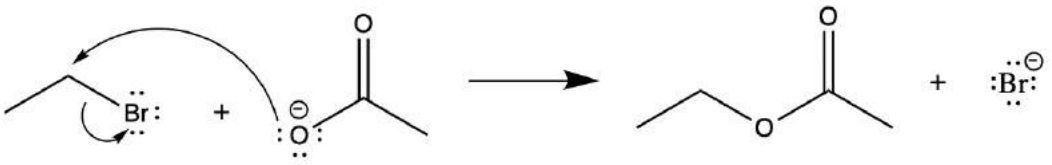
Chapter 7: Alkyl Halides and Nucleophilic Substitution

SN2 Reaction

Mechanism:

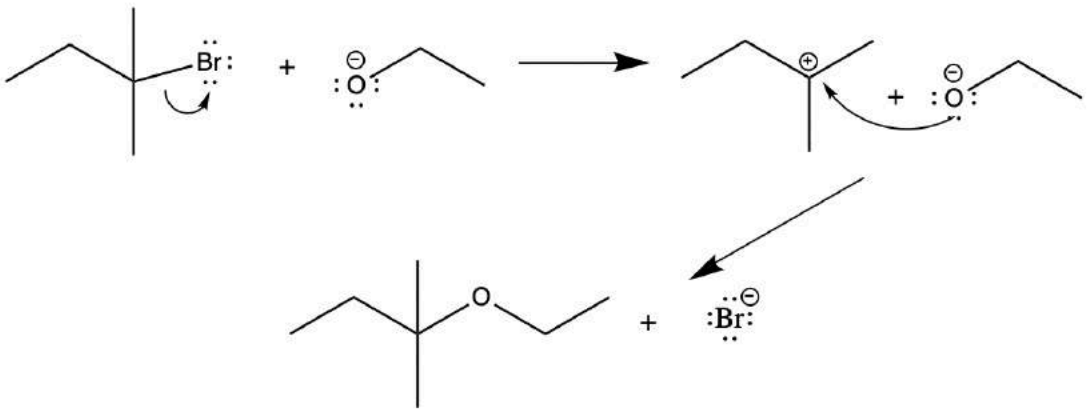


Notes:

- One step reaction
- Order of reactivity: **Methyl** > **Primary** > **Secondary** > Tertiary
- Stereochemistry: Inversion of configuration at stereogenic center (because of backside attack)
- Better leaving group = faster reaction
- Favors: Strong nucleophiles
- Favors: Not-sterically-hindered alkyl halides
- Favors: Polar aprotic solvents (cannot hydrogen bond)

SN1 Reaction

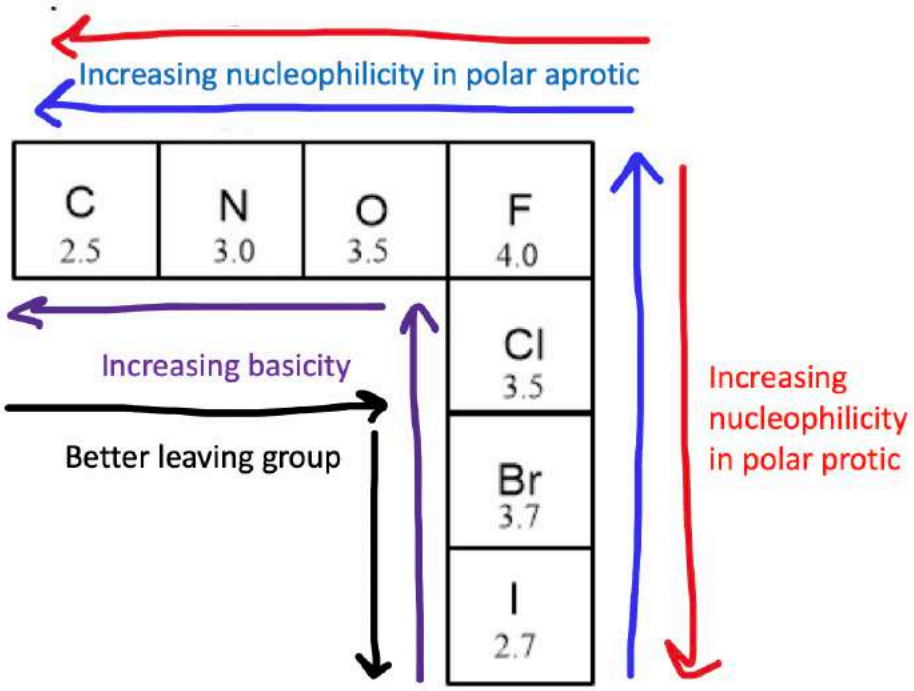
Mechanism:



Notes:

- Two step reaction
- Order of reactivity: **Tertiary** > **Secondary** > Primary > Methyl
- Stereochemistry: Racemization (because the carbocation is planar)
- Better leaving group = faster reaction
- Favors: Weak nucleophiles
- Favors: Sterically hindered alkyl halides
- Favors: Polar protic solvents (can hydrogen bond)

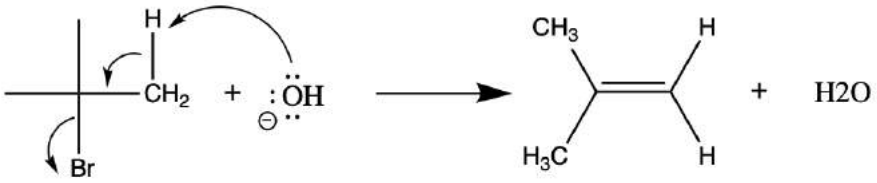
Important Trends



Chapter 8: Alkyl Halides and Elimination Reactions

E2 Reaction

Mechanism:

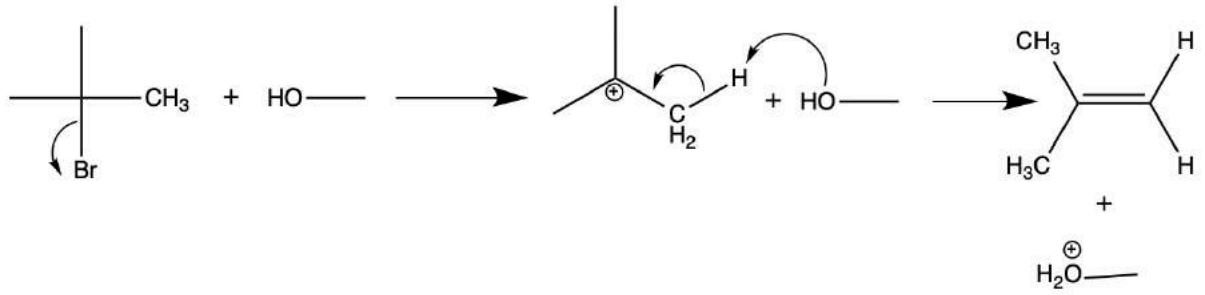


Notes:

- One step reaction
- Order of reactivity: **Tertiary** > **Secondary** > **Primary**
- Stereochemistry: antiperiplanar arrangement of H and X
- Better leaving group = faster reaction
- Favors: Polar aprotic solvents, **strong bases**
- Products follow Zaitsev rule (more substituted alkene is the major product)

E1 Reaction

Mechanism:



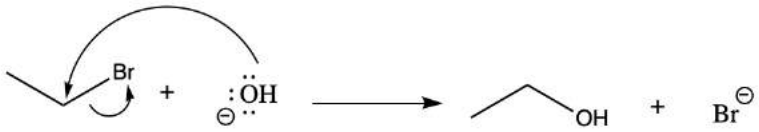
Notes:

- Two step reaction
- Order of reactivity: **Tertiary** > **Secondary** > Primary
- Stereochemistry: Trigonal planar carbocation intermediate
- Better leaving group = faster reaction
- Favors: Polar protic solvents, **weak bases**
- Products follow Zaitsev rule

Chapter 9: Alcohols, Ethers, and Epoxides

Preparation of Alcohols

Mechanism:

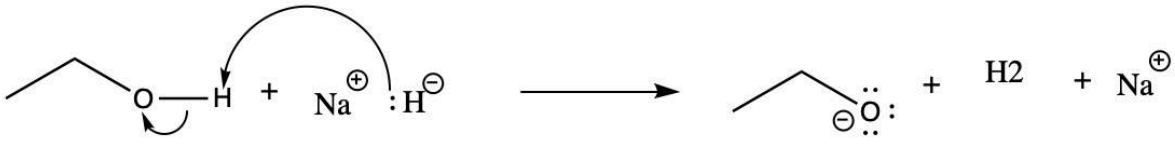


Notes:

- SN2 mechanism

Preparation of Alkoxides

Mechanism:



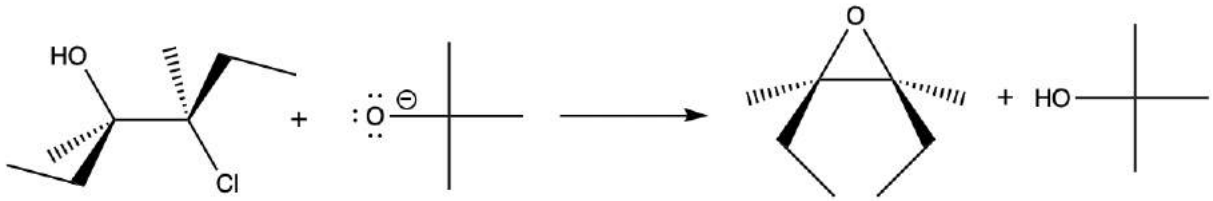
Preparation of Ethers (Williamson Ether Synthesis)

Mechanism:

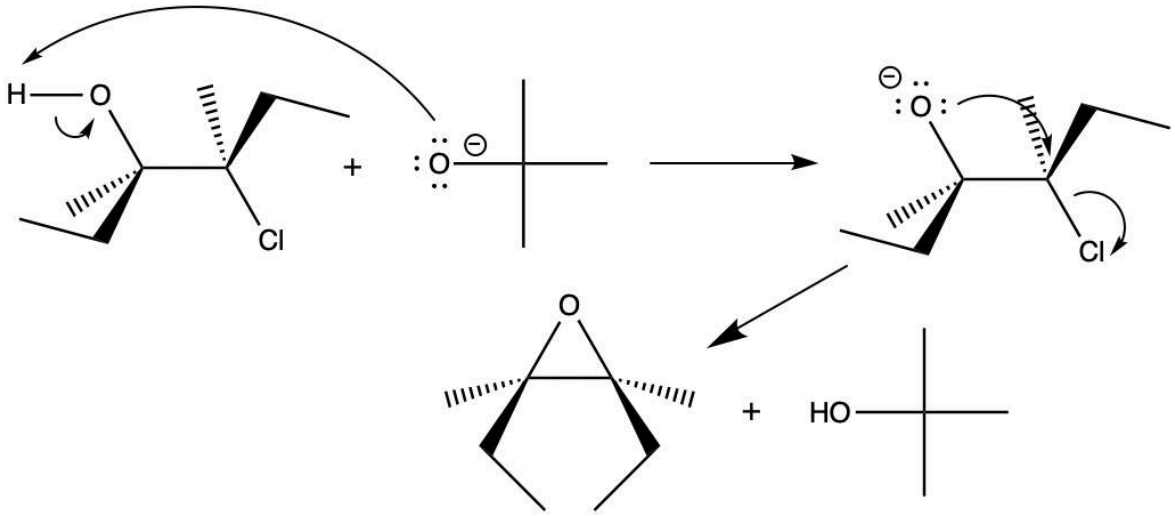
Notes:

- SN2 mechanism

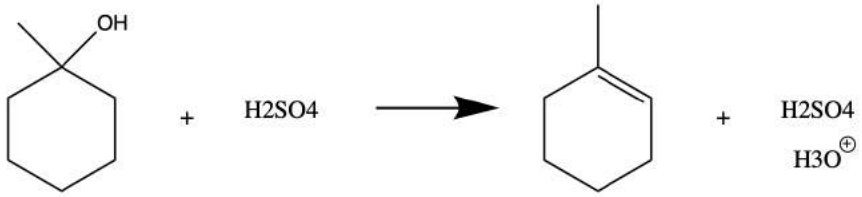
Preparation of Epoxides



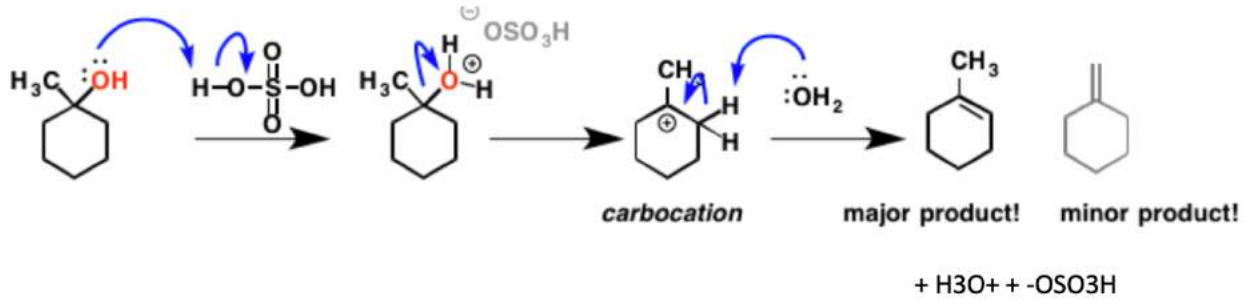
Mechanism:



Alcohol Dehydration: Secondary and Tertiary



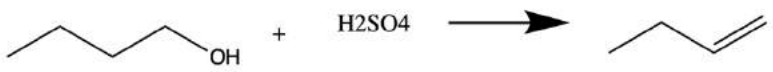
Mechanism:



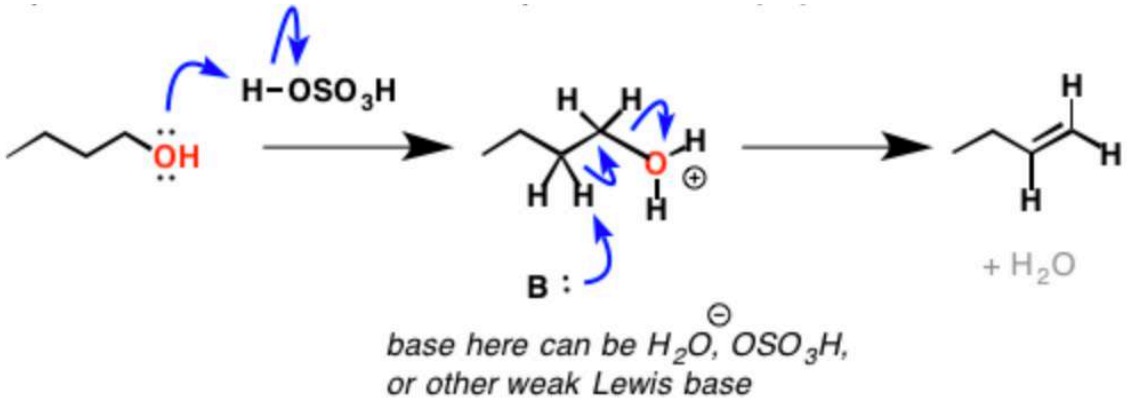
Notes:

- E1 mechanism
- Zaitsev rule applies (the most substituted product is the major product)
- Carbocation rearrangements are possible

Alcohol Dehydration: Primary



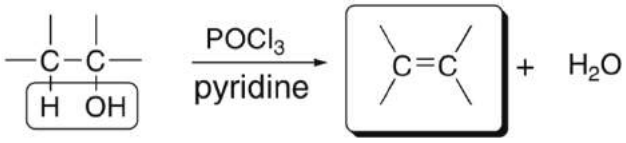
Mechanism:



Notes:

- E2 mechanism
- Zaitsev rule applies

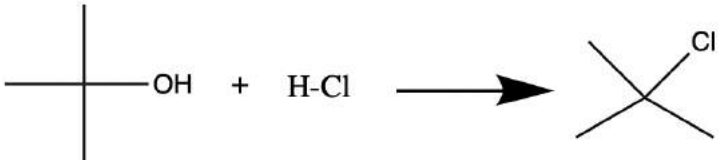
Other Reagents to Form Alkenes: POCl3 and Pyridine



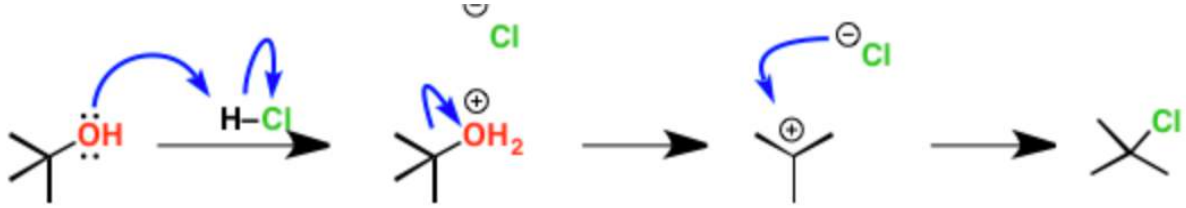
Notes:

- E2 mechanism

Alkyl Halides Formation from Alcohols: Secondary and Tertiary



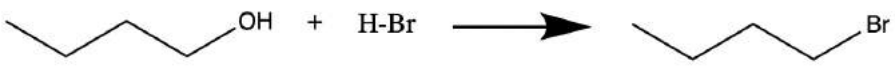
Mechanism:



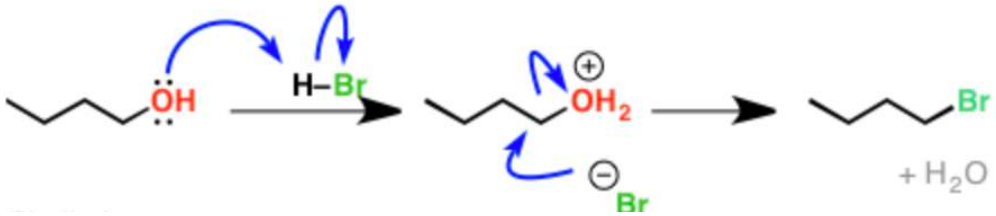
Notes:

- SN1 mechanism
- Carbocation rearrangements are possible

Alkyl Halides Formation from Alcohols: Primary



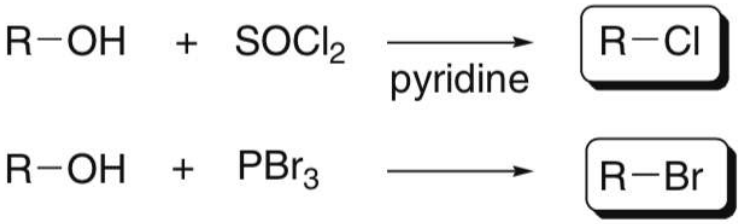
Mechanism:



Notes:

- SN2 mechanism (inversion of stereochemistry)

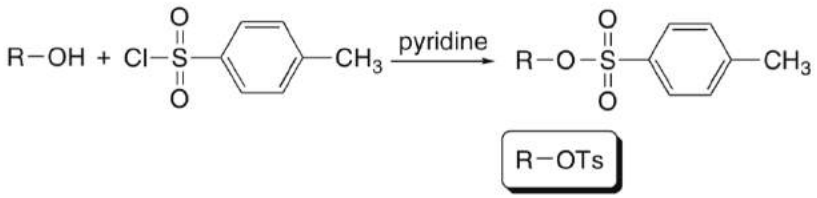
Other Reagents to Form Alkyl Halides: SOCl2 and PBr3



Notes:

- SN2 reaction, both reagents will lead to inversion of stereochemistry

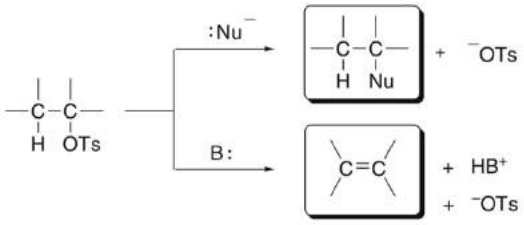
Reaction with Alkyl Tosylates



First step:

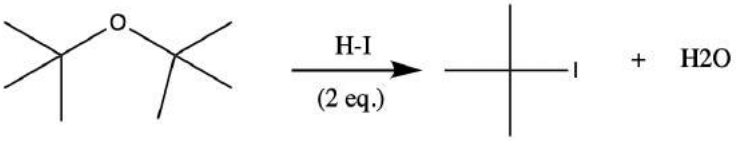
- Note: Stereochemistry is retained

Second step:

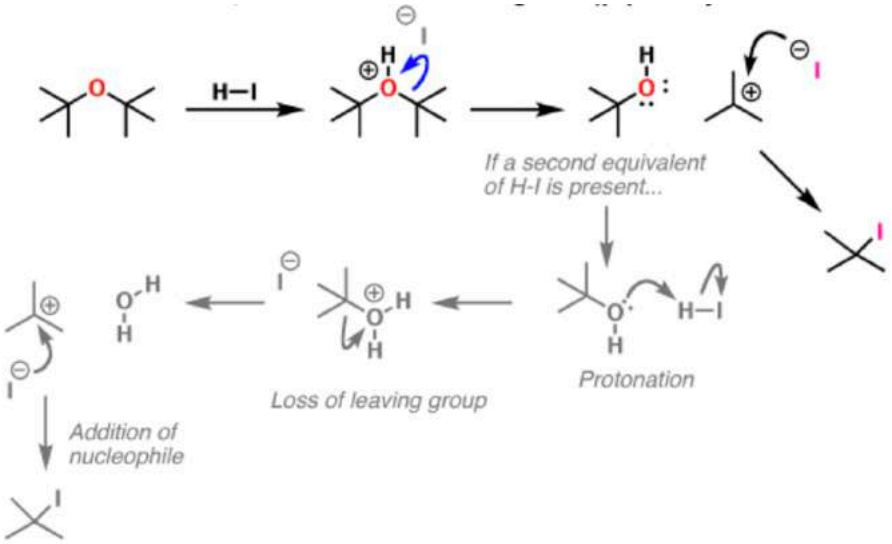


- Substitution is carried out with strong :Nu⁻, so the mechanism is S_N2.
- Elimination is carried out with strong bases, so the mechanism is E2.

Ether Cleavage with Strong Acids: Secondary and Tertiary



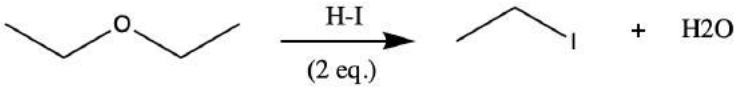
Mechanism:



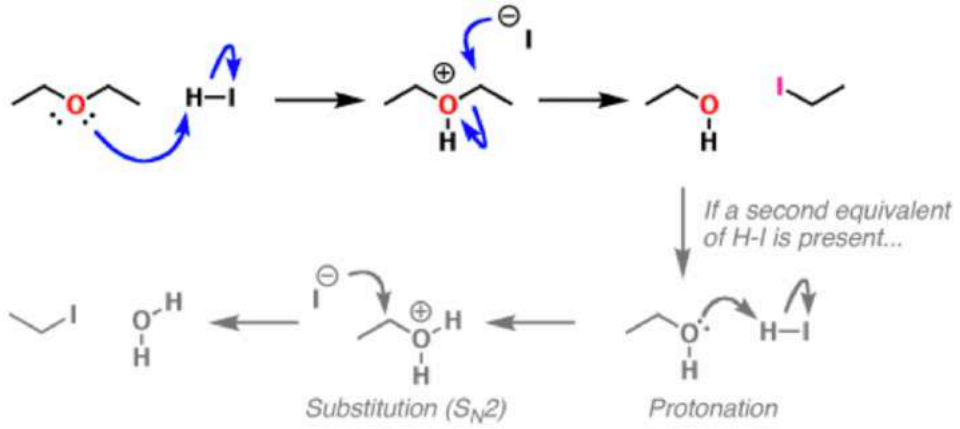
Notes:

- SN1 mechanism

Ether Cleavage with Strong Acids: Primary



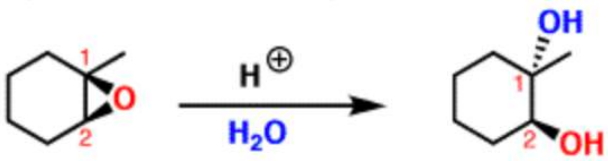
Mechanism:



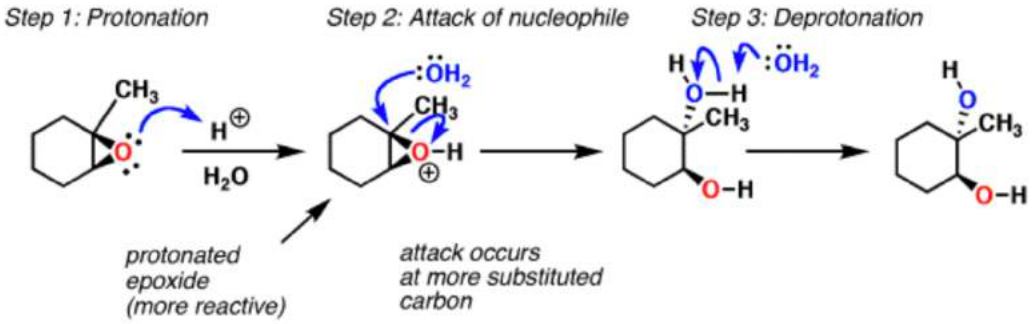
Notes:

- SN2 mechanism

Epoxide Reactions with Acids



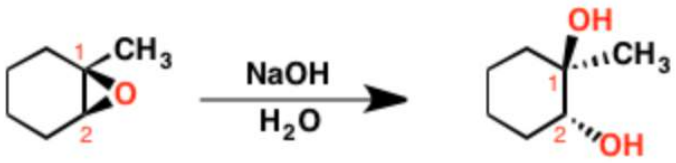
Mechanism:



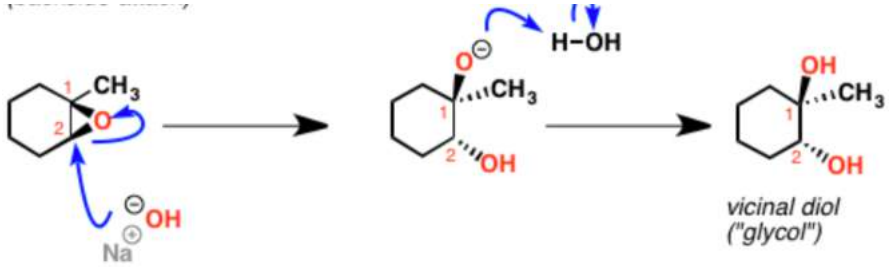
Notes:

- SN1/SN2 mechanism
- Attacks at the more substituted carbon
- Backside attack = inversion of configuration

Epoxide Reactions with Strong Nucleophiles



Mechanism:

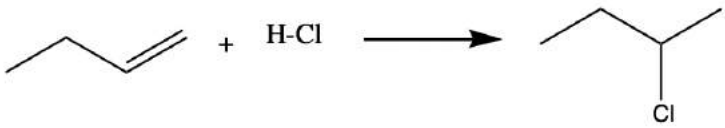


Notes:

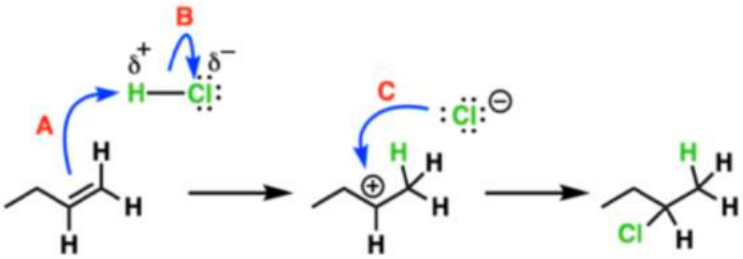
- SN2 mechanism
- Attacks the less substituted carbon
- Backside attack = inversion of configuration

Chapter 10: Alkenes

Hydrohalogenation



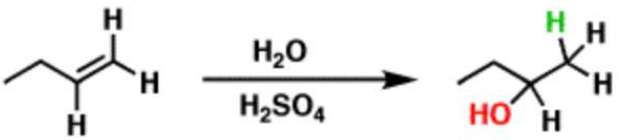
Mechanism:



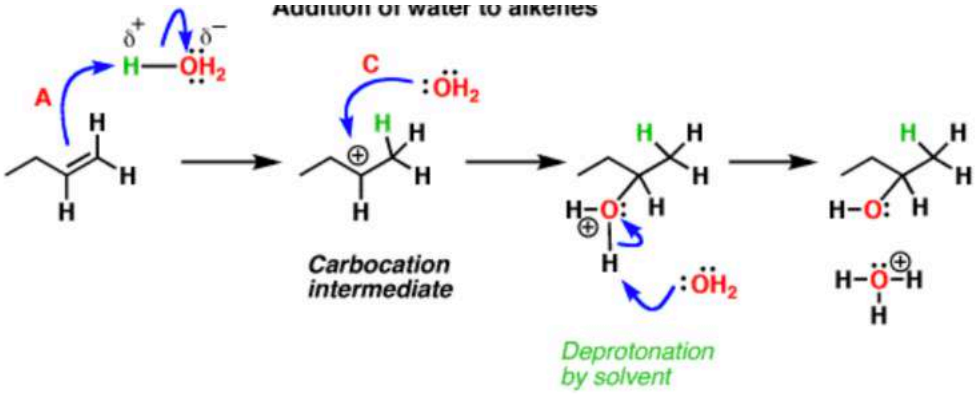
Notes:

- Carbocation rearrangements are possible
- Markovnikov's rule is followed (H bonds to less subbed carbon, X bonds to more subbed carbon)
- Stereochemistry: Syn (added to same sides) and anti (add to opposite sides) addition

Hydration



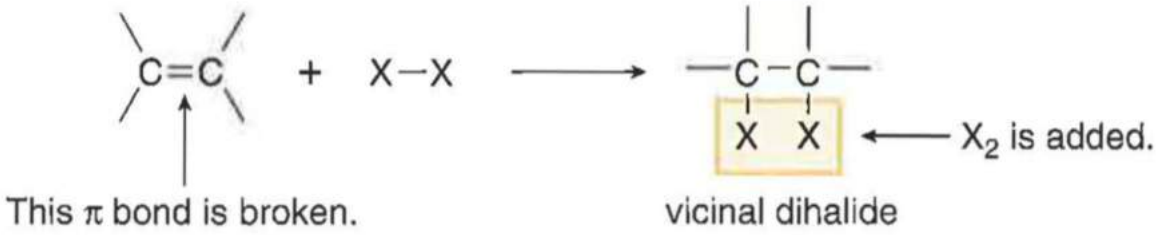
Mechanism:



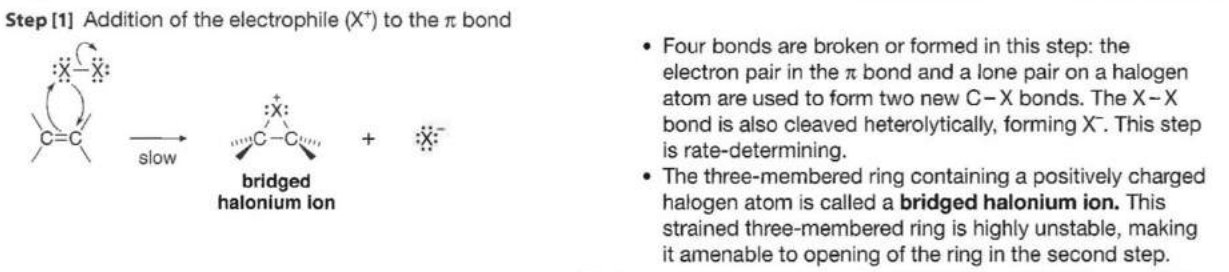
Notes:

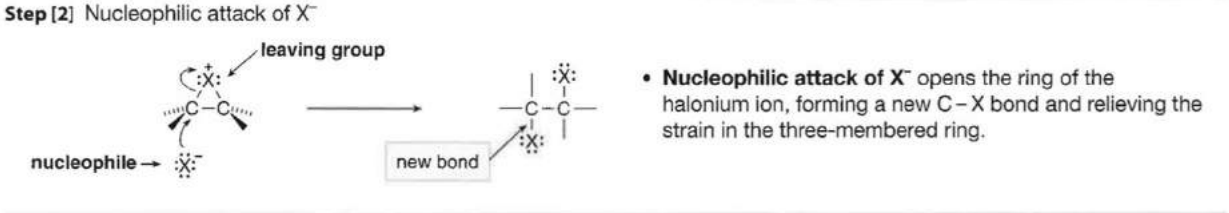
- Carbocation rearrangements are possible
- Markovnikov's rule is followed
- Same mechanism if using alcohol instead of water to make ethers
- Stereochemistry: Syn and anti-addition occur

Halogenation



Mechanism:

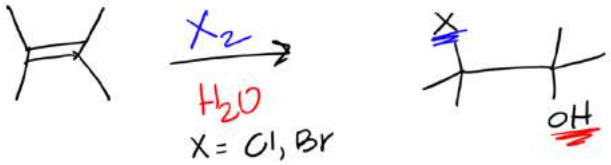




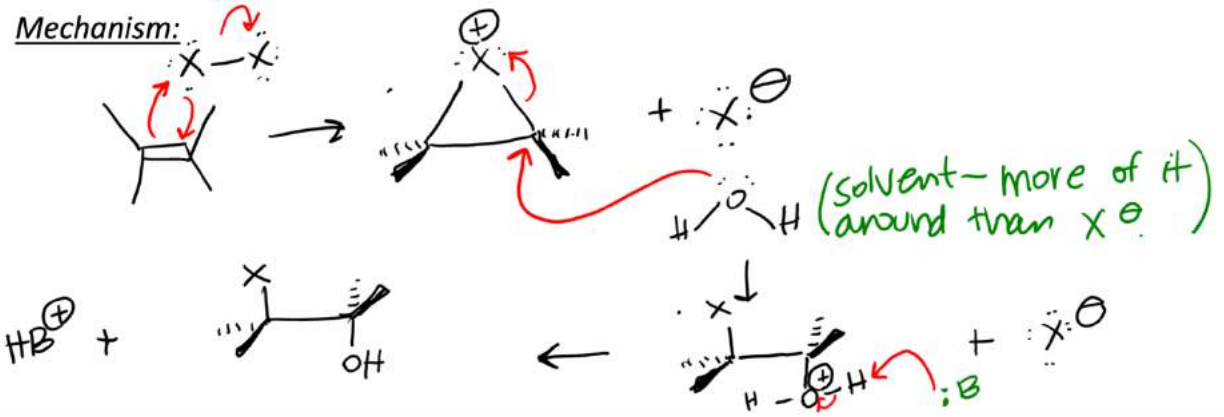
Notes:

- Halogen attacks most subbed carbon in halonium ion
- No carbocation rearrangements
- Stereochemistry: anti-addition

Halohydrin Formation

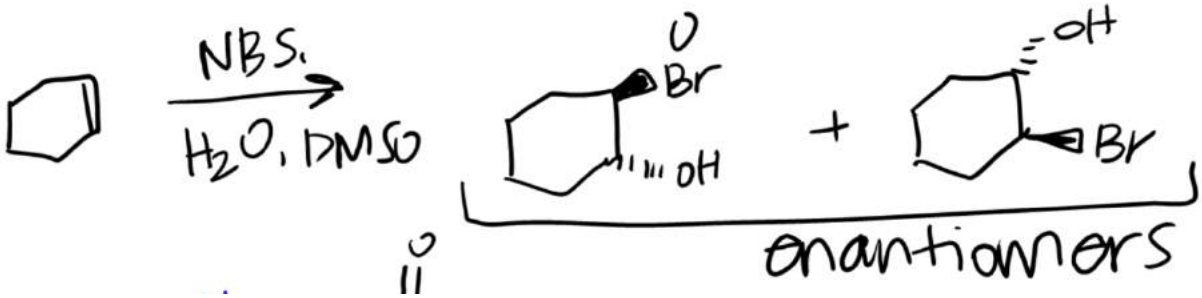


Mechanism:

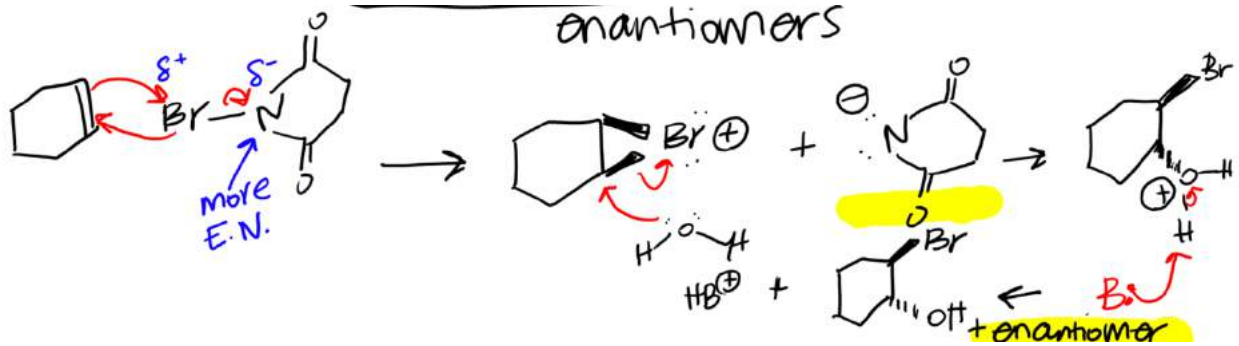


Notes:

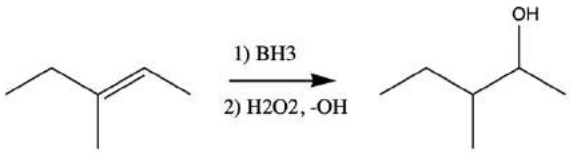
- H2O attacks more subbed carbon (recall acid-catalyzed ring opening of an epoxide)
- No carbocation rearrangements
- Stereochemistry: Anti-addition
- Special reagent: NBS



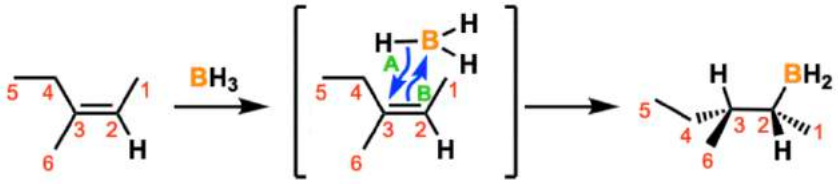
  - Mechanism:



Hydroboration-Oxidation



Mechanism:

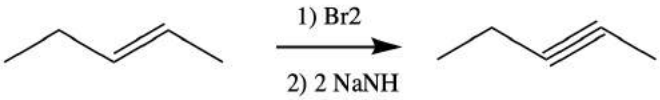


Notes:

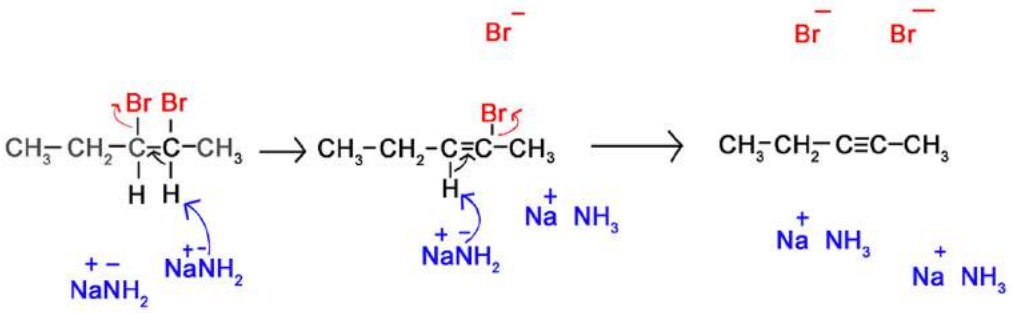
- You only need to know the hydroboration step, not the oxidation step
- Anti-markovnikov (OH is added to less subbed carbon)
- No carbocation rearrangements
- Syn-addition
- Retention of configuration
- Same mechanism as 9-BBN

Chapter 11: Alkynes

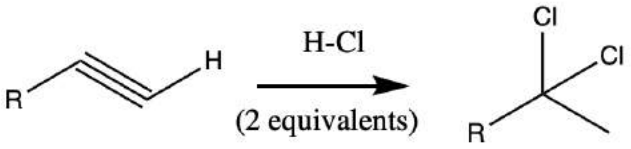
Preparation of Alkynes



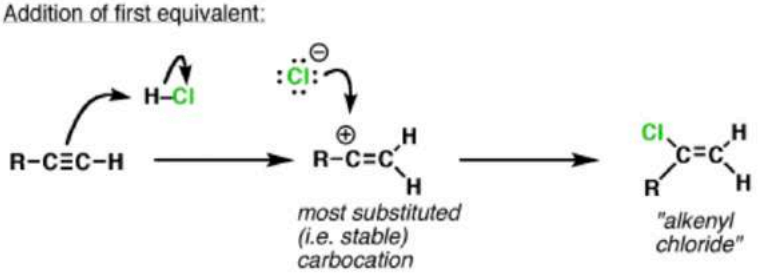
Mechanism (2nd step):

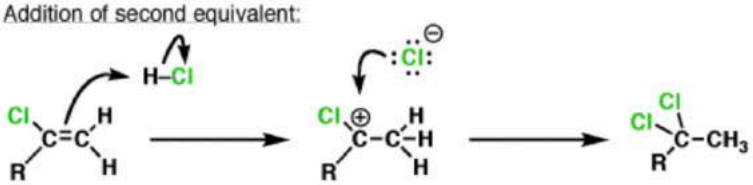


Hydrohalogenation



Mechanism:

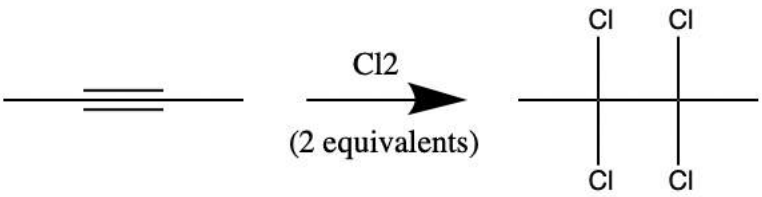




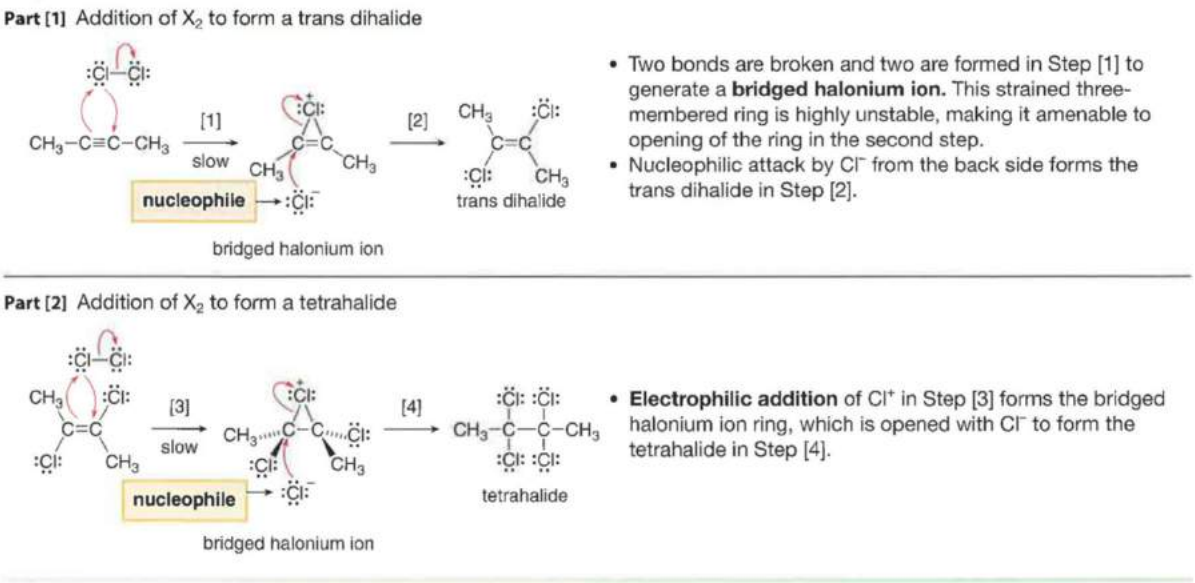
Notes:

- Markovnikov's rule is followed
- The carbocation will form on the more substituted or resonance-stabilized carbon

Halogenation



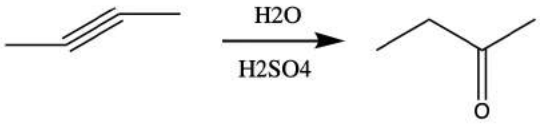
Mechanism:



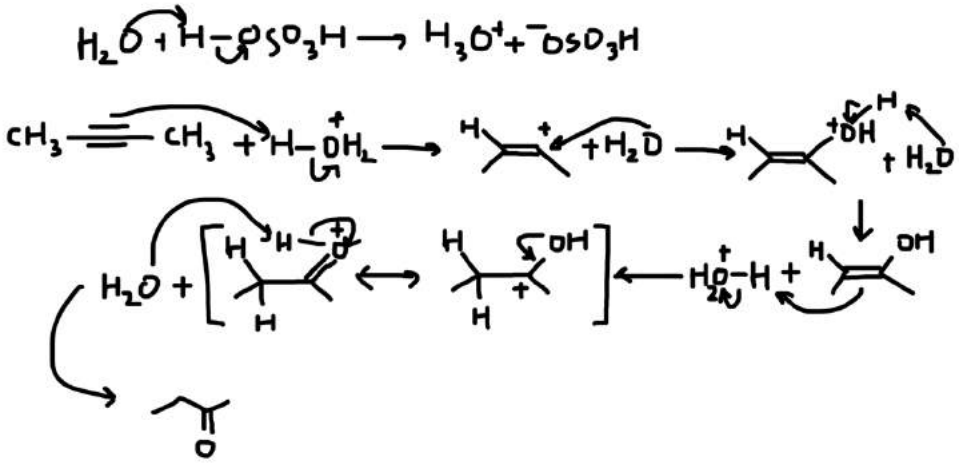
Notes:

- Anti-addition
- Halogens will attack the more substituted or resonance-stabilized side

Hydration



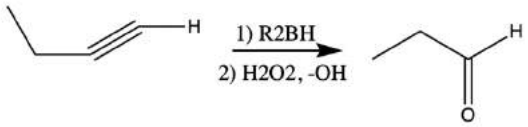
Mechanism:



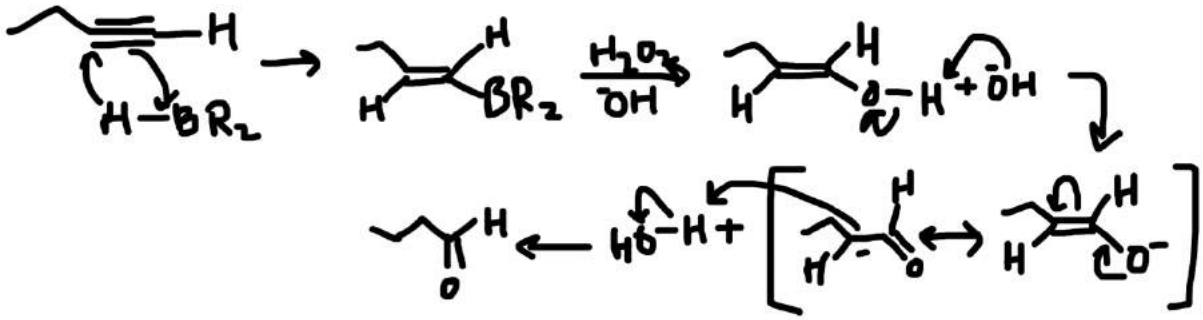
Notes:

- Markovnikov's rule is followed
- Unstable enol
- End product is a ketone
- Acid-catalyzed

Hydroboration-Oxidation



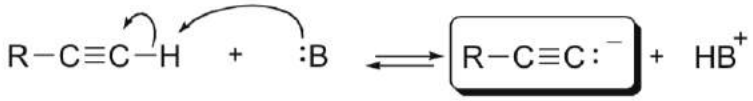
Mechanism:



Notes:

- Anti-markovnikov
- Unstable enol
- End product is aldehyde (if it's a terminal alkyne) or ketone

Formation of Acetylide Anions

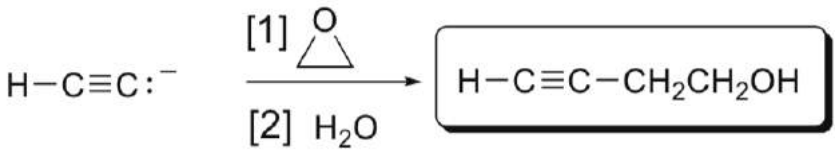


- Typical bases used are NaNH2 and NaH

Acetylide Anion Reactions with Alkyl Halides

- SN2 if primary alkyl halide, secondary or tertiary alkyl halide = E2

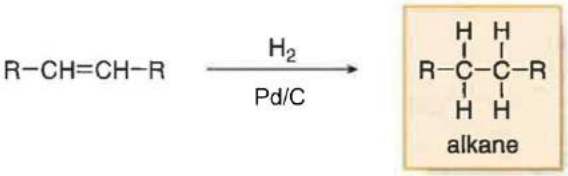
Acetylide Anion Reactions with Epoxides



- SN2 mechanism
- Acetylide attacks the less substituted carbon on the epoxide

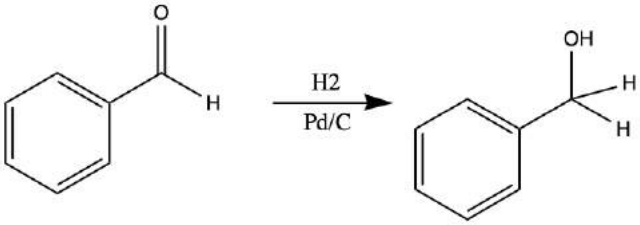
<u>Chapter 12: Oxidation and Reduction</u>

Reduction of Alkenes

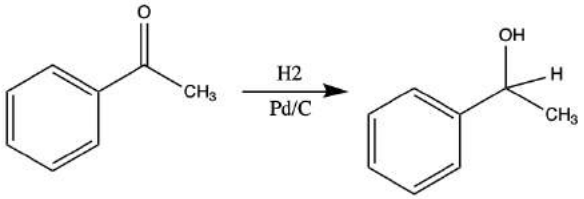


- Syn addition occurs

Reduction of Aldehydes

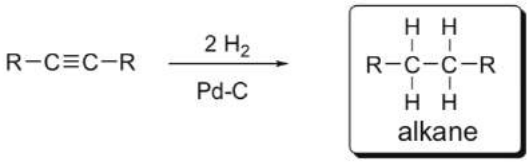


Reduction of Ketones

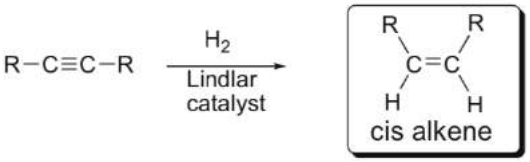


- Stereochemistry: Racemic mixture

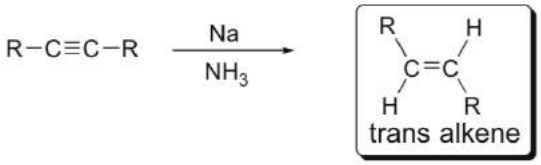
Reduction of Alkynes



- 2 equivalents of H2 are required
- 4 new C-H bonds are formed

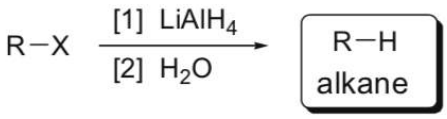


- Syn addition occurs = cis alkene product



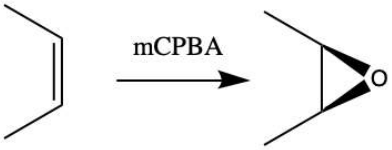
- Anti-addition occurs = trans alkene product

Reduction of Alkyl Halides

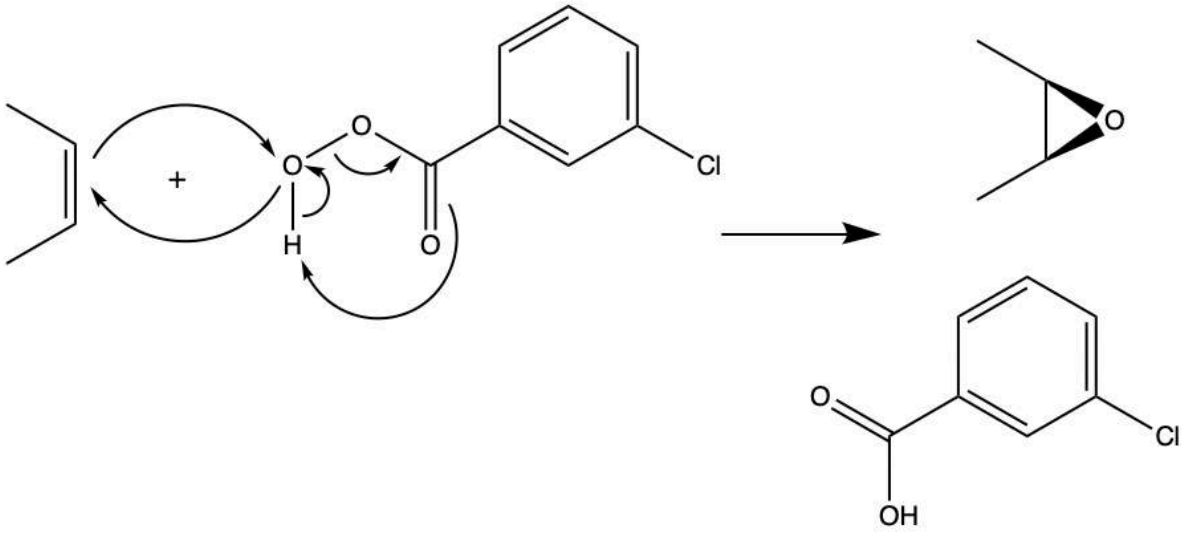


- SN2 mechanism
- Attacks the less substituted carbon if attacking epoxides

Epoxidation



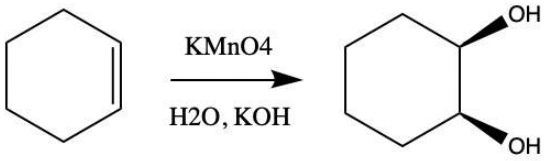
Mechanism:



Notes:

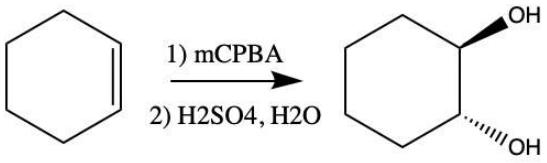
- One step reaction
- Syn addition
- Reaction is stereospecific (syn alkene = cis product, trans alkene = trans product)

Syn Dihydroxylation



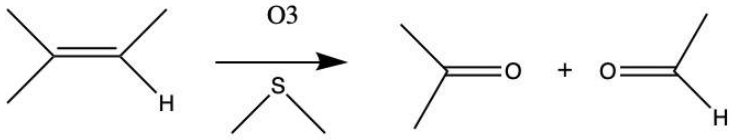
- Cis products
- Stereochemistry: Racemic mixture (but for the example above the products are identical)

Trans Dihydroxylation

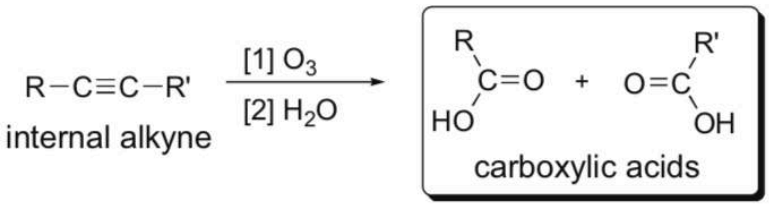


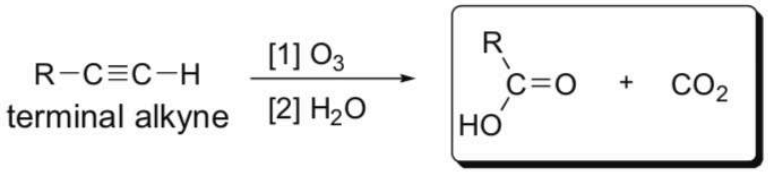
- Trans products
- Stereochemistry: Racemic mixture
- Step 2 can also use KOH instead of sulfuric acid and water

Oxidative Cleavage of Alkenes

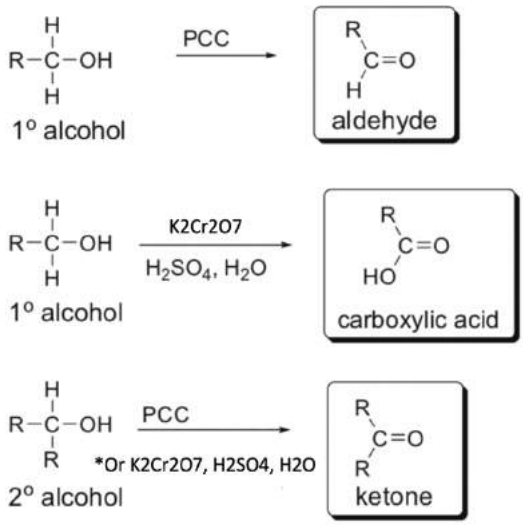


Oxidative Cleavage of Alkynes



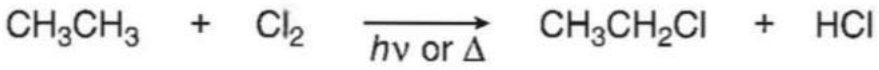


Oxidation of Alcohols



Chapter 15 Radical Reactions

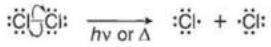
Halogenation of Alkanes



Mechanism:

Initiation

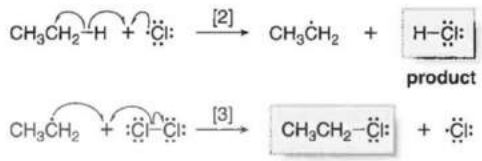
Step [1] Bond cleavage forms two radicals.



- Homolysis of the weakest bond in the starting materials requires energy from light or heat.
- Thus, the Cl – Cl bond ($\Delta H°$ = 242 kJ/mol), which is weaker than either the C – C or C – H bond in ethane ($\Delta H°$ = 368 and 410 kJ/mol, respectively), is broken to form two chlorine radicals.

Propagation

Steps [2] and [3] One radical reacts and a new radical is formed.

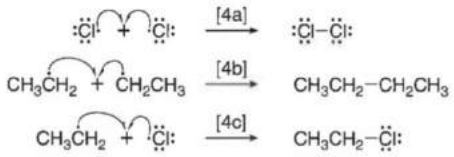


Repeat Steps [2], [3], [2], [3], again and again.

- The Cl· radicals abstract a hydrogen atom from ethane (Step [2]). This forms H – Cl and leaves one unpaired electron on carbon, generating the ethyl radical (CH_3CH_2·).
- CH_3CH_2· abstracts a chlorine atom from Cl_2 (Step [3]), forming CH_3CH_2Cl and a new chlorine radical (Cl·).
- The Cl· radical formed in Step [3] is a reactant in Step [2], so Steps [2] and [3] can occur repeatedly without an additional initiation reaction (Step [1]).
- In each propagation step, one radical is consumed and one radical is formed. The two products—CH_3CH_2Cl and HCl—are formed during propagation.

Termination

Step [4] Two radicals react to form a σ bond.

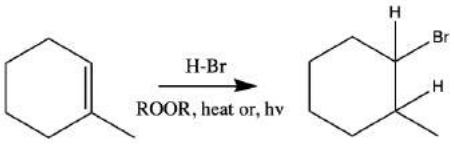


- To terminate the chain, two radicals react with each other in one of three ways (Steps [4a, b, and c]) to form stable bonds.

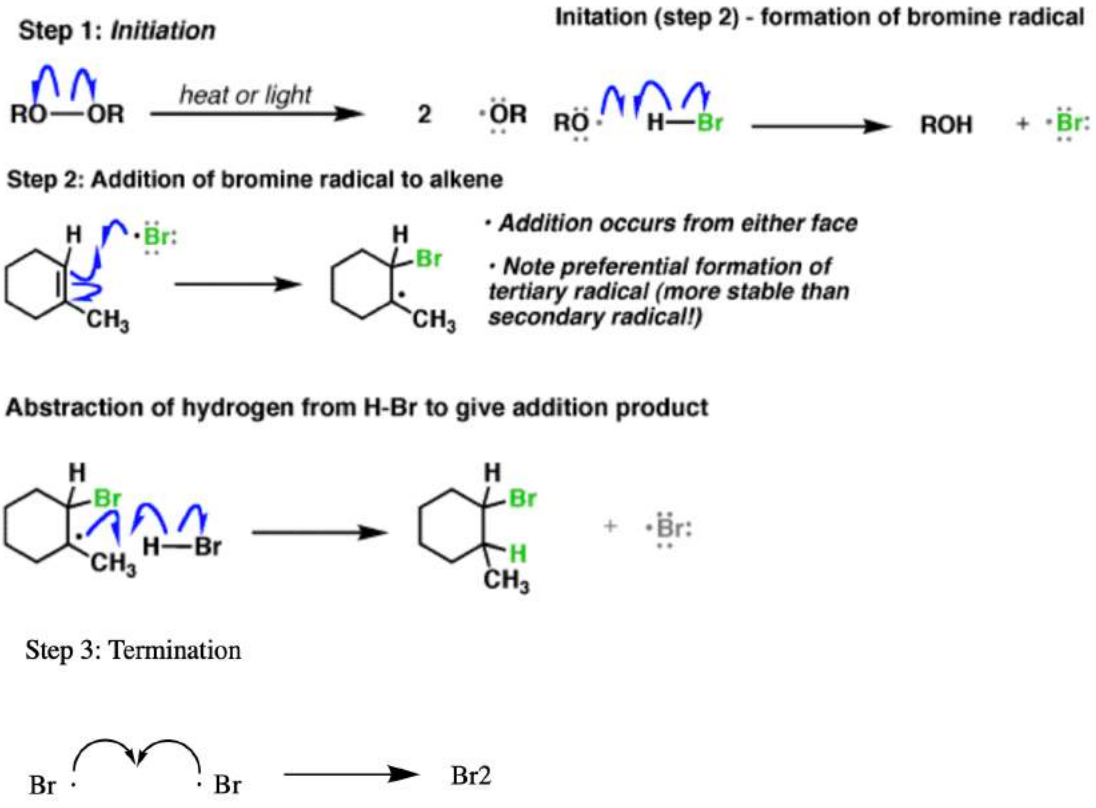
Notes:

- Must be Br2 or Cl2
- Chlorination is faster and less selective than bromination = 2+ products
- Bromination = 1 product (most substitued carbon is chosen)
- Stereochemistry: Racemic mixture

Radical Addition of HBr to an Alkene



Mechanism:

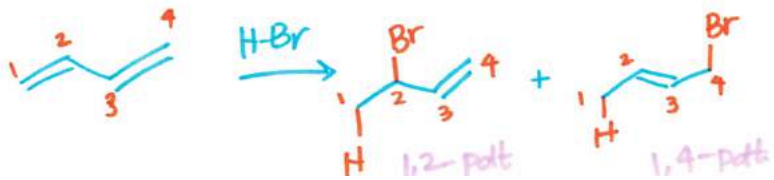


Notes:

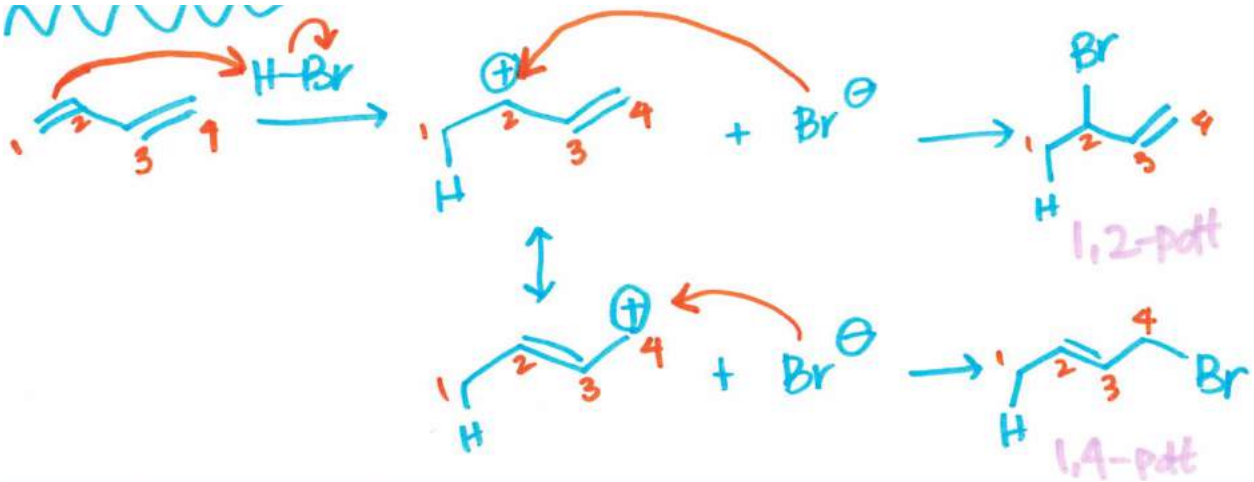
- Bromine gets added to the less substituted side (vs adding to the most substituted side with only H-Br)

Chapter 16: Conjugation, Resonance, and Dienes

1,3 Diene Electrophilic Addition



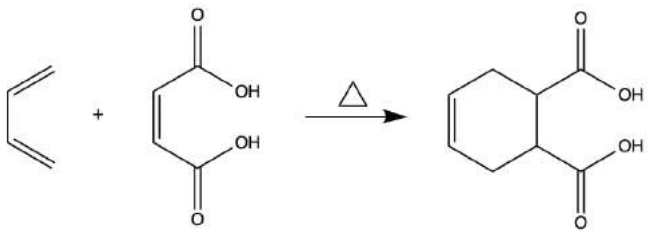
Mechanism:



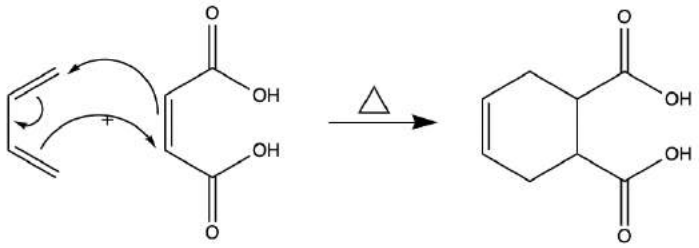
Notes:

- Markovnikov's rule is followed
- Kinetic product: 1,2 product. More formed at lower temperatures
- Thermodynamic product: 1,4 product. More formed at higher temperatures

Diels-Alder Reaction



Mechanism:



Notes:

- Reaction is one-step (concerted)
- Diene must be in s-cis conformation
- Trans diene = no reaction
- Stereochemistry is retained

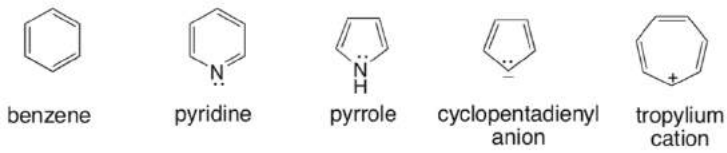
- (ie. If the dienophile was trans, product will be trans)

Chapter 17: Benzene and Aromatic Compounds

Huckel's Rule

Aromatic compound	• A cyclic, planar, completely conjugated compound that contains $4n + 2$ π electrons ($n = 0, 1, 2, 3$, and so forth). • An aromatic compound is more stable than a similar acyclic compound having the same number of π electrons.
Antiaromatic compound	• A cyclic, planar, completely conjugated compound that contains $4n$ π electrons ($n = 0, 1, 2, 3$, and so forth). • An antiaromatic compound is less stable than a similar acyclic compound having the same number of π electrons.
A compound that is not aromatic	• A compound that lacks one (or more) of the requirements to be aromatic or antiaromatic.

Examples of aromatic compounds with 6 π electrons (17.8)



Examples of compounds that are not aromatic (17.8)