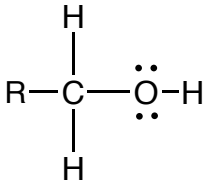
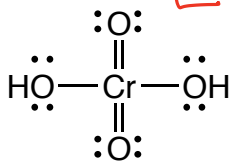
Chromic Acid Oxidation of Alcohols

Called "Jones Reagent" ($CrO_3 + H_2O$ or K_2CrO_7) + H_2SO_4

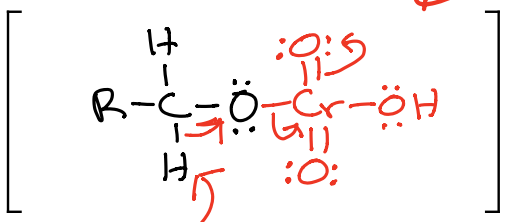
Not responsible for first step

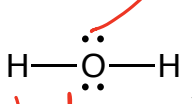


1° Alcohols



"H_2CrO_4" or "Chromic Acid"

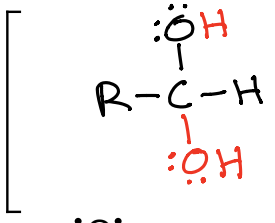




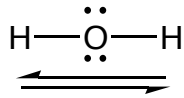
Take a proton away and break a bond

Aldehyde

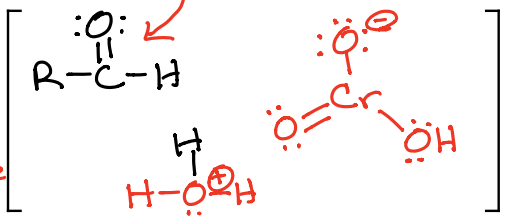
Not responsible for this step

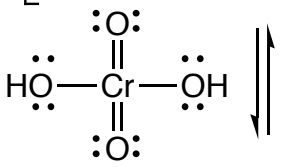


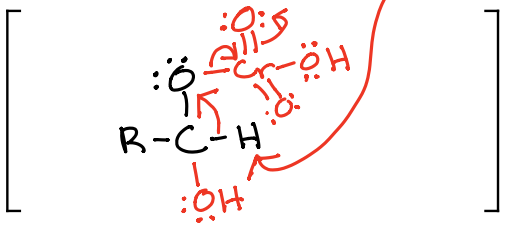
Called a geminal diol

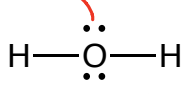


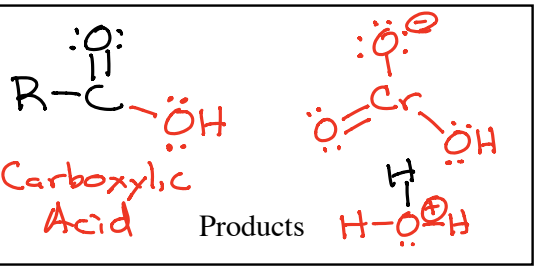
Water reacts with aldehyde – will learn next semester







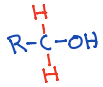




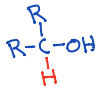
Carboxylic Acid

Products

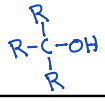
Summary:



1° alcohols ⇒ Carboxylic Acid → 



2° alcohols ⇒ Ketone → 

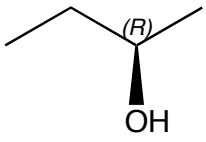


3° alcohols ⇒ NO REACTION

Regiochemistry: N/A

Stereochemistry: N/A

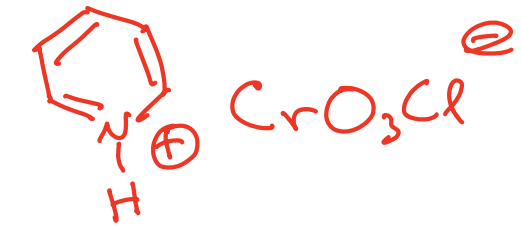
Example:



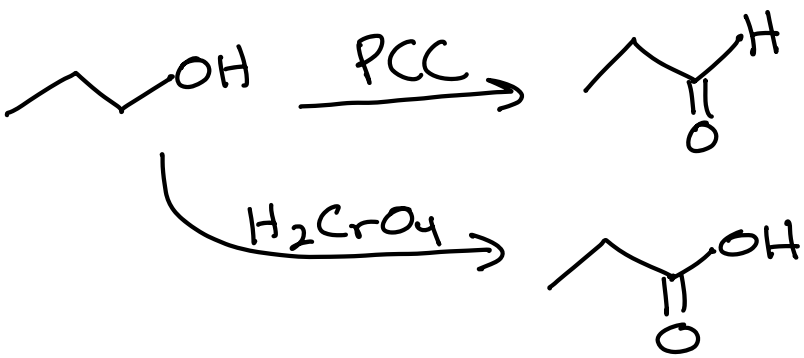
H_2CrO_4

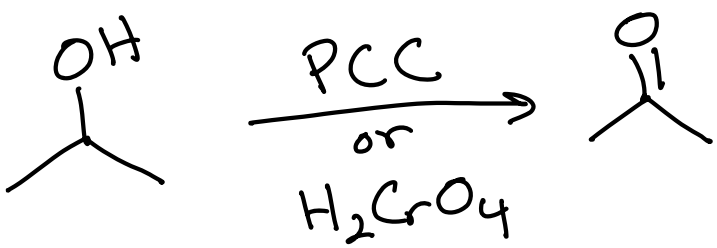
Ketone

A chromic acid-like reagent WITHOUT WATER will stop at the when using a as starting material



PCC





<u>Organic Chemistry</u> 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

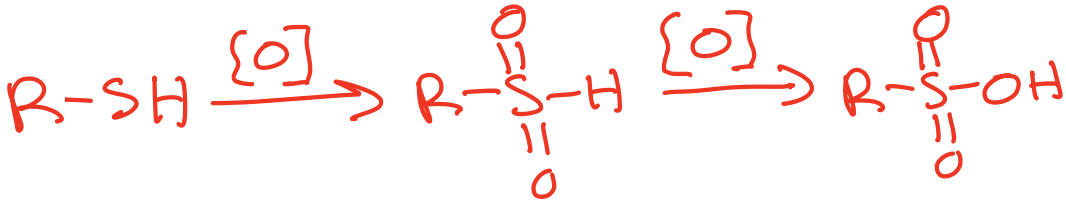
You will learn reactions that can make antifreeze from vodka. 11/12/25

You will learn a reaction that can make nail polish remover from rubbing alcohol.

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.

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.

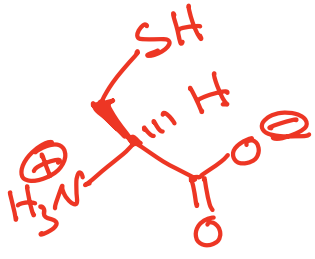
Thiols → R–S–H



In the presence of O_2:

$$2\ R\text{-}SH + \tfrac{1}{2}O_2 \longrightarrow R\text{-}S\text{-}S\text{-}R + H_2O$$

Dissulfide Bond



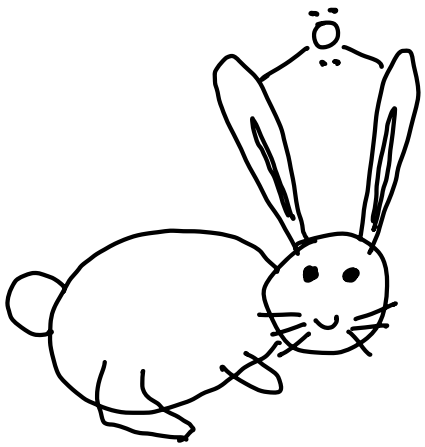
The amino acid cysteine (Cys)

Dissulfide bonds between cysteine residues that are far apart in the sequence, but overlap in three-dimensions, provide covalent links that stabilize folded protein structures

Ethers → R–Ö–R

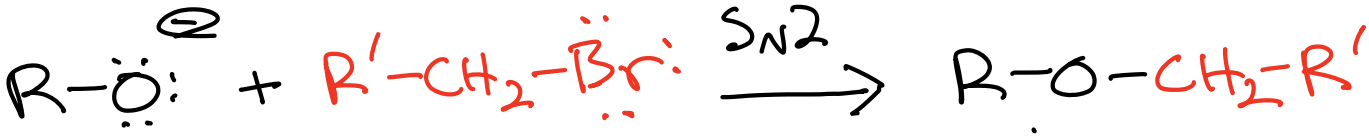
↳ Unreactive under most conditions

Diethyl ether



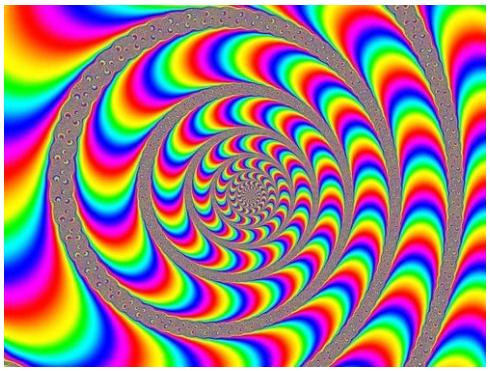
How to make ethers

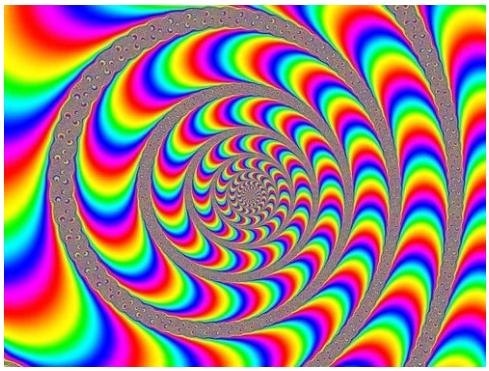
Williamson Ether Synthesis

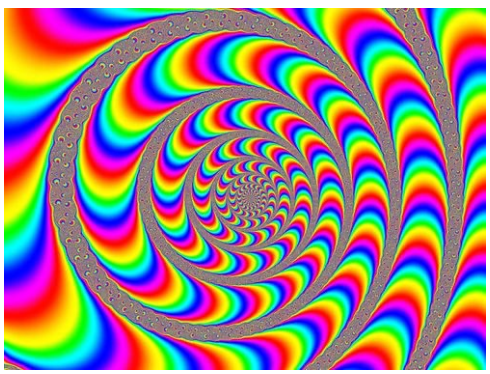


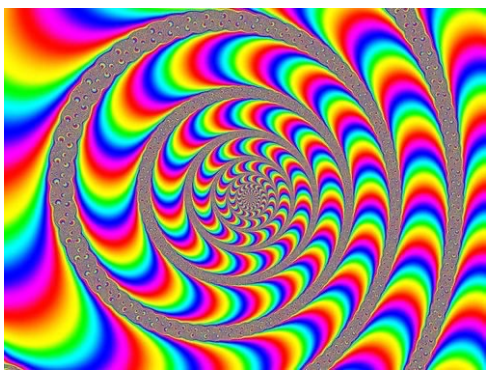
You can also react alkenes with alcohols in the presence of catalytic amounts of H_2SO_4 to make ethers:

Flashback!!



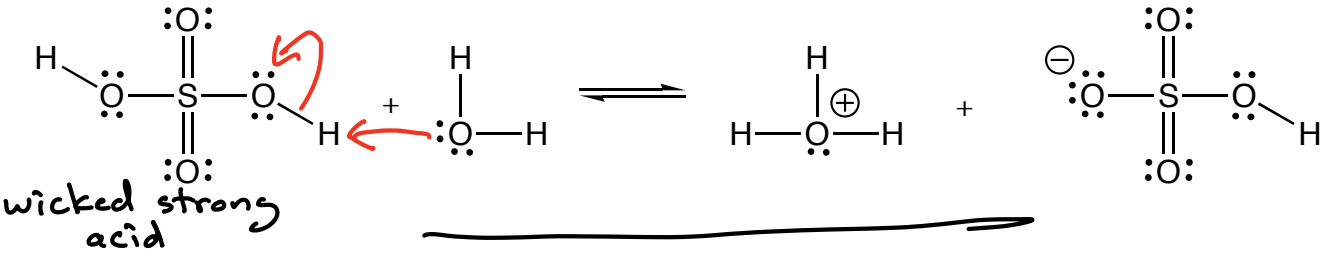


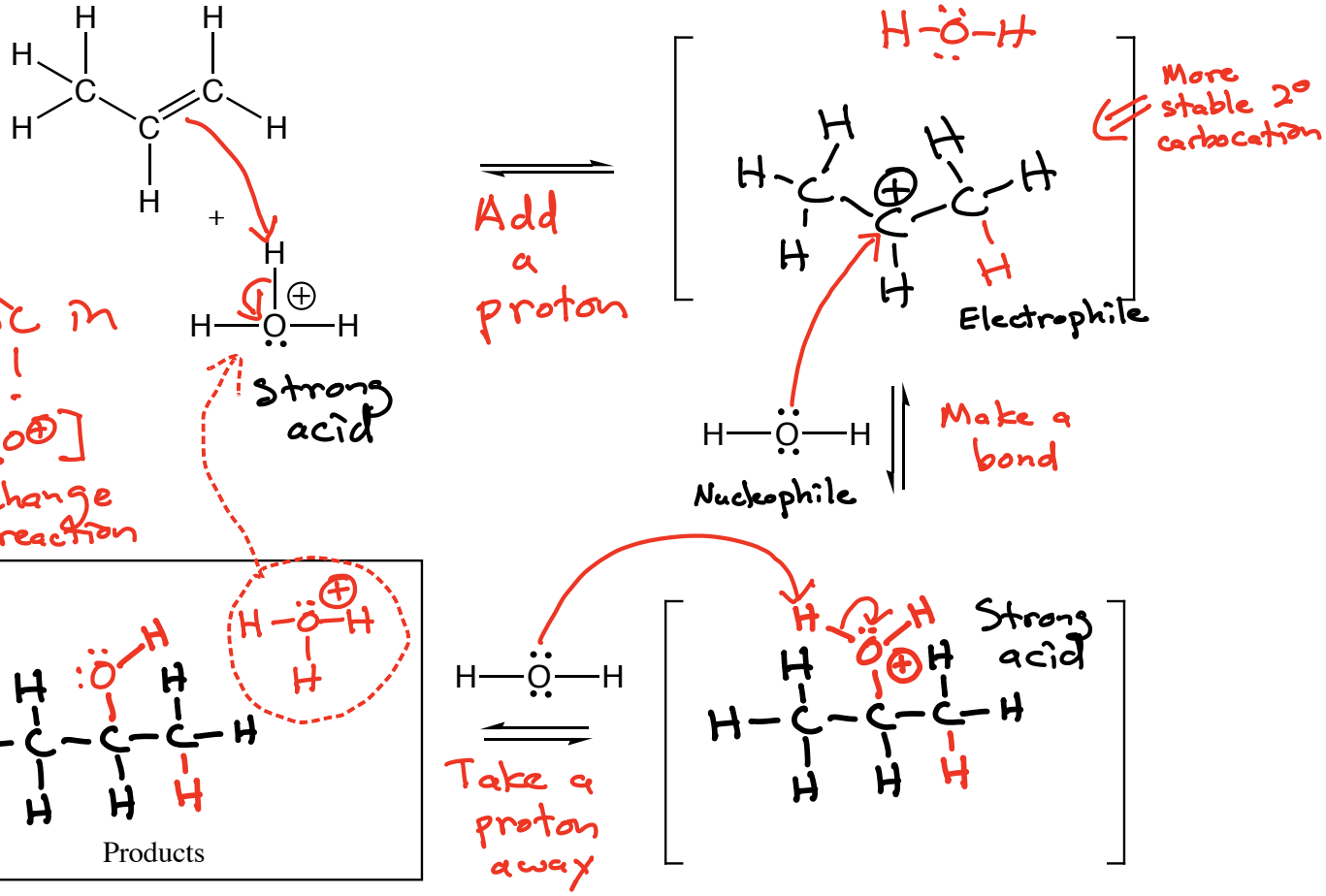




Flashback!!

Acid-catalyzed Hydration of an Alkene

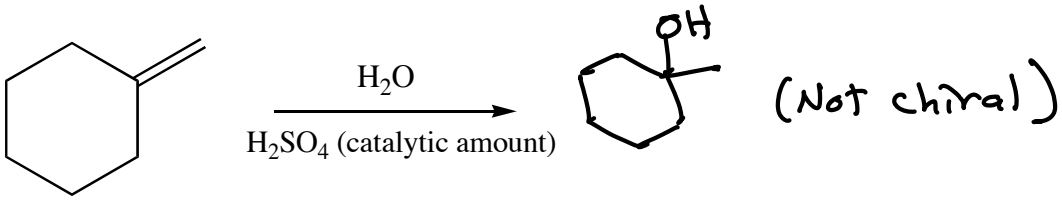




Catalytic in Acid!
⇒ The $[H_3O^{\oplus}]$ does not change during the reaction

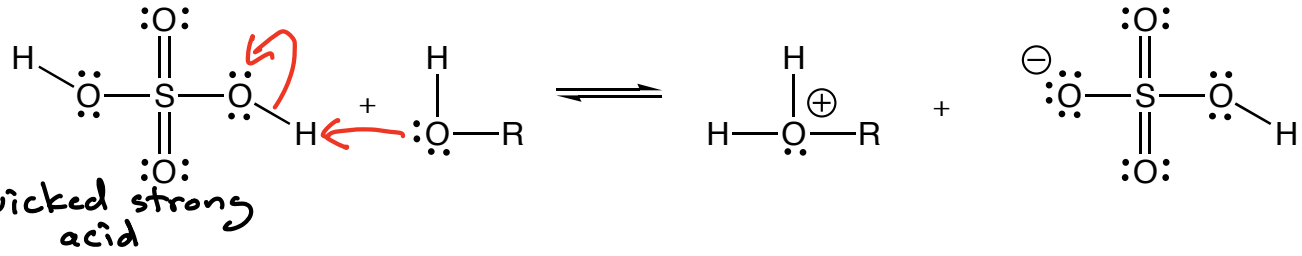
Summary:	Proton adds to make a carbocation intermediate, water attacks to make a new bond, take a proton away to make the product alcohol. Catalytic in $H_3O^{\oplus}$
Regiochemistry:	Markovnikov's Rule
Stereochemistry:	Mixed (time capsule)

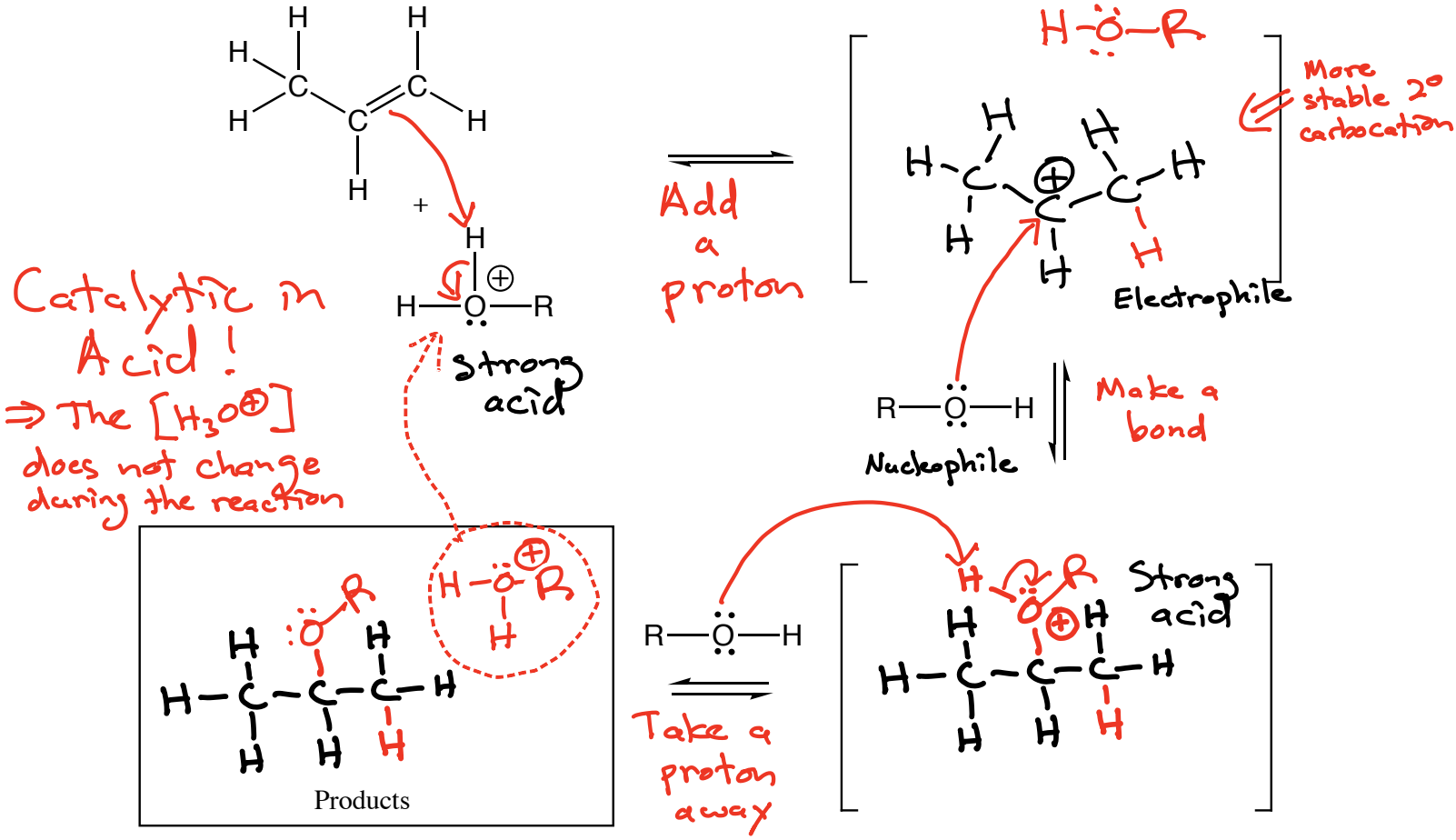
Example:



-OH on more substituted C atom ⇒ Markovnikov's Rule

Acid-catalyzed Reaction of an Alcohol with an Alkene



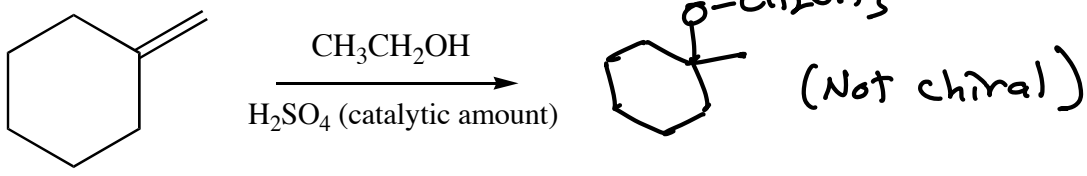


Summary: Proton adds to make a carbocation intermediate, alcohol attacks to make a new bond, take a proton away to make the product ether. Catalytic in $H_3O^{\oplus}$

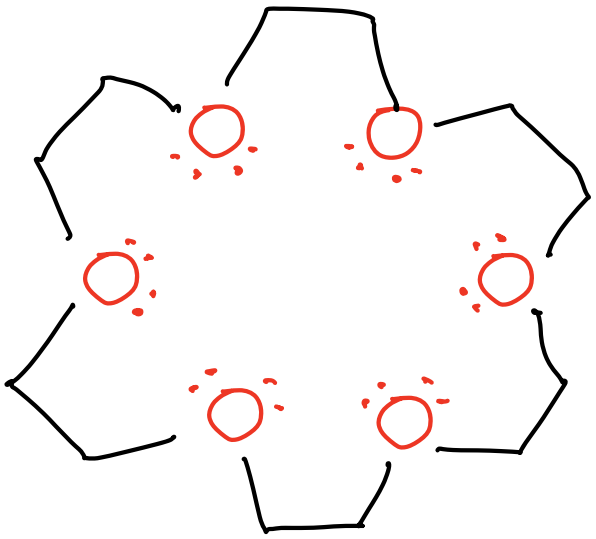
Regiochemistry: Markovnikov's Rule

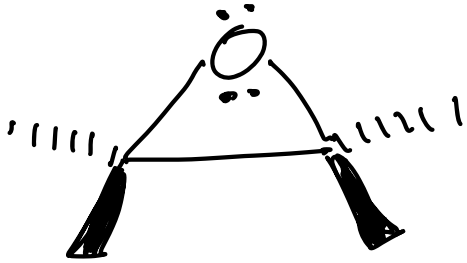
Stereochemistry: Mixed

Example:



Crown Ethers → bind cations based on



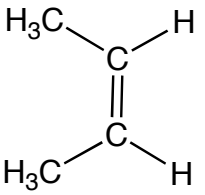


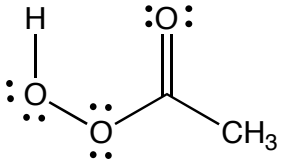
Epoxide

Important because they can be formed from alkenes or halohydrins AND

Epoxides are also involved in a number of biological processes including oxidative damage

Epoxide Formation





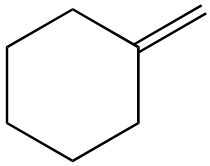
Products

Summary: Alkenes react with peracids in a single concerted step

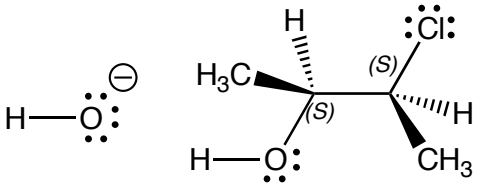
Regiochemistry: N/A

Stereochemistry: Mixed when new chiral centers are created

Example:



CH_3CO_3H



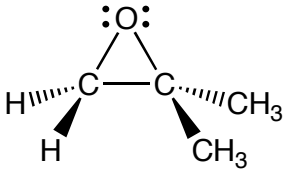
Products

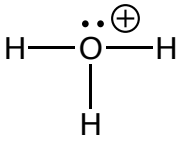
Summary: Halohydrins react in base to give the alkoxide that reacts antiperiplanar to give the epoxide.

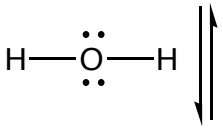
Regiochemistry: N/A

Stereochemistry: Antiperiplanar transition state

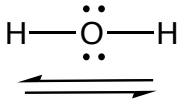
Acid-Catalyzed Epoxide Opening







Products

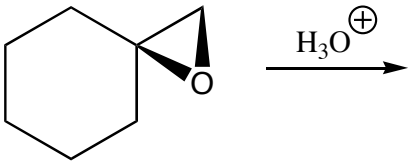


Summary: In acid, epoxides are protonated to give a highly reactive cation intermediate that reacts with nucleophiles at the more highly substituted carbon atom

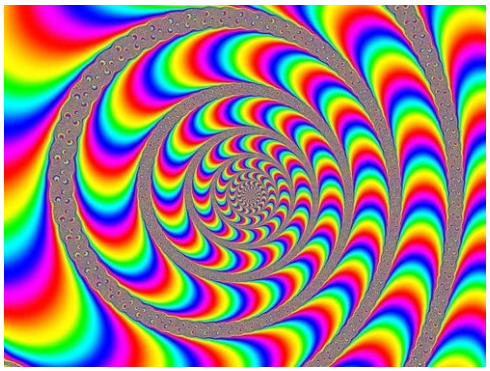
Regiochemistry: "Markovnikov" Attack at more highly substituted C atom

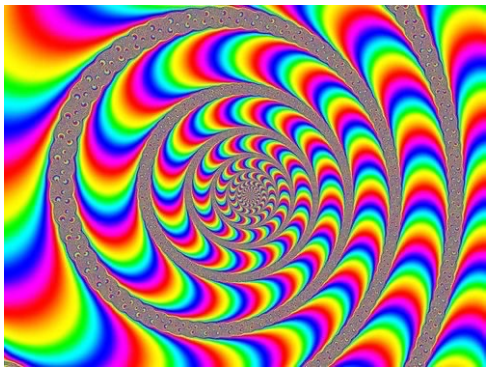
Stereochemistry: Anti

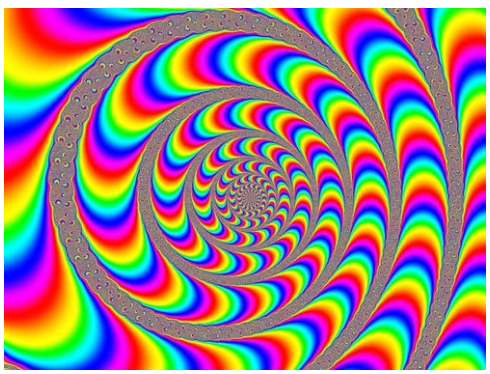
Example:

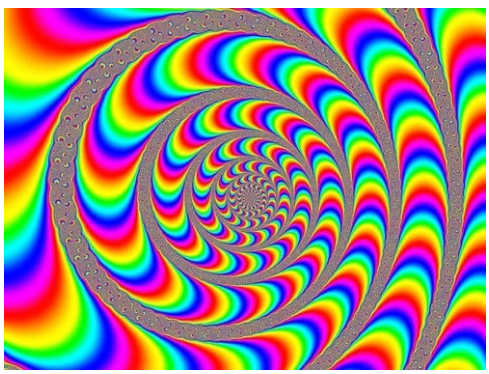


Flashback!!



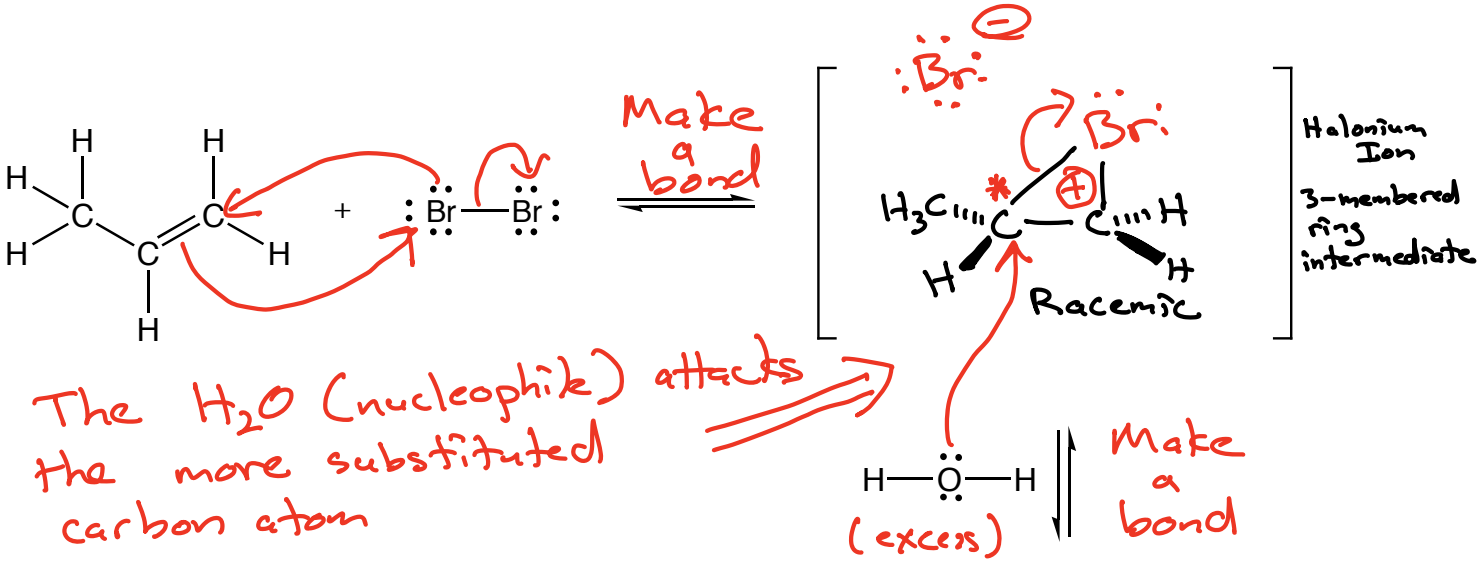


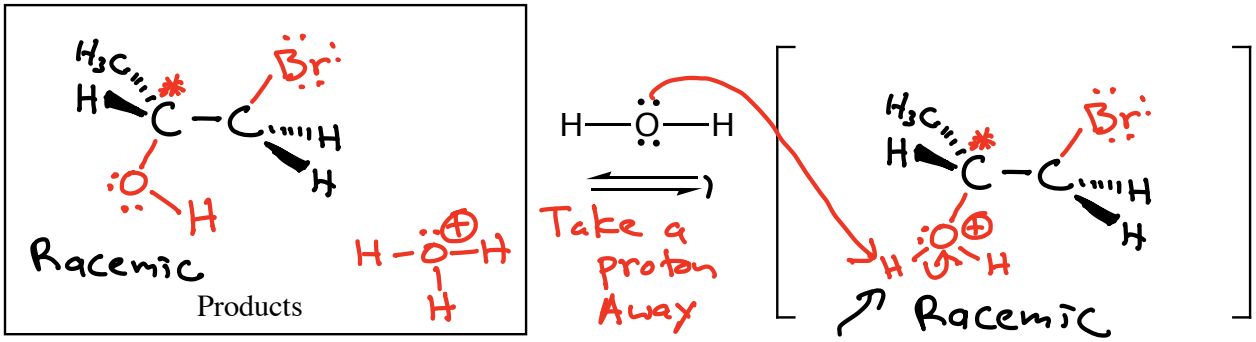




Flashback!!

Alkene Hydrohalogenation





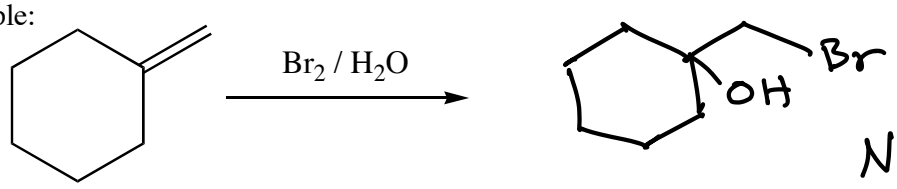
pH drops during the reaction!

Summary: Alkene reacts with X_2 to give a 3-membered ring intermediate (halonium ion) → H_2O attacks the more substituted C atom and we take a proton away to give the halohydrin product.

Regiochemistry: Markovnikov (OH on more substituted C atom)

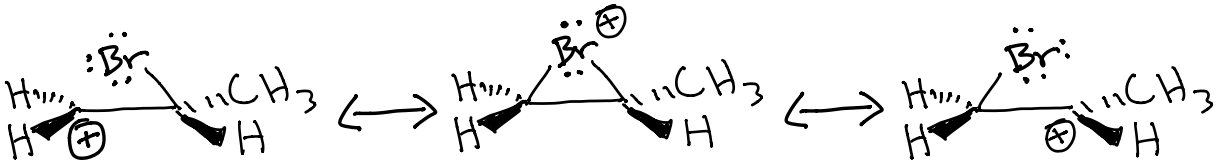
Stereochemistry: Anti

Example:



Not Chiral

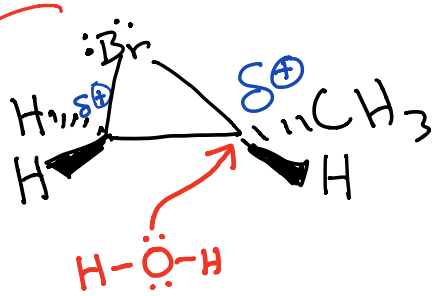
Flashback → Halohydrin Mechanism



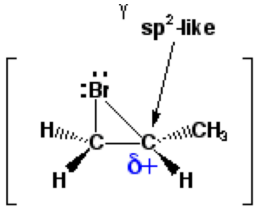
Minor Contributor

Major Contributor

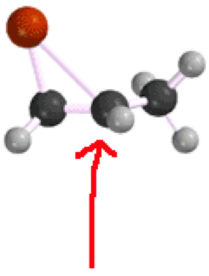
Resonance Hybrid

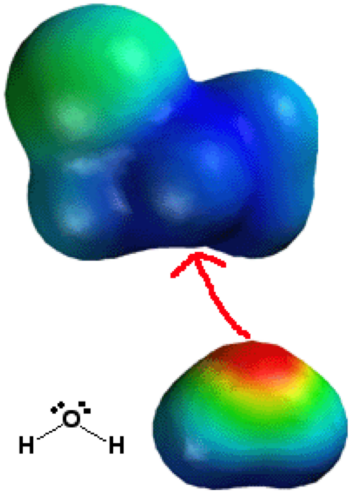


Water attacks the more substituted carbon atom because there is more partial ⊕ charge



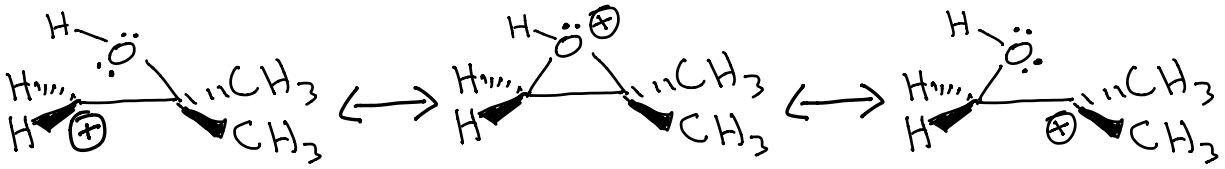
Resonance hybrid

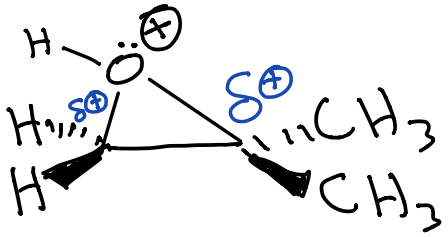


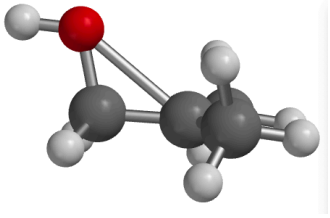


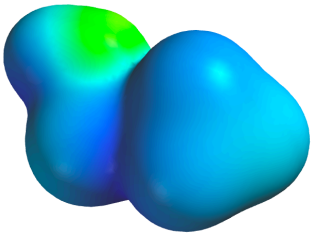
Nucleophiles Attack the More Positively-Charged Carbon Atom From This Face Leading to Markovnikov Regiochemistry and Trans Stereochemistry of Addition

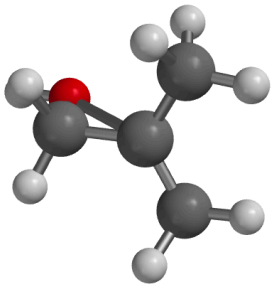
Epoxide in acid

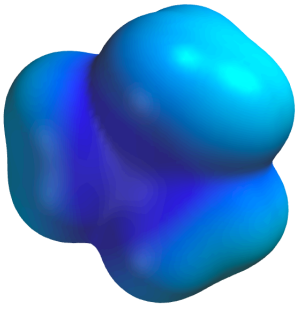




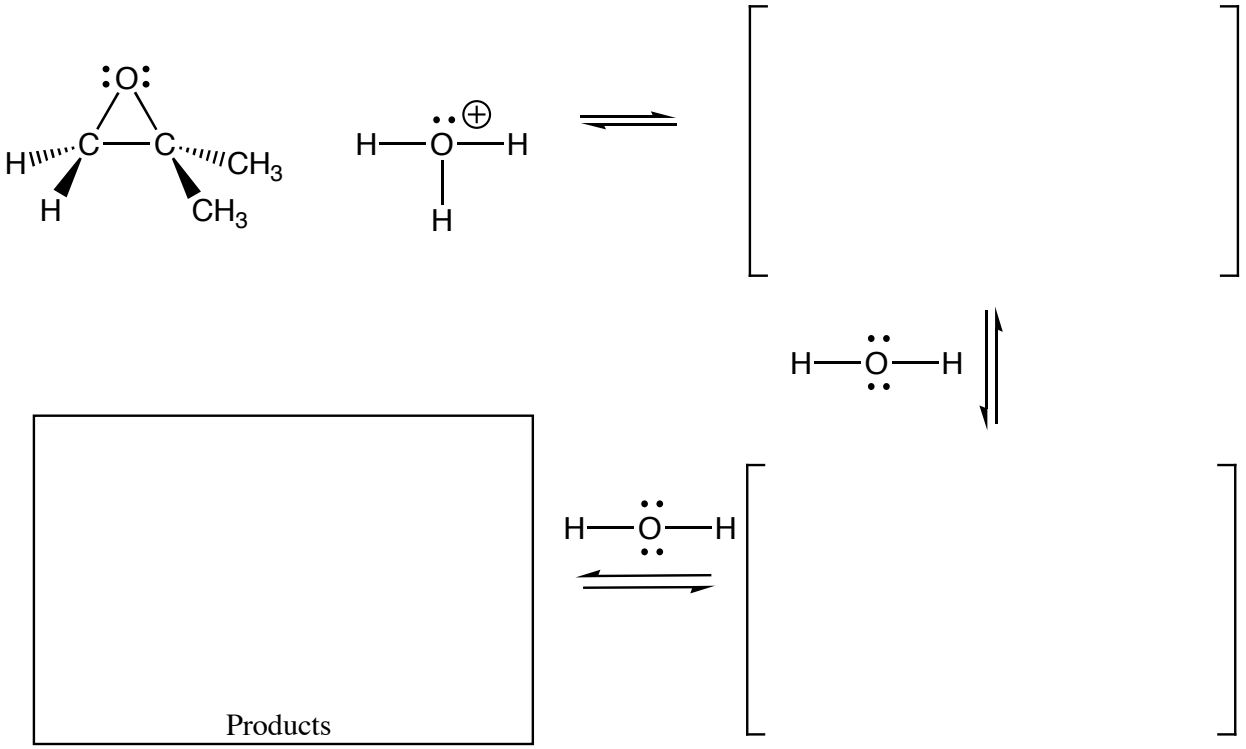






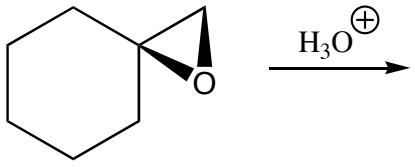


Acid-Catalyzed Epoxide Opening

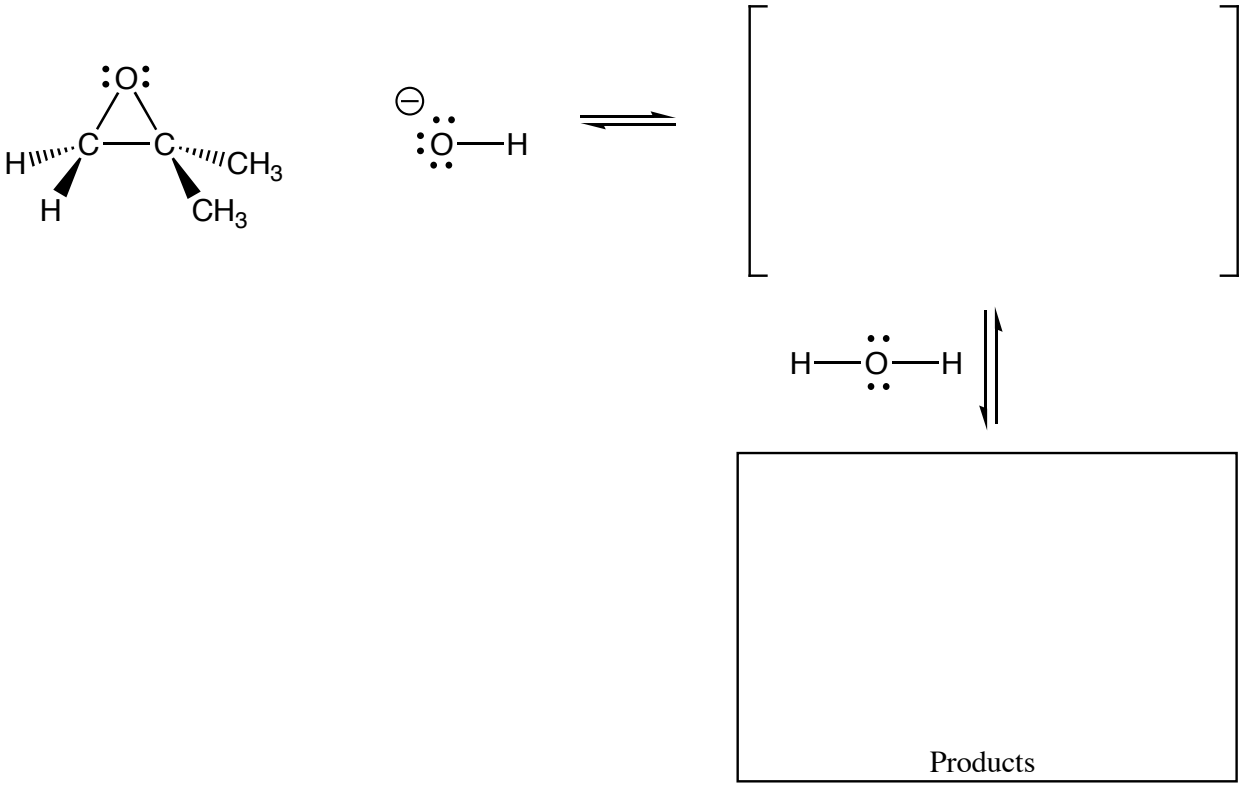


Summary:	In acid, epoxides are protonated to give a highly reactive cation intermediate that reacts with nucleophiles at the more highly substituted carbon atom
Regiochemistry:	"Markovnikov" Attack at more highly substituted C atom
Stereochemistry:	Anti

Example:

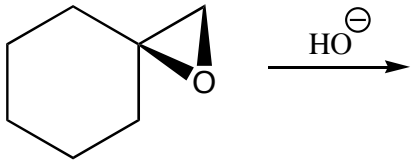


Nucleophilic ~~Base Promoted~~ Epoxide Opening

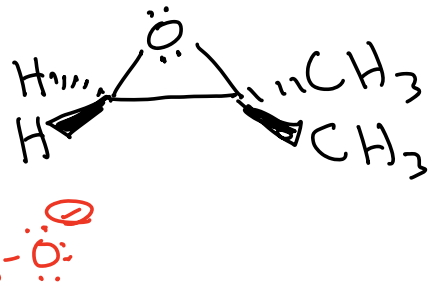


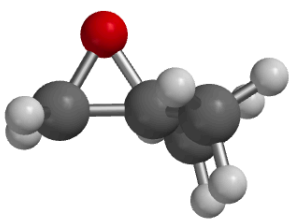
Summary:	Epoxides add strong nucleophiles at the less hindered carbon atom
Regiochemistry:	Less hindered (non-Markovnikov)
Stereochemistry:	Anti addition

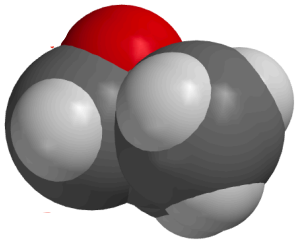
Example:



Epoxide reacting with nucleophile

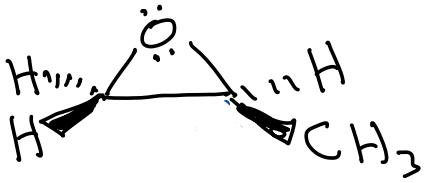






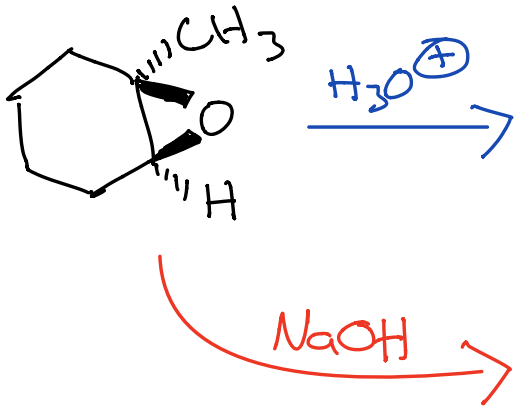
H-O⊖

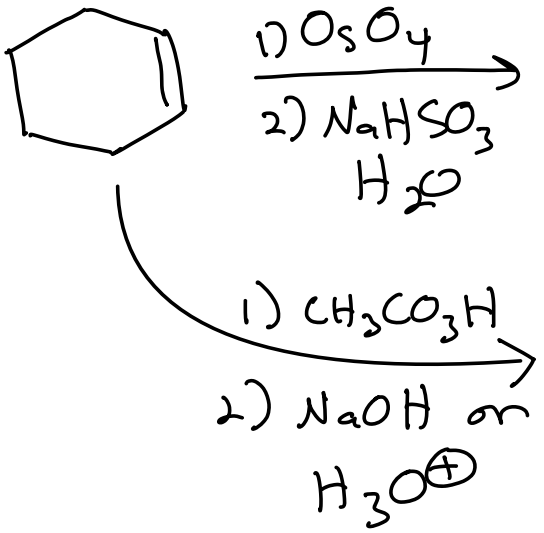
Watch out for the stereochemistry!



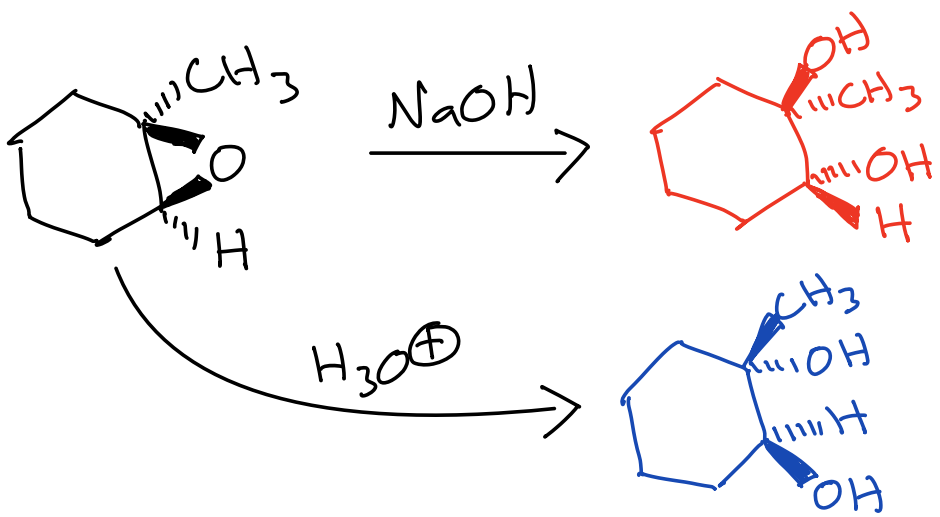
$H_3O^{\oplus}$ →

NaOH →

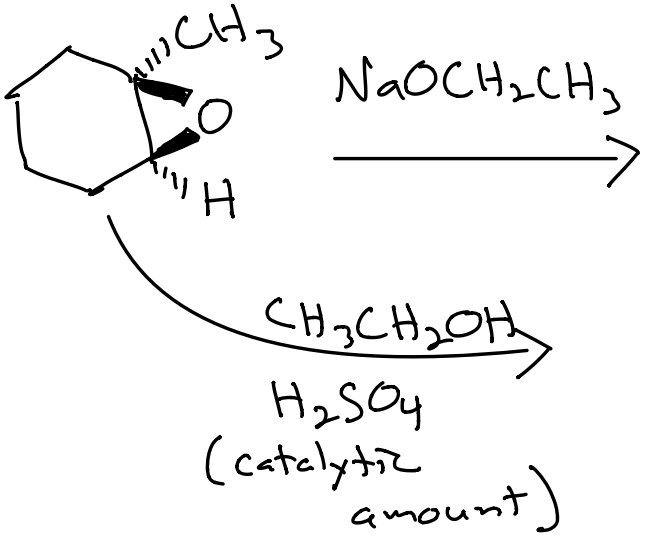

CH3
O
H
H3O⊕
NaOH



Watch out for the stereochemistry!

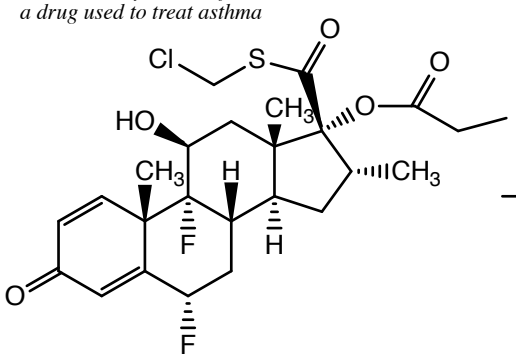


Works with alkoxides and alcohols as well



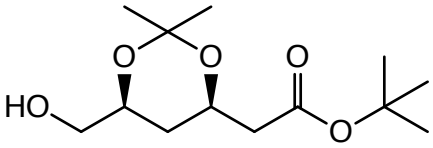
Reactions in the Context of Complex Molecules

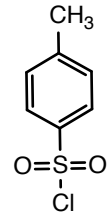
Used in the synthesis of Fluticasone (Flonase), a drug used to treat asthma



NaI

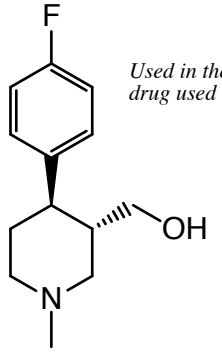
acetone





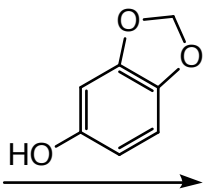
Used in the synthesis of Lipitor

NaCN



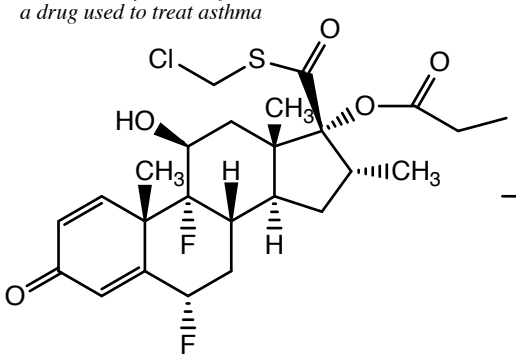
Used in the synthesis of Paxil, a drug used to treat depression

$SOCl_2$



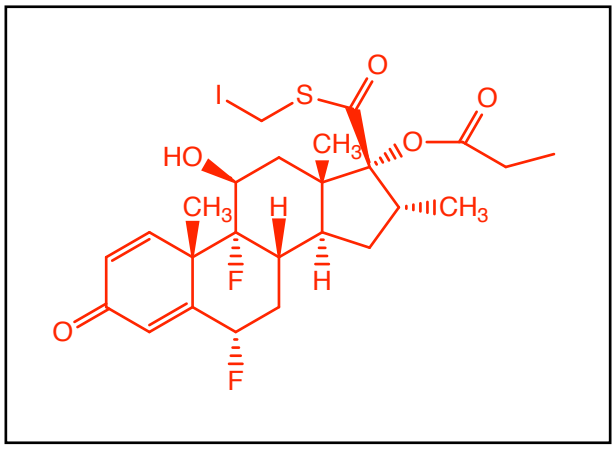
Reactions in the Context of Complex Molecules

Used in the synthesis of Fluticasone (Flonase), a drug used to treat asthma

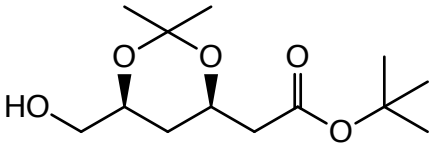


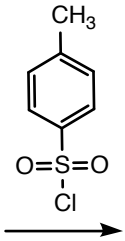
NaI

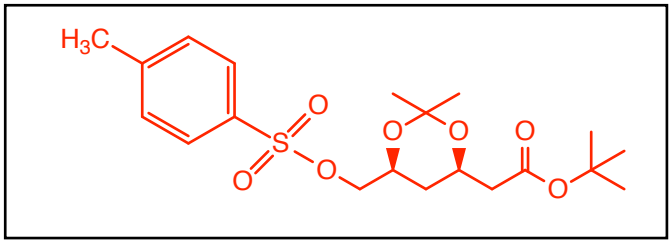
acetone



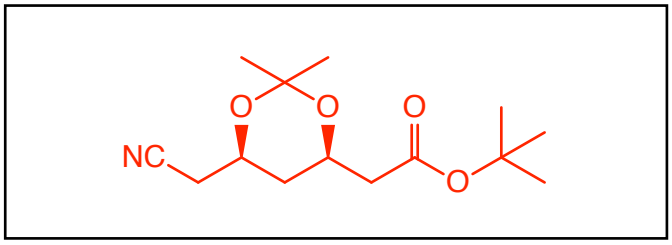
Used in the synthesis of Lipitor



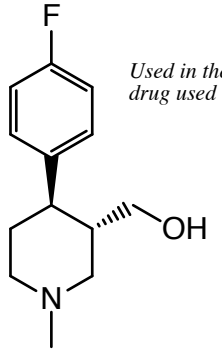




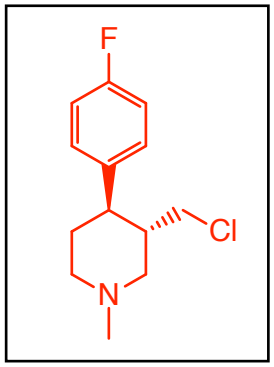
NaCN

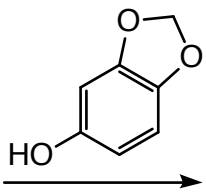


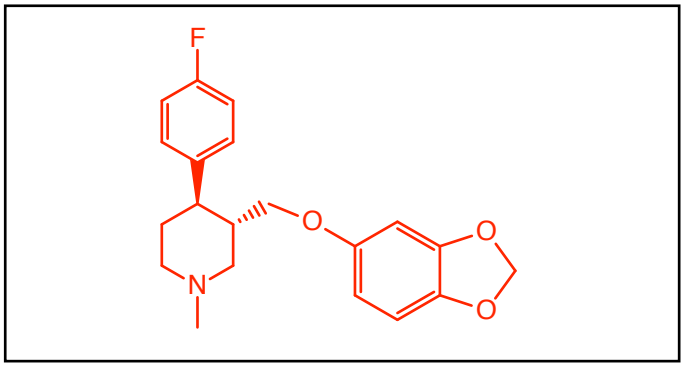
Used in the synthesis of Paxil, a drug used to treat depression



$SOCl_2$

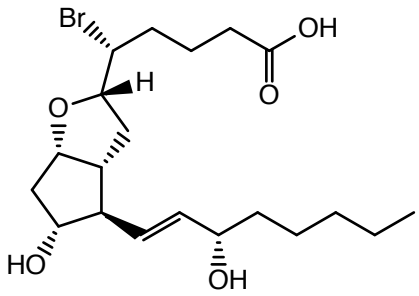






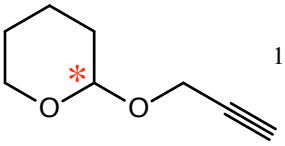
Reactions in the Context of Complex Molecules

Used in the synthesis of several protaglandins

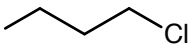


excess KO*t*Bu
*t*BuOH

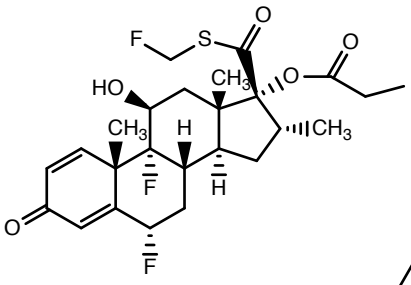
Used in the synthesis of protaglandin C_2



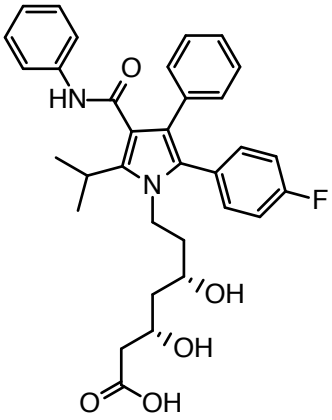
(racemic)

1. 1 eq. $NaNH_2$ THF (ether solvent)
2. 

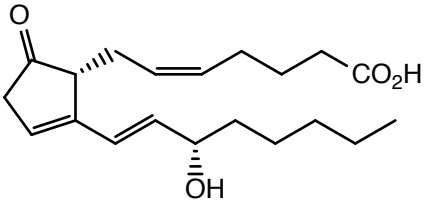
DMSO (polar aprotic solvent) NaCN



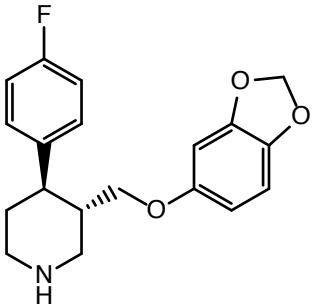
Fluticasone (Flonase)



Atorvastatin (Lipitor)



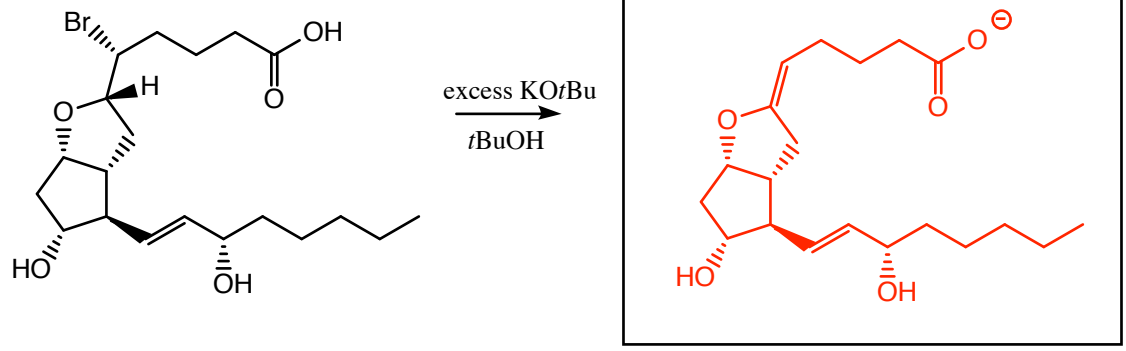
Prostaglandin C_2



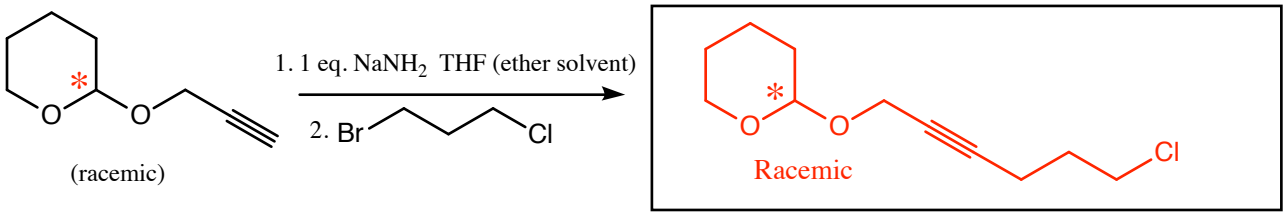
Paroxetine (Paxil)

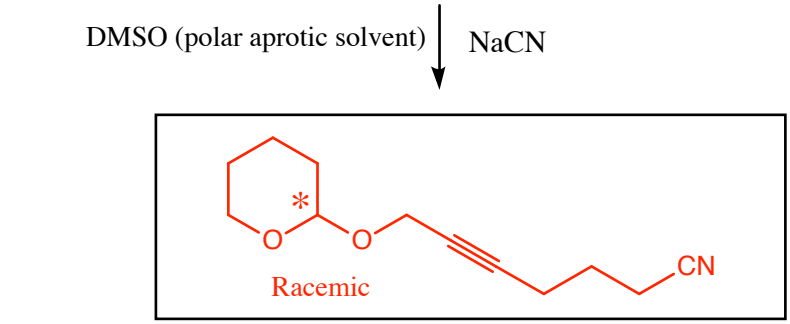
Reactions in the Context of Complex Molecules

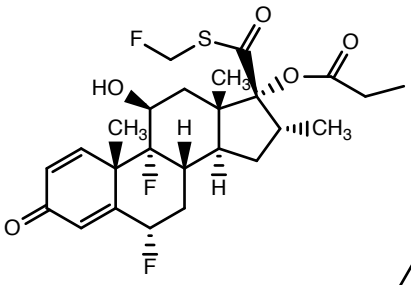
Used in the synthesis of several protaglandins



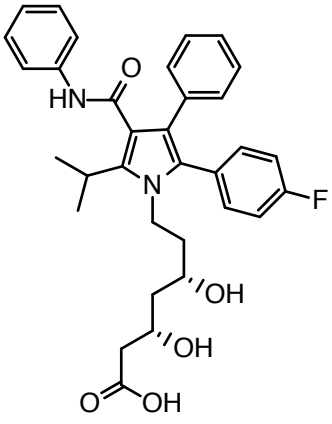
Used in the synthesis of protaglandin C_2



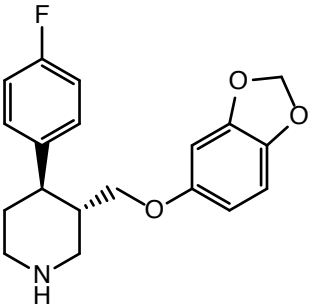




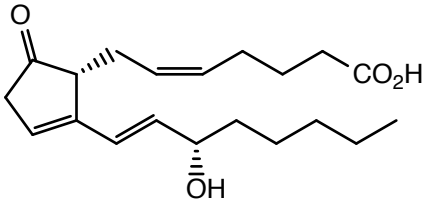
Fluticasone (Flonase)



Atorvastatin (Lipitor)



Paroxetine (Paxil)



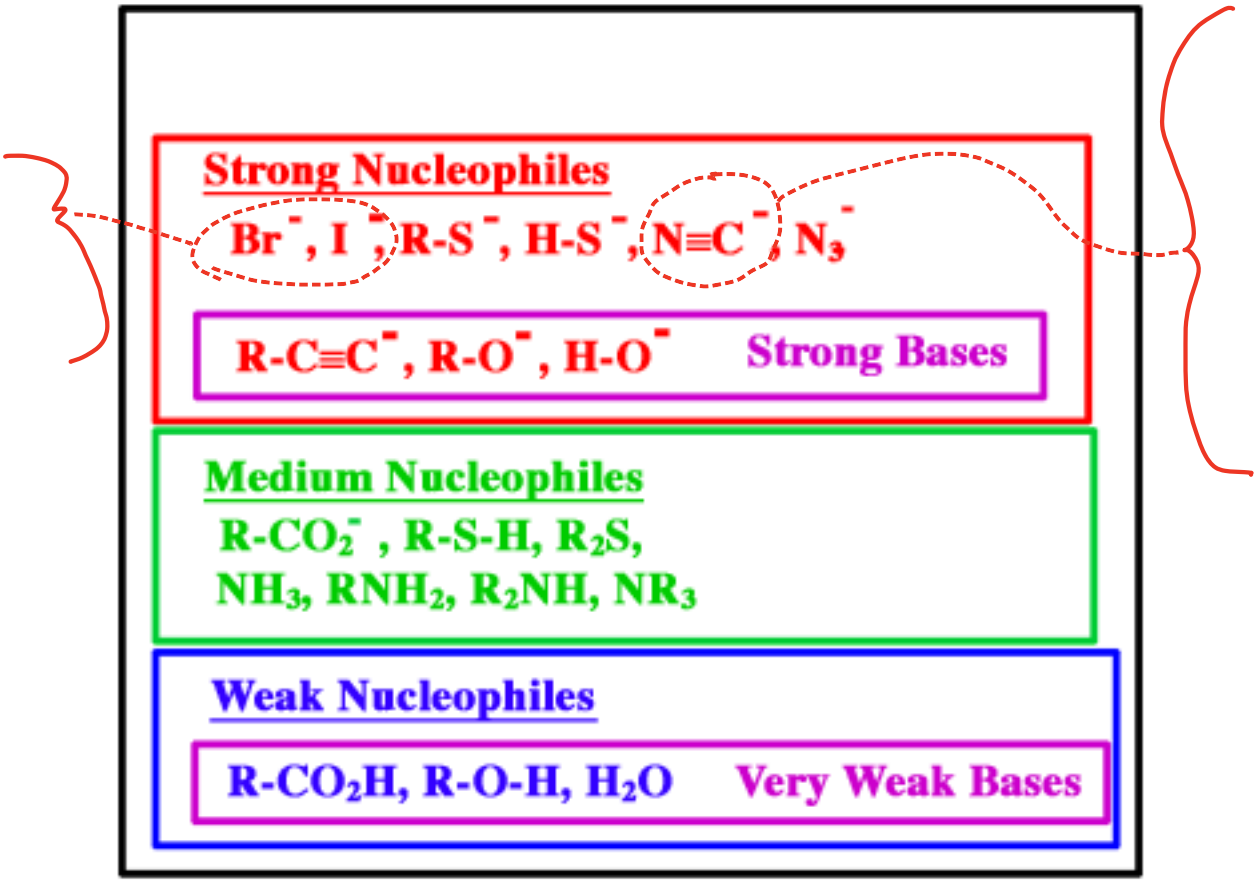
Prostaglandin C_2

Here are some things I wish I had said when we were talking about substitution and elimination reactions:

Good leaving group →

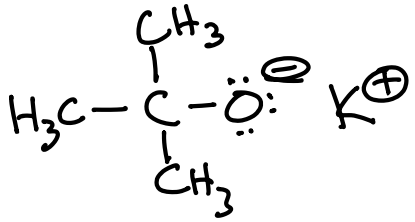
Nucleophiles → not simple to explain what makes a good nucleophile → the Table for reference

Table of Nucleophiles



Special Case

***Tert*-Butoxide ($tBuO^-$) is a strong base, but is not a nucleophile due to steric hindrance.**



"KOtBu" or "$tBuO^-$"

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.

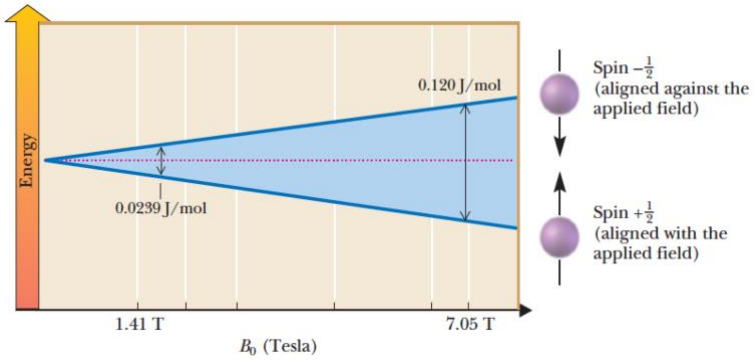
B. Atomic nuclei, like electrons, have a quantum mechanical property of "spin". Spin can be thought of as a small magnetic field around the nucleus created as if the positive charge of the nucleus were circulating.

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 higher values to the left!!***

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

.

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

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

Nuclei in the are of lower energy and nuclei in the are of higher energy in a magnetic field.

The between the $+1/2$ and $-1/2$ spin states

experienced by the nuclei

of exactly the right energy (i.e. frequency) is by $+1/2$ spin state nuclei causing them to to the $-1/2$ spin state.

NMR experiment →

 $-\frac{1}{2}$

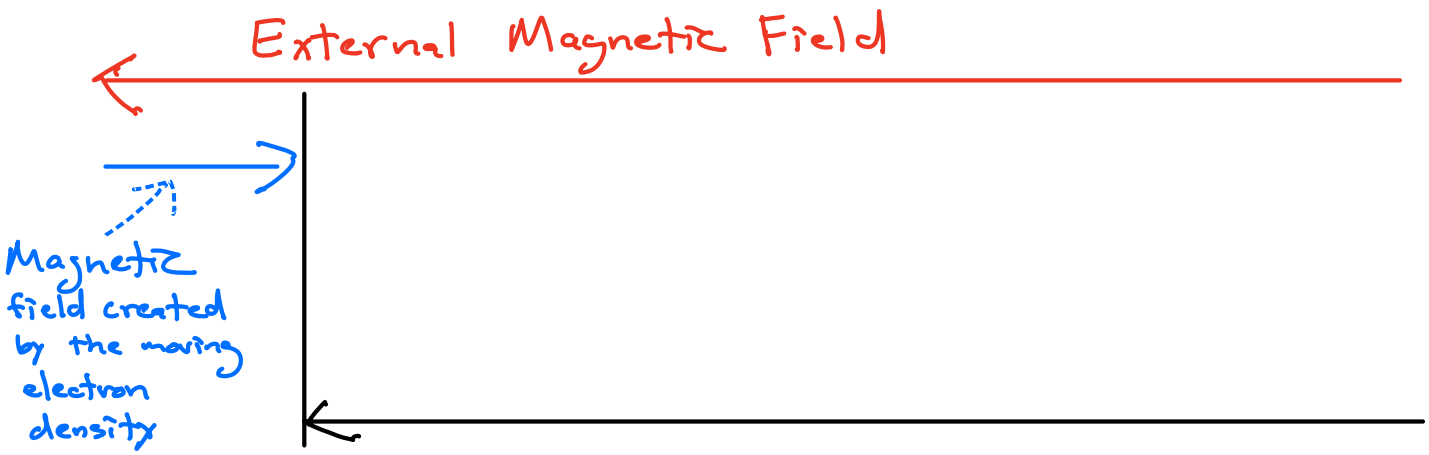
 $+\frac{1}{2}$

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 →

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

Shielding →



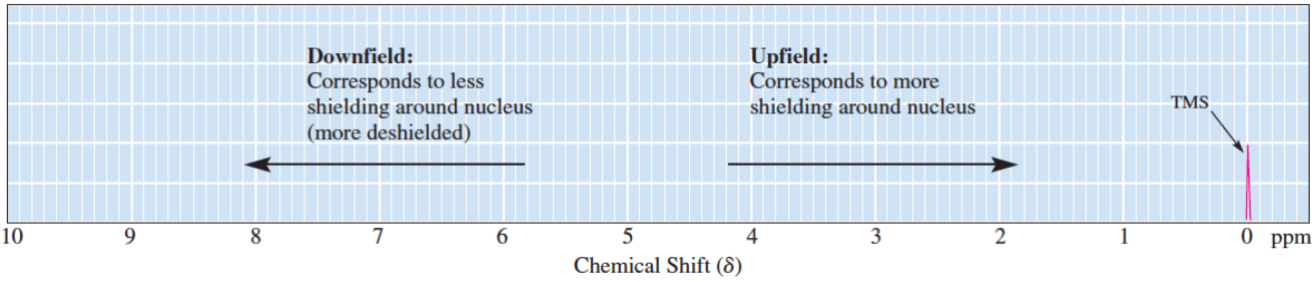
The magnitude of the magnetic field experienced by a nucleus under the electron density.

Shielding Bottom Line ⟶

⇒ More electron density generates a

so a nucleus under more electron density experiences a

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



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	Alkyl	0.8–1.7
$R_2C{=}C(R)CHR_2$	Allylic	1.6–2.6
$RC{\equiv}CH$	Acetylenic	2.0–3.0
$R_2C{=}CHR$, $R_2C{=}CH_2$	Vinylic	4.6–5.7
RCHO	Aldehydic	9.5–10.1

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	$RCOCH_3$	3.7-3.9
RCH_2R	1.2-1.4	$RCOCH_2R$	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
$RCCH_3$	2.1-2.3	$R_2C{=}CHR$	5.0-5.7
$RCCH_2R$	2.2-2.6	$H_2C(O)CH_2$	3.3-4.0
$ArCH_3$	2.2-2.5	RCH	9.5-10.1
RCH_2NR_2	2.3-2.8	$RCOH$	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.

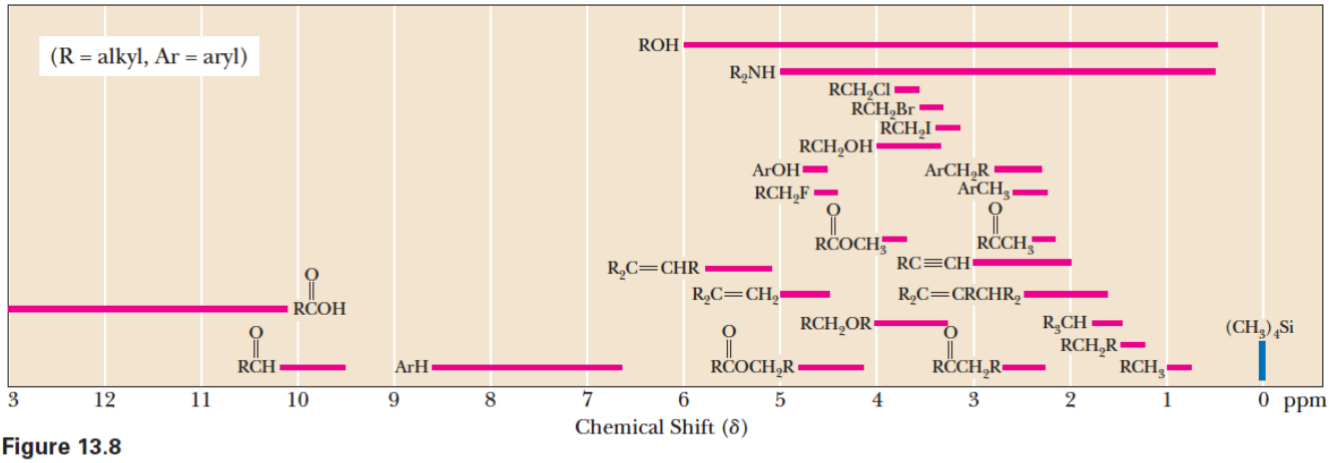


Figure 13.8
Average values of chemical shifts of representative types of hydrogens. These values are approximate. Other atoms or groups in the molecules may cause signals to appear outside of these ranges.

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.

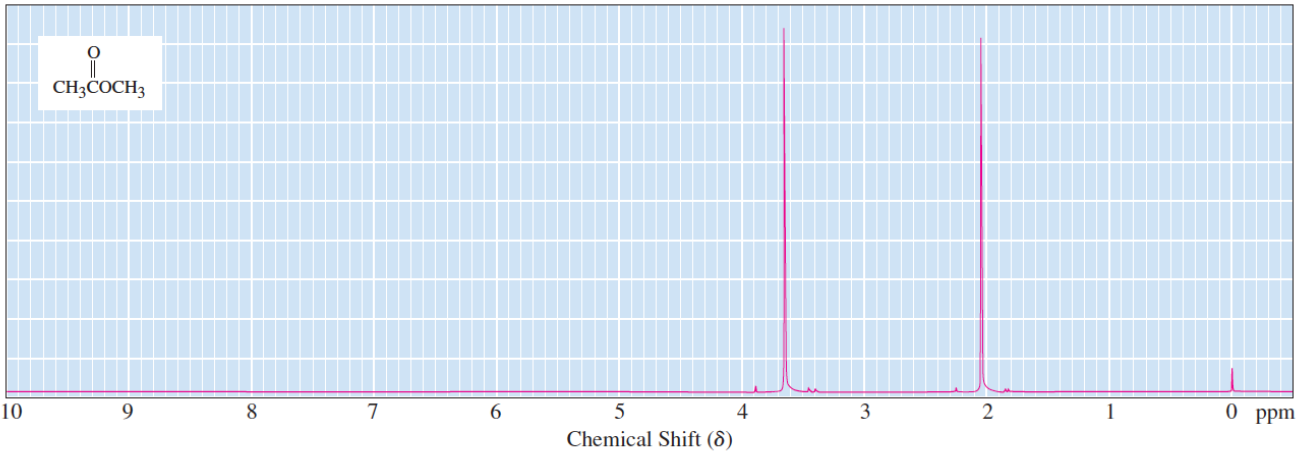


Figure 13.5
^{1}H-NMR spectrum of methyl acetate

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

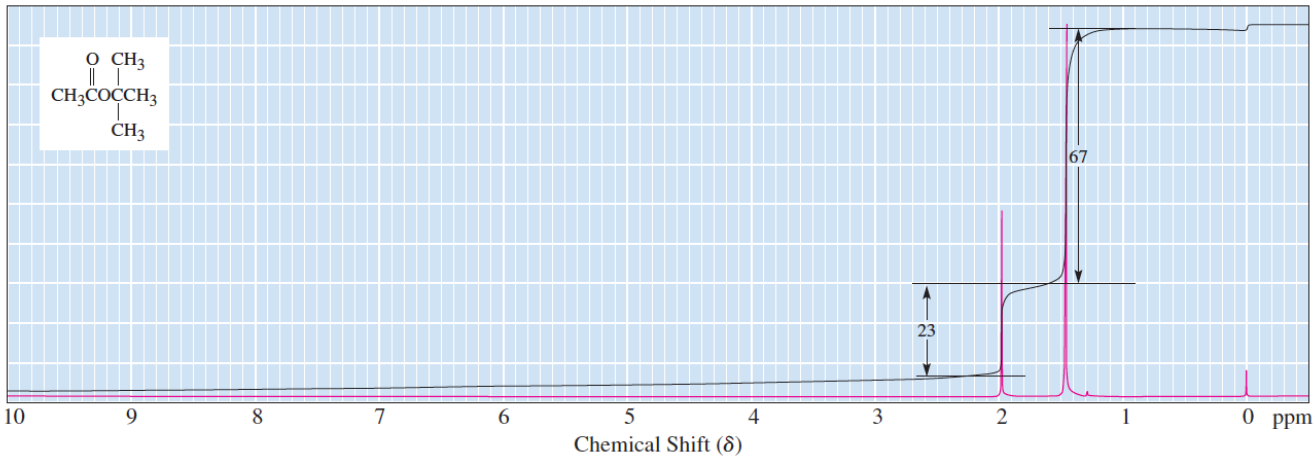
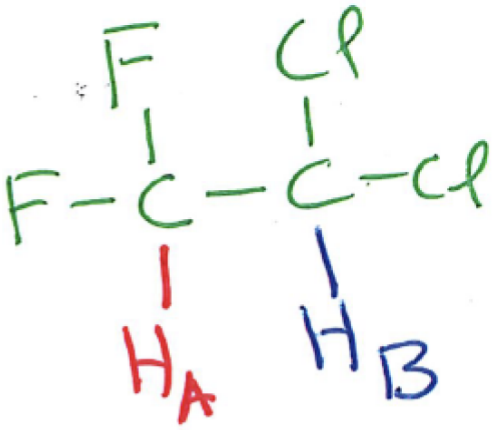


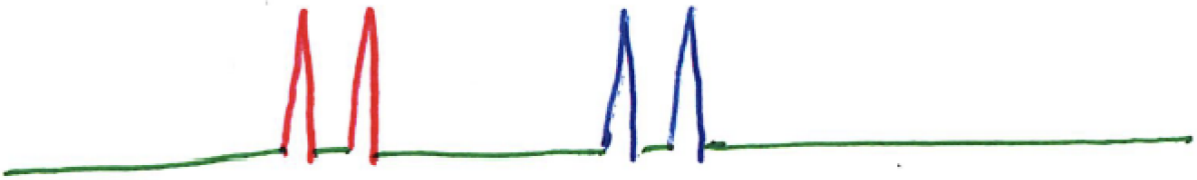
Figure 13.7
^{1}H-NMR spectrum of *tert*-butyl acetate showing the integration. The total vertical rise of 90 chart divisions corresponds to 12 hydrogens, 9 in one set and 3 in the other.

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

Definition →

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.





General case → For "n" equivalent adjacent H atoms a signal is split into "n+1" peaks

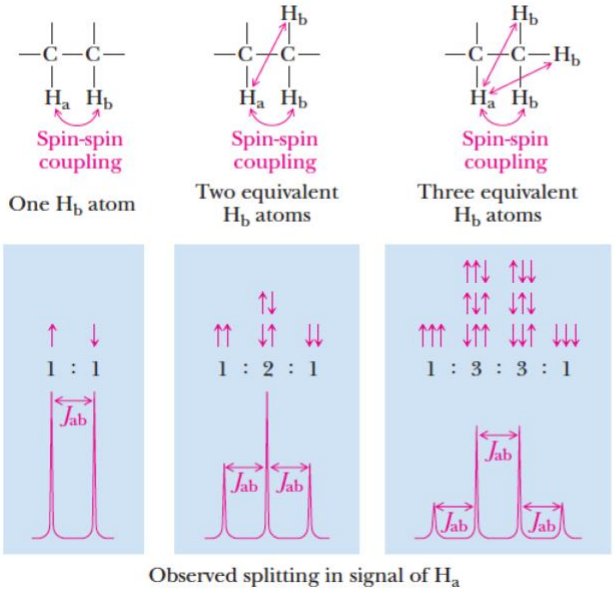


Figure 13.15
The origins of signal splitting patterns. Each arrow represents an H_b nuclear spin orientation.

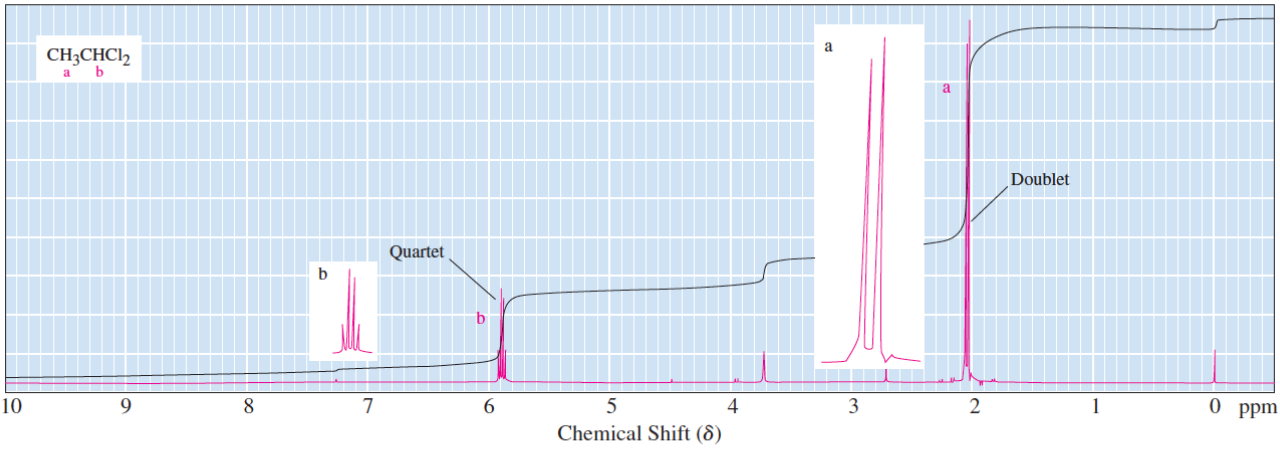
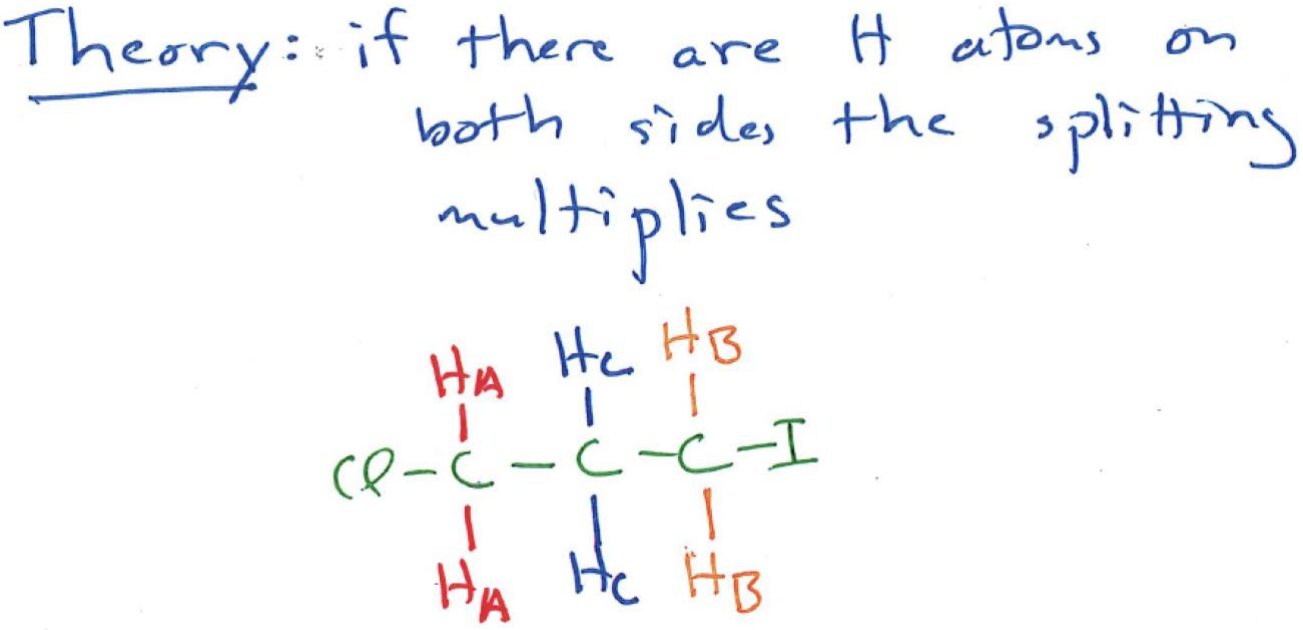
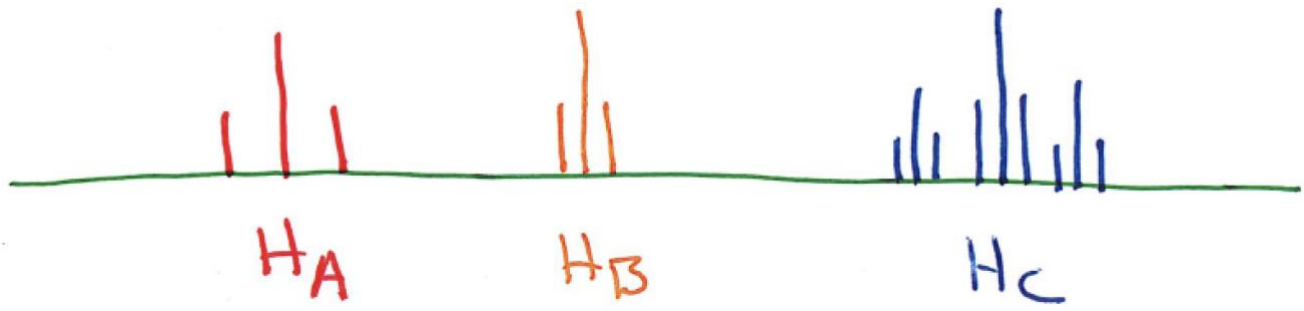


Figure 13.12
^{1}H-NMR spectrum of 1,1-dichloroethane.

O. THEORY: When there are two sets of adjacent H atoms, the number of peaks multiply. For example, a CH_2 group with a CH_2 group and a CH_3group on either side should show 3 x 4 = 12 splittings! You can say this group is a "triplet of quartets" (or a "quartet of triplets").

P. WHAT YOU WILL SEE IN REALITY : For alkyl groups complex splittings simplify because coupling constants ("J") are all about the same. In practice, if there are n adjacent H atoms, equivalent or not, you will see n+1 peaks. This is an approximation, but almost always true on spectra taken with all but the most sophisticated NMR spectrometers.

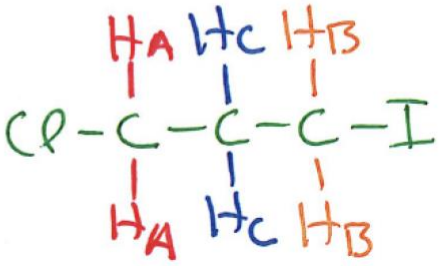


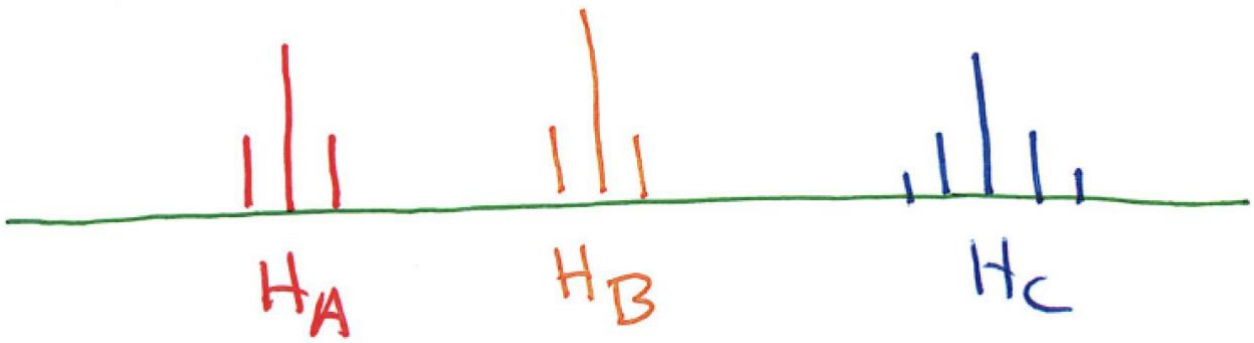


Reality: The splitting does multiply, but $J_{AC} = J_{BC}$ causing overlap of peaks

$\Rightarrow$ we observe $n+1$ peaks

(n = total # of adjacent H atoms)





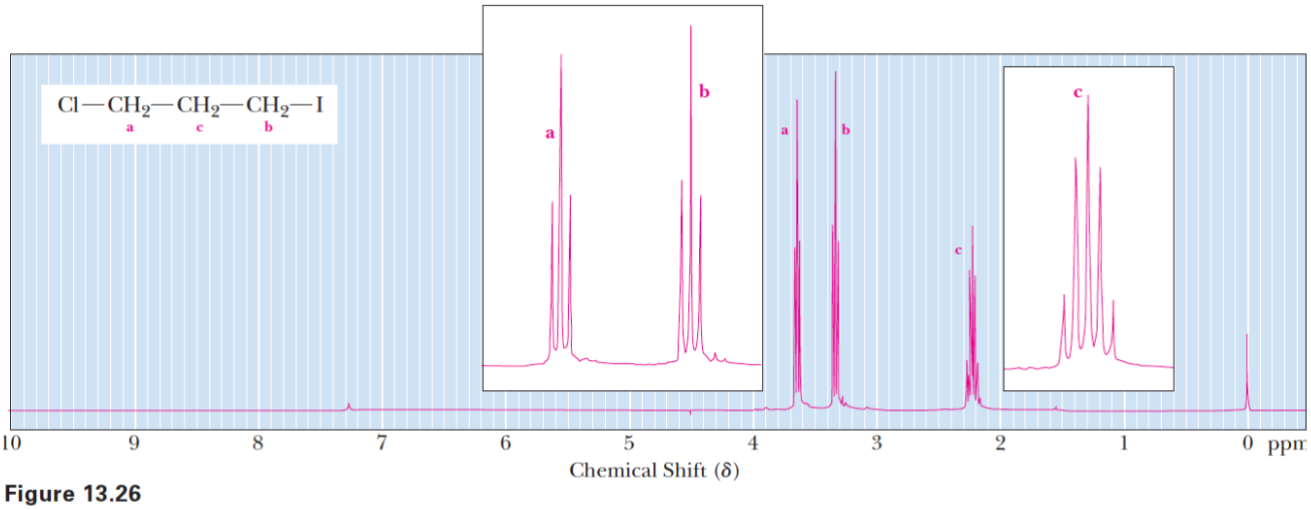


Figure 13.26
300 MHz ^{1}H-NMR spectrum of 1-chloro-3-iodopropane

Recap:

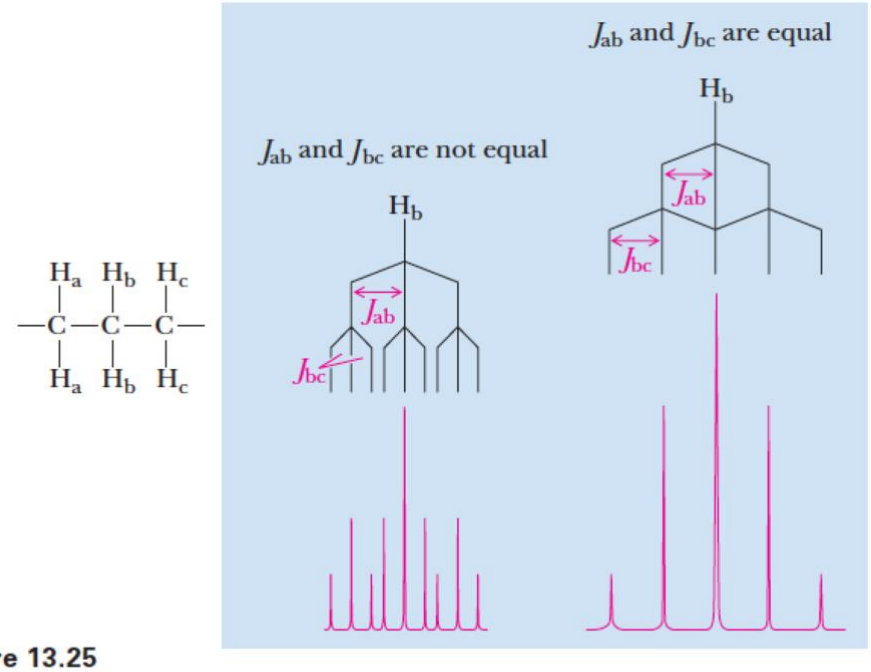


Figure 13.25
Simplification of signal splitting that occurs when coupling constants are the same.

Q. Non-equivalent H atoms on the same C atom can split each other (called geminal coupling), for example on alkenes or small rings. This coupling usually has very small coupling constants, so is difficult to see on some spectra.

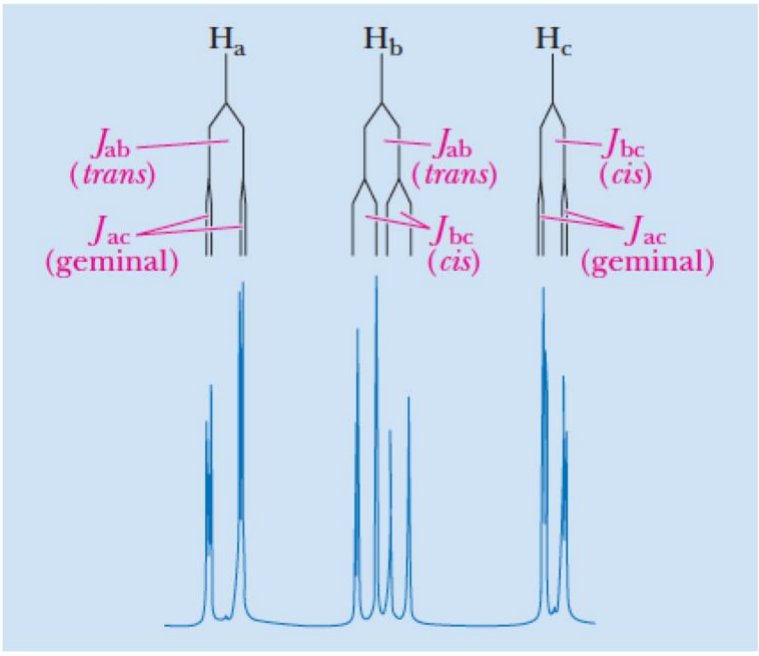


Figure 13.22
Tree diagrams for the complex coupling seen for the alkenyl H atoms in the ^{1}H-NMR spectrum of ethyl propenoate.

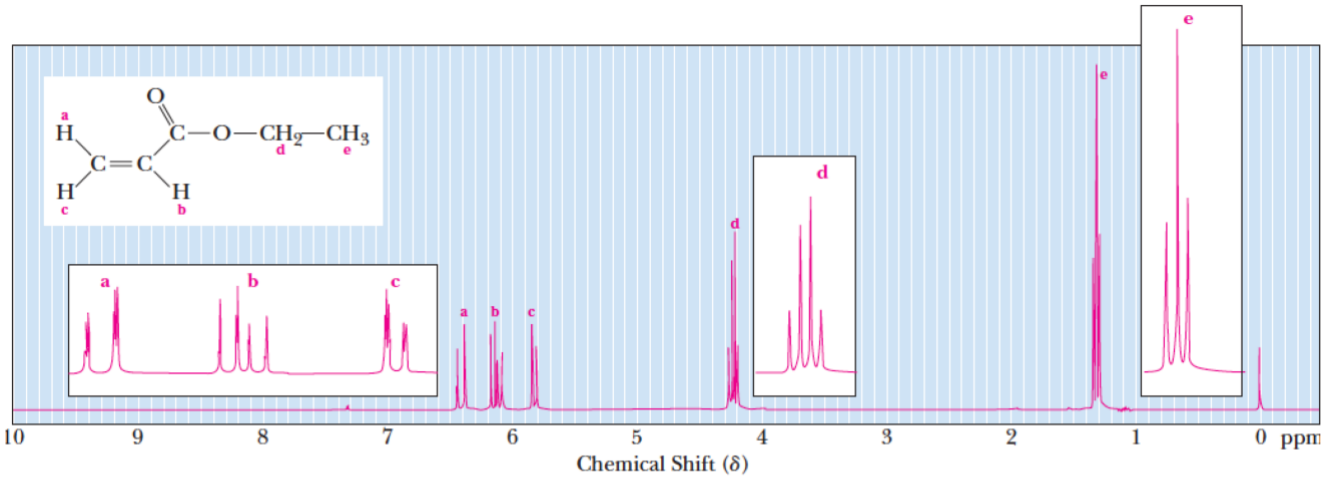


Figure 13.21
300 MHz ^{1}H-NMR spectrum of ethyl propenoate.