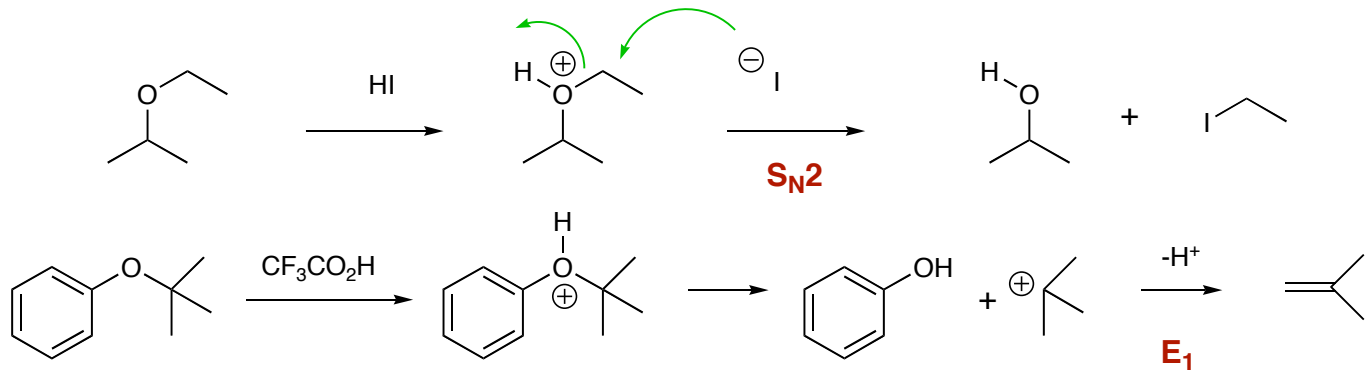
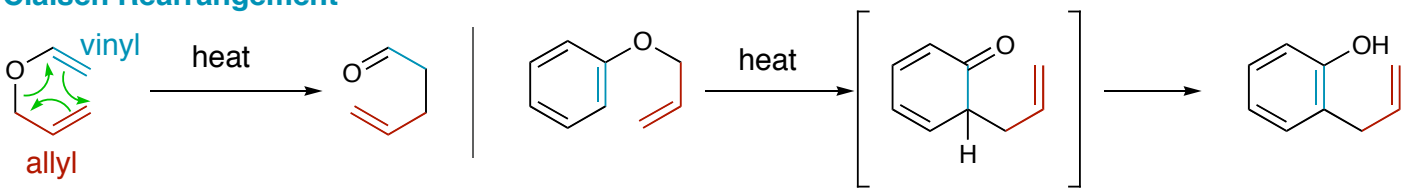
Chapter 18 - Ethers and Epoxides; Thiols and Sulfides

Reactions of Ethers

Ethers are very stable and often used as solvents to carry out organic reactions. However, under strong acid conditions with a nucleophilic conjugate base, they can be cleaved by an S_N2 reaction. Tertiary ethers undergo cleavage by an E_1 mechanism. Allyl Vinyl Ethers undergo a Claisen Rearrangement when heated.

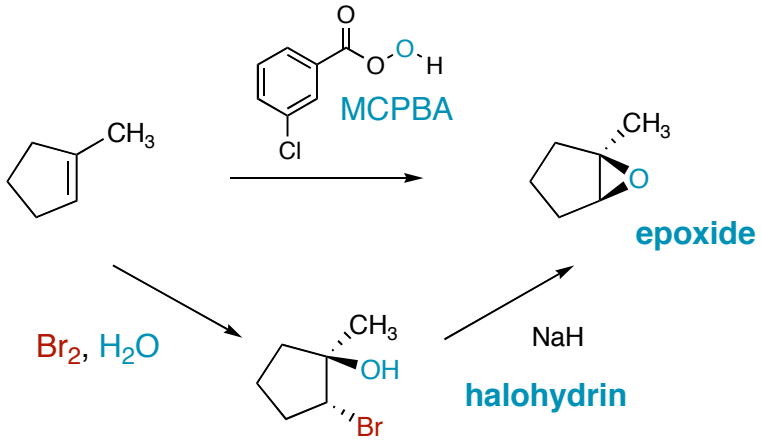


Claisen Rearrangement



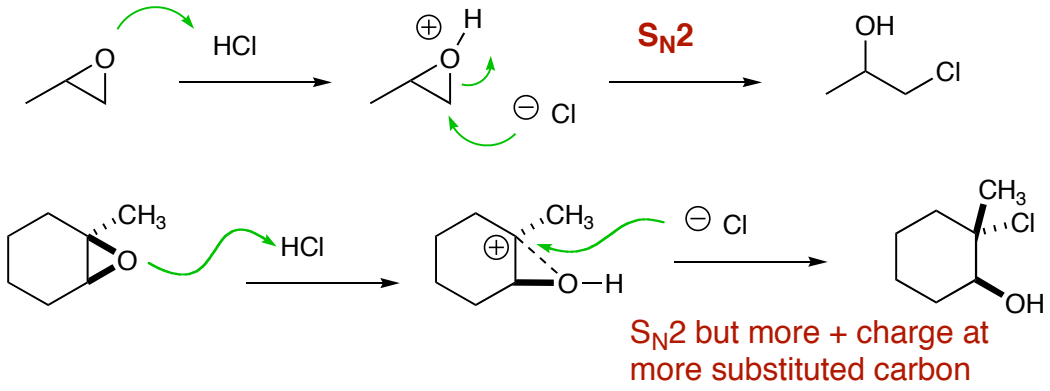
Preparation of Epoxides

Epoxides can be made in one step by reaction with meta-chloroperbenzoic acid (MCPBA). This is a stereospecific reaction and both C-O bonds are formed at the same time. They can also be prepared in two steps by formation of a halohydrin followed by treatment with NaH (a Williamson Ether Synthesis).

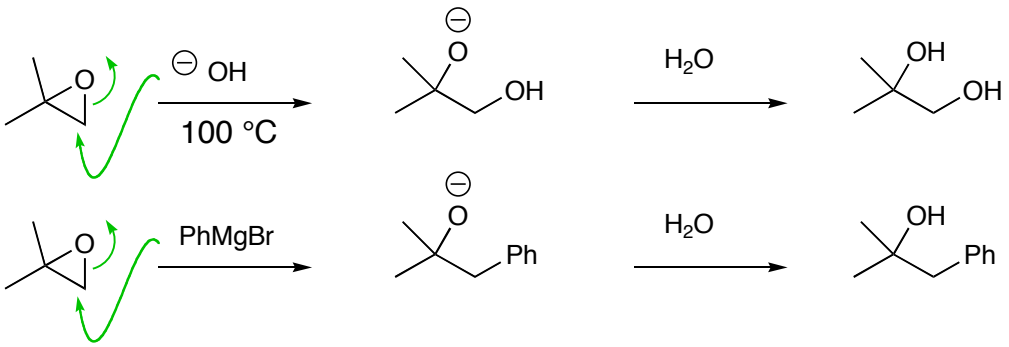


Reactions of Epoxides

Epoxides are more reactive than typical ethers due to ring strain. Under acidic conditions, primary and secondary protonated epoxides will be attached by nucleophiles via a S_N2 mechanism - thus the nucleophile will add to the less hindered carbon. If there is a tertiary carbon in the epoxide, there will be more positive charge at that carbon so nucleophiles will add to the more hindered carbon. Note that this is still a stereospecific anti addition as there is not a full carbocation formed. It is somewhere in between a S_N2 and S_N1 mechanism.



Base catalyzed or nucleophilic opening of epoxides can be done. It generally requires strong nucleophiles and heat. Epoxides are not as electrophilic as typical alkyl halides.



Thiols and Sulfides

The sulfur analogs of alcohols are called thiols and the sulfer analogs of ethers are called sulfides. The amino acid cysteine is an important amino acid in proteins and affect their folding structure and stability.