Synthesis of Ethers and Sulfides

Williamson ether synthesis

\[
\text{Cyclic ether} + \text{NaH} \rightarrow \text{Nu}^- + \text{alkyl halide} \rightarrow \text{Ether}
\]

tosylate may be used instead of alkyl halide
alkyl halide or tosylate must be 1° to avoid E2 products
instead of NaH, Na (methyl or 1°) or K (2° or 3°) may be used

Alkoxymercuration-reduction

\[
\text{Cyclic ether} + \text{alkynol} + 1. \text{Hg(OAc)}_2 + 2. \text{NaBH}_4 \rightarrow \text{Ether}
\]

same as oxymercuration-reduction with an alcohol replacing water
ether always goes to the more substituted side

Synthesis of sulfides

\[
\text{Cyclic sulfide} + \text{Cl}^- + \text{alkynol} \rightarrow \text{Sulfide}
\]

tosylate may be used instead of alkyl halide
sulfides are poor bases, so 2° alkyl halides can be used without E2 products forming

Reactions of Ethers and Sulfides

Cleavage of ethers with HX

\[
\text{Ether} + 2\text{eq HBr} \rightarrow \text{Alkyl halides}
\]

only works with HI and HBr
symmetrical ethers form only one alkyl halide; unsymmetrical ethers form two
aryl ethers give phenol instead of an aryl halide
Synthesis of Epoxides

Oxidation of alkenes with peroxycacid

\[
\text{alkene} + \text{peroxycacid} \rightarrow \text{epoxide}
\]

alkene is oxidized and peroxycacid is reduced
syn addition is observed
PhCO_3H is often used because it is soluble in organic solvents
MMPP is often used because the byproduct crystallizes out of solution

Cyclization of halohydrins

\[
\text{halohydrins} \xrightarrow{\text{NaH (or K)}} \text{epoxide}
\]

halohydrins are formed from alkenes and X_2, H_2O
the C with the halogen is inverted

Reactions of Epoxides

Ring opening by a strong Nu

\[
\begin{align*}
\text{epoxide} & \xrightarrow{\text{NaOH}} \text{OH} \xrightarrow{\text{H}_2\text{O}} \\
\text{epoxide} & \xrightarrow{\text{RONa}} \text{OH} \xrightarrow{\text{ROH}} \\
\text{epoxide} & \xrightarrow{\text{RMgBr}} \text{OH} \xrightarrow{2\cdot\text{H}_2\text{O}^+}
\end{align*}
\]

Nu attacks the less substituted side
the C that gets attacked is inverted

Ring opening by a weak Nu

\[
\begin{align*}
\text{epoxide} & \xrightarrow{\text{H}_2\text{SO}_4} \text{OH} \xrightarrow{\text{H}_2\text{O}} \\
\text{epoxide} & \xrightarrow{\text{H}_2\text{SO}_4} \text{OH} \xrightarrow{\text{ROH}}
\end{align*}
\]

Nu attacks the more substituted side