

5.46 (NMR Spectroscopy and Organic Structure Determination) Notes

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Week 1

1D NMR Principles and Practices

1.1 Underlying Principles of NMR

- 1/4:
- Philosophy: NMR is a complicated and useful set of tool for chemists.
 - Background on Walt.
 - Training: Masters, PhD, Postdoc, and 5 jobs in NMR.
 - 20 years industry experience, 10 years academia experience, some small company experience.
 - Considers himself somewhere in the middle between knowing nothing and everything about NMR.
 - Experience in natural products discovery, drug discovery, biological NMR, etc.
 - Goal of the class: Distill what's most important for us to know.
 - Announcements.
 - Syllabus now posted on Canvas!
 - Everything important will be posted on Canvas.
 - MestReNova is what we should use; TopSpin is what Walt is more comfortable with.
 - Slides posted to Canvas at the end of the day.
 - This week: The fundamentals.
 - Chemical shift, coupling constants, correlations (new), NMR relaxation
 - The NMR periodic table.
 - ^1H has almost 100% spin 1/2.
 - ^{12}C is 99% abundant and has spin 0.
 - Thus, we can only do NMR with ^{13}C .
 - The resonant frequency depends on an absolutely fundamental physical property called the **gyromagnetic ratio** (γ).
 - Highest gyromagnetic ratio is tritium (^3H), then fluorine, then a whole bunch, then phosphorus, carbon, nitrogen (with a bunch in between these three as well).
 - Higher magnetic field gives more signal.
 - But 1/4 as much for ^{13}C as for ^1H , because γ for ^{13}C is 1/4 what it is for ^1H .
 - The highest field NMR systems commercially available are at 1.2 GHz.
 - Walt will typically only go up to 600 MHz in this class, corresponding to a 14.1 T magnet.

- Range of chemical shifts.

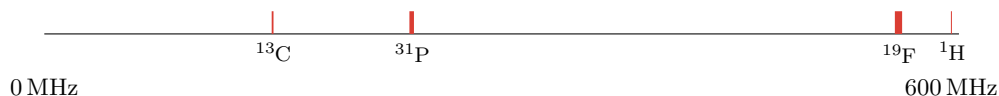


Figure 1.1: Chemical shift ranges of common nuclei.

- The range of chemical signals we'll see is tiny, though; only about 6000 Hz if we're talking about a 10 ppm window.
- Different nuclei appear in different windows and with different ranges (think of how carbon is 0-200 ppm vs. proton -5-15!!).
- Note that the ranges in Figure 1.1 are to scale relative to each other, but have been scaled up absolutely by 10 times.
- All atoms' spins are active as soon as we magnetize the sample in the magnet bore. Differentiating between them is now an electronics problem.
- α - and β -D-glucose's anomeric protons have significantly different chemical shifts (4.6 ppm vs. 5.1 ppm, roughly).
- Oxygen is virtually all spin 0 ^{16}O , but protons will couple to each other and to ^{13}C (giving carbon satellites).
 - 1% of the time, the proton is coupled to ^{13}C , and gets massively split.
 - All couplings exist; it's just a question of whether we can see them!
 - 170 Hz coupling for the 1-bond carbon-to-proton coupling.
 - 2-bond connection is then expected to be much smaller, maybe 25-30 Hz.
 - Protons are present in much higher concentration, though, so we see their splitting much more (but it's also smaller because they're farther away!). This is why vicinal protons couple in 4-8 Hz instead of 200 Hz.
- Sergei: Why no coupling to the alcohol protons?
 - Because the sample is in D_2O , we get exchange everywhere to OD.
 - Since deuterium is spin 1, it should split the spin 1/2 nucleus into a triplet. But it also has 1/6 the gyromagnetic ratio. Additionally, fast exchange prevents any meaningful coupling from developing.
 - Dissolving the sample in (very dry) DMSO-d_6 will *not* lead to proton exchange, and we *can* observe the couplings to the hydroxyl protons!
- Equations.
 - 5/2 exponent for gyromagnetic ratio means it *really* matters for sensitivity.
- 600 MHz denotes the resonance for protons at the set magnetic field.
 - Carbon would be at 150 MHz in this case (because 1/4 gyromagnetic ratio)!
 - 140-150 A of current in the magnetic.
- A 4 Hz coupling is on the order of parts per billion, so to discern it, we need parts per billion homogeneity in the magnetic field. This is why we need shimming.
 - Shimming is done with additional coils that impart additional magnetism to parts of the sample.

- Shimming is done for all of the few dozen coils every once in a while, and then with some of the coils for each particular sample.
 - To shim, you measure the deuterium lock signal and how broad or narrow/high the peak is and then you fiddle with the coils!
 - All you really have to look at is the height because the area is the same, so the height of the lock signal correlates to how good the shimming is.
 - Today, we do **radian shimming**, which tells us how to change the current in the coils to make the shimming better.
 - Shim coils can only be adjusted so far; if there's no sample below the coil, the shimming likely can't compensate enough to get a good spectrum.
- Administrivia.
 - There will be some kind of group project.
 - Final project is for us to use our skills to do something useful.
 - Write up our PSets independently, but we can work together on them.

1.2 Recording NMR Data

- 2/6:
- Deuterated solvents are used both to remove the proton background *and* for lock.
 - If you run a sample automatically, everything we do in the next 20 minutes is gonna be automated.
 - Locking.
 - If your sample doesn't lock in automation, the sample will fail.
 - If you've got 50:50 CDCl₃ to MeOD, the system may or may not lock on the chloroform signal, specifically.
 - The spectrometer is sweeping resonant frequencies across a relatively small range for deuterium.
 - x -axis is frequency, y -axis is intensity; perhaps an FID??
 - When lock is on, we're picking a deuterium frequency. If DMSO-d₆ resonates at 2.49 ppm, we relate everything else back to that.
 - Shimming.
 - We don't use R_f pulses, but rather magnetic gradient pulses.
 - A constant gradient across the measured window will give a broad line because samples at one part will go at one frequency, and samples at another part will go at a different frequency.
 - Various currents for various gradients that you add together properly can be added together, like Fourier analysis! Creating a straight line as the sum of nonstraight lines!
 - There's error in the machine picking the deuterium sample exactly right.
 - This is what makes the machine say CHCl₃ is at 7.19-7.28 ppm.
 - There's a difference between robustness and precision; the machine probably loses some precision for the sake of robustness.
 - Tuning.
 - Looking at the response of the entire R_f system.
 - Is that response maximum at the frequency at which I'm looking?
 - You need to tune the system to your sample, because otherwise, your sample's response will be much weaker.

- Phasing.
 - Maximizing the real and imaginary components.
- The FID.
 - The FID goes down due to a **relaxation effect** (t_2) that we'll discuss more later.
 - Exponential multiplication of 0.5 Hz, i.e., (reciprocal) 2 s.
 - Hertz/seconds conversions are good math to practice on.
 - Getting rid of the signal after 2 seconds gives less noise, but you lose signal intensity.
 - Losing 0.5 Hz couplings is fine if you're mainly looking for 3-5 Hz couplings.
 - Zero-filling gives an increase in resolution, but it has limited advantages.
 - The further out you go in time, the more frequency discrimination you get. But lose S/N as well.
- t_2 is the relaxation to equilibrium perpendicular to the magnetic field.
- t_1 is the relaxation to equilibrium parallel to the magnetic field.
 - This determines if spins actually get back to equilibrium after you do something with them (e.g., pulses).
- Pulse length.
 - 5 μ s by default.
 - What if we lengthen it to 500 μ s?
 - Things get out of phase. Manual phasing allows you to see it, but you get a broad background.
 - At 5 ms, you don't get anything really interpretable, although the peaks are in roughly the same space.
 - 1/5 μ s is 20 kHz, which is parts per million on a 600 MHz spectrum.
- Project #1.
 - Task: Prepare a presentation for the class, and a report for the class.
 - Purpose: Share as much information about a range of useful nuclei as we can with each other.
 - We're not gonna touch the stuff in this class for a long time, so it will be good for our future selves to have resources.
 - List of references that people can go to is really important (online, published articles, etc.).
 - Stay within the allotted time no matter what.
 - Report and slides can be the same, but just make sure that all of your references go in the slides, too.