

## Lab 3B • 04/19/12

Problem 1: C<sub>6</sub>H<sub>13</sub>Br – delta 3.460, d, 2H; 1.45, quint, 1H; 1.427, dq, 4H; 0.895, t, 6H

What degree of unsaturation do we have for that compound? Zero. Let's review the formula for degree of unsaturation. When we have something that's fully saturated, that means it doesn't have any double or triple bonds; it also means it doesn't have any rings. If I had a [saturated] organic hydrogen, what is the number of hydrogens it should have based on the number of carbons?  $2C + 2$ . We start out with degree of unsaturation being compared to the number of hydrogens it normally would have, which is  $2C + 2$ , but we have to make some adjustments, because this assumes no heteroatoms. Some heteroatoms change the count, some don't. For example, chalcogens like oxygen and sulfur, how would they affect the count here? Would we need to adjust the number of hydrogens we expect if we have oxygen or sulfur on the molecule? No, because they're both divalent atoms, so if you have a carbon-hydrogen bond, you can insert an oxygen in that bond and it doesn't change the number of hydrogens you'd need to keep everything neutral.

What if you had a halogen, chlorine or something like that, would we change the number of hydrogens? We would subtract one for each halogen, so I'll say 'minus X'. What about pnictogens like nitrogen and phosphorus? Then we would add.  $2C + 2 - X + N$  is the base number that we'd expect for a fully saturated compound. We then compare to how many hydrogens we really do have. Since one degree of unsaturation involves a pair of hydrogens, we then take that difference and divide it by two. In this case, six carbons,  $2C + 2$ , that would give us 14, but we do have a halogen, so we subtract and that gives us 13, which is how many we do have, which is why it's a degree of unsaturation of zero. We know that means there's no rings and there's no double or triple bond. We know we have a halogen which is going to be the reason we have such high chemical shift. The fact that we do have such a high chemical shift is a good clue we do have the halogen on the same carbon as there are hydrogens.

There is one thing here that stands out that is related to one of the problems-solving approaches [towards NMR problems]. What's notable in the peaks that are given to us? Six hydrogens; why is that noteworthy? It means there is some sort of symmetry, because you can't have one carbon that has more than four hydrogens on it, and never would you have four itself unless you have the molecule methane. Normally, the maximum of hydrogens – which means the maximum integration – would be three. The fact that we have six means one of a few things: either we have two methyl groups, which is the most likely thing given the small number of atoms; it's not out of the ordinary to have two methyl groups the same, so two times three gives us six. We could, in theory, have three methylenes, three CH<sub>2</sub> groups, but that would mean they would all have to be identical, which given the number of other peaks we have which implies the number of other types of hydrogens that we have (and given that limited number of atoms), not likely to be three pairs. The even more unlikely case for this problem would be having six equivalent hydrogens. If you had the molecule benzene, that does have six equivalent hydrogens, six individual hydrogens; not likely to happen here. Based on the integration of six, the molecule likely has two equivalent methyl groups.

Here are two methyl groups. In these situations, the most common thing to have happen is the two methyl groups are part of some sort of branch – in other words, you'll have some kind of common carbon that then splits off in two directions, and those two directions are identical. Let's see what we can do here. Here's the six hydrogens [purple]. What kind of splitting are these six hydrogens going to cause? Quartet, because even though there's six hydrogens, there's only three in either location, so whatever group I put next to it is not going to experience all six hydrogens [unless the branch directly connects the two methyl groups], so it's fine that we don't have a heptet here. We know there needs to be a quartet; there's only one place we can find a quartet here, that's the third peak that's listed. I'm going to go ahead and circle the quartet [purple] to show that it's this first set of methyl groups that cause that.

We could also look at the methyl groups themselves and see that they have triple splitting. The type of absorbance that you get is all due to the magnetic field that is around the nucleus being scanned. Not only, though, is there the main magnetic field that's part of the machine, there's the environment around it, what the other nuclei have as their own spins. If you have a neighbor that has a spin aligned with the magnetic field, that's going to add to the overall magnetic field that's experienced by the nucleus being scanned, or the neighbor's oriented opposite, then it's going to end up subtracting from that magnetic field. Since both possibilities are likely, and on average they're equally likely, that means given a solution, a sample that's got zillions of molecules, it will experience both of those things. By having one neighbor, you'll get two different absorbances. That's the origin of this  $n + 1$  rule; it turns out that if you have two neighbors, you get three absorbances; three neighbors, four absorbances. The fact that we have a triplet here means there's two neighbors. The fact that we have two equivalent methyl groups that have two neighbors means that this peak that integrates to four is going to correspond to the next thing up the chain, so let's write those hydrogens in [blue]. That's what causes the methyl groups to be a triplet, and because of symmetry they integrate to four.

Look at what other piece of information we have next: the neighbor only has one hydrogen on it; we know because there's only a doublet. We had a doublet of quartets, which means on one side of the last set of hydrogens we looked at, we have that methyl group, that's the quartet, but on the other side of it, we only have one hydrogen that's there. Think about the number of carbons we have.

We could wonder if there are again two carbons equivalent to each other, each one with just one hydrogen; that would correspond integrating to two, and we do have a peak that integrates to two. That peak that integrates into two is split into just a doublet; that means there'd be one neighbor and we do have one peak that integrates to one. But, if we had the two side chains, each of which had three carbons, that's all six carbons in the compound; where are we going to put one bromine left over but somehow have everything be symmetric, so it doesn't add up. Notice also that we have quintet splitting on one of these peaks. Quintet means you have four equivalent neighbors. We could have four equivalent neighbors if, at this point in the compound, we join those side chains. This new hydrogen here, if we allow there only to be one hydrogen, that would match the splitting of the [blue] protons that we just came from. If there's only one hydrogen, that would correspond to an integration of one, which because it has those four equivalent neighbors would explain the quintet. The fact it's a triplet shows it has another carbon neighbor, which is why it only has one hydrogen its own self. At this point, all that's left is that carbon, two remaining hydrogens, and then the bromine, which means the structure of the compound is this. Let's finish the assignments to make sure this makes sense. This last peak has two hydrogens that matches this peak with an integral of two, and it also matches the fact that its neighbor [green] has a triplet in it. And, because the neighbor is only a single hydrogen, that's why that last carbon is itself split into a double.

Problem 2: C<sub>6</sub>H<sub>10</sub>O – delta 5.79, ddt, 1H; 5.02, dd, 1H; 4.97, dd, 1H; 2.52, t, 2H; 2.34, dt, 2H; 2.149, s, 3H

We can work most of this problem purely off of spitting and integration; you then have to make a small but logical leap. Before we take the systematic approach, let's see if there's any of these tricks or observations, these realizations, that would help us come up with some possible structural pieces of this molecule. Is there anything about the chemical shift that strikes you in this compound? What's the degree of unsaturation? Two. Given its chemical formula and the fact that it's got a degree of unsaturation of two, that means we could have a triple bond – if we did, that means we have either an ether or an alcohol; we could have a carbonyl and an alkene; we could have a carbonyl and a ring; we could have an alkene and a ring; or we could have two different rings. Does that last option of just having two rings make sense with the chemical shift values that we've got? Not particularly, especially given that we have three different absorbances, each of them almost at five. We'd need some really strange molecule that has lots of different inequivalent carbons to be able to generate something like that if all we had was an oxygen, not a double bond or something else to cause those chemical shifts. I'm suggesting that the double ring option is not that valid. [not an alkyne cause we haven't covered them]

All of the other options have some kind of double bond in them. What is roughly the range of hydrogens alpha to a carbonyl? What would a ketone be as far as its chemical shift? It's about 2.0 - 2.3; notice that we have a singlet integrating to three that has a chemical shift within that range. Why do I point this out? Because any time you have a singlet, that means you have no hydrogen neighbors on the next carbon over. If we have a singlet that integrates to three, it could be something like these different methyl groups, because on their neighbors, there are no hydrogens. We could have an ether, if we had just one degree of unsaturation in an alkene or a ring; then, the oxygen would have to be saturated. But that chemical shift, it's strange to have it all the way up at 5, that is a little high, and having three different hydrogens, just single hydrogens. You can't have an ether that has more than two carbons on it, so somehow making two of the hydrogens on the same carbon different from each other to generate these chemical shifts, that's a complicated problem. The carbonyl looks like a really strong candidate for explaining the singlet in this case.

Let's return one last time to these high chemical shifts. What functional group that we can get out of this degree of unsaturation would make sense having that high chemical shift? Where does an alkene show up? About 5 to 6. This is right in the range for one. What about the integrations would support the idea of having an alkene? What kind of alkene would this be, based on the integrations? Terminal. Why? Because only a terminal alkene would have three hydrogens on it, and the very end carbon, because the configuration is locked in by that double bond, the two hydrogens on that same carbon would be different from each other, because one would have cis interactions with its neighbor, the other would have trans interactions; they would be different. That would explain the three singlet absorbances and, also, the complicated splitting pattern: doublet of doublets of triplets. I'm going to guess there's a double bond in there. I'm also going to suggest there's some good evidence for there being a ketone in here. This molecule likely contains an alkene, since there are multiple peaks with a chemical shift about 5, each of which only integrates to one. The alkene will be terminal since that is the only way to have three individual hydrogens. The compound also appears to have a carbonyl, based on the singlet that integrates to three with a chemical shift between 2.0 and 2.3.

Now that I've made these guesses, let's go back and try do it systematically. Let's take that singlet integrated to three and figure out what the significance of that is. You would have a carbon with three hydrogens [black] that would have some kind of neighbor that would have no hydrogens on it. Where would we go next? My suggestion would be to handle the triplet. Why? Because the fact that it's only a triplet and not a triplet of doublets, a triplet of quartets, some complex splitting – it means it only has neighbors on one side. But since itself only integrates to two, that means that position also has something next to it that is blocking splitting. There's the strong likelihood that it's going to be the same thing that blocked the splitting for the methyl group. We can't make that assumption yet, but given the limited number of atoms, very high likelihood. We have a carbon with two hydrogens on it; that would explain the integration of two. The fact that it's a triplet means it has a neighbor, [and] that neighbor has two hydrogens on it.

There is one other peak that integrates to two, so we must have automatically figured out which peak that is. We look at that peak: it is split into a triplet, which would match with the methylene that we just came from, but it's also got a doublet. A doublet means that it's got one individual hydrogen on its neighbor. We have three peaks that have an integration of 1. Which one would this [green] hydrogen be? The one with the doublet of doublet of triplets, because of the methylene group that we just came from. It has two neighbors on one side, so it has to have a triplet somewhere. The fact that it's a doublet of doublets meshes with this idea that the molecule is an alkene, because we've used up four carbons already, and the molecule only has six. We know that if there's a doublet of doublets, that means there is a neighboring carbon that has two different hydrogens on it.

There is another way to get two hydrogens, which is if they are somehow enantiotopic or diastereotopic, but even if they were enantiotopic, it would only matter in chiral solvents. Based on the degree of unsaturation and chemical shift, we're going to guess this is really a double bond that's here. Here's that [green] hydrogen that is split by the methylene group. We do have these two remaining hydrogens, but we don't have enough information to tell which of the remaining two peaks corresponds to which of the two hydrogens, cause they have the same splitting, the same integration, and virtually the same chemical shift. It is not always true that something cis and a lower chemical shift than trans, nor the reverse; it's more complicated than that. For them, they would have needed to have identified this much, and then whatever they said for the remaining hydrogens would have been OK. What's left? We've used up five of the carbons, and all ten of the hydrogens. We haven't used one carbon, we haven't used the oxygen. That's a carbonyl. Fits right in where the question marks [are], so that means the answer is this.

#### pKa values

Let me write down a sequence of compounds, including an ester – there's nothing special about these examples, I'm trying to make them as generic as possible to just get us a range for a pKa value – ketone, aldehyde, alcohol. Now, another sequence of molecules: a diester, a molecule that has two carboxylate groups on either end; versus an oxoester, a compound that has a ketone on one ester, [an] ester on the other; versus a diketone; versus an oxoaldehyde, one side a ketone one side an aldehyde; versus a dialdehyde. Let me indicate on each one of these compounds which of the hydrogens I'm actually worried about. [pKas: ketone, 19; aldehyde, 16; alcohol, 16] What is the origin of the difference in acidity between the ketone and the aldehyde? Hyperconjugation. I'm going to make a blanket statement that's going to be true in two different ways. The statement is this: the carbonyl stabilizes whatever enolate is formed, but if the carbonyl is distracted, you could say, by some other group next to it – to be less anthropomorphic, if something donates electron density to the carbonyl, then the carbonyl is less able to delocalize an enolate; if it's less able to delocalize, that means it doesn't want to form, if it doesn't want to form, that means the hydrogen doesn't ever want to come off, meaning it's not as acidic. A ketone has two alkyl groups on it, one on each side of the carbonyl. Both of those alkyl groups are able to undergo hyperconjugation. Hyperconjugation is electron density for the carbonyl, that means the carbonyl can't tolerate the enolate as well, which means the hydrogen doesn't come off as easily, which is why a ketone is not as acidic as an aldehyde, because an aldehyde only has one alkyl group that can undergo hyperconjugation, because the hydrogen on the other side is 90° to the pi bond and therefore can't undergo hyperconjugation – automatically less stabilization and automatically, therefore, the aldehyde is more acidic.

Based on what I just said, predict the pKa of the ester. Less than 16 for the ester? Why would you say less than 16; what would that mean about the ester? Both oxygens are really electronegative, so we have the one carbonyl oxygen that's pulling electron density away and, of course, it's delocalizing. But, even though oxygen's electronegative, it also has the ability to do resonance. What would resonance do to this carbonyl? It would make it harder for the carbonyl to tolerate the enolate. So, the oxygen's electronegative, but overall, it provides more electron density – more than hyperconjugation could, cause this is actual delocalization. So, if the difference between an aldehyde and a ketone was because of simply hyperconjugation, there's going to be at least that much difference between the ketone and the ester. There is, because the pKa is roughly 24 or 25. Resonance is both the answer here for why something is less acidic, but also for why in this next set of compounds something is more acidic. Resonance is making this less acidic, but resonance is making this more acidic. It's not a contradiction, because resonance is occurring even before the hydrogen comes off of an ester. It is not a good resonance structure that I'm about to write, because I'm taking a molecule in which everything formally has a neutral charge, and I am now generating something that has charge separation. If you have charge separation, that means you have a poorer resonance structure – but poorer does not mean insignificant. Poorer just means that's not the main way we would describe the structure of the molecule. But, there's charge that's delocalizing. Consider what would happen in this case: you've deprotonated and made the enolate; you still have the lone pair. Both of them are competing for the carbonyl. If you have something other than the enolate that is interacting with that carbonyl, it makes that carbonyl less able to interact with the enolate, making it less stable, making it less likely to form, meaning that it's not as acidic to start with. When electron density is provided to the carbonyl by either hyperconjugation or delocalization, the partial positive charge on the carbonyl carbon is reduced, meaning that delocalization of a neighboring negative charge is less likely or less favorable – meaning an enolate would be more difficult to form, meaning the corresponding alpha proton would be less acidic. This is due to hyperconjugation or resonance before the hydrogen comes off.

Look at this next set of compounds. We have two carbonyls, one on either side of the hydrogen, which means the hydrogen is double alpha. If being alpha is what caused these hydrogens to be acidic in the first place, what's double alpha gonna mean? They're even more acidic because of resonance.

We just got done saying that resonance made something less acidic; why is it now more acidic? Because the resonance doesn't even happen until that hydrogen comes off. There is no delocalization going on between the two carbonyls – well, there is, there's a tautomerization that is favorable for some of these compounds. But, if I take the hydrogen off, you then form a negative charge that then will delocalize. Because that delocalization only happens once the hydrogen comes off, then if you make it easier to delocalize, you make it easier for the hydrogen to come, which means you've made it more acidic. In all of these compounds, even the diester, they're more acidic than any of the compounds we saw before. [13, 11, 9, 7, 7, 5] The same trend as far as whether we have an alkoxy or an alkyl or a hydrogen group next door, that same trend of becoming more and more acidic from alkoxy to alkyl to hydrogen is present. For this group, resonance stabilizes the anion formed, so the alpha hydrogens are more acidic.

[lab directions; review for lab quiz]

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$$\text{DOU} = (2C + 2 - X + N) - H / 2$$

C<sub>6</sub>H<sub>13</sub>Br: delta 3.460, d, 2H; 1.45, t, quint, 1H; 1.427, dq, 4H; 0.895, t, 6H – no D.O.U.

Based on integration of 6, the molecule likely has two equivalent methyl groups (based on small # of atoms & the # of other peaks).

C<sub>6</sub>H<sub>10</sub>O: delta 5.79, ddt, 1H; 5.02, dd, 1H; 4.97, dd, 1H; 2.52, t, 2H; 2.34, dt, 2H; 2.149, s, 3H – 2 D.O.U.  
C≡C; C=O + C=C; C=O + ring; C=C + ring; 2 rings

This molecule likely contains an alkene, since:

- There are multiple peaks with delta ~ 5, each of which only integrates to 1.
- The alkene would be terminal, since that is the only way to have 3 individual hydrogens.

The compound also appears to have a carbonyl, based on the singlet that integrates to 3 with  $2.0 \leq \delta \leq 2.3$ .

- Resonance stabilizes the anion formed, so the alpha-H are more acidic.

When electron density is provided to a C=O by either hyperconjugation or delocalization, the delta + on the C=O carbon is reduced, meaning the delocalization of a neighboring negative charge is less favorable, meaning an enolate would be more difficult to form, meaning the corresponding alpha-hydrogen would be less acidic.

The presence of two C=O makes the circled hydrogens more acidic because more delocalization is possible after the H is removed.

If a C=O has electron density provided to it, it will reduce the delta+ on the C=O carbon. Since the ability to form an enolate depends on the C=O, stabilizing the C=O through either hyperconjugation or delocalization will make the enolate more difficult to form, making it less acidic.

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Structures – Identical to those from lab 3A (04/18/12)