18.0 Introduction

18.1 Names and Properties of Ethers

18.1 Exercises

Questions

Q18.1.1

Give the IUPAC name for the following chemical structures.

(a)

(b)

(c)

O

SH
Q18.1.2

Draw structures of the following.

(a) 3-isopropoxypentane  (b) 1-(4-chlorophenoxy)-3-methylbenzene (c) 2-(tert-butoxy)-2-methylpropane

Q18.1.3

Name the following ethers and sulfides.

(a)

(b)

(c)

(d)

(e)
Solutions

S18.1.1

(a) oxydicyclopentane (b) 2-phenyloxirane (c) 1-cyclohexylethane-1-thiol

S18.1.2

(a)

(b)

(c)

S18.1.3

(a) diisopropylsulfide (b) 1,3-dimethoxybenzene (c) 2-Methyltetrahydro-2H-pyran (d) methyl 3-sulfanylbenzoate (e) methyl(phenyl)sulfide

18.2 Synthesis of Ethers
18.2 Exercises

Questions

Q18.2.1
When preparing ethers using the Williamson ether synthesis, what factors are important when considering the nucleophile and the electrophile?

Q18.2.2
How would you synthesize the following ethers? Keep in mind there are multiple ways. The Williamson ether synthesis, alkoxymercuration of alkenes, and also the acid catalyzed substitution.

(a)

(b)

(c)

(d)
Q18.2.3

Draw the electron arrow pushing mechanism for the formation of diethyl ether in the previous problem.

Q18.2.4

Ether C from problem 26 can also be prepared from an alkene and an alcohol, draw these two. (There are two possibilities for the alcohol and alkene)

Q18.2.5

Epoxides are often formed intramolecularly. Take for example this large ring, in a publication from 2016 [J. Org. Chem., 2016, 81 (20), pp 10029–10034]. If subjected to base, what epoxide would be formed? (Include stereochemistry)

Q18.2.6

What reagents would you use to perform the following transformations?

(a)

(b)
Q18.2.7
Predict the product of the following.

\[ \text{HO} \rightarrow \text{H}_2\text{SO}_4 \text{(conc.)} \]

Q18.2.8
If the following epoxide were subjected to a general nucleophile, Nu, what would be the major product?

Solutions
S18.2.1
The nucleophile ideally should be very basic, yet not sterically hindered. This will minimize any elimination reactions from occurring. The electrophile should have the characteristics of a good Sn2 electrophile, preferably primary to minimize any elimination reactions from occurring.

S18.2.2
The Williamson ether syntheses require added catalytic base. Also, most of the halides can be interchanged, say for example for a -Br or a -Cl. Although, typically -I is the best leaving group.
Note, there is only one ether (also called a silyl ether, and often used as an alcohol protecting group.) The other group is an ester.

(e)

\[ \text{OH} + \text{OH} + \text{H}_2\text{SO}_4^{\text{(conc.)}} \]
While both are possible, the top route is likely easier because both starting materials are a liquid.

Note the cis addition.
An oxidation to an alcohol through hydroboration, and subsequent substitution with 2-bromopropane could also work, but this route provides the least likelihood of an elimination reaction occurring.

(d)

Lindlar's catalyst reduces alkynes to cis/Z alkenes. This stereochemistry is retained after epoxidation.

S18.2.7

The result is the production of dioxane, a common solvent.

S18.2.8

The regiochemistry is determined by the slight electron withdrawing effect of the adjacent benzene ring. The stereochemistry is determined by the stereospecific Sn2 mechanism.

18.3 Reactions of Ethers: Acidic Cleavage

18.4 Reactions of Ethers: Claisen Rearrangement

18.5 Cyclic Ethers: Epoxides

18.6 Reactions of Epoxides: Ring-opening
18.6 Exercises

Questions

Q18.6.1

Given the following, predict the product assuming only the epoxide is affected. (Remember stereochemistry)

\[
\text{\begin{tikzpicture}
  \draw (0,0) circle (1cm);
  \draw (0,0) -- (-1,-1) -- (1,-1) -- (0,0);
  \draw (0,0) -- (0,2);
  \draw (0,0) -- (0.5,0.5);
  \draw (0,0) -- (-0.5,0.5);
  \filldraw (0,0) circle (0.1cm);
  \filldraw (-0.5,0.5) circle (0.1cm);
  \filldraw (0.5,0.5) circle (0.1cm);
  \draw (-0.5,0.5) -- (0.5,0.5);
  \draw (0,0) -- (0,-1);
  \node at (-2,-1.5) {HBr};
\end{tikzpicture}}
\]

Q18.6.2

Predict the product of the following, similar to above but a different nucleophile is used and not in acidic conditions. (Remember stereochemistry)

\[
\text{\begin{tikzpicture}
  \draw (0,0) circle (1cm);
  \draw (0,0) -- (-1,-1) -- (1,-1) -- (0,0);
  \draw (0,0) -- (0,2);
  \draw (0,0) -- (0.5,0.5);
  \draw (0,0) -- (-0.5,0.5);
  \filldraw (0,0) circle (0.1cm);
  \filldraw (-0.5,0.5) circle (0.1cm);
  \filldraw (0.5,0.5) circle (0.1cm);
  \draw (-0.5,0.5) -- (0.5,0.5);
  \draw (0,0) -- (0,-1);
  \node at (-2,-1.5) {1. CH\textsubscript{2}CH\textsubscript{2}MgBr}
  \node at (-2,0.5) {2. H\textsubscript{3}O^{+}};
\end{tikzpicture}}
\]

Q18.6.3

Epoxides are often very useful reagents to use in synthesis when the desired product is a single stereoisomer. If the following alkene were reacted with an oxyacid to form an epoxide, would the result be a enantiomerically pure? If not, what would it be?

\[
\text{\begin{tikzpicture}
  \draw (0,0) circle (1cm);
  \draw (0,0) -- (-1,-1) -- (1,-1) -- (0,0);
  \draw (0,0) -- (0,2);
  \draw (0,0) -- (0.5,0.5);
  \draw (0,0) -- (-0.5,0.5);
  \filldraw (0,0) circle (0.1cm);
  \filldraw (-0.5,0.5) circle (0.1cm);
  \filldraw (0.5,0.5) circle (0.1cm);
  \draw (-0.5,0.5) -- (0.5,0.5);
  \draw (0,0) -- (0,-1);
\end{tikzpicture}}
\]

Solutions

S18.6.1
Note that the stereochemistry has been inverted

S18.6.2

First, look at the symmetry of the alkene. There is a mirror plane, shown here.

Then, think about the mechanism of epoxidation with an oxyacid, take for example \textit{mCPBA}. The mechanism is concerted, so the original \textit{cis} stereochemistry is not changed. This leads to "two" epoxides.
However, these two mirror images are actually identical due to the mirror plane of the *cis* geometry. It is a meso compound, so the final result is a single stereoisomer, but not a single enantiomer.

18.7 Crown Ethers

18.8 Thiols and Sulfides

18.9 Spectroscopy of Ethers