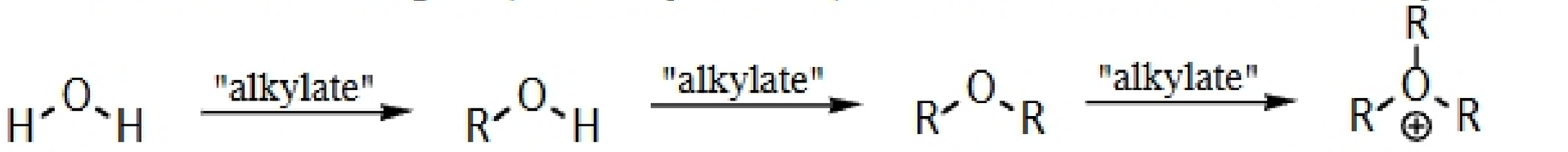
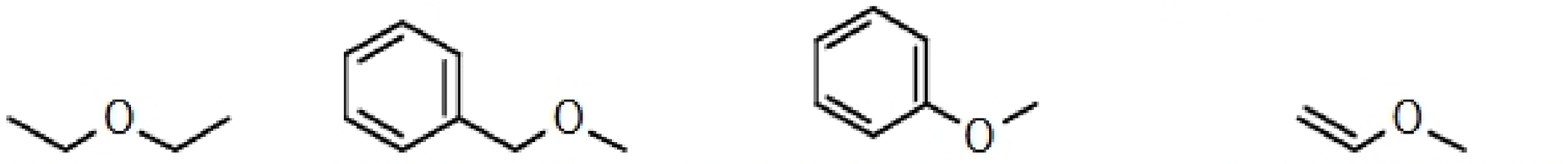
Ethers, epoxides and sulfides

An ether is the logical (and nearly terminal) conclusion of a series of water alkylations:



Water — Alcohol — **Ether** — Trialkyloxonium Salt (YECH!)

Ethers come in a couple of flavors. There is the standard, dialkyl type:



Ether,
Diethyl Ether
Ethyl ether
(all 3 in common usage)

Benzyl Methyl Ether

Anisole
(Phenyl Methyl Ether)

Vinyl Methyl Ether

And then there are the cyclic ethers – the names of these can be ugly, because they are often based on the molecule from which the ether was derived, rather than as an accurate description of the ether:

Furan — Tetrahydrofuran (THF) — Trimethylene Oxide (Oxetane) — Ethylene Oxide, Oxirane, Epoxide — Propylene Oxide

Uses of ethers:

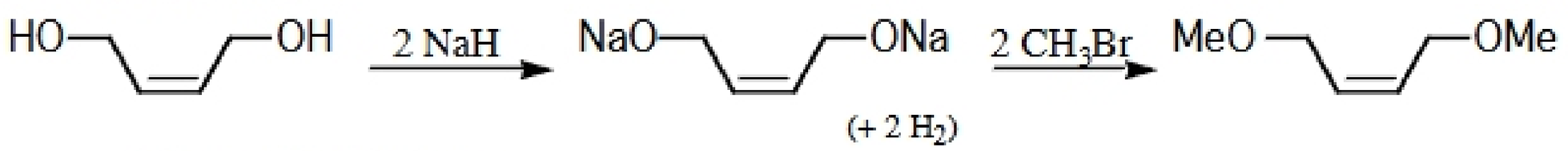
Unlike alcohols, ethers in general are unreactive. They are more commonly used as reaction *solvents* than as reactants – ethers thus make great protecting groups! The only real exceptions to this rule are the epoxides - the three-membered ring ethers. We will talk more about the reactivity of these compounds later.

Preparation of Ethers:

The most common preparation of simple ethers uses the Williamson Ether Synthesis. In short, this preparation utilizes a deprotonated alcohol and an alkyl halide:

In General:

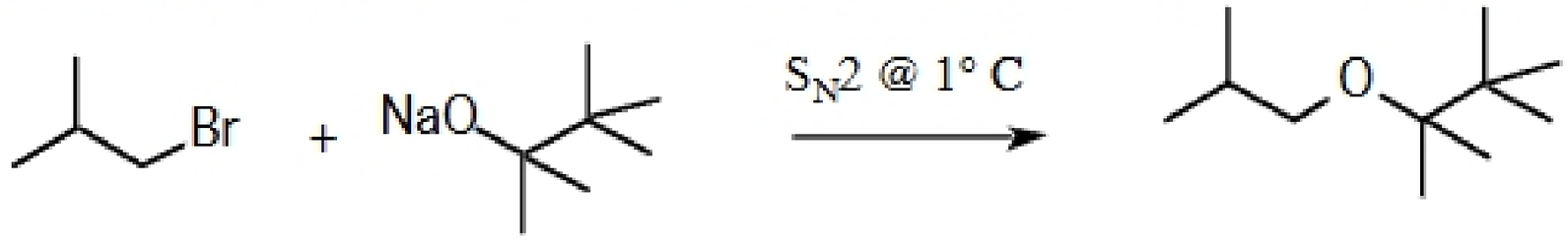
An Example:

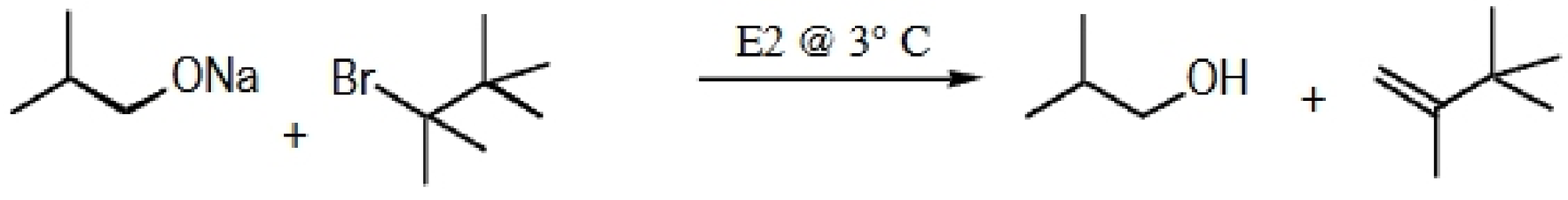


Notes and Restrictions:

The alkoxide portion of the starting material is generally produced by the action of sodium hydride (NaH). This hydride is the reagent of choice because the only by-product is

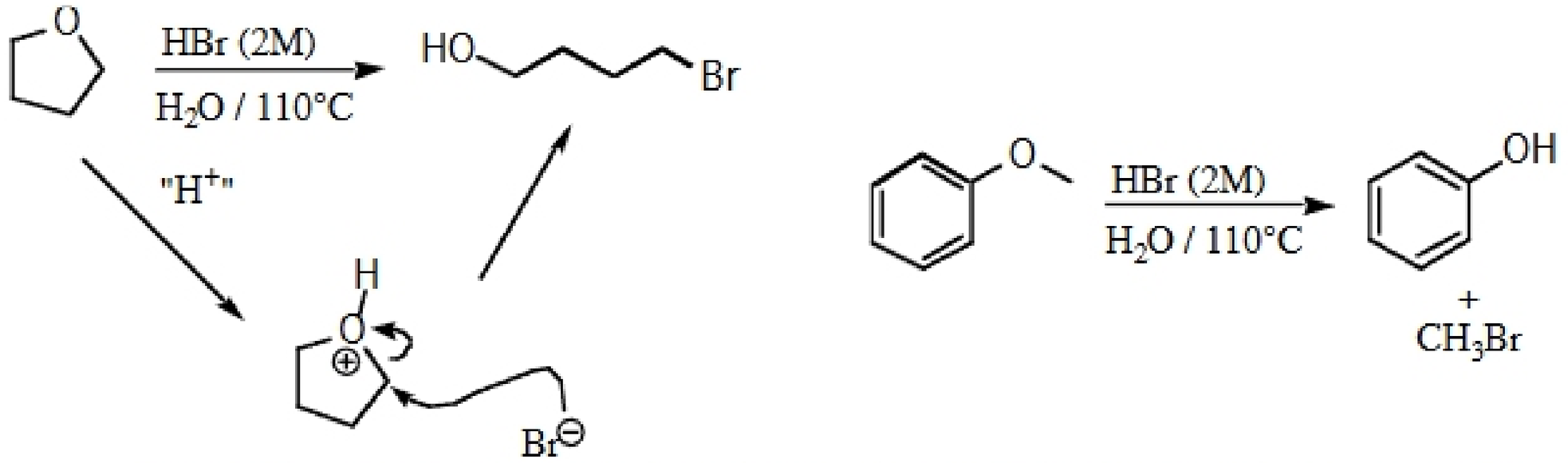
hydrogen gas (a very strong driving force!) Because the alkoxide is very basic, the alkyl halide *should* be primary - otherwise, deprotonation rather than nucleophilic attack is likely:





Destruction of Ethers:

Now that you've gone through all the trouble of making an ether, we're going to talk about how you tear them back apart. Ethers are generally cleaved by strong acids at high temperatures (i.e. at LEAST 2M acid at 100+°C). HBr and HI are the reagents of choice:



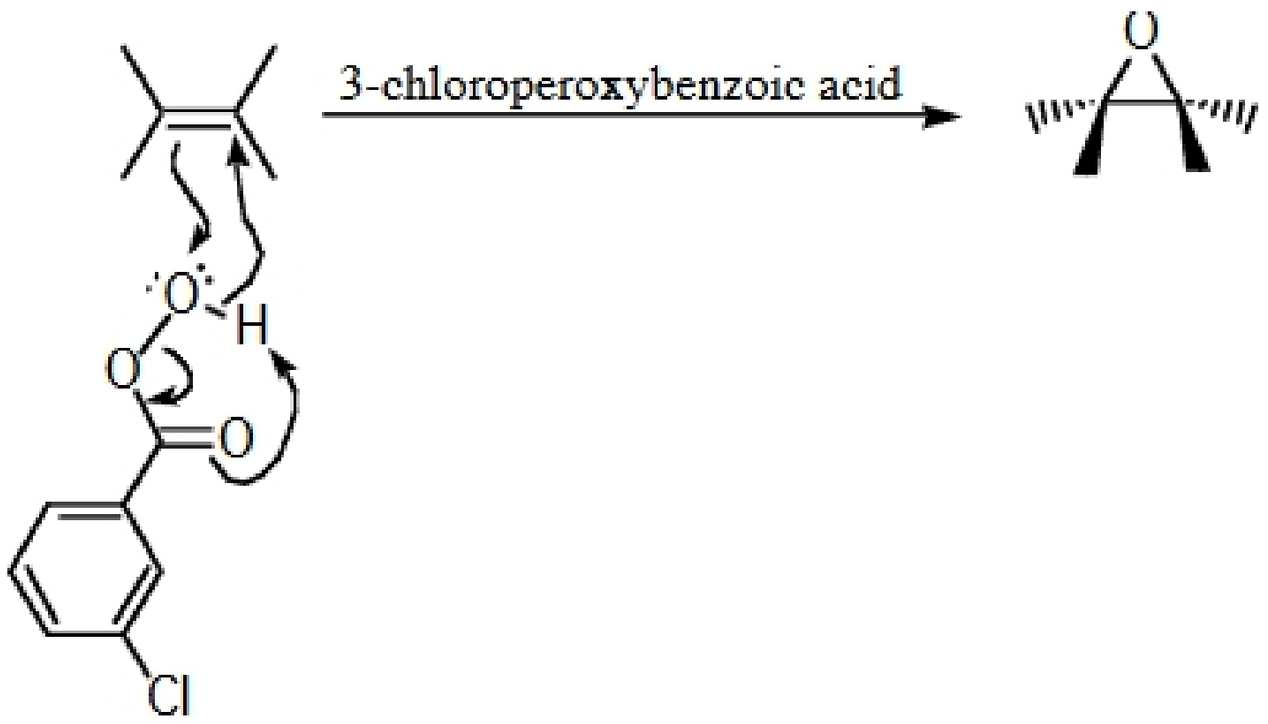
Because they can form stable carbocations, tertiary, allylic and benzylic ethers can be cleaved under much milder conditions, and form an alkene in place of the alkyl halide.

Epoxides: ()

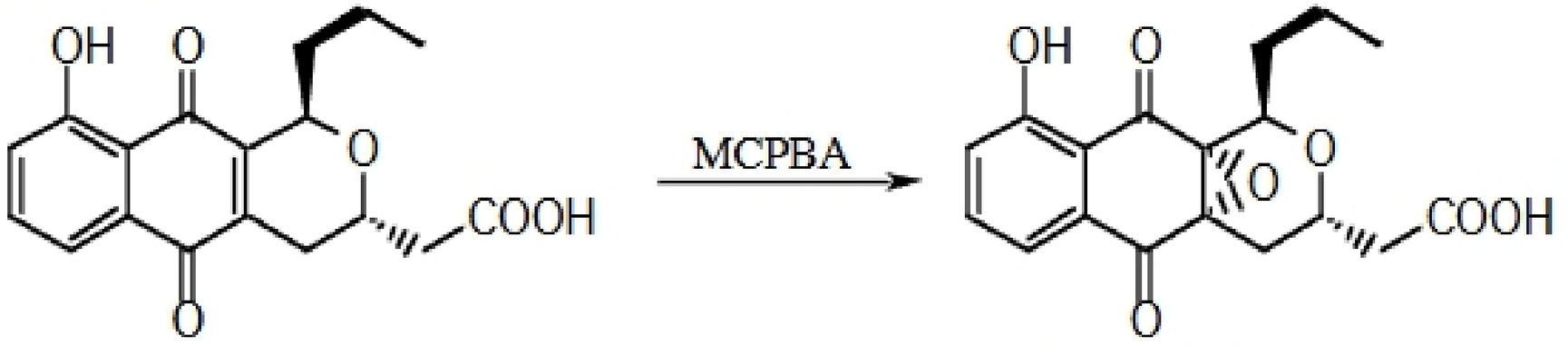
Because of the strain induced by the presence of a three-membered ring, epoxides are significantly more reactive than other ethers. Thus, they become useful in organic synthesis.

Preparation:

Epoxides are easily prepared from alkenes, by oxidation with a peroxyacid (often called a peracid). This is really the only *non-stereospecific* epoxidation method currently in use:



For example:



Frenolicin

Ring-Opening of epoxides:

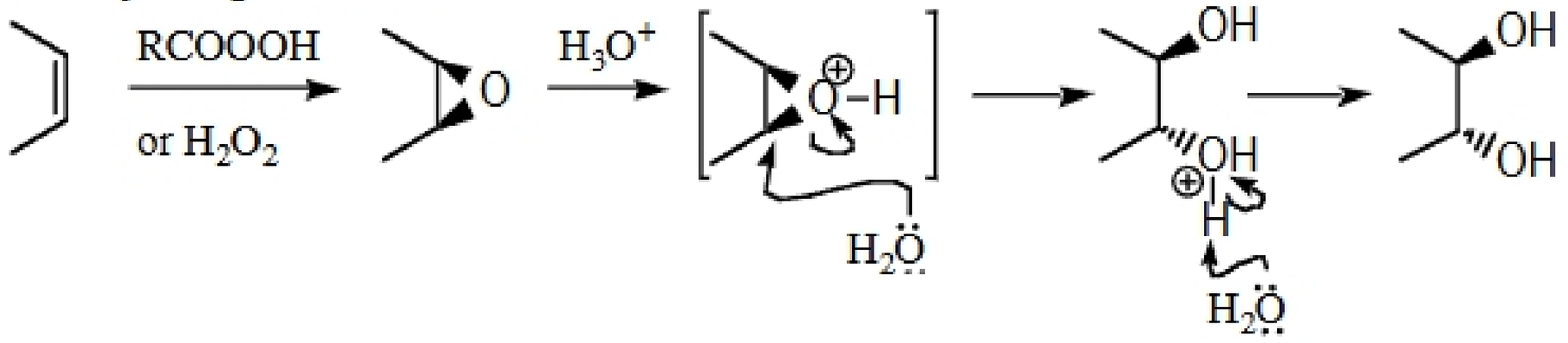
This is where the real synthetic utility of epoxides comes into play. As we discussed earlier:

1) Epoxides can be ring-opened to *trans* (or *anti*) 1,2-diols
2) Metallated Species (**RM**) can be added to epoxides, to form primary alcohols.

Here we will discuss a little more about the mechanism of these reactions, as well as how to predict where incoming nucleophiles will add.

A) Acid-catalyzed ring-opening of epoxides.

With simple, aqueous acids, epoxides ring-open to give the *anti* 1,2-diol. The mechanism is relatively straightforward:



In this case, obviously, the nature of the epoxide is unimportant – the result is always the *anti*-diol.