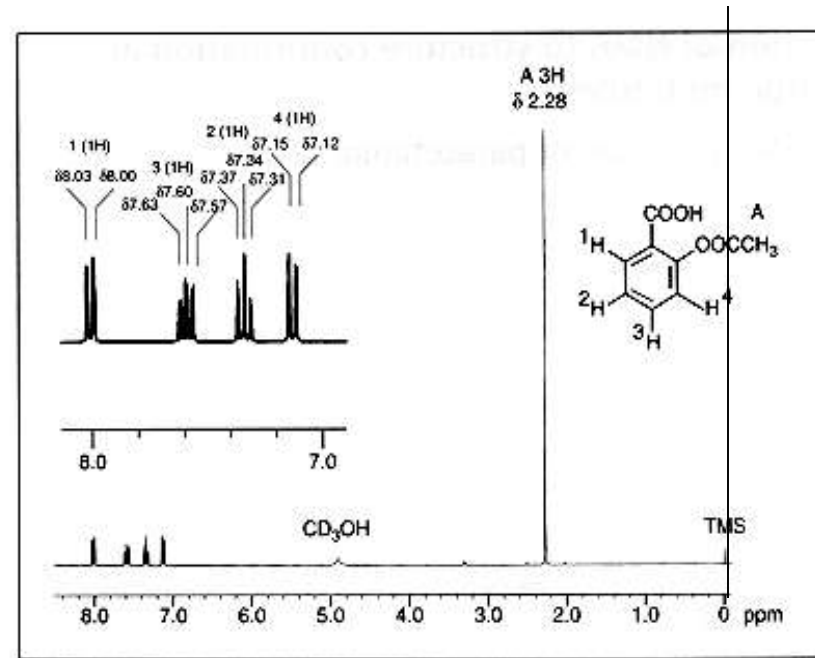
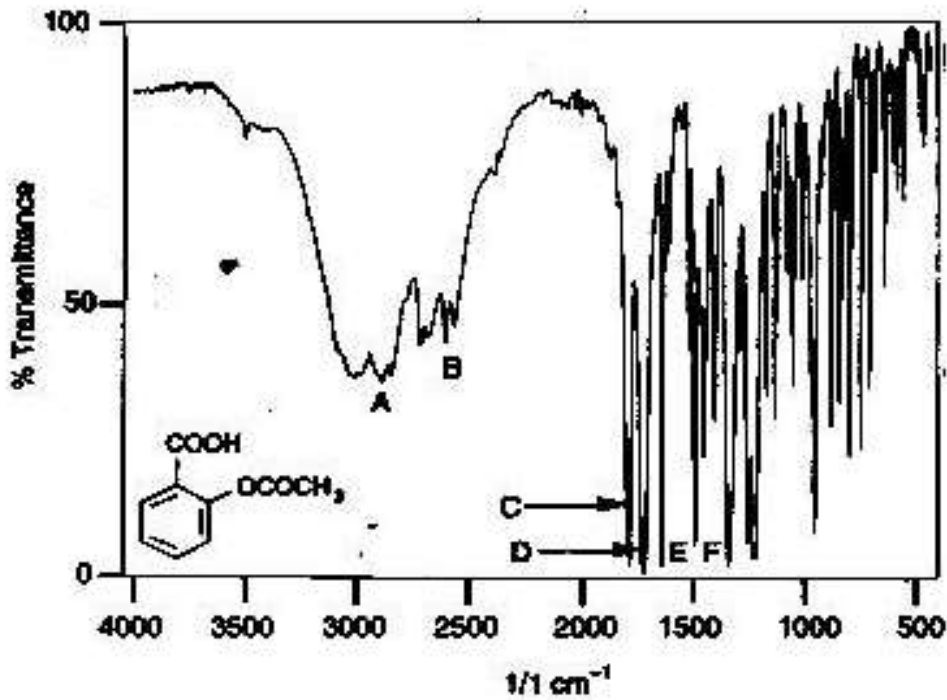


Nuclear Magnetic Resonance Spectroscopy

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**CHEBROLU HANUMAIAH INSTITUTE
OF PHARMACEUTICAL SCIENCES**

IR vs. NMR



NMR vs. IR

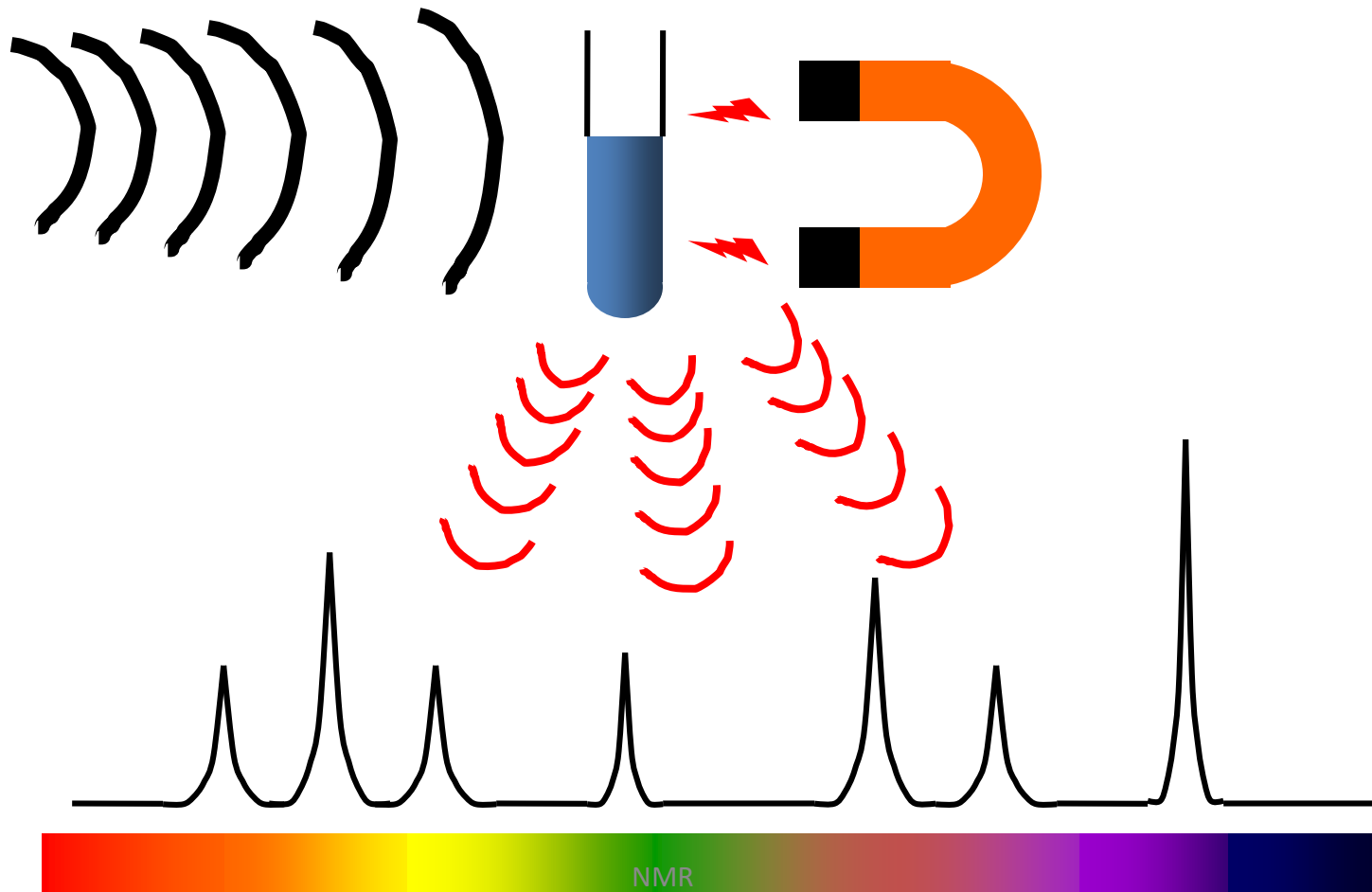
- NMR has narrower peaks relative to IR
- NMR yields far more information than IR
- NMR allows you to collect data on solids & liquids but not gases
- NMR samples are easier to prepare

Introduction

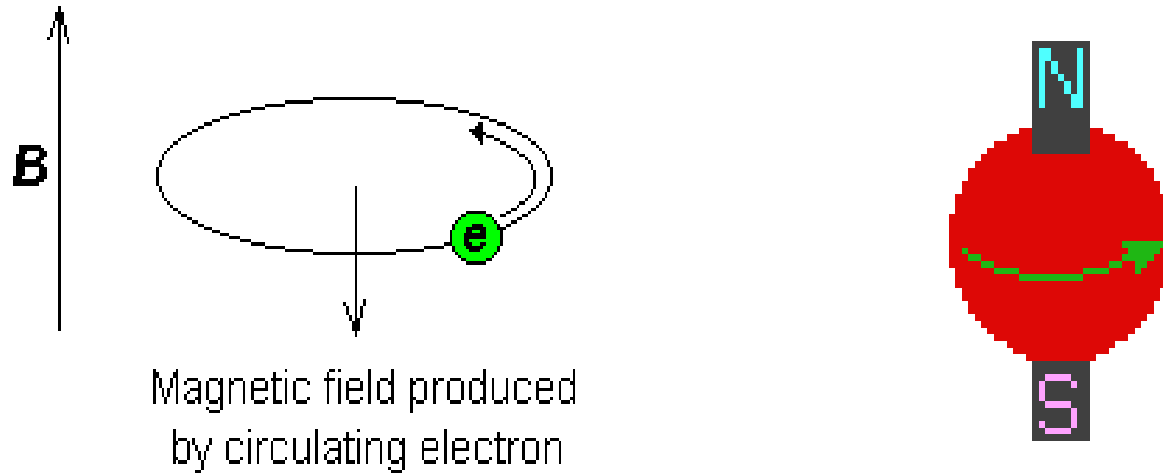
- NMR is the most powerful tool available for organic structure determination.
- It is used to study a wide variety of nuclei:
 - ^1H
 - ^{13}C
 - ^{15}N
 - ^{19}F
 - ^{31}P
 - ^{23}Na
 - ^{25}Mg
 - ^{27}Al
 - ^{29}Si
 - ^{31}P
 - ^{33}S
 - ^{109}Ag

I	Atomic Mass	Atomic Number	Example (I)
Half-integer	Odd	Odd or even	${}^1_1\text{H}(\frac{1}{2})$, ${}^{17}_8\text{O}(\frac{5}{2})$, ${}^{15}_7\text{N}(\frac{1}{2})$
Integer	Even	Odd	${}^2_1\text{H}(1)$, ${}^{14}_7\text{N}(1)$, ${}^{10}_5\text{B}(3)$
Zero	Even	Even	${}^{12}_6\text{C}(0)$, ${}^{16}_8\text{O}(0)$, ${}^{34}_{16}\text{S}(0)$

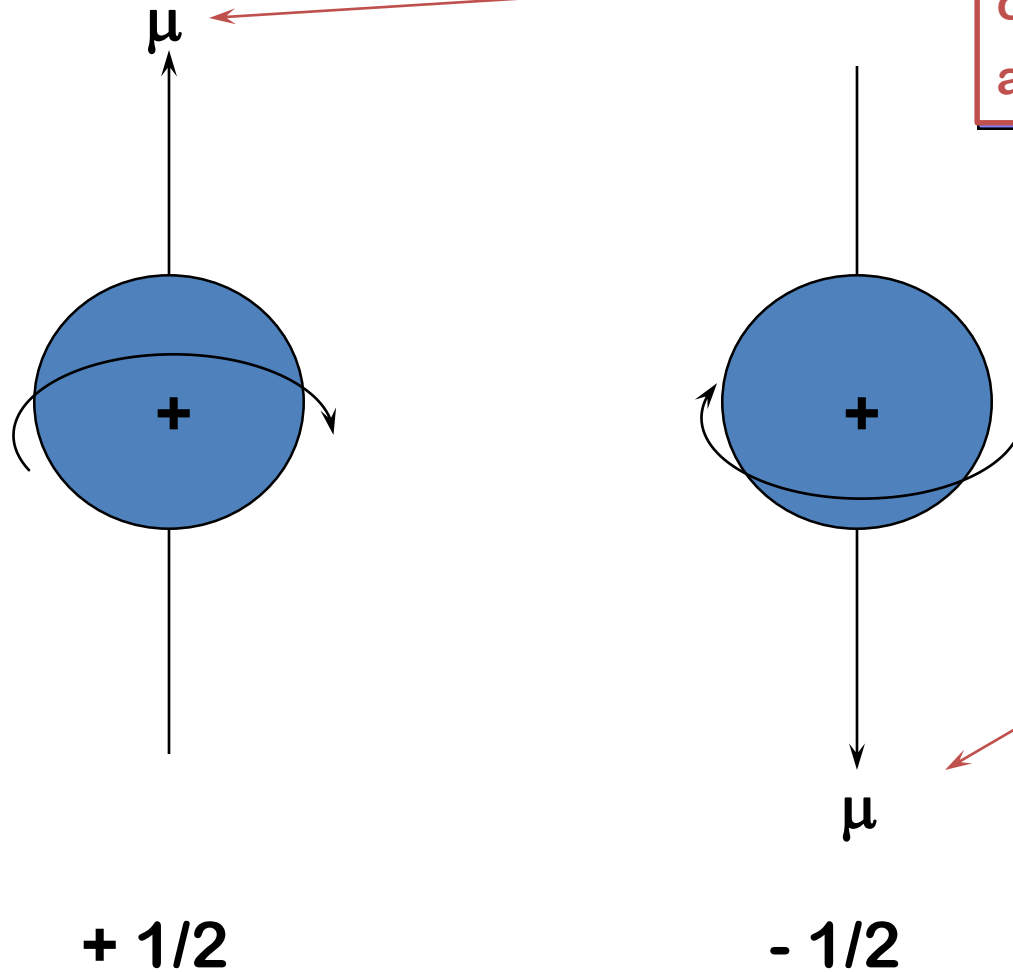
Explaining NMR



Explanation of spinning properties of nuclei



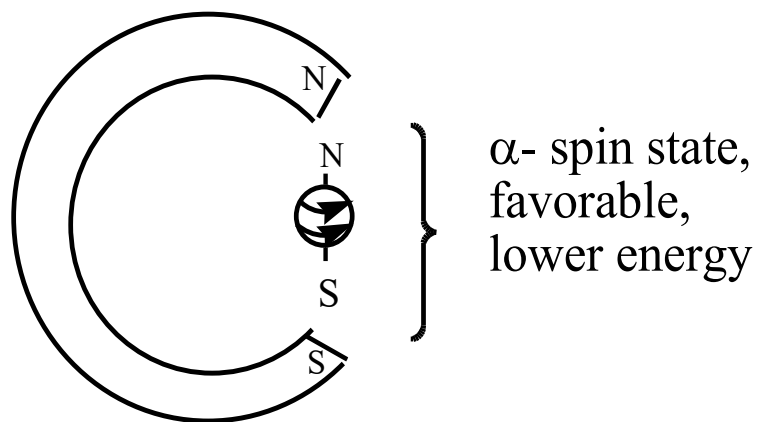
Nuclear spin states - hydrogen nucleus



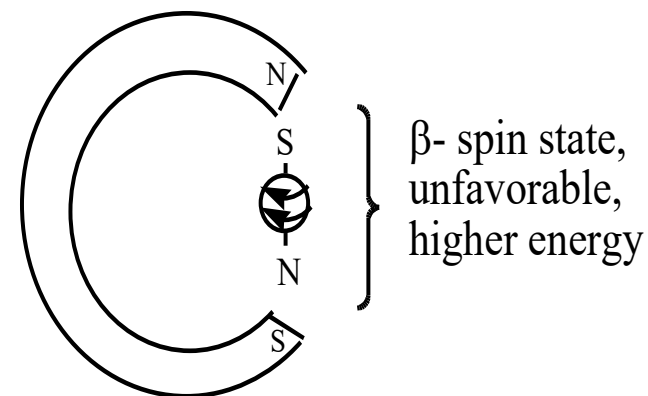
The spin of the positively charged nucleus generates a magnetic moment vector, μ .

The two states are equivalent in energy in the absence of a magnetic or an electric field.

TWO SPIN STATES

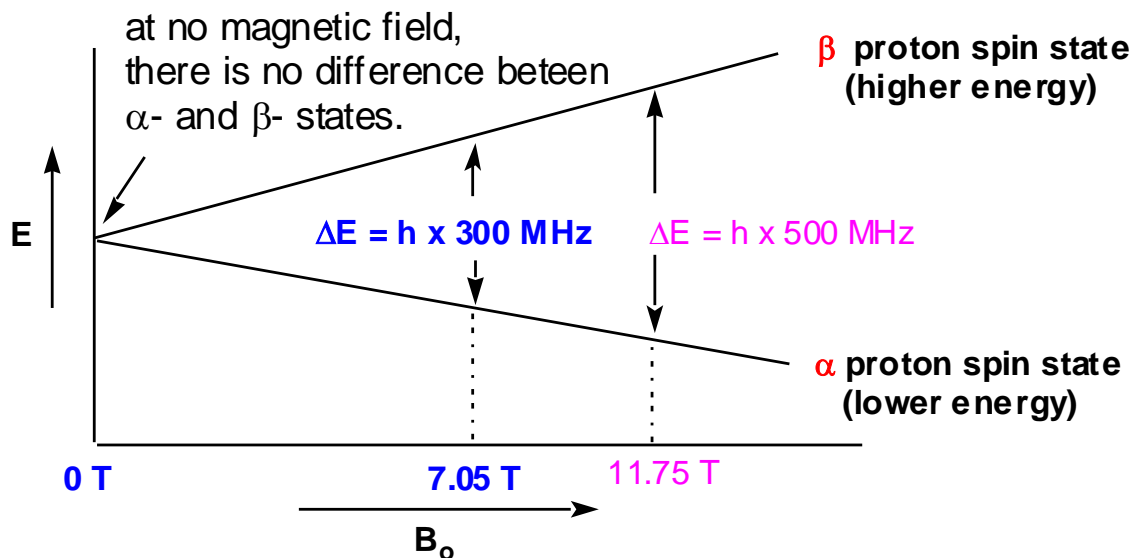


A spinning nucleus with its magnetic field aligned **with** the magnetic field of a magnet



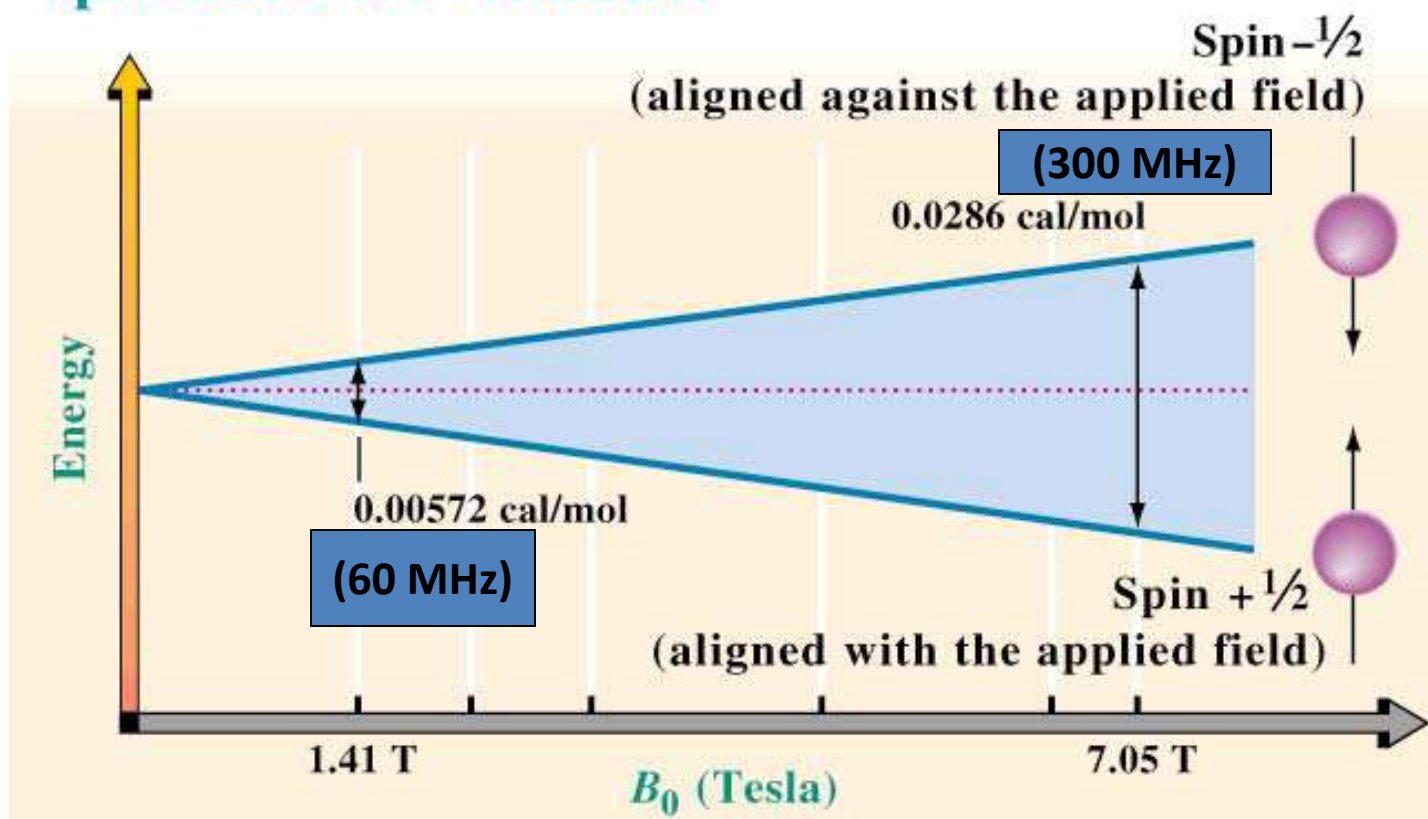
A spinning nucleus with its magnetic field aligned **against** the magnetic field of a magnet

Graphical relationship between magnetic field (B_o) and frequency (ν) for ^1H NMR absorptions



Influence of external magnetic field

Energy difference between allowed nuclear spin states for ^1H nuclei



Resonance

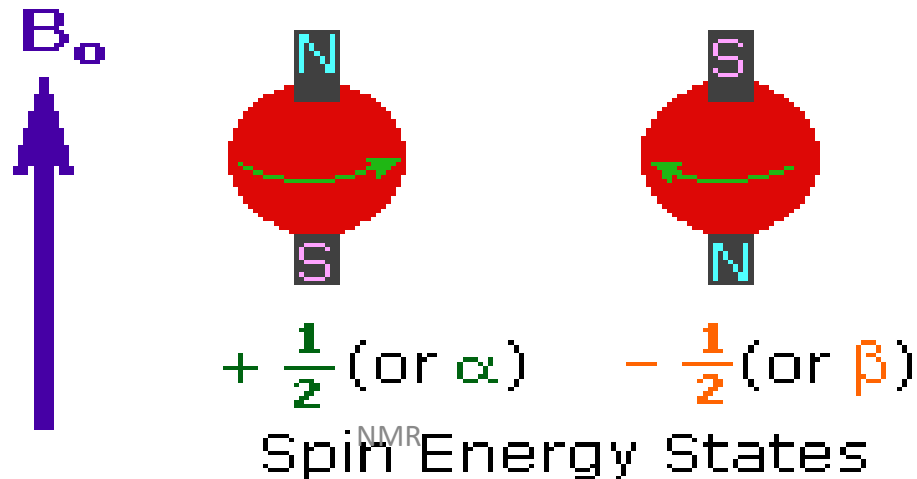
- Resonance: Matching of natural frequency with the applied frequency.
- In NMR the applied radio frequency has to be match with the **precessional frequency** of nuclei (which is the consequences of applied external magnetic field)
- Absorption of radio frequency occur by nuclei after resonance is achieved.

Precessional frequency (ν)

The number of revolution per second made by magnetic moment vector of the nucleus around the external magnetic field B_0

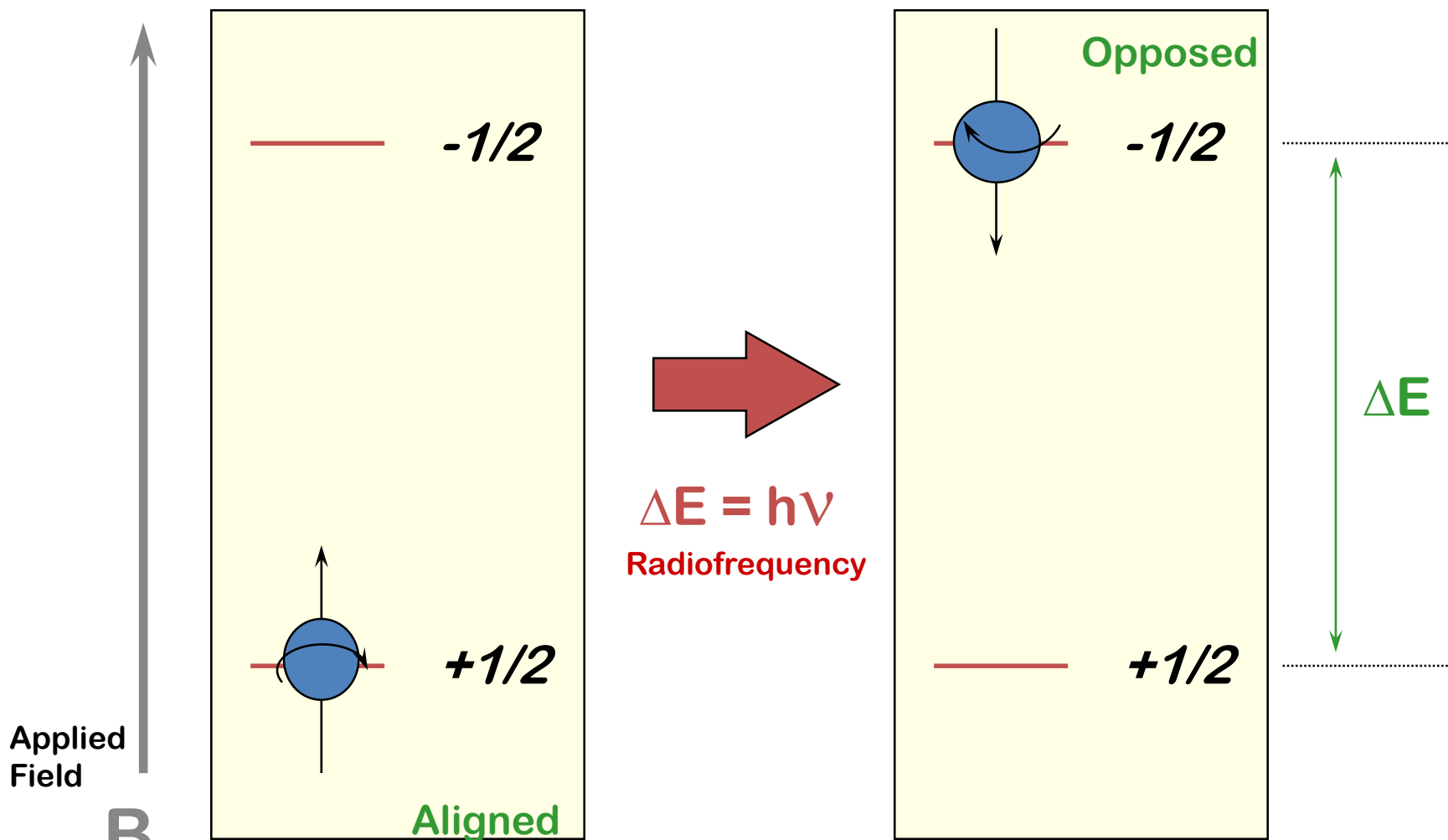
OR

Precessional frequency is equal to the frequency of electromagnetic radiation in MHz (Mega cycles/sec) necessary to induce a transition from one spin state to other.



Absorption of Energy

quantized



Mathematical Expression.

$$\omega = \gamma B_0$$

ω = Angular Precessional velocity

B_0 = Applied field in gauss

γ = Gyromagnetic ratio

ν = Precessional frequency

But,

$$\omega = 2\pi\nu$$

$$\gamma = \frac{2\pi\mu}{hI}$$

So,

$$\gamma B_0 = 2\pi\nu$$

$$\nu = \frac{\gamma B_0}{2\pi}$$

$$1 \text{ T} = 10^4 \text{ G}$$

$$\Delta E = \frac{h\gamma}{2\pi} B_0$$

The Larmor Equation

Stronger magnetic fields (B_0) cause the instrument to operate at higher frequencies (ν).

frequency

field strength

$$E = h\nu = h \left(\frac{\gamma}{2\pi} \right) B_0$$

constants

$\nu \propto B_0$

NMR Field Strength	^1H Operating Frequency
1.41 T	60 MHz
2.35 T	100 MHz
7.05 T	300 MHz

Isotope	Natural % Abundance	Spin (I)	Magnetic Moment (μ)	Magnetogyric Ratio (γ)
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^1H	99.9844	1/2	2.7927	26.753
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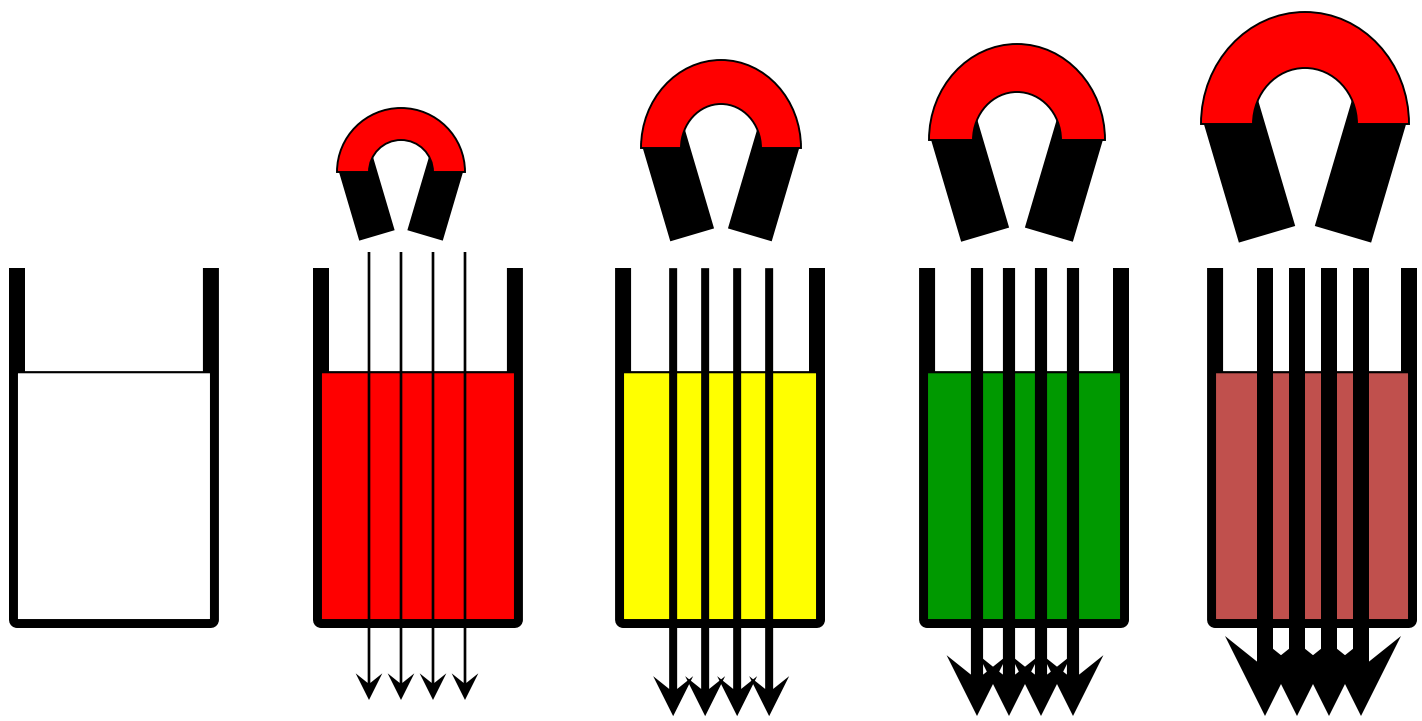
^2H	0.0156	1	0.8574	4,107
--------------	--------	---	--------	-------

^{13}C	1.108	1/2	0.7022	6,728
-----------------	-------	-----	--------	-------

^{19}F	100.0	1/2	2.6273	25,179
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^{31}P	100.0	1/2	1.1305	10,840
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Increasing magnetic field strength



low frequency

high frequency

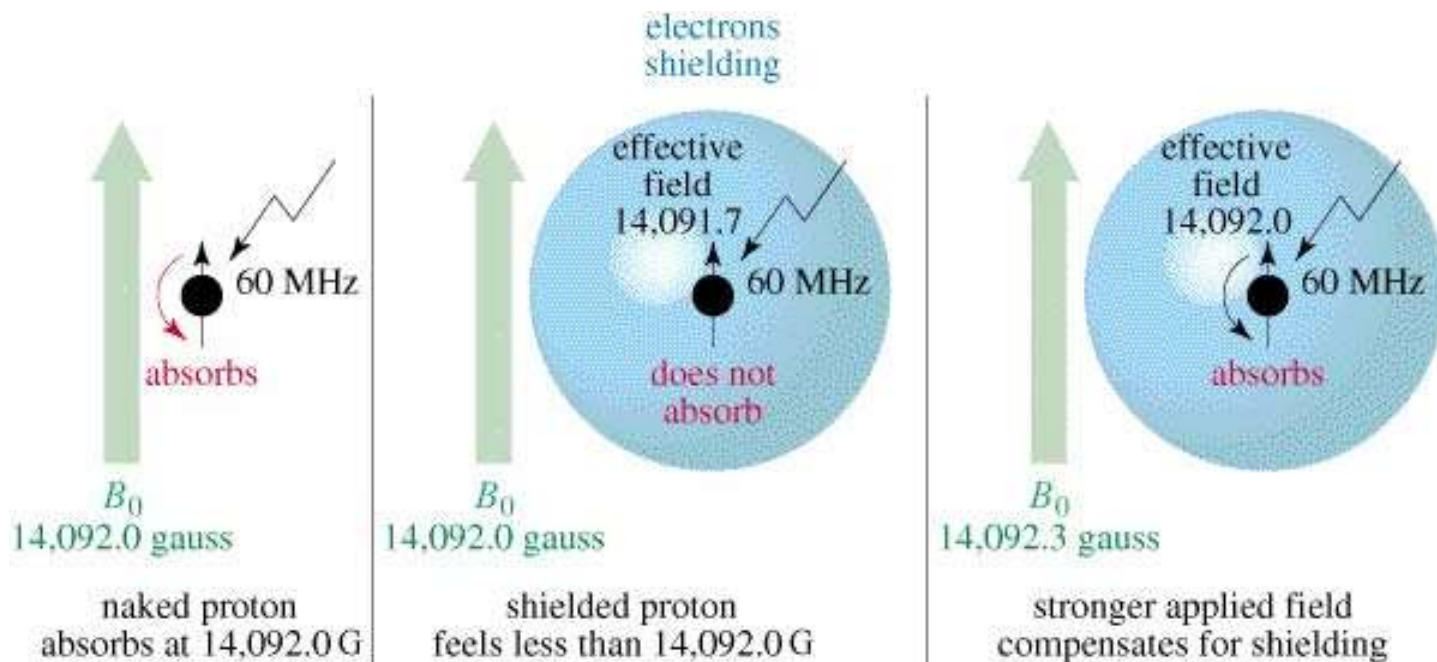


Magnetic Shielding

- If all protons absorbed the same amount of energy in a given magnetic field, not much information could be obtained.
- But protons are surrounded by electrons that shield them from the external field.
- Circulating electrons create an induced magnetic field that opposes the external magnetic field.

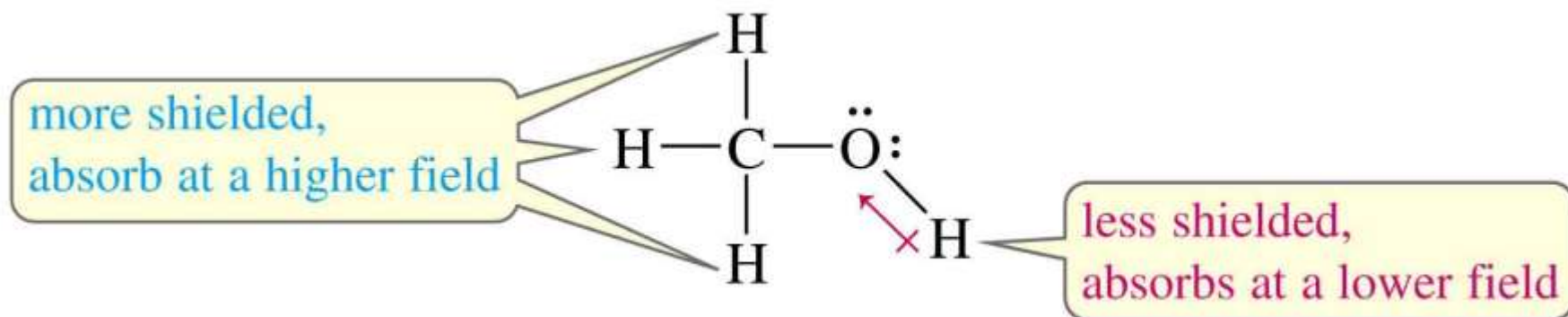
Shielded Protons

Magnetic field strength must be increased for a shielded proton to flip at the same frequency.



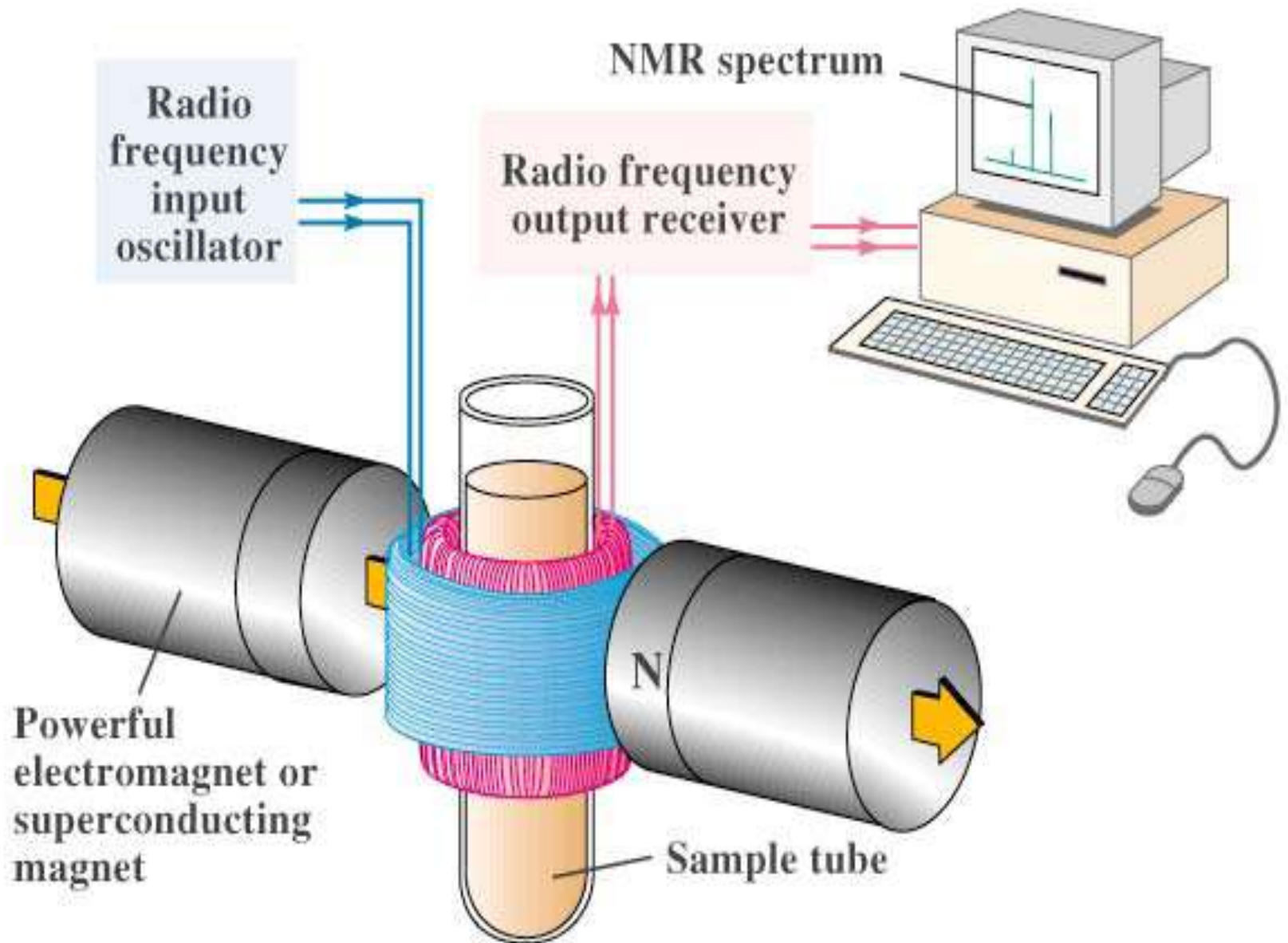
Protons in a Molecule

Depending on their chemical environment, protons in a molecule are shielded by different amounts.



NMR Signals

- The *number* of signals shows how many different kinds of protons are present.
- The *location* of the signals shows how shielded or deshielded the proton is.
- The *intensity* of the signal shows the number of protons of that type.
- Signal *splitting* shows the number of protons on adjacent atoms.

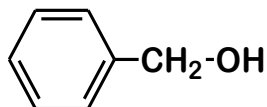


Number of signal

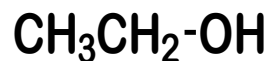
Number of signal α number of magnetically equivalent proton

Compound

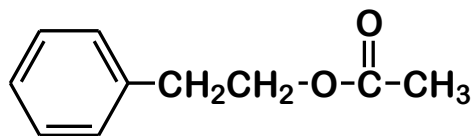
No.of signal



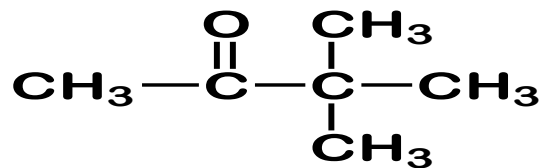
3



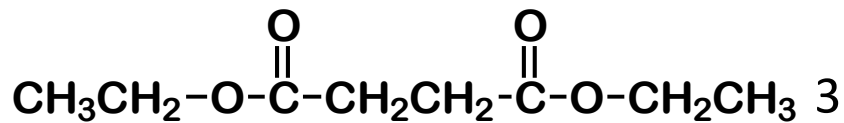
3



4



2

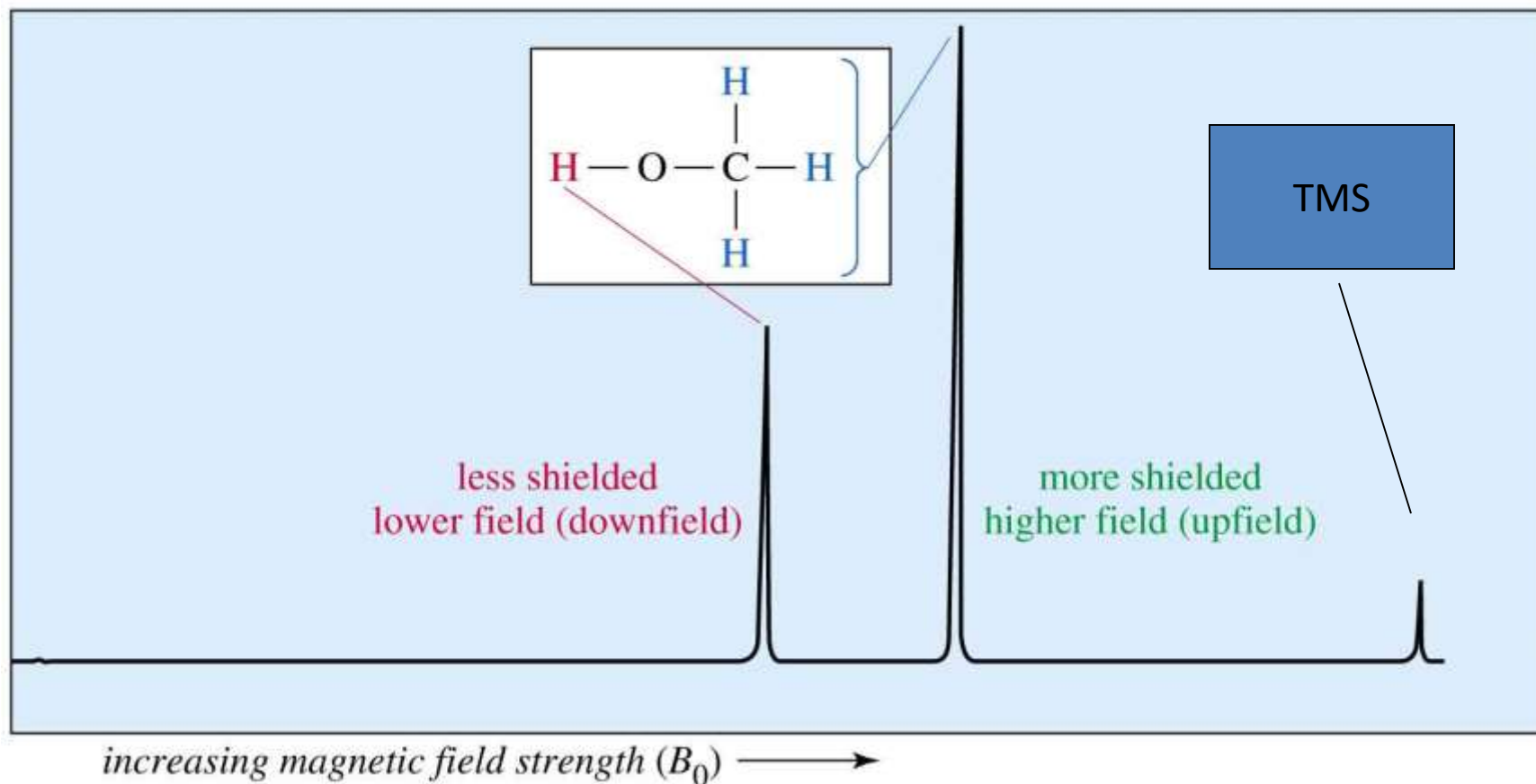


3

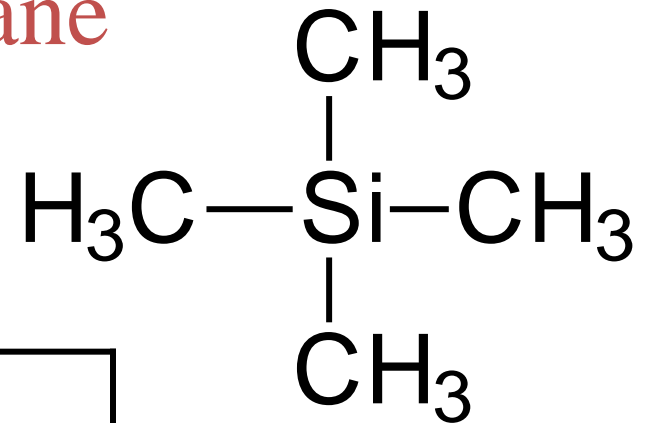
The NMR Graph

Downfield: the shift of an NMR signal to the left on the chart paper

Upfield: the shift of an NMR signal to the right on the chart paper



Tetramethylsilane



Chemically inert

Highly shielded

Miscibility large range of solvent

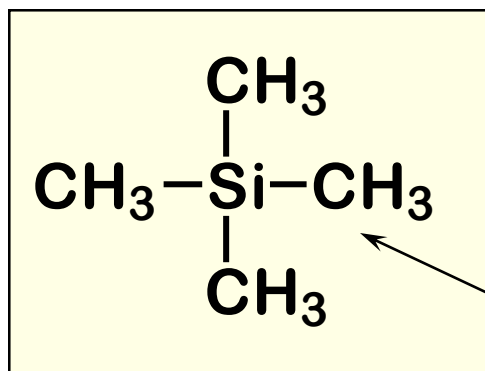
Highly volatile

Does not take part in intermolecular association

For water soluble compound Sodium salt of 3-(trimethyl silyl)propane sulphonate is used as internal standard

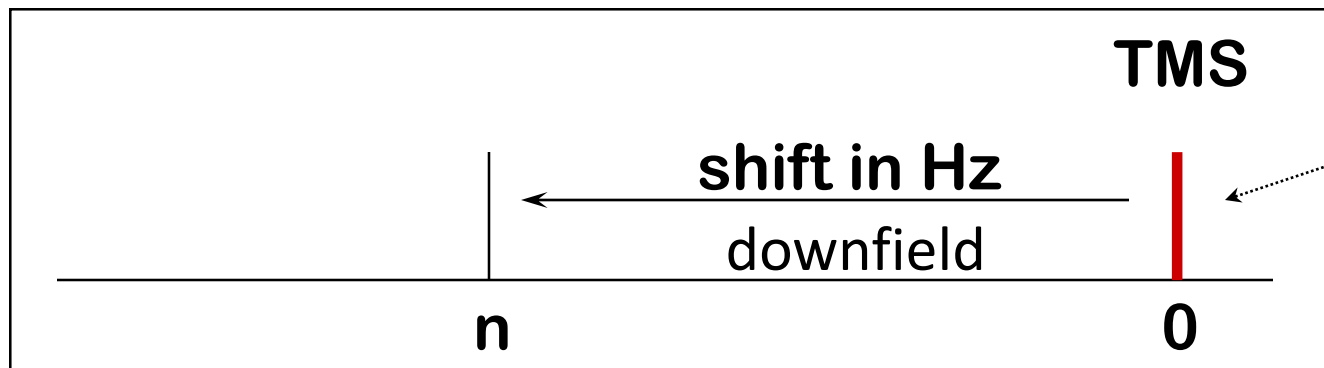
Peaks are measured relative to TMS

Rather than measure the exact resonance position of a peak, we measure how far downfield it is shifted from TMS.



reference compound
tetramethylsilane
“TMS”

Highly shielded
protons appear
way upfield.



no other
compound would
come at a higher
field than TMS.

The chemical shift

The shifts from TMS in Hz are bigger in higher field instruments (300 MHz, 500 MHz) than they are in the lower field instruments (100 MHz, 60 MHz).

$$\text{chemical shift} = \delta = \frac{\text{shift in Hz (sample- Ref)}}{\text{spectrometer frequency in MHz}} = \text{ppm}$$

parts per million

This division gives a number independent of the instrument used.

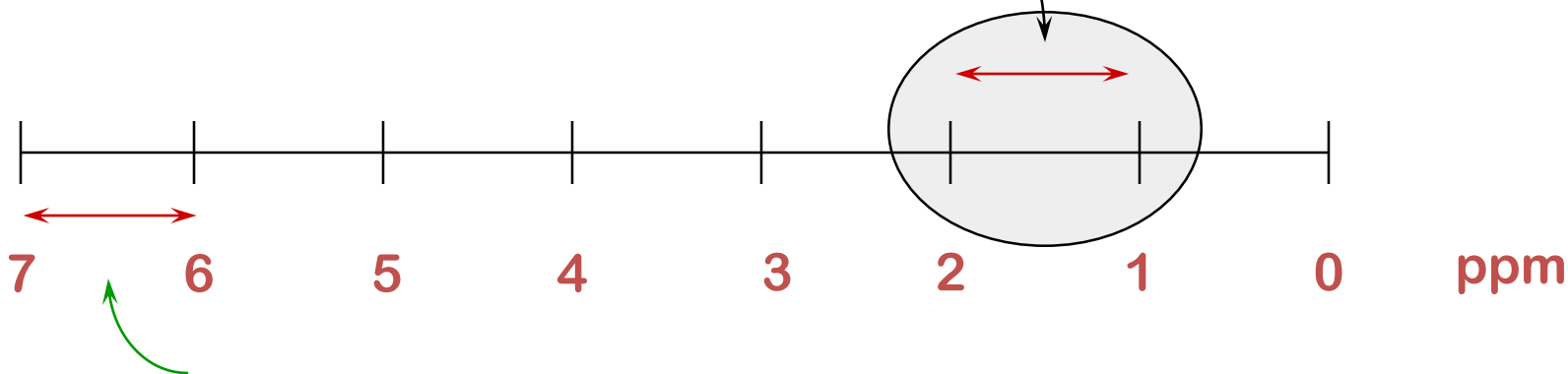
The Chemical Shift independent upon applied magnetic field strength

Imagine that we have a magnet where our standard absorbs at 300,000,000 Hz (300 megahertz), and our sample absorbs at 300,000,300 Hz. The difference is 300 Hz, so we take $300/300,000,000 = 1/1,000,000$ and call that 1 part per million (or 1 PPM). Now let's examine the same sample in a stronger magnetic field where the reference comes at 500,000,000 Hz, or 500 megahertz. The frequency of our sample will increase proportionally, and will come at 500,000,500 Hz. The difference is now 500 Hz, but we divide by 500,000,000 ($500/500,000,000 = 1/1,000,000 = 1$ PPM).

Hertz Equivalence Of 1 ppm

¹ H Operating Frequency	Hz Equivalent of 1 ppm
60 MHz	60 Hz
100 MHz	100 Hz
300 MHz	300 Hz

1 part per million of n MHz is n Hz
$$n \text{ MHz} \left(\frac{1}{10^6} \right) = n \text{ Hz}$$

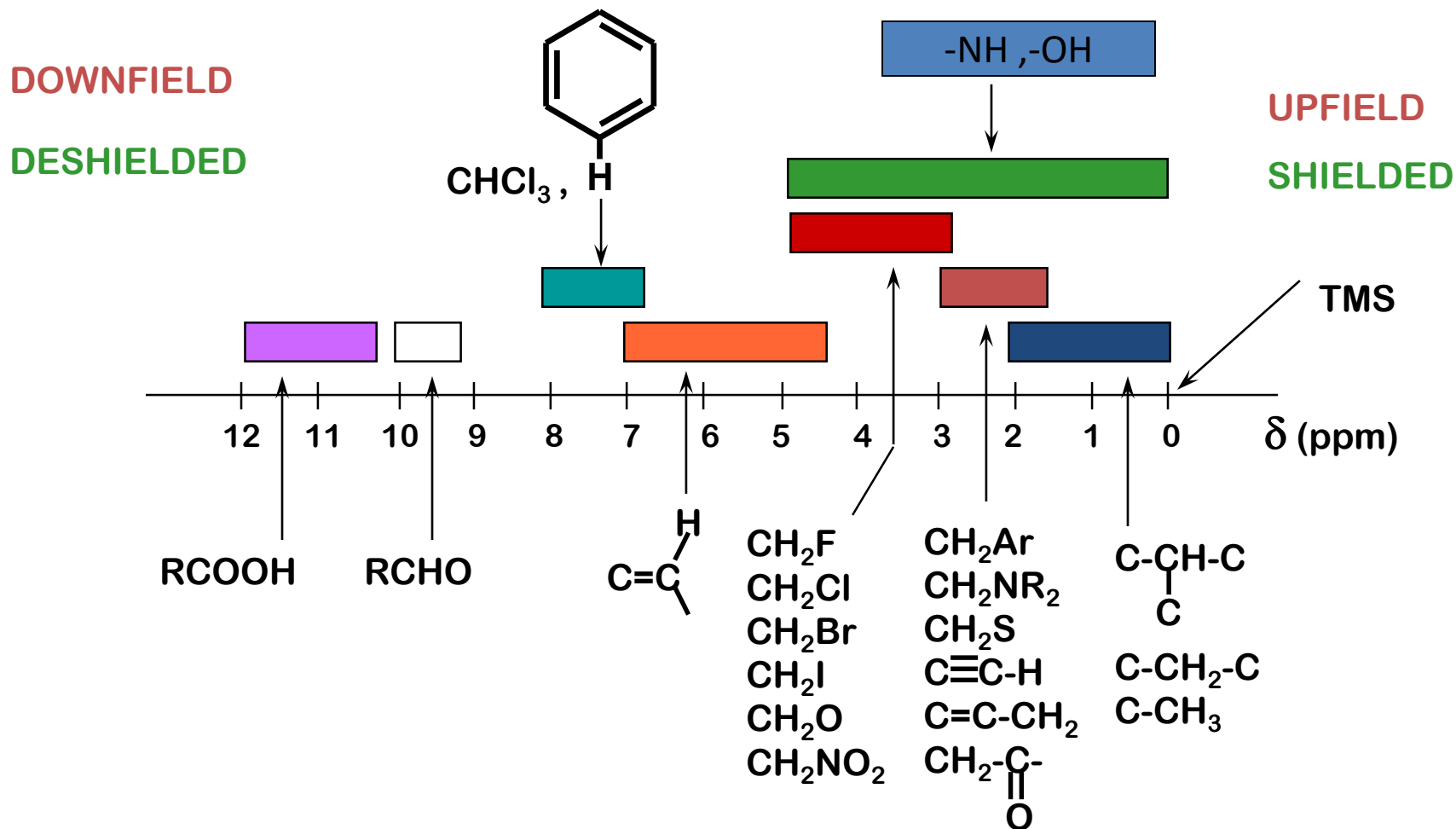


Each ppm unit represents either a 1 ppm change in B_0 (magnetic field strength, Tesla) or a 1 ppm change in the precessional frequency (MHz).

Approximate Chemical Shift(δ) Ranges (ppm) For Selected Types Of Protons

Cyclopropane	0.2	Ethers	3.3-4.0
1 ^o hydrogen	0.9	Esters	2.0-2.2
Vinylic	4.6-5.8	Acids	2.0-2.5
Acetylinic	2.0-3.5	Aldehydic	9.0-10
Aromatic	6.0-9.0	Hydroxy	1.0-5.5
Fluorides	4.0-4.5	Phenolic	4.0-12
Chlorides	3.0-4.0	Carboxylic	10.5-12
Alcohols	3.4-4.0		

NMR Correlation Chart



Factors affecting chemical shift

- Inductive effect
- Vanderwaal's deshielding
- Anisotropic/space effect
- Hydrogen bonding

Substitution Effects on Chemical Shift (inductive effect)

Dependence of the Chemical Shift of CH_3X on the Element X

Compound CH_3X	CH_3F	CH_3OH	CH_3Cl	CH_3Br	CH_3I	CH_4	$(\text{CH}_3)_4\text{Si}$
Element X	F	O	Cl	Br	I	H	Si
Electronegativity of X	4.0	3.5	3.1	2.8	2.5	2.1	1.8
Chemical shift δ	4.26	3.40	3.05	2.68	2.16	0.23	0

most deshielded

← TMS

deshielding increases with the electronegativity of atom X

Electronegativity Dependence of Chemical Shift

most
deshielded

CHCl₃	CH₂Cl₂	CH₃Cl	
7.27	5.30	3.05	ppm

The effect increases with greater numbers of electronegative atoms.

most
deshielded

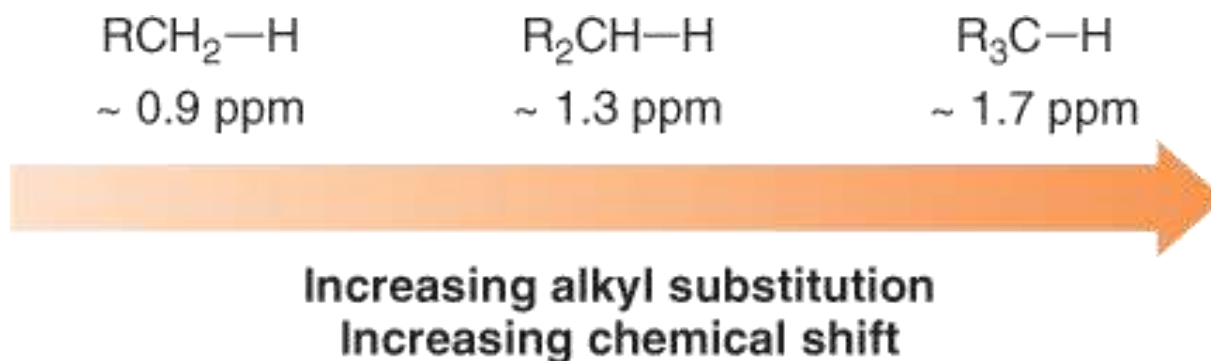
-CH₂-Br	-CH₂-CH₂Br	-CH₂-CH₂CH₂Br	
3.30	1.69	1.25	ppm

The effect decreases with increasing distance.

Nuclear Magnetic Resonance Spectroscopy

^1H NMR—Chemical Shift Values

- The chemical shift of a C—H bond increases with increasing alkyl substitution.



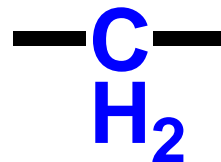
Nuclear Magnetic Resonance Spectroscopy

Calculating ^1H NMR—Chemical Shift Values

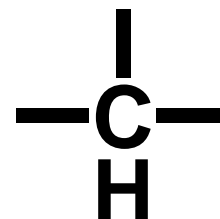
- The chemical shift of a C—H can be calculated with a high degree of precision if a chemical shift additivity table is used.
- The additivity tables starts with a base chemical shift value depending on the structural type of hydrogen under consideration:



Methylene



Methine



Base Chemical Shift 0.87 ppm

1.20 ppm

1.20 ppm

Nuclear Magnetic Resonance Spectroscopy

Calculating ^1H NMR—Chemical Shift Values

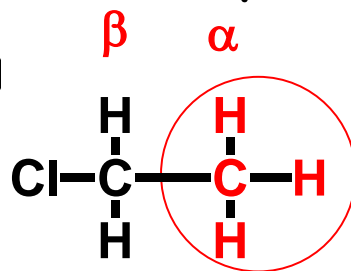
- The presence of nearby atoms or groups will effect the base chemical shift by a specific amount:
 - The carbon atom bonded to the hydrogen(s) under consideration are described as alpha (α) carbons.
 - Atoms or groups bonded to the same carbon as the hydrogen(s) under consideration are described as alpha (α) substituents.
 - Atoms or groups on carbons one bond removed from the a carbon are called beta (β) carbons.
 - Atoms or groups bonded to the β carbon are described as alpha (β) substituents.



Nuclear Magnetic Resonance Spectroscopy

Calculating ^1H NMR—Chemical Shift Values

Added Chemical Shifts			
Substituent	Type of Hydrogen	α -Shift	β -Shift
$\text{C}=\text{C}-$	CH_3	0.78	—
	CH_2	0.75	-0.10
	CH	—	—
$\begin{array}{c} \text{Y} \\ \\ \text{RC}-\text{C}-\text{C}- \\ \\ [\text{Y} = \text{C or O}] \end{array}$ Aryl- Cl-	CH_3	1.08	—
	CH_2	1.40	0.95
	CH	1.45	0.59
	CH_3	1.99	—
	CH_2	2.49	0.69
	CH	2.90	0.59
	CH_3	2.55	0.09
	CH_2	2.90	0.59
	CH	2.55	0.09
Br-	CH_3	1.80	0.89
	CH_2	2.18	0.60
	CH	2.68	0.25
I-	CH_3	1.28	1.29
	CH_2	1.95	0.58
	CH	2.75	0.00
OH-	CH_3	2.50	0.99
	CH_2	2.90	0.19
	CH	2.20	—
	CH_3	2.49	0.99
R-O- (R is saturated)	CH_3	2.49	0.99
	CH_2	2.95	0.15
	CH	2.00	—
	CH_3	2.88	0.98
$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{CO}- \text{ or } \text{ArO}- \end{array}$	CH_2	2.98	0.49
	CH	3.49	—
		(ester only)	
$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}- \end{array}$ where R is alkyl, aryl, OH, OR', H, CO, or N	CH_3	1.29	0.18
	CH_2	1.05	0.91
	CH	1.05	—



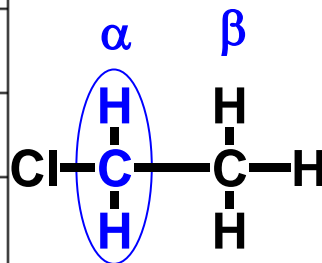
(Hydrogen under consideration)

Base Chemical Shift = 0.87 ppm

no α substituents = 0.00

one β -Cl (CH_3) = 0.63

TOTAL = 1.50 ppm



(Hydrogen under consideration)

Base Chemical Shift = 1.20 ppm

one α -Cl (CH_2) = 2.30

no β substituents = 0.00

TOTAL = 3.50 ppm

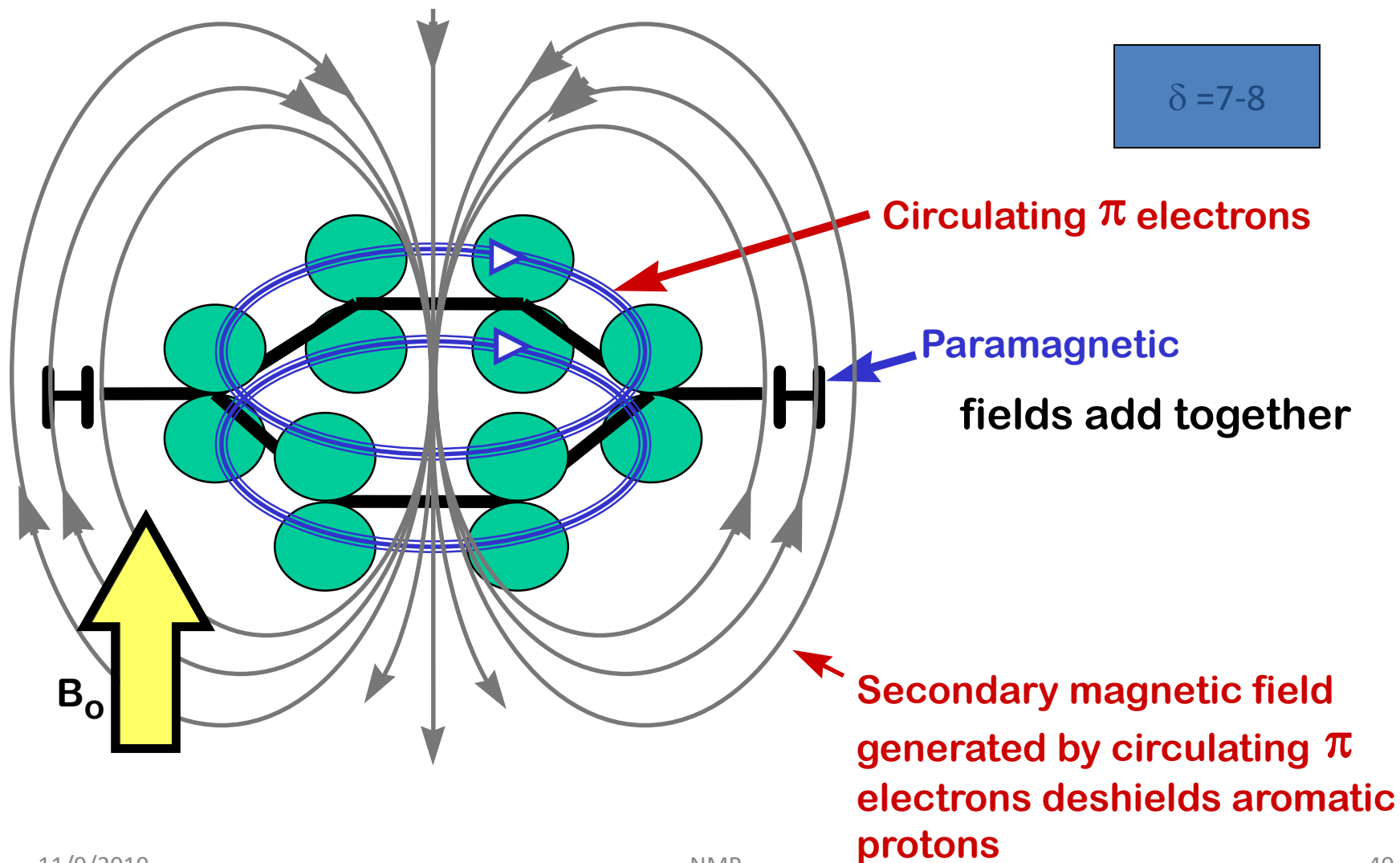
Anisotropic/Space effect

Due To The Presence Of Pi Bonds

The presence of a nearby pi bond or pi system greatly affects the chemical shift.

Benzene rings have the greatest effect.

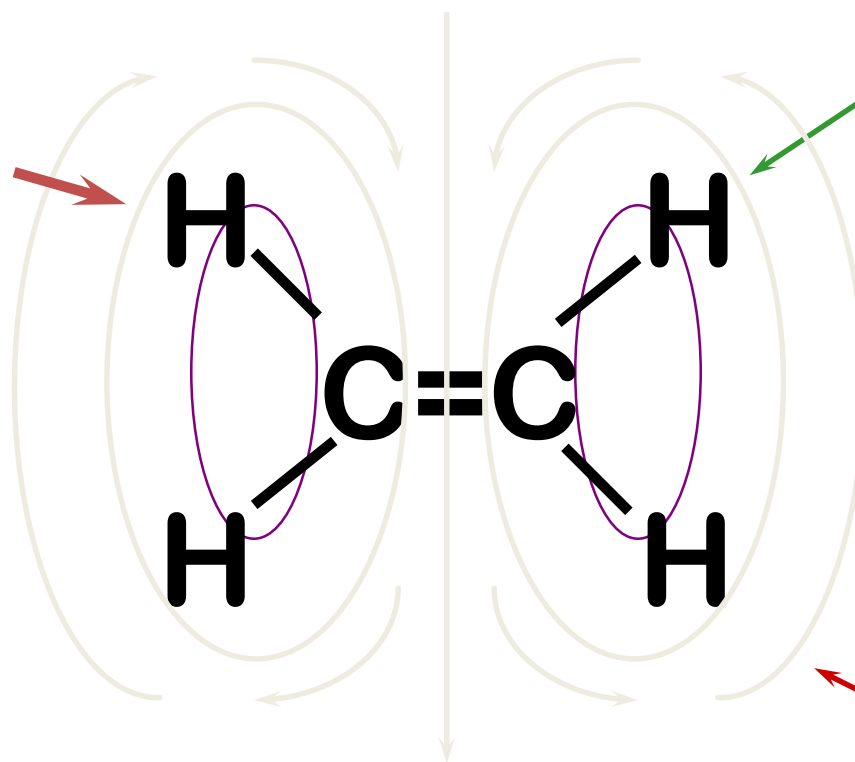
Ring Current in Benzene



Anisotropic field in alkene

$$\delta = 5 - 6$$

Paramagnetic
fields add



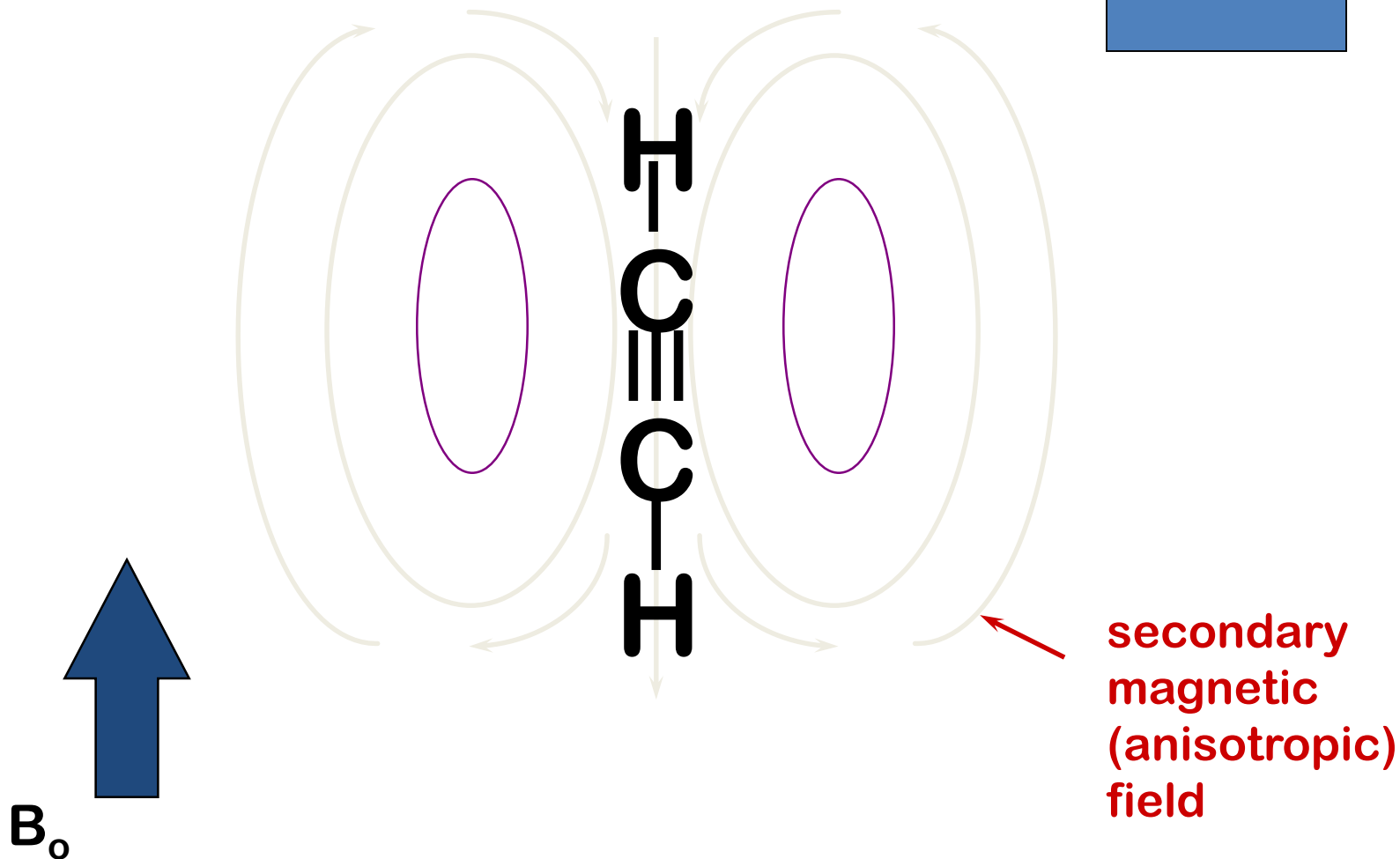
protons are
deshielded

shifted
downfield

secondary
magnetic
(anisotropic)
field lines

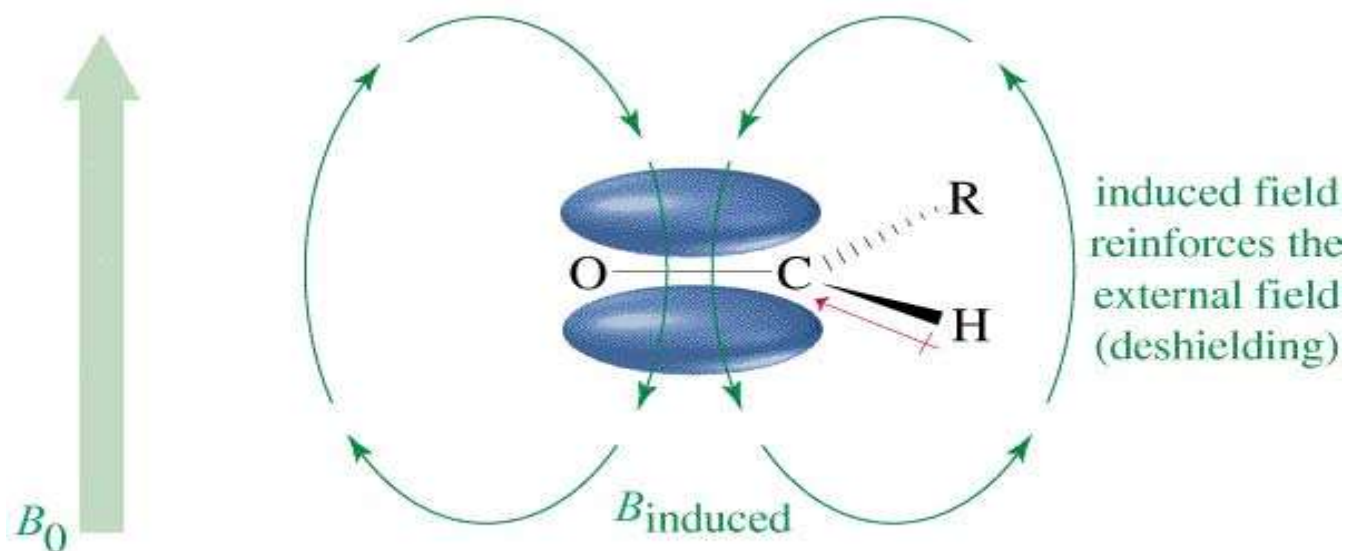
Anisotropic field for acetylene

$\delta=2.5$

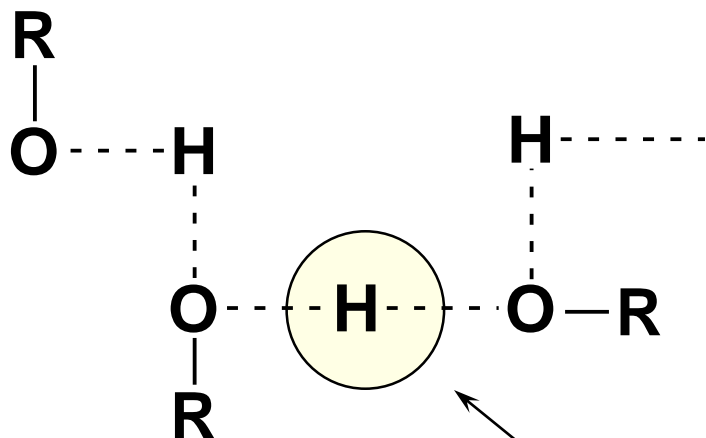


Anisotropic field for aldehyde

$\delta = 9-10$

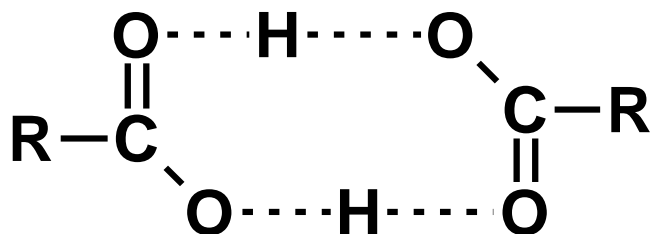


Hydrogen bonding deshields protons



Hydrogen bonding lengthens the O-H bond and reduces the valence electron density around the proton - it is deshielded and shifted downfield in the NMR spectrum.

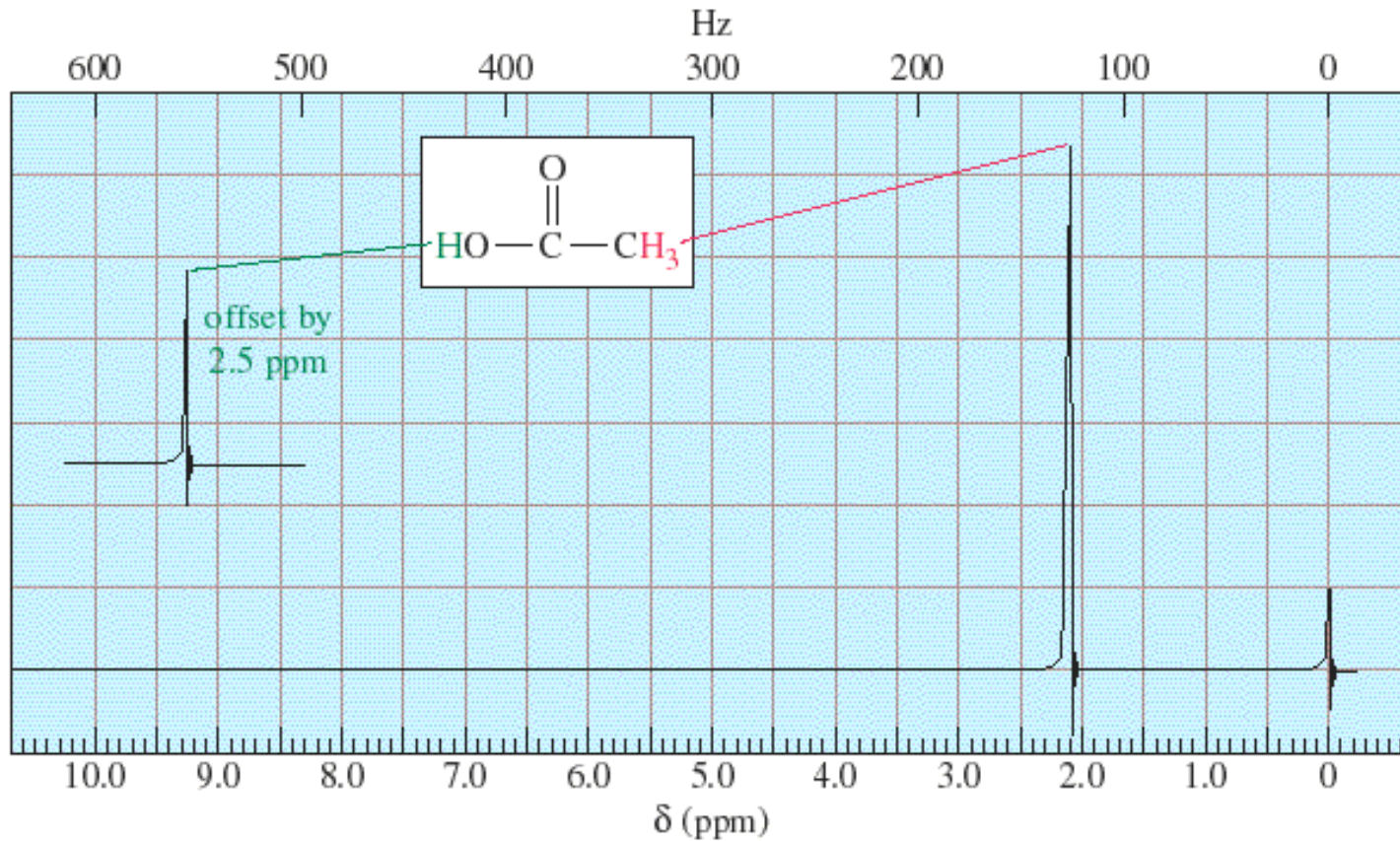
Hydrogen bonding in carboxylic acids



Carboxylic acids have strong hydrogen bonding – they form dimers.

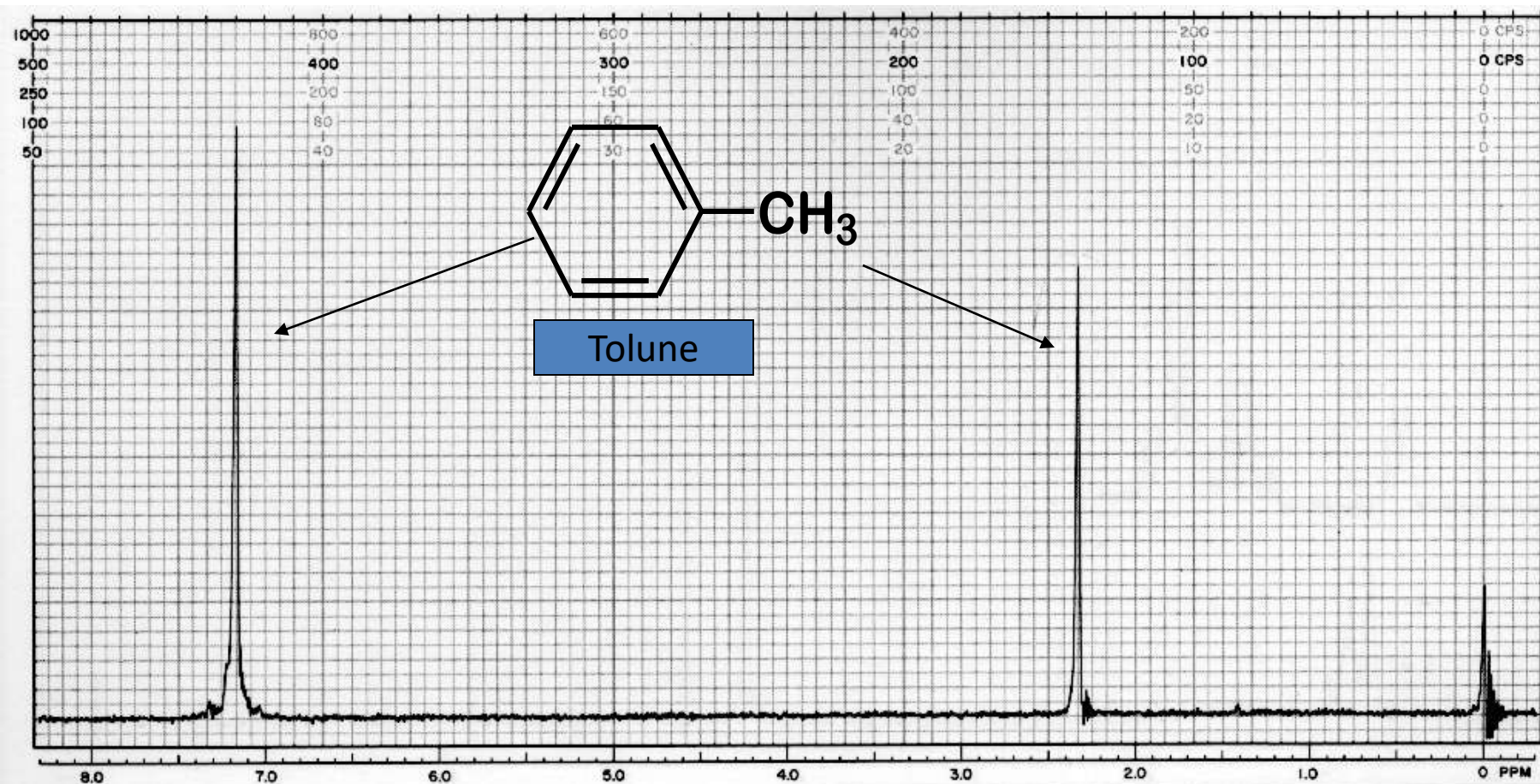
With carboxylic acids the O-H absorptions are found between 10 and 12 ppm.

Carboxylic Acid Proton, $\delta 10+$



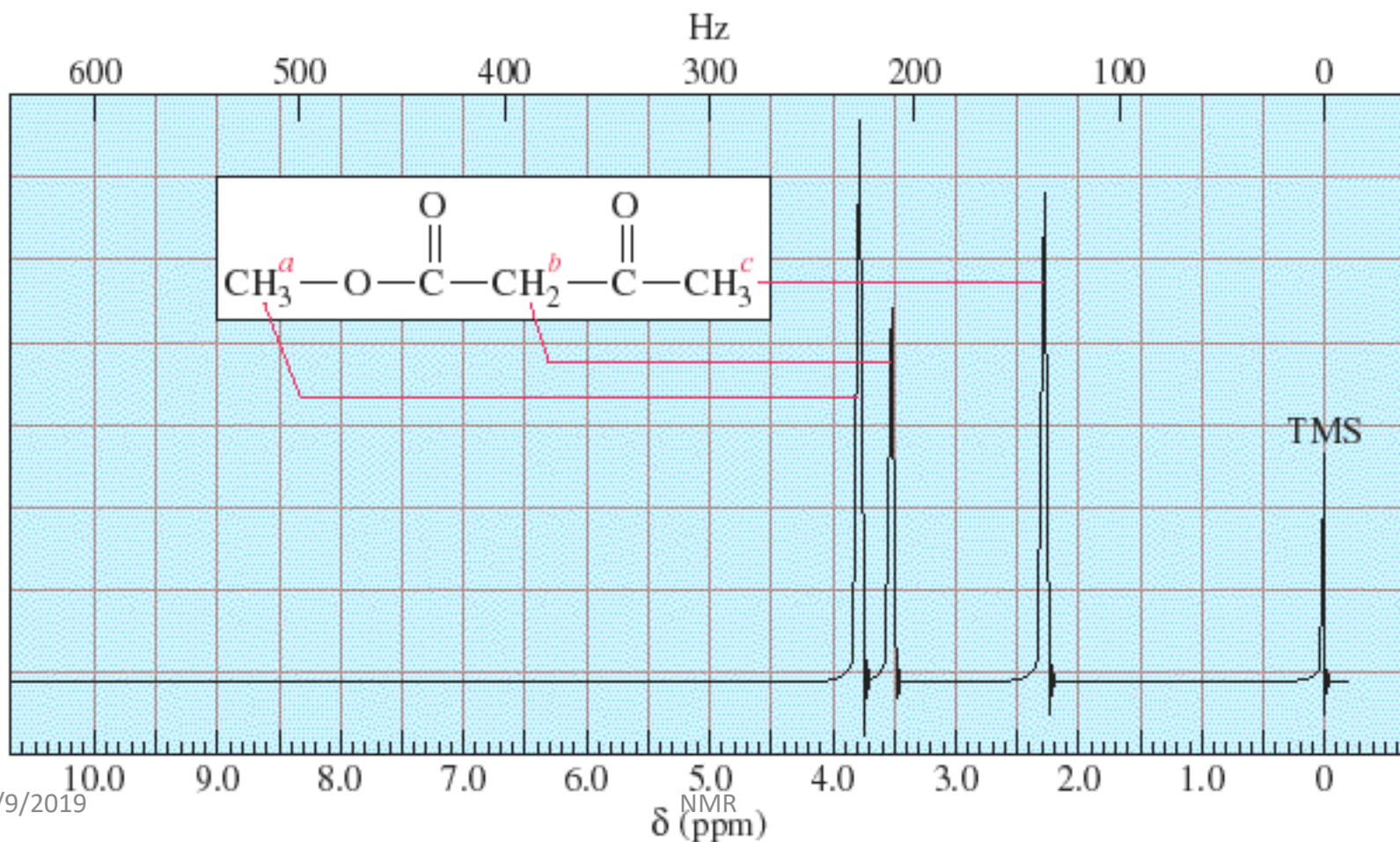
Peak area and proton counting

- Number of proton \propto peak area



Number of Signals

Equivalent hydrogens have the same chemical shift.



Spin-Spin Splitting in ^1H NMR Spectra

- Peaks are often split into multiple peaks due to *magnetic interactions* between nonequivalent protons on adjacent carbons, The process is called **spin-spin splitting**
- The splitting is into one more peak than the number of H's on the adjacent carbon(s), This is the "**n+1 rule**"
- The relative intensities are in proportion of a binomial distribution given by Pascal's Triangle
- The set of peaks is a **multiplet** (2 = doublet, 3 = triplet, 4 = quartet, 5=pentet, 6=hextet, 7=heptet.....)

The Origin of ^1H NMR—Spin-Spin Splitting

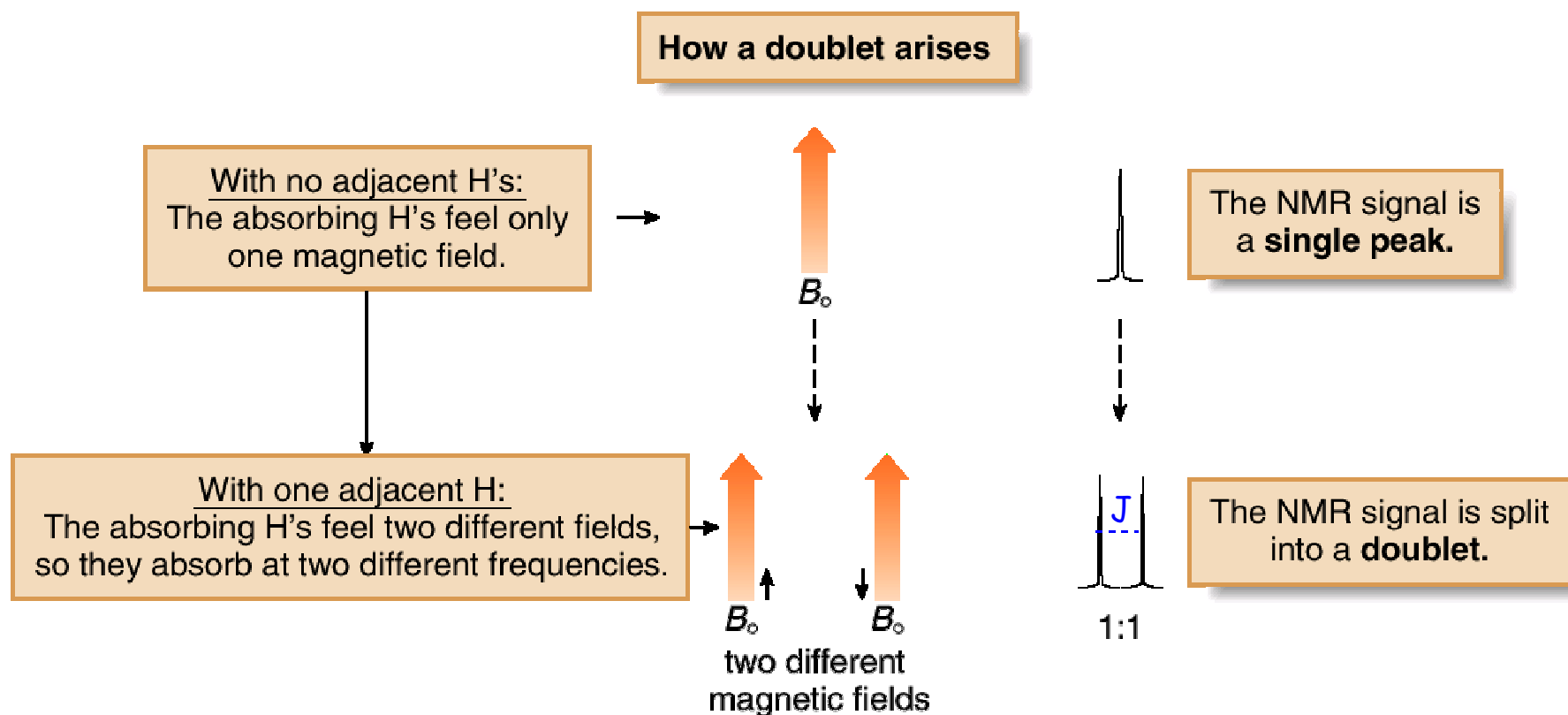
- Spin-spin splitting occurs only between nonequivalent protons on the same carbon or adjacent carbons.

Let us consider how the doublet due to the CH_2 group on $\text{BrCH}_2\text{CHBr}_2$ occurs:

- When placed in an applied field, (B_0), the adjacent proton (CHBr_2) can be aligned with (\uparrow) or against (\downarrow) B_0 . The likelihood of either case is about 50% (i.e., 1,000,006 \uparrow vs 1,000,000 \downarrow).
- Thus, the absorbing CH_2 protons feel two slightly different magnetic fields—one slightly larger than B_0 , and one slightly smaller than B_0 .
- Since the absorbing protons feel two different magnetic fields, they absorb at two different frequencies in the NMR spectrum, thus splitting a single absorption into a doublet, where the two peaks of the doublet have equal intensity.

The Origin of ^1H NMR—Spin-Spin Splitting

The frequency difference, measured in Hz, between two peaks of the doublet is called the **coupling constant, J** .



- One adjacent proton splits an NMR signal into a doublet.

The Origin of ^1H NMR—Spin-Spin Splitting

Let us now consider how a triplet arises:



- When placed in an applied magnetic field (B_0), the adjacent protons H_a and H_b can each be aligned with (\uparrow) or against (\downarrow) B_0 .
- Thus, the absorbing proton feels three slightly different magnetic fields—one slightly larger than B_0 ($\uparrow_a \uparrow_b$), one slightly smaller than B_0 ($\downarrow_a \downarrow_b$) and one the same strength as B_0 ($\uparrow_a \downarrow_b$).

The Origin of ^1H NMR—Spin-Spin Splitting

- Because the absorbing proton feels three different magnetic fields, it absorbs at three different frequencies in the NMR spectrum, thus splitting a single absorption into a triplet.
- Because there are two different ways to align one proton with B_0 , and one proton against B_0 —that is, $\uparrow_a\downarrow_b$ and $\downarrow_a\uparrow_b$ —the middle peak of the triplet is twice as intense as the two outer peaks, making the ratio of the areas under the three peaks 1:2:1.
- Two adjacent protons split an NMR signal into a triplet.
- When two protons split each other, they are said to be coupled.
- The spacing between peaks in a split NMR signal, measured by the J value, is equal for coupled protons.

The Origin of ^1H NMR—Spin-Spin Splitting

How a triplet arises

With no adjacent H's:
The absorbing H feels only one magnetic field.



B_0



The NMR signal is a **single peak**.

With two adjacent H's:
The absorbing H feels three different fields, so it absorbs at three different frequencies.



B_0

$\uparrow_a \downarrow_b$

or

$\downarrow_a \uparrow_b$

$\downarrow_a \downarrow_b$



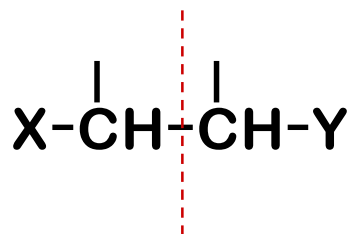
1:2:1

The NMR signal is split into a **triplet**.

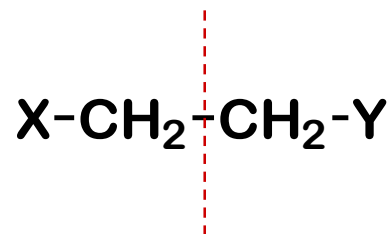
three different magnetic fields

EXCEPTIONS TO THE N+1 RULE

- 1) Protons that are equivalent by symmetry usually do not split one another

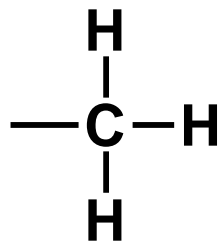


no splitting if x=y

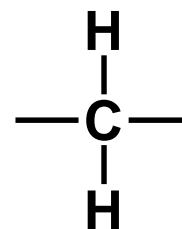


no splitting if x=y

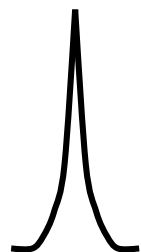
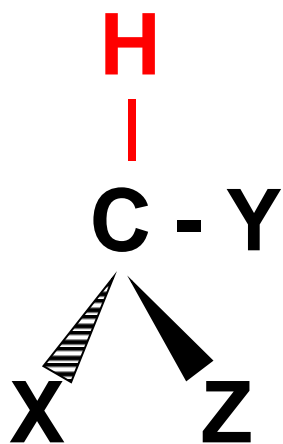
- 2) Protons in the same group usually do not split one another



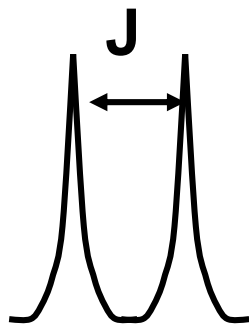
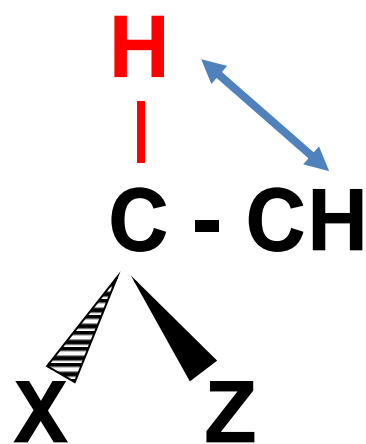
or



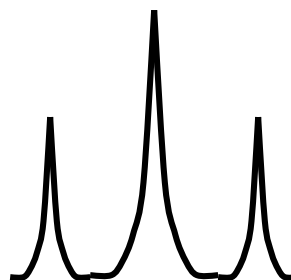
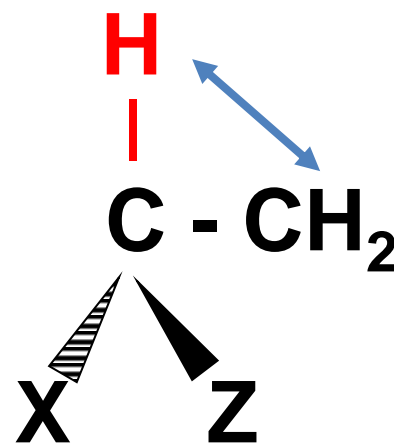
Examples



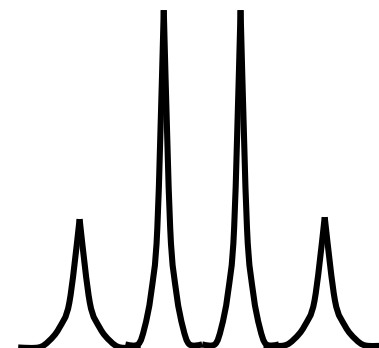
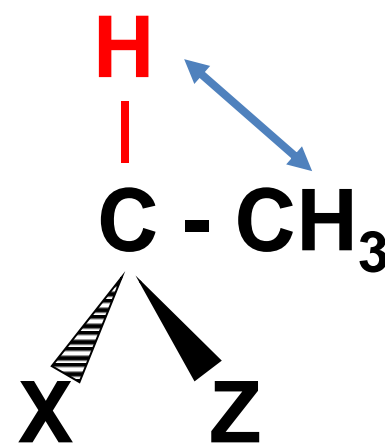
singlet



doublet



triplet

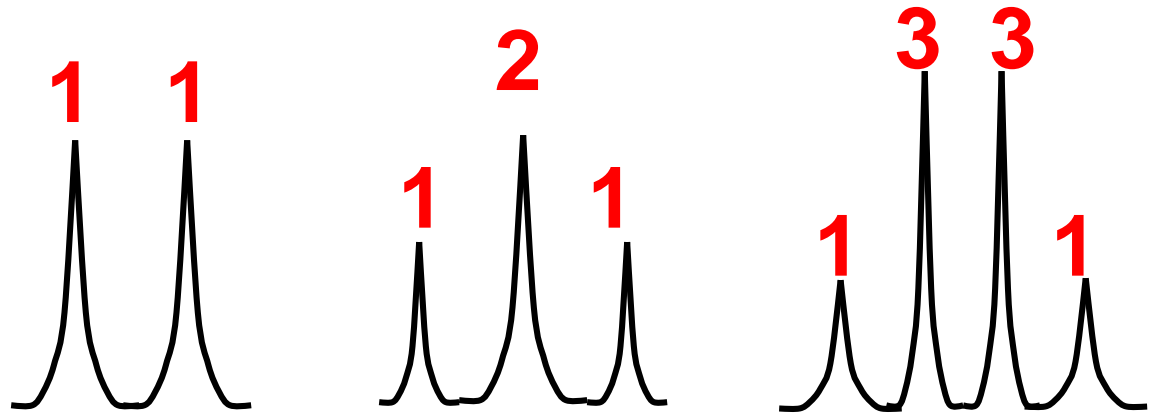


quartet

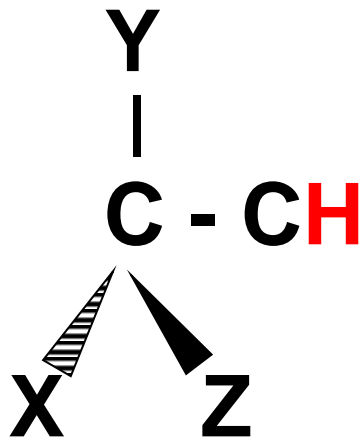
Intensities

1
1 1
1 2 1
1 3 3 1
1 4 6 4 1
1 5 10 10 5 1

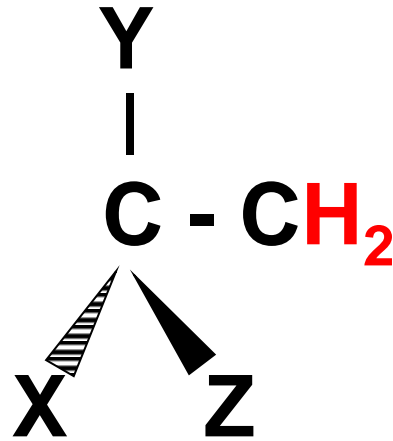
Pascal's Triangle



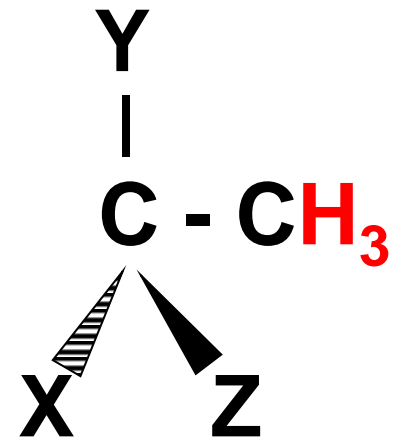
NMR Peak Intensities



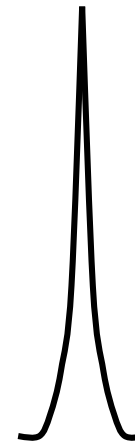
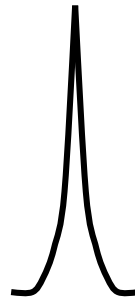
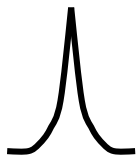
AUC = 1



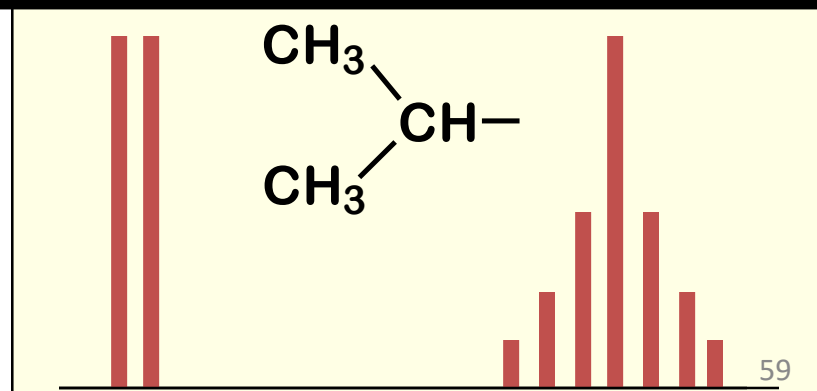
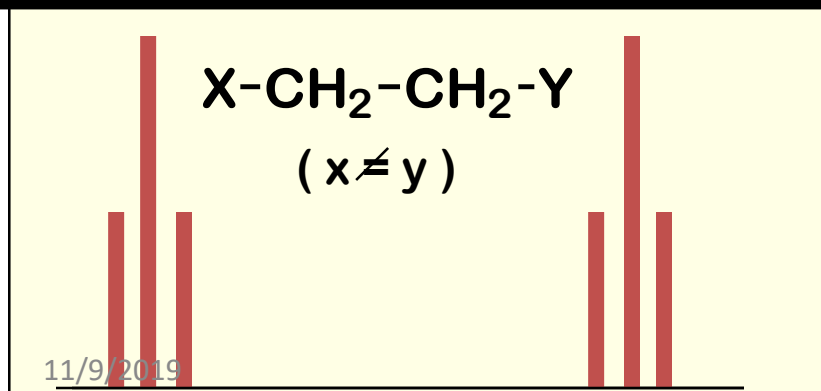
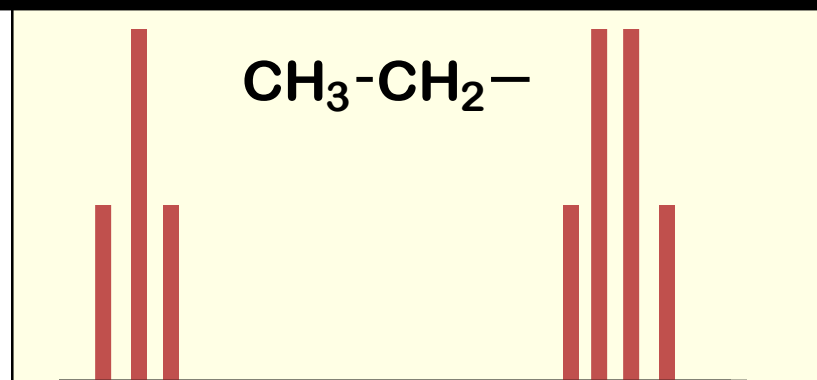
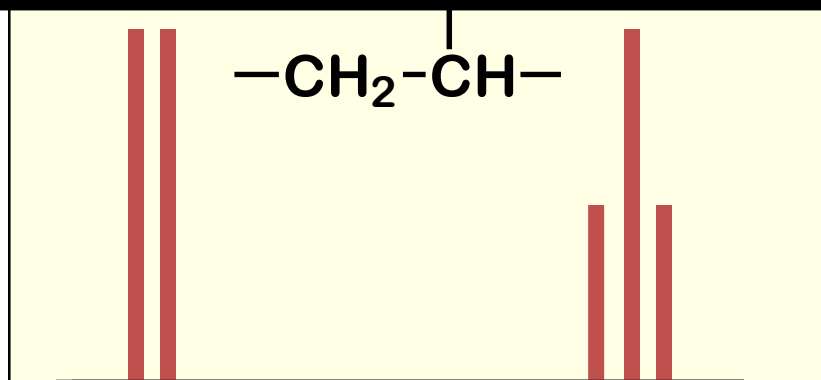
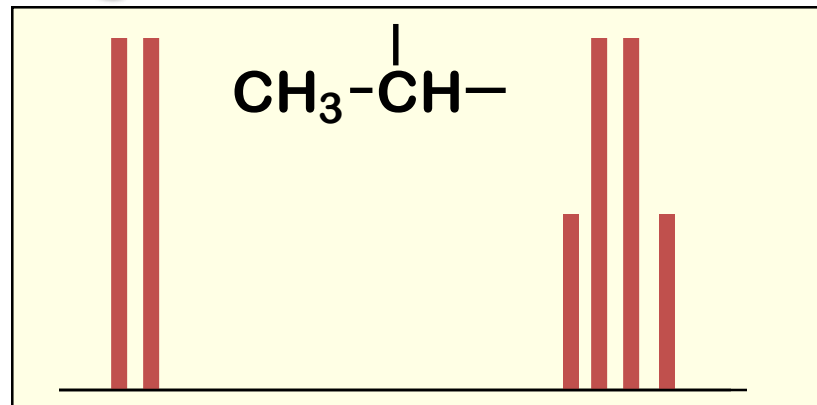
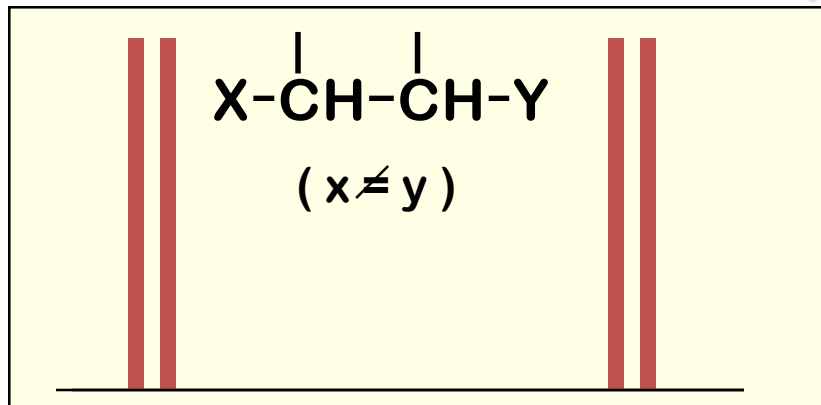
AUC = 2



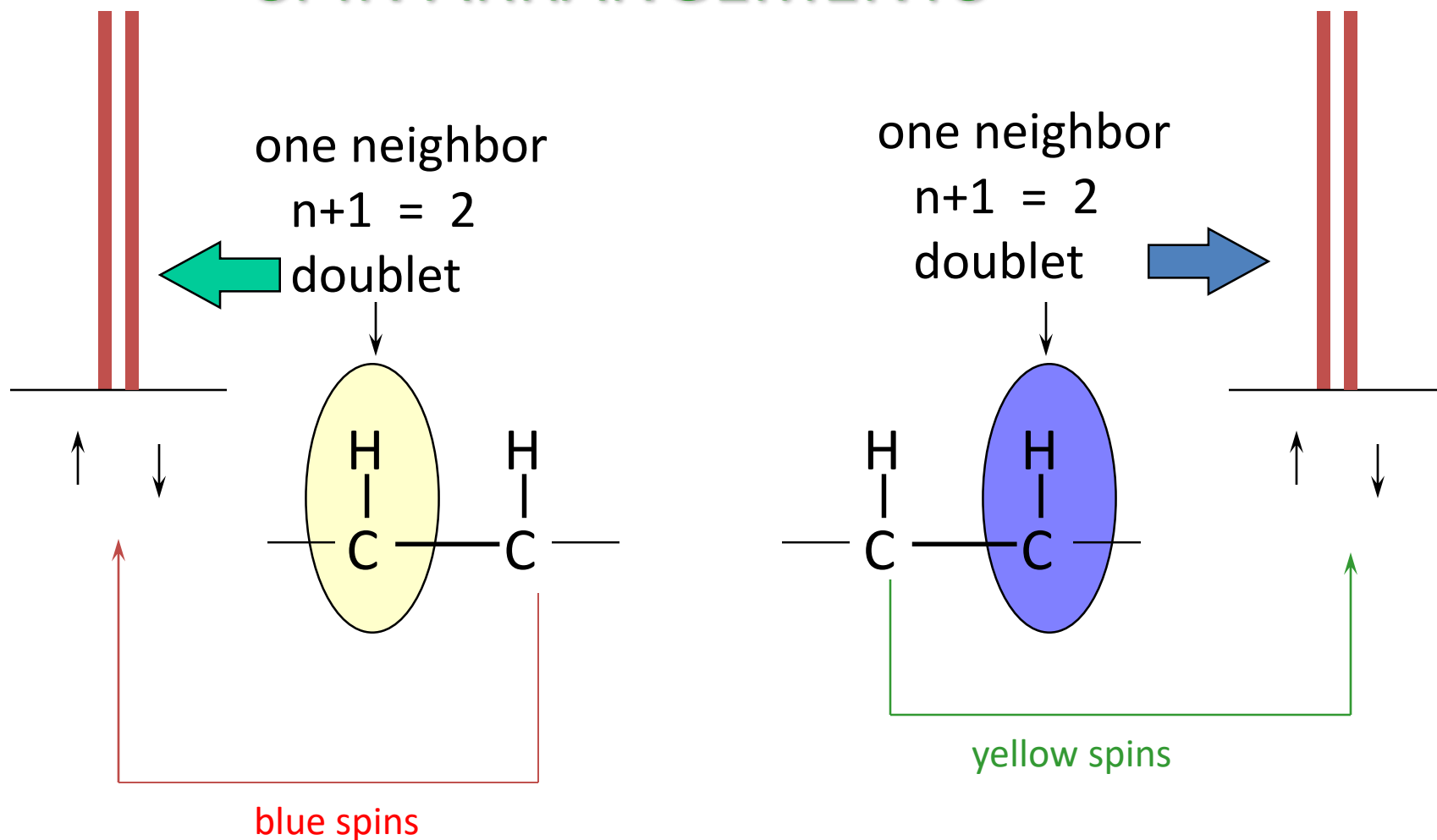
AUC = 3



Some Common Splitting Patterns

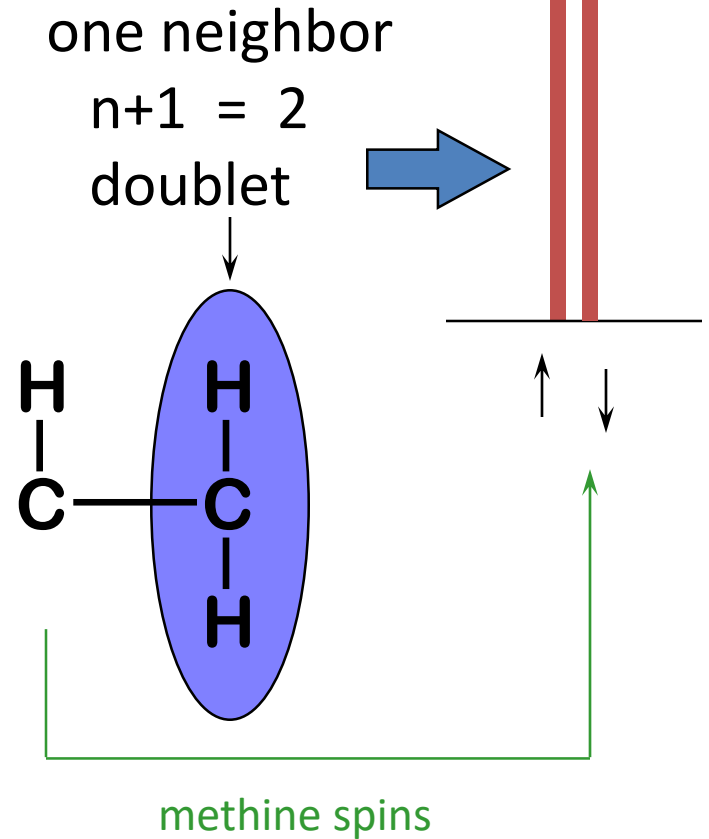
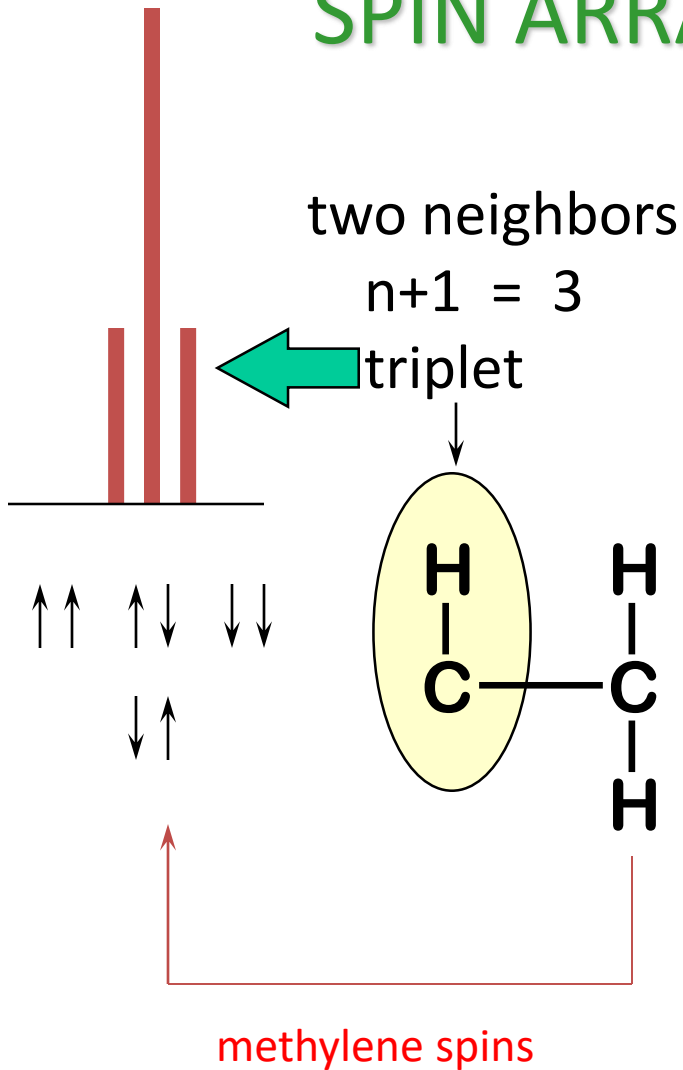


SPIN ARRANGEMENTS

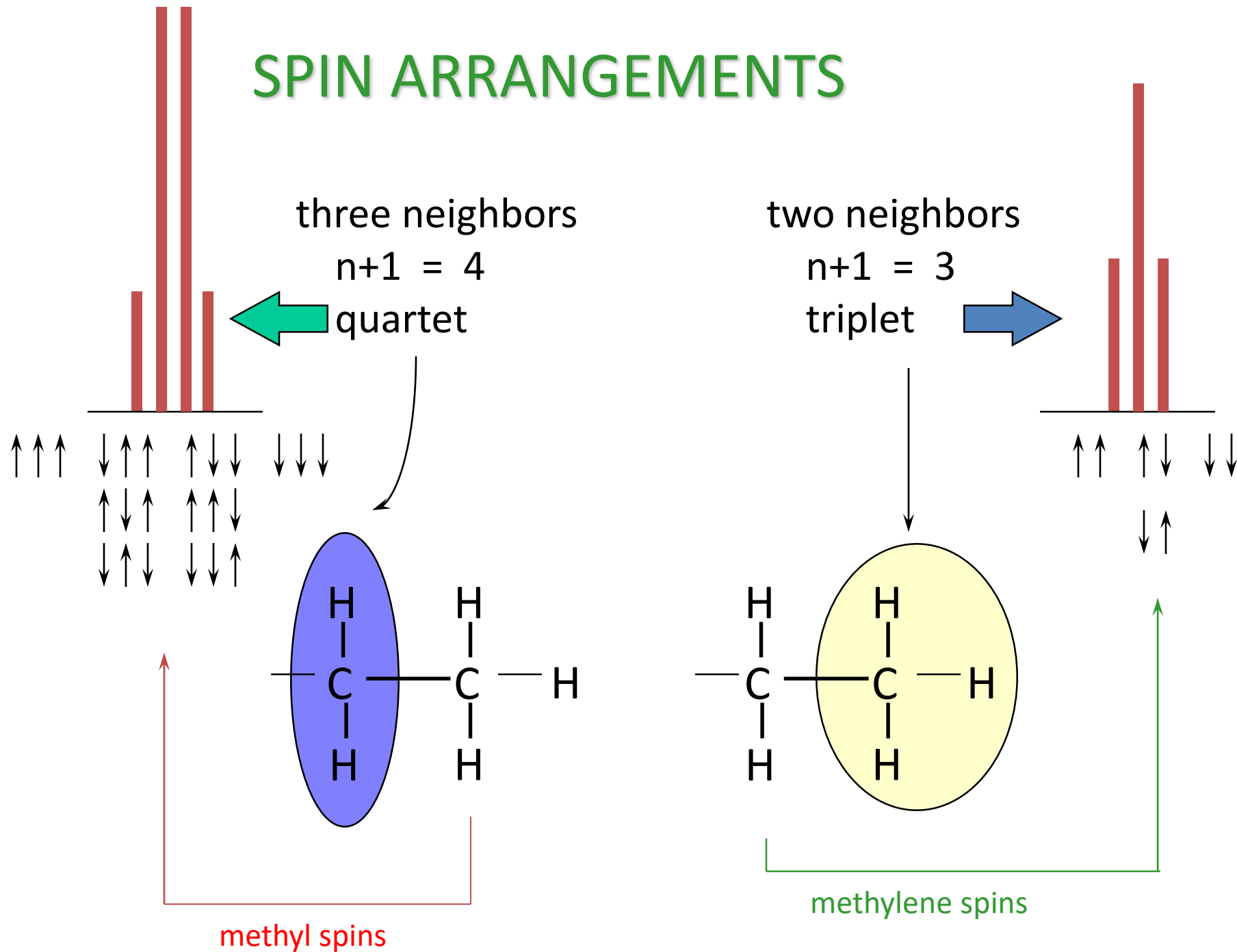


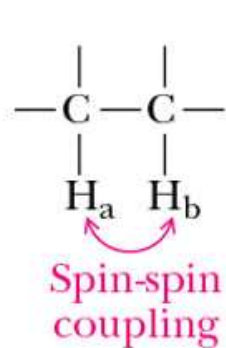
The resonance positions (splitting) of a given hydrogen is affected by the possible spins of its neighbor.

SPIN ARRANGEMENTS

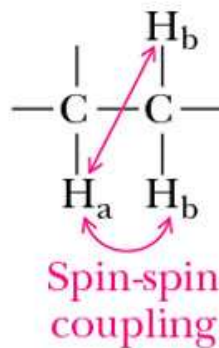
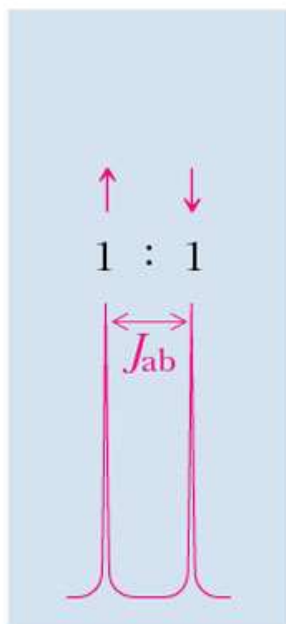


SPIN ARRANGEMENTS

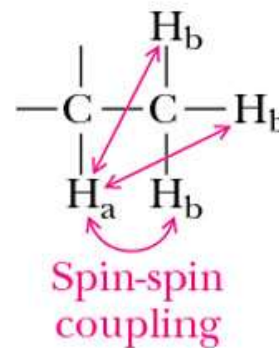
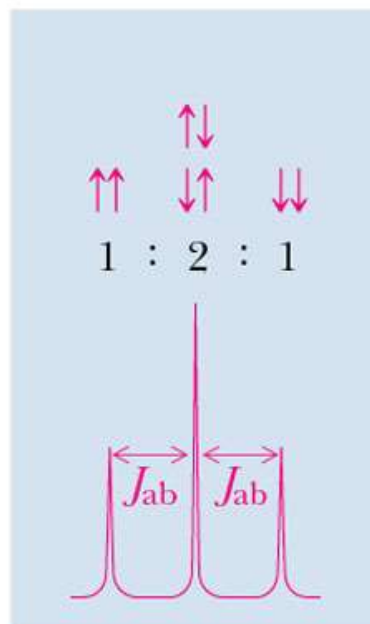




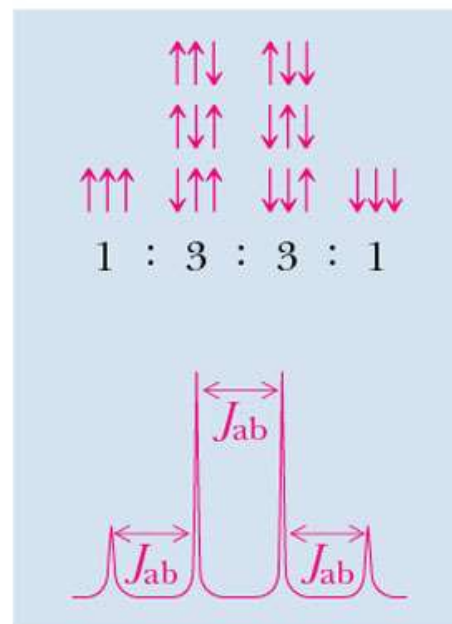
One H_b atom



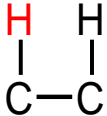
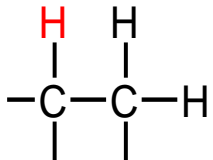
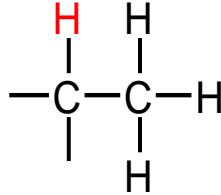
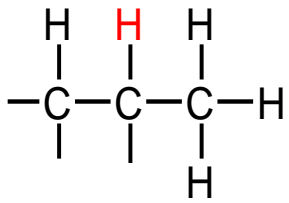
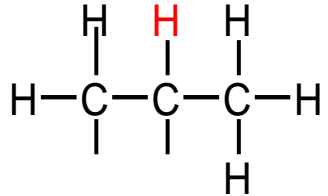
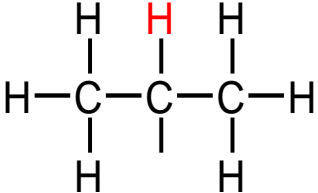
Two equivalent H_b atoms



Three equivalent H_b atoms



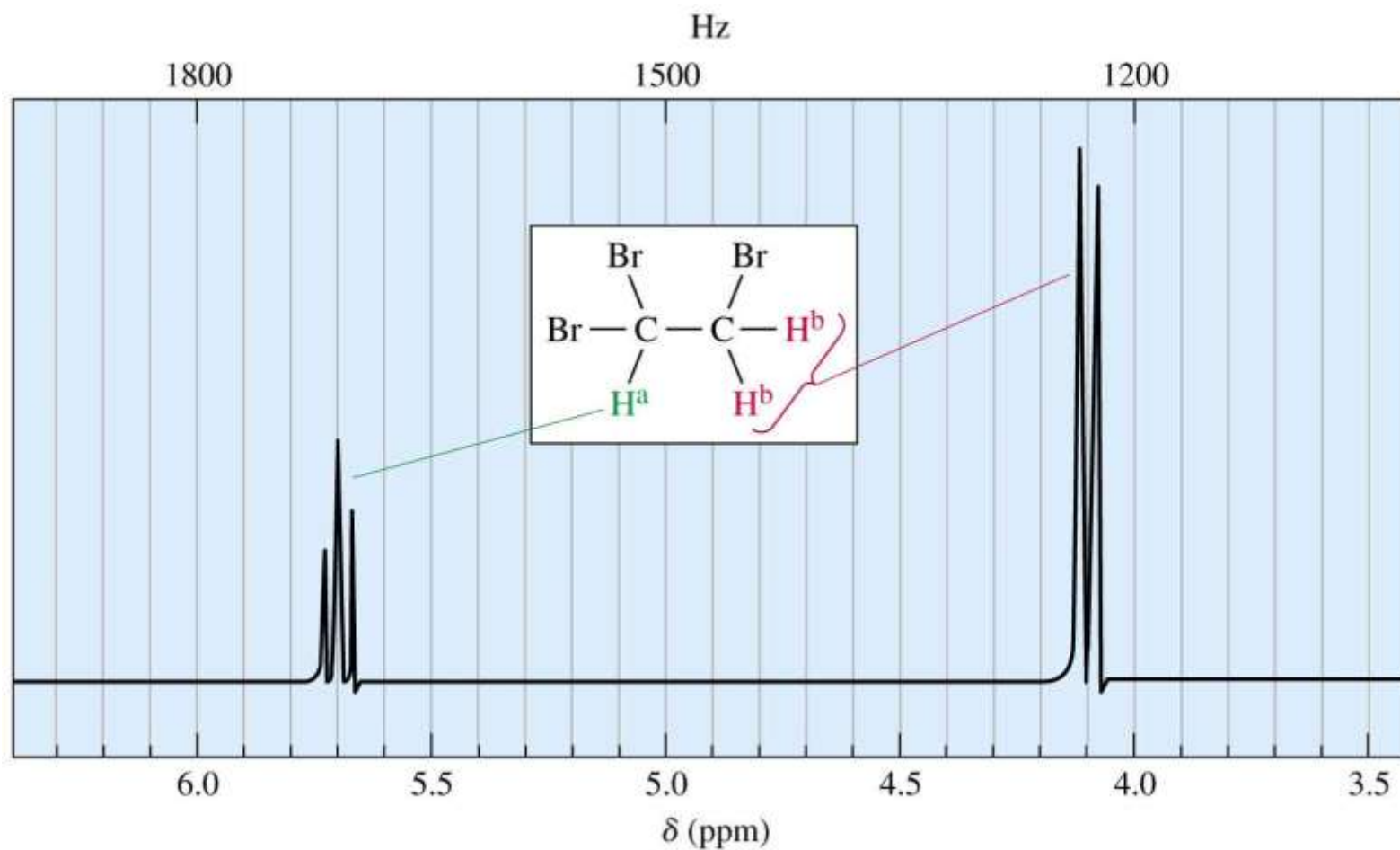
Observed splitting in signal of H_a

no. of neighbors	relative intensities	pattern	example
0	1	singlet (s)	
1	1 1	doublet (d)	
2	1 2 1	triplet (t)	
3	1 3 3 1	quartet (q)	
4	1 4 6 4 1	pentet	
5	1 5 10 10 5 1	sextet	
6	1 6 15 20 15 6 1	septet	

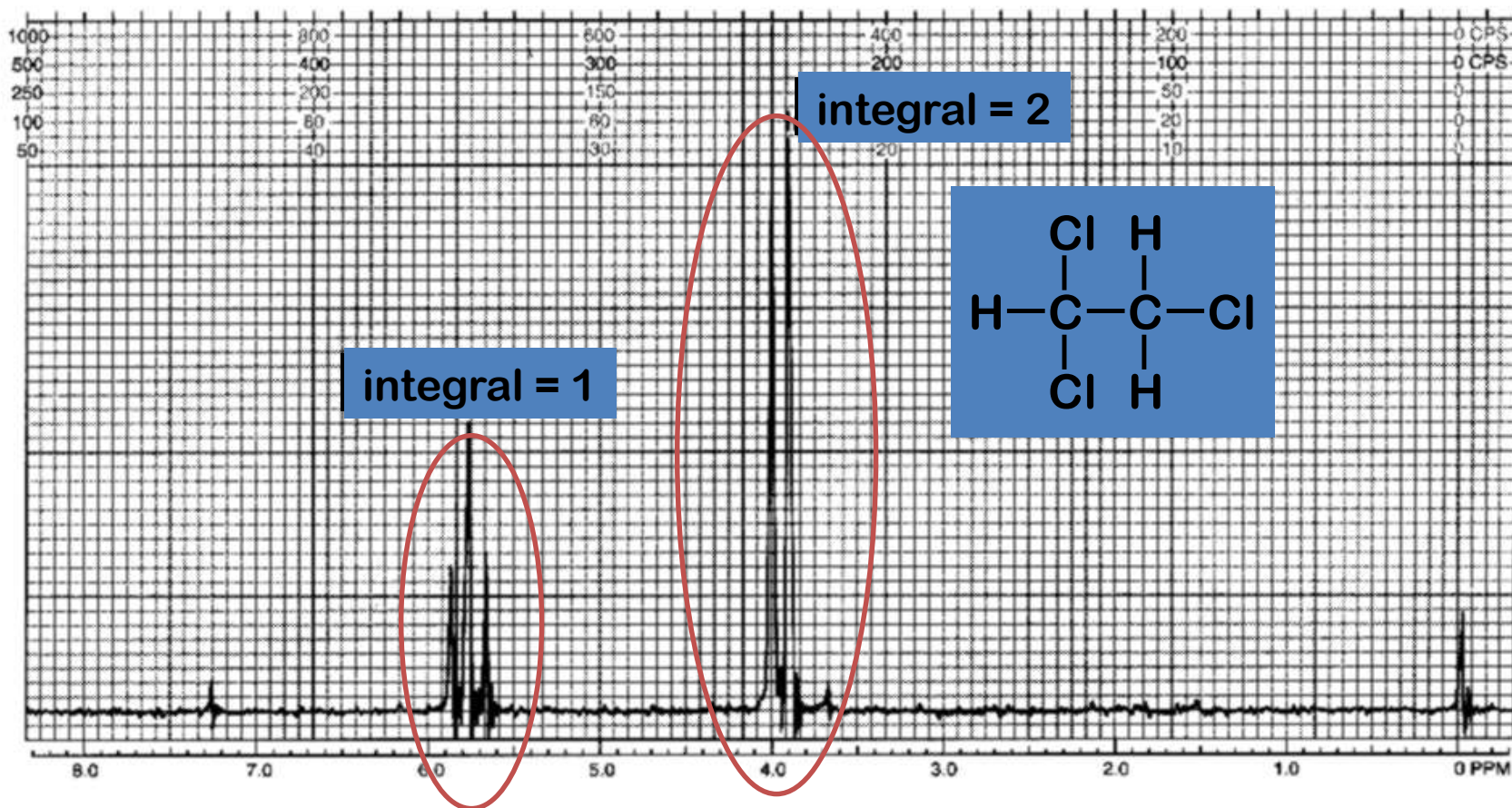
Relative Peak Intensities of Symmetric Multiplets

<i>Number of Equivalent Protons Causing Splitting</i>	<i>Number of Peaks (multiplicity)</i>	<i>Area Ratios (Pascal's triangle)</i>
0	1 (singlet)	1
1	2 (doublet)	1 1
2	3 (triplet)	1 2 1
3	4 (quartet)	1 3 3 1
4	5 (quintet)	1 4 6 4 1
5	6 (sextet)	1 5 10 10 5 1
6	7 (septet)	1 6 15 20 15 6 1

1,1,2-Tribromoethane



1,1,2-Trichloroethane

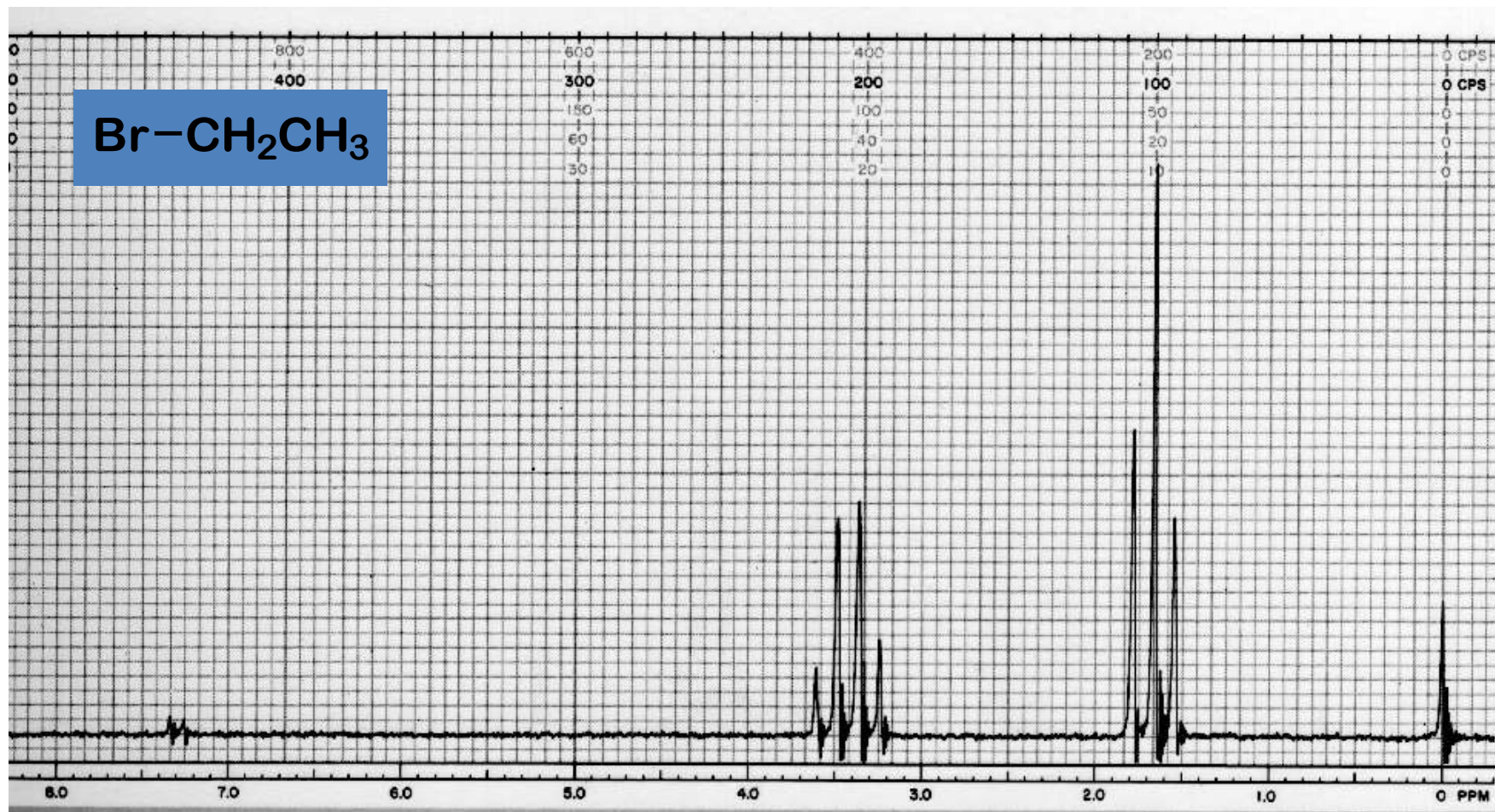


triplet

doublet

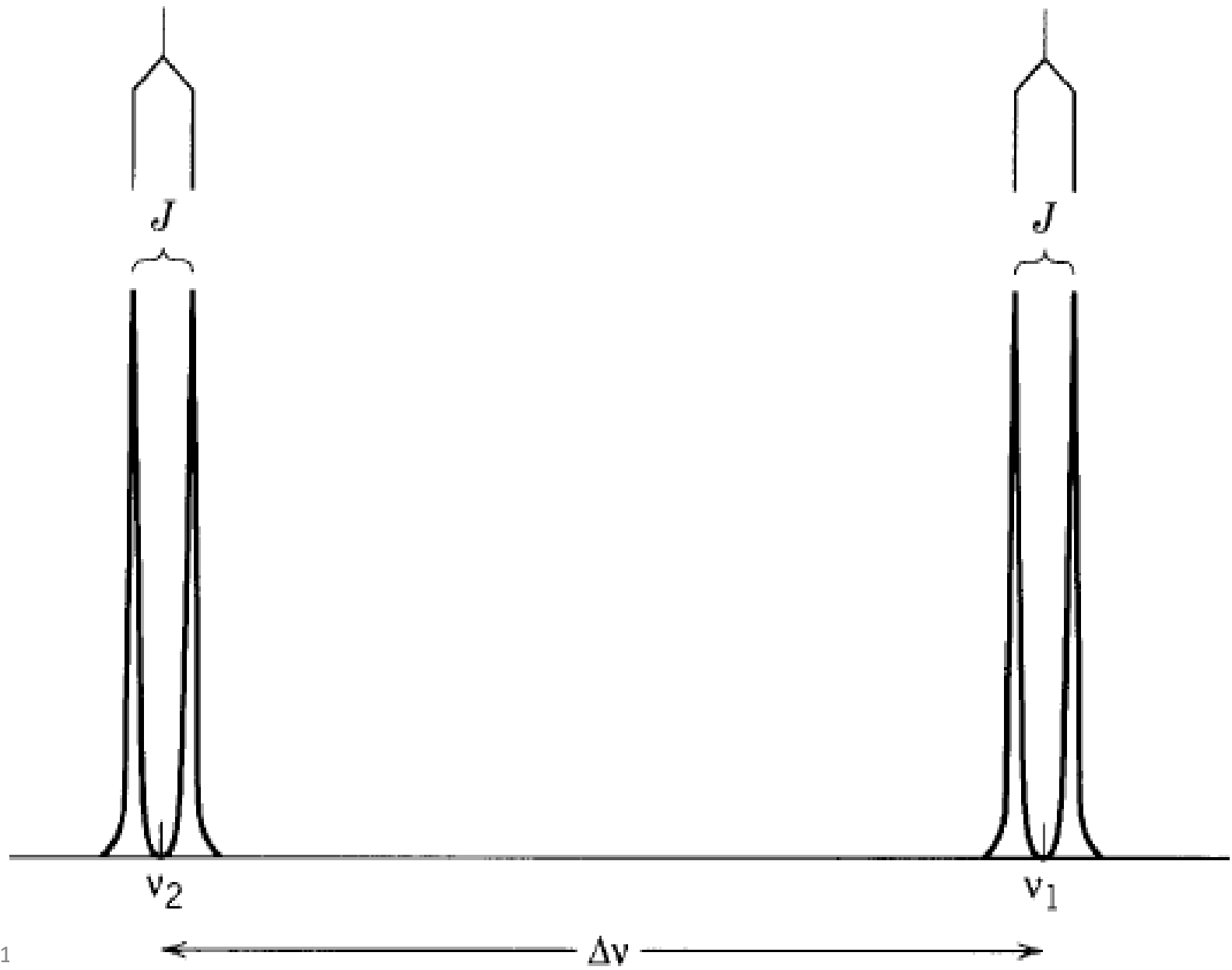
The subpeaks are due to spin-spin splitting and are predicted by the $n+1$ rule.

NMR Spectrum of Bromoethane



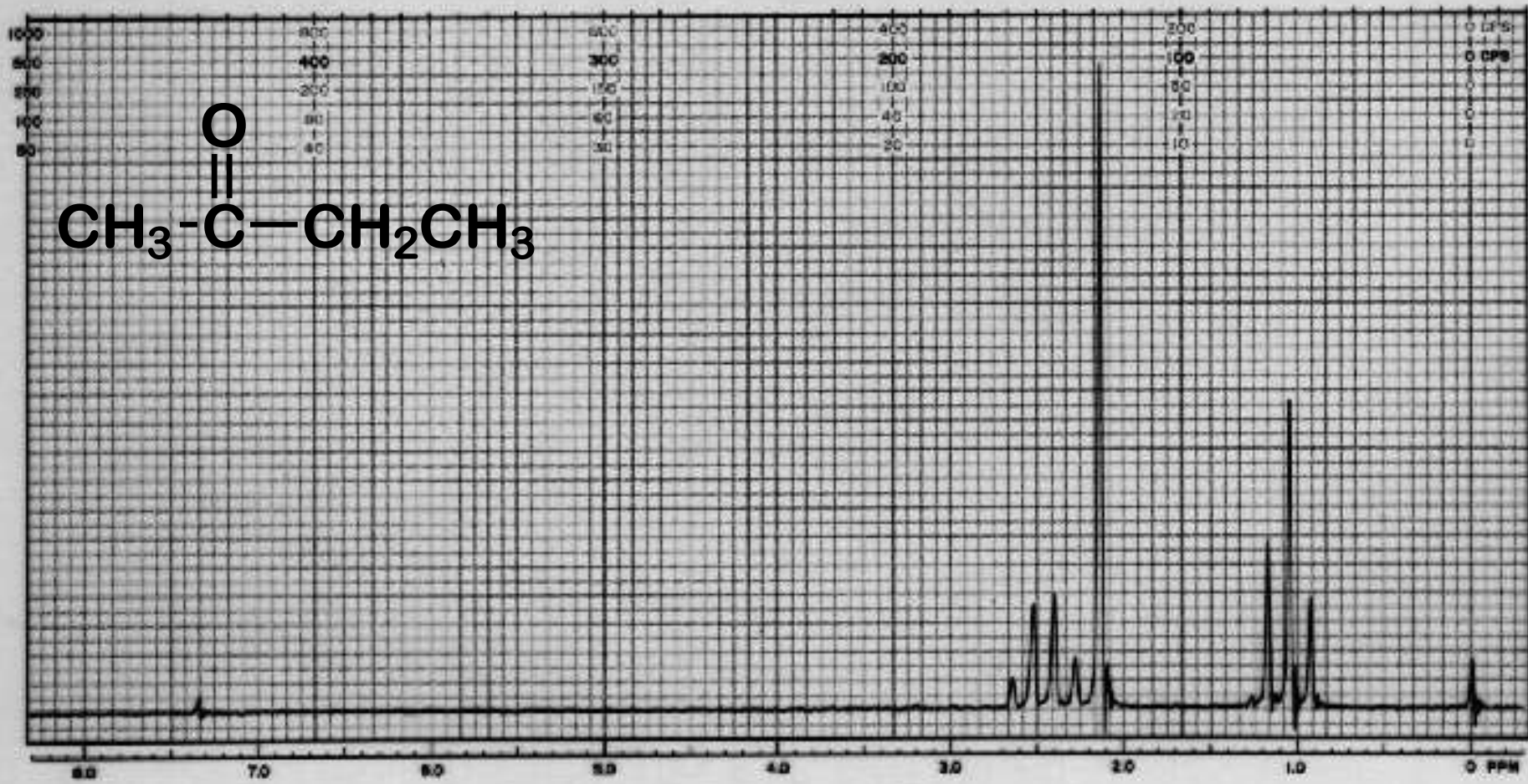
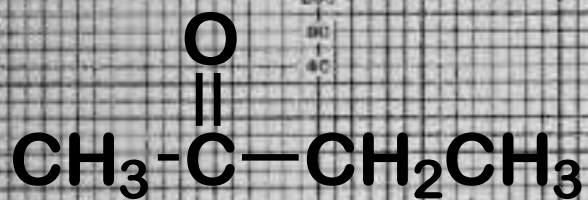
Coupling Constant(J)

- Distance between the peaks of multiplet
- Measured in Hz (0-20 Hz for PMR)
- Not dependent on strength of the external field
- For symmetrical peaks $\Delta\nu / J > 8$

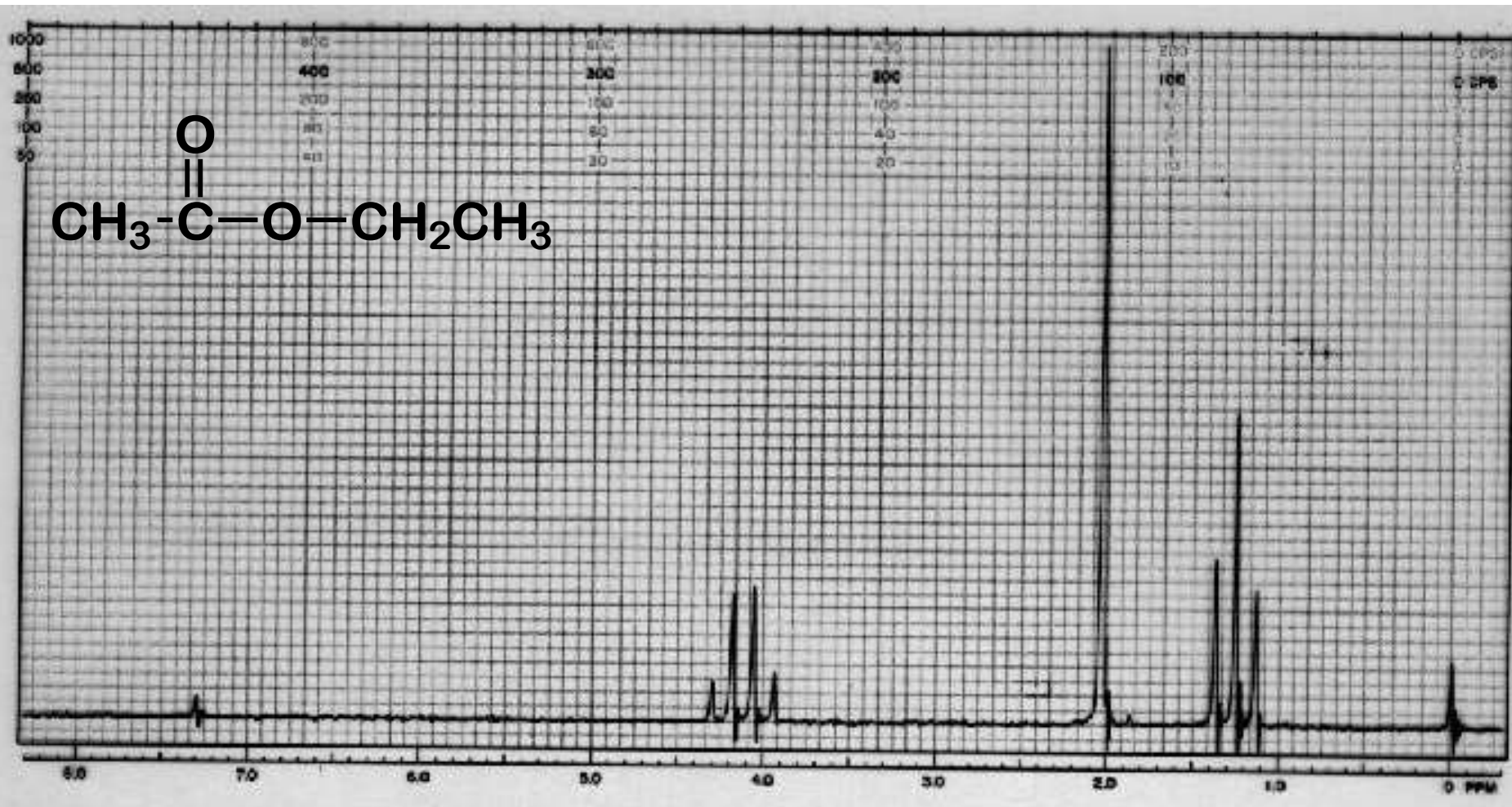
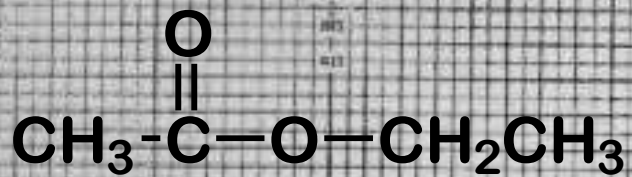


Example spectra for discussion

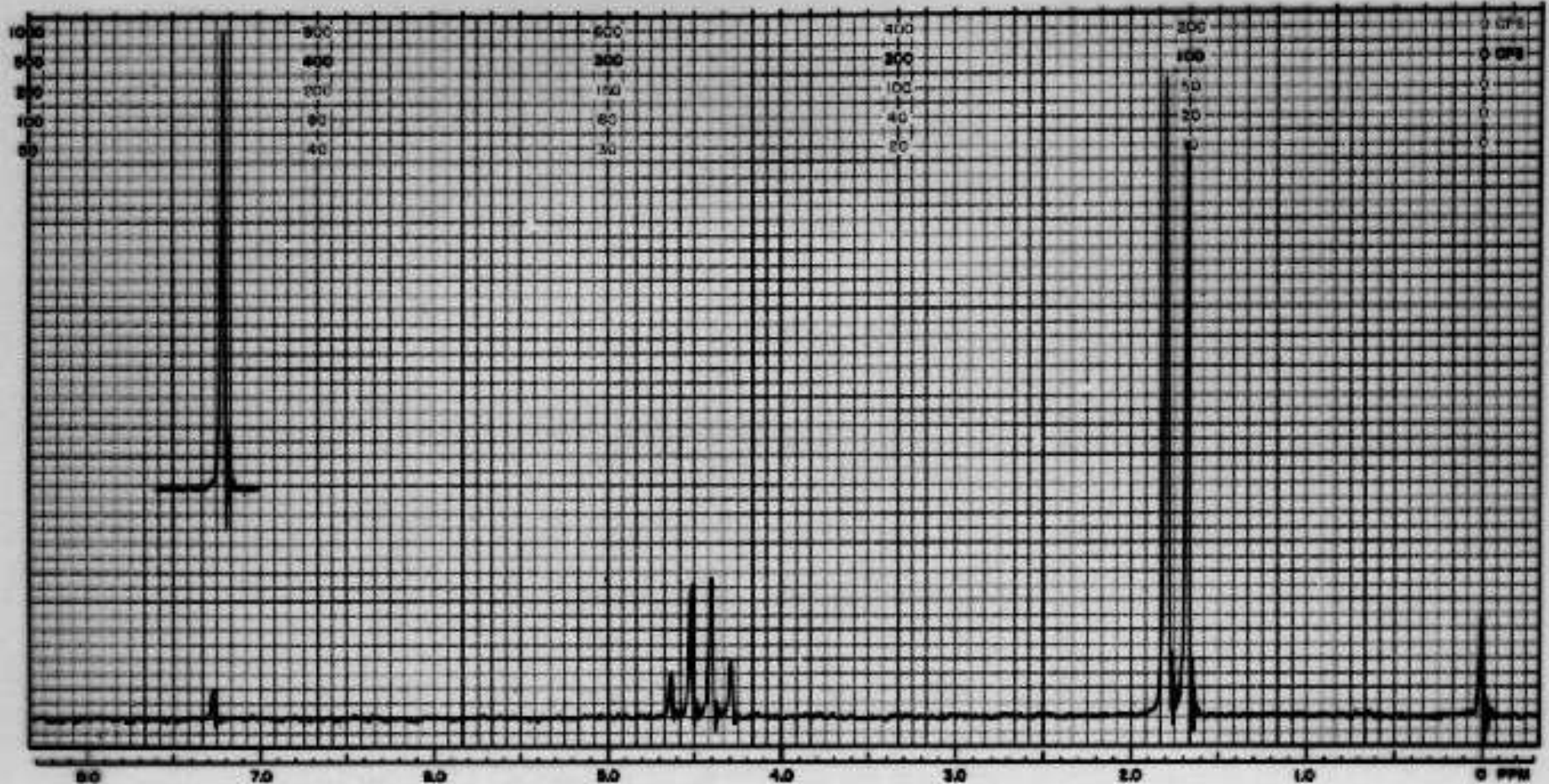
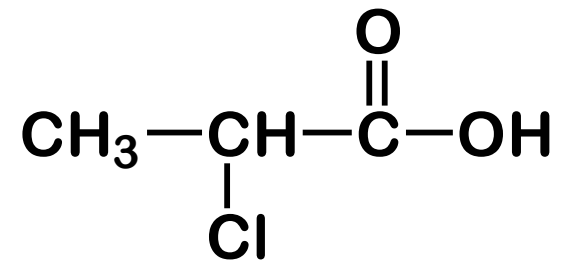
Methyl Ethyl Ketone



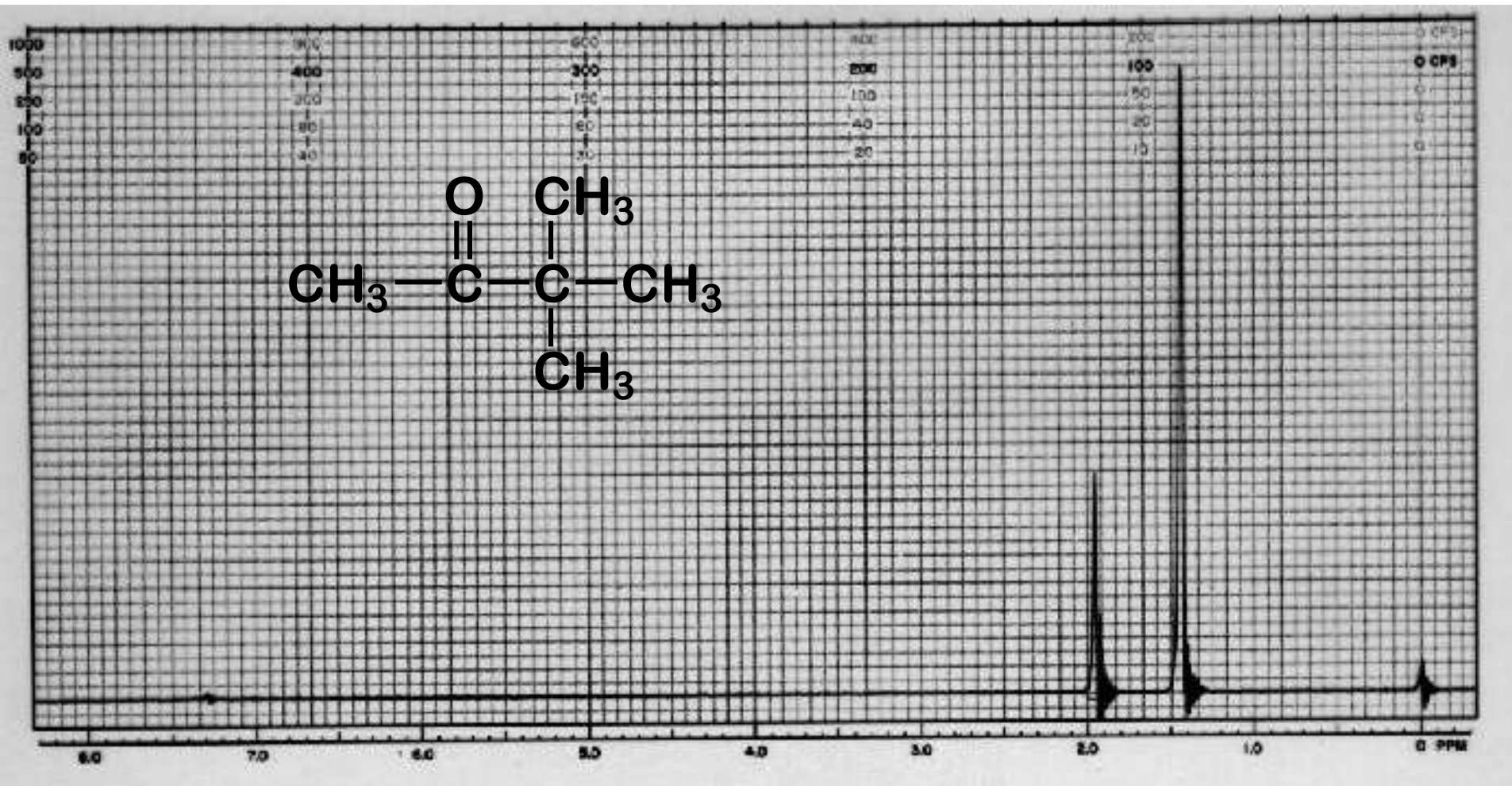
Ethyl Acetate



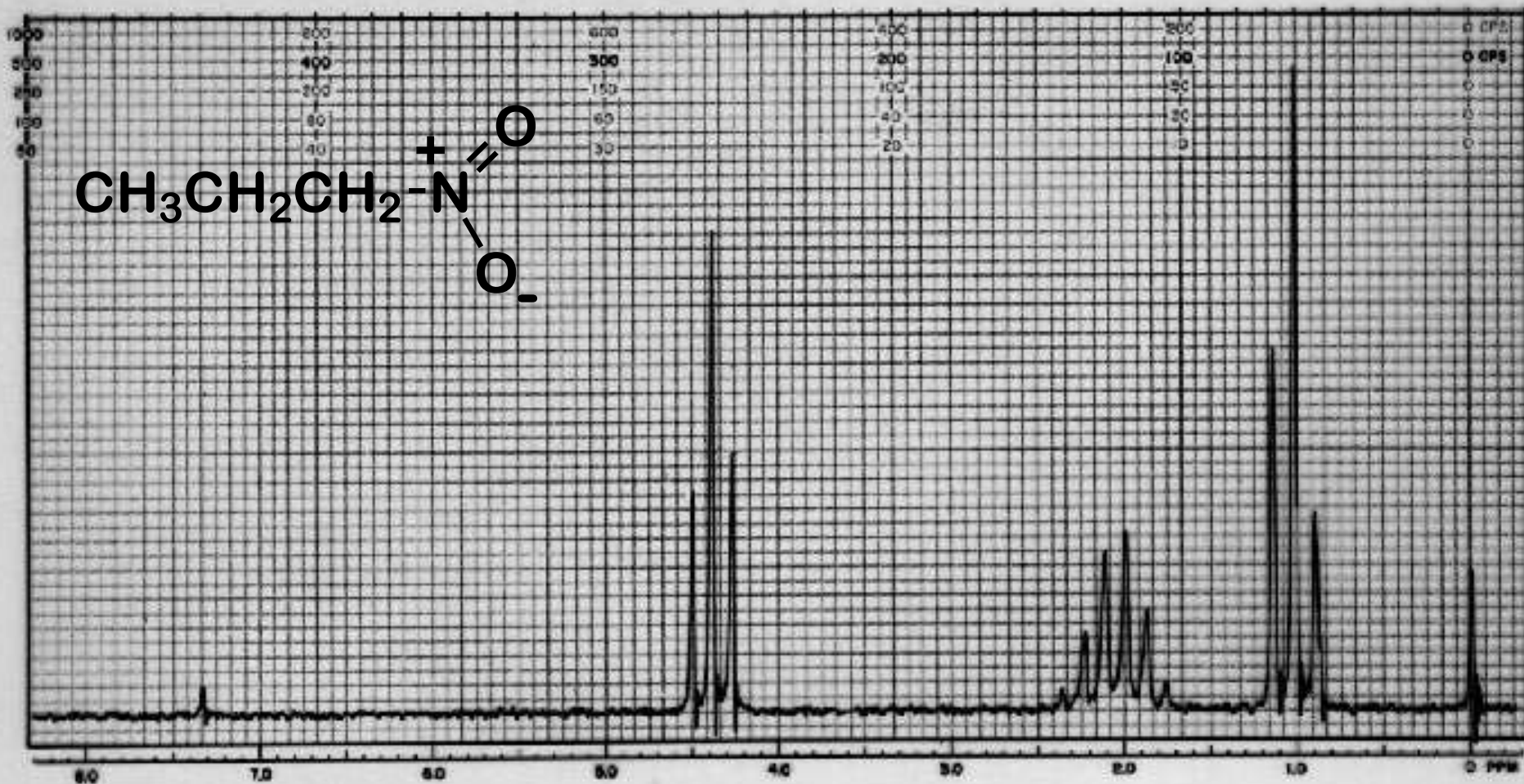
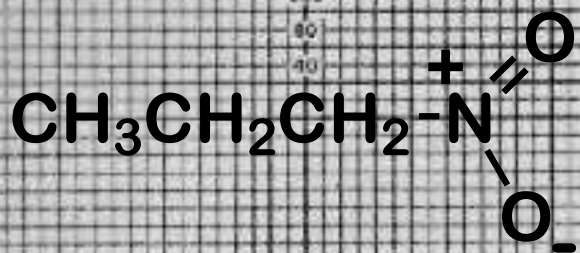
α -Chloropropionic Acid



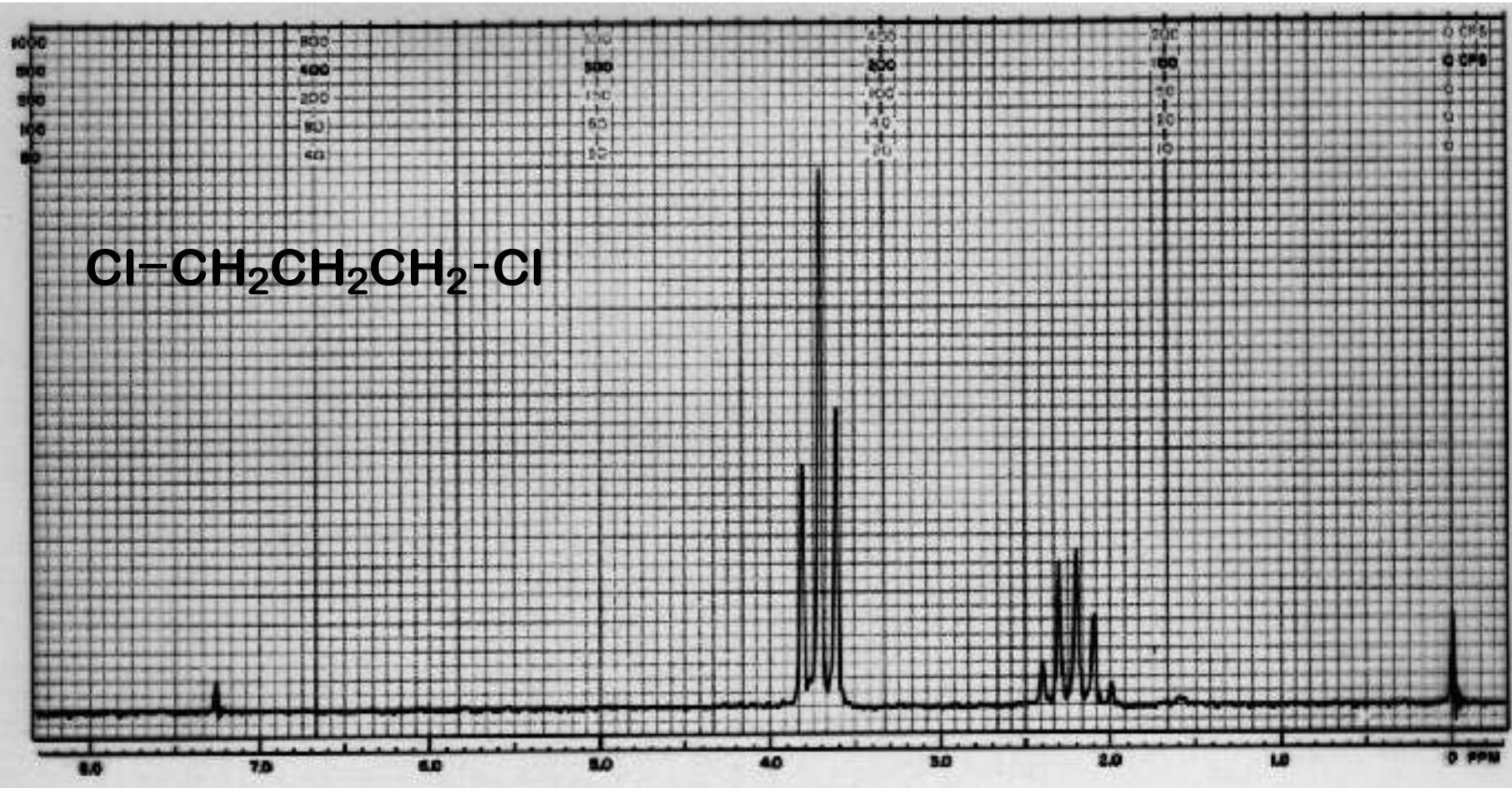
t-Butyl Methyl Ketone (3,3-dimethyl-2-butanone)



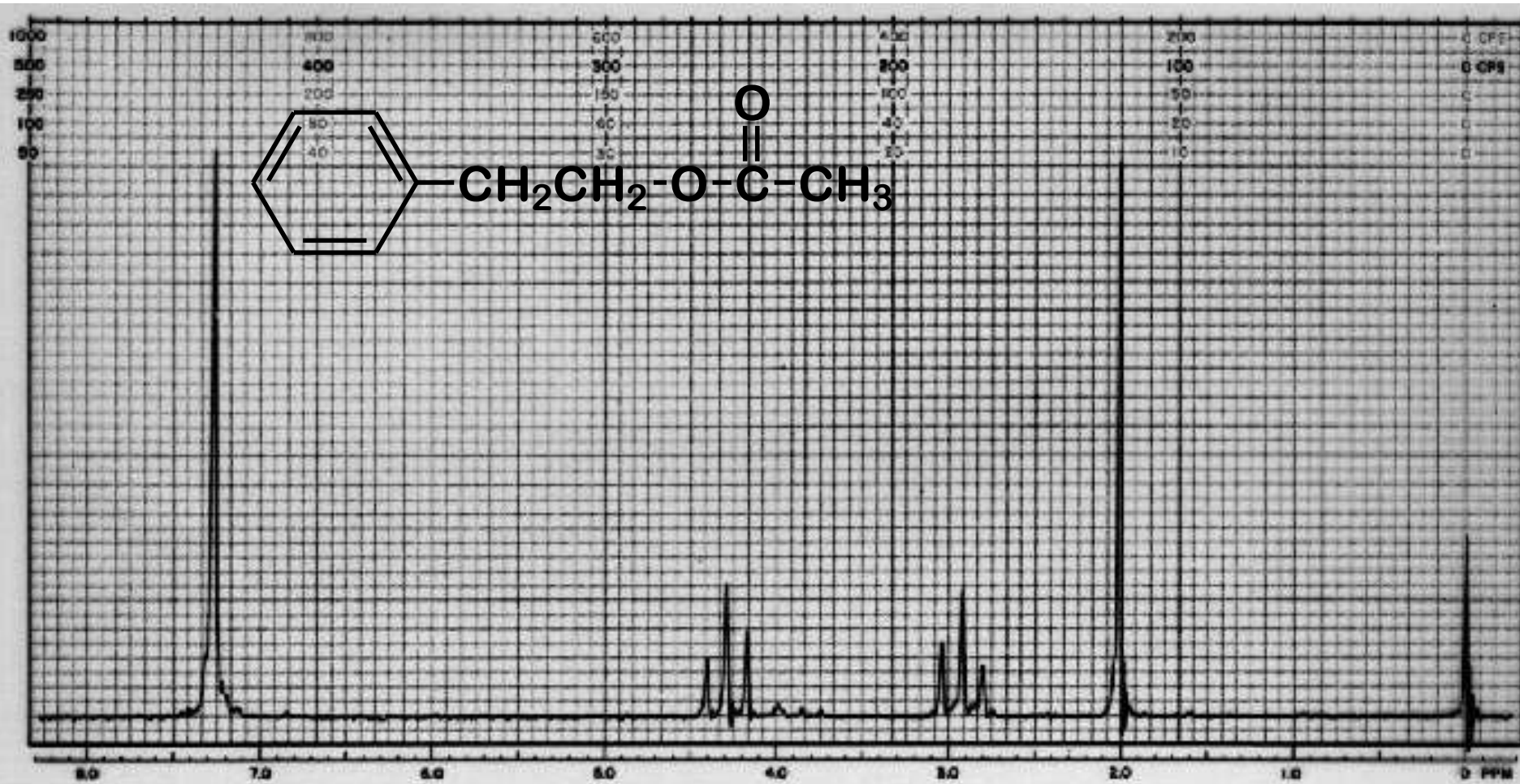
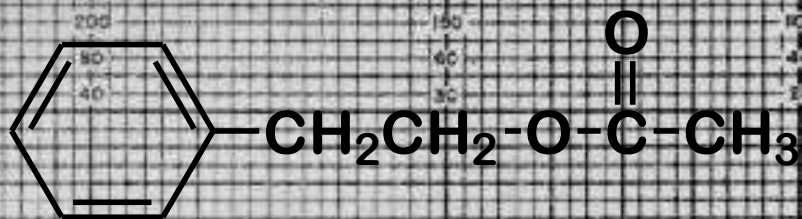
1-Nitropropane



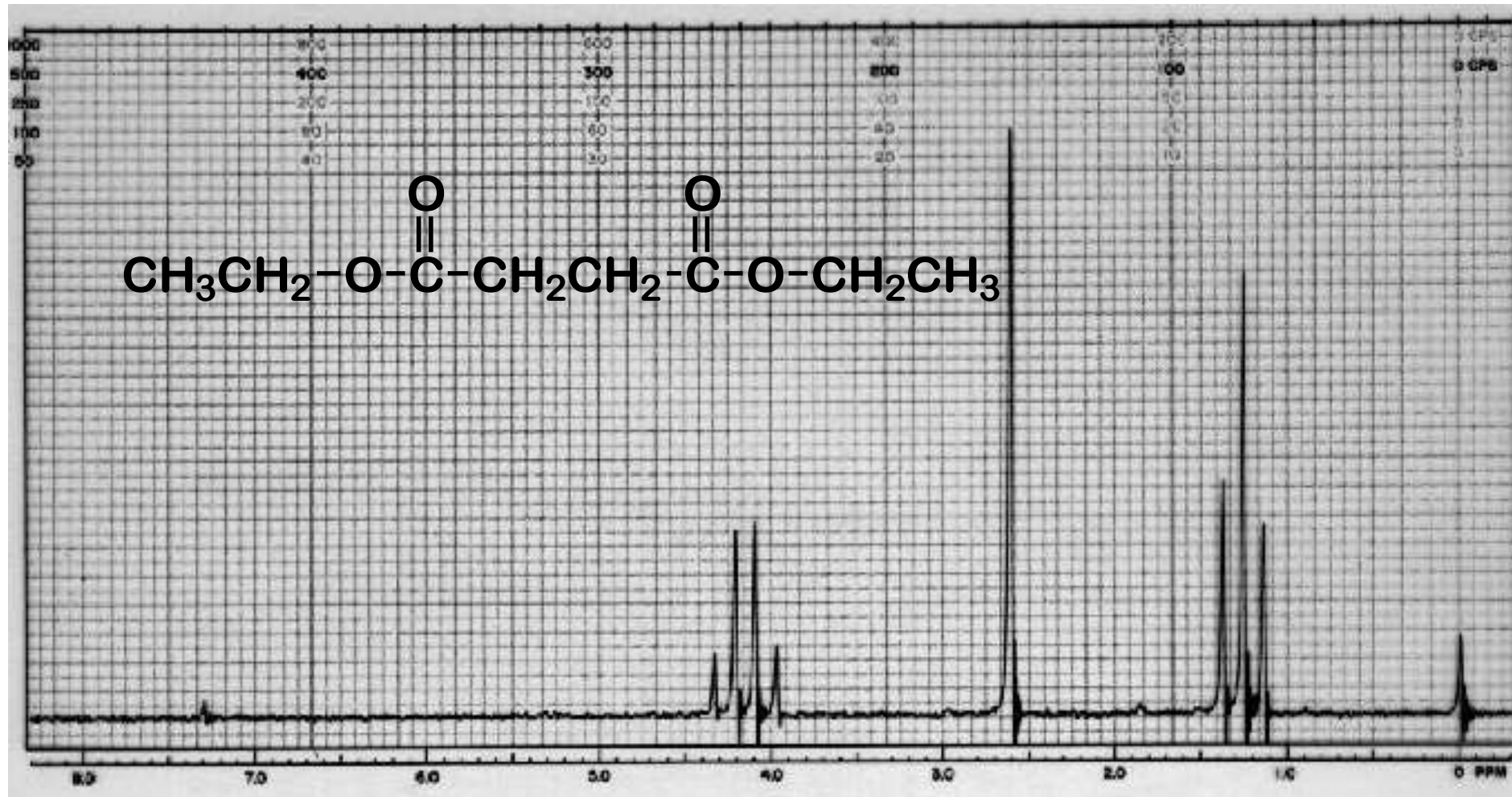
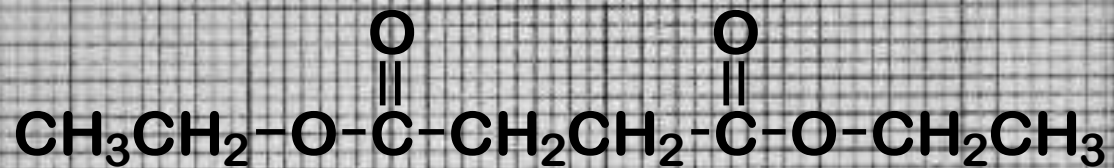
1,3-Dichloropropane



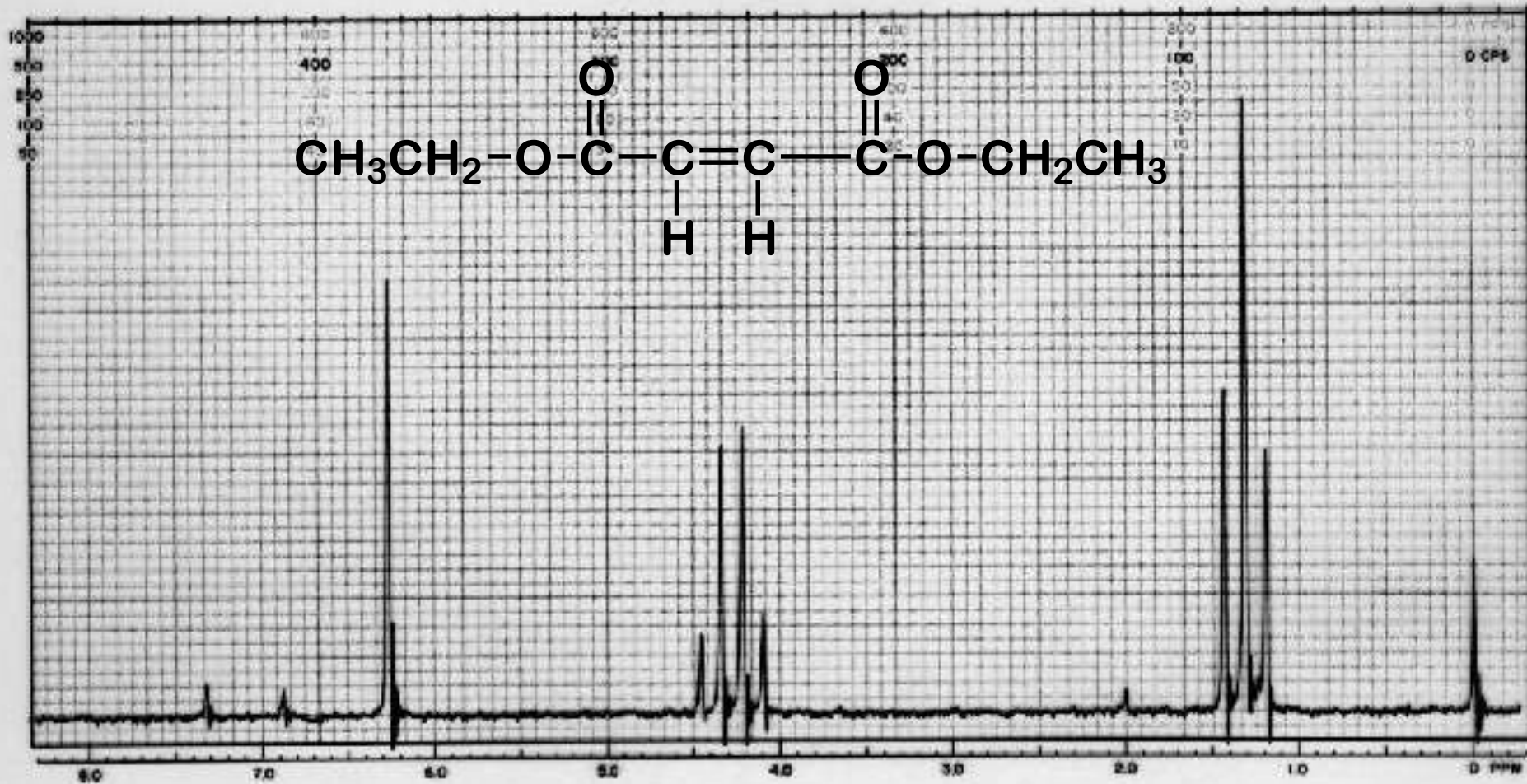
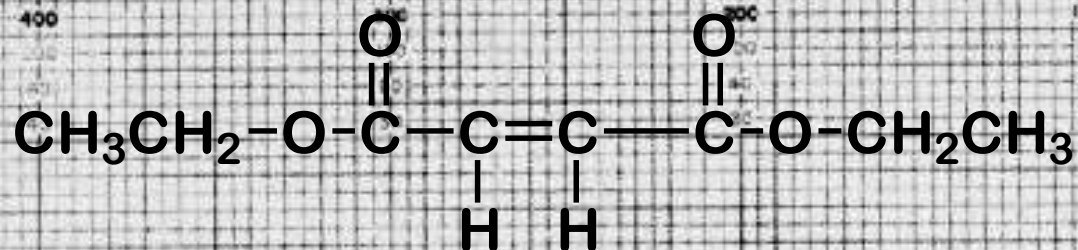
Phenylethyl Acetate



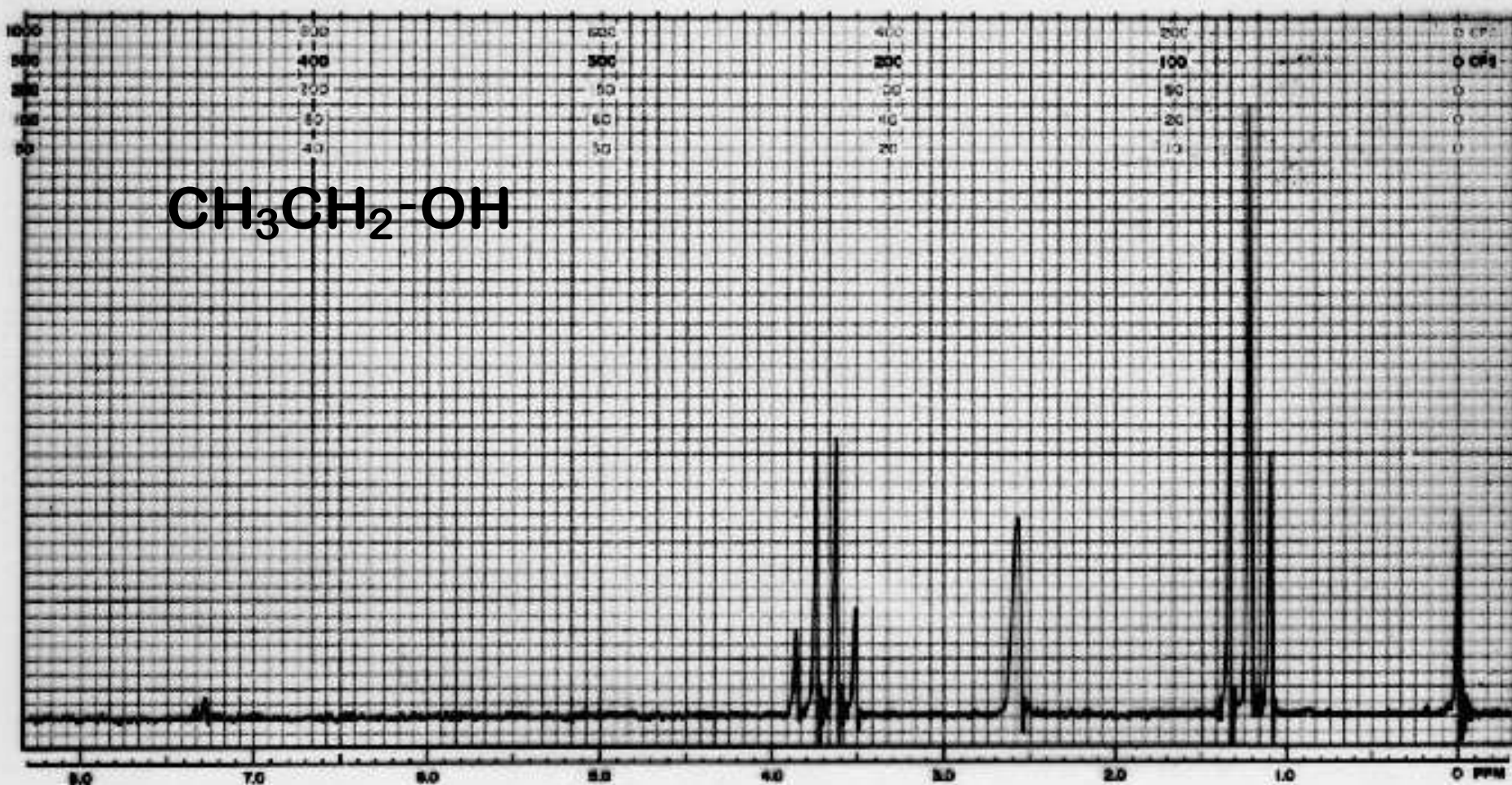
Ethyl Succinate



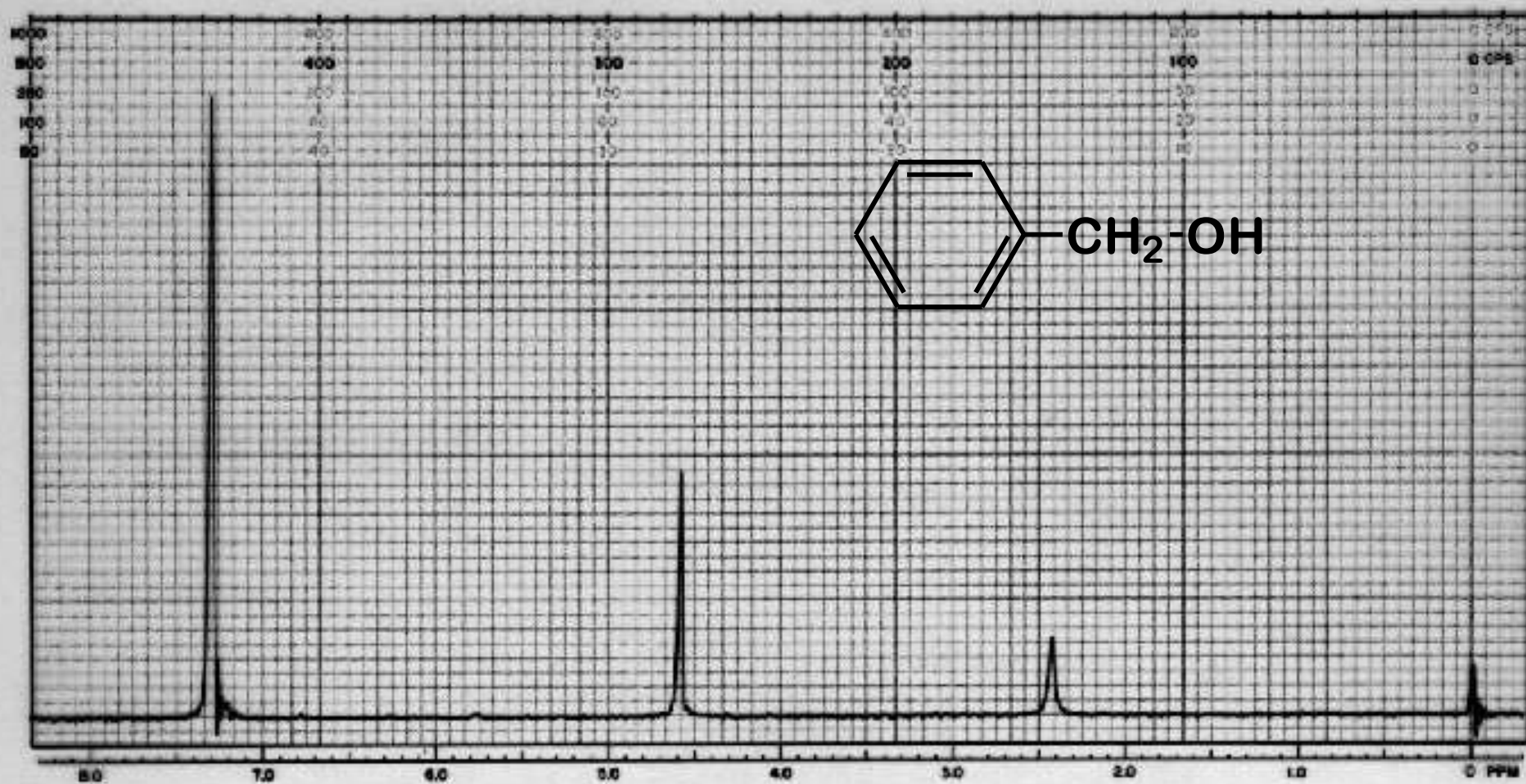
Diethyl Maleate



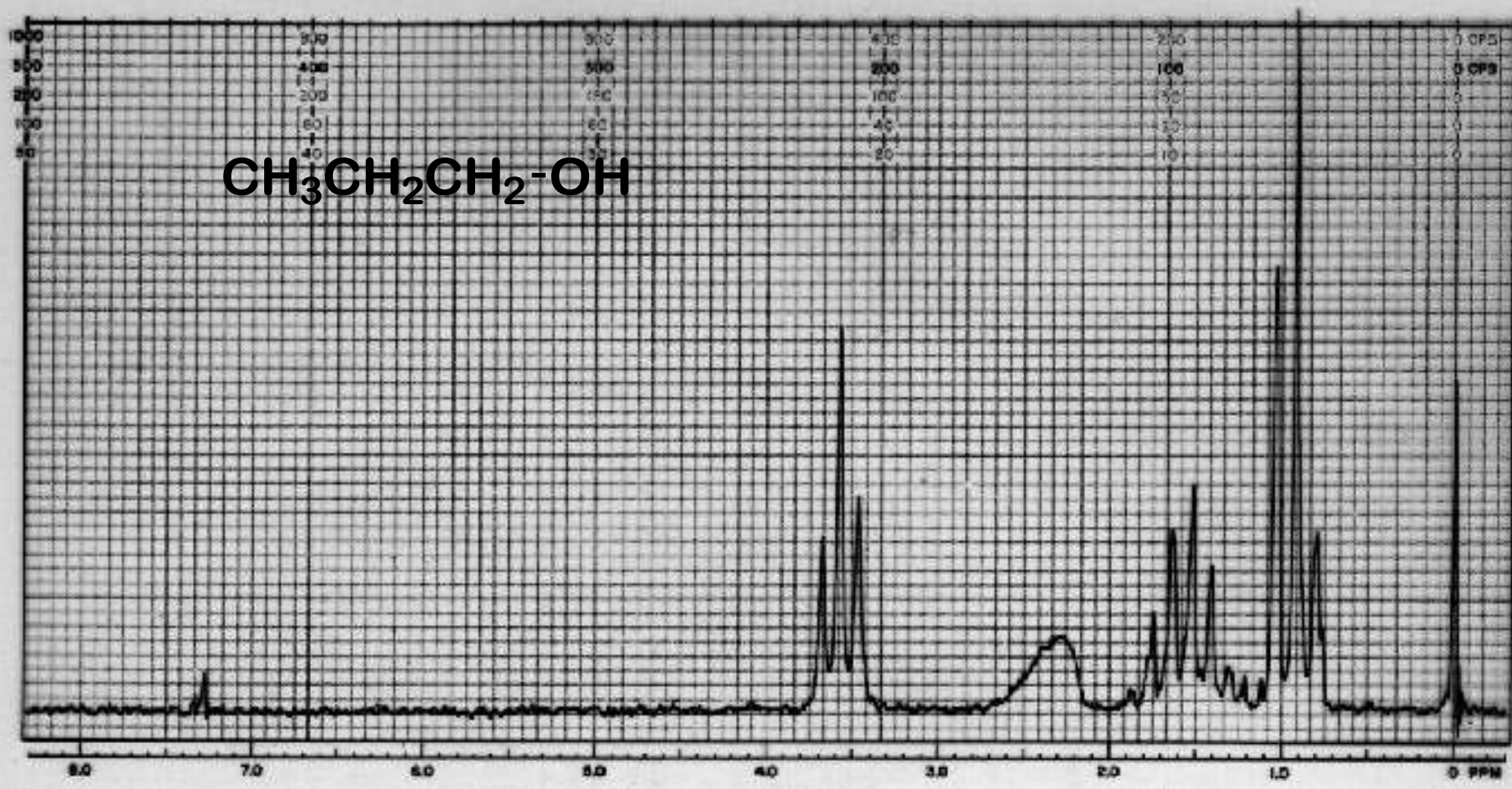
Ethanol



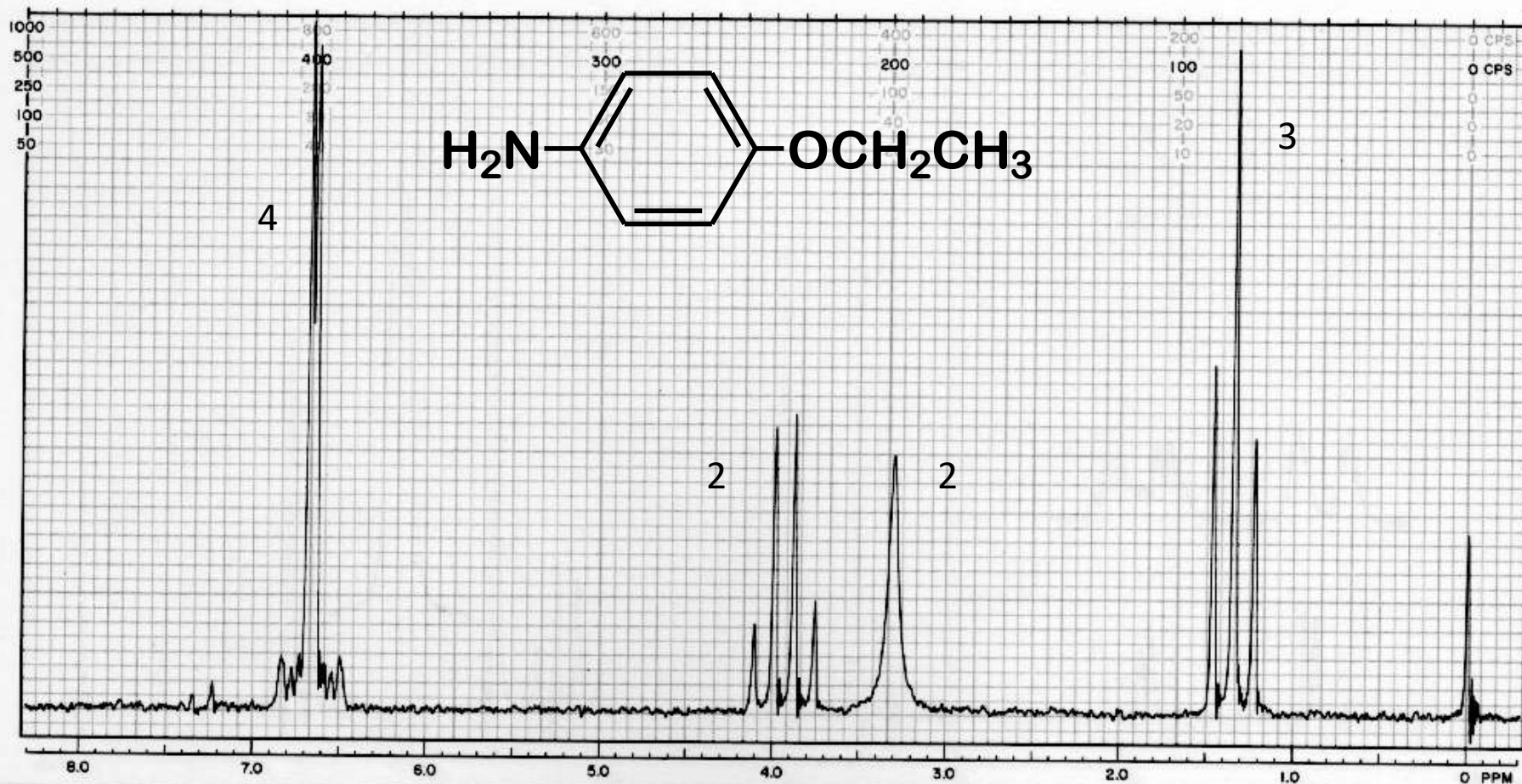
Benzyl Alcohol



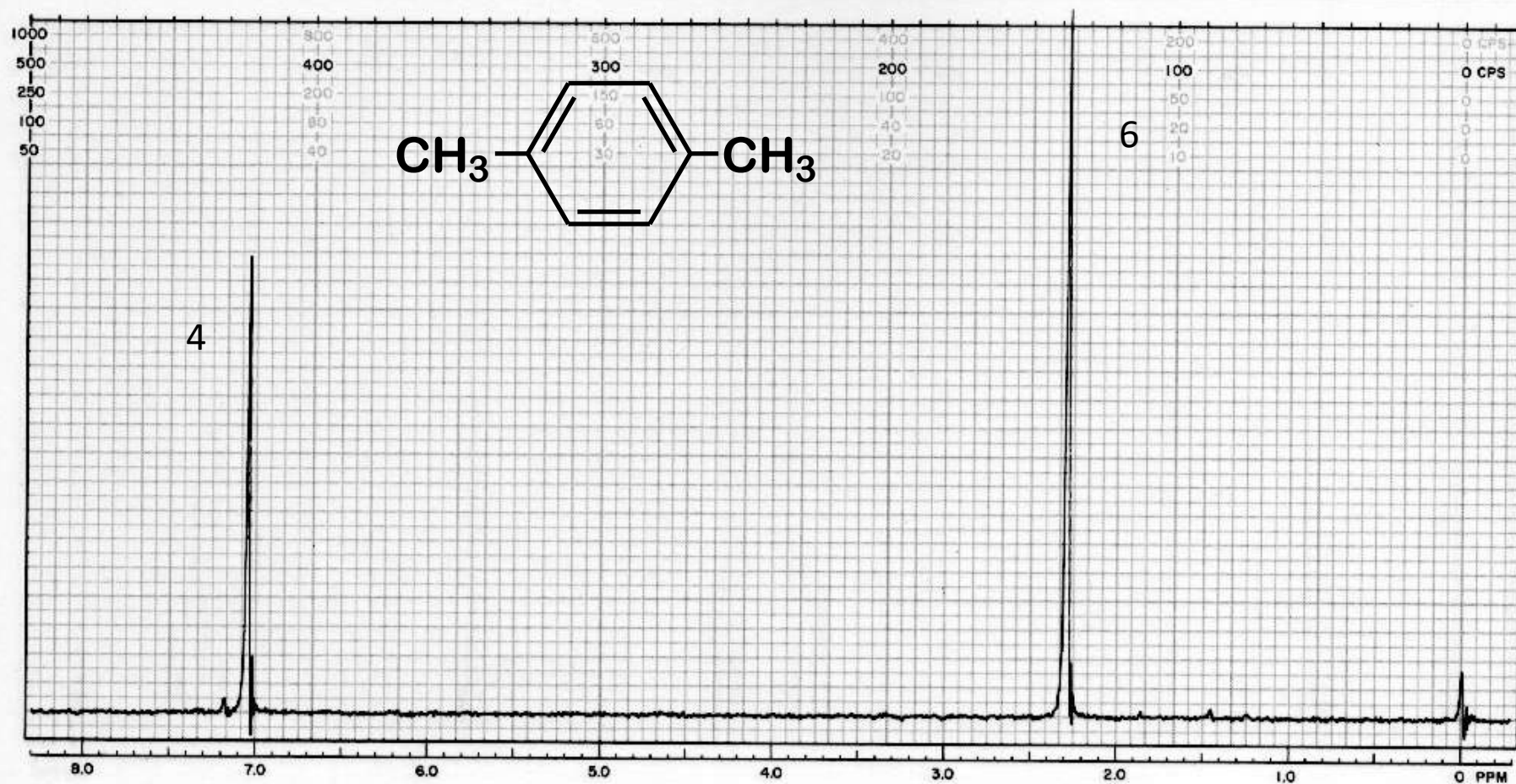
n-Propyl Alcohol



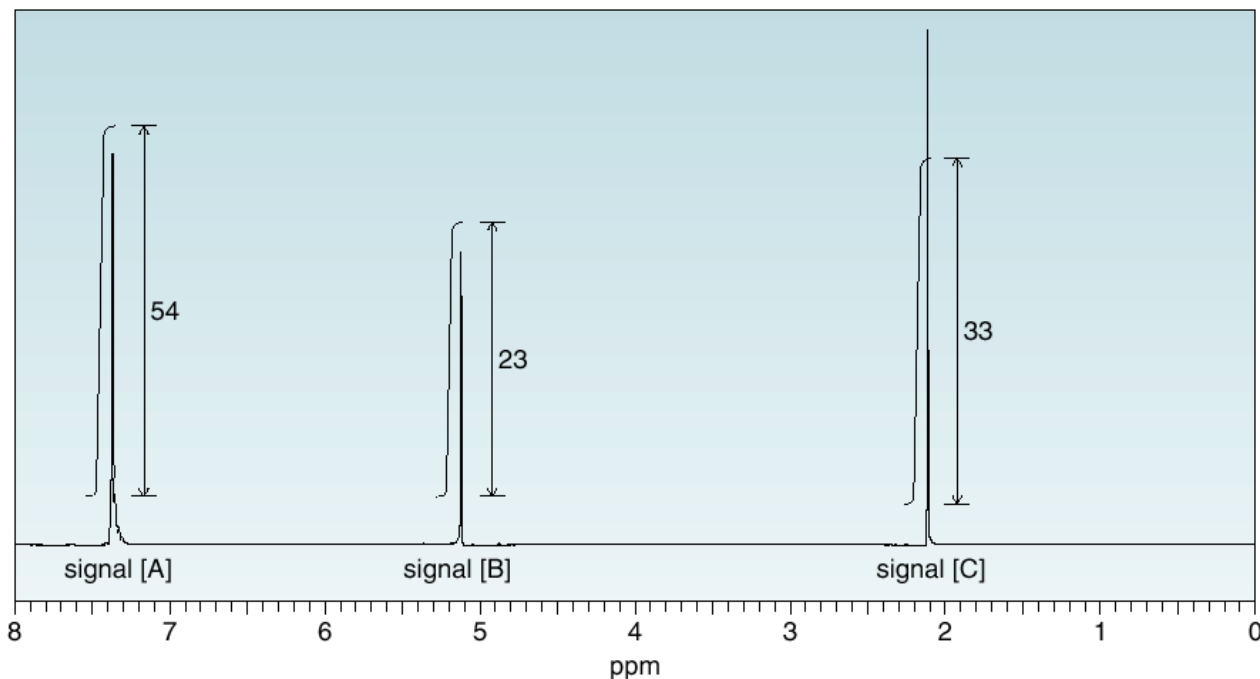
NMR Spectrum of 1-amino-4-ethoxybenzene



NMR Spectrum of *p*-Xylene (1,4-dimethylbenzene)



Example A compound of molecular formula $C_9H_{10}O_2$ gives the following integrated 1H NMR spectrum. How many protons give rise to each signal?



Step [1] Determine the number of integration units per proton by dividing the total number of integration units by the total number of protons.

- Total number of integration units: $54 + 23 + 33 = 110$ units
- Total number of protons = 10
- Divide: $110 \text{ units} / 10 \text{ protons} = \mathbf{11 \text{ units per proton}}$

Step [2] Determine the number of protons giving rise to each signal.

- To determine the number of H atoms giving rise to each signal, divide each integration value by the answer of Step [1] and round to the nearest whole number.

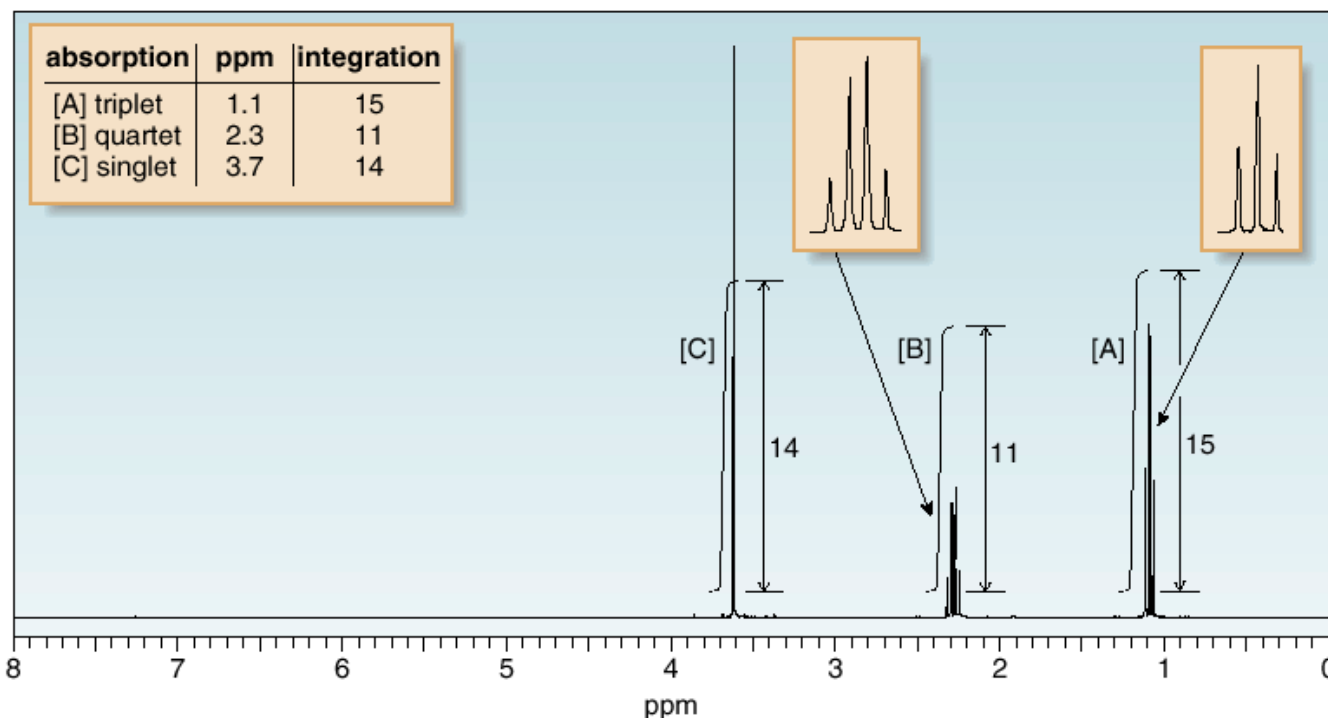
$$\text{Answer: } \frac{54}{11} = 4.9 \approx \mathbf{5 \text{ H}} \quad \left| \quad \frac{23}{11} = 2.1 \approx \mathbf{2 \text{ H}} \quad \left| \quad \frac{33}{11} = \mathbf{3 \text{ H}}$$

Nuclear Magnetic Resonance Spectroscopy

^1H NMR—Structure Determination

How To Use ^1H NMR Data to Determine a Structure

Example Using its ^1H NMR spectrum, determine the structure of an unknown compound X that has molecular formula $\text{C}_4\text{H}_8\text{O}_2$ and contains a $\text{C}=\text{O}$ absorption in its IR spectrum.



Step [1] Determine the number of different kinds of protons.

- The number of NMR signals equals the number of different types of protons.
- This molecule has three NMR signals ([A], [B], and [C]) and therefore **three** types of protons (H_a , H_b , and H_c).

Nuclear Magnetic Resonance Spectroscopy

^1H NMR—Structure Determination

How To, continued . . .

Step [2] Use the integration data to determine the number of H atoms giving rise to each signal (Section 14.5).

- Total number of integration units: $14 + 11 + 15 = 40$ units
- Total number of protons = 8
- Divide: $40 \text{ units} / 8 \text{ protons} = 5 \text{ units per proton}$
- Then, divide each integration value by this answer (5 units per proton) and round to the nearest whole number.

$$\frac{15}{5} = 3 \text{ H}_a \text{ protons}$$

signal [A]



Three equivalent H's usually means a CH_3 group.

$$\frac{11}{5} = 2.2 \approx 2 \text{ H}_b \text{ protons}$$

signal [B]



Two equivalent H's usually means a CH_2 group.

$$\frac{14}{5} = 2.8 \approx 3 \text{ H}_c \text{ protons}$$

signal [C]



Three equivalent H's usually means a CH_3 group.

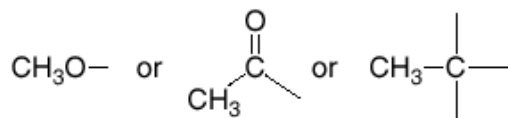
Nuclear Magnetic Resonance Spectroscopy

^1H NMR—Structure Determination

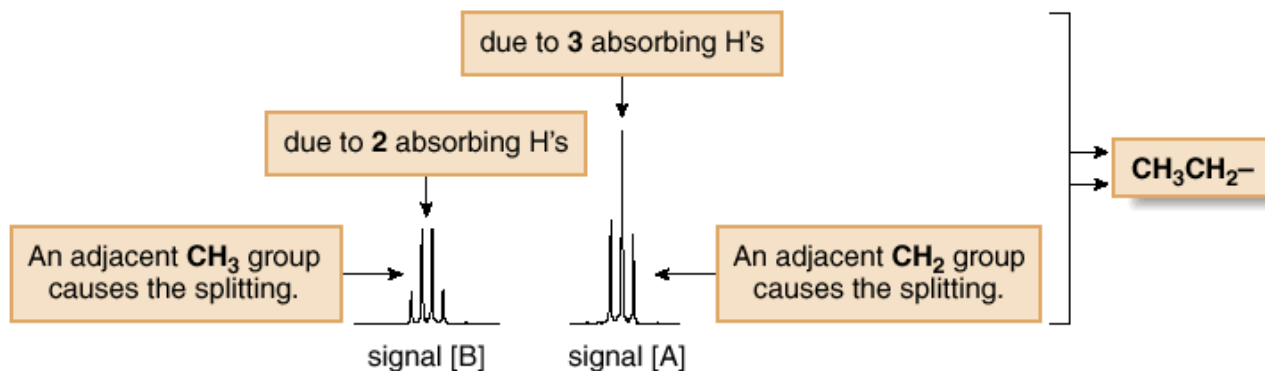
How To, continued . . .

Step [3] Use individual splitting patterns to determine what carbon atoms are bonded to each other.

- Start with the singlets. Signal [C] is due to a CH_3 group with no adjacent nonequivalent H atoms. Possible structures include:



- Because signal [A] is a **triplet**, there must be **2 H's** (CH_2 group) on the adjacent carbon.
- Because signal [B] is a **quartet**, there must be **3 H's** (CH_3 group) on the adjacent carbon.
- This information suggests that **X** has an **ethyl** group $\text{---} \rightarrow \text{CH}_3\text{CH}_2\text{---}$.



To summarize, **X** contains $\text{CH}_3\text{---}$, $\text{CH}_3\text{CH}_2\text{---}$, and $\text{C}=\text{O}$ (from the IR). Comparing these atoms with the molecular formula shows that one O atom is missing. Because O atoms do not absorb in a ^1H NMR spectrum, their presence can only be inferred by examining the chemical shift of protons near them. O atoms are more electronegative than C, thus deshielding nearby protons, and shifting their absorption downfield.

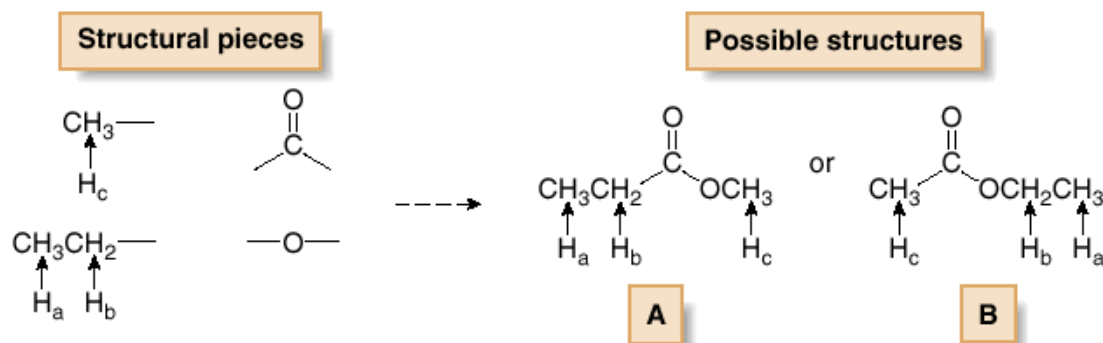
Nuclear Magnetic Resonance Spectroscopy

^1H NMR—Structure Determination

How To, continued . . .

Step [4] Use chemical shift data to complete the structure.

- Put the structure together in a manner that preserves the splitting data and is consistent with the reported chemical shifts.
- In this example, two isomeric structures (**A** and **B**) are possible for **X** considering the splitting data only:

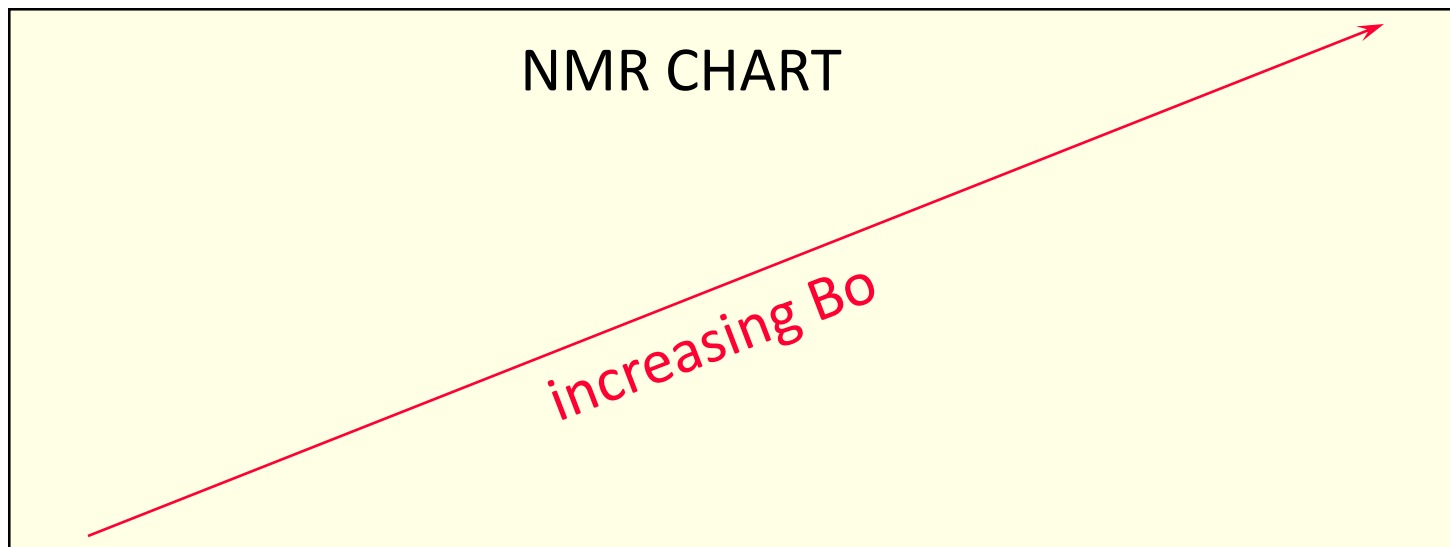


- Chemical shift information distinguishes the two possibilities. The electronegative O atom deshields adjacent H's, shifting them downfield between 3 and 4 ppm. If **A** is the correct structure, the singlet due to the CH_3 group (H_c) should occur downfield, whereas if **B** is the correct structure, the quartet due to the CH_2 group (H_b) should occur downfield.
- Because the NMR of **X** has a singlet (not a quartet) at 3.7, **A is the correct structure**.

IN THE CLASSICAL NMR EXPERIMENT THE INSTRUMENT
SCANS FROM “LOW FIELD” TO “HIGH FIELD”

LOW
FIELD

HIGH
FIELD



DOWNFIELD

UPFIELD



scan

Solvents used in PMR

- Carbon tetrachloride
- Carbon Disulphide
- Deuteriochloroform
- Hexachloroacetone

Characteristics of solvents:

- It should be chemically inert
- It should be devoid of hydrogen atom
- It should dissolve sample to reasonable extent (at least 10%)

Proton Exchange Reaction

- In a molecule, if a proton shuttles between two magnetic environments at a rate which is much faster in comparison with nmr coupling times , then the resonance observed for that proton will be simply that of average effective field in the two environments.
- Thus, only one resonance will be observed, although proton will shuttle between two different magnetic environments
- -OH proton in water has different chemical shift as compared to that –OH proton in acetic acid.

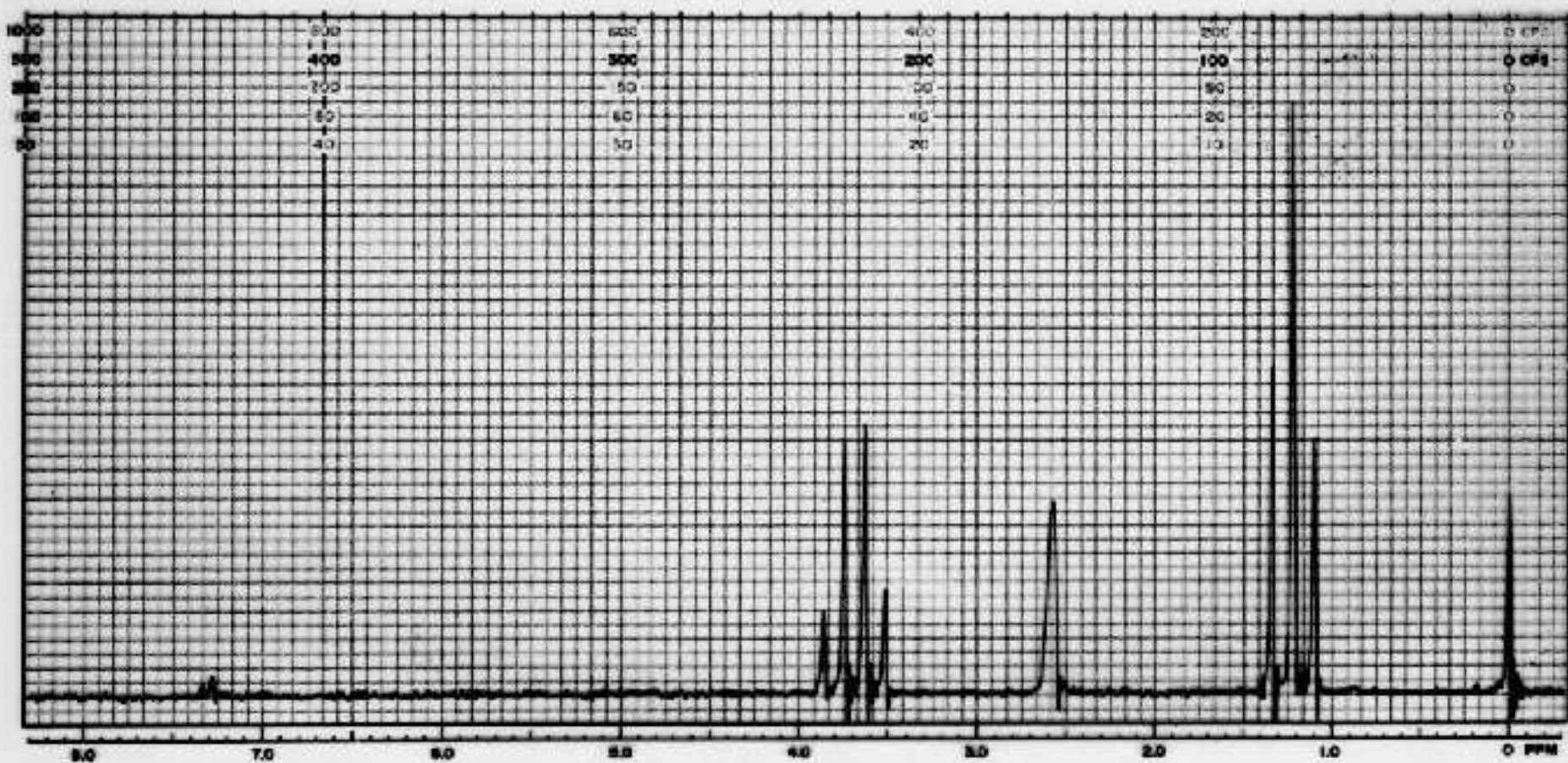
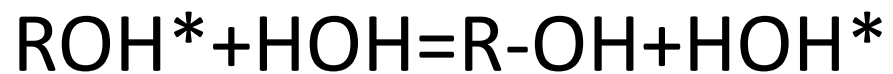
But one signal is seen in nmr spectrum for acetic acid in water at an average position according to following formula

$$N_a \delta_a + N_b \delta_b$$

N_a, N_b = mole fraction of proton a,b respectively

δ_a, δ_b = Chemical shift for unexchanged proton a,b.

Example : Ethanol vs. anhydrous Ethanol



Spin decoupling by double resonance

- Powerful tool for simplification of spectra in complex molecule
- This technique involves the irradiation of a proton or a group of equivalent protons with sufficiently intense radio frequency energy to eliminate completely the observed coupling due to the neighbouring protons.
- The rate of transition between energy states (spin state) becomes much faster, so that the life time of nucleus in any one spin state will be too short to resolve coupling with neighbouring proton

↓ (irradiate)



Triplet Sextet Triplet

Triplet Quartet

↓ (irradiate)



Singlet

Singlet

↓ (irradiate)

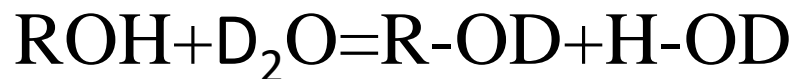


Triplet

Triplet

Deuterium Exchange Reaction

If a few drop of deuterium oxide are added in the sample, the D₂O exchanges with labile proton such as –OH, -NH, -SH.



The signal for –OH proton normally observed in ROH will be missing and instead ,a signal for proton in H-OD will appear.



This technique is employed for detecting the presence of -OH, -NH group etc.

Application of NMR spectroscopy

1. Identification of structural isomers
2. Detection of hydrogen bonding
3. Detection of aromaticity
4. Distinction between cis and trans isomer
5. Detection of electronegative atom/group
6. Detection of some double bond character due to resonance
7. Importance in quantitative analysis

$$\text{Amt. of drug} = \frac{\text{Area signal for drug protons}}{\text{Area signal for int. std. protons}} \times \text{mass of int. std. added} \times \frac{\text{MW drug}}{\text{MW int.std.}} \times \frac{\text{No. protons from int. std.}}{\text{No. protons from drug}}$$

Types of information from the NMR spectrum

1. Each different type of hydrogen gives a peak or group of peaks (multiplet).
2. The chemical shift (δ , in ppm) gives a clue as to the type of hydrogen generating the peak (alkane, alkene, benzene, aldehyde, etc.)
3. The integral gives the relative numbers of each type of hydrogen.
4. Spin-spin splitting gives the number of hydrogens on adjacent carbons.
5. The coupling constant J also gives information about the arrangement of the atoms involved.

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