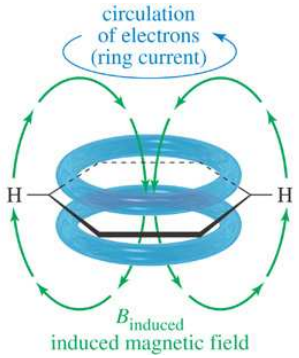
Organic Chemistry, 6th Edition
L. G. Wade, Jr.



Chapter 13
Nuclear Magnetic Resonance Spectroscopy

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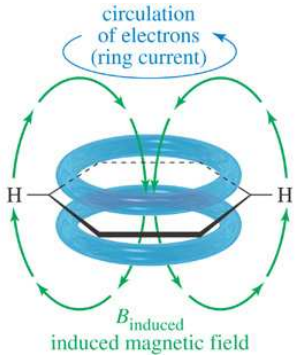
Introduction



- 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

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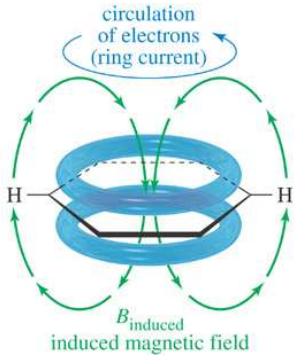
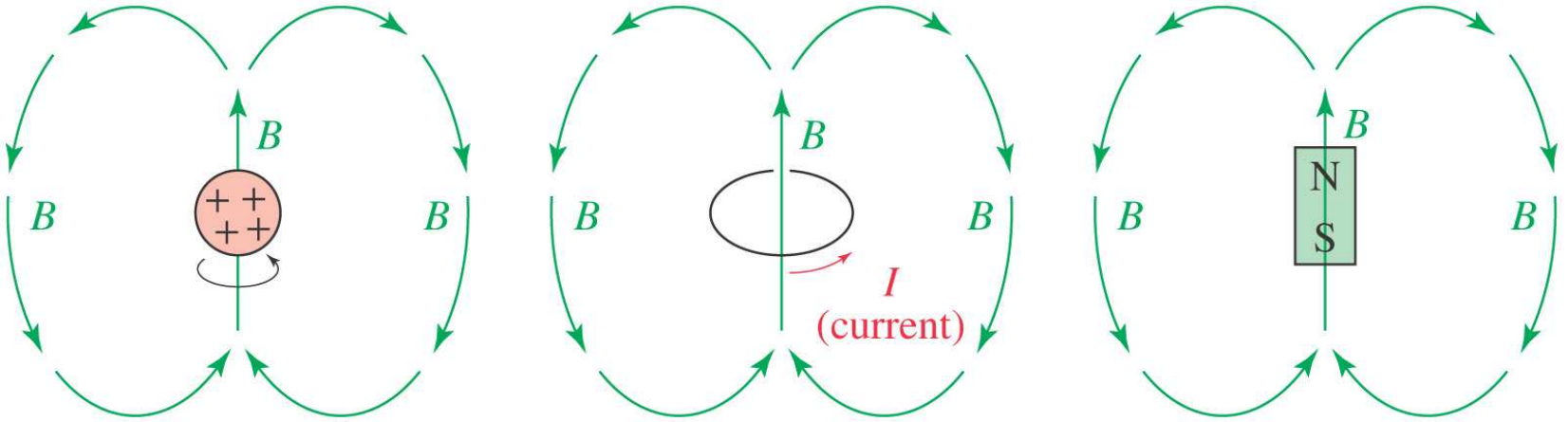
Nuclear Spin



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



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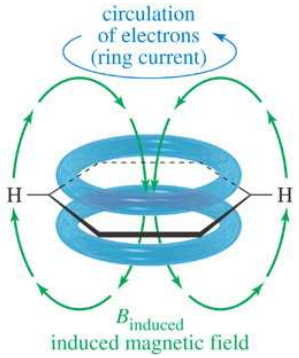
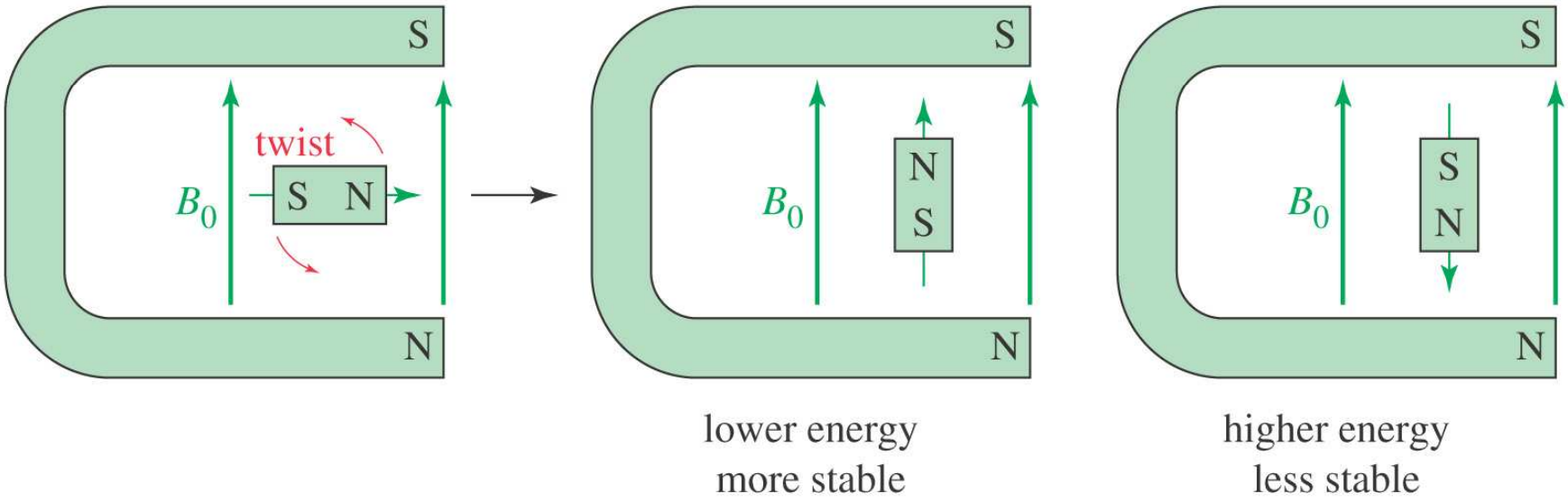
External Magnetic Field



When placed in an external field, spinning protons act like bar magnets.



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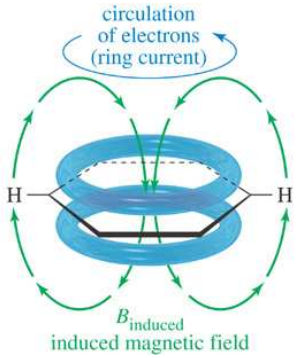
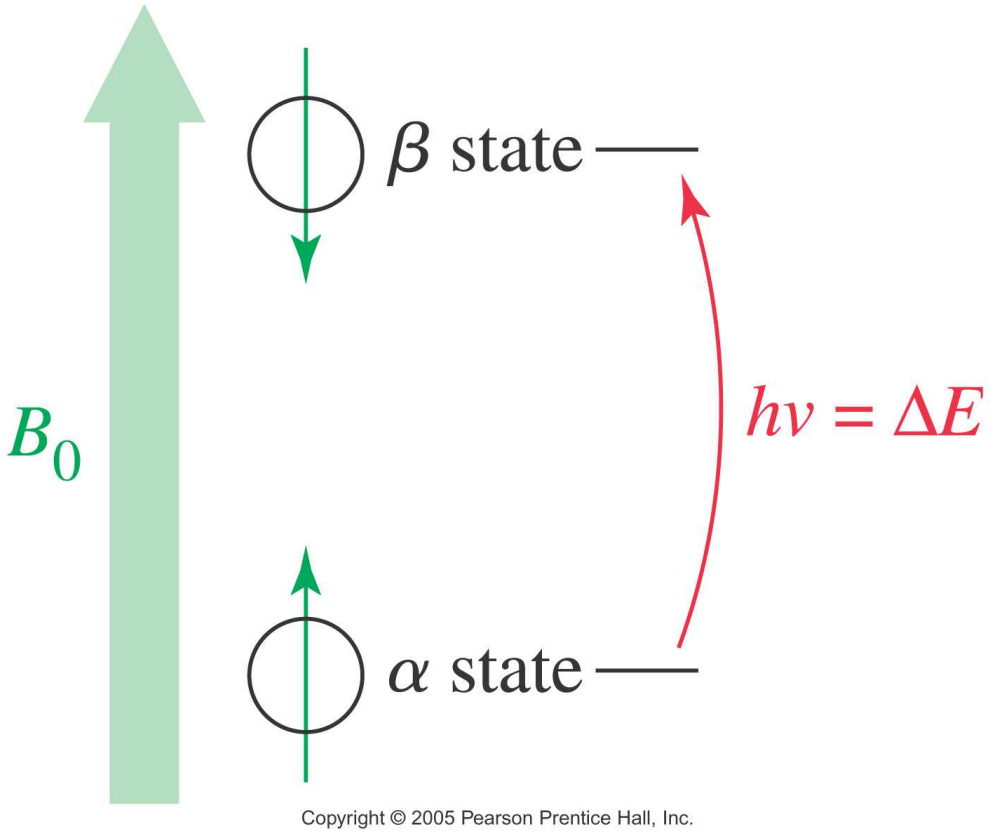
Two Energy States

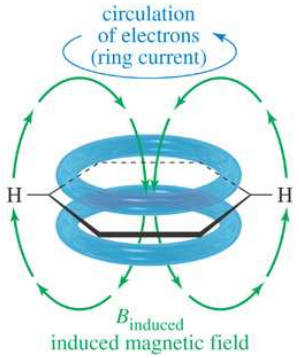


The magnetic fields of the spinning nuclei will align either *with* the external field, or *against* the field.

A photon with the right amount of energy can be absorbed and cause the spinning proton to flip. =>

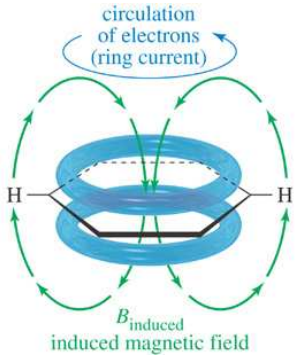


ΔE and Magnet Strength



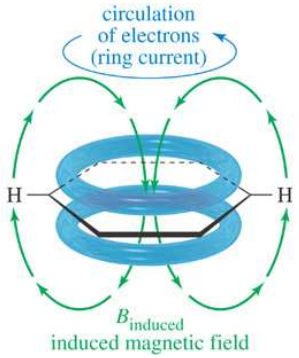
- Energy difference is proportional to the magnetic field strength.
- $\Delta E = h\nu = \gamma \frac{h}{2\pi} B_0$
- Gyromagnetic ratio, γ, is a constant for each nucleus (26,753 $s^{-1}gauss^{-1}$ for H).
- In a 14,092 gauss field, a 60 MHz photon is required to flip a proton.
- Low energy, radio frequency. =>

Magnetic Shielding

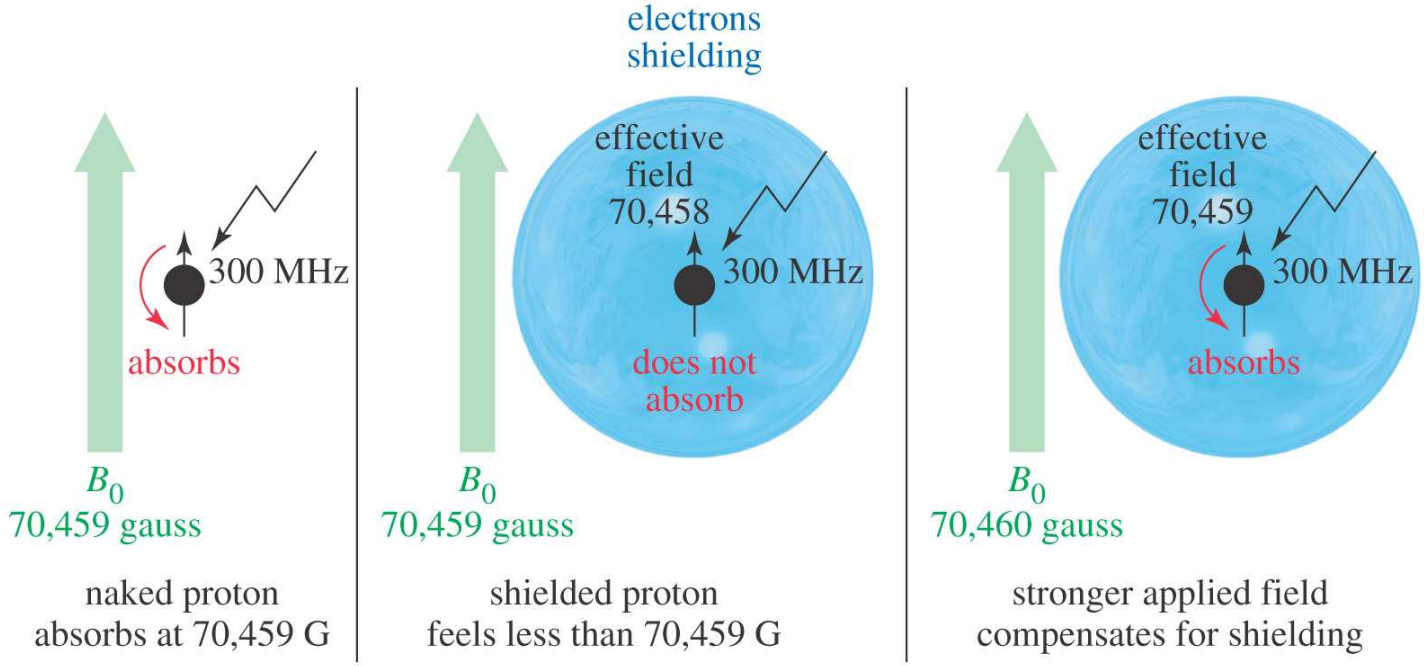


- If all protons absorbed the same amount of energy in a given magnetic field, not much information could be obtained.
- But protons are surrounded by electrons that shield them from the external field.
- Circulating electrons create an induced magnetic field that opposes the external magnetic field.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

Shielded Protons



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



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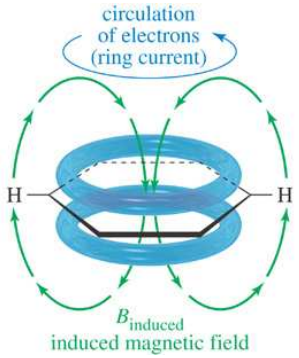
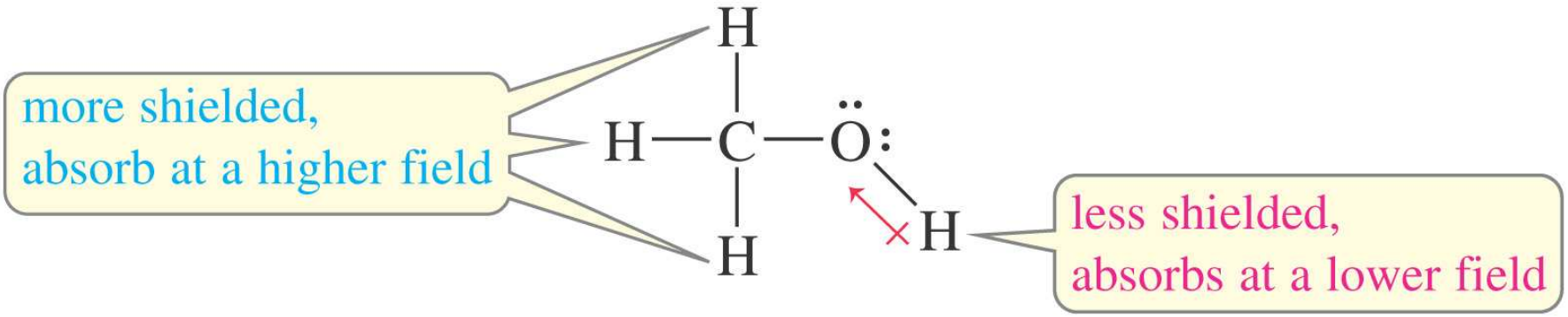
Protons in a Molecule



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



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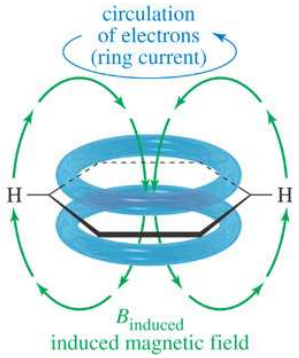
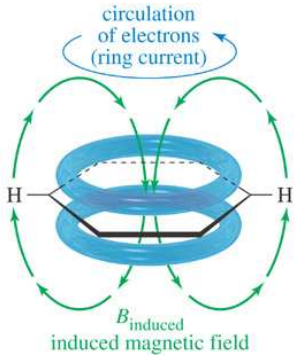
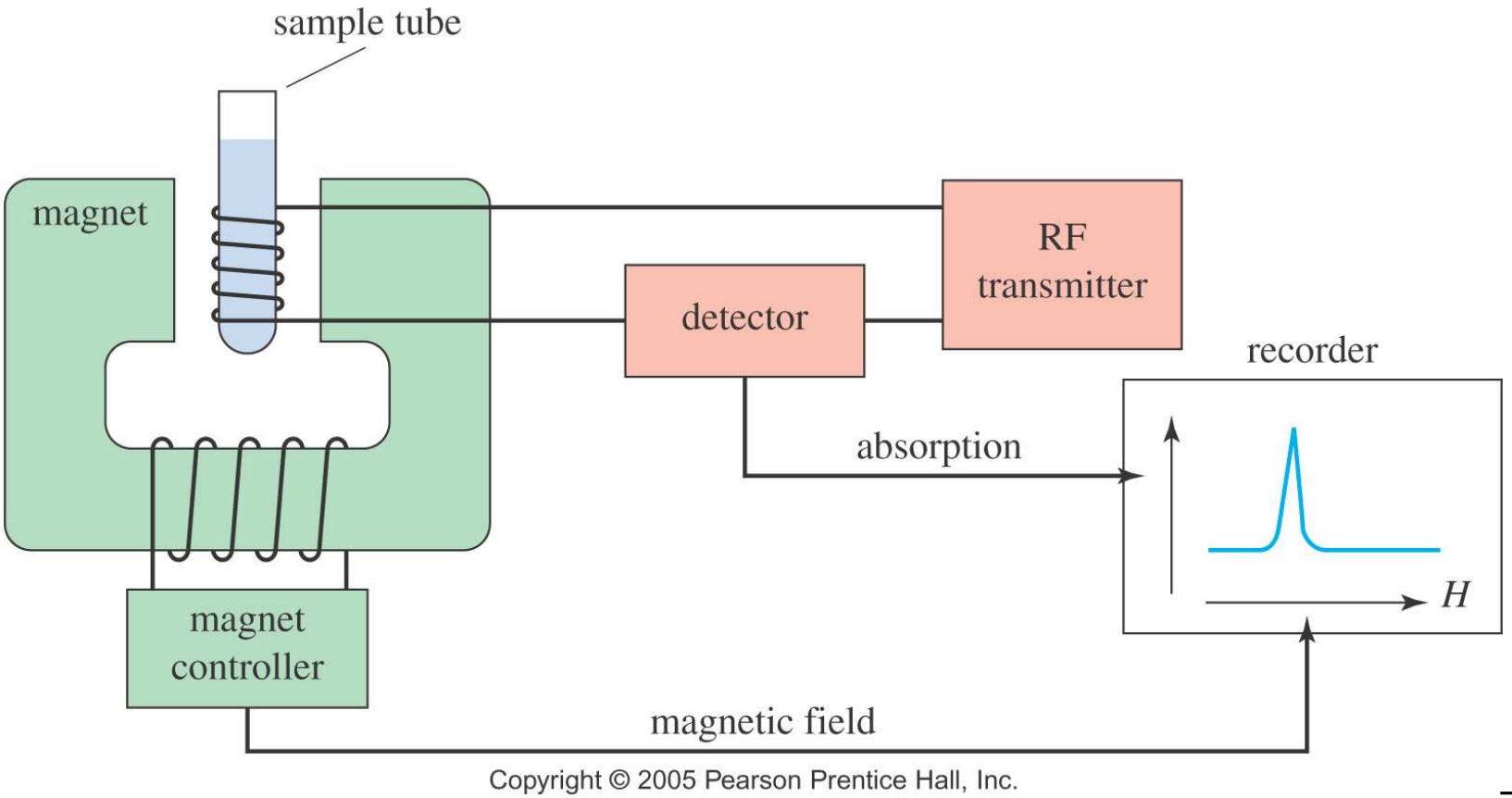
NMR Signals



- 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





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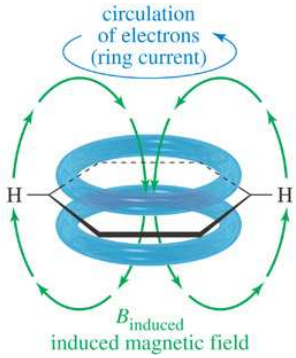
The NMR Spectrometer



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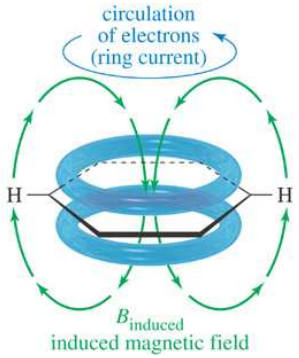
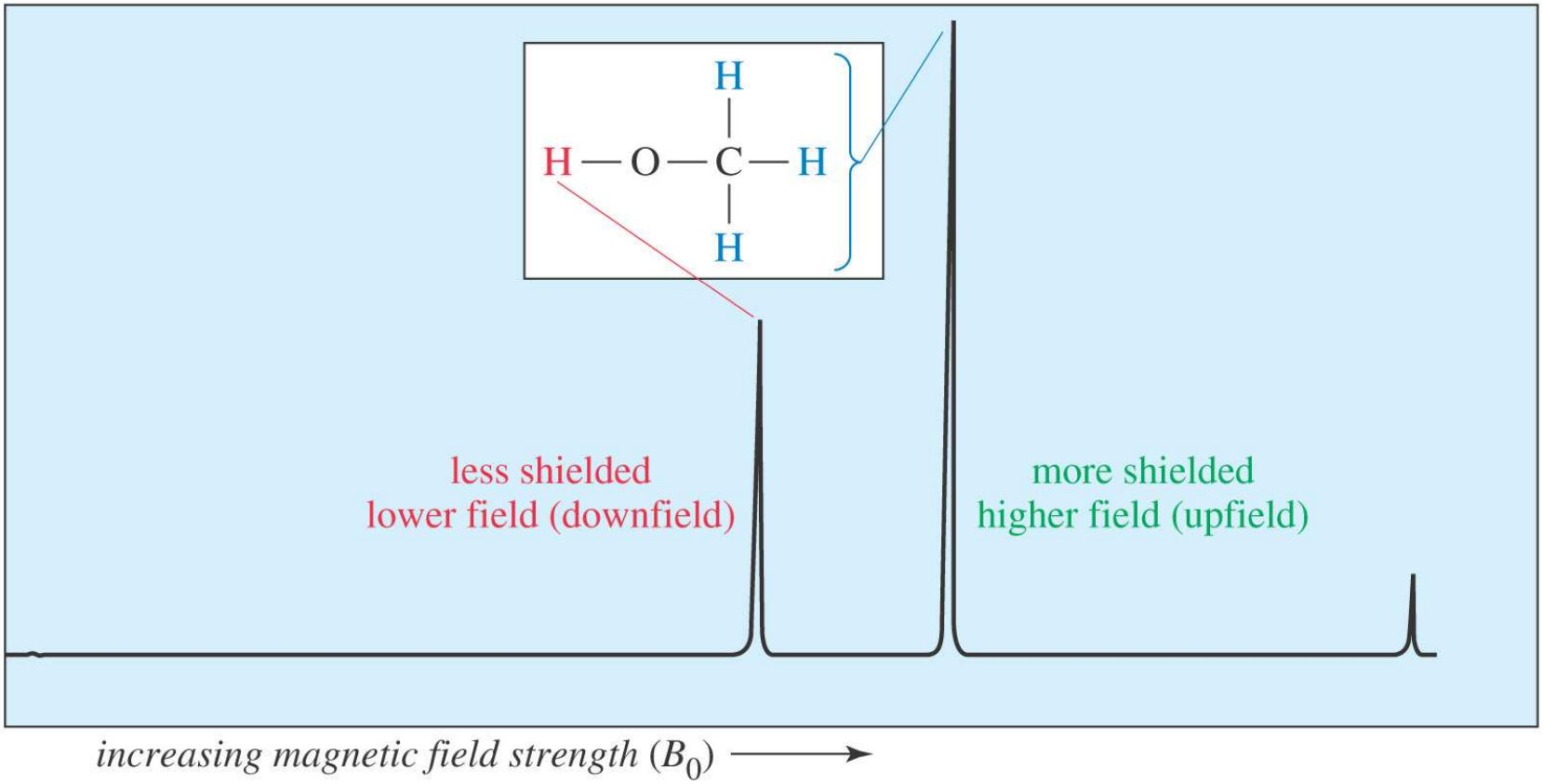
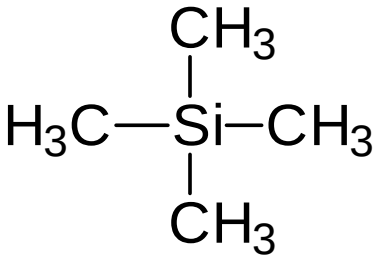
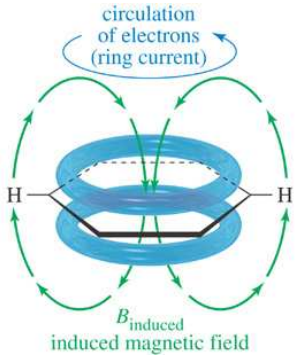
The NMR Graph







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.

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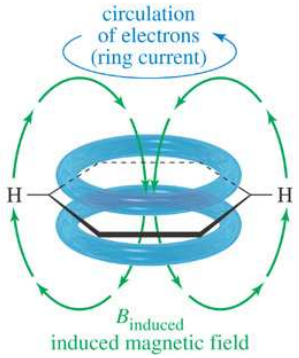
Chemical Shift



- 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.

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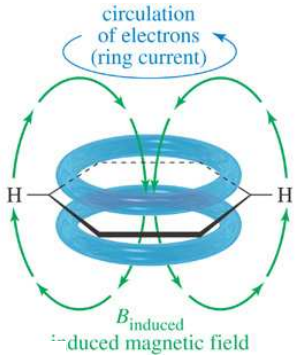
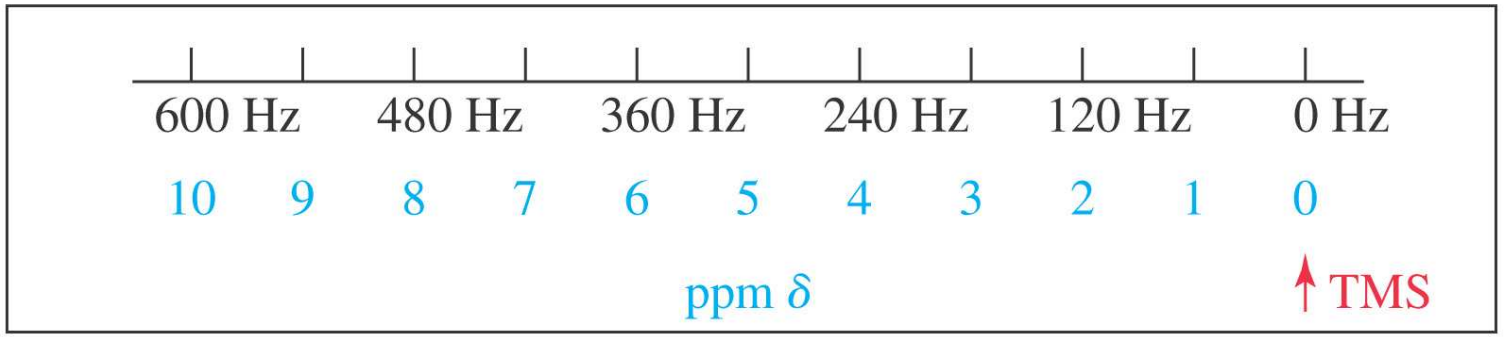
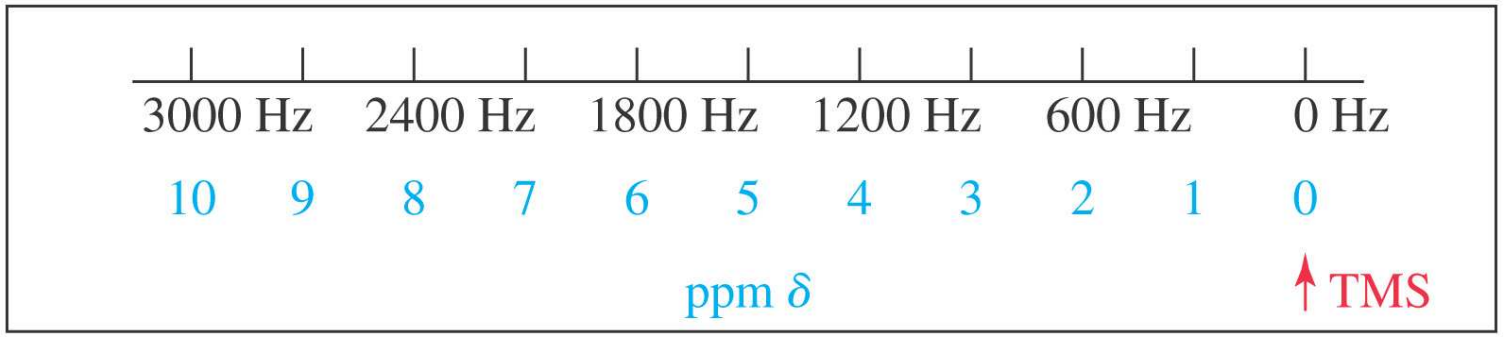
Delta Scale



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



60 MHz



300 MHz

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Location of Signals

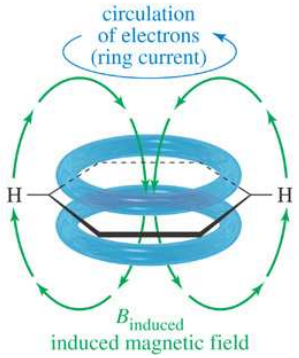

TABLE 13-2 Chemical Shifts of the Chloromethanes

Compound	Chemical Shift	Difference
CH_4	δ0.2	
		2.8 ppm
CH_3Cl	δ3.0	
		2.3 ppm
CH_2Cl_2	δ5.3	
		1.9 ppm
$CHCl_3$	δ7.2	

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

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

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Typical Values

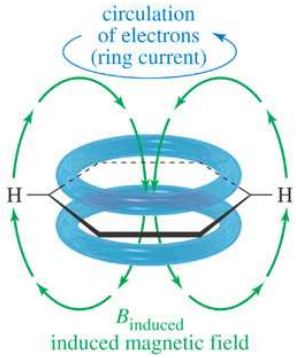
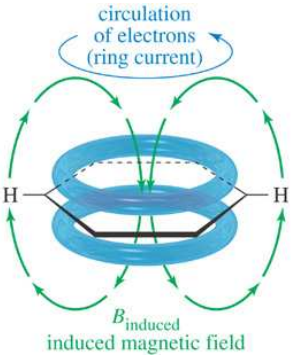


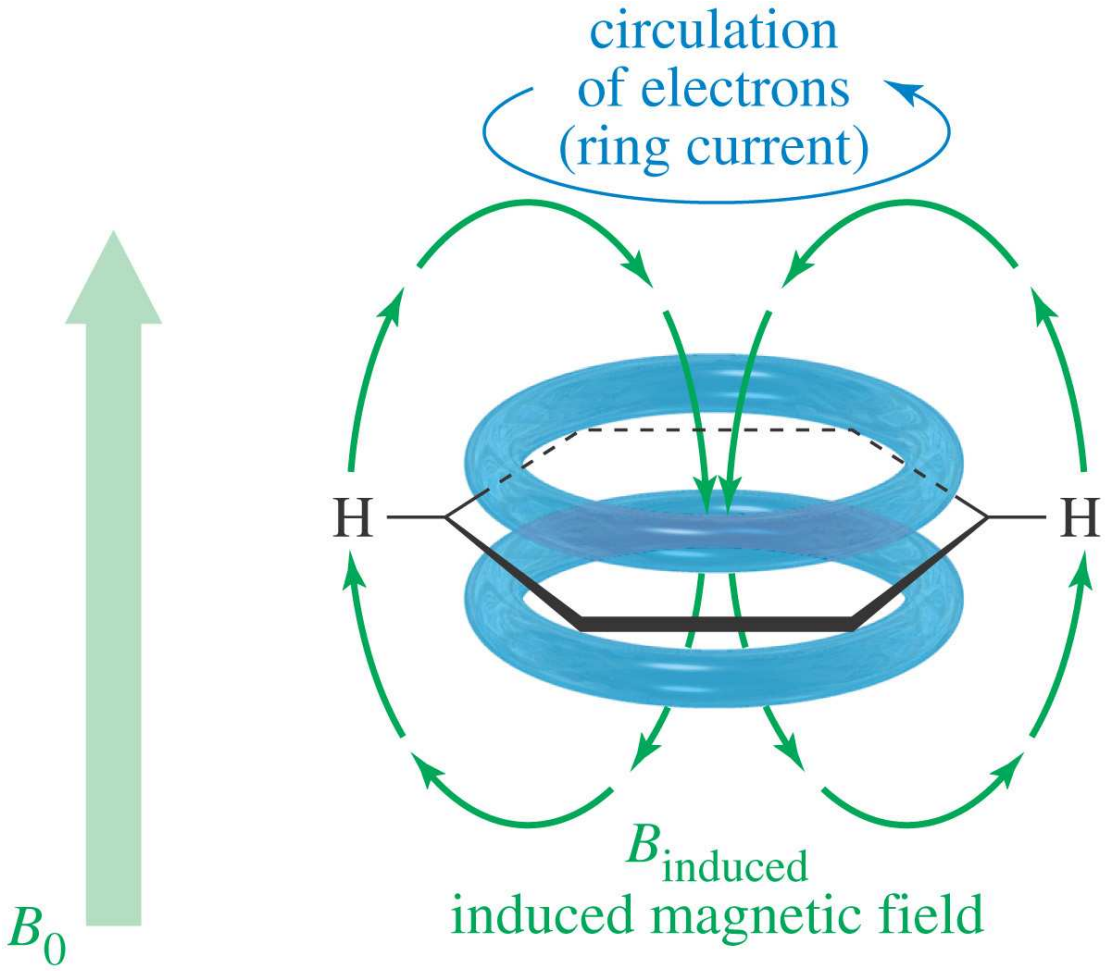
TABLE 13-3 Typical Values of Chemical Shifts

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 ($-\underset{|}{CH}-$)	1.4	Ph—CH_3	2.3
$-C(=O)-CH_3$	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





induced field reinforces the external field (deshielding)

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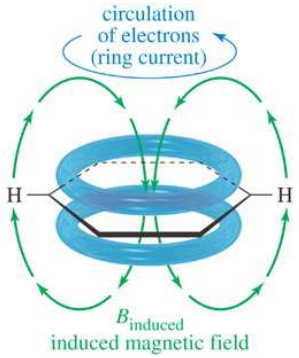
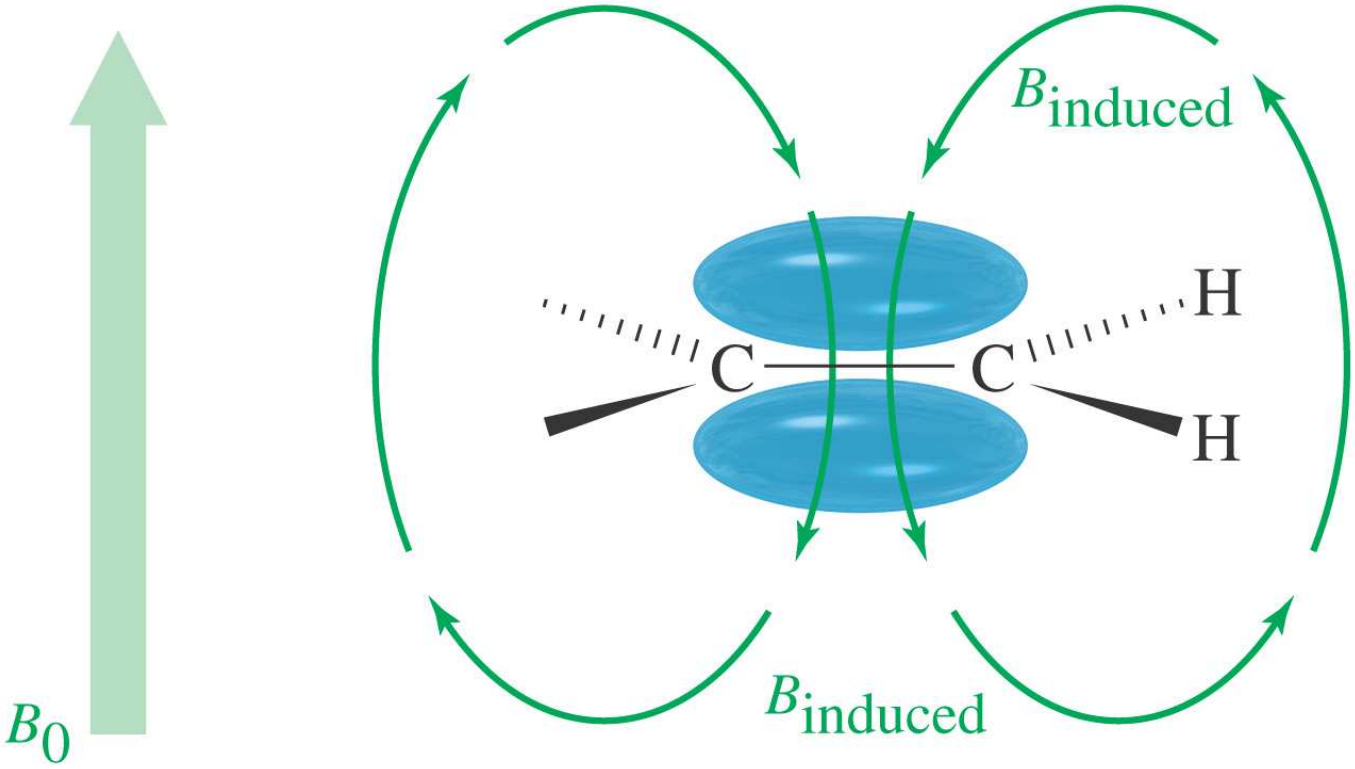
Vinyl Protons, δ5-δ6





induced field reinforces the external field (deshielding)

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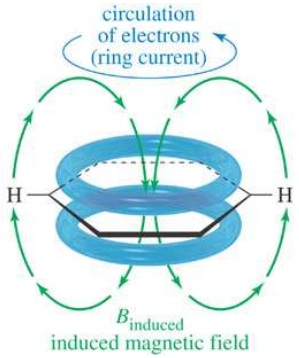
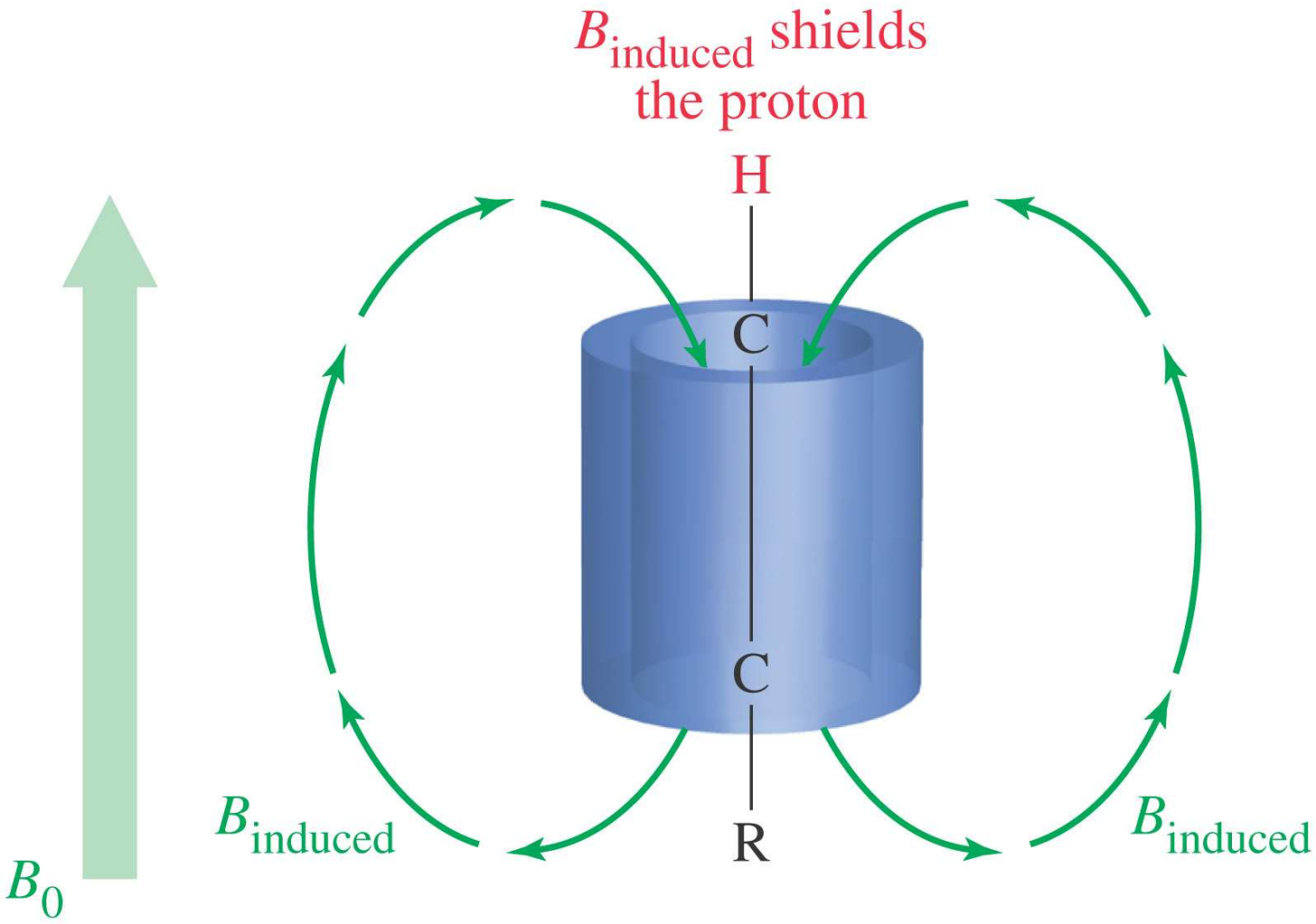
Acetylenic Protons, δ2.5





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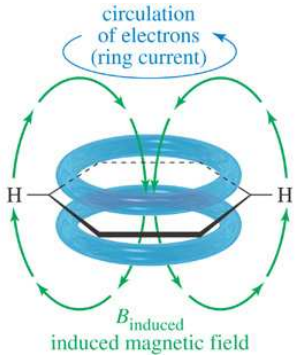
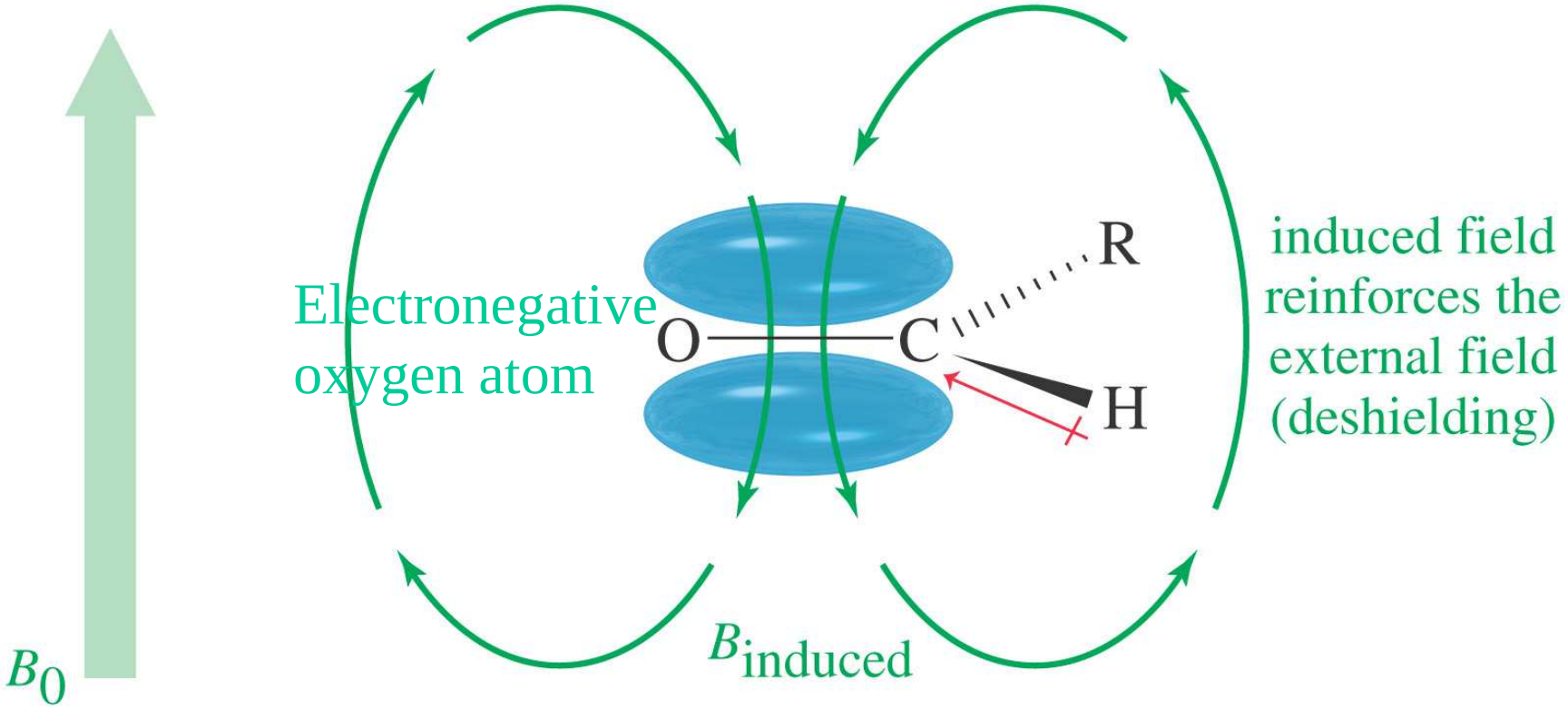
Aldehyde Proton, δ9-δ10





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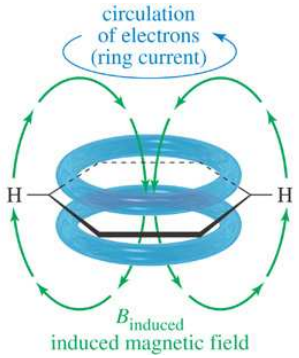
O-H and N-H Signals



- Chemical shift depends on concentration.
- Hydrogen bonding in concentrated solutions deshield the protons, so signal is around δ3.5 for N-H and δ4.5 for O-H.
- Proton exchanges between the molecules broaden the peak.

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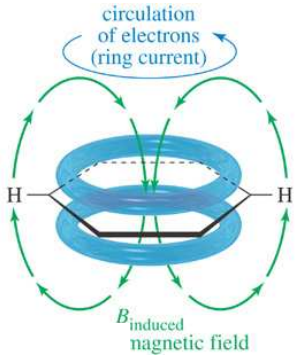
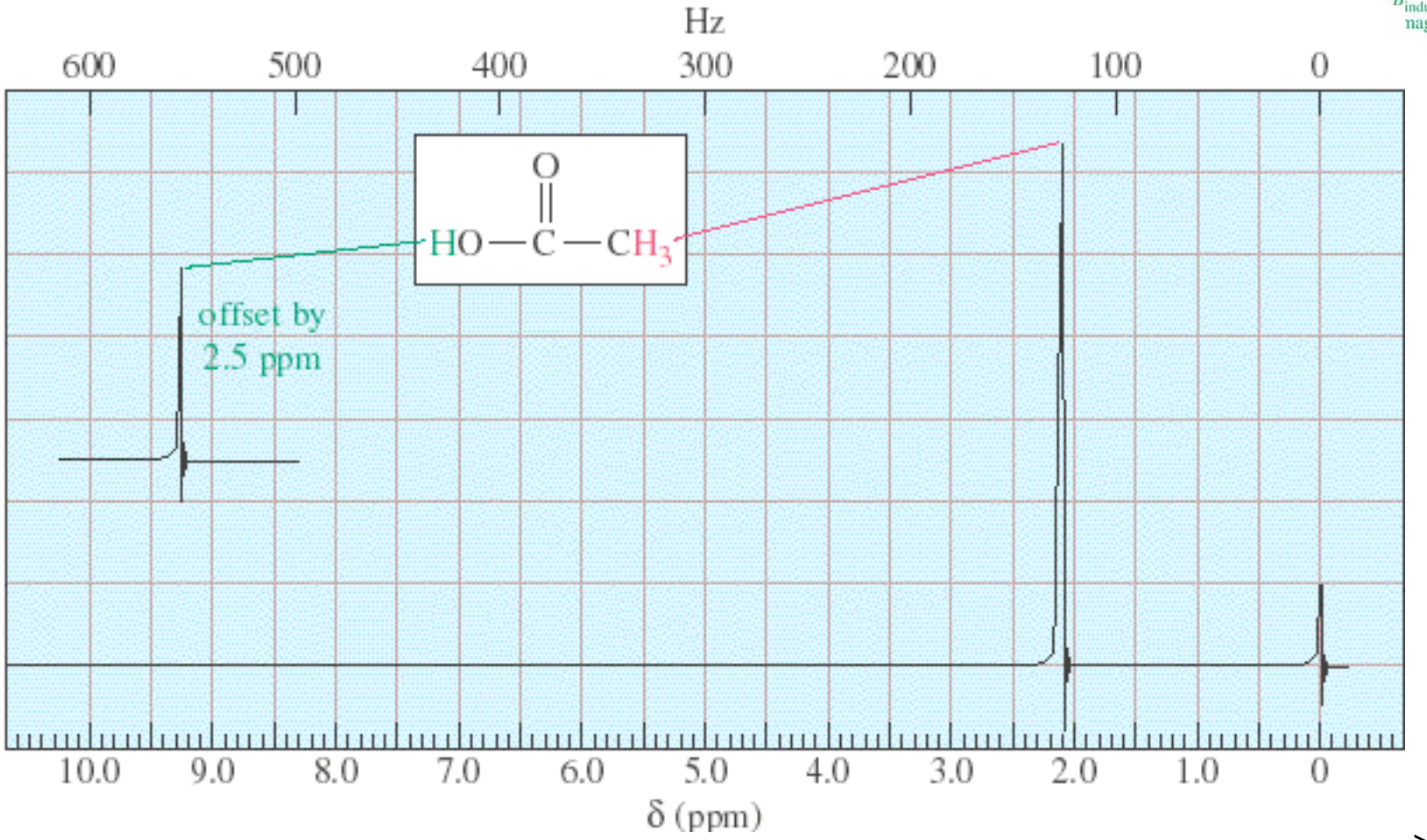
Carboxylic Acid Proton, δ10+





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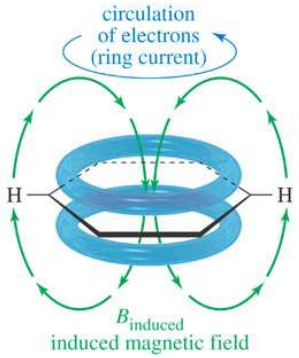
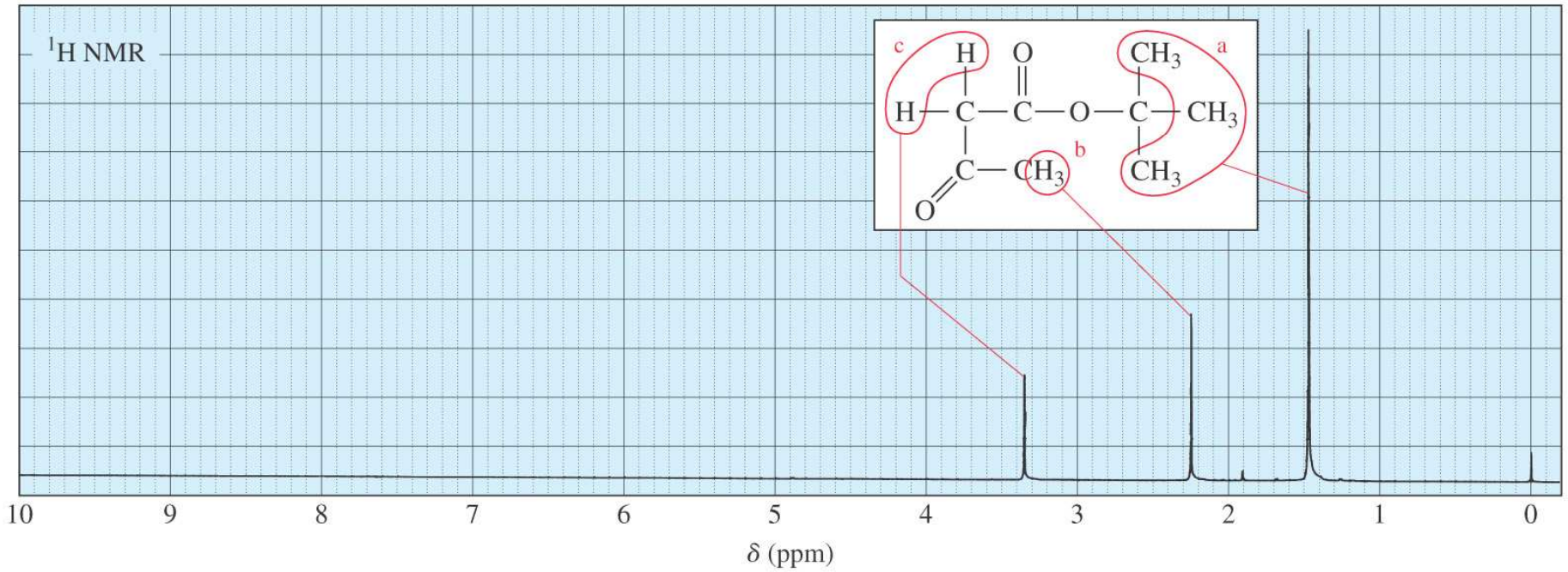
Number of Signals



Equivalent hydrogens have the same chemical shift.



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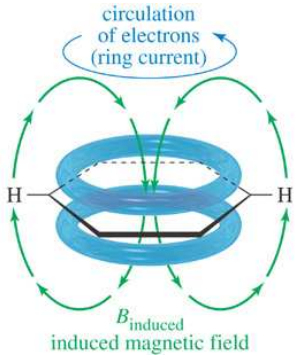
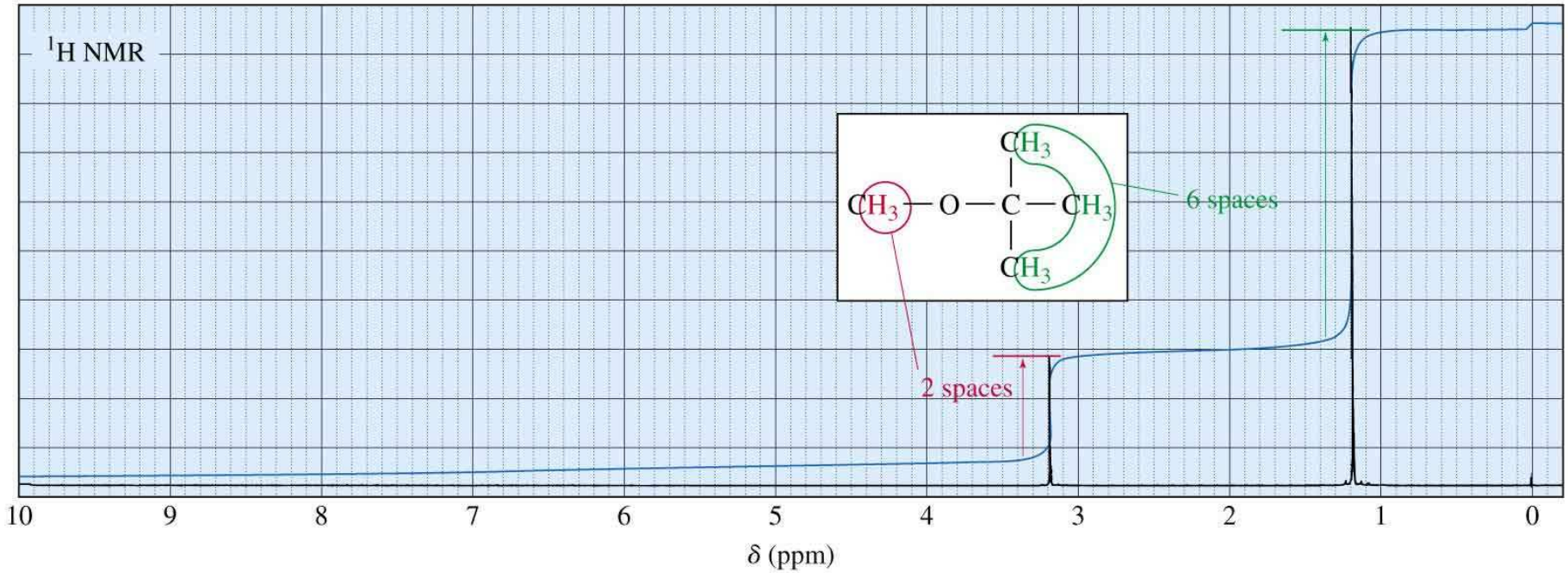
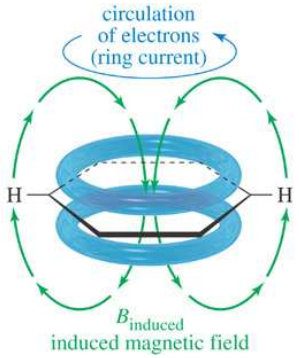
Intensity of Signals



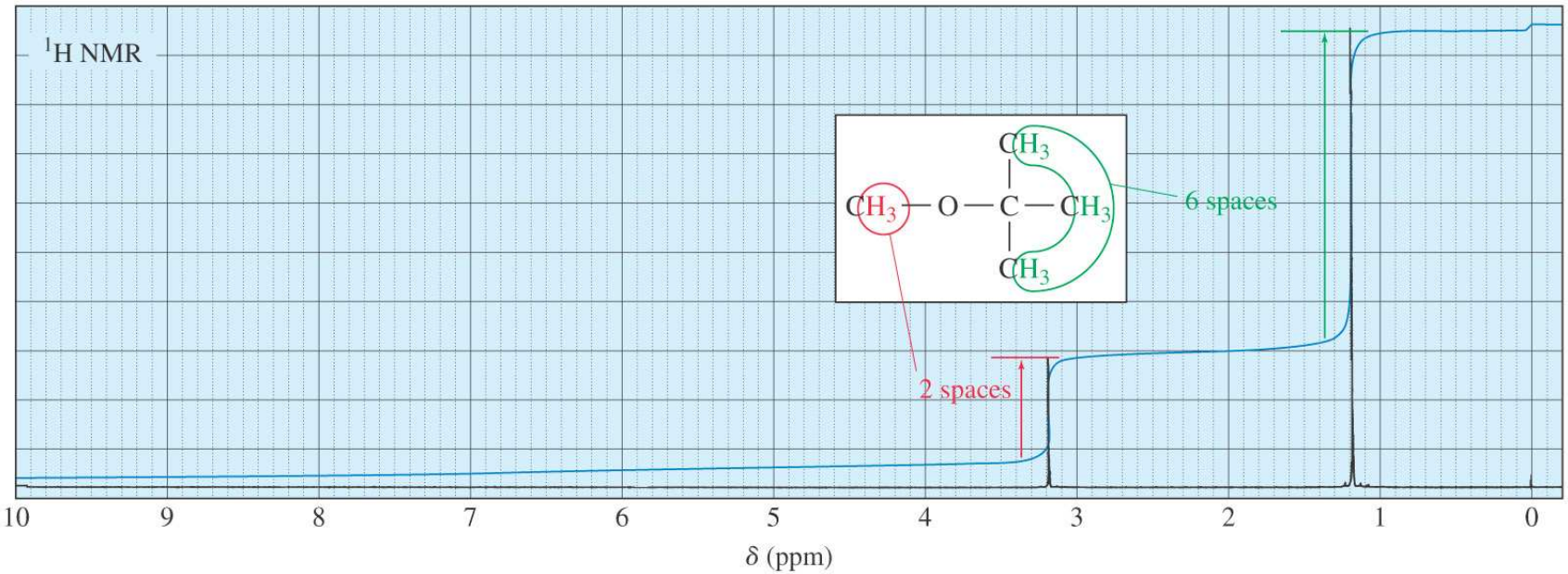
- The area under each peak is proportional to the number of protons.
- Shown by integral trace.



How Many Hydrogens?



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



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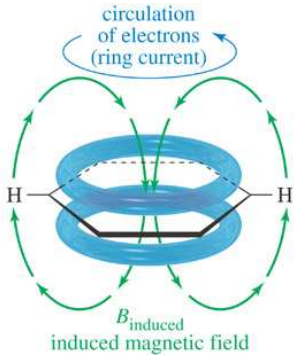
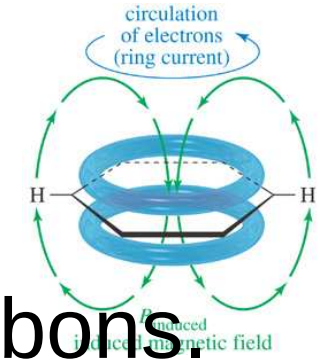
Spin-Spin Splitting

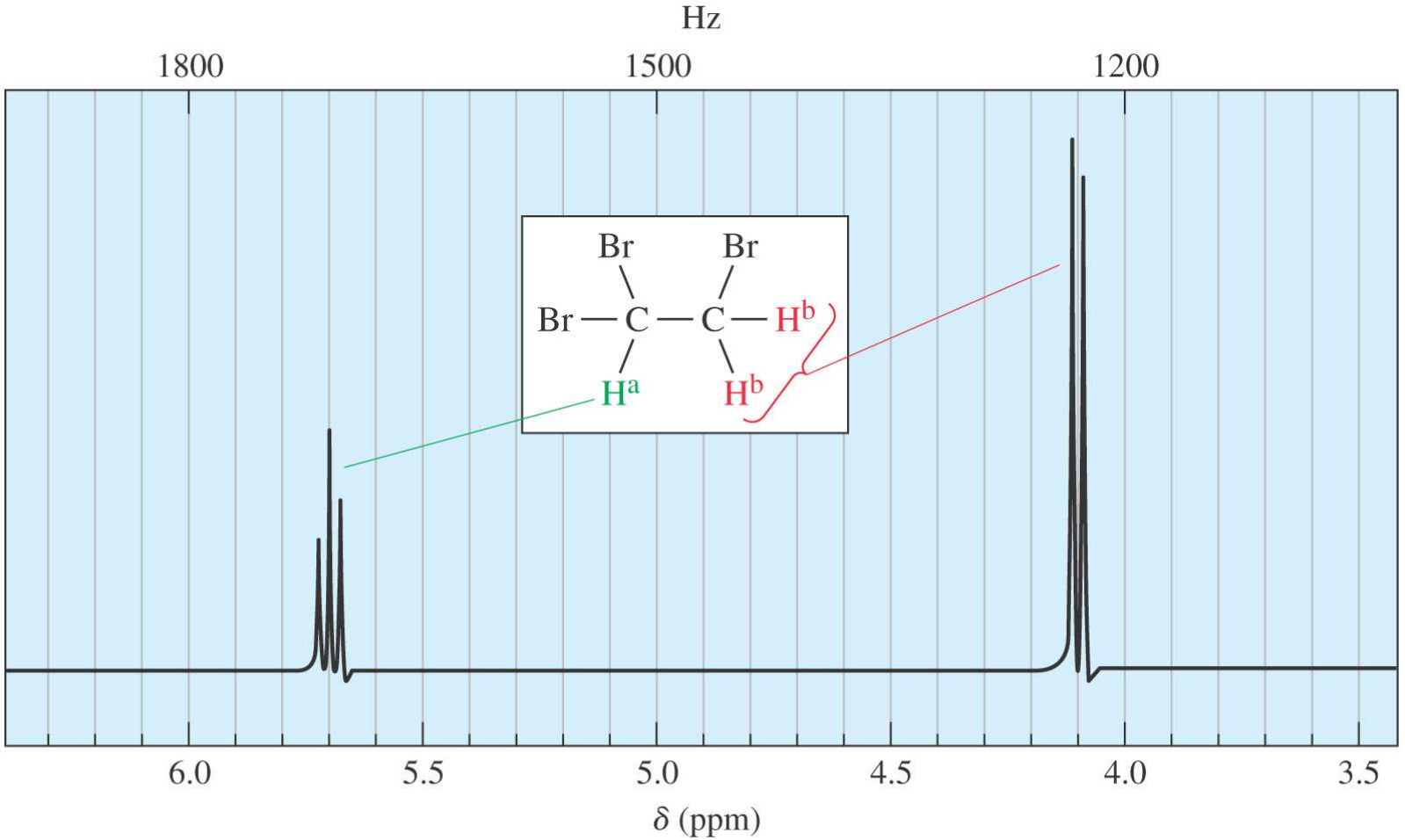


- Nonequivalent protons on adjacent carbons have magnetic fields that may align with or oppose the external field.
- This magnetic coupling causes the proton to absorb slightly downfield when the external field is reinforced and slightly upfield when the external field is opposed.
- All possibilities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

1,1,2-Tribromoethane



Nonequivalent protons on adjacent carbons.



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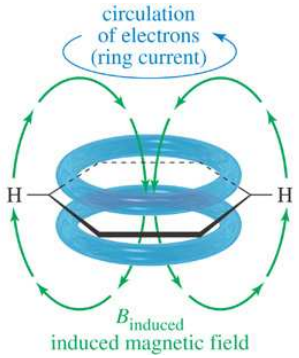
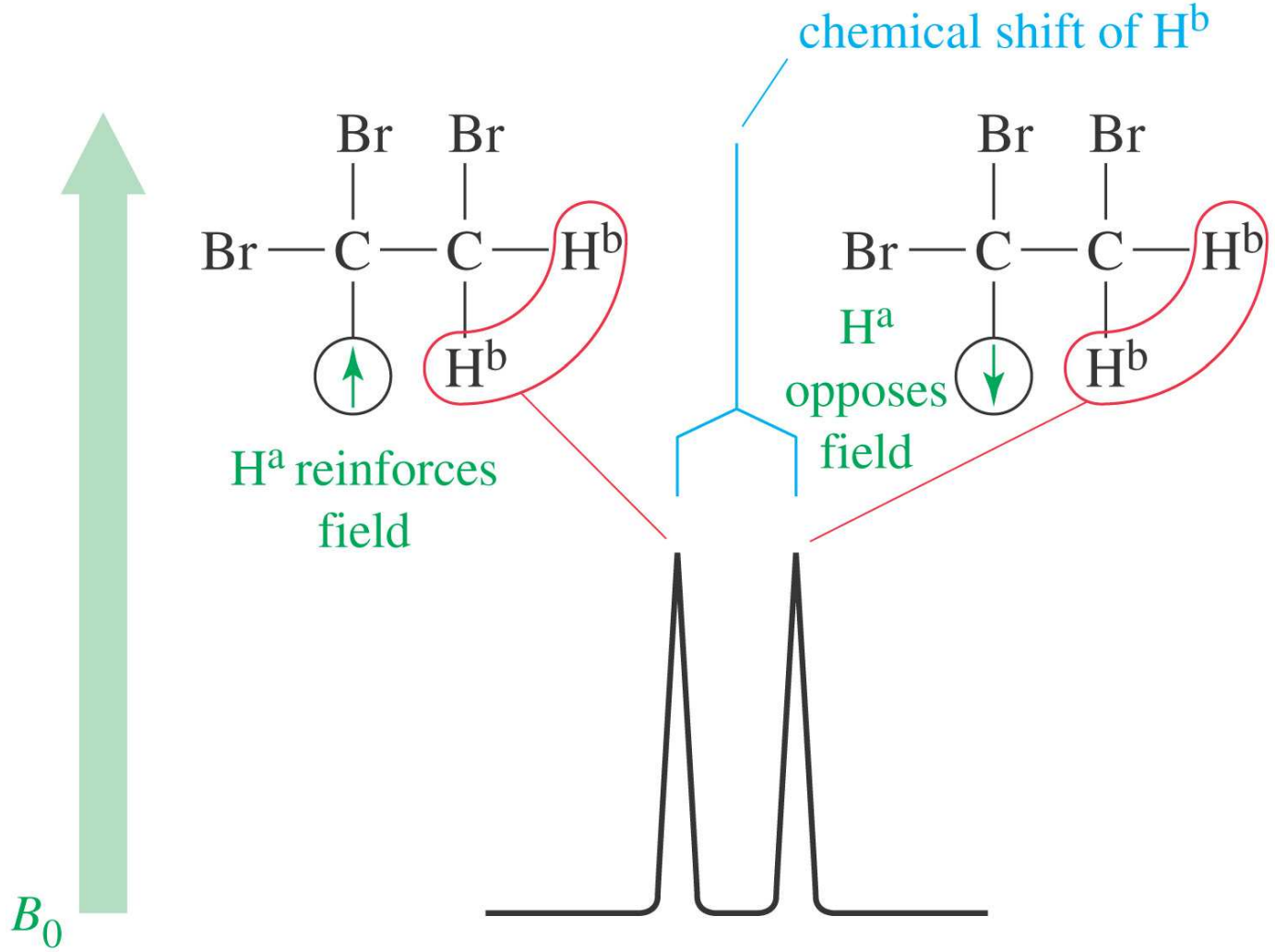
Doublet: 1 Adjacent Proton





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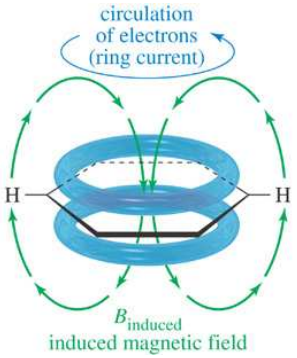
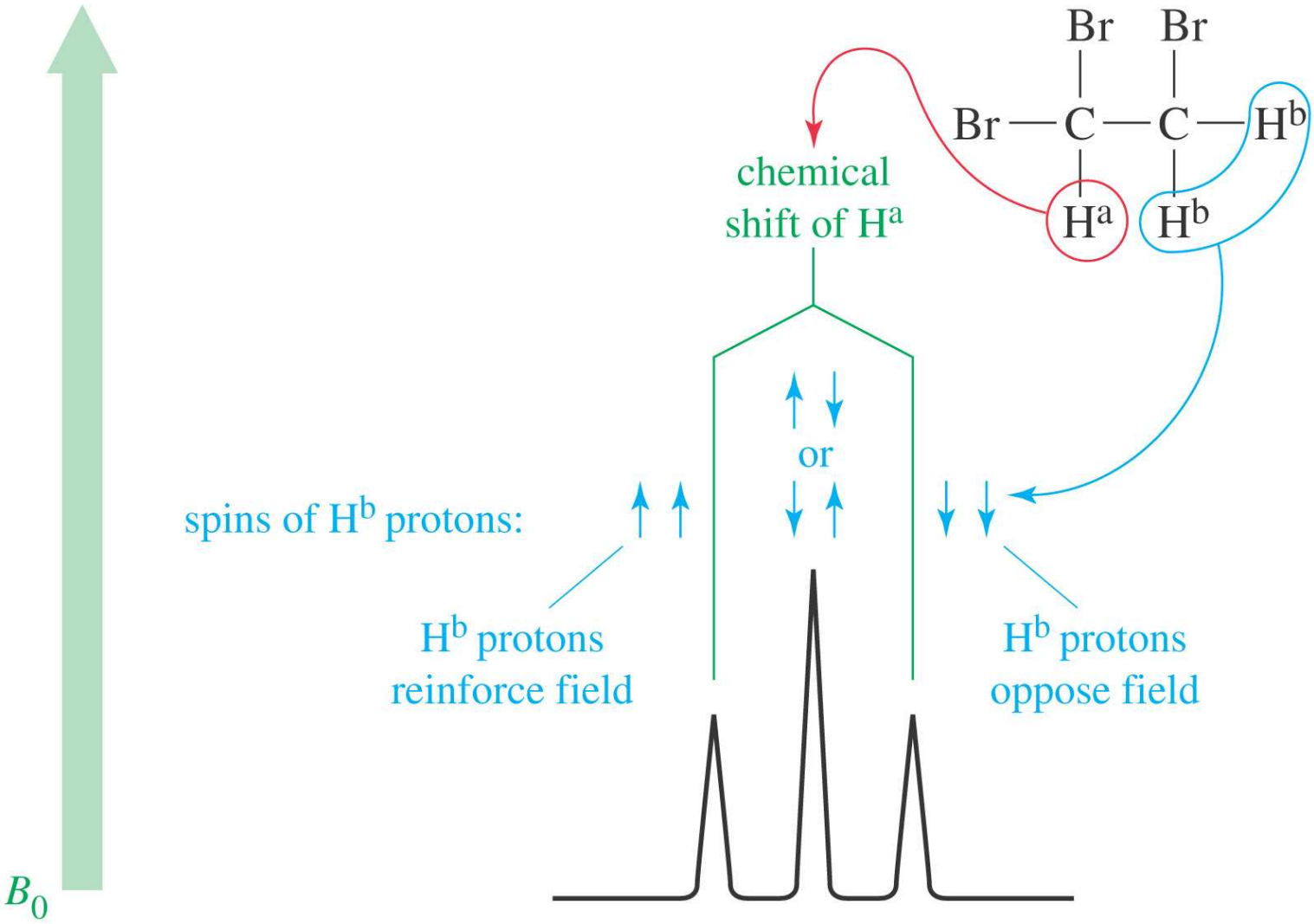
Triplet: 2 Adjacent Protons





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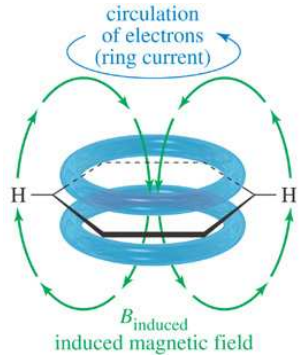
The *N* + 1 Rule

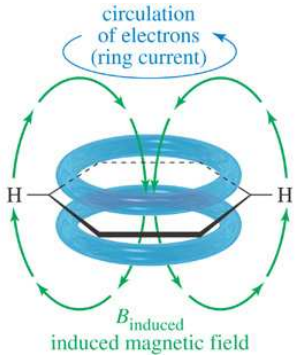


If a signal is split by *N* equivalent protons, it is split into *N* + 1 peaks.

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

=>

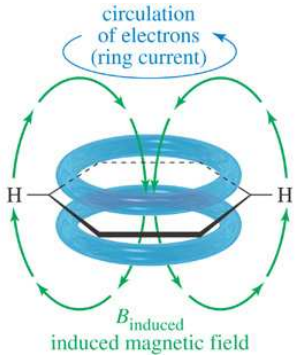
Range of Magnetic Coupling

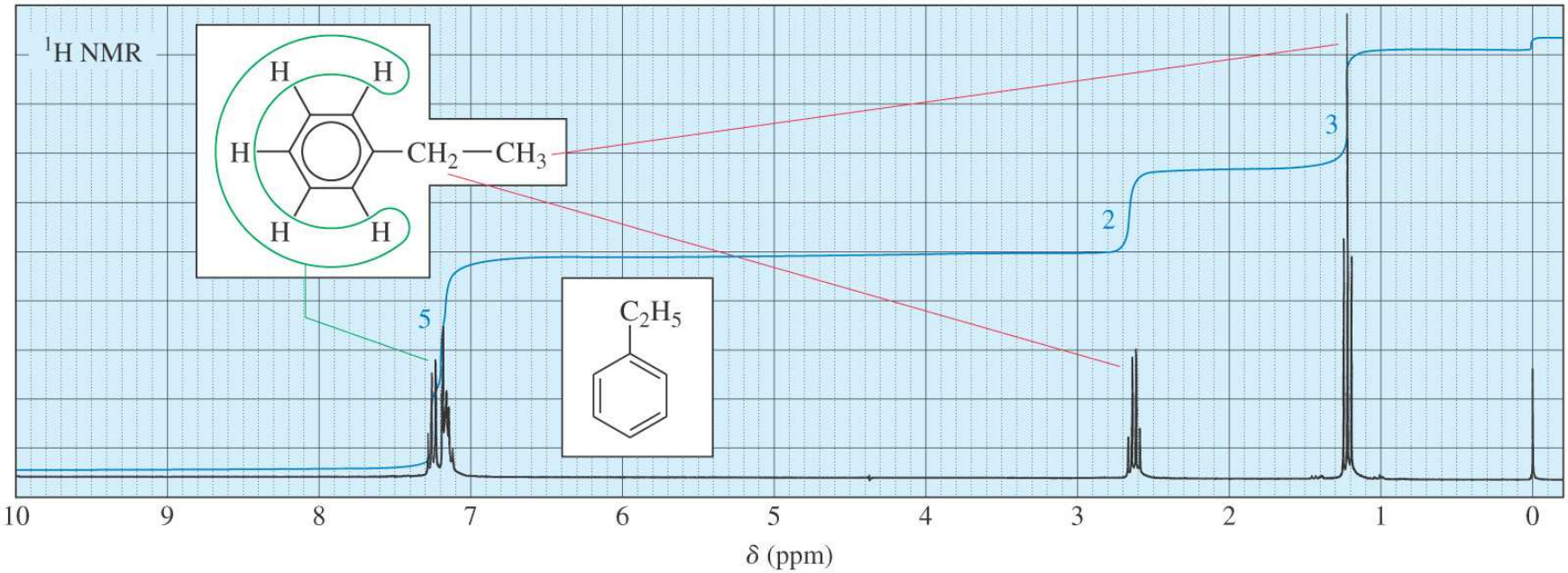


- Equivalent protons do not split each other.
- Protons bonded to the same carbon will split each other only if they are not equivalent.
- Protons on adjacent carbons normally will couple.
- Protons separated by four or more bonds will not couple.

=>

Splitting for Ethyl Groups





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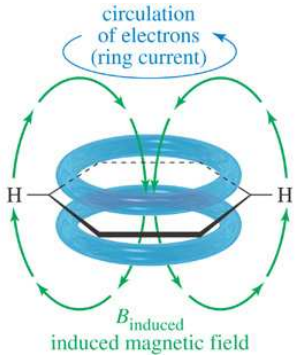
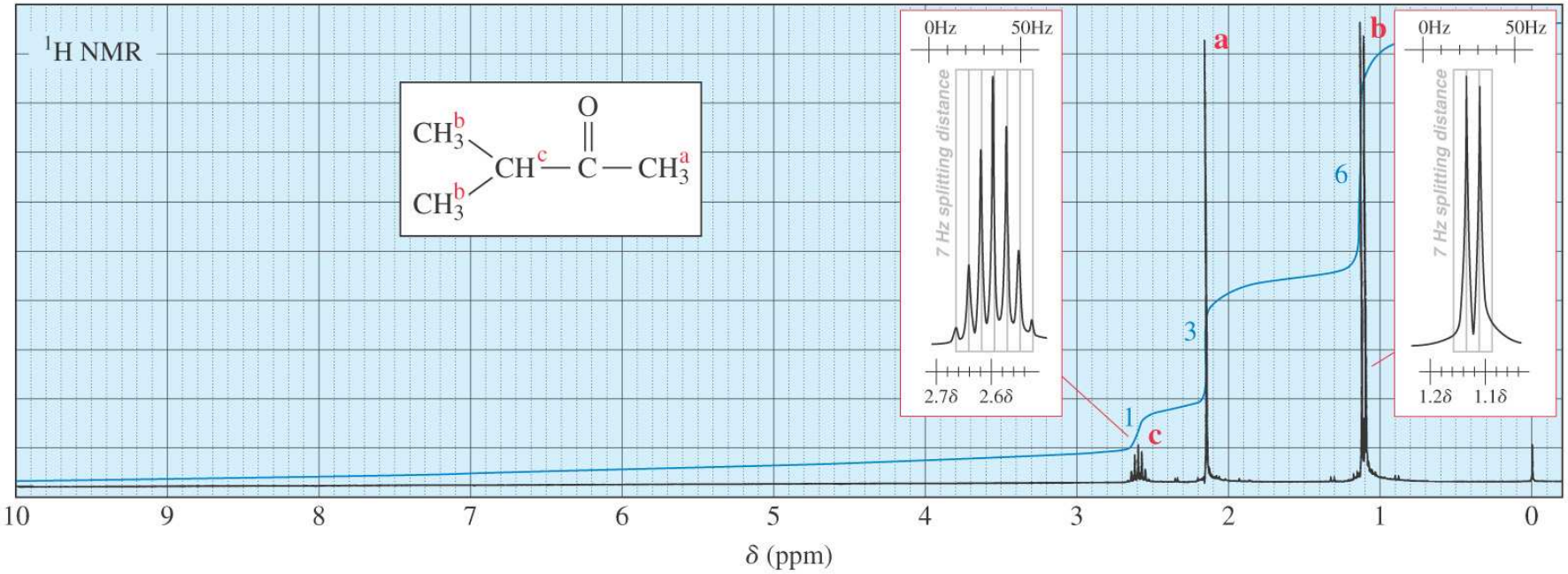
Splitting for Isopropyl Groups





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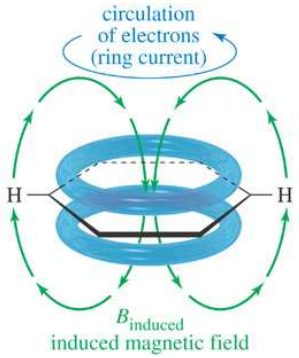
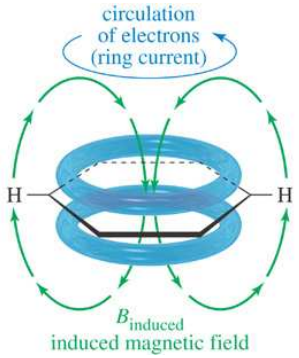
Coupling Constants

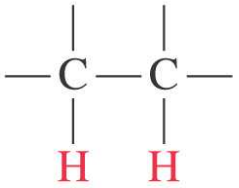
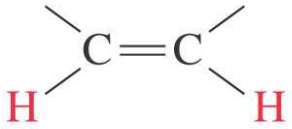
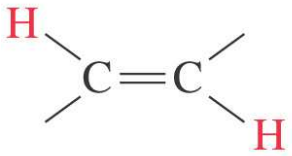
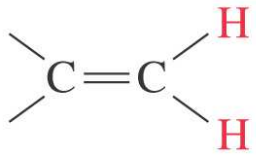


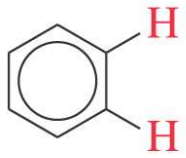
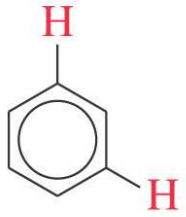
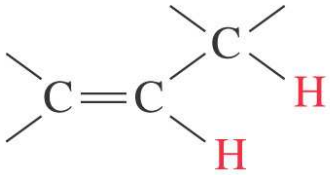
- Distance between the peaks of multiplet
- Measured in Hz
- Not dependent on strength of the external field
- Multiplets with the same coupling constants may come from adjacent groups of protons that split each other.

=>

Values for Coupling Constants

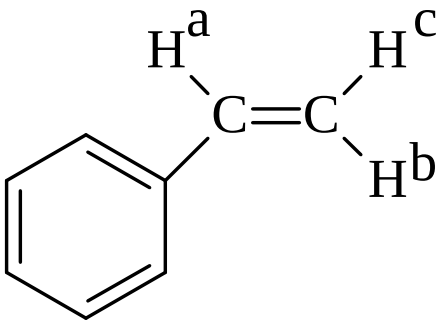


		Approx. J
	(free rotation)	7 Hz[a]
	(cis)	10 Hz
	(trans)	15 Hz
	(geminal)	2 Hz

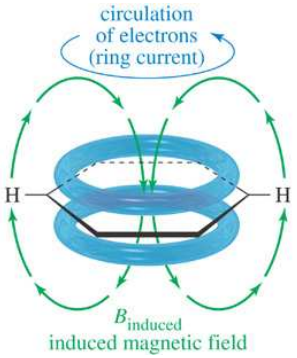
		Approx. J
	(ortho)	8 Hz
	(meta)	2 Hz
	(allylic)	6 Hz

[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.

=>



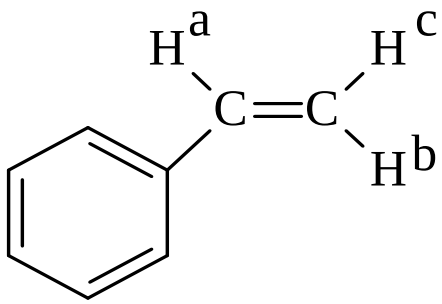
Complex Splitting

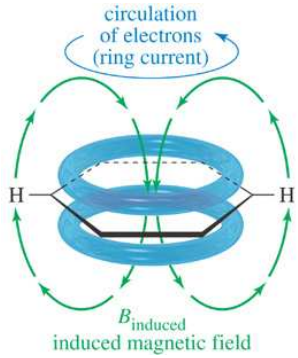


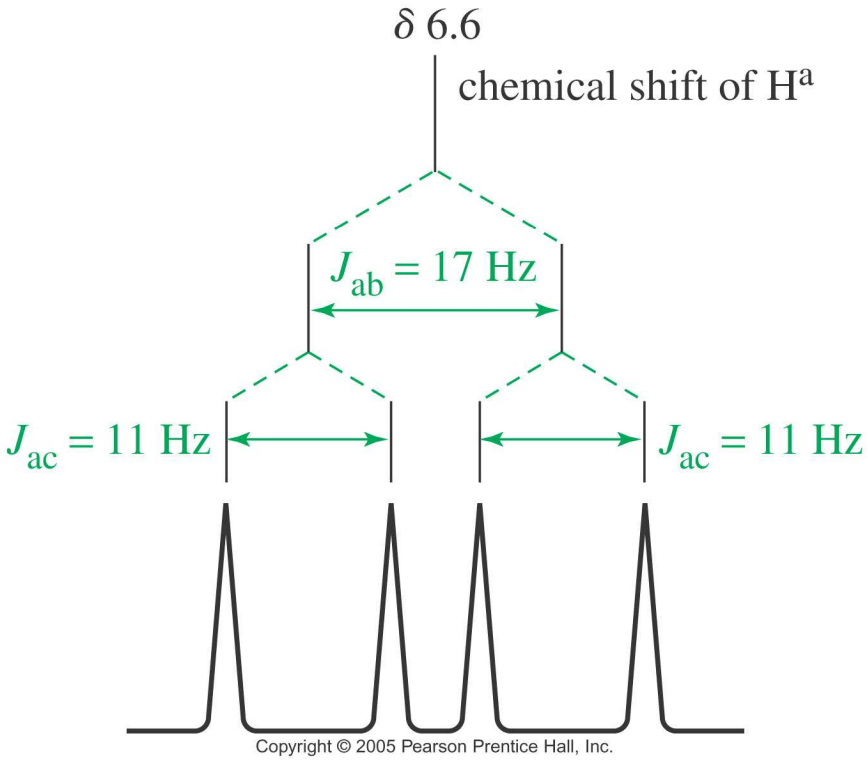
- Signals may be split by adjacent protons, different from each other, with different coupling constants.
- Example: H^a of styrene which is split by an adjacent H *trans* to it (J = 17 Hz) and an adjacent H *cis* to it (J = 11 Hz).

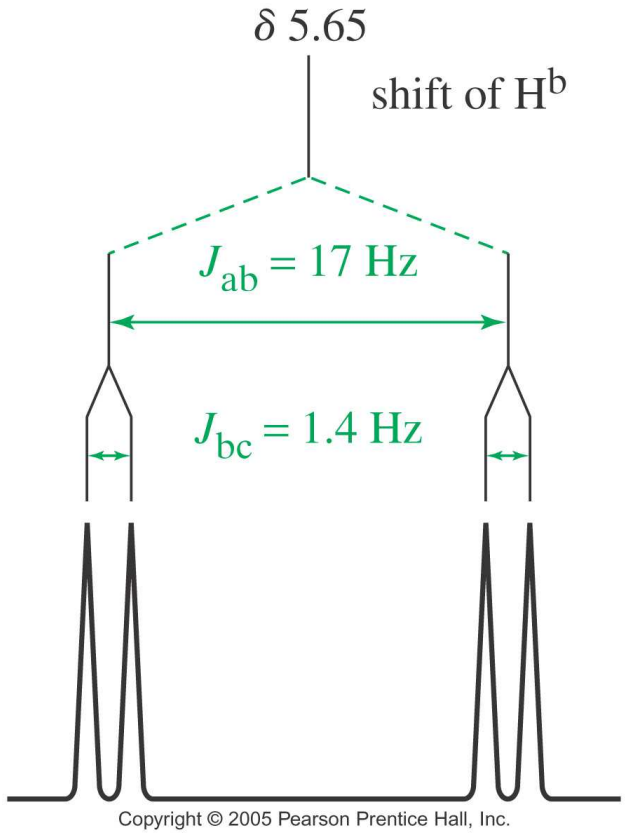
=>

Splitting Tree

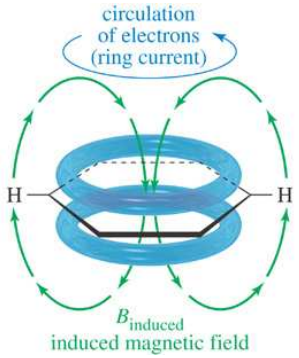


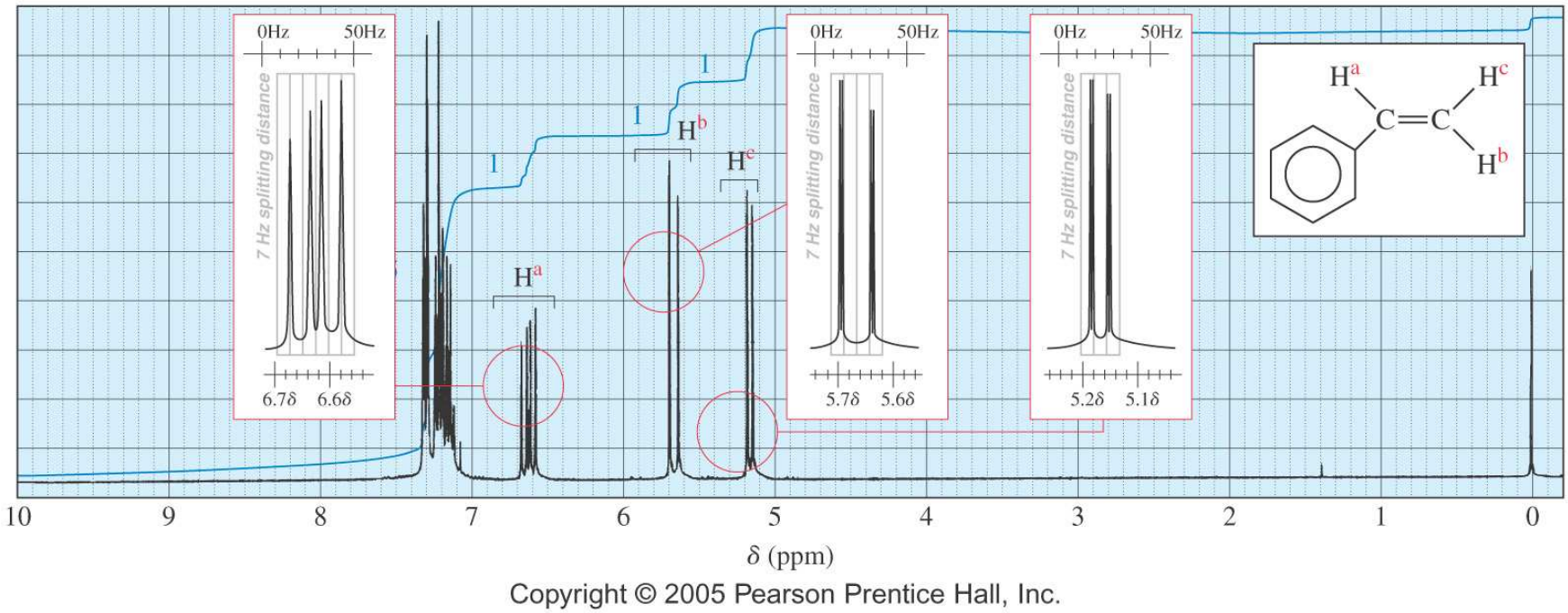






Spectrum for Styrene





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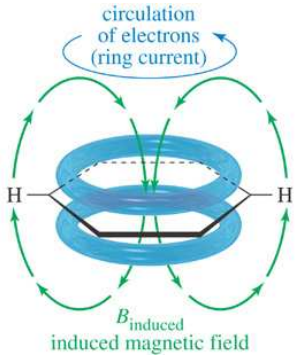
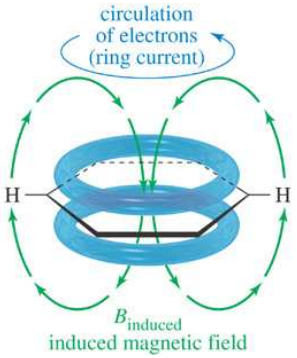
Stereochemical Nonequivalence

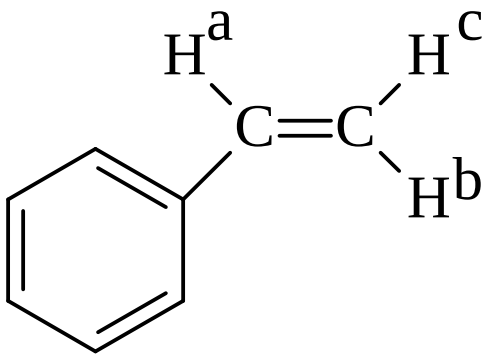


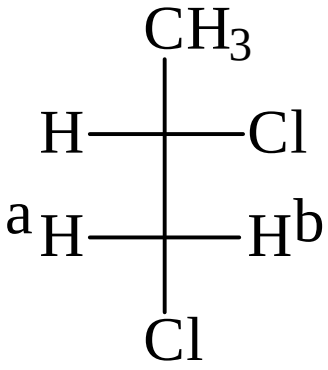
- Usually, two protons on the same C are equivalent and do not split each other.
- If the replacement of each of the protons of a -CH_2 group with an imaginary “Z” gives stereoisomers, then the protons are non-equivalent and will split each other.

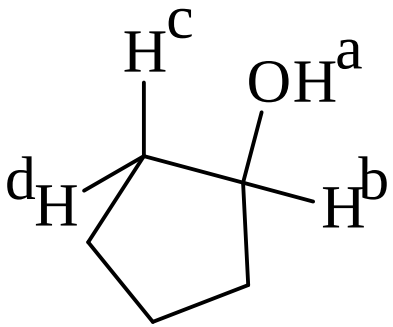
=>

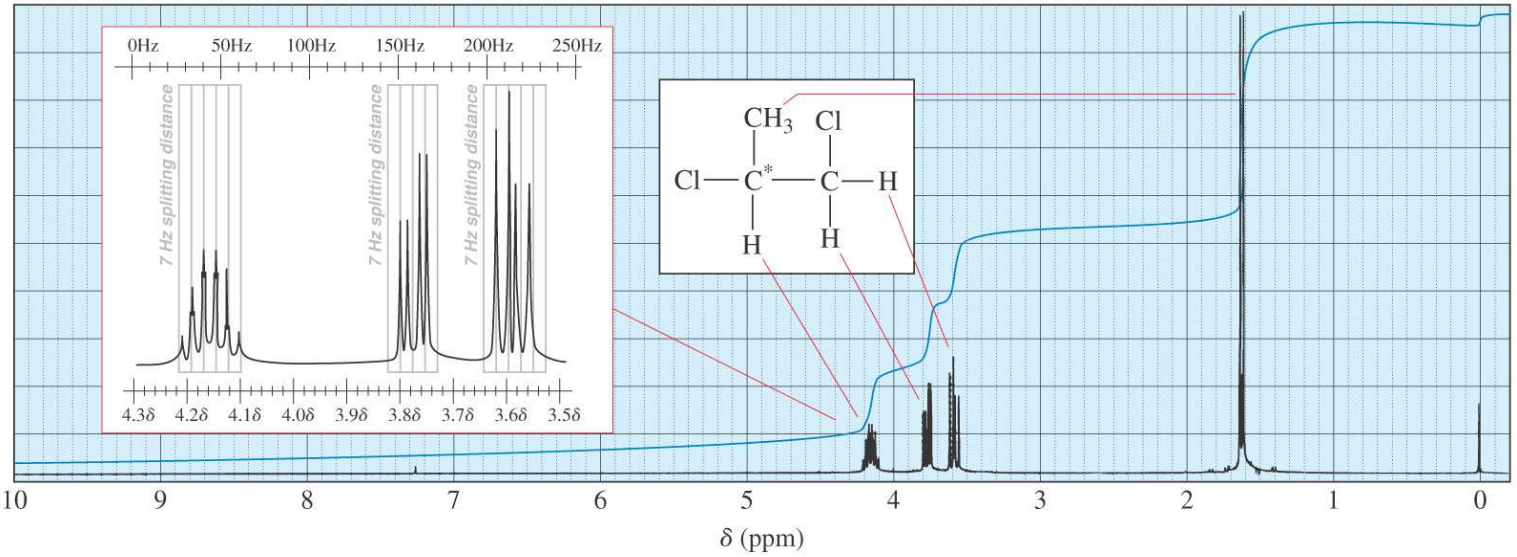
Some Nonequivalent Protons











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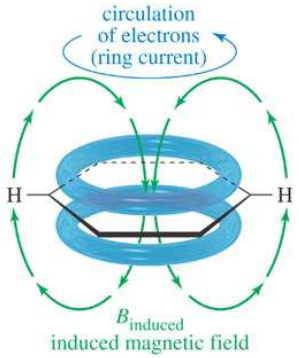
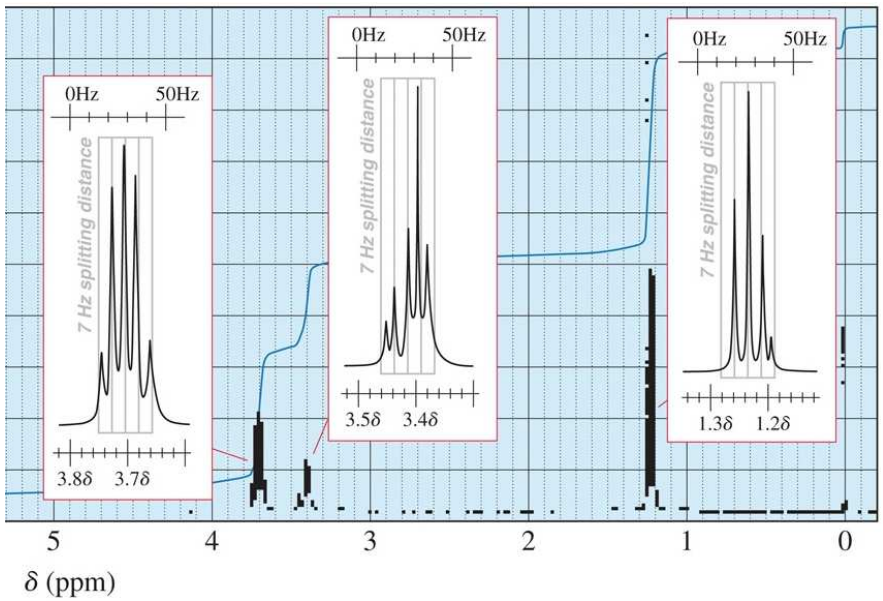
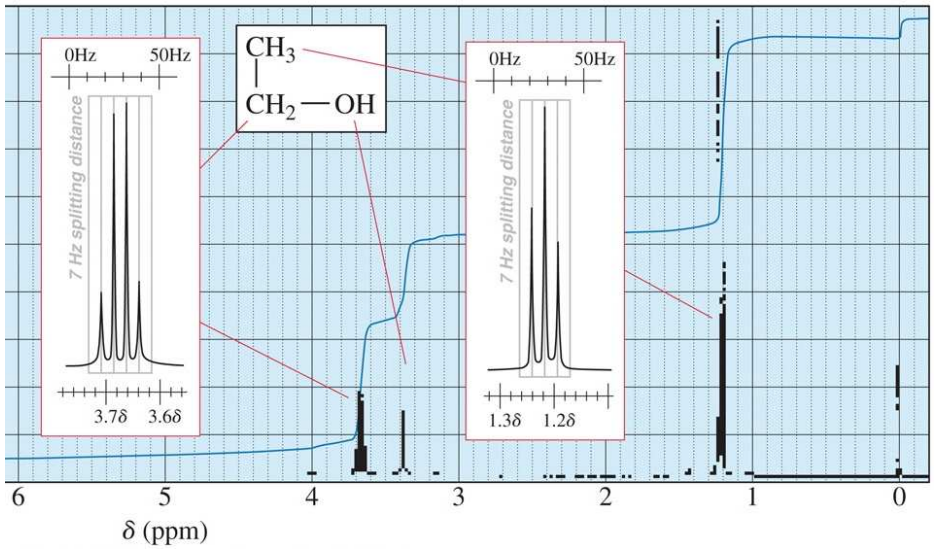
Time Dependence



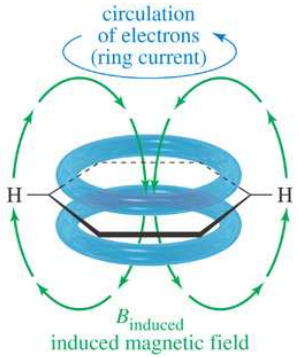
- Molecules are tumbling relative to the magnetic field, so NMR is an averaged spectrum of all the orientations.
- Axial and equatorial protons on cyclohexane interconvert so rapidly that they give a single signal.
- Proton transfers for OH and NH may occur so quickly that the proton is not split by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

=>



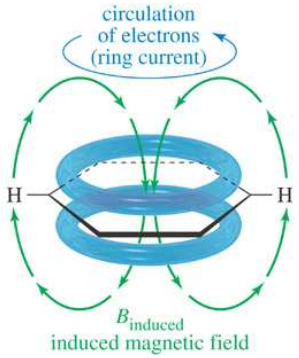


Hydroxyl Proton

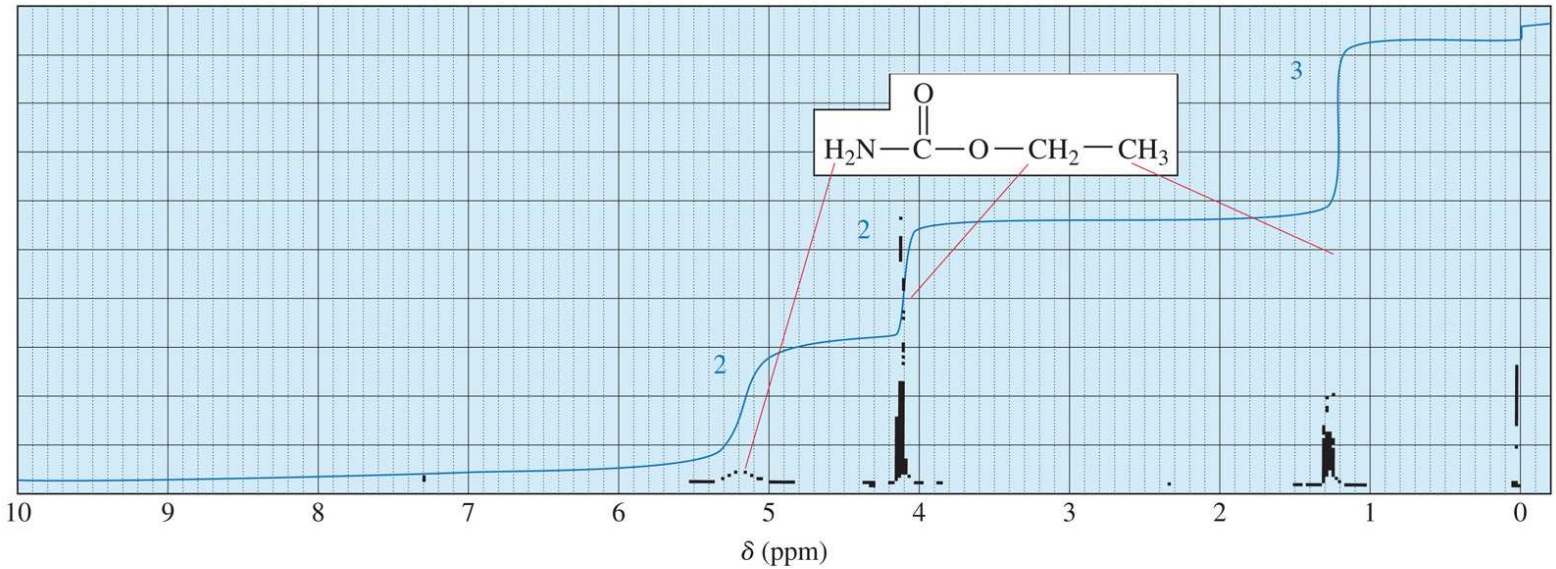


- Ultrapure samples of ethanol show splitting.
- Ethanol with a small amount of acidic or basic impurities will not show splitting.

N-H Proton



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



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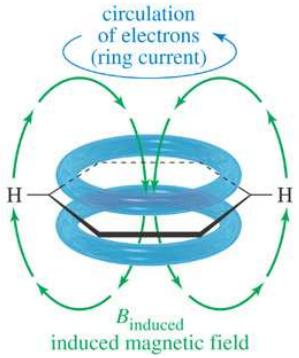
Identifying the O-H or N-H Peak



- 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.

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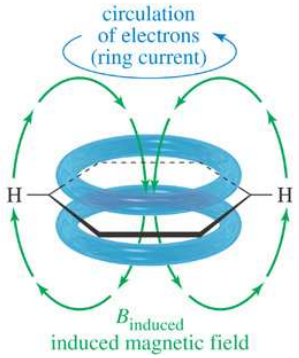
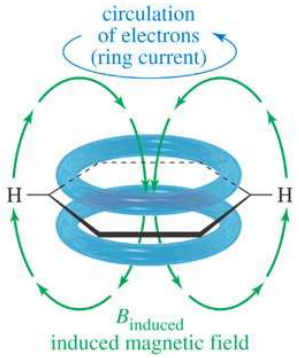
Carbon-13



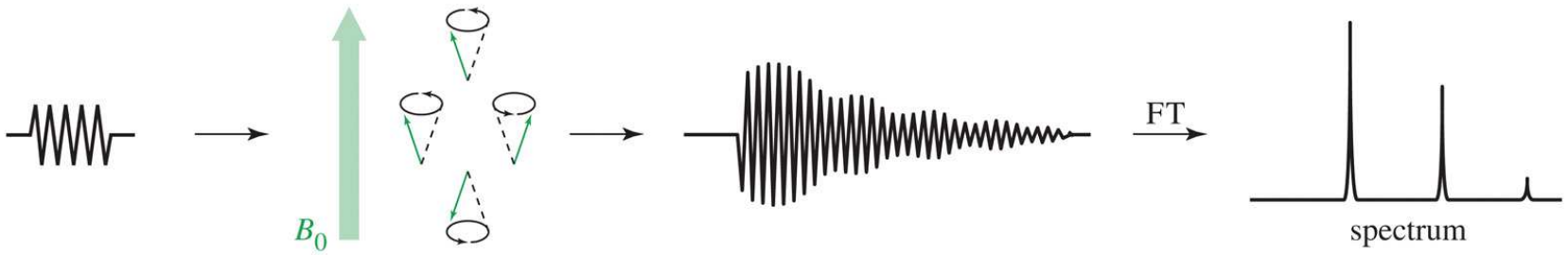
- ^{12}C has no magnetic spin.
- ^{13}C has a magnetic spin, but is only 1% of the carbon in a sample.
- The gyromagnetic ratio of ^{13}C is one-fourth of that of ^{1}H.
- Signals are weak, getting lost in noise.
- Hundreds of spectra are taken, averaged.

=>

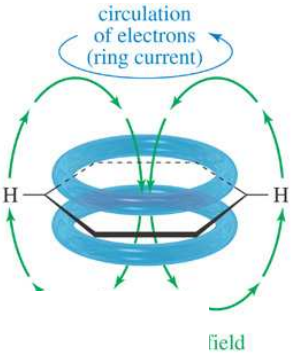
Fourier Transform NMR

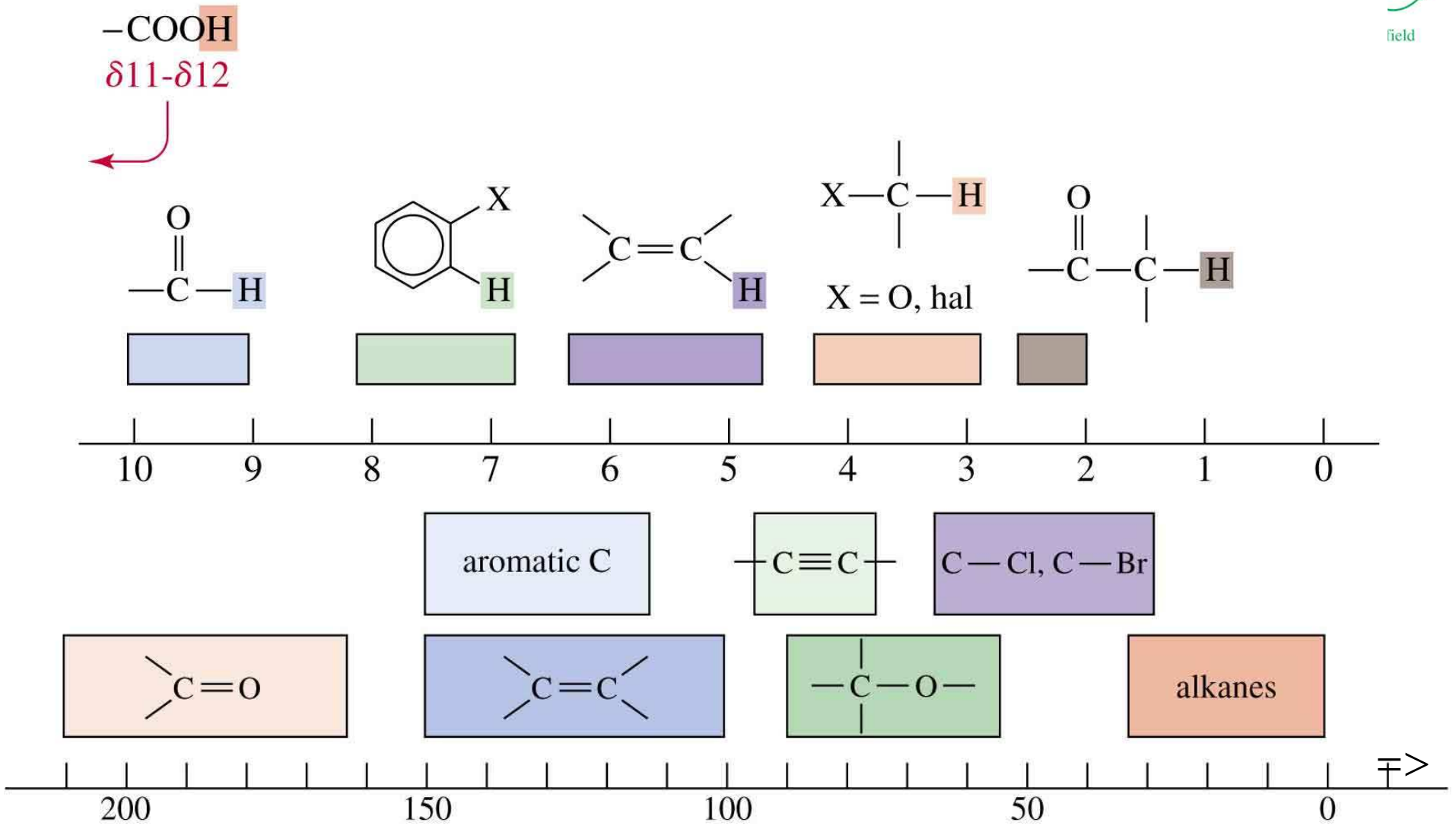


- Radio-frequency pulse given.
- Nuclei absorb energy and precess (spin) like little tops.
- A complex signal is produced, then decays as the nuclei lose energy.
- Free induction decay is converted to spectrum. =>

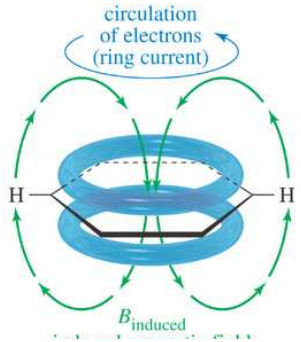


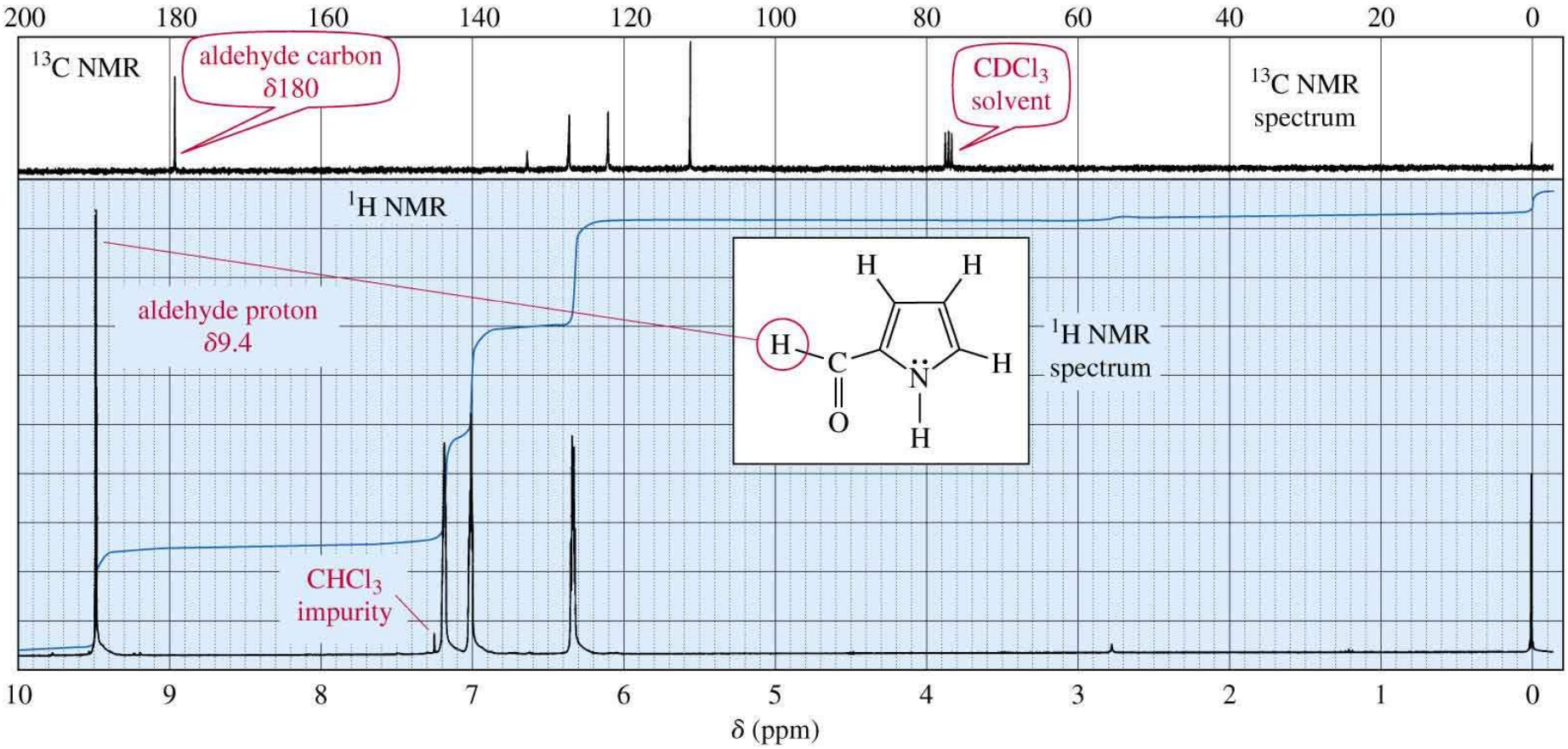
Hydrogen and Carbon Chemical Shifts





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





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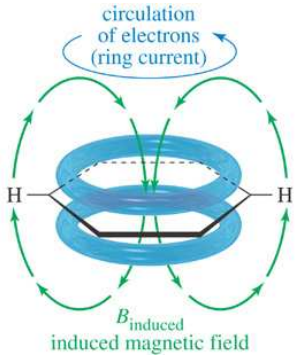
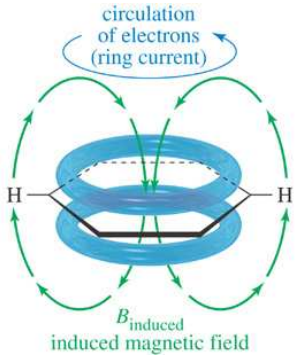
Differences in ^{13}C Technique



- 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.

=>

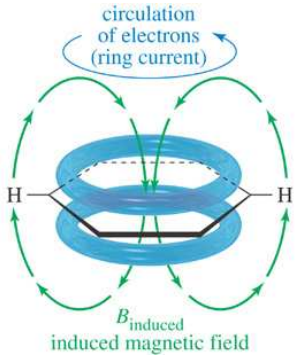
Spin-Spin Splitting



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

=>

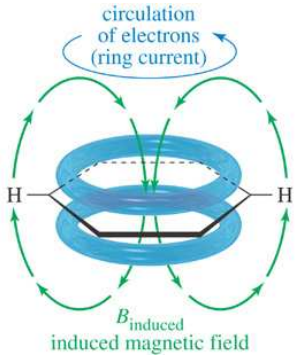
Proton Spin Decoupling



- 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.

=>

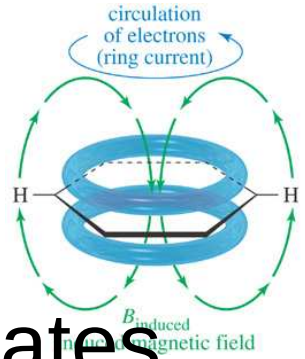
Off-Resonance Decoupling



- ^{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.

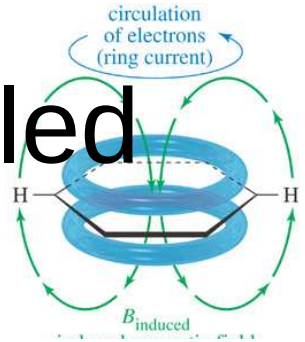
=>

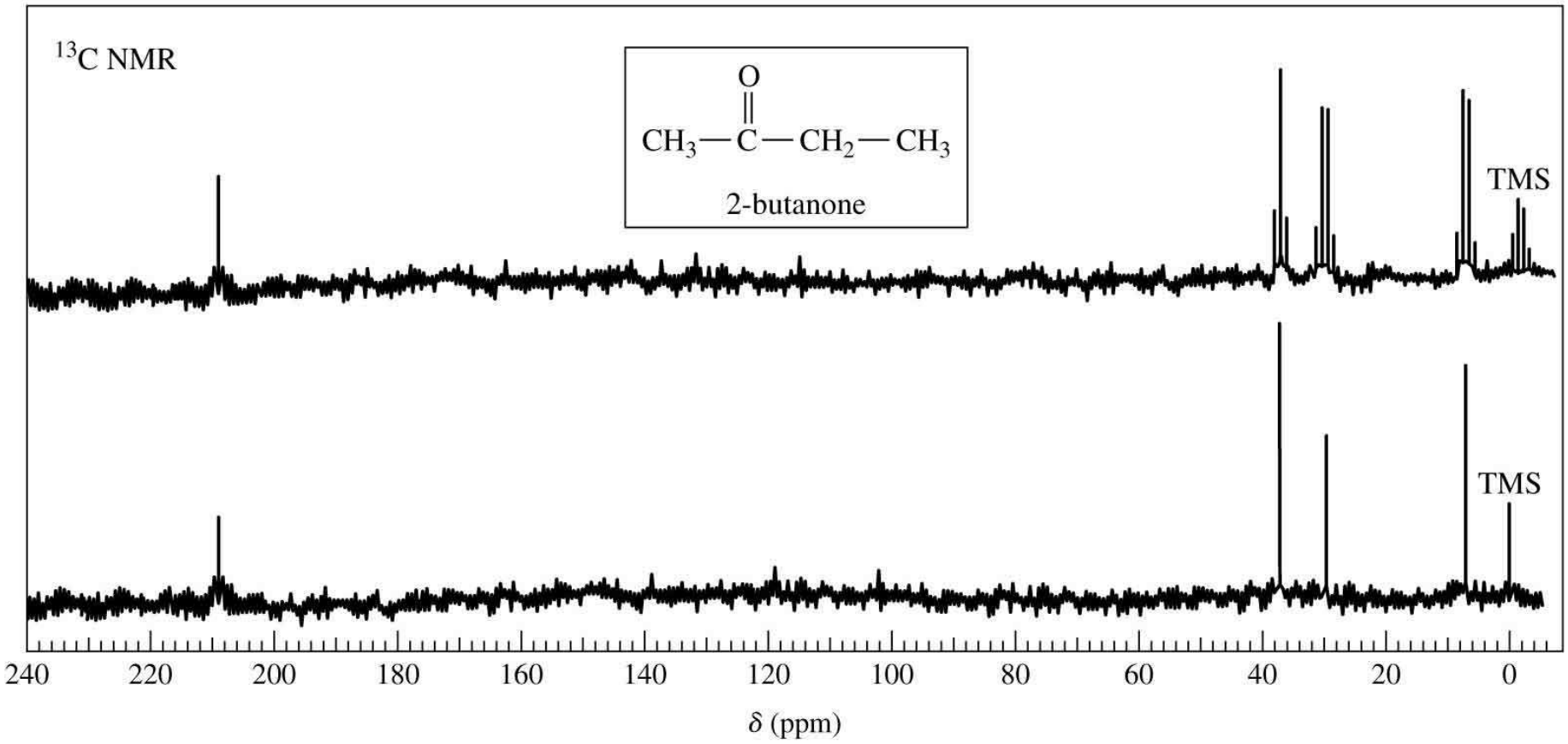
Interpreting ^{13}C NMR



- 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). – **Not always true.**
- The splitting pattern of off-resonance decoupled spectrum indicates the number of protons attached to the carbon. =>

Two ^{13}C NMR Spectra (coupled to hydrogen and decoupled)





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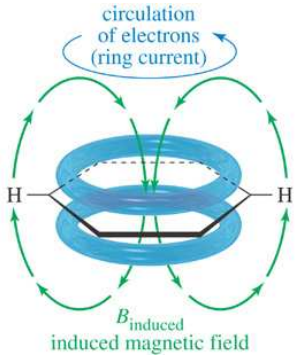
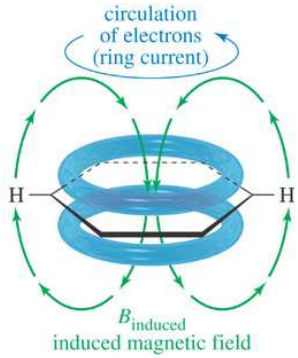
MRI

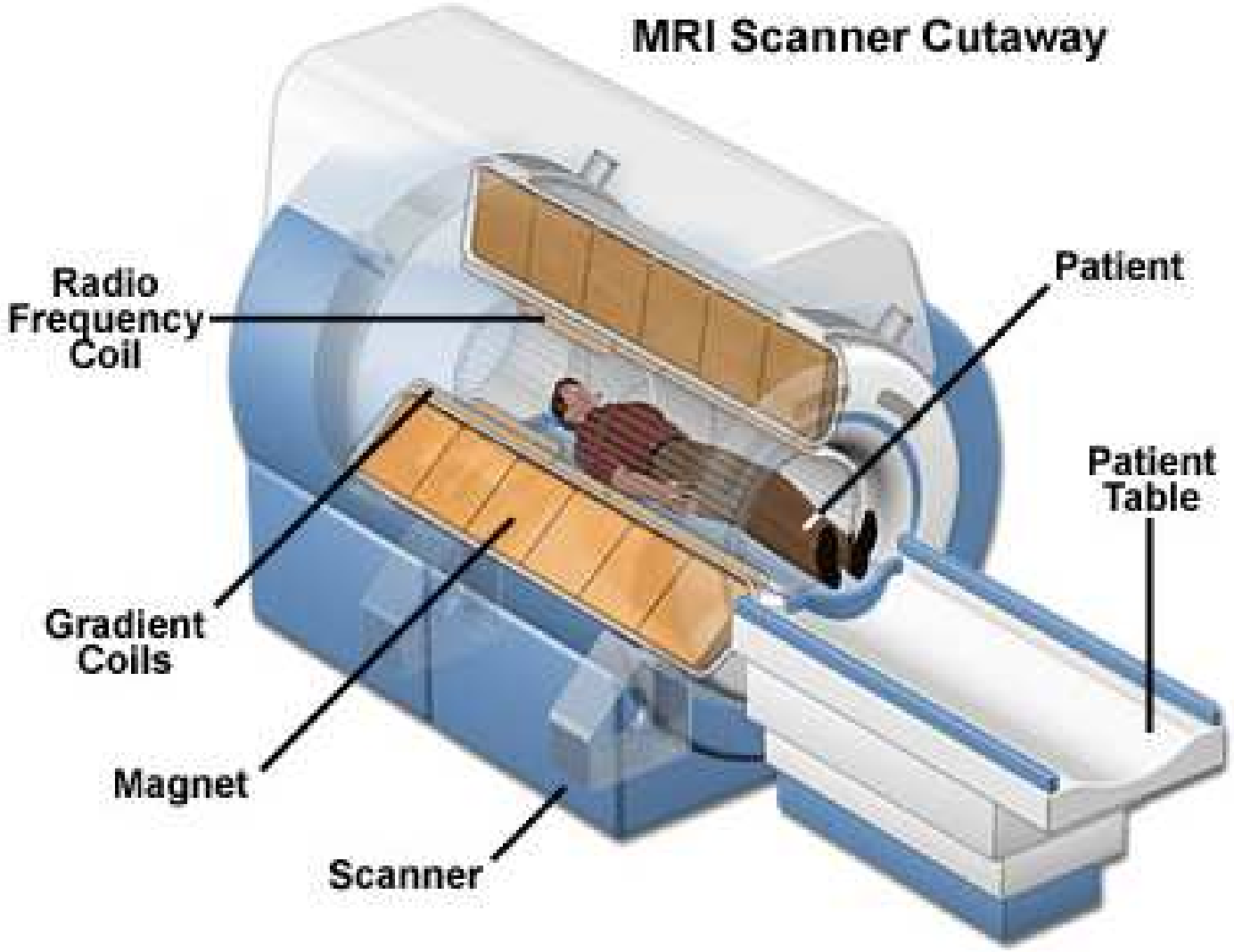


- Magnetic resonance imaging, noninvasive
- “Nuclear” was omitted because of public’s fear that it would be radioactive.
- Only protons in one plane can be in resonance at one time.
- Computer puts together “slices” to get 3D.
- Tumors readily detected.

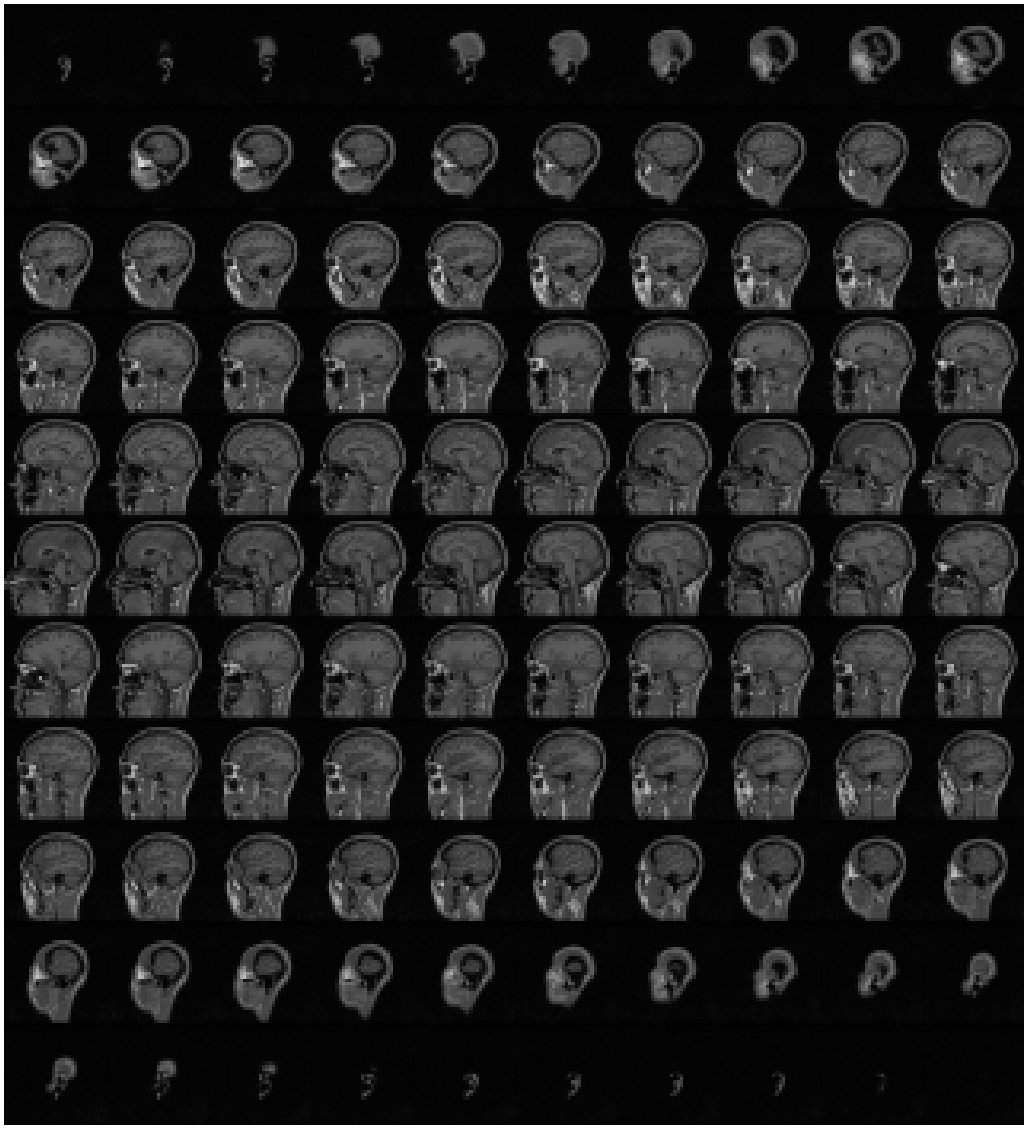
=>

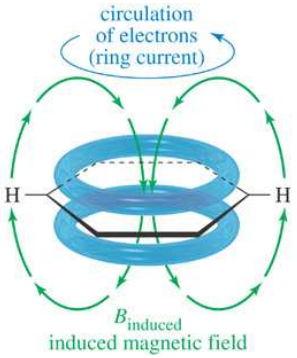
MRI

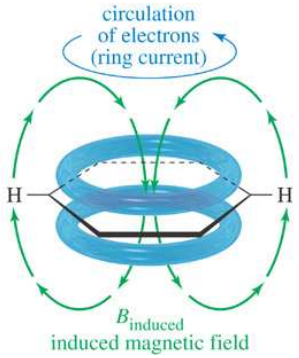

circulation
of electrons
(ring current)
H
H
$B_{induced}$
induced magnetic field


MRI Scanner Cutaway
Radio
Frequency
Coil
Patient
Patient
Table
Gradient
Coils
Magnet
Scanner

MRI




circulation
of electrons
(ring current)
H
H
B_{induced}
induced magnetic field



End of Chapter 13