

## Lab 12A • 03/05/12

### Structural elucidation

The first compound has a formula  $C_4H_8O$ , and it's got three absorptions:  $\delta$  2.449, q, 2H; 2.34, s, 3H; 1.58, t, 3H. With that information, what is the structure of the compound? What should we do first? Before we even look at the absorption information, notice that I've given us the chemical formula. How do we work the problem if you don't know the formula? It's a lot, lot harder problem. Realize that if even if we had a unknown compound, if we were in a real analytic lab, besides from NMR, IR, those types of techniques, you also have in-house – which means in the same facility – or by mail, you can do elemental analysis. [Remember a common Chem 1A problem:] a compound has 73% carbon, 18% oxygen, whatever percent oxygen and molecular mass of whatever, determine both the empirical and molecular formulas. If you had that, if you did that analysis, you would have the chemical formula available. Why is that chemical formula useful? Because we could calculate something known as the degree of unsaturation. In this particular case, what does saturated or unsaturated mean? It means you could have a double bond or triple bond. But when we're talking about the phrase "degree of unsaturation", there's actually one other type of structure that we count: a ring. Why? Because in order to take two parts of a compound and wrap them around into a ring, you'd have to take a hydrogen off of each of the ends, so rings, technically, also count as a degree of unsaturation. Colloquially, when we use the phrase, it does refer just to the absence of double and triple bonds, so when we talk about saturated fat, it doesn't mean ringless fat in that case. For degree of unsaturation, it refers to double bonds, triple bonds, or rings.

Remember that there's a formula that we have that we can calculate the degree of unsaturation:  $2C + 2$ , that's an important value: that is the maximum number of hydrogens possible, given a certain number of carbons. It should make sense, that calculation, because, think of a straight-chain alkane, for example, no branches. All of the carbons in the middle, each [is] going to have two hydrogens. The two ends are each going to have three hydrogens. If you can think of it, therefore, as two hydrogens plus an extra one because they're at the end, so if you have ten carbons, you're going to have ten pairs of hydrogens, plus the other two and the ends:  $2C + 2$ . Sometimes, though, this formula has to be adjusted a bit. What else would you put there?  $+ N - X$ . Why? Because if you put a halogen on a molecule, you have to take a hydrogen off; that's not unsaturation, that's just what you have to do in order a [halogen] even to be connected up; you have to remove that hydrogen. The opposite is true for nitrogen. Nitrogen is trivalent normally, so if you have a carbon here and a hydrogen there and you put a nitrogen between the two, in order to end up with a balanced structure, you have to have one more hydrogen on there. So each nitrogen, we need an extra hydrogen; for each halogen, we remove one. What I've written up there now is the adjusted count, once you take heteroatoms into account. Now, this is supposed to be a comparison; that's how many we're supposed to have. We would then subtract out the hydrogens that you really have, cause we're going to find out the difference.

Heteroatom – if we're referring to compounds as hydrocarbons, that means they should only have hydrogen and carbon. For organic molecules, that's all they have to have, hydrogen and carbon. Anything that's not hydrogen or carbon, that's different, that's what the prefix hetero- means: heteroatom means different atom, something other than carbon or hydrogen.

Once we take this difference, we divide the whole thing by two, because each degree of unsaturation is a pair of hydrogens. For this compound  $C_4H_8O$ , what is the degree of unsaturation? One, because for four carbons, we should have 10 hydrogens. We only have 8 hydrogens instead, so  $10 - 8$  is 2, divided by 2 is one. With one degree of unsaturation, we have three possibilities: a ring, a carbon-carbon double bond, or a carbon-oxygen double bond. Let's see what would happen if we had a ring; let's just look at a couple of structures that would have a ring that has the right number of atoms, just as a place to start the discussion. One possibility is cyclobutanol; another possibility, THF. As I'm about to show you, neither of these would be acceptable. If a ring is present, then there can't be a carbon-carbon double bond or carbon-oxygen double bond, since there's only one degree of unsaturation. Let's start with the compound on the right; it's a little bit easier to analyze. How many sets of equivalent hydrogens are on that compound? If we have two equivalent hydrogens, what does that mean? It's two atoms that have the exact same chemical environment, which means they have the same neighbors – the same neighbors no matter how far down the structure we look, every single position – the first position way, second, third, fourth – are identical completely between those two different hydrogens.

Looking at THF, just on the basis of position, how many different types of hydrogens are there on THF? If I wanted to label Ha and Hb, how many As, Bs, Cs, how many of them am I going to need? What is one set of hydrogens? The ones right next to where the oxygen is; those are equivalent because the molecule is symmetric. Since the molecule's got a mirror plane through the whole darn thing, the two halves are exactly equal with each other. The hydrogens just to the left of the oxygen are identical to the ones on the right. They're not the same as the remaining hydrogens, because the ones that I just wrote down are one position away from the oxygen, the others are two positions away, so they automatically have a different chemical environment. If it has two types of protons, how many unique signals will it generate (singlet, doublet, triplet, all the splitting patterns, assume those count as one)? Two, because the number of sets of hydrogens in the number of signals. What about cyclobutanol – how many different types of hydrogens do I have there? Three? Four? Four. Why?

Cause you've got the carbon that's the furthest away from the alcohol, you have one position closer, where there's two places that have that same kind of environment, there's the hydrogen on the position where the alcohol is, and then, the one that people often forget, the hydrogen that is the alcohol itself – just because it's on an oxygen doesn't mean anything, it's still a hydrogen, so it'd still count. If I have four types of hydrogens, then I have four NMR signals, which means neither of these two compounds is the right structure, because I only have three NMR signals, but one of these has four, one of these have two. They don't match, so they're not the right structure.

We could try to investigate other cyclic structure, and what's going to turn out is none of them are going to match. There's only a limited number of other possibilities, even, because we've only got a handful of carbons that we're working with. Let's take a guess about whether the compound might have a carbon-carbon double bond or a carbon-oxygen bond, because if it doesn't have a ring, it has to have one of those two others. [From a chemical shift table,] that would be really useful right now, because we could find out three pieces of information – if we had a hydrogen on an alkene, that has a chemical shift of roughly 4.6 through 5.9; if we have a carbonyl, and we have an aldehyde, then that has a chemical shift of between 9 and 10; if we have a carbonyl, but we don't have the hydrogen right on the carbonyl, but it's a ketone hydrogen instead, then that has a chemical shift of between 2.0 and 2.7. Based on those chemical shift values, do we have a carbon-carbon double bond? It told you that the compound has a chemical shift of 2.5, 2.3, and 1.1; do any of those numbers fit 4.6 through 5.9? Does this have an alkene or not? Does the fact that we don't have an alkene peak mean we don't have an alkene? Let me show you what I'm getting at. It is possible to have an alkene without seeing alkene hydrogens, if you had 2,3-dimethylbut-2-ene, then you have four methyl groups. In this particular case, they'd happen to all be symmetric, they'd all be identical, so you'd only get one signal, but it wouldn't be between 4.6 and 5.9, because the hydrogens not on the alkene, the hydrogen is one off the alkene. But in order to end up in that situation, you'd have to have at least six carbons in your compound, or six atoms of some sort – technically, we could put an oxygen on there (but not in our specific case). In our case, we just don't have enough atoms, period.

If you were to put an oxygen on there and made it an alcohol, realize you would make something that tautomerizes, so you've got to be a little bit careful about what you try to guess. Since this compound does not have enough atoms, and since it does not have a peak in the right range, there is no carbon-carbon double bond – which automatically means it has a carbon, cause it has a degree of unsaturation, and we've shown it doesn't have a ring, and if it doesn't have an alkene, it has to have a carbonyl. We didn't look at all possibilities with rings. [good problem to try others] There's no ring. There's a degree of unsaturation, so that means there's a carbon-carbon double bond or a carbon-oxygen double bond. There is no carbon-carbon double bond, cause we can't make a structure that would lack that peak, and, given our limited number of atoms, that means we would have to have that peak show up. We don't have it, so it's not there, so that means we have to have a carbonyl. Does the compound have an aldehyde in it? No, because look at what the chemical shift is for an aldehyde – between 9 and 10. Our highest number is 2.5, nowhere close to 9 or 10, so there's no aldehyde. That means this is a ketone, which means there's two butanone, because there's only one ketone possible with four carbons. Notice I didn't even use any of the splitting information; I didn't even get that far, didn't have to, because I used the other information I had to rationalize it. Since there is no peak with a chemical shift greater than 9, the carbonyl must be part of a ketone. There's only one possible four-carbon ketone with the right degree of unsaturation; you could have cyclobutanone, but that's two degrees of unsaturation. This is the only answer possible.

How could we help prove that? Let's see the fact that there are three types of hydrogens. Let's rewrite the chemical shift information with a little color coding. The reason I want to do that is because it's going to help you when you solving problems to know which atoms split which other ones; that's what we want to keep track off. The three absorbances were chemical shift 2.449, 2.343, and 1.058. Right there, we could identify which hydrogen is which, even without the rest of the information. Look at 2.5 versus 2.3; those have to be H<sub>a</sub> and H<sub>b</sub>, one or the other. Why? Because those are the protons closest to the carbonyl. The carbonyl causes hydrogens to have a range of 2.0 to 2.7. The higher of the two numbers is going to be the one that's on the interior of the molecule. Usually, when you have a terminal functional group, it's lower chemical shift; internal, higher. When we're comparing the two, the usual best guess is the higher chemical shift is the internal one, which means this is going to be H<sub>b</sub>, and this is going to be H<sub>a</sub>. H<sub>c</sub> would be the one with the lowest chemical shift, which makes sense because it's the further from the carbonyl. Why would any of these have higher chemical shift because of the carbonyl? Because the carbonyl's a delta positive, which means it's an electron withdrawing group, which means it deshields whatever's next to it, and deshielding causes larger chemical shift.

What were the splittings? The first hydrogen got split into a quartet, which makes sense if it's being caused by the green protons, H<sub>c</sub>. There is no splitting for the second peak; why? Because there's no neighbors; if we look at the carbonyl, this particular carbonyl has no hydrogens on it. That carbonyl, in fact, blocks splitting between neighbors. H<sub>c</sub> has got two neighbors to it; it's going to be a triplet, due to those blue hydrogens. Everything matches; that is our answer.

I've got two more left. The first one has exactly the same chemical formula, but it's got different chemical shifts and splitting patterns. This one has a peak at 9.57, d, 1H; 2.39, d, 6H; 1.06, d, 6H. Is it possible to have six hydrogens on one carbon? Then how the heck do we end up with an integration of 6? Two methyl groups attached to the same point, the two methyl groups are equivalent. Each methyl group's got three hydrogens, so there's six hydrogens. At least, that's one way you could do it. You could also have three carbons that are all identical, each with two hydrogens.

What it means is there are multiple chemically-equivalent carbons. When you have an integral ever that's greater than three, it means you have symmetry of some sort in the molecule. The only way that integration can be greater than three is if there are multiple chemically equivalent carbons that will have those chemically equivalent hydrogens. With that one statement, we can solve the compound's structure in one step. I want to do it a different way. [Previously, we started out] with degree of unsaturation. This is the same formula, so same degree of unsaturation, which is one. What kind of compound is this? What if we look at the chemical shift? Chemical shift of 9 means what functional group? Aldehyde. The only other functional group with hydrogens that high up are carboxylic acids, which have to have two oxygens. If we have the fact that we have a chemical shift that's that high, and we know we have a degree of unsaturation, we know it's an aldehyde. Let's start with that.

I'm going to rewrite my peak information and colorize it. First one, we'll have our carbonyl hydrogen, which is split into a doublet. The carbonyl only had one hydrogen on it; there another carbon that only had one hydrogen; then there's something that integrates to 6. If the carbonyl's a doublet, which is the only hydrogen which could have done that splitting, did the blue ones or the green ones split the carbonyl? Why blue? There's only one of them; a doublet comes from the fact that you have one neighbor, one neighbor – that spin might be up or down relative to the magnetic field, that's what causes a doublet to form. If the greens one split it, it would cause the heptet, which is what we have in another situation. One neighbor makes a doublet, so we know that it has to be the blue that split it. That means that, right next door here, we have H<sub>b</sub>, and we have no other hydrogens, because if you did, it would be a different splitting for the carbonyl. If we didn't have any other hydrogens, the only other atoms we could put there is carbon, which once we put two carbons there, we've used all four up, that's the answer. We again don't need the rest of the information. We know it's a carbonyl, because of chemical shift greater than 9. With that carbonyl, we have a splitting pattern of a doublet – a doublet means there's one and exactly one neighbor – one hydrogen neighbor. That means there can't be more than one hydrogen there; the only thing that we could put, because we already used the oxygen up, is to put carbons there. Once we put carbons there, we've used all of the carbons up, and that's it – we've figured out the structure of the compound. Since the aldehyde hydrogen was split into a doublet, it has exactly one and only one neighboring hydrogen, which means the other two atoms at the neighbor position must be carbons.

We can verify this is correct. Two methyl groups attached to the same position, they're chemically equivalent, so the hydrogens on both methyl groups are the same, which is how we end up with that integration of six. That's what's causing the heptet; the carbonyl carbon causes the doublet. The blue hydrogens, there's only one of them, and that's what splits all six of the carbons into just a doublet. Carbonyls block splitting, if we're talking about carbonyls in ketones. But if you look, H<sub>a</sub> is only one position away from H<sub>b</sub>, so even though it's on a carbonyl, it's close enough. If you looked at the first example we did, we had carbon with hydrogen, carbon with nothing, and carbon with hydrogen; that's why they didn't split. But here, we've got carbon with hydrogen, carbon with hydrogen – splitting happens.

Last problem. C<sub>6</sub>H<sub>10</sub>O. It only has three absorbances: 2.55, t, 4H; 2.05, tt, 4H; 1.06, quint, 2H. Start with the degree of unsaturation – what is the degree of unsaturation? 2, because it's C<sub>6</sub>: 2 times 6 is 12 plus 2 is 14, we only have 10 hydrogens, so 14 - 10 is 4 divided by 2 is 2. If we had two degrees of unsaturation, what kinds of things could we have? Could be cyclic; could be bicyclic; could be a ketone. If you have a ketone, you have to have something else, cause there's two degrees of unsaturation. We only have one oxygen, so it can't be two carbonyls, so we could have a carbonyl and a ring, or we could have a carbonyl and a carbon-carbon double bond. What if we had an ether or an alcohol? Then that means we could have a carbon-carbon double bond and a ring; we could have two carbon-carbon double bonds, and we could have a triple bond, because a triple bond itself would count for 2 degrees of unsaturation. Doesn't look like this is helping us a lot, does it? This pretty much is telling us: you could have anything. Instead of trying to do one of these creative tricks, we could go to the chemical shifts. Do we have an aldehyde? No, because we don't have anything chemical shift high enough. Does it appear that we have an alkene? No. We technically have enough carbons that we could end up in one of those alkene hydrogenless situations. But, that's not the situation either. If there's no aldehyde, and there's no carbon-carbon double bond, based on the chemical shift, what might we guess is there? A ketone, because if we had an alcohol, what kind of integration should we have? We should have an integration of one somewhere, because we only have one oxygen, so we can only have only one alcohol, so we should have an integration of one show up at some place or another. But we don't have that; we have integrations of 4, 4, and 2, so there's no alcohol. There might be an ether there; that's a tricky case. Based on the chemical shift, let's guess that it's a ketone.

If we have a ketone, our first peak, the largest chemical shift, has an integration of 4. What is the only way possible to have an integration of four, given the limited number of atoms in this compound? If it's symmetric. That means whatever I do on one side, I have to do on the other. If I have the four hydrogens there, here's how we make [them] equivalent. Since the hydrogen next to the carbonyl integrates to four, the carbonyl must be completely symmetric. Not only must it be symmetric this first position out, but if all four of these are chemically equivalent, then whatever is next to them must also be chemically equivalent, then these hydrogens themselves would not be equivalent. [tummy eraser][ $\int$   $\int$   $\int$   $\int$ ] I have these four hydrogens that are chemically equivalent, and the only way to keep them chemically equivalent is if the next thing over is the same. What do we got left? We have a triplet of triplets, and we also have two more hydrogens that are left after that [are split into] a quintet. Here's a little bit of logic: if we have a quintet, that means it has to be next to four neighbors. There's only two neighbors here, two neighbors here, so unless we pull this whole thing into a circle, we're never going to end up where we can get four neighbors again. That's the point. The compound is cyclohexanone. [H<sub>a</sub>] The blue hydrogens, it's the next peak down, because it's the next position away from the carbonyl.

The furthest position away, the lowest chemical shift, only has two hydrogens on it, which matches what I just drew. Rewriting the absorption information with the color coding, the peak at 2.55, the ones closest to the carbonyl, I'm making those the purple ones, those integrate to four, cause they're symmetric, so they're all equivalent. They're split into a triplet by the blue hydrogens, the next one over, that also are chemically equivalent, and that's why they also integrate to four; they have a chemical shift of 2.5. They are split into a triplet first by the purple hydrogens, where there are only two of them at one time that split; that's why the purples only split into a triplet, cause two over there, two over there, only two acting on the neighbor at once. The red ones down below, they're on the other side of the blues, they're in a different environment, they're not the same as the purple ones, so that's why they have their own splitting – it's a triplet of triplets. We have that last peak, [chemical shift] 1.06, integrates to 2, and they're split by those blue ones. All four of those blue hydrogens are neighboring the red ones at the same time; if you've got four equivalent neighbors, that's why this ends up being a quintet. Cyclohexanone.

[three examples – degree of unsaturation and chemical shift, no integration or splitting; worked problem just on one peak's worth of information; symmetry, integrals greater than 3]  
[lab directions]

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C<sub>4</sub>H<sub>8</sub>O – delta 2.449, q, 2H; 2.34, s, 3H; 1.058, t, 3H

Degree of unsaturation – 1 D.O.U. → must have a ring or C=C or C=O

– If a ring is present, there can be no C=C or C=O, since there is only 1 D.O.U.

These are incorrect structures for this example since the # of signals does not match.

If the compound doesn't have a ring, it must have a C=C or C=O.

It is possible to have an alkene without seeing alkene hydrogens:

Since this compound does not have enough carbons for the above exception, and since there are no hydrogens with the appropriate delta, the compound does not have [a] C=C, which, if it also does not have a ring, it must have a C=O since it has a D.O.U.

Since there is no peak with delta ≥ 9 the C=O must be part of a ketone

H<sub>b</sub> delta 2.449, q, 2H; H<sub>a</sub> delta 2.34, s, 3H; H<sub>c</sub> delta 1.058, t, 3H

C<sub>4</sub>H<sub>8</sub>O – delta 9.57, d 1h; 2.39, dsept, 1H; 1.06, d, 6H

The only way integration can be greater than 3 is if there are multiple chemically-equivalent carbons.

– Since there is one D.O.U. and there is a peak with delta ≥ 9, the compound is an aldehyde.

H<sub>a</sub> delta 9.57, d, 1H; H<sub>b</sub> delta 2.39, dsept, 1H; H<sub>c</sub> delta 1.06, d, 6H

Since the aldehyde hydrogen was split into a doublet, it has exactly one and only one neighboring hydrogen, which means the other two atoms @ the neighbor position must be carbons.

C<sub>6</sub>H<sub>10</sub>O → 2 D.O.U. – 2 rings; C=O & ring; C=O & C=C; C=C & ring, 2 C=C; C≡C

delta 2.55, t, 4H; 2.05, tt, 4H; 1.06, quintet, 2H

Based on delta (nothing delta ≥ 9)(nothing 4.6 ≤ delta ≤ 5.9)(is 2.0 ≤ delta ≤ 2.7) – Guess that it is a ketone

Since the hydrogen next to C=O integrates to 4, the C=O must be completely symmetric.

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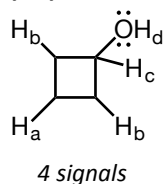
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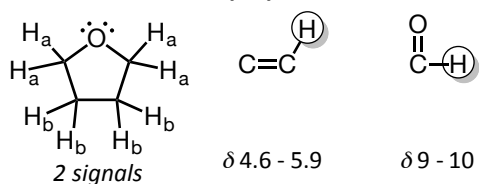
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Structures

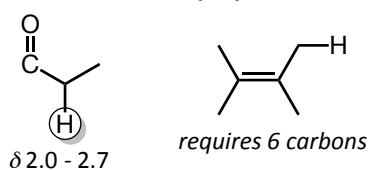
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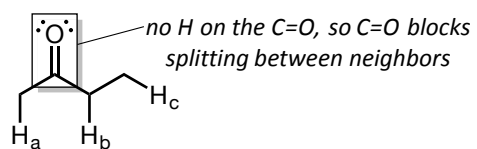
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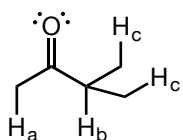
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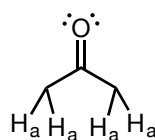
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