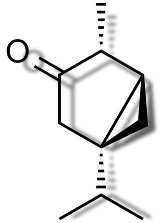
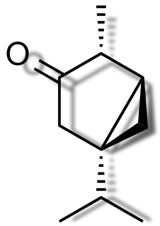


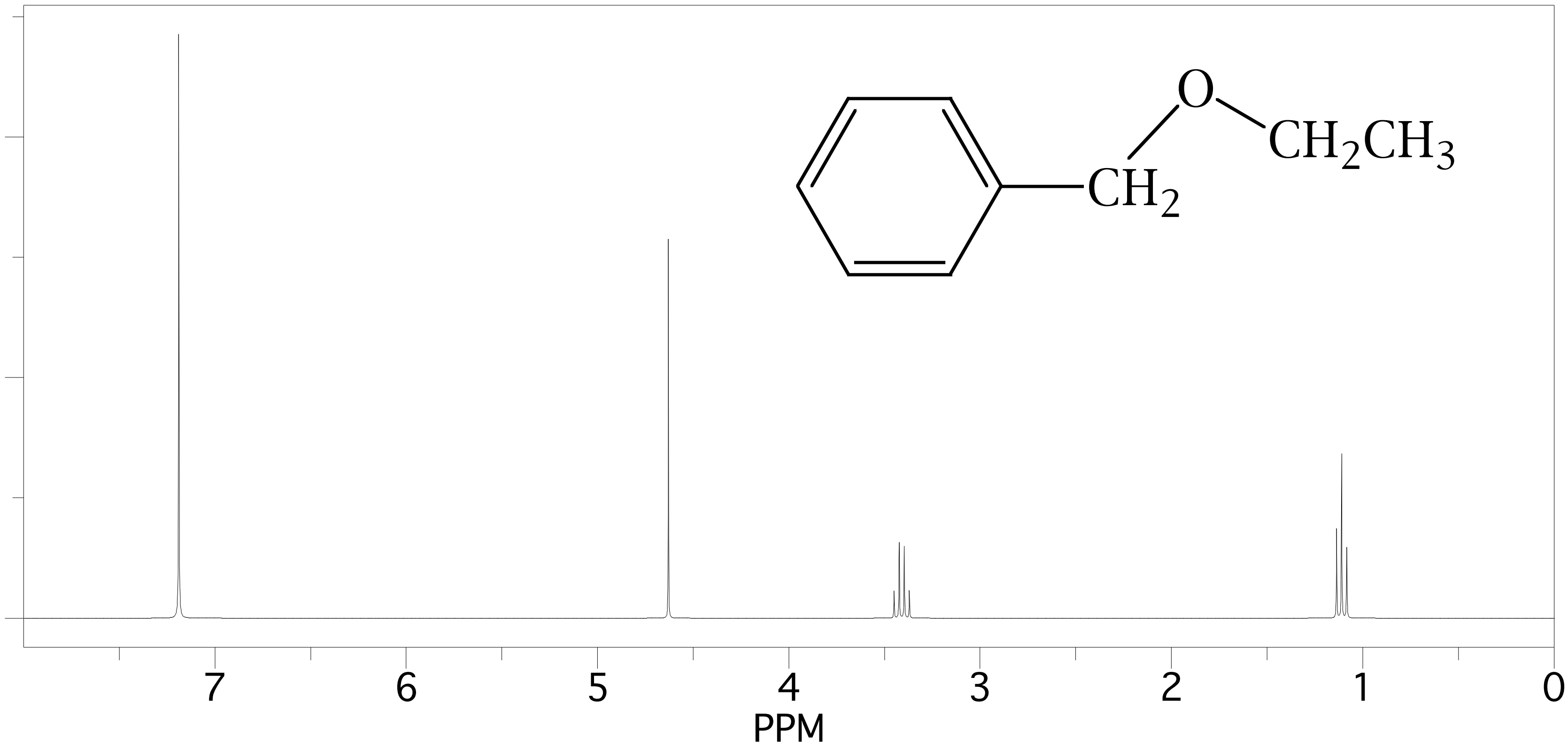
Chemistry 2600

Chapter 13

Nuclear Magnetic Resonance (NMR) Spectroscopy

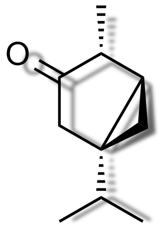
Nuclear Magnetic Resonance Spectroscopy

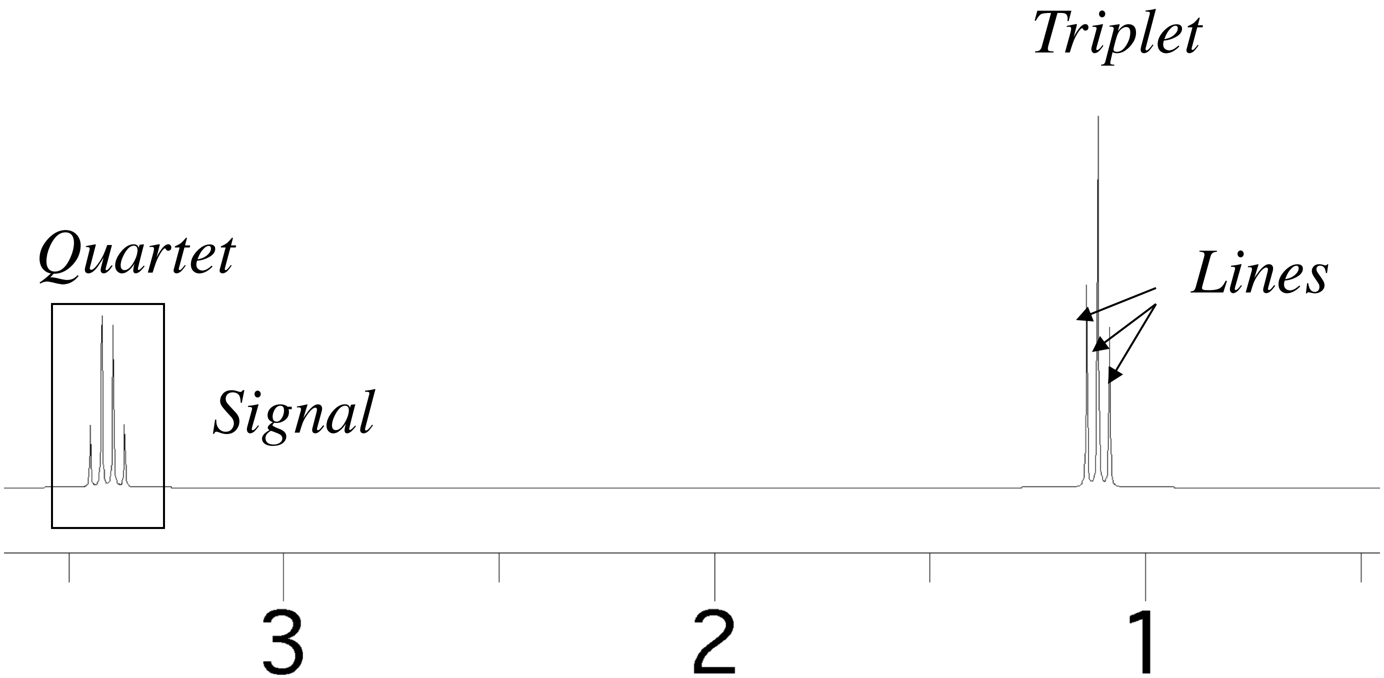




A proton NMR spectrum. Information from peaks:

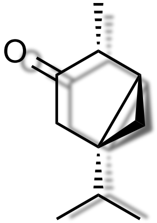
magnitude (integration), position and multiplicity.



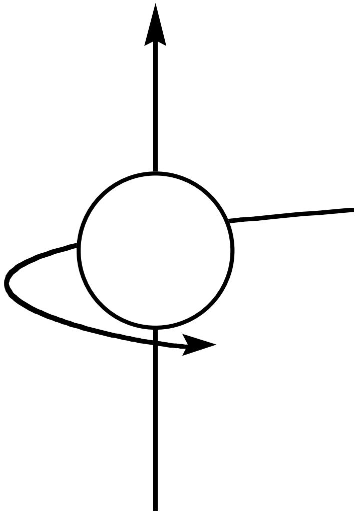


Signal…	*The line or group of lines that result from the absorption of particular set of nuclei*.
Lines…	*The peaks that appear in a particular signal*.
Multiplicity…	*The number of lines in a signal and/or the pattern of the lines*

How does NMR work?

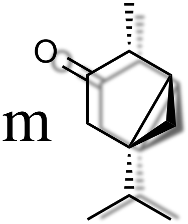


Nuclei behave as if they spin…



Nuclear spin is quantized and described by the quantum no. I, where I = 0, 1/2, 1, 3/2, 2, ….

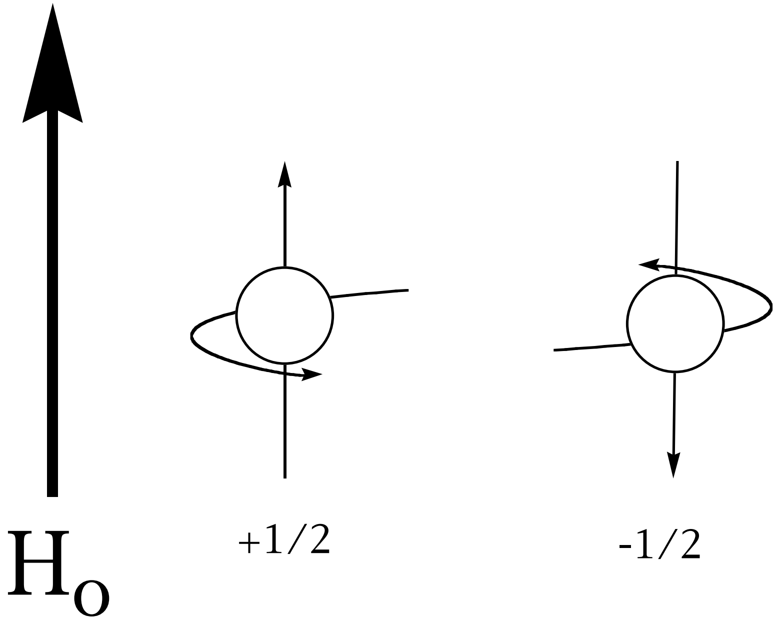
Spin 1/2 nuclei: ^{1}H (proton), ^{13}C, ^{19}F, ^{31}P
Spin 0 nuclei: ^{12}C, ^{16}O
Spin 1 nuclei: ^{14}N, ^{2}H
Spin 5/2: ^{17}O
Spin 3: ^{10}B

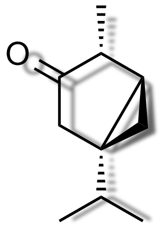


In a given sample of a compound **in solution**, spins are random and their fields…

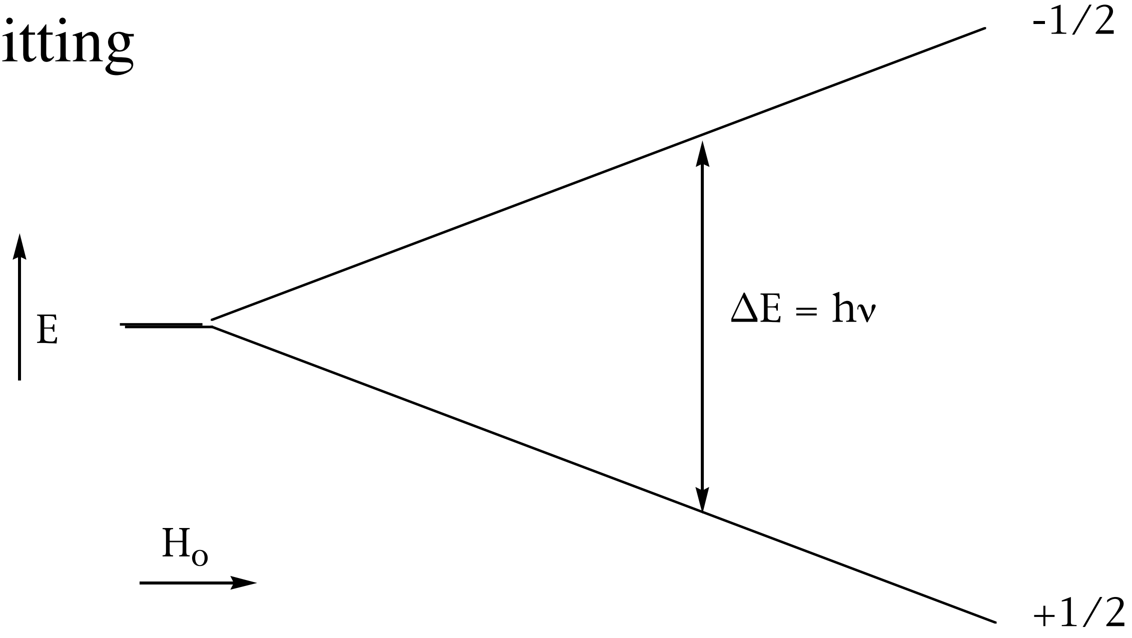
In the presence of an externally applied magnetic field (H_o), a nucleus will adopt 2I + 1 orientations having differing energies.

For the proton, there are two “spin states”.





Zeeman splitting



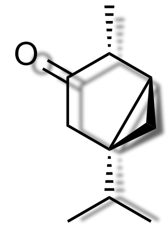
The relative number of nuclei in the different spin states (proton, 14 kGauss - 60 MHz) is:

$$\Delta E = h\nu = \frac{h\gamma}{2\pi} H_o$$

$$\frac{N_{upper}}{N_{lower}} = e^{\frac{-\Delta E}{kT}} = \frac{1,000,000}{1,000,009}$$

$$\nu = \frac{\gamma}{2\pi} H_o$$

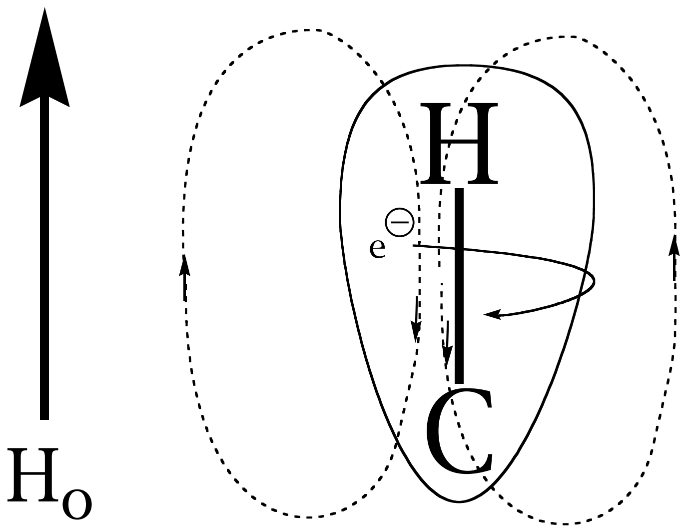
The actual resonance frequency for a given nucleus depends on its LOCAL CHEMICAL ENVIRONMENT



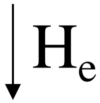
These local magnetic effects are due to:

- σ electrons
- π electrons
- other magnetically active nuclei - especially protons

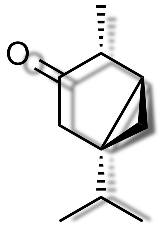
σ electrons

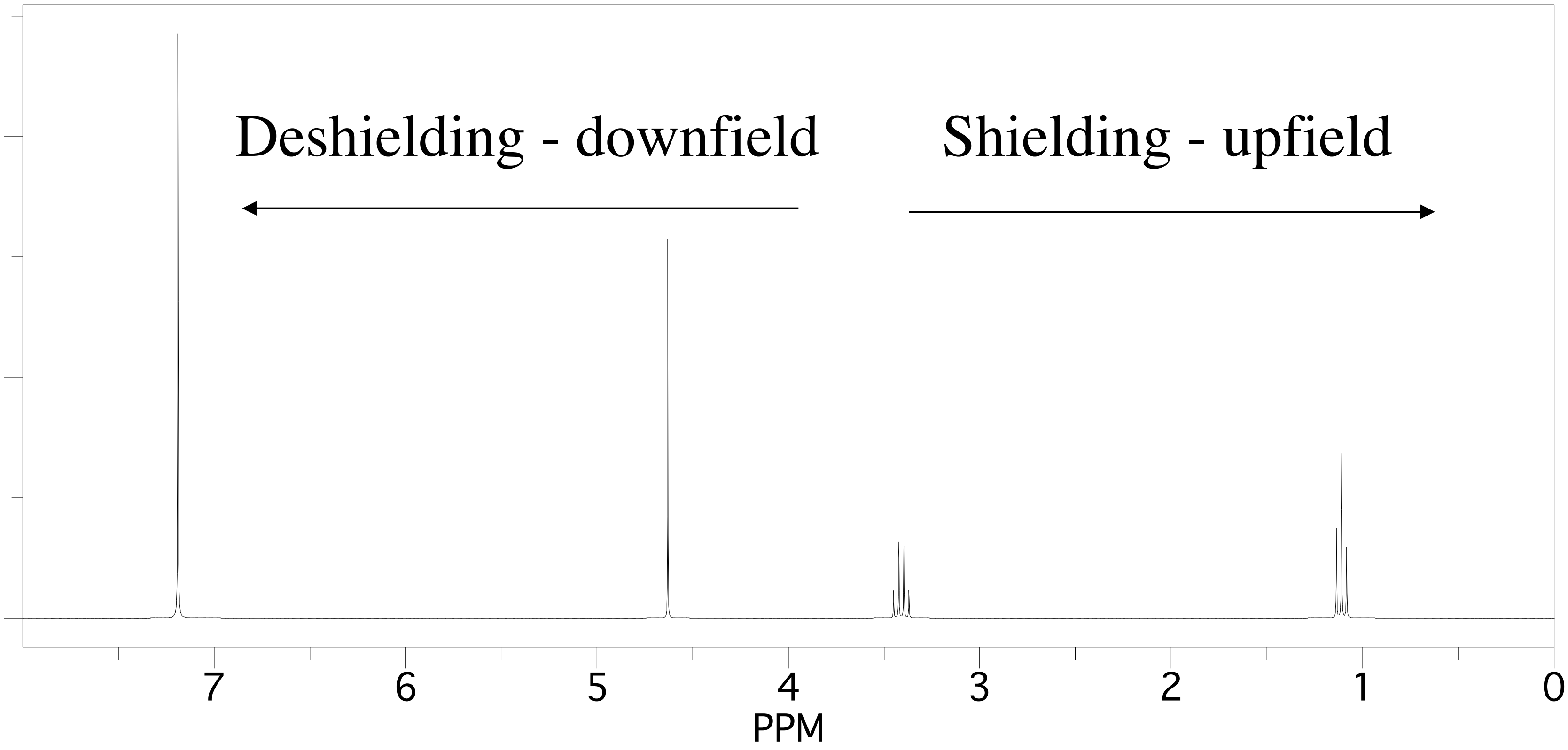


In the locale of the proton, the field lines are opposed to the applied magnetic field. This has the effect of “shielding” the proton from the full effect of H_o.



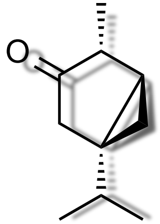
Chemical shielding has the effect of moving signals to the right on an NMR spectrum. We refer to this as…



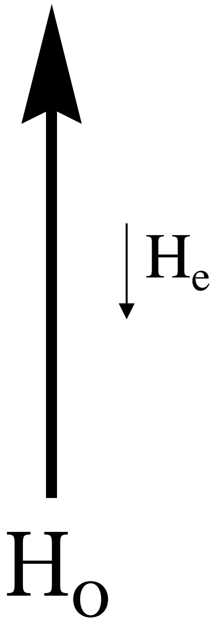

Deshielding - downfield

Shielding - upfield

Chemical Shift



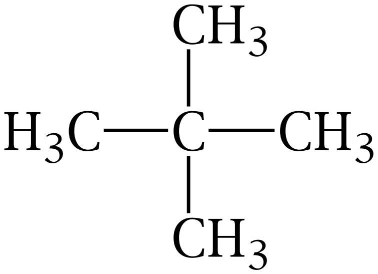
The magnitude of H_e is proportional to the electron density in the σ bond.



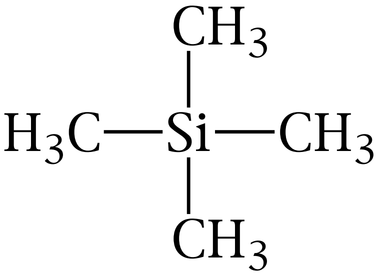
Consider…

Tetramethylsilane
aka TMS

$H_3C—O—CH_3$

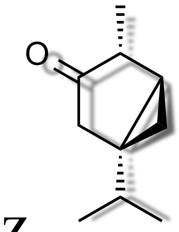


$$H_3C—C(CH_3)_2—CH_3$$



$$H_3C—Si(CH_3)_2—CH_3$$

So, in NMR spectroscopy, inductive effects play a key role in chemical shift.



Because almost all proton resonance frequencies are found downfield of the TMS signal, TMS is used as an internal reference. All peak positions are measured as frequencies in Hz downfield of TMS, with TMS at zero.

There is a problem however is that the ν is proportional to H_o

- H_o = 60 MHz, ν = 162 Hz downfield of TMS
- H_o = 100 MHz, ν = 270 Hz downfield of TMS

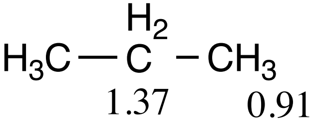
We define the δ scale:

$$\delta = \frac{\nu_{\text{signal downfield of TMS}}}{\text{spectrometer frequency in MHz}} = ppm$$

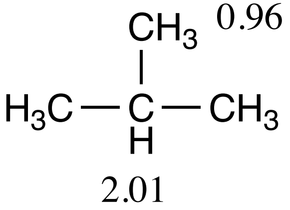
$$\delta = \frac{162\,Hz}{60\,MHz} = \frac{270\,Hz}{100\,MHz} = 2.70\,ppm$$

CH_4 0.23

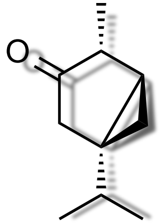
H_3C-CH_3 0.86



$H_3C-\overset{H_2}{C}-CH_3$



$H_3C-\overset{CH_3}{\underset{H}{C}}-CH_3$



Chemical shift correlates well with electronegativity…

$$H_3C\text{—}X$$

	F	O	Cl	Br	I	H	TMS
EN	4.0	3.5	3.1	2.8	2.5	2.1	1.8
δ ppm	*4.26*	*3.40*	*3.05*	*2.68*	*2.16*	*0.23*	*0*

$CHCl_3$	CH_2Cl_2	CH_3Cl
7.27	5.30	3.05

$\text{—}CH_2Br$	$\text{—}C\underline{H_2}CH_2Br$	$\text{—}C\underline{H_2}CH_2CH_2Br$	$C\underline{H_2}CH_2CH_3$
3.30	1.69	1.25	1.20

π Electron Effects - Diamagnetic Anisotropy

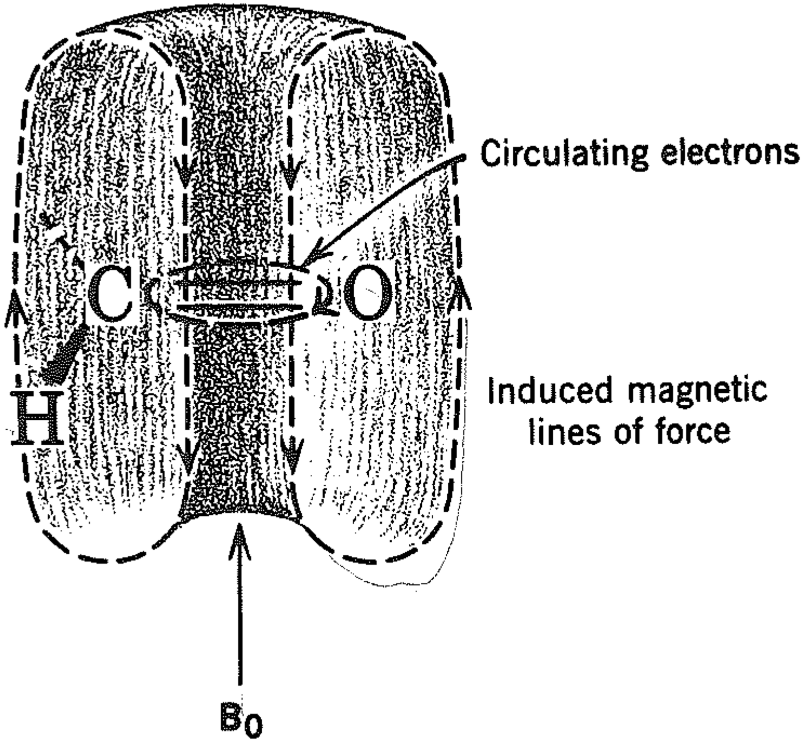
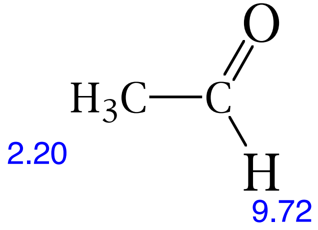
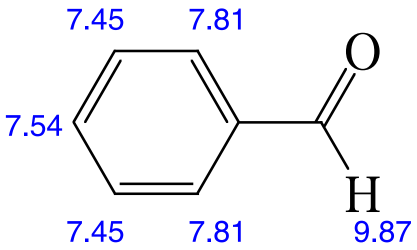


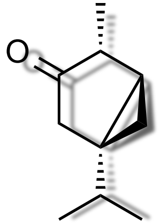
FIGURE 4.16. Deshielding of aldehydic protons.





*graphics from ‘***Spectrometric Identification of Organic Compounds***’ , 5th Ed. Silverstein et al.

π Electron Effects - Diamagnetic Anisotropy



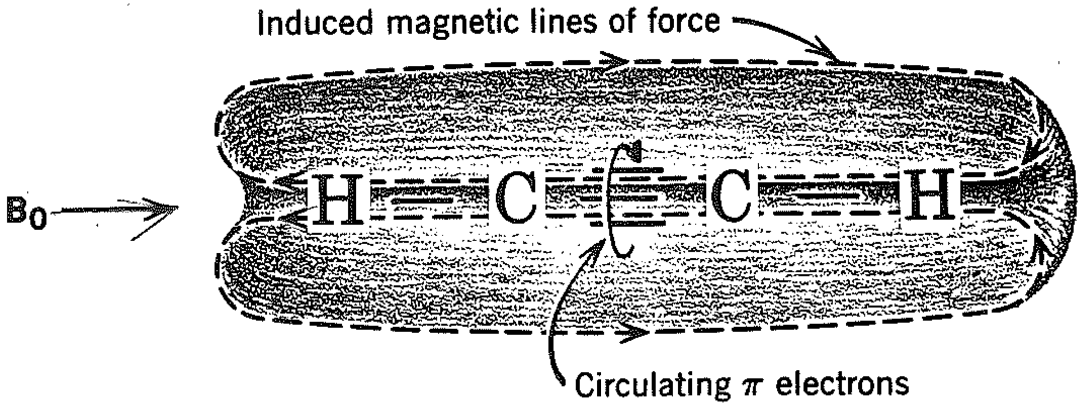


FIGURE 4.15. Shielding of alkyne protons.

1.80 $H_3C—C{\equiv}C—H$ 1.82

*graphics from ‘***Spectrometric Identification of Organic Compounds***’, 5th Ed. Silverstein et al.

π Electron Effects - Diamagnetic Anisotropy

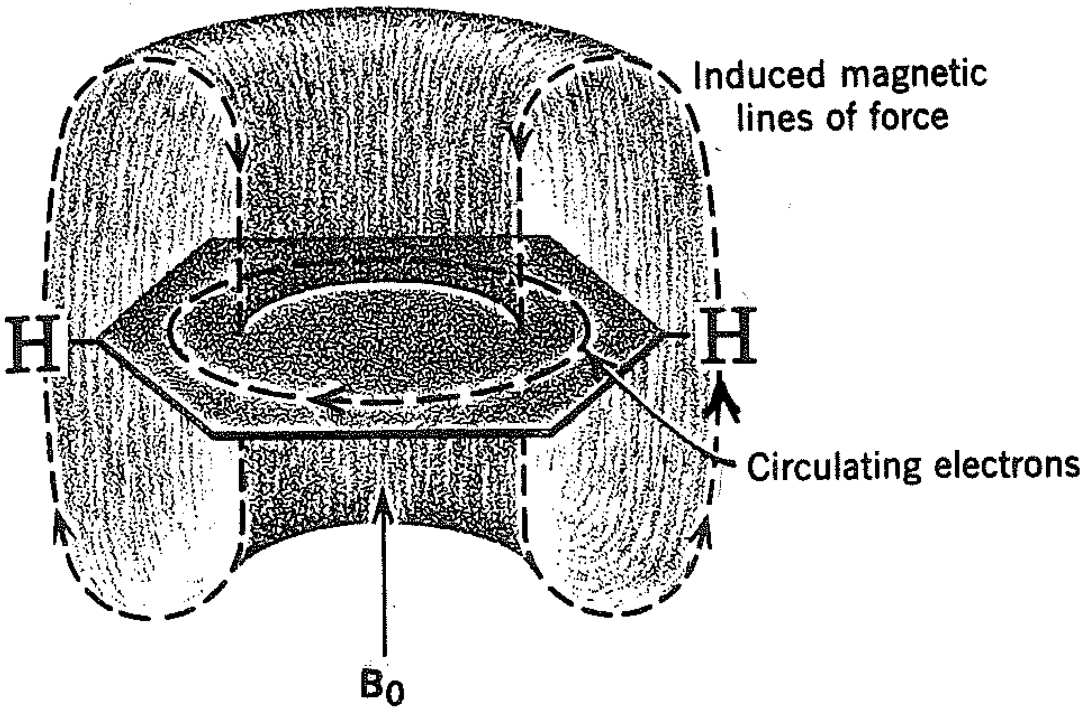
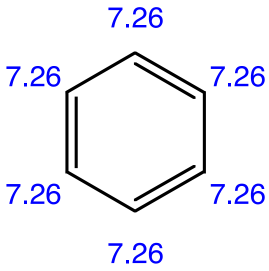
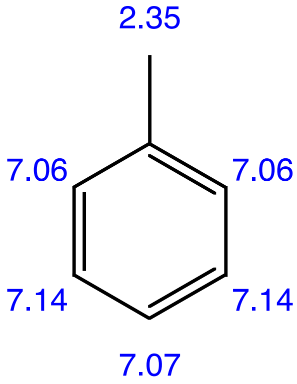


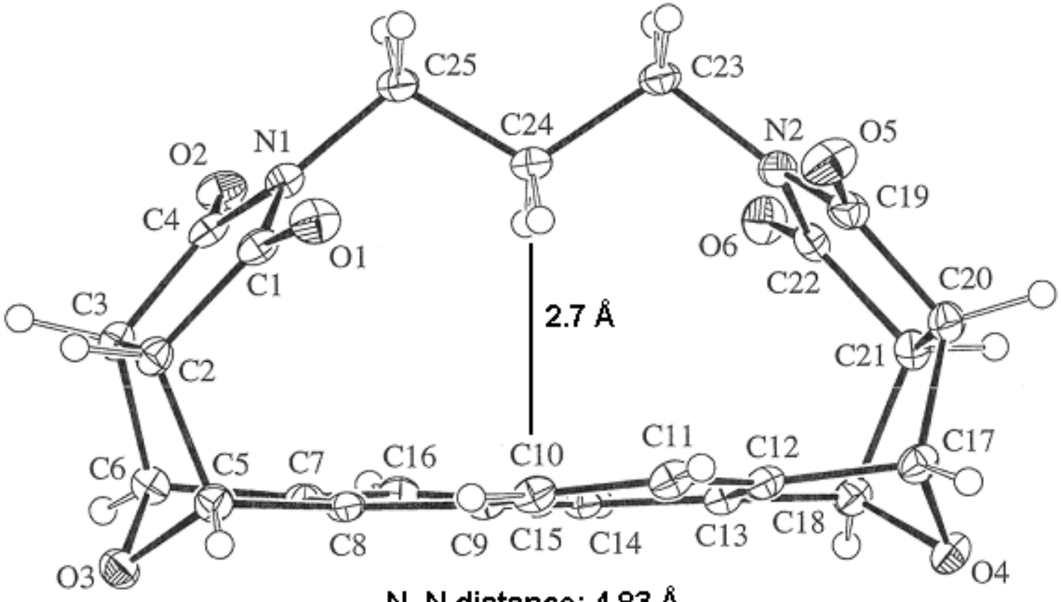
FIGURE 4.17. Ring current effects in benzene.



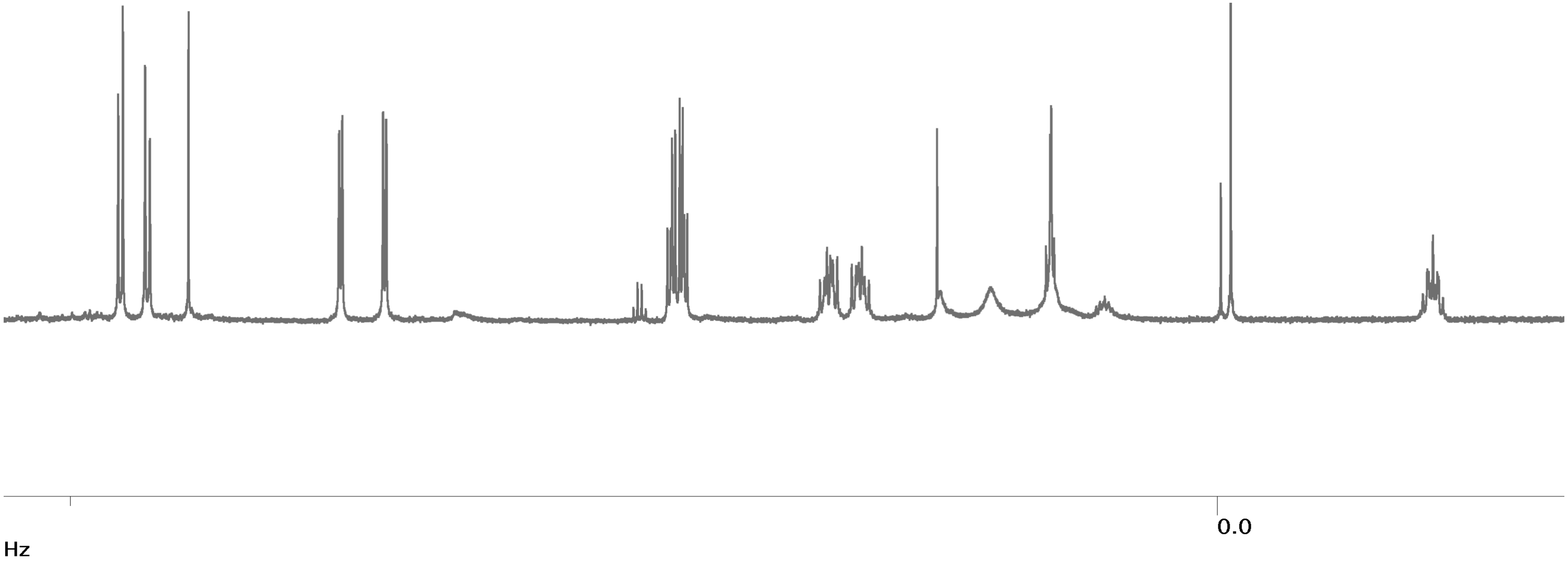


*graphics from '***Spectrometric Identification of Organic Compounds***', 5th Ed. Silverstein et al.

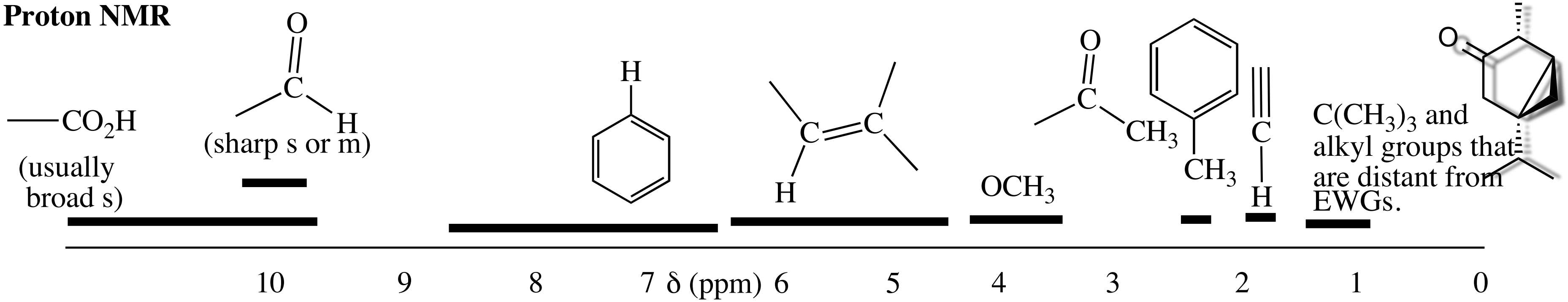
X-ray Structure of the 3C Naphthodifuran Cyclophane



N–N distance: 4.83 Å



Proton NMR



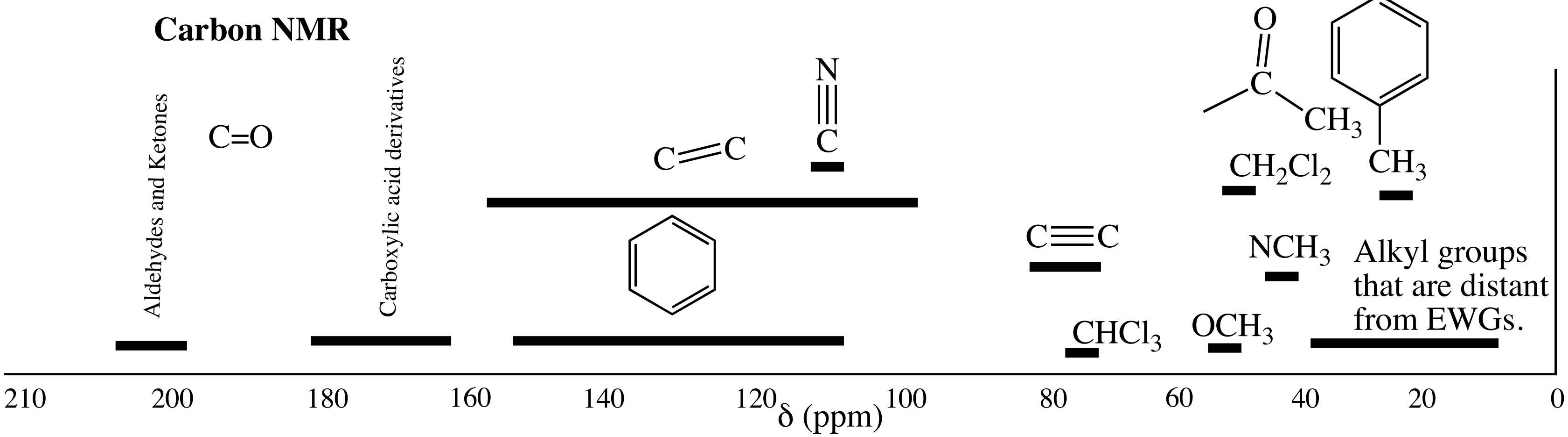
Alkyl protons cover a range of chemical shifts depending on the natrue and number of the electron-withdrawing groups (EWGs) that are nearby. Methyl groups are found between 0.9 and 4.2 ppm (pentane to C**H**$_3$OCOAr). Methylene (CH$_2$) groups are found between 1.2 (pentane) and 5.2 ppm (CH$_2$Cl$_2$). Methine (CH) groups range between 1.5 ppm ((CH$_3$)$_3$C**H**) to 5.6 ppm (PhC**H**(OCH$_3$)$_2$) to 7.27 ppm (CHCl$_3$) depending on the three substituents.

IF YOUR SPECTRUM HAS A BROAD PEAK then it is almost certinaly an NH, NH$_2$ or OH gropu and not CH. These peaks can occur anywhere between 1.5-14 ppm and vary even from sample to sampe of the same compound! Only carboxylic acids are somewhat consistent at ~10 ppm.

Ethynyl (vinyl C=C**H**) protons are usually found at 5-6.5 ppm. They are found in the upfield portion of this range if an O or N atom is directly attached (beta to H, i.e. ROCH=C**H**) and downfield in this range if a carbonyl, nitro or CN group is attached to the double bond (i.e. O=C-C=C**H**).

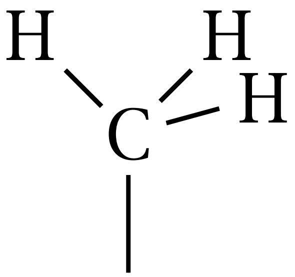
Aromatic protons (PhH) are usually found around 7-7.5 ppm. They may be shielded upfield of this range (as far as 6.5) by lone-pair donating groups (OH and NH - strong o/p directing ring activators)or downfield of this range (7.5-8.5 ppm) by electron-withdrawing groups(C=O, NO$_2$, SO$_3$H i.e. strong meta-directing deactivators).

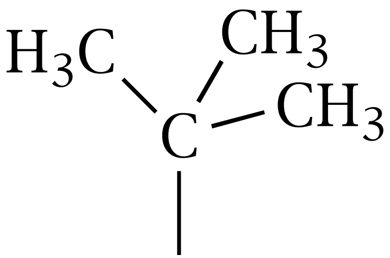
Carbon NMR



Chemical shift equivalence of atoms or groups.

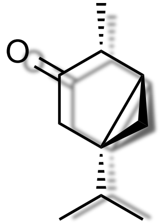
Groups or nuclei are shift equivalent if they can be exchanged by a bond rotation without changing the structure of the molecule.



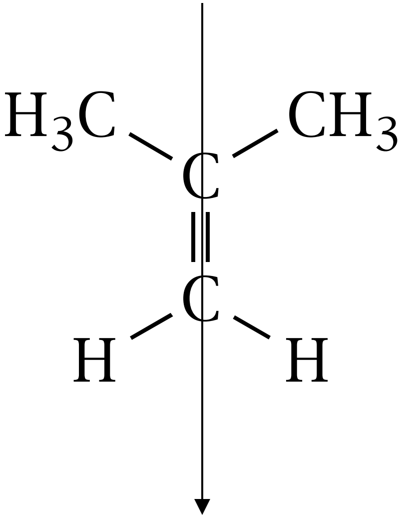


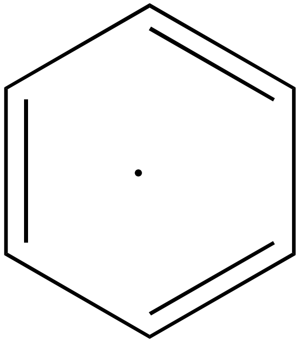
These atoms/groups are said to be “homotopic”. Homotopic atoms/groups are always shift equivalent.

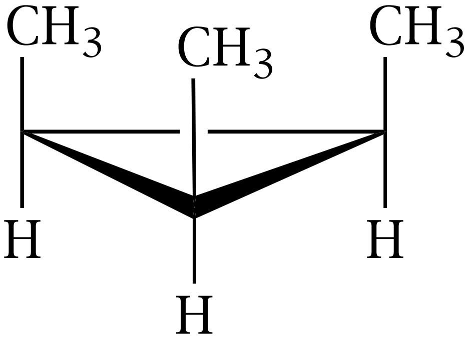
Shift equivalence can also be determined by symmetry properties of the molecule known as symmetry elements.



A proper axis of rotation…

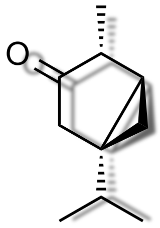


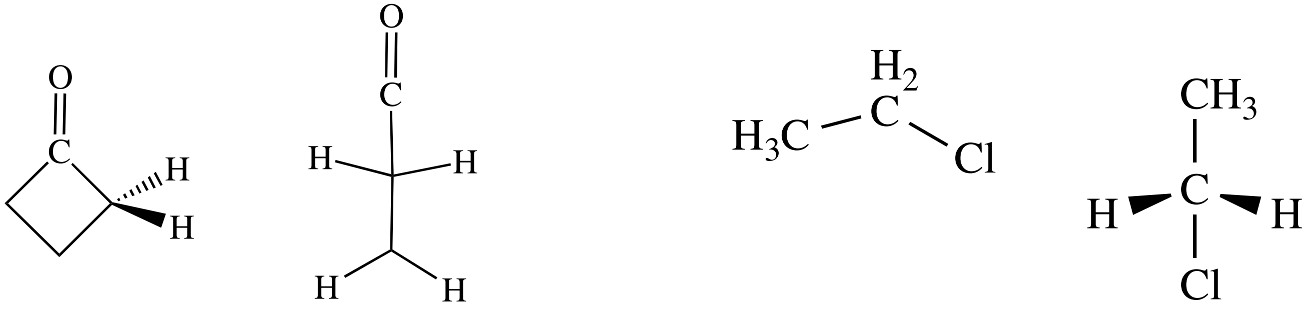




Nuclei or groups that are related by a proper axis of rotation are homotopic.

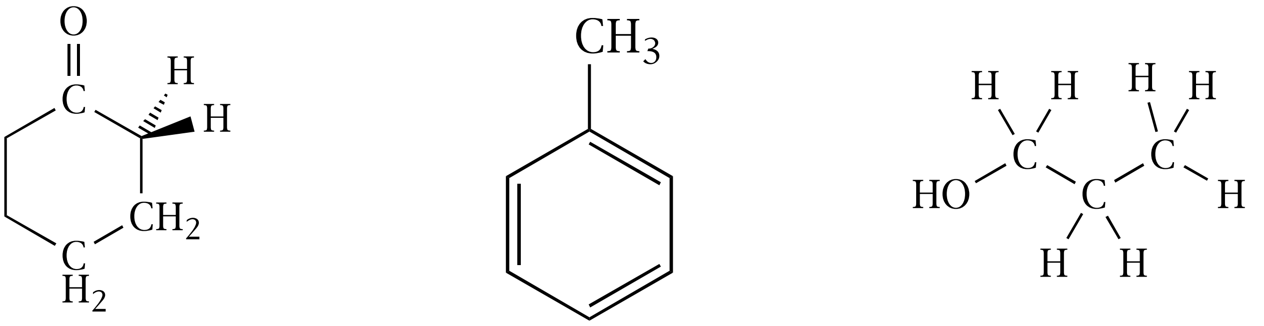
Atoms/groups that can be reflected in an internal mirror plane of symmetry, but not exchanged by bond rotation or a proper axis of symmetry are "enantiotopic".

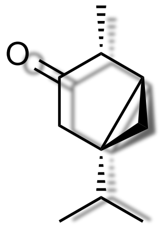




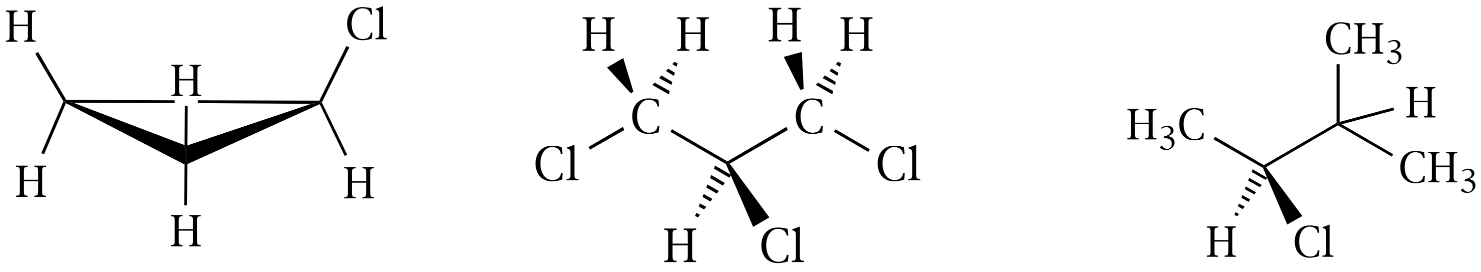
For our current purposes, enantiotopic protons are shift equivalent.

Constitutionally different atoms/groups are not shift equivalent. It is typically easy to recognize atoms/groups that are constitutionally different.



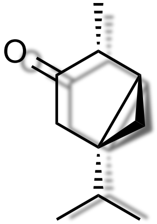


Protons that are not constitutionally different, that cannot be exchanged by bond rotation or by molecular symmetry are “diastereotopic”.

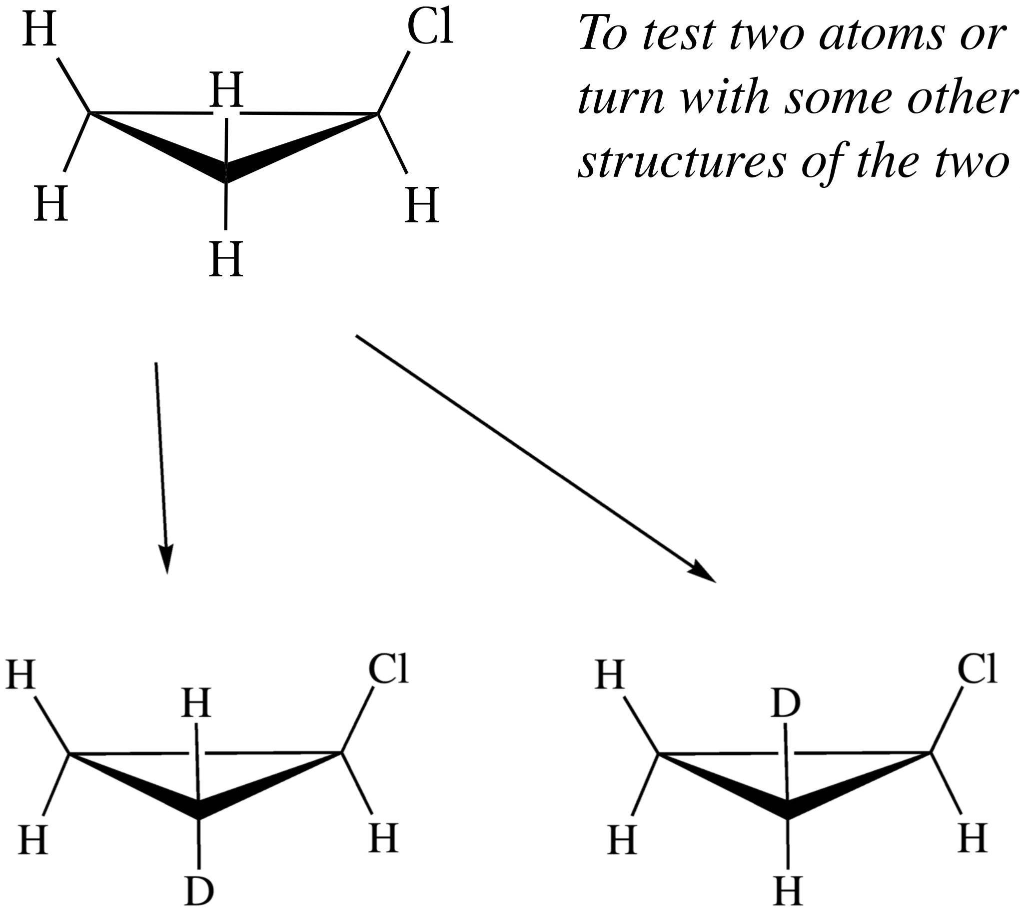


Diastereotopic atoms/groups are NOT shift equivalent, except by coincidence (i.e. they happen to have the same chemical shift by accident).

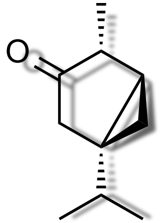
The "topicity" of groups or atoms can be determined using the substitution test.

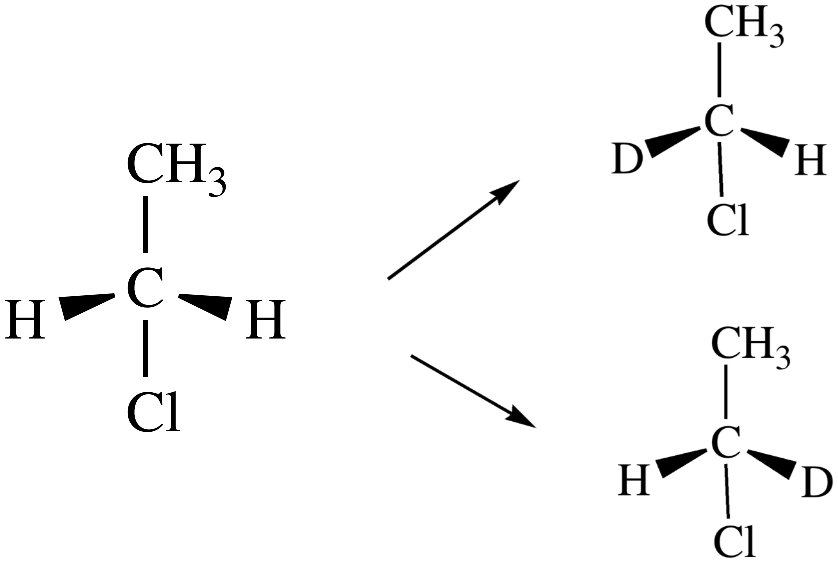


To test two atoms or groups, replace each in turn with some other group and compare the structures of the two products…

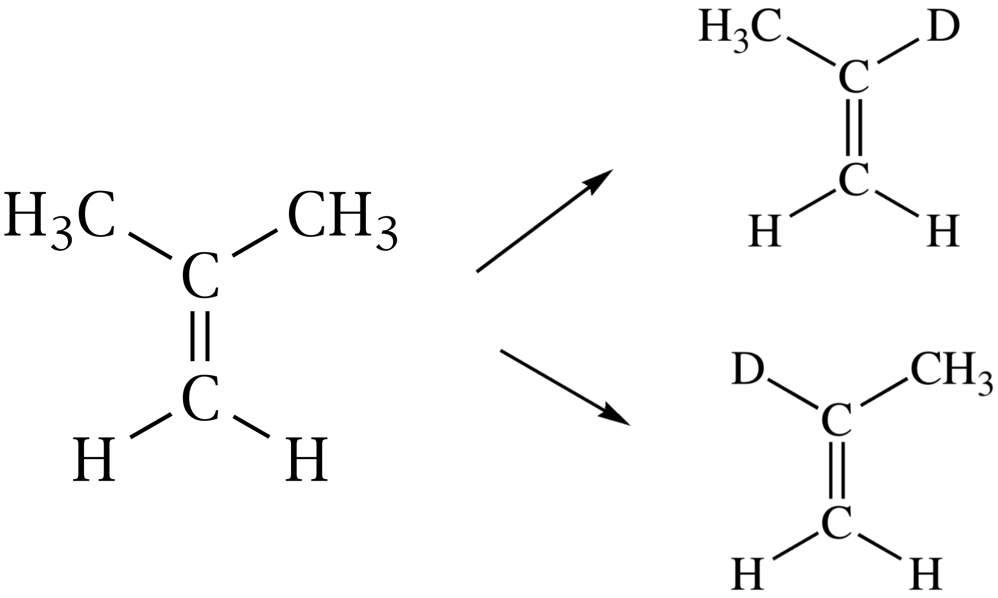


If the structures are identical, then the atoms/groups are homotopic. If the structures are enantiomers the atoms/groups are enantiotopic. If the structures are diastereomers as in this example, then the atoms/groups are diastereotopic.



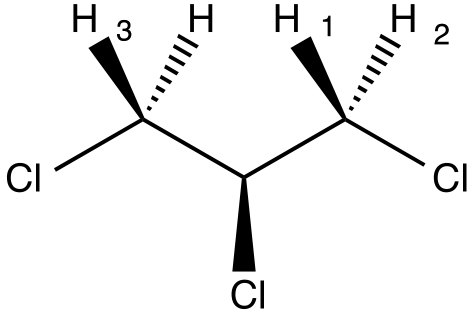


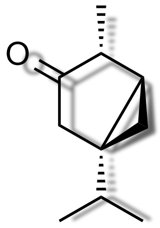
These structures are enantiomers so the protons on the CH_2 are enantiotopic.



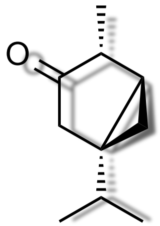
These structures are superimposable making the methyl groups homotopic.

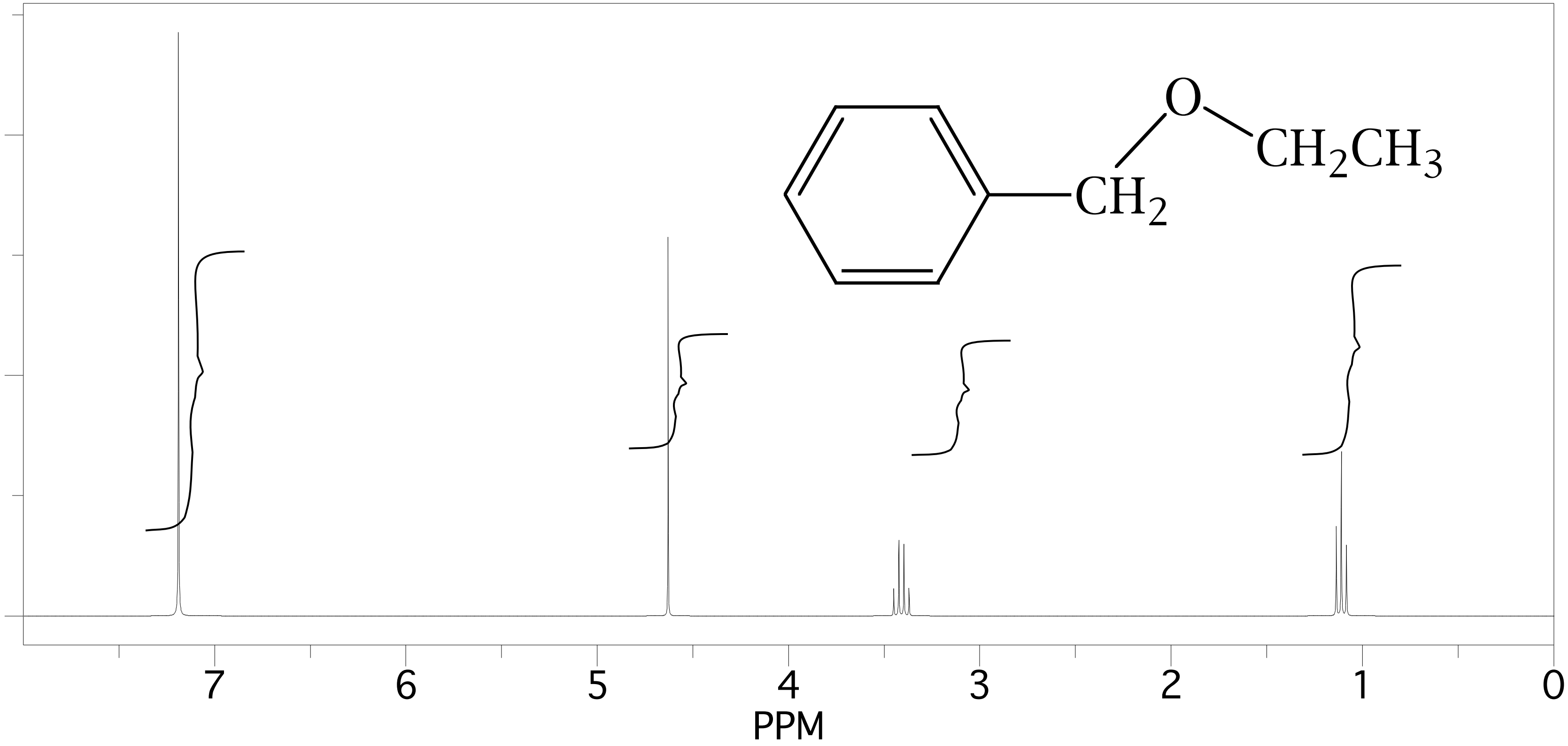
Determine the topicity of H_1 and H_2.
Determine the topicity of H_1 and H_3.





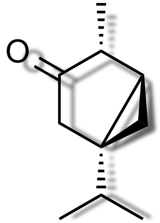
Integration.



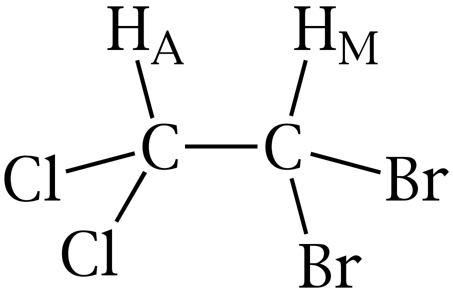


Raw integrals: 8.5:3.5:3.4:5.0

Chemical shift effects of neighbouring magnetic fields - spin-spin coupling

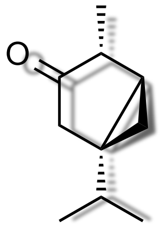


Consider the vicinal protons in the molecule:



In the absence of any influence by H_M, H_A will resonate at ν_A.

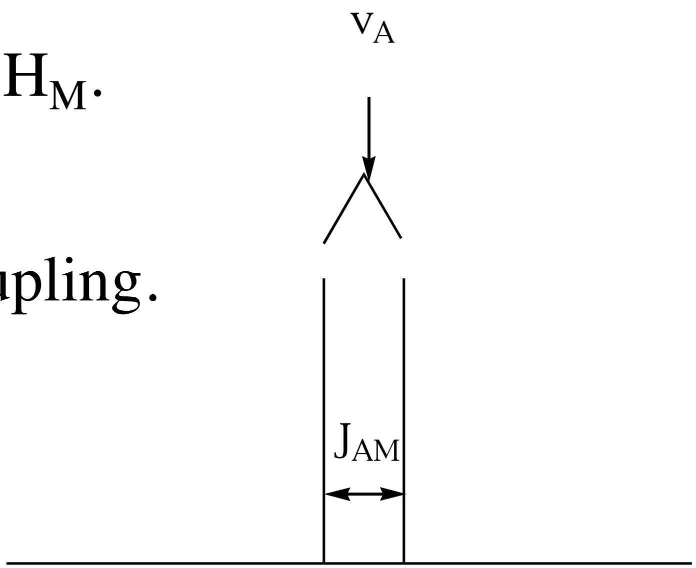
But proton H_M generates its own magnetic field which will affect ν_A. Is this field aligned with H_o or against H_o i.e. will it shield or deshield H_A?



Remember that the population of the two spin states are nearly equal. In the total of all molecules, half of the H_M protons will be aligned with H_o and half against.

So in half the molecules, H_M shields H_A and in the other half H_M deshields H_A. We therefore see two peaks for H_A, of equal intensity; one upfield of ν_A and one downfield of ν_A.

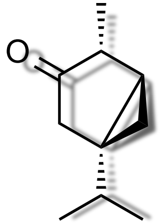
We call this type of signal a … “doublet”.
We say that H_A is “split” into a doublet by H_M.



This effect is referred to as “spin-spin” coupling.

The distance between the two peaks in Hz is J, the coupling constant.

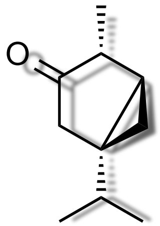
Important aspects of coupling:



- coupling always goes both ways. If H_A is split by H_M, then H_M must also be split by H_A and J must be equal in both cases.
- coupling is a through-bond and not a through-space effect.
- coupling between shift-equivalent nuclei is not observed.
- coupling constants are independent of field strength: a coupling constant of 7 Hz on a 300 MHz instrument will be 7 Hz on a 500 MHz machine.

The magnitude of J can be extremely useful in determining structure. It depends on:

- number of bonds between nuclei
- type of bonds between nuclei
- type of nuclei
- conformation



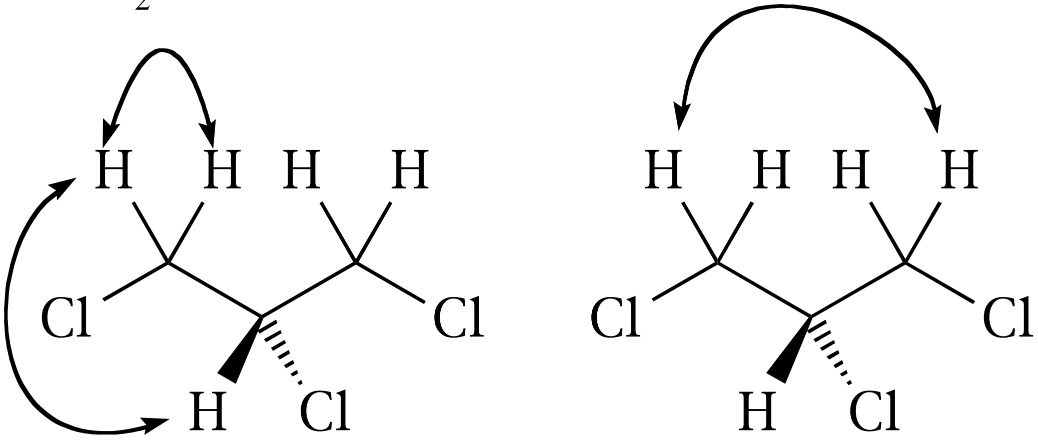
Because coupling is a through bond effect, the magnitude of J depends on the number of bonds between coupling nuclei. One bond couplings are larger than two bond couplings, two larger than three. In proton-proton couplings, four bond couplings are not usually observed.

Geminal $J_2 = 12\text{-}14$ Hz

$J_4 = 0$ Hz Long range

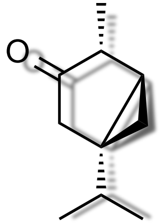
Vicinal

$J_3 = 7$ Hz*

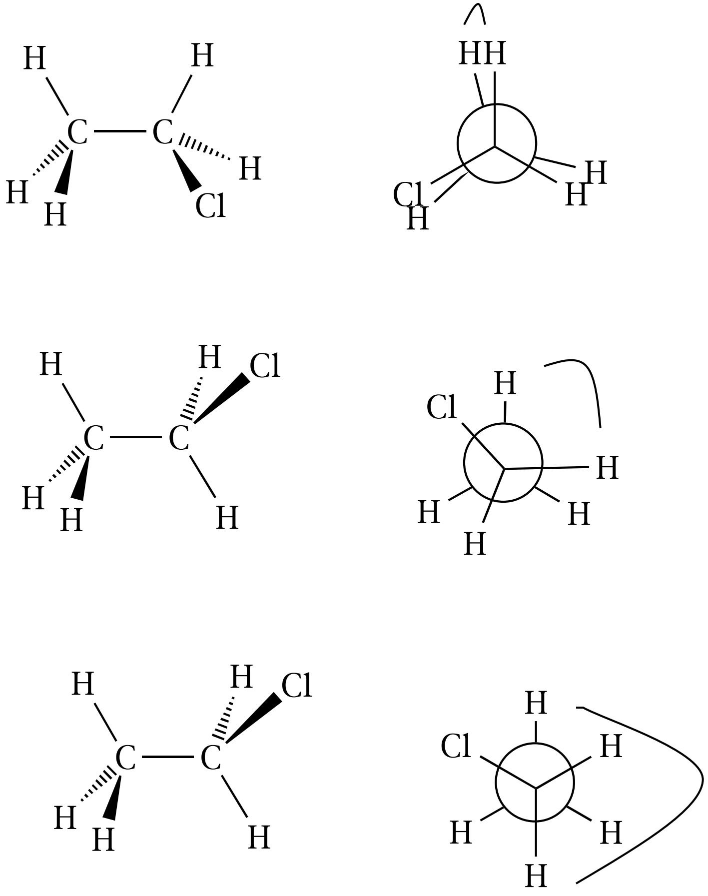


* In conformationally averaged systems.

The magnitude of vicinal couplings depends strongly on the overlap between adjacent C-H bonds.



The Dihedral Karplus Curve



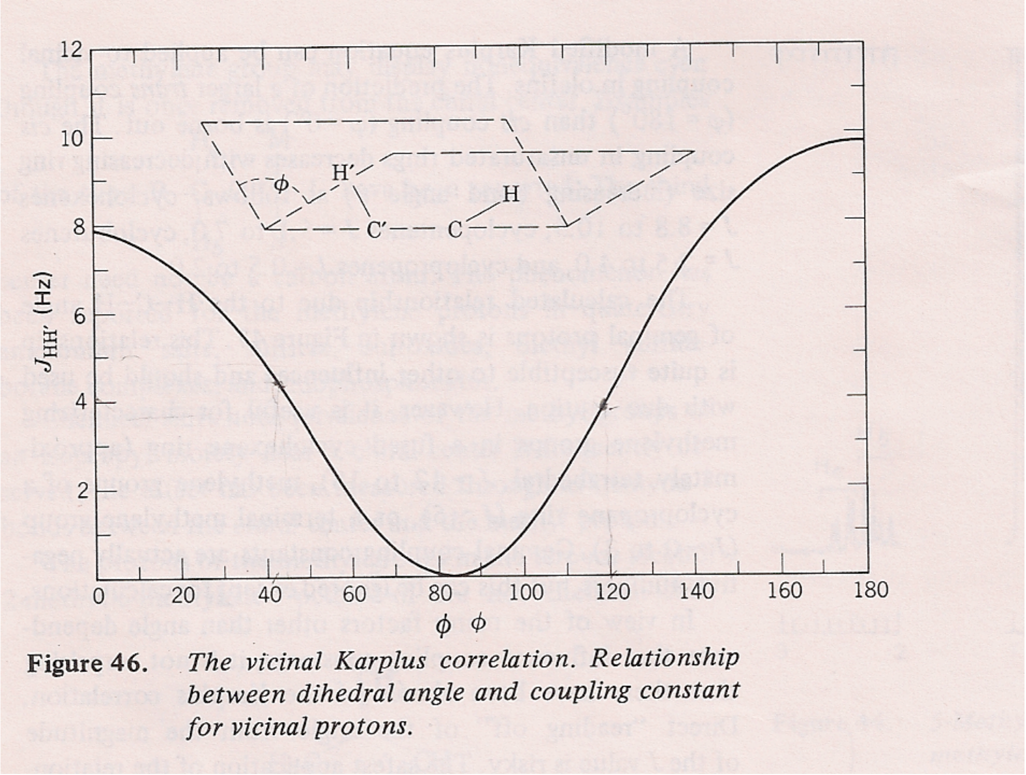
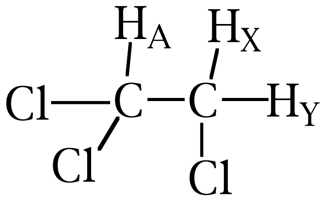
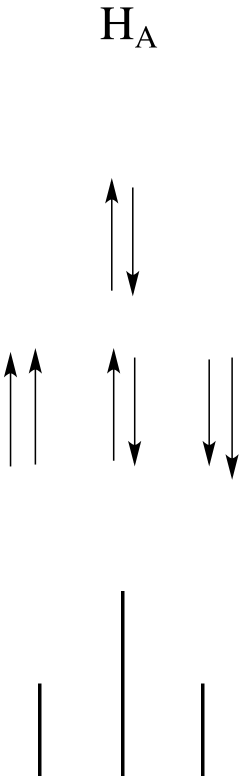


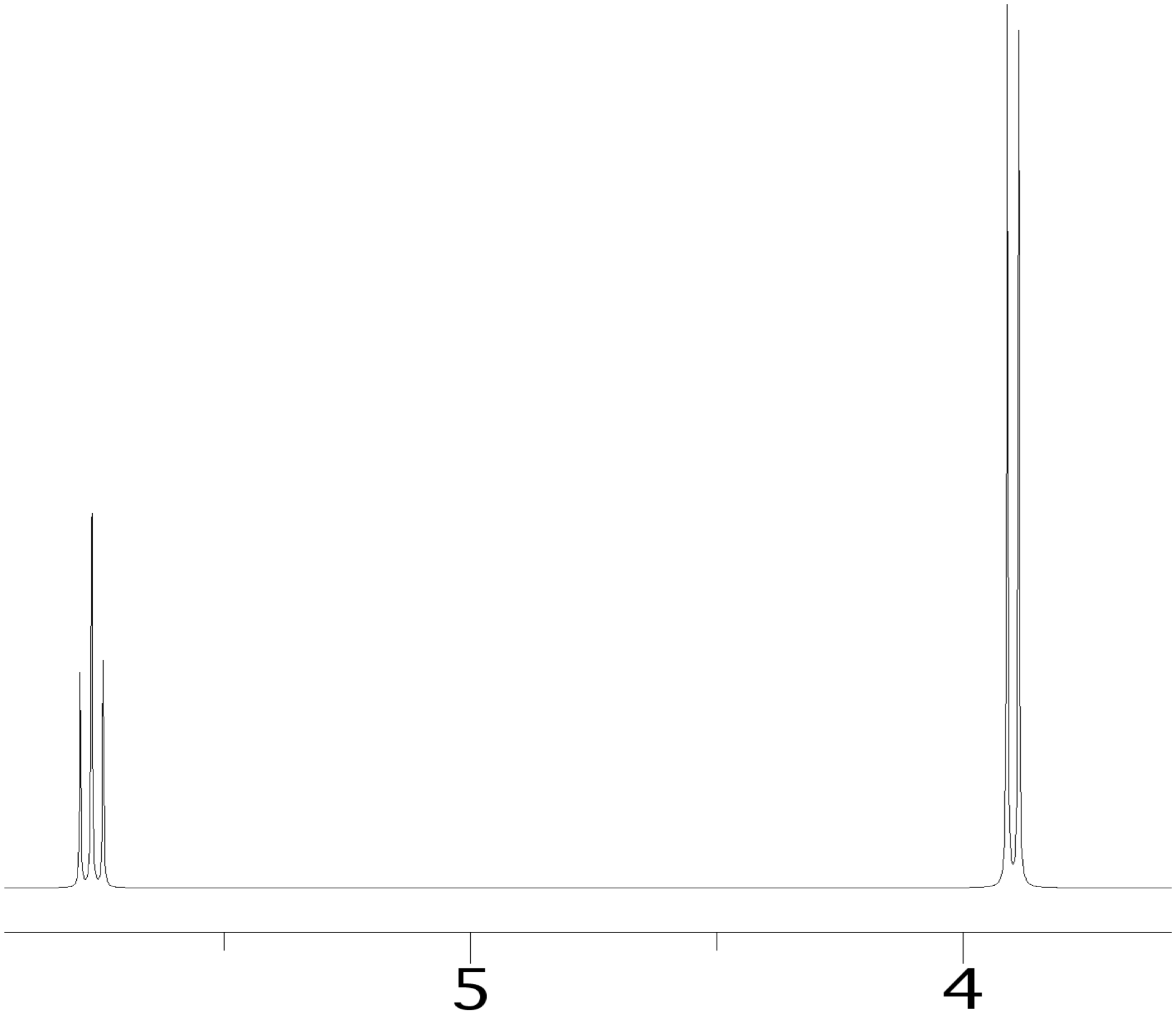
Figure 46. *The vicinal Karplus correlation. Relationship between dihedral angle and coupling constant for vicinal protons.*

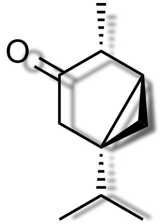
From Silverstein, Bassler and Morrill.

Consider the following molecule:





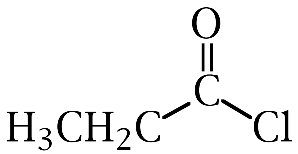




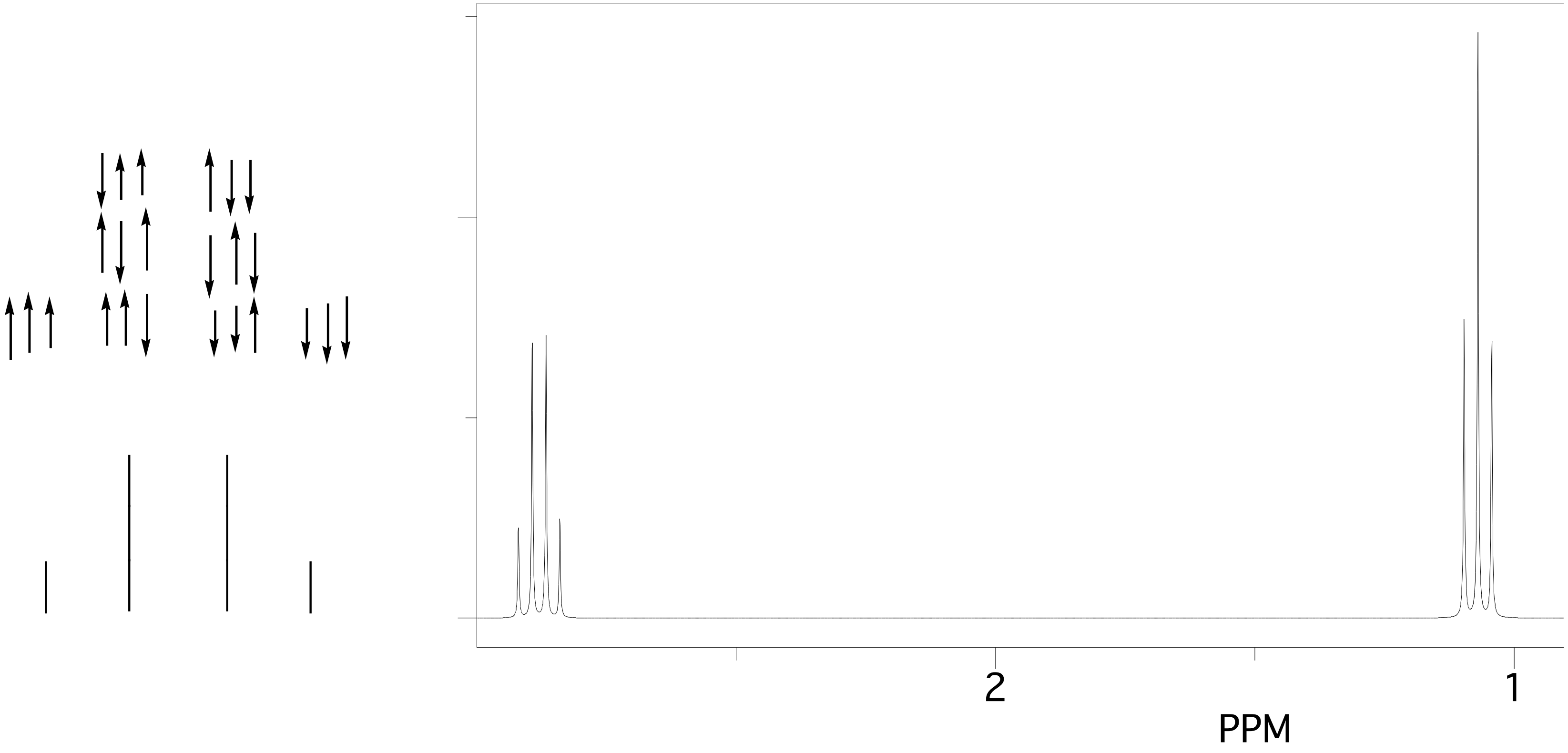
NOTE:
The SIGNAL INTEGRATION tells you about the number of protons that give rise to a particular signal. MULTIPLICITY tells you about the number of NEIGHBOURING NUCLEI.

The n + 1 rule (Pascal's Triangle: for simple aliphatic systems, the number of lines in a given signal is n+1 where n is the no. of neighbouring protons.

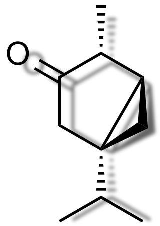
Consider the following molecule:



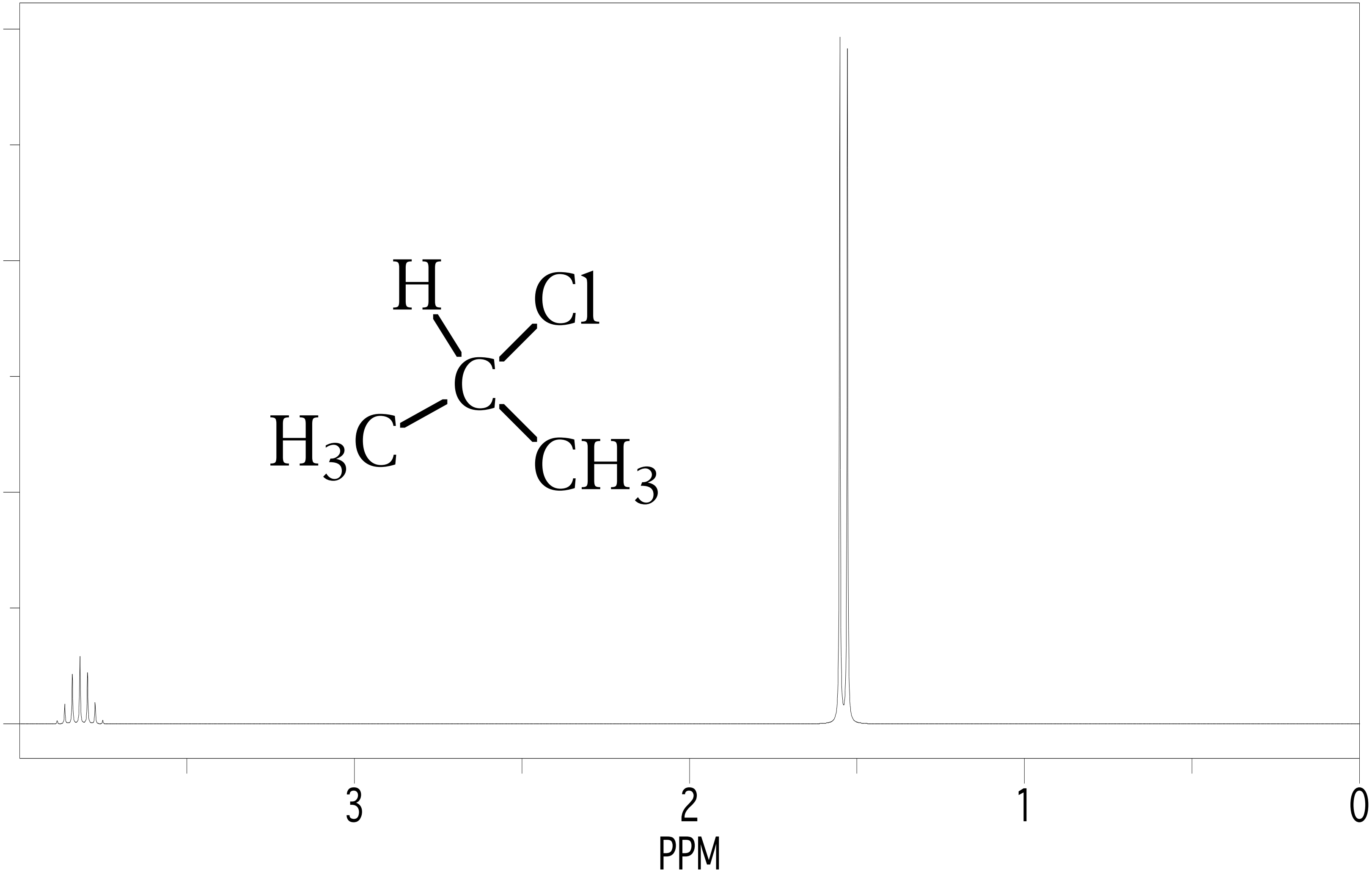
$H_3CH_2C-C(=O)-Cl$



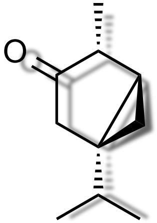
The combination of a 2 proton quartet and a 3 proton triplet is characteristic of the presence of an ethyl group.

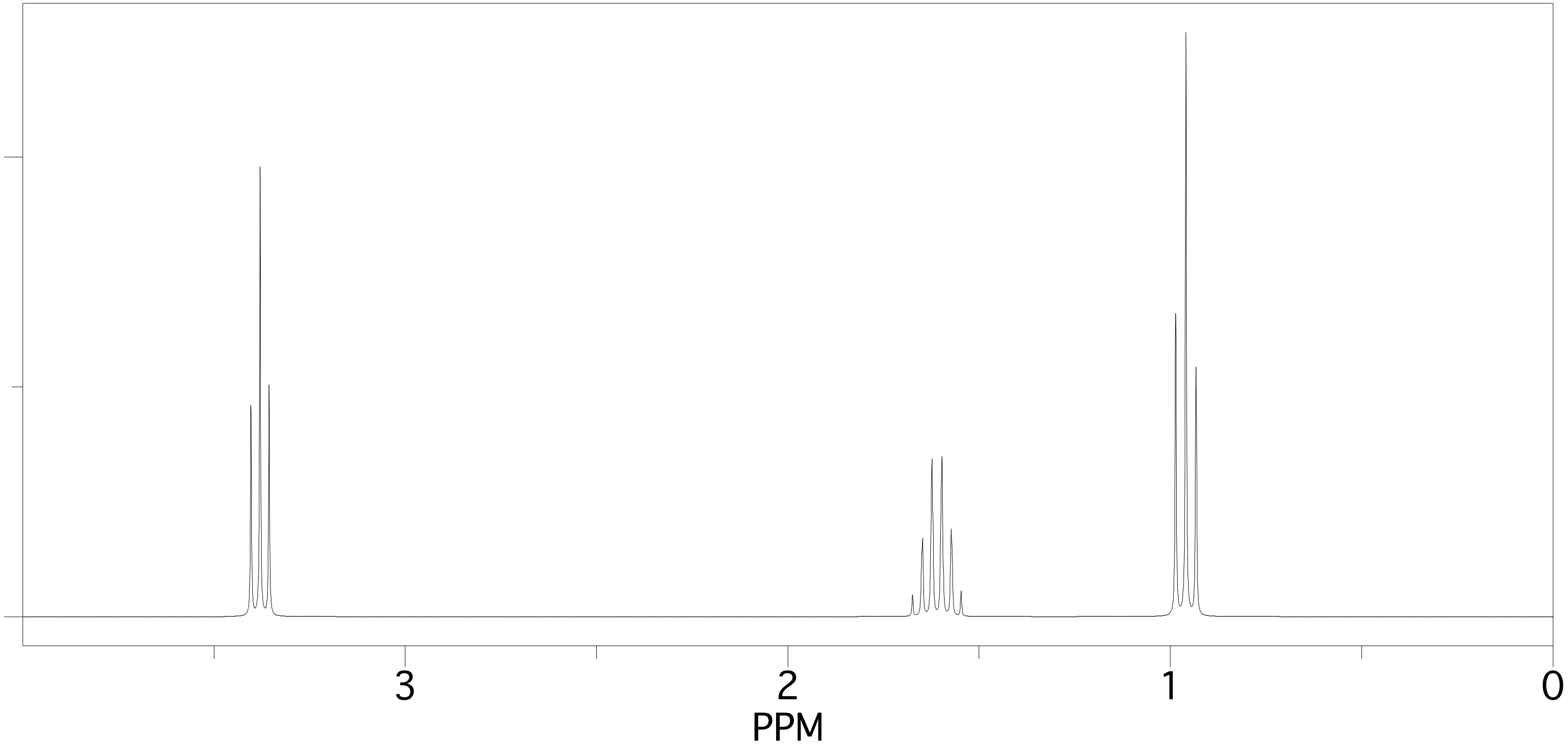


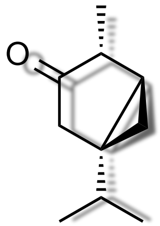
The isopropyl group.



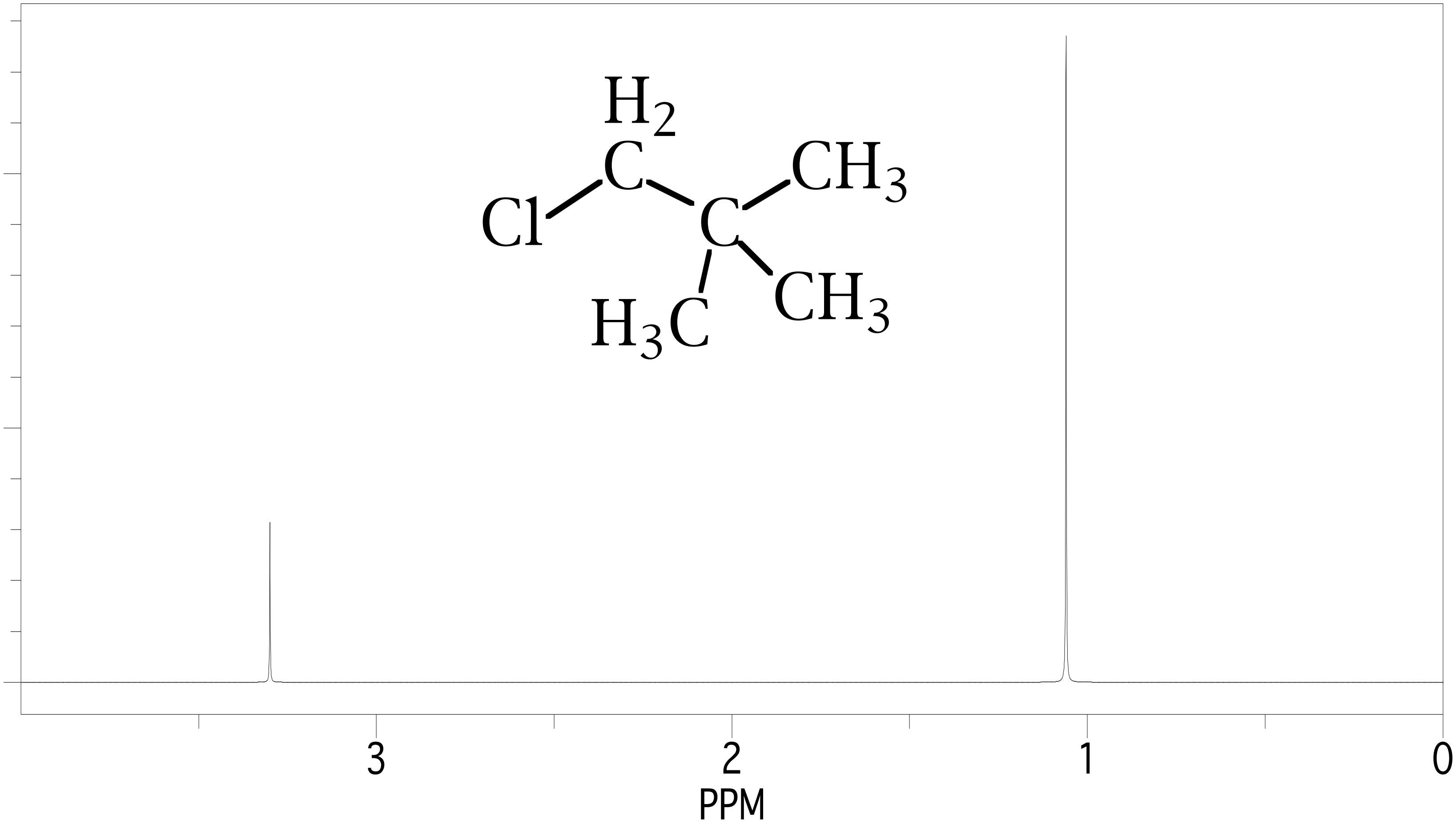
The n-propyl group. $CH_3CH_2CH_2Cl$

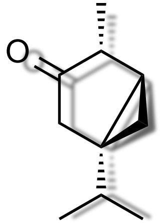






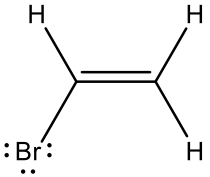
The t-butyl group.

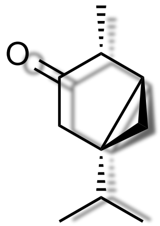


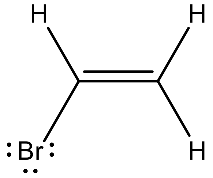


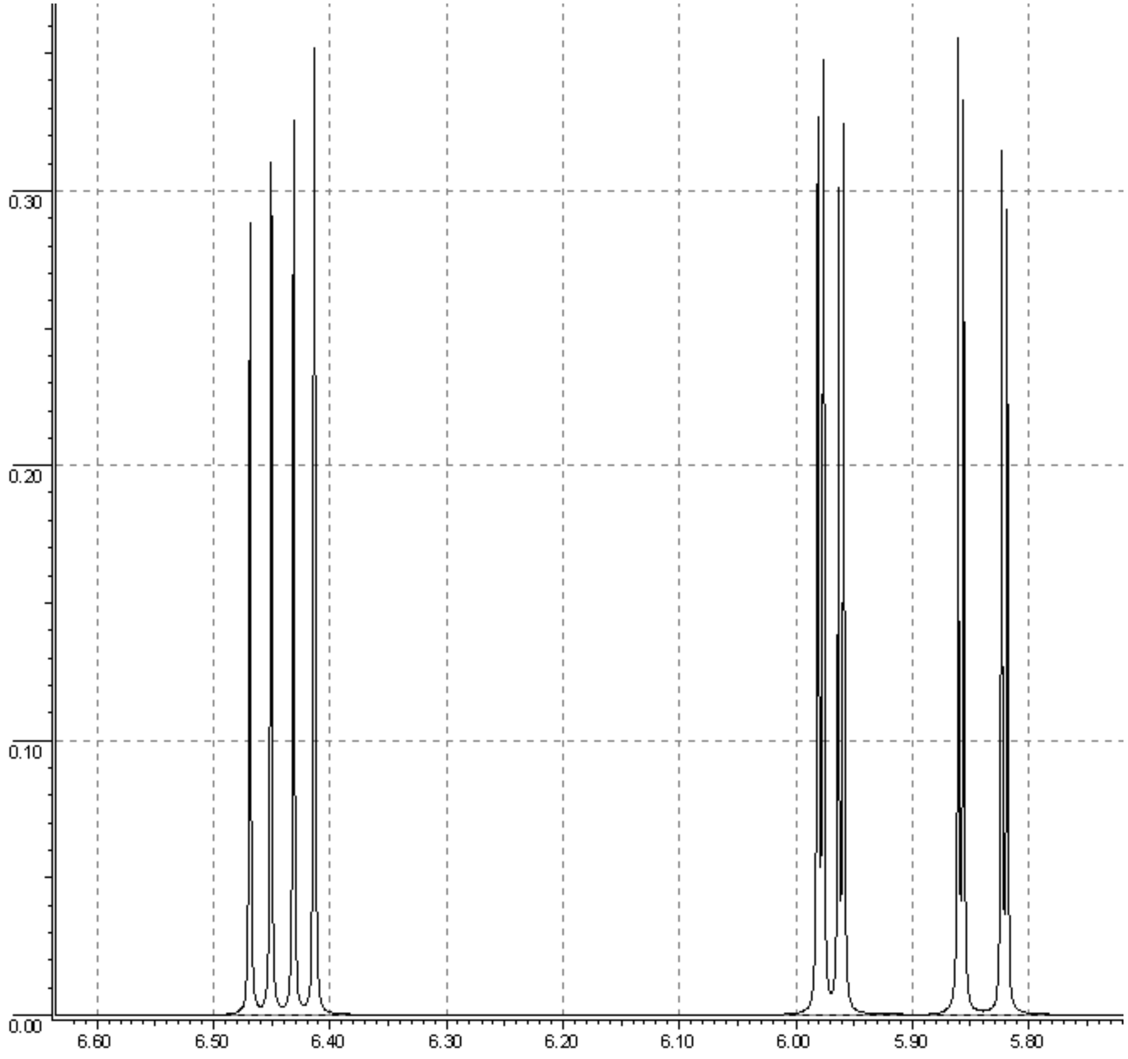
For more complex splitting patterns we use tree diagrams (Pascal's triangles within Pascal's triangle).

e.g.



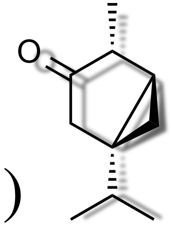

O


H
H
Br
H


0.30
0.20
0.10
0.00
6.60
6.50
6.40
6.30
6.20
6.10
6.00
5.90
5.80

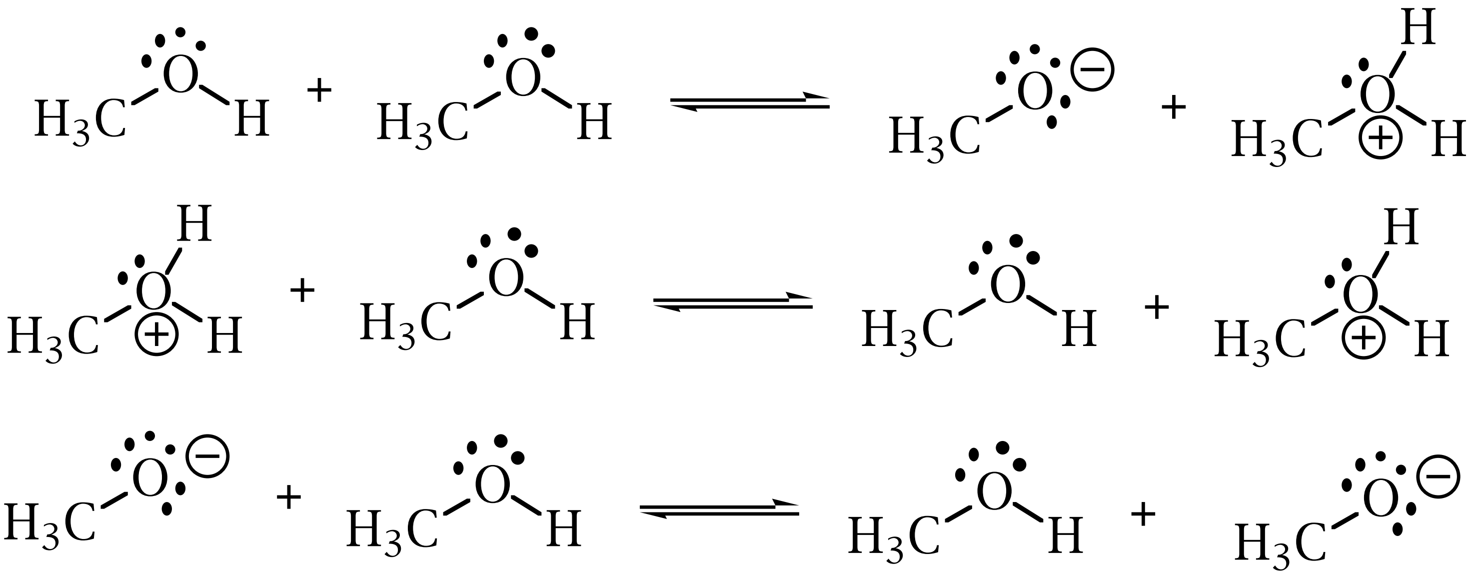
Chemical exchange processes - protons attached to O and N.

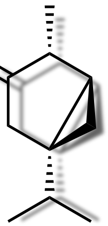
(Alcohols, phenols, carboxylic acids, amines - but not amides)



Unlike most spectroscopic methods, the acquisition of signal in NMR spectroscopy takes about three seconds (proton).

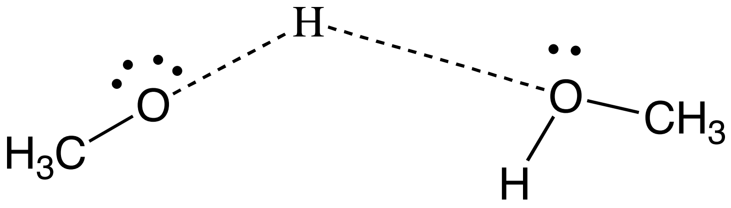
In that time, protons attached to O or N can be transferred from one molecule to another via the autoionization process…



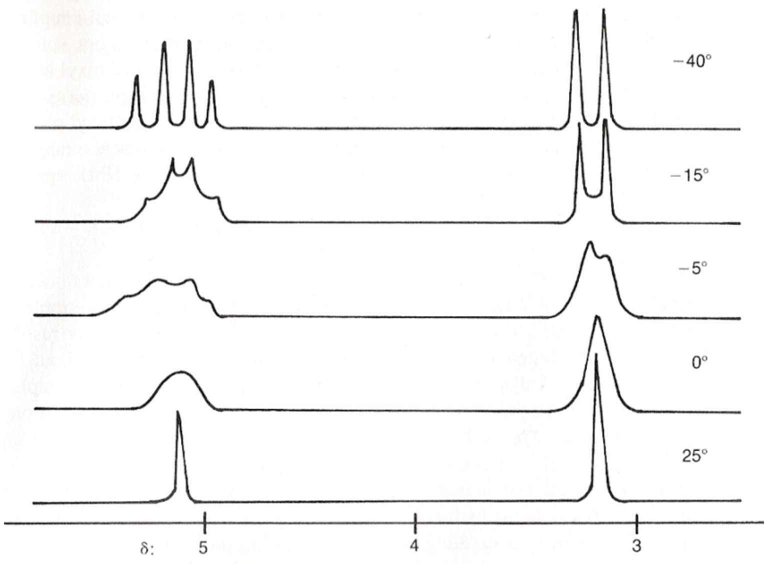


If the rate of exchange is slow compared to the time scale of the NMR experiment (I.e. three seconds) then the spectrum is that expected of CH_3OH. Under these conditions, vicinal OH:CH coupling is observed. This is rarely the case.

If the rate of exchange is comparable to the NMR time scale, then one observes the exchanging proton in a *range* of environments and at a range of chemical shift postions.

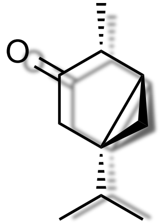


Under these conditions, the OH peak is broad and coupling is not observed.



▶ **FIGURE 5.19** NMR spectra of methanol at various temperatures.

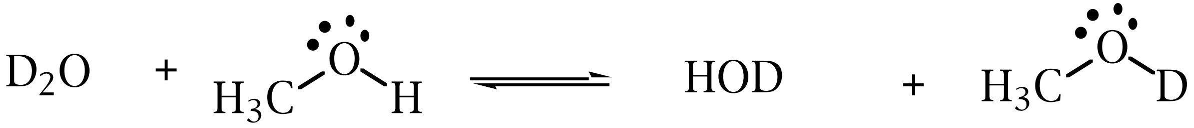
Figure from Pavia, Lampman & Kriz (1996) “Introduction to Spectroscopy” 2nd ed. p.206



The rate of exchange is catalyzed by acids and bases, depends on solvent, temperature, concentration, purity, and lunar phase.

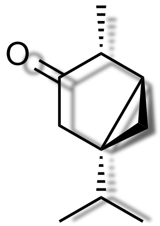
Exchangeable protons:

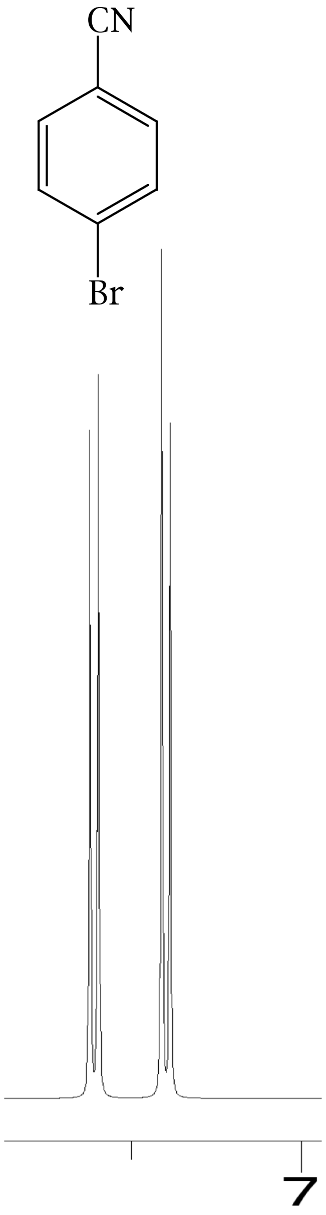
- do not couple
- have variable shift positions
- are observed as broad peaks
- exchange with D_2O

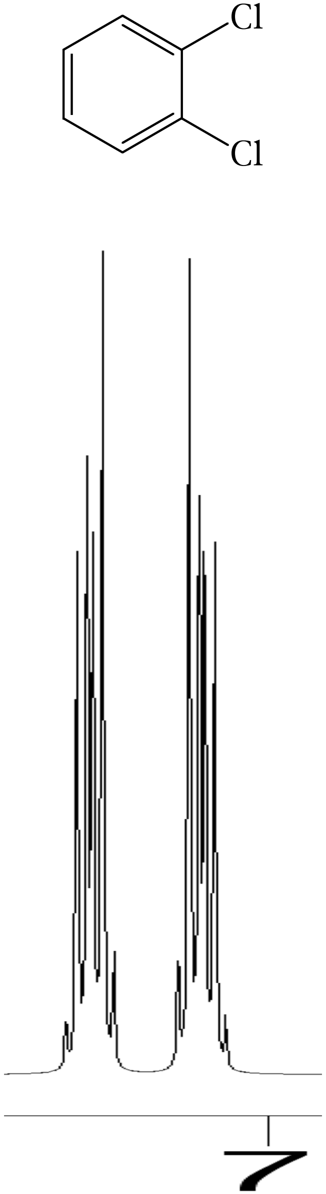


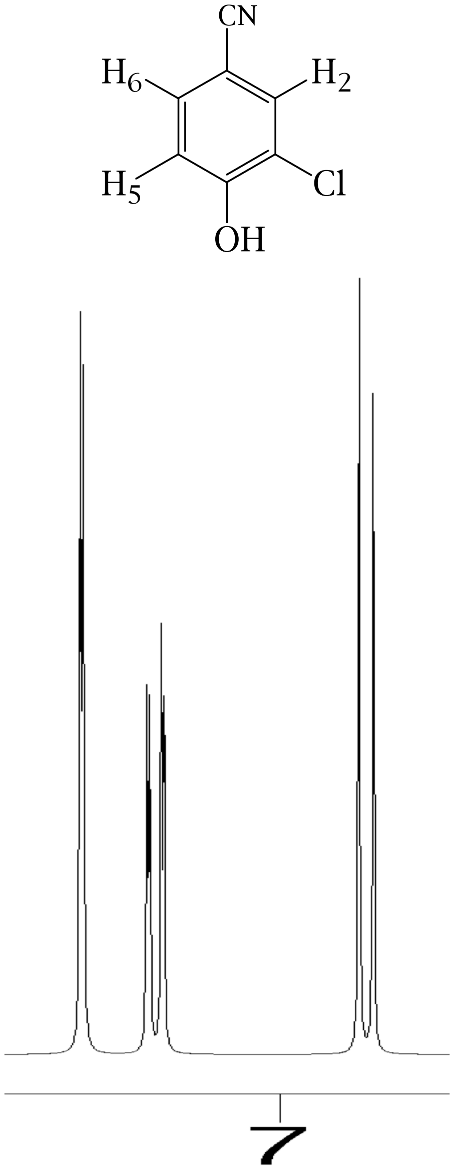
Typically: Alcohols 1-5 ppm
Phenols 3.5-6 ppm
Carboxylic acids 10-12 ppm
NH (amines) 0.5 - 5 ppm

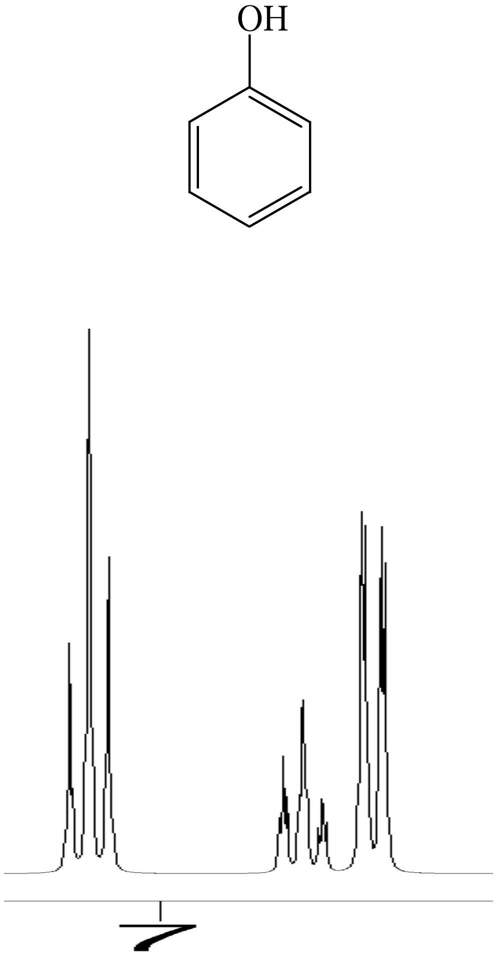
Substituted benzenes.



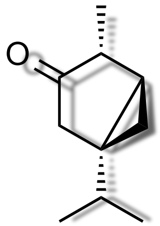


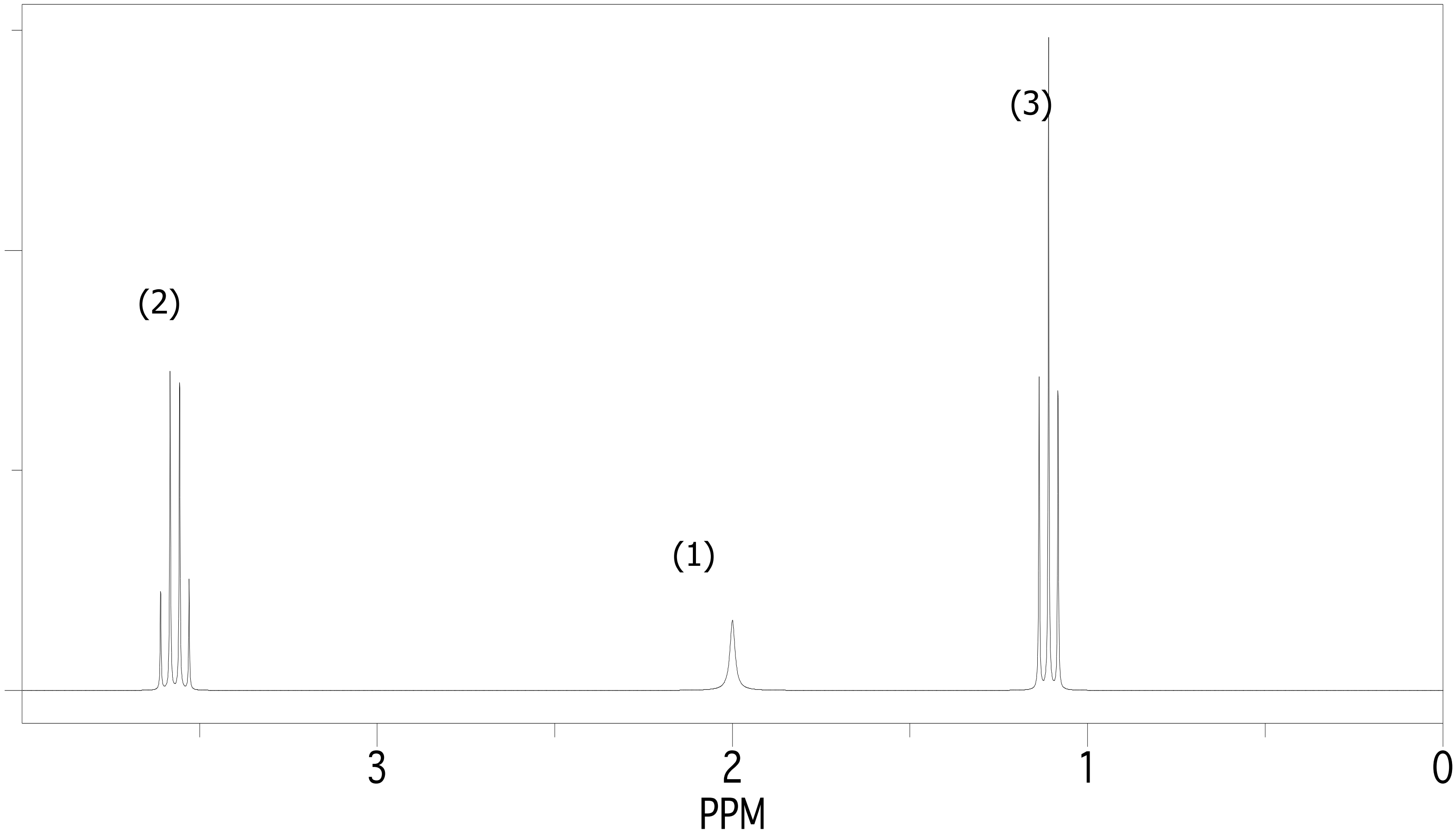




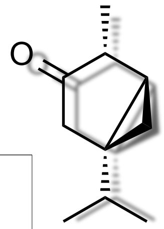


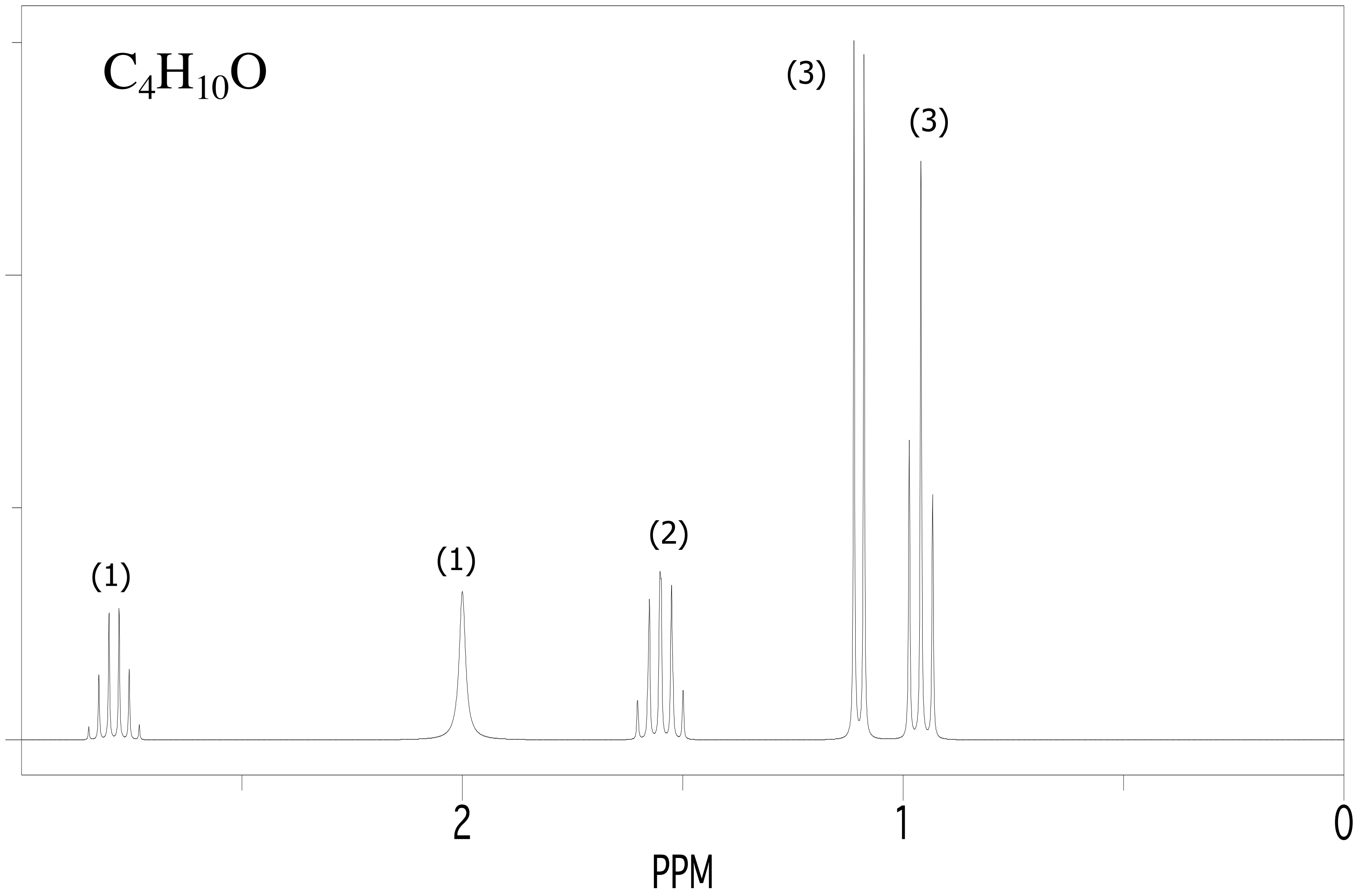
Analyzing Spectra:





Analyzing Spectra:

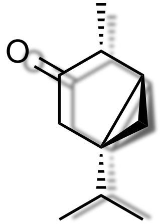




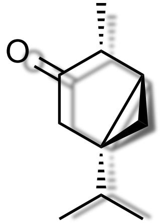
$C_4H_{10}O$

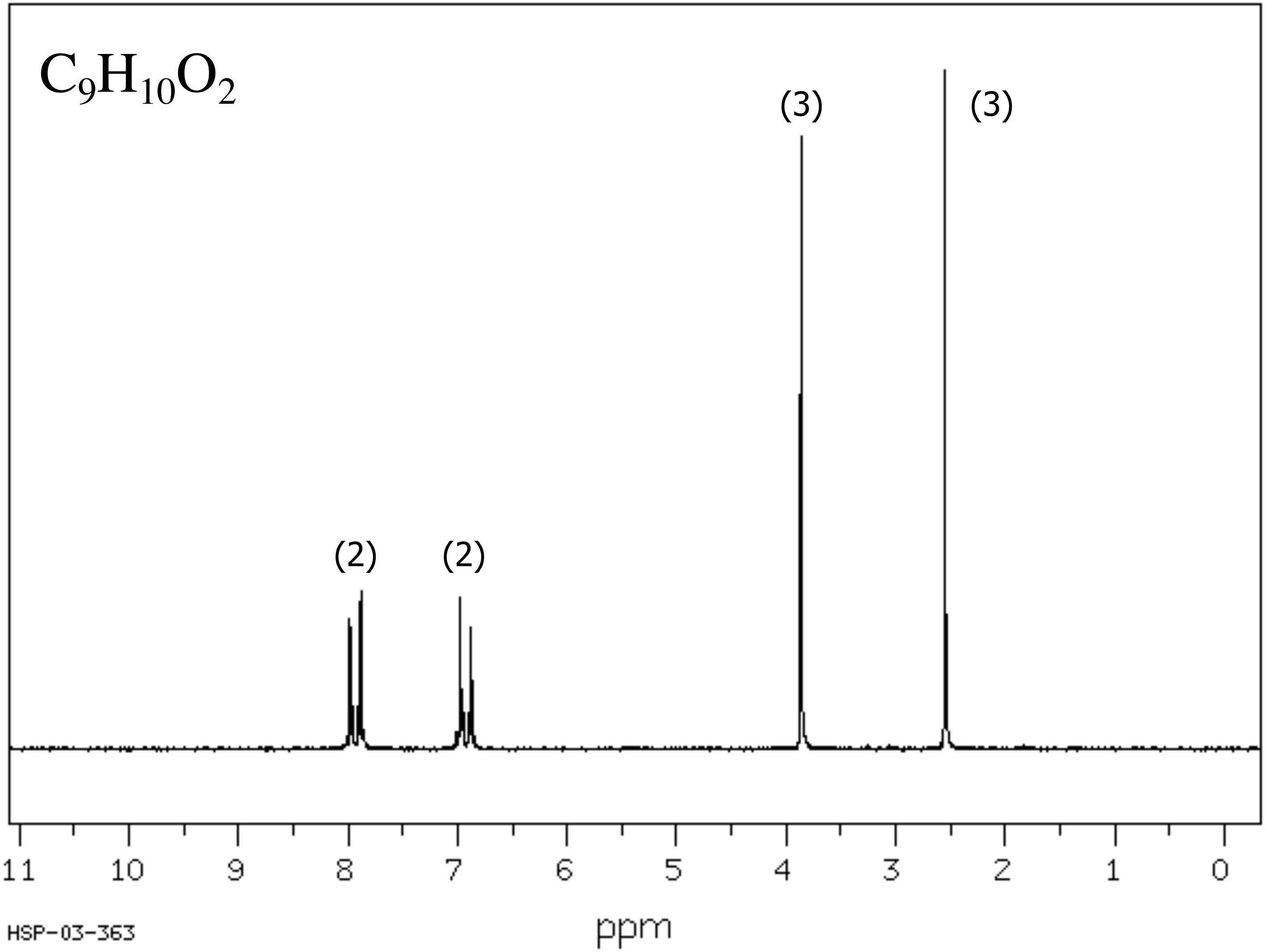
Analyzing Spectra:

C_7H_{12}



Analyzing Spectra:

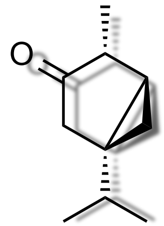


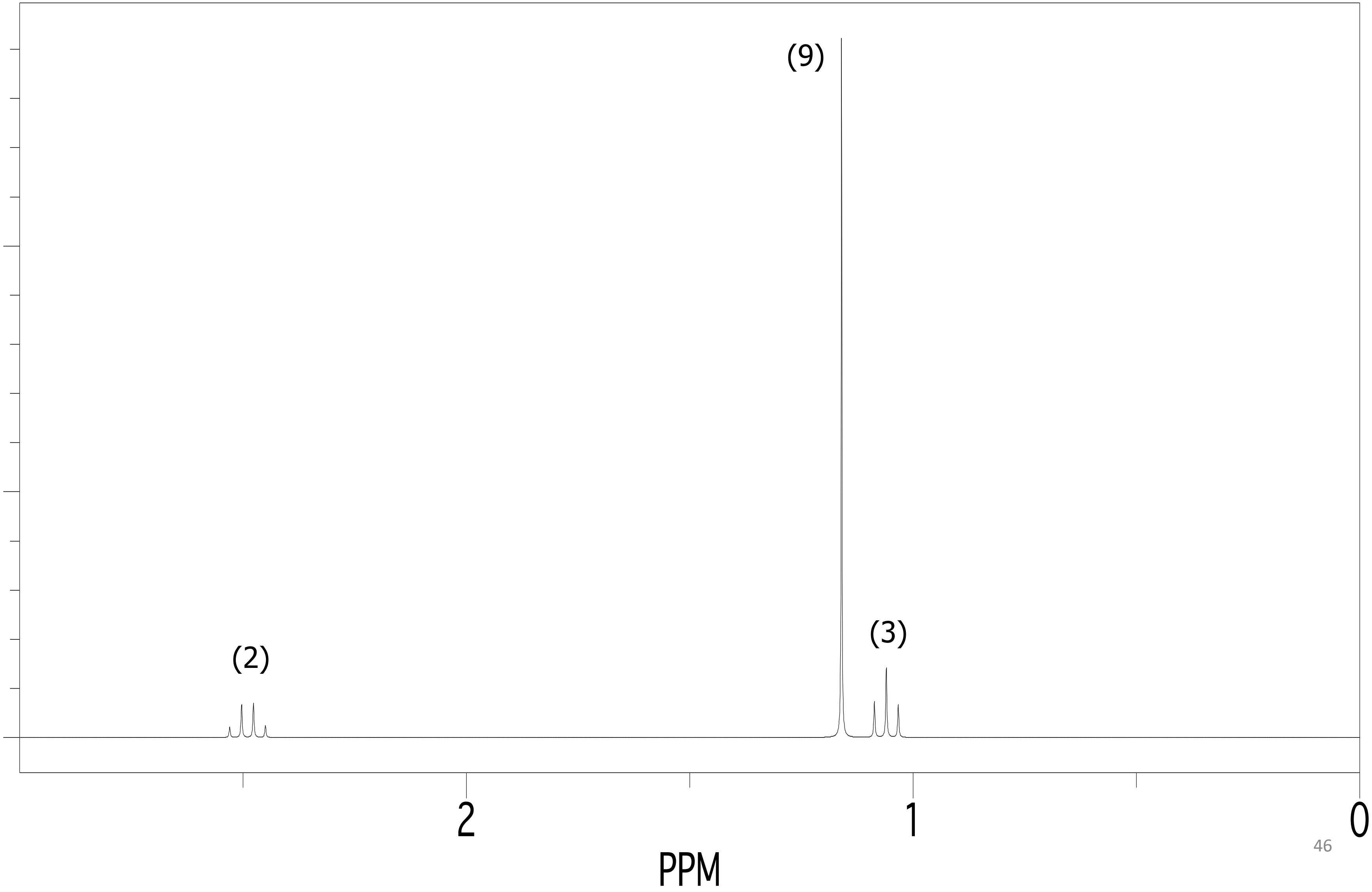


$C_9H_{10}O_2$

Analyzing Spectra:

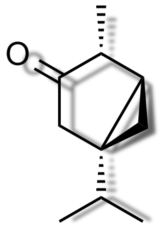
$C_7H_{14}O$

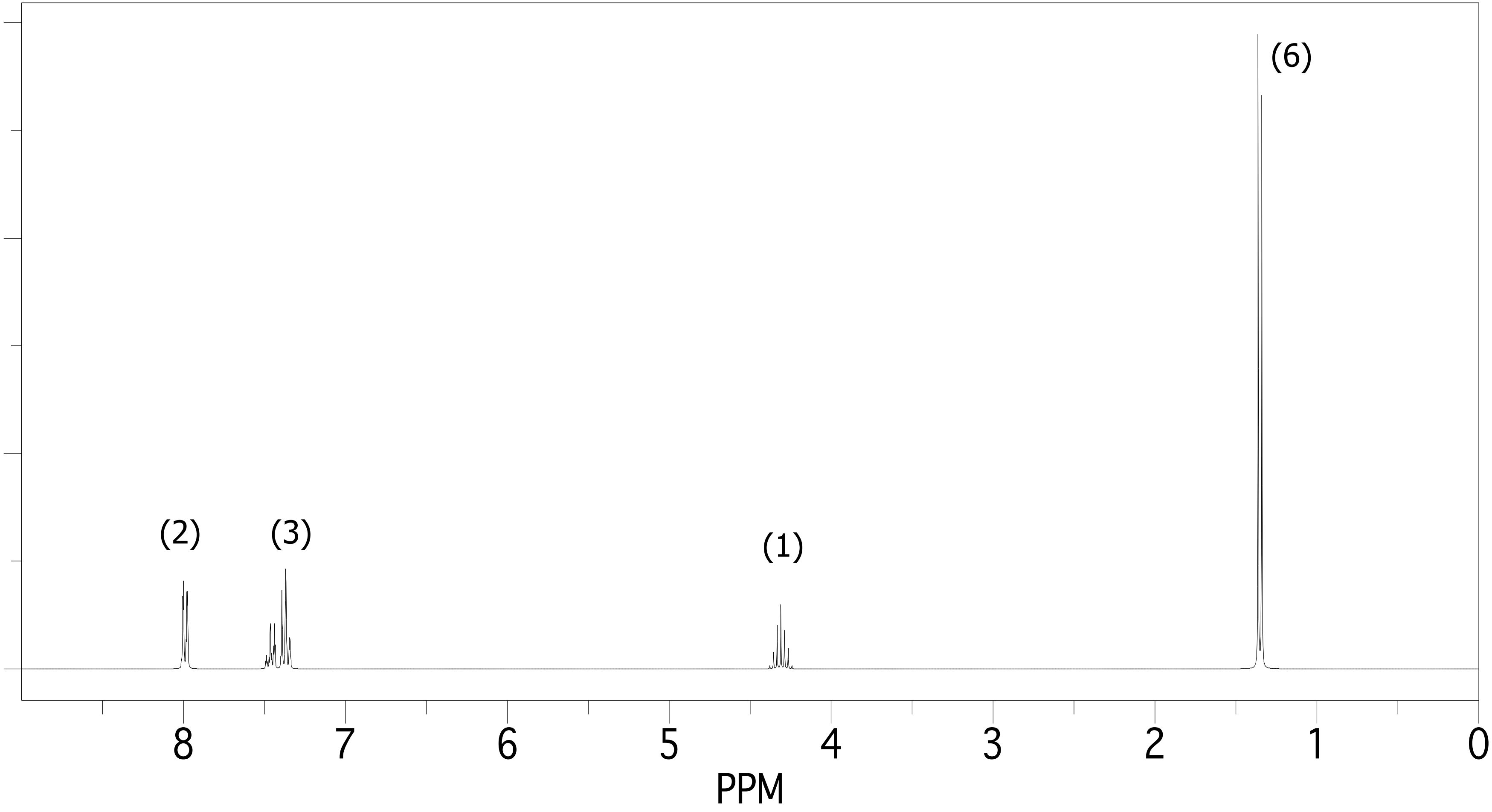




Analyzing Spectra:

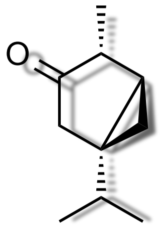
$C_{10}H_{12}O_2$

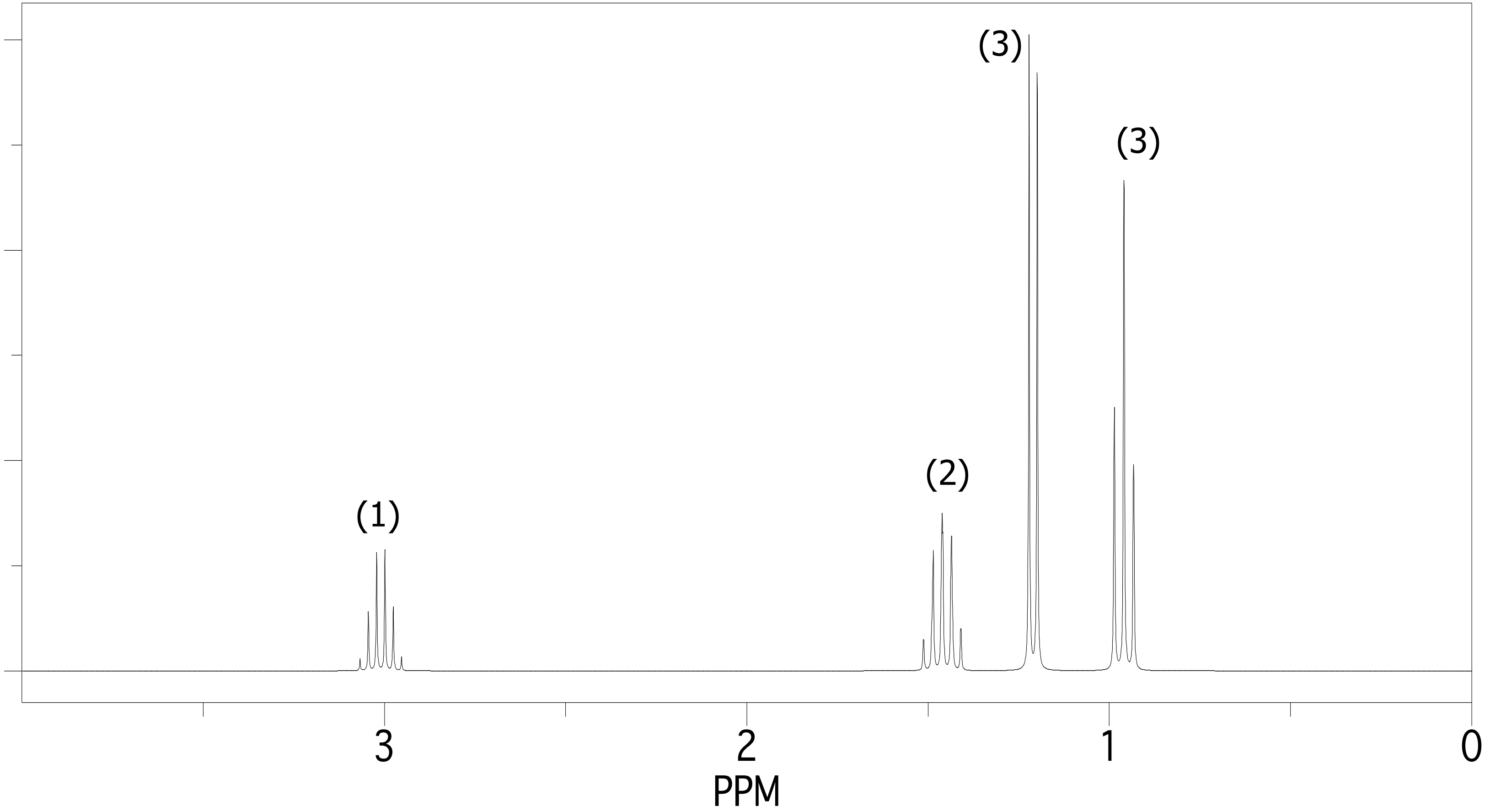


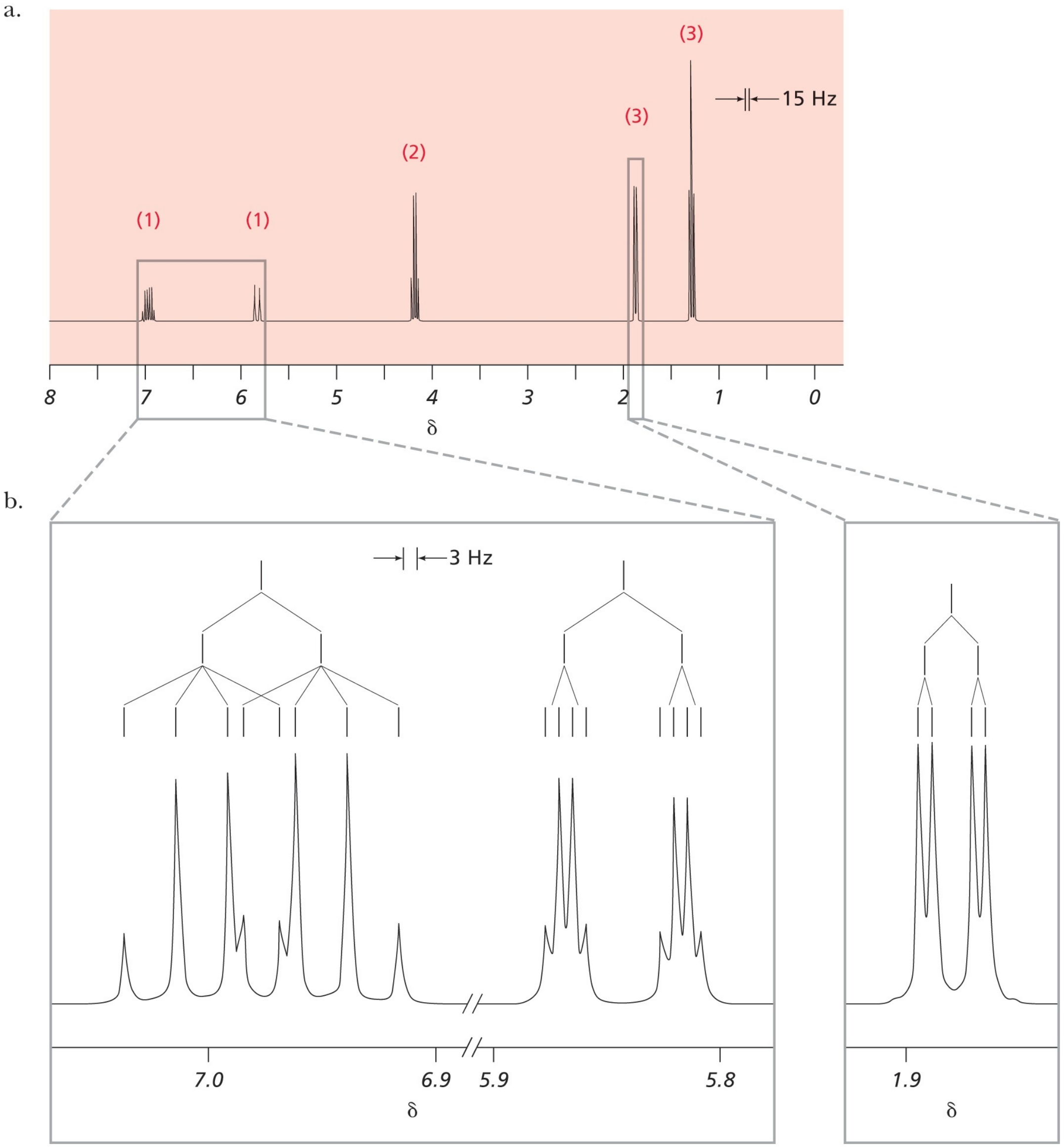


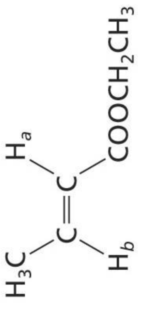
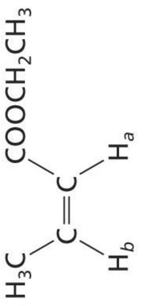
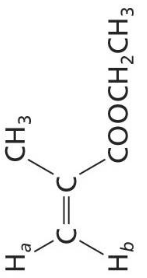
Analyzing Spectra:

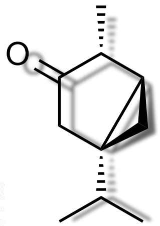
$C_8H_{18}O$



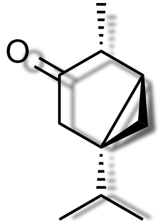




			
$J(CH_3, H_a)$	2	2	2
$J(CH_3, H_b)$	7	7	2
$J(H_a, H_b)$	15	7	2



Carbon 13 NMR (^{13}C)



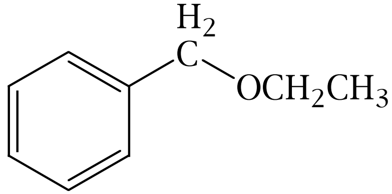
- ^{12}C has no spin and therefore is unobservable by NMR therefore we rely on ^{13}C.
- ^{13}C is only 1% abundant.
- ^{13}C is ~1/4 as sensitive as ^{1}H.

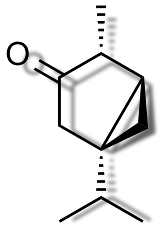
^{1}H and ^{13}C NMR similarities:

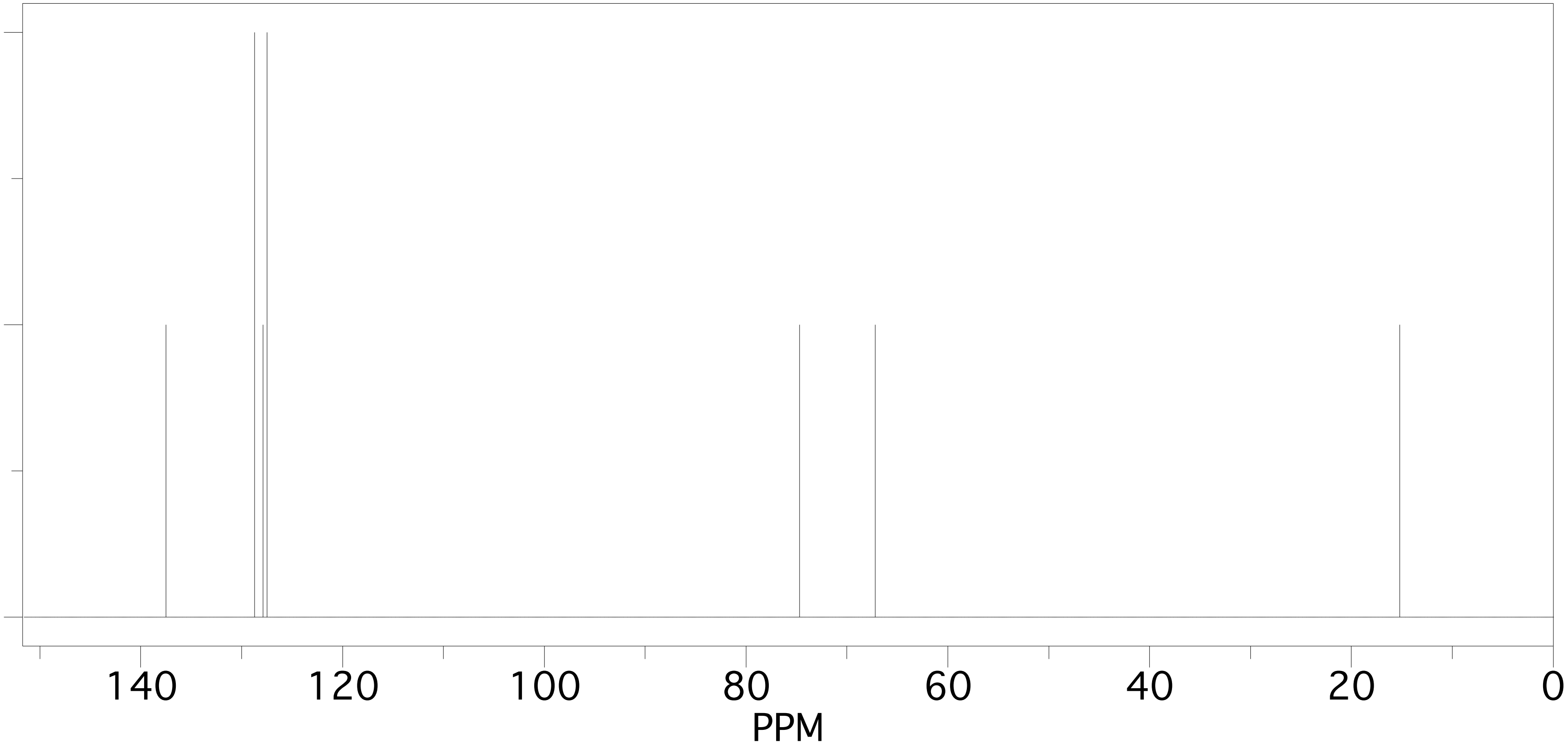
  - chemical shift effects are the same but over a much larger scale (spectral width is about 220 ppm)
  - scale is defined in the same way

^{1}H and ^{13}C NMR differences:

  - integrations are not valid
  - ^{13}C-^{13}C coupling is not observed
  - ^{13}C-^{1}H coupling is usually eliminated

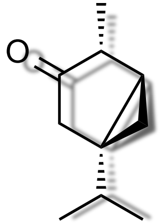

H_2
C
OCH_2CH_3

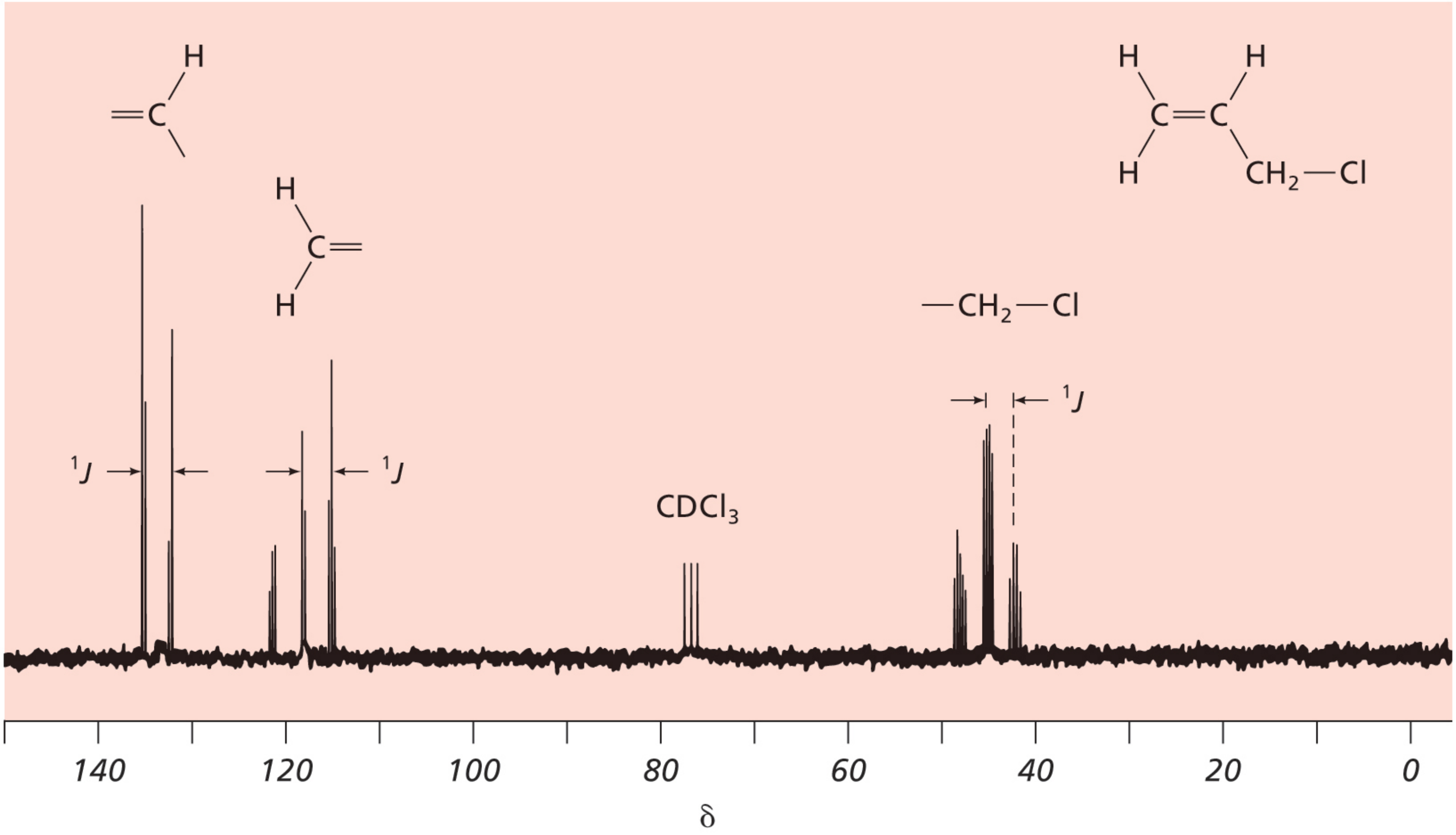

O


140
120
100
80
60
40
20
0
PPM

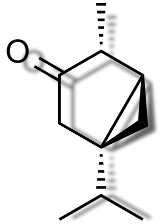
Coupling ‘allowed’:

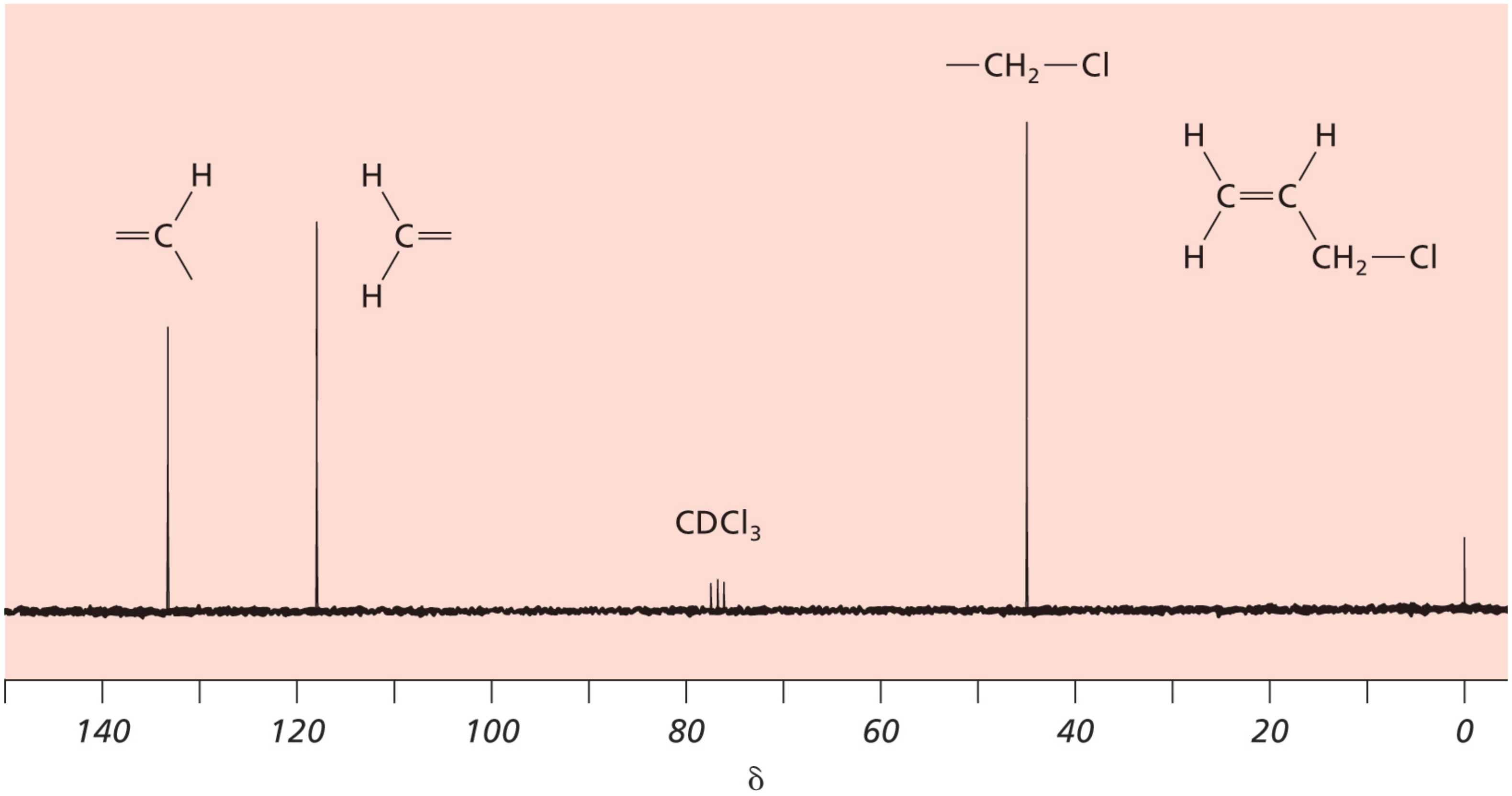
$^1J_{CH}$	$^2J_{CH}$	$^3J_{CH}$
$^{13}C—H$	$^{13}C—C—H$	$^{13}C—C—C—H$
$J \approx 125–150$ Hz	$J \approx 5–10$ Hz	$J \approx 0–1$ Hz



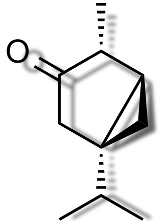


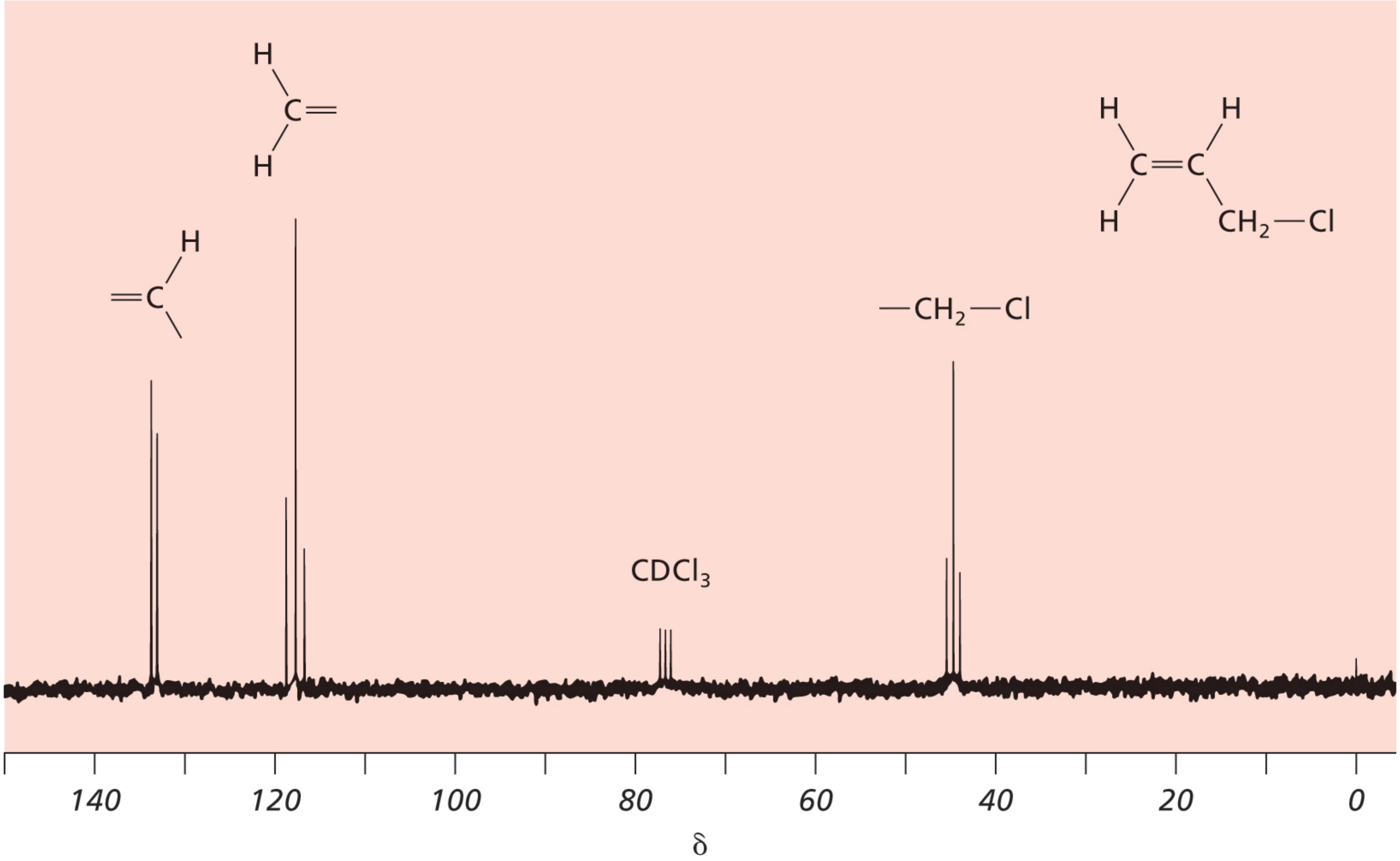
Broadband decoupled:





Off resonance decoupling:





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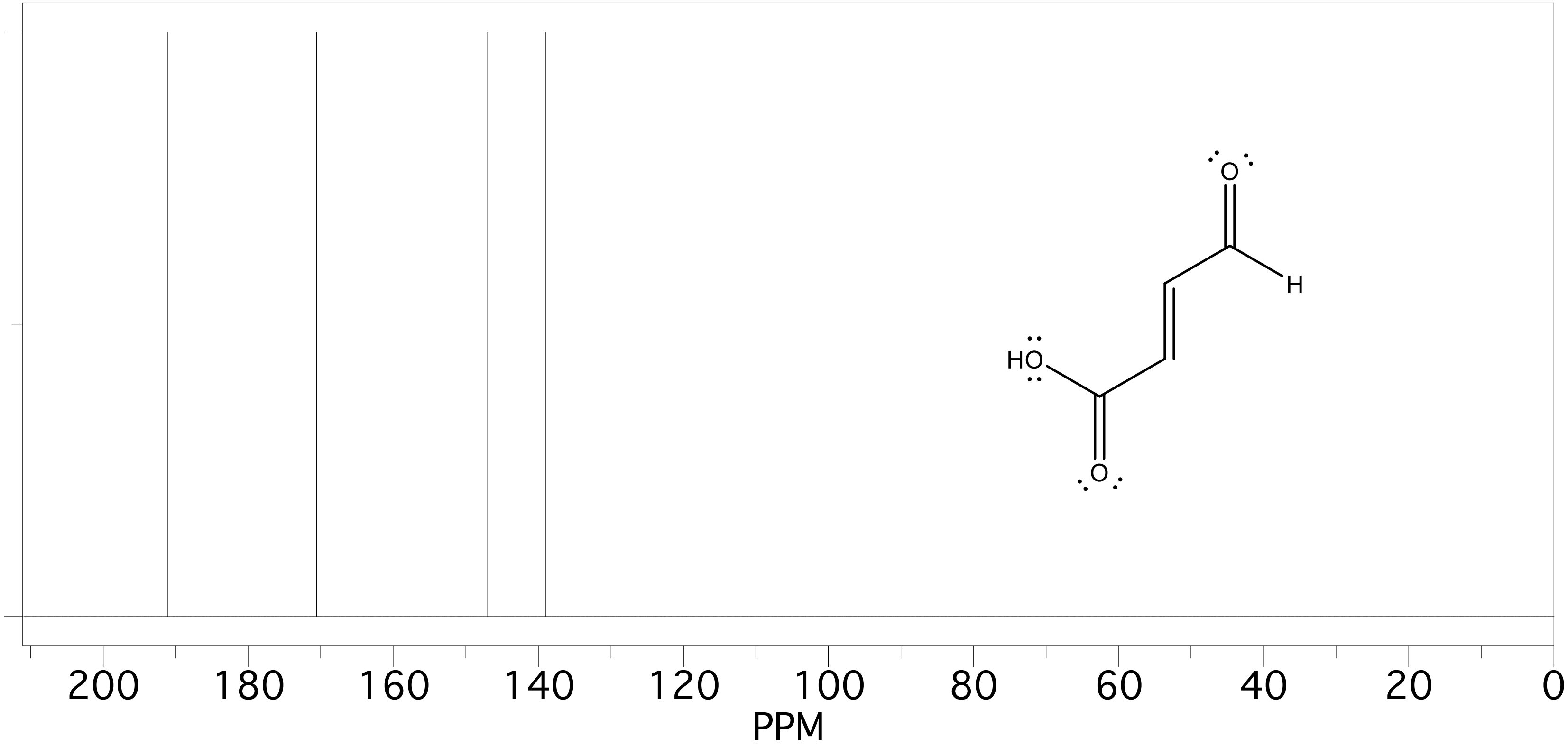
O
H
HO
O
200
180
160
140
120
100
80
60
40
20
0
PPM

Analyzing Spectra: