

Welcome to an NMR tutorial focused on electronic and magnetic effects with a healthy dose of some pretty odd multiplets. So far, I have shown you plenty of nice, well-behaved spectrum. Also some that are a little bit confusing. rotamers and atropisomers. Those signals originate in the shape of the molecule, and the timescale of the measurements. Let's talk about some have some slightly different roots. So if you've made 1,4-substituted aromatics before, you've probably seen this complex structure, and you may have observed that it's hard to measure any J values. You shouldn't try, and we'll talk about why. But this is a pretty common observation. We're going to see some peaks that are a great deal more complicated than you would initially expect from the molecule. On some peaks with pretty odd shapes. What this is feeding into is: does my spectra look as expected? Well, if it doesn't, is that the wrong compounds or is something more complicated going on? So we've got to start with the idea, really, of magnetic equivalence. So we're all used to the idea of chemical equivalence. In these isomers of dichlorobenzene here, all of the 'a' protons are equivalent to the other 'a' protons and the b's are equivalent to the other 'b' proton. And this is because if we rotate the molecule, they would be equal to one another, they couple to equivalent, chemically equivalent nuclei. So you'll notice that although the couple to nuclei that appeared equivalent, we don't actually coupled to the same nuclei. So Ha, coupled to Hb, Ha prime, which couples Hb prime. This means that these are magnetically inequivalent. So these protons are in fact, not magnetically identical, although they are chemically equivalent. Same is true in the 1,2 isomer - 'a' will couple to Both 'b' signals.

As can 'a' prime, However, the relationships are different, the J values for h 'a' prime to 'b' prime are different to those from ha to hb prime. By contrast, if we take the 1,3 isomer, so we could have a line of symmetry through here. Hbs are in fact magnetically equivalent as well as chemically equivalent. You can see they were both couple in equivalent fashion to Ha and to Hc. All of the nuclei that are magnetically equivalent are chemically equivalent, but not all nuclei that are chemically equivalent. are in fact magnetically equivalent. You can see here, this is difluoroethylene. And you'd think at first glance, that these two protons are equivalent - and chemically they are. However, each has a different coupling relationship to each of the two fluorines. So this is not the same as that. And these protons are thereforw magnetically inequivalent. If we instead to take try trifluoroethane: In this case, rotation around this bond is sufficiently quick that The relationship of each proton to each fluorine averages out to be the same over the course of an NMR experiment. So in fact, these protons are magnetically equivalent. One way to think of this is that if we draw where our lines of our axes of symmetry are for these dichlorobenzene analogues, We can see that although they all have lines of symmetry, these two, the 1,4, and 1,2 isomers those lines of symmetry are through bonds, it is only in the 1,3 isomer where everything is magnetically equivalent that you can see this plane of symmetry is through the nuclei to which each of our signal couples Before moving on, I wanted to spend a little bit of time on nomenclature. Now.

I know that nomenclature is deathly boring. Chemistry nomenclature is even more boring than a lot of other of nomenclature. That said, you will hear these descriptions, and it is worth understanding what people mean when they quote them. So spin systems can be classified by the number of distinct spins. Or Chemical shifts. Now, there is one lengths are given for each chemically inequivalent spin in the spin system.. And the alphabetic distance between the letters denotes the chemical shift difference. To give you an example, phosphorus and hydrogen here have very different chemical shifts, but they are coupled to one another. This would be an AX system, part of the same system because they're coupled but their chemical shifts are very different. If you go back to this old example here, these two diastereotopic protons are coupled to one another, they are different. But their chemical shifts are not very much different. And so this would be an AB system. Now the letters used are comprised of three pairs. So typically AB, M and

N, and X and Y. You can have more than two in a system, so for example, here we have an AMX system, the M denoting the nuclei that is sort of in-between the very far away and very close in terms of chemical shifts. And in this example, we have a chlorobenzene. And having that on one face makes A and M sufficiently different that you label them as A and M. And then you have an additional coupling for both to X. So this is an AMX system. If we then take away that phenyl ring and just have a chloro substituent, in this case A is less influenced and A and B are closer in chemical shift. And this is an ABX system. In addition to the lettering based on chemical shift, we also add primes to denote magnetic equivalence. So here we have a system, a difluoromethane system. The hydrogen atoms are always equivalent to one another on the Fs, B, are always equivalent to one another. You could call this A₂X₂ if you preferred. By contrast, if you take our difluoroethene system, symmetrical through here, And in fact the coupling of those nuclei are different. So again, we have a different coupling pattern. Different set nuclei being coupled to for each proton. And as a result, these are A₂, They are magnetically inequivalent. So this is an A, A prime. Then fluorine shift is very different, but they are also inequivalent for the same reason, So X, X prime system. And here we can see again our dichlorobenzene 1,2 dichlorobenzene example. And for the same reasons we discussed earlier. A couples to these two Differently.

To the way A prime does, magnetically inequivalent. Depending on the size of the chemical shift, This could be an A, A prime, BB prime system. This is probably an AA prime BB prime system. However, if we were to look at the 1,4-chloronitro analogue, nitro has a larger effect on a chemical shift. And A and B or X is more different. And so this might be instead called an A, A prime X, X prime system. The reason for doing all of this labeling is to allow generalized observations. So we can talk about spin systems in the abstract. So our magnetically inequivalent nuclei are chemically equivalent, They have identical shifts and patterns and they're going to be on top of each other. Is this distinction, more than pedantry? Unfortunately, yes it is. Because these nuclei are not identical. They can coupled to one another. This causes something called second-order effects. So you will observe that may signals are more complex. than the rules we've seen so far would suggest, I'm talking about complex signals and incorrect J values like the aromatic peak we started with. Now often these are due to a phenomena called strong coupling, which causes second-order effects. Now this is seen where the difference in chemical shift between coupled signals converges on the J value. And typical effects are roofing and additional lines. So here is our Difluoroethylene spectra As you can see, it is a lot more complicated than the nice singlet you might expect to see. And in this case, this is our AB system because these are rather close to one another, the J value is actually quite large. You can see that these doublets are sloped. Some, but not all, second-order effects are dependent on magnetic field strength. So let's start with the first, The more useful of the phenomenon that I just mentioned. This is the slanting - this is usually quite helpful actually. As the chemical shifts of coupled protons converge, the closer line in each signal to the other gets stronger, and the further line gets weaker. And this creates a slanting effect where they slant towards one another. And you can use this to identify coupled signals. So if we take a series of epoxides, in this case, we have this absurd huge charged heterocycle coming out of the front face. And this has really quite a big effect on this proton. And its chemical shift is quite different to that observed for this other green proton here. As a result, these are very far apart. And you see only the slightest tiny bit of slanting, Perhaps. We then reduce that size to a phenyl group. This has a smaller effect on the proton on this face. And you can see the signals coming closer together.

Incidentally, I should mention that each of these is showing up as a doublet as a doublet of doublets coupled with each other and to this proton here. So you can start to see the beginning of the slant here. I should mention that because we have a sequence of doublets, so this is one doublet, and this is another doublet. together they form a doublet of doublets, you can see the slanting pattern repeated

in each doublet. So if we then make this group smaller still, we go to a chlorine. You can see very clearly that we have a pretty serious slant. We're, we would be able to tell these are coupled based on this.

A bit further still and we go to a borane system. In this case, we're starting to see other second order effects. The shape of the signal is being distorted somewhat by the second-order effect. But even so, you can still see the slant although I would suggest, I'm maybe not measuring the J in this case. And finally, we have a special non-coupling fluorine, just for simulation purposes. And in this case you can see there's a very significant slant. And in fact, the signals are overlapping and starting to produce something a bit different. Now I mentioned the dependence on field strength. J values, coming from coupling between nuclei, are dependent on the properties of those nuclei - The overlap that allows them to effect one another. They are actually independent of field strength, so they come from the properties of the molecule. Now, you're used to seeing spectra in a format where chemical shift is displayed and this is also independent field strength. However, chemical shift is a useful normalization tool we employ, where we essentially normalize out the difference in frequency. What your NMR spectra actually measures for the nuclei, is the frequency. And the frequency is not independent of magnetic field. And it is the frequency differences, not the chemical shift differences, which actually denote the difference between the signals. And the way this shows up in your spectra is that you will see the standard chemical shift. But if you were to actually look, the frequency range contained within one to two ppm is different on a 400 megahertz spectrometer to 100 megahertz spectrometer. So it'll be four times greater. The effect of this in terms of what you practically see then is that your signals are narrower and chemical shift terms on higher fields spectrometers. And so the frequency differences between signals are larger, but the J values are the same. This means that if nuclei are chemically inequivalent Increasing the field strength is likely to increase the chemical shift difference. So they will converge less often on the J value and you will get less second order effects. And I think it's easier to show this illustration. So here we have our chloroepoxide example. And this is the same signal. It is simulated from 60-1000 megahertz. We can see at 60 megahertz We end up with a strange, fairly complicated signal. And it's very wide. As we go to a 100 megahertz, it changes a little bit. It's narrow, sharper, a bit It is still ultimately second-order in nature. When we get to 200 and we're starting to see a shape kind of like we saw for the fluorine before, And its a bit more distinct and a lot narrower. And then by the time we get to 300, we're seeing quite distinct roofing doublets. And this one we've seen before, 400. And these signals are quite distinct and you can take J values and so on from them. And then as you increase up to 600 and eventually a 1000 megahertz. You can see that what happens is the signal gets narrower and actually, the degree of roofing is reduced as the frequency difference between two signals increases. But wait a minute. I told you that for A, A prime, B, B prime systems like the one I'm showing you that they are chemically equivalent and magnetically inequivalent. This means that their chemical shifts are always the same. And indeed, as a result of this, A and A prime are chemically equivalent, magnetically inequivalent, always have identical chemical shifts. This means that they will always be both on top of each other and coupling. They will always display strong coupling and second-order effects will result. And this is independent of the magnetic field strength. And again, we can demonstrate this by simulation. We can see for our 60 megahertz signal our quite distinctive standard second-order shape for one of these signals. And as we go from 60 all the way down to 1000 megahertz, you can see the signal gets a great deal narrower. But actually, if we blow it up, Here, if you look, although its sharper, the shape for this signal, even at 1000 megahertz, is actually the same. These will always give a second order effect. So the last of these phenomena that I wanted to talk about is something called virtual coupling. So second-order or strong coupling can actually affect the other couplings of the nuclei involved. So that strong coupling can then distort otherwise first-order multiplets. And I think I can show you this with an ABX system. So A and B start

coupled and become strongly so as their signals converge.

converge. A and X are further apart and not coupled. As B disrupts A it produces more inequivalent transitions and makes the signal more complicated. But I think it's easier to show you this with an illustration. So here we have A and B. They're signals are 0.5 ppm apart. This is much larger than the J value. And you can see little bit of roofing. And you'd see the signal for X is a nice doublet. that suggests this is the BX coupling. Now, as we move to a gap of 0.2 PPM, you can see that this roofing, much more pronounced. But again, still have a nice doublet just for B-X coupling here. However, once we get to 0.1 PPM, This is still a much larger gap than the J value. However, we are now starting to see the appearance of another small doublet. This does not mean A and X are coupled. It means that the stronger coupling between A and B is starting to distort the B-X coupling. And this is more pronounced as we get down to where the J coupling is getting closer to the chemical shift difference here we can see what looks like quite a pronounced set doublet of doublets until finally at 0.01 ppm, the chemical shift difference and the J value are quite similar. And here we have what looks like a big doublet of doublets. And if we take this all the way to the extreme and make the chemical shifts of A and B identical, then the J value is obviously much larger than the chemical shift difference. And we end up what looks like a triplet. And that is something you might alternatively expect to see from this system where Ha is coupling to equivalent B and X. And it'd be quite hard to distinguish these two. I do just to point out these tiny bumps here, they are no artifacts or impurities. They are characteristic of this process. They are also very small. And if you do happen to spot them, they might indicate that you're observing virtual coupling. I hope that was useful to you. Second-order effects are somewhat less common with modern high field spectrometers but there's still something, especially in aromatic systems you come across quite regularly. You can see my earlier talk for a list of resources if you need more information on various NMR phenomena that's it until next time.