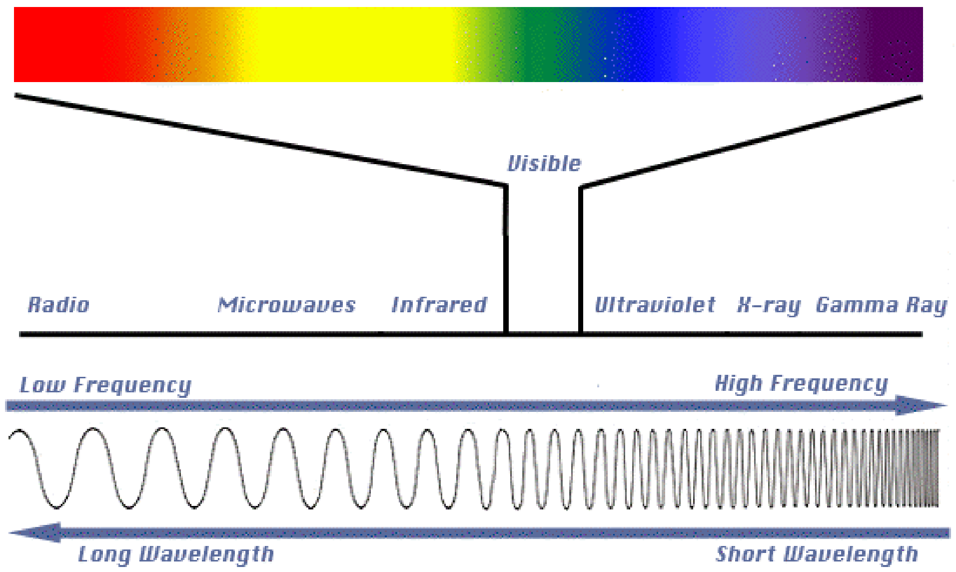
Nuclear Magnetic Resonance Spectroscopy

NMR Spectroscopy

NMR spectroscopy is a form of ***absorption*** spectrometry.



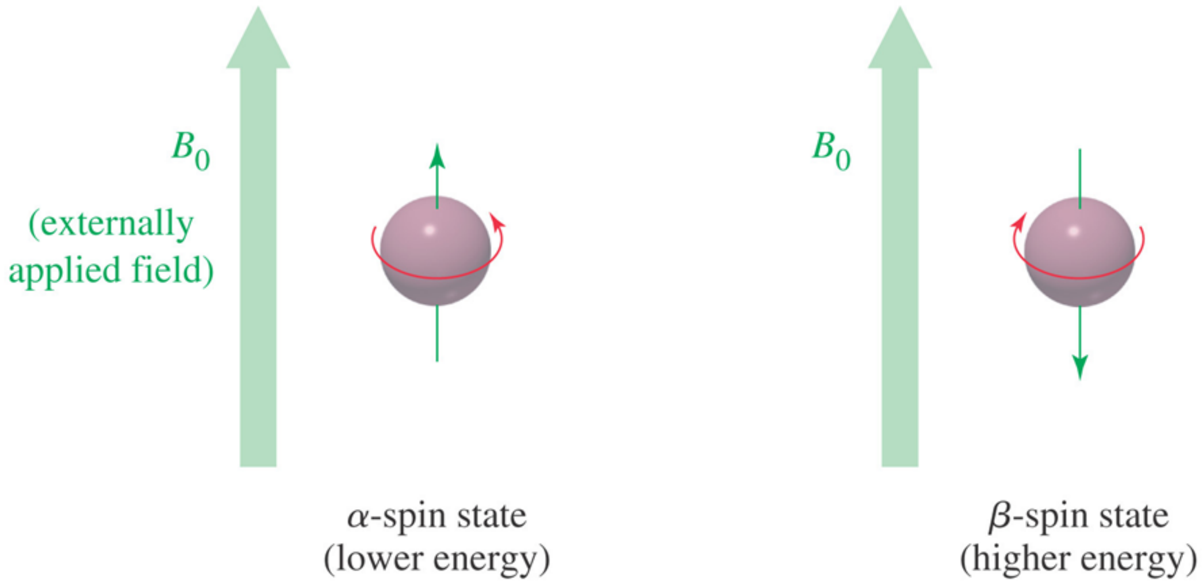
Most absorption techniques (*e.g.* – Ultraviolet-Visible and Infrared) involve the electrons… in the case of NMR, it is the ***nucleus*** of the atom which determines the response.

An applied (***magnetic***) field is necessary for the absorption to occur.

Nuclear Magnetic Resonance (NMR) Spectroscopy

direct observation of the H’s and C’s of a molecules

Nuclei are positively charged and spin on an axis; they create a tiny magnetic field



Not all nuclei are suitable for NMR.

^{1}H and ^{13}C are the most important NMR active nuclei in organic chemistry

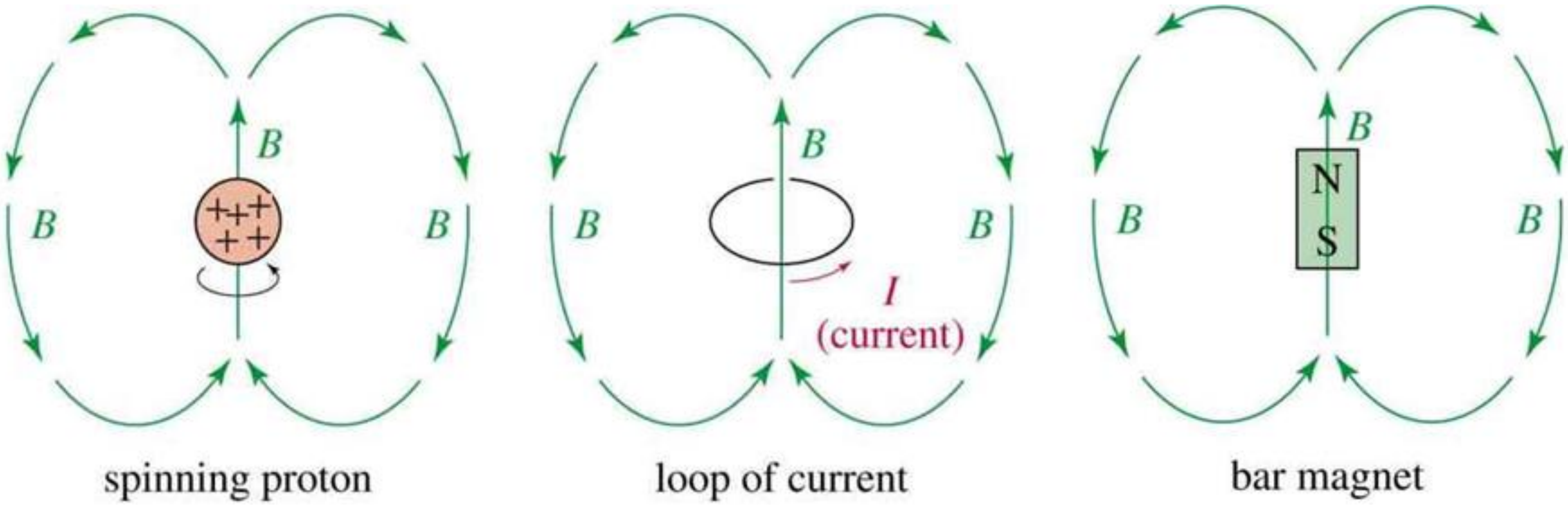
Natural Abundance

^{1}H 99.9% ^{13}C 1.1%

^{12}C 98.9% (not NMR active)

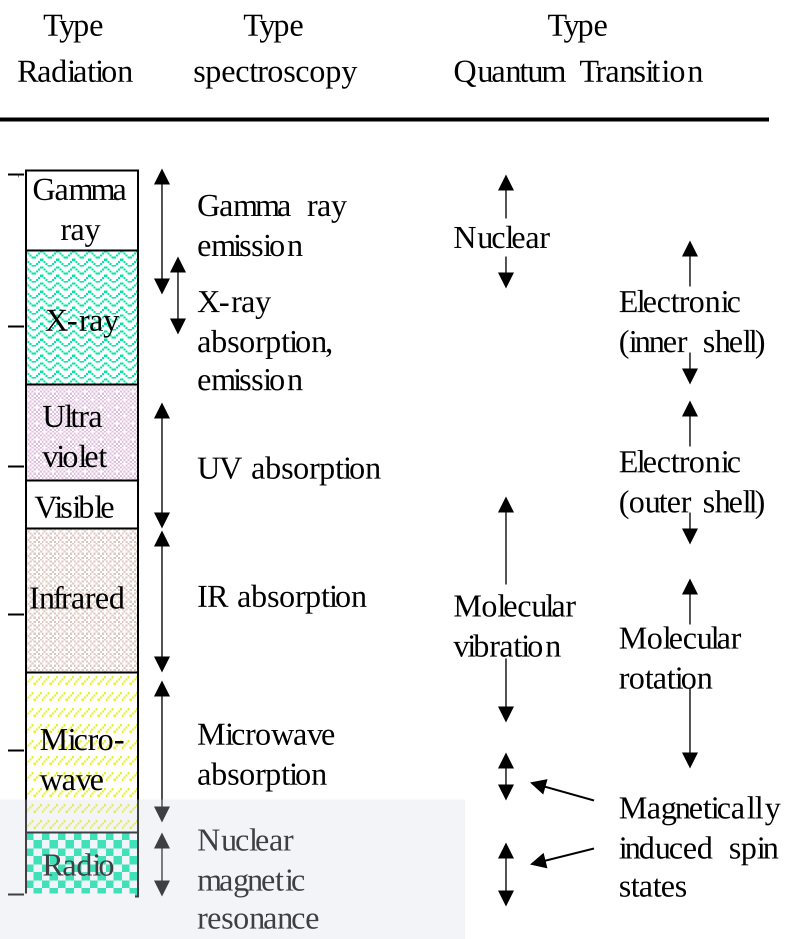
Nuclear Spin

- A nucleus with an odd atomic number or an odd mass number has a nuclear spin.
- The spinning charged nucleus generates a magnetic field.



Spectral Properties, Application and Interactions of Electromagnetic Radiation

Energy		Wave Number V	Wavelength λ	Frequency υ
Kcal/mol	Electron volts, eV	cm^{-1}	cm	Hz
9.4×10^{7}	4.9×10^{6}	3.3×10^{10}	3×10^{-11}	10^{21}
9.4×10^{3}	4.9×10^{2}	3.3×10^{6}	3×10^{-7}	10^{17}
9.4×10^{1}	4.9×10^{0}	3.3×10^{4}	3×10^{-5}	10^{15}
9.4×10^{-1}	4.9×10^{-2}	3.3×10^{2}	3×10^{-3}	10^{13}
9.4×10^{-3}	4.9×10^{-4}	3.3×10^{0}	3×10^{-1}	10^{11}
9.4×10^{-7}	4.9×10^{-8}	3.3×10^{-4}	3×10^{3}	10^{7}


Type Radiation

Type spectroscopy

Type Quantum Transition

Gamma ray

X-ray

Ultra violet

Visible

Infrared

Micro-wave

Radio

Gamma ray emission

X-ray absorption, emission

UV absorption

IR absorption

Microwave absorption

Nuclear magnetic resonance

Nuclear

Electronic (inner shell)

Electronic (outer shell)

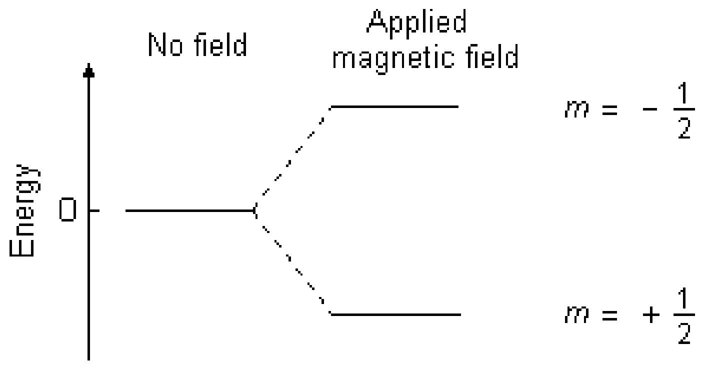
Molecular vibration

Molecular rotation

Magnetically induced spin states

Spin Quantum Numbers

The number of spin states is 2I + 1, where I is the spin quantum number.


Energy levels for a nucleus with spin quantum number 1/2

- If the number of neutrons **and** the number of protons are both even, then the nucleus has **NO** spin.
- If the number of neutrons **plus** the number of protons is odd, then the nucleus has a half-integer spin (i.e. 1/2, 3/2, 5/2)
- If the number of neutrons **and** the number of protons are both odd, then the nucleus has an integer spin (i.e. 1, 2, 3)

SPIN QUANTUM NUMBERS OF SOME COMMON NUCLEI

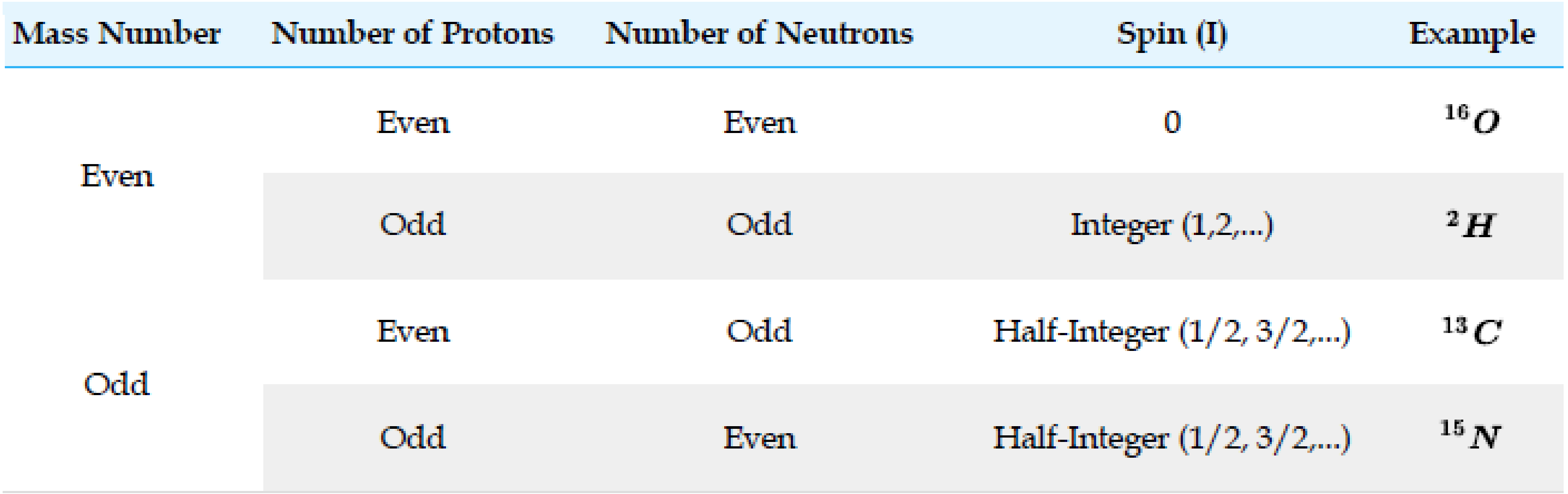
The most abundant isotopes of C and O do not have spin.

Element	P=1, N=0 ^{1}H	P=1, N=1 ^{2}H	P=6, N=6 ^{12}C	P=6, N=7 ^{13}C	P=7, N=7 ^{14}N	P=8, N=8 ^{16}O	P=9, N=10 ^{19}F
Nuclear Spin Quantum No (I)	1/2	1	0	1/2	1	0	1/2
No. of Spin States	2	3	0	2	3	0	2

Elements with either odd number of protons or neutrons (odd mass number or odd atomic number) have the property of nuclear “spin”.

The number of spin states is 2I + 1, where I is the spin quantum number.

Table. General rules for determination of nuclear spin quantum numbers



Mass Number	Number of Protons	Number of Neutrons	Spin (I)	Example
Even	Even	Even	0	^{16}O
	Odd	Odd	Integer (1,2,...)	^{2}H
Odd	Even	Odd	Half-Integer (1/2, 3/2,...)	^{13}C
	Odd	Even	Half-Integer (1/2, 3/2,...)	^{15}N

Atoms active in NMR

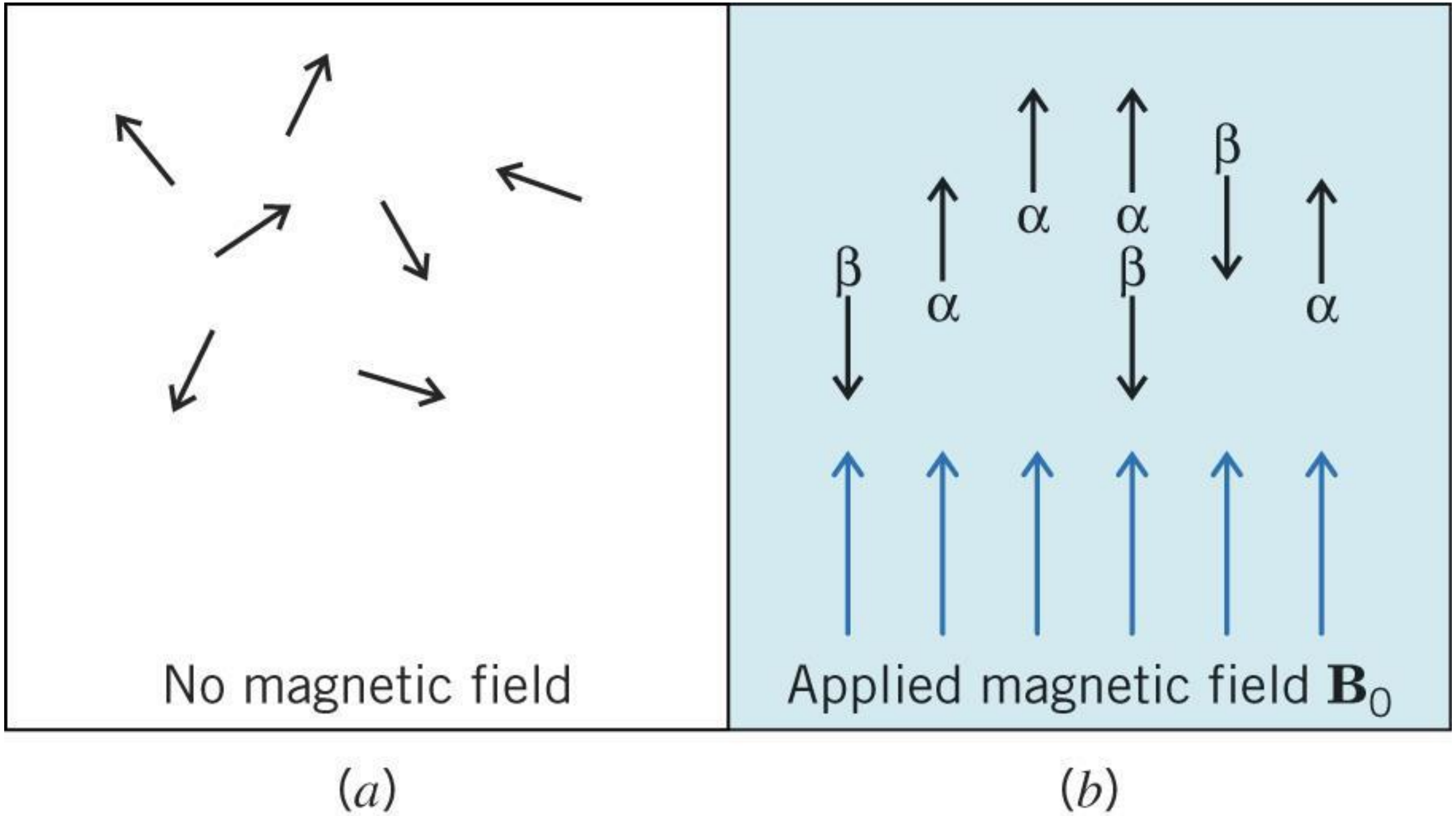
I = 1/2: ^{1}H, ^{13}C, ^{19}F, ^{31}P

I = 1: ^{2}H, ^{14}N

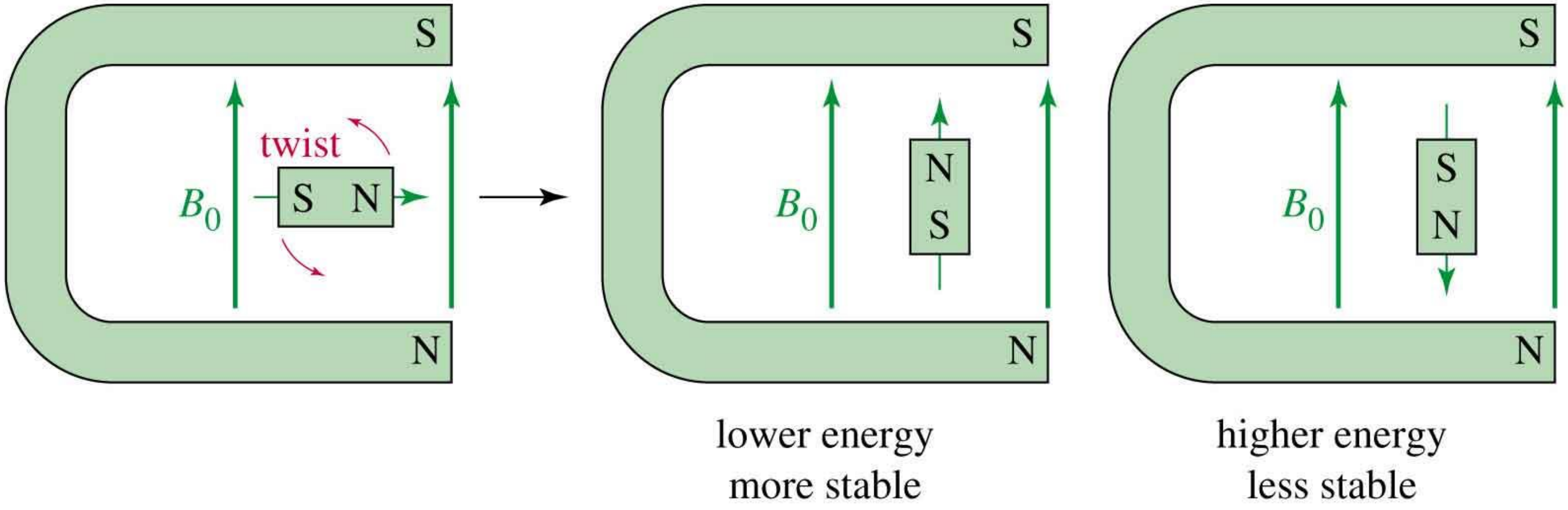
I = 3/2: ^{15}N

Atoms active in NMR

I= 0: ^{12}C, ^{16}O


No magnetic field
β
α
α
α
β
β
α
Applied magnetic field $\mathbf{B}_0$
(a)
(b)

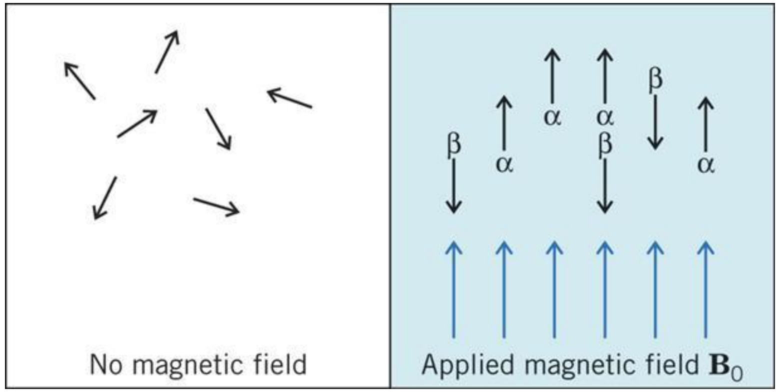
Behavior of spinning protons with external magnetic field



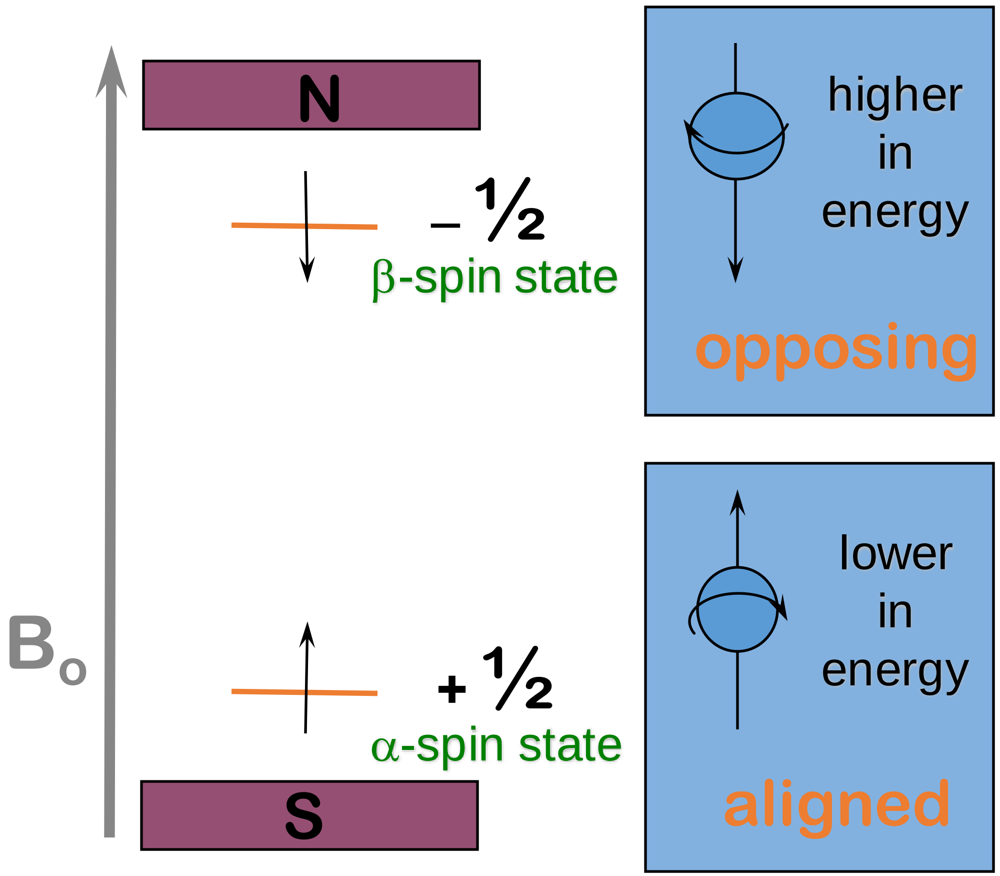
(α-spin state) **(β-spin state)**

THE NUCLEUS IN A MAGNETIC FIELD

When nuclei are exposed to external magnetic field of strength B_0, their spins line up parallel to the applied field, either spin aligned (α-spin state) or spin opposed (β-spin state) to the external field.



Nuclear Spin Energy Levels



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

Energy of spinning nuclei

The energy of the nucleus in these two states (orientations) is given by:

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

Energy of α-state
(spin aligned)

$$E_{+\frac{1}{2}} = -\frac{\gamma(+\frac{1}{2})h}{2\pi} B_0$$

$$E_{+\frac{1}{2}} = -\frac{\gamma h}{4\pi} B_0$$

Energy of β-state
(spin opposed)

$$E_{-\frac{1}{2}} = -\frac{\gamma(-\frac{1}{2})h}{2\pi} B_0$$

$$E_{-\frac{1}{2}} = \frac{\gamma h}{4\pi} B_0$$

Energy difference between the two state

$$\Delta E = \frac{\gamma h}{4\pi} B_0 - \left(-\frac{\gamma h}{4\pi} B_0\right) = \frac{\gamma h}{2\pi} B_0$$

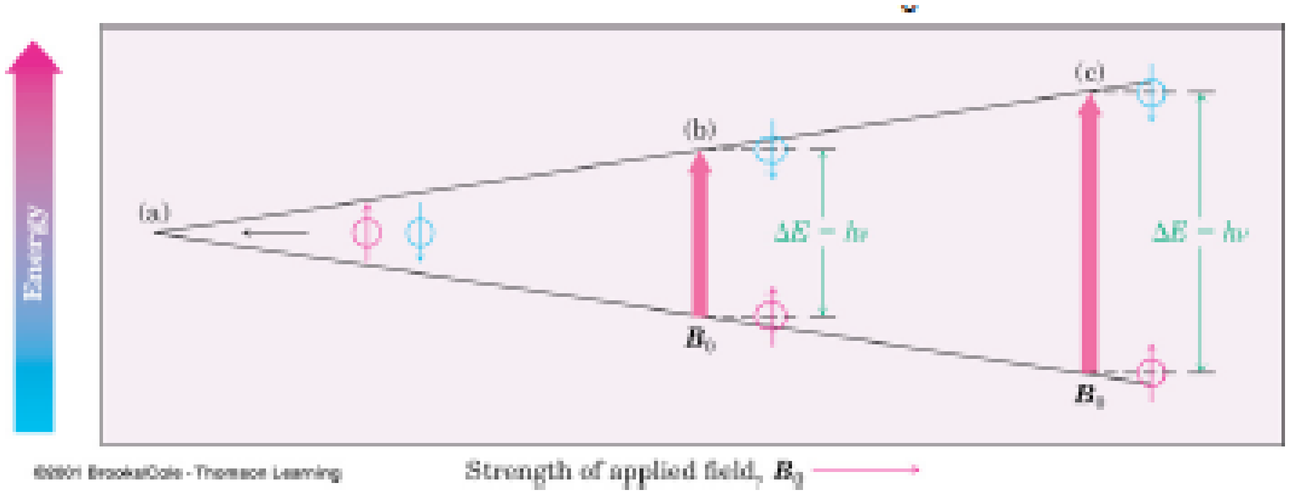
Absorption of electromagnetic radiation of frequency ν that correspond to in energy to ΔE

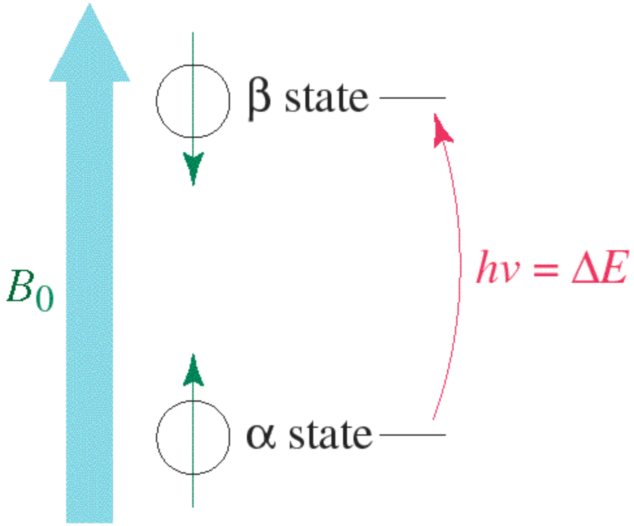
$$\Delta E = \cancel{h}\nu = \frac{\gamma \cancel{h}}{2\pi} B_0$$

Δ*E* and Magnet Strength

The energy difference between aligned and opposed to the external magnetic field (Bo) is generally small and is dependent upon Bo

Applied EM radiation (radio waves) causes the spin to flip and the nuclei are said to be in ***resonance*** with Bo





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

B_o = external magnetic field strength
γ = gyromagnetic ratio
^1H = 26,752 $s^{-1}gauss^{-1}$
^{13}C = 6.7 $s^{-1}gauss^{-1}$

. **In a 14,092 gauss field, a 60 MHz (60,000,000) photon is required to flip a proton.**

. **Low energy, radio frequency.**

Magnetic Shielding

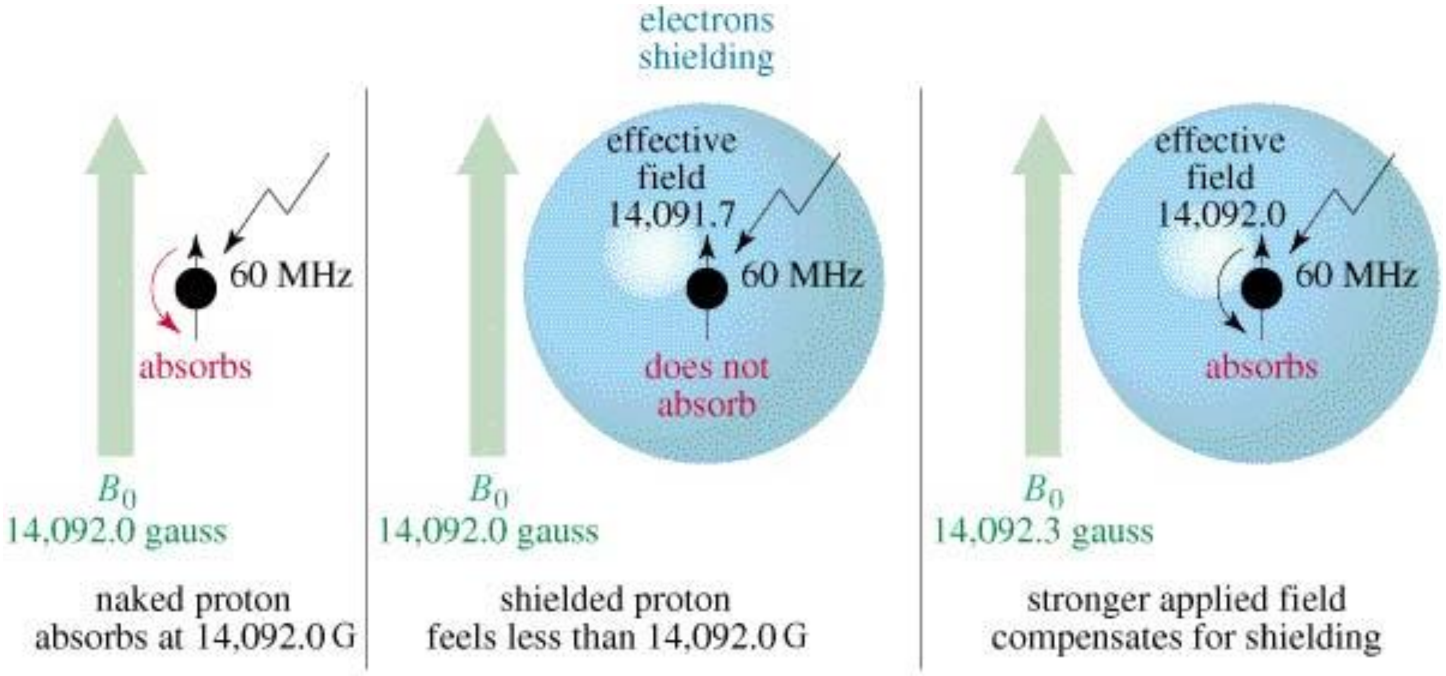
If all protons absorbed the same amount of energy in a given magnetic field, not much information could be obtained.

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.



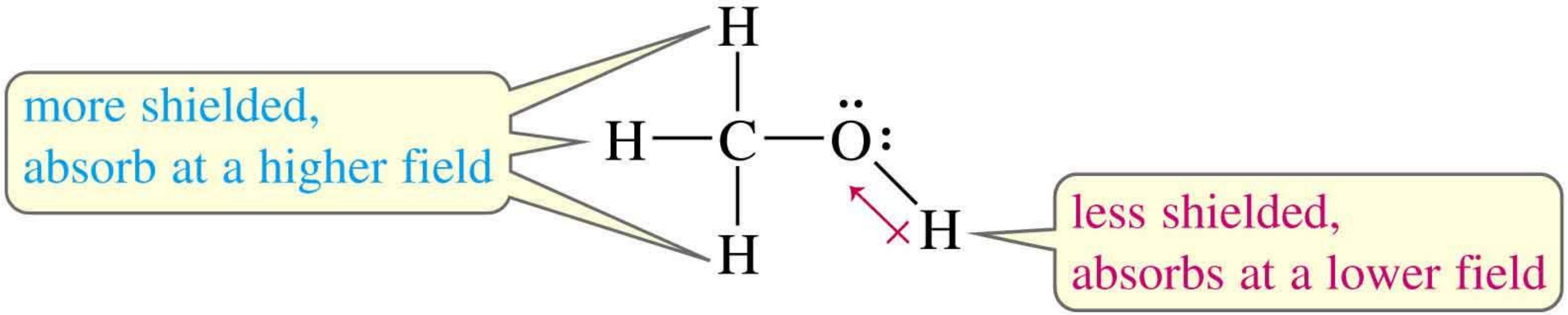
naked proton absorbs at 14,092.0 G

shielded proton feels less than 14,092.0 G

stronger applied field compensates for shielding

Protons in a Molecule

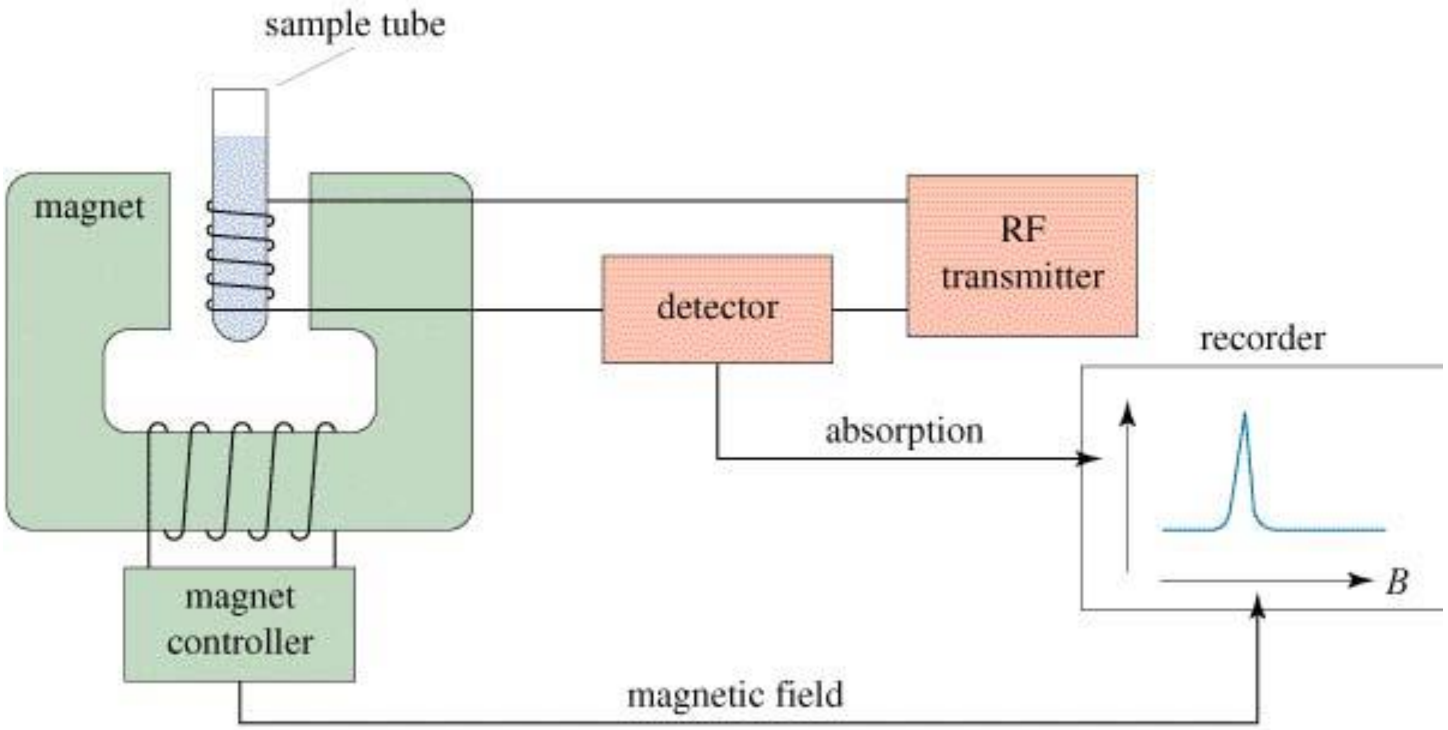
Depending on their chemical environment, protons in a molecule are shielded by different amounts.



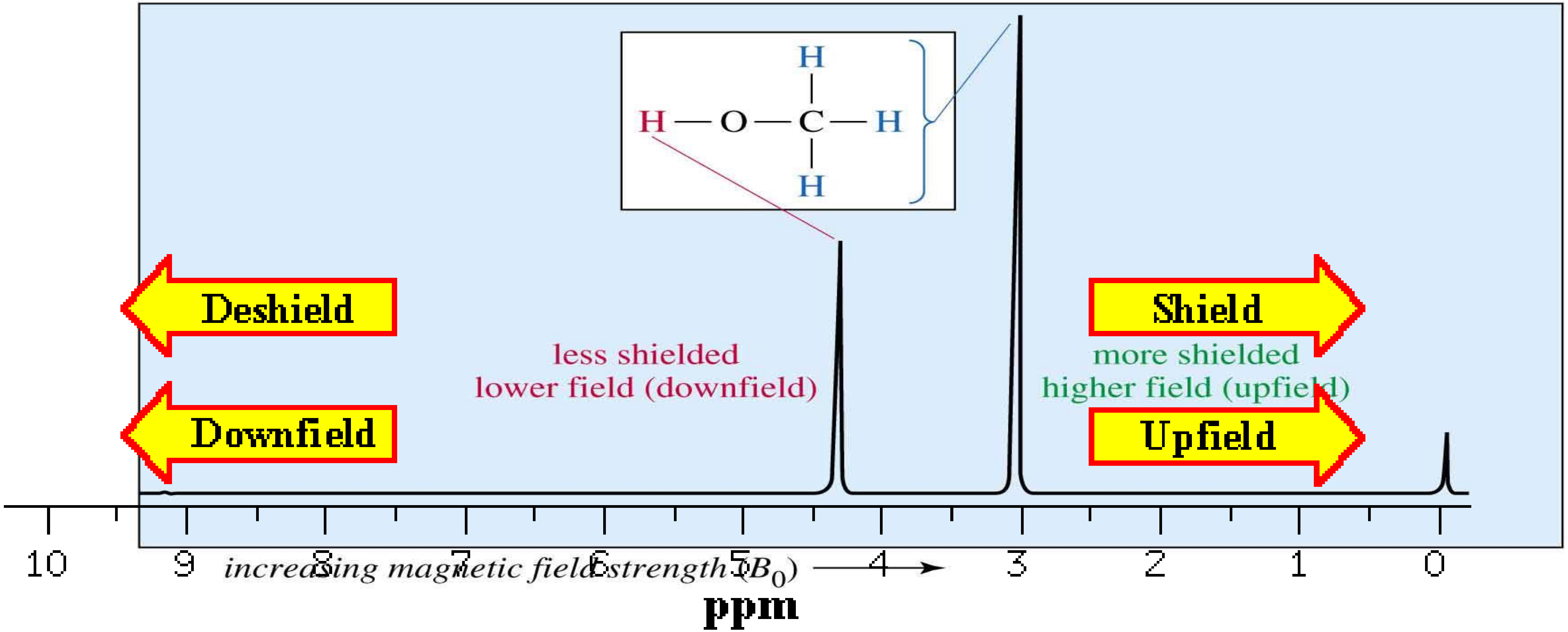
NMR Signals

- 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.

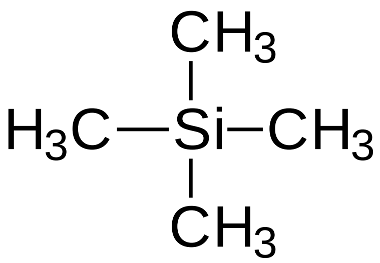
The NMR Spectrometer



The NMR Graph



Tetramethylsilane



- TMS is added to the sample.
- Since silicon is less electronegative than carbon, TMS protons are highly shielded. Signal defined as zero.
- Organic protons absorb downfield (to the left) of the TMS signal.

Chemical Shift

- Measured in parts per million.
- Ratio of shift downfield from TMS (Hz) to total spectrometer frequency (Hz).
- Same value for 60, 100, or 300 MHz machine.
- Called the delta scale (δ).

Chemical Shift calculation

$\delta = V_H - V_{TMS} / V_{NMR} \times 10^6$ ppm

δ= Chemical shift (ppm)

V_H= Frequency of proton

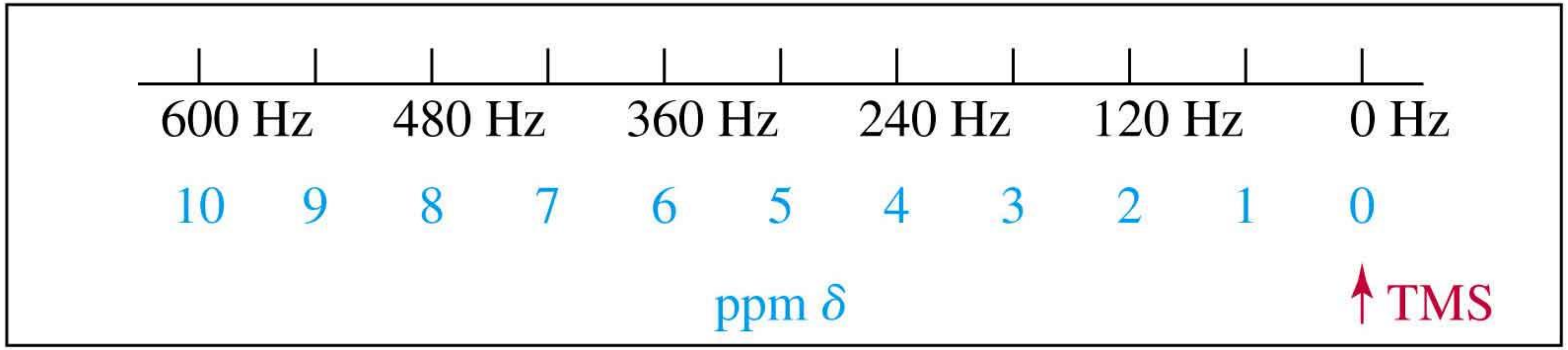
V_{TMS}= 0

V_{NMR}= 60 MHz or 100MHZ or 300 MHz

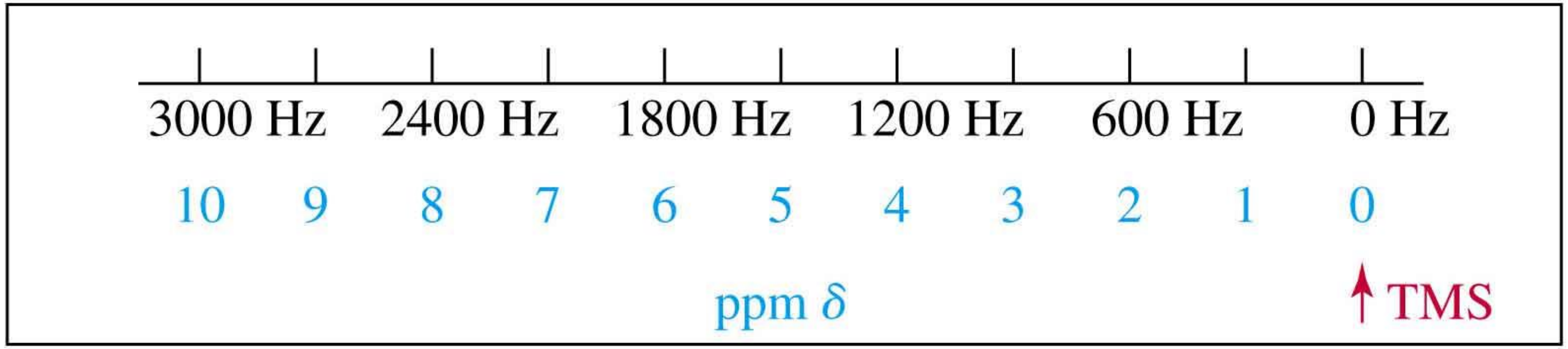
1MHz= 10^6 Hz

Delta Scale

$$\text{chemical shift, ppm } \delta = \frac{\text{shift downfield from TMS (in Hz)}}{\text{spectrometer frequency (in MHz)}}$$



60 MHz



300 MHz

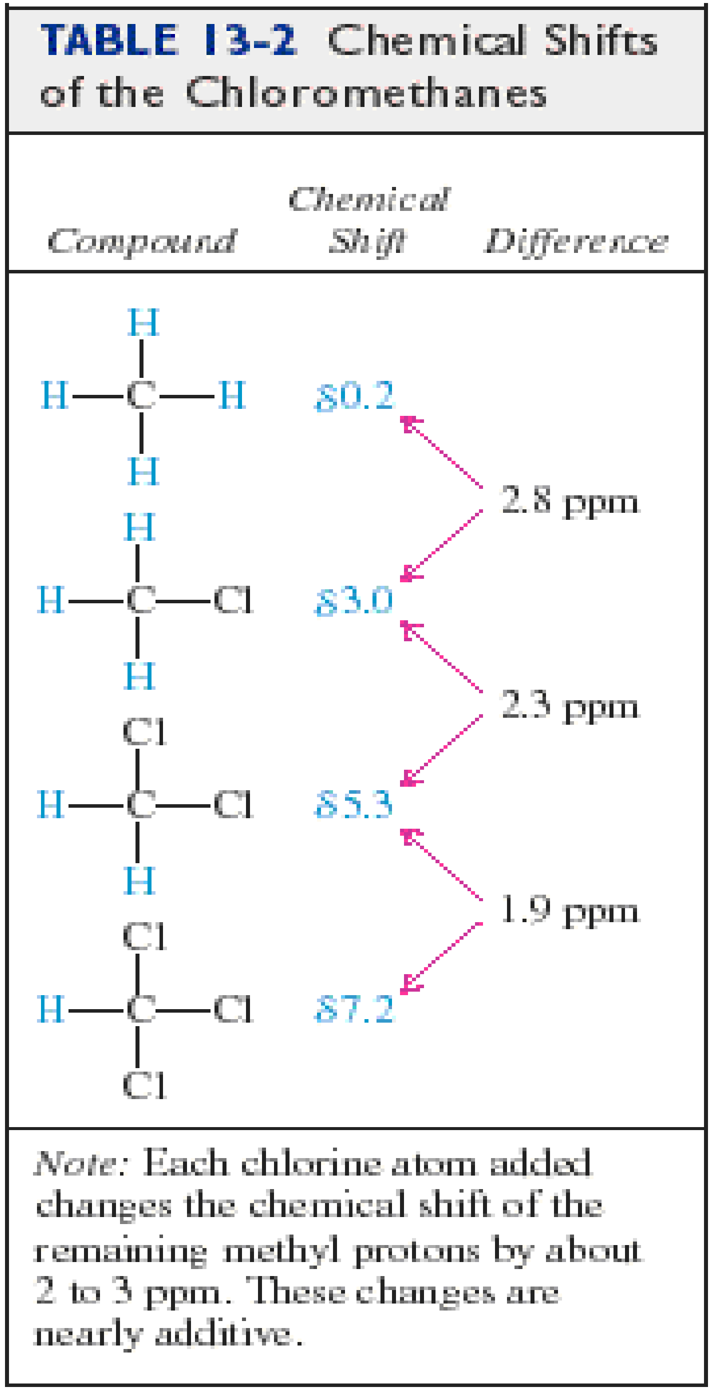


TABLE 13-2 Chemical Shifts of the Chloromethanes

Compound	*Chemical Shift*	*Difference*
	δ0.2	
		2.8 ppm
	δ3.0	
		2.3 ppm
	δ5.3	
		1.9 ppm
	δ7.2	

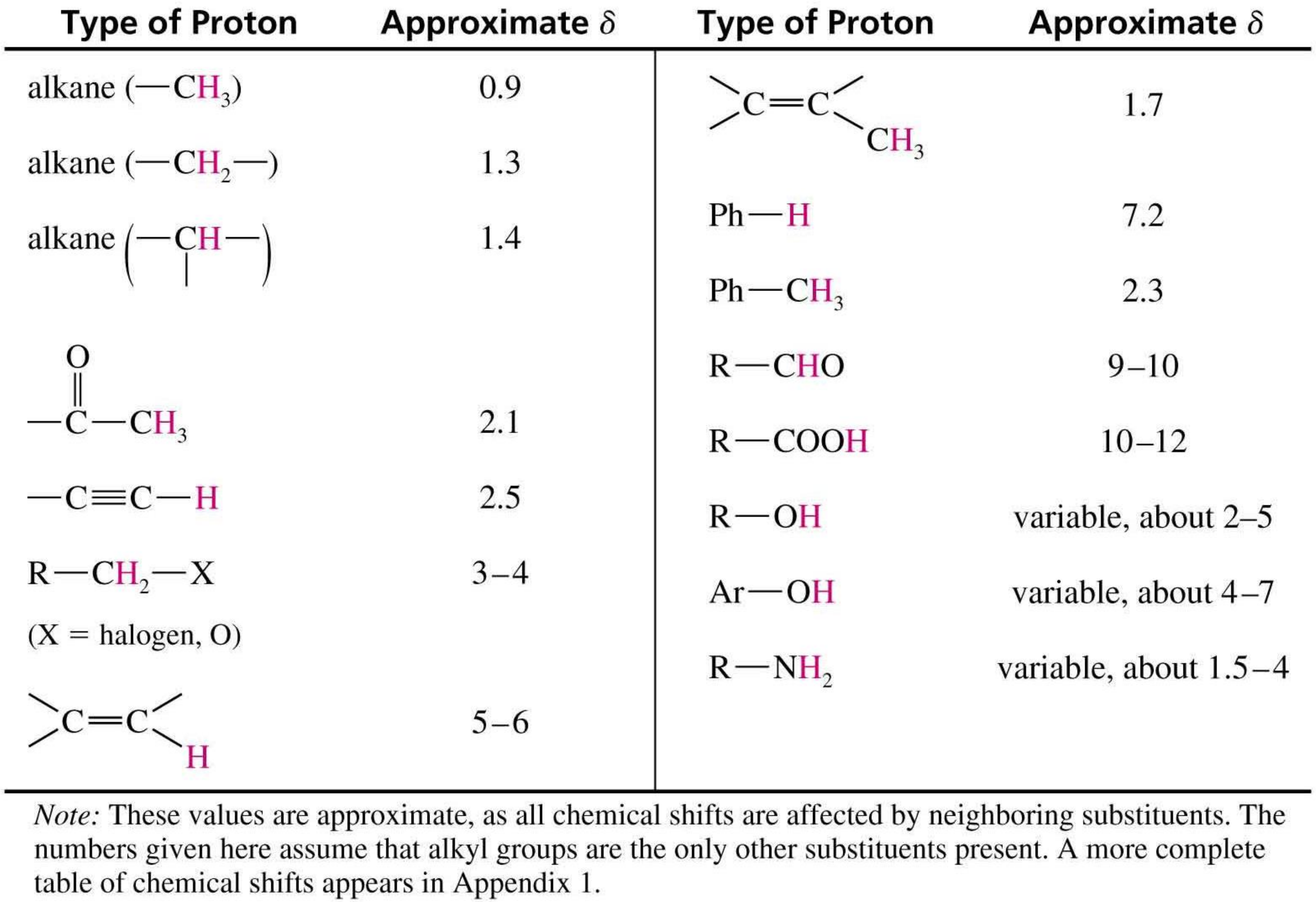
Note: Each chlorine atom added changes the chemical shift of the remaining methyl protons by about 2 to 3 ppm. These changes are nearly additive.

Location of Signals

- More electronegative atoms deshield more and give larger shift values.
- Effect decreases with distance.
- Additional electronegative atoms cause increase in chemical shift.

$CHCl_3$	CH_2Cl_2	CH_3F	CH_3OH	CH_3Cl	CH_3Br	CH_3I	CH_4	$(CH_3)_4Si$
7.27	5.30	4.26	3.4	3.05	2.68	2.16	0.23	0

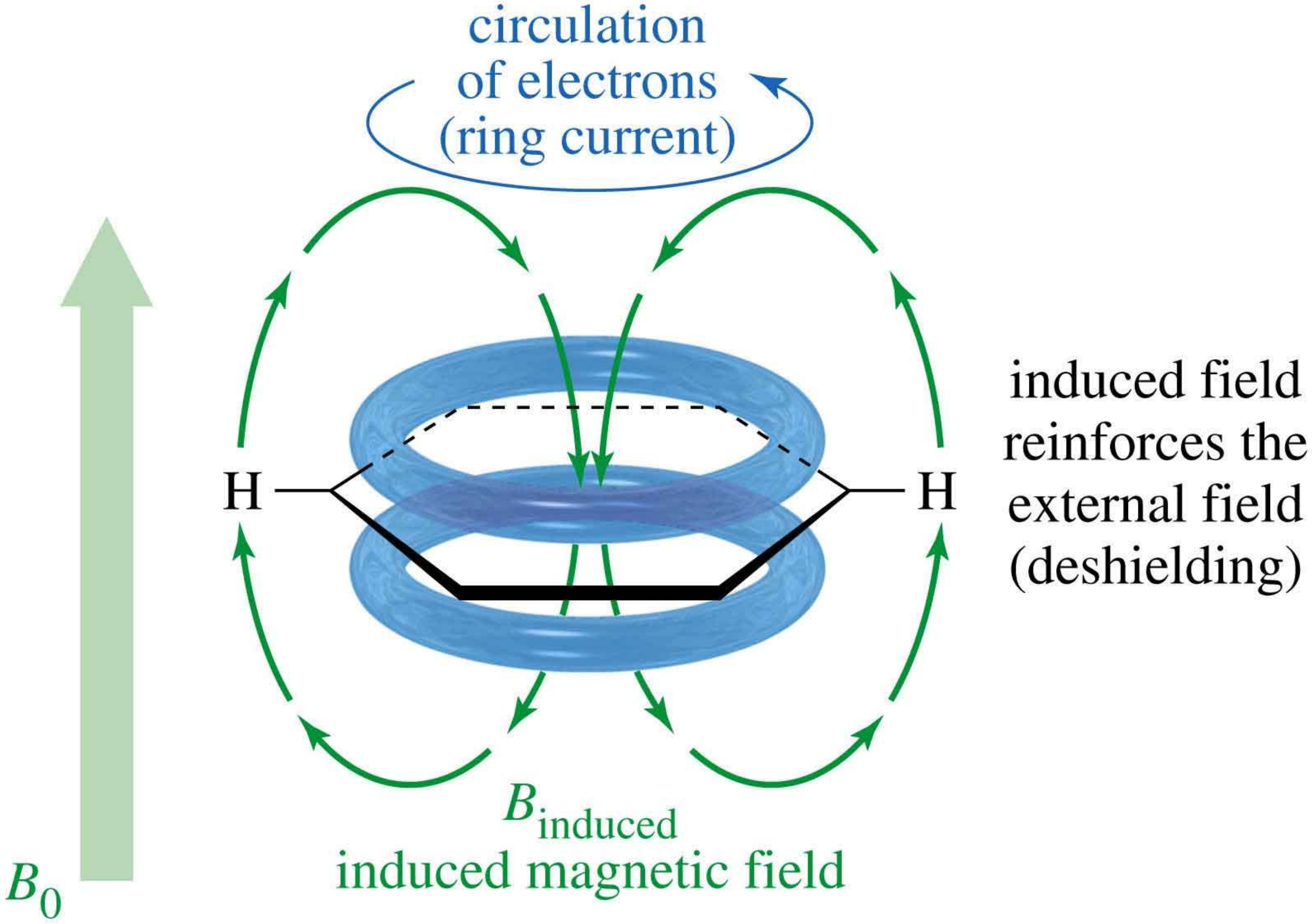
Typical Values



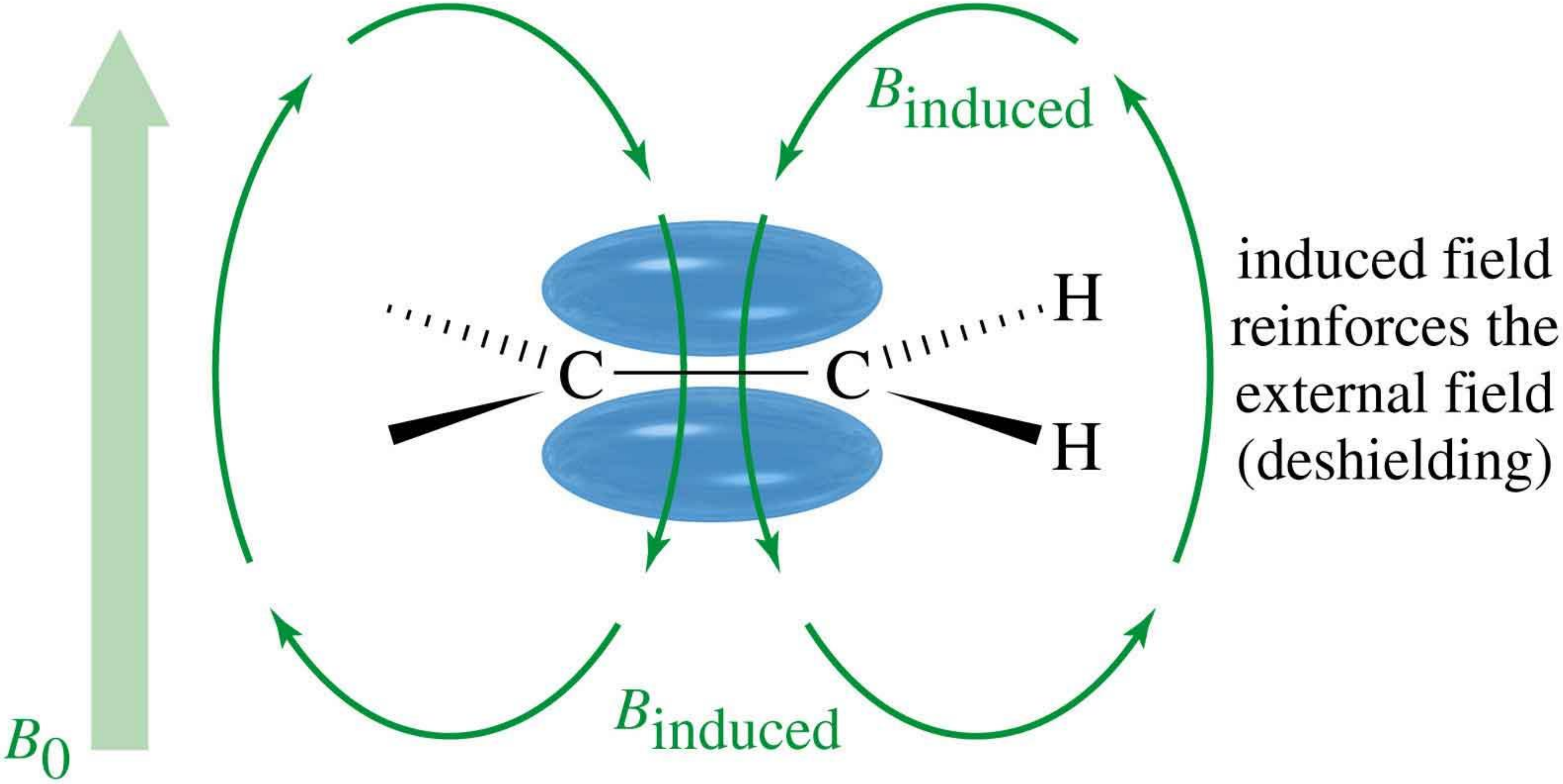
Type of Proton	Approximate δ	Type of Proton	Approximate δ
alkane ($-CH_3$)	0.9	$>C{=}C<CH_3$	1.7
alkane ($-CH_2-$)	1.3	$Ph-H$	7.2
alkane $\left(-\underset{\vert}{CH}-\right)$	1.4	$Ph-CH_3$	2.3
$-\overset{\overset{O}{\Vert}}{C}-CH_3$	2.1	$R-CHO$	9–10
$-C{\equiv}C-H$	2.5	$R-COOH$	10–12
$R-CH_2-X$ (X = halogen, O)	3–4	$R-OH$	variable, about 2–5
$>C{=}C<H$	5–6	$Ar-OH$	variable, about 4–7
		$R-NH_2$	variable, about 1.5–4

Note: These values are approximate, as all chemical shifts are affected by neighboring substituents. The numbers given here assume that alkyl groups are the only other substituents present. A more complete table of chemical shifts appears in Appendix 1.

Aromatic Protons, δ7-δ8

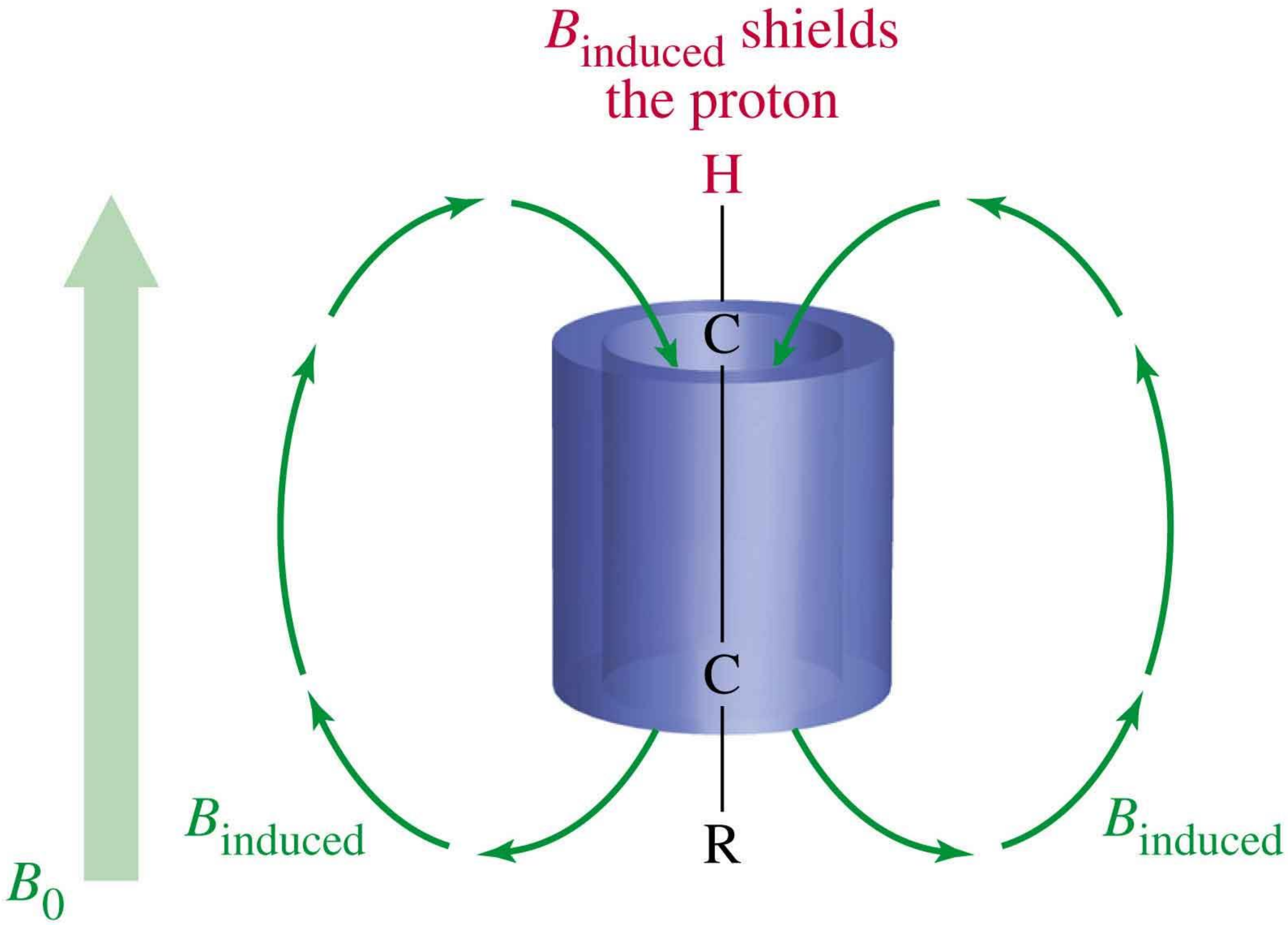


Vinyl Protons, δ5-δ6

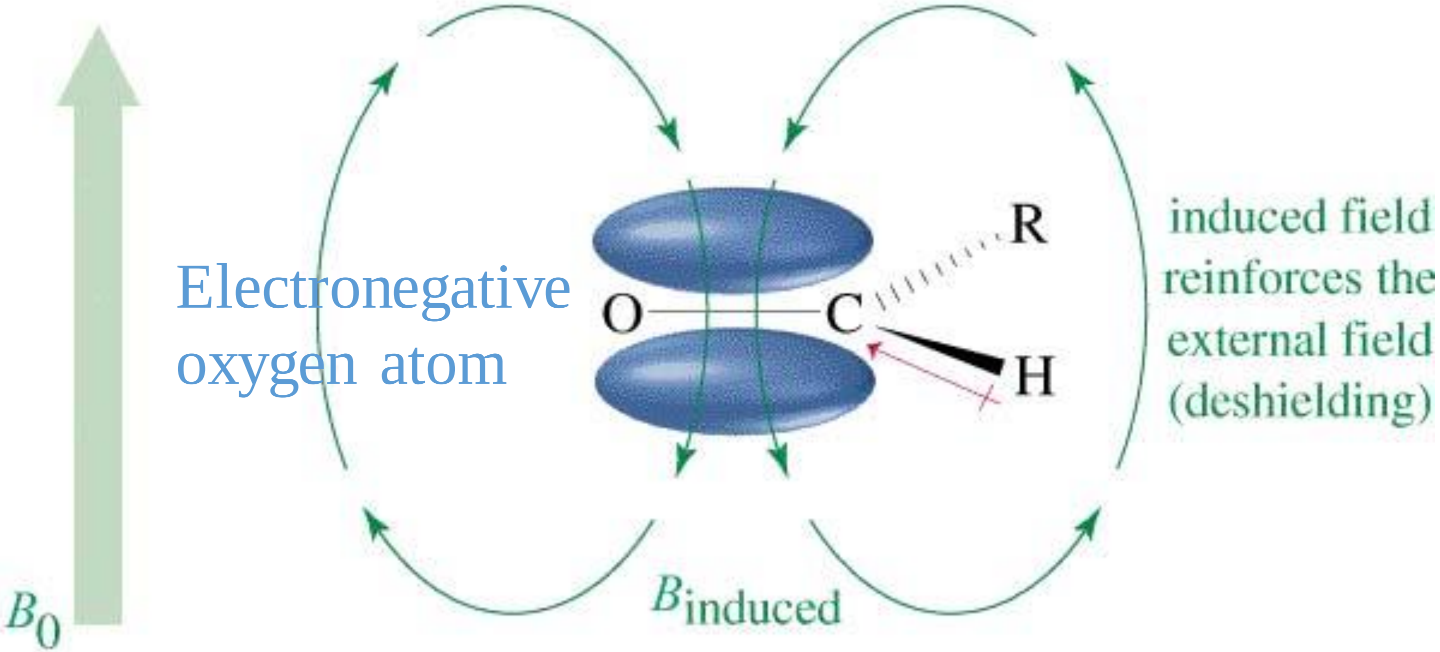


induced field reinforces the external field (deshielding)

Acetylenic Protons, δ2.5



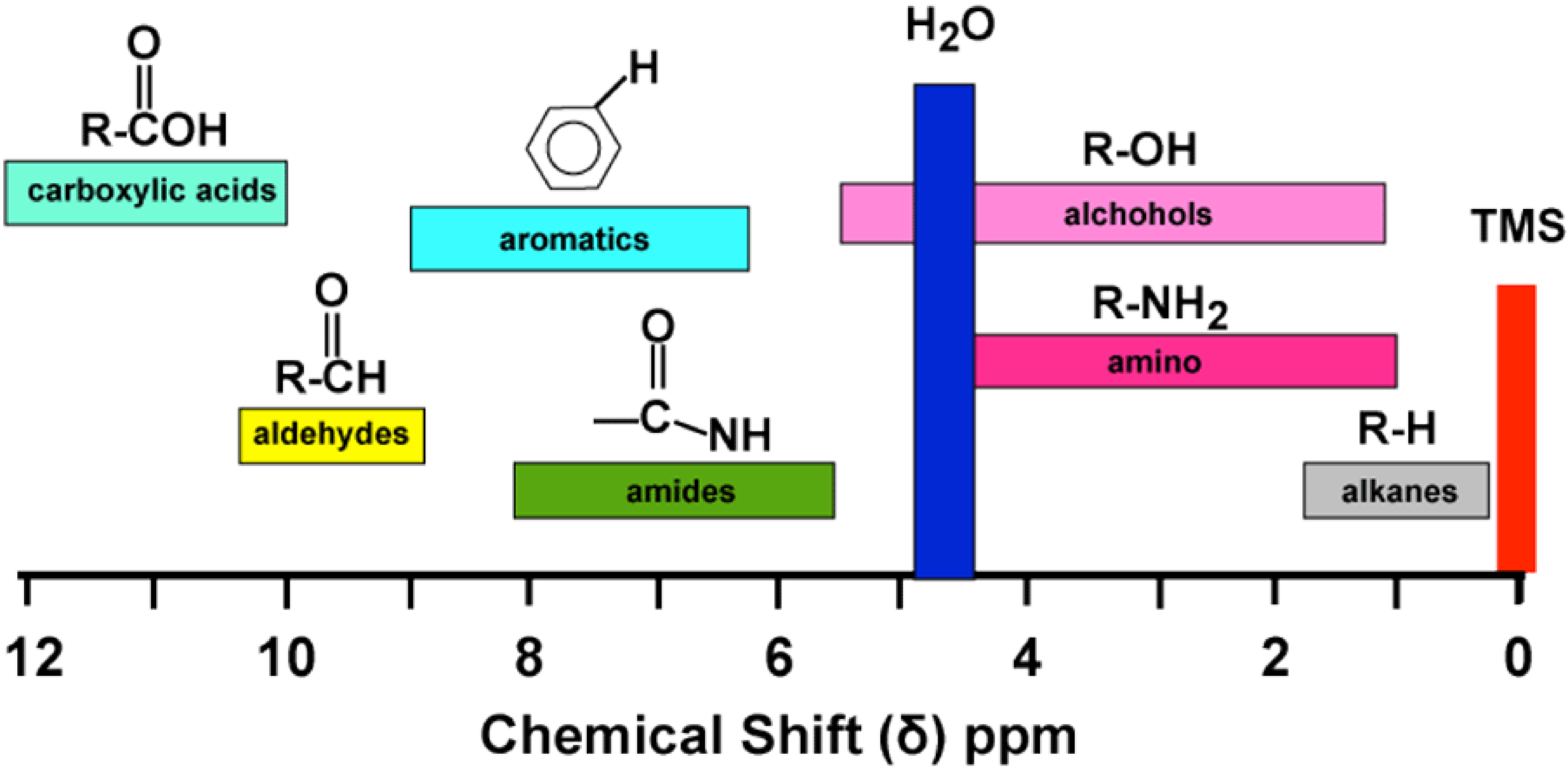
Aldehyde Proton, δ9-δ10



Electronegative oxygen atom

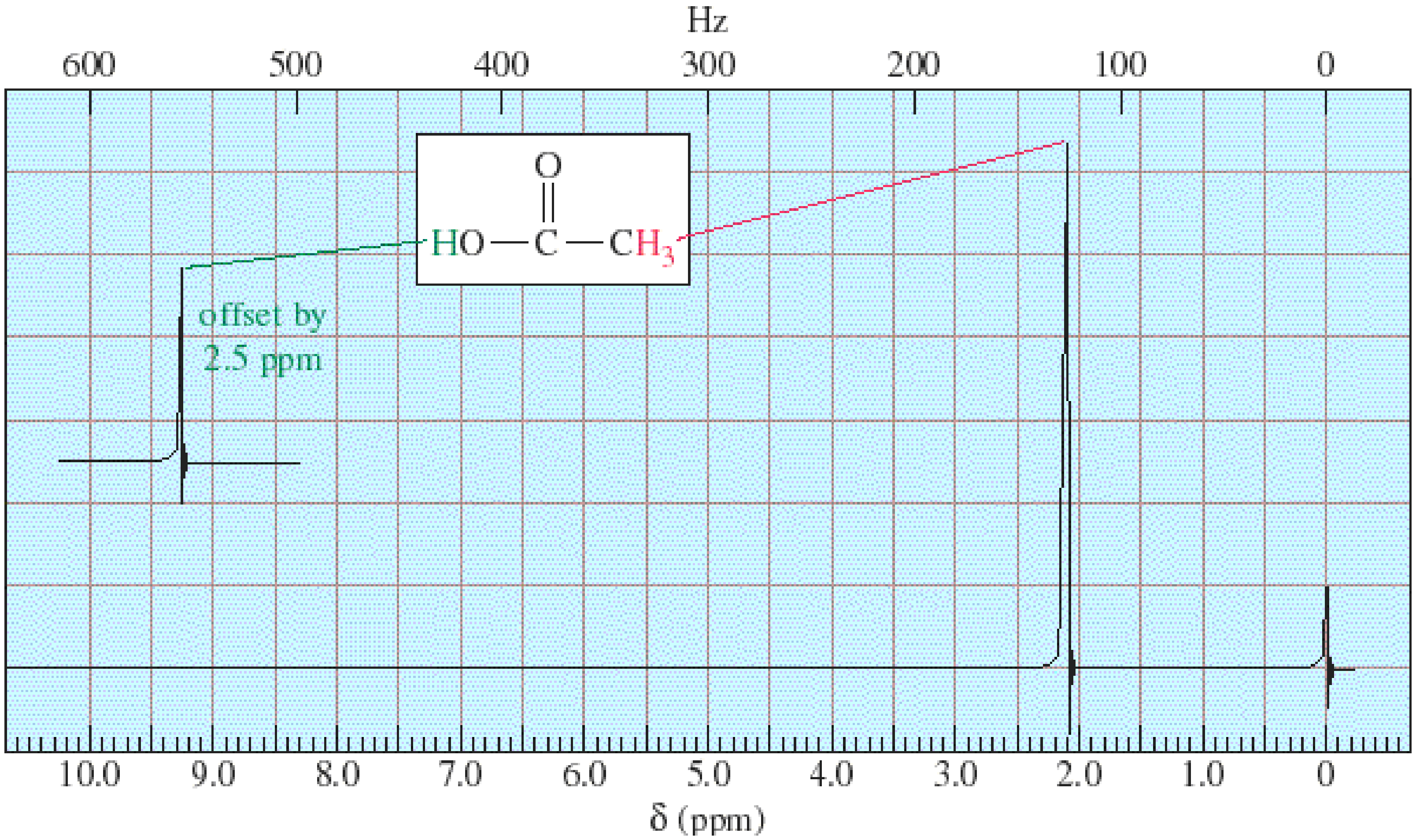
O-H and N-H Signals

- Chemical shift depends on concentration.
- Hydrogen bonding in concentrated solutions deshield the protons, so signal is around $\delta 3.5$ for N-H and $\delta 4.5$ for O-H.
- Proton exchanges between the molecules broaden the peak.



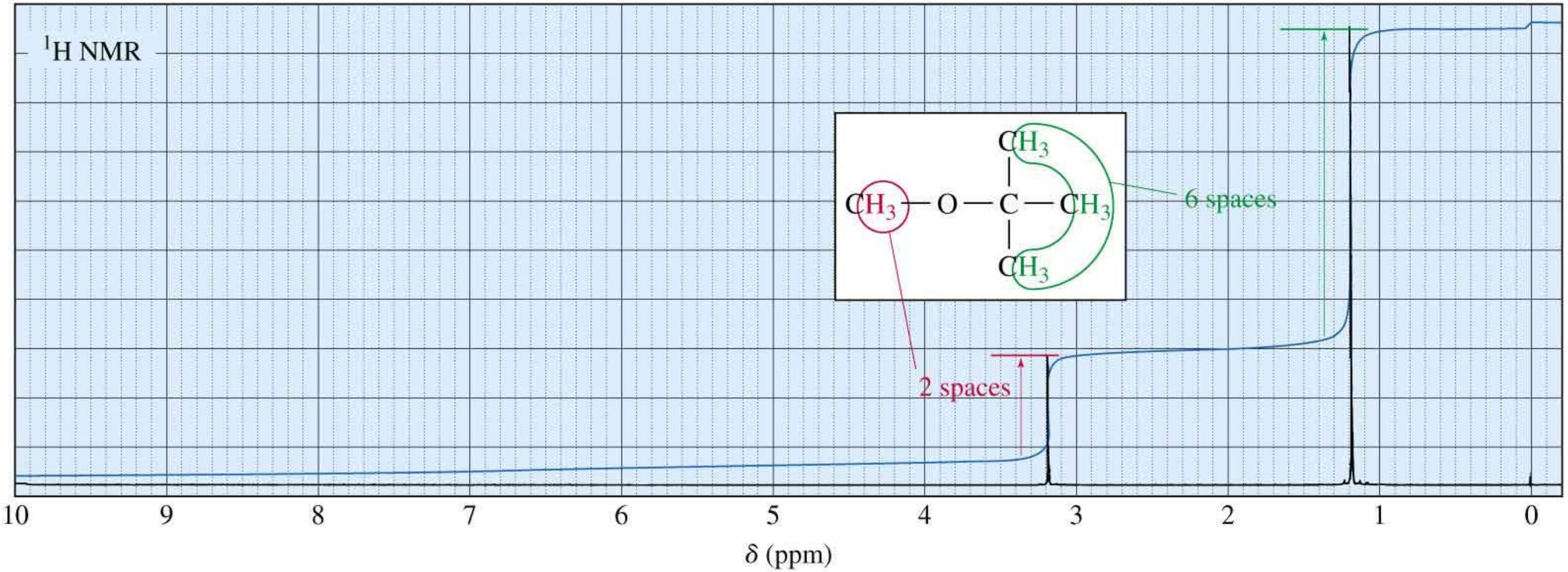
H$_2$O
R-COOH
carboxylic acids
H
aromatics
R-OH
alchohols
TMS
R-CH
aldehydes
C
NH
amides
R-NH$_2$
amino
R-H
alkanes
12
10
8
6
4
2
0
Chemical Shift (δ) ppm

Carboxylic Acid Proton, δ10+



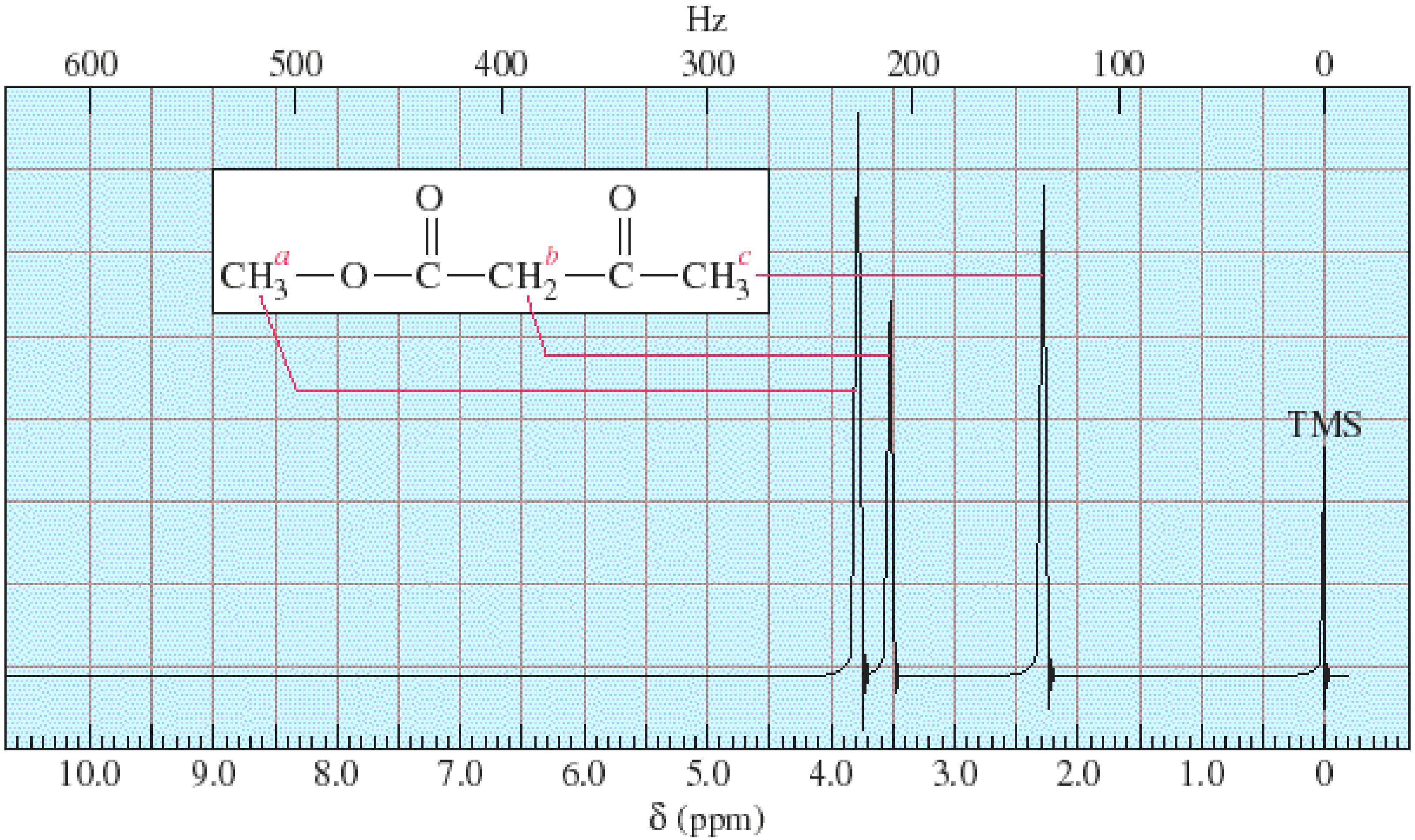
Intensity of Signals

- The area under each peak is proportional to the number of protons.
- Shown by integral trace.



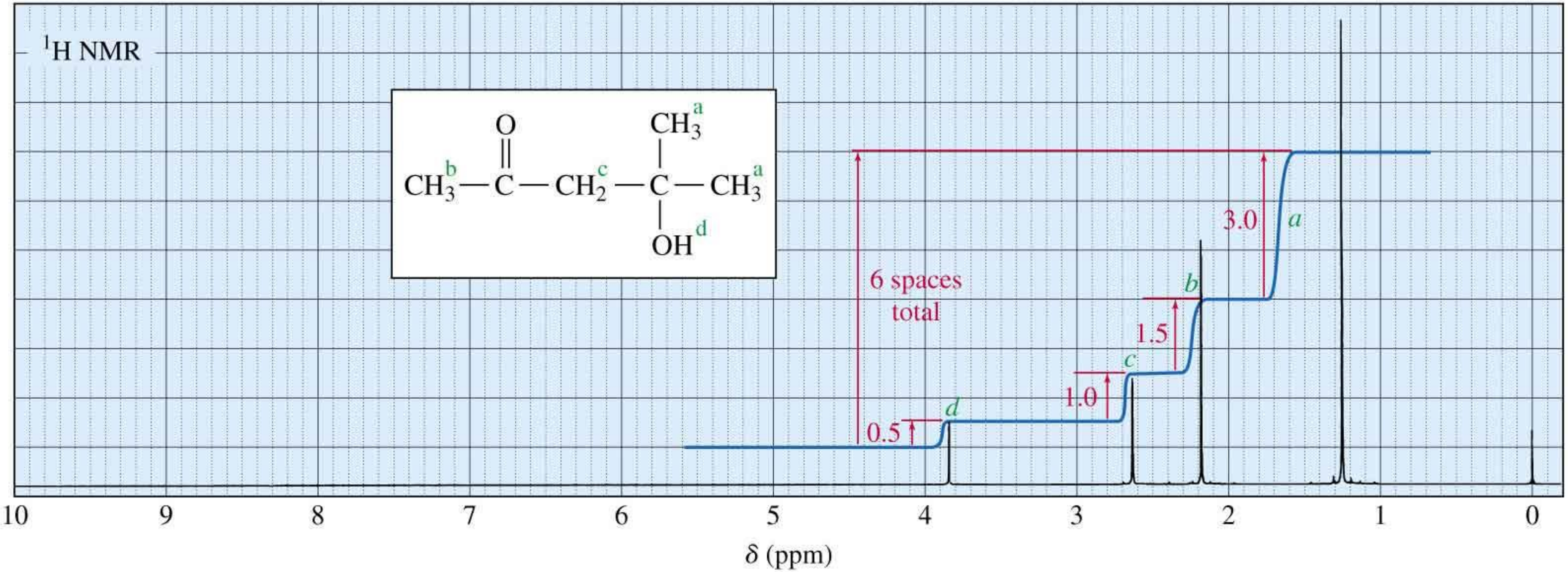
Number of Signals

Equivalent hydrogens have the same chemical shift.



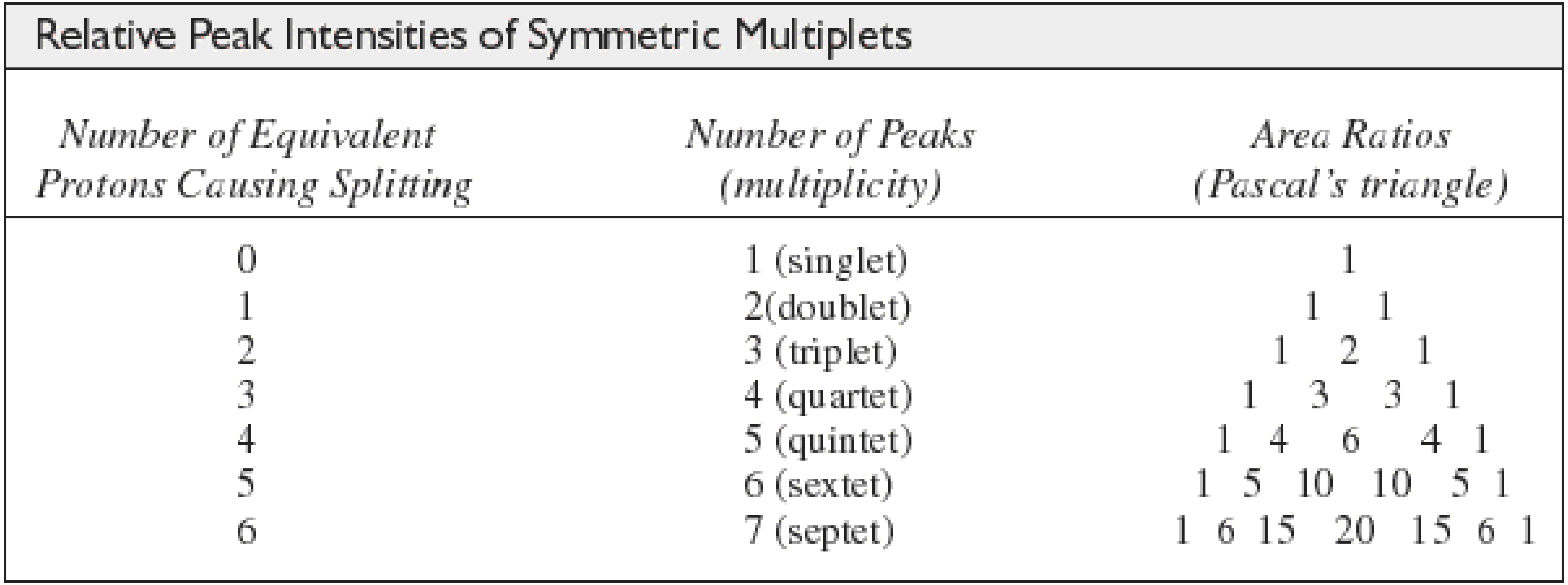
How Many Hydrogens?

When the molecular formula is known, each integral rise can be assigned to a particular number of hydrogens.



The *N* + 1 Rule

If a signal is split by *N* equivalent protons, it is split into *N* + 1 peaks.



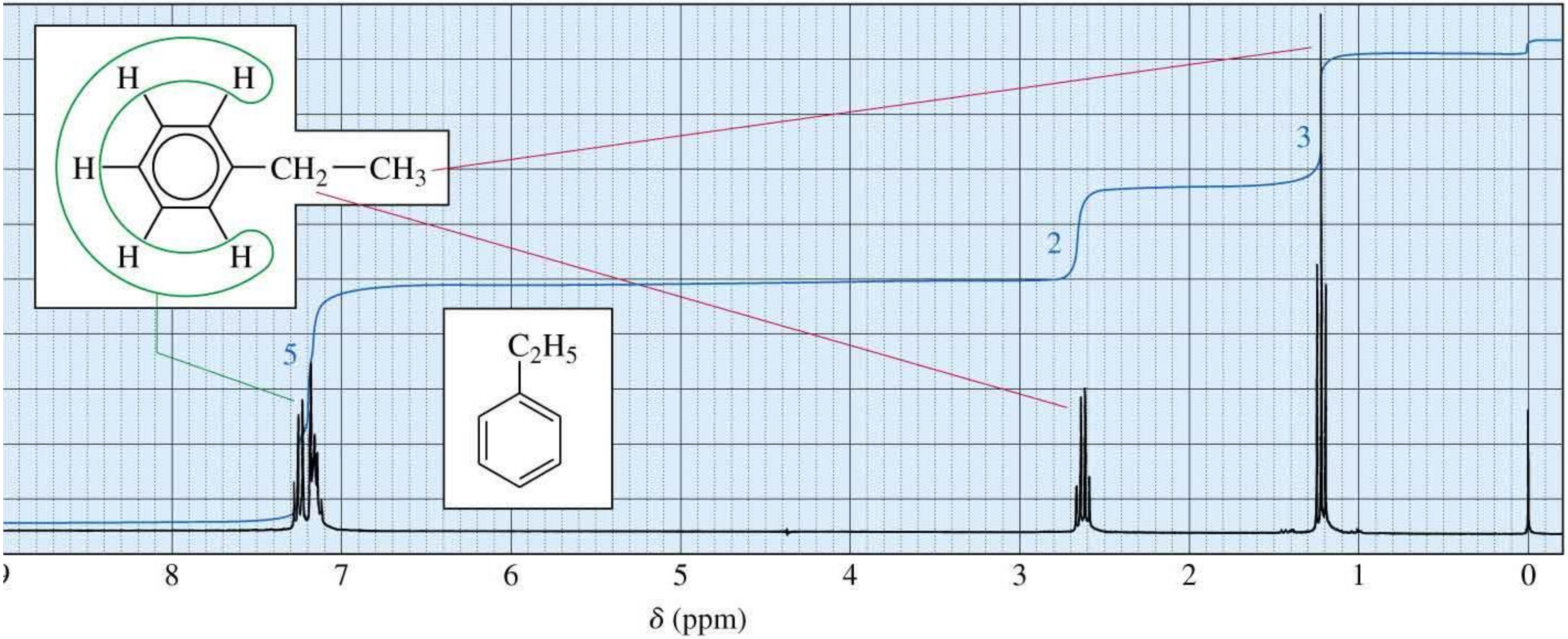
Relative Peak Intensities of Symmetric Multiplets

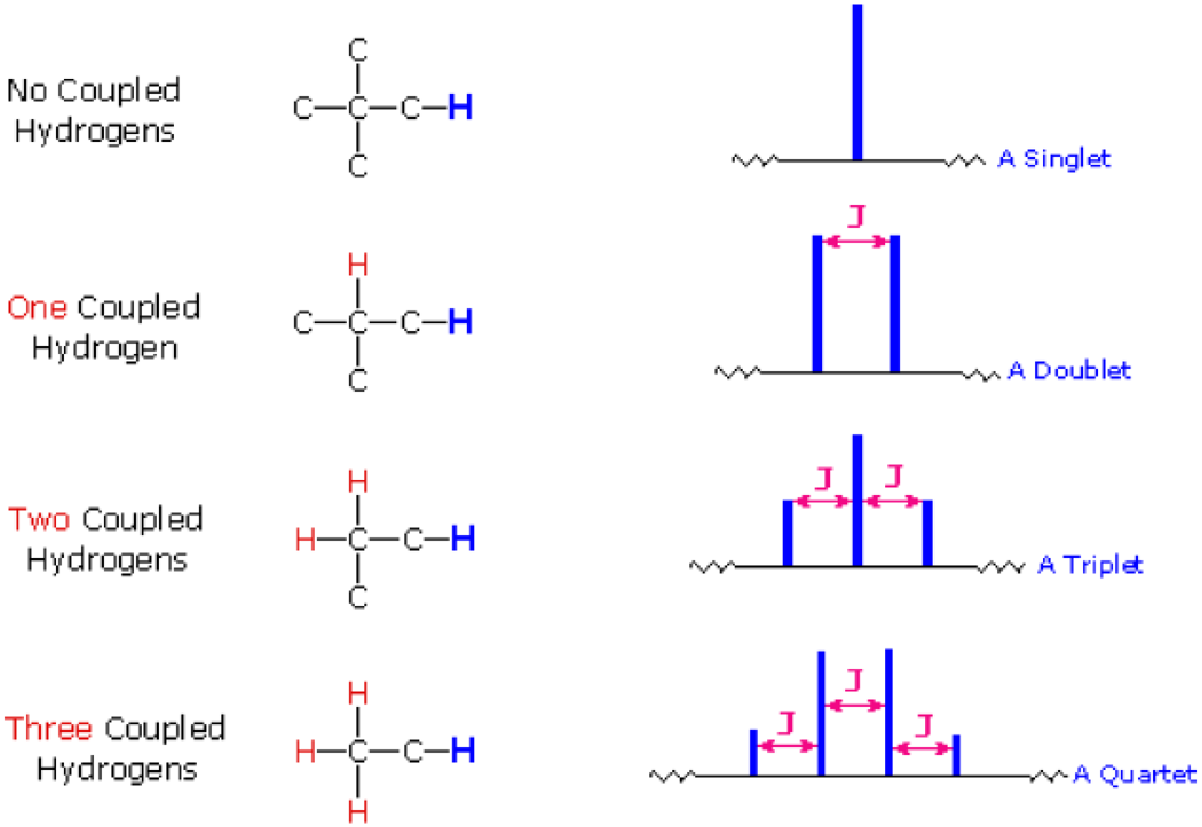
Number of Equivalent Protons Causing Splitting	*Number of Peaks (multiplicity)*	*Area Ratios (Pascal's triangle)*
0	1 (singlet)	1
1	2(doublet)	1 1
2	3 (triplet)	1 2 1
3	4 (quartet)	1 3 3 1
4	5 (quintet)	1 4 6 4 1
5	6 (sextet)	1 5 10 10 5 1
6	7 (septet)	1 6 15 20 15 6 1

Range of Magnetic Coupling

- Equivalent protons do not split each other.
- Protons bonded to the same carbon will split each other only if they are not equivalent.
- Protons on adjacent carbons normally will couple.
- Protons separated by four or more bonds will not couple.

Splitting for Ethyl Groups





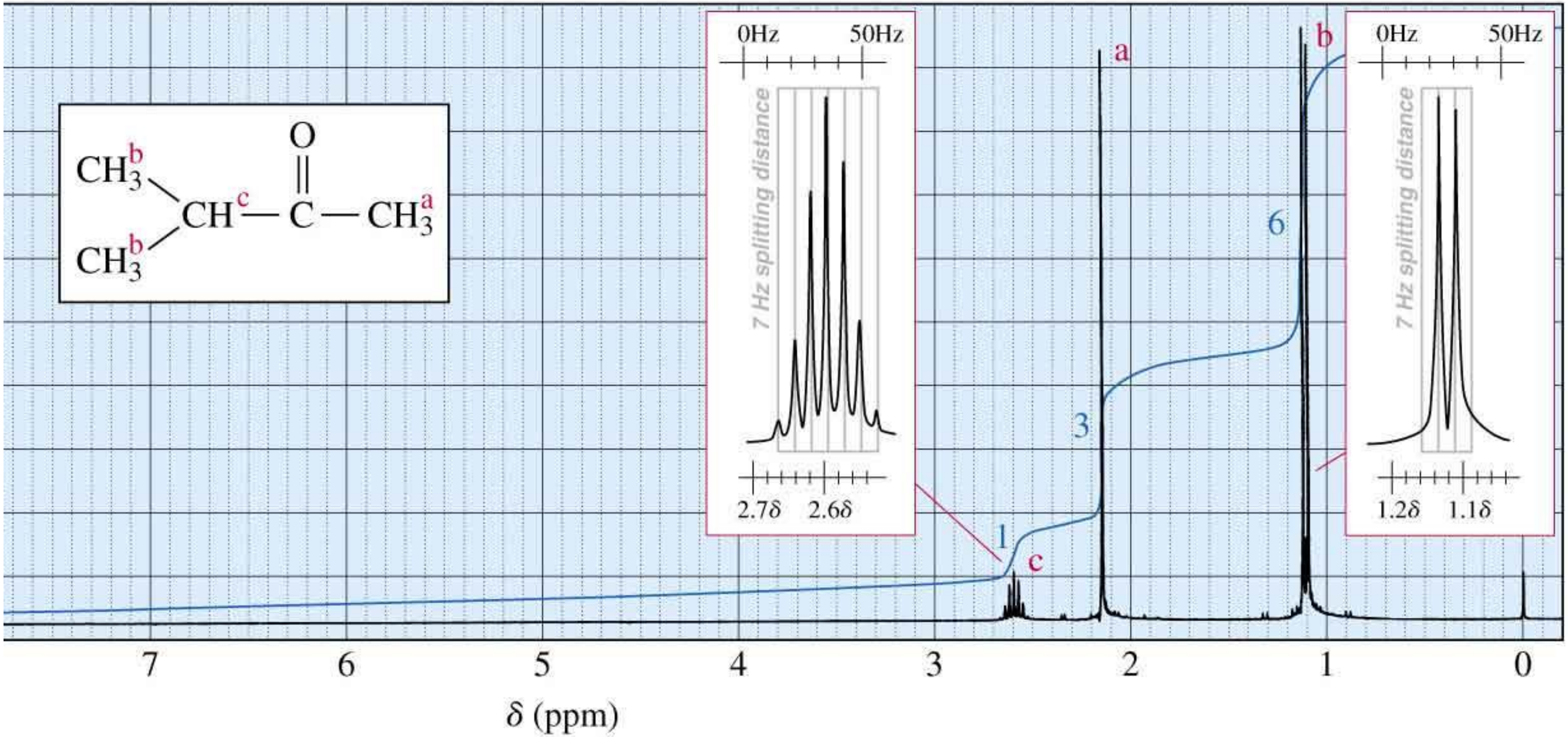
No Coupled Hydrogens

One Coupled Hydrogen

Two Coupled Hydrogens

Three Coupled Hydrogens

Splitting for Isopropyl Groups

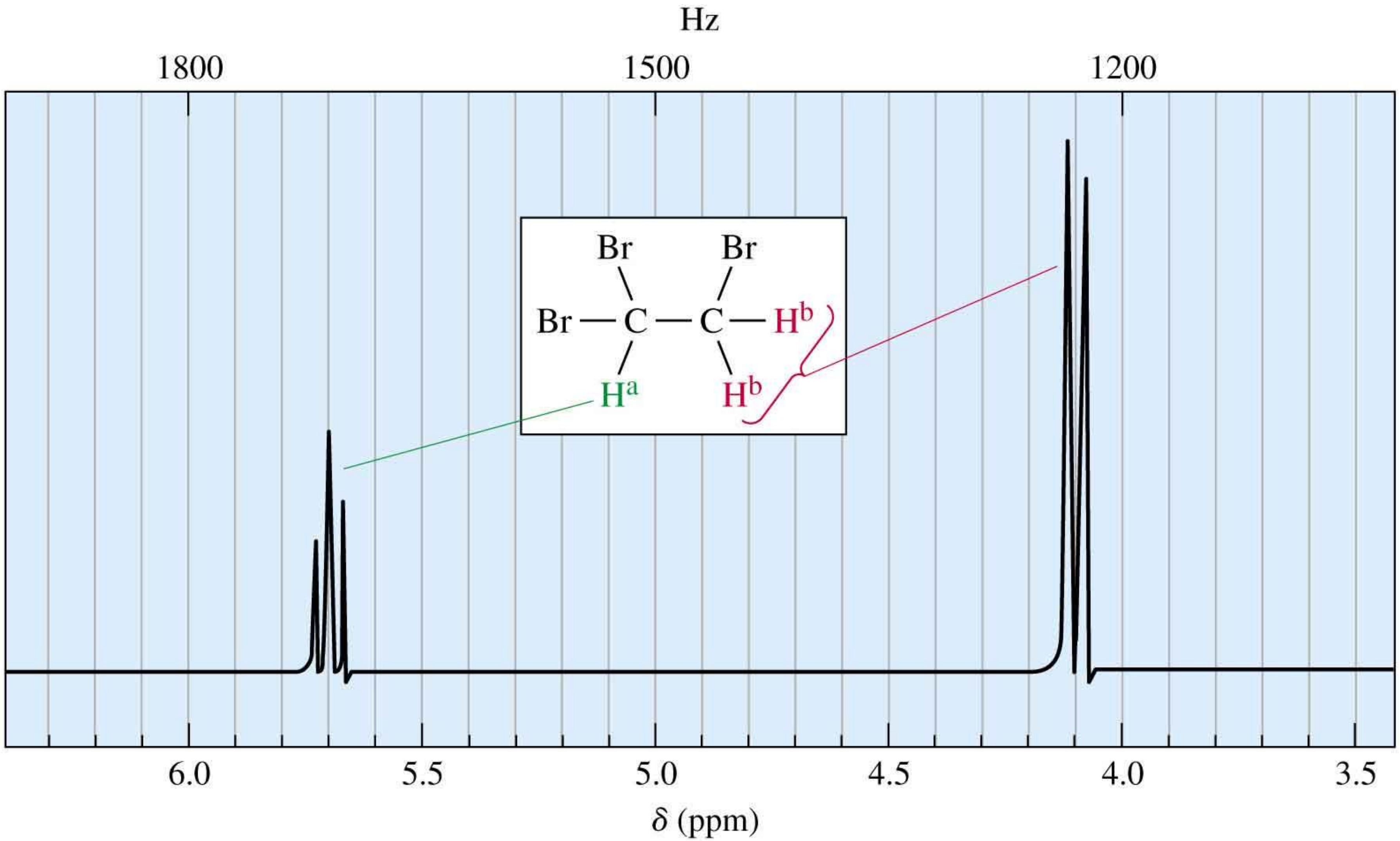


Spin-Spin Splitting

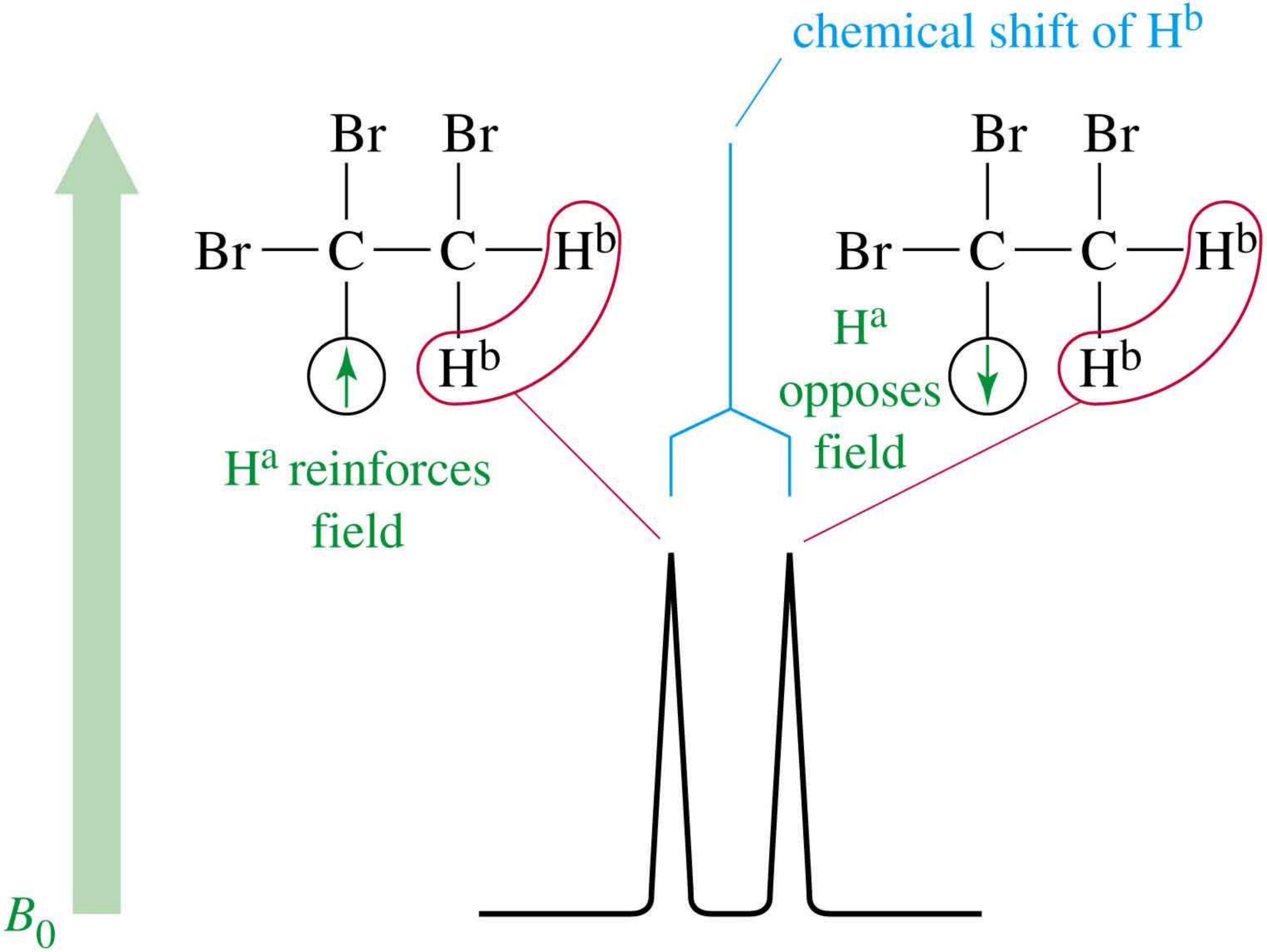
- Nonequivalent protons on adjacent carbons have magnetic fields that may align with or oppose the external field.
- This magnetic coupling causes the proton to absorb slightly downfield when the external field is reinforced and slightly upfield when the external field is opposed.
- All possibilities exist, so signal is split.

1,1,2-Tribromoethane

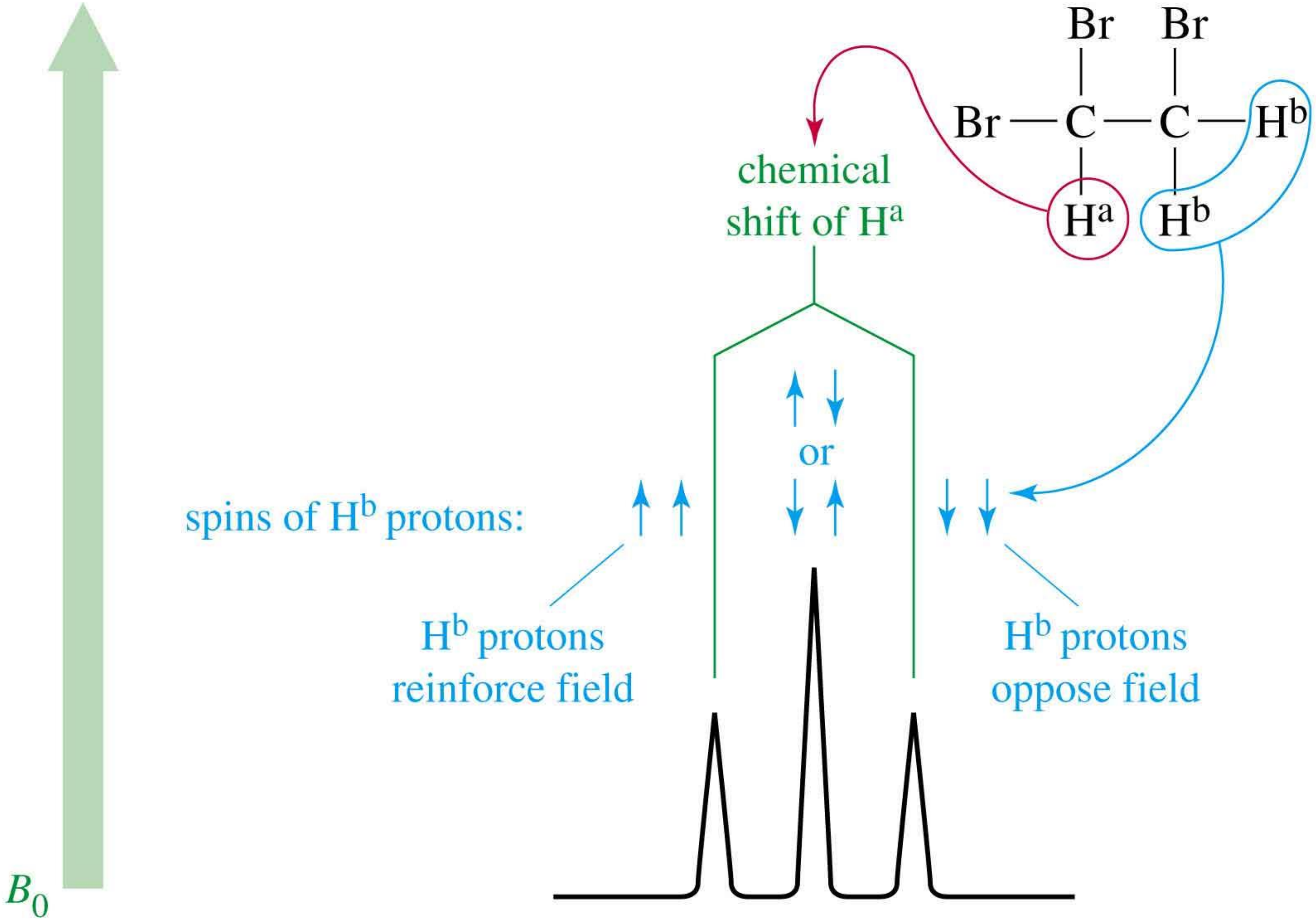
Nonequivalent protons on adjacent carbons.



Doublet: 1 Adjacent Proton



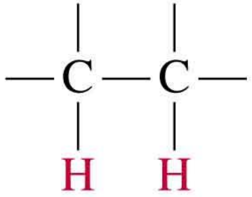
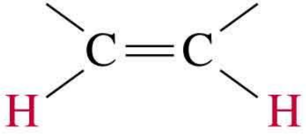
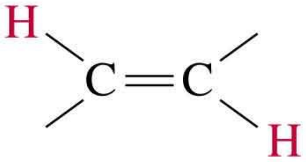
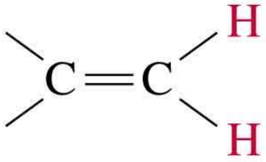
Triplet: 2 Adjacent Protons

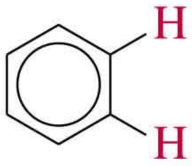
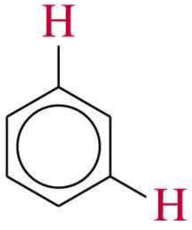
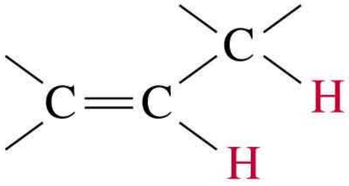


Coupling Constants

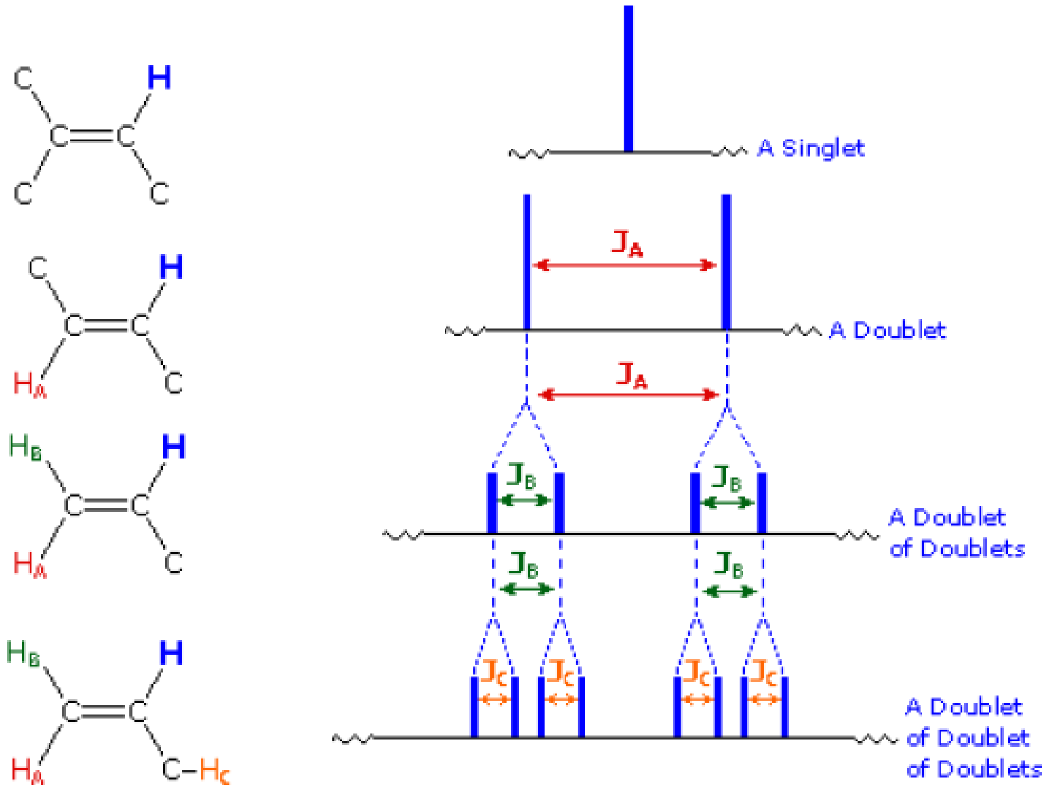
- Distance between the peaks of multiplet
- Measured in Hz
- Not dependent on strength of the external field
- Multiplets with the same coupling constants may come from adjacent groups of protons that split each other.

Values for Coupling Constants

		Approx. *J*
	(free rotation)	7 Hz[a]
	(cis)	10 Hz
	(trans)	15 Hz
	(geminal)	2 Hz

	Approx. *J*
 (ortho)	8 Hz
 (meta)	2 Hz
 (allylic)	6 Hz

[a] The value of 7 Hz in an alkyl group is averaged for rapid rotation about the carbon–carbon bond. If rotation is hindered by a ring or bulky groups, other splitting constants may be observed.



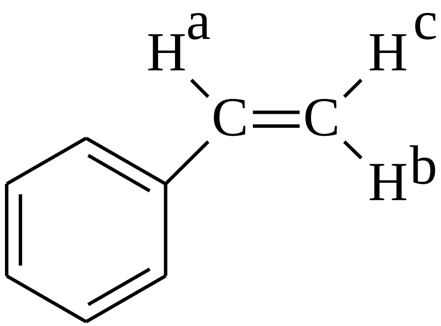
No Coupled
Hydrogens

One Coupled
Hydrogen

Two Coupled
Hydrogens

Three Coupled
Hydrogens

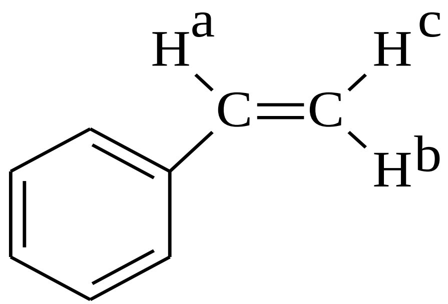
Complex Splitting

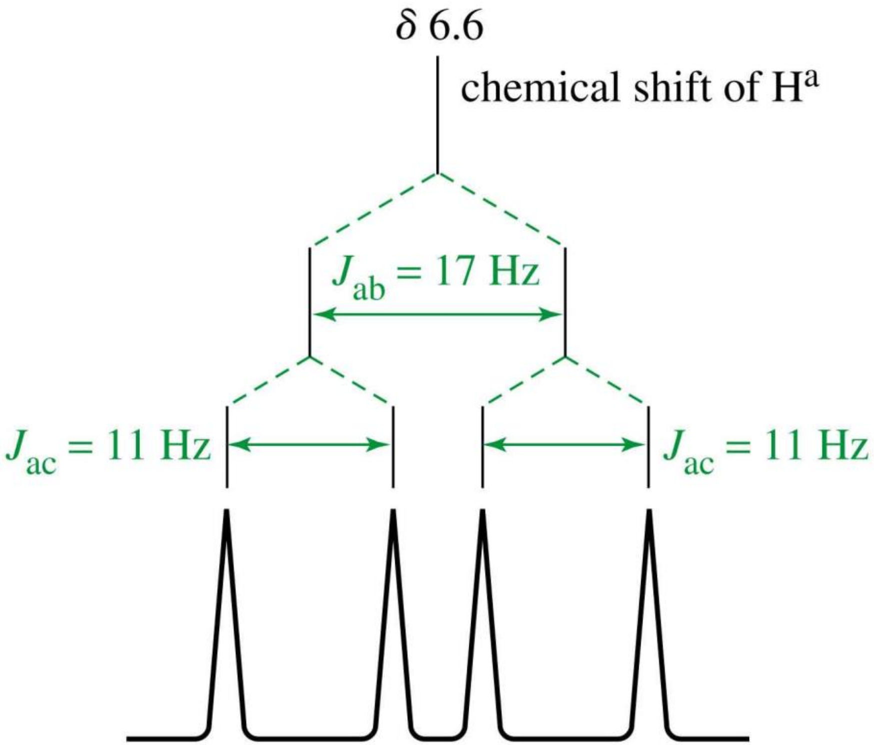


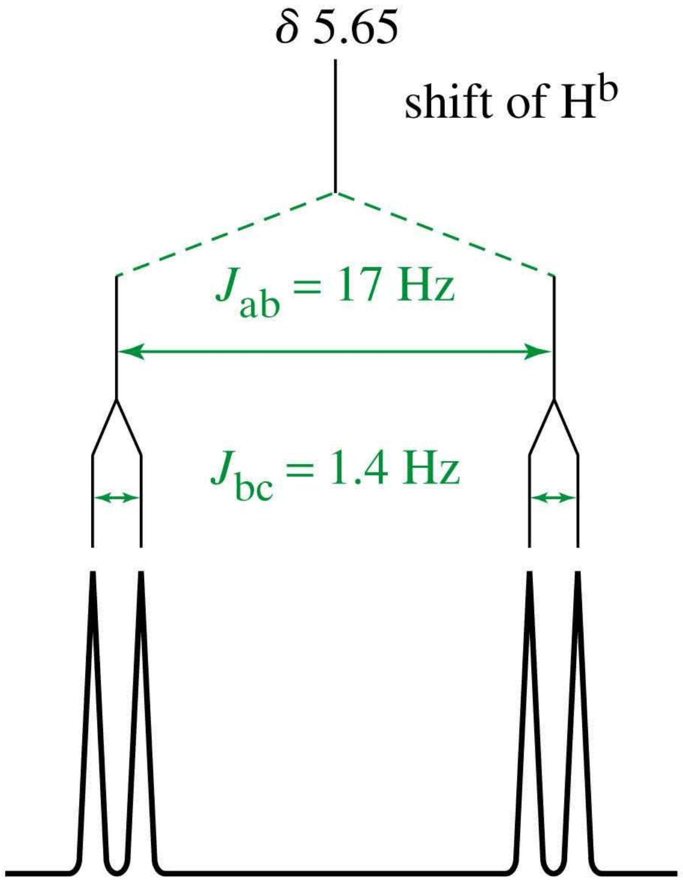
- Signals may be split by adjacent protons, different from each other, with different coupling constants.

- Example: H^a of styrene which is split by an adjacent H *trans* to it (J = 17 Hz) and an adjacent H *cis* to it (J = 11 Hz).

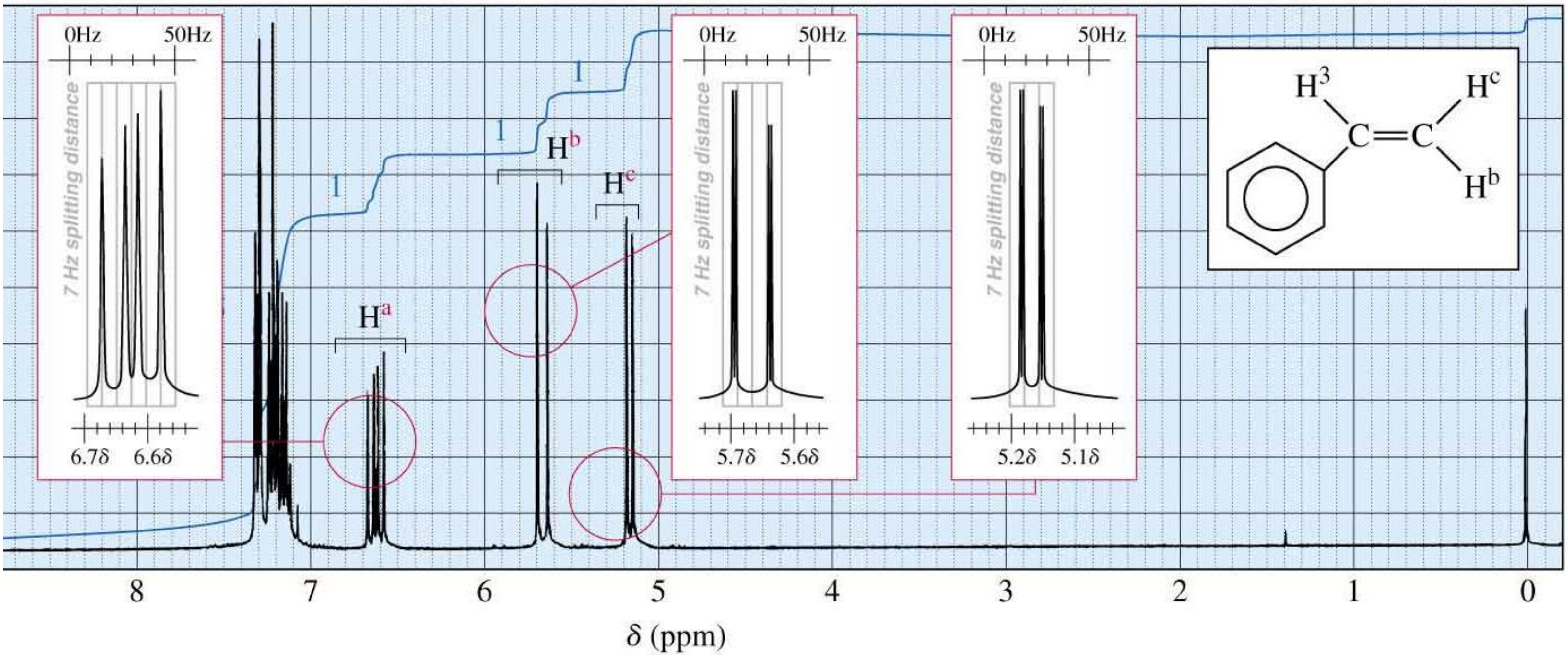
Splitting Tree







Spectrum for Styrene

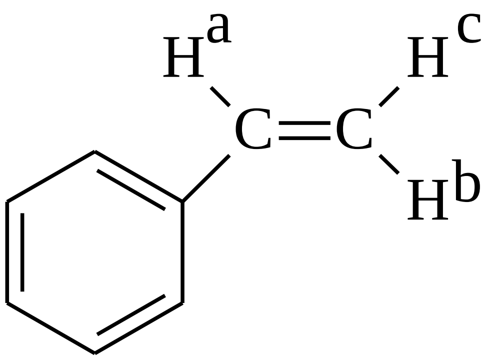


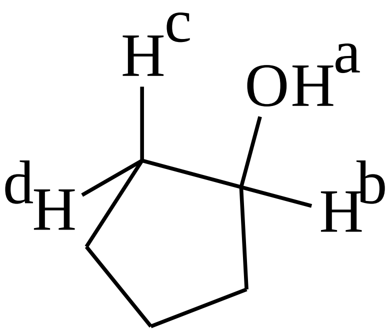
Stereochemical Nonequivalence

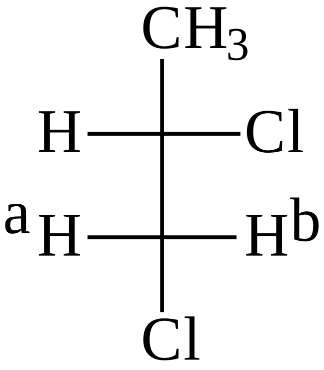
- Usually, two protons on the same C are equivalent and do not split each other.

- If the replacement of each of the protons of a -CH_2 group with an imaginary “Z” gives stereoisomers, then the protons are non-equivalent and will split each other.

Some Nonequivalent Protons

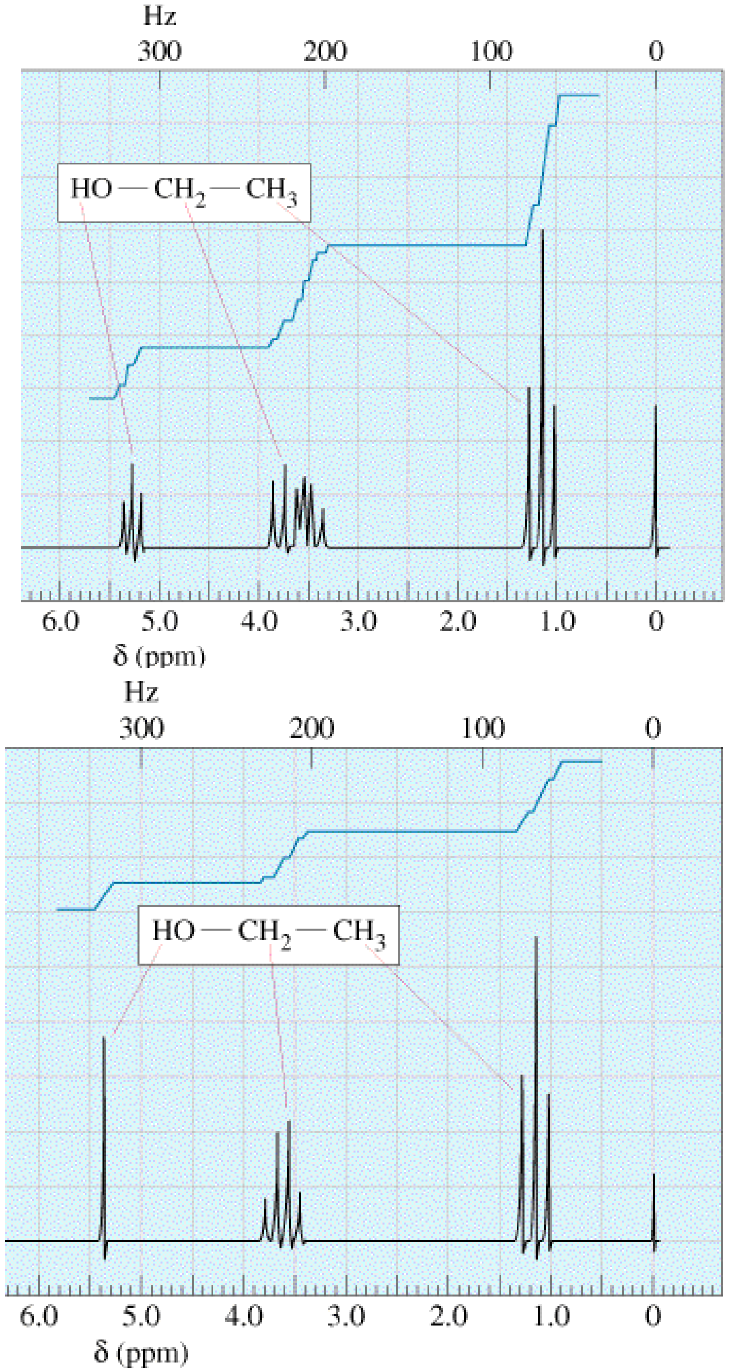






Time Dependence

- Molecules are tumbling relative to the magnetic field, so NMR is an averaged spectrum of all the orientations.
- Axial and equatorial protons on cyclohexane interconvert so rapidly that they give a single signal.
- Proton transfers for OH and NH may occur so quickly that the proton is not split by adjacent protons in the molecule.

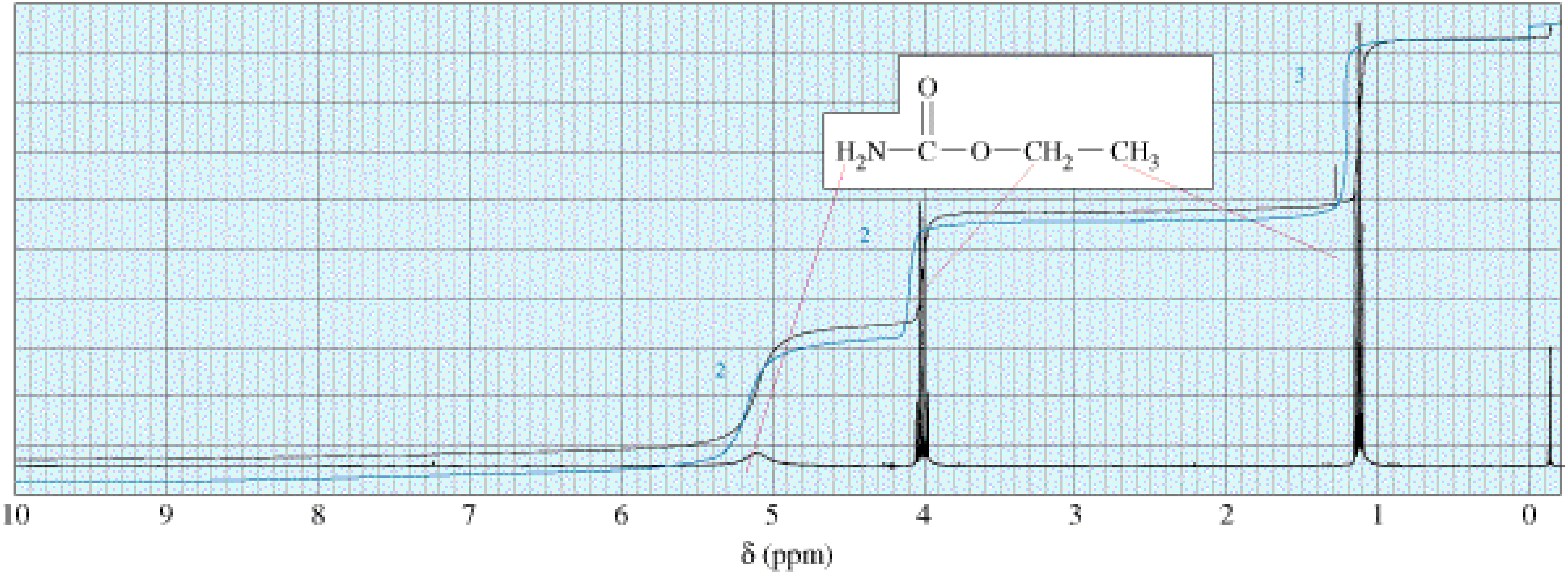


Hydroxyl Proton

- Ultrapure samples of ethanol show splitting.
- Ethanol with a small amount of acidic or basic impurities will not show splitting.

N-H Proton

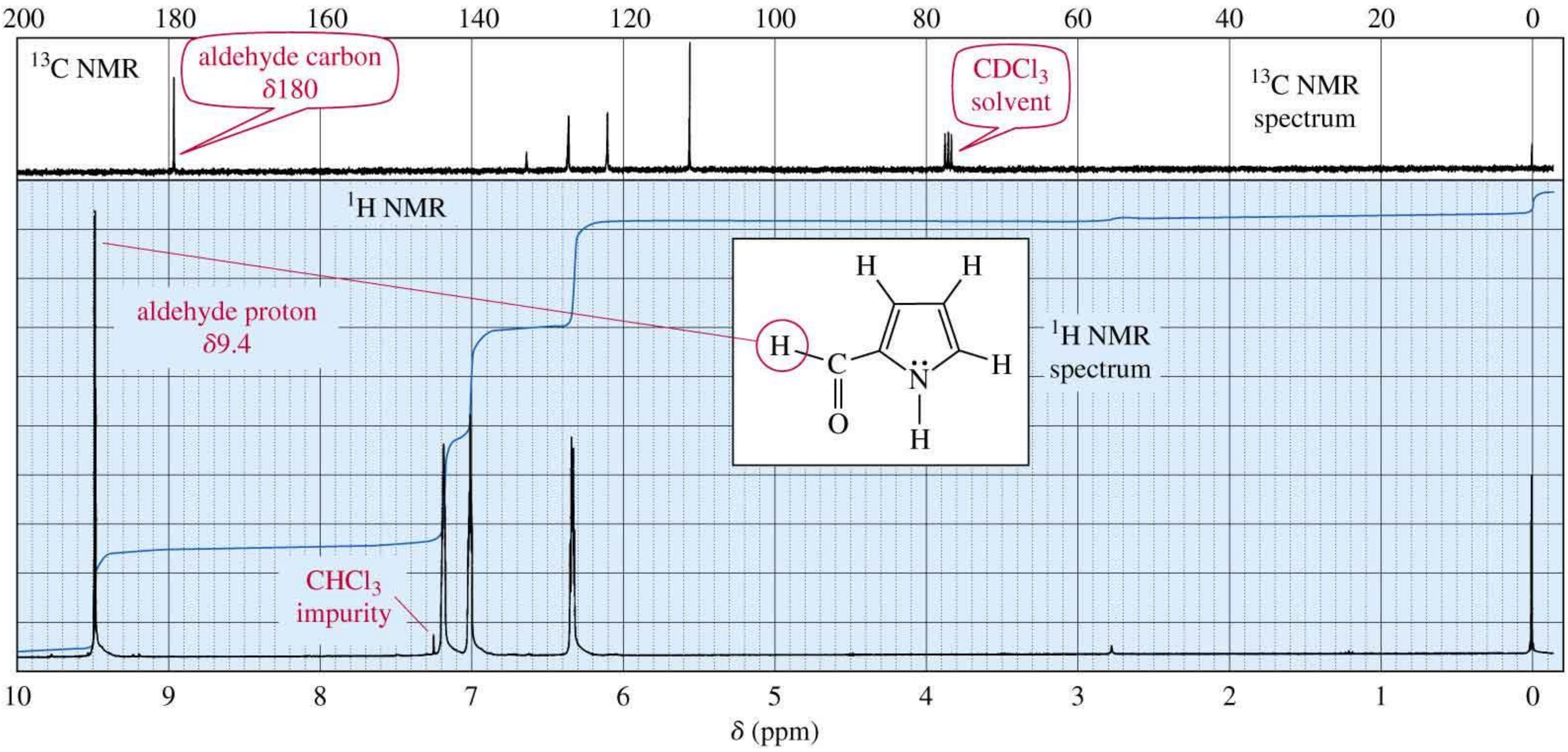
- Moderate rate of exchange.
- Peak may be broad.



Identifying the O-H or N-H Peak

- Chemical shift will depend on concentration and solvent.
- To verify that a particular peak is due to O-H or N-H, shake the sample with D_2O
- Deuterium will exchange with the O-H or N-H protons.
- On a second NMR spectrum the peak will be absent, or much less intense.

Combined ^{13}C and ^{1}H Spectra



Differences in ^{13}C Technique

- Resonance frequency is ~ one-fourth, 15.1 MHz instead of 60 MHz.
- Peak areas are not proportional to number of carbons.
- Carbon atoms with more hydrogens absorb more strongly.

Spin-Spin Splitting

- It is unlikely that a ^{13}C would be adjacent to another ^{13}C, so splitting by carbon is negligible.
- ^{13}C will magnetically couple with attached protons and adjacent protons.
- These complex splitting patterns are difficult to interpret.

Proton Spin Decoupling

- To simplify the spectrum, protons are continuously irradiated with “noise,” so they are rapidly flipping.
- The carbon nuclei see an average of all the possible proton spin states.
- Thus, each different kind of carbon gives a single, unsplit peak.

Off-Resonance Decoupling

- ^{13}C nuclei are split only by the protons attached directly to them.

- The $N + 1$ rule applies: a carbon with N number of protons gives a signal with $N + 1$ peaks.

Interpreting ^{13}C NMR

- The number of different signals indicates the number of different kinds of carbon.
- The location (chemical shift) indicates the type of functional group.
- The peak area indicates the numbers of carbons (if integrated).
- The splitting pattern of off-resonance decoupled spectrum indicates the number of protons attached to the carbon.

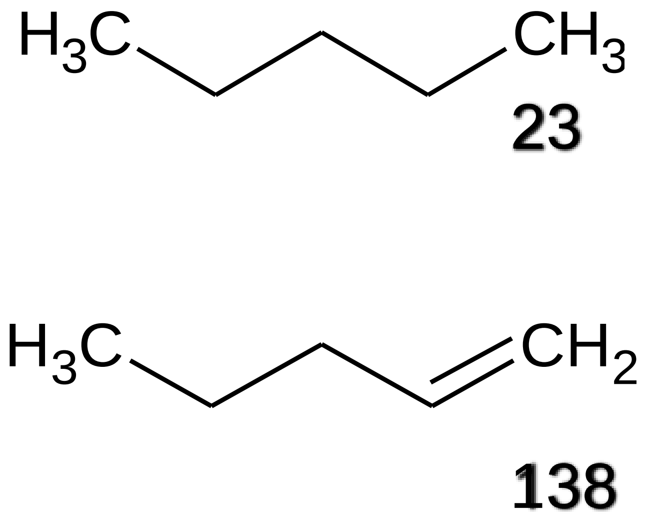
^{13}C Chemical Shifts

are measured in ppm (δ) from the carbons of TMS

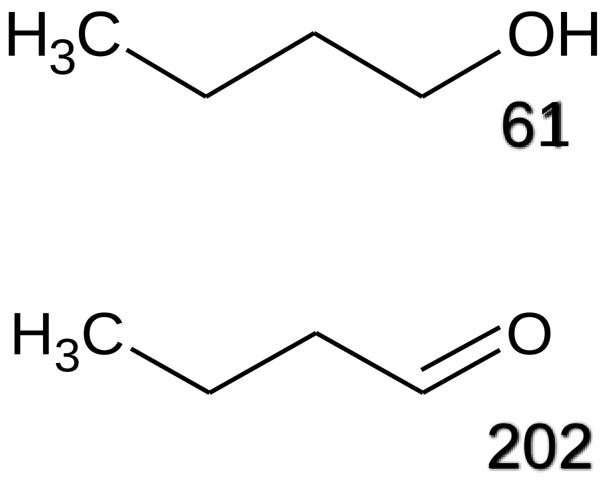
^{13}C Chemical shifts are most affected by:

- hybridization state of carbon
- electronegativity of groups attached to carbon

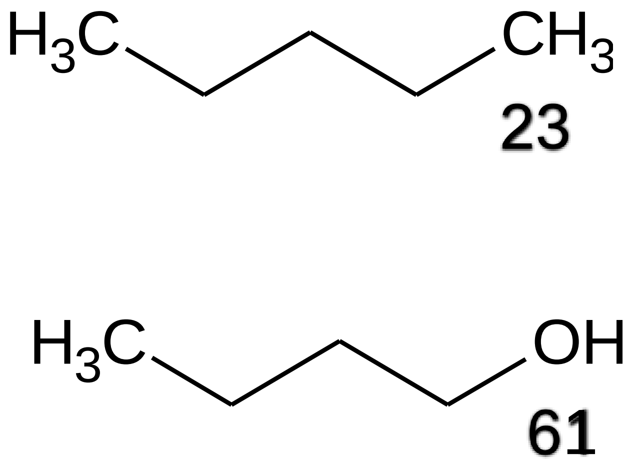
Examples (chemical shifts in ppm from TMS)



sp^3 hybridized carbon is more shielded than sp^2

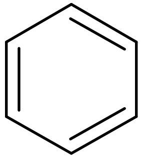


sp^3 hybridized carbon is more shielded than sp^2

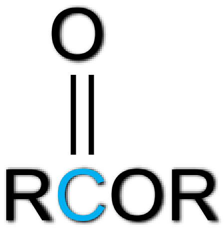
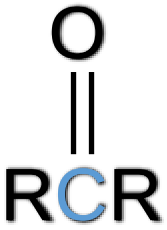


an electronegative atom deshields the carbon to which it is attached

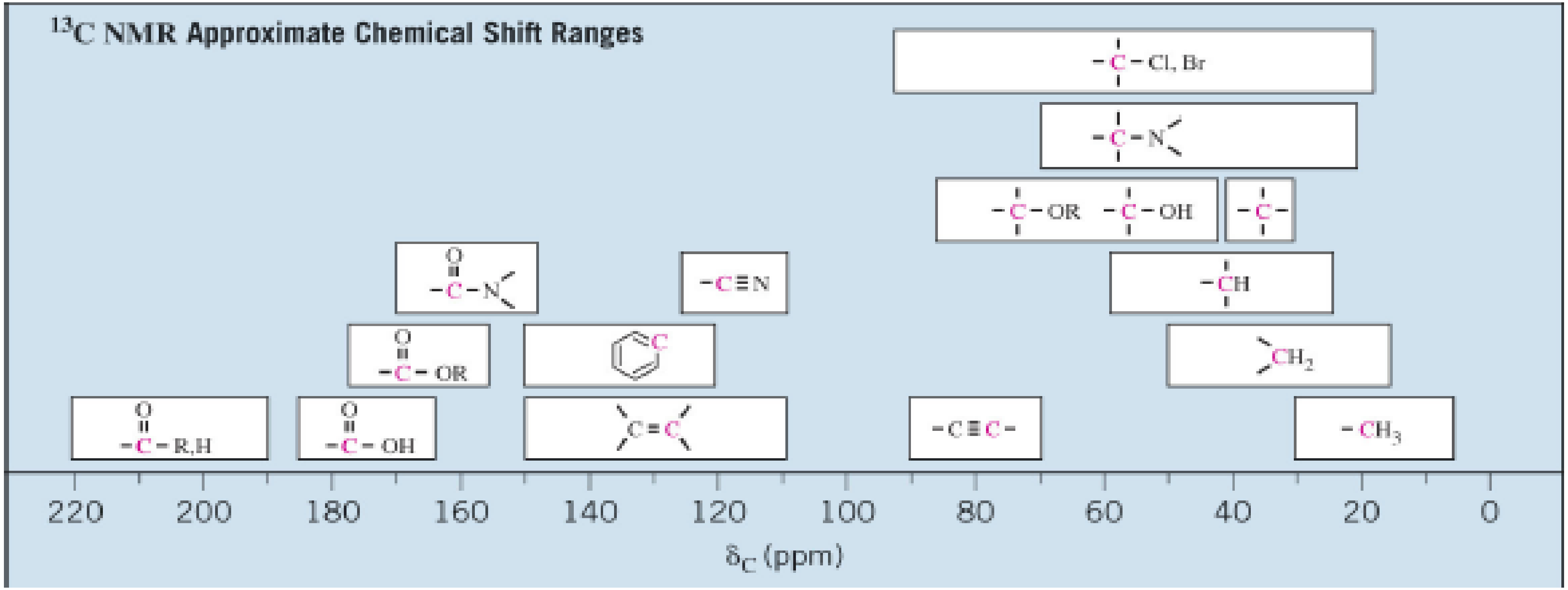
Type of carbon	Chemical shift (δ) ppm
RCH_3	0-35
R_2CH_2	15-40
R_3CH	25-50
R_4C	30-40

Type of carbon	Chemical shift (δ) ppm
$RC\equiv CR$	65-90
$R_2C=CR_2$	100-150
	110-175

Type of carbon	Chemical shift (δ) ppm
RCH_2Br	20-40
RCH_2Cl	25-50
RCH_2NH_2	35-50
RCH_2OH	50-65
RCH_2OR	50-65

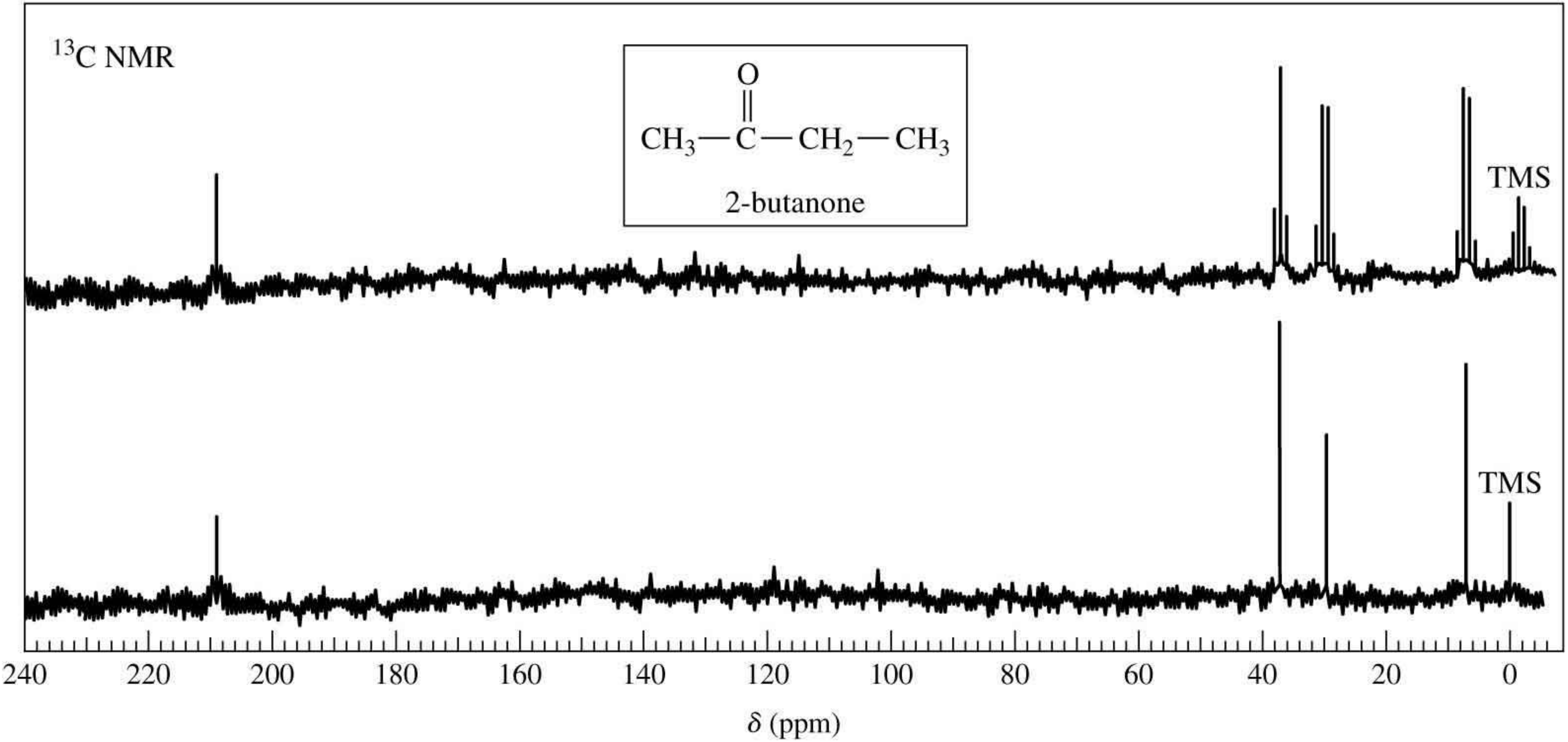
Type of carbon	Chemical shift (δ) ppm
 $R\overset{\overset{O}{\|}}{C}OR$	160-185
 $R\overset{\overset{O}{\|}}{C}R$	190-220

- **^{13}C Chemical Shifts**
  - ➔ Just as in ^{1}H NMR spectroscopy, chemical shifts in ^{13}C NMR depend on the electron density around the carbon nucleus
    - Decreased electron density causes the signal to move downfield (*desheilding*)
    - Increased electron density causes the signal to move upfield (*sheilding*)



- ➔ Because of the wide range of chemical shifts, it is rare to have two ^{13}C peaks coincidentally overlap
- ➔ A group of 3 peaks at δ 77 comes from the common NMR solvent deuteriochloroform and can be ignored

Two ^{13}C NMR Spectra



Hydrogen and Carbon Chemical Shifts