What is the main starting material in this reaction? 4-methyl-2-pentanol. What is the main reagent that you're reacting with it? Sulfuric acid. Really the only logical thing that's going to happen in this case is the –OH group is going to get protonated. The next step will be for the water to come off. This is our first introduction to a process known as elimination. Before I write the last step of the mechanism, I want to draw a SMOG just for this portion of the molecule that I've circled. The carbocation position itself is going to be sp2-hybridized; remember that the positive charge there, that represents a hydrogen that's been pulled off along with the electrons, that's what would cause it to be positively charged. There's still, therefore, one more hydrogen on there, so there are three single bonds, three sigma bonds, that's why it's sp2-hybridized. The carbon on either side of that carbocation would be sp3-hybiridized. Since I'm trying to draw a simplified diagram, I'll write R to show the rest of the molecule. Because this is a secondary position, that means there's going to be two different neighbors with which that p orbital can have hyperconjugation. I'm going to only write one of the in, because now we're going to use hyperconjugation to explain what this elimination mechanism is. Hyperconjugation is just this partial donation of charge. But imagine that, after that partial donation starts, what if some were to start to pull on that hydrogen. The electron donation into that p orbital that had begun with hyperconjugation, you could say, would then be allowed to be completed; the lone pair could move totally into now not just being hyperconjugated but in a bonding interaction with that p orbital. In other words, mechanistically, I've wrote the following: I can show something in solution pulling that hydrogen off. In response, the pair of electrons that used to be in that bond can move into the carbocation, which means we're going to produce an alkene. This is the first time that we're seeing the formation of an alkene, and an alkene is the product of an elimination reaction. A [true] elimination reaction start with an alkyl halide or some other leaving group, so this is similar to that mechanism. The important point here is that this interaction between neighbors can, by removing that hydrogen, be increased to the point where you form a new bond. It's not shown in the SMOG because this is from before the hydrogen's removed. But once that hydrogen's removed, that carbon would go from being sp3-hybridized to sp2-hybridized.

This is not the only result of the fact that we have this hyperconjugation interaction. Now imagine this possibility: instead of the hydrogen being pulled off, what if somehow, in this hyperconjugation interaction, the hydrogen just moved on over. This lets me introduce the concept of a hydride shift or a carbocation rearrangement. Imagine that you have this interaction going on and somehow the hydrogen just moves over. Why might there be a driving force for this process? Imagine that we had enough hydride shifts occur where we could move the carbocation from being in a secondary position to, instead, being in a tertiary position. If on the same molecule you're comparing a secondary versus tertiary position, you're comparing isomers; you're allowed, therefore, to make a direct energetic comparison; you can really use that word stable. The tertiary carbocation would be more energetically stable that the secondary carbocation. At room temperature or, because in real life we're doing this above room temperature, there's plenty of heat available for the migration of that hydrogen to occur. That's one of the facets of a cationic reaction that you're going to have to be familiar with for every carbocation reaction that we learn. Any time that a carbocation forms, there's always – almost without an exception – the possibility that it's going to migrate around.

There's actually five products that are going to form; I'd like to write the mechanism for all of them. First, let me show you the sequence of hydride shifts that are going to lead to this tertiary carbocation, and then I'll go back and write the whole mechanism for all of the products. Here's the secondary carbocation. The first hydride shift would produce something that like is not going to be much different in energy, because you're exchanging one secondary carbocation for another one. Note that this is not resonance, because resonance structure you don't break or form single bonds; you're not just moving double bonds and lone pairs, a bond is moving over, it is a different molecule. Let's say that happened a second time. Now, we would have our more stable carbocation. This process is referred to as a hydride shift; hydride means a negatively-charged hydrogen, which means it's going to have a pair of electrons. It's also referred to as carbocation rearrangement. Let's see how carbocation rearrangement leads to the formation of five different products.

Starting with the original alcohol, it gets protonated first; water leaves, and we form a carbocation. To save a little space, I am going to write multiple possibilities coming from some of these structures. Let's start with the hydrogen on the carbon that's on the rightmost side. Water could remove that hydrogen, which if it did, you'd form a double bond at the very end of the molecule. Or, we could do what I showed originally, where this secondary hydrogen might get removed instead. We'll call this possibility number 1 where the end hydrogen came off, and we'll call this possibility number 2 where the secondary hydrogen comes off. That will actually make two different products: one will be the one I wrote up above, but you'll also get, at the same time, an isomer, the cis isomer. So the first one I wrote was trans, the second one I wrote was cis. There's a third possibility, though. I'm going to rewrite the structure. Let's say that the third possibility is that we have that hydride shift, that we have that carbocation rearrangement. Now there are again two possibilities: possibility number 3 is that water removes the tertiary hydrogen. Then the last possibility is, instead of that tertiary hydrogen simply being removed, it instead moves over – yet another carbocation shift. Once it's in that position, now the last possible product can form, if water removes this primary hydrogen. [mention of future discussion of thermodynamics]

Let's go back and name these compounds. Before I name them, let's remind ourselves of a little bit of terminology. Let's say I have a molecule like this, and let's say I want to talk about the position of one substituent relative to another.

The word 'side' itself could be a bit ambiguous because you could thin the top side versus the bottom or the left versus the right. The terminology that I defined is that, when I use the word 'side', I'm going to mean one carbon of that double bond versus another. You can only use the terms cis and trans in certain cases. In fact, in this molecule, you couldn't use them, because we have more than two substituents, and we have two substituents on one side, one carbon. We would try to look at how those substituents are located relative to each other in terms of their face. On the left side, I have a substituent on the top and the bottom face; on the right side, I have substituent on the top face. That means I have both a cis interaction and a trans interaction, so we can't use the terms cis or trans because they're relative terms that only compare two objects, not three. This is where the E/Z system comes in. We're going to use the same Cahn-Ingold-Prelog rules when we name using E/Z that we use for R and S.

In all of the molecules that are formed here, we don't have a situation where we have to use E/Z. All I'll say for the moment that, roughly, the term cis is interchangeable with Z, and the term trans is roughly interchangeable with the term E. The idea being that cis refers to two things being on the same face, and trans to two things being on opposite faces. Now let's look at our set of molecules. The red one, the one possibility #1, is that cis or trans? No is the correct answer. That question was not really was it cis 'or' trans; the question really is, is it 'cis or trans', either one of them? The answer's no, because you have two hydrogens on one side of the molecule. If you flip the position of the two hydrogens, you'd make exactly the same molecule again, which means it doesn't matter which way you write the substituents; there's only one of them. You'd always get the same double bond back, so you don't need the terms cis or trans to unambiguously express what's one that double bond. We don't even use the terms. The double bond is the most important feature of this molecule, so we're going to number from the position where the double bond is, in this case from the right. When naming the double bond itself, there's always two numbers involved, and we always use the lower of the two numbers, so we're going to use the 1, not the 2. We don't need to use both numbers, because it would be automatically understood that the second carbon of the double bond follows the first carbon. This is a five-carbon chain with a methyl group. Five carbons would be pentene. The double bond's at the 1 position so it's pent-1-ene, and we have a methyl substituent, so the full name is 4-methylpent-1-ene. Cis and trans you don't need and therefore should not use, cause there is no cis or trans relationship in this molecule.

The next two, the green ones, possibility 2. They're both forms of 4-methylpent-2-ene, but the one on the left, because the groups on the different sides are on opposite faces, that's trans; the one where the groups are on the same face on opposite sides, that is cis. I'm almost universally going to use E and Z, though, instead to name compounds, because when you can use cis trans you can always use E/Z. The other way that's not true; there's sometimes where you have to use E/Z that you can't use cis or trans. The one on the left is going to be (E)-4-methylpent-2-ene, and the one on the right will be (Z)-4-methylpent-2-ene. Possibility number 3, molecule written in black: is this 'cis or trans'? No, because you have two methyl groups on the same side, and if you flip them, you would not make a different molecule. It doesn't matter which way you write the methyl groups, so you don't need the cis or trans or E/Z labels. This would be 2-methylpent-2-ene. Because the double bond is now closer to the left than the right, we now have to number from the opposite direction. The last case has neither cis nor trans because you have two hydrogens attache to the same side, so this would be 2-methylpent-1-ene.

[physical set-up for this experiment]

Heating at reflux

Imagine the following: say that we have a reaction flask that we want to heat up as much as we possibly. In those situations, we'll often use some form of condenser. In this case, I'm showing a water condenser, which has two different completely isolated pathways in that piece of glassware; there's the channel that goes right through the middle, but then there's this jacket around it which water flows through but it's completely sealed off from that inner chamber. Here's what happens when you're heating at reflux: you put in your solvent, your reaction mixture, and you start heating it. As you heat it, some of the molecules are going to have enough energy that they become vapor. Some of the vapor will have molecules that are moving slow enough that they recondense. When they recondense on the glassware, that process is exothermic, it releases energy to the glassware. That means that, over time, wherever that limit of condensation is, the glassware starts to heat up. As it starts to heat up, that means that condensation doesn't start to occur as ready, so that means the vapor will rise up a little more before it condenses. Where it condenses there, it releases heat, therefore the vapor keeps on rising and rising and rising. As it's rising, though, you're also going to have condensation, so what you'll see is this continual cycle of vapor coming up and then liquid dropping back down on the sides of the glassware. That is what is called heating at reflux, this constant up and down process. What's the point of the water condenser? To ensure that the vapor doesn't rise so far up your glassware that it just completely evaporates. What this allows you to do is to heat a solution at its boiling point without losing much of the solvent because it keeps recondensing, so you're able to keep the reaction flask at a higher temperature. But there's also a sort of self-limiting effect here, because unless you put so much heat that you just destroy your compound and burn all the solvent off, the solvent's gonna keep trying to recondense. It will never really heat up past, therefore, its boiling point.

If we were using a water condenser, then the cold water that we use is going to go in closer to the point of heating; that way, we can be sure that there's at least some interaction between that cold water and the vapor, and we catch that vapor closer to the reaction flask.

Because if, instead, we had cold water coming in from the top, we could imagine a scenario where the water warms up by the time it gets down to the bottom of the flask, it doesn't have as much change, therefore, to catch the vapor since the cold part's already up in the top, so there's more potential for solvent loss. In real life, you would take a hose connected up to your fume hood (your fume hoods do have cold water ports); you'd attach that to the bottom port of your condenser, and then the top,, where the eater comes back out, you would feed that into the sink that's in your fumehood. The vapor is going to rise at first, condense at some point and then fall back down; you can actually see the line where that condensation has reached. That is heating at reflux – heating a solution to its boiling point then recollecting the solution by using a condenser. If you have a reaction that takes a long time but is guaranteed to work, you often would set these up at the end of your work day, let them run overnight, come back the next day and you have your completed reaction. just a real-life note : there are clips that they made t ensure the hoes stay attached to your condenser. [story of flooding a office because of a water condenser]

You're going to be heating this solution mixture, but distilling. A distillation apparatus might look something like this. You have a distilling adaptor, something where vapor is going to rise up just like under reflux, but then there's a pathway coming off from that so that as the vapor rises and then falls, not all of it returns to the original flask, but some of it goes on this side channel. To encourage condensation after that point, you'll often put an air- or, I'll draw the case of, a water-condensor. I you were to use a water condenser, again water wold go in the side closest to where the heat source is. And then we would have a collecting flask. So what happens in distillation? Generally, we use distillation to purify materials. We purify them on the basis of boiling points. Compounds with lower boiling point have higher vapor pressure, are going to evaporate first; so as your heating up this mixture, first the low boiling point materials start to rise; they'll rise, condense, fall, rise, condense, fall. They'll reflux – until that level reaches hight enough where now it can spill over this arm and come out the side of the distillation apparatus. It'll then condense and be collected in that flask. That portion of the liquid will keep coming over until you run out of that lowest boiling point material. What you could then do is pull of the collection flask, put a clean one on, wait for the next compound to heat up enough where it starts to rise up, it starts to reflux and then it is collected over.

[We're going to use distillation in today's lab to separate], because the alcohol that you start with – because of the hydrogen bonding in that alcohol – it's got a much higher boiling point than the alkenes that you're going to form. So as the reaction progresses, the alkenes will rise up first, they'll condense over and be collected in your product flask. The alcohol should remain in your starting material flask. At the same time the alkenes are going to therefore being separated, what other specific piece of equipment are you supposed to attach to this set-up? A drying tube. Why? Because what's one of the products of this reaction? Look at the mechanism again. The second step of the reaction, water comes off. The drying tube is going to catch that water, not let it re-enter the reaction mixture. Much of this process is technically reversible, but if I'm removing water as it's formed, that's exactly the type of Le Châtelier's principle we talked about. We continuously remove a product, the product concentration never builds up enough so that you reach equilibrium, so it keeps moving more and more forward. That's why the drying tube is here in this reaction, to help influence the reaction and pull the reaction forward. In this experiment, distillation is being used to separate the lower boiling point alkenes from the higher boiling point starting material, which is the alcohol. Part of the reason we're doing this, and not just letting it sit there being heated up, is because with enough heat, alkenes can react with each other and we can get a number of by-products. Even just the heating of the alcohol itself is going to produce by-products that are going to accumulate the longer the reaction continues. You're not really supposed to react until everything comes over in the distillation apparatus. With extensive heating, you can end up forming polymers, this black goo that's going to be hard to get out of your reaction flask. In general, it's bad to do what is called heating to dryness, that you heat a reaction mixture so much that all of the liquid removed – the liquid, the solvent even if it's boiling, it's still providing some mechanism by which heat can flow, that heat can be transfered. Once you get rid of that, you're applying the full heat of your apparatus to whatever by-products might be left, which that can often cause unwanted – and sometimes explosive – reactions.

When you have carbocations being formed in a dehydration reaction, the carbocations can be attacked by an alkene that might be formed. That's again why we're distilling the alkenes out of the solution, to help prevent that side reaction. But with enough time and enough heat, there are side reactions that we're going to be unable to control, unable to avoid. If we just kept going and going and going and didn't stop, we're going to get this goo that's hard to recover out of our flask. [skipping second distillation]

We're going to discuss how we can see evidence of these five different alkenes in our IR spectra, so we can confirm even that they formed. But then we're also going to be doing gas chromatography. That's going to be a technique that we're going to be able to use figure out how much of each of the compounds we have in our mixture.

Since the purpose of this distillation is not separate out every compound from each other, but simply to separate the alkenes out from the alcohols, we're going to give this distillation a boost. If you had a large set of glassware, and if you set everything up and then turn the heat on, it may be half an hour or so before any of the liquid starts to come over. To help this process, we're going to do a couple of things. Do not forget your stirbar. Unless your mixing, you're not agitating the liquid enough for it to evaporate cleanly, so either you'll have a case where evaporation occurs but it's slow, or if you don't have any mixing, you can end up with bumping occurring, which means the solution all suddenly gushes up at once. You don't want to that happen.

Make sure you bury your reaction flasks well into the sand bath, so that you really get good heat transfer from the sand to your equipment. On top of that, from the top of where your sand bath is to a bit below where the junction of your distillation apparatus is, you're going to insulate it with cotton and aluminum foil. This would defeat the ability of distillation to better separate your compounds. The more that you make your vapor rise up and go through the stages of condensation, the more separation you get from your compounds. But, we're not trying separate all the different alkenes from each other, we're separating the whole group of them from the much higher boiling point alcohols. In this case, if we insulate it, we're going to speed up the process of getting those alkenes to rise up and then be separated. [lab procedure]

The system cannot be closed off, because you'd be heating a closed system, which means you'd be building up pressure which mean, well, exploding glassware. There are cases, though, where you'll put the system under vacuum; there are what are known as vacuum distillations. Sometimes you can have a mixture of organic products that are heavy enough or at high enough boiling point that, by the time that you heat them up enough, they would start decomposing before you could purify them. But, since boiling point is the point at which vapor pressure equals surrounding pressure, if we drop the surrounding pressure by putting the system under vacuum, you significantly drop the vapor pressure you have to reach up to before boiling occurs. Many organic solvents, you just put them under vacuum, they'll be gone. [In vacuum distillation], you would close off the system. In a vacuum distillation, you would seal the thermometer joint and then, in between the condenser and the collection flask, we would have a vacuum adapter.

NMR

The first place we're going to start is what physically is going on inside a sample inside an NMR spectrometer. Some nuclei have spin in the same way that electrons have spin, which doesn't really mean that the nucleus is sitting there physically spinning around, but it has some of the effects, some of the physical behavior as if something has spin. More specifically, some nuclei have the same magnitude of spin as electrons – specifically 1/2. There are other nuclei that have other spin numbers, and the number that it has depends on the balance between the number of protons and neutrons in the nucleus. For our purposes, we're going to be focused on two nuclei – regular old protium, the major form of hydrogen, 1H; and then carbon-13, because these two nuclei have spin of 1/2. 1H and 13C are atoms with nuclei of spin 1/2. What happens when a charge sits there and spins? What gets generated? A magnetic field. Similarly, if you had a coil of wire that you pass charge around, you're going to generate a magnetic field – that's called an electromagnet. These nuclei that have these spins also therefore have their own itty bitty tiny magnetic fields that they generate. That means they're susceptible to interacting with a stronger external magnetic field.

If you had a collection of nuclei, if we have a set of atoms that are out in the middle of space, so we can say for all [practical] purposes that there's no magnetic fields around, no electric fields around. Then there's going to be no particular reason that the spins are going to point one way or another. They'll just be totally randomly arranged. They'll start out randomly arranged, but as soon as we do put the sample in a strong magnetic field, it's going to force the spins to become oriented. One way you can imagine this – there's a couple of analogies – one that's sometimes used is a wind analogy. Imagine that you have a weathervane [definition] that is not parallel with the direction of wind; the wind is going to apply torque to that weathervane, which is going to cause it to spin, until it reaches the point where it's aligned with the wind. Technically, the wind could push it one way or, if somehow it gets pushed the opposite direction, as long as it's pointing one way or another, if it's a flat piece of metal, then it will no longer turn as long as it's aligned somehow with the wind. The same thing goes on with nuclear spins. If these spins are not parallel or anitparallel to the magnetic field, they're going to be forced to turn. They're going to align up in one of those two orientations. We start out with random spins, but now, they're going to be lined up in the direction – or opposite the direction – of the magnetic field. More of them are going to be aligned with the field than against it, because if they're aligned with the magnetic field, they're effectively going to be at lower energy, like they're flowing down the river with the main magnetic field. Or, if they're turned exactly opposite, if they're antiparallel, it's like they're fighting upstream a little bit that external magnetic field.

What happens in terms of energy is that when you have the random situation, when they're not aligned, you'll have one averaged out energy level for the whole sample. But as soon as you put it into a magnetic field, you're going to split the energies into two leves. This graph I'm drawing is for the case of spin 1/2; for other spins, the diagram is more complicated, but we won't see any non-half-spin nuclei, so this will be the only energy graph we'll worry about. The bottom one would be where the spin is aligned with the magnetic field, the lower energy level. The higher energy level would be when it's oriented oppositely. That energy gap has a specific energy, which means it has a specific frequency that corresponds to it. This is exactly what is excited in a molecule when you do NMR spectroscopy – you're zapping the nuclei, and their spins invert and then relax; the energy's absorbed, then as it gets released, the spins revert back – more of them – to being in the lower configuration.

There are three main factors that affect this energy gap, which means it affects the frequency that you measure. One of the major factors is the strength of the magnetic field itself. Different machines have different magnet strengths; those will generate different energy gaps, and so they operate at different acquisition frequencies. Another major factor is the identity of the nucleus itself. Some nuclei are more likely to get turned around by an external magnetic field; this is something known a the magnetogyric constant – how sensitive is a nucleus to the magnetic field.

Gyric, gyrate, to spin, move; magnetio, related to magnetic fields; so magnetogyric is just a fancy way of saying does a nucleus spin in a magnetic field. The most subtle effect, the most subtle factor, but the most important as far as our ability to determine structure, is the fact that that energy gap partially depends on what the local environment, the local chemical environment, is around the nucleus being observed. In a sense, you can say it's the one variable, because once you choose a spectrometer, once you choose a nucleus to observe, then the differences in frequency you're going to see are due entirely to these differences in chemical environment. For example, if you had a very electronegative atom next to a nucleus that you're trying to observe, that electronegative atom is going to pull some electron density away from the nucleus. That nucleus, then is somewhat more exposed to that external magnetic field; if it is, that means the energy gap's going to be increased.

I want to talk about what physically an NMR spectrometer looks like in just very plain terms. If I wanted to hypersimplify it, an NMR machine would look like this. Most NMR is done in the liquid phase, so you have what's referred to as an NMR tube – a specially milled tube that you fill a solution and it's suspended within a chamber within your spectrometer. That chamber is then surrounded by a ginmormous magnet. In the case of the spectrometers we have, they're what are known as fixed magnets – they're just big, hulking pieces of metal, iron core magnets. But those are actually somewhat weak magnetic fields. For true research purposes, a modern NMR spectrometer is a superconducting magnet, which means you have a coil of wires that are inside a dewar of liquid helium that's inside a dewar of liquid nitrogen that's inside a insulation tank. It has to be kept that cold or otherwise you don't have superconductivity. You then apply a massive charge to this coil of wire which, since they're being superconducting, they don't lose any energy, so that charge just keeps going and going and going, which generates the magnetic field. As you can imagine, these are somewhat pricey machines – because they're very sophisticated, and there's also the maintenance involved. [story of spectroscopist at berkeley] Those kinds of superconducting magnets are so powerful that in new buildings, new research facilities that they're being put into, often they'll be put in the basement (where basements can be built) and then there won't even be a floor above then, the next floor would be the next story up to give that room away from the metal in the building – and way from people, because some of those magnets are so powerful that if you have a pacemaker and you walk up against it you wouldn't necessarily be walking much longer, because the pacemaker would be interfered with by the magnetic field. Or, if you're wearing jewelry that's of the wrong type, you might find yourself being drawn to those machines. At the very least, for our magnets, they're not that powerful, but I'd recommend not sitting on them and getting your wallets next to those magnets so that your credit cards [don't] get erased.

What happens when you put the sample inside the spectrometer? All of these different nuclei end up having splits in their energy levels. What we do is we zap the whole sample with a range of different frequencies. Only those frequencies that correspond to the energy gaps that are there are going to be absorbed. Once you zap the sample with radiation, you then flip the switch, turn it off and – you can say – listen to the radiation that comes back off of the sample. Each of those frequencies that you get corresponds to a different energy gap, and we're going to learn how to interpret that information to determine the structure of a compound.

In most modern NMR spectrometers, a sample that is suspended in a magnetic field is irradiated with a range of electromagnetic frequencies, light of different frequencies. Only those frequencies that correspond to the energy gaps that form are going to be absorbed. After being irradiated, those different frequencies are going to be released again by the sample and then detected by the spectrometer. This brings us to an interesting point about these modern NMR spectrometers. Back when this technique was first developed, we didn't have the computing power available to do what I've described here. Instead, there were two options: one was that you could vary the strength of the magnetic fields. For an iron core magnet, you could do that by changing the amount of iron or moving some of the iron around, shimming the magnet. As you changed the magnetic field, you could observe at just one frequency. As you increase or decrease the magnetic field, the different energy gaps which shrink or grow until they would match that frequency. Another way of doing it is to set one fixed magnetic field and then scan at different range of frequencies, one at a time. Problem with that method is that, let's say that each scan would only take 10 seconds to zap it and then acquire a signal and then give it enough time before you then zap it again. If each one of those times took 10 seconds, and if you had 1000 frequencies you were going to scan at to get a decent resolution spectrum, 1000 times 10, that's 10,000 seconds which is two and half hours. An afwul long time just to scan one compound. That's if it only takes 10 seconds per scan; on some compounds with transition metals it can maybe take a minute, and then you're just sunk as far as time.

The modern approach is to what I've described, where you don't scan at one frequency at a time, you zap it with a whole bunch of frequencies at once. There's a couple of analogies I could make for that. Most of them – because it's the only comparison I could make a good relation to – are musical examples. For example, fill a wine glass up and tap it; it's going to ring. But it's only going to ring at one particular frequency. It didn't matter how you tapped it, though, your tapping, you could say, excited the glass, and then it resonated at the frequency it was natural for it to resonate at. Another maybe better example, but obscure, is the following. Have any of you ever lived in a place where you have a stereosystem next to a piano – not an electronic piano, but a real wood full-on piano? Have you ever listened to the music in a room like that and suddenly turned the music off? What happens (or what do you guess is going to happen)? Some of the piano strings will resonate, because if the sound waves coming from the stereo match the vibration frequencies of these piano strings it's going to cause the strings to vibrate a little bit.

You've got this wall of sound coming at it that all of these different frequencies will be excited, but only if they're found in that blast coming at it. That's kinda what's going on here. You blast it with a whole bunch of different frequencies and then some of them respond.

But then there's the reverse problem, on figuring out what do you have in the signal coming back off of the samples? Because you have all of these different frequencies stacked on top of each other. In fact, the signal that you acquire from an NMR spectrometer looks kinda like this. If we're talking about acquiring a signal, then we're going to be looking at the intensity of that electromagnetic radiation versus time. Often, this graph will have what appears to be like waves within waves, kinda like the way that I've drawn it here. This is called the free induction decay (FID). This doesn't have frequency. This is something that is based in time. Does anybody known what an equalizer is, an EQ? It used to be in car stereoes, that would be the thing that you tried to impress each other with, with how fancy the panels on your stereo players were. How many of you have ever used iTunes and played with the equalizer in iTunes? It's the same thing, just a software version. Essentially what these are are either software or hardware devices where each of these different frequency ranges – for those of you not totally into music, you might know what treble and base are, low sounds, high sounds. So you tweak those knobs and change the sound that you're listening to. Or, the way these equalizers used to work is that each different frequency range – 60 Hz, 120 Hz, 240, whatever – would have a stack of LEDs and they'd blink with how much of that signal shows up in that frequency.

That's exactly what's done in a [modern] NMR spectrometer. Mathematically what happens is you take that whole signal and you superimpose on top of it each individual frequency that you want to pull out of that signal. [Fourier transform] You take an integral that involves your reference frequency and your complex signal and it will pull out of that signal how much of that frequency is in it. In other words, you convert from a graph that has time as its x-axis into a graph that now has frequency – which is 1/t – as its axis. The amount of response at each one of the frequencies will be shown, and you end up with these graphs that have relatively clean and predictable patterns. It's these patterns that we're going to have to learn to interpret. [A Fourier transform] is a mathematical operation that allows you to convert between these two domain spaces. In English, you convert from a mishmash of frequencies to figuring out how much of each of those frequencies is around. Because this requires computing power, NMR didn't really take off as a technique until we had more modern computers. You could probably control a spectrometer with an iPhone, that's how far we've come technology-wise. The only limiting factor is that for good NMR spectrometers, the problem of having a superconducting magnet. If they ever make a room-temperature [superconductor], then we're going to have NMR boxes on our desktops.

[The Fourier transform] involves the Dirac delta function, which is a form of integral that has a non-zero value if the two functions being integrated match, and it has zero value if there's no overlay between the two functions. That's how it's used to pick and tease out frequency individually; you integrate over all possible frequencies, and that's a Fourier transform. The y-axis is intensity, how much signal is coming back. The amount if signal is related to how many atoms are responding at that frequency.

Let's get a little more complicated. As it turns out, it's not actually frequency that we use for our x axis. Why? Because each machine's magnetic field strength is different. Magnetic field strength is one of the main causes for different energy gaps, so if each spectrometer has its own magnetic field, it's going to generate it's own unique forms of energy gaps, which means it's going to measure things at different frequencies, which would make it awfully tough to compare results from one spectrometer to another. There's this unit created called chemical shift. Chemical shift is the unit of measure, but sometimes that phrase is used instead of chemical environment. The fact that we're going to change these energy gaps, that's sometimes called chemical shift, and the unit of measure is sometimes called chemical shift. Unit of measure is usually given the symbol delta, lower casse delta, and it is the observed frequency of a particular nucleus machine frequency, divided by that machine frequency, multiplied by a million. Since you're taking frequency and dividing by frequency, you end up with sometime that has no units. Because you multiply it by a million, we would say the units are parts per million (ppm). Why are we multiplying by a million? Because if, for example, you had a 90 MHz machine, a machine whose nominal operating frequency is 90 MHz, out of that, the differences between different atoms might only be 100 – 200 Hz, just fractions. For hydrogen, it's usually between 0 and 10 ppm – not very large differences, that's why we want large magnetic fields, so we can better see the differences between the energy gaps.

What is the machine frequency? It's just a reference point. If we're going to have a spectrum, it might be easier as humans to interpret the spectrum if we could put a zero somewhere on the graph. What the machine frequency is is, really, defining the zero point. It is the frequency measured on a particular spectrometer for a particular reference compound. For organic molecules, the reference compound is almost always tetramethylsilane (TMS) [not to be confused with the trimethylsilyl protecting group]. Silane is kinda like alkane; it represents compounds that are saturated. But the sil- prefix indicates that it's focused on silicon compounds. Imagine that you have silicon connected to silicon and those were covered by hydrogens; those are silanes. Many silanes are incredibly explosive; SiH4, the silicon equivalent of methane, is supremely explosive. This compound is not.

Why are we defining one frequency by another in this unit of measure? If we define the machine frequency as zero, and then we're comparing it to some other frequency that we're observing for a nucleus, that might make sense.

What's the point of dividing by machine frequency? Machine frequency is linearly related to the energy gap (E = h • nu); that energy gap is affected by the magnetic field strength, it's linearly affected by the magnetic field strength. Frequency is related to the energy gap, which related to the magnetic field strength. That means frequency depends on the magnetic field strength. If you're operating with the same magnetic fields strength, then when you divide one frequency by another, you're canceling out the effect of that magnetic field. If we were to write the equations down, we would see that the magnetic field would be in the numerator and the denominator, because it's related to frequency. Since it cancels out, that means that no matter what machine you measure it on, chemical shift is going to be the same. Chemical shift is a machine-independent quantity, meaning the same value will be obtained regardless of the spectrometer used.

The next thought. What do these graphs have in the way of their x-axis. We started out saying here's the signal being acquired; we do this Fourier transform to get it in terms of frequency. But not I'm saying we don't really use frequency, we instead use this unit of chemical shift. But, curiously enough, on spectra, the convention is zero is on the righthand side of the spectrum, meaning that both frequency and chemical shift increase to the left. There's a historical reason why this is true. Let's talk about this term called deshielding. This concept is what chemical environment is about – the interaction of a nucleus with it neighbors is going to cause changes in its chemical environment, which is going to show up in chemical shift. Imagine that we have fluoroethane, and let's say that we wanted to observe the carbon that's right next to that fluorine. Fluorine, because it's electronegative, can pull electron density away from that carbon that's being observed. That carbon, therefore, effectively experiences a greater interaction with the surrounding magnetic field, the spectrometer's magnetic field. Because it's interacting more strongly with that magnetic field, that means the energy gap is going to increase. If that energy gap increases, that means the frequency of radiation needed to bridge that gap increases. SInce chemical shift comes from frequency, that means that chemical is going to increase. When a nucleus being observed is close to an atom that is electron-withdrawing, electron density will be pulled away from that nucleus. The nucleus is effectively, therefore, more exposed to the spectrometer's magnetic field. When we say more exposed, we can use this term deshielded. Since it is more exposed, it experiences a larger energy gap, which causes a larger frequency of light being absorbed, which corresponds to a larger chemical shift. Put something next to that nucleus that pulls electrons away from that nucleus; that nucleus feels more of the magnetic field. Because the energy gap is related to the magnetic field, if it experiences more magnetic field, it experiences a greater energy gap. The energy gap has a correspondence to a photon that corresponds to a particular frequency of light. Since chemical shift is calculated from frequency, that means it's going to have a greater chemical shift.

Let's turn the whole story backwards. Where, relative to carbon, is silicon located on the periodic table? Right below it. Which is more electronegative, carbon or silicon? Carbon is more electron negative. To the right of carbon, what do we have? Nitrogen, oxygen, fluorine. Below each of those – phosphorus, sulfur, chlorine. This six atoms are more electronegative than silicon, because they're to the right and/or above silicon's position on the periodic table. Tat means that silicon is less electronegative than almost any atom that typically shows up in organic compounds. Now let's say we have a nucleus that's bing observed that's next to silicon. Silicon doesn't pull electrons away, so we could say that the atom's more shielded. Since that atom is shielded, it doesn't experience as much of that magnetic field, which means the energy gap is smaller, which means the frequency observed for that gap is smaller, which means the chemical shift is smaller. Since silicon's less electronegative than anything, practically, in an organic molecule, that means the smallest frequency you will observed will be for alkyl salines; that's why TMG is defined as the zero point, because almost any other compound you acquire will have higher frequencies. Silicon is less electronegative than most elements commonly found in organic molecules. Atoms attached to silicon are therefore shielded by comparison, which means the nuclei are not as exposed to the magnetic field, which means the energy gap is not as large, which results in a lower observed frequency and chemical shift.

[Referring to graph above:] deshielded on the left, shielded on the right. Atoms that have deshielding going on – more exposed, bigger gap, bigger chemical shift – on the left of the spectrum. Atoms that are shielded don't have electrons being pulled away – smaller gap, small frequency, smaller chemical shift – the righthand side of the graph. Coming back to silicon specifically, since silicon is less electronegative and by comparison would make atoms more shielded, that's why TMS would be used as a reference standard, because the frequency observed for TMS would be lower than almost any other organic compound.

Aside from these terms shielded and deshielded, there are these historical terms upfield and downfield that you'll still see in texts sometimes and still hear people refer to. This one's a little more complicated to describe. Chemical shift increases to the left; we already had the terms deshielded on the left and shielded on the right. Now, we're going to talk about downfield and upfield. Let me start with this comparison of three random nuclei. Let's say that we have some nucleus that has a particular energy gap to it. Let's say that we have, in the same sample, a nucleus that's experiencing deshielding. Deshielding, larger energy gap, more exposure to the magnetic field. Let's say that we also have something in that same sample that is shielded, which means it's going to have a smaller energy gap. Let's go back, for the moment, to the case where we have a spectrometer that can only observe at a fixed frequency. That means it's only going to be able to detect one kind of energy gap. Let's say it was tuned perfectly to make the nucleus I have in the middle of these three. That means that, at that set of conditions, at that particular strength magnetic field, you're not going to see the shielded or deshielded nuclei, they just won't show up at the right frequency. In modern spectrometers, we get all of the frequencies at once, but I'm explaining where these terms come from, which is from the old days of spectrometers where it often was fixed frequency of observance. What's the only way we could see these different nuclei, then, is to change the magnetic field.

In the case of something that's shielded, we would have to increase the magnetic field in order to bring the energy large enough to be observed at this fixed-energy point. Conversely, the deshielded nucleus, we'd have to decrease the magnetic field in order to drop the gap low enough so it's the right amount of energy to correspond to the frequency that you're observing at.

If a spectrometer can only scan at a fixed frequency, then the magnetic field used must be varied in order to make the energy gap for different nuclei match the observation frequency. If an atom is shielded, it's going to need a larger magnetic field in order to get this right energy gap; that's why we say it's upfield; it needs a stronger magnetic field. The opposite is true: if an atom is deshielded, you don't need as strong of a magnetic field to get that correct energy gap, which is why it's called downfield. Since downfield mean lower field, upfield means greater field, that means magnetic field strength increases the natural direction along the x-axis. Since spectrometers used to be built with magnetic field strengths that were variable, that's how we ended up with magnetic fields strength being left to right. Once you fix the magnetic field at a particular strength, then in relation, the frequency observed would therefore be from right to left. That's why the spectrum is backwards.

[mentioning chemical equivalency; chemical shift tables; splitting]

NMR solvents

If you were to take normal ethanol, acetone, benzene, ethyl acetate, any of the common lab solvents, and put them into an NMR spectrometer, we're going to get a huge signal off of those solvents if we're going proton NMR. If we had some compound dissolved in that solvent, we might not be able to see that compound, because its signal is being flooded out by the solvent itself. In order to prepare a sample, we have to use isotopically prepared solvents – in other words, deuterated solvents. Why deuterium? Because there are sets of reactions that we convert regular organic compounds into deuterated compounds. Deuterium has a different magnetogyric constant than hydrogen, and it's spin 1, so it has a completely different kind of interaction than hydrogen. In other words, if you're looking for hydrogen and you've got deuterium there, the hydrogen probe can't see it.

What are some common examples of NMR solvents? One of the most common, because it's the easiest to make and a bunch of compounds are soluble in it – deuterated chloroform (chloroform-d). The 'd' afterwards refers to the fact that its hydrogen has been replaced by deuterium. Not everything's soluble in chloroform unfortunately, so there are some other common solvents. Some of the more common ones would be deuterated benzene (benzene-d6) and acetone (acetone-d6). Producing 100% fully-deuterated compounds is expensive; producing 99.9% is not as expensive. If you need to ensure that you really have 100%, that requires more careful techniques than 99+, which is [many] cases is good enough. You might sometimes purposely want a solvent that is only 99.9% deuterated. Can you think of a reason why it might be use to use a not quite exhaustively deuterated solvent? These solvents have been well-studied; they have very well-defined chemical shift values. What you can do is use the residual signal that comes from that solvent and calibrate your spectrum against it. Sometimes, 100% deuterated solvents are used, but frequently solvents that are 99+% deuterated at used. In these cases the residual signal caused by the non-deuterated solvent is used to calibrate a spectrum. Of course, there's TMS, the compound itself, which is zero reference on most organic applications. Sometimes you'll add maybe 1% of TMS to a solvent. That would give you yet another reference point.

If you're looking for hydrogens, you won't see deuterium, because different nuclei show up at different frequency ranges. If you had 100% deuterated solvent, the solvent would be invisible to proton NMR. By having a little bit of solvent left that does have hydrogen, those hydrogens can be spotted and then that's what you use to calibrate your spectrum.

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hydride shift = carbocation rearrangement; H:- ≣ hydride

E ⟺ trans; Z ⟺ cis

Heating at reflux – Heating a sol'n to its boiling point then recollecting the solution by using a condenser.
In this experiment, distillation is being used to separate the lower boiling point alkenes from the higher boiling point starting material (alcohol)

NMR – 1H and 13C are atoms with nuclei of spin 1/2
Factors that affect this energy gap: strength of the magnetic field (B); magnetogyric constant (gamma) (how sensitive a nucleus is to magnetic fields); chemical environment; NMR Tube

In most modern NMR spectrometers, a sample suspended in a magnetic field is irradiated with a range of EM frequencies. Only those frequencies that correspond to the energy gaps generated by the sample being in the magnetic field will be absorbed. After being irradiated, the various frequencies of re-emitted by the sample are observed.

Chemicals shift (ppm) : delta = observed frequency - machine frequency / machine frequency x 1,000,000
Machine frequency – the frequency measured on a particular spectrometer for a particular reference compound. For organic compounds, the reference is almost always tetramethylsilane (TMS).
Chemical shift is a machine-independent quantity, meaning the same value will be obtained regardless of the spectrometer used.

Deshielded: Whenn a nucleus being observed is close to an atom that is electron-withdrawing, electron density will be pulled away from the nucleus being observed. The nucleus is therefore more exposed (deshielded) to the spectrometer's magnetic field. Since it interacts more greatly with the magnetic field, energy gap increases, which corresponds to a greater observation frequency, which corresponds to a larger chemical shift.

Silicon is less electronegative than most elements typically found in organic compounds. Atoms attached to silicon are therefore shielded by comparison, which means the nuclei are not as exposed to the magnetic field, which means the energy gap is not as large, which results in a lower observed frequency and chemical shift. ∴ TMS is used as a reference compound since the frequencies generated by the carbons & hydrogens on TMS would be lower than those observed for nearly any other organic compounds.

If a spectrometer can only scan at a fixed frequency, then the magnetic field used must be varied in order to make the energy gaps for different nuclei match the observation frequency.
If an atom is shielded, a larger magnetic field will be required to generate the appropriate energy gap –> upfield.
If an atom is deshielded, a weaker magnetic field must be used to generate the appropriate energy gap –> downfield.

NMR Solvents
For liquid NMR experiments, deuterated solvents (solvents in which hydrogen is replaced by deuterium) must be used, otherwise the signals from the solvent could mask the signals of the compound being observed.

Sometimes, 100% deuterated solvents are used, but frequently solvents that are only 99+% deuterated are used. In these cases, the residual signal caused by the non-deuterated solvent is used to calibrate a spectrum. Sometimes, TMS is included in NMR solvents so that it can be used to calibrate a spectrum.

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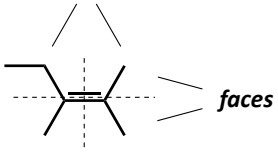
Structures *(remaining structures identical to lab 11A)*

11/03/11 lab • 1

sides



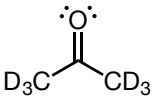
faces

11/03/11 lab • 2

Common solvents

$CDCl_3$ ***chloroform-d***

C_6D_6 ***benzene-d***



acetone-d