

## Lab 14B • 03/13/12

C<sub>4</sub>H<sub>10</sub>O – What degree of unsaturation do we have? Zero. There are four peaks: 3.337, 3H, singlet; 3.336, 2H, triple; 1.59, 2H, tq; 0.93, 3H, t.

Let's start out with degree of unsaturation. Since the degree of unsaturation is equal to zero, the compound must be either an alcohol or an ether. Those are the only two functional groups that have a single oxygen and also don't have any degrees of unsaturation, so no aldehydes, no ketones. Also, this not going to be a cyclic ether [or alcohol], there is no ring because there is no degree of unsaturation. Let's think of the different ways we could put a single oxygen in with four carbons. It turns out there's not that many structures. We could have an isopropyl group on one end and a methyl group on the other. We could have something more symmetric – good old diethyl ether. We could have something like this. We can't have an alcohol. Why not? There's nothing that integrates to one. If you look at the integrations: 3, 2, 2, 3, we only have one oxygen. This might not be such a simple trick if I had more than one oxygen, cause then I'd have to worry about whether I might had two alcohols. But since you only have one oxygen, which could be one alcohol, that would give me an integration of one somewhere. But I don't have that. That's why I'm looking at these example ethers.

Knowing that it has to be an ether, this is the only three possibilities it could be. Is there any way we can move anything around to generate a different molecule without making an alcohol? Doesn't look like it. Let's do the same trick we've done for several problems and count unique signals. For any of these problems that we're doing, we're always going to assume that we're dealing with achiral solvents. We don't have to worry about enantiotopic protons at all; I'll carefully choose problems where you don't have to worry about diastereotopic protons. How many unique types of hydrogen are there on the first compound? Three: we have the methyl group; we have the position where the [ether] is attached; and then we have the two equivalent methyl groups. We could stop right there even without counting the peaks, because if we have two equivalent methyl groups, we have something that integrates to six, so we know it can't be that. But, more to the way that I'm working this problem, we'll say that there's three absorbances.

The next compound, does that give us the right number of absorbances? How many types of hydrogens do we have here? Only two, cause it's symmetric. Just so we don't clutter the diagrams so much, I'm not writing every hydrogen in, so be careful when you're studying this that you recognize that; I'm just trying to show types of hydrogens. Here we only have two absorbances. That must mean that this last one is going to end up being the correct answer. The methyl group is its own hydrogens; the position next to the oxygen is different; two positions away is different; three positions away is also unique. This has a total of four absorbances. This is going to turn out to be the correct answer.

1) realization of integration – since there is only one oxygen in the compound, it is either an ether or a monoalcohol. If it was an alcohol, it must have a peak that integrates to one. It doesn't have it, which means it must be an ether. We could solve the problem looking at integration, because we do have a peak that integrates to three. Because if that, it can't be diethyl ether, because that would have an integration of six. And then, this first compound, two methyl groups that are the same, yet again also would generate an integration of six. Only the last compound would give us an integration of three, without having an integration of six.

What about chemical shift? How does chemical shift information help us? If we look at [a] table, a few absorbances that would matter: if you have an alcohol, if you look at that alcohol absorbance, that can show up between 4.5 and 9.0. Practical experience, I don't remember seeing an alcohol that has an absorbance at such a high chemical shift. [phenol?] In fact, I've seen compounds that have significantly lower chemical shift. If you know you have an alcohol because of process of elimination, then known this chemical shift might be a back-up piece of information to help you solve the structure. Otherwise, sometimes, since it is such a broad range, that might not be too helpful. But, if we look at the range for a range next to where the alcohol is, on the carbon where it's attached, that has a tighter range of 3.4 to 4. Let's just wonder for a moment: why might an alcohol have a broad range of chemical shifts?

What would happen if we put some D<sub>2</sub>O in a sample that has an alcohol that we were trying to scan? Alcohols, even though they're not very much so, they're acidic; they have pK<sub>a</sub> values of 16 to 18. They do undergo dissociation. It's an equilibrium; it doesn't like to be dissociated permanently, but those protons can hop on and off very rapidly. What can happen is that at room temperature, if you put D<sub>2</sub>O into a sample, deuterium will exchange with the hydrogens that you're trying to scan for. It'll actually make the peak disappear, effectively. If you're trying to confirm whether or not you've got an alcohol peak, you can put a drop of D<sub>2</sub>O, watch for the peak to disappear; that's the alcohol peak. Since the chemical shift for an alcohol itself isn't always that useful, that trick with D<sub>2</sub>O is. Alcohols undergo rapid proton exchange in solution, which means they can temporarily dissociate and then acquire a proton again.

Now we need one more piece of information: a hydrogen two positions away from an alcohol has a chemical shift about 1.2.

There's one more fact: because of this rapid exchange that's going, it can occur rapidly enough that the proton – even when it's there, even if you don't add D<sub>2</sub>O, so you do get an integration – because of that rapid exchange, it doesn't do any splitting. Even if you have a hydrogen like this that technically is only one position away from a carbon that has hydrogen neighbors on it, those neighbors are not going to split the alcohol proton, which can make a problem confusing. At a far below room temperature scan, here's what a spectrum looks like; when you slow things down, there's not as much exchange going on, so you would see splitting then. This proton exchange causes alcohol hydrogens to not participate in splitting. Splitting with appear again if the solution is cooled sufficiently so that proton exchange stops.

If D<sub>2</sub>O – a fairly significant quantity of D<sub>2</sub>O, because you want to have the possibility of flooding an alcohol and turning it into a deuterium. If D<sub>2</sub>O is added to an NMR sample of an alcohol, the peak for the alcohol hydrogen effectively disappears; since the deuterium replaces hydrogen, it will not be scanned since it is a different nucleus and would appear at an entirely different frequency.

Getting back to the chemical shift aspect of things: we've already identified it's not an alcohol. We've got hydrogens next to an oxygen. The range for an alcohol or ether – as far as a hydrogen next to those functional groups – are virtually indistinguishable ranges. Attaching an alkyl group to an oxygen only has a minimal effect on whatever neighbors might be next to that functional group. If we've already identified that we don't have an alcohol, then we have two different peaks that have a chemical shift of 3.4. We only have one oxygen; the only way we could have one oxygen but have two peaks that have that chemical shift value is if we have an ether. Since the compound has two peaks that have a [chemical shift] of roughly 3.4, the compound must be an ether, since there's only one oxygen and therefore only one way to generate two peaks with that chemical shift.

There's one last approach we could take, which is to look at the splitting. A singlet that integrates to three usually indicates a methyl group with blocked splitting. There's a couple of different ways to block splitting: we could have a carbon that has no hydrogens attached to it. It's possible to come up with a structure like that here, but .... all of these pieces of information, of course, are conflated together. If we look at the fact that we have an oxygen there, putting an oxygen right next to a methyl group, that oxygen wouldn't have any [hydrogen] neighbors as long as it's an ether; that would therefore explain why we have a methyl group with that chemical shift that is a singlet that, since it's a methyl group, integrates to three. It's a reasonable guess to make.

Let's try to take just the splitting information and see if from that we can build the structure of a compound. We'll then use chemical shift to verify whether we've made a logical structure. We'll verify that both integration and splitting match. This is the style that, in the future, more of these problems are going to look like. We have a singlet; we have a triplet; we have a triplet of quartets; and we have a triple that integrates to three. What's a triplet integrating to three mean that we have? If we integrate to three, what does that likely mean that we have? A methyl group. If it has a triplet, what does that mean about the environment of that methyl group? It's only going to have two neighbors. If I start with a triplet that integrates to three, here are those three hydrogens; here's the triplet aspect of it – that it only has two neighbors. We have two peaks that integrate to two: one of them is a triplet, one of them is a triplet of quartets. Which peak must correspond to the blue protons, then? Which peak would be compatible with the two hydrogens? We have to have a quartet because there are three neighbors to the blue protons.

Now that we know that it's a triplet of quartets, and the quartet is caused by the methyl neighbor, we know it's a triplet as well. What does the triplet mean? That on the other side, we only have two hydrogen neighbors. There's only one other peak that integrates to two. If it's only a triplet, what does that mean about its neighbors? It has to be oxygen, because if you put a carbon there, that carbon's going to have hydrogens on it. That would cause the green protons to be split. They are split, but only by the methylene group, the blue protons that we've already established. The fact that we've now crawled to the end of a chain, the fact that we're not longer being split, that means there must be an oxygen here. If I color code the spectral information, it'll end up looking like this.

[lab directions]

Aluminum trichloride is a really noxious solid. If you think of the structure of aluminum trichloride, it's electron deficient, so it's really reactive with water. Even if you just open a bottle of the solid up, it starts reacting with water – enough so so that if you take a piece of pH paper and you were to wave it over the mouth of that bottle, the pH paper would turn pink because of the amount of hydrochloric acid that's being generated.

[lab directions]

An anhydride, even though it is not an acyl halide, because it's got an oxygen attached to a carbonyl, it has the same ability to react with aluminum as an acyl halide would. Anhydrides aren't as bad as acyl halides; they are one step lower in terms of reactivity. But, anhydride means without water. It's a compound that was formed by heating up and removing water from it, so it would be something that would readily react with water.

[lab directions]

Why wouldn't you pour a bunch of water into a concentrated acid? What happens when you mix water with acid? It dilutes the acid, but there's an immense amount of interaction with strong acids, at least, and water. Think of HCl. HCl dissociates the way it does because it gets so favorably surrounded with water, so if you throw water into a concentrated acid, there's usually a large amount of heat released. If you have a large amount of heat in just a little bit of water, that means you splatter. If you take some concentrated acid and pour some drops of water on it, that can splatter out and get on you. That's why you never add water to acid, you pour acid into water so the water helps disperse the heat as that heat of solution is evolved.

[Friedel-Crafts volcano]

We're going to start talking about alkenes. Alkenes have a feature of their spectra that we normally don't discuss with other functional groups. It's not that other functional groups don't have this behavior – what I'm referred to is splitting, but not just the fact that there's splitting, but how much splitting – in other words, the splitting constants. For just plain hydrogen-hydrogen splitting, there is some splitting constant there, but generally we don't refer to it, because normally it doesn't provide any extra information. All of the problems we've worked so far, have we even thought of coupling constants at all? No, we've just used the splitting information as-is. But with alkenes, the situation's a little different, because there's three types of hydrogen-hydrogen interactions that potentially could occur on an alkene.

One of those interactions is a cis interaction, if you happen to have a double bond that has two hydrogens that are cis to each other. I've used this terminal double bond as an example because it has all three of the forms of interactions that are possible. A cis double bond ends up generating a coupling constant in the range of [6-14] Hz. [why is Hz used?] Another interaction is trans[, with a coupling constant of 12-18 Hz]. But there's one more interaction that we never really talked about before, because before we were just naming double bonds; we weren't talking about the structure of double bonds. There is this geminal interaction that occurs. Realize that the two hydrogens are different from each other, cause one is closer to the top hydrogen, one is further from it, so automatically since they're locked into that position since it's a double bond, they're distinct hydrogens from each other. Since they're distinct hydrogens from each other, they split each other. That geminal splitting has a splitting constant between 0 and 3 Hz.

How could that be used in a problem? Let's start with a simple one: C<sub>8</sub>H<sub>8</sub>. This is an unusual peak; you haven't seen one like this before. That m stands for multiplet. Multiplet, we use that designation if the splitting pattern is so complicated that we can't determine it, or, if it doesn't really matter and it's really complicated. Notice that we have this integration of 5, and look at the chemical shift range. With the degree of unsaturation, the chemical shift range, and the integration, what kind of compound is this? What is the degree of unsaturation? 5, cause  $8 \times 2 = 16 + 2 = 18 - 8 = 10 / 2 = 5$ , so five degrees of unsaturation. We have a chemical shift in the 7 range. Yes, benzene, which has a degree of unsaturation of 4 by itself, which show up in that range. If I had an integration of 5 with benzene, what does that mean? I have a monosubstituted benzene ring. If I have a degree of unsaturation of 5, and I have 8 atoms and a mono-substituted benzene ring, that means the molecule is styrene. Let's investigate further, cause there's three other peaks that appear. [order of peak listing]

We have a doublet of doublets that integrates to 1 that has two splitting constants. In fact, we have three peaks in that situation – slightly different chemical shifts, slightly different combination[s] of coupling constants. Based on degree of unsaturation and chemical shift, it's likely the compound contains benzene. An integration of 5 suggests the compound is a monosubstituted benzene. Given the limited number of atoms, if I use up 6 atoms and I know that there's only one substituent, the other two carbons have to go on there, I know I have one more degree of unsaturation, and so that's how I can jump straight to styrene. But now let's try to match the different hydrogens on styrene to the spectral information. Notice that these hydrogens are not equivalent, not at all; that's why we end up with a multiplet, and that's why we have a range for chemical shift. That is not unusual for benzene compounds, because this is a frequent result. Any monosubstituted benzene potentially could have this kind of complication, so it's not unusual to report benzene in this way. That's the only reason I'm writing all these hydrogens with the same color, because they correspond just to one absorbance.

We do have the three other hydrogens: the one that is right next to the benzene ring, and then the two that are terminal. Which one is which? We know from process of elimination which one is the hydrogen closest to the benzene ring, cause the one closest to the benzene ring can have a cis interaction and a trans interaction, but it can't have a geminal interaction. If we look at the three different peaks, notice that they are two of them that have a coupling constant of 2 [Hz]; that's right in the range of where a geminal proton would show up, so those two with the coupling constant of 2 [Hz] are the geminal hydrogens. The one that does not have a coupling constant of 2 [Hz] is not the geminal, which means it is the one right next to the benzene ring. How do we tell from the other two? One has a splitting constant of 7 [Hz], one has a splitting constant of 12 [Hz]. Turns out it's the trans that has the larger coupling constant range, so the coupling constant of 12 [Hz] corresponds to trans, and the at 7 corresponds to cis. Cis, then, would have to be the one that I've circled in green, and trans would be the one that I've circled in red.

First problem – C<sub>6</sub>H<sub>12</sub>: 5.45, dt, 1H, 14 Hz; 5.42, dq, 1H, 14 Hz; 1.95, dt, 2H; 1.643, d, 3H; 1.360, tq, 2H; 0.885, t, 3H

Second problem – 6.342, d, 1H, 6.2 Hz; 4.644, dt, 1H, 6.2 Hz; 3.957, t, 2H; 1.984, dt, 2H; 1.846, tt, 2H

C<sub>4</sub>H<sub>10</sub>O – delta 3.337, 3H, s; 3.336, 2H, t; 1.59, 2H, tq; 0.93, 3H, t → D.O.U. = 0

Method 1: Degree of unsaturation

Since D.O.U. = 0, the compound must be either an alcohol or an ether; also, the compound cannot be cyclic.

Method 2: Integration

Since there is only one oxygen in the compound, it is either an ether or a monoalcohol. If it is an alcohol, it must have a peak that integrates to one. It doesn't have it, so it must be an ether.

Method 3: Chemical shift [delta]

Alcohols undergo rapid proton exchange in solution, in which the alcohol momentarily becomes deprotonated then reprotonated again. This proton exchange causes alcohol hydrogens to not participate in splitting (splitting will again appear if the sol'n is cooled sufficiently to slow or stop exchange). If D<sub>2</sub>O is added to a NMR sample of an alcohol [or amine], the peak for the alcohol hydrogen effectively disappears since if deuterium replaces hydrogen, it will not be scanned since it is a different nucleus and would appear at an entirely different frequency. Since the compound has two peaks that have delta ≈ 3.4, the compound must be an ether since there is only one oxygen and therefore only one way to generate two peaks with that delta.

Method 4: Splitting

\*A singlet that integrates to 3 usually indicates a methyl group with blocked splitting. Since there is delta ~ 3.4 and an oxygen is present, it is a reasonable guess that the compound is a methyl ether.

C<sub>8</sub>H<sub>8</sub>: delta 7.10 – 7.5, m [multiplet], 5H; 6.992, dd, 1H, J<sub>1</sub> = 7 Hz, J<sub>2</sub> = 12 Hz [trans]; 5.737, dd, 1H, J<sub>1</sub> = 2 Hz, J<sub>2</sub> = 12 Hz; 5.225, dd, 1H, J<sub>1</sub> = 2 Hz, J<sub>2</sub> = 7 Hz [cis]

Based on delta and D.O.U., the compound likely contains benzene. An integration of 5 suggests the compound is a monosubstituted benzene.

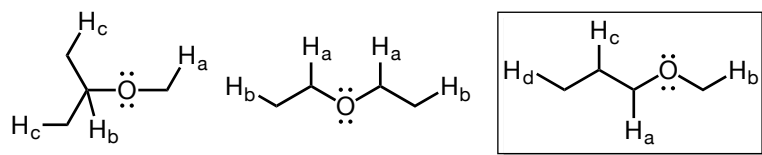
C<sub>6</sub>H<sub>12</sub> : delta 5.45, dt, 1H, J = 14 Hz; 5.42, dq, 1H, J = 14 Hz; 1.95, dt, 2H; 1.643, d, 3H; 1.360, tq, 2H; 0.885, t, 3H

C<sub>5</sub>H<sub>8</sub>O: delta 6.342, d, 1H, J = 6.2 Hz; 4.644, dt, 1H, J = 6.2 Hz; 3.957, t, 2H; 1.984, dt, 2H; 1.846, t, 2H

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Structures

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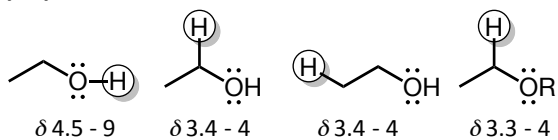


3 absorptances

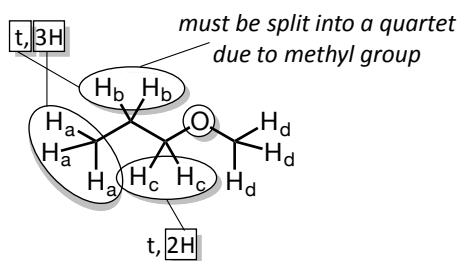
2 absorptances

4 absorptances

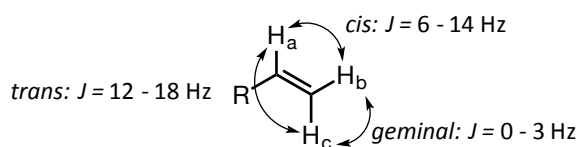
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