

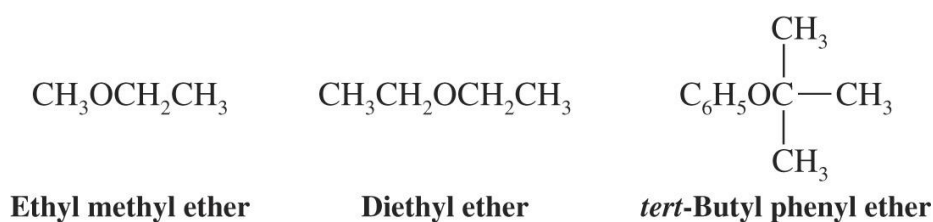
## Chapter 11 Alcohols and Ethers

### † Nomenclature:

- | Nomenclature of Alcohols (Given in Chapter 4)
- | Nomenclature of Ethers

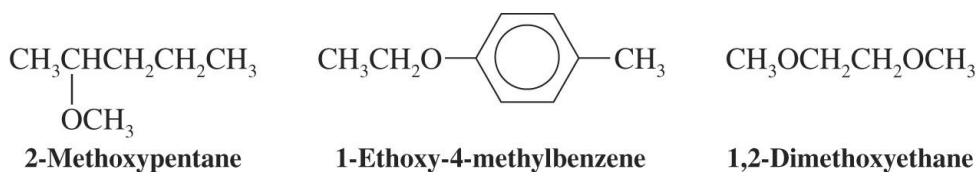
- Common Names

§ The groups attached to the oxygen are listed in alphabetical order



- IUPAC

§ Ethers are named as having an alkoxyl substituent on the main chain



§ Cyclic ethers can be named using the prefix oxa-

§ Three-membered ring ethers can be called oxiranes.

§ Four-membered ring ethers can be called oxetanes



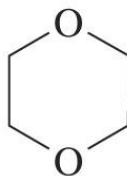
**Oxacyclopropane  
or oxirane  
(ethylene oxide)**



**Oxacyclobutane  
or oxetane**



**Oxacyclopentane  
(tetrahydrofuran)**



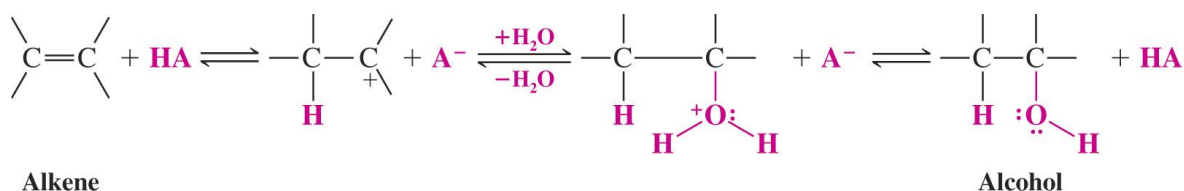
**1,4-Dioxacyclohexane  
(1,4-dioxane)**

## † Physical Properties of Alcohols and Ethers:

- Alcohols have considerably higher boiling points than ethers:  
The former (e.g. alcohols) can form hydrogen bonding.
- Both alcohols and ethers can hydrogen bond to water and have similar solubilities in water

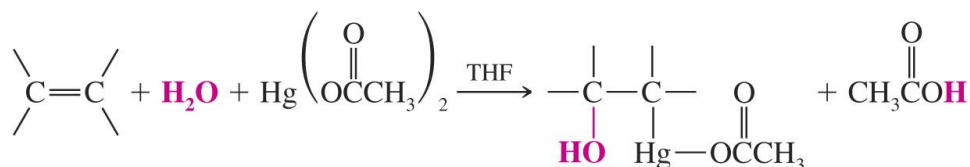
## † Synthesis of alcohols from alkenes:

### a) Addition of Water to Alkenes: (Hydration of alkenes)

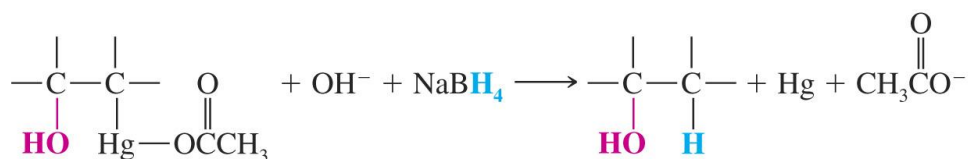


## b) Oxymercuration-Demercuration: Markovnikov Addition

### Oxymercuration

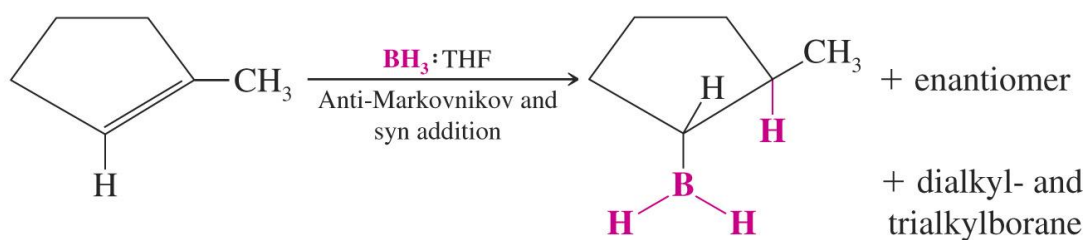


### Demercuration

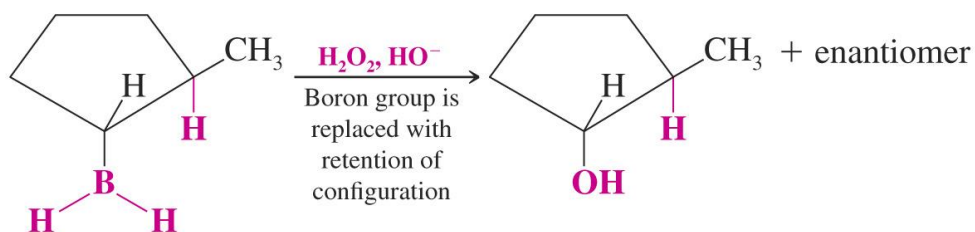


## c) Hydroboration-Oxidation: Anti-Markovnikov Syn Hydration

### Hydroboration



### Oxidation



## † Alcohols as Acids:

- Alcohols have acidities similar to water.
- Sterically hindered alcohols such as *tert*-butyl alcohol are less acidic (have higher  $pK_a$  values): (The conjugate base is not well solvated and so is not as stable)

Acid	$pK_a$
$CH_3OH$	15.5
$H_2O$	15.74
$CH_3CH_2OH$	15.9
$(CH_3)_3COH$	18.0

- Alcohols are stronger acids than terminal alkynes and primary or secondary amines

### *Relative Acidity*

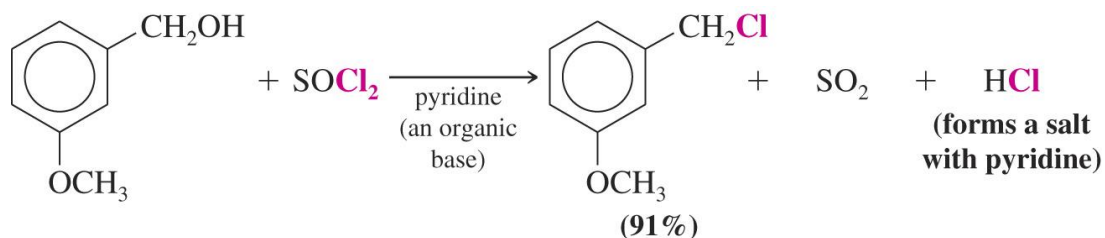
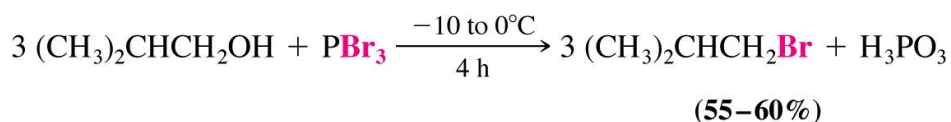
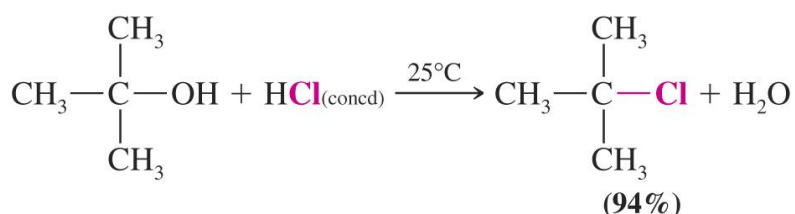


- An alkoxide can be prepared by the reaction of an alcohol with sodium or potassium metal

## † Conversion of Alcohols into Alkyl Halides:

The hydroxyl groups are poor leaving groups, and are often converted to alkyl halides when a good leaving group is needed

Three general methods exist for conversion of alcohols to alkyl halides, depending on the classification of the alcohol and the halogen desired



### t Alkyl Halides from the Reaction of Alcohols with Hydrogen Halides:

| The order of reactivity is as follows

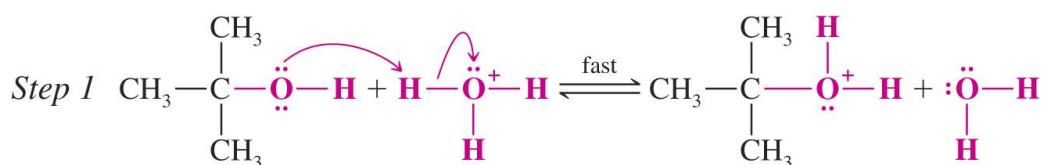
§ Hydrogen halide  $\text{HI} > \text{HBr} > \text{HCl} > \text{HF}$  (Unreactive)

§ Type of alcohol  $3^\circ > 2^\circ > 1^\circ < \text{methyl}$

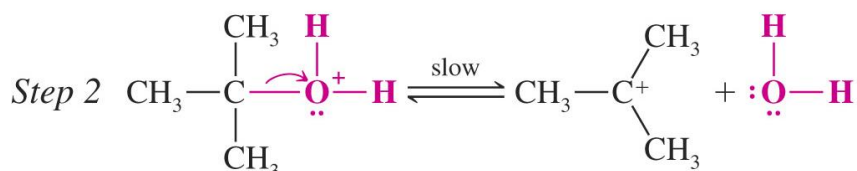
**| Mechanism of the Reaction of Alcohols with HX:****a) S<sub>N</sub>1 mechanism for 3°, 2°, allylic and benzylic alcohols**

- These reactions are prone to carbocation rearrangements

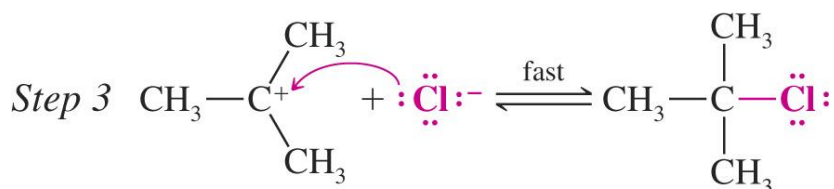
**In step 1 the hydroxyl is converted to a good leaving group**

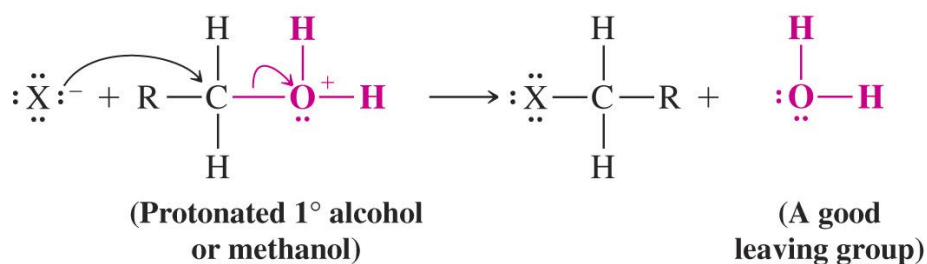


**In step 2 the leaving group departs as a water molecule, leaving behind a carbocation**

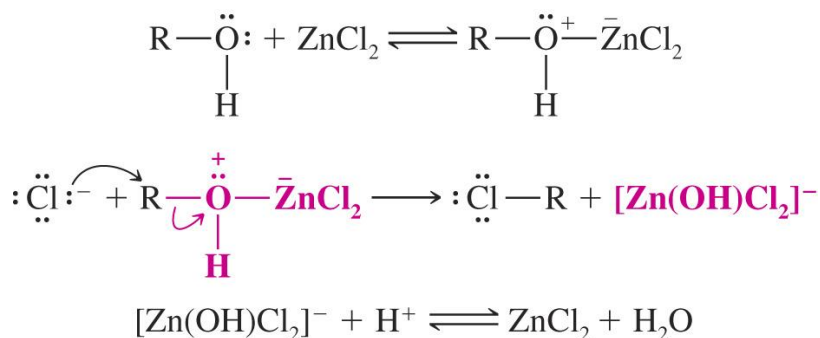


**In step 3 the halide, a good nucleophile, reacts with the carbocation**



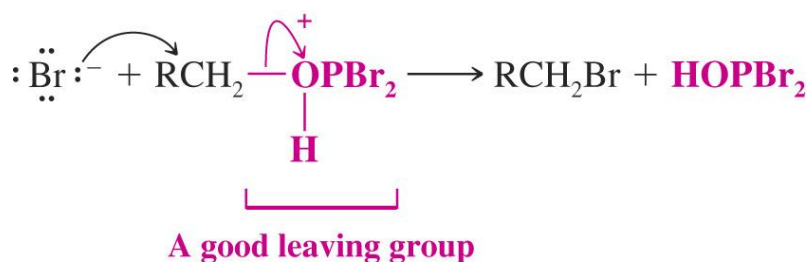
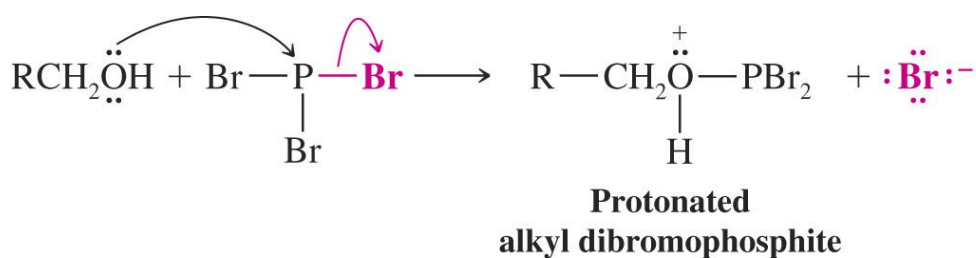
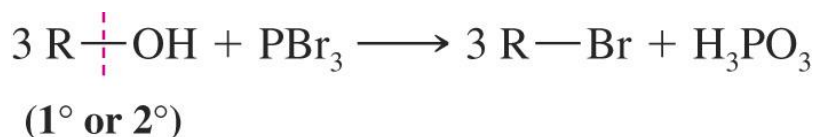
b) S<sub>N</sub>2 mechanism for 1° and methyl alcohols

## c) 1° and 2° alkyl chlorides can only be made with the assistance of a Lewis acid such as zinc chloride

† Alkyl Halides from the Reaction of Alcohols with PBr<sub>3</sub> and SOCl<sub>2</sub>:

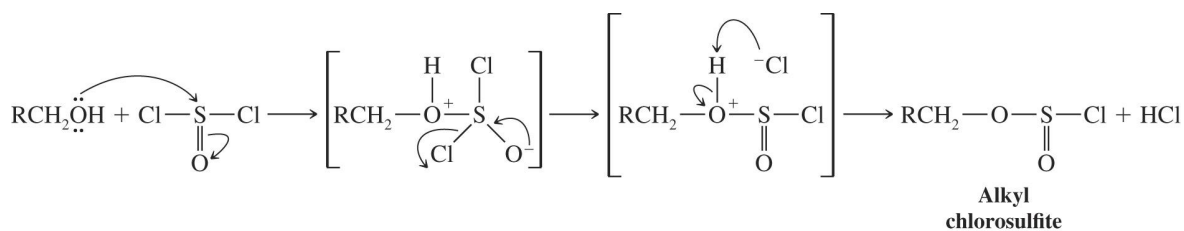
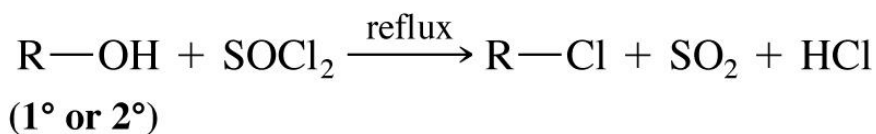
These reagents only react with 1° and 2° alcohols in S<sub>N</sub>2 reactions, without seeing any arrangement, to convert the hydroxyl to an excellent leaving group

| **Reaction of phosphorous tribromide (PBr<sub>3</sub>) to give alkyl bromides**

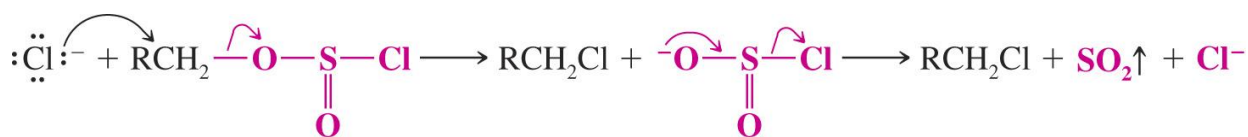


| **Reaction of thionyl chloride to give alkyl chlorides:**

Often an amine is added to react with HCl formed in the reaction

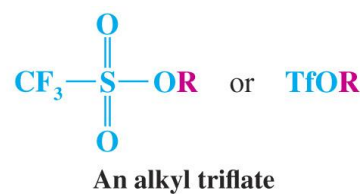
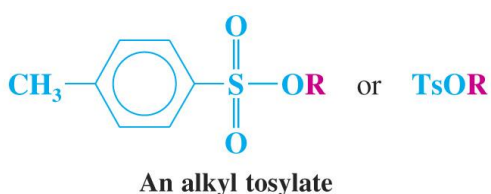
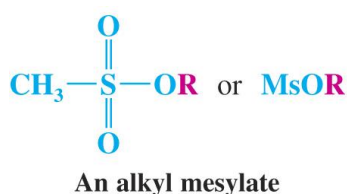




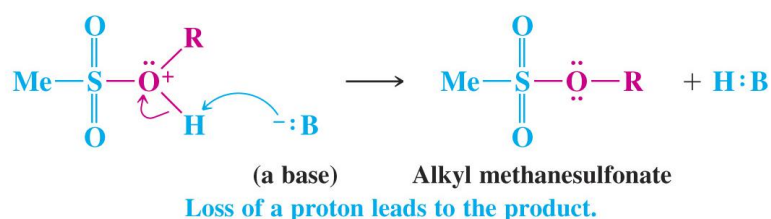
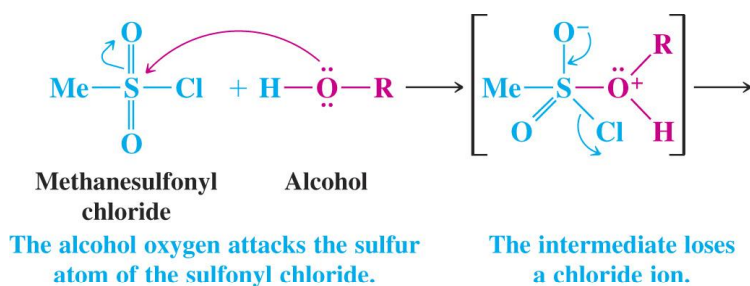


**Tosylates, Mesylates, and Triflates: Leaving Group Derivatives of Alcohols:**

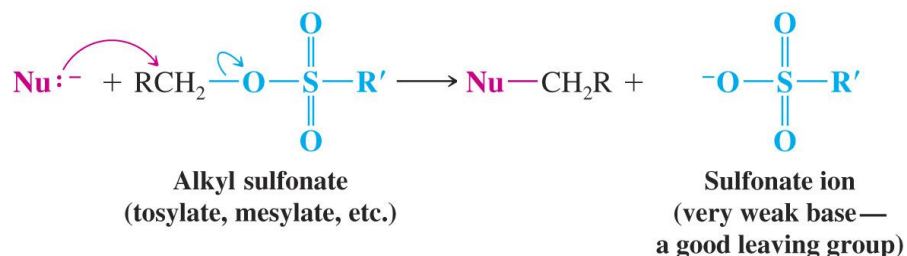
The OH group of an alcohol can be converted to a good leaving group by conversion to a sulfonate ester



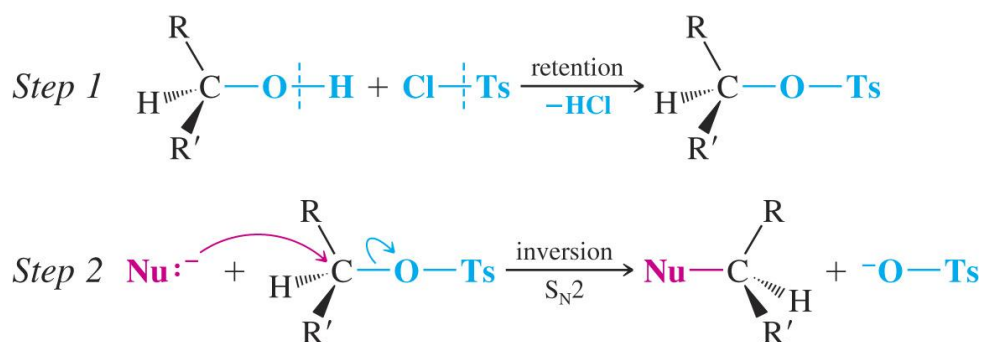
**Sulfonyl chlorides are used to convert alcohols to sulfonate esters. (Base is added to react with the HCl generated)**



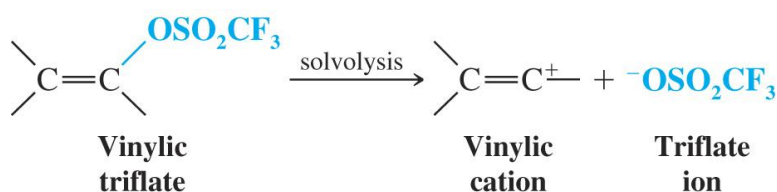
| **A sulfonate ion (a weak base) is an excellent leaving group**



| **If the alcohol hydroxyl group is at a stereogenic center then the overall reaction with the nucleophile proceeds with inversion of configuration**



| **Triflate anion is such a good leaving group that even vinyl triflates can undergo S<sub>N</sub>1 reaction**



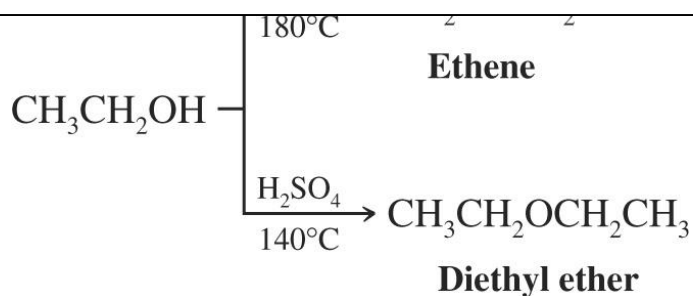
## † Synthesis of Ethers:

### a) Ethers by Intermolecular Dehydration of Alcohol

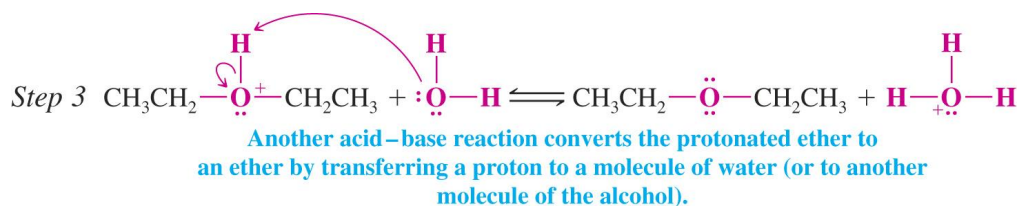
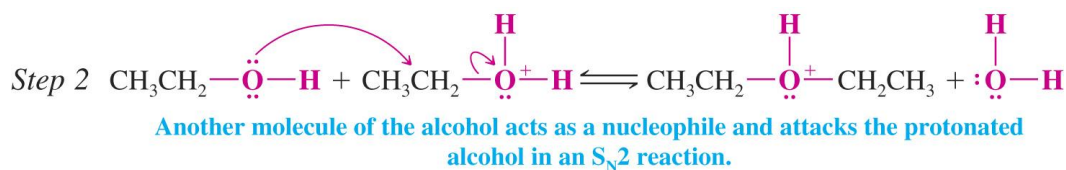
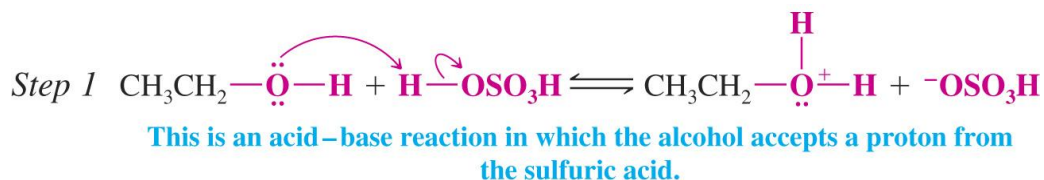
§ Primary alcohols can dehydrate to ethers

§ This reaction occurs at lower temperature.

§ This method generally does not work with 2° or 3° alcohols because elimination competes strongly

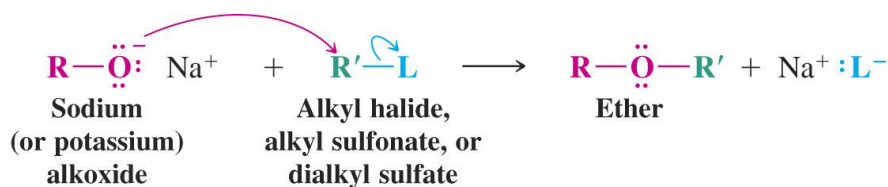


§ The mechanism is an S<sub>N</sub>2 reaction



## b) Williamson Ether Synthesis

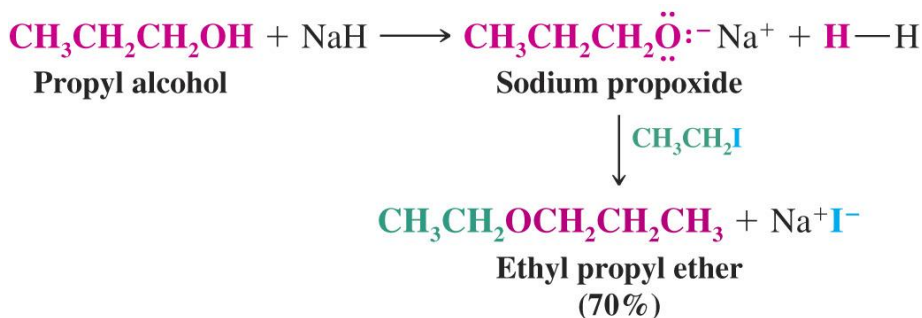
**This is a good route for synthesis of unsymmetrical ethers**



The alkoxide ion reacts with the substrate in an  $\text{S}_{\text{N}}2$  reaction, with the resulting formation of an ether. The substrate must be unhindered and bear a good leaving group. Typical substrates are  $1^\circ$  or  $2^\circ$  alkyl halides, alkyl sulfonates, and dialkyl sulfates, that is,



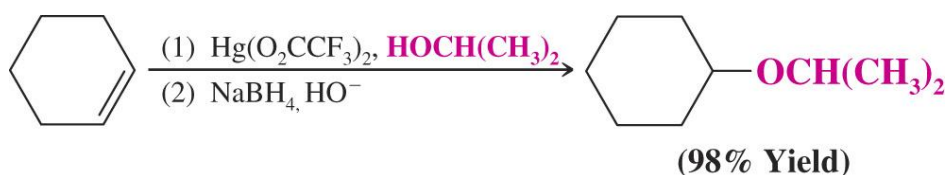
Example:



- The alkyl halide (or alkyl sulfonate) should be  $1^\circ$  to avoid  $\text{E}_2$  reaction
- Substitution is favored over elimination at lower temperatures

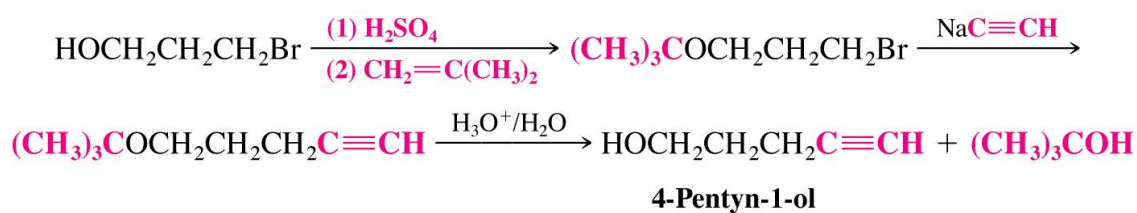
## c) Synthesis of Ethers by Alkoxymercuration-Demercuration

**Alcohol is used as nucleophile instead of water**



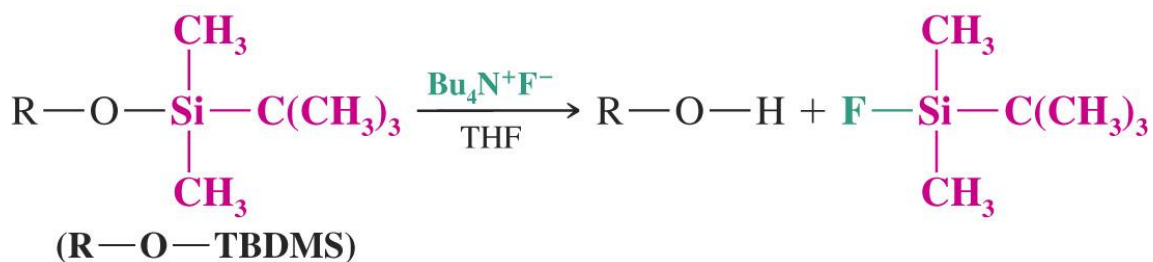
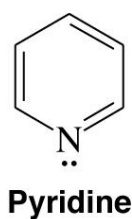
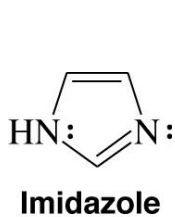
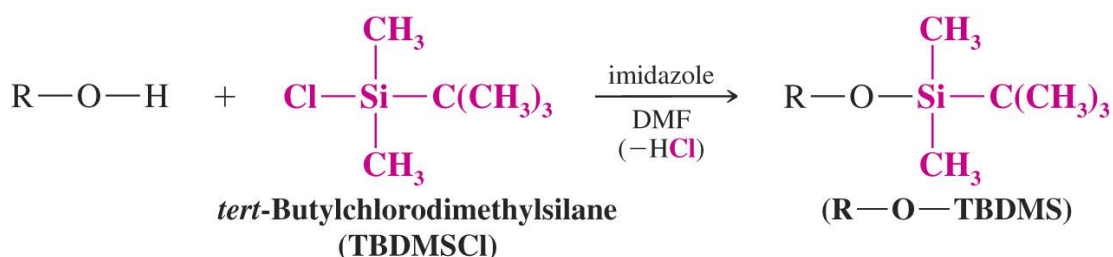
### d) *tert*-Butyl Ethers by Alkylation of Alcohols: Protecting Groups

This method is used to protect primary alcohols (The protecting group is removed using dilute acid)



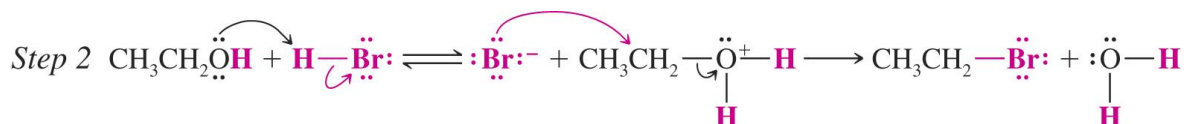
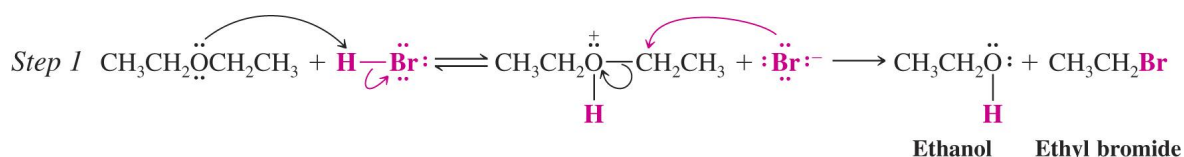
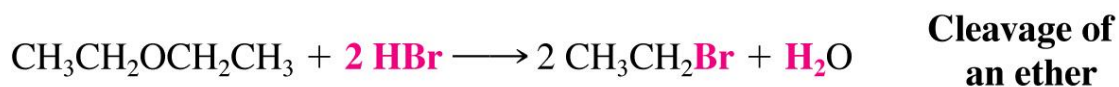
### e) Silyl Ether Protecting Groups

Silyl ethers are widely used protecting groups for alcohols



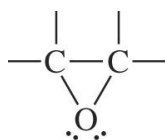
## † Reactions of Ethers:

- Acyclic ethers are generally unreactive, except for cleavage by very strong acids to form the corresponding alkyl halides
- Dialkyl ethers undergo  $S_N2$  reaction to form 2 equivalents of the alkyl bromide

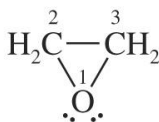


## † Epoxides:

- | Epoxides are three-membered ring cyclic ethers (These groups are also called oxiranes)



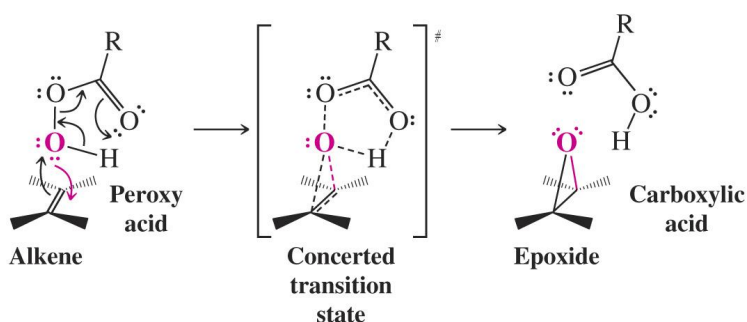
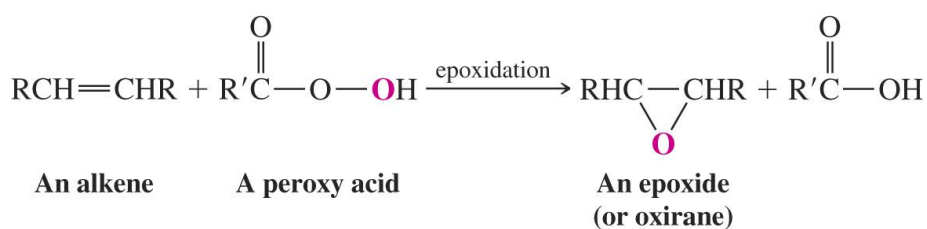
An epoxide



IUPAC name: oxirane  
Common name: ethylene oxide

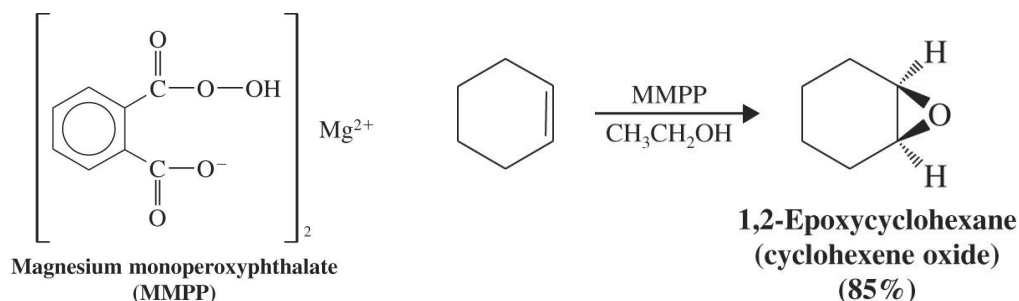
a) Epoxides are usually formed by reaction of alkenes with peroxy acids

This process is called epoxidation and involves syn addition of oxygen



The peroxy acid transfers an oxygen atom to the alkene in a cyclic, single-step mechanism. The result is the syn addition of the oxygen to the alkene, with the formation of an epoxide and a carboxylic acid.

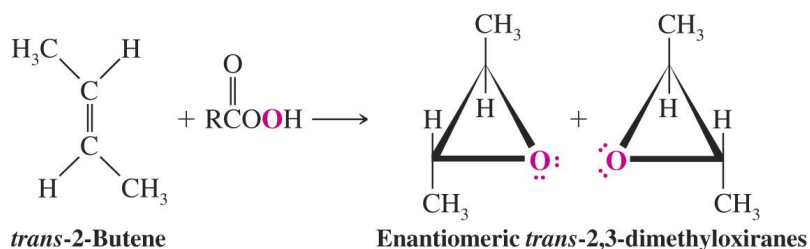
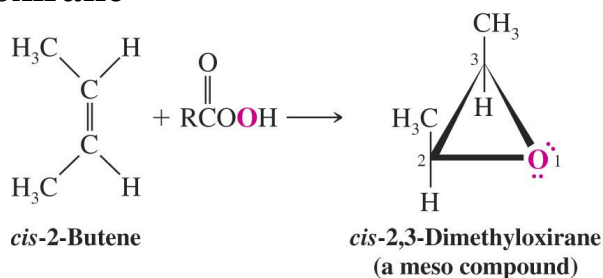
b) Magnesium monoperoxyphthalate (MMPP) is a common and safe peroxy acid for epoxidation



### c) Epoxidation is stereospecific

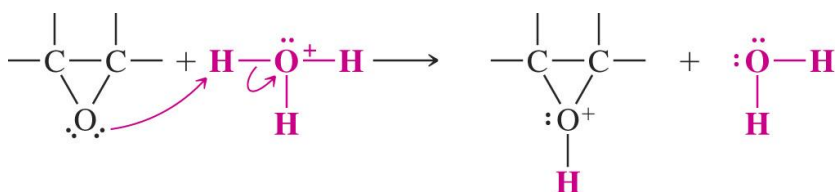
§ Epoxidation of *cis*-2-butene gives the meso *cis* oxirane

§ Epoxidation of *trans*-2-butene gives the racemic *trans* oxirane



### † Reaction of Epoxides:

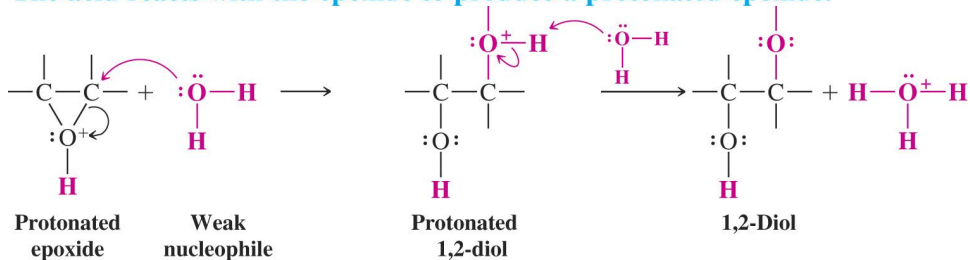
a) Acid-catalyzed hydrolysis of an epoxide leads to a 1,2-diol



Epoxide

Protonated epoxide

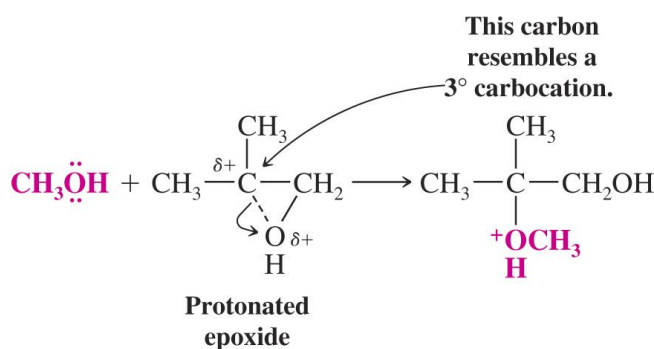
The acid reacts with the epoxide to produce a protonated epoxide.



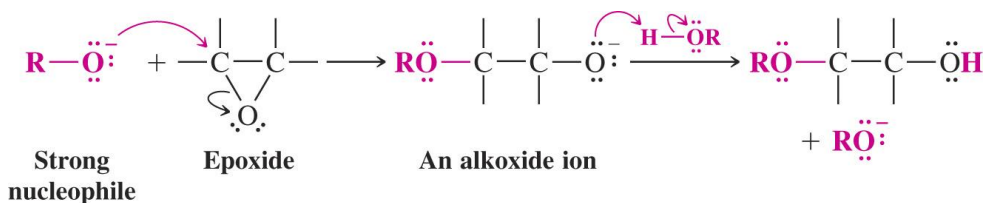
The protonated epoxide reacts with the weak nucleophile (water) to form a protonated 1,2-diol, which then transfers a proton to a molecule of water to form the 1,2-diol and a hydronium ion.



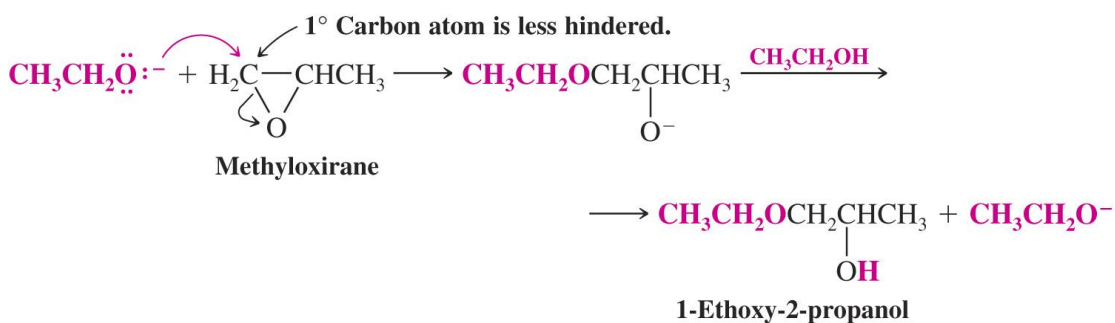
b) In unsymmetrical epoxides, the nucleophile attacks primarily at the most substituted carbon of the epoxide



c) Base-catalyzed reaction with strong nucleophiles (*e.g.* an alkoxide or hydroxide) occurs by an  $\text{S}_{\text{N}}2$  mechanism

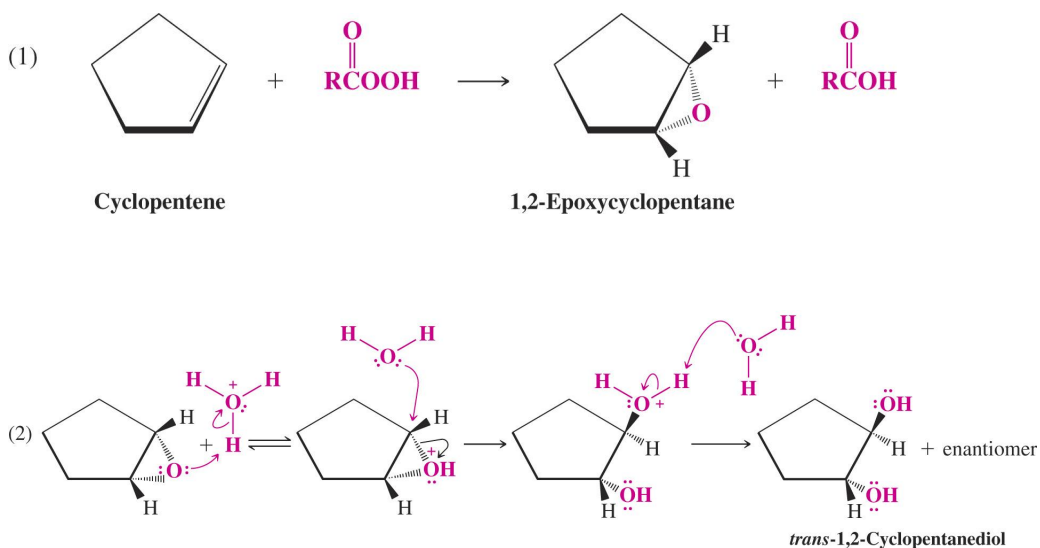


A strong nucleophile such as an alkoxide ion or a hydroxide ion is able to open the strained epoxide ring in a direct  $\text{S}_{\text{N}}2$  reaction.



# † Anti 1,2-Dihydroxylation of Alkenes via Epoxides:

a) Opening of the following epoxide with water under acid catalyzed conditions gives the trans diol.



b) Epoxide ring-opening is a stereospecific process

