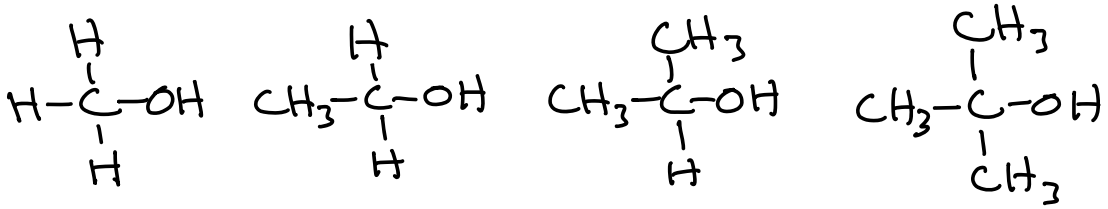
Alcohols → Reaction mechanisms depend on the number of alkyl groups attached on the C atom of C-OH bond.

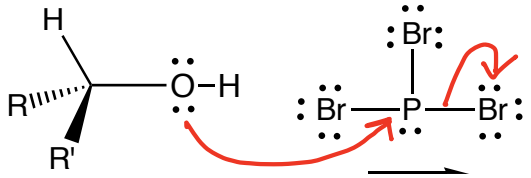


Methyl 1° 2° 3°

★ The -OH is not a leaving group but several reactions involve conversion of the -OH group into a good leaving group

⟹ Recall, the -OH group is a weak nucleophile and weak base (in strong acid)

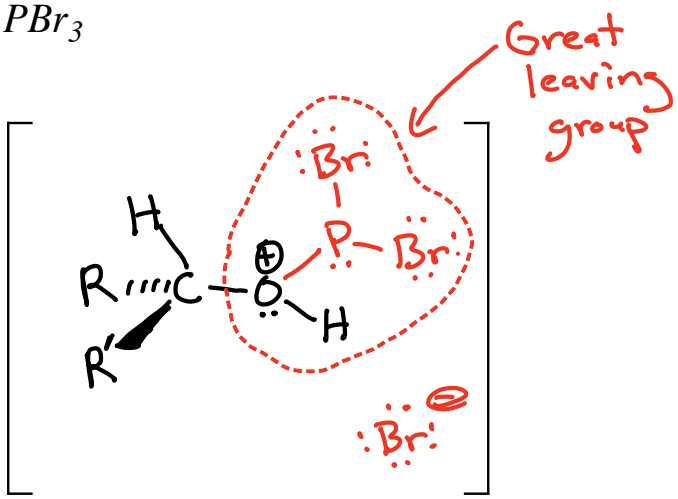
Alcohols + PBr_3



1° or 2° Alcohols

S_N2

Great leaving group



S_N2

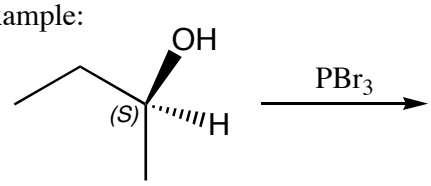
Products

Summary:

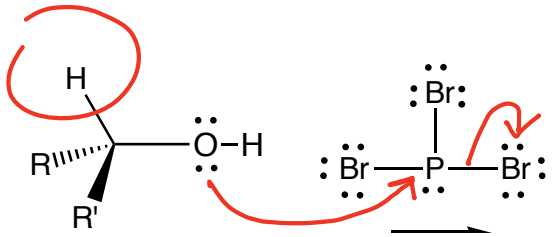
Regiochemistry:

Stereochemistry:

Example:

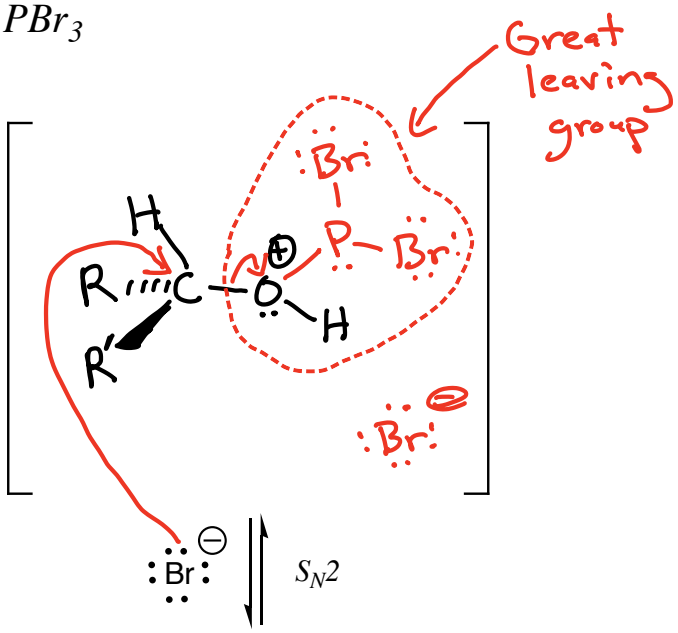


Alcohols + PBr_3



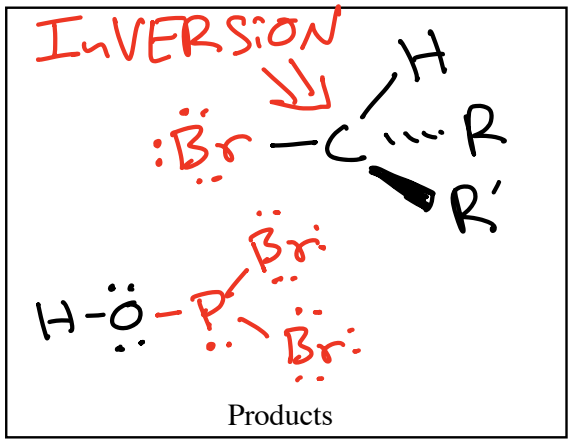
1° or 2° Alcohols

S_N2



Does NOT work with 3° alcohols

★ There is an analogous reaction with $SOCl_2$ that converts alcohols into chloroalkanes

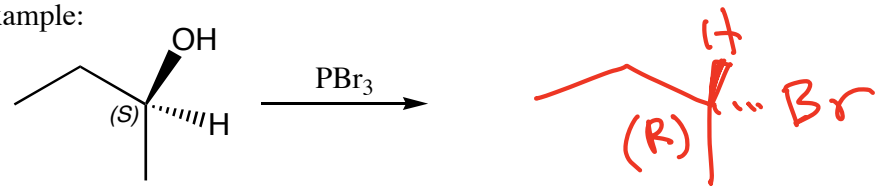


Summary: 1° or 2° alcohols react with PBr_3 via an S_N2 reaction on the P atom to create a good leaving group that undergoes an S_N2 reaction with $Br^\ominus$ at the C atom

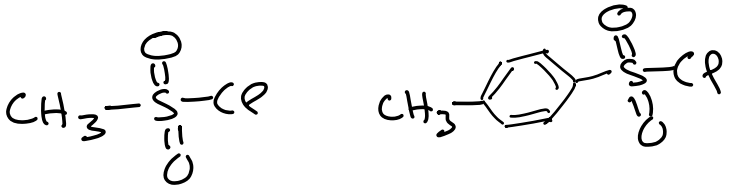
Regiochemistry: N/A

Stereochemistry: INVERSION

Example:

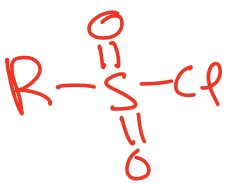


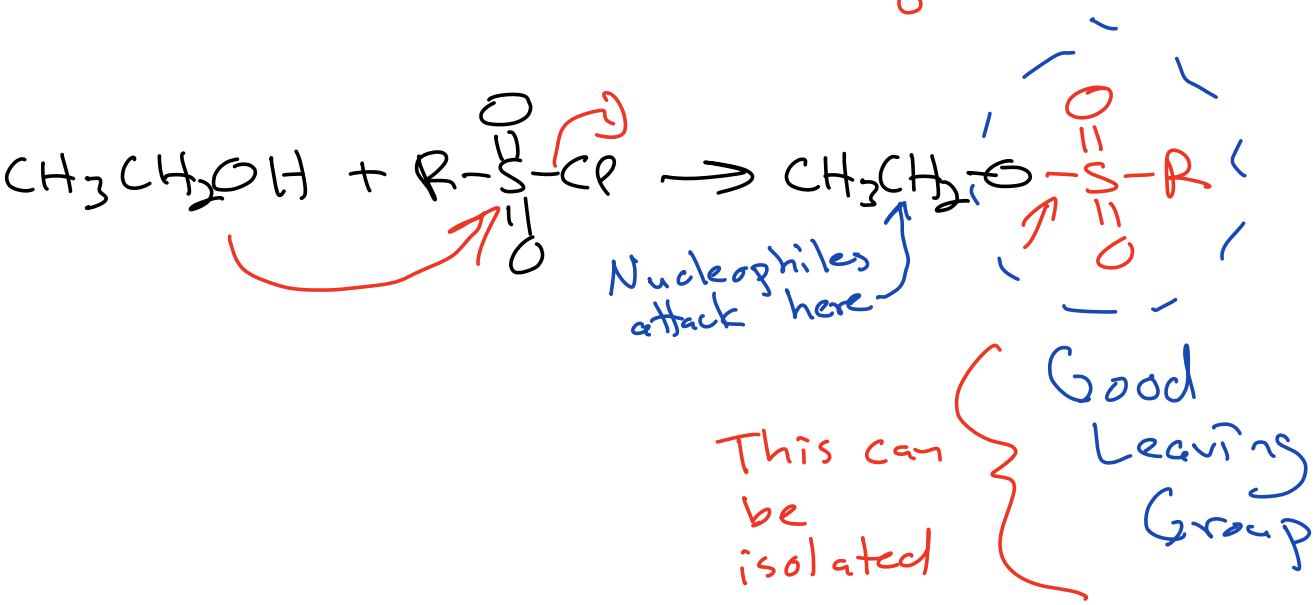
Alkyl Sulfonates



Methanesulfonyl Chloride

p-Toluenesulfonyl Chloride



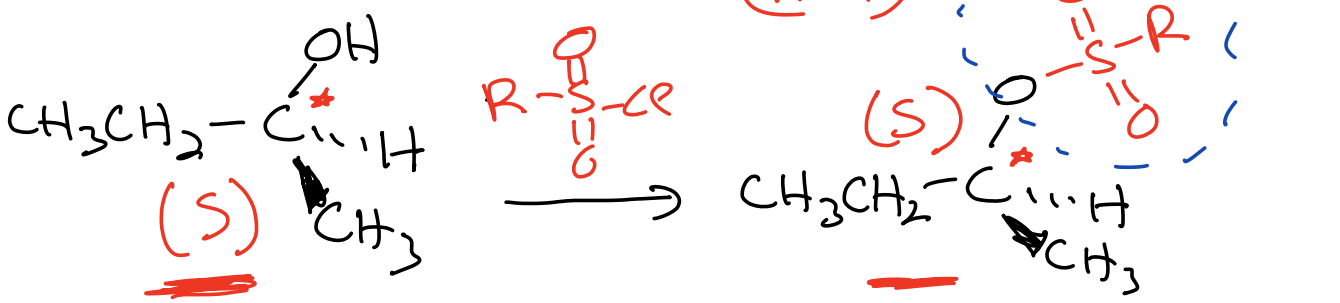


Stereochemistry

Byproduct of the reaction

(HCl)

This reacts like -Br



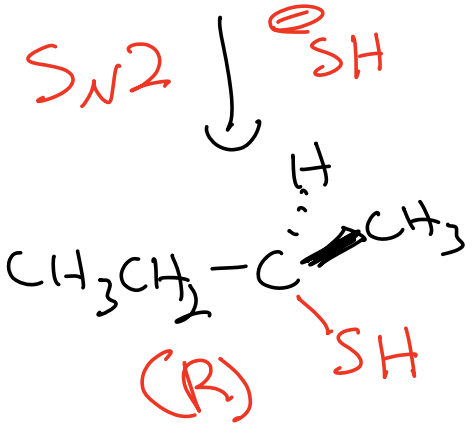
(S)

(S)

Net ⇒

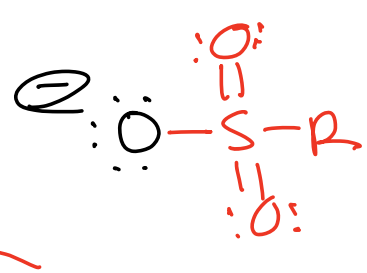
INVERSION

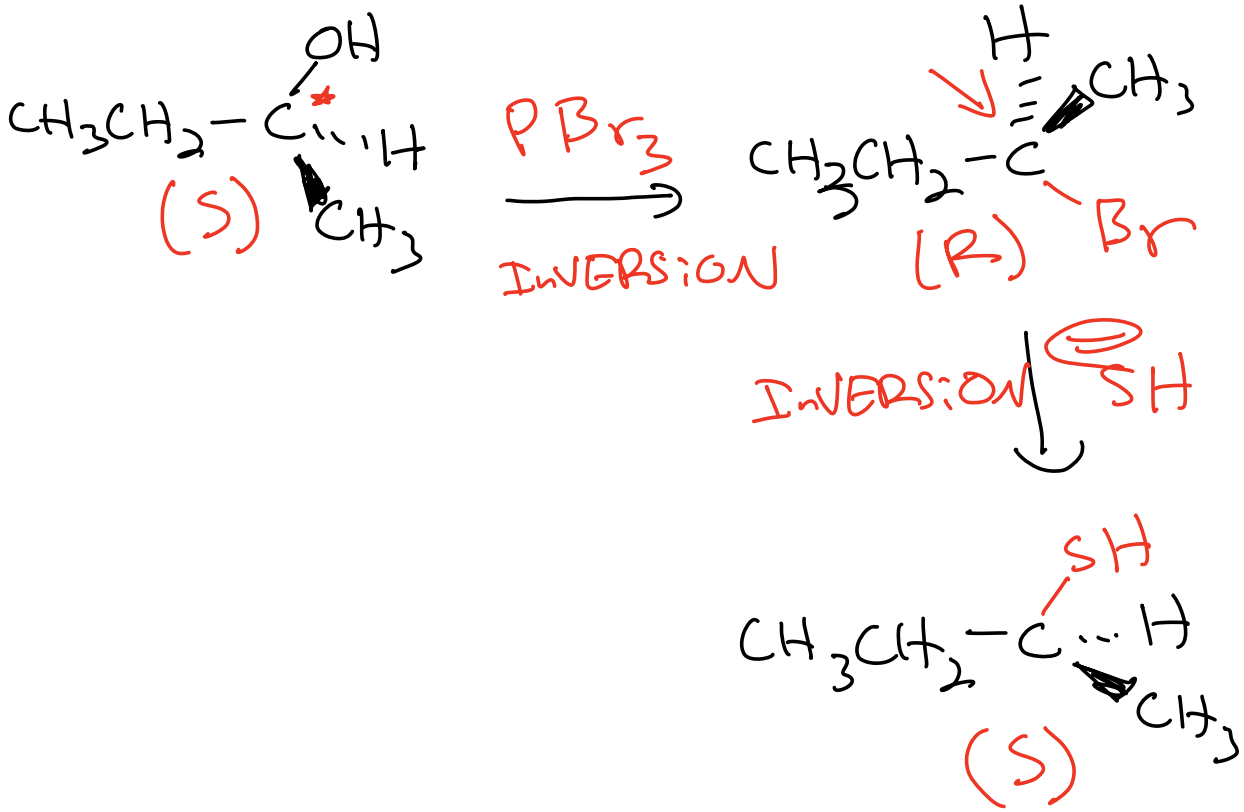
S_N2



(R)

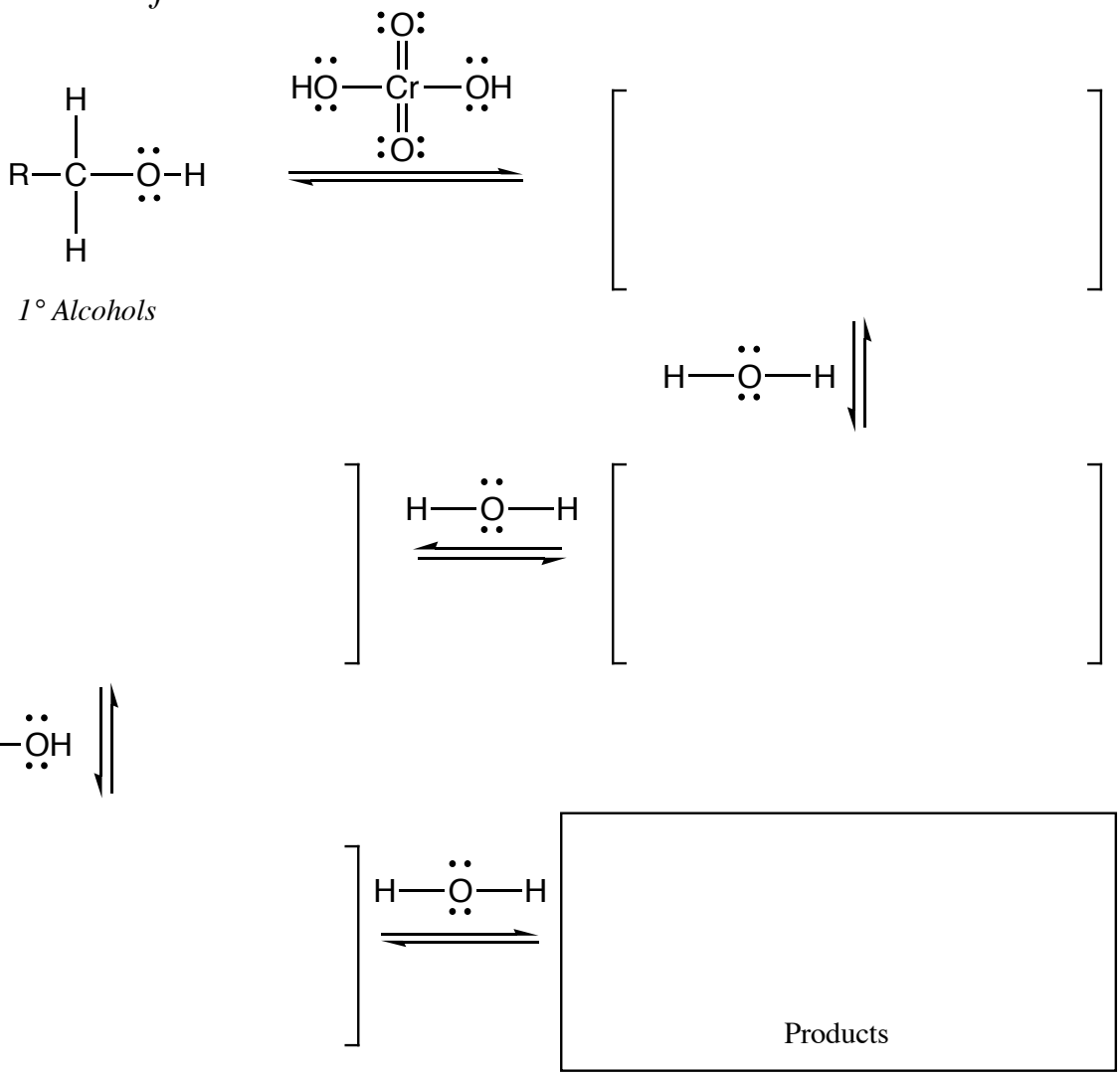
stabilized by resonance delocalization ⇒ relatively stable anion, explaining why it is such a good leaving group





⟹ You can not invert or retain the stereochemistry of a chiral alcohol taking part in S_N2 reactions

Chromic Acid Oxidation of Alcohols

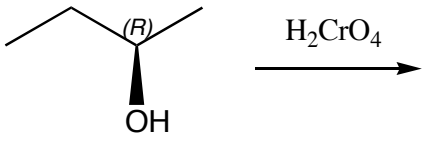


Summary:

Regiochemistry:

Stereochemistry:

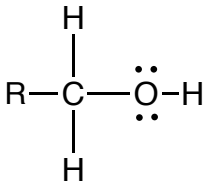
Example:



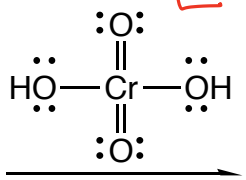
Chromic Acid Oxidation of Alcohols

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

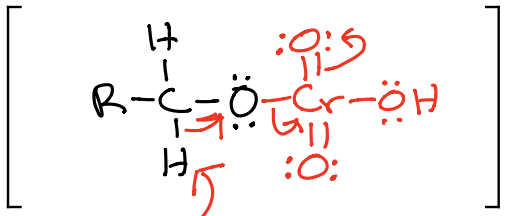
Not responsible for first step

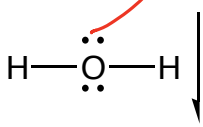


1° Alcohols



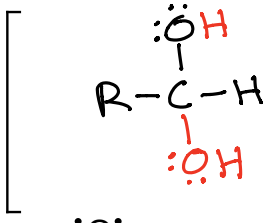
"H_2CrO_4" or "Chromic Acid"



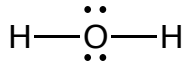


Take a proton away and break a bond

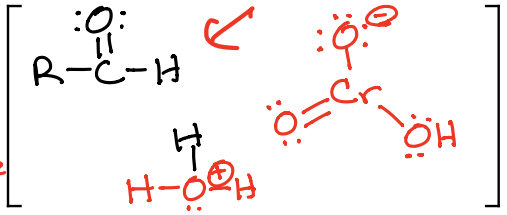
Not responsible for this step

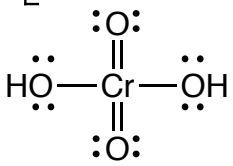


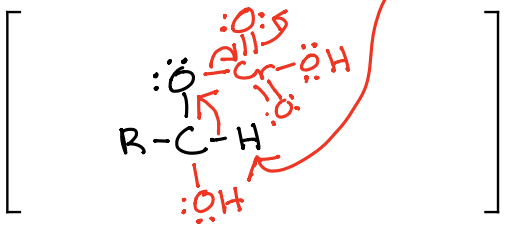
Called a geminal diol

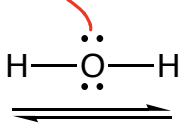


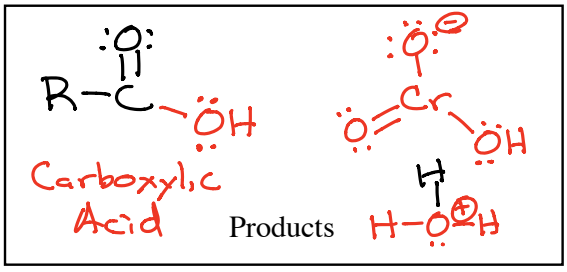
Water reacts with aldehyde – will learn next semester







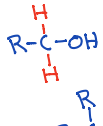




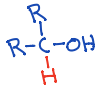
Carboxylic Acid

Products

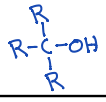
Summary:



1° alcohols ⇒ Carboxylic Acid



2° alcohols ⇒ Ketone

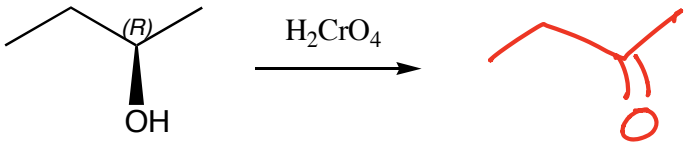


3° alcohols ⇒ NO REACTION

Regiochemistry: N/A

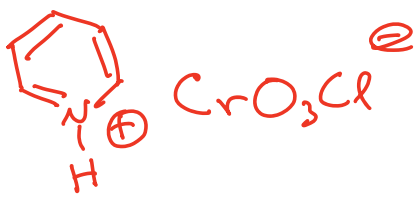
Stereochemistry: N/A

Example:



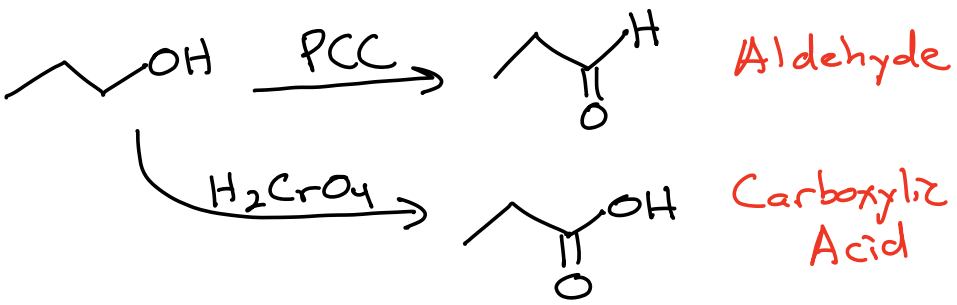
Ketone

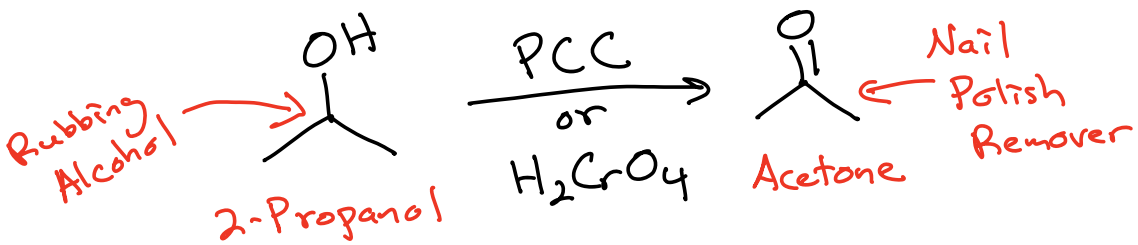
A chromic acid-like reagent WITHOUT WATER will stop at the aldehyde when using a primary alcohol as starting material



Pyridinium Chlorochromate

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. 8/25/2022

You will learn the secret structural reason proteins, the most important molecular machines in our bodies, can support the chemistry of life. 9/6/22

You will learn why when you take Advil for pain, exactly half of what you take works, and the other half does nothing. 9/20/22

You will learn how toothpaste works. 9/29/22

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. 10/27/22

You will learn how medicines like Benadryl, Seldane, and Lipitor work. 11/10/22

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. 10/4/22

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. 10/27/22

You will learn reactions that can make antifreeze from vodka. 11/10/22

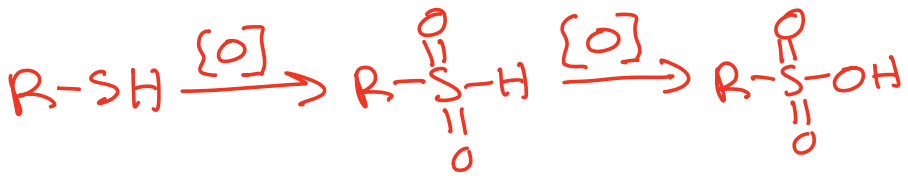
You will learn a reaction that can make nail polish remover from rubbing alcohol. 11/15/22

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.

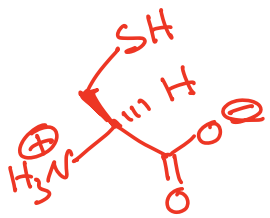
Thiols → R–S–H

The sulfur atom can be oxidized!



In the presence of O_2:

This is a slow but spontaneous reaction!



The amino acid cysteine (Cys)

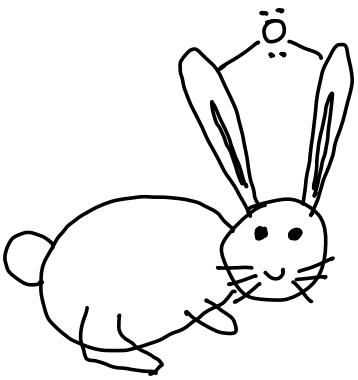
Disulfide bonds between cysteine residues that are far apart in the sequence, but overlap in three-dimensions, provide covalent links that stabilize folded protein structures — especially common in proteins that are outside of cells ex. antibodies ← In bloodstream

Ethers → R–Ö–R

↳ Unreactive under most conditions

Diethyl ether

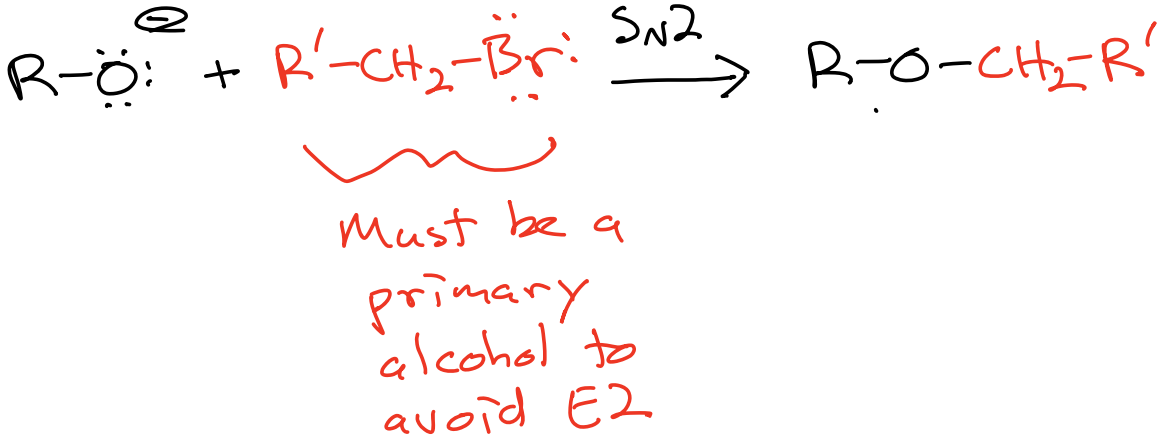
Good solvent – polar but not protic – can interact with cations but not anions



Ether Bunny!

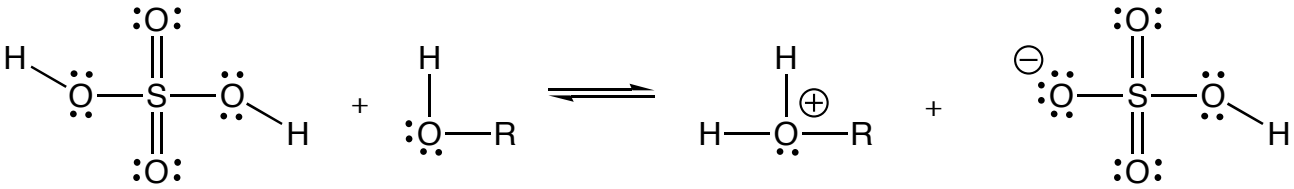
How to make ethers

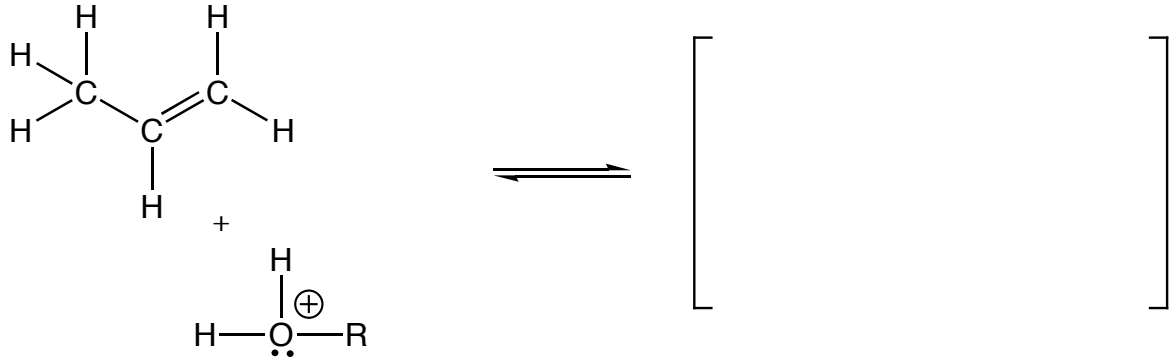
Williamson Ether Synthesis

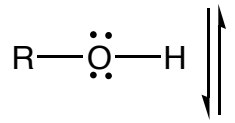


You can also react alkenes with alcohols in the presence of catalytic amounts of H_2SO_4 to make ethers:

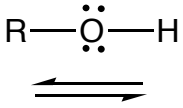
Acid-catalyzed Reaction of an Alcohol with an Alkene







Products

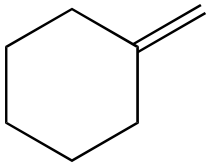


Summary:

Regiochemistry:

Stereochemistry:

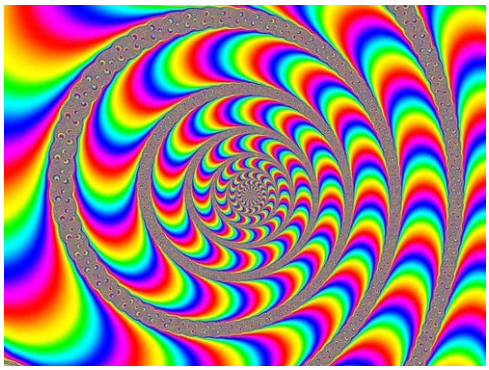
Example:

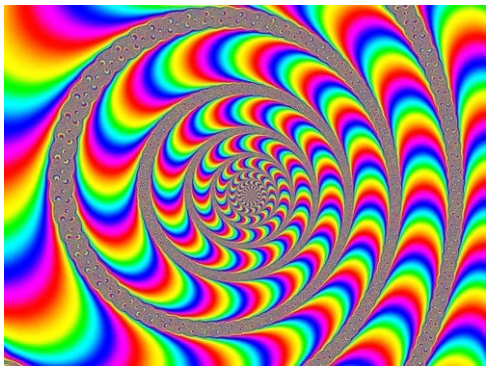


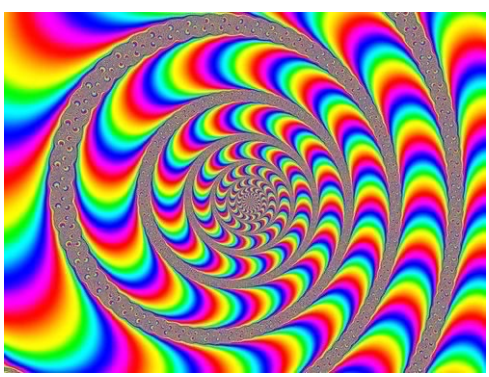
CH_3CH_2OH

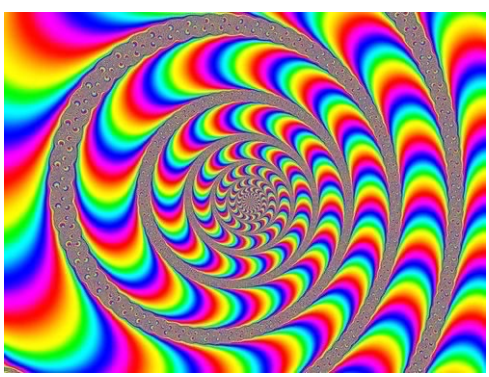
H_2SO_4 (catalytic amount)

Flashback!



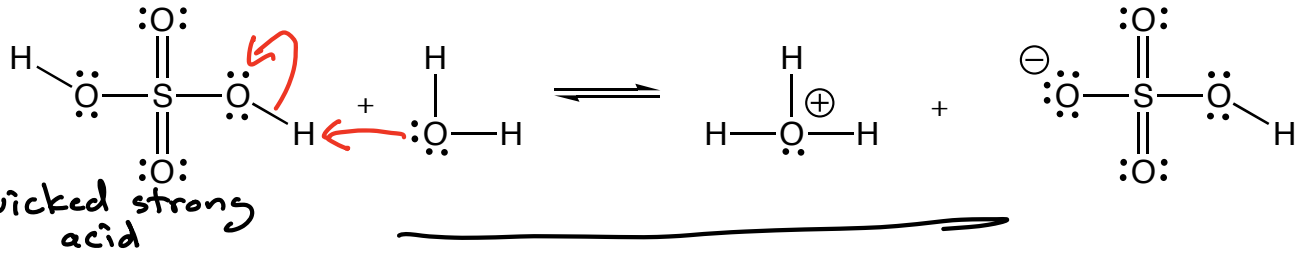


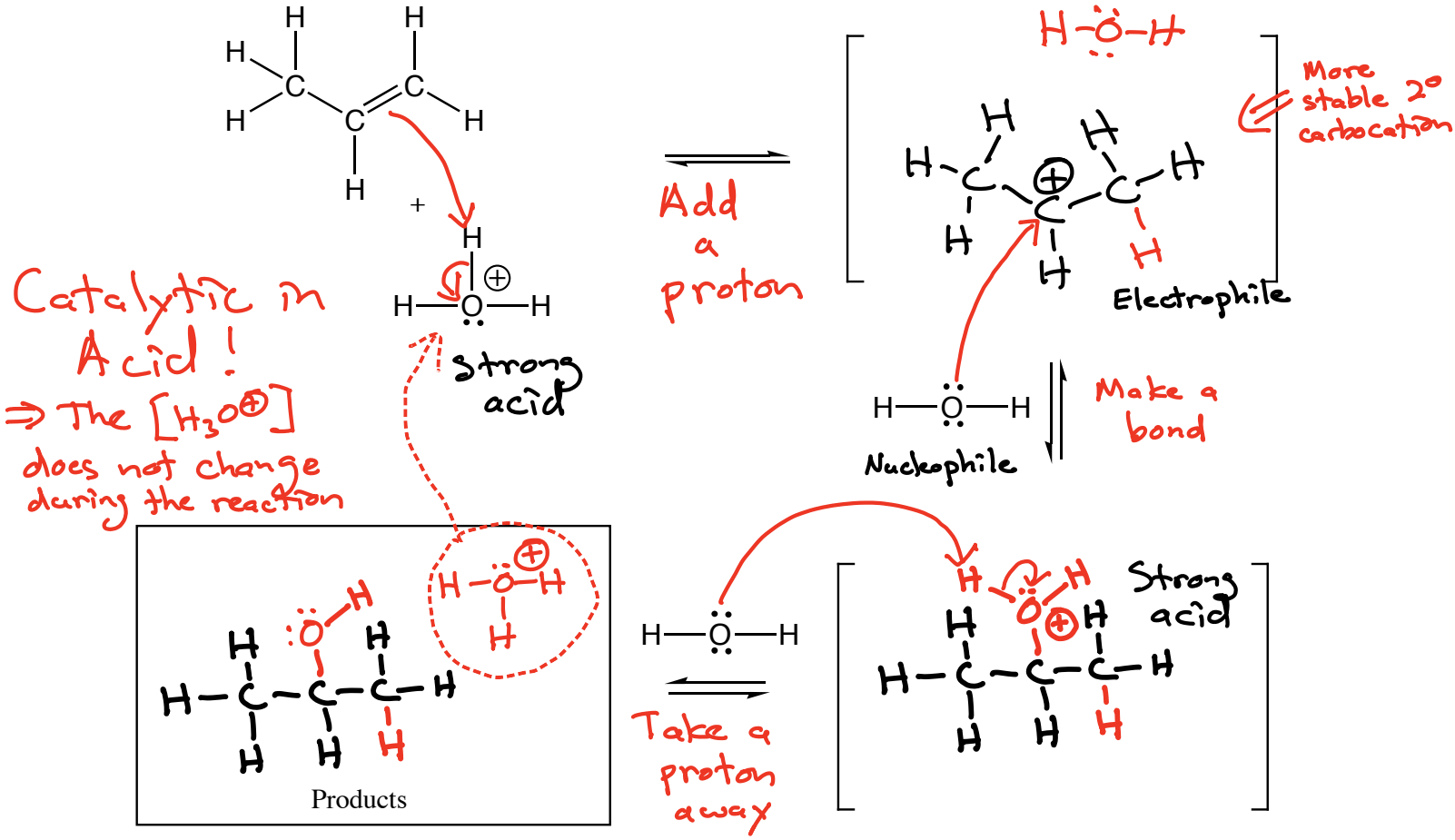




Flashback to October 4

Acid-catalyzed Hydration of an Alkene



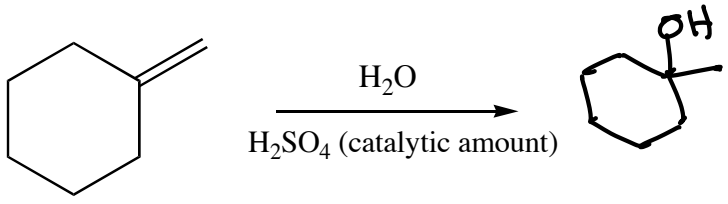


Summary: Proton adds to make a carbocation intermediate, water attacks to make a new bond, take a proton away to make the product alcohol. Catalytic in $H_3O^{\oplus}$

Regiochemistry: Markovnikov's Rule

Stereochemistry: Mixed (time capsule)

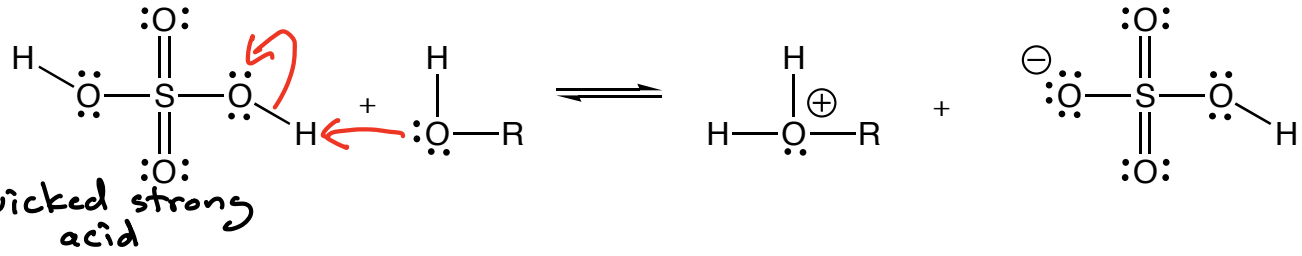
Example:

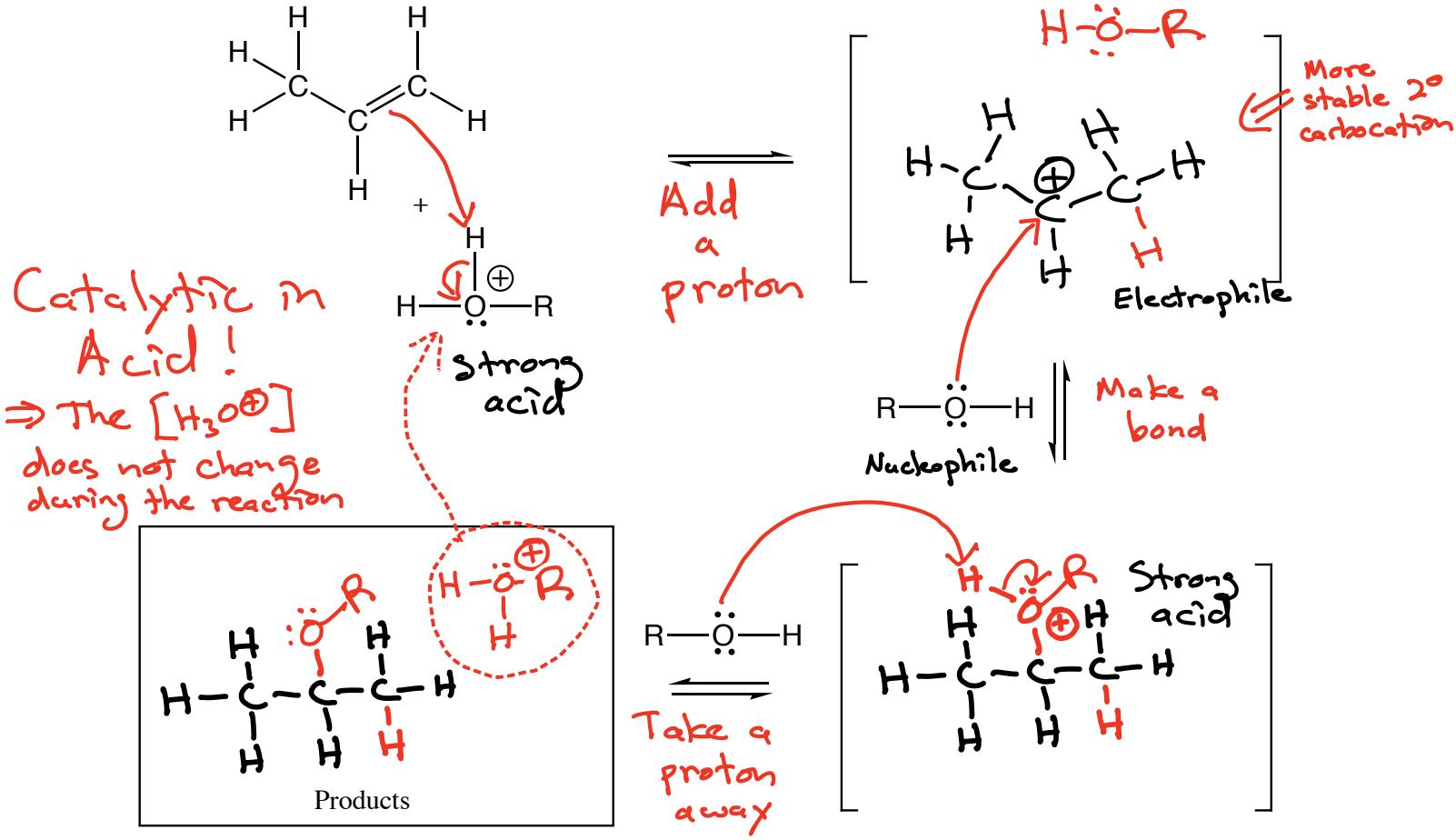


(Not chiral)

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

Acid-catalyzed Reaction of an Alcohol with an Alkene



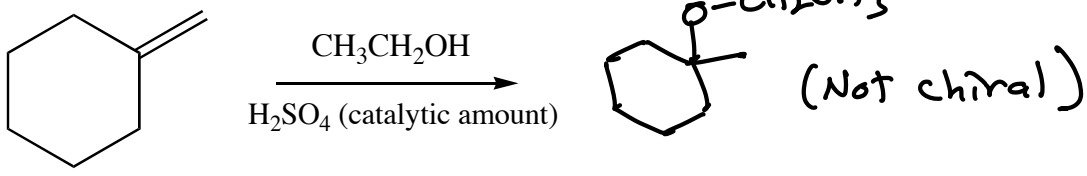


Summary: Proton adds to make a carbocation intermediate, alcohol attacks to make a new bond, take a proton away to make the product ether. Catalytic in $H_3O^{\oplus}$

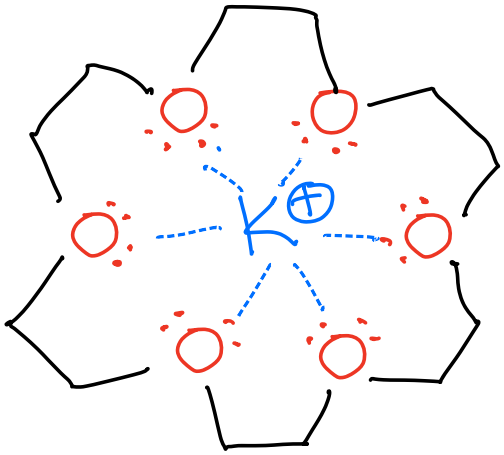
Regiochemistry: Markovnikov's Rule

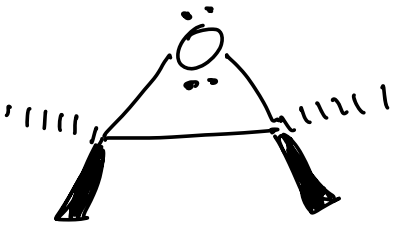
Stereochemistry: Mixed

Example:



Crown Ethers → bind cations based on the radius of the ion





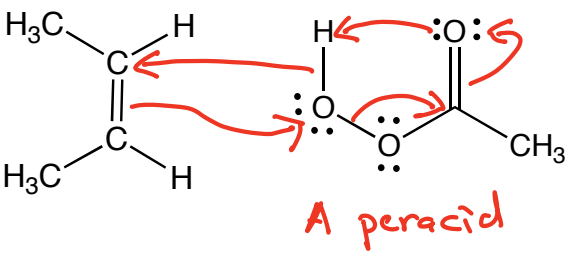
Epoxide

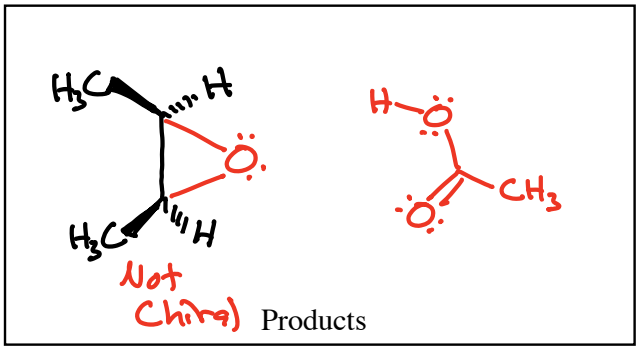
Important because they can be formed from alkenes or halohydrins AND they are good electrophiles → reactions open up three-membered ring, relieving angle strain

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

Synthesis of epoxides

Epoxide Formation



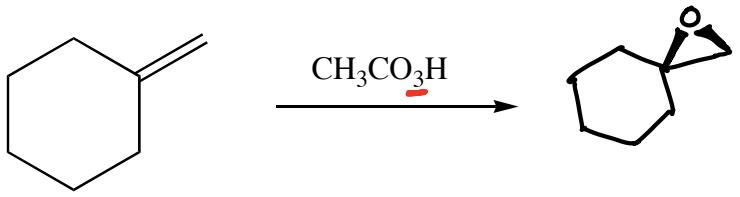


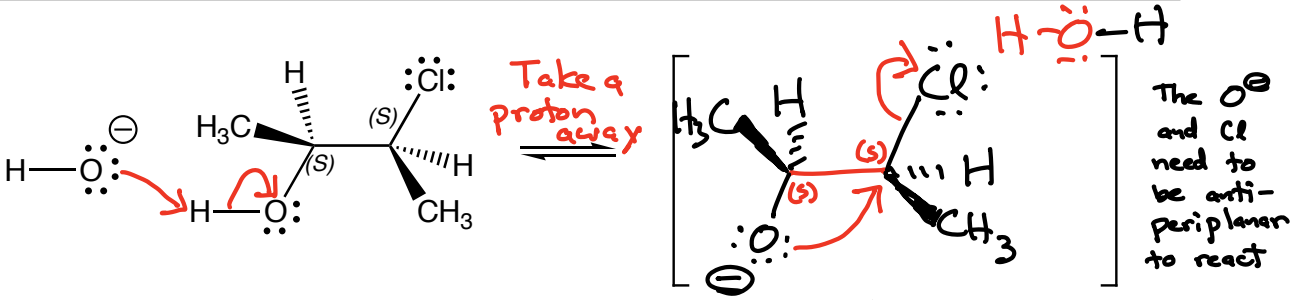
Summary: Alkenes react with peracids in a single concerted step

Regiochemistry: N/A

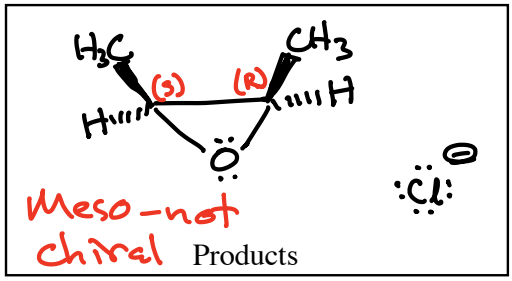
Stereochemistry: Mixed when new chiral centers are created

Example:





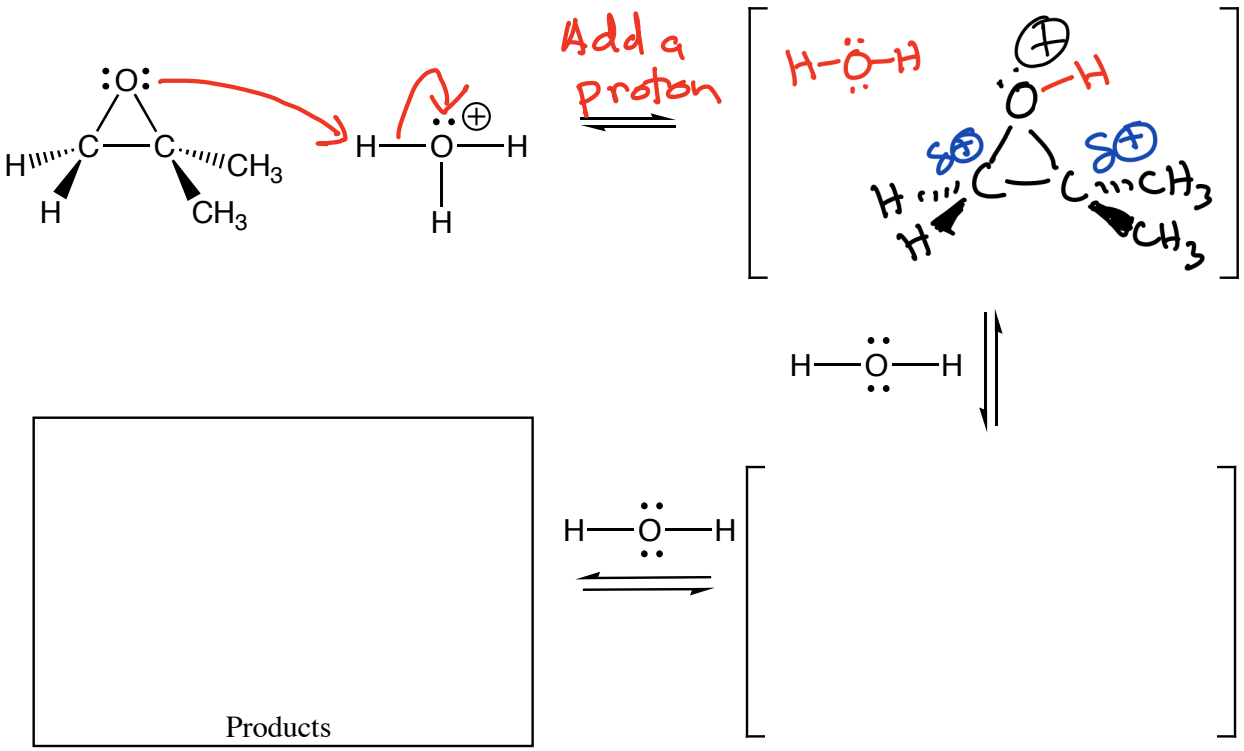
Summary: Halohydrins react in base to give the alkoxide that reacts antiperiplanar to give the epoxide.



Regiochemistry: N/A

Stereochemistry: Antiperiplanar transition state

Acid-Catalyzed Epoxide Opening

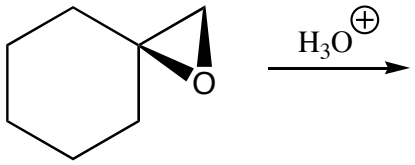


Summary: In acid, epoxides are protonated to give a highly reactive cation intermediate that reacts with nucleophiles at the more highly substituted carbon atom

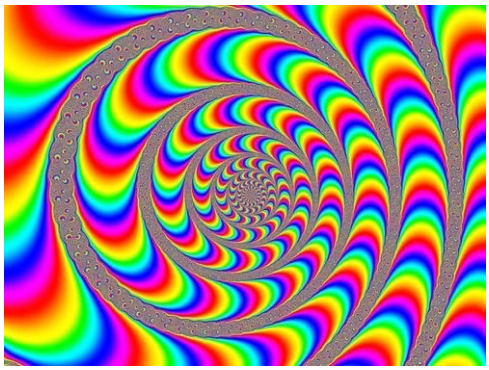
Regiochemistry: "Markovnikov" Attack at more highly substituted C atom

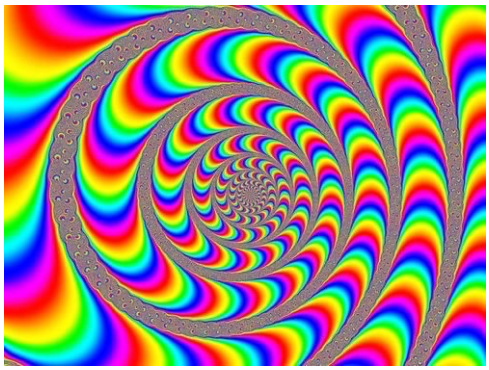
Stereochemistry: Anti

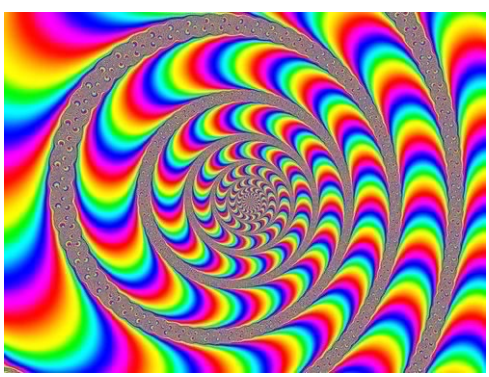
Example:

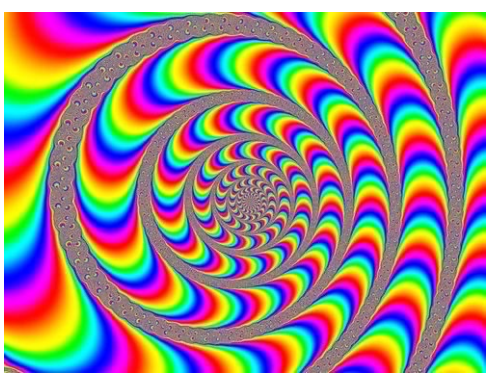


Flashback!



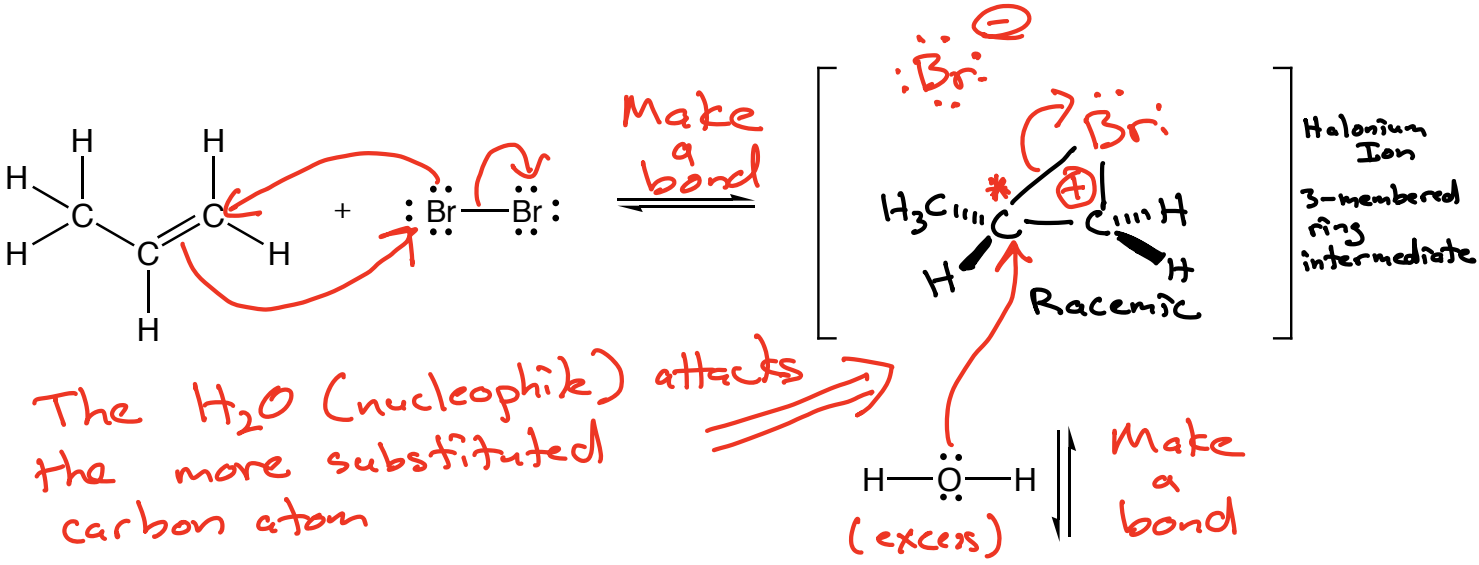


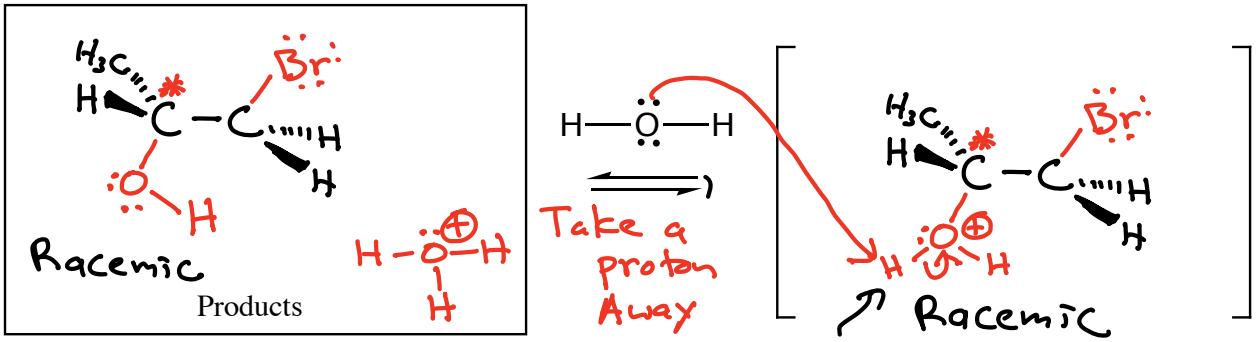




Flashback to October 11

Alkene Hydrohalogenation





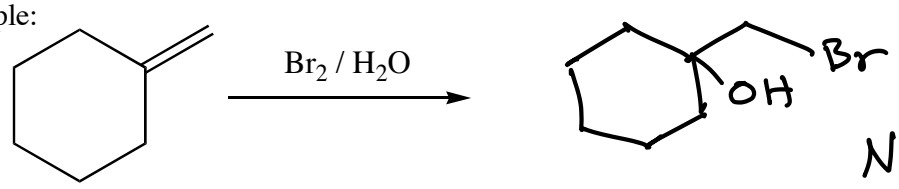
pH drops during the reaction!

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)

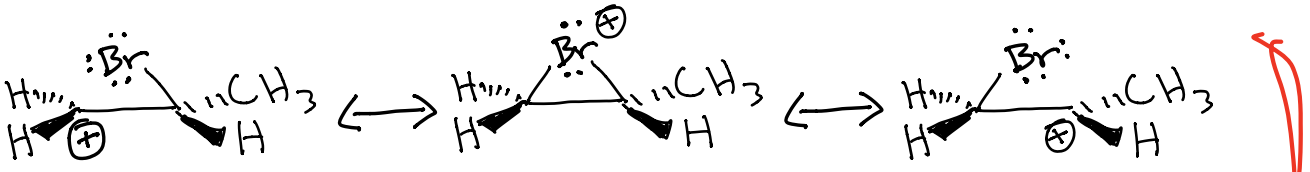
Stereochemistry: Anti

Example:



Not Chiral

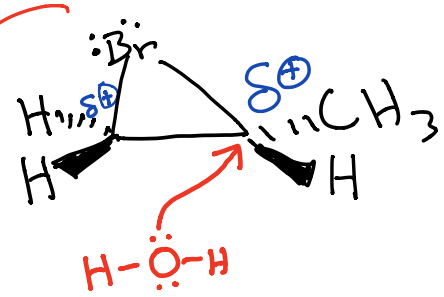
Flashback → Halohydrin Mechanism



Minor Contributor

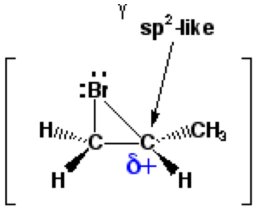
Major Contributor

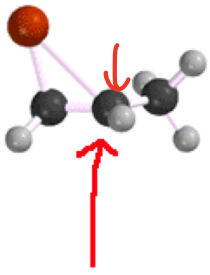
Resonance Hybrid

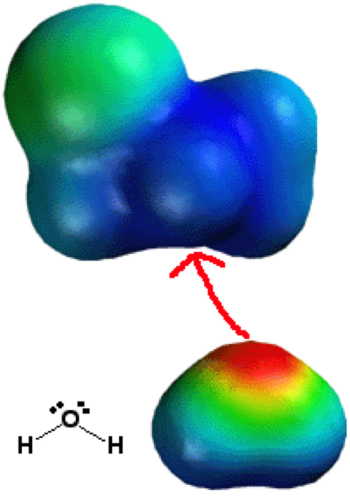


Water attacks the more substituted carbon atom because there is more partial ⊕ charge

From "Pictures of the Day (POTD)" 10-9-20

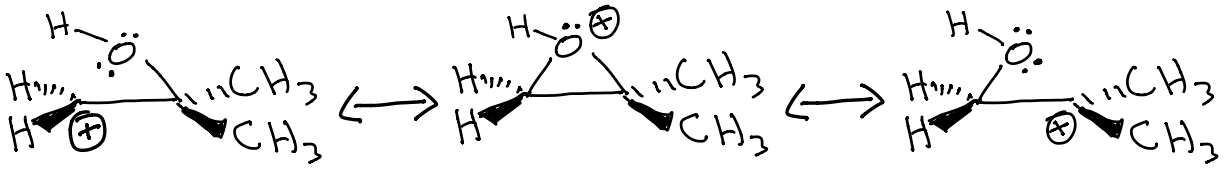






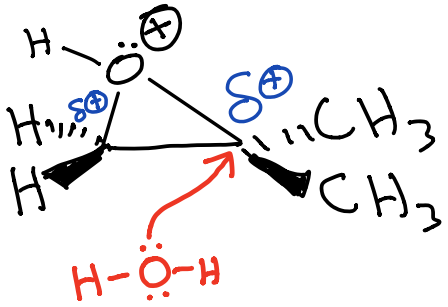
Nucleophiles Attack the More Positively-Charged Carbon Atom From This Face Leading to Markovnikov Regiochemistry and Trans Stereochemistry of Addition

Epoxide in acid



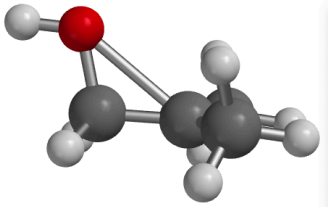
Minor Contributor

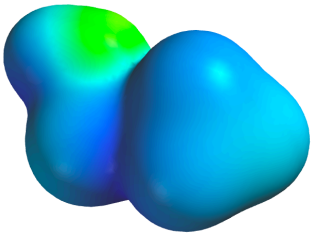
Major Contributor



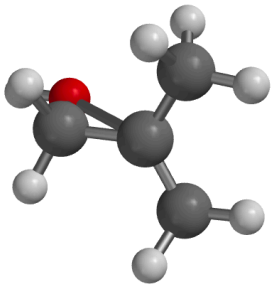
Water attacks the more substituted carbon atom because there is more partial ⊕ charge

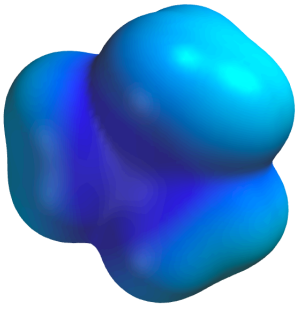
Side View



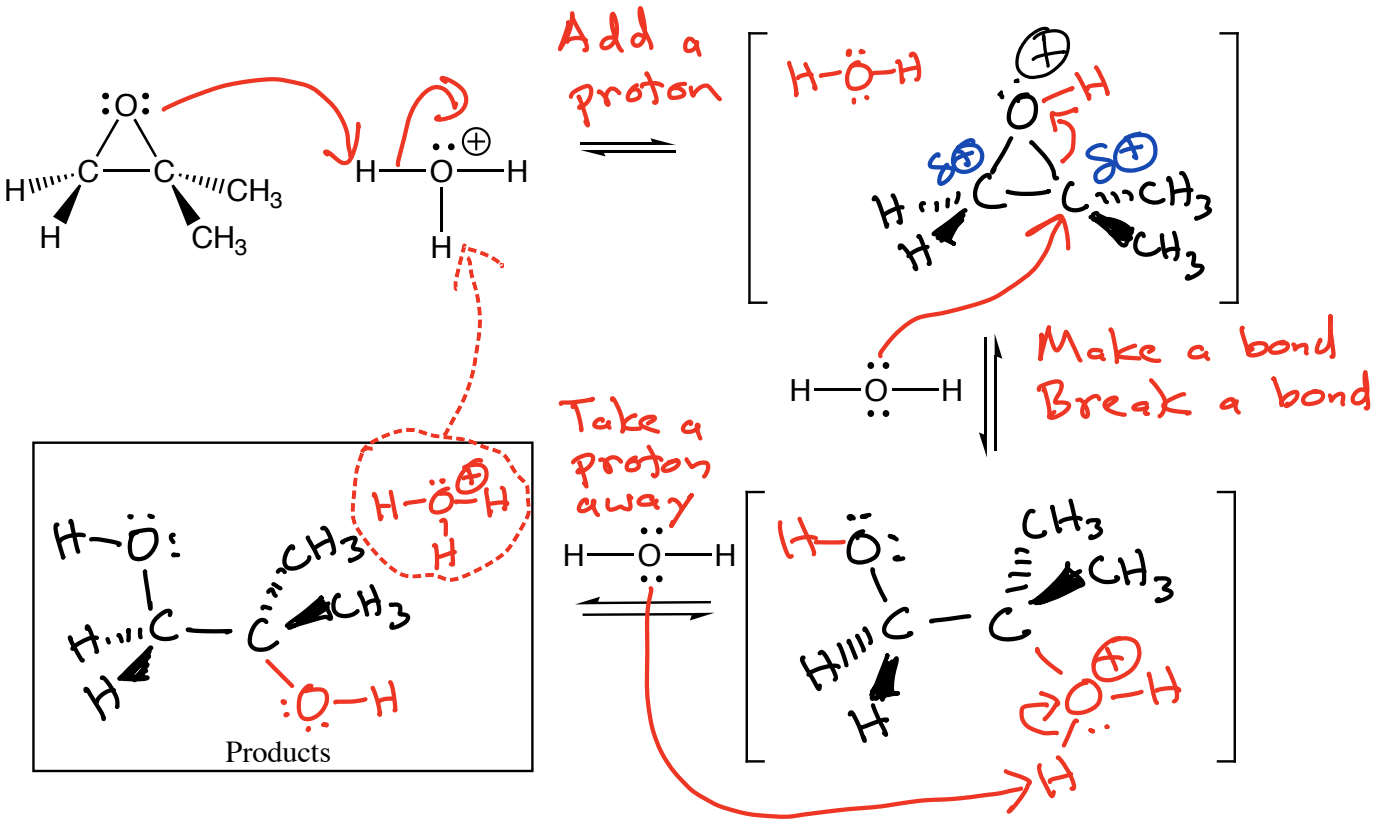


View from Bottom



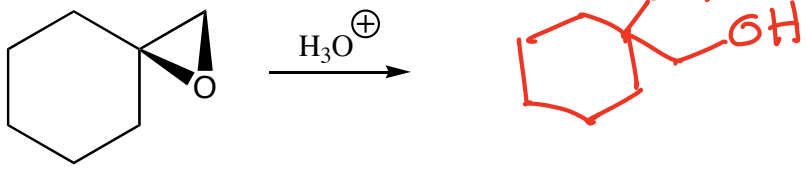


Acid-Catalyzed Epoxide Opening

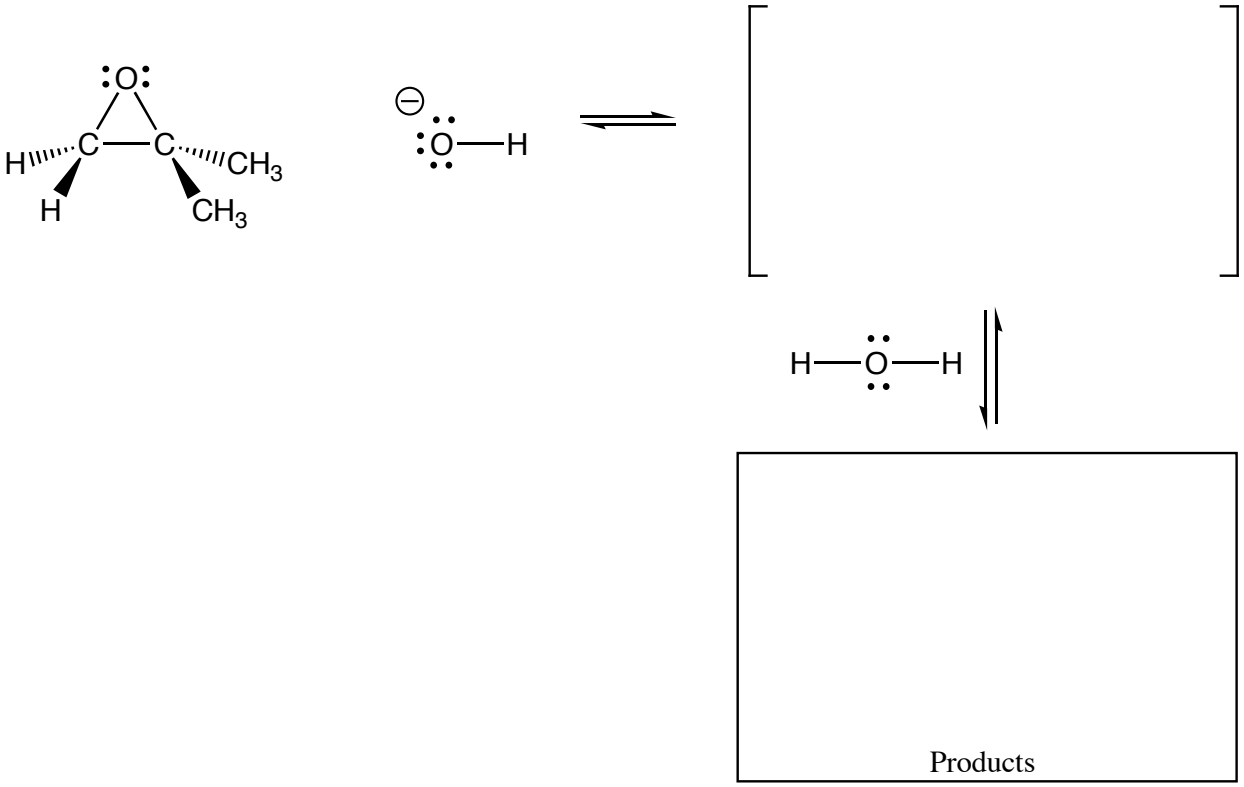


Summary:	In acid, epoxides are protonated to give a highly reactive cation intermediate that reacts with nucleophiles at the more highly substituted carbon atom
Regiochemistry:	"Markovnikov" Attack at more highly substituted C atom
Stereochemistry:	Anti

Example:

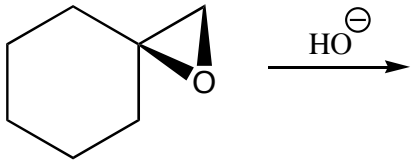


Nucleophilic ~~Base Promoted~~ Epoxide Opening

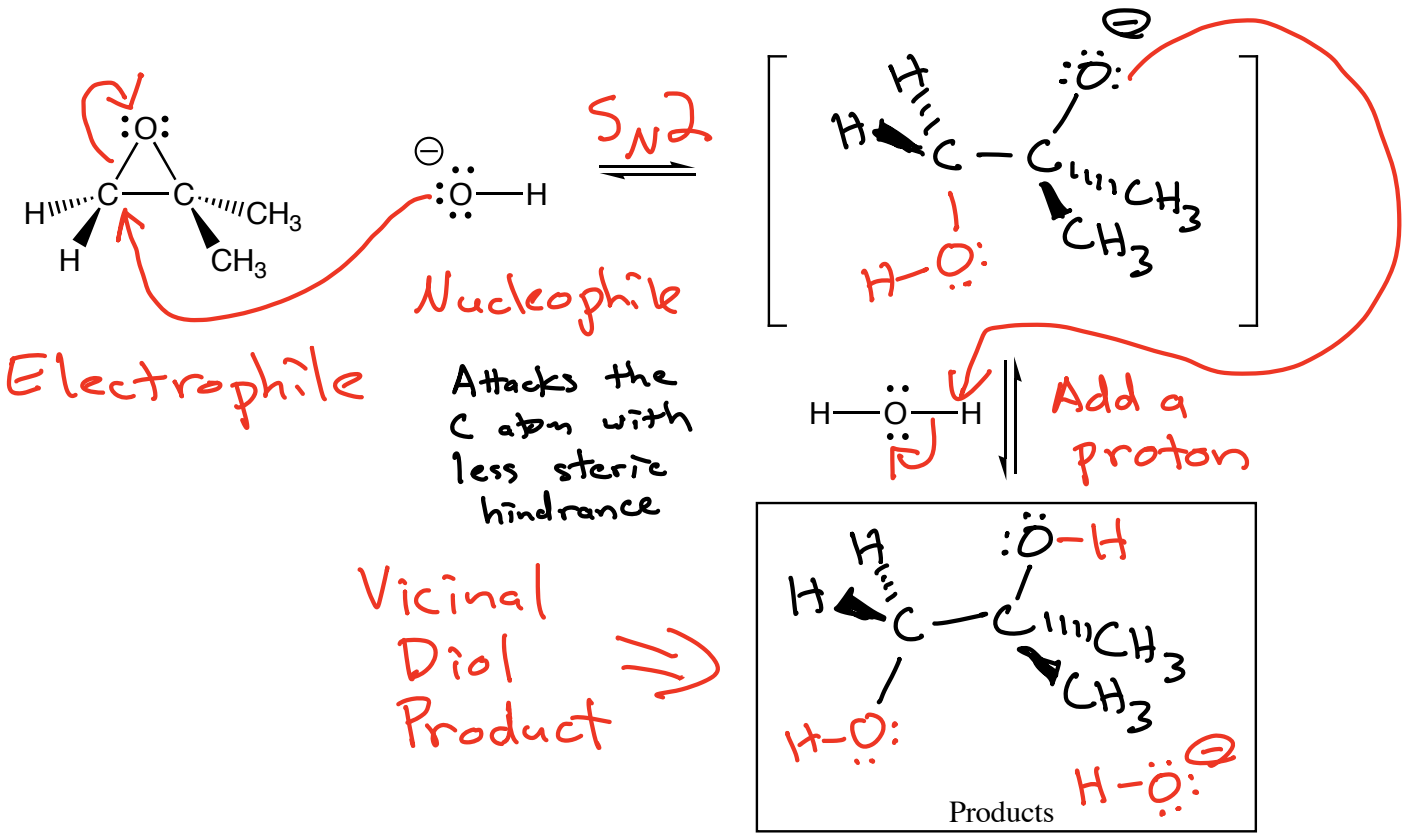


Summary:	Epoxides add strong nucleophiles at the less hindered carbon atom
Regiochemistry:	Less hindered (non-Markovnikov)
Stereochemistry:	Anti addition

Example:

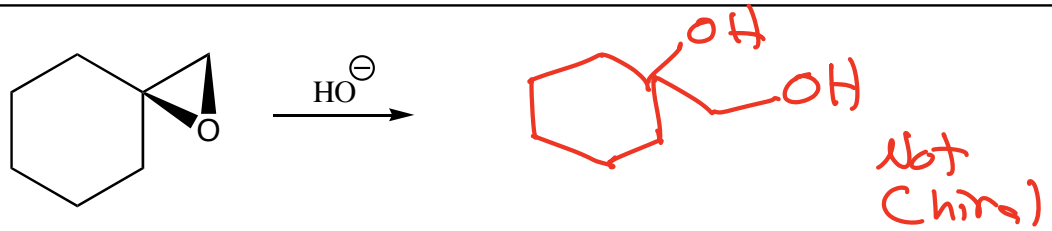


Nucleophilic ~~Base Promoted~~ Epoxide Opening

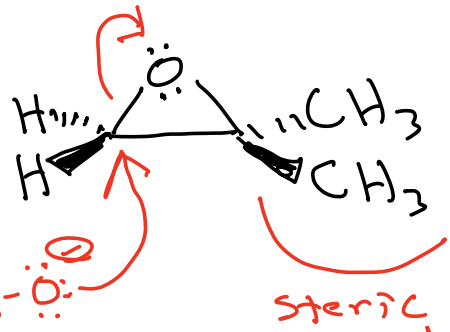


Summary:	Epoxides add strong nucleophiles at the less hindered carbon atom
Regiochemistry:	Less hindered (non-Markovnikov) ✓
Stereochemistry:	Anti addition

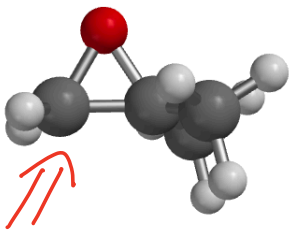
Example:



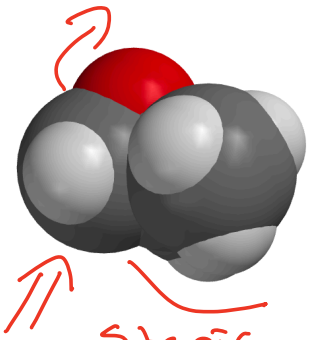
Epoxide reacting with nucleophile



Nucleophile attacks less hindered carbon

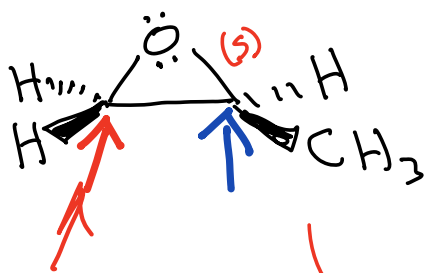


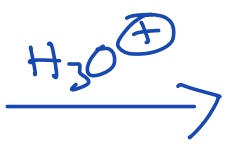
Steric Hindrance → blocks attack at this carbon



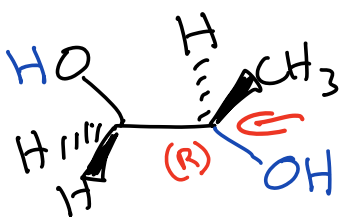
Steric Hindrance

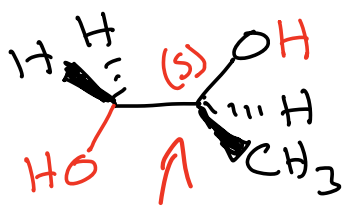
Watch out for the stereochemistry!



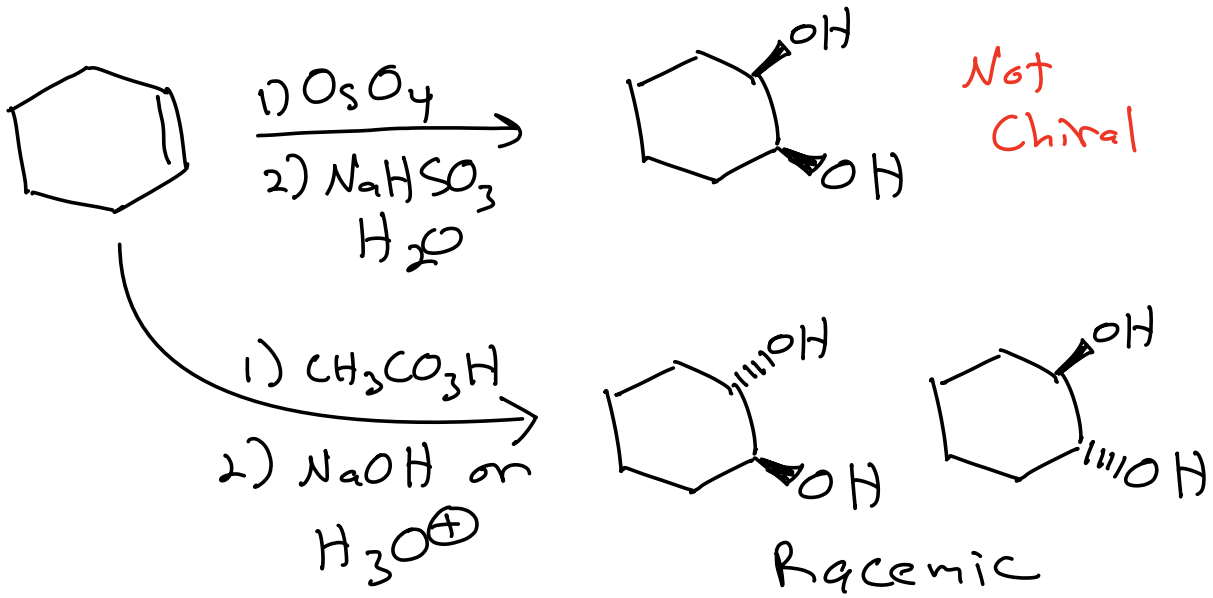


INVERSION





Attack will always be from underneath → back of C-O bond



Watch out for the stereochemistry!