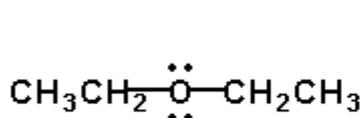
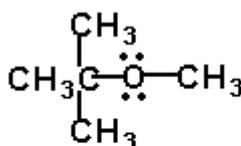


Ethers

Ethers like alcohols are organic derivatives of water, but lack the labile -OH group. As a result, ethers, except for epoxides, are usually not very reactive and are often used as solvents for organic reactions. The word ether is used for both the functional group and diethyl ether, the most familiar member of this family. Ether usually brings to mind the anesthetic, but the flammability and side-effects have led to the use of other compounds for surgery. Methyl t-butyl ether is used as an octane booster in gasoline. Dioxin and tetrahydrofuran are cyclic ethers commonly used as solvents in the laboratory. The environmental pollutant dioxin is an ether.



diethyl ether

methyl t-butyl ether
(MTBE)

dioxin

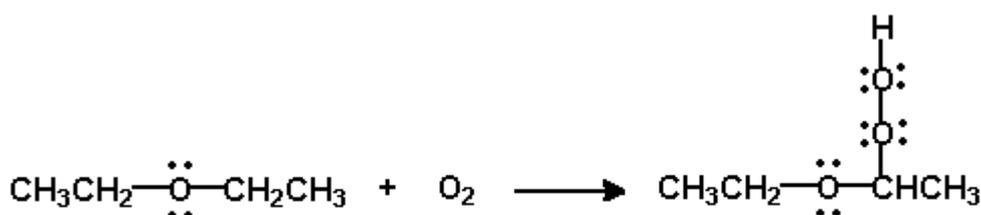


tetrahydrofuran

Chemical Properties of Ethers

Ethers make good solvents in the laboratory because they are relatively resistant to oxidizing agents and acids and bases. The lone pairs of electrons, make them good Lewis bases which complex with metal ions and helps solubilize important reagents like Grignard reagents and lithium aluminum hydride. An important class of ethers are the crown ethers which complex with sodium and potassium ions and can permit polar inorganic salts such as potassium permanganate to dissolve in nonpolar organic solvents like benzene producing "purple benzene".

One disadvantage of ethers is their flammability and ability to form explosive peroxides in the presence of oxygen. This process can be prevented by adding stabilizers to ethers or by excluding oxygen. Chemists should keep bottles of ether tightly sealed, date each container when it is opened, and dispose within a few weeks of opening. Special care must be taken when distilling or evaporating ethers to make sure they are peroxide free.



diethyl ether

diethyl ether hydroperoxide

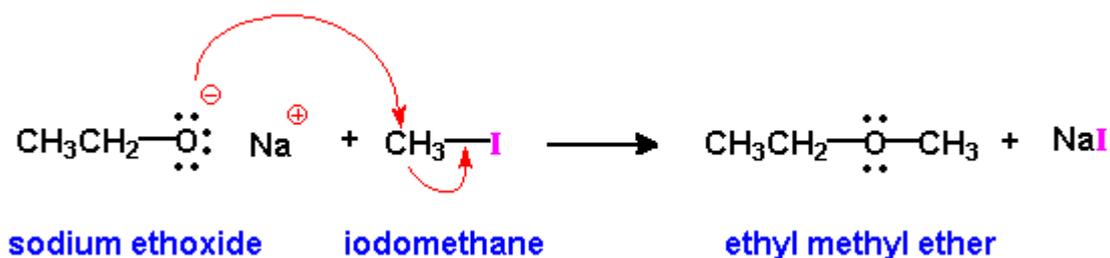
Synthesis of Ethers

Williamson Ether Synthesis

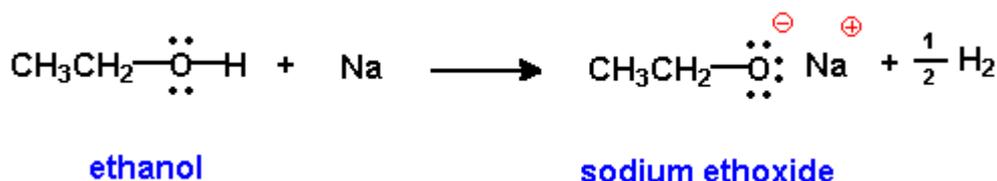
The Williamson ether synthesis is the most general way of preparing ethers. This reaction involves two steps:

- formation of an alkoxide anion
- S_N2 reaction of the alkoxide anion with an unhindered alkyl halide (usually primary)

For example, ethyl methyl ether can be prepared by the nucleophilic substitution of iodomethane with sodium ethoxide.

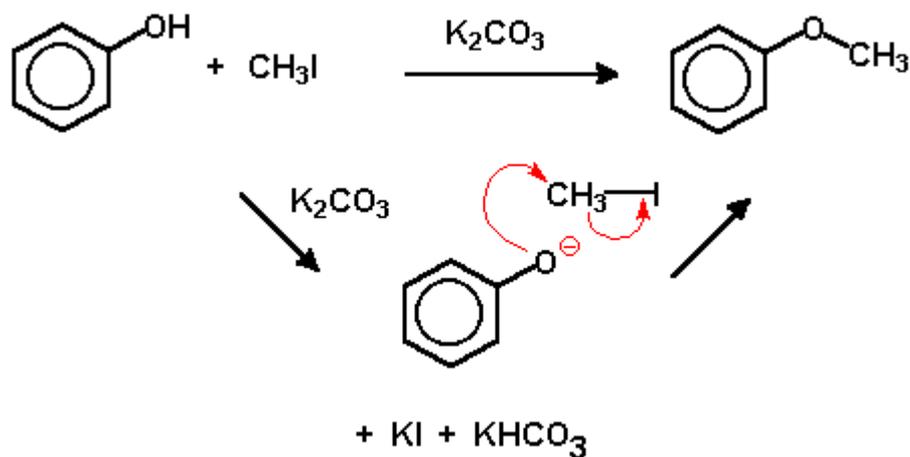


Sodium ethoxide can be prepared by the reaction of sodium metal with ethanol.



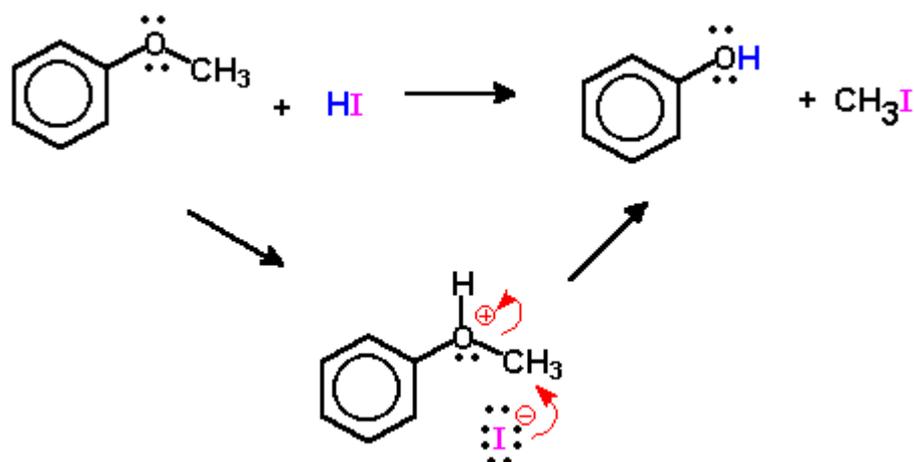
With secondary halides, E2 elimination competes. The reaction fails for tertiary halides.

Phenols can be used as the alcohol in the Williamson ether synthesis. The higher acidity of phenols allows the phenoxide anion to be formed directly in the reaction mixture by mild bases such as potassium carbonate.



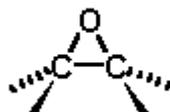
Cleavage of Ethers

Ethers can be cleaved by HI, HBr, and HCl. This reaction involves protonation of the ether oxygen followed by S_N2 displacement at the alkyl group as shown for the cleavage of methyl phenyl ether.



Epoxidation

Epoxides are cyclic ethers in which the oxygen atom is part of a strained three-membered ring called an oxirane.

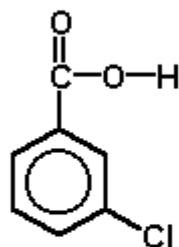


As predicted from the strain energy of small rings, epoxides are usually very reactive species and provide a rich variety of chemical reactivity.

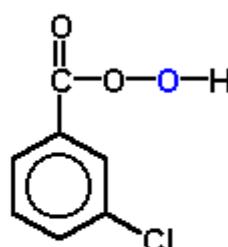
Epoxide may be prepared from alkenes by several routes:

- **direct oxidation of the double bond**

Organic peracids (peroxyacids) convert alkenes to epoxides. Peracids are carboxylic acids with an extra oxygen atom inserted between the carbonyl group and the OH group. A very common reagent is m-chloroperbenzoic acid which is available commercially. Many other peracids are unstable and must be prepared as needed.

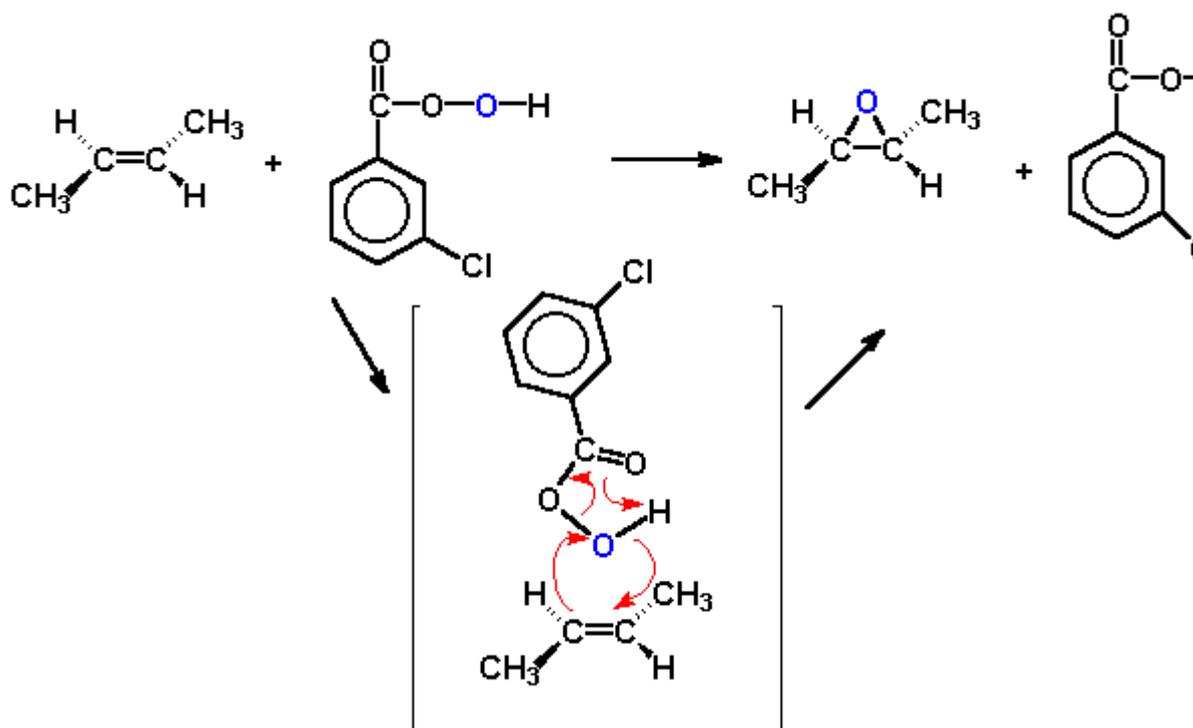


m-chlorobenzoic acid

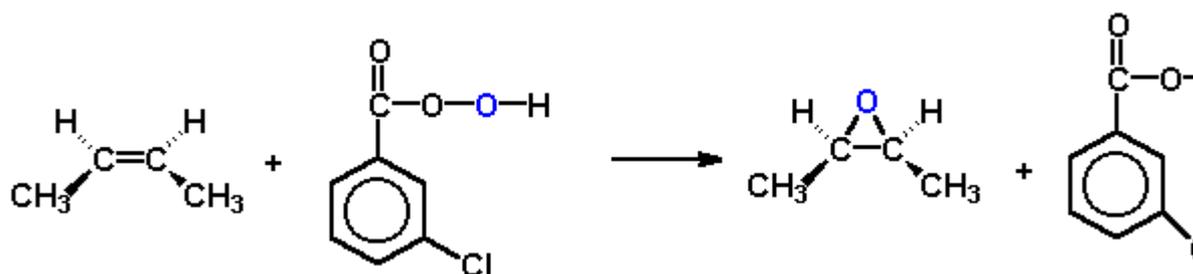


m-chloroperbenzoic acid

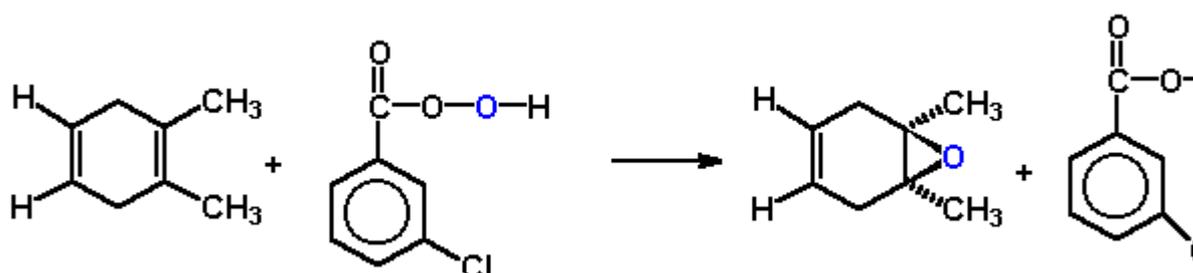
The peracid transfers an oxygen atom to the alkene in a single step so the stereochemistry of the double bond is retained. Thus, *trans*-2-butene gives *trans*-1,2-dimethyloxirane.



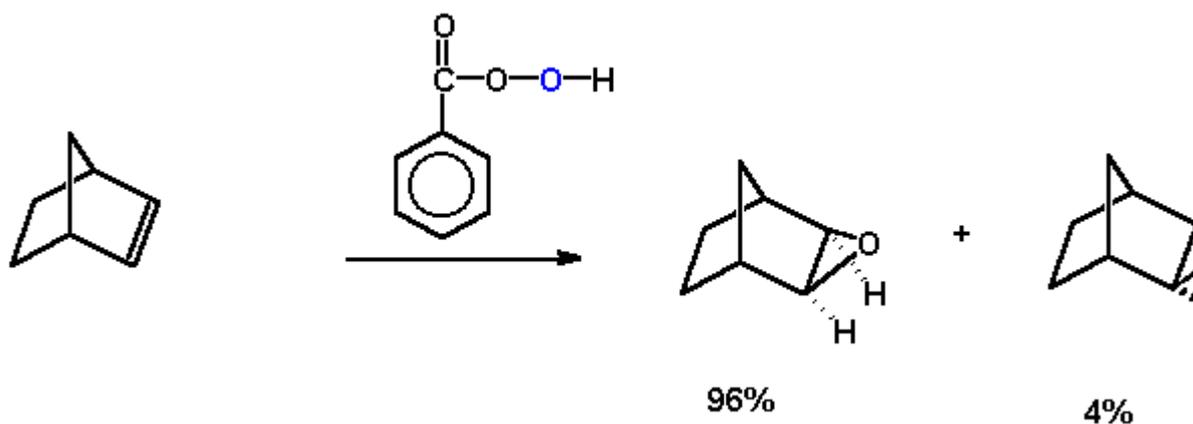
Correspondingly, peracid epoxidation of *cis*-2-butene gives *cis*-1,2-dimethyloxirane.



The mechanism of peracid epoxidation involves nucleophilic attack of the pi-electrons from the double bond. As predicted, the rate of epoxidation increases with increasing alkyl substitution. For example, 1,2-dimethyl-1,4-cyclohexadiene reacts at the tetrasubstituted instead of the disubstituted double bond.

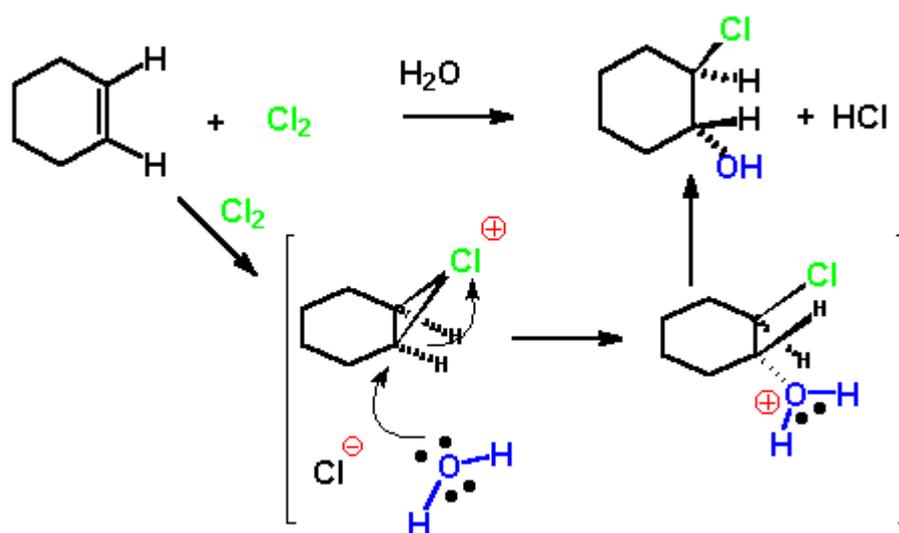


With cyclic olefins the epoxide oxygen is usually added from the least hindered side of the double bond. For example, epoxidation of norbornene gives 96% of the exo diol.



- nucleophilic displacement of halohydrins

Halohydrins are prepared by the addition of aqueous hypochlorous acid (HOCl) or hypobromous acid (HOBr) to alkenes. Conveniently this is done by using aqueous solutions of the halogen. This electrophilic addition proceeds by formation of the intermediate halonium ion as we have seen in the case of direct addition of halogens to alkenes. In the presence of water, this reactive intermediate undergoes nucleophilic addition of water by an $\text{S}_{\text{N}}2$ mechanism giving an anti-orientation of the halide and hydroxyl group.



The reaction of halohydrins with base produces epoxides by an $\text{S}_{\text{N}}2$ mechanism. Base forms the hydroxide anion and the trans-arrangement of nucleophile and leaving group favors the $\text{S}_{\text{N}}2$ process.

