

## Chapter 18: Ethers & Epoxides

### *Learning Objective & Key Concepts*

1. Nomenclature of Ethers
2. Williamson Ether synthesis
3. Acid-catalyzed cleavage of ethers
4. Reactivity of epoxide rings
5. Laboratory preparation of epoxides
6. Acid-catalyzed and base catalyzed epoxide ring opening

**Keywords:** *Alkoxymercuration, Claisen Rearrangement, Ether.*

### *Tutorial Questions*

*These are a subset of EOC questions, hand these in for extra credit, but I strongly advise you to complete the full set of EOC questions as well as in-text questions too.*

18.24      18.25    18.27    18.29 a, c & e    18.32                  18.49

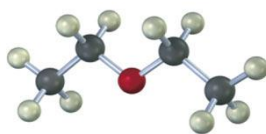
### *In-Text Questions*

18.1                  18.3                  18.7                  18.8                  18.10  
18.11                18.14

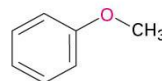
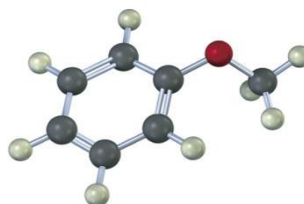
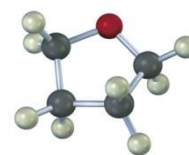
### *End-of-Chapter Problems*

- 18.19                  18.21 (don't worry about major and minor product)  
18.23                  18.24 (skip sulfur containing ones)  
18.25                  18.27  
18.29 (very good question, must try)  
18.30  
18.31 18.32 (Challenging, good practice on mechanisms)  
18.34 (make models if this helps)  
18.41  
18.49 (challenging, but just follow section on Claisen rearrangement)  
18.50 (Seems difficult but it's more a question on stereochemistry than epoxide reaction, once you've determined product structure it's straightforward).  
18.57 parts C and D only.

Like alcohols and phenols, **Ethers** are also organic derivatives of water. Structurally, ethers have a single oxygen atom bonded to two carbons. The carbons may be alkyl, vinyl or aryl. The structure may be cyclic or acyclic. **Epoxides** are 3-membered ether rings (two carbon atoms and one oxygen). Because of extra reactivity due to small ring strain, epoxides have very different chemical properties compared to ethers. Epoxides are discussed starting in section 18.5



Diethyl ether

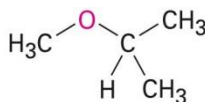
Anisole  
(methyl phenyl ether)

Tetrahydrofuran

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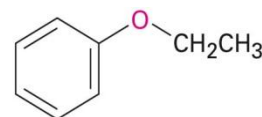
## 18.1 Names and Properties of Ethers

Simple ethers are named as “*alkyl alkyl ether*”, for example:



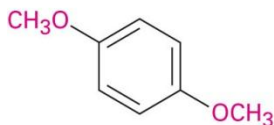
Isopropyl methyl ether

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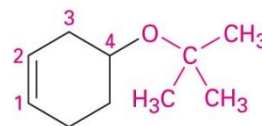


Ethyl phenyl ether

If functional groups are present, the ether link is considered an alkoxy substituent:

*p*-Dimethoxybenzene

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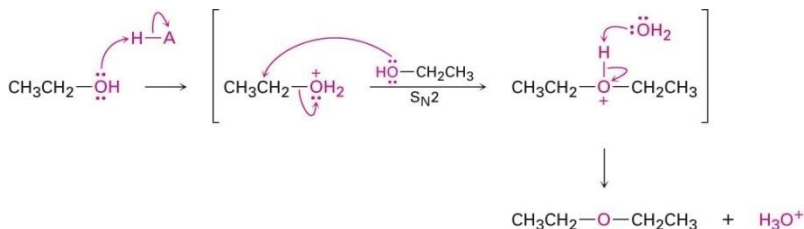
4-*tert*-Butoxy-1-cyclohexene

Ethers are slightly polar, they have slightly higher boiling point than corresponding alkanes. They are relatively stable and unreactive and the simple ones are commonly used as organic solvents (see examples shown earlier: diethyl ether, tetrahydrofuran).

❖ Try problem 18.1

## 18.2 Synthesis of Ethers

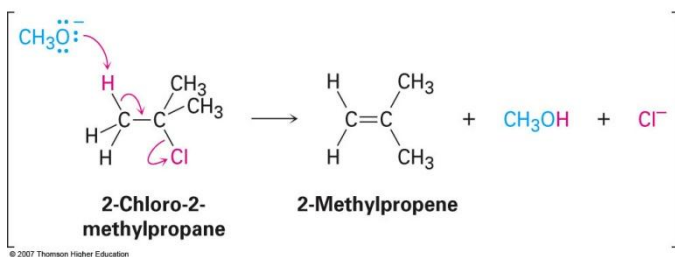
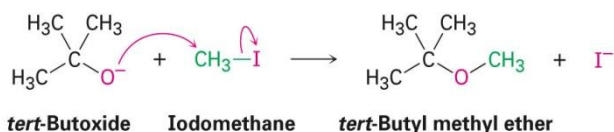
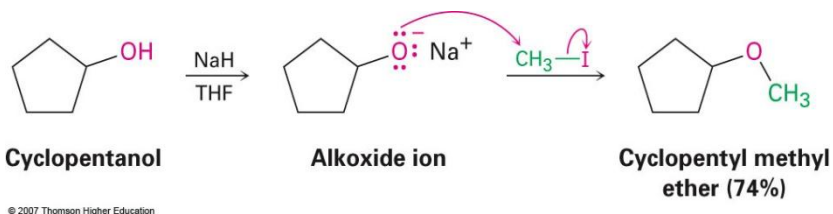
Industrially, simple symmetrical ethers are prepared by acid-catalyzed dehydration of alcohol: one protonated alcohol undergoes SN2 reaction by a second alcohol acting as nucleophile. (Note: do not confuse this with an elimination reaction of alcohol to give alkene - which is also a dehydration reaction!)



This ether production method is limited to primary alcohols – secondary and tertiary alcohols would undergo E1 elimination as noted above.

## The Williamson Ether Synthesis

For asymmetrical ether, the most useful method is the Williamson ether synthesis: primary halide or tosylate undergoes SN2 reaction by an alkoxide ion.

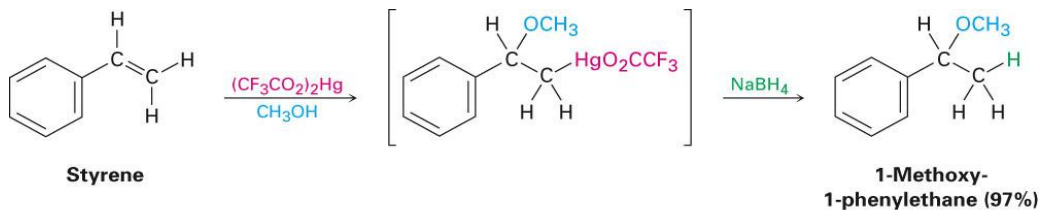


The Williamson ether synthesis has all the limitations of SN2 reactions – ie: competition from elimination and rearrangement. This mostly means choosing the halide/tosylate and alkoxide pair to avoid a secondary or tertiary halide/tosylate substrate. For example, in the synthesis of *tert*-butyl methyl ether (TMBE), *tert*-butoxide and iodomethane is preferable to methoxide and *tert*-butyl halide which would give elimination instead.

❖ Try problem 18.3

## Alkoxymercuration of Alkenes

This reaction is an extension of the reaction we saw in section 7.4: an alkene is treated with an alcohol in the



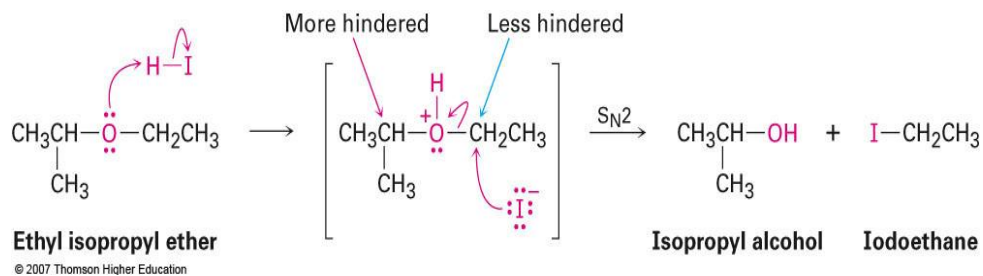
presence of mercuric acetate or mercuric trifluoroacetate  $(\text{CF}_3\text{CO}_2)_2\text{Hg}$  and then demercurated using sodium borohydride ( $\text{NaBH}_4$ ) to give an ether. This reaction follows Markovnikov's rule (*which means hydrogen adds to alkene carbon already carrying more hydrogen atom*). This reaction is highly versatile and can be used for making primary, secondary and tertiary alcohols. Dertiary alcohols cannot be readily formed by this method because of steric hindrance.

❖ Go through worked example 18.1

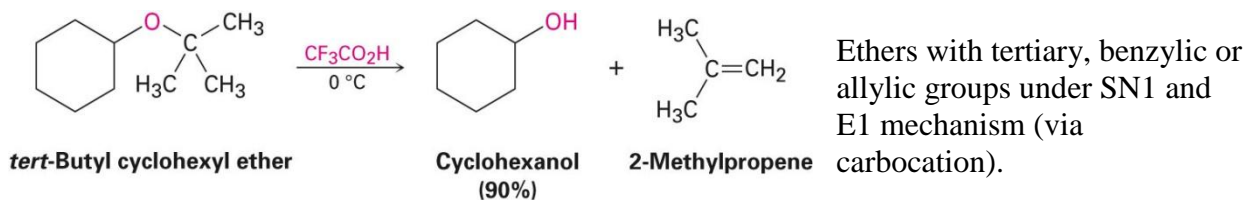
❖ Try problem 18.5

## 18.3 Reactions of Ethers: Acidic Cleavage

As noted before, ethers are unreactive and inert to dilute acids and bases as well as most nucleophiles.



Strong acids however, can cause ethers to react. Strong acid of choice may be HI or HBr but HCl not usually strong enough. See example: the mechanism is  $\text{S}_{\text{N}}2$  – favored by primary and secondary alkyl groups. Note nucleophile (iodide ion) attacks least hindered alkyl group.



Ethers with tertiary, benzylic or allylic groups under  $\text{S}_{\text{N}}1$  and  $\text{E}1$  mechanism (via carbocation).

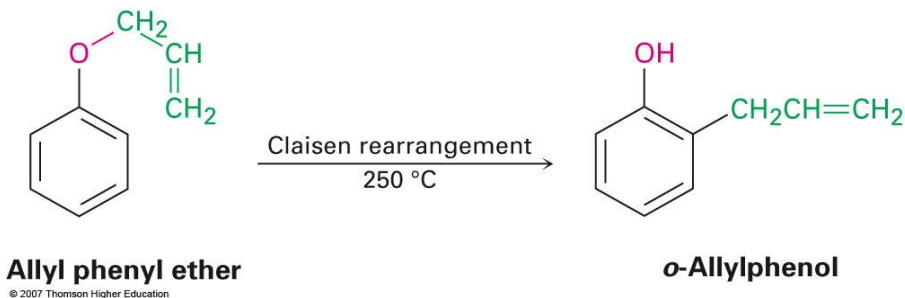
❖ Go through worked example 18.2

❖ Try problem 18.7

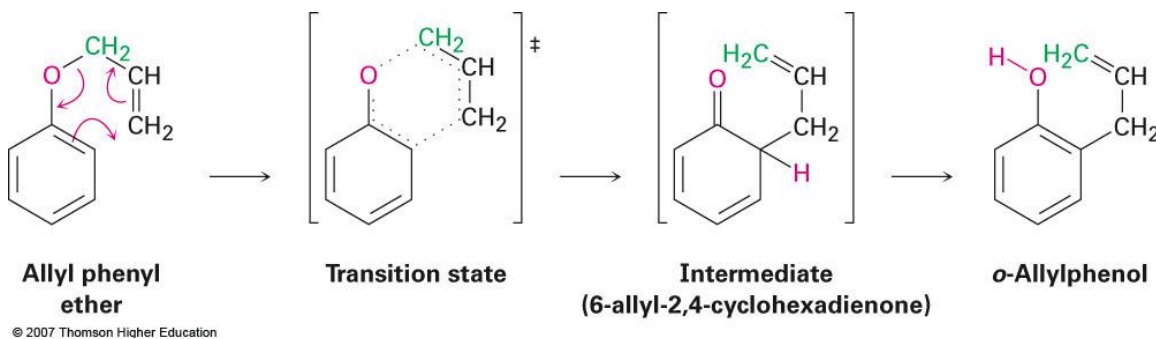
❖ Try problem 18.8

## 18.4 Reactions of Ethers: Claisen Rearrangement

When heated, allyl aryl ethers undergo the **Claisen rearrangement** reaction to give an allylphenol. This reaction is the basis for o-alkylation of phenols.



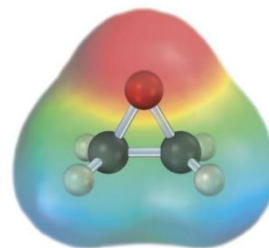
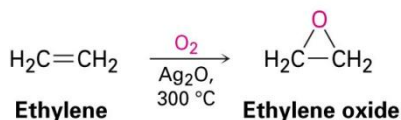
The reaction takes place through a **pericyclic** mechanism: a concerted organization of bonding electrons through a 6-membered cyclic intermediate.



❖ Try problem 18.10

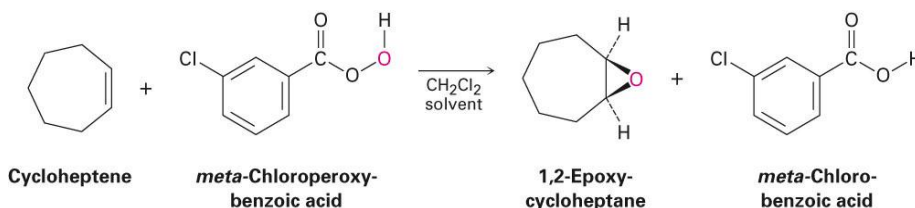
## 18.5 Cyclic Ethers: Epoxides

Three-membered ring cyclic ethers are called epoxides or oxiranes. They are usually reactive due to ring strain. The simplest oxirane is called ethylene oxide (note this is a non-systematic name; it is NOT an alkene). Industrially, this is made by air oxidation of ethene using a silver catalyst. The IUPAC name for ethylene oxide is 1,2-epoxyethane.



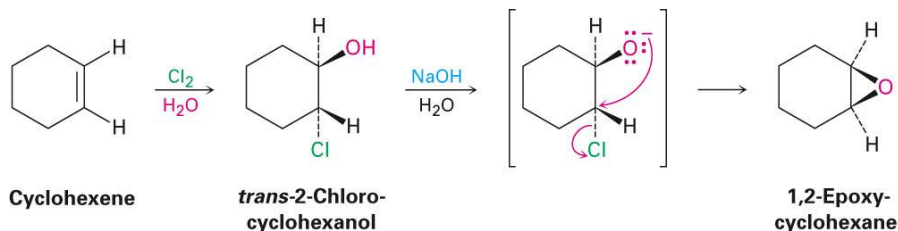
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For laboratory preparations: we've already seen  
a) the reaction between an alkene and peroxyacid to form epoxides and



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b) formation of an epoxide from a vicinal halohydrin (which we can now refer to as an intramolecular Williamson synthesis).



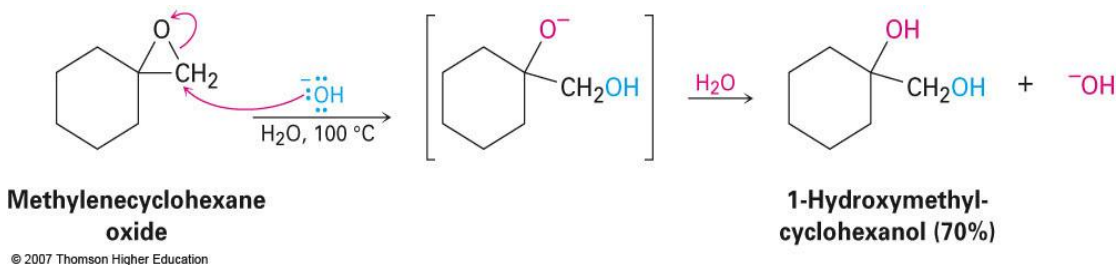
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❖ Try problem 18.11 (hint: stereochemistry!)

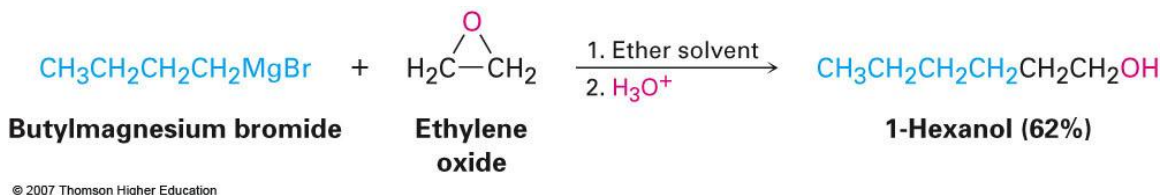


### Base-Catalyzed Epoxide Opening

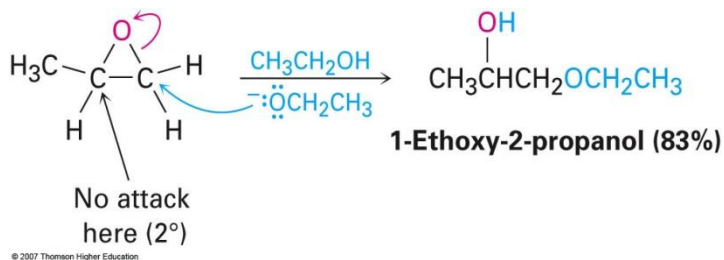
Epoxides can be cleaved by base as well as by acids. In aq. base, the product is also a vicinal diol.



The most common – and synthetically useful – example is the reaction between an epoxide and a Grignard reagent.



Unlike acid-catalyzed epoxide opening, the base-catalyzed version has more predictable stereochemical outcome: the reaction is typically  $\text{S}_{\text{N}}2$ , so steric hindrance is more important than carbocation stability and nucleophilic attack is at the less-hindered epoxide carbon.



❖ Try problem 18.14

## 18.5 Crown Ethers

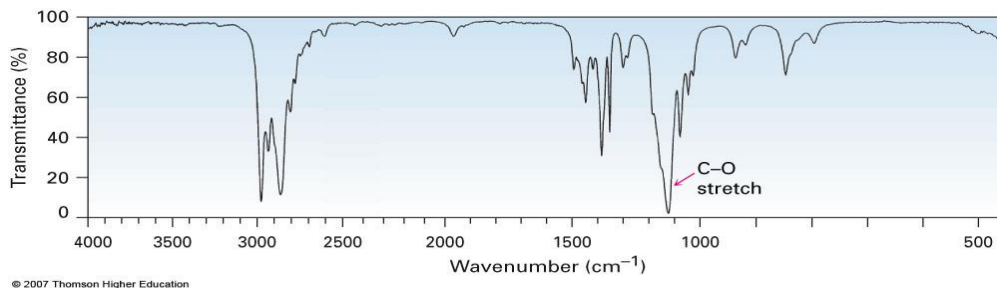
*Fascinating, but beyond scope of chem232. Strongly recommend you read this section for interest. This may be an extra-credit self-study topic too.*



## 18.9 Spectroscopy of Ethers and Epoxides

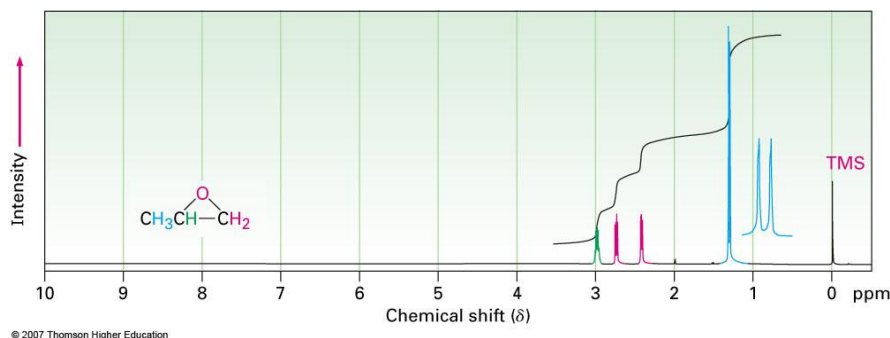
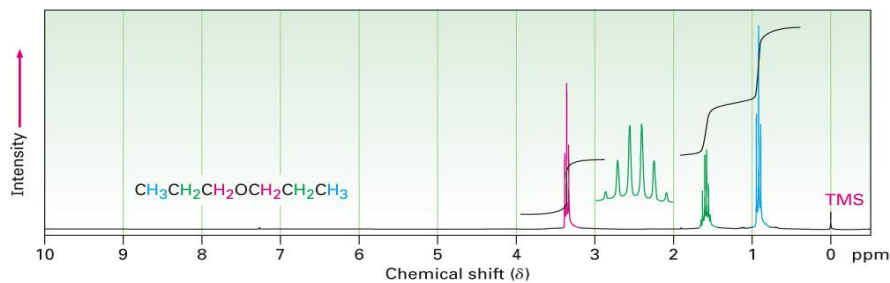
### Infrared Spectroscopy

The ether bond does not give characteristic stretches outside of fingerprint region, so IR not very useful in confirming present of C-O-C bond.



### Nuclear Magnetic Resonance Spectroscopy

$^1\text{H-NMR}$  – typically 3.4 to 4.5  $\delta$  for ethers but 2.5 to 3.5  $\delta$  for epoxides



$^{13}\text{C-NMR}$  – typically 50 to 80  $\delta$  for both ethers and epoxides

