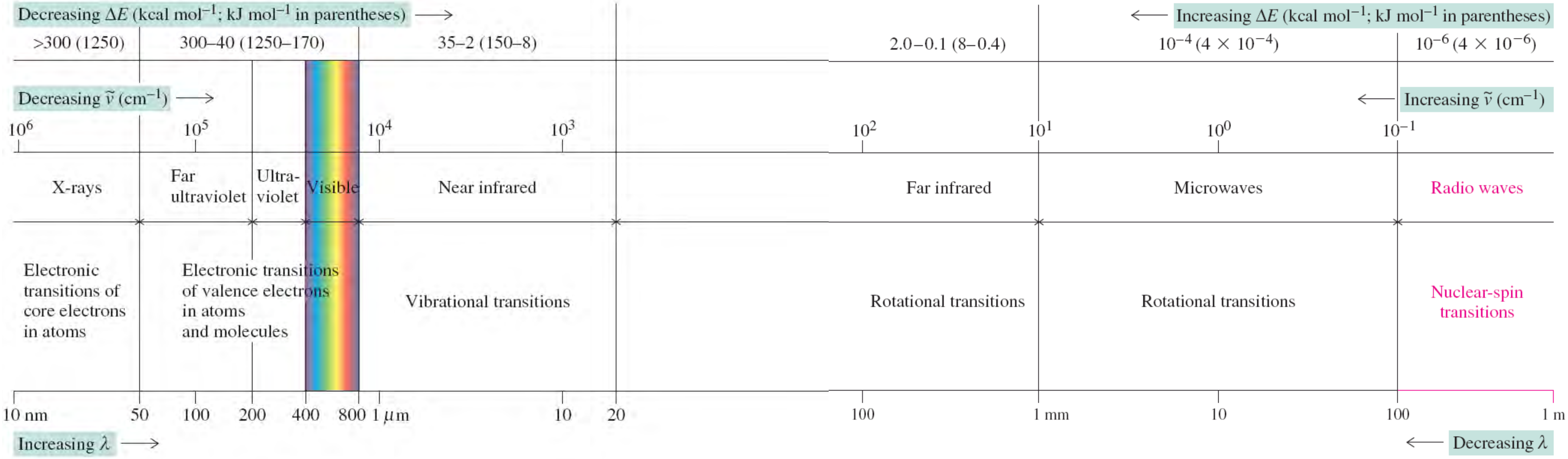
CHAPTER 10

Using Nuclear Magnetic Resonance Spectroscopy to Deduce Structure

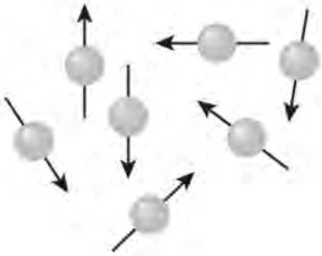


In this diagram, frequency is specified in units of wavenumbers, defined as 1/λ, which is the number of waves per centimeter.

Wavenumbers are used to specify energy in infrared spectroscopy.

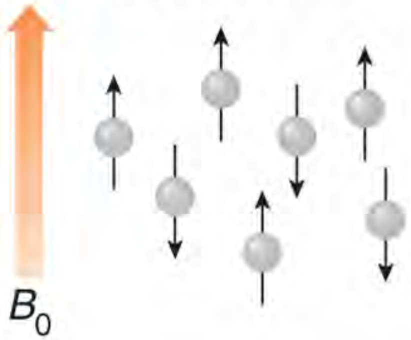
A spinning proton creates a magnetic field.

With no external magnetic field...

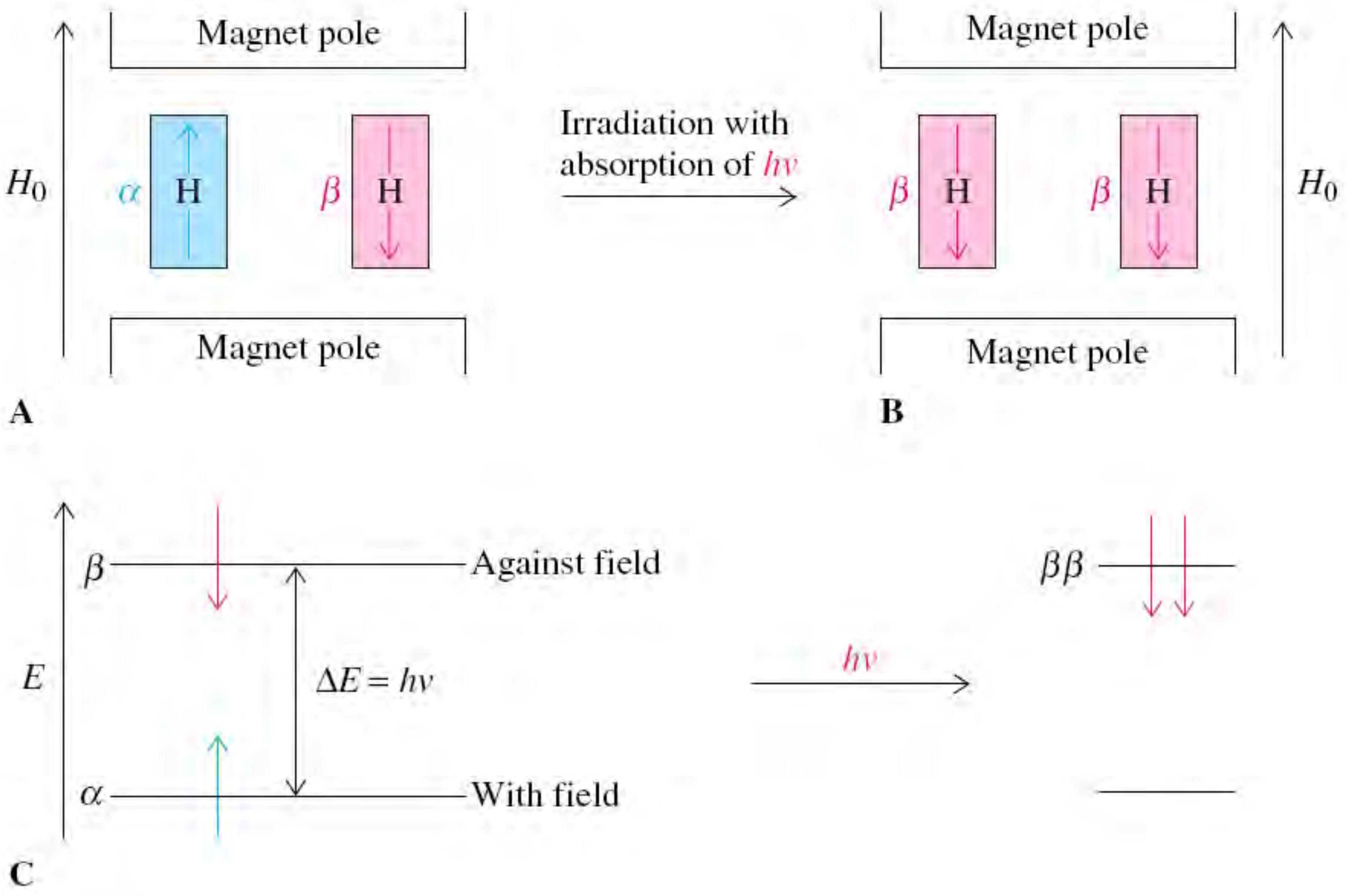


The nuclear magnets are randomly oriented.

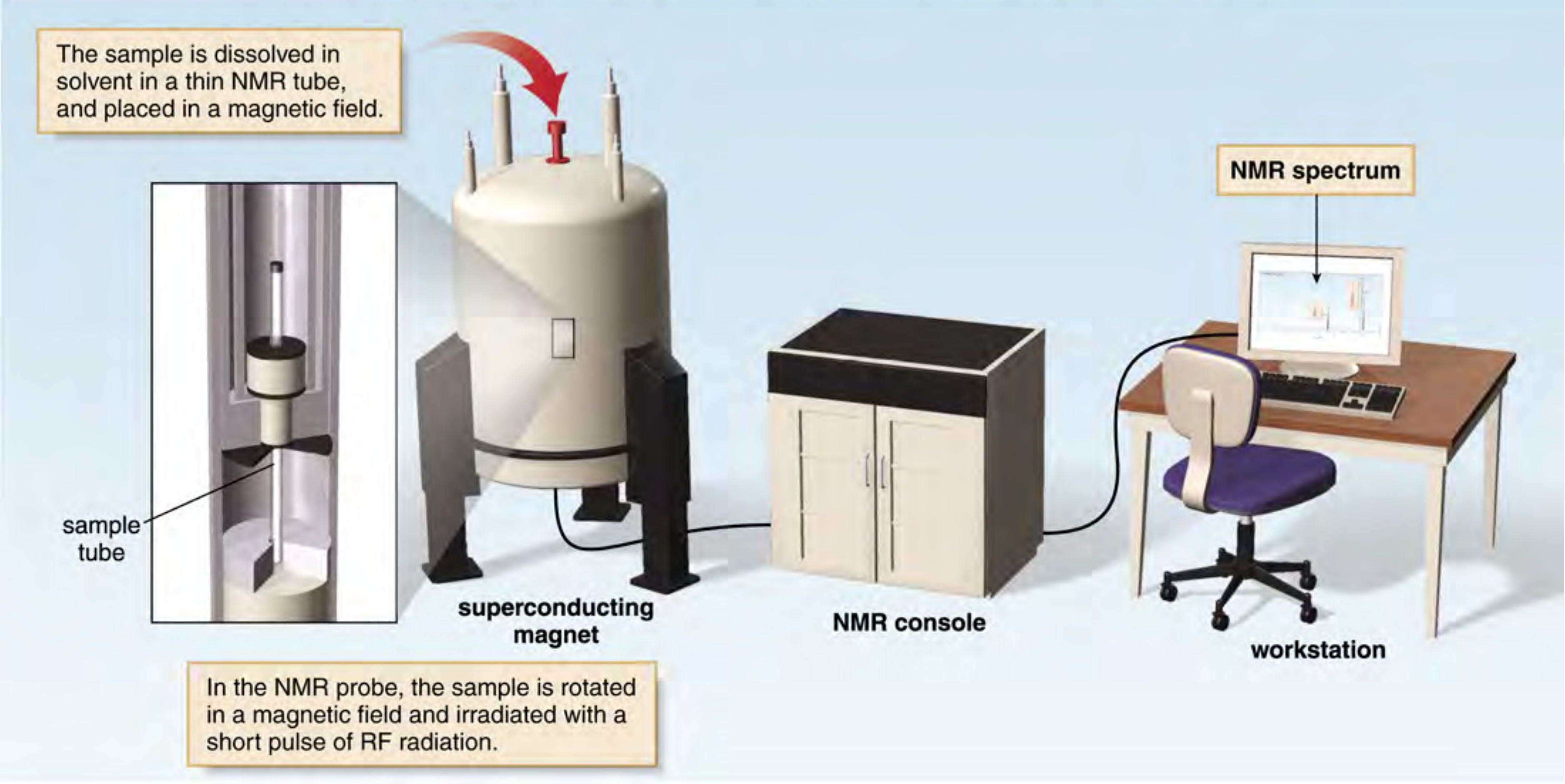
In a magnetic field...



The nuclear magnets are oriented **with or against B_0.**


H_0
Magnet pole
α
H
β
H
Magnet pole
A
Irradiation with absorption of $h\nu$
Magnet pole
β
H
β
H
Magnet pole
H_0
B
E
β
Against field
$\Delta E = h\nu$
α
With field
C
$h\nu$
$\beta\beta$

NMR Schematic


The sample is dissolved in solvent in a thin NMR tube, and placed in a magnetic field.

In the NMR probe, the sample is rotated in a magnetic field and irradiated with a short pulse of RF radiation.

An NMR spectrometer. The sample is dissolved in a solvent, usually $CDCl_3$ (deuterochloroform), and placed in a magnetic field. A radiofrequency generator then irradiates the sample with a short pulse of radiation, causing resonance. When the nuclei fall back to their lower energy state, the detector measures the energy released, and a spectrum is recorded. The superconducting magnets in modern NMR spectrometers have coils that are cooled in liquid helium and conduct electricity with essentially no resistance.

Many nuclei undergo magnetic resonance.

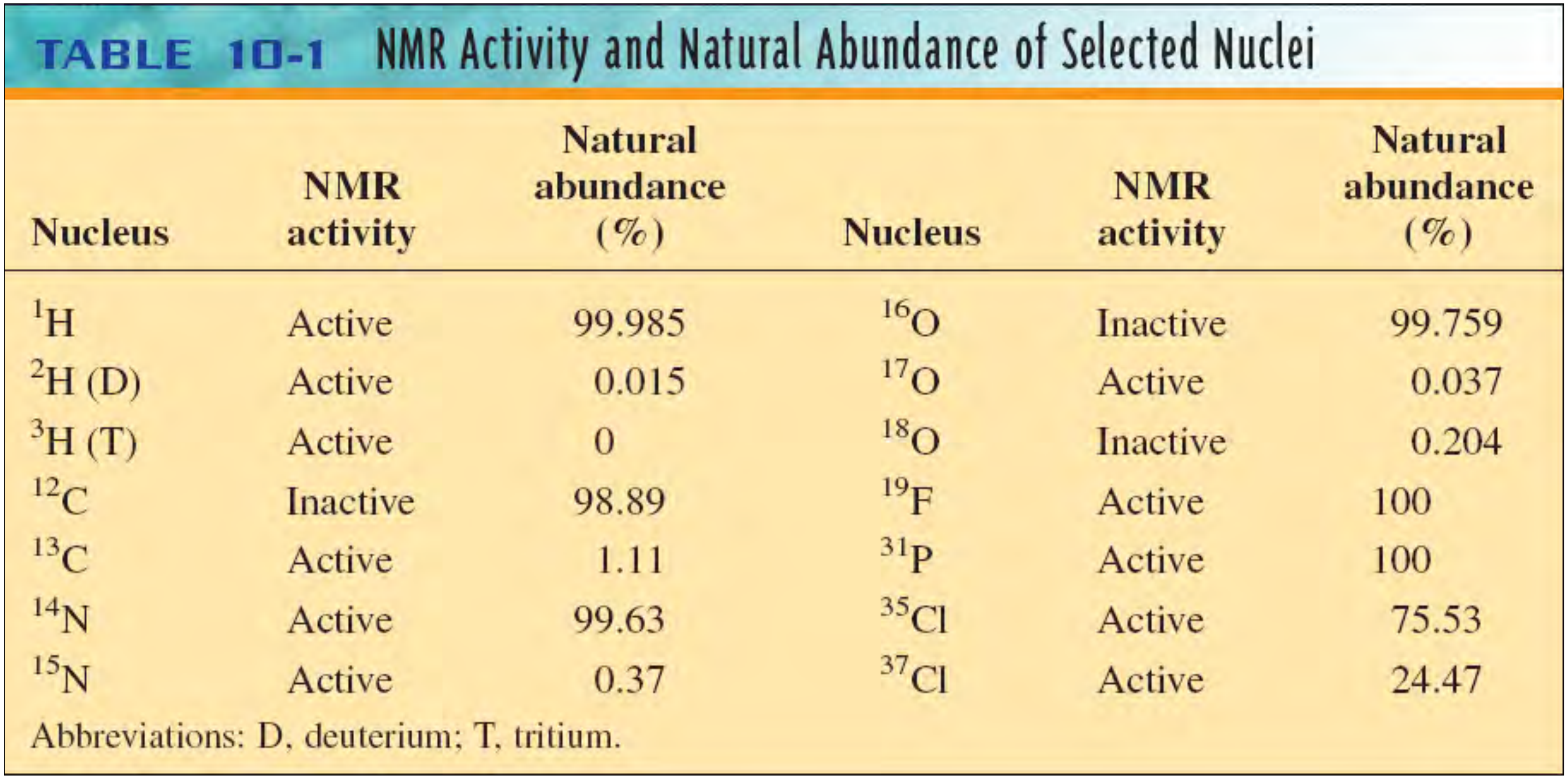


TABLE 10-1 NMR Activity and Natural Abundance of Selected Nuclei

Nucleus	NMR activity	Natural abundance (%)	Nucleus	NMR activity	Natural abundance (%)
^{1}H	Active	99.985	^{16}O	Inactive	99.759
^{2}H (D)	Active	0.015	^{17}O	Active	0.037
^{3}H (T)	Active	0	^{18}O	Inactive	0.204
^{12}C	Inactive	98.89	^{19}F	Active	100
^{13}C	Active	1.11	^{31}P	Active	100
^{14}N	Active	99.63	^{35}Cl	Active	75.53
^{15}N	Active	0.37	^{37}Cl	Active	24.47

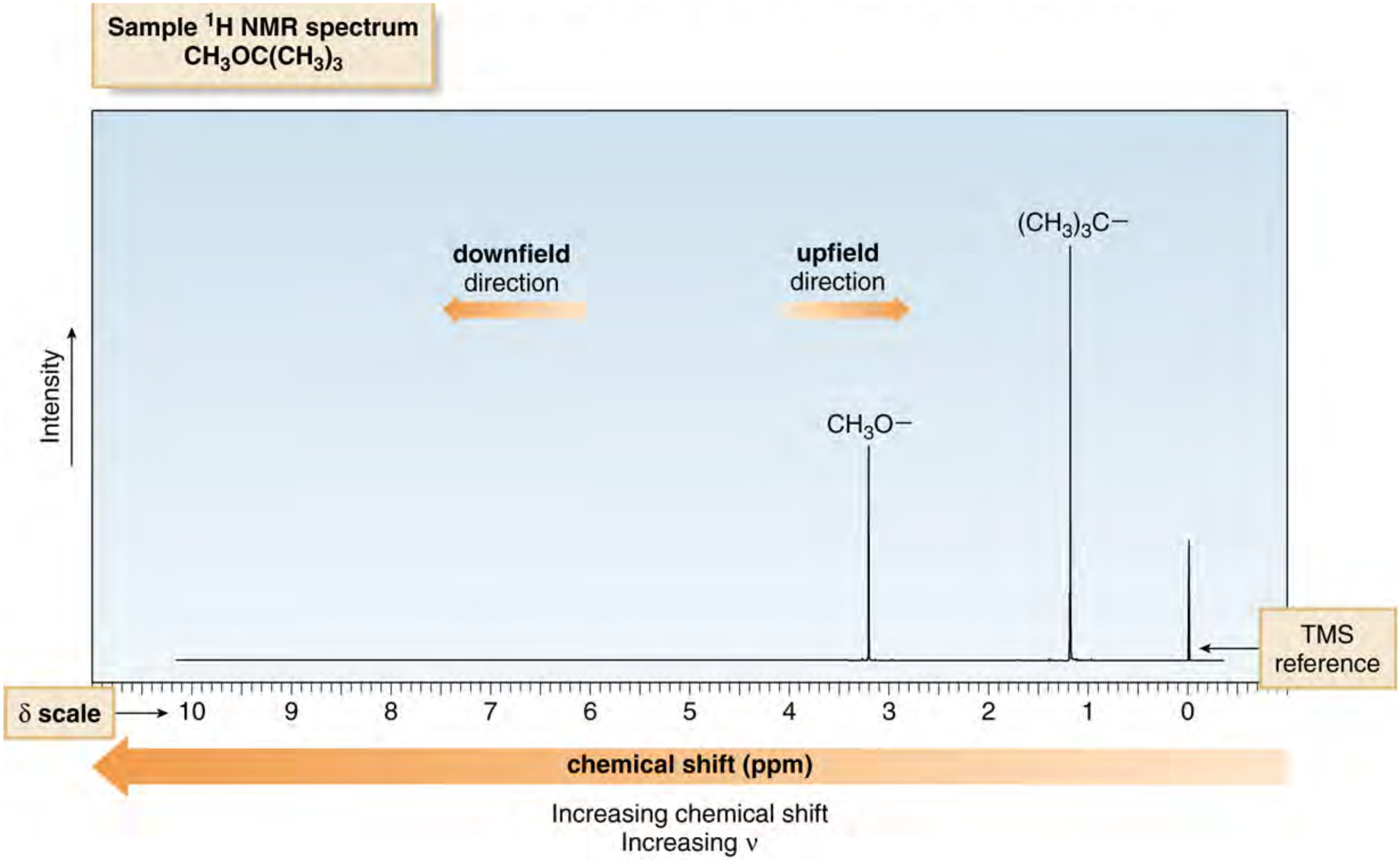
Abbreviations: D, deuterium; T, tritium.

In general, nuclei composed of an odd number of protons (^{1}H and its isotopes, ^{14}N ^{19}F, and ^{31}P) or an odd number of neutrons (^{13} C) show magnetic behavior.

If both the proton and neutron counts are even (^{12}C or ^{16}O) the nuclei are non-magnetic.

^{1}H NMR Spectra

- **An NMR spectrum is a plot of the intensity of a peak against its chemical shift, measured in parts per million (ppm).**

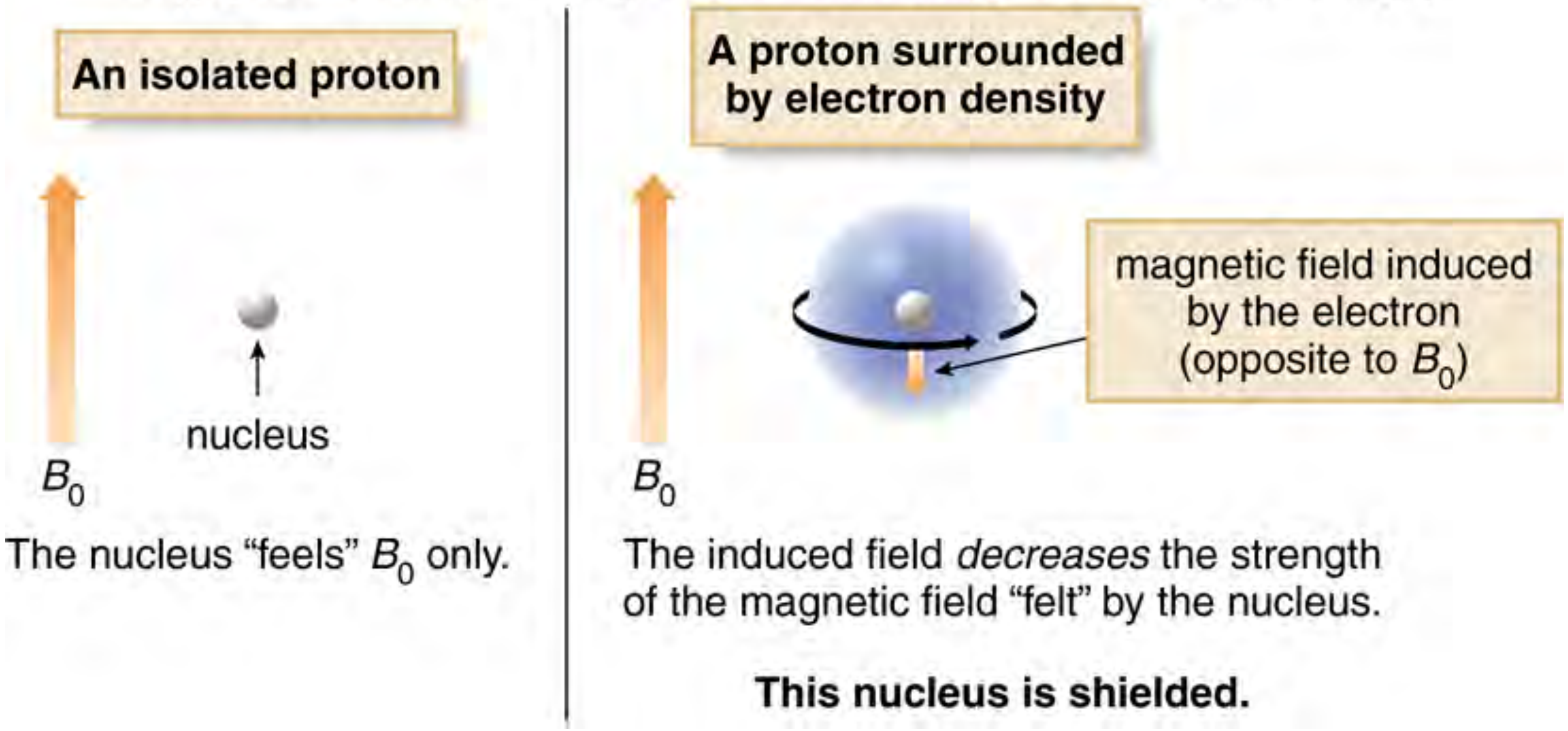


Structural Information from Features of a ^{1}H NMR Spectrum

- **Position of signals**: indicates what types of hydrogen the molecule contains.
- **Number of signals**: indicates the number of **different types** of hydrogen in a molecule.
- **Intensity of signals**: indicates the relative amounts (how many) of each kind of hydrogen in the molecule.
- **Spin-spin splitting of signals**: gives further information of the neighboring environment for the various hydrogens in the molecule.

Shielding and Chemical Shift

- **Protons in a given environment absorb in a predictable region in an NMR spectrum.**
- **Two important factors: electronegativity and magnetic anisotropy**



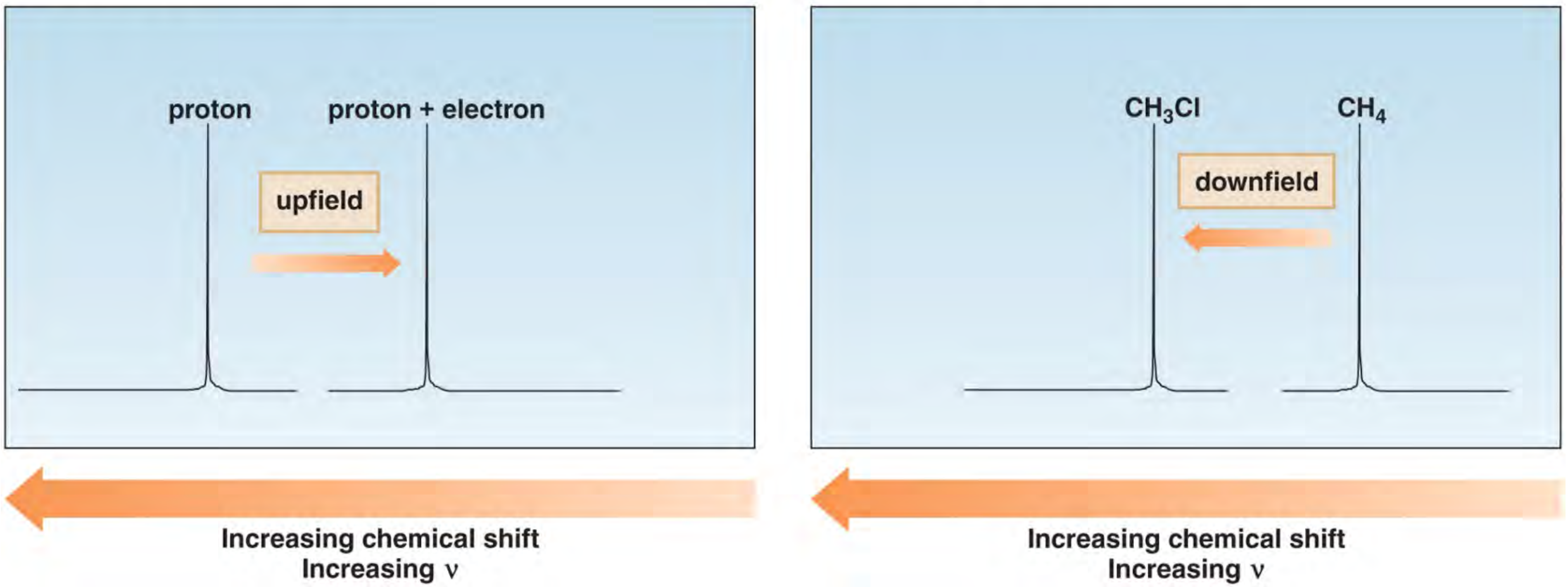
Shielding and Chemical Shift

a. Shielding effects

- An electron shields the nucleus.
- The absorption shifts *upfield*.

b. Deshielding effects

- Decreased electron density deshields a nucleus.
- The absorption shifts *downfield*.

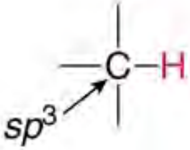
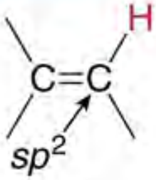
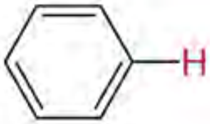
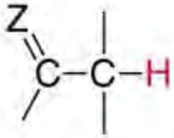
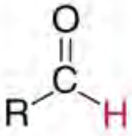
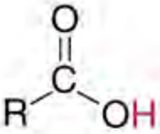
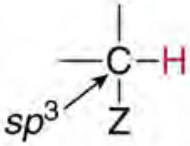


The degree of shielding of a nucleus depends upon its surrounding electron density.

Adding electrons increases shielding.

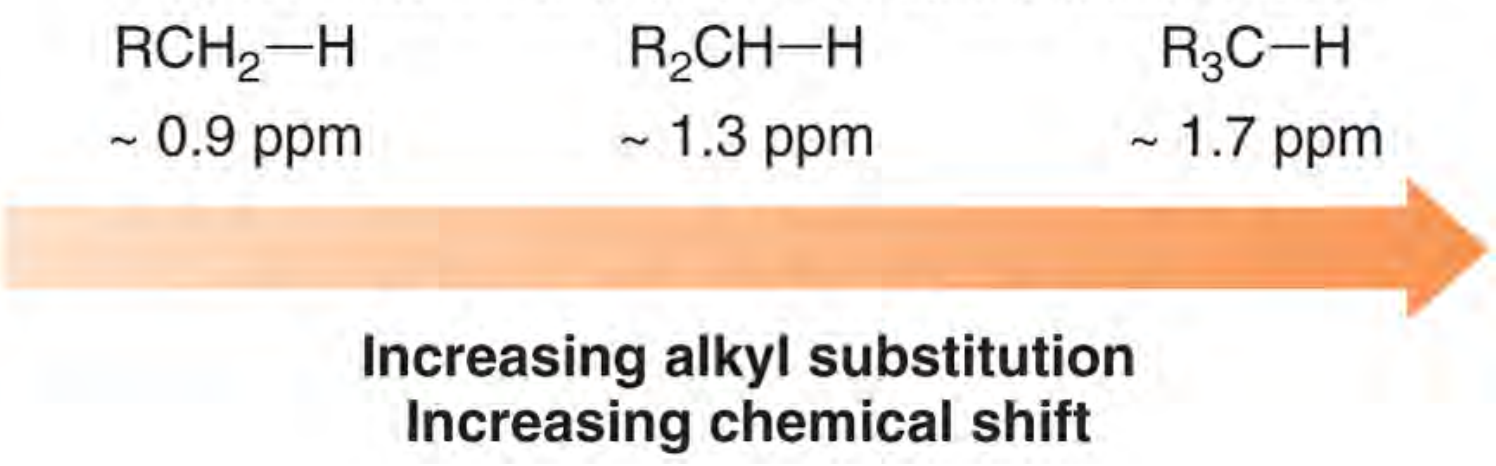
Removing electrons causes deshielding.

Characteristic Chemical Shifts Relative to TMS (0 ppm)

Type of proton	Chemical shift (ppm)	Type of proton	Chemical shift (ppm)
	0.9–2		4.5–6
- RCH_3 - R_2CH_2 - R_3CH	~0.9 ~1.3 ~1.7		6.5–8
 Z = C, O, N	1.5–2.5		9–10
—C≡C—H	~2.5		10–12
 Z = N, O, X	2.5–4	RO—H or R—N—H	1–5

Electronegativity and Chemical Shift

- **The chemical shift of a C−H bond increases with increasing alkyl substitution or electronegative atoms attached.**



RCH_2-H RCH_2-OH

The absorptions of alkane hydrogens occur at relatively high field.

Hydrogens close to an electron withdrawing group (halogen or oxygen) are shifted to relatively lower field (deshielding).

The more electronegative the atom, the more the deshielded methyl hydrogens are relative to methane.

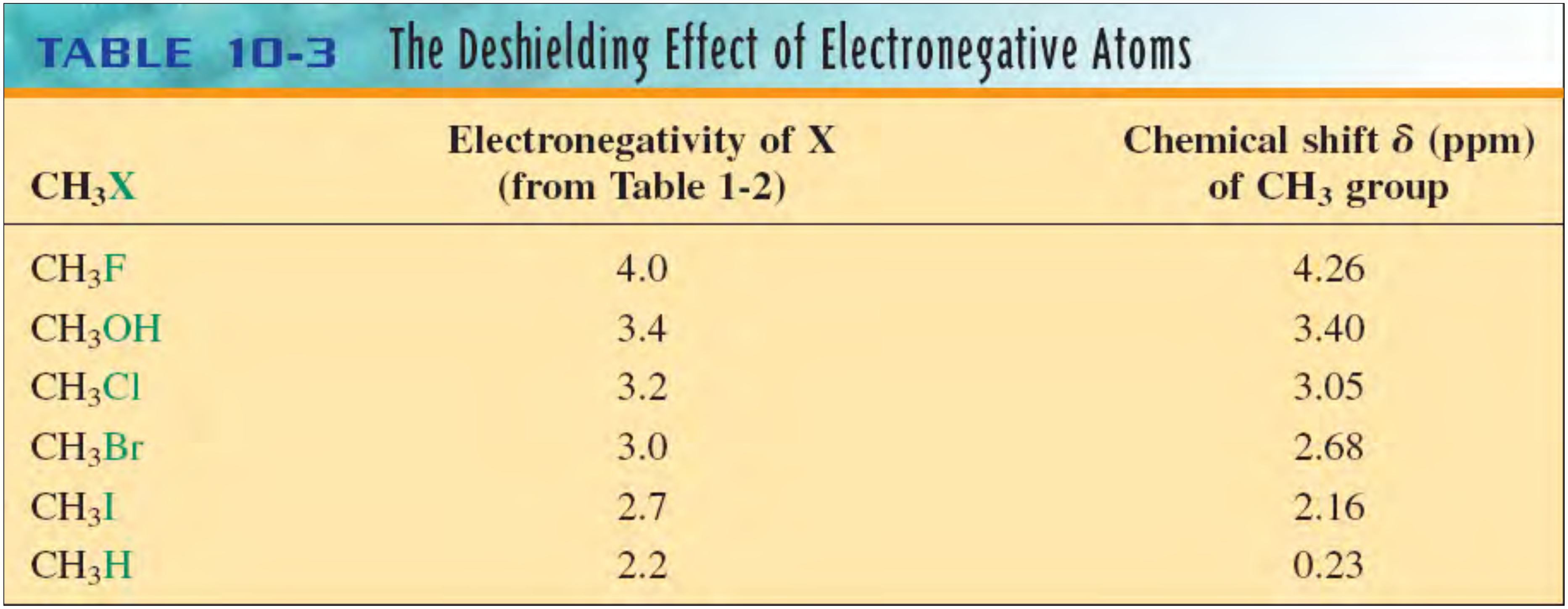
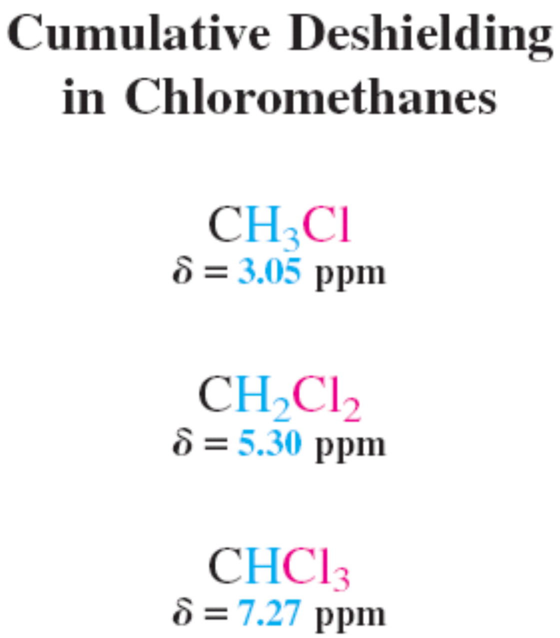


TABLE 10-3 The Deshielding Effect of Electronegative Atoms

CH_3X	Electronegativity of X (from Table 1-2)	Chemical shift δ (ppm) of CH_3 group
CH_3F	4.0	4.26
CH_3OH	3.4	3.40
CH_3Cl	3.2	3.05
CH_3Br	3.0	2.68
CH_3I	2.7	2.16
CH_3H	2.2	0.23

Multiple substituents exert a cumulative effect.



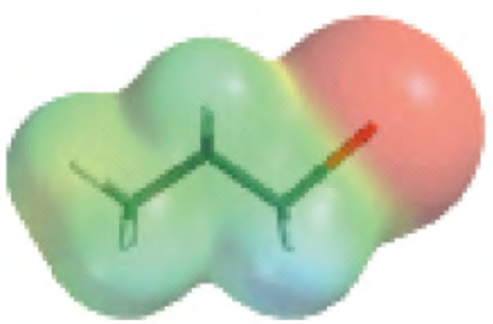
Cumulative Deshielding in Chloromethanes

CH_3Cl
$\delta = 3.05$ ppm

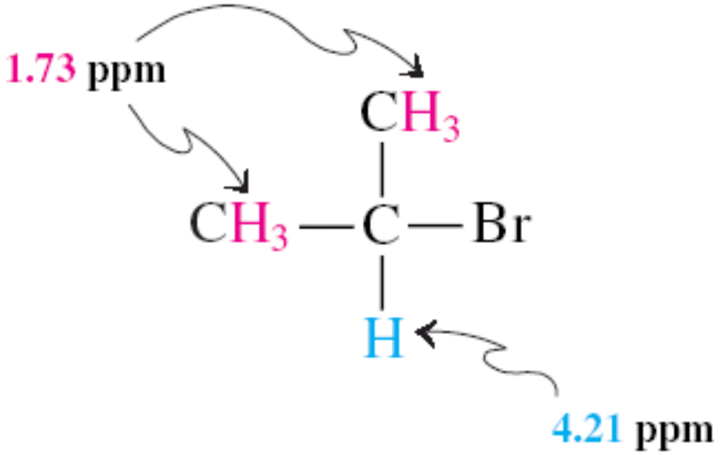
CH_2Cl_2
$\delta = 5.30$ ppm

$CHCl_3$
$\delta = 7.27$ ppm

The deshielding influence of electron withdrawing groups diminishes rapidly with distance.



1-Bromopropane



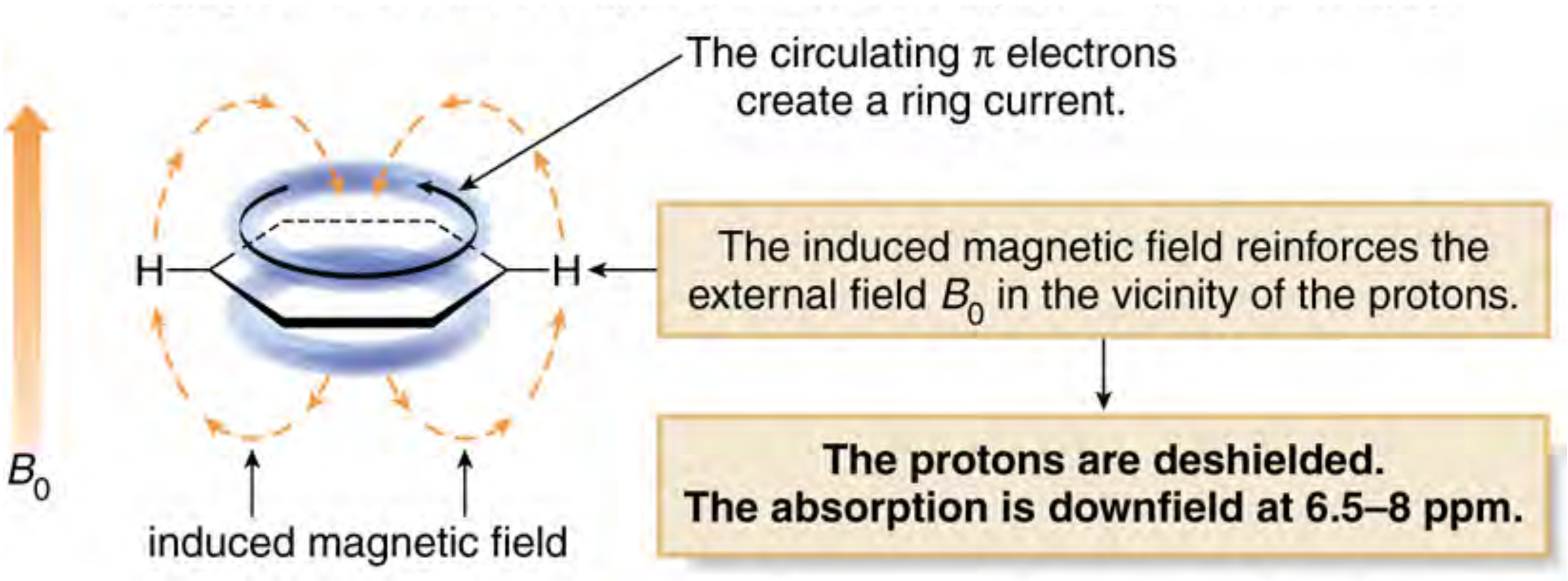
$$CH_3-\overset{\displaystyle CH_3}{\underset{\displaystyle H}{C}}-Br$$

$CH_3-CH_2-CH_2-Br$

$\delta =$ 1.03 1.88 3.39 ppm

Aromatic Deshielding and Anisotropy

- In a magnetic field, the six π electrons in benzene circulate around the ring creating a ring current.
- The magnetic field induced by these moving electrons reinforces the applied magnetic field in the vicinity of the protons.
- The protons thus feel a stronger magnetic field and a higher frequency is needed for resonance meaning they are deshielded and absorb downfield.



The circulating π electrons create a ring current.

The induced magnetic field reinforces the external field B_0 in the vicinity of the protons.

**The protons are deshielded.
The absorption is downfield at 6.5–8 ppm.**

Alkyne Chemical Shifts

- In a magnetic field, the π electrons of a carbon-carbon triple bond are induced to circulate, but in this case the induced magnetic field opposes the applied magnetic field (B_0).
- The proton thus feels a weaker magnetic field, so a lower frequency is needed for resonance.
- The nucleus is shielded and the absorption is upfield.

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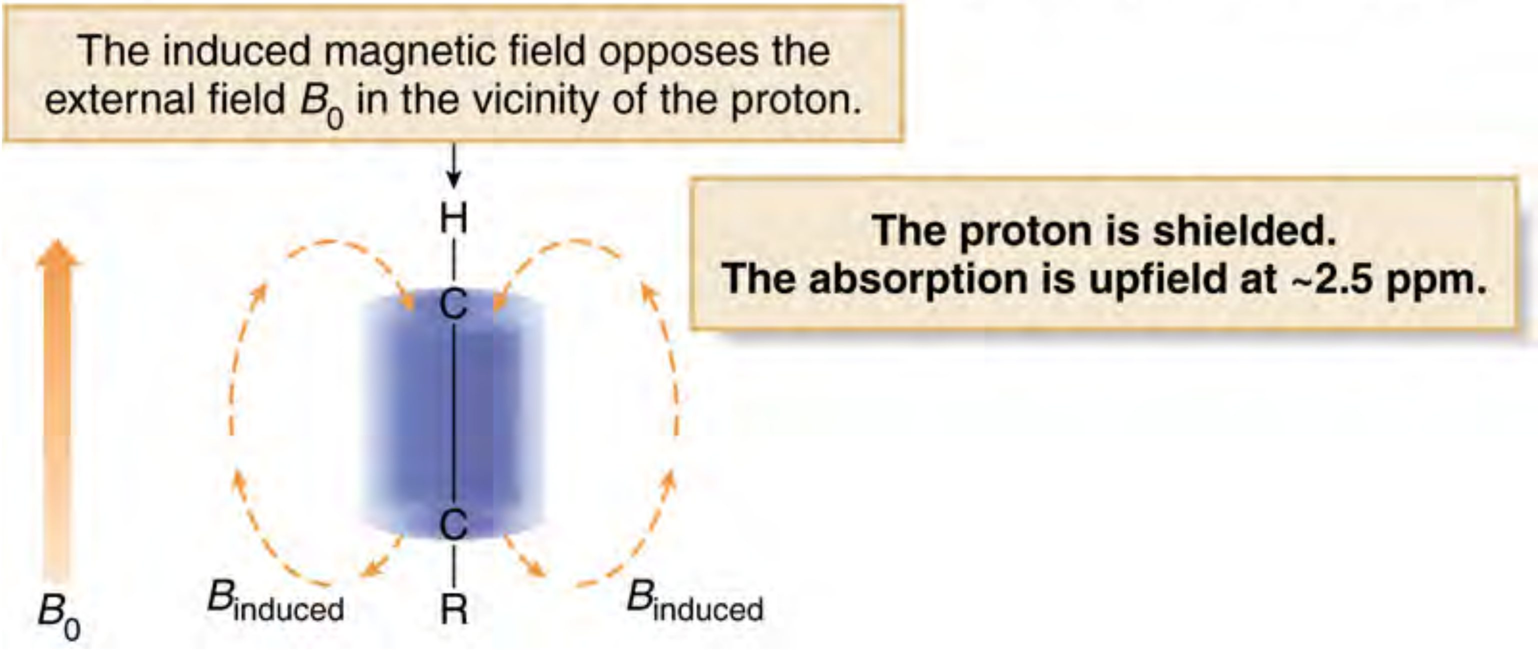
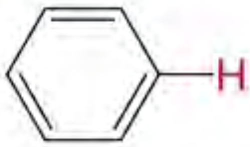
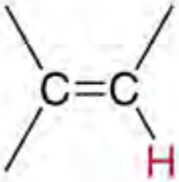


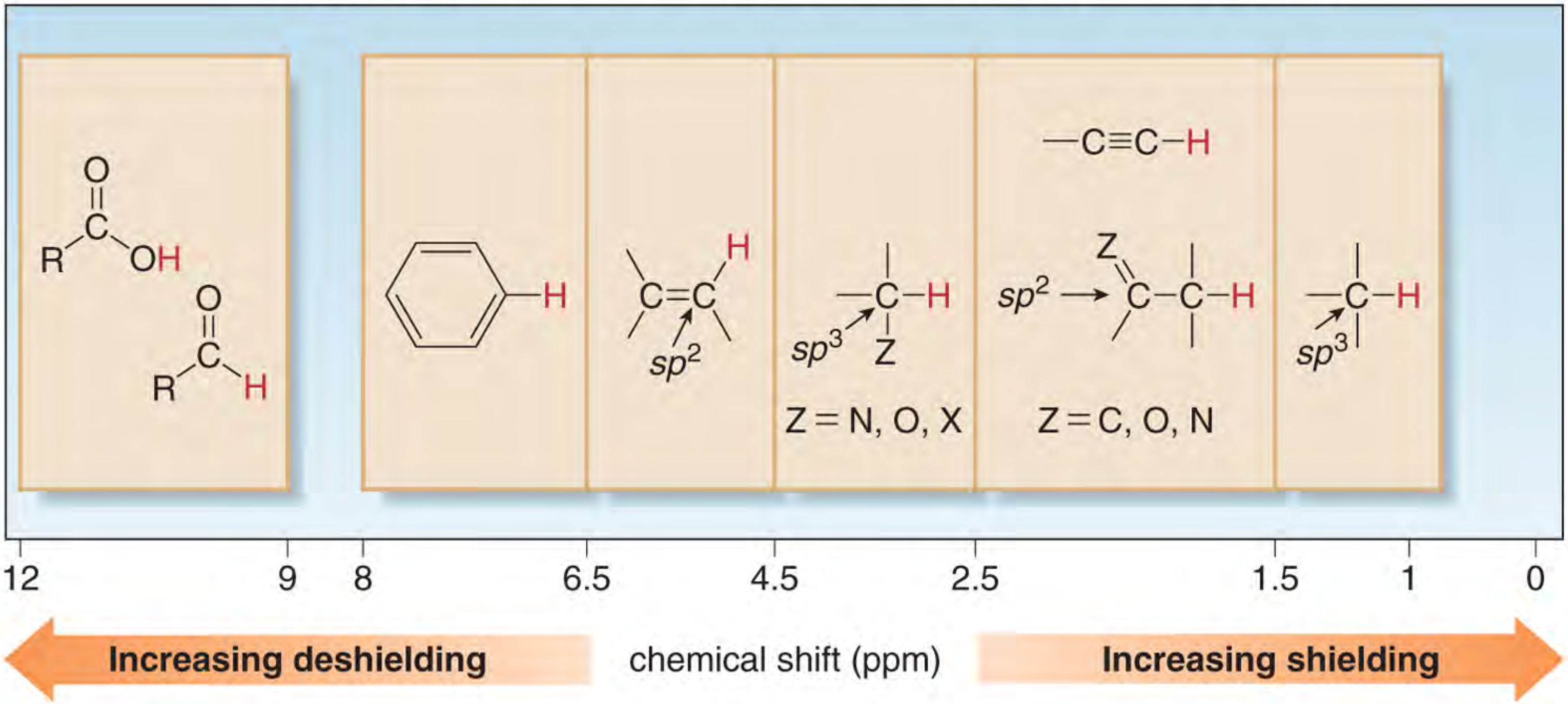
The induced magnetic field opposes the external field B_0 in the vicinity of the proton.

The proton is shielded. The absorption is upfield at ~2.5 ppm.

Summary of π Electron and Chemical Shift

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

Regions in the ^{1}H NMR Spectrum



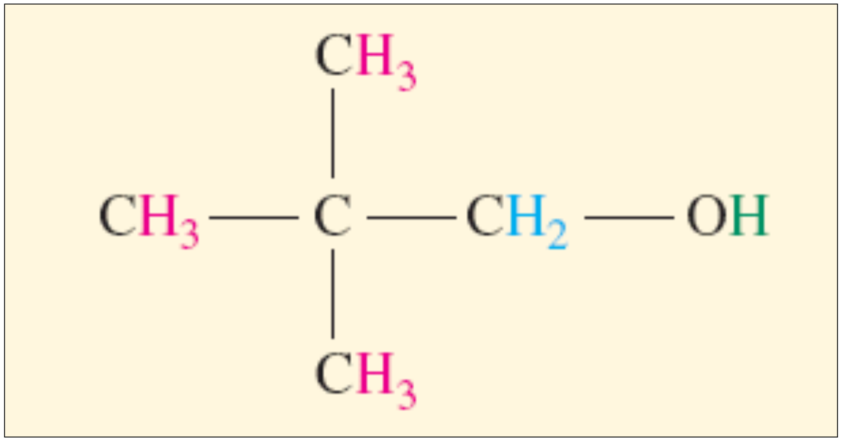
- Shielded protons absorb at lower chemical shift (to the right).
- Deshielded protons absorb at higher chemical shift (to the left).

Structural Information from Features of a ^{1}H NMR Spectrum

- Position of signals: indicates what types of hydrogen the molecule contains.
- Number of signals: indicates the number of different types of hydrogen in a molecule.
- Intensity of signals: indicates the relative amounts (how many) of each kind of hydrogen in the molecule.
- Spin-spin splitting of signals: gives further information of the neighboring environment for the various hydrogens in the molecule.

20

Chemically equivalent hydrogens in a molecule all have identical electronic environments and therefore show NMR peaks at the same position.



In the NMR spectrum of 2,2-dimethyl-a-propanol, there are three different peaks due to absorptions by:

Nine equivalent methyl hydrogens on the butyl group (most shielded);

One hydrogen on the OH;

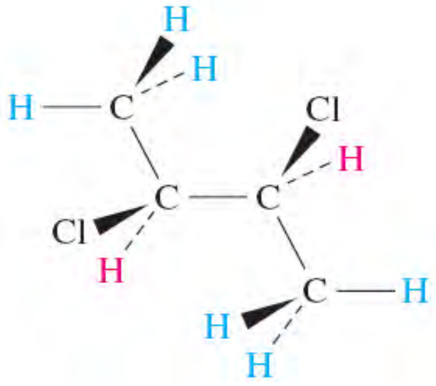
Two equivalent methylene hydrogens.

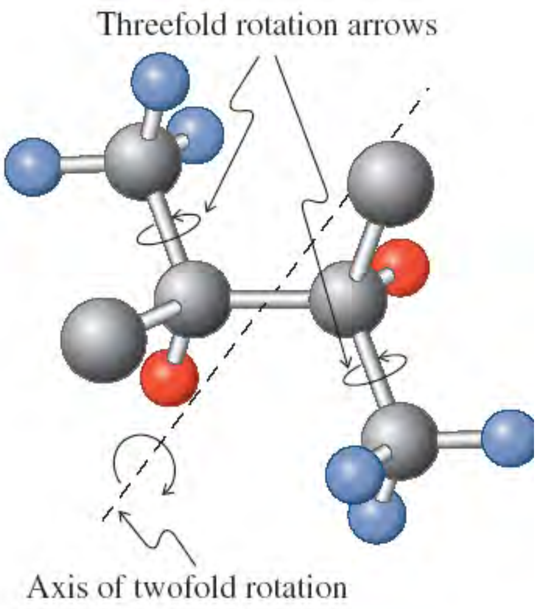
10-5 Tests for Chemical Equivalence

Molecular symmetry helps establish chemical equivalence.

Rotational symmetry results in equivalent protons when the group of protons is rapidly rotating, as in a methyl group.

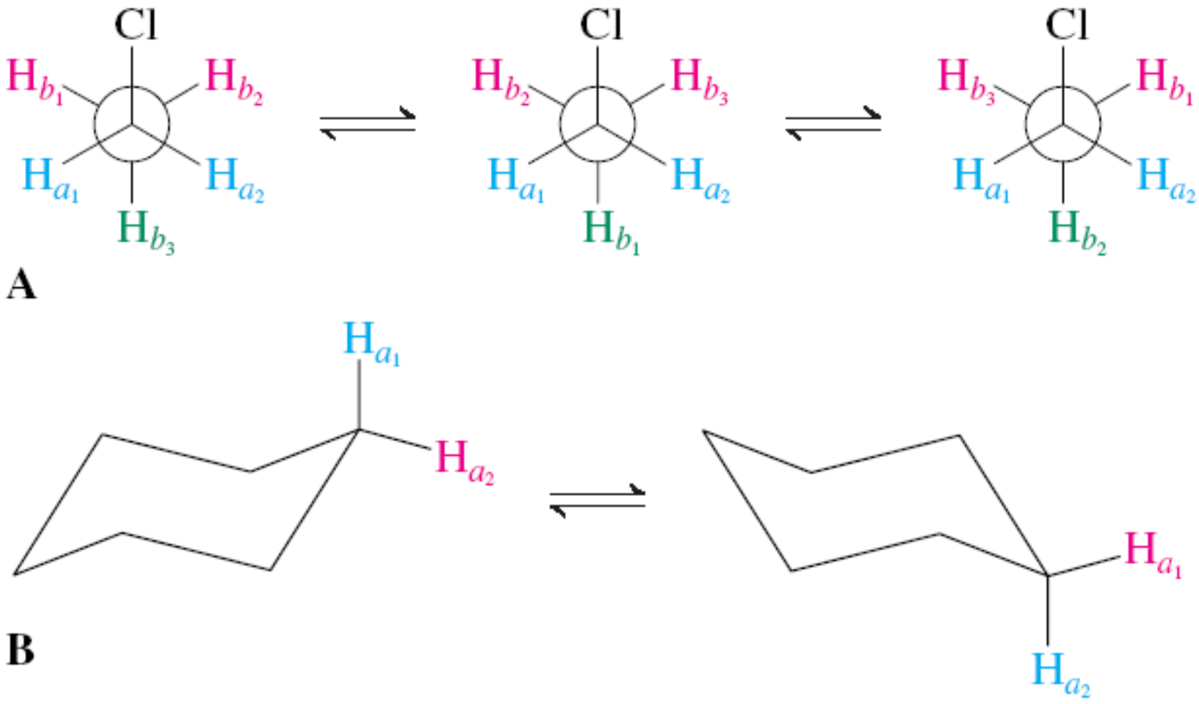
Figure 10-12 Rotation of a methyl group as a test of symmetry.





Conformational interconversion may result in equivalence on the NMR time scale.

In the case of the rapid rotation of the methyl group in chloroethane, or the rapid conformation flip in cyclohexane, the observed chemical shifts are the averages of the values that would be observed without the rapid rotation or flip.



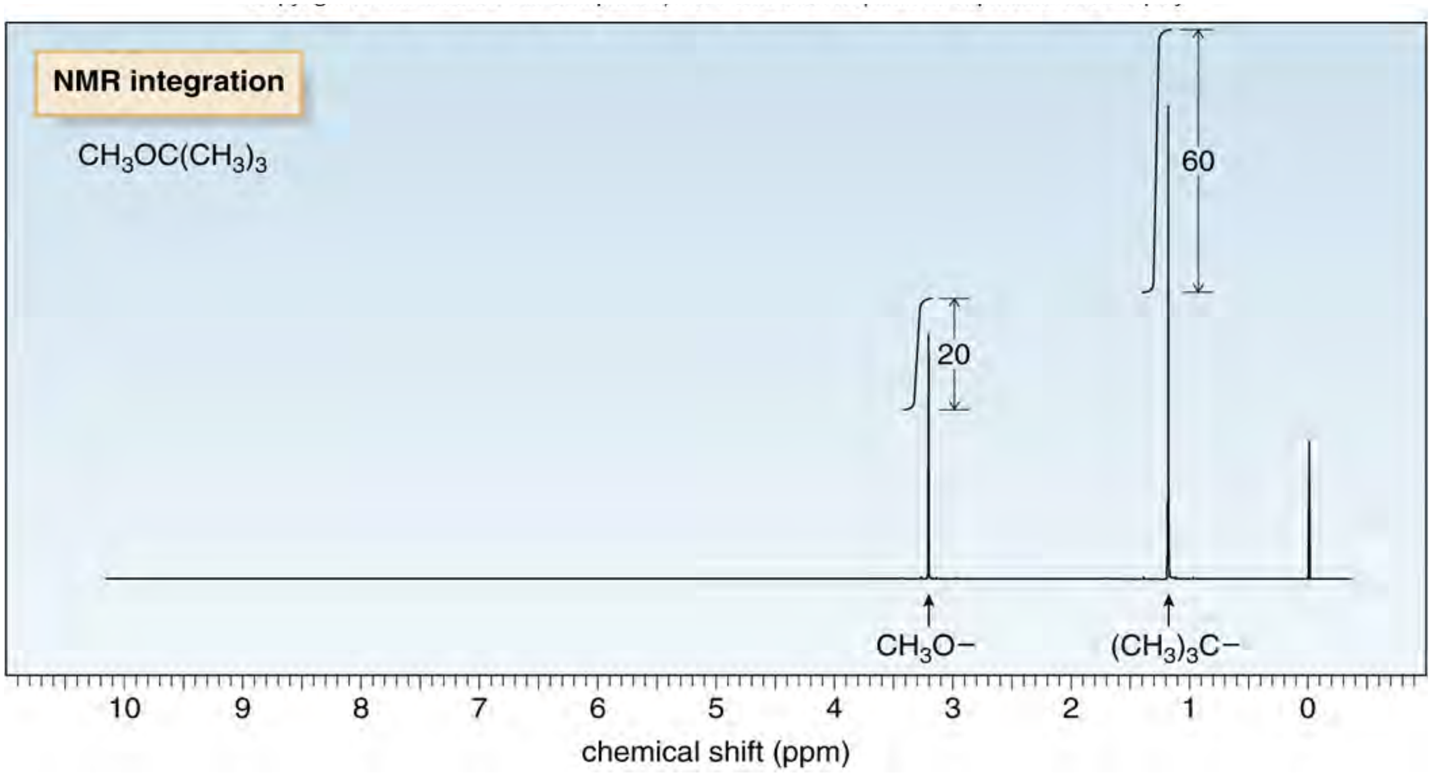
For cyclohexane, the single line in the NMR spectra at δ = 1.36 ppm at room temperature becomes two lines at a temperature of -90º C, one at δ = 1.12 ppm for the six axial hydrogens and one at δ = 1.60 for the six equatorial hydrogens.

Structural Information from Features of a ^{1}H NMR Spectrum

- **Position of signals**: indicates what types of hydrogen the molecule contains.
- **Number of signals**: indicates the number of **different types** of hydrogen in a molecule.
- **Intensity of signals**: indicates the relative amounts (how many) of each kind of hydrogen in the molecule.
- **Spin-spin splitting of signals**: gives further information of the neighboring environment for the various hydrogens in the molecule.

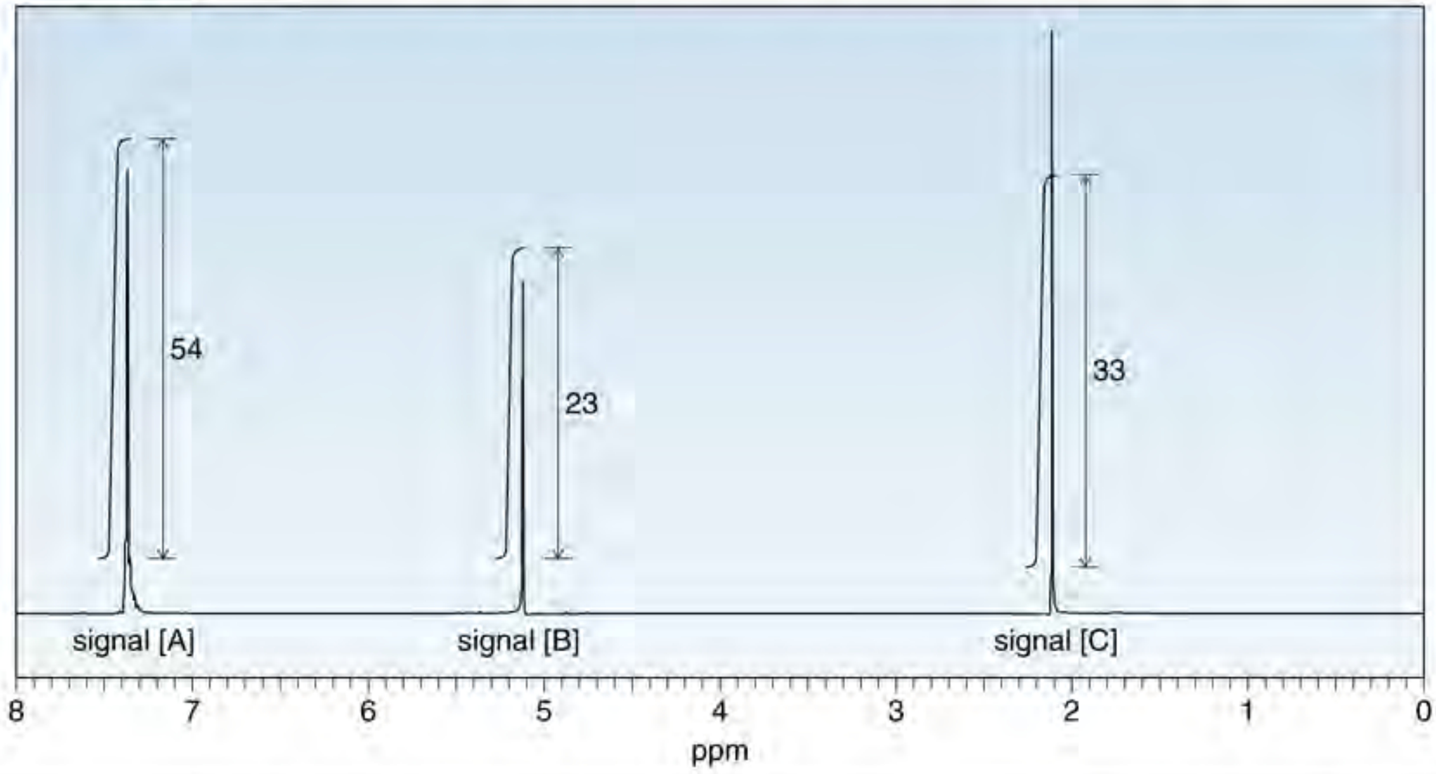
^{1}H NMR Integration

- **Modern NMR spectrometers automatically calculate and plot the value of each integral in arbitrary units.**
- **The ratio of integrals to one another gives the ratio of absorbing protons in a spectrum.**
- **Note that this gives a ratio, and not the absolute number, of absorbing protons.**



HOW TO Determine the Number of Protons Giving Rise to an NMR Signal

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



2.35 1.0 1.43

Structural Information from Features of a ^{1}H NMR Spectrum

- **Position of signals**: indicates what types of hydrogen the molecule contains.
- **Number of signals**: indicates the number of **different types** of hydrogen in a molecule.
- **Intensity of signals**: indicates the relative amounts (how many) of each kind of hydrogen in the molecule.
- **Spin-spin splitting of signals**: gives further information of the neighboring environment for the various hydrogens in the molecule.

^{1}H NMR—Spin-Spin Splitting

- **The spectra up to this point have been limited to single absorptions called singlets.**
- **Often signals for different protons are split into more than one peak.**

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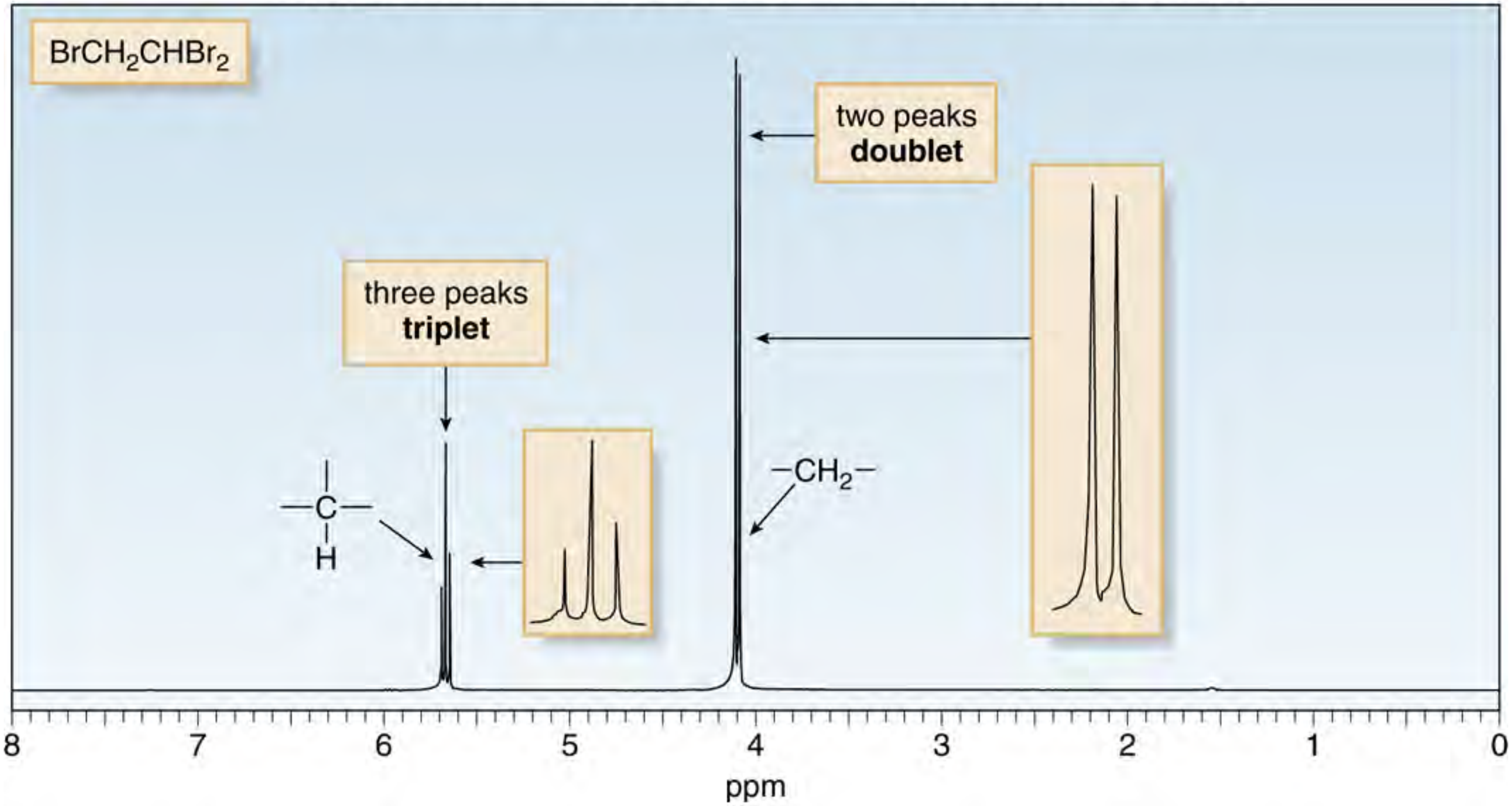


10-7 Spin-Spin Coupling: The Effect of Non-Equivalent Neighboring Hydrogens

When non-equivalent hydrogen atoms are not separated by at least one carbon or oxygen atom, an additional phenomenon called "spin-spin splitting" or "spin-spin coupling" occurs.

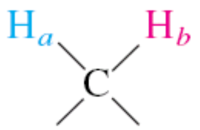
Instead of single peaks (singlets), more complex patterns occur called multiplets (doublets, triplets or quartets).

The number and kind of hydrogen atoms directly adjacent to the absorbing nuclei can be deduced from the multiplicity of the peak.

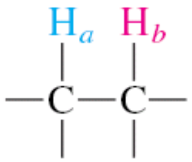
Spin-spin splitting is usually observed only between hydrogen atoms bound to the same carbon (geminal coupling) or to adjacent carbons (vicinal coupling).

Hydrogen nuclei separated by more than two carbon atoms (1,3 coupling) is usually negligible.

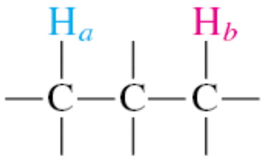
Coupling Between Close-Lying Hydrogens



J_{ab}, geminal coupling, variable 0–18 Hz



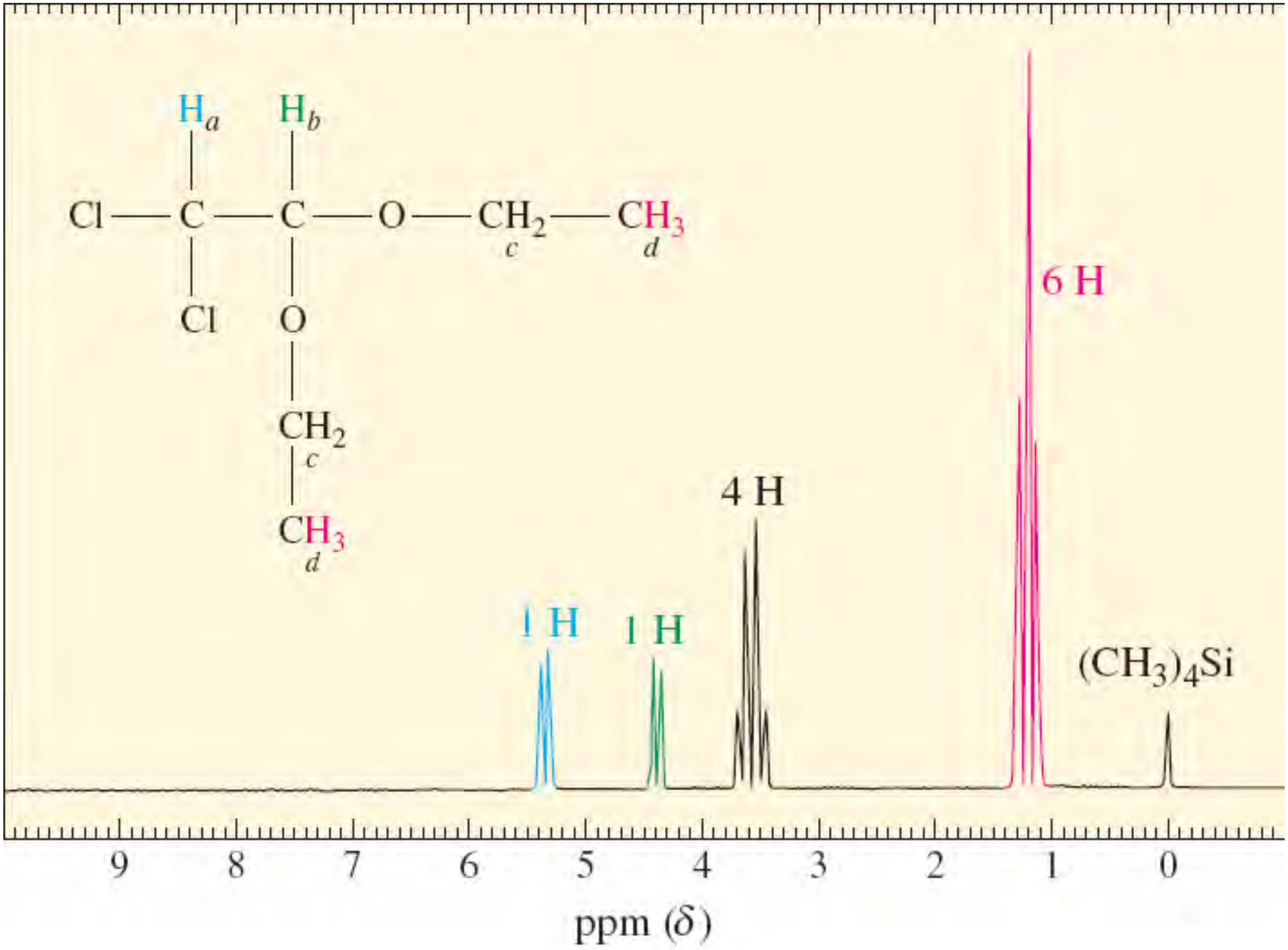
J_{ab}, vicinal coupling, typically 6–8 Hz



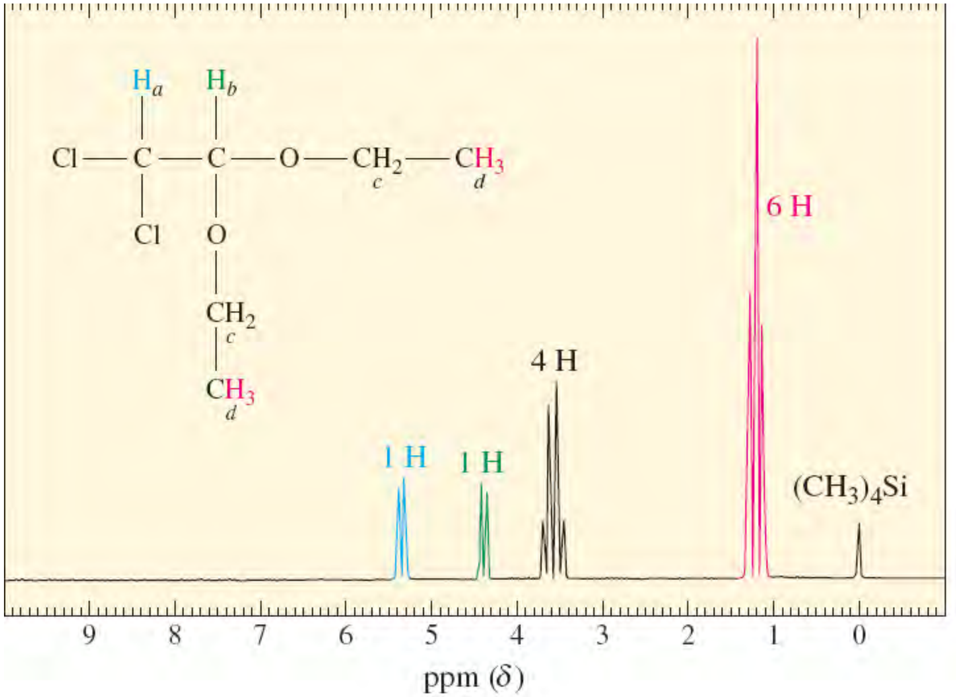
J_{ab}, 1,3-coupling, usually negligible

Finally, equivalent nuclei do not exhibit mutual spin-spin splitting. Ethane exhibits only a single line at δ = 0.85 ppm.

Splitting is observed only between nuclei with different chemical shifts.

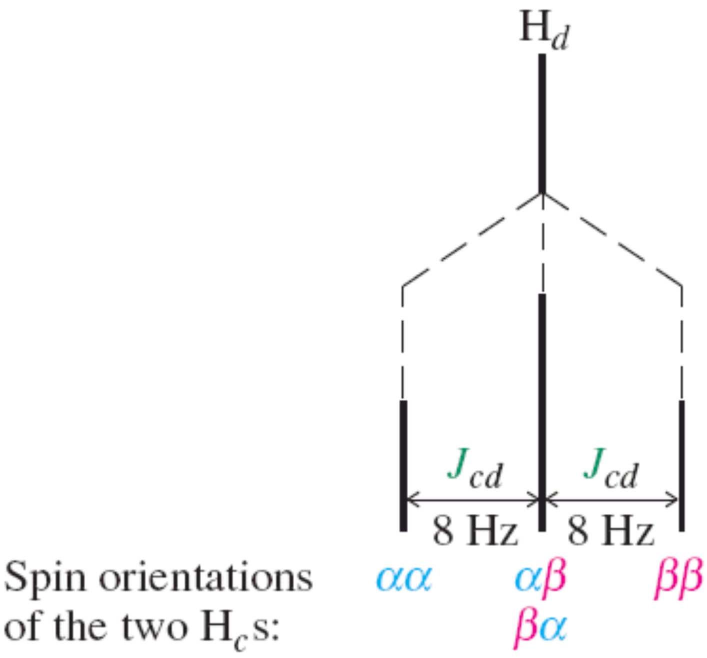

H a
H b
Cl — C — C — O — CH2 — CH3
c
d
Cl
O
CH2
c
CH3
d
6 H
4 H
1 H
1 H
(CH3)4Si
9
8
7
6
5
4
3
2
1
0
ppm (δ)

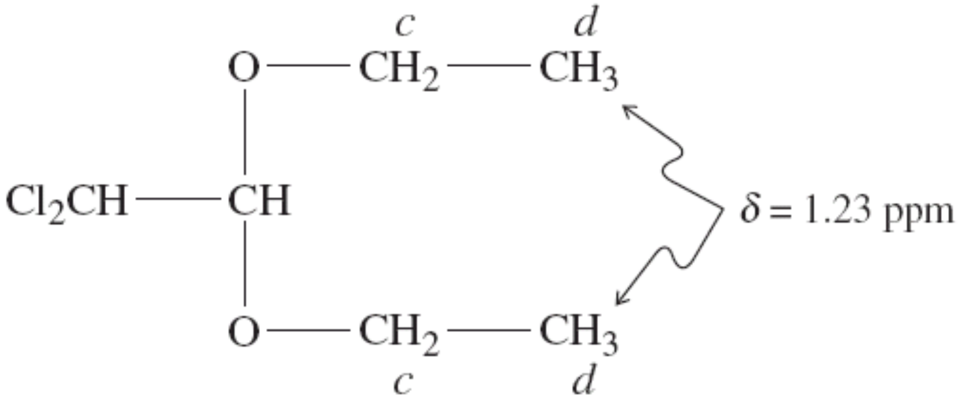
Local-field contributions from more than one hydrogen are additive.



Consider the triplet above. It corresponds to the methyl protons being split by the methylene protons.

The methylene proton spins will statistically orient in the external magnetic field as αα, αβ, βα and ββ. Each methyl proton will see an increased field 25% of the time (αα), no change 50% of the time (αβ and βα), and a decreased field 25% of the time (ββ).

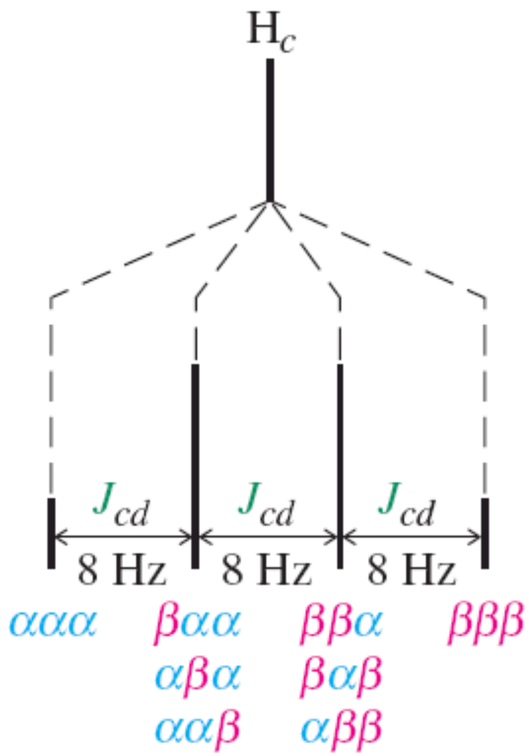


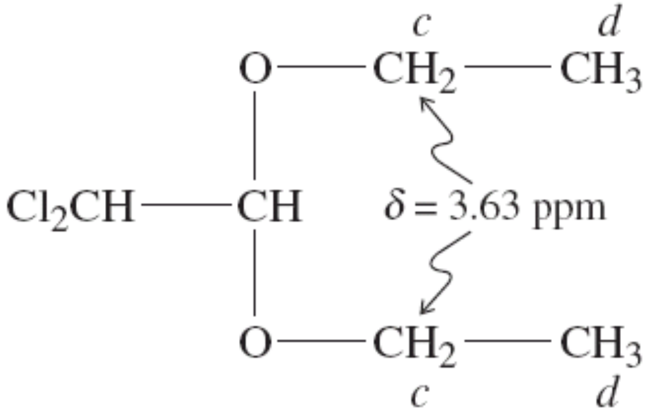


The integrated intensity of the triplet will be 6 since there are a total of 6 equivalent methyl protons.

In the case of the methylene protons, the methyl proton spins will statistically distribute as ααα, ααβ, αβα, βαα, αββ, βαβ, ββα, and βββ.

This will result in a 1:3:3:1 quartet of peaks.





The integrated intensity of the quartet will be 4, corresponding to the 4 equivalent methylene protons.

In many cases, spin-spin splitting is given by the N+1 rule.

A simple set of rules:

- Equivalent nuclei located adjacent to one neighboring hydrogen resonate as a doublet.
- Equivalent nuclei located adjacent to two hydrogens of a second set of equivalent nuclei resonate as a triplet.
- Equivalent nuclei located adjacent to a set of three equivalent hydrogens resonate as a quartet.

In many cases, spin-spin splitting is given by the N+1 rule.

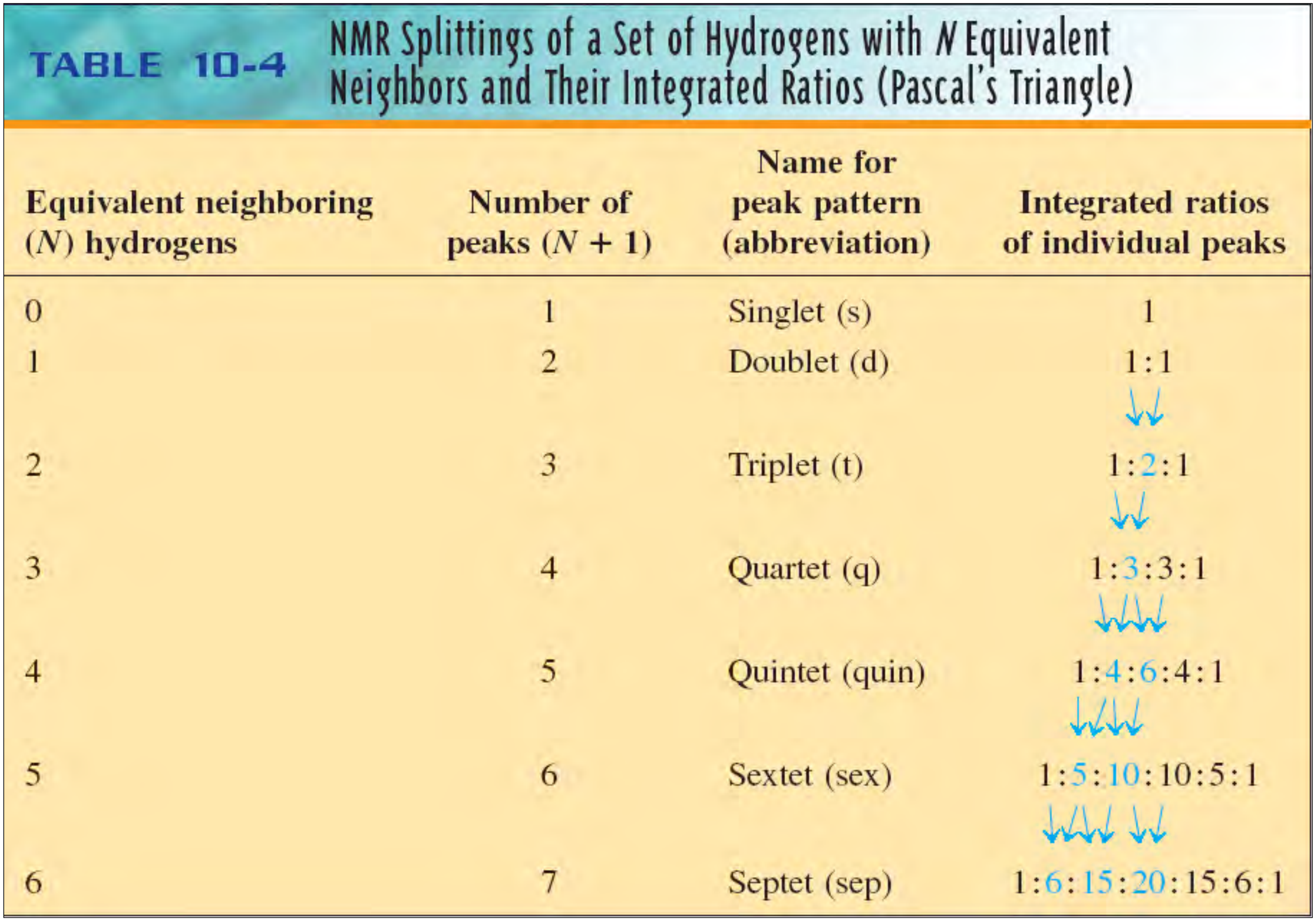


TABLE 10-4 NMR Splittings of a Set of Hydrogens with *N* Equivalent Neighbors and Their Integrated Ratios (Pascal's Triangle)

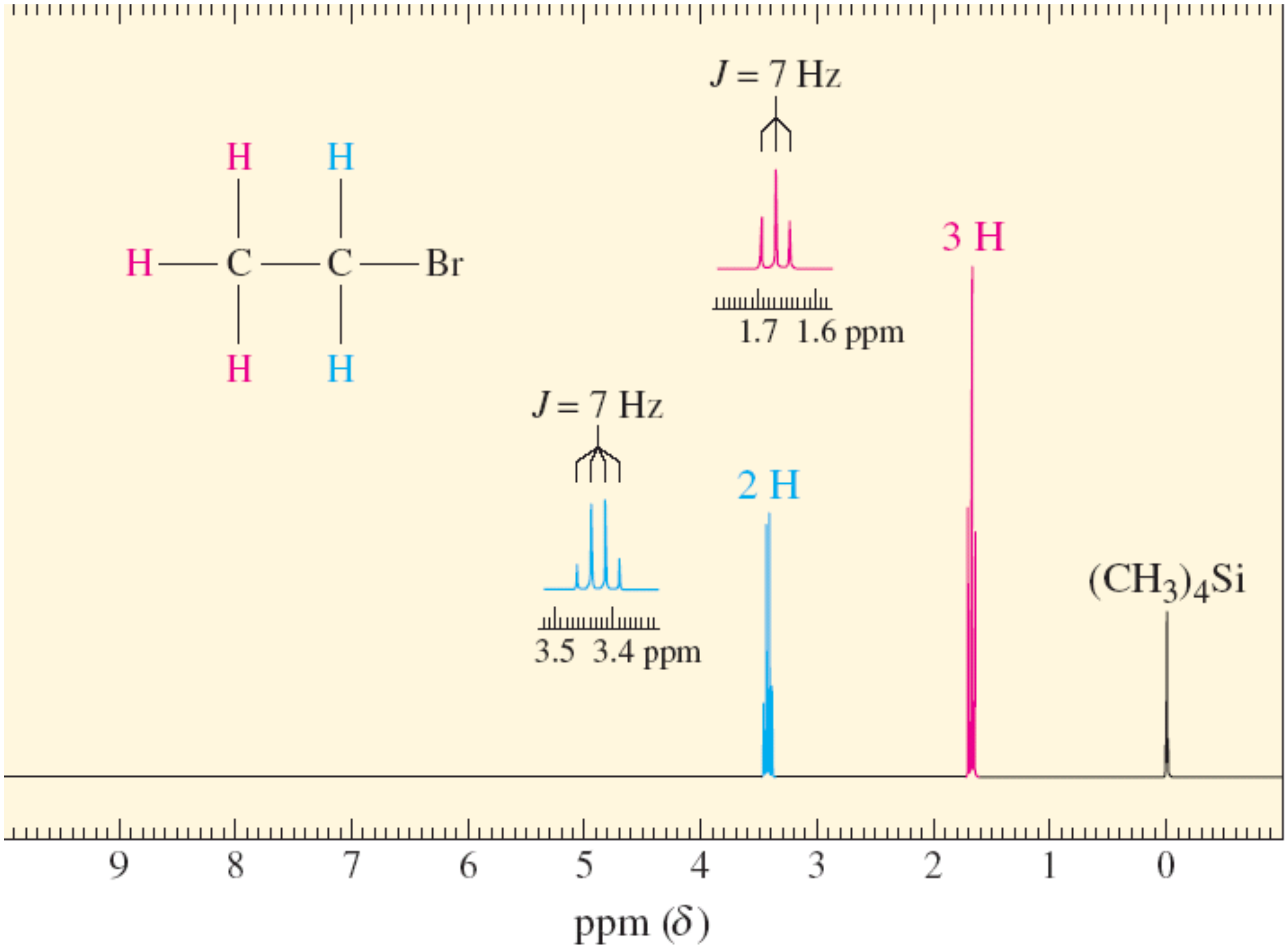
Equivalent neighboring (*N*) hydrogens	Number of peaks (*N* + 1)	Name for peak pattern (abbreviation)	Integrated ratios of individual peaks
0	1	Singlet (s)	1
1	2	Doublet (d)	1 : 1
2	3	Triplet (t)	1 : 2 : 1
3	4	Quartet (q)	1 : 3 : 3 : 1
4	5	Quintet (quin)	1 : 4 : 6 : 4 : 1
5	6	Sextet (sex)	1 : 5 : 10 : 10 : 5 : 1
6	7	Septet (sep)	1 : 6 : 15 : 20 : 15 : 6 : 1

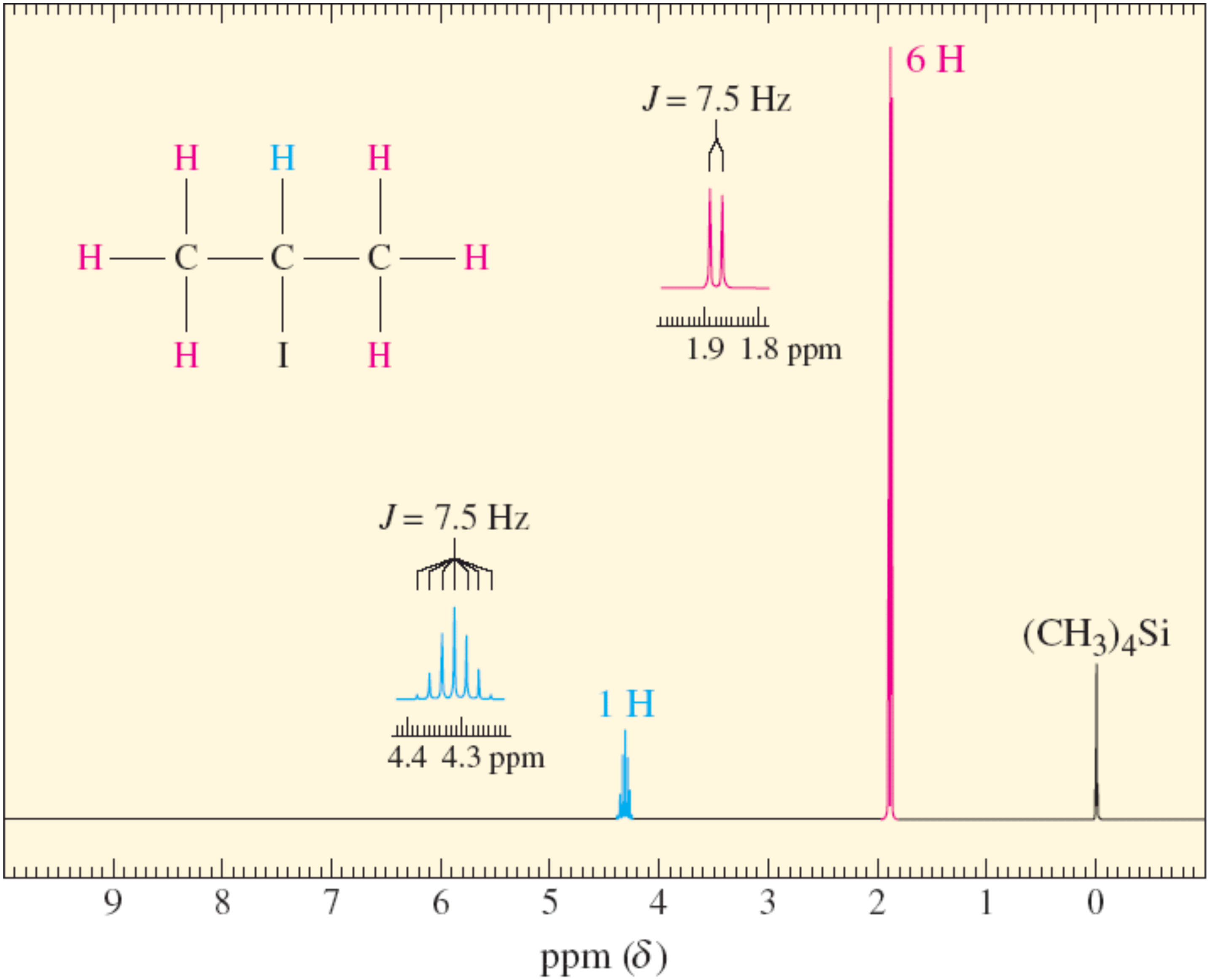
This table illustrates the N+1 rule: Nuclei having N adjacent equivalent neighbors split into N+1 peaks. The heights of the N+1 peaks follow Pascal's triangle.

It is important to note that non-equivalent nuclei split each other.

A split in one requires a split in the other. In addition, the coupling constants will be the same for each type of nuclei.

Two additional examples:

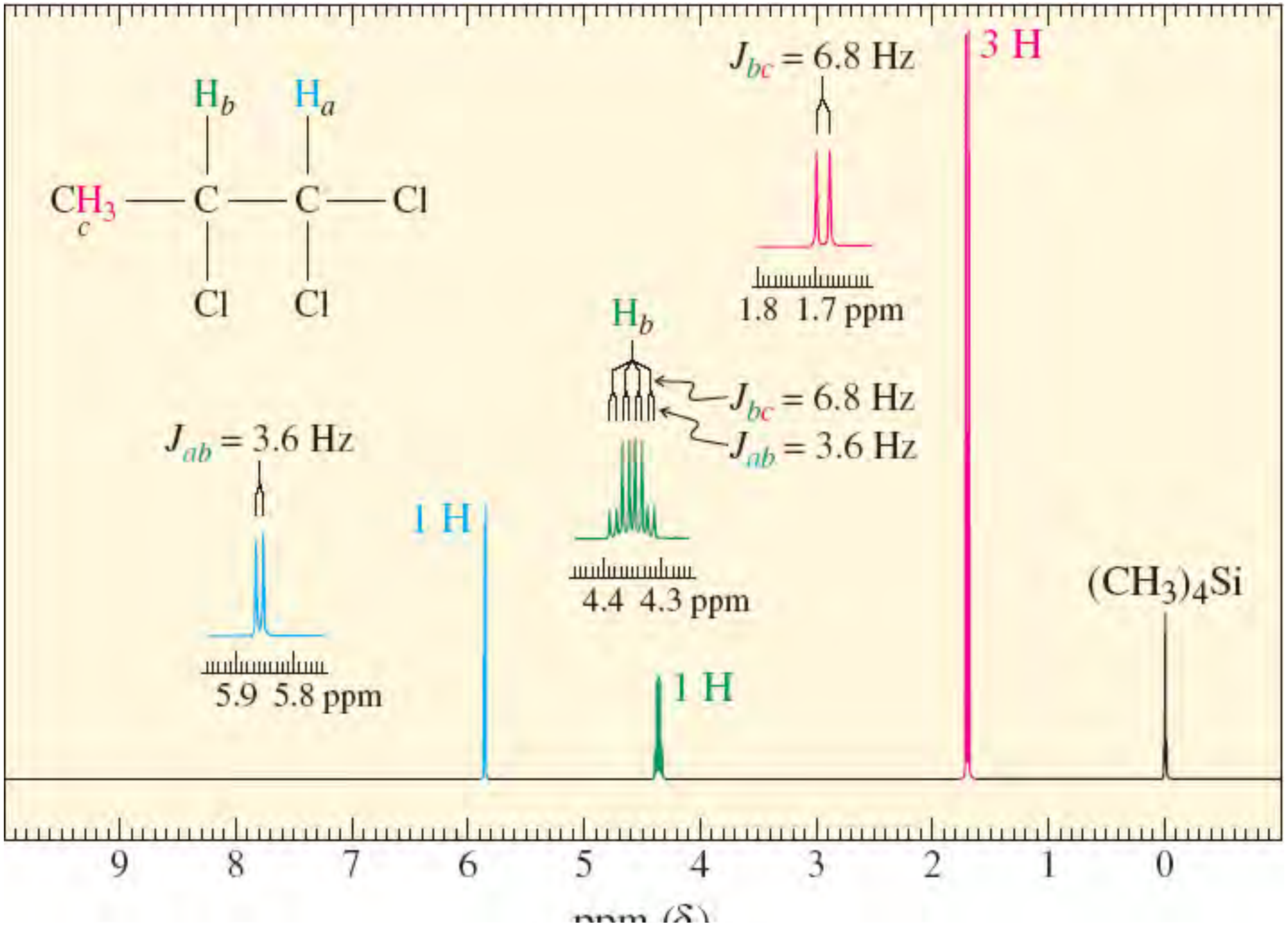



H
H
H
H
C
C
C
H
H
I
H
J = 7.5 Hz
1.9 1.8 ppm
6 H
J = 7.5 Hz
4.4 4.3 ppm
1 H
(CH3)4Si
9
8
7
6
5
4
3
2
1
0
ppm (δ)

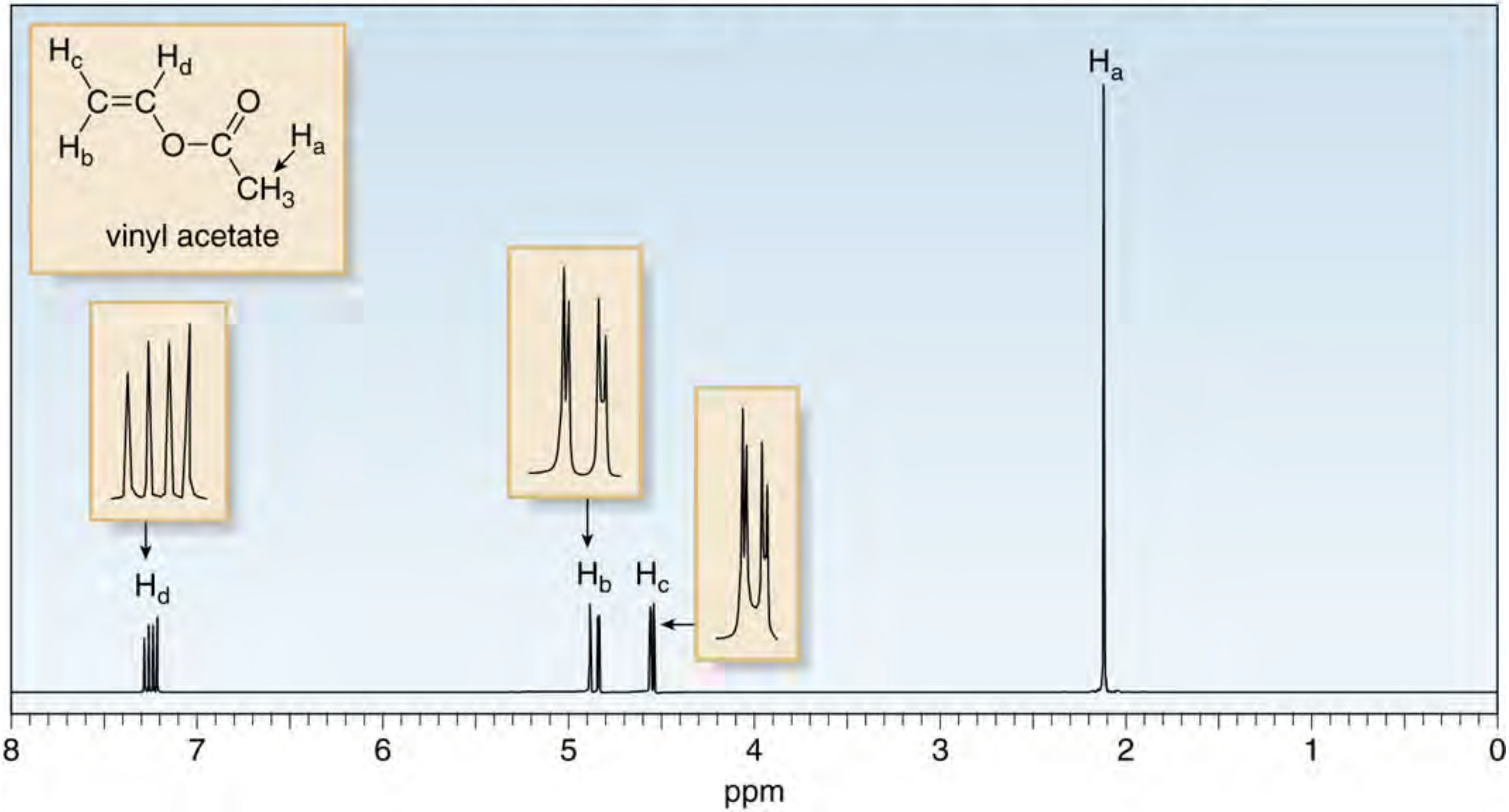
10-8 Spin-Spin Splitting: Some Complications

The N+1 rule may not apply in a direct way if several neighboring hydrogens having fairly different coupling constants are coupled to the resonating nucleus.

In this case, the rule is revised to (n1+1) * (n2 + 1).

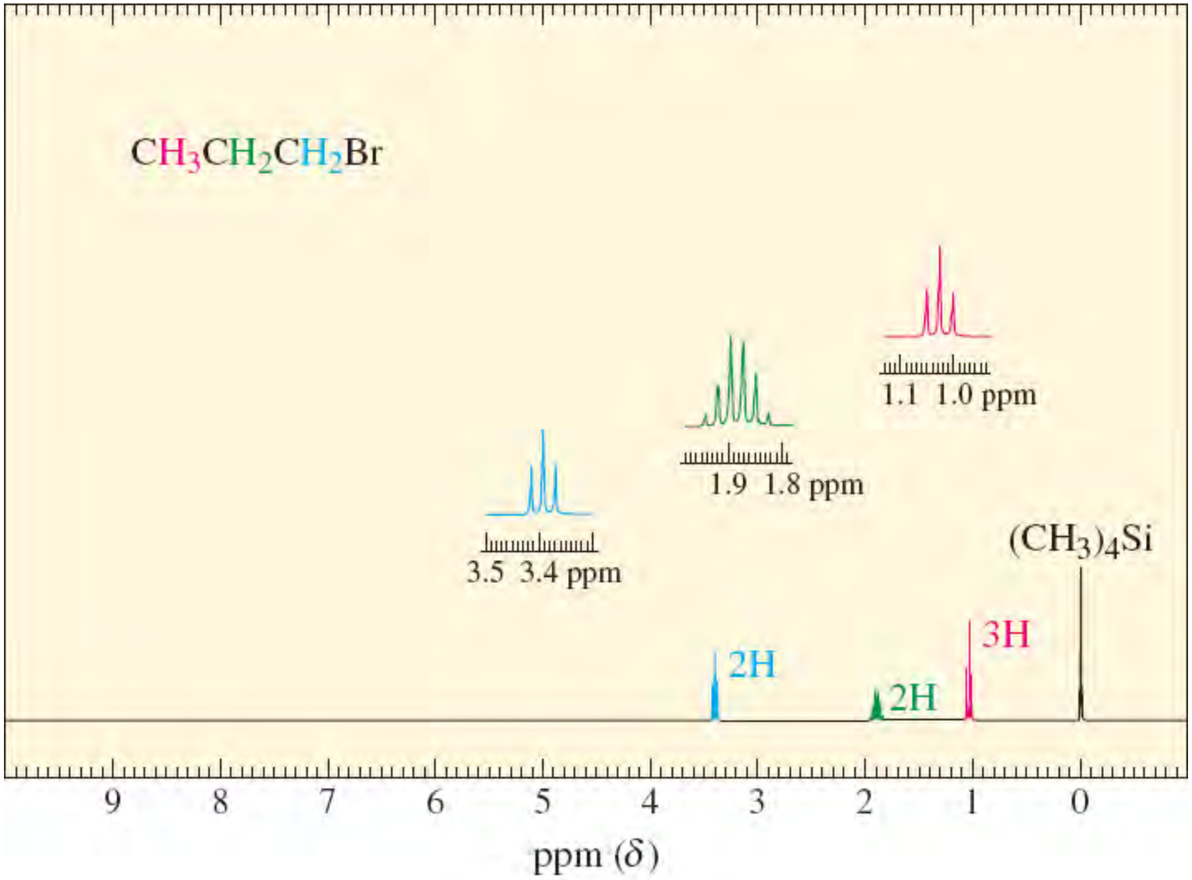


^{1}H NMR of Vinyl Acetate



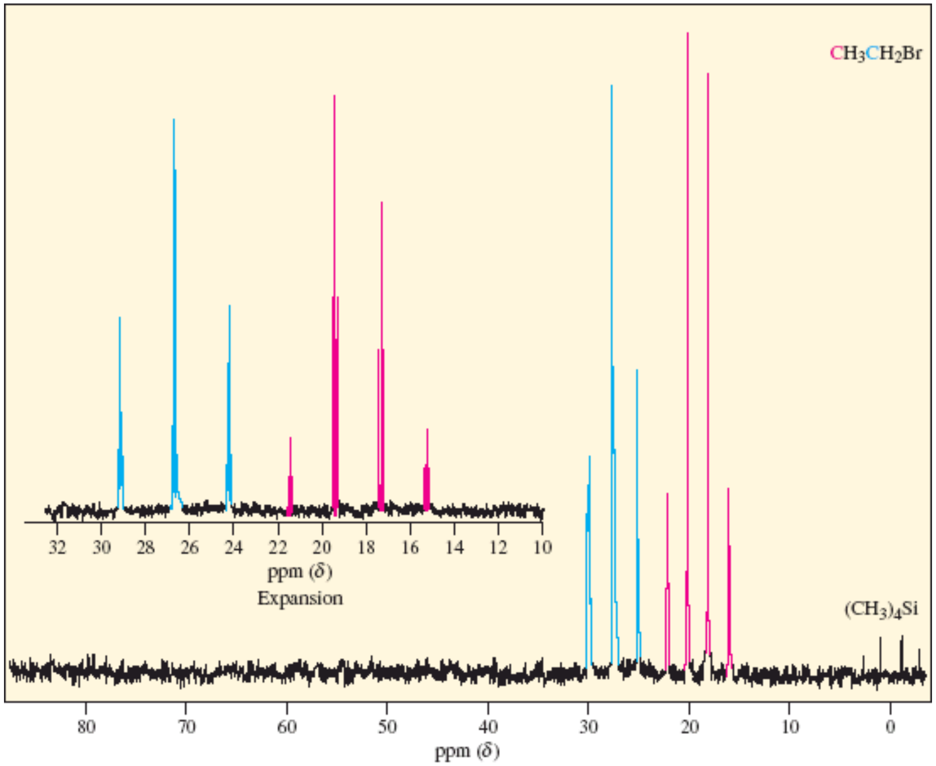
In the case of 1-bromopropane, the hydrogens on C2 are also coupled to two non-equivalent sets of neighbors. A theoretical analysis of this resonance would predict as many as 12 lines (a quartet of triplets).

Because the coupling constants are very similar, however, many of the lines overlap, thus simplifying the pattern.

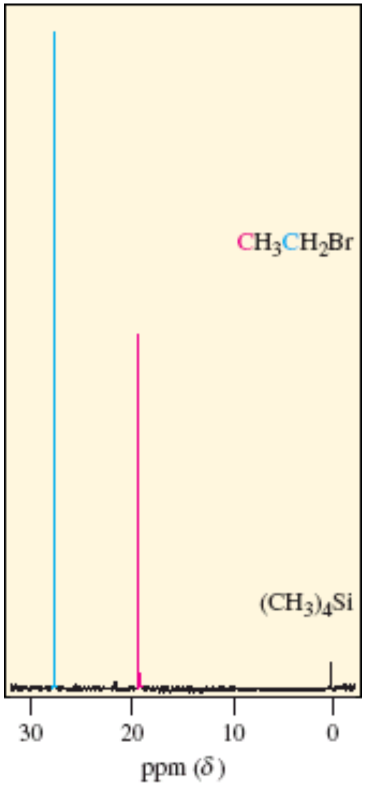


10-9 Carbon-13 Nuclear Magnetic Resonance

The NMR spectroscopy of ^{13}C is very useful for structural determination.

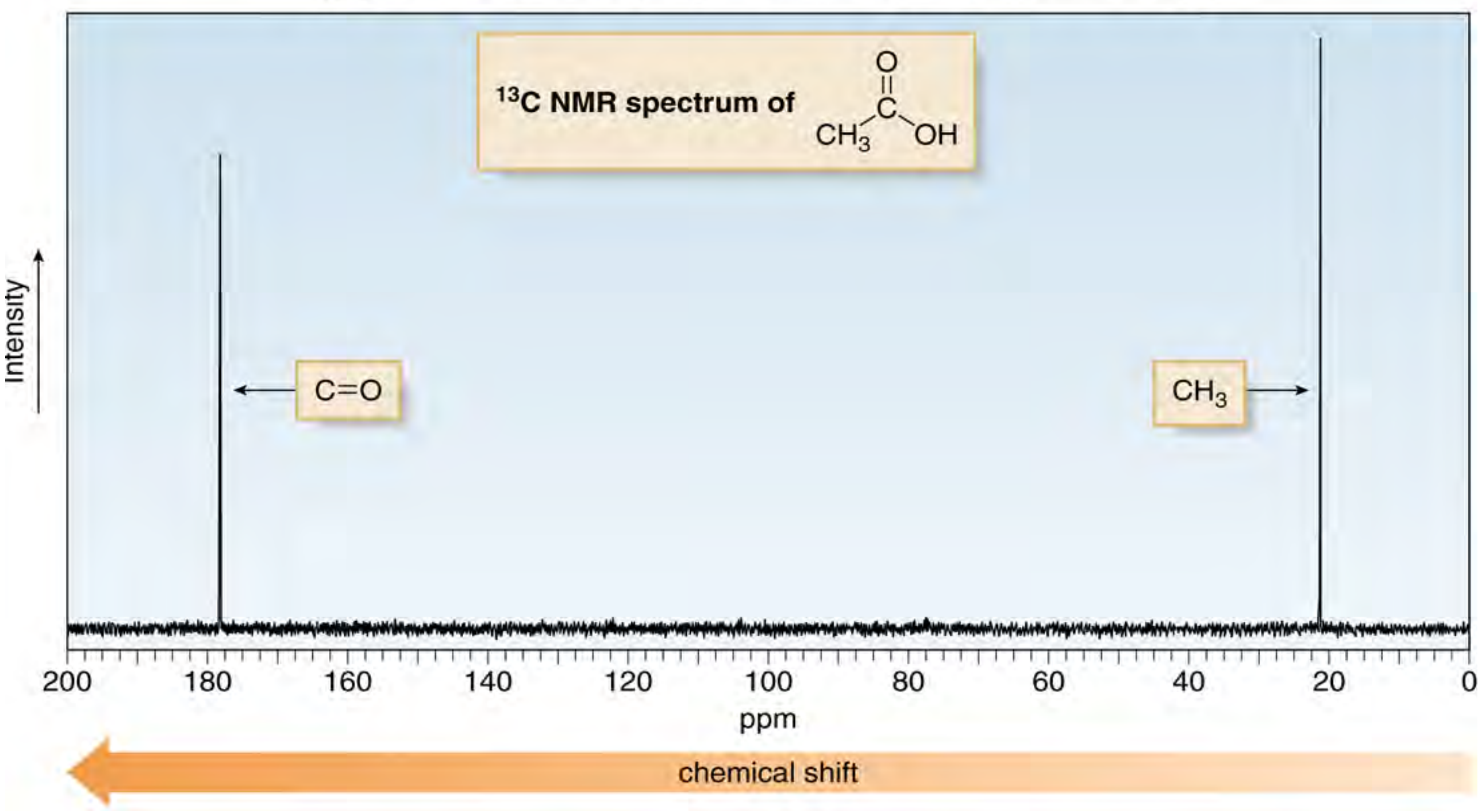


^1H-Decoupling

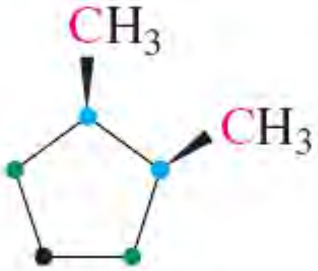


^{13}C NMR Spectrum Example

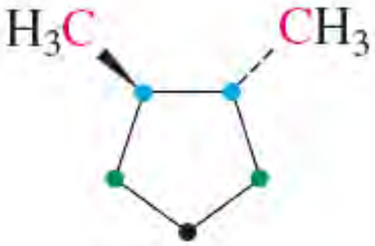
- ^{13}C Spectra are easier to analyze than ^{1}H spectra because the signal splitting can be avoided.
- Each type of carbon atom appears as a single peak with 1H-decoupling.



The numbers of non-equivalent carbons in the isomers of C_7H_{14} are clearly demonstrated by the numbers of ^{13}C peaks in their NMR spectra.



Four peaks



Four peaks

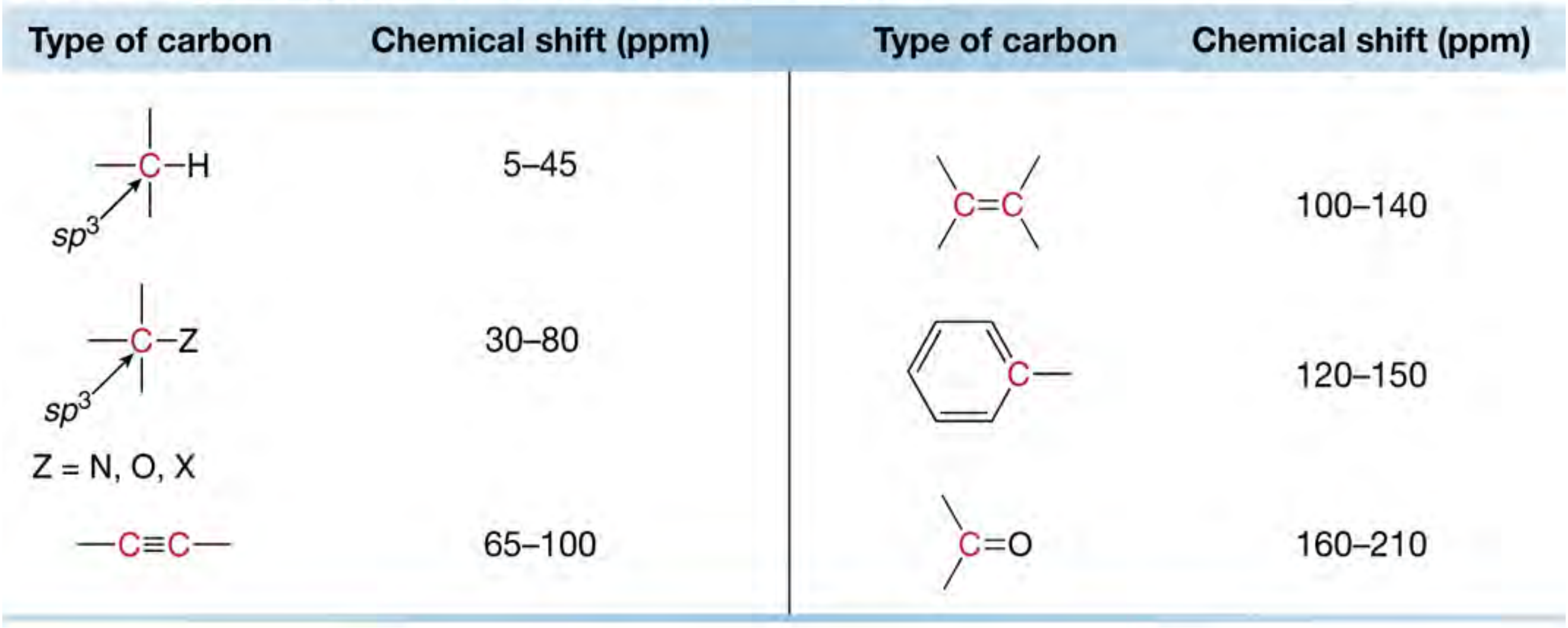
Three peaks

One peak

Chemical Shifts in ^{13}C NMR

- **In contrast to the small range of chemical shifts in ^{1}H NMR (1-10 ppm usually), ^{13}C NMR absorptions occur over a much broader range (0-220 ppm).**
- **The chemical shifts of carbon atoms in ^{13}C NMR depend on the same effects as the chemical shifts of protons in ^{1}H NMR.**

Common ^{13}C-NMR chemical shift values



Type of carbon	Chemical shift (ppm)	Type of carbon	Chemical shift (ppm)
—C–H sp^3	5–45	C=C	100–140
—C–Z sp^3 Z = N, O, X	30–80	C—	120–150
—C≡C—	65–100	C=O	160–210

^{13}C NMR of 1-Propanol

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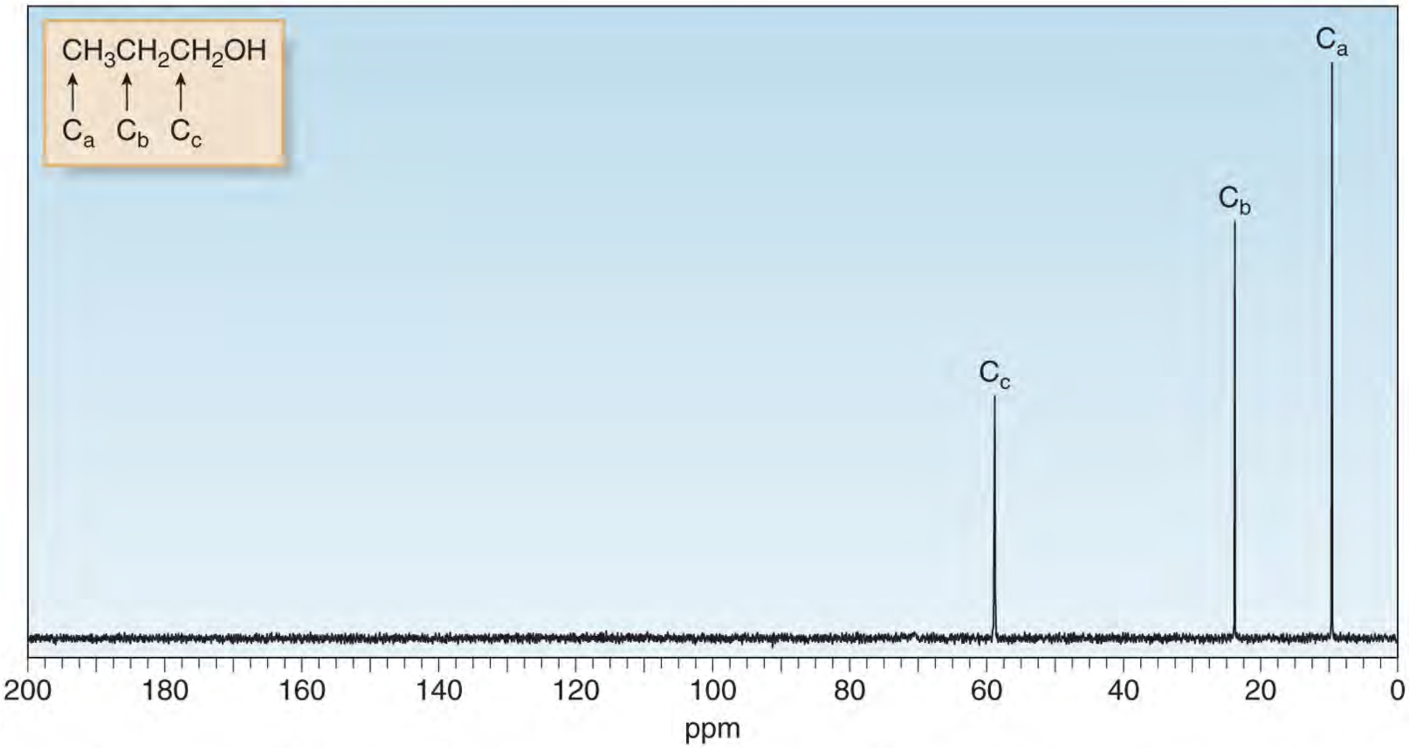
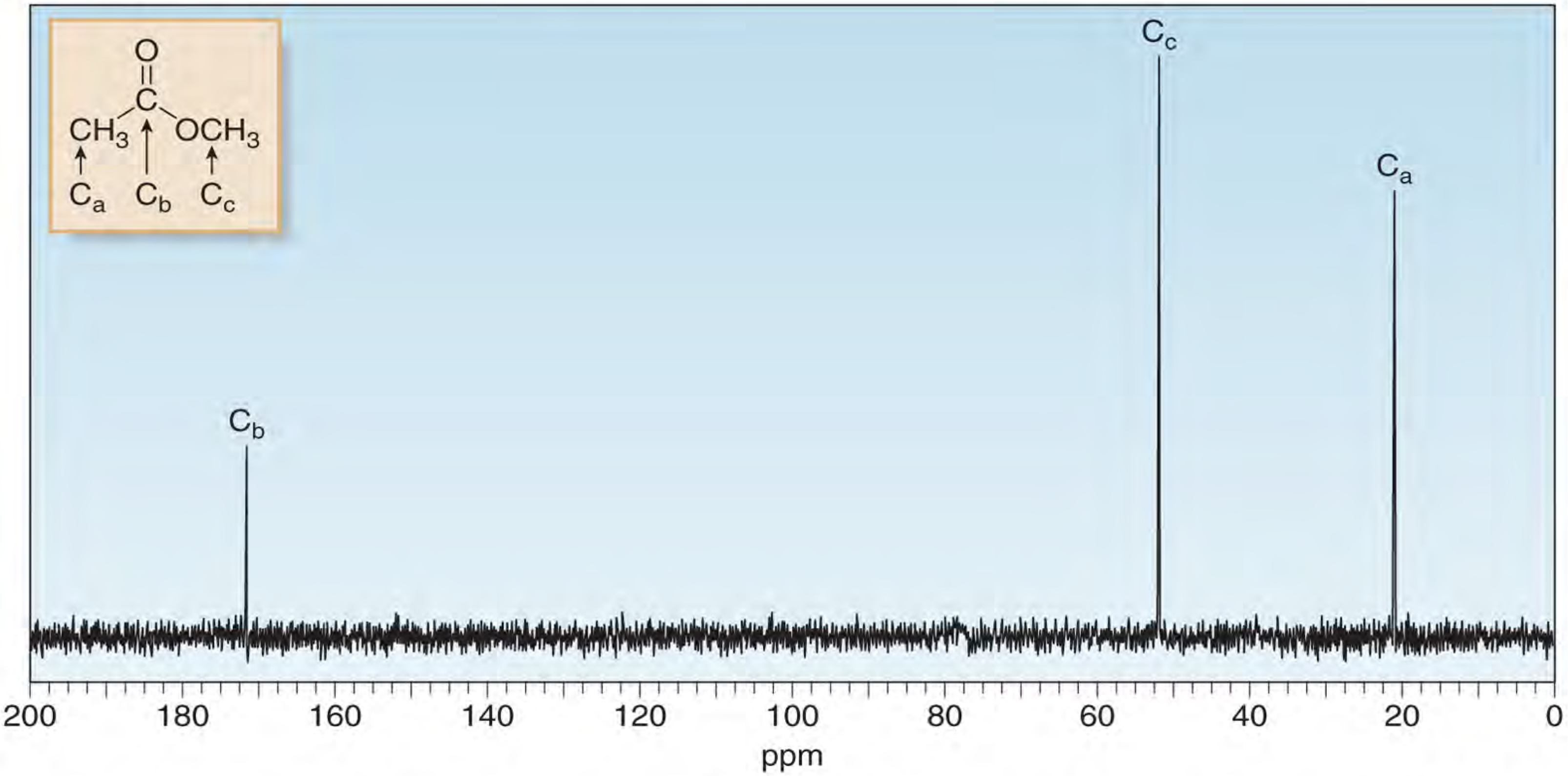


a. 1-Propanol

- The three types of C's in 1-propanol—identified as C_a, C_b, and C_c—give rise to three ^{13}C NMR signals.
- Deshielding increases with increasing proximity to the electronegative O atom, and the absorption shifts downfield; thus, in order of increasing chemical shift: $C_a < C_b < C_c$.

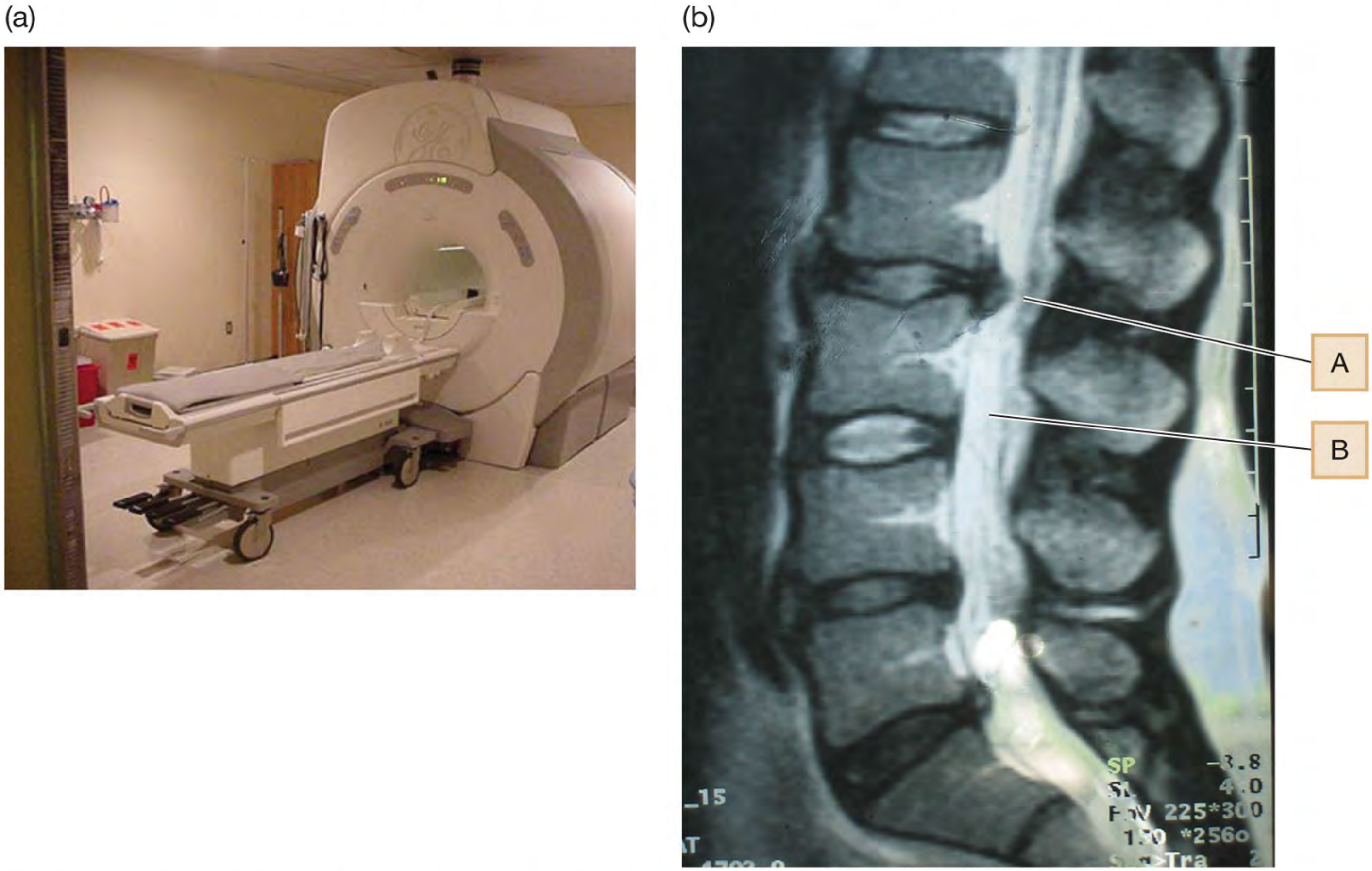
^{13}C NMR of Methyl Acetate

b. Methyl acetate



- The three types of C's in methyl acetate—identified as C_a, C_b, and C_c—give rise to three ^{13}C NMR signals.
- The carbonyl carbon (C_b) is highly deshielded, so it absorbs farthest downfield.
- C_a, an sp^3 hybridized C that is not bonded to an O atom, is the most shielded, and so it absorbs farthest upfield.
- Thus, in order of increasing chemical shift: $C_a < C_c < C_b$.

Magnetic Resonance Imaging (MRI)



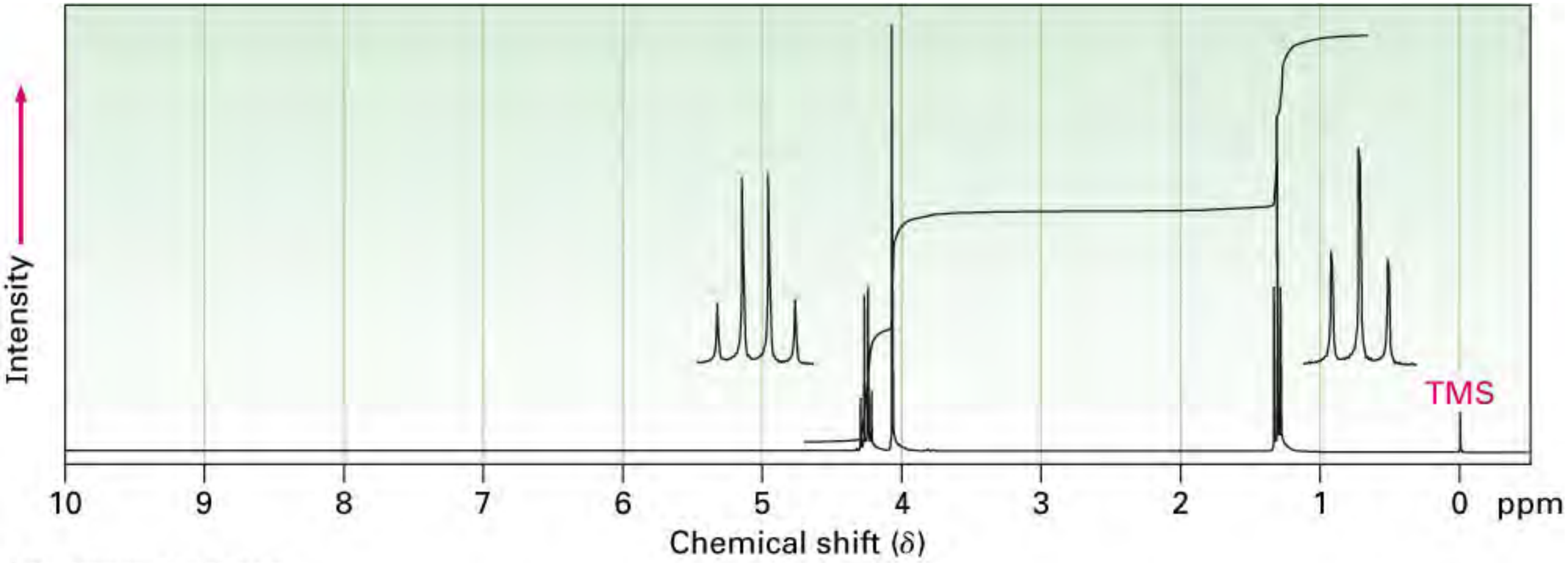
a. An MRI instrument: An MRI instrument is especially useful for visualizing soft tissue. In 2002, 60 million MRI procedures were performed. The 2003 Nobel Prize in Physiology or Medicine was awarded to chemist Paul C. Lauterbur and physicist Sir Peter Mansfield for their contributions in developing magnetic resonance imaging.

b. An MRI image of the lower back: **A** labels spinal cord compression from a herniated disc. **B** labels the spinal cord, which would not be visualized with conventional X-rays.

How to determine structures of compounds from their spectra?

1. Determine the molecular formula and degree of unsaturation
2. From ^{13}C-NMR, determine # of signals and chemical shifts
3. From ^{1}H-NMR, determine # of signals, # of protons in each signal, peak splitting patterns and chemical shifts

Molecular formula: $C_4H_7O_2Cl$



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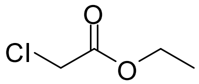
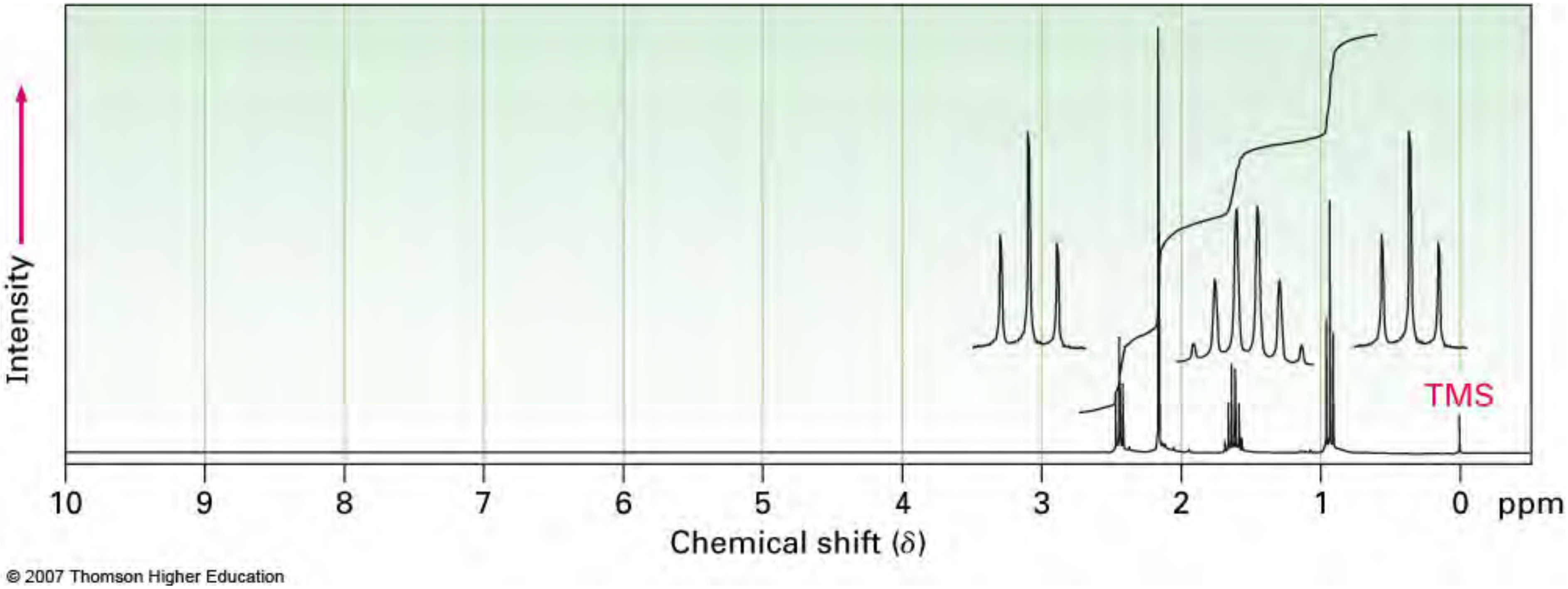


Molecular formula: C5H10O



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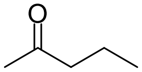
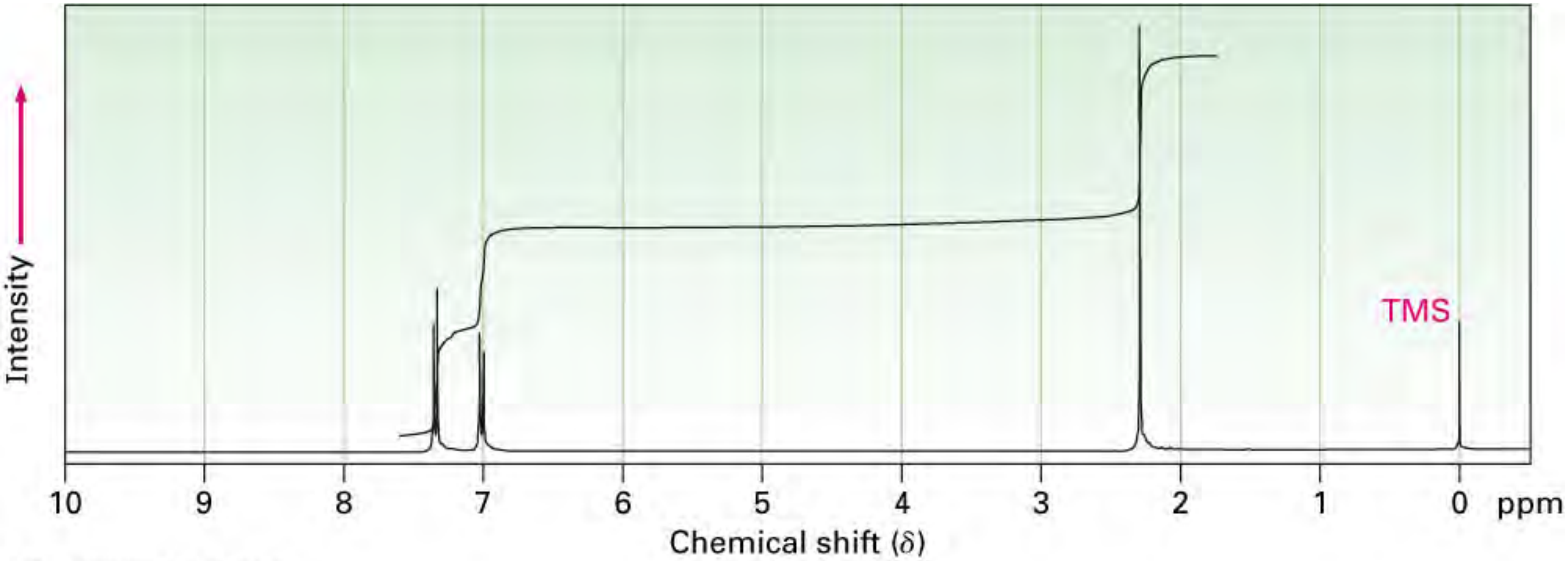


Molecular formula: C_7H_7Br



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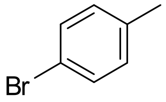

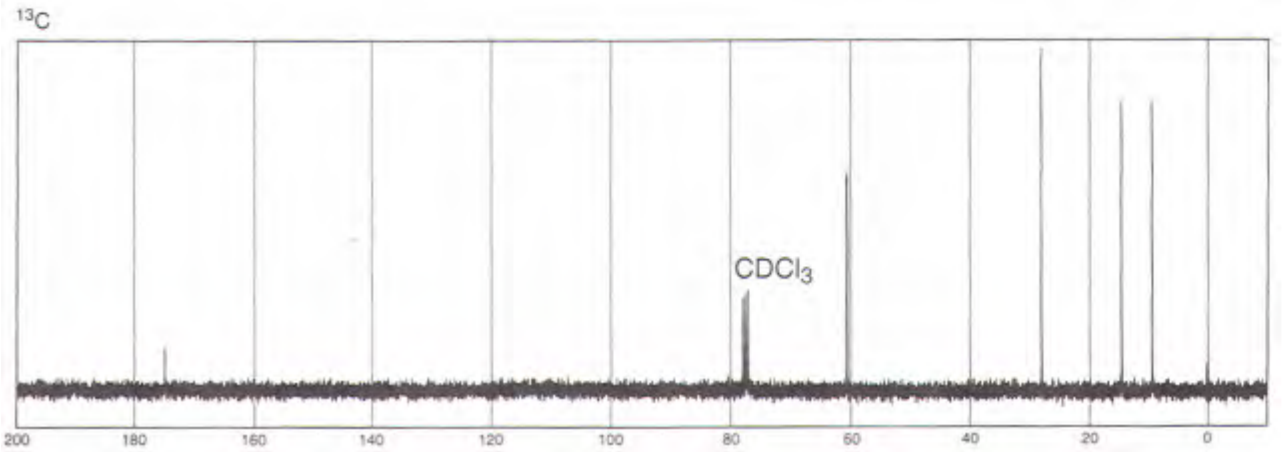

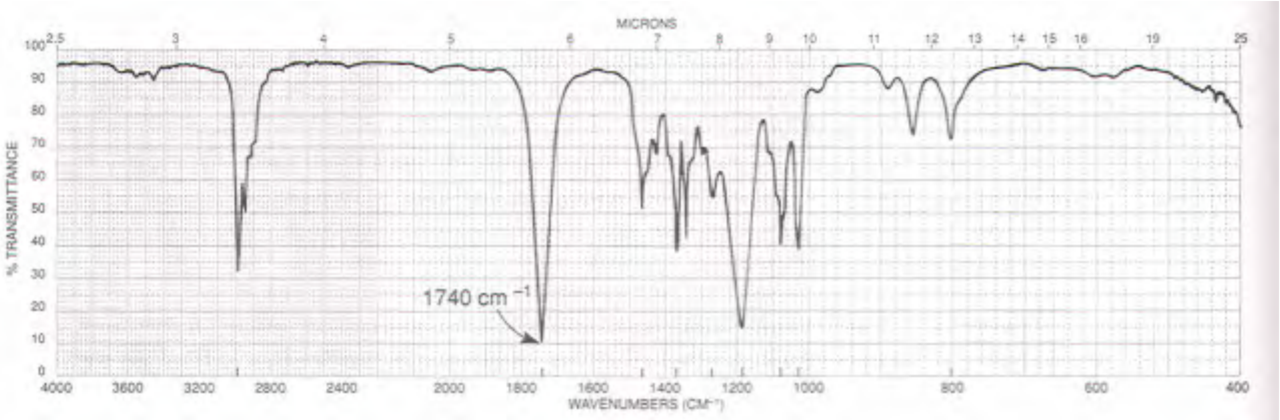

Formula
$C_5H_{10}O_2$