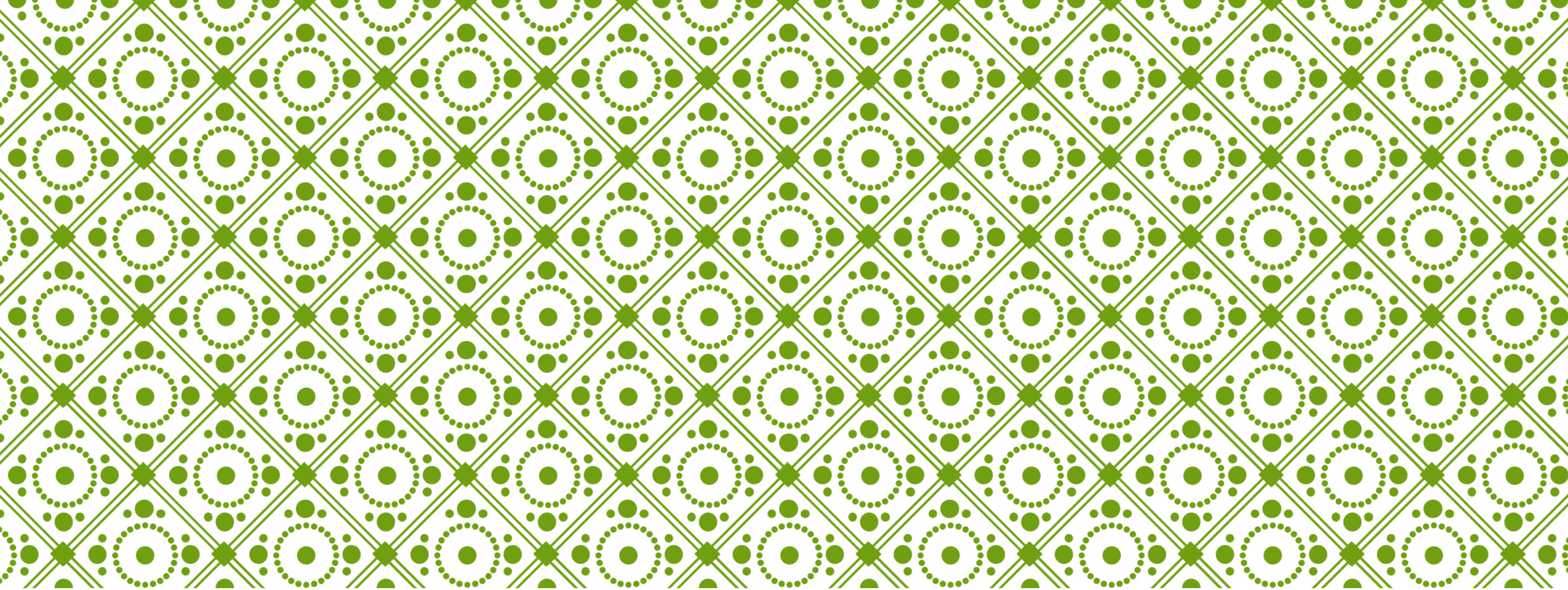


NMR SPECTROSCOPY: A BRIEF INTRODUCTION

Dr. Darshana Mehta
School of Studies in Chemistry and Biochemistry,
Vikram University, Ujjain – 456 010, Madhya Pradesh, India

Introduction to NMR Spectroscopy

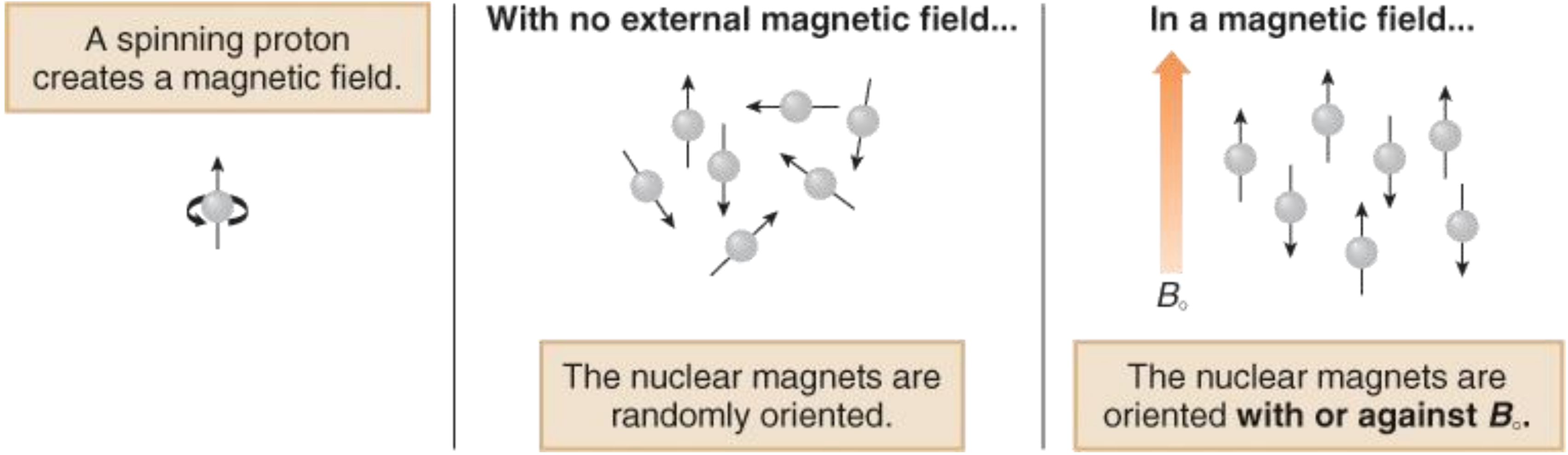
- **Nuclear magnetic resonance spectroscopy is a powerful analytical technique used to characterize organic molecules by identifying carbon-hydrogen frameworks within molecules.**

- **Two common types of NMR spectroscopy are used to characterize organic structure: ^{1}H NMR is used to determine the type and number of H atoms in a molecule; ^{13}C NMR is used to determine the type of carbon atoms in the molecule.**

- **The source of energy in NMR is radio waves which have long wavelengths, and thus low energy and frequency.**

- **When low-energy radio waves interact with a molecule, they can change the nuclear spins of some elements, including ^{1}H and ^{13}C.**

Introduction to NMR Spectroscopy



- When a charged particle such as a proton spins on its axis, it creates a magnetic field. Thus, the nucleus can be considered to be a tiny bar magnet.

- Normally, these tiny bar magnets are randomly oriented in space. However, in the presence of a magnetic field B_0, they are oriented with or against this applied field. More nuclei are oriented with the applied field because this arrangement is lower in energy.

- The energy difference between these two states is very small (<0.1 cal).

Introduction to NMR Spectroscopy

Nuclear spin

$$\mu = \hat{y} I h$$

μ - magnetic moment

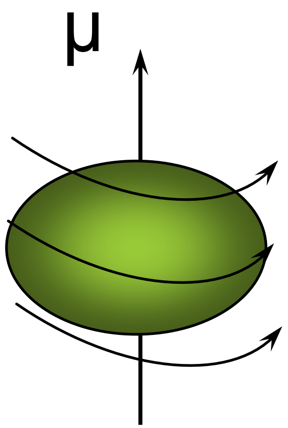
$\hat{y}$ - gyromagnetic ratio

I - spin quantum number

h - Planck’s constant

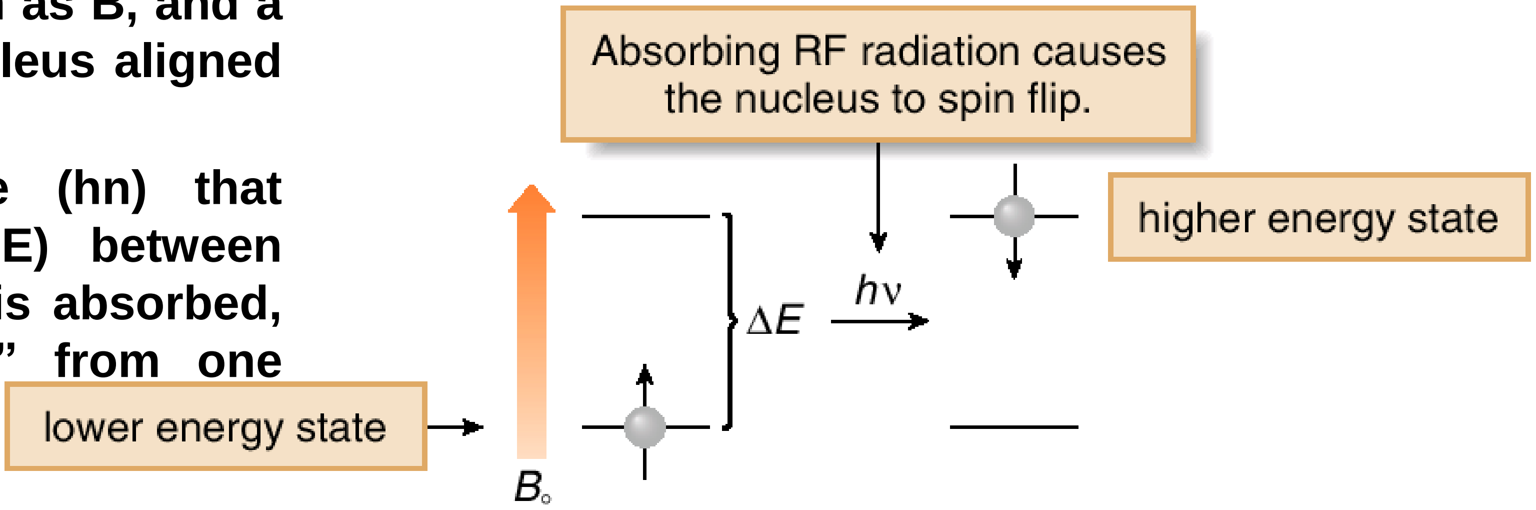
I is a property of the nucleus

Mass No.	Atomic No.	I
Odd	Even or odd	1/2, 3/2, 5/2,…
Even	Even	0
Even	Odd	1, 2, 3



Introduction to NMR Spectroscopy

- **In a magnetic field, there are now two energy states for a proton: a lower energy state with the nucleus aligned in the same direction as B, and a higher energy state in which the nucleus aligned against B.**
- **When an external energy source (hn) that matches the energy difference (DE) between these two states is applied, energy is absorbed, causing the nucleus to "spin flip" from one orientation to another.**


Absorbing RF radiation causes the nucleus to spin flip.

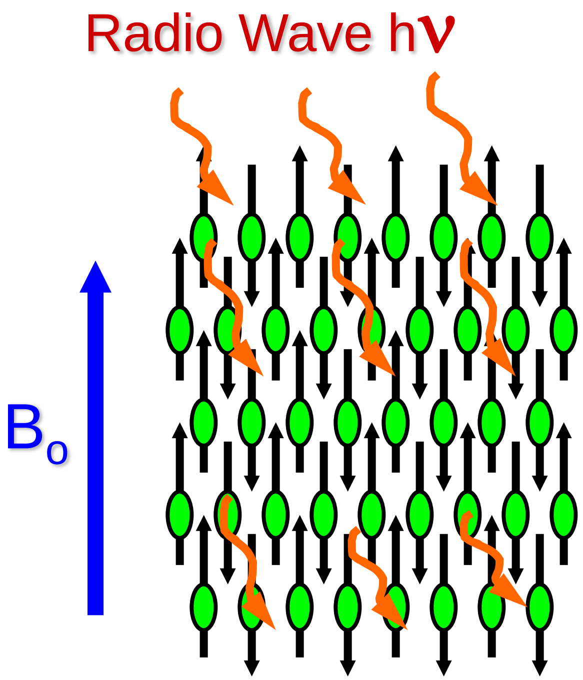
lower energy state

higher energy state

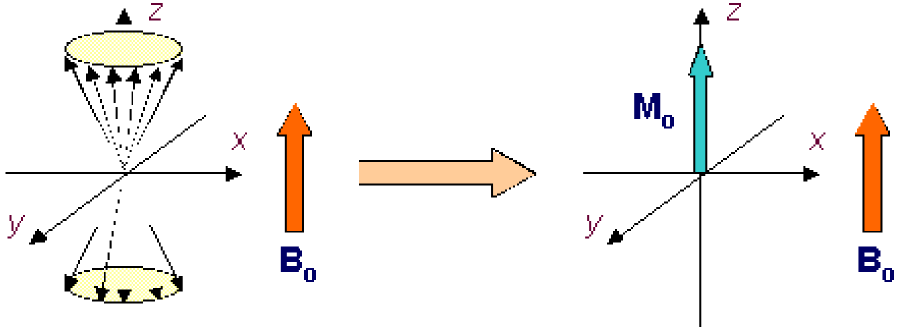
- **The energy difference between these two nuclear spin states corresponds to the low frequency RF region of the electromagnetic spectrum.**

- **Thus, two variables characterize NMR: an applied magnetic field B0, the strength of which is measured in tesla (T), and the frequency n of radiation used for resonance, measured in hertz (Hz), or megahertz (MHz)—(1 MHz = 10^6 Hz).**

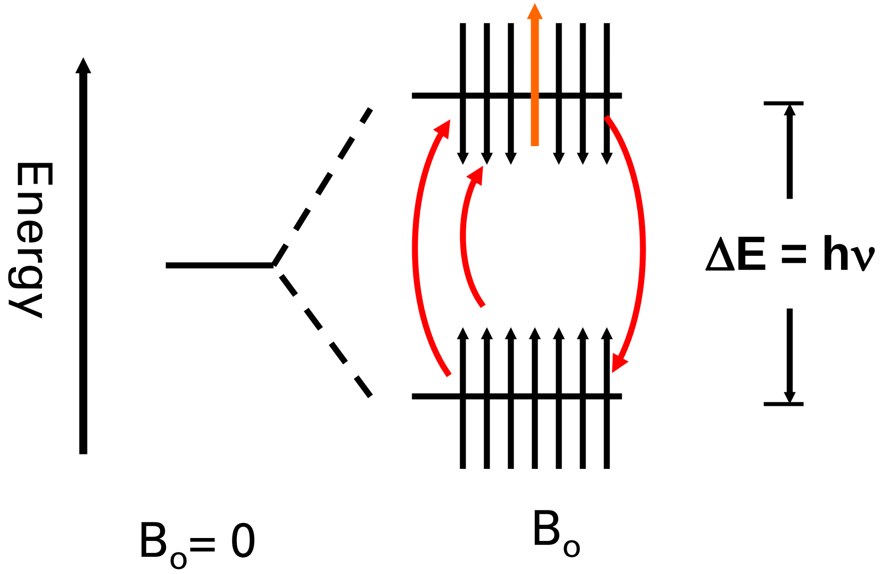
Introduction to NMR Spectroscopy



Classical view



Quantum mechanical view



Larmor Equation:

$$\nu = \gamma B_o / 2\pi$$

ν = Larmor frequency;

γ = nuclear gyric ratio

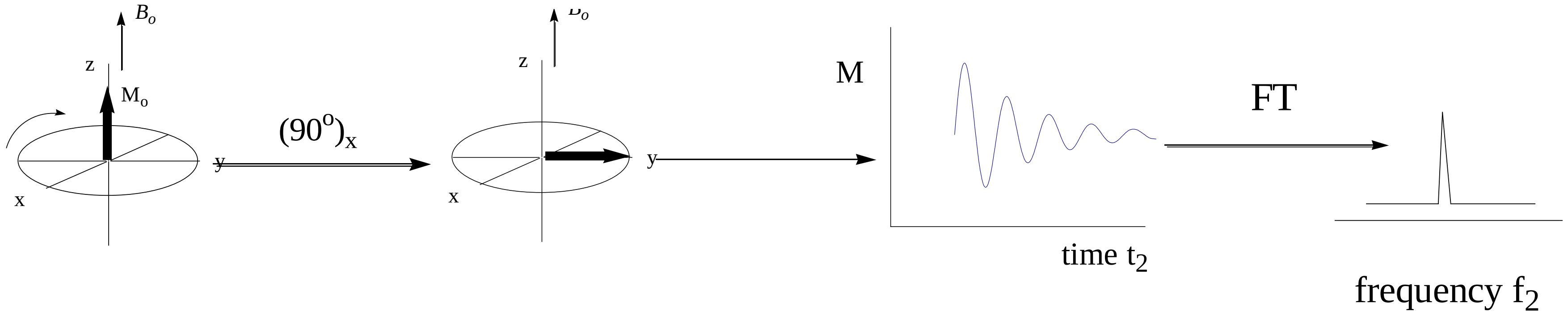
B_o = magnetic field strength (Telsla)

ONE-PULSE SEQUENCE

- *NMR pulse sequences* composed of a series of RF pulses, delays, gradient pulses and phases
- In a 1D NMR experiment, the FID acquisition time is the time domain (t_1)
- Multidimensional NMR experiments may also use multiple nuclei (^{2}D, ^{13}C,^{15}N) in addition to ^{1}H, but usually detect ^{1}H

$$F(\nu) \propto \int_{-\infty}^{\infty} f(t) e^{-i2\pi\nu t}\, dt$$

Fourier Transform is a mathematical procedure that transforms time domain data into frequency domain



Excess of spin population along the direction of applied magnetic field.

After 90^{o} pulse magnetization is tipped into the *xy* plane.

M=Magnetization which produces the FID. It decays as magnetization in *xy* plane diminishes after resonance

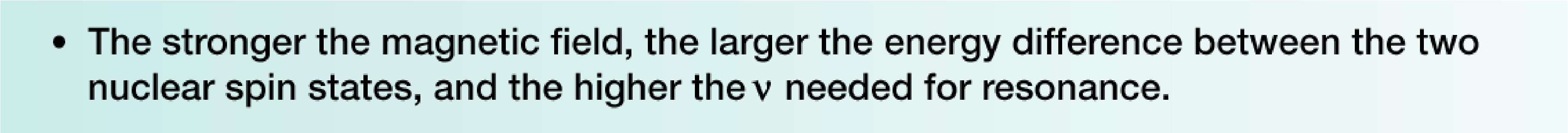
preparation

detection

Introduction to NMR Spectroscopy

- The frequency needed for resonance and the applied magnetic field strength are proportionally related:

$$\nu \propto B_o$$

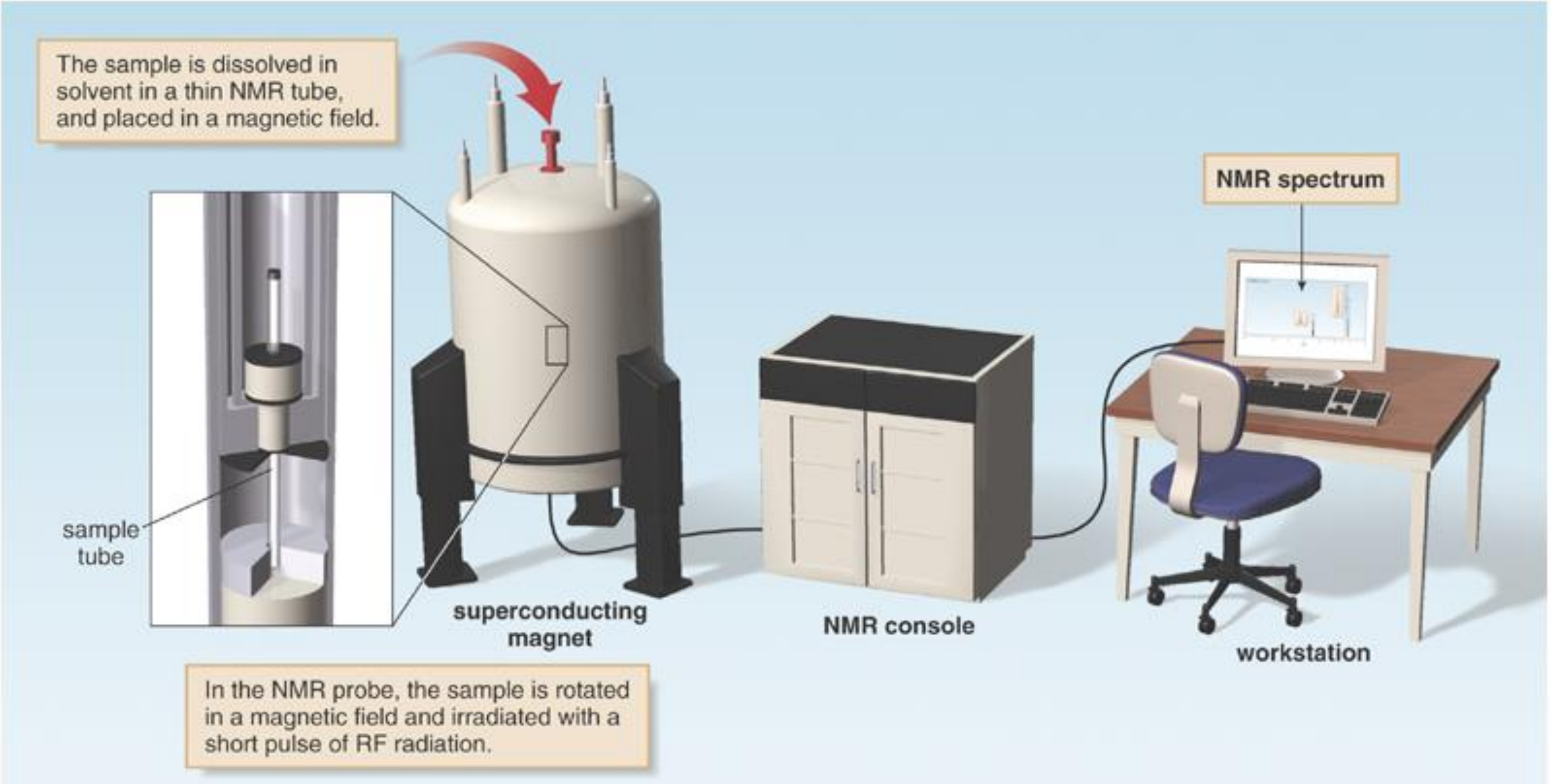


- The stronger the magnetic field, the larger the energy difference between the two nuclear spin states, and the higher the ν needed for resonance.

- NMR spectrometers are referred to as 300 MHz instruments, 500 MHz instruments, and so forth, depending on the frequency of the RF radiation used for resonance.

- These spectrometers use very powerful magnets to create a small but measurable energy difference between two possible spin states.

Introduction to NMR Spectroscopy


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.

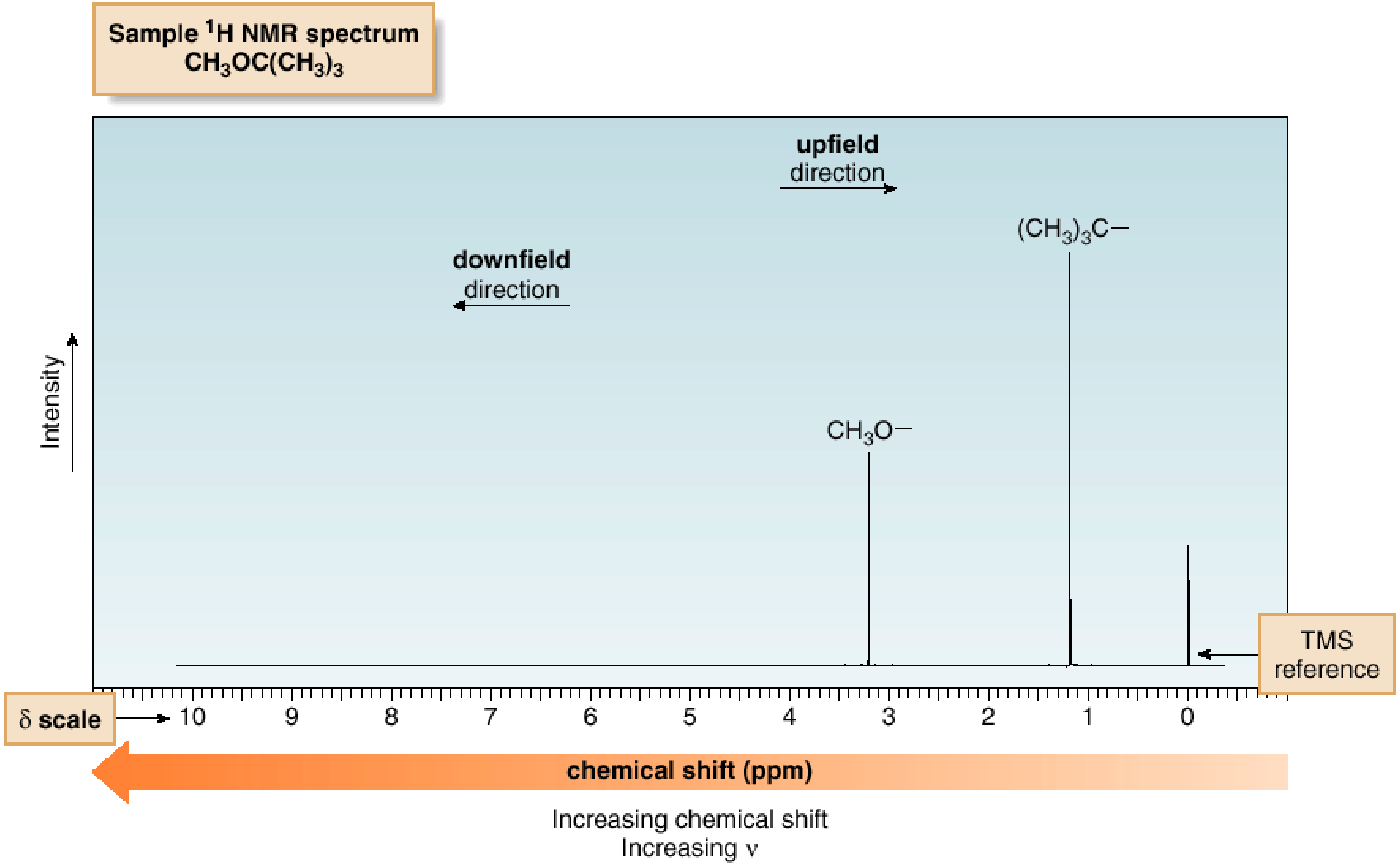
An NMR spectrometer. The sample is dissolved in a solvent, usually $CDCl_3$ (deuterochloroform), and placed in a magnetic field. A radiofrequency generator then irradiates the sample with a short pulse of radiation, causing resonance. When the nuclei fall back to their lower energy state, the detector 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.

Introduction to NMR Spectroscopy

- **Protons in different environments absorb at slightly different frequencies, so they are distinguishable by NMR.**
- **The frequency at which a particular proton absorbs is determined by its electronic environment.**
- **The size of the magnetic field generated by the electrons around a proton determines where it absorbs.**
- **Modern NMR spectrometers use a constant magnetic field strength B_0, and then a narrow range of frequencies is applied to achieve the resonance of all protons.**
- **Only nuclei that contain odd mass numbers (such as ^1H, ^{13}C, ^{19}F and ^{31}P) or odd atomic numbers (such as ^2H and ^{14}N) give rise to NMR signals.**

^{1}H NMR—The Spectrum

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

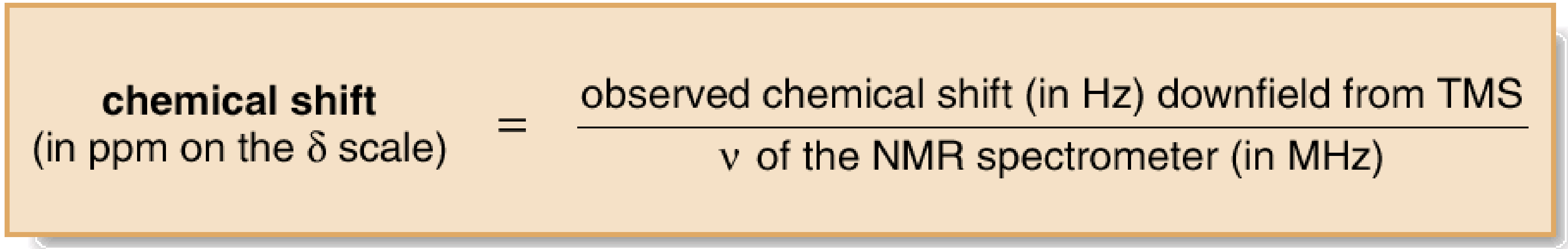


^{1}H NMR—The Spectrum

- NMR absorptions generally appear as sharp peaks.
- Increasing chemical shift is plotted from left to right.
- Most protons absorb between 0-10 ppm.
- The terms “upfield” and “downfield” describe the relative location of peaks. Upfield means to the right. Downfield means to the left.
- NMR absorptions are measured relative to the position of a reference peak at 0 ppm on the δ scale due to tetramethylsilane (TMS). TMS is a volatile inert compound that gives a single peak upfield from typical NMR absorptions.

^{1}H NMR—The Spectrum

- **The chemical shift of the *x* axis gives the position of an NMR signal, measured in ppm, according to the following equation:**

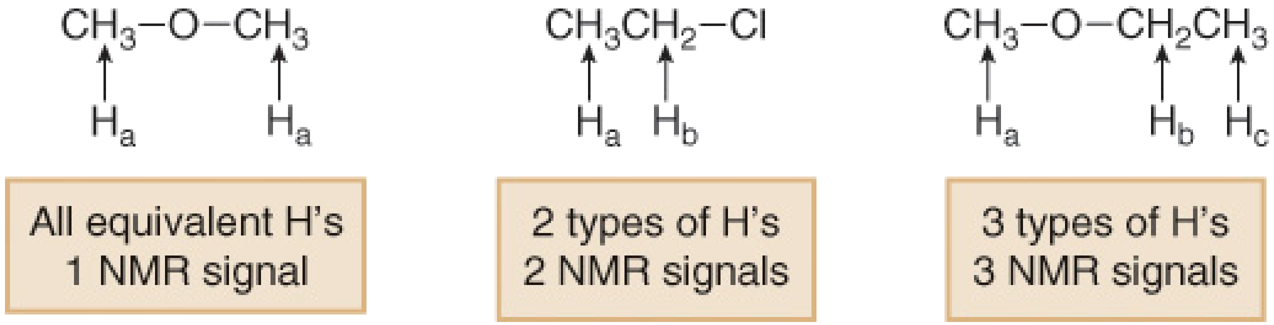


$$\begin{array}{c}\textbf{chemical shift}\\ \text{(in ppm on the } \delta \text{ scale)}\end{array} = \frac{\text{observed chemical shift (in Hz) downfield from TMS}}{\nu \text{ of the NMR spectrometer (in MHz)}}$$

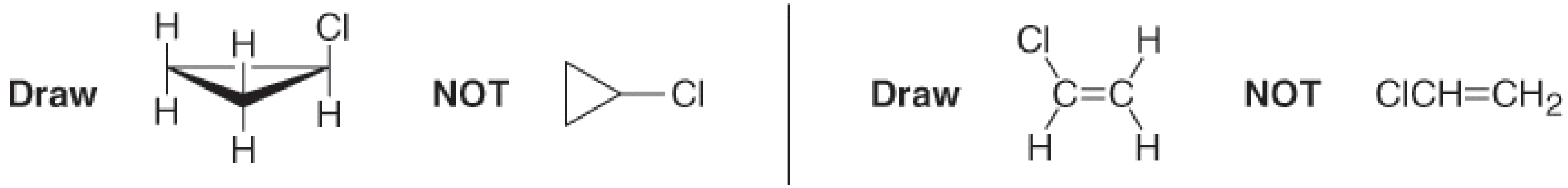
- **By reporting the NMR absorption as a fraction of the NMR operating frequency, we get units, ppm, that are independent of the spectrometer.**
- **Four different features of a ^{1}H NMR spectrum provide information about a compound's structure:**
  a. **Number of signals**
  b. **Position of signals**
  c. **Intensity of signals.**
  d. **Spin-spin splitting of signals.**

^{1}H NMR—Number of Signals

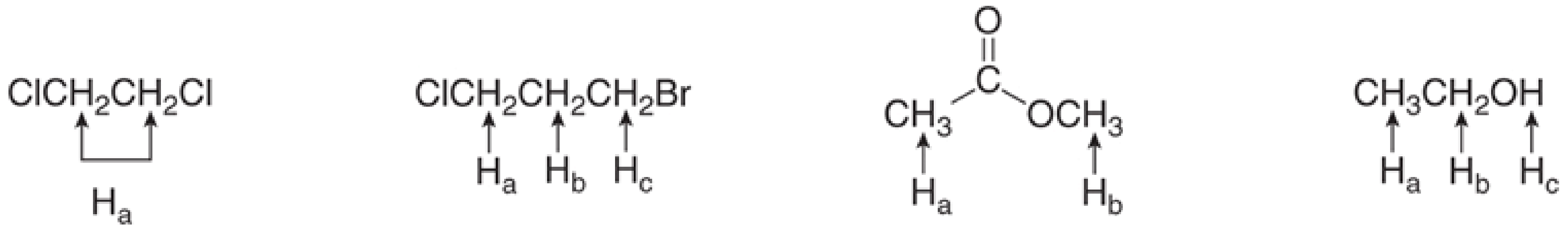
- **The number of NMR signals equals the number of different types of protons in a compound.**
- **Protons in different environments give different NMR signals.**
- **Equivalent protons give the same NMR signal.**



- **To determine equivalent protons in cycloalkanes and alkenes, always draw all bonds to hydrogen.**



^1H NMR—Number of Signals



1 type of H
1 NMR signal

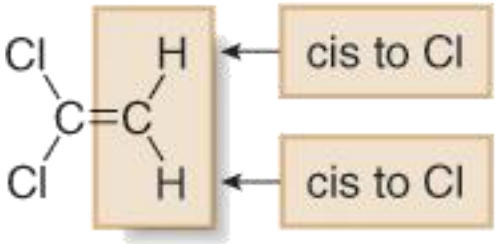
3 types of H's
3 NMR signals

2 types of H's
2 NMR signals

3 types of H's
3 NMR signals

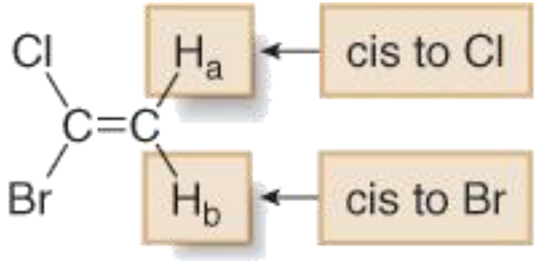
^{1}H NMR—Number of Signals

- In comparing two H atoms on a ring or double bond, two protons are equivalent only if they are cis (or trans) to the same groups.



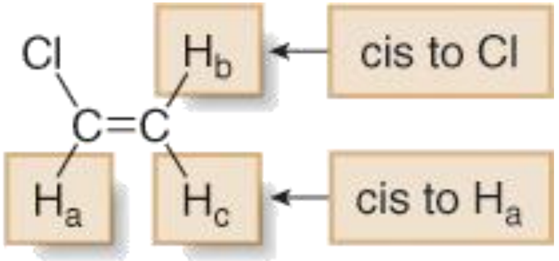
1,1-dichloroethylene

1 type of H
1 NMR signal



1-bromo-1-chloroethylene

2 types of H's
2 NMR signals

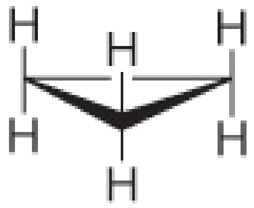


chloroethylene

3 types of H's
3 NMR signals

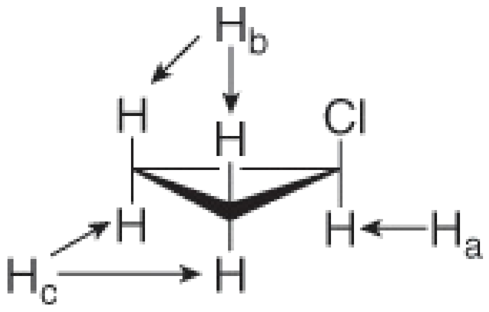
^{1}H NMR—Number of Signals

- **Proton equivalency in cycloalkanes can be determined similarly.**



cyclopropane

All H's are equivalent.
1 NMR signal

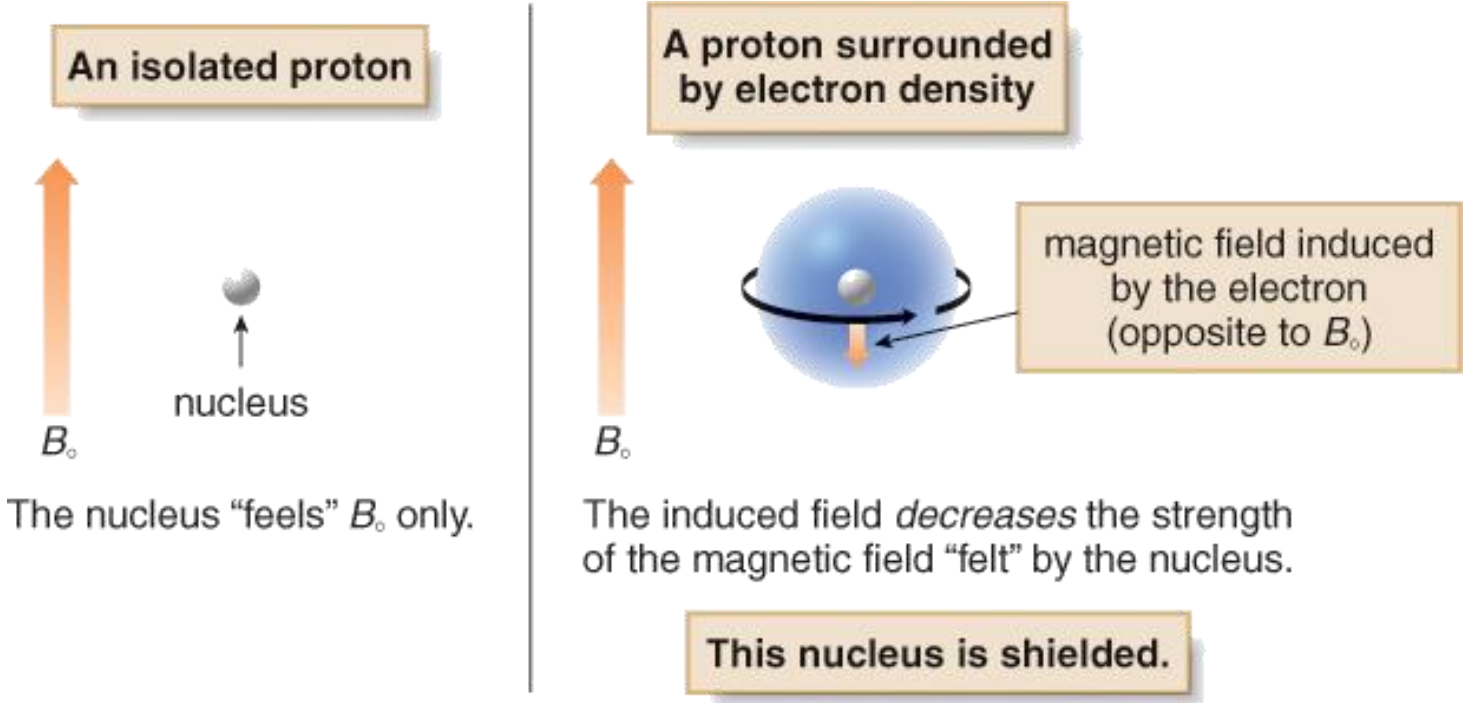


chlorocyclopropane

3 types of H's
3 NMR signals

^{1}H NMR—Position of Signals

- In the vicinity of the nucleus, the magnetic field generated by the circulating electron decreases the external magnetic field that the proton "feels".
- Since the electron experiences a lower magnetic field strength, it needs a lower frequency to achieve resonance. Lower frequency is to the right in an NMR spectrum, toward a lower chemical shift, so shielding shifts the absorption upfield.



^{1}H NMR—Position of Signals

- **The less shielded the nucleus becomes, the more of the applied magnetic field (B_0) it feels.**
- **This deshielded nucleus experiences a higher magnetic field strength, to it needs a higher frequency to achieve resonance.**
- **Higher frequency is to the left in an NMR spectrum, toward higher chemical shift—so deshielding shifts an absorption downfield.**
- **Protons near electronegative atoms are deshielded, so they absorb downfield.**

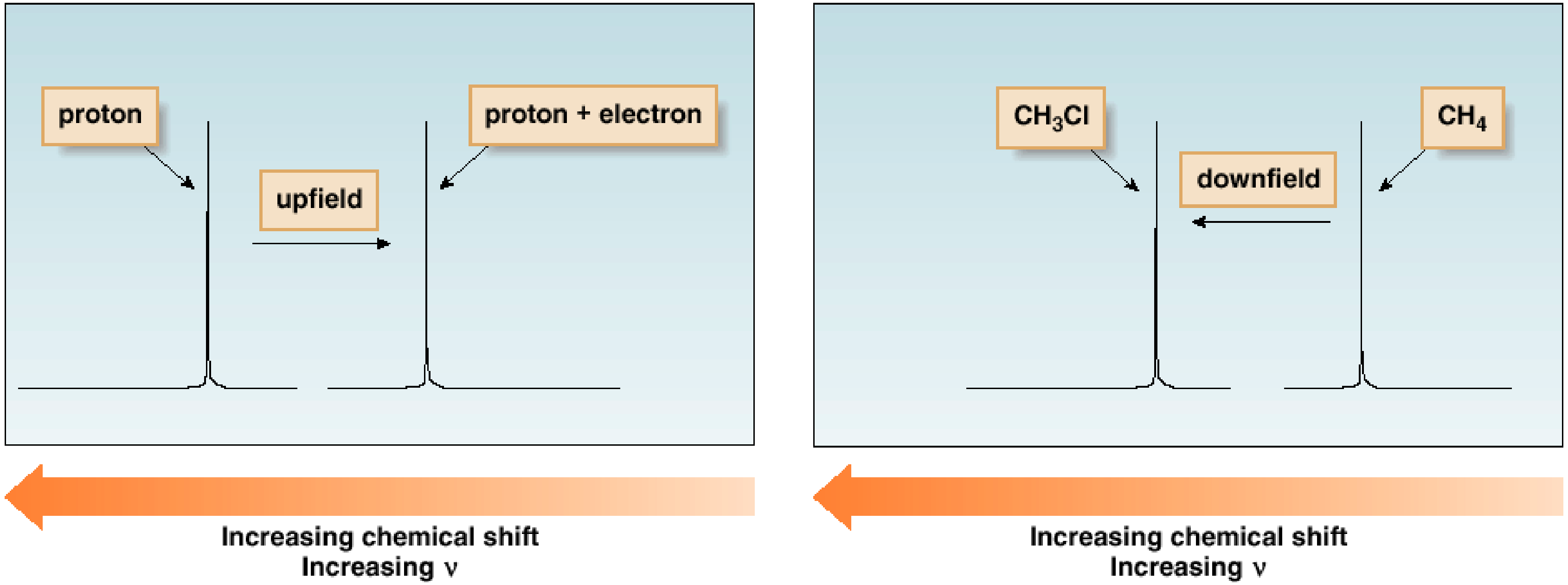
^1H NMR—Position of Signals

a. Shielding effects

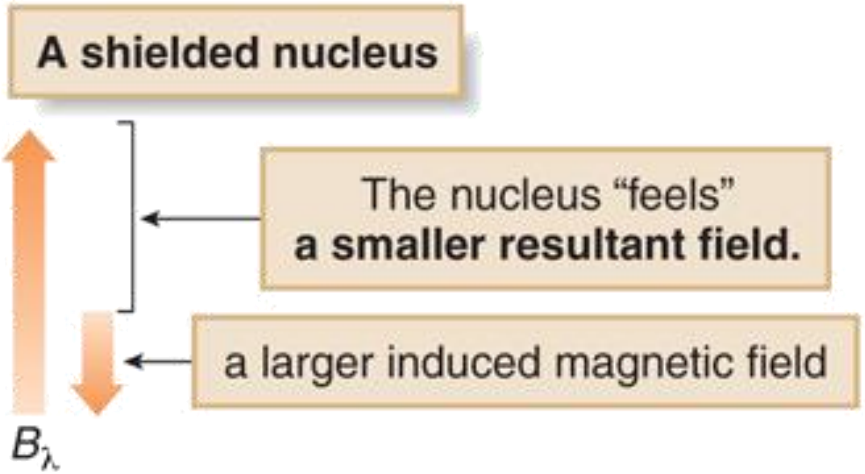
- An electron shields the nucleus.
- The absorption shifts *upfield*.

b. Deshielding effects

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



^{1}H NMR—Position of Signals



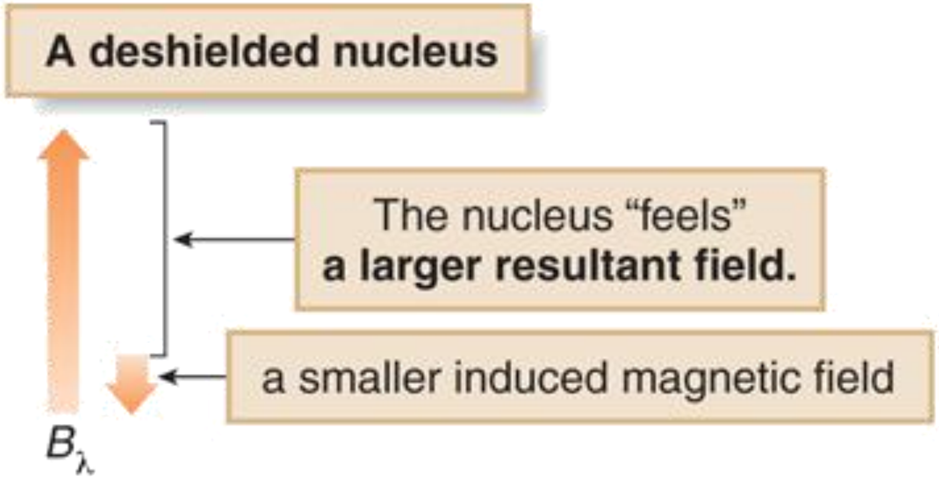
A shielded nucleus

The nucleus “feels”
a smaller resultant field.

a larger induced magnetic field

B_λ

- As the electron density around the nucleus increases, the nucleus feels a smaller resultant magnetic field, so a lower frequency is needed to achieve resonance.
- **The absorption shifts upfield.**



A deshielded nucleus

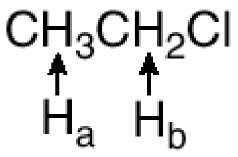
The nucleus “feels”
a larger resultant field.

a smaller induced magnetic field

B_λ

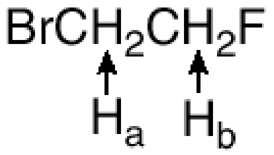
- As the electron density around the nucleus decreases, the nucleus feels a larger resultant magnetic field, so a higher frequency is needed to achieve resonance.
- **The absorption shifts downfield.**

^{1}H NMR—Position of Signals



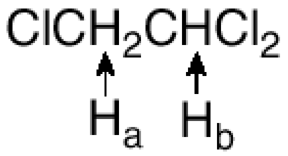
$\underset{\overset{\uparrow}{H_a}}{CH_3}\underset{\overset{\uparrow}{H_b}}{CH_2}Cl$

- The H_b protons are **deshielded** because they are closer to the electronegative Cl atom, so they absorb **downfield** from H_a.



$Br\underset{\overset{\uparrow}{H_a}}{CH_2}\underset{\overset{\uparrow}{H_b}}{CH_2}F$

- Because F is more electronegative than Br, the H_b protons are more **deshielded** than the H_a protons and absorb farther **downfield.**

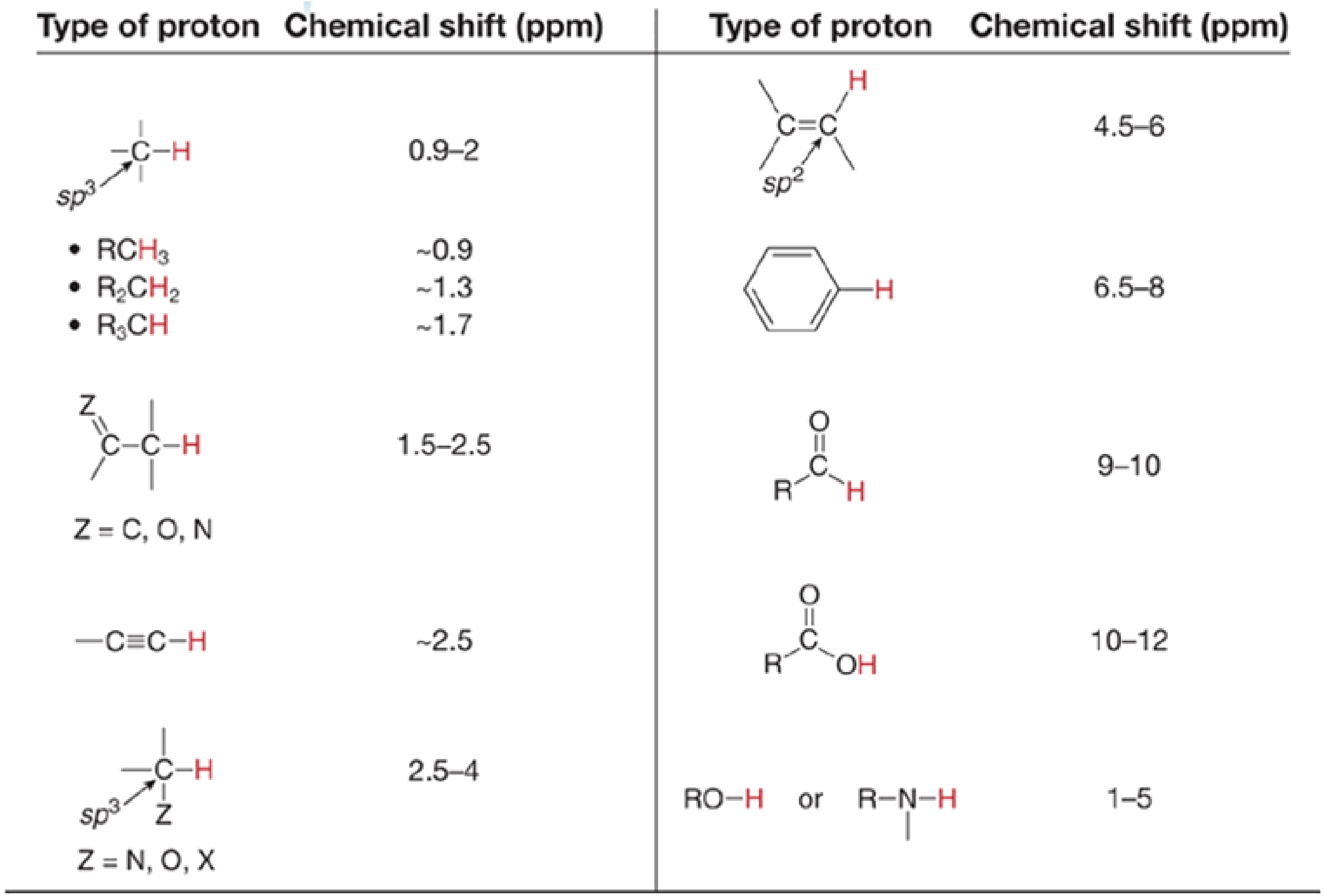


$Cl\underset{\overset{\uparrow}{H_a}}{CH_2}\underset{\overset{\uparrow}{H_b}}{CH}Cl_2$

- The larger number of electronegative Cl atoms (two versus one) **deshields** H_b more than H_a, so it absorbs **downfield** from H_a.

^1H NMR—Chemical Shift Values

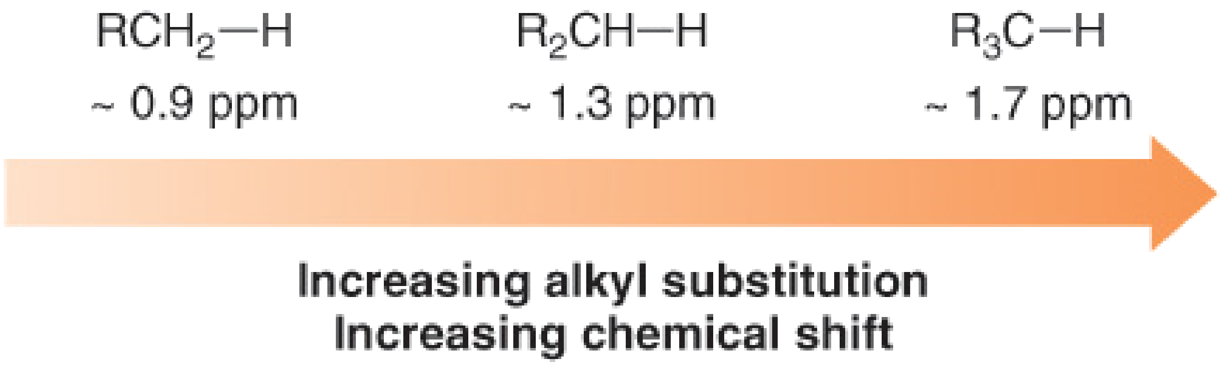
- **Protons in a given environment absorb in a predictable region in an NMR spectrum.**



Type of proton	Chemical shift (ppm)	Type of proton	Chemical shift (ppm)
$-C-H$ sp^3	0.9–2	$C=C-H$ sp^2	4.5–6
• RCH_3 • R_2CH_2 • R_3CH	~0.9 ~1.3 ~1.7	C_6H_5-H	6.5–8
$Z=C-C-H$ Z = C, O, N	1.5–2.5	$RC(=O)H$	9–10
$-C\equiv C-H$	~2.5	$RC(=O)OH$	10–12
$Z-C-H$ sp^3 Z = N, O, X	2.5–4	$RO-H$ or $R-N-H$	1–5

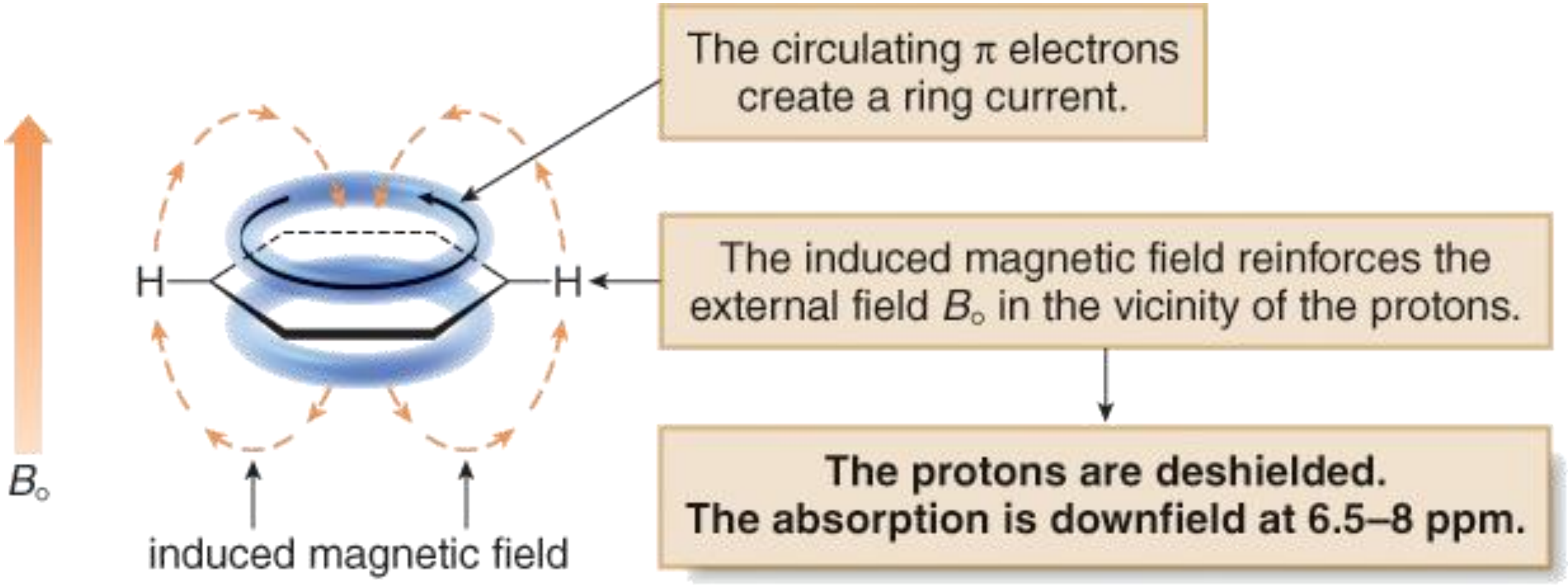
^{1}H NMR—Chemical Shift Values

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



^{1}H NMR—Chemical Shift Values

- 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. Thus they are deshielded and absorb downfield.



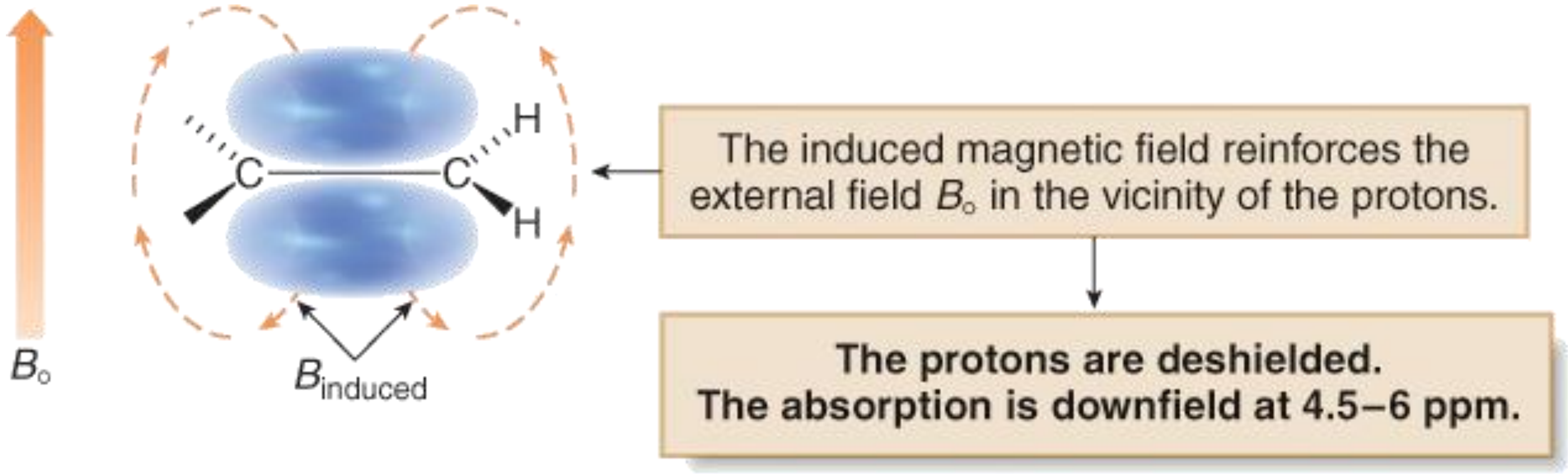
The circulating π electrons create a ring current.

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

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

^{1}H NMR—Chemical Shift Values

- In a magnetic field, the loosely held π electrons of the double bond create a magnetic field that reinforces the applied field in the vicinity of the protons.
- The protons now feel a stronger magnetic field, and require a higher frequency for resonance. Thus the protons are deshielded and the absorption is downfield.

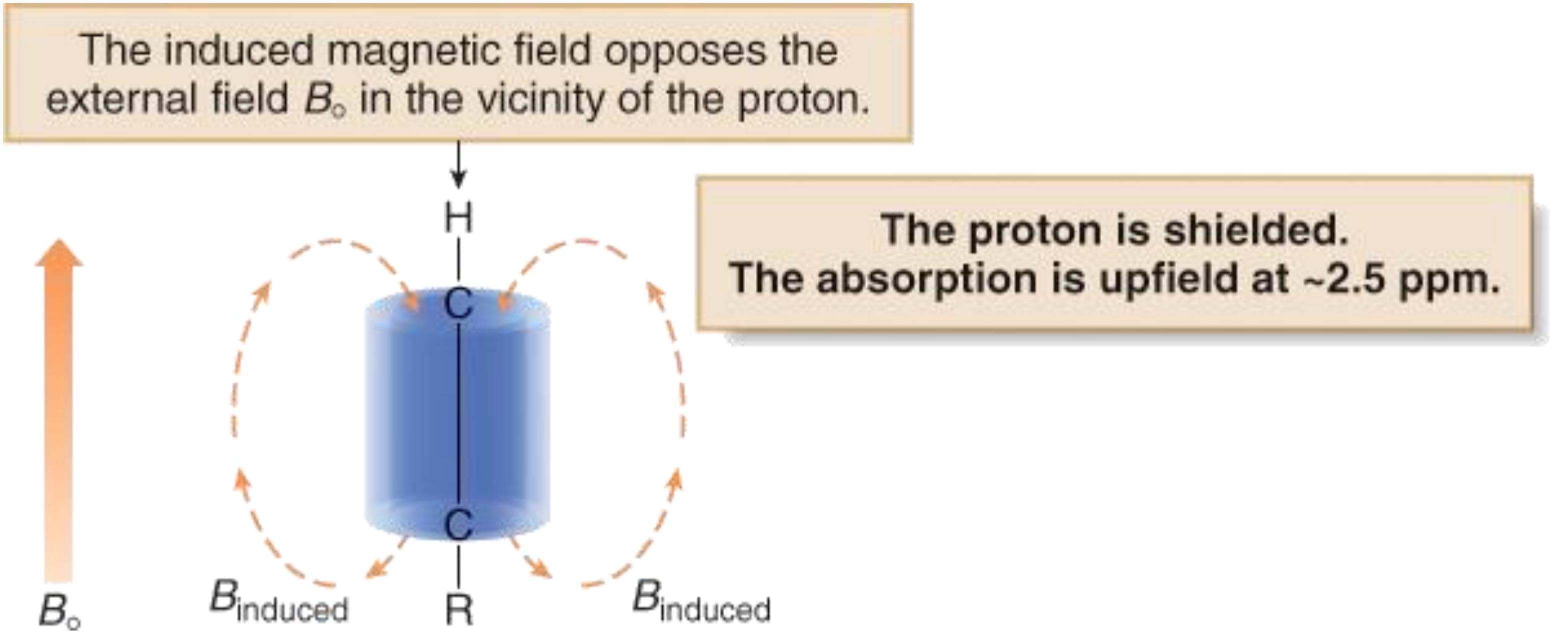


The induced magnetic field reinforces the external field B_o in the vicinity of the protons.

The protons are deshielded.
The absorption is downfield at 4.5–6 ppm.

^{1}H NMR—Chemical Shift Values

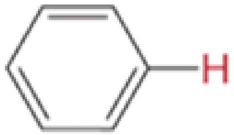
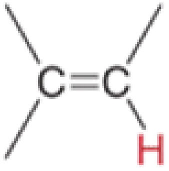
- In a magnetic field, the π electrons of a carbon-carbon triple bond are induced to circulate, but in this case the induced magnetic field opposes the applied magnetic field (B_0).
- Thus, the proton feels a weaker magnetic field, so a lower frequency is needed for resonance. The nucleus is shielded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



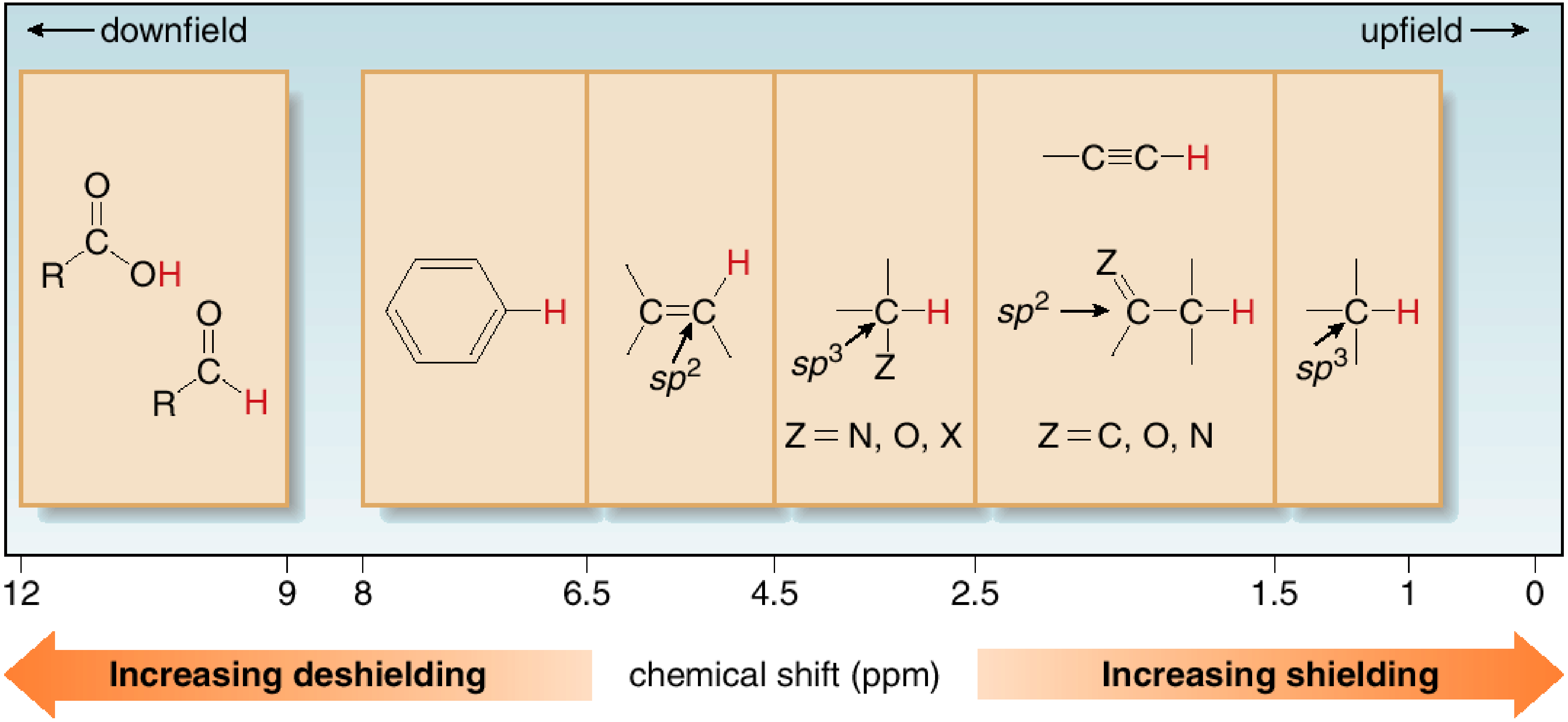
The induced magnetic field opposes the external field B_o in the vicinity of the proton.

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

^{1}H NMR—Chemical Shift Values

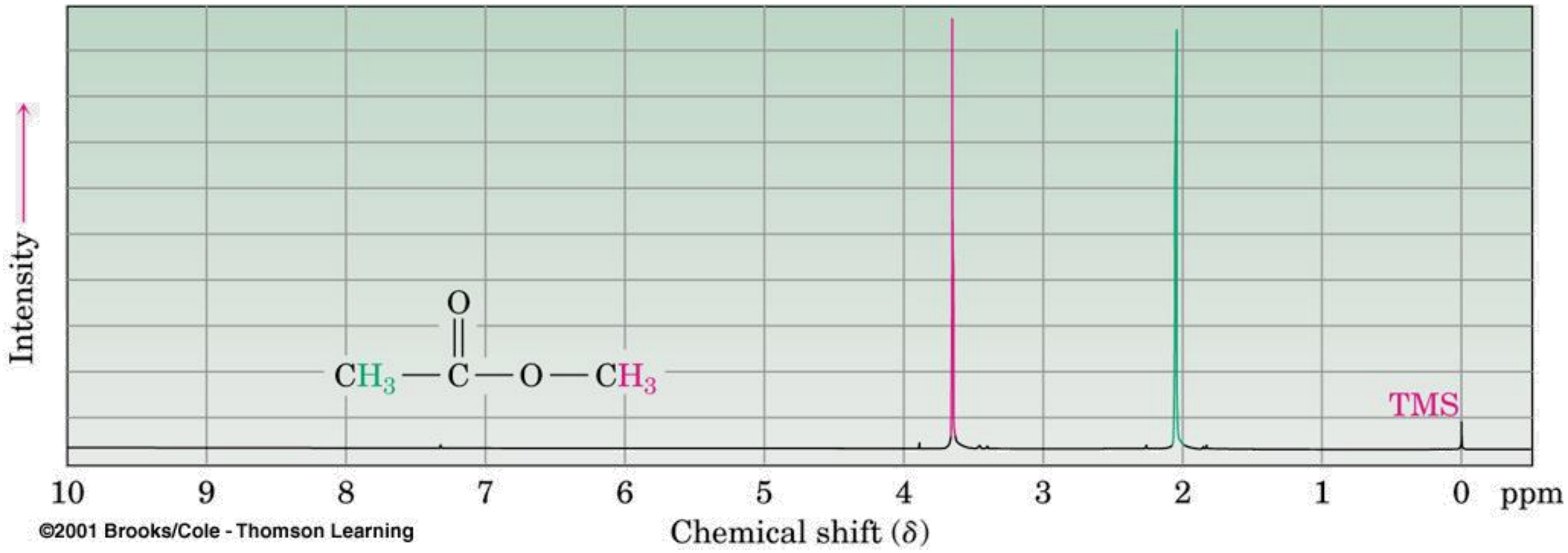
Proton type	**Effect**	**Chemical shift (ppm)**
	highly deshielded	6.5–8
	deshielded	4.5–6
$-C\equiv C-H$	shielded	~2.5

^{1}H NMR—Chemical Shift Values



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

^{1}H NMR OF METHYL ACETATE



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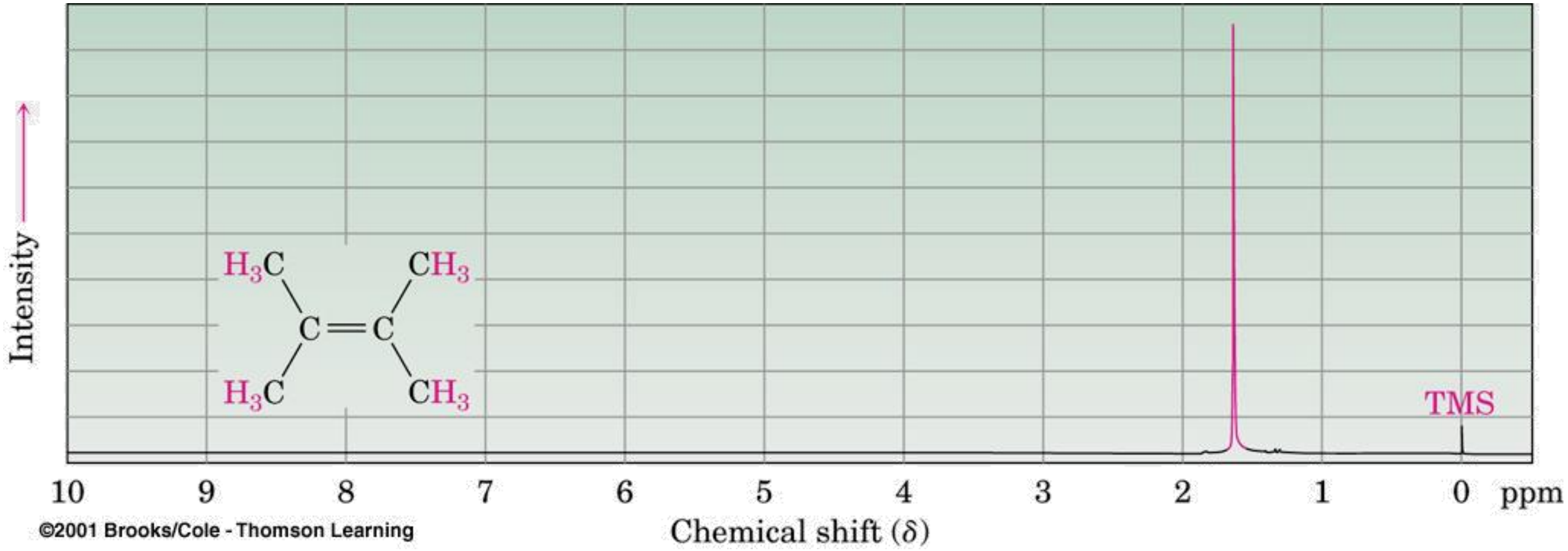
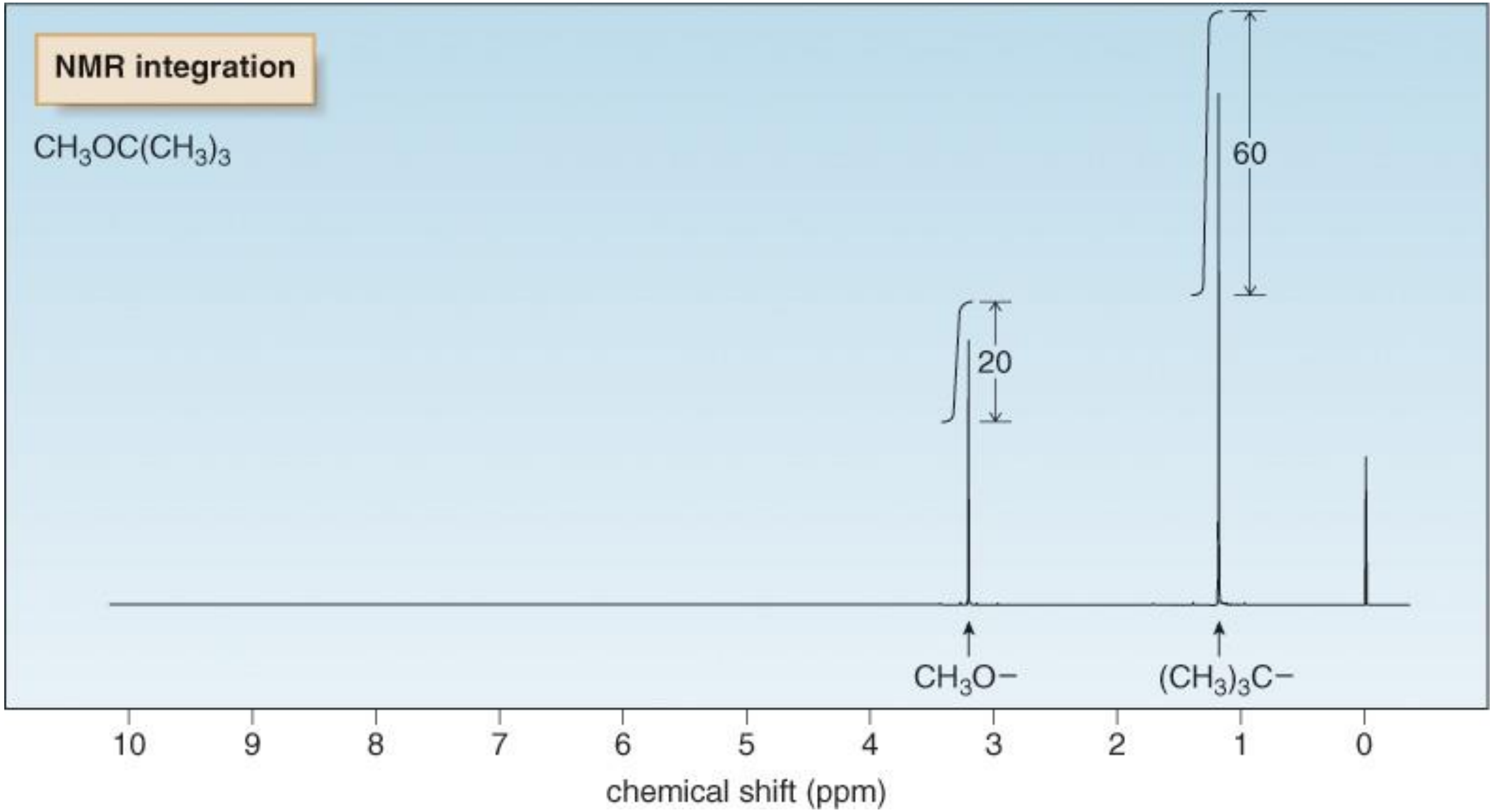
2,3-DIMETHYL-2-BUTENE



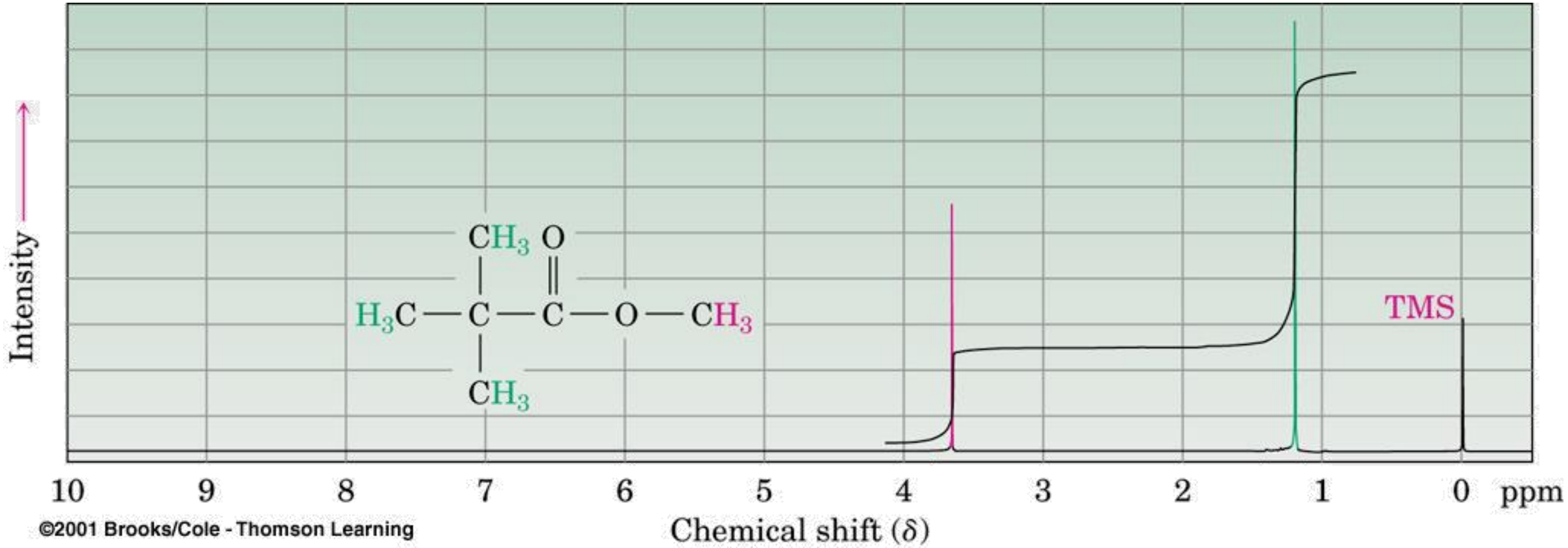
^{1}H NMR—Intensity of Signals

- The area under an NMR signal is proportional to the number of absorbing protons.
- An NMR spectrometer automatically integrates the area under the peaks, and prints out a stepped curve (integral) on the spectrum.
- The height of each step is proportional to the area under the peak, which in turn is proportional to the number of absorbing protons.
- 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.

^{1}H NMR—Intensity of Signals

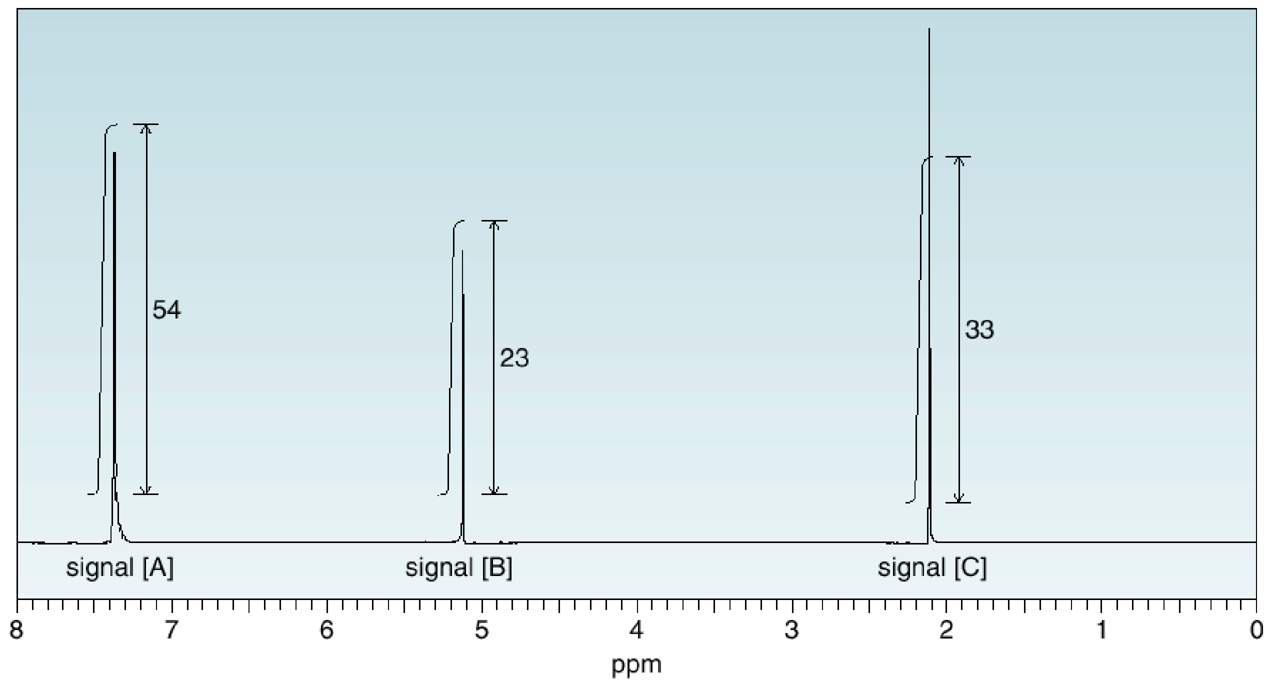


METHYL A,A-DIMETHYLPROPIONATE



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?



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

- Total number of integration units: 54 + 23 + 33 = 110 units
- Total number of protons = 10
- Divide: 110 units/10 protons = **11 units per proton**

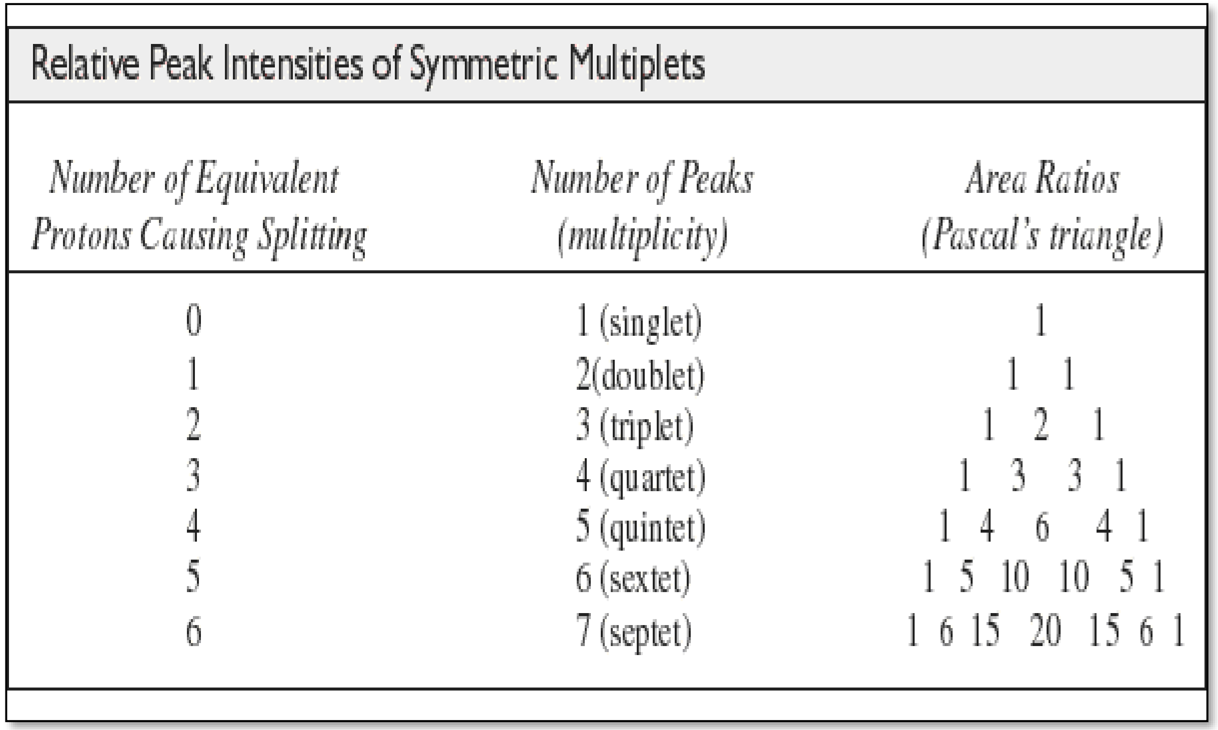
Step [2] Determine the number of protons giving rise to each signal.

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

	Signal [A]:	Signal [B]:	Signal [C]:
Answer:	$\frac{54}{11} = 4.9 \approx$ **5 H**	$\frac{23}{11} = 2.1 \approx$ **2 H**	$\frac{33}{11} =$ **3 H**

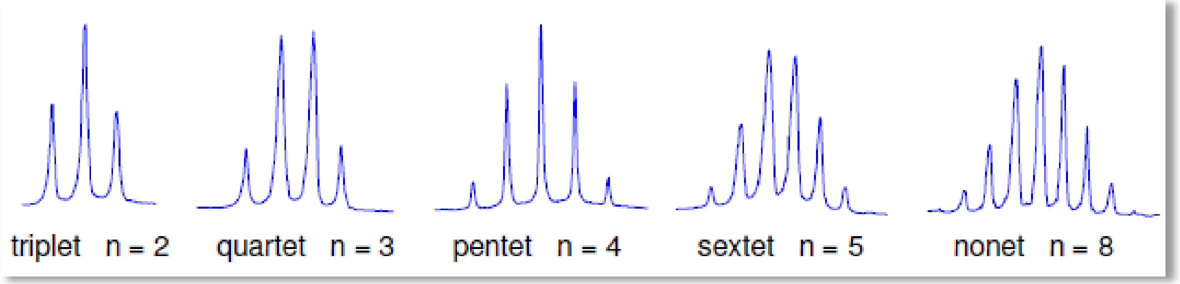
SPIN-SPIN SPLITTING IN ^{1}H NMR SPECTRA

- Peaks are often split into multiple peaks due to ***magnetic interactions*** between nonequivalent protons on adjacent carbons, The process is called **spin-spin splitting**
- **Indirect spin-spin coupling** (indirect dipole-dipole interaction, J-coupling) - a magnetic interaction between individual nuclear spins transmitted by the bonding electrons through which the nuclear spins are indirectly connected.
- The splitting is into one more peak than the number of H’s on the adjacent carbon(s), This is the **“n+1 rule”**
- The relative intensities are in proportion of a binomial distribution given by **Pascal’s Triangle**
- The set of peaks is a **multiplet** (2 = doublet, 3 = triplet, 4=quartet, 5=pentet, 6=hextet, 7=heptet…..)



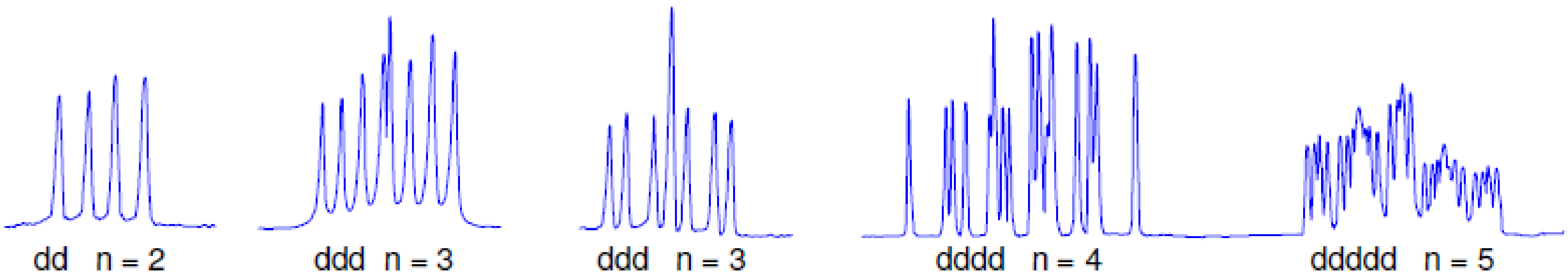
Relative Peak Intensities of Symmetric Multiplets

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



SPIN-SPIN SPLITTING IN ^{1}H NMR SPECTRA

- ❖ If all couplings are different, then the number of peaks is 2^n for ^{1}H, and the intensities are 1:1:1: . . .. Thus a proton coupled to two others by different couplings gives a dd (doublet of doublets).
- ❖ This pattern is never called a quartet. As the number of couplings gets larger, accidental superpositions of lines will sometimes occur, so that the 1:1:1... intensity ratio no longer applies.



SPIN-SPIN SPLITTING IN ^{1}H NMR SPECTRA

- **There are two distinct types of magnetic interaction (coupling) between nuclei (A and X) with a non-zero spin:**
  - **The direct interaction (dipole-dipole coupling: D)**
  - **The indirect or scalar coupling (spin-spin splitting: J)**

- **The direct interaction is about 1000 times as large as the scalar coupling (e.g. at 2 Å distance H-H dipolar coupling is ca 30,000 Hz).**

- **These direct couplings make the observation of high-resolution NMR spectra in solids and very viscous liquids difficult, and make NMR spectra in liquid crystals (where molecules are partially oriented, and the dipolar coupling is only partially averaged) very complex.**

- **In mobile isotropic liquids the random motion of molecules completely averages the dipolar coupling, so no direct effects are seen.**

SPIN-SPIN SPLITTING IN ^{1}H NMR SPECTRA

- The scalar coupling *J* is a through-bond interaction, in which the spin of one nucleus perturbs (polarizes) the spins of the intervening electrons, and the energy levels of neighboring magnetic nuclei are in turn perturbed by the polarized electrons.
- This leads to a lowering of the energy of the neighboring nucleus when the perturbing nucleus has one spin, and a raising of the energy when it has the other spin.
- The J coupling (always reported in Hz) is field-independent (i.e. *J* is constant at different external magnetic field strength), and is mutual (i.e. $J_{AX} = J_{XA}$).
- Because the effect is usually transmitted through the bonding electrons, the magnitude of *J* falls off rapidly as the number of intervening bonds increases.
- Coupling over one (^1J), two (^2J) and three (^3J) bonds usually dominates the fine structure of NMR spectra, but coupling across four (^4J) and five (^5J) bonds is often seen, especially through π bonds (double and triple bonds, aromatic carbons).

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

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

- ❖ Let us consider how the doublet due to the CH_2 group on $BrCH_2CHBr_2$ occurs:

- ❖ When placed in an applied field, (B_0), the adjacent proton ($CHBr_2$) can be aligned with (↑) or against (↓) B_0. The likelihood of either case is about 50% (i.e., 1,000,006↑ vs 1,000,000↓).

- ❖ Thus, the absorbing CH_2 protons feel two slightly different magnetic fields—one slightly larger than B_0, and one slightly smaller than B_0.

- ❖ Since the absorbing protons feel two different magnetic fields, they absorb at two different frequencies in the NMR spectrum, thus splitting a single absorption into a doublet, where the two peaks of the doublet have ***equal*** intensity.