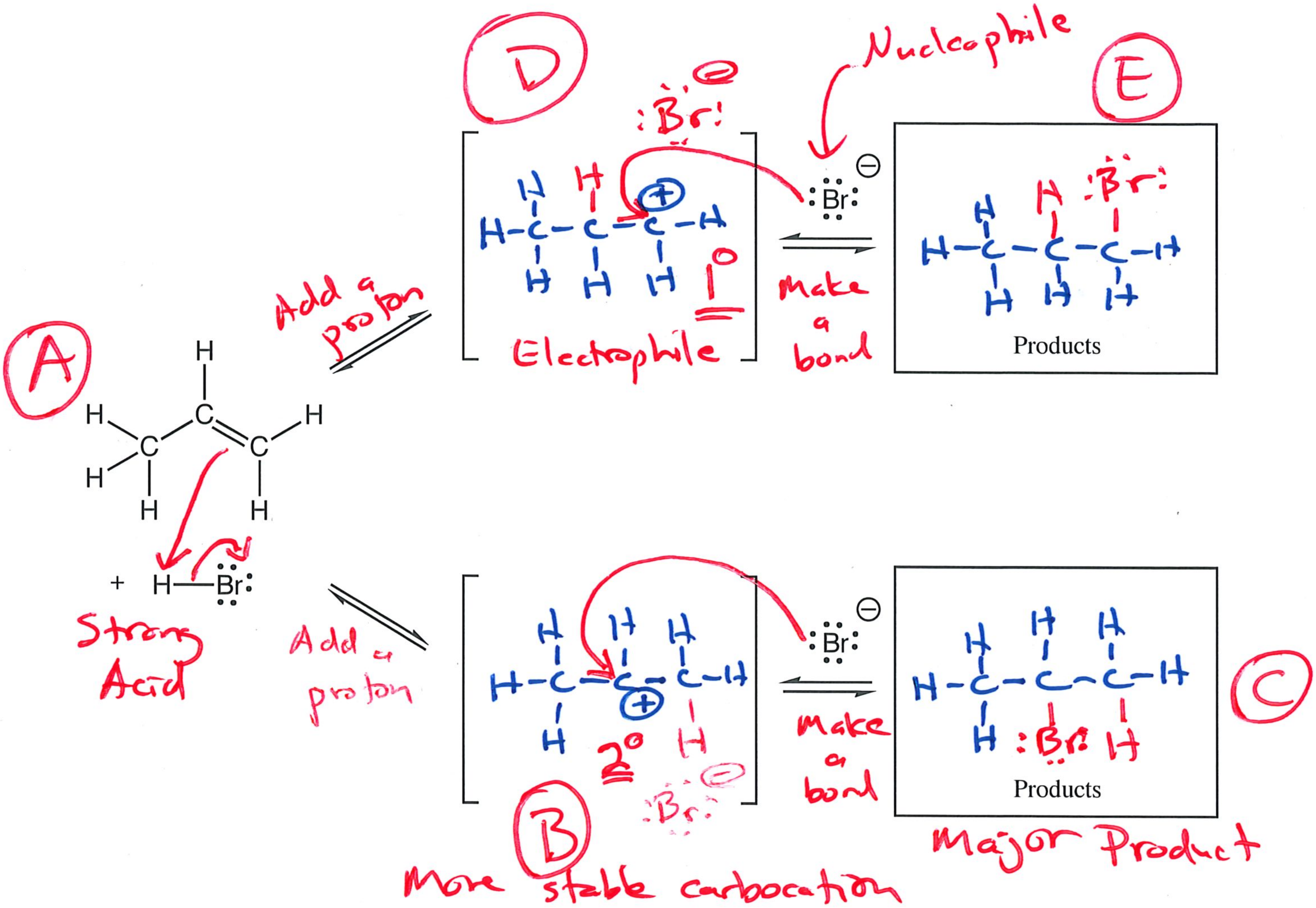
Addition of H-X to an Alkene

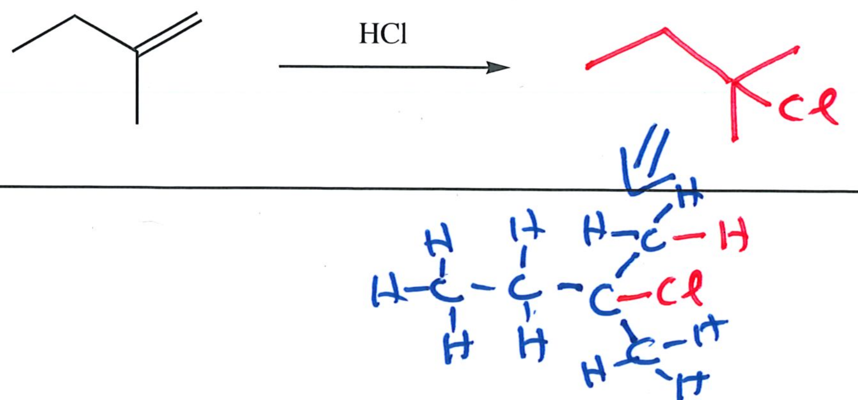


Summary: Alkene pi bond reacts with H-X (X=Cl, Br, I) to give a carbocation intermediate that makes a bond with X⊖ to give product

Regiochemistry: Markovnikov's Rule

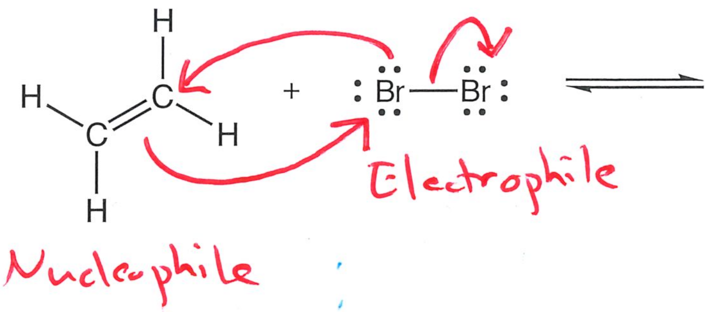
Stereochemistry: Mixed (time kapsule) → Racemic Product

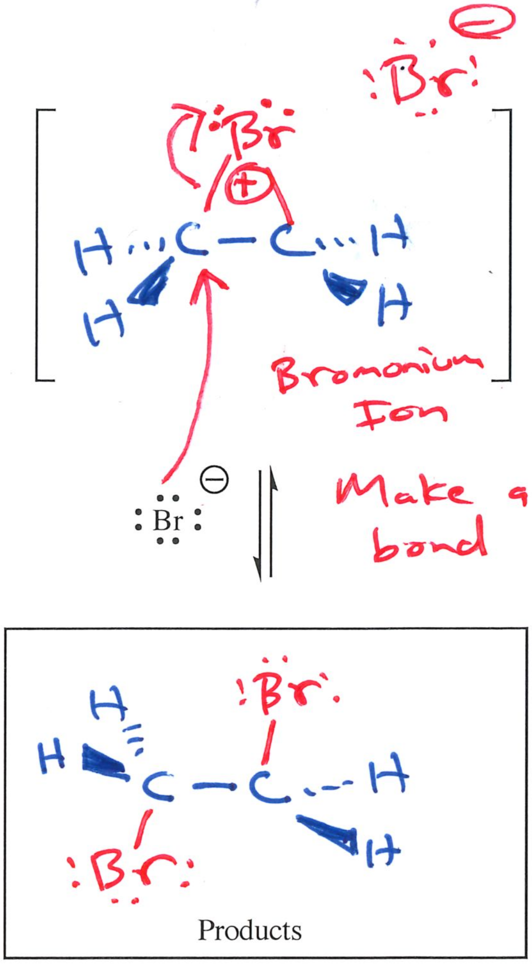
Example:



Add X_2 to alkene

Alkene Halogenation





⟹ The top face of the intermediate is blocked by the Br atom → $Br^{\ominus}$ must attack from underneath

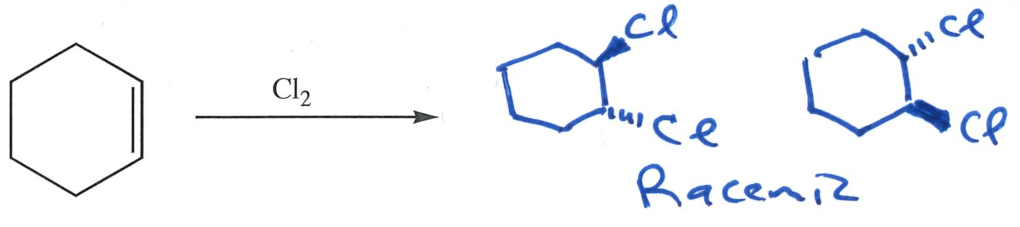
anti geometry

Summary: Alkenes react with the electrophile X_2 ($X = Cl, Br, I$) to give a three-membered ring intermediate, that reacts with $X^{\ominus}$ to give product

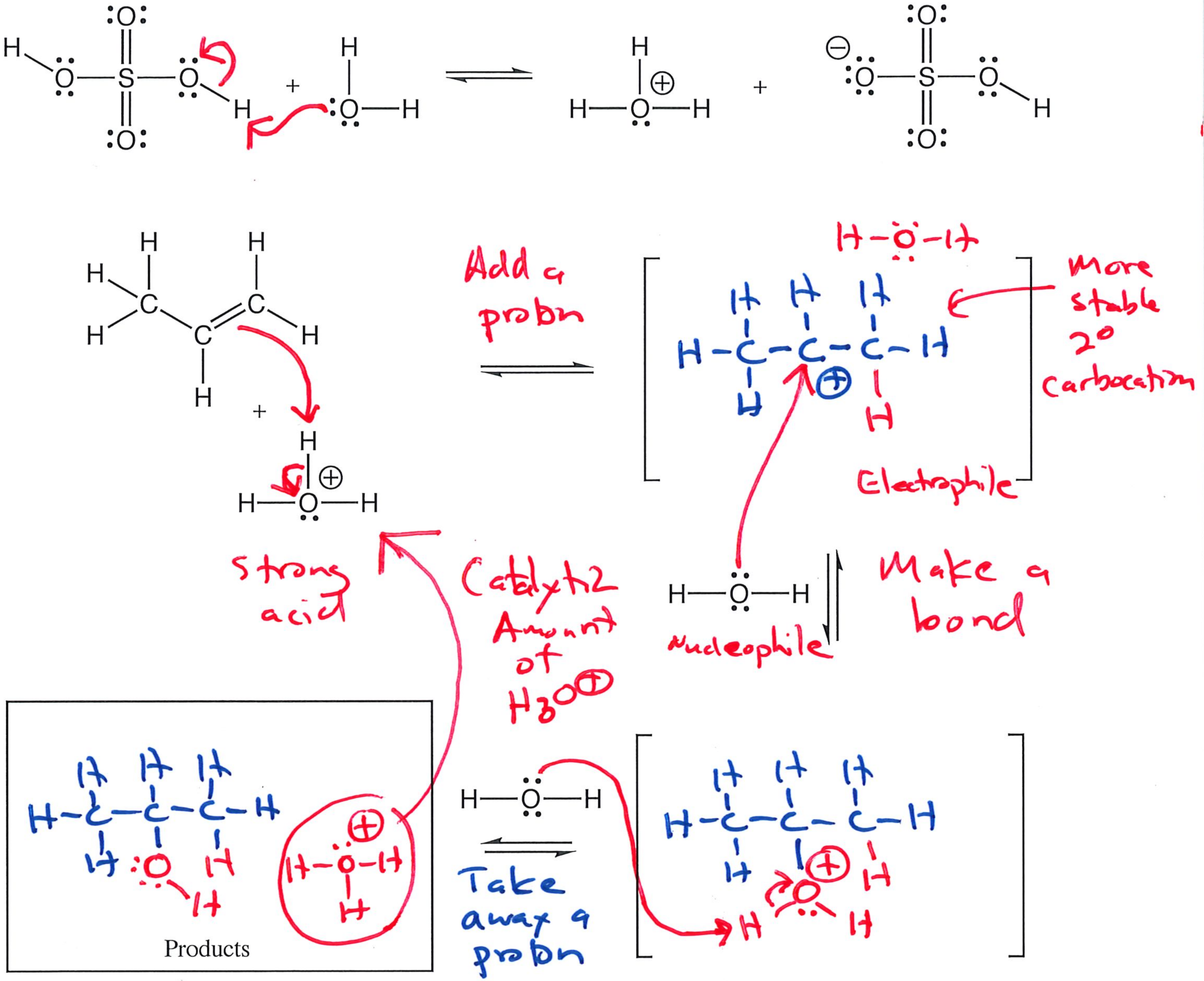
Regiochemistry: N/A (Br on both atoms)

Stereochemistry: Anti addition → trans products

Example:



Acid-catalyzed Hydration of an Alkene

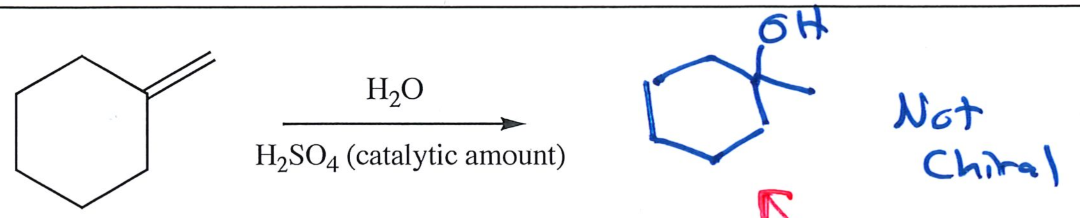


Summary: Proton adds to make a carbocation, a bond is made to water, a proton is removed to give alcohol

Regiochemistry: Markovnikov's Rule

Stereochemistry: Mixed

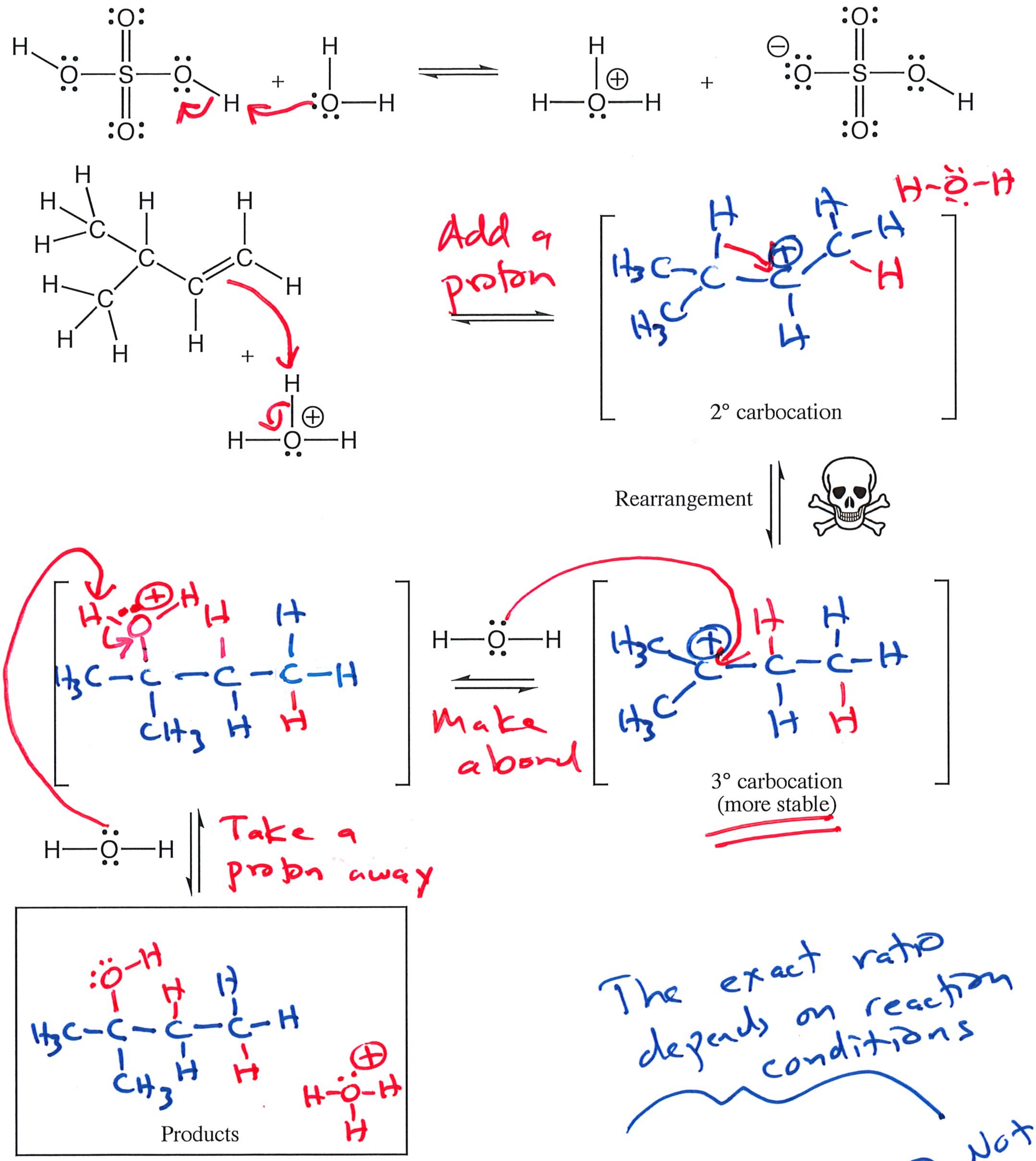
Example:



OH is on more substituted C atom → Markovnikov

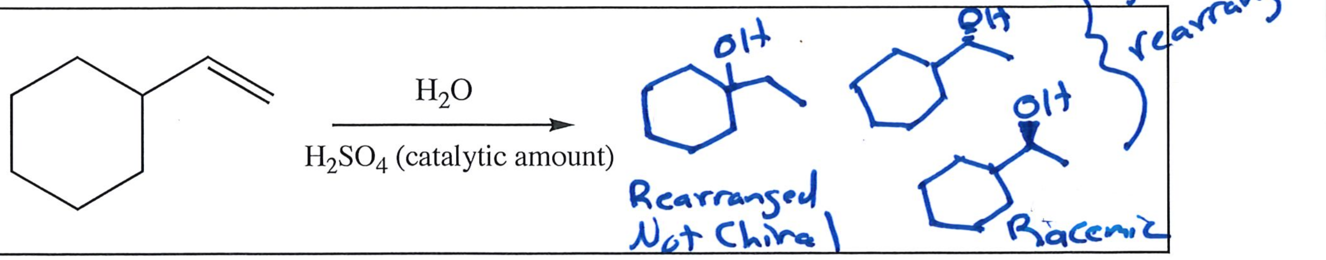
pH does not change during reaction

Cation Rearrangement



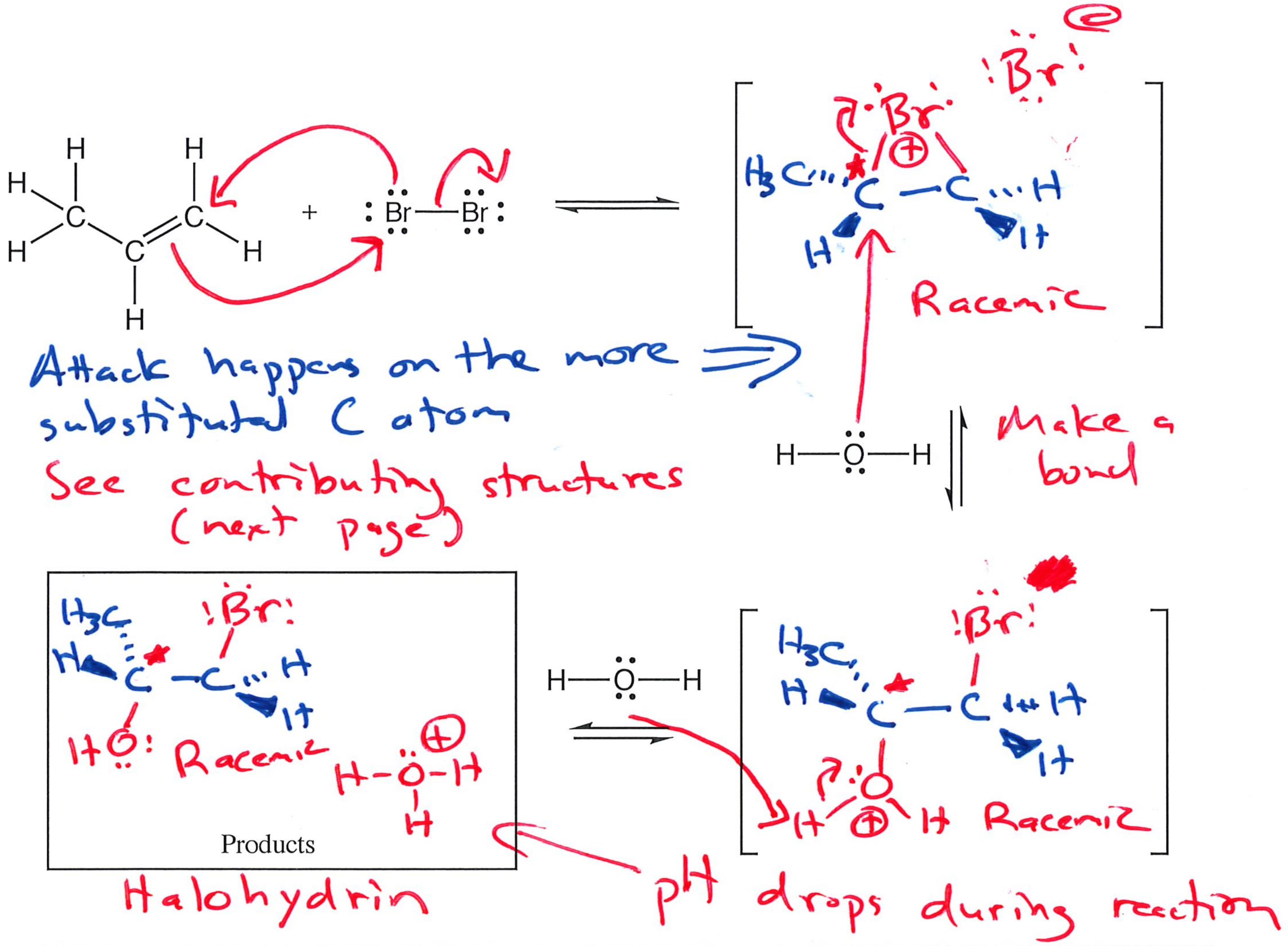
The exact ratio depends on reaction conditions

Example:



Add X_2 in the presence of excess H_2O

Alkene Hydrohalogenation



Attack happens on the more substituted C atom

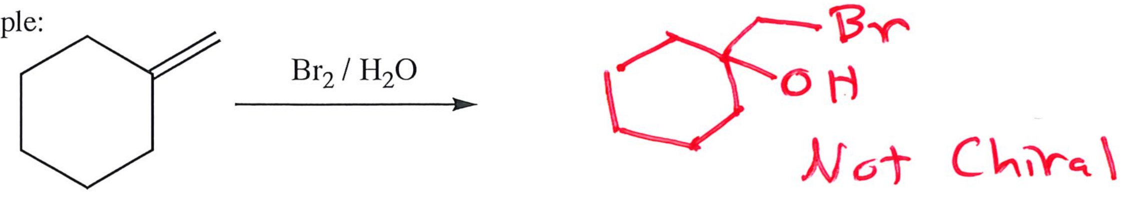
See contributing structures (next page)

Summary: Alkene reacts with X_2 to give three-membered ring intermediate, H_2O adds to the more substituted C atom, water removes proton to give product

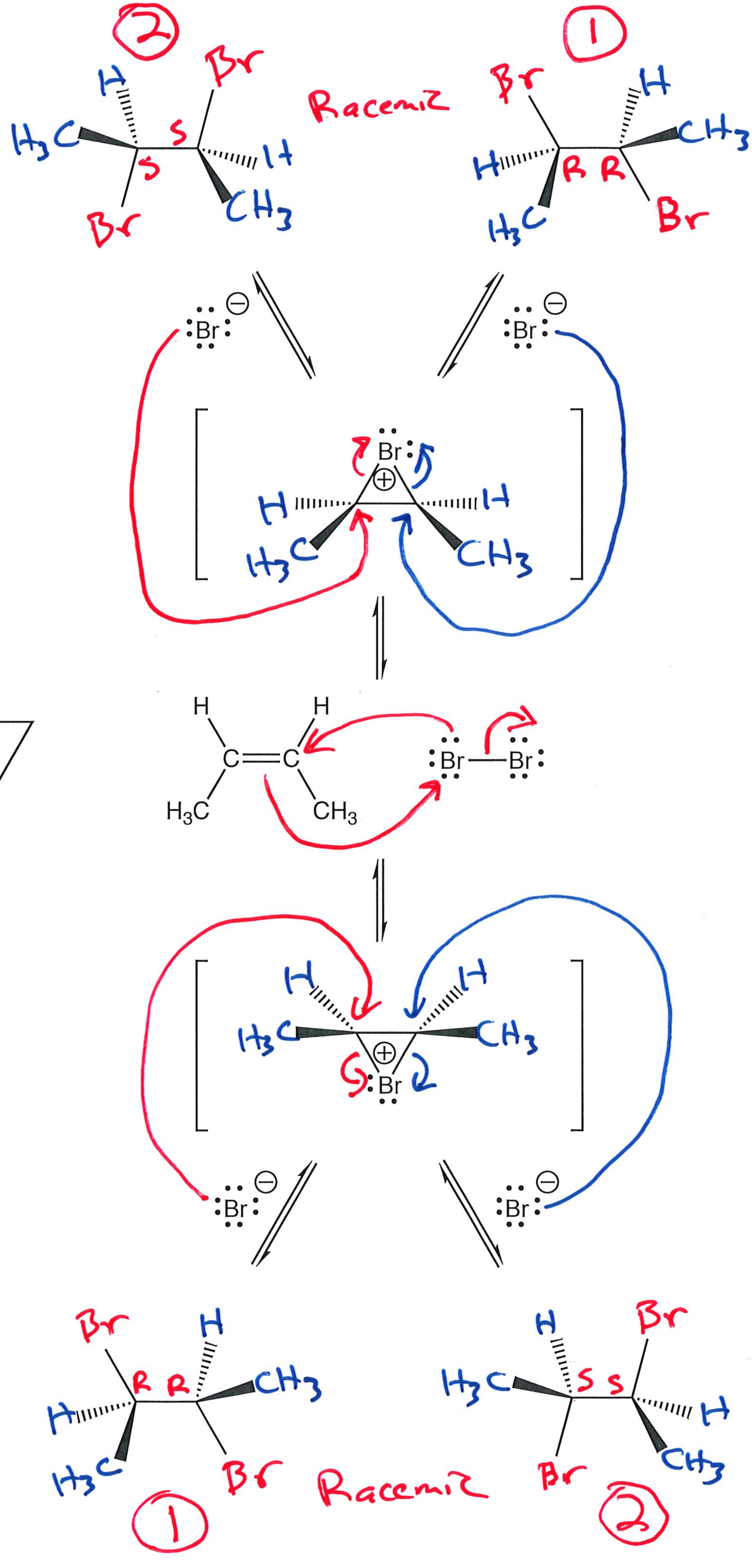
Regiochemistry: Markovnikov

Stereochemistry: Anti addition

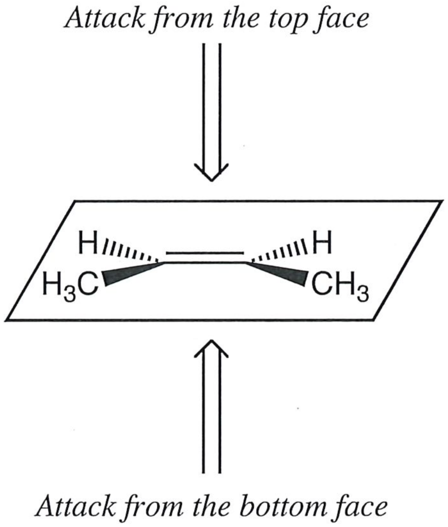
Example:



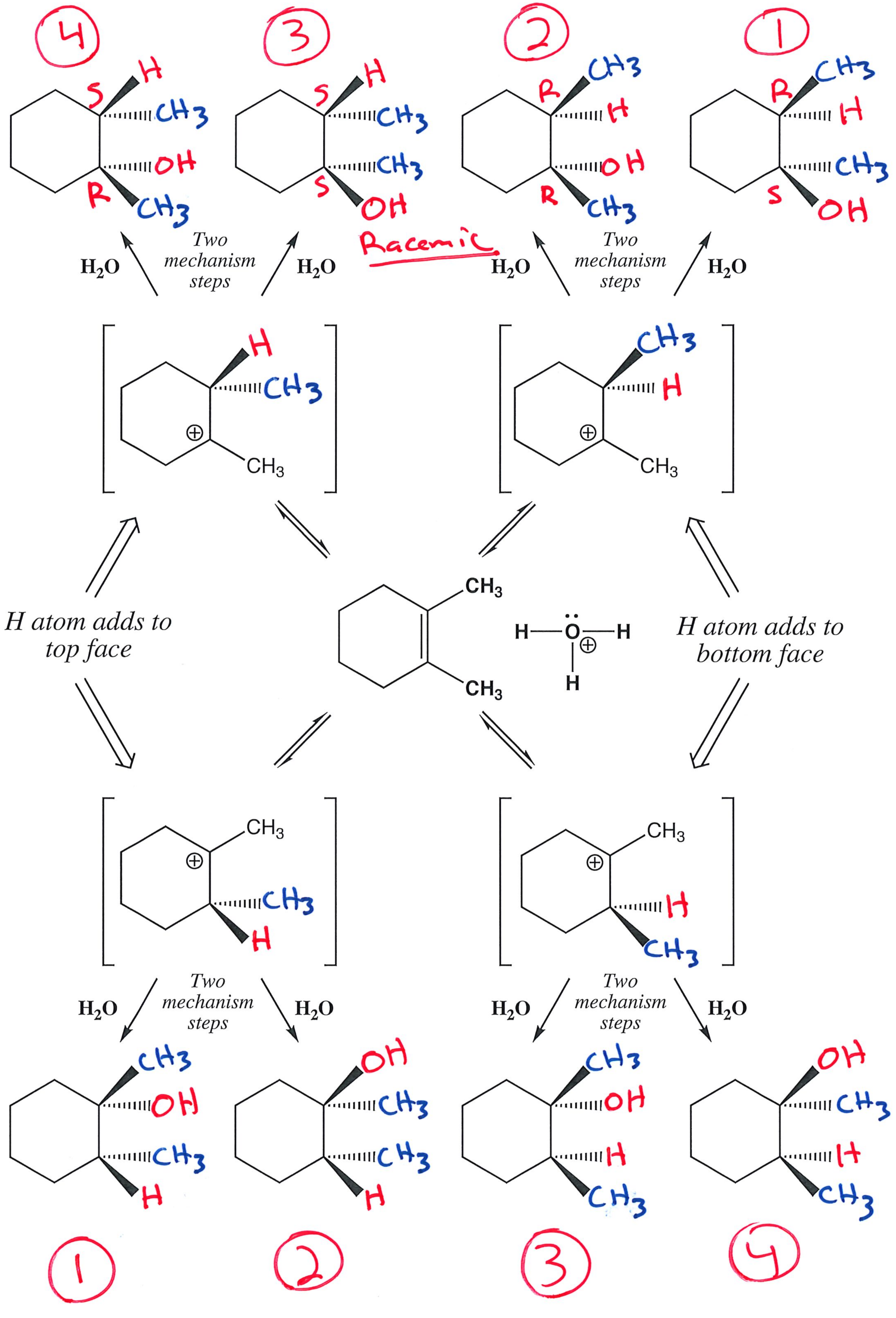
There is more H_2O present, so H_2O reacts in second step, not $Br^{\ominus}$



②
①
Racemic
S
S
R R
Br
H
H_3C
CH_3
Br⊖
Br⊕
C=C
Br—Br
R R
S S
Racemic
①
②

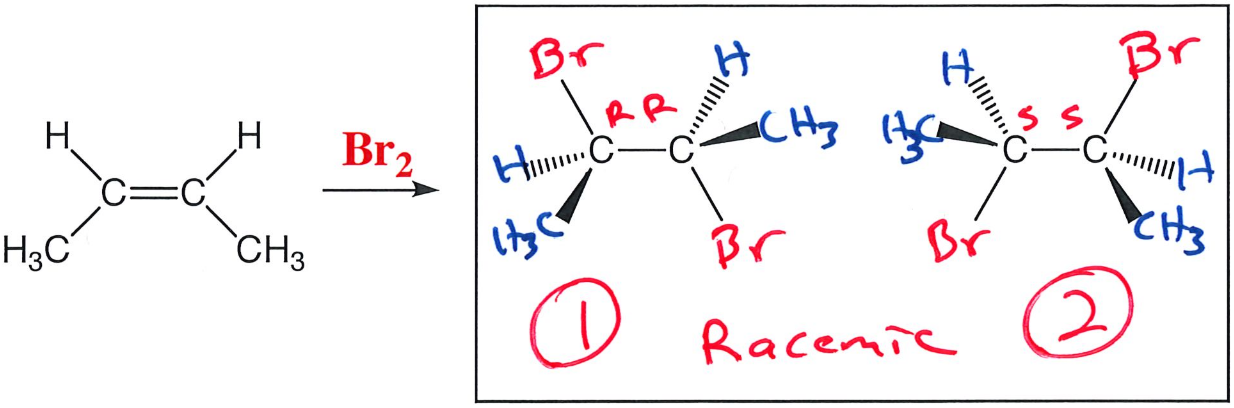


Attack from the top face
H_3C
H
H
CH_3
Attack from the bottom face


④
③
②
①
S
R
H
CH3
OH
Two mechanism steps
H2O
Racemic
H atom adds to top face
H atom adds to bottom face
CH3
⊕
H—Ö—H
H
①
②
③
④

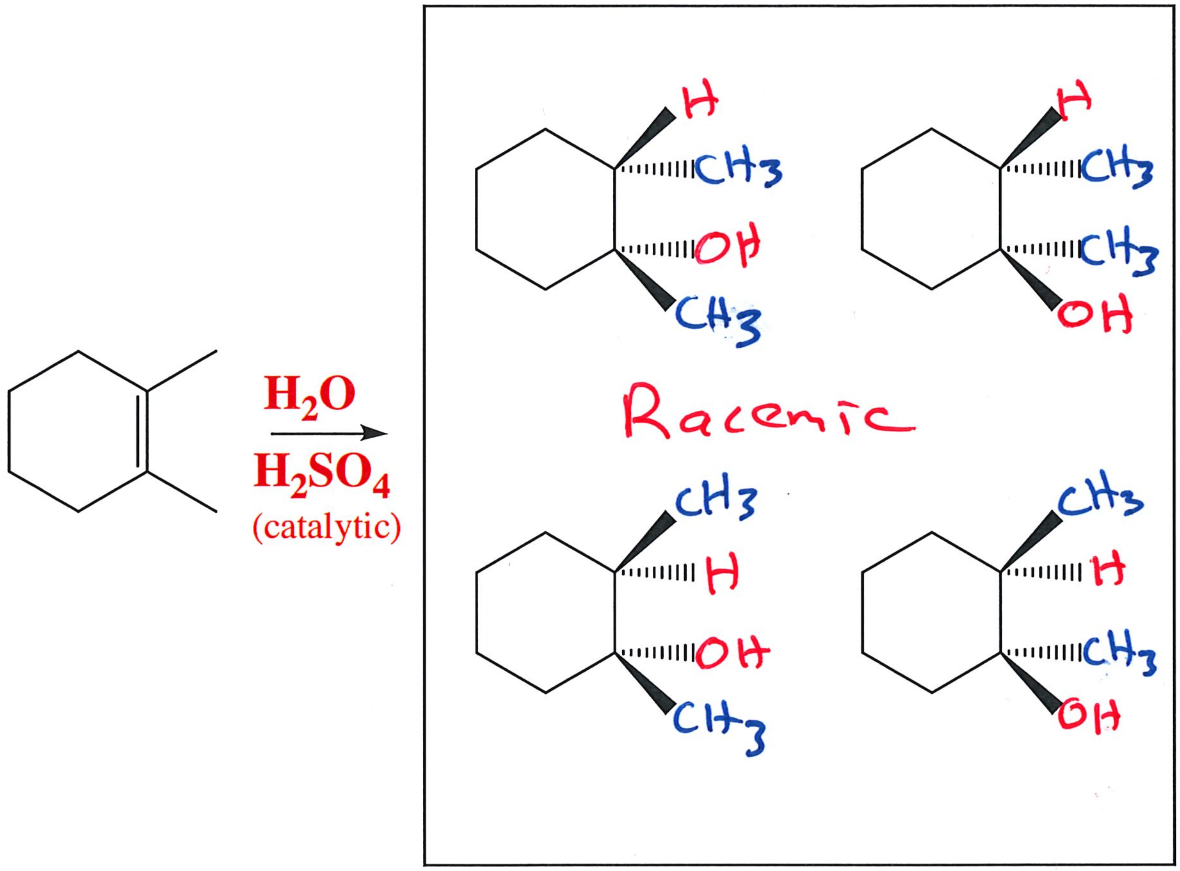
Examples

1)



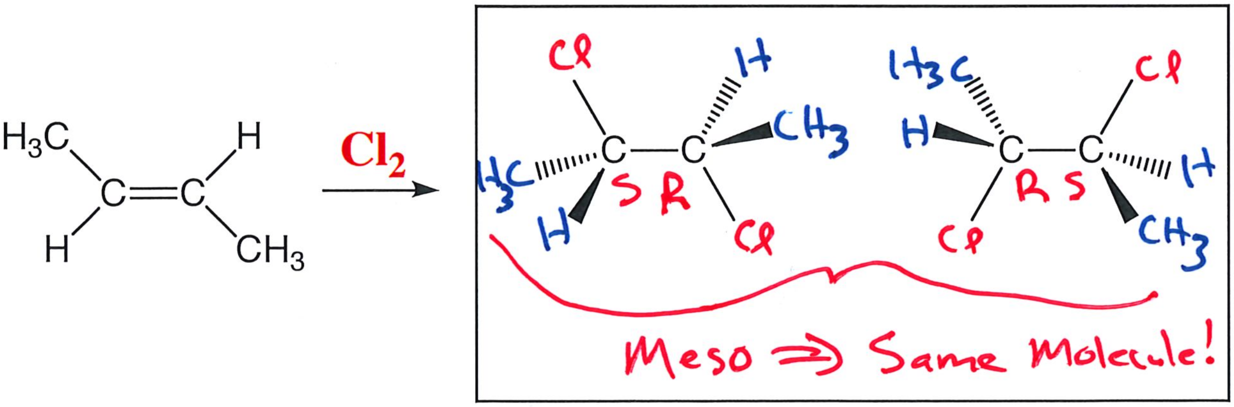
Racemic

2)



Racemic

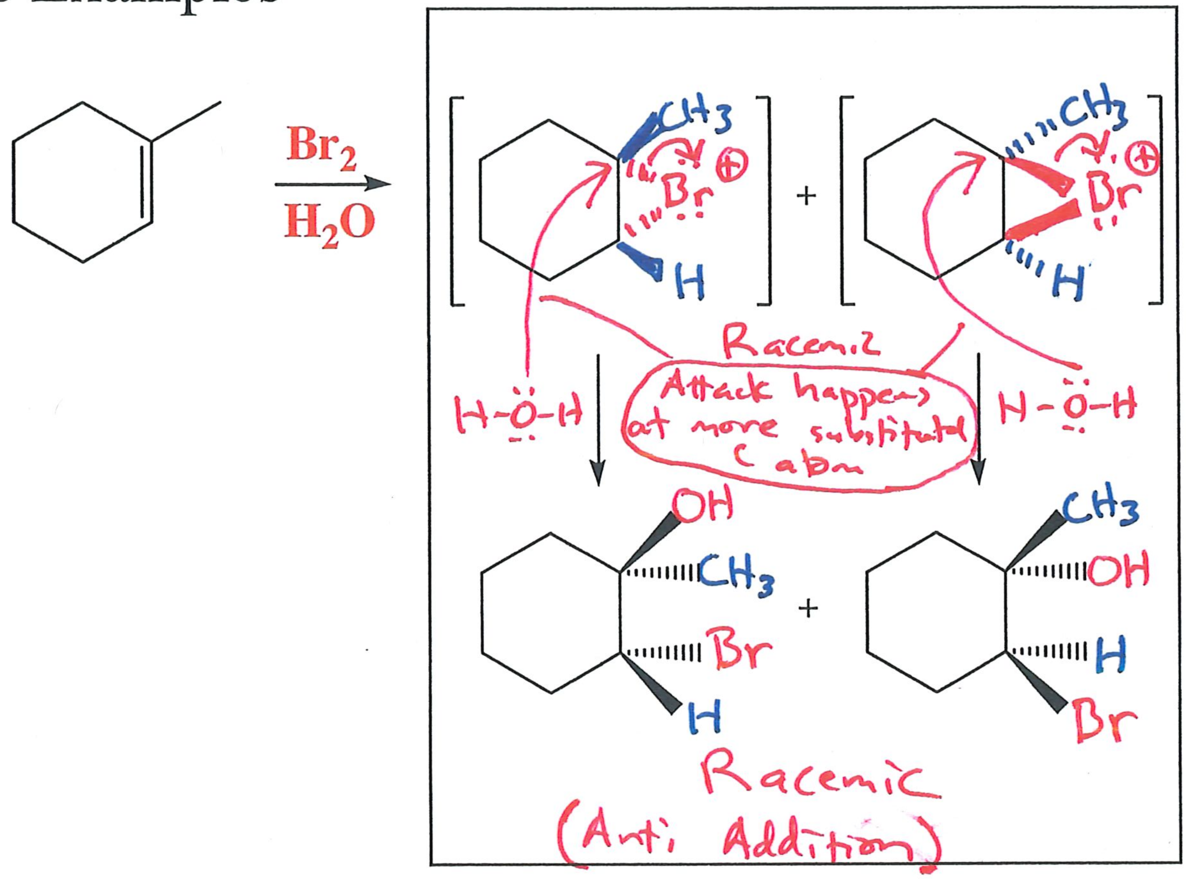
3)



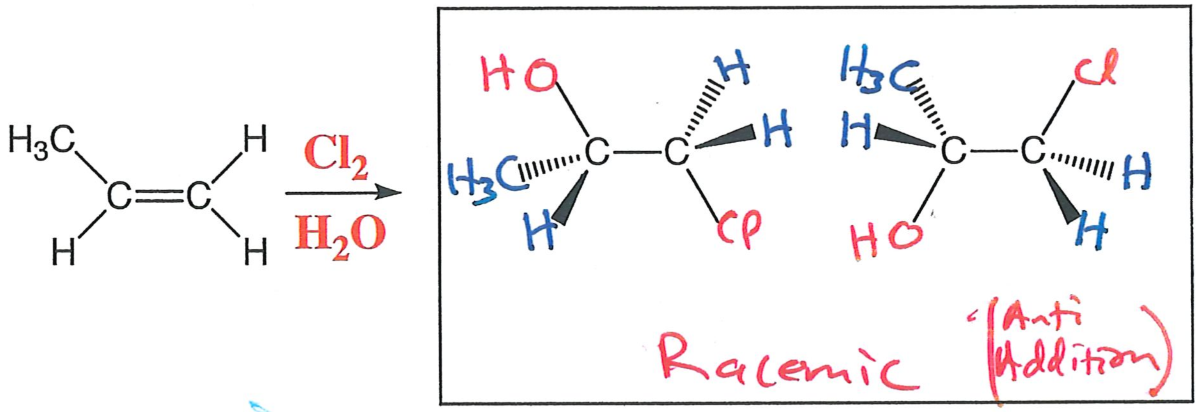
Meso ⇒ Same Molecule!

More Examples

4)

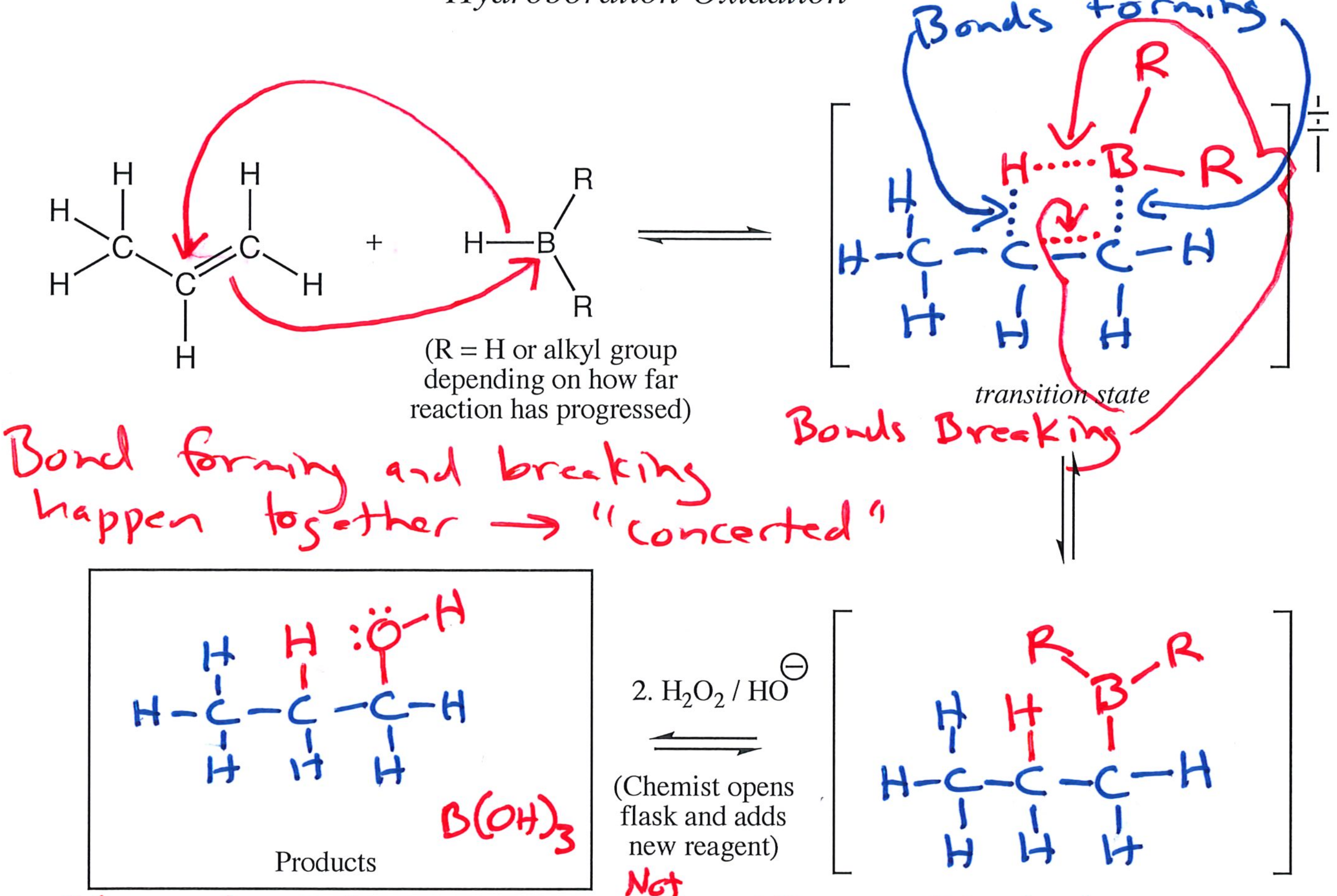


5)



Home of the 4-membered ring Transition State

Hydroboration-Oxidation



(R = H or alkyl group depending on how far reaction has progressed)

Bond forming and breaking happen together → "concerted"

(Chemist opens flask and adds new reagent)

Stereochemistry is NOT mixed in this last step

Not responsible for this step

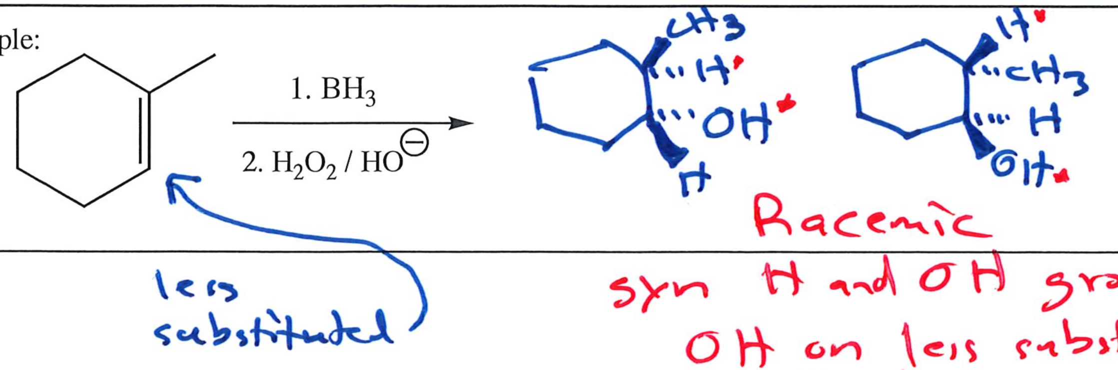
Alkyl borane

Summary: The pi bond of the alkene reacts with BH_3 ~~to~~ ~~put~~ via a four-membered ring transition state to give the alkyl borane

Regiochemistry: non-Markovnikov

Stereochemistry: syn

Example:

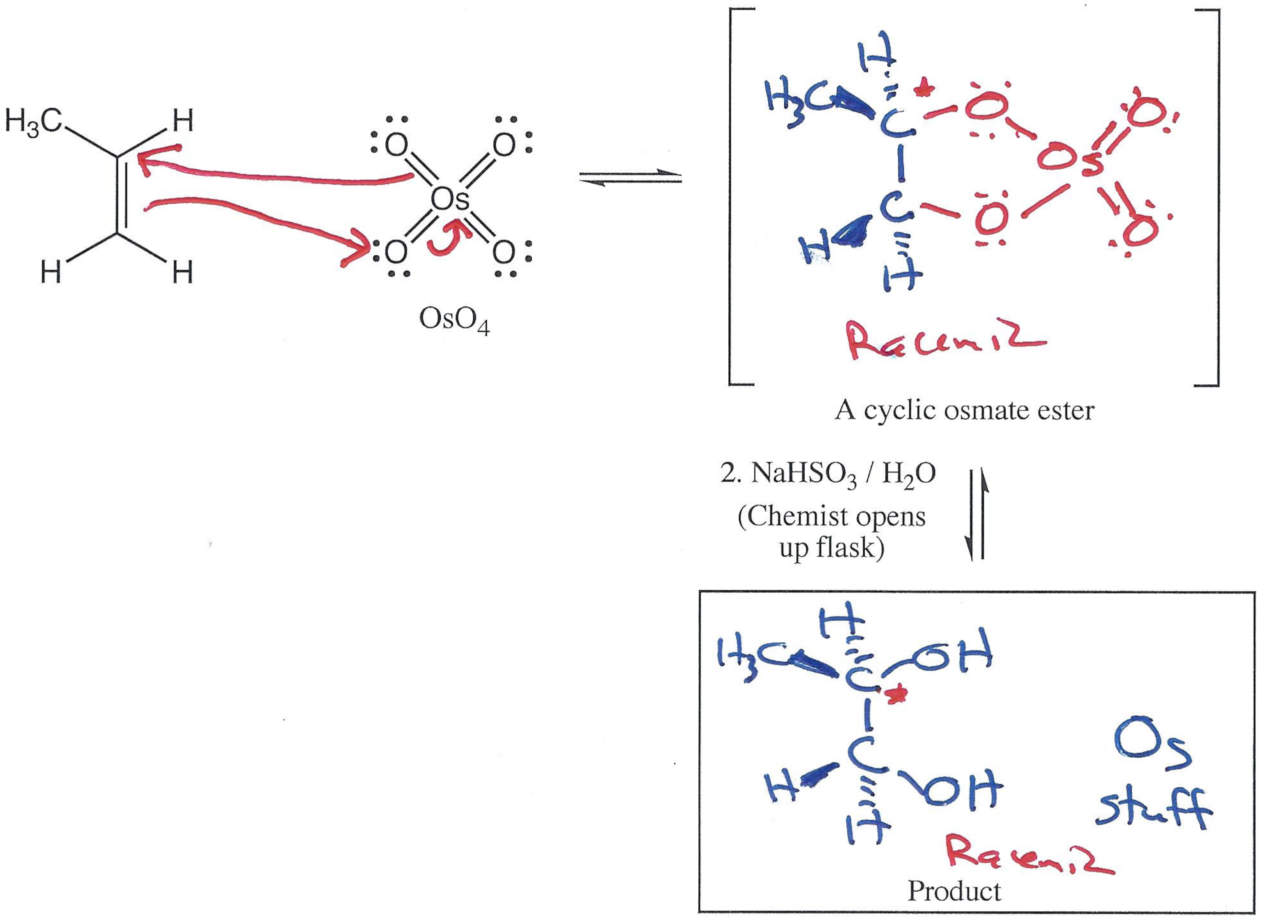


Racemic

syn H and OH groups added

OH on less substituted C atom

OsO_4 Partial Mechanism

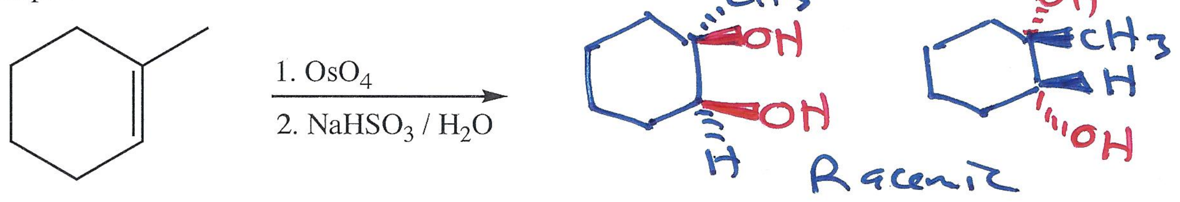


Summary: Mechanism involves a cyclic osmate ester leading to syn stereochemistry

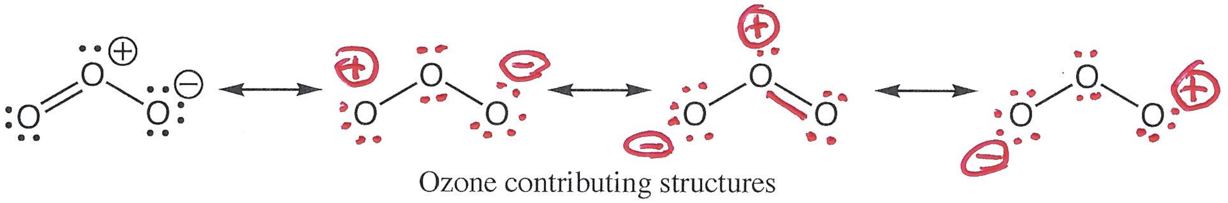
Regiochemistry: N/A

Stereochemistry: Syn

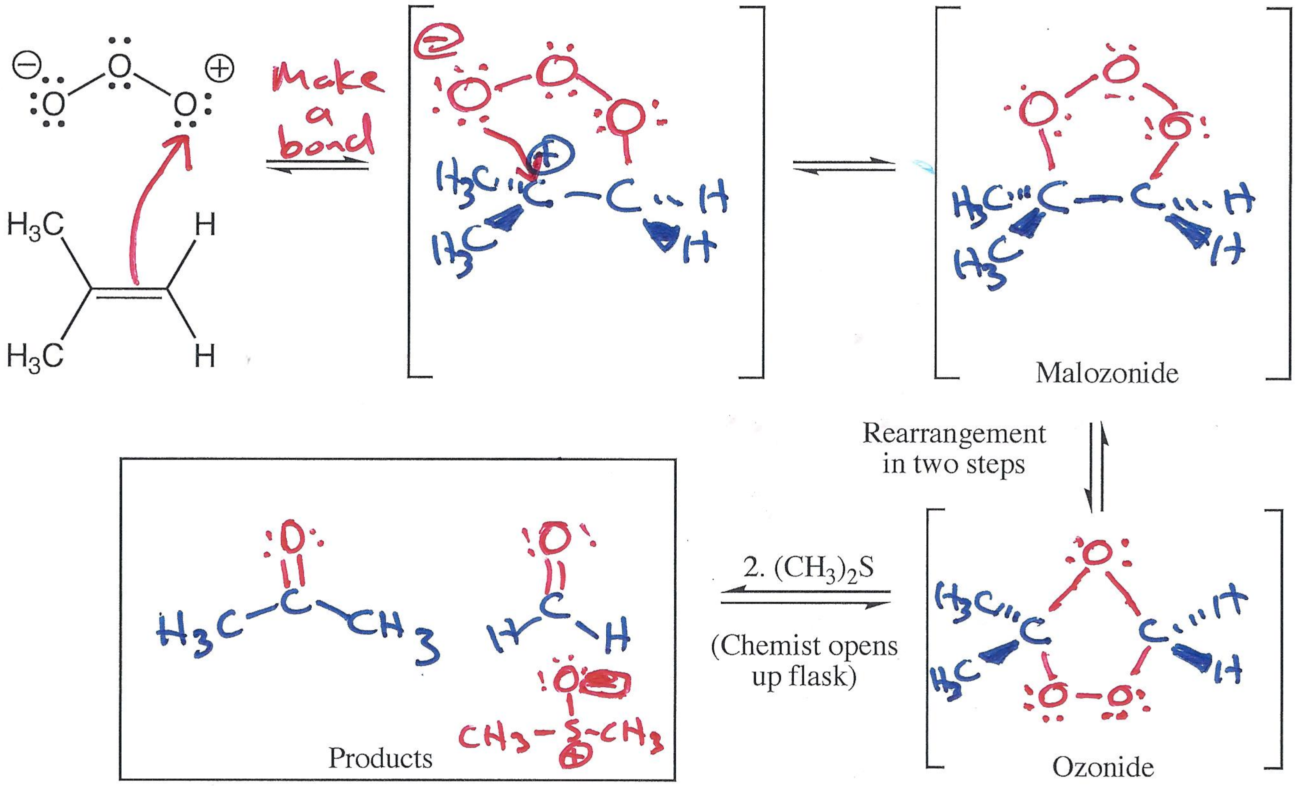
Example:



Ozonolysis Partial Mechanism



Ozone contributing structures

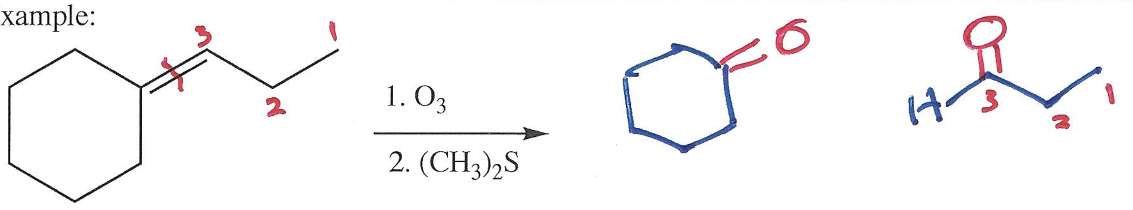


Summary: Ozone reacts with alkenes to give malozonide then ozonide intermediates that react with $(CH_3)_2S$ to give products

Regiochemistry: N/A

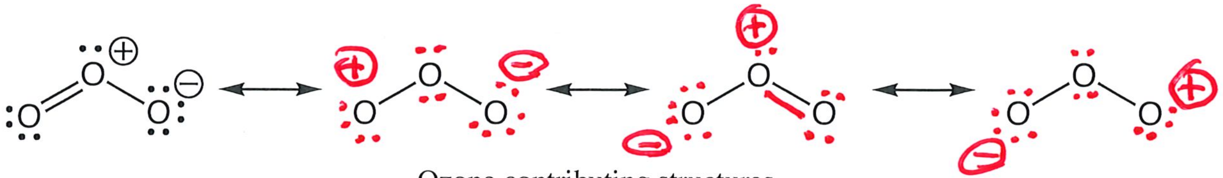
Stereochemistry: N/A

Example:

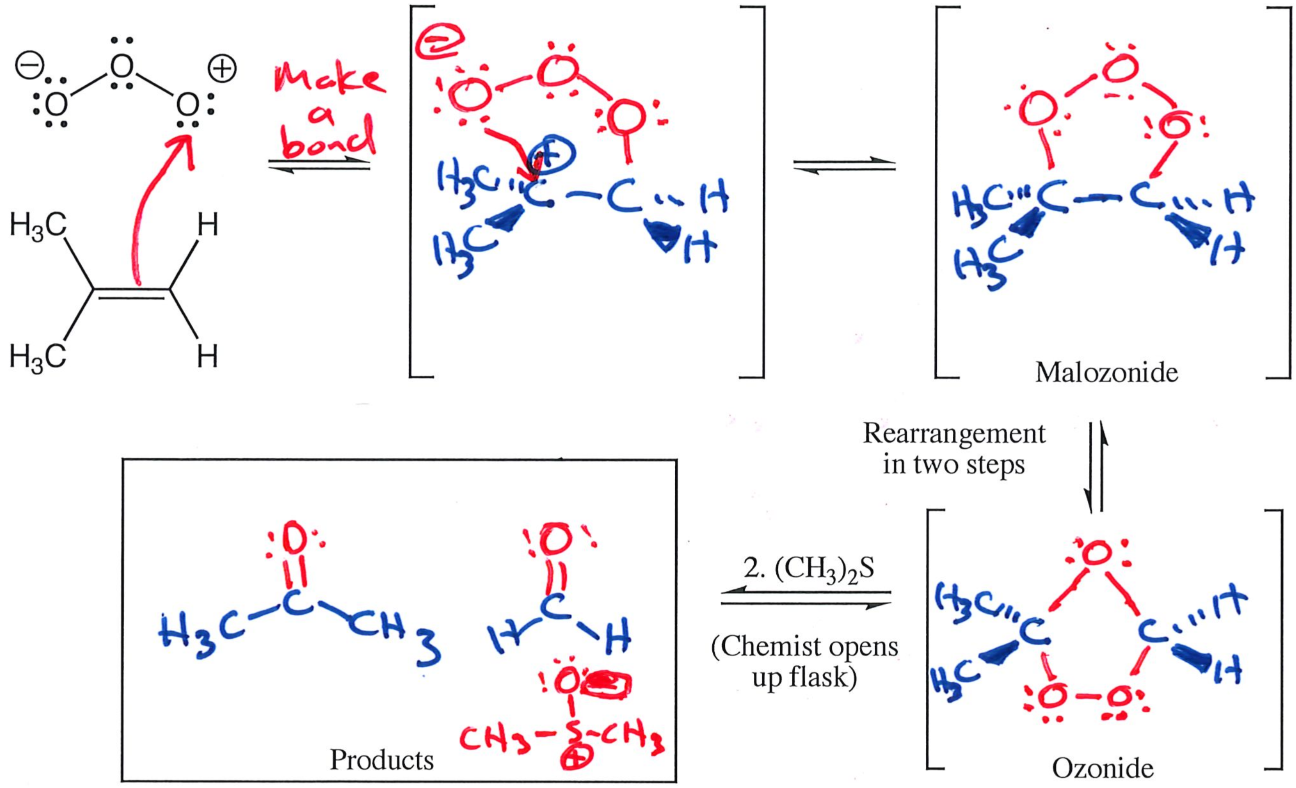


The only reaction you will learn that breaks C=C bonds (or any C–C bond)

Ozonolysis Partial Mechanism



Ozone contributing structures

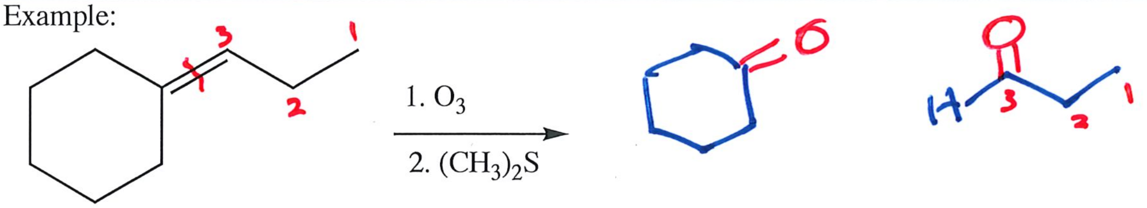


Summary: Ozone reacts with alkenes to give malozonide then ozonide intermediates that react with $(CH_3)_2S$ to give products

Regiochemistry: N/A

Stereochemistry: N/A

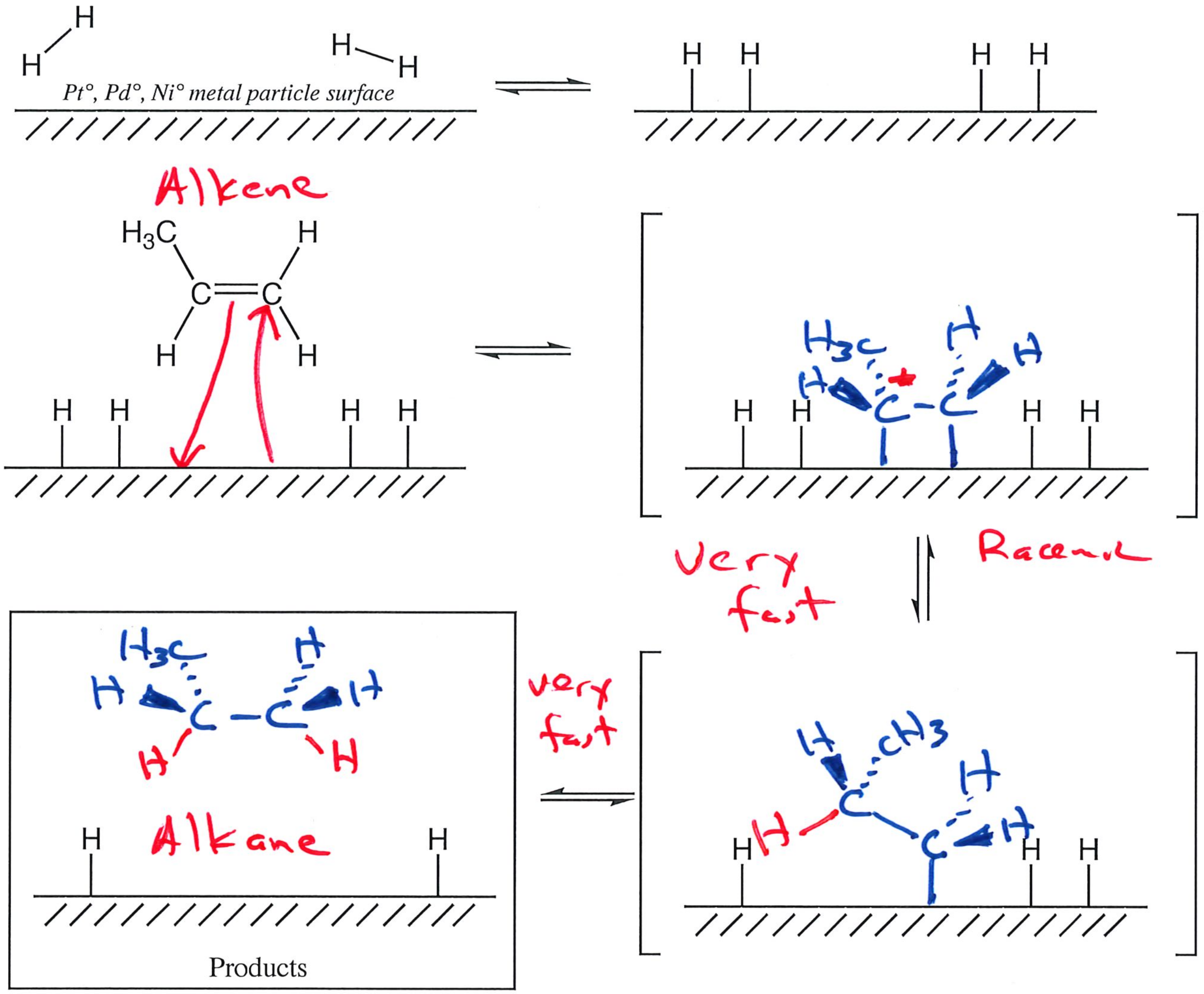
Example:



The only reaction you will learn that breaks C=C bonds (or any C–C bond)

Converts alkenes to alkanes

Hydrogenation: H_2 with Pt°, Pd°, Ni°

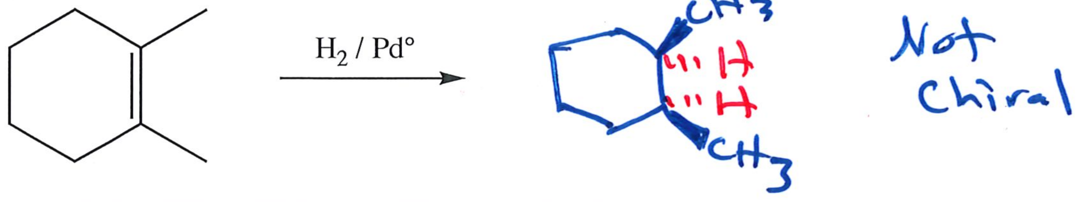


Summary: H_2 adsorbs onto the metal surface → alkene adsorbs onto the metal surface → H atoms transfer to both C atoms of the original C=C

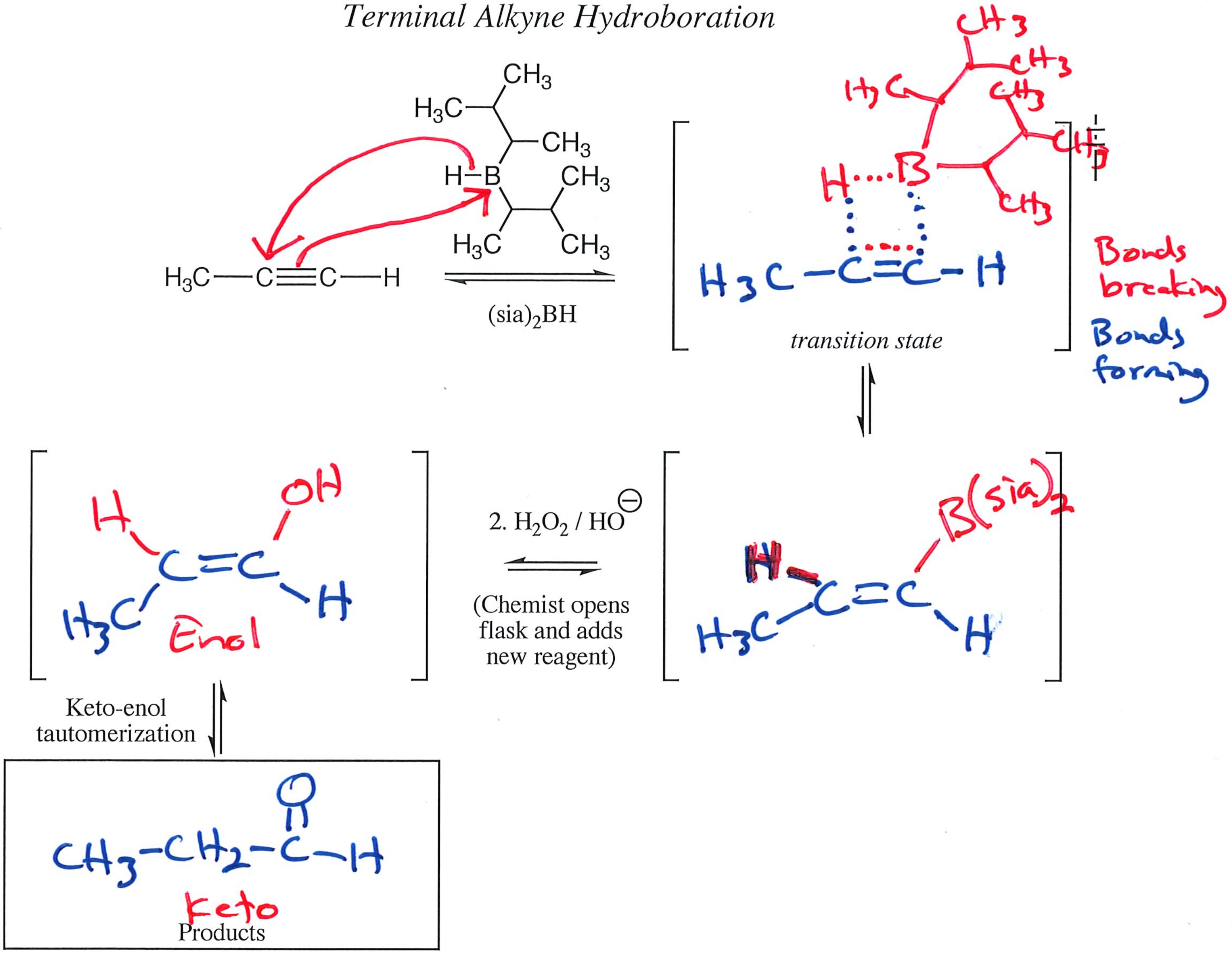
Regiochemistry: N/A

Stereochemistry: Syn → both H atoms add to same face

Example:



Terminal Alkyne Hydroboration

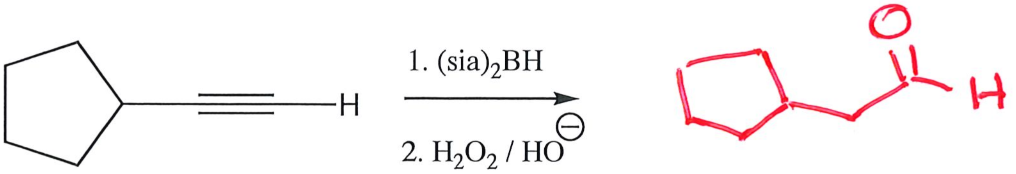


Summary: 1) $(sia)_2BH$ 2) $H_2O_2/HO^\ominus$ gives syn additon of H and OH, to create an enol that spontaneously gives the more stable keto product

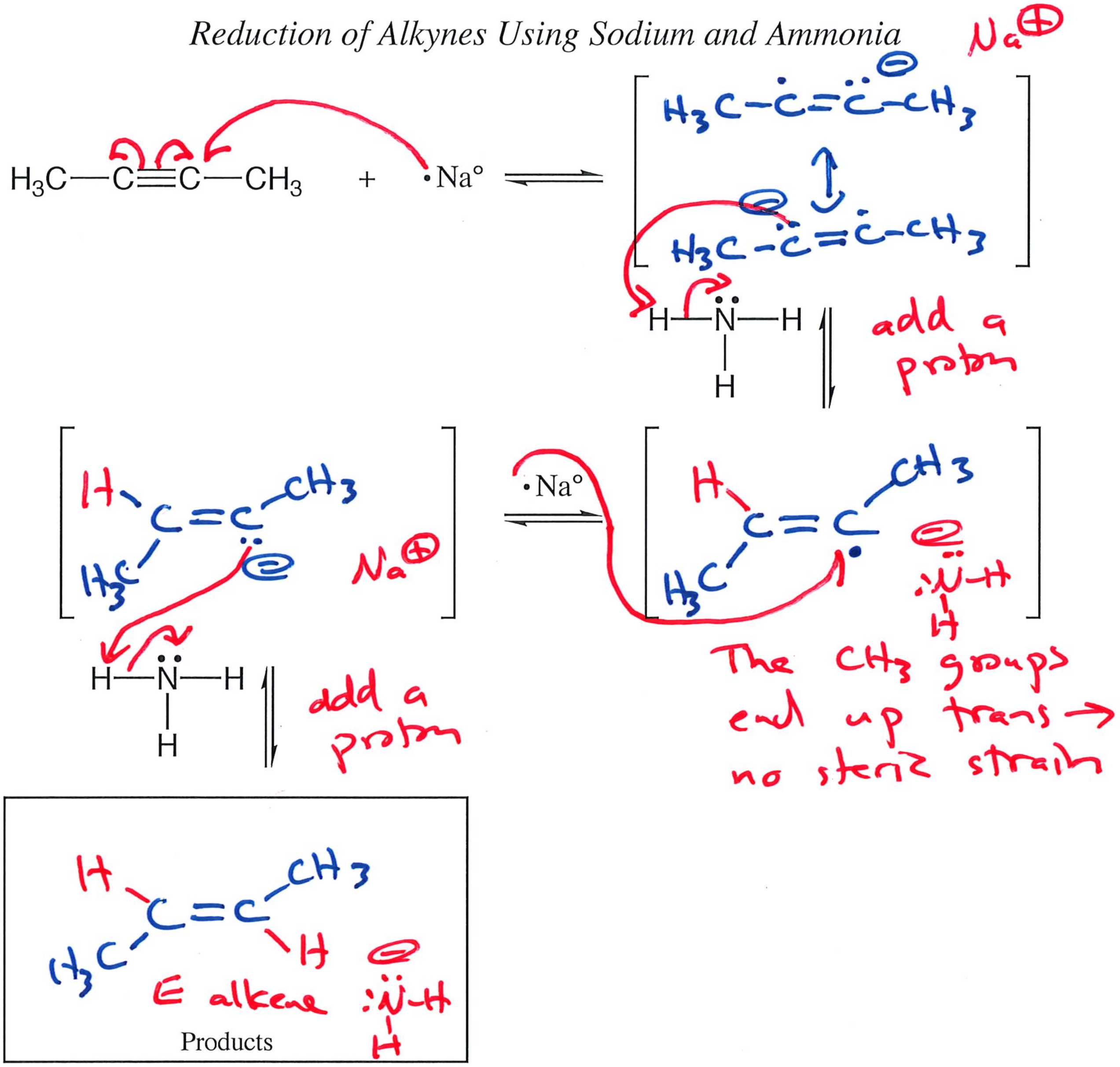
Regiochemistry: Terminal alkynes → non-Markovnikov

Stereochemistry: N/A

Example:



Reduction of Alkynes Using Sodium and Ammonia

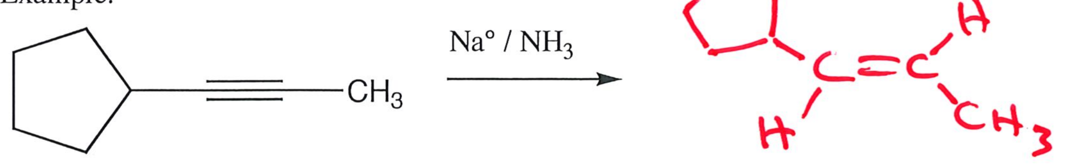


Summary: Alkynes are reduced to an E alkene by two single electrons from Na° and two protons from :NH_3

Regiochemistry: – N/A

Stereochemistry: anti → E alkenes

Example:

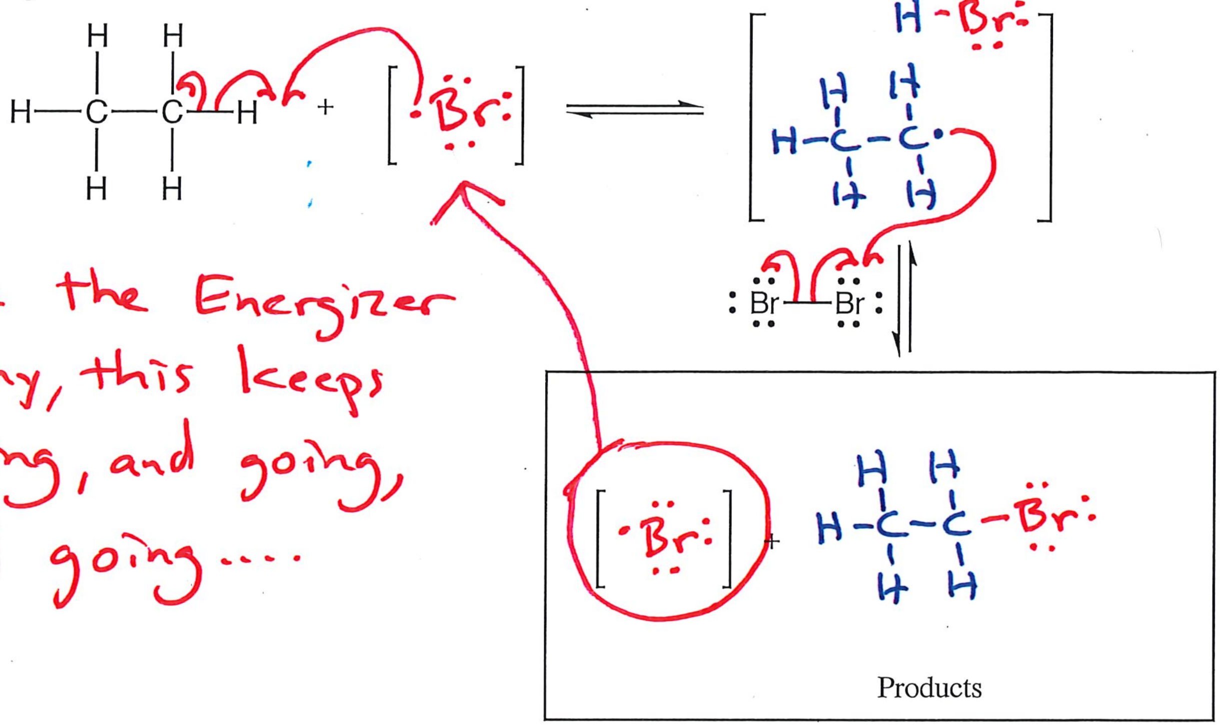


The only reaction that starts with an alkane

Alkane Free Radical Halogenation

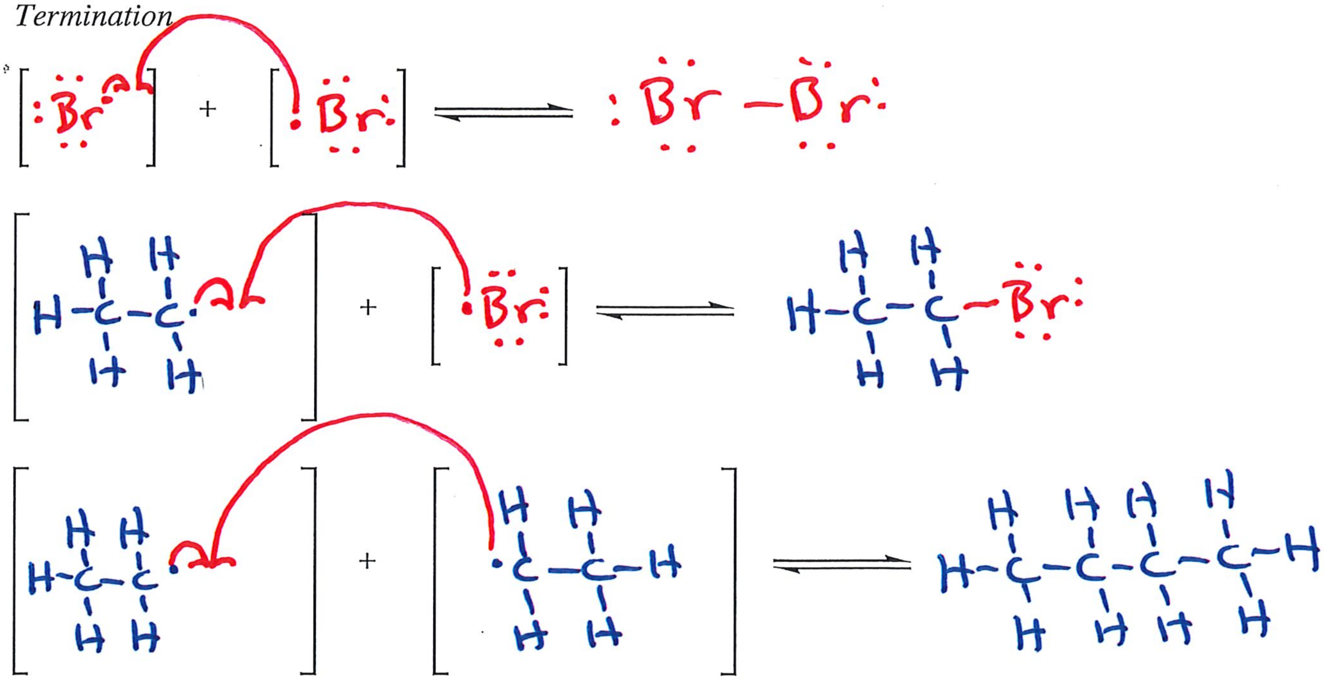
Initiation

Propagation



Like the Energizer bunny, this keeps going, and going, and going....

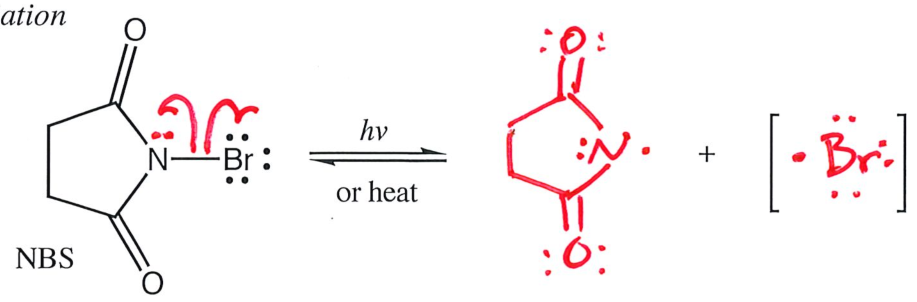
Termination



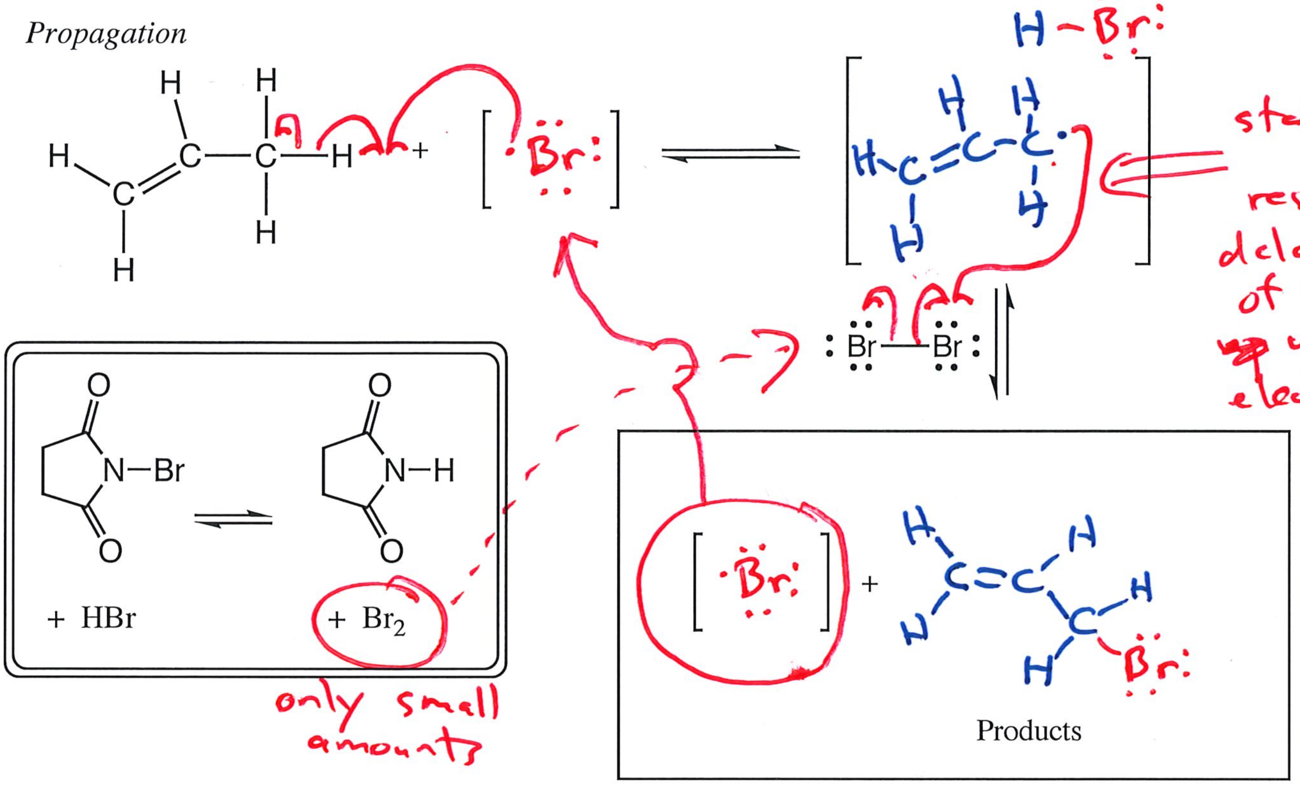
When two radicals collide → they form a new bond, ending the radical chain process

Allylic Halogenation

Initiation



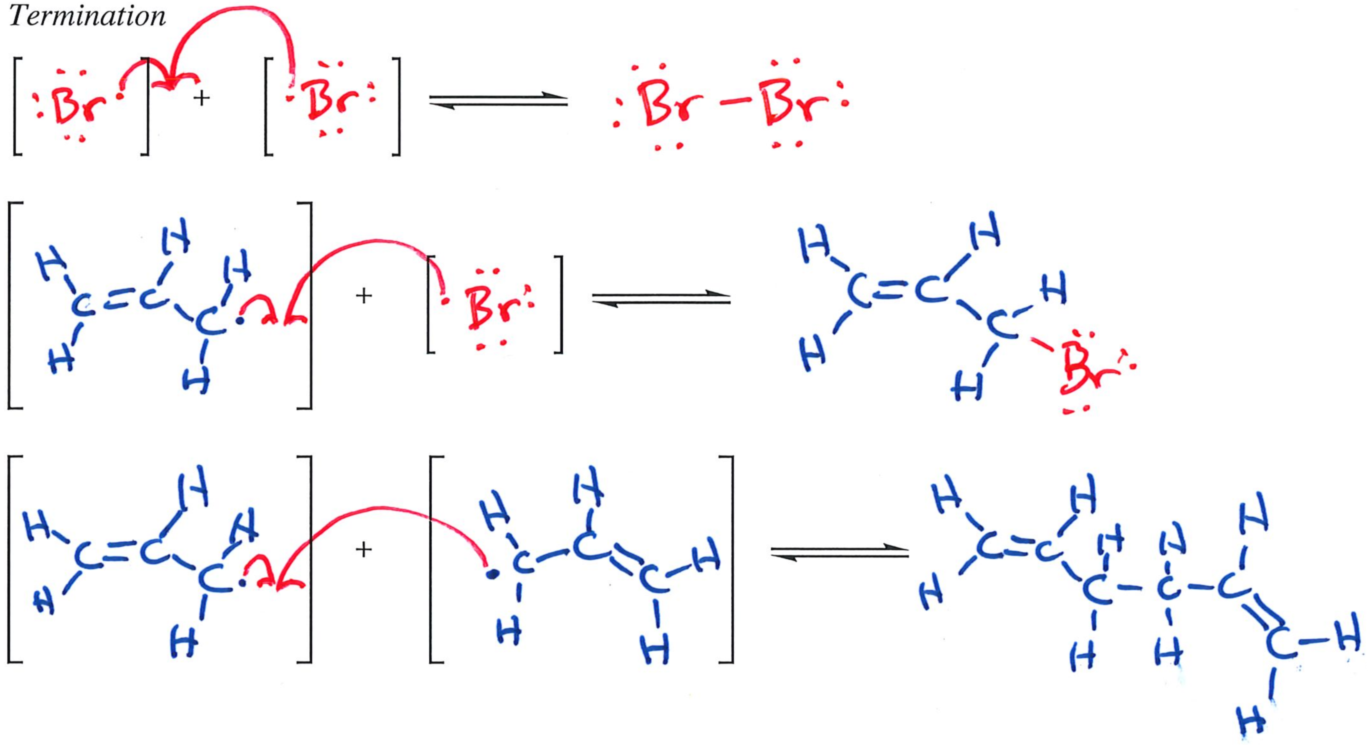
Propagation



stabilized by resonance delocalization of the unpaired electron density

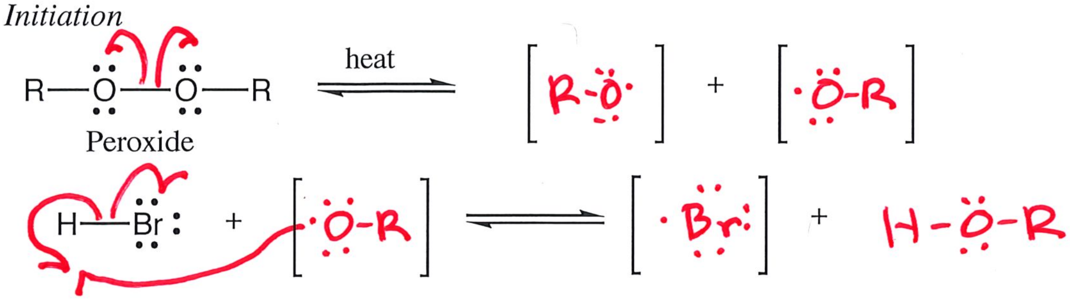
only small amounts

Termination

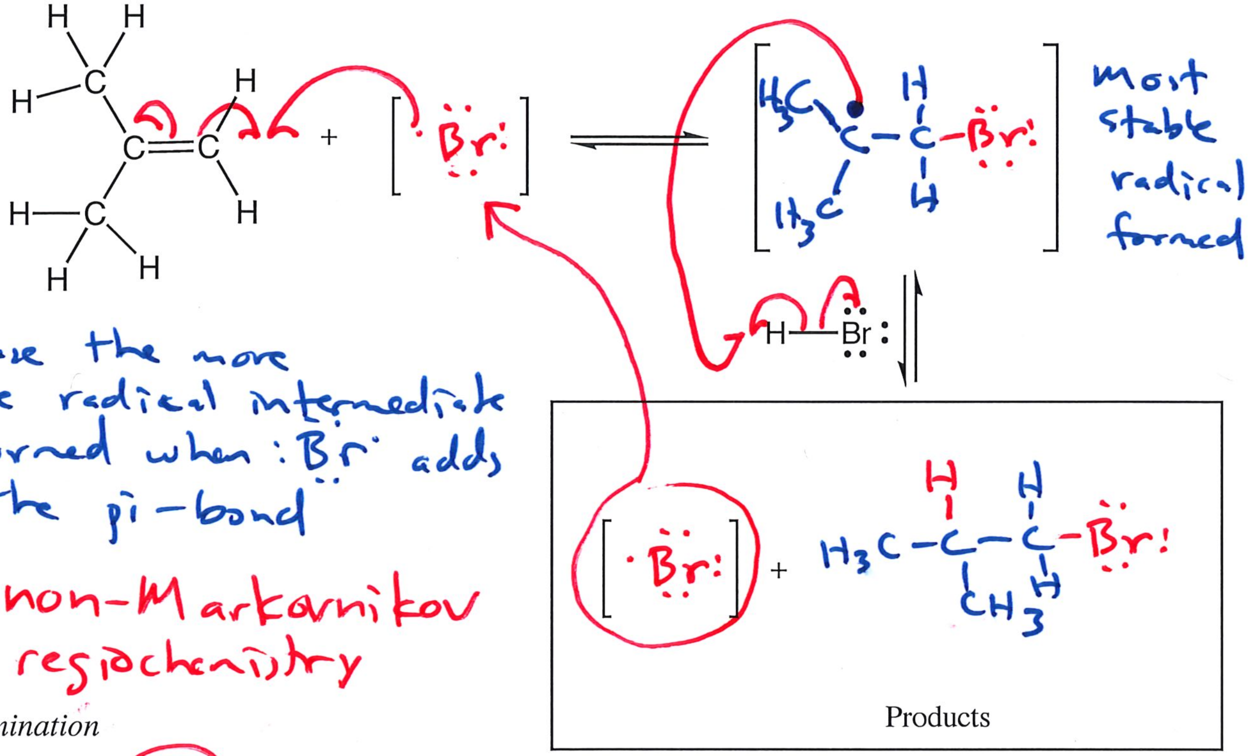


Non-Markovnikov Addition of HBr to an Alkene

Initiation



Propagation

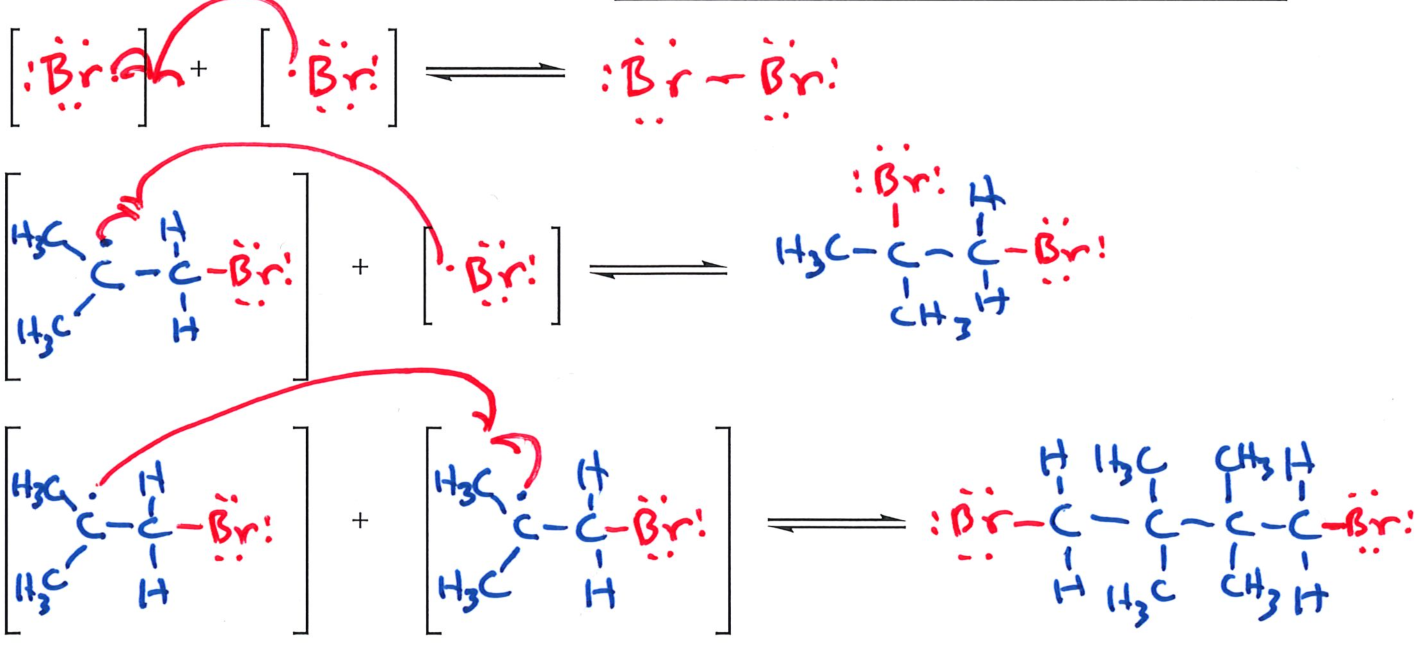


most stable radical formed

Because the more stable radical intermediate is formed when :Br· adds to the pi-bond

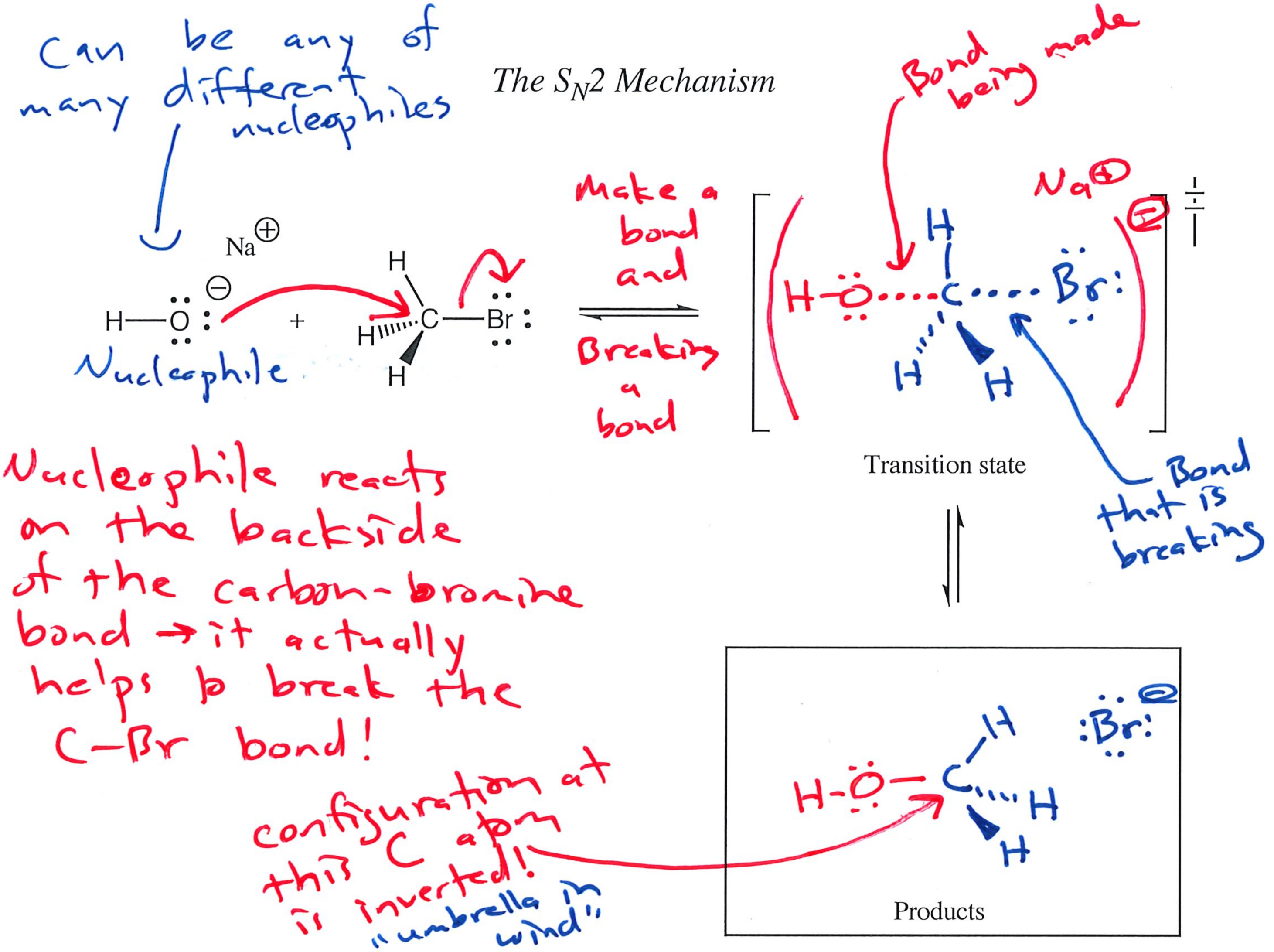
⇒ non-Markorvnikov regiochemistry

Termination



Stereochemistry is mixed

The S_N2 Mechanism



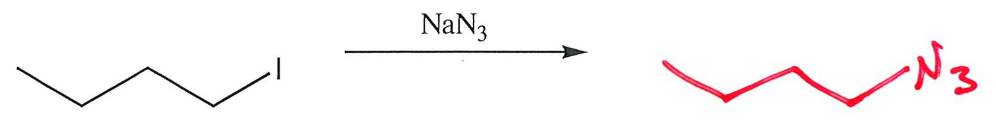
Nucleophile reacts on the backside of the carbon-bromine bond → it actually helps to break the C–Br bond!

Summary: Backside attack by a nucleophile forms a new bond to carbon, and helps break the carbon-leaving group bond.

Regiochemistry: N/A

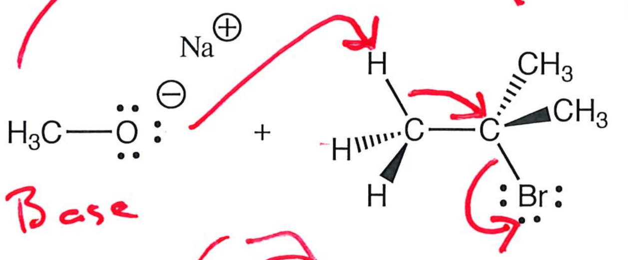
Stereochemistry: INVERSION at site of reaction

Example:



The E2 Mechanism

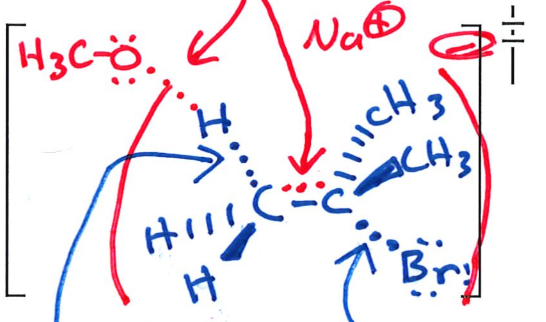
Both of these are part of rate determining step



Base

Take a proton away

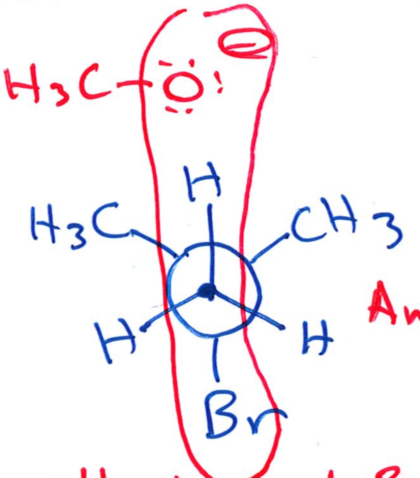
Break a bond



Transition state

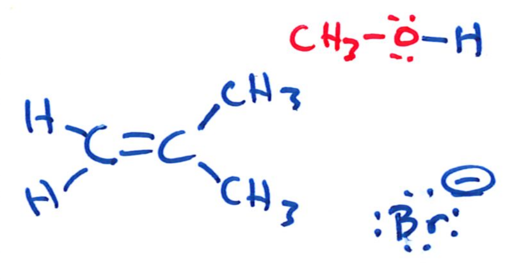
Bonds forming

Bonds breaking



Antiperiplanar

The base, H atom and Br must be in the same plane



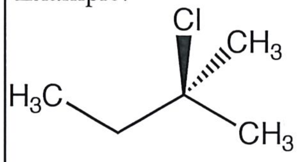
Products

Summary: Base remove H atom from carbon adjacent to leaving group in one step leading to formation of an alkene. All atoms involved must be in the same plane (antiperiplanar)

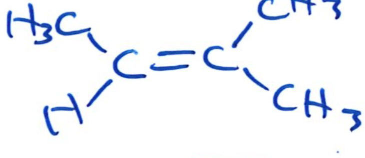
Regiochemistry: Zaitsev's Rule → Make most stable alkene

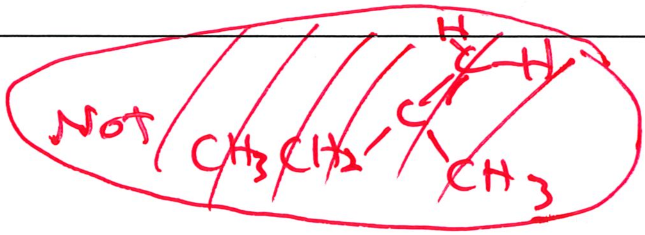
Stereochemistry: Determined by antiperiplanar reaction geometry

Example:

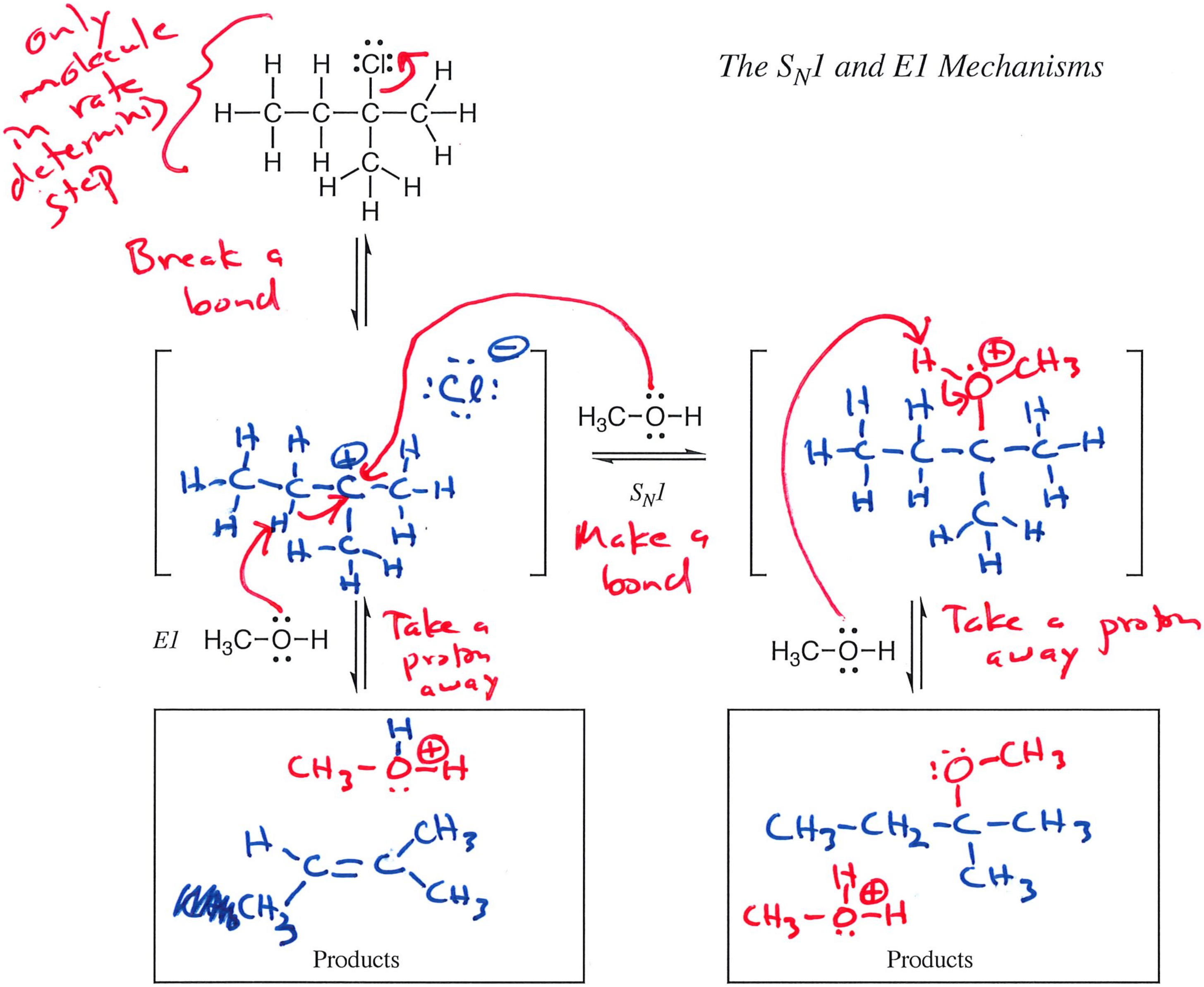


NaOH →





The S_N1 and E1 Mechanisms

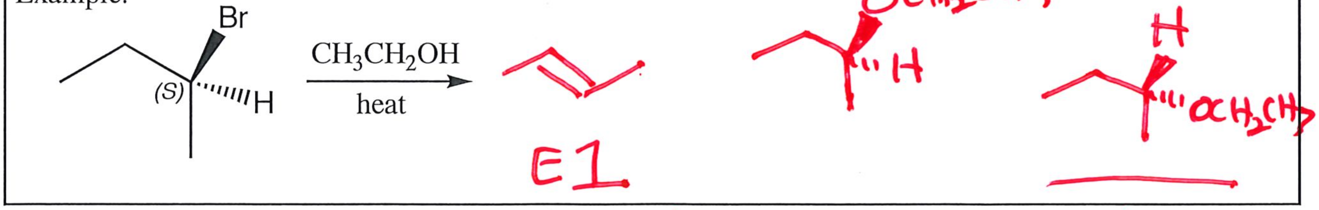


Summary: For sterically hindered haloalkenes, nothing reacts in a week base, week nucleophile untill the C–X bond breaks, creating a carbocation intermediate that adds a nucleophile (S_N1) or has a proton taken away (E1) → Compete

Regiochemistry: E1 Zaitsev's Rule

Stereochemistry: S_N1 Scrambled → not exactly 1:1

Example:

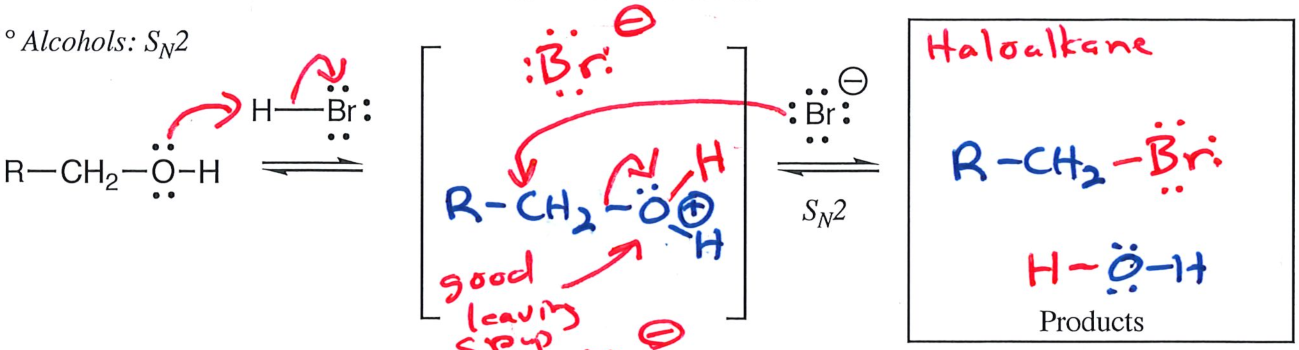


you get both stereoisomers → not racemic → some excess of INVERSION → but not much

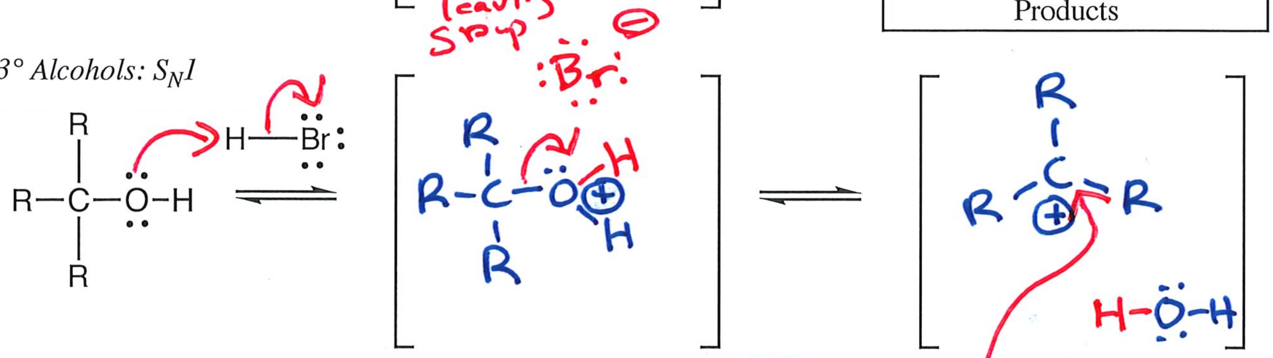
X = Cl, Br, I

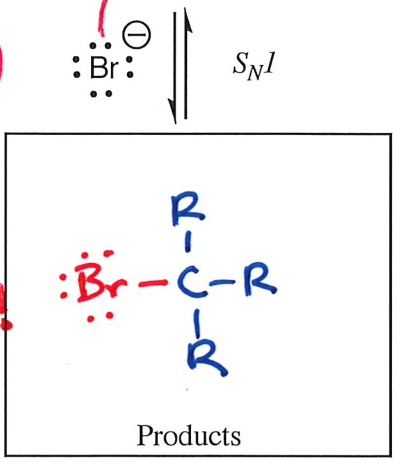
Alcohols + H-X

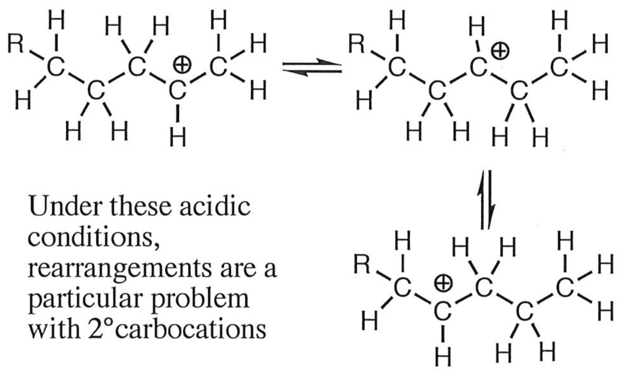
1° Alcohols: S_N2



2°/3° Alcohols: S_N1







Under these acidic conditions, rearrangements are a particular problem with 2°carbocations

No E1

⇓

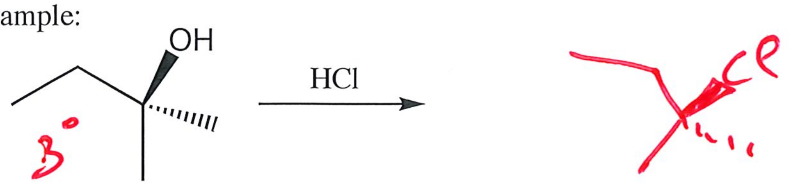
the conditions are acidic!

Summary: Reaction of the OH with H-X converts the OH group into a good leaving group 1° → S_N2 2°, 3° → S_N1 to give haloalkanes

Regiochemistry: N/A

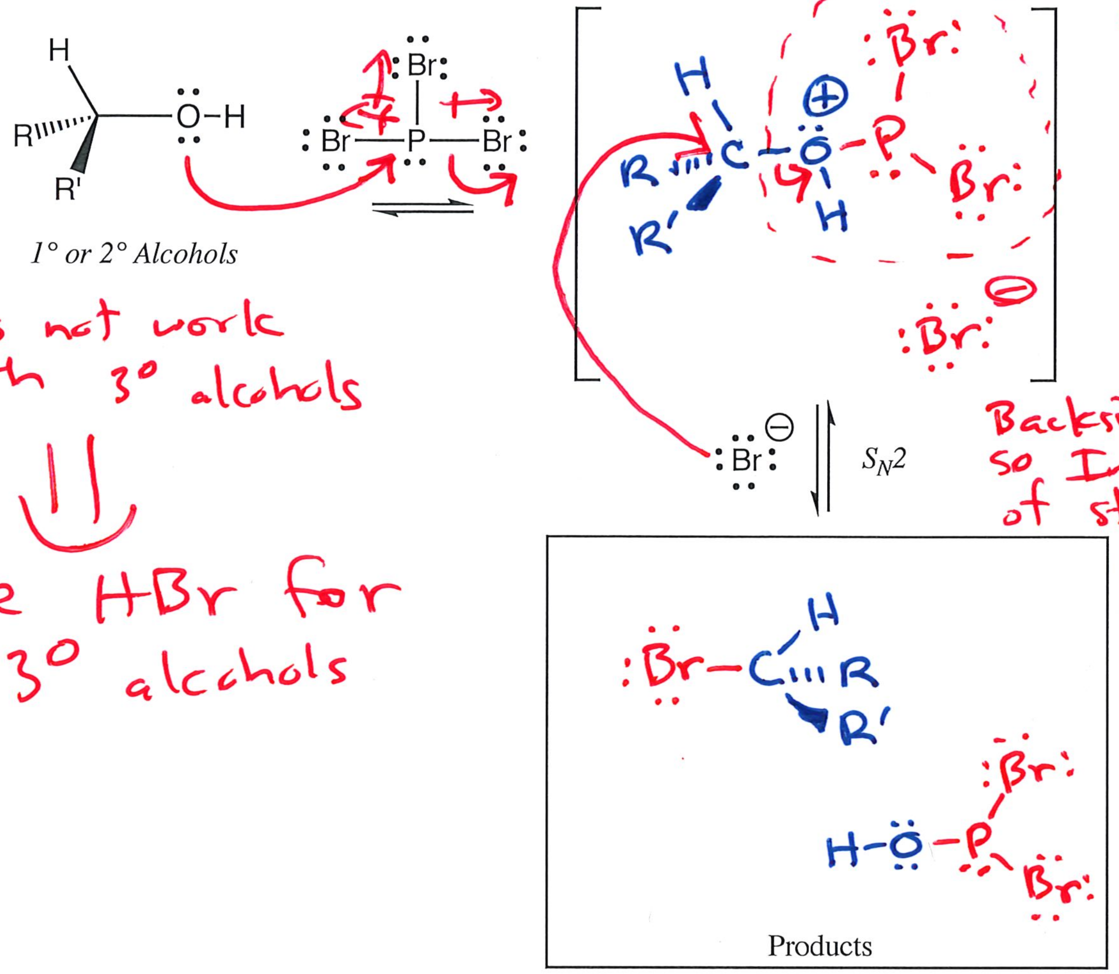
Stereochemistry: Chiral 3° alcohols will give scrambled products

Example:



Not Chiral

Alcohols + PBr$_3$



Great leaving group

Backside attack so INVERSION of stereochemistry

Does not work with 3° alcohols

⇓

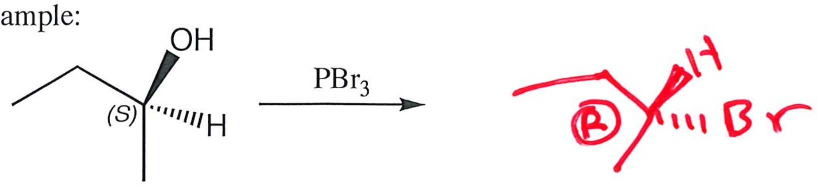
use HBr for 3° alcohols

Summary: 1° or 2° (not 3°) alcohols react with PBr$_3$, followed by S_N2 with $Br^{\ominus}$ to give a ~~haloalkane~~ bromoalkane product

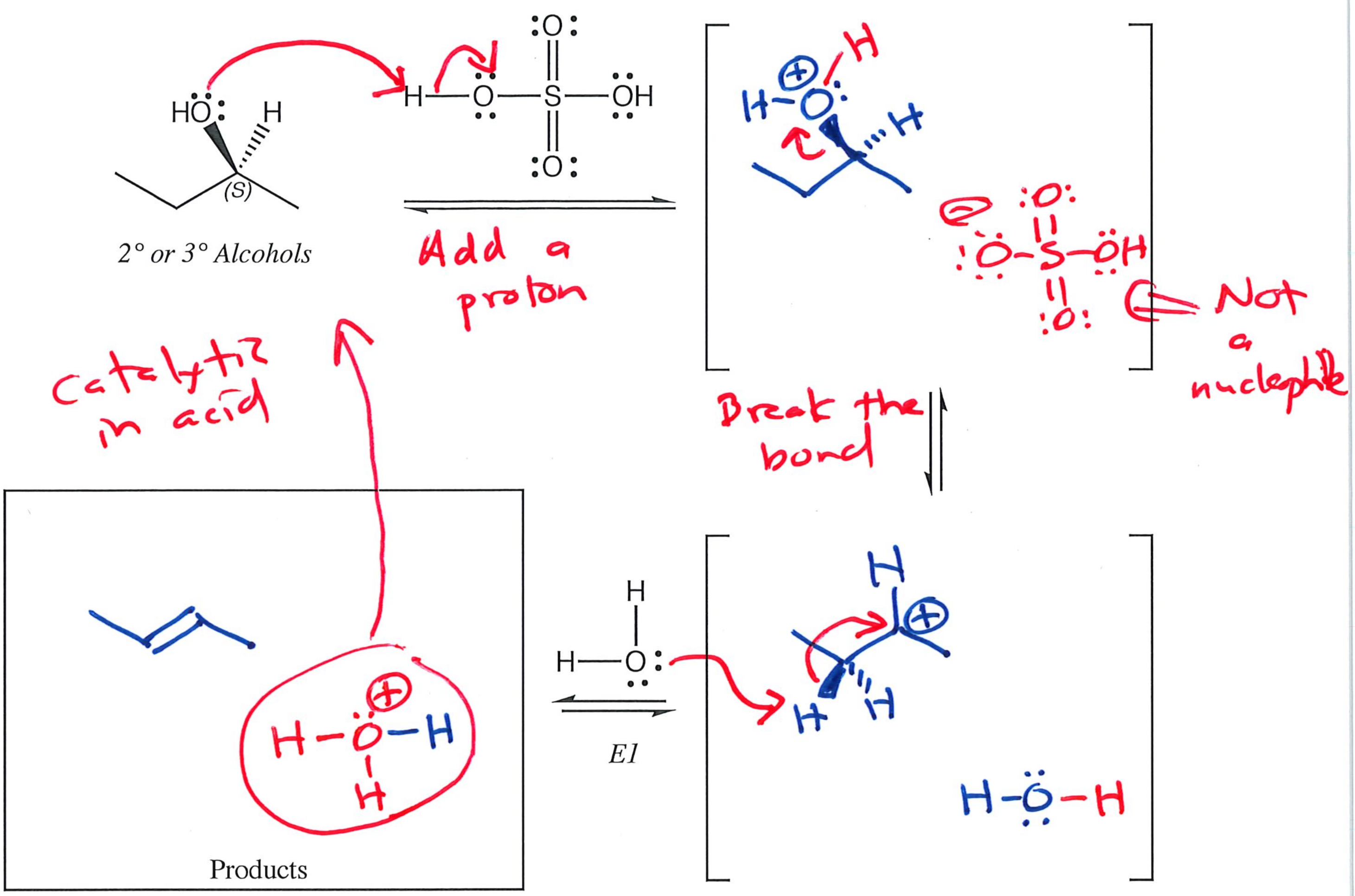
Regiochemistry: N/A

Stereochemistry: INVERSION

Example:



2° or 3° Alcohol Dehydration

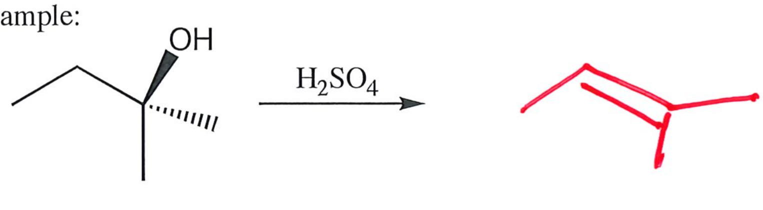


Summary: OH group is protonated in strong acid, H_2O departs to give the carbocation intermediate, that undergoes an E1 to give the alkene

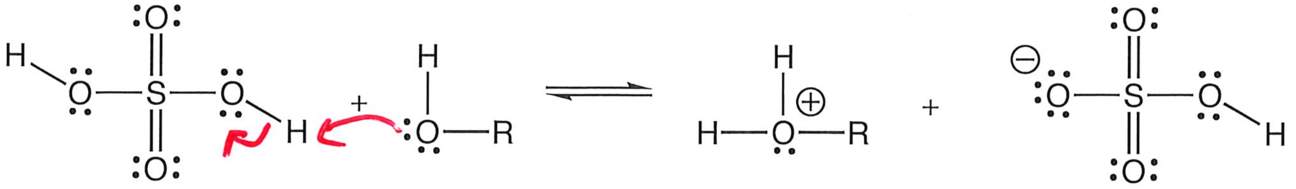
Regiochemistry: Zaitsev's Rule

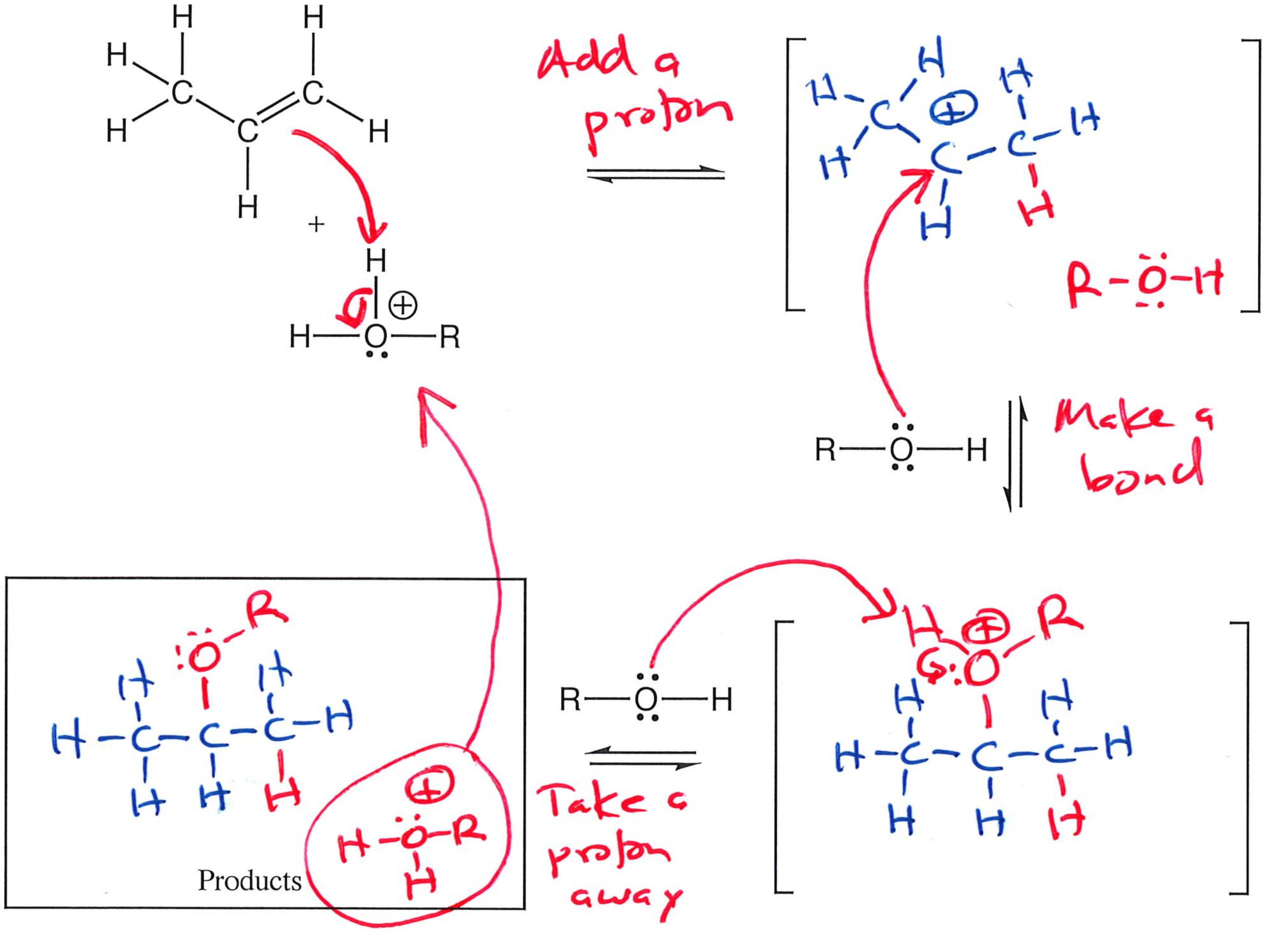
Stereochemistry: N/A

Example:



Acid-catalyzed Reaction of an Alcohol with an Alkene



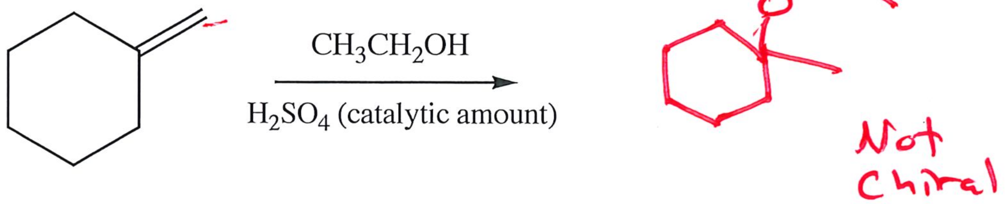


Summary: Alkene is protonated to give carbocation, ROH makes a bond, proton taken away to give ether

Regiochemistry: Markovnikov

Stereochemistry: Mixed

Example:

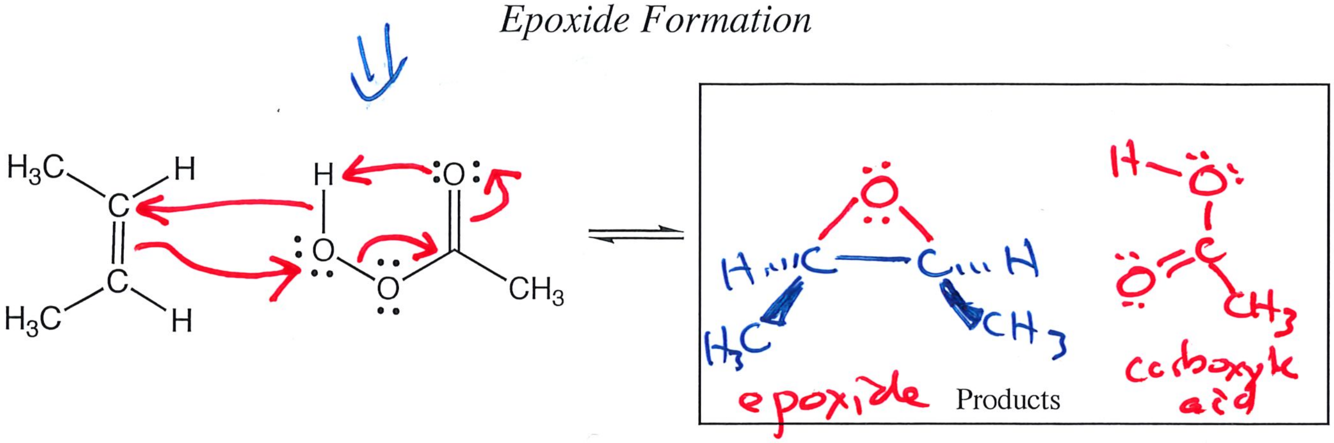


Not Chiral

Will not work if both "sides" of ether are "primary"

$CH_3CO_3H = RCO_3H$

Epoxide Formation

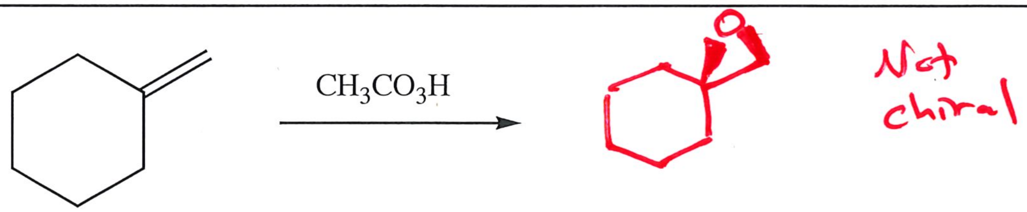


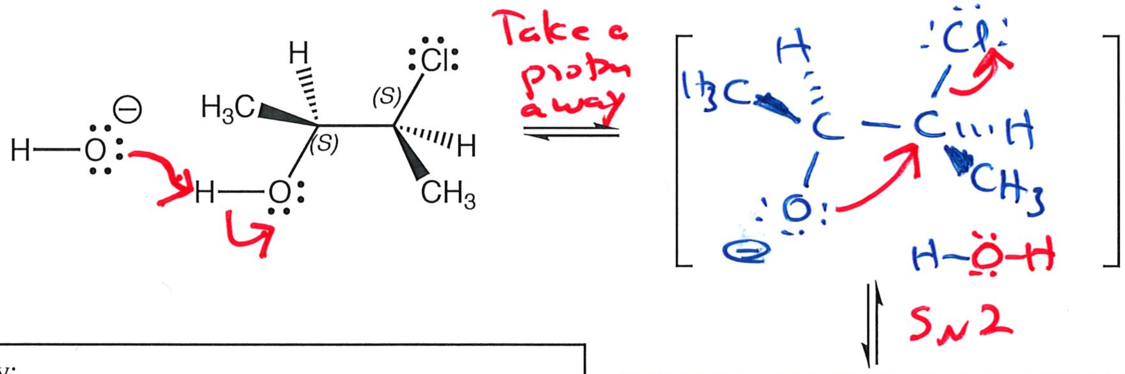
Summary: Alkenes react in one step to give an epoxide and carboxylic acid

Regiochemistry: N/A

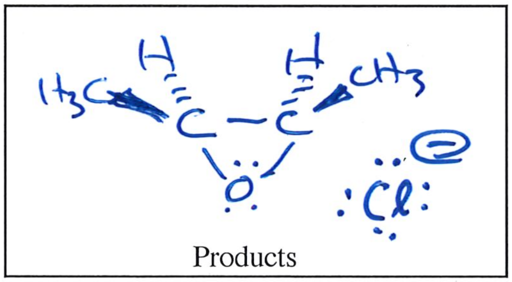
Stereochemistry: Racemic mixtures

Example:





Summary: Halohydrins react in base to give alkoxide that undergoes an intramolecular SN2 to give epoxide

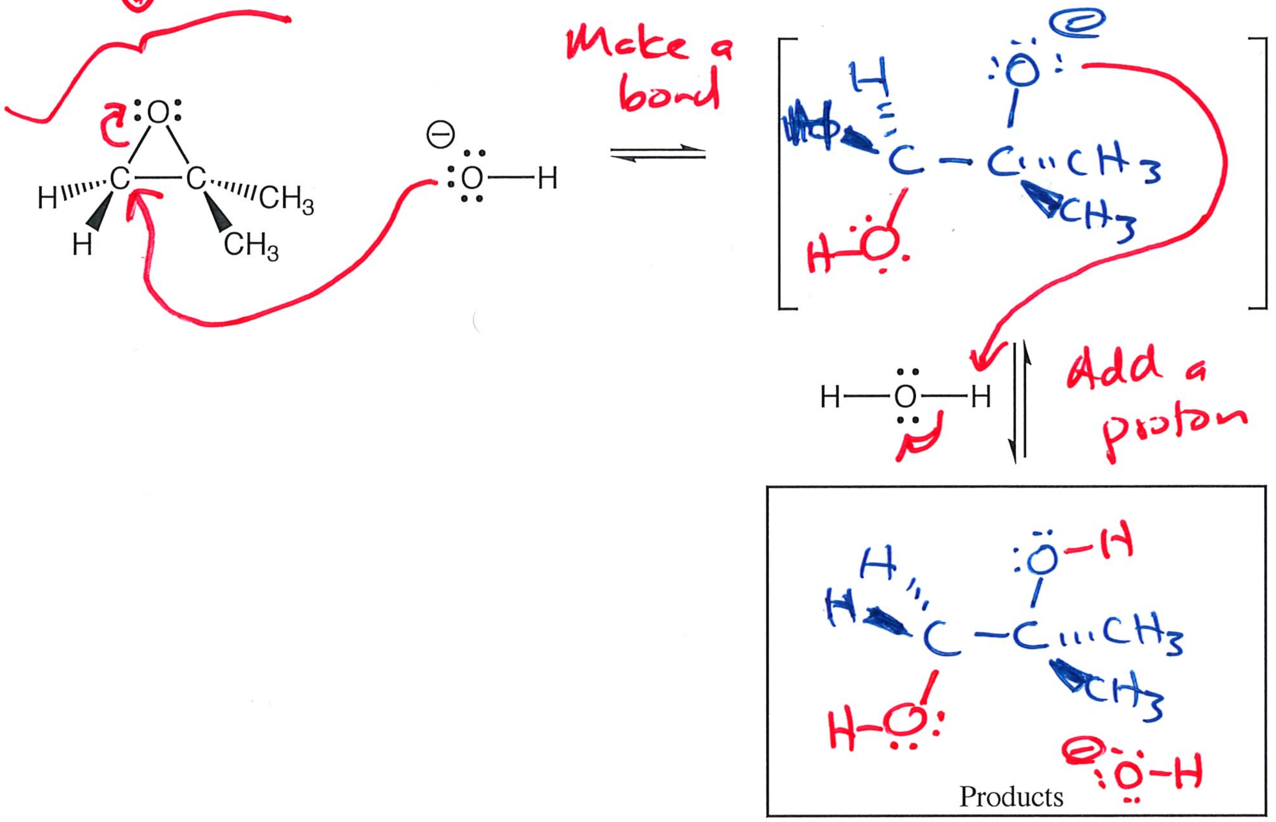


Regiochemistry: N/A

Stereochemistry: Antiperiplanar transition state

Nucleophilic ~~Base-Promoted~~ Epoxide Opening

ring strain makes these good electrophiles

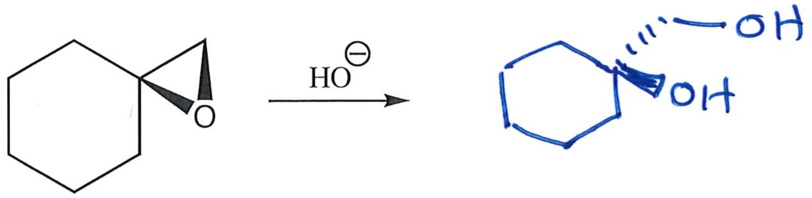


Summary: Nucleophiles react at the least hindered ~~[illegible]~~ carbon of an epoxide

Regiochemistry: Less hindered

Stereochemistry: Anti addition

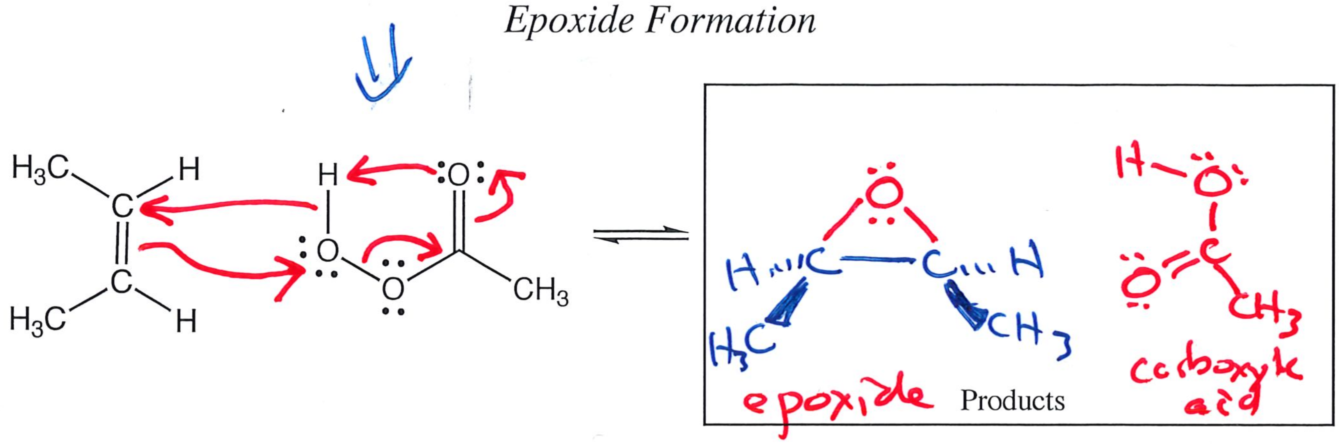
Example:



Not chiral

$CH_3CO_3H = RCO_3H$

Epoxide Formation

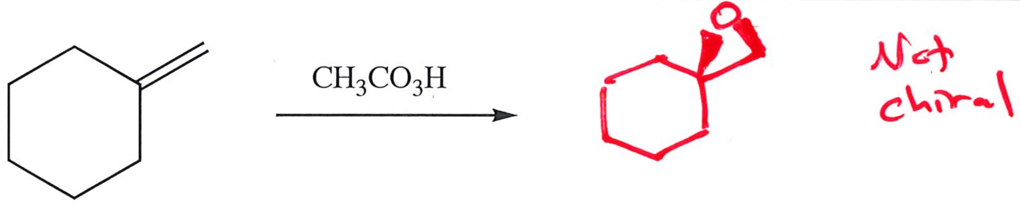


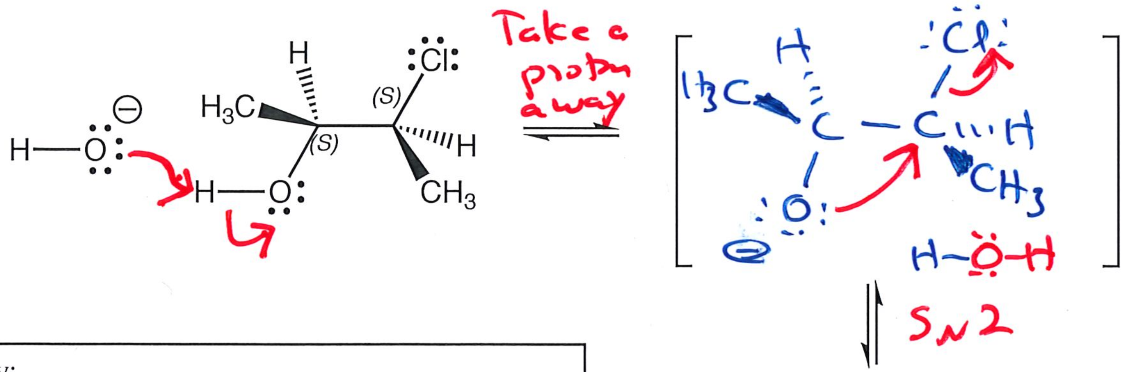
Summary: Alkenes react in one step to give an epoxide and carboxylic acid

Regiochemistry: N/A

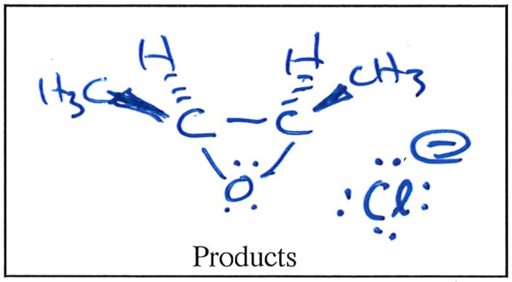
Stereochemistry: Racemic mixtures

Example:





Summary: Halohydrins react in base to give alkoxide that undergoes an intramolecular SN2 to give epoxide

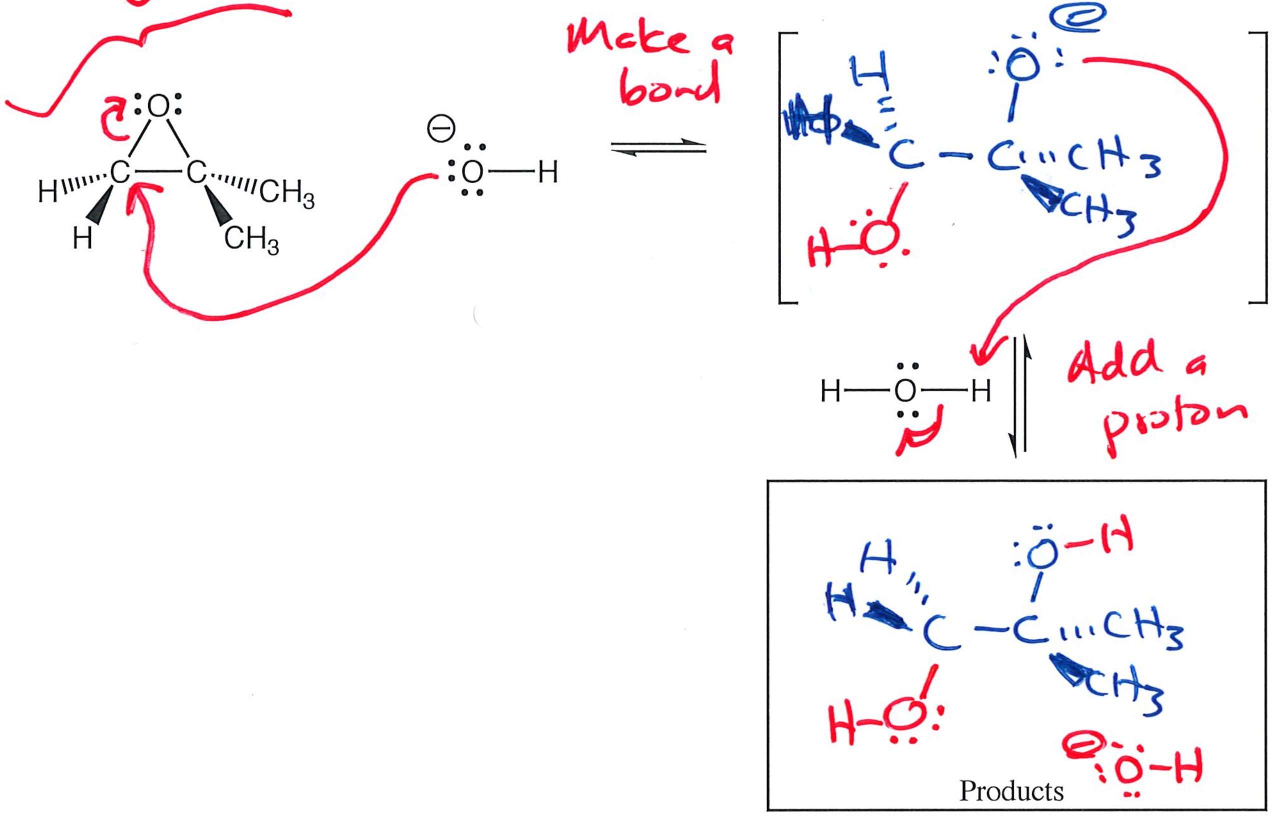


Regiochemistry: N/A

Stereochemistry: Antiperiplanar transition state

~~Base-Promoted~~ Nucleophilic Epoxide Opening

ring strain makes these good electrophiles

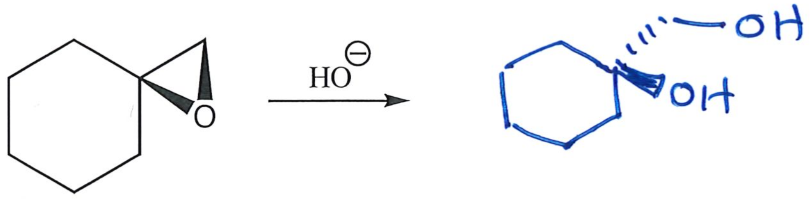


Summary: Nucleophiles react at the least hindered carbon of an epoxide

Regiochemistry: Less hindered

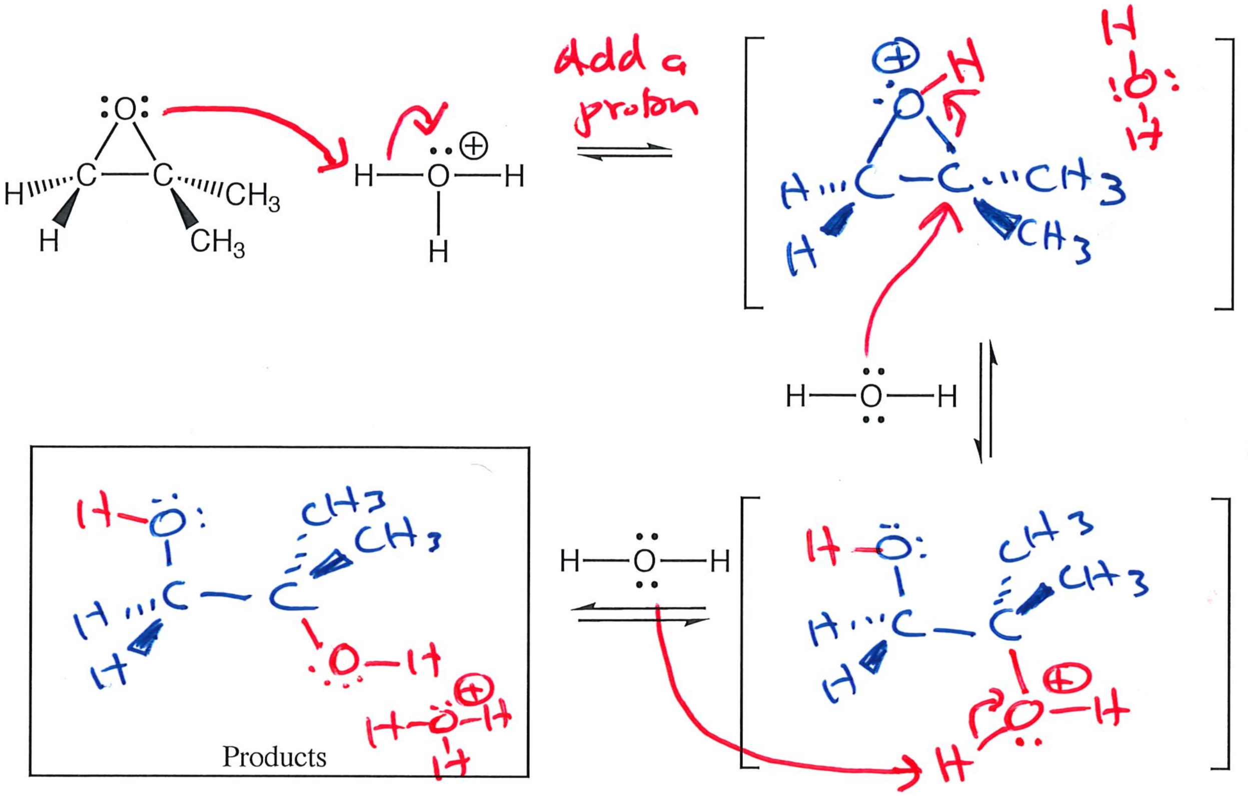
Stereochemistry: Anti addition

Example:



Not chiral

Acid-Catalyzed Epoxide Opening

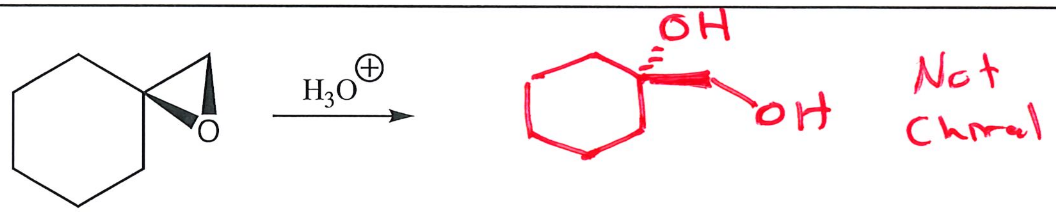


Summary: In acid, epoxides are protonated then water attacks the more substituted C atom

Regiochemistry: Attacks more substituted C atom ⇒ Markovnikov

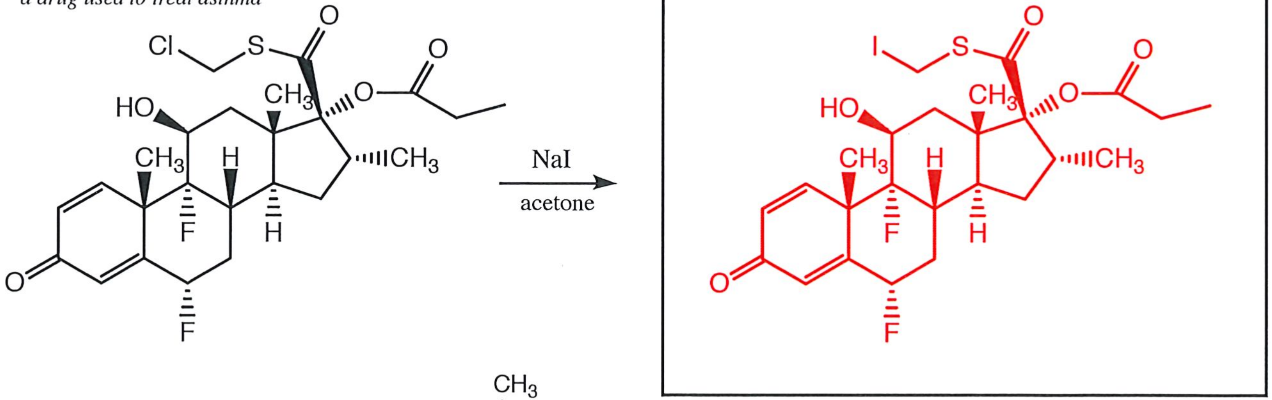
Stereochemistry: Anti

Example:

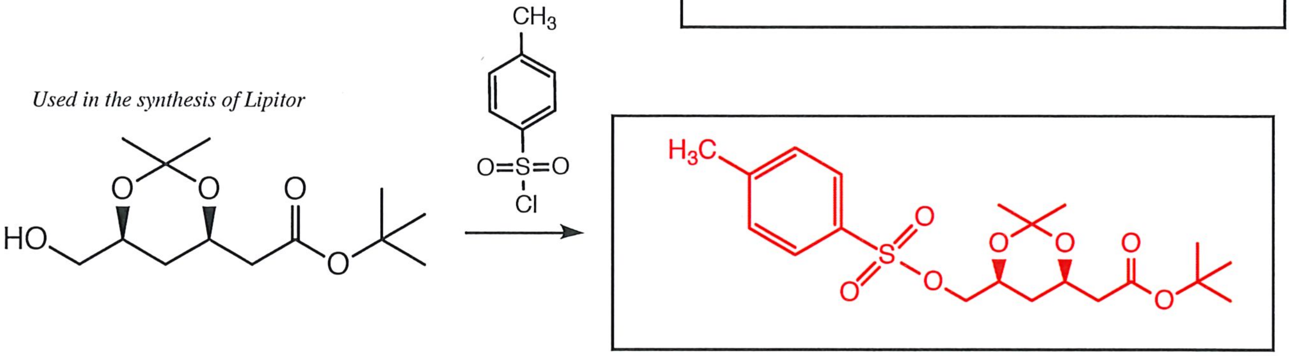


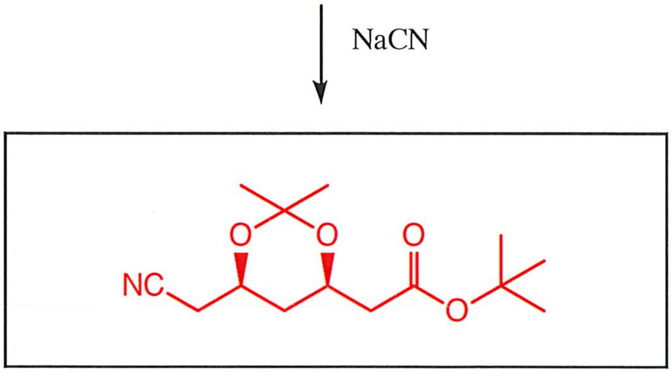
Reactions in the Context of Complex Molecules

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

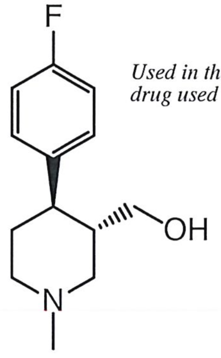


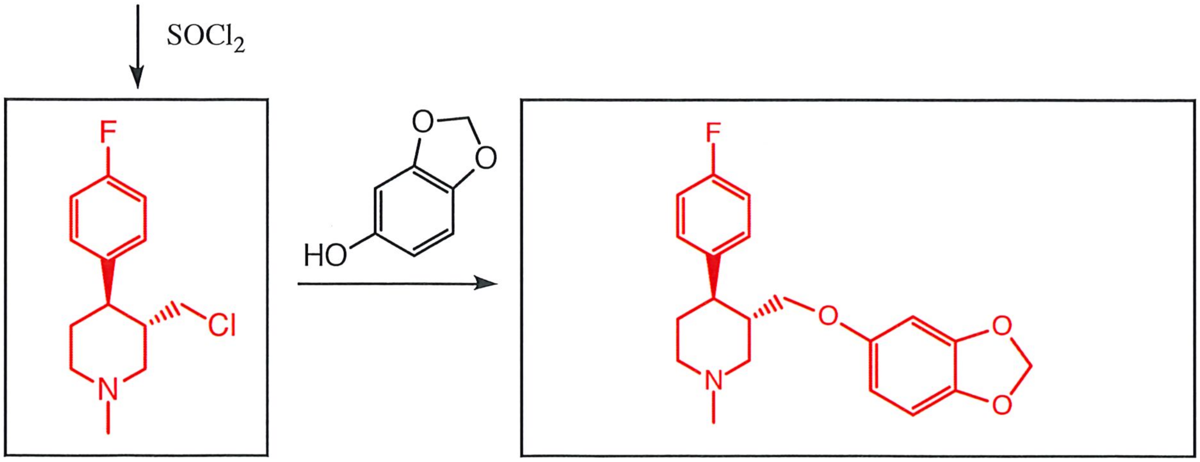
Used in the synthesis of Lipitor





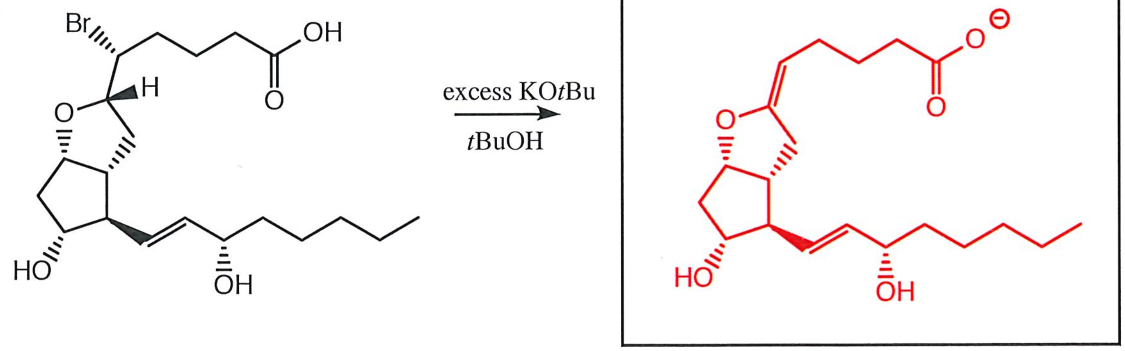
Used in the synthesis of Paxil, a drug used to treat depression



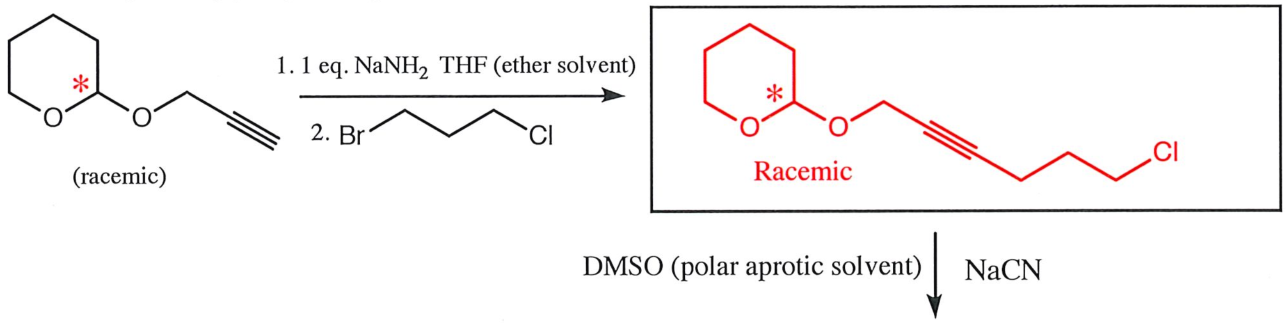


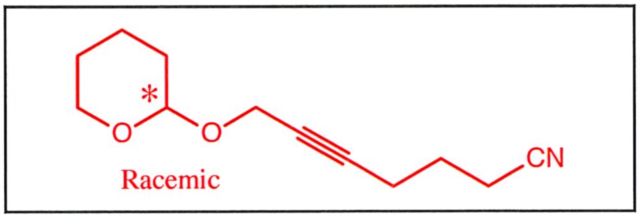
Reactions in the Context of Complex Molecules

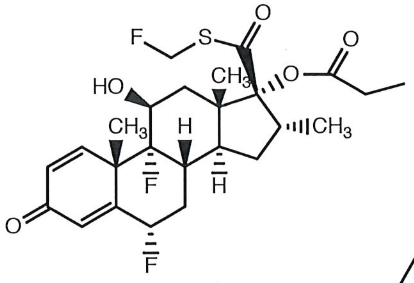
Used in the synthesis of several protaglandins



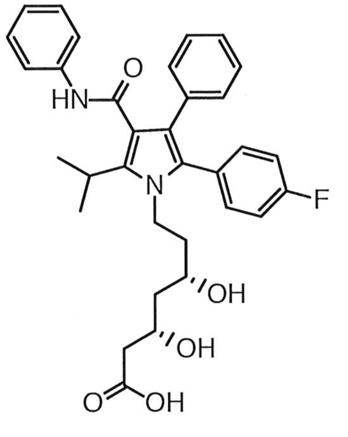
Used in the synthesis of protaglandin C_2

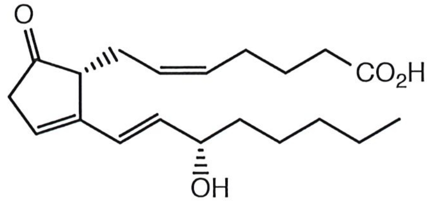




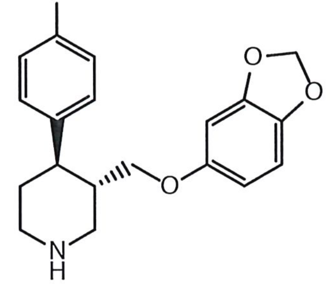


Fluticasone (Flonase)





Prostaglandin C_2



Paroxetine (Paxil)

Atorvastatin (Lipitor)