Nuclear Magnetic Resonance
H-NMR
Part 1
Introduction to NMR, Instrumentation, Sample Prep, Chemical Shift

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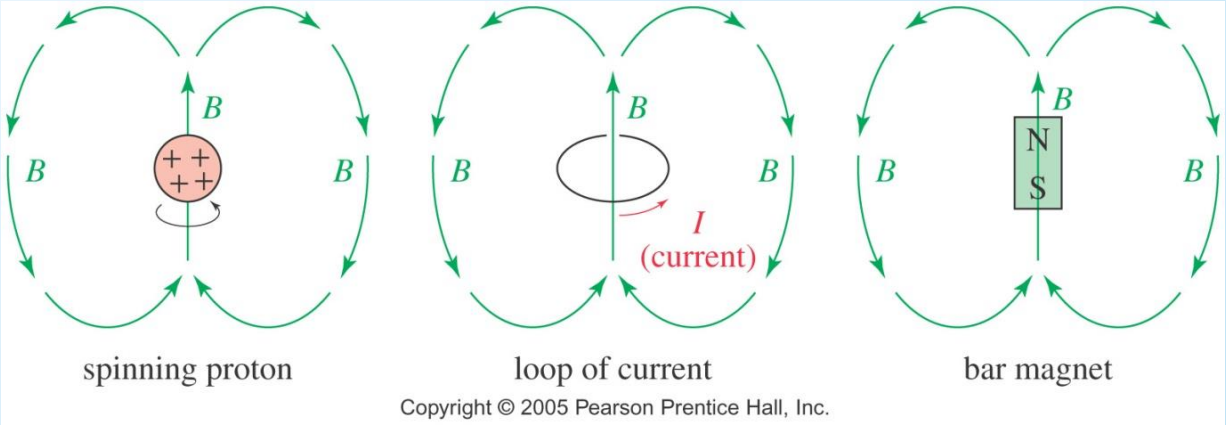
Introduction

- NMR is the most powerful tool available for organic structure determination.
- It is used to study a wide variety of nuclei:
  $^{1}H, ^{13}C, ^{15}N, ^{19}F, ^{31}P$

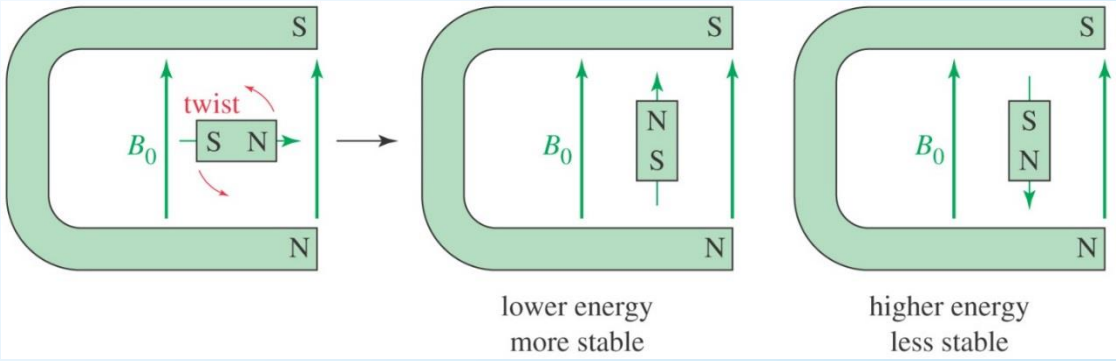
Nuclear Spin

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



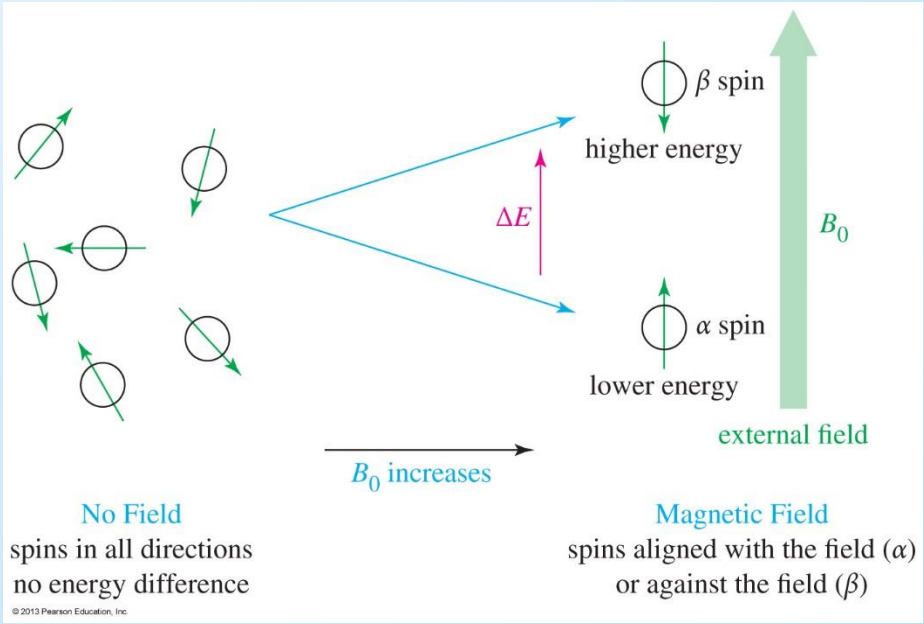
External Magnetic Field

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



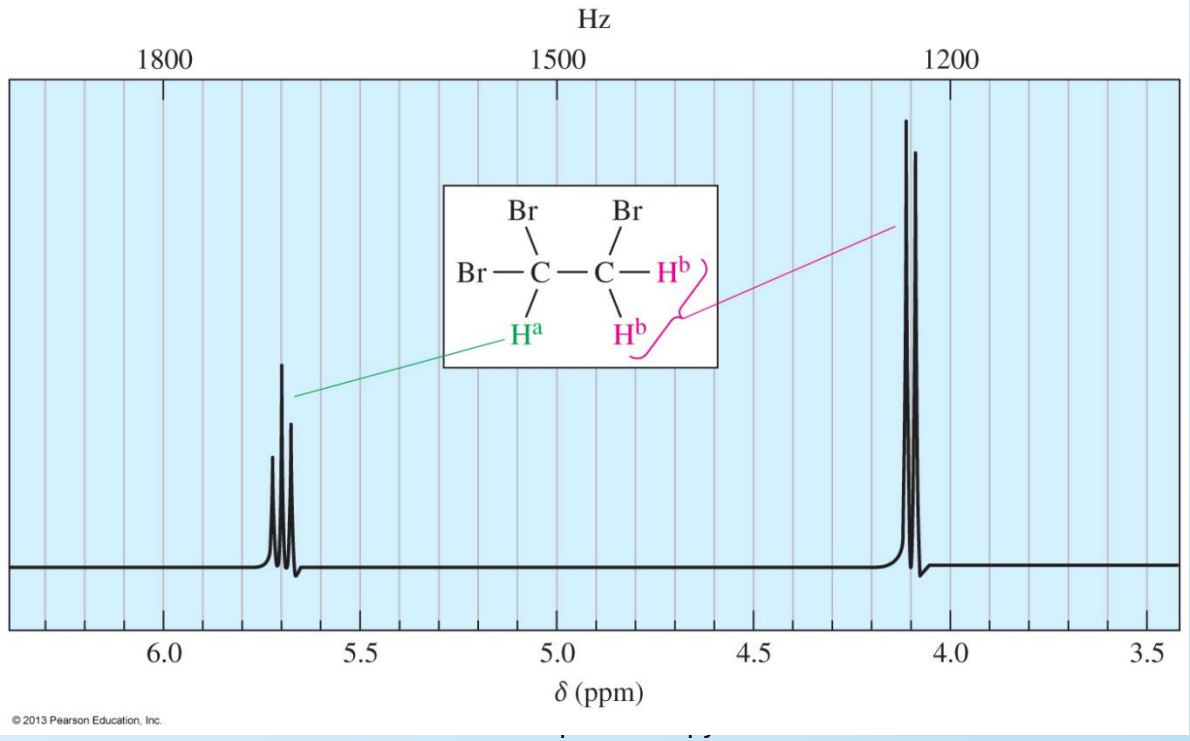
Two Energy States

- 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.



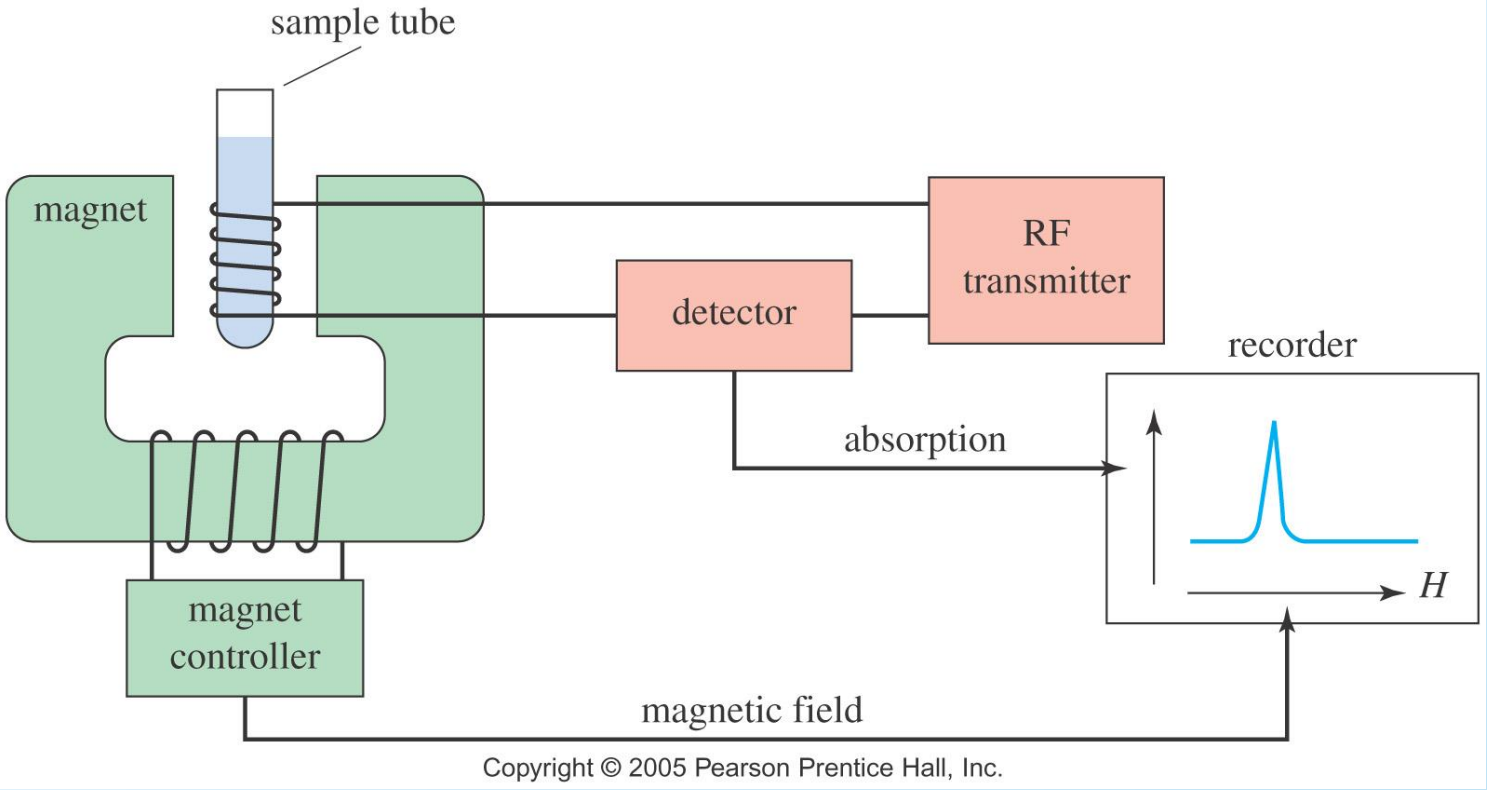
NMR Spectrum

- The ***number*** of signals shows how many different kinds of protons are present.
- The ***location*** (chemical shift) of the signals shows how shielded or deshielded the proton is.
- The ***intensity*** (integration) of the signal shows the number of protons under a signal.
- Signal ***splitting*** (coupling) shows the number of protons on adjacent atoms.



The NMR Spectrometer

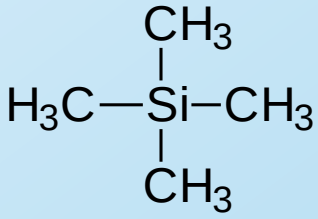
See photos at:
http://biophysics.bumc.bu.edu/facilities/nmrspectroscopy/nmrvirtualtour.html



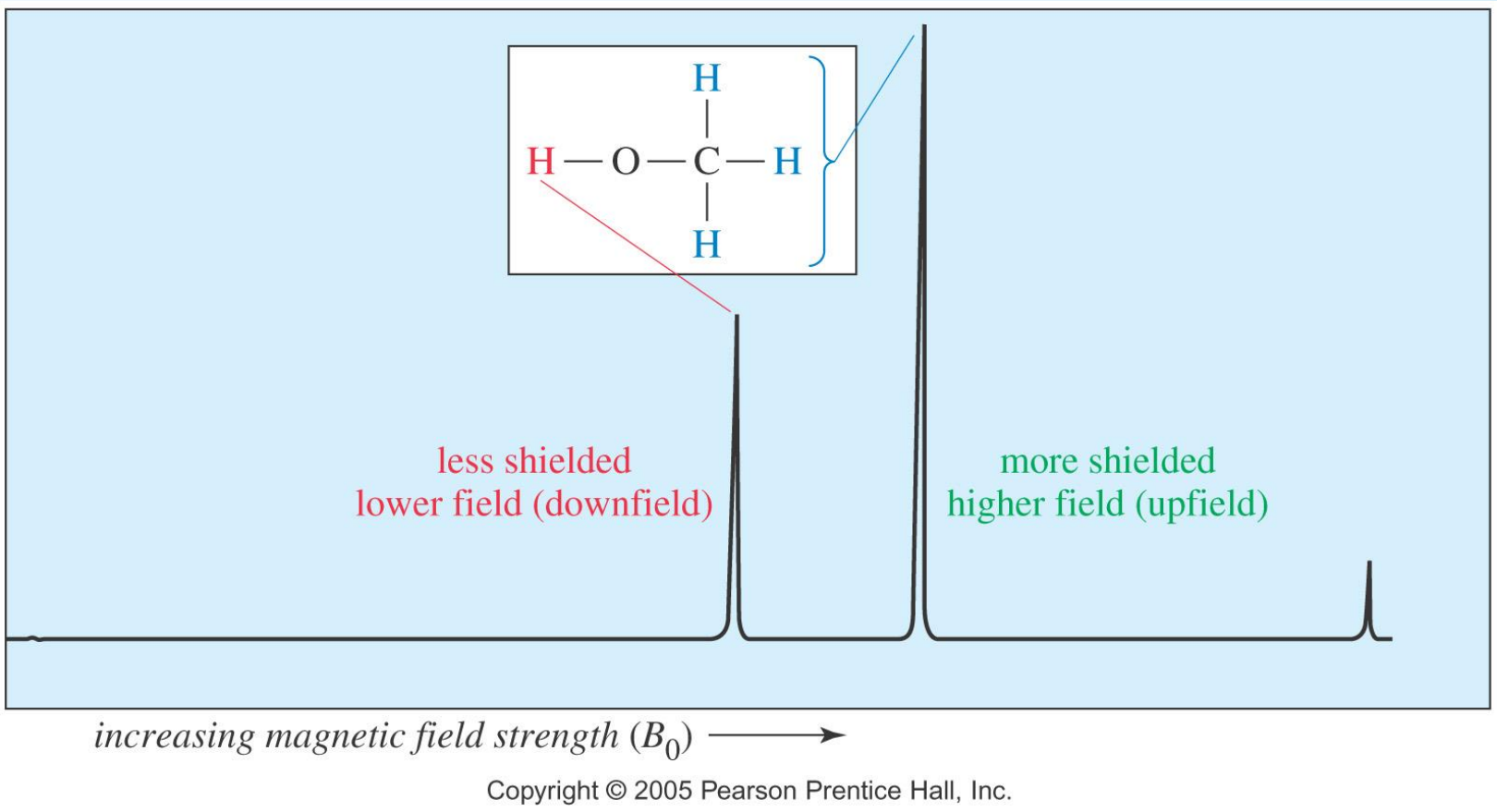
NMR at PNNL *(Pacific Northwest National Lab)*

Making the Sample

- A NMR tube (shown on the right) is used to make the sample. Samples are not destroyed during the analysis.
- Sample is dissolved in a solvent that is NMR inactive.
- Most solvents for organic compounds are hydrocarbons, e.g. chloroform ($CHCl_3$), dichloromethane (CH_2Cl_2), methanol (CH_3OH) and in some cases water (H_2O). These solvents are treated with deuterium (D; a NMR inactive isotope of H), so that the solvent solubility properties don't change drastically. $CHCl_3$ is $CDCl_3$ and H_2O is D_2O etc.
- Tetramethyl Silane (TMS) is added to the sample as a reference.
- 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.



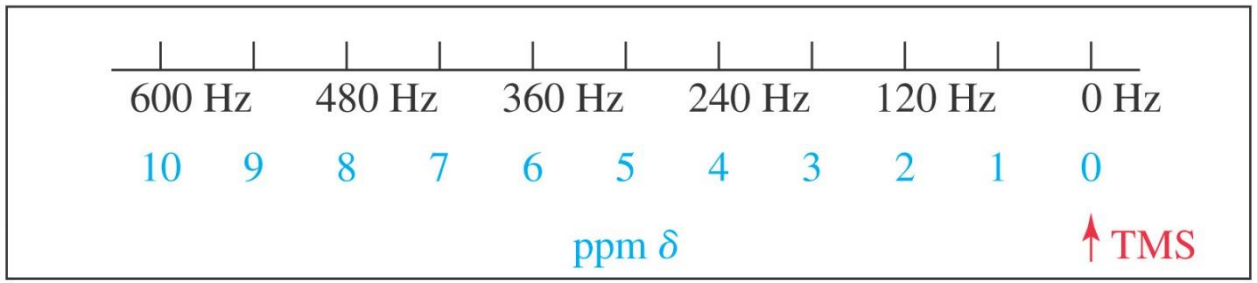
The NMR Graph



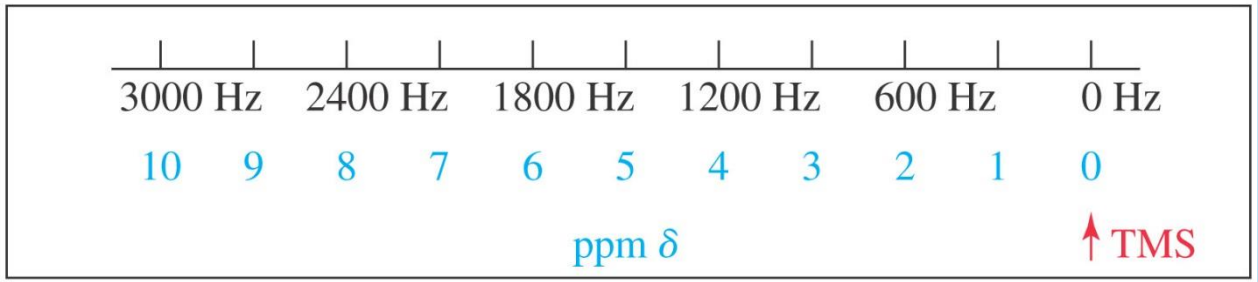
Chemical Shift

- Measured in parts per million (ppm, δ).
- It is the 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.

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



60 MHz



300 MHz

Chemical Shift – Shielding/Deshielding

TABLE 13-2 Chemical Shifts of the Chloromethanes

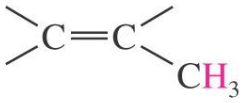
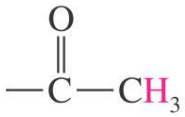
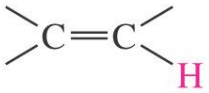
Compound	Chemical Shift	Difference
CH_4	$\delta 0.2$	
		2.8 ppm
CH_3Cl	$\delta 3.0$	
		2.3 ppm
CH_2Cl_2	$\delta 5.3$	
		1.9 ppm
$CHCl_3$	$\delta 7.2$	

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 (left side of spectrum).
- Effect decreases with distance.
- Additional electronegative atoms cause increase in chemical shift.

Chemical Shift - Typical Values

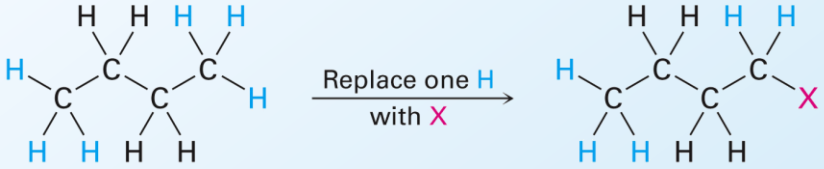
TABLE 13-3 Typical Values of Chemical Shifts

Type of Proton	Approximate δ	Type of Proton	Approximate δ
alkane ($-CH_3$)	0.9		1.7
alkane ($-CH_2-$)	1.3	Ph—H	7.2
alkane 	1.4	Ph—CH_3	2.3
	2.1	R—CHO	9–10
—C≡C—H	2.5	R—COOH	10–12
R—CH_2—X (X = halogen, O)	3–4	R—OH	variable, about 2–5
	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.

Equivalent and Non Equivalent Protons

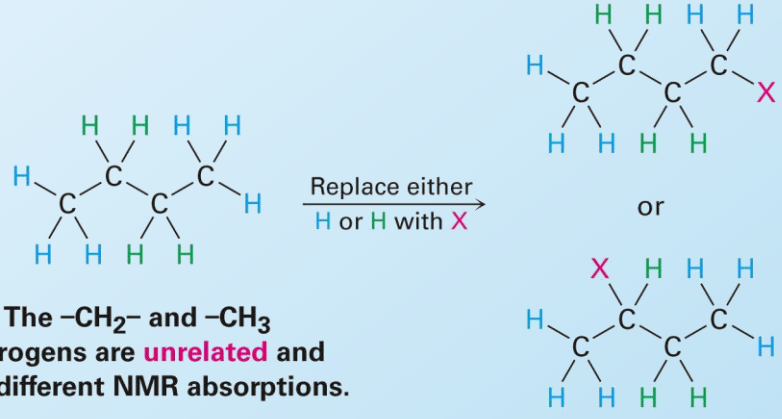
- Two H's that are in identical environments (**homotopic**) have the **<u>same NMR signal</u>**
- Test by replacing each with X (halogen)
  - if they give the identical result, they are equivalent then protons are considered **homotopic**



The six $-CH_3$ hydrogens are homotopic and have the same NMR absorption.

Only one substitution product is possible.

If replacement of each H with "X" gives a different constitutional isomer then the H's are in **constitutionally heterotopic** environments and will have **<u>different chemical shifts</u>** – they are nonequivalent under all circumstances

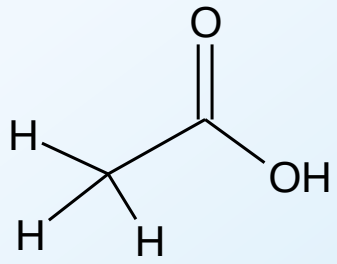


The $-CH_2-$ and $-CH_3$ hydrogens are unrelated and have different NMR absorptions.

The two substitution products are constitutional isomers.

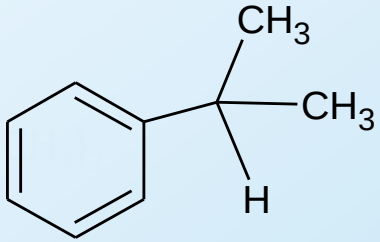
Equivalent and Non Equivalent Protons

(a) CH_3COOH



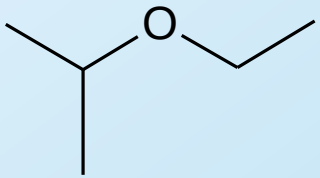
Two different Hs

(b) $C_6H_5CH(CH_3)_2$



Three different Hs

(c) $(CH_3)_2CHOCH_2CH_3$



Four different Hs

Magnetic Shielding

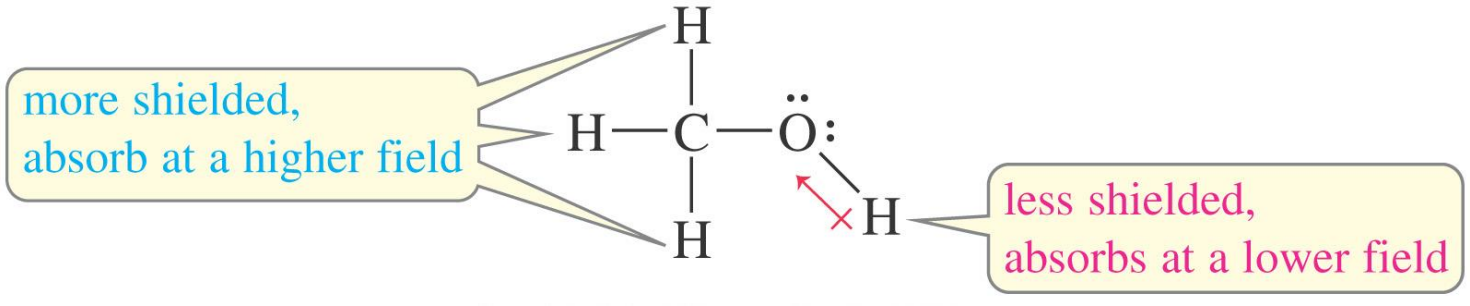
- If all protons absorbed the same amount of energy in a given magnetic field, not much information could be obtained.
- But protons are surrounded by electrons that shield them from the external field.
- Circulating electrons create an induced magnetic field that opposes the external magnetic field.

Shielded Protons

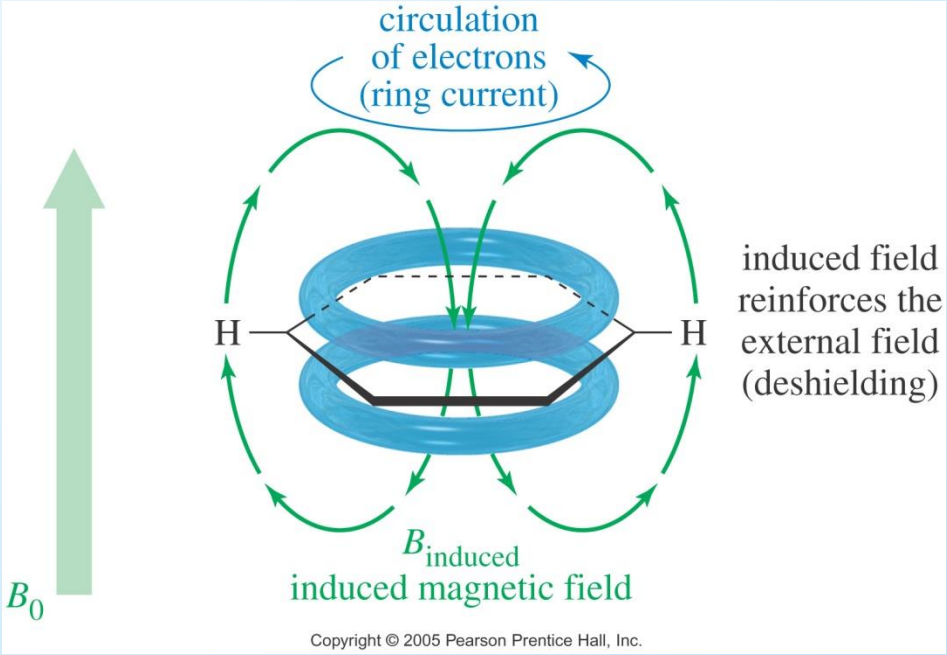
Magnetic field strength must be increased for a shielded proton to flip at the same frequency.

Protons in a Molecule

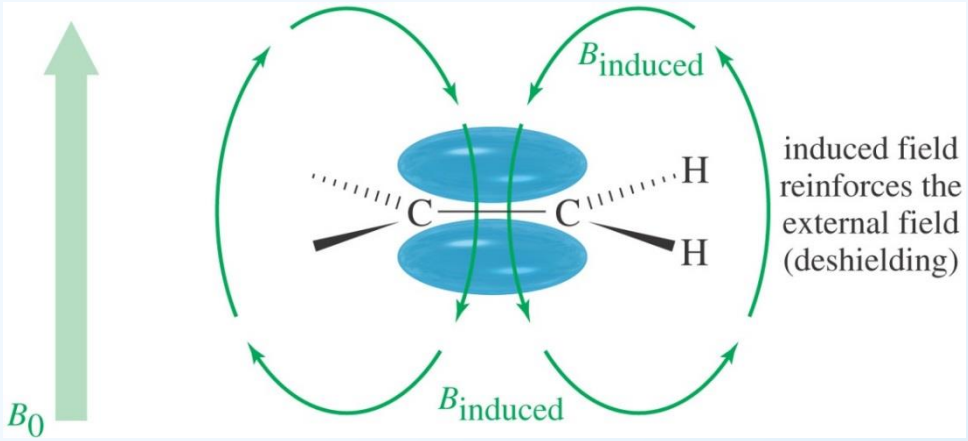
Depending on their chemical environment, protons in a molecule are shielded by different amounts.



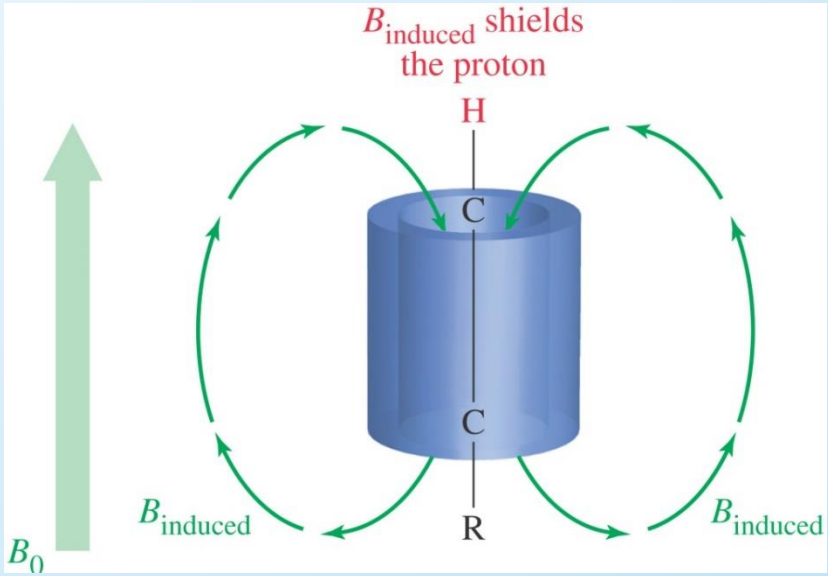
Aromatic Protons,
δ7-δ8



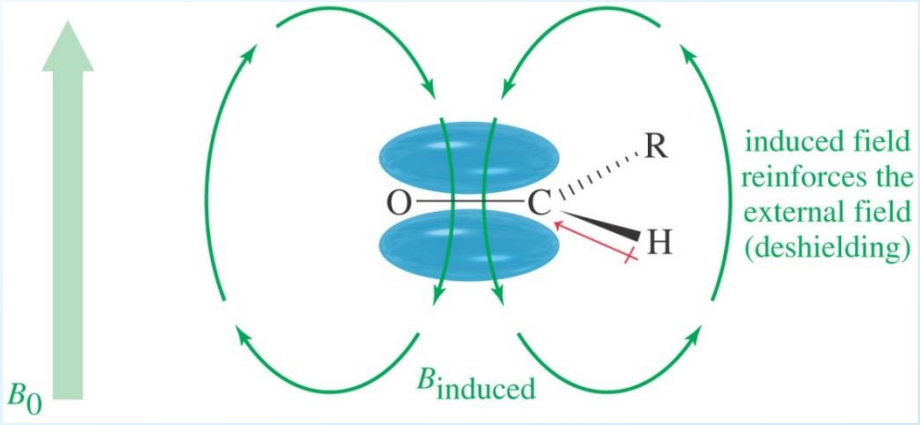
Vinyl Protons, δ5-δ6



Acetylenic Protons, δ2.5



Aldehyde Proton, δ9-δ10

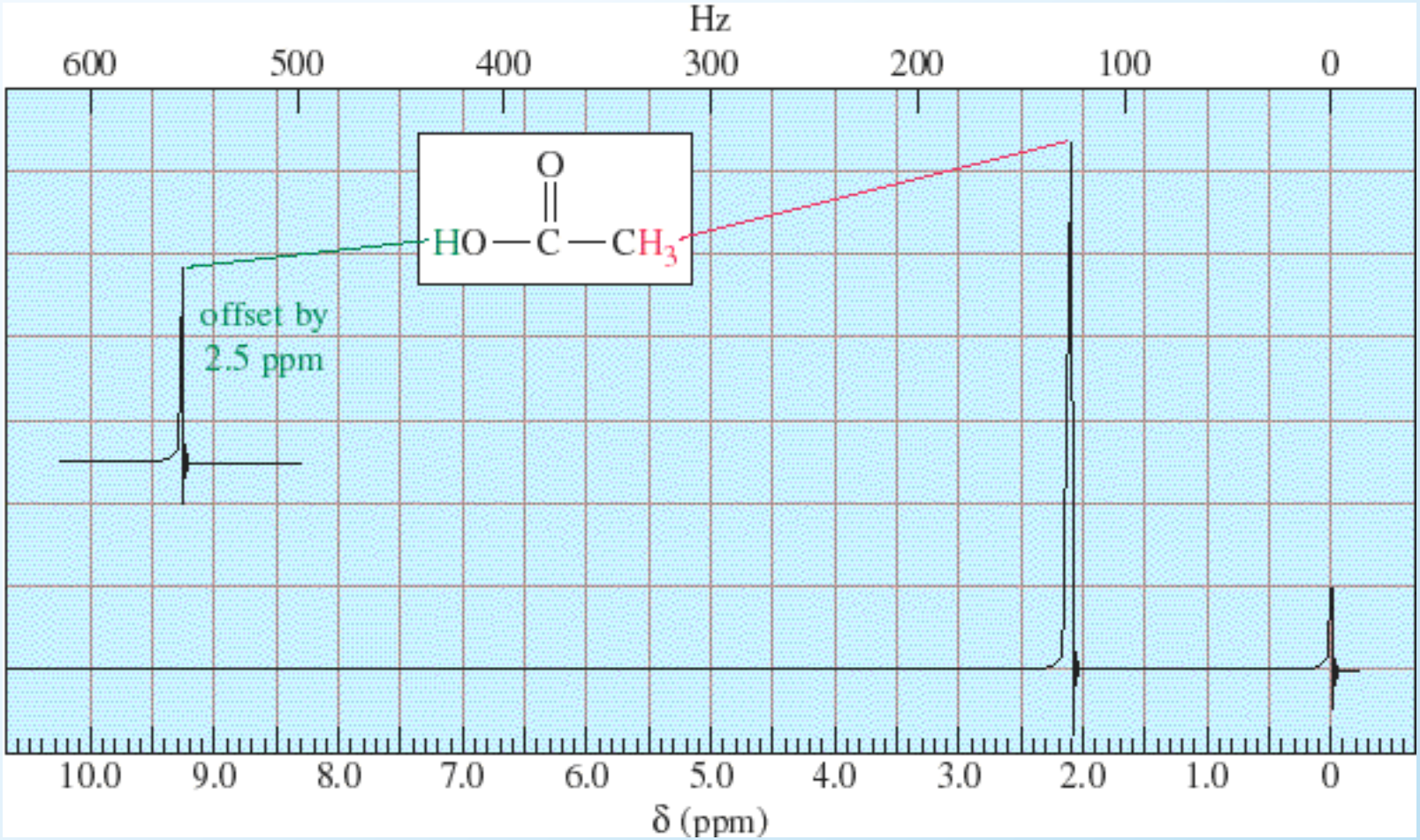


Electronegative
oxygen atom

O-H and N-H Signals

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

Carboxylic Acid Proton, δ10+



Key Concepts

- Fundamentals of NMR
- Equivalent and Non equivalent Protons
- Shielding and Deshielding
- Chemical Shift