Lab 3A • 04/18/12

[pre-lab for Robinson annulation]

Chem 12B Lab Quiz #2 NMR problems

Section 1 Problem 1 : C6H13Br – 3.460, d, 2H; 1.45, tquintet, 1H; 1.427, dq, 4H; 0.895, t, 6H

How many degrees of unsaturation do we have? Zero. Let's review what the way to determine the degree of unsaturation would be. There is a formula we could use, where we're going to compare how many hydrogens we should, versus how many we do have. When I say should have, we're talking about compounds that are fully saturated, which means no double bonds and also no rings. For simple compound, how do you figure out how many hydrogens there should be? 2C + 2 – the number of carbons you have, times two, plus two. But, we have to make certain adjustments for certain functioanl groups. Do we need to do anything for chalcogens like oxygen and sulfur? No, because they're divalent, so insertion of a chalcogen into a molecule doesn't change the hydrogen count, so oxygen and sulfur we ignore. What about halogens, though? We subtract one for each halogen, cause the halogen has to take the place of a hydrogen. What about pnictogens, like nitrogen and phosphorus? Then we add one. This first clump of numbers – 2C + 2 - X + N – is how many hydrogens we would have for a fully saturated compound. We then subtract how many hydrogens we have, and since a degree of unsaturation represents a pair of hydrogens, we're going to divide this whole thing by two. C6, that means we'd normally expect 14 hydrogens, but we have a bromine so it makes it 13, which we have 13, so no degrees of unsaturation – which means no rings, no double bonds or triple bonds.

What else do we have in terms of pieces of information? We've got several places we could start. You might recall we did see a sequence of small problems where we used degree of unsatuation or symmetry or chemical shift, some key piece of information that led to almost the entire structure being solved instantly. This doesn't necessarily fall into one of those nice categories, but there's several pieces of information that jump out at me. What looks like a really logical place to start? Symmetry? What leads us to guess that there might be symmetry in this case? 6H for integration. It is not possible to have a carbon that has more than four hydrogens on it, [and] the only case where you have four itself is methane. We obviously don't have methane, so the maximum integration we should have for any one type of hydrogen is three. The way that we can get six is only if we have equivalent neighbors, equivalent carbons somewhere on the molecule, which normally means we have a branch point, where the two branches are equivalent to each other. With an integration of six, the most likely guess would be that it's two methyl groups, because technically six could also be six equivalent hydrogens, but no way we're going to get that with only six carbons, not unless we have benzene, which we certianly don't in this case. Or, we could, in theory, have three equivalent caebons, each one with only two hydrogens; given, again, the limited number of carbons present in this compound, not verly likely. The most likely thing that we would have is two methyl groups that are identical to each other. Let's start with that.

Two methyl groups that I'll draw somewhat close togehter, because we're expecting that they're probably from two related chains. I'll throw some color coding on here. That purple hydrogen is corresponding to these six hydrogens. We get some other piece of information from that same absorbance; we see that it's a triplet. Why is it signicant that we have a triplet? What does a triplet mean? That next to each of those methyl groups, we have exactly two hydrogens. To briefly revisit the story of splitting: if we have some hydrogen that we're observing, it's going to have an energy gap that proportional to the overall magnetic field that the sample is put in. But, it can also be influenced by other atoms around it. Say, for example, there's a neighboring hydrogen that has a spin oriented the same way as the main magnetic field. From the perspective of that hydrogen that you're trying to scan, then, you're going to have a greater magnetic field, because its neighbor adds to the one that the entire sample is part of. If we had a neighbor instead that had a spin opposite the main magnetic field, then it effectively subtracts from that main magnetic field. When you have one neighbor, either possibility could occur, and statistically both occur, so where you only had one absorbance previously, you're going to see two. If you have two neighbors, that would make a split of the peak into three; if we have three neighbors, it splts the peak in to four. This is that (n + 1) rule.

The fact that we have a triplet – this is the point of telling the splitting story – means there are two neighbors. Which peak on here is going to correspond to the two neighbors? The one that integrates to four. [You might say] that since we have an integration of four, it makes sense that we have a quintet, but those hydrogens are also responsible for a triplet, because, compared to the methyl group, there are only of those hydrogens right next to it – yes, there's another two of them, but they're next to the other methyl group. Since only two hydrogens are interacting at one time with methyl group, that's why it's split into a triplet, even though the integration is four. Notice that, even though we have an integration of six for these methyl groups, these two hydrogens are themselves only split into a doublet of quartets; I'll circle these blue, and it's going to correspond to those four hydrogens. The quartet of those hydrogens comes from the two methyl groups; again, since only one methyl group is next to each of those pairs of hydrogens, that's why, even though in total it integrates to six, indiviually, you only have splitting into a quartet.

Where can we go from here? We look at these blue hydrogens, the ones that we just identified are split into a quartet. Those four hydrogens, again, correspond to a triplet, but those four hydrogens also have a double. What does the doublet mean? That yes, we have a neighbor here, but we also have a neighbor on the other side of these methylene groups; that neighbor can only have one and exactly one hydrogen on it. If you're really sharp, you'll realize that means the structure of the compound is the following; why? Because, there is only one peak that integrates to one; if we have a doublet, it means we have to have one of two possibitiles: either both side chains have that doublet – which means we need something that integrates to two, and we do have something that integrates to two, but it only itself is split into a doublet, which wouldn't match the fact that we've got these two hydrogens as neighbors; we also can look and see that the two side chains, we've alredy made four carbons, we've used up four carbons of only six that we have. At some point, we need to join these two side chains together, which, as you can see, if we do that through a commnon carbon, there'd be only one carbon left for the whole compound, [so] I've written that down. There's only room for one hydrogen, which matches the splitting pattern. That one hydrogen is responsible for the doublet of the blue hydrogens; it also would split the remaining carbon's hydrogens just into a doublet. The green on I just circled, it has the blues as neighbors, which not all four of them are acting at the same time, so we would end up with a quintet. There are two remaining hydrogens next door that would cause the triplet. We've identified all of the hydrogens. This makes sense in terms of chemical shift. Bromine is the only electronegative element on this compound; the hydrogens closest to the bromine are the highest chemical shift. The next highest hydrogens are the ones a little futher away, and so on and so forth. The answer is this. [through space effects]

Section 1 Problem 2: C6H10O – 5.79, ddt, 1H; 5.02, dd, 1H; 4.97, dd, 1H; 2.52, t, 2H; 2.34, dt, 2H; 2.149, s, 3H

How many degrees of unsaturation [do] we have? Two degrees of unsaturation. Given we do have one oxygen, it means we have the following possibilities: we have a triple bond and either an alcohol or an ether; we have a carbonyl and a carbon-carbon double bond; we have a carbonyl and a ring; or we have a carbon-carbon double bond and a ring; or we have two rings. [eliminating alkynes only because we didn't discuss them] Is there any information there that seems to give us a hint as to whether we might have a ring or a carbonyl or an alkene? Any one of those three things, do we see evidence of one of them here? Is there ever going to be direct evidence that we have a ring? No; there's nothing that's going to jump out and say automatically: oop, this is a ring; that we figure out through elucidation, through solving the problem. Do we have any information that could tell us right away that we have a carbonyl? Maybe. There would be a better situation that would more obviously tell us that we have a carbonyl, which would be if we have an aldehyde. Why are aldehydes so easily identifiable? High chemical shift – 9 or greater; they're one of the few functional groups, other than carboxylic acids, that even have a chemical shift that high. But do we have something as high as ten or nine; no, so we don't have an aldehyde. What about ketones? Ketones don't have hydrogens directly on the carbonyl, so they won't have a chemical shift that high. [What is the chemical shift for the alpha hydrogen of a ketone?] Usually between 2.0 and 2.3. Do we have anything in the 2.0 through 2.3 range? Yes. In fact, we have a singlet, which the significance of that singlet we'll come back to. It's a clue that maybe we do have a carbonyl. But, other functional groups can have chemical shift in the 2 range, so when we revisit that singlet, we'll understand why that broadcasts to me the possibility of a carbonyl.

Do we have any firm evidence of an alkene? Yes, because few functional groups have a chemical shift in the range of 5.8. It is a little risky automatically assuming an alkene, because it's not totally impossible to have an oxygen group that would make the chemical shift that high. But, there's two other pieces of evidence that would go along with it. What other evidence do we have that we have an alkene? Three separate neighbors: doublet of doublet of triplets. We've never seen a situation like that before. Even though that's a good clue, that by itself doesn't automatically make it an alkene; I'll show you just as an aside here a molecule where we'll end up with doublets of doublets of triplets. The hydrogens I've written out in this compound, none of them are equivalent to each other; that means that the hydrogen in the middle here will be split into a doublet of doublet of triplets. So, there's no double bonds there, but you can generate triple splitting. But, the chemical shift being greater than five, along with that complex splitting, along with the fact that we have three hydrogens that all integrate to one. When you see all three hydrogens having a chemical shift greater than five, and integrating just to one, and having complex splitting, all that put together screams alkene, screams terminal alkene, because a terminal alkene's the only way we can get three individual hydrogens.

What if we weren't sure still? Can we solve this structure just looking at integration and splitting? Let's try.

Given that there are three different hydrogen, each with a chemical shift greater than five and each with complex splitting, the molecule likely contains a terminal alkene.

If we weren't sure of that still, there is a way to it systematically. When you're totally lost in an NMR problem, some of the places I suggested to start at the following: places where you have an integration of three, because very frequently that means you have a methyl group. If you have a methyl group, that means you can start at one end of the molecule and try to solve your way to the other end of the molecule; sometimes that makes it easier. If you don't have an integration of three, then I recommend starting with peaks that only have one kind of splitting; we've got two of those here: we've got a singlet, and we have a triplet. When you only have individual splitting like that, that means there's only one type of neighbor [except in cases of symmetry]. In the case of a singlet, that means there's no hydrogens on any neighbor; that's a special case.

Recall that if you have a singlet, that can occur if you have a ketone, if you have an ether, or if you have a quaternary carbon. All three of these examples, the circled methyl group will be a singlet because its neighbor has no hydrogens.

Let's take that last peak – the singlet that integrates to three – cause what that means is we have a methyl group that is connecte to something; we don't know for sure yet what that something is, but we know that there's no hydrogens on that neighbor. Let's look at the next peak over, the one above it, the one that's just a triplet. If you have a triplet that integrates to two, then here's what that means: you have two hydrogens – that's what integration of two means. The two hydrogens are a triplet; a triplet means you have two neighbors. There is only one other peak that integrates to two, so we know which of those two neighbors they are. Since that carbon – the one that was in blue – the hydrogens on that position, there's only two of them, there's only a neighbor with a triplet, but a carbon has to have four bonds. That means there's again something on the other side that is preventing splitting from occurring, which again the possibilities I've shown up above are a carbonyl, an ether, or a quarternary carbon. I've already suggested there's some chemical shift evidence for a carbonyl, cause there are chemical shifts of 2.1, 2.3, which would be in the range for a ketone's alpha protons. But let's continue working first before we try to guess what might that question mark might be.

Since we now know the neighbor, that there's two hydrogens there, we can see what it's splitting is: it's a doublet of triplets. The triplet matches the fact that we just came from those blue hydrogens; the double means that there's a carbon that only has one hydrogen on it. We have three groups that integrate one: which of the three groups would correspond to this red hydrogen that I just circled? Why the first one? We have a triplet, and triplet corresponds to two neighbors, the two green hydrogens. What else could we learn from that peak? It's a single hydrogen; there can't be any other hydrogen on there. We could try to put an oxygen on there, but that's going to change it's chemical shift, and it's also going to change why type of functional group. At this point, if we go back and make our assumption that there's an alkene, that would fit perfectly right here, cause that would leave us with just one hydrogen where I've circled the red hydrogen. There would only be two more hydrogens left, and those two would not be equivalent to each other, because the double bond permanently locks one hydrogen closer to the red circled hydrogen than the other one would be.

What you could not solve with the information I've given you is which one of those last two hydrogens corresponds to which of the last two peaks, cause they're both an integration of one, they're both doublet of doublets, and they're both almost the same chemical shift value. When something is cis versus trans, there's not always a clear trend of how that translates into chemical shift changes, so you wouldn't have been able to solve that much of the problem. But, look at how many carbons we've used up: five; there's only one more carbon left. Look how many hydrogens we've used up: ten; that's all of the hydrogens. The only thing we haven't used, then, is that single carbon and an oxygen, which means we have a carbonyl, which means this is the answer.

[why not a singlet of triplets? the only time you have a singlet is when you have no splitting, period] What you're trying to say is: there's zero neighbors on this side, so shouldn't we say singlet? No, because you can't see a singlet, because it's a singlet. The two neighbors that split it into a triplet, each one of those peaks, if you split into a singlet, it's still just a triplet, just like three times one is three, so we don't put in the one, we don't put in the singlet, because it doesn't mean anything.

Alpha protons

A smørgasbord of pKa. We know a few of these values already. [pKas can vary by reference; aldehyde – 16.7 listed as 16 or 17] Aldehyde – 16; alcohol – also 16; ketone left of the aldehyde – 19. Why is the ketone pKa 19, instead of the aldehyde's 16? What is different structurally that causes a difference in the acidity of those compounds? This ketone has two alkyl groups on it, each of which can hyperconjugate with the carbonyl's carbon. Hyperconjugation means the partial donation of electron density to some kind of neighbor. If you're giving electron density to the carbonyl carbon, you're making the carbonyl carbon less positively charged. When you form an enolate, the enolate tries to delocalize with that carbonyl. If you have already satisfied the carbonyl's carbon, that means it has less of a likelihood to react, to try to delocalize a negative charge next to it.

Use the same logic and predict whether the ester's alpha proton is going to me more or less acidic than the ketone even. Less acidic, higher pKa; it has a pKa of 25; why? This alpha hydrogen is less acidic than that one. Hyperconjugation is only a partial donation of electron density; delocalization, resonance, that's a much more robust donation of electron density. Another way to explain this: that even before anything happens, in terms of acid-base reaction, there's already delocalization possible. As we can see, it's not going to be the most favorable thing, because we do separate charge; when you separate charge, that makes for a poorer structure – poorer, but not impossible, and not something that can be totally ignored, either. There is some delocalization going on. If that delocalization is going on, now imagine this situation: we deprotonated the ester to make an enolate. Now we have both a negative charge and a lone pair, both of them competing to do resonance with that carbonyl. In the case of the aldehyde and the ketone, yeah, there was hyperconjugation, but there was nothing resonance-wise that the anion would have to compete with. Stabilizing that positive charge of the carbonyl makes the carbonyl less able to tolerate a negative charge next to it, which means the negative charge won't want to form as much, which means the hydrogen won't want to come off, and that means it's less acidic. I said the same thing with the difference between an aldehyde and a ketone, but the operative word there was hyperconjugation; for the oxygen, it's delocalization, it's resonance.

If a carbonyl has electron density provided to it, it will reduce the positive charge on the carbonyl carbon. Since the ability to form an enolate depends on the carbonyl, stabilizing the carbonyl through either hyperconjugation or delocalization will make the enolate more difficult to form, making the compound less acidic. Conjugation, delocalization, much more donation of electrons than hyperconjugation; that's why there's a more dramatic effect, that's why esters are less acidic than ketones.

We have one other sequence of compounds; notice the thing that distinguishes them from the first set of compounds: they all have two carbonyls. I just got done explaining how resonance can make something less acidic; for these dicarbonyl compounds, they're more acidic, but it's because the resonance is doing a different job. In the case of an ester, you have resonance even before the acid, base reaction occurs; that resonance stabilizes the carbonyl, makes the compound less reactive. In these other cases, there is no resonance going on with where the middle hydrogen is located. These all differ by whether we have a methoxy, a methyl, or a hydrogen at the end, but just look at the interior, where that hydrogen is that's circled. No resonance goes on there – until the hydrogen comes off. Once the hydrogen comes off, then because we have resonance, that makes it easier for that anion to have formed in the first place, which means that hydrogen is more acidic. All five of these are more acidic than a plain aldehyde. [pKa values somewhat rounded] Notice the same patterns: where we have methoxy groups on the carbonyl, it's less acidic, because the oxygens are undergoing resonance. Where we have methyl groups, it's less acidic, because we have hyperconjugation. Where we have the dialdehyde, the most acidic, because there's the least stabilization of all. Realize that that aldehyde is almost as acidic as acetic acid – acetic acid, pKa 4.75. It will do resonance with both, which is why all of these are more acidic than a compound with only one carbonyl. The presence of two carbonyls makes these circled hydrogens more acidic, because more delocalization is possible after the hydrogen is removed. Here, after it's removed, since it stabilizes the anion formed, that's why it makes these more acidic, and, in the ester case, because there's stabilization before the hydrogen's removed off, that why it's harder to remove, and that's why it's less acidic.

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DOU = (2C + 2 - X + N) - H / 2

C6H13Br: delta 3.460, d, 2H; 1.45, t, quint, 1H; 1.427, dq, 4H; 0.895, t, 6H – no D.O.U.
Integration of 6 –> symmetry; most likely two equivalent methyl groups

C6H10O: 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

Given that there are 3 different hydrogens – each with delta > 5 and each with complex splitting – the molecule likely contains a terminal alkene.

The presence of two C=O makes the circled hydrogens more acidic because more delocalization is possible after the H is removed.
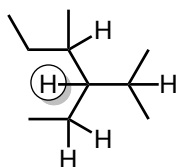
If a C=O has electron density provided to it, it will reduce the delta+ on the C=O carbon. Since the ability to form an enolate depends on the C=O, stabilizing the C=O through either hyperconjugation or delocalization will make the enolate more difficult to form, making it less acidic.
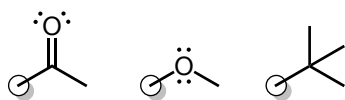
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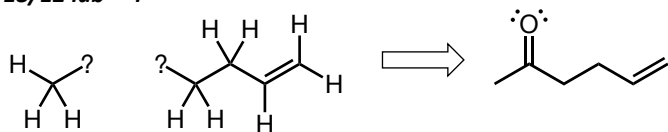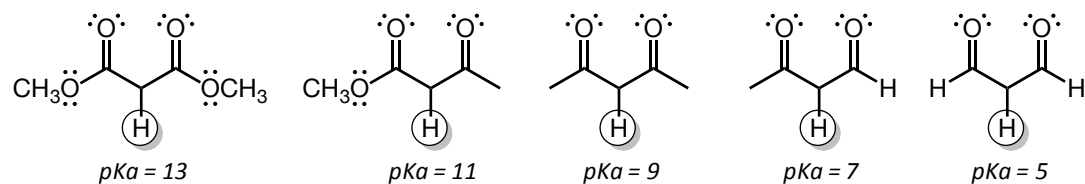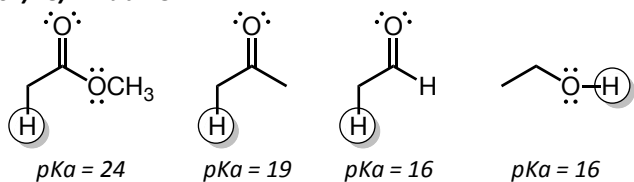
04/18/12 lab • 1
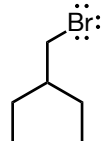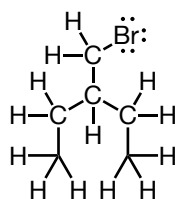
04/18/12 lab • 2

04/18/12 lab • 3

These methyl groups are singlets since their neibhbor has no hydrogens.

04/18/12 lab • 4

04/18/12 lab • 5

pKa = 24   pKa = 19   pKa = 16   pKa = 16

pKa = 13   pKa = 11   pKa = 9   pKa = 7   pKa = 5

04/18/12 lab • 6

04/18/12 lab • 7