a carbon-carbon double bond, it has to have a carbonyl. If it has a carbonyl, there's only one answer, because for a four-carbon non-cyclic compound, there is only one ketone possible, that's automatically the answer. There's a degree of unsaturation of one, so it has to show up somewhere. In this example, it's the carbonyl. Because there's no aldehyde, and the only way for it to be an aldehyde is if you do have a chemical shift that's above 9; there isn't, so it has to be a ketone. We didn't even use splitting information at all; we just used the chemical formula and a little bit of logic. Are you going to have to go through this type of thing for every problem? Yes and no. Some problems, some formulas with some information that you're given, you may more quickly identify a structure by messing around with the splitting patterns. But, it is often the case for smaller molecules you can solve structures just by logic.

Walking through the logic one last time: a degree of unsaturation of one means there's a ring or a double bond. If there's a double bond, it might be carbon-carbon or carbon-oxygen. We tried some ring structures, analyzing them, none of them worked, so that means there's a double bond. There's no alkene because there's nothing in the right chemical shift range and there's not enough atoms to create an alkene that would lack hydrogens; that means there's a carbonyl.

In the case of a carbonyl, if the chemical shift were high enough, it could be an aldehyde, but it's not high enough, so it's not an aldehyde, so it's a ketone automatically. In this case, because there's only four carbons, there's only one ketone possible.

Let's double-check this is the right one by looking at the splitting patterns. I'll label the three types of hydrogens this compound has. What I want to go back and do is rewrite the chemical shift information but color code it; it might help you keep track of what's going on by color coding. Chemical shift of 2.5, 2.3, and 1.1. The lowest chemical shift's going to be for the hydrogens that are furthest from the carbonyl. Why would the carbonyl cause anything to have a higher chemical shift? We have an electronegative oxygen which is causing a slight positive charge on the carbon, which means that carbon's drawing electron density from its neighbors, so it's causing deshielding. The closer the carbonyl, the higher the chemical shift; the further from the carbonyl, lower chemical shift. Hc will be the chemical shift of 1.1; that one integrated to three, which matches because we've got a methyl group. We have two other carbons left: one that's a methyl group, one that's not. The methyl group integrates to three, so that matches the middle peak; the middle one is the purple one, the three hydrogen. That follows the normal pattern that a terminal hydrogen is a slightly lower chemical shift than an internal one. There's only one other type of hydrogen left, which would be the one that I colored in blue, which is on a methylene position – in general, –CH2– is called methylene; there are only two hydrogens on that blue position.

I left the splitting out because what I'm going to do is colorize based on which hydrogens are causing the splitting. If you look at that purple one, Ha, the middle peak, it's a singlet, so that one I won't color in at all. Why is it a singlet? Because its neighbor, the carbonyl, has no hydrogen on it. We're going to see another example where just because you have a carbonyl doesn't mean you can't have splitting, but if you have a ketone, that carbonyl blocks splitting. What about the other two positions? There's the blue ones that a have a methyl group as a neighbor. The methyl group, since it has three hydrogens, that means it's going to split the blue into a quartet. Then the other way around: the methyl group has those two blue hydrogens as neighbors; two neighbors causes a triple to form. Everything matches.

Let's move on to our next example, which is the same chemical formula, but a different set of chemical shifts. Chemical shift of 9.57 that's a doublet that integrates to 1; 2.39 that is a double of heptets (which means 7); then we have a chemical shift of 1.06 that's a double that integrates to 6. So what's the structure of this compound? If you make one key observation, you can actually solve this problem in just seconds. Hopefully you're starting out the way we started the previous problem: you're looking at the chemical formula first. Since it's the same chemical formula, we still have just that one degree of unsaturation, which again means a ring, a carbon-carbon [double] bond, or a carbonyl. Which one of those three things do we likely have based on the signal information that we're given? Why a carbonyl? Because it's an aldehyde. It turns out only aldehydes and carboxylic acids can show up that high of a number. We don't have a carboxylic acid because we've only got one oxygen. Based on chemical shift, the compound is an aldehyde, which means it has no rings or carbon-carbon double bonds. Why? Because it's only got one degree of unsaturation, and we already used it up. If it has an aldehyde, we know this much: that there's one hydrogen on that carbonyl, which I'll call Ha. How many neighbors does that carbonyl have? In terms of hydrogens, one and exactly and only one; why? What's the splitting of that carbonyl hydrogen? A double. A doublet means there's only one neighbor. If we put any more than that number of hydrogens next door, we change the splitting pattern. Turn that back around: we've already used an oxygen up, and I'm saying that there can only be one hydrogen on its neighbor. The only other thing we can put there is two carbons, which since there are only the two more carbons available, that's structure of the compound. I'll say that again: there's only one hydrogen at this position. If there's only one hydrogen at that position, that means the other two atoms there must be carbon. In this specific case, since the carbonyl had a carbon and an oxygen, since the neighbor has a carbon which we only put one hydrogen on, and since we used the other two carbons up, that's it, that is the structure of the compound.

Let's go back and verify this by trying to match up the splitting patterns. There's a third type of hydrogen which shows up in two places, cause the two methyl groups are identical to each other – which is actually one of the important things about this example compound. We solved the structure through logic again, but notice that we have an integration of 6. Is it possible to have one type of hydrogen on one carbon? No. But is it possible to have six of one type of hydrogen? Yes, as long as they're on different carbons. It happens in a case just like this: the two methyl groups are joined to one position. From that one position, it's just one molecule, one chain, so from either of the methyl groups, since you end up at the same place, those are two chemically equivalen positions. Anytime that you have any kind of local symmetry, two of the same group attached to the same position, or a ring that's got symmetry to it – those are the cases where you're going to end up with an integration greater than three. It's not possible to have an integration greater than three without some form of symmetry. We've got a carbonyl there, so how is it that Ha is not a singlet? The only way that integration can be greater than three is if the molecule has some symmetry. Since two methyl groups are attached to the same common position, they are chemically equivalent.

As far as the splitting, the previous example, we had a carbonyl, and then we had groups on either side of the carbonyl, but no hydrogens on the carbonyl. So, since from one side of the carbonyl to the other was two positions away, there was no splitting. But in this case, we have a hydrogen on the carbonyl, and so the next position over is just the next position over, on which there is a hydrogen. Since you have two different hydrogens that are only separated by one position, that's the normal situation in which you can have splitting. It's because, again, the hydrogen is on the carbonyl not next to the carbonyl; that's why this one will experience it.

Carbonyls themselves don't prevent splitting; it's the fact that carbonyls in ketones that lack hydrogens – that causes a lack of splitting. In this case, Ha has Hb as its only neighbor, so that's why that first peak at delta 9.57, which integrates to one, is split by that blue neighbor into a doublet. Skipping over one peak, let's go to the 1.06. Again, it makes sense that that would correspond to these green hydrogens, cause they're the further away from the carbonyl, so furthest away from that electron withdrawing effect. They integrate to six, which that is a piece of information we would have used to show that there's symmetry in the molecule. If I hadn't started with the aldehyde first, I could have looked at that six and said: ok, there must be two methyl groups there. Why do I guess two methyl groups? Because three time two is six. How do I know it might not be some other thing that there's three of? Cause we've only got a limited number of atoms. Those six hydrogens have only that one blue neighbor, so that explains why they are just split into a doublet. The last peak, the one at 2.39, the one I colored in blue, has the purple neighbor on one side – that's what caused the doublet – it has the six hydrogens on the other side – that's what causes the heptet.

What does a doublet of heptets mean, or a doublet of triplets? Double of triplets doesn't mean that you have two triplets; it means you have one kind of hydrogen over here, and that hydrogen is causing the doublet; we have a different kind of hydrogen, a pair of different hydrogens over here, and they're causing the triplet. When you have those multiple splitting symbols, each symbol means you've got a different neighbor. That's also useful information, because if somehow we were trying to reconstruct from the middle of the molecule out, we could look at that one absorbance and say: six equal hydrogen? The only way possible is when we've got two methyl groups attached. And look and see that there's a doublet, that means on the other side I've only got one hydrogen attached. A doublet of triplets might look something like this. It would be really possible to confuse that with two separate triplets, but with some experience, knowing what you're looking for, you could identify that as a doublet of triplets.

Let's do the last example, which is C6H10O. It's got these three absorbances: delta 2.55, triple, integrates to 4; an absorbance at 2.05, that's a triplet of triplets, that also integrates to 4; and then delta 1.07 that is a quintet – quint meaning five – and that peak integrates to two. [erasing board with stomach; $D0 || !$D0] How many degrees of unsaturation? Two. 6 * 2 = 12 + 2 = 14 - 10 = 4 / 2 = 2. Two degrees of unsaturation, which means it could have what? It could have a carbonyl and a ring, or it could have a carbon-carbon double bond and a ring, or it could have two rings, or, potentially, it could have two carbon-carbon double bonds. It can't have two carbonyls, though, because there's only one oxygen. But you could have a triple bond. One more possibility – a carbonyl and a carbon-carbon double bond. Looks like it's not helping us a heck of a lot this time, is it, the degree of unsaturation information. Let's see if we can do anything with the chemical shift information, then. Do we have an alkene? Based on chemical shift, do we likely have an alkene? Probably not. There's always the situation where you can have a completely substituted alkene, but unless we have that, no we don't have an alkene because nothing's high enough in chemical shift. Do we have an aldehyde? No, cause, again, we don't have anything that's high enough in chemical shift. Let's start there. The compound does not have an aldehyde because no delta > 3, and unless it is completely substituted, there's no alkene – again, because there's no detla > 3.

So let's guess that we have a ketone. We could have two rings, but realize that if we had two rings, it would have to be a compound kinda like that, which is not impossible, but unlikely. If we have a ketone, though, let's look at the chemical shift information. As I explain this, you might think, how was I supposed to know this? That's why I'm showing you this, so you know this trick to look out for. Each of these problems we've done so far is to show you one trick – the first problem, how you use chemical formula to almost identify a compound without even look at splitting; the second problem was to use splitting to solve the structure without looking at all of the information, honing in on the key functional group and the key structural feature that allows us to solve the compound. The trick that we're learning here is symmetry. We have a chemical shift of 2.5; that's kinda at the high end of that carbonyl, that ketone absorbance range, delta 2.0 – 2.7. But it's got an integration of four. What is the only way we can have a integration of four? It's if we have symmetry on either side of the carbonyl. Since the likely integration for the ketone hydrogens is four, there must be symmetry. We take what we know – or what we're guessing – that we have a carbonyl, and we're going to guess that we have four hydrogens that are all equivalent. But wait, the only way that these can be equivalent is if their neighbors are identical to each other. If you had one neighbor on either side that had two hydrogens, that's four hydrogens, that would correspond to the second peak. It turns out that a ring is the only way that this problem's going to be solved. Let's continue that thought, that we could have two hydrogens here and two hydrogens here, then the compound could continue on. But look, you've used up five carbons already, and the oxygen; there's only one more carbon left, and the molecule has to be symmetric in order for these integrations to work out. The answer is cyclohexanone.

Let's look at the three types of the hydrogens and see how that matches the three peaks that we had. Delta 2.55, 2.05, 1.70. First one was closest to the carbonyl, that's why I'm coloring it purple, matching it with Ha. Notice that on whichever Ha we're looking, there are only two neighbors to each individual Ha. So yes, in total there are four Hbs, but only two of them are neighbors at a time to Ha; that explains the triplet. This is an example of how splitting pattern doesn't match integration always, from one hydrogen to another. Because you do have Hbs on either side, that's why they are four hydrogens. Looking further down to Hc, Hc has only two hydrogens, and it's split into that quintet by the blue ones, because this time, both sets of blue hydrogens are interacting with Hc at once. They're both neighbors, so now all four get involved. If you look at the blues, they have the two Has on one side, the two Hcs on the other, and that's what explains the triplet of triplets. Why are there only three types of hydrogens? It is due to symmetry.

You look on either side of the carbonyl, those positions are equally distant from the carbonyl and equally distant if you went the other way around as well. The next position down, since it's symmetric, those two are equal to each other; then that one carbon that's exactly opposite, the mirror plane passes through, so ignoring stereochemistry, that's why there's only three types of hydrogens.

[lab directions]

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C4H8O – delta 2.449, q, 2H; 2.34, s, 3H; 1.058, 5, 3H
Degree of unsaturation – due to double bonds, triple bonds, and rings.
1 D.O.U. – must have a ring or C=C or C=O
what if there was a ring?
– If there is no ring, compound must have a C=C or C=O.
It is possible to have an alkene without having alkene hydrogens if the alkene is fully substituted.
In this case, due to the limited # of atoms and the fact no delta > 3, there is no alkene –> must have C=O
If there is a C=O –> Can only be an aldehyde if delta ≥ 9. In this case, since max delta < 3, must be a ketone.
Hb delta 2.449, q, 2H; Ha delta 2.34, s, 3H; Hc delta 1.058, t, 3H

C4H8O – delta 9.57, d, 1H; 2.39, dhept, 1H; 1.06, d, 6H
The only way integration can be greater than 3 is if the molecule has some symmetry.*
1 D.O.U. –> ring, C=C, C=O
Based on delta ≥ 9, compound is an aldehyde, which means it has no rings or C=C.
Based on the splitting of the aldehyde hydrogen, there can only be exactly one H @ this position, which means the other two atoms connected must be carbons.
*Since two methyl groups are attached to take same common position, they are chemically equivalent.
Ha delta 9.57, d, 1H; Hb delta 2.39, dhept, 1H; delta 1.06, d, 6H

C6H10O – delta 2.55, t, 4H; 2.05, tt, 4H; 1.70, quint, 2H
#D0 || !$D0; try
try: command not found
2 D.O.U. – C=O & ring; C=C & ring; 2 rings; C=C & C=O; C=C & C=C; C≡C
Compound does not have an aldehyde (no delta > 3) and, unless it is completely substituted, no alkene (no delta > 3)
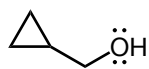Guess: ketone
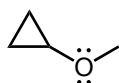Since the likely integration for the ketone Hs is 4, there must be symmetry.
Ha delta 2.55, t, 4H; Hb delta 2.05, tt, 4H; Hc delta 1.70, quint, 2H

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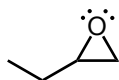**Structures** *(remaining structures identical to lab 12A)*

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| 4 signals | 3 signals, but wrong integration | 4 signals |