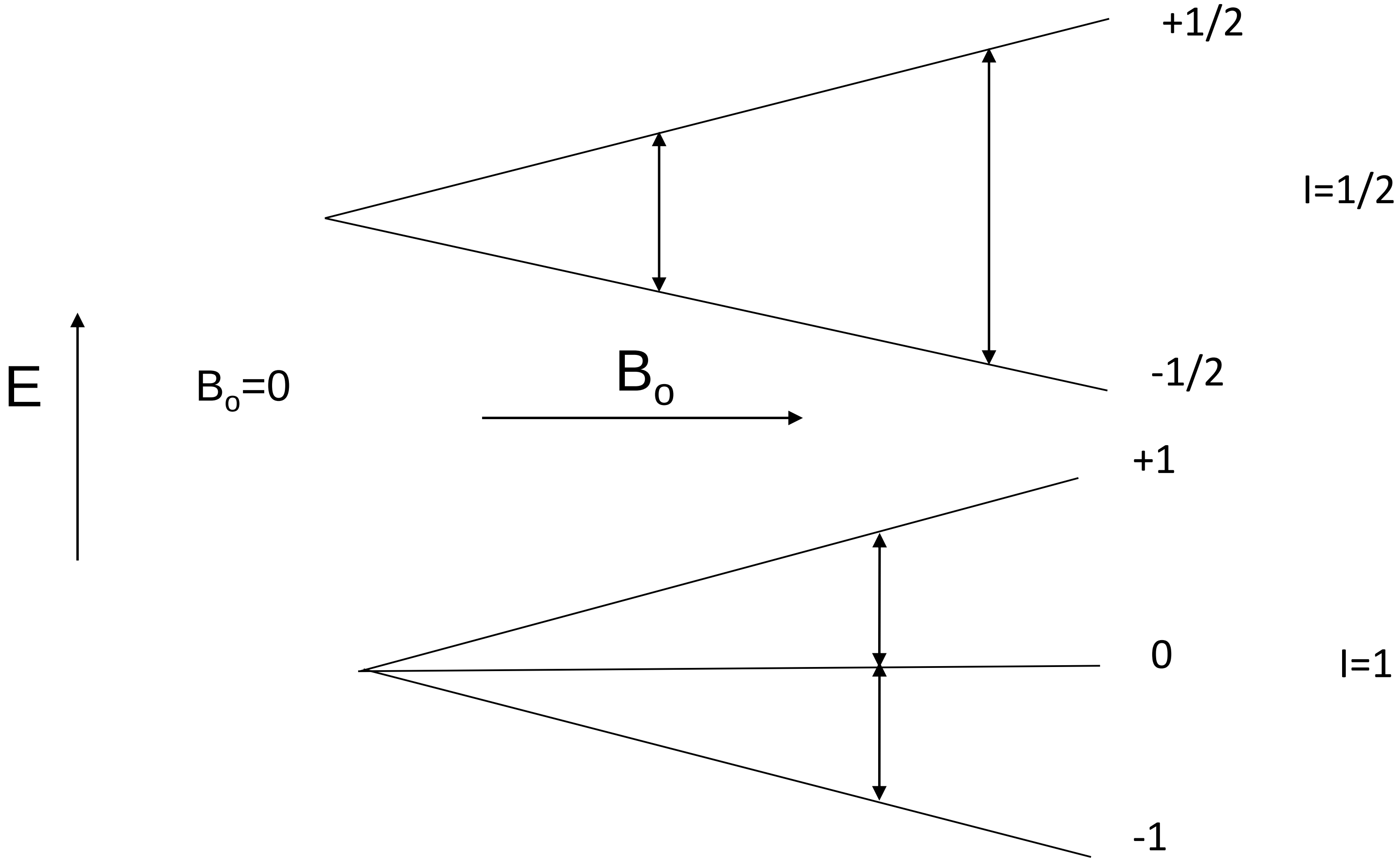
Nuclear Magnetic Resonance

Some atomic nuclei possess angular momentum also referred to as spin. This is given the quantum # I which can have integer and half integer values.

Atomic Mass	Atomic Number	I	Examples
odd	odd	1/2,3/2,..	^{1}H, ^{19}F, ^{31}P
odd	even	1/2,3/2,..	^{13}C, ^{17}O, ^{29}Si
even	odd	1,2,3,	^{2}H, ^{14}N,^{10}B
even	even	0	^{12}C, ^{16}O

When a nucleus is placed in a magnetic field the energy splits based on the magnetic quantum # m where m goes from I to –I in steps of 1 so that there are 2I+1 levels.



The energy difference between the levels is

$\Delta E=\gamma(h/2\pi)B_0=h\nu$

Where γ (magnetogyric ratio) is a constant for a specific nucleus.

$\nu=(\gamma/2\pi)B_0$ is the Larmor Relationship

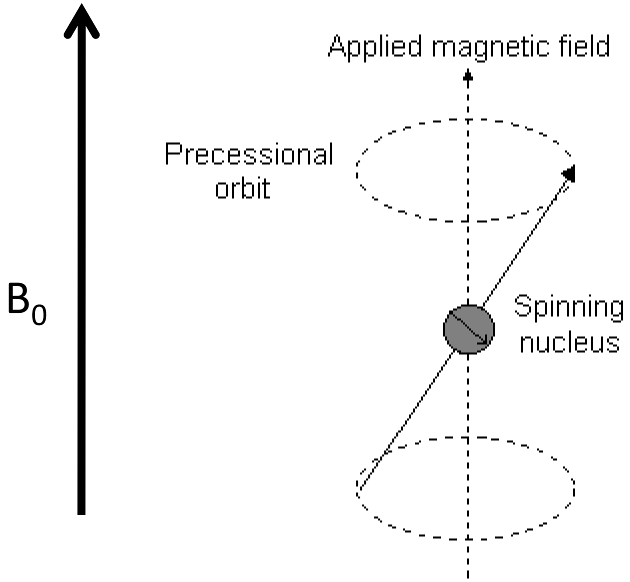
$\nu=(\gamma/2\pi)B_0$ the Larmor Relationship

For ^{1}H in a 7 T magnet

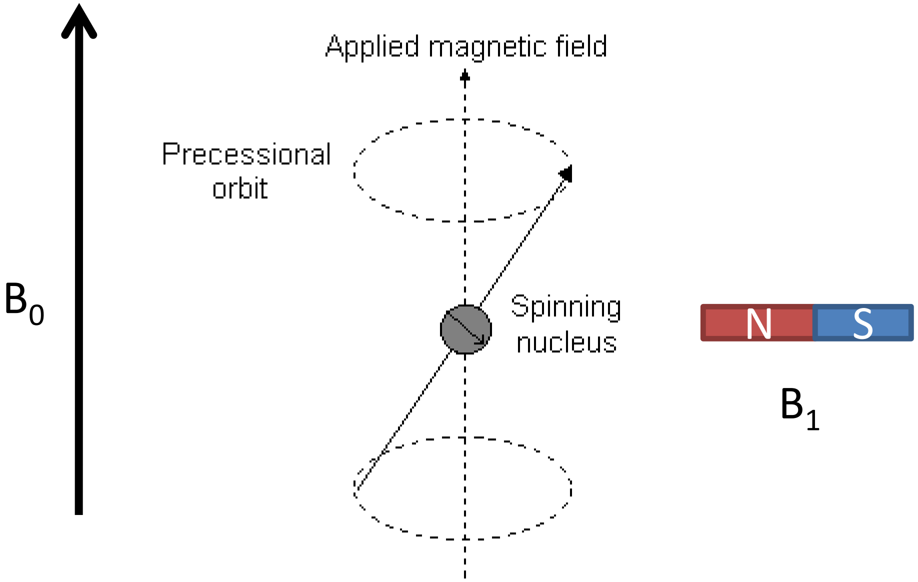
$\nu=26.75\text{X}10^{7}$ Rad, T^{-1},S^{-1} X 7T / 2π = 298.2 MHz

For ^{13}C

$\nu=6.728\text{X}10^{7}$ Rad, T^{-1},S^{-1} X 7T / 2π = 74.99 MHz

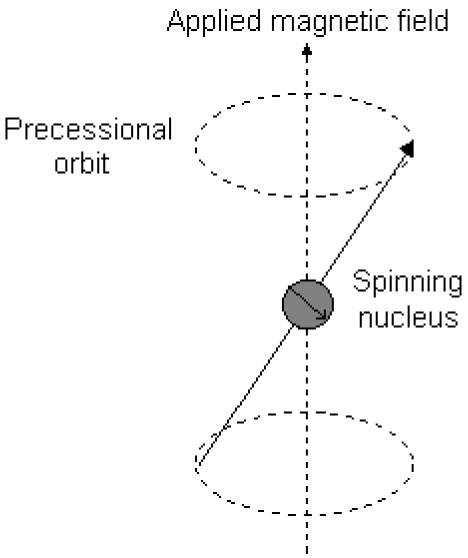


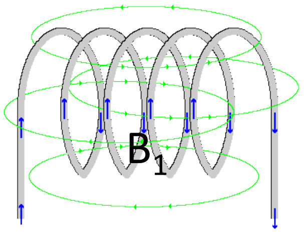
$\nu=(\gamma/2\pi)B_0$ is the Larmor frequency A stationary magnetic field perpendicular to B_0 cannot interact with the precessing nucleus.

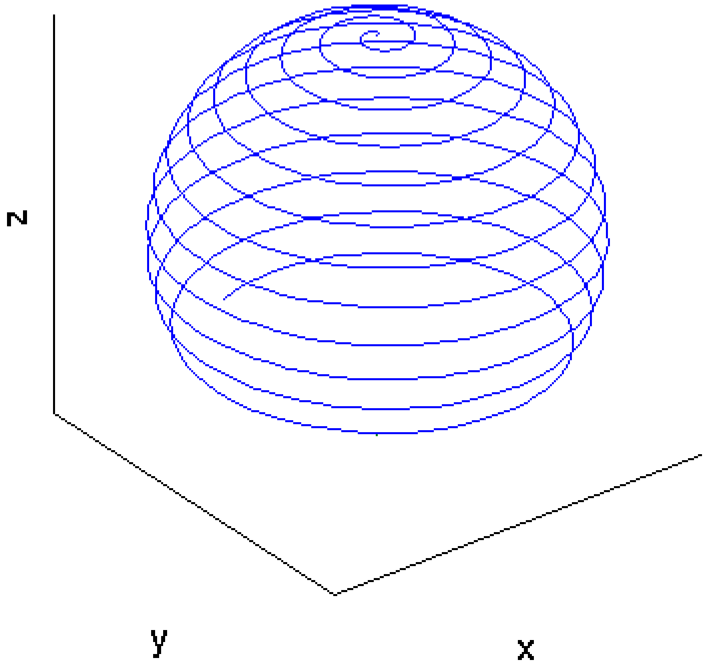


Oscillating Magnetic Field

A magnetic field rotating at the resonance frequency ν causes the nucleus to nutate into the XY plane.



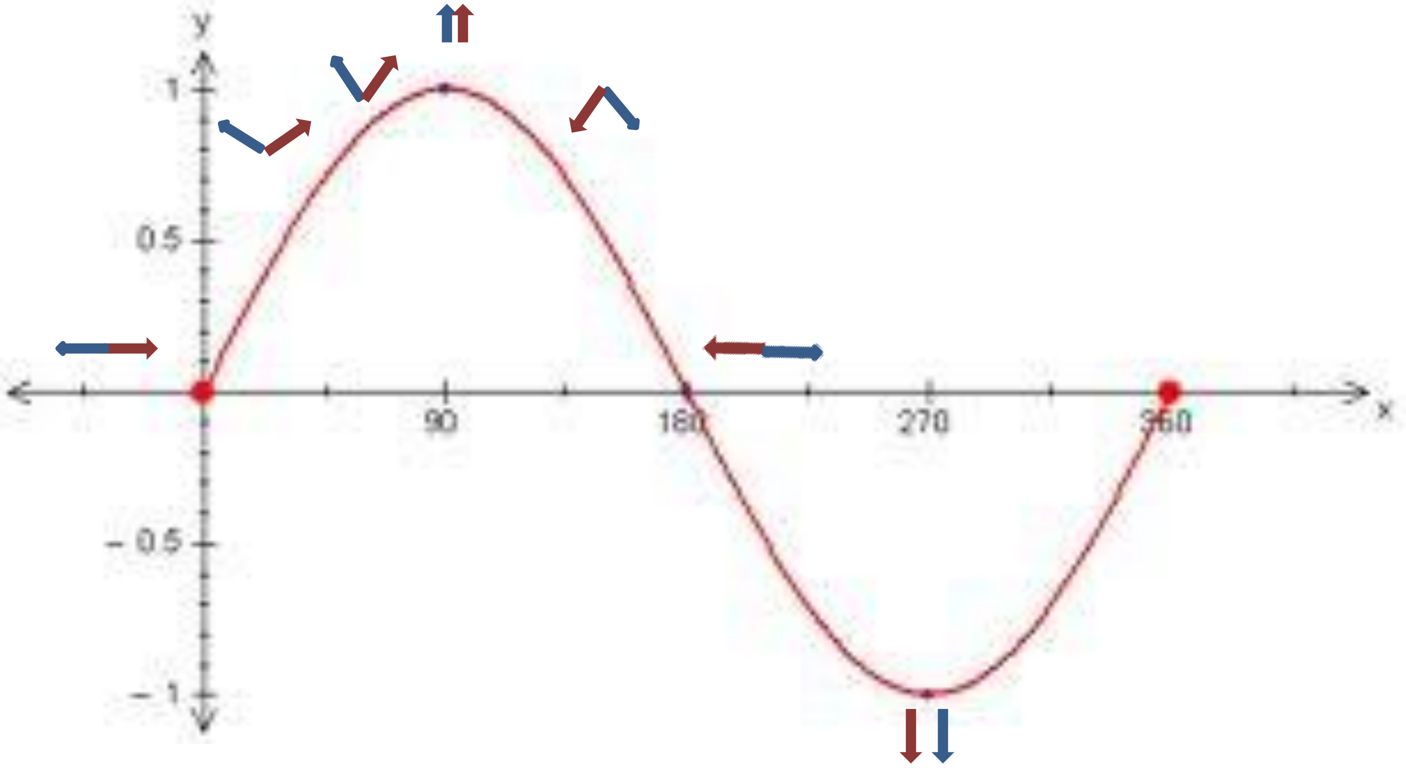




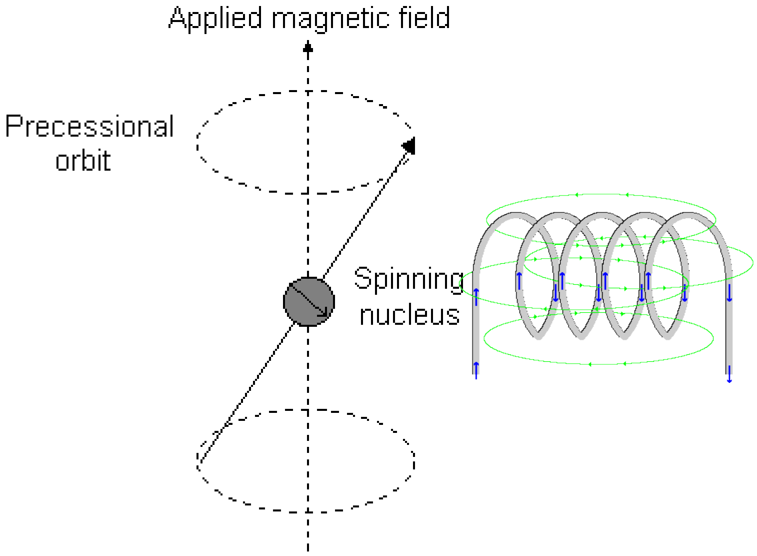
Nuclear vector nutates into XY plane

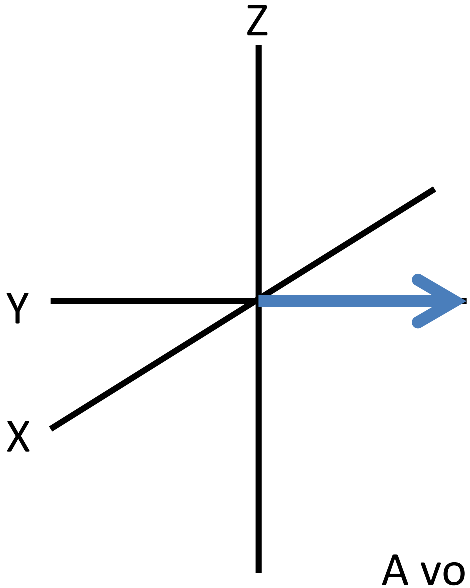
http://www.fis.unipr.it

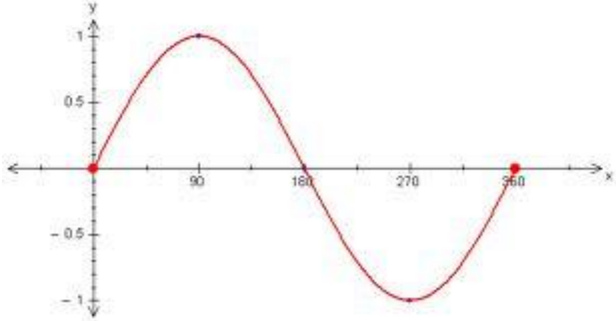
How can one make a rotating magnetic field at the Larmor frequency? An RF signal is an electromagnetic wave. The sine curve can be decomposed into two counter rotating magnetic fields.



$\nu=(\gamma/2\pi)B_0$ the Larmor Relationship

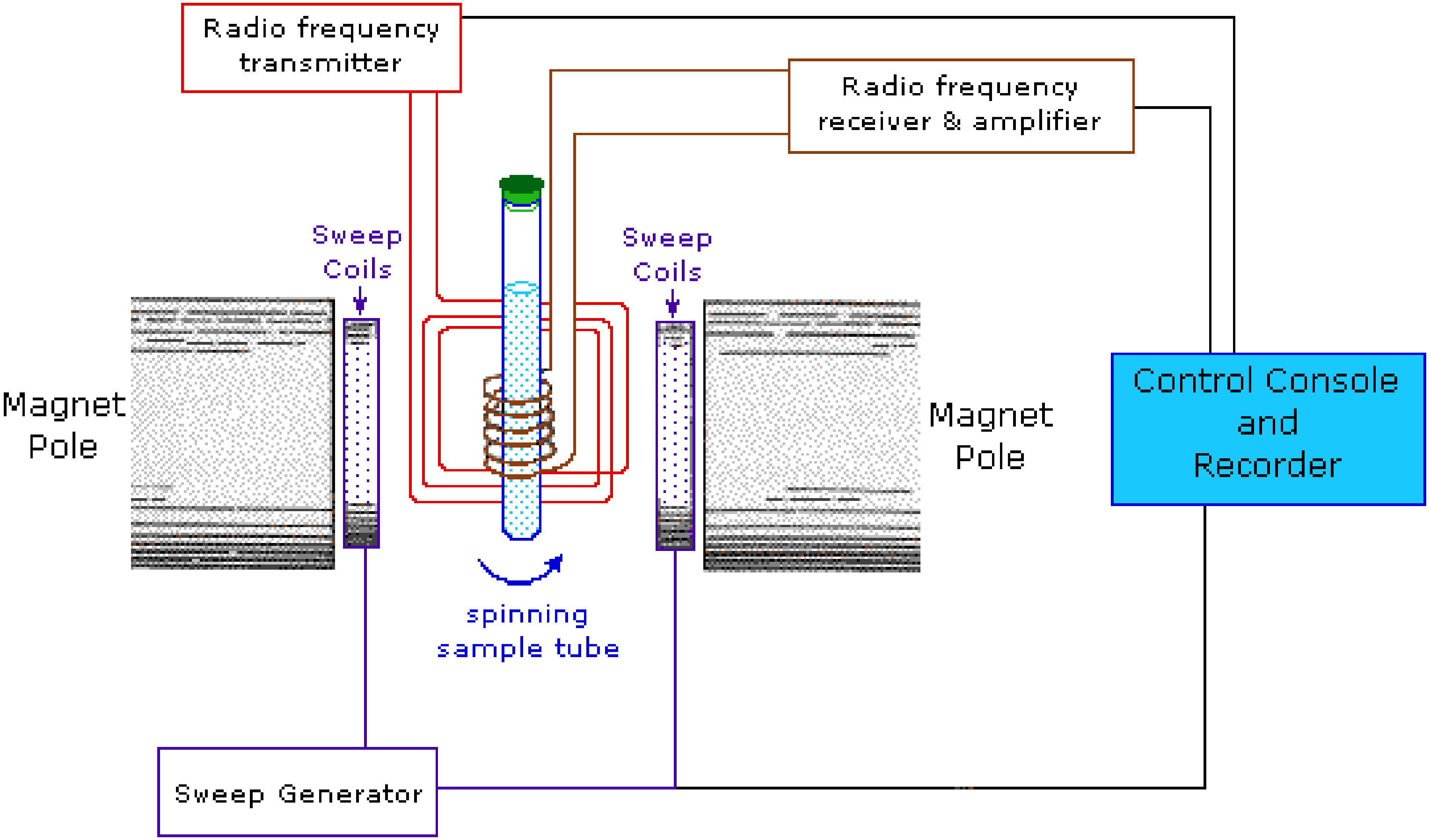






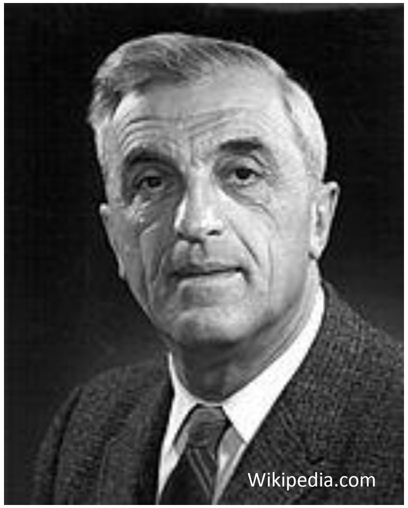
A voltage is produced in the coil that oscillates at the precessional frequency ν.

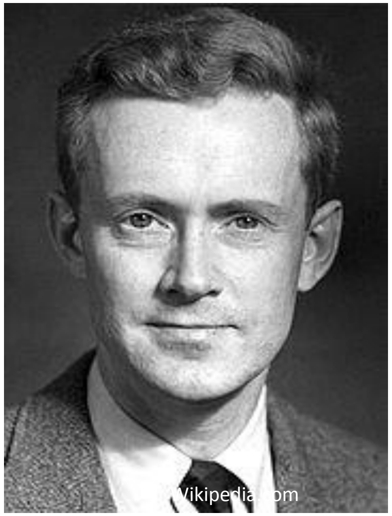
Continuous Wave NMR



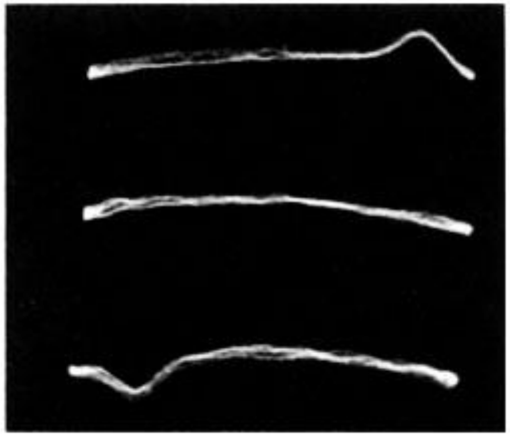
Felix Bloch (1905-1983)

Edward Mills Purcell (1912-1997)


Wikipedia.com


Wikipedia.com

Nobel Prize in Physics, 1955.

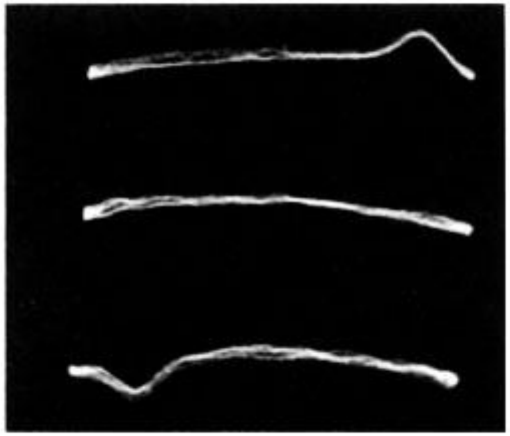


First NMR signals of water

Bloch, F., Hansen, W. W. and Packard, M. *Phys. Rev.* **70**, 474–485 (1946);

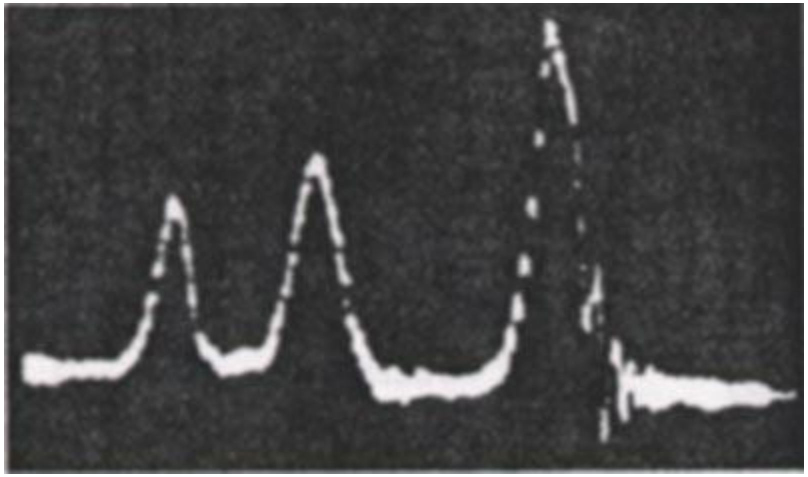
$\omega = \gamma\,(1-\sigma)\,B_0$

σ: Chemical Shift



First NMR signals of water

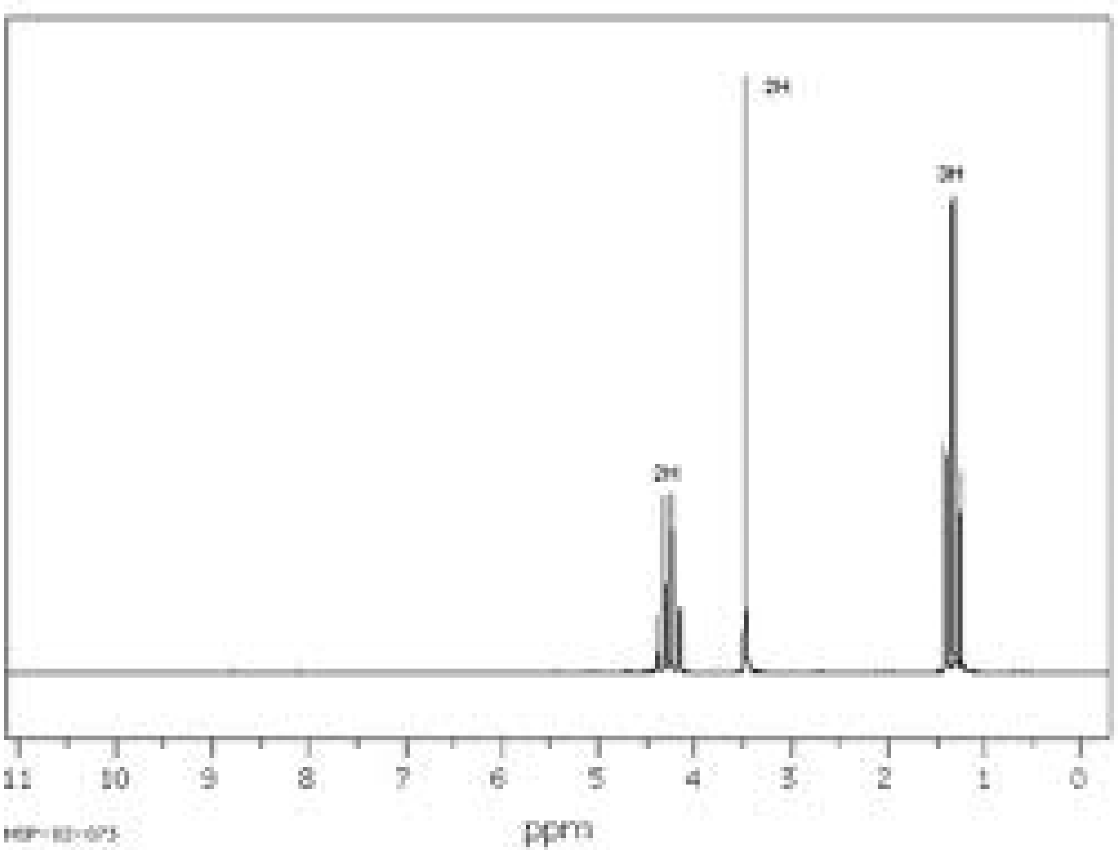
Bloch, F., Hansen, W. W. and Packard, M. *Phys. Rev.* **70**, 474–485 (1946);



First NMR signals of ethanol (1951)

$CH_3\text{-}CH_2\text{-}OH$

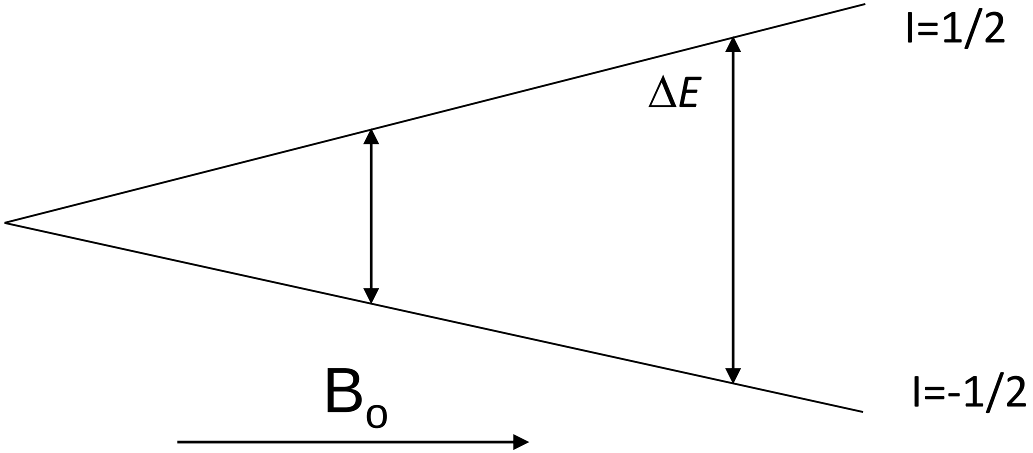
NMR spectrum



low field → high field

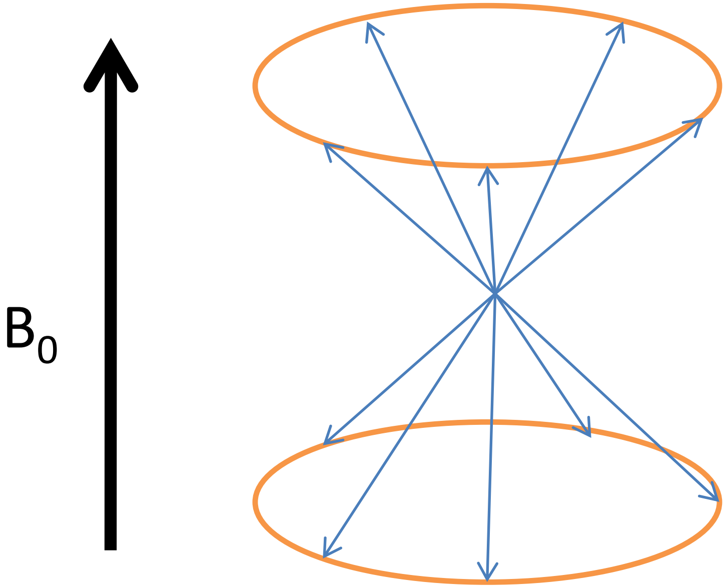
$$\text{ppm} = \frac{\nu \text{ of the peaks} - \nu \text{ of the reference}}{\nu \text{ of the spectrometer MHz}}$$

Boltzmann Distribution of Spins

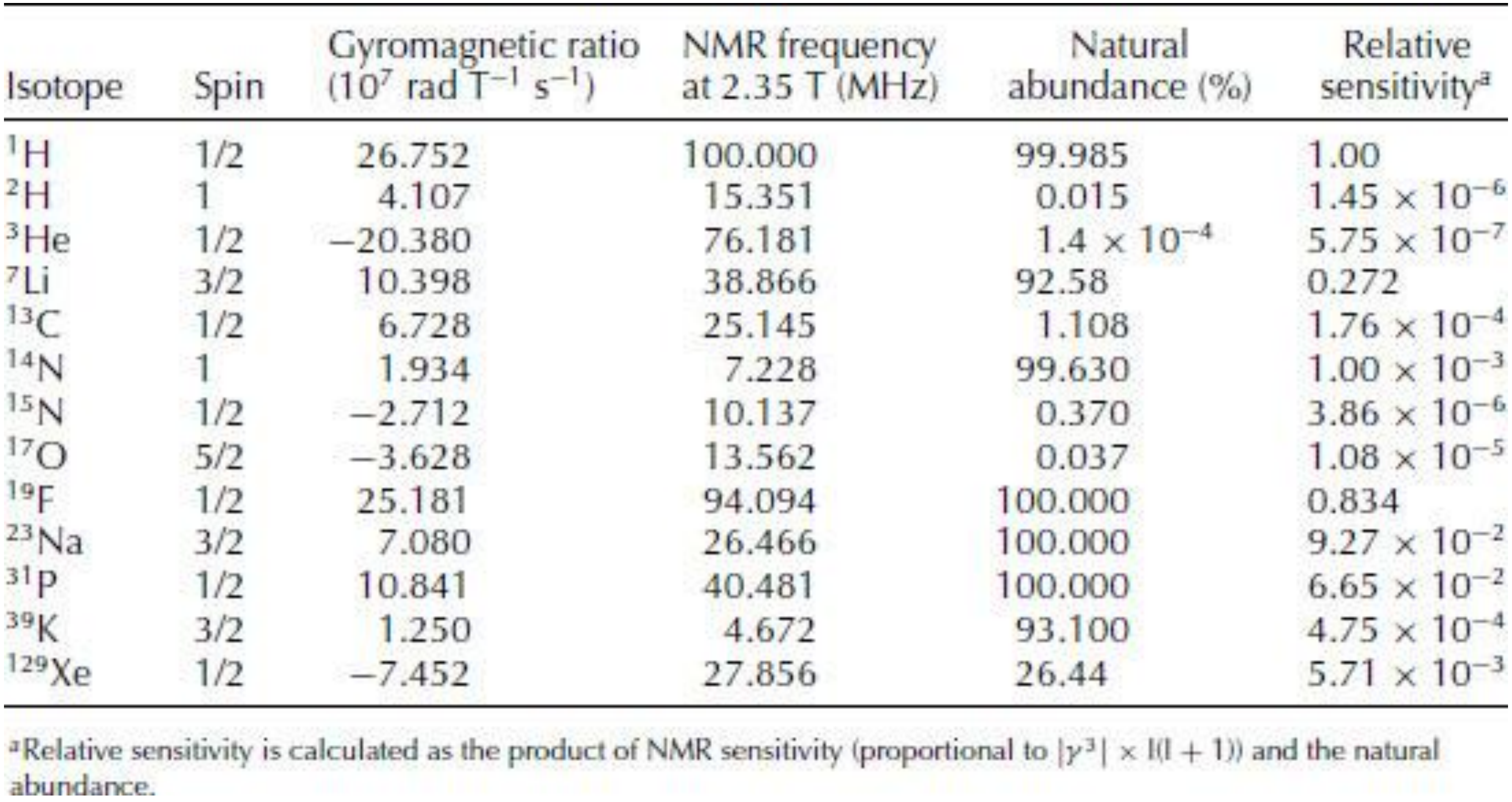


$$\frac{N_{\text{upper}}}{N_{\text{lower}}} = e^{-\Delta E/kT} = e^{-h\nu/kT}$$

For ^1H at 400 MHz this comes to 1,000,000/1,000,090 therefore NMR is very insensitive



Sensitivity of some common NMR nuclei



Isotope	Spin	Gyromagnetic ratio (10^7 rad T^{-1} s^{-1})	NMR frequency at 2.35 T (MHz)	Natural abundance (%)	Relative sensitivity[a]
^{1}H	1/2	26.752	100.000	99.985	1.00
^{2}H	1	4.107	15.351	0.015	1.45×10^{-6}
^{3}He	1/2	−20.380	76.181	1.4×10^{-4}	5.75×10^{-7}
^{7}Li	3/2	10.398	38.866	92.58	0.272
^{13}C	1/2	6.728	25.145	1.108	1.76×10^{-4}
^{14}N	1	1.934	7.228	99.630	1.00×10^{-3}
^{15}N	1/2	−2.712	10.137	0.370	3.86×10^{-6}
^{17}O	5/2	−3.628	13.562	0.037	1.08×10^{-5}
^{19}F	1/2	25.181	94.094	100.000	0.834
^{23}Na	3/2	7.080	26.466	100.000	9.27×10^{-2}
^{31}P	1/2	10.841	40.481	100.000	6.65×10^{-2}
^{39}K	3/2	1.250	4.672	93.100	4.75×10^{-4}
^{129}Xe	1/2	−7.452	27.856	26.44	5.71×10^{-3}

[a] Relative sensitivity is calculated as the product of NMR sensitivity (proportional to $|\gamma^3| \times I(I+1)$) and the natural abundance.

What is the Problem with Continuous Wave NMR?

If we want to observe a peak 1 Hz wide

$\Delta E = h\nu$

If ν = 1Hz than $\Delta E = h$

Uncertainty principle states $\Delta E \Delta t \sim h$

If $\Delta E = h$ then $\Delta t = 1$ sec.

For 60 MHz NMR 10ppm = 600 Hz so a scan of 1 hz resolution takes 600 seconds or 10 min.

What are the consequences of this problem?

NMR is weak so we have a poor signal to noise (S/N) ratio.
We can increase the S/N by adding up a number of scans.

The rule is that the S/N increases as the square root of the change in the # of scans.

So to increase the signal to noise by a factor of 2 you need to collect 4 times the number of scans.

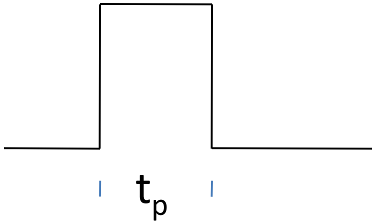
Therefore, for a 60 MHz spectrum that takes 10 minutes you would need to collect 4 scans or 40 minutes and for an increase of S/N of 4 times you would need 16 scans or 160 min (2hours 40 min).

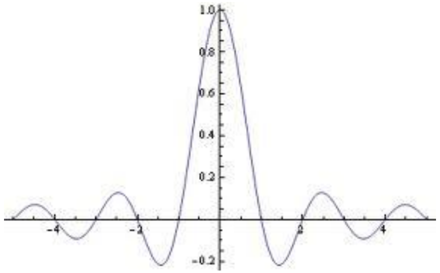
Solution to this problem

If we could observe all frequencies at one time we could collect a complete NMR spectrum in one second.

How can we generate all frequencies at one time?

Very short square pulses produce a range of frequencies.



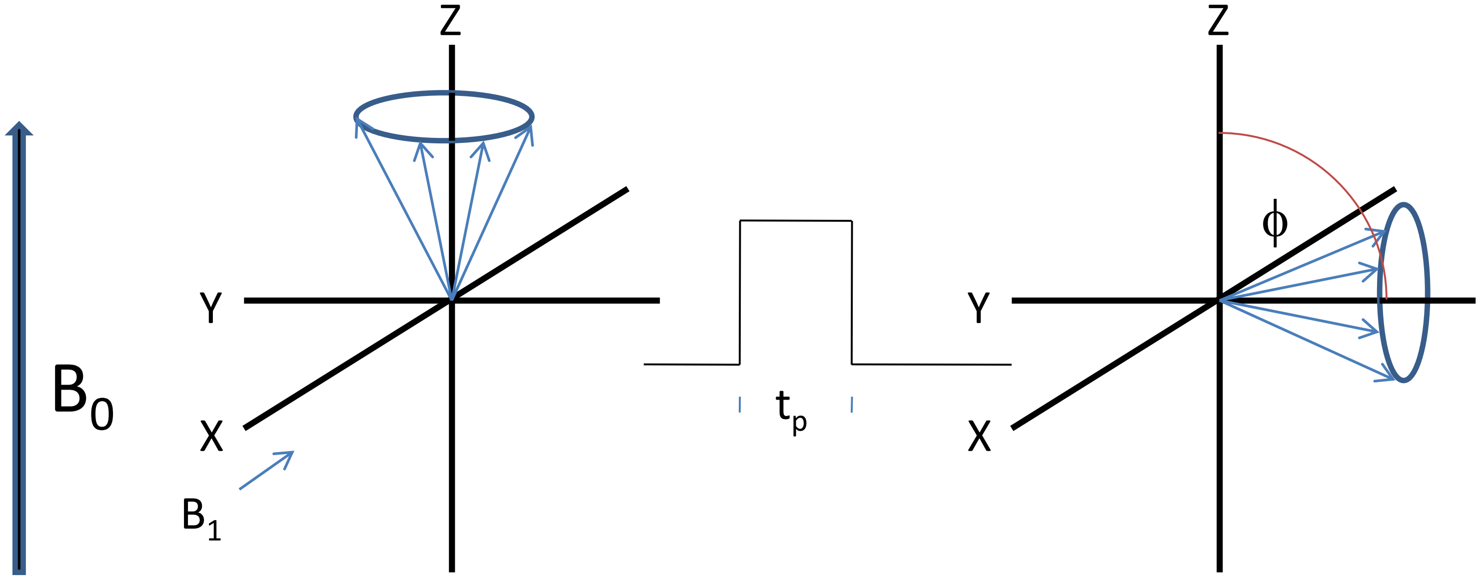


dsprelated.com

Frequency range = +/- $1/t_p$

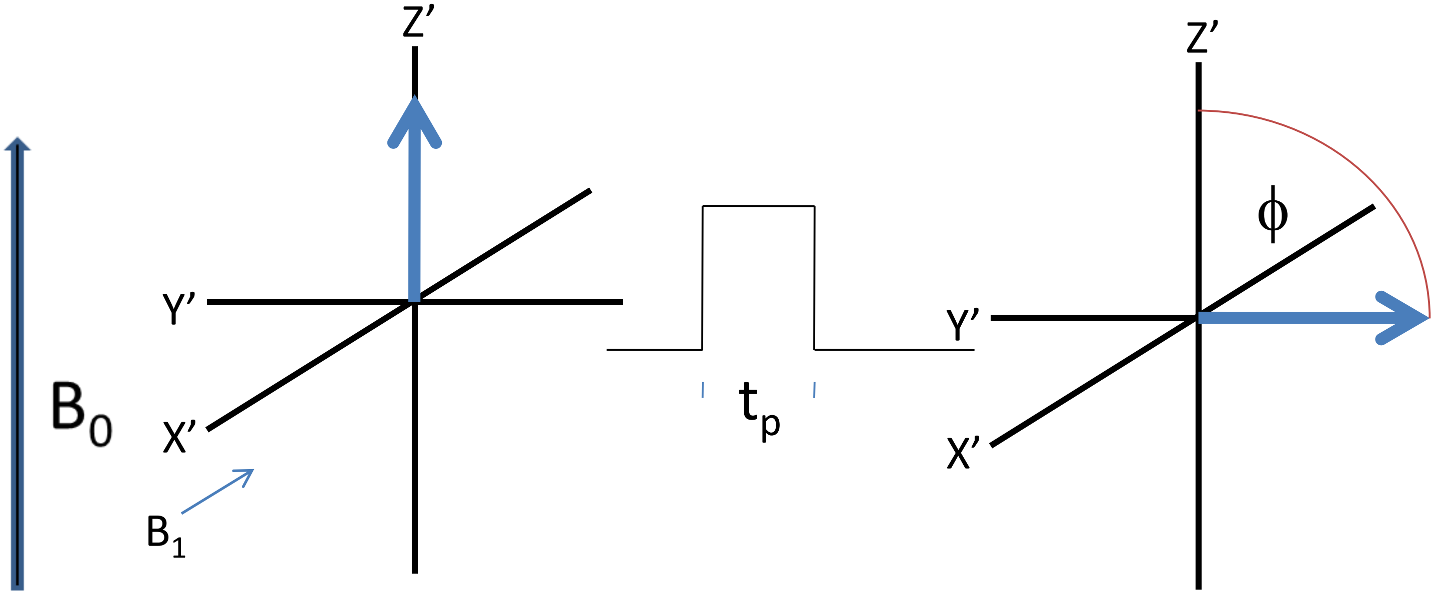
Therefore a 10 μsec pulse produces
a frequency range of +/- 100,000 hz

NMR in the Laboratory Frame



$$\phi = \gamma B_1 t_p$$

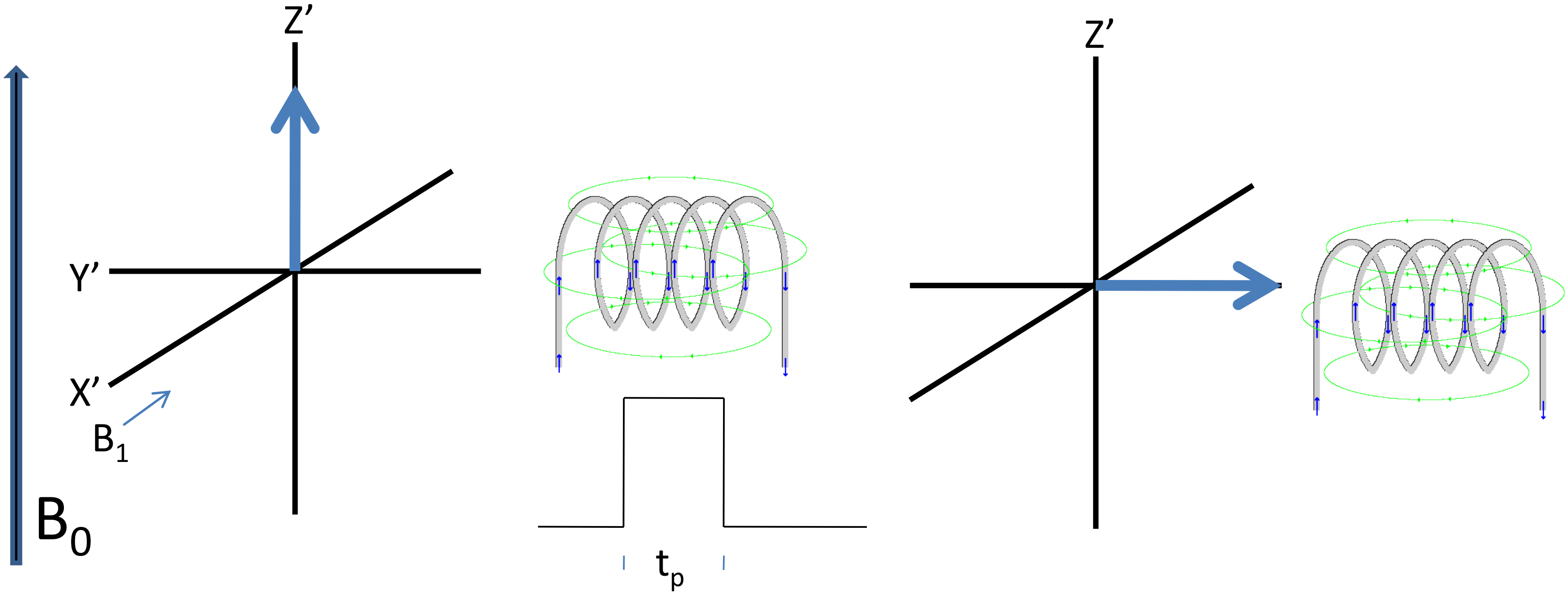
NMR in the Rotating Frame



$$\phi = \gamma B_1 t_p$$

Axes are rotating at the Larmor frequency

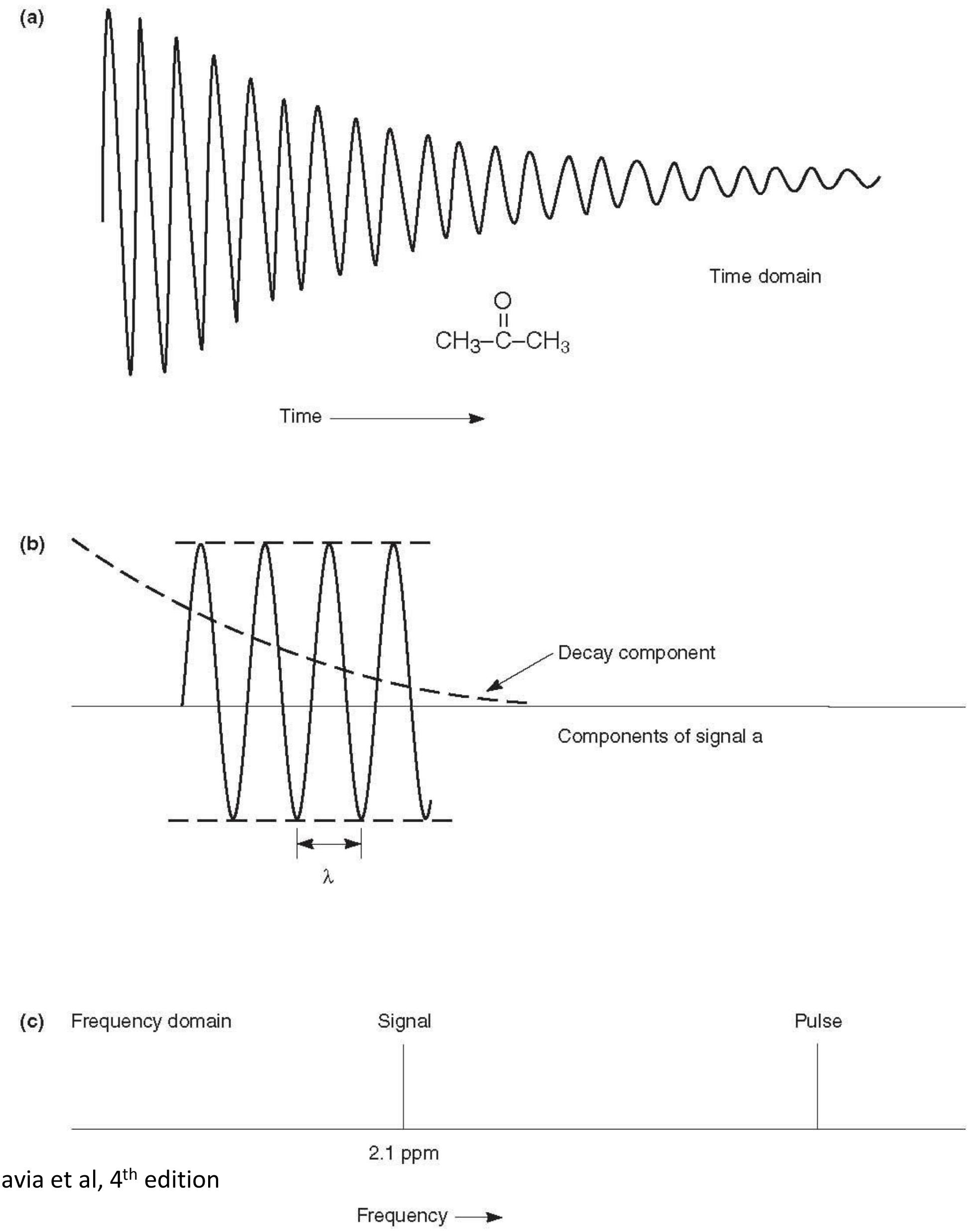
Signal Detection in NMR



$\phi=\gamma B_1 t_p$

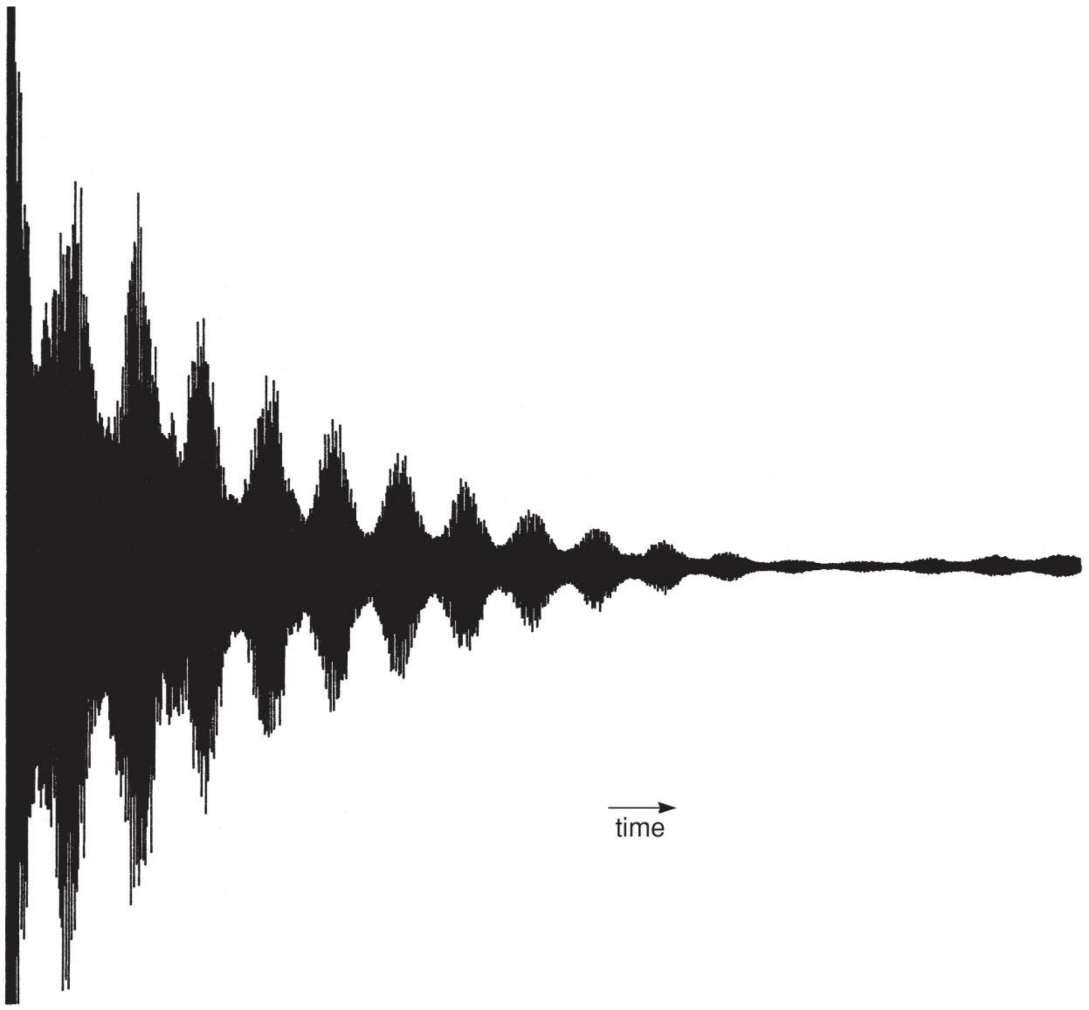
A voltage is produced in the coil that oscillates at the precessional frequency ν.

Free Induction Decay (FID)



Introduction to Spectroscopy, Pavia et al, 4th edition

Free Induction decay (FID) from many frequencies



Introduction to Spectroscopy, Pavia et al, 4th edition

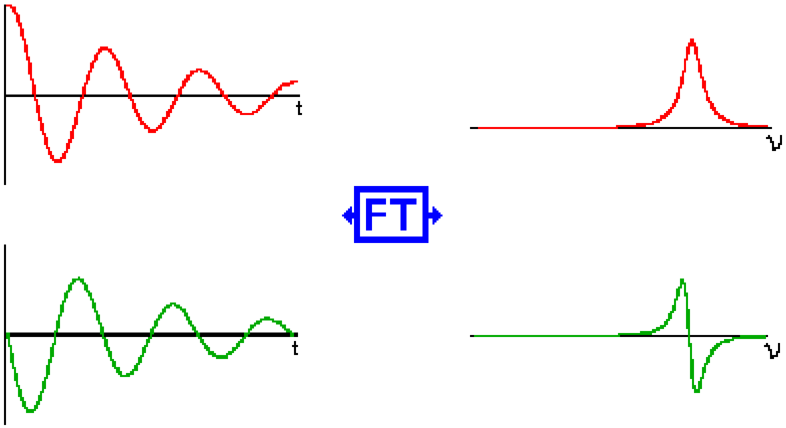
Fourier Transform

$$f(\omega) = \int_{-\infty}^{\infty} f(t)e^{-i\omega t}\, dt$$

$$e^{-i\omega t} = \cos\omega t + i\sin\omega t$$

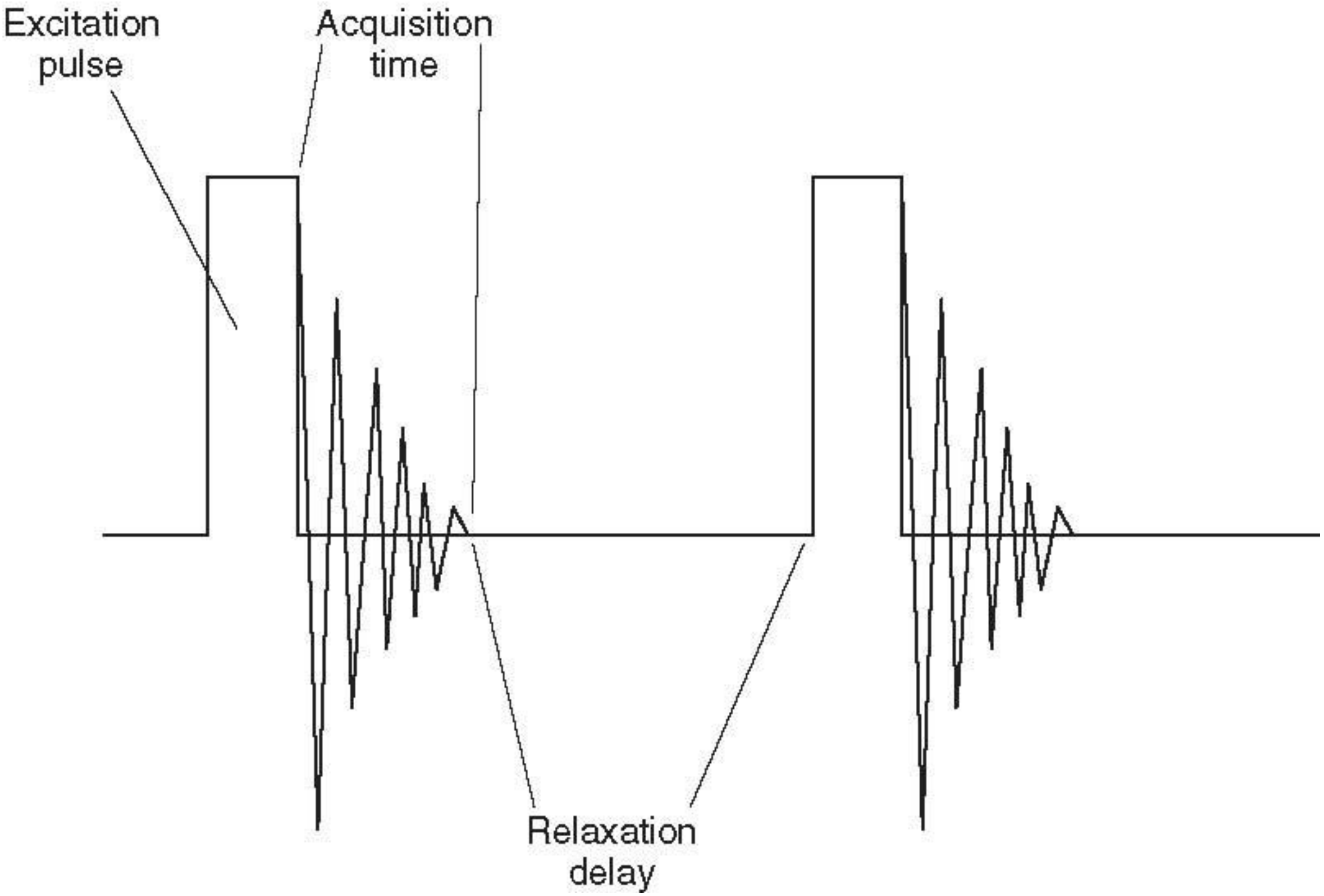
$$\mathrm{Re}[f(\omega)] = \int_{-\infty}^{\infty} f(t)\cos\omega t\, dt$$

$$\mathrm{Im}[f(\omega)] = \int_{-\infty}^{\infty} f(t)\sin\omega t\, dt$$

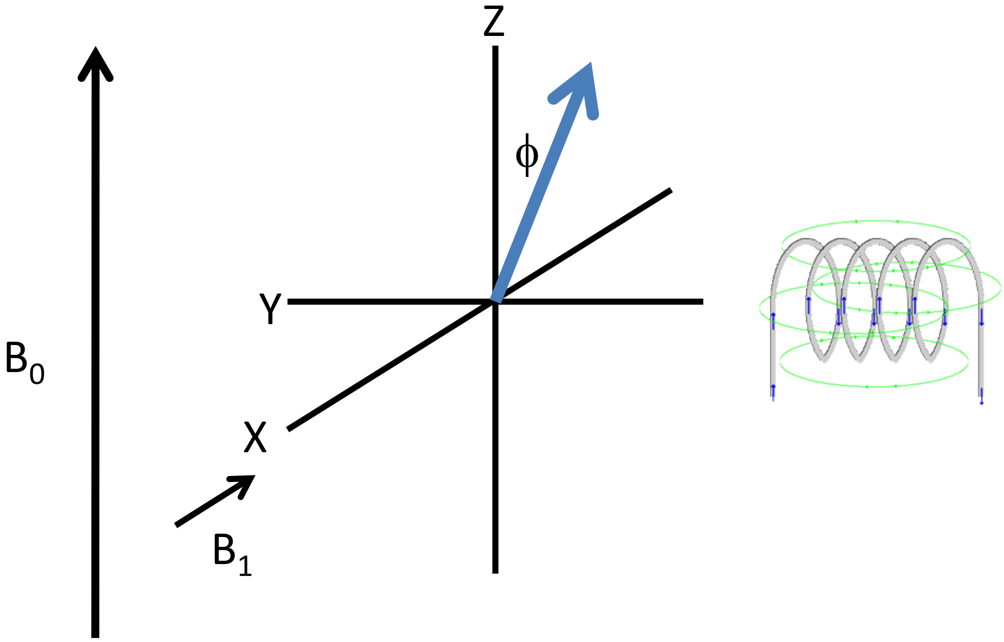


www.cis.rit.edu/htbooks/nmr/

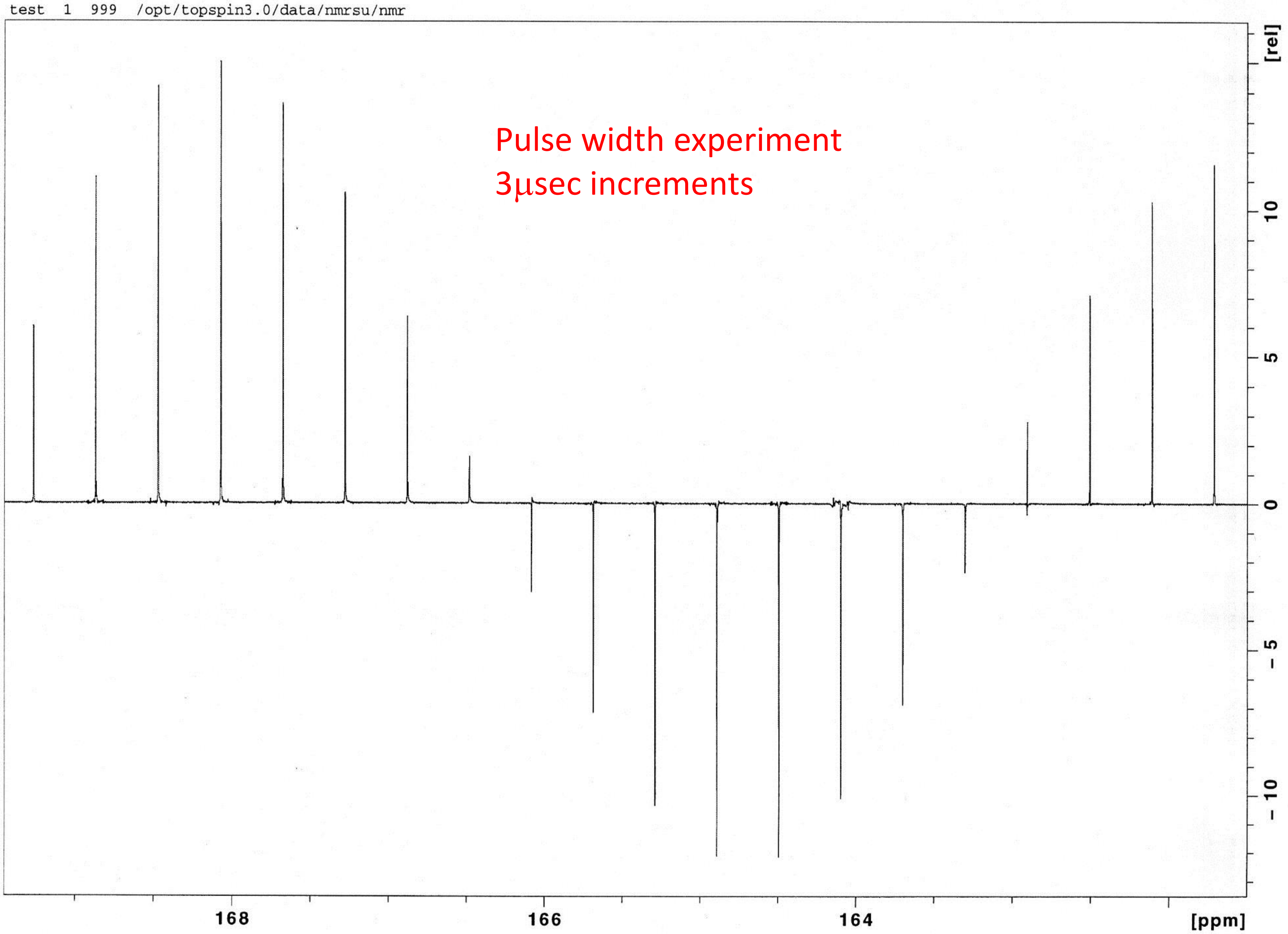
Actual NMR Experiment



Affect of Pulses on the nuclear vector



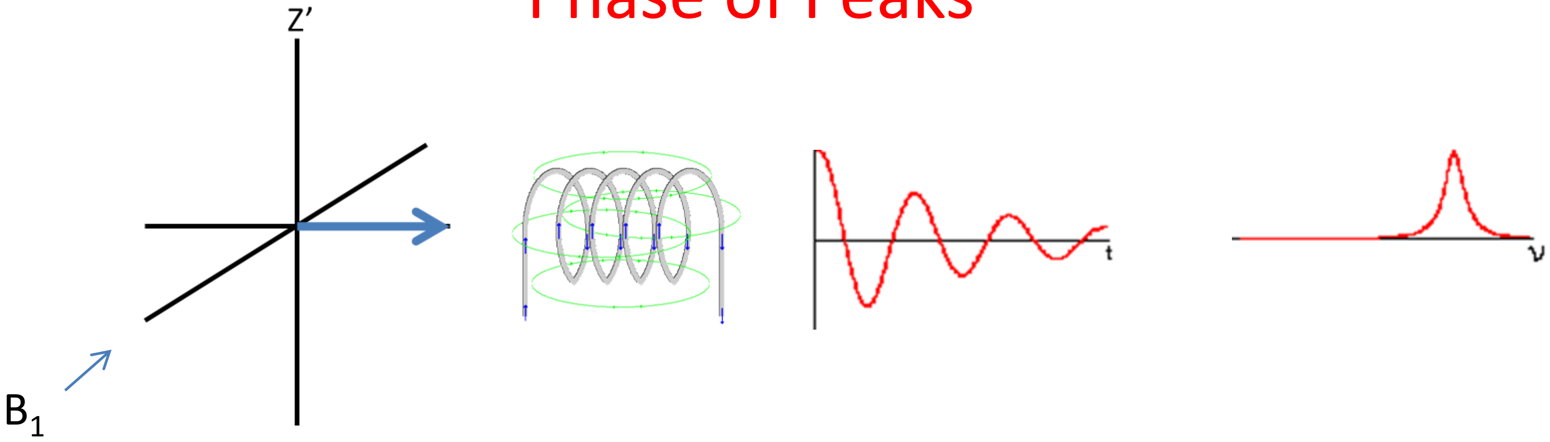
$$\phi=\gamma B_1 t_p$$

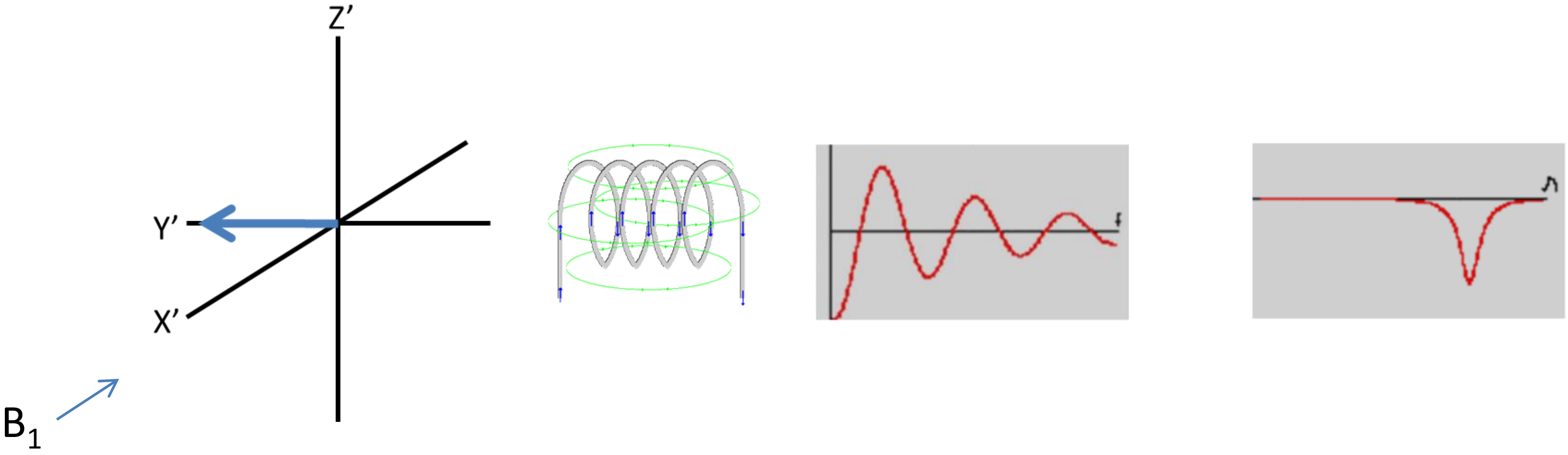


Pulse width experiment

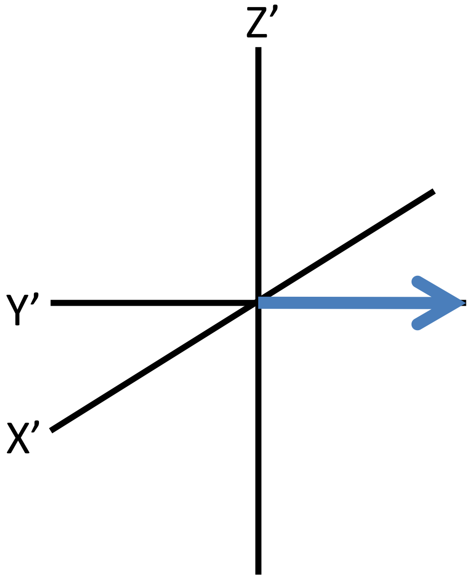
3µsec increments

Phase of Peaks

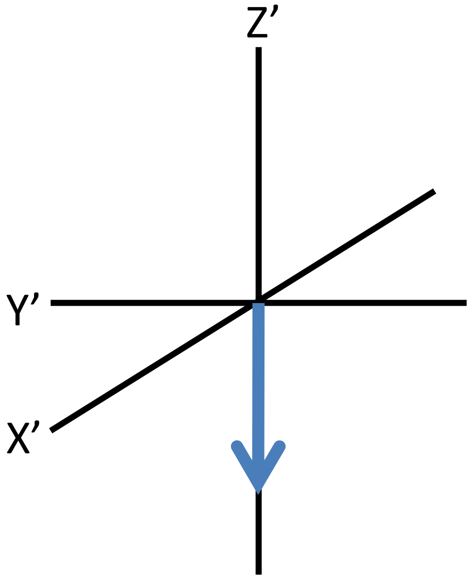




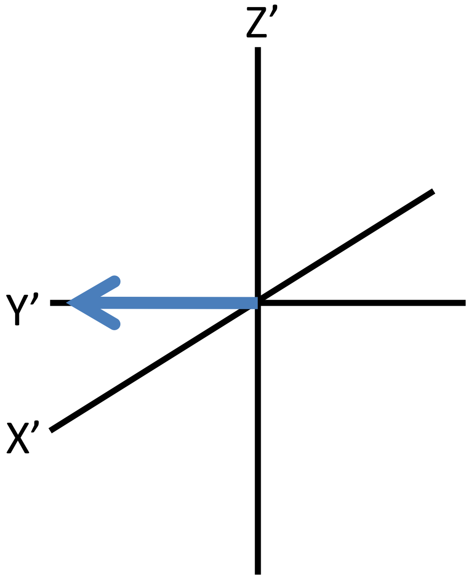
Selecting Pulse Angles



90^0 $\pi/2$ x pulse



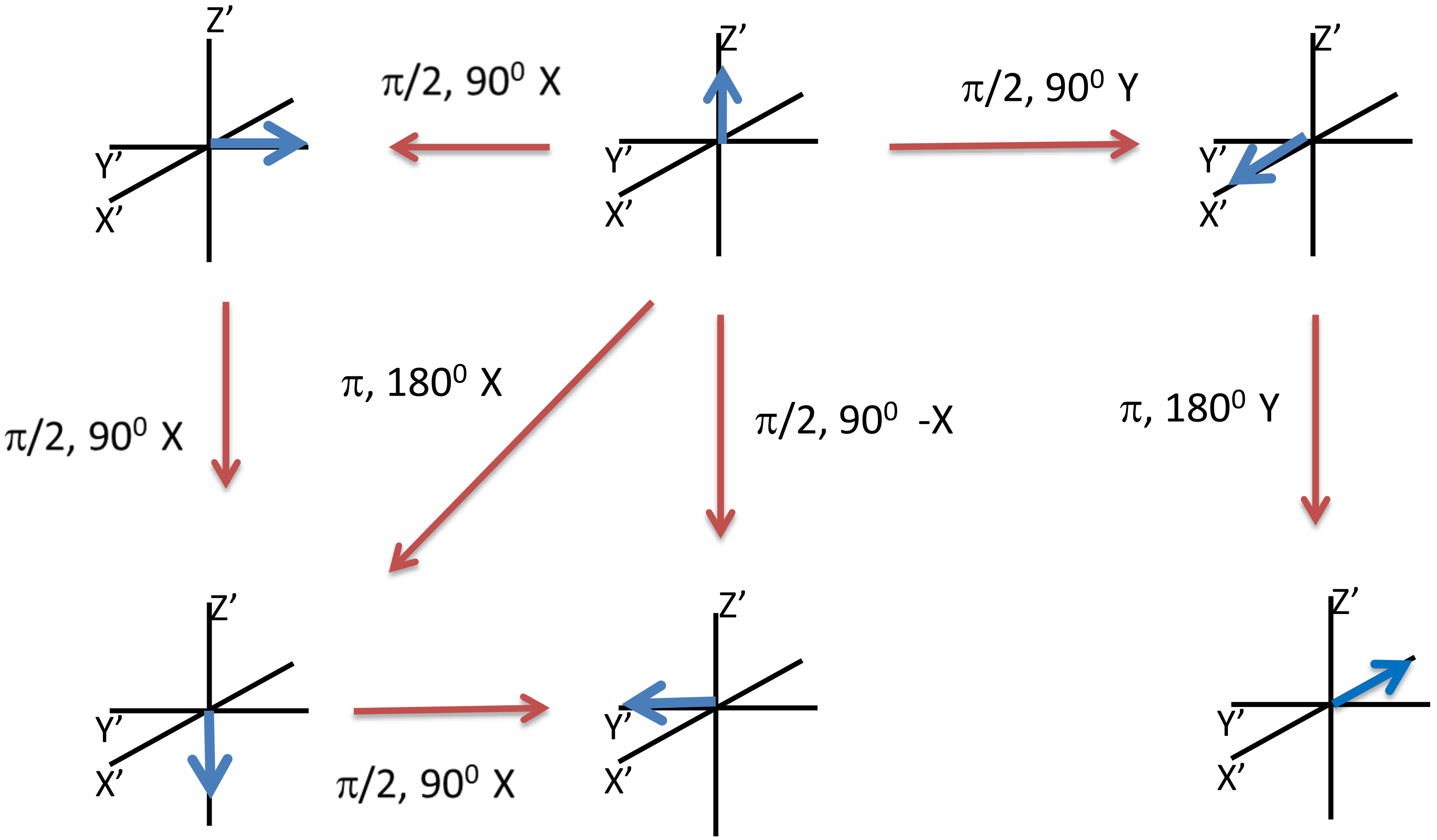
180^0 π x pulse



270^0 $3/2\pi$ x pulse

$$\phi=\gamma B_1 t_p$$

Phases



$\pi/2$, 90^0 X

$\pi/2$, 90^0 Y

$\pi/2$, 90^0 X

π, 180^0 X

$\pi/2$, 90^0 -X

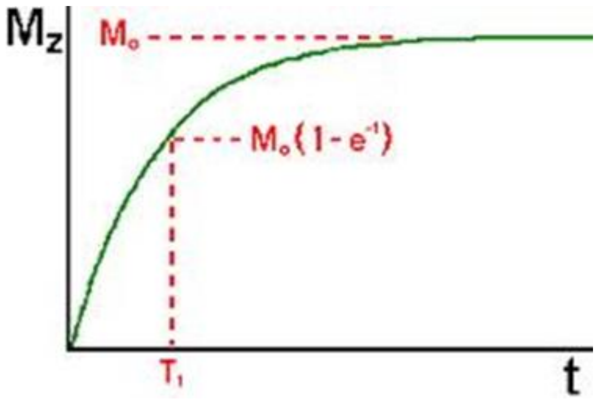
π, 180^0 Y

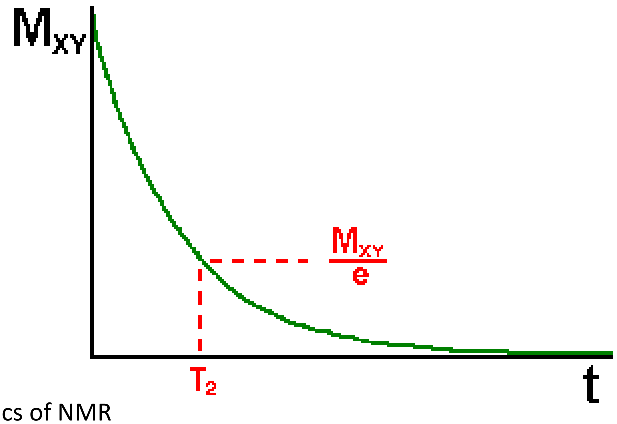
$\pi/2$, 90^0 X

Relaxation

Relaxation is the time that it takes the nuclei to returns to the equilibrium state.

There are two types of relaxation T_1 and T_2. T_1 is referred to as Longitudinal or spin lattice and T_2 is referred to a transverse or spin spin relaxation.



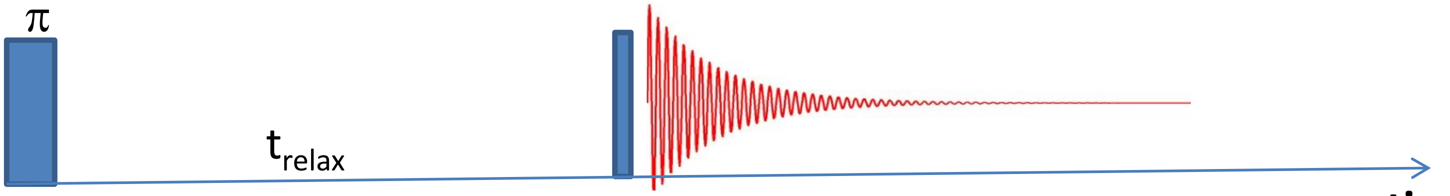


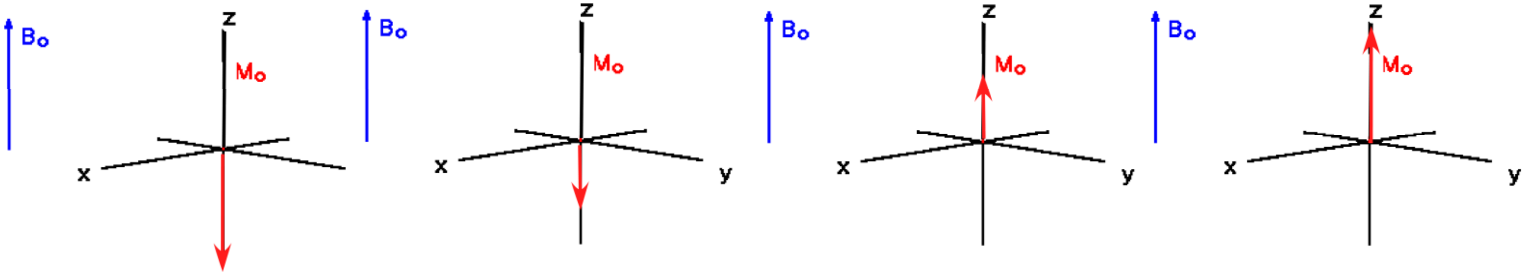
Hornak, Basics of NMR

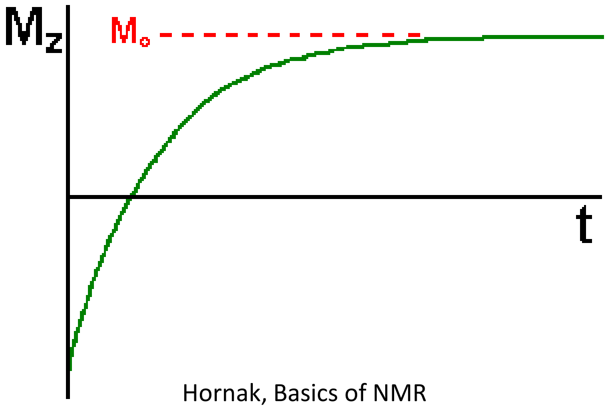
How to measure T_1 ?

- accurate integrations
- must know approximate T_1 before experiment

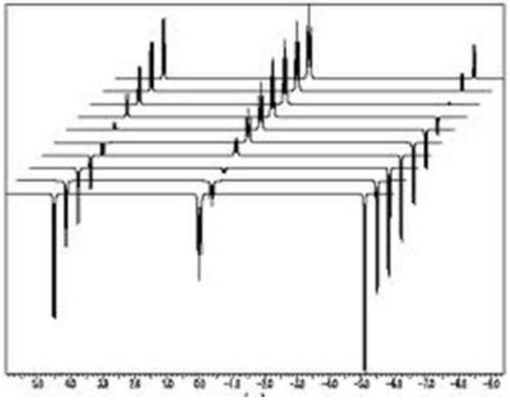
Inversion Recovery



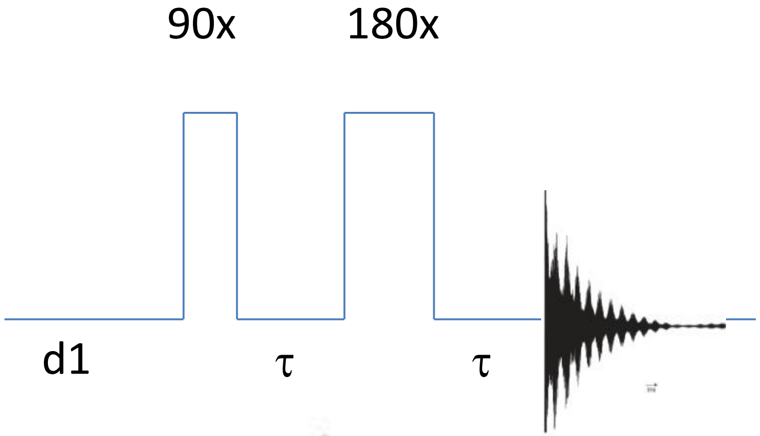




Hornak, Basics of NMR

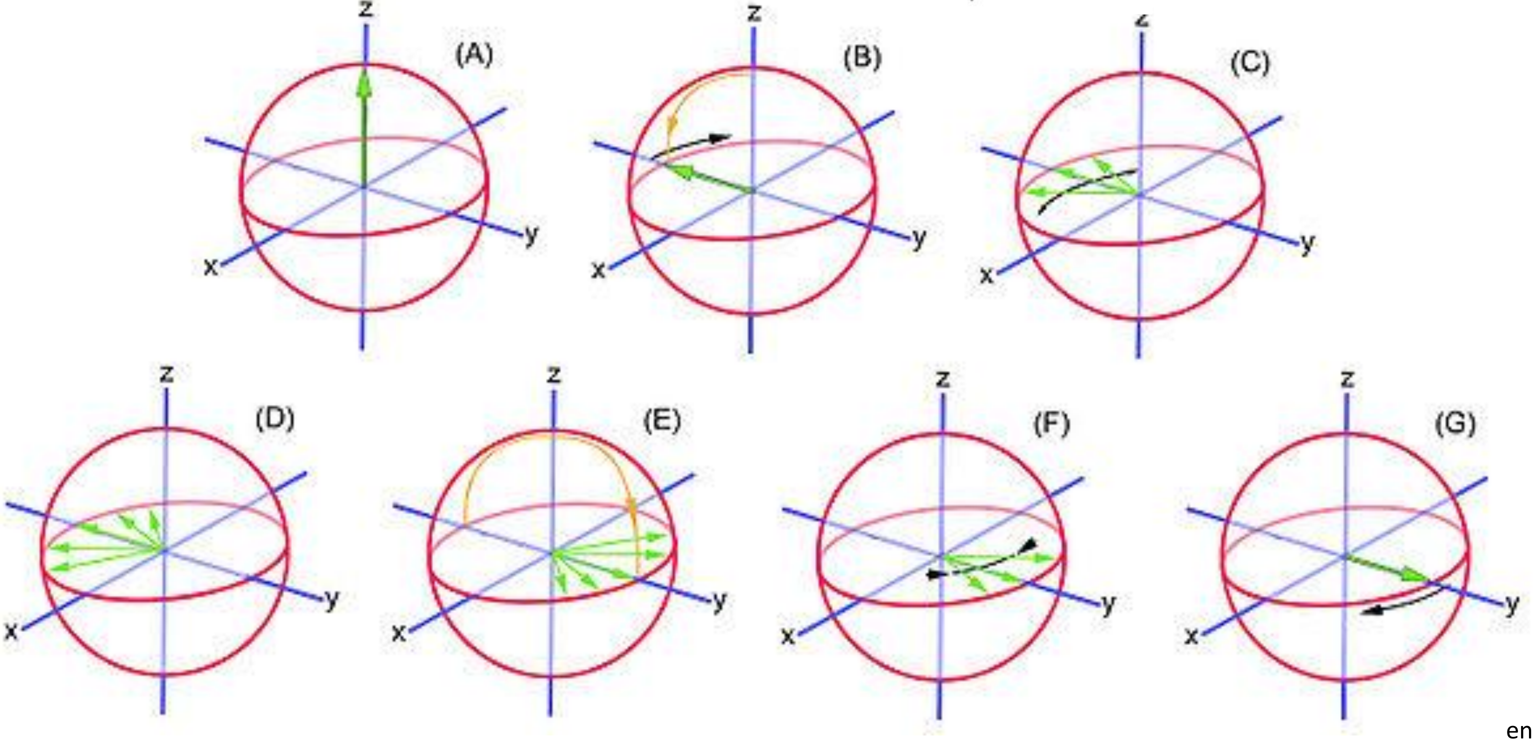


Spin Echo Experiment



90x 180x

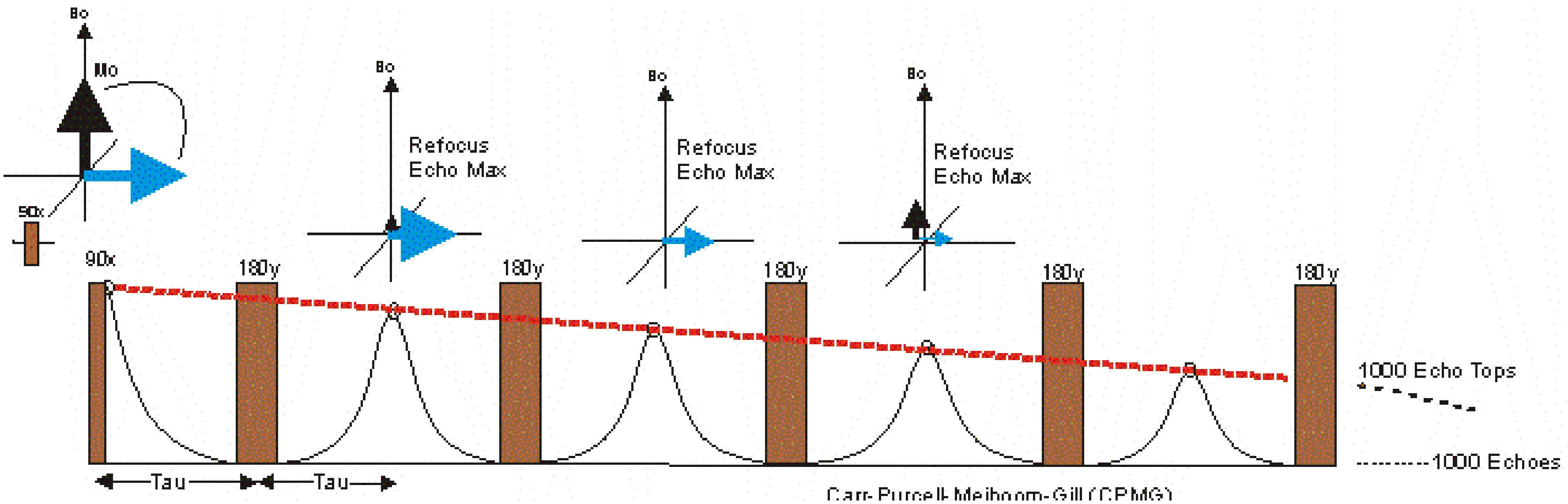
d1 τ τ



en.wikipedia.org

CPMG sequence to measure T_2

(Carr Purcell Meiboom Gill)



Source: http://www.process-nmr.com/TD-NMR1.gif

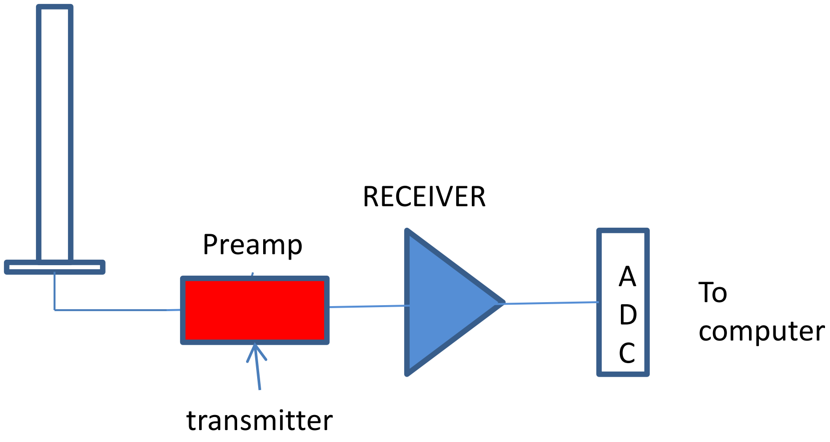
Instrumentation
Some of the Nuts and Bolts

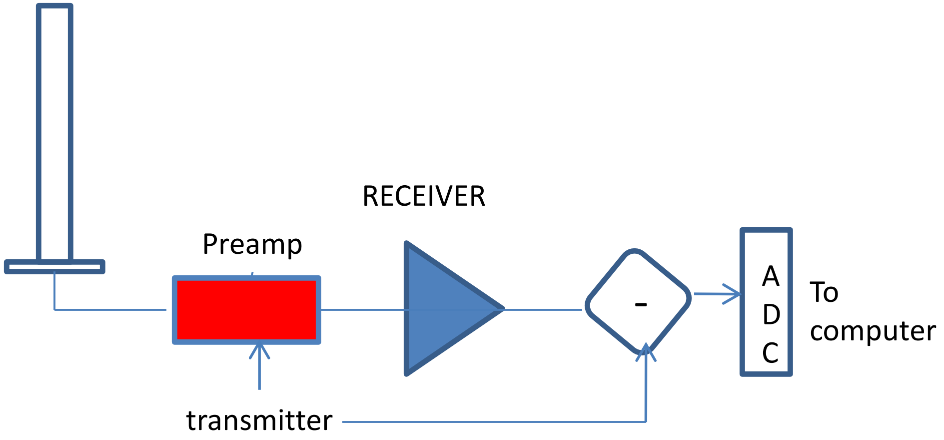
The signal coming back from the sample is in volts but computers do not understand volts.

In order to do this we need an ADC (analog to digital converter) but these have limitations in frequency range and voltage.

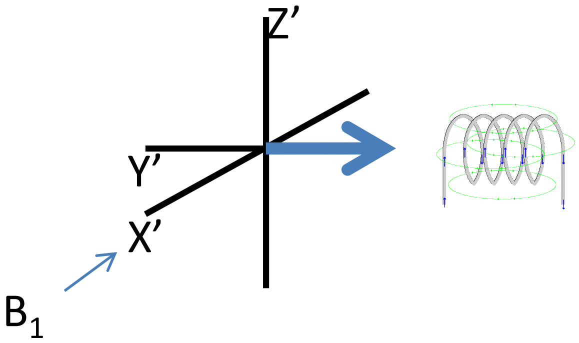
If you have a 500 MHz NMR and are observing ^{1}H the actual signal varies from 500,000,000 Hz to 500,005,000 Hz for a 10 PPM window.

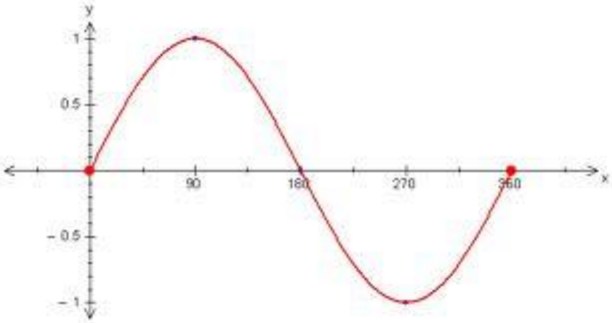
If you could subtract the 500 MHz from this you would only need to look at 0 to 5000 Hz, the audio frequency range.





What does the nmr actually see?

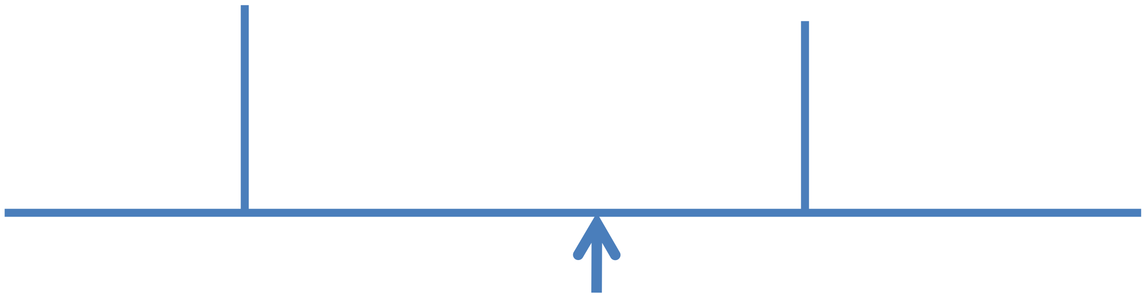




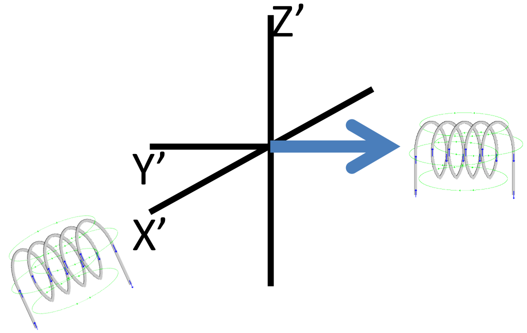
Frequency of transmitter

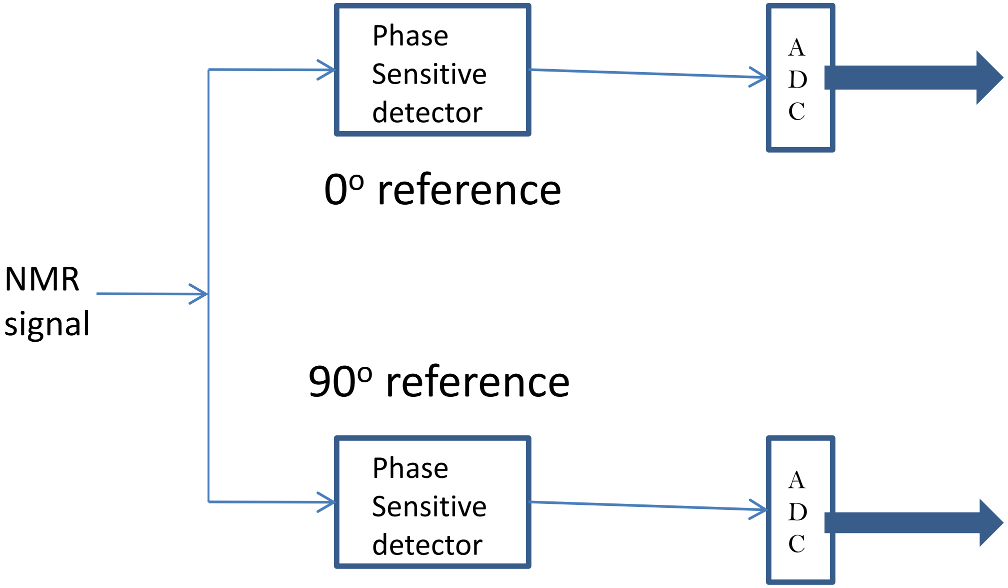
Where do we put the transmitter?

Frequency of transmitter



Frequency of transmitter





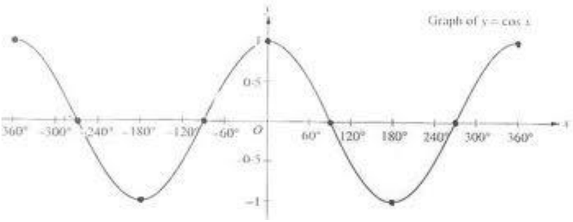
NMR signal

Phase Sensitive detector

0º reference

ADC

Computer Memory A

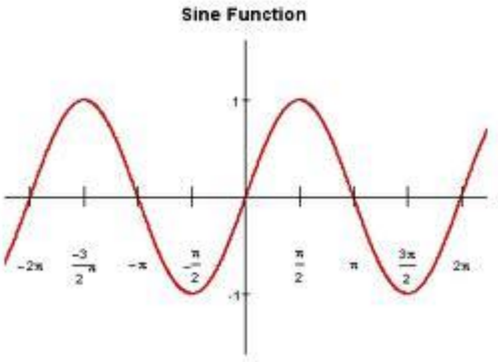


90º reference

Phase Sensitive detector

ADC

Computer Memory B



How do we convert the fid into a spectrum?

$$\text{Re}[f(\omega)]=\int_{-\infty}^{\infty} f(t)\cos\omega t\,dt$$

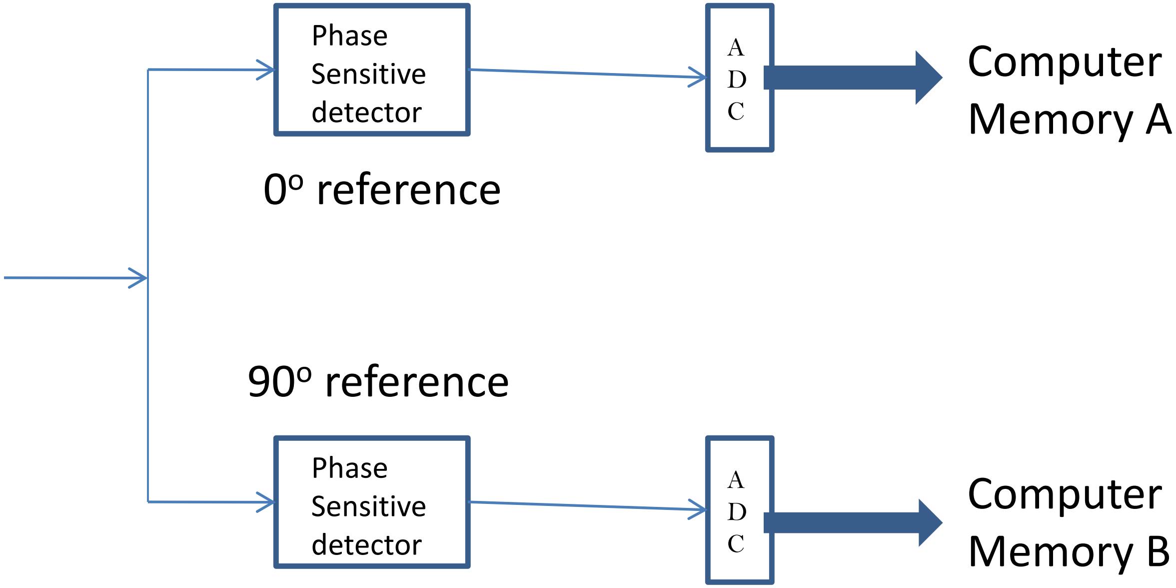
A

$$\text{Im}[f(\omega)]=\int_{-\infty}^{\infty} f(t)\sin\omega t\,dt$$

B

Sum

New Problem



Phase Sensitive detector

0° reference

A D C

Computer Memory A

90° reference

Phase Sensitive detector

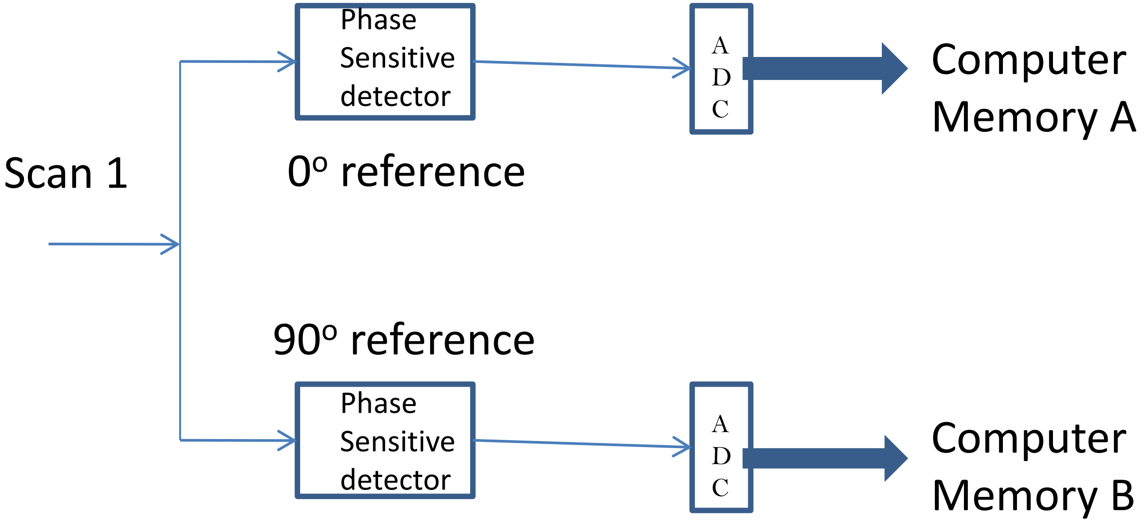
A D C

Computer Memory B

What if ADC’s are not exactly matched?

Sum

Ghost peak



Scan 1

Phase Sensitive detector

0° reference

ADC

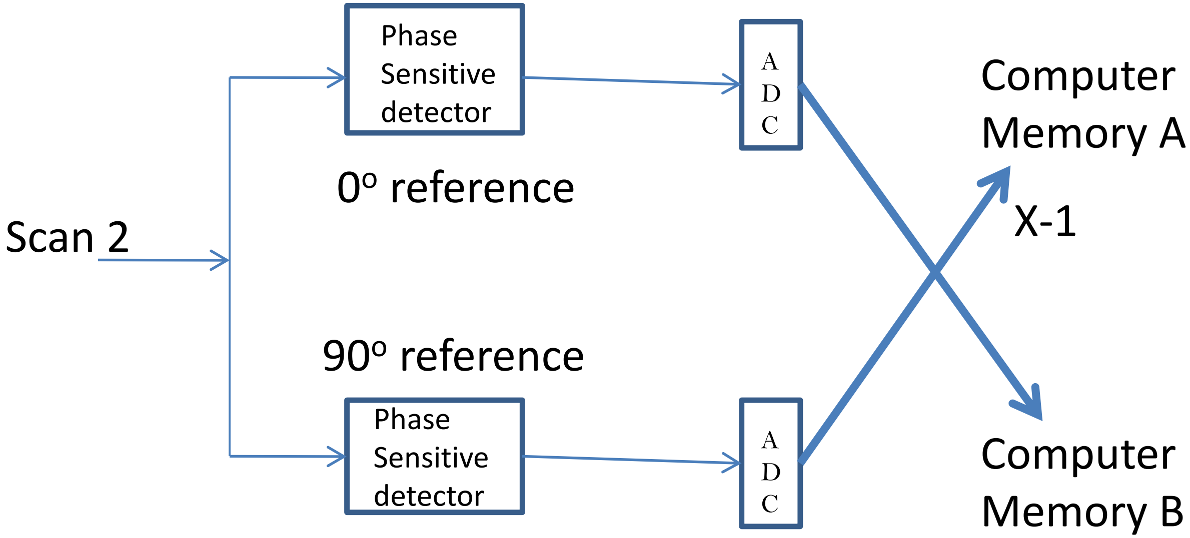
Computer Memory A

90° reference

Phase Sensitive detector

ADC

Computer Memory B



Scan 2

Phase Sensitive detector

0° reference

ADC

Computer Memory A

X-1

90° reference

Phase Sensitive detector

ADC

Computer Memory B

Cyclops Phase Cycling

Scan	pulse phase	receiver	A	B
1	X	X	+1	+2
2	Y	Y	-2	+1
3	-X	-X	-1	-2
4	-Y	-Y	+2	-1

A and B are separate memory locations
1 stores the cos and 2 stores the sin

PAVIA 4th Ed.

Spin states – 3.1

Magnetic Moments – 3.2

Absorbance – 3.3

Resonance – 3.4

Populations – 3.5

Spectrometers, FIDs – 3.7

PAVIA 5th Ed. In Chap. 5

Chemical Shifts – 3.6

Chemical Shift Equivalence – 3.8

Integration – 3.9

Chemical Environment and Chemical Shift – 3.10, 3.11 A,B

Splitting (“n+1 rule”) – 3.13, 3.16, 3,17

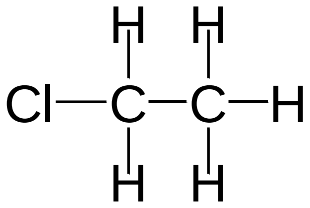
PROBLEMS AT THE END OF CHAP 3

Preview: Types of Information available from a ^{1}H NMR spectrum

A ^{1}H nuclear magnetic resonance spectrum contains information about the:

(a) number of different types of proton

(b) relative number of each type of proton

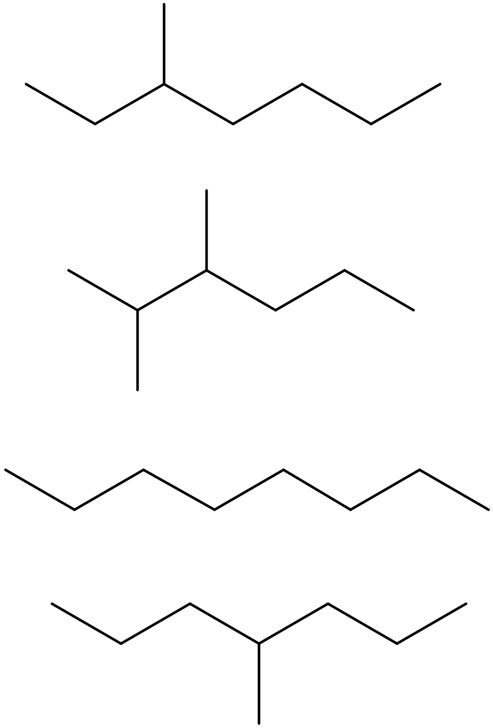


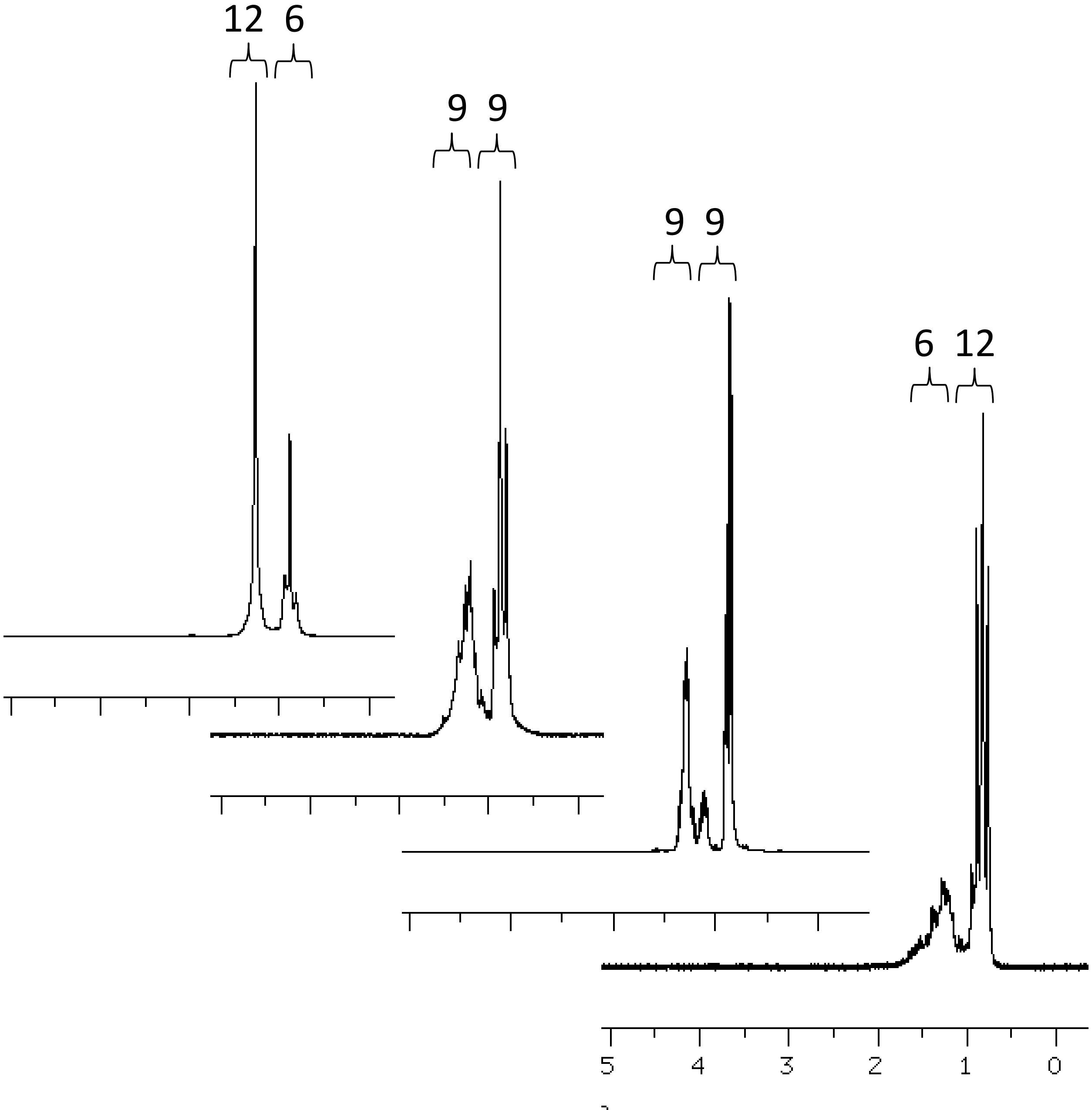
(c) proximity to functional groups

(d) the number of *adjacent* nuclei with spin

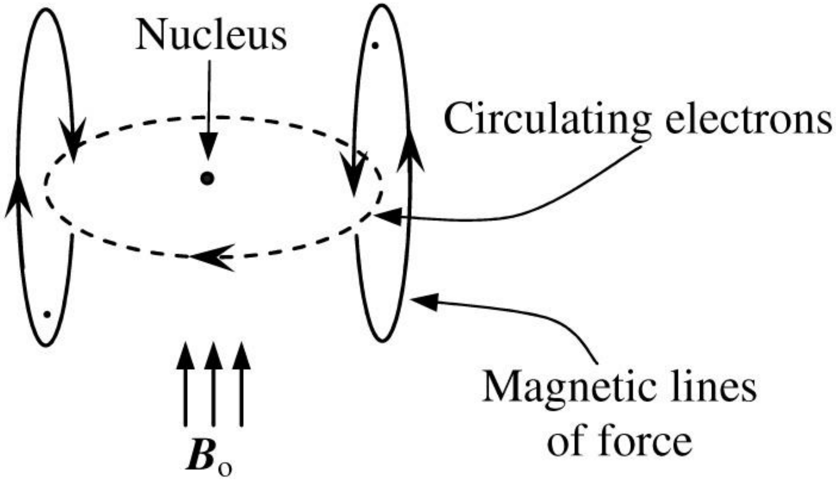
(b) relative number of each type of proton

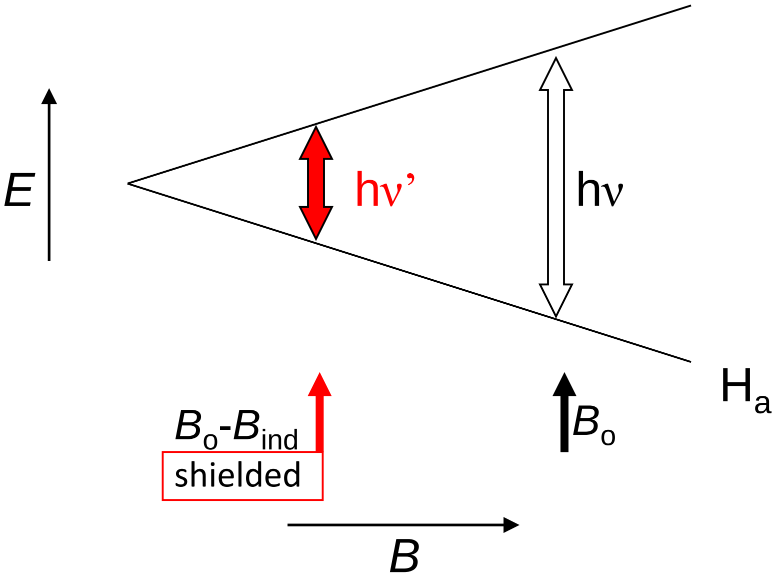
Which alkane is which?

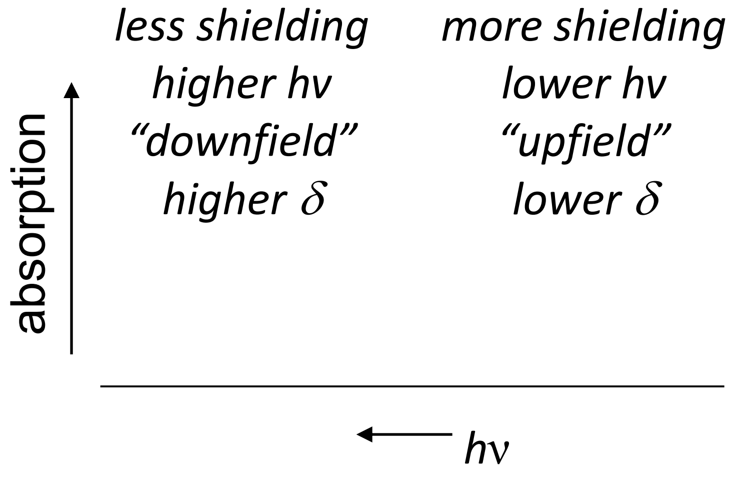




(c) proximity to functional groups - *shielding and deshielding*





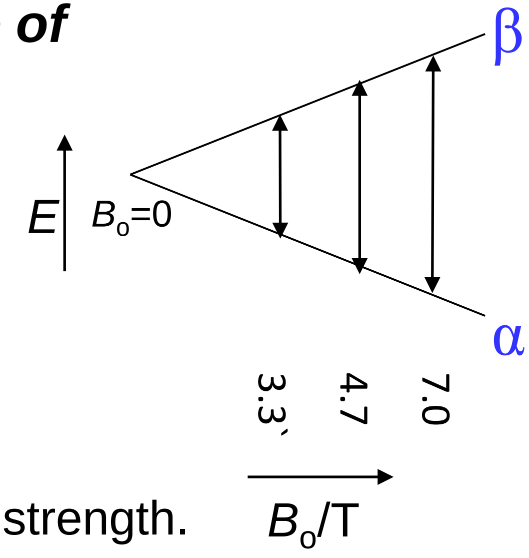


less shielding
higher hν
"downfield"
higher δ

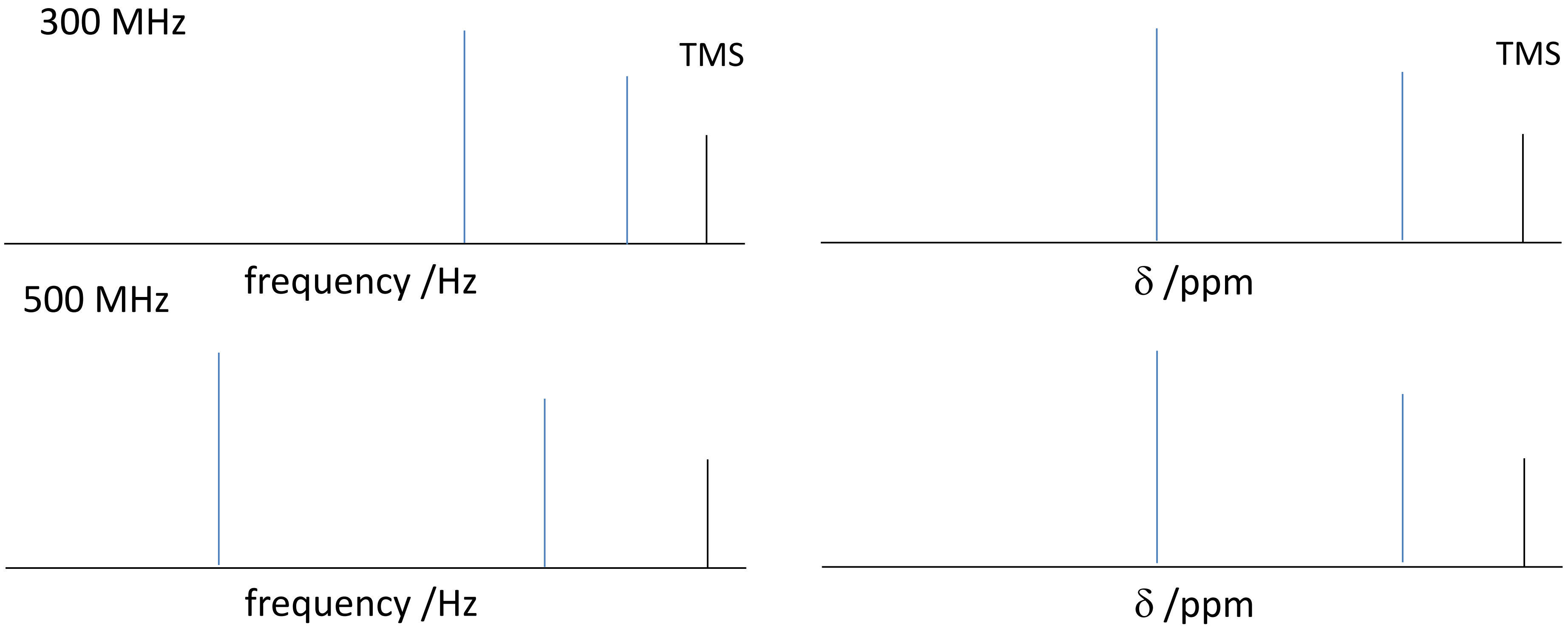
more shielding
lower hν
"upfield"
lower δ

The effect of magnet field strength on the appearance of spectra (1): chemical shift

B_0 / T	υ_{TMS} / Hz	$\upsilon_{C_2H_6}-\upsilon_{TMS}$/ Hz	$\delta_{C_2H_6}$ / ppm
5.87	250×10^6	215	0.86
7.00	300×10^6	258	0.86
11.74	500×10^6	430	0.86

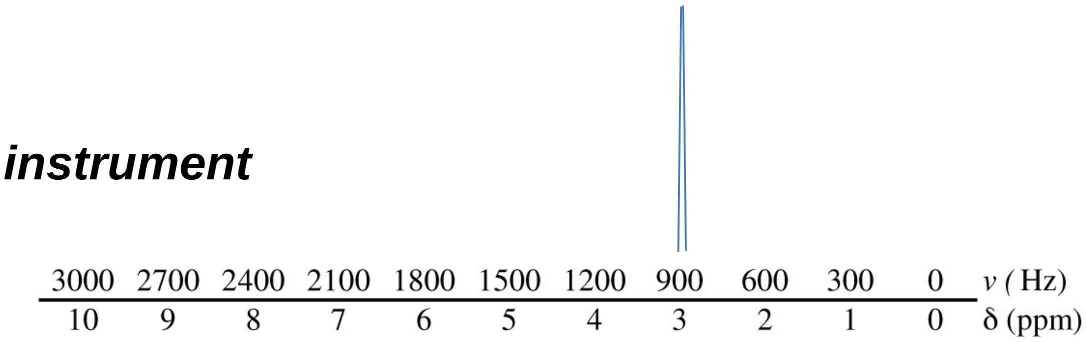


- The *resonance frequency* (in Hz) depends on the magnet field strength.
- The *chemical shift* (δ) is <u>independent</u> of magnet strength.



DISPERSION AT DIFFERENT FREQUENCIES

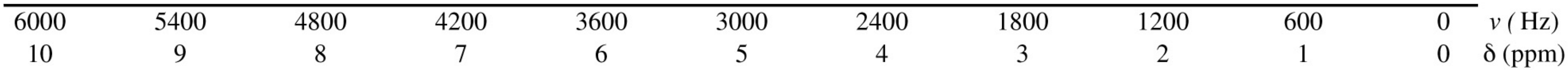
7 T, 300 MHz instrument



Higher frequency
less shielding
deshielded

Lower frequency
more shielding
shielded

14 T, 600 MHz instrument



Effect of structure on chemical shift (δ scale, ppm)

$CH_3–CH_3$
0.9

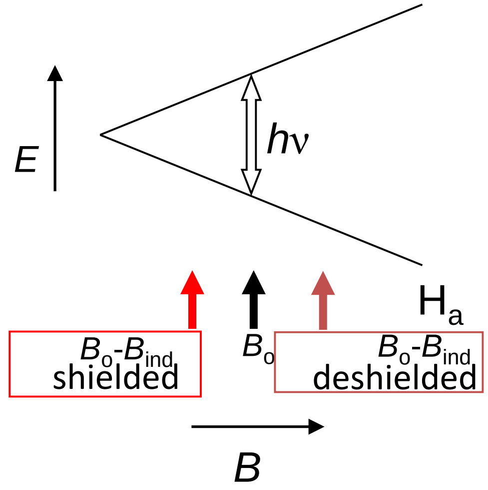
$CH_3–N(CH_3)_2$
2.2

$CH_3–OCH_3$
3.2

$CH_3–F$
4.3

$CH_3–Si(CH_3)_3$
0.0

$CH_3–Cl$
3.1


E

$h\nu$

H_a

B_o-B_{ind}
shielded

B_o

B_o-B_{ind}
deshielded

B

$CH_3–Br$
2.7

$CH_3–I$
2.2

$CHCl_3$
7.3

CH_2Cl_2
5.3

CH_3Cl
3.1

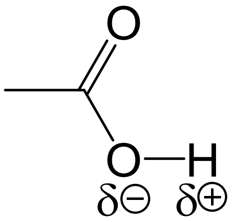
Typical ^{1}H NMR chemical shifts

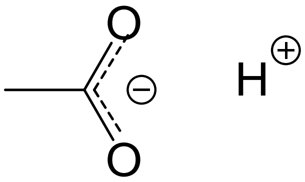
Type of proton	chemical shift (δ)
$(CH_3)_4Si$	0.00
CH_3-C-R (sp^3)	0.9 - 1.8
-CH_2-C-R (sp^3)	1.1 - 2.0
-CH-C-R (sp^3)	1.3 - 2.1
H-C-N	2.2 - 2.9
H-C-O	3.3 - 3.7
H-C-Cl	3.1 - 4.1
H-C-Br	2.7 - 4.1
H-C-C=O	2.1 - 2.5
H-C-C=C	1.6 - 2.6
H-C-Ar	2.3 - 2.8
H-C=O (sp^2)	9 - 10
H-C=C (sp^2)	4.5 - 6.5
H-Ar (sp^2)	6.5 - 8.5
H-C≡C (sp)	2.5
H-N (amine)	1 - 3
H-OR (alcohol)	0.5 - 5
H-OAr (phenol)	6 - 8
H-O_2CR (acid)	10 - 13

You will be provided with a copy of Table 9.1 on exams. This provides approximate ranges for values of chemical shifts for particular types of protons. Remember that protons adjacent to two (or more) electron withdrawing groups will appear further downfield than a proton adjacent to only one.

^1H nuclei with very low and very high surrounding electron density

CH_3CO_2H

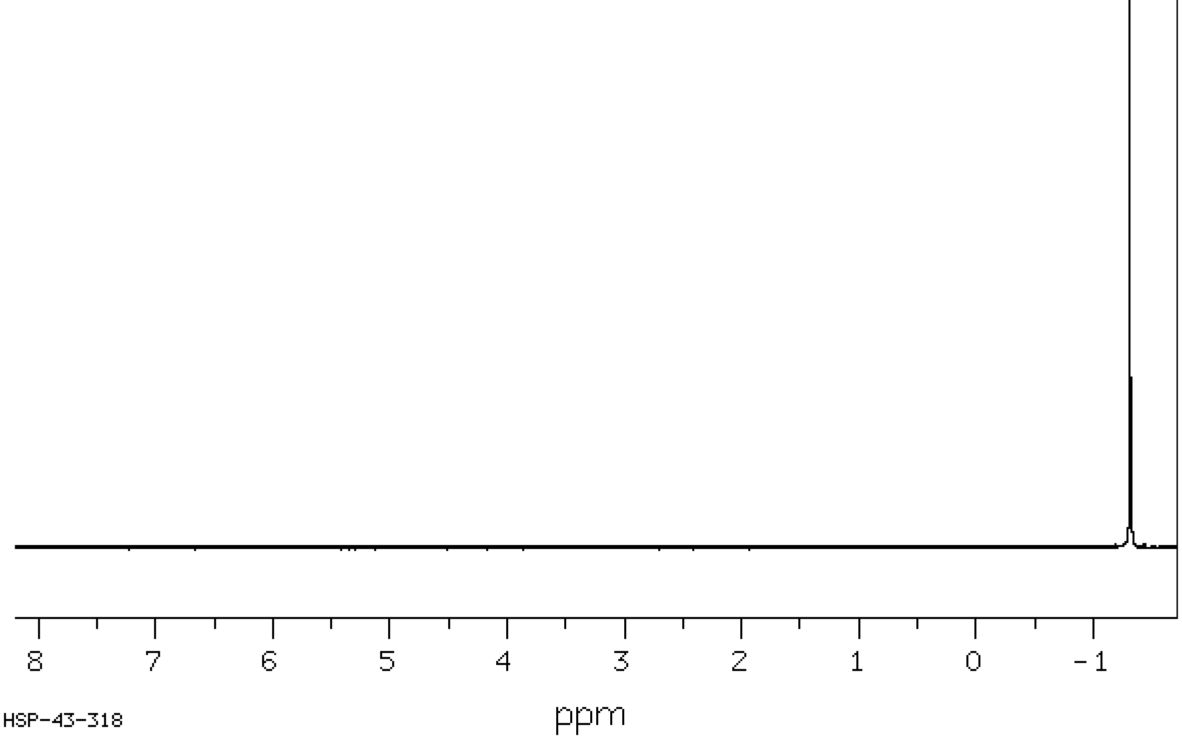




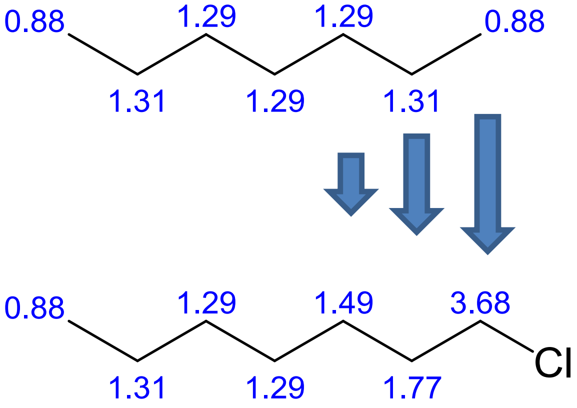
CH_3Li

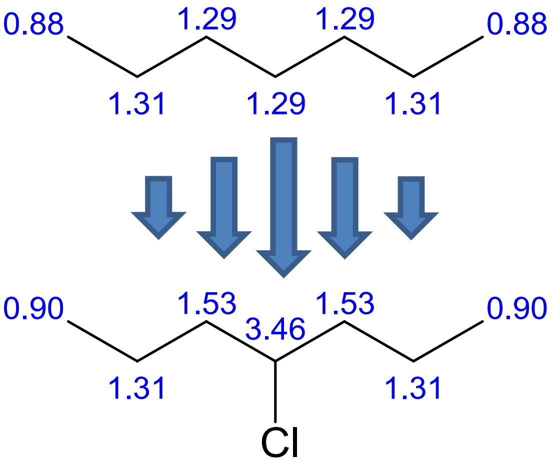
$\underset{\delta\ominus}{H_3C}-\underset{\delta\oplus}{Li}$

$\underset{\ominus}{H_3C}\quad\underset{\oplus}{Li}$



The effect of a substituent on ^{1}H NMR chemical shift drops off rapidly





Chemical Shifts are not additive

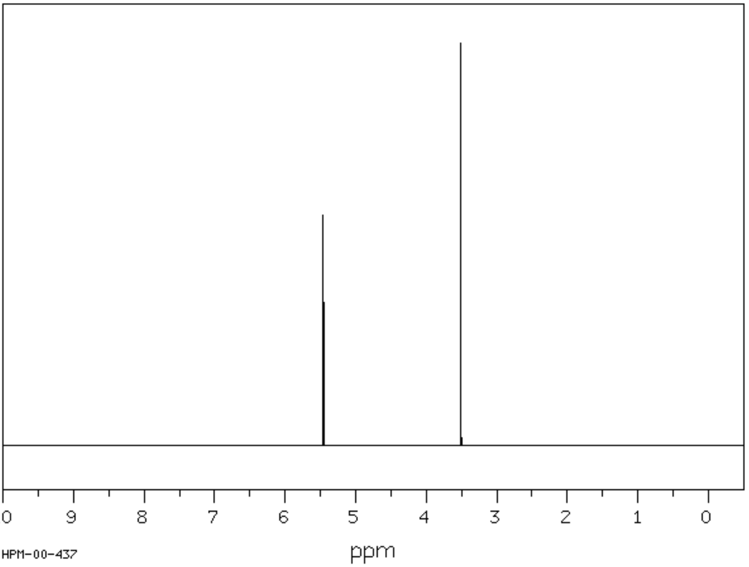
$H_3C{-}Cl$

3.1

$Cl{-}CH_2{-}OCH_3$

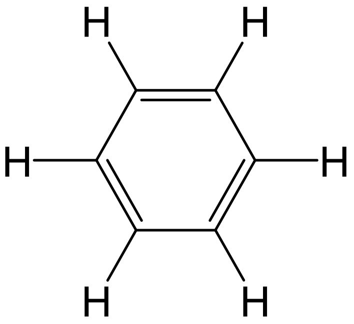
$H_3C{-}OCH_3$

3.2

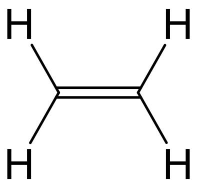


Chemical Shift Anisoptropy

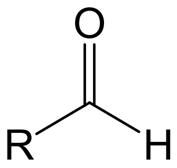
Ring currents lead to significant downfield shifts of hydrogen nuclei on *sp*^{2} carbon atoms



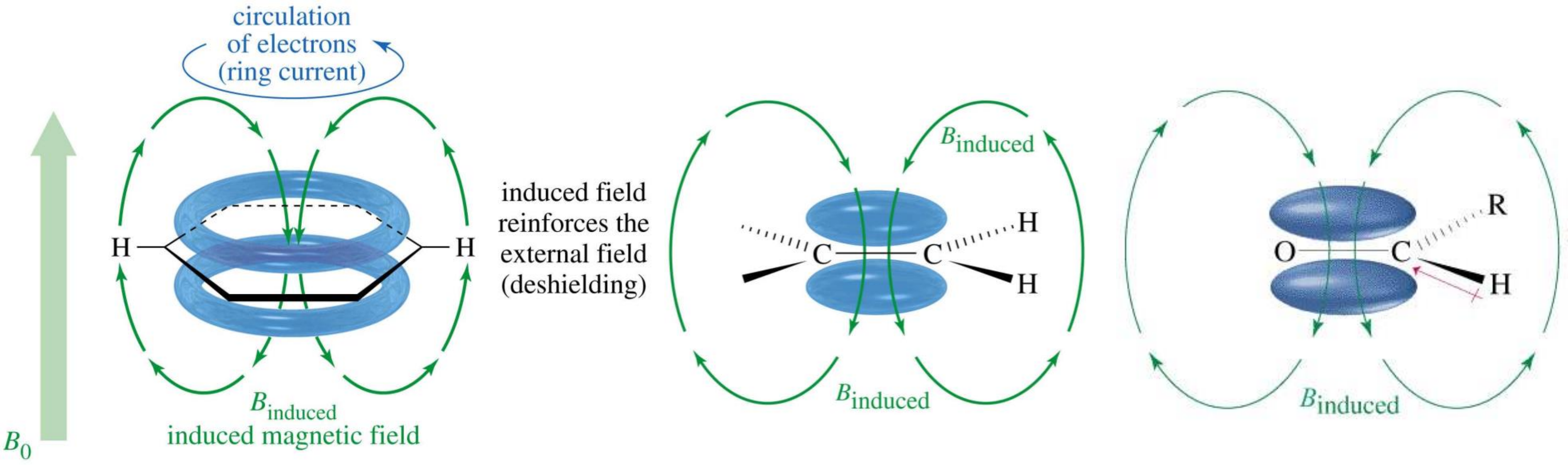
7.3



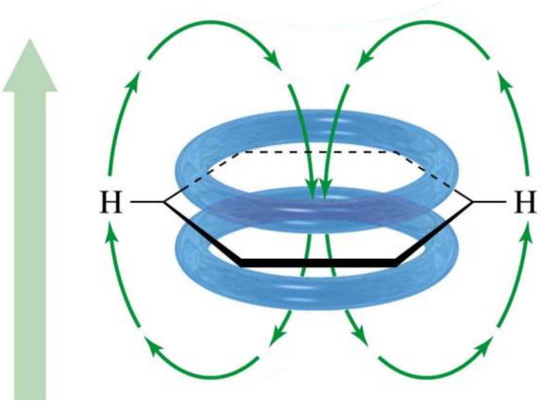
5.3

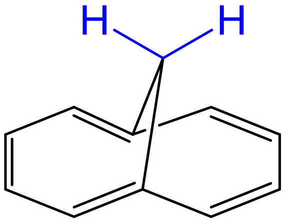


9.5-10.5

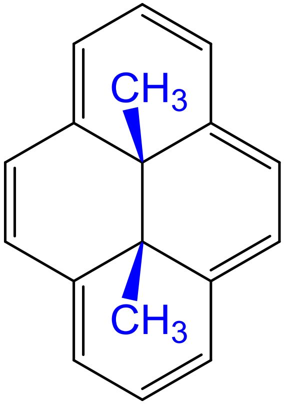


^{1}H NMR AROMATIC SHIELDING AND DESHIELDING EFFECTS

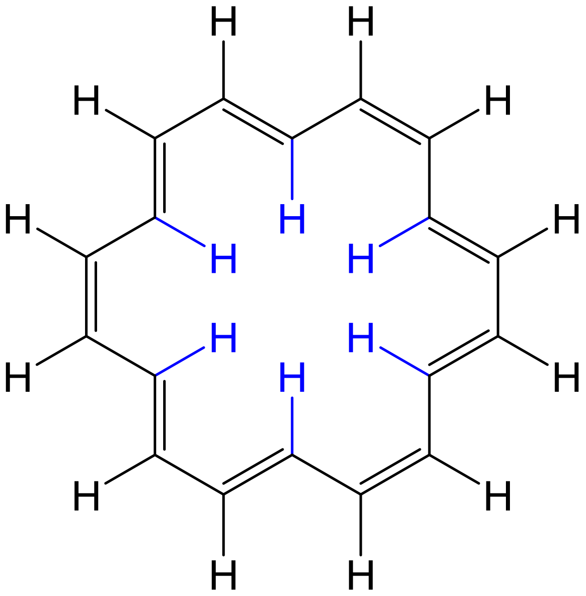




δ_{ring} 7.27–6.95 ppm
δ_{CH2} –0.51 ppm



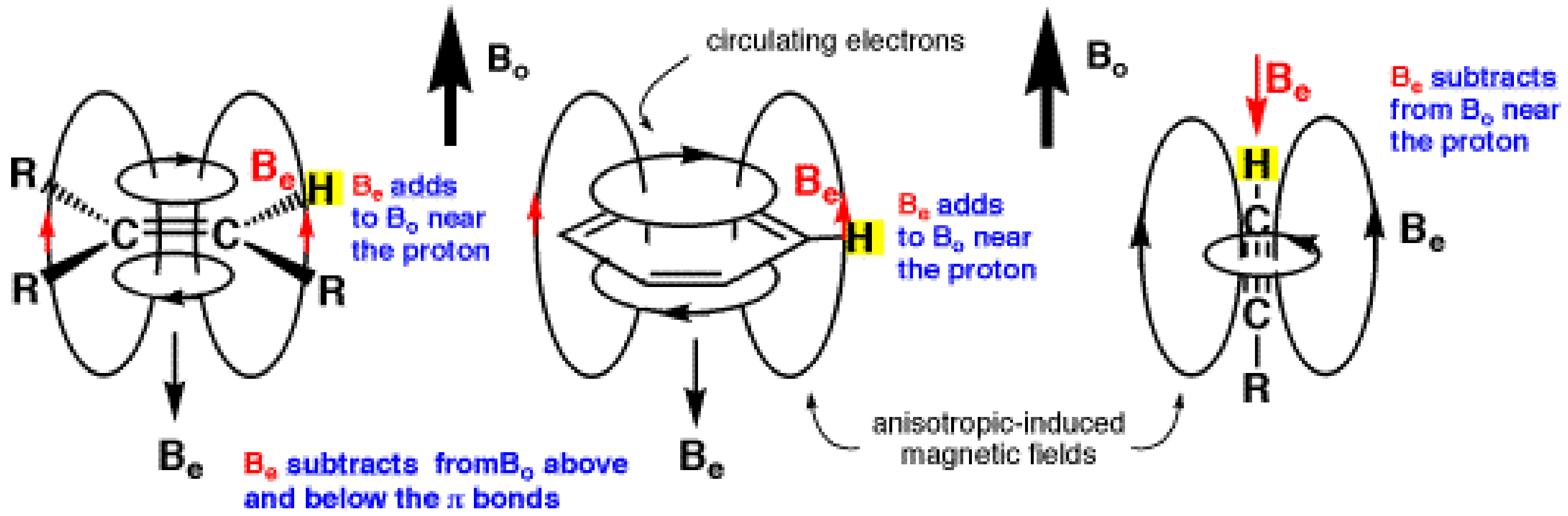
δ_{ring} 8.14–8.64 ppm
δ_{Me} –4.25 ppm



δ_{out} 9.28 ppm
δ_{in} –2.99 ppm

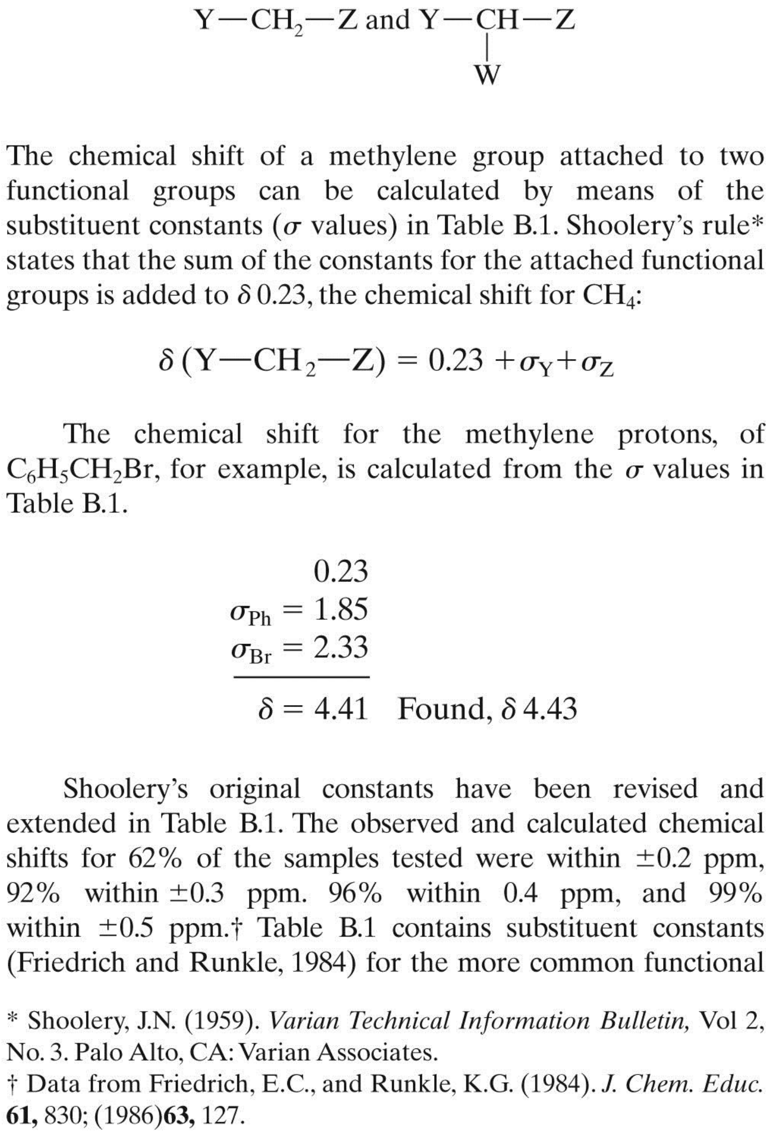
What about the chemical shift of sp systems

Figure 7. Components of the B_e field produced by the circulation of π-electrons in alkenes, aromatics, and alkynes as a function of orientation relative to the applied field B_o. The major anisotropic contribution to the total B_e field from circulation of π-electrons adds to (alkene or aromatic) or subtracts from B_o (alkyne).



http://orgchem.colorado.edu/Spectroscopy/nmrtheory/protonchemshift.html

Estimating chemical shifts of $–CH_2–$ by calculation using empirical contributions of each substituent



$$\mathrm{Y{-}CH_2{-}Z} \text{ and } \mathrm{Y{-}\underset{\underset{\textstyle W}{|}}{C}H{-}Z}$$

The chemical shift of a methylene group attached to two functional groups can be calculated by means of the substituent constants (σ values) in Table B.1. Shoolery's rule* states that the sum of the constants for the attached functional groups is added to δ 0.23, the chemical shift for CH_4:

$$\delta\,(\mathrm{Y{-}CH_2{-}Z}) = 0.23 + \sigma_Y + \sigma_Z$$

The chemical shift for the methylene protons, of $C_6H_5CH_2Br$, for example, is calculated from the σ values in Table B.1.

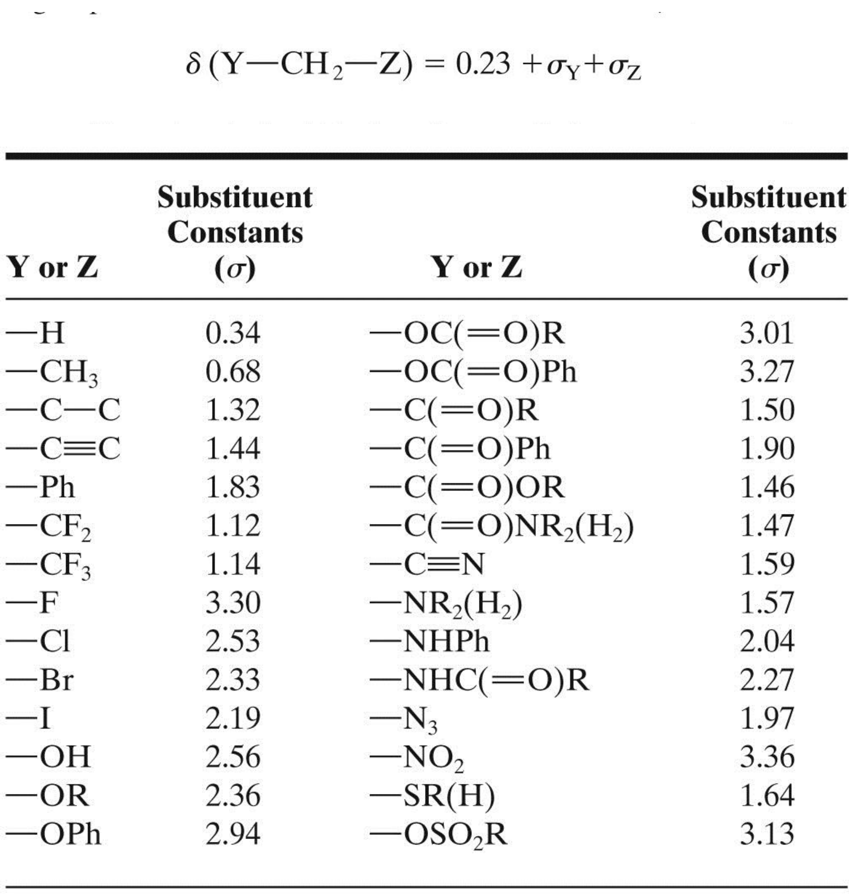
$$\begin{array}{r} 0.23 \\ \sigma_{Ph} = 1.85 \\ \underline{\sigma_{Br} = 2.33} \\ \delta = 4.41 \end{array} \quad \text{Found, } \delta\ 4.43$$

Shoolery's original constants have been revised and extended in Table B.1. The observed and calculated chemical shifts for 62% of the samples tested were within ±0.2 ppm, 92% within ±0.3 ppm. 96% within 0.4 ppm, and 99% within ±0.5 ppm.† Table B.1 contains substituent constants (Friedrich and Runkle, 1984) for the more common functional

---

* Shoolery, J.N. (1959). *Varian Technical Information Bulletin,* Vol 2, No. 3. Palo Alto, CA: Varian Associates.

† Data from Friedrich, E.C., and Runkle, K.G. (1984). *J. Chem. Educ.* **61,** 830; (1986)**63,** 127.



$$\delta\,(\mathrm{Y{-}CH_2{-}Z}) = 0.23 + \sigma_Y + \sigma_Z$$

Y or Z	**Substituent Constants (σ)**	**Y or Z**	**Substituent Constants (σ)**
—H	0.34	—OC(=O)R	3.01
$—CH_3$	0.68	—OC(=O)Ph	3.27
—C—C	1.32	—C(=O)R	1.50
—C≡C	1.44	—C(=O)Ph	1.90
—Ph	1.83	—C(=O)OR	1.46
$—CF_2$	1.12	$—C(=O)NR_2(H_2)$	1.47
$—CF_3$	1.14	—C≡N	1.59
—F	3.30	$—NR_2(H_2)$	1.57
—Cl	2.53	—NHPh	2.04
—Br	2.33	—NHC(=O)R	2.27
—I	2.19	$—N_3$	1.97
—OH	2.56	$—NO_2$	3.36
—OR	2.36	—SR(H)	1.64
—OPh	2.94	$—OSO_2R$	3.13

Substituent	*Substituent constant*
-R	0.68
$-C_6H_5$	1.83
$-NO_2$	3.36
-C(O)R	1.50
-OC(O)R	3.01
-Cl	2.53

$$\delta(\mathrm{Y{-}CH_2{-}Z}) = 0.23 + \sigma_{\mathrm{Y}} + \sigma_{\mathrm{Z}}$$

$\mathrm{Cl{-}\mathbf{CH_2}{-}Cl}$

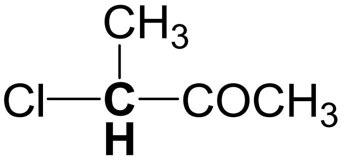
$\delta_{\mathrm{H}} = 0.23 +$ $=$ ppm

Observed: 5.30 ppm

$\mathrm{C_6H_5{-}\mathbf{CH_2}{-}OCOCH_3}$

$\delta_{\mathrm{H}} = 0.23 +$ $=$ ppm

Observed: 5.10 ppm



$$\mathrm{Cl{-}\underset{\mathbf{H}}{\overset{CH_3}{\mathbf{C}}}{-}COCH_3}$$

$\delta_{\mathrm{H}} = 0.23 +$ $=$ ppm

Observed: 5.11 ppm

$\mathrm{CH_3CH_2{-}\mathbf{CH_2}{-}NO_2}$

$\delta_{\mathrm{H}} = 0.23 +$ $=$ ppm

Observed: 4.38 ppm

Instructions to download, install and launch ChemDraw

The ChemBioOffice software package is downloadable direct from CambridgeSoft (NOT from GT's OIT). Access their site using Internet Explorer or Firefox:

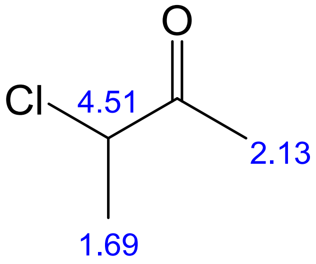
http://scistore.cambridgesoft.com/sitelicense.cfm?sid=100)

(i) Register with the site (button in top left)

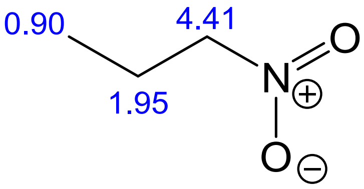
(ii) Once registered, go back to the site licence page (http://scistore.cambridgesoft.com/sitelicense.cfm?sid=100), enter you gatech.edu email address. Follow directions to download the software installer ("ChemBioOffice" for a PC; or "ChemBioDraw" for a Mac)

(iii) Install the software. You will be asked for a verification/activation code during the installation. *This will have been emailed to you (your email program might have placed the message in your junk mail box - so check there as well!)* Enter the info in the installation process and proceed. Launch the program to make sure it works.

Estimating chemical shifts using ChemDraw



```
CH   4.51          1.50        methine
                   0.17        1 alpha -C
                   1.98        1 alpha -Cl
                   0.86        1 alpha -C=O
```



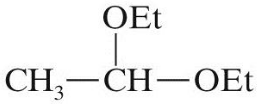
```
CH2  4.41          1.37        methylene
                   3.08        1 alpha -N(=O)=O
                  -0.04        1 beta -C
```

Estimating chemical shifts of –$\overset{|}{\text{C}}$H– by calculation using empirical contributions of each substituent

The table gives the substituent constants* to be used with the formulation

$$\delta\,\text{CHXYZ} = 2.50 + \sigma_X + \sigma_Y + \sigma_Z$$

which is satisfactory if at least two of the substituents are electron-withdrawing groups. In other words, only a single substituent may be an alkyl group (R). Within these limits, the standard error of estimate is 0.20 ppm. For example, the chemical shift of the methine proton in



$CH_3\text{—}\overset{\text{OEt}}{\overset{|}{\text{CH}}}\text{—OEt}$

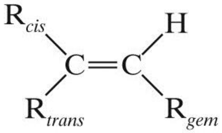
is calculated from Table B.2a as follows:

$$\delta = 2.50 + 1.14 + 1.14 + 0.00 = 4.78$$

The found value is 4.72.

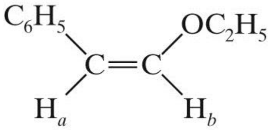
Group	(σ)
—F	1.59
—Cl	1.56
—Br	1.53
—NO_2	1.84
—NH_2	0.64
—NH_3^+	1.34
—NHCOR	1.80
—OH, —OR	1.14
—OAr	1.79
—OCOR	2.07
—Ar	0.99
—C=C	0.46
—C≡C	0.79
—C≡N	0.66
—COR, —COOR, —COOH	0.47
—$CONH_2$	0.60
—COAr	1.22
—SH, —SR	0.61
—SO_2R	0.94
—R	0

Estimating chemical shifts of vinylic hydrogen atoms by calculation using empirical contributions of each substituent



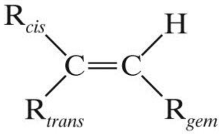
$\delta_H = 5.25 + Z_{gem} + Z_{cis} + Z_{trans}$

For example, the chemical shifts of the alkene protons in

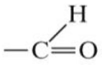
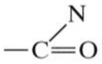
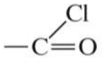
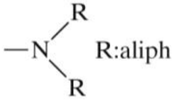
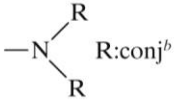


are calculated:

H_a	$C_6H_{5\ gem}$	1.35	5.25
	OR_{trans}	−1.28	0.07
		0.07	δ 5.32
H_b	OR_{gem}	1.18	5.25
	$C_6H_{5\ trans}$	−0.10	1.08
		1.08	δ 6.33



$\delta_H = 5.25 + Z_{gem} + Z_{cis} + Z_{trans}$

Substituent R	Z gem	Z cis	Z trans	Substituent R	Z gem	Z cis	Z trans
—H	0	0	0				
—Alkyl	0.44	−0.26	−0.29	 $-\mathrm{C}(\mathrm{H})=\mathrm{O}$	1.03	0.97	1.21
—Alkyl-ring[a]	0.71	−0.33	−0.30				
$-CH_2O$, $-CH_2I$	0.67	−0.02	−0.07				
$-CH_2S$	0.53	−0.15	−0.15	 $-\mathrm{C}(\mathrm{N})=\mathrm{O}$	1.37	0.93	0.35
$-CH_2Cl$, $-CH_2Br$	0.72	0.12	0.07				
$-CH_2N$	0.66	−0.05	−0.23	 $-\mathrm{C}(\mathrm{Cl})=\mathrm{O}$	1.10	1.41	0.99
$-C\equiv C$	0.50	0.35	0.10				
$-C\equiv N$	0.23	0.78	0.58	—OR, R: aliph	1.18	−1.06	−1.28
$-C=C$	0.98	−0.04	−0.21	—OR, R: conj[b]	1.14	−0.65	−1.05
$-C=C$ conj[b]	1.26	0.08	−0.01	—OCOR	2.09	−0.40	−0.67
$-C=O$	1.10	1.13	0.81	—Aromatic	1.35	0.37	−0.10
$-C=O$ conj[b]	1.06	1.01	0.95	—Cl	1.00	0.19	0.03
—COOH	1.00	1.35	0.74	—Br	1.04	0.40	0.55
—COOH conj[b]	0.69	0.97	0.39	 $-NR_2$ R:aliph	0.69	−1.19	−1.31
—COOR	0.84	1.15	0.56	 $-NR_2$ R:conj[b]	2.30	−0.73	−0.81
—COOR conj[b]	0.68	1.02	0.33	—SR	1.00	−0.24	−0.04
				$-SO_2$	1.58	1.15	0.95

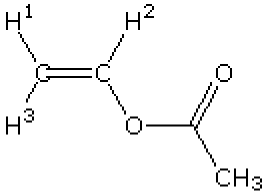
[a] Alkyl ring indicates that the double bond is part of the ring  .

[b] The *Z* factor for the conjugated substituent is used when either the substituent or the double bond is further conjugated with other groups.

Source: Pascual C., Meier, J., and Simon, W. (1966) *Helv. Chim. Acta,* **49,** 164.

$\delta_H = 5.25 + Z_{gem} + Z_{cis} + Z_{trans}$

Z	*substituent constant*		
	gem	*cis*	*trans*
-OC(O)R	2.09	-0.40	-0.67
-C(O)OR$_2$	0.84	1.15	0.56



$\delta_H{}^1 = 5.25$ = ppm

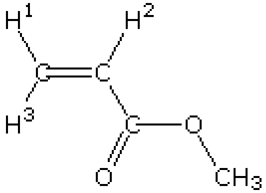
Observed: 4.55 ppm

$\delta_H{}^2 = 5.25$ = ppm

Observed: 7.25 ppm

$\delta_H{}^3 = 5.25$ = ppm

Observed: 4.85 ppm



$\delta_H{}^1 = 5.25$ = ppm

Observed: 5.82 ppm

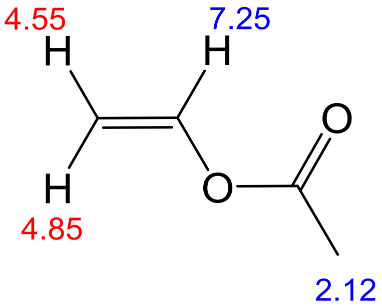
$\delta_H{}^2 = 5.25$ = ppm

Observed: 6.14 ppm

$\delta_H{}^3 = 5.25$ = ppm

Observed: 6.4 ppm

Using ChemDraw to estimate chemical shifts

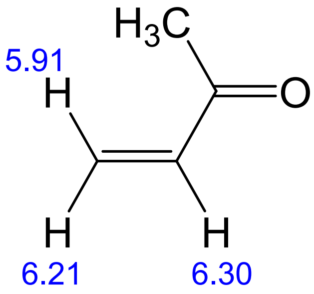


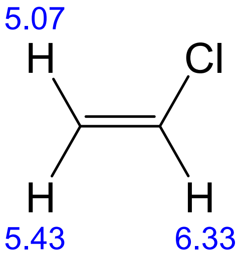
```
H    7.25                     5.25       1-ethylene
                              2.03       1 -OC(=O)-C gem
                             -0.03       general corrections

H    4.85                     5.25       1-ethylene
                             -0.37       1 -OC(=O)-C cis
                             -0.03       general corrections

H    4.55                     5.25       1-ethylene
                             -0.69       1 -OC(=O)-C trans
                             -0.01       general corrections
```

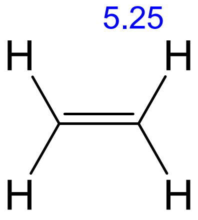
__Understanding__ the effect of substituents on the chemical shifts of peaks for protons of alkenes

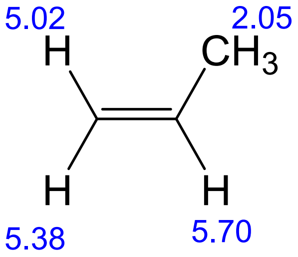
hi

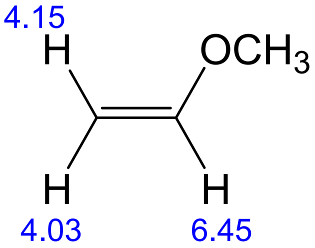
lo









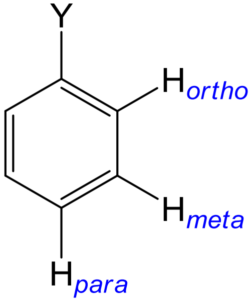


hi

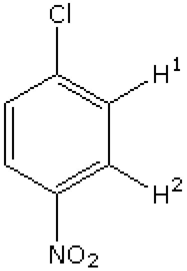
lo

Estimating chemical shifts of hydrogen atoms on benzene rings

$\delta_H = 7.27 + \Sigma d_i$



substituent	*substituent constant*		
	o-	*m-*	*p-*
-C(O)OR	-0.25	0.03	-0.13
$-NO_2$	0.95	0.26	0.38
-Cl	0.03	-0.02	-0.09

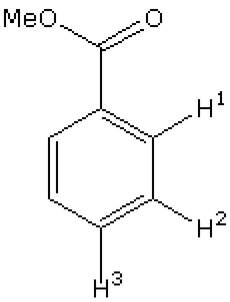


$\delta_H^1 = 7.27 +$ = ppm

Observed: 7.50 ppm

$\delta_H^2 = 7.27 +$ = ppm

Observed: 8.20 ppm



$\delta_H^1 = 7.27 +$ = ppm

Observed: 8.03 ppm

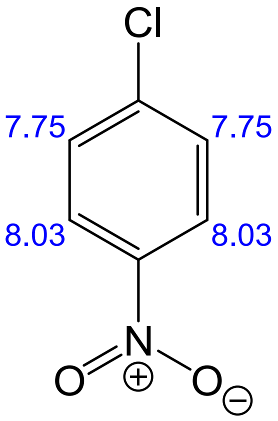
$d_H^2 = 7.27 +$ = ppm

Observed: 7.42 ppm

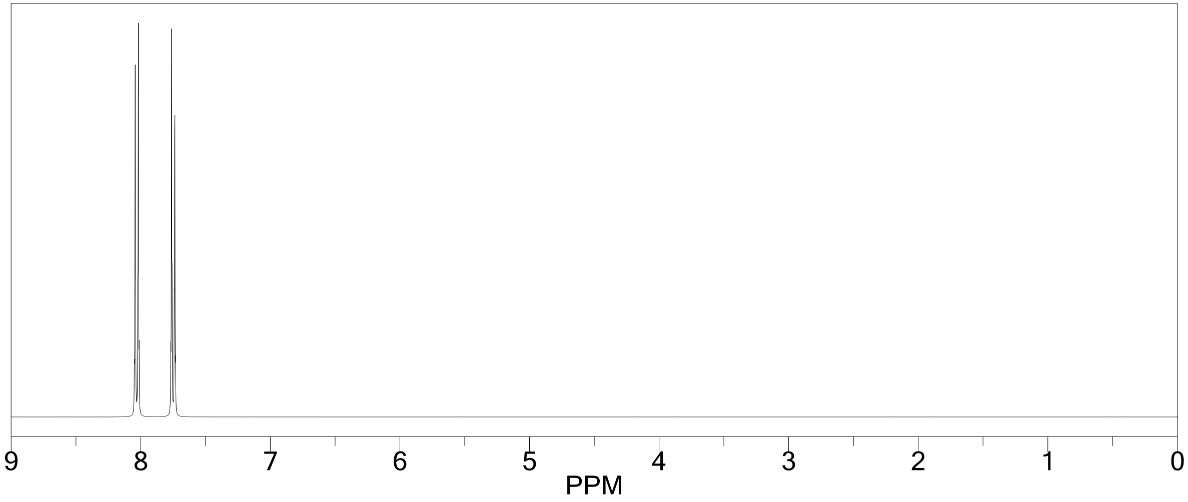
$d_H^3 = 7.27 +$ = ppm

Observed: 7.53 ppm

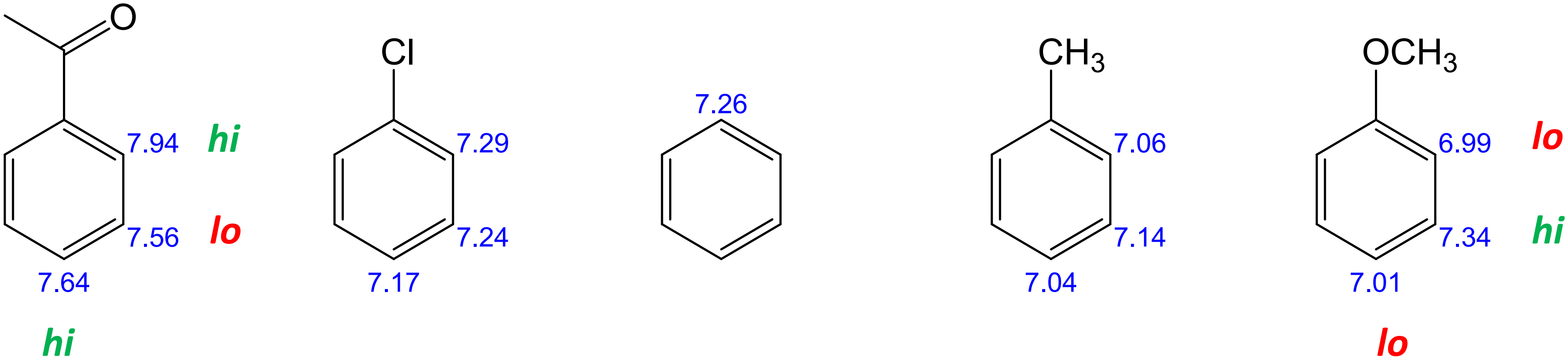
Estimating ^{1}H NMR shifts by ChemDraw



```
CH  7.75              7.26     1-benzene
                      0.01     1 -Cl
                      0.26     1 -N(=O)=O
                      0.22     general corrections

CH  8.03              7.26     1-benzene
                     -0.06     1 -Cl
                      0.93     1 -N(=O)=O
                     -0.10     general corrections
```



Understanding the effect of substituents on the chemical shifts of peaks for protons on substituted benzenes



Draw suitable resonance structures that explain the variation of charge distribution around the benzene rings to explain the trends in chemical shift

PAVIA 4th Ed. *PAVIA 5th Ed. Chapter 7*

Coupling constants – 5.1

Mechanism of coupling – 5.2,6,17

Magnetic Equivalence – 5.3

Multiplets of Multiplets – 5.4,5

Protons on O – 5.7,8

Protons on N – 5.9-11

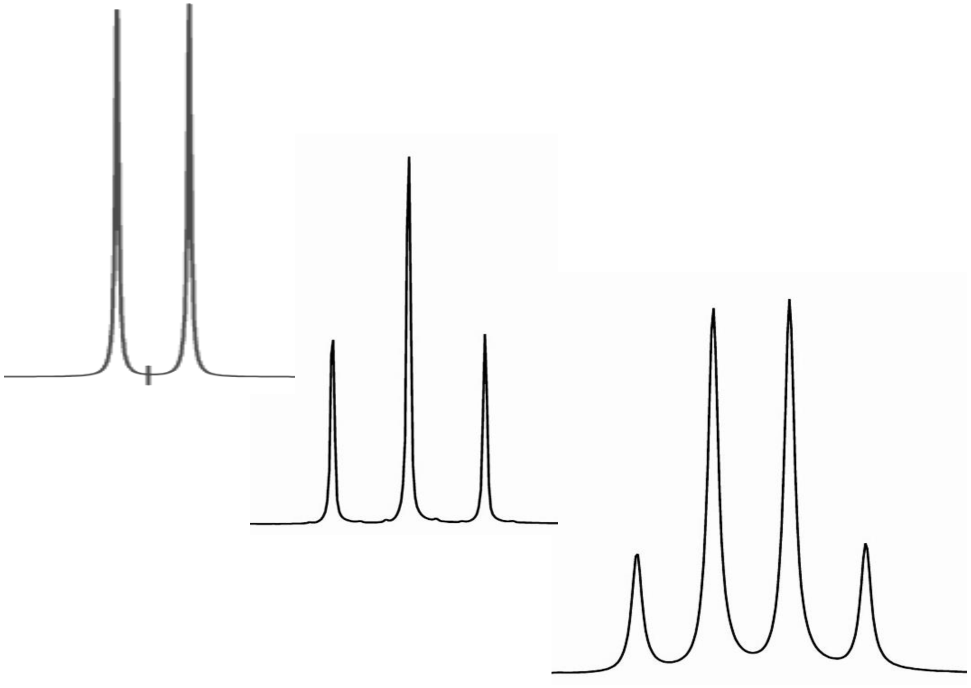
Second Order Spectra 5.12

Aromatic Compounds 5.13

Enatiotopic and Diastereotopic Protons 5.14,15,18,19

Coupling is only observed between non-equivalent protons.

The signal for a *proton* coupling to a set of *N* protons will be split into a *multiplet* consisting of *N*+1 lines. The relative area of each peak *within* a multiplet can be determined from Pascal’s triangle.

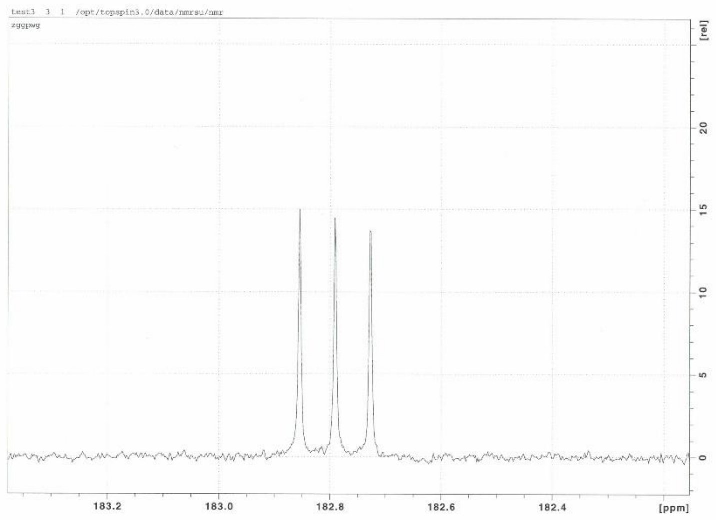


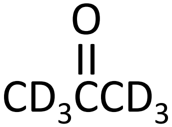
This is often referred to as the “*N*+1 rule” – but this only works for nuclei with nuclear spin quantum numbers, I = + ½ and –½ (e.g., ^{1}H)

This is a special case of a more general “2*NI*+1 rule” (for all values of I).

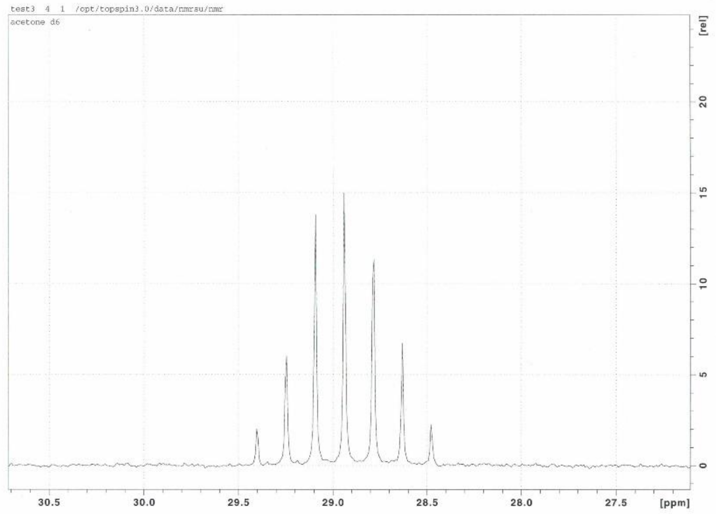
Coupling with spins other than 1/2

$CDCl_3$



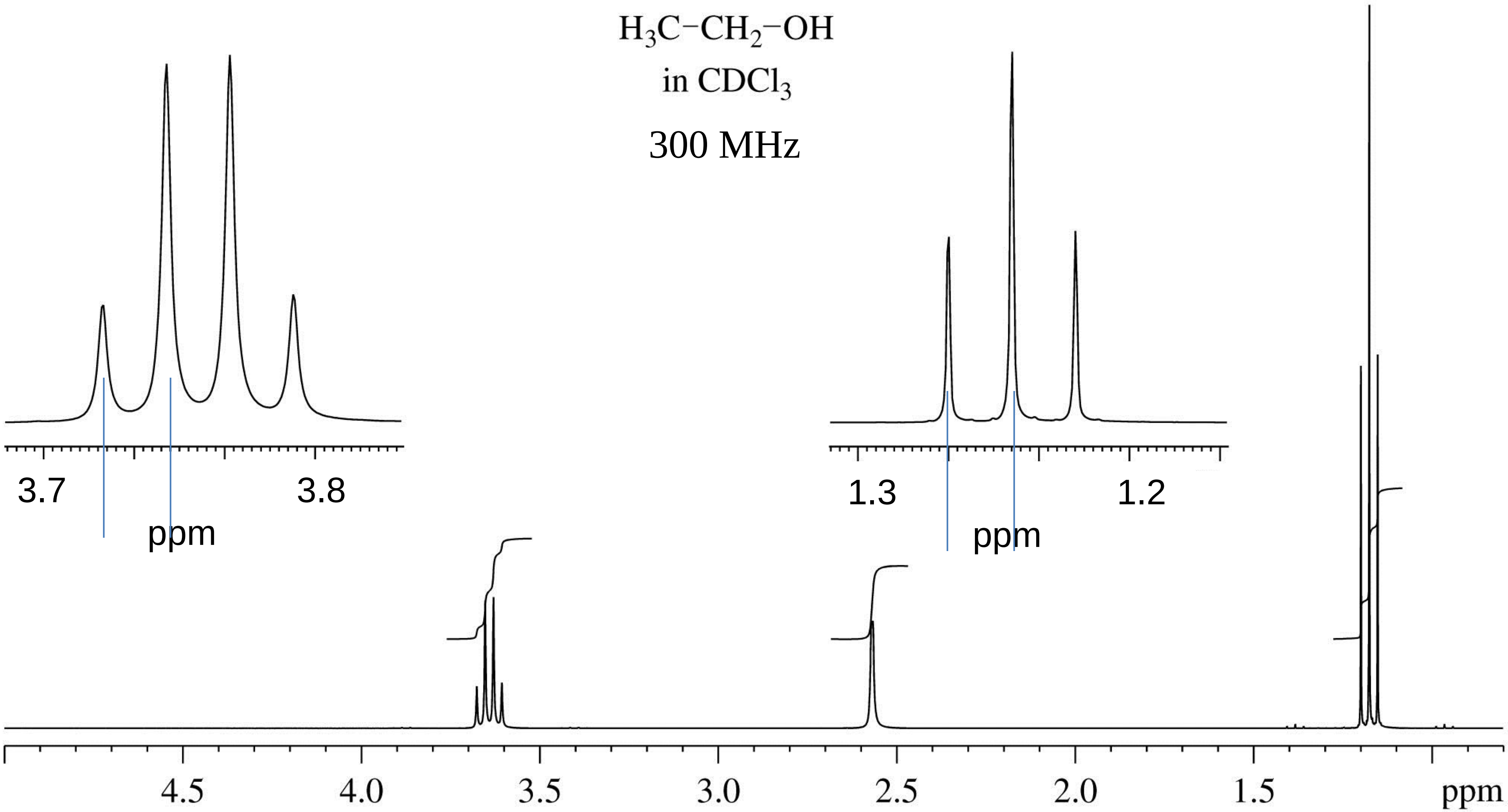


$CD_3C(=O)CD_3$

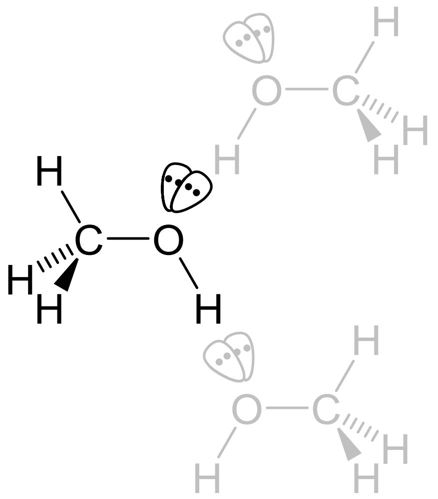


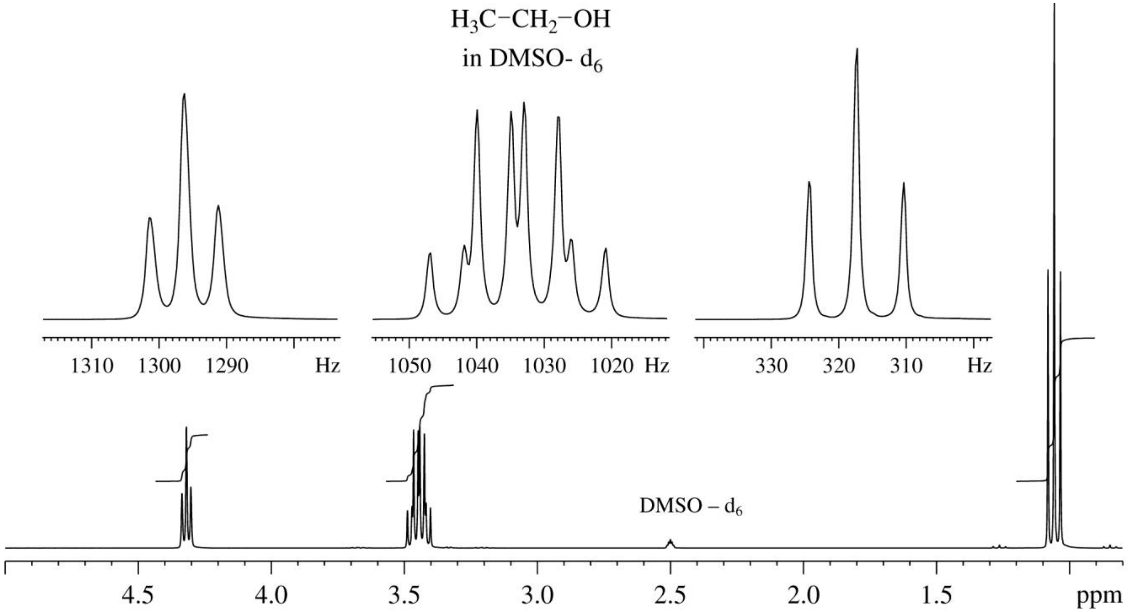
Measuring the Coupling Constants

Pavia 5.1



O-H of alcohols does not usually couple to neighboring protons in $CDCl_3$ (they sometimes do in DMSO-d_6)



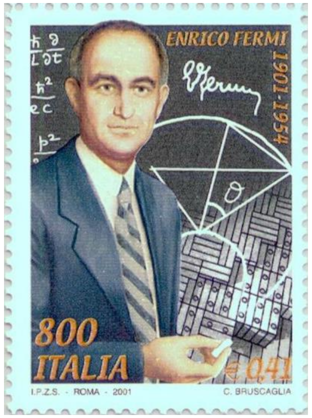


Protons on O (alcohols, carboxylic acids) and N (amines) are exchangable

$$\mathrm{RO{-}H} + \mathrm{D_2O} \longrightarrow \mathrm{RO{-}D} + \mathrm{HOD}$$

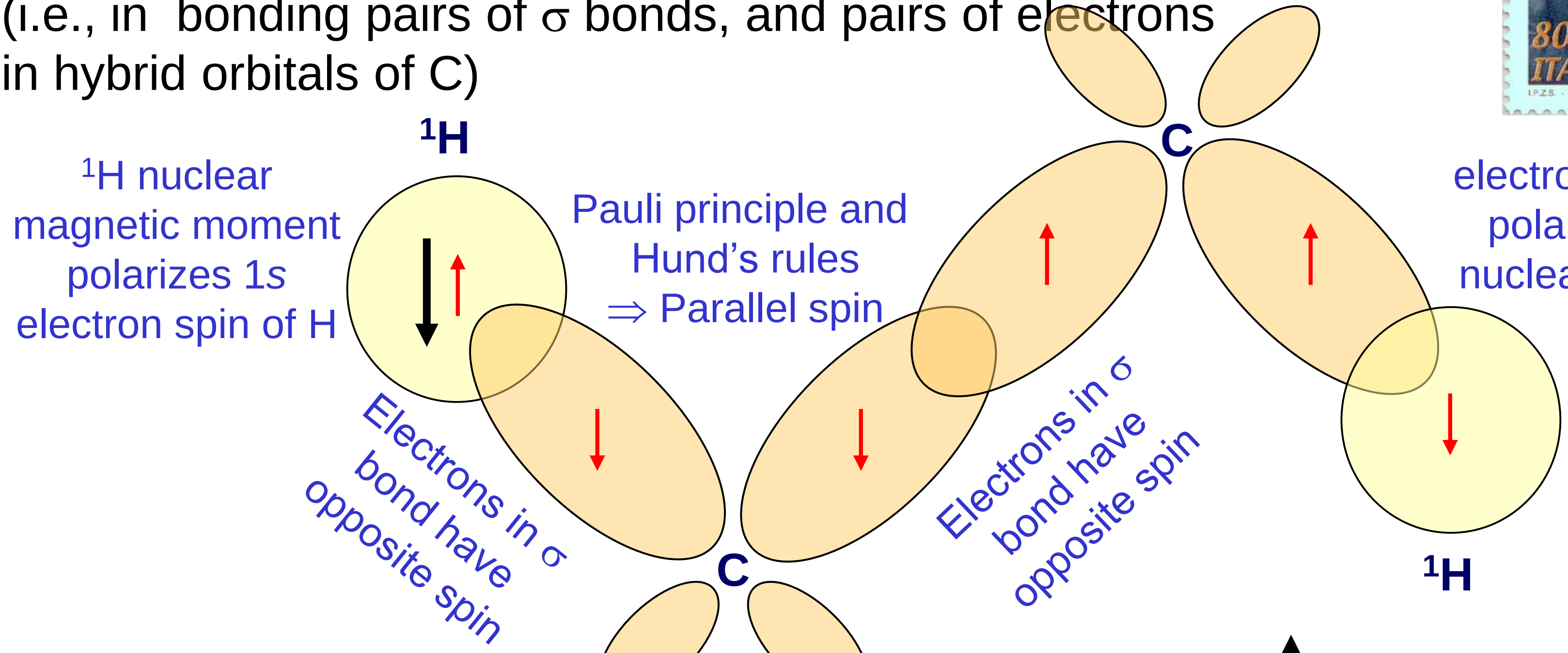
The Origin of Coupling: Fermi contact interaction

Pavia 5.2



e.g., three-bond coupling , ${}^3J$

^{1}H nuclear magnetic moment polarizes spin of H1*s* electron. Electrons with polarized spin then influence other electrons (i.e., in bonding pairs of σ bonds, and pairs of electrons in hybrid orbitals of C)



^{1}H nuclear magnetic moment polarizes 1*s* electron spin of H

Pauli principle and Hund's rules ⇒ Parallel spin

electron spin polarizes nuclear spin

Electrons in σ bond have opposite spin

Electrons in σ bond have opposite spin

Nuclear spin

Electron spin

Coupling is a *through-bond* effect

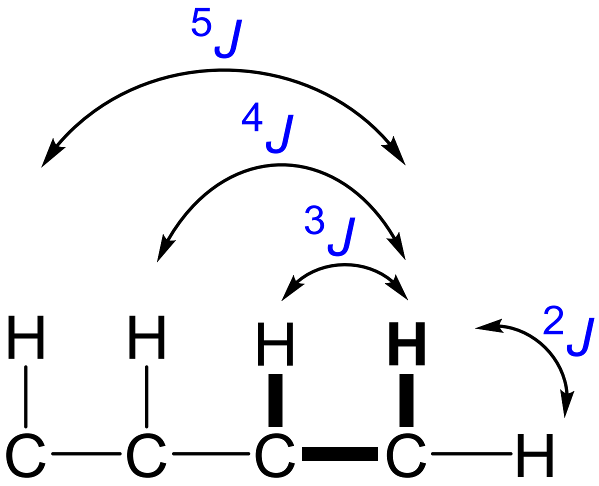
The extent of interaction between protons is the "coupling constant" (*J*) , measured in Hz

Coupling is only observed between chemically non-equivalent protons – protons that give peaks at different chemical shifts

J is *independent* of magnet strength (spectrometer frequency)

The extent of interaction between ^{1}H nuclei (i.e., ^{1}H-^{1}H coupling) drops off rapidly with number of bonds.

Coupling is a *through-bond* effect



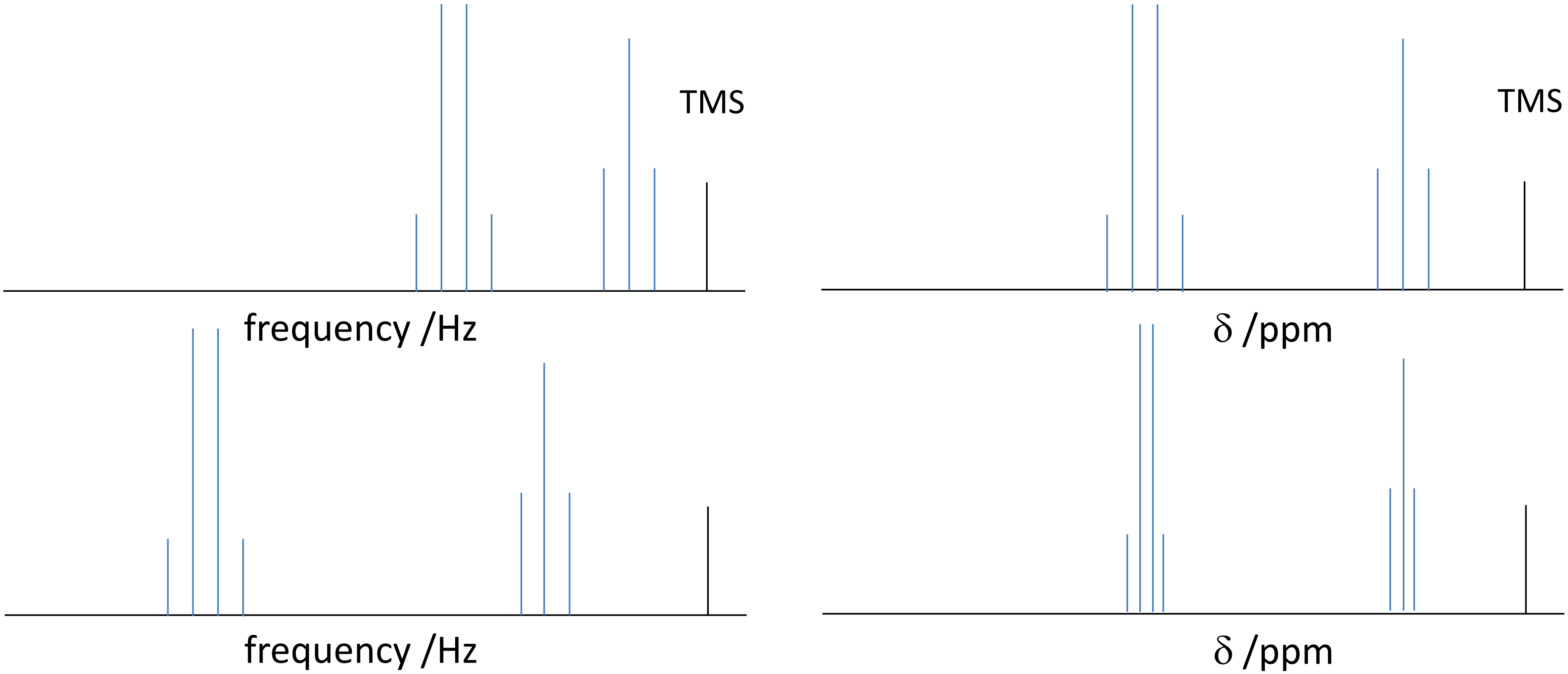
Typical ^{1}H-^{1}H coupling constants

^2J: 12 – 15 Hz for H–sp^3C–H
0 – 2 Hz for H–sp^2C–H

^3J: 0 – 14 Hz, depending on dihedral angle
~7 Hz for freely rotating H–sp^3C–sp^3C–H

^4J : 0 – 1 Hz, "long-range coupling"

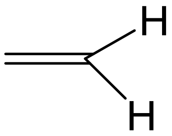
The effect of magnet strength on the appearance of spectra (2): Coupling constants are not effected by field strength (spectrometer frequency)



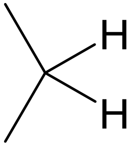
The *resonance frequency* is proportional to the magnet strength.
Coupling constants are *not* effected by the magnet strength.

Some Common ^{1}H-^{1}H Coupling Constants, J (in Hz)

Two-bond coupling (geminal hydrogen atoms)



typically 0-2 hz



typically 12-15 hz

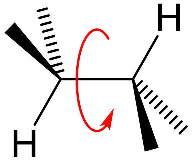
Remember – only chemically non-equivalent nuclei couple one another

Three-bond coupling between hydrogen atoms on sp^3 carbon atoms

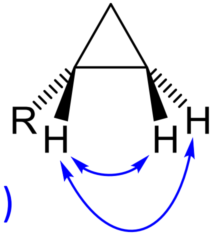
Three-bond coupling (*vicinal hydrogen atoms*)

Free rotation

Fixed conformations

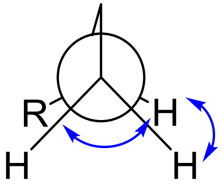


typically ~7 Hz



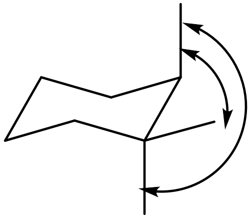
J_{cis} ~9 Hz (6-12)

J_{trans} ~6 Hz (4-8)



ϕ_{cis} ~0°

ϕ_{trans} ~120°

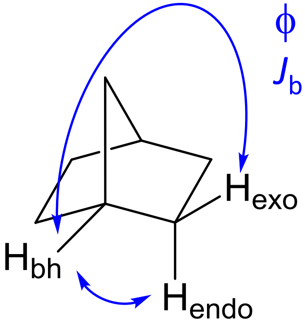


aa 180° J ~10 Hz

ae 60° J ~2 Hz

ϕ ~78°

$J_{bh\text{-}end}$ ~3 Hz



ϕ ~45°

$J_{bh\text{-}exo}$ ~8 Hz

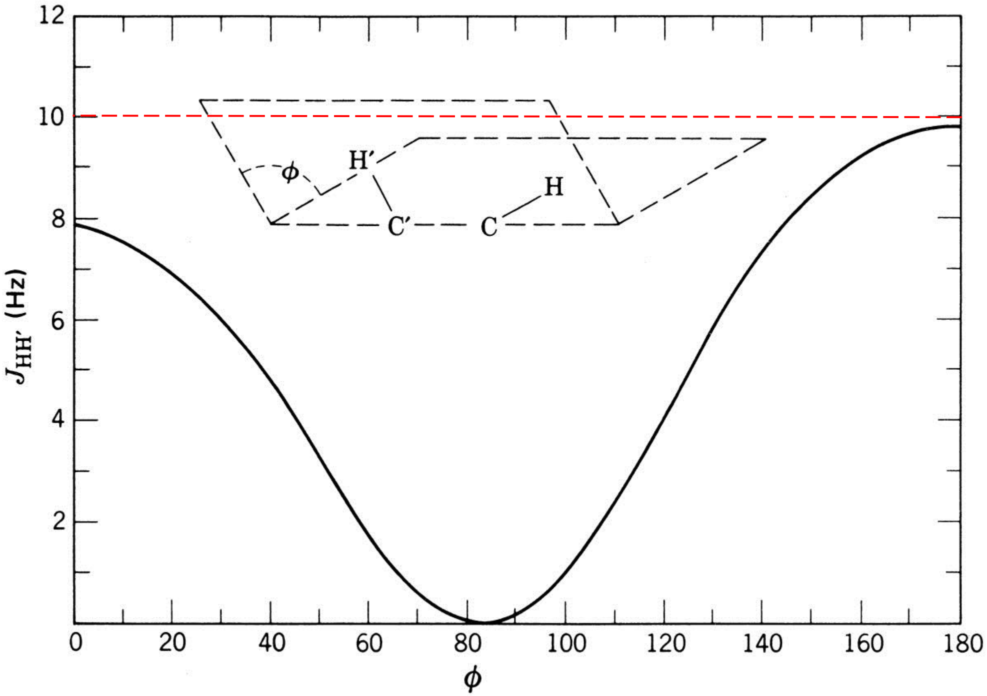
Remember – only chemically non-equivalent nuclei couple one another

The Karplus equation

$^{3}J = A\cos^{2}\Phi + B\cos\Phi + C$

where:
J is the coupling constant
Φ is the dihedral angle between two hydrogen atoms

J. Am. Chem. Soc., **85,** 2870 (1963)

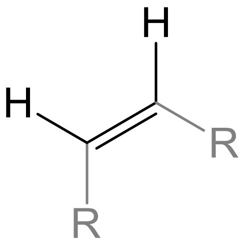


Values of A, B and C depend on substituents

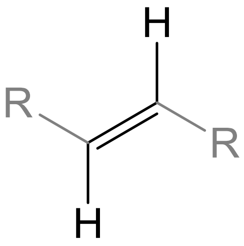
Online tool Calculation for coupling based on substituents and **dihedral** angle: *www.stenutz.eu/conf/jhh.html*

Coupling between hydrogen atoms on sp^2 carbon atoms

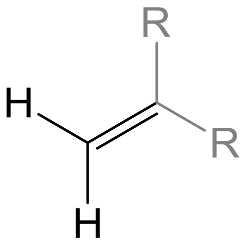
Vinylic coupling



$^{3}J_{\text{cis}}$ ~10 Hz (6-15)

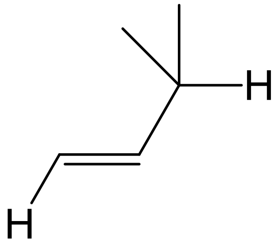


$^{3}J_{\text{trans}}$ ~16 Hz (11-18)

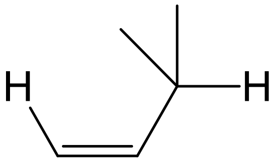


$^{2}J_{\text{gem}}$ ~1 Hz (0-5)

Long-range (4-bond) allylic couplings



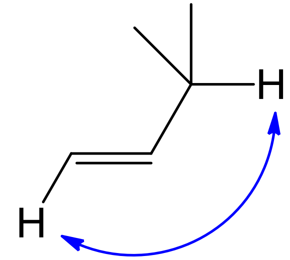
$^{4}J_{\text{trans}}$ ~1-2 Hz



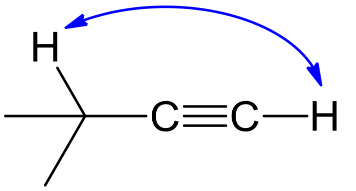
$^{4}J_{\text{cis}}$ ~1 Hz

Remember – only chemically non-equivalent nuclei couple one another

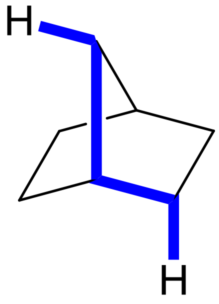
Long-range (four-bond) couplings



J_{allylic} ~1 Hz (0.3)

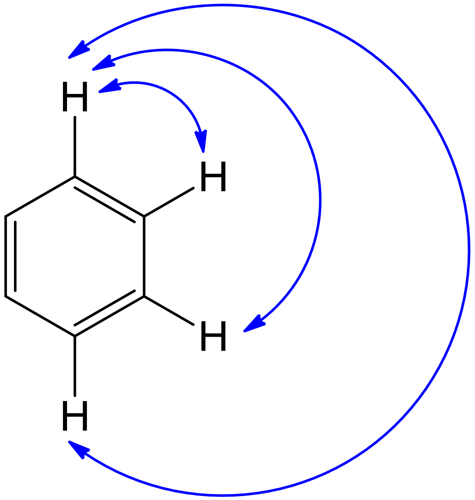


J ~0 Hz (0-1.5)



J_W ~1 Hz

Couplings between hydrogen atoms on substituted benzenes



^3J_o ~8 Hz (6-10)
^4J_m ~3 Hz (1-4)
^5J_p ~<1 Hz (0-2)

Remember – only chemically non-equivalent nuclei couple one another

Two-spin systems

e.g. $A_3 X_2$

J/Hz ~7

$CH_3–CH_2–Cl$

A_3 X_2

δ 1.49 3.42

ν at 300 MHz

1026 447

Δν/*J* 83

A X

e.g., AX_2, A_2X_2, A_2X_3, …
"first order systems"
can be analyzed
In a straightforward manner

A B

e.g., AB_2, A_2B_2, A_2B_3, …
"higher order systems"
cannot be interpreted
by simple inspection

Three spin systems

e.g, $A_3M_2X_2$

$CH_3–CH_2–CH_2–Cl$

A_3 M_2 X_2

A M X

e.g.,
AMX, AM_2X_3, A_2MX_2 , …
"first order systems" can be analyzed in a straightforward manner

A B X

e.g.,
ABX_2, A_2B_2X, $A_3B_2X_2$, …
"higher order systems"
cannot be interpreted by simple inspection

The effect of magnet strength on the appearance of spectra (2): second order spectra **($\Delta\nu/J < 8$)** *can be converted to first order spectra upon increasing the field strength (spectrometer frequency)*

J (Hz) ~7 ~7

$CH_3–CH_2–CH_2–Cl$

	A_3	M_2	X_2
δ	0.90	1.61	3.68

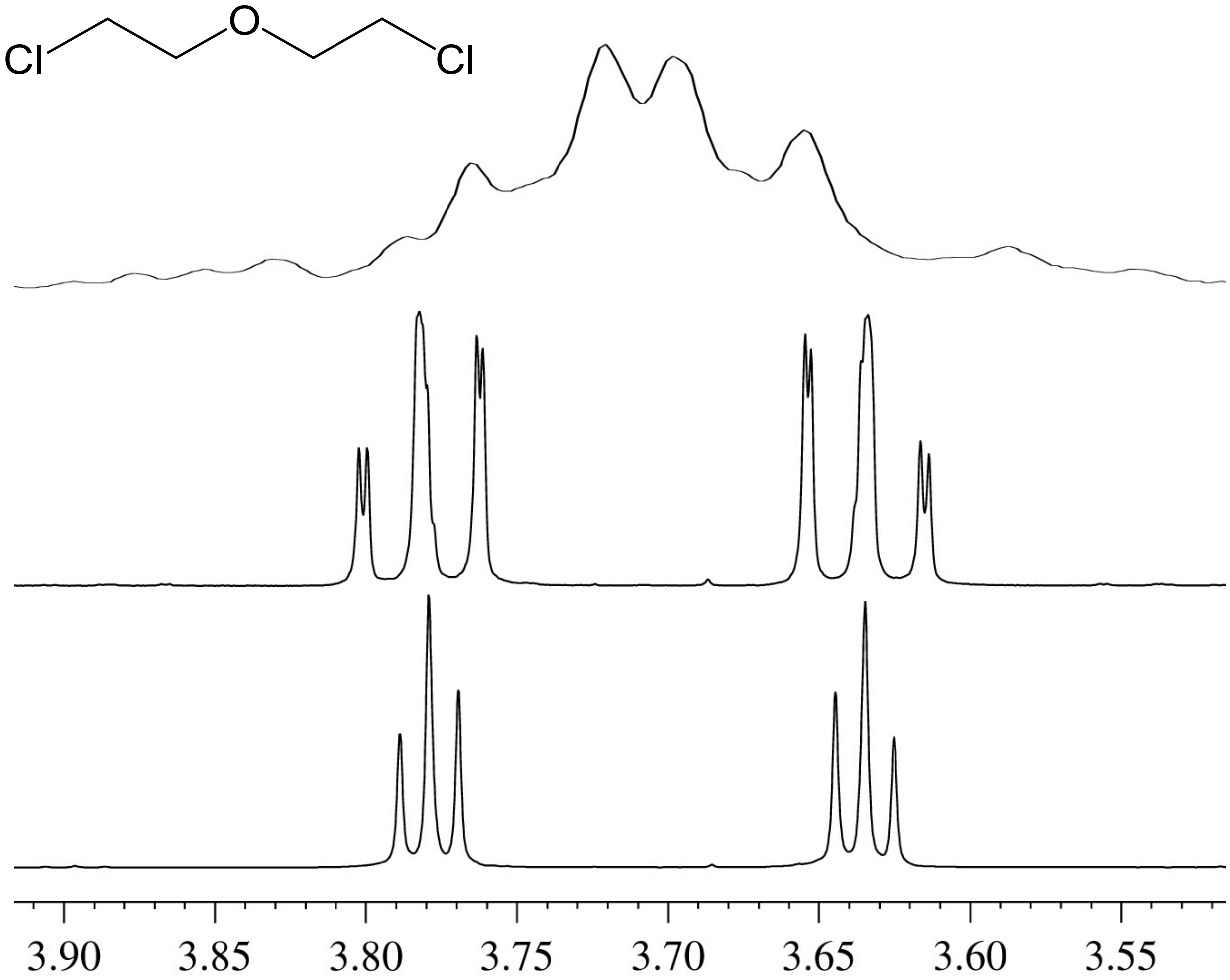
ν at 300 MHz

ν	270	483	1104
$\Delta\nu$	213	621	
$\Delta\nu/J$	30	89	

ν at 60 MHz

ν	54	97	221
$\Delta\nu$	43	124	
$\Delta\nu/J$	6	18	

Converting a A_2B_2 spin system to an A_2X_2



J/Hz ~7

…–O–CH_2–CH_2–Cl

δ 3.78 3.63

ν at 60 MHz

227 218

Δν/*J* 1.3 A_2B_2

ν at 300 MHz

1134 1089

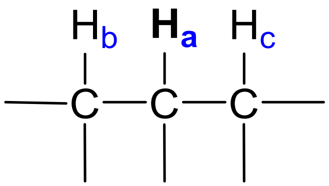
Δν/*J* 6.4

ν at 600 MHz

2267 2178

Δν/*J* 12.9 A_2X_2

Tree Diagrams



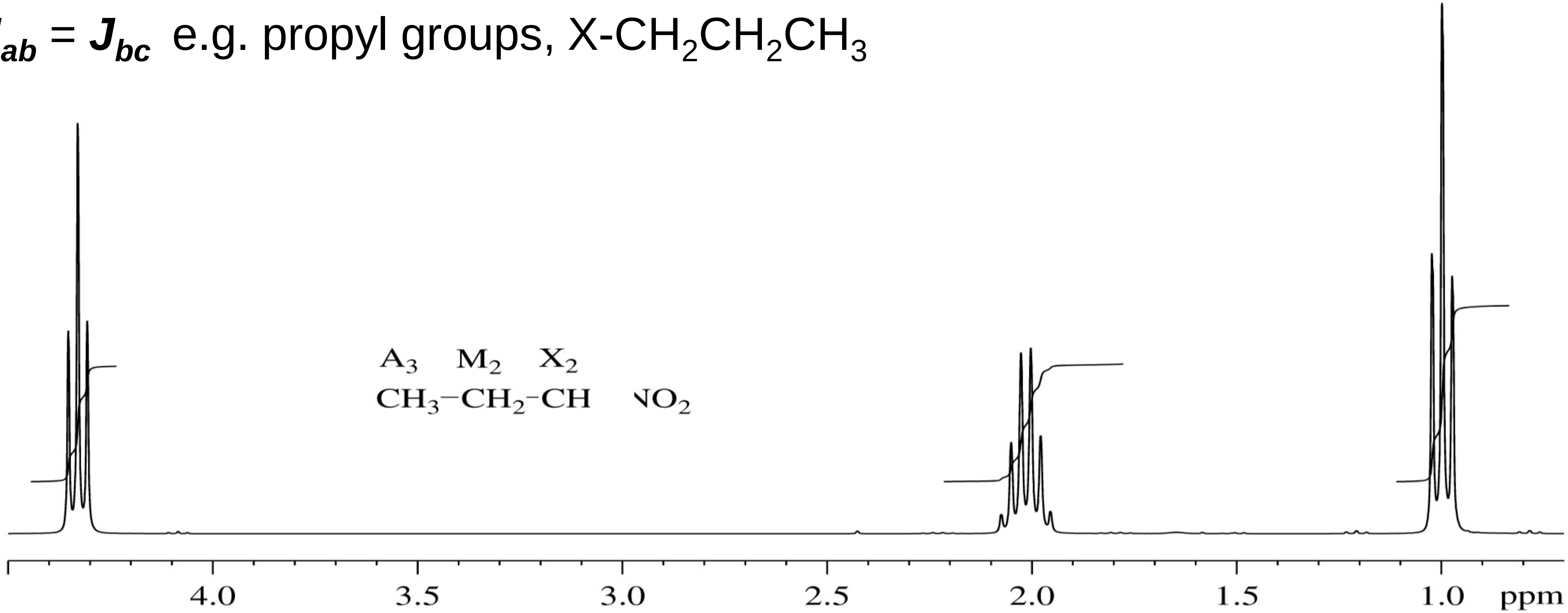
$J_{ab} = J_{ac}$

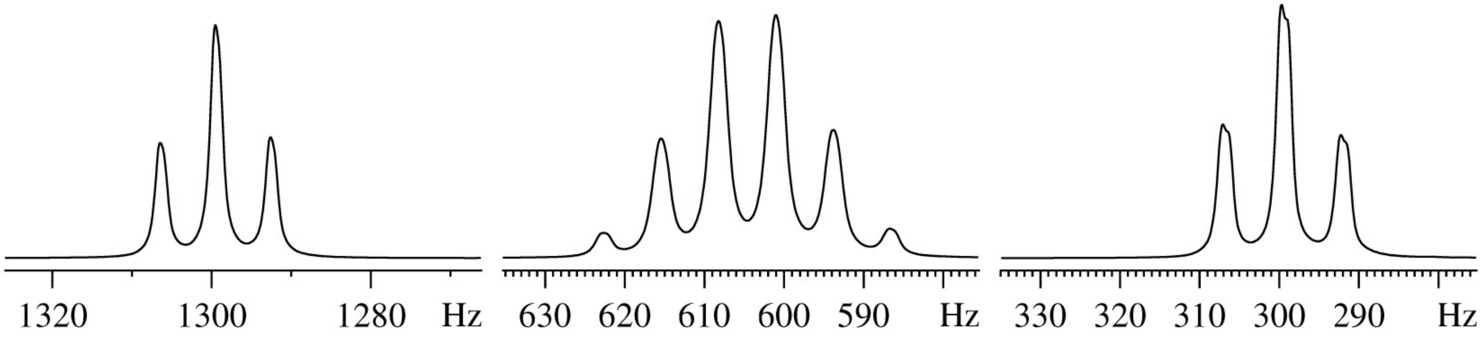
most common when carbons have the same hydridization and free rotation (~7Hz is common)

$J_{ab} \neq J_{ac}$

most common when carbons have the different hydridization or restricted rotation.

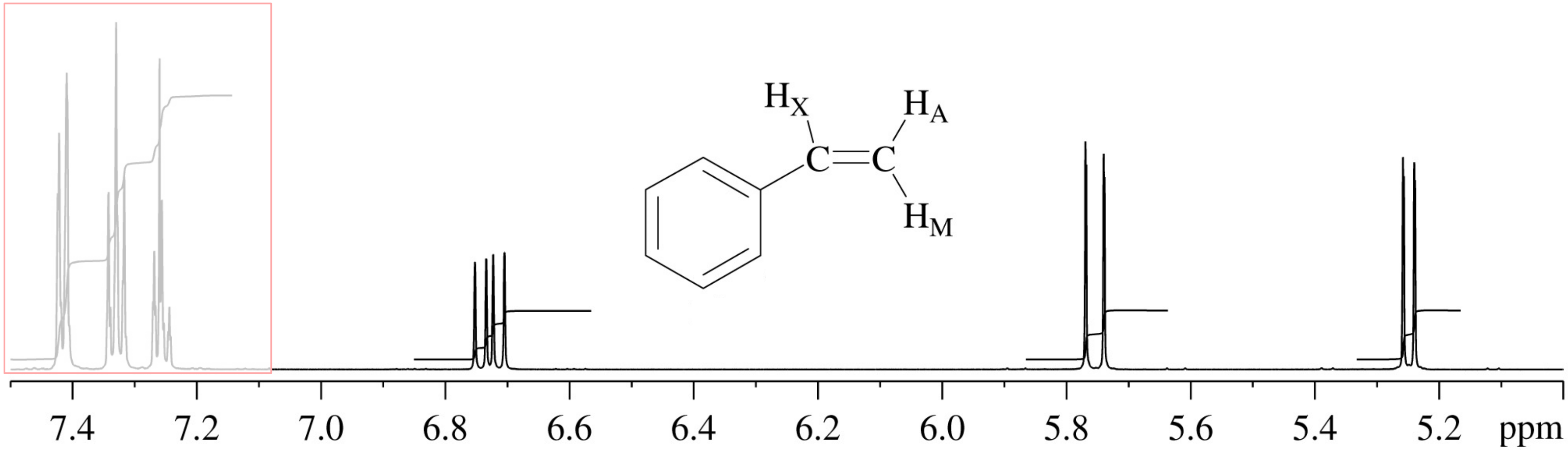
$\boldsymbol{J_{ab} = J_{bc}}$ e.g. propyl groups, X-$CH_2CH_2CH_3$

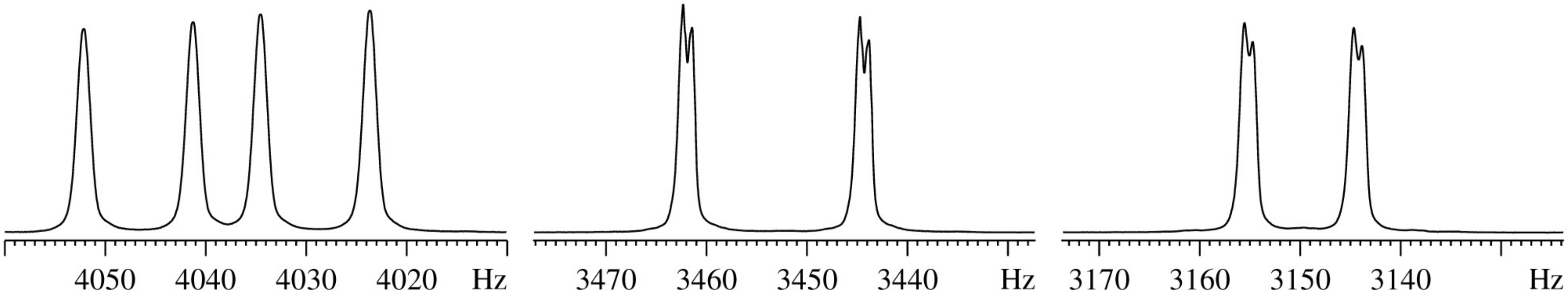




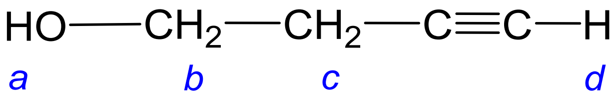
$J_{XA} \neq J_{XB}$ e.g. vinyl groups

Pavia 5.5

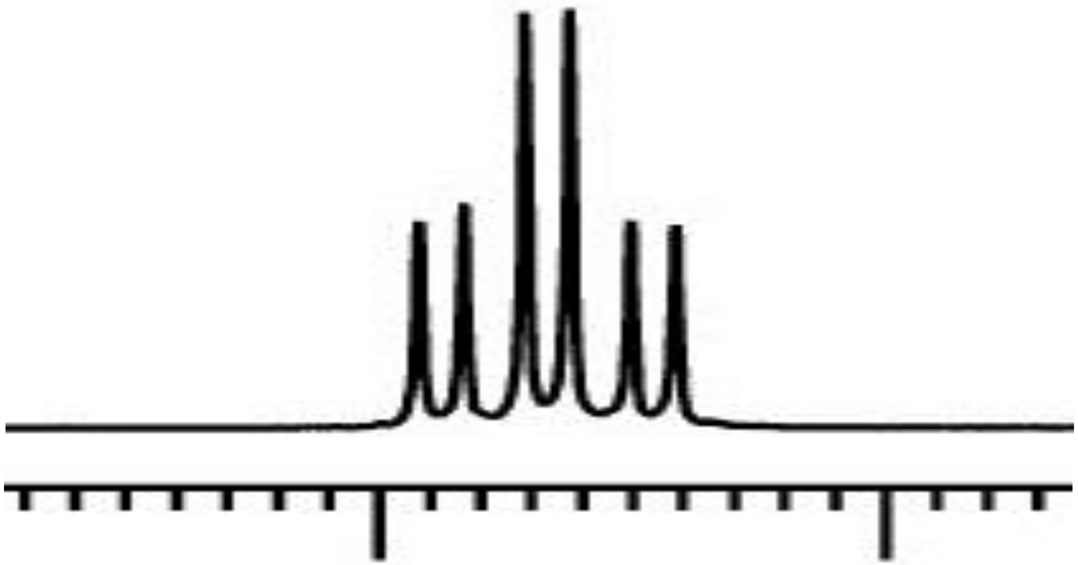


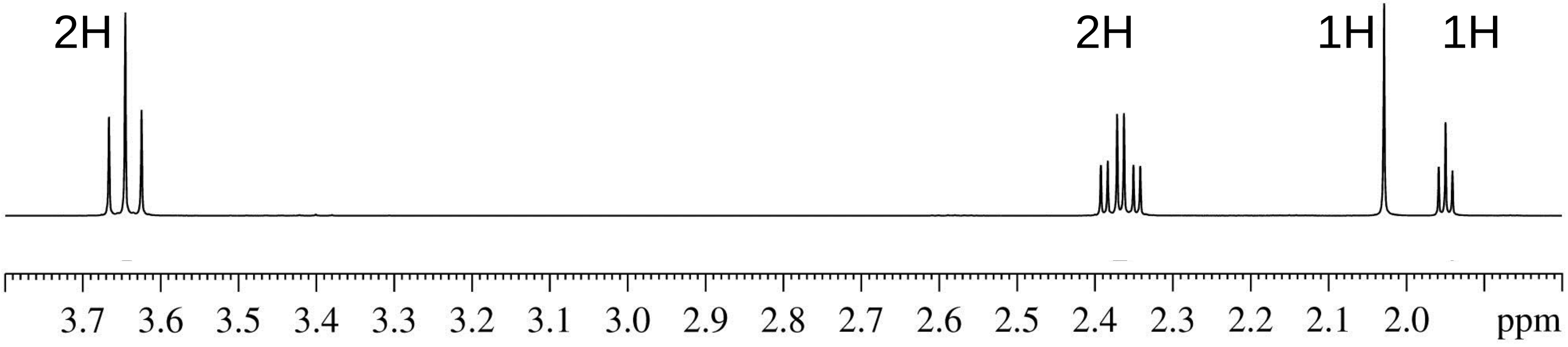


How do you describe the multiplicity of the following signal?



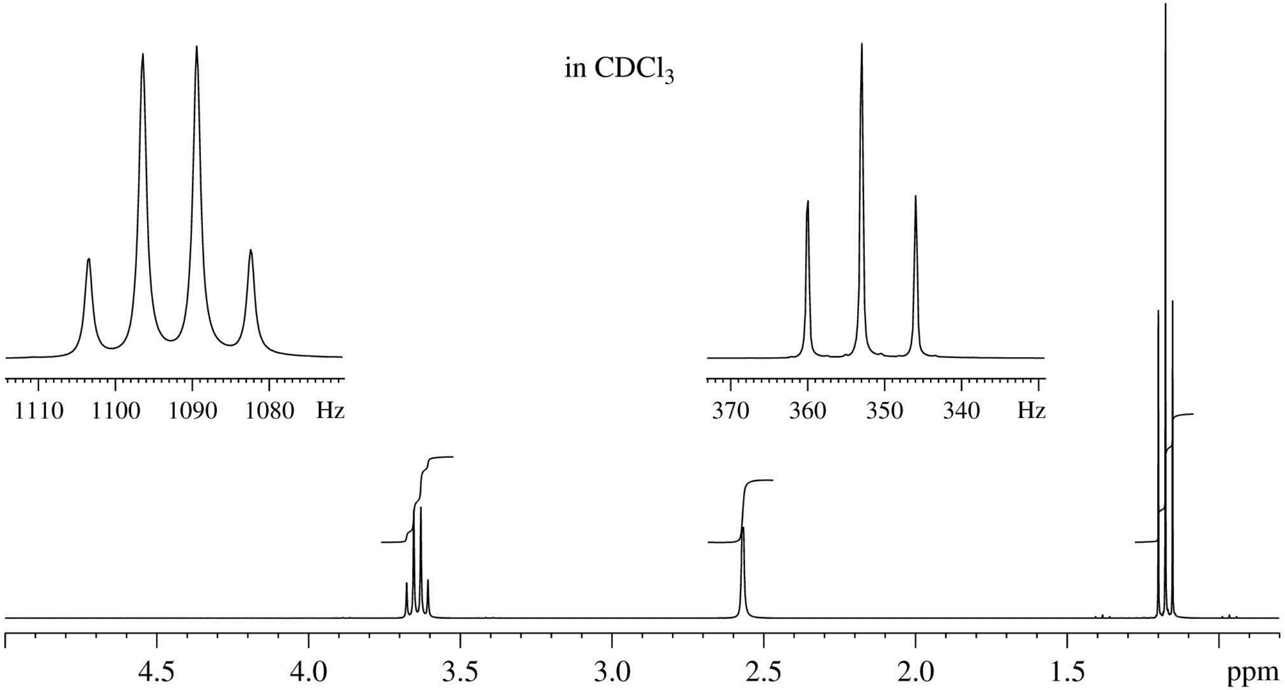
$HO{-}CH_2{-}CH_2{-}C{\equiv}C{-}H$

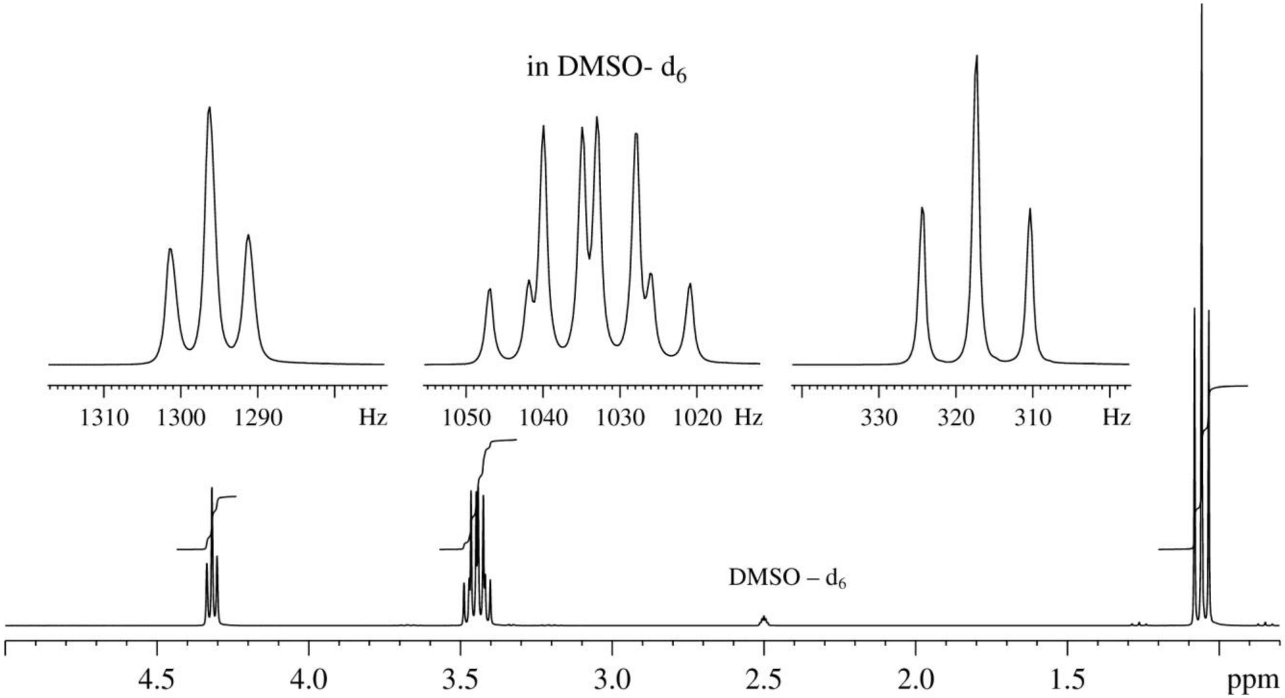


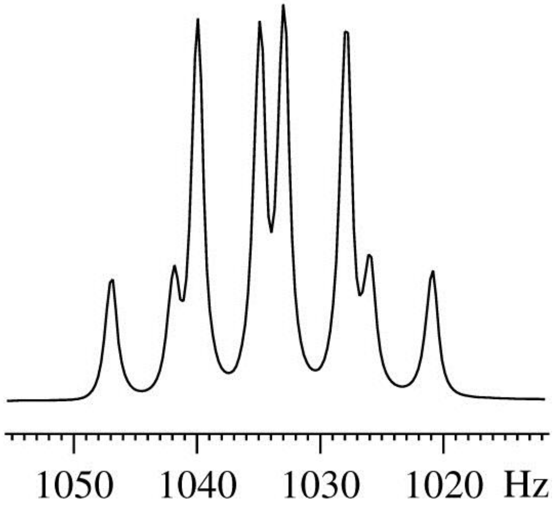


$HO—CH_2—CH_3$

a *b* *c*



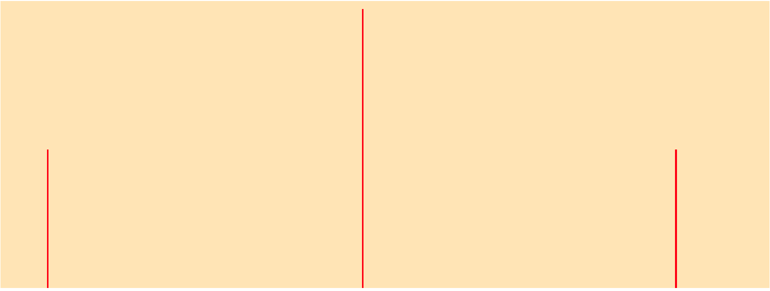




Predicting the Appearance of First Order Multiplets

Online tool www.colby.edu/chemistry/NMR/jmmset.html

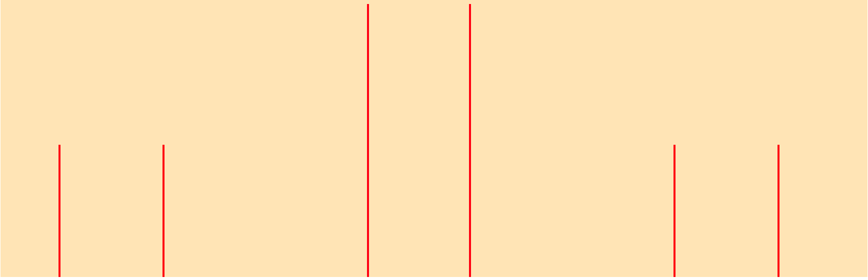
AX_2, J = 7 Hz



AMX_2

J_{AM} = 6 Hz

J_{AX} = 1 Hz



AMX_2

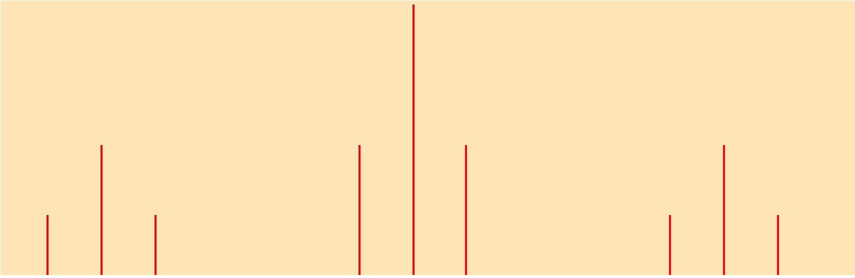
J_{AM} = 6 Hz

J_{AX} = 3 Hz

AM_2X_2

J_{AM} = 6 Hz

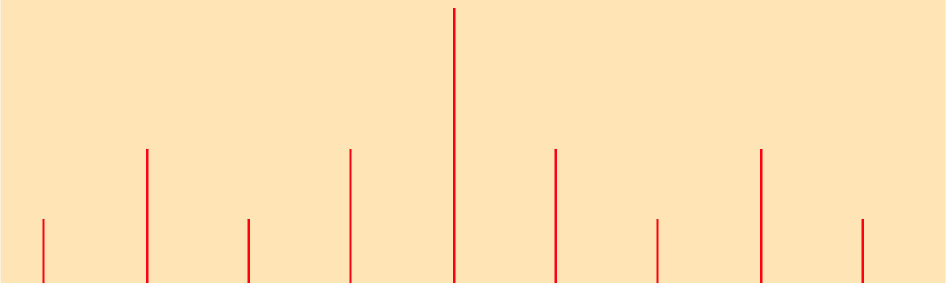
J_{AX} = 1 Hz



AM_2X_2

J_{AM} = 6 Hz

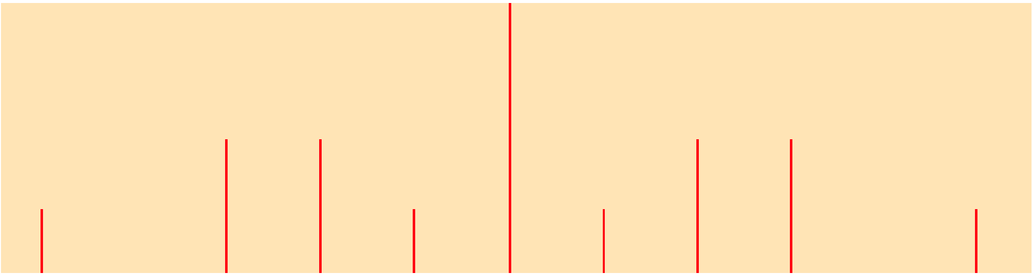
J_{AX} = 2 Hz



AM_2X_2

J_{AM} = 6 Hz

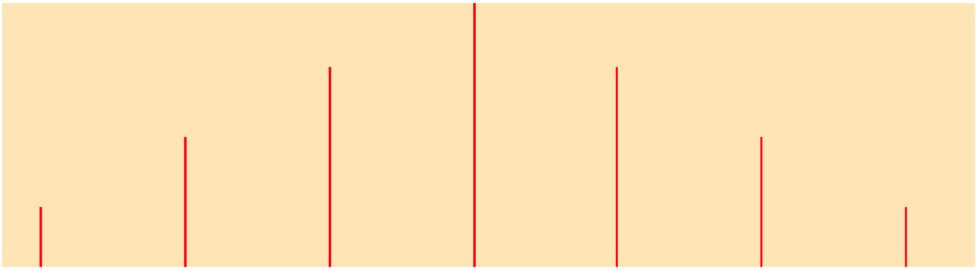
J_{AX} = 4 Hz



AM_2B_2

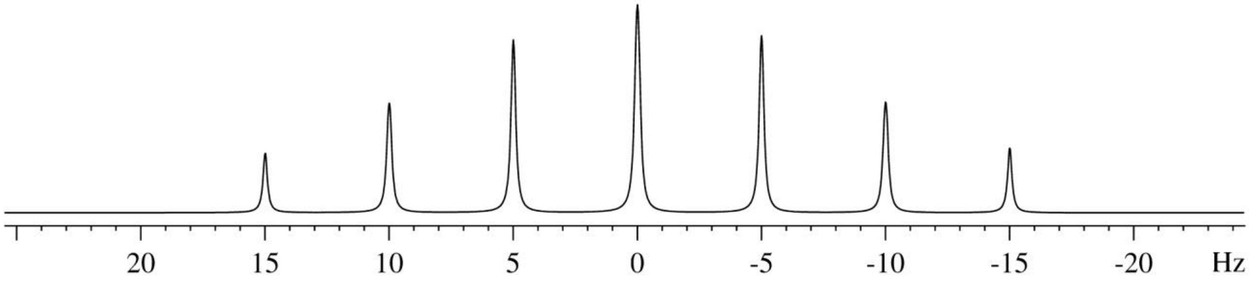
J_{AM} = 6 Hz

J_{AX} = 3 Hz

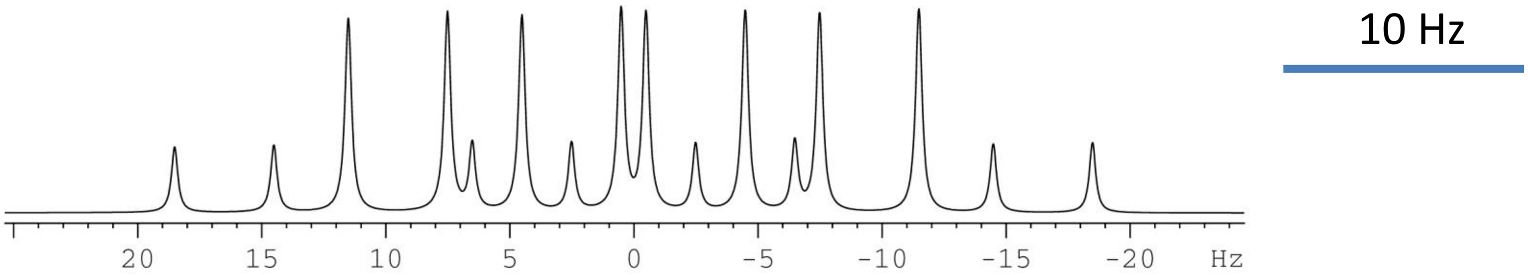


B. E. Mann, “The Analysis of First-Order Coupling Patterns in NMR Spectra, *J. Chem. Educ.*, **1995**, *72(7)*, 614. DOI: 10.1021/ed072p614

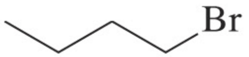
How do you describe the multiplicity of the following signal?



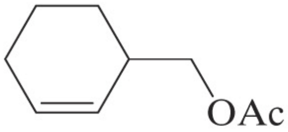
How do you describe the multiplicity of the following signal?



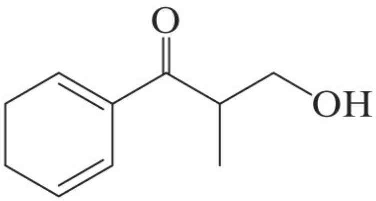
Problems: Describe the spin systems of the following molecules using the Pople notation.



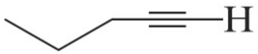
a



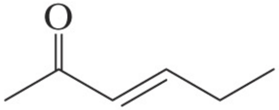
b



c

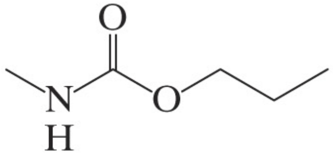


d



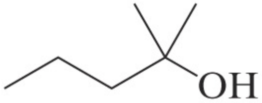
e

f

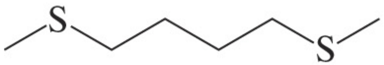


g

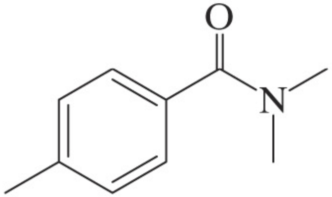
h



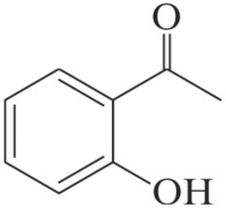
i



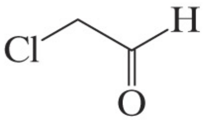
j



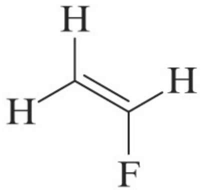
k



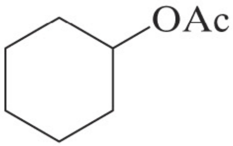
l



m



n



o

Problems

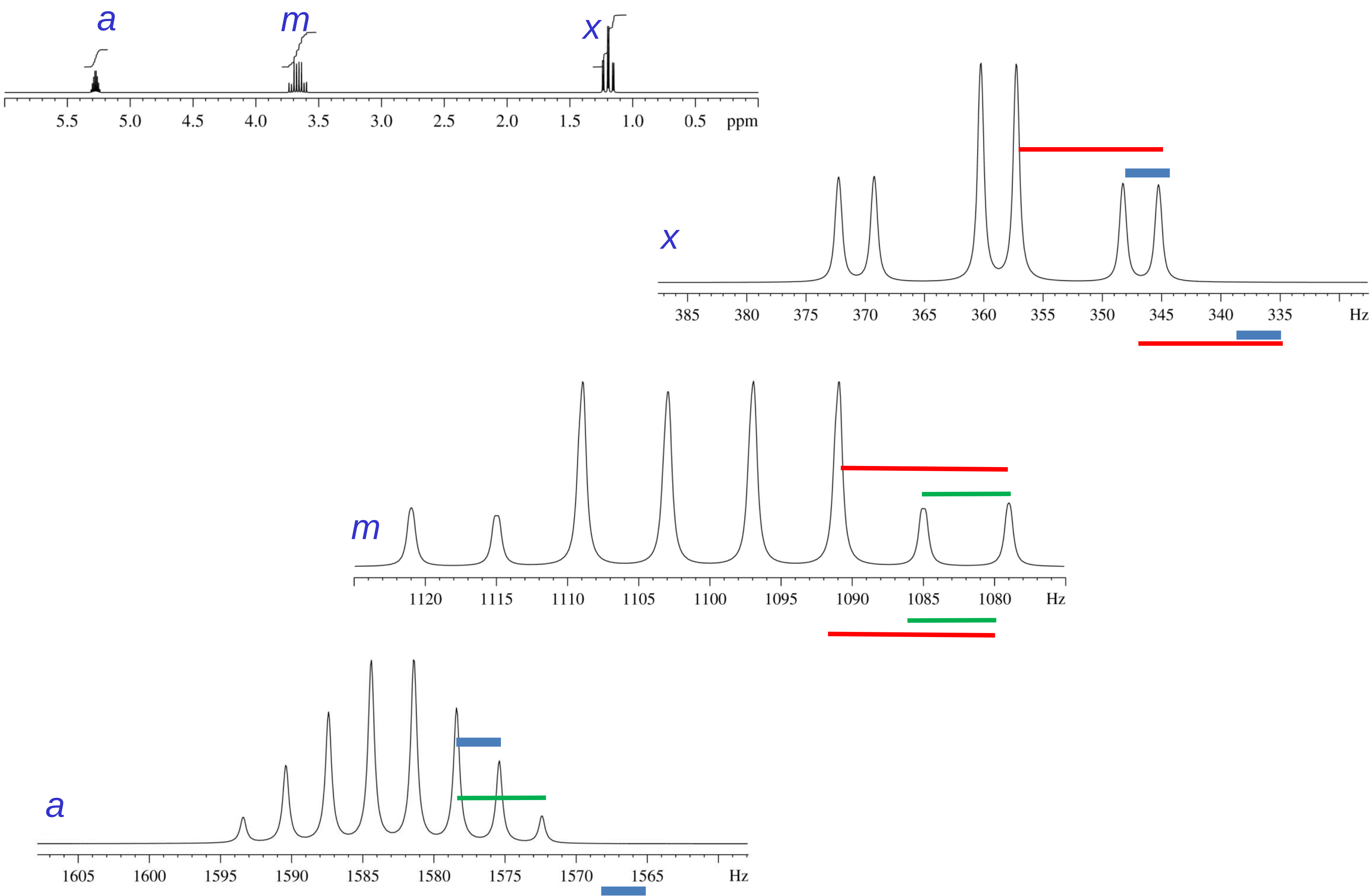
Sketch the spectra you expect for AX, A_2X, A_3X, A_2X_2, A_3X_2 spin systems.

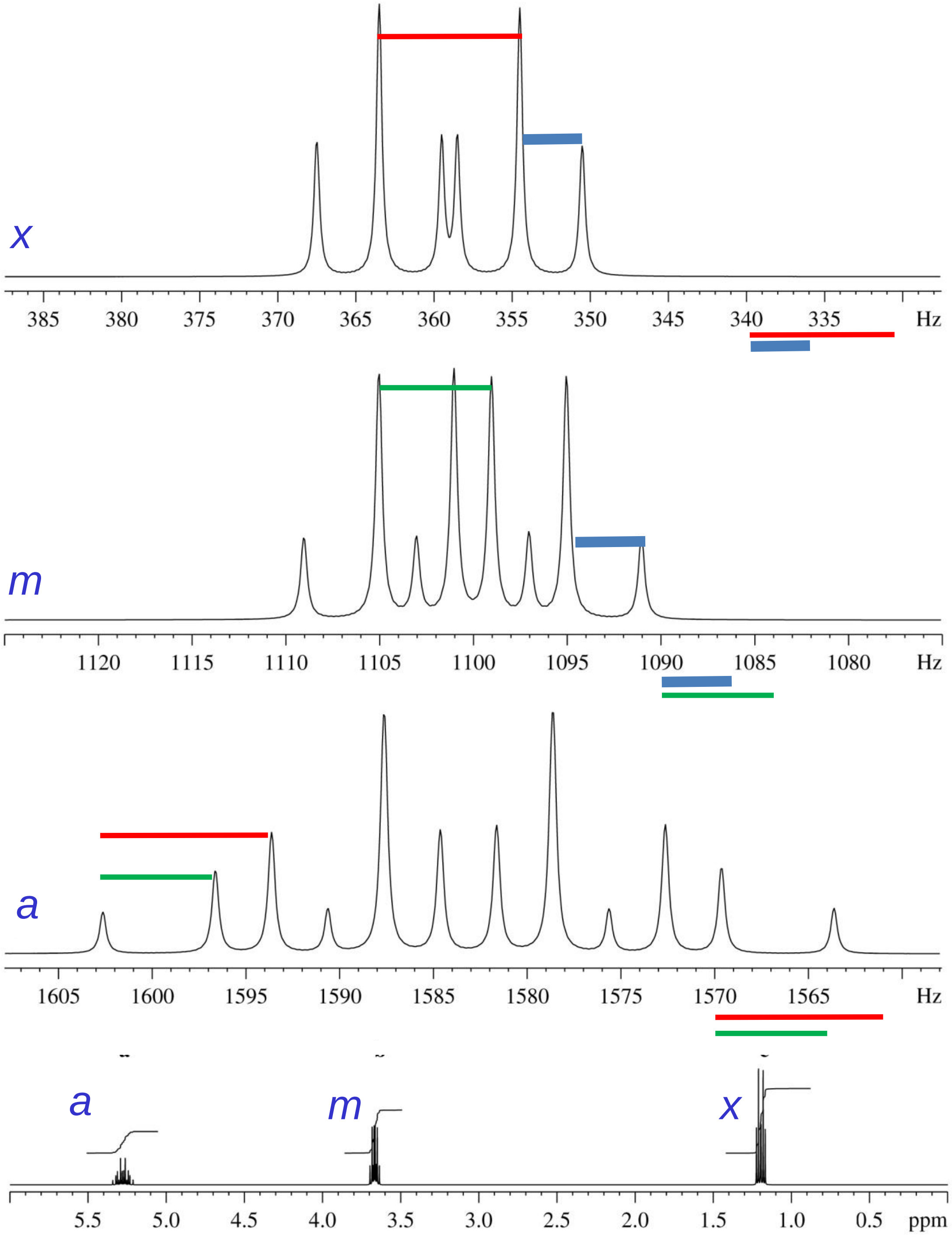
Sketch the spectra you expect for AMX, A_2MX, A_3MX, A_2MX_2, A_3MX_2 spin systems, where A does not couple X, and $J_{AM} = J_{MX}$

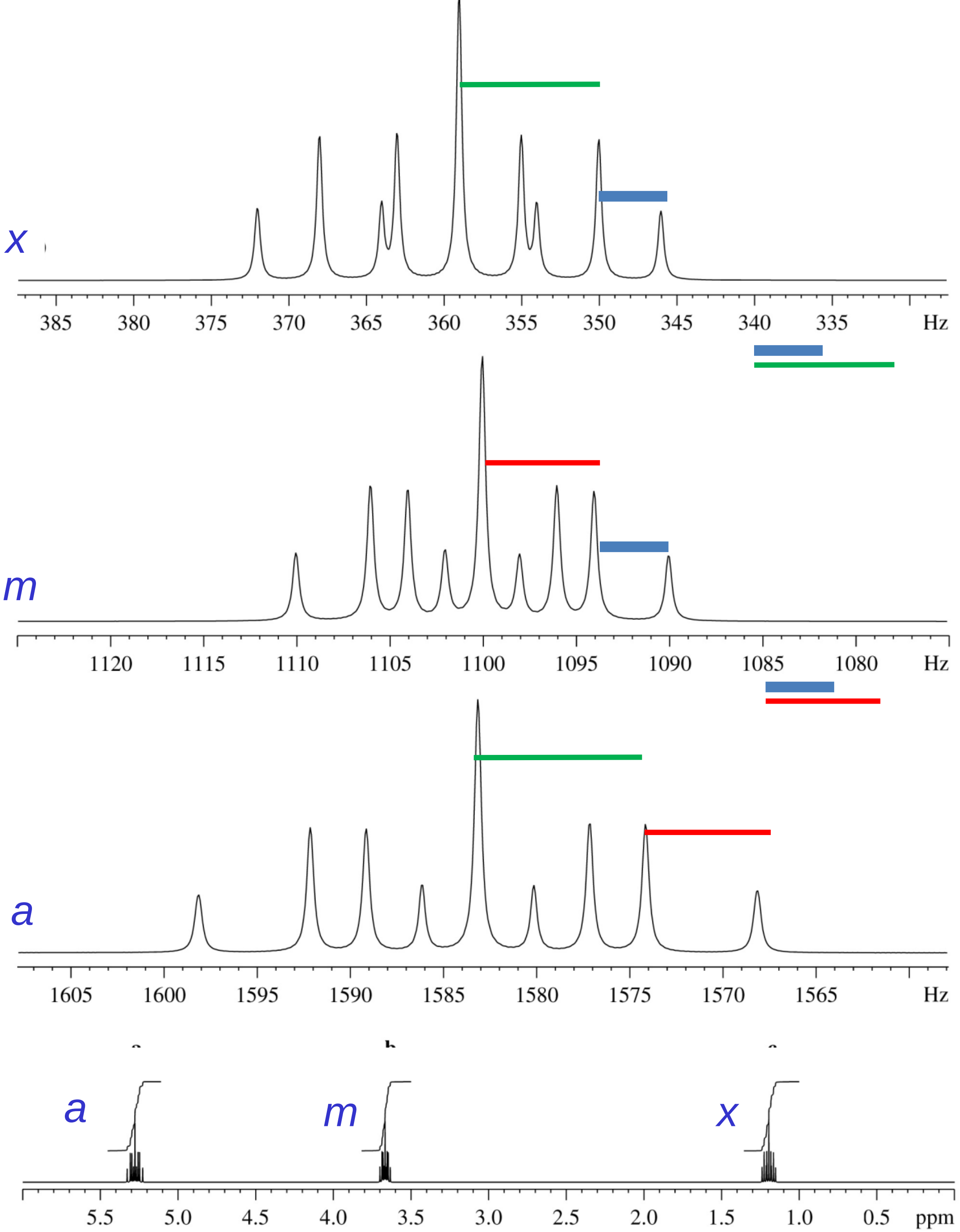
Sketch the spectra you expect for AMX, A_2MX, A_3MX, A_2MX_2, A_3MX_2 spin systems, where A does not couple X, and $J_{AM} =$ 10 Hz, and $J_{MX} =$ 5 Hz.

Problems

Determine structural features based on the appearance of peaks in the following spectra.




x
385
380
375
370
365
360
355
350
345
340
335
Hz
m
1120
1115
1110
1105
1100
1095
1090
1085
1080
Hz
a
1605
1600
1595
1590
1585
1580
1575
1570
1565
Hz
a
m
x
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

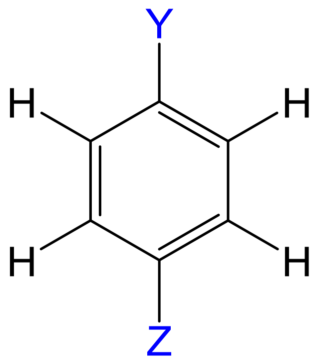

x
385
380
375
370
365
360
355
350
345
340
335
Hz
m
1120
1115
1110
1105
1100
1095
1090
1085
1080
Hz
a
1605
1600
1595
1590
1585
1580
1575
1570
1565
Hz
a
m
x
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

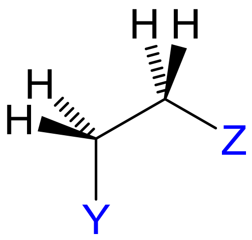
Magnetic Inequivalent Nuclei

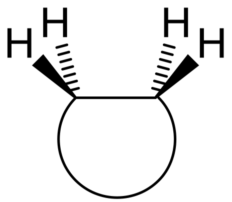
Pavia 5.4,13

- Two protons which are chemical shift equivalent (i.e., related by symmetry) can be split by a second set of protons
  e.g., an A_2X_2 system gives a *t* of *t*

- However, each proton of type A might couple differently to each proton X. In this case, the two A protons are said to be "magnetically inequivalent", and are labeled A and A'. Protons X will also be magnetically inequivalent (i.e., X and X').



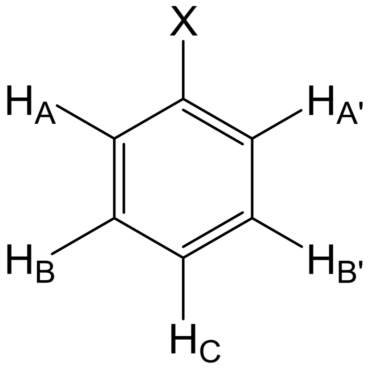


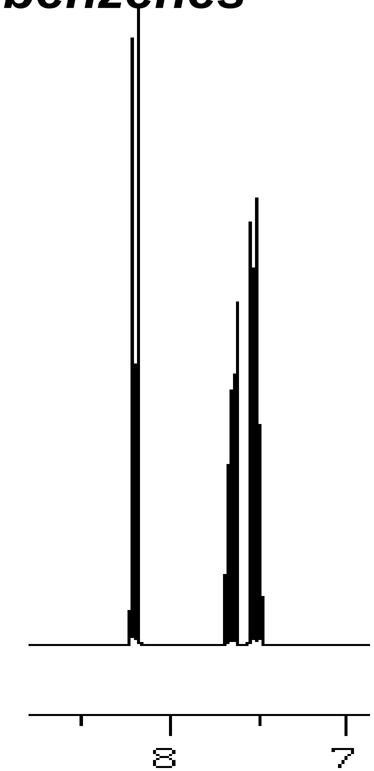


Remember, complex sets of peaks are observed (higher order spectra) if the chemical shifts of the peaks are similar.

Multiplicity of peaks for protons on substituted benzenes

Monosubstituted benzenes





δ(A) 8.193
δ(B) 7.519
δ(C) 7.650

Spectral Database for Organic Compounds (SDBS)

H_A and $H_{A'}$ are chemical shift equivalent. However they are "magnetically inequivalent” - they couple to H_B and $H_{B'}$ differently. So, while

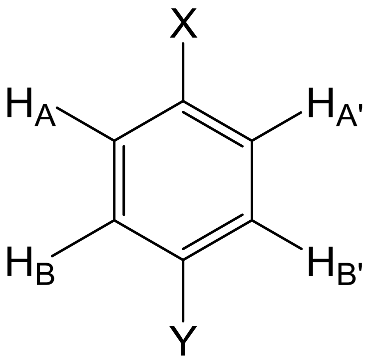
$J(H_A\text{-}H_B) = J(H_{A'}\text{-}H_{B'}) \approx$ 7-10 Hz

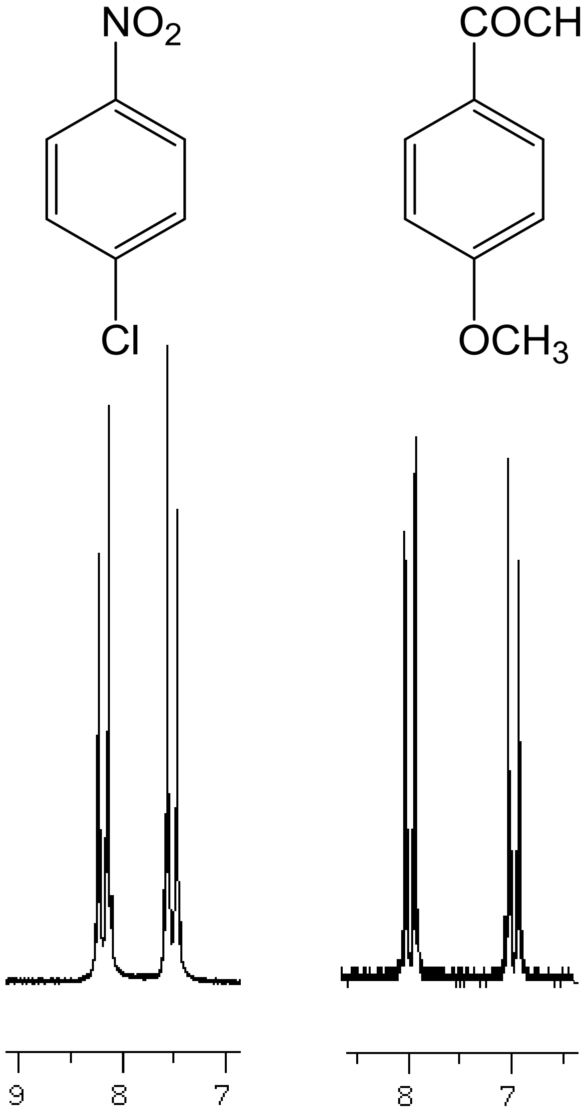
and $J(H_A\text{-}H_{B'}) = J(H_{A'}\text{-}H_B) \approx$ 0-1 Hz

$J(H_A\text{-}H_B) \neq J(H_A\text{-}H_{B'})$

So, H_A (and $H_{A'}$) should be split by coupling to H_B ($J \approx$ 7-10 Hz), H_C ($J \approx$ 1-3 Hz), and to $H_{B'}$ ($J \approx$ 0-1 Hz). However, the difference in chemical shifts is small and while the peak for H_A might appear as an AB system,it may be more complex

Unsymmetrically para-disubstituted benzene





Spectral Database for Organic Compounds (SDBS)

H_A and $H_{A'}$ are chemical shift equivalent. However they are "magnetically inequivalent" - they couple to H_B and $H_{B'}$ differently. So, while

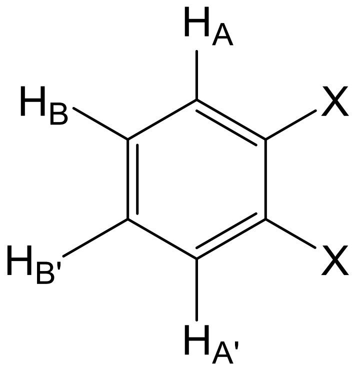
$J(H_A\text{-}H_B) = J(H_{A'}\text{-}H_{B'}) \approx$ 7-10 Hz

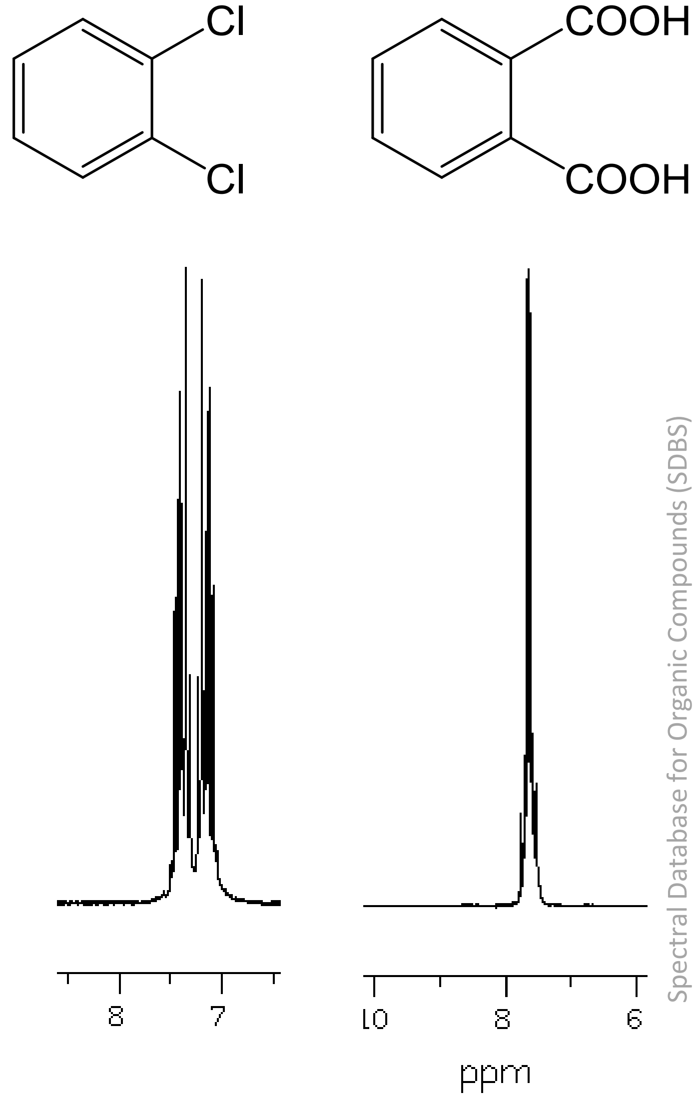
and $J(H_A\text{-}H_{B'}) = J(H_{A'}\text{-}H_B) \approx$ 0-1 Hz

$J(H_A\text{-}H_B) \neq J(H_A\text{-}H_{B'})$

So, H_A (and $H_{A'}$) should be split by coupling to H_B ($J \approx$ 7-10 Hz) and to $H_{B'}$ ($J \approx$ 0-1 Hz). However, the difference in chemical shifts is small and while the peak for H_A might appear as AB system, it may be more complex

Symmetrical ortho disubstituted benzene





Spectral Database for Organic Compounds (SDBS)

H_A and $H_{A'}$ are chemical shift equivalent. However they are "magnetically inequivalent" - they couple to H_B and $H_{B'}$ differently. So, while

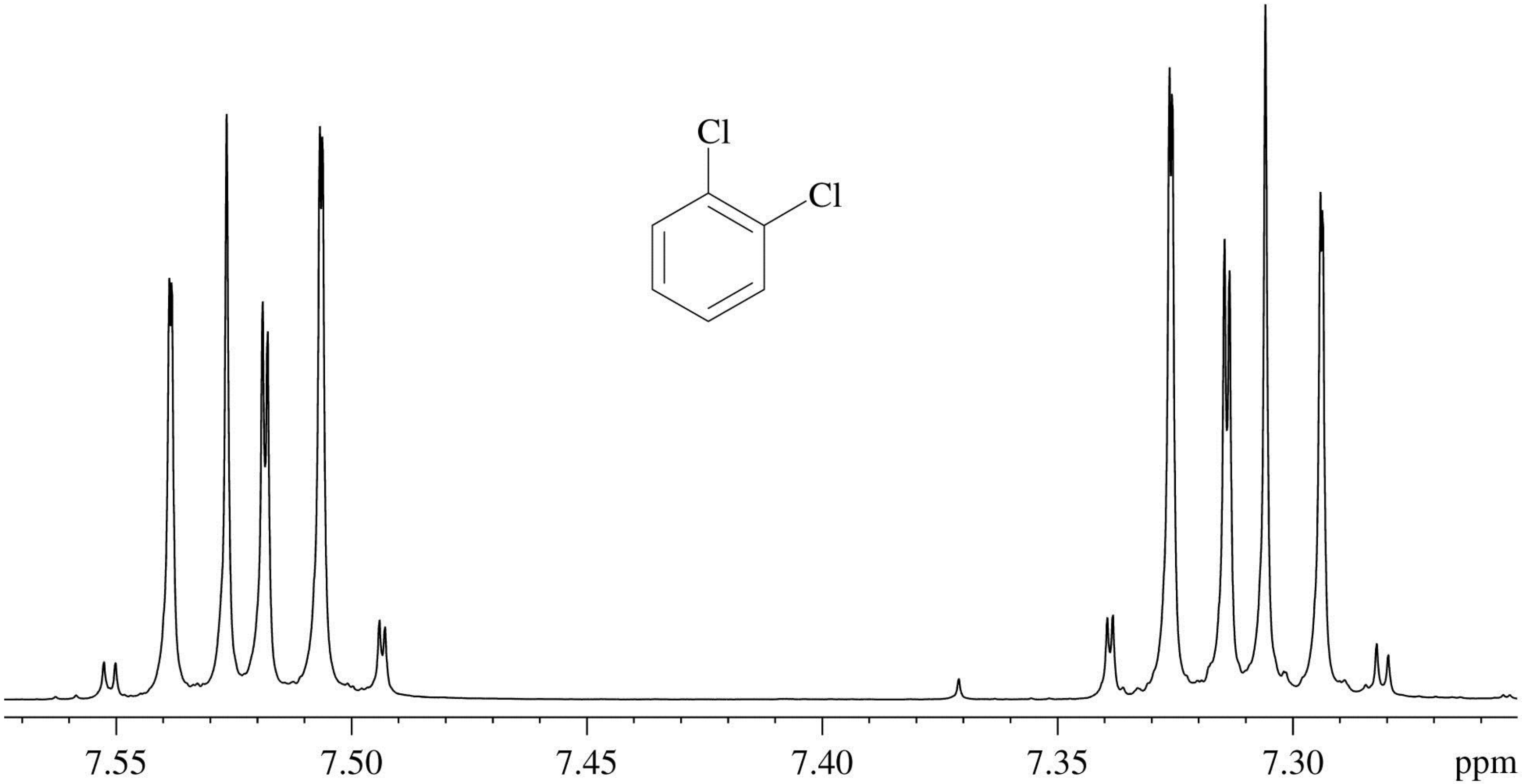
$J(H_A\text{-}H_B) = J(H_{A'}\text{-}H_{B'}) \approx$ 7-10 Hz

and $J(H_A\text{-}H_{B'}) = J(H_{A'}\text{-}H_B) \approx$ 0-1 Hz

$J(H_A\text{-}H_B) \neq J(H_{A'}\text{-}H_{B'})$

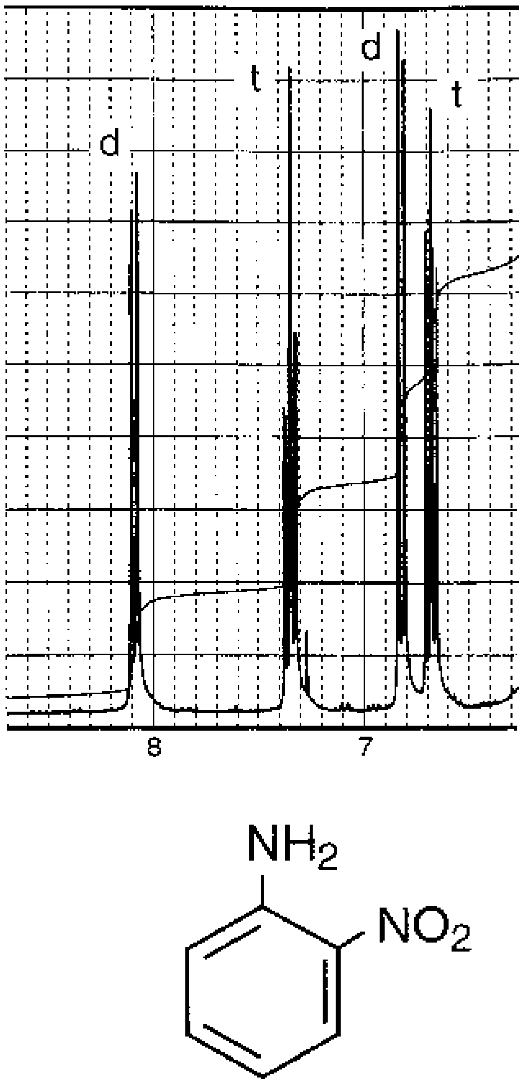
So, H_A (and $H_{A'}$) should be split by coupling to H_B ($J \approx$ 7-10 Hz) and to $H_{B'}$ ($J \approx$ 0-1 Hz). However, the difference in chemical shifts is small and while the peak for H_A might appear as AB system, it may be more complex

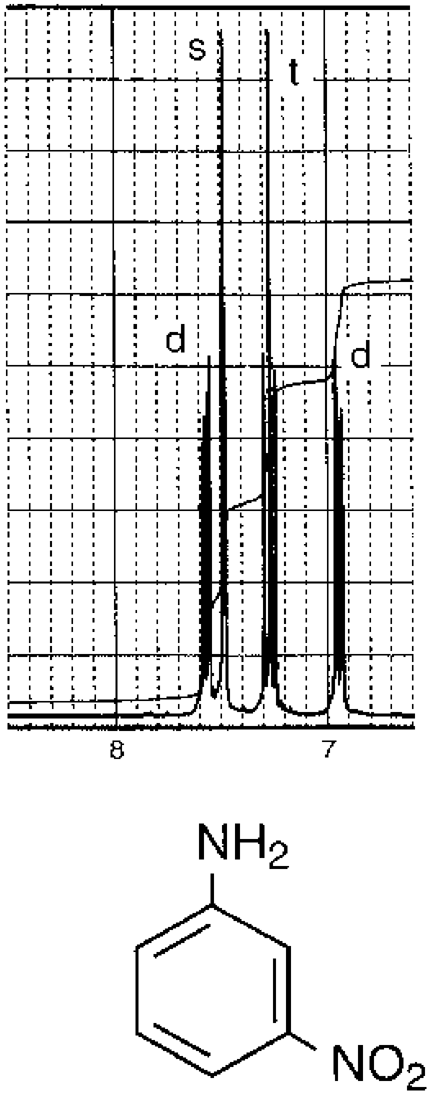
AA'XX' spin system of 1,2-dichlorobenzene

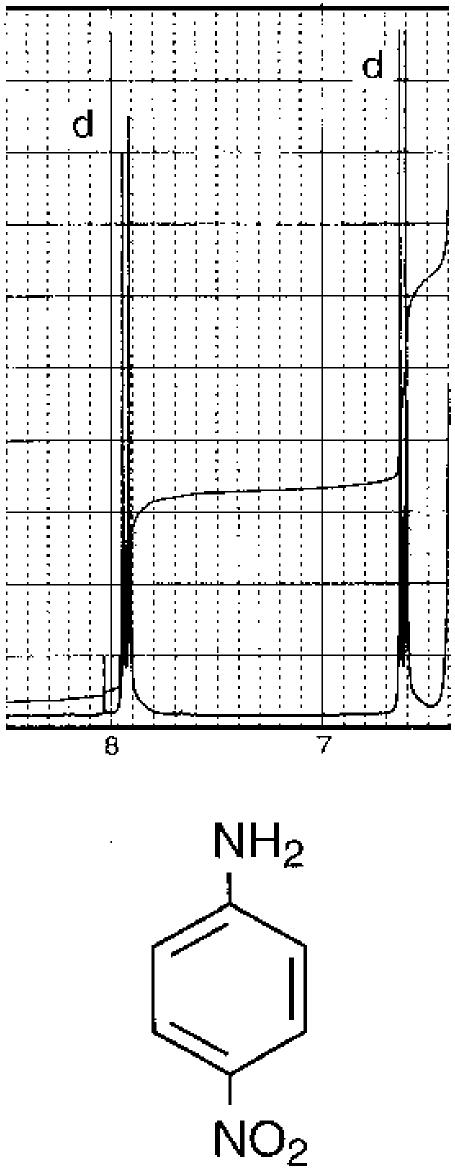


Determining substitution patterns – Which one is which?

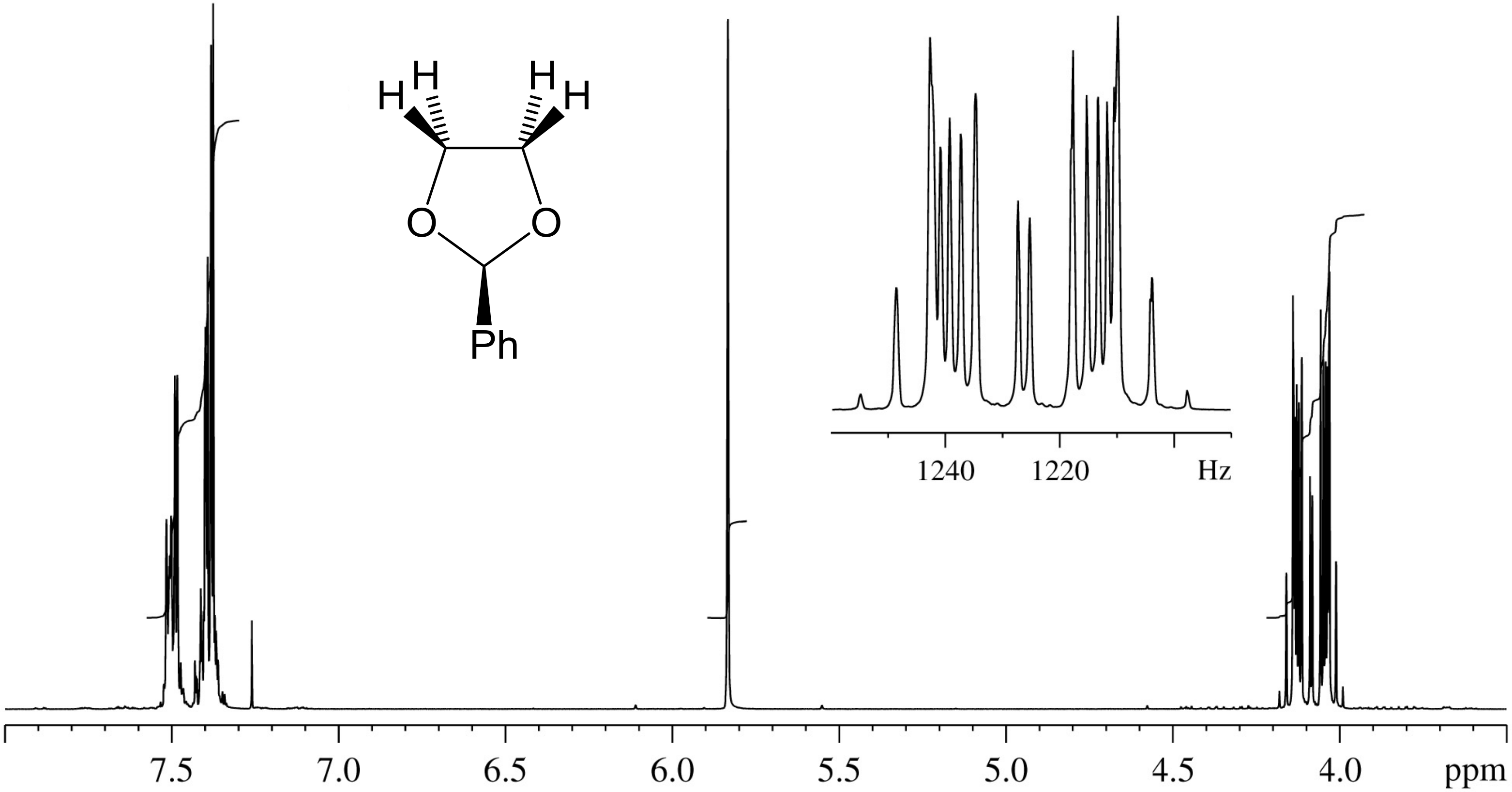
Pavia 5.13







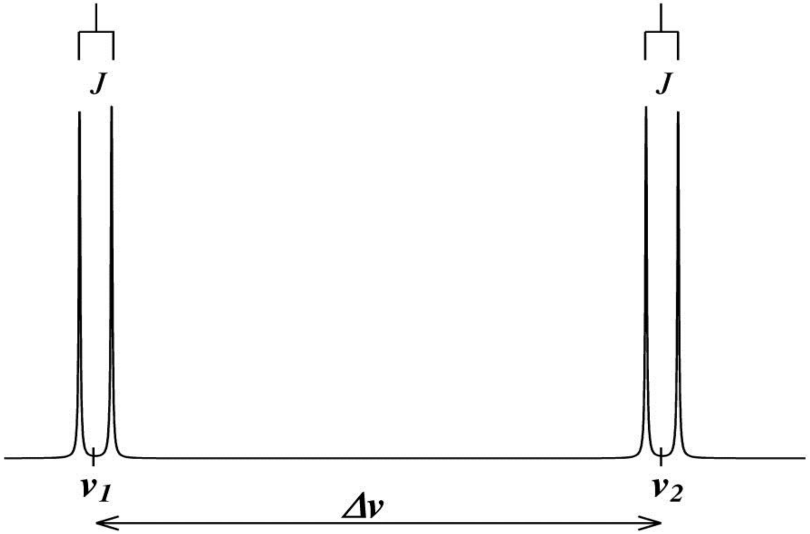
AA’BB’ spin system of a cyclic system



More second order effects: “Tenting” of multiplets

e.g. The effect of $\Delta\nu/J$ on the appearance of a pair of doublets

The two peaks in each doubletof an AX system with $\Delta\nu/J >> 10$ are the same height (Pascal’s triangle):

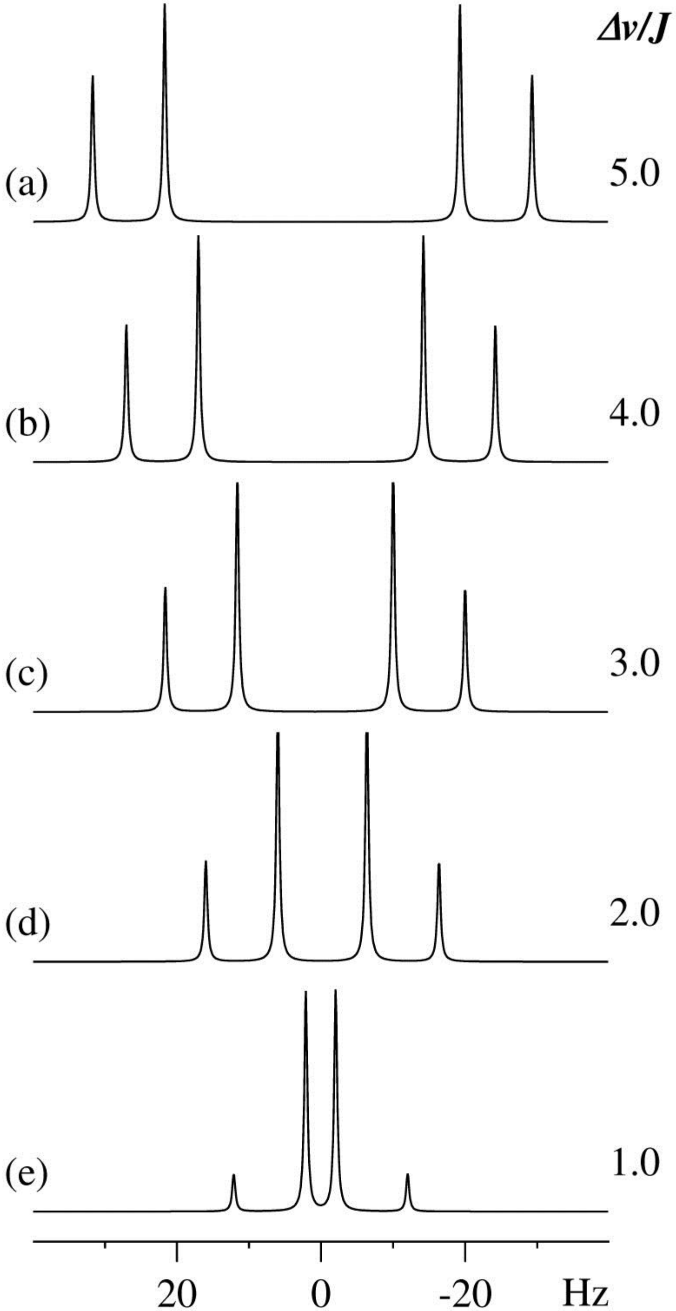


⇓ ⇓

δ_1 δ_2

but…

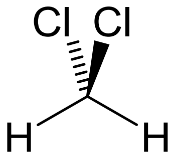
… as $\Delta\nu/J$ becomes < 8, the inside peaks increase in intensity relative to the outside peaks.



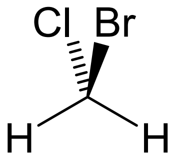
The effect of stereogenic centers

Pavia 5.14-19

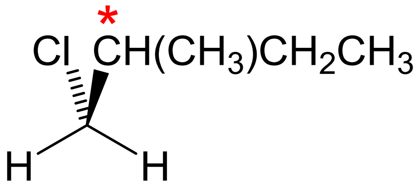
Homotopic Protons have the same electronic environment and the same chemical shift.



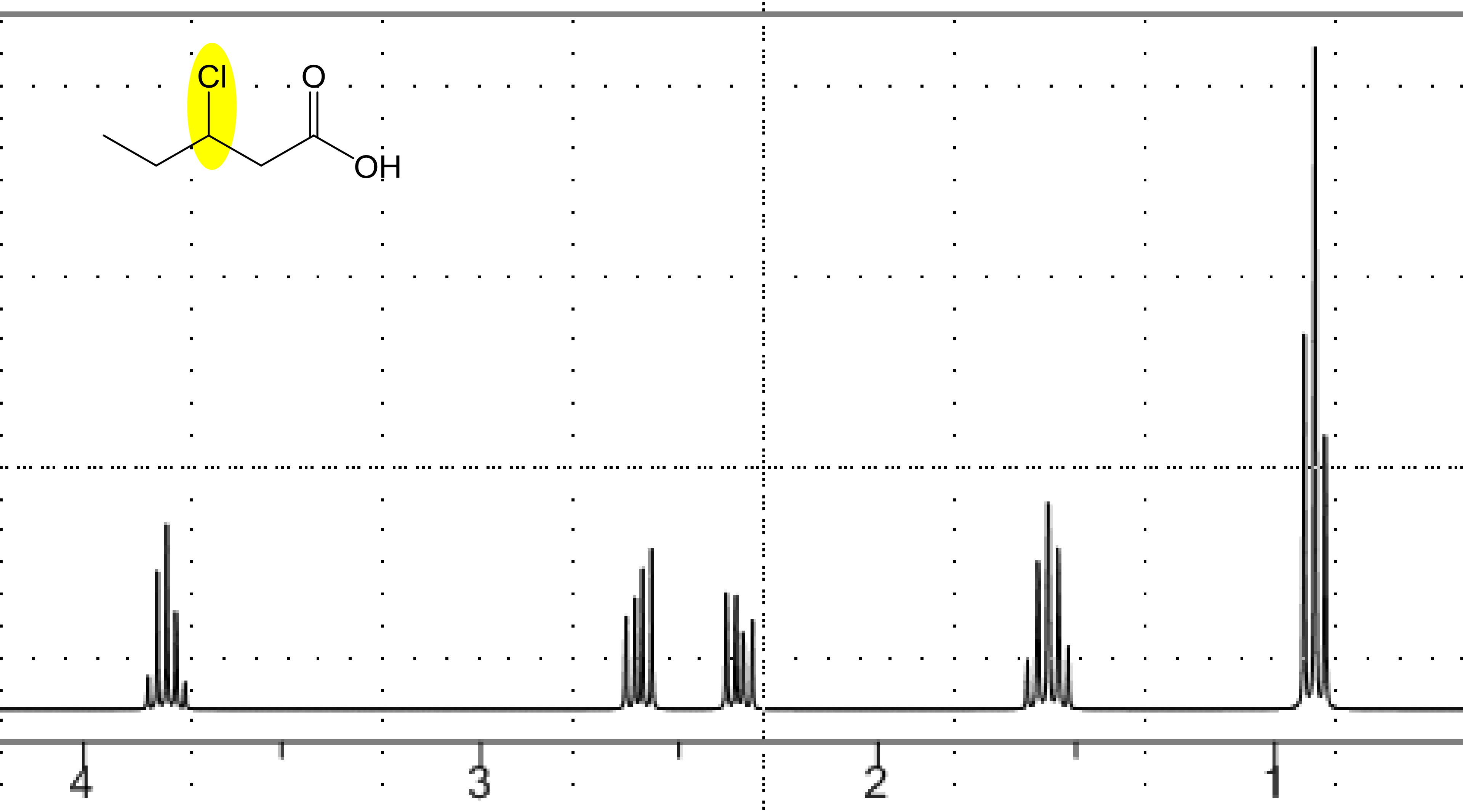
Enantiotopic protons are equivalent in an achiral environment (e.g., in a simple solvent such as $CDCl_3$), but are non-equivalent in a chiral environment (such as when dissolved in an optically active solvent or in the presence of a "chiral shift reagent")

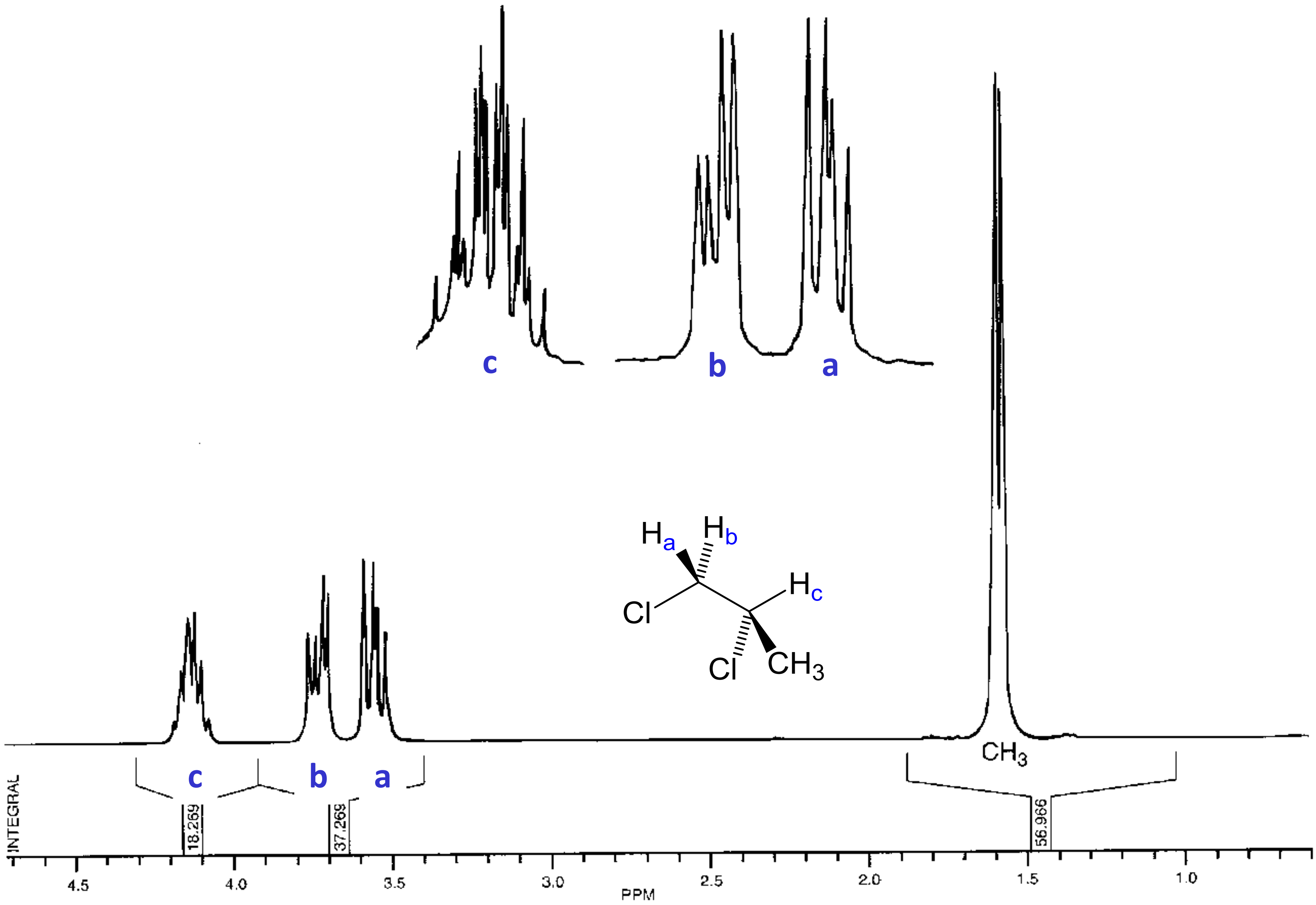


Diastereotopic protons are non-equivalent protons that can not be exchanged by any symmetry element: They will appear as separate signals (i.e., with different chemical shifts), and they will couple with one another.

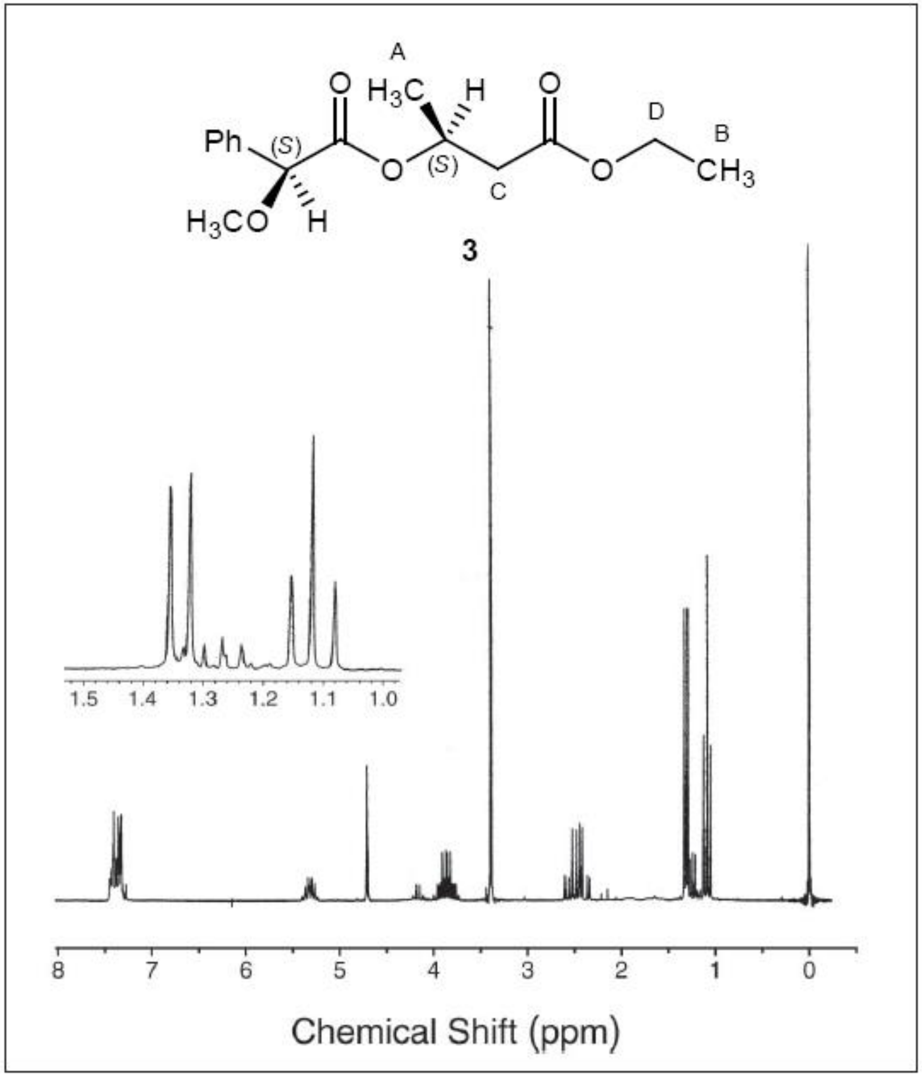


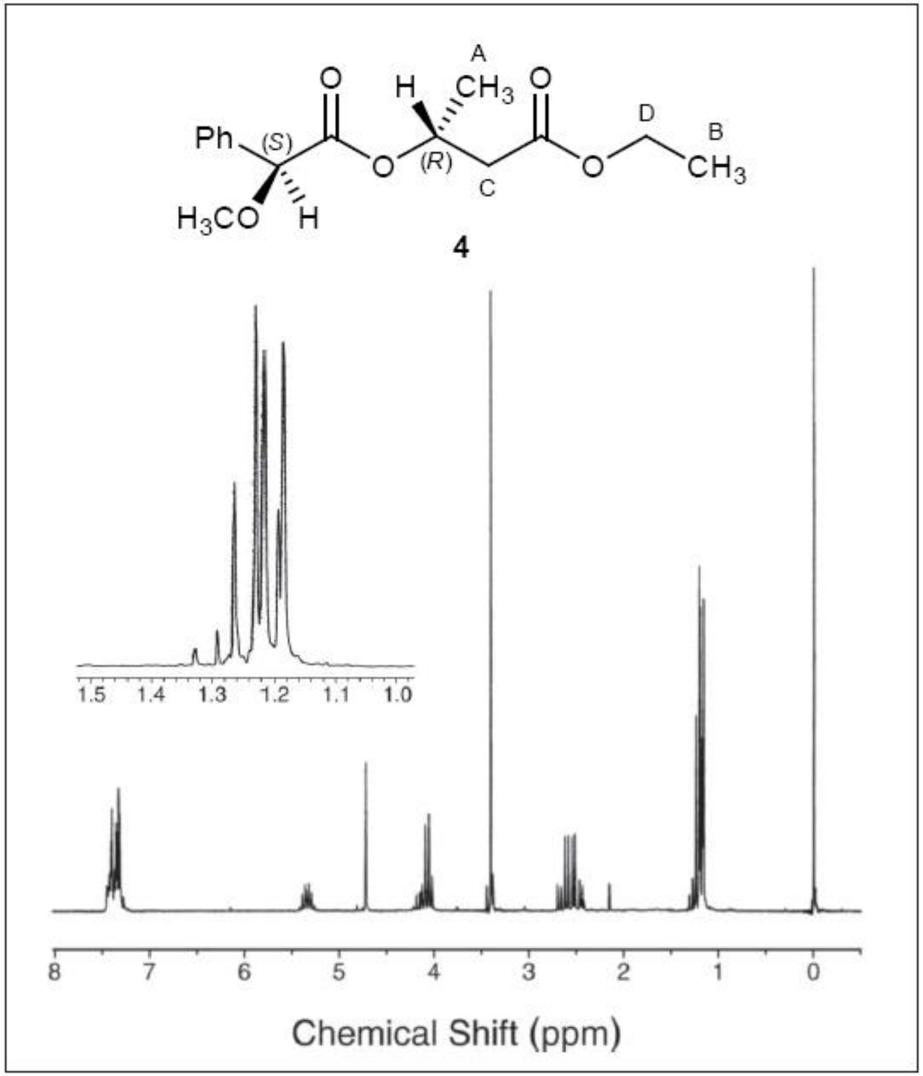
Diastereotopic protons




c
b
a
H a
H b
H c
Cl
Cl
CH3
c
b
a
CH3
INTEGRAL
18.269
37.269
56.966
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
PPM

Diastereomeric esters

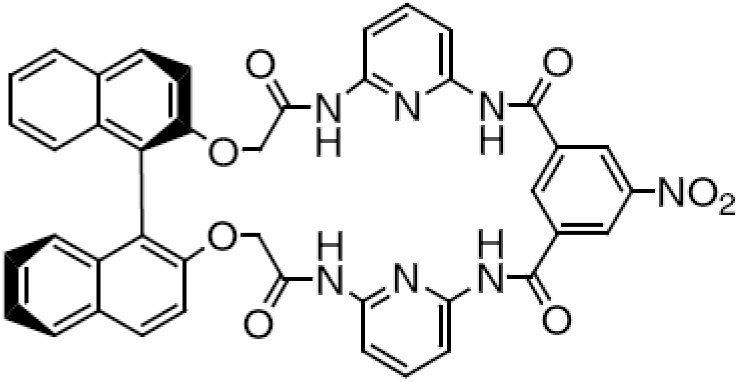

3


4

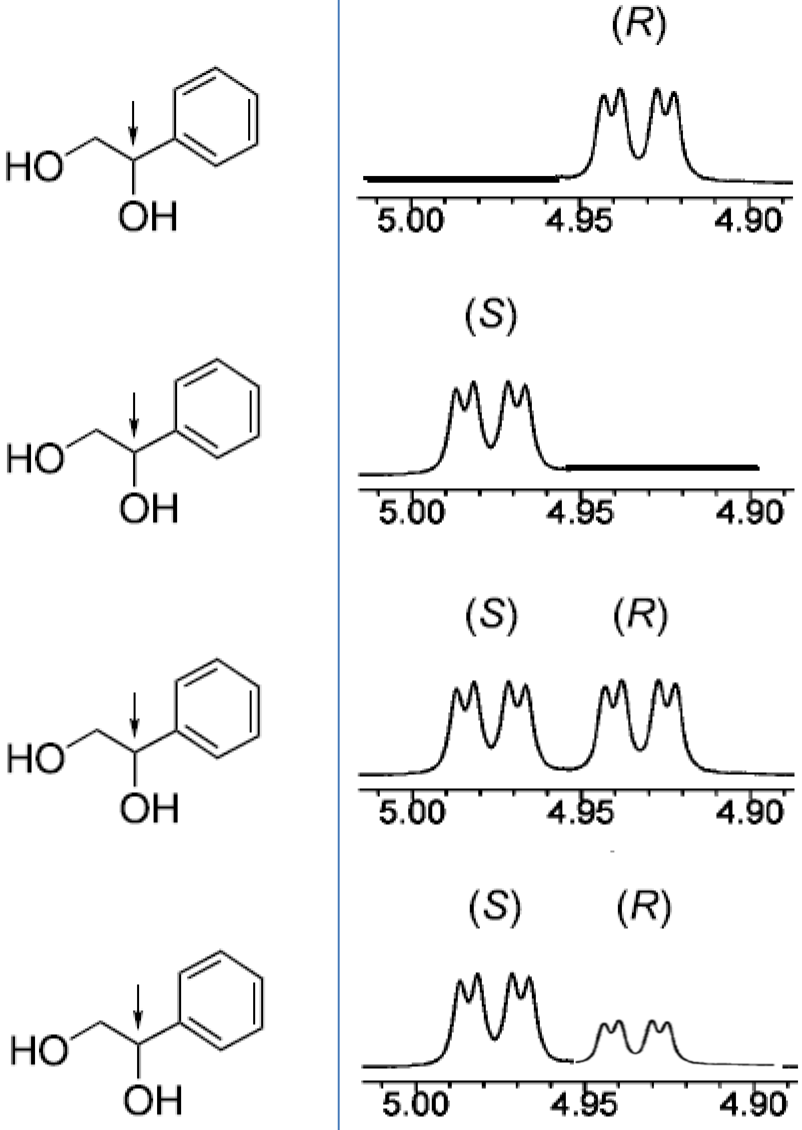
Journal of Chemical Education **2005**, *85(7)* , 1049.

Diastereomeric complexes formed between two enantiomers

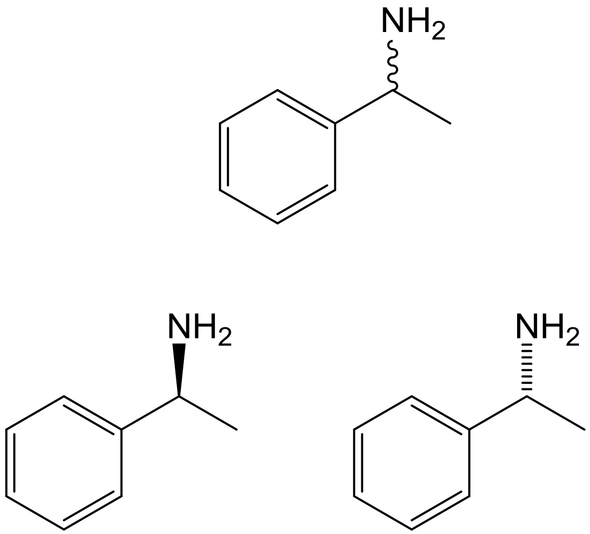
TCI Product Literature

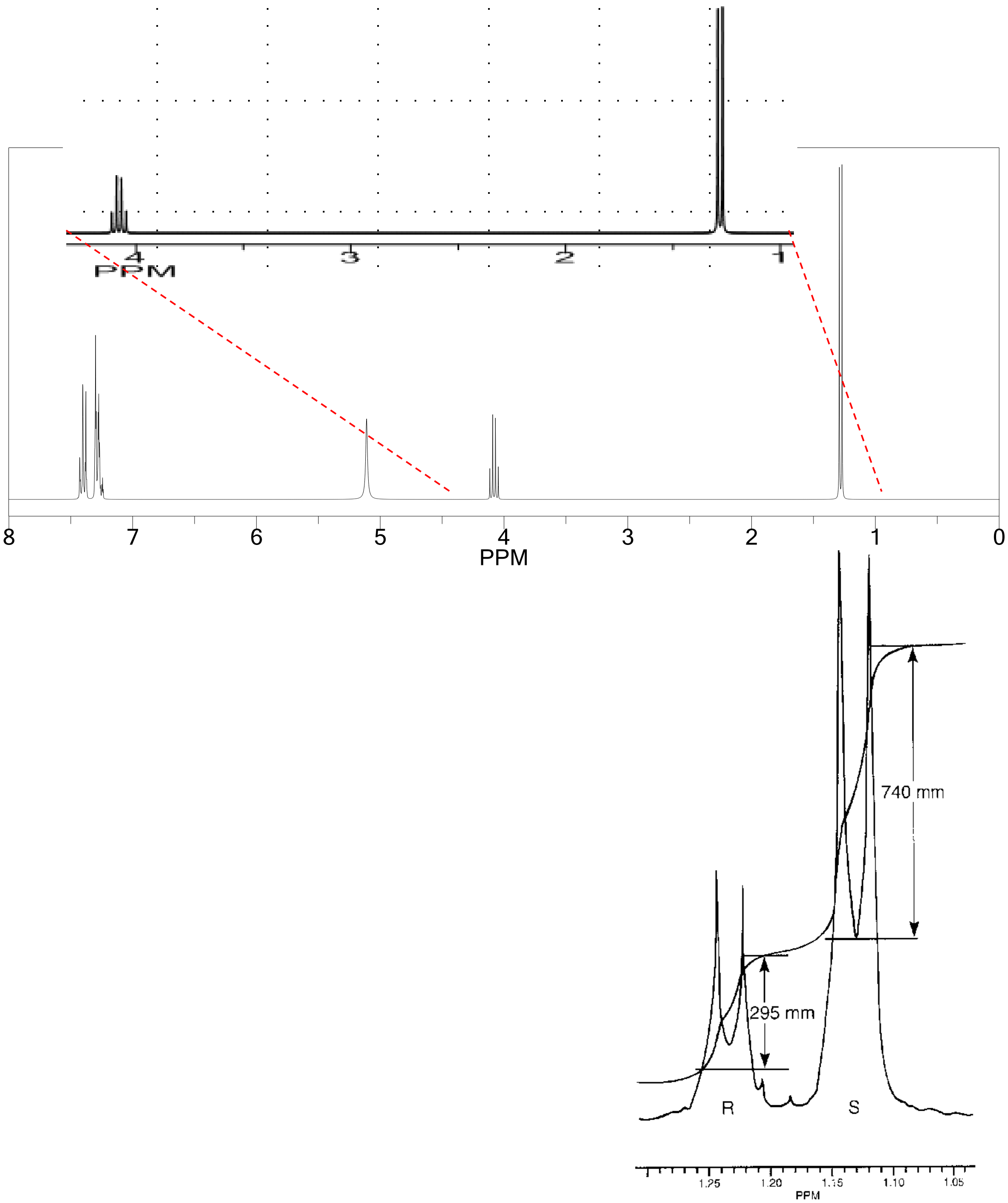


C2184 Chirabite-AR **1**



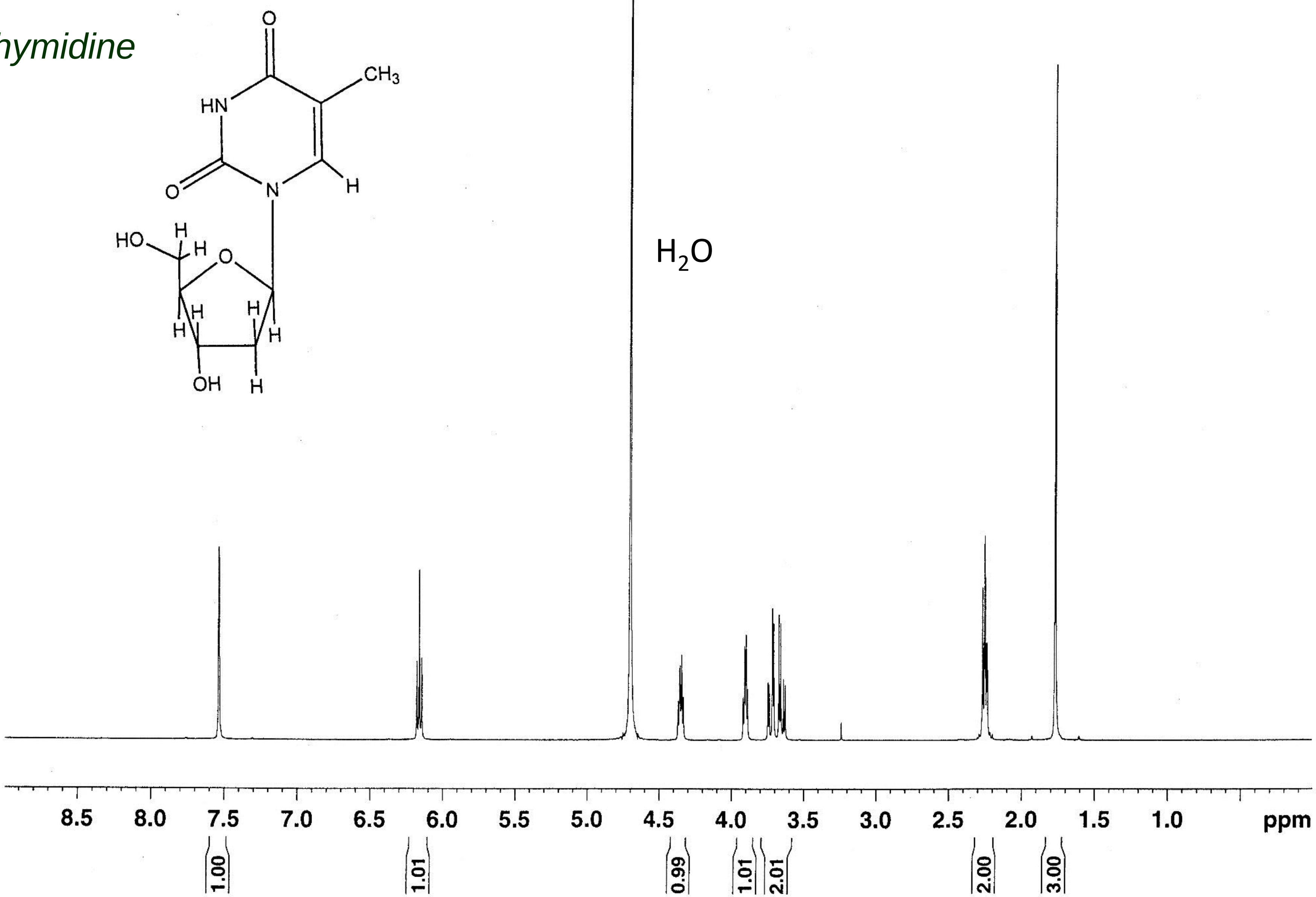
Chiral Eu(III) complexes



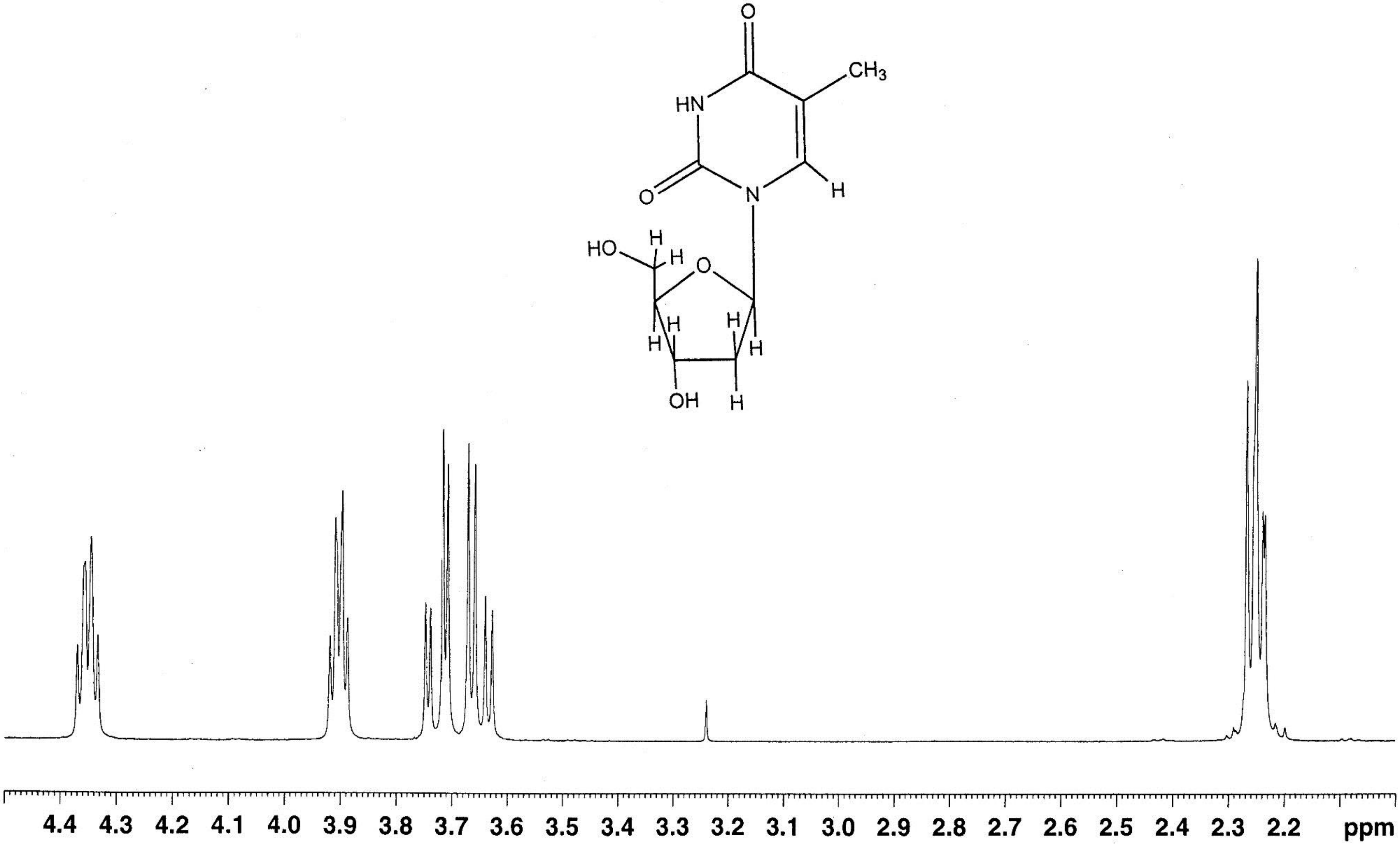


MORE COMPLEX STRUCTURES
CHALLENGES AND NEW TOOLS

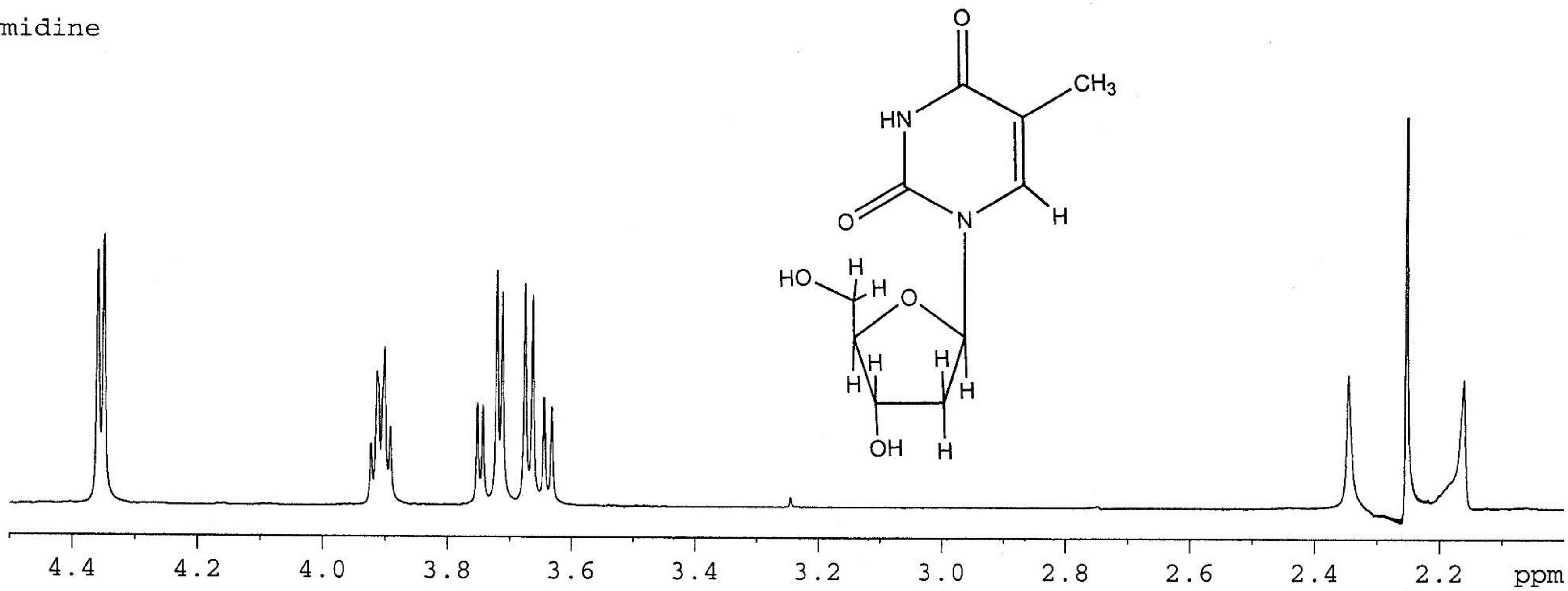
Thymidine

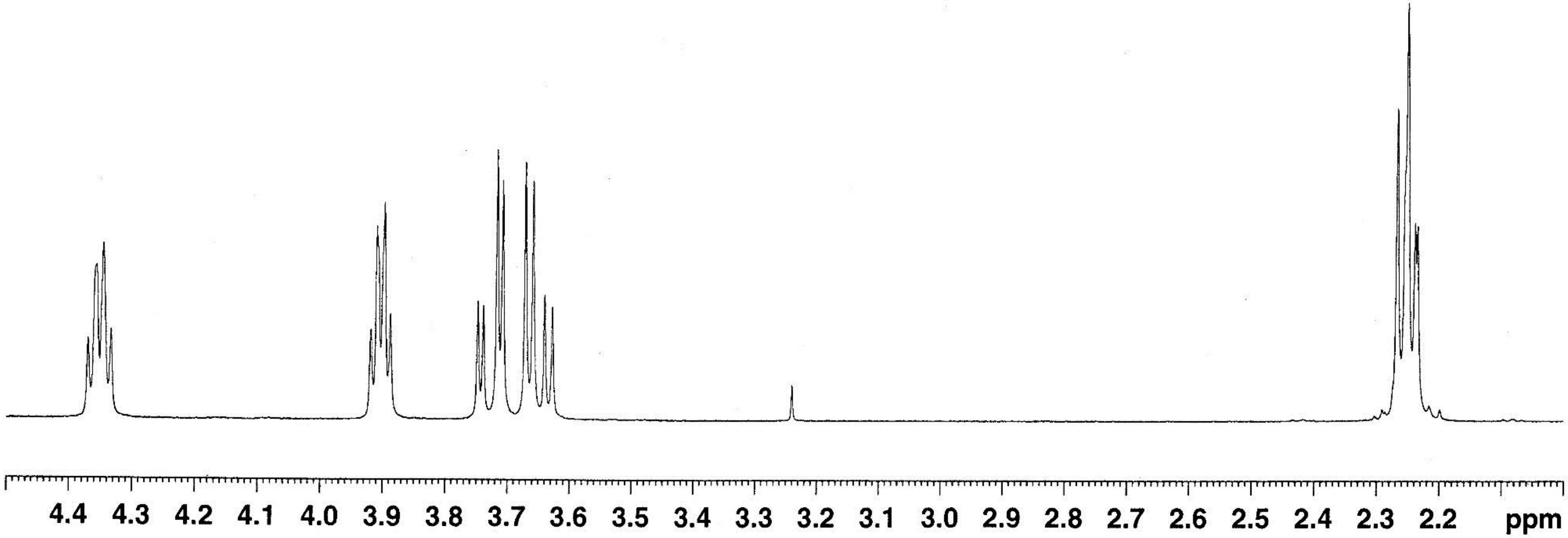


thymidine


O
CH3
HN
O
N
H
HO
H
H
O
H
H
H
H
OH
H
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
ppm

thymidine


O
CH3
HN
O
N
H
HO
H
H
O
H
H
H
H
OH
H
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
ppm


4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
ppm

Nuclear Overhauser Effect

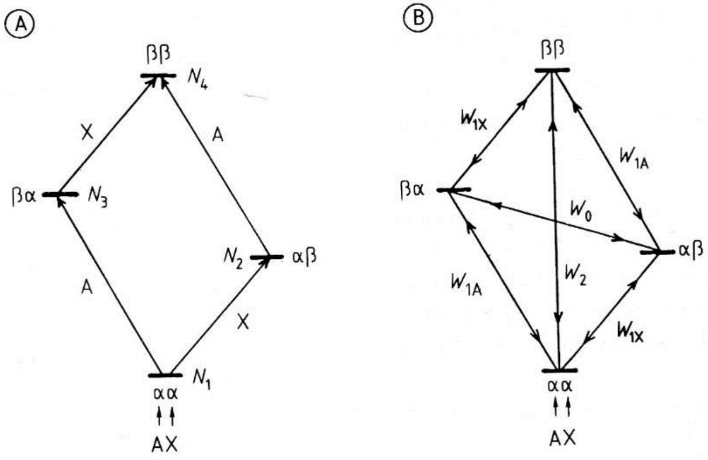


Figure 10-1. Energy level schemes for a two-spin AX system with $J_{AX} = 0$. A: The frequencies of the two A transitions are equal, as are those of the two X transitions. N_1 to N_4 are the populations of the energy levels. B: The probabilities W for the six allowed relaxation transitions are shown. Those with a subscript 1 correspond to single quantum transitions, while W_0 corresponds to a zero quantum transition and W_2 to a double quantum transition.

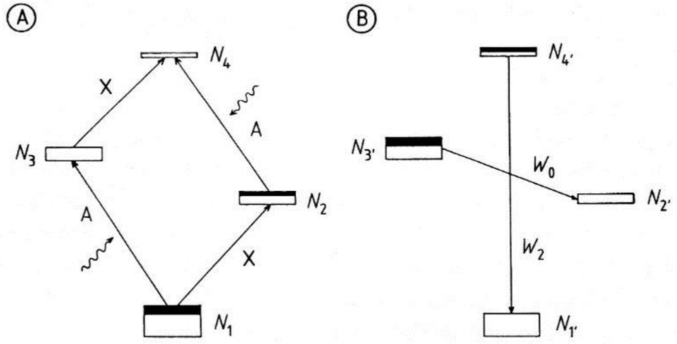


Figure 10-2. Changes occurring in the population ratios in an NOE experiment. The energy level scheme A shows the initial situation, and B shows the situation when the two A transitions of equal energy are saturated. The relative thicknesses of the slabs represent the populations N_1 to N_4 and $N_{1'}$ to $N_{4'}$. Of the transition probabilities for relaxation only W_2 and W_0, corresponding to double quantum and zero quantum transitions, are shown.

Basic One and Two Dimensional NMR spectroscopy, 5th Ed., Friebolin, Wiley-VCH

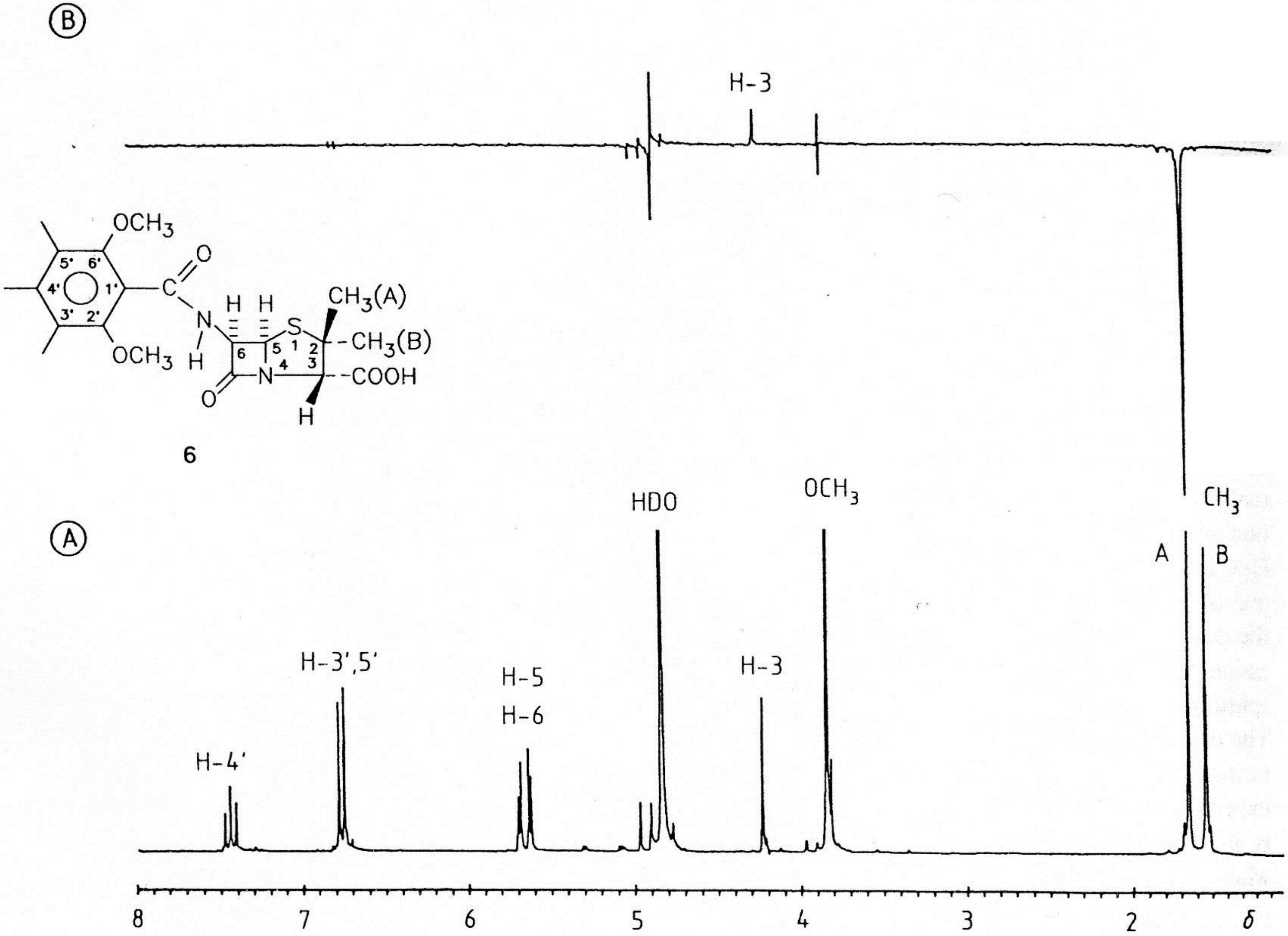


Figure 10-5.
A: 250 MHz ^{1}H NMR spectrum of methicillin (**6**) in 0.2 M sodium acetate buffer (D_2O; pD 7.0), with assignments. On saturating the methyl signal ($\delta \approx 1.7$ ppm) the NOE difference spectrum shows an increase in the intensity of the H-3 signal ($\delta \approx 4.25$ ppm). The negative signal in the NOE difference spectrum corresponds to the irradiating frequency. Strong signals, such as the residual solvent signals (HDO) or those of the methyl groups, are often found to be not exactly cancelled to zero in the difference spectrum.

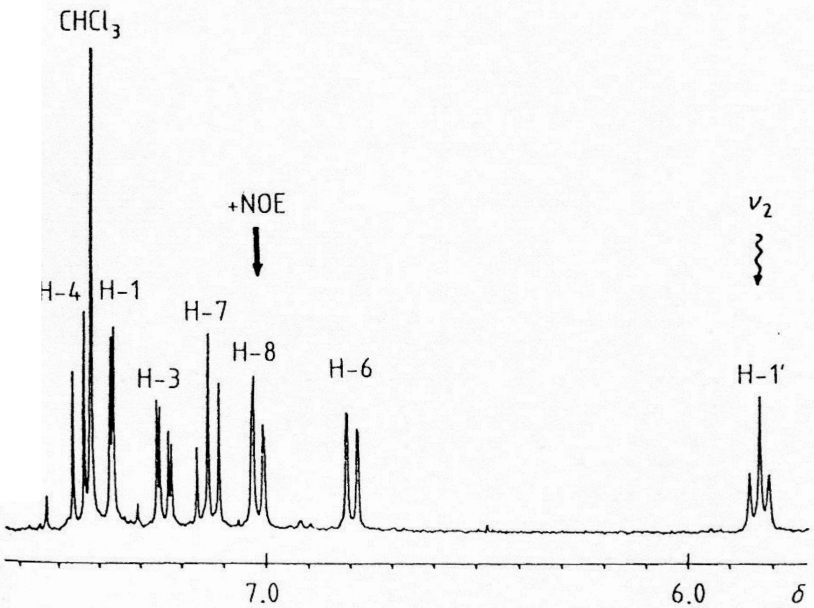
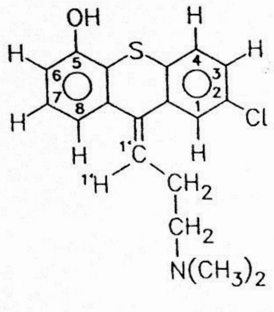
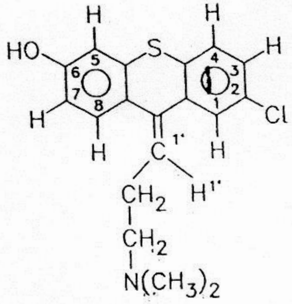


Figure 10-4.
Portion of the 300 MHz ^1H NMR spectrum of chloroprothixene (**4**) in $CDCl_3$ with assignments. When the H-1′ resonances (δ = 5.84 ppm) are saturated the intensity of the doublet of doublets at δ = 7.02 ppm is increased due to the NOE.



4



5

OTHER PEAKS

Sample

Typically 1-5 mg sample in 0.75-1.00 mL solvent in a 5 mm diameter NMR tube.

Too dilute – noisy spectra

Too concentrated – poor spectra

Viscous samples, and samples containing insoluble articles – broadened peaks

Signals from presence of the other compounds

Standards added to reference chemical shift

Tetramethylsilane: $(C\mathbf{H}_3)_4Si$

Sodium 3-(trimethylsilyl)-1-propanesulfonate $(C\mathbf{H}_3)_3SiCH_2CH_2CO_2^{-}\,Na^{+}$

Residual ^{1}H impurities of deuterated solvents

Chemical shift of residual ^{1}H in deuterated solvents

$CDCl_3$	δ 7.26 (1)
benzene-d_6	7.15 (br)
acetone-d_6	2.04 (5)
DMSO-d_6	2.74 (5)
DMF-d_7, THF-d_8, Nitrobenzene-d_5	

Water (H_2O) in the sample/solvent gives a peak

Chemical shift of residual H_2O in deuterated solvents

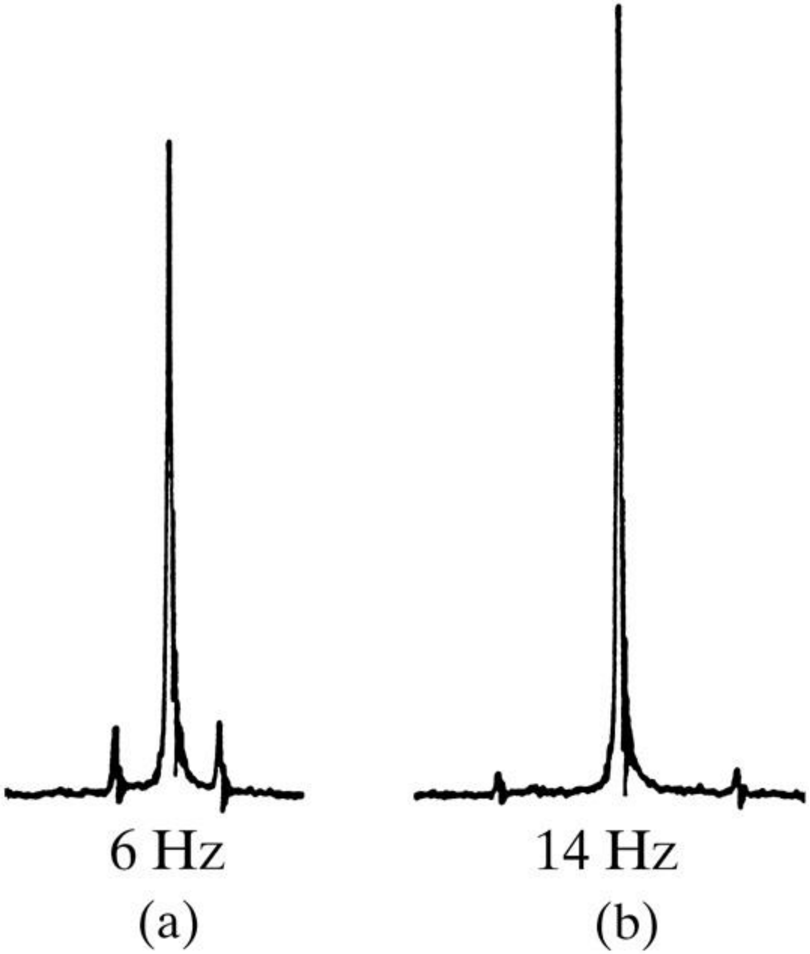
$CDCl_3$	δ 1.56
benzene-d_6	0.40
acetone-d_6	2.84
D_2O	4.79

Other impurities

Peaks (in $CDCl_3$)

Acetone	δ 2.17
DMF	8.02, 2.96. 2.88
DMSO	2.62
Paraffin joint grease	0.86 (m), 1.26 (br. s)
Silicone grease	0.70
THF	3.76 (m), 1.85 (m)

Spinning side bands



Georgia Tech NMR Center

Bruker Avance IIID - 800 MHz 1H, 201 MHz, 13C (18.8 Tesla magnet)
multidimensional spectral acquisition of complex samples; ^{1}H NMR when improved sensitivity or spectral dispersion are needed.

Bruker Avance III Solutions and Solid- 700 MHz 1H, 176 MHz, 13C (11.7 Tesla magnet**)**
multidimensional spectral acquisition of complex samples; ^{1}H NMR when improved sensitivity or spectral dispersion are needed.

Bruker Avance IIIHD Solutions and solids - 500 MHz 1H, 125 MHz, 13C (11.7 Tesla magnet)
multidimensional spectral acquisition of complex samples; ^{1}H NMR when improved sensitivity or spectral dispersion are needed.

Bruker Avance III HD - 500 MHz 1H, 125 MHz, 13C (11.7 Tesla magnet)
multidimensional spectral acquisition of complex samples; 1H NMR when improved sensitivity or spectral dispersion are needed.

Bruker Avance III Solids - 400 MHz ^{1}H, 100 MHz ^{13}C (9.4 Tesla)
Primary use: high-resolution NMR of solids including quadrupolar nuclei; NMR imaging (i.e., MRI), especially of fluids in solid substrates.

Bruker DSX 300 Solids - 300 MHz ^{1}H, 75 MHz ^{13}C (7 Tesla)
Primary use: solid-state NMR; high-resolution and wideline NMR of molecular structure, dynamics and orientation.

Bruker Avance III - 400 MHz ^{1}H, 100 MHz ^{13}C (9.4 Tesla)
Primary use: high-resolution multinuclear NMR of liquids; ^{1}H and ^{109}Ag to ^{31}P NMR .

Varian Mercury Vx 300 (7 Tesla)
Primary use: routine ^{1}H and ^{13}C liquids acquisitions.

Varian Mercury Vx 400 (9.4 Tesla) *[IBB 3325A]*
Primary use: routine ^{1}H, ^{13}C, ^{19}F and ^{31}P liquids acquisitions.

http://web.chemistry.gatech.edu/~gelbaum/nmr/nmr.html

Reporting ^1H NMR Spectra in Papers and Progress Reports

Ⓐ Ⓑ Ⓒ Ⓓ Ⓔ Ⓕ

^1H NMR ($CDCl_3$, 400 MHz): δ12.1-12.7 (br. s, 1H, -COOH), 7.29 (d, *J* = 9 Hz, 2H, C-2,6), δ6.98 (d, *J* = 9 Hz, 2H, C-3,5), 2.7 (s, 3H, $-CH_3$).

Ⓐ Solvent: e.g., $CDCl_3$, C_6D_6, acetone-d_6, THF-d_8, CD_3CN, 1,4-dichlorobenzene-d_4, CD_2Cl_2. Frequency used in the experiment (and temperature if not r.t. or 25 °C)

Ⓑ List *all* peaks, providing *a single value of* δ to any multiplet that you define – provide δ to two decimal places. Only give a *range* of δ if a peak is being defined as an ill-defined "m" multiplet (in which case, it might be appropriate to report to nearest one tenth of a ppm.

Ⓒ Describe the multiplicity: s, d, t, q, p, sextet, septet, dd, dt, ddd, etc. If describing a multiplet of multiplets it is customary to list the one with the larger coupling constant first. Only describe a peak as an ill-defined multiplet (m) if you really cannot determine the multiplicity. This is most common when there are overlapping peaks. O-H peaks might be described as broad singlets (br. s). Specify the origin of the couplings if it is not obvious (*e.g.*, for long range coupling).

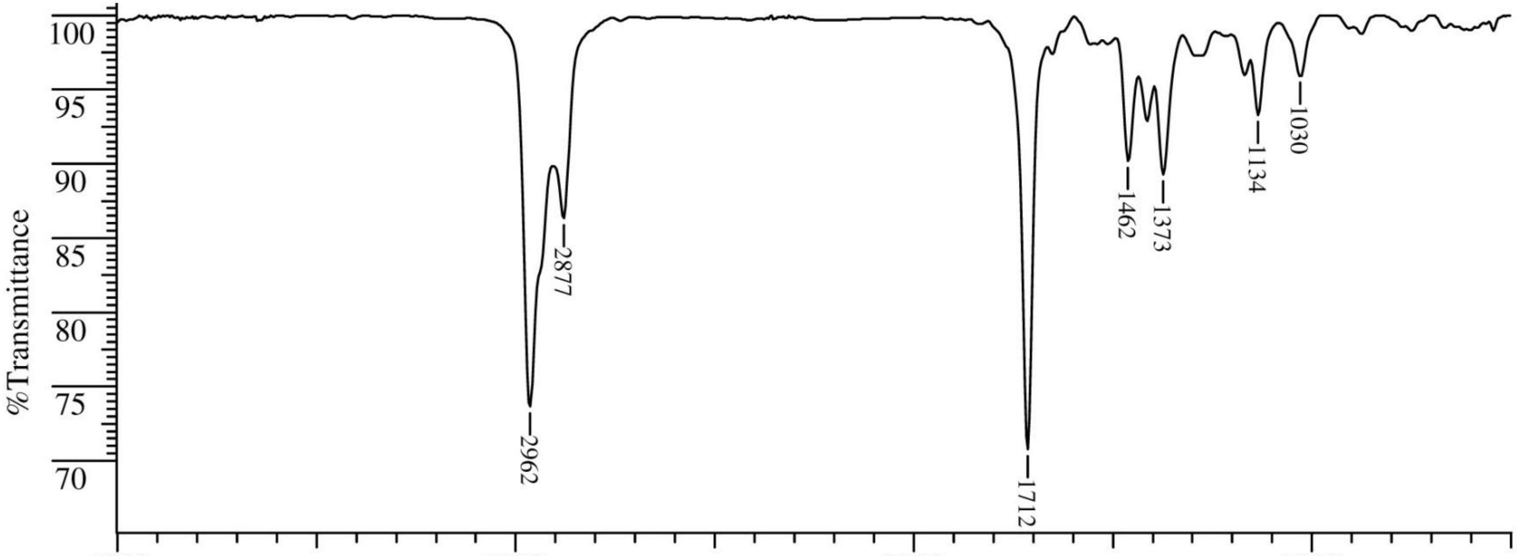
Ⓓ Give the values of coupling constants in the multiplet (unless it is a s or m). Give values to nearest one Hz, unless it is <1 Hz, or there is particular significance to a more accurate number. Remember, you need to provide a coupling constant for *every coupling within the multiplet*, *e.g.*, a ddt has three coupling constants.

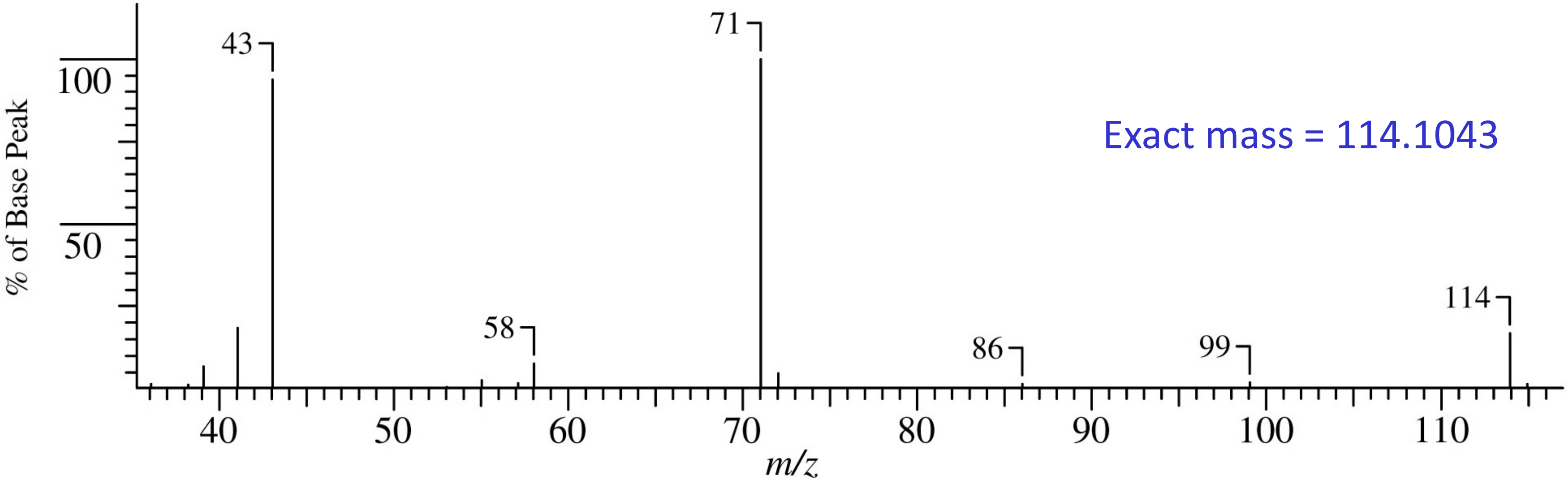
Ⓔ Indicate how many hydrogen atoms to which the peak corresponds. Make sure that the total number of hydrogens is correct.

Ⓕ Provide a succinct, but accurate, assignment of a peak to a particular type of hydrogen in the molecule. This can be difficult, and might not always be possible.

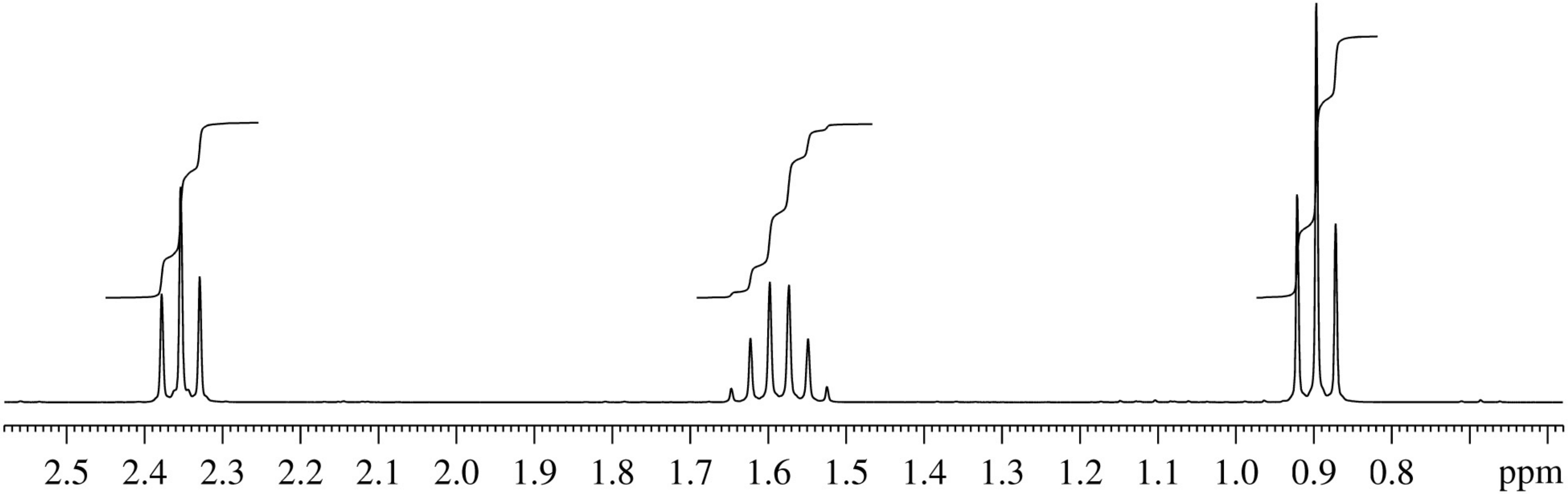
Determine the *structures* of the compounds for which the spectra are provided on the following slides. You considered the IR spectra alone, and the IR and MS together, in previous sections. Now, with NMR data, you should be able to identify a single compound.

Compound A

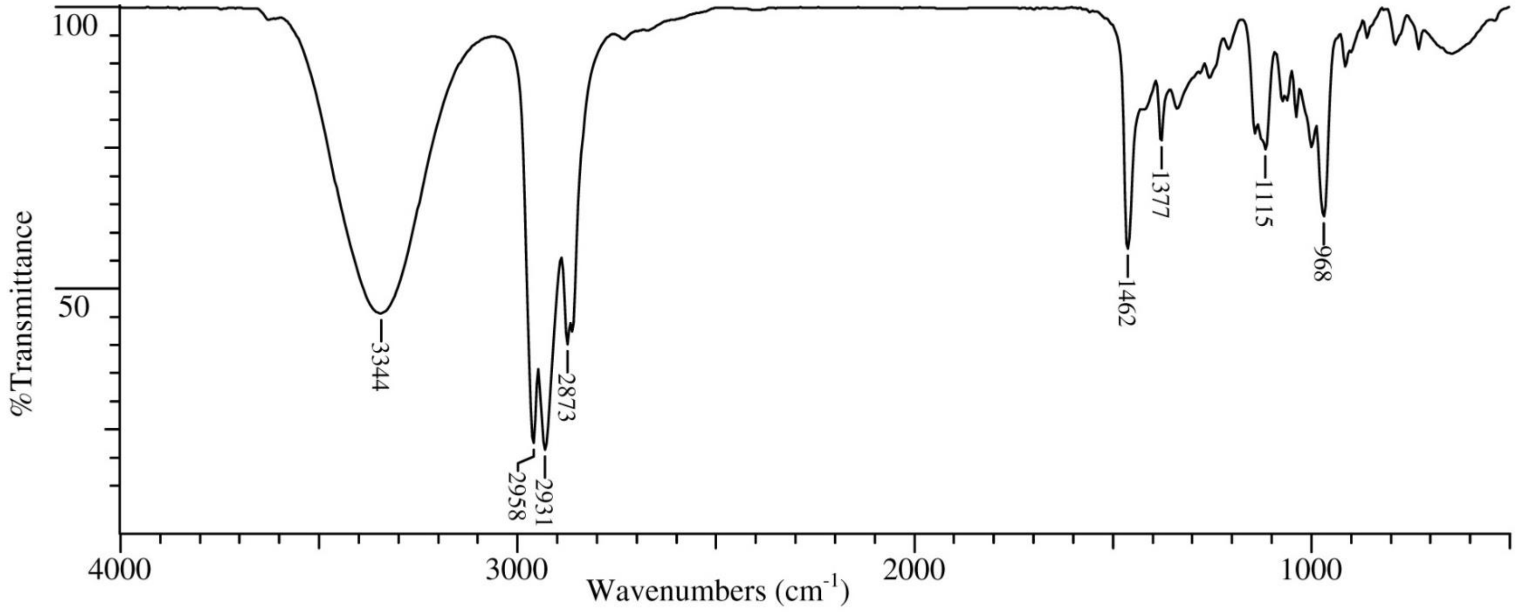


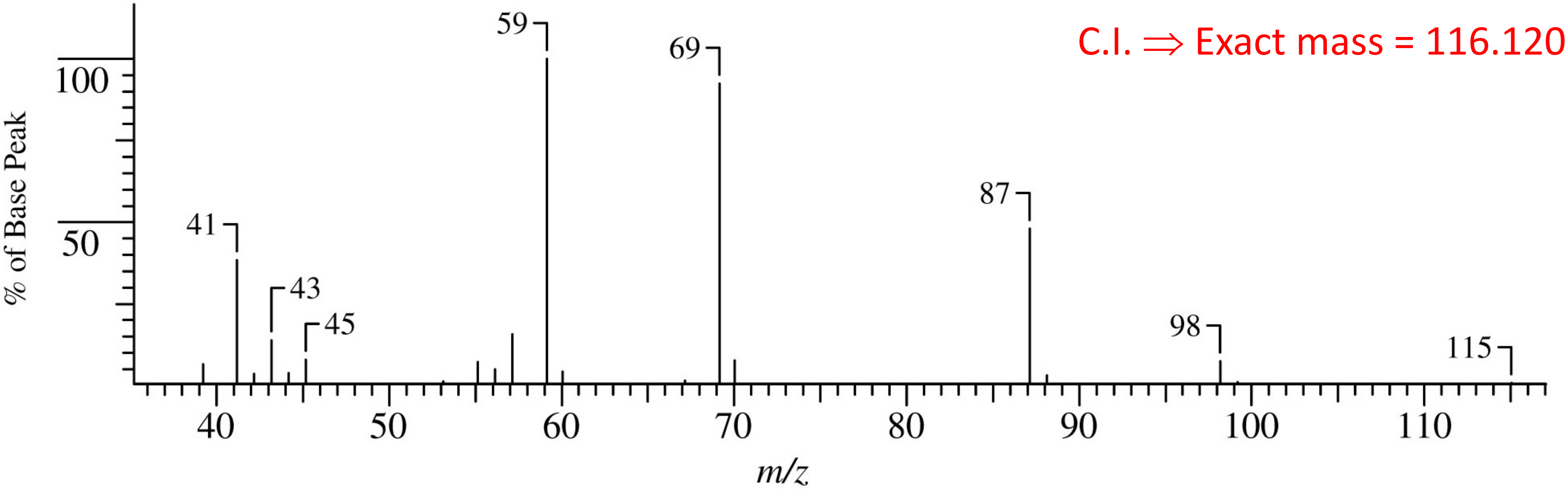


Exact mass = 114.1043

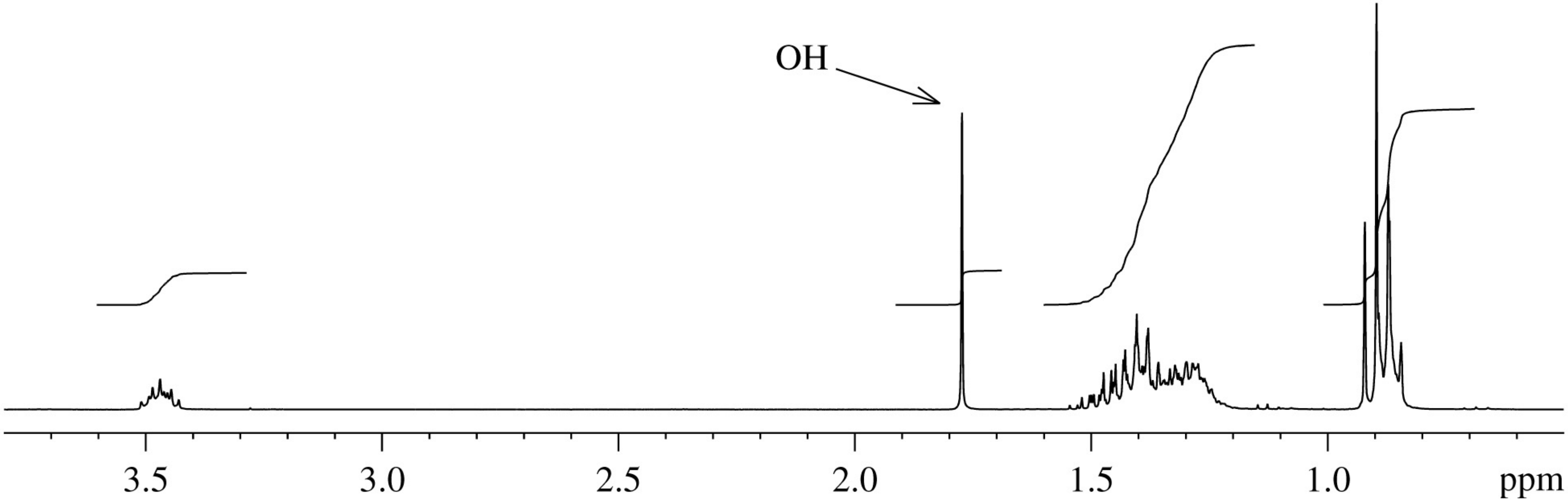

2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
ppm

Compound B



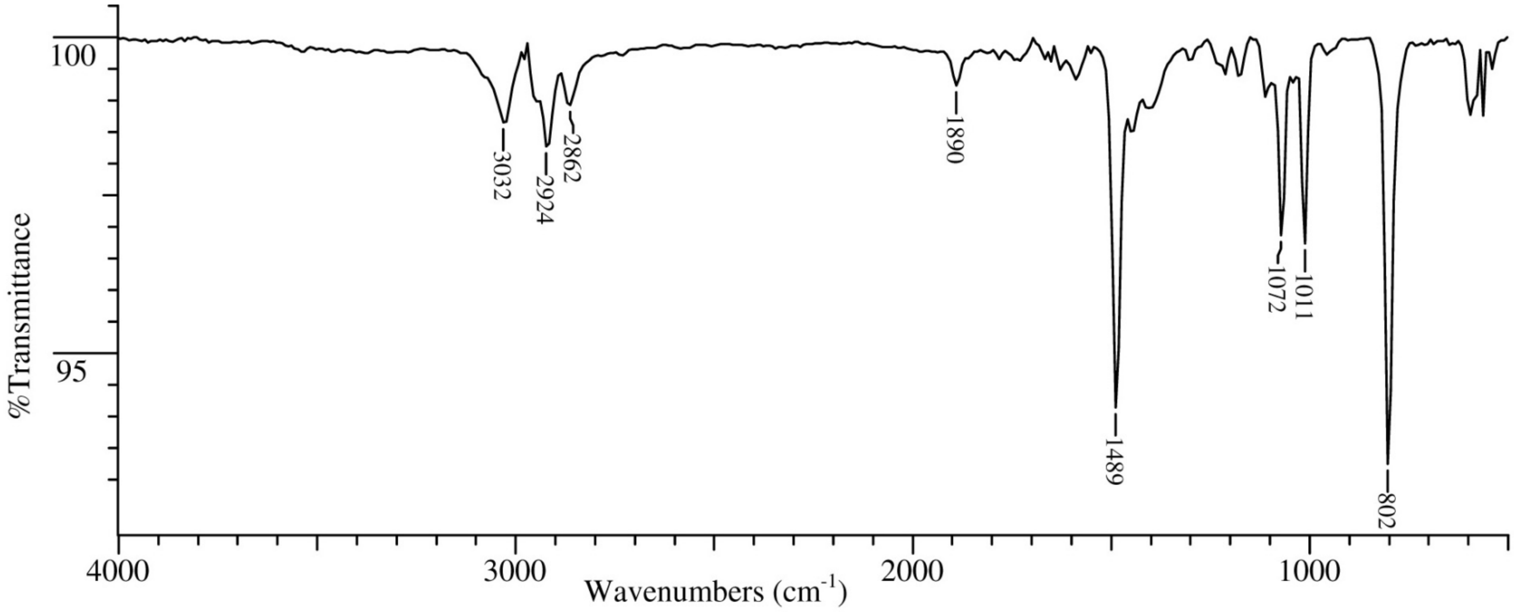


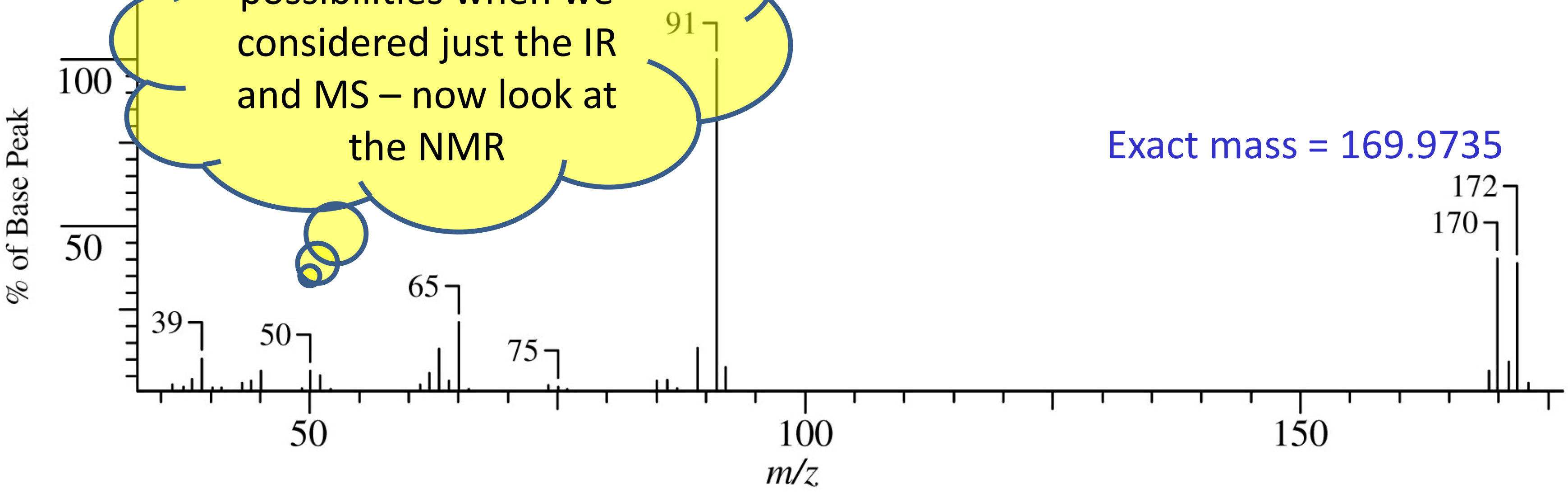
C.I. ⇒ Exact mass = 116.1203



Mass spec probably lets you identify the exact isomer

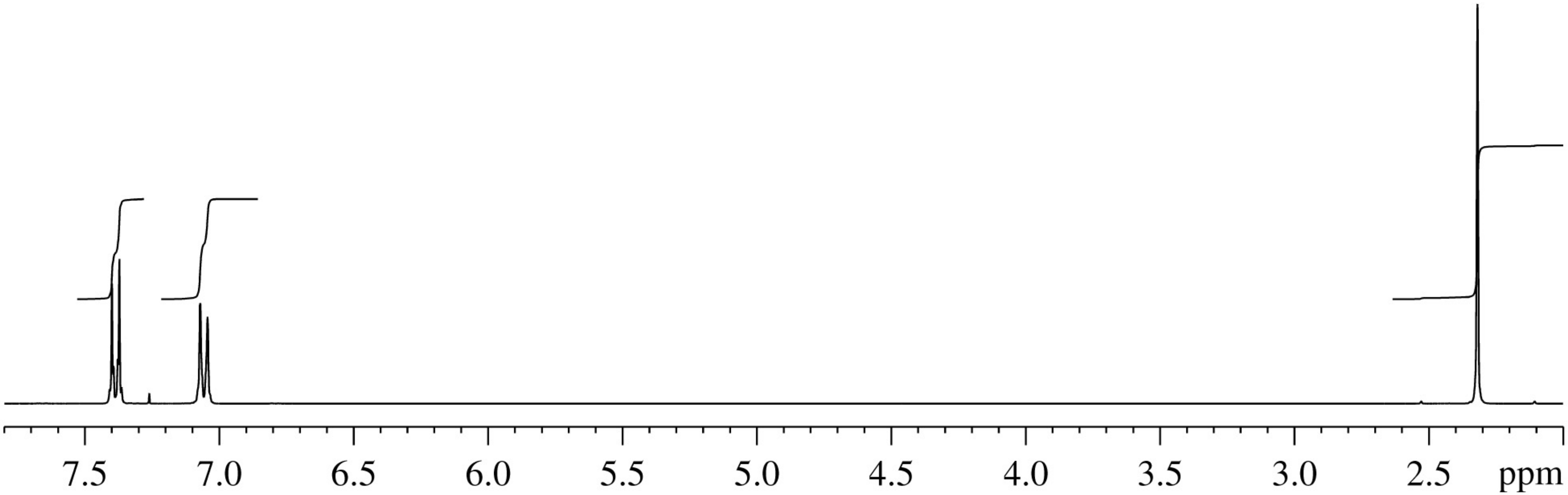
Compound C



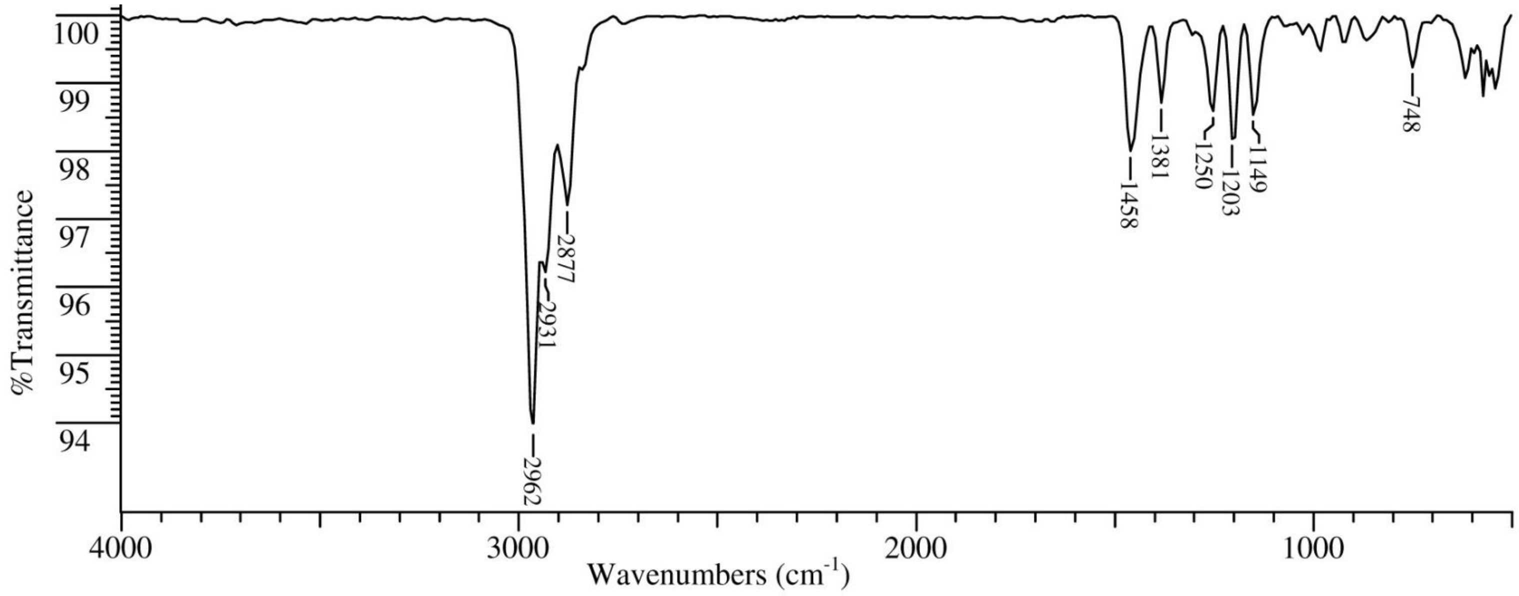


There were probably 4 possibilities when we considered just the IR and MS – now look at the NMR

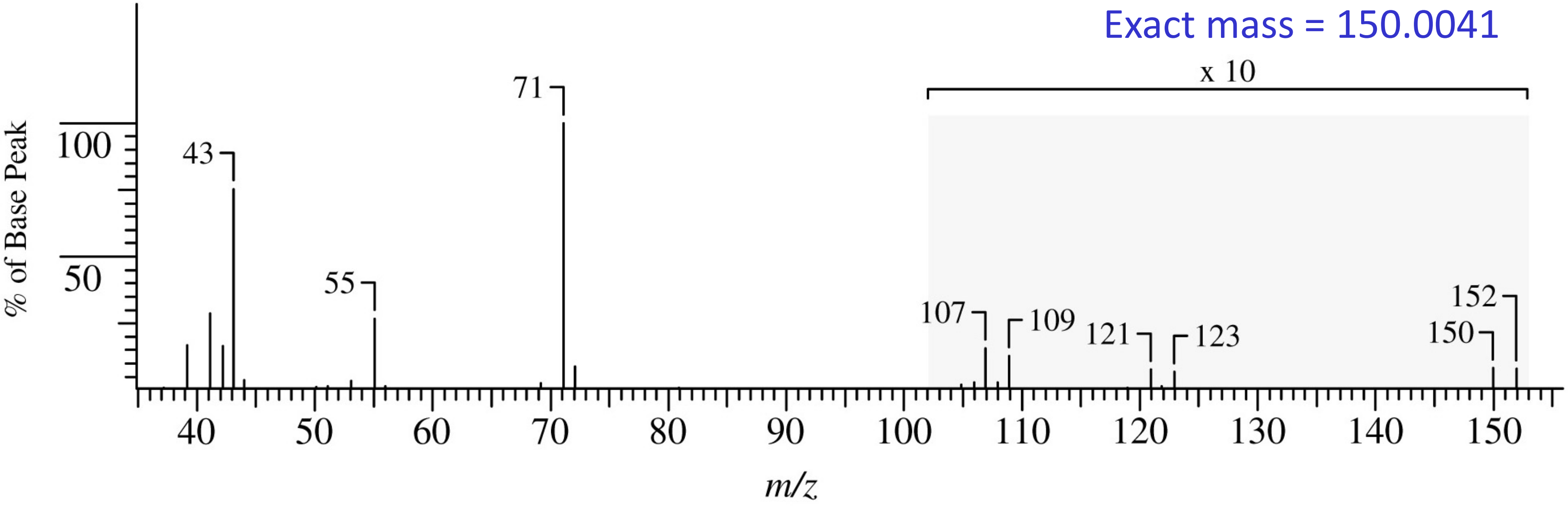
Exact mass = 169.9735

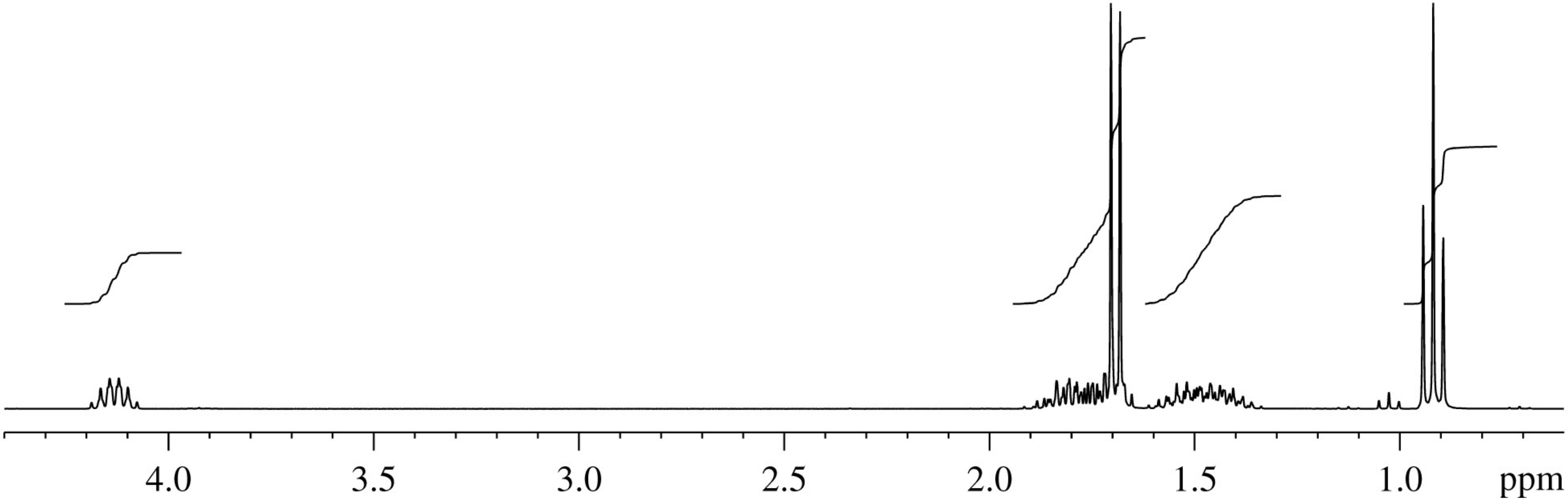

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm

Compound D



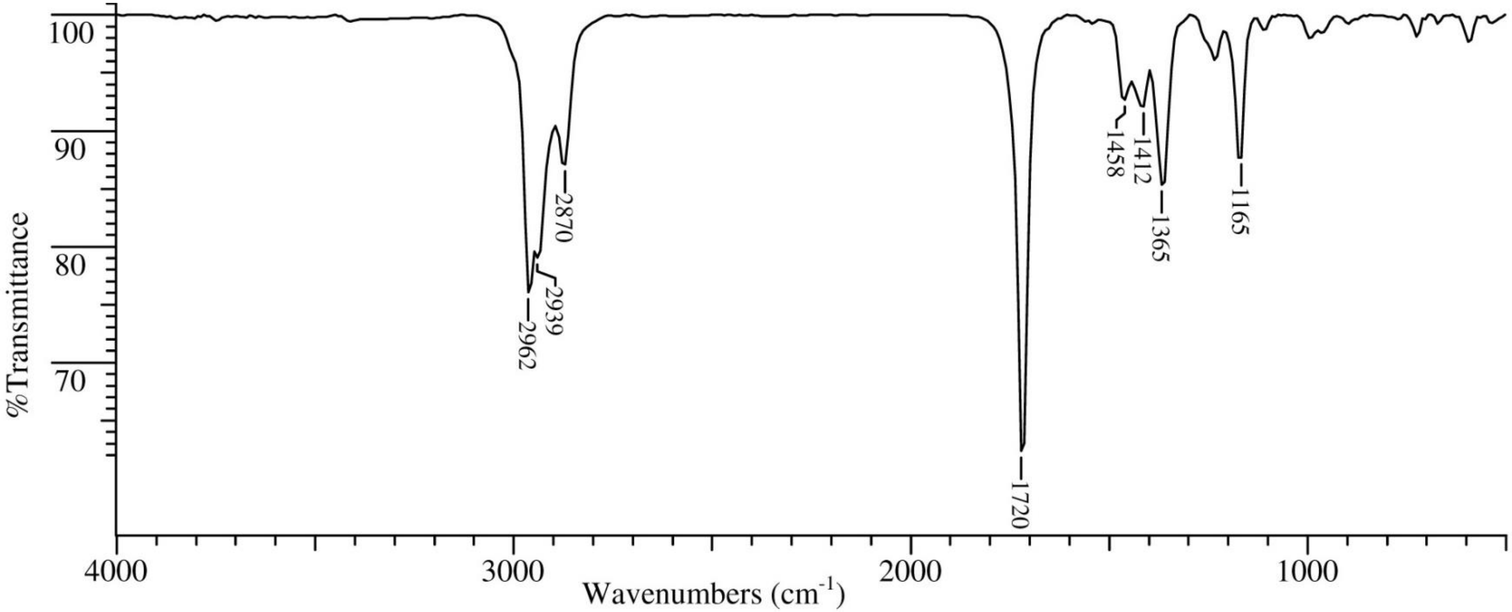
Exact mass = 150.0041

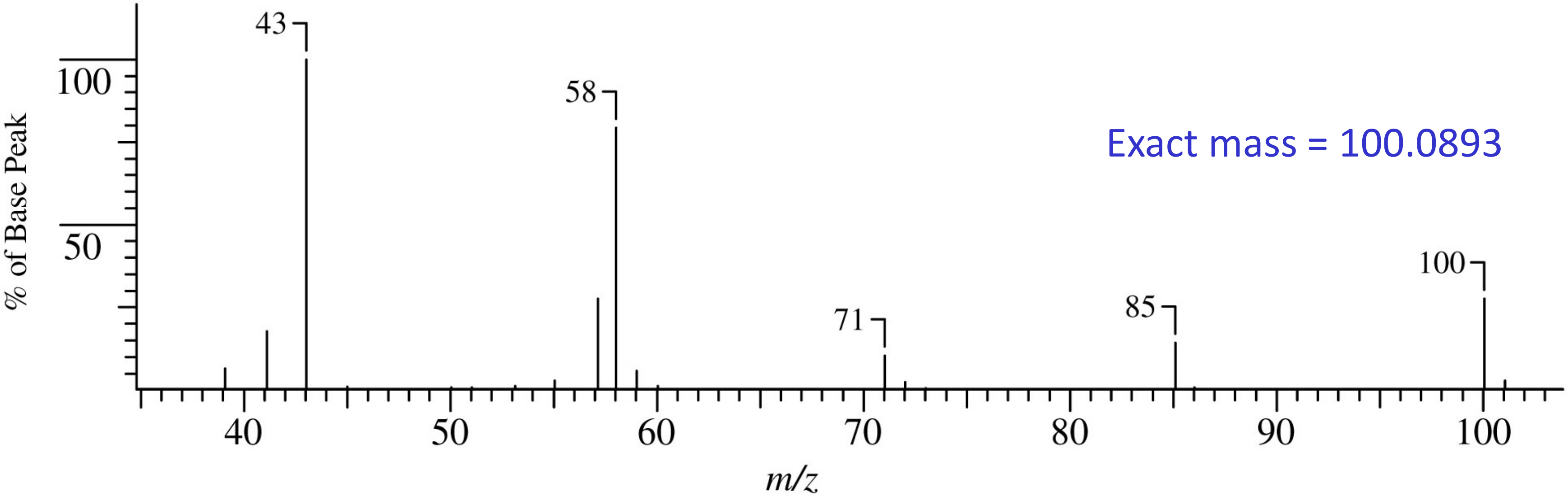




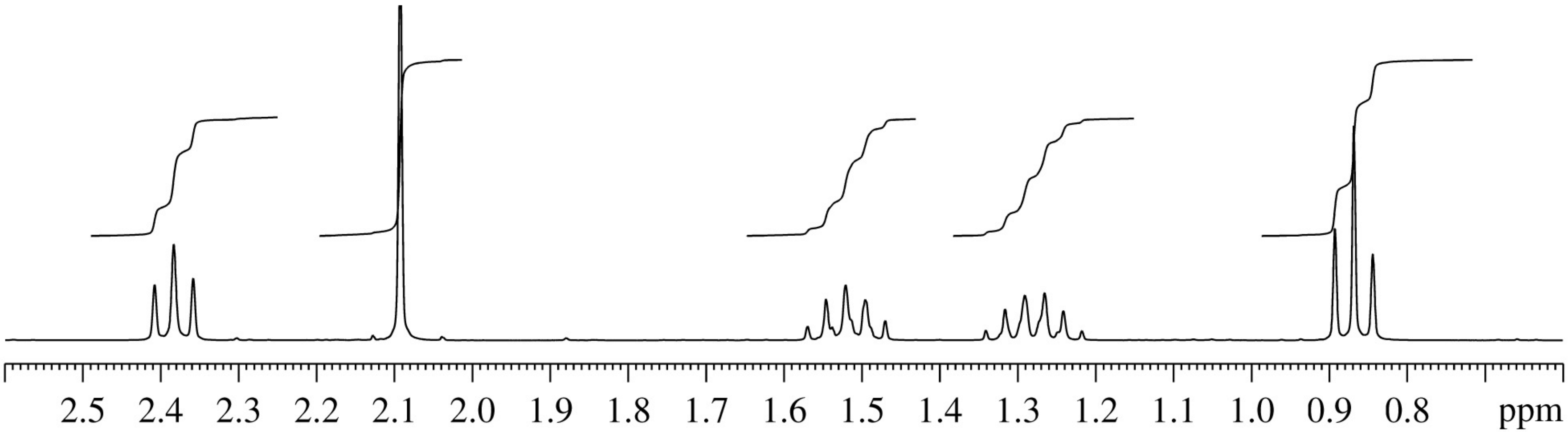
You *might* have nailed this one with the MS alone – does the NMR confirm your choice?

Compound E



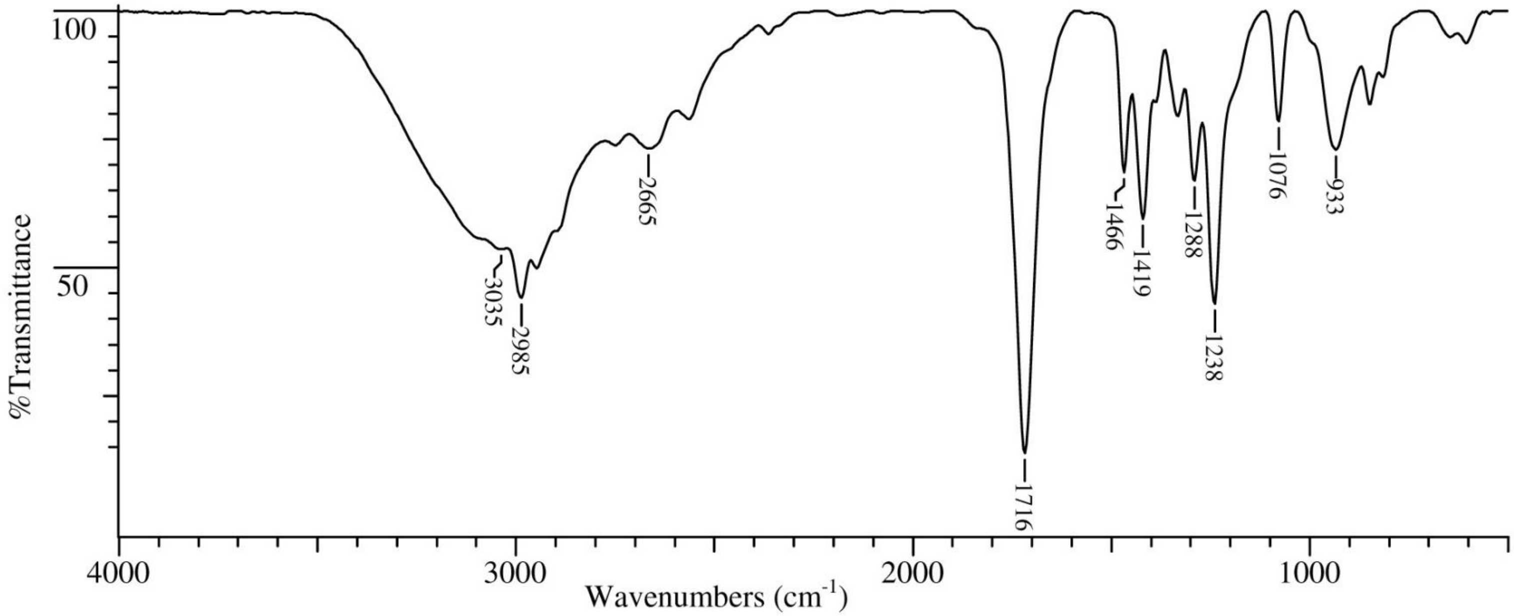


Exact mass = 100.0893



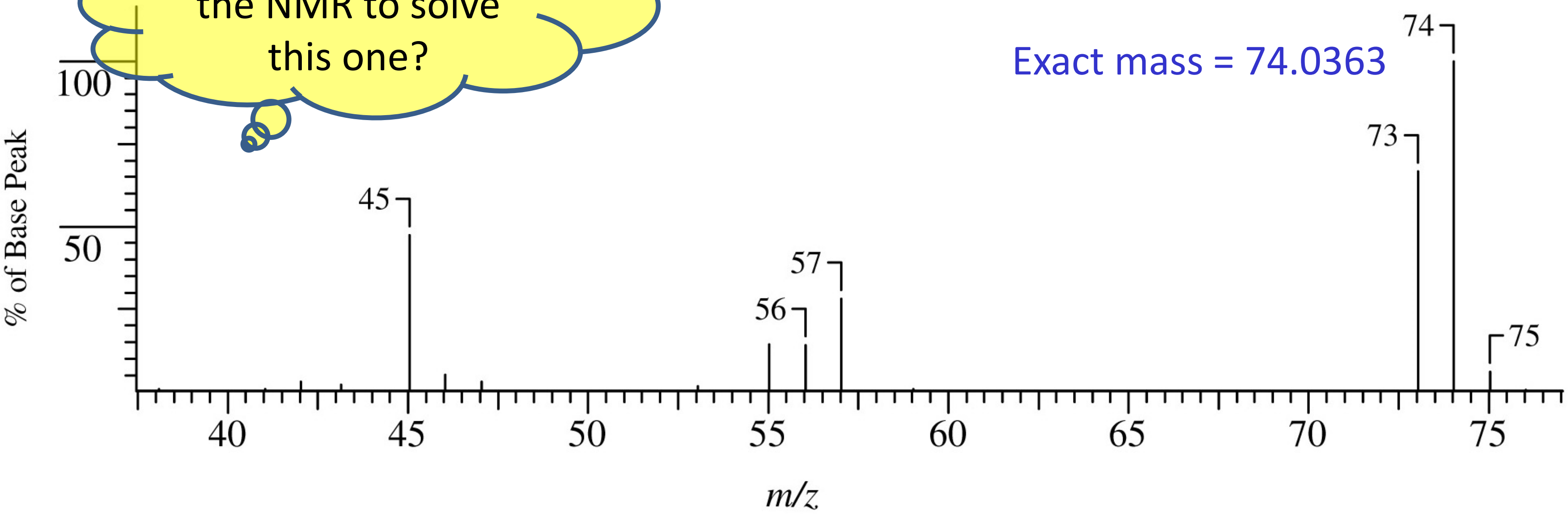
Again, you *might* have got this structure using only the MS and IR, but the NMR should reassure you that you have the correct structure

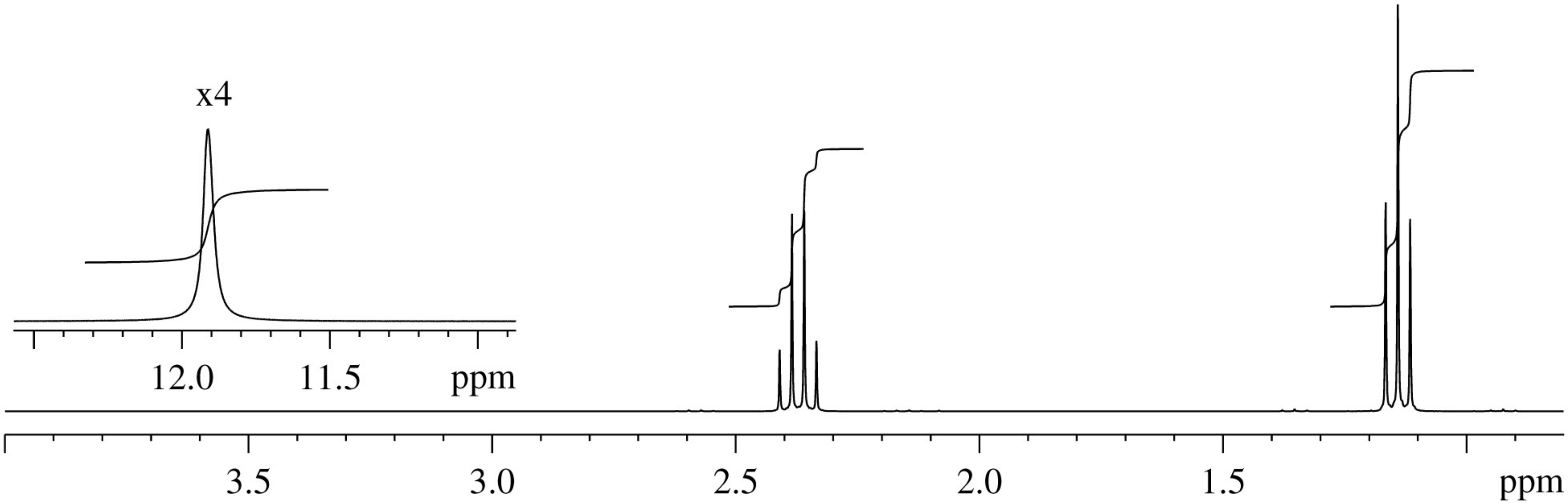
Compound F



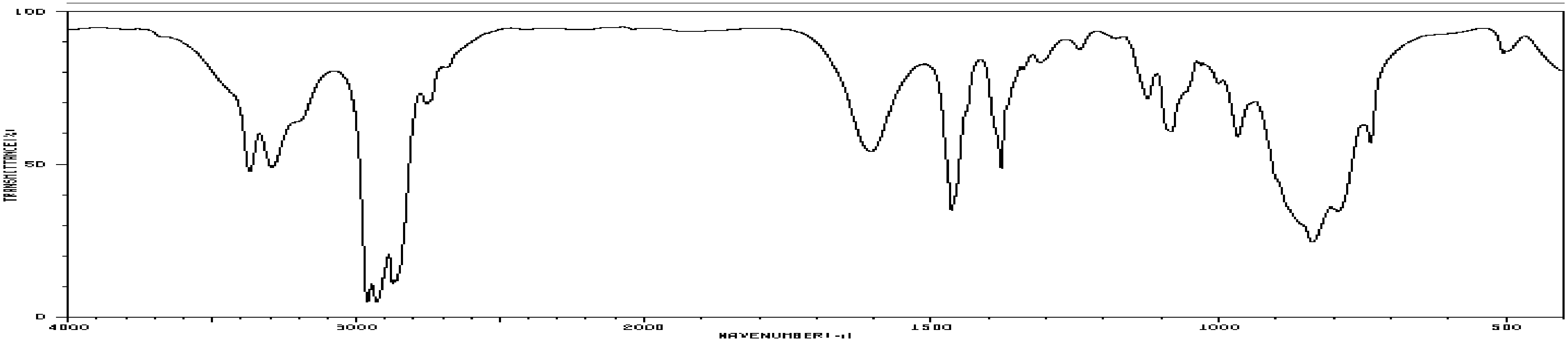
Do you really need the NMR to solve this one?

Exact mass = 74.0363

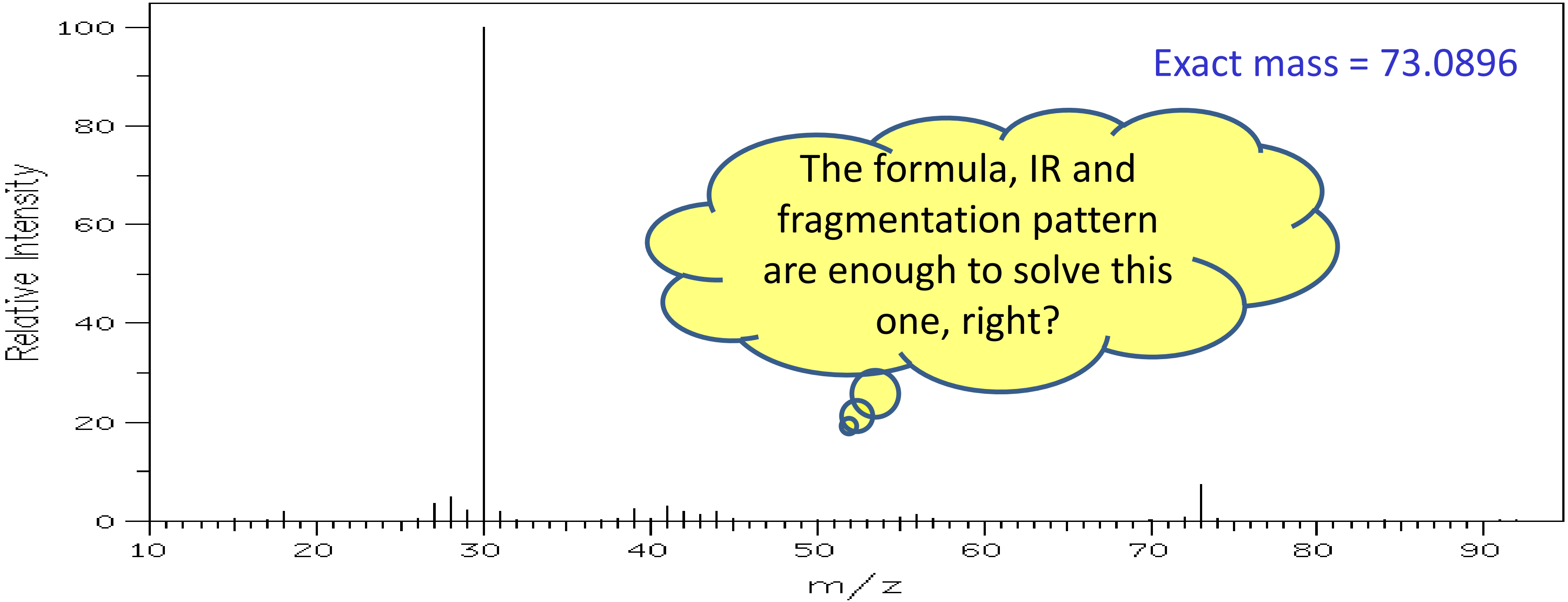



x4
12.0
11.5
ppm
3.5
3.0
2.5
2.0
1.5
ppm

Compound G

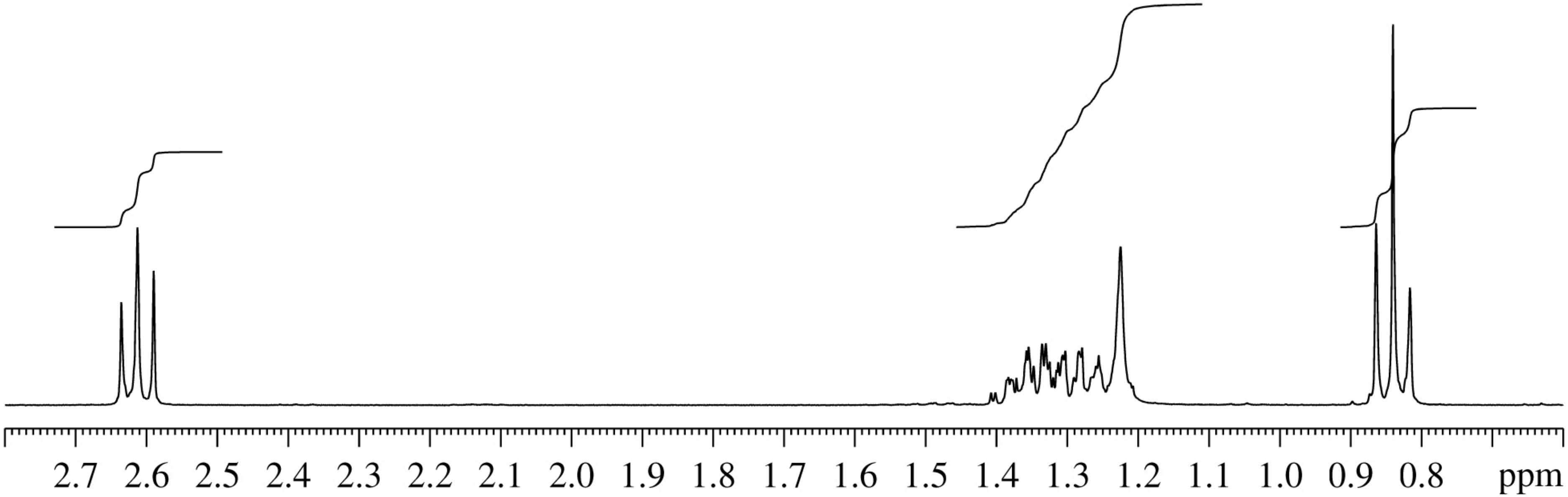


3369	46	1606	52	1083	58	498	84
3293	47	1465	33	1001	74		
2960	4	1379	46	967	57		
2928	4	1340	77	837	23		
2874	10	1312	79	792	33		
2862	10	1243	84	736	55		
2767	66	1124	68	606	84		

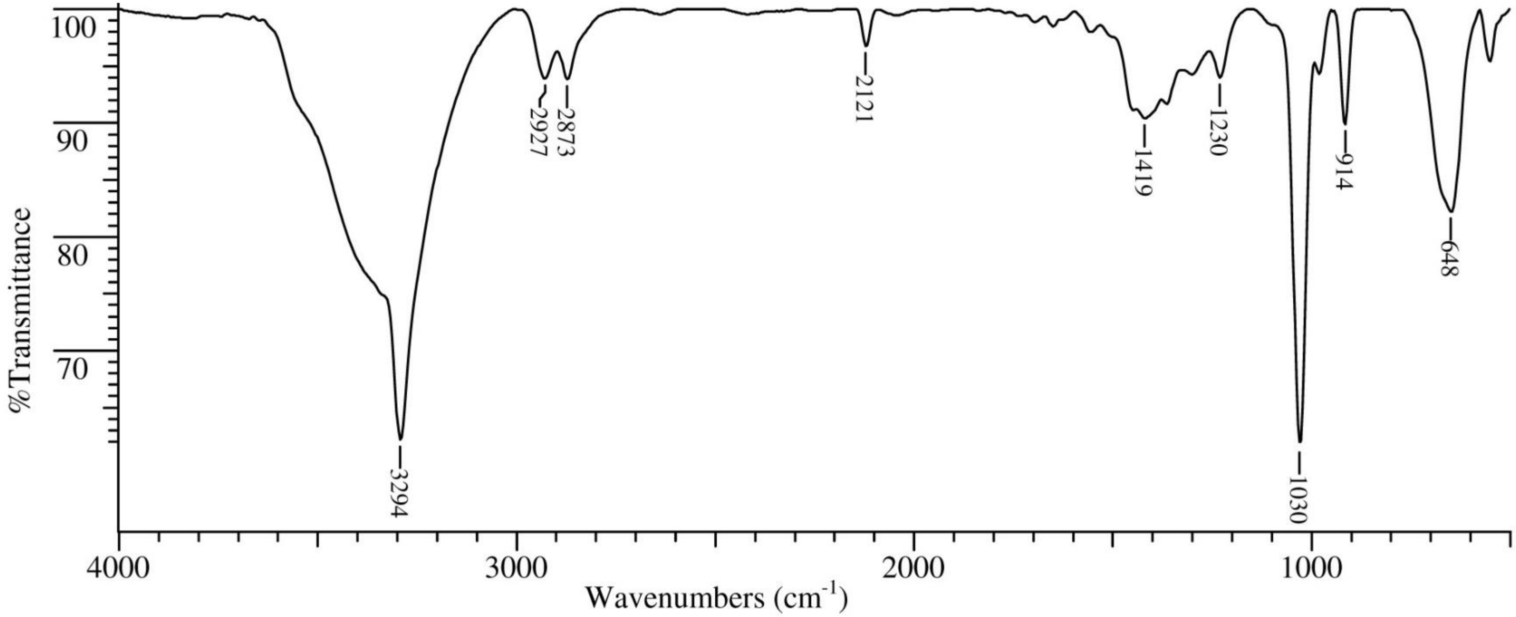


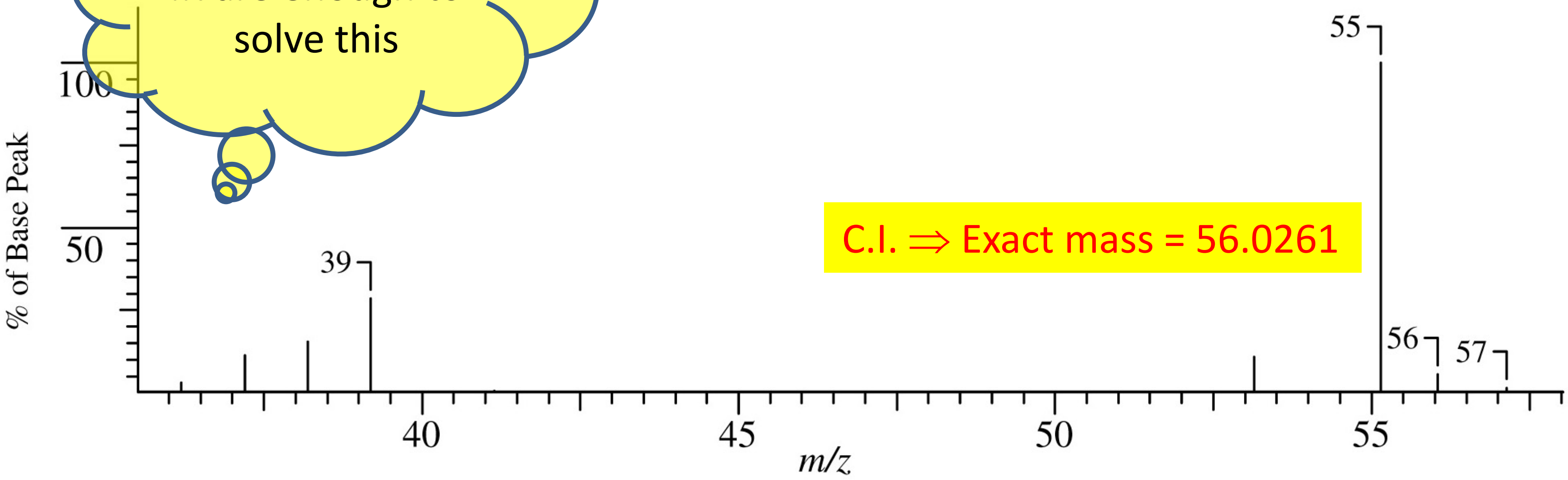
Exact mass = 73.0896

The formula, IR and fragmentation pattern are enough to solve this one, right?


2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
ppm

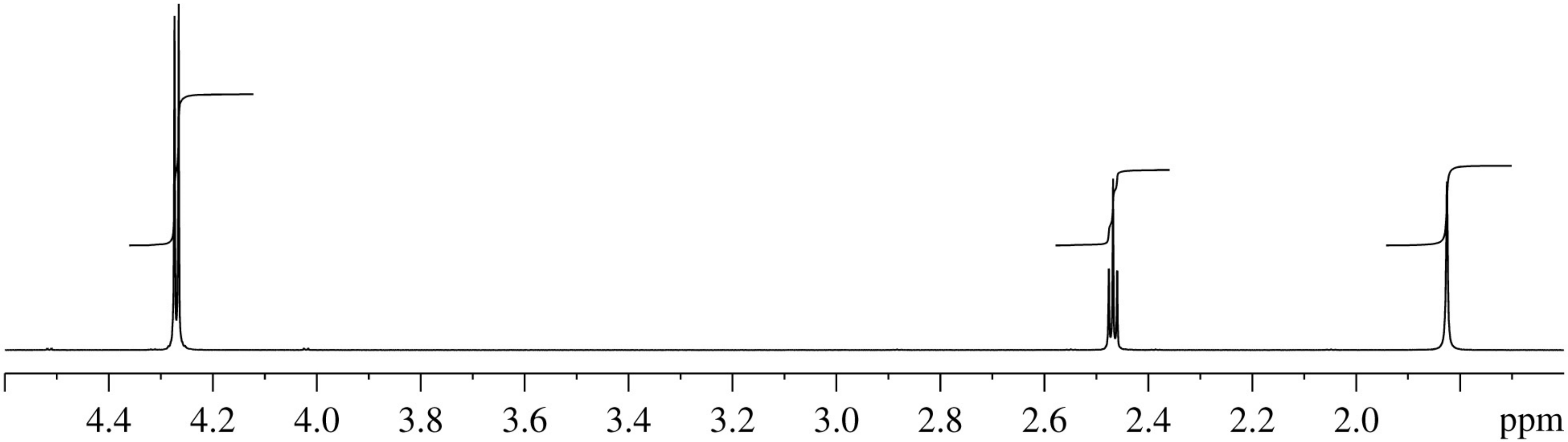
Compound H



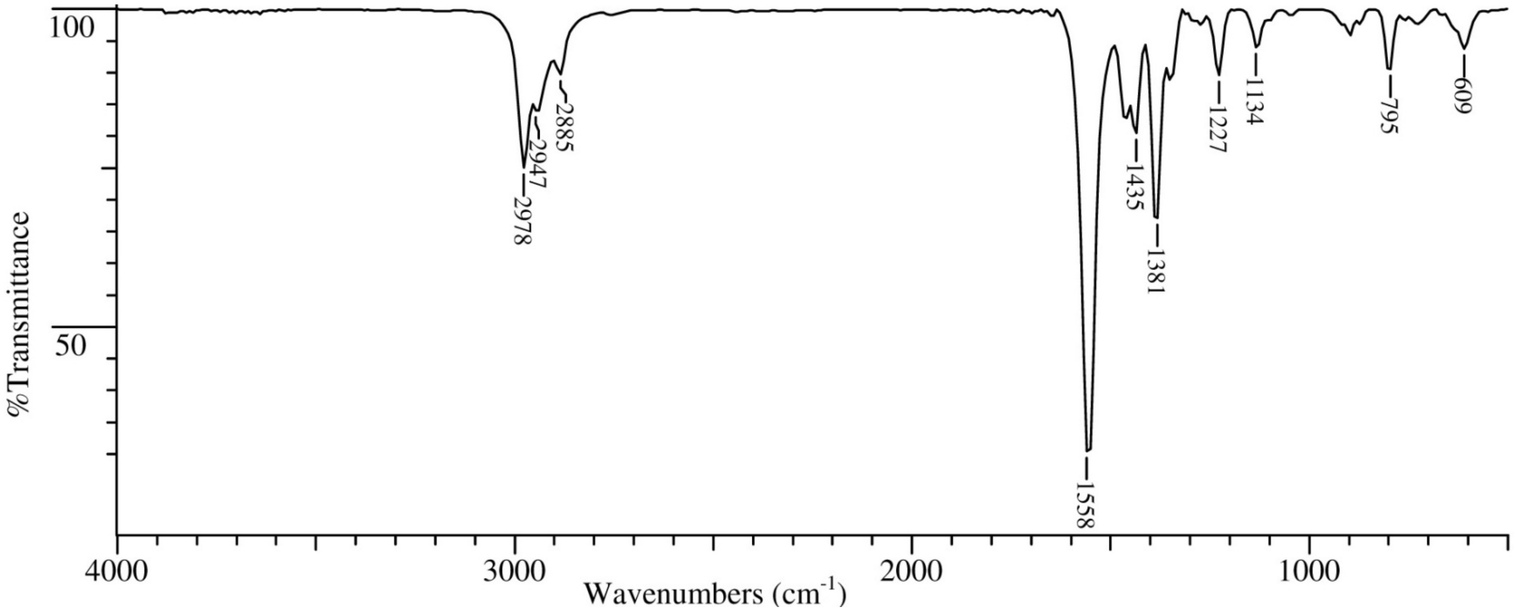


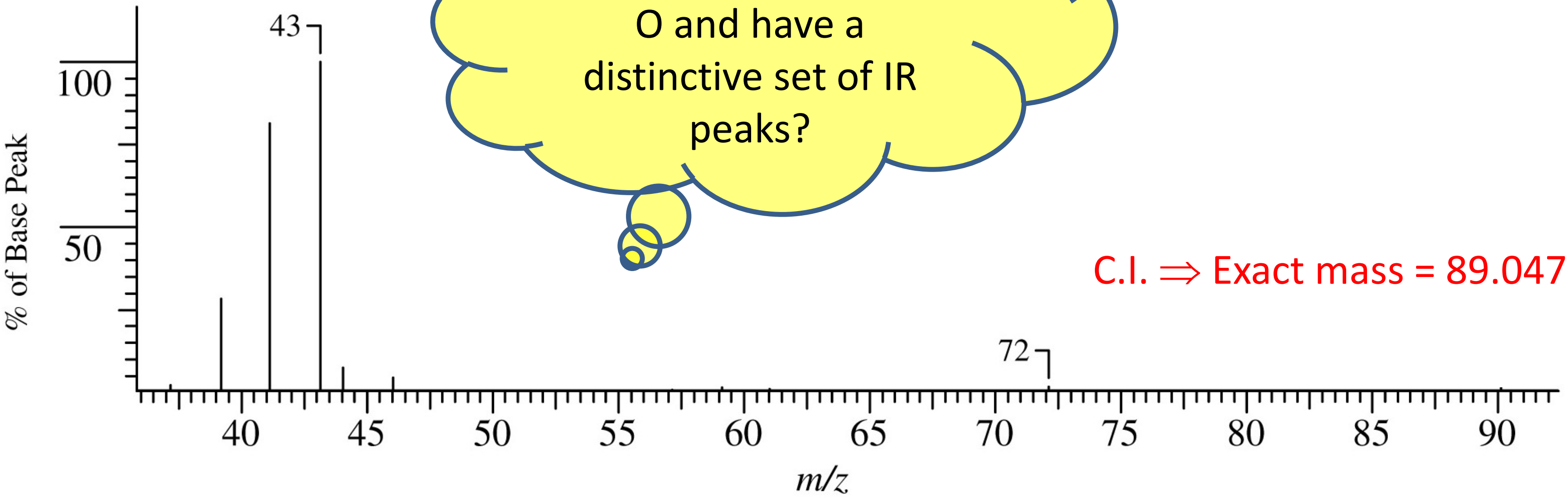
The formula and IR are enough to solve this

C.I. ⇒ Exact mass = 56.0261


4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
ppm

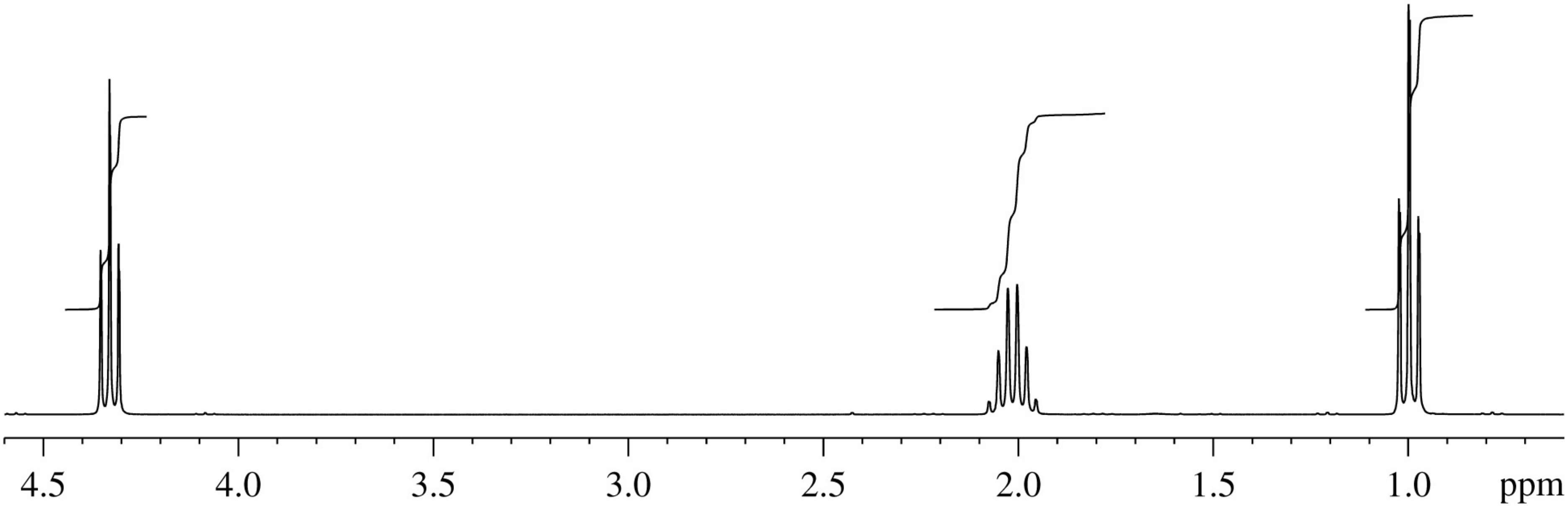
Compound I



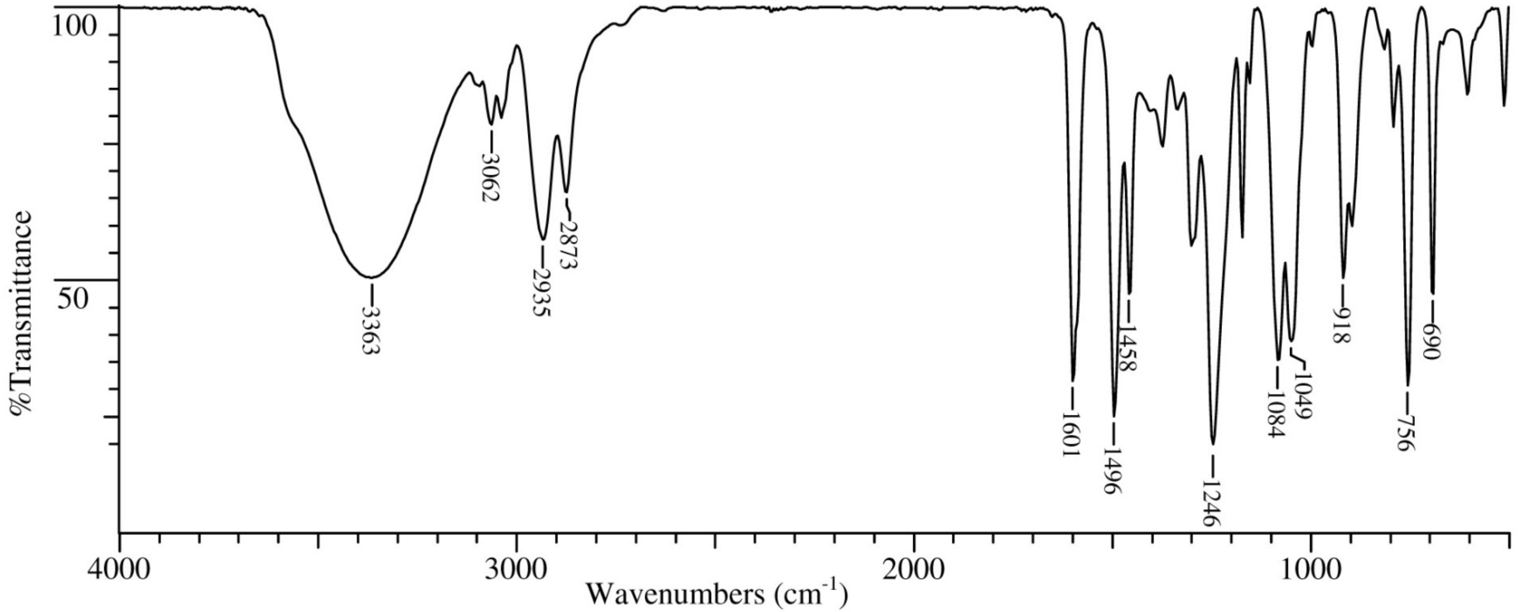


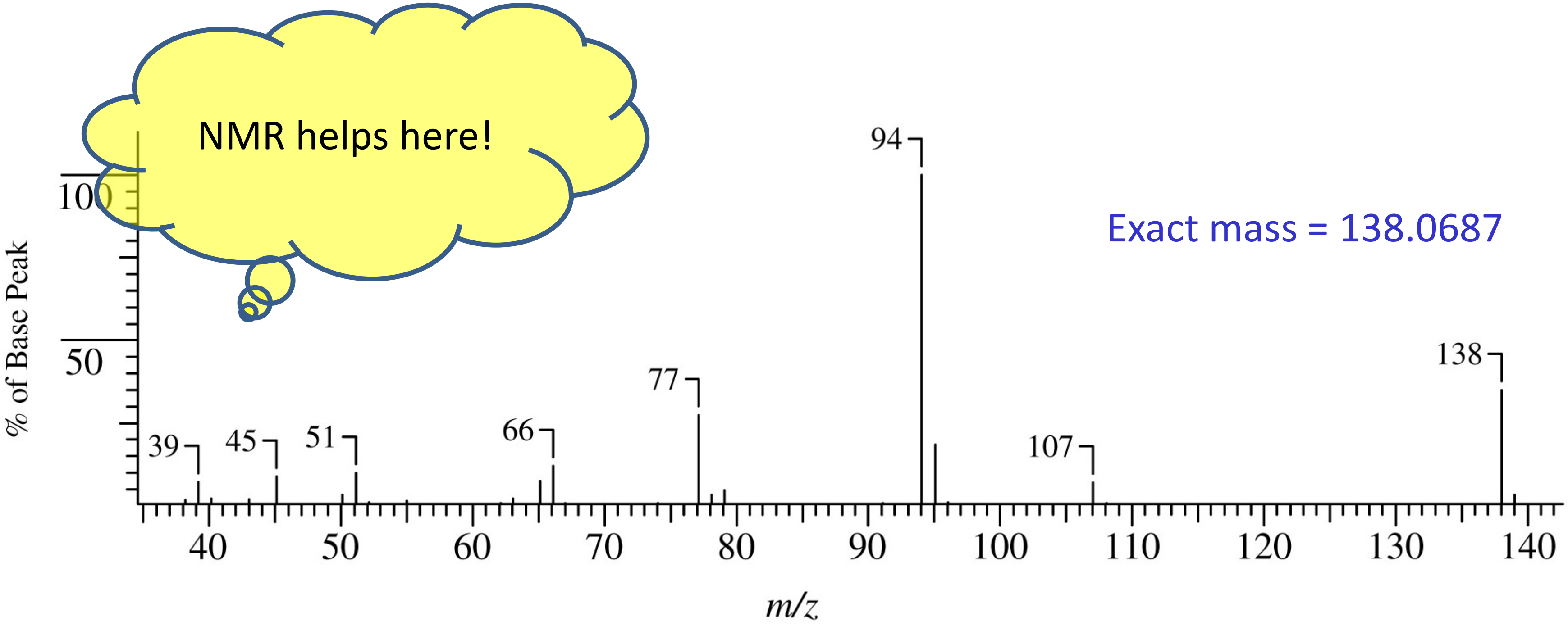
Which functional groups contains N and O and have a distinctive set of IR peaks?

C.I. ⇒ Exact mass = 89.0474


4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

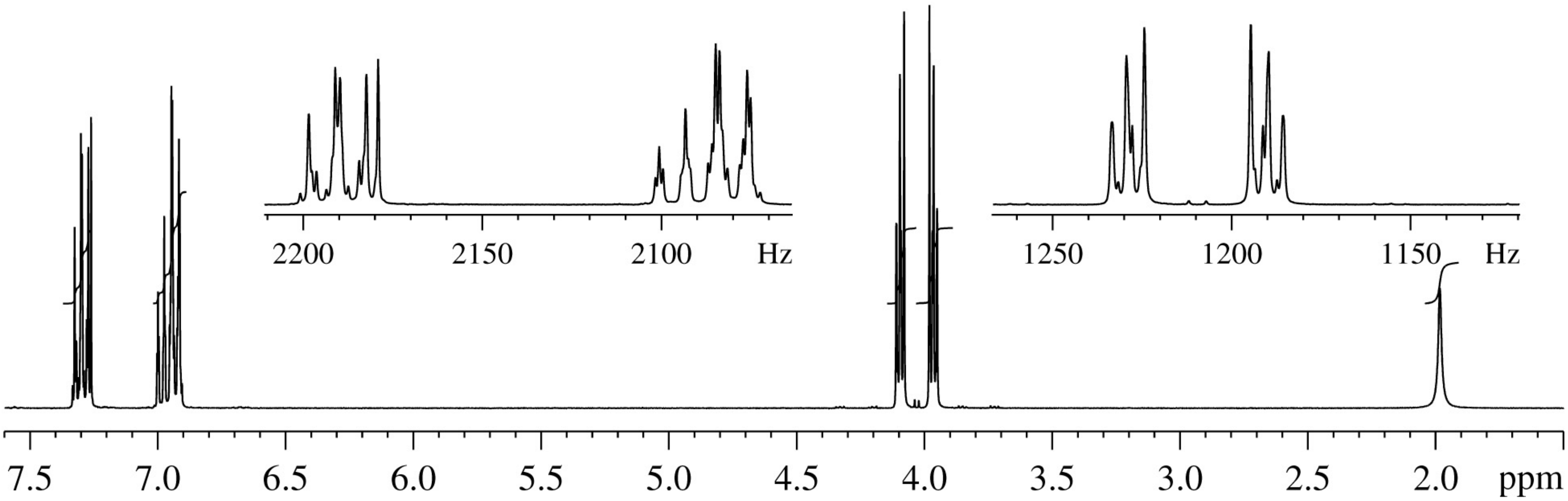
Compound J



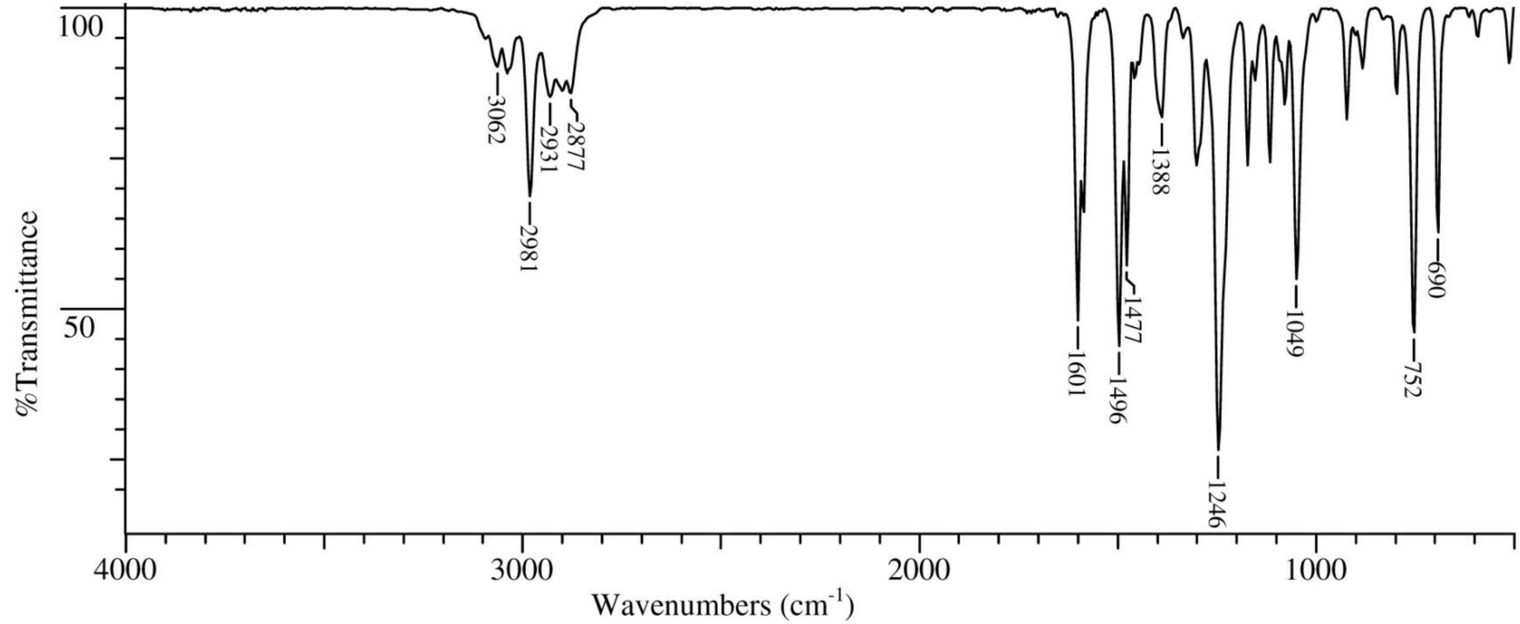


NMR helps here!

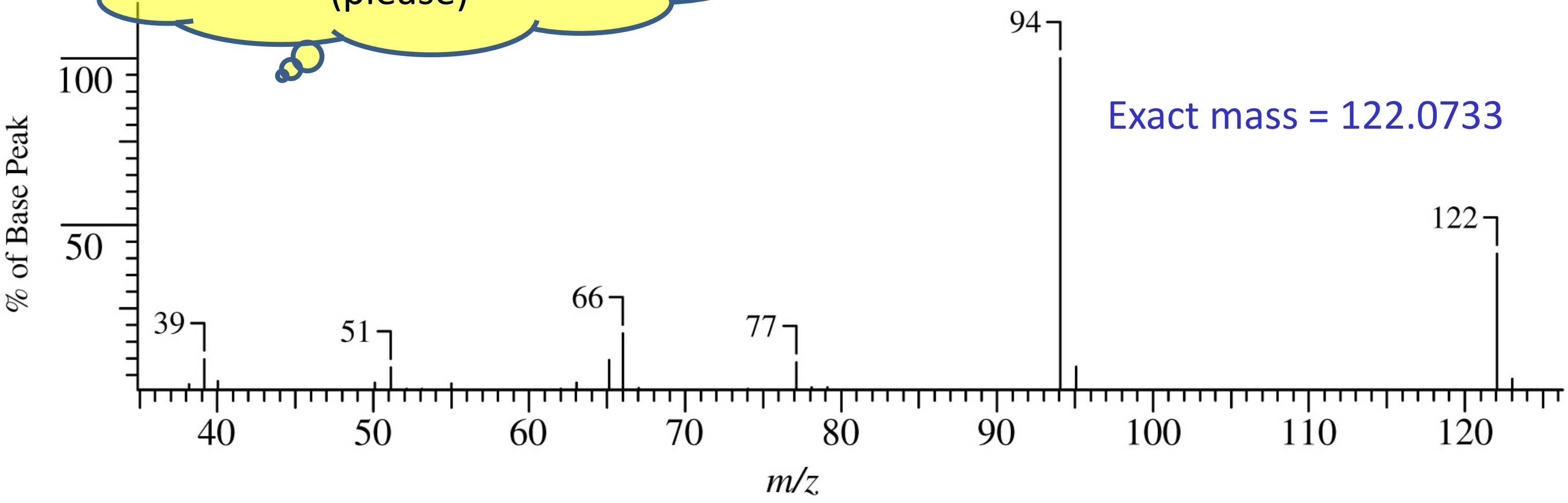
Exact mass = 138.0687


2200
2150
2100
Hz
1250
1200
1150
Hz
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm

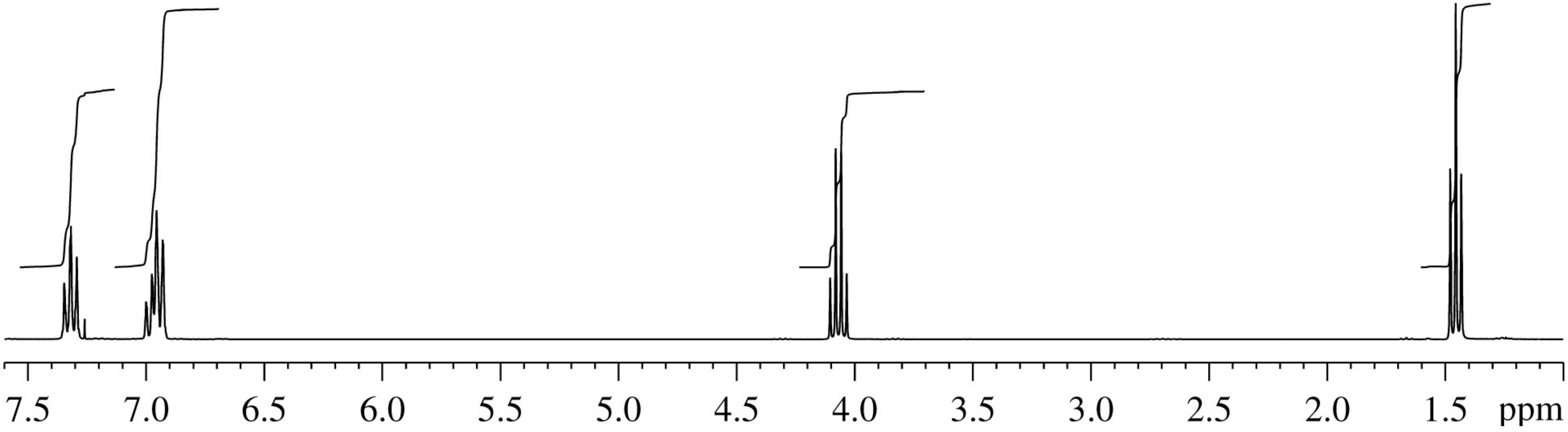
Compound K



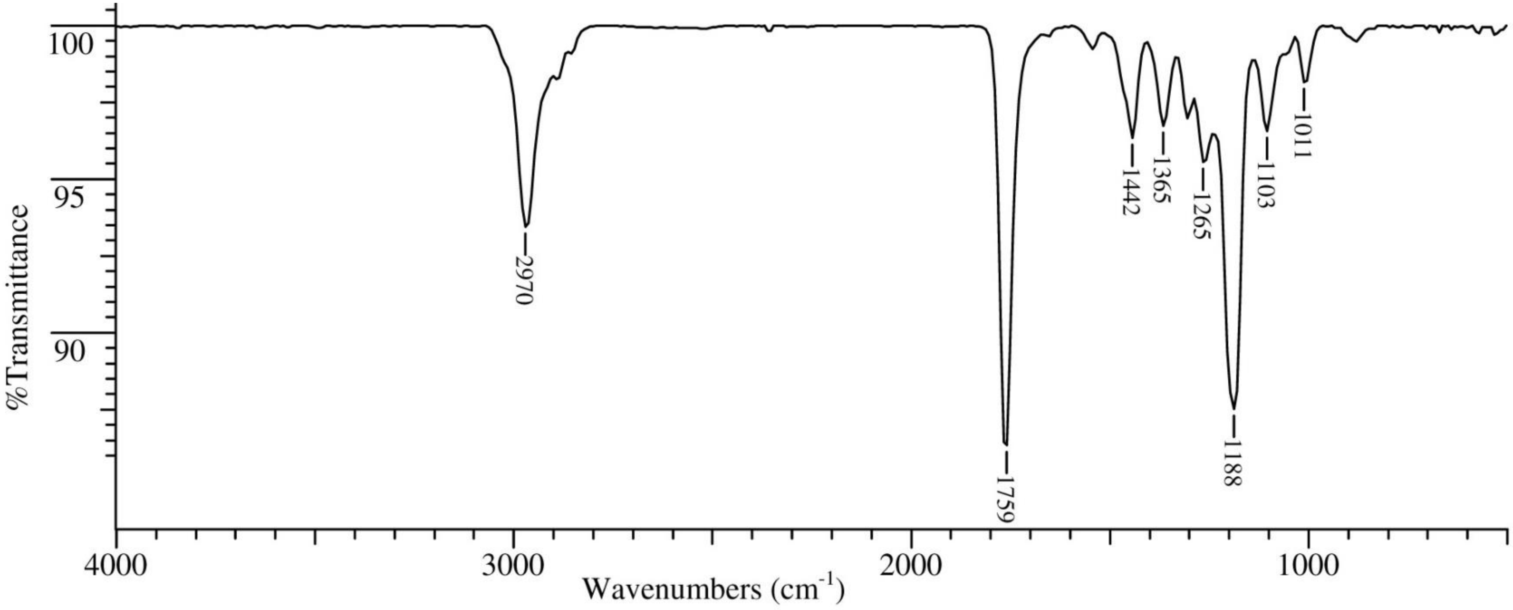
Gimme the NMR!
(please)

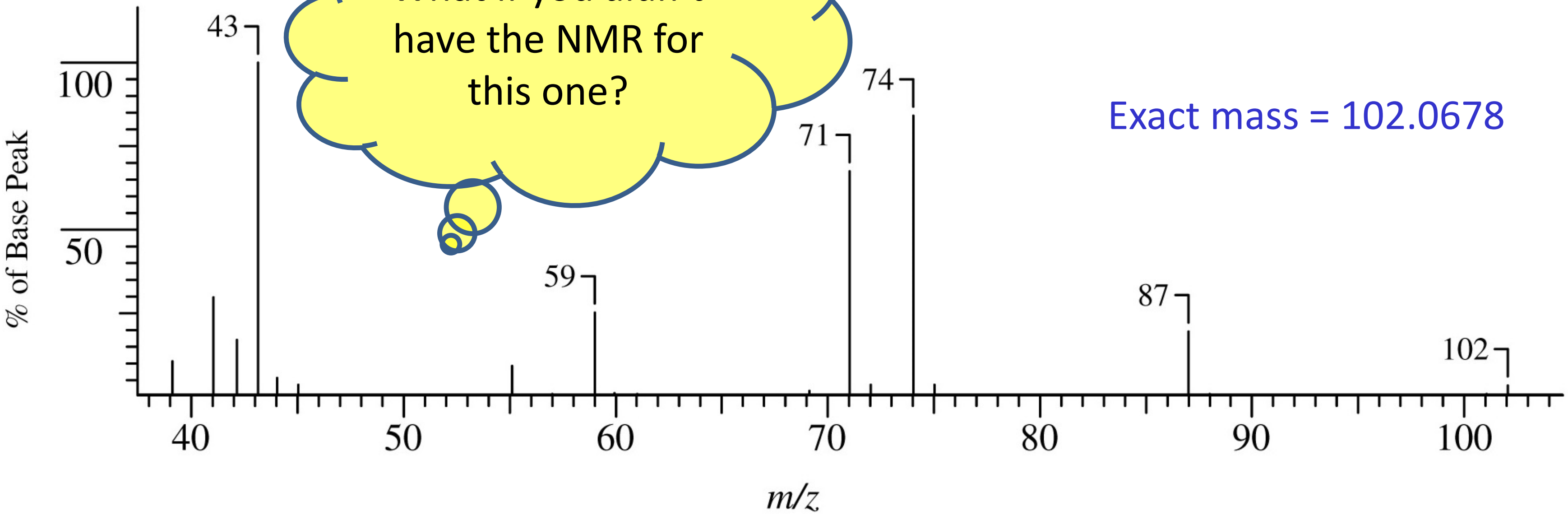


Exact mass = 122.0733


7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm

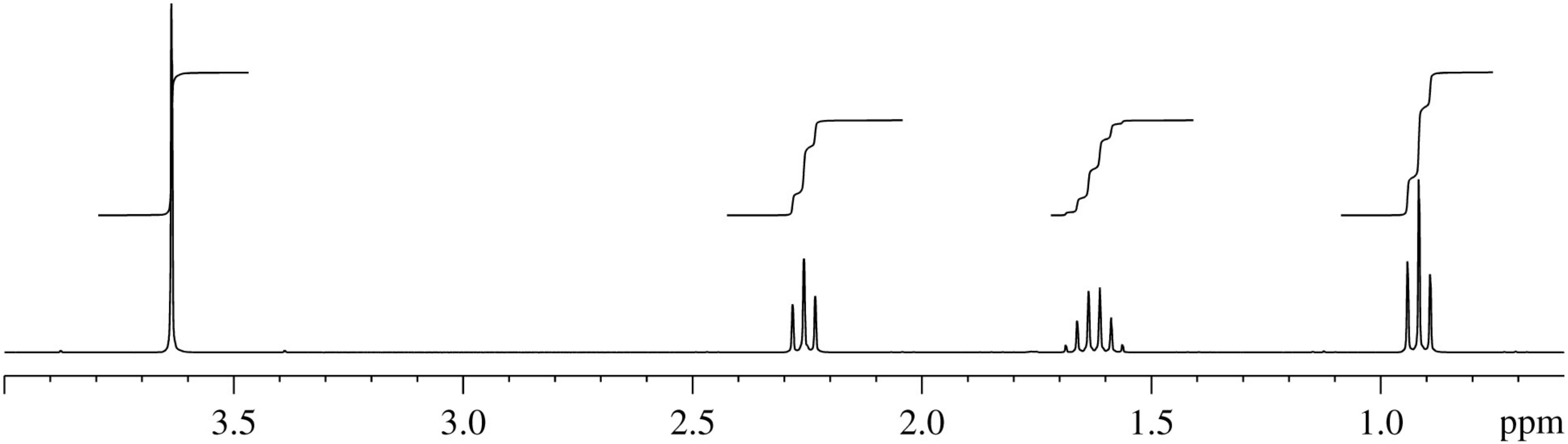
Compound L



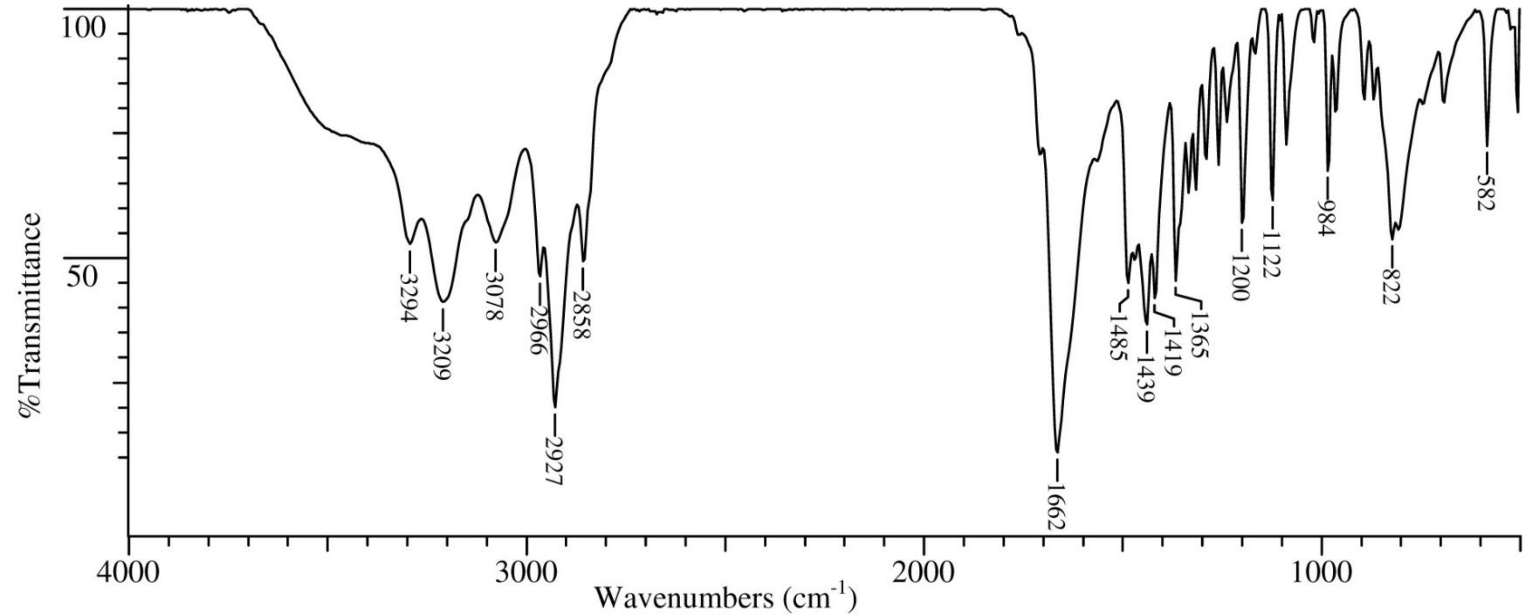


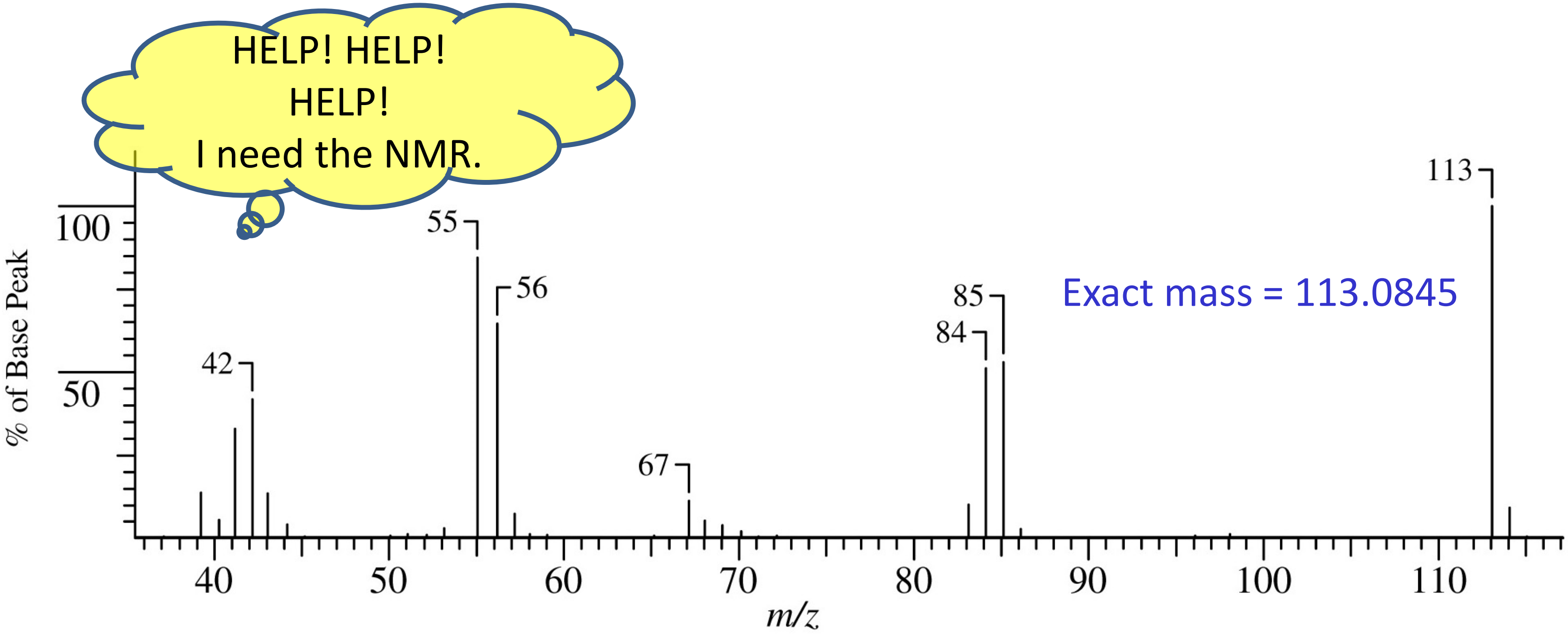
What if you *didn't* have the NMR for this one?

Exact mass = 102.0678

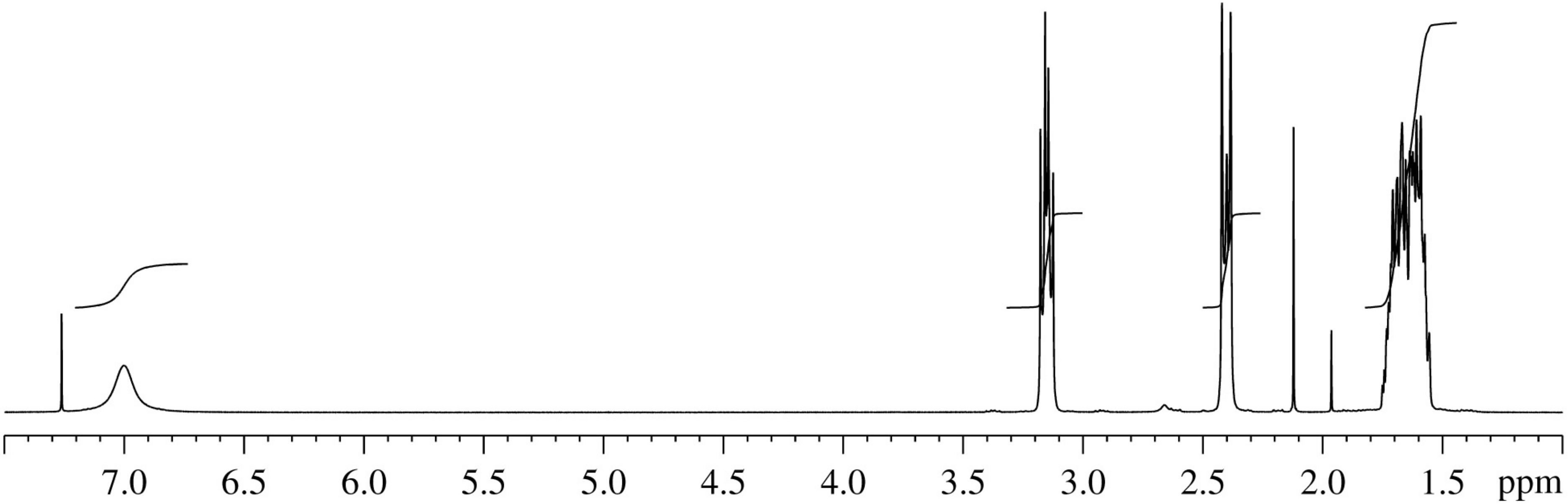

3.5
3.0
2.5
2.0
1.5
1.0
ppm

Compound M



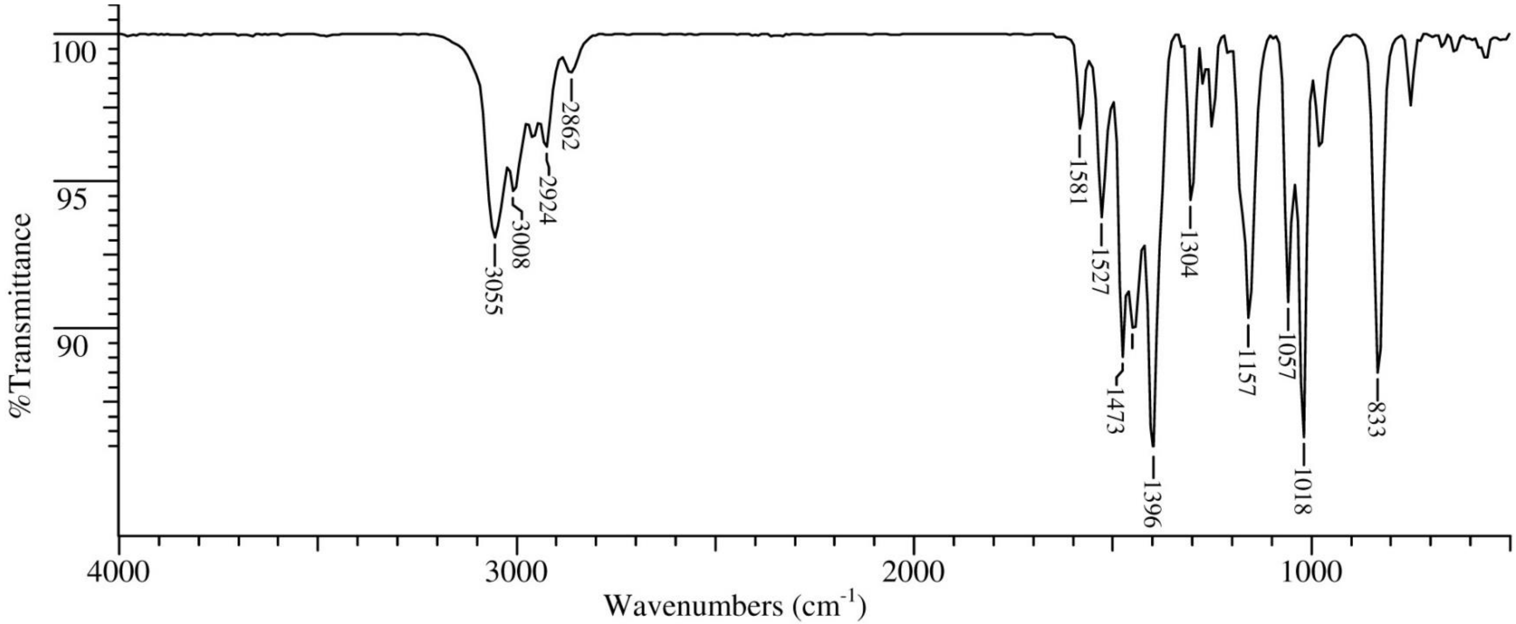


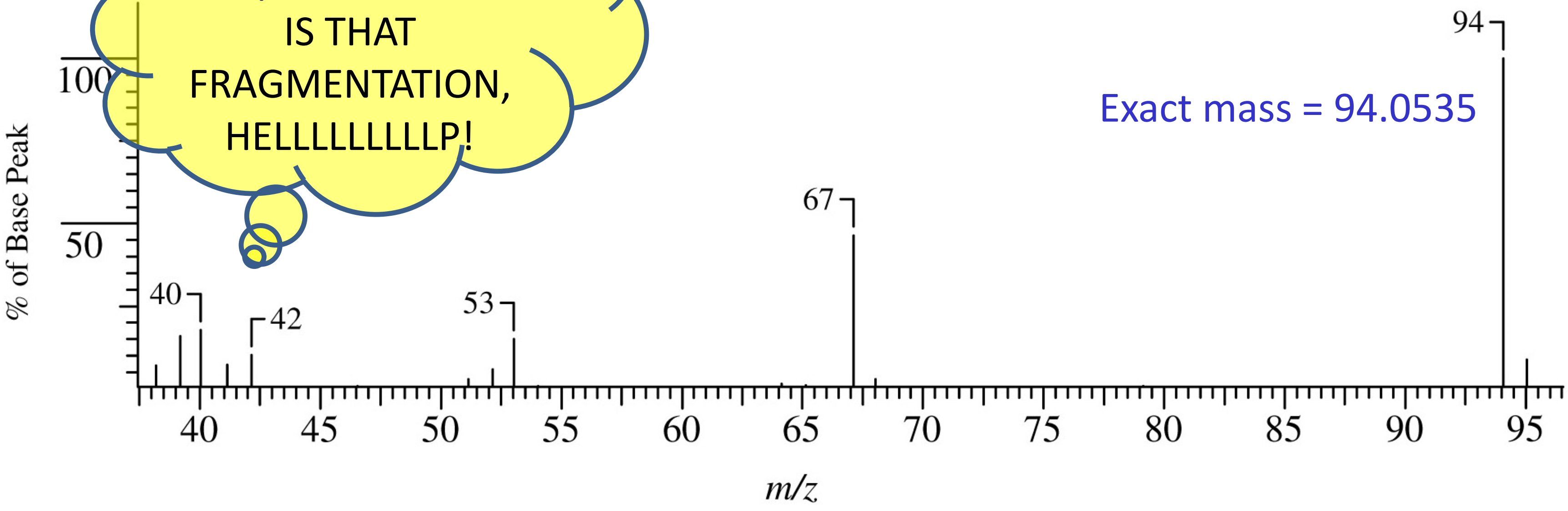
Exact mass = 113.0845



....got it.

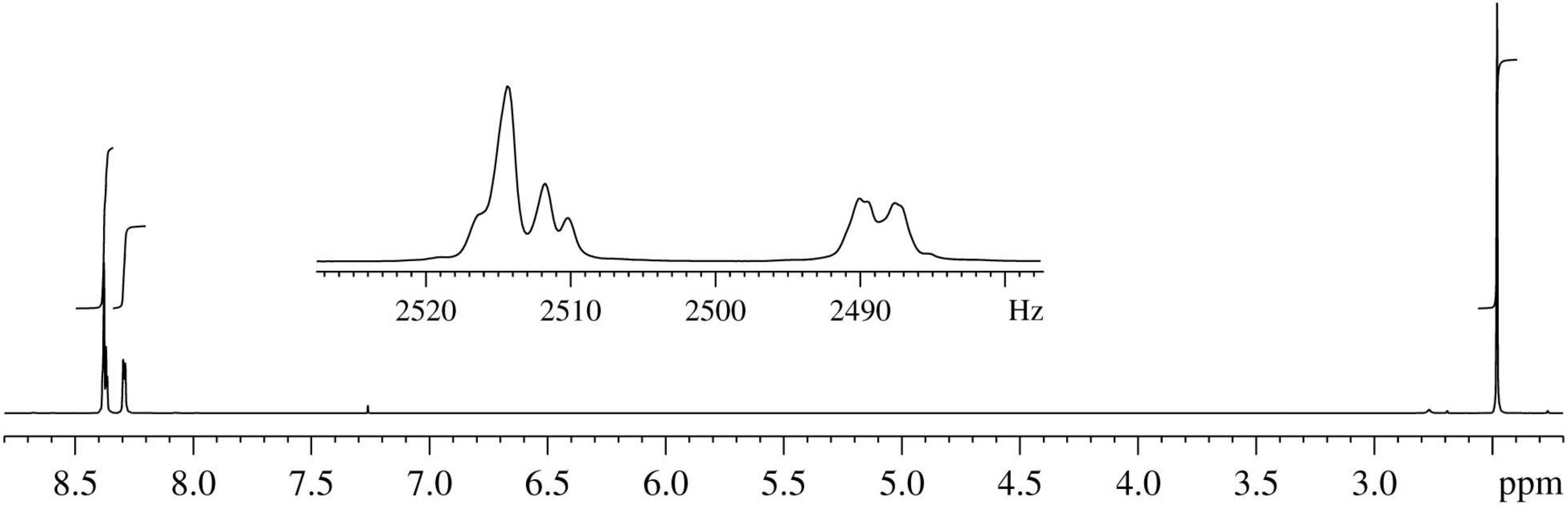
Compound N





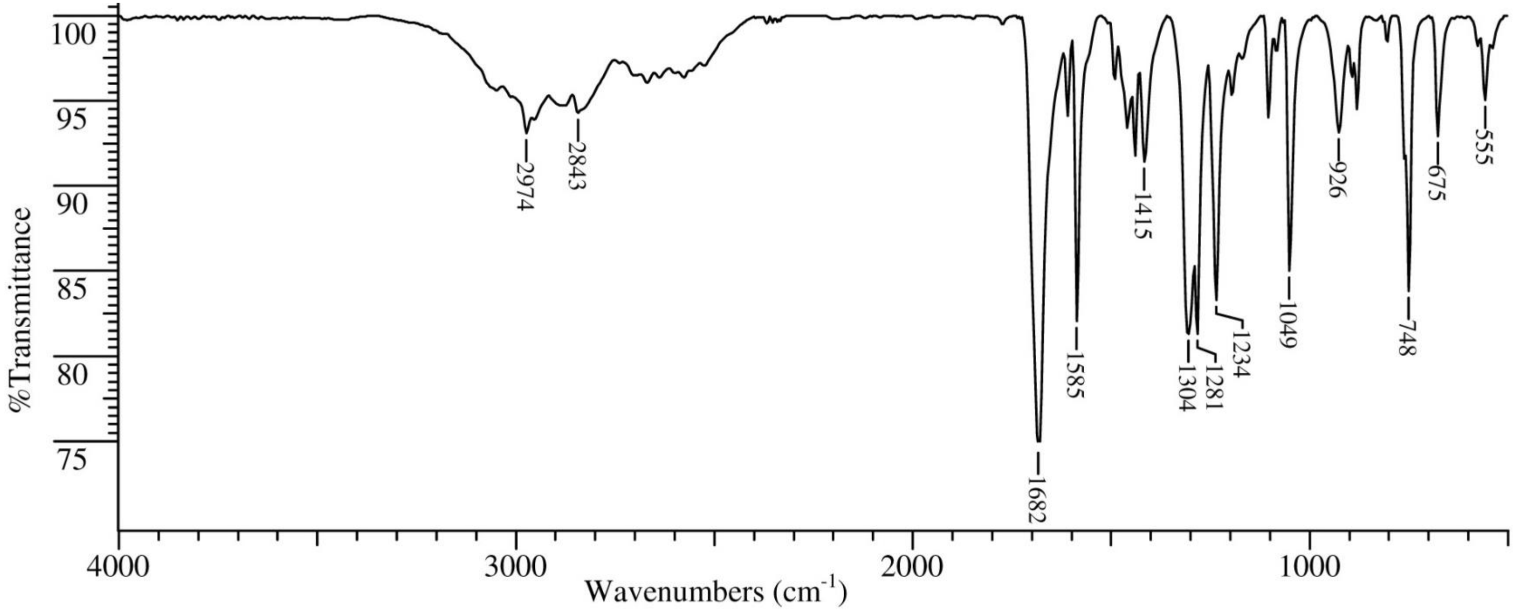
Small formula … simple IR …WHAT IS THAT FRAGMENTATION, HELLLLLLLLLP!

Exact mass = 94.0535

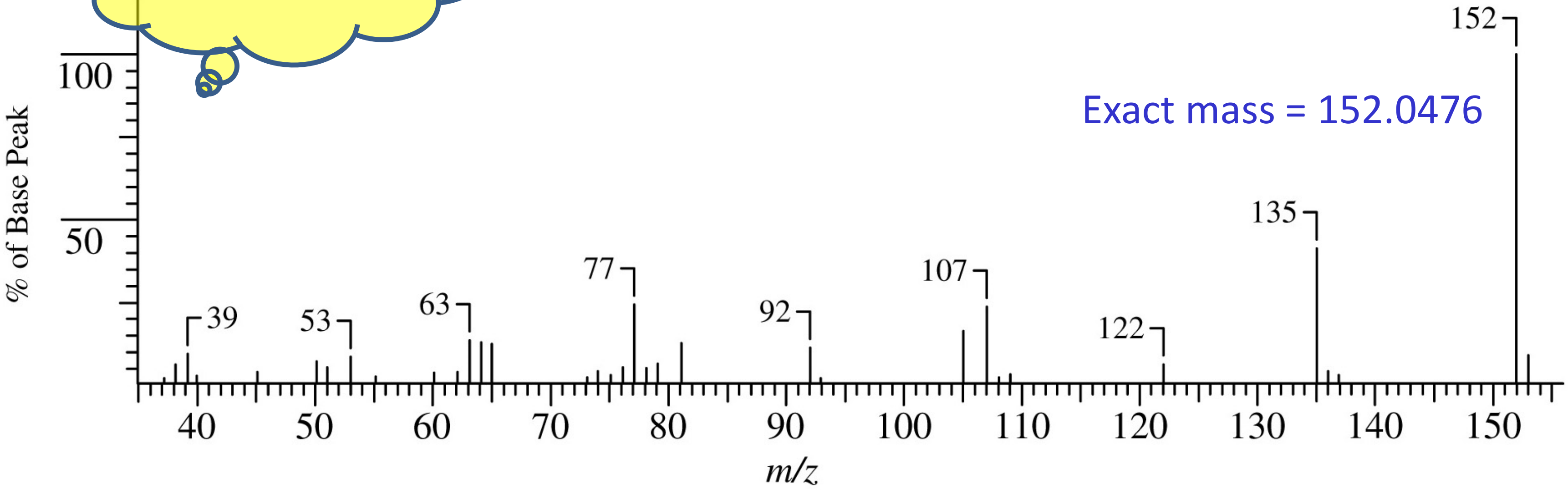


Does this help?

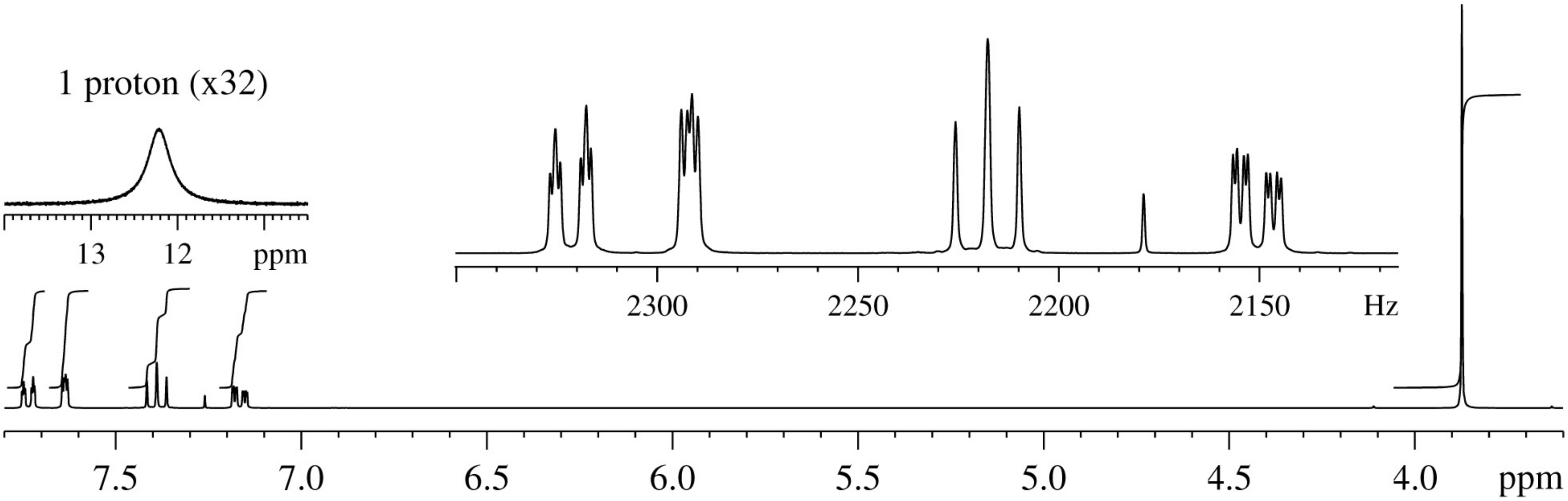
Compound O



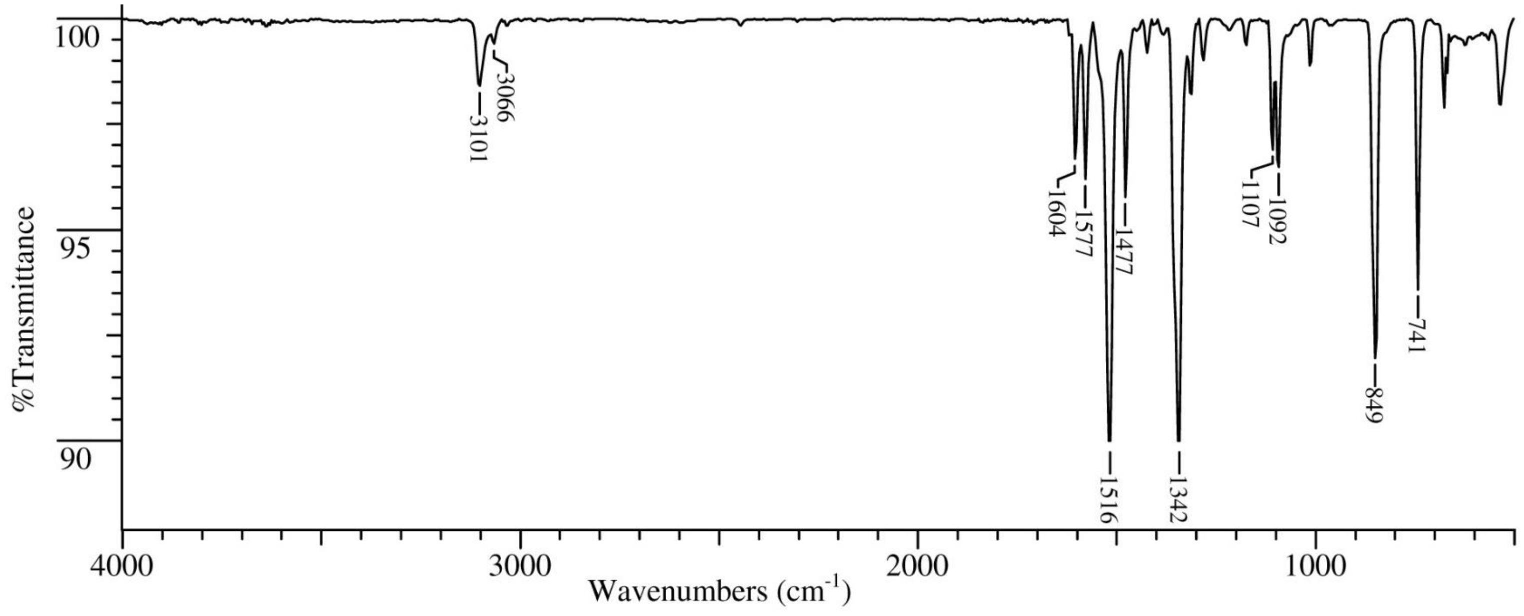
....need-N-M-R

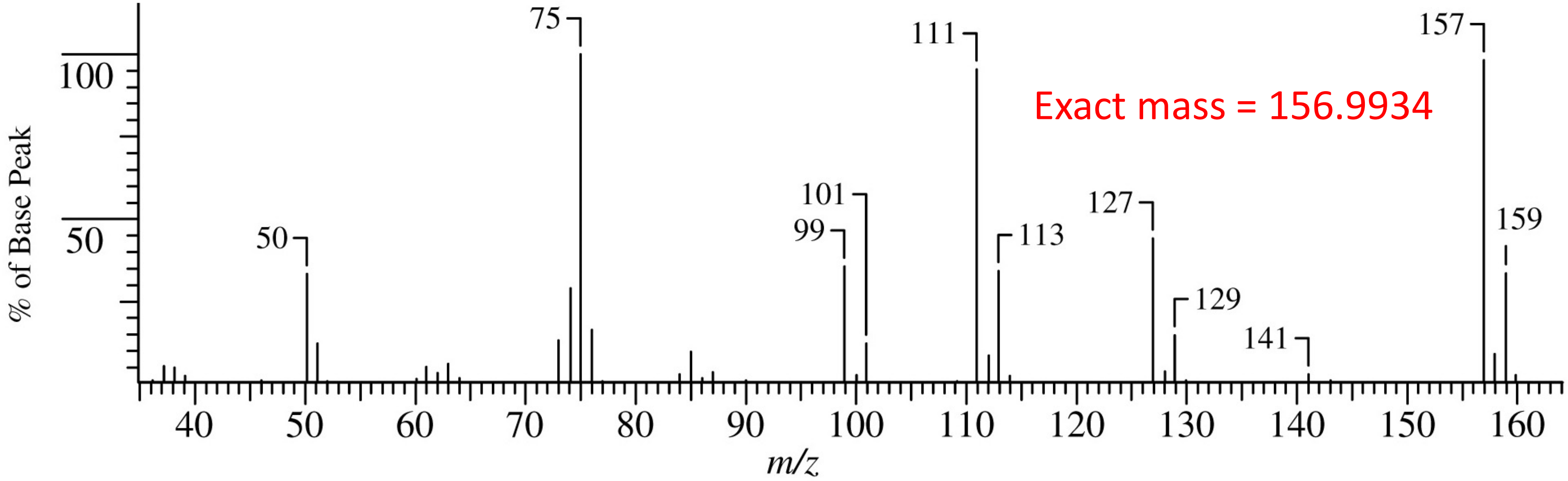


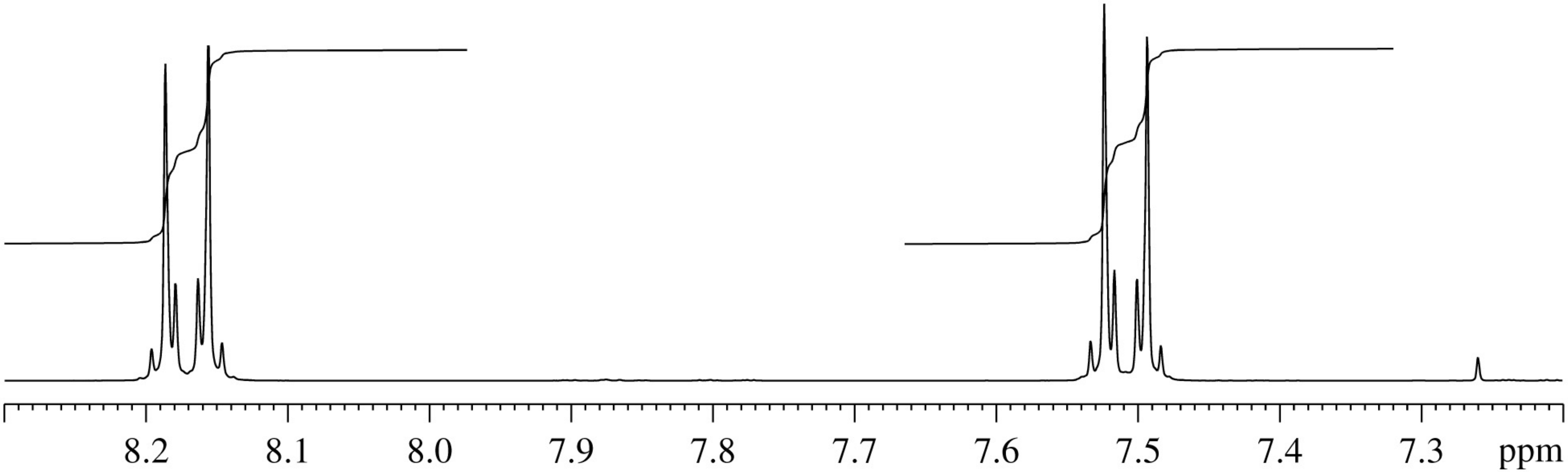
Exact mass = 152.0476


1 proton (x32)
13
12
ppm
2300
2250
2200
2150
Hz
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
ppm

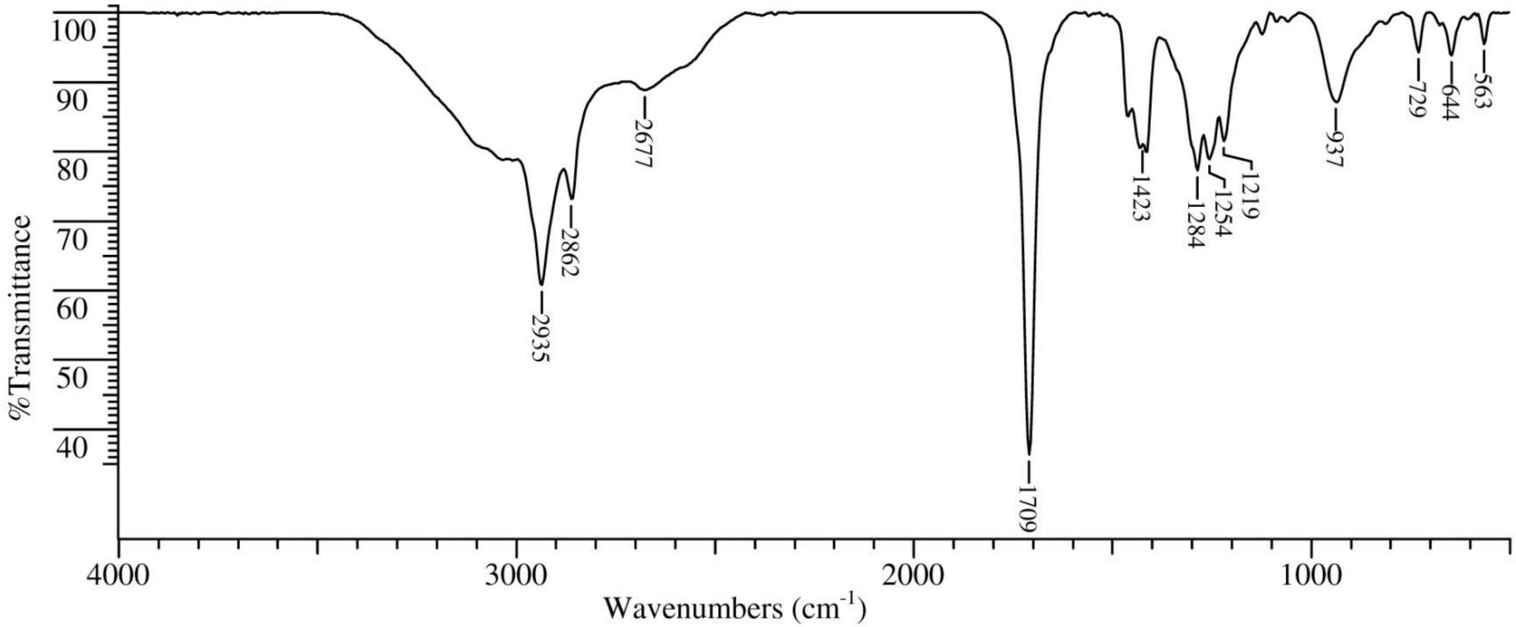
Compound P

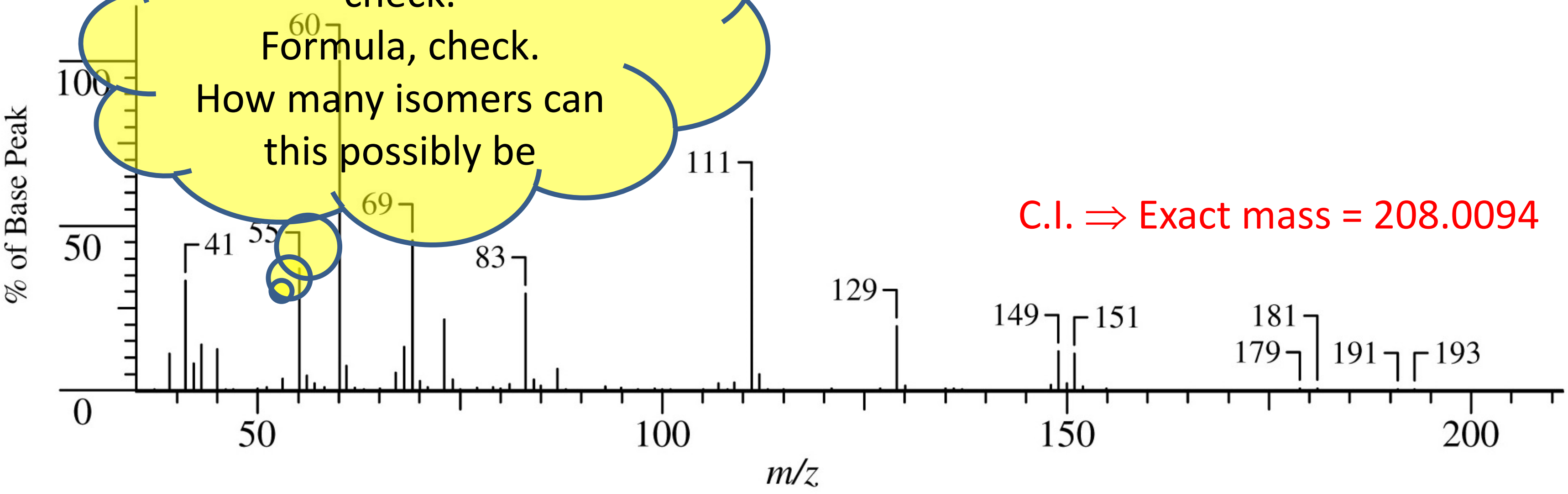



Exact mass = 156.9934


8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
ppm

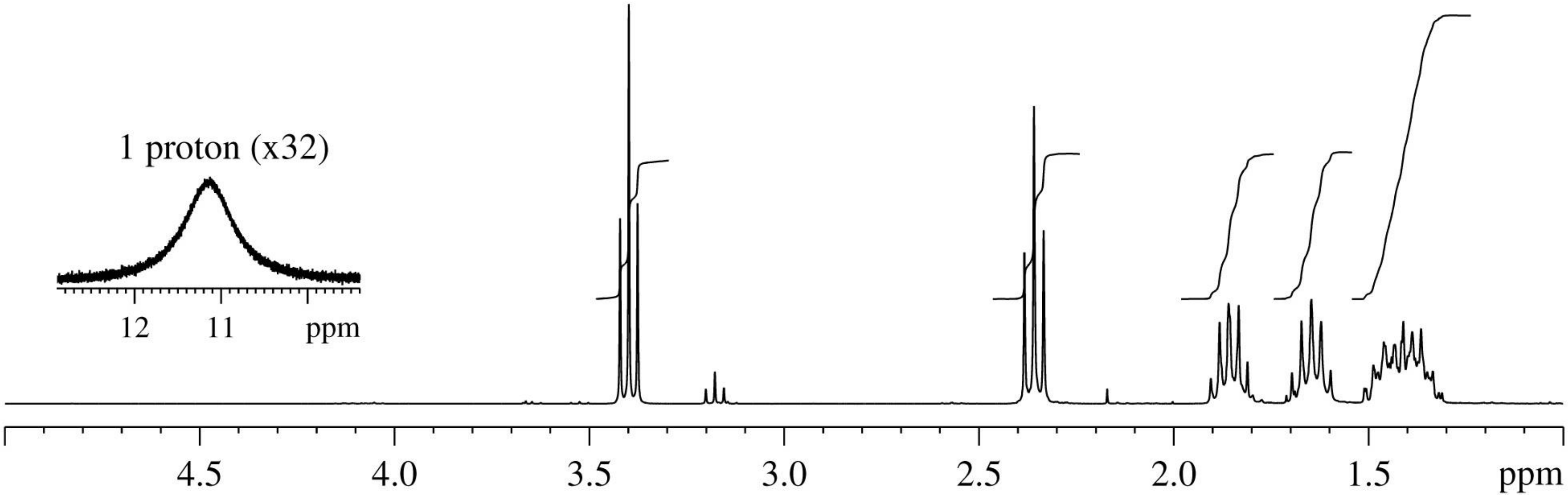
Compound Q





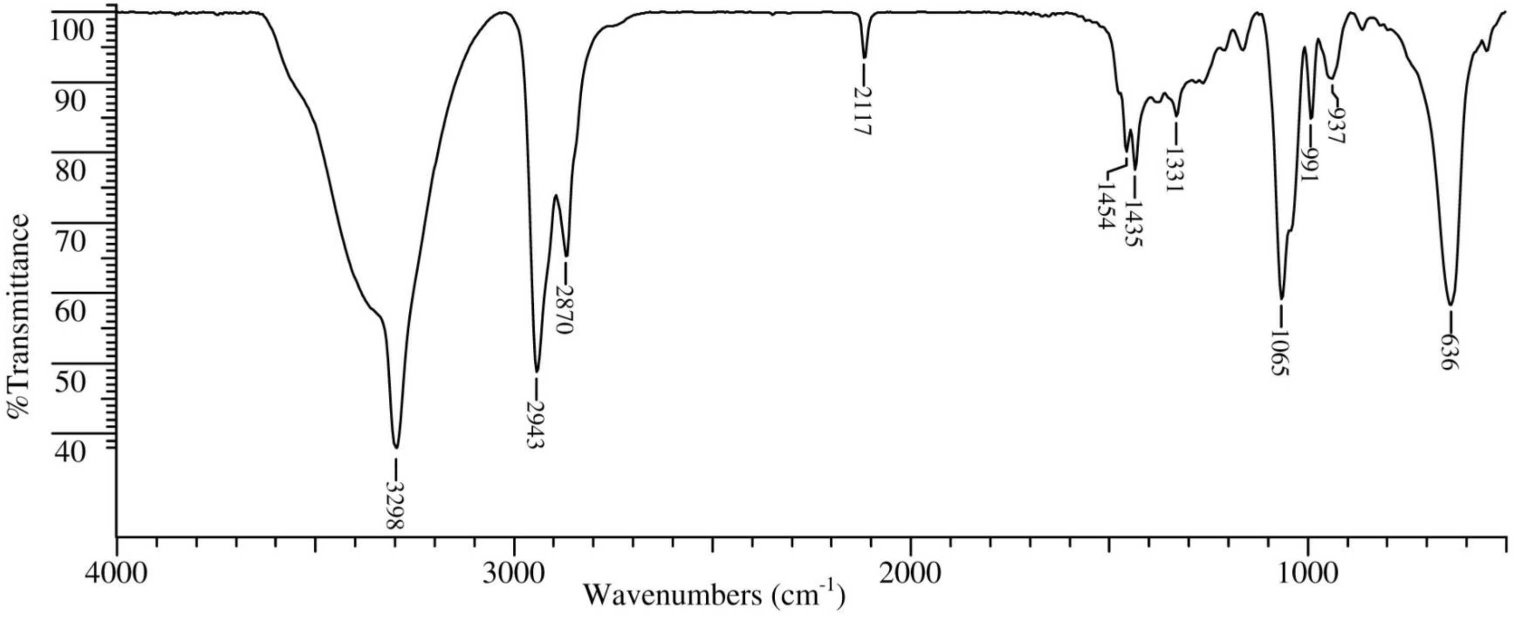
Acid, check. Bromine, check.
Formula, check.
How many isomers can this possibly be

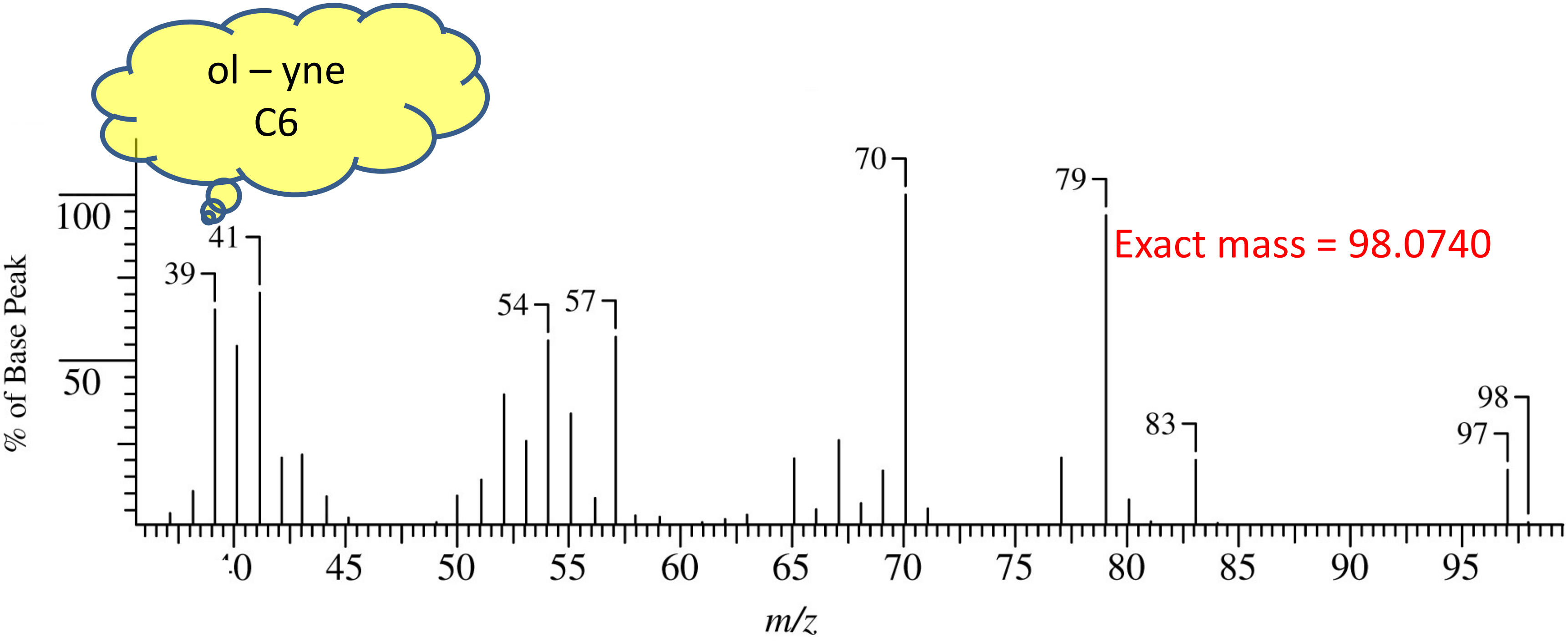
C.I. ⇒ Exact mass = 208.0094



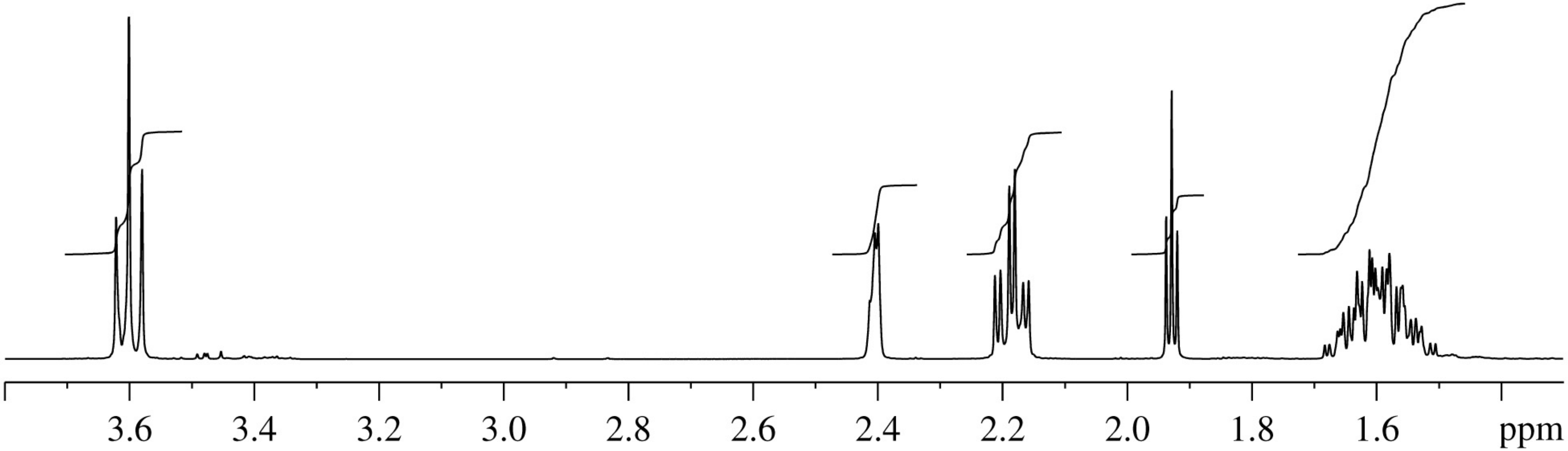
UNO!

Compound R

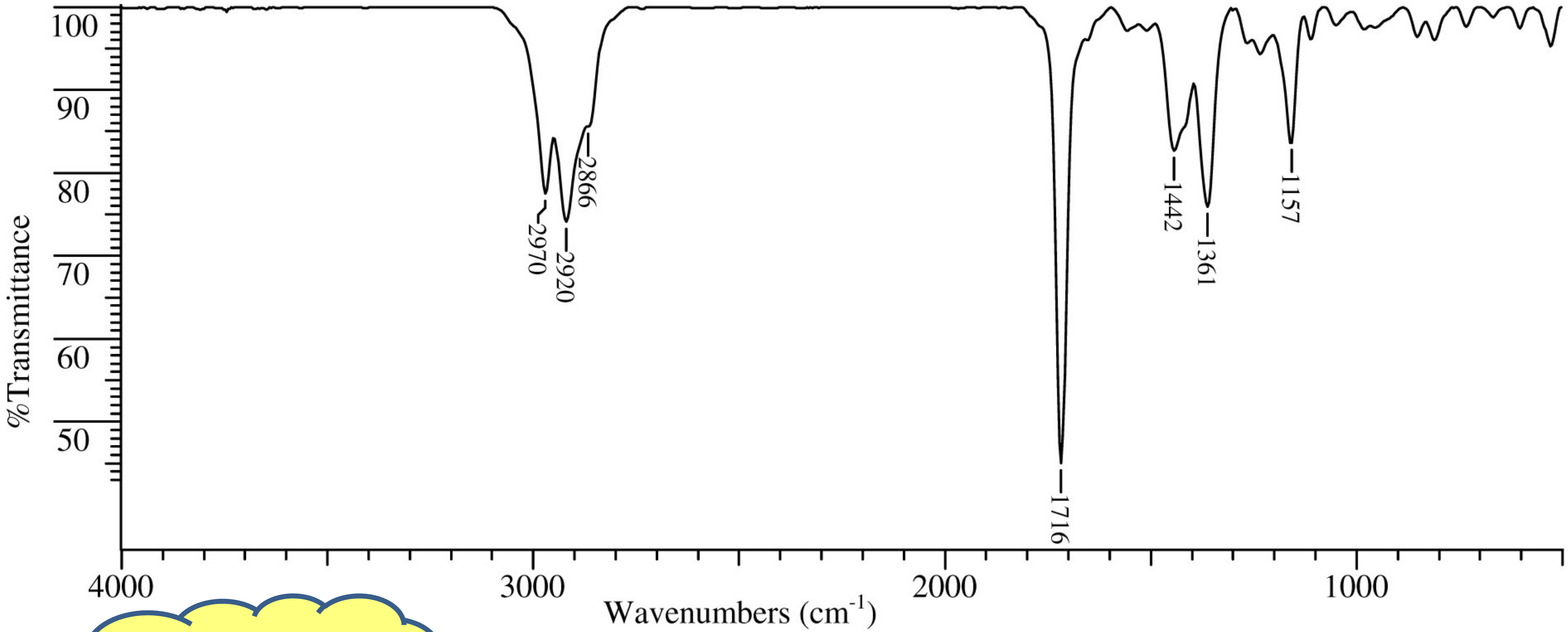



ol – yne
C6

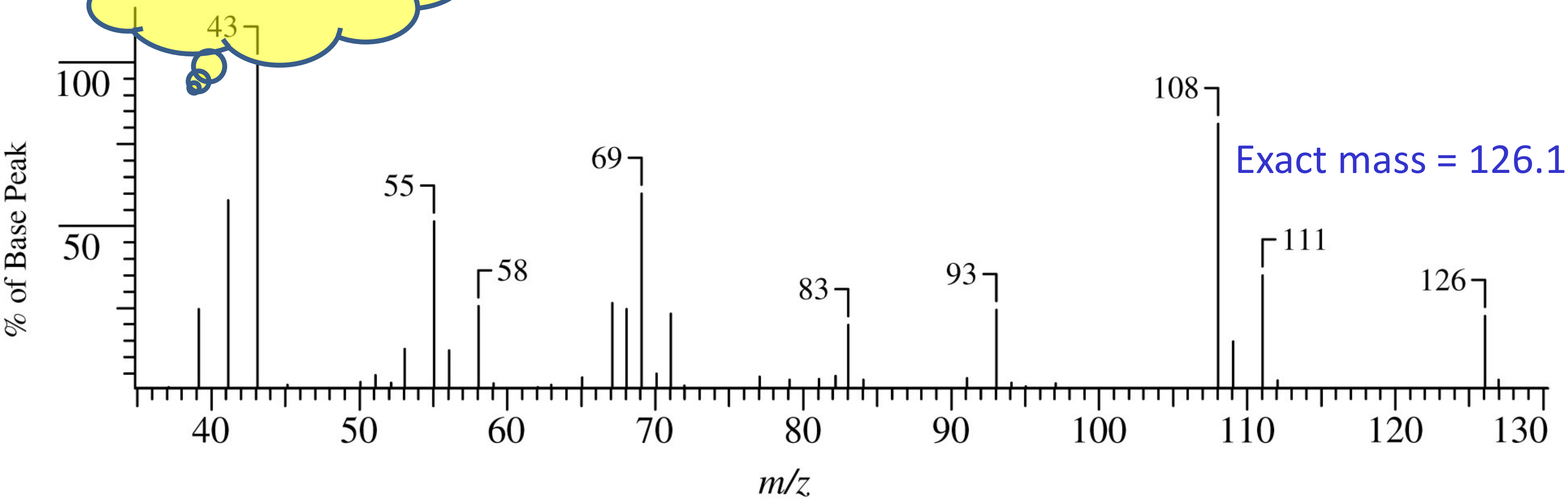
Exact mass = 98.0740


3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
ppm

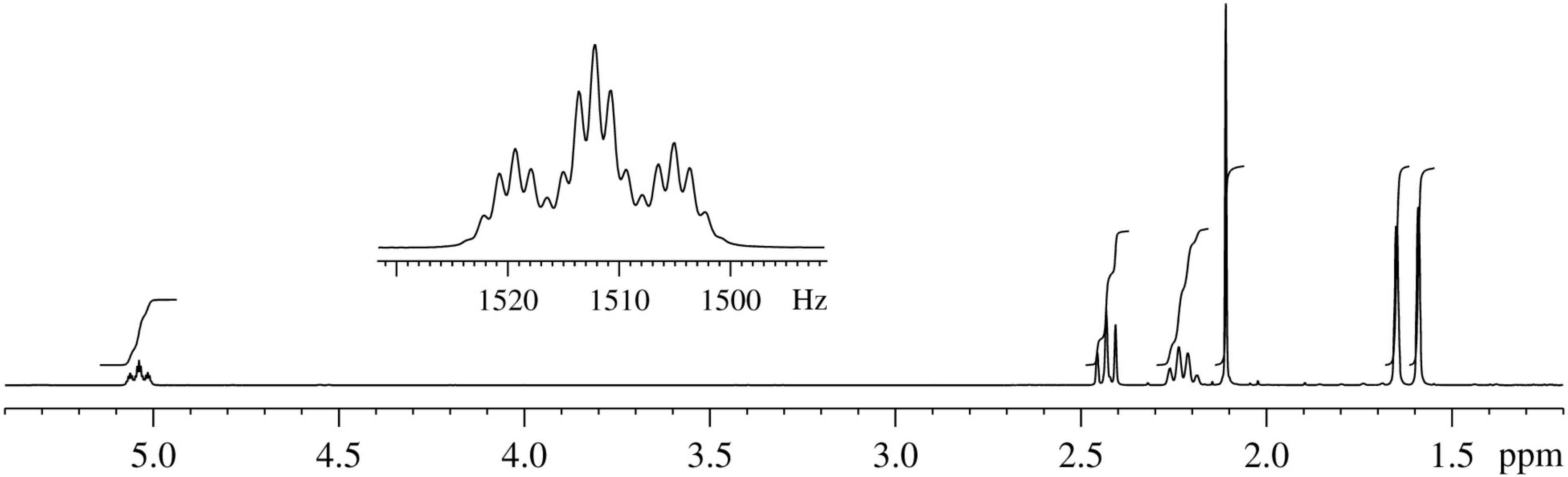
Compound S



ketone

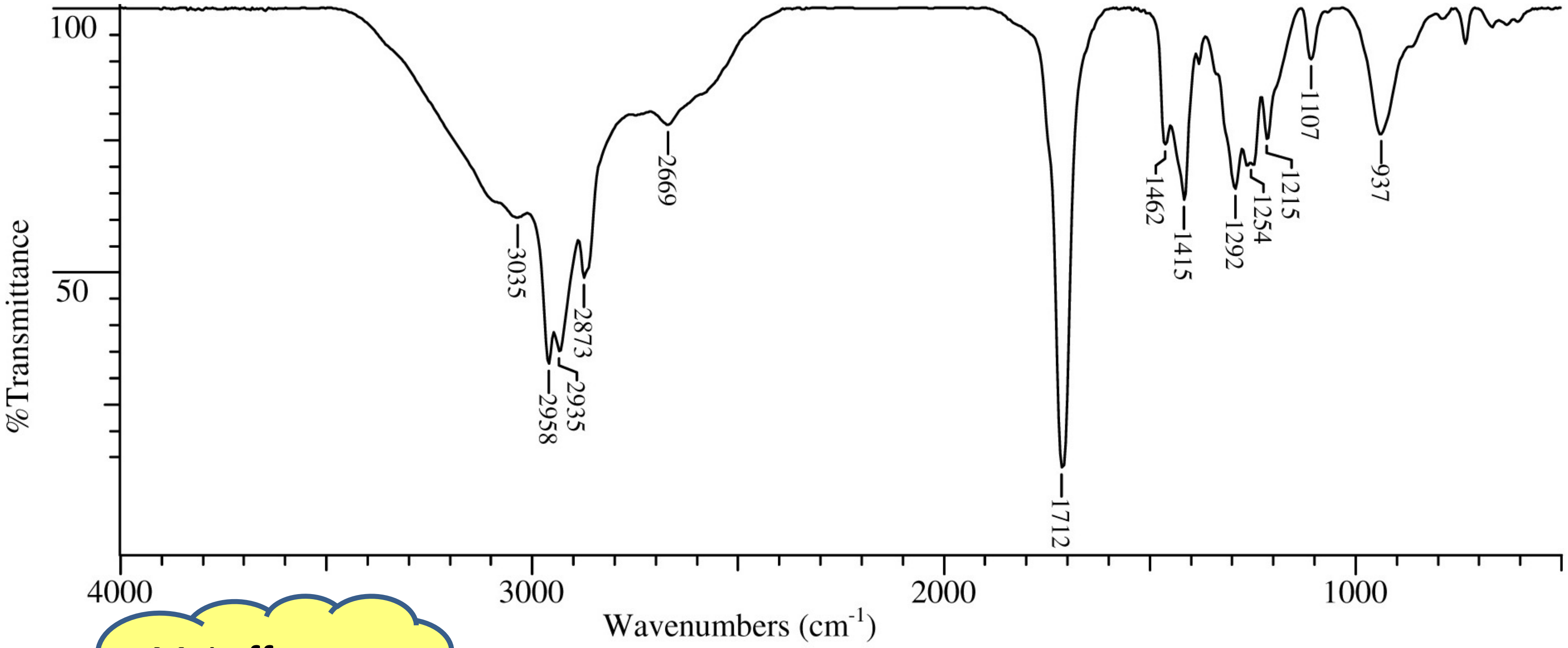


Exact mass = 126.1041

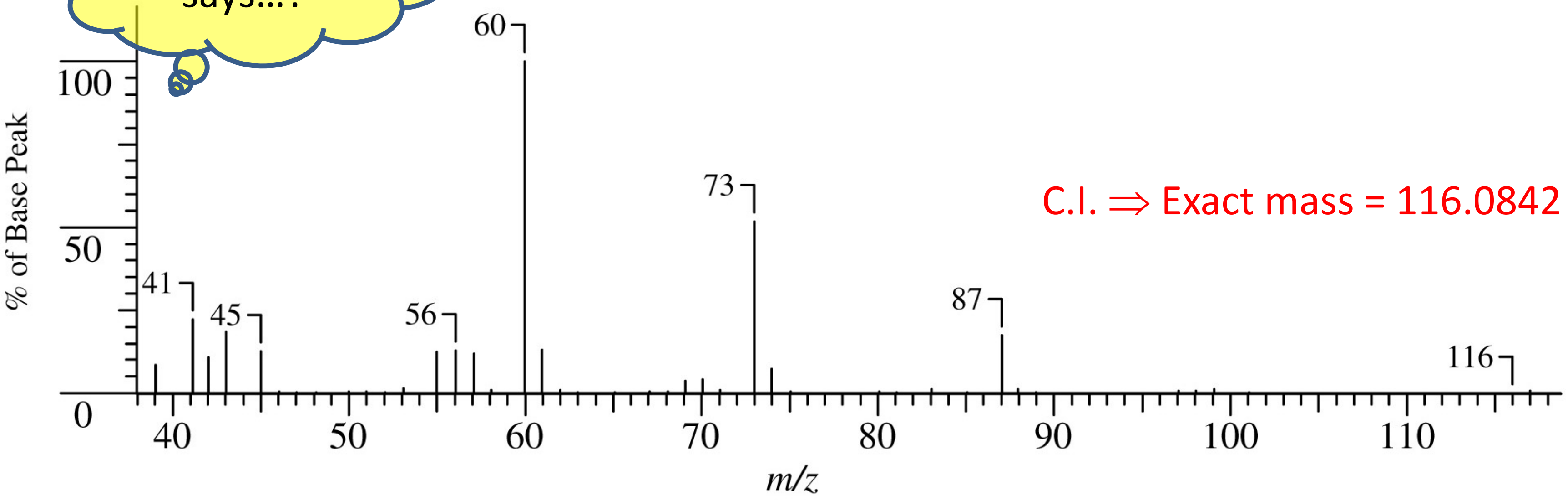


Cool 1H signal at 5.05!

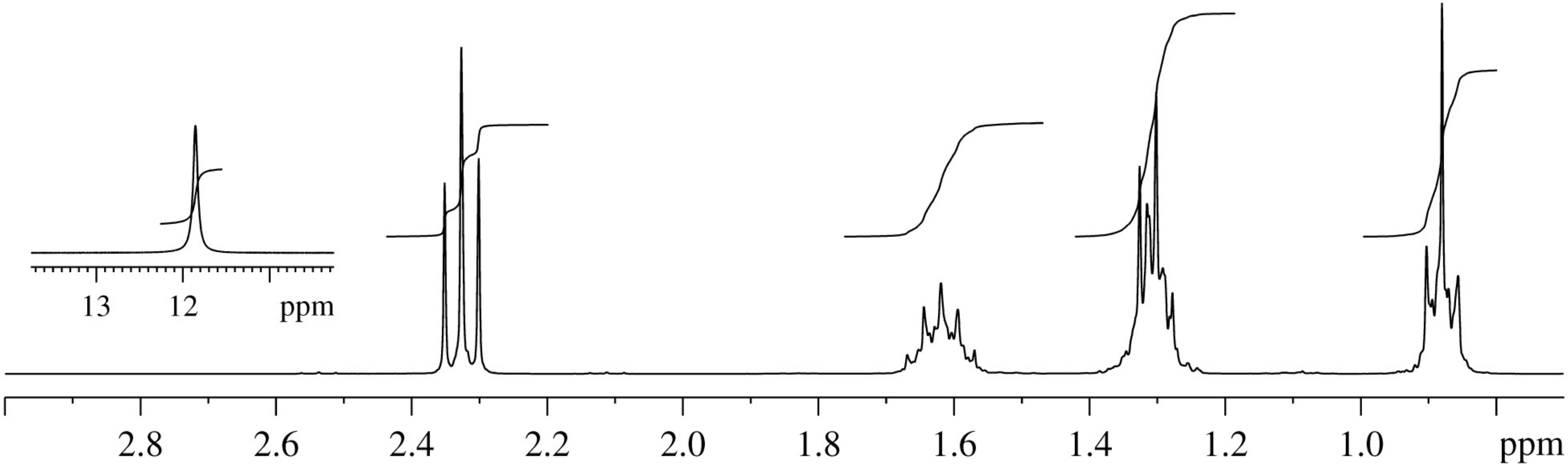
Compound T



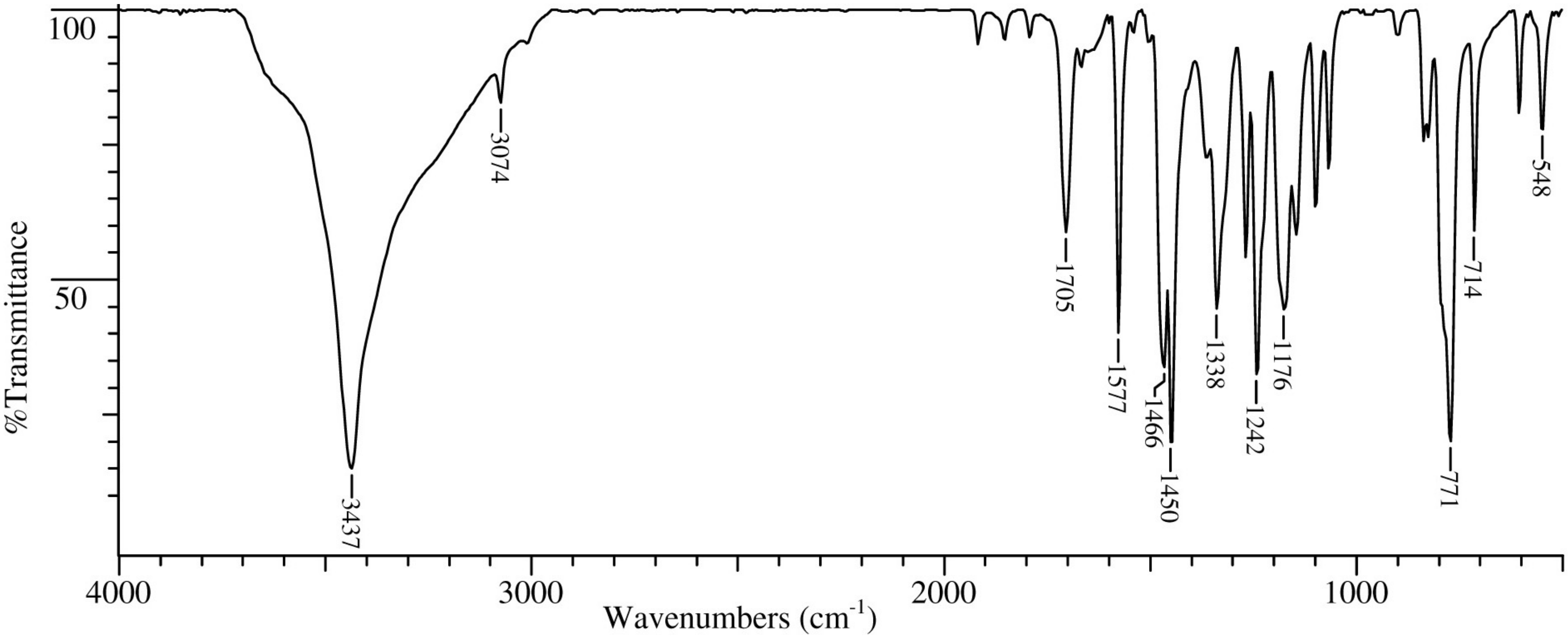
McLafferty says…?



C.I. ⇒ Exact mass = 116.0842

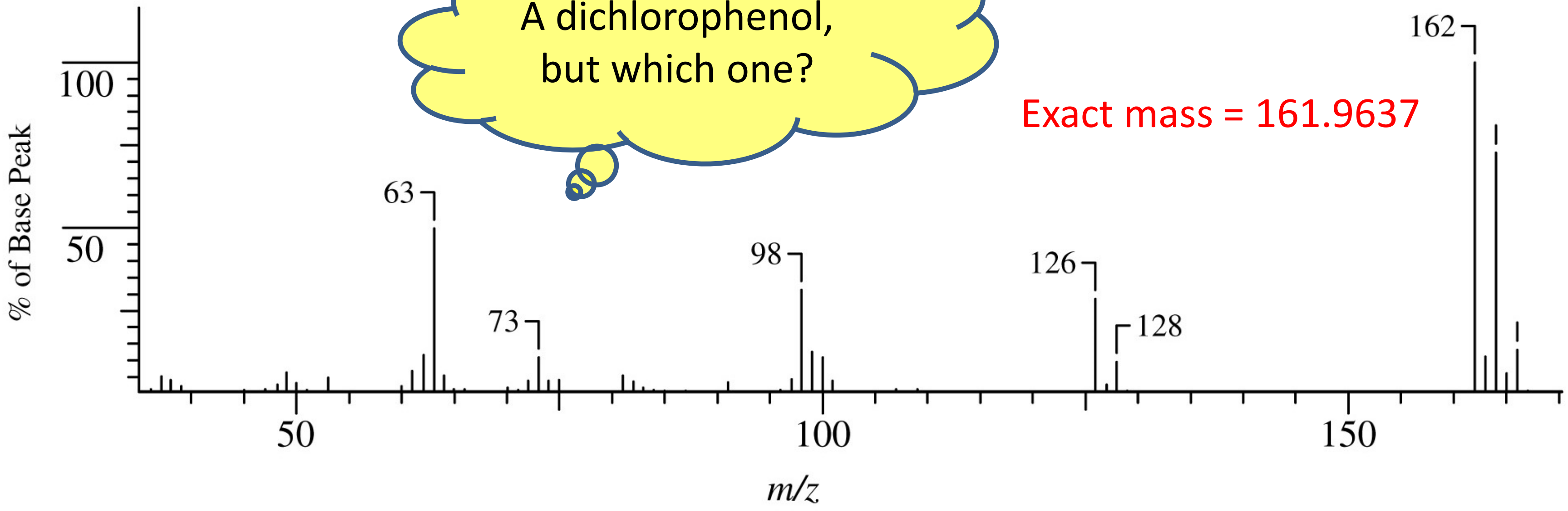

13
12
ppm
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
ppm

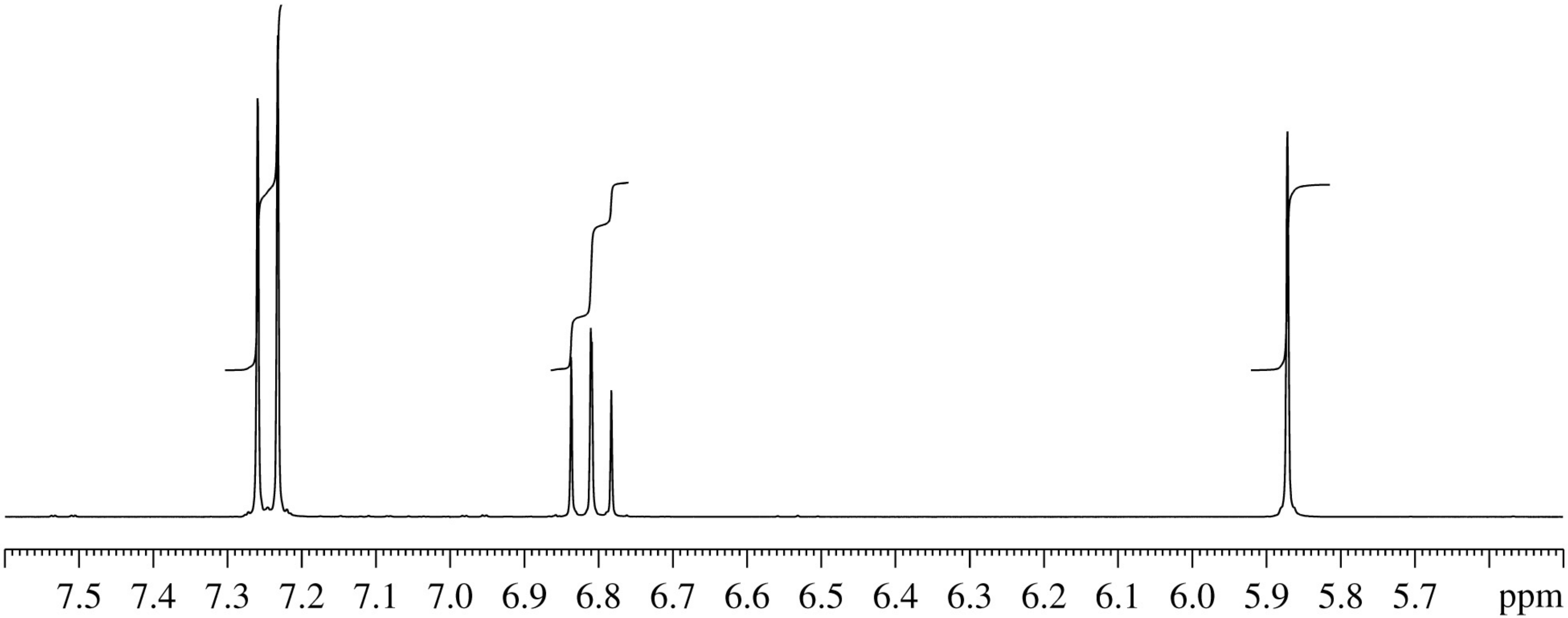
Compound U



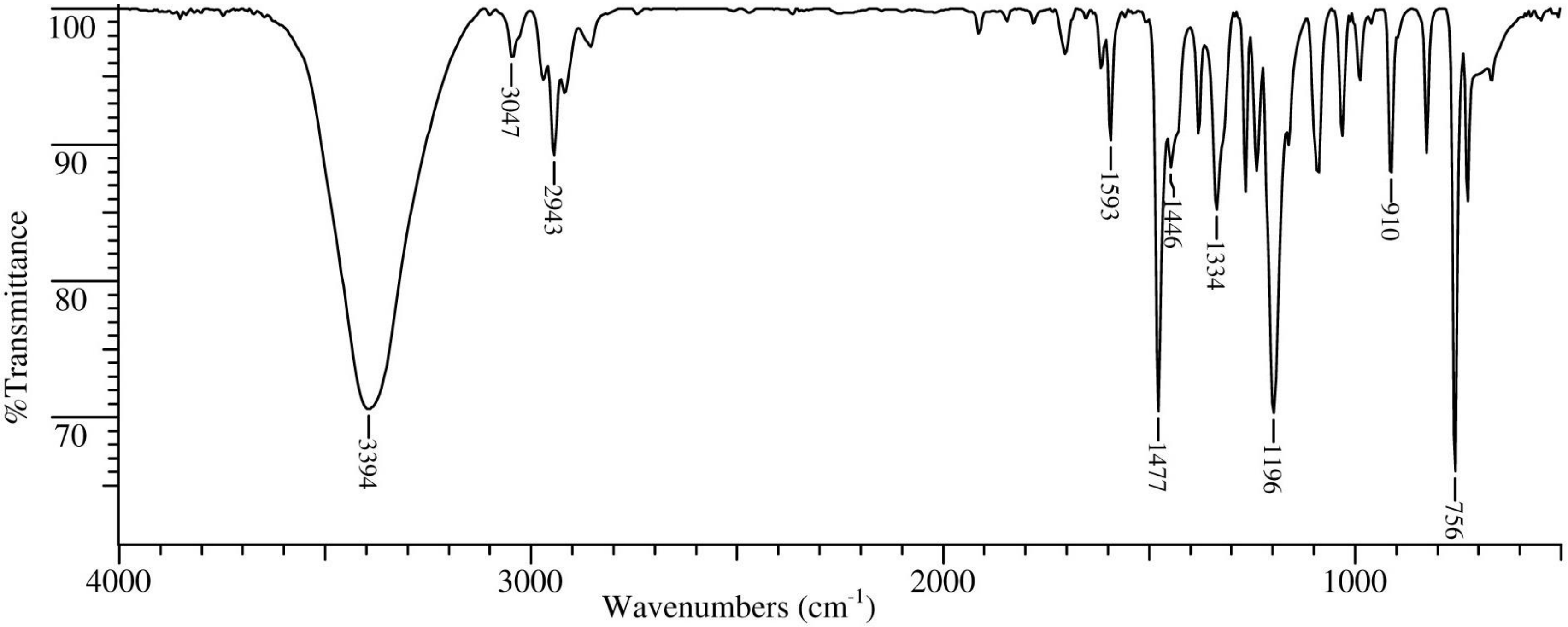
A dichlorophenol,
but which one?

Exact mass = 161.9637

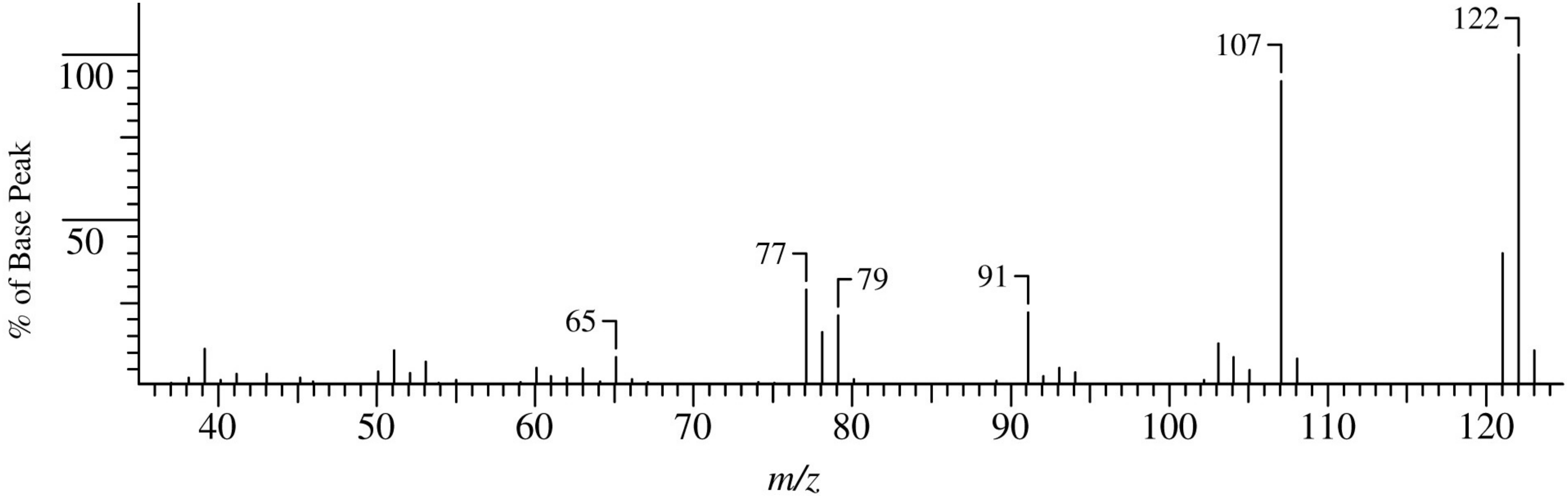


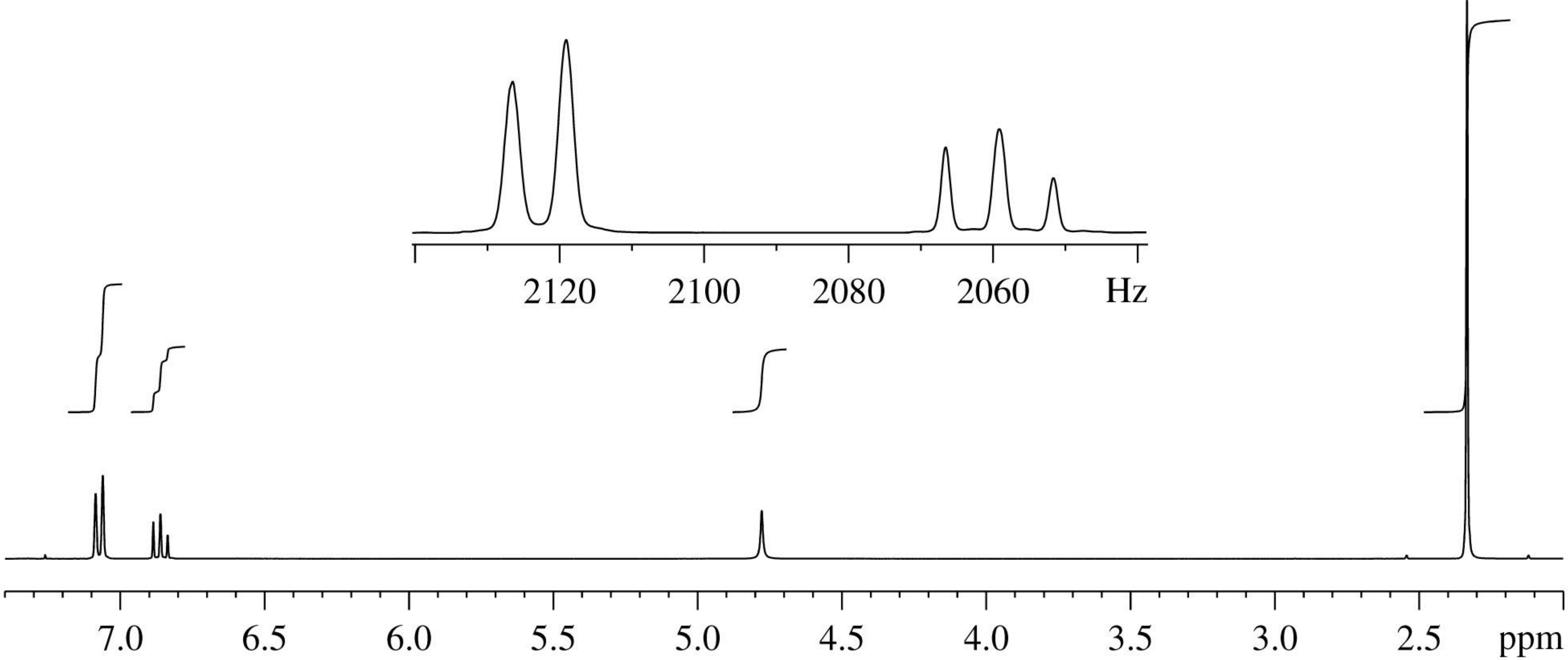

7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
6.5
6.4
6.3
6.2
6.1
6.0
5.9
5.8
5.7
ppm

Compound V

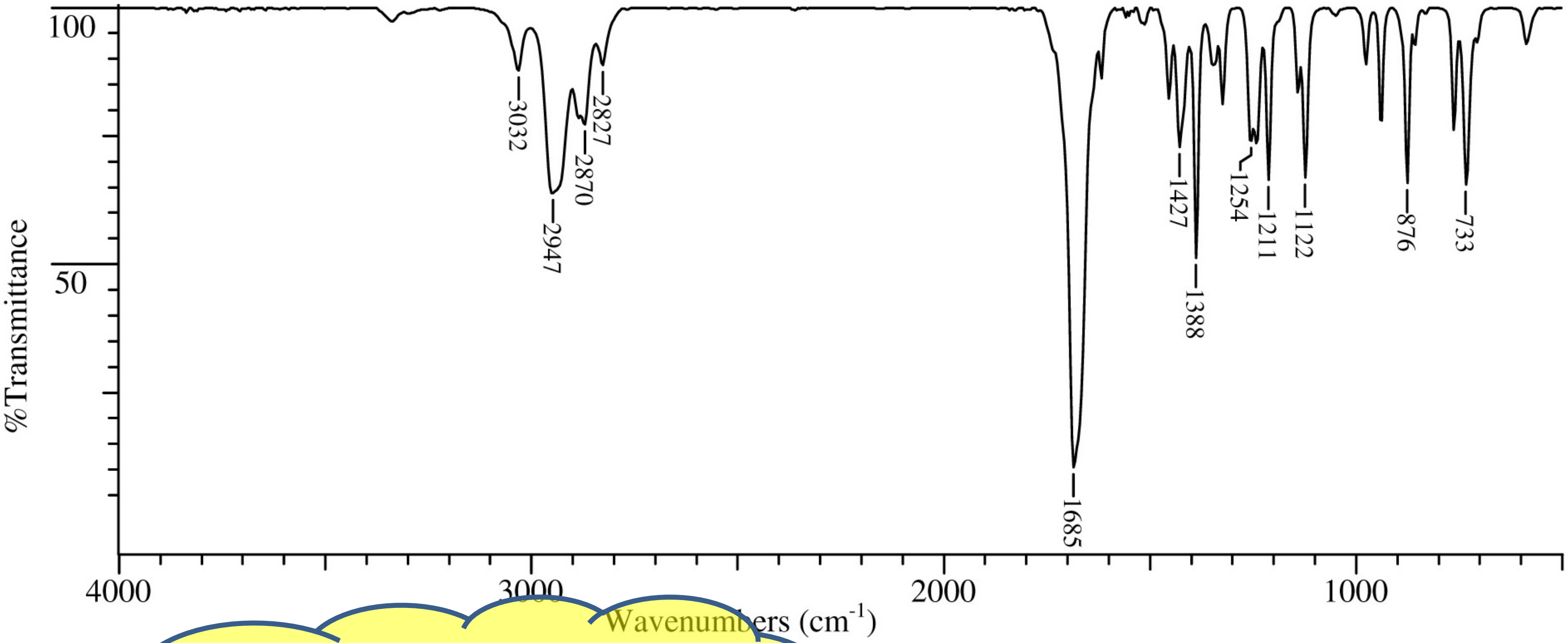


Exact mass = 122.0733

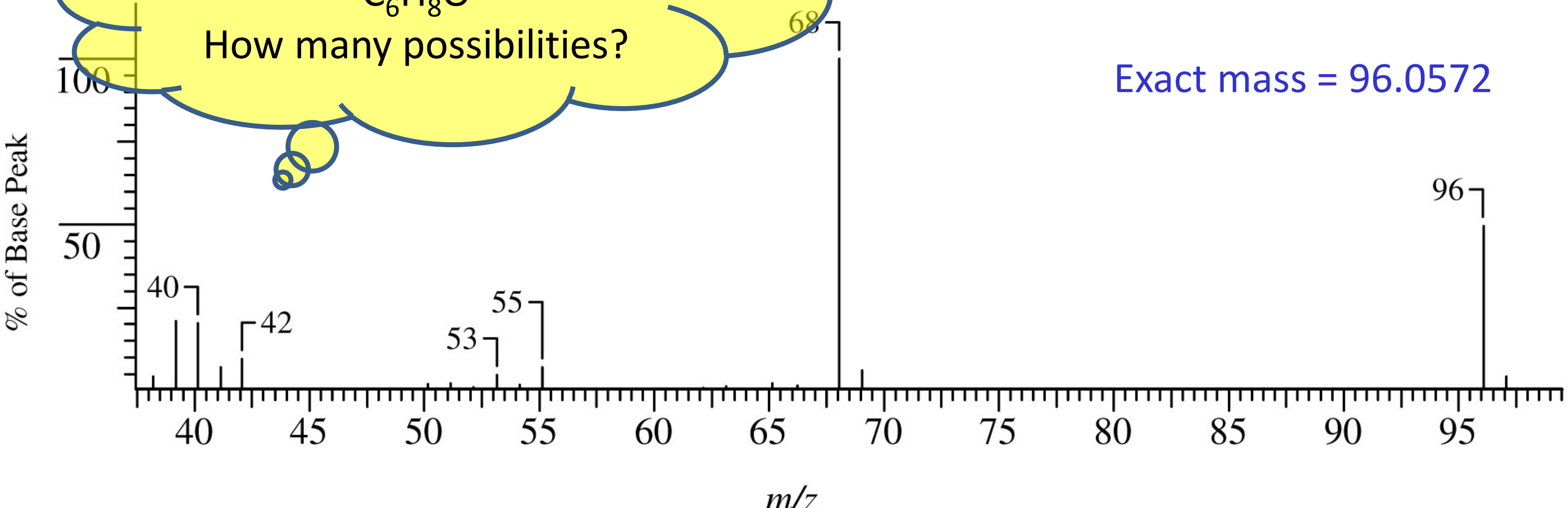



2120
2100
2080
2060
Hz
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm

Compound W



C=O (low freq?); M-28;
C_6H_8O
How many possibilities?



Exact mass = 96.0572

^{13}C NMR SPECTROMETRY

Introduction

^{13}C has nuclear spin (not ^{12}C)

However, ^{13}C is only present at 1.1% abundance

- Signals are weak, sample needs to be more concentrated
- Spectra *usually* acquired without multiplicity information

- Larger range of chemical shifts (0 to >200 ppm)

CHAPTER 4

NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

PART TWO: CARBON-13 SPECTRA, INCLUDING HETERONUCLEAR COUPLING WITH OTHER NUCLEI 177

Types of information available from a ^{13}C NMR spectrum

A ^{13}C nuclear magnetic resonance spectrum contains information about the:

(a) number of different types of carbon

- Each peak corresponds to a different *type* of carbon

(b) type of carbons and proximity to functional groups

- Chemical shift provides information about the type of carbon present

Unlike ^{1}H NMR spectra, simple ^{13}C NMR spectra *do not* provide information about the:

relative number of each type of proton

(no integrals)

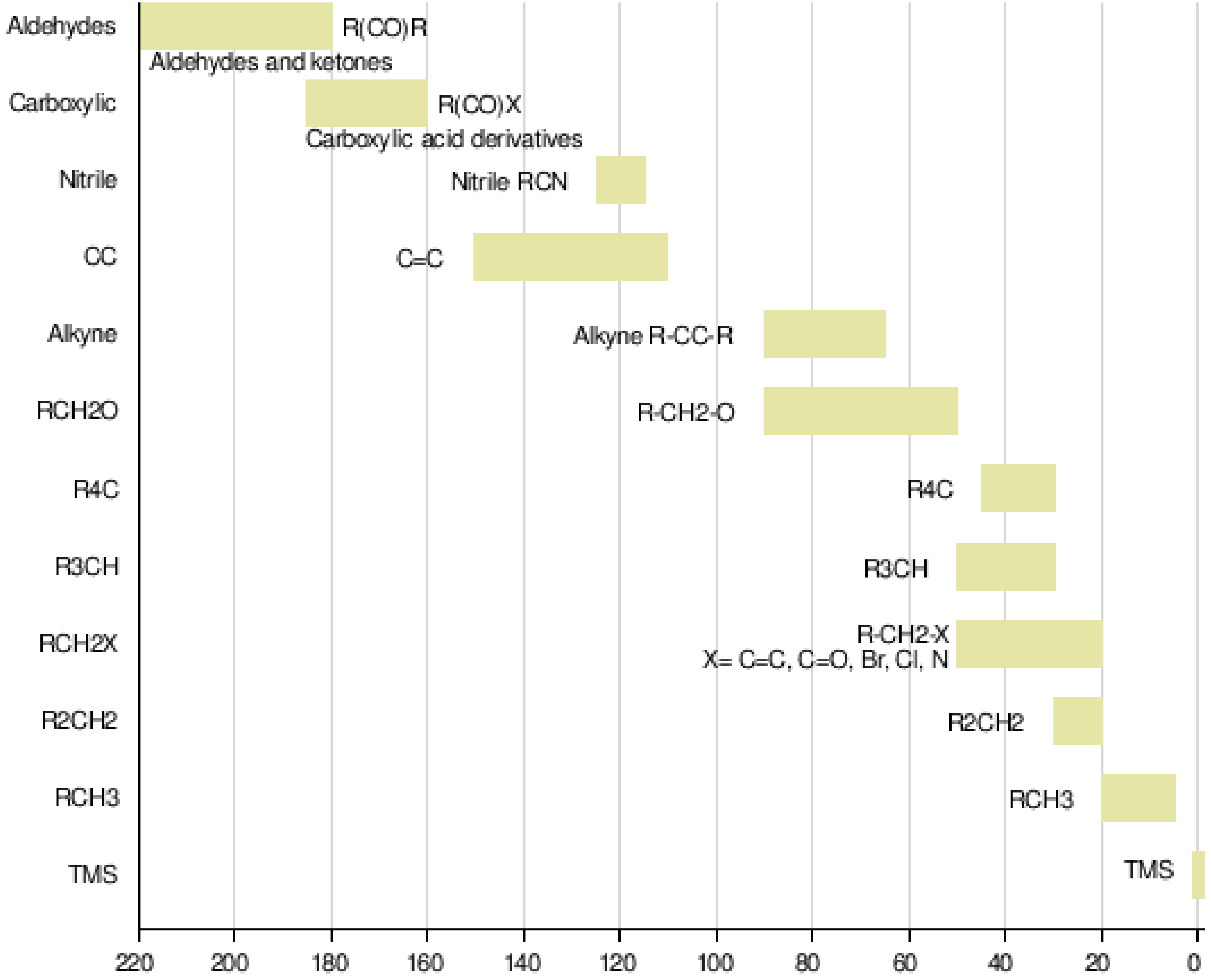
or

number of adjacent protons or carbons

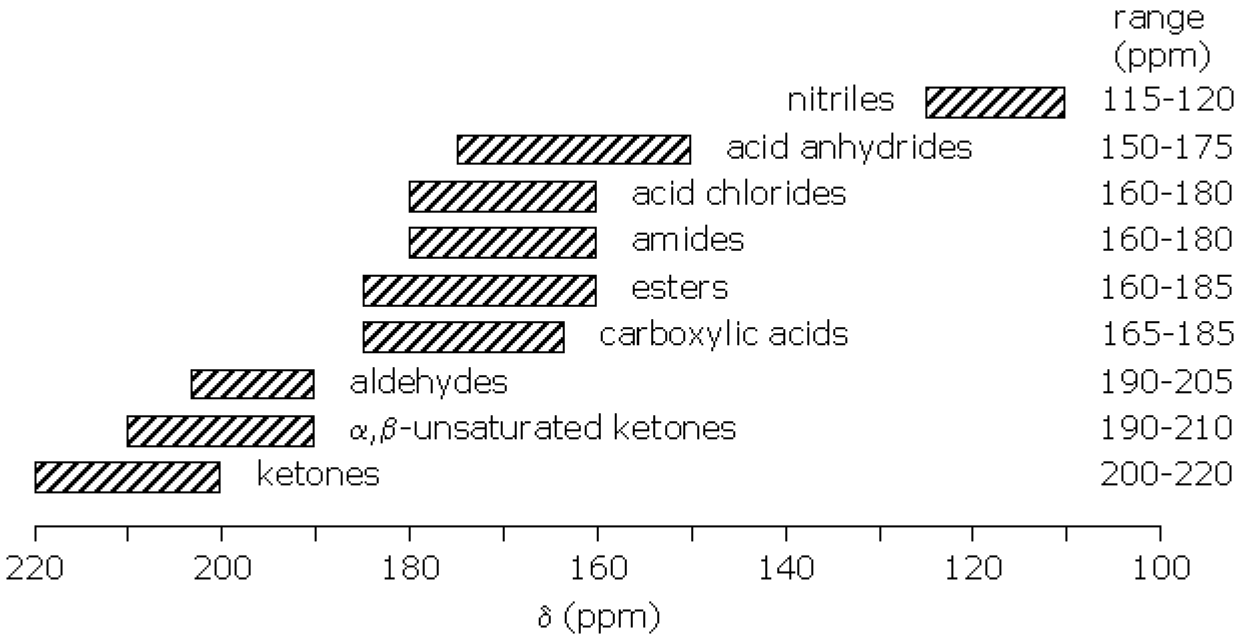
(no coupling)

More advanced techniques, covered later in the class, allow you to collect this information. This might be useful In solving some structural problems.

Chart of general ^{13}C chemical shifts



^{13}C chemical shifts: Carbonyls



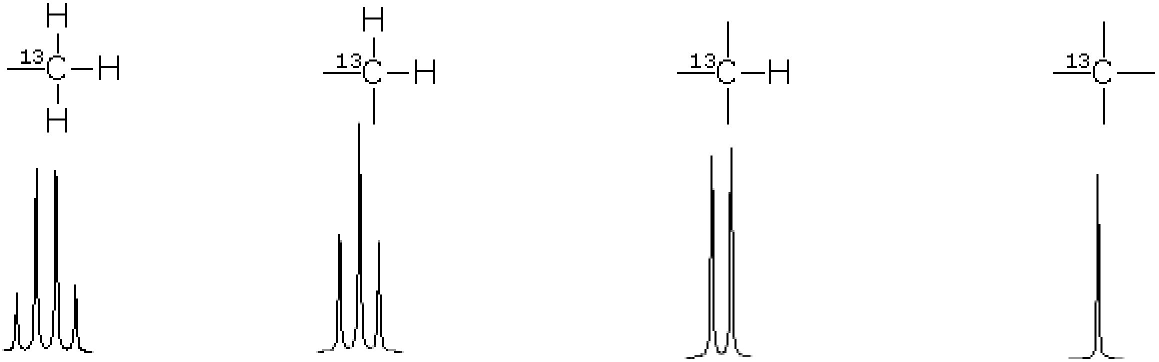
http://www.chemistry.ccsu.edu/glagovich/teaching/316/nmr

^{1}H-coupled and “decoupled” ^{13}C spectra

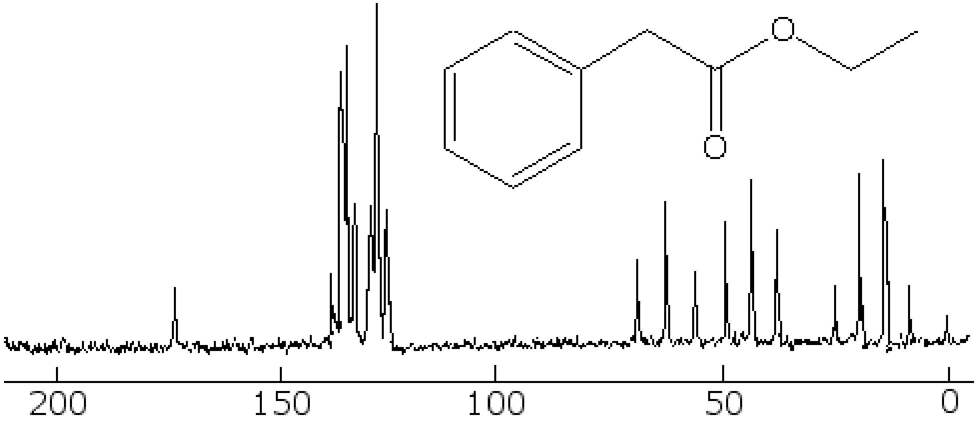
Coupling Constants

^{13}C–^{1}H	^{2}J (Hz)
sp^{3}	115-125
sp^{2}	150-170
sp	240-270

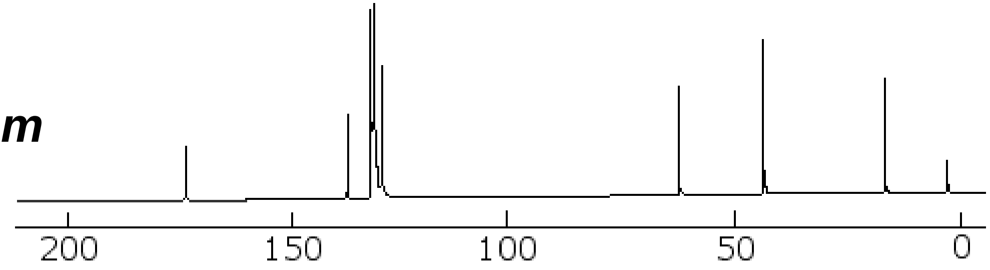
Splitting due to attached ^{1}H



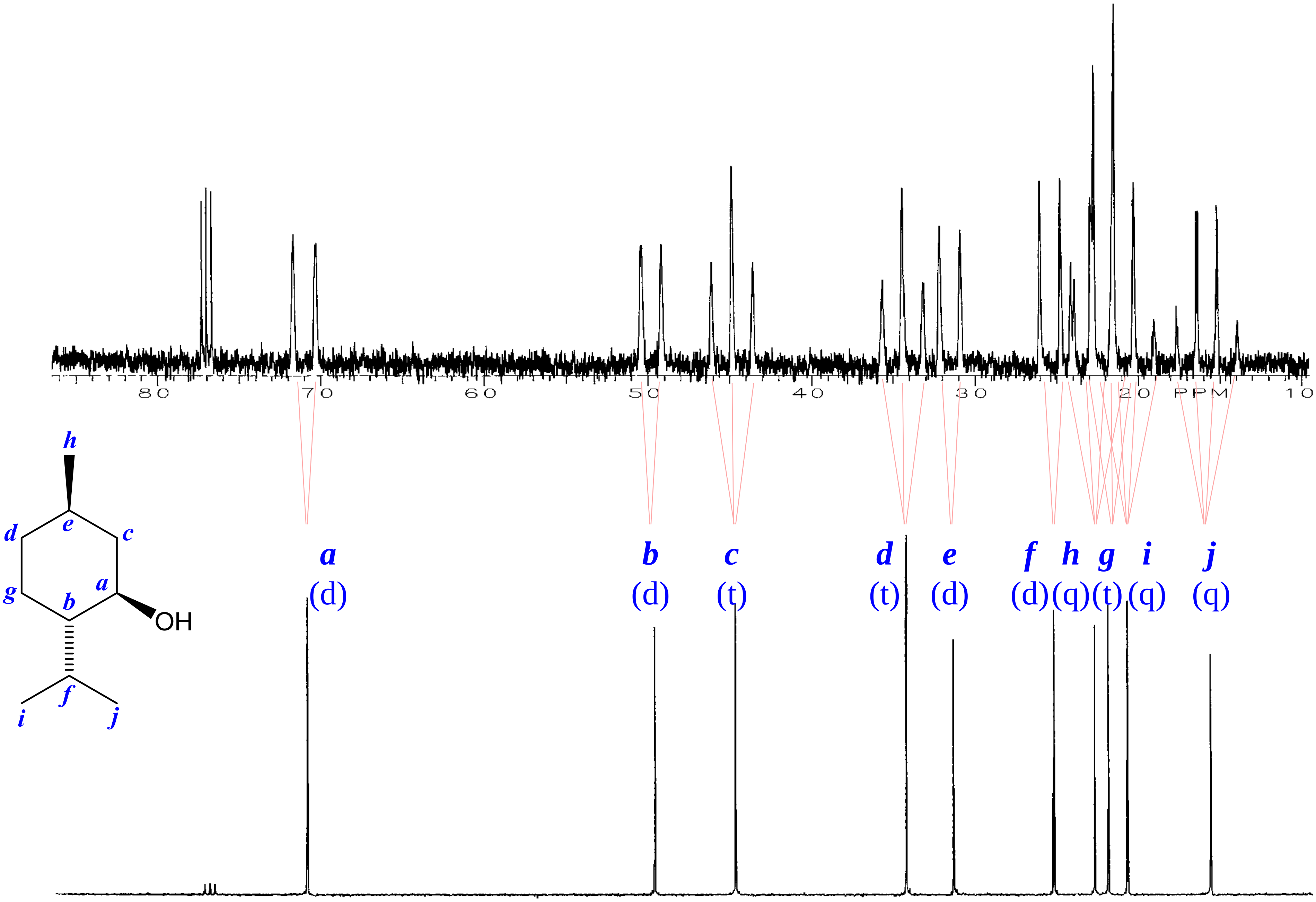
^{1}H coupled ^{13}C spectrum



^{1}H decoupled ^{13}C spectrum



http://www.chemistry.ccsu.edu/glagovich/teaching/316/nmr



80
70
60
50
40
30
20
PPM
10
h
e
d
c
a
g
b
OH
f
i
j
a (d)
b (d)
c (t)
d (t)
e (d)
f (d)
h (q)
g (t)
i (q)
j (q)

Attached Proton Test (APT)

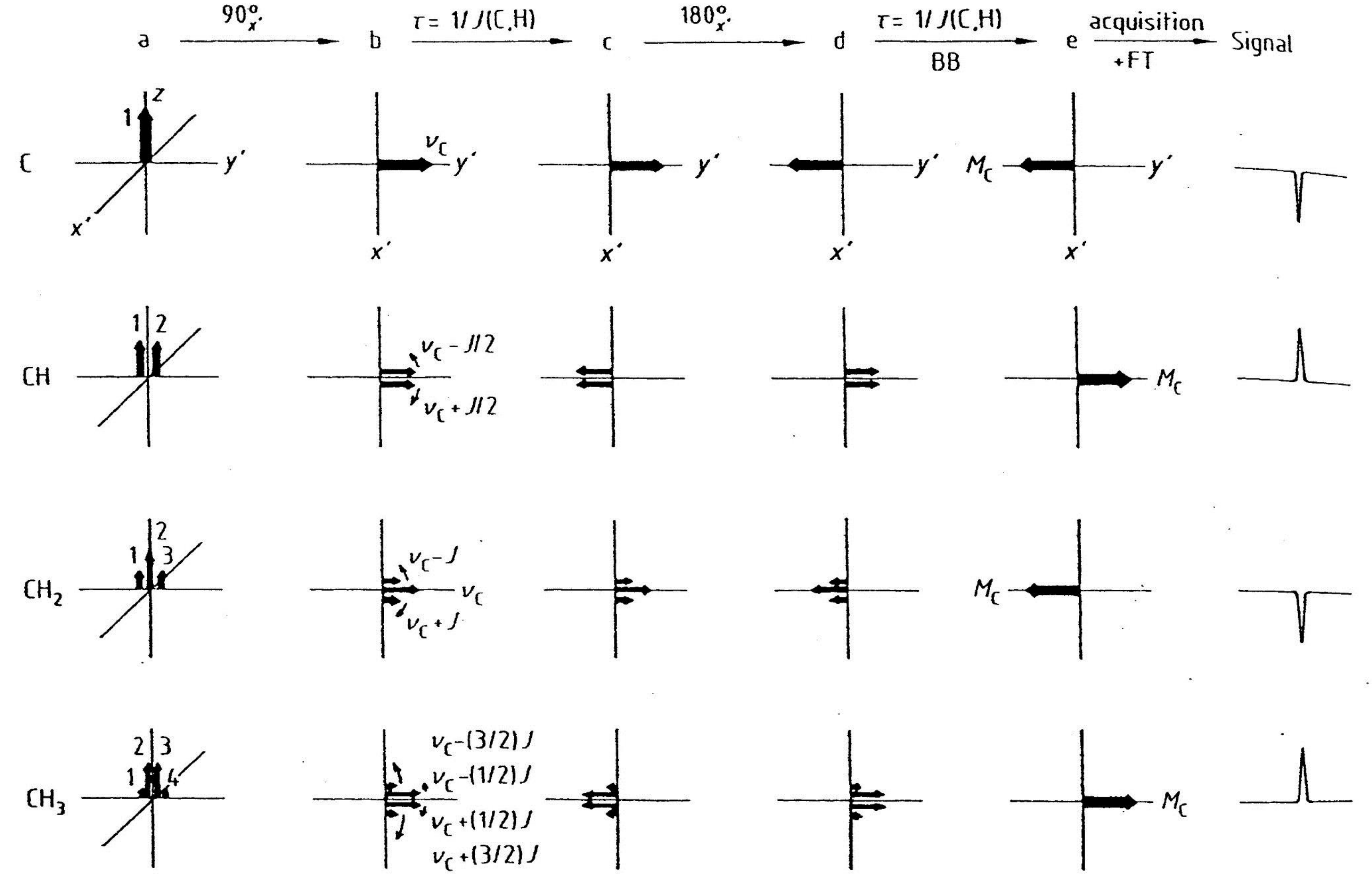


Figure 8-11

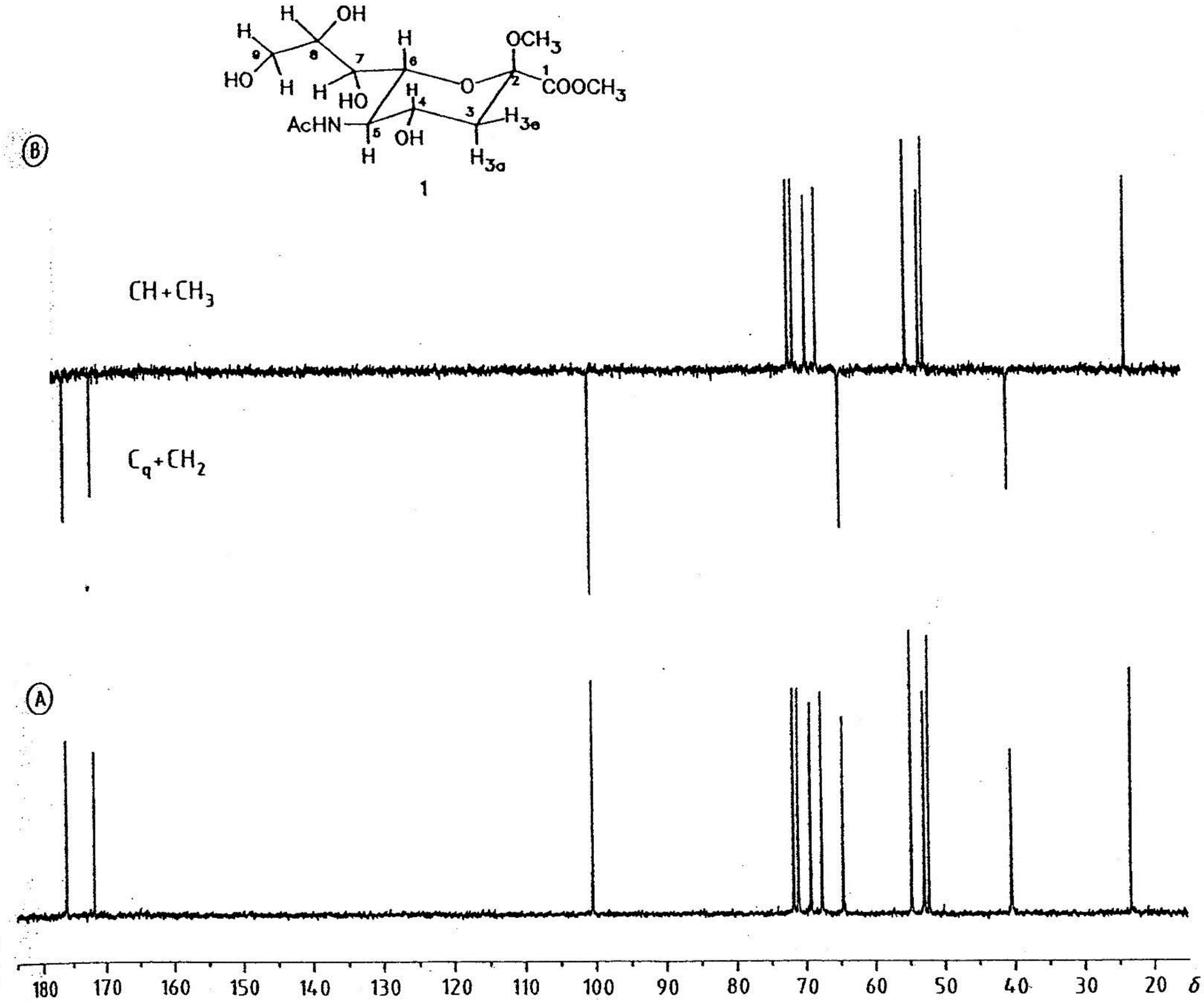


Figure 8-12.
Example of a *J*-modulated spin-echo experiment.
A: 50.3 MHz ^{13}C NMR spectrum of the neuraminic acid derivative **1** with ^{1}H BB decoupling.
B: 50.3 MHz ^{13}C NMR spectrum of the same sample, recorded using the *J*-modulated spin-echo pulse sequence (Fig. 8-9 A). Signals with positive amplitudes are assigned to CH or CH$_3$ groups, those with negative amplitudes

Selective Population Inversion (SPI)

Polarization transfer and spectrum

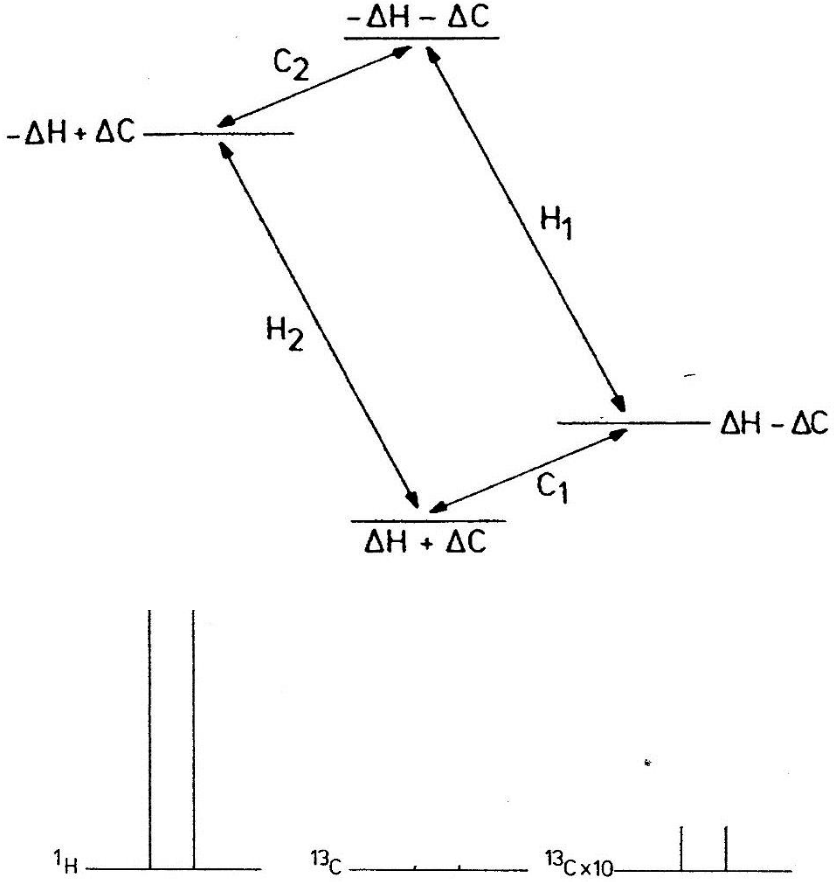


Figure 6.1 Energy levels and populations of a heteronuclear AX system.

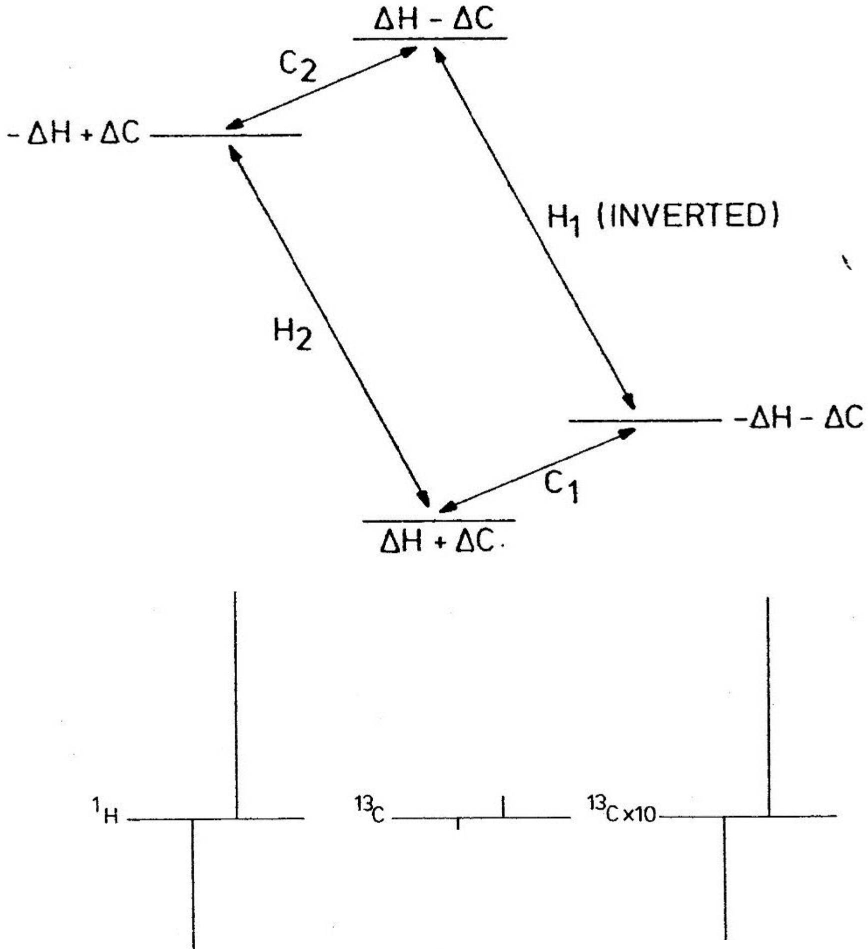
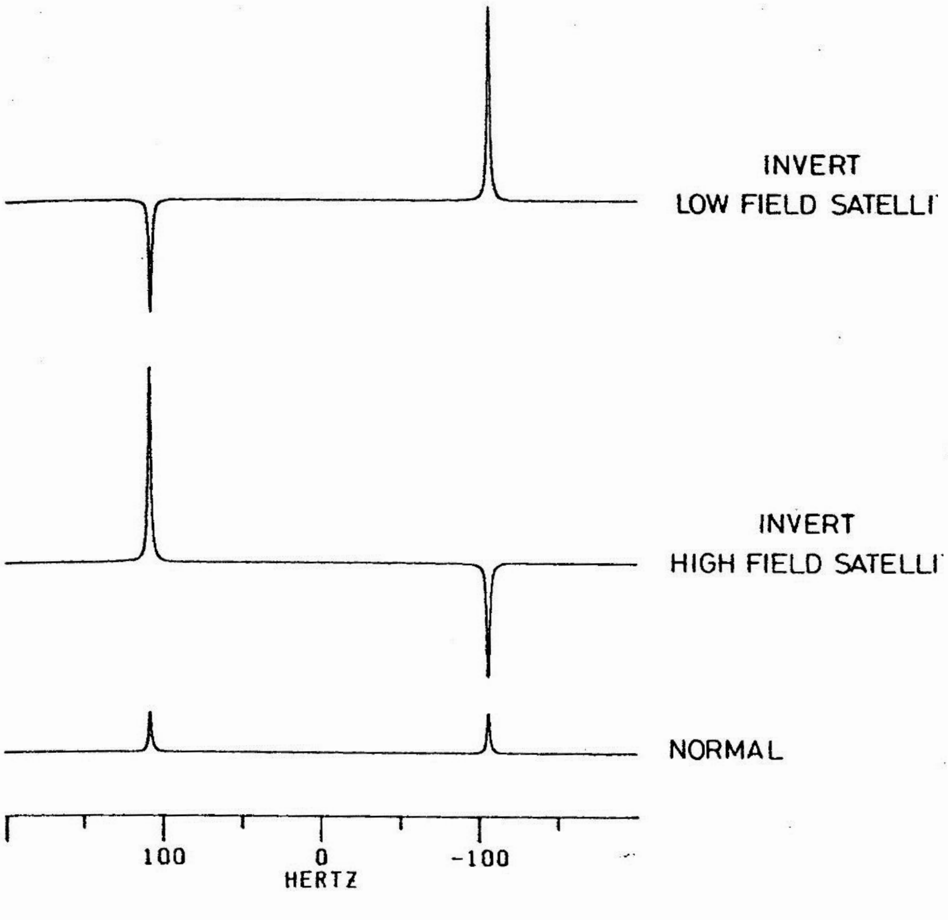


Figure 6.2 The new populations after inverting one of the H transitions.

Spectrometric Identification of Organic Compounds,7th Ed. Silverstein etal, Wiley ,2005

Insensitive Nucleus Enhancement through Polarization Transfer (INEPT)



The basic idea

The major limitation of SPI is its lack of generality. If we could find some way to set up the appropriate polarisation of *all* proton transitions regardless of frequency, we would evidently have a very promising experiment. We need a sequence which puts pairs of proton transitions into antiphase, as in SPI, but using non-selective pulses and in a manner independent of chemical shifts. This can be done using a spin echo to prepare multiplet components along selected axes:

$$\begin{array}{lccccccc} \text{S:} & \left(\frac{\pi}{2}\right)_x & — \tau — & \pi_x & — \tau — & \left(\frac{\pi}{2}\right)_y & \\ \text{I:} & & & \pi_x & & \left(\frac{\pi}{2}\right)_x & \textit{Acquire} \cdots \end{array}$$

In this notation, which was used in the first paper on INEPT[2] (Insensitive Nuclei Enhanced by Polarisation Transfer), S stands for the sensitive nucleus and I for the insensitive one (^{1}H and ^{13}C respectively in our example). Irritatingly this convention is not always followed, and it is common to see the source nucleus labelled I and the destination S in many of the huge number of publications that have been stimulated by the original idea. It is only an arbitrary convention, of course, but it would be nice if a little consistency could be achieved. Throughout this chapter, S will be used to label the source nucleus, and I that to which magnetisation is transferred (irrespective of whether S is in fact more 'sensitive' than I).

We can follow the effect of this sequence easily for an AX system with coupling constant J (Figure 6.4). The delay τ is set to $1/4J$, so doublet components (which precess in the rotating frame at $\pm J/2$ Hz) move through 1/8'th of a cycle up to the π pulses. The S spin π pulse rotates these components into the second half of the x-y plane, while that on the I spins ensures that the coupling is not refocused by reversing the sense of their precession. During the second τ interval chemical shifts and inhomogeneity *are* refocused of course, so they have been omitted from consider-

Spectrometric Identification of Organic Compounds,7th Ed. Silverstein etal, Wiley ,2005

Figure 6.4 INEPT sequence for an AX system.

one up and one down. This corresponds with the desired antiphase polarisation of the doublet, so the $\pi/2$ pulse on I elicits an enhanced response as in SPI (Figure 6.5).

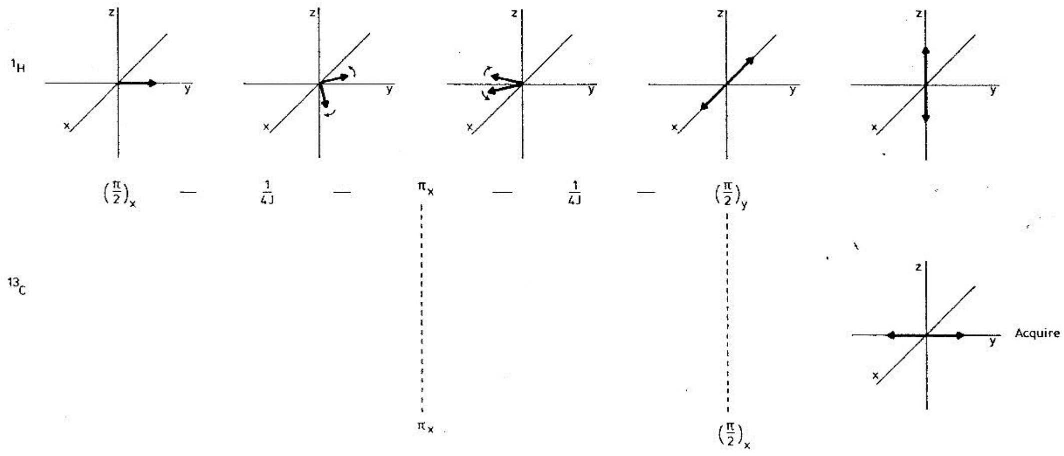
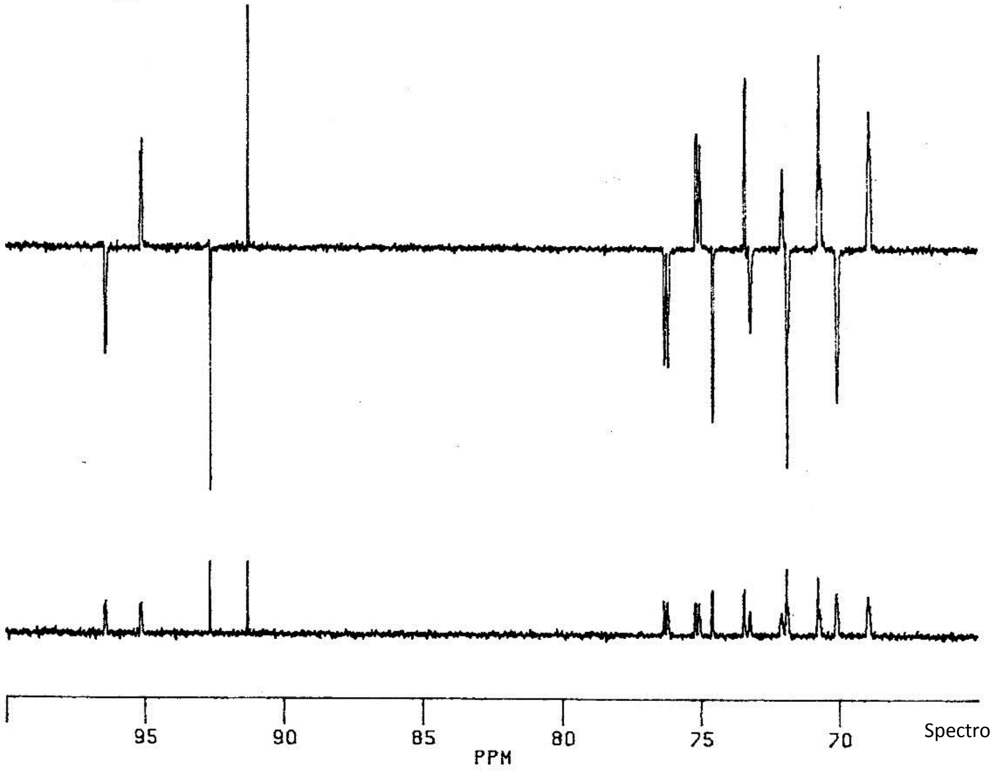


Figure 6.5 INEPT does for many doublets what SPI did for one.



Spectrometric Identification of Organic Compounds,7th Ed. Silverstein etal, Wiley ,2005

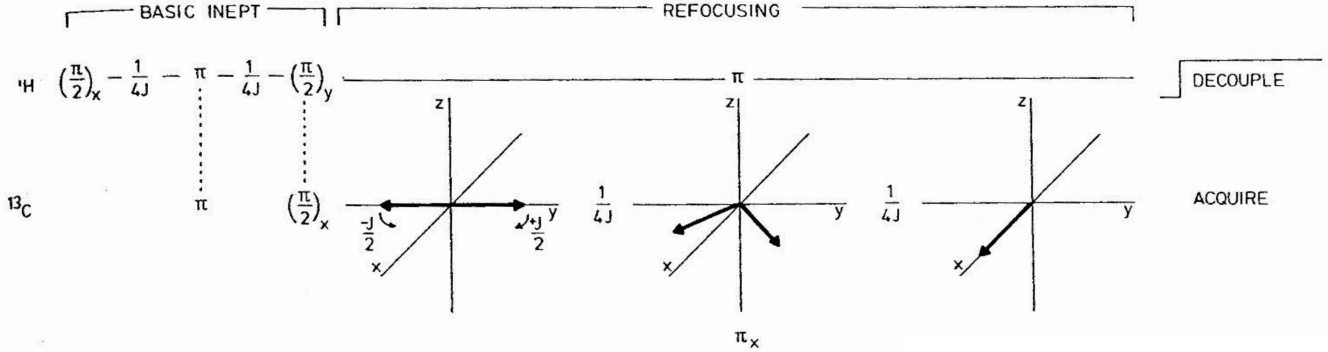


Figure 6.8 Refocusing for an AX system; this allows the use of broadband decoupling during acquisition.

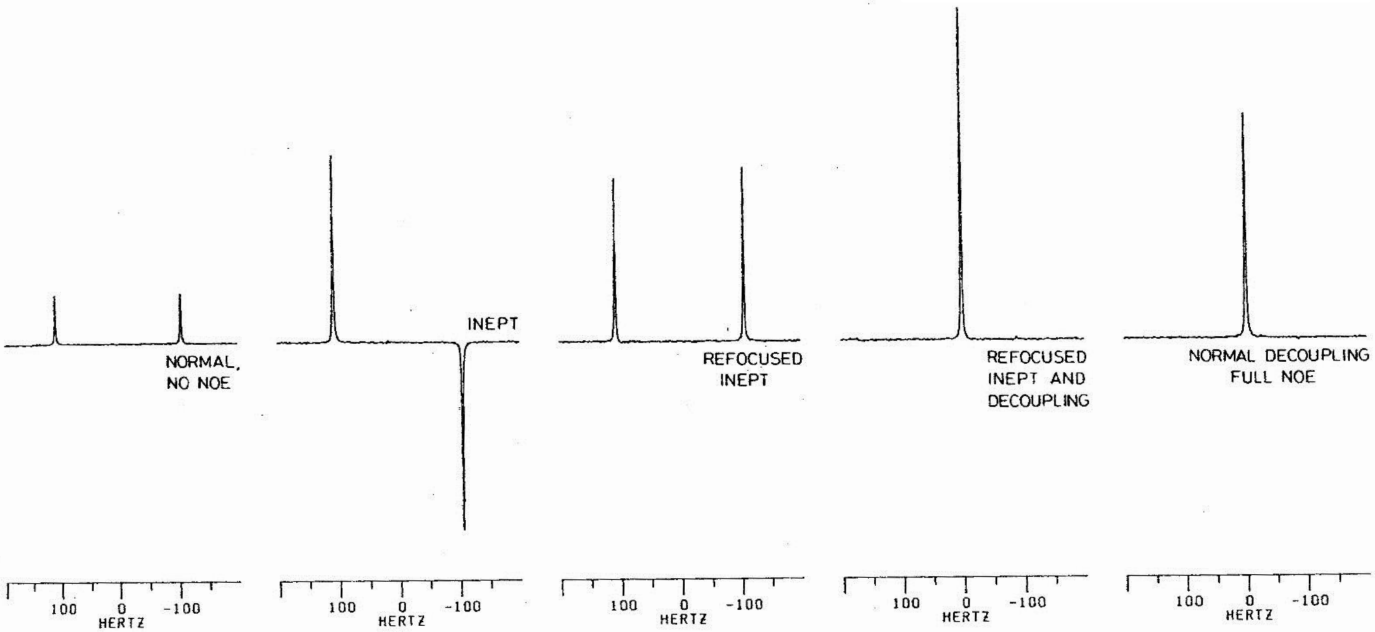


Figure 6.9 Permutations on the spectrum of chloroform. It can be seen that the refocused INEPT spectrum shows some loss of intensity as compared with simple INEPT; this is partly due to transverse relaxation during the refocusing period, and partly to imperfections in pulses.

on the ratio of gyromagnetic ratios, so the true comparison we should make is:

INEPT†: $$I = I_0 \left| \frac{\gamma_S}{\gamma_I} \right|$$

NOE: $$I = I_0 \left(1 + \frac{\gamma_S}{2\gamma_I} \right)$$

Spectrometric Identification of Organic Compounds,7th Ed. Silverstein etal, Wiley ,2005

Distortionless Enhancement through Polarization Transfer (DEPT)

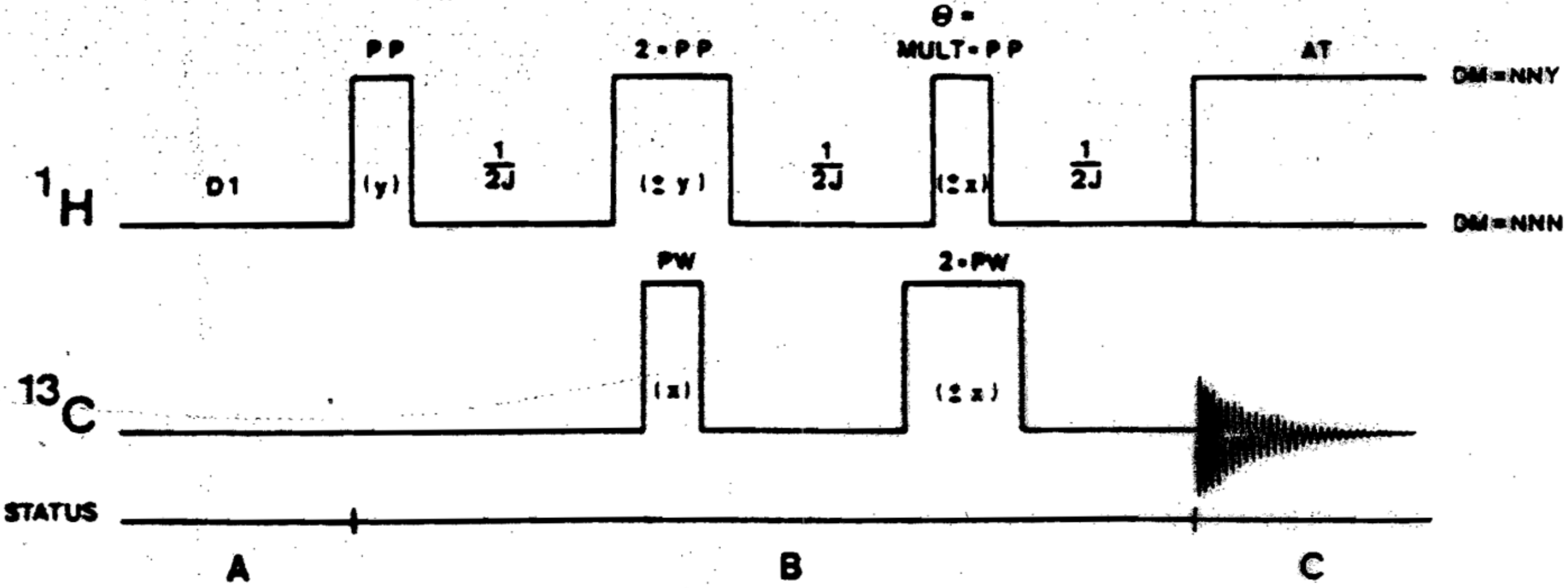


Figure 2-24. Pulse Sequence Diagram for the Basic DEPT Experiment (3)

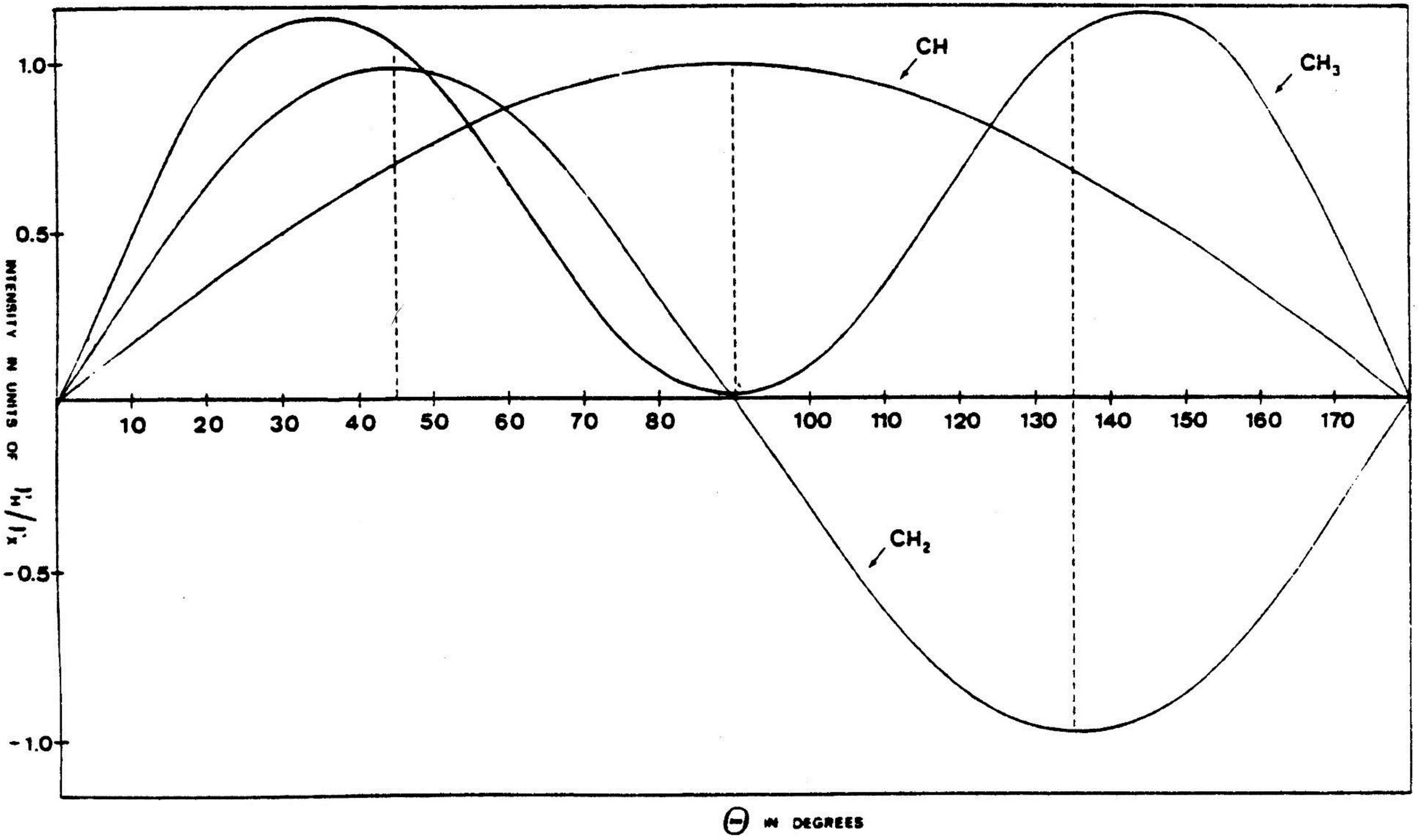
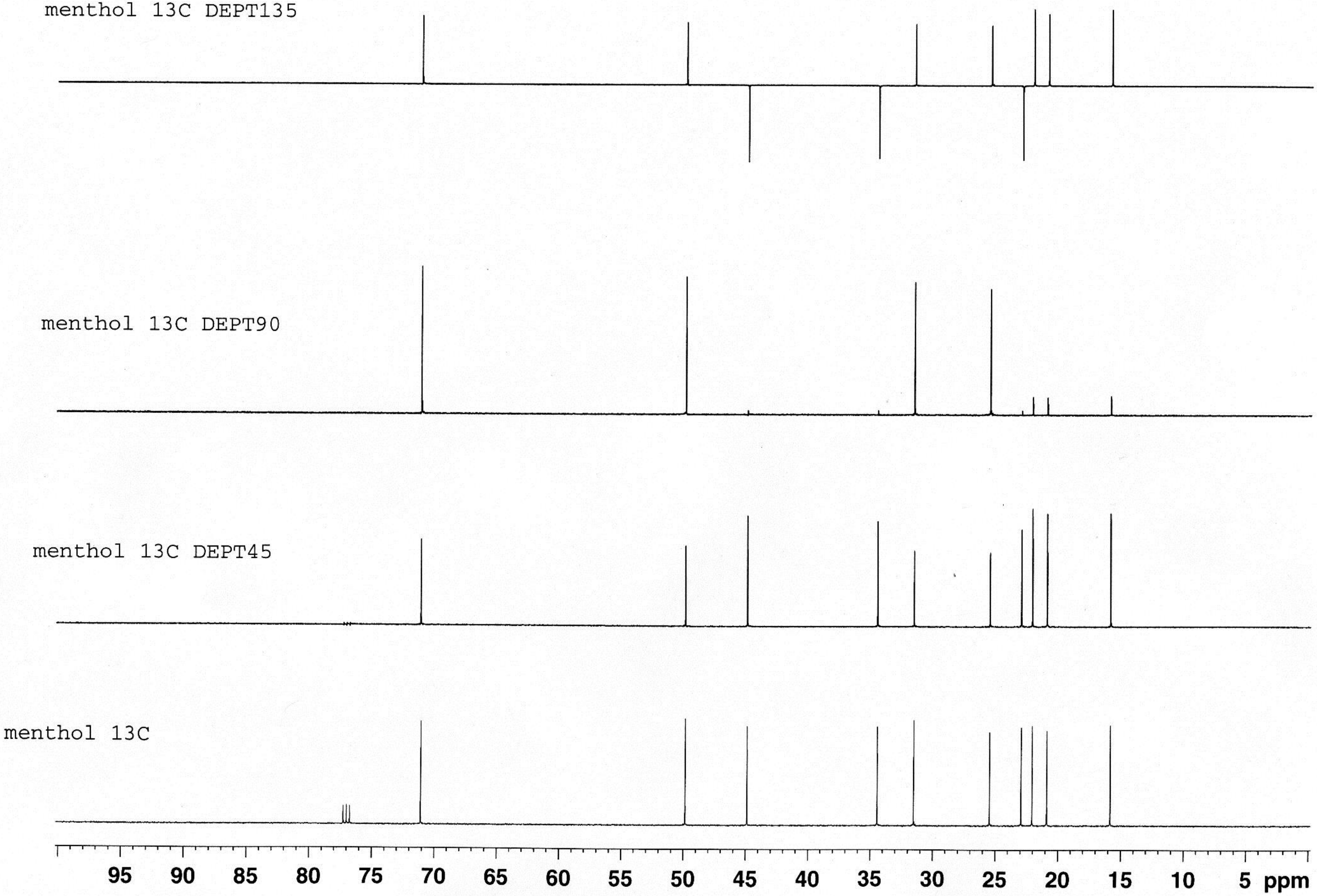
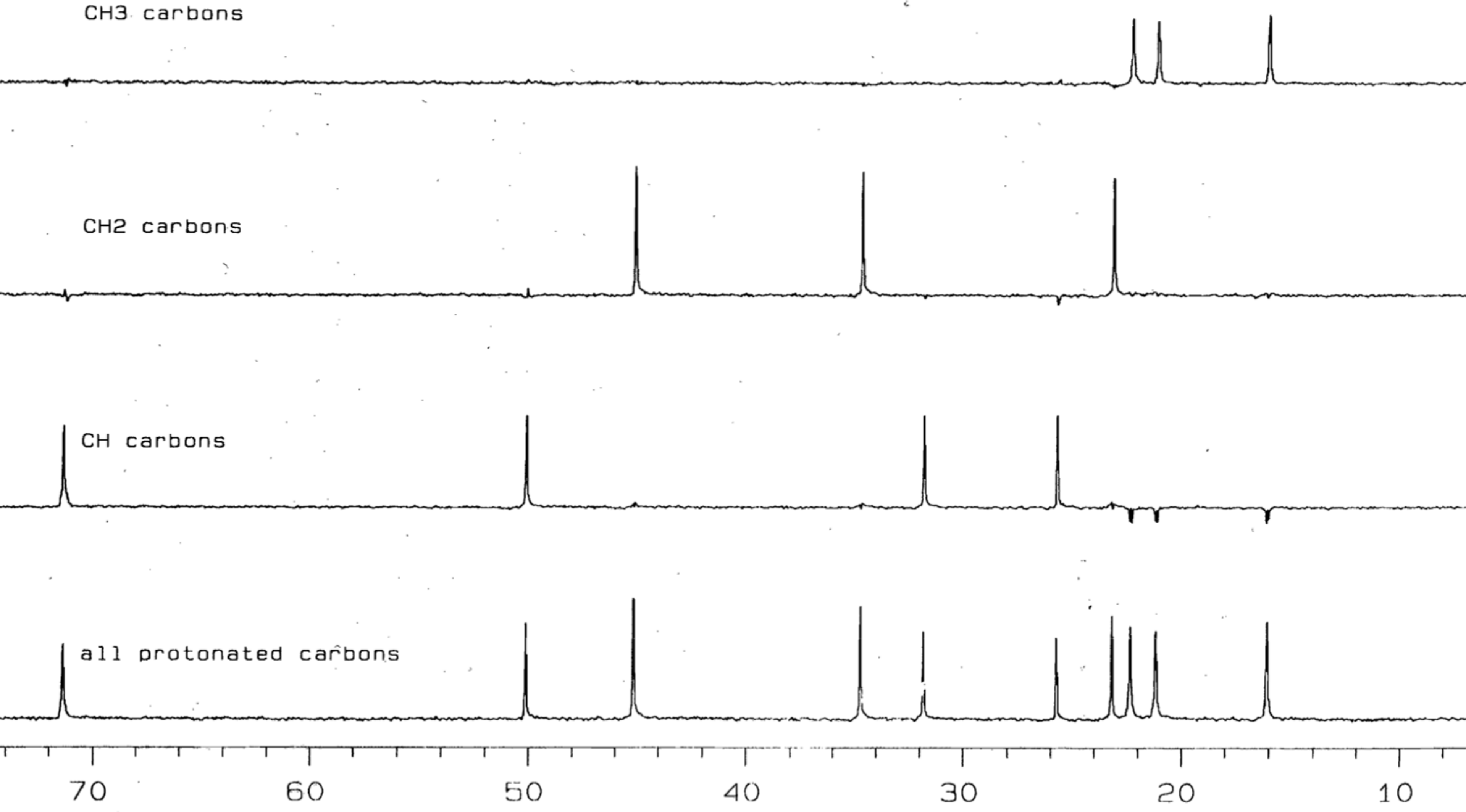


Figure 2-25. Signal Enhancements. ^{13}C doublets, triplets, and quartets as a function of the theta pulse flip angle, in units of $^{\delta H}/_{\delta C}$.

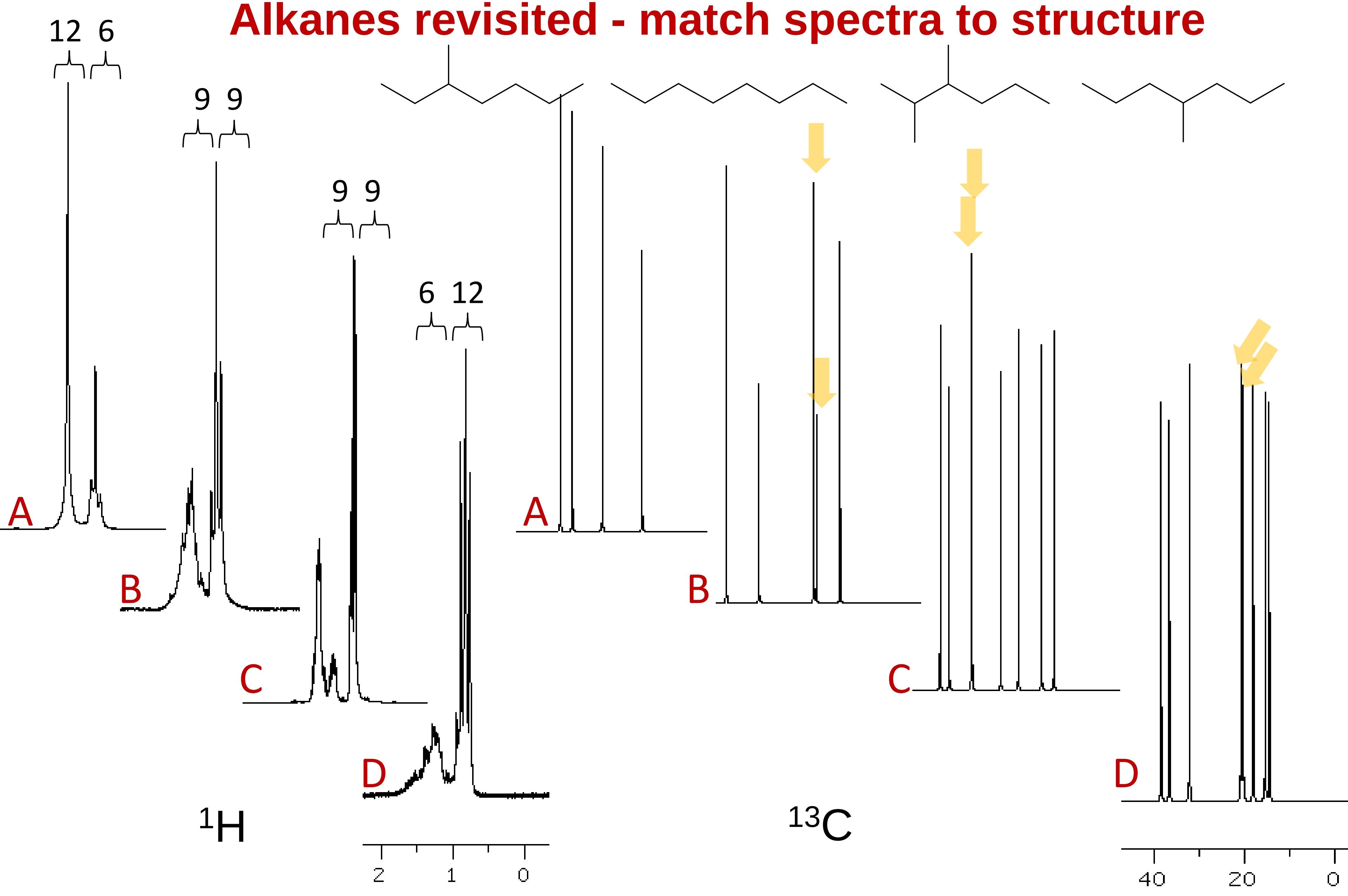

menthol 13C DEPT135
menthol 13C DEPT90
menthol 13C DEPT45
menthol 13C
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
ppm


CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
70
60
50
40
30
20
10

(a) number of different types of carbon

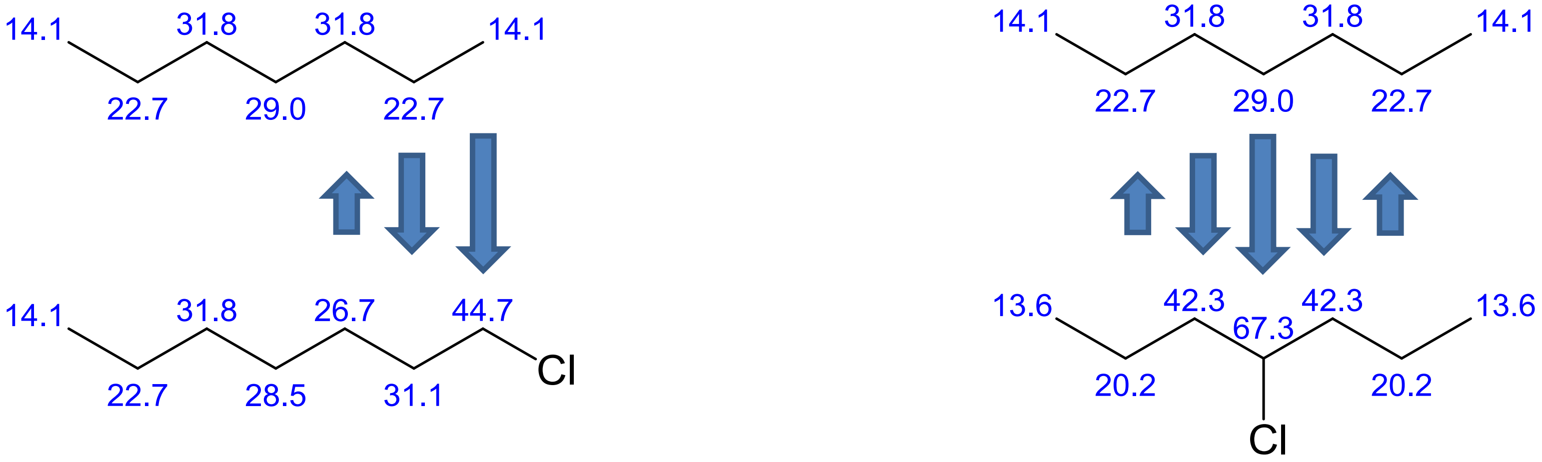
- Each peak corresponds to a different *type* of carbon groups

Alkanes revisited - match spectra to structure



(b) type of carbons and proximity to functional groups

The effect of a substituent on ^{13}C NMR chemical shift drops off rapidly



Estimating ^{13}C chemical shifts of alkanes

$$C_{\varepsilon}–C_{\delta}–C_{\gamma}–C_{\beta}–C_{\alpha}–\mathbf{C}–C_{\alpha}–C_{\beta}–C_{\gamma}–C_{\delta}–C_{\varepsilon}$$

$$\delta_{C}\ (\text{ppm}) = -2.3 + 9.1\alpha + 9.4\beta - 2.5\gamma + 0.3\delta + 0.1\varepsilon + S$$

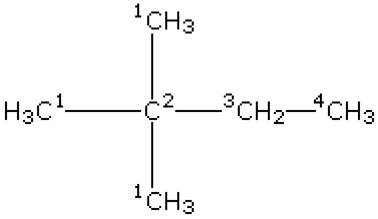
where α, β, γ, δ, and ε, are the numbers of carbon atoms in these positions relative to the carbon atom observed.

S represents steric corrections are derived from the following table (use all that apply, even if they apply more than once).

Steric corrections

Observed	*type of attached carbon atom*			
Carbon Atom	Primary	Secondary	Tertiary	Quaternary
Primary	0.0	0.0	-1.1	-3.4
Secondary	0.0	0.0	-2.5	-7.5
Tertiary	0.0	-3.7	-9.5	-15.0
Quaternary	-1.5	-8.4	-15.0	-25.0

δ_C (ppm) = $-2.3 + 9.1\alpha + 9.4\beta - 2.5\gamma + 0.3\delta + 0.1\varepsilon + S$



$\delta_C{}^1$ = -2.3 + 9.1•__ + 9.4•__ - 2.5•__ + 0.3•__ + 0.1•__+ S = ppm

Observed: 29.1 ppm

$\delta_C{}^2$ = -2.3 + 9.1•__ + 9.4•__ - 2.5•__ + 0.3•__ + 0.1•__+ S = ppm

Observed: 30.6 ppm

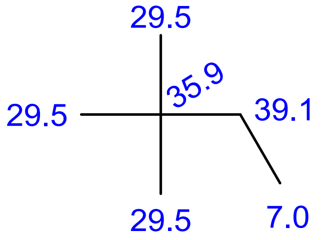
$\delta_C{}^3$ = -2.3 + 9.1•__ + 9.4•__ - 2.5•__ + 0.3•__ + 0.1•__+ S = ppm

Observed: 36.9 ppm

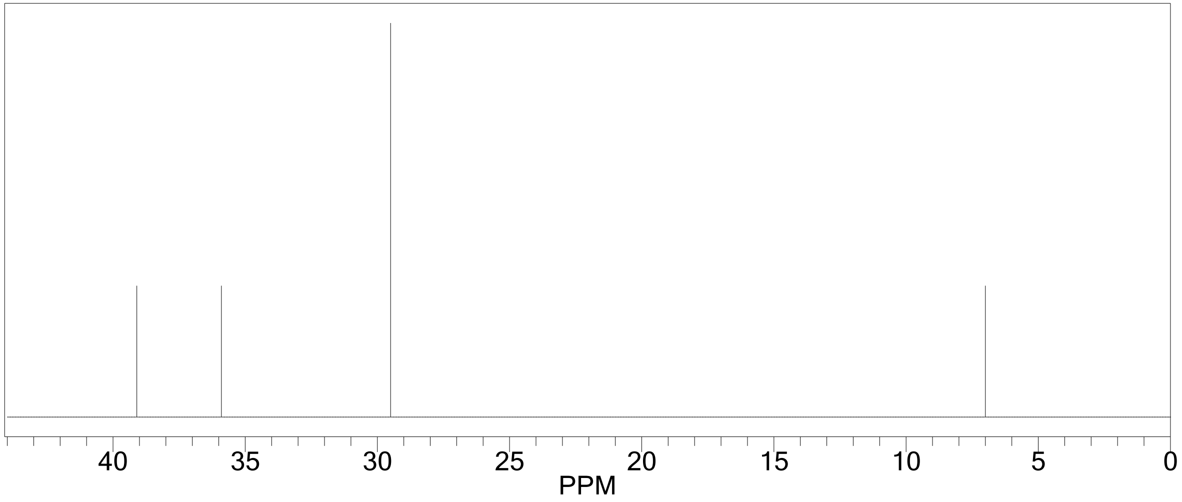
$\delta_C{}^4$ = -2.3 + 9.1•__ + 9.4•__ - 2.5•__ + 0.3•__ + 0.1•__+ S = ppm

Observed: 8.9 ppm

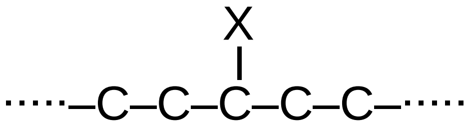
ChemDraw predictions of chemical shift



```
C   35.9          -2.3      aliphatic
                  36.4      4 alpha -C
                   9.4      1 beta -C
                  -7.6      general corrections

CH2 39.1          -2.3      aliphatic
                  18.2      2 alpha -C
                  28.2      3 beta -C
                  -5.0      general corrections

(CH3)3 29.5       -2.3      aliphatic
                   9.1      1 alpha -C
                  28.2      3 beta -C
                  -2.5      1 gamma -C
                  -3.0      general corrections

CH3 7.0           -2.3      aliphatic
                   9.1      1 alpha -C
                   9.4      1 beta -C
                  -7.5      3 gamma -C
                  -1.7      general corrections
```



Estimating ^{13}C chemical shifts of substituted chains



δ_C = base value + substituent effects

Base Values

compound	C_1	C_2	C_3	C_4	C_5
methane	-2.3				
ethane	5.7				
propane	15.8	16.3			
butane	13.4	25.2			
pentane	13.9	22.8	34.7		
hexane	14.1	23.1	32.2		
heptane	14.1	23.2	32.6	29.7	
octane	14.2	23.2	32.6	29.9	
nonane	14.2	23.3	32.6	30.0	30.3
decane	14.2	23.2	32.6	31.1	30.5
2-methylpropane	24.5	25.4			
2-methylbutane	22.2	31.1	32.0	11.7	
2-methylpentane	22.7	28.0	42.0	20.9	14.3
2,2-dimethylpropane	31.7	28.1			
2,2-dimethylbutane	29.1	30.6	36.9	8.9	
2,3-dimethylbutane	19.5	34.4			

cyclopropane	-3.0
cyclobutane	22.4
cyclopentane	25.6
cyclohexane	26.9
cycloheptane	28.4
cyclooctane	26.9
cyclononane	26.1
cyclodecane	25.3

Substituent coefficients

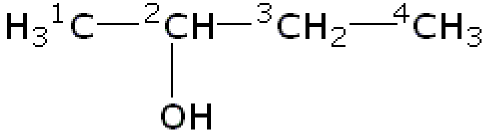
	terminal			*internal*		
	$Y-C_\alpha-C_\beta-C_\gamma$			$C_\gamma-C_\beta-C_\alpha(Y)-C_\alpha-C_\beta-C_\gamma$		
Substituent Y	α	β	γ	α	β	γ
$-CH_3$	9	10	-2	6	8	-2
$-CH=CH_2$	20	6	-0.5			-0.5
$-CCH$	4.5	5.4	-3.5			-3.5
$-C_6H_5$	23	9	-2	17	7	-2
$-CHO$	31	0	-2			
$-C(O)CH_3$	30	1	-2	24	1	-2
$-CO_2H$	21	3	-2	16	2	-2
$-CO_2R$	20	3	-2	17	2	-2
$-C(O)NH_2$	22	2.52	-0.52			-0.5
$-CN$	4	3	-3	1	3	-3
$-NH_2$	29	11	-5	24	10	-5
$-NHR$	37	8	-4	31	6	-4
$-NR_2$	42	6	-3			-3
$-NO_2$	63	4		57	4	
$-OH$	48	10	-5	41	8	-5
$-OR$	58	8	-4	51	5	-4
$-OC(O)CH_3$	51	6	-3	45	5	-3
$-F$	68	9	-4	63	6	-4
$-Cl$	31	11	-4	32	10	-4
$-Br$	20	11	-3	25	10	-3
$-I$	-6	11	-1	4	12	-1

Base ^{13}C values for linear chains

Compound	*C_1*	*C_2*	*C_3*	*C_4*	*C_5*
butane	13.4	25.2	..	..	..

	terminal			internal		
	$Y\text{-}C_\alpha\text{-}C_\beta\text{-}C_\gamma$			$C_\gamma\text{-}C_\beta\text{-}C_\alpha(Y)\text{-}C_\alpha\text{-}C_\beta\text{-}C_\gamma$		
Substituent Y	α	β	γ	α	β	γ
-OH	48	10	-5	41	8	-5

δ_C^1 = base value + substituent effects


$H_3{}^{1}C-{}^{2}CH(OH)-{}^{3}CH_2-{}^{4}CH_3$

δ_C^1 = + = ppm
observed: 22.6 ppm

δ_C^2 = + = ppm
observed: 68.7 ppm

δ_C^3 = + = ppm
observed: 32.0 ppm

δ_C^4 = + = ppm
observed: 9.9 ppm

$HO-{}^{1}CH_2-{}^{2}CH_2-{}^{3}CH_2-{}^{4}CH_3$

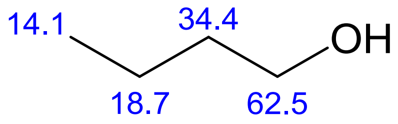
δ_C^1 = 13.4 + 48 = 61.4 ppm
observed: 61.4 ppm

δ_C^2 = 25.2 + 10 = 35.2 ppm
observed: 35.0 ppm

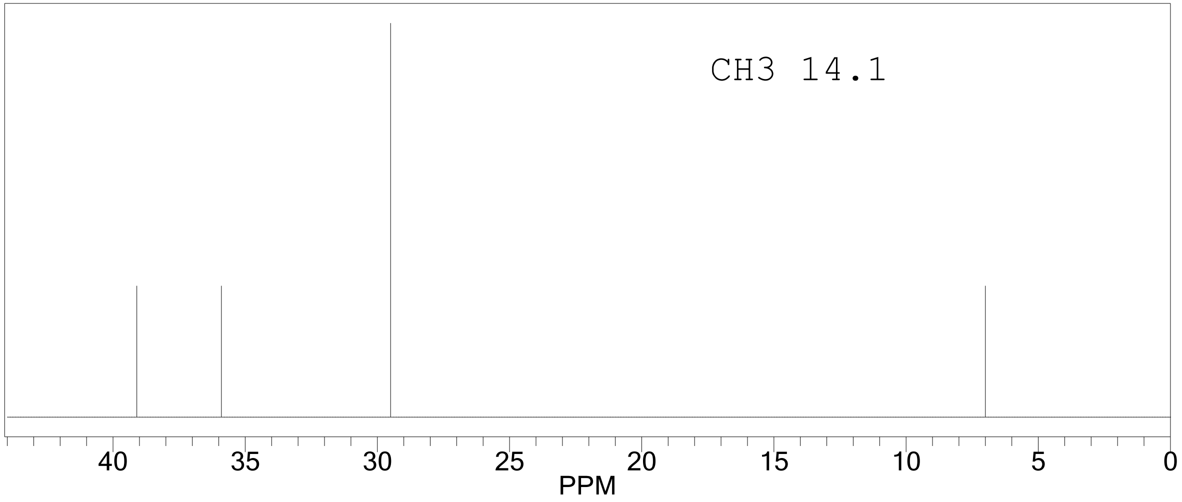
δ_C^3 = 25.2 + (-5) = 20.2 ppm
observed: 19.1 ppm

δ_C^4 = 13.4 = 13.4 ppm
observed: 13.6 ppm

ChemDraw predictions of chemical shift



```
CH2 62.5        -2.3     aliphatic
                 9.1     1 alpha -C
                49.0     1 alpha -O
                 9.4     1 beta -C
                -2.5     1 gamma -C
                -0.2     general corrections

CH2 34.4        -2.3     aliphatic
                18.2     2 alpha -C
                 9.4     1 beta -C
                10.1     1 beta -O
                -1.0     general corrections

CH2 18.7        -2.3     aliphatic
                18.2     2 alpha -C
                 9.4     1 beta -C
                -6.2     1 gamma -O
                -0.4     general corrections

CH3 14.1        -2.3     aliphatic
                 9.1     1 alpha -C
                 9.4     1 beta -C
                -2.5     1 gamma -C
                 0.3     1 delta -O
                 0.1     general corrections
```



Estimating ^{13}C chemical shifts of carbons in alkenes

$$C_\gamma{-}C_\beta{-}C_\alpha{-}\mathbf{C^1}{=}C^2{-}C_{\alpha'}{-}C_{\beta'}{-}C_{\gamma'}$$

$$\delta_{C}{}^{1}\ (\text{ppm}) = 123.3 + [\,10.6\alpha + 7.2\beta - 1.5\gamma] - [\,7.9\alpha' + 1.8\beta' - 1.5\gamma'] + S$$

where: α, β, γ and α', β', γ' are the number of carbon atoms at these positions relative to the carbon atom observed

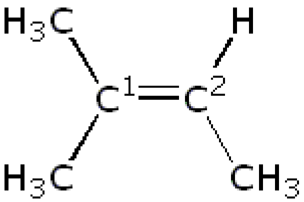
Steric corrections

C_α and $C_{\alpha'}$ are *trans* (*E*-configuration)	0
C_α and $C_{\alpha'}$ are *cis* (*Z*-configuration)	-1.1
Two alkyl substituents at C^1 (i.e., two C_α)	-4.8
Two alkyl substituents at C^2 (i.e., two $C_{\alpha'}$)	2.5
Two or more alkyl substituents at C_β)	2.3

Steric corrections

C_α and $C_{\alpha'}$ are *trans* (*E*-configuration)	0
C_α and $C_{\alpha'}$ are *cis* (*Z*-configuration)	-1.1
Two alkyl substituents at C^1 (i.e., two C_α)	-4.8
Two alkyl substituents at C^2 (i.e., two $C_{\alpha'}$)	2.5
Two or more alkyl substituents at C_β)	2.3

$$\delta_C{}^1\ \text{(ppm)} = 123.3 + [\,10.6\alpha + 7.2\beta - 1.5\gamma] - [\,7.9\alpha' + 1.8\beta' - 1.5\gamma'] + S$$



$$\delta_C{}^1 = 123.3 + [10.6(2)] - [7.9(1)] + [(-4.8) + (-1.1)] = 130.7\ \text{ppm}$$

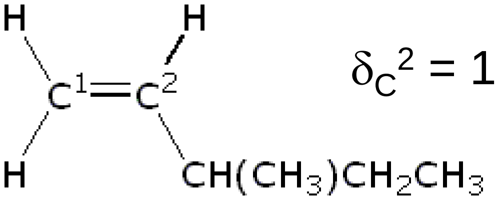
Observed: 131.4 ppm

$$\delta_C{}^2 = 123.3 + [10.6(1)] - [7.9(2)] + [(2.5) + (-1.1)] = 119.5\ \text{ppm}$$

Observed: 118.7 ppm

$$\delta_C{}^1 = 123.3 + [0] - [7.9(1) + 1.8(2) - 1.5(1)] + [0] = 113.3\ \text{ppm}$$

Observed: 112.9 ppm

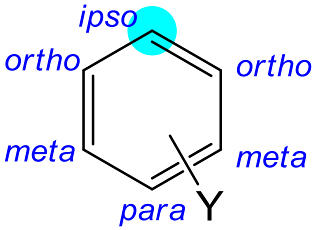


$$\delta_C{}^2 = 123.3 + [10.6(1) + 7.2(2) - 1.5(1)] - [0] + [0] = 146.8\ \text{ppm}$$

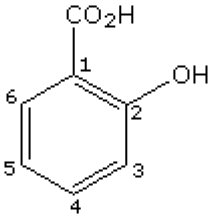
Observed: 144.9 ppm

Estimating ^{13}C chemical shifts of carbons of substituted benzenes

$\delta_C = 128.5 + \Sigma d_i$



Substituent (R)	d_{ipso}	d_{ortho}	d_{meta}	d_{para}
$-CO_2H$	2.9	1.3	0.4	4.3
-OH	26.6	-12.7	1.6	-7.3



$\delta_C^{1} = 128.5 + \quad + \quad =$ ppm

observed: 121.0 ppm

$\delta_C^{2} = 128.5 + \quad + \quad =$ ppm

observed: 161.4 ppm

$\delta_C^{3} = 128.5 + \quad + \quad =$ ppm

observed:117.4 ppm

$\delta_C^{4} = 128.5 + 1.6 + 5.8 =$ ppm

observed: 136.6 ppm

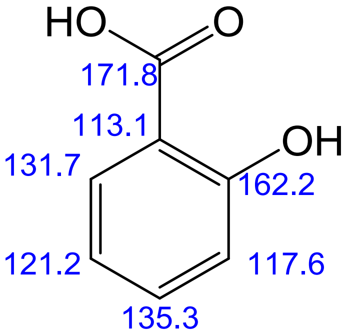
$\delta_C^{5} = 128.5 + (-7.3) + 0.6 =$ ppm

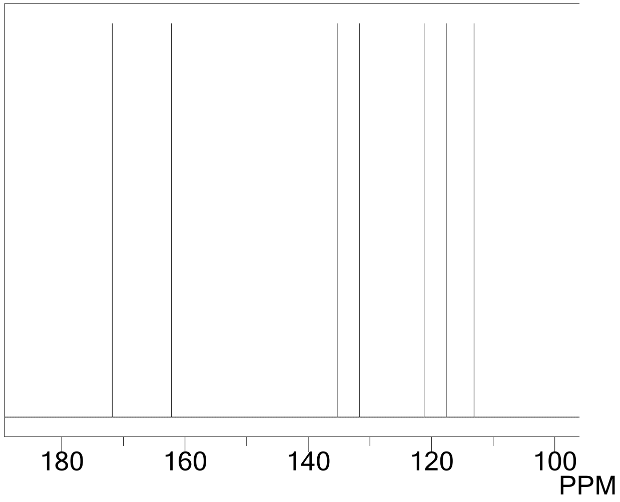
observed: 119.6 ppm

$\delta_C^{6} = 128.5 + 1.2 + 1.6 =$ ppm

observed: 133.6 ppm

ChemDraw predictions of chemical shift



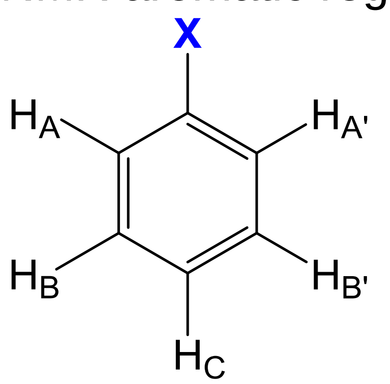


```
C    113.1          128.5      1-benzene
                    -12.8      1 -O
                      2.1      1 -C(=O)-O
                     -4.7      general corrections

C    162.2          128.5      1-benzene
                     28.8      1 -O
                      1.6      1 -C(=O)-O
                      3.3      general corrections

CH   117.6          128.5      1-benzene
                    -12.8      1 -O
                     -0.1      1 -C(=O)-O
                      2.0      general corrections

CH   135.3          128.5      1-benzene
                      1.4      1 -O
                      5.2      1 -C(=O)-O
                      0.2      general corrections

CH   121.2          128.5      1-benzene
                     -7.4      1 -O
                     -0.1      1 -C(=O)-O
                      0.2      general corrections

CH   131.7          128.5      1-benzene
                      1.4      1 -O
                      1.6      1 -C(=O)-O
                      0.2      general corrections
```

Multiplicity of peaks for protons on substituted benzenes

Monosubstituted benzenes

^{1}H NMR aromatic region - 5H

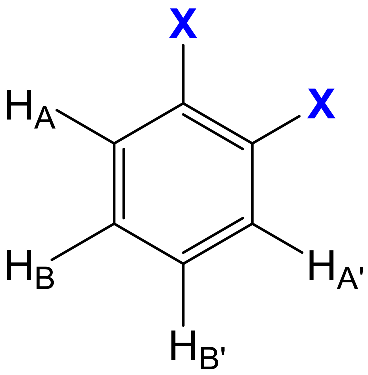


^{1}H NMR - AA'BB'C,
2H t, 2H d of d, and 1H d of d,
or more complex

^{13}C NMR - 4 signals

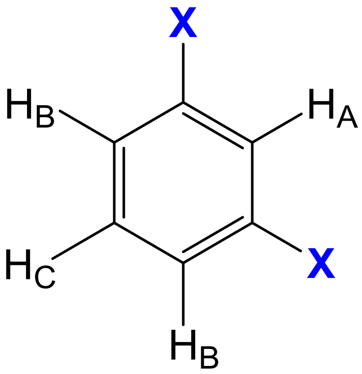
Symmetrically disubstituted benzenes

^{1}H NMR aromatic region - 4H



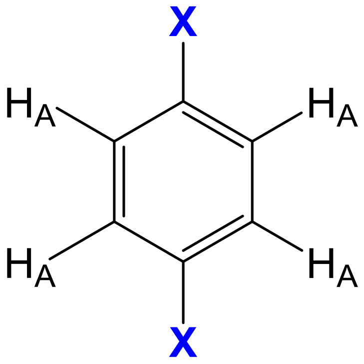
^{1}H NMR - AA'BB', might appear as pair of d, or more complex

^{13}C NMR - 3 signals



^{1}H NMR - AB$_2$C, might appear as: 1H d, 2H d of d, and 1H t, or more complex

^{13}C NMR - 4 signals

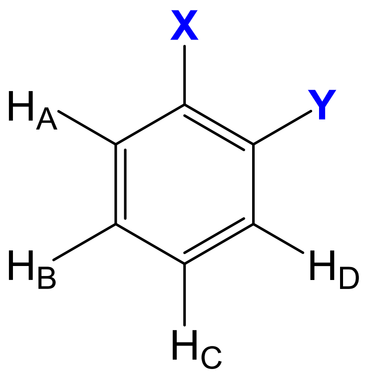


^{1}H NMR - singlet

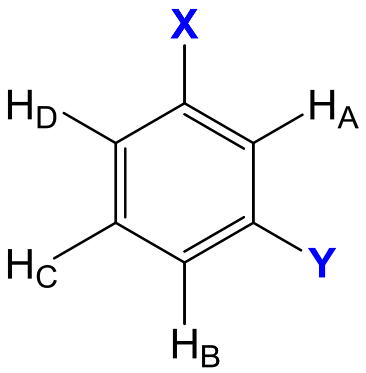
^{13}C NMR - 2 signals

Unsymmetrically disubstituted benzenes

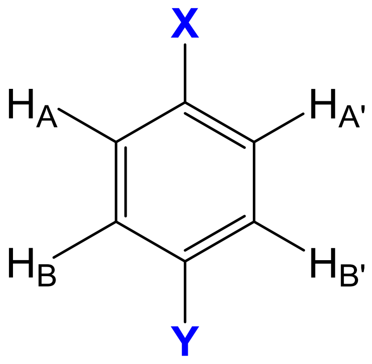
^{1}H NMR aromatic region - 4H



^{13}C NMR - 6 signals
^{1}H NMR – ABCD, might appear as two doublets and two triplets or more complex



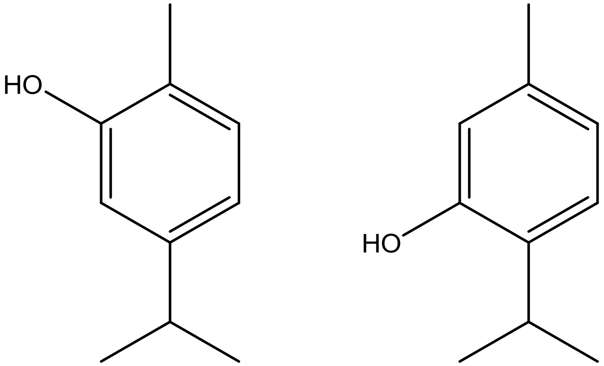
^{13}C NMR - 6 signals
^{1}H NMR – ABCD, might appear as two doublets, one triplet and a singlet, or more complex

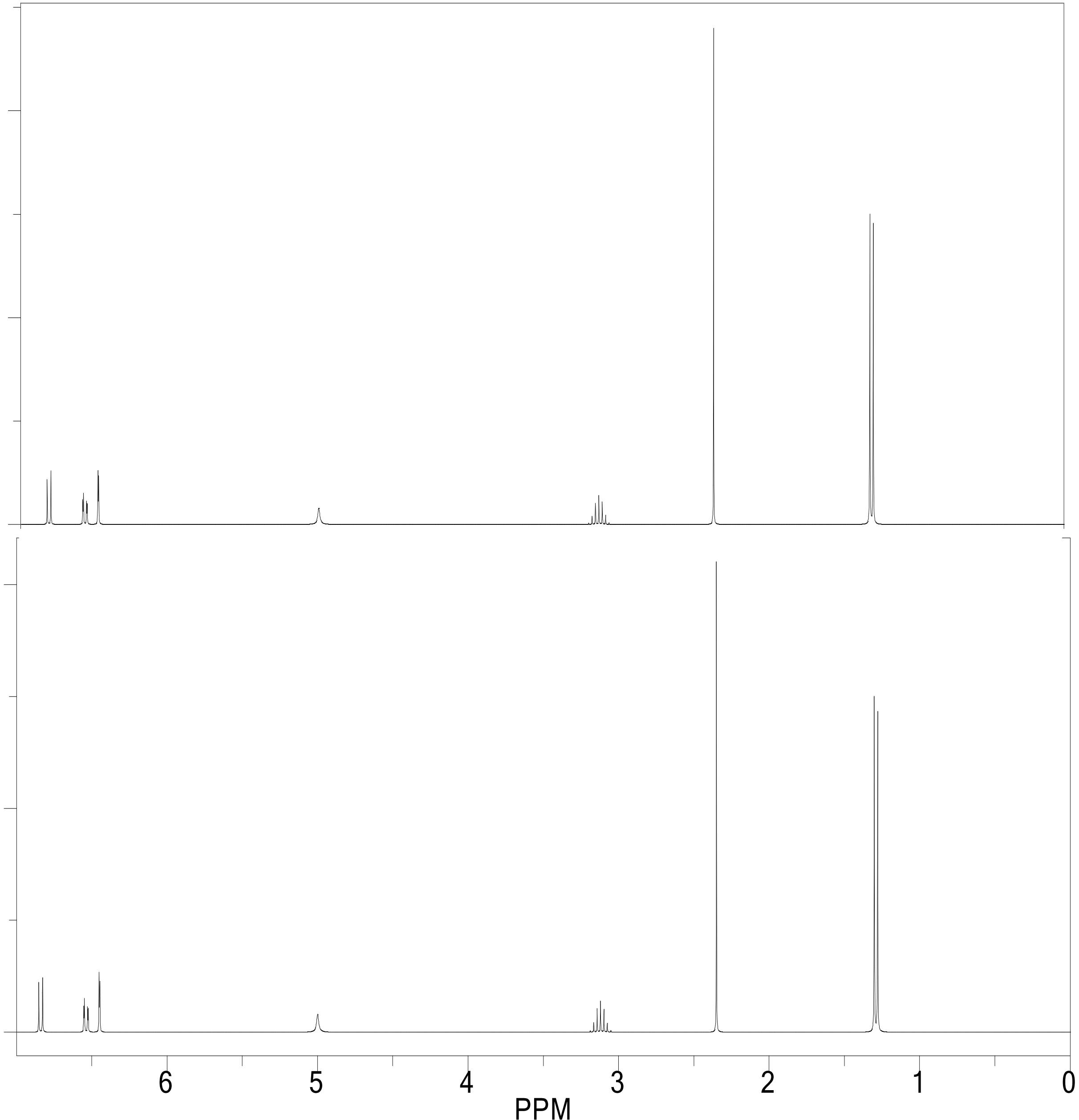


^{13}C NMR - 4 signals
^{1}H NMR - AA’BB’, might appear as pair of d, or more complex

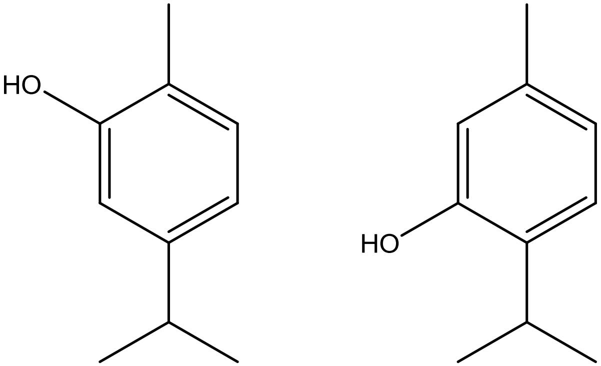
^{13}C NMR to the rescue!!!

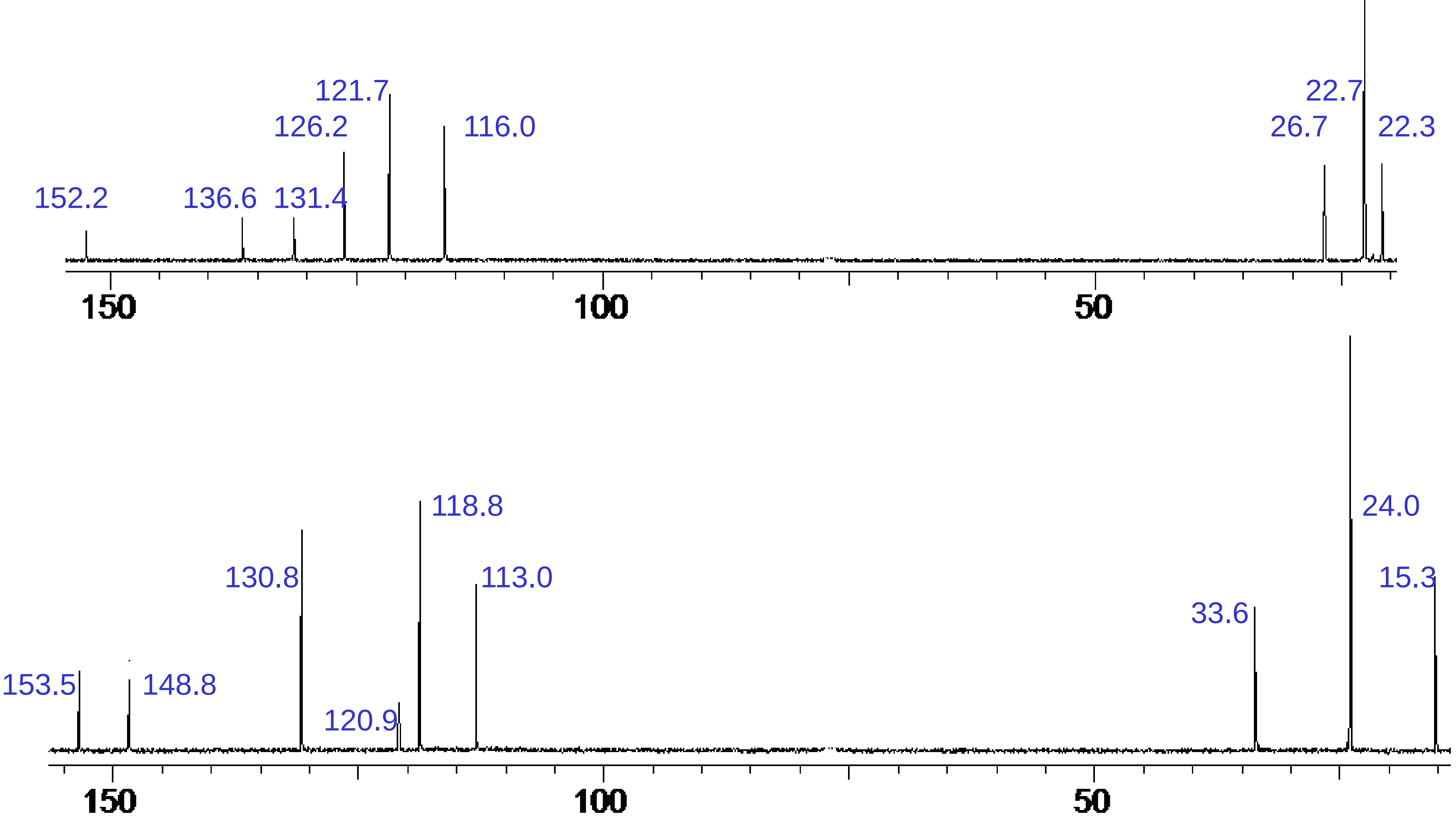
^{1}H NMR does not let you determine which structure you have

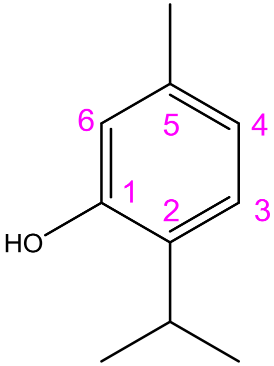




How does ^{13}C NMR help?

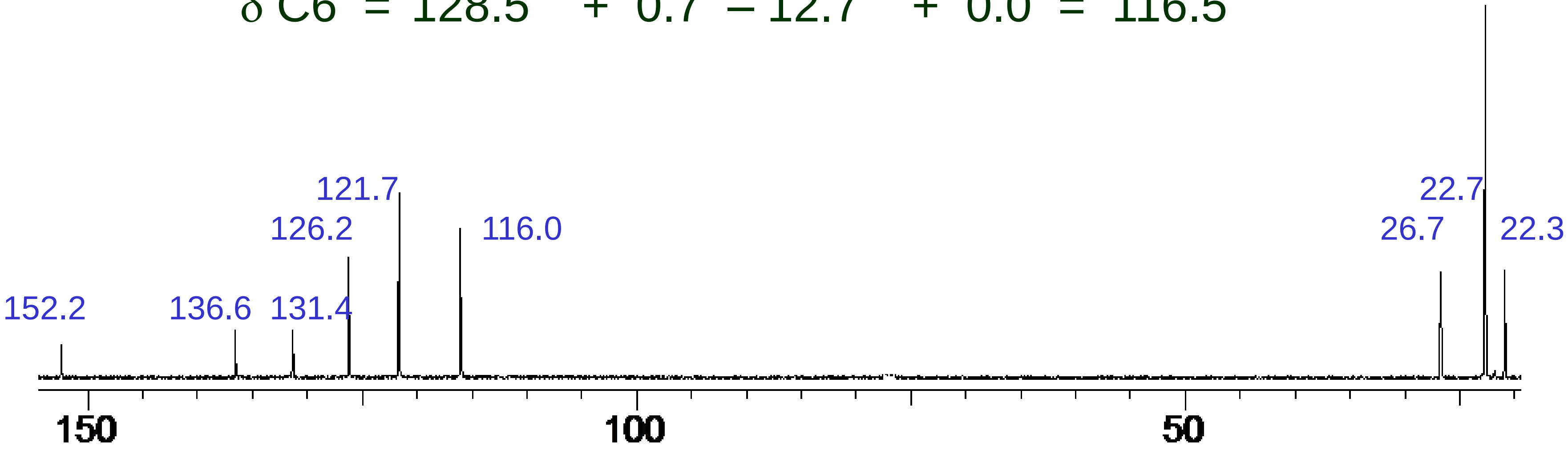


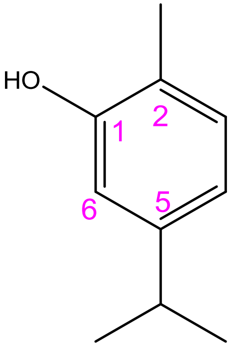




Substituent (R)	d_{ipso}	d_{ortho}	d_{meta}	d_{para}
-OH	26.6	-12.7	1.6	-7.3
-Me	9.3	0.7	-0.1	-2.9
$-CH(Me)_2$	20.1	-2.0	0.0	-2.5

δ C1 = 128.5 + 26.6 – 2.0 + 0.1 = 153.0
δ C2 = 128.5 + 20.1 –12.7 – 2.9 = 133.0
δ C3 = 128.5 – 2.0 + 1.6 – 0.1 = 128.0
δ C4 = 128.5 + 0.7 – 0.0 – 7.3 = 121.9
δ C5 = 128.5 + 9.3 + 1.6 – 2.5 = 136.9
δ C6 = 128.5 + 0.7 – 12.7 + 0.0 = 116.5





Substituent (R)	d_{ipso}	d_{ortho}	d_{meta}	d_{para}
-OH	26.6	-12.7	1.6	-7.3
-Me	9.3	0.7	-0.1	-2.9
$-CH(Me)_2$	20.1	-2.0	0.0	-2.5

δ C1 = 128.5 + 26.6 + 0.7 + 0.0 = 155.8

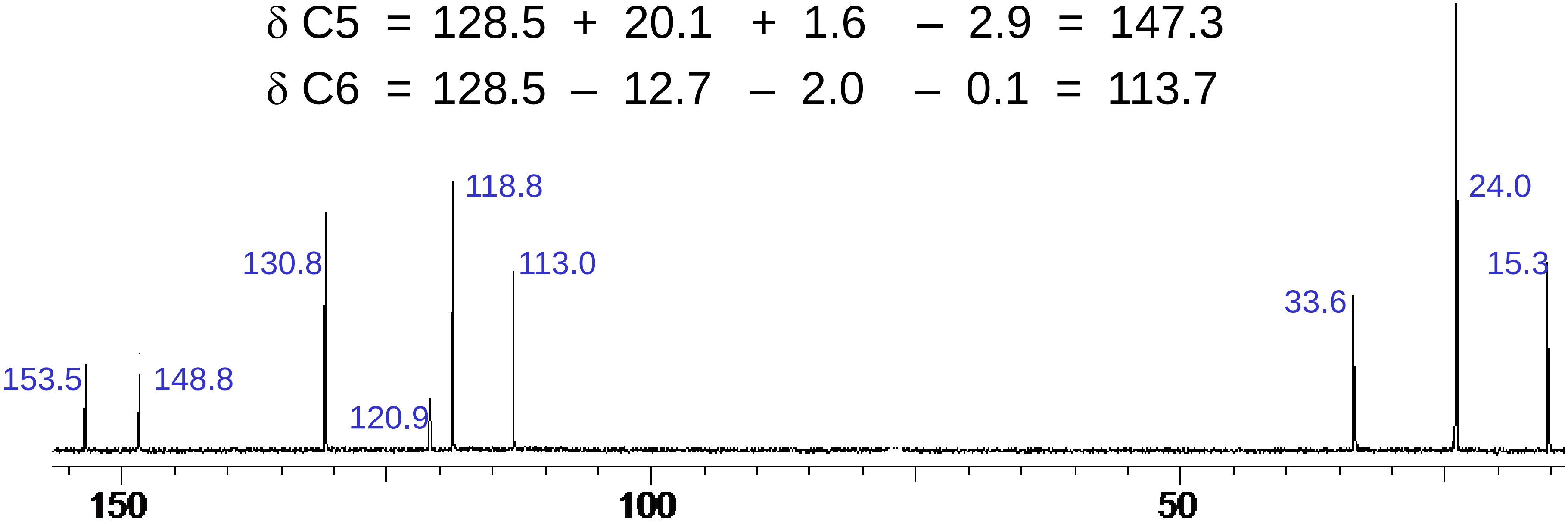
δ C2 = 128.5 + 9.3 – 12.7 – 2.5 = 122.6

δ C3 = 128.5 + 0.7 + 1.6 + 0.0 = 130.8

δ C4 = 128.5 – 0.1 – 2.0 – 7.1 = 119.3

δ C5 = 128.5 + 20.1 + 1.6 – 2.9 = 147.3

δ C6 = 128.5 – 12.7 – 2.0 – 0.1 = 113.7



ADDITIONAL PEAKS

Signals from the presence of the other compounds

Standards added to reference chemical shift

Tetramethylsilane: $(C\mathbf{H}_3)_4Si$

Sodium 3-(trimethylsilyl)-1-propanesulfonate $(C\mathbf{H}_3)_3SiCH_2CH_2CO_2^- Na^+$

Residual ^{13}C of deuterated solvents

Chemical shift of ^{13}C in deuterated solvents

$CDCl_3$ δ 77 ppm - 3 lines ***!?***

Remember: peaks are not integrated. In general, H-substituted ^{13}C give taller peaks

Sample

Typically 10-50 mg sample in 0.75-1.00 mL solvent in a 5 mm diameter NMR tube. Too little, or too much, sample »» poor spectra

Reporting ^{1}H decoupled ^{13}C NMR Spectra in Papers and Progress Reports

Ⓐ Ⓑ Ⓒ

^{13}C NMR ($CDCl_3$, 100 MHz): δ123.2 (###), 121.1 (###)….

Ⓐ Solvent: e.g., $CDCl_3$, C_6D_6, acetone-d_6, THF-d_8, CD_3CN, 1,4-dichlorobenzene-d_4, CD_2Cl_2. Frequency used in the experiment (and temperature if not r.t. or 25 °C). Remember, a “400 MHz” spectrometer refers to the frequency for ^{1}H NMR, which corresponds to 100 MHz for ^{13}C NMR.

Ⓑ List *all* peaks – provide δ to one decimal place. If the number of peaks is less than the number of types of carbon atoms, because of coincidence chemical shifts, can you assign any of the peaks to more than one type of carbon atom?

Ⓒ Provide a succinct, but accurate, assignment of a peak to a particular type of hydrogen in the molecule. This can be difficult, and might not always be possible.

WORK PROBLEMS!!

Pavia: Chapters 3, 4 and 5 (not questions dealing with ^{19}F and ^{31}P)

Do as many of the problems on these sites (except those with COSY spectra)

www.nd.edu/~smithgrp/structure/workbook.html

www.chem.ucla.edu/~webspectra/index.html