

Lab 12A • 11/09/11

Chemical equivalency

How many different types of hydrogens are there on this compound, 2-methylbutane? The way we can figure that out is to imagine that we put something like chlorine at each carbon, and we can decide whether or not that's going to generate a unique compound. In general, if we have two atoms that we say are chemically equivalent, that means if you go from either atom that you're comparing and examine the structure, the whole molecule relative to where that atom is positioned, if when you compare two atoms and they have exactly the same neighbors and then neighbors of neighbors and so on and so forth across the molecule, then those two atoms are chemically equivalent, they are identical. If the chemical environment around two atoms is identical, meaning that the neighbors for both atoms are identical across the whole molecule, the atoms are chemically equivalent. The reason that's important for NMR is that, other than some exceptions that we'll talk about, every chemically inequivalent hydrogen or carbon, every one that's not the same, generates its own signal. A unique NMR signal is generated for each unique type of atom.

If we find four different kinds of hydrogens, in principle we're going to find NMR peaks. Later, we'll discover that if the environments are incredibly similar, that maybe you won't be able to distinguish them by NMR, but, technically, if they're inequivalent, they're inequivalent. Let's look at this example molecule and let's identify the different types of hydrogens that are on here. One way we can differentiate between the different positions on this molecule is just to focus on the fact that we have primary versus secondary versus tertiary carbons. I can identify right away that I have this tertiary hydrogen, which is definitely going to be different in nature than a secondary hydrogen. But then we have three methyl groups, three ends of the molecules. Are all three of those the same? Are any of them the same as each other? Let's say I start here; if I see what its neighbor is, it's a tertiary carbon; if I look at the methyl group up above it, it also has the same tertiary carbon as its neighbor; on top of that, since they are joined at the same branch, the rest of the molecule's structure is identical for both of those of atoms; because their immediate neighbor is the same, and because therefore the rest of the molecule is the same, those two methyl groups are chemically equivalent. But, if I look at this other position, this methyl group, it has as a neighbor a secondary carbon, not a tertiary carbon. That's going to have a chemical effect, it's going to have a different kind of reactivity. Related to NMR, that means it's going to have a different magnetic environment. So the methyl group on the righthand side of the molecule is not the same as the methyl groups on the lefthand side of the molecule. Put a chlorine on one methyl group versus another, you'd get two unique products, which means they were two different hydrogens to begin with. If I put a chlorine at either of the lefthand methyl groups, though, the two products would be identical, which means the hydrogens were identical. The reason we care about this is if I identify four different kinds of hydrogens, that, in principle, means that I'm going to have four different NMR signals when I analyze this compound.

Now let's see a slightly more complicated example. Another molecule that's not totally symmetric. The reason I'm showing you this example is that it's not the immediate neighbor alone that matters, but it matters all up and down the molecule. If you go from the two positions that you're comparing, if you find any differences as you travel the paths, that means they're two different atoms. For example, the two methyl groups on the left and the two methyl groups on the right. If you weren't paying close attention, you might say that all four of them are exactly the same, because all four of them are connected to a tertiary carbon. But are those the same tertiary carbons? Because look one more position away. On the lefthand side, that first tertiary carbon's located next to another tertiary carbon, but on the righthand side, that tertiary carbon's connected instead to a secondary carbon. Since these junctions, these tertiary carbons, are not the same as each other, anything that's attached to them is automatically not equivalent either. You can start from the lefthand methyl group, I could go to carbon with a chain and a methyl, carbon with a chain and methyl group; from the other side, I get to carbon with a chain and a methyl group, then I get to something that just has the rest of the chain, no methyl group there. From either side of the molecule, those are different hydrogens.

Back to what we had in the first example, since these two methyl groups on the left are attached to a common point, these two are equivalent to each other, because you would get the same exact structure if you started from either point. This one is not identical to that one, but it is identical to this one. Let me mark out all the different types of hydrogens on this molecule. We have the methyl groups on the left – realize I'm only writing in one of the hydrogens that might be at these different positions – then we have the tertiary position, we have the next tertiary position over, we have the methyl group attached at that point, which is unique, we have the secondary position, we have the next tertiary position, and then we have the last type of methyl group. So, there are seven different types of hydrogens in this molecule, so in theory we're going to get seven different signals.

This is the simple case of what causes things to be inequivalent – by having primary versus secondary or functional groups around. If I put an –OH group right here, now the two methyl groups would no longer be the same, cause one has a functional group, one doesn't. But there's a sneakier case of how many equivalent hydrogens we have or don't have, which is this: what do you think is the number of different hydrogens on here? Five? The oxygen has a hydrogen its own self, doesn't it? That hydrogen counts. Let's label that as one of our hydrogens, then. We have a methyl group on the left; is it different from the methyl group on the right?

Yes, because the one I just wrote a hydrogen for is only one position away from the –OH group, the other end of the molecule is two positions away, so they're definitely different from each other. There's the hydrogen where the –OH group is located; and then we have one more carbon that has two more hydrogens. But notice the note I just made below here: they're not equivalent to each other. Five is a correct first guess; but why is the answer really six? Why are the two protons at what I've labeled as He not the same as each other? It might help if I draw a rotamer. Now the way I've drawn it, could you come up with a reason why those two might not be the same as each other? The –OH group is closer to one of the hydrogens than the other. If you have an electron-withdrawing group nearby, it's going to pull electron density away and cause a higher chemical shift. One of these two hydrogens is pointed the same way as that –OH group, and it's going to be closer to the electron withdrawing effect of oxygen. Even if it's not through the bond, there are what are known as through-space effects – that electron density can be pulled even if it's not along a bond. The other hydrogen, the one written with a dash, pointed away from the –OH group, further from the –OH group, close enough that the oxygen's still going to have a big inductive effect, but further away, so it is a different effect than the proton that is pointed the same direction. Because, in space, if you could stop that molecule just for a moment can keep that orientation the same, one interaction with hydrogen and the –OH group is different than the other hydrogen and the –OH so they're not chemically equivalent.

The interactions between the two indicated hydrogens – meaning the two hydrogens I wrote in – are different, since the two hydrogens are different distances from the –OH group. Therefore, the hydrogens are chemically inequivalent. There's a term that can be used in general to describe exactly this kind of situation. Let me tell you where this term comes from and then relate it back to what's physically going on. We had something like this chiral alcohol, and let's there was some kind of process that occurred (magic). I'm going to replace one or the other of the hydrogens at that secondary position with some mythical functional group, which I'll call Z. I've taken one molecule and turned it into two different whats? What is the relationship between the two molecules I just wrote? Diastereomer, because I've only changed one of the two stereocenters on this molecule. Because of that, these are called diastereotopic protons. What term means is: if you replace either of the hydrogens, you're going to generate diastereomers. If, by replacing one hydrogen with another, a pair of diastereomers is formed, the hydrogens are called diastereotopic. Because we have this different interaction of the chiral center that really is there versus its neighbor – that's why this term diastereotopic matters. It's not that somehow magically a reaction is going to happen; no reaction's really happening, we're just talking about a structural relationship. That relationship is exactly the fact that, in this example molecule, the two neighboring hydrogens are different distances from the –OH group. Because any time that you have diastereotopic protons, you would have that potential difference of behavior, diastereotopic protons are always chemically inequivalent.

[There is also the term] enantiotopic. If we had something like plain old butane, if I asked you how many different types of protons are on that molecule, what would the answer be? Two? Is the molecule symmetric? Yes it is. From one end of the molecule versus the other, would you get the same structure if you walked along the molecule either direction? Yes. But we do have a secondary versus a primary carbon, so they are two different positions, so normally, yes, we would say there are two different types of hydrogen. But it actually depends on what solvent you're in. Let me write out what the term enantiotopic means. Enantiotopic means that if you replace one hydrogen versus another and you end up making enantiomers, they're called enantiotopic. If by replacing one hydrogen versus another a pair of enantiomers are formed, the hydrogens are called enantiotopic. Why would it matter? If you started out with something that's achiral, who cares if it has the potential to be chiral if it was substituted? It's not that we're really going to substitute it; it's trying to get a particular structural relationship. Here's the relationship, except this case we're not going to compare two things on the same molecule; I'm going to take butane (I'll write out two of its hydrogens) and now let me examine its interactions with a chiral molecule.

Let's say [butane] is dissolved in this chiral form of butan-2-ol. In this particular interaction between these two molecules, now the –OH group would have a different interaction with a hydrogen on a different molecule, versus the hydrogen in back, which would have a different interaction with the hydrogen that's in back. Another way of looking at it is this –OH group, when oriented with butane the way it's being written, will be closer to one hydrogen of butane than the other. That means, for that moment that the molecules are interacting that the hydrogens are no longer equivalent to each other, because of the molecule they're interacting with. Take the alcohol away, they go back to being equivalent again. Enantiotopic protons are chemically equivalent in achiral environments, but they're chemically inequivalent in chiral environments. Since most of the time we're going to use achiral solvents, enantiotopic protons are normally chemically equivalent.

There is one more case, the simplest case, where no matter which hydrogen on the position you might replace, you always get the same molecule, which means there's no possibility that, by the different hydrogen that you substitute, you're going to generate different interactions. This is what would be true for a methyl group, for example. Even on a chiral molecule, if we have something like the methyl group I'm pointing to on the righthand side, it doesn't matter whether you replace on or the other or the other of those three hydrogens with some mythical group Z, you'd get the same molecule. No matter which of the hydrogens at the end of this molecule are replaced, the exact same product would result, meaning no stereocenter is formed. Therefore, the three hydrogens at that position are entirely equivalent, so they're called homotopic protons, homo meaning the same – the same result comes from substituting any of those hydrogens. Because it doesn't matter which one that you substitute, you always have the same structure that results. It doesn't matter if you're in an achiral environment or a chiral environment, there'll be no difference in interaction. Homotopic protons are always chemically equivalent.

Just one more problem in terms of chemical equivalency to think about today. Cyclohexane. How many different types of protons exist in cyclohexane? Two. Why? Axial versus equatorial protons, correct. But if you examine this compound at room temperature, you only get one NMR signal. In an NMR spectrum, remember that the y-axis is intensity, chemical shift starts at zero on the right, increases towards the left. At room temperature, you'll see a signal; below room temperature, that'll turn into a sort of broader signal. Way below room temperature, it starts to resolve into two different peaks; way, way, way below room temperature, you'd actually get two distinct signals. What do you think's going on here? Why would it only look like one type of hydrogen at room temperature but two types of hydrogens show up below room temperature? Ring flips. Ring flip is just changing from one conformer to another, isn't it? If you played with your molecular models, you know that to do a ring flip, all that you're really doing is making different rotomers; you're just twisting different single bonds. If you drop the temperature low enough, there's not enough energy to allow the single bonds to move; they're frozen, almost literally, in position, there's not enough energy for that twist to occur. So they cyclohexane ring isn't flipping back and forth, you'll have axial protons that are always axial, equatorial protons that are always equatorial, and two axial protons have a different interaction with each other, what would lead to a steric interaction if you put any kind of substituent there, versus if you have an equatorial hydrogen that's pointed away from everything else. Way below room temperature, the ring flip isn't possible, and so you can distinguish the axial versus equatorial interactions. But at room temperature, the flip is happening so quickly that the machine, by the time it acquires the information, the molecule's already wiggled, already flipped a few times, and so you end up getting an average of the two signals. This is a problem with spectroscopy call the time scale problem, where if what you're doing to scan takes longer than what the molecule itself is doing, you won't see it. This is a very classic example of that. At room temperature, ring flips are occurring rapidly enough that the two types of hydrogen – axial and equatorial – cannot be distinguished, so only one averaged signal results. Far below room temperature, the ring no longer flips, and so the two hydrogen types can be distinguished. Besides being an example of this time scale issue, it's also an example of how, just because you identify a certain number of inequivalent protons, it doesn't always mean you're going to see that number of signals in your spectrum.

Chemical equivalency

If the chemical environment around two atoms is identical – meaning that the neighbors for both atoms are identical across the whole molecule – the atoms are chemically equivalent. A unique NMR signal is generated for each unique (chemically inequivalent) type of atom.

The interactions between the two indicated hydrogens are different, since the two hydrogens are different distances from the OH group. ∴ The hydrogens are chemically inequivalent.

Diastereotopic – If, by replacing one hydrogen versus another, a pair of diastereomers are formed, the hydrogens are called diastereotopic. Diastereotopic protons are always chemically inequivalent.

If, by replacing one hydrogen versus another, a pair of enantiomers are formed, the hydrogens are called enantiotopic. Enantiotopic protons are chemically equivalent in achiral environments and chemically inequivalent in chiral environments.

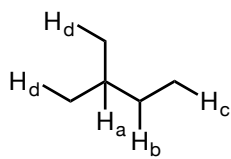
No matter which of the hydrogens at the end of this molecule are replaced, the exact same product would result (no stereocenter is form[ed]). Therefore the three hydrogens at that position are entire[ly] equivalent → homotopic. Homotopic protons are always equivalent.

@ RT, ring flips are occurring rapidly enough that the two types of hydrogens cannot be distinguished, so only one averaged signal results.

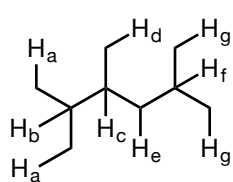
Far below RT, the ring no longer can flip, so the two types of hydrogens can be distinguished.

Structures

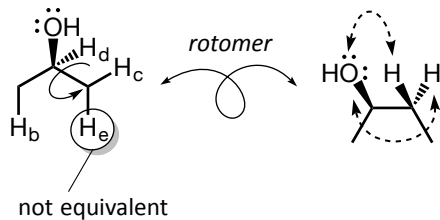
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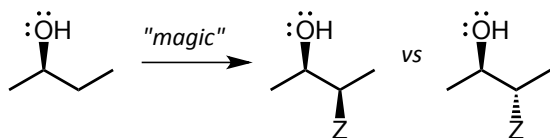
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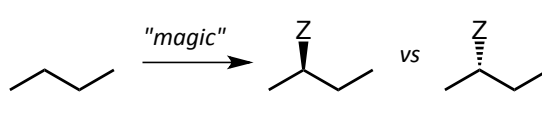
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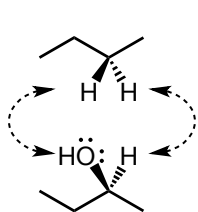
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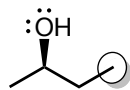
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