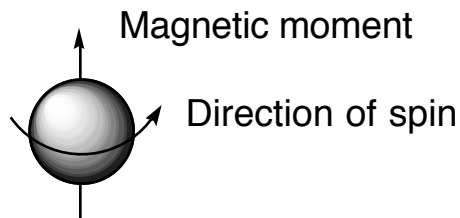


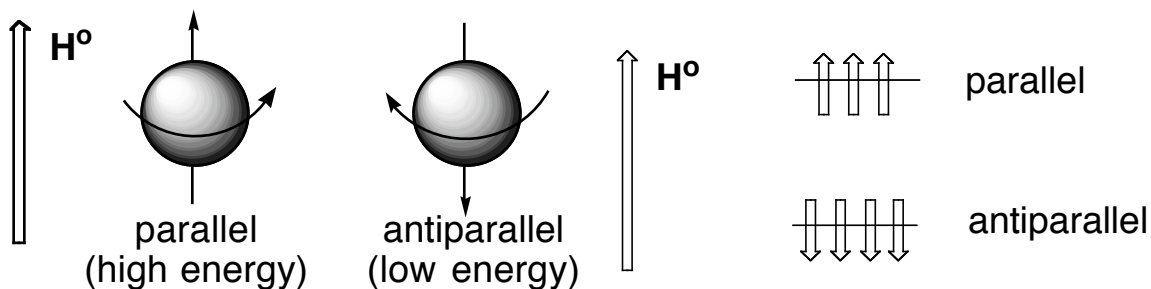
CHEM 3306
Nuclear Magnetic Resonance (NMR) Spectroscopy

Physics

Nuclear Spin: It is experimentally observed that some nuclei act as small magnets. Nuclei have a charge, and a spinning charged particle generates a magnetic field, so it is said that these nuclei have "spin". Only nuclei with an odd number of protons (atomic number) or an odd number of neutrons (isotope) have spin.

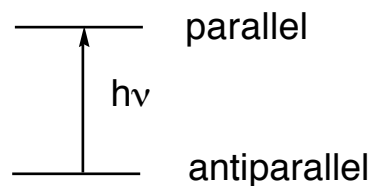


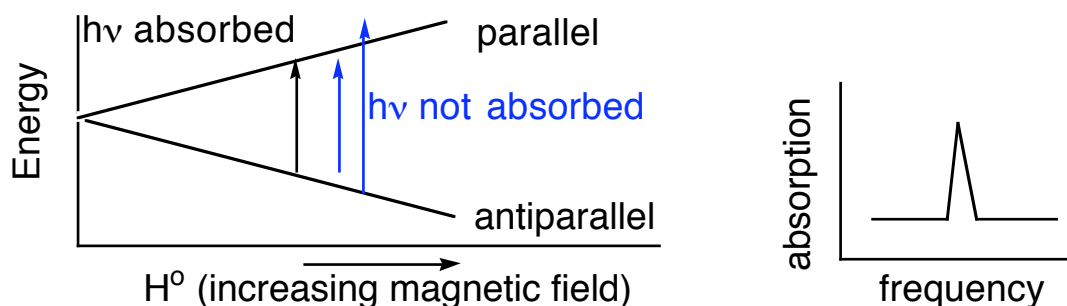
Observation of nuclear spin: Most macroscopic manifestations of magnetism are due to electron spin. Nuclear spin is usually observed by first placing a nucleus in an external magnetic field (H^0). The nuclear magnetic moment is quantized and can either line up parallel to H^0 or antiparallel to it. Remember that the north pole of a magnet is attracted to the south pole. Thus the antiparallel alignment is more stable.



As with any situation with more than one energy level, there will be a Boltzmann distribution, with a majority of nuclei in the low energy state, but some nuclei in the higher energy state. In fact, as the energy differences are quite small (radio frequency) the equilibrium is close to 1:1.

As with any quantized phenomenon, absorption of a photon can occur from the low energy state to the high-energy state. It happens that in this case, the photon is in the radio frequency range. The frequency depends on a number of factors, including the strength of H^0 and the identity of the nucleus. At higher magnetic field, the energy difference between parallel and antiparallel is larger and the population difference is similarly larger, so higher field instruments are inherently more sensitive.

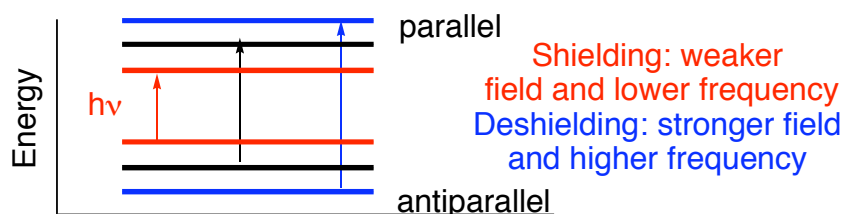




¹³C NMR Spectroscopy

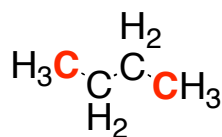
Perhaps the easiest place to start is with ¹³C NMR. The natural abundance of the magnetic ¹³C isotope is only about 1%, while 99% is the non-magnetic ¹²C. This means that for a ¹³C nucleus in a molecule, there is a 99% chance that a neighboring carbon is ¹²C and non-magnetic. Most ¹³C NMR spectra are "proton-decoupled", meaning that we don't see the ¹H nuclei, even though they are also magnetic. More on coupling later.

Chemical Shift: The nuclei are (almost always) in an atom or a molecule and are thus surrounded by electrons. The magnetic spin of the electrons "shield" the nuclei so they do not see quite as strong a magnetic field as is applied outside the molecule. This means that it takes a lower energy photon to cause the absorption.

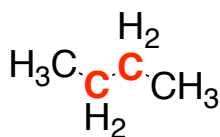


Changes in the electron density change the "effective field" the nucleus sees and change the frequency of the absorption. These changes are quite small, only 1 to 200 parts per million (ppm) for ¹³C, but they are observable. Indeed, you know of many factors, which influence the electron density or partial charge on an atom. These are manifest in the NMR spectra and are referred to as "upfield" or "downfield" shifts relative to tetramethylsilane [(CH₃)₄Si; TMS].

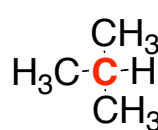
There are a few trends to remember. More substitution generally shifts the chemical shift downfield. The reasons for this are subtle – meaning I can't give you a simple explanation. Just remember the trend.



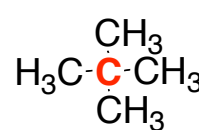
methyl
0-30 ppm



methylene
15-55 ppm

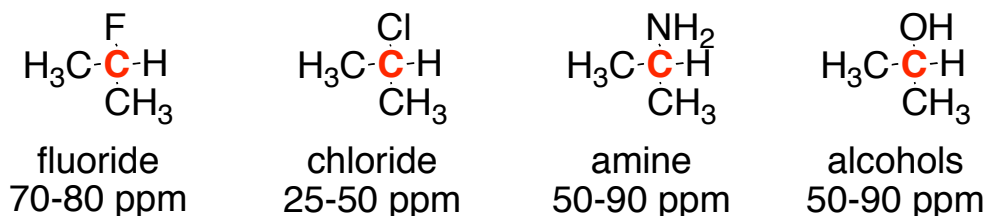


methine
25-55 ppm

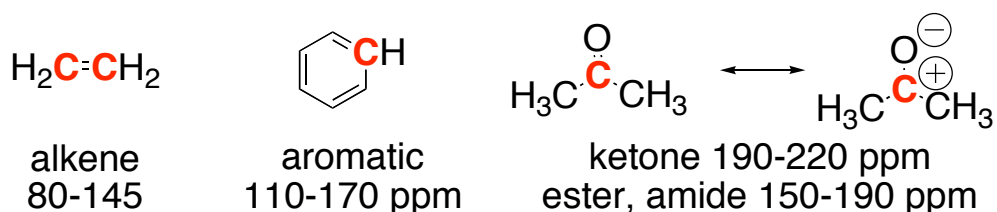


quaternary
30-40 ppm

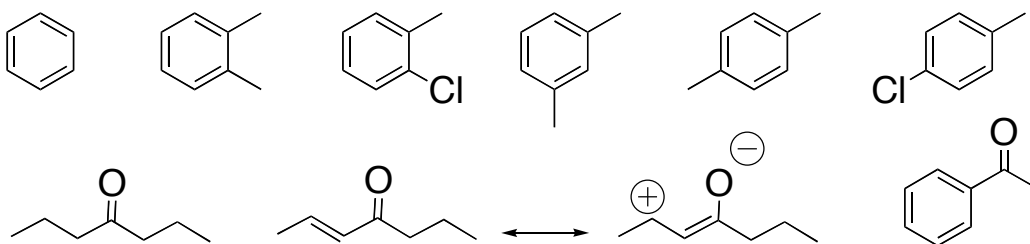
More logically, adding an electronegative group removes electron density from the carbon and thus moves the chemical shift downfield. So halides, amines and alcohols will all be shifted downfield from an alkane. The effects are remarkably additive, so the carbon in a 3° alcohol will be more downfield than the carbon in a 1° alcohol.



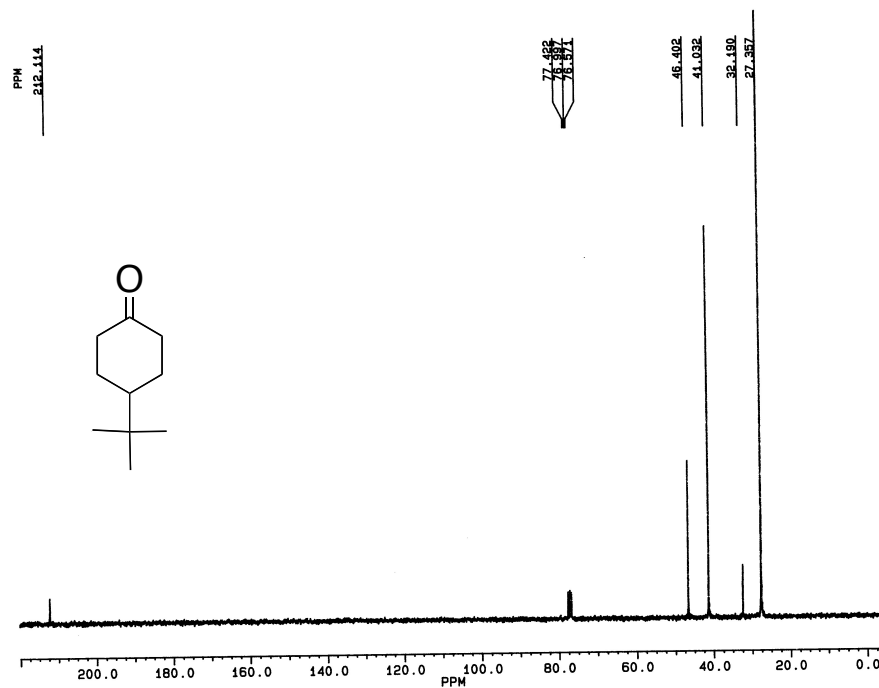
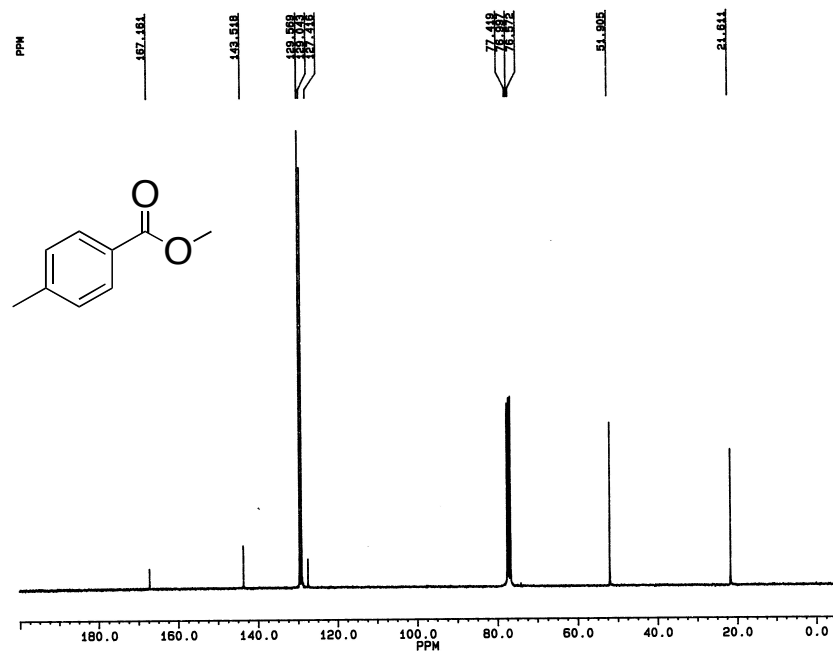
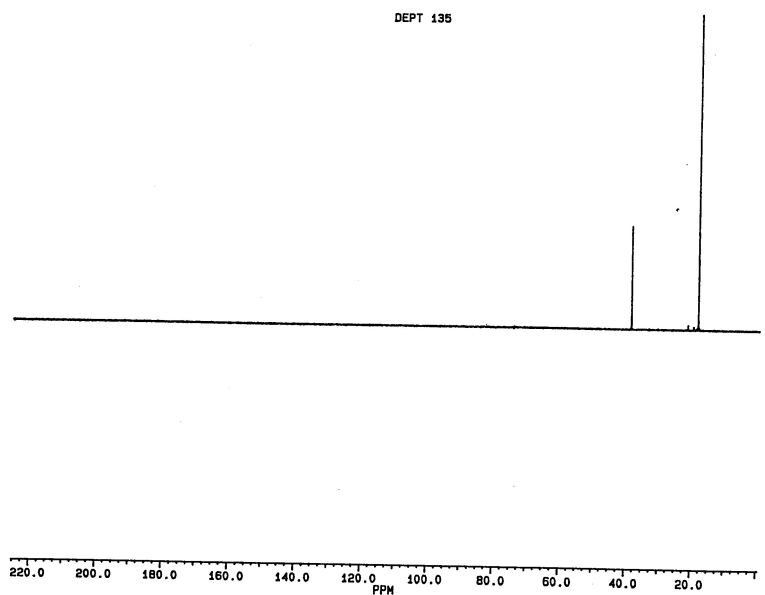
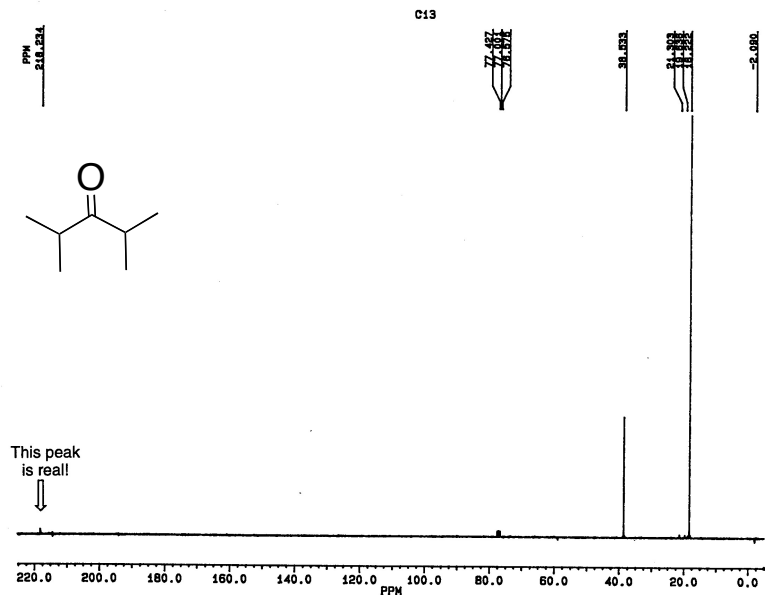
Hybridization also makes a difference – sp^2 carbons are further downfield than sp^3 . As a simple rule of thumb, 100 ppm is a convenient dividing line in the spectrum; generally sp^3 carbons are to the right of 100 ppm and sp^2 carbons are to the left. Carbons in an aromatic ring are even further downfield; this is attributed to an induced “ring current” in the aromatic ring that leads to a separate deshielding magnetic field. The furthest downfield carbons are generally carbonyl carbons, since they are sp^2 hybridized and bonded to an electronegative group. (Consider the charge separated resonance structure shown below.)



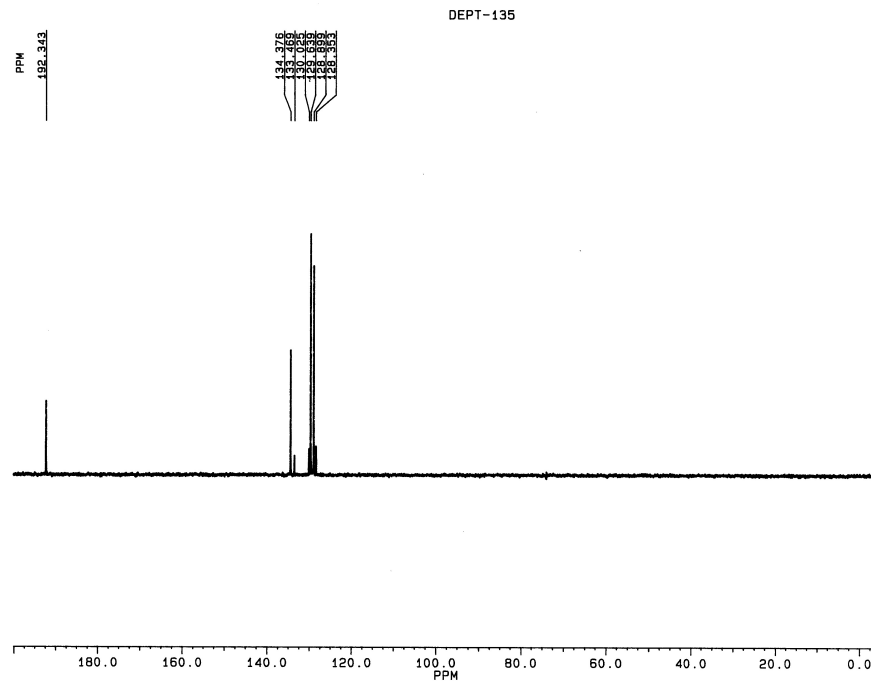
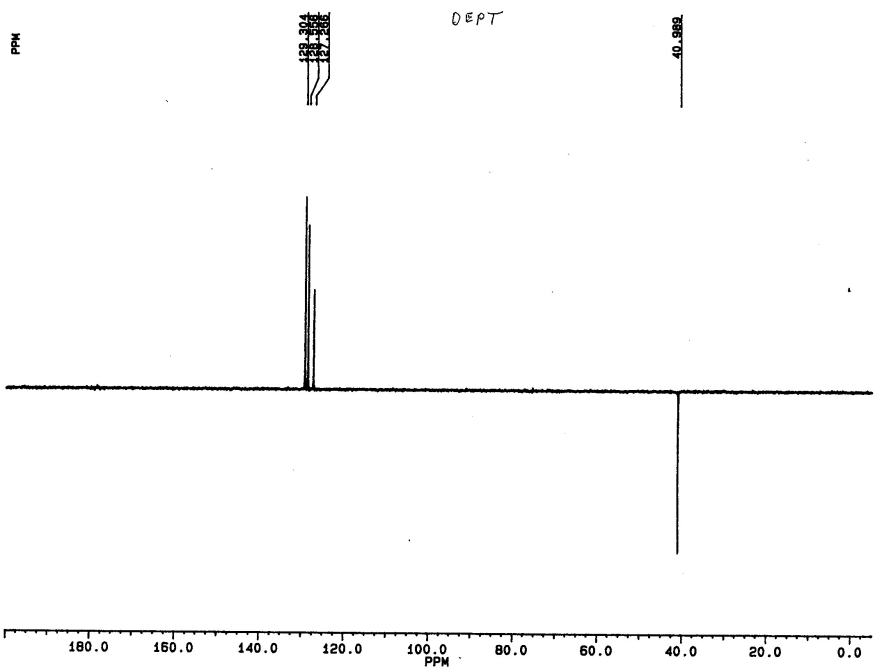
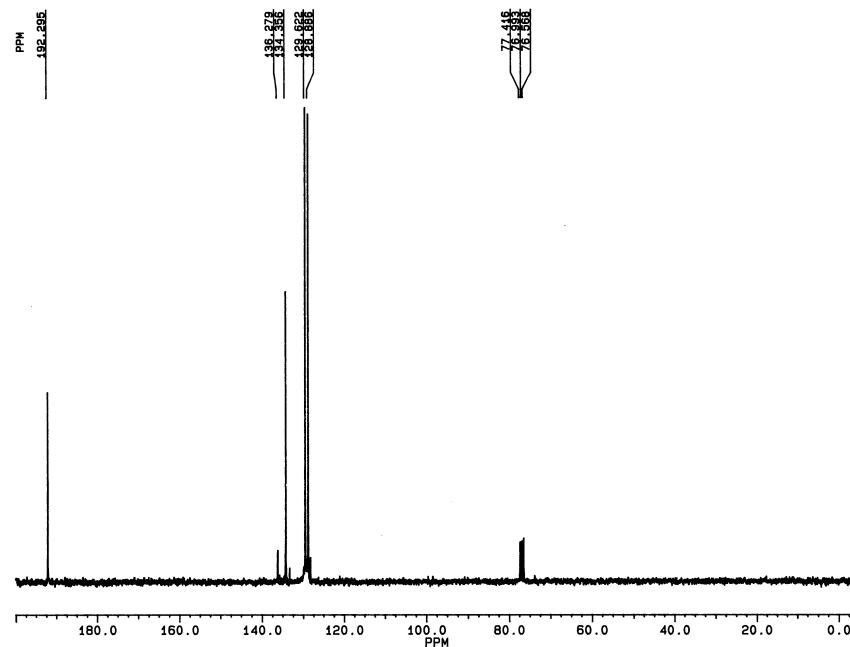
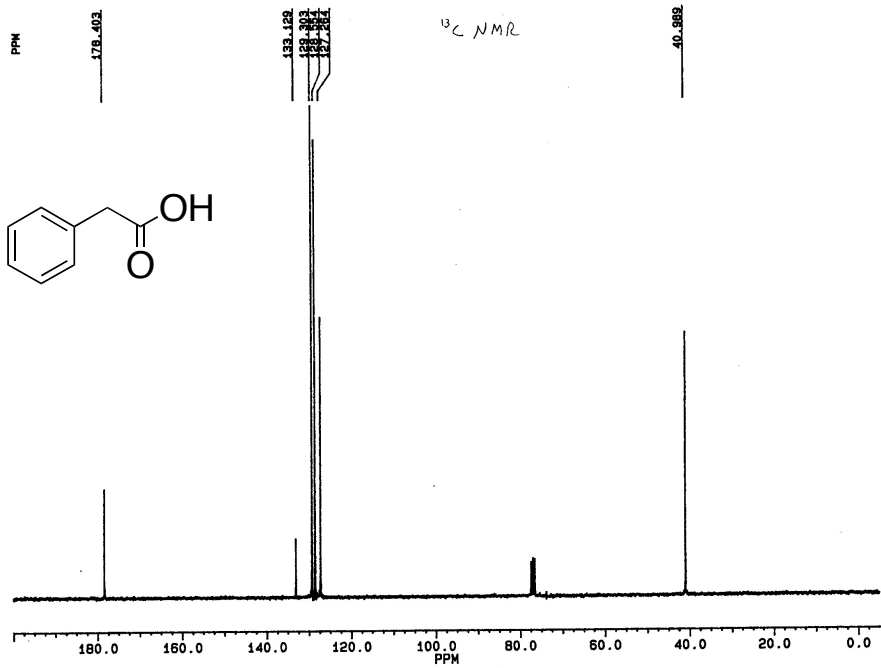
Symmetry: One of the most important aspects of ^{13}C NMR is simply counting carbons. However, symmetry becomes important, so that carbons that are in exactly the same environment by symmetry will have exactly the same chemical shift and look like a single peak. How many peaks will be observed in the ^{13}C NMR of these compounds? What are the approximate chemical shifts?



DEPT-135: This experiment gives positive peaks for methyl and methine carbons, negative peaks for methylene carbons and quaternary carbons disappear.



DEPT-135: This experiment gives positive peaks for methyl and methine carbons, negative peaks for methylene carbons and quaternary carbons disappear.

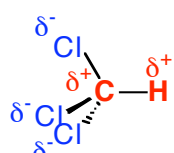


¹H NMR: (Proton NMR)

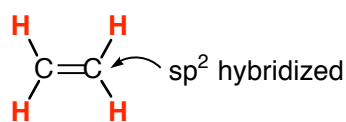
Fortunately for organic chemists, the most abundant isotope of hydrogen (¹H) is "NMR active", i.e. the nucleus has a spin of 1/2, while ¹²C and ¹⁶O have no spin. Thus in the simplest NMR experiments to conduct, one only "sees" the hydrogens. However, these are seen in exquisite detail! This makes the interpretation more difficult.

Chemical Shift: The trends in chemical shifts are very similar in both ¹³C NMR and ¹H NMR spectra. A group that is more electron withdrawing removes electron density and shifts the proton signal "downfield". The range is smaller, generally 0 – 10 ppm.

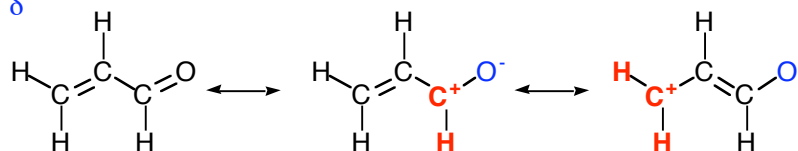
Electron withdrawing groups



Hybridization



Resonance



Bold indicates a downfield shift.

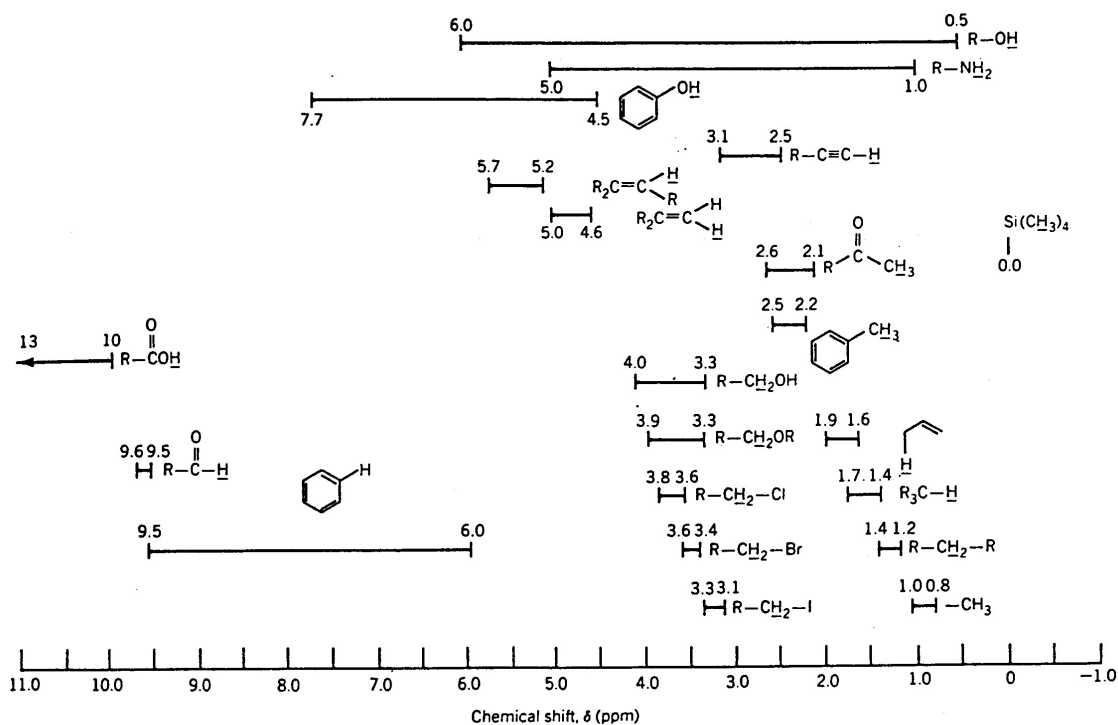
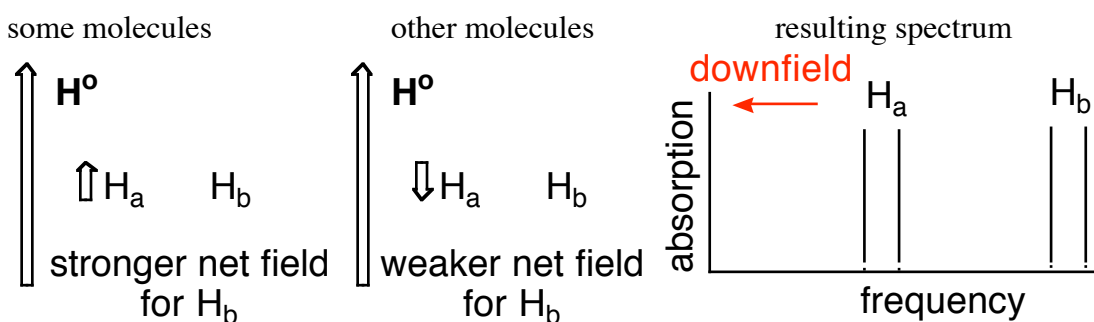


FIGURE 9.59 NMR ¹H chemical shifts. From Zubrick, J. W. *The Organic Lab Survival Manual, 3rd ed.*; Wiley: New York, 1992. (Reprinted by permission of John Wiley & Sons, New York.)

Integration: The more hydrogens, the stronger the absorption. Within a given compound, the integrated signal intensity for a given hydrogen will be proportional to the number of equivalent hydrogens. Thus, the relative intensities of different hydrogens give the relative numbers of hydrogens in the molecule. So a methyl group should integrate to three hydrogens and a methine to one hydrogen. (Note: in ^{13}C NMR spectroscopy, intensity does not necessarily reflect the number of carbons.)

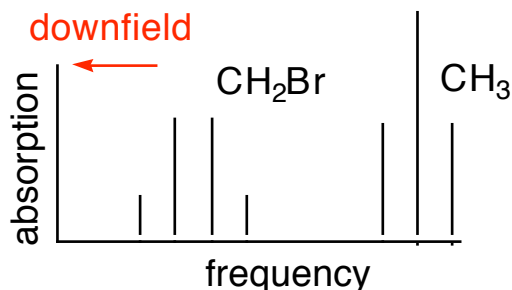
Spin-Spin Coupling: There is an even more subtle, and very important effect that is observed in ^1H NMR spectroscopy. If there are two ^1H nuclei in a molecule, they both are magnets and influence each other! Consider a sample containing $\text{H}_a\text{-C-C-H}_b$ and the effect that the two spins of H_a can have on H_b .



Coupling Constants. Note that the separation between the two peaks from H_a are the same as those from H_b . This is the coupling constant, J (in units of Hz). The magnitude of J is **always** the same in the two nuclei that are coupled to each other and it depends *only* on the relationship between the two nuclei. Thus the magnitude of J provides significant information about that relationship. If there are more hydrogens, each contributes to the splitting, in a predictable way.

Ethyl group splitting. Consider a molecule such as bromoethane ($\text{CH}_3\text{CH}_2\text{Br}$). First, the methylene hydrogens (CH_2) will be shifted further downfield than the methyl hydrogens (CH_3) because they are closer to the electron withdrawing Br (chemical shift). Second, each of the methylene hydrogens has the same chemical shift and do not couple with each other. Third, each of the methylene hydrogens is next to three methyl hydrogens and is coupled to them.

	$\text{CH}_3\text{CH}_2\text{Br}$	
+++		1
++-	+ - +	3
+--	- + -	3
---		1



This gives four peaks, in a 1:3:3:1 ratio.

Based on these two examples, it is apparent that the splitting of a hydrogen (or several equivalent hydrogens) will reflect the number of *neighboring* hydrogens.

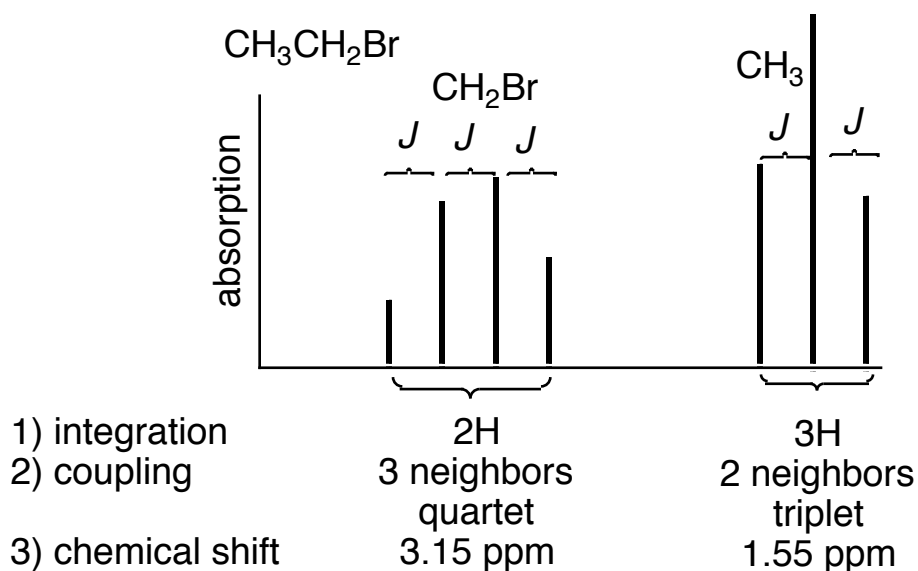
<u>Neighbors</u>	<u>splitting</u>	<u>Intensity</u>
0	singlet	1
1	doublet	1 1
2	triplet	1 2 1
3	quartet	1 3 3 1
4	quintet	1 4 6 4 1

Pascal's triangle

Second order effects: Note that intensity pattern is not perfect, but that the peaks tend to lean towards each other. Indeed, as the chemical shifts of two peaks approach each other, they eventually coalesce into a single peak.

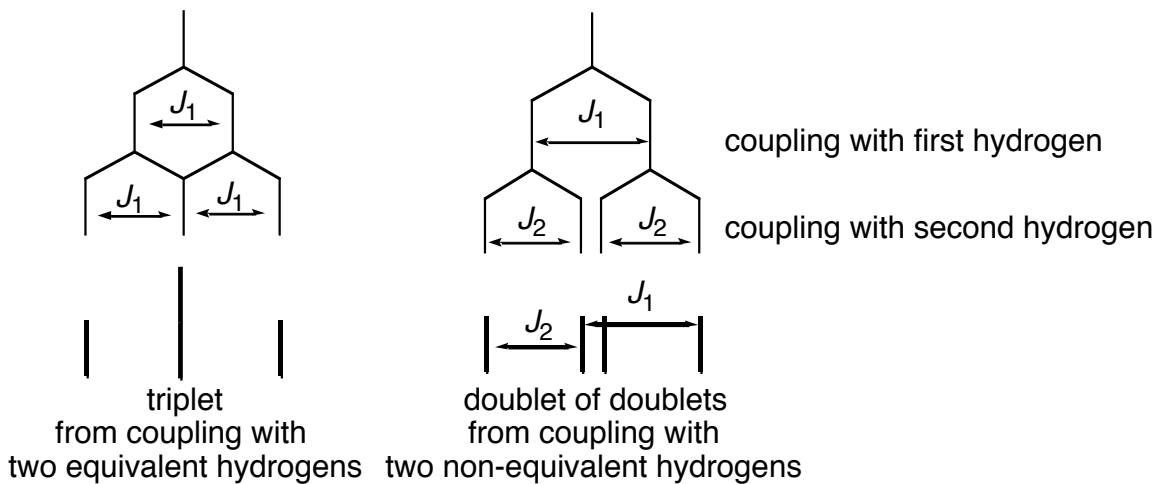


Thus, the actual NMR spectrum of bromoethane will look like this:

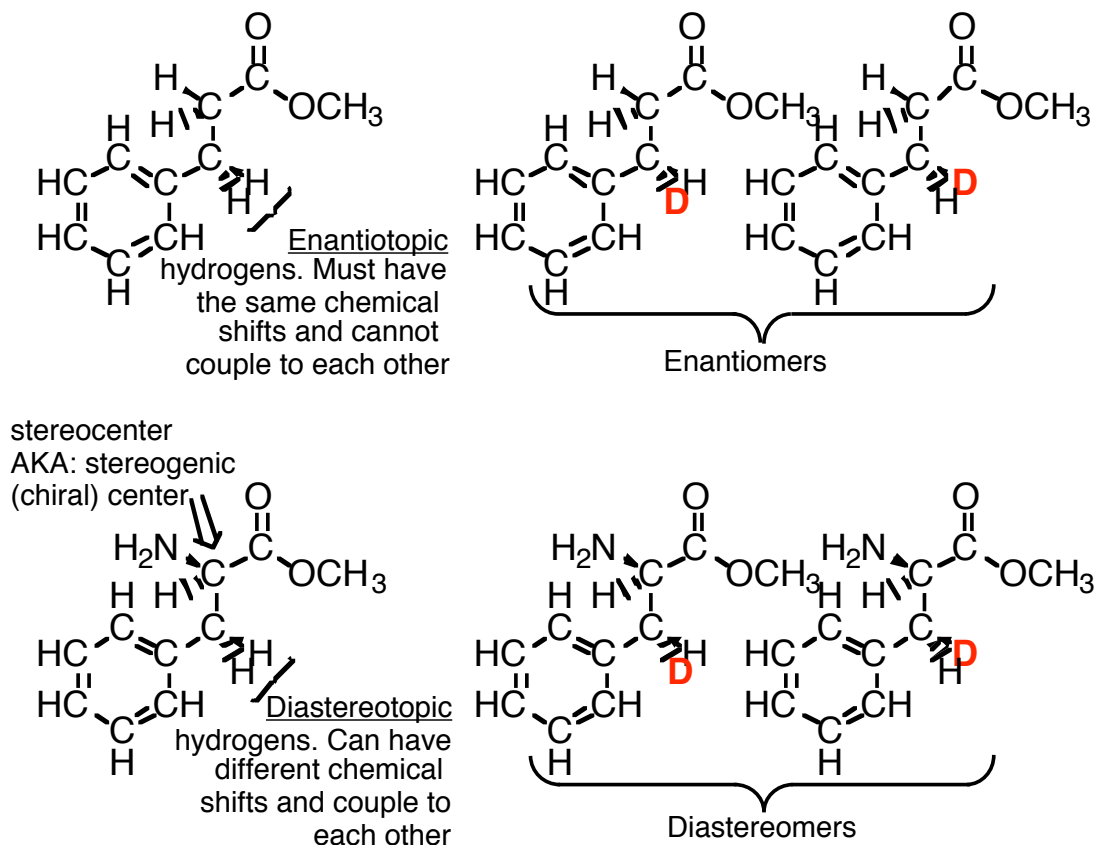


In summary, the things to look for in the spectrum are (1) the integration, which tells you how many equivalent hydrogens there are (2) the couplings, which tell you how many neighboring hydrogens there are and (3) the chemical shift (frequency) which tells you something about what electron withdrawing groups are near the hydrogens.

Real life couplings are sometimes more complicated. If hydrogens have different neighboring hydrogens, they may experience different couplings (coupling constants, J_1 and J_2) with each neighbor. Fundamentally, this is the same as what we have seen before. In both examples below, one peak is split into a doublet by one hydrogen, and then each peak of the doublet is split by a second hydrogen into another doublet. On the left, the two couplings are identical; this gives rise to the expected triplet from two identical neighboring hydrogens. On the right, the second coupling is smaller than the first. This gives rise to a doublet of doublets.



Equivalent hydrogens and stereochemistry: It is important to be able to look at a structure and determine whether some hydrogens will have the same chemical shift and/or are magnetically equivalent, as this determines the coupling patterns that are observed in the NMR spectrum. The first example shown below is of enantiotopic hydrogens. They have the same chemical shift and do not couple to each other. The spectrum of the indicated hydrogens would simply be a triplet, from coupling to the adjacent hydrogens. The second example shows diastereotopic hydrogens. The actual NMR spectrum for this compound is shown on the following page.



Homotopic protons will have the same chemical shift. They may or may not be magnetically equivalent. In a methyl group for example, they are magnetically equivalent and are considered as a unit.

Diastereotopic hydrogens can accidentally have the same chemical shift, but usually they will have different chemical shifts. Thus they can be, and often are, magnetically nonequivalent. **Think:** What makes compounds diastereomers? The same factors make hydrogens diastereomeric.

Enantiotopic hydrogens have the same chemical shift in achiral environments.

