تشخيص المركبات بواسطه طيف الرنين النووي للبرتون H-NMR

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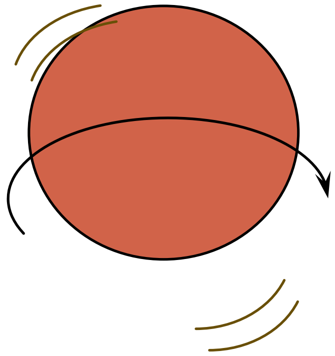
Introduction

- NMR is the most powerful tool available for organic structure determination.

- It is used to study a wide variety of nuclei:
  - ^{1}H
  - ^{13}C
  - ^{15}N
  - ^{19}F
  - ^{31}P

Nuclear Spin

The nuclei of some atoms have a property called “Spin”.



- Elements with either odd mass or odd atomic number have the property of nuclear “spin”.

- Each spin-active nucleus has a number of spins defined by its spin quantum number, **I**

- The number of spin states is 2**I** + 1

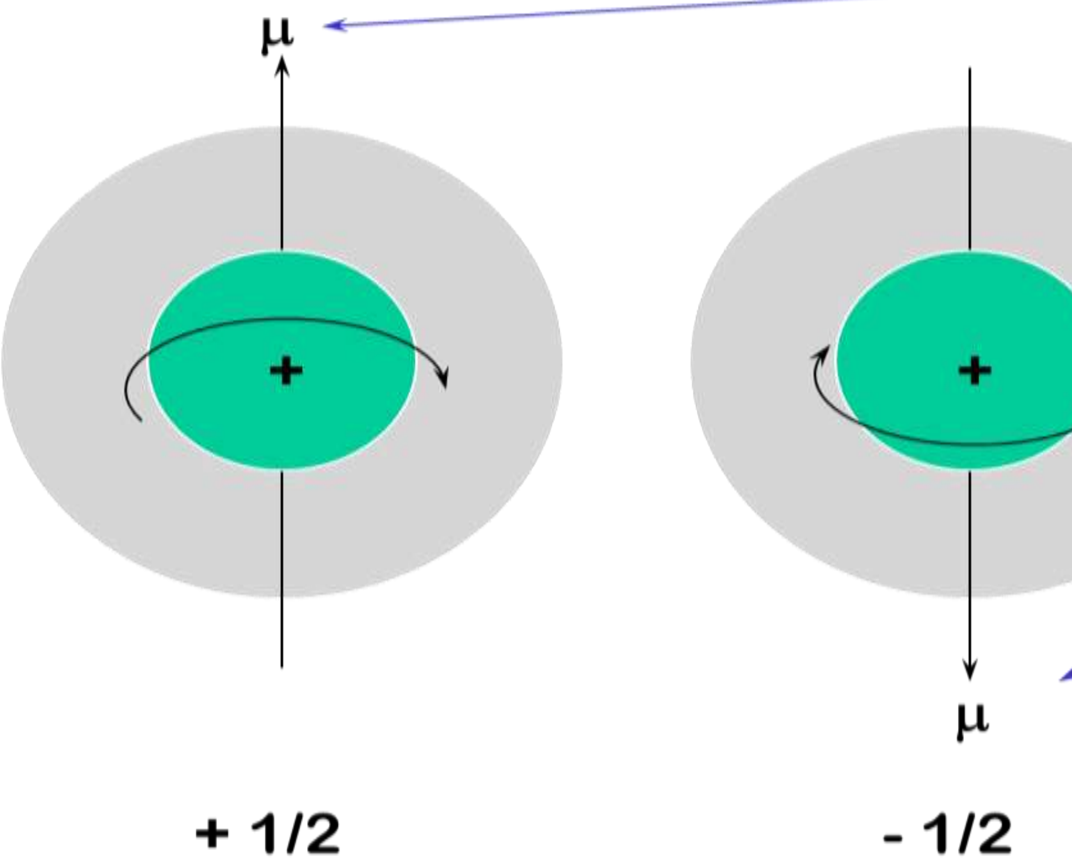
Spin Quantum Numbers of Some Common Nuclei

Mass No	**Atomic No**	**I**
Odd	Odd or Even	1/2 , 3/2, 5/2
Even	Even	0
Even	Odd	1 , 2 ,3

Element	**^{1}H**	**^{2}H**	**^{12}C**	**^{13}C**	**^{14}N**	**^{16}O**	**^{17}O**	**^{19}F**	**^{31}P**
Nuclear Spin Quantum No (I)	1/2	1	0	1/2	1	0	5/2	1/2	1/2
No. of Spin States	2	3	0	2	3	0	6	2	2

The Proton

Nuclear Spin States - Hydrogen Nucleus



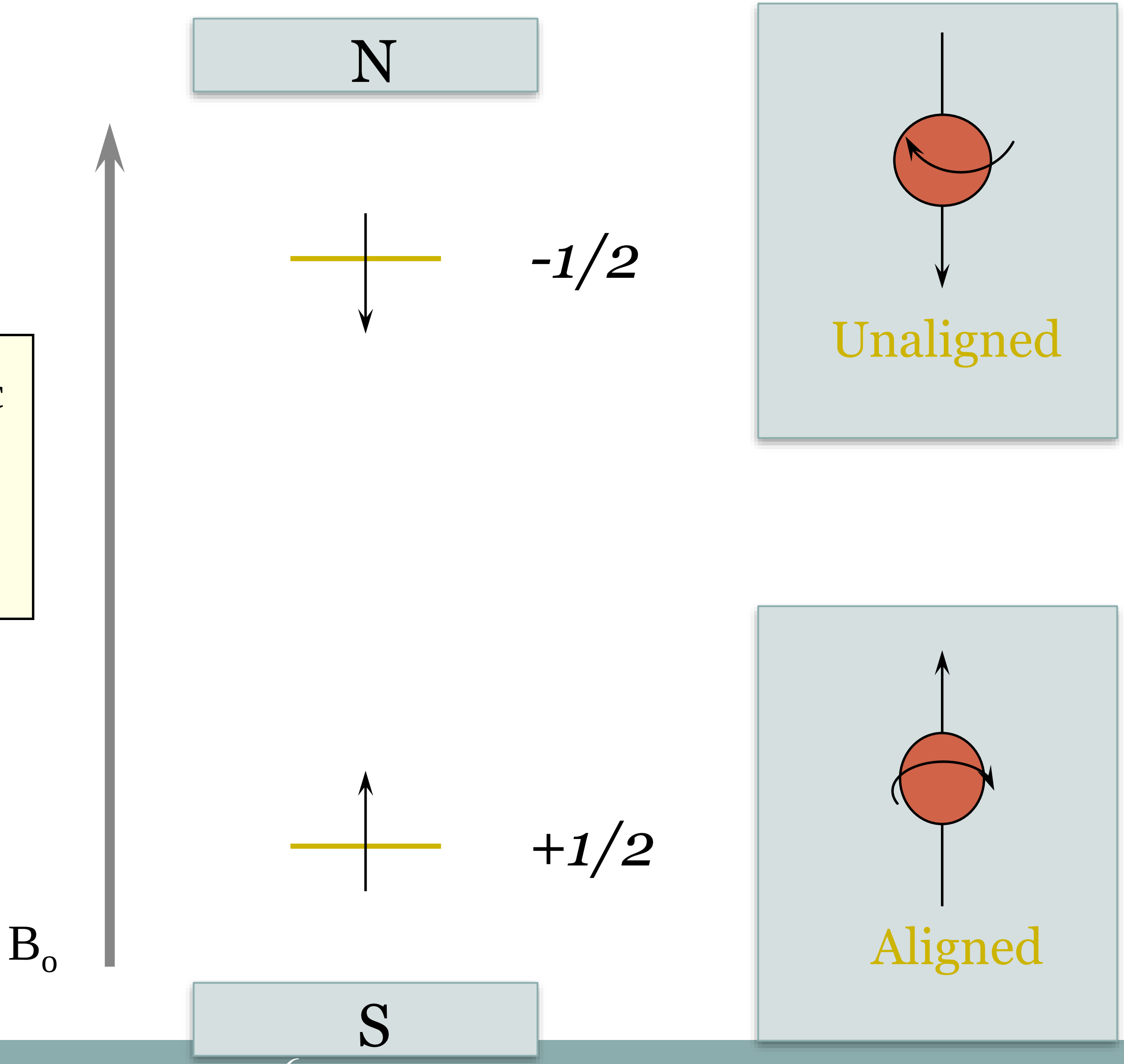
The spin of the positively charged nucleus generates a magnetic moment vector, μ.

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

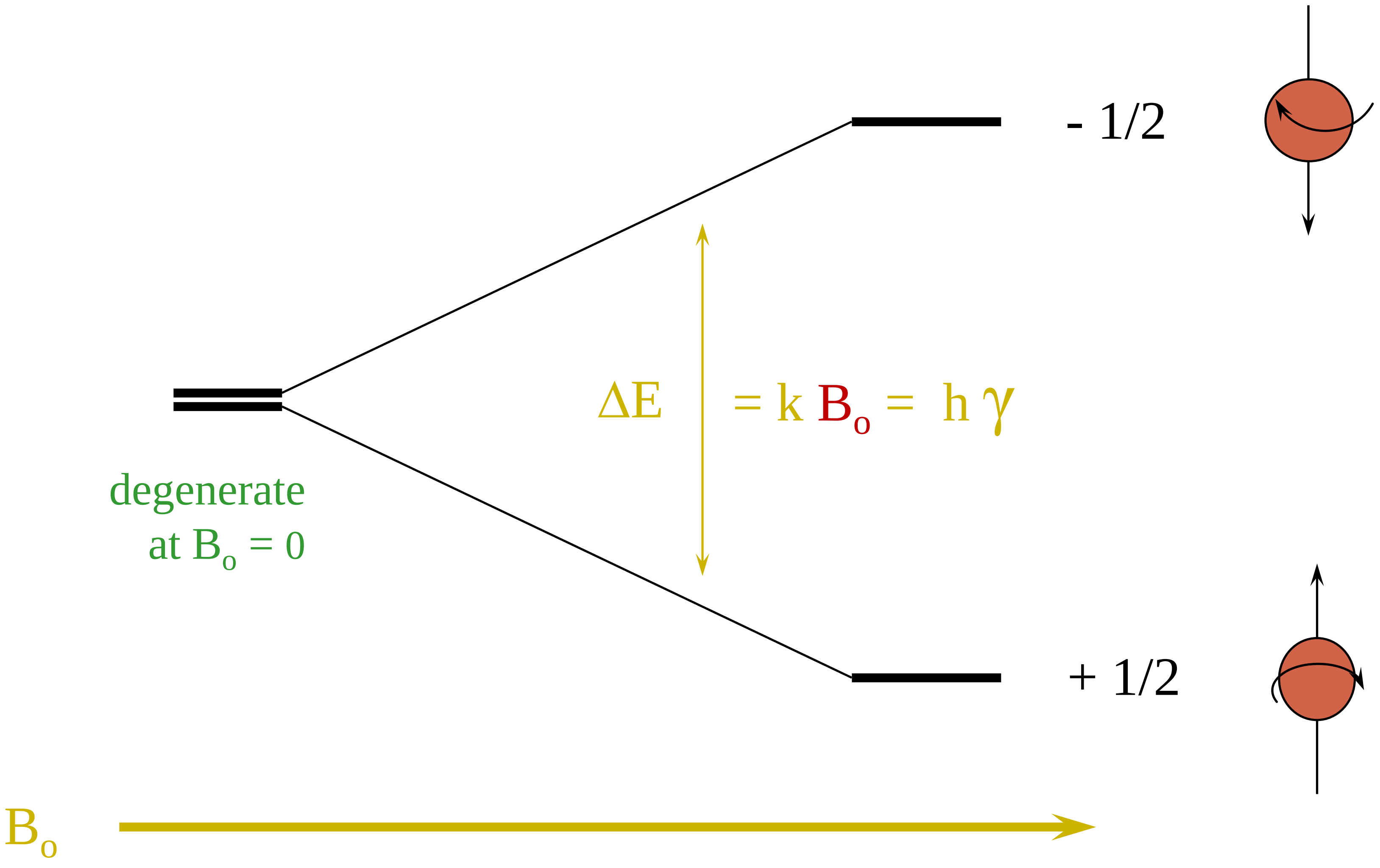
TWO SPIN STATES

Nuclear Spin Energy Levels

In a strong magnetic field (B_o) the two spin states differ in energy.



The Energy Separation Depends on B_o



$- 1/2$

$\Delta E = k B_o = h\gamma$

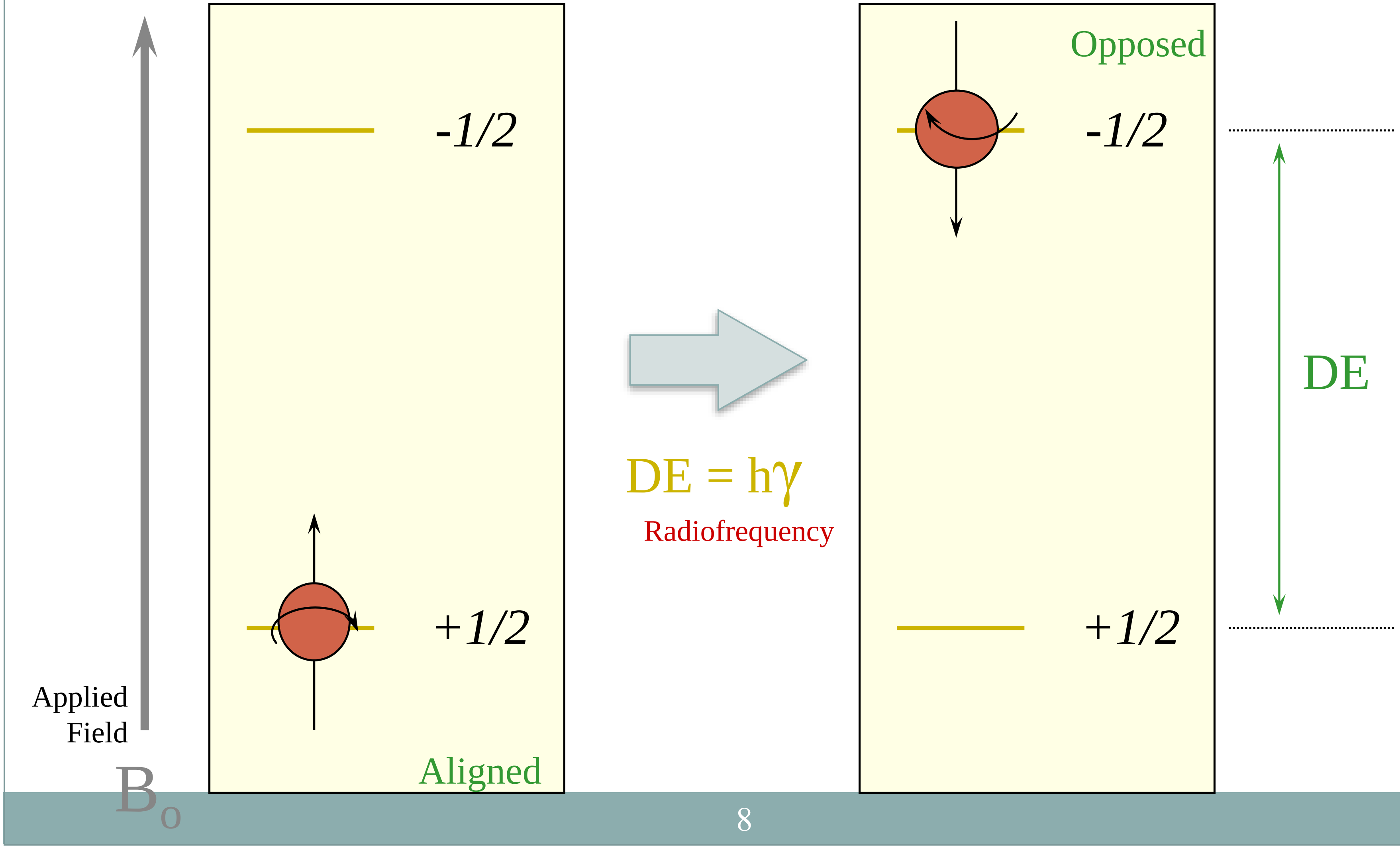
degenerate
at $B_o = 0$

$+ 1/2$

B_o

increasing magnetic field strength

Absorption of Energy



-1/2

+1/2

Aligned

Applied Field

B_o

DE = hγ

Radiofrequency

Opposed

-1/2

+1/2

DE

The Larmor Equation!!!

$\Delta E = kB_o = h\nu$ can be transformed into

$$\nu = \left(\frac{\gamma}{2\pi}\right) B_o$$

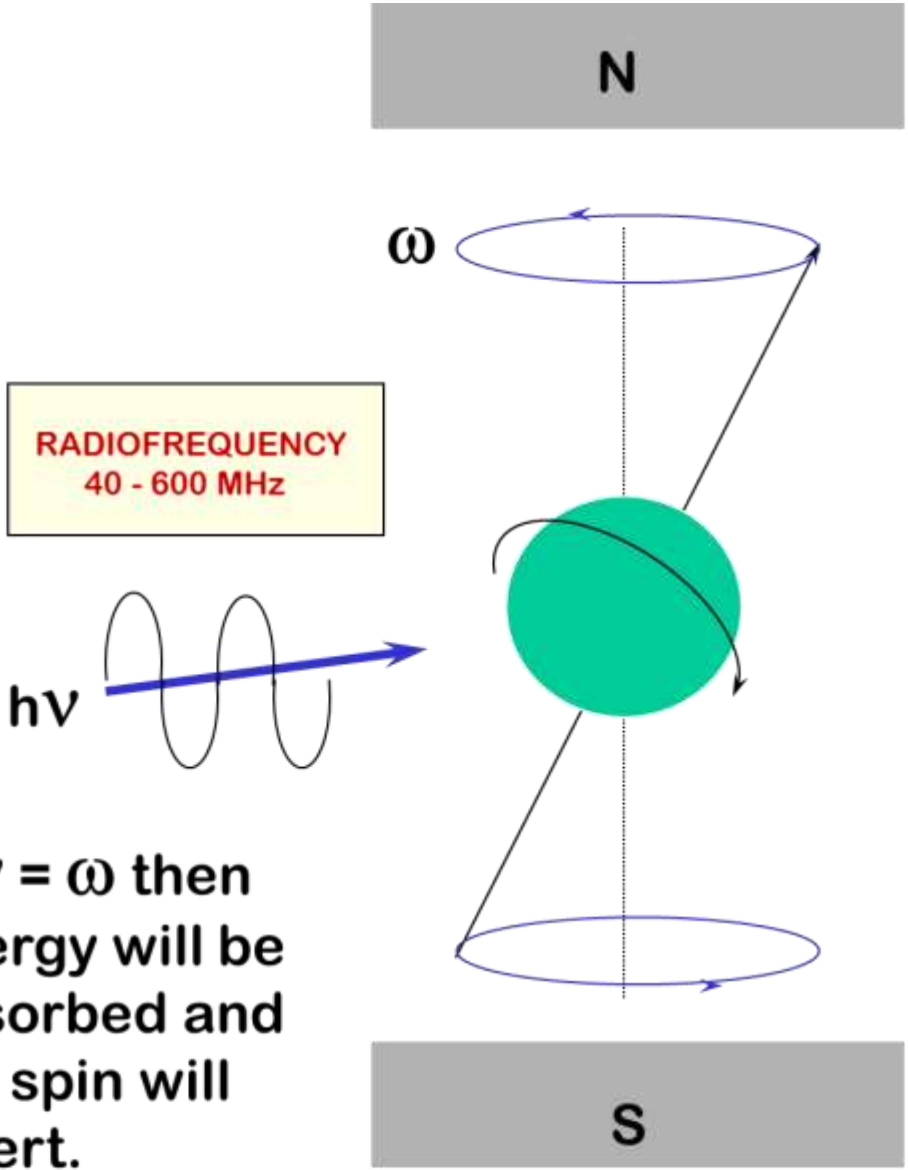
frequency of the incoming radiation that will cause a transition

gyromagnetic ratio γ

strength of the magnetic field

γ is a constant which is different for each atomic nucleus (H, C, N, etc)

The “Resonance” Phenomenon



RADIOFREQUENCY
40 - 600 MHz

Nuclei precess at frequency ω when placed in a strong magnetic field.

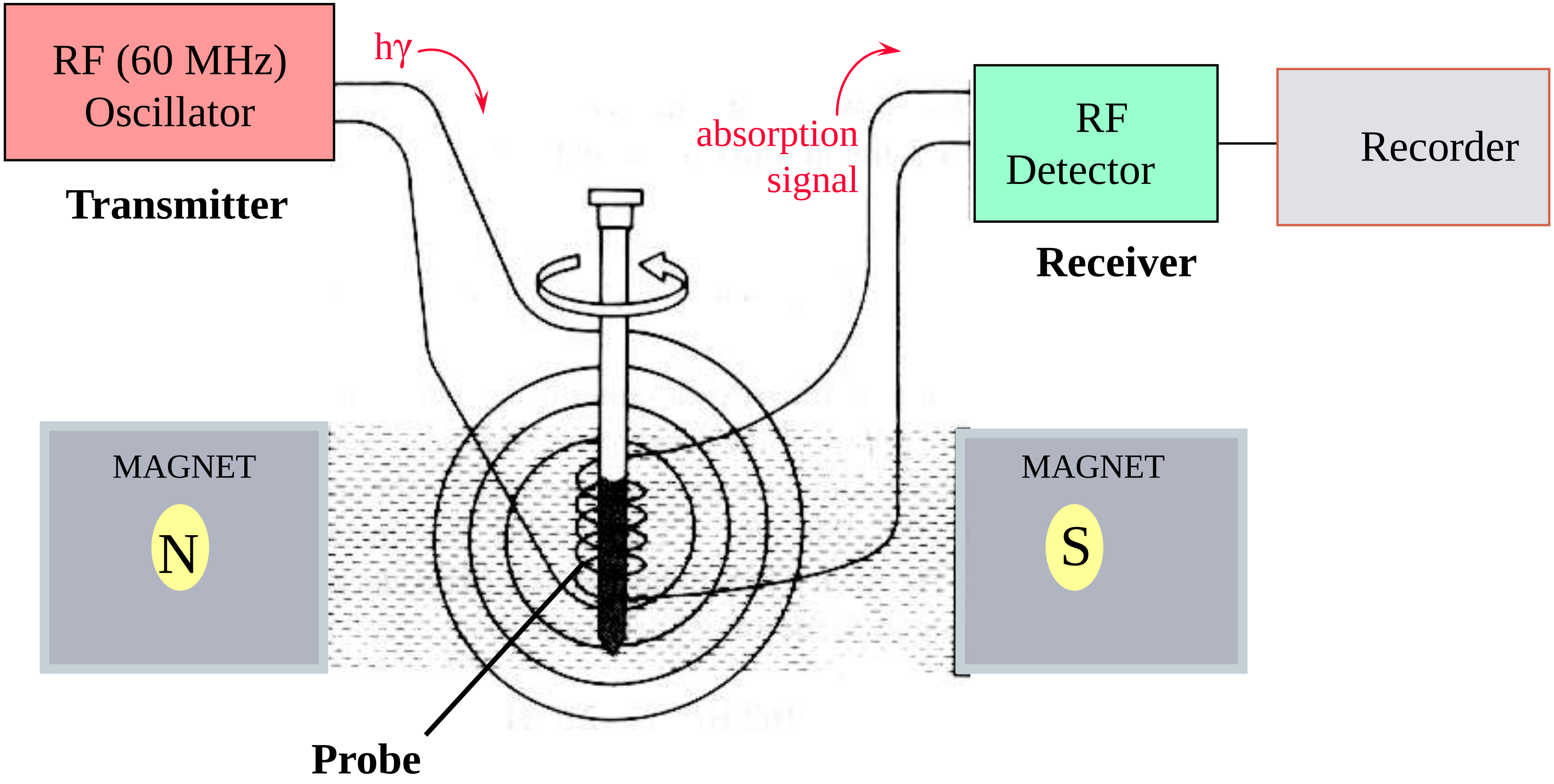
If ν = ω then energy will be absorbed and the spin will invert.

NUCLEAR MAGNETIC RESONANCE

NMR

NMR Spectrometers

1- The Continuous-Wave (CW) Instruments



RF (60 MHz) Oscillator

Transmitter

hγ

absorption signal

RF Detector

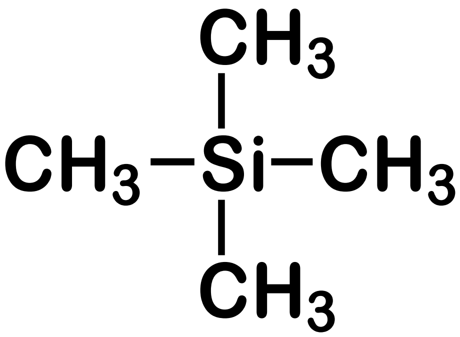
Receiver

Recorder

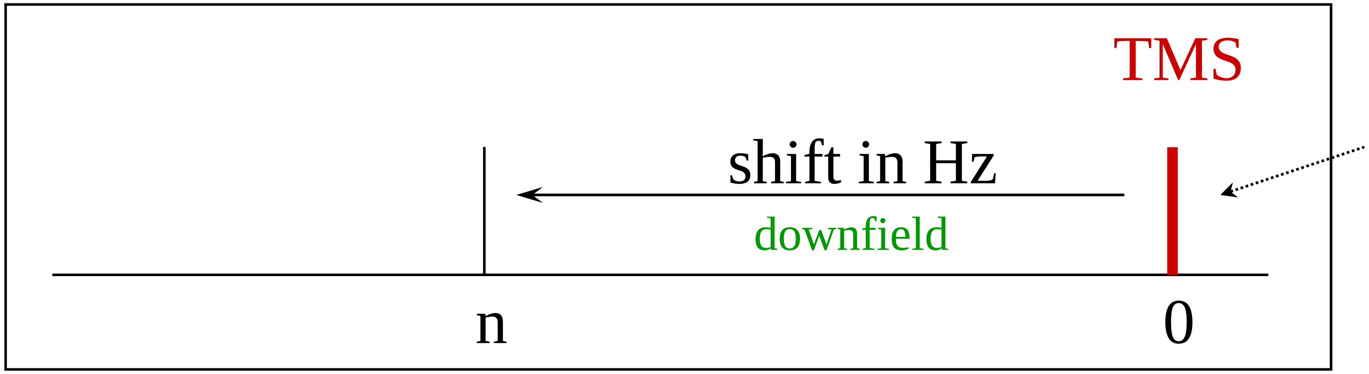
Probe

Peaks are Measured Relative to TMS (Tetramethylsilane)

Reference compound



$$CH_3-\underset{CH_3}{\overset{CH_3}{Si}}-CH_3$$



TMS

shift in Hz

downfield

n

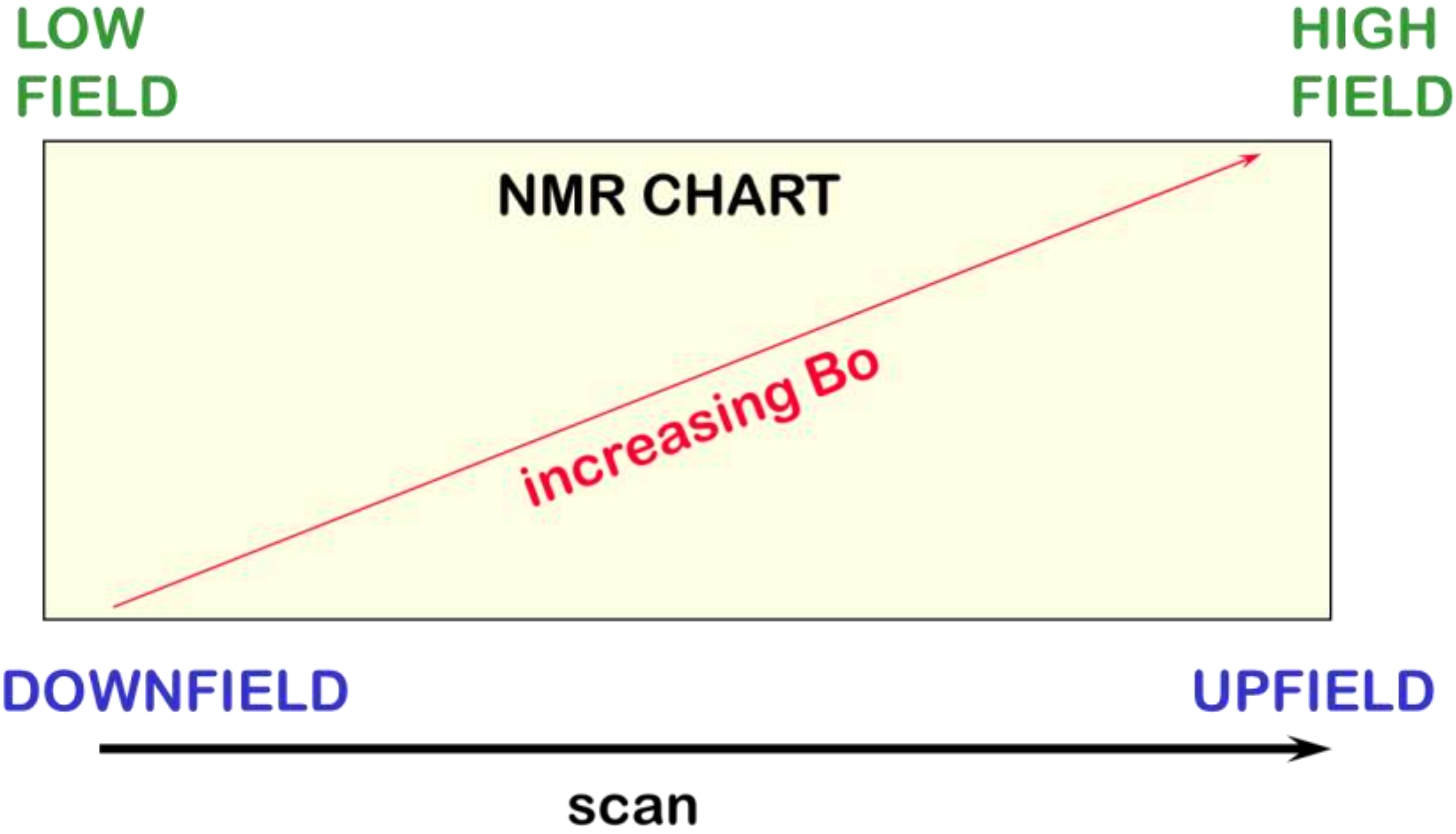
0

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

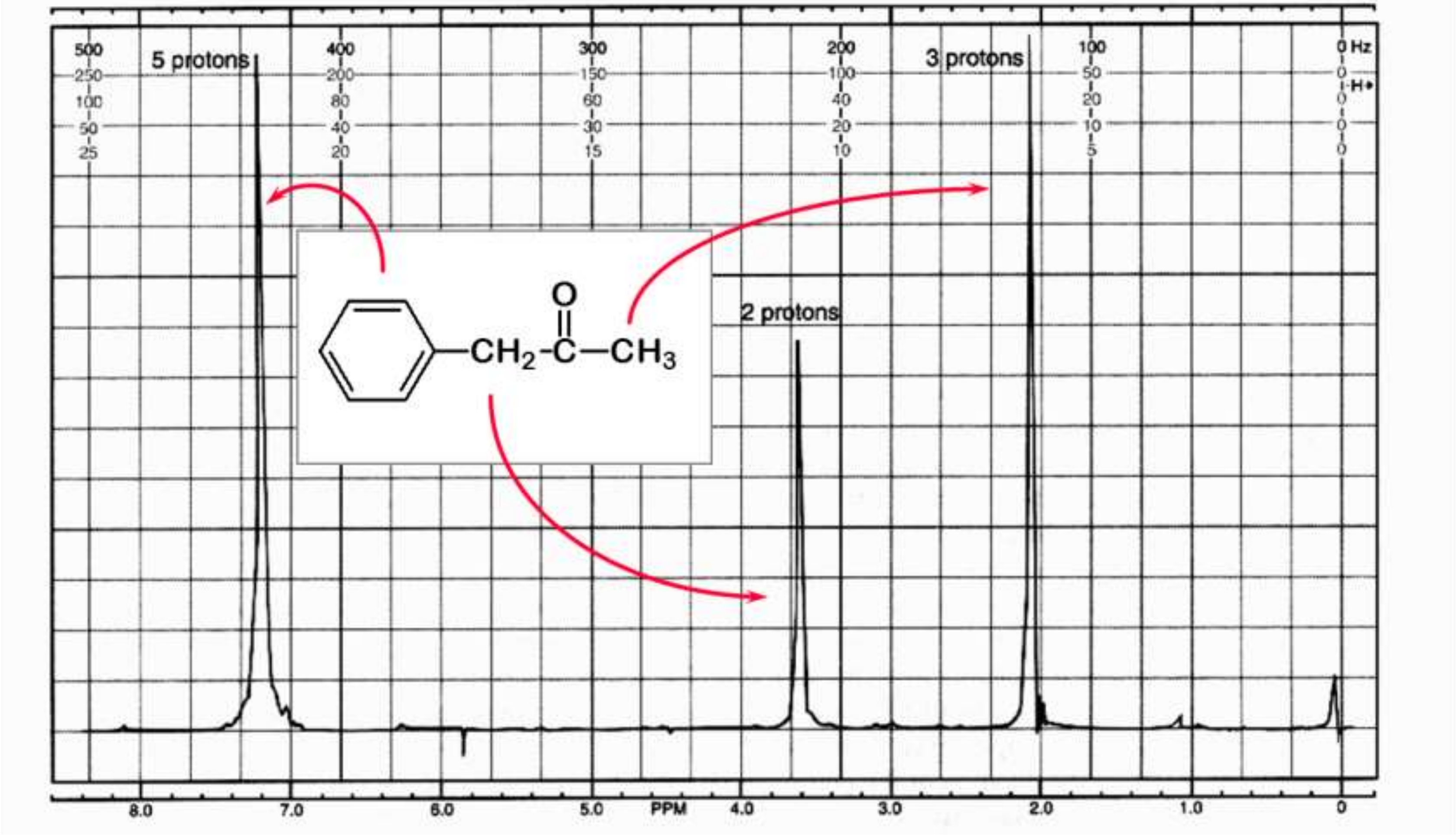
Solvents

Solvent		δ value
Tetrachlorocarbon	CCl_4	-
Carbon disulfide	CS_2	-
Acetone	$(CD_3)_2CO$	2.0
Dimethysulfoxide	$(CD_3)_2SO$	2.0
Acetonitrile	CD_3CN	2.0
Water	D_2O	5.0
Chloroform	$CDCl_3$	7.2
Benzene	C_6D_6	7.3

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



NMR Spectrum of Phenylacetone



NMR Spectrometers

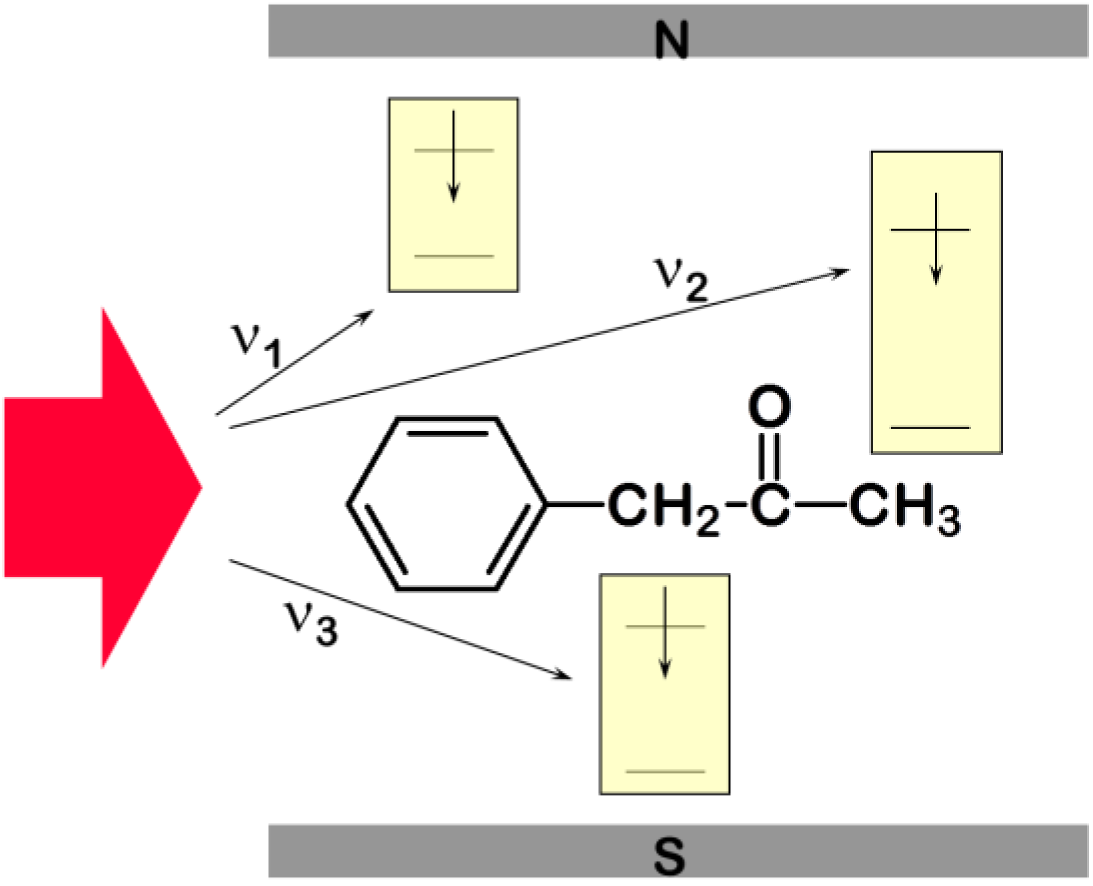
2- Fourier Transform (FT) Instruments

PULSED EXCITATION

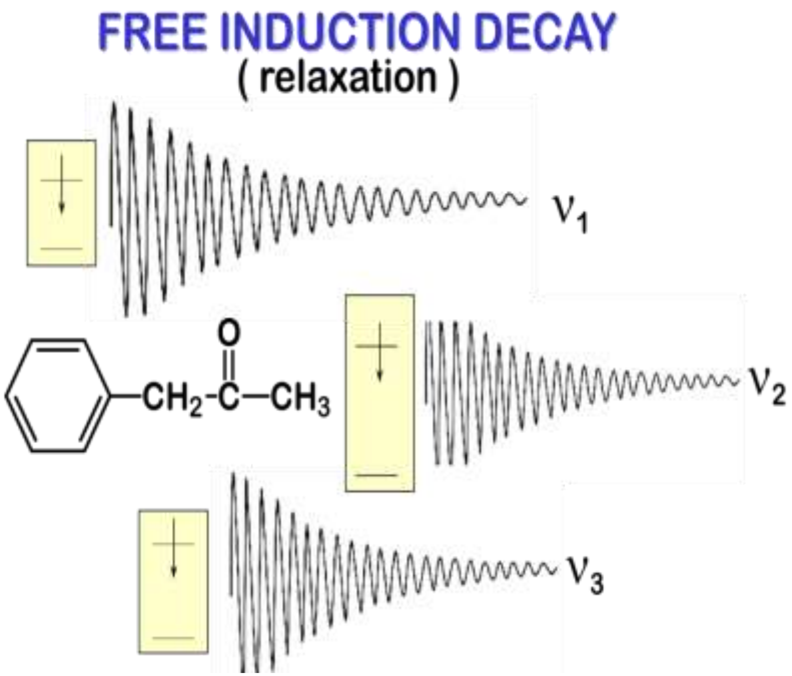
BROADBAND RF PULSE

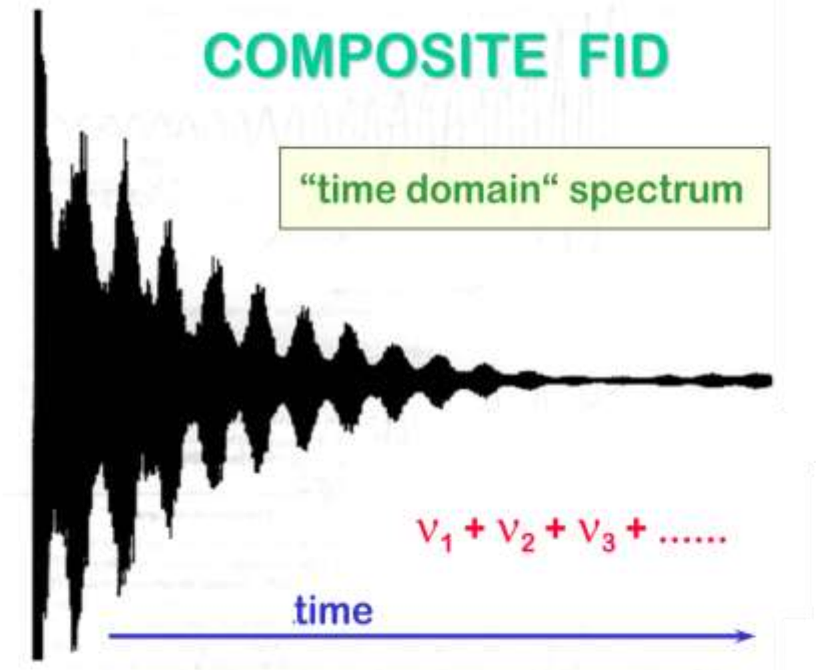
contains a range of frequencies

$(\nu_1 \ldots\ldots \nu_n)$



All types of hydrogen are excited simultaneously with the single RF pulse.





A mathematical technique that resolves a complex FID signal into the individual frequencies that add together to make it.

TIME DOMAIN converted to → **FREQUENCY DOMAIN**

FID — NMR SPECTRUM

DOMAINS ARE MATHEMATICAL TERMS

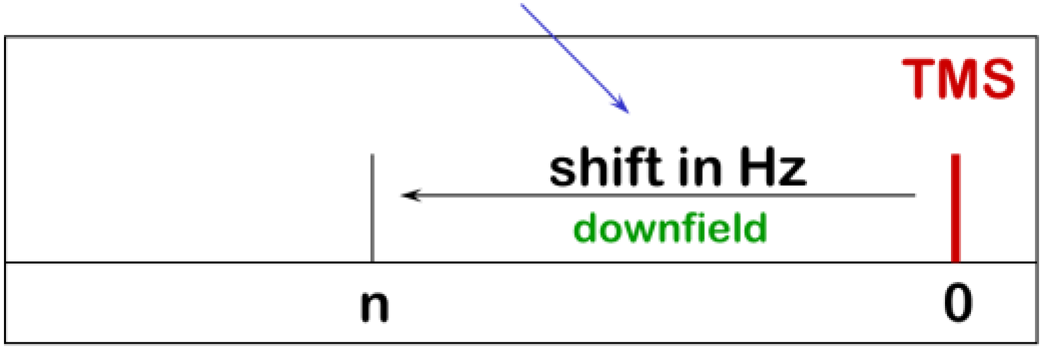
NMR—The Spectrum

There are three kinds each of which we will consider each of these separately:

- Position of Signals (Chemical shift)
- Integrations
- Coupling constant

1- Position of Signals (Chemical shift)

- The shift observed for a given proton in Hz also depends on the frequency of the instrument used.



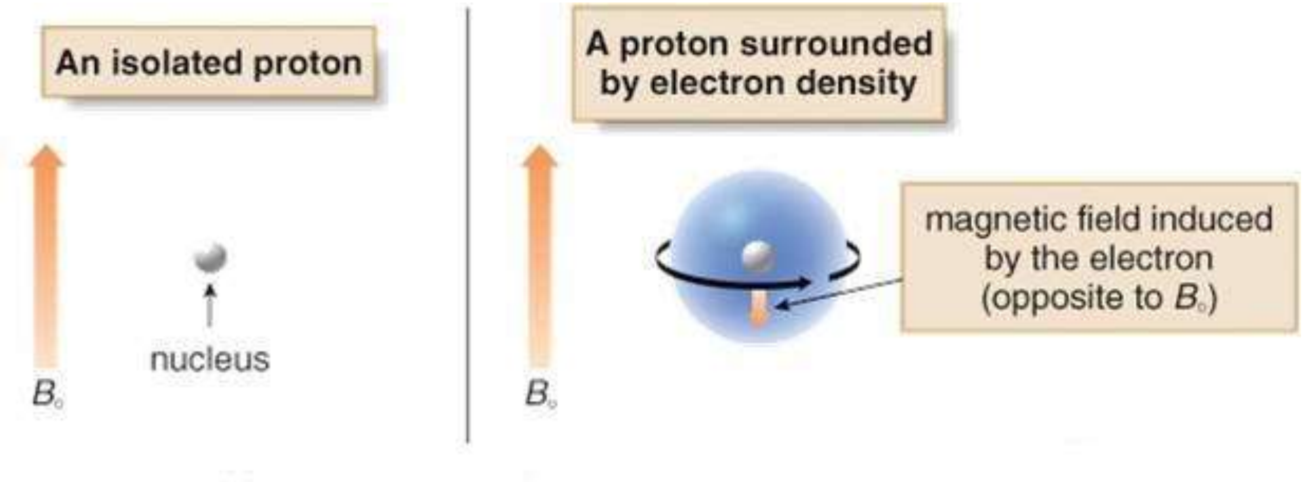
Higher frequencies = larger shifts in Hz.

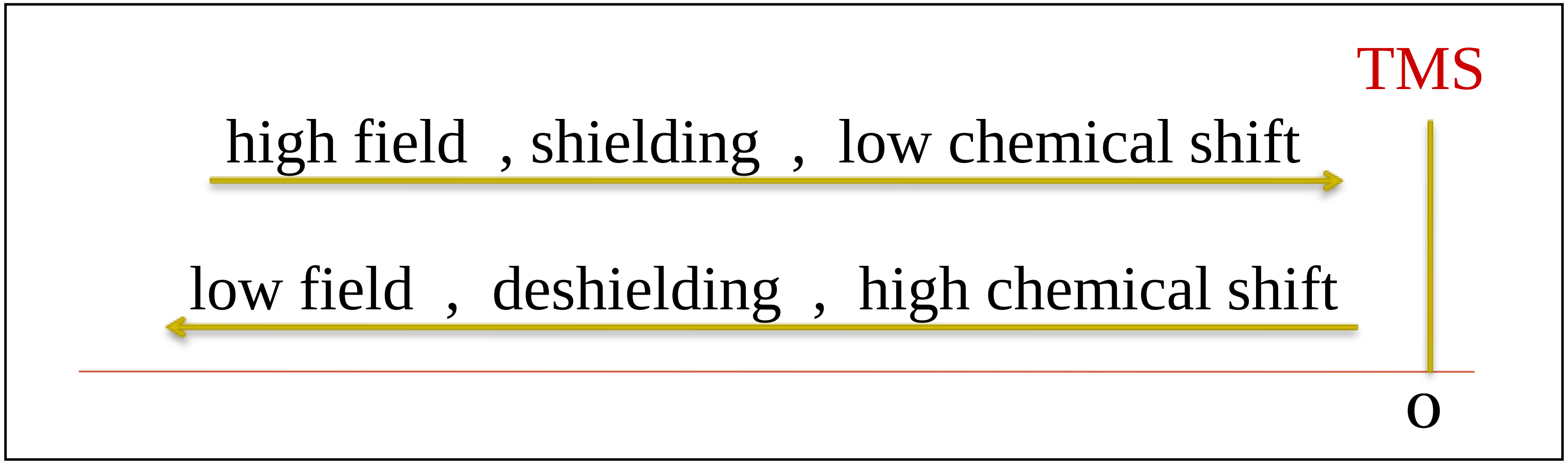
- We can adjust the shift to a field-independent value, the "chemical shift" in the following way:

$$\text{Chemical shift} = \delta = \frac{\text{shift in Hz}}{\text{spectrometer frequency in MHz}} = \textbf{ppm}$$

Protons Differ in Their Shielding

- All different types of protons in a molecule have a different amounts of shielding.
- They all respond differently to the applied magnetic field and appear at different places in the spectrum.
- This is why an NMR spectrum contains useful information (different types of protons appear in predictable places).





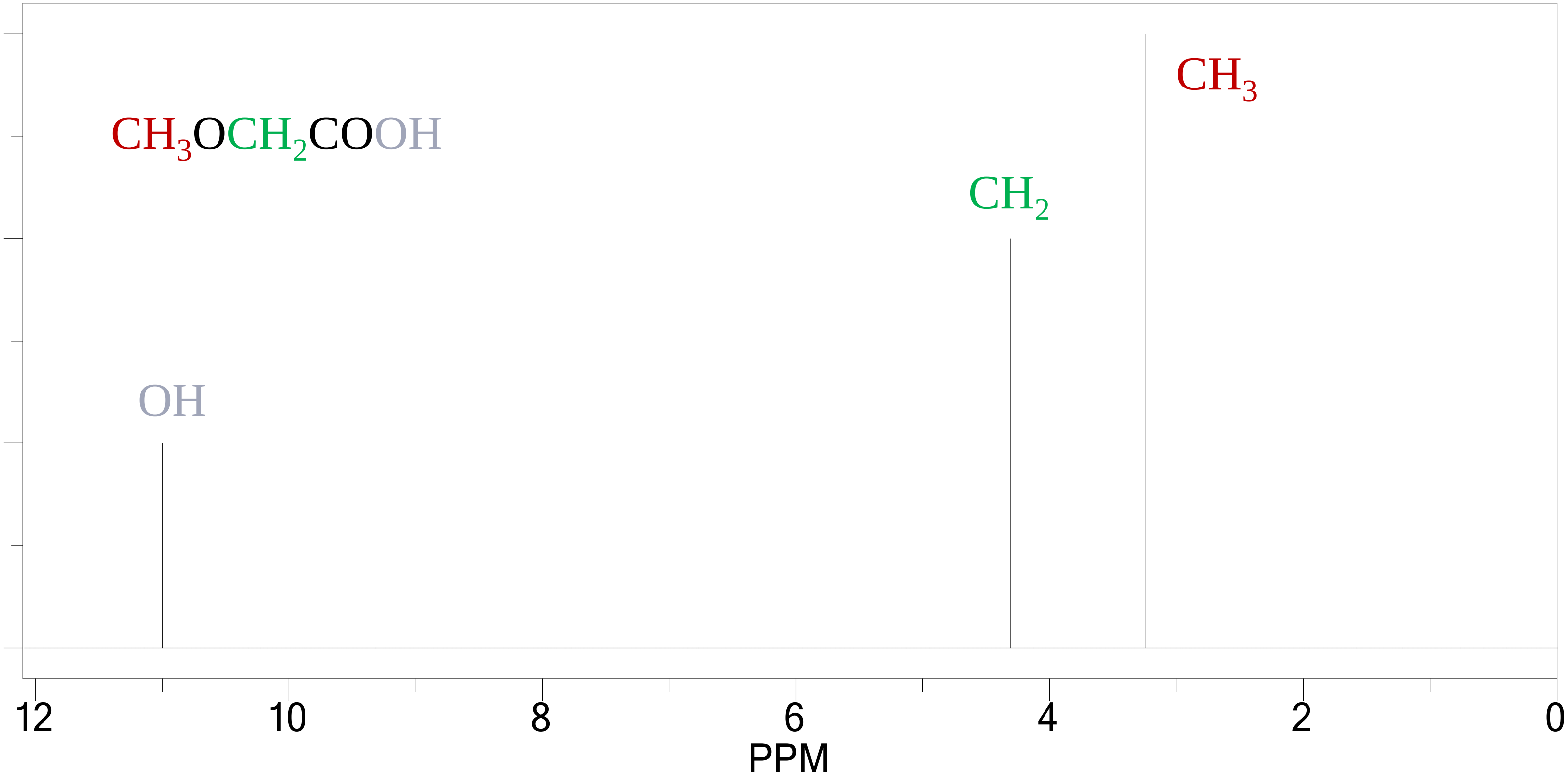
TMS

high field , shielding , low chemical shift

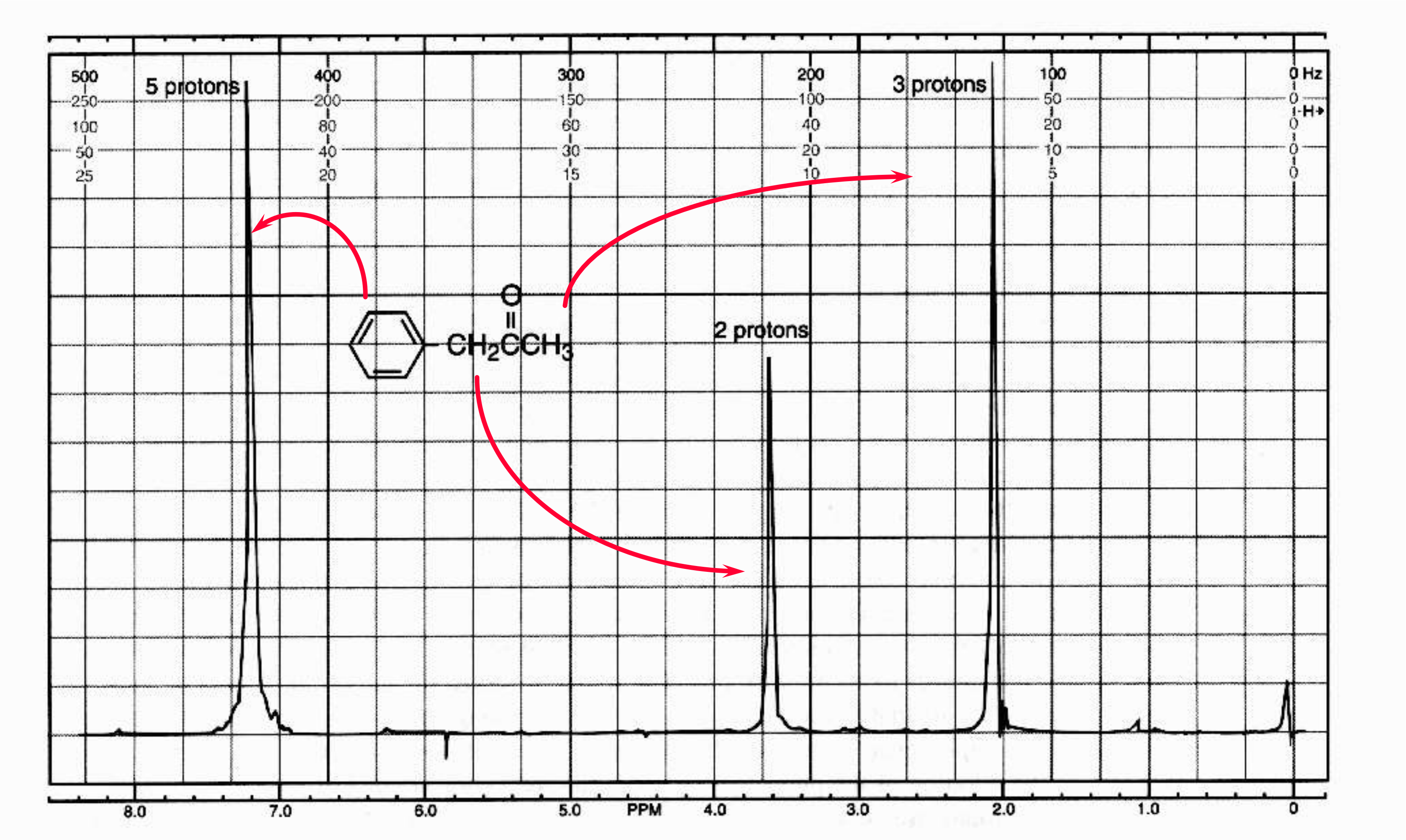
low field , deshielding , high chemical shift

0

NMR Spectrum of Methylacetic acid



NMR Spectrum of Phenylacetone

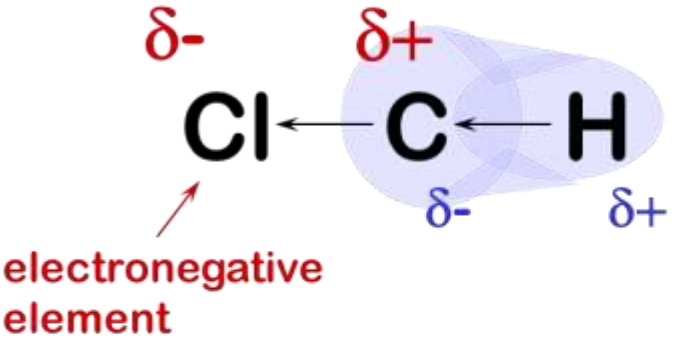


Factors Influencing Chemical Shifts

- Three major factors account for the resonance positions (on the ppm scale) of most protons.

1. Deshielding by electronegative elements.
2. Anisotropic fields usually due to pi-bonded electrons in the molecule.
3. Deshielding due to hydrogen bonding.

1. Deshielding by electronegative elements.



Chlorine “deshields” the proton, that is, it takes valence electron density away from carbon, which in turn takes more density from hydrogen deshielding the proton.

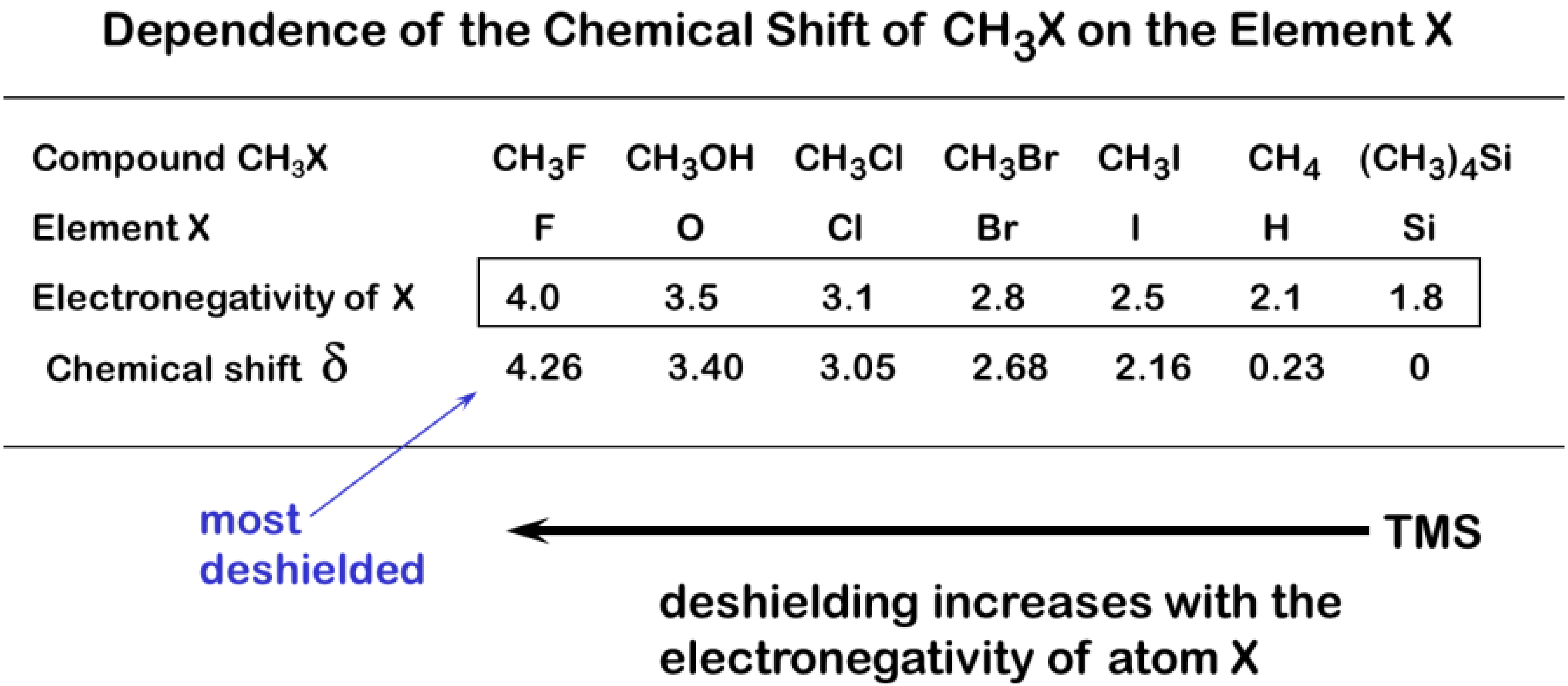
NMR CHART

“deshielded“ protons appear at low field

highly shielded protons appear at high field

deshielding moves proton resonance to lower field

Electronegativity Dependence of Chemical Shift



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	$(CH_3)_4Si$
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

deshielding increases with the electronegativity of atom X

Substitution Effects on Chemical Shift

most deshielded

$CHCl_3$	CH_2Cl_2	CH_3Cl	
7.27	5.30	3.05	ppm

The effect increases with greater numbers of electronegative atoms.

most deshielded

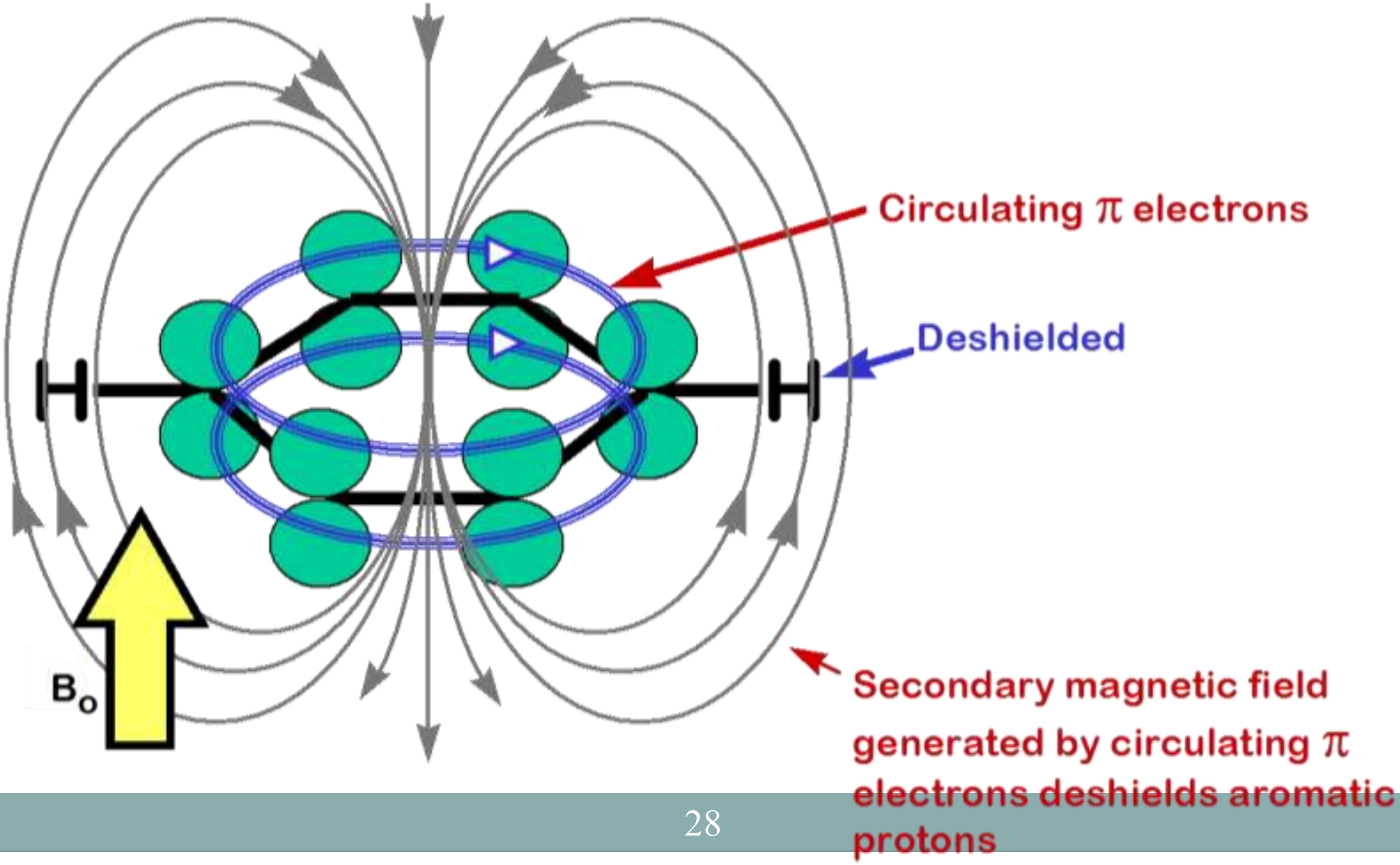
$-CH_2-Br$	$-CH_2-CH_2Br$	$-CH_2-CH_2CH_2Br$	
3.30	1.69	1.25	ppm

The effect decreases with incresing distance.

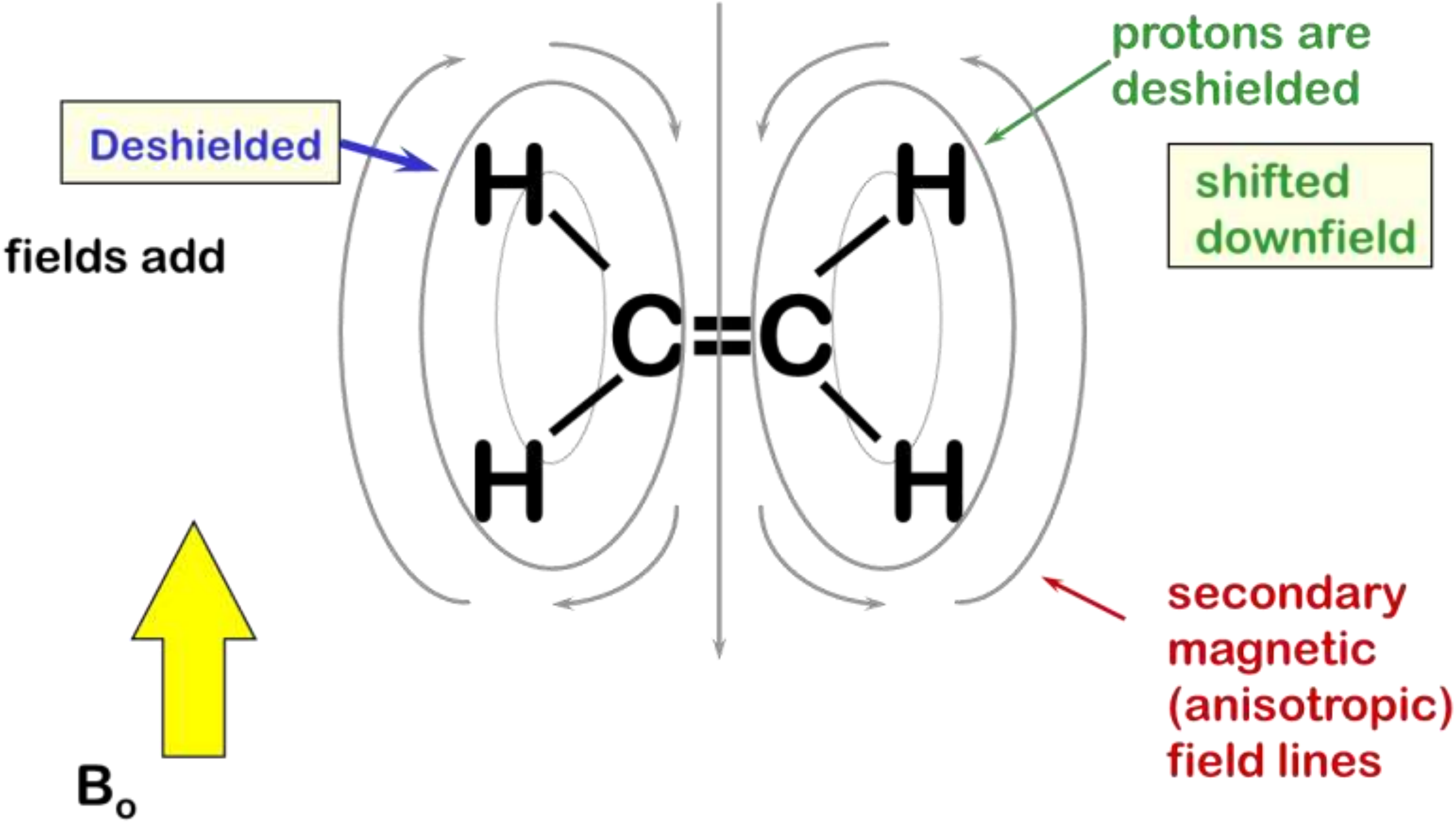
2. Anisotropic fields

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

Benzene rings have the greatest effect



Anisotropic fields in an Alkene



Deshielded

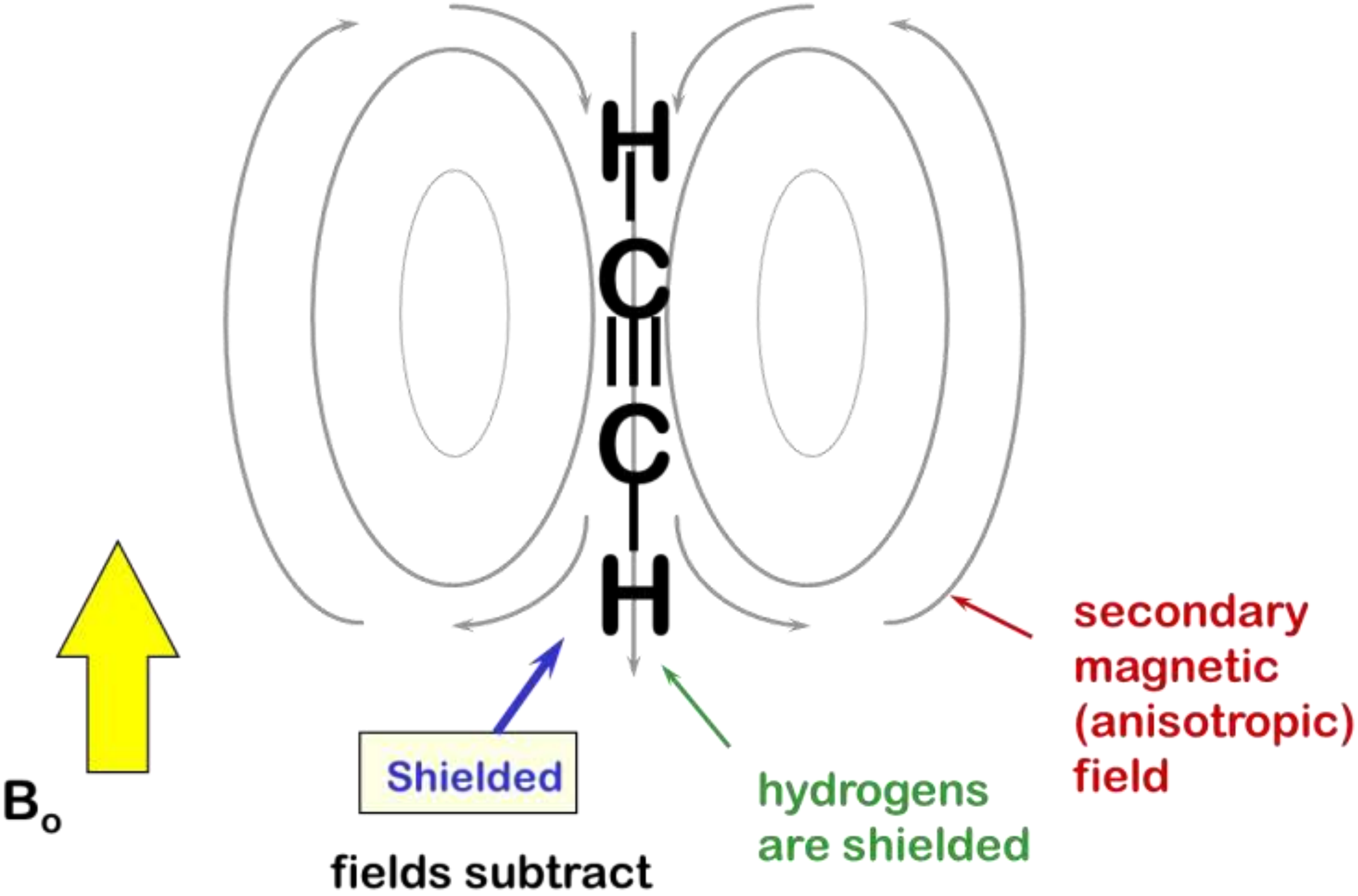
fields add

protons are deshielded

shifted downfield

secondary magnetic (anisotropic) field lines

Anisotropic fields in an Alkyne

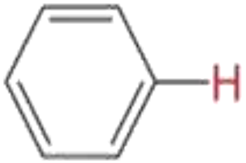
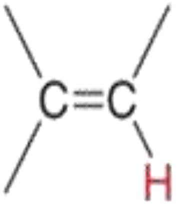


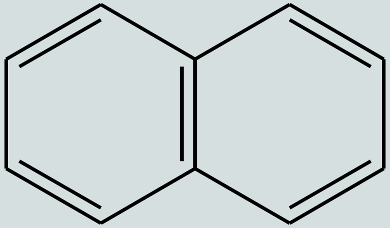
Shielded

fields subtract

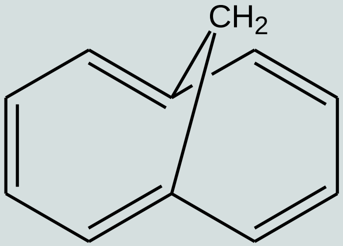
hydrogens are shielded

secondary magnetic (anisotropic) field

Proton type	Effect	Chemical shift (ppm)
	highly deshielded	6.5–8
	deshielded	4.5–6
$—C\equiv C—H$	shielded	~2.5



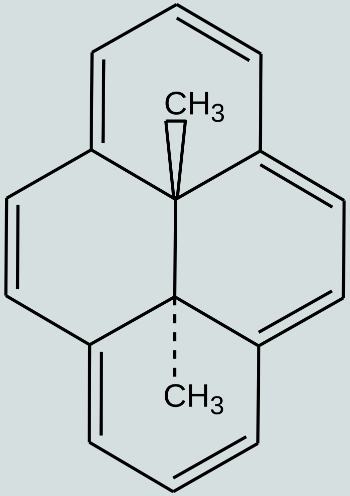
Naphthalene



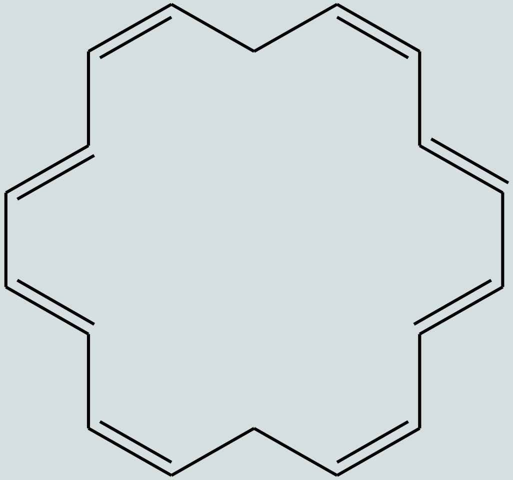
Bicyclo[4.4.1]undeca-1(10),2,4,6,8-pentaene

>7.27δ

CH_2 at ~ -1.2 δ



10b,10c-Dimethyl-10b,10c-dihydro-pyrene



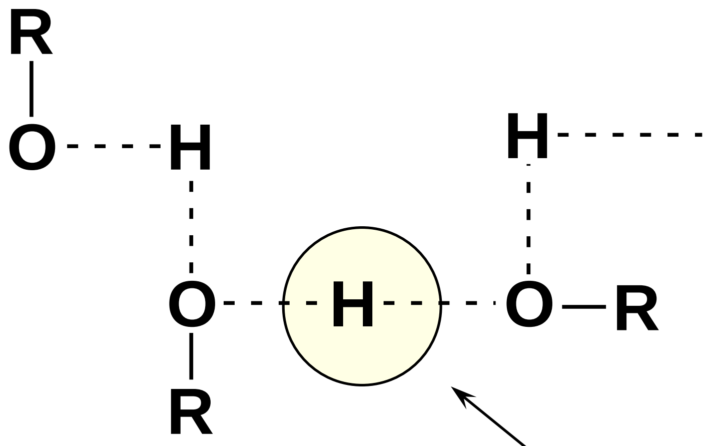
Cyclooctadecanonaene

2CH_3 at ~ -4.2 δ

Inner hydrogens ~ -1.8 δ
Outer hydrogens ~ 8.9 δ

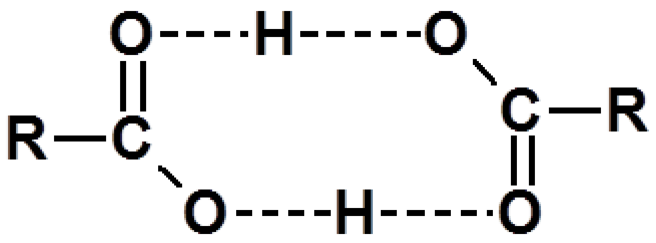
3. Deshielding due to hydrogen bonding

The chemical shift depends on how much hydrogen bonding is taking place.



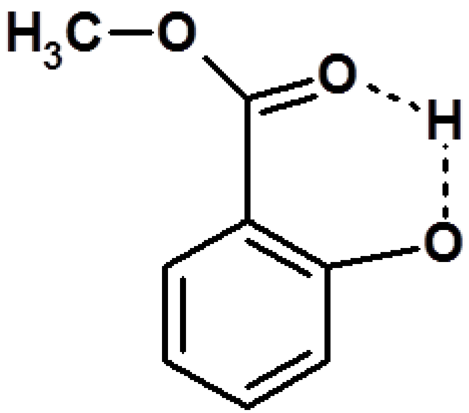
Alcohols vary in chemical shift from 0.5 ppm (free OH) to about 5.0 ppm (lots of H bonding).

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.



Carboxylic acids have strong hydrogen bonding – they form dimers.

With carboxylic acids the O-H absorptions are found between 10 and 12 ppm very far downfield



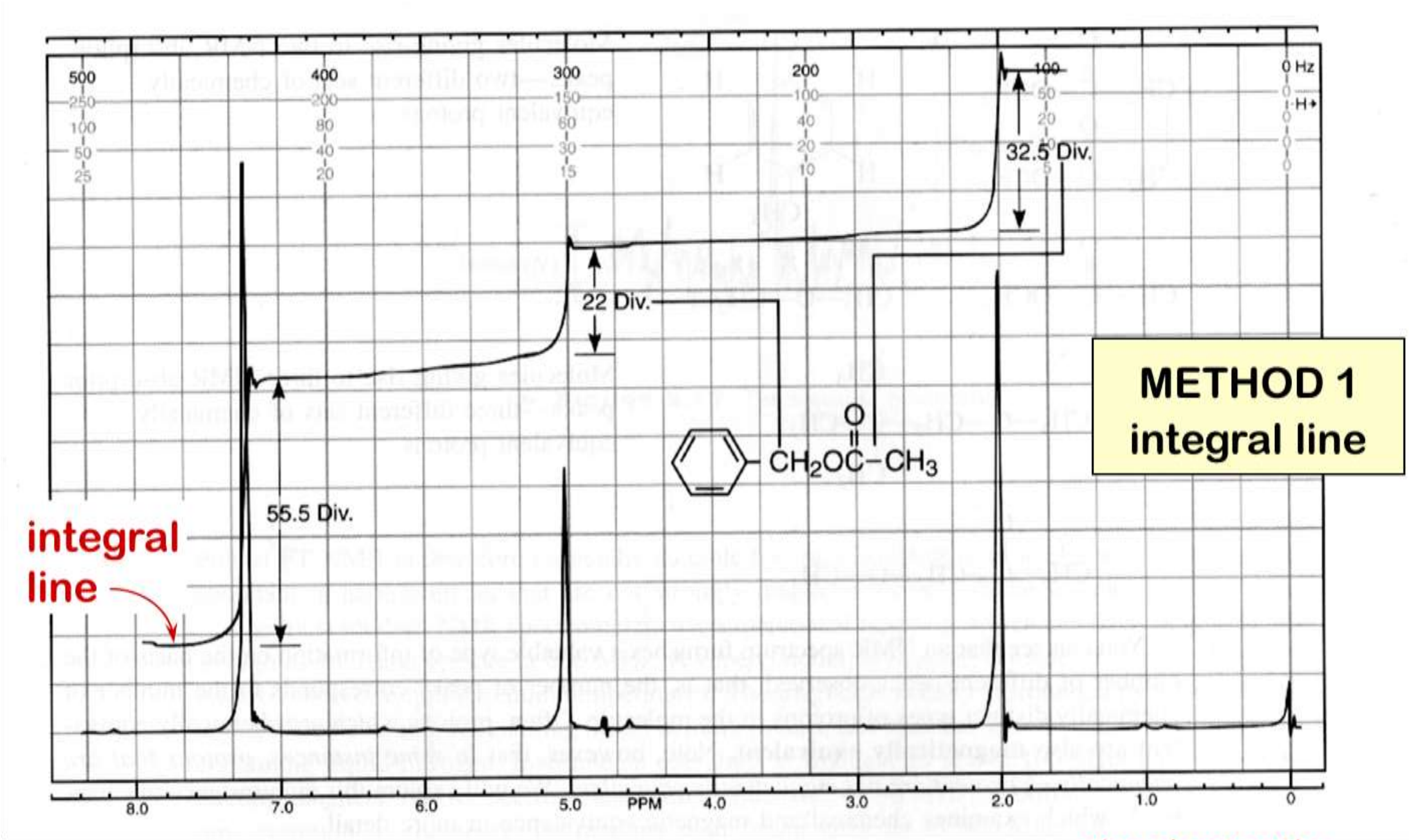
In methyl salicylate, which has strong internal hydrogen bonding, the NMR absortion for O-H is at about 14 ppm, very far downfield.

2- Integration of Peak

- The NMR spectrum can also tell the relative numbers of each type of hydrogen by a process called Integration.

Integration = determination of the area under a peak

The integral line rises an amount proportional to the number of H in each peak



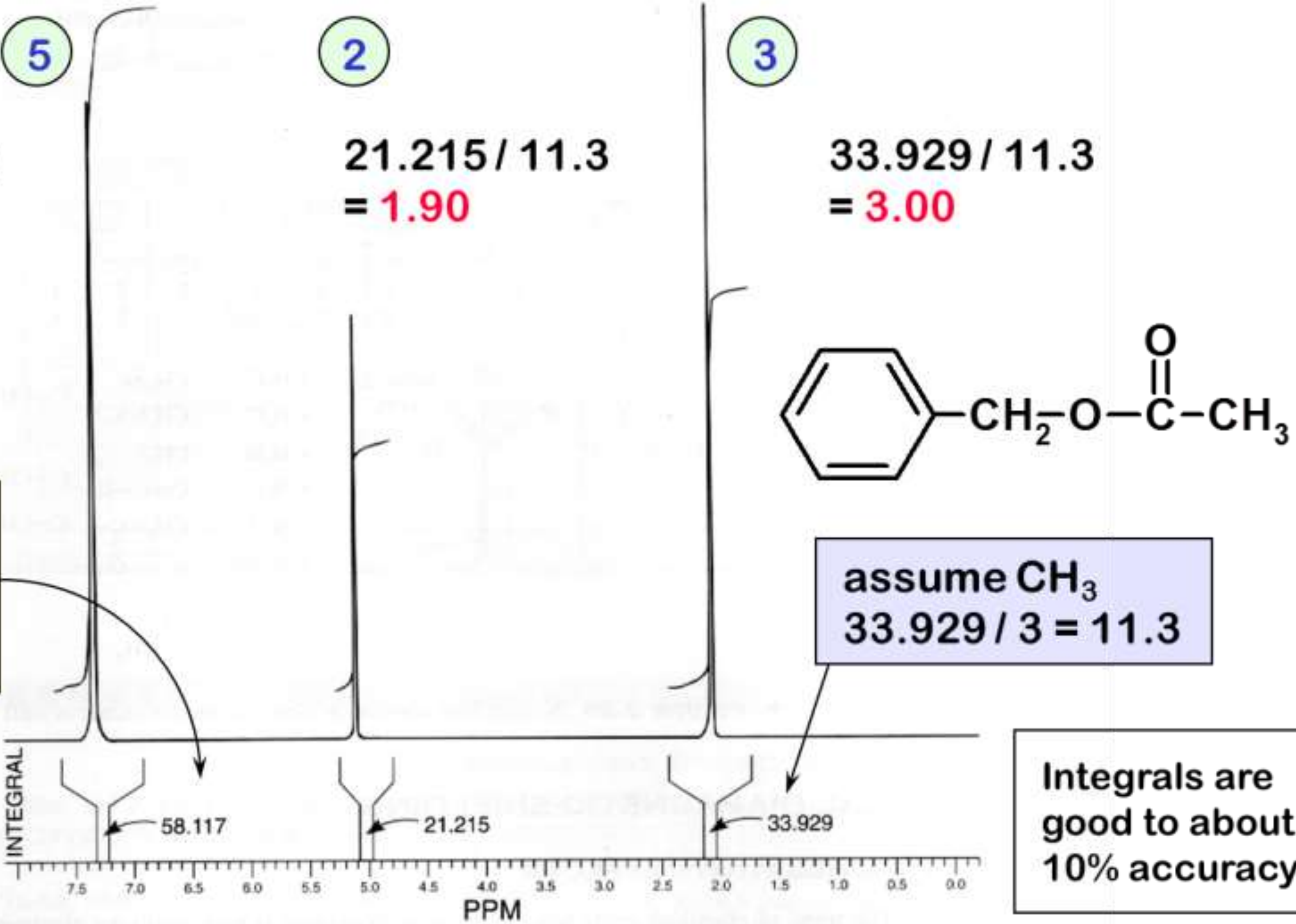
METHOD 1
integral line

integral line

55 : 22 : 33 = 5 : 2 : 3

simplest ratio of the heights

Modern instruments FT-NMR report the integral as a number



Actually : ⑤ ② ③

58.117 / 11.3
= 5.14

21.215 / 11.3
= 1.90

33.929 / 11.3
= 3.00

METHOD 2

digital integration

assume CH_3
33.929 / 3 = 11.3

Integrals are good to about 10% accuracy.

NMR - Position of Signals (Chemical shift values)

Chart .1 Chemical shifts of Protons

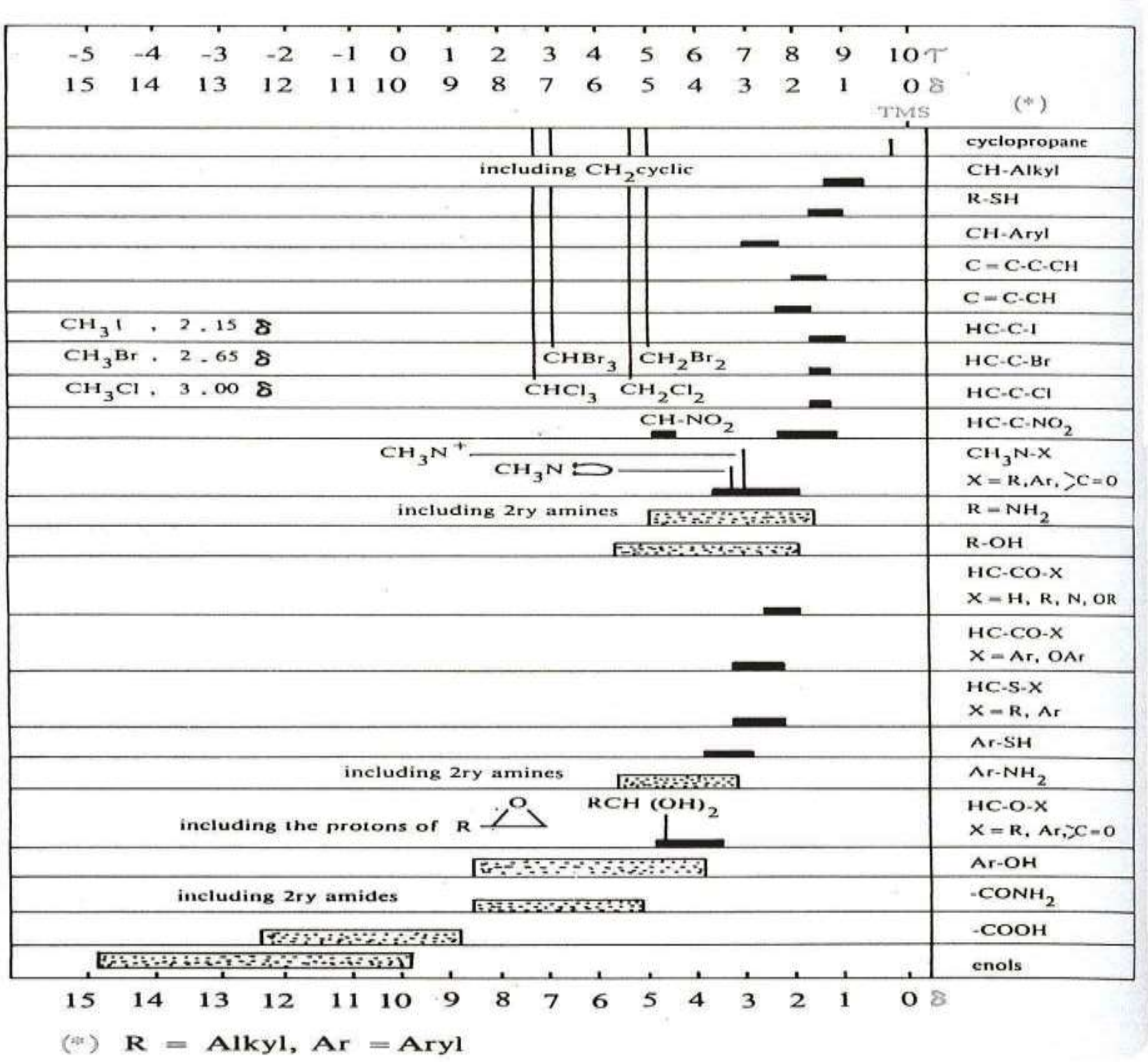
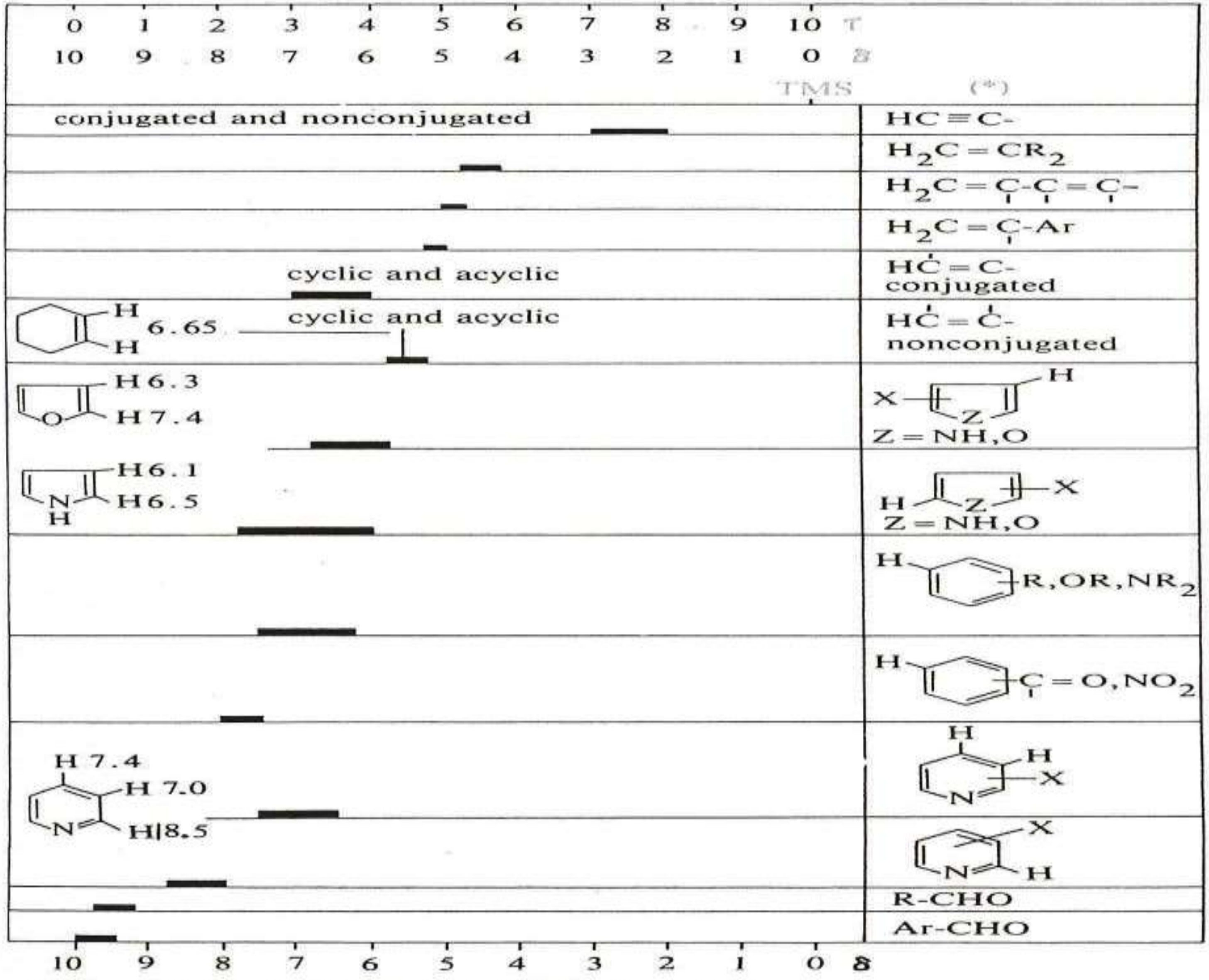
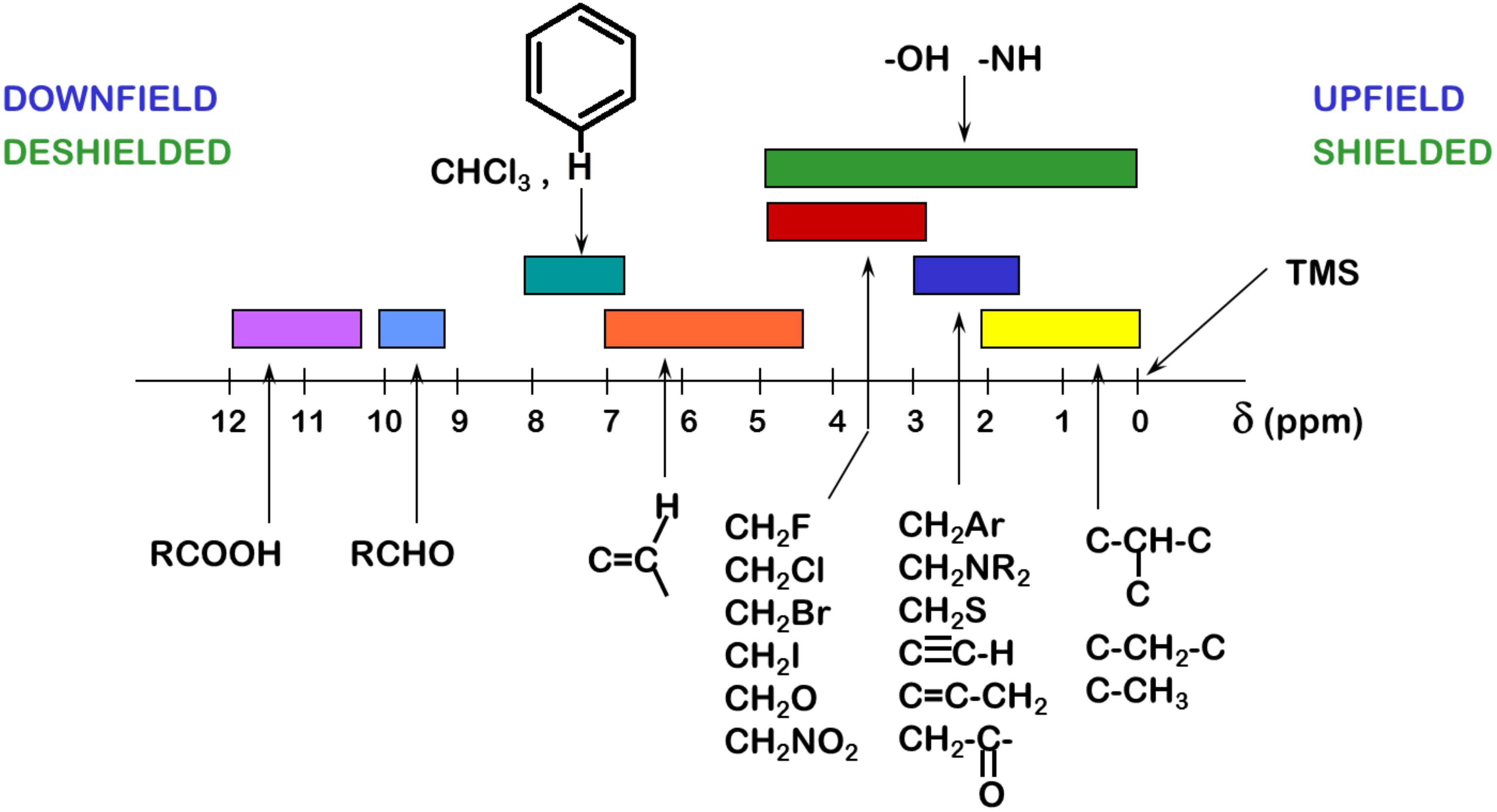


Chart .2 Chemical shifts of Protons

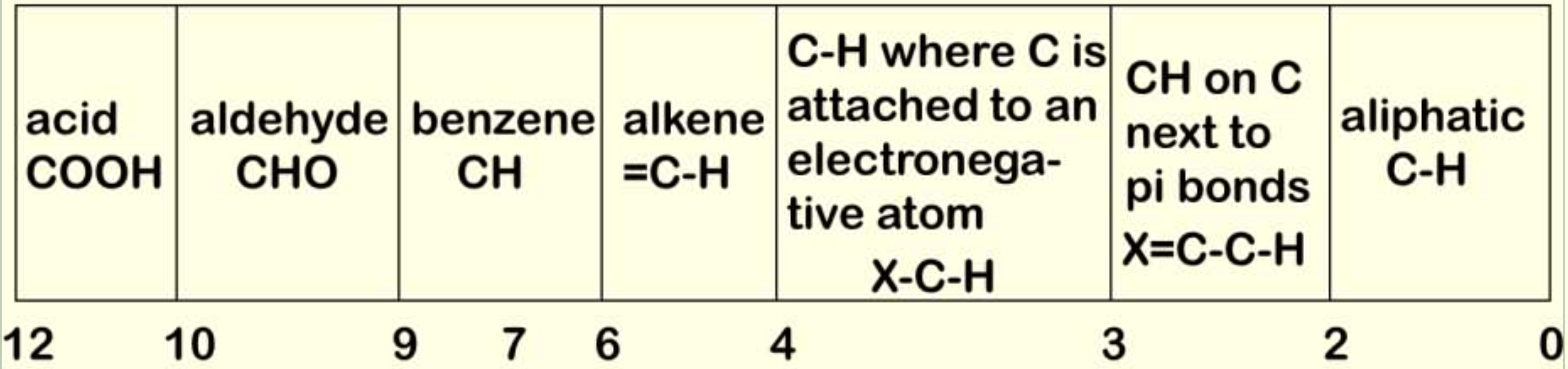


(*) X = Common Group, R = Alkyl, Ar = Aryl

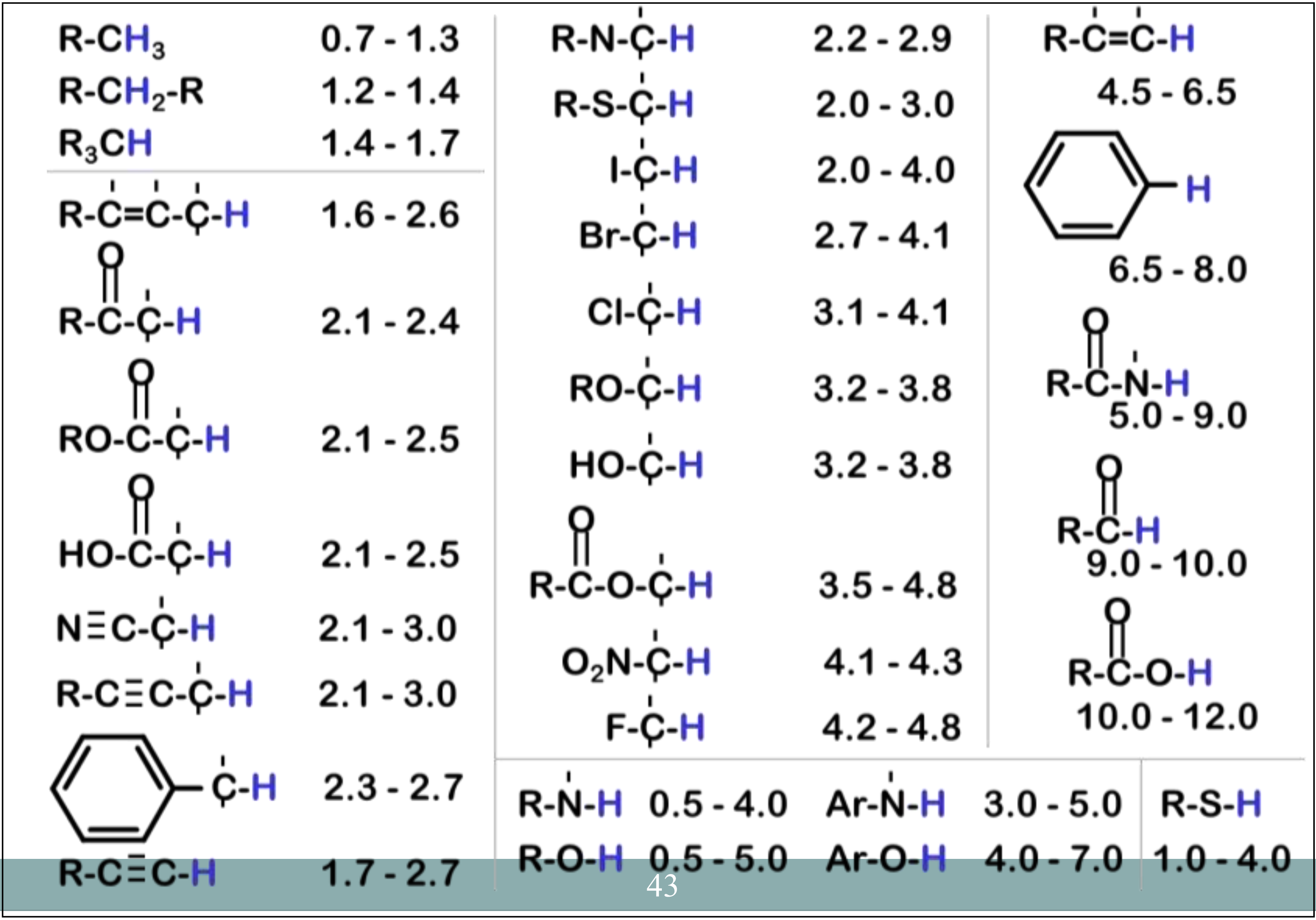
NMR Correlation Chart



It is usually sufficient to know what types of Hydrogens come in selected areas of the NMR Chart.



Approximate Chemical Shift Ranges (ppm) for Selected Types of Protons.



$R\text{-}CH_3$	0.7 - 1.3
$R\text{-}CH_2\text{-}R$	1.2 - 1.4
R_3CH	1.4 - 1.7
R-C=C-C-H	1.6 - 2.6
R-$\overset{O}{C}$-C-H	2.1 - 2.4
RO-$\overset{O}{C}$-C-H	2.1 - 2.5
HO-$\overset{O}{C}$-C-H	2.1 - 2.5
N≡C-C-H	2.1 - 3.0
R-C≡C-C-H	2.1 - 3.0
C-H	2.3 - 2.7
R-C≡C-H	1.7 - 2.7
R-N-C-H	2.2 - 2.9
R-S-C-H	2.0 - 3.0
I-C-H	2.0 - 4.0
Br-C-H	2.7 - 4.1
Cl-C-H	3.1 - 4.1
RO-C-H	3.2 - 3.8
HO-C-H	3.2 - 3.8
R-$\overset{O}{C}$-O-C-H	3.5 - 4.8
$O_2N\text{-}C\text{-}H$	4.1 - 4.3
F-C-H	4.2 - 4.8
R-C=C-H	4.5 - 6.5
H	6.5 - 8.0
R-$\overset{O}{C}$-N-H	5.0 - 9.0
R-$\overset{O}{C}$-H	9.0 - 10.0
R-$\overset{O}{C}$-O-H	10.0 - 12.0
R-N-H	0.5 - 4.0
R-O-H	0.5 - 5.0
Ar-N-H	3.0 - 5.0
Ar-O-H	4.0 - 7.0
R-S-H	1.0 - 4.0

Spin-Spin Splitting

- Often a group of hydrogens will appear as a multiplet rather than as a single peak.

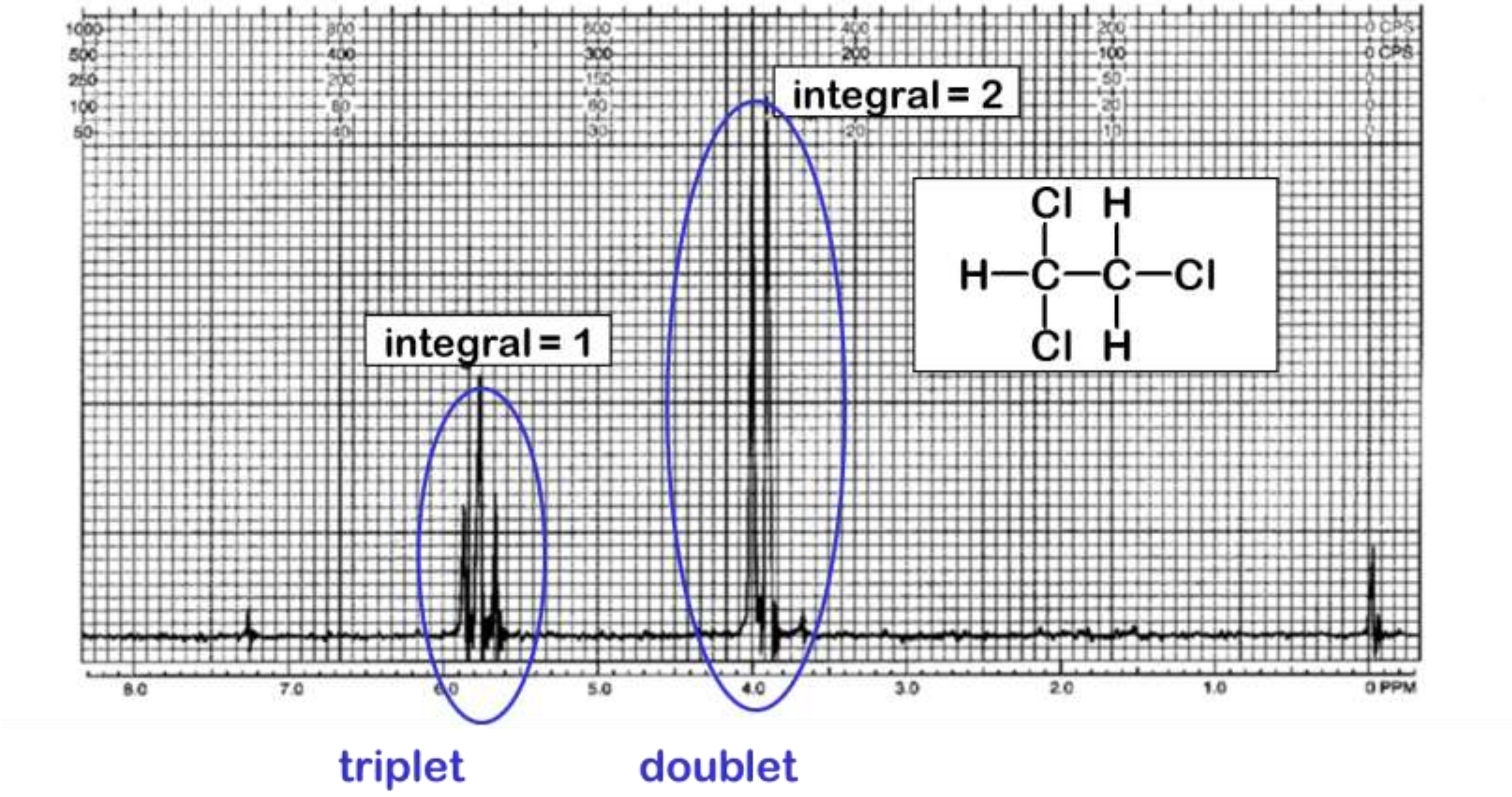
- Multiplets are named as follows:

Single
Doublet
Triplet
Quartet
Quintet
Sextet
Septet
Octet
Nonet

- This happens because of interaction with neighboring hydrogens and is called Spin-Spin Splitting

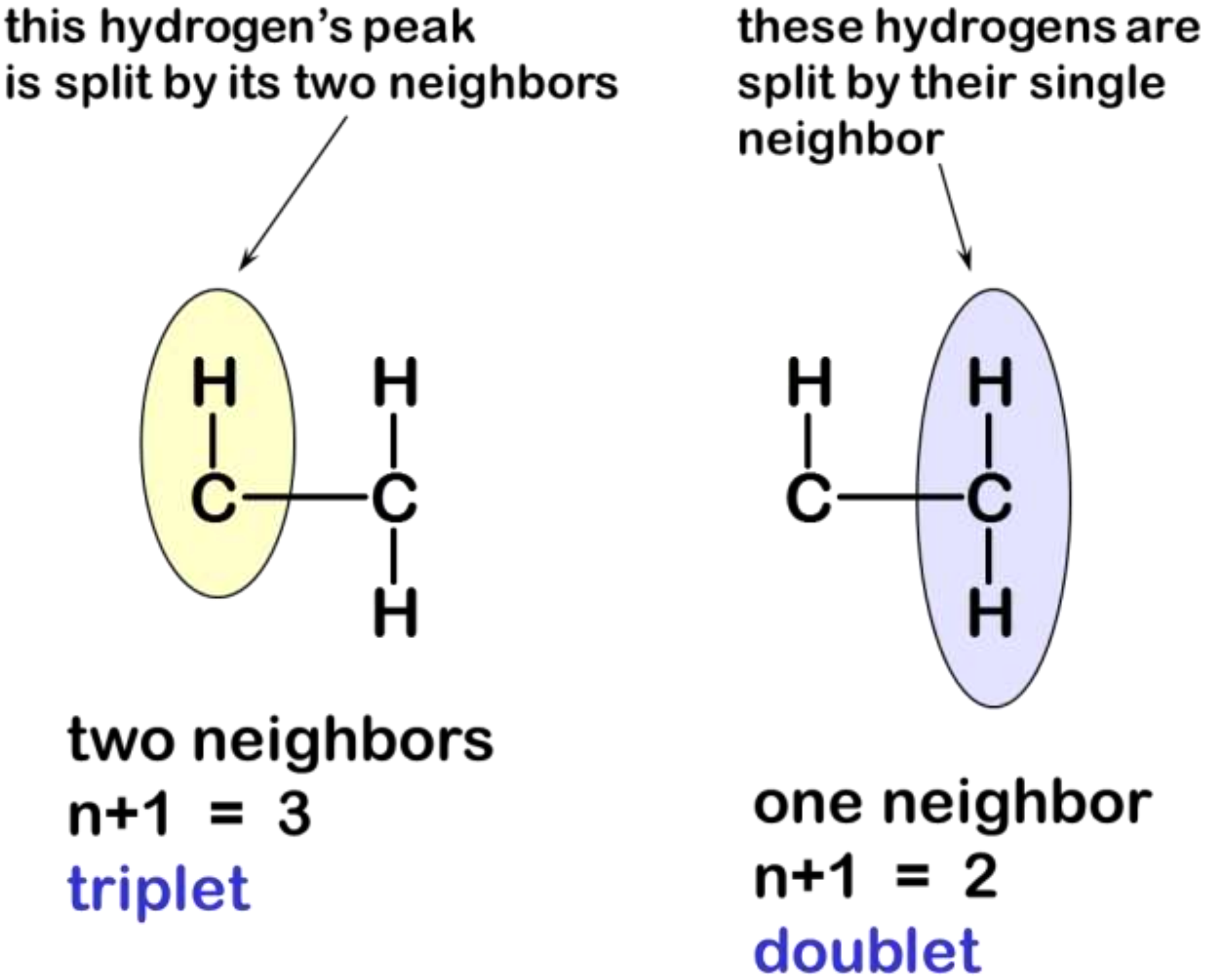
1,1,2-Trichloroethane

The two kinds of hydrogens do not appear as single peaks, rather there is a "triplet" and a "doublet".



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

n + 1 Rule



this hydrogen's peak is split by its two neighbors

two neighbors
n+1 = 3
triplet

these hydrogens are split by their single neighbor

one neighbor
n+1 = 2
doublet

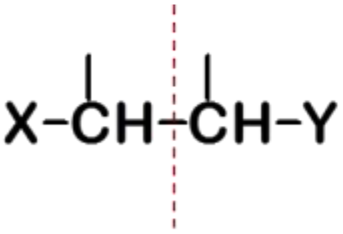
Multiplets

- singlet
- doublet
- triplet
- quartet
- quintet
- sextet
- septet

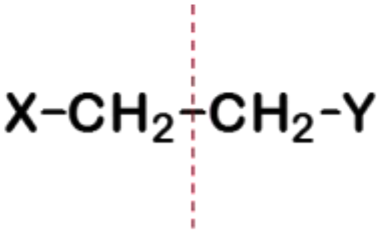
Exceptions to the n+1 Rule

IMPORTANT !

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

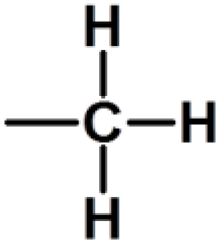


no splitting if x=y

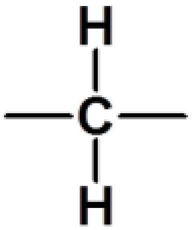


no splitting if x=y

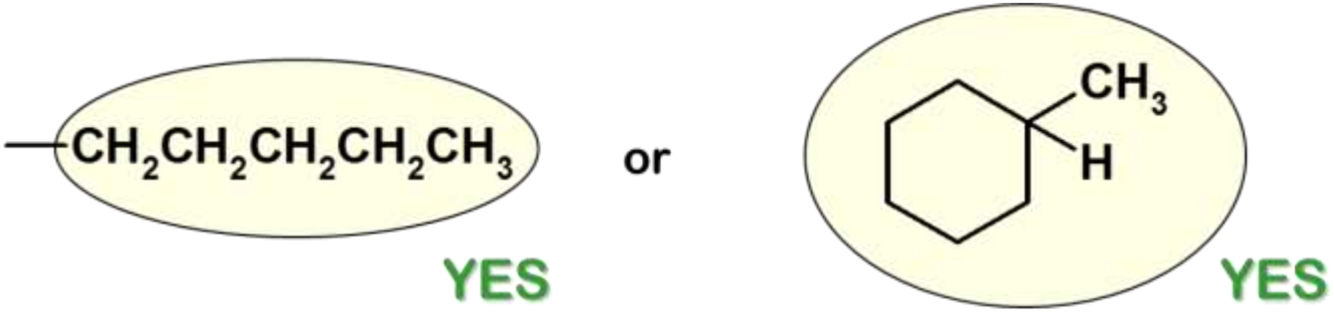
2) Protons in the same group usually do not split one another.



or

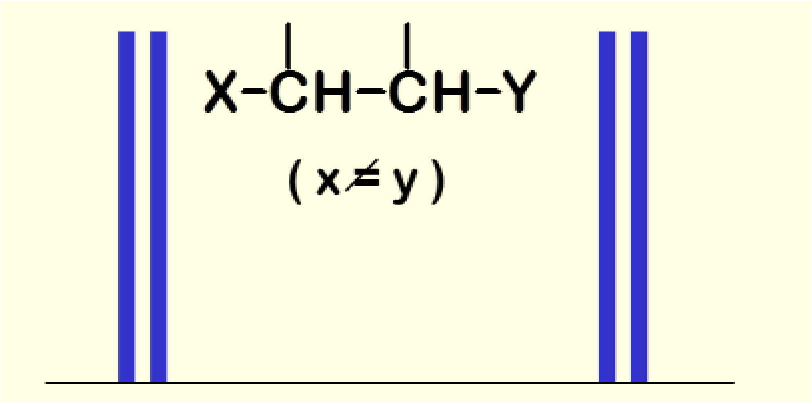


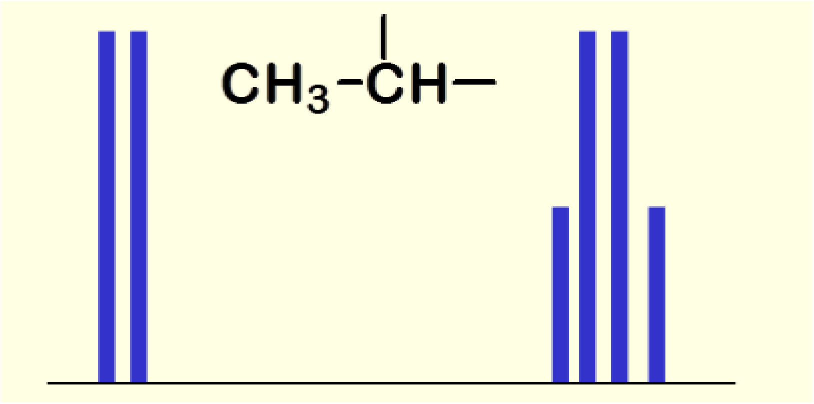
3) The n+1 rule applies principally to protons in aliphatic (saturated) chains or on saturated rings.

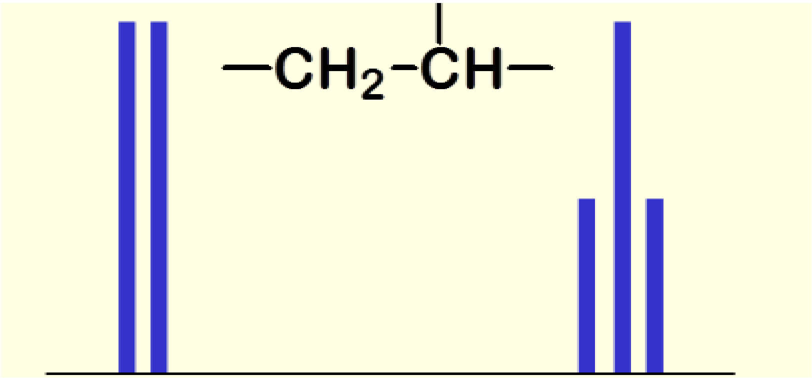


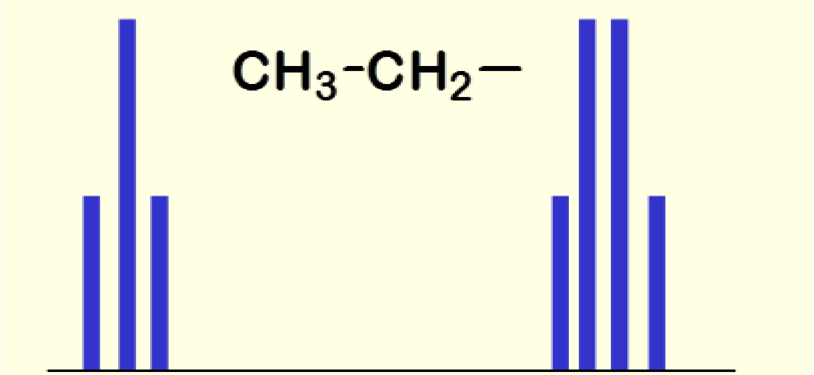
but does not apply (in the simple way shown here) to protons on double bonds or on benzene rings.

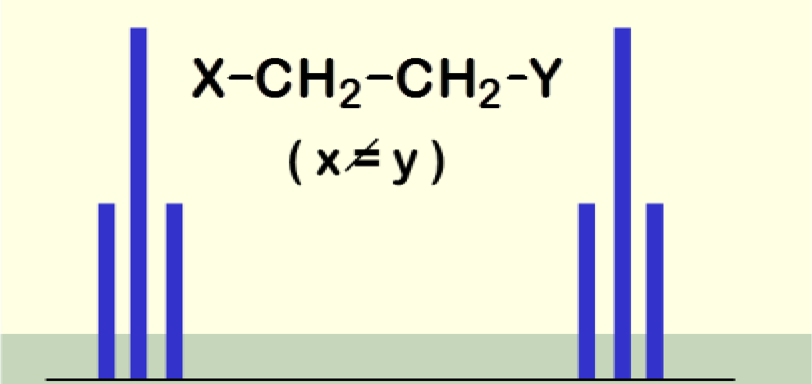
Some Common Splitting Patterns

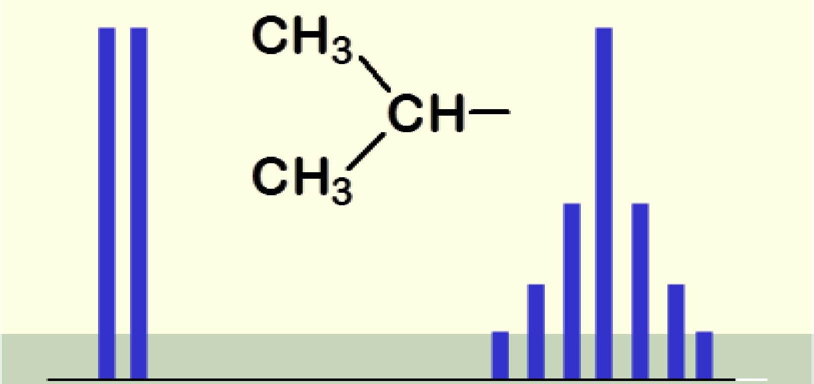








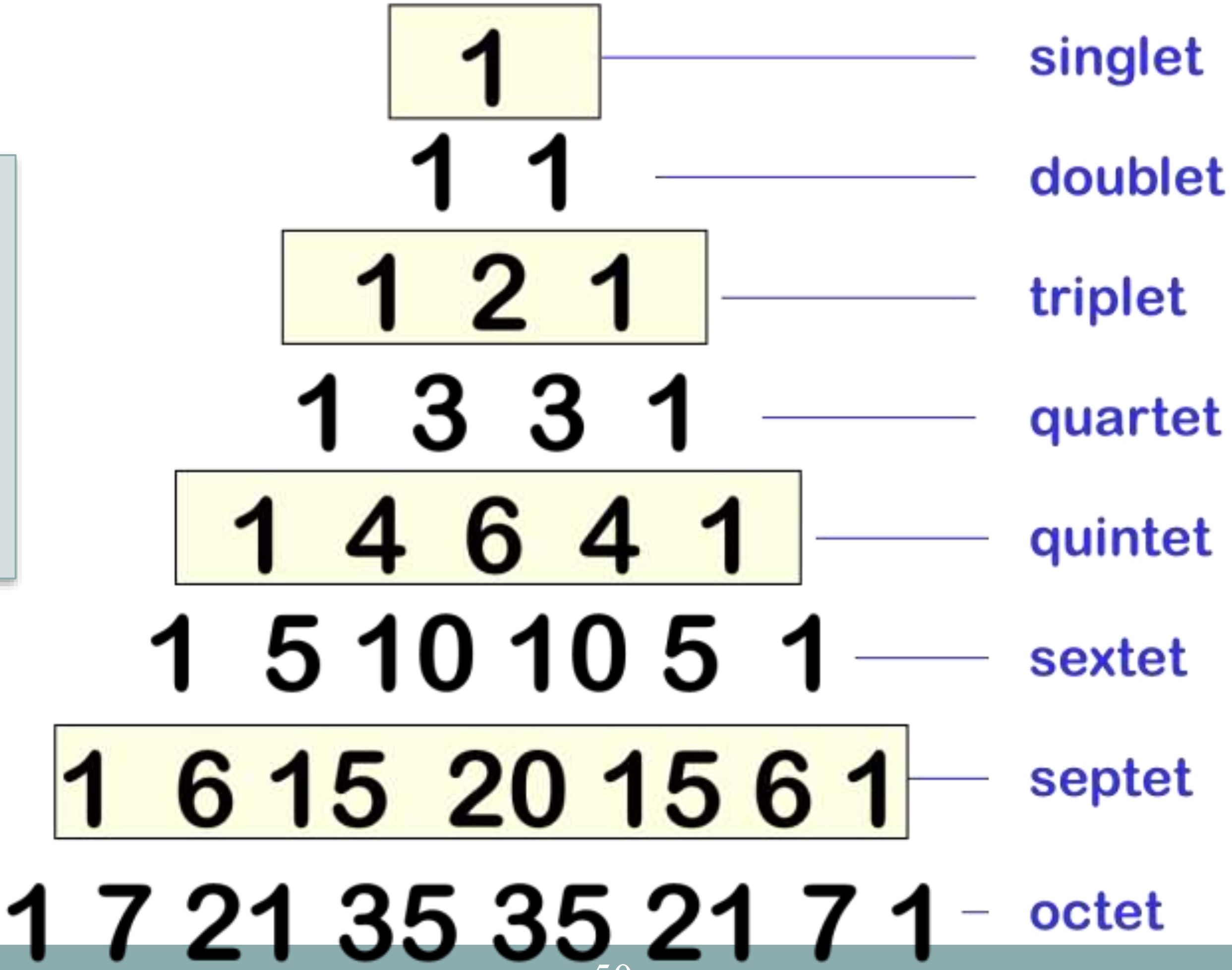




Intensities of multiplet peaks

PASCAL'S TRIANGLE

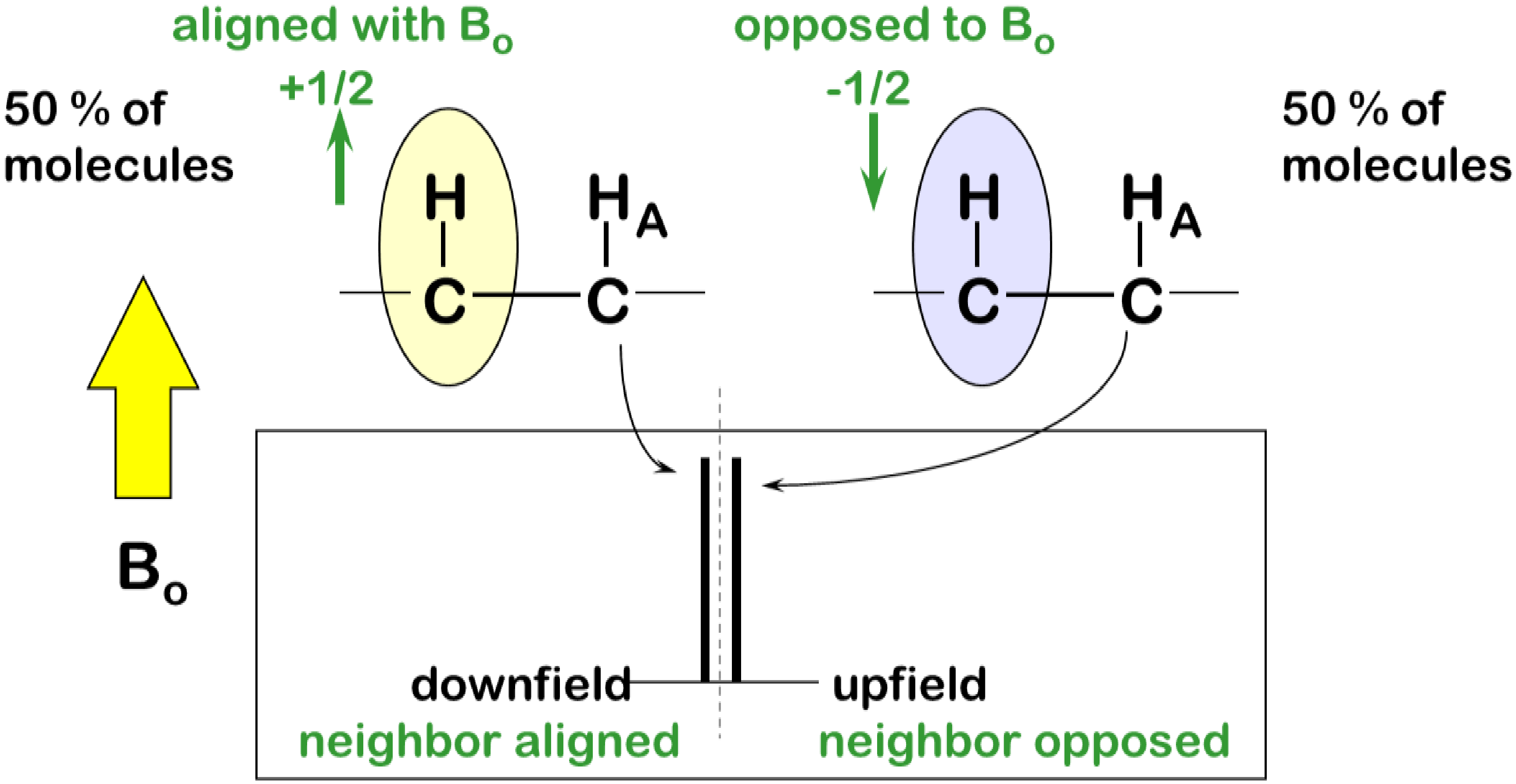
The interior entries are the sums of the two numbers immediately above.

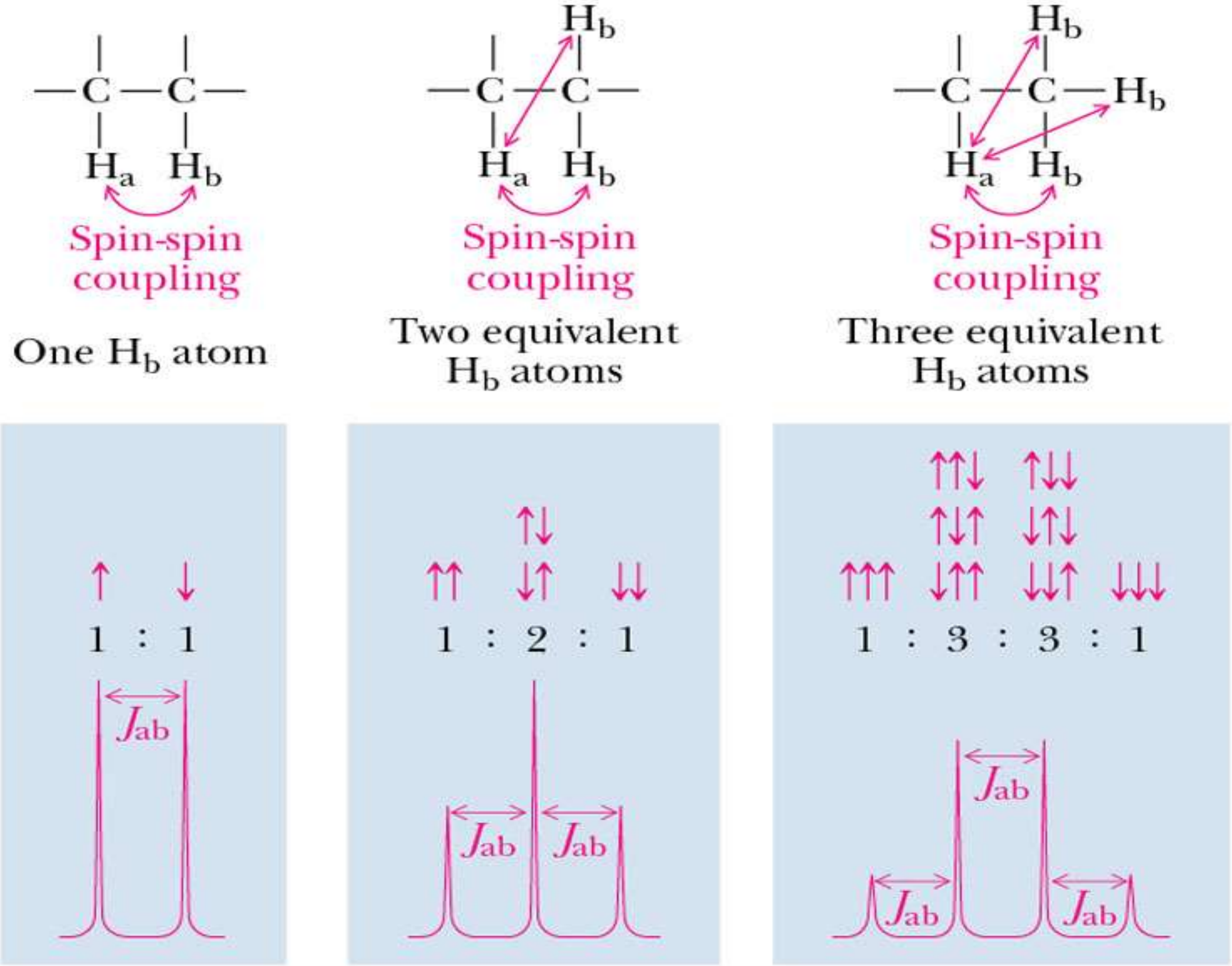


1	singlet
1 1	doublet
1 2 1	triplet
1 3 3 1	quartet
1 4 6 4 1	quintet
1 5 10 10 5 1	sextet
1 6 15 20 15 6 1	septet
1 7 21 35 35 21 7 1	octet

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

The Chemical Shift of Proton H_A is affected by the Spin of its Neighbors.



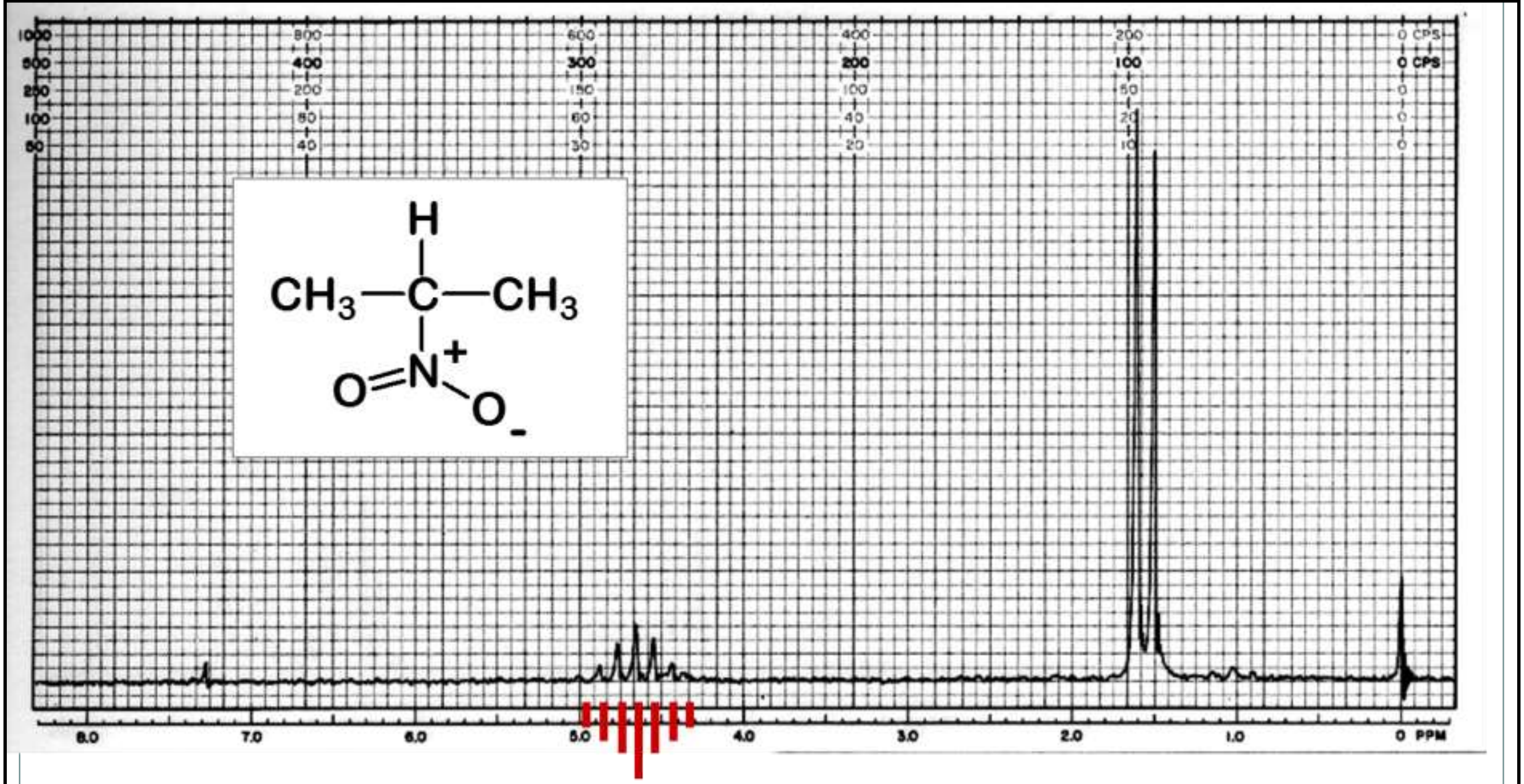


Observed splitting in signal of H_a

Some Example Spectra with Splitting

NMR Spectrum of Bromoethane

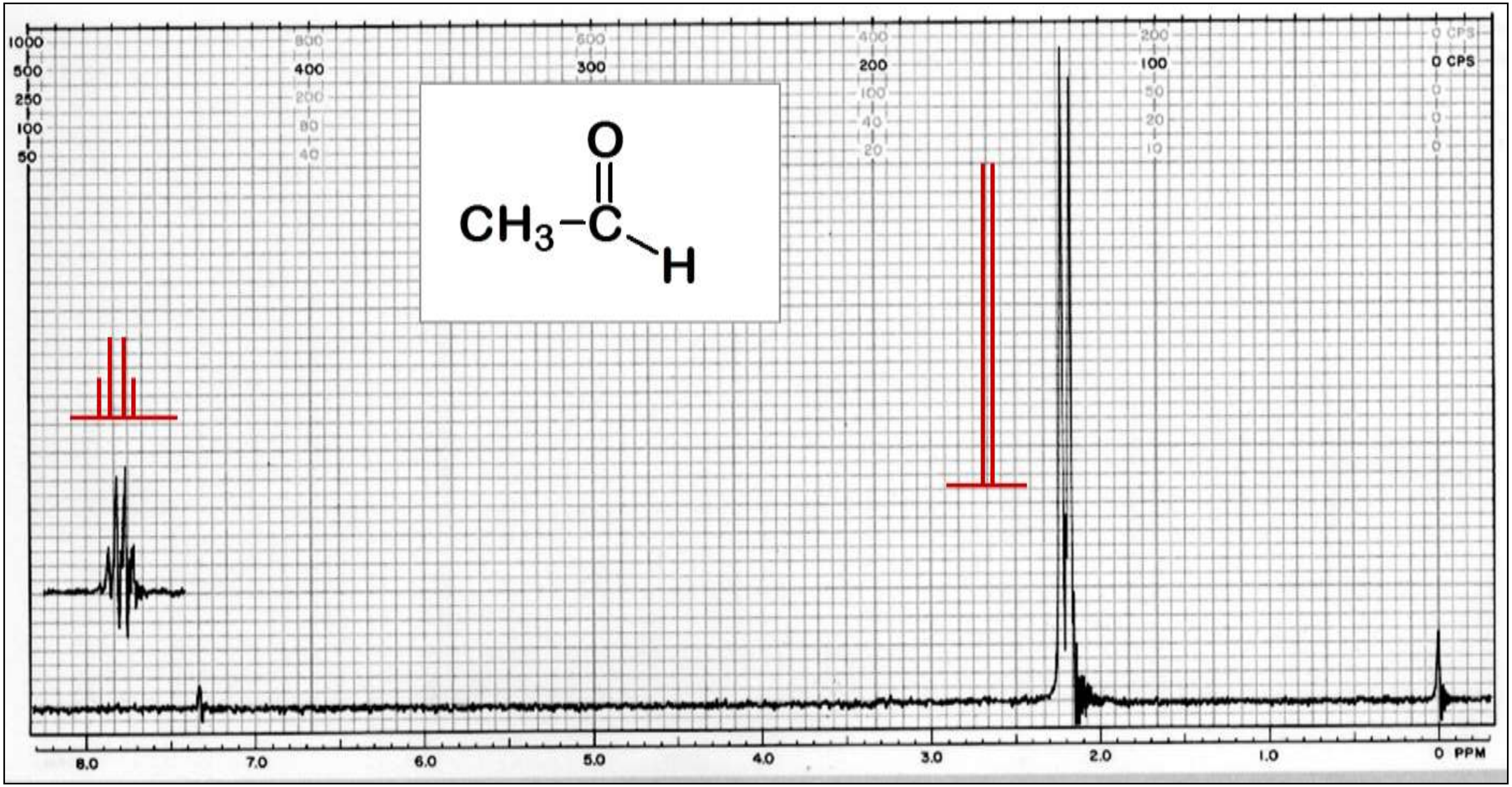
NMR Spectrum of 2-Nitropropane



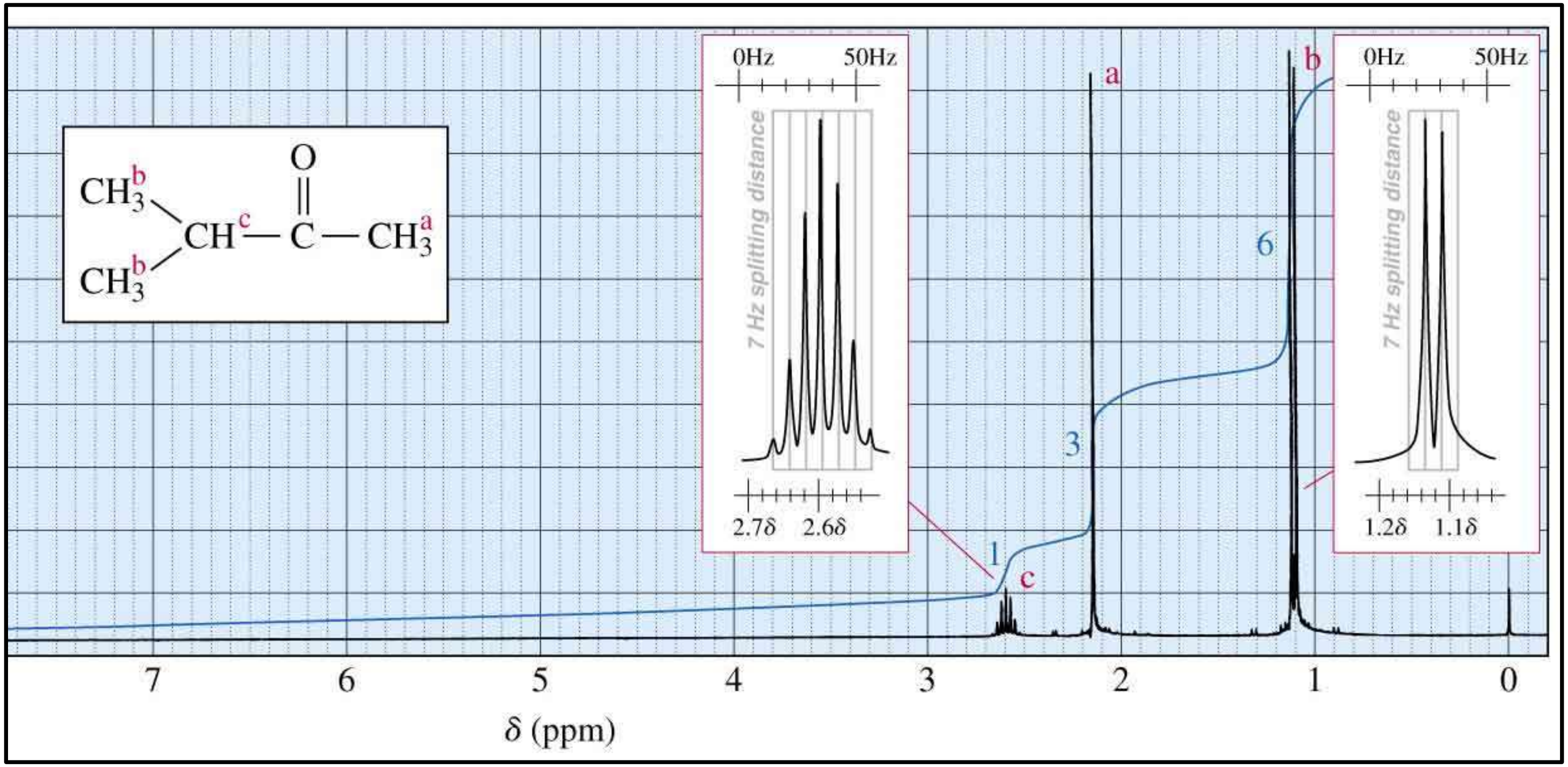
1:6:15:20:16:6:1

in higher multiplets the outer peaks are often nearly lost in the baseline

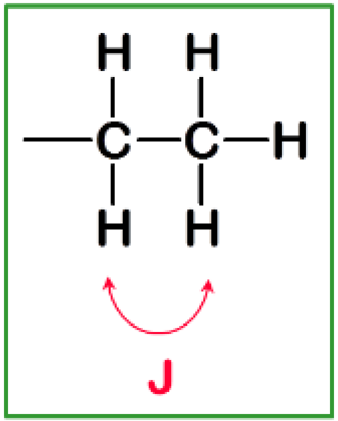
NMR Spectrum of Acetaldehyde



NMR Spectrum of 3-Methyl-butan-2-one

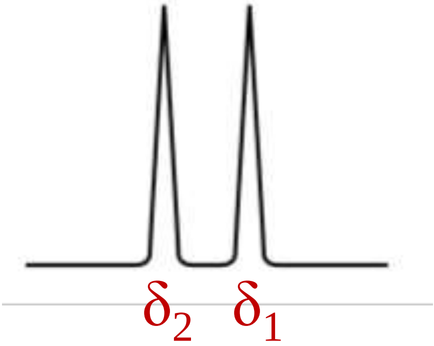


Coupling Constants



- Distance between the peaks of multiplet
- Measured in Hz
- J is a measure of the amount of interaction between the two sets of hydrogens creating the multiplet.
- Not dependent on strength of the external field

How to count J from spectrum:

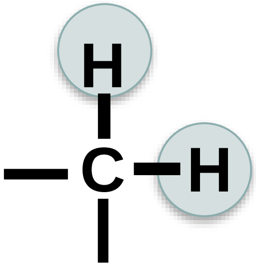


$J = (\delta_2 - \delta_1)$ x spectrometer frequency Hz

Types of Coupling Constants

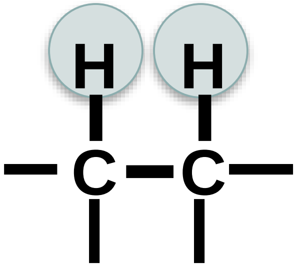
1. ^{2}J or geminal coupling

It is designated ^{2}J since two bonds intervene between the two hydrogens but the two hydrogens are not equivalent



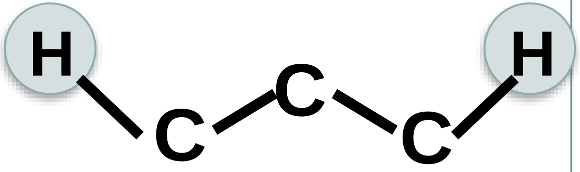
2. ^{3}J or vicinal coupling

It is designated ^{3}J since three bonds intervene between the two hydrogens

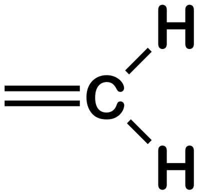
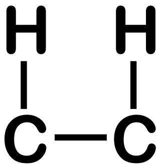
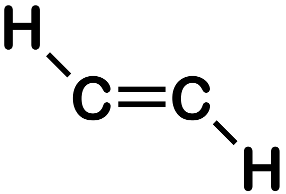
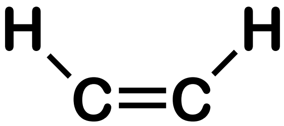
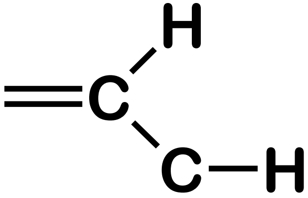


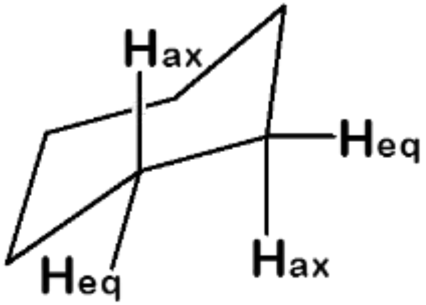
3. ^{4}J - ^{n}J or Long Range Coupling

Couplings larger than ^{3}J since more than three bonds intervene between the two hydrogens



Some Representative Coupling Constants

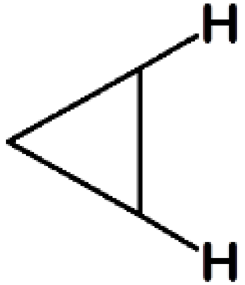
geminal		0 to 5 Hz	two bond	^2J
vicinal		6 to 8 Hz	three bond	^3J
trans		11 to 18 Hz	three bond	^3J
cis		6 to 15 Hz	three bond	^3J
vicinal		4 to 10 Hz	three bond	^3J



Hax , Hax = 8 to 14

Hax , Heq = 0 to 7 three bond ^3J

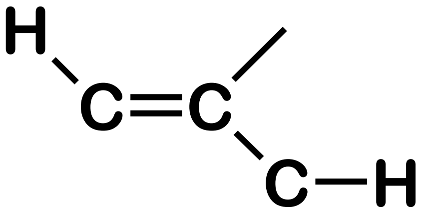
Heq , Heq = 0 to 5



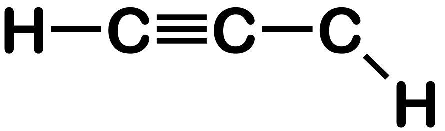
cis 6 to 12 Hz

trans 4 to 8 Hz

three bond ^3J



0 to 3 Hz four bond ^4J



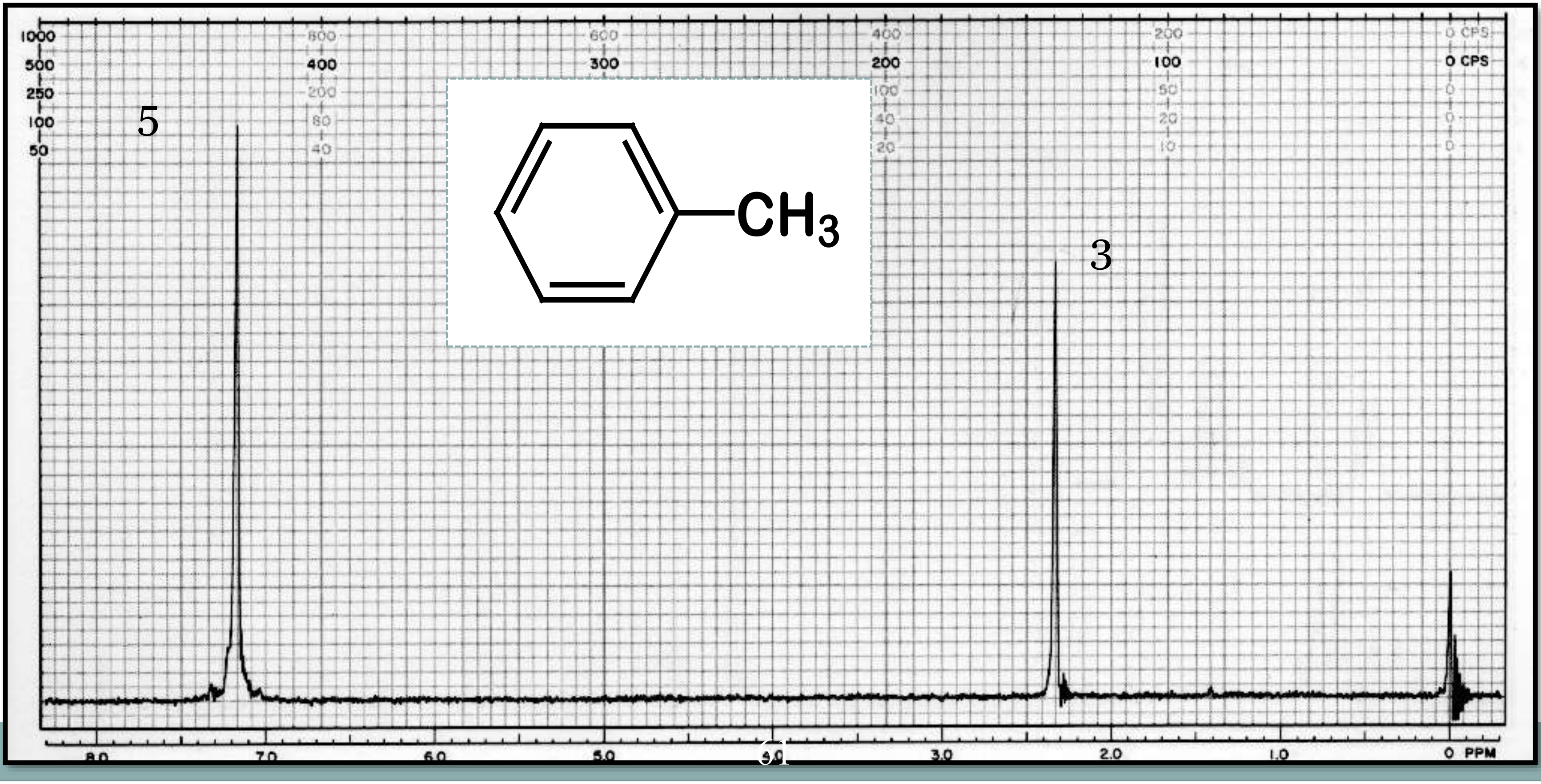
0 to 3 Hz four bond ^4J

Spectra of Aromatic Compounds

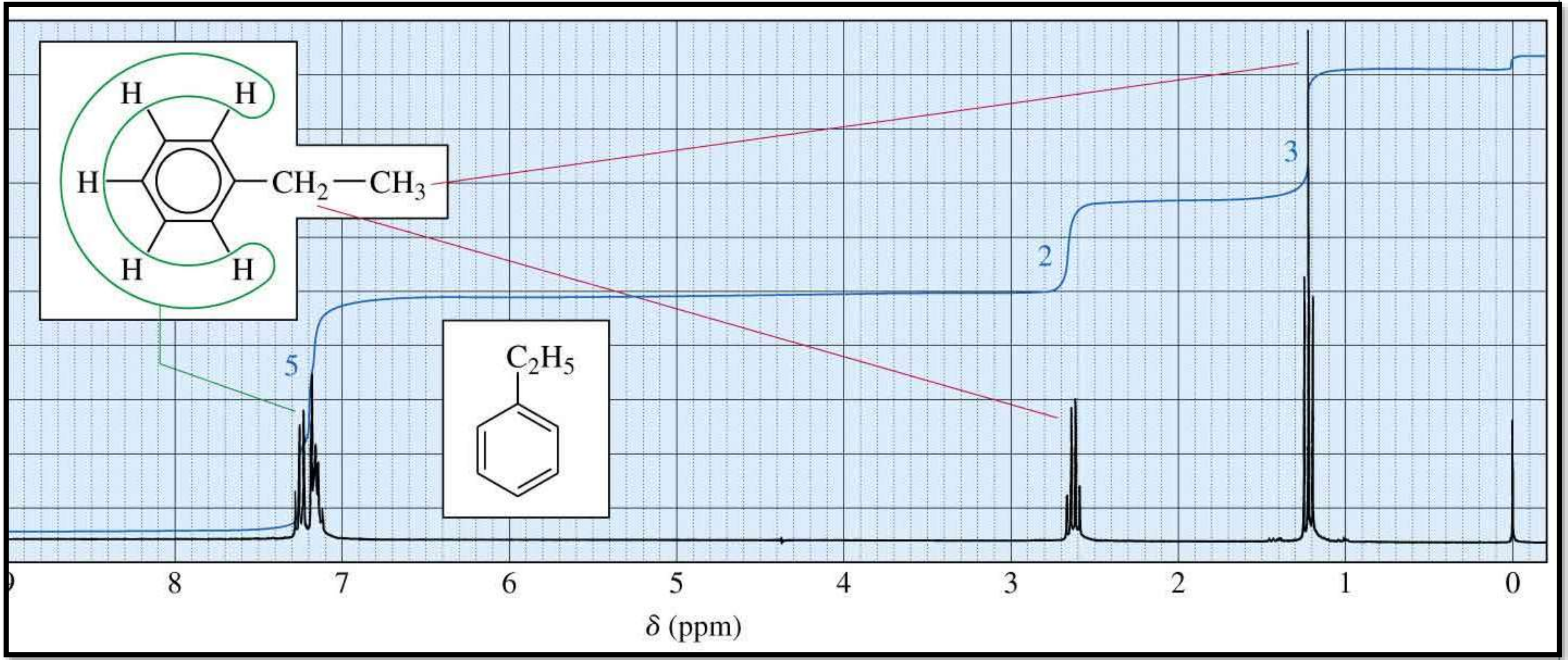
The *mono*-substituted Pattern

Alkyl - Substituted Rings

NMR Spectrum of Toluene

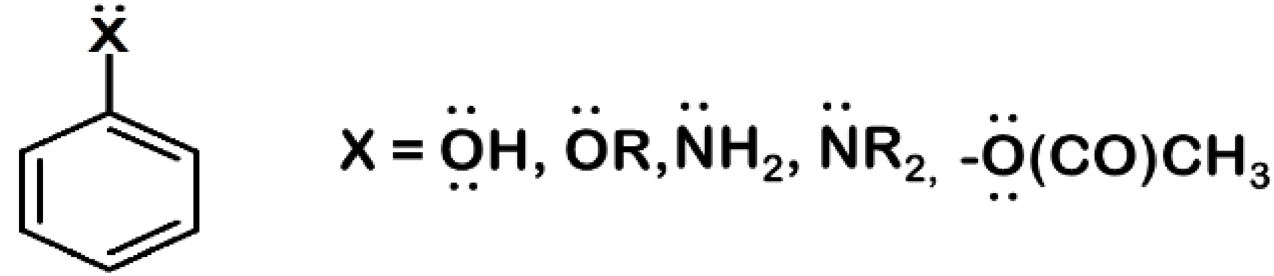


NMR Spectrum of Ethyl-benzene



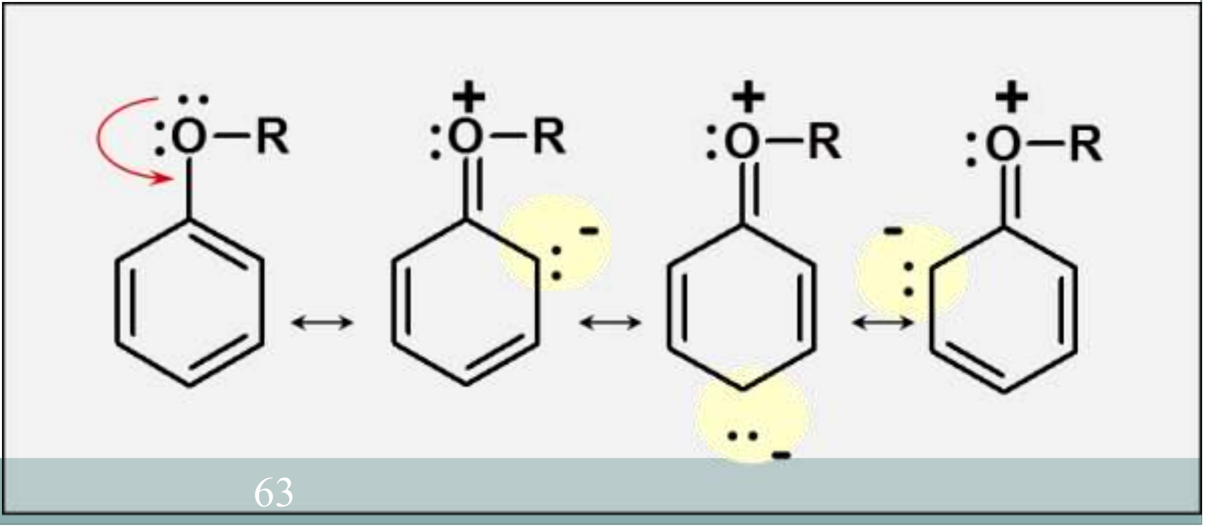
Substituents with Unshared Pairs

- Electronegative elements with unshared pairs shield the *o*- and *p*- ring positions

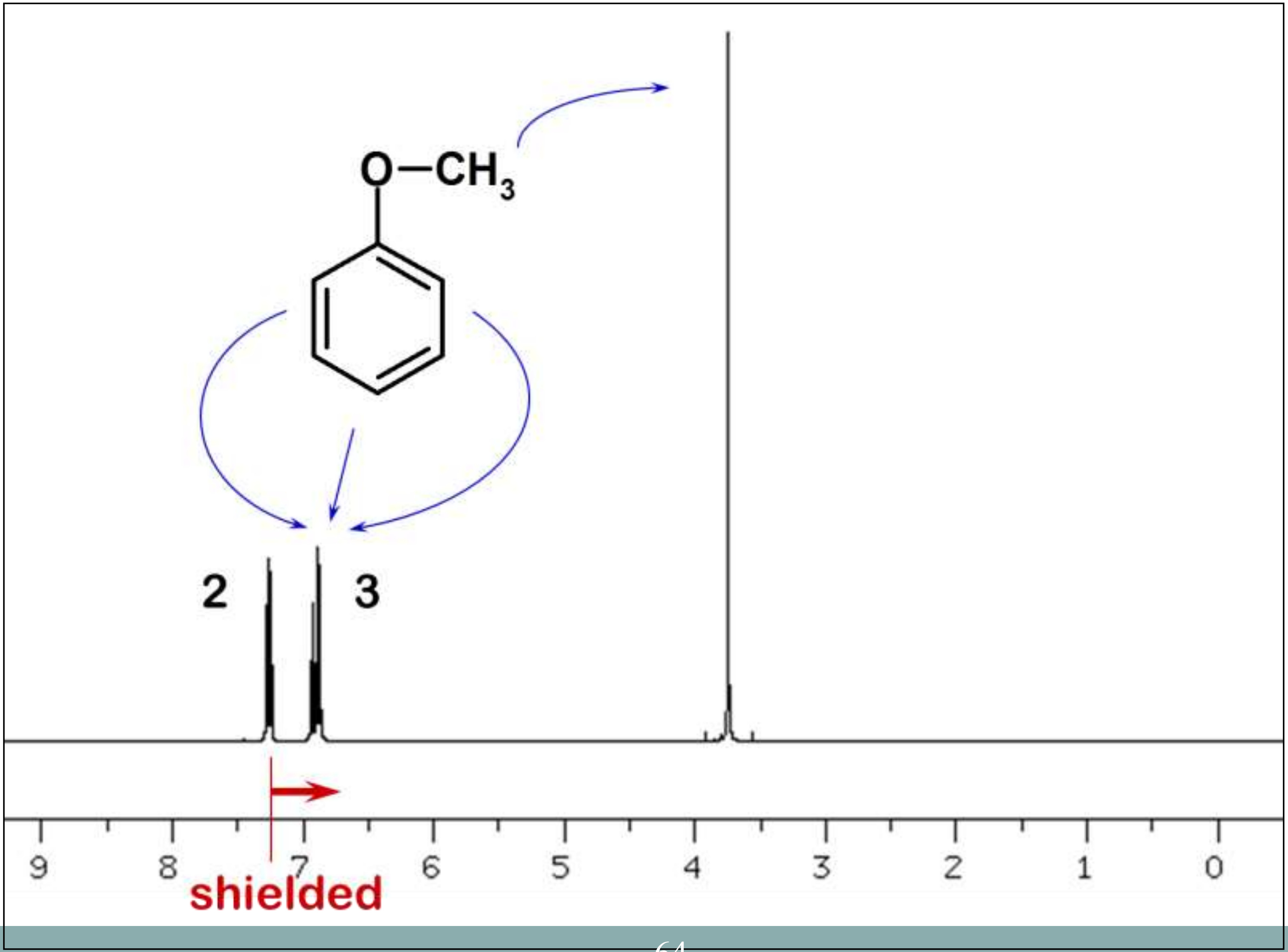


$X = \ddot{O}H, \ddot{O}R, \ddot{N}H_2, \ddot{N}R_2, -\ddot{O}(CO)CH_3$

Electron-donating groups shield the *o*-, *p*- positions due to resonance

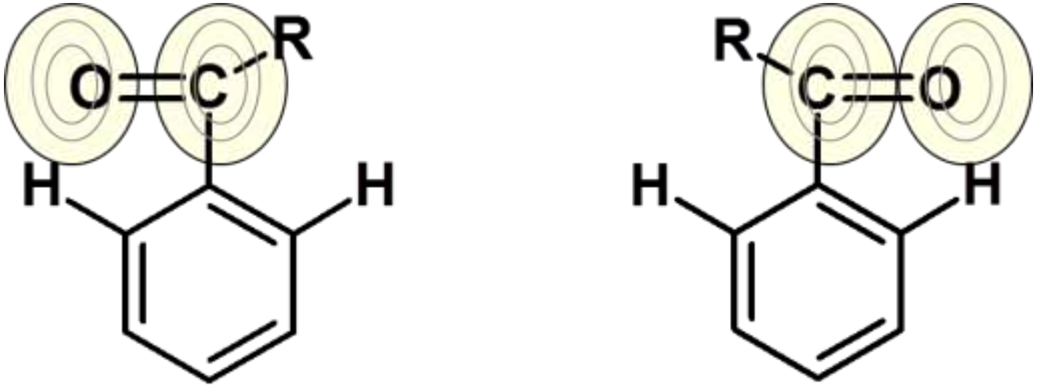


NMR Spectrum of Anisole



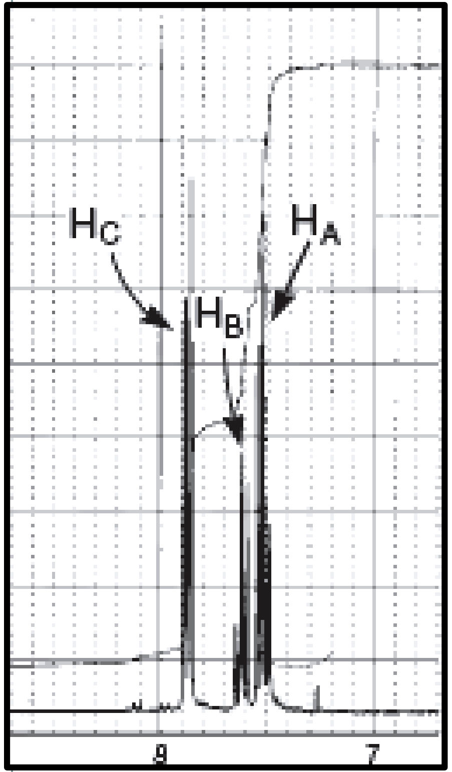
The Effect of Carbonyl Substituents

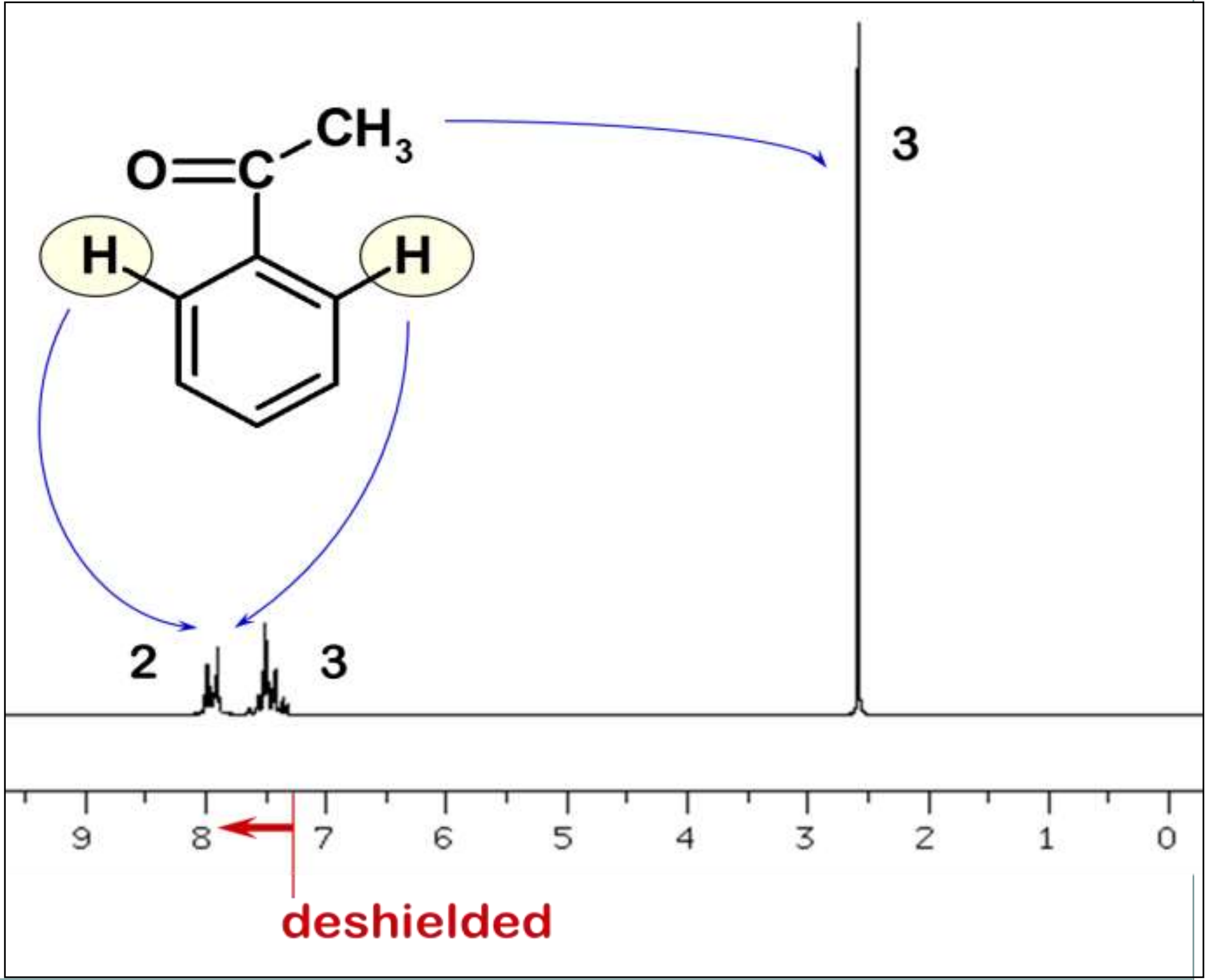
- When a carbonyl group is attached to the ring the *o*- and *p*- protons are deshielded by the anisotropic field of C=O



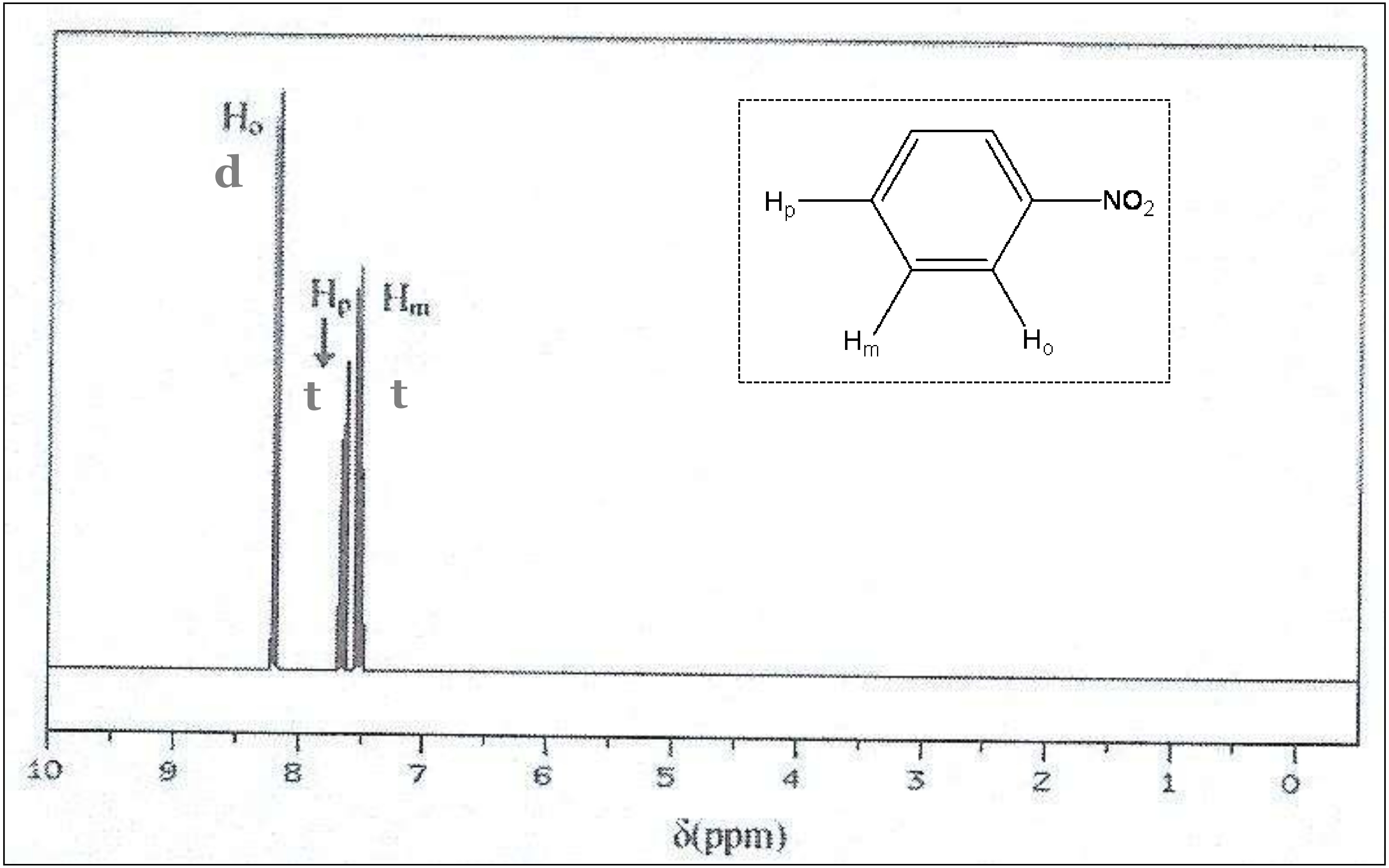
- The same effect is sometimes seen with C=C bonds.

NMR Spectrum of Acetophenone

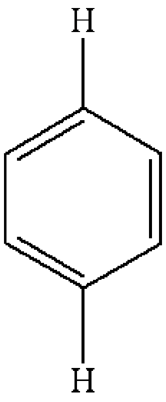




NMR Spectrum of Nitrobenzene

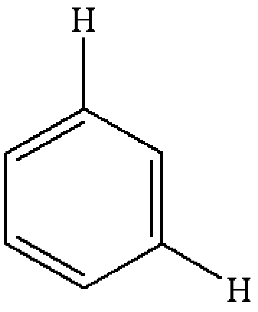


Coupling Constants in Aromatic Rings



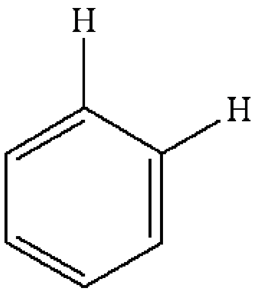
Para-

$^{5}J = 0\text{-}1$ Hz



Meta-

$^{4}J = 1\text{-}3$ Hz

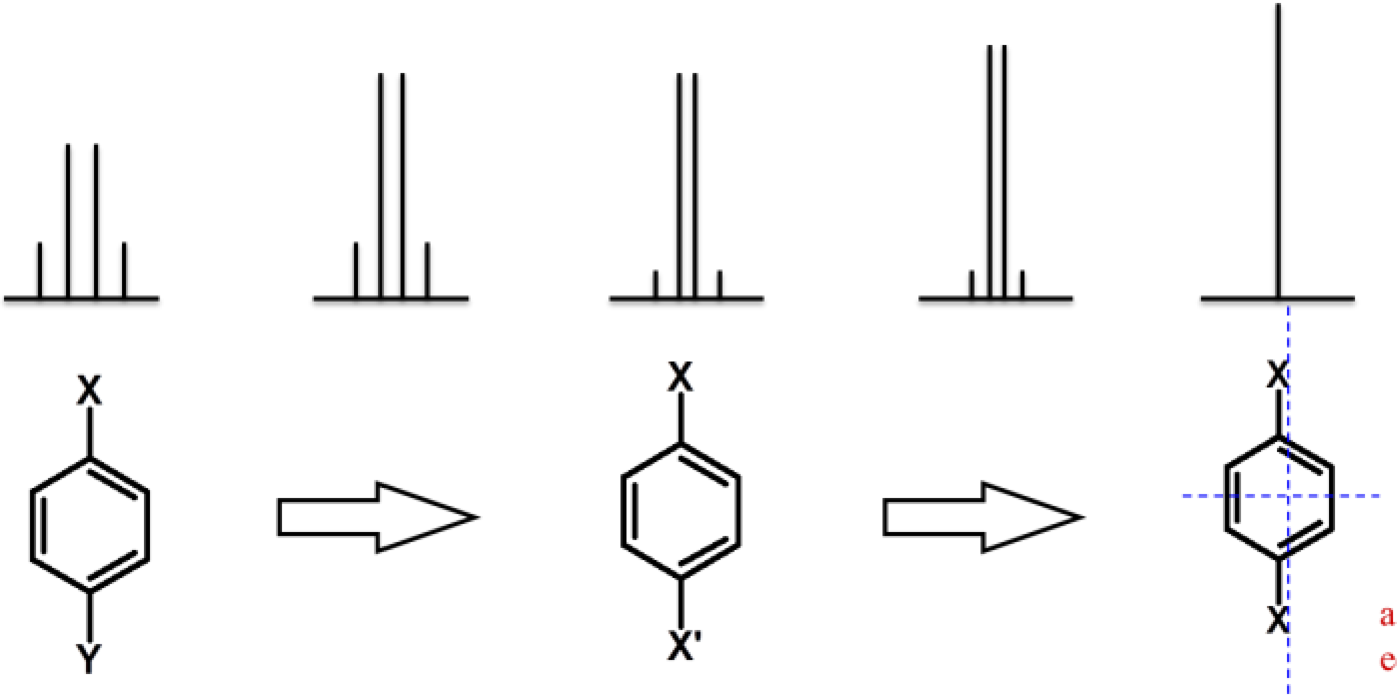


Ortho-

$^{3}J = 6\text{-}10$ Hz

The *p*-Disubstituted Rings

- 1,4-Disubstituted benzene rings will show a pair of doublets, when the two groups on the ring are very different



all H equivalent

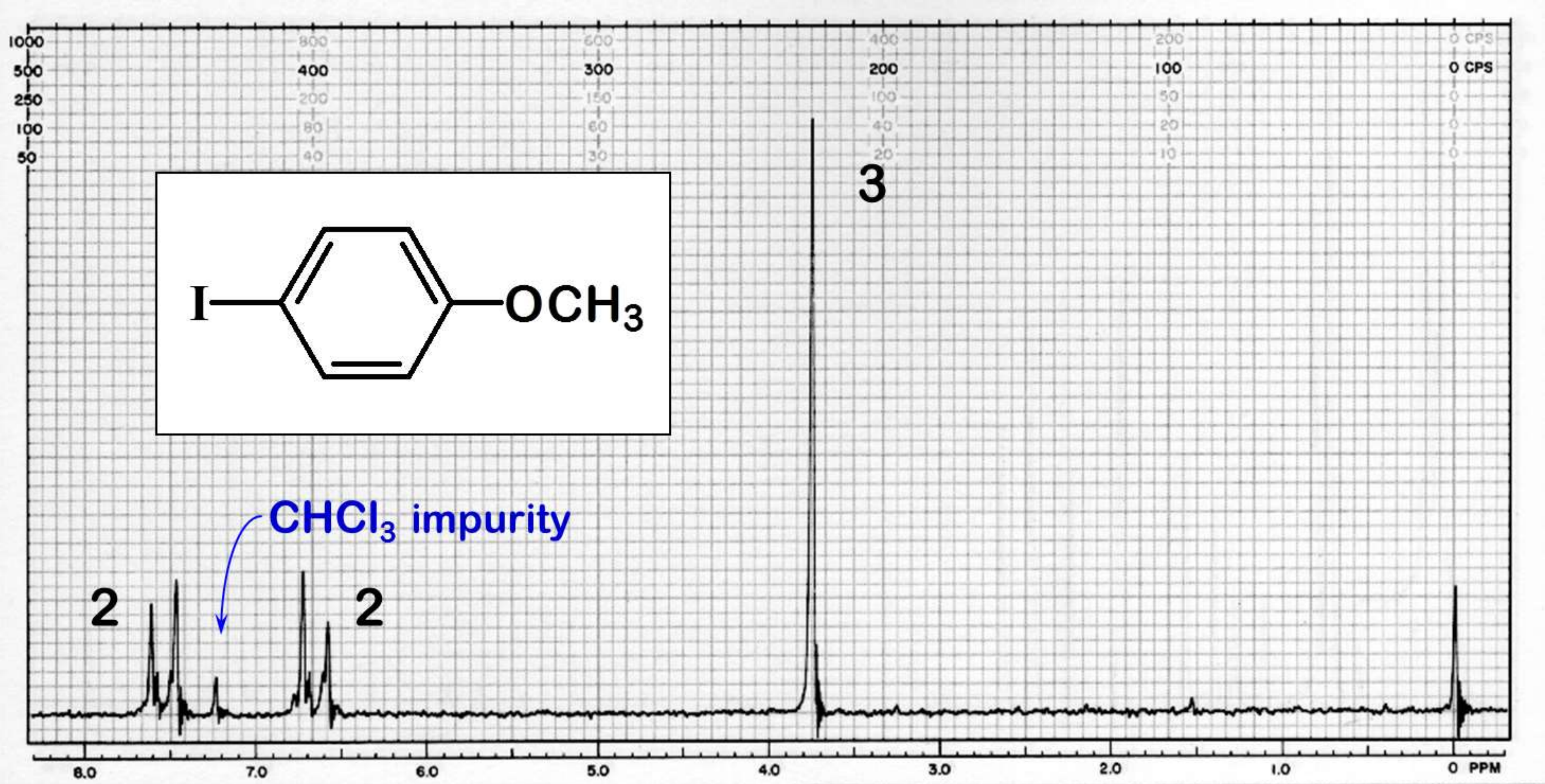
X ≠Y

X ≈ X'

X = X

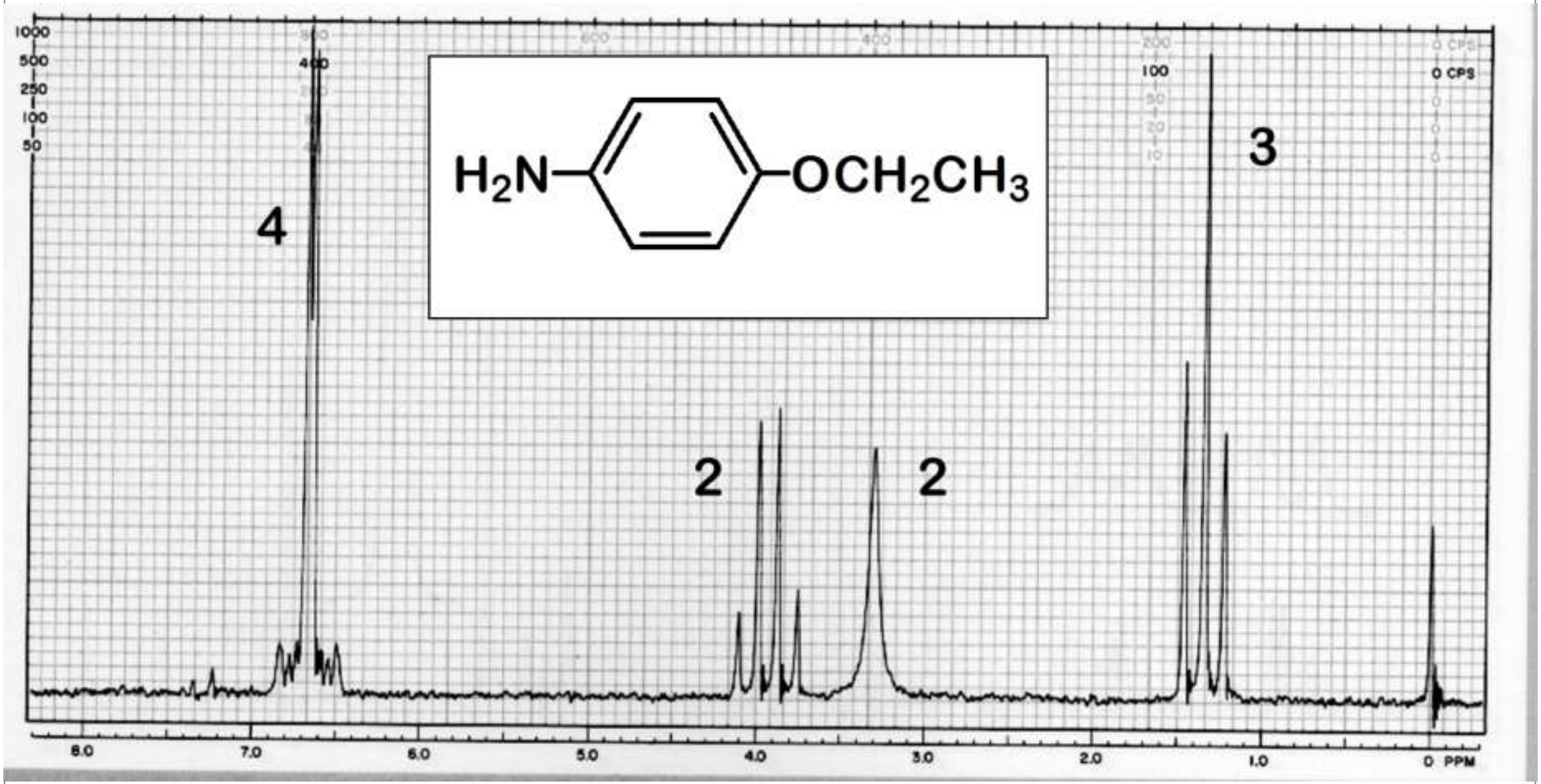
same groups

NMR Spectrum of 1-iodo-4-methoxybenzene

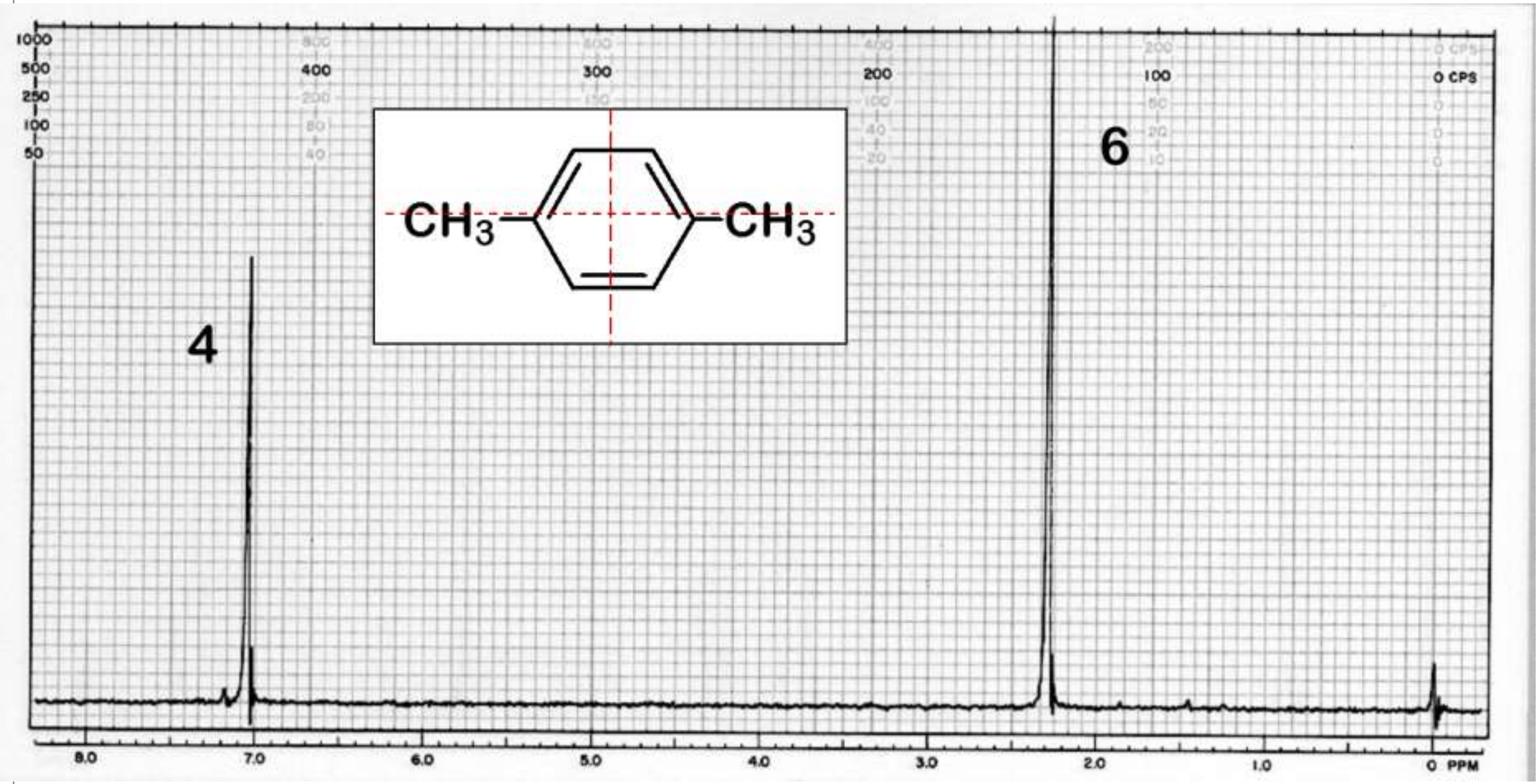


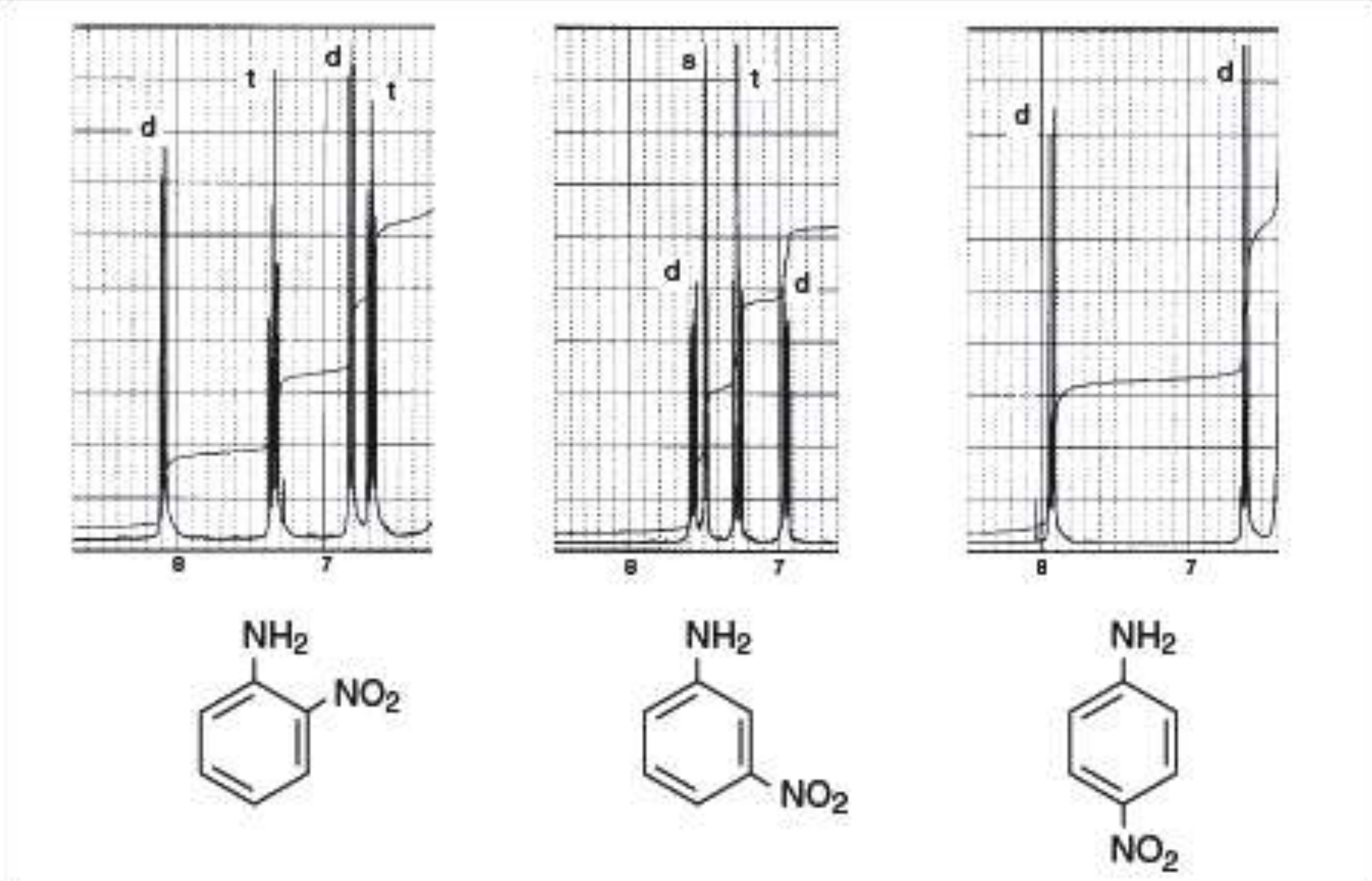
AA‘BB‘ pattern

NMR Spectrum of 1-amino-4-ethoxybenzene

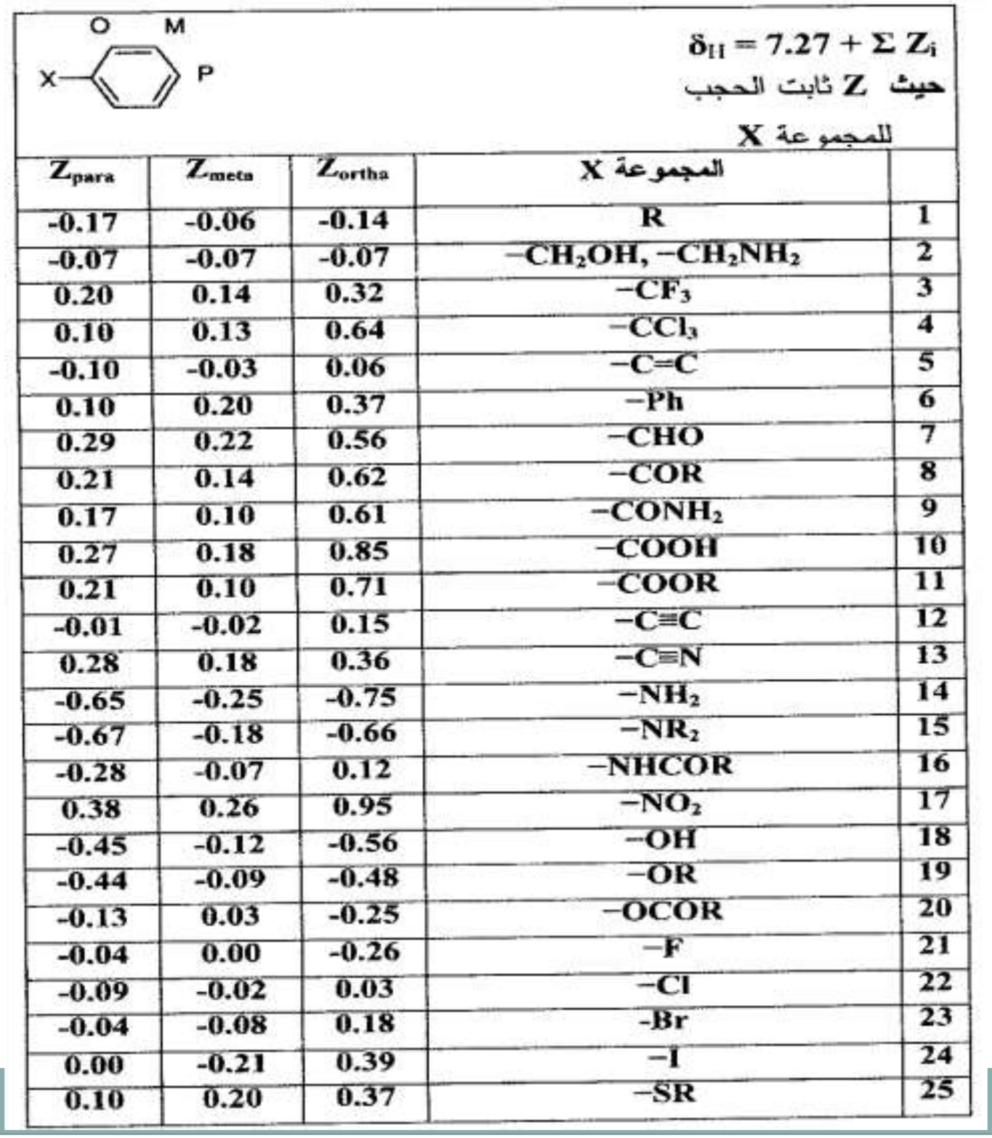


NMR Spectrum of *p*-Xylene (1,4-dimethylbenzene)




d
t
d
t
8
7
NH2
NO2
s
t
d
d
8
7
NH2
NO2
d
d
8
7
NH2
NO2

Estimation of Proton Chemical shifts in Substituted Benzene



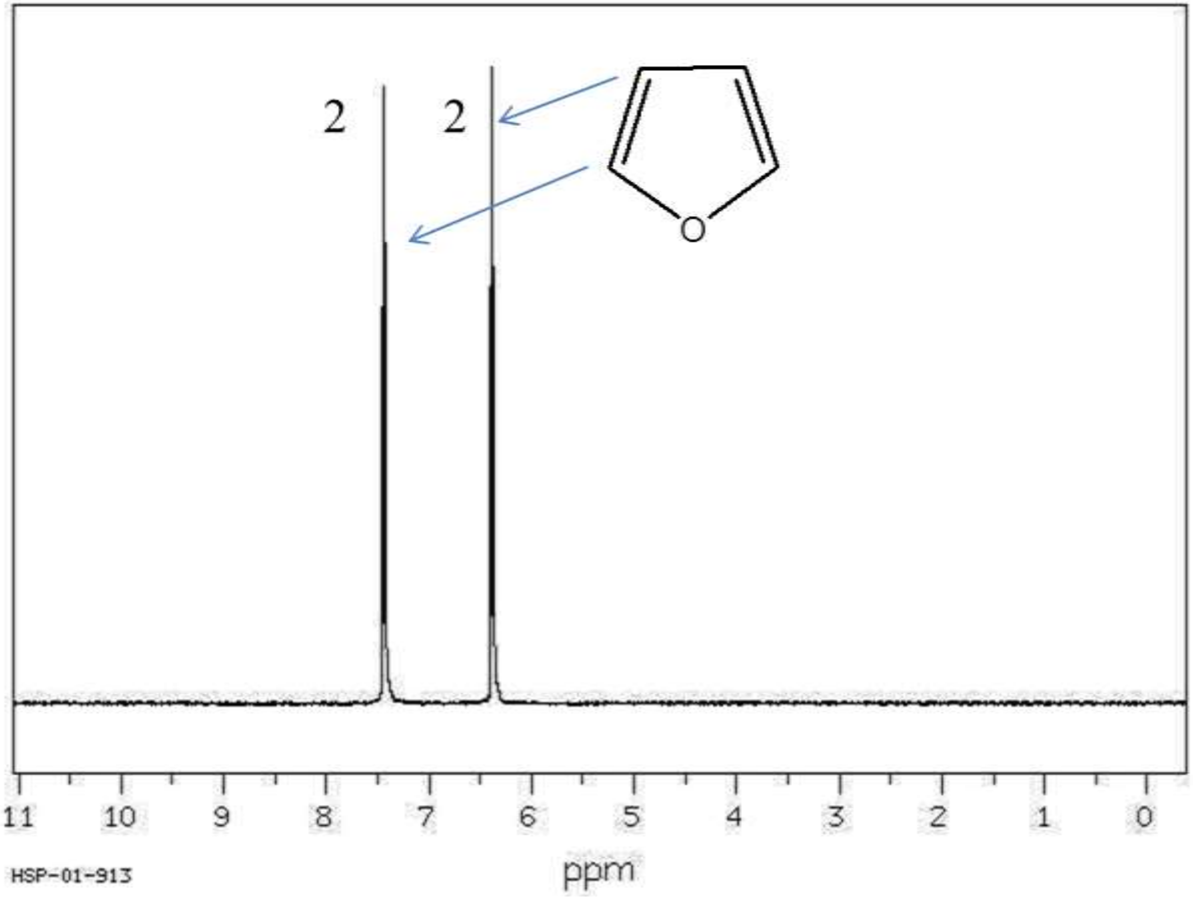
$\delta_H = 7.27 + \Sigma Z_i$

حيث Z ثابت الحجب

للمجموعة X

	المجموعة X	Z_{ortho}	Z_{meta}	Z_{para}
1	R	-0.14	-0.06	-0.17
2	$-CH_2OH$, $-CH_2NH_2$	-0.07	-0.07	-0.07
3	$-CF_3$	0.32	0.14	0.20
4	$-CCl_3$	0.64	0.13	0.10
5	$-C=C$	0.06	-0.03	-0.10
6	$-Ph$	0.37	0.20	0.10
7	$-CHO$	0.56	0.22	0.29
8	$-COR$	0.62	0.14	0.21
9	$-CONH_2$	0.61	0.10	0.17
10	$-COOH$	0.85	0.18	0.27
11	$-COOR$	0.71	0.10	0.21
12	$-C\equiv C$	0.15	-0.02	-0.01
13	$-C\equiv N$	0.36	0.18	0.28
14	$-NH_2$	-0.75	-0.25	-0.65
15	$-NR_2$	-0.66	-0.18	-0.67
16	$-NHCOR$	0.12	-0.07	-0.28
17	$-NO_2$	0.95	0.26	0.38
18	$-OH$	-0.56	-0.12	-0.45
19	$-OR$	-0.48	-0.09	-0.44
20	$-OCOR$	-0.25	0.03	-0.13
21	$-F$	-0.26	0.00	-0.04
22	$-Cl$	0.03	-0.02	-0.09
23	$-Br$	0.18	-0.08	-0.04
24	$-I$	0.39	-0.21	0.00
25	$-SR$	0.37	0.20	0.10

NMR Spectrum of Furan



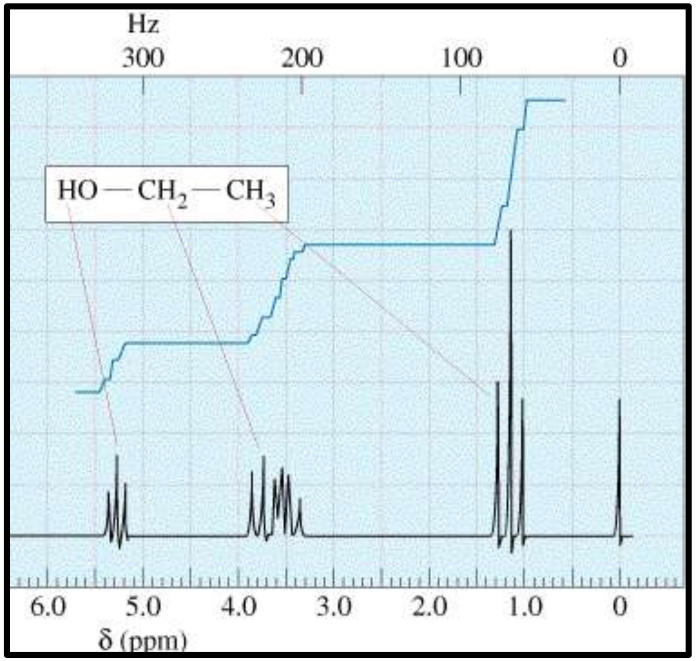
Hydroxyl and Amino Protons

- Hydroxyl and amino protons can appear almost anywhere in the spectrum (H-bonding).

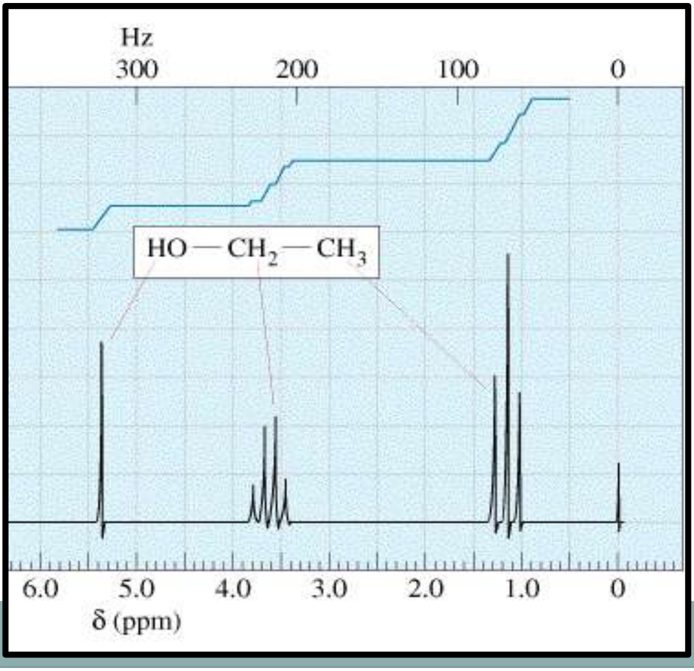
- These absorptions are usually broader than other proton peaks and can often be identified because of this fact.

- Carboxylic acid protons generally appear far downfield near 10 to 12 ppm.

O-H Proton

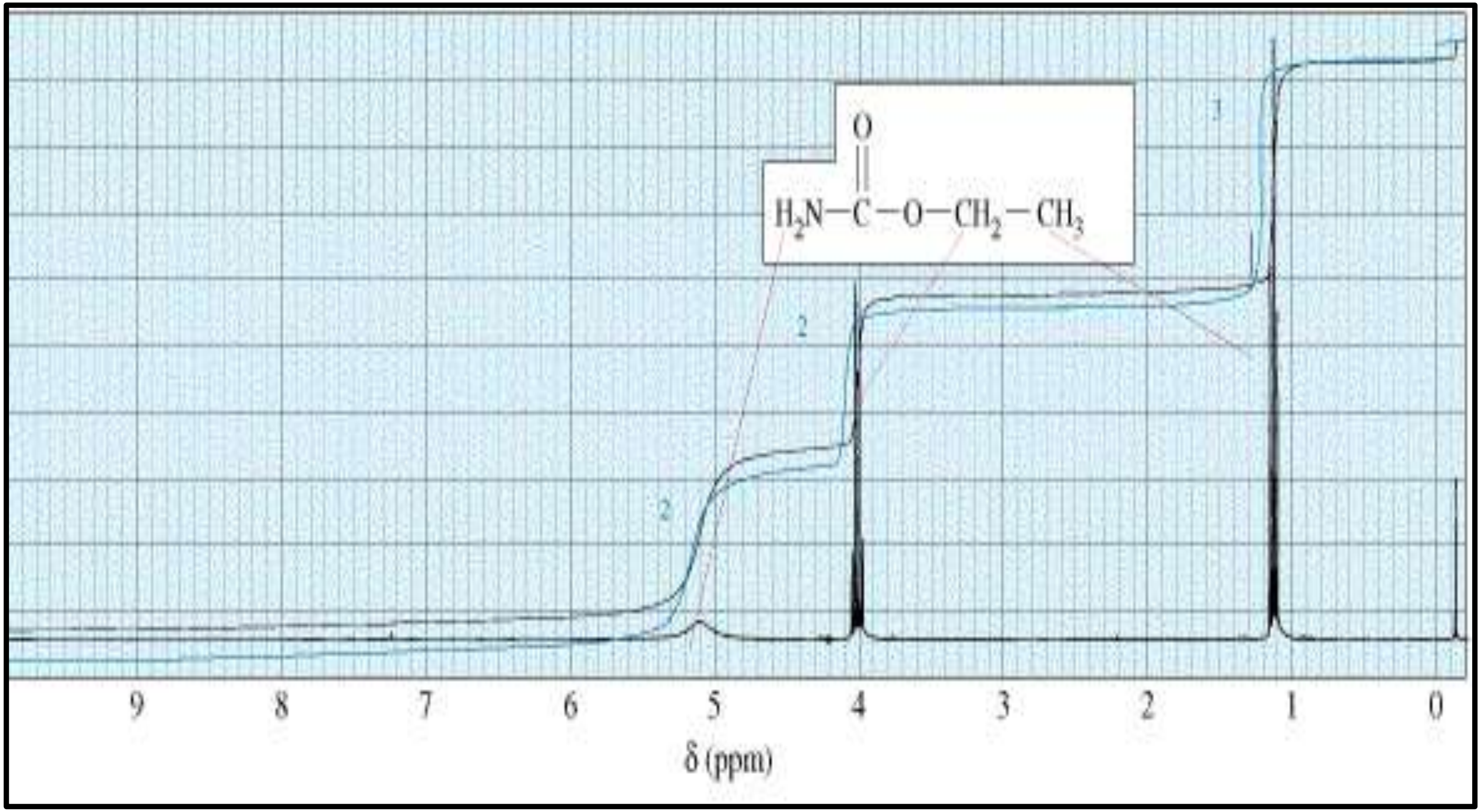


Ultrapure samples of ethanol show splitting.

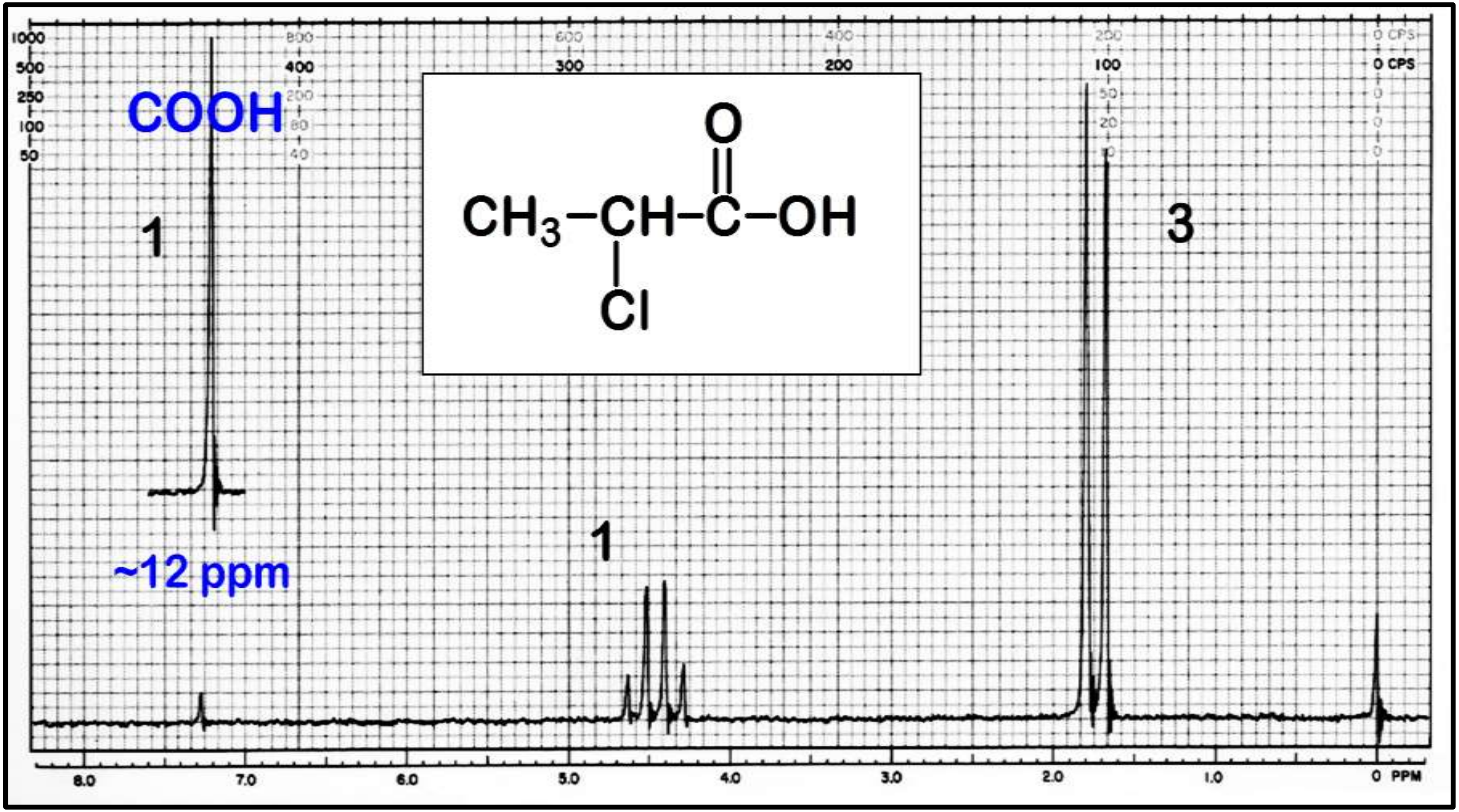


Ethanol with a small amount of acidic or basic impurities will not show splitting.

N-H Proton



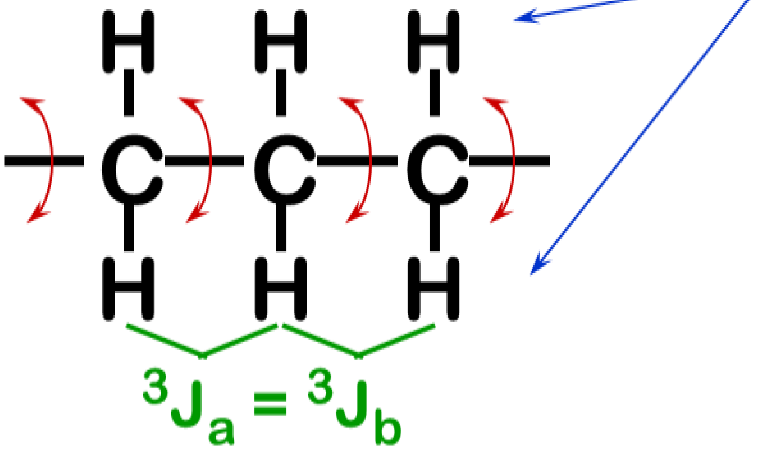
NMR Spectrum of 2-Chloropropanoic Acid



Unequal Coupling Tree Diagrams

Splitting Diagrams aka “ Tree Diagrams ”

The Typical Situation where the n+1 Rule Applies



Hydrogens can interchange their positions by rotations about the C-C bonds.

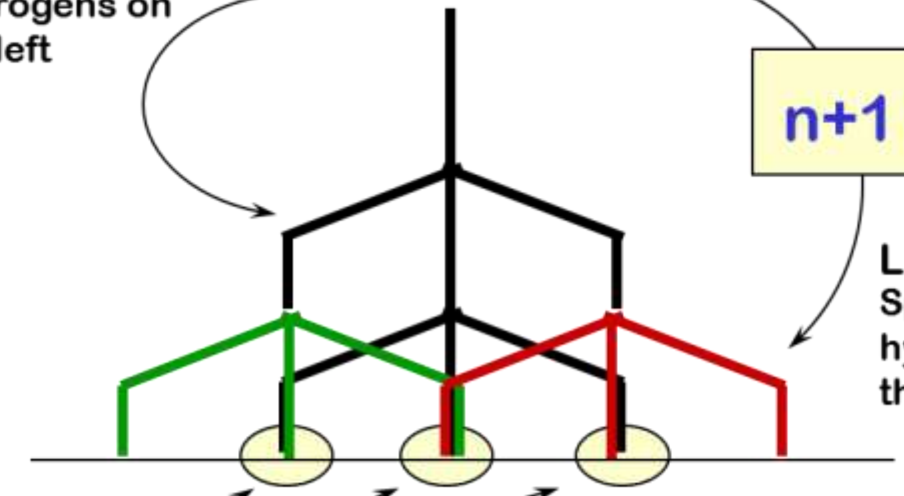
This makes all the hydrogens on each of the carbon atoms equivalent.

All the couplings along the chain have the same J value.

The n+1 rule is followed .....

LEVEL ONE
Splitting from
hydrogens on
the left

$-CH_2-CH_2-CH_2-$



$n+1 = (4 + 1) = 5$

LEVEL TWO
Splitting from
hydrogens on
the right

INTENSITIES

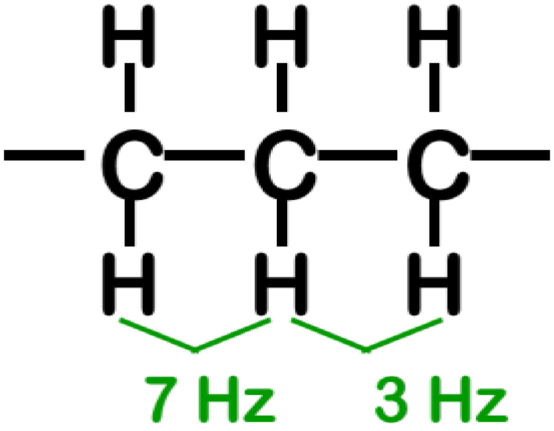
1:2:1
1:2:1
1:2:1
\+ 1:2:1

1:4:6:4:1

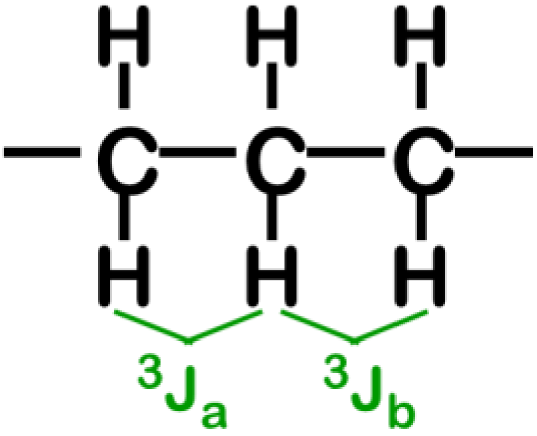
Splittings
overlap

..... because of overlapping legs. You get the quintet predicted by the n+1 rule.

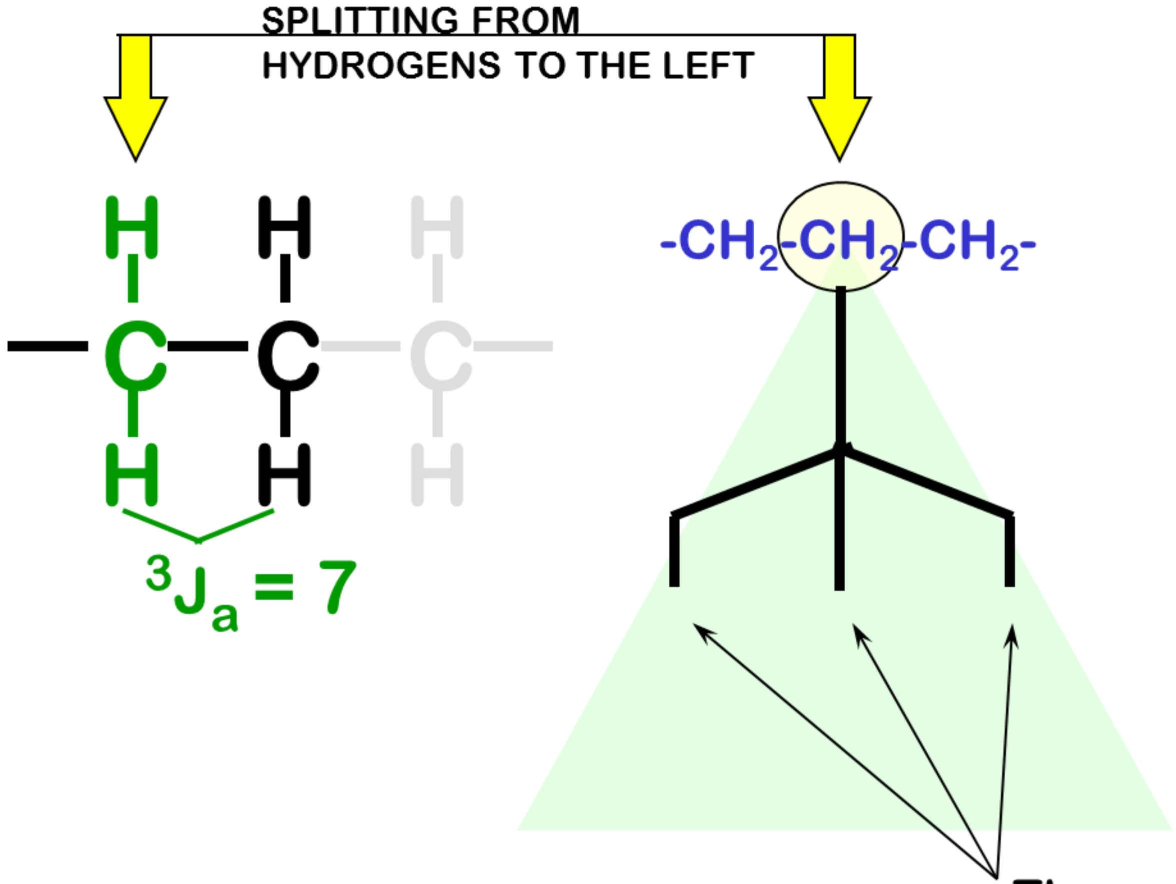
What happens when the J values are not equal ?



$^3J_a \neq {}^3J_b$



A “ Splitting Tree ” is constructed



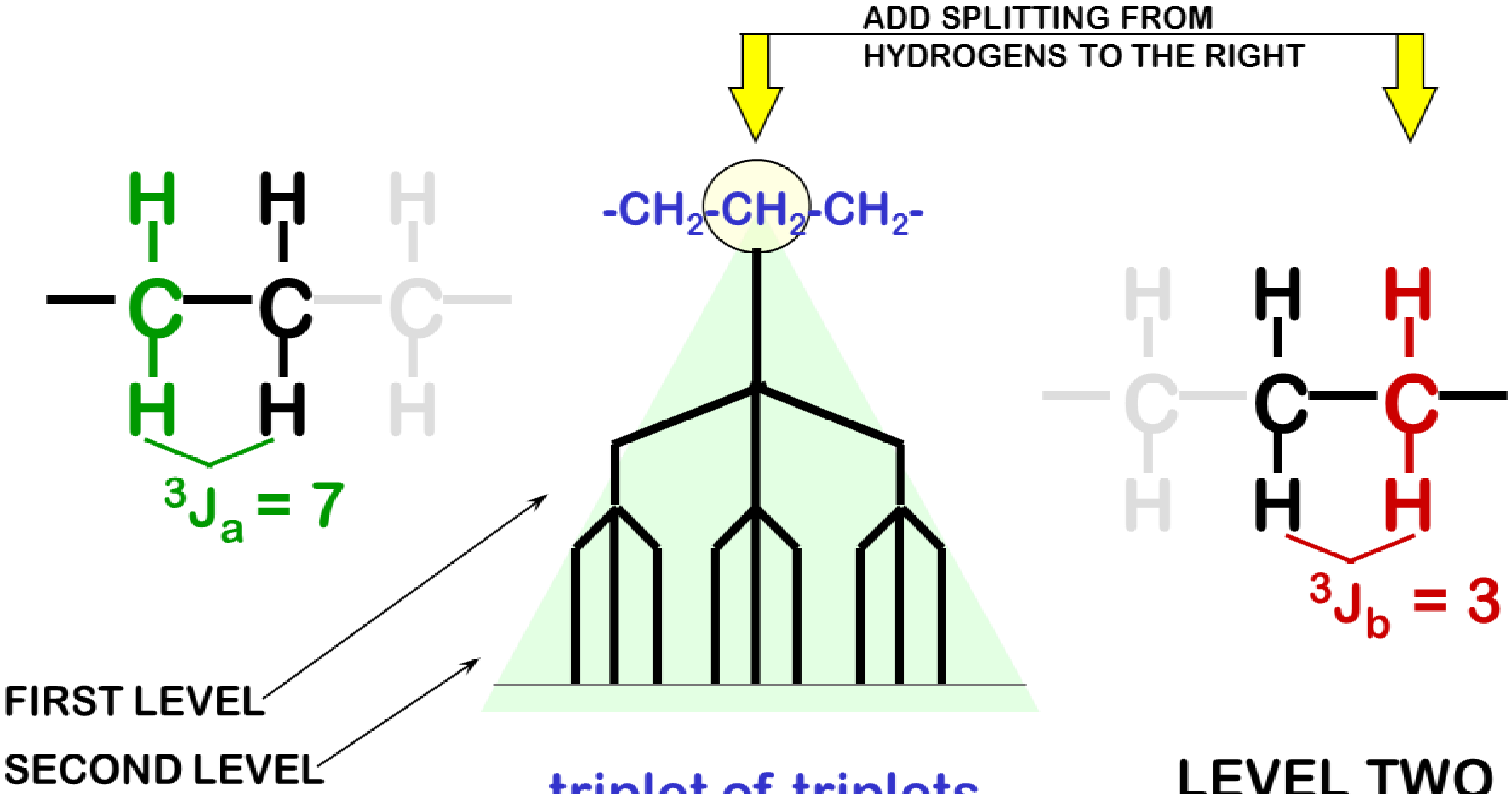
LEVEL ONE

The largest J value is usually used first.

Two neighbors gives a triplet.

The next splittings will be added to <u>each</u> <u>leg</u> of the first splitting.

Each level of the splitting uses the n+1 rule.



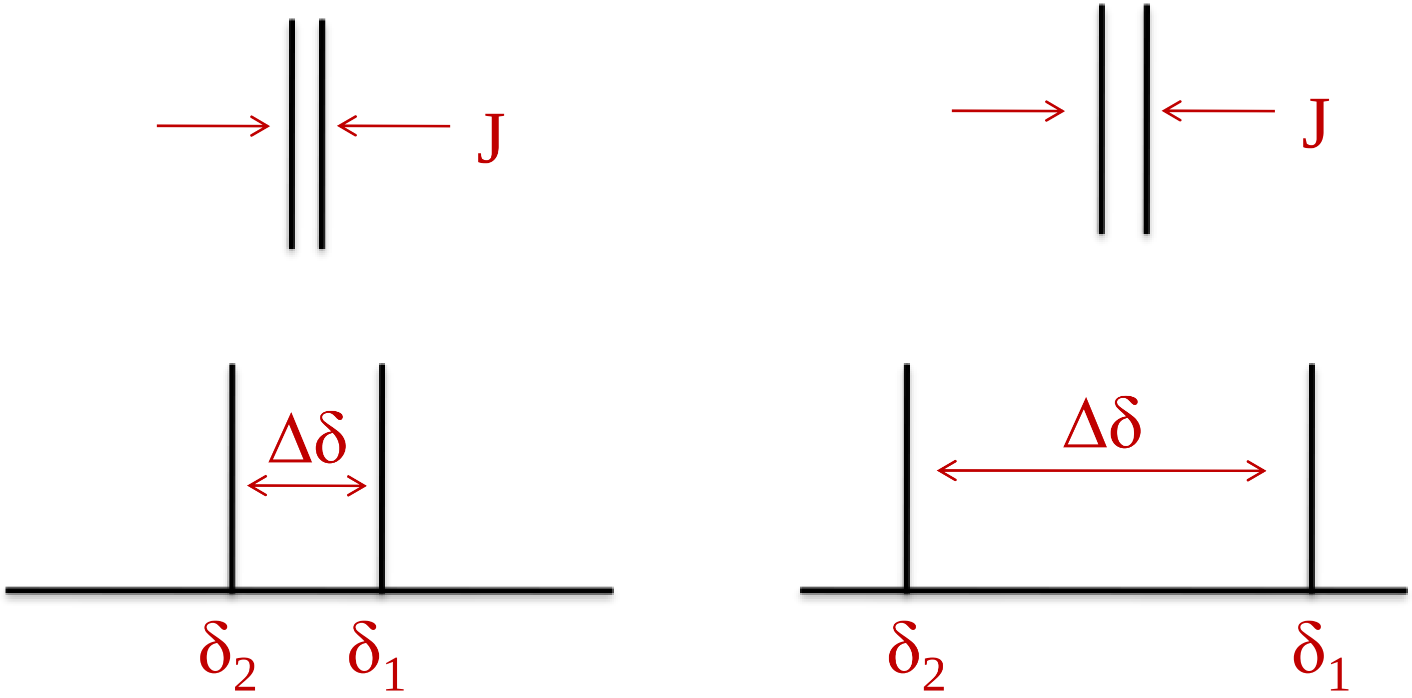
triplet of triplets

LEVEL TWO

The smaller splitting is used second.

It is also a triplet.

Simple and Complex Spectra



$\Delta\delta/J < 10$

Second-order spectra

$\Delta\delta/J > 10$

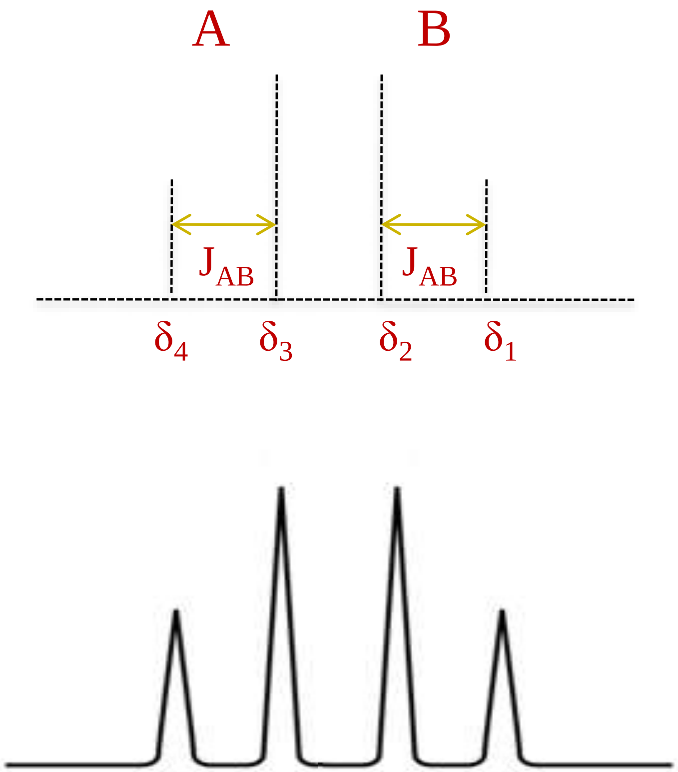
First-order spectra

Classification of splitting systems

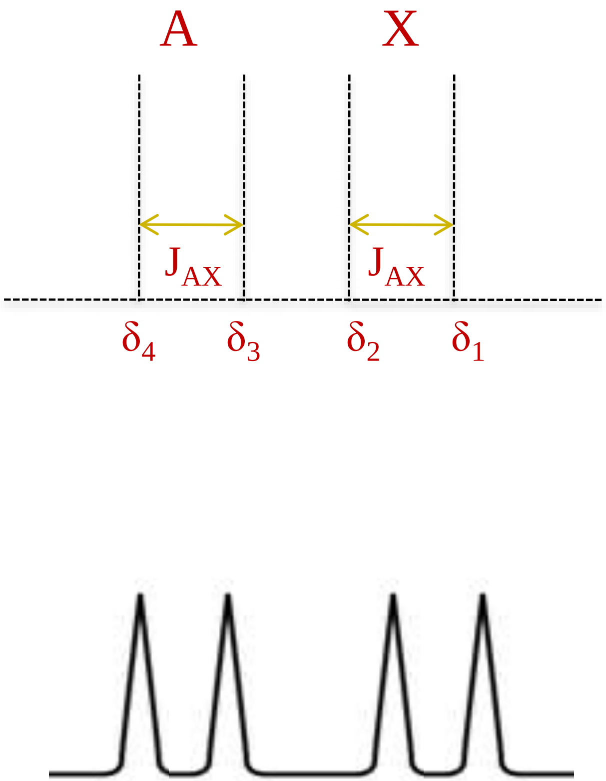
- AB pattern
- AX pattern
- ABC pattern
- ABX pattern
- AMX pattern

AB and AX patterns

$\Delta\delta \approx J$

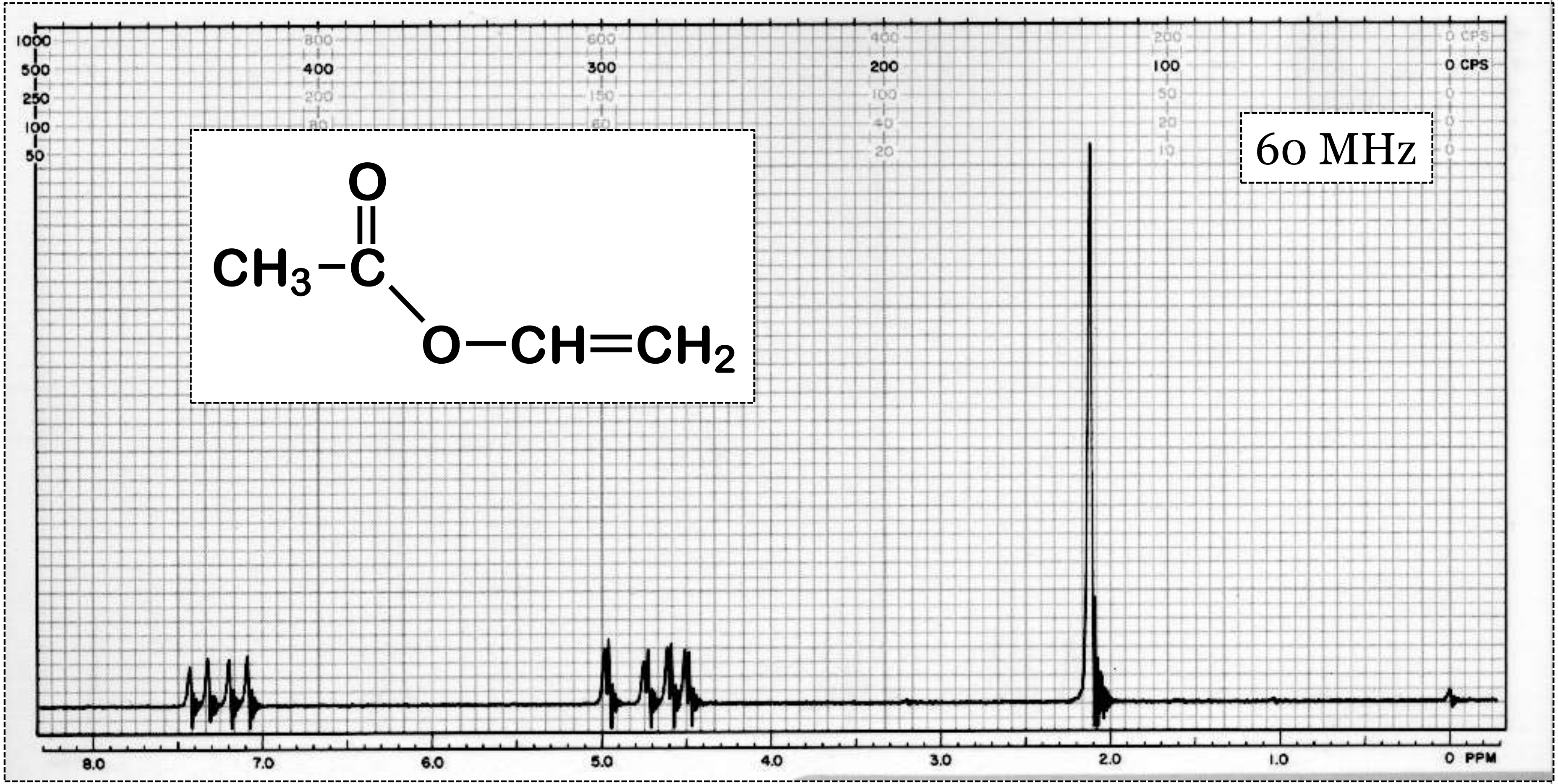


$\Delta\delta > J$



AMX pattern

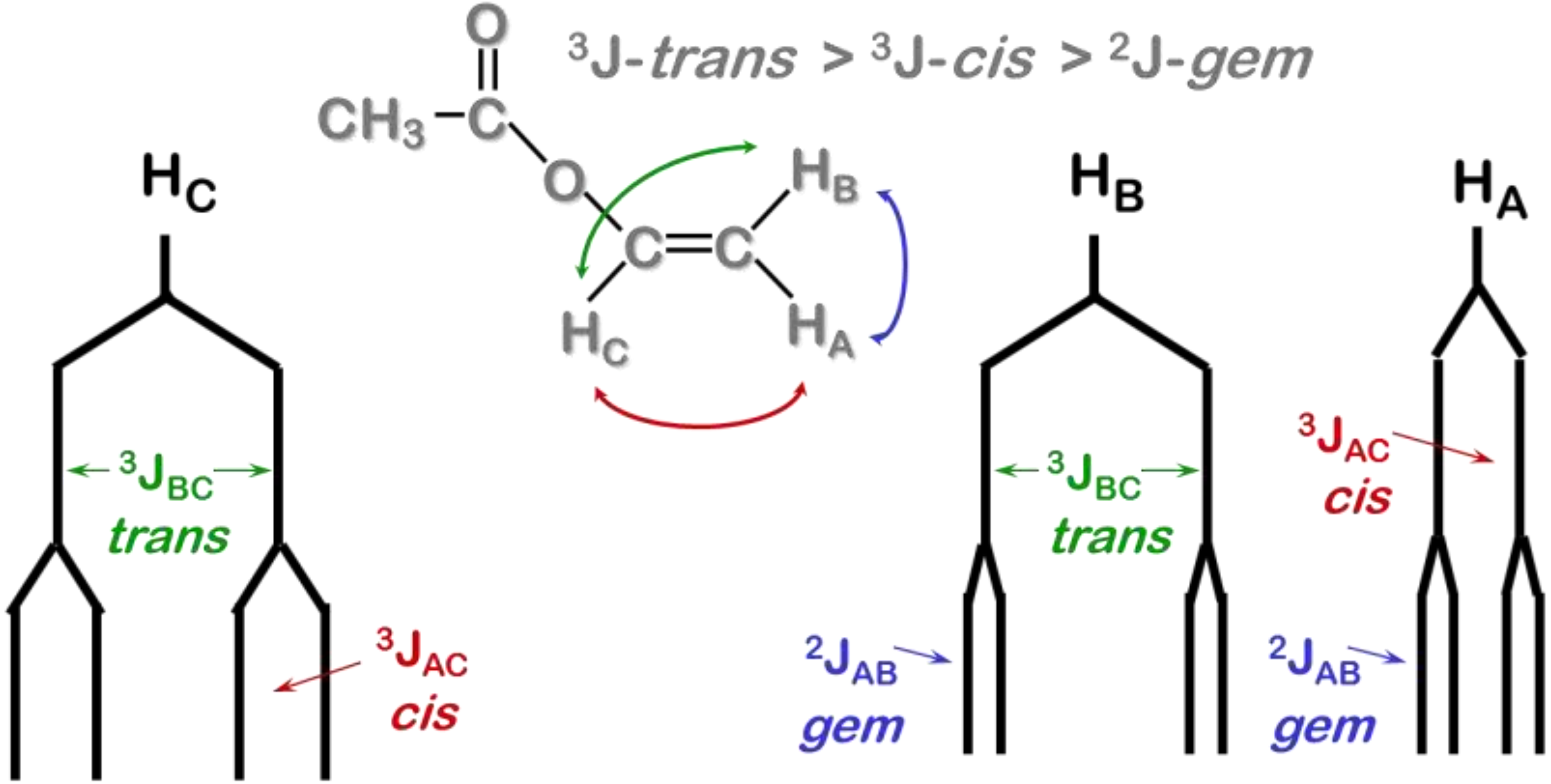
NMR Spectrum of Vinyl Acetate



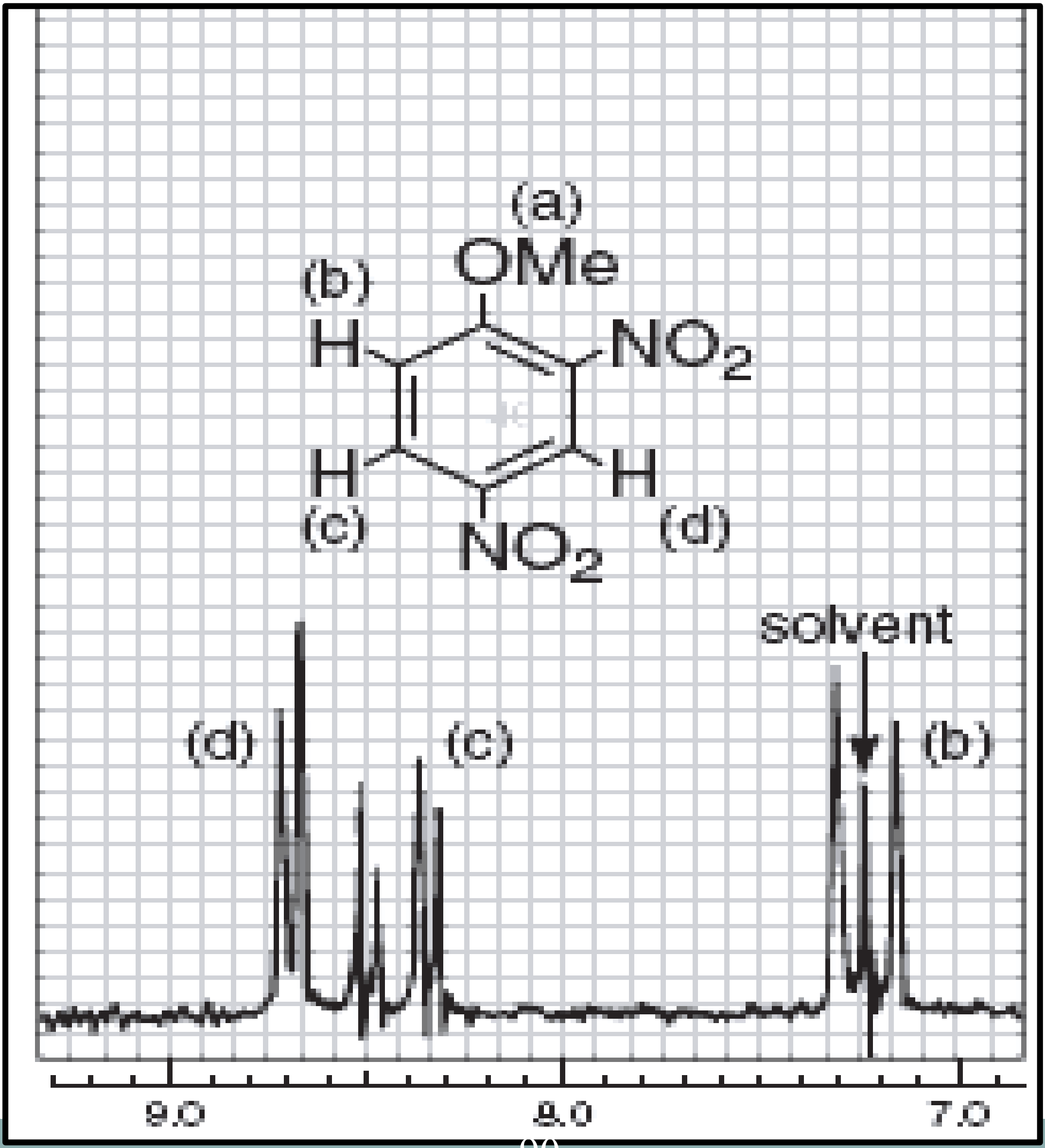
$CH_3-C(=O)-O-CH=CH_2$

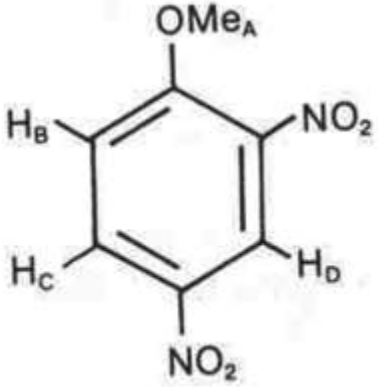
60 MHz

^{3}J-*trans* > ^{3}J-*cis* > ^{2}J-*gem*



2,4-Dinitroanisole

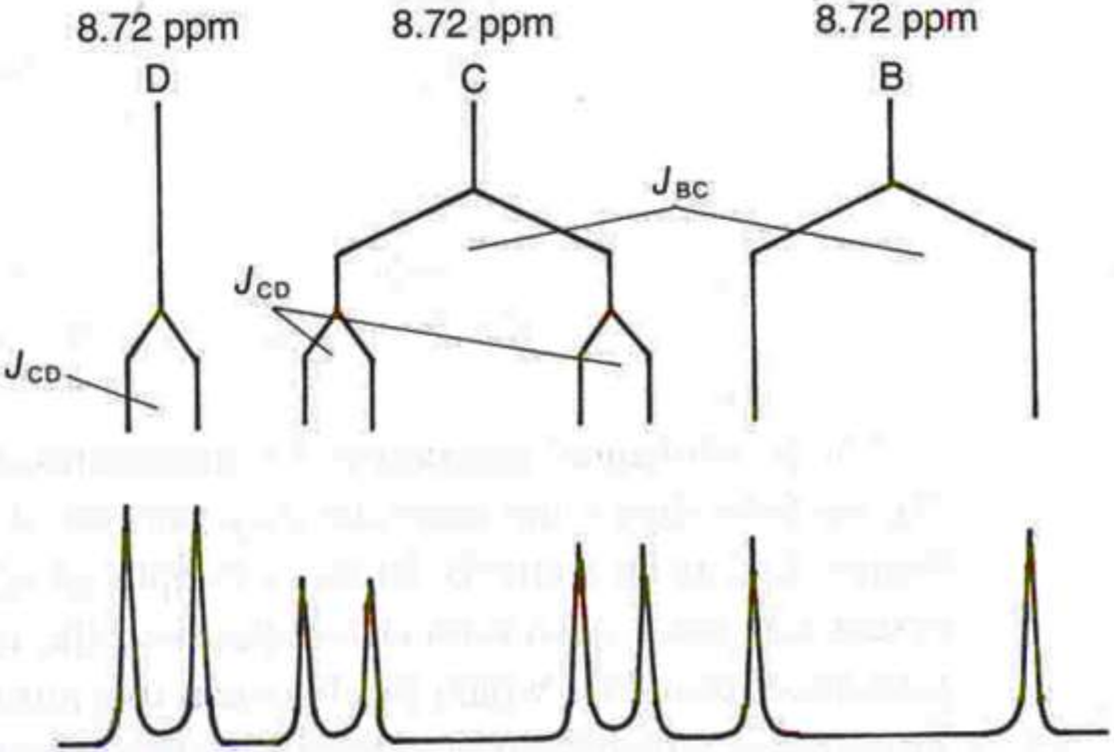




$^3J_{BC}$ ~ 8 *ortho*

$^4J_{CD}$ ~ 2 *meta*

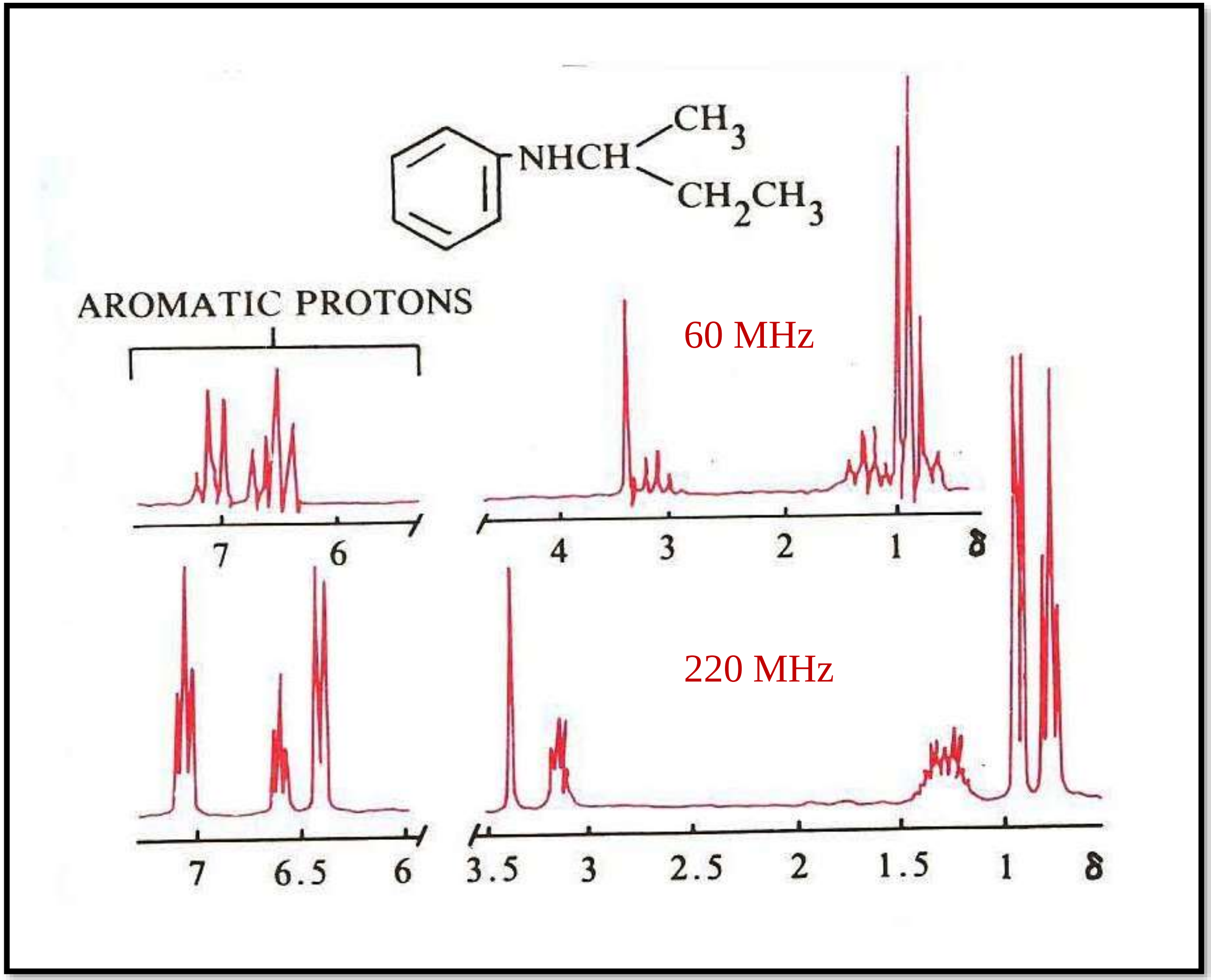
$^5J_{BD}$ ~ 0 *para*



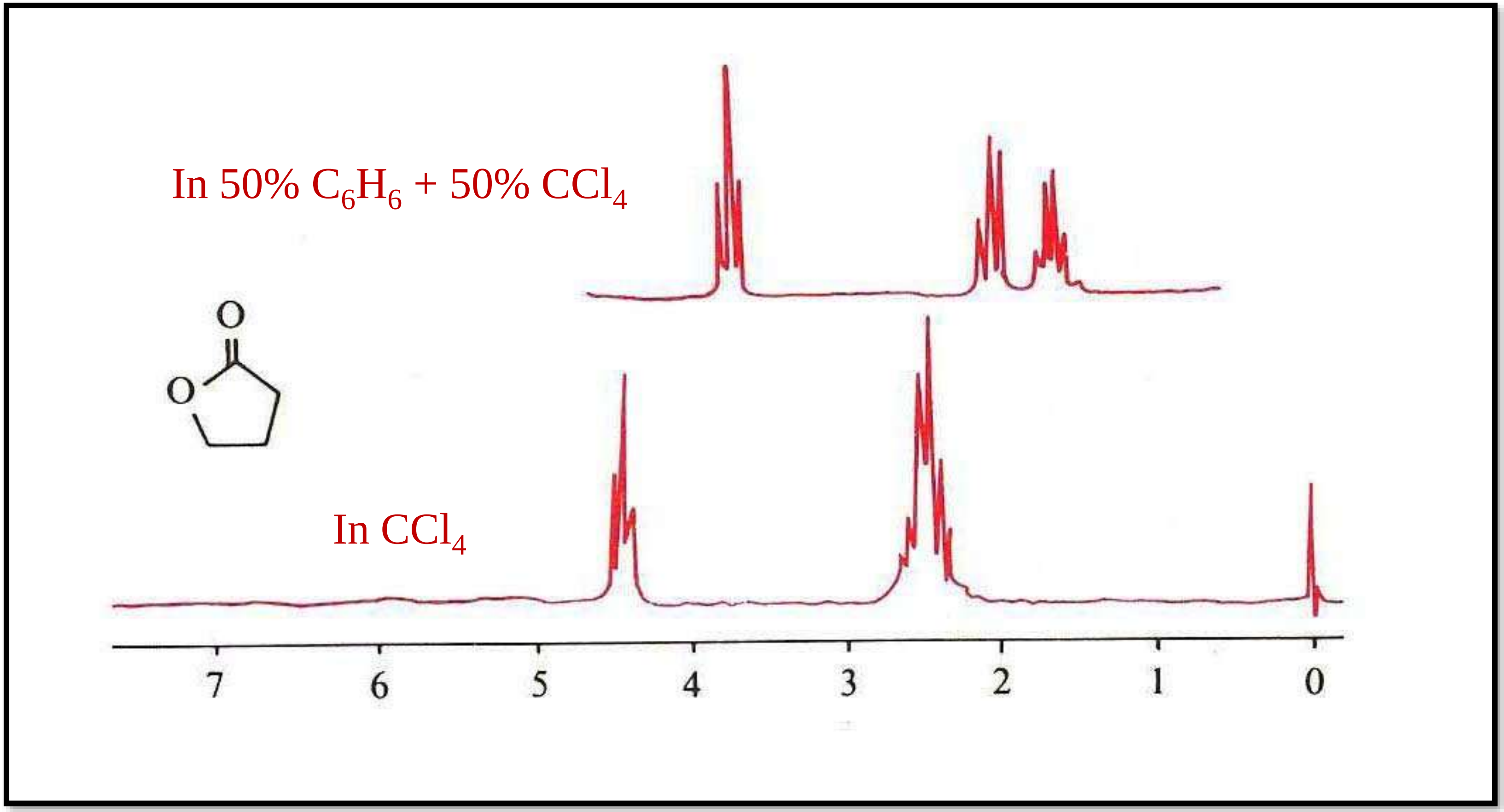
Simplification of Complex ^{1}H-NMR Spectra

- Increasing the Frequency of the Instrument
- Deuteration
- Change the Solvent
- Double resonance
- Shift reagents

Increasing the Frequency of the Instrument



Change the Solvent



Double resonance