Chem 135: Spectroscopy Study Guide

Eugene Kwan, 2015

Description This describes the bare essentials of what you need to know about spectroscopy in the organic chemistry lab. I don't talk much about how any of it works.

How to Study To do well in the spectroscopy component of Chem 135, you should:

(1) Read this document first. It will give you a general idea of what's going on. Then you can learn the specifics.

(2) Carefully read Organic Structures from Spectra (Field *et al.*), pages 1-80. Make sure you understand everything. The mid-term will be closed-book, so you should be familiar with all the general trends and a handful of specific numbers. (*Note:* the figures in this handout are taken from this book.)

(3) Do the problems in the book! Practice makes perfect! The mid-term exam will include at least three problems from the book. Yes, that's right! You have some of the mid-term in front of you right now! I will *not* hand out answers to

(4) You aren't responsible for everything. I will not ask about EIMS fragmentation patterns, any specifics about the absorption maxima of UV-vis chromophores (other than calculating an ε), or the specific contents of any data table. You *will* be asked to assign spectral data or elucidate structures. So, don't memorize things *per se*, but you should do enough problems so you know the most common numbers. I also won't ask you about how any of the experiments work. (If you're interested, I can tell you more. More than you ever wanted to know…)

(5) You should know how to deconvolute any first-order multiplet. Read Hoye and Zhao, *J. Org. Chem.* **2002**, *67*, 4014-4016. It's only three pages, quite straightforward, and you must understand it. Do all the practice multiplet questions! Multiplets are guaranteed to appear on the mid-term exam. (Also see *JOC* **1994**, *59*, 4096-4103 for more practice.)

(6) Read the notes on ^{13}C-^{19}F couplings in ^{13}C spectra. In the lab, you will synthesize a compound that displays these couplings. On the mid-term, you will be asked to assign the carbon spectrum of a compound containing fluorine. It will be analogous to the examples shown in the notes.

(7) Have fun! Each problem is like a crossword puzzle. There is exactly one correct answer, and most people enjoy figuring out what it is. It is all completely logical.

Two Kinds of Workflows

To business! In the day-to-day lab, there are basically two kinds of things we can do with spectroscopy: **structural verification** and **structural elucidation**. In structural verification, we have a good idea of what the molecule's structure is already, and we're just trying to make sure the compound is what we think it is. This is the most frequent task, because every time we perform a reaction, we want to know if we have the product before moving to the next step. In structural elucidation, we don't have any idea of the structure going in. This might happen if we've isolated a surprising side product in a reaction, or perhaps if we've isolated a natural product from a plant. Of course, structural elucidation will be harder than structural verification. The problems in the book are all structural elucidation (if you can do elucidation, you can do verification).

The Tools

We have four routine tools at our disposal. Each of them answers different questions:

A. UV-vis (ultraviolet-visible spectroscopy): observes electronic transitions; is there conjugation in the molecule?

B. IR (infrared spectroscopy): observes vibrational transitions; identifies functional groups.

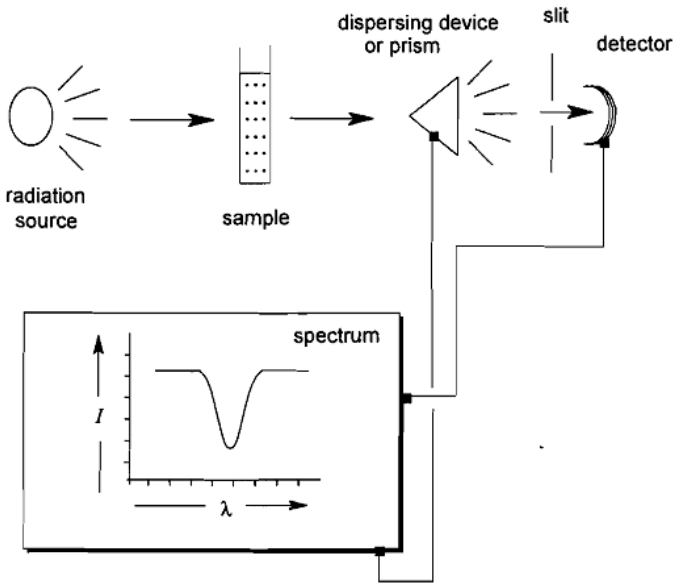
C. MS (mass spectrometry): observes mass to charge ratio; determines molecular weight.

D. NMR (nuclear magnetic resonance spectroscopy): observes nuclear spin transitions; determines structural connectivity, stereochemistry, and functional groups present.

As you can see, NMR gives the most information, but the other methods are also helpful. Below, I give you the bare essentials of what you need to know about each method.

A. UV-vis

In UV-vis, we shine light on a sample. For every wavelength going in, we figure out how much light comes out at that same wavelength:



The amount of light coming out is always lower than the amount of light going in because some of the light gets absorbed. So we define the **absorbance** A as:

$$A = -\log\left(\frac{I}{I_0}\right)$$

where I is the intensity going out and I_0 is the intensity going in. Absorbance does not have units. The bigger the dip in the spectrum, the bigger the absorbance.

If we think about putting food coloring in water, it seems obvious that one drop will color the water less than ten drops. The water coloration should also depend on the kind of food coloring used; surely some are

darker than others! This idea is described by the **Beer-Lambert Law**: $A = \varepsilon cl$, where ε is the molar absorptivity (how colored the compound is intrinsically, $M^{-1}\ cm^{-1}$), c is the concentration (M), and l is the path length (cm). This means that the intensity declines *exponentially* as more stuff is added.

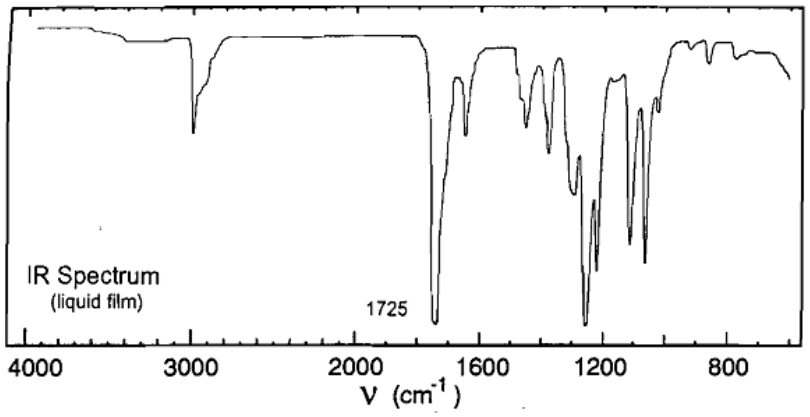
Where does the color come from? It comes from electronic transitions between filled n, σ, or π orbitals and empty σ^* or π^* orbitals. The closer the filled and empty orbitals are in energy, the longer the wavelength of the transition will be. This means that highly conjugated compounds are visibly colored and have large ε values.

There are a lot of data tables showing the wavelengths of the absorption maxima (λ_{max}) of various compounds, but they are not terribly illuminating. If there's a long wavelength (>220 nm) absorption that has a big ε ($>10^4$), I suspect conjugation, but that's all. UV-vis don't have much fine structure, so it is a pretty limited form of information.

Things to Know: how to calculate ε given a UV spectrum and how to determine if a molecule contains conjugation.

B. IR

IR is similar to UV-vis, but has several important differences. The first is obvious: instead of using UV/visible light, we use IR light. Second, for historical reasons, instead of using absorbance, we report the transmittance $T = I / I_0$ and wavenumbers (cm^{-1}) instead of wavelength (nm). Finally, IR observes vibrational transitions instead of electronic ones. As a result, IR is most useful for detecting the presence of functional groups. Here's a sample IR spectrum:



In the book, you'll find a lot of IR tables, but here are some key facts to know:

(a) The bigger the dip, the more intense the peak. Peaks are classified by weak (w), medium (m), strong (s), or broad (br).

(b) Broad absorptions above 3100 cm^{-1} indicate OHs or NHs. Occasionally, they can be sharp. Carboxylic acids tend to give broader absorptions at a lower wavenumber range: 2500-3300 cm^{-1}. Amines have weaker and sharper absorptions than alcohols.

(c) Alkane C-H stretches are in virtually every molecule and appear from 2850-3000 cm^{-1}. If there's an alkene, it will appear from 3000 cm^{-1} to 3100 cm^{-1}. Alkynes appear higher still at around 3300 cm^{-1}.

(d) Carbonyls appear from 1600-1800 cm^{-1} as very sharp and strong absorptions. These are quite diagnostic:

ketone, aldehyde, or carboxylic acid	1700-1740 cm^{-1}
ester	1735-1750 cm^{-1}
amide	1630-1690 cm^{-1}
acid chloride	1770-1815 cm^{-1}

Unfortunately, sometimes things will appear at unexpected frequencies, so you should use the ^{13}C NMR to corroborate your guess. Additionally, sometimes one carbonyl can appear as a slight doublet due to a phenomenon known as "Fermi resonance." Again, use the ^{13}C NMR as your guide; carbonyls will not be split there.

(e) Aromatics have complex bands, but there is a distinctive pattern of weak and wavy "overtones" at 1650-2000 cm^{-1}. If you get good, you can figure out the substitution pattern from these, but I normally just figure it out from the NMR spectra.

(f) Some special groups have frequencies worth knowing:

nitro group	1500-1650 cm^{-1}
C-O stretch	1050-1260 cm^{-1}
nitrile	2215-2280 cm^{-1}
allene	1900-2000 cm^{-1}
imine	1480-1690 cm^{-1}

(g) Other absorptions below 1400 cm^{-1} may be worth looking at if you're an expert, but it can be pretty complicated. This is called **the fingerprint region**.

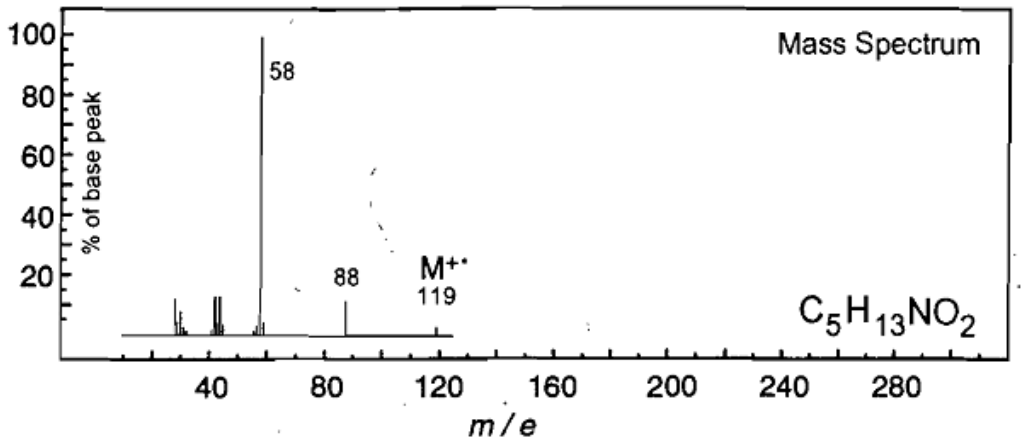
Things to Know: how to identify the most common functional groups from IR spectra. Memorize the numbers I gave above and reinforce it by practicing like crazy.

C. MS

MS is nothing like UV-vis or IR, as it doesn't involve light at all. Instead, we take a sample and ionize it in the gas phase. We then use electric fields to measure the mass to charge ratio (m/z) of the resulting ions (generally, z=+1, but other values are possible). One way to do this is called **electron impact (EI)**:

$$M + e \rightarrow \quad [M]^{+\cdot} \quad + \; 2e$$

This means that we bombard the molecules with electrons, making them lose electrons to form radical cations. This is quite an energetic process, so the molecular ion usually fragments. Fragmentation will try to make relatively stable cations (e.g., benzyl cation), but it is common to see less stable ones (e.g., methyl radical). The fragments can also rearrange in complex ways that we will not discuss. In the molecule below, the molecular ion is dwarfed by the fragment ions:



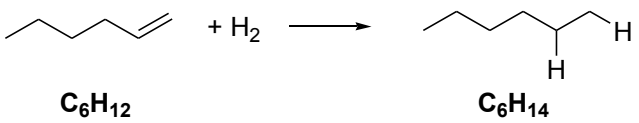
Because the purpose of MS is generally to establish the molecular formula, it is often desirable ionize in a "softer," lower energy way. In the lab, we will use **electrospray ionization**, which vaporizes a solution of the sample through an electrically charged nozzle. The molecular ion will generally not fragment and will be observed as an adduct with components of the solution:

$[M+H]^+$	m/z = M+1
$[M+NH_4]^+$	m/z = M+18
$[M+Na]^+$	m/z = M+23
$[2M+H]^+$	m/z = 2M+1

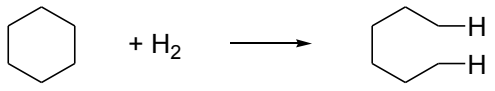
where M is the mass of the molecular ion. Dimer peaks are usually observed if the sample is too concentrated.

Every element has a distribution of known isotopes. For example carbon is 98.9% carbon-12 and 1.1% carbon-13. That means that the molecular ion appears as a small histogram of peaks, with a distribution that reflects the statistics of randomly drawing isotopes from a bag. On "high-resolution" instruments, each mass is accurate to four decimal places, so we can determine the molecular formula with high confidence.

The molecular formula is a useful piece of information because it tells us how many double bonds, triple bonds, or rings are in the molecule. This might seem surprising, so let me explain. As you know, alk*anes* have a general formula of C_nH_{2n+2} and alk*enes* have a formula of C_nH_{2n}. I can think of the alkane as having more hydrogen than the alkene:



Another way to say this is the alkene is more "saturated" with hydrogen. I can also achieve the same effect by forming a ring:



C_6H_{12} C_6H_{14}

The reason is that when I connect the ends of the ring, I have to get rid of two hydrogens to make the bond. So, I can tell from the fact that the formula is C_6H_{12} instead of C_6H_{14} that the molecule has a double bond or a ring in it. We say this the molecule has "one unit of unsaturation." In general, we can figure out how many units of unsaturation (*U*) a molecule has using this formula:

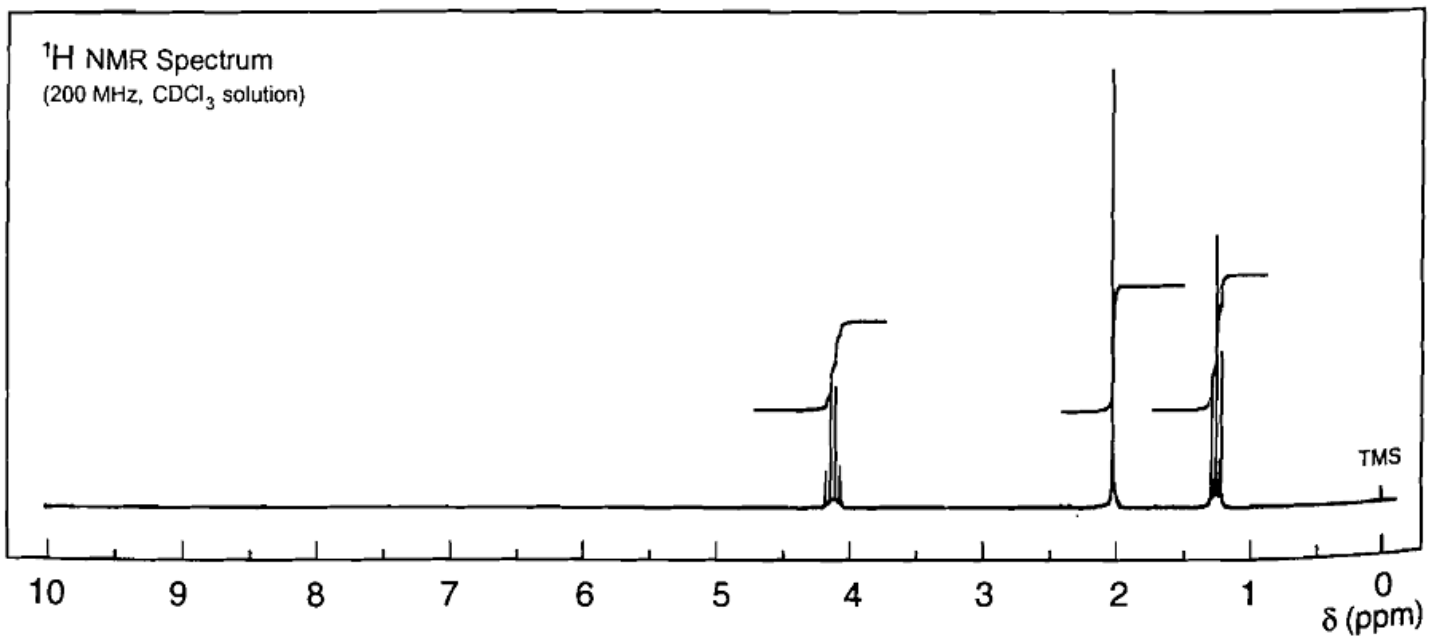
$$U = C + 1 - 0.5\,(H + X - N)$$

C is the number of carbons, *H* is the number of hydrogens, *X* is the number of other mono-valent atoms (e.g., halogens), and *N* is the number of nitrogens. *This is worth memorizing.* Double bonds (e.g., alkenes, carbonyls) count as one unit of unsaturation, while triple bonds (alkynes, nitriles) count as two. Rings always count as one.

Things to know: understand what an EIMS spectrum is and why it shows more than one peak; how molecular formula is determined from ESIMS data; and how to calculate the unsaturation number of a formula.

D. NMR

NMR is the most useful of the spectroscopy experiments for organic chemists. It depends on the fact that when common organic nuclei such as ^1H and ^{13}C are placed in a magnetic field, they precess. Not all nuclei are NMR active; for example, ^{12}C (98.9% abundant) is NMR-silent. The precession phenomenon is pretty complicated, but suffice it to say, when the nuclei are given the appropriate stimulus, they give off radiofrequency (RF) waves whose amplitude and frequency depends in a very specific way on their chemical environment. Here is a typical ^1H NMR spectrum (ethyl acetate, $C_4H_8O_2$):



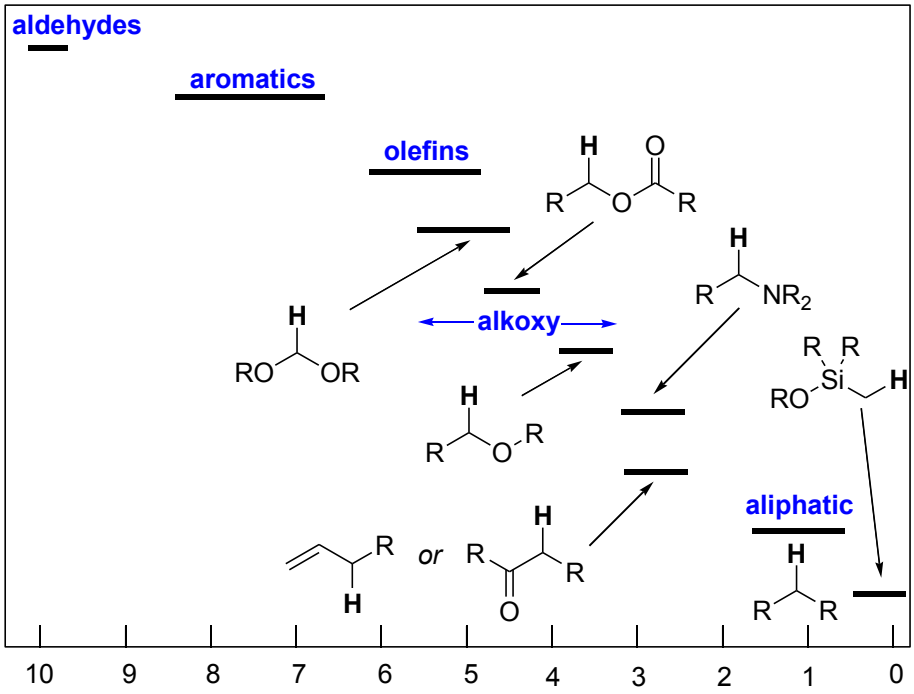
The x-axis reflects the frequency of the precession and is called **chemical shift** (ppm). For historical reasons, moving left means bigger numbers is called "going downfield." Bigger numbers mean the protons are more electron poor. For example, the ones near 4 ppm are next to oxygen, but the ones near 1 ppm are next to another carbon. Note that some of the peaks have a fine structure. The spacings between the sub-peaks reflect the **coupling constants** of the proton and give an indication of the connectivity of the molecule. For example,

the peaks at 4 and 1 ppm have the same spacings. This is because they represent the CH_2 and CH_3 of an OCH_2CH_3 group. Note that the area under each peak, given by the **integrals** above, are directly proportional to the number of protons. In this case, the ethoxy group protons have a ratio of 2:3. Ratios of integrals are proportional to the *empirical* formula, not the *molecular* formula. This means we don't know if the actual number of protons is 2:3, 4:6, or a higher multiple.

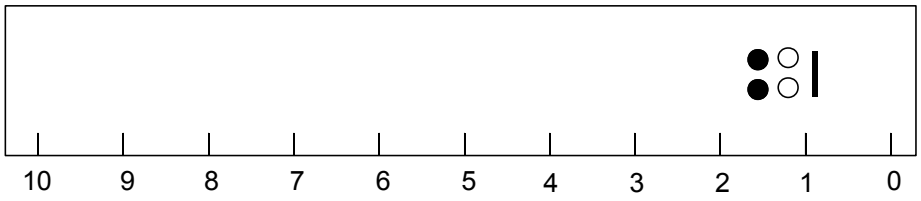
For our purposes, NMR spectra can only be recorded in the solution state. Therefore, one generally uses solvents that do not contain protons. This might mean choosing a liquid like carbon tetrachloride, or more commonly, the use of deuteration. This works because deuterium (^2H) is NMR active at a very different frequency than proton (^1H). Typical deuterated solvents include deuterochloroform ($CDCl_3$), dimethyl sulfoxide (d_6-DMSO), and water (D_2O). The frequency of TMS (tetramethylsilane) is defined to be 0 ppm and serves as an internal standard from which all the other chemical shifts in the spectrum can be calculated. However, it is common practice to omit TMS and reference all chemical shifts to residual, non-deuterated solvent. A small amount of protiated chloroform ($CHCl_3$) is always present in $CDCl_3$, resulting in a small signal at 7.26 ppm in proton spectra and 77 ppm in carbon spectra. A comprehensive list of solvent residual signals can be found in *Organometallics*, **2010**, *29*, 2176-2179. It would be worth knowing the solvent residual signals for chloroform, dimethyl sulfoxide, and water.

Tip: The solvent used can be a clue as to the polarity of the substance. Most non-polar compounds will be dissolved in chloroform, while polar compounds will require dimethyl sulfoxide or water. Furthermore, if you find yourself proposing a crazy-looking molecule, you should keep thinking. The compounds chosen for problems are usually commercially available compounds you will have heard of. One way to turn your thinking around is to ask what commodity chemicals or cheap natural products will have the properties you're seeing.

Most **proton chemical shifts** fall between 0 and 10 ppm. Knowing the chemical shifts of typical protons is absolutely essential:

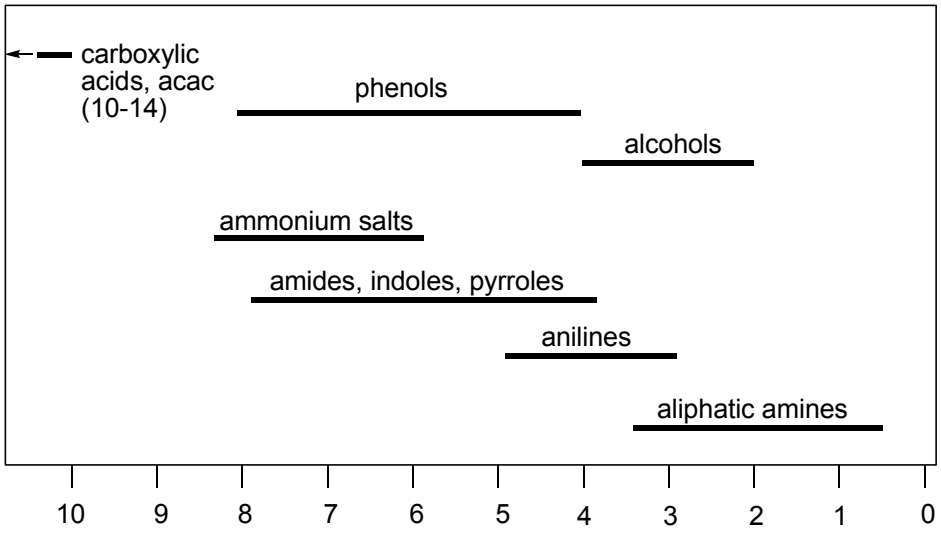


For more specific information, you have several choices. You can look up comprehensive tables of chemical shifts, such as the ones given in the book or class handouts. Functional group listings can also be useful. Silverstein gives charts that show where methine (CH), methylene (CH_2), and methyl (CH_3) groups resonate when adjacent to various functional groups. For example, for alkyl protons of the form MCH_2R:



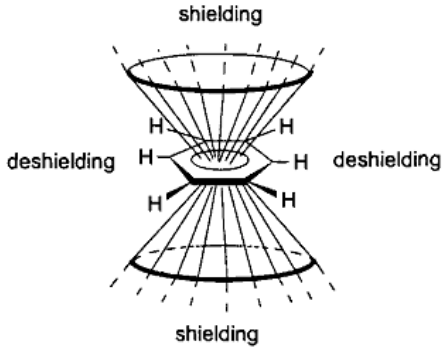
This follows the notation in Silverstein, where a solid bar means M=CH3, two open circles means M=CH2, and two shaded circles means M=CH. For other groups, the spread in chemical shifts will be much more pronounced. In general, chemical shifts will follow the ordering CH > CH_2 > CH_3. This parallels the trend that more electron-poor protons are more downfield (bigger chemical shift).

Exchangeable protons are those that are directly bonded to heteroatoms, such as alcohols or amines. Because of hydrogen bonding, their chemical shifts are quite sensitive to temperature, concentration, and solvent. This contrasts with most non-exchangeable protons, which are quite insensitive to these factors. Assuming a 5-20% solution in $CDCl_3$, there are some characteristic shifts that are worth knowing:



Because exchangeable protons are in chemical exchange (see below) with residual water, they can give broad signals. One way to verify whether a signal is exchangeable is to add a drop of D_2O. By mass action, the compound will incorporate a large amount of exchangeable deuterium. As a result, any exchangeable protons should disappear from the spectrum. (The other product of this reaction, water, will not be visible because of the immiscibility of chloroform and water.)

The chemical shift of a proton is greatly affected by what is around it. One important factor is called **magnetic anisotropy**. The classic example of this is aromatic rings, where protons above the plane of the ring will be shifted upfield (smaller shift) and protons in the plane of the ring will be shifted downfield (larger shift). This effect is transmitted through space, meaning that it doesn't matter whether the proton being affected is bonded to the aromatic ring or not: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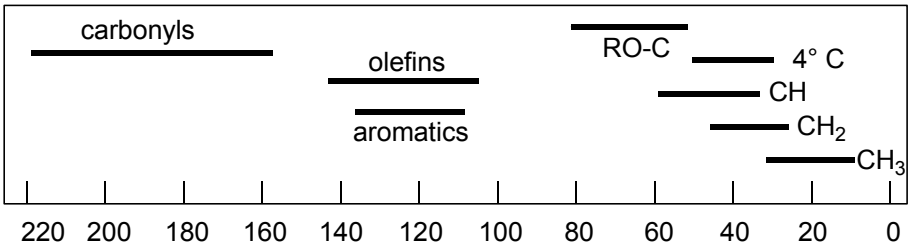
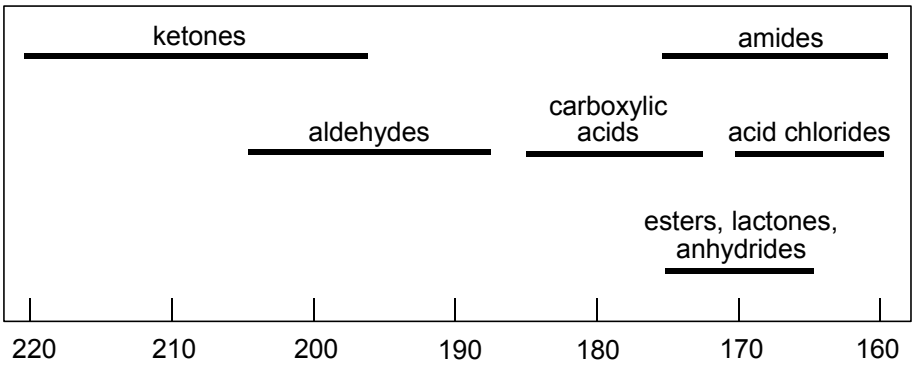
Carbon-13 chemical shifts cover a much larger range:

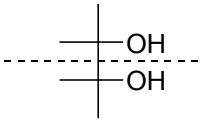


Unfortunately, the shifts of many common functional groups overlap. The two primary uses of a carbon spectrum are to (a) identify functional groups and (b) count the number of unique carbons. Like IR, there are characteristic shifts for different kinds of carbonyl groups:



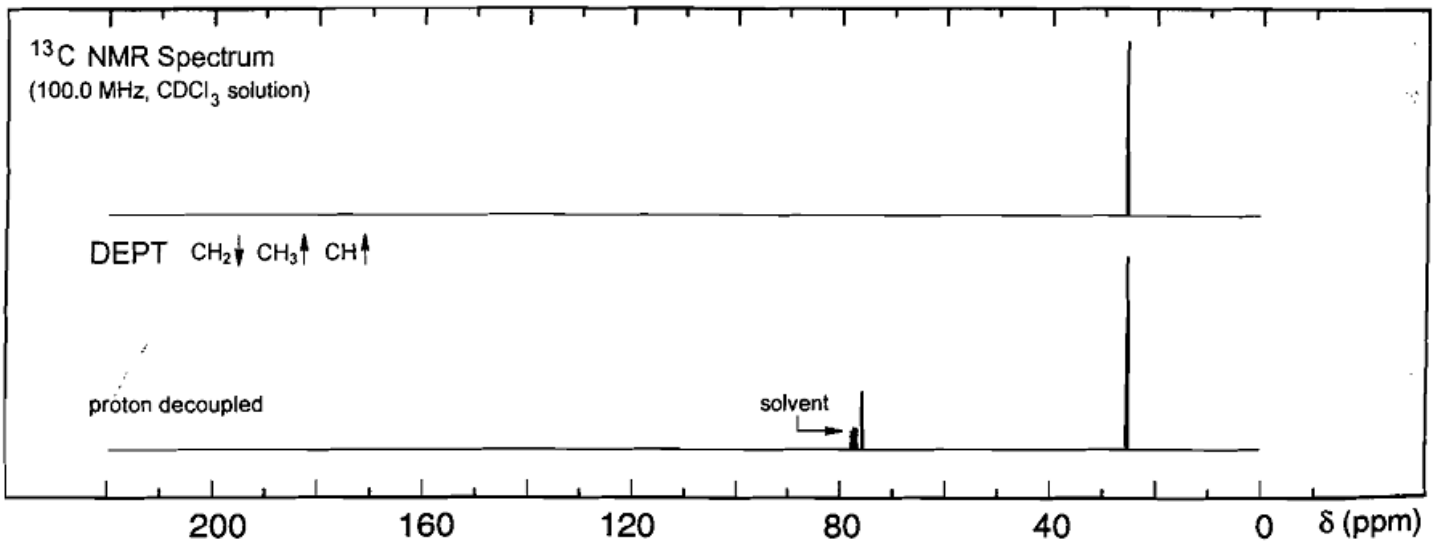
Just as in proton spectra, the number of carbon signals can be smaller than the number of carbons in the molecular formula if there is symmetry present. For example, consider this spectrum of pinacol:

six carbons, but only two signals!



$C_6H_{14}O_2$

pinacol



Note the residual chloroform at 77 ppm. In this case, an additional experiment called **DEPT (distortionless enhancement by polarization transfer)** has been performed. Specifically, this is a DEPT-135 spectrum,

where the methines and methyl groups appear with positive phase and methylenes appear with negative phase. Quaternary carbons (i.e., those with no attached protons) do not appear. The book will occasionally show some "off-resonance decoupled" spectra. This is an older technique where quartets represent methyl groups, triplets represent methylene groups, doublets represent methines, and singlets represent quaternary carbons. Under normal conditions, *carbon-13 spectra cannot be integrated*.

The fine structure within peaks is related to its **coupling constants**. This is a complicated topic, but I can summarize the essentials as follows:

1. One proton will couple to, or "split," another proton only if they have different chemical shifts. We can determine whether a pair of protons will split each other by applying the following definitions:

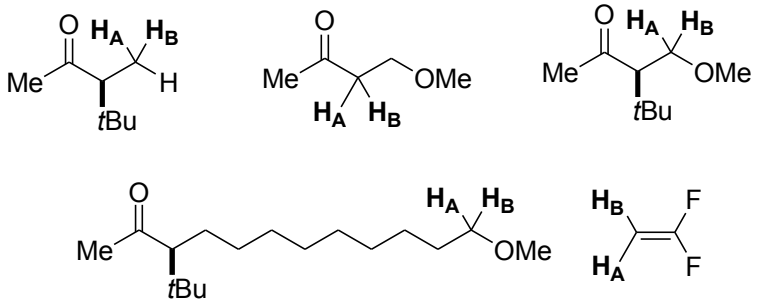
   Homotopic protons are related by rotational symmetry (e.g., those in a methyl group). They have the same chemical shift and will not split each other. *Test:* replace one proton with a deuterium. No chiral center is produced.

   Enantiotopic protons are related by reflection symmetry and will have the same chemical shift. *Test:* replace one proton with a deuterium. One of a pair of enantiomers is produced.

   Diastereotopic protons are neither homotopic nor enantiotopic. They *may* have different chemical shifts.

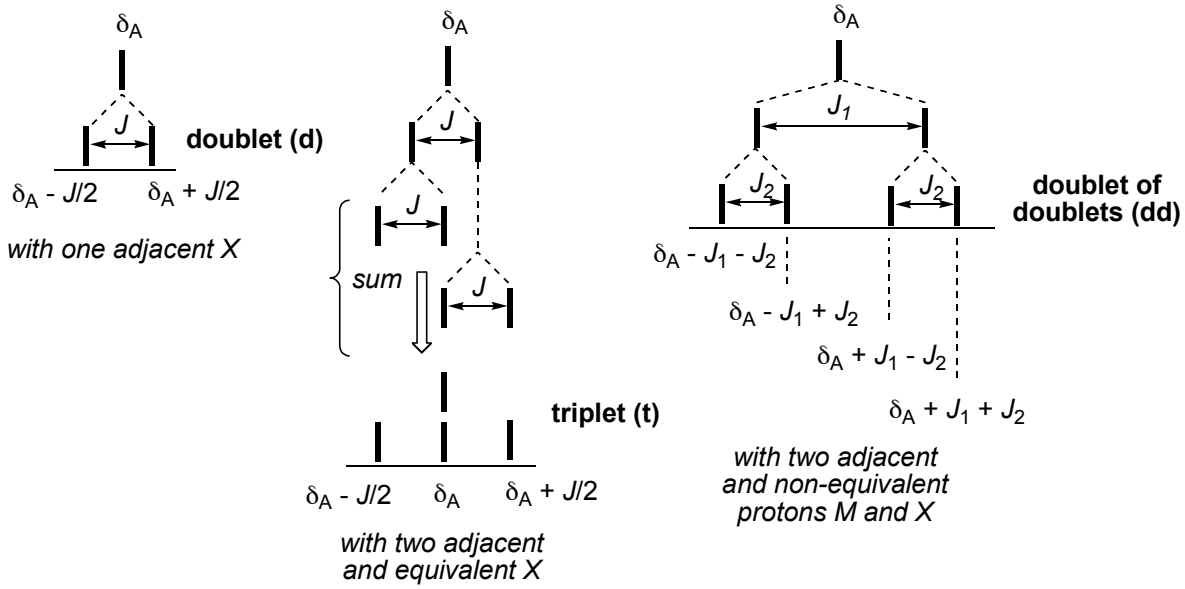
   Note that enantiomers have the same NMR spectrum but diastereomers have different NMR spectra. Two protons are considered **chemically equivalent** if they have the same chemical shift. However, they may or may not also be **magnetically equivalent**, which demands that they also have the same coupling constant to any other NMR-active nucleus in the molecule. For two protons to be considered "the same" for the purposes of determining whether they split each other, they must be both chemically equivalent *and* magnetically equivalent.

   Here are some examples. For each of the compounds below, determine if the indicated protons are (a) homo-, enantio-, or diastereotopic, (b) chemically equivalent, and (c) magnetically equivalent:



   Answers (left to right, top to bottom):
   homotopic/yes/yes; enantiotopic/yes/yes; diastereotopic/no/no; diastereotopic, but effectively enantiotopic; homotopic/yes/no (they have different coupling to the fluorines).

2. The ***n*+1 rule** states that a proton split by *n* equivalent protons will give a multiplet with *n*+1 lines. The intensity of these lines will follow those of Pascal's Triangle. Here's why:



Consider a proton A that is adjacent (vicinal) to another proton X of a different chemical shift. These protons will split each other with a coupling constant *J* (Hz). The result will be a four line spectrum, a doublet centered at δ_A (shown) and a doublet centered at δ_X (not shown).

If A is adjacent to two identical protons X, then we can figure out what happens by repeating the splitting process twice. A and X_1 will form a doublet with spacing *J*. A and X_2 will also form a doublet with spacing *J*. Because the spacings are the same, the two center lines will coincide, leading to a triplet with intensity 1:2:1. Higher-order versions of this process will produce 1:3:3:1 and the higher levels of Pascal's Triangle.

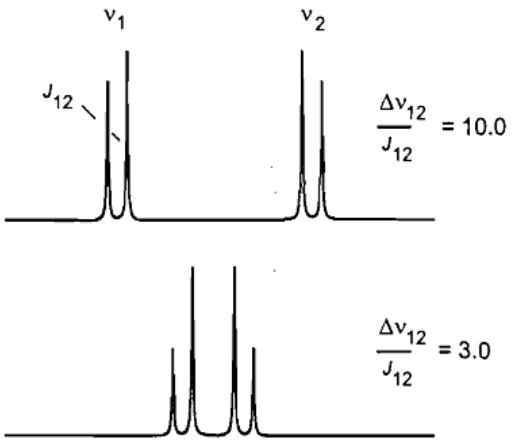
The more general case is that A is next to two *different* protons, M and X. In that case, the center lines will *not* overlap. We then see a doublet of doublets. You should consider all Pascal-type multiplets to be degenerate doublets of doublets of …

3. The coupling constants are a property of the molecule and fixed quantities in Hz, while chemical shifts depend on the magnetic field strength and are in ppm. The conversion is:

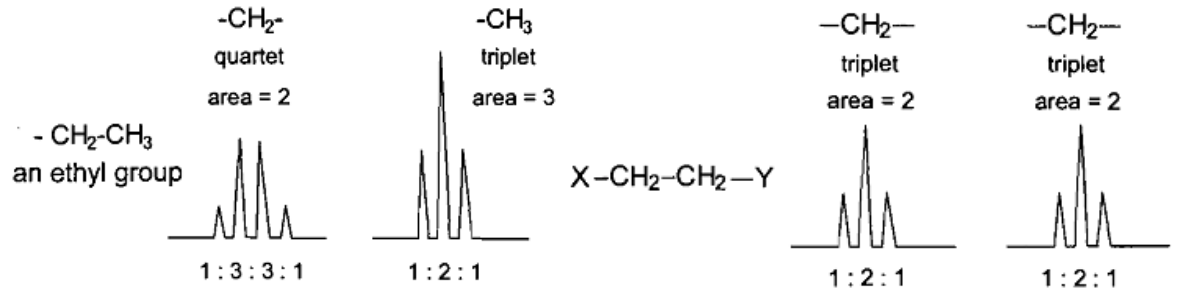
chemical shift (ppm) * field strength (MHz) = chemical shift (Hz)

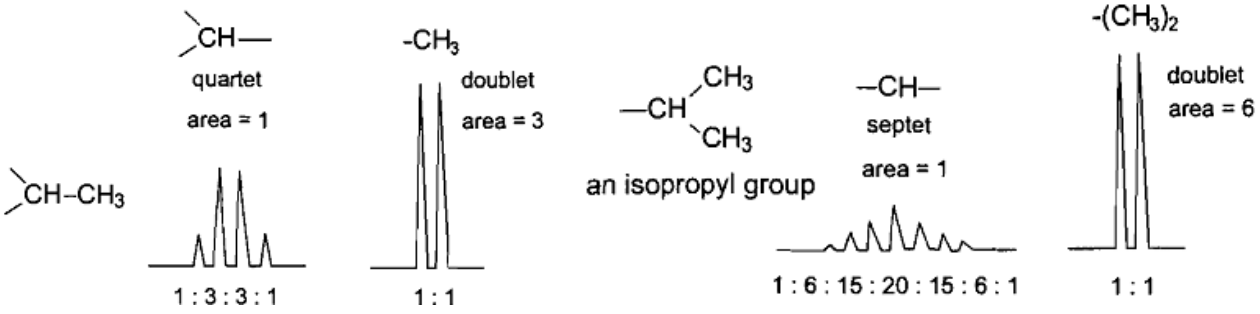
For example, a 0.01 ppm spacing between peaks at 500 MHz might represent a 5 Hz coupling. The true chemical shift of any multiplet is the center of the multiplet, regardless of whether there is actually a peak there.

4. As a rule of thumb, if the frequency separation (Hz) between the coupled peaks is less than ten times the coupling constant, then the above rules will not apply. Such spectra are called **second-order**. Second-order peaks may be centrosymmetric, but will not have intensities assignable to *n*-th order doublet of doublets. A common indication of this problem in a doublet of doublets is a "roof-like" tilting of the peaks (see Figure 5.10):



5. It's worth knowing some of the common coupling patterns, since this will let you identify molecular fragments easily:

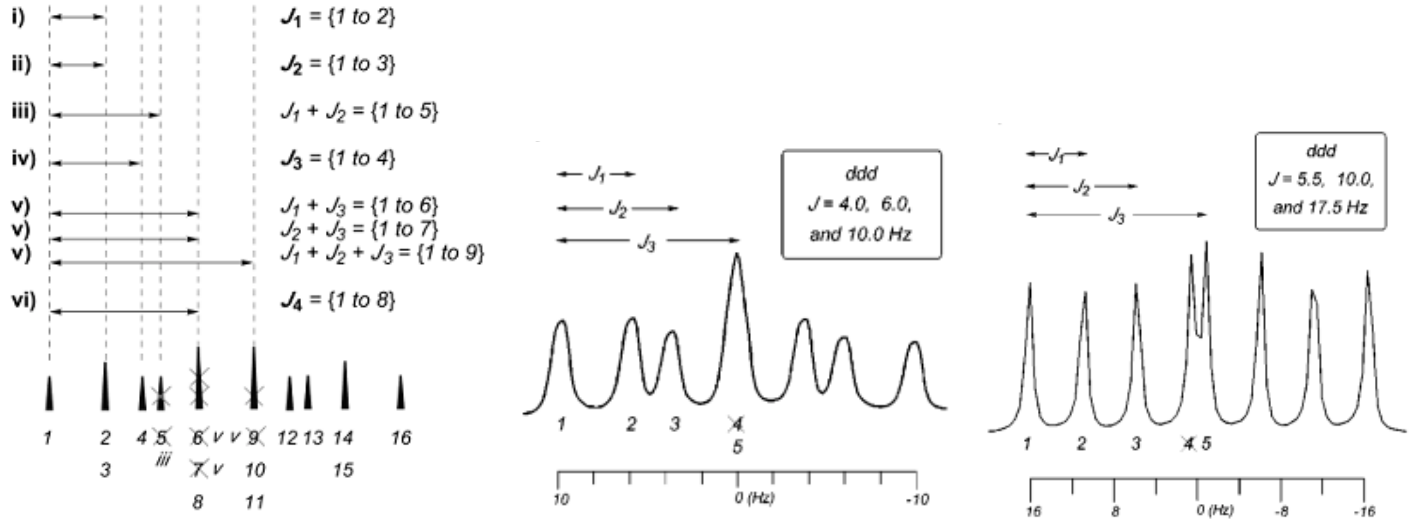




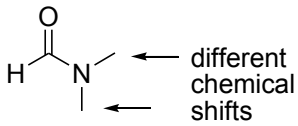
6. To extract coupling constants from a first-order peak, follow the procedure of Hoye (see the references in point 5 on the first page). I summarize it here:

   (a) Confirm the peak is first-order.
   (b) View the peak as an *n*-th order doublet of doublets. Determine *n* by assigning components.
   (c) The distance from component 1 to 2 is J_1. The distance from component 1 to 3 is J_2.
   (d) Look J_1+J_2 Hz right from component 1. If there is a peak there, remove *one* of its components from consideration. (If there's more than one component there, then only remove one. If there's no component there, then don't do anything.)
   (e) The distance from component 1 to the next component is J_3.
   (f) Repeat (d) and eliminate one component for each of J_1+J_3, $J_2 + J_3$, and $J_1 + J_2 + J_3$. Do not remove J_1+J_2 again. The distance from component 1 to the next component is J_4. Repeat until all *n* components have been found. You may verify your answer by constructing a coupling tree.

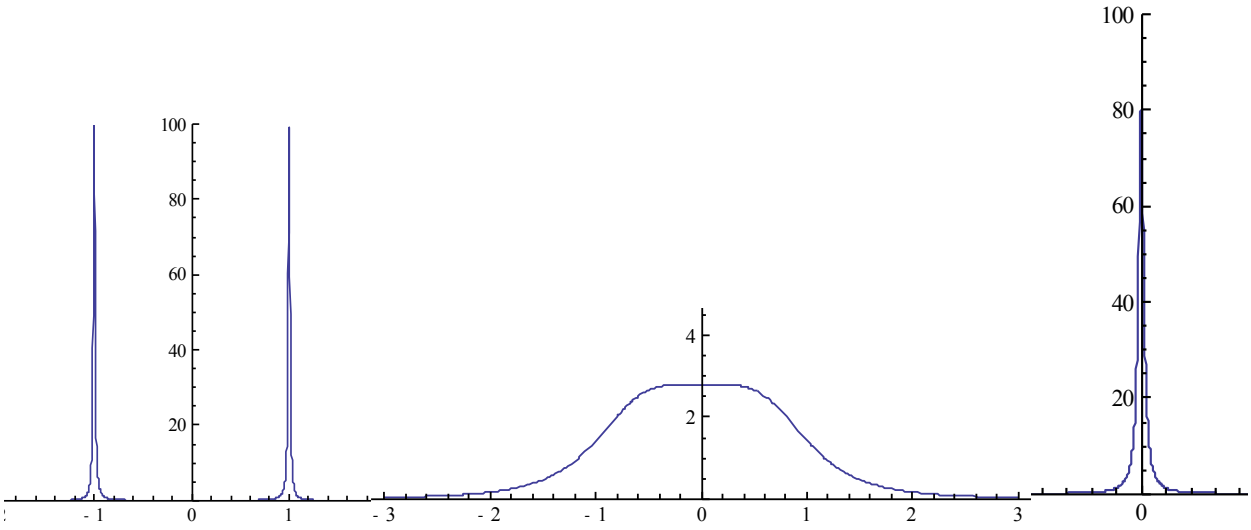
Here are some examples from the paper:



Sometimes peaks will become broad because there are two species present in solution, rather than *J*-coupling. This is called **chemical exchange**. A classic example is the spectrum of *N*,*N*-dimethylformamide:



The two methyl groups are at different locations with respect to the magnetically anisotropic carbonyl group and have different chemical shifts. If amide rotation is very slow, then we will see two distinct peaks for the methyl groups. If amide bond rotation becomes very fast, the different chemical shifts will become averaged and we will see one chemical shift. Since temperature controls the rate of rotation, it is possible to be at an intermediate temperature where we are somewhere between slow and fast. When this happens, the two peaks will be in the process of coalescing into one. The diagram below shows the transition from slow to intermediate to fast exchange for two exchanging chemical shifts at -1 ppm and +1 ppm:



Review Questions

These are basic questions you should be able to answer after reading this study guide. Answering them will not be enough; you'll have to practice applying these ideas on the problems in the book.

1. Given an absorbance, concentration, and path length, how do you calculate ε? What kinds of absorptions are indicative of significant conjugation?

2. Where do the following functional groups absorb in the infrared?

(a) OHs and NHs (b) alkanes, alkenes, and alkynes (c) carbonyl groups
(d) aromatics (e) nitro groups

3. What are the key differences between EIMS and ESIMS? How do you calculate the unsaturation number given a molecular formula?

4. What are typical proton chemical shifts for (a) alkanes, (b) ethers, (c) olefins, (d) aromatics, and (e) aldehydes? Which would you expect to be more downfield, a methine adjacent to an ether oxygen or a methylene adjacent to the same ether oxygen?

5. How would you distinguish between a ketone and an amide carbonyl group with carbon-13 NMR? A methine and a methylene group? Can carbon spectra be integrated?

6. Sketch the expected spectra for (a) an isopropyl group, (b) the fragment $–CH_2-CHR-$ where the CHR fragment is a chiral center, and (c) a *tert*-butyl carbamate.

In-Class Practice Problem Answer Key: