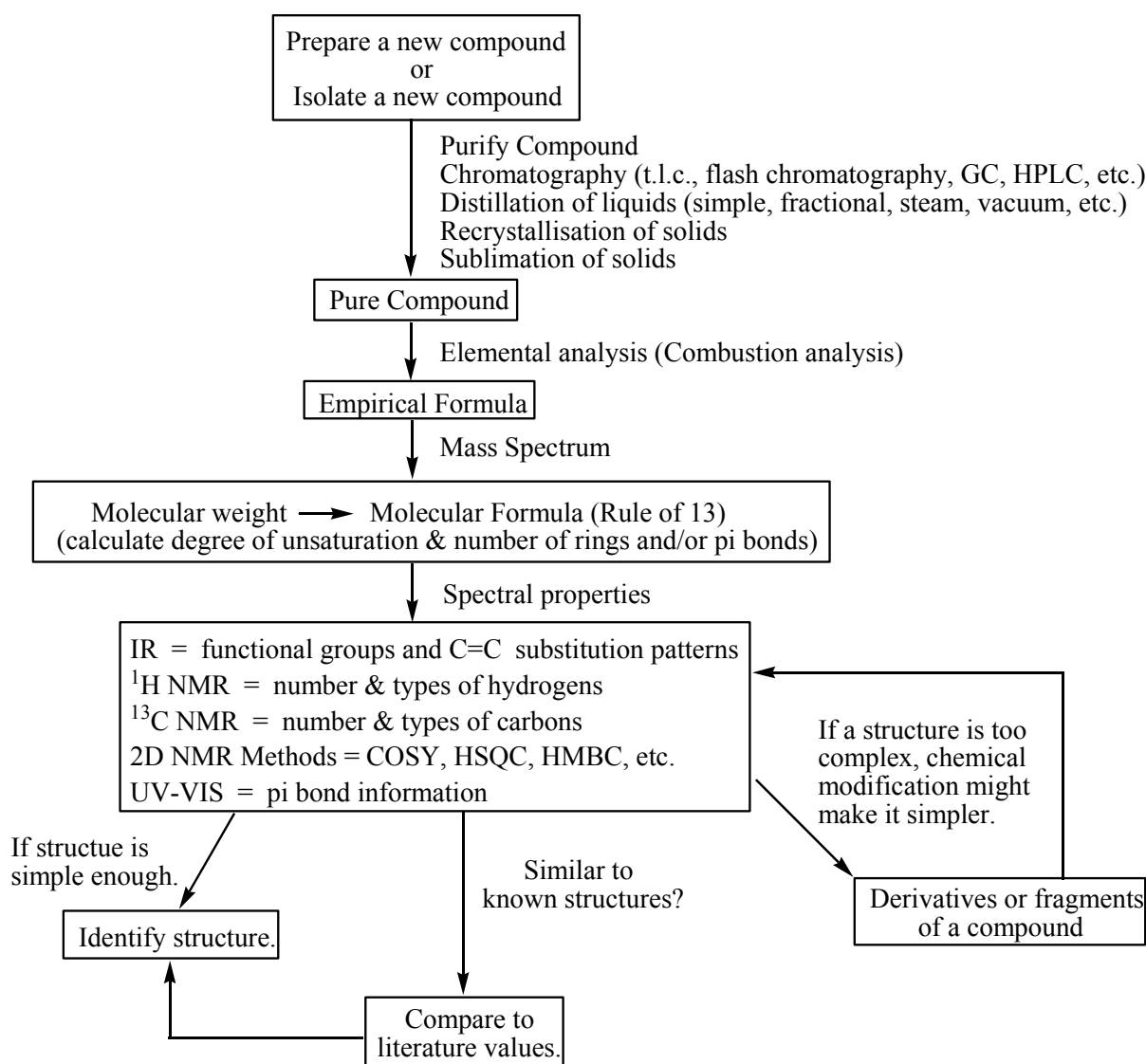


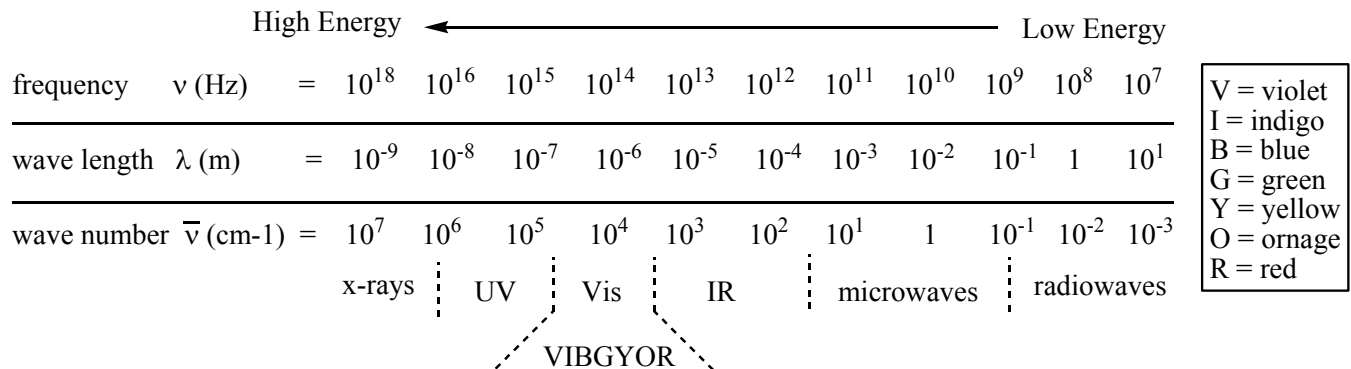
General Procedure For Structure Identification

New organic compounds are most often encountered as a sequential progression of steps in a chemical synthesis, or alternatively in natural product isolation from plants or animals or other environmental source in nature. In a synthetic sequence, usually a known starting material is mixed with reagents of well understood chemistry in a highly purified solvent under controlled reaction conditions (i.e. temperature, pressure, etc.). The researchers have reasonable expectations of what possible products could form. Usually they are confirming what they already suspect. However, surprises are common enough and these can often lead to new directions for a research project. In natural product isolation, the world is the limit. The nature of the extraction procedure may suggest classes of compounds such as proteins, carbohydrates, lipids, nucleic acids, terpenoids, steroids, alkaloids and the like. However, rarely will there be much of a clue concerning a specific structure until one actually begins to acquire spectroscopic data. In either case, highly purified material is desired for spectra to be useful. From this starting point, an overview of a possible strategy from preparation or isolation of a compound to identification of its structure is presented below. You usually learn about some of the purification techniques listed below in the organic laboratory.



Common Features of Electromagnetic Radiation

The following figure illustrates the usual spectroscopic divisions of the electromagnetic spectrum.



There are a few aspects common to the entire electromagnetic spectrum.

Electromagnetic Radiation as Energy

$$E = h \nu$$

$$E = h (c / \lambda) = h c (1 / \lambda)$$

$$E = h c \bar{\nu}$$

$$c = \nu \lambda$$

The variables are ν , λ and $\bar{\nu}$. Changes in these values will change the energy of electromagnetic radiation.

ν = frequency (#/sec = Hz, used in NMR)

λ = wave length (in m, cm, nm, etc., nm used in UV-Vis)

$\bar{\nu}$ = wave number (#/distance = #/cm used in IR)

$h = 6.62 \times 10^{-34}$ joule-sec

$c = 3.0 \times 10^{10}$ cm/sec = 3.0×10^8 m/sec

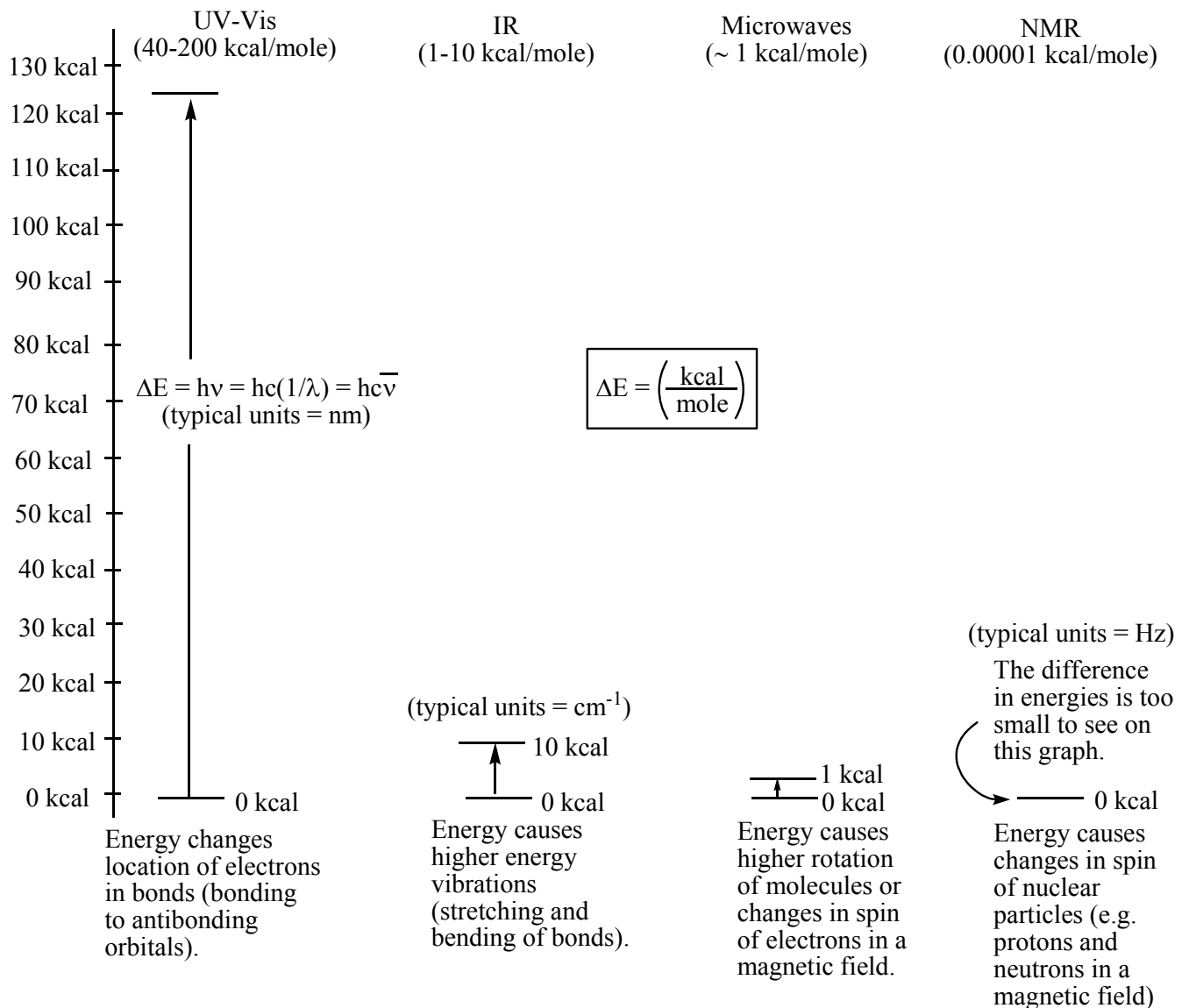
} These two
are constants.

Where Does the Energy Go?

The energy of the electromagnetic radiation (light) absorbed is transferred into a particular energy transition of the molecule with a matching (resonant) frequency. In a molecule, this increase in energy can be electronic excitation in ultraviolet-visible light, vibrational stretching and bending in infrared light or proton and carbon-13 nuclear spin inversion in the presence of a magnetic field with radio waves of nuclear magnetic resonance spectroscopy.

The figure below shows the electromagnetic spectrum with relevant energies, frequencies, wavelengths and wavenumbers. The effects on molecules, atoms, electrons and nuclei are listed in the appropriate regions.

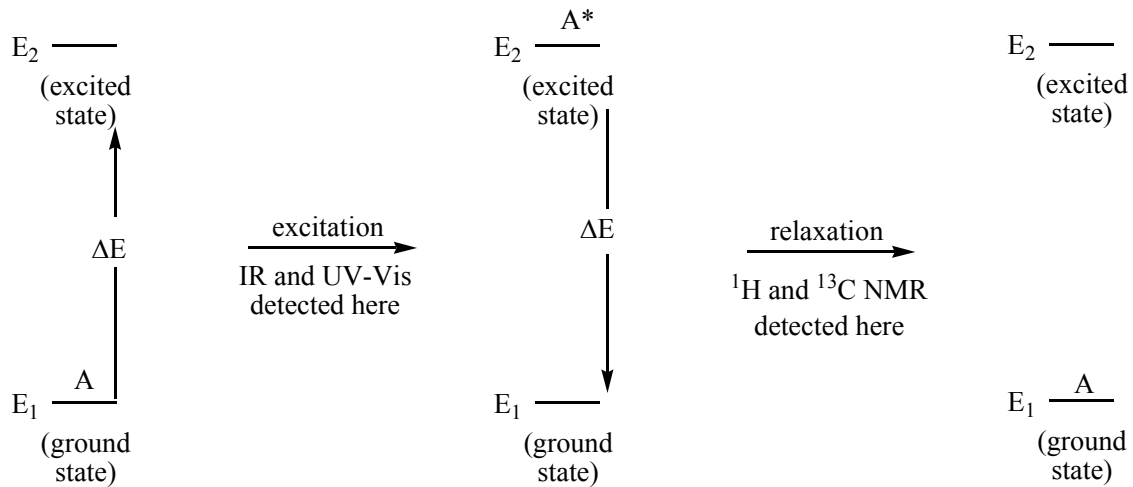
Spectroscopic Techniques



Other Ways of Looking at Energy (ν = frequency, $\bar{\nu}$ = wave number, λ = wavelength)

Parameter	X-rays	UV	Vis	IR	Microwave	Radiowaves
E (kcal/mole)	24,000	200	50	10	3×10^{-3}	6×10^{-6}
E (kJ/mole)	100,000	800	200	40	1.2×10^{-2}	2×10^{-5}
E (eV/photon)	1,200	8	2	0.4	1×10^{-4}	3×10^{-7}
ν (Hz)	3×10^{17}	2×10^{15}	5×10^{14}	1×10^{14}	3×10^{10}	3×10^8
$\bar{\nu}$ (cm^{-1})	1×10^7	50,000	17,000	3,000	1	0.01
λ (nm)	1	200	600	3,000	1×10^7	1×10^9

From the moment a molecule gets in an excited state (electronic, vibrational, rotational or nuclear spin), it is seeking a way to get back to the lower energy ground state. This process is called relaxation. Relaxation can occur by a number of mechanisms, which include producing heat (radiationless heat transfer) or emitting a photon of energy (fluorescence or phosphorescence). Our observation of the interaction of the photon with the molecule is sometimes detected in the event of excitation (UV-Vis and IR) and sometimes detected in the relaxation of the excited state (^1H and ^{13}C NMR).



A = molecule of interest in ground state
 A* = molecule of interest in excited state
 $E_2 > E_1$ = energy states of the molecule
 $\Delta E = (E_2 - E_1)$

$\Delta E \approx 50\text{-}100$ kcal/mole

Electron excitation occurs from a bonding to an antibonding orbital. Usually in pi bonds or conjugated pi systems, but it also can be from lone pair electrons or weak sigma bonds.

UV-VIS

$\Delta E \approx 1\text{-}5$ kcal/mole

Excitation of stretching and bending vibrations of functional group patterns.

IR

$\Delta E \approx 10^{-5}$ kcal/mole

Excitation corresponds to nuclear particle spin flips in the presence of a magnetic field: ^1H isotope of hydrogen and ^{13}C isotope of carbon.

NMR

Spectrometers

In each spectroscopic technique there are essential elements of instrumentation. It is not possible to cover the details of such instrumentation here and our ultimate goal is interpretation.

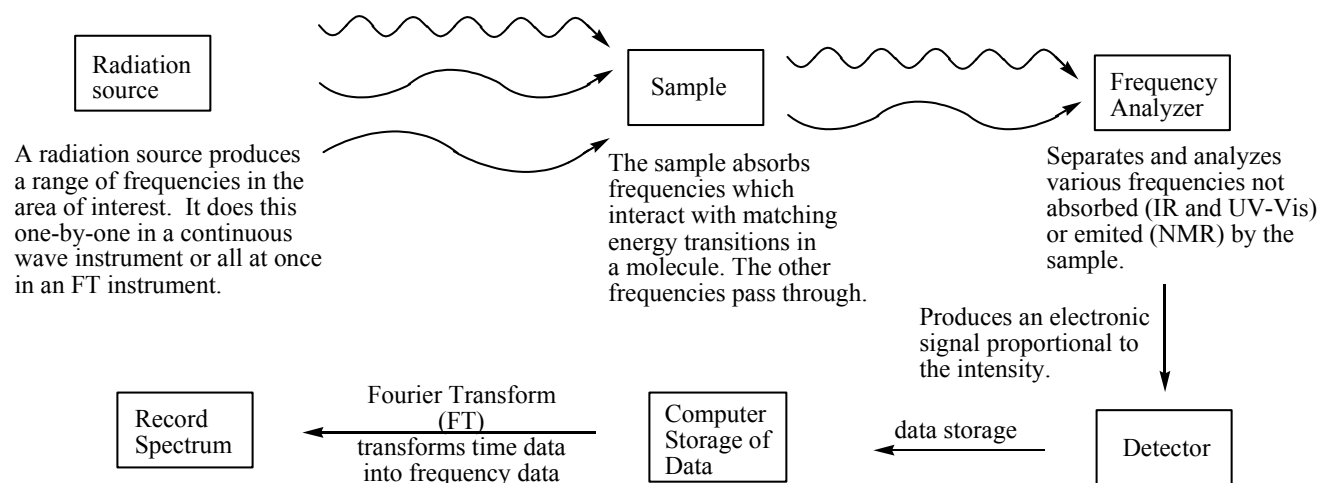
There are some common general features. All of the instruments have a source of electromagnetic radiation (except mass spectrometry). This can be ultraviolet light, visible light, infrared light or radiowaves in NMR. There is a sample holder which contains the sample to be studied and allows the radiation to pass through the sample. This allows for any relevant interactions to occur. Any frequencies that are absorbed are converted into energetic transitions in the sample that is irradiated.

The efficiency of energy transfer to the sample determines the strength of absorption that occurs, for a particular frequency of radiation. A very efficient transfer will lead to a strong absorption and a less efficient transfer will produce a weaker absorption. If a particular frequency does not interact with the sample at all, then none of the radiation will be absorbed. Alternatively, we could say all of the electromagnetic radiation is transmitted. Absorption and transmission are inversely related, as shown below. Some instruments record absorption and some record transmission. Absorbance units are usually given as 2 minus the log scale value of the percent transmission (Beer's law).

$A = 2 - \log(T)$	$A = \text{absorbance}$ $T = \text{transmittance}$
-------------------	---

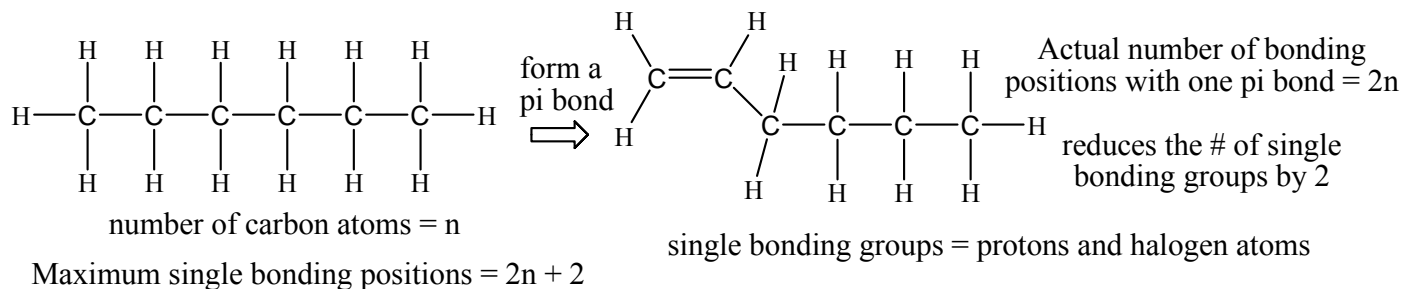
100% transmission	0% absorption	(Absorbance = $2 - \log(100\%) = 0.00$)
80% transmission	20% absorption	(Absorbance = $2 - \log(80\%) = 0.10$)
60% transmission	40% absorption	(Absorbance = $2 - \log(60\%) = 0.21$)
40% transmission	60% absorption	(Absorbance = $2 - \log(40\%) = 0.40$)
20% transmission	80% absorption	(Absorbance = $2 - \log(20\%) = 0.70$)
1% transmission	99% absorption	(Absorbance = $2 - \log(1\%) = 2.00$)

In addition to detecting the intensity of transmission (or absorption), the instrument must also separate the many different frequencies to be recorded (referred to as resolution). This requires a frequency analyzer of some sort. Modern spectroscopic instruments allow extremely fine divisions to be recorded. The finer the detail, the greater the resolution that is possible for the chemist to make distinguishing determinations. Once the frequencies have been separated, they must be detected in a manner that also allows the intensity to be measured. There are a variety of detectors that stir up electrons (excite them) to generate electrical signals that can be amplified. These signals are routed to either a computer data storage area or a recording chart that can print out the final result, which is called a spectrum. An experienced spectroscopist (soon to be you) can then analyze the details in the spectrum to develop conclusions about structural features of the unknown sample. This is shown in the simplistic diagram below.

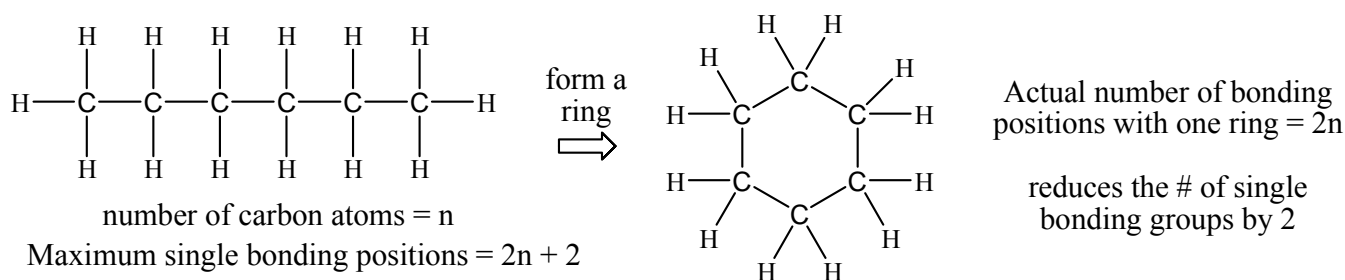


Finding a Molecular Formula and Degrees of Unsaturation

Degrees of Unsaturation – details that can help solve our structure



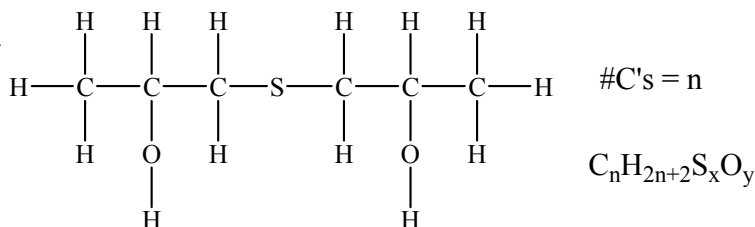
$$\text{Degree of unsaturation} = \frac{(2n + 2) - (2n)}{2} = \frac{2}{2} = 1 \text{ degree of unsaturation}$$



$$\text{Degree of unsaturation} = \frac{(2n + 2) - (2n)}{2} = \frac{2}{2} = 1 \text{ degree of unsaturation}$$

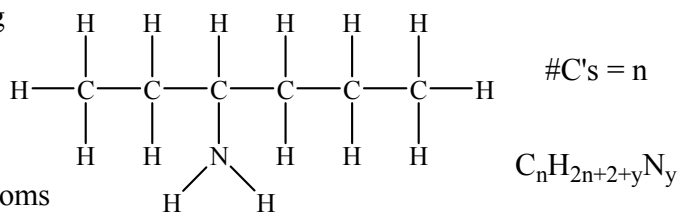
Oxygen atoms (or divalent sulfur), in any amount, do not change the above calculation. They merely act as spacer atoms. We just ignore them when calculating the degree of unsaturation.

Maximum bonding positions on n carbon atoms = $2n + 2$



Every single nitrogen atom will add an extra bonding position. Also, an odd number of nitrogen atoms (1,3,5...) will lead to an odd molecular weight.

Maximum bonding positions on n carbon atoms with nitrogen present = $2n + 2 + \#N$ atoms



$$\text{degrees of unsaturation} = \frac{\left(\begin{array}{l} \text{maximum number of} \\ \text{single bonding positions} \\ \text{on a carbon skeleton} \end{array} \right) - \left(\begin{array}{l} \text{actual number of single} \\ \text{bonding atoms on a carbon} \\ \text{skeleton, includes Hs and} \\ \text{halogens} \end{array} \right)}{2}$$

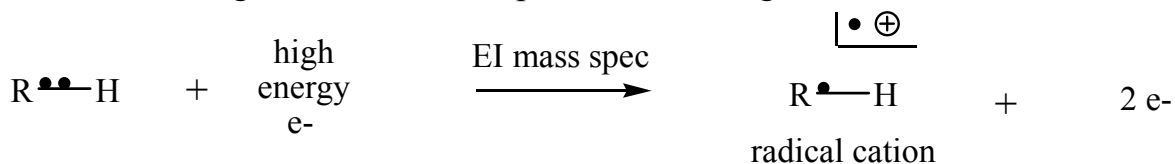
Possibilities if 2 degrees of unsaturation,	
pi bonds	rings
2	0
1	1
0	2

$$\text{degrees of unsaturation} = \frac{(2n + 2 + \#N) - (\text{single bond atoms})}{2}$$

n = the number of carbon atoms
 $\#N$ is the number of nitrogen atoms
 single bonding atoms = H and halogens

Mass Spectroscopy – can help generate a molecular formula

MS is different from the other routine spectroscopies (UV-Vis, IR, H and C NMR) in that absorption or emission of electromagnetic radiation is not used. Rather, the sample (molecule) is ionized by a high energy electron beam in a process referred to as electron impact (EI). An electron is knocked out of a bonding molecular orbital (MO), forming a radical cation. There are many other modern and important variations of mass spectroscopy, which we won't cover. Our present purpose in using mass spectroscopy is limited to obtaining a molecular formula and the degrees of unsaturation, leading to the number of pi bonds and rings.



The atomic weights listed in the periodic table are average masses based on the abundance and mass of all of the isotopes. However, molecules are made of specific isotopes, which vary by some interger multiple of atomic mass units (amu). Molecular weights in our problems will be based on exact masses of the isotopes, not average masses of the atoms. We need to be precise in our calculation of possible masses for each collection of atoms. For example the atomic weight of bromine in the periodic table is 79.9, though there is no bromine isotope with a mass of 80. The 79.9 atomic weight is a result of an approximate 50/50 mixture of two stable isotopes of mass 78.9 and 80.9. Because of this complication we will require data on the exact masses and the relative abundance of the common isotopes that we expect to encounter. The elements most useful to us in organic chemistry and biochemistry are listed below with the most abundant isotope listed as 100% and the other isotopes as a fraction of that amount.

<u>Element</u>	<u>Atomic Weight</u>	<u>Nuclide</u>	<u>Mass</u>	<u>Relative Abundance</u>
hydrogen	1.00797	¹ H	1.00783	100.0
		² H (D)	2.01410	0.015
carbon	12.01115	¹² C	12.00000	100.0
		¹³ C	13.00336	1.11
nitrogen	14.0067	¹⁴ N	14.0031	100.0
		¹⁵ N	15.0001	0.37
oxygen	15.9994	¹⁶ O	15.9949	100.0
		¹⁷ O	16.9991	0.04
		¹⁸ O	17.9992	0.20
fluorine	18.9984	¹⁹ F	18.9984	100.0

silicon	28.086	²⁸ Si	27.9769	100.0
		²⁹ Si	28.9765	5.06
		³⁰ Si	29.9738	3.36
phosphorous	30.974	³¹ P	30.9738	100.0
sulfur	32.064	³² S	31.9721	100.0
		³³ S	32.9715	0.79
		³⁴ S	33.9679	4.43
chlorine	35,453	³⁵ Cl	34.9689	100.0
		³⁷ Cl	36.9659	31.98
bromine	79.909	⁷⁹ Br	78.9183	100.0
		⁸¹ Br	80.9163	97.3
iodine	126.904	¹²⁷ I	126.9045	100.0

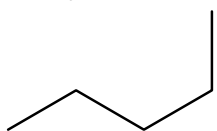
In every molecular example we encounter, the highest percent isotopomer has the lowest molecular weight mass, which we call the M+ peak. Higher mass isotopomers with heavier isotopes can have molecular weights of M+1, M+2, M+3, M+4 and more. An odd molecular weight is indicative of an odd number of nitrogen atoms (1, 3, 5, etc.).

The atomic values of M+1, M+2 and M+4 in the following table are based 'only' on the isotopes of each indicated atom(s). These are typical atoms one might find in an organic structure. In a molecule, M+ is the molecular weight peak and referenced as 100% no matter what its real size is relative to the base peak (the base peak is the largest peak in the mass spectrum) and the M+1, M+2, M+3, etc. peaks are reported as a percent of the M+ peak and will depend on what type and how many of each isotope there are. In most problems you will be given an exact mass (the M+ peak) and M+1, M+2, etc. peaks to determine if and how much sulfur, chlorine and/or bromine is present.

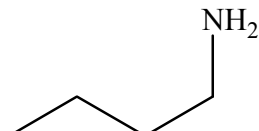
	H	C	N	O	S	F	Cl	Br	I
M+	100%	100%	100%	100%	100%	100%	100%	100%	100%
M+1	0.02%	1.1%	0.38%	0.04%	0.8%	0%	0%	0%	0%
M+2	0%	0%	0%	0.20%	4.5%	0%	32%	97%	0%
M+4	0%	0%	0%	0%	0%	0%	0%	0%	0%
	(Cl) ₂	(Br) ₂	(Br,Cl)	(S,Cl)	(S,Br)				
M+	100%	100%	100%	100%	100%				
M+1	0%	0%	0%	0.7%	0.7%				
M+2	64%	194%	129%	36%	102%				
M+4	10%	95%	31%	1.4%	4.4%				

The relative percents of these peaks can indicate what other atoms are present and in what amount they are present. For this to work the M^+ peak must be big enough to see, and the $M+1$ and higher peaks must be big enough to be significant to estimate the relative percent of the M^+ peak. We assume this is the case in our problems, even though there are many exceptions where it is not true. There are alternative ways of obtaining a molecular weight, such as chemical ionization, CI, that can more reliably provide this information, but are not covered in our brief discussions.

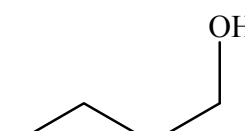
A rough estimate of the number of carbon atoms can be obtained by dividing the $M+1$ percent is divided by 1.1, which is the percent abundance of the ^{13}C isotope relative to the ^{12}C isotope. In a similar way, the $M+2$ and $M+4$ peaks are helpful at indicating if and how much S, Cl and/or Br is present. Lower molecular weight sulfur compounds are easily detected by their foul smell.



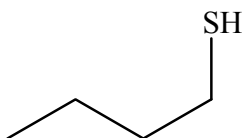
Chemical Formula: C_5H_{12}
 Exact Mass: 72.09
 $M^+ = 72.09$ (100.0%),
 $M+1 = 73.10$ (5.5%)



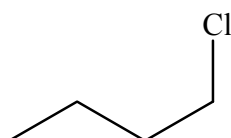
Chemical Formula: $\text{C}_4\text{H}_{11}\text{N}$
 Exact Mass: 73.09
 $M^+ = 73.09$ (100.0%),
 $M+1 = 74.09$ (4.7%)



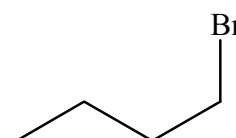
Chemical Formula: $\text{C}_4\text{H}_{10}\text{O}$
 Exact Mass: 74.07
 $M^+ = 74.07$ (100.0%),
 $M+1 = 75.08$ (4.5%)



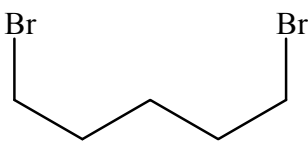
Chemical Formula: $\text{C}_4\text{H}_{10}\text{S}$
 Exact Mass: 90.05
 $M^+ = 90.05$ (100.0%),
 $M+1 = 91.05$ (5.1%),
 $M+2 = 92.05$ (4.6%)



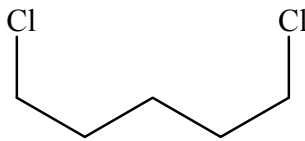
Chemical Formula: $\text{C}_4\text{H}_9\text{Cl}$
 Exact Mass: 92.04
 $M^+ = 92.04$ (100.0%),
 $M+1 = 93.04$ (4.3%),
 $M+2 = 94.04$ (32.0%),
 $M+3 = 95.04$ (1.4%)



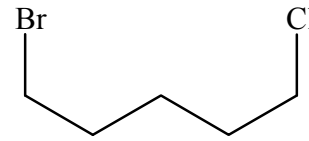
Chemical Formula: $\text{C}_4\text{H}_9\text{Br}$
 Exact Mass: 135.99
 $M^+ = 135.99$ (100.0%),
 $M+1 = 136.99$ (4.3%),
 $M+2 = 137.99$ (97.3%),
 $M+3 = 138.99$ (4.3%)



$\text{C}_5\text{H}_{10}\text{Br}_2$
 Exact Mass: 227.91
 $M^+ = 227.91$ (100.0%),
 $M+1 = 228.92$ (5.4%),
 $M+2 = 229.91$ (194.6%),
 $M+3 = 230.92$ (10.7%),
 $M+4 = 231.91$ (94.6%),
 $M+5 = 232.91$ (5.1%)



$\text{C}_5\text{H}_{10}\text{Cl}_2$
 Exact Mass: 140.02
 $M^+ = 140.02$ (100.0%),
 $M+1 = 141.02$ (5.5%),
 $M+2 = 142.01$ (63.9%),
 $M+3 = 143.02$ (3.5%),
 $M+4 = 144.01$ (10.2%),



$\text{C}_5\text{H}_{10}\text{BrCl}$
 Exact Mass: 183.97
 $M^+ = 183.97$ (77.4%),
 $M+1 = 184.97$ (5.6%),
 $M+2 = 185.96$ (129.2%),
 $M+3 = 186.97$ (7.1%),
 $M+4 = 187.96$ (31.1%),
 $M+5 = 188.96$ (1.7%)

Finding a Molecular Formula

Our approach to obtaining a molecular formula will be as follows.

1. Determine if ^{35}Cl , ^{79}Br or ^{32}S are present (and how many) using the mass spec information listed above (M+2 peaks, etc.).
2. A proton count can be determined by using the proton integration from the H NMR. This will be given until H NMR is covered.
3. A carbon count can be estimated by dividing the M+1 mass spec peak by 1.1, since the ^{13}C isotope is 1.1% of the ^{12}C isotope. This can be confirmed by counting the number of carbon peaks in the proton decoupled ^{13}C NMR (taking into account any symmetry features). This will be given until ^{13}C is covered. A minor complication is that ^{33}S is 0.8% of ^{32}S and two ^{15}N is about 0.8% of ^{14}N . Both of these possibilities can appear as an extra carbon atom in a formula unless subtracted from the M+1 percent.
4. The total masses of any ^{35}Cl , ^{79}Br , ^{32}S (use the exact masses of the lower atomic mass isotopes), plus the total mass of hydrogen (^1H) and carbon (^{12}C) is subtracted from the exact mass, the M+ peak. This will leave a residual mass most likely composed of ^{14}N and/or ^{16}O . Usually, how many of each element becomes clear by inspection, looking for some combination of 14 and 16 to equal the residual mass.
5. Once all of the atoms are determined, one uses the formula to calculate the total degrees of unsaturation, which equals the total pi bonds and rings.
6. Pi bonds are estimated from the chemical shifts in the ^{13}C NMR, looking for alkene, alkyne, aromatic, nitrile and C=O functionality. Certain types of pi bonds will not show up in the ^{13}C , such as N=O and N=N pi bonds (nitro, nitroso, azido, etc.). Most of these are rare for us, but the nitro ($-\text{NO}_2$) is common enough and can be seen in the IR spectrum (1550 cm^{-1} and 1350 cm^{-1}). The number of pi bonds is subtracted from the total degrees of unsaturation to find out how many rings are present.

The procedure described here is a good first step towards finding an unknown structure. Two examples are provided below.

Having an IR and/or NMR data will give us many additional clues to help decide what a structure is. We'll look at those techniques after the formula examples below.

Example 1 – finding a molecular formula and the number of pi bonds and rings

Mass spec data:

Exact Mass: 369.06

M+ = 369.06 (100.0%),
 M+1 = 370.06 (17.7%),
 M+2 = 371.06 (99.6%),
 M+3 = 372.06 (17.2%),

An odd mass indicates
 an odd number of nitrogen
 atoms.

1. $M+ \approx M+2$ so bromine is present (exact mass = 79).
2. Proton count from ^1H NMR = 20 (given for now, until a H NMR is provided)
3. Carbon count from MS data = $(17.7)/(1.1) = 16$
 Carbon count from ^{13}C NMR is 16 (given for now, until a C NMR is provided)
4. Total mass of $^{79}\text{Br} + 20 \text{ H} + 16 \text{ }^{12}\text{C} = 291$
5. Residual mass = $369 - 291 = 78 = 64 + 14 = 4 \times \text{O} + 1 \times \text{N}$
 Molecular formula = $\text{C}_{16}\text{H}_{20}\text{BrNO}_4$
 maximum single bonding positions = $2(16) + 2 + 1 = 35$
 degrees of unsaturation = $[(35) - (21)] / 2 = 14 / 2 = 7$ degrees
6. ^{13}C NMR shows 6 x (=C) in alkene/aromatic region = 3 x (C=C)
 and 1 x (C=O) for a total of 4 pi bonds. However, there are two absorptions in the IR at 1550 and 1350 cm^{-1} , indicate that a nitro group might be present. That brings the total pi bonds to 5. The number of rings = (total unsaturation) - (pi bonds) = $7 - 5 = 2$ rings

Example 2

Mass spec data:

Exact Mass: 414.13

M+ = 414.13 (100.0%),
 M+1 = 415.13 (22.9%),
 M+2 = 416.12 (36.5%),
 M+3 = 417.13 (8.3%),
 M+4 = 418.12 (1.5%),

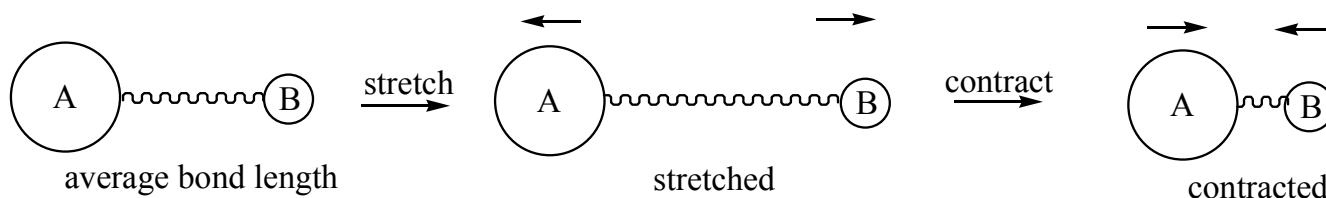
An even mass indicates
 no nitrogen atoms or an
 even number of nitrogen
 atoms.

1. $M+2 = (M+) \times (36.5\%)$ so Cl (32%) and S (4.5%) are likely present (exact mass = $35+32 = 67$).
 Also $M+4 = 1.5\%$, supports this conclusion. This also adds 0.8% to M+1 peak.
2. Proton count from ^1H NMR = 27 (given for now, until an H NMR is provided)
3. Carbon count from MS data = $(22.9-0.8)/(1.1) = 20$ (subtract 0.8 for each sulfur atom present)
 Carbon count from ^{13}C NMR is 20 (given for now, until a C NMR is provided)
4. Total mass of $^{35}\text{Cl} + ^{32}\text{S} + 27 \text{ H} + 20 \text{ }^{12}\text{C} = 334$
5. Residual mass = $414 - 334 = 80 = 5 \times 16 = 5 \times \text{O}$
 Molecular formula = $\text{C}_{20}\text{H}_{27}\text{ClO}_5\text{S}$
 maximum single bonding positions = $2(20) + 2 = 42$
 degrees of unsaturation = $[(42) - (28)] / 2 = 14 / 2 = 7$ degrees
6. ^{13}C NMR shows 6 x (=C) in alkene/aromatic region = 3 x (C=C)
 and 2 x (C=O) for a total of 5 pi bonds. The number of rings = (total unsaturation) - (pi bonds) = $7 - 5 = 2$ rings

Infrared Spectroscopy

Vibrational bands in the IR are a result of stretching (symmetric and asymmetric) and bending of bonds commonly found in organic and biological molecules.

In a stretching vibration the two atoms stretch away from one another or contract towards one another.



The frequency of this stretching vibration is simply how many times this occurs per second (visible light = 10^{14} /sec). Electromagnetic radiation with this energy can induce a specific vibration. In IR spectra this is reported as wavenumbers (cm^{-1}).

$c = v \lambda$
$v = c / \lambda = c \bar{\nu}$
$\bar{\nu} = v / c$

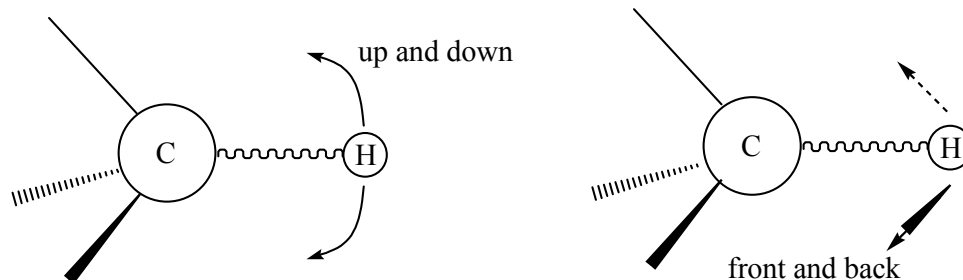
c = speed of light = 3.0×10^8 m/sec

v = frequency = # per second = Hz in NMR

λ = wave length of light (various units, nm in UV-Vis)

$\bar{\nu}$ = wave number = # per distance (cm^{-1} in IR)

Additionally, a two atom bond can also bend. If we arbitrarily fix a carbon atom, then the hydrogen atom can move up and down or front and back (relative to the rest of the molecule).



Generally, stretching vibrations are more energetic than bending vibrations and require higher energy photons for a specified pair of bonded atoms. The following examples are some typical values, but are not always useful in determining structures.

Typical IR Stretching Wavenumbers, $\bar{\nu}$

sp^3 C-H	2850-3000 cm^{-1}
sp^2 C-H	3000-3100 cm^{-1}
sp C-H	3250-3340 cm^{-1}
N-H	3100-3500 cm^{-1}
O-H	3200-3500 cm^{-1}

↑
Usually higher in energy.

Typical IR Bending Wavenumbers, $\bar{\nu}$

sp^3 C-H	1380, 1450 cm^{-1}
sp^2 C-H	650-1000 cm^{-1}
sp C-H	600-700 cm^{-1}
N-H	1550-1640 cm^{-1}
O-H	1000-1300 cm^{-1}

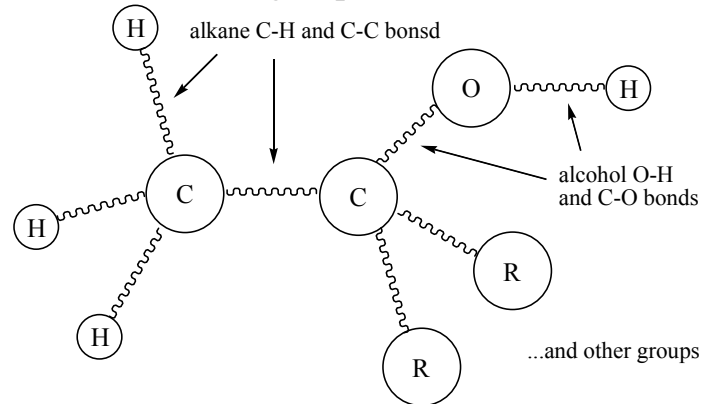
higher energy photons mean:

shorter λ , (distance)

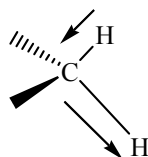
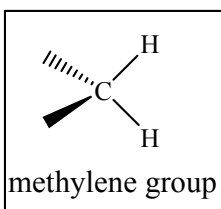
higher v , (# / sec)

higher $\bar{\nu}$ (# / distance)

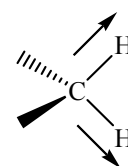
Real organic molecules are much more complicated than simple two atom pairs. Many atoms are present and numerous bonds can approximate a whole collection of vibrating springs. Commonly encountered arrangements of atoms are called functional groups and produce reasonably predictable IR wavenumbers. These IR bands can be used to identify the presence of a functional group when detected in the IR spectrum.



Nearby atoms and bonds tend to act as subgroups in concert with one another. By increasing our atom pattern from two vibrating atoms to three, we can gain an appreciation of the increased complexity. A simple methylene, CH₂ subgroup illustrates some of the possibilities. Simultaneous stretching of the two hydrogen atoms away from and towards the carbon is a symmetric stretching vibration, which has a characteristic range of wave numbers. When one hydrogen stretches away and the other hydrogen moves toward the carbon an asymmetric stretch occurs. For each particular three atom system the asymmetric stretch is usually the higher energy vibration.



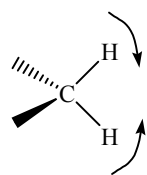
CH₂ asymmetrical stretch $\approx 2930 \text{ cm}^{-1}$



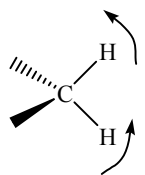
CH₂ symmetrical stretch $\approx 2850 \text{ cm}^{-1}$

Usually the wave number of asymmetric stretch > symmetric stretch

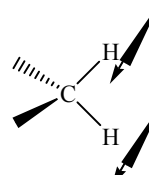
Several bending vibrations are also IR active in a methylene subunit. These bending modes are shown below along with their approximate resonant wavenumber.



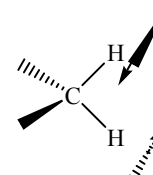
CH₂ scissoring
 $\sim 1450 \text{ cm}^{-1}$
in the plane



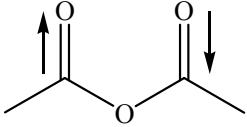
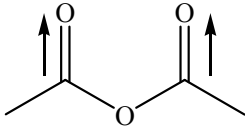
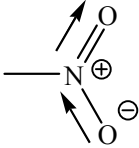
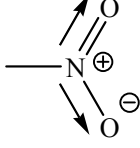
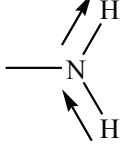
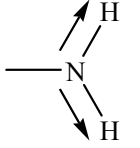
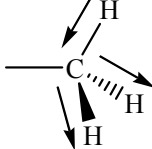
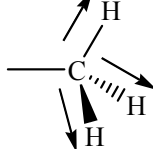
CH₂ rocking
 $\sim 720 \text{ cm}^{-1}$
in the plane



CH₂ wagging
 $\sim 1250 \text{ cm}^{-1}$
out of the plane

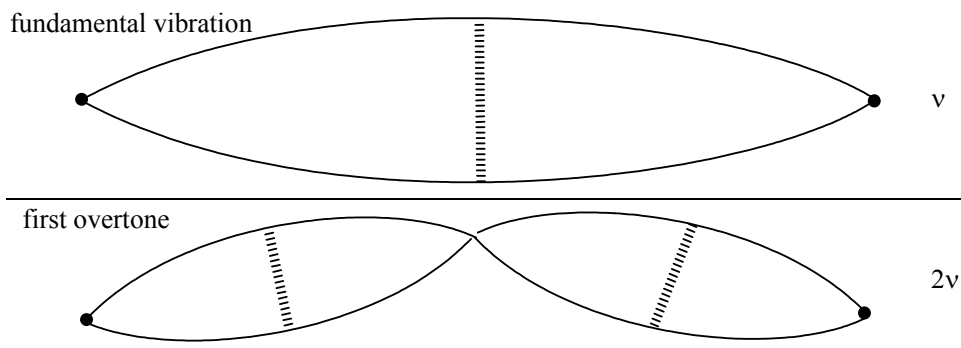


CH₂ twisting
 $\sim 1250 \text{ cm}^{-1}$
out of the plane

asymmetrical stretching	symmetrical stretching
 <p>anhydride asymmetrical stretching $\approx 1800 \text{ cm}^{-1}$</p>	 <p>anhydride symmetrical stretching $\approx 1760 \text{ cm}^{-1}$</p>
 <p>nitro asymmetrical stretching $\approx 1550 \text{ cm}^{-1}$</p>	 <p>nitro symmetrical stretching $\approx 1350 \text{ cm}^{-1}$</p>
 <p>primary amine and amide (NH_2) asymmetrical stretching $\approx 3400 \text{ cm}^{-1}$</p>	 <p>primary amine and amide (NH_2) symmetrical stretching $\approx 3300 \text{ cm}^{-1}$</p>
 <p>methyl asymmetrical stretching $\approx 2960 \text{ cm}^{-1}$</p>	 <p>methyl symmetrical stretching $\approx 2870 \text{ cm}^{-1}$</p>

Vibrations such as these are called fundamental vibrations because they involve a direct transition from a low energy ground state to a higher energy excited state. The energy (frequency/wavenumber) of the exciting electromagnetic photon matches the energy (frequency/wavenumber) of the vibrating system. The two frequencies are said to be in resonance.

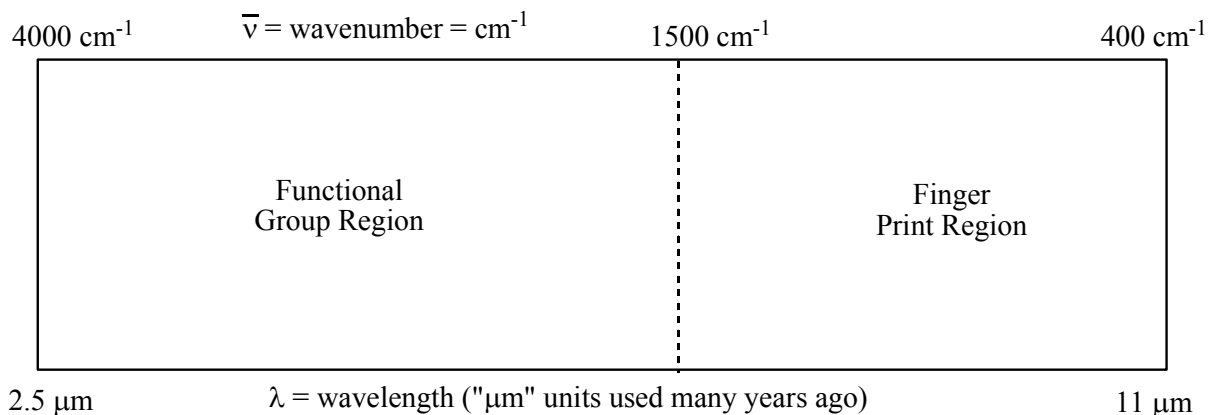
In actuality, real life is more complicated than our simplistic picture. Absorptions occur at other wavenumbers due to overtones, combination bands and difference bands. If you have ever played a guitar (or other stringed instrument), then you have probably learned how to tune the strings using harmonics or overtones by lightly touching the vibrating string at the halfway point. A different note is heard due to higher frequency vibrations also occurring in addition to the fundamental vibration. The other frequency vibrations are integer multiples of the main vibration due to the fixed points of attachments at the end of the strings.



A particularly intense IR absorption can produce a small, but easily detectable vibration band at twice the frequency. For example, an intense carbonyl, C=O, absorption band at $\approx 1700 \text{ cm}^{-1}$ can often produce a small but observable overtone band at $\approx 3400 \text{ cm}^{-1}$ ($\approx 2 \times 1700 \text{ cm}^{-1}$). This is sometimes mistaken for an O-H or N-H absorption.

Combination bands are also possible. When two different frequencies couple together, they may produce an IR active absorption band which is a combination of their two frequencies, i.e. $\nu_{\text{combo}} = \nu_1 + \nu_2$. Difference bands are similar, but in the opposite sense. Two different frequencies can act together in opposition and partially cancel one another forming an IR active absorption band, i.e. $\nu_{\text{difference}} = \nu_1 - \nu_2$.

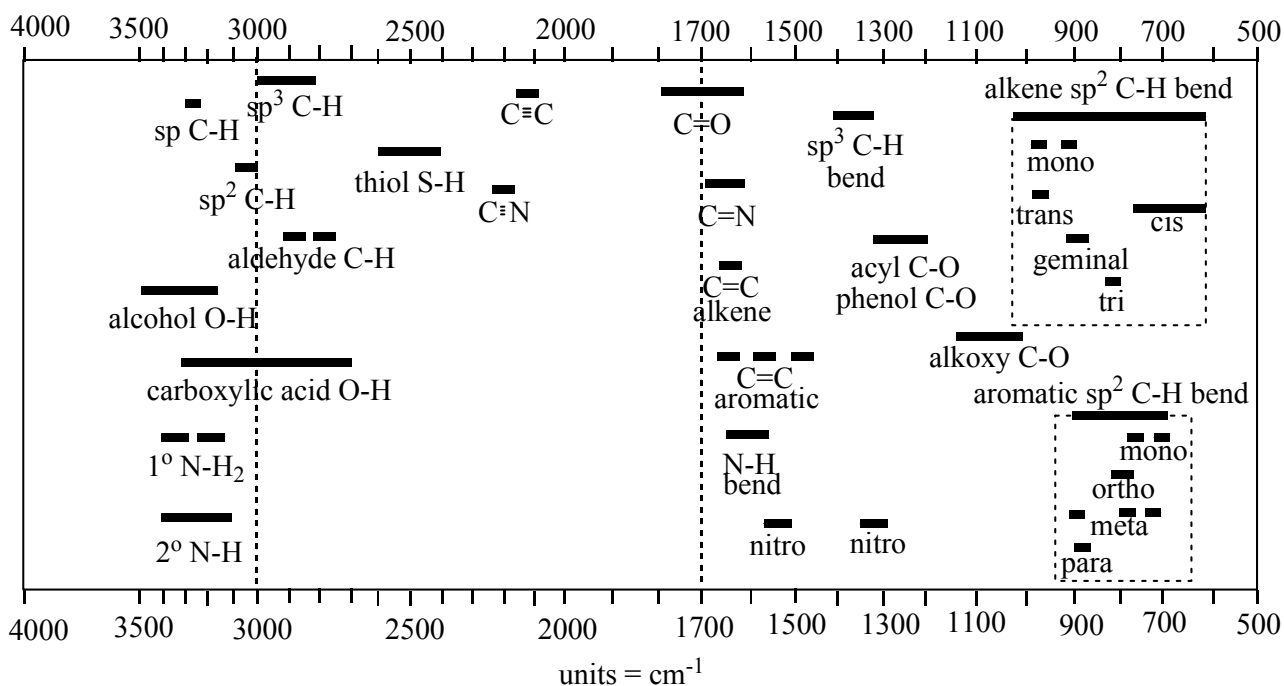
Overtone, combination bands and difference bands can make an IR spectrum much more complicated than a simple consideration of the fundamental bands would lead us to believe. They can hide or confuse an otherwise straight forward analysis. On the other hand, the complicated patterns generated tend to be unique for each arrangement of atoms. The patterns of absorption bands generated can be used in much the same way as our fingerprints are for exact identification. The lower wavenumber region of an IR spectrum ($1500\text{-}400 \text{ cm}^{-1}$) is often called the finger print region for this reason. Many of the fundamental bands of functional groups appear above 1500 cm^{-1} and are useful in identifying the functional groups present. Accordingly, this region is often called the functional group region ($1500\text{-}4000 \text{ cm}^{-1}$).



We will ignore the specifics of these extra absorption bands and try to identify mainly the fundamental functional group absorption bands. However, there are some overtone bands that are useful for identifying organic structure. One such group is the aromatic overtones around $1660\text{-}2000 \text{ cm}^{-1}$ produced from C-H bending of hydrogen atoms around the aromatic ring. Even though they can be helpful, they are usually weak and are partially covered up when in the presence of strong carbonyl bands.

The values given in the tables that follow are typical values. I gave you a choice of tables. Use the one that works best with your way of thinking. Specific substituents may cause variations in absorption frequencies due to resonance, inductive and/or steric effects. Absorption intensities may be stronger or weaker than expected, often depending on dipole moments. In general, a stronger dipole moment means a stronger absorption. Additional bands (combination and overtones) may confuse an interpretation. In very symmetrical compounds there may be fewer than the expected number of absorption bands, (it is even possible that all bands of a functional group may disappear, i.e. a symmetrically substituted alkyne!). Infrared spectra are generally informative about functional groups that are present, but not always. ^{13}C NMR is often just as informative about which functional groups are present, and sometimes even more so. IR is often helpful in the solution of a structure, but not always. Information obtained from one spectroscopic technique should be verified or expanded by consulting the other spectroscopic techniques.

IR - typical functional group absorptions (full range, mainly stretching bands)



Energy of left side of spectrum

$$\left(\frac{4000}{\text{cm}}\right)\left(\frac{100\text{ cm}}{\text{m}}\right)\left(\frac{3 \times 10^8 \text{ m}}{\text{sec}}\right)\left(6.6 \times 10^{-34} \text{ j-sec}\right)\left(\frac{6 \times 10^{23}}{\text{mole}}\right) = 48,000 \text{ j} \left(\frac{1 \text{ kj}}{1000 \text{ j}}\right)\left(\frac{1 \text{ kcal}}{4.2 \text{ kj}}\right) = 11 \frac{\text{kcal}}{\text{mole}}$$

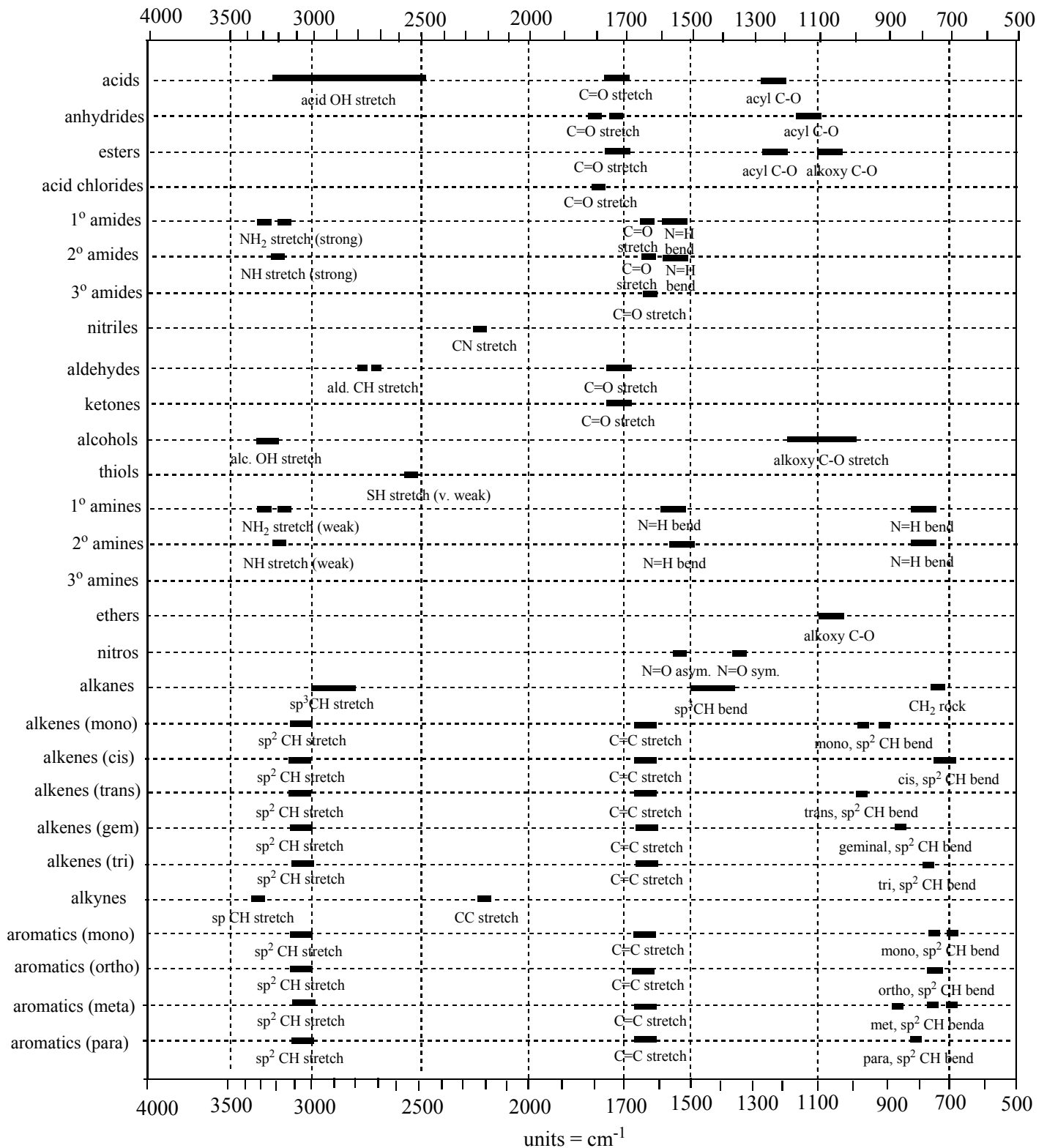
Energy of right side of spectrum

$$\left(\frac{400}{\text{cm}}\right)\left(\frac{100\text{ cm}}{\text{m}}\right)\left(\frac{3 \times 10^8 \text{ m}}{\text{sec}}\right)\left(6.6 \times 10^{-34} \text{ j-sec}\right)\left(\frac{6 \times 10^{23}}{\text{mole}}\right) = 4,800 \text{ j} \left(\frac{1 \text{ kj}}{1000 \text{ j}}\right)\left(\frac{1 \text{ kcal}}{4.2 \text{ kj}}\right) = 1.1 \frac{\text{kcal}}{\text{mole}}$$

This is not enough energy to break typical organic bonds.

The only wave numbers (cm^{-1}) reported are for the specific functional group indicated. Other functionality will be mixed in, as appropriate in a real IR.

IR - typical functional group absorptions (full range, mainly stretching bands)



IR Flowchart to Determine Functional Groups in a Compound (all values in cm^{-1})

IR Spectrum (all values are approximate, \pm)	
has C=O band (1650-1800 cm^{-1}) very strong	has a triple bond
does not have C=O band	
<p>aldehydes</p> <p>C-H stretch (two weak bands) 2860-2800 2760-2700</p> <p>C=O stretch ~1740-1720, saturated ~1700-1660, conjugated</p>	<p>nitriles</p> <p>stretch simple ~2250 conjugated ~2220</p>
<p>ketones</p> <p>stretch ~1720-1710, when saturated ~1700-1660, when conjugated ~1810-1720, when in rings</p>	<p>alkanes</p> <p>stretch 3000-2840 bend CH₂ ~1450 CH₃ ~1370</p>
<p>esters - rule of 3</p> <p>stretch 1750-1730, saturated 1740-1680, conjugated 1820-1720, in rings</p> <p>acyl C-O 1350-1150 alkoxy C-O 1200-1050</p>	<p>alkenes</p> <p>stretch 3100-3000 bend 1000-650 (see table)</p> <p>1660-1600 not present or weak when symmetrical</p>
<p>acids</p> <p>stretch 1730-1700, saturated 1700-1680, conjugated</p> <p>acyl C-O 1320-1150 acid O-H 3400-2500 very broad</p>	<p>aromatics</p> <p>stretch 3100-3000 bend 900-690 (see table)</p> <p>stretch 1600-1470</p> <p>overtone patterns (weak) between 2000-1660</p>
<p>amides</p> <p>1680-1630, always conjugated with nitrogen lone pair, higher in small rings (4 atom = 1745)</p> <p>1^o ~3350 & ~3180, 2 bands for 1^o amides, 3300, one band for 2^o amides stronger than in amines, sometimes an extra overtone \approx3200, no bands for 3^o amides</p> <p>~1640-1550, N-H bend, strong in amides with polar resonance form</p>	<p>alcohols</p> <p>C-O stretch 1200-1050 O-H stretch \approx 3600-3650, phenyl > 3^o > 2^o > 1^o sharp when no H bonding \approx 3400-3300, broad with H bonding</p>
<p>acid chlorides</p> <p>stretch (very high) 1810-1770, when saturated 1780-1760, when conjugated</p> <p>C-Cl 730-550 not real useful when many peaks are present</p>	<p>thiols</p> <p>stretch ~2550, weak S-H stretch</p>
<p>anhydrides</p> <p>1830-1800 1770-1740,</p> <p>acyl C-O 1300-900 strong</p>	<p>amines</p> <p>stretch 1^o 3500 & 3300, two bands for 1^o amines, one band for 2^o amines, weaker than in amides, sometimes an extra overtone about 3100 due to N-H bend, no N-H bands for 3^o amines</p> <p>1640-1550, N-H bend, weaker in amines 800 N-H bend</p>
	<p>ethers</p> <p>C-O stretch aliphatic \approx1120 (variable) aromatic \approx1250</p>
	<p>nitro compounds (does not show in H or C NMR, look for nitro in the IR)</p> <p>1500-1600, asymmetric stretch, strong 1300-1390, symmetric stretch, medium</p>
	<p>X = halogen</p> <p>variable bands, usually mixed in among other bands, not real useful (sp³ = 500-1000 range) (sp² = 1000-1250 range)</p>

All IR values are approximate and have a range of possibilities depending on the molecular environment in which the functional group resides. Resonance often modifies a peak's position because of electron delocalization (C=O lower, acyl C=O higher, etc.). IR peaks are not 100% reliable. Peaks tend to be stronger (more intense) when there is a large dipole associated with a vibration in the functional group and weaker in less polar bonds (to the point of disappearing in some completely symmetrical bonds).

Alkene sp² C-H bending patterns

monosubstituted alkene (985-1000, 900-920)
trans disubstituted (960-990)
cis disubstituted (670-730)
gem disubstituted (880-900)
trisubstituted (790-840)
tetrasubstituted (none, no sp² C-H)

Aromatic sp² C-H bending patterns

monosubstituted (730-770, 690-710)
ortho disubstituted (730-770)
meta disubstituted (880-900, sometimes 750-810, 680-730)
para disubstituted (790-840)

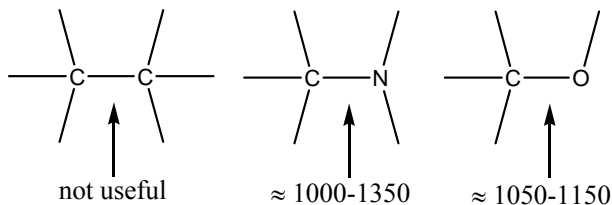
There are also weak overtone bands between 1660 and 2000, but are not shown here. You can consult pictures of typical patterns in other reference books. If there is a strong C=O band, they may be partially covered up.

For convenience, photoreduce pages 19 and 20 to a single page for a good overview of IR peaks.

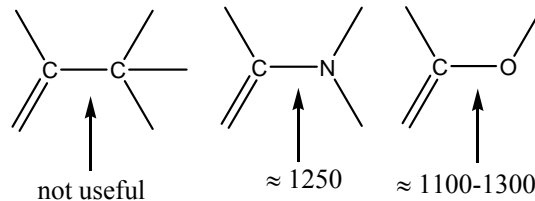
Infrared Tables (short summary of common absorption frequencies)

Bonds to Carbon (stretching bands)

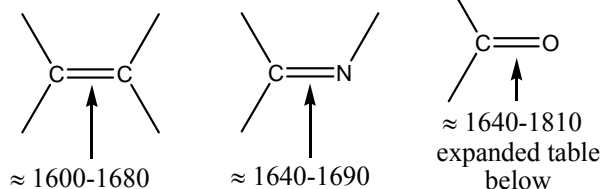
sp³ C-X single bonds



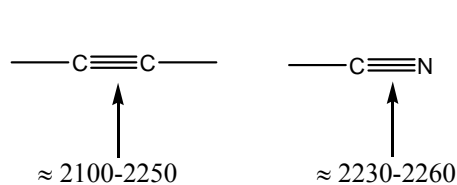
sp² C-X single bonds



sp² C-X double bonds

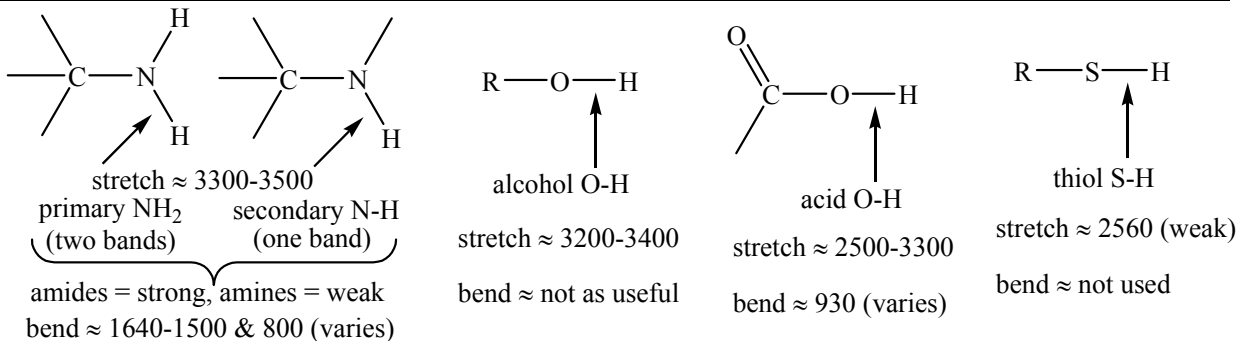
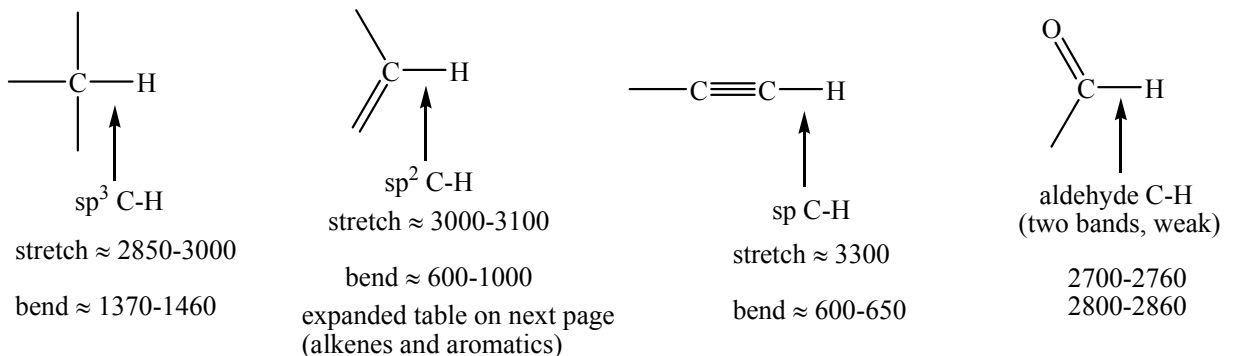


sp C-X triple bonds

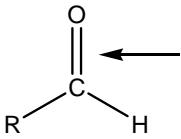
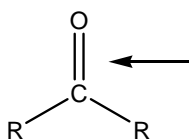
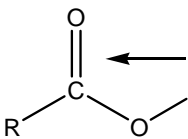
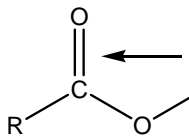
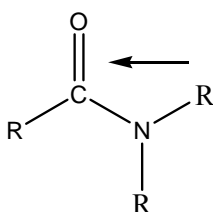
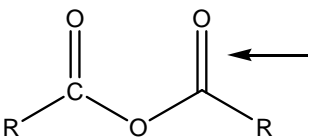
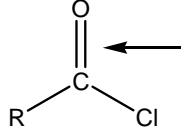


Stronger dipoles produce more intense IR bands and weaker dipoles produce less intense IR bands. When a dipole completely disappears, the IR band may also disappear.

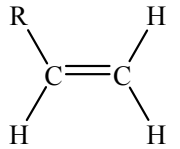
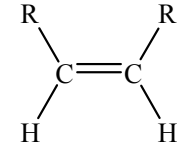
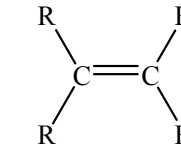
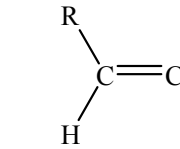
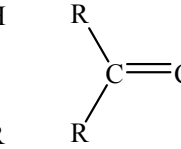
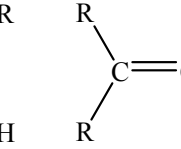
Bonds to Hydrogen (stretching and bending bands)



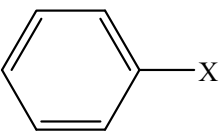
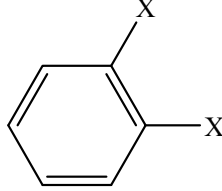
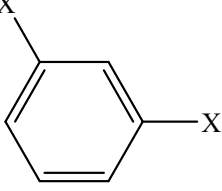
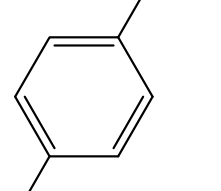
Carbonyl Highlights (stretching bands, approximate values in cm^{-1} , usually very strong)

<p>Aldehydes</p>  <p>saturated = 1725 conjugated = 1690 aromatic = 1700</p>	<p>Ketones</p>  <p>saturated = 1715 conjugated = 1680 aromatic = 1690 6 atom ring = 1715 5 atom ring = 1745 4 atom ring = 1780 3 atom ring = 1850</p>	<p>Esters</p>  <p>saturated = 1735 conjugated = 1720 aromatic = 1720 6 atom ring = 1735 5 atom ring = 1775 4 atom ring = 1840</p>	<p>Acids</p>  <p>saturated = 1715 conjugated = 1690 aromatic = 1690</p>
<p>Amides</p>  <p>saturated = 1650 conjugated = 1660 aromatic = 1660 6 atom ring = 1670 5 atom ring = 1700 4 atom ring = 1745 3 atom ring = 1850</p>	<p>Anhydrides</p>  <p>saturated = 1760, 1820 conjugated = 1725, 1785 aromatic = 1725, 1785 6 atom ring = 1750, 1800 5 atom ring = 1785, 1865</p> <p>2 bands (symmetric and asymmetric)</p>	<p>Acid Chlorides</p>  <p>saturated = 1800 conjugated = 1770 aromatic = 1770</p>	

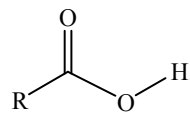
Alkene Substitution Patterns (C-H bending frequencies)

 <p>monosubstituted</p> <p>985-1000 900-920</p>	 <p>cis disubstituted</p> <p>675-730 (broad)</p>	 <p>geminal disubstituted</p> <p>880-900</p>	 <p>trans disubstituted</p> <p>960-990</p>	 <p>trisubstituted</p> <p>790-840</p>	 <p>tetrasubstituted</p> <p>none</p>
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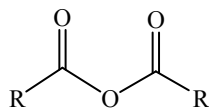
Aromatic Substitution Patterns (C-H bending frequencies)

 <p>monosubstituted</p> <p>690-710 730-770</p>	 <p>ortho disubstituted</p> <p>735-770</p>	 <p>meta disubstituted</p> <p>680-725 750-810 880-900 (sometimes)</p>	 <p>para disubstituted</p> <p>790-840</p>
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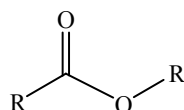
(Characteristic weak overtone patterns often show between 1650-2000, not used in this book)

IR Problem – Match the structures with the spectra that follow.

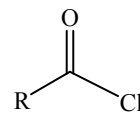
carboxylic acid



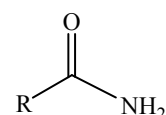
anhydride



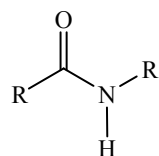
ester



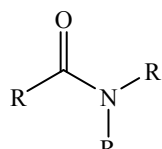
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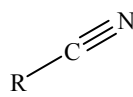
1° amide



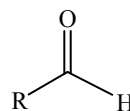
2° amide



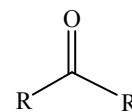
3° amide



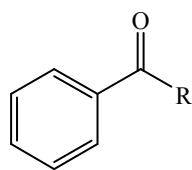
nitrile



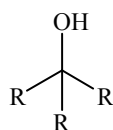
aldehyde



simple ketone



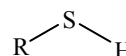
aromatic ketone



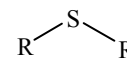
3° alcohol



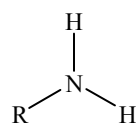
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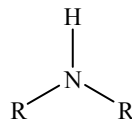
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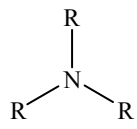
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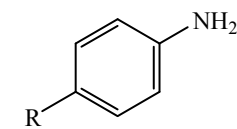
1° amine



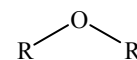
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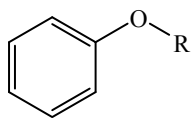
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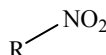
para-aromatic 1° amine



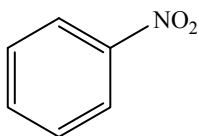
ether



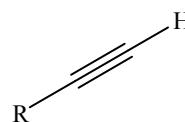
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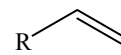
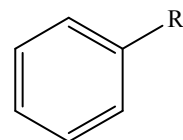
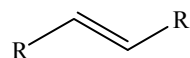
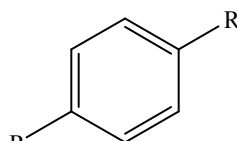
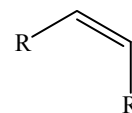
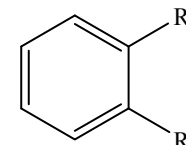
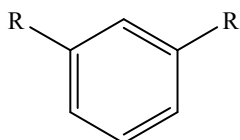
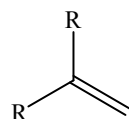
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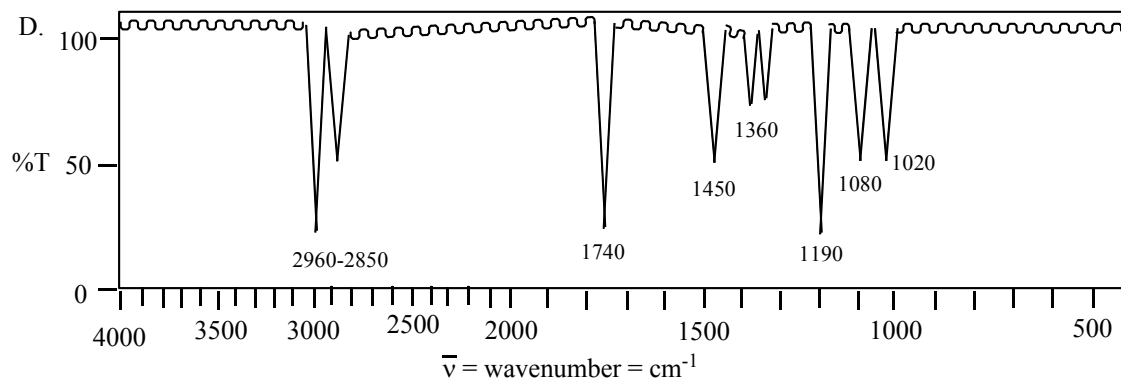
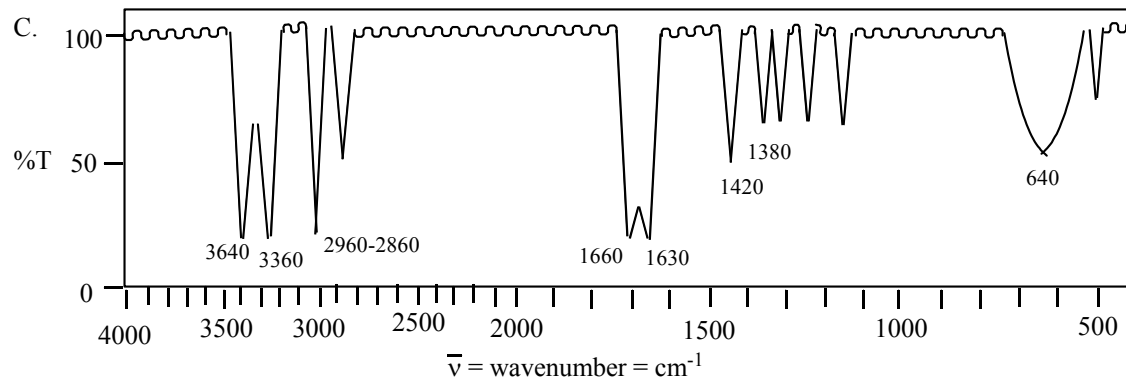
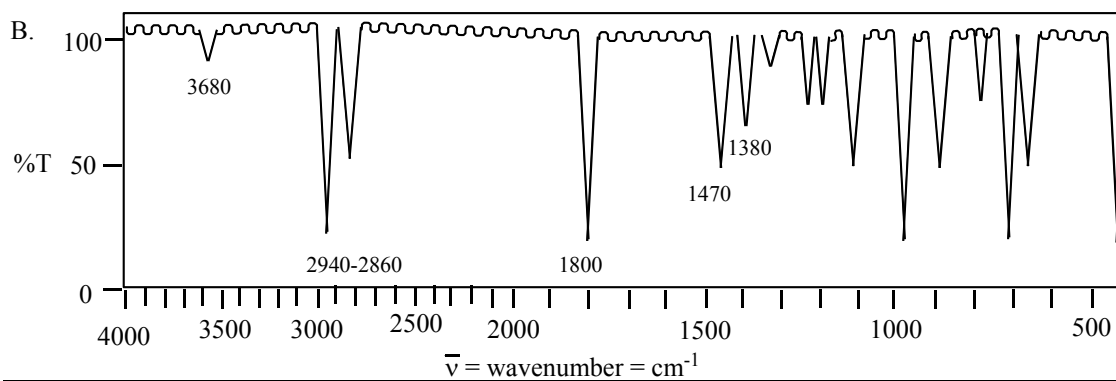
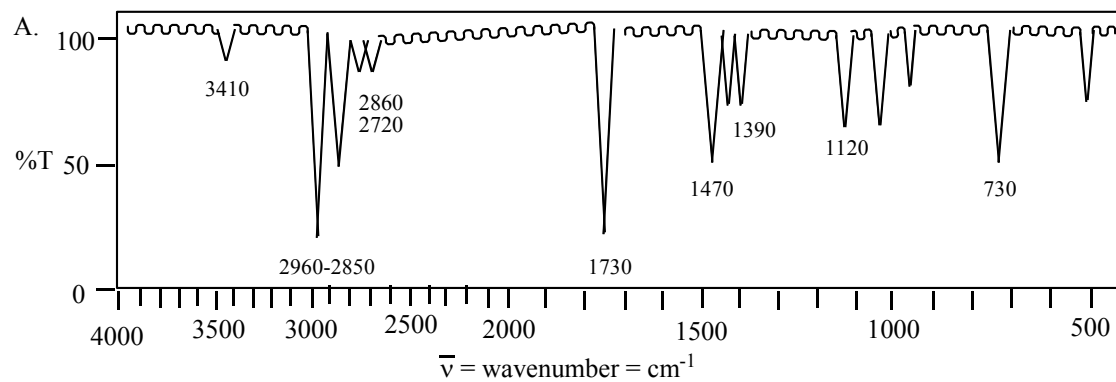


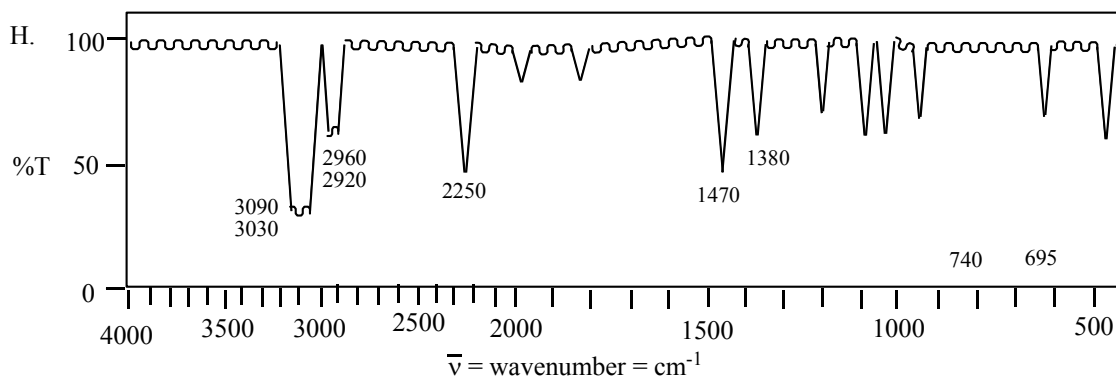
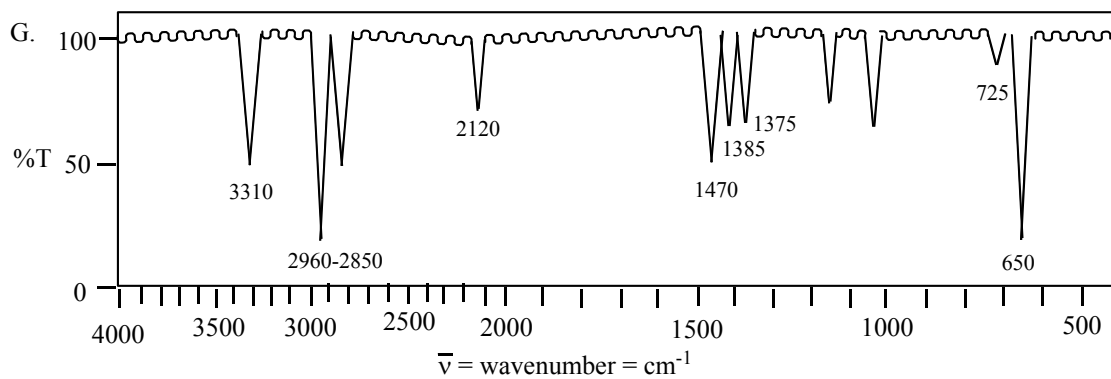
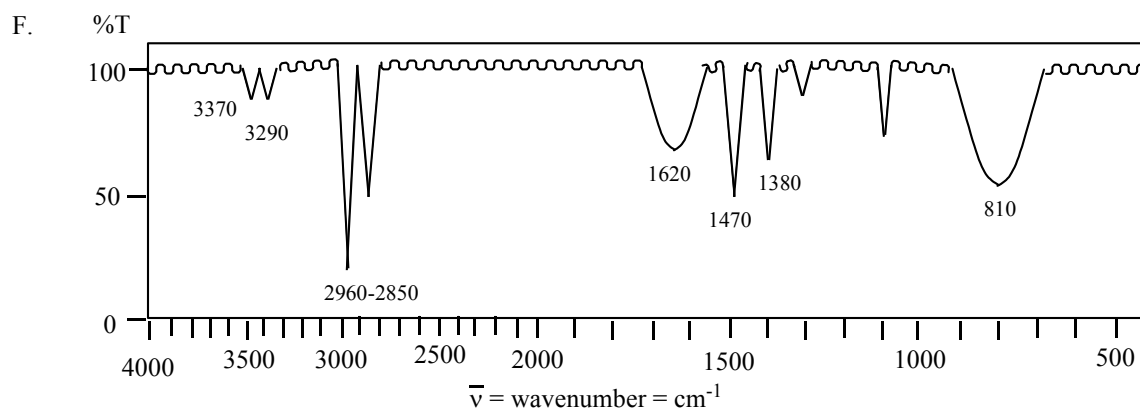
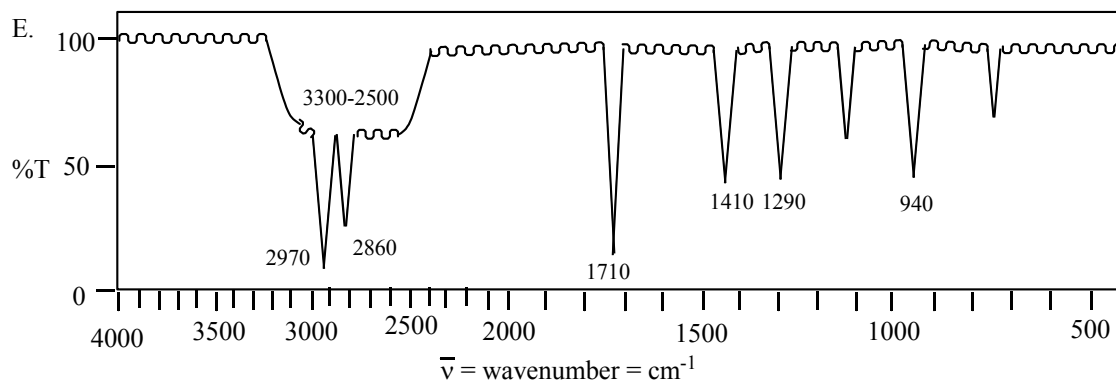
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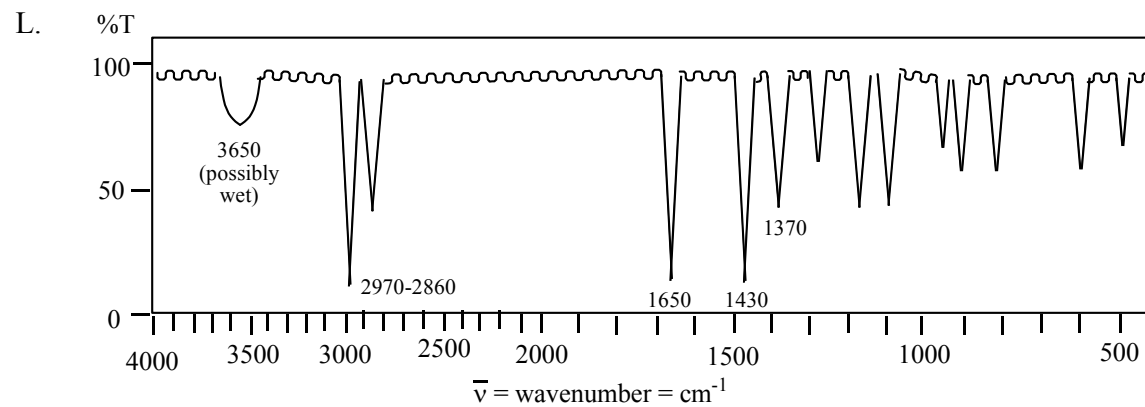
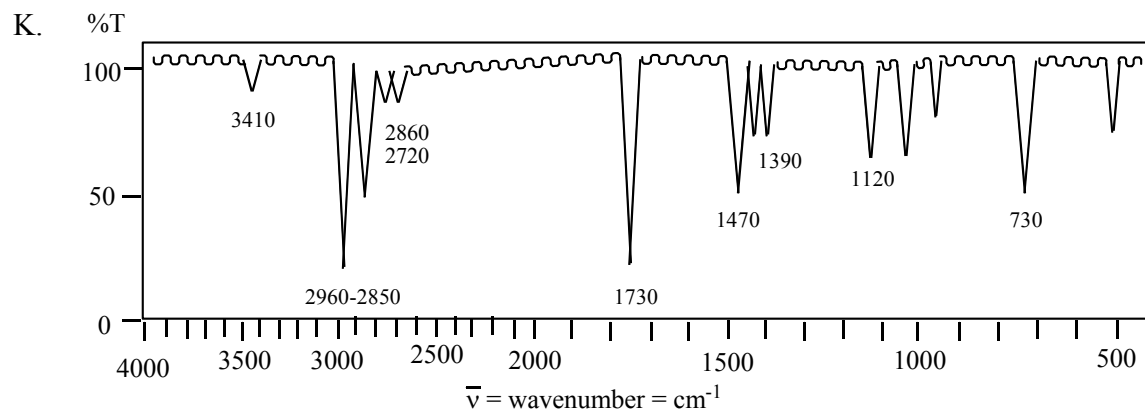
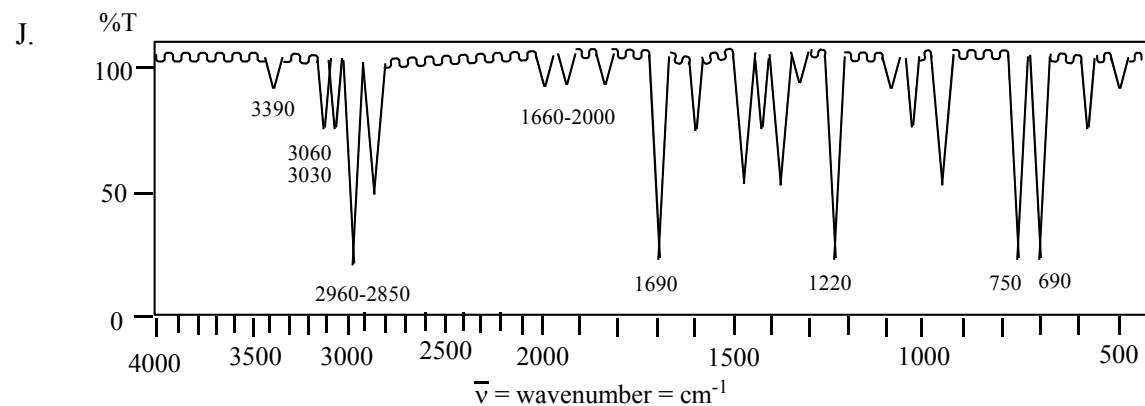
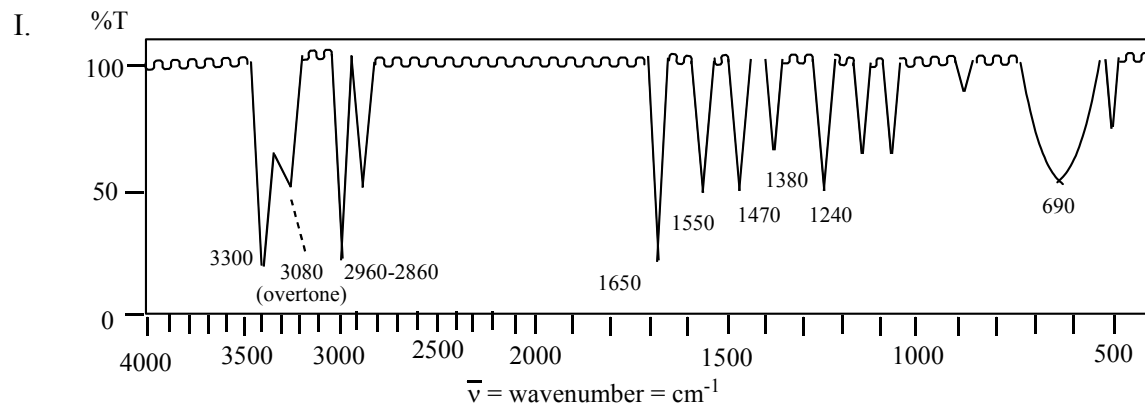


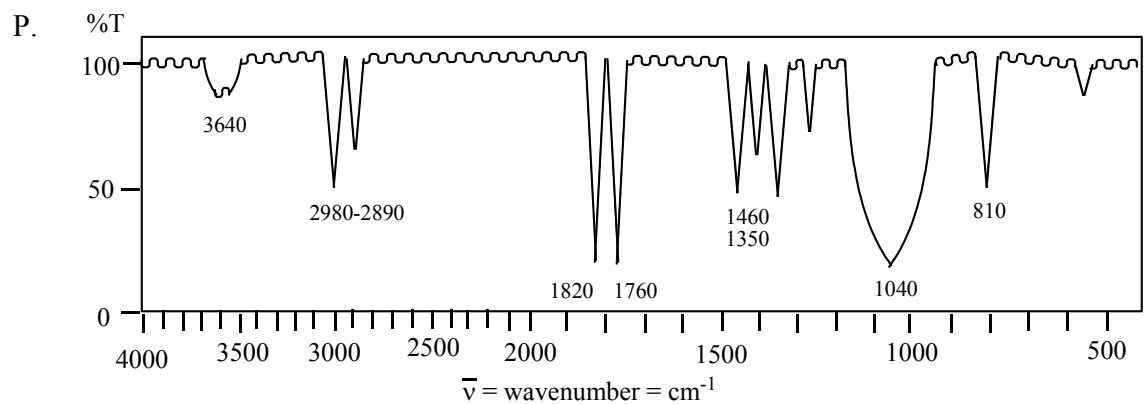
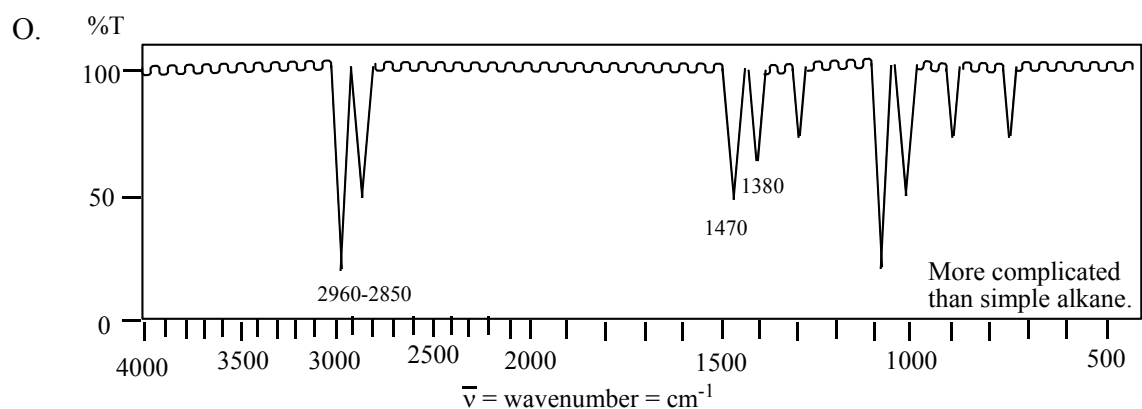
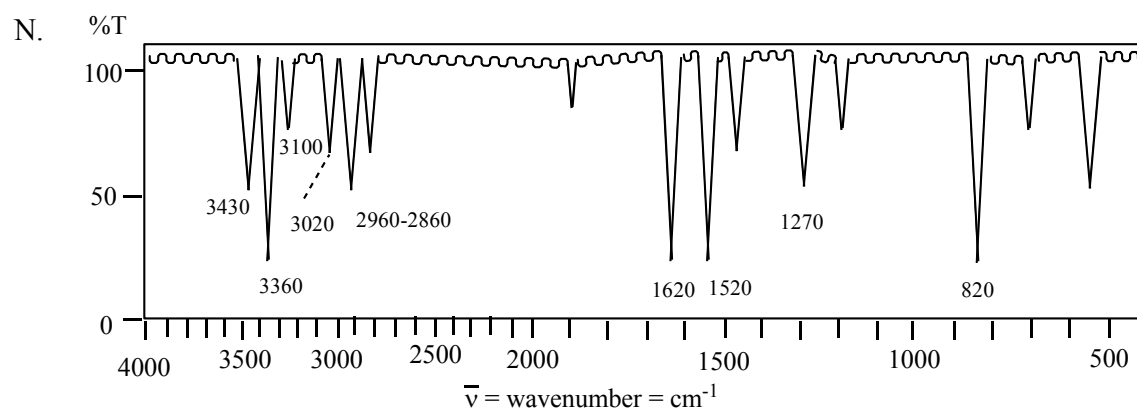
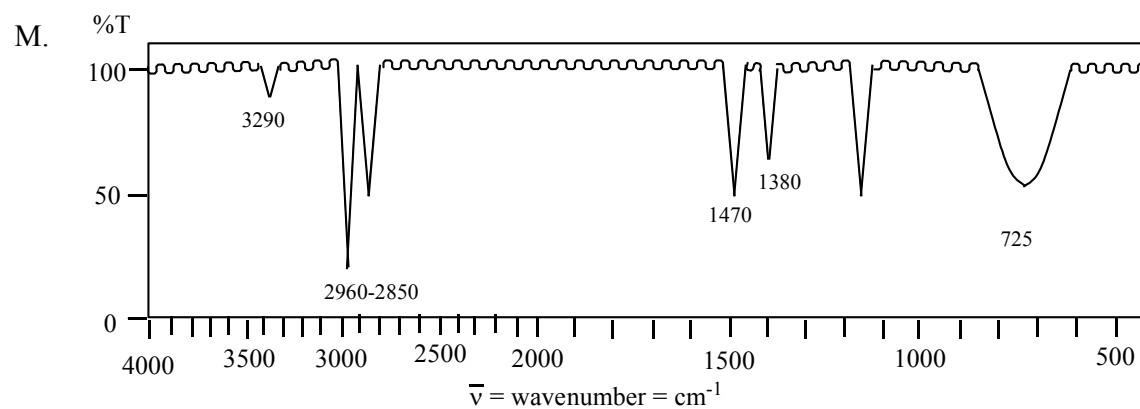
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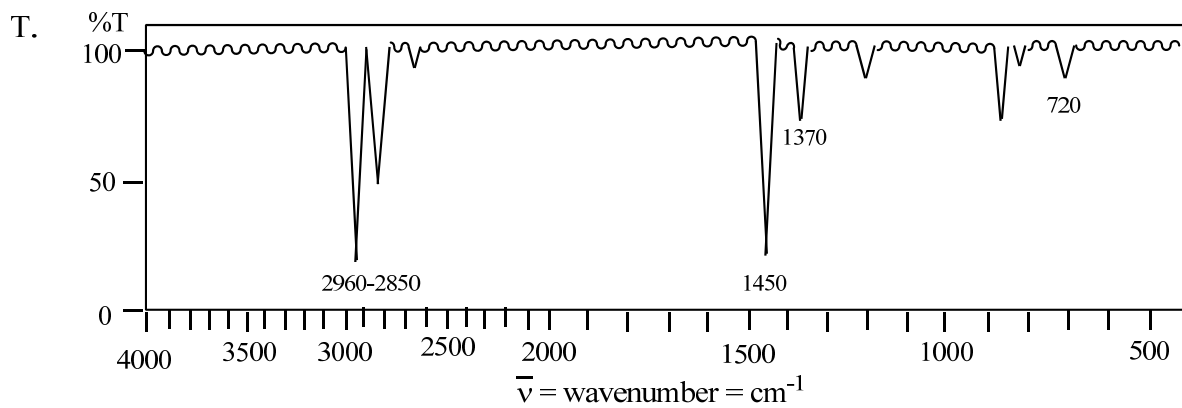
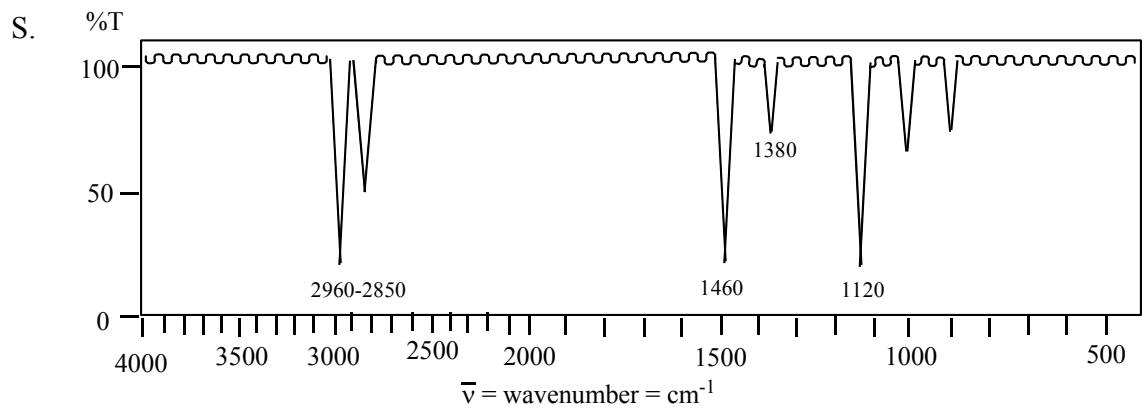
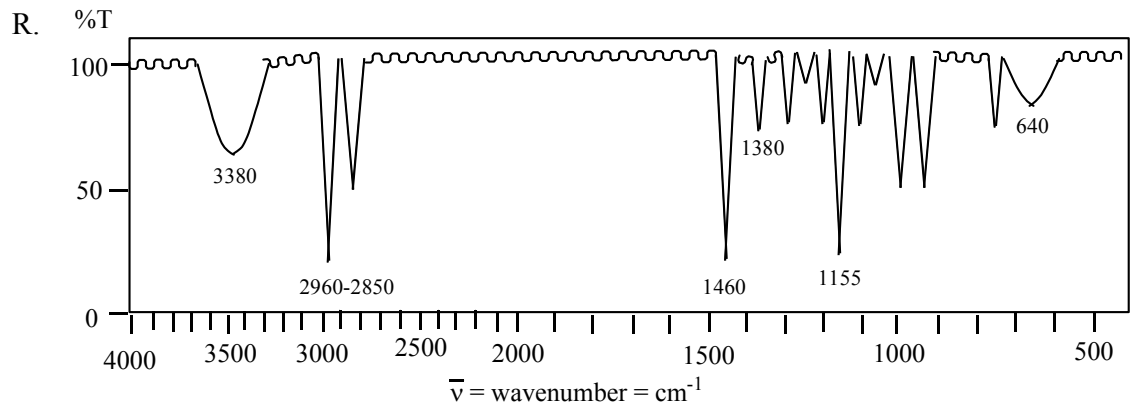
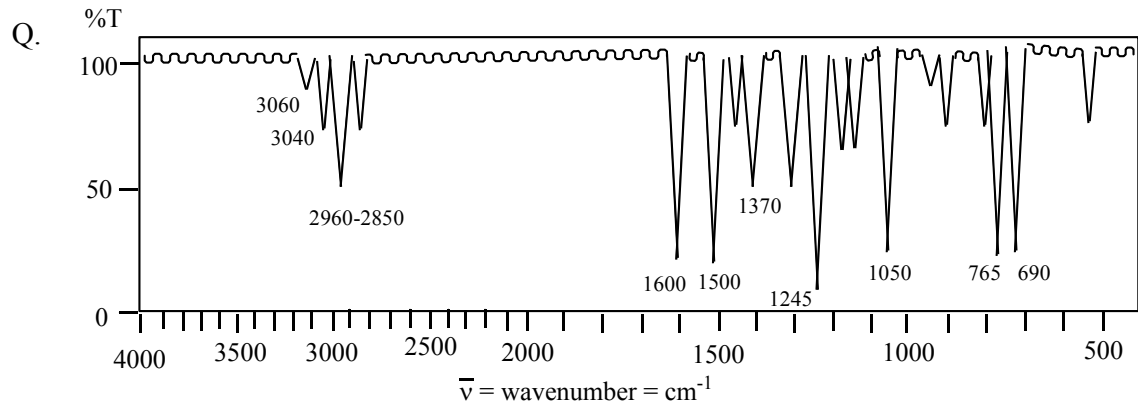
mono substituted
alkenemonosubstituted
aromatictrans substituted
alkenepara substituted
aromaticcis substituted
alkeneortho substituted
aromaticmeta substituted
aromaticgeminal substituted
alkene

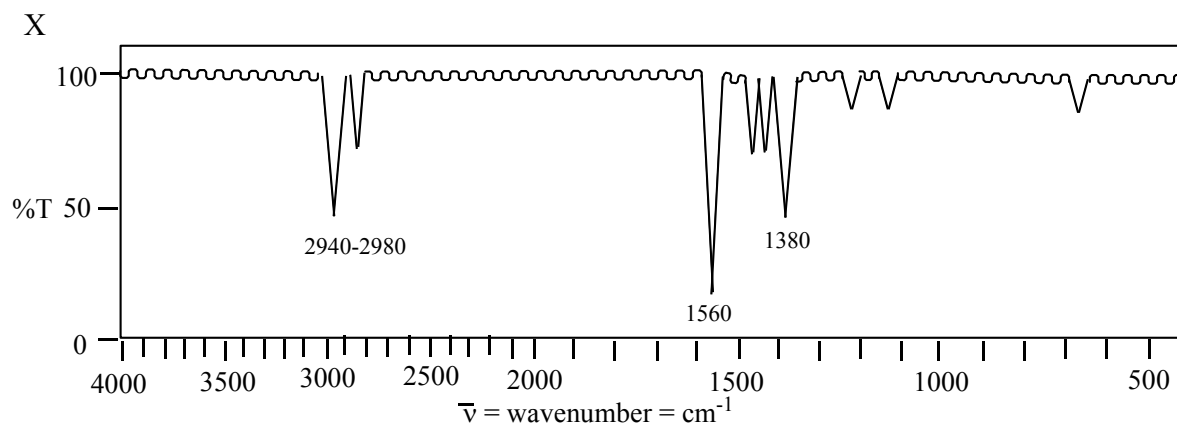
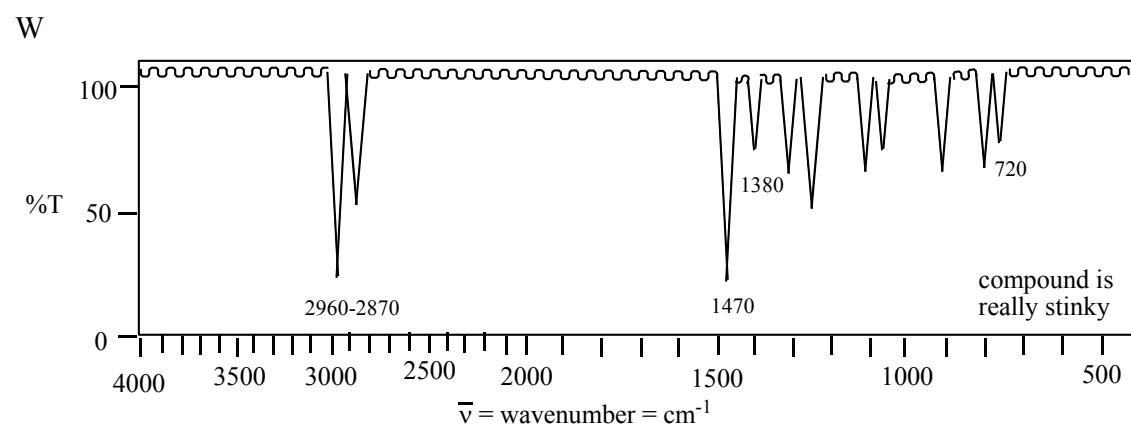
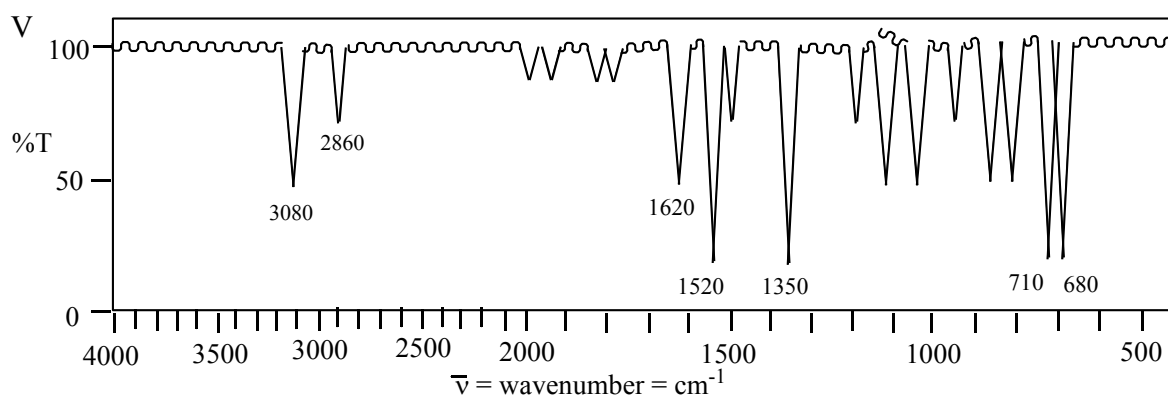
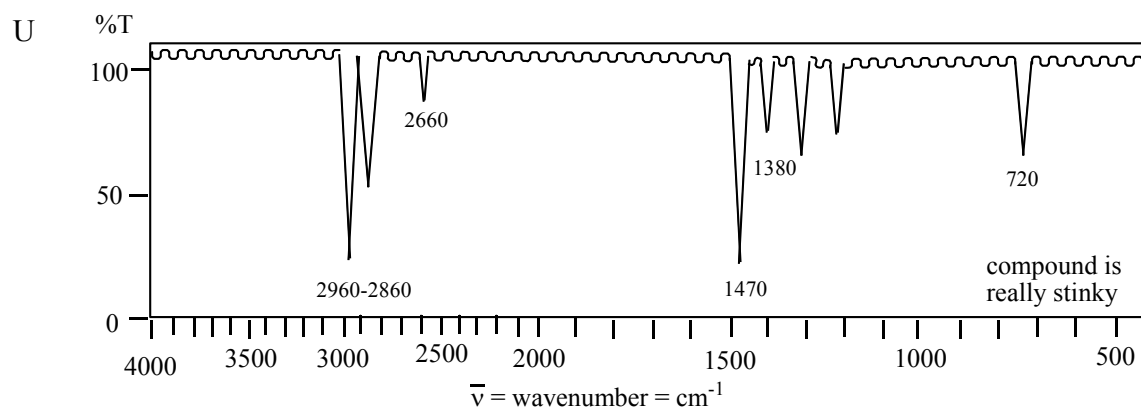


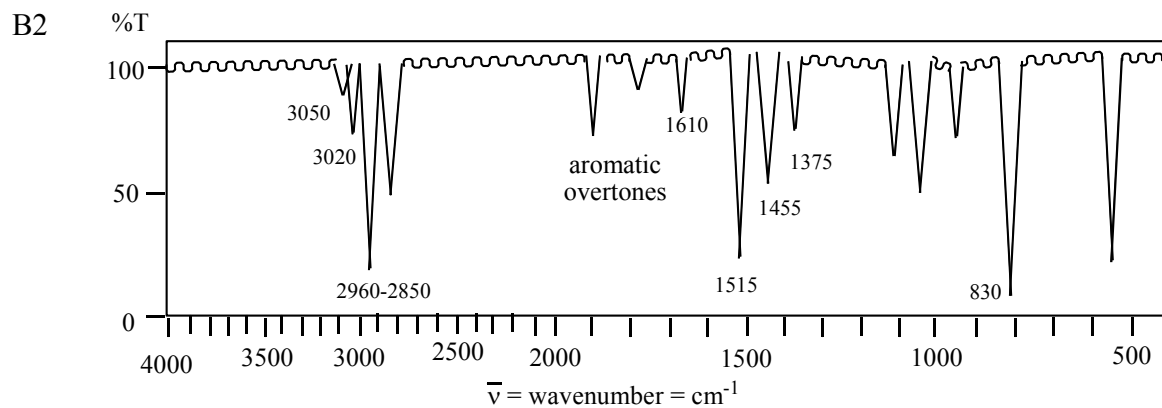
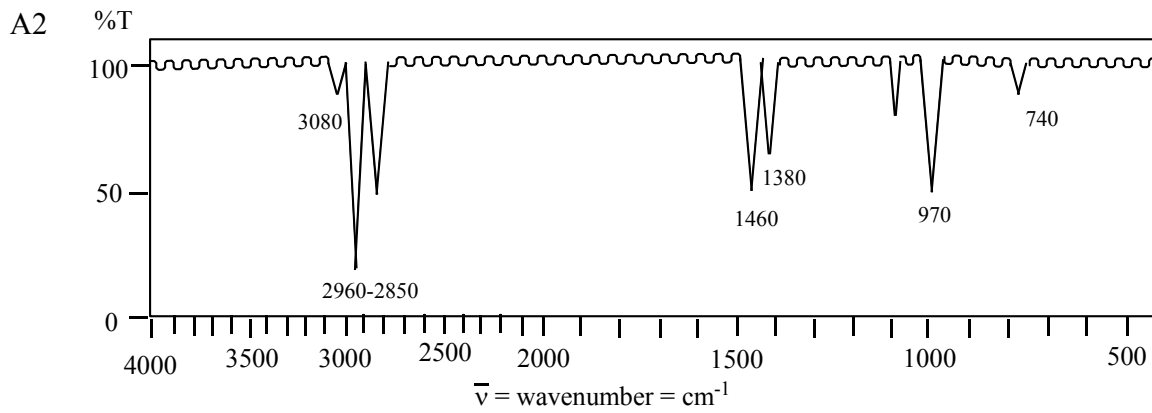
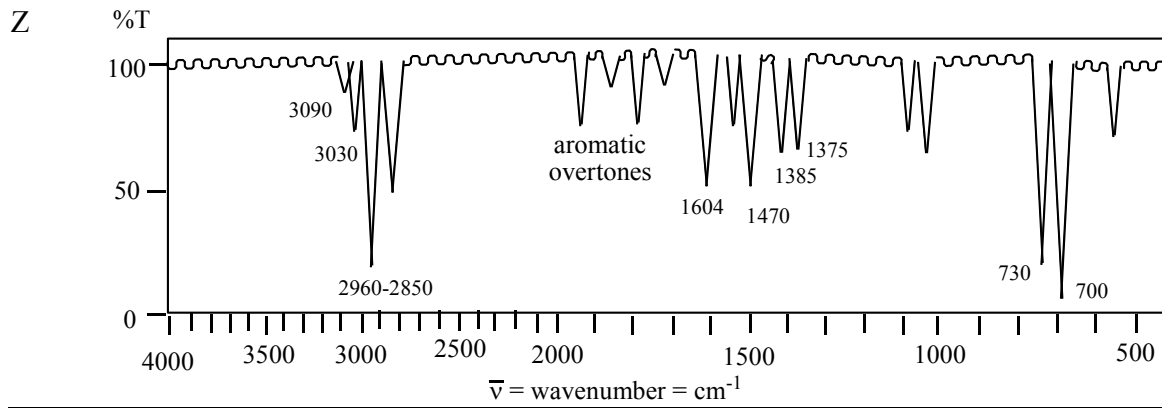
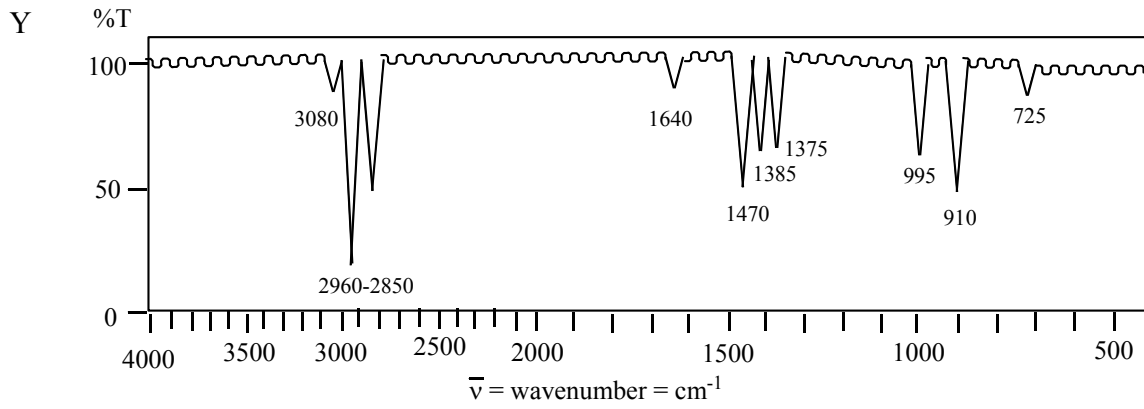


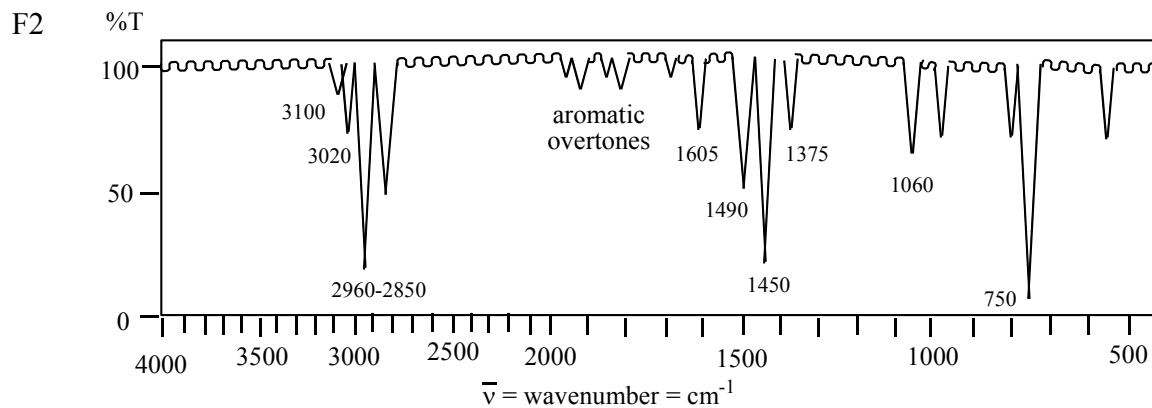
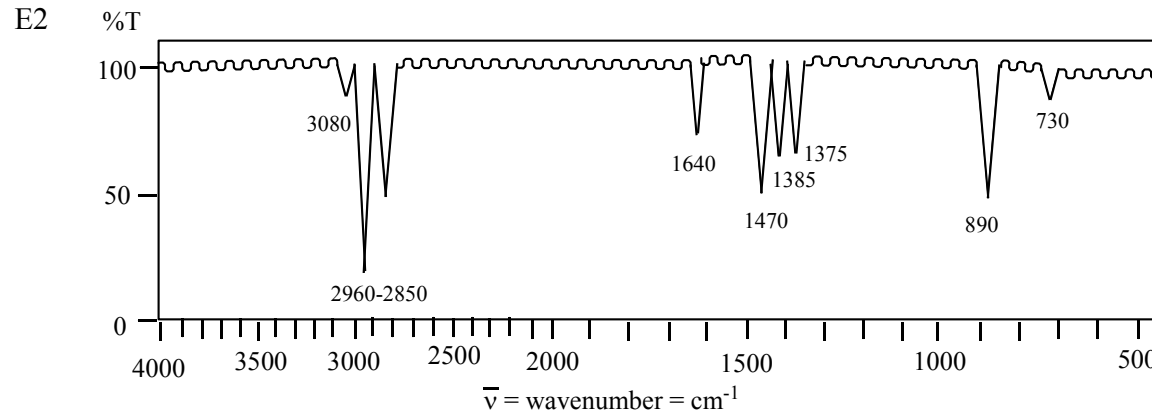
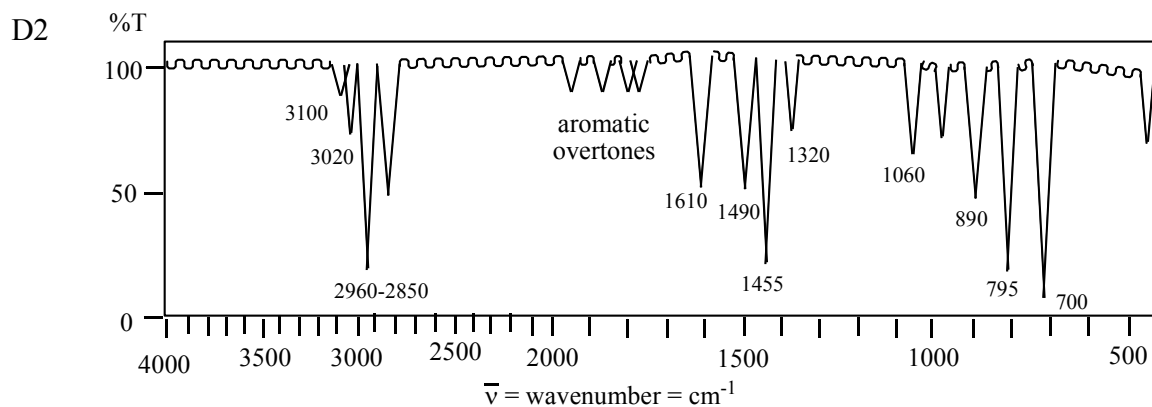
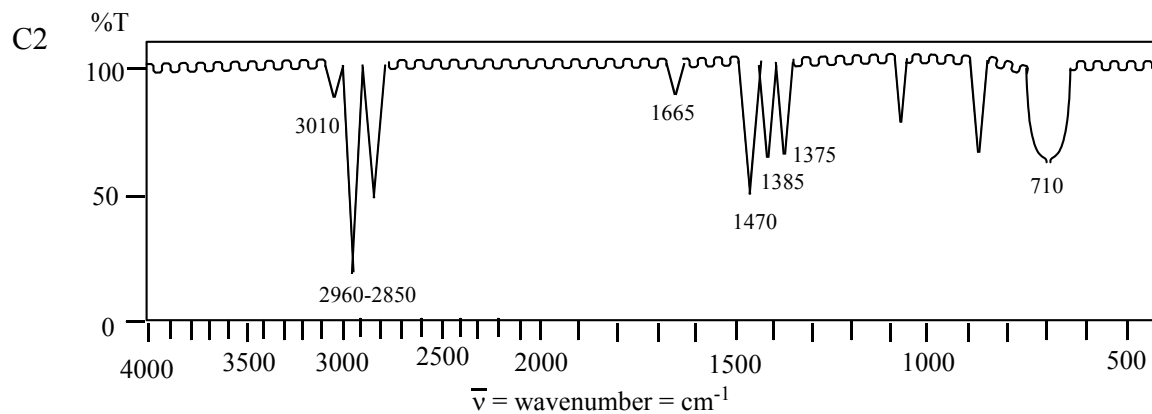












What does NMR tell us?

$^1\text{H-NMR}$

Provides information on:

1. The types of protons present (δ = chemical shift and is given in parts per million, ppm, of the energy to flip a nuclear spin in a magnetic field, the usual range is $\delta = 0$ -12 ppm).
2. The number of such protons (integration counts the relative numbers of hydrogen atoms as a whole number ratio by summing the area under the peaks).
3. How many neighbor protons are immediately adjacent to a specific center.
 - a. splitting patterns = multiplicity = number of peaks (singlet = s, doublet = d, triplet = t, quartet = q,...etc.)
 - b. J values = coupling constants (distance that peaks in a multiplet are separated in frequency units, given in Hz = cycles per second). These provide information about neighboring nuclei (protons and carbons).

$^{13}\text{C-NMR}$

Provides information on:

1. The types of carbon atoms present (δ = chemical shift is given in parts per million, the usual range $\delta = 0$ -250 ppm). Carbons are more dispersed than protons (have a wider range of chemical shifts, so there is less overlap of peaks).
2. The number of distinct kinds of carbon atoms present equals the number of peaks in a proton decoupled ^{13}C spectra. All carbon peaks appear as singlets when decoupled from the protons.
3. Reveals how many protons are on each carbon.
 - a. DEPT experiment (Distortionless Enhancement by Polarization Transfer) is a series of three ^{13}C experiments with different mixing of proton coupling to display CH, CH₂ or CH₃'s as distinct patterns. Carbons without hydrogen do not show up and are determined by comparison with a normal proton decoupled ^{13}C spectrum.
 - b. Off resonance experiment reveals coupling between protons and carbons which shows up in the multiplicity of a ^{13}C peak as follows: a singlet = C (quaternary carbon), doublet = CH (methine carbon), triplet = CH₂ (methylene carbon) or quartet = CH₃ (methyl carbon). This is an older method that is seldom used anymore.

2D Methods of NMR that we will consider

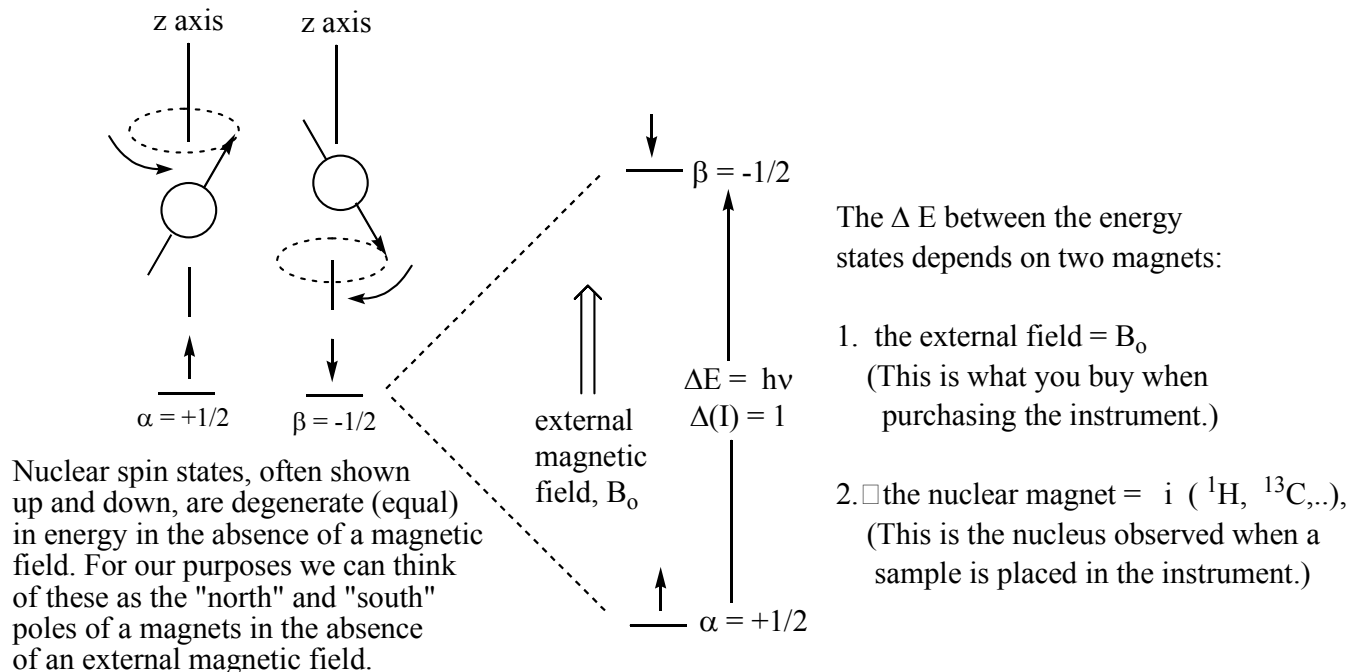
1. COSY: Proton-proton correlation spectroscopy provides proton connectivity patterns using proton spin systems based on coupling between interacting protons.
2. HETCOR or HSQC: Indicates what protons are on what carbon atoms via direct one bond coupling ($^1J_{\text{CH}}$).
3. HMBC: Indicates what protons are two or three bonds away from a carbon atom ($^2J_{\text{CH}}$, $^3J_{\text{CH}}$). It is especially helpful for connecting spin systems through quaternary carbon centers and heteroatoms.

Observing the Signal

The energy changes in NMR occur when magnetically active nuclear particles (protons and/or neutrons) alter their orientation in a magnetic field. This is a quantum mechanical event that can partly be explained pictorially with a vector model. Quantized magnetic energy states are represented with vector pictures to represent different "magnetic" possibilities. When there are only two magnetic quantum states, which is true for both ^1H and ^{13}C , we can simplistically think of these spin states as the two poles of a magnet (north and south).

In the absence of a magnetic field the two magnetic spin states have the same energy (chemists say they have degenerate energy states). However, just as two little magnets pointed in opposite directions would have different energy states if a large third magnet were brought close to them, the spinning nuclei have different energies if placed in a large magnetic field. This creates the possibility of seeing transitions between these energy states when we apply the proper radiowave frequency ($E=h\nu$) to stimulate transitions (using the resonant frequency $= \nu$). In NMR this is called the Larmor frequency.

The spinning electrical charge generates an oscillating magnetic field which precesses (rotates) at the Larmor frequency, ν , dependent on the nucleus, γ_i , and the external magnetic field, B_0 .



In the presence of a magnetic field these two magnetic quantum states are different in energy. The spin aligned with the external field, B_0 , is lower in energy than the spin aligned against the field. An input of energy with the exact frequency of this energy difference ($\Delta E = h\nu$) will stimulate a transition of the energy levels and invert the population levels. NMR actually detects the transition in relaxation back to the ground state energy. α is used to represent the lower energy state and β is used to represent the higher energy state.

Proton (^1H) and carbon (^{13}C) "magnets"

"I" represents the angular momentum (spin) quantum number. The spin quantum number is related to the number of spin states (energy states) of a particular nucleus in a magnetic field. Values of I can vary by units of $\pm 1/2$ ($0, \pm 1/2, \pm 1, \pm 3/2$, etc.).

$$\text{Number of Spin States} = 2(I) + 1$$

Nuclei with $I = 1/2$ are the most useful spin states and the most commonly used. Both ^1H and ^{13}C are in this group. Other commonly used nuclei include ^{15}N , ^{31}P and ^{19}F . These are especially useful in biochemistry and pharmaceutical chemistry, but we won't study them here.

Number of spin states = $2(1/2) + 1 = 2$ spin states for both ^1H and ^{13}C nuclei

$$I = 1/2 = ^1\text{H}, ^{13}\text{C}, ^{15}\text{N}, ^{19}\text{F}, ^{31}\text{P},$$

(these are all observable on a typical broadband NMR)

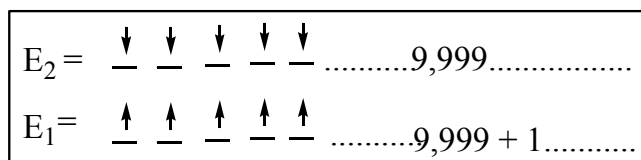
Relative Boltzman Energy Populations (for protons in a magnetic field)

Because ΔE is very small in NMR transitions, there is not much of a difference in the populations between the two energy states; it is very close to a 50/50 mixture. This fact will become very important when explaining multiplicities of peaks. Evenso, there is a very slight excess in the lower energy state (more stable, parallel spin state). How much excess depends on ΔE in the Boltzman energy expression (shown below). While the difference in populations is very small, it is very important because it is that tiny excess that we observe in the NMR experiment. A larger B_0 creates a larger ΔE and a greater relative difference in the two populations, making the NMR experiment more sensitive. This makes it easier to detect the signals we want to measure. All it takes to get a larger B_0 is money (...and someone to take care of the instrument).

$\nu_{\text{H}} = 300 \text{ MHz}$

$$\text{Boltzman distribution} = \frac{N_2}{N_1} = \exp\left(\frac{-\Delta E}{RT}\right) = \exp\left(\frac{-\left(\frac{0.028 \text{ cal / mole}}{(1.98 \text{ cal / mol-K})(298 \text{ K})}\right)}{1}\right) = \left(\frac{0.99995}{1.00000}\right)$$

N_i = number of nuclei in a particular energy state.



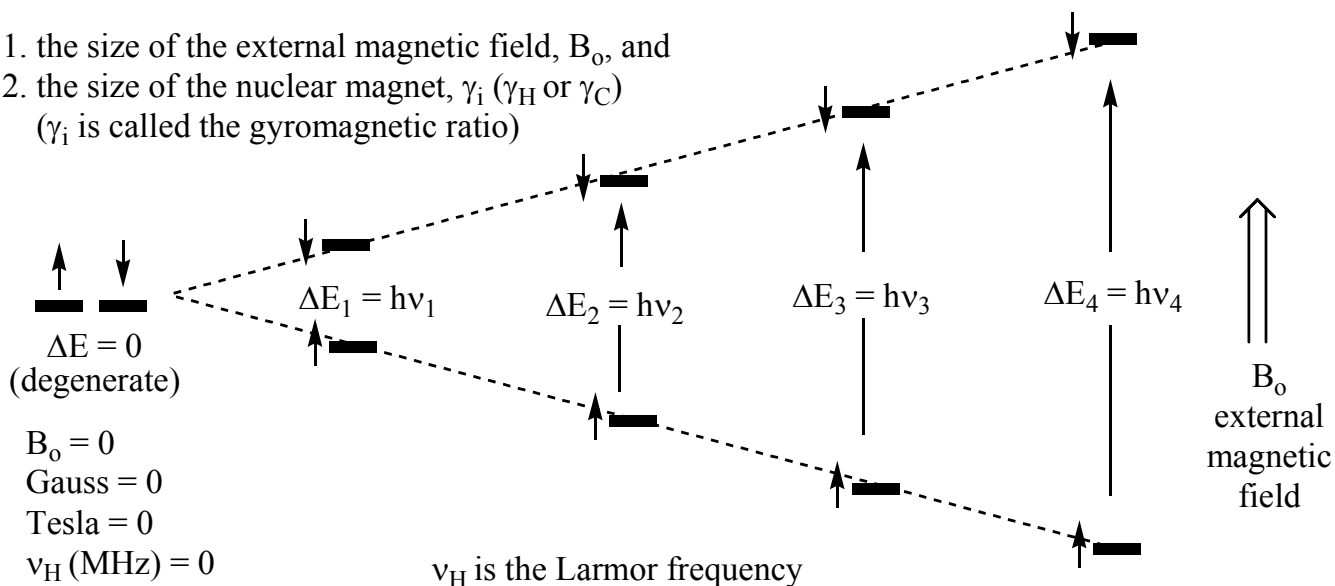
A difference of 1 out of about 20,000 because of ΔE , though the populations levels are still about 50/50.

We can stimulate energy transitions between these two energy states via an input of radio waves with matching energy (having the resonant frequency). The size of an NMR instrument is specified by the frequency of the **proton** transition in Mega hertz (Mega = 1,000,000 = 10^6 Hz). For any NMR instrument, the frequency of the carbon transition is $\frac{1}{4}$ of the proton value (because the size of the carbon magnet is about $\frac{1}{4}$ the size of the proton magnet).

Nuclei that have an even number of protons and neutrons in their nucleus only have one spin state ($I=0$) and are not magnetically active. In a sense, we are fortunate that most of carbon is isotope ^{12}C ($\sim 99\%$) and most of oxygen is isotope ^{16}O ($> 99\%$) because it simplifies our interpretation of routine ^1H and ^{13}C NMR spectra. Both ^{16}O and ^{12}C have an even number of protons and neutrons (^{12}C : $p = n = 6$ and ^{16}O : $p = n = 8$) and are magnetically invisible.

The size of ΔE depends on:

1. the size of the external magnetic field, B_o , and
2. the size of the nuclear magnet, γ_i (γ_H or γ_C)
(γ_i is called the gyromagnetic ratio)

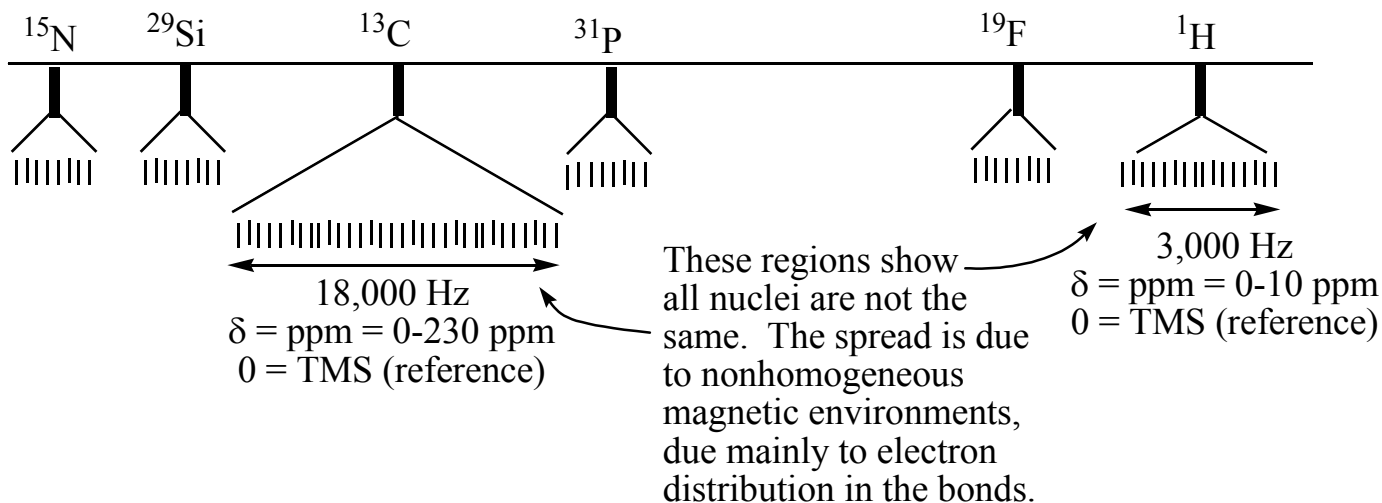


Size of external magnetic field =	Gauss = 14,100	Gauss = 23,500	Gauss = 70,500	Gauss = 141,500
	Tesla = 1.4	Tesla = 2.4	Tesla = 7.1	Tesla = 14.2
	ν_H (MHz) = 60*	ν_H (MHz) = 100*	ν_H (MHz) = 300*	ν_H (MHz) = 600*
	ν_C (MHz) = 15*	ν_C (MHz) = 25*	ν_C (MHz) = 75*	ν_C (MHz) = 150*
	Original commercial instrument	Largest solid core electromagnet	Current routine instruments range from 300-400 MHz	Very large field magnet, very expensive
	* assumes a proton nucleus			

The NMR Radio Dial

The energy of a 300 MHz NMR instrument (based on the energy differences of protons) is in the radio wave region of the electromagnetic spectrum and is determined by the size of the external magnetic field, B_0 . Think of the other nuclei as appearing at different positions on your radio dial and each magnetogyric ratio, γ_i , as the number you tune into on your radio. The parameter γ_i is a ratio of a particle's dipole moment and its nuclear angular momentum, something we won't emphasize. We focus mainly on the interpretation of proton and carbon NMR data.

$$\Delta E = h\nu = \left(\frac{h}{2\pi}\right) (\gamma_i) (B_0) = (\text{constants}) \times (\text{type of nucleus}) \times (\text{external magnetic field})$$



$\gamma_H = 26,751$ radians/(sec-gauss)
$\gamma_{F19} = 25,166$ radians/(sec-gauss)
$\gamma_{P31} = 10,829$ radians/(sec-gauss)
$\gamma_{C13} = 6,726$ radians/(sec-gauss)
$\gamma_D = 4,106$ radians/(sec-gauss)
$\gamma_{N15} = 2,712$ radians/(sec-gauss)

γ_i = magnetogyric ratio

(Think of this as the number on your radio dial.)

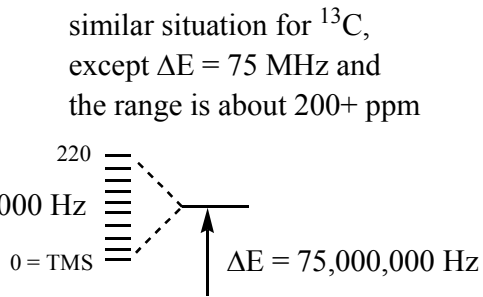
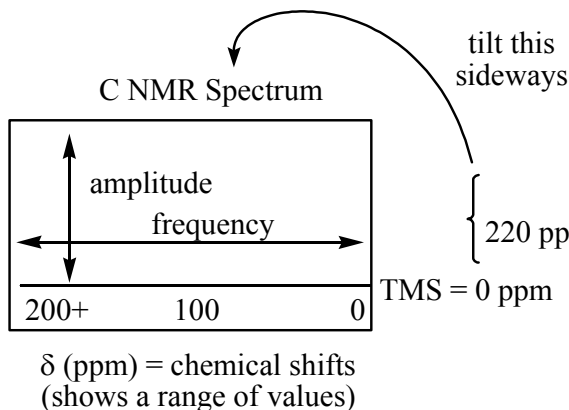
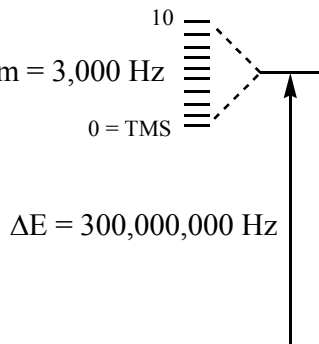
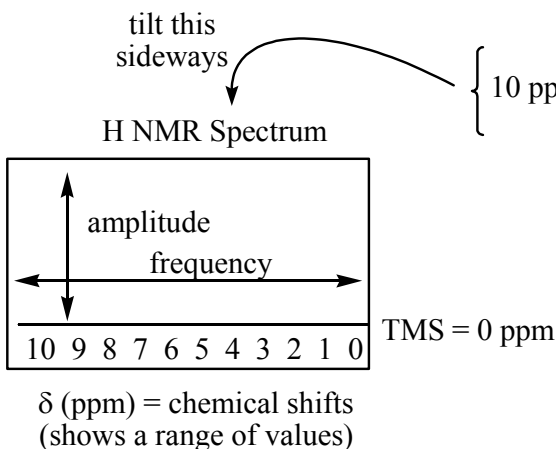
Why are there differences in chemical shifts? – Two main reasons for us.

Almost all of the proton chemical shifts in organic chemistry come in a very narrow range of the full ΔE to excite a proton. On a 300,000,000 Hz instrument, the full range of proton *differences* in energy of excitation is about 3,000 Hz. One millionth of the full ΔE is 300 Hz, so the full range of chemical shifts is about 10 parts per million (ppm). Rather than report the frequency differences in Hertz which would change with the size of the instrument, NMR spectroscopists report the differences in ppm, which is the same value on all instruments. Tetramethylsilane (TMS) has an exceptional frequency in H and C NMR spectra on the right side and is used to reference zero ppm. A chemical shift that lies 2 ppm to the left of TMS would be 200 Hz away on a 100 MHz instrument, 600 Hz away on a 300 MHz instrument and 1200 Hz away on a 600 MHz instrument. A bigger magnet produces a proportionately bigger energy difference between the spin states of the nuclei, in hertz, but not as ppm of the energy field. Chemical shift in ppm, is a unitless parameter that is the same for each type of hydrogen atom (or carbon atom), no matter what size instrument the spectrum is acquired on.

1 ppm in Hz depends on B_0 (size of the external magnetic field: 1/1,000,000 of ΔE of ν in Hz).

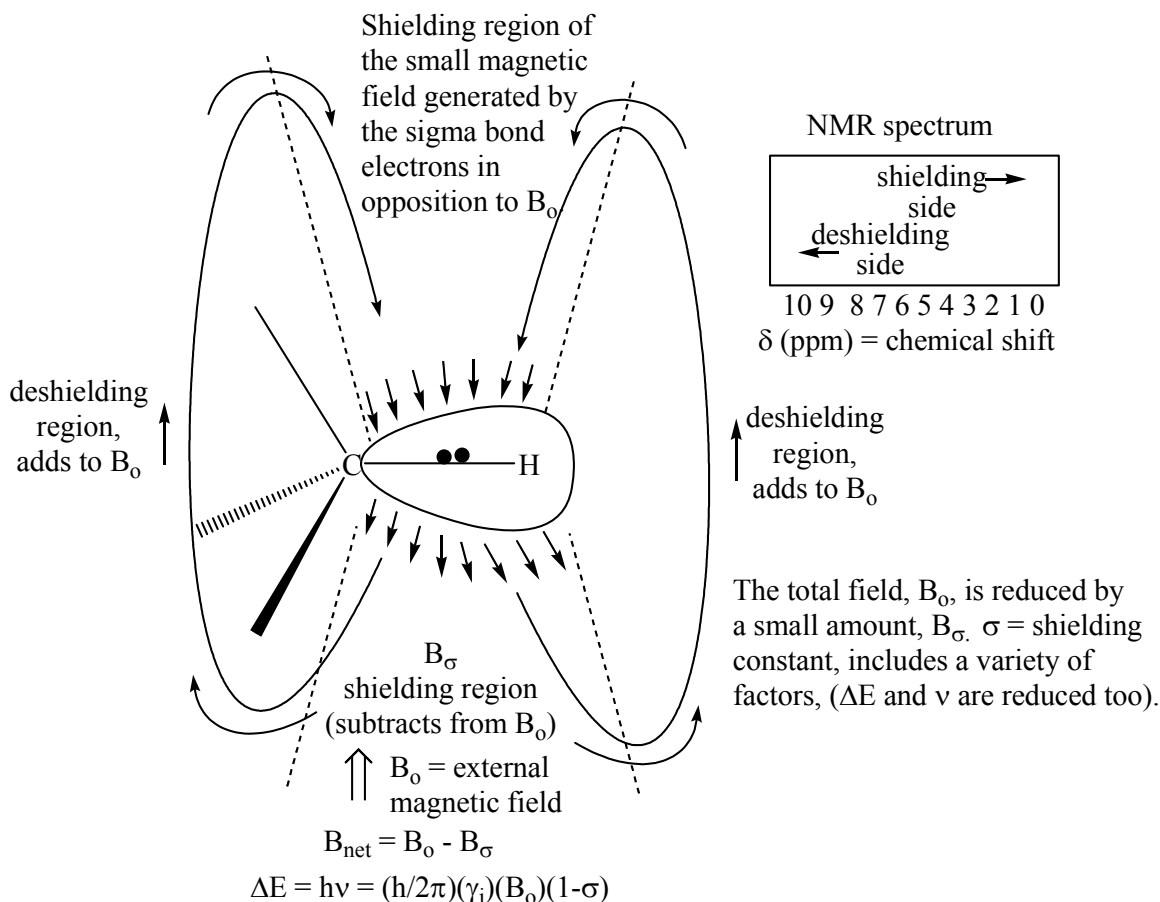
B_0	1.0 ppm (= Hz)
60 MHz	60 Hz = 1 ppm
100 MHz	100 Hz = 1 ppm
300 MHz	300 Hz = 1 ppm
600 MHz	600 Hz = 1 ppm

On a 300 MHz instrument the range of differences in chemical shifts is about 3000 Hz. This is only a small portion of the total energy to cause a proton to flip (about 300,000,000 Hz = 300 MHz).



1. Electronegativity Effects

Electrons moving in chemical bonds create their own small opposition magnetic field to the external magnetic field. This is called shielding. The more electron density there is, the stronger is this opposition field (the shielding effect). Any nearby electron withdrawing groups can steal some of this electron density away from sigma C-H bonds and change the net magnetic field each proton experiences, which then changes the chemical shift, δ , where a proton is excited.



Some typical proton chemical shifts for methyl groups attached to different atoms are shown below. Clearly there is some sort of electronegativity effect working here. Electronegative atoms reduce electron density in the sigma bond and cause deshielding effects (δ moves to the left = downfield). Electropositive atoms (Si) increase electron density in the sigma bond and cause shielding effects (δ moves to the right = upfield).

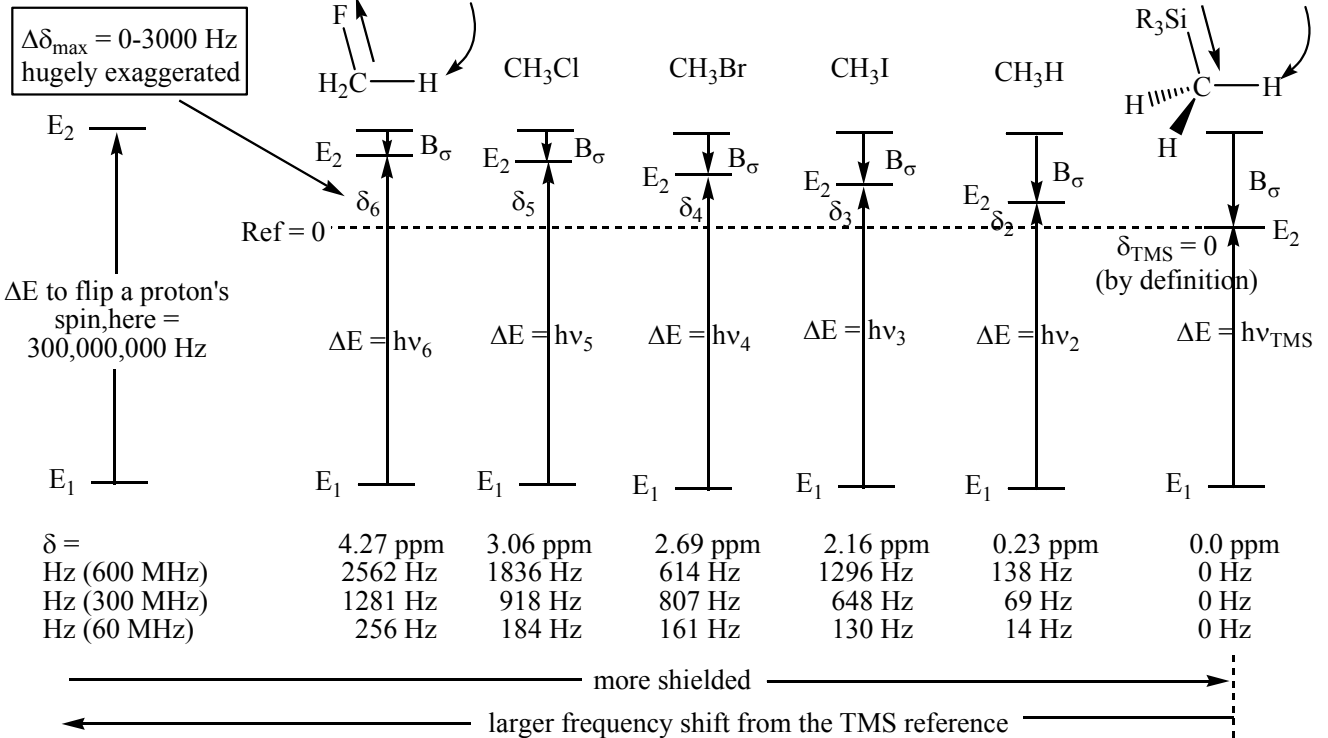
proton chemical shift (δ) =	$\text{CH}_3\text{-F}$	$\text{CH}_3\text{-OR}$	$\text{CH}_3\text{-Cl}$	$\text{CH}_3\text{-Br}$	$\text{CH}_3\text{-I}$	$\text{CH}_3\text{-H}$	$(\text{CH}_3)_4\text{Si} = \text{TMS}$
	↑	↑	↑	↑	↑	↑	↑
	4.27 ppm	3.39 ppm	3.06 ppm	2.69 ppm	2.16 ppm	0.23 ppm	0.0 ppm
	← deshielding direction ———						
	————— shielding direction →						

TMS is zero by definition = relative reference point for both protons and carbons in NMR.

$$\Delta E_{\text{actual}} = B_{\text{net}} = (1 - \sigma) B_0 \quad (B_0 \text{ is reduced a little by a } \sigma_{\text{diamagnetic}} \text{ shielding term)}$$

These protons are least shielded because of the inductive pull of fluorine (deshielded)

These protons are most shielded because of the inductive push of silicon.

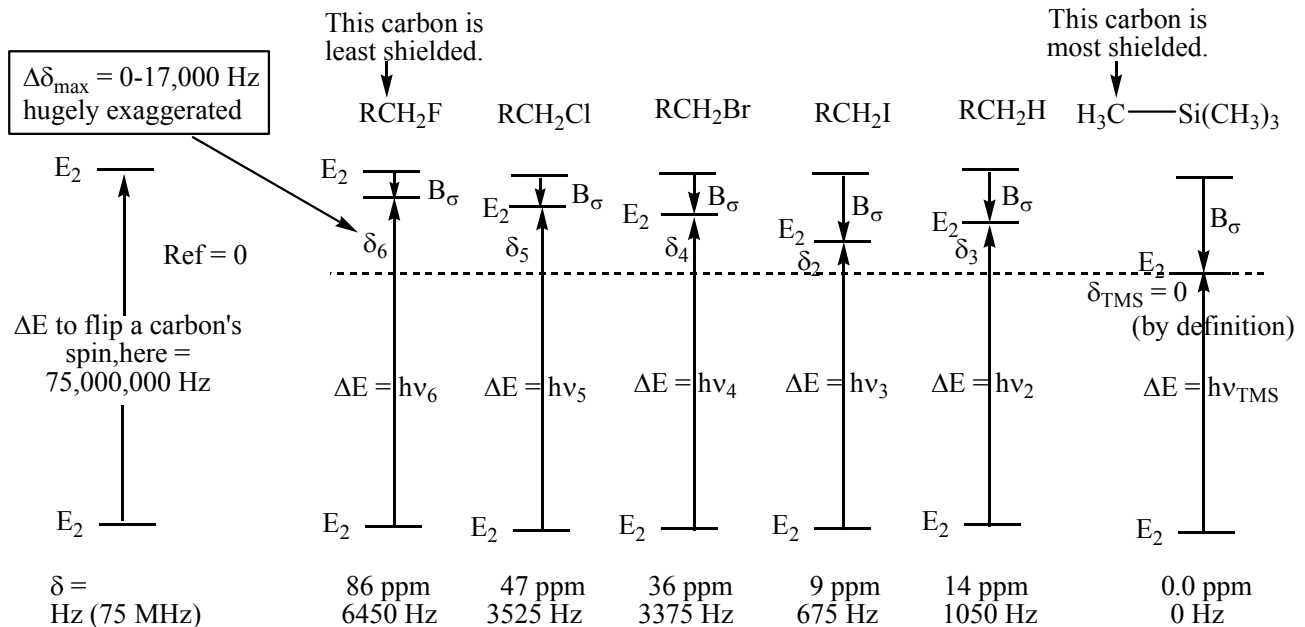


$\Delta E = 300,000,000 \text{ Hz}$ (energy to flip proton spin)

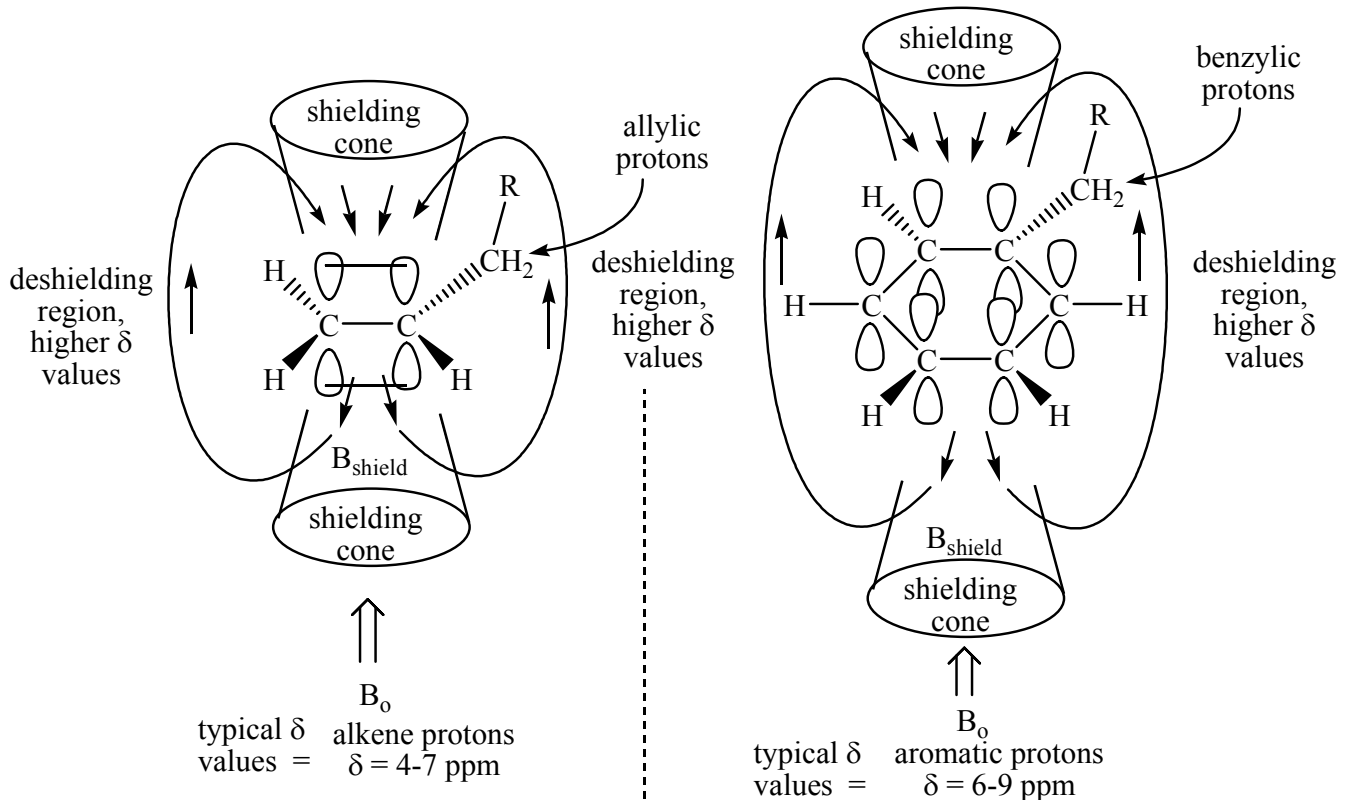
$\Delta\delta = 0-3,000 \text{ Hz} = 0-10 \text{ ppm}$ (the scale is greatly exaggerated above), we can measure δ to about 0.1 Hz out of 300,000,000 Hz, that's about 1 part out of 3 billion!

We are assuming a constant magnetic field strength of B_0 (=70,500 gauss here) and variable frequencies, ν 's, detected all at once and converted by Fourier transformation NMR.

Similar information for ^{13}C shifts on a 300 MHz NMR ($^{13}\text{C} = 75 \text{ MHz}$)



Pi bond anisotropy: certain orientations of the molecule (relative to B_0) add to the external magnetic field and others cancel with a net contribution of what is shown below in the following figures.



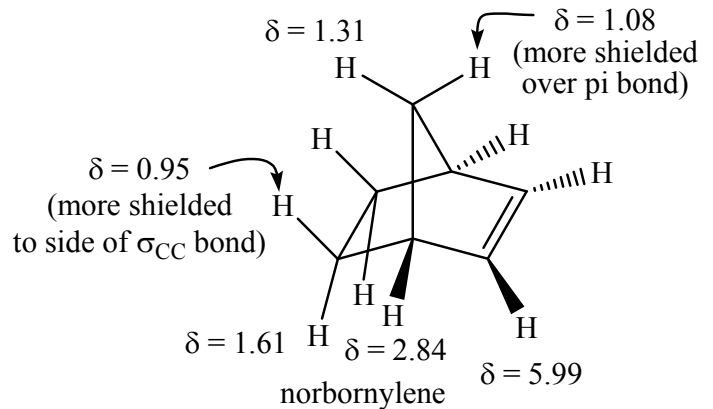
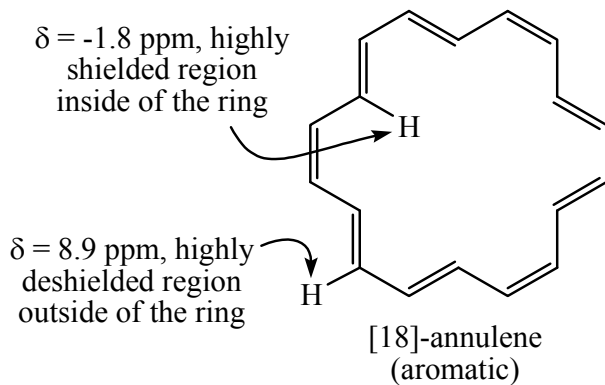
Protons to the side of an alkene pi bond are deshielded and shifted to a larger chemical shift = δ . Allylic protons are shifted in a similar direction but by a smaller amount because they are farther away from the pi bond.

Ring current in aromatics has a larger effect than a single pi bond in a typical alkene. Aromatic protons usually have a larger chemical shift than alkene protons. Benzylic protons are shifted in a similar direction but by a smaller amount because they are farther away from the pi bonds.

B_{pi} = induced magnetic field due to pi bond electrons

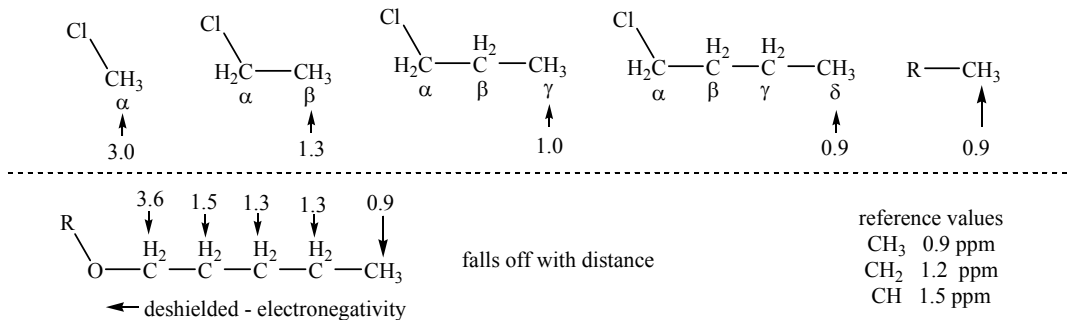
a. B_{shield} opposes B_0 in shielding cone; B_0 is effectively made smaller and a smaller δ is the result

b. $B_{deshielded}$ adds to B_0 in the deshielding region; B_0 is effectively made larger and a larger δ is the result.

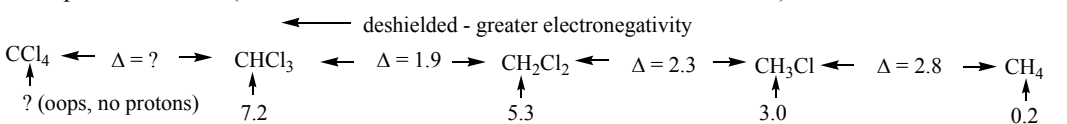


Electronegativity and Resonance Effect – Experimental Data

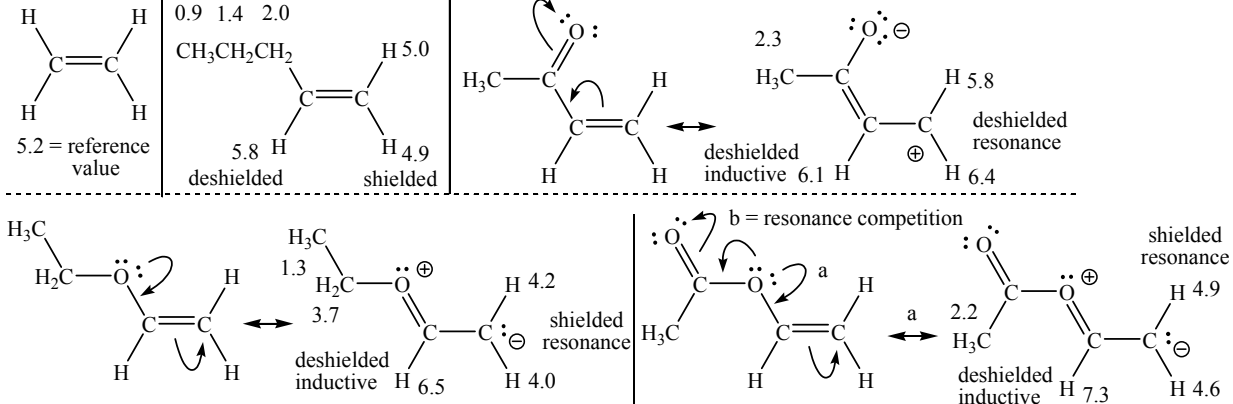
Electronegative substituent and distance from protons



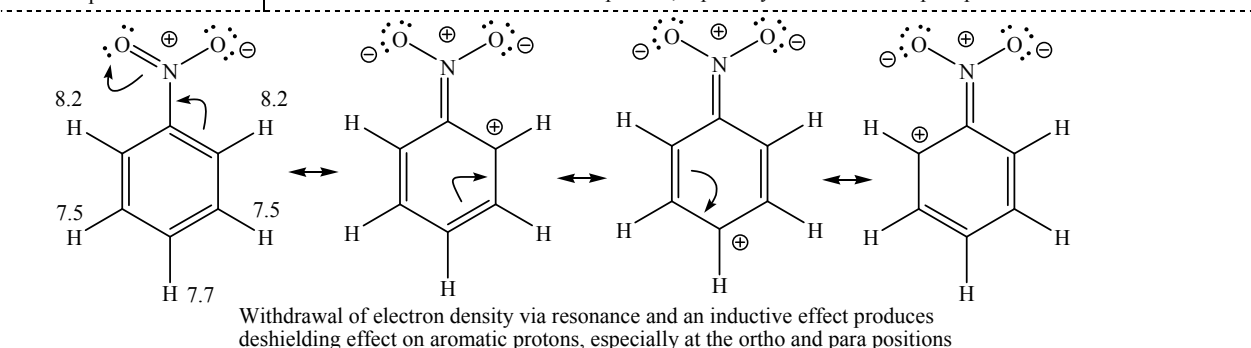
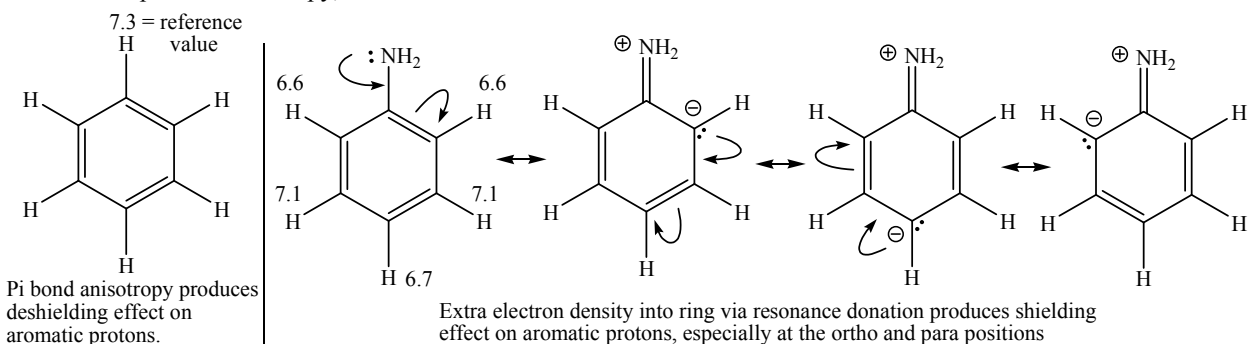
Multiple substituents (often each additional substituent has a smaller effect)



Alkene substituents - pi bond anisotropy, resonance and inductive effects



Aromatics - pi bond anisotropy, resonance and inductive effects



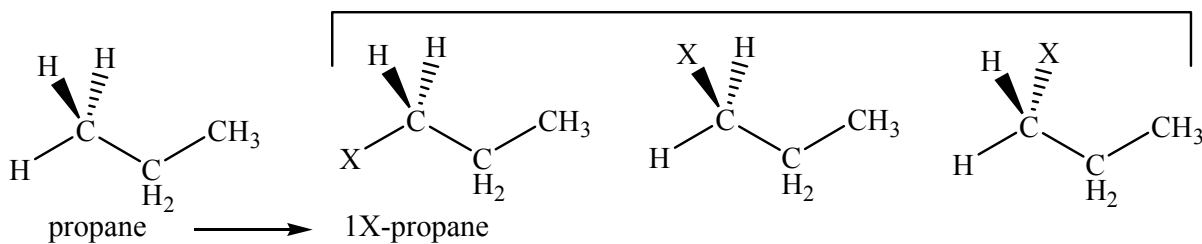
Recognizing different types of protons and carbons

Replace each proton being compared with "X", as a different group, and evaluate the new structures obtained with X at each position according to the following guidelines. The same is true for carbon atoms, but mostly shown for protons below.

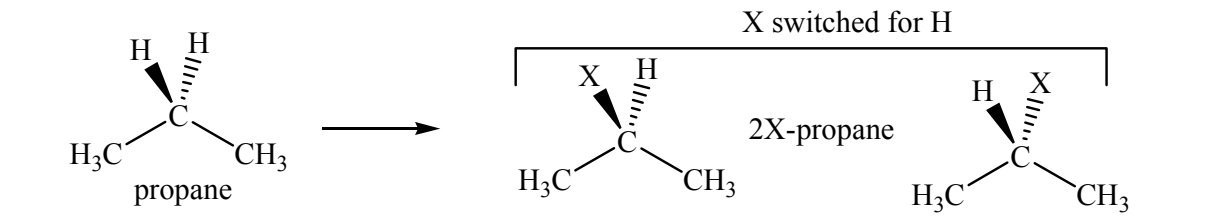
Classification of Protons (and Carbons) by Group Topology

1. **homotopic groups** – Do the switches produce the same end result? If so, the protons are homotopic protons and have the same chemical shift and do not split one another. This generally produces straight forward splitting patterns based on the simple N+1 rule (explained later).

Replace each methyl proton with "X" and compare. X switched for H produces the same molecule

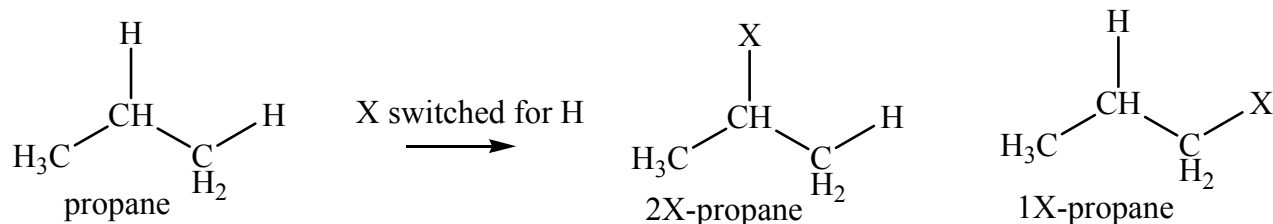


Replace each methylene proton with "X" and compare. In propane this produces the same molecule.



2. **heterotopic groups** – When substitution of each atom produces structural or positional isomers, the atoms are heterotopic. Such groups do not generally have the same chemical shifts, but may coincidentally have the same chemical shifts (accidental equivalence).

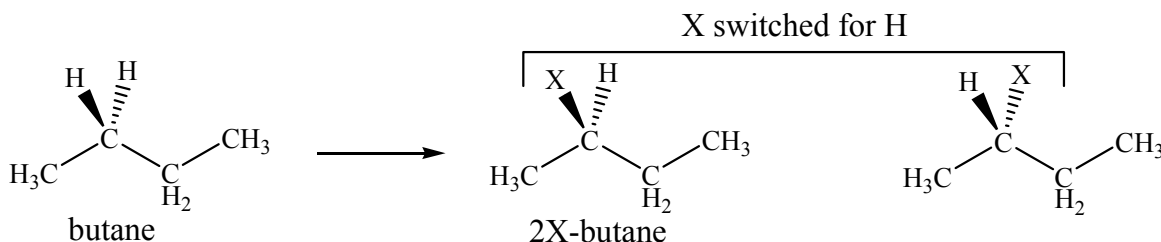
Replace methylene proton with "X" and compare to replacing methyl proton with "X".



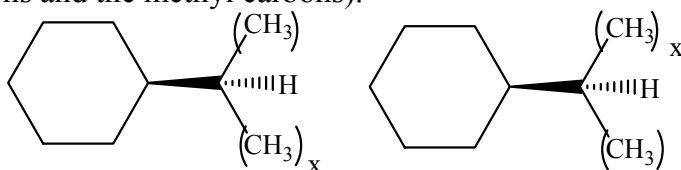
These two molecules are isomers, but the methylene hydrogen is completely different from the methyl hydrogen. Those protons (and carbons) are heterotopic and will very likely have different chemical shifts and split one another when neighbors.

3. **enantiotopic groups** – Do the switches produce different molecules, as enantiomers? If so, the protons are enantiotopic protons. In the absence of a chiral environment these protons still have identical chemical shifts and will not split one another. However in the presence of a chiral environment (an adjacent chiral center or another molecule that is chiral such as a reagent or a solvent molecule), they will become nonequivalent (diastereotopic) and may or may not have different chemical shifts (they could coincidentally have the same chemical shift, but probably not). If their chemical shifts are different, they may split one another (couple) and make the spectrum appear more complicated.

The methyl protons are all homotopic, as in propane, and simple to consider. Next, replace each methylene proton with "X" and compare. These two molecules are enantiomers and, in this example the methylene hydrogen atoms are enantiotopic. In the absence of any chiral environment they would not split one another because they have the same chemical shift. In the presence of any other chiral center they would become diastereotopic and could split one another and split their neighboring hydrogen atoms differently. However in this example that is not the case.



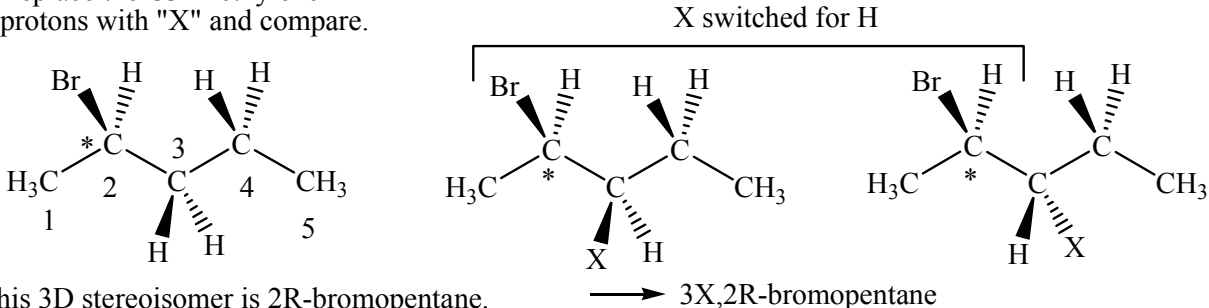
In a similar way the two methyl groups in isopropylcyclohexane are also enantiotopic (both the methyl protons and the methyl carbons).



4. **diastereotopic groups** – Do the switches produce different molecules, as diastereomers? If so, the protons are diastereotopic protons, and will be different and quite likely have different chemical shifts. This would cause them to split one another and to possibly split neighboring protons differently, leading to a more complicated spectrum than expected. Of course, there is always the possibility that there exist coincidental (or accidental) equivalence, and then they would not split one another.

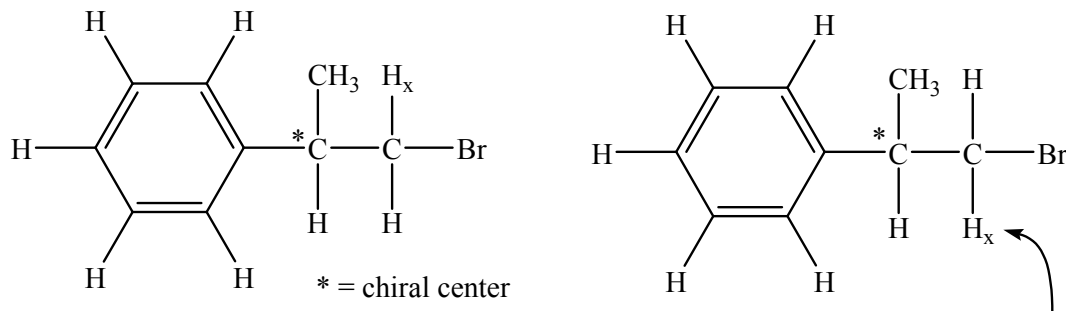
2-bromopentane * = chiral center

Replace the C3 methylene protons with "X" and compare.

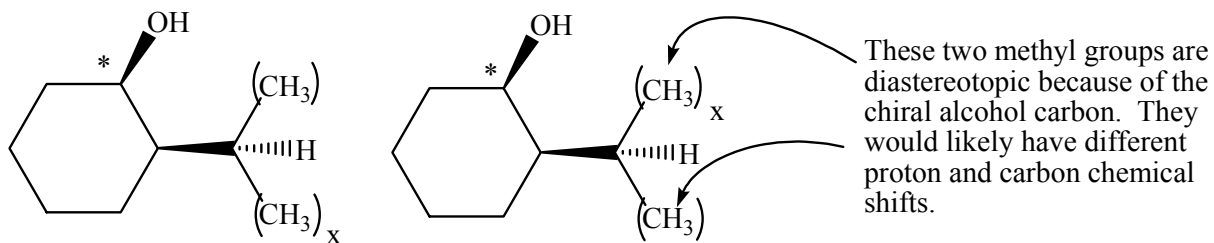


This 3D stereoisomer is 2R-bromopentane.

Because of the chiral center at C2, switching H for X at C3 forms diastereomers and, in this example the C3 methylene hydrogen atoms are diastereotopic. They could split one another if they have different chemical shifts and they could split their neighboring hydrogen atoms differently. This would make the spectrum more complicated. A similar result would be obtained with 2S-bromopentane. A similar result occurs with the C4 protons. This means there are seven different kinds of hydrogen in 2-bromopentane! Each of the methyl groups has a different type of proton, the methine hydrogen is different and all four methylene hydrogens are different.



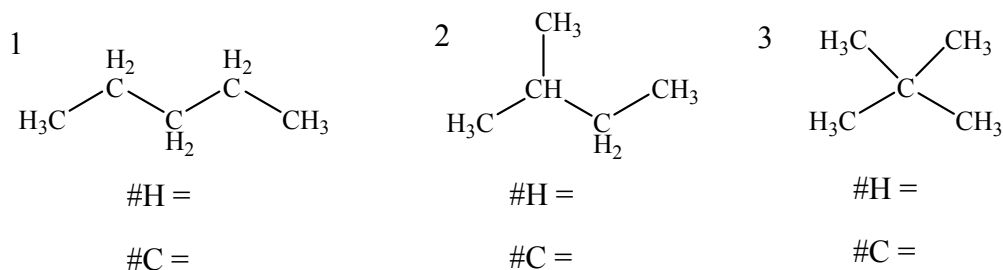
The CH₂ protons are diastereotopic because of the chiral benzylic center. Switching each of these protons with X produces a pair of diastereomers. These protons would likely have different chemical shifts and split one another and split the neighboring benzylic proton differently. (You can substitute "split" for "interact with" until we explain what "coupling" means.)



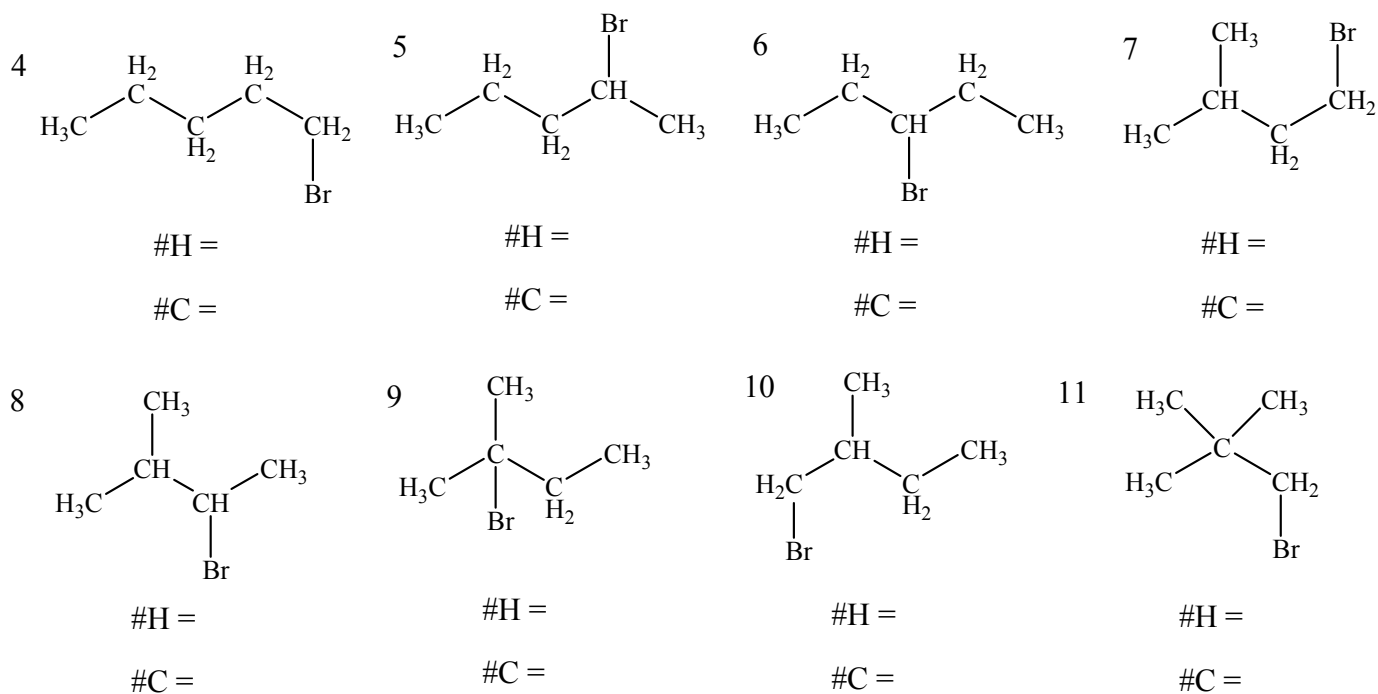
These two methyl groups are diastereotopic because of the chiral alcohol carbon. They would likely have different proton and carbon chemical shifts.

11 simple (?) examples: How many different protons and carbons are in each of the C_5H_{12} isomers and $C_5H_{11}Br$ isomers?

There are three C_5H_{12} isomers



There are eight $C_5H_{11}Br$ isomers



Calculating Proton Chemical Shifts (alkane, alkene and aromatic protons)

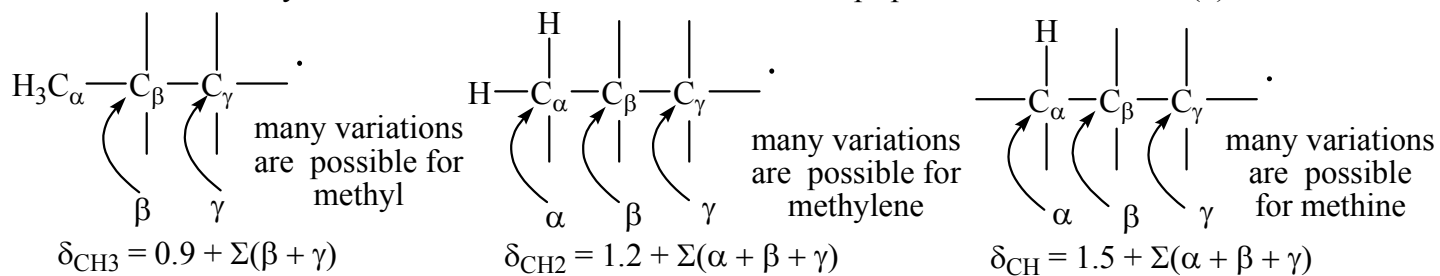
Just below are tables of parameters to modify given starting values for sp^3 C-H (start at 0.9 ppm for CH_3 , 1.2 ppm for CH_2 and 1.5 ppm for CH), alkene sp^2 C-H (start at 5.2 ppm) and aromatic sp^2 C-H (start at 7.3 ppm). Most common organic functionality can be found in the tables. The effect of each substituent falls off with distance away from the proton whose chemical shift is being calculated. The α column is used when the proton shift we are calculating and the substituent are on the same carbon. The β column is used if the proton and substituent are on adjacent carbon atoms (vicinal), and the γ column is used when the proton and substituent have a 1,3 substitution pattern. The estimated chemical shifts are very close to experimental values for a single substituent, but become progressively poorer as more substituents are included. Usually the chemical shift is overestimated a little with multiple substituents.

Any substituent directly attached to a methyl has a unique value. There are no additional bonds to consider further. Almost any common methyl pattern and chemical shift adjustment can be found directly in the list below using the α parameters and adding 0.9 ppm as in the equation below.

$$\delta_{CH_3} = 0.9 + \alpha \quad CH_3-X \quad (\text{There is only one possibility for each X.})$$

If a methyl is part of a longer chain with an additional substituent (or several substituents) at a β or γ position (or both positions), use the 0.9 ppm chemical shift for a simple methyl as a starting point and add the appropriate parameters for any number of substituents within three carbons as shown. In a similar manner we can calculate chemical shifts for methylene hydrogen atoms (CH_2) and a methine hydrogen atom (CH) using the following formulas.

Σ is the summation symbol for all substituents used to estimate sp^3 proton chemical shifts (δ).



Chemical Shifts Correction Factors for Protons on sp³ carbon atoms

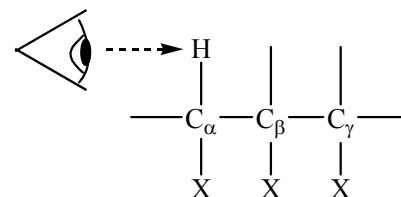
Estimation of sp³ C-H chemical shifts for one to multiple substituent parameters for protons within 3 Cs of consideration.

Relative position of calculated proton and substituent(s)

α = hydrogen and substituent are attached to the same carbon

β = hydrogen and substituent are on adjacent (vicinal) carbons

γ = hydrogen and substituent have a 1,3 substitution pattern

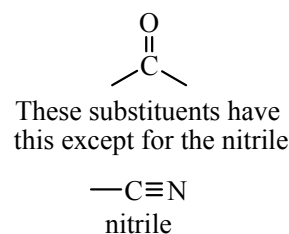
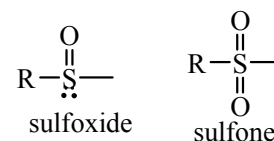
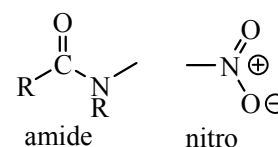
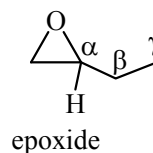


Substituent's positions relative to calculated proton chemical shift. X = substituent from table.

X = substituent	α	β	γ
substituent atom is a carbon			
R- (alkyl substituent)	0.0	0.0	0.0
R ₂ C=CR- (alkene)	0.8	0.2	0.1
RCC- (alkyne)	0.9	0.3	0.1
Ar- (aromatic)	1.4	0.4	0.1
substituent atom is a halogen			
F-	3.2	0.5	0.2
Cl-	2.2	0.5	0.2
Br-	2.1	0.7	0.2
I-	2.0	0.9	0.1
substituent atom is an oxygen			
HO- (alcohol)	2.3	0.3	0.1
RO- (simple ether)	2.1	0.3	0.1
R ₂ C=CRO- (enol ether)	2.5	0.4	0.2
ArO- (aromatic ether)	2.8	0.5	0.3
epoxide	1.5	0.4	0.1
RCO ₂ - (simple ester, oxygen side)	2.8	0.5	0.1
ArCO ₂ - (aromatic ester, oxygen side)	3.1	0.5	0.2
ArSO ₃ - (sulfonate, oxygen side)	2.8	0.4	0.0
substituent atom is a nitrogen			
R ₂ N- (amine, R = H or C)	1.5	0.2	0.1
ArRN- (aromatic amine, R = H or C)	1.9	0.1	0.1
R'CONR- (amide, nitrogen side)	2.1	0.3	0.1
ArCONR- (aromatic amide, nitrogen side)	2.1	0.3	0.1
O ₂ N- (nitro)	3.2	0.8	0.1
substituent atom is a sulfur			
HS- (thiol)	1.3	0.4	0.1
RS- (sulfide)	1.3	0.4	0.1
ArS- (aromatic sulfide)	1.4	0.4	0.1
RSO- (sulfoxide)	1.6	0.5	0.2
ArSO- (aromatic sulfoxide)*	1.7	0.5	0.1
RSO ₂ - (sulfone)	1.9	0.3	0.2
ArSO ₂ - (aromatic sulfone)*	2.2	0.6	0.1
substituent atom is a carbonyl group or nitrile			
OHC- (aldehyde)	1.1	0.4	0.1
RCO- (ketone)	1.2	0.3	0.0
ArCO- (aromatic ketone)	1.7	0.3	0.1
HO ₂ C- (carboxylic acid)	1.1	0.3	0.1
RO ₂ C- (ester, carbon side)	1.1	0.3	0.1
R ₂ NOC- (amide carbon side)	1.0	0.3	0.1
ClOC- (acid chloride)	1.8	0.4	0.1
NC- (nitrile)	1.1	0.4	0.2

* value from ChemDraw

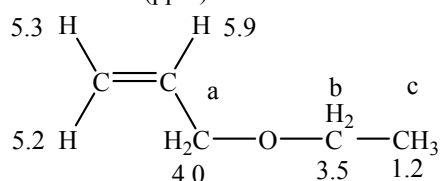
In general, multiple substituents do not add their entire values. Each additional substituent adds a smaller portion of its listed increment. Even so, the calculated values are typically close to the experimental values.



The calculated chemical shifts are often quite close to the experimental values, but can vary as much as 0.5 ppm with multiple substituents. A few examples are provided to show how to do the calculations. We are only calculating sp^3 C-H at this point. When calculating δ for diastereotopic CH_2 protons next to a chiral center, use the regular calculated value for the first proton, H_a , and use $(\delta_a - 0.3 \text{ ppm})$ for the second proton, H_b . Alkene and aromatic sp^2 C-H will be considered after this problem.

Problem 3 – Use the above table to estimate the chemical shifts of each type of sp^3 C-H in the structures below.

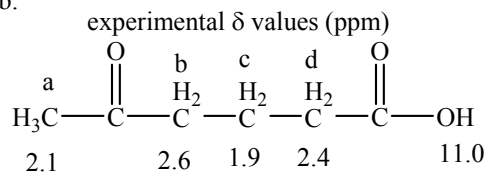
a. experimental δ values (ppm)



Only sp^3 C-H calculations shown here.

	a	b	c
calculated sp^3	1.2	1.2	0.9
C-H δ values (ppm) =	0.8 (α)	0.1 (γ)	0.0 (-) alkene
	2.1 (α)	2.1 (α)	0.3 (β) ether "O"
	4.1	3.4	1.2

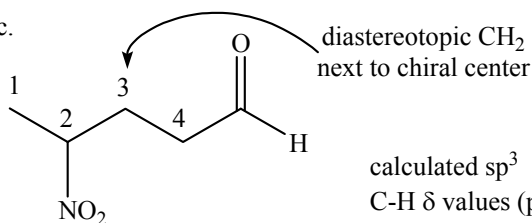
b.



Only sp^3 C-H calculations shown here.

	a	b	c	d
calculated sp^3	0.9	1.2	1.2	1.2
C-H δ values (ppm) =	1.2 (α)	1.2 (α)	0.3 (β)	0.0 (γ) ketone
	0.0 (-)	0.1 (γ)	0.3 (β)	1.1 (α) acid
	2.1	2.5	1.8	2.3

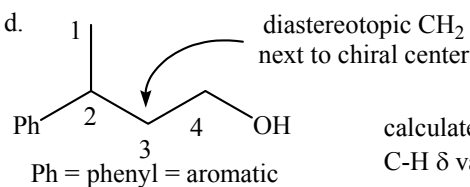
c.



Only sp^3 C-H calculations shown here.

	1	2	3a	3b	4
calculated sp^3	0.9	1.2	1.2	1.2	1.2
C-H δ values (ppm) =	0.8 (β)	3.2 (α)	0.8 (β)	0.8 (β)	0.1 (γ) nitro
	0.0 (-)	0.1 (γ)	0.4 (β)	0.4 (β)	1.1 (α) aldehyde
	1.7	4.5	2.4	2.4	2.4
				-0.3	
				2.1	

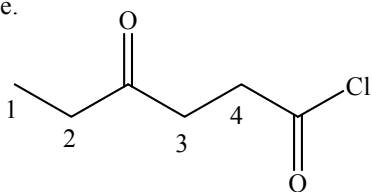
d.



Only sp^3 C-H calculations shown here.

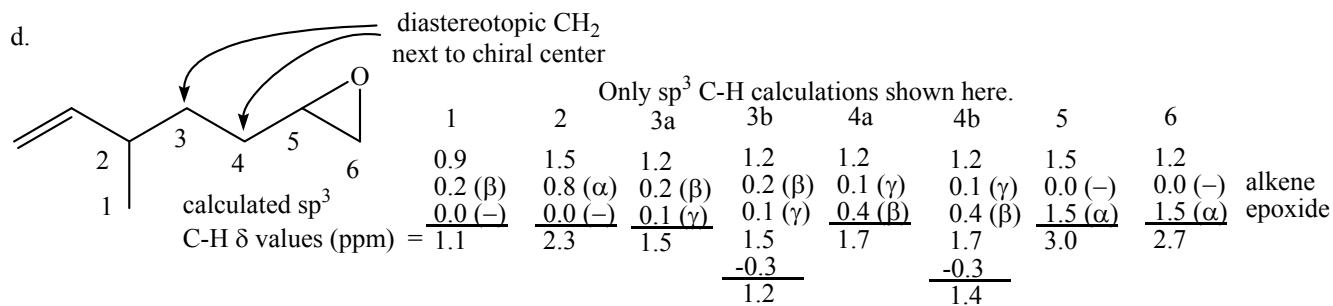
	1	2	3a	3b	4
calculated sp^3	0.9	1.2	1.2	1.2	1.2
C-H δ values (ppm) =	0.4 (β)	1.4 (α)	0.4 (β)	0.4 (β)	0.1 (γ) aromatic
	0.0 (-)	0.1 (γ)	0.3 (β)	0.3 (β)	2.3 (α) alcohol
	1.3	2.7	1.9	1.9	3.6
				-0.3	
				1.6	

e.

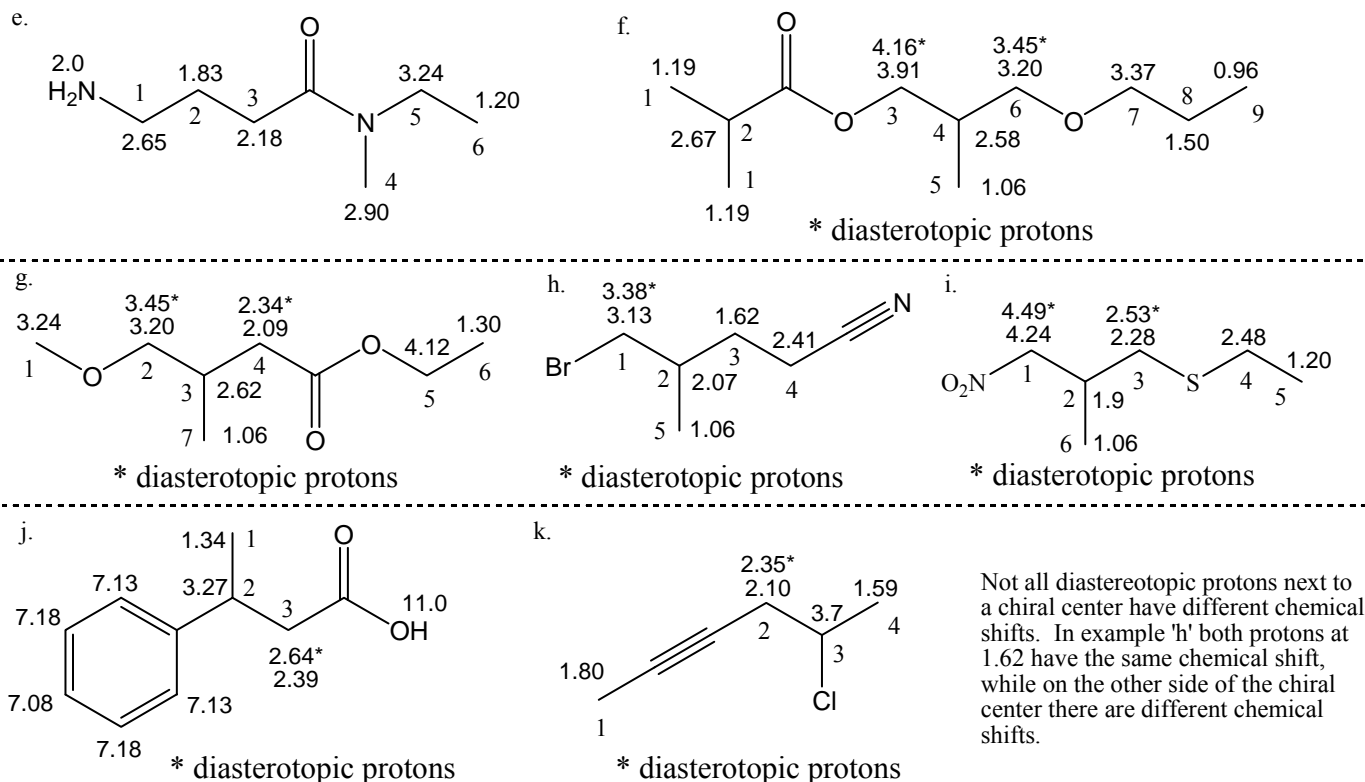


Only sp^3 C-H calculations shown here.

	1	2	3	4
calculated sp^3	0.9	1.2	1.2	1.2
C-H δ values (ppm) =	0.4 (β)	1.2 (α)	1.2 (α)	0.4 (β) ketone
	0.0 (-)	0.0 (-)	0.4 (β)	1.8 (α) acid chloride
	1.3	2.4	2.8	3.4



Additional Problems - chemical shifts are calculated values from ChemDraw

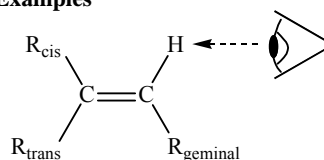


Similar tables are presented for calculating alkene and aromatic sp² C-H chemical shifts (just below). Alkene chemical shift calculations will start at 5.2 ppm and make adjustments if substituents are geminal, cis or trans. Aromatic chemical shift calculations will start at 7.3 ppm and make adjustments if substituents are ortho, meta or para. A few example calculations are presented with the tables. Any other C-H chemical shift values will be estimated from our generic table of chemical shift values (presented after shift calculations on page 50, protons and carbons).

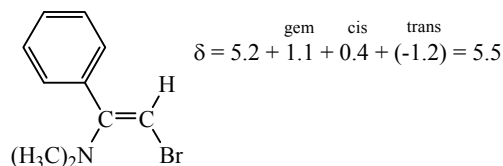
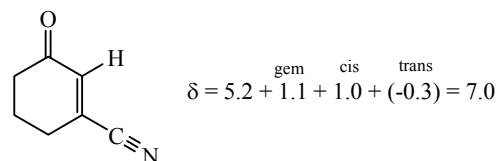
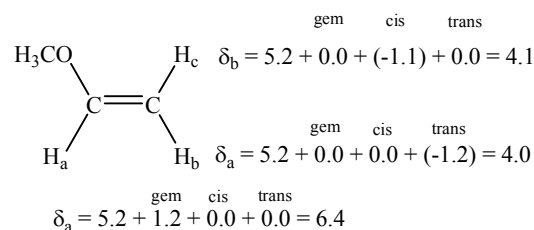
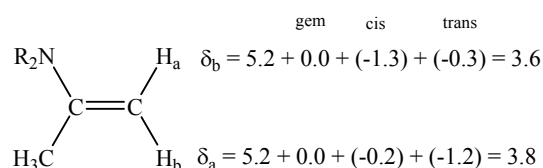
Estimated Chemical Shifts for Protons on Alkene sp^2 Carbon Atoms

X = substituent	geminal	cis	trans
H-	0.0	0.0	0.0
hydrogen			
R-alkyl	0.5	-0.2	-0.3
C ₆ H ₅ CH ₂ -benzyl	1.0	-0.3	-0.3
X-CH ₂ -halomethyl (X = F, Cl, Br, I)	0.7	0.1	0.0
(H)/ROCH ₂ -hydroxy/alkoxy methyl	0.6	0.0	0.0
(H ₂)/R ₂ NCH ₂ -aminomethyl	0.6	-0.1	-0.1
RCOCH ₂ -carbonyl methyl	0.7	-0.1	-0.1
NCCCH ₂ -cyanomethyl	0.7	-0.1	-0.1
R ₂ C=CR-alkenyl	1.0	-0.1	-0.2
RCC-alkynyl	0.5	0.4	0.1
C ₆ H ₅ -phenyl	1.4	0.4	-0.1
F-fluoro	1.5	-0.4	-1.0
Cl-chloro	1.1	0.2	0.1
Br-bromo	1.1	0.4	0.6
I-iodo	1.1	0.8	0.9
RO-alkoxy	1.2	-1.1	-1.2
RCO ₂ -ester, oxygen side	2.1	-0.4	-0.6
R ₂ N-amino	0.8	-1.3	-1.2
RCONH-amide, nitrogen side	2.1	-0.6	-0.7
O ₂ N-nitro	1.9	1.3	0.6
RS-sulfide	1.1	-0.3	-0.1
RSO-sulfoxide	1.3	0.7	0.4
RSO ₂ -sulfone	1.6	1.2	0.9
OHC-aldehyde	1.0	1.0	1.2
ROC-ketone	1.1	1.1	0.9
HO ₂ C-carboxylic acid	1.0	1.4	0.7
RO ₂ C-ester, carbon side	0.8	1.2	0.6
H ₂ NOC-amide, carbon side	1.4	1.0	0.5
ClOC-acid chloride	0.3	0.8	0.6
NC-nitrile	0.5	1.0	0.9

Examples



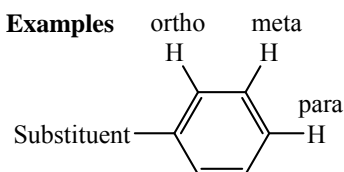
$$\delta(\text{ppm}) = 5.2 + \text{gem} + \text{cis} + \text{trans}$$



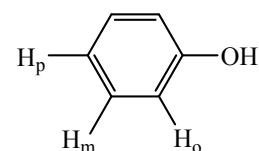
Estimated chemical shifts for protons at aromatic sp^2 carbon atoms

X = substituent	ortho	meta	para
H- hydrogen	0.0	0.0	0.0
R- alkyl	-0.1	-0.1	-0.2
XCH ₂ - halomethyl (X = F,Cl,Br,I)	0.3	0.1	-0.1
(H)/ROCH ₂ - hydroxy/alkoxy methyl	-0.1	-0.1	-0.1
R ₂ C=CR- alkenyl	0.0	0.0	-0.2
RCC- alkynyl	0.5	0.4	-0.1
C ₆ H ₅ - phenyl	0.2	0.0	0.0
F- fluoro	-0.3	0.0	-0.2
Cl- chloro	0.0	-0.1	-0.1
Br- bromo	0.2	-0.1	-0.1
I- iodo	0.4	-0.2	0.0
RO- alkoxy	-0.5	-0.1	-0.4
HO- hydroxy	-0.5	-0.2	-0.4
RCO ₂ - ester, oxygen side	-0.2	0.0	-0.2
(H ₂ N)R ₂ N- amino	-0.8	-0.2	-0.7
RCONH- amide, nitrogen side	0.4	0.0	-0.3
ON- nitroso	0.6	0.3	0.4
O ₂ N- nitro	0.9	0.3	0.4
RS-/HS- sulfide / thiol	-0.1	-0.2	-0.2
XO ₂ S- sulfonyl X (R,HO,RO,H ₂ N)	0.7	0.3	0.4
OHC- aldehyde	0.6	0.2	0.4
ROC- ketone	0.6	0.1	0.2
HO ₂ C- carboxylic acid	0.9	0.2	0.3
RO ₂ C- ester, carbon side	0.7	0.1	0.2
H ₂ NOC- amide, carbon side	0.7	0.2	0.2
CIOC- acid chloride	0.8	0.2	0.4
NC- nitrile	0.3	0.2	0.3

Examples



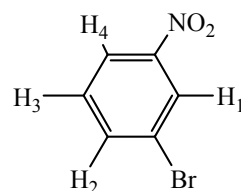
$$\delta(\text{ppm}) = 7.3 + \text{ortho} + \text{meta} + \text{para}$$



$$\delta_o = 7.3 + (-0.5) = 6.8$$

$$\delta_m = 7.3 + (-0.2) = 7.1$$

$$\delta_p = 7.3 + (-0.4) = 6.9$$

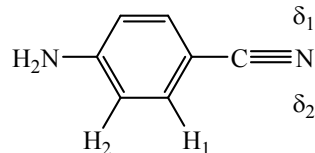


$$\delta_1 = 7.3 + 0.2 + 1.0 = 8.5$$

$$\delta_2 = 7.3 + 0.2 + 0.4 = 7.9$$

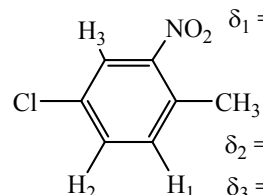
$$\delta_3 = 7.3 + (-0.1) + 0.3 = 7.5$$

$$\delta_4 = 7.3 + 1.0 + 0.0 = 8.3$$



$$\delta_1 = 7.3 + (-0.8) + 0.2 = 6.7$$

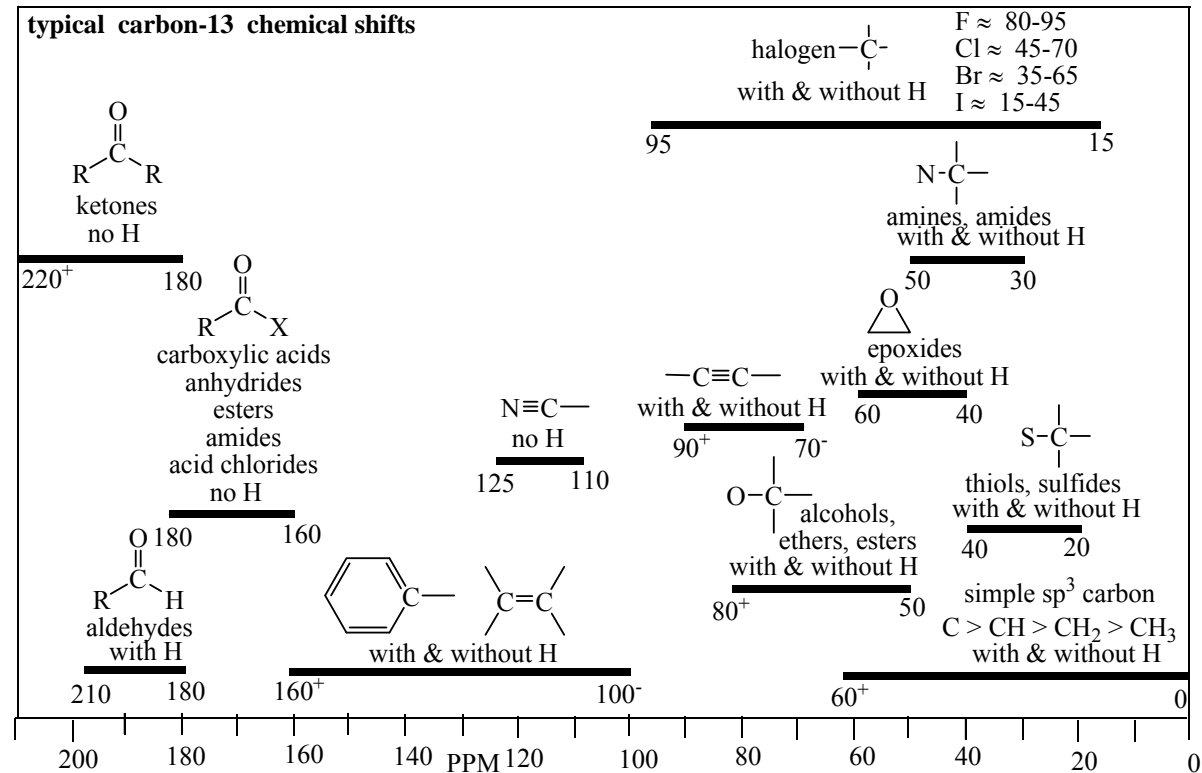
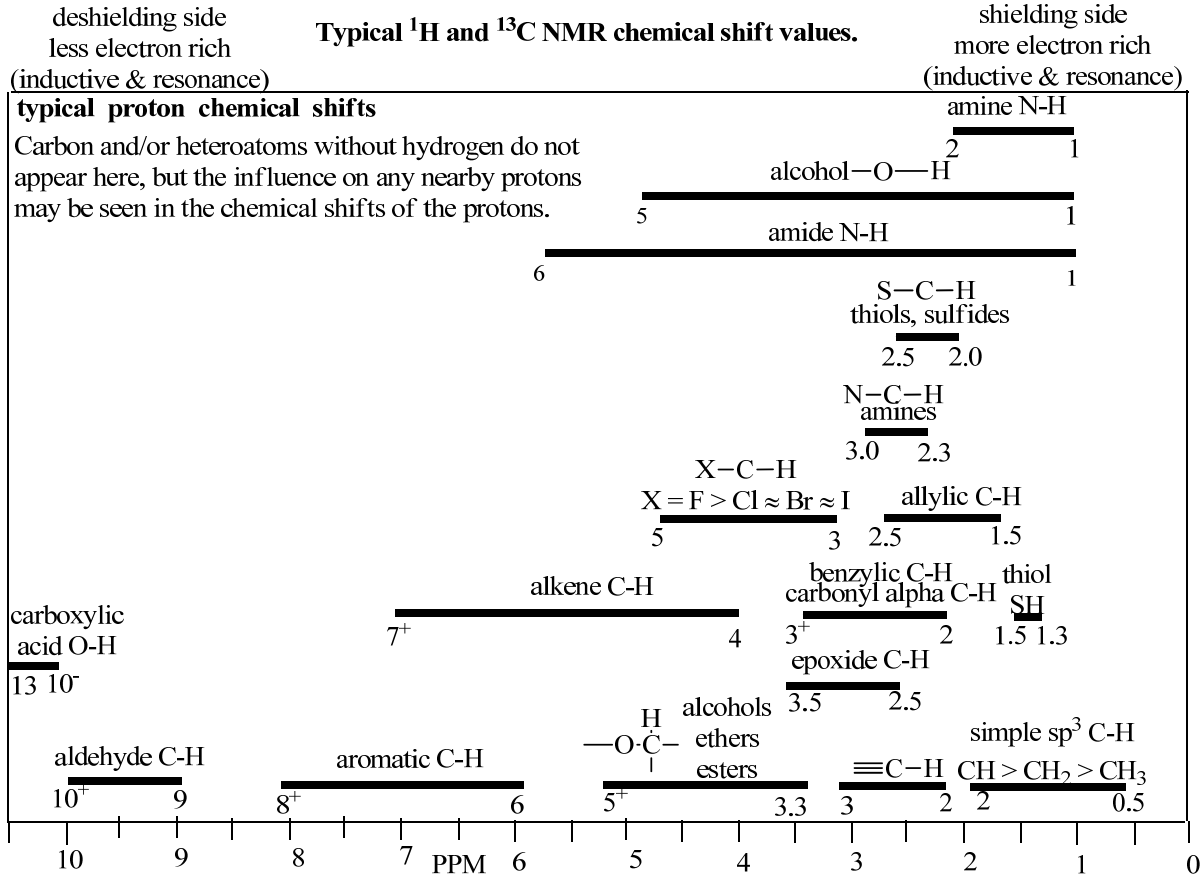
$$\delta_2 = 7.3 + (-0.2) + 0.4 = 7.5$$



$$\delta_1 = 7.3 + (-0.1) + 0.0 + 0.3 = 7.5$$

$$\delta_2 = 7.3 + 0.0 + (-0.1) + 0.4 = 7.6$$

$$\delta_3 = 7.3 + 0.0 + 1.0 + (-0.1) = 8.2$$



Proton Coupling / Splitting Patterns / Multiplicities - Perturbations by nearby neighbor protons

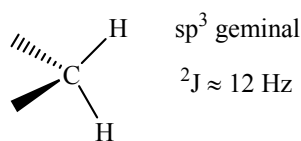
Very often there is more than one peak associated with a certain type of proton (called splitting). This makes the NMR spectrum more complicated, but it also makes it much more useful. The splitting pattern of a 'type' of proton can tell us which other protons are neighbors and how many neighbors there are. Recognizing these features provides a way of linking together separate parts of our structure into a more complete structure. There is an even better way called COSY (2D correlation spectroscopy), but we will discuss that later.

An important distinction must be understood between an observed proton and its neighbor protons. When discussing the observed proton we are looking at the tiny excess that has spin aligned with the field (1 out of 20,000). However, each neighbor proton is like a tiny magnet that alters the very large external magnetic field, B_0 , experienced by the observed proton. Remember that the population of higher energy protons (oriented against B_0 or subtracting from B_0) and lower energy protons (oriented with B_0 or adding to B_0) is about 50/50.

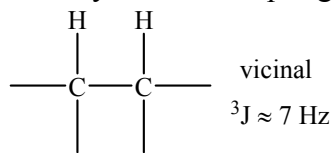
You could flip of a 'fair' coin to decide if the neighbor proton magnet was up or down, and that's the way we will look at it. These little neighbor proton magnets will create perturbations that divide the 'observed' proton into various populations based on probabilities of a coin flip when the protons are close enough to influence one another (usually 2-3 bonds apart) and that will produce multiple peaks, where one was expected. One proton neighbor equals two equal possibilities (with or against the external fields = heads or tails in coin flips). More extensive examples are provided, just below.

When the two protons are on the same carbon atom they are called geminal (twins). If there is a nearby chiral center, they will be diastereotopic. If they are cis/trans in a ring or part of a pi bond, they can also have different chemical shifts. When the geminal chemical shifts are different they will each split the other into two peaks. The separation between the peaks is their J value (discussed just below), and written as 2J because they are two bonds apart. Typical alkane $sp^3 J_{\text{geminal}}$ has a range of values from about 0-20 Hz, but we will use 12 Hz in our problems when diastereotopic splitting is present. Typical alkene $sp^2 J_{\text{geminal}}$ values will be 2 Hz in our problems. The numerical value of J (in Hz) is called a coupling constant.

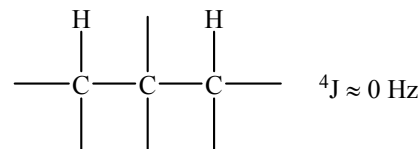
The most common pattern of coupling is vicinal interaction (neighbors) between nonequivalent protons on adjacent carbon atoms. Vicinal protons are always three bonds apart, and vicinal coupling is usually shown as 3J or J_{vicinal} . Vicinal coupling constants are typically about 7 Hz. This is the value we will use in our problems later. Real J_{vicinal} coupling can appear over a range from about 0-12 Hz. When protons are over three bonds apart, the coupling is commonly too small to see and we will consider such patterns to have zero coupling, e.g. $^nJ = 0$ Hz ($n \geq 4$). However, there are some special exceptions that we will show in a summary table of coupling constants, but rarely use in our problems.



Geminal protons, (twins), are on the same carbon, and 2J values can range from 0 Hz when equivalent to quite large, near 20 Hz when diastereotopic. When present, we will use $^2J = J_{\text{gem}} = 12$ Hz as our typical value.



Vicinal protons (neighbors, Latin) are on adjacent carbons and 3J values for freely rotating neighbors are typically around 7 Hz. In more rigid systems 3J values can range from 0 Hz to over 12 Hz. We will use $^3J = J_{\text{vicinal}} = 7$ as our typical value.

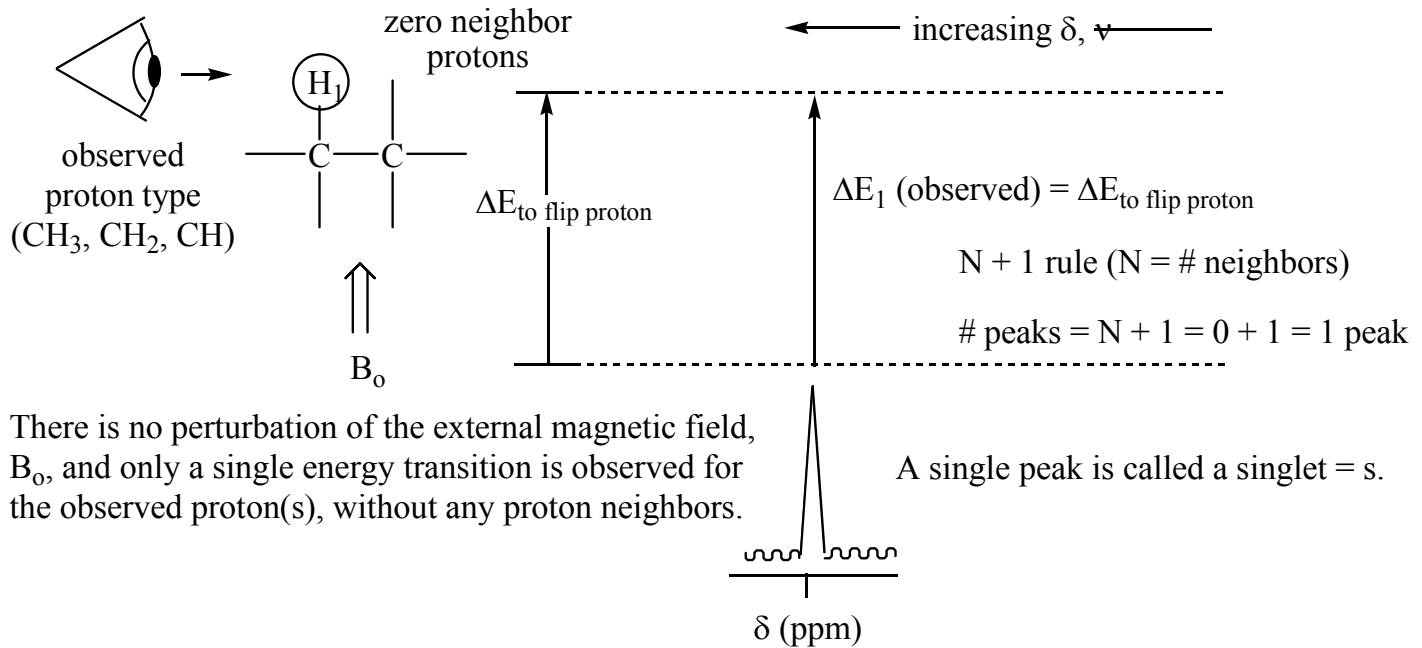


We can usually ignore 4 bond coupling (and higher) because any coupling is so small we can't see it. However, when special conformations are rigidly held (e.g. W coupling) there may be small J values of 1-2 Hz (very rarely can be as high as 7 Hz).

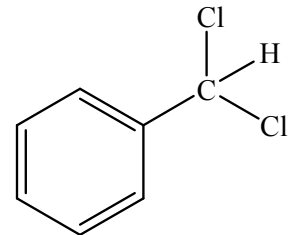
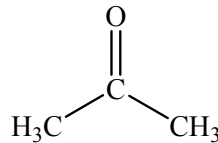
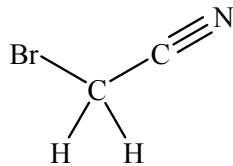
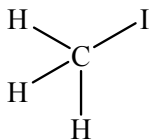
Coupling and multiplicity may be the most difficult aspect of NMR for beginning students. A few examples should help clarify the common patterns. If you don't get it the first time then read it again (...and again). A simplistic N+1 rule is often invoked to interpret NMR spectra, but a deeper understanding is necessary to appreciate the many exceptions to the N+1 rule. Simply stated, the N+1 rule says there will be 1 more peak than there are coupled neighbors (# of peaks = N+1, where N = # of neighbor protons).

Zero neighbors

- Proton(s) with zero nearest neighbor protons do not have any perturbation of B_0 . They appear all together as a single peak. A special-case rule, where all the coupling constants are equal (usually $^3J = 7\text{Hz}$) is called the N+1 rule, where N is the number of neighbor protons. With zero neighbors the N+1 rule correctly predicts there will be one peak.

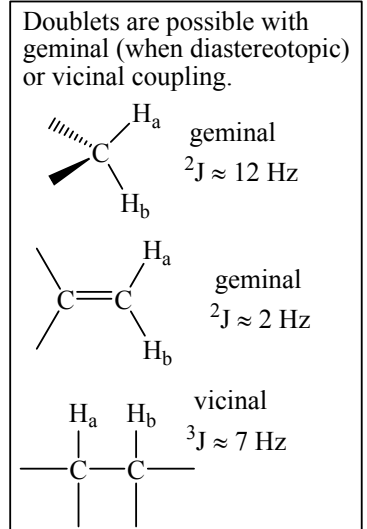
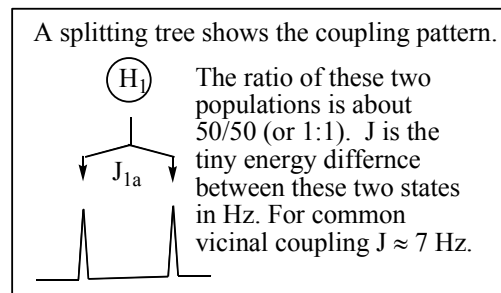
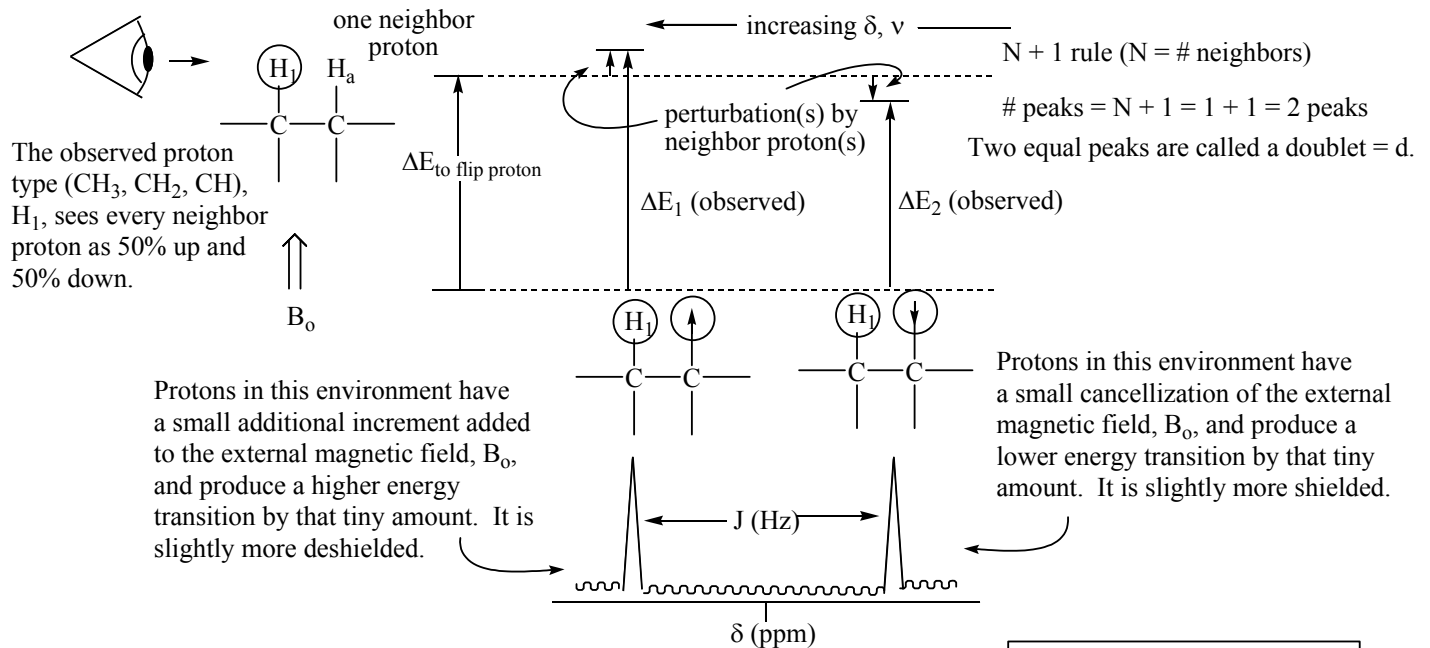


Some proton examples with zero proton neighbors:



One Neighbor – There are several examples of coupling on page 60.

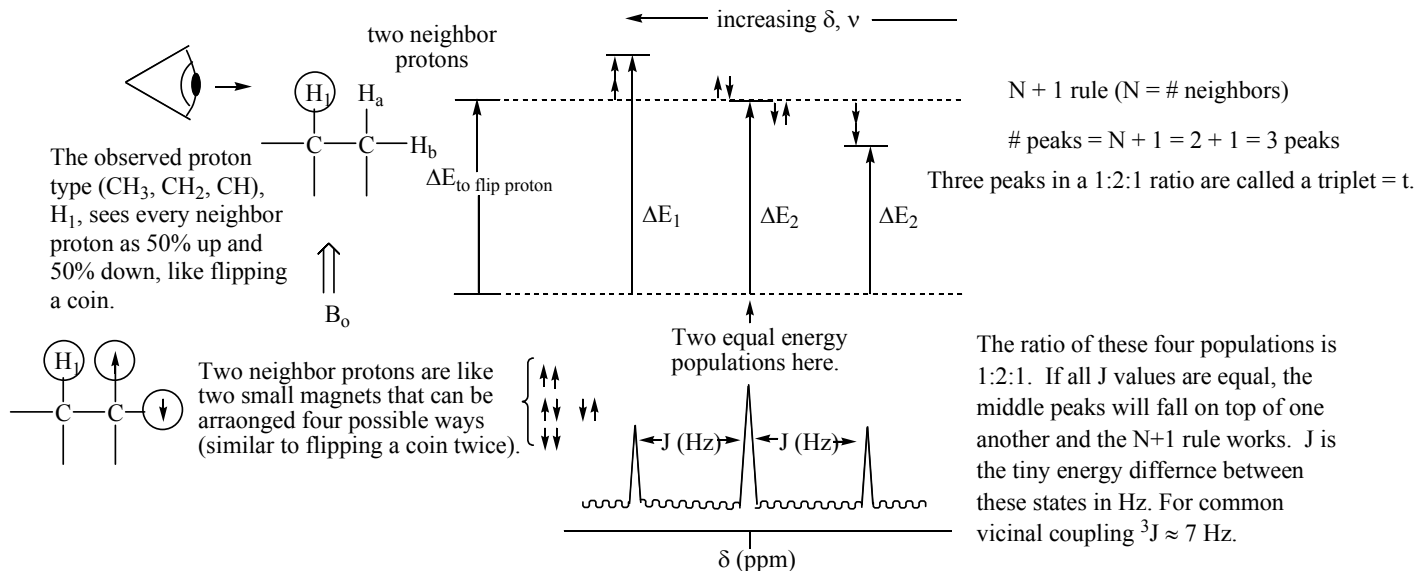
2. Proton(s) with one nearest neighbor proton are split into two populations (like flipping a coin, heads or tails). This can be vicinal ($^3J=7$ Hz) or geminal, when different ($^2J=12$ Hz). With one neighbor the N+1 rule correctly predicts there will be two equal area peaks separated by distance in Hz, called a J value or coupling constant.



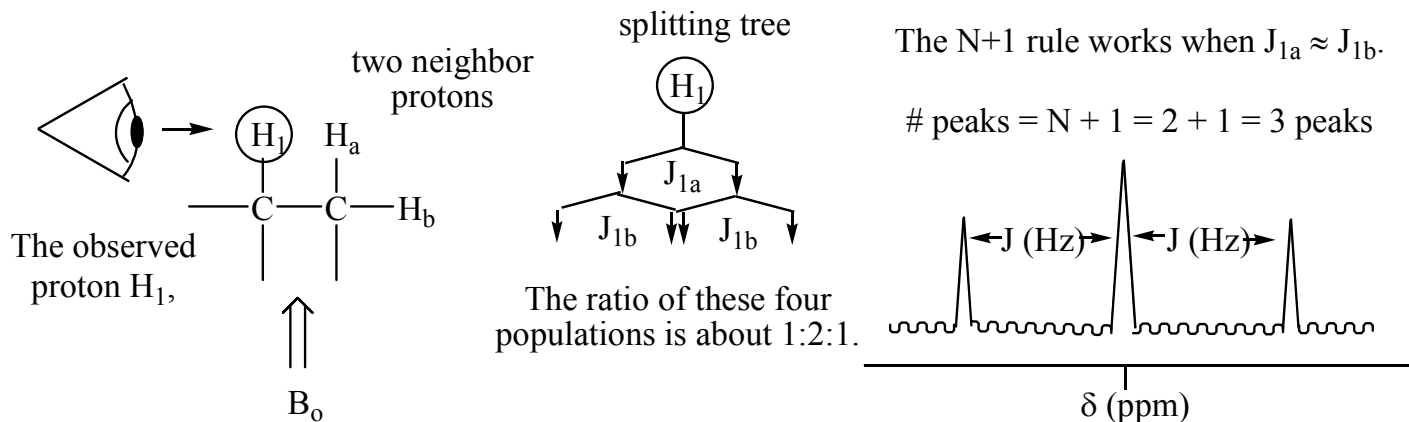
J values do not change when moving from instrument to instrument. The $\Delta\delta$ values in a multiplet only depend on the neighbor atom, as a very small magnet. Because J values are the same (and very small) they are always reported in units of Hz.

Two Neighbors

3. Protons with two nearest neighbor protons split into four populations (like two coin flips). Both neighbor protons can be on the same carbon or one each on separate neighbor carbons. With two neighbors the N+1 rule correctly predicts there will be three peaks in a 1:2:1 ratio, since the middle two populations are equal in energy.

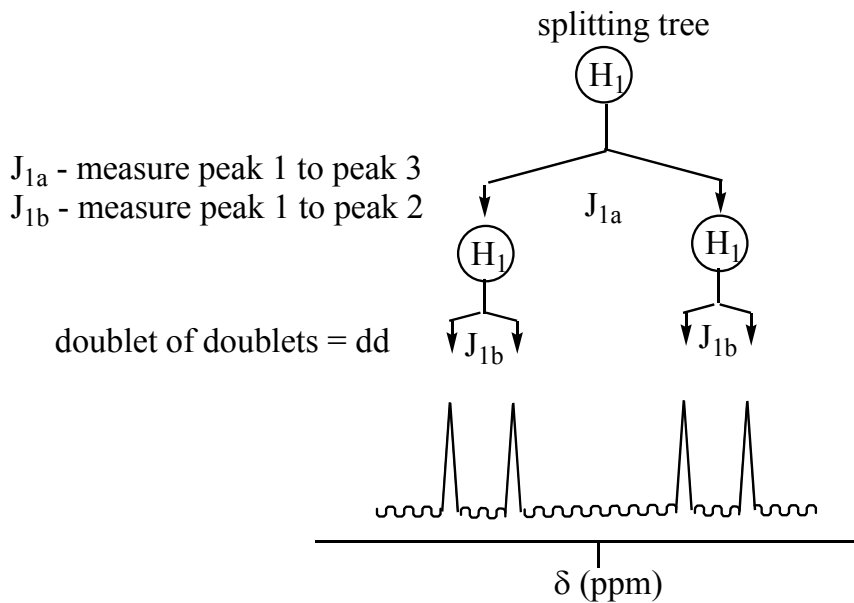


When two nearest neighbor protons are next to (vicinal) to $\text{H}_{\text{observed}} = \text{H}_1$ (above) it really produces a doublet of doublets = dd. Proton H_1 is split into two populations because of neighbor H_a and each of those populations is further split into two populations because of H_b ($2 \times 2 = 4$ populations). The four peaks look like three because the coupling constants are same and the middle two peaks fall on top of one another. If it were not for the coincidence of identical coupling constants, we would be able to see all four peaks (populations).



Neighbors with different coupling constants:

When the coupling constants are different ($J_{1a} \neq J_{1b}$), all four peaks will be observed as two sets of doublets called a doublet of doublets (dd). Each peak will be approximately the same size. The coupling constant of the larger difference (J_{1a} below) can be measured from the first to the third peaks (or second to the fourth peaks) and the coupling constant of the smaller difference (J_{1b} below) can be measured from the first to the second peaks (or the third to the fourth peaks). The splitting pattern (splitting tree) is drawn using the largest coupling constant first and then the smaller coupling constant(s) so there is no crossing of lines.

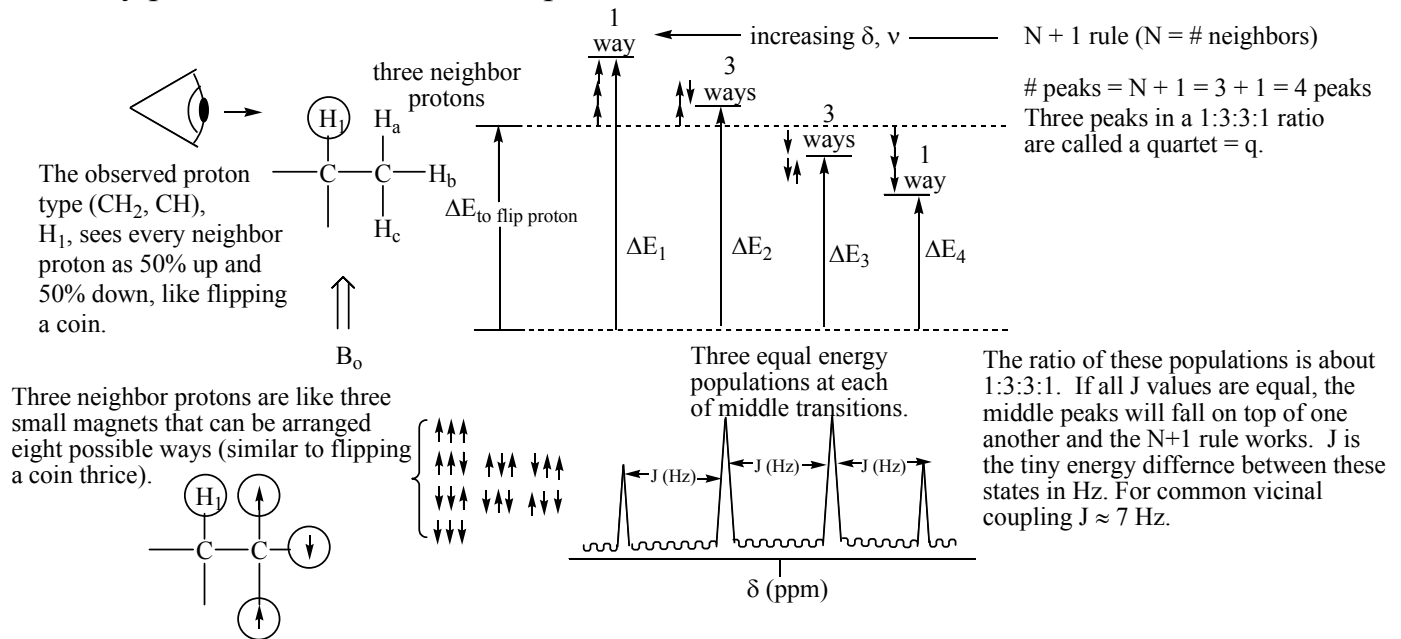


When the J values are not equal all four peaks are observed. The ratio of these four populations is 1:1:1:1. Draw splitting trees with the largest coupling at the top and the smallest coupling at the bottom.

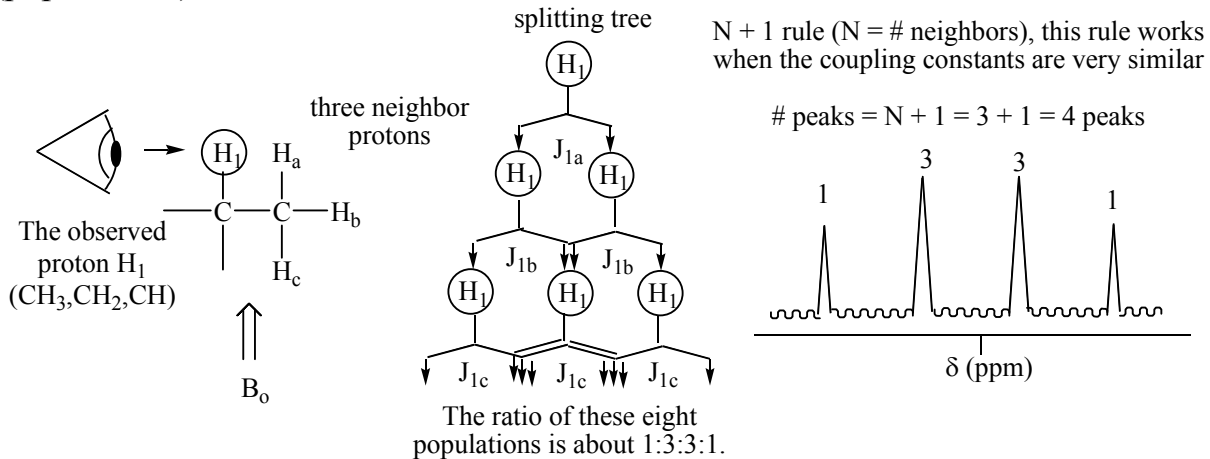
$$J_{1a} > J_{1b}$$

Three Neighbors

4. Protons with three nearest neighbor protons split into eight populations (like three coin flips). Neighbor protons can be on the same carbon or two on one and one on another or one each on three separate carbons. With three neighbors the N+1 rule correctly predicts there will be four peaks in a 1:3:3:1 ratio.

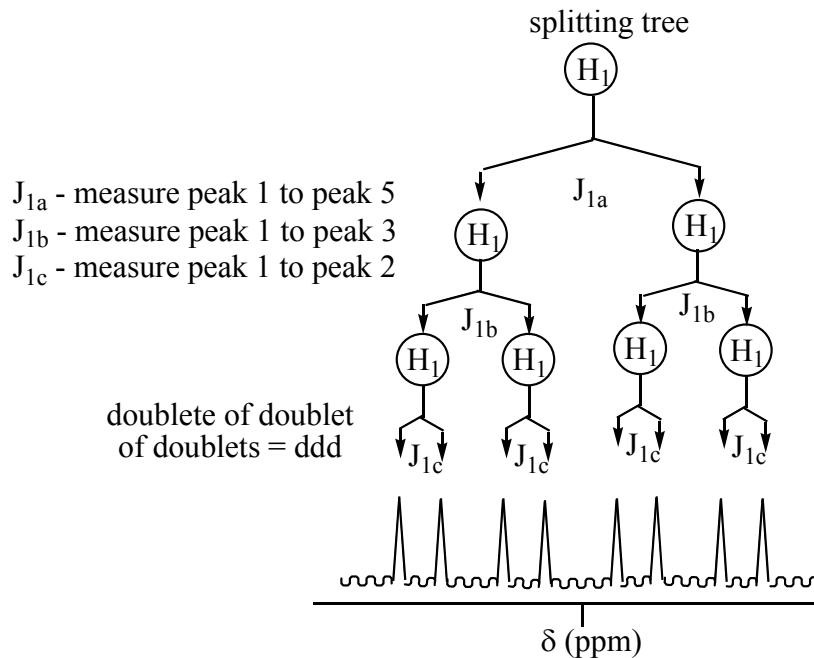


Three nearest neighbor protons to $\text{H}_{\text{observed}}$ (H_1) really produce a doublet of doublet of doublets = ddd. Proton H_1 is split into two populations because of neighbor H_a and each of those populations is further split into two populations because of H_b and each of those populations is further split into two populations because of H_c ($2 \times 2 \times 2 = 8$ populations). The eight peaks look like four because the coupling constants are the same and the middle peaks continue to fall on top of one another. If it were not for the coincidence of identical coupling constants, we would be able to see all eight peaks (populations).



Neighbors with different coupling constants:

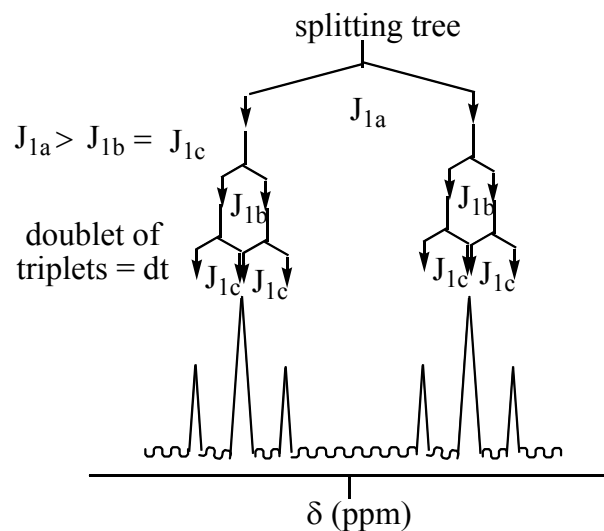
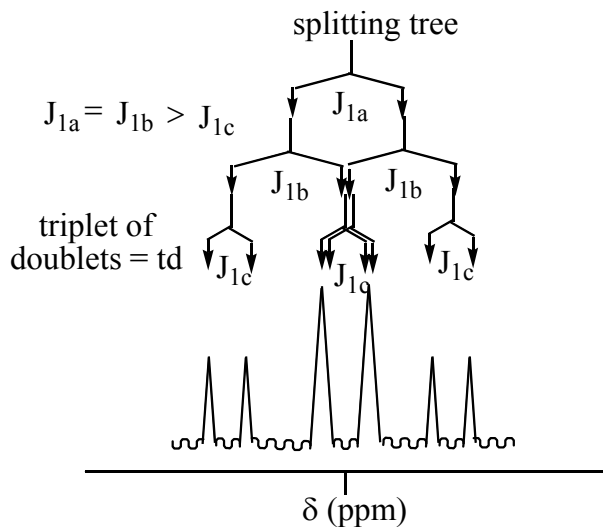
The splitting tree below shows what can happen when all of the coupling constants are different, called a doublet of doublets of doublets (ddd). Each peak will be approximately the same size. The splitting tree is drawn using the largest coupling constant first and then the smaller coupling constant(s).



When the J values are not equal all eight peaks are observed. The ratio of these eight populations is 1:1:1:1:1:1:1:1. Draw splitting trees with the largest coupling at the top and the smallest coupling at the bottom.

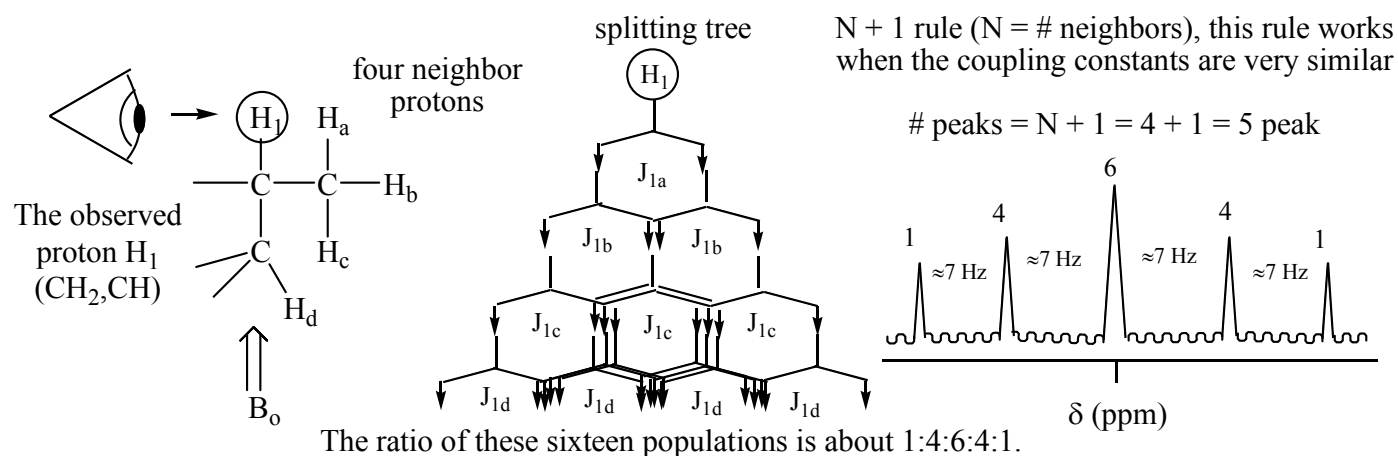
$$J_{1a} > J_{1b} > J_{1c}$$

If two of the three coupling constants happen to be equal, then different splitting patterns will be observed. In the first splitting tree below $J_{1a} = J_{1b} > J_{1c}$ producing a triplet of doublets and in the second splitting tree $J_{1a} > J_{1b} = J_{1c}$ producing a doublet of triplets. In all cases there are eight populations resulting from three neighbors.



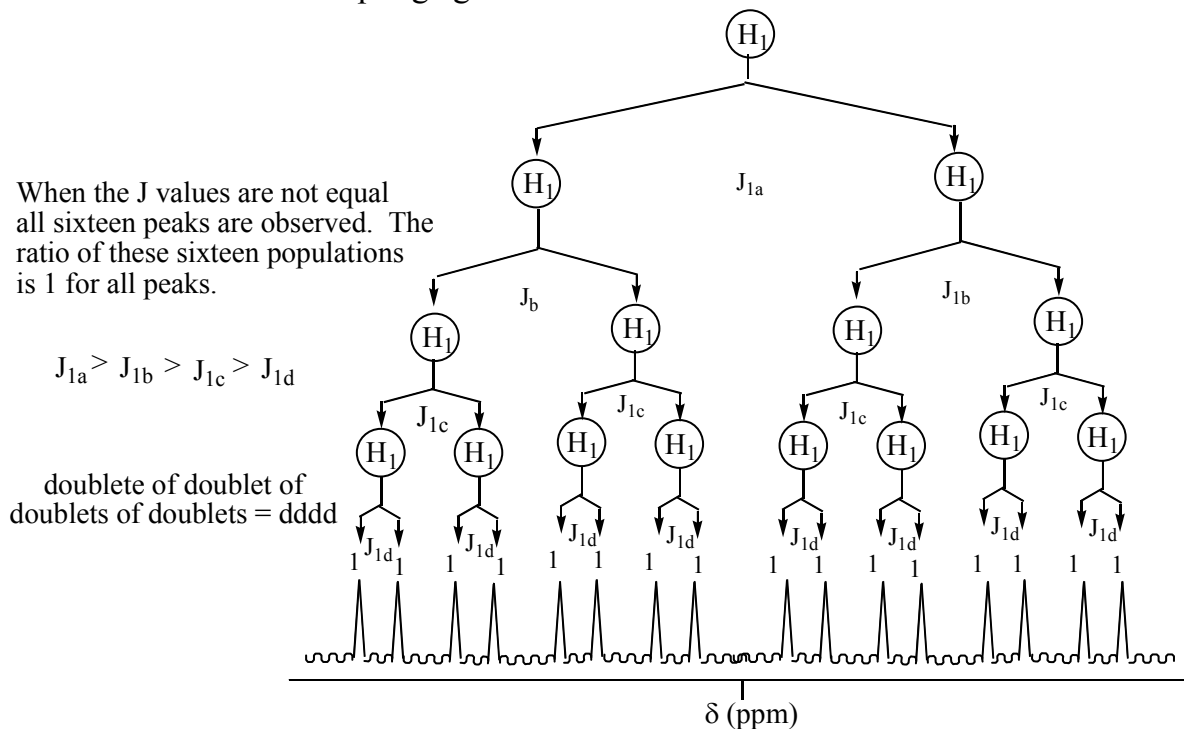
Four Neighbors

Four nearest neighbor protons to H_{observed} (H_1) really produce a doublet of doublet of doublet of doublets = dddd. Proton H_1 is split into two populations because of neighbor H_a and each of those populations is further split into two populations because of H_b and each of those populations is further split into two populations because of H_c and each of those doublets is further split into two populations because of H_d ($2 \times 2 \times 2 \times 2 = 16$ populations). The 16 peaks look like five because the coupling constants are same and the middle peaks continue to fall on top of one another. If it were not for the coincidence of identical coupling constants, we would be able to see all sixteen peaks (populations), as shown on the next page.



Four Neighbors with different coupling constants:

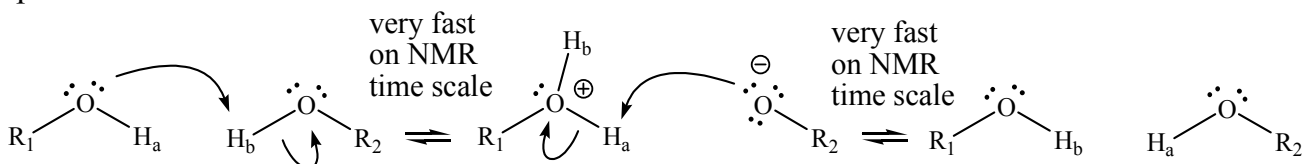
The splitting tree below shows what can happen when all of the coupling constants are different, called a doublet of doublet of doublet of doublets (dddd). Each peak should be approximately the same size. The splitting pattern (splitting tree) is drawn using the largest coupling constant first and then the smaller coupling constant(s) to prevent overlap. Sometimes the coupling constants are close, but not exactly the same. Partial multiplets can be observed and the number of peaks is less than 16. There are several variations in appearance of these 16 peaks if some of the coupling constants are equal to one another, but we won't draw any. I hope you get the idea how this works by now. If not, go back and reread this section on coupling again.



¹H NMR patterns having protons following the N+1 rule are shown on the next page.

Exchangeable Protons on Heteroatoms (O-H and N-H)

It is possible for O-H (and N-H) protons to exchange with one another (via acid/base reactions) randomizing the spin up or spin down next to any H on an adjacent carbon. If this occurs on the NMR time scale (thousands per second) or faster, any coupling (observable interaction) that might have been present before exchange is lost in the exchange and these peaks often appear as broad singlets (reported as #H,brd s). If D₂O is added to the mixture, deuterium can substitute in and the O-H or N-H can completely disappear from the NMR spectrum.

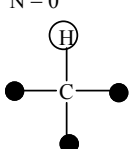
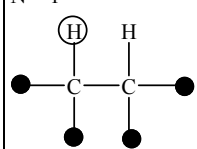
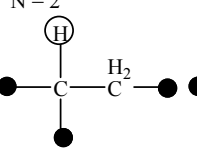
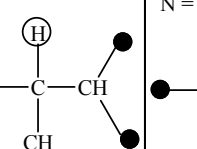
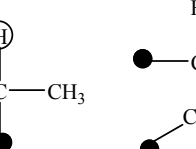
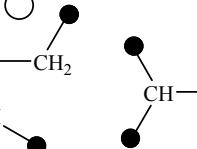
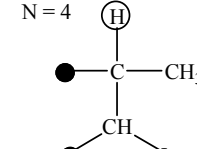
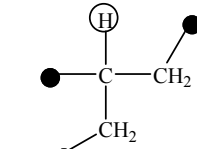
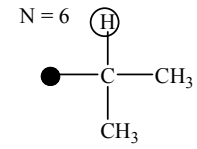


Here are some of the more common splitting patterns that we will encounter using the N+1 rule. Pascal's triangle at the bottom shows the relative size of peaks in the multiplets. Only $^3J_{\text{vicinal}}$ are shown.

● = group without any coupled proton(s)

⊕ = observed proton

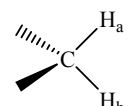
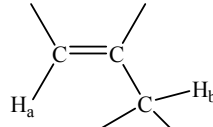
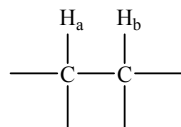
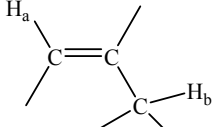
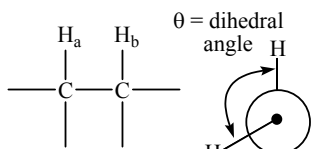
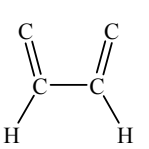
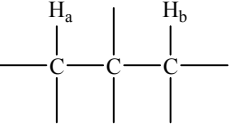
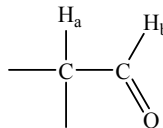
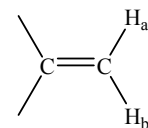
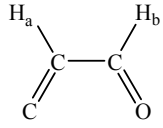
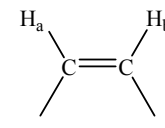
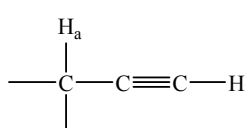
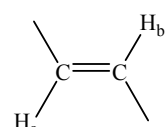
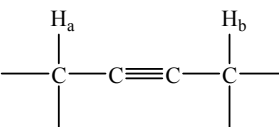
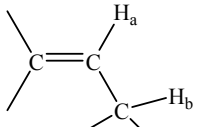
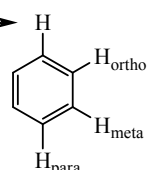
I = integration (number of protons)
N = number of nearest neighbors

<p>N = 0</p>  <p>s, J=none I=1H N=0</p> <p style="text-align: center;"> </p> <p style="text-align: center;">singlet</p> <p>δ = calc or exp</p>	<p>N = 1</p>  <p>d, J=7 I=1H N=1</p> <p style="text-align: center;"> </p> <p style="text-align: center;">doublet</p> <p>δ = calc or exp</p>	<p>N = 2</p>  <p>t, J=7 I=1H N=2</p> <p style="text-align: center;"> </p> <p style="text-align: center;">triplet</p> <p>δ = calc or exp</p>	<p>N = 3</p>  <p>q, J=7 I=1H N=3</p> <p style="text-align: center;"> </p> <p style="text-align: center;">quartet</p> <p>δ = calc or exp</p>	<p>N = 4</p>  <p>qnt, J=7 I=1H N=4</p> <p style="text-align: center;"> </p> <p style="text-align: center;">quintet</p> <p>δ = calc or exp</p>	<p>N = 5</p>  <p>sex, J=7 I=1H N=5</p> <p style="text-align: center;"> </p> <p style="text-align: center;">sextet</p> <p>δ = calc or exp</p>																				
<p>N = 6</p>  <p>sep, J=7 I=1H N=6</p> <p style="text-align: center;"> </p> <p style="text-align: center;">septet</p> <p>δ = calc or exp</p>	<p>N = 7</p>  <p>oct, J=7 I=1H N=7</p> <p style="text-align: center;"> </p> <p style="text-align: center;">octet</p> <p>δ = calc or exp</p>																								
<p>N = 8</p>  <p>non, J=7 I=1H N=8</p> <p style="text-align: center;"> </p> <p style="text-align: center;">nonet</p> <p>δ = calc or exp</p>	<p>Pascal's triangle = coefficients of variable terms in binomial expansion $(x + y)^n$, n = integer</p> <p style="text-align: center;">Multiplets when the N + 1 rule works (all J values are equal).</p> <table style="margin-left: auto; margin-right: auto;"> <tr> <td style="padding-right: 10px;">s = singlet</td> <td style="text-align: center;">1</td> <td style="padding-left: 10px;">↖ 1 peak = 100%</td> </tr> <tr> <td>d = doublet</td> <td style="text-align: center;">1 1</td> <td style="padding-left: 10px;">↖ 1 peak = 50%</td> </tr> <tr> <td>t = triplet</td> <td style="text-align: center;">1 2 1</td> <td style="padding-left: 10px;">↖ 1 peak = 25%</td> </tr> <tr> <td>q = quartet</td> <td style="text-align: center;">1 3 3 1</td> <td style="padding-left: 10px;">↖ 1 peak = 12%</td> </tr> <tr> <td>qnt = quintet</td> <td style="text-align: center;">1 4 6 4 1</td> <td style="padding-left: 10px;">↖ 1 peak = 6%</td> </tr> <tr> <td>sex = sextet</td> <td style="text-align: center;">1 5 10 10 5 1</td> <td style="padding-left: 10px;">↖ 1 peak = 3%</td> </tr> <tr> <td>sep = septet</td> <td style="text-align: center;">1 6 15 20 15 6 1</td> <td style="padding-left: 10px;">↖ 1 peak = 1.5%</td> </tr> <tr> <td>o = octet</td> <td style="text-align: center;">1 7 21 35 35 21 7 1</td> <td style="padding-left: 10px;">↖ 1 peak = 0.8%</td> </tr> </table> <p style="text-align: right; margin-top: 10px;">Relative sizes of the peaks in multiplets (% edge peak shown). As the multiplets get larger, it gets harder to see the edge peaks so you have to be careful interpreting large multiplets.</p>	s = singlet	1	↖ 1 peak = 100%	d = doublet	1 1	↖ 1 peak = 50%	t = triplet	1 2 1	↖ 1 peak = 25%	q = quartet	1 3 3 1	↖ 1 peak = 12%	qnt = quintet	1 4 6 4 1	↖ 1 peak = 6%	sex = sextet	1 5 10 10 5 1	↖ 1 peak = 3%	sep = septet	1 6 15 20 15 6 1	↖ 1 peak = 1.5%	o = octet	1 7 21 35 35 21 7 1	↖ 1 peak = 0.8%
s = singlet	1	↖ 1 peak = 100%																							
d = doublet	1 1	↖ 1 peak = 50%																							
t = triplet	1 2 1	↖ 1 peak = 25%																							
q = quartet	1 3 3 1	↖ 1 peak = 12%																							
qnt = quintet	1 4 6 4 1	↖ 1 peak = 6%																							
sex = sextet	1 5 10 10 5 1	↖ 1 peak = 3%																							
sep = septet	1 6 15 20 15 6 1	↖ 1 peak = 1.5%																							
o = octet	1 7 21 35 35 21 7 1	↖ 1 peak = 0.8%																							

Combinations of these are possible.

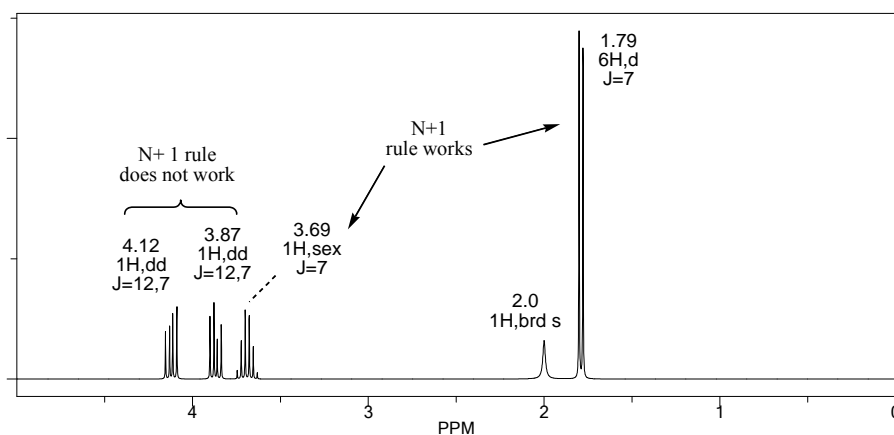
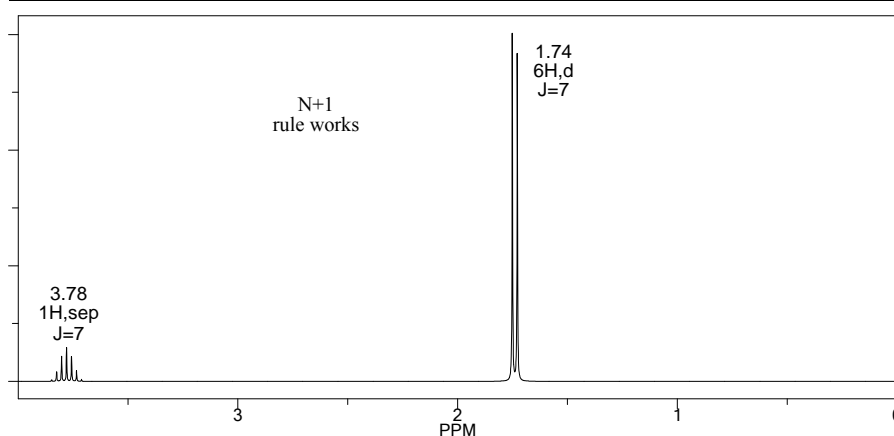
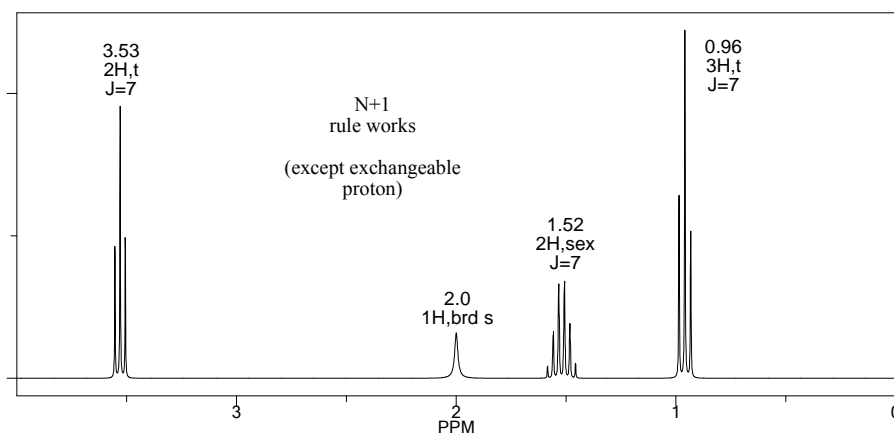
dd = doublet of doublets; ddd = doublet of doublet of doublets; dddd = doublet of doublet of doublet of doublets; dt = doublet of triplets, td = triplet of doublets; etc.

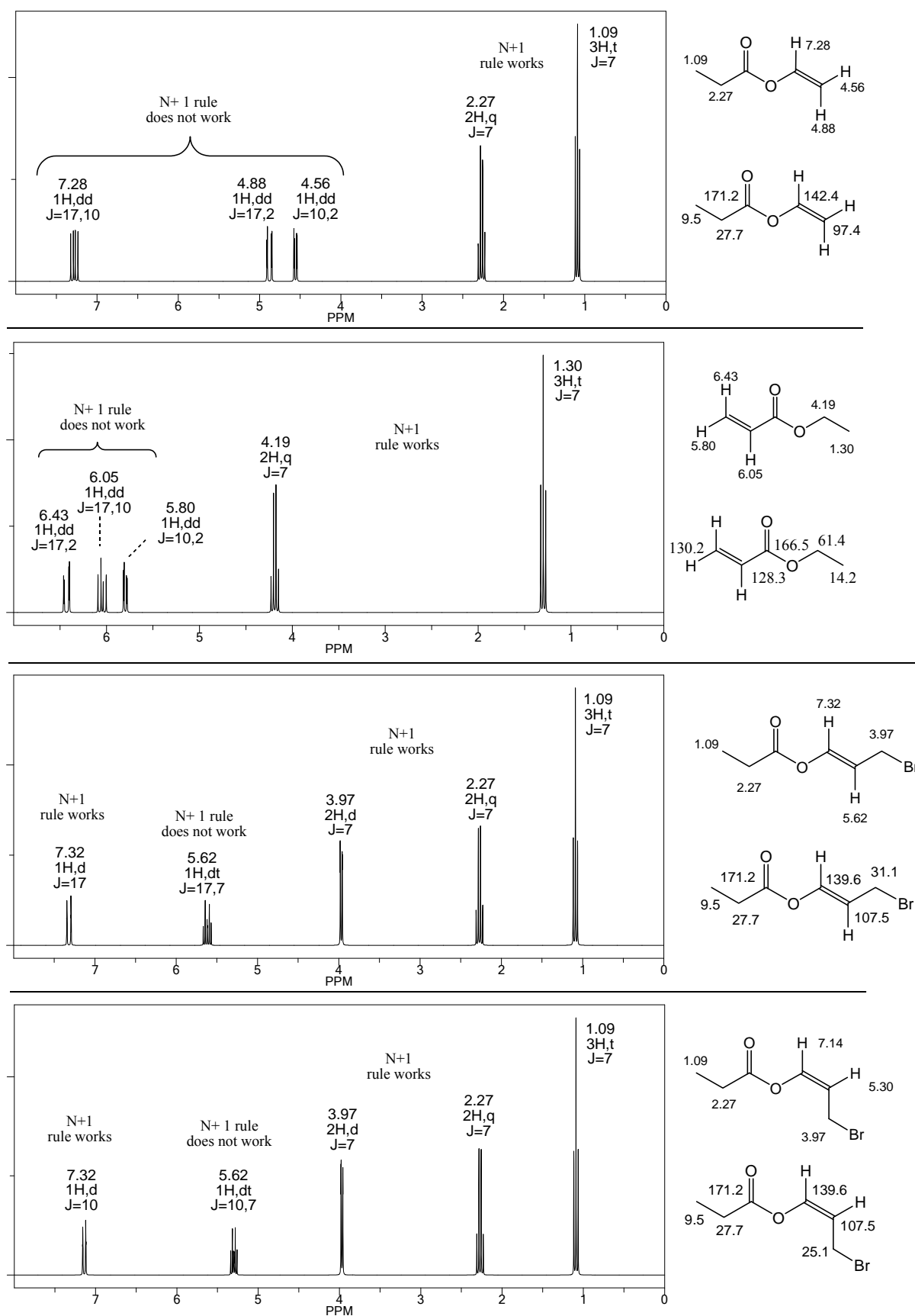
Typical Coupling Constants (used in the problems in this book)

 <p>Range Typical 0-30 Hz 12 Hz</p> <p>Geminal protons can have different chemical shifts and split one another if they are diastereotopic.</p>	 <p>Range Typical 0-3 Hz 1 Hz</p> <p>cis / allylic coupling, notice through 4 bonds (not used in our simulated spectra)</p>
 <p>Range Typical 6-8 Hz 7 Hz</p> <p>Vicinal protons are on adjacent atoms, when freely rotating coupling averages out to about 7 Hz.</p>	 <p>Range Typical 0-3 Hz 1 Hz</p> <p>trans / allylic coupling, notice through 4 bonds (not used in our simulated spectra)</p>
 <p>$\theta =$ dihedral angle</p> <p>Range Typical 0-12 Hz 7 Hz</p> <p>vicinal coupling depends on dihedral angle, see plot of Karplus equation, p 41</p>	 <p>Range Typical 9-13 Hz 10 Hz</p> <p>sp² vicinal coupling (different pi bonds)</p>
 <p>Range Typical 0-1 Hz 0 Hz</p> <p>Protons rarely couple through 4 chemical bonds unless in a special, rigid shape (i.e. W coupling)</p>	 <p>Range Typical 1-3 Hz 2 Hz</p> <p>sp³ vicinal aldehyde coupling</p>
 <p>Range Typical 0-3 Hz 2 Hz</p> <p>sp² geminal coupling</p>	 <p>Range Typical 5-8 Hz 6 Hz</p> <p>sp³ vicinal aldehyde coupling</p>
 <p>Range Typical 5-11 Hz 10 Hz</p> <p>sp² cis (acyclic) coupling (always less than the trans isomer)</p>	 <p>Range Typical 2-3 Hz 2 Hz</p> <p>sp / propargylic coupling, notice through 4 bonds</p>
 <p>Range Typical 11-19 Hz 17 Hz</p> <p>sp² trans coupling (always larger than the cis alkene)</p>	 <p>Range Typical 2-3 Hz 3 Hz</p> <p>bis-propargylic coupling, notice through 5 bonds (not used in our simulated spectra)</p>
 <p>Range Typical 4-10 Hz 7 Hz</p> <p>sp² / sp³ vicinal coupling</p>	<p>ortho, meta and para coupling to this proton,</p>  <p>only ortho coupling is used in our simulated spectra</p> <p>Range Typical ortho 6-10 Hz 9 Hz meta 2-3 Hz 2 Hz para 0-1 Hz 0 Hz</p>

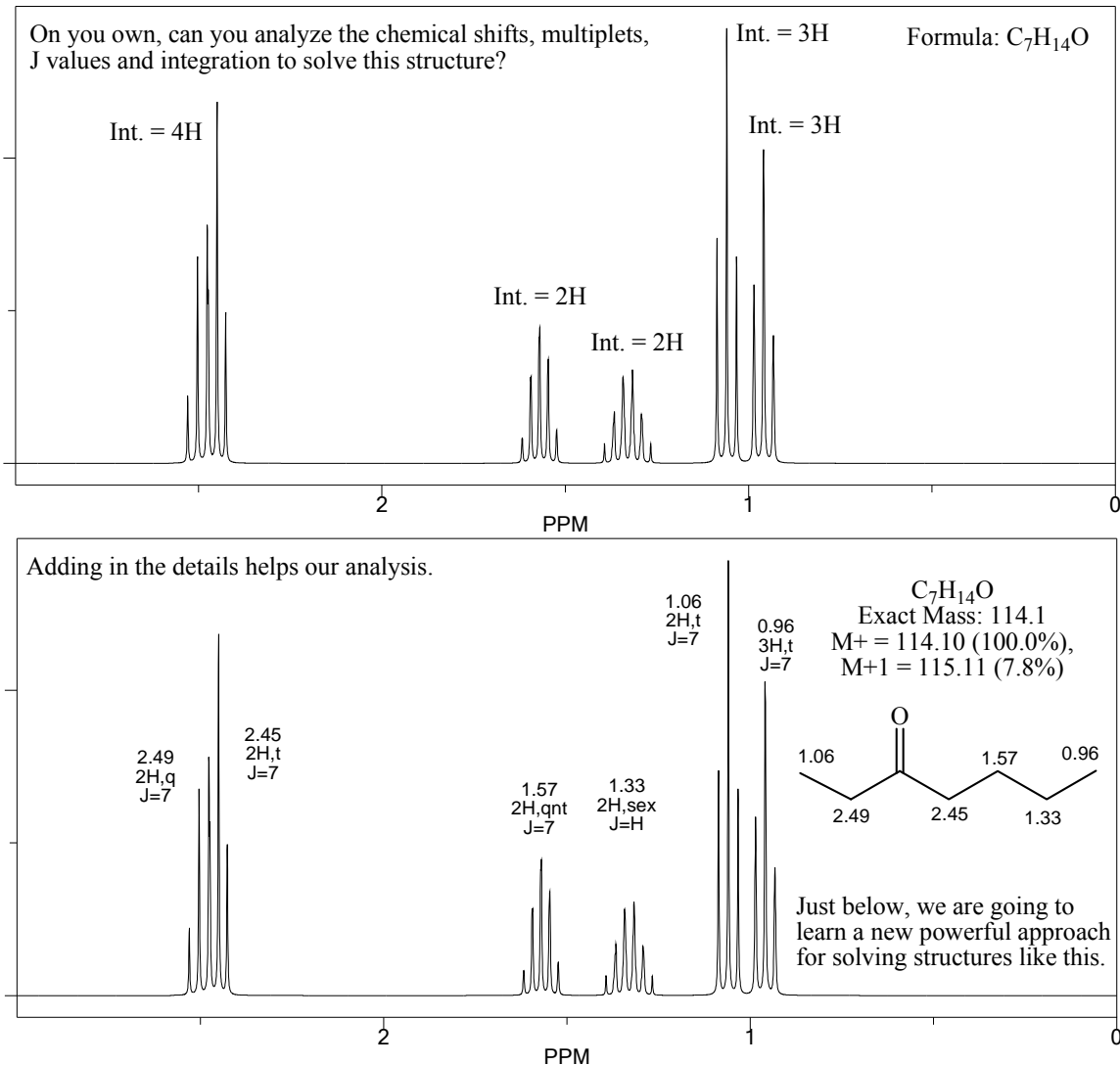
When J values are less than 1 Hz it is often difficult to resolve the peaks and a peak may merely appear wider and shorter.

The following spectra show examples where the N+1 rule is followed and where there are deviations of the N+1 rule. There are examples of nonequivalent geminal protons that have different coupling constants combined with the usual expected vicinal coupling constants. The sp^3 geminal coupling from one neighbor leads to a doublet, ($J=12$ Hz) and the vicinal coupling from a second neighbor also leads to a doublet ($J=7$ Hz). Overall each geminal proton in the bottom example appears as a doublet of doublets ($J=12,7$ Hz). All other couplings are vicinal, following the N+1 rule with $J=7$ Hz. On the following page are alkene examples. The coupling in alkenes (protons on sp^2 carbons) is different ($J_{trans} = 17$ Hz, $J_{cis} = 10$ Hz and $J_{gem} = 2$ Hz). In any aromatic examples, we only use J_{ortho} coupling ($= 9$ Hz), ignoring possible J_{meta} ($= 0-3$ Hz) and J_{para} ($= 0-1$ Hz).

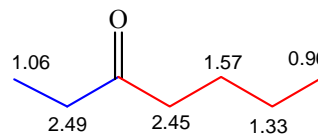
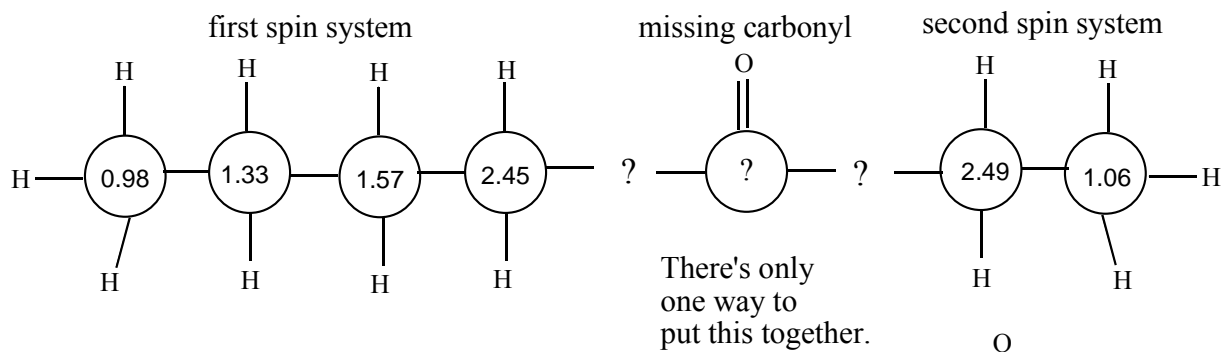




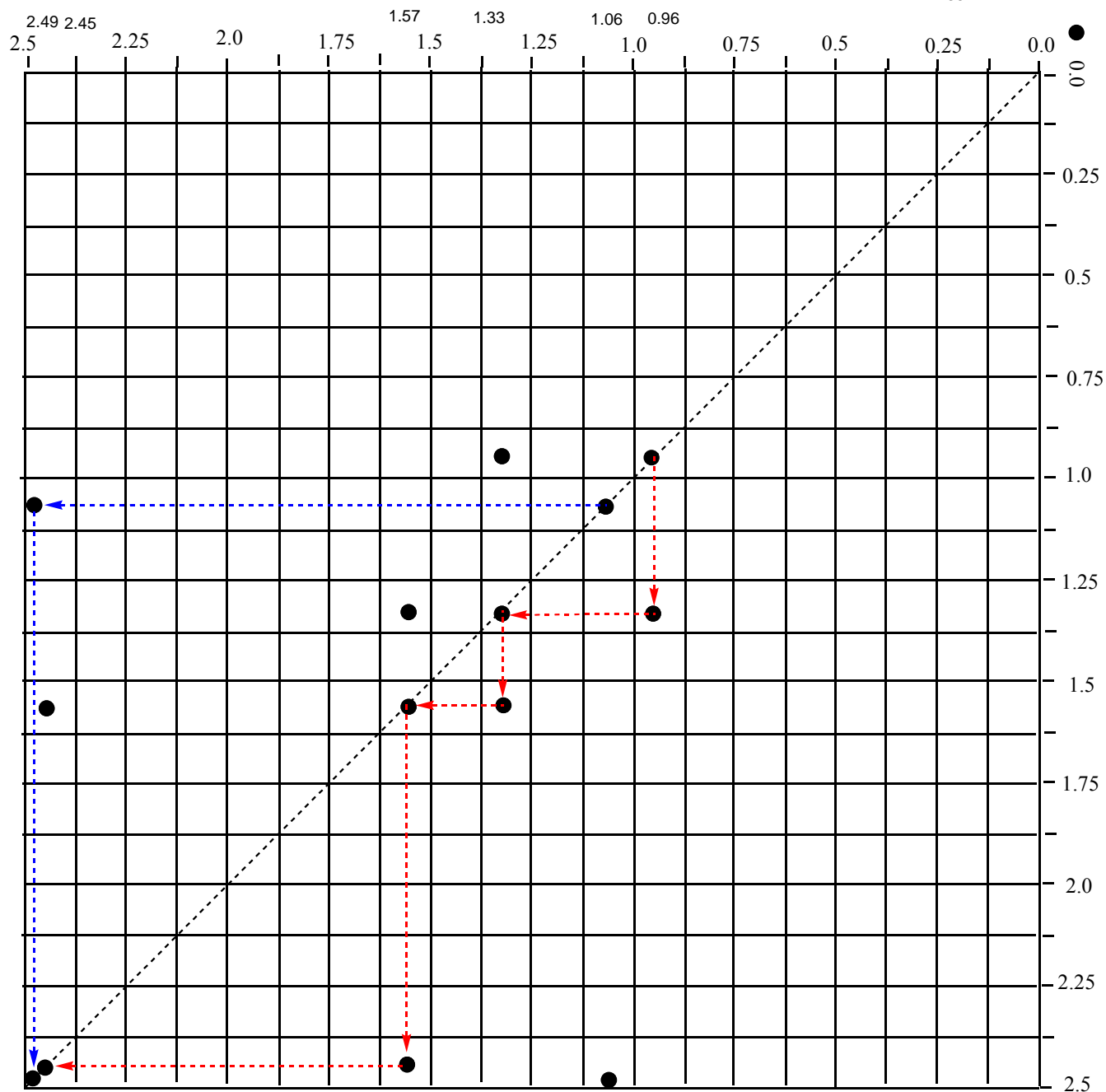
Example : Heptan-3-one shows a simple example of two common problems in H NMR spectra, similar multiplets that look alike and overlapping multiplets that make it hard to interpret what they really are.



A 2D COSY NMR experiment (H/H correlation spectrum) on the next page shows how both of these disadvantages can be overcome. The equivalent of a 1D proton spectrum lies along each axis. There are diagonal peaks that serve as place holders for what we already know about the locations of multiplets in our 1D NMR (the intersection of equivalent protons shifts). The nondiagonal peaks are called cross peaks and appear wherever protons are coupled. This valuable information allows us to trace out coupled spin systems. When possible, it is helpful to start a COSY analysis at an end position of a spin system. The two methyl groups work well here at 0.96 ppm and 1.06 ppm. Trace vertically or horizontally from a diagonal peak to find a cross peak. Only one is expected because they are methyls. Trace in a perpendicular direction back towards the diagonal to find the coupled partner on the diagonal. Continue in this manner until there are no other cross peaks. If a diagonal type of proton is next to two or three neighbors you may have to trace out more than one path. It is less obvious, but the two CH_2 groups next to the carbonyl group could also serve as starting points since there is only one open bond. However, because they partially overlap one another, neither is as good a starting point as the two methyl groups.

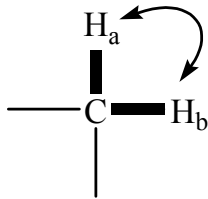


COSY correlations



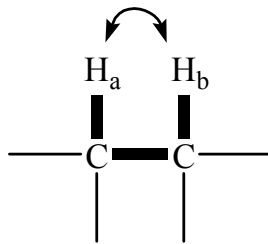
2D Methods of NMR that we will consider: 2D NMR experiments work because of coupling between interacting neighbors.

1. COSY (correlation spectroscopy): Proton-proton correlation spectroscopy provides proton connectivity patterns using proton spin systems based on coupling between interacting protons. A COSY spectrum typically shows which protons are close to one another (within 2-3 bonds).



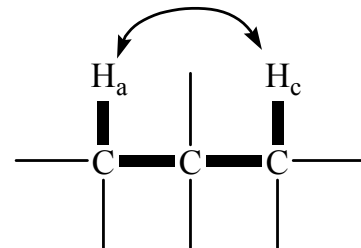
$$J_{\text{geminal}} = {}^2J$$

2 bond coupling only occurs when the protons are diastereotopic



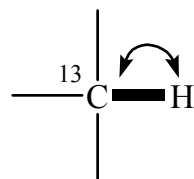
$$J_{\text{vicinal}} = {}^3J$$

3 bond coupling is very common when H_a and H_b are different.



4J is usually too small to see (but not always)

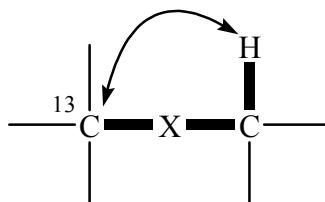
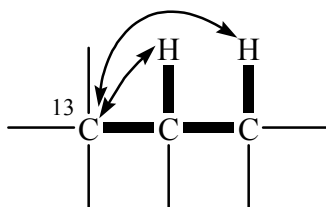
2. HETCOR (heteronuclear correlation spectroscopy) or HSQC (heteronuclear single quantum correlation): Indicates what protons are on what carbon atoms via direct one bond C-H coupling (${}^1J_{\text{CH}}$).



1J coupling shows what Hs are on what Cs.

$${}^1J_{\text{CH}} \approx 140 \text{ Hz}$$

3. HMBC (heteronuclear multiple bond correlation): Indicates what protons are two or three bonds away from a carbon atom (${}^2J_{\text{CH}}$, ${}^3J_{\text{CH}}$). It is especially helpful for connecting spin systems through quaternary carbon centers (which do not have any attached protons) and across heteroatoms (N and O).



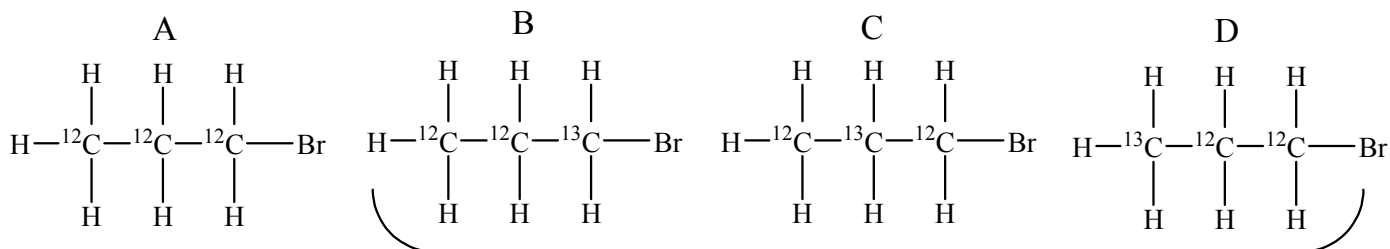
X = nitrogen, oxygen or sulfur atom

$${}^2J_{\text{CH}}, {}^3J_{\text{CH}} \approx 7-10 \text{ Hz}$$

^{13}C NMR

Probability of finding a ^{12}C at any different position = 0.989

Probability of finding a ^{13}C at any different position = 0.011



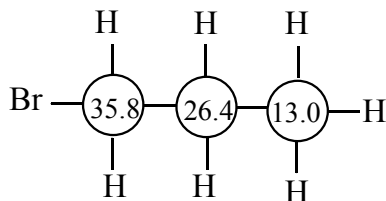
$$(0.989)(0.989)(0.989) \approx 0.967$$

This isotopomer represents about 96.7% of the molecules and does not have any observable carbon in the ^{13}C NMR spectrum.

$$(0.989)(0.989)(0.011) \approx 0.011$$

Each of these isotopomers represent about 1% of the molecules and produce the observable carbons in the ^{13}C NMR spectrum. Each signal comes from a different isotopomer. Compound B has ^{13}C at C_3 , compound C has ^{13}C at C_2 , and compound D has ^{13}C at C_1 .

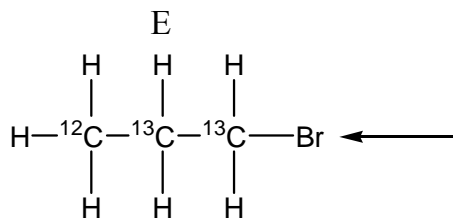
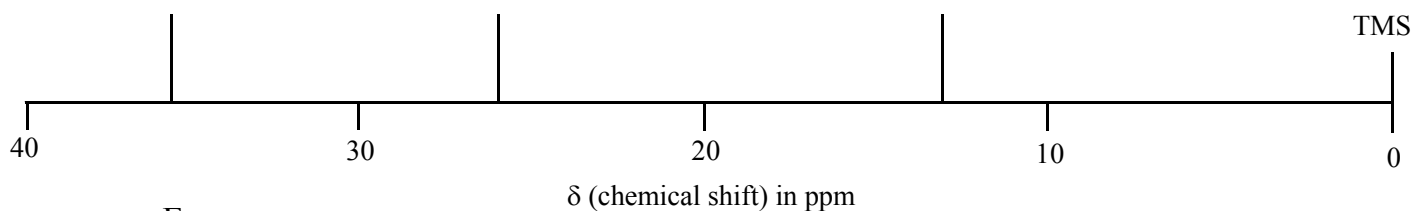
Structure "A" is invisible in the ^{13}C NMR



$\delta = 35.8$ ppm
(from B)

$\delta = 26.4$ ppm
(from C)

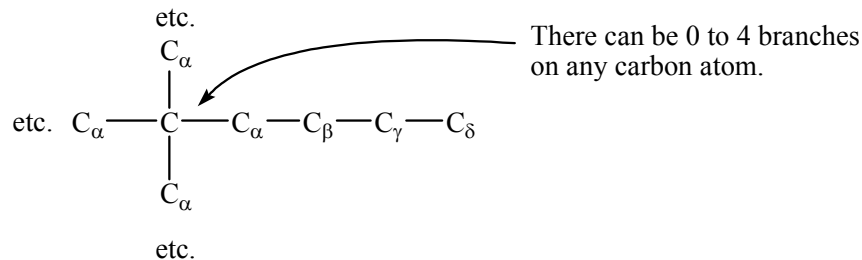
$\delta = 13.0$ ppm
(from D)



The odds of two ^{13}C atoms in the same molecule are $(0.011)^2 = 0.00012$ or about 1 out of 8300 structures. We will assume that this is not observable in a typical ^{13}C NMR spectrum. However, it is the basis for a rarely used INADEQUATE NMR experiment which can map out a carbon skeleton in a similar way to how a COSY shows proton correlations. However, space does not permit a discussion of INADEQUATE NMR.

sp³ Carbon Chemical Shift Calculations from scratch

Calculations of the individual ¹³C shifts of any alkane can be estimated starting from the chemical shift of methane (approximately -2 ppm). Using a simplified approach, I converted all the numerical corrections to integer values. Correction factors are included for every directly attached carbon atom (C_α = +9), every once removed carbon atom (C_β = +9) and every twice removed carbon atom (C_γ = -2). There are even some corrections for C_δ carbons, but they are generally smaller than the uncertainties in our estimations so I ignore those. Steric corrections are also necessary, which I also simplified to integer values.



The simplified equation for calculating a chemical shift for an sp³ carbon looks as follows.

$$\delta_C = (-2) + (9)(\#C_\alpha + \#C_\beta) + (\#C_\gamma)(-2) + (\text{simplified steric corrections}) \text{ ppm}$$

Simplified steric corrections:


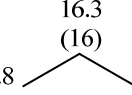
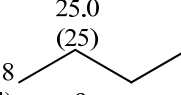
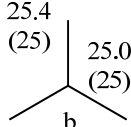
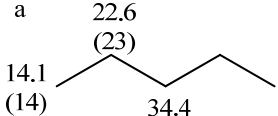
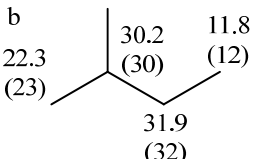
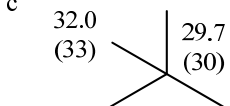
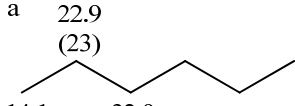
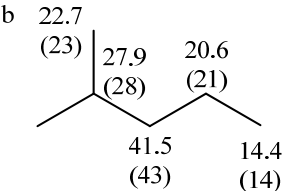
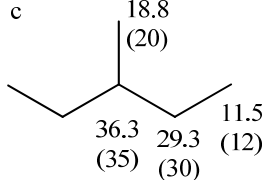
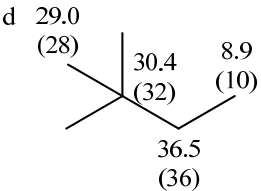
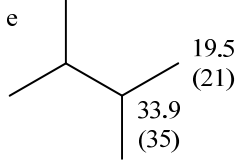
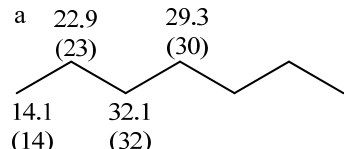
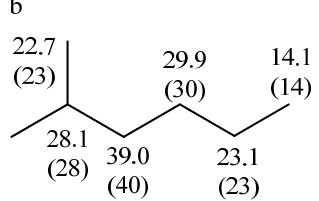
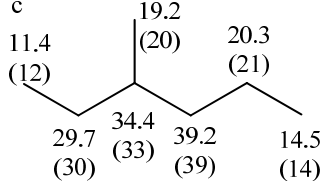
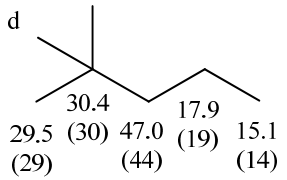
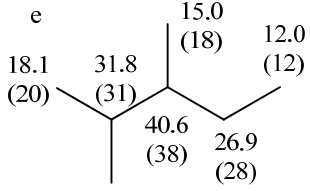
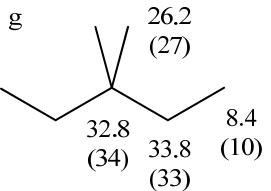
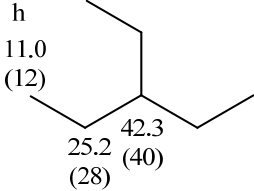
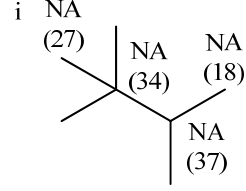
The attached C_α carbons are:
(make a correction for each attached carbon)

The calculated carbon atom is: ↓	primary	secondary	tertiary	quaternary
primary	0	0	-1	-3
secondary	0	0	-2	-8
tertiary	0	-4	-10	-15
quaternary	-1	-8	-15	-25

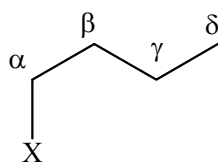
I calculated all of the estimated values for the C₁ → C₇ molecules on the next page using the simplified equation, supplemented by the simplified steric table of corrections (in parentheses). You can see that most estimated values are close to the experimental values provided (no parentheses).

sp^3 Carbon Chemical Shift Calculations from a known carbon skeleton

Examples of real carbon chemical shifts in $C_1 \rightarrow C_7$ alkanes are listed as possible starting points for calculation of carbon chemical shifts in substituted molecules (all ^{13}C shifts in ppm). Estimated values using the simplified formula provided above are listed in parentheses for comparisons.

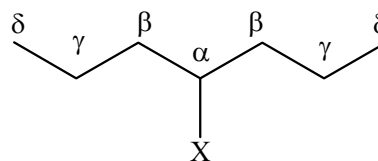
C_1 skeleton	C_2 skeleton	C_3 skeleton	C_4 skeletons	
CH ₄ -2.3 (-2)	 5.9 (7)	 16.3 (16) 15.8 (16)	 25.0 (25) 13.8 (14)	 25.4 (25) 25.0 (25)
C_5 skeletons				
 14.1 (14) 22.6 (23) 34.4 (34)	 22.3 (23) 30.2 (30) 11.8 (12) 31.9 (32)	 32.0 (33) 29.7 (30)		
C_6 skeletons				
 14.1 (14) 22.9 (23) 32.9 (32)	 22.7 (23) 27.9 (28) 20.6 (21) 41.5 (43) 14.4 (14)	 18.8 (20) 36.3 (35) 29.3 (30) 11.5 (12)	 29.0 (28) 30.4 (32) 8.9 (10) 36.5 (36)	 19.5 (21) 33.9 (35)
C_7 skeletons				
 14.1 (14) 22.9 (23) 29.3 (30) 32.1 (32)	 22.7 (23) 28.1 (28) 29.9 (30) 14.1 (14) 39.0 (40) 23.1 (23)	 11.4 (12) 19.2 (20) 20.3 (21) 29.7 (30) 34.4 (33) 39.2 (39) 14.5 (14)	 29.5 (29) 30.4 (30) 47.0 (44) 17.9 (19) 15.1 (14)	 18.1 (20) 31.8 (31) 15.0 (18) 12.0 (12) 40.6 (38) 26.9 (28)
 26.2 (27) 32.8 (34) 33.8 (33) 8.4 (10)	 11.0 (12) 42.3 (40) 25.2 (28)	 NA (27) NA (34) NA (18) NA (37)		

The following table presents many functional group correction factors. These will be applied to the carbon atoms in the appropriate skeletons presented above that are near each functional group. Two sets of correction values are provided for each substituent, depending on whether a substituent is at the end of a chain (terminal) or in the middle of a chain (internal). These are provided in side-by-side tables that follow ($\alpha > \beta > \gamma$). With only a couple of exceptions, the α and β corrections are deshielding (positive) and the γ corrections are shielding (negative). The correction factors are only reported to whole number values because estimated chemical shifts are not generally reliable to more than a few ppm.



terminal substituent

X = a substituent

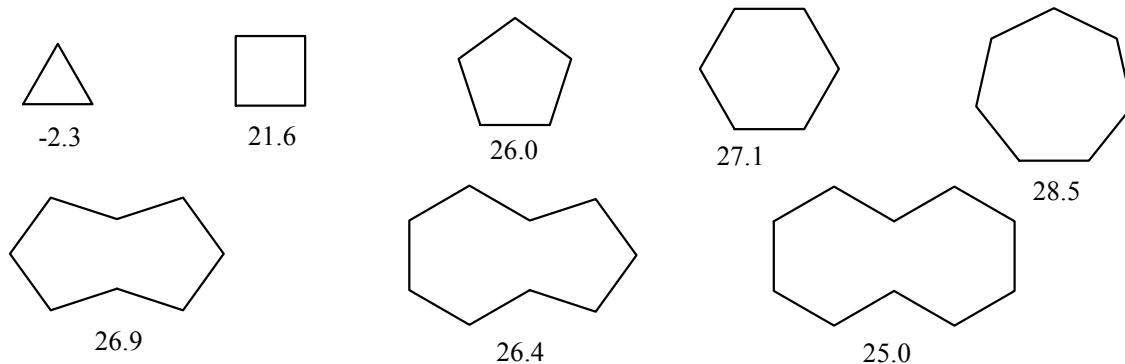
 δ values are assumed to be zero.

internal substituent

Substituent = X	X is attached to a terminal carbon atom (ppm)			X is attached to an internal carbon atom (ppm)		
	C_α correction	C_β correction	C_γ correction	C_α correction	C_β correction	C_γ correction
-CH=CH ₂ alkenes	20	6	-1	15	5	-1
-CCH alkynes	5	5	-4	2	6	-4
-C ₆ H ₅ aromatic	23	9	-2	17	7	-2
-OH alcohol	48	10	-6	44	7	-4
-OR ether	60	7	-6	57	5	-6
-O ₂ CR ester,oxygen side	51	6	-6	49	5	-6
-NH ₂ 1° amine	28	10	-5	24	8	-5
-NRH 2° amine	38	8	-5	32	5	-4
-NR ₂ 3° amine	45	5	-5	37	3	-4
-RNOCR amide,nitrogen side	26	7	-5	21	5	-5
-NO ₂ nitro	62	5	-5	58	2	-5
-F fluoro	70	8	-7	67	5	-7
-Cl chloro	31	10	-5	36	8	-5

Substituent = X	X is attached to a terminal carbon atom (ppm)			X is attached to an internal carbon atom (ppm)		
	C _α correction	C _β correction	C _γ correction	C _α correction	C _β correction	C _γ correction
-Br bromo	20	10	-4	28	10	-4
-I iodo	-7	11	-2	7	11	-2
-CH=O aldehyde	30	0	-3	24	-1	-3
-CR=O ketone	31	1	-3	26	0	-3
-C(OH)=O acid	22	2	-3	18	1	-3
-C(OR)=O ester, carbon side	20	2	-3	16	2	-3
-C(NR ₂)=O amide, carbon side	25	3	-3	19	2	-3
-CN nitrile	3	3	-3	3	3	-3
-C(Cl)=O acid chloride	33	2	-3	30	2	-3
-SH thiol	11	10	-3	12	8	-3
-SR sulfide	22	8	-3	20	6	-3

Here are some possible starting values for C_n cycloalkanes (ppm). Use the internal correction factors from the table when calculating rings with substituents.



Three examples are provided, starting from scratch, with a substituent at an end position and an internal position. Remember too, generic ^{13}C shifts are provided on page 50.

$$\delta_{\text{C}} = (-2) + (9)(\#C_{\alpha} + \#C_{\beta}) + (\#C_{\gamma})(-2) + (\text{simplified steric corrections}) \text{ ppm}$$

	C1	C2	C3	C4	C5	C6	C7
start =	-2	-2	-2	-2	-2	-2	-2
$\alpha + \beta =$	18	36	45	63	45	36	27
$\gamma =$	-2	-2	-6	-2	-4	-2	-4
steric =	0	-2	-8	-10	-11	-3	-1
subst. =	48	10	-6	0	0	0	0
calc. $\delta =$	62	40	23	49	28	29	20
exp. $\delta =$	61.0	42.4	26.0	51.5	31.1	30.0	22.7

	C1	C2	C3	C4	C5	C6	C7	C8
start =	-2	-2	-2	-2	-2	-2	-2	-2
$\alpha + \beta =$	27	36	45	36	36	36	27	18
$\gamma =$	-2	-2	-2	-6	-4	-2	-2	-2
steric =	-1	-4	-2	0	0	0	0	0
subst. =	-4	7	44	7	-4	0	0	0
calc. $\delta =$	18	35	83	35	26	32	23	14
exp. $\delta =$	17.2	33.6	76.8	34.3	25.9	32.1	22.8	14.1

	C1	C2	C3	C4
27.1 ppm				
start =	27	27	27	27
subst. =	44	7	-4	0
steric =	0	0	0	0
calc. $\delta =$	71	34	23	27
exp. $\delta =$	70.1	35.5	24.4	25.6

Problem – Estimate the sp^3 carbon chemical shifts of the following molecules. If real values are known, they are listed next to the appropriate carbon atom (experimental), otherwise estimated values are from ChemDraw (estimated).

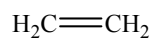
experimental	experimental	estimated	experimental	estimated
experimental	experimental	estimated	estimated	

Calculating Alkene ^{13}C Chemical Shifts (ppm)

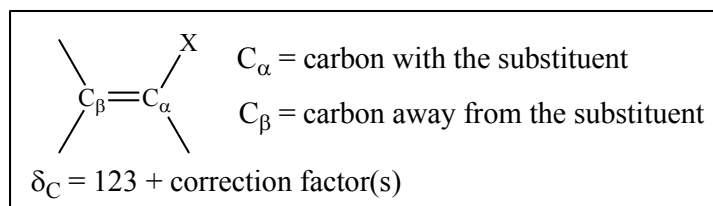
To calculate alkene carbon chemical shifts, there are two types of substituent corrections. The alpha values are used when a substituent is directly attached to the carbon and the beta values are used when a substituent is attached to the other carbon of the double bond. Since there are four bonding positions at any alkene it is possible that 1-4 corrections might be needed.

Correction factors for sp^2 alkene shifts

alkene starting point = ethene



123.3



Substituent = X	X is attached to the alkene carbon atom (ppm)		Substituent = X	X is attached to the alkene carbon atom (ppm)	
	C_α correction	C_β correction		C_α correction	C_β correction
H_3C -methyl	13	-7	-OR ether	29	-38
CH_3CH_2 -ethyl	17	-10	$-\text{O}_2\text{CR}$ ester, oxygen side	18	-25
$\text{CH}_3\text{CH}_2\text{CH}_2$ -propyl	17	-9	$-\text{NR}_2$ enamine	28	-32
$(\text{H}_3\text{C})_2\text{CH}$ -isopropyl	23	-12	$-\text{NO}_2$ nitro	22	-1
$(\text{H}_3\text{C})_3\text{C}$ -t-butyl	26	-15	$-\text{SR}$ sulfide	14	-13
$-\text{CH}=\text{CH}_2$ alkenes	14	-7	$-\text{CH}=\text{O}$ aldehyde	15	14
$-\text{CCH}$ alkynes	-6	6	$-\text{CR}=\text{O}$ ketone	14	5
$-\text{C}_6\text{H}_5$ aromatic	12	-11	$-\text{C}(\text{OH})=\text{O}$ acid	5	10
* $\text{X}-\text{CH}_2$ - allylic X	≈ 14	≈ -7	$-\text{C}(\text{OR})=\text{O}$ ester, carbon side	6	7
$-\text{F}$ fluoro	25	-34	$-\text{C}(\text{NR}_2)=\text{O}$ amide, carbon side	6	5
$-\text{Cl}$ chloro	3	6	$-\text{C}(\text{Cl})=\text{O}$ acid chloride	8	14
$-\text{Br}$ bromo	-9	-1	$-\text{CN}$ nitrile	-6	14
$-\text{I}$ iodo	-38	7			

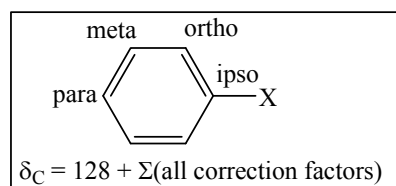
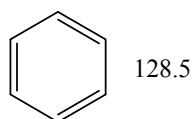
*X = Cl, Br, I, OH, OR

Calculating Aromatic ^{13}C Chemical Shifts (ppm),

To calculate aromatic carbon chemical shifts, there are four types of substituent corrections depending on a carbons location in an aromatic ring relative to a substituent. Ipso values are used when a substituent is directly attached to the carbon, ortho values are used when the calculated carbon and substituent carbon are adjacent to one another, meta values used when the calculated carbon is the second carbon over from the substituent carbon, and para values are used when the substituent carbon and calculated carbon are on opposite sides of the aromatic ring. Since there are six bonding positions in any aromatic ring it, is possible that 1-6 corrections might be needed for each carbon of the aromatic ring. Generally, the more corrections that are made, the less reliable is the estimated chemical shift.

Correction factors for sp^2 aromatic shifts

aromatic starting point = benzene



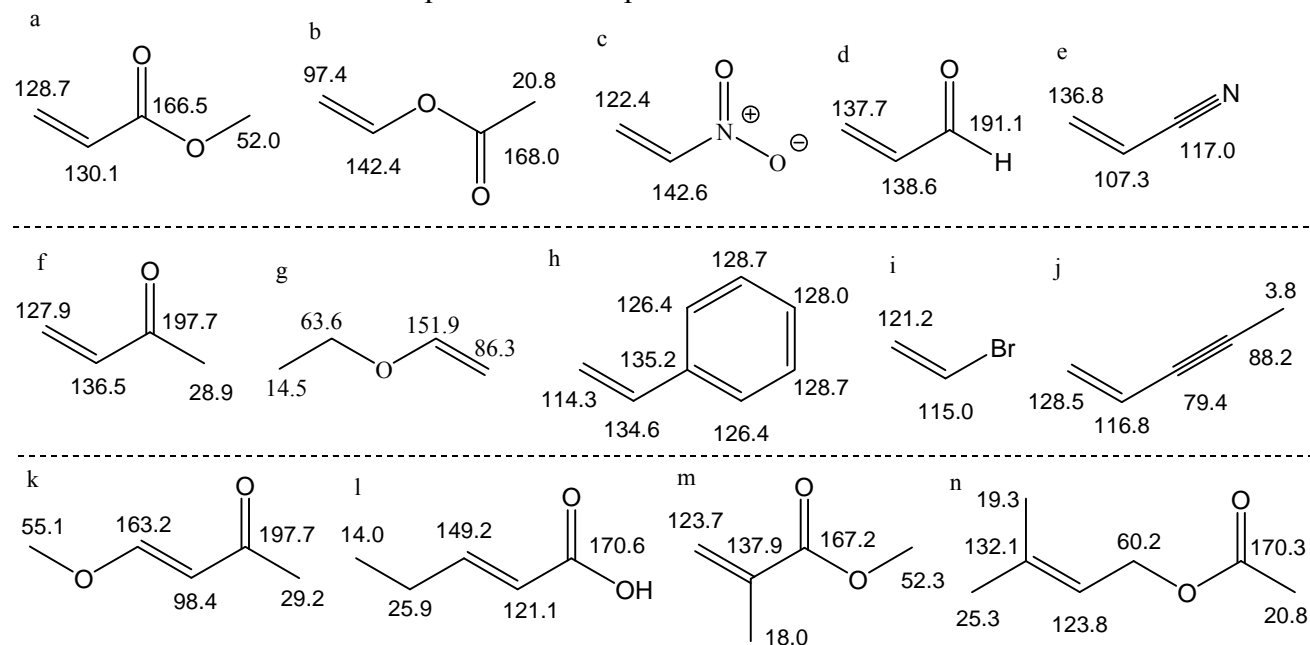
X is attached to an aromatic carbon atom (ppm)

Substituent = X	ipso	ortho	meta	para
H_3C -methyl	9	1	0	-3
CH_3CH_2 -ethyl	12	-1	0	-3
$\text{CH}_3\text{CH}_2\text{CH}_2$ -propyl	10	0	0	-3
$(\text{H}_3\text{C})_2\text{CH}$ -isopropyl	20	-2	0	-3
$(\text{H}_3\text{C})_3\text{C}$ -t-butyl	19	-3	0	-3
$-\text{CH}=\text{CH}_2$ alkenes	9	-2	0	-1
$-\text{CCH}$ alkynes	-6	4	0	0
$-\text{C}_6\text{H}_5$ aromatic	8	-1	0	-1
* $\text{X}-\text{CH}_2$ -allylic X	≈ 10	≈ -1	0	-1
$-\text{F}$ fluoro	34	-13	2	-4
$-\text{Cl}$ chloro	5	0	1	-2
$-\text{Br}$ bromo	-5	3	2	-1
$-\text{I}$ iodo	-31	9	2	-1
$-\text{OH}$ phenol	29	-13	2	-7
$-\text{OR}$ ether	34	-14	1	-8
$-\text{O}_2\text{CR}$ ester, oxygen side	22	-7	0	-3

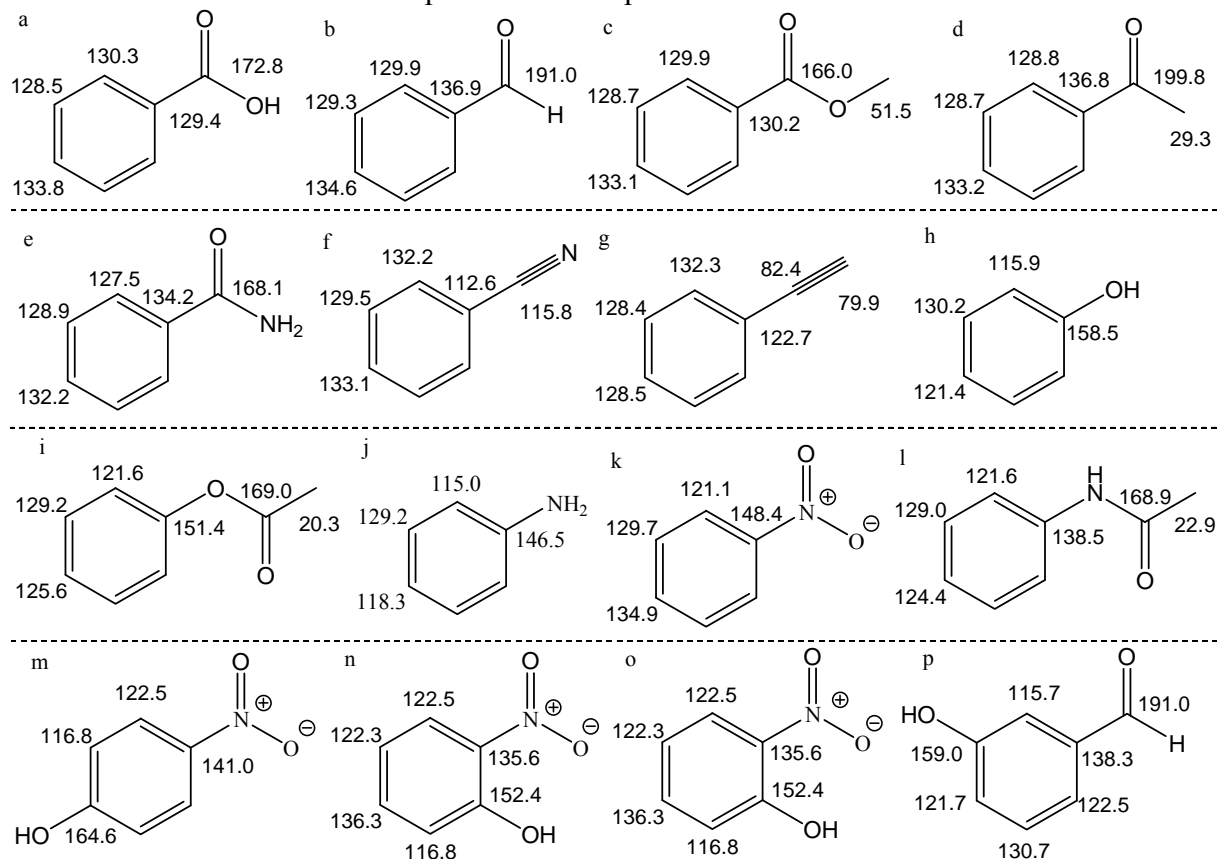
Substituent = X	ipso	ortho	meta	para
$-\text{NR}_2$ amines	16	-15	1	-10
$-\text{RNOCR}$ amide, nitrogen side	10	-8	0	-4
$-\text{NO}_2$ nitro	20	-5	1	6
$-\text{NO}$ nitroso	37	-8	1	7
$-\text{SH}$ thiol	4	1	0	-3
$-\text{SR}$ sulfide	8	4	0	0
$-\text{SOR}$ sulfoxide	18	-5	1	2
$-\text{SO}_2\text{R}$ sulfone	12	-1	1	5
$-\text{CH}=\text{O}$ aldehyde	8	1	0	6
$-\text{CR}=\text{O}$ ketone	9	0	0	4
$-\text{C}(\text{OH})=\text{O}$ acid	2	2	0	5
$-\text{C}(\text{OR})=\text{O}$ ester, carbon side	2	1	0	4
$-\text{C}(\text{NR}_2)=\text{O}$ amide, carbon side	5	-1	0	3
$-\text{C}(\text{Cl})=\text{O}$ acid chloride	5	3	0	7
$-\text{CN}$ nitrile	-16	4	1	4

*X = Cl, Br, I, OH, OR

Problem – Calculate the alkene carbon chemical shifts in the following structures. If you don't find an exact match for a particular substituent, look for a close analog to use in place of the actual substituent. The chemical shifts provided are experimental or come from ChemDraw estimates.

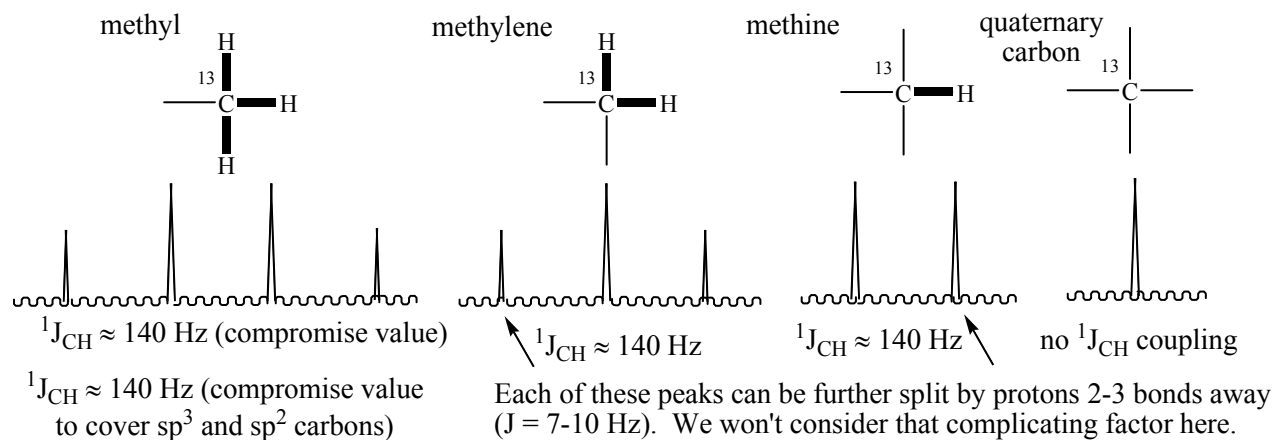


Problem – Calculate the aromatic proton chemical shifts in the following structures. If you don't find an exact match for a particular substituent, look for a close analog to use in place of the actual substituent. The chemical shifts provided are experimental or come from ChemDraw estimates.

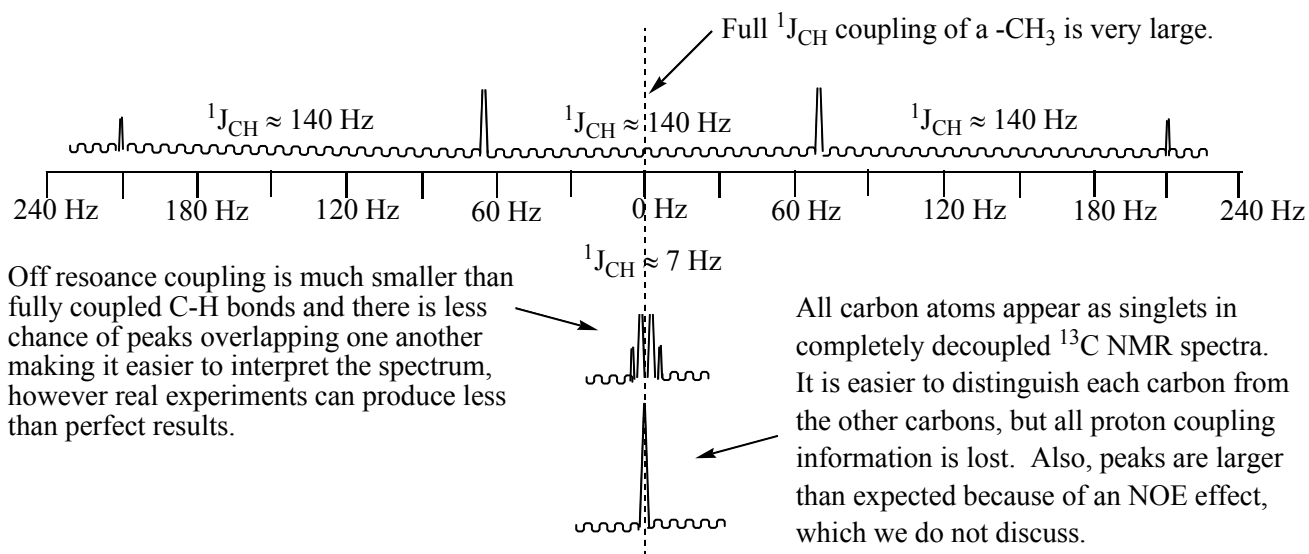


C-H Coupling

^{13}C atoms can fully couple with their proton neighbors, following the N+1 rule. They can also be partially decoupled (still follow the N+1 rule) or be completely decoupled from their proton neighbors (only single peaks). One bond C-H coupling, $^1J_{\text{CH}}$, is large (typically 120-165 Hz, but 140 Hz is used as a compromise value). Two and three bond coupling, $^2J_{\text{CH}}$ and $^3J_{\text{CH}}$, constants are smaller and similar (about 7-10 Hz). These differences in coupling constants are also the basis of some important C/H correlation experiments using $^1J_{\text{CH}}$ (HETCOR or HSQC) and $^2J_{\text{CH}}$ and $^3J_{\text{CH}}$ (HMBC) to be discussed later.

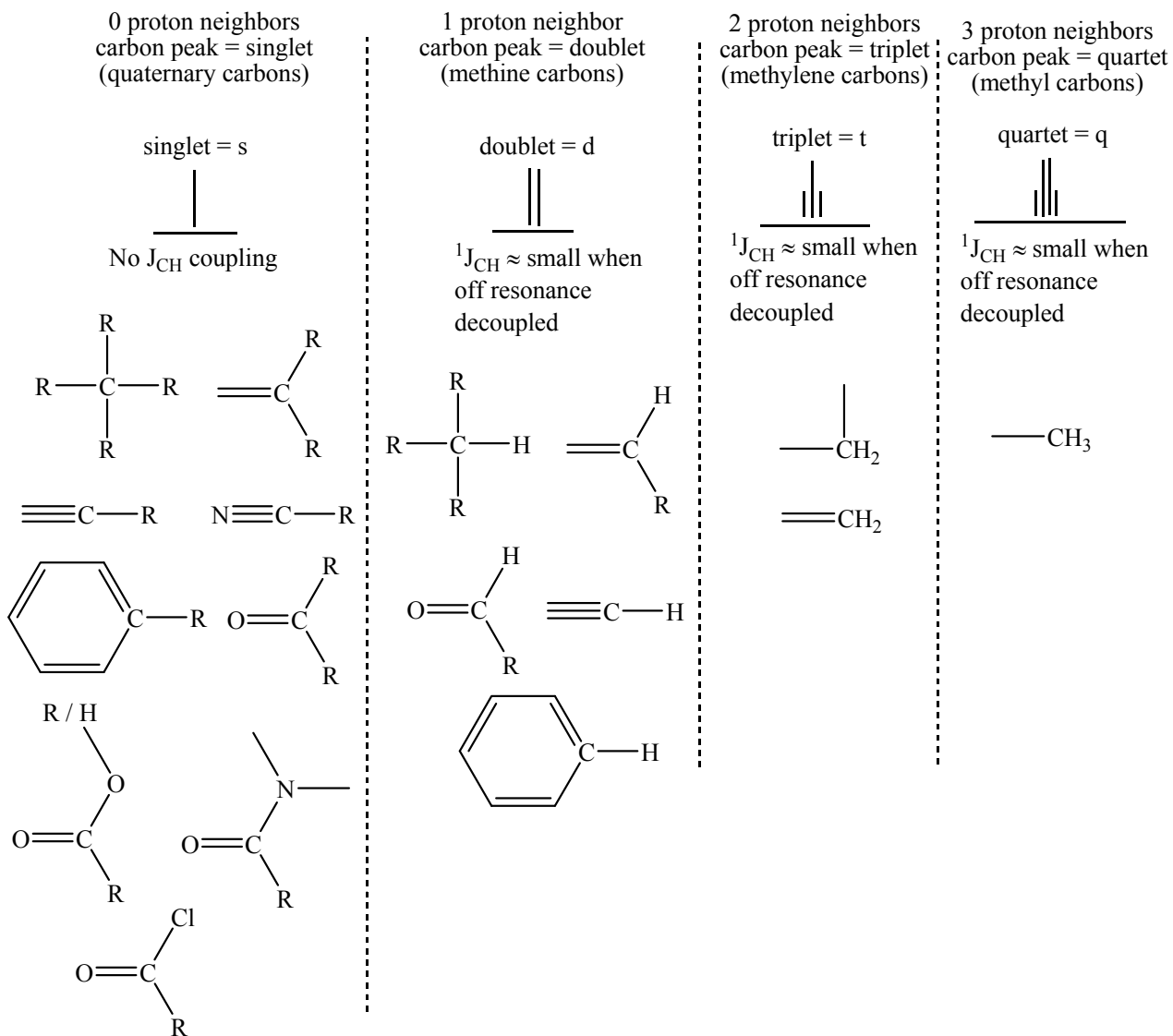


	1J	2J	3J			
sp^3 C-H J values	≈ 120	$\approx 7-10$	$\approx 7-10$			
sp^2 C-H J values	≈ 165	$\approx 7-10$	$\approx 7-10$			
sp C-H J values	≈ 240	-	-			
				1 bond coupling ($^1J = 120-240$ Hz)	2 bond coupling ($^2J = 7-10$ Hz)	3 bond coupling ($^3J = 7-10$ Hz)

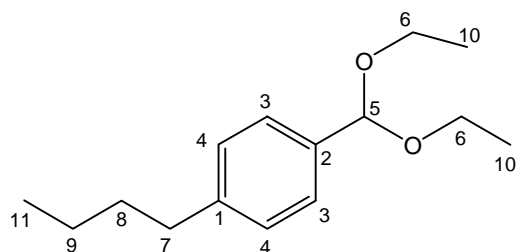


The following table shows the common proton substituted carbon patterns you are likely to encounter in a structure problem. The multiplets are what you would see if an off resonance spectrum was acquired. However, DEPT experiments have almost completely supplanted off resonance spectra and show only singlets, though occasionally carbon peaks are still identified with s, d, t and q to indicate the number peaks expected according to the number of attached protons (N+1 rule). You will also encounter this terminology in the older literature.

The N+1 rule works perfectly for C-H bonds when fully or partially decoupled.

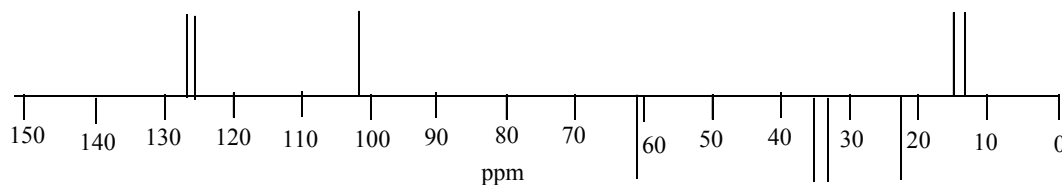


To determine how many protons are on each carbon atom, chemists have almost completely switched to the DEPT experiment (distortionless enhancement by polarization transfer), where all the carbon peaks remain as easy to read singlets. To explain what we see in a DEPT, we need two additional ^{13}C spectra obtained with different pulse sequences, which we will call DEPT-90 and DEPT-135. The normal decoupled ^{13}C spectrum shows all the carbon atoms as single peaks. Often the quaternary carbons are smaller because of slow relaxation. The DEPT-90 spectrum only shows methine carbons (CH) as positive peaks. The DEPT-135 spectrum shows both methyl (CH_3) and methine (CH) carbons as positive peaks and methylene (CH_2) carbons as negative peaks. The quaternary carbons are easy to assign because they do not appear in either of the extra DEPT experiments. The methine carbons are easy to assign because they are the only peaks in the DEPT-90. The methylene carbons are easy to assign because they are the negative peaks in the DEPT-135 and finally the methyl carbons are assigned because they appear in the DEPT-135 but not the DEPT-90.

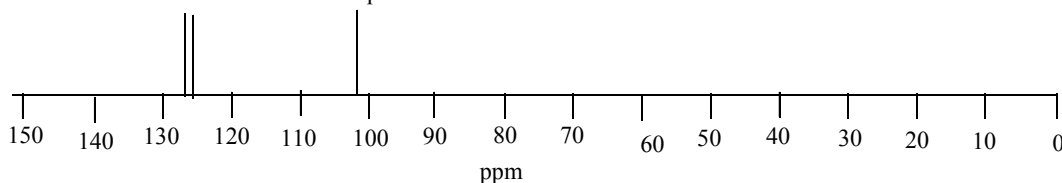


p-butylbenzaldehyde diethyl acetal

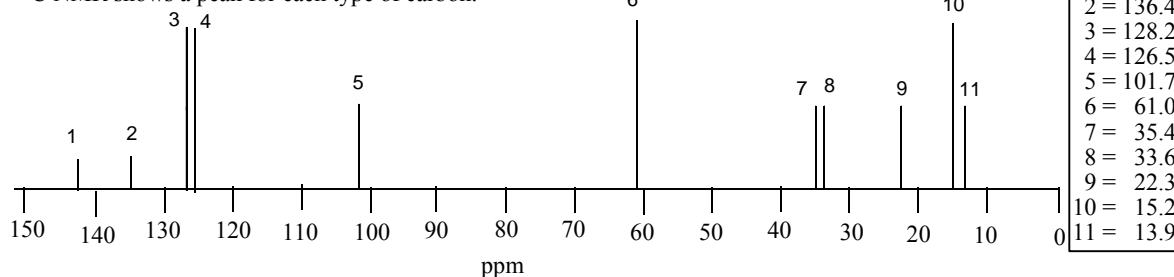
DEPT-135 shows CH and CH_3 carbon atoms up and CH_2 carbon atoms down.



DEPT-90 shows CH carbon atoms up .

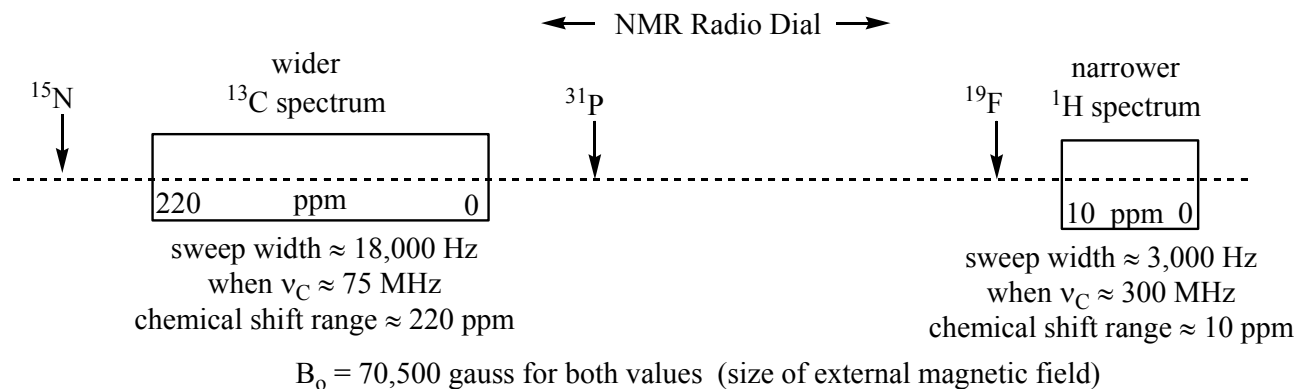


^{13}C NMR shows a peak for each type of carbon.



HETCOR and HSQC - greater carbon dispersion, a carbon advantage transferred to protons

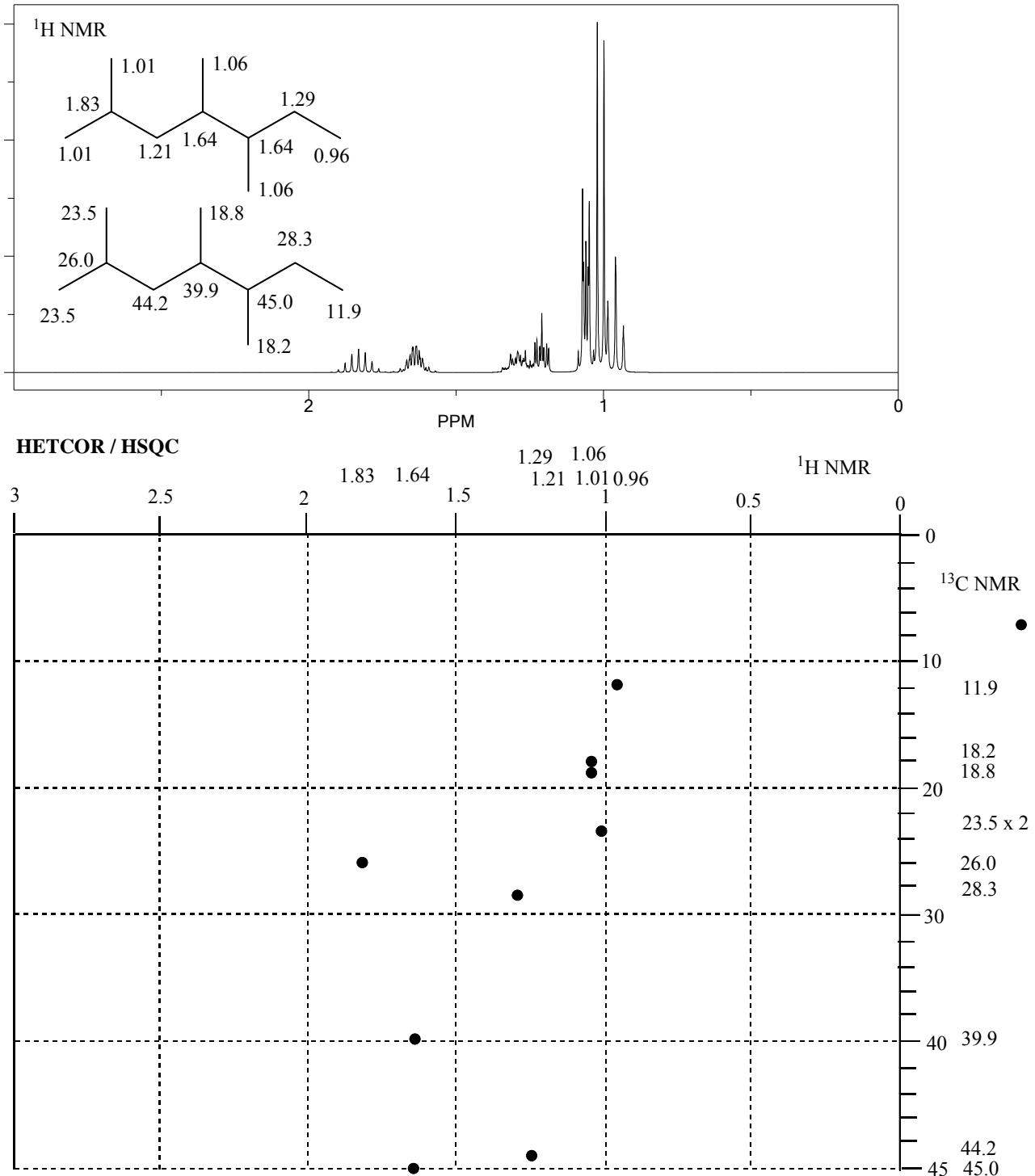
HETCOR or HSQC experiments take advantage of the large carbon dispersion by transferring the wide carbon chemical shift differences to the protons narrow range. There is a good chance that some proton chemical shifts may lay on top of one another, making interpretation difficult. If we can connect the carbons with the protons, we can use the wider dispersion of ^{13}C peaks to spread out the proton peaks so there is less chance of overlap of NMR signals than is found in ^1H NMR.



HETCOR (heteronuclear correlation spectroscopy) and **HSQC** (heteronuclear single quantum correlation) are two versions of C/H correlation NMR experiments that will show peaks resulting from one bond C-H connections. Like the COSY they are 2D NMR experiments. Both experiments correlate each type of proton to the carbon it is attached to via their one bond coupling interactions, $^1J_{\text{CH}}$. Proton chemical shifts are plotted along one axis and carbon chemical shifts along the other, with correlations between protons and carbons appearing as NMR peaks. There is no diagonal line in a HETCOR or HSQC because the axes are completely different. Both axes use ppm, $^1\text{H} = 10$ ppm and $^{13}\text{C} = 220$ ppm. Where ever a peak appears there is one bond coupling between that carbon atom and its attached protons. With this extra information, the COSY does much more than reveal couplings between protons in a spin system. Now, we will be connecting their carbon atoms at the same time. Except for quaternary carbons, that have no protons, we will be able to construct the carbon skeleton (including the protons) of all the spin systems.

Simple Example of HETCOR/HSQC information: 2,4,5-trimethylheptane

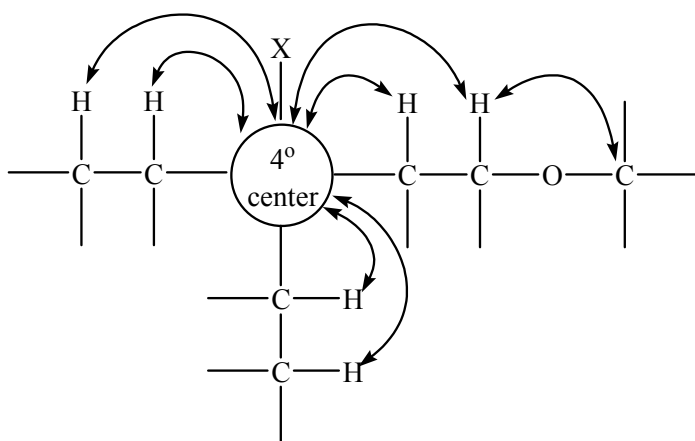
Proton peaks overlap, while carbon peaks are far apart. In a HETCOR or HSQC the carbon axis helps to separate out the overlapping proton signals. HETCOR and HSQC spectra pull the overlapping proton shifts far apart through their correlation with the carbon peaks.



HMBC

Our final 2D correlation experiment is called **HMBC (heteronuclear multiple bond correlation)**. It looks at two and three bond correlations between carbon and hydrogen, $^2J_{CH}$ and $^3J_{CH}$. HMBC will help us complete the construction of the carbon skeleton by connecting the spin systems to the quaternary centers and across heteroatoms. HMBC will put us well on our way to being able to solve complex organic structures (except for stereochemistry considerations). The types of interactions we are looking for are shown in the following figure.

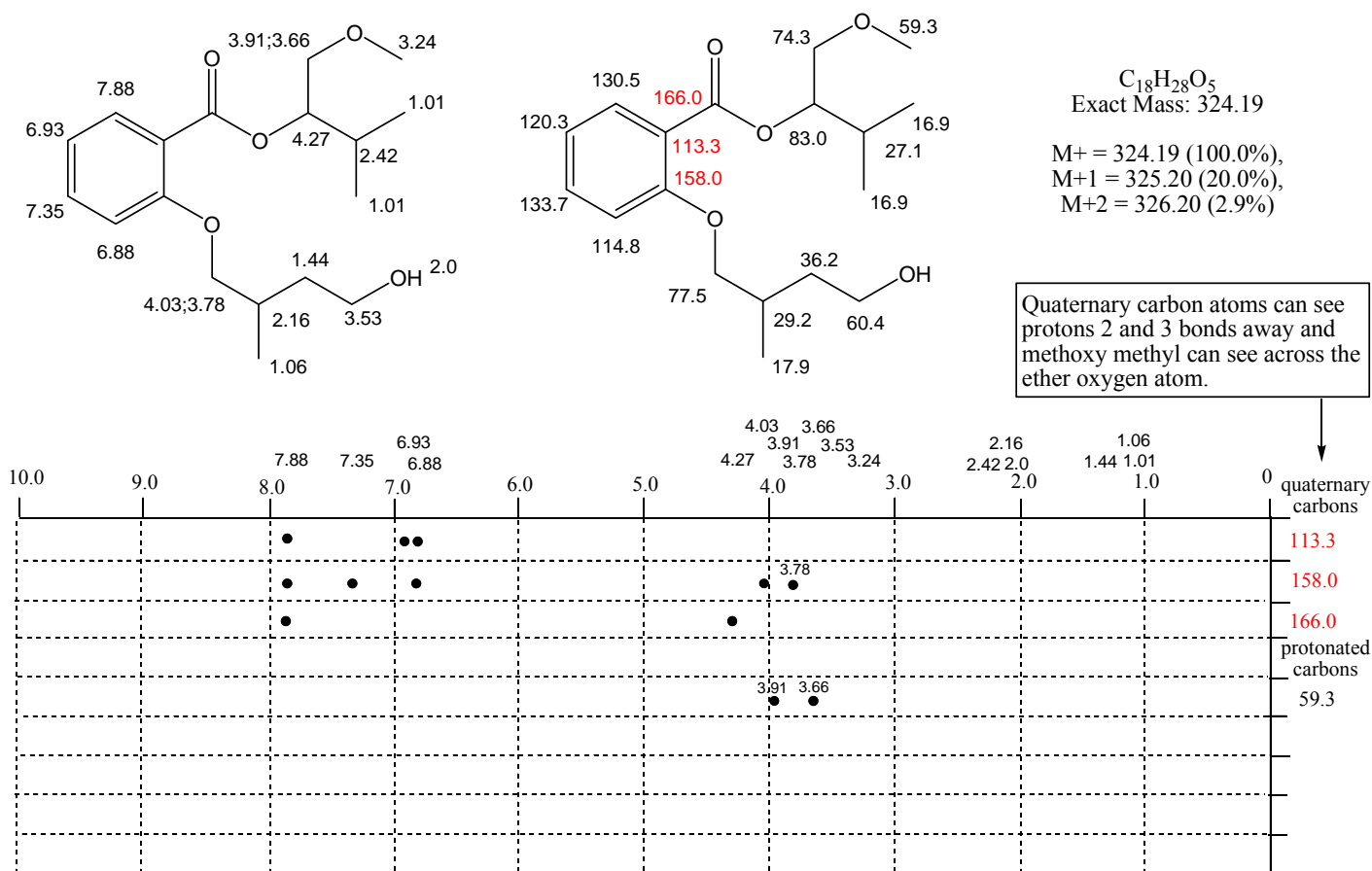
Typical Strategy for connecting spin systems to quaternary atoms and across heteroatoms using $^2J_{CH}$ and $^3J_{CH}$.



We are looking for correlations that answer questions about which way spin systems are connected to the quaternary centers and across heteroatoms. There can be many possibilities.

Recall that there were large $^1J_{CH}$ values (140 Hz) and smaller $^2J_{CH}$ and $^3J_{CH}$ values (7-10 Hz) that were similar. It turns out that the small two and three bond C-H couplings are the key to solving this problem. One simple example shows some of the potential value of an HMBC experiment to finish the connectivity of a structure.

HMBC example – selected carbons



It is finally time for an actual problem. An organizing table is provided to summarize all of the spectral information on one page. This way you can rapidly check “What if...?” speculations that run through your head as you work toward a solution to the structure, instead of flipping back and forth among different spectra. The columns are listed in an order you might find useful. First tabulate all of the carbon shifts and then solve their substructure using the DEPT. Use the HETCOR/HSQC to connect the protons with their carbon atoms and then complete all of the spin systems using the COSY, splicing together the protons and carbons at the same time. The final step connects the spin systems through quaternary centers and across heteroatoms using the HMBC. There are still important questions left unanswered, such as stereochemical features and 3D spatial proximity of uncoupled protons. Experiments like NOESY and ROESY can answer these, but are beyond our simplistic, simulated approach. There’s always something more to learn.

In actual structure problems, the spectral information is arranged as follows: MS information to help decide a molecular formula and the degrees of unsaturation, an IR spectrum to provide hints about which functional groups are present and the NMR data: 1H NMR, ^{13}C /DEPT, COSY, HETCOR and HMBC to fully solve the structures.

Data worksheet

^{13}C	DEPT structural unit	HETCOR	COSY	HMBC, NOE, other	^1H fragments from ^1H NMR

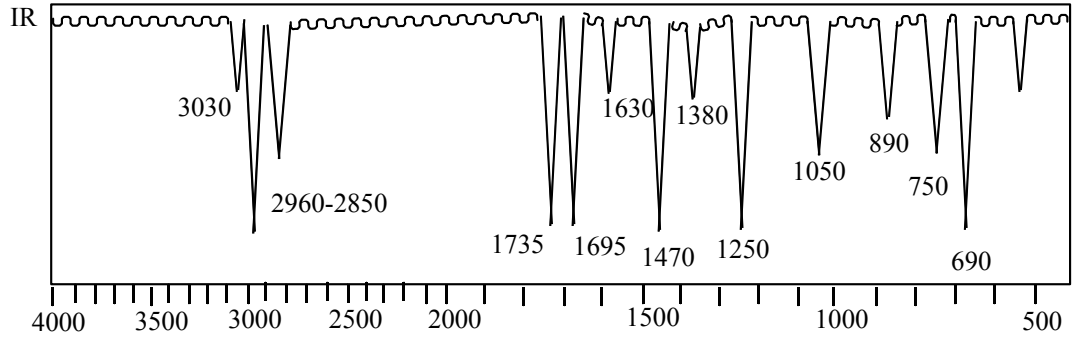
Example problem - Predict a reasonable structure from the spectral information provided below. As much as possible match the spectral information to the part of the structure that it explains. Show all of your work.

MW and IR Spectrum: Interpret as fully as possible from structure. Not every peak is interpretable. (units = cm^{-1})

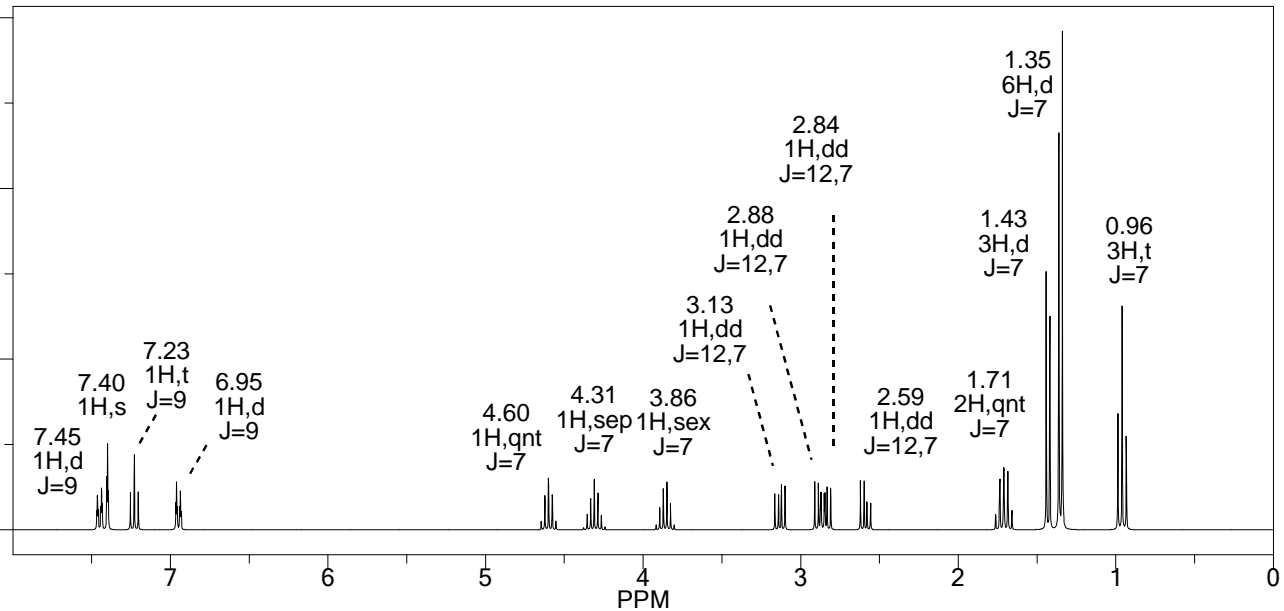
mass spec data
(exact mass)

MW = 384.1

M+ = 100%
M+1 = 19.9%
M+2 = 97.3%
M+3 = 18.9%

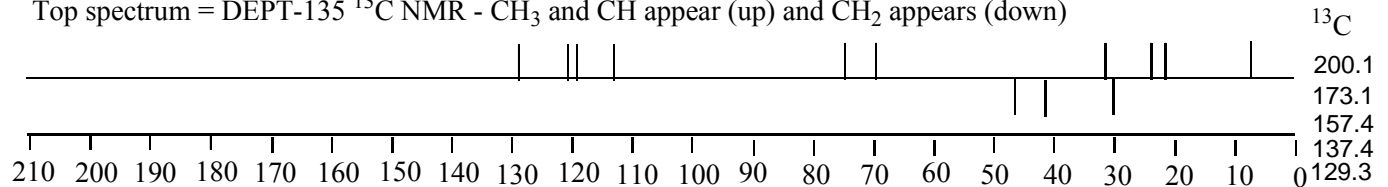


Proton NMR: interpret data (calculate chemical shifts to confirm they match actual values, N = # neighbors)

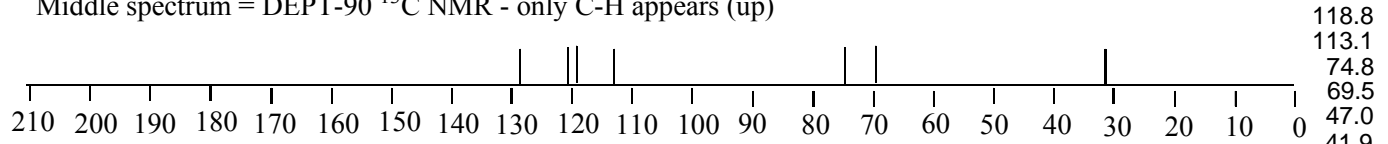


^{13}C and DEPT NMR: As much as possible match the ^{13}C peaks to carbons in your structure.

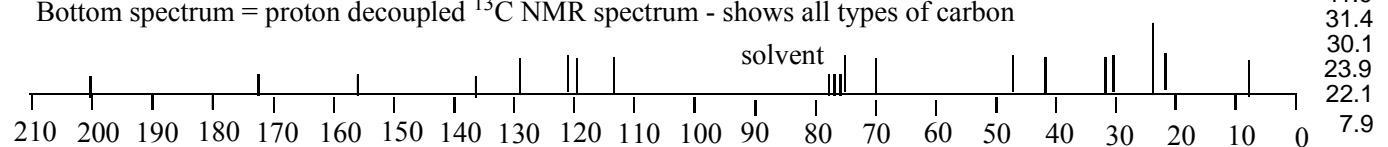
Top spectrum = DEPT-135 ^{13}C NMR - CH_3 and CH appear (up) and CH_2 appears (down)

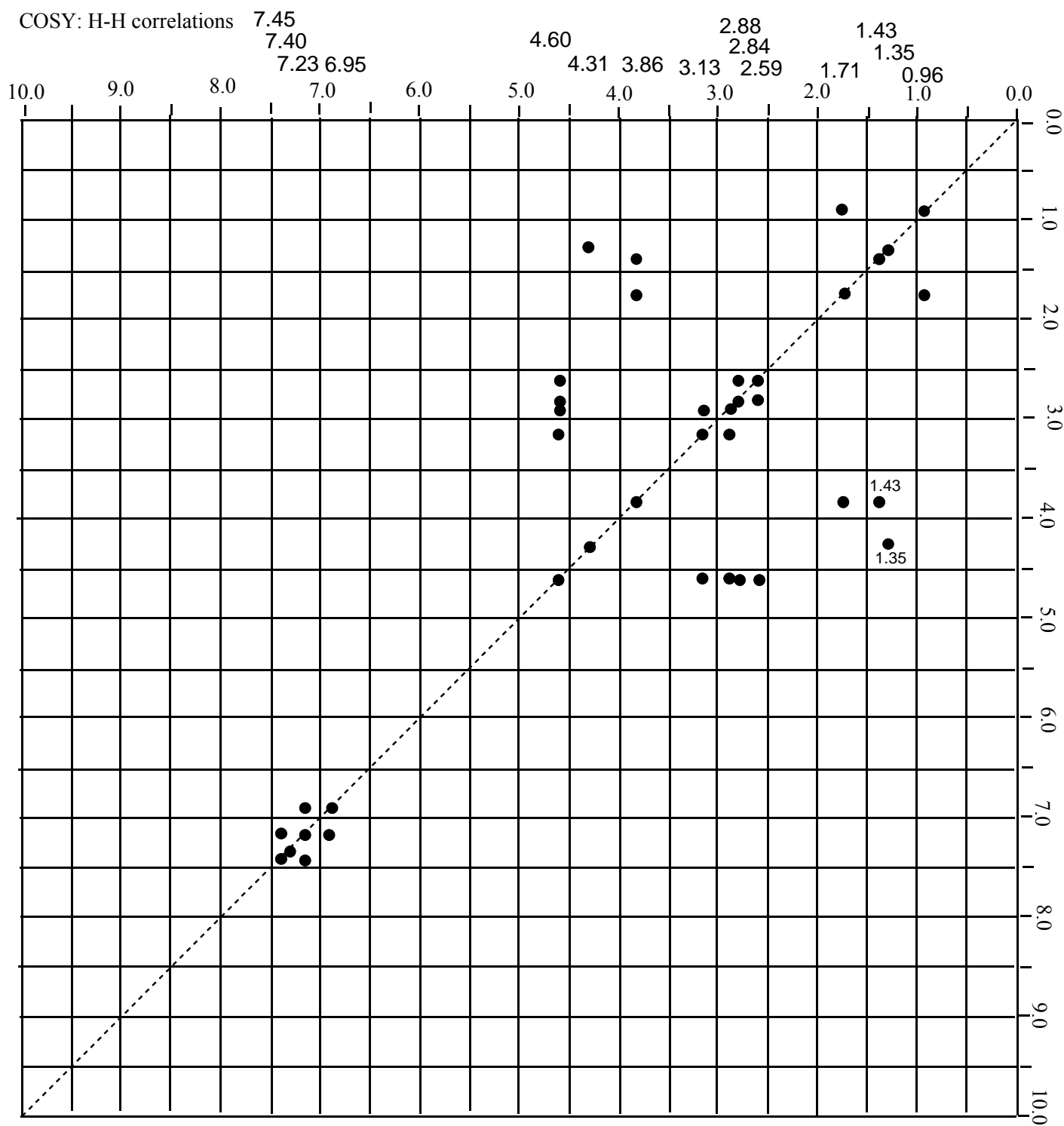


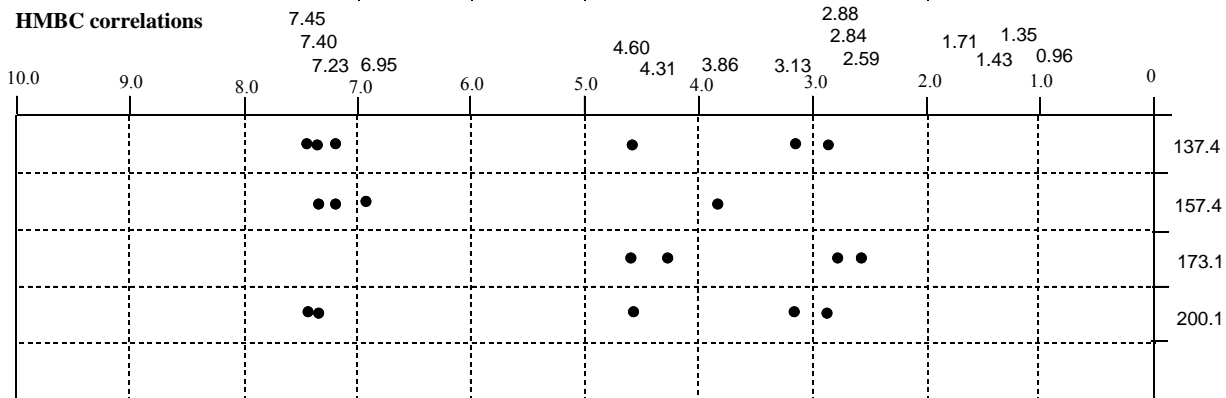
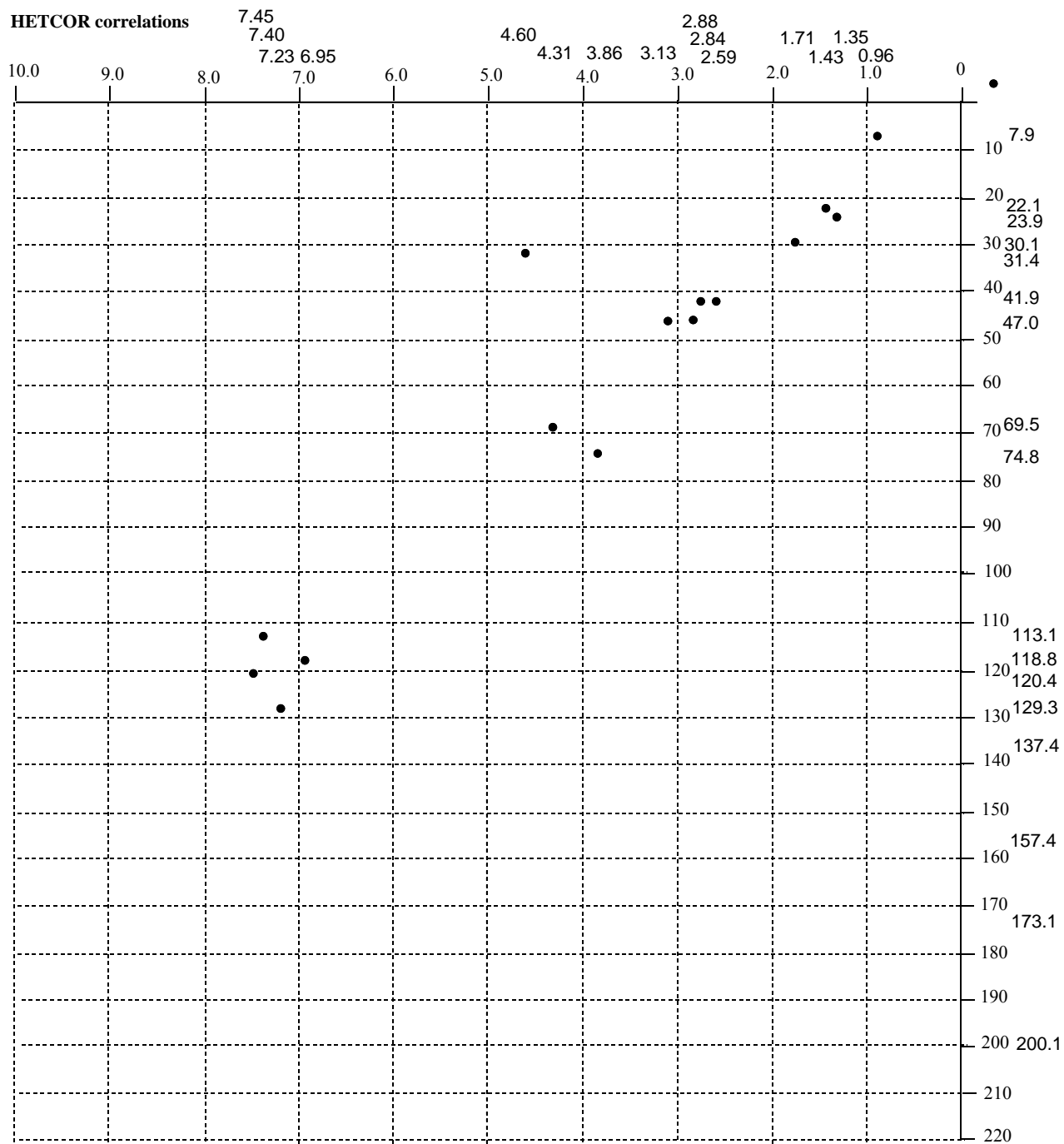
Middle spectrum = DEPT-90 ^{13}C NMR - only C-H appears (up)



Bottom spectrum = proton decoupled ^{13}C NMR spectrum - shows all types of carbon







Don't look at the answer until you try to solve the structure. An ideal answer would look as follows.

Solve for a molecular formula and degrees of unsaturation.

M+ and M+2 peaks are approximately equal so there is one Br present.

The M+1 peak divided by 1.1 = $19.9/1.1 = 18$ = approximate number of carbon atoms.

The proton NMR shows 25 protons and the ^{13}C NMR shows 18 carbon atoms (confirms MS data).

This all totals to $79 + 25 + 216 = 320$ grams

Residual mass = (total mass) - (320) = $384 - 320 = 64$.

This indicates four oxygen atoms so the formula is $\text{C}_{18}\text{H}_{25}\text{BrO}_4$

2 points

Degrees of unsaturation = $[(2 \times 18 + 2) - (26)] / 2 = 12/2 = 6$

Examination of the ^{13}C NMR shows six =C carbons (3 C=C bonds) and two C=O bonds (total of 5 pi bonds), so the number of rings = (total degrees of unsaturation) - (pi bonds) = $6 - 5 = 1$ ring

IR data:

3030 = sp^2 CH stretch, 1630 = (C=C), 890, 750, 690 possible meta substituted aromatic ring

2960-2850 = sp^3 CH stretch, 1470, 1380 CH bend

1735 = probable ester C=O, 1250 = acyl C-O 1050 = alkoxy C-O

2 points

Tabulated 2D NMR Information

^{13}C	DEPT	HETCOR	COSY	HMBC
200.1	C=O	none	none	7.45 7.40 4.60 3.13,2.88
173.1	O-C=O	none	none	4.60 4.31 2.84,2.59
157.4	=C-O	none	none	7.40 7.23 6.95 3.86
137.4	=C-	none	none	7.45 7.40 7.23 4.60 3.13,2.88
129.3	=C-H	7.23	7.45 6.95	
120.4	=C-H	7.45	7.23	
118.8	=C-H	6.95	7.23	
113.1	=C-H	7.40	none	
74.8	O-CH	3.86	1.71 1.43	
69.5	O-CH	4.31	1.35	
47.0	CH2	3.13,2.88	4.60, gem	
41.9	CH2	2.84,2.59	4.60, gem	
31.4	Br-CH	4.60	3.13,2.88 2.84,2.59	
30.1	CH2	1.71	3.86 0.96	
23.9	CH3	1.35	4.31	
22.1	CH3	1.43	3.86	
7.9	CH3	0.96	1.71	

2 points

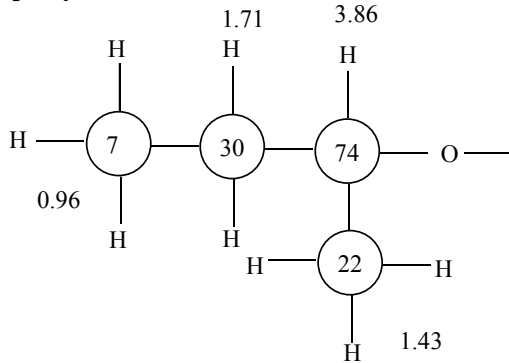
2 points

2 points

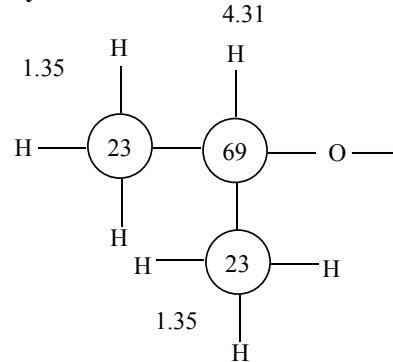
2 points

Connect proton spin systems using the COSY, which also connects the carbon atoms they are attached to from the HETCOR/HSQC. (2 points)

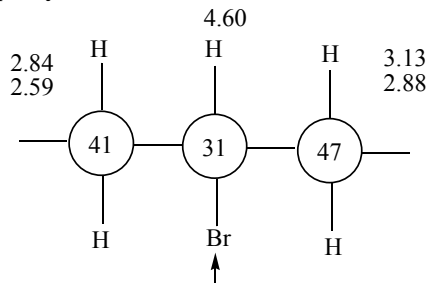
spin system 1



spin system 2

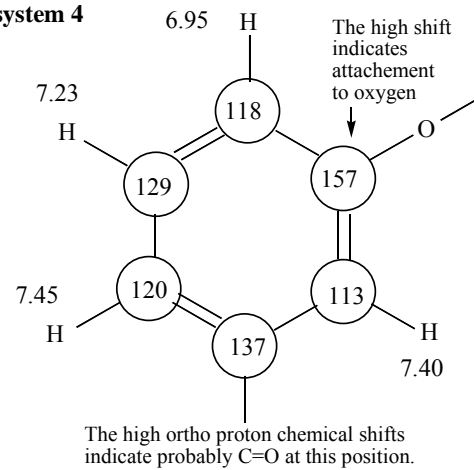


spin system 3

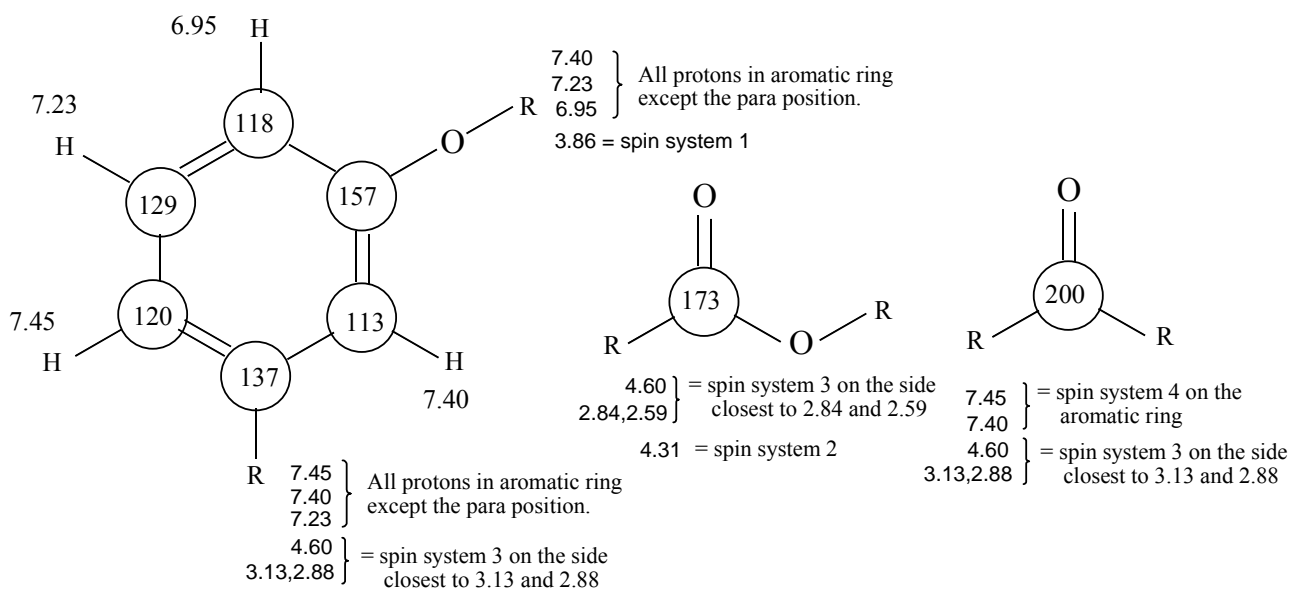


The low carbon shift and high proton shift indicate the Br is here.

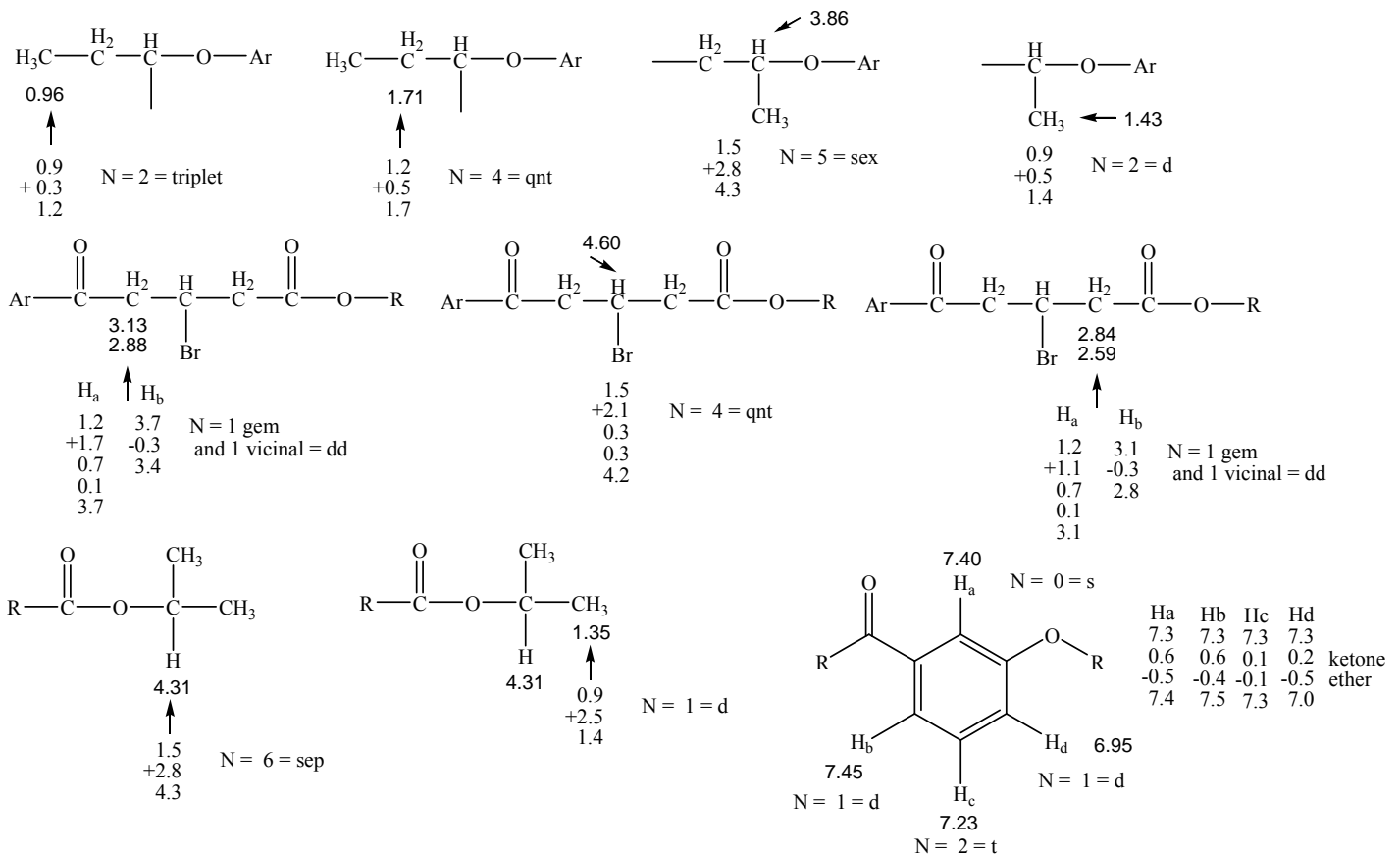
spin system 4



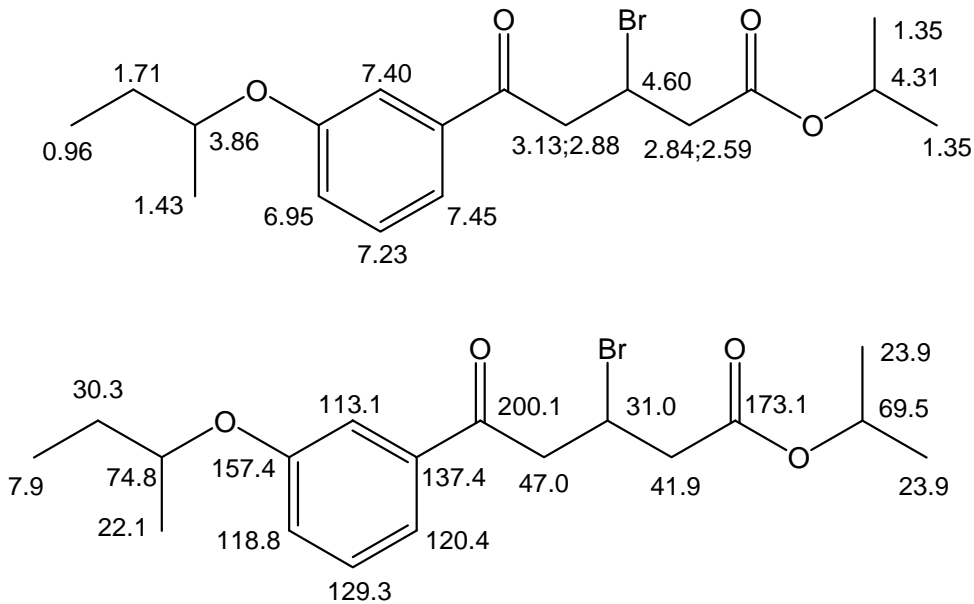
Use the HMBC to see what protons (and their spin systems) are close to any quaternary carbons. (2 points)



Interpretation of Proton NMR Data (4 points)



The actual structure is:



$C_{18}H_{25}BrO_4$
 Exact Mass: 384.09
 $M^+ = 384.09$ (100.0%),
 $M+1 = 385.10$ (19.9%),
 $M+2 = 386.09$ (97.3%),
 $M+3 = 387.09$ (18.9%),

correct structure

4 points

Total = 24 points