

Chapter 6: Reactions of Alcohols, Ethers and Epoxides

Conversion of Alcohols To Alkyl Bromides With PBr_3

General Reaction:

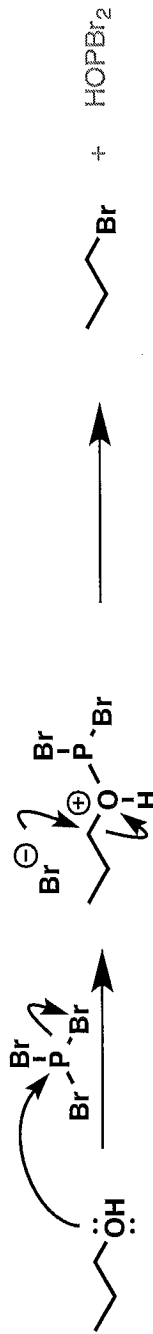


Works for primary and secondary alcohols

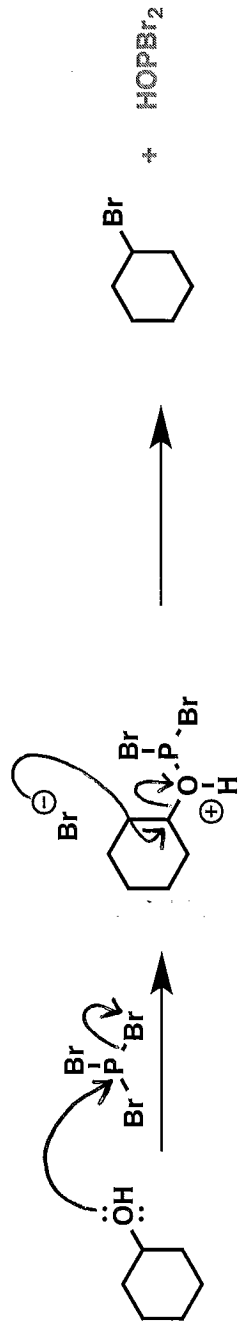
Mechanism Basics Box:

- Reaction works best with primary and secondary alcohols
- Mechanism is comprised of two consecutive $\text{S}_{\text{N}}2$ reactions
- Since it proceeds through $\text{S}_{\text{N}}2$, inversion of configuration occurs at the alcohol carbon

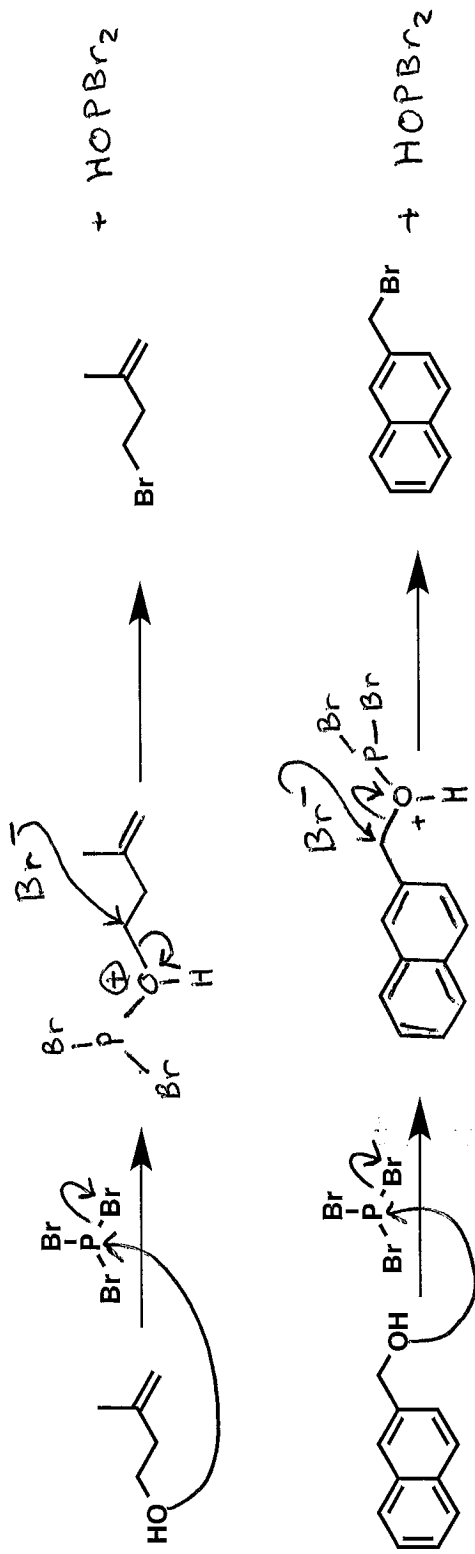
General Mechanism:



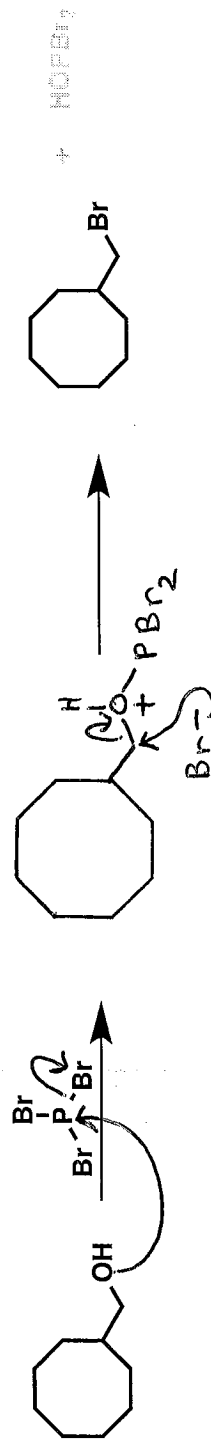
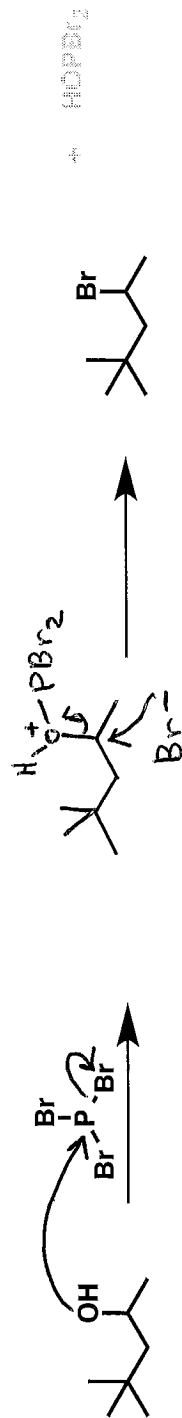
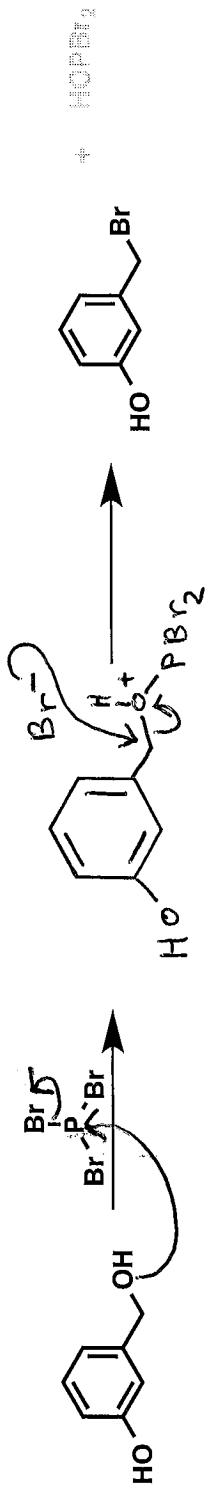
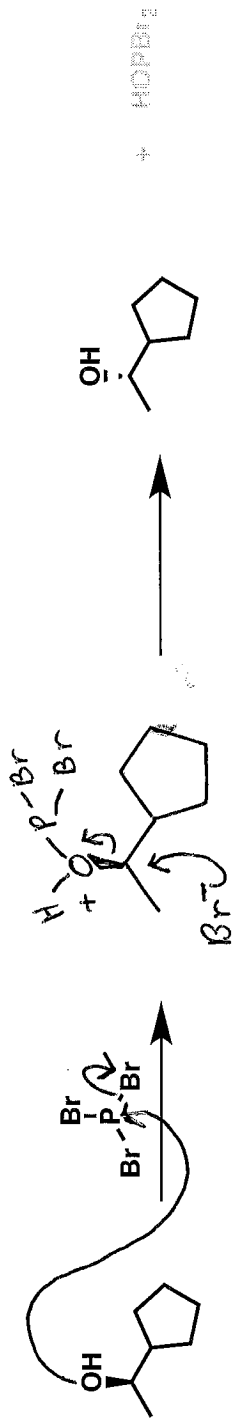
Fill in the missing mechanism arrows.



Complete the mechanism by following the pattern (draw arrows and intermediate).

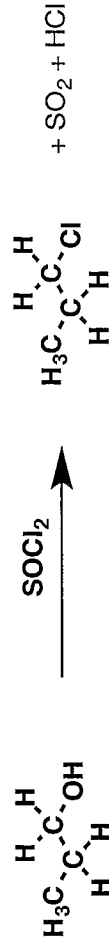


Complete the mechanism by following the pattern (draw arrows and intermediate).



Conversion of Alcohols To Alkyl Chlorides With SOCl_2

General Reaction:

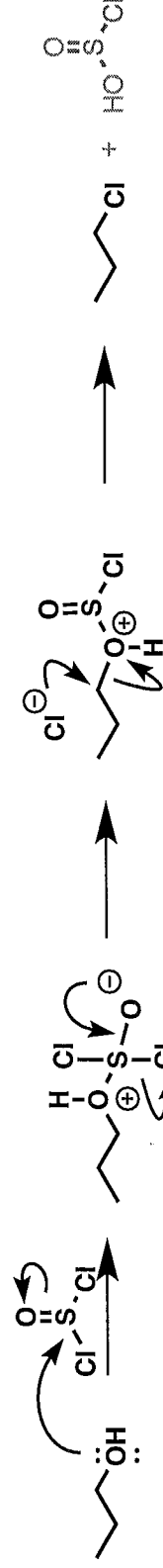


Works best for primary and secondary alcohols

Mechanism Basics Box:

- This $\text{S}_{\text{N}}2$ reaction proceeds with inversion of configuration at the alcohol-bearing carbon
- The reaction works best with primary and secondary alcohols
- Pyridine may be added to the reaction to scavenge any residual HCl produced
- A variation on this mechanism is sometimes taught, involving a mechanism called $\text{S}_{\text{N}}1\text{R}$

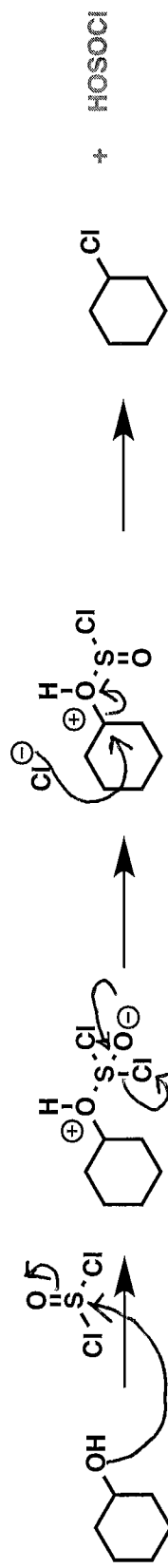
General Mechanism:



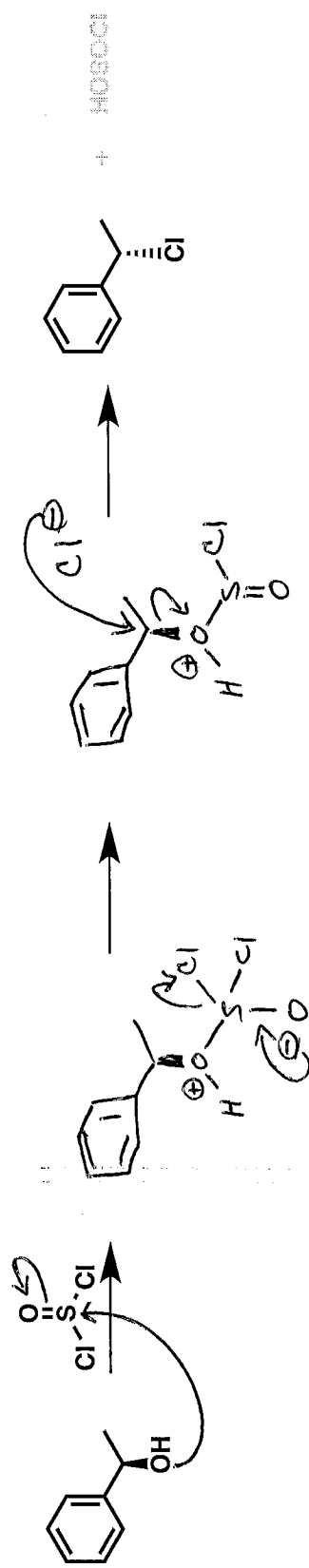
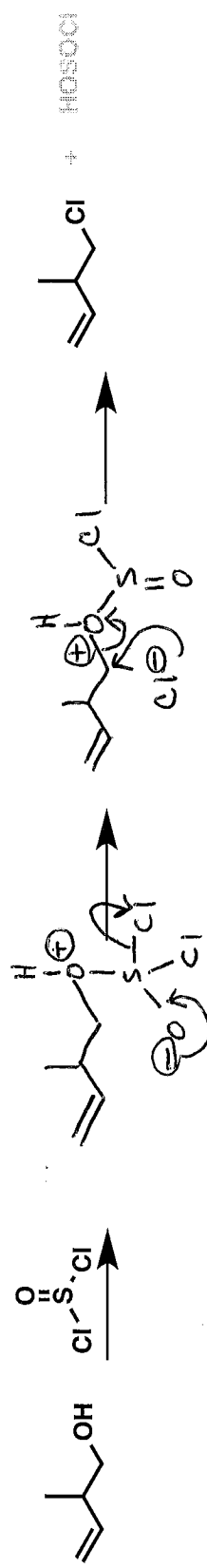
Decomposition of HOS(O)Cl to HCl and SO_2



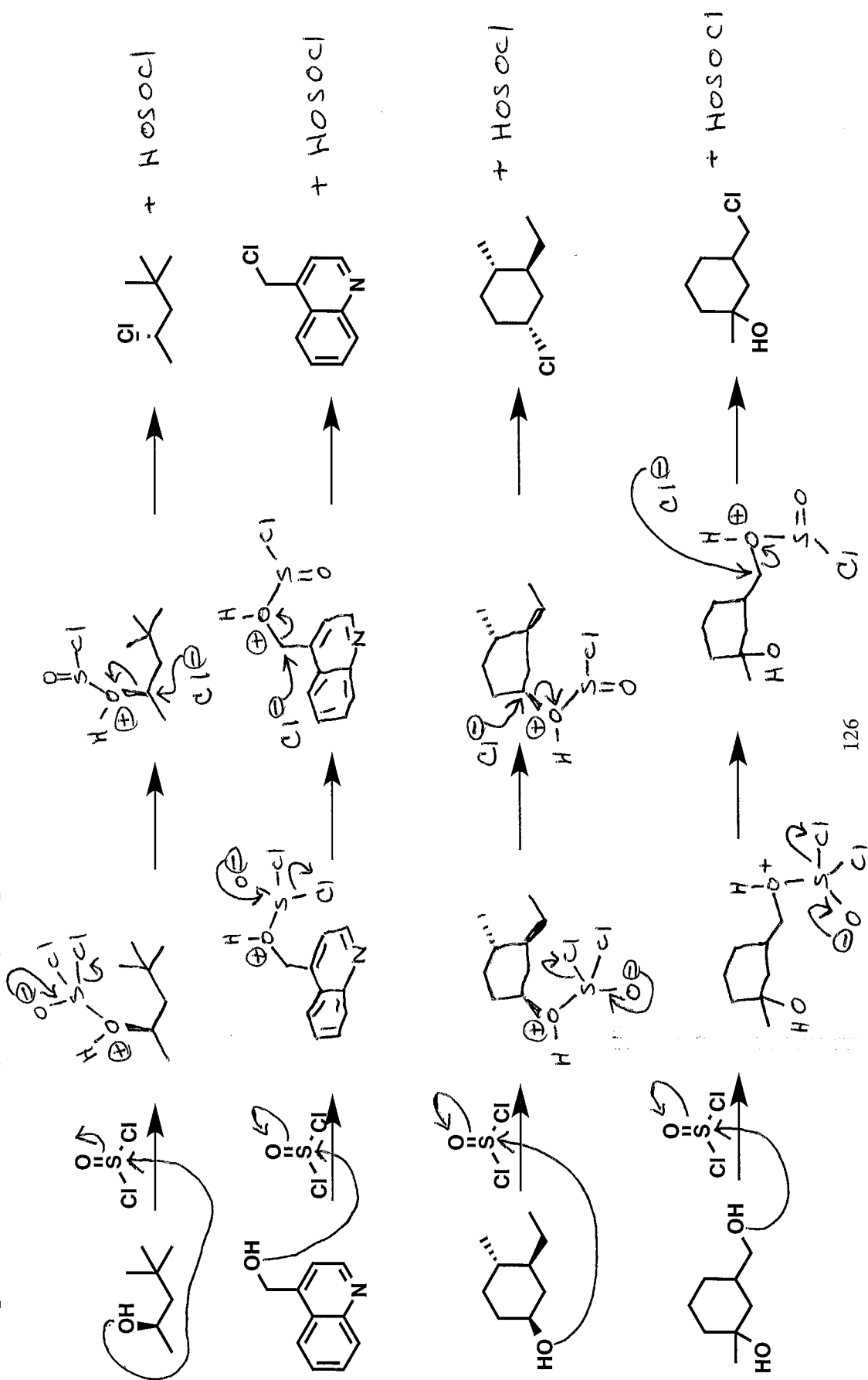
Fill in the missing mechanism arrows.



Complete the mechanism by following the pattern (draw arrows and intermediates).

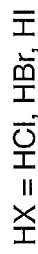
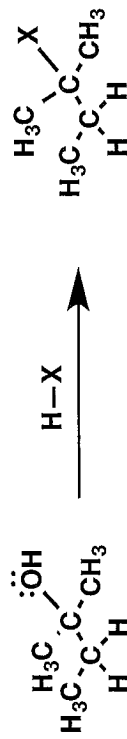


Complete the mechanism by following the pattern (draw arrows and intermediate).



Conversion Of Alcohols To Alkyl Halides With HX

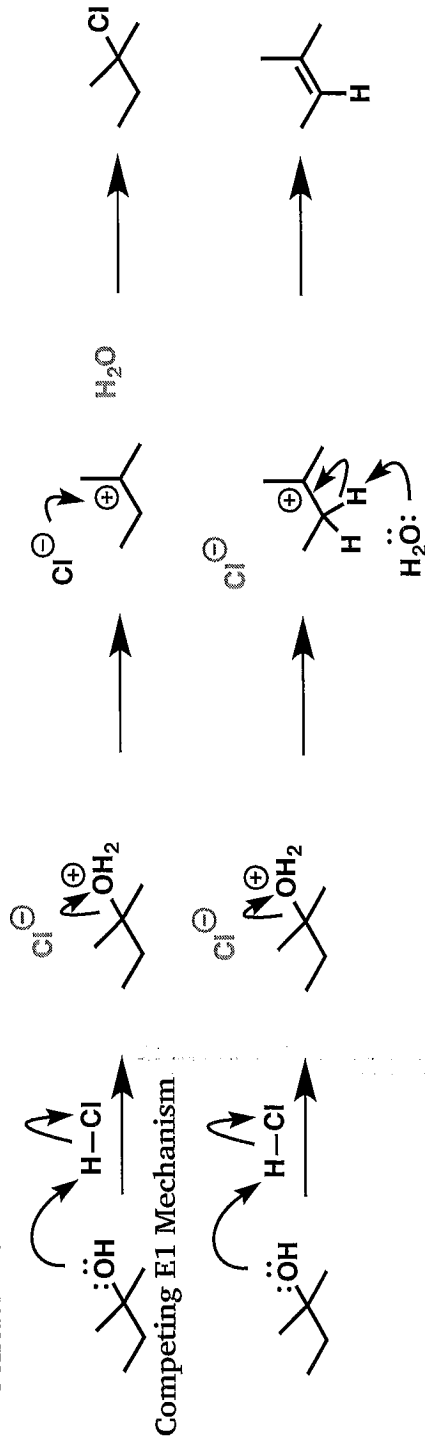
General Reaction:



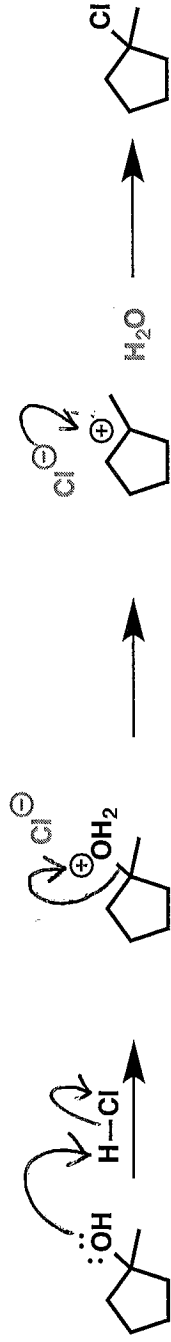
Mechanism Basics Box:

- This proceeds via an S_N1 mechanism
- The reaction works best with tertiary, allylic, and secondary alcohols
- The carbocation intermediate may rearrange leading to multiple products
- A common competing reaction with this substitution is E1 elimination, especially when the reaction is conducted with polar solvents and added heat

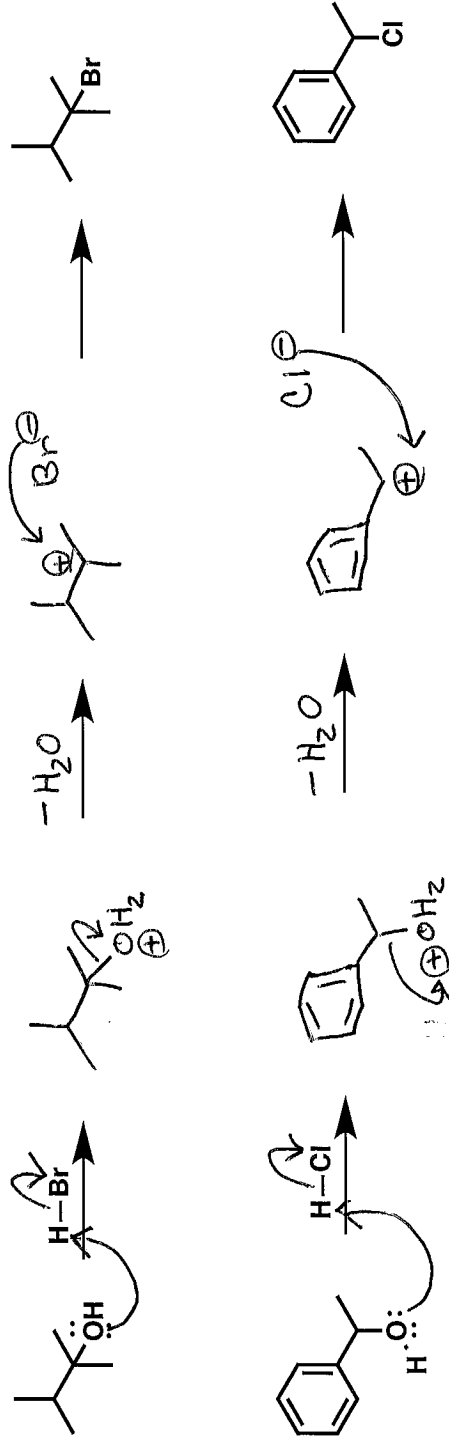
General Mechanism:



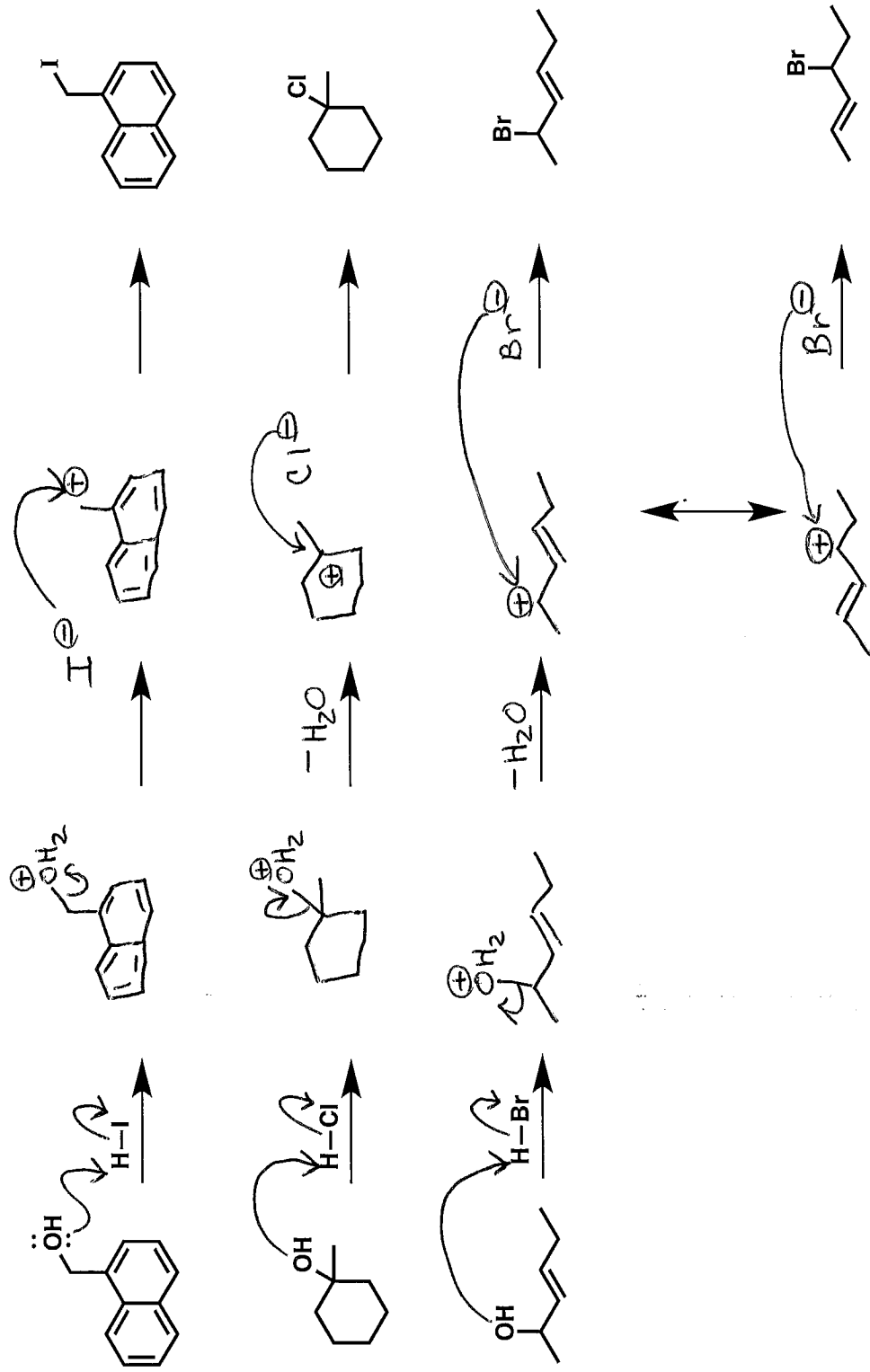
Fill in the missing mechanism arrows.



Complete the mechanism by following the pattern (draw arrows and intermediates).

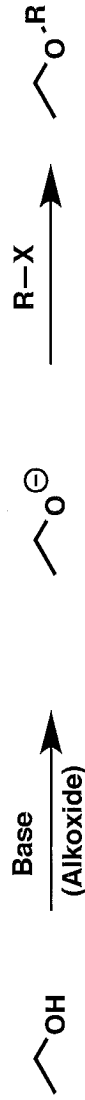


Complete the mechanism by following the pattern (draw arrows and intermediates).



Williamson Ether Synthesis

General Reaction:



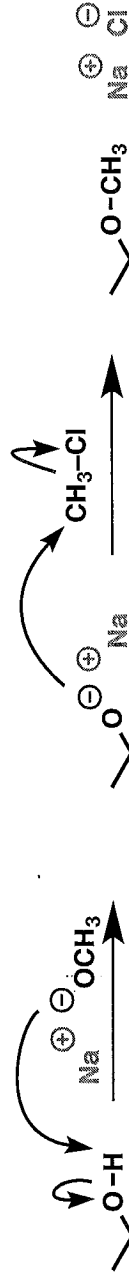
R-X is generally a primary alkyl halide

Base is usually an alkoxide (RO⁻) or hydride (e.g. NaH or KH)

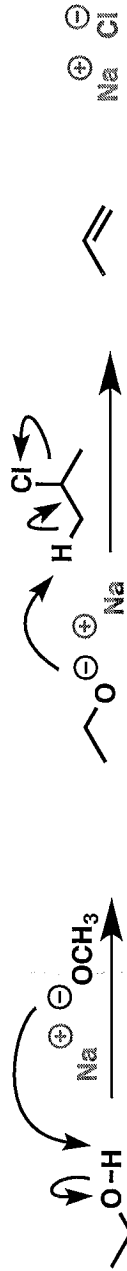
Mechanism Basics Box:

- Reaction works best for methyl and primary alkyl halides. Secondary and tertiary alkyl halides lead to elimination products.
- Since the carbon-oxygen bond forming reaction is an S_N2, it proceeds with inversion of configuration at the carbon bearing the leaving group.
- The alkoxide may be primary, secondary, or tertiary.

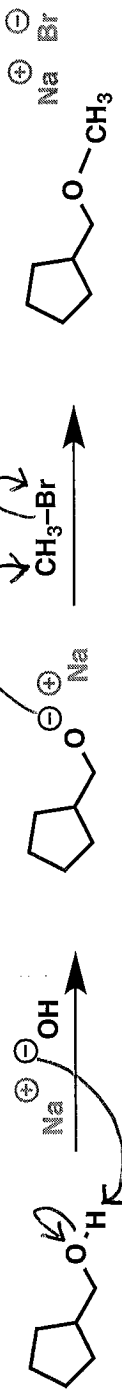
General Mechanism:



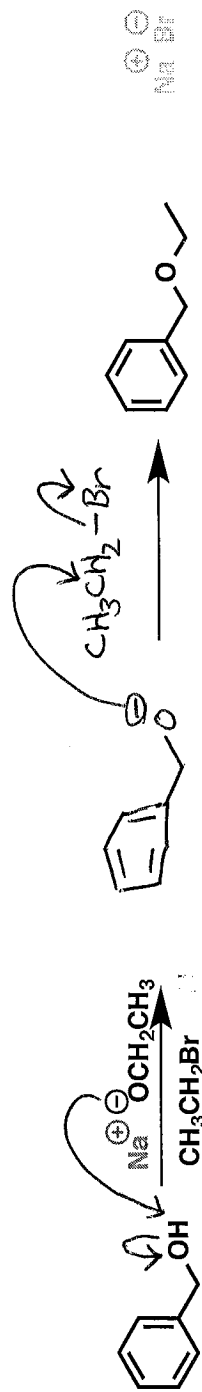
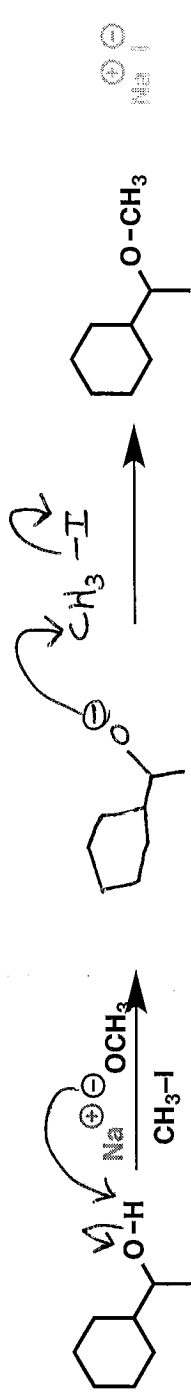
Competing elimination mechanism (for secondary alkyl halides)



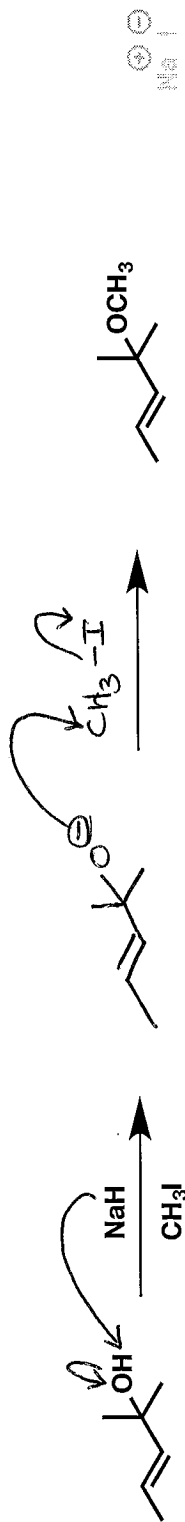
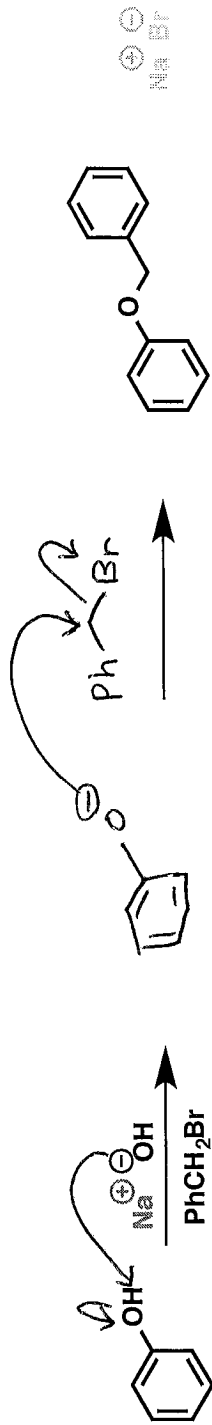
Fill in the missing arrows.



Complete the mechanism by following the pattern (draw arrows and intermediate).



Complete the mechanism by following the pattern (draw arrows and intermediate)



Ether Cleavage

General Reaction:

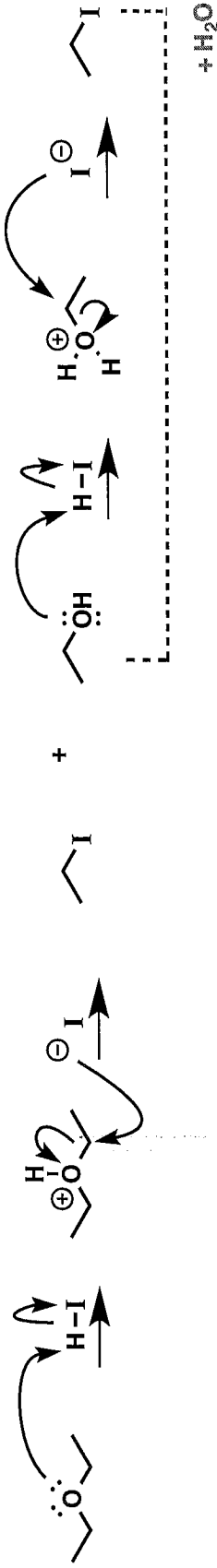


With excess HI, the alcohol is converted to an alkyl iodide under these conditions.

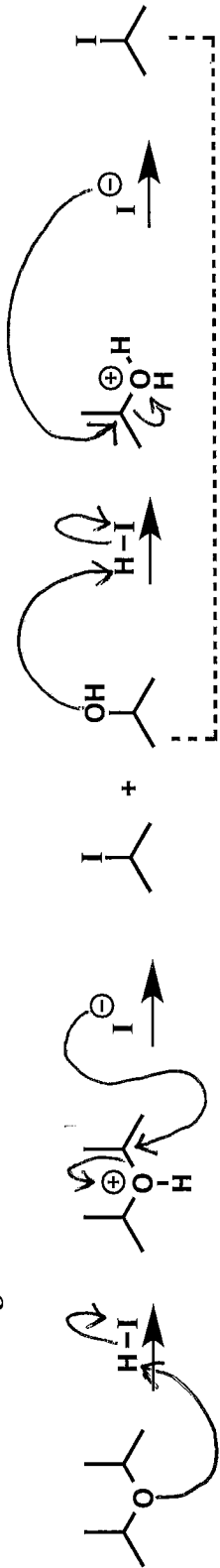
Mechanism Basics Box:

- Ether cleavage occurs when these molecules are exposed to highly acidic conditions such as HI, HBr, or H_2SO_4
- Cleavage of primary ethers yields an alcohol and a halide. The alcohol then undergoes an acid catalyzed $\text{S}_{\text{N}}2$ reaction to yield another equivalent of the alkyl halide.
- Cleavage of ethers with primary or secondary sites results in halide substitution. However cleavage with ethers that have a tertiary carbon typically undergo E1 elimination.

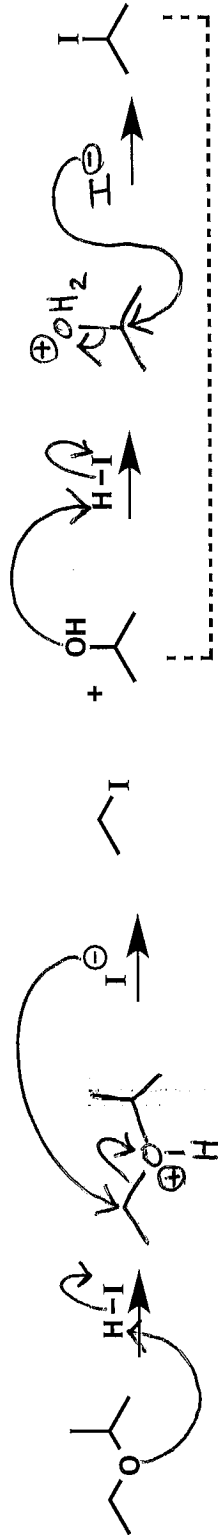
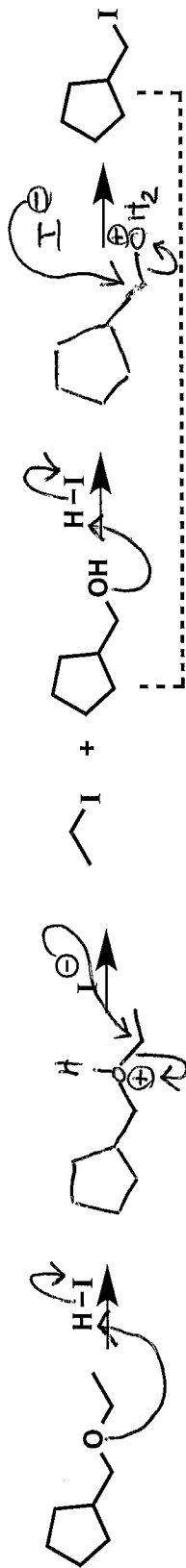
General Mechanism:



Fill in the missing arrows.

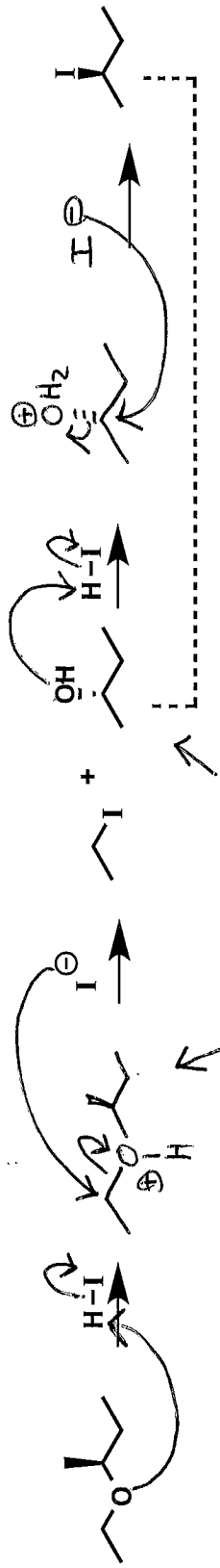
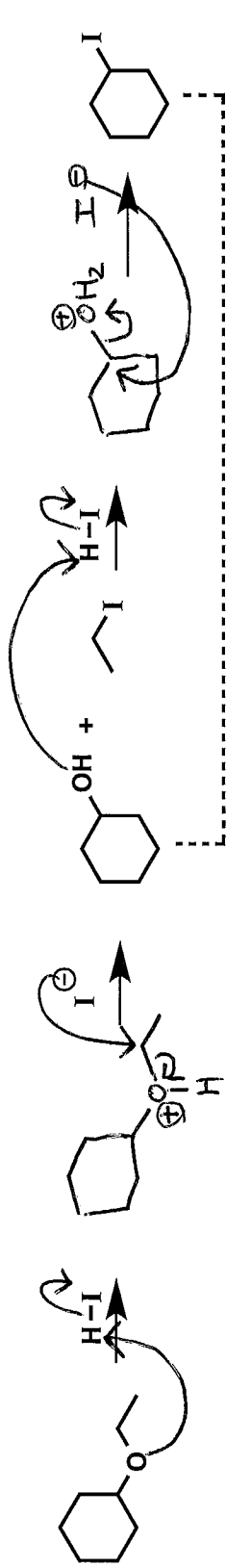


Complete the mechanism by following the pattern (draw arrows and intermediate)

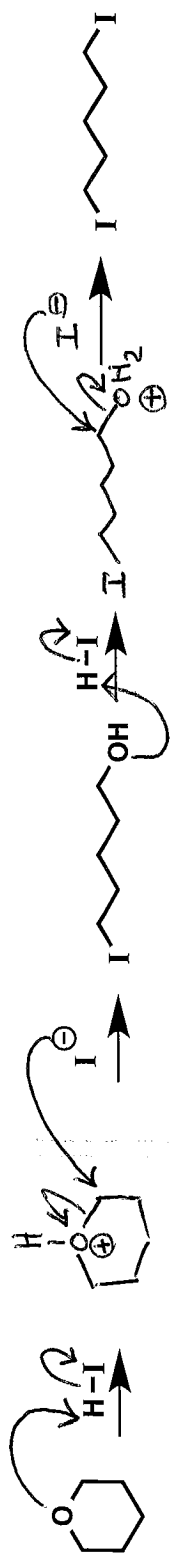
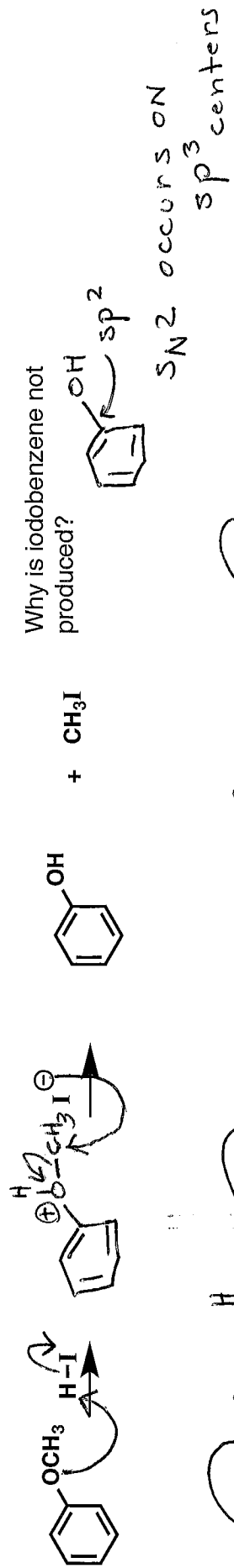


This is an SN2 reaction, so the iodide nucleophile will initially attack the least substituted carbon adjacent to the protonated ether oxygen

Fill in the missing intermediates and mechanism arrows.

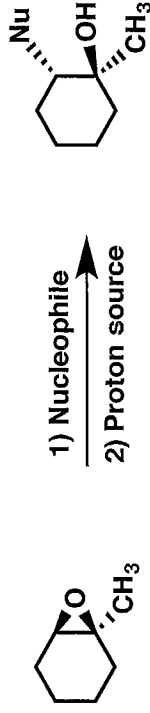


"S stereocenter in both cases"



Base Catalyzed Epoxide Opening

General Reaction:



Nucleophiles are generally negatively charged species, **or** uncharged amines

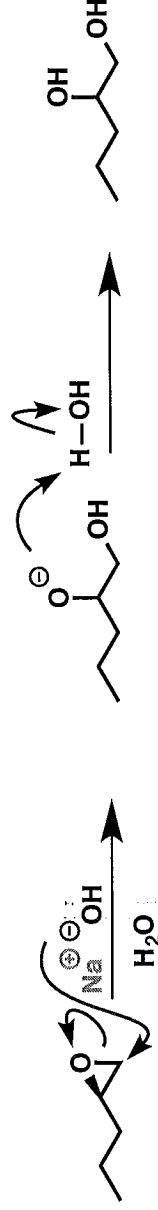
Common examples: NaOH , NaOCH_3 , NaSH ,
 NaSCH_3 , LiAlH_4 , NH_3 , NaCN

Mechanism Basics Box:

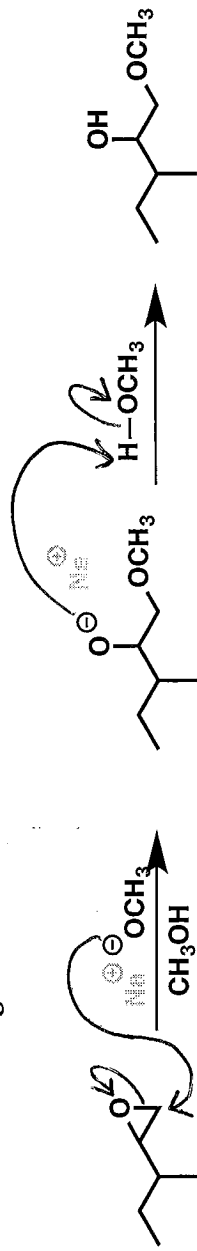
- Under basic conditions the nucleophile attacks the epoxide at the least substituted carbon (due to lesser steric hindrance)
- This is essentially an $\text{S}_{\text{N}}2$ reaction. Inversion of configuration occurs on the site that is attacked by the nucleophile
- The product alcohol retains the stereochemistry of the original epoxide
- The product alcohol and nucleophile have an anti orientation

The proton source is usually water (H_2O) or other mild acid

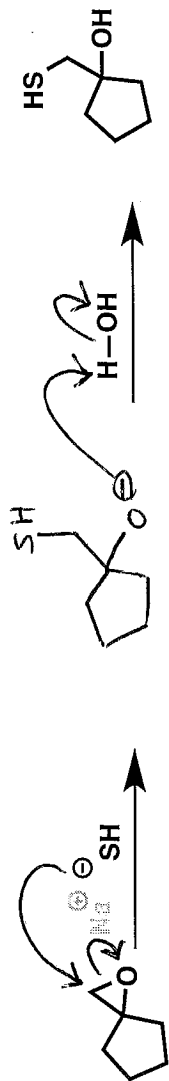
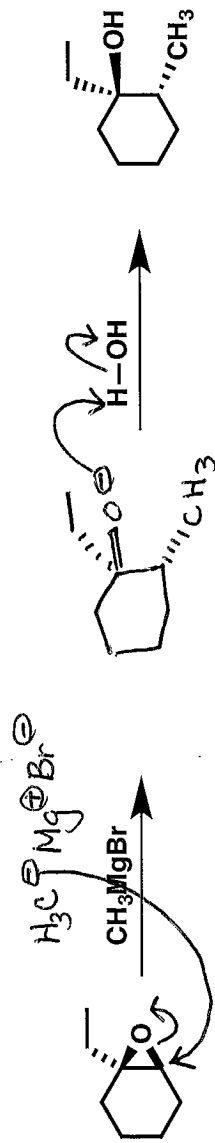
General Mechanism:



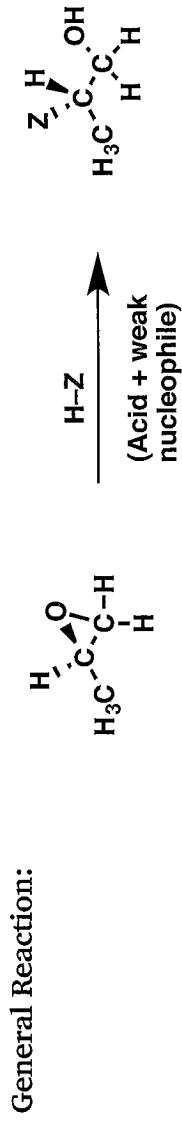
Fill in the missing arrows.



Complete the mechanism by following the pattern (draw arrows and intermediate)



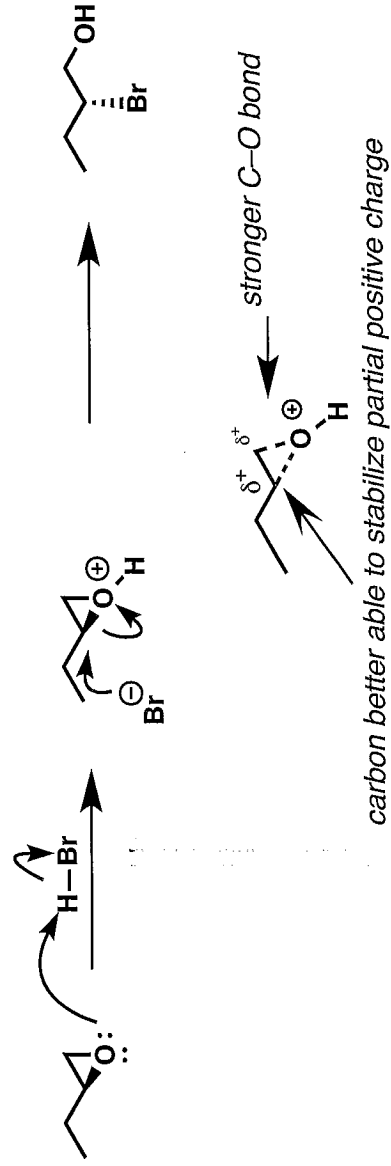
Acid Catalyzed Opening of Epoxides



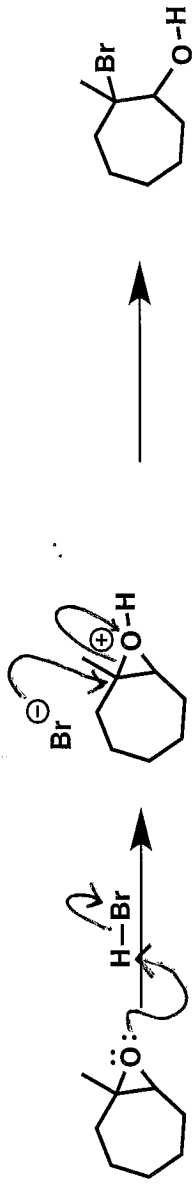
Mechanism Basics Box:

- Under acidic or neutral conditions, the nucleophile attacks the epoxide at the most substituted site
- Inversion of configuration occurs at the carbon where the nucleophile attacks
- The product alcohol retains the stereochemistry of the original epoxide

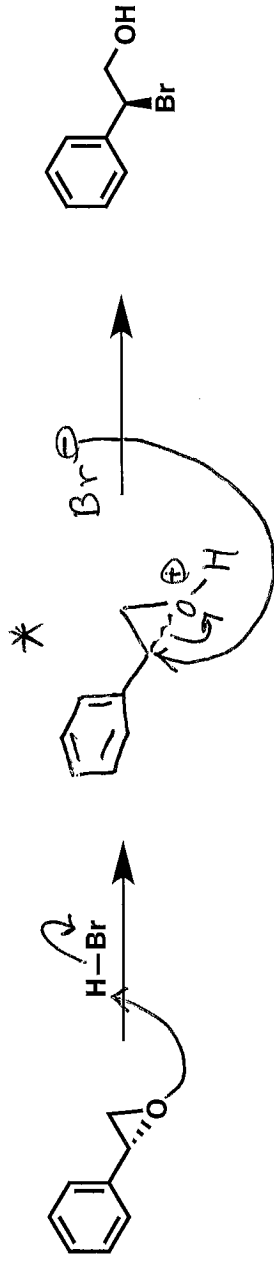
General Mechanism:



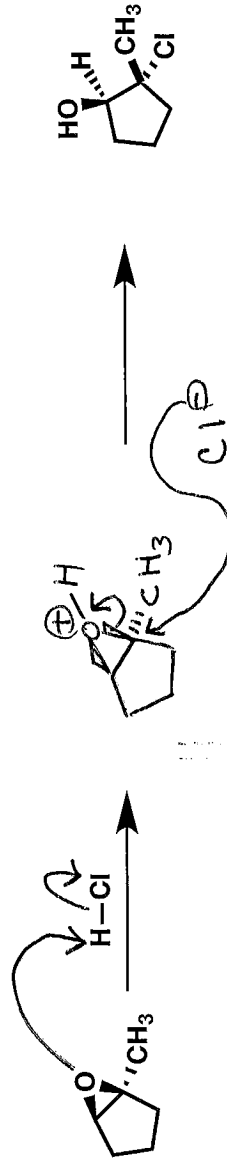
Fill in the missing arrows.



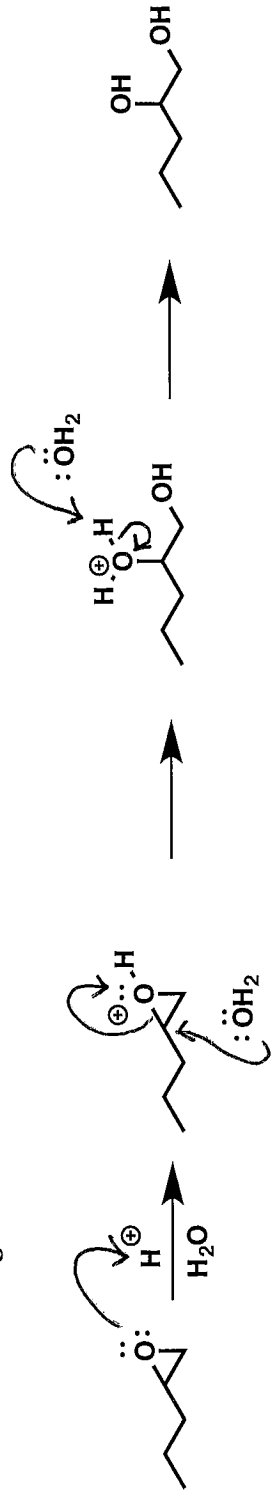
Complete the mechanism by following the pattern (draw arrows and intermediate)



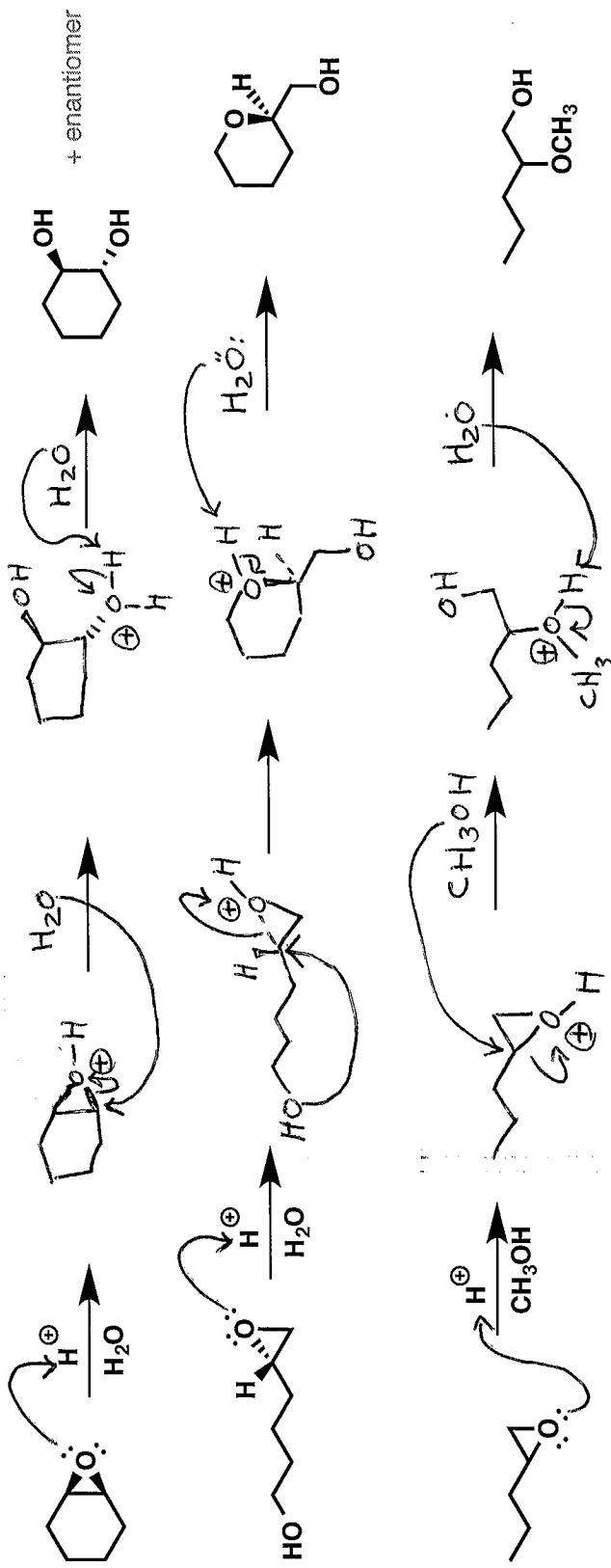
* resonance form



Fill in the missing arrows.

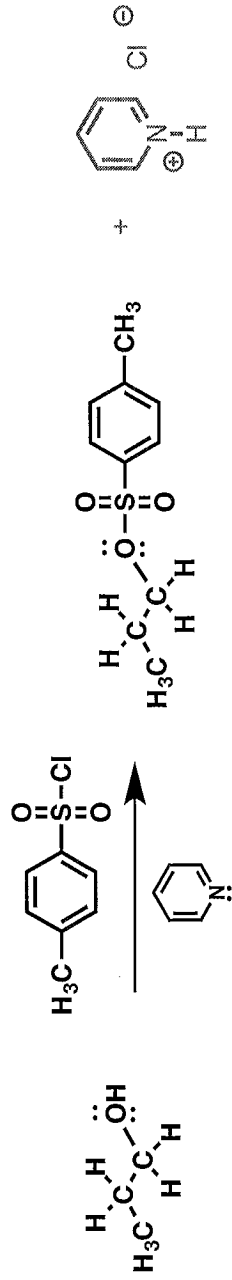


Complete the mechanism by following the pattern (draw arrows and intermediates).



Formation of Tosylates (Alkyl Sulfonates)

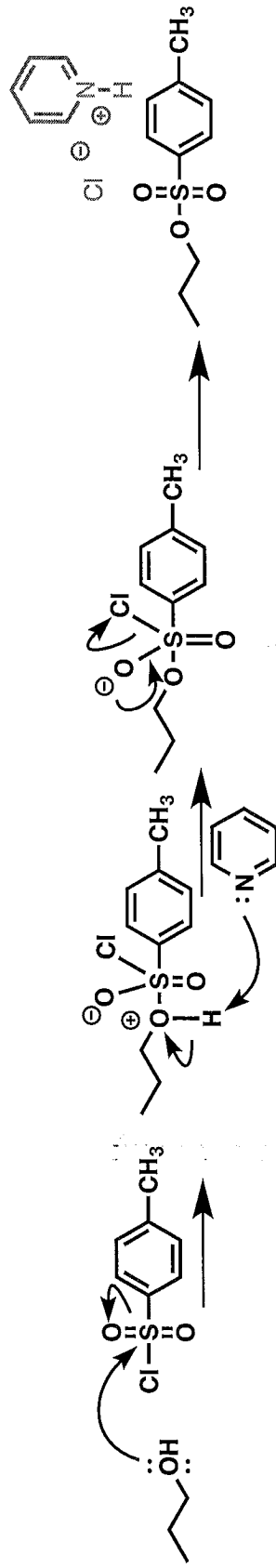
General Reaction:



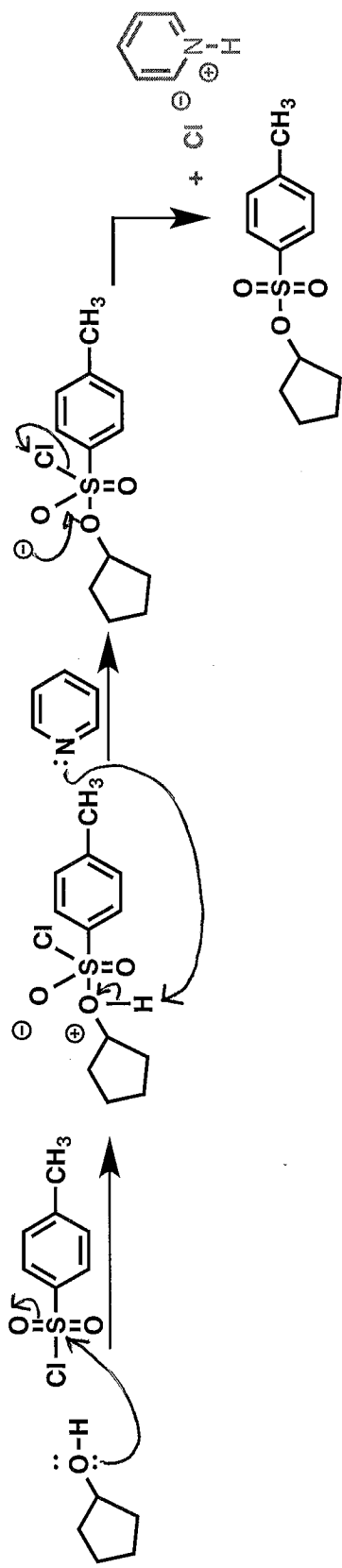
Mechanism Basics Box:

- Alcohols can be converted into good leaving groups for $\text{S}_{\text{N}}2$ and E2 reactions by transforming them into tosylates or mesylates ("alkyl sulfonates")
- In these species the leaving group (OTs) is very stable as it is resonance-stabilized.

General Mechanism:



Fill in the missing arrows.



Complete the mechanism by following the pattern (draw arrows and intermediate)

