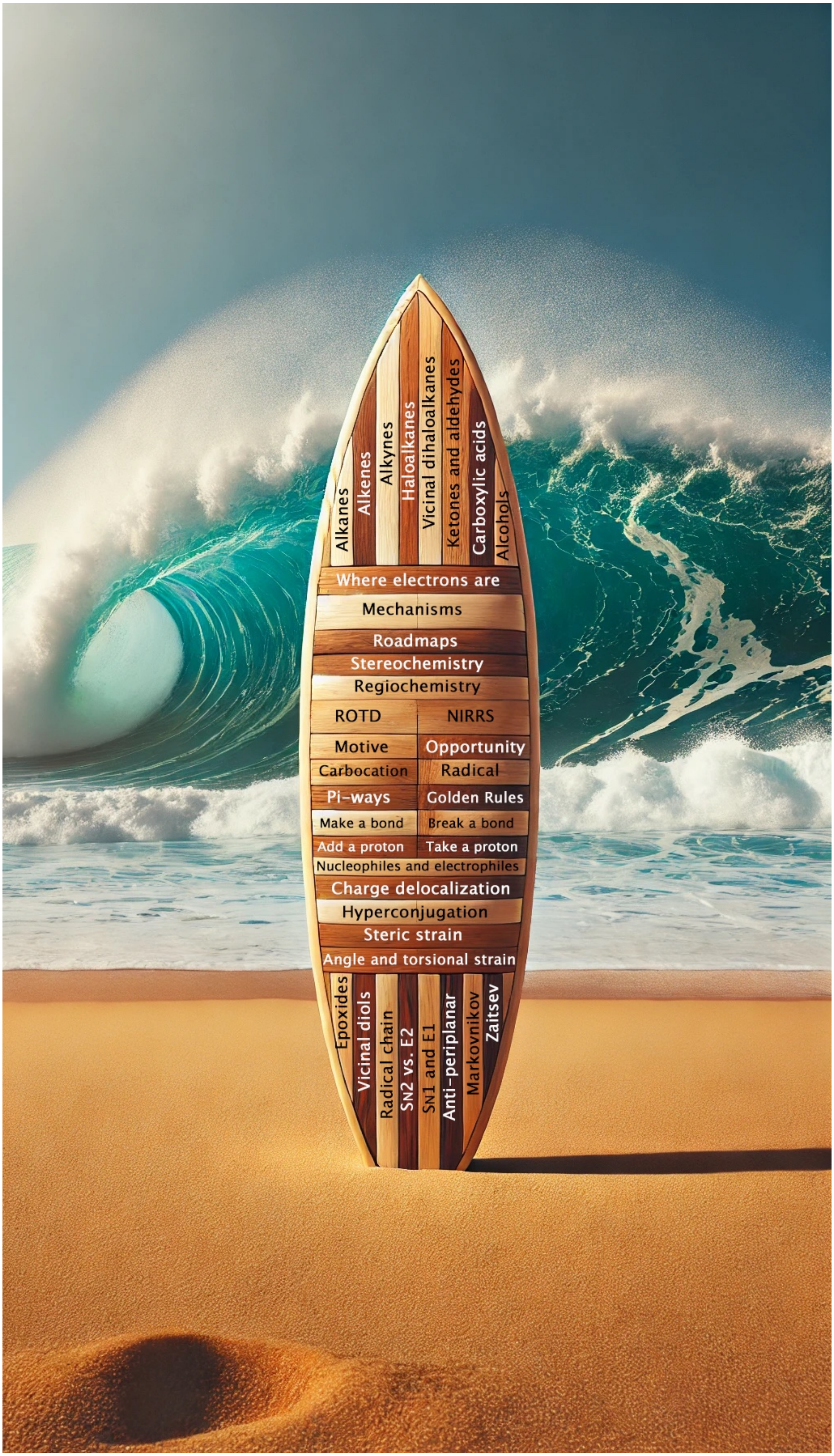
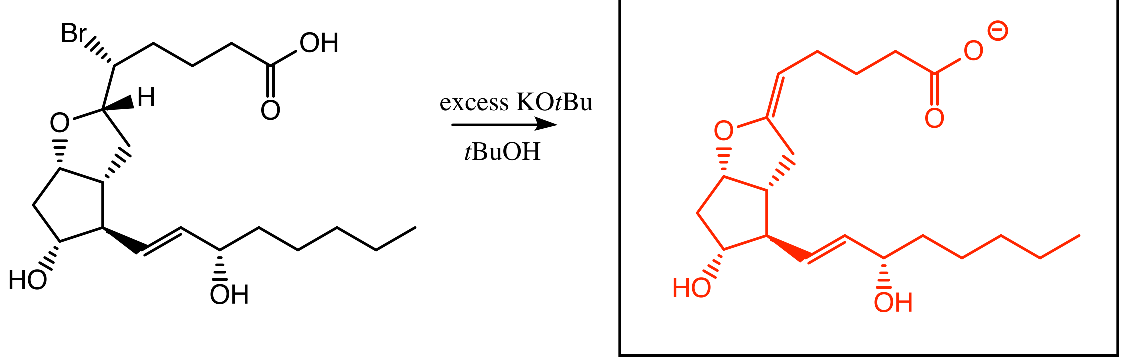
“You can’t stop the waves, but you can learn to surf”

Jon Kabat-Zinn

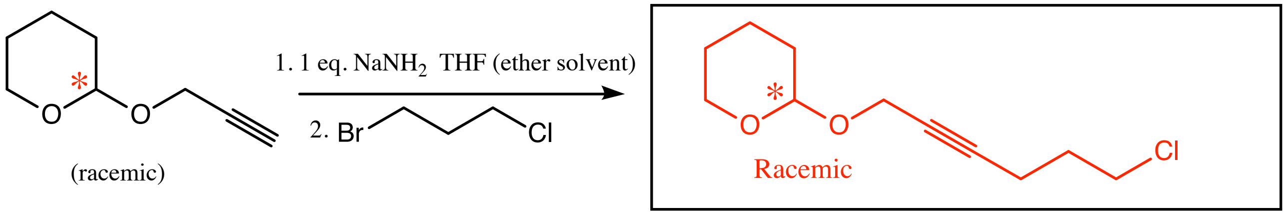

Alkanes
Alkenes
Alkynes
Haloalkanes
Vicinal dihaloalkanes
Ketones and aldehydes
Carboxylic acids
Alcohols
Where electrons are
Mechanisms
Roadmaps
Stereochemistry
Regiochemistry
ROTD
NIRRS
Motive
Opportunity
Carbocation
Radical
Pi-ways
Golden Rules
Make a bond
Break a bond
Add a proton
Take a proton
Nucleophiles and electrophiles
Charge delocalization
Hyperconjugation
Steric strain
Angle and torsional strain
Epoxides
Vicinal diols
Radical chain
SN2 vs. E2
SN1 and E1
Anti-periplanar
Markovnikov
Zaitsev

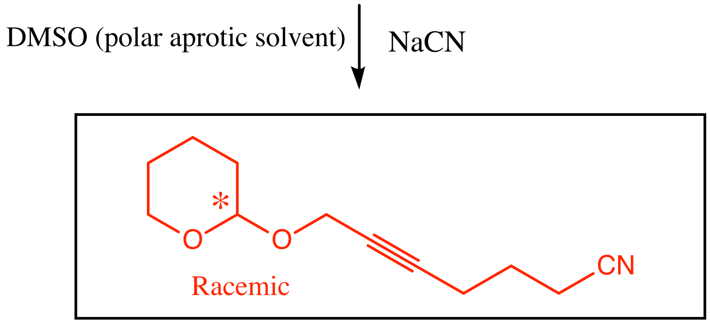
Reactions in the Context of Complex Molecules

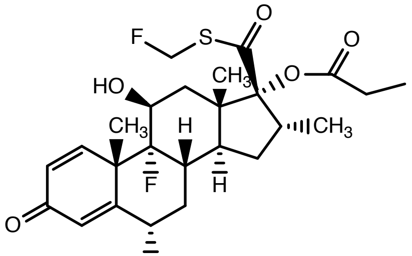
Used in the synthesis of several protaglandins



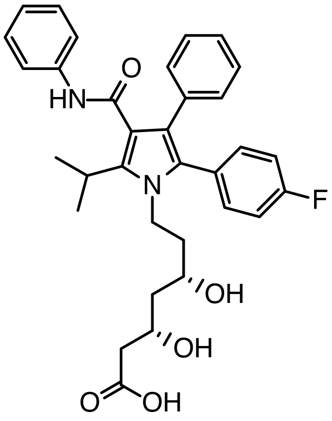
Used in the synthesis of protaglandin C_2

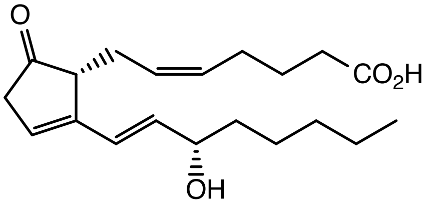




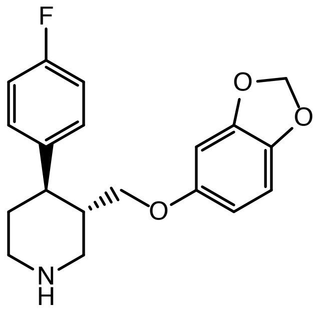


Fluticasone (Flonase)





Prostaglandin C_2



Paroxetine (Paxil)

Atorvastatin (Lipitor)

Organic Chemistry is the study of carbon-containing molecules.

This class has two points.

The first point of the class is to understand the organic chemistry of living systems. We will teach you how to think about and understand the most amazing things on the planet!!

Water is essential for life, you will learn why water has such special properties. 8/27/25

You will learn the secret structural reason proteins, the most important molecular machines in our bodies, can support the chemistry of life. 9/10/25

You will learn why when you take Advil for pain, exactly half of what you take works, and the other half does nothing. 9/24/25

You will learn how toothpaste works. 10/6/25

You will learn how a single chlorofluorocarbon refrigerant molecule released into the atmosphere can destroy many, many ozone molecules, leading to an enlargement of the ozone hole. 10/29/25

You will learn how medicines like Benadryl, Seldane, and Lipitor work. 11/12/25

You will learn how Naloxone is an antidote for an opioid overdose.

You will learn why Magic Johnson is still alive, decades after contracting HIV.

You will learn how MRI scans work.

The second point of organic chemistry is the synthesis of complex molecules from simpler ones by making and breaking specific bonds.

You will learn how to understand movies of reaction mechanisms like alkene hydration. 10/8/25

You will learn reactions that once begun, will continue reacting such that each product molecule created starts a new reaction until all the starting material is used up. 10/29/25

You will learn reactions that can make antifreeze from vodka. 11/12/25

You will learn a reaction that can make nail polish remover from rubbing alcohol. 11/17/25

You will learn how to look at a molecule and accurately predict which atoms will react to make new bonds, and which bonds will break during reactions. 11/19/25

You will learn how to analyze a complex molecule's structure so that you can predict ways to make it via multiple reactions starting with less complex starting molecules. 11/19/25

To understand NMR you need to know the following:

A. Physics: Moving charge generates a magnetic field, and a moving magnetic field causes charges to move in a conductor.

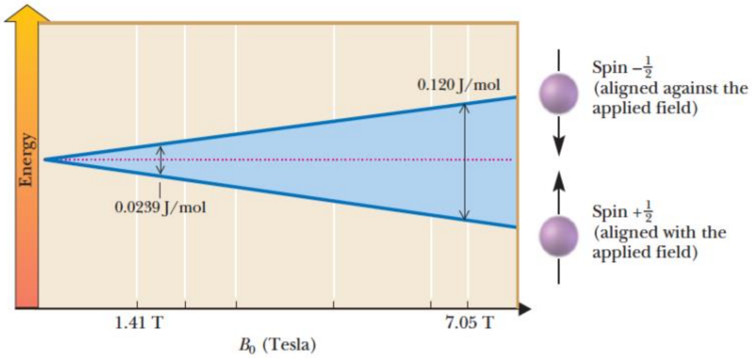
B. Atomic nuclei, like electrons, have a quantum mechanical property of "spin". Spin can be thought of as a small magnetic field around the nucleus created as if the positive charge of the nucleus were circulating.

C. NMR, nuclear magnetic resonance, is used to assign structures of organic molecules.

D. We care about the nuclei ^{1}H and ^{13}C since these are commonly found in organic molecules and they have spin quantum numbers of 1/2.

E. Nuclei with spin quantum number 1/2 are quantized in one of two orientations, "+1/2" (lower energy) or "-1/2"(higher energy) in the presence of an external magnetic field, that is, with and against the external field, respectively.

F. **The difference in energy between the +1/2 and -1/2 nuclear spin states is proportional to the strength of the magnetic field felt by the nucleus.**



G. Electron density is induced to circulate in a strong external magnetic field, which in turn produces a magnetic field that opposes the external magnetic field. This **shields** nuclei from the external magnetic field. The greater the electron density around a nucleus, the more shielded it is, and the lower the energy (frequency) of electromagnetic radiation required to flip its nuclear spin.

H. In the classic ^{1}H-NMR experiment, the molecule of interest is placed in solvent (the solvent has deuterium atoms in place of H atoms so the solvent molecules will not show up in the spectra, see R.) then is put in a spinning tube in a very strong magnetic field. The sample is exposed to radiofrequency irradiation and if it is of exactly the right frequency energy is absorbed and spins flip from +1/2 to -1/2 (come into resonance). The absorbed energy is plotted in the spectra.

I. All ^{1}H-NMR spectra are recorded as **chemical shift (∂, delta)** in the units of **ppm** (parts per million). Shielding magnetic field effects are around 1 millionth as large as the external magnetic field in which the sample is placed. Tetramethylsilane (TMS, $(CH_3)_4Si$)) is placed in the sample as a standard and assigned the value of 0.0 ppm. ***Warning the NMR scale is plotted "backwards", with <u>higher values to the left</u>!!***

Certain nuclei such as ^1H nuclei have a quantum mechanical property called spin that comes with an associated magnetic field.

^1H nuclei can exist in two different spin states, $+1/2$ and $-1/2$.

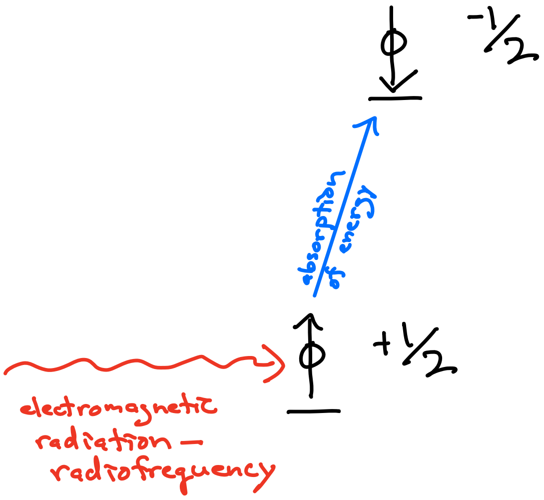
In a strong magnetic field, the nuclei with spin line up with $(+1/2)$ and against $(-1/2)$ the magnetic field.

Nuclei in the $+1/2$ spin state are of lower energy and nuclei in the $-1/2$ spin state are of higher energy in a magnetic field.

The difference in energy between the $+1/2$ and $-1/2$ spin states is directly proportional to the strength of the magnetic field experienced by the nuclei

Radiofrequency electromagnetic radiation of exactly the right energy (i.e. frequency) is absorbed by $+1/2$ spin state nuclei causing them to "flip" to the $-1/2$ spin state. $\Rightarrow$ A process called "resonance"

NMR experiment → place sample of a molecule in a very strong magnetic field



The energy absorption/nuclear spin flipping phenomenon is called "Resonance"

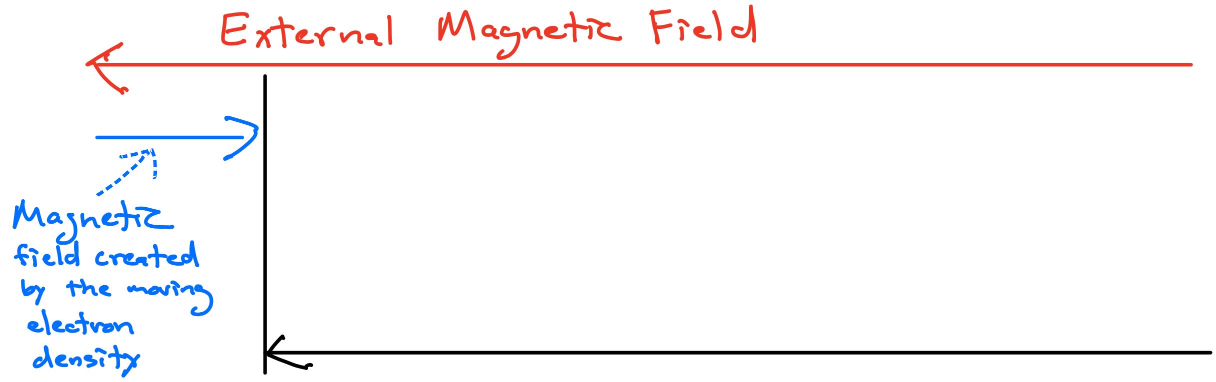
The ^1H nucleus of spin state $+\frac{1}{2}$ absorbs a quanta of energy of precisely the correct frequency and the nucleus is "excited" to the $-\frac{1}{2}$ spin state

Key Point → The energy of the of electronagnetic energy that is absorbed must match exactly the energy difference between the $+1/2$ and $-1/2$ nuclear spin states for resonance to happen

We monitor the energy that is absorbed by the nuclear spins as they flip

Shielding → explanation

The external magnetic field induces electron density to circulate, which creates its own small magnetic field that will always directly oppose the external magnetic field.



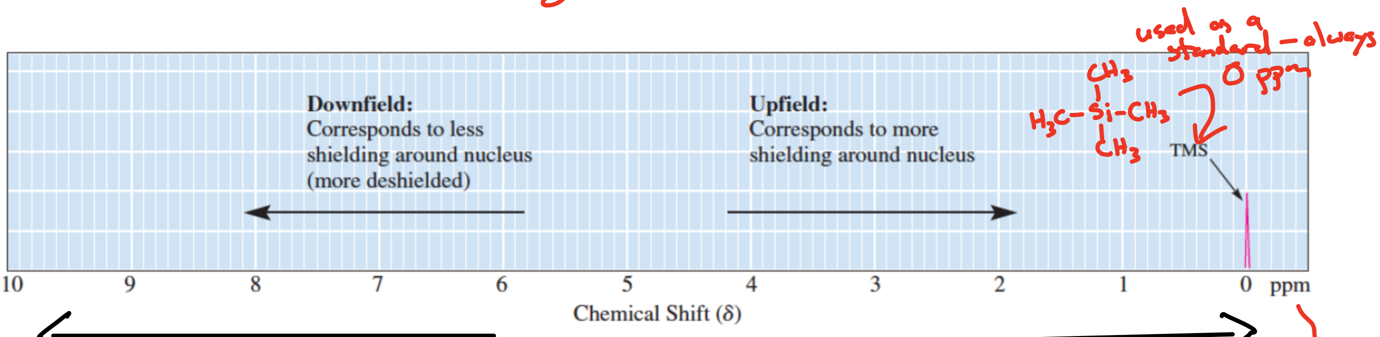
The magnitude of the magnetic field experienced by a nucleus under the electron density.

Shielding Bottom Line →

⇒ More electron density generates a larger opposing magnetic field so a nucleus under more electron density experiences a smaller magnetic field.

⇒ More electron density around a nucleus provides more shielding of the external magnetic field

Plot is backwards → larger values to the LEFT!



"parts per million"

Deshielding

Less electron density

Larger difference in energy between +½ and −½ nuclear spin state

Shielding

More electron density

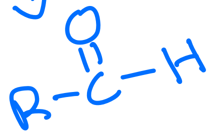
Smaller difference in energy between +½ and −½ nuclear spin state

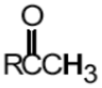
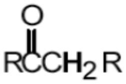
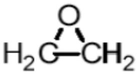
J. The hybridization state of carbon atoms attached to an H atom influences shielding in predictable ways by removing differing amounts of electron density around adjacent nuclei.

K. Electron density in pi bonds also has a large effect on H atom shielding because pi electrons are more free to circulate in an a magnetic field compared to electron density in sigma bonds. Geometry of the pi bond is important.

Table 13.3 The Effect of Hybridization on Chemical Shift

Type of Hydrogen (R = alkyl)	Name of Hydrogen	Chemical Shift (δ)
RCH_3, R_2CH_2, R_3CH sp^3	Alkyl	0.8–1.7
$R_2C{=}C(R)CHR_2$	Allylic	1.6–2.6
$RC{\equiv}CH$ sp	Acetylenic	2.0–3.0
sp^2 → $R_2C{=}CHR$, $R_2C{=}CH_2$	Vinylic	4.6–5.7
$RCHO$	Aldehydic	9.5–10.1


$R-\overset{O}{\overset{\|}{C}}-H$

Type of Hydrogen (R = alkyl, Ar = aryl)	Chemical Shift (δ)*	Type of Hydrogen (R = alkyl, Ar = aryl)	Chemical Shift (δ)*
		RCH_2OH	3.4-4.0
R_2NH	0.5-5.0	RCH_2Br	3.4-3.6
ROH	0.5-6.0	RCH_2Cl	3.6-3.8
RCH_3	0.8-1.0	 $R\overset{O}{\overset{\|}{C}}OCH_3$	3.7-3.9
RCH_2R	1.2-1.4	 $R\overset{O}{\overset{\|}{C}}OCH_2R$	4.1-4.7
R_3CH	1.4-1.7	RCH_2F	4.4-4.5
$R_2C{=}CRCHR_2$	1.6-2.6	$ArOH$	4.5-4.7
$RC{\equiv}CH$	2.0-3.0	$R_2C{=}CH_2$	4.6-5.0
 $R\overset{O}{\overset{\|}{C}}CH_3$	2.1-2.3	$R_2C{=}CHR$	5.0-5.7
 $R\overset{O}{\overset{\|}{C}}CH_2R$	2.2-2.6		3.3-4.0
$ArCH_3$	2.2-2.5	 $R\overset{O}{\overset{\|}{C}}H$	9.5-10.1
RCH_2NR_2	2.3-2.8	 $R\overset{O}{\overset{\|}{C}}OH$	10-13
RCH_2I	3.1-3.3		
RCH_2OR	3.3-4.0		

* Values are relative to tetramethylsilane. Other atoms within the molecule may cause the signal to appear outside these ranges.

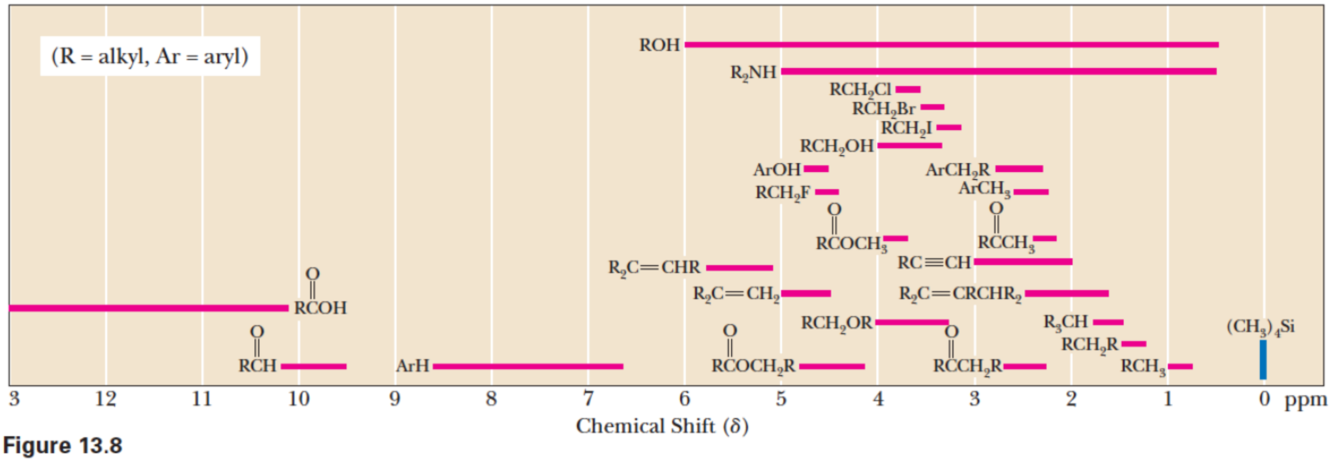
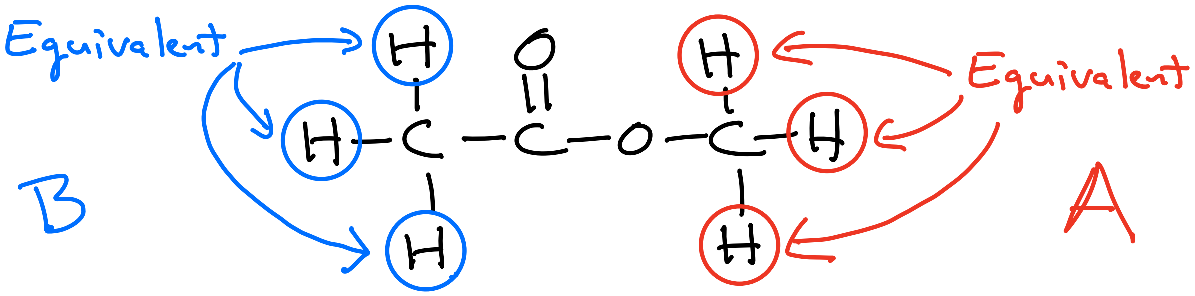
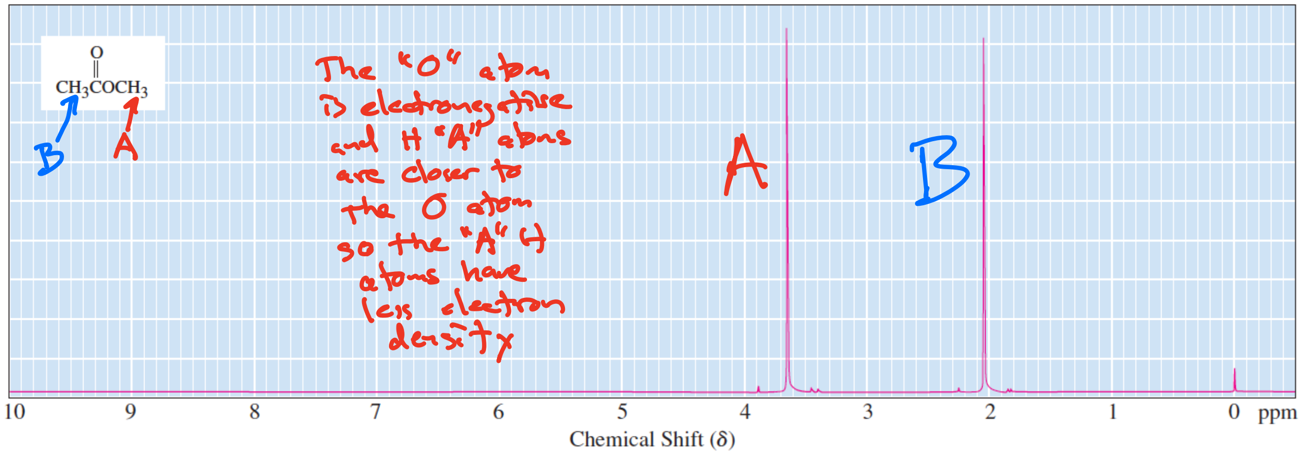


Figure 13.8
Average values of chemical shifts of representative types of hydrogens. These values are approximate. Other atoms or groups in the molecules may cause signals to appear outside of these ranges.

L. Chemically **equivalent** H atoms give rise to the same ^{1}H-NMR signal. **Equivalent** H atoms have the same chemical environment because they are bonded to the same freely rotating *sp*^{3} C atom (molecular motion, nanosecond, is fast compared the time it takes for a spin to flip, microsecond) OR they are equivalent due to symmetry in the molecule.



Less Electron Density ←

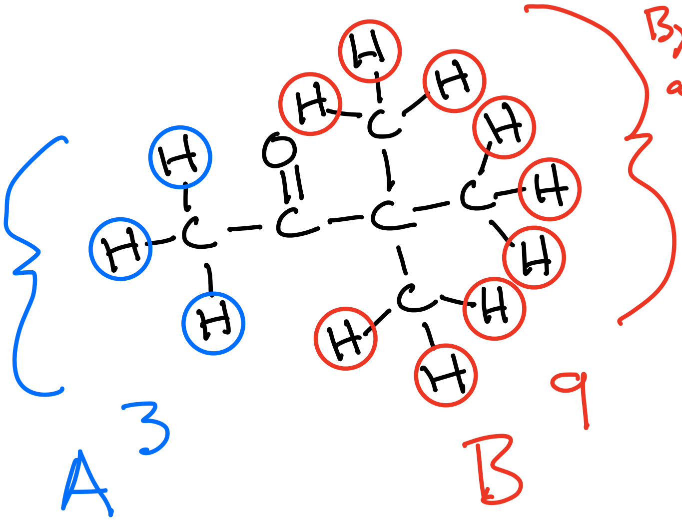


The "O" atom is electronegative and H "A" atoms are closer to the O atom so the "A" H atoms have less electron density

Figure 13.5
^{1}H-NMR spectrum of methyl acetate

M. The area of a ^{1}H-NMR signal is proportional to the number of equivalent H atoms that give rise to that signal.

These 3 H atoms are equivalent



By symmetry all 9 of these H atoms are equivalent

The entire molecule will have 2 signals with a ratio of areas equal to 3:9 or 1:3

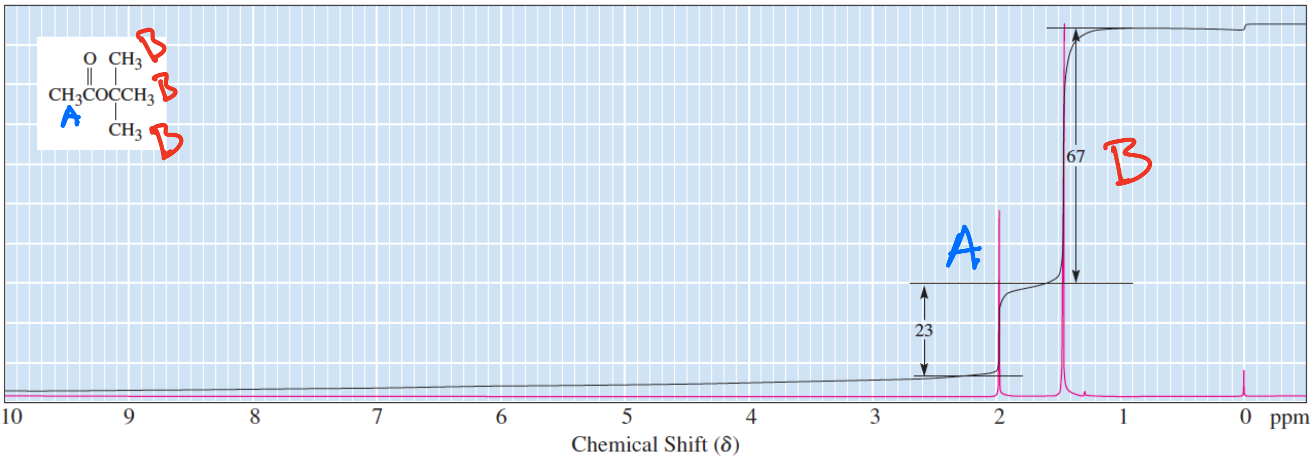


Figure 13.7
^{1}H-NMR spectrum of *tert*-butyl acetate showing the integration. The total vertical rise of 90 chart divisions corresponds to 12 hydrogens, 9 in one set and 3 in the other.

Surprising Fact → The absolute energy difference between ^1H nuclei in a $+1/2$ and $-1/2$ spin state is so small → according to the Boltzmann distribution, at any one time there is only a small excess of ^1H nuclear spins in the $+1/2$ spin state

Nearly 1:1

The magnetic field produced by a ^1H nucleus in a $+1/2$ spin state is different than that produced by a ^1H nucleus in a $-1/2$ spin state.

Definition → "Adjacent" means no more than 3 bonds away.

N. Adjacent nuclei have magnetic fields associated with their spins. The spins of equivalent adjacent nuclei can be either +1/2 or -1/2, and at room temperature they are found in about a 50:50 mixture at any given nucleus (very slight excess of lower energy +1/2). These can add to give n+1 different spin **combinations** in the proportions predicted by Pascal's triangle. Each different spin combination produces a different magnetic field, which leads to n+1 splittings in the peaks of the NMR spectra of the adjacent (no more than three bonds away) nuclei.

Cl is less electronegative than F, so there will be more electron density around H_B compared to H_A → The H_B signal will be closer to 0 than the signal for H_A