^{1}H and ^{13}C NMR Material

(Chem 318, 319, 422, 424)

Beauchamp

(updated 9-14-10)

Nuclear Magnetic Resonance (NMR): ^{1}H = proton NMR and ^{13}C = carbon-13 NMR

^{1}H-NMR

Provides information on:

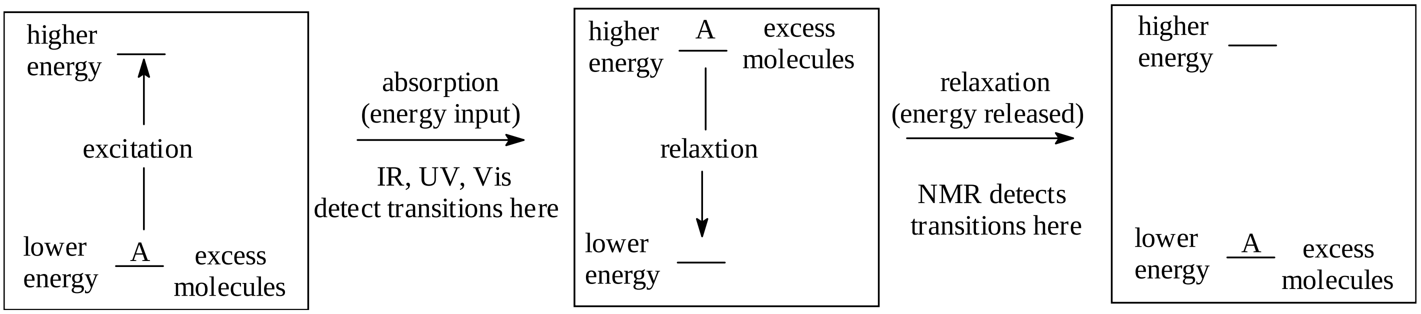
1. The types of protons present (δ = chemical shift is given in parts per million, the usual range = 0-10 ppm, a few chemical shifts extend to 10-15 ppm).
2. The number of such protons (integration counts the relative numbers of hydrogen atoms as a ratio by summing the area under the peaks).
3. How many neighbor protons are immediately adjacent to a specific center.
    a. splitting patterns = multiplicity = number of peaks (singlet, doublet, triplet, quartet, quintet, etc.) can indicate how many neighbor protons there are. When simple (first order) the number of peaks is one more than the number of neighbors (N+1 rule). When complicated (second order) the appearance of the peaks is hard to interpret.
    b. J values = coupling constants (distance in Hz that peaks are separated, given in frequency units, Hz = cycles per second).

^{13}C-NMR

Provides information on:

1. The types of carbon atoms present (chemical shift is given in parts per million, the usual range = 0-250 ppm).
2. The number of distinct kinds of carbon atoms present equals the number of peaks in proton decoupled 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 four ^{13}C experiments with different mixing of proton coupling to display CH, CH_2 or CH_3'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 (coupling between protons and carbons shows up in a multiplicity of a ^{13}C peak as a singlet, doublet, triplet or quartet "= N+1 rule"). This is an old fashioned method that is seldom used anymore, but much simpler to understand.

As in other spectroscopy, detection is due to energy transitions. In NMR, the detection is observed in the relaxation of the excited state. The transitions in NMR are of very low energy (radiowaves). They are a result of two magnetic quantum states resulting from the spin of nuclear particles (protons and/or neutrons) in the presence of a magnetic field.



Energy = Electromagnetic Radiation

	ultraviolet	visible	infrared	radiowave
$\Delta E \left(\frac{\text{kcal}}{\text{mole}}\right)$	100	40	10	0.000006
ν (frequency) (per sec. = Hz)	10^{15}	10^{15}	10^{14}	**10^{7}** **NMR**
λ (wave length) (nm)	**300** **UV**	**600** **VIS**	3000	20,000,000,000 (20m)
$\bar{\nu} = (1/\lambda)$ (cm^{-1}, wavenumber)	30,000	17,000	**3300** **IR**	0.0005

Bold units are "typical" units for that spectrocsopic method.

ΔE = energy ν = frequency λ = wavelength $\bar{\nu}$ = wavenumber

$\Delta E = h\nu = hc(1/\lambda) = hc\bar{\nu}$ $c = (\nu)(\lambda) = 3.0 \times 10^{8}$ m/sec $= 3.0 \times 10^{10}$ cm/sec

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

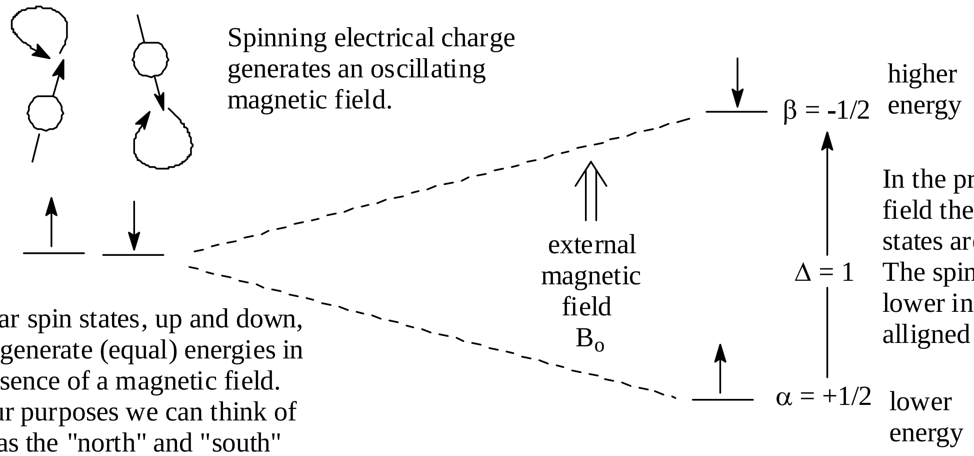
"I" is the spin quantum number.

Number of Spin States = 2(I) + 1

In practice, I = 1/2 is the most commonly encountered spin state, which is the value for both ^{1}H and ^{13}C, the nuclei presented in this book. Other commonly used nuclei include N-15, P-31 and F-19. These are especially useful in biochemistry and pharmaceutical chemistry.

Number of spin states = 2(1/2) + 1 = 2 spin states for both proton and carbon nuclei

I = 1/2 = **^{1}H, ^{13}C**, ^{15}N, ^{19}F, ^{31}P,....(these are all observable on a typical broadband NMR)



Spinning electrical charge generates an oscillating magnetic field.

Nuclear spin states, up and down, are degenerate (equal) energies in the absence of a magnetic field. For our purposes we can think of these as the "north" and "south" poles of a magnet.

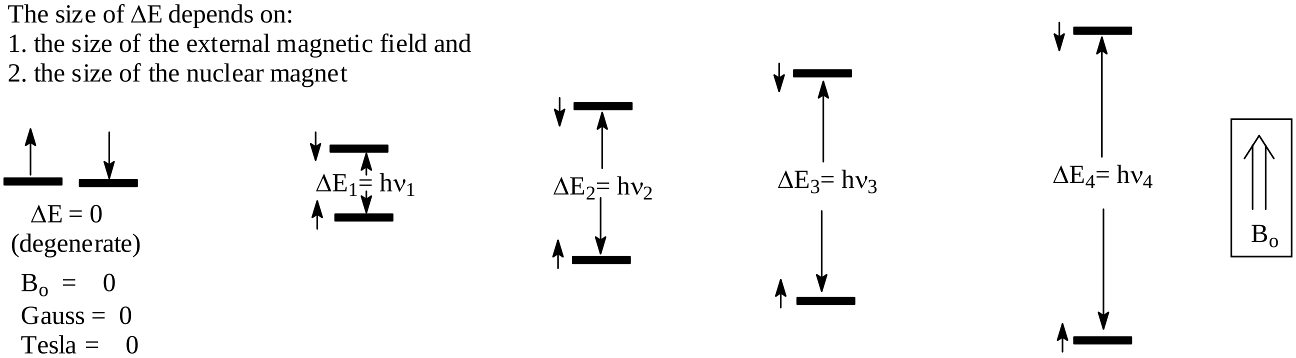
In the presence of a magnetic field these two magnetic quantum states are different in energy. The spin aligned with the field is lower in energy than the spin alligned against the field.

Some nuclei only have one spin state. We are fortunate that most of carbon is isotope ^{12}C and most of oxygen is isotope ^{16}O. Both have and even number of protons and neutrons and are magnetically invisible. This greatly simplifies our interpretation of routine ^{1}H and ^{13}C NMR spectra.

I = 0 = ^{12}C, ^{16}O, = no magnetic moment (magnetically invisible)

The two magnetically degenerate energy states become split in the presence of an external magnetic field. We can stimulate energy transitions between these two energy states (ΔE) via an input of radiowaves. Most NMR instruments describe ΔE in MHz based on a proton nucleus.

The size of ΔE depends on:
1. the size of the external magnetic field and
2. the size of the nuclear magnet



B_o = 0

Size of external magnetic field ⇒					
Gauss =	0	14,100	23,500	70500	176,300
Tesla =	0	1.4	2.4	7.1	17.7
ν_H(MHz) =	0	60*	100*	300*	750*
		Original commercial instrument (1960)	Largest solid core electromagnetic	Our Instrument cost (1990) $220,000	Largest known instrument (2004) about 1000 MHz = 1 Giga Hz cost? probably $ millions

M = mega = 1,000,000 = 10^6

* assumes a proton nucleus

The ΔE between the energy states depends on two magnets:

a. the external field = B_o (This is what you buy when purchasing the instrument.)
b. the nuclear magnet = γ_i (γ_{1H}, γ_{13C},..),(This is the nucleus observed when a sample is placed in the instrument.)

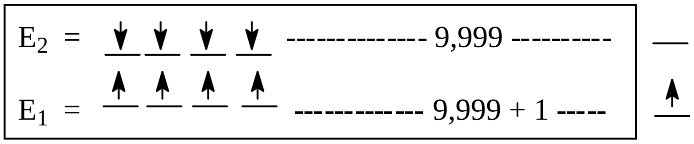
Relative Boltzman Energy Populations (protons)

Because ΔE is very small in NMR transitions, there is not much of a difference in the populations of the two energy states.

300 MHz – a bigger magnetic field and a bigger energy difference

$$\frac{N_2}{N_1} = \exp^{-\left(\frac{\Delta E}{RT}\right)} = \exp^{-\left(\frac{(0.028\ \text{cal / mole})}{(1.98\ \text{cal / mol-K})(289\ \text{K})}\right)} = \frac{0.99995}{1.00000}$$

N_i = number of nuclei in a particular energy state.

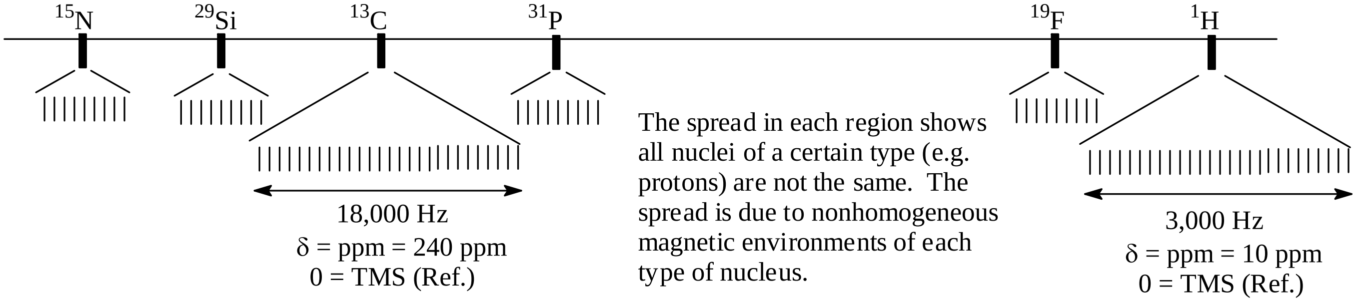


We see a difference of 1 out of about 20,000 because of ΔE. This is the signal we detect, but, the population levels are essentially 50/50.

The NMR Radio Dial

The energy difference (ΔE) of a 300 MHz NMR instrument is in the radiowave region of the electromagnetic spectrum. Think of the other nuclei as appearing at different positions on your radio dial and γ_i as the number you tune into. You can tune in a nuclei, like you tune in a radio station.

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



The spread in each region shows all nuclei of a certain type (e.g. protons) are not the same. The spread is due to nonhomogeneous magnetic environments of each type of nucleus.

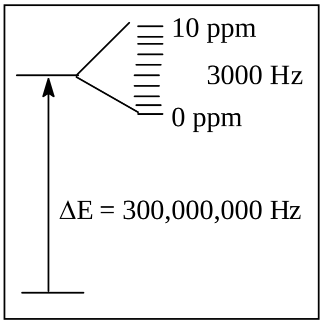
Protons

1 ppm depends on B_o (size of external magnetic field, 1 / 1,000,000 of ΔE of ν in Hz)

$$\frac{1}{1,000,000} \text{ x } (300,000,000 \text{ Hz}) = 300 \text{ Hz} = 1 \text{ ppm}$$

B_o	1.0 ppm (= Hz)
60 MHz	60 Hz
100 MHz	100 Hz
300 MHz	300 Hz
600 MHz	600 Hz

The range of differences in chemical shifts (about 3000 Hz = 10 ppm) is only a small portion of the total energy to cause a proton to flip (about 300,000,000 Hz = 300 MHz) on a 300 MHz instrument.



Most protons are detected within a 10 ppm range of the entire ΔE of excitation.

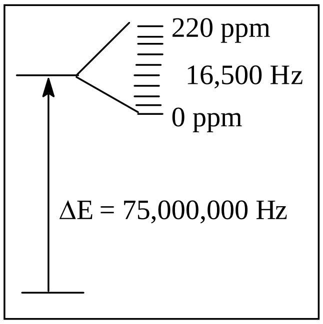
Carbon-13 - (μ_{13C}) = 1/4 x (μ_{1H}) in the same external magnetic field (the carbon magnet = 1/4 the proton magnet)

1 ppm depends on B_o (size of external magnetic field, 1 / 1,000,000 of ΔE of ν in Hz)

$$\frac{1}{1,000,000} \text{ x } (75,000,000 \text{ Hz}) = 75 \text{ Hz} = 1 \text{ ppm}$$

B_o	1.0 ppm (= Hz)
15 MHz	15 Hz
25 MHz	25 Hz
75 MHz	75 Hz
150 MHz	150 Hz

The range of differences in chemical shifts (about 16,500 Hz = 220 ppm) is only a small portion of the total energy to cause a carbon to flip (about 75,000,000 Hz = 75 MHz) on a 75 MHz instrument. The differences among the carbons is wider than the differences among the protons in ppm (greater dispersion).



Most ^{13}Cs are detected within a 220 ppm range of the entire ΔE of excitation.

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

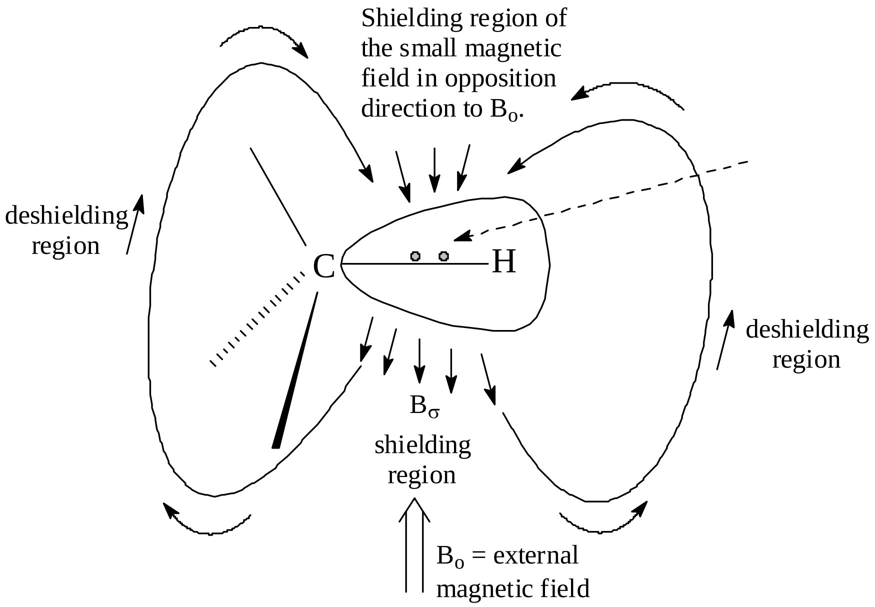
1. Electronegativity Effects

Some typical chemical shifts for methyl groups attached to different atoms are shown below. Clearly there is some sort of electronegativity effect working.

	CH_3-F	CH_3-OR	CH_3-Cl	CH_3-Br	CH_3-I	CH_3-H	$(CH_3)_4$Si = TMS
chemical shift (δ) =	4.27ppm	3.39ppm	3.06ppm	2.69ppm	2.16ppm	0.23ppm	0.0ppm

zero by definition = relative reference point for both hydrogen and carbon NMR.

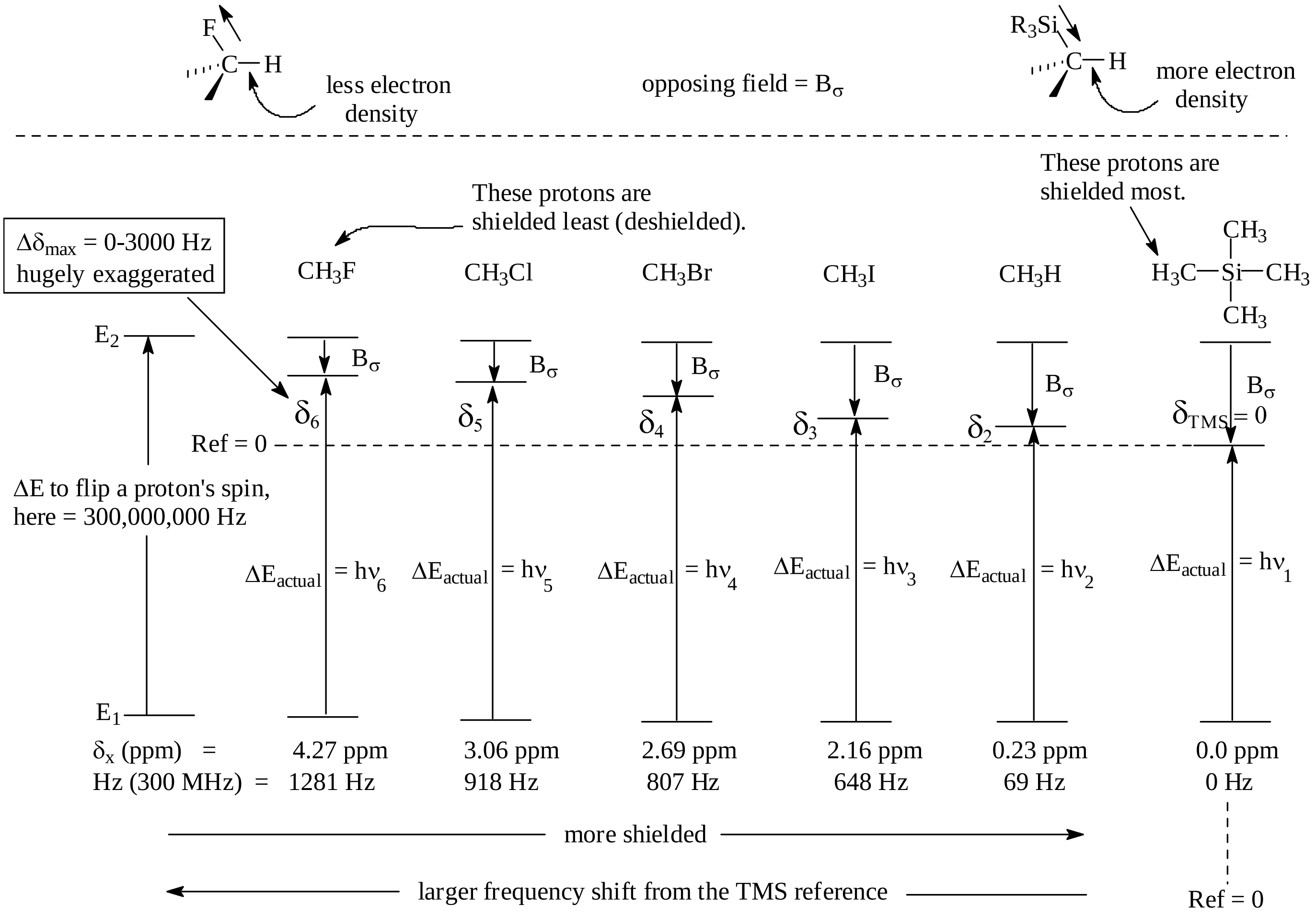
Electrons moving in chemical bonds create their own small opposition magnetic field to the external magnetic field. The more electron density there is, the stronger is this opposition field. Any nearby electron withdrawing groups can steal some of this electron density away from sigma bonds with protons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

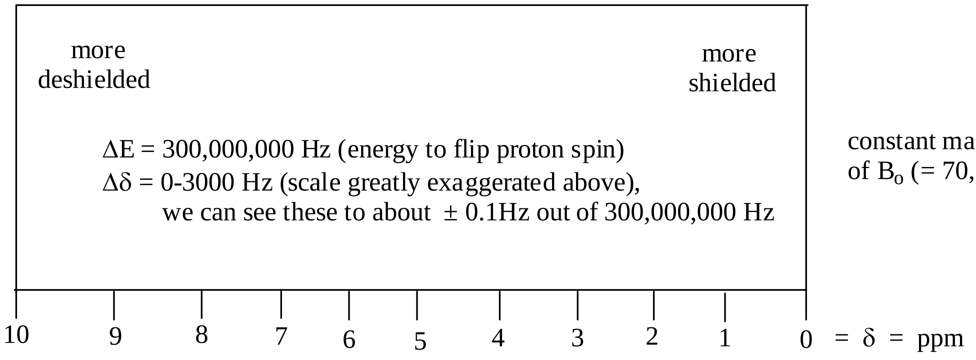


Sigma, σ, is a shielding constant that includes a variety of factors that change the energy of transition of nuclei. Diamagnetic shielding is most important for spherical shapes, like the proton (1s orbital), but paramagnetic shielding becomes important when electrons are in orbitals that are not spherical, like carbon-13 (2p orbitals). We will not discuss this aspect, except to point out that this weak shielding effect produces a small variable reduction in the size of the external field, B_o, and produces a net effective field, B_{net}, because of shielding by electrons. Differences in σ lead to differences in the chemical shifts of protons in H-NMR (or differences in carbon shifts in ^{13}C NMR).

Because the electronegativity of silicon is less than carbon, the carbon and the protons are more electron rich, thus more shielded than in routine organic compounds. The peak for both carbon and hydrogen in TMS is far to the right of most signals and defined as “zero” parts per million.

Differences in proton chemical shifts (due to electronegativity or inductive effects)



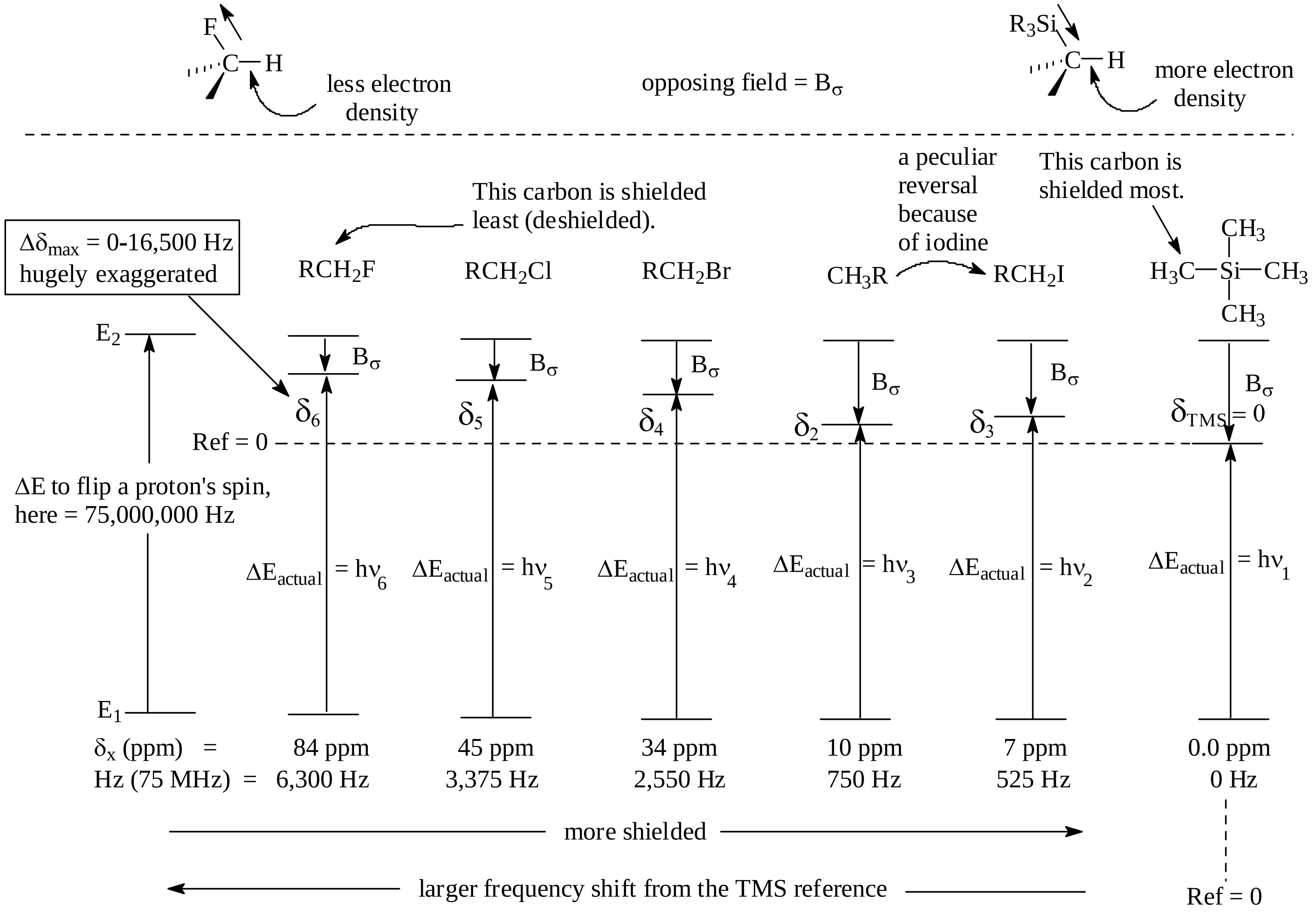


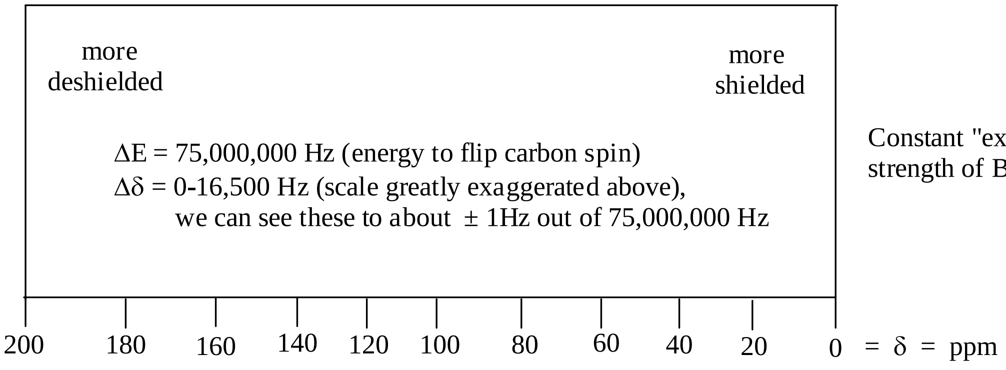
ΔE = 300,000,000 Hz (energy to flip proton spin)

Δδ = 0-3000 Hz (scale greatly exaggerated above),
we can see these to about ± 0.1Hz out of 300,000,000 Hz

constant magnetic field strength of B_o (= 70,500 gauss) assumed

Differences in carbon chemical shifts (due to electronegativity or inductive effects)



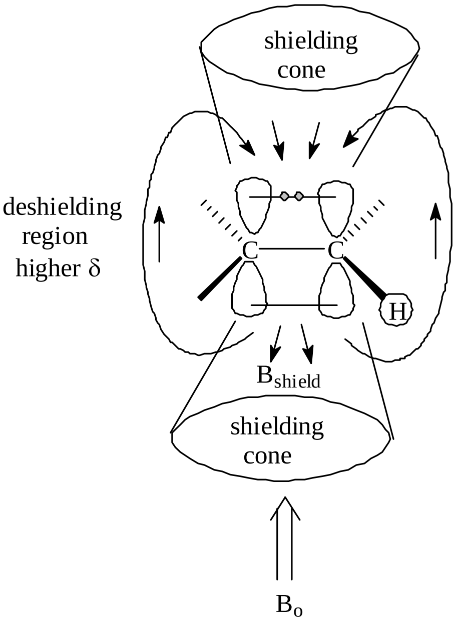


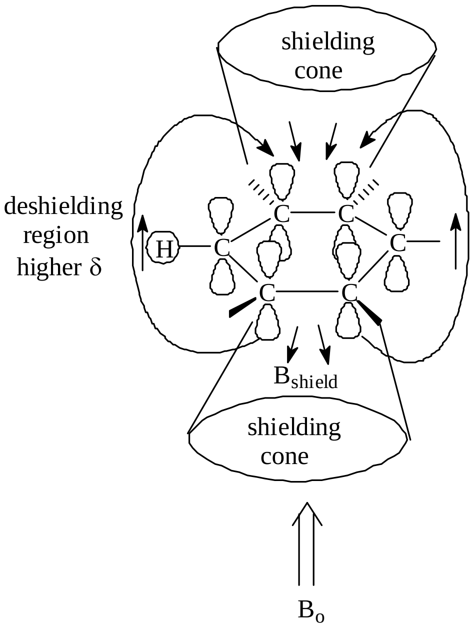
Constant "external" magnetic field strength of B_o (= 70,500 gauss) assumed.

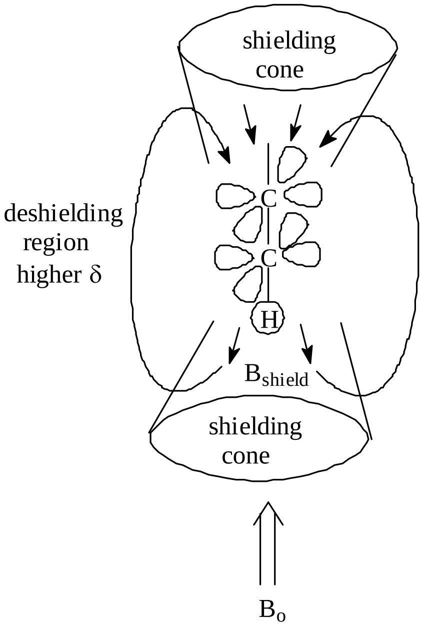
2. π bond anisotropy = a second type of effect causes changes in local magnetic environments

Certain molecule orientations (relative to B_o) add and others cancel relative to the external magnetic field. The molecules are tumbling and changing orientations to B_o on the order of 10^8-10^{12} times per second (how fast depends on the size, shape, solvent viscosity, temperature, etc.) The net *contributing* orientations are shown below for pi systems (alkenes, aromatics and terminal alkynes).

π bond anisotropy: certain orientations (relative to B_o) add, others cancel with a net contribution of what is shown in the following diagrams.







typical: alkene protons δ = 4-6 ppm

aromatic protons δ = 7-8 ppm

terminal alkyne protons δ = 2-3 ppm

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 by a smaller amount because they are farther away.

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

Alkyne protons have a smaller δ than expected based on the greater electronegativity of an sp orbital, but the net orientation of the pi bonds causes the end of a triple bond to be shielded. Nitriles show similar effects.

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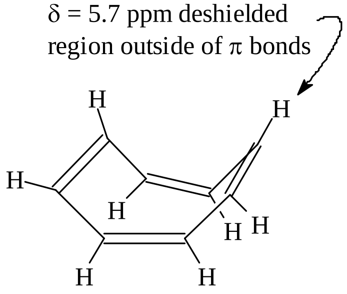
Examples

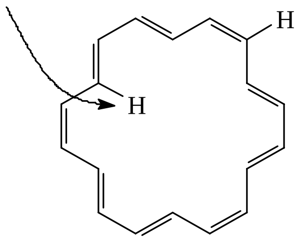
δ = 5.7 ppm deshielded region outside of π bonds



1,3,5,7-cyclooctatetrene
(a cycloalkene)

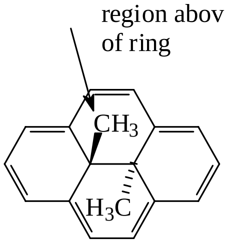
δ = -1.8 ppm highly shielded region inside of ring

δ = 8.9 ppm deshielded region outside of ring



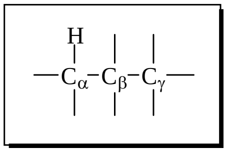
[18]-annulene
(aromatic)

δ = - 4.2 ppm highly shielded region above and inside of ring



trans-10b,10c-dimethyldihydropyrene

Calculation of chemical shifts for protons at sp^3 carbons



Estimation of sp^3 C-H chemical shifts with multiple substituent parameters for protons within 3 C's of consideration.

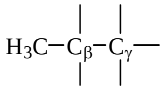
α = directly attached substituent, use these values when the hydrogen and substituent are attached to the same carbon
β = once removed substituent, use these values when the hydrogen and substituent are on adjacent (vicinal) carbons
γ = twice removed substituent, use these values when the hydrogen and substituent have a 1,3 substitution pattern

X = substituent	α	β	γ
R- (alkyl)	0.0	0.0	0.0
R_2C=CR- (alkenyl)	0.8	0.2	0.1
RCC- (alkynyl)	0.9	0.3	0.1
Ar- (aromatic)	1.4	0.4	0.1
F- (fluoro)	3.2	0.5	0.2
Cl- (chloro)	2.2	0.5	0.2
Br- (bromo)	2.1	0.7	0.2
I- (iodo)	2.0	0.9	0.1
HO- (alcohol)	2.3	0.3	0.1
RO- (ether)	2.1	0.3	0.1
epoxide	1.5	0.4	0.1
R_2C=CRO- (alkenyl ether)	2.5	0.4	0.2
ArO- (aromatic ether)	2.8	0.5	0.3
RCO_2- (ester, oxygen side)	2.8	0.5	0.1
$ArCO_2$- (aromatic ester, oxygen side)	3.1	0.5	0.2
$ArSO_3$- (aromatic sulfonate, oxygen)	2.8	0.4	0.0
H_2N- (amine nitrogen)	1.5	0.2	0.1
RCONH- (amide nitrogen)	2.1	0.3	0.1
O_2N- (nitro)	3.2	0.8	0.1
HS- (thiol, sulfur)	1.3	0.4	0.1
RS- (sulfide, sulfur)	1.3	0.4	0.1
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_2C- (carboxylic acid)	1.1	0.3	0.1
RO_2C- (ester, carbon side)	1.1	0.3	0.1
H_2NOC- (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
RSO- (sulfoxide)	1.6	0.5	0.3
RSO_2- (sulfone)	1.8	0.5	0.3

Starting value and equations for CH_3's

$\delta\, CH_3 = 0.9 + \alpha$ $H_3C—\alpha$

$\delta\, CH_3 = 0.9 + \Sigma(\beta + \gamma)$

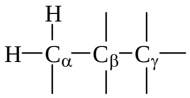


Σ is the summation symbol for all substituents considered

Starting value and equation for CH_2's

In a similar manner we can calculate chemical shifts for methylenes (CH_2) using the following formula

$\delta\, CH_2 = 1.2 + \Sigma(\alpha + \beta + \gamma)$

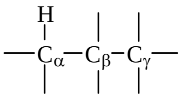


Σ is the summation symbol for all substituents considered

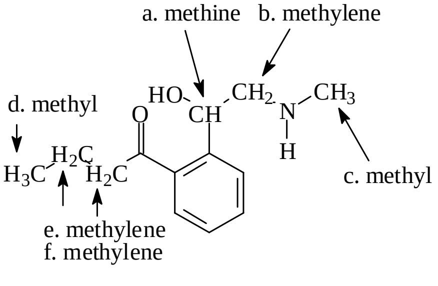
Starting value and equation for CH's

In a similar manner we can calculate chemical shifts for methines (CH) using the following formula

$\delta\, CH = 1.5 + \Sigma(\alpha + \beta + \gamma)$



Σ is the summation symbol for all substituents considered



Calculations are generally close to actual chemical shifts for a single substituent, but are less reliable as the number of substituent factors goes up. Multiple substituent factors tend to overestimate an actual chemical shift.

a. methine = $1.5 + (1.4)_\alpha + (2.3)_\alpha + (0.2)_\beta = 5.4$ ppm
actual = 5.2

b. methylene = $1.2 + (1.5)_\alpha + (0.4)_\beta + (0.3)_\beta = 3.4$ ppm
actual = 3.0 and 3.2

c. methyl = $0.9 + (1.5)_\alpha = 2.4$ ppm
actual = 2.6

d. methyl = $0.9 + (0.1)_\alpha = 1.0$ ppm
actual = 1.0

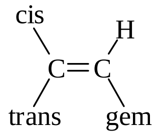
e. methylene = $1.2 + (0.3)_\alpha = 1.5$ ppm
actual = 1.7

f. methylene = 1.2. + $(1.7)_\alpha = 2.9$ ppm
actual = 2.9

Estimated chemical shifts for protons at alkene sp^2 carbons

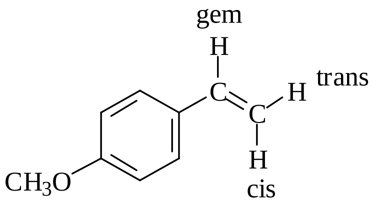
Substituent	$\alpha_{geminal}$	α_{cis}	α_{trans}
H- Hydrogen	0.0	0.0	0.0
R- Alkyl	0.5	-0.2	-0.3
$C_6H_5CH_2$- Benzyl	0.7	-0.2	-0.2
X-CH_2- Halomethyl	0.7	0.1	0.0
(H)/ROCH_2- alkoxymethyl	0.6	0.0	0.0
$(H)_2/R_2NCH_2$- aminomethyl	0.6	-0.1	-0.1
RCOCH_2- α-keto	0.7	-0.1	-0.1
NCCH_2- α-cyano	0.7	-0.1	-0.1
R_2C=CR- Alkenyl	1.2	0.0	0.0
C_6H_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- akoxy (ether)	1.2	-1.1	-1.2
RCO_2- O-ester	2.1	-0.4	-0.6
$(H)_2/R_2N$- N-amino	0.8	-1.3	-1.2
RCONH- N-amide	2.1	-0.6	-0.7
O_2N- Nitro	1.9	1.3	0.6
RS- Thiol	1.1	-0.3	-0.1
OHC- Aldehyde	1.0	1.0	1.2
ROC- Ketone	1.1	0.9	0.7
HO_2C- C-acid	0.8	1.0.	03
RO_2C- C-ester	0.8	1.0	0.5
H_2NOC- C-amide	0.4	1.0	0.5
NC- Nitrile	0.3	0.8	0.6

Substitution relative to calculated "H"



δ(ppm) = 5.2 + α_{gem} + α_{cis} + α_{trans}

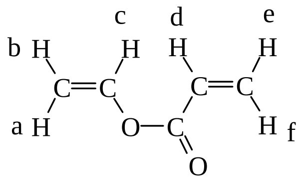
Example Calculation



δ gem = 5.2 + 1.4 = 6.6
actual = 6.6

δ trans = 5.2 - 0.1 = 5.1
actual = 5.1

δ cis = 5.2 + 0.4 = 5.7
actual = 5.6



δ_a = 5.2 + (-0.4) = 4.8
actual = 4.9 (J = 14, 1.6 Hz)

δ_b = 5.2 + (-0.6) = 4.6
actual = 4.6 (J = 6, 1.6 Hz)

δ_c = 5.2 + 2.1 = 7.3
actual = 7.4 (J = 14, 6 Hz)

δ_d = 5.2 + 0.8 = 6.0
actual = 6.2 (J = 18, 11 Hz)

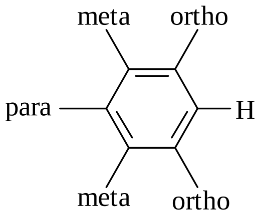
δ_e = 5.2 + 0.5 = 5.7
actual = 5.8 (J = 11, 1.4 Hz)

δ_f = 5.2 + 1.0 = 6.2
actual = 6.4 (J = 18, 1.4 Hz)

Estimated chemical shifts for protons at aromatic sp^2 carbons

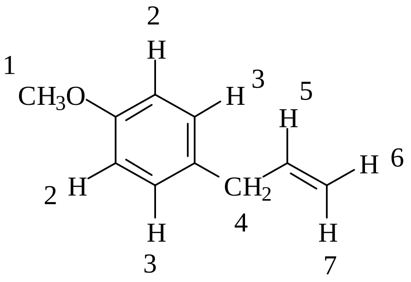
Substituent	α ortho	α meta	α para
H- Hydrogen	0.0	0.0	0.0
CH_3- Methyl	-0.2	-0.1	-0.2
$ClCH_2$- Cholromethyl	0.0	0.0	0.0
Cl_3C- Halomethyl	0.6	0.1	0.1
$HOCH_2$- Hydroxymethyl	-0.1	-0.1	-0.1
$R_2C{=}CR$- Alkenyl	0.1	0.0	-0.1
C_6H_5- Phenyl	1.4	0.4	-0.1
F- Fluoro	-0.3	0.0	-0.2
Cl- Chloro	0.0	0.0	-0.1
Br- Bromo	0.2	-0.1	0.0
I- Iodo	0.4	-0.2	0.9
HO- Hydroxy	-0.6	-0.1	-0.5
RO- Alkoxy	-0.5	-0.1	-0.4
RCO_2- O-ester	-0.3	0.0	-0.1
$(H)_2/R_2N$- N-amino	-0.8	-0.2	-0.7
RCONH- N-amide	0.1	-0.1	-0.3
O_2N- Nitro	1.0	0.3	0.4
RS- thiol/sulfide	-0.1	-0.1	-0.2
OHC- Aldehyde	0.6	0.2	0.3
ROC- Ketone	0.6	0.1	0.2
HO_2C- C-acid	0.9	0.2	0.3
RO_2C- C-ester	0.7	0.1	0.2
H_2NOC- C-amide	0.6	0.1	0.2
NC- Nitrile	0.4	0.2	0.3

Substitution relative to calculated "H"

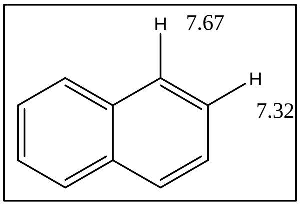


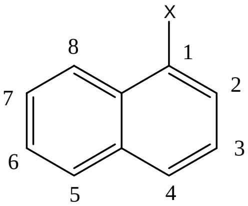
$$\delta(\text{ppm}) = 7.3 + \alpha_{\text{ortho}} + \alpha_{\text{meta}} + \alpha_{\text{para}}$$

Example Calculation



1. $\delta\ (CH_3) = 0.9 + 2.8 = 3.7$
   actual = 3.8
2. $\delta\ (2) = 7.3 + (-0.5)_{\text{ortho}} + (-0.1)_{\text{para}} = 6.7$
   actual = 6.8
3. $\delta\ (3) = 7.3 + (-0.2)_{\text{ortho}} + (-0.4)_{\text{para}} = 6.7$
   actual = 7.1
4. $\delta\ (CH_2) = 1.2 + (0.8)\alpha + (1.4)\alpha = 3.4$
   actual = 3.3
5. $\delta\ (5) = 5.2 + (0.7)_{\text{gem}} = 5.9$
   actual = 5.9
6. $\delta\ (6) = 5.2 + (-0.2)_{\text{trans}} = 5.0$
   actual = 5.1
7. $\delta\ (7) = 5.2 + (-0.2)_{\text{cis}} = 5.0$
   actual = 5.1

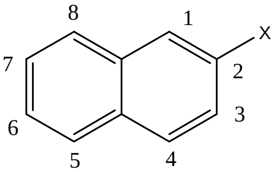




starting values for calculations:

H1, H4, H5, H8 = 7.67
H2, H3, H6, H7 = 7.32

Naphalene position	H-2	H-3	H-4	H-5	H-6	H-7	H-8
H hydrogen	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CH_3- (R-) methyl (alkyl)	-0.2	-0.1	-0.2	0.0	0.0	0.0	0.1
F- fluoro	-0.2	0.0	-0.1	0.1	0.1	0.2	0.4
Cl- chloro	0.2	0.0	0.0	0.1	0.1	0.2	0.5
Br- bromo	0.4	-0.1	0.0	0.0	0.1	0.2	0.5
I- iodo	0.1	-0.5	0.2	-0.2	-0.1	0.0	0.3
HO- hydroxy	-0.7	-0.2	-0.4	0.0	0.0	0.1	0.4
RO- alkoxy	-0.7	-0.1	-0.4	0.0	0.0	0.0	0.5
RCO_2- O-ester	-0.2	0.1	-0.1	0.0	-0.1	0.1	0.2
(H2) / R2N- amino	-0.8	-0.2	-0.5	-0.1	0.0	0.0	0.0
RCONH- N-amide	0.4	0.2	0.1	0.3	0.2	0.2	0.4
O_2N- nitro	0.8	0.1	0.2	0.3	0.2	0.3	0.7
NC- nitrile	0.5	0.1	0.3	0.2	0.2	0.3	0.5
OHC- aldehyde	0.4	0.1	0.2	0.1	0.1	0.2	1.5
RCO- ketone	0.4	-0.1	0.1	0.0	0.0	0.1	1.1
HO_2C- acid	1.1	0.2	0.4	0.2	0.2	0.3	1.4
RO_2C- C-ester	0.8	0.0	0.2	0.1	0.1	0.2	1.3
ClOC- acid chloride	1.2	0.2	0.4	0.2	0.2	0.3	1.0

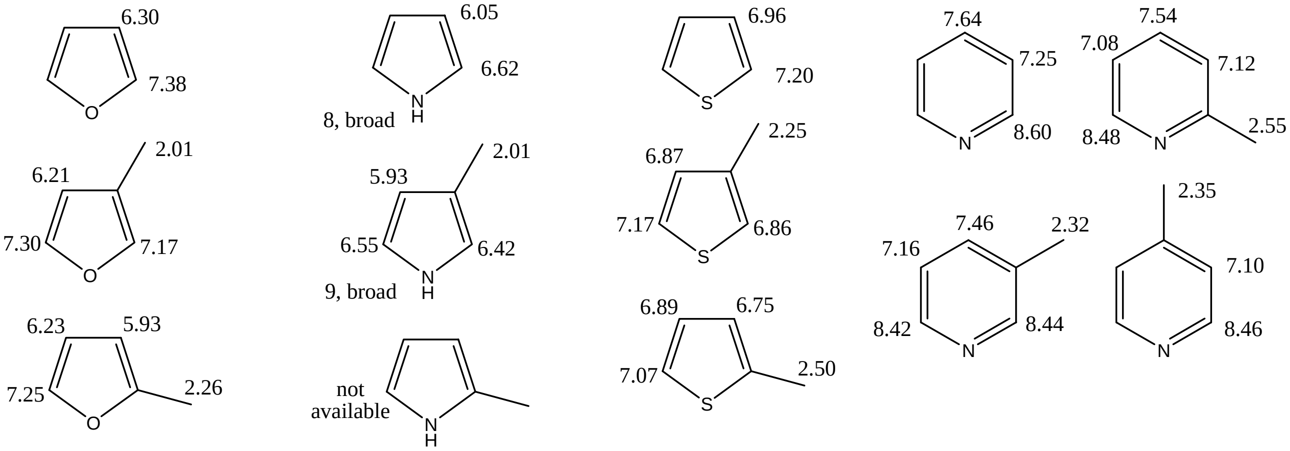


starting values for calculations:

H1, H4, H5, H8 = 7.67
H2, H3, H6, H7 = 7.32

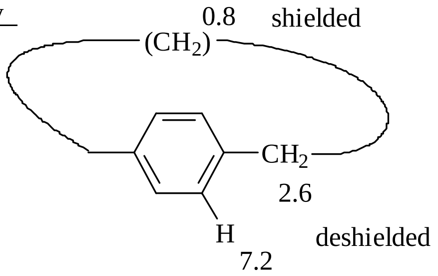
Naphalene position	H-1	H-3	H-4	H-5	H-6	H-7	H-8
H hydrogen	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CH_3- (R-) methyl (alkyl)	-0.2	-0.1	-0.1	0.0	0.0	0.0	0.0
F- fluoro	-0.4	-0.3	0.0	0.0	0.0	0.0	0.0
Cl- chloro	0.1	0.1	0.1	0.1	0.1	0.2	0.0
Br- bromo	0.2	0.1	-0.1	-0.1	0.1	0.1	0.1
I- iodo	0.1	-0.5	0.2	-0.2	-0.1	0.0	0.3
HO- hydroxy	-0.7	-0.3	0.0	0.0	-0.1	0.0	-0.1
RO- alkoxy	-0.7	-0.3	0.0	0.0	-0.1	0.0	-0.1
RCO_2- O-ester	-0.2	-0.1	0.0	0.1	0.0	0.1	0.1
(H2) / R2N- amino	-0.9	-0.6	-0.2	-0.1	-0.2	-0.1	-0.2
RCONH- N-amide	0.5	0.1	0.1	0.1	0.1	0.1	0.1
O_2N- nitro	1.0	0.8	0.2	0.2	0.3	0.2	0.3
NC- nitrile	0.5	0.2	0.2	0.2	0.3	0.3	0.2
OHC- aldehyde	0.6	0.6	0.2	0.2	0.3	0.2	0.3
RCO- ketone	0.8	-0.7	0.2	0.2	0.3	0.2	0.3
HO_2C- acid	1.0	0.7	0.4	0.4	0.4	0.3	0.5
RO_2C- C-ester	0.8	0.7	0.1	0.1	0.2	0.1	0.2
ClOC- acid chloride	1.0	0.7	0.4	0.5	0.3	0.4	0.4

Starting point chemical shifts for a few common heterocycles.

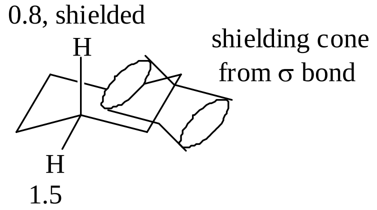


Real Examples of Combination Effects on Chemical Shifts

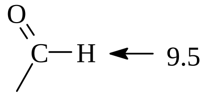
π bond anisotropy

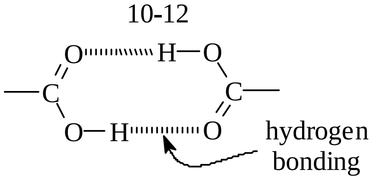


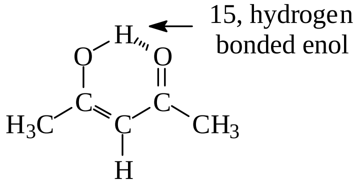
σ bond example too



electronegativity and π bond







electronegative substituent and distance from protons

$-O-CH_2CH_2CH_2CH_2CH_3$ — 3.6, 1.5, 1.3, 1.3, 0.9

CH_3-Cl — 3.0

CH_3CH_2-Cl — 1.3

$CH_3CH_2CH_2-Cl$ — 1.0

$CH_3CH_2CH_2CH_2-Cl$ — 0.9

CH_3CH_2-R — 0.9

multiple substituents

CH_4 CH_3Cl CH_2Cl_2 $CHCl_3$ CCl_4

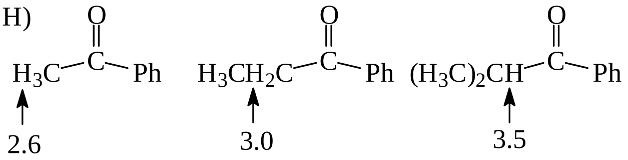
0.2 ← Δ = 2.8 → 3.0 ← Δ = 2.3 → 5.3 ← Δ = 1.9 → 7.2 ← Δ = ? → ? (oops)

substituents at methyl (CH_3), methylene (CH_2) and methine (CH)

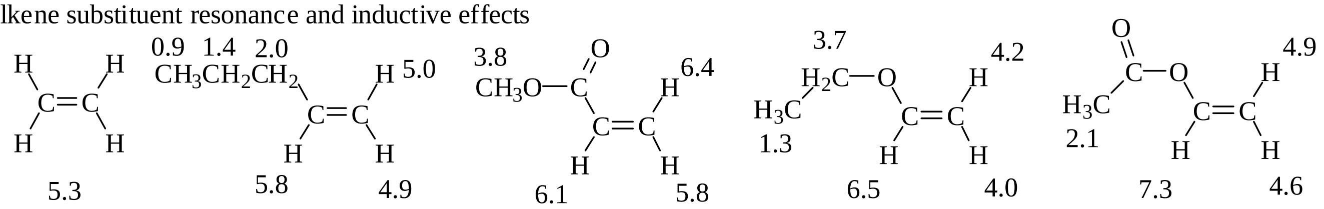
CH_3Cl — 3.0

CH_3CH_2Cl — 3.5

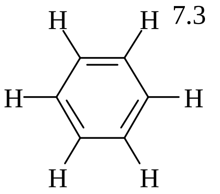
$(CH_3)_2CHCl$ — 4.1



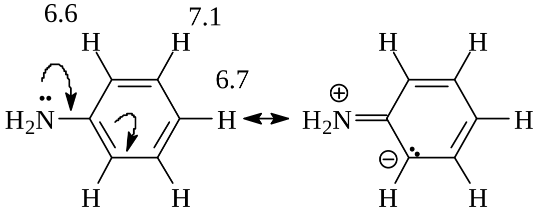
alkene substituent resonance and inductive effects



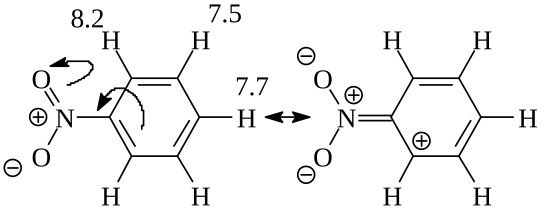
aromatic resonance and inductive effects



π bond anisotropy produces deshielding effect on aromatic protons.



Extra electron density via resonance produces shielding effect on aromatic protons, especially at ortho/para positions.



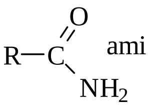
Withdrawal of electron density via resonance produces deshielding effect on aromatic protons, especially at ortho/para positions.

sp C-H

H—C≡C—H	2.4
R—C≡C—H	1.9
Ar—C≡C—H	3.0

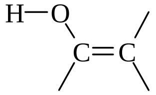
RO—H	alcohol H = 1-5
ArO—H	phenol H = 4-10
RS—H	thiol H = 1-2.5
ArS—H	aromatic thiol H = 3-4

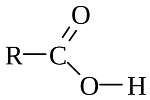
R_2N-H amine H = 1-5



amide H = 5-8

enol H = 10-17

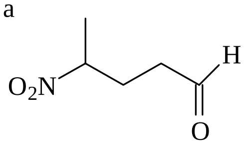




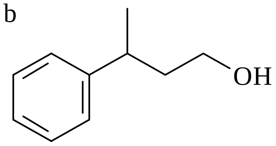
acid H = 10-13

Problem– Calculate the expected chemical shifts for the following protons attached to sp^3 carbon.

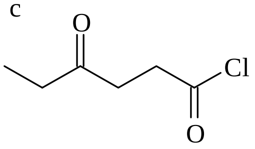
a



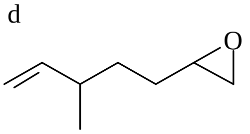
b



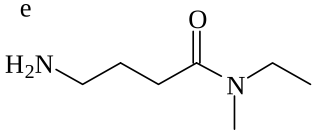
c



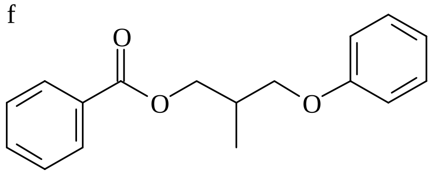
d



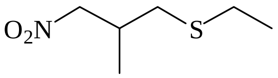
e



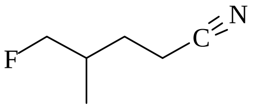
f



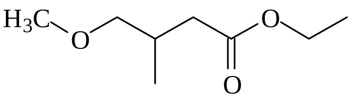
g



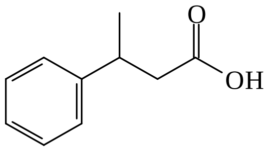
h



i



h



Problem

a. How many different isomers are there in C_5H_{12}? How many different types of hydrogen atoms are there in each isomer? How many different types of carbon atoms are there in each isomer?

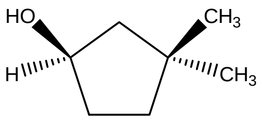
	isomer 1	isomer 2	isomer 3
number of distinct kinds of ^1H			
number of distinct kinds of ^{13}C			

b. How many different isomers are there for $C_5H_{11}Br$? (Hint: Use the carbon skeletons generated in part a as a starting point.) How many different types of hydrogen atoms (and carbon atoms) are there in each isomer of $C_5H_{11}Br$? Nuclei can be nonequivalent, chemically equivalent and magnetically equivalent. There can also be several types of groups: homotopic, heterotopic, enantiotopic, diastereotopic and rototopic. The types of protons (or carbons) present will affect the appearance of the NMR spectrum, sometimes dramatically. The interpretation is sometimes straight forward, but occasionally it is very complicated. Some of the details are too complicated for us to easily evaluate, but we need to be aware of them so that we know exceptions exist for our simplistic rules (e.g. the N+1 rule that we will study later). Generally each distinct type of ^1H (and ^{13}C) will have its own chemical shift (δ). Occasionally two different types of ^1H (and ^{13}C) will fall on top of one another and obscure the information. This is much more common in ^1H NMR (spread over 10 ppm) than ^{13}C NMR (spread over 220 ppm) because the proton range is so much smaller. As you are working out the different types of protons, do the same with the carbon atoms.

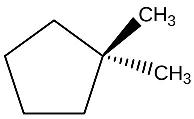
	isomer 1	isomer 2	isomer 3	isomer 4	isomer 5	isomer 6	isomer 7	isomer 8
number of distinct kinds of ^1H								
number of distinct kinds of ^{13}C								

Problem x – How many different types of hydrogen atoms and carbon atoms are in the following structures. Classify each comparison as homotopic, heterotopic, enantiotopic or diastereotopic atoms.

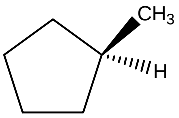
a.



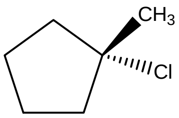
b.



c.



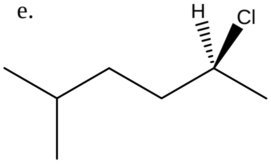
d.



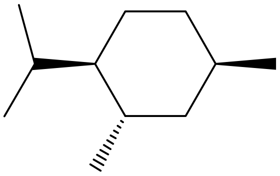
Different types of H = ?

Different types of C = ?

e.



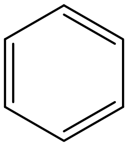
f.



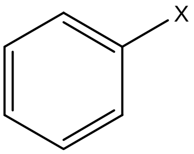
Different types of H = ?

Different types of C = ?

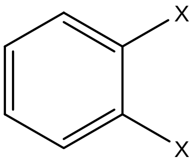
g.



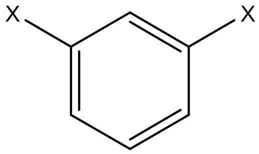
h.



i.



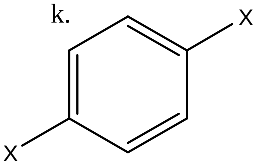
j.



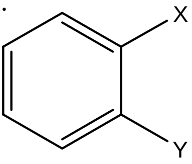
Different types of H = ?

Different types of C = ?

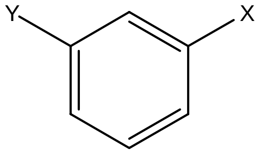
k.



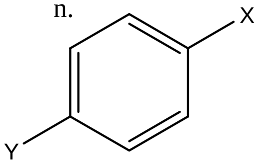
l.



m.



n.



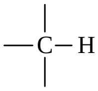
Different types of H = ?

Different types of C = ?

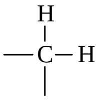
Summary of Generic Proton Shifts

Proton chemical shifts of hydrogen on sp^3 carbons depend on two main factors (electronegativity and pi bond anisotropy). All values listed below are only approximate and have a small plus or minus range about the listed value.

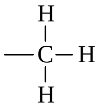
All things being equal, methine protons (CH) have greater chemical shifts than methylene protons (CH_2) which have greater chemical shifts than methyl protons (CH_3).



$\delta \approx$ 1.5 ppm
methine protons



$\delta \approx$ 1.2 ppm
methylene protons

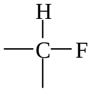


$\delta \approx$ 0.9 ppm
methyl protons

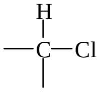
Chemical shifts in an only "alkane" environment.

1. **sp^3 C-H** Electronegative atoms in the vicinity of hydrogen deshield protons and produce a larger chemical shift. If the electronegative atom is in resonance with an adjacent pi system that further withdraws electron density, and the chemical shift is increased (look at ethers vs. esters).

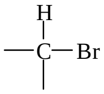
a. next to a halogen



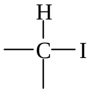
$\delta \approx$ 4.1 - 4.7 ppm
fluoro alkanes



$\delta \approx$ 3.1 - 3.7 ppm
chloro alkanes

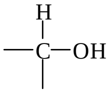


$\delta \approx$ 3.0 - 3.6 ppm
bromo alkanes

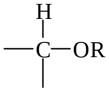


$\delta \approx$ 2.9 - 3.5 ppm
iodo alkanes

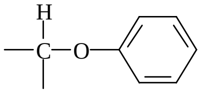
b. next to a oxygen



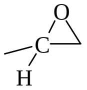
$\delta \approx$ 3.1 - 3.7 ppm
alcohol



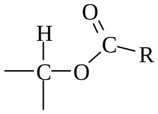
$\delta \approx$ 3.0 - 3.6 ppm
alkyl ether



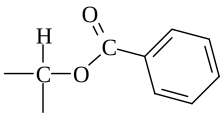
$\delta \approx$ 3.7 - 4.3 ppm
aromatic ether
(resonance withdrawal)



$\delta \approx$ 2.5 - 3.2 ppm
epoxide ether

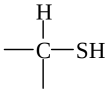


$\delta \approx$ 3.7 - 4.3 ppm
alkyl ester
(oxygen side)
(resonance withdrawal)

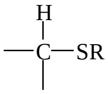


$\delta \approx$ 4.0 - 4.6 ppm
aromatic ester
(oxygen side)
(resonance withdrawal)

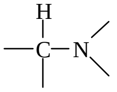
c. next to a sulfur or nitrogen



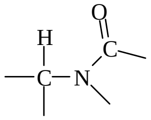
$\delta \approx$ 2.2 - 2.8 ppm
thiol



$\delta \approx$ 2.2 - 2.8 ppm
alkyl ether

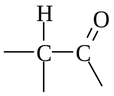


$\delta \approx$ 2.3 - 3.1 ppm
amines

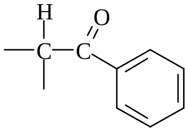


$\delta \approx$ 3.0 - 3.6 ppm
(resonance withdrawal)
amides

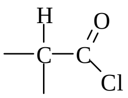
2. **sp^3 C-H** Pi bonds in the vicinity of hydrogen also deshield protons via pi bond anisotropy and produce a larger chemical shift. The closer the sp^3 C-H is to the pi bond the greater chemical shift observed. When an electronegative atom is part of the pi bond, the chemical shift further increases (look at C=C vs C=O).



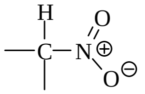
$\delta \approx$ 1.9 - 2.7 ppm
aldehydes, ketones,
carboxylic acids, amides,
alkyl ester (oxygen side)



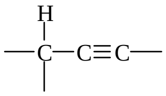
$\delta \approx$ 2.6 - 3.3 ppm
aromatic ketones
(resonance withdrawal)



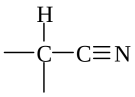
$\delta \approx$ 2.7 - 3.4 ppm
acid chlorides
(resonance withdrawal)



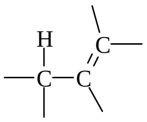
$\delta \approx$ 2.7 - 3.4 ppm
nitro compounds
(resonance withdrawal)



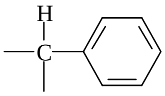
$\delta \approx$ 1.8 - 2.4 ppm
propargylic protons



$\delta \approx$ 2.3 - 2.8 ppm
propargylic protons



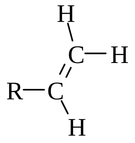
$\delta \approx$ 1.7 - 2.3 ppm
allylic protons



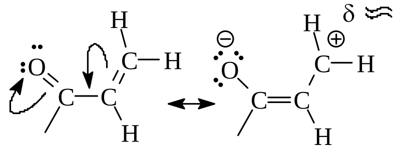
$\delta \approx$ 2.3 - 2.9 ppm
benzylic protons

3. **<u>sp^2 C-H</u>** Hydrogens at the side of a pi bond are deshielded even more than above via pi bond anisotropy. An aldehyde produces the largest effect due to the electronegative oxygen, followed by an aromatic ring, followed by alkenes and finally terminal alkynes. (sp C-H, partially shielded)

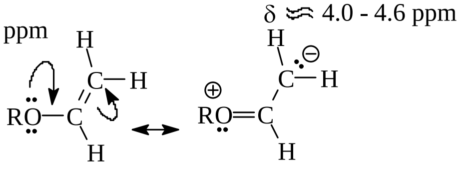
alkene C-H



δ ≈ 5.7 ppm
simple vinylic protons



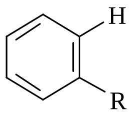
δ ≈ 6.0 - 6.3 ppm
vinylic protons (resonance and inductive withdrawal)



δ ≈ 6.4 - 7.4 ppm
vinylic protons (resonance donation and inductive withdrawal)

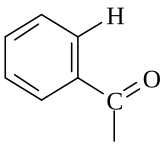
aromatic C-H

δ ≈ 7.1 - 7.3 ppm



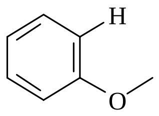
simple aromatic protons

δ ≈ 7.9 - 8.3 ppm

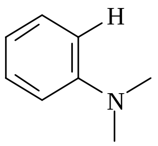


aromatic protons (resonance and inductive withdrawal)

δ ≈ 6.7 - 7.0 ppm

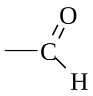


δ ≈ 6.5 - 7.0 ppm



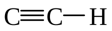
aromatic protons (resonance donation and inductive withdrawal)

aldehyde C-H



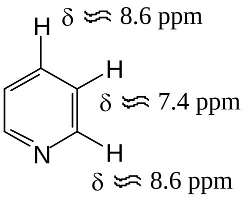
δ ≈ 9 - 10 ppm
aldehydes

alkyne C-H

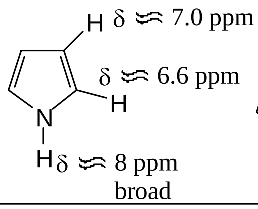


δ ≈ 1.9 - 3.2 ppm
terminal alkyne protons

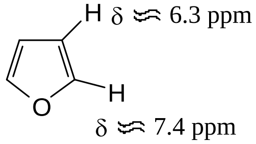
pyridine C-H



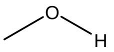
pyrrole C-H



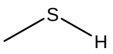
furan C-H



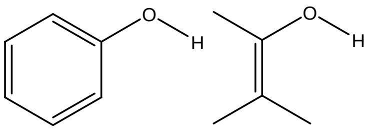
4. There are several kinds of hydrogen attached to heteroatoms. Some of these are listed below. Often these hydrogens do not follow the N+1 rule because they exchange very fast on the NMR time scale via acid/base proton exchanges and are not next to neighbor protons long enough to allow coupling to be observed. They are often observed as broad singlets (sometimes so broad they are not easily seen in a spectrum). If the exchange rate is very fast among all of the exchangeable protons on the NMR time scale, all of the exchangeable protons may appear together at a single, averaged chemical shift.



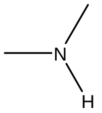
δ ≈ 1-5 ppm
alcohols



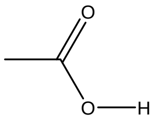
δ ≈ 1-3 ppm
thiols



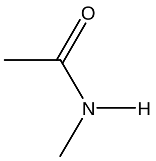
δ ≈ 5-15 ppm
phenols and
enol protons



δ ≈ 1-2 ppm
amines



δ ≈ 10-12 ppm
carboxylic acids

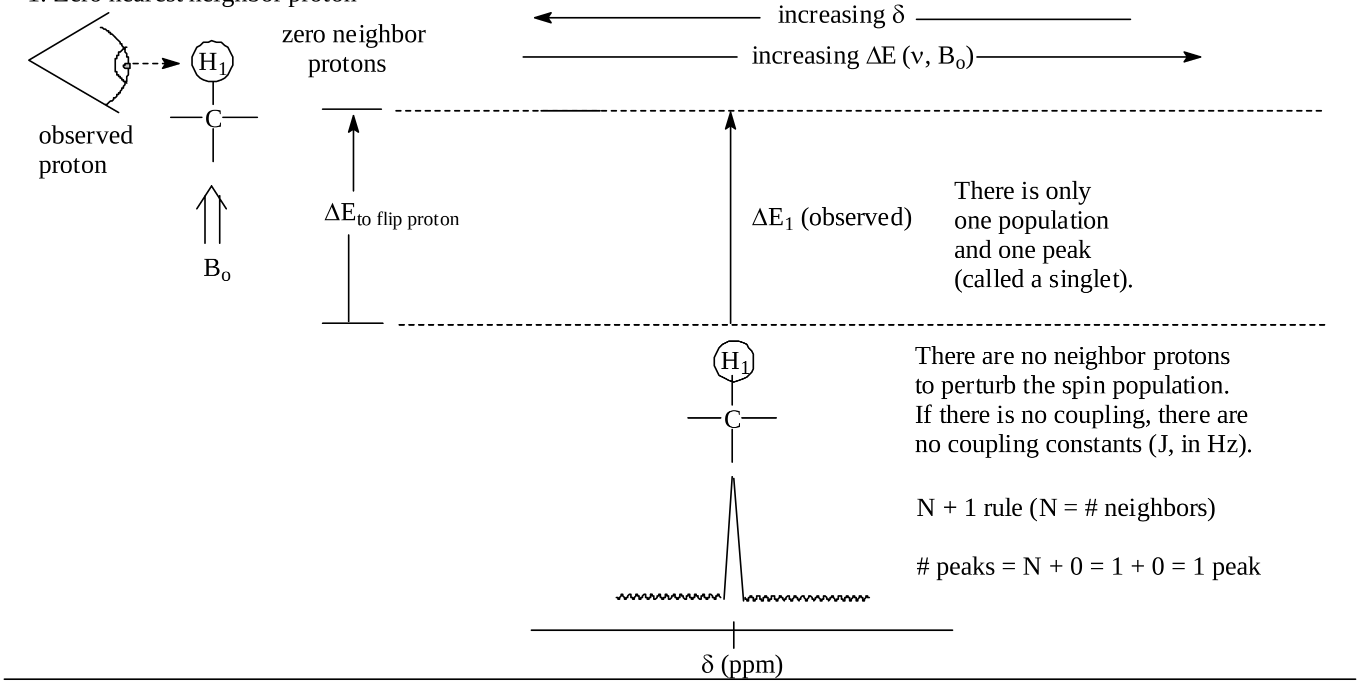


δ ≈ 1-6 ppm
amides

The actual chemical shift (δ) depends on solvation, hydrogen bonding, exchange, etc.

Splitting patterns of coupled protons

1. Zero nearest neighbor proton



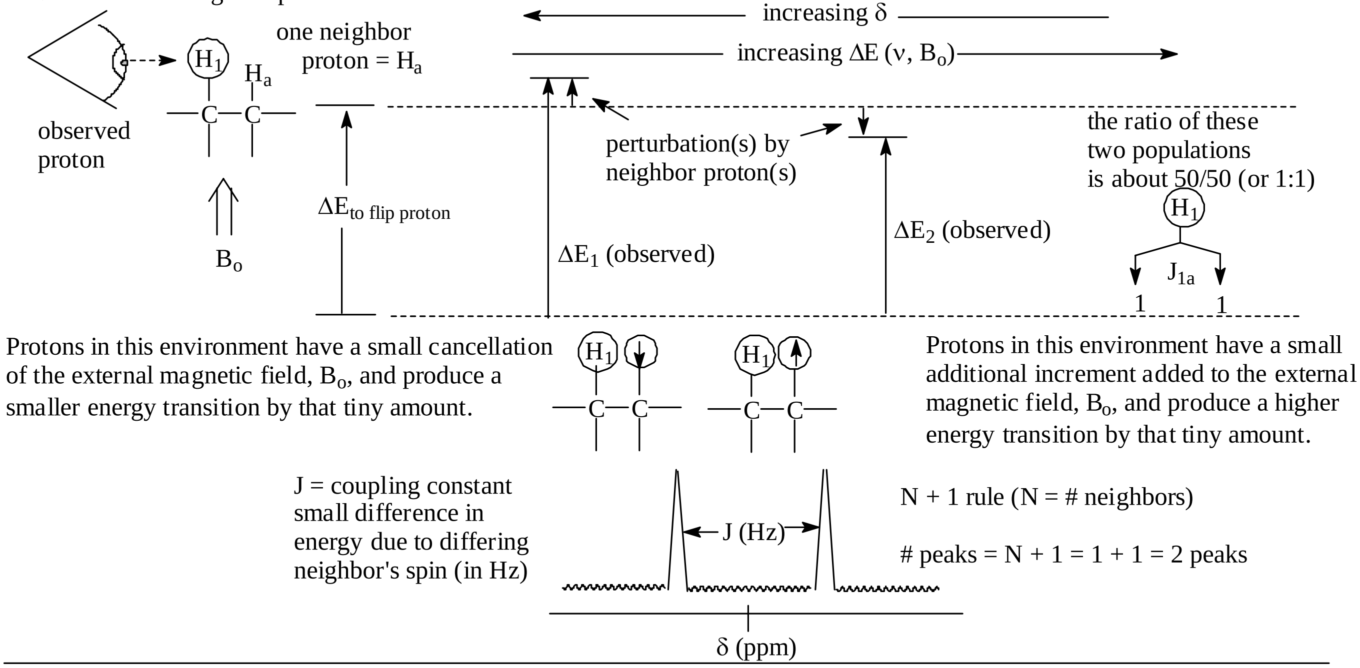
There is only one population and one peak (called a singlet).

There are no neighbor protons to perturb the spin population. If there is no coupling, there are no coupling constants (J, in Hz).

N + 1 rule (N = # neighbors)

peaks = N + 0 = 1 + 0 = 1 peak

2. One nearest neighbor proton



the ratio of these two populations is about 50/50 (or 1:1)

Protons in this environment have a small cancellation of the external magnetic field, B$_o$, and produce a smaller energy transition by that tiny amount.

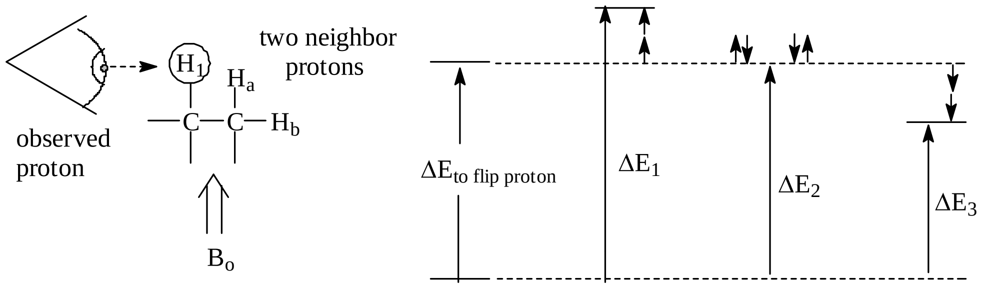
Protons in this environment have a small additional increment added to the external magnetic field, B$_o$, and produce a higher energy transition by that tiny amount.

J = coupling constant small difference in energy due to differing neighbor's spin (in Hz)

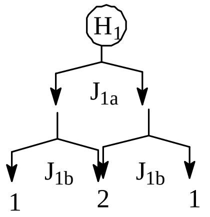
N + 1 rule (N = # neighbors)

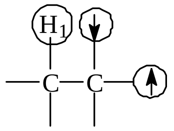
peaks = N + 1 = 1 + 1 = 2 peaks

3. Two nearest neighbor protons (both on same carbon or one each on separate carbons)

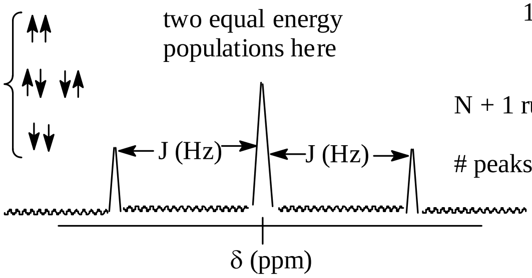


the ratio of these four populations is about 1:2:1





two neighbor protons are like two small magnets that can be arranged four possible ways (similar to flipping a coin twice)

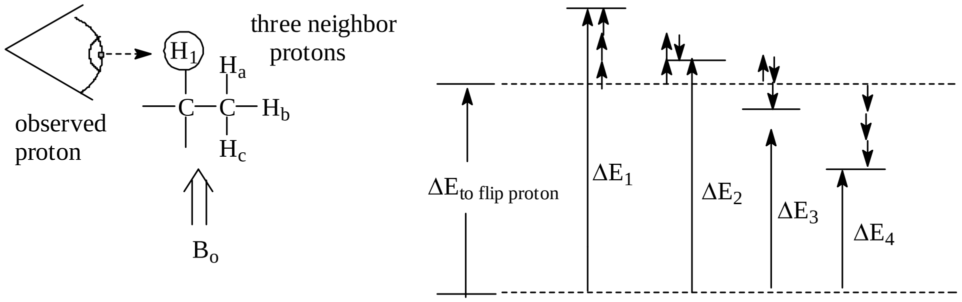


N + 1 rule (N = # neighbors)

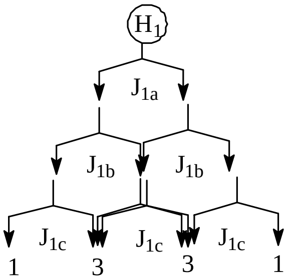
peaks = N + 1 = 2 + 1 = 3 peaks

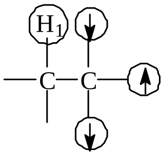
---

4. Three nearest neighbor protons (on same carbon, or two on one and one on another, or one each on separate carbons)

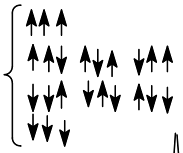


the ratio of these eight populations is about 1:3:3:1

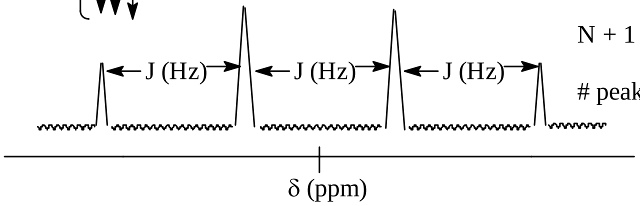




three neighbor protons are like three small magnets that can be arranged eight possible ways (similar to flipping a coin thrice)



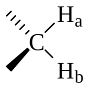
three equal energy populations at each of middle transitions



N + 1 rule (N = # neighbors)

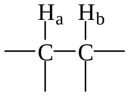
peaks = N + 1 = 3 + 1 = 4 peaks

Typical Coupling Constants (for this book, reality is more complicated)



Range	Typical
0-30 Hz	12 Hz

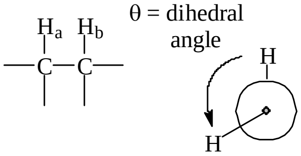
geminal protons - can have different chemical shifts and split one another if they are diastereotopic



Range	Typical
6-8 Hz	7 Hz

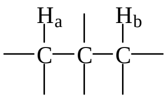
vicinal protons are on adjacent atoms, when freely rotating coupling averages out to about 7 Hz

θ = dihedral angle



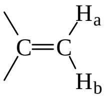
Range	Typical
0-12 Hz	7 Hz

depends on dihedral angle, see plot of Karplus equation



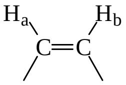
Range	Typical
0-1 Hz	0 Hz

protons rarely couple through 4 chemical bonds unless in a special, rigid shapes (i.e. W coupling)



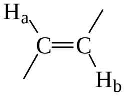
Range	Typical
0-3 Hz	2 Hz

sp^2 geminal coupling



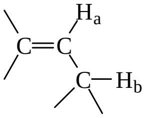
Range	Typical
5-11 Hz	10 Hz

sp^2 cis (acylic) coupling (always smaller than the trans isomer)



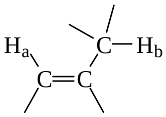
Range	Typical
11-19 Hz	17 Hz

sp^2 trans coupling (always larger than the cis isomer)



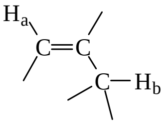
Range	Typical
4-10 Hz	7 Hz

sp^2 / sp^3 vicinal coupling



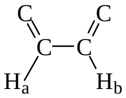
Range	Typical
0-3 Hz	1 Hz
	(0 Hz, for us)

cis / allylic coupling, notice through 4 bonds



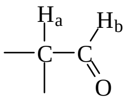
Range	Typical
0-3 Hz	1 Hz
	(0 Hz, for us)

trans / allylic coupling, notice through 4 bonds



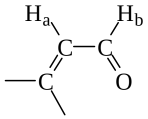
Range	Typical
9-13 Hz	10 Hz

sp^2 vicinal coupling (different π bonds)



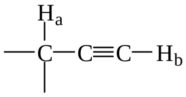
Range	Typical
1-3 Hz	2 Hz

sp^3 vicinal aldehyde coupling



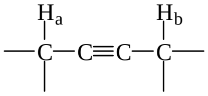
Range	Typical
5-8 Hz	6 Hz

sp^2 vicinal aldehyde coupling



Range	Typical
2-3 Hz	2 Hz

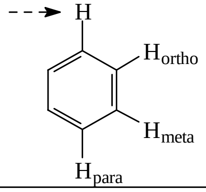
sp / propargylic coupling notice through 4 bonds



Range	Typical
2-3 Hz	3 Hz

bis-propargylic coupling notice through 5 bonds

ortho, meta and para coupling to this proton



	Range	Typical
ortho	6-10 Hz	9 Hz
meta	1-3 Hz	1 Hz
para	0-1 Hz	0 Hz

(J_{meta} & J_{para} = 0 Hz, for us)

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

Multiplets when the N + 1 rule works.

s = singlet	1	1 peak = 100%
d = doublet	1 1	edge peak = 50% of total area
t = triplet	1 2 1	edge peak = 25% of total area
q = quartet	1 3 3 1	edge peak = 12%
qnt = quintet	1 4 6 4 1	edge peak = 6%
sex = sextet	1 5 10 10 5 1	edge peak = 3%
sep = septet	1 6 15 20 15 6 1	edge peak = 1.5%
o = octet	1 7 21 35 35 21 7 1	edge peak = 0.8%

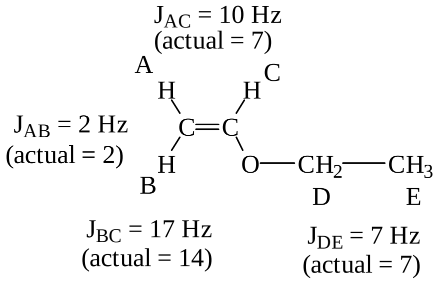
<u>Combinations or these are possible.</u>

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.

Predicted appearance of proton NMR spectrum (J values can all be different or J values can coincidently be the same = N+1 rule)

Protons A, B and C are coupled to one another, but not to protons D and E. Protons D and E are coupled to one another.



J_{AC} = 10 Hz (actual = 7)

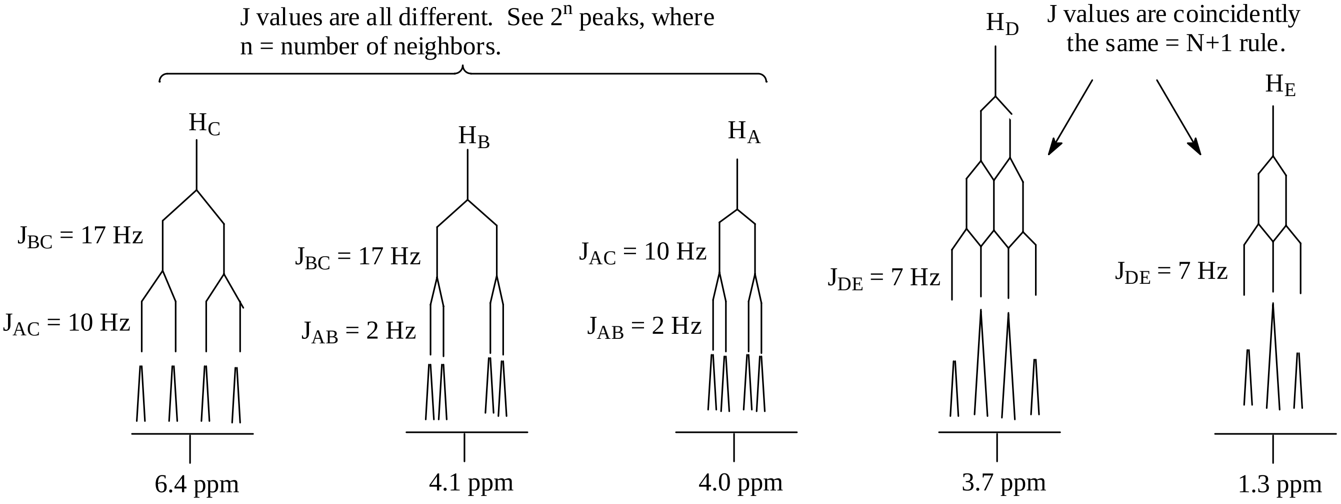
J_{AB} = 2 Hz (actual = 2)

J_{BC} = 17 Hz (actual = 14)

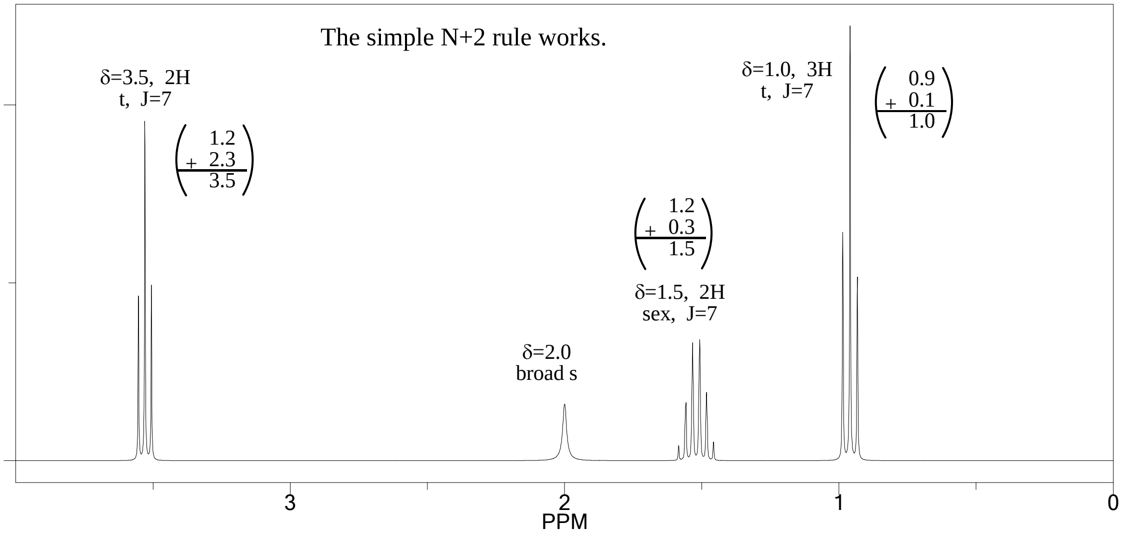
J_{DE} = 7 Hz (actual = 7)

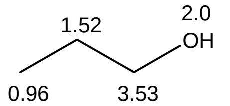
approximate chemical shifts (from tables)

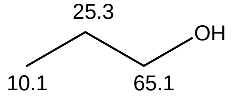
δ_A = 5.2 - 1.2 = 4.0 ppm (actual = 4.0)
δ_B = 5.2 - 1.1 = 4.1 ppm (actual = 4.2)
δ_C = 5.2 + 1.2 = 6.4 ppm (actual = 6.5)
δ_D = 1.2 + 2.5 = 3.7 ppm (actual = 3.7)
δ_E = 0.9 + 0.4 = 1.3 ppm (actual = 1.3)



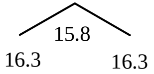
Calculated proton and carbon chemical shifts (δ) from our data are also shown in parentheses.

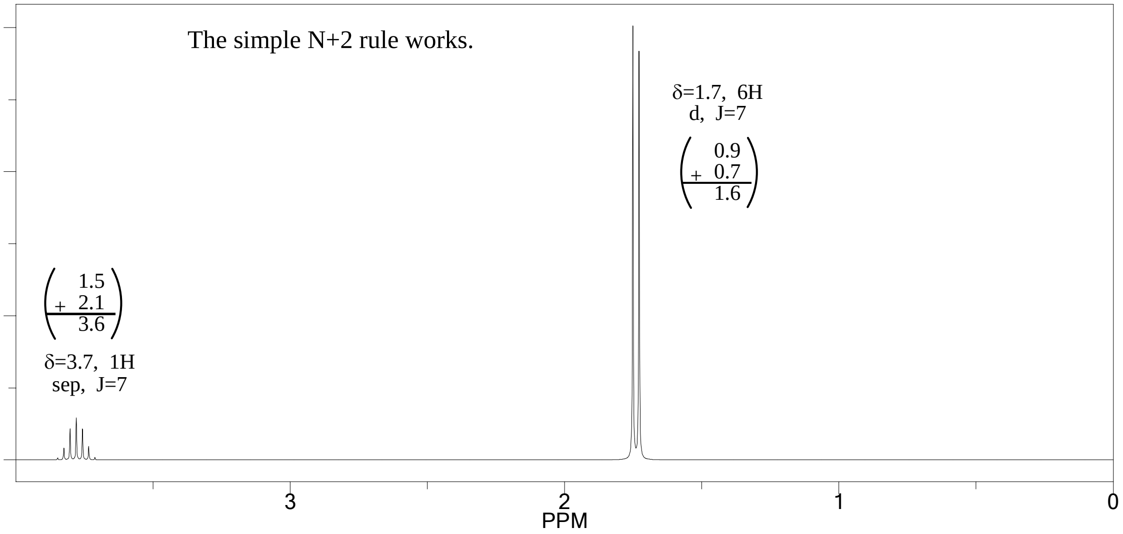

The simple N+2 rule works.

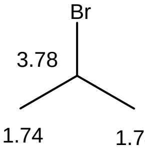


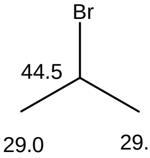


Starting ^{13}C
shifts for propane

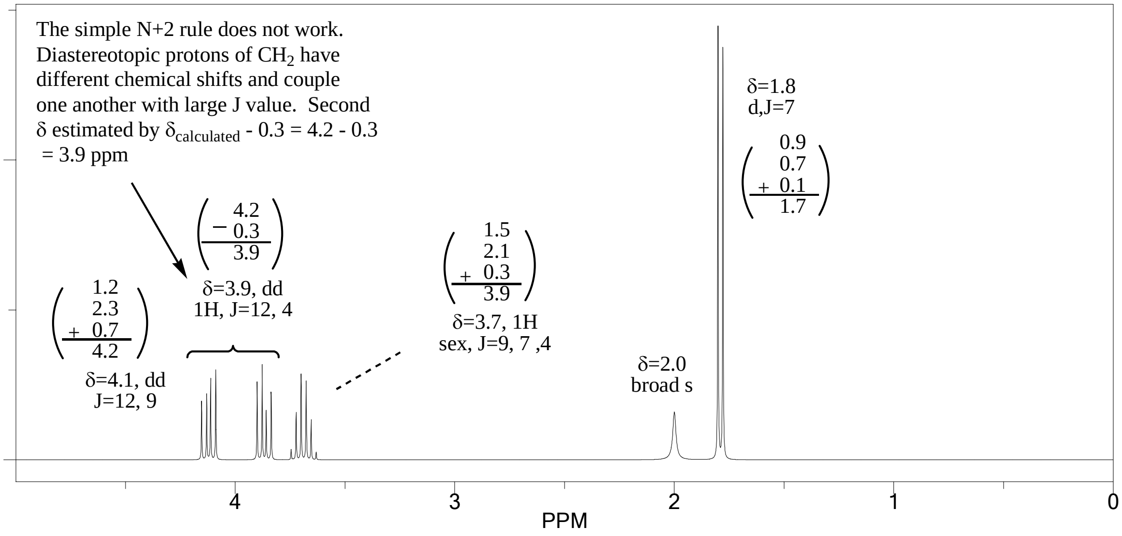


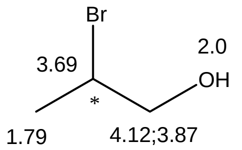

The simple N+2 rule works.

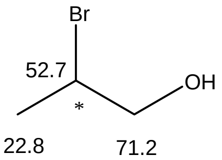




* = chiral center

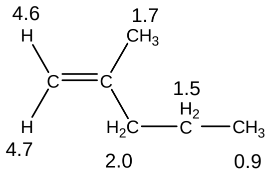

The simple N+2 rule does not work. Diastereotopic protons of CH_2 have different chemical shifts and couple one another with large J value. Second δ estimated by $\delta_{calculated}$ - 0.3 = 4.2 - 0.3 = 3.9 ppm



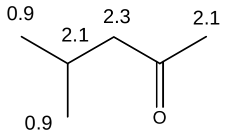


Problem - Predict approximate NMR's for the following compounds. Draw a sketch of your estimated NMR. Include calculations of ^{1}H chemical shifts, estimates of coupling constants (J values) and multiplicities (s, d, t, q, dd, etc.), as well as the number of hydrogens to be integrated at each chemical shift (by writing the appropriate number of hydrogens above the multiplet, e.g. 2H). The actual chemical shifts are written by each type of hydrogen to check your calculations.

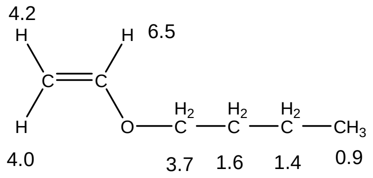
a.



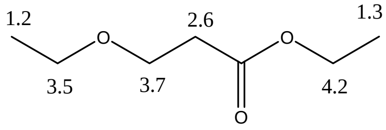
b.



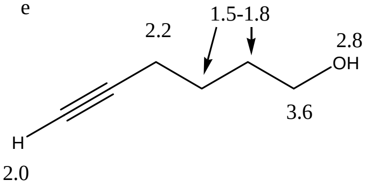
c.



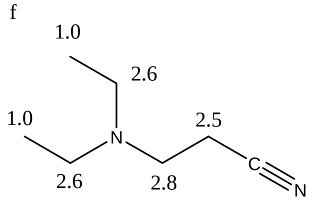
d.



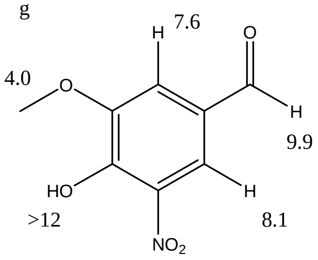
e



f

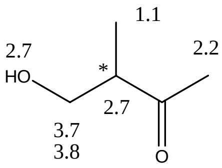


g

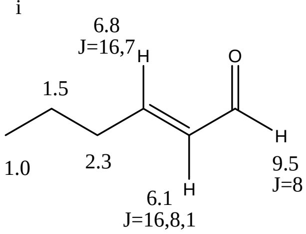


h

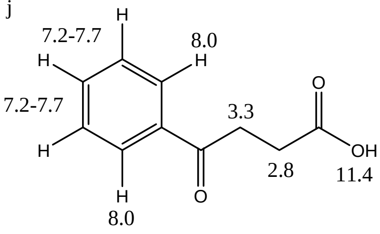
* = chiral center



i



j



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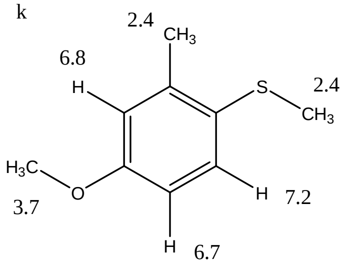

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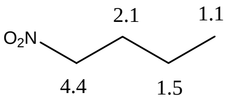
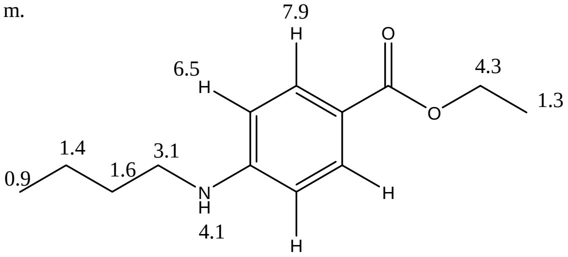
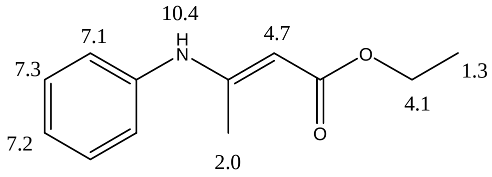


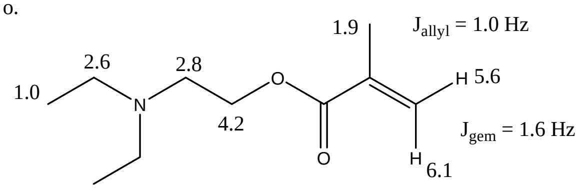
m.



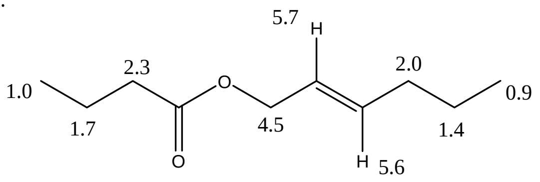
n.



o.

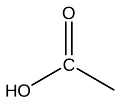


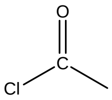
p.

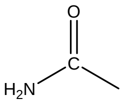


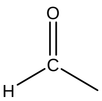
Examples of Functional Group Possibilities

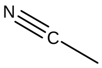
1. One point connection to isolated spin systems.

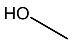

carboxylic acid

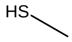

acid chloride

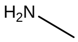

1° amide

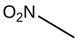

aldehyde

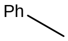

nitrile

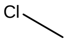

alcohol

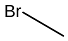

thiol

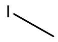

1° amine


nitro

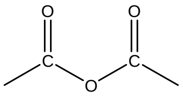

phenyl

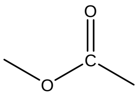

chloro

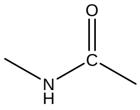

bromo

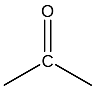

iodo

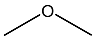
2. Two point connection to isolated spin systems.

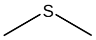

anhydride

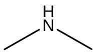

ester

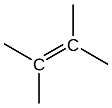

2° amide

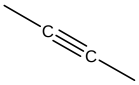

ketone

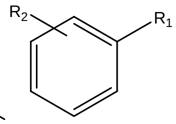

ether


sulfide

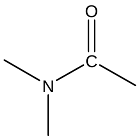

2° amine

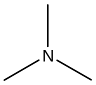

alkenes with 2H and 2 substituents as geminal, cis or trans

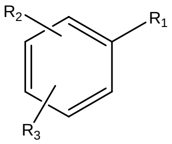

disubstituted alkyne


disubstituted aromatic (o, m, p)

3. Three point connection to isolated spin systems (just a sampling).


3° amide


3° amine


trisubstituted aromatic

Consider a diastereotopic CH_2 or $C(CH_3)_2$ *next to a chiral center* to have different chemical shifts. Calculate the δ_1 chemical shift and then subtract 0.3 ppm to estimate a value for the δ_2 chemical shift.

Use the following "typical" J values in your prediction of spectra. By keeping our values "typical" we simplify our analysis of presented spectra. Real examples can be much more complicated, with every single coupling constant different from "typical" leading to an undecipherable number of peaks that we end up calling a multiplet, because of its complexity.

$^2J_{geminal}$ = 12 Hz
$^3J_{vicinal}$ = 7 Hz
^4J = 0 Hz

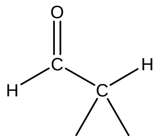
sp^3 coupling

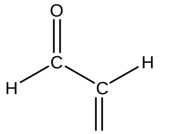
$^2J_{geminal}$ = 2 Hz
$^3J_{cis}$ = 10 Hz
$^3J_{trans}$ = 17 Hz
$^4J_{allylic}$ = 0 Hz (in this book,but typicall ≈ 1 Hz)

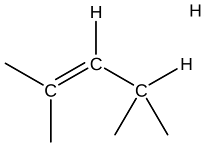
alkene coupling

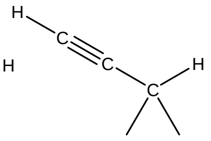
$^3J_{ortho}$ = 9 Hz
$^4J_{para}$ = 0 Hz (in this book,but typicall ≈ 1 Hz)
$^5J_{para}$ = 0 Hz

aromatic coupling

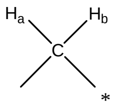

$^3J_{vicinal}$ = 2 Hz


$^3J_{vicinal}$ = 6 Hz


$^3J_{vicinal}$ = 7 Hz


$^4J_{propargylic}$ = 2 Hz

miscellaneous coupling

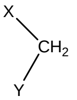

* = chiral center

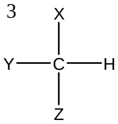
H_a and H_b are diastereotopic in a chiral environment. If they have different chemical shifts they will split one another with $J_{geminal}$ = 12 Hz.

Examples of possible sp^3 spin systems (C1 through C6) that could be connected to the functional group patterns shown above. There are a LOT of possibilities when di- or tri- substituted. We will try "some" of these. For possible specific examples consider: Br, CN and Ar (in any combinations). (Remember, in our course $J_{vicinal}$ = 7 Hz and $J_{geminal}$ = 12 Hz when diastereotopic)

1 Carbon - mono-, di-, tri- substituted

1 $H_3C—X$

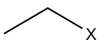
2


3


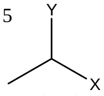
$Y—\overset{X}{\underset{Z}{C}}—H$

X = Y = Z
or
X, Y, Z varies

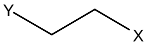
2 Carbons - mono-, di-, tri- substituted

4


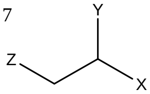
(1-)

5


(1,1-)

6


(1,2-)

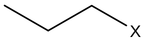
7


(1,1,2-)

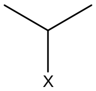
X = Y = Z
or
X, Y, Z varies

3 Carbons - mono-, di-, tri- substituted

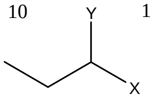
X = Y = Z
or
X, Y, Z varies

8


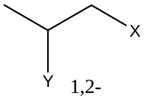
1-

9


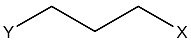
2-

10


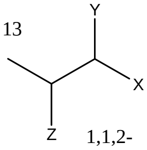
1,1-

11


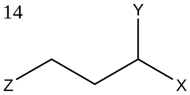
1,2-

12


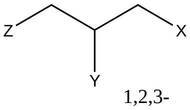
1,3-

13


1,1,2-

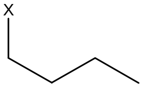
14


1,1,3-

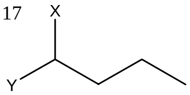
15


1,2,3-

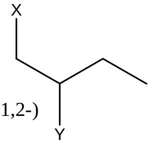
4 Carbons - mono-, di-, tri- substituted

16


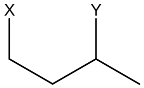
(1-)

17


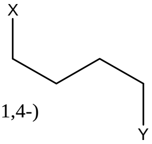
(1,1-)

18


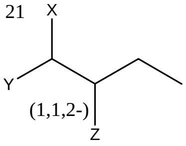
(1,2-)

19


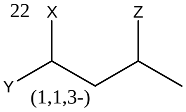
(1,3-)

20


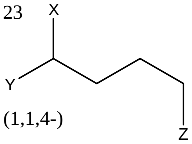
(1,4-)

21


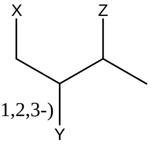
(1,1,2-)

22


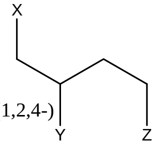
(1,1,3-)

23


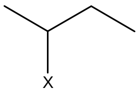
(1,1,4-)

24


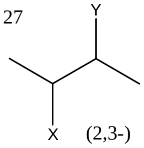
(1,2,3-)

25


(1,2,4-)

26


(2-)

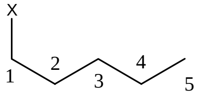
27


(2,3-)

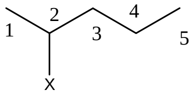
X = Y = Z
or
X, Y, Z varies

Only using examples with continuous spin systems

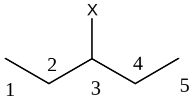
5 Carbons - mono-, di-, tri- substituted



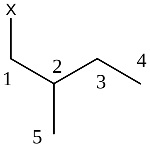
(1-substituted,
disubstituted = 1,1-, 1,2-, 1,3-, 1,4-, 1,5-,
trisubstituted = 1,1,2-, 1,1,3-, 1,1,4-, 1,1,5-, 1,2,3-, 1,2,4-, 1,2,5-, 1,3,4-, 1,3,5-)



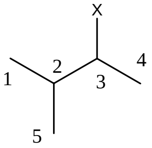
(2-substituted,
disubstituted = 2,3-, 2,4-)



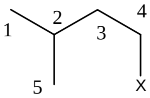
(3-substituted)



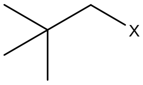
(1-substituted,
disubstituted = 1,1-, 1,3-, 1,4-, 1,5-,
trisubstituted = 1,1,3-, 1,1,4-, 1,1,5-, 1,3,4-, 1,3,5-, 1,4,4-, 1,4,5-)



(3-substituted,
disubstituted = 3,4-,
trisubstitued = 3,4,4-, 2,3,4-)

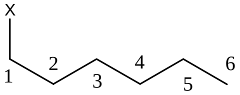


(4-substituted)

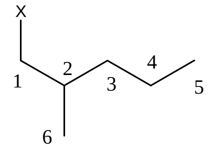


No continuous spin system possible.

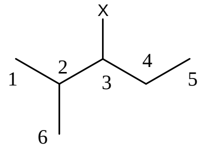
6 Carbons - mono-, di-, tri- substituted



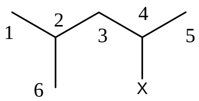
(1-substituted,
disubstituted = 1,1-, 1,2-, 1,3-, 1,4-, 1,5-, 1,6-,
trisubstituted = 1,1,2-, 1,1,3-, 1,1,4-, 1,1,5-, 1,1,6-, 1,2,3-, 1,2,4-, 1,2,5-, 1,2,6-, 1,3,4-, 1,3,5-, 1,3,6-)



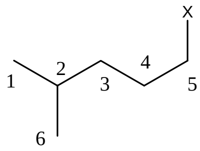
(1-substituted,
disubstituted = 1,1-, 1,3-, 1,4-, 1,5-, 1,6-,
trisubstituted = 1,1,3-, 1,1,4-, 1,1,5-, 1,1,6-, 1,3,4-, 1,3,5-, 1,3,6-, 1,4,5-, 1,5,5-, 1,5,6-)



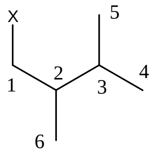
(3-substituted,
disubstituted = 3,4-, 3,5-,
trisubstituted = 3,4,5-, 3,5,5-)



(4-substituted,
disubstitituted = 4,5-,
trisubstituted = 4,5,5-)

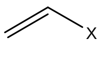


(5-substituted,
disubstituted = 5,5-)

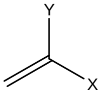


(1-substituted,
disubstituted = 1,5-, 1,6-,
trisubstituted = 1,1,5-, 1,1,6-,)

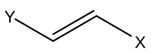
Alkene sp^2 H & C example patterns

1


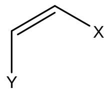
mono-

2


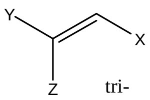
geminal-

3


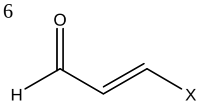
trans-

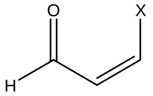
4


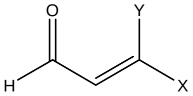
cis-

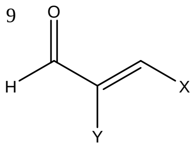
5


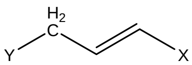
tri-

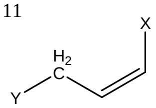
6


7


8


9


10


11


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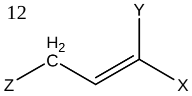

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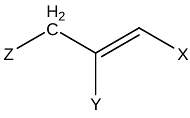

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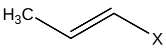

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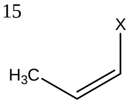

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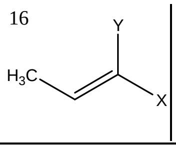

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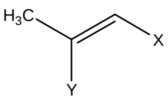
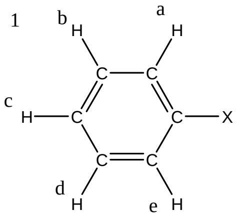


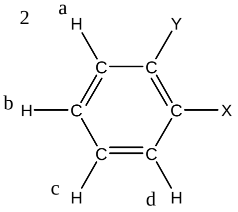
X = Y = Z
or
X, Y, Z varies

$J_{gem} \approx 2$ Hz
$J_{cis} \approx 10$ Hz
$J_{trans} \approx 17$ Hz
$J_{allylic} \approx 0$ (for us), (typically = 1 Hz)
$J_{sp3\text{-}sp2} = 7$ Hz
$J_{ald\text{-}sp2} = 6$ Hz

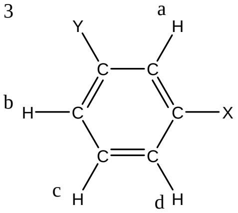
Aromatic sp^2 H & C example patterns

1


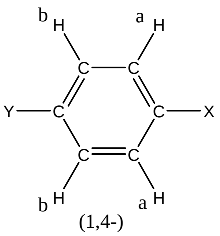
(1-)

2


(1,2-)

3


(1,3-)

4


(1,4-)

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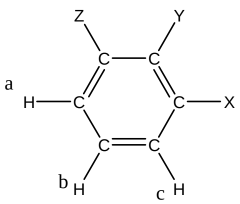
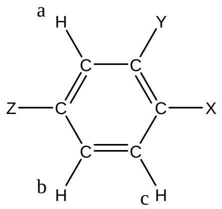
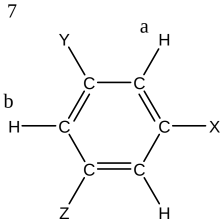


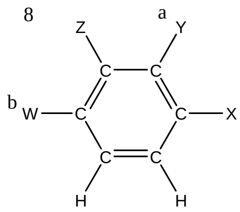
(1,2,3-)

6


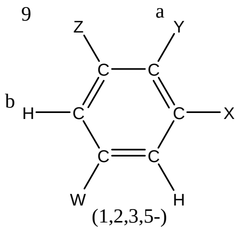
(1,2,4-)

7


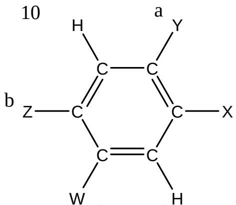
(1,3,5-)

8


(1,2,3,4-)

9


(1,2,3,5-)

10


(1,2,5,6-)

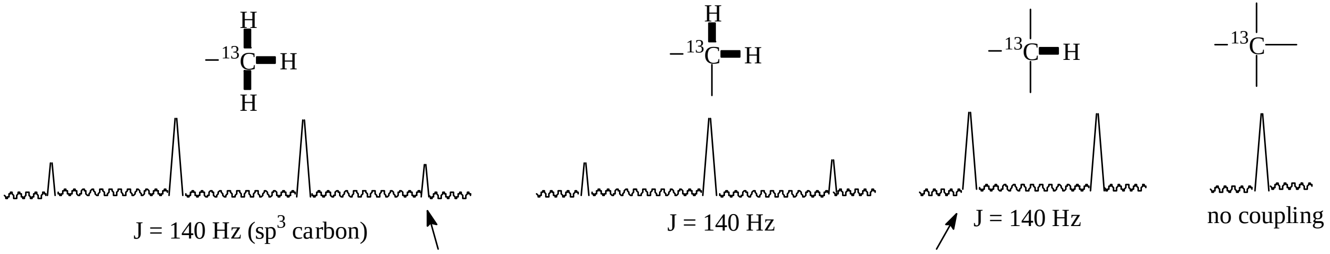
$J_{ortho} \approx 9$ Hz
$J_{meta} \approx 0$ Hz (for us), (typically = 1 Hz)
$J_{para} \approx 0$ Hz

X = Y = Z = W
or
X, Y, Z, W varies

^{13}C NMR - Appearance of ^{13}C carbons with directly attached proton neighbors (not commonly done)

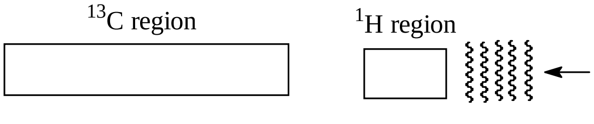
1. Full coupling = larger J values, (versus off resonance decoupling = partially proton decoupled = smaller J values, not common anymore.)

Full one bond Coupling ($^{1}J_{CH}$) is large (140-250 Hz), gives multiplets similar to H NMR's N+1 rule

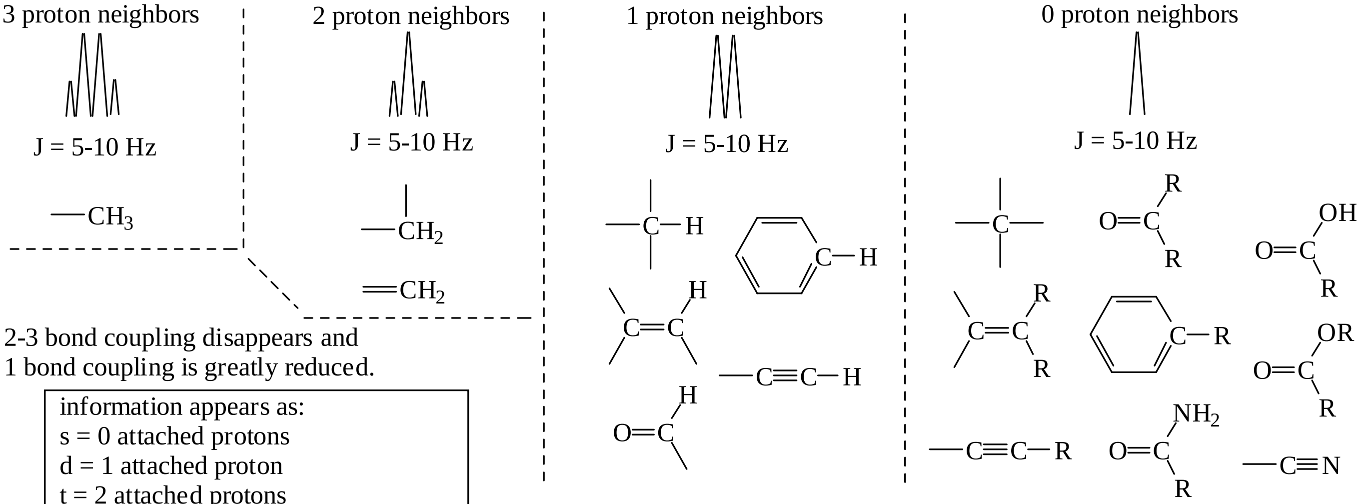


Each of these peaks can be further split by protons 2-3 bonds away (J = 7 Hz). We won't consider that complication factor here.

2. Off Resonance Coupling (reduced one bond coupling by partial irradiation of protons, smaller $^{1}J_{CH}$ = 5-10 Hz) (used to be common and simple to interpret from the N+1 rule, but not used much now, DEPT is used instead)



irradiation near proton region partially decouples protons from carbons in an off resonance experiment and shrinks the coupling constant to a much smaller value so there is less overlap and it is easier to interpret.

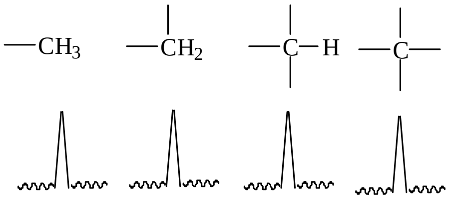


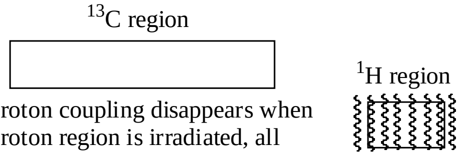
2-3 bond coupling disappears and
1 bond coupling is greatly reduced.

information appears as:
s = 0 attached protons
d = 1 attached proton
t = 2 attached protons
q = 3 attached protons (methyl group)

3. **Fully Proton Decoupled Carbon Spectrum only have singlets for each carbon** (the usual way of running a carbon 13 NMR**).**

All carbons above would appear as singlets in a fully proton decoupled ^{13}C spectrum. Strong irradiation of the proton region can be thought of as rapid interchange of population states so each carbon sees an average of up/down proton spins with no net splitting (coupling). Simplifies spectrum ,but lose C-H information.





proton coupling disappears when proton region is irradiated, all carbons become singlets

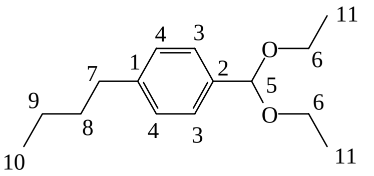
direct irradiation of proton region fully decouples protons from carbons

DEPT = distortionless enhanced by polarization transfer: This is a more recent multiple pulse experiment. It is easier to read and interpret than off resonance ^{13}C. However, it is much more difficult to understand the theory behind the DEPT experiment (and we won’t try). The data can be presented in unprocessed (shown below) or processed form (not shown). DEPT is equivalent to running multiple carbon-13 NMR’s and it takes more time.

A full spectrum is needed to determine all distinct types of carbon

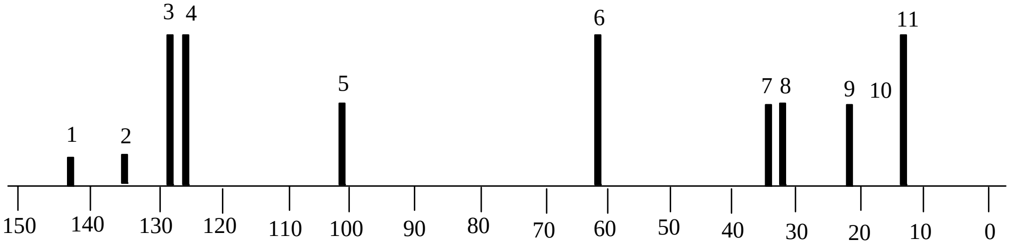
p-butylbenzaldehyde diethyl acetal

Fully decoupled ^{13}C, all carbons show as singlets.

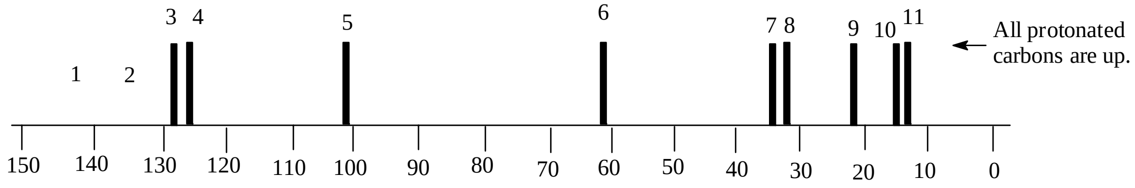


$C_{15}H_{24}O_2$

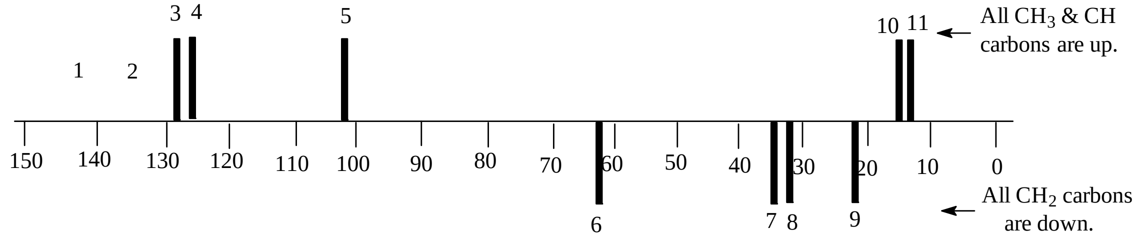
ppm
143.0
136.4
128.2
126.5
101.7
61.0
35.4
33.6
22.3
15.2
13.9



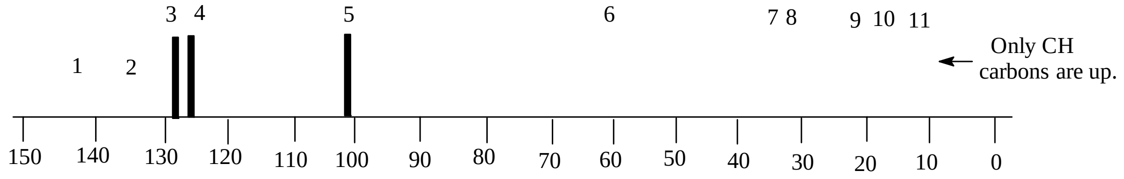
Variation 1 of DEPT: All protonated carbons appear as singlet up peaks, but C's without hydrogen do not appear.



Variation 2 of DEPT: All CH_3's and CH's appear as singlet up peaks and CH_2's are singlet down peaks. Again, C's without hydrogens do not appear.



Variation 3 of DEPT: Only CH's show as singlet up peaks. No other C's appear in this spectrum.



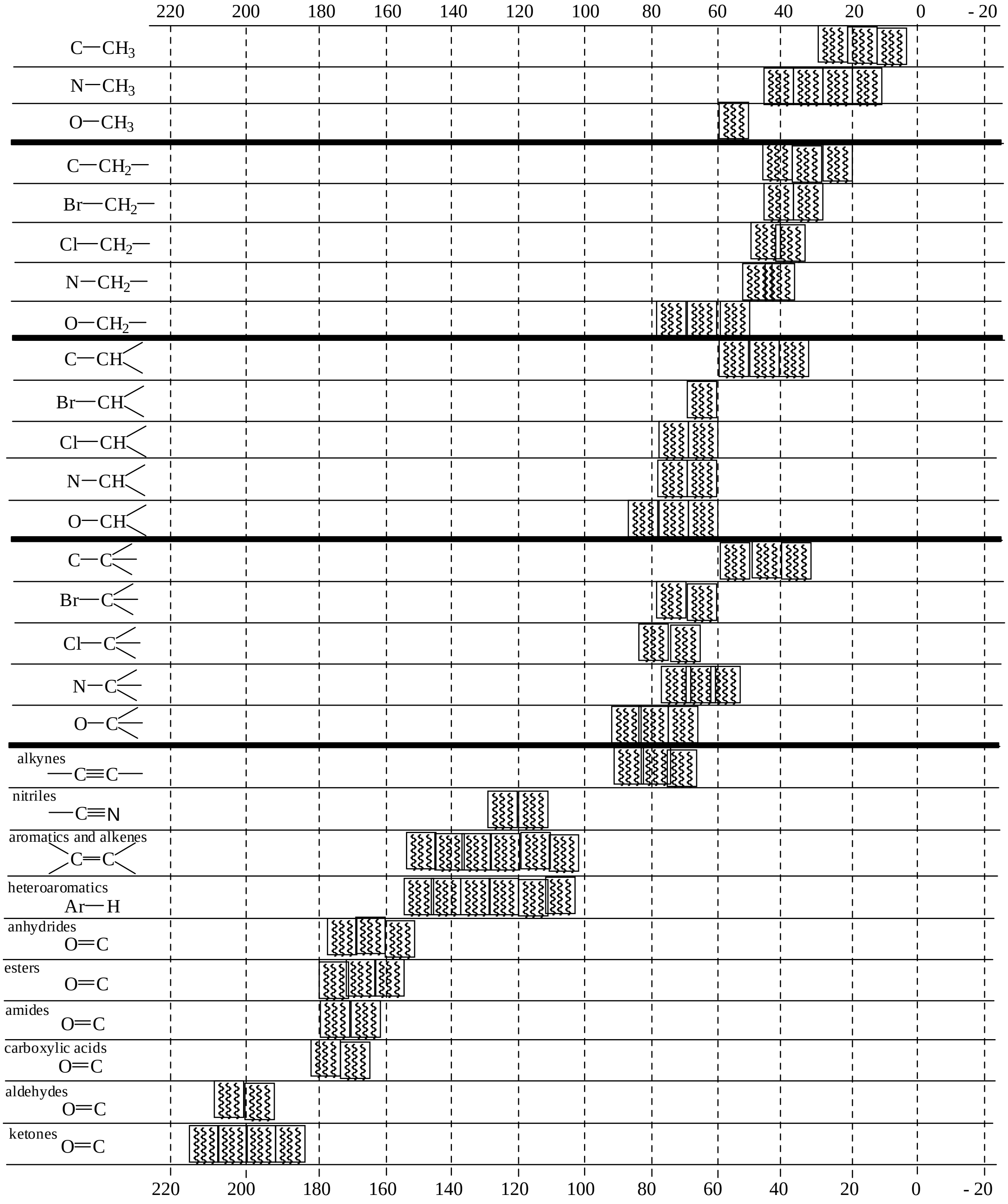
Variation 3 shows the CH carbons. Variation 2 - Variation 3 leaves only CH_3 carbons pointing up and CH_2 carbons pointing down.

A processed DEPT separates out each type of carbon and displays them as up peaks in a separate spectrum (not shown here).

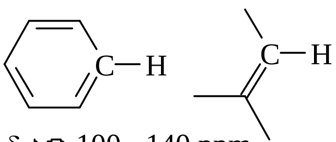
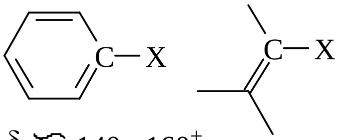
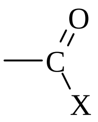
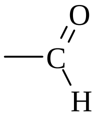
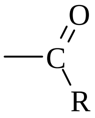
Chemical shifts of carbons vary based on similar reasons used to explain differing proton chemical shifts (i.e. electronegativity of environment and π bond anisotropy). Carbon chemical shifts occur over a wider range than proton chemical shifts showing greater dispersion due to σ_{para}. This means there is less chance of overlap in decoupled ^{13}C spectrum, (but occasionally it is still happens).

Typical ^{13}C shift values are provided below. As with proton chemical shifts, ^{13}C chemical shift values can be calculated (predicted) with a fair amount of accuracy and there are a variety of ways to do so.

Generic values of ^{13}C chemical shifts relative to TMS = 0 ppm



Similar chemical shift information presented in a different format. Remember, proton decoupled carbons appear as singlets. When carbons are coupled to their hydrogens, carbons follow the N+1 rule. Methyls = q, methylenes = t, methines = d, and carbons without hydrogen appear as singlets = s. DEPT provides the same information. Carbon chemical shifts are spread out over a larger range than proton chemical shifts (they are more dispersed), so it is less likely that two different carbon shifts will fall on top of one another. The relative positions of various types of proton and carbon shifts have many parallel trends (shielded protons tend to be on shielded carbons, etc.)

Simple alkane carbons	CH_3- d ≈ 0 - 30 ppm (q)	$\underset{\vert}{C}H_2-$ d ≈ 20 - 40 ppm (t)	$-\underset{\vert}{C}H-$ d ≈ 30 - 50 ppm (d)	$-\underset{\vert}{\overset{\vert}{C}}-$ d ≈ 30 - 60 ppm (s)
sp^3 carbon next to oxygen	CH_3-O d ≈ 50 - 60 ppm (q)	$\underset{\vert}{C}H_2-O$ d ≈ 55 - 80 ppm (t)	$-\underset{\vert}{C}H-O$ d ≈ 60 - 80 ppm (d)	$-\underset{\vert}{\overset{\vert}{C}}-O$ d ≈ 70 - 90 ppm (s)
sp^3 carbon next to nitrogen	CH_3-N d ≈ 10 - 50 ppm (q)	$\underset{\vert}{C}H_2-N$ d ≈ 35 - 55 ppm (t)	$-\underset{\vert}{C}H-N$ d ≈ 50 - 70 ppm (d)	$-\underset{\vert}{\overset{\vert}{C}}-N$ d ≈ 50 - 70 ppm (s)
sp^3 carbon next to bromine or chlorine (X = Cl, Br)		$\underset{\vert}{C}H_2-X$ d ≈ 25 - 50 ppm (t)	$-\underset{\vert}{C}H-X$ d ≈ 60 - 80 ppm (d)	$-\underset{\vert}{\overset{\vert}{C}}-X$ d ≈ 60 - 80 ppm (s)
sp carbon (alkynes)	$-C{\equiv}C-$ δ ≈ 70 - 90 ppm	sp carbon (nitriles)	$-C{\equiv}N$ δ ≈ 110 - 125 ppm	
sp^2 carbon (alkenes and aromatics)	 δ ≈ 100 - 140 ppm simple sp^2 carbon resonance donation moves δ lower, resonance withdrawal moves δ higher	 δ ≈ 140 - 160^+ ppm sp^2 carbon attached to an electronegative atom (X = oxygen, nitrogen, halogen) or C_β carbon conjugated with a carbonyl group		
 δ ≈ 160 - 180 ppm carboxyl carbons (acids, esters, amides) (s)	 δ ≈ 180 - 210 ppm aldehyde carbons, lower values when conjugated (d)	 δ ≈ 180 - 220 ppm ketone carbons, lower values when conjugated (s)		

Calculations of alkane ^{13}C chemical shifts not listed above.

sp^3 Carbon Chemical Shift Calculations

Calculations for sp^3 carbon ^{13}C chemical shifts of functionalized carbon skeletons can be performed starting from the actual shifts found in the corresponding alkane skeleton, and introducing corrections factors based on the functionality present in the molecule. This assumes that the alkane ^{13}C shifts are available, which is why several examples are provided below.

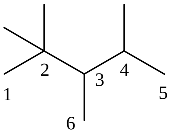
Examples of C_n alkanes as possible starting points for calculation ^{13}C shifts in ppm.

Steric Corrections for sp^3 carbon chemical shift calculations

The calculated carbon atom is: ↓	The attached C_α carbons are:			
	primary	secondary	tertiary	quaternary
primary	0	0	-1.1	-3.4
secondary	0	0	-2.5	-7.5
tertiary	0	-3.7	-9.5	-15.0
quaternary	-1.5	-8.4	-15.0	-25.0

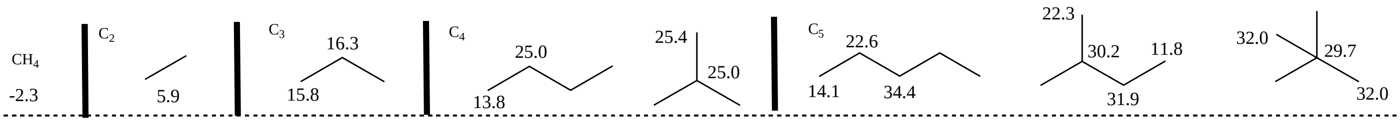
Approximate ^{13}C shift calculation from scratch.

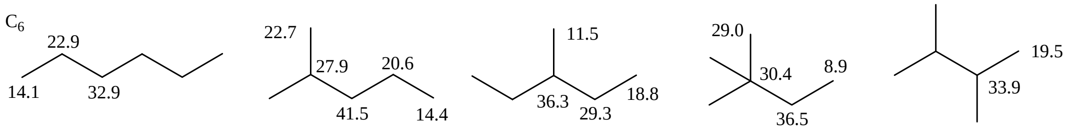
$$\boxed{\delta_C = -(2) + 9x(\#\alpha + \#\beta) - 2x(\#\gamma) + \text{steric corrections}}$$

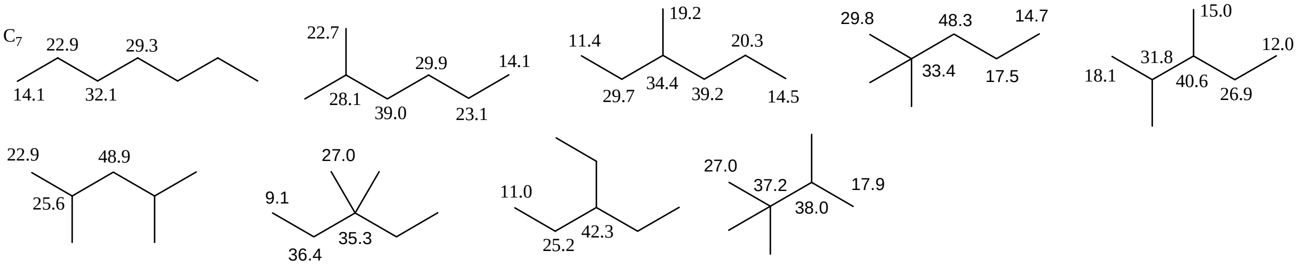


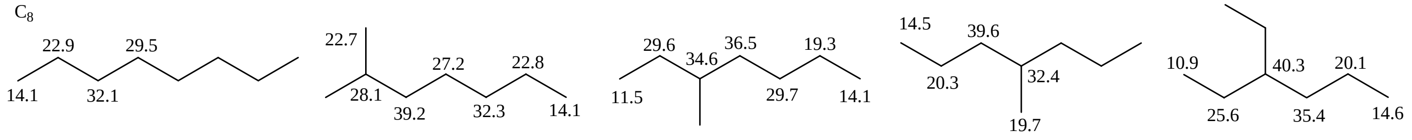
C1 = -2 + 9(1+3) - 2(2) + (-3) = 29 (actual = 28.3)
C2 = -2 + 9(4+2) - 2(2) + [3x(-1.5)+(-15.0)] = 28 (actual = 34.0)
C3 = -2 + 9(3+5) - 0(2) + [(-9.5)+(-15.0)] = 45 (actual = 47.9)
C4 = -2 + 9(3+2) - 3(2) + (-9.5) = 27 (actual = 27.2)
C5 = -2 + 9(1+2) - 2(2) + (-1) = 20 (actual = 19.5)
C6 = -2 + 9(1+2) - 5(2) + (-1) = 14 (actual = 8.5)

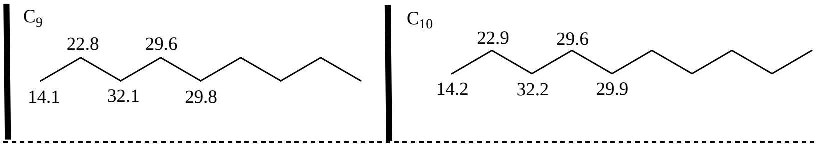
^{13}C shifts for various carbon alkane skeletons - useful starting points for calculating sp3 carbon chemical shifts











If such a starting point is not available, then calculations of the individual ^{13}C shifts of the corresponding alkane can be approximated starting from the chemical shift of methane (-2.3 ppm). Correction factors are included for directly attached carbon atoms (C_α = +9.1), once removed carbon atoms (C_β = +9.4) and twice removed carbon atoms (C_γ = -2.5). Steric corrections are also made when there is a greater density of highly substituted carbons near one another. Finally, the alkane ^{13}C shift values are then modified by correction factors for any appropriate substituent(s). The example alkane, just below, is not present in those listed above. The actual chemical shifts of this alkane are known, so we can check how accurate our calculated values compare with the real values. Once we have demonstrated how to calculate the ^{13}C chemical shifts of an alkane, we will introduce a few substituents to show how they change the chemical shifts of nearby carbons.

An alkane carbon atom's ^{13}C shift is affected most by the directly attached carbons (C_α), and carbons once removed (C_β). Both types of carbon neighbors are deshielding by about 9 ppm. Any carbon atoms just beyond the C_β carbons are called C_γ carbons, and are slightly shielding by about -2.5 ppm. Finally, there is a steric correction factor required when there is a dense collection of near-by C_α and C_β carbon atoms.

The starting point (methane) for ^{13}C chemical shift calculations = -2.3 ppm
There is a C_α correction for all directly attached carbon atoms, C_α = +9.1 ppm
There is a C_β correction for carbons attached to C_α, C_β = +9.4 ppm
There is a C_γ correction for carbons attached to C_β, C_γ = -2.5 ppm

Steric corrections are made according to substitution patterns of the carbon for which the calculation is being made and substitution patterns of all C_α positions, as indicated in the table below. Include a steric correction factor for each C_α carbon attached, if it is indicated.

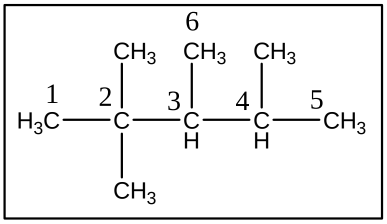
The calculated carbon atom is: ↓	The attached C_α carbons are: primary	secondary	tertiary	quaternary
primary	0	0	-1.1	-3.4
secondary	0	0	-2.5	-7.5
tertiary	0	-3.7	-9.5	-15.0
quaternary	-1.5	-8.4	-15.0	-25.0

The "more precise" formula for calculating an sp^3 carbon ^{13}C chemical shift is as follows.

$$\delta_C = (-2.3) + (\#C_\alpha)(9.1) + (\#C_\beta)(9.4) + (\#C_\gamma)(-2.5) + (\text{steric corrections})\ \text{ppm}$$

The ^{13}C chemical shift calculations of 2,2,3,5-tetramethylpentane are provided as examples. The actual chemical shifts are also provided for comparison. The calculated carbon shifts in this example range from 0.4 ppm to 5.6 ppm off.

$$\delta_C = -2.3 + (\#C_\alpha)(9.1) + (\#C_\beta)(9.4) + (\#C_\gamma)(-2.5) + (\text{steric corrections})\ \text{ppm}$$



C_α C_β C_γ steric $\delta_{calculated}$ (δ_{real})

$C_1 = -2.3 + (1)(9.1) + (3)(9.4) + (2)(-2.5) + (-3.4)$ ppm = 26.7 (actual = 28.3)

$C_2 = -2.3 + (4)(9.1) + (2)(9.4) + (2)(-2.5) + (-15.0) + (3)(-1.5)$ ppm = 28.4 (actual = 34.0)

$C_3 = -2.3 + (3)(9.1) + (5)(9.4) + (0)(-2.5) + (-15.0) + (-9.5)$ ppm = 47.5 (actual = 47.9)

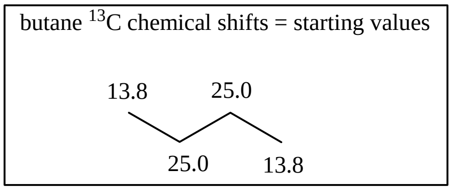
$C_4 = -2.3 + (3)(9.1) + (2)(9.4) + (3)(-2.5) + (-9.5)$ ppm = 26.8 (actual = 27.2)

$C_5 = -2.3 + (1)(9.1) + (2)(9.4) + (2)(-2.5) + (-1.1)$ ppm = 19.5 (actual = 17.7)

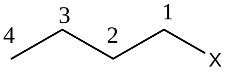
$C_6 = -2.3 + (1)(9.1) + (2)(9.4) + (5)(-2.5) + (-1.1)$ ppm = 12.0 (actual = 8.5)

As mentioned above, the known or calculated chemical shifts of a similar alkane structure can serve as a starting point for estimating the chemical shifts of a similar functionalized carbon skeleton. This requires making a correction to the carbons near-by the functional group. Two correction values are provided for each substituent, depending on whether the substituent is at the end of a chain (terminal) or in the middle of a chain (internal). Several substituent values are provided in side-by-side tables that follow.

An example showing how a substituent value can be estimated.

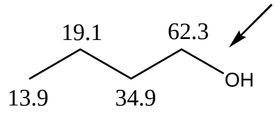


X is attached to a terminal carbon atom of a freely rotating chain.



X = -OH

compare to butane



X = OH

δ (ppm) - δ (alkane) = Δ(correction factor)

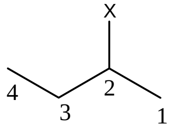
1 = 62.3 - 13.8 = +48.5 C_α correction

2 = 34.9 - 25.0 = + 9.9 C_β correction

3 = 19.1 - 25.0 = - 5.9 C_γ correction

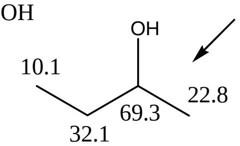
4 = 13.9 - 13.8 = + 0.1 C_δ correction

X is attached to a terminal carbon atom of a freely rotating chain.



X = -OH

compare to butane



X = OH

δ (ppm) - δ (alkane) = Δ(correction factor)

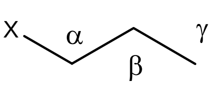
1 = 22.8 - 13.8 = + 9.0 C_β correction

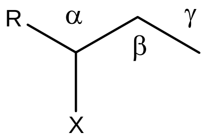
2 = 69.3 - 25.0 = +44.3 C_α correction

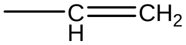
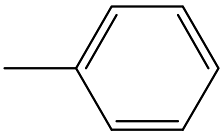
3 = 32.1 - 25.0 = + 7.1 C_β correction

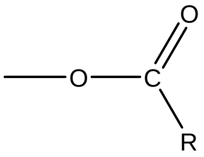
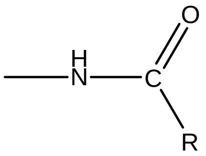
4 = 10.1 - 13.8 = - 3.7 C_γ correction

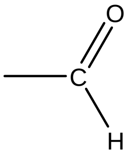
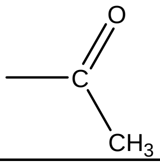
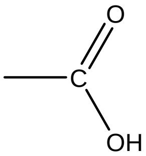
A table of corrections factors for “X” substituents on alkane skeletons (in terminal and internal positions) is provided on the next two pages. Average correction factors for C_α, C_β and C_γ carbons relative to substituent. C_δ is assumed small enough to ignore (not always true). We are also not considering the influence of conformational factors (shapes), which can be significant in relatively rigid systems (e.g. chair conformations can influence chemical shifts).

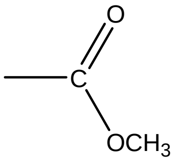
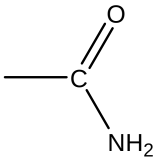
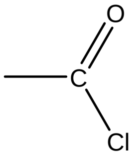




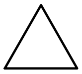
	X is attached to a terminal carbon atom (ppm)			X is attached to an internal carbon atom (ppm)		
Substituent = X	C_α correction	C_β correction	C_γ correction	C_α correction	C_β correction	C_γ correction
$-CH_3$	9	9	-2	6	8	-2
$-CH_2CH_3$	18	7	-2	9	6	-2
$-CH(CH_3)_2$	26	4	-2	14	3	-2
$-C(CH_3)_3$	32	2	-2	20	1	-2
 $-CH{=}CH_2$	20	6	-1	15	5	-1
$-C{\equiv}CH$	5	5	-4	2	6	-4
	23	9	-2	17	7	-2

	X is attached to a terminal carbon atom (ppm)			X is attached to an internal carbon atom (ppm)		
Substituent = X	C_α correction	C_β correction	C_γ correction	C_α correction	C_β correction	C_γ correction
$-OH$	48	10	-6	44	7	-4
$-OR$	60	7	-6	57	5	-6
	51	6	-6	49	5	-6
$-NH_2$	28	10	-5	24	8	-5
$-NH(CH_3)$	38	8	-5	32	5	-4
$-N(CH_3)_2$	45	5	-5	37	3	-4
	26	7	-5	21	5	-5
$-NO_2$	62	5	-5	58	2	-5

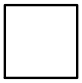
Substituent = X	X is attached to a terminal carbon atom (ppm)			X is attached to an internal carbon atom (ppm)		
	C_α correction	C_β correction	C_γ correction	C_α correction	C_β correction	C_γ correction
—F	70	8	-7	67	5	-7
—Cl	31	10	-5	36	8	-5
—Br	20	10	-4	28	10	-4
—I	-7	11	-2	7	11	-2
	30	0	-3	24	-1	-3
	31	1	-3	26	0	-3
	22	2	-3	18	1	-3

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
	20	2	-3	16	2	-3
	25	3	-3	19	2	-3
—C≡N	3	3	-3	3	3	-3
	33	2	-3	30	2	-3
—SH	11	10	-3	12	8	-3
—SR	22	8	-3	20	6	-3

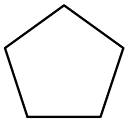
Possible starting point values for calculating ^{13}C chemical shifts (ppm) in cycloalkanes. Use internal substituent corrections from table above. Rigid or preferred conformations may alter these calculated values in a real structure.



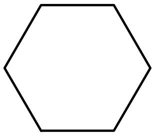
-2.3



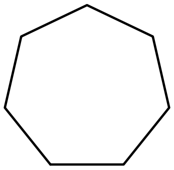
21.6



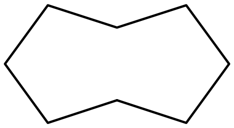
26.0



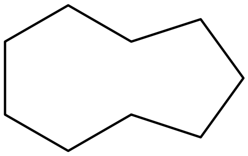
27.1



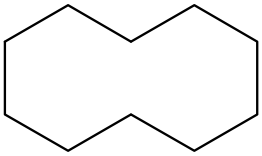
28.5



26.9



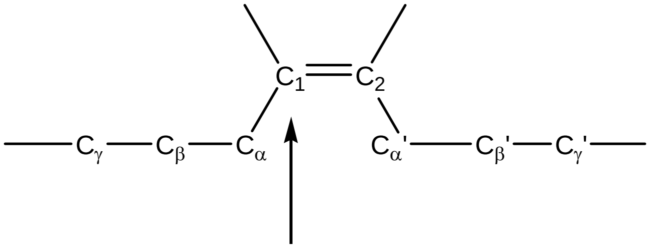
26.4



25.0

Correction factors for calculating alkene ^{13}C chemical shifts. The starting point value is 123.3 from ethane (ethlylene). The first table assumes a hydrocarbon skeleton, which can then be modified using the alkane substituent correction factors above. The second table looks at specific substituents on alkene carbon atoms. Two columns are listed in each table. One column (α, β, γ) for when the substituent is directly attached to the carbon whose chemical shift is being calculated, and a second column (α’, β’, γ’) for when the substituent is on the other carbon of the double bond.

Alkene corrections for alkane branches.

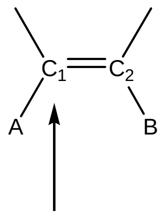


δ_{C1} calculated chemical shift = $123.3 + [10.6\alpha + 7.2\,\beta - 1.5\gamma] - [7.9\,\alpha' + 1.8\beta' - 1.5\,\gamma']$ + (steric corrections)

Steric corrections:

C_α and C_α' are trans	0
C_α and C_α' are are cis	-1.1
2 x alkyl substituents at C_1	-4.8
2 x alkyl substituents at C_2	+2.5
(2 or more) x substituents at C_β	+2.3

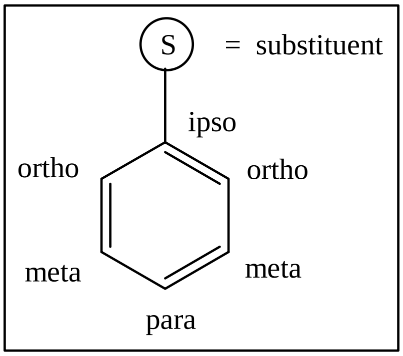
Alkene corrections for specific substituents. If you don't find an exact match for your substituent, you might be able to approximate it using one of the values below.



δ_{C1} calculated chemical shift = 123.3 + any corrections listed below.

Substituent	A	B
$-H$	0	0
$-CH_3$	12.9	-7.4
$-CH_2CH_3$	19.2	-9.7
$-CH_2CH_2CH_3$	15.7	-8.9
$-CH(CH_3)_2$	12.9	-7.4
$-C(CH_3)_3$	26.5	-14.5
$-CH=CH_2$	13.6	-7
$-C_6H_5$	12.5	-11
$-CCH$	-6.5	+5.2
$-CH_2Cl$	10.2	-6
$-CH_2Br$	10.9	-4.5
$-CH_2\ I$	14.2	-4.0
$-CH_2OH$	14.2	-8.4
$-CH_2NH_2$	16.7	-9.8
$-CH_2OCH_3$	29.4	-38.9
$-CH_2OCH_2CH_3$	28.6	-36.9
$-CH_2C_5H_6$	14.2	-7.5
$-COOH$	5.0	-9.8
$-COOCH_3$	5.2	+7.3
$-CONH_2$	6.0	+7.1
$-COCl$	8.1	+14.0
$-CH=O$	15.3	+14.0
$-COCH_3$	13.8	+4.7
$-CN$	-15.1	+14.2
$-OCH_3$	29.4	-38.9
$-OCH_2CH_3$	28.6	-36.9
$-OCOCH_3$	18.4	-26.7
$-NO_2$	22.3	-0.9
$-Si(CH_3)_3$	16.9	+6.7
$-F$	24.9	-34.3
$-Cl$	2.6	-6.1
$-Br$	-8.6	-0.9
$-I$	-38.1	7.0
$-H$	12.9	-7.4

Correction factors for calculating aromatic ^{13}C chemical shifts. The starting point value is 128.5 from benzene. Four columns are listed. The first column is called “ipso” corrections and is used when the substituent is directly attached to the carbon in the benzene ring. The other columns are used when the carbon shift being calculated is ortho, meta or para to the substituent carbon. Multiple corrections should be made when multiple substituents are present. Each substituent may have a different relationship with each of the carbon atoms in the benzene ring. The more substituents that are present, the less reliable is the chemical shift calculation.



δ_C calculated chemical shift = 128.5 + any corrections listed below.

Substituent	ipso	ortho	meta	para
$-H$	0	0	0	0
$-CH_3$	9.3	0.7	-0.1	-2.9
$-CH_2CH_3$	11.7	-0.5	0	-2.6
$-CH_2CH_2CH_3$	14.2	0	-0.2	-2.8
$-CH(CH_3)_2$	20.3	-2.1	-0.2	-2.7
$-C(CH_3)_3$	22.5	-3.1	-0.3	-3.1
$-CH=CH_2$	9.2	-2.3	0	-0.7
$-C_6H_5$	8.1	-1.1	-0.5	-1.1
$-CCH$	-6.3	3.6	-0.2	-0.2
$-CH_2F$	7.9	-1	0.1	0.2
$-CH_2Cl$	9.0	0.2	0	-0.2
$-CH_2Br$	9.2	0.5	0.2	-0.2
$-CH_2OH$	12.4	-1.5	-0.1	-1.1
$-CH_2NH_2$	14.9	-1.5	0	-1.8
$-CH_2OCH_3$	9.8	-0.1	-0.8	-0.9
$-CH_2C_5H_6$	12.9	0.4	-0.1	-2.5
$-COOH$	2.1	-1.6	-0.1	5.2
$-COOCH_3$	2.0	1.2	-0.1	4.3
$-CONH_2$	5.7	-1.0	0.4	3.7
$-COCl$	4.7	2.9	0.5	6.9
$-CH=O$	8.2	1.2	0.6	5.8
$-COCH_3$	8.9	-0.1	-0.1	4.4
$-CN$	-16.0	3.6	0.6	4.3
$-OCH_3$	33.5	-14.4	1.0	-7.7
$-OCH_2CH_3$	30.5	-13.9	0.9	-7.9
$-OCOCH_3$	22.4	-7.1	-0.4	-3.2
$-NO_2$	19.8	-5.0	0.9	6.2
$-Si(CH_3)_3$	11.9	4.8	-0.7	0.3
$-F$	33.6	-13.0	1.6	-4.5
$-Cl$	5.3	0.4	1.4	-1.9
$-Br$	-5.4	3.4	2.2	-1.0
$-I$	-31.2	8.9	1.6	-1.1

^{13}C NMR Problems Name________________________________

Beauchamp

Use the molecular formulas along with the ^{13}C chemical shifts and multiplicities to determine a reasonable structure for the following molecules (There may be more than one reasonable possibility.) The multiplicities are s = singlet, d = doublet, t = triplet, q = quartet. The degree of unsaturation can help determine the possible number of rings and/or π bonds. Draw an approximate sketch of each spectrum. Use arrows drawn from each type of carbon pointing to the appropriate chemical shift to indicate the correct correspondence.

1. C_8H_{18} - 24.9d, 25.5q, 30.2q, 31.2s, 53.4t

2. $C_5H_{11}Cl$ - 22.0q, 25.7d, 41.6t, 43.1t

3. $C_4H_8O_2$ - 14.4q, 20.9q, 60.4t, 170.7s

4. C_4H_7Br - 17.5q, 32.9t, 127.8d, 131.0d

5. C_6H_8O - 18.7q, 130.2d, 130.4d, 141.6d, 153.3d, 193.0d

6. C_9H_{12} - 21.2q, 127.2d, 137.5s

7. $C_6H_{15}NO$ - 27.0t, 27.9t, 34.2t, 34.9t, 43.2t, 62.9t

8. $C_9H_{10}O$ - 8.2q, 31.6t, 128.0d, 128.6d, 132.8d, 137.2s, 200.0s

9. $C_5H_8O_2$ - 14.4q, 60.4t, 129.3t, 130.0d, 166.0s

10. $C_9H_{10}O_3$ - 56.0q, 56.1q, 109.4d, 110.7d, 126.5d, 130.3s, 149.8s, 154.6s, 190.7d

11. $C_{12}H_{14}O_4$ - 14.2q, 61.5t, 129.0d, 131.1d, 132.7s, 167.5s

12. $C_9H_8O_3$ - 115.4d, 115.9d, 125.4s, 130.0d, 144.2d, 159.7s, 168.1s

13. $C_8H_{11}N$ - 13.0q, 23.9t, 115.4d, 118.6d, 126.8d, 128.0s, 128.4d, 144.3s

14. $C_{11}H_{14}O$ - 14q, 23t, 26t, 38t, 128d, 129d, 132d, 136s, 201s

15. $C_4H_{11}N$ - 13q, 44q, 52t

16. C_4H_8O - 14q, 16t, 45t, 202d

17. $C_5H_{12}O$ - 22q, 24t, 42d, 62t

18. $C_{10}H_9NO_2$ - 15q, 62t, 116s, 118s, 129d, 132d, 134s, 165s

19. C_9H_9ClO - 39t, 41t, 127d, 128d, 133d, 136s, 196s

20. $C_{13}H_{20}N_2O_2$ - 12q(x2), 46t(x2), 51t, 63t, 114d, 120s, 131d, 151s, 166s

21. $C_{11}H_{14}O$ - 27q, 44s, 127d, 127.5d, 131d, 138s, 209s

22. $C_3H_4Br_2O_2$ - 28.8t, 40.4d, 173.6s

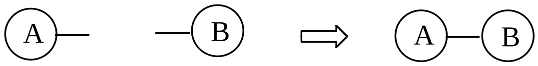
23. C_3H_5Br - 32.6t, 118.8t, 134.2d

24. $C_3H_6Cl_2$ - 22.4q, 49.5t, 55.8d

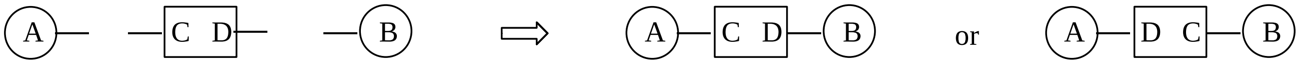
Possible approach for solving a structure problem.

Each structure is a puzzle made of an unknown number of pieces that you create. Your goal is to use the spectral data to make the pieces of your puzzle as few as possible (big pieces make fewer pieces). It's easier to solve a 25 piece puzzle than a 1000 piece puzzle. Your goal is to make a two piece puzzle that only fits together one way. It's not always possible, but that's the goal. The more pieces there are, the more difficult your choices.

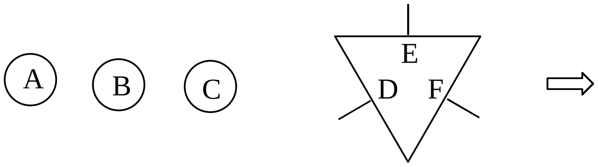
The Goal: only one way to connect.



...two ways to connect,



...or more ways? (six ways here)



6 ways to connect these pieces

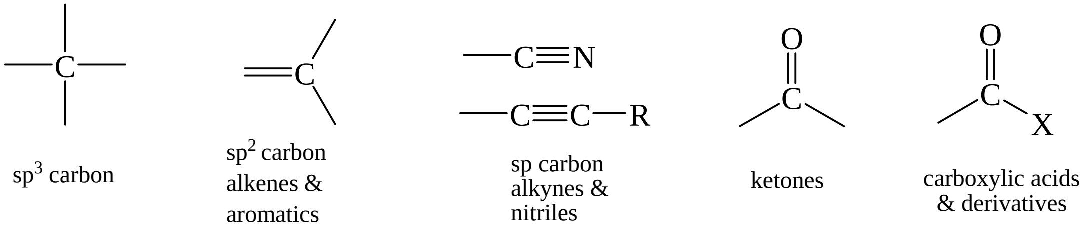
If you have access to some of the more modern NMR experiments, it can make your job of structure determination relatively straightforward. However, there is a lot of information to organize (organized = easy, unorganized = impossible). My strategy for "organizing" the information is provided in the next pages.

1. From the ^{13}C and DEPT data identify each carbon piece. Look for aspects of symmetry that will make some carbon atoms equivalent. Chemical shifts of protons and carbons provide clues about nearby functionality.

2. Use the HETCOR to pair up carbons with their attached protons. Double check assignments with DEPT.

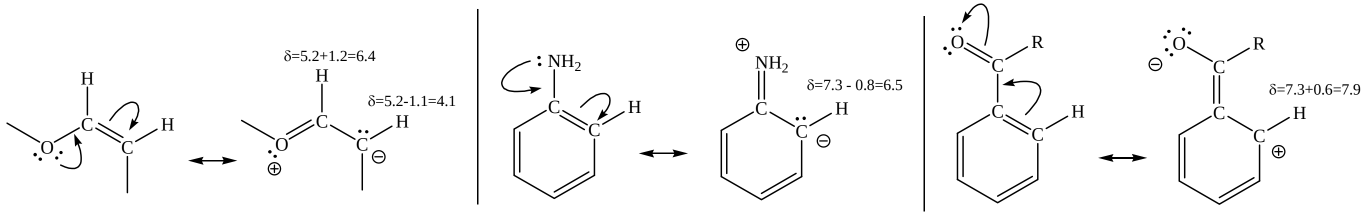
3. Use the COSY cross peaks to connect the coupled proton/carbon pieces from the HETCOR data (#2). Double check the COSY fragment patterns with the multiplicities in the proton NMR spectrum to see if they are consistent.

4. Proton and carbon chemical shifts provide hints and suggestions about nearby heteroatoms (N,O,halogens,etc.) and pi bond patterns (alkenes, alkynes, aromatics, carbonyl groups, nitriles, etc.). Multiple functionality producing smaller shifts can produce a large shift from a single stronger influencing functional group. Using chemical shifts this way may help locate quaternary carbon centers and heteroatoms (e.g. next to ester carbon side or next to ester oxygen side). HMBC (explained later) is very helpful for placing quaternary carbon atoms.

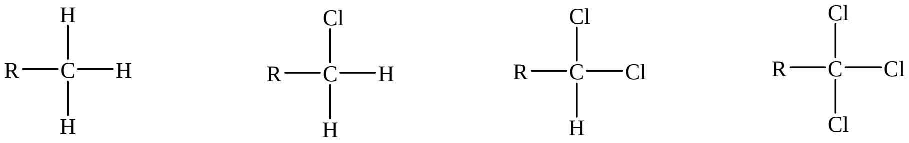


These are all considered "quaternary" centers (carbon atoms without any attached hydrogen atom). The lack of an attached hydrogen takes away connectivity clues in the COSY and HETCOR spectra (explained later).

Remember resonance effects can be both shielding (more electron density, smaller δ) and deshielding (less electron density, larger δ).



Inductive withdrawing effects are deshielding and not usually completely additive.


$R-CH_3$ $\quad$ $R-CH_2Cl$ $\quad$ $R-CHCl_2$ $\quad$ $R-CCl_3$

proton shifts:	0.9 ppm	Δ=2.6	3.5 ppm	Δ=2.6	5.9 ppm	Δ=NA	no protons
carbon shifts :	14 ppm	Δ=31	45 ppm	Δ=24	69 ppm	Δ=26	95 ppm

5. Look for symmetry features in the proton and carbon NMR spectra. Count the number of carbon atoms in the ^{13}C NMR and the number of protons in the H NMR to help make a formula (rule of 13). Estimate the number of heteroatoms (N,O,halogens) to modify your formula (use the IR functional groups and the H NMR and ^{13}C NMR chemical shifts). Calculate a degree of unsaturation and use the ^{13}C to estimate the number of pi bonds, and by difference determine the number of rings in your structure.

6. Look for end pieces of your puzzle that only connect one way, and middle pieces that connect 2, 3, or more ways and try to fit them together based on expected chemical shifts.

A possible worksheet to help solve your structure problems is provided just below.

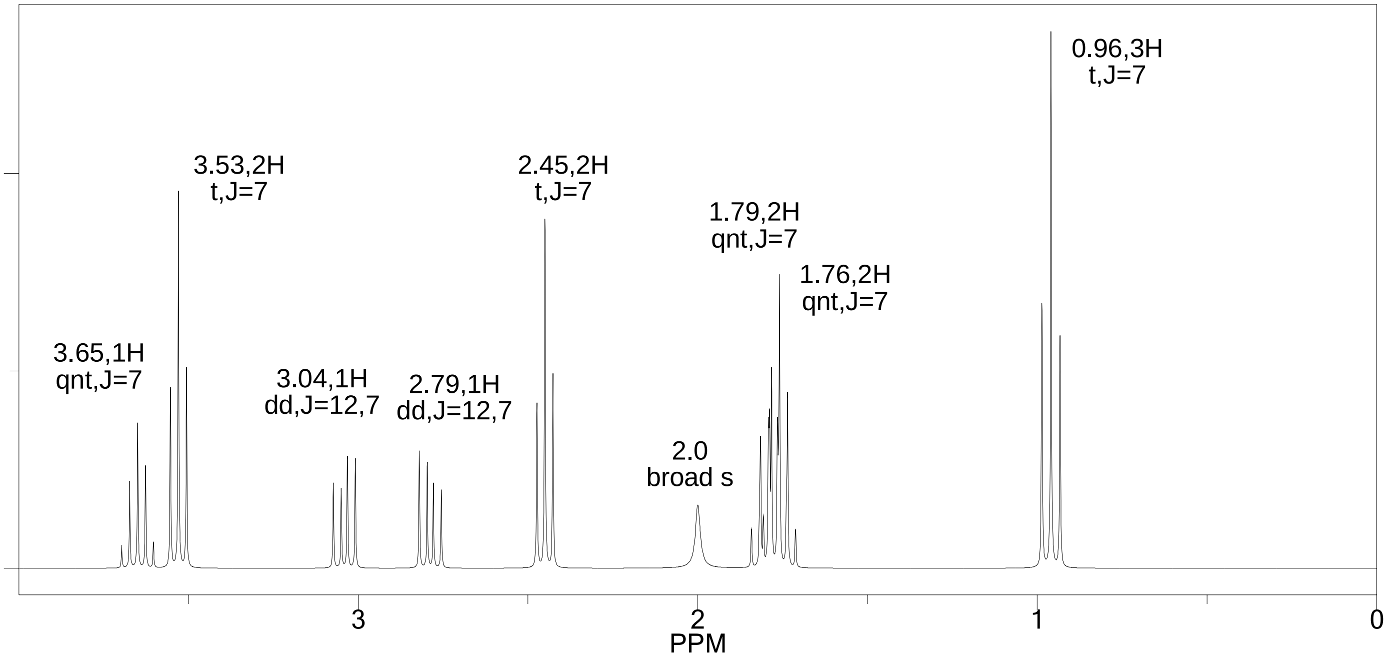
Structure Problem Worksheet

^{13}C / DEPT		HETCOR	COSY	HMBC	NOE and/or NOESY

Advantages of other 1D and 2D NMR experiments: DEPT, COSY, HETCOR, HMBC – An Example

^{1}H NMR – Integration indicates the number of hydrogen atoms at each chemical shift. The chemical shift provides information about the functional group environment around the protons, and the multiplicity provides information about neighboring "coupled" protons having different chemical shifts. Typical coupling includes geminal (2 bond coupling, both hydrogen atoms attached to the same carbon atom, as $=CH_2$ or as $*-CH_2$, where * = chiral center), vicinal coupling (3 bond coupling) and a few 4 bond couplings (allylic, meta, para, etc.) that we mostly ignore.

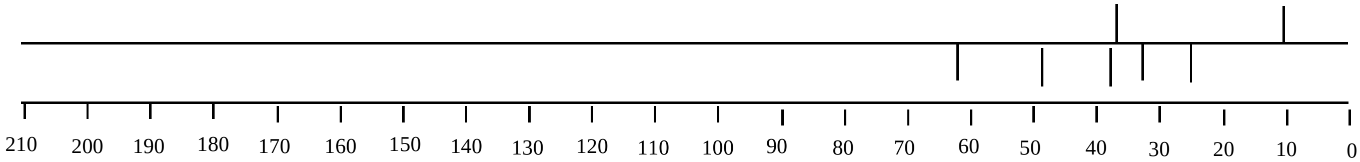
MW = 223.1 (bromine is present)



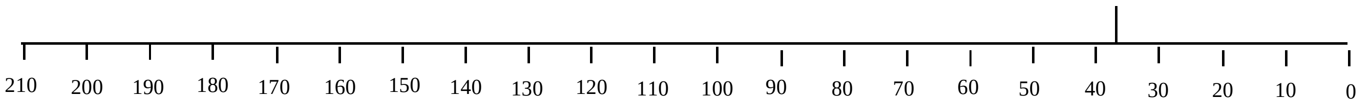
^{13}C NMR and DEPT (distortion enhancement by polarization transfer) data

The ^{13}C NMR shows each distinct type of carbon atom. If atoms are equivalent, by symmetry, they will appear as a single peak, often at approximately "n" times the intensity, where "n" is the number of similar carbons. When a carbon atom does not have any attached hydrogen atom its intensity is often weaker (a smaller peak appears), because it relaxes so slowly it does not give a full intensity response with each pulse (excitation). Such carbons are often referred to as "quaternary" carbon atoms. DEPT shows the number of hydrogens on each carbon, as indicated below.

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

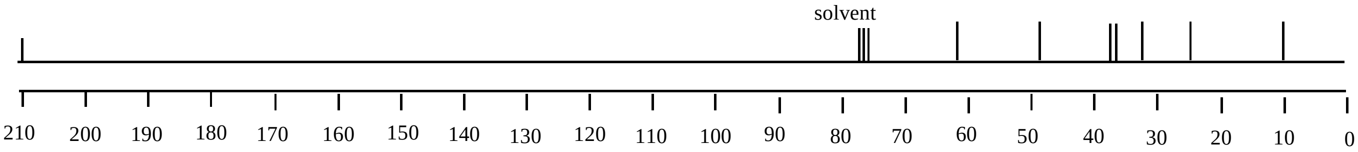


Middle spectrum = DEPT-90 ^{13}C NMR - only C-H appears (up)



210.1
62.4
49.3
38.1
37.0
32.6
25.5
10.0

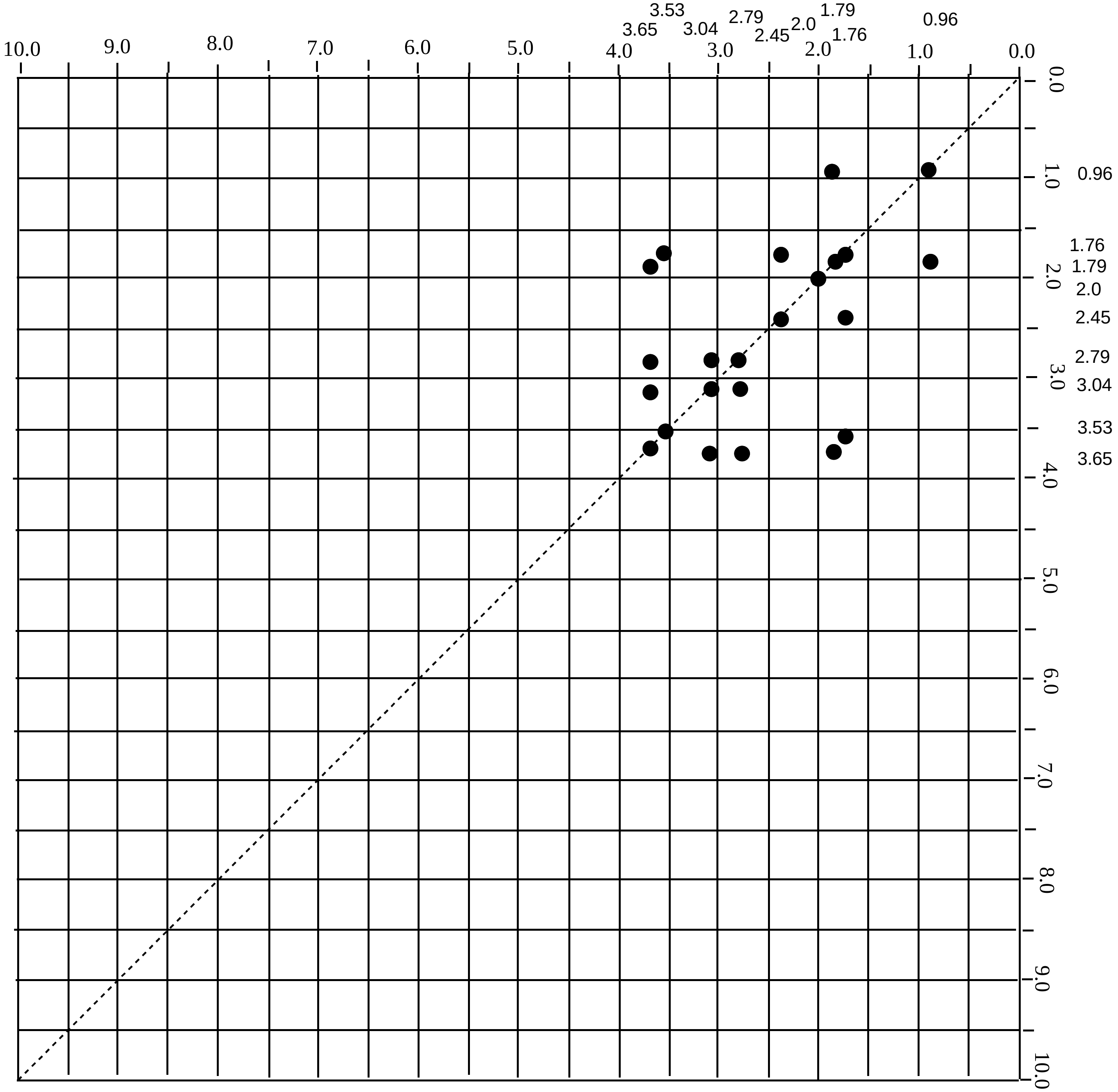
Bottom spectrum = proton decoupled ^{13}C NMR spectrum - shows all types of carbon



HH COSY spectrum (Proton-Proton Correlation Spectroscopy)

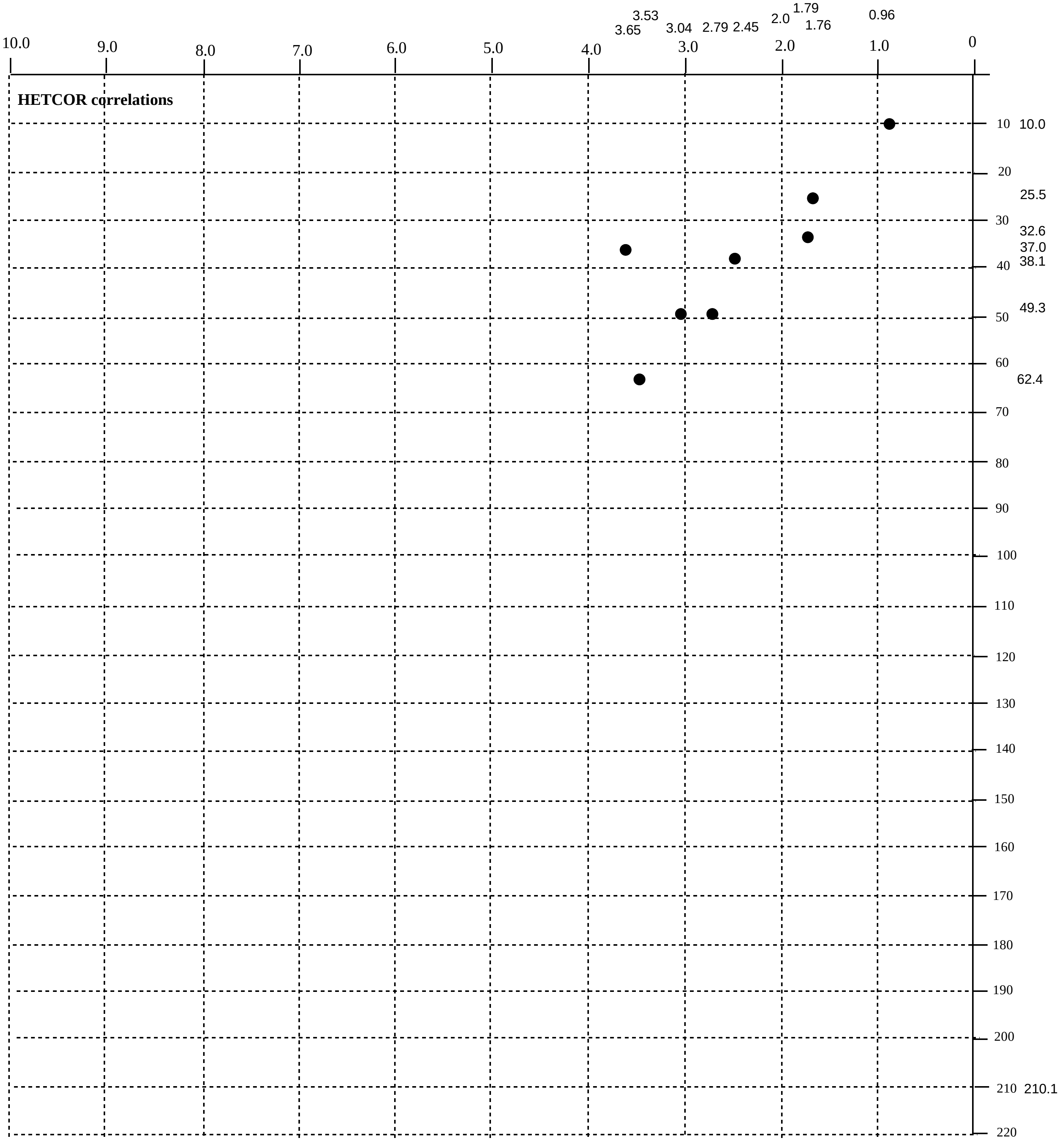
The diagonal peaks show the same peaks and chemical shifts that are seen in the normal proton NMR, and are not helpful. However, the *cross peaks* (off diagonal peaks) show proton/proton correlations with "coupled neighbor" protons, and can trace out a path of connectivity in each spin system (a spin system is a continuous path of coupled protons). *Connect the dots* to construct the *spin systems* within a structure.

COSY: H-H correlations: diagonal peaks do not provide any additional information, but cross peaks appear whereever different neighbor protons are coupled. ●



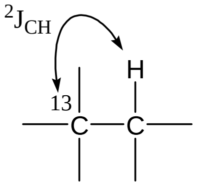
HETCOR spectrum

The peaks (dots) show carbon atoms and proton atoms that are directly attached to one another (one bond coupling), as in a direct C-H bond. This is detected via one bond C-H coupling constants ($^1J_{CH}$), which are large (around 120-160 Hz). In a sense, you could say that we are looking for the coupling patterns about 140 times per second and these interactions are repeatedly reinforced, while other coupling is random (sometimes + and sometimes -) and cancels out. Once you have made these C-H connections, the COSY spectrum will not only show neighbor protons, but it will also show neighbor carbon atoms attached to those protons.

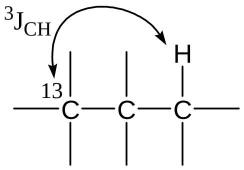


HMBC spectrum

The peaks (dots) show carbon atoms and proton atoms that are two and three bonds away from one another (2 and/or 3 bond coupling). This is detected via two and three bond C-H coupling constants ($^{2/3}J_{CH}$ around 7-10 Hz), which are much smaller than one bond coupling. This is especially helpful for quaternary carbon atoms which do not show coupling to neighbor carbons or protons, (in our course).



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

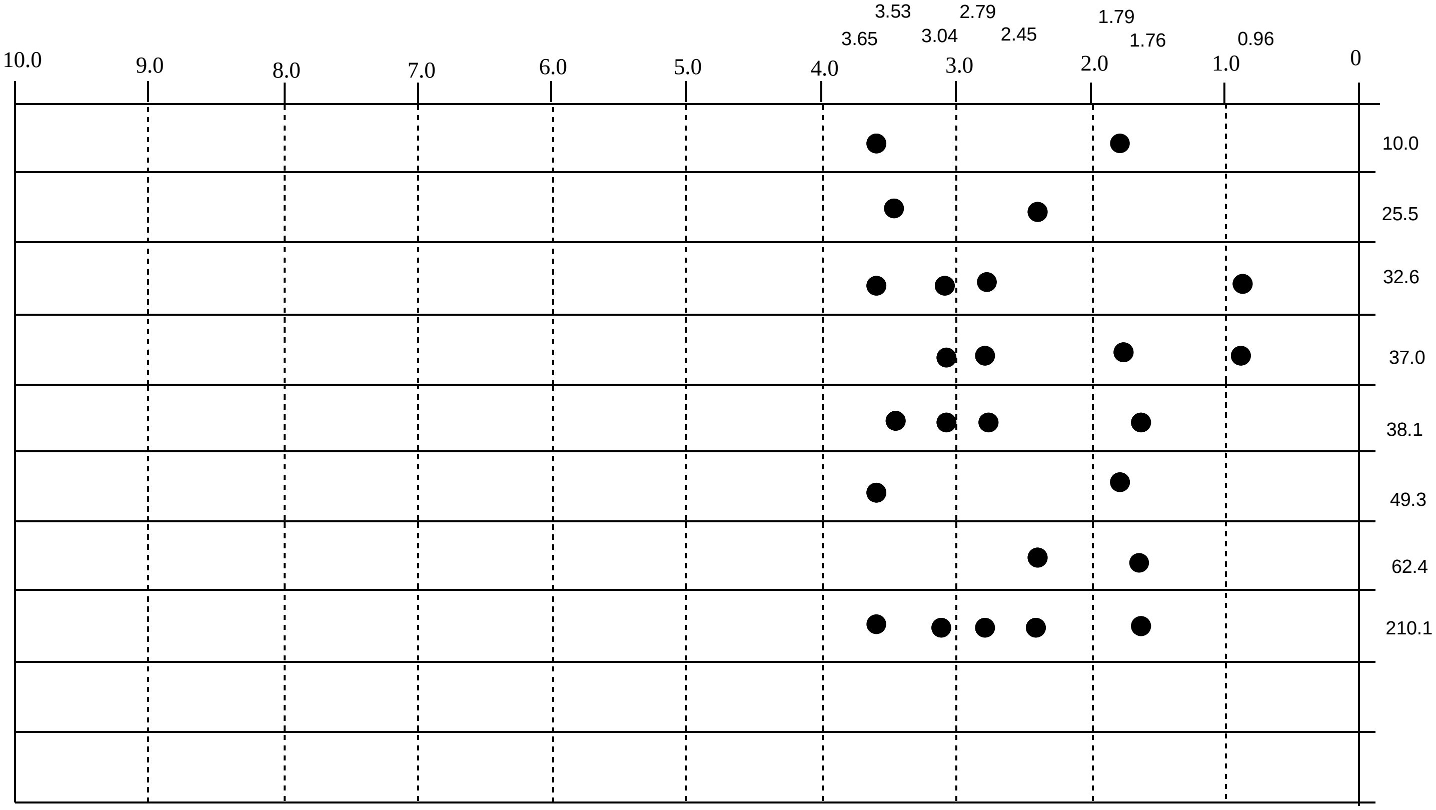


$^{3}J_{CH} \approx$ 7-10 Hz

HMBC = heteronuclear multiple bond correlation

Detection of CH coupling is timed to the approximate coupling between the coupled atoms. In this case of HMBC this is approximately 10 Hz. In a sense we are looking for a signal 10 times per second. Smaller or larger coupling usually tends to average towards zero. It is possible that expected coupling will not be present and unexpected coupling will appear. These complications are excluded in our simple approach to problems. Correlations with quaternary carbons (no attached hydrogen atoms) are especially helpful.

HMBC correlations = ● Shows carbon couplings to protons 2 and 3 bonds away.



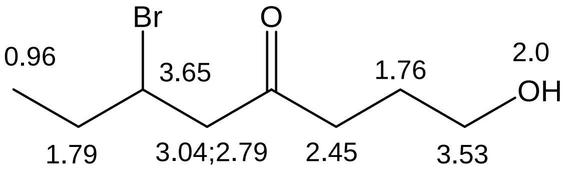
If you organize all of this information in a compact way (the one page worksheet) so you can confirm or reject structure possibilities, it becomes quite straight forward to construct a reasonable structure of the molecule. Left out of our discussion are issues of relative stereochemistry. There are other NMR experiments (NOE, NOESY, ROESY) that help resolve these details, but we will not discuss them in this course.

Structure Problem Worksheet

^{13}C	DEPT	HETCOR	COSY	HMBC	NOE and/or NOESY
210.1	C=O ketone			3.65, 3.04, 2.79, 2.45, 1.76	
62.4	CH_2-O	3.53	1.76	3.65, 2.45, 1.76	
49.3	CH_2	2.79 3.04	3.04 , 3.65 2.79 , 3.65	3.65, 2.45, 1.79	
38.1	CH_2	2.45	1.76	3.53, 3.04, 2.79, 1.76	
37.0	CH	3.65	3.04, 2.79, 1.79	3.04, 2.79, 2.45, 1.76	
32.6	CH_2	1.79	3.65, 0.96	3.65, 3.04, 2.79, 1.79, 0.96	
25.5	CH_2	1.76	2.45, 3.53	3.53, 2.45	
10.0	CH_3	0.96	1.79	3.65, 1.79	

Answer

Proton Data



^{13}C Data