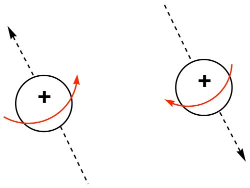
Chapter 13: Nuclear Magnetic Resonance (NMR) Spectroscopy

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

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



Not all nuclei are suitable for NMR.

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

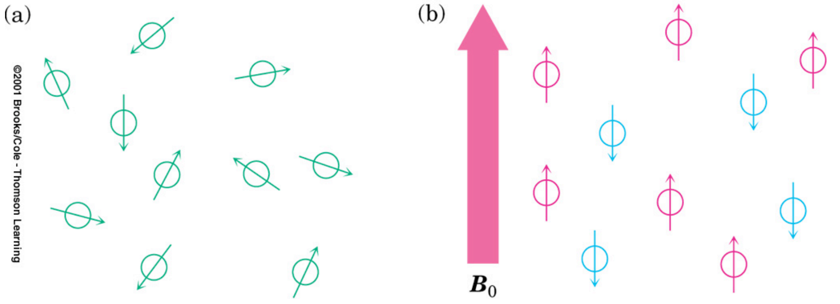
Natural Abundance

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

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

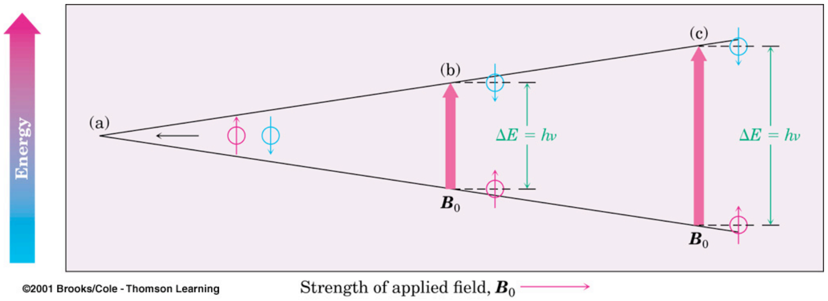
(a) Normally the nuclear magnetic fields are randomly oriented

(b) When placed in an external magnetic field ($\mathbf{B_o}$), the nuclear magnetic field can either be aligned with the external magnetic or oppose the external magnetic field



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

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



$\Delta E = h\nu$ $\quad \Delta E = \dfrac{\gamma B_o h}{2\pi}$

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

Note that $\dfrac{h}{2\pi}$ is a constant and is sometimes denoted as ħ

NMR Active Nuclei: nuclear spin quantum number (I)
atomic mass and atomic number

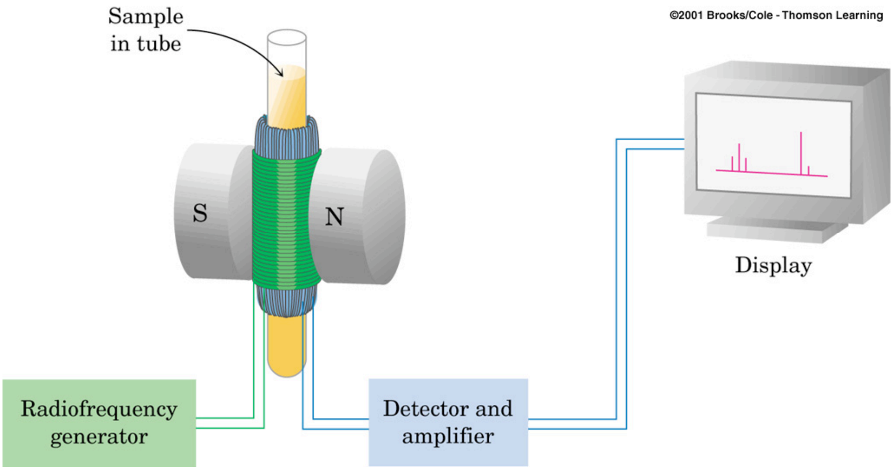
Number of spin states = 2I + 1 (number of possible energy levels)

Even mass nuclei that have even number of neutron have I = 0 (NMR inactive)

Even mass nuclei that have odd number of neutrons have an integer spin quantum number (I = 1, 2, 3, etc)

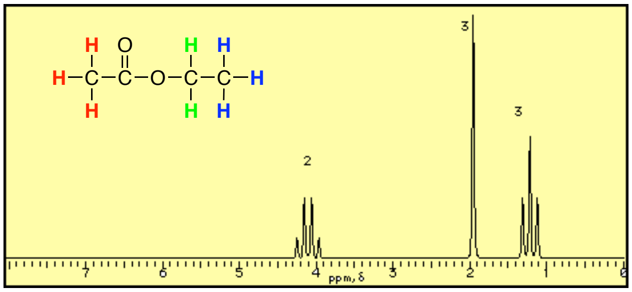
Odd mass nuclei have half-integer spin quantum number (I = 1/2, 3/2, 5/2, etc)

I= 1/2: ^{1}H, ^{13}C, ^{19}F, ^{31}P
I= 1: ^{2}H, ^{14}N
I= 3/2: ^{15}N
I= 0: ^{12}C, ^{16}O



Continuous wave (CW) NMR
Pulsed (FT) NMR

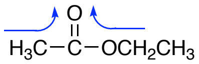
Different nuclei absorb EM radiation at different wavelength (energy required to bring about resonance)
Nuclei of a given type, will resonate at different energies depending on their chemical and electronic environment.
The position (*chemical shift*, δ) and pattern (*splitting* or *multiplicity*) of the NMR signals gives important information about the chemical environment of the nuclei

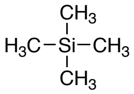


Chemical shift: the exact field strength (in ppm) of a nuclei comes into resonance relative to a reference standard (TMS

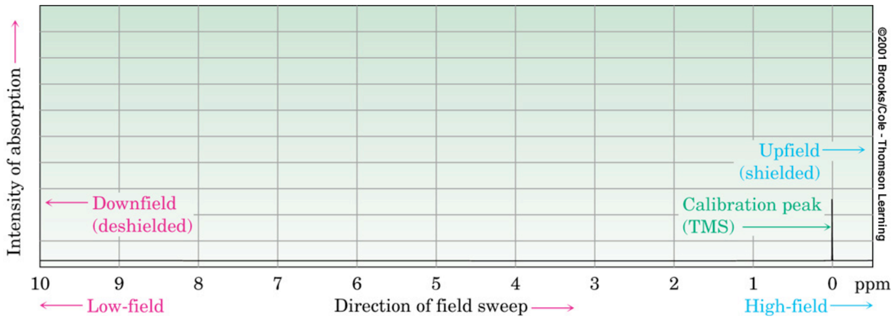
Electron clouds “shield” nuclei from the external magnetic field causing then to absorb at slightly higher energy

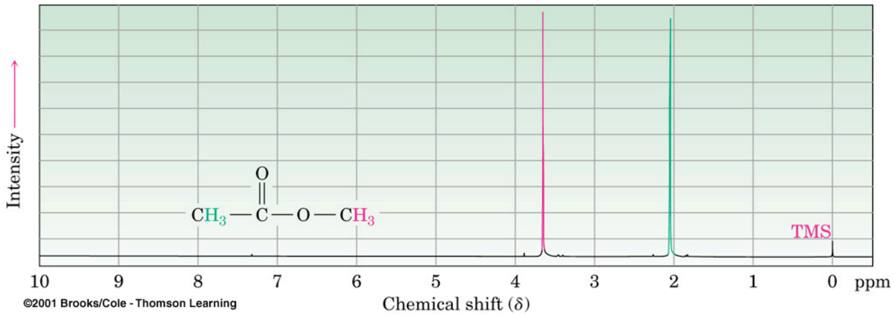
Shielding: influence of neighboring functional groups on the electronic structure around a nuclei and consequently the chemical shift of their resonance.


$H_3C-\overset{O}{\overset{\|}{C}}-OCH_2CH_3$


$H_3C-\overset{CH_3}{\underset{CH_3}{Si}}-CH_3$

Tetramethylsilane (TMS);
Reference standard δ = 0
for ^1H NMR





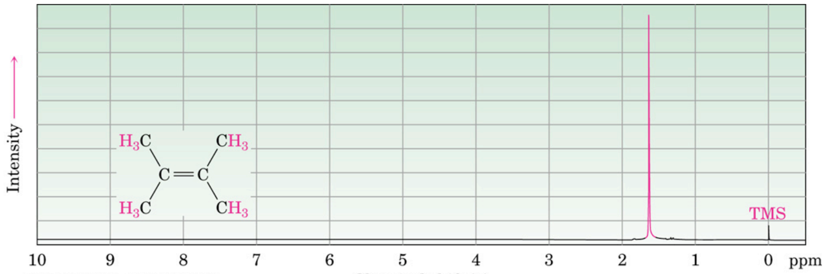
Vertical scale= intensity of the signal

Horizontal scale= chemical shift (δ), dependent upon the field strength of the external magnetic field; for ^1H, δ is usually from 1-10 ppm

$$\delta = \frac{\nu - \nu_{TMS}}{\nu_0} = \frac{\text{chemical shift in Hz}}{\text{operating frequency in MHz}}$$

14,100 gauss: 60 MHz for ^1H (60 million hertz) ppm= 60 Hz
15 MHz for ^{13}C
140,000 gauss: 600 MHz for ^1H ppm = 600 Hz
150 MHz for ^{13}C

Equivalence: chemically and magnetically equivalent nuclei resonate at the same energy and give a single signal or pattern



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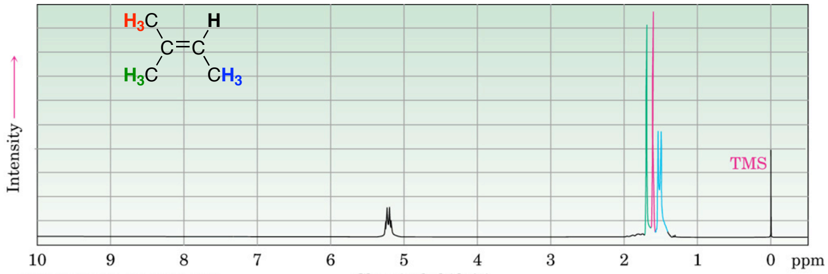

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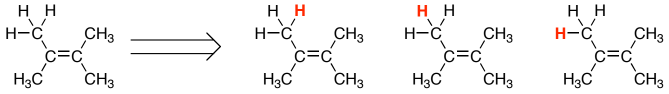
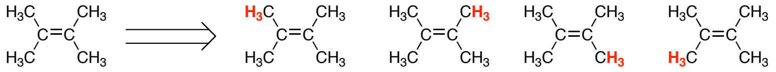
Test of Equivalence:

1. Do a mental substitution of the nuclei you are testing with an arbitrary label (your book uses X)
2. Ask what is the relationship of the compounds with the arbitrary label
3. If the labeled compounds are identical (or enantiomers), then the original nuclei are chemically equivalent and will normally give rise to a single resonance in the NMR spectra

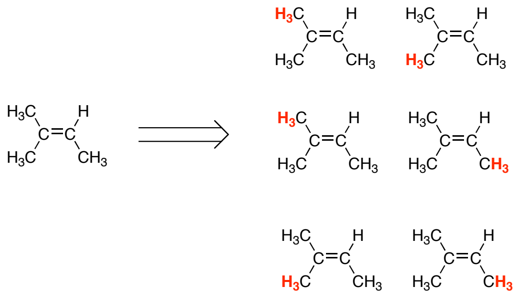
   If the labeled compounds are not identical (and not enantiomers), then the original nuclei are not chemically equivalent and can give rise to different resonances in the NMR spectra



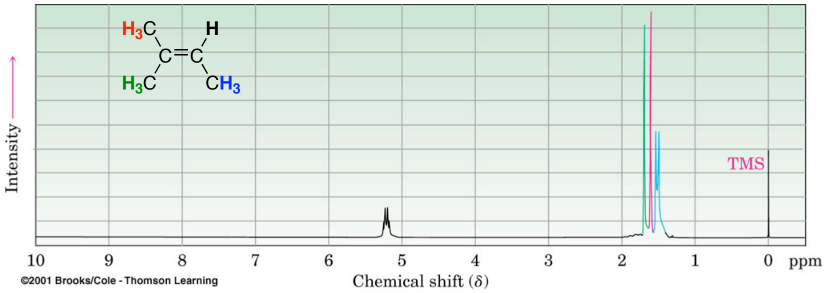
Identical, so the protons are equivalent

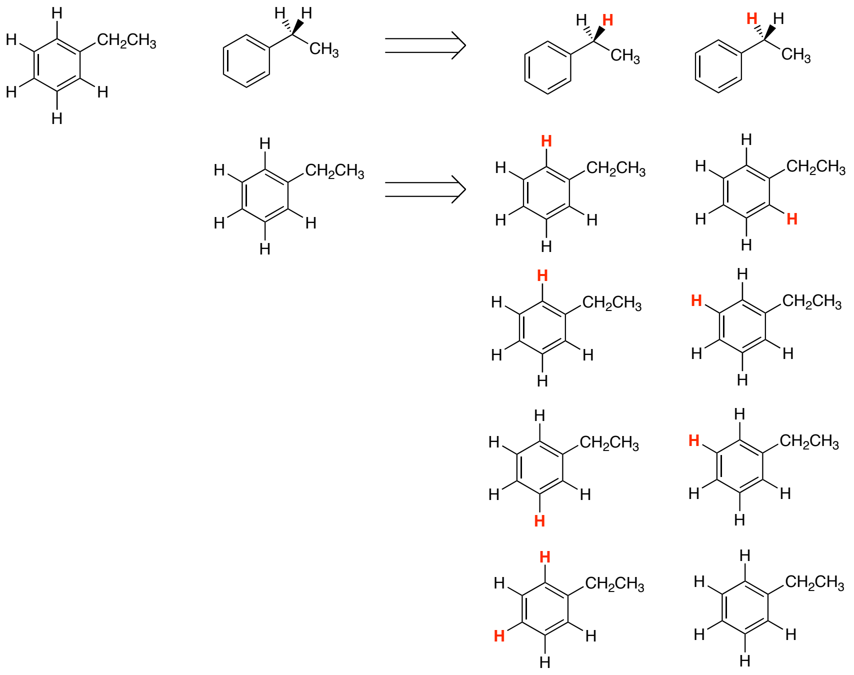


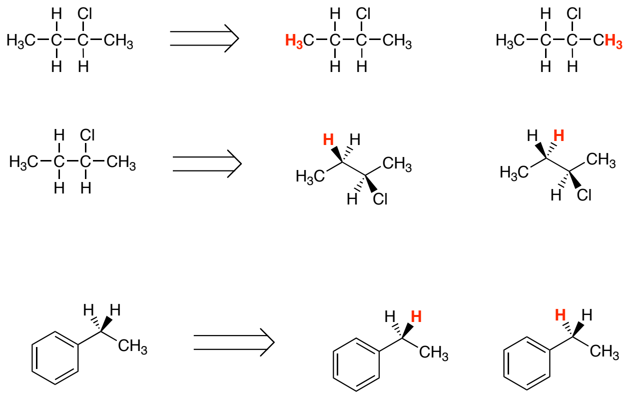
Identical, so the methyl groups are equivalent



These are geometric isomers (not identical and not enantiomers). The three methyl groups are therefore not chemically equivalent and *can* give rise to different resonances

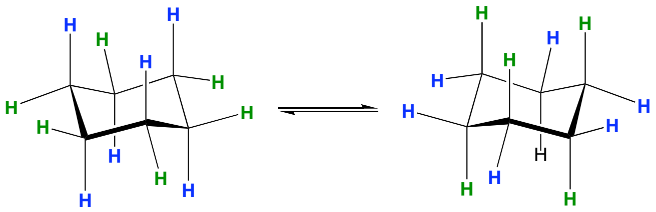






Homotopic: equivalent
Enantiotopic: equivalent
Diastereotopic: non-equivalent

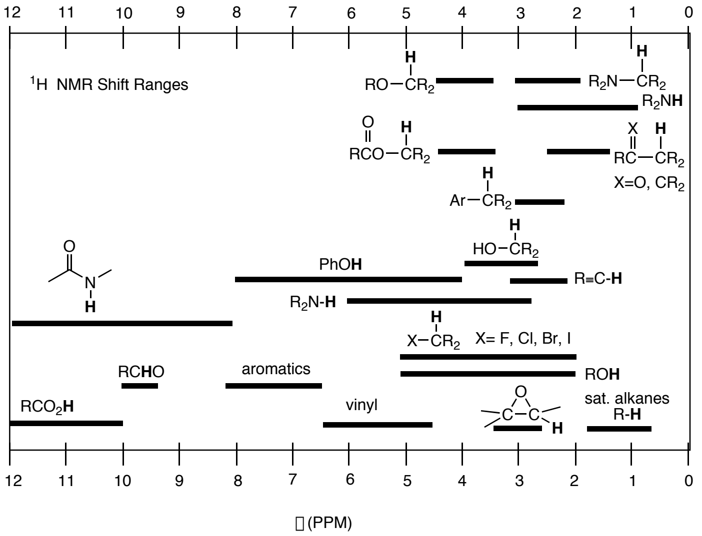
Cyclohexane: two different types of protons, axial and equitorial



The chair-chair interconversion interchanges the axial and equatorial protons and is a fast process at room temperature. NMR is like a camera with a slow shutter speed and a blurred image of fast processes is observed.

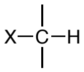
At room temperature the cyclohexane protons are observed as a time-average and appear as a single resonance. At -90 °C the chair-chair interconversion is sufficiently slow that axial and equatorial are observed as two separate resonances.

Typical ^{1}H NMR chemical shifts ranges
also see Table 13.2 and 13.3 (pages 495-6)



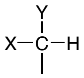
The influence of neighboring groups (deshielding) on ^{1}H chemical shifts is additive (to an extent)

Shoolery's additivity rules for predicting the chemical shift of protons of the type:



$X-C-H$

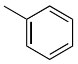
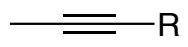
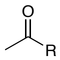
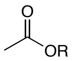
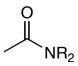
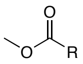
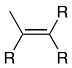
- or -

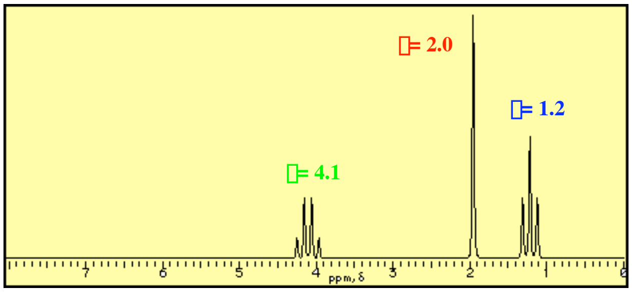


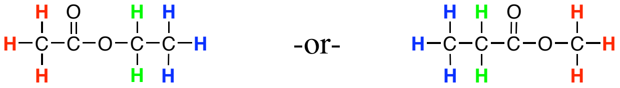
$X-C(Y)-H$

for protons on sp3 carbons only

$$\square\text{(ppm)} = 0.233 + \square\ \square_i$$

Funtional Group (X,Y)	$\square_i$ (ppm)	Funtional Group (X,Y)	$\square_i$ (ppm)
-Cl	2.53		1.85
-Br	2.33		1.44
-I	1.82		1.70
-OH	2.56		1.55
-OR	3.23		1.59
	3.13	$-CF_3$	1.14
-SR	1.64	-CN	1.70
$-NR_2$	1.57		
$-CH_3$	0.47		
	2.53		



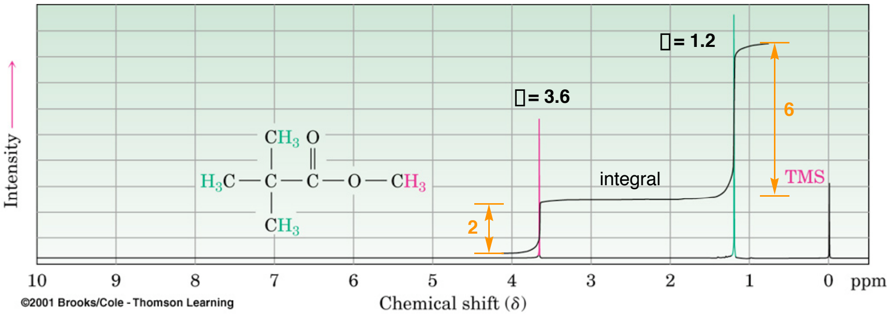


□= 0.233 + 3.13 + 0.47 = 3.833
□= 0.233 + 1.70 = 1.933

□= 0.233 + 1.70 + 0.47 = 2.43
□= 0.233 + 3.13 = 3.363

Integration of ^{1}H NMR resonances

The area under an NMR resonance is proportional to the number of nuclei that give rise to that resonance.



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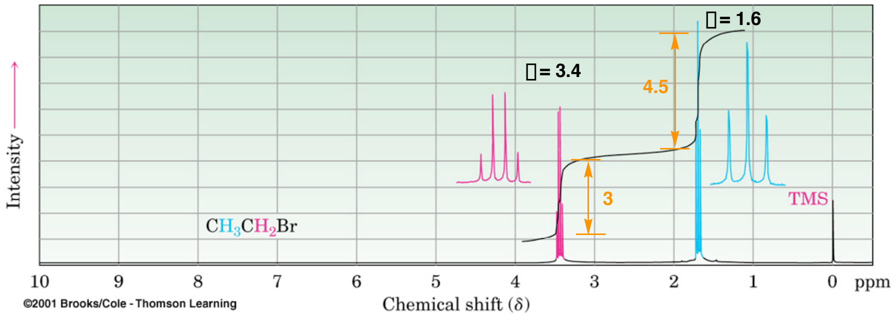
The relative area under the resonances at □= 3.6 and 1.2 is 1:3

The integral is superimposed over the spectrum as a “stair-step” line.
The height of each “step” is proportional to the area under the resonance.



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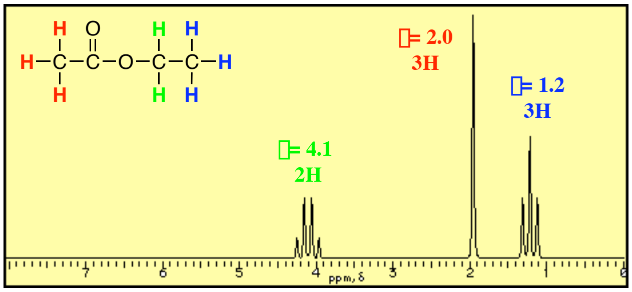
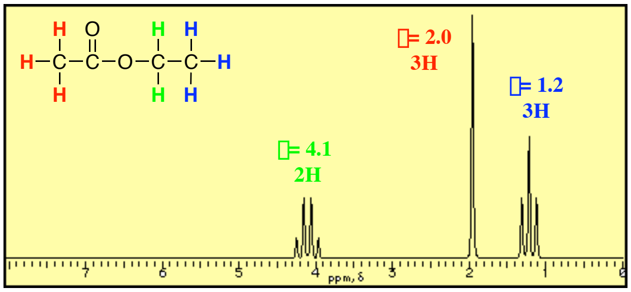


Spin-Spin Coupling (splitting)

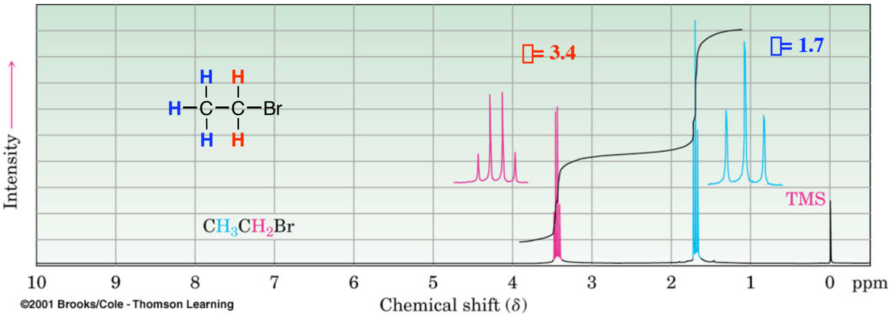
protons on adjacent carbons will interact and "split" each others resonances into multiple peaks (multiplets)

n + 1 rule: equivalent protons that have n equivalent protons on the adjacent carbon will be "split" into n + 1 peaks.



Resonances always split each other. The resonance at δ= 4.1 splits the resonance at δ= 1.2, therefore the resonance at δ= 1.2 must split the resonance at δ= 4.2.

The *multiplicity* is defined by the number of peaks and the pattern



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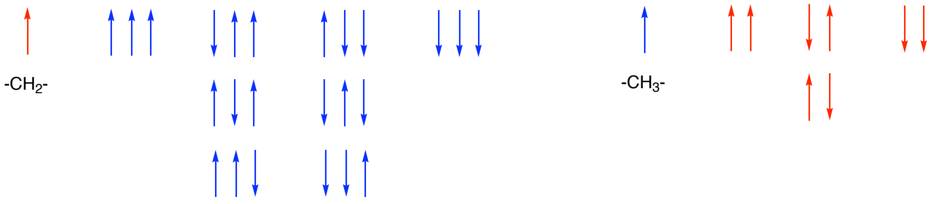


1 : 3 : 3 : 1

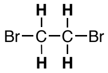
1 : 2 : 1

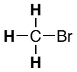
One proton on an adjacent carbon will split a proton into a **doublet** (d), two peaks of 1:1 relative intensity

Two proton on an adjacent carbon will split a proton into a **triplet** (t), three peaks of 1:2:1 relative intensity

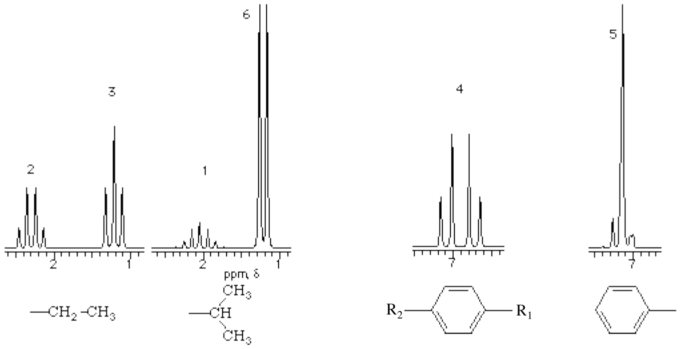
Three proton on an adjacent carbon will split a proton into a **quartet** (q), four peaks of 1:3:3:1 relative intensity

Equivalent protons do not show spin-spin coupling



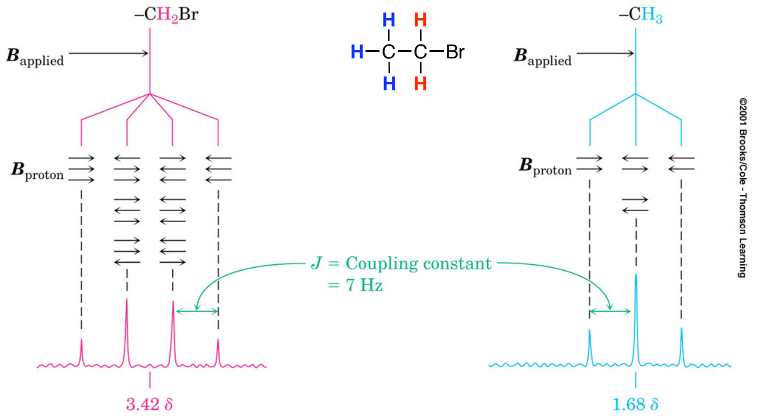


Singlet (s)



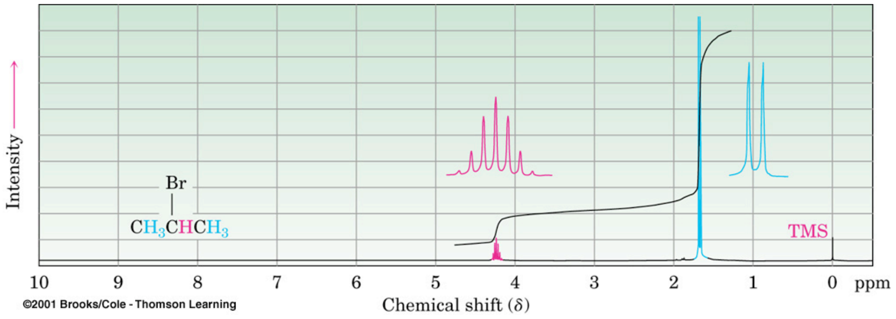
The resonance of a proton with n equivalent protons on the adjacent carbon will be “split” into n + 1 peaks with a *coupling constant J*.

Coupling constant: distance between peaks of a split pattern; expressed in Hz. Protons coupled to each other have the same coupling constant J.



Quartet due to coupling with $-CH_3$

Triplet due to coupling with $-CH_2Br$



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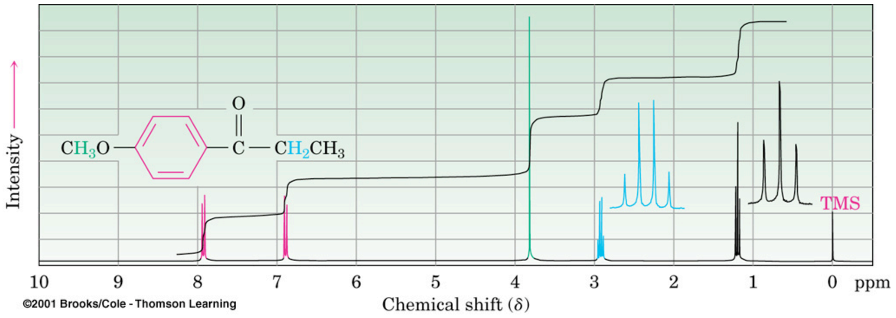

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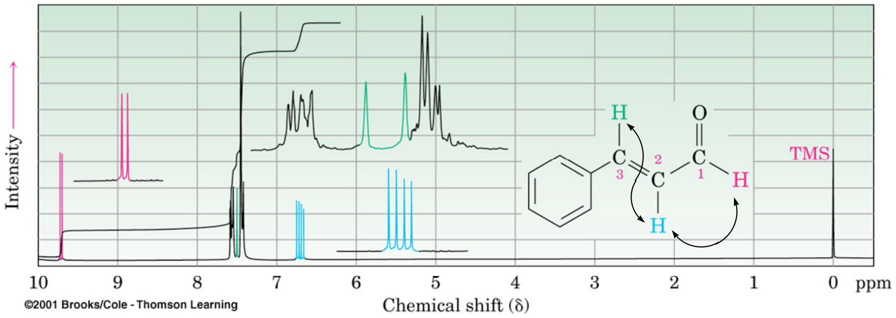
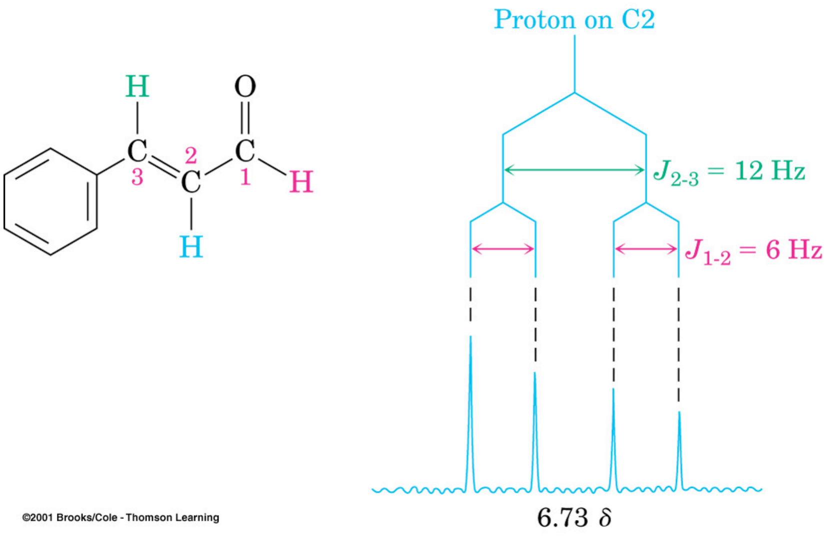
More complex spin-spin coupling: non equivalent protons will couple independently.



H_2 splits H_3 into a doublet with coupling constant $J_{2\text{-}3}$

H_2 splits H_1 into a doublet with coupling constant $J_{1\text{-}2}$

H_1 splits H_2 into a doublet; H_3 splits H_2 into a doublet (doublet of doublets) with coupling constants $J_{1\text{-}2}$ and $J_{2\text{-}3}$.



Summary of ^{1}H-^{1}H spin-spin coupling

- chemically equivalent protons do not exhibit spin-spin coupling to each other.
- the resonance of a proton that has n equivalent protons on the adjacent carbon is split into n+1 peaks (multiplicity) with a coupling constant *J*.
- protons that are coupled to each other have the same coupling constant
- non-equivalent protons will split a common proton independently. complex coupling.

Spin-spin coupling is normally observed between nuclei that are one, two and three bonds away. Four-bond coupling can be observed in certain situations but is not common.

Summary of ^{1}H-NMR Spectroscopy

- the number of proton resonances equals the number of non-equivalent protons
- the chemical shift (δ, ppm) of a proton is diagnostic of the chemical environment (shielding and deshilding)
- Integration: number of equivalent protons giving rise to a resonance
- spin-spin coupling is dependent upon the number of equivalent protons on the adjacent carbon

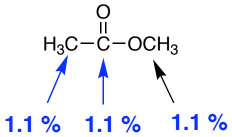
^{13}C NMR Spectroscopy:

Natural Abundance

^{1}H 99.9% (I= 1/2)

^{12}C 98.9% (I= 0)

^{13}C 1.1% (I= 1/2)



$H_3C{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OCH_3$

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

B_o = external magnetic field strength

γ= gyromagnetic ratio

^{1}H= 26,752

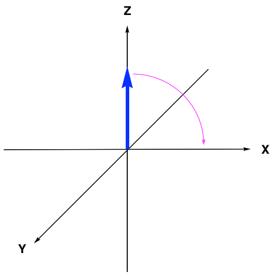
^{13}C= 6.7

^{13}C is a <u>much</u> less sensitive nuclei than ^{1}H for NMR spectroscopy

New techniques (hardware and software) has made ^{13}C NMR routine

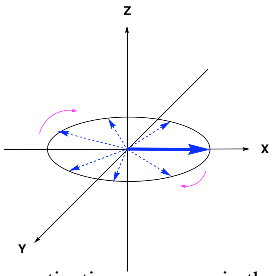
- Pulsed NMR techniques (FT or time domain NMR)
- Signal averaging (improved signal to noise)

Pulsed NMR Techniques:



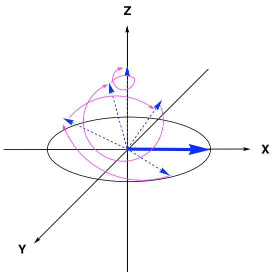
EM pulse “tips” the magnetization 90 ° into the XY-plane

The magnetization is detected in the X-axis



The magnetization precesses in the XY-plane at the **Larmor frequency** of the nuclei, which is directly related to the chemical shift (δ) of the nuclei

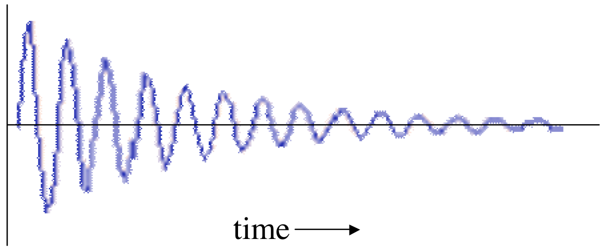
relaxation (recovery)



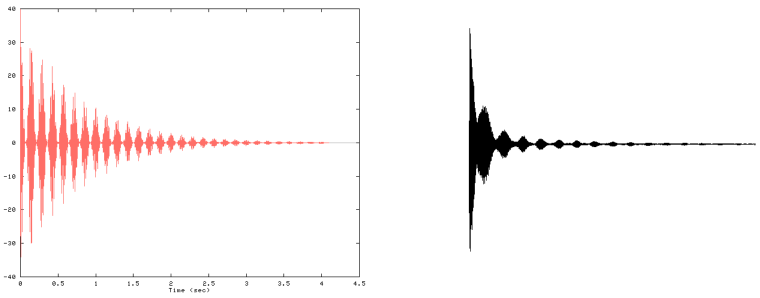
The magnetization will relax (recover) back to the Z-axis. As the magnetization precesses in XY-plane, it “spirals” back to the Z-axis.

Animation: http://www.nmr.ethz.ch/education/PCV/anim/puls_evol.html
http://www.nmr.ucdavis.edu/BCM230_F2001/Flash/PresentationSecondWeek.swf

Free Induction Decay (FID)- time domain NMR



In pulse (FT) NMR, all nuclei are tipped at the same time and the FID's are superimposed.



Fourier Transform (FT) deconvolutes all of the FID's and gives an NMR spectra.

Signal averaging: pulsed NMR allows for many FID's (NMR spectra) to be accumulated over time. These FID's are added together and averaged. Signals (resonances) build up while the "noise" is random and cancels out during the averaging.

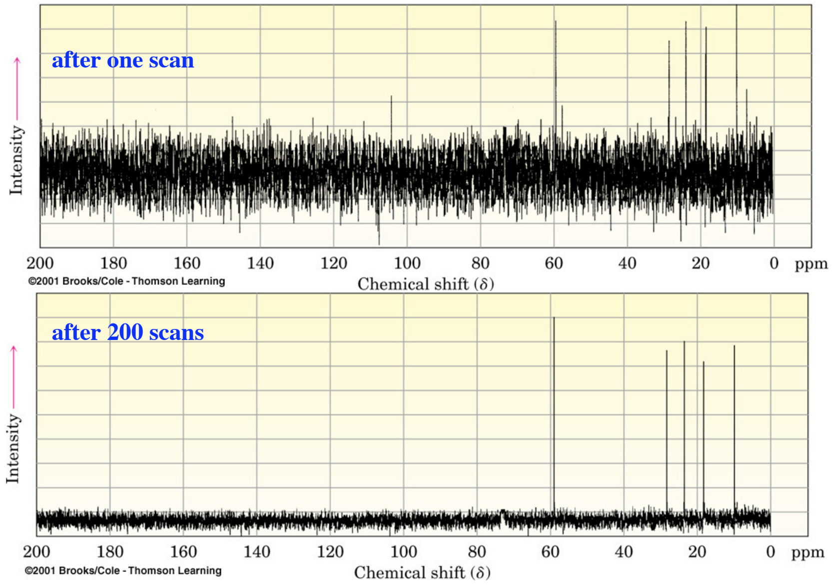
Enhanced signal to noise ratio and allows for NMR spectra to be collected on insensitive nuclei such as ^{13}C and small samples.

Chemical shifts give an idea of the chemical and electronic environment of the ^{13}C nuclei due to shielding and deshielding effects
range: 0 - 220 ppm from TMS

^{13}C NMR spectra will give a map of the carbon framework. The number of resonances equales the number of non-equivalent carbons.

Signal-Averaging

^{13}C-spectra of $CH_3CH_2CH_2CH_2CH_2OH$



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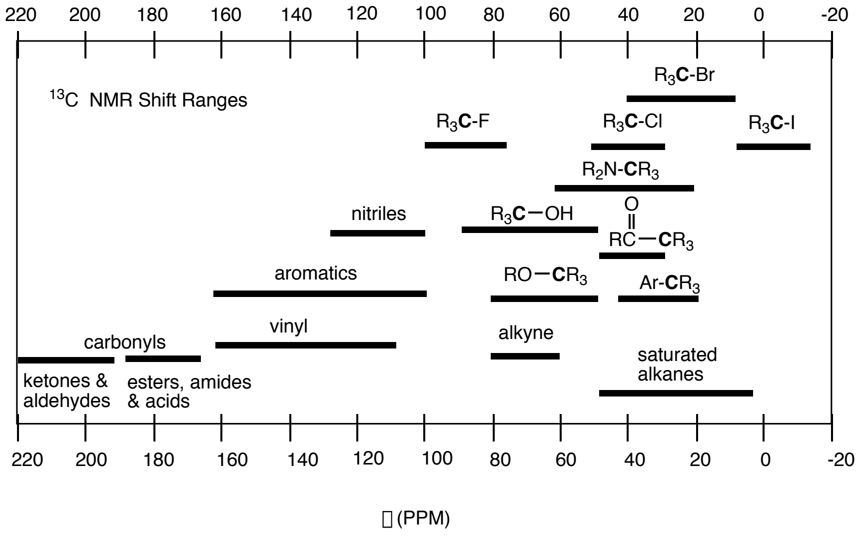
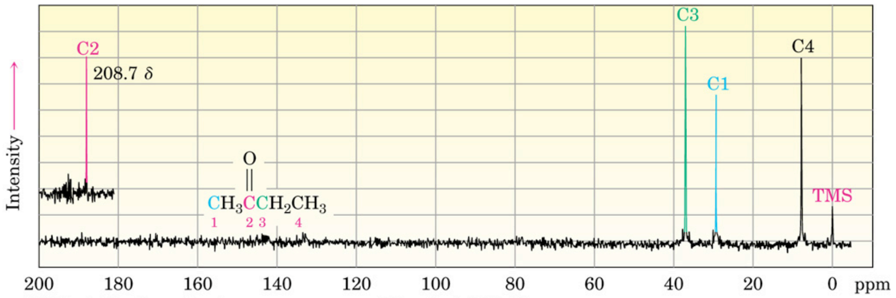
Chemical Shift Range of ^{13}C



Note the carbonyl range



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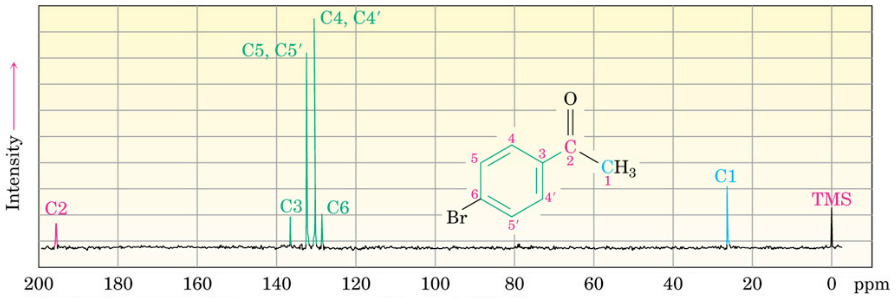

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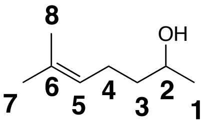
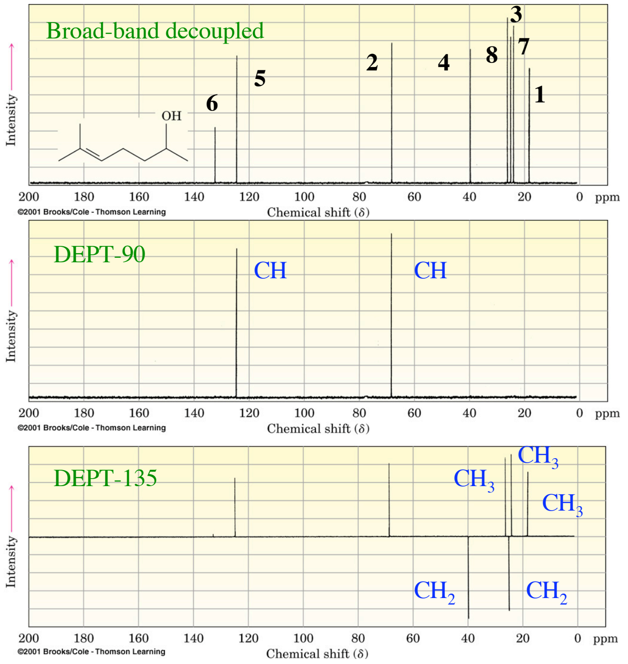
^{1}H-^{13}C spin-spin coupling: spin-spin coupling tells how many protons are attached to the ^{13}C nuclei. (i.e., primary, secondary tertiary or quaternary carbon)

^{13}C spectra are usually collected with the ^{1}H-^{13}C coupling "turned off" (broad band decoupled). In this mode all ^{13}C resonances appear as singlets.

DEPT spectra (**D**istortionless **E**nhancement by **P**olarization **T**ransfer) a modern ^{13}C NMR spectra that allows you to determine the number of attached hydrogens.

Run: broad-band decoupled spectra
    DEPT-90: only CH's show up
    DEPT-135: CH's and CH_3's give positive resonances
        CH_2's give negative resonances





Solving Combined Spectra Problems:
Mass Spectra:
- Molecular Formula
  - Nitrogen Rule □ # of nitrogen atoms in the molecule
  - M+1 peak □ # of carbons
- Degrees of Unsaturation: # of rings and/or □-bonds

Infrared Spectra:
- Functional Groups
  - C=O
  - C=C
  - C≡C

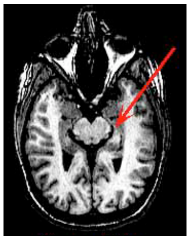
^{1}H NMR:
- Chemical Shift (□) □ chemical environment of the H's
- Integration □ # of H's giving rise to the resonance
- Spin-Spin Coupling (multiplicity) □ # of non-equivalent H's on the adjacent carbons (vicinal coupling).
- Shoolery's Rules: finial check on the structure assignment by ^{1}H NMR

^{13}C NMR:
- # of resonances □ symmetry of carbon framework
- Type of Carbonyl

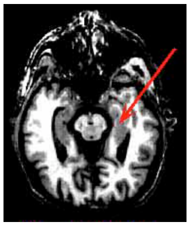
Each piece of evidence gives a fragment (puzzle piece) of the structure. Piece the puzzle together to give a proposed structure. The proposed structure should be consistent with all the evidence.

Magnetic Resonance Imaging (MRI): uses the principles of nuclear magnetic resonance to image tissue

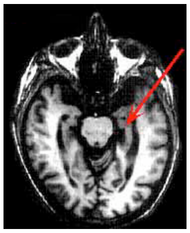
MRI normally used the magnetic resonance of protons on water and very sophisticated computer methods to obtain images. Other nuclei within the tissue can also be used (^{31}P) or a imaging (contrast) agent can be administered



Normal
25 years old



Normal
86 years old



Alzheimer’s Disease
78 years old