

## Ch 18 Ethers and Epoxides

Ethers (R-O-R') are compounds with two organic groups attached to an  $sp^3$  oxygen. Epoxides are cyclic ethers where the  $sp^3$  O is a part of a 3-membered ring. Thiols (R-S-H') and thioethers (R-S-R') are the analogous sulfur compounds.

### General Characteristics of Ethers

- The substituents are typically alkyl, but can be alkenyl or aromatic as well.
- Ethers are unreactive in general, but can cause explosions.
- Ethers react with  $O_2$  in air to create ether peroxides (R-O-O-R').
- It is the ether peroxides that are explosive.
- Common small ethers also have low boiling points, just above room temperature.
- So, it is best to keep ethers cold, contained, and away from air.
- If these precautions are met, ethers are very useful solvents.

### Naming Ethers

1. Name ethers containing only simple organic groups by identifying both groups alphabetically, then following with ether.  
For example, *t*-butyl methyl ether is a common additive in gasoline.
2. If both groups are identical, precede their name (singular) with di, such as diethyl ether, a common laboratory solvent.
3. If one group is large or complex enough to be a parent, the name the smaller group, along with its O, as an alkoxy group.  
For example, 2-(3,4,5-trimethoxyphenyl)ethanamine is the systematic name for mescaline.
4. If there are two identical alkoxy groups on one parent chain, precede the groups' name (singular) with di, and include their location as well.  
For example, 1,2-dimethoxyethane.

### Properties of Ethers

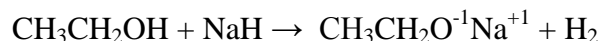
- Ethers (R-O-R') are structurally analogous to water (H-O-H).
- The ether O is  $sp^3$  and has tetrahedral geometry.
- The two C-O bonds are polar due to the larger electronegativity of O, and the ether molecules have small dipole moments.  
This increases boiling points somewhat in comparison to analogous alkanes.
- The steric hindrance due to the organic groups makes the O's two lone pairs less available, and this tends to decrease intermolecular bonding somewhat.

### Industrial Preparation

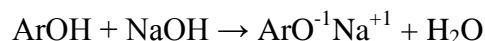
- Small symmetrical ethers are prepared from the alcohol with  $H_2SO_4$ .
- The first step is protonation of the alcohol O, which creates a good stable leaving group for an  $S_N2$  reaction, where a second alcohol molecule is the entering Nu.
- This only works with small  $1^\circ$  alcohols. Why  $1^\circ$ ?
- What kind of reaction would be favored if  $2^\circ$  and  $3^\circ$  alcohols were used with  $H_2SO_4$ ?

## Williamson Ether Synthesis

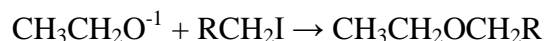
- This essentially creates an ether through an S<sub>N</sub>2 reaction.
- An alkoxide anion (R-O<sup>-1</sup>) is the entering Nu, which reacts with a 1° alkyl halide, such as CH<sub>3</sub>I.
- The alkoxide is generally prepared by deprotonating an alcohol using very strong bases, such as Na and NaH, generally with THF (tetrahydrofuran) as the solvent.



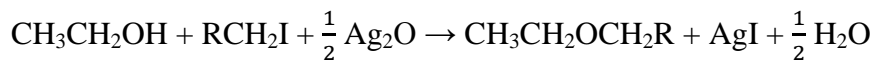
- Phenoxides are more acidic and can be deprotonated with NaOH.



- The alkoxide will then react by S<sub>N</sub>2 with a 1° alkyl halide.

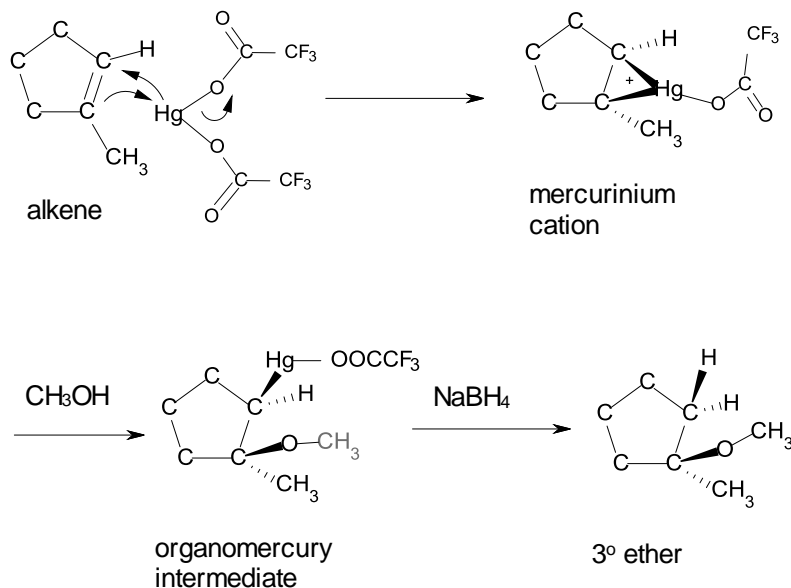


- Considering that alkoxides are strongly basic, what kind of reaction would be favored if they are used with 2° and 3° alkyl halides?
- This reaction can also be done in one step using Ag<sub>2</sub>O, so that the alkoxide does not need to be created first.



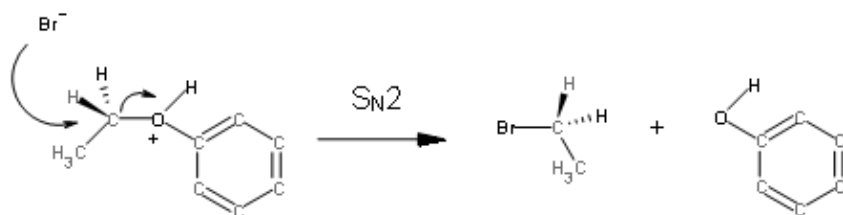
## Alkoxymercuration of Alkenes

- This reaction is similar to oxymercuration of alkenes with Hg(OAc)<sub>2</sub>, which creates 2° and 3° alcohols by hydration of alkenes.
- The major difference with alkoxymercuration is that it adds an alcohol (R-O-H), rather than water (H-O-H), to the alkene.
- The first step to add mercury (II) trifluoroacetate, Hg(OOCCF<sub>3</sub>)<sub>2</sub>, along with the alcohol, to the alkene to react both the alkoxy group and the Hg across the double bond.
- Then, the -Hg(OOCCF<sub>3</sub>) is removed from the less substituted C by reduction in the second step with NaBH<sub>4</sub>.
- The product is Markovnikov, that is, the more substituted ether predominates.
- The alcohol can be 1°, 2°, or 3°, but ditertiary ethers do not form due to steric hindrance.

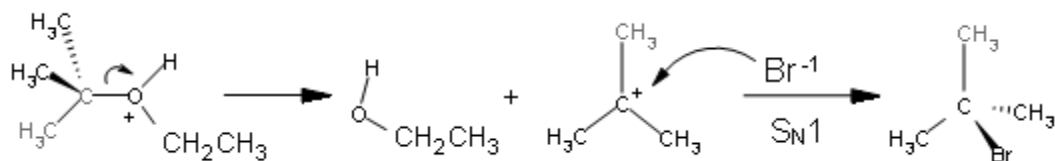


## Acidic Cleavage of Ethers

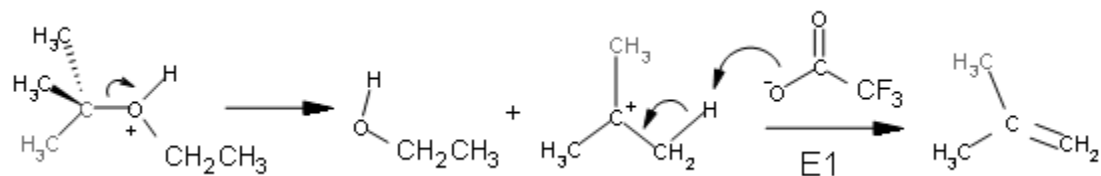
- This reaction occurs by refluxing ethers with HBr or HI (not HCl).
- It is essentially the reverse of the Williamson ether synthesis.
- The first step is protonation, where the acid donates  $H^{+1}$  to ether O.
- This creates the leaving group (ROH).
- The halide ( $Br^{-1}$  or  $I^{-1}$ ) is the entering Nu in a substitution reaction.
- If there is no  $3^{\circ}$  alkyl group present, the reaction is  $S_N2$ , where the alcohol with lesser-substituted ( $1^{\circ}$ ) C connected to the O will be the substrate that acquires the halogen.



- If, however, there is a  $3^{\circ}$  alkyl group present, the reaction is  $S_N1$ . The  $3^{\circ}$  C will become a carbocation, which will acquire the  $Br^{-1}$  or  $I^{-1}$ .



- If the acid used with the  $3^{\circ}$  ether has a sterically-hindered (non-Nu) conjugate base, such as the trifluoroacetate anion (the conjugate base of  $CF_3COOH$ ), then E1 will predominate.



- Except for epoxides, ethers are not cleaved by bases.

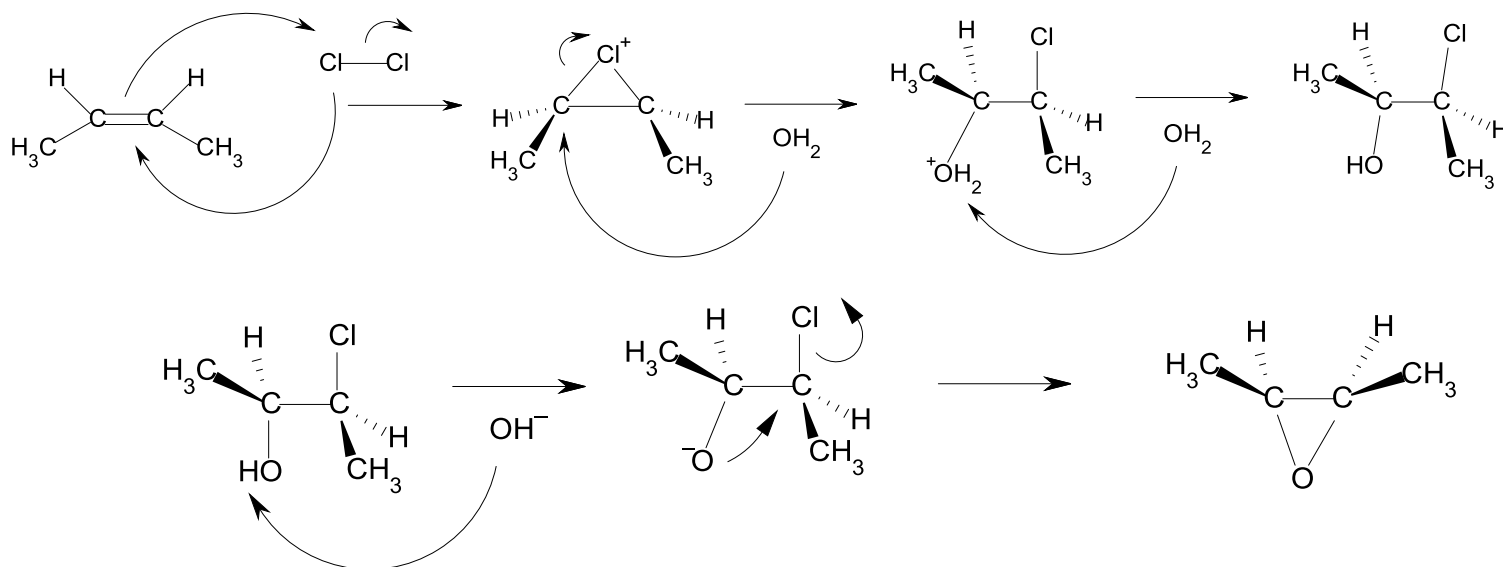
## Epoxides

- Generally, cyclic ethers behave like acyclic ethers, except for epoxides.
- The 3-membered ring containing the O is strained, which makes epoxides reactive.
- One way to create epoxides is from a halohydrin by an internal Williamson reaction.

Halohydrin are created from alkenes using  $\text{Cl}_2$  and  $\text{H}_2\text{O}$ .

The halohydrin is treated with aqueous  $\text{NaOH}$ , which deprotonates the halohydrin's O.

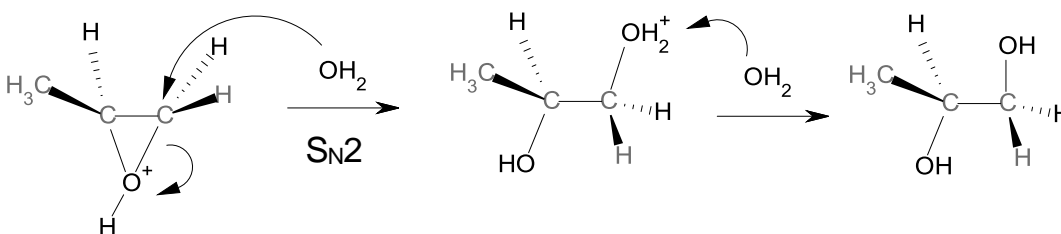
The anionic  $\text{O}^-$  is a Nu, which replaced the leaving  $\text{Cl}^-$  on the adjacent C.



- Epoxides can also be created by oxidizing an alkene with a peroxyacid ( $\text{RCOOOH}$ ).
- Epoxides can be cleaved (opening the ring) by acid or base. The result is typically a diol or halohydrin.

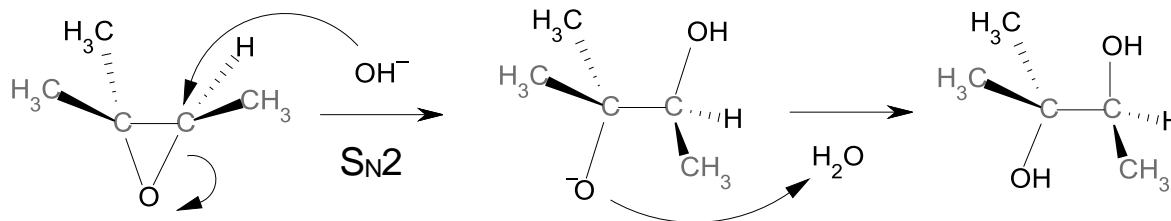
## Acid-Catalyzed Ring-Opening

- The first step is protonation of the epoxide O with the acid.
- If the acid is aqueous (aq) and no other Nu is present, then  $\text{H}_2\text{O}$  will act as the Nu and it will bond to one of the two epoxide C's. The OH simultaneously detaches from the same C, but remains attached to the other C.
- $\text{H}^+$  is removed from the added  $\text{H}_2\text{O}$  by another  $\text{H}_2\text{O}$  molecule to create a 1,2-diol.
- If an anhydrous hydrogen halide ( $\text{HCl}$ ,  $\text{HBr}$ , or  $\text{HI}$ ) is used (in ether), the halide is the Nu. The result is a halohydrin.
- If there is no  $3^\circ$  alkyl group present, the reaction is  $\text{S}_{\text{N}}2$ , where the lesser-substituted ( $1^\circ$ ) C will be the substrate that acquires the halide. The more-substituted C will acquire the OH.
- If, however, there is a  $3^\circ$  alkyl group present, the reaction is more like  $\text{S}_{\text{N}}1$ . The  $3^\circ$  C will become partially positive ( $\delta^+$ ), and will acquire the Nu. The lesser-substituted C will acquire the OH.



### Base-Catalyzed Ring-Opening

- The reaction of an epoxide with NaOH is always  $S_N2$ , where the  $\text{OH}^-$  is the entering Nu, which attacks the lesser-substituted C.
- The epoxide O is the LG, and it is left as an anion (negative).
- Typically,  $\text{H}_2\text{O}$  will add  $\text{H}^+$  to the anionic  $\text{O}^-$ , converting it to a hydroxyl (OH). The result is a 1,2-diol.
- A Grignard reagent ( $\text{RMgBr}$ ) can be used so that the entering Nu is a carbanion ( $\text{R}^-$ ). The result is a larger alcohol molecule where the more-substituted C will acquire the OH, and the lesser-substituted C will acquire the alkyl group from the Grignard reagent.



### Crown Ethers

- Crown ethers are cyclic multi-oxygen ethers.
- They are named as x-crown-y, where x is the total number of ring atoms, and y is the number of oxygen atoms in the ring.
- For instance, 18-crown-6 ether has an 18-membered ring containing 6 O's. How many C's are in the ring?
- The large number of lone pairs in the ring makes crown ethers able to solvate metal cations by containing them with the ring.
- As a result,  $\text{KMnO}_4$  will dissolve in toluene with 18-crown-6 present. With the  $\text{K}^+$  stuck inside the crown ether's ring, the  $\text{MnO}_4^-$  is left free. This allows the  $\text{MnO}_4^-$  to be used for oxidizing (or cleaving) alkenes.