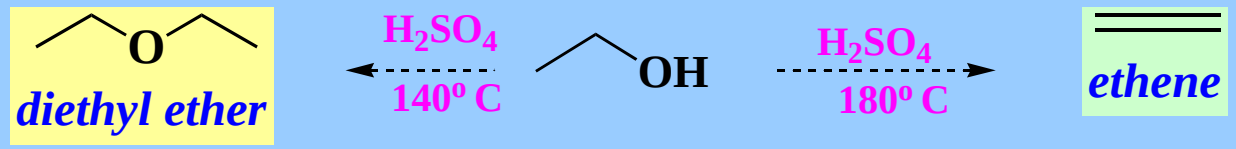
Section 11--Synthesis of Ethers

Synthesis of Ethers--The Sulfuric Acid Dehydration Method

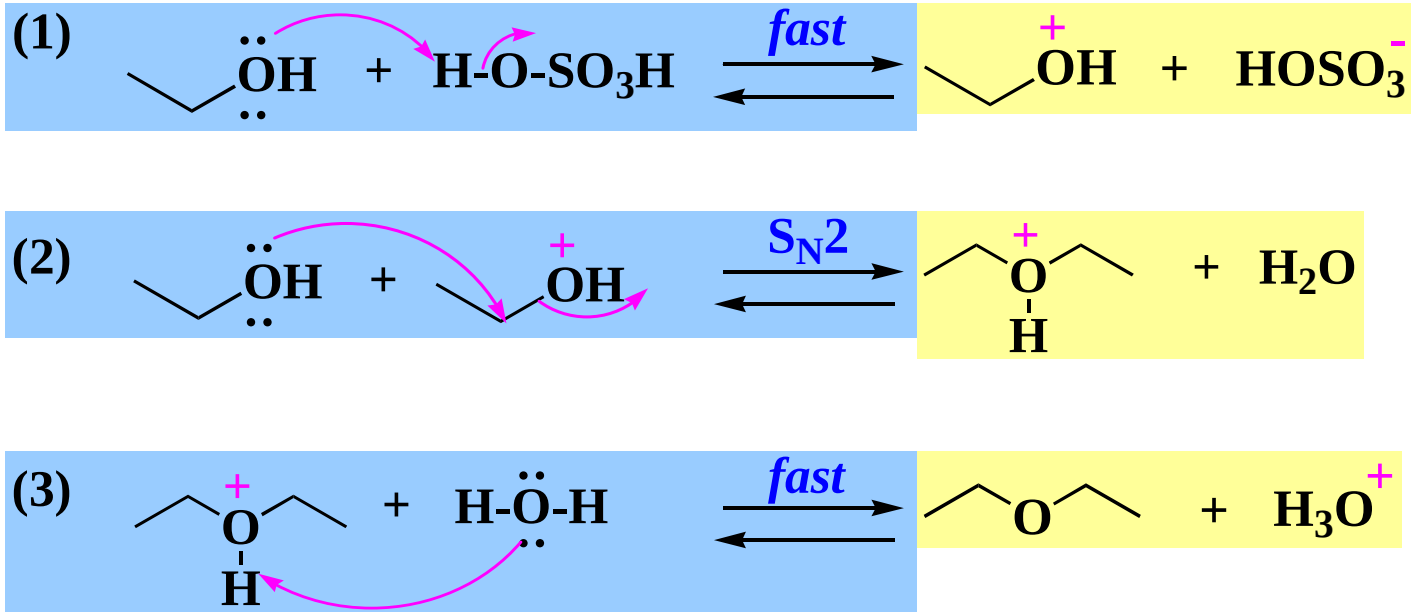
Symmetrical ethers may be prepared from the dehydration of primary alcohols in the presence of sulfuric acid. The synthesis of commercially important ethers, such as diethyl ether, are carried out under carefully designed conditions that minimize side reactions.

Reaction of Ethanol and Sulfuric Acid

The major product produced in this reaction depends on the reaction conditions:



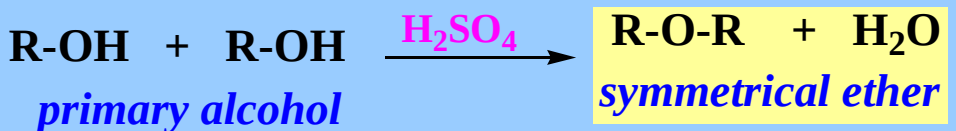
Mechanism: Acid-Catalyzed S_N2



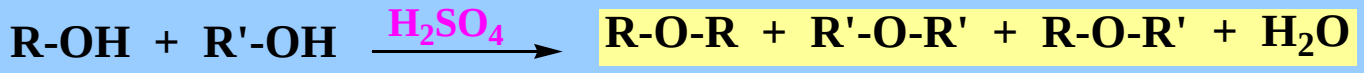
In the commercial synthesis of diethyl ether, ethanol is constantly added to the reaction mixture to maintain a high concentration of the needed nucleophile, and diethyl ether is removed.

Limitations of the Sulfuric Acid Dehydration Synthesis

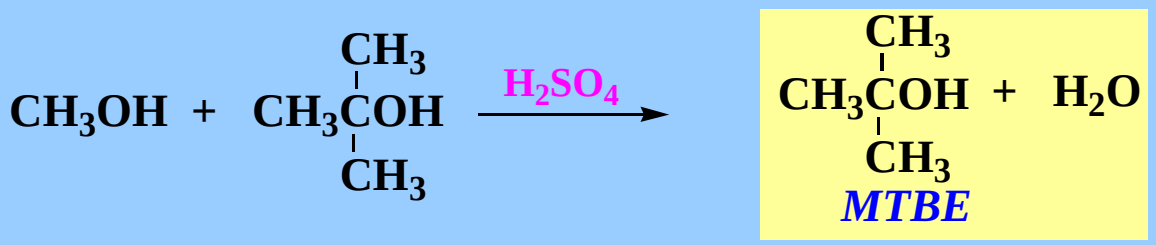
In general, symmetrical ethers can be prepared from primary alcohols by this method:



In most cases, unsymmetrical ethers are not prepared by this procedure because of the potential of three products:

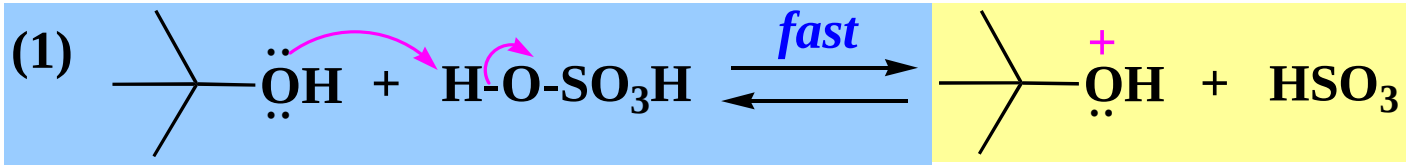


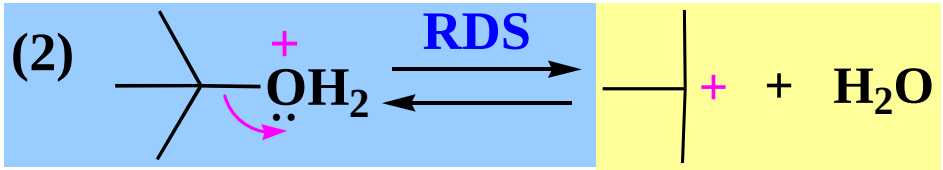
An exception is the synthesis of unsymmetrical primary-tertiary ethers such as methyl tert-butyl ether (MTBE):



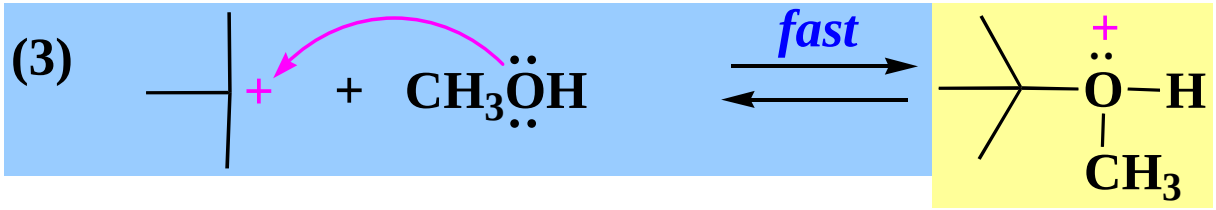
Mechanism of the Reaction between Methanol and tert-Butyl Alcohol

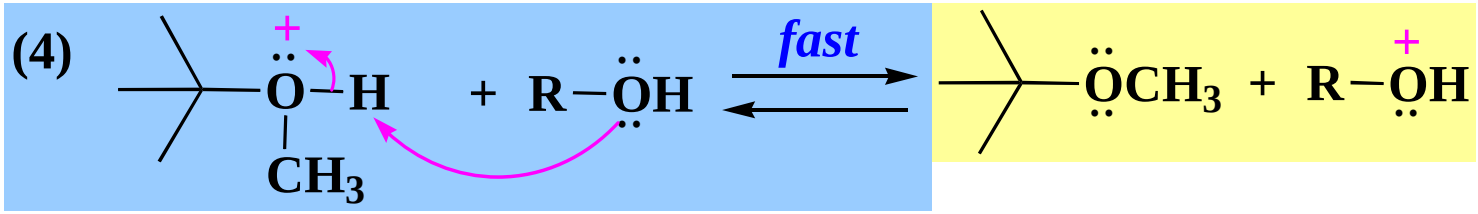
Because of the stability of the tert-butyl carbocation, the following acid-catalyzed dehydration mechanism dominates:





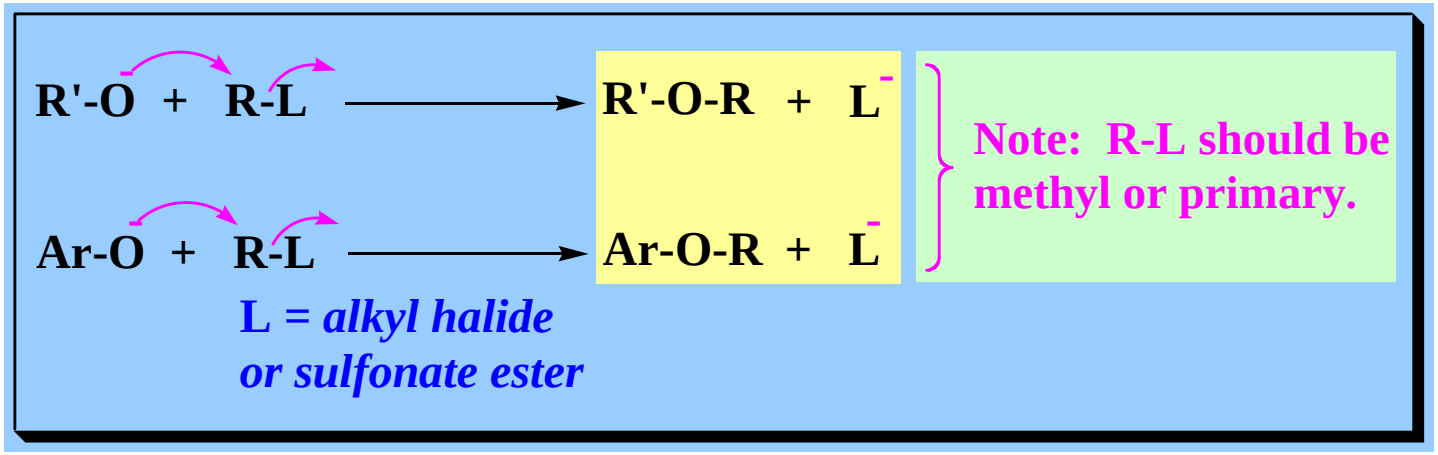
This is an S_N1 mechanism where bond heterolysis in the RDS yields a tertiary carbocation intermediate.



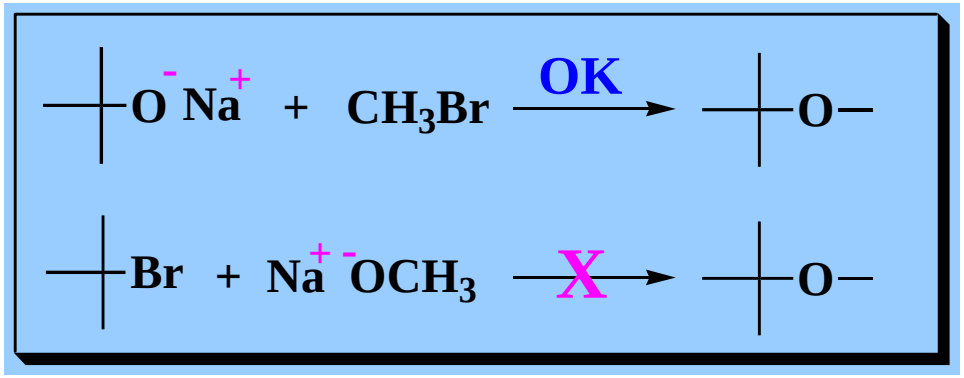


Williamson Synthesis of Unsymmetrical Ethers

This S_N2 reaction of an alkoxide and an alkyl halide (or the equivalent) may be used to prepare unsymmetrical ethers.



Example



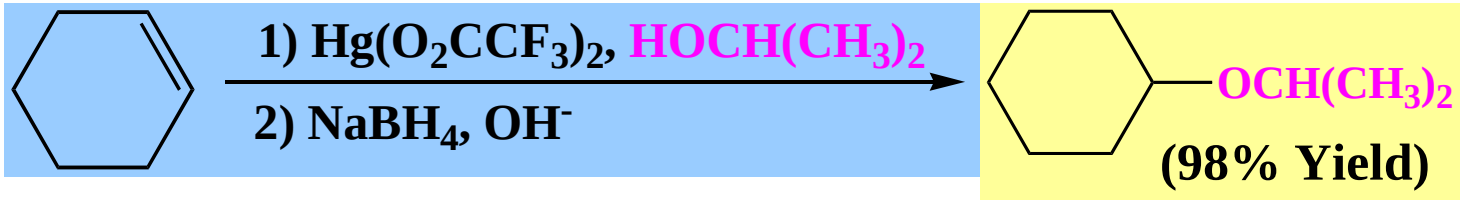
Synthesis of Ethers by Alkoxymercuration-Demercuration

Alkoxymercuration-demercuration is another method for synthesizing ethers. This is a version of the oxymercuration-demercuration discussed earlier.

If water is used, then the alkene is converted into an alcohol (oxymercuration-demercuration).

If an alcohol is the solvent, then the alkene is converted into an ether (alkoxymercuration-demercuration).

Example

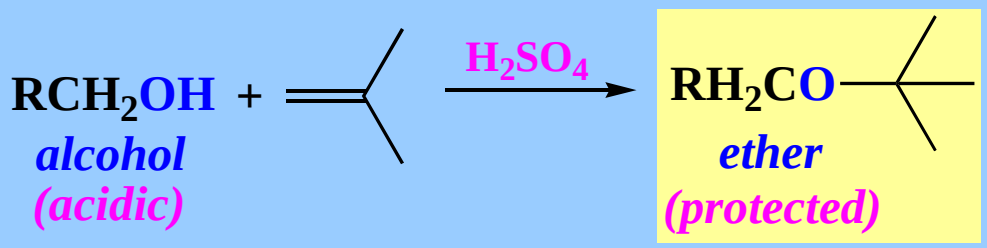


Tert-Butyl Ethers as Protecting Groups of Alcohols

Protecting groups are widely used in organic synthesis when it is necessary to temporarily mask the chemical properties of a functional group during a reaction with another functional group.

The hydroxyl group in alcohols is relatively acidic and often is temporarily transformed into a function that is not affected by strong bases during organic syntheses.

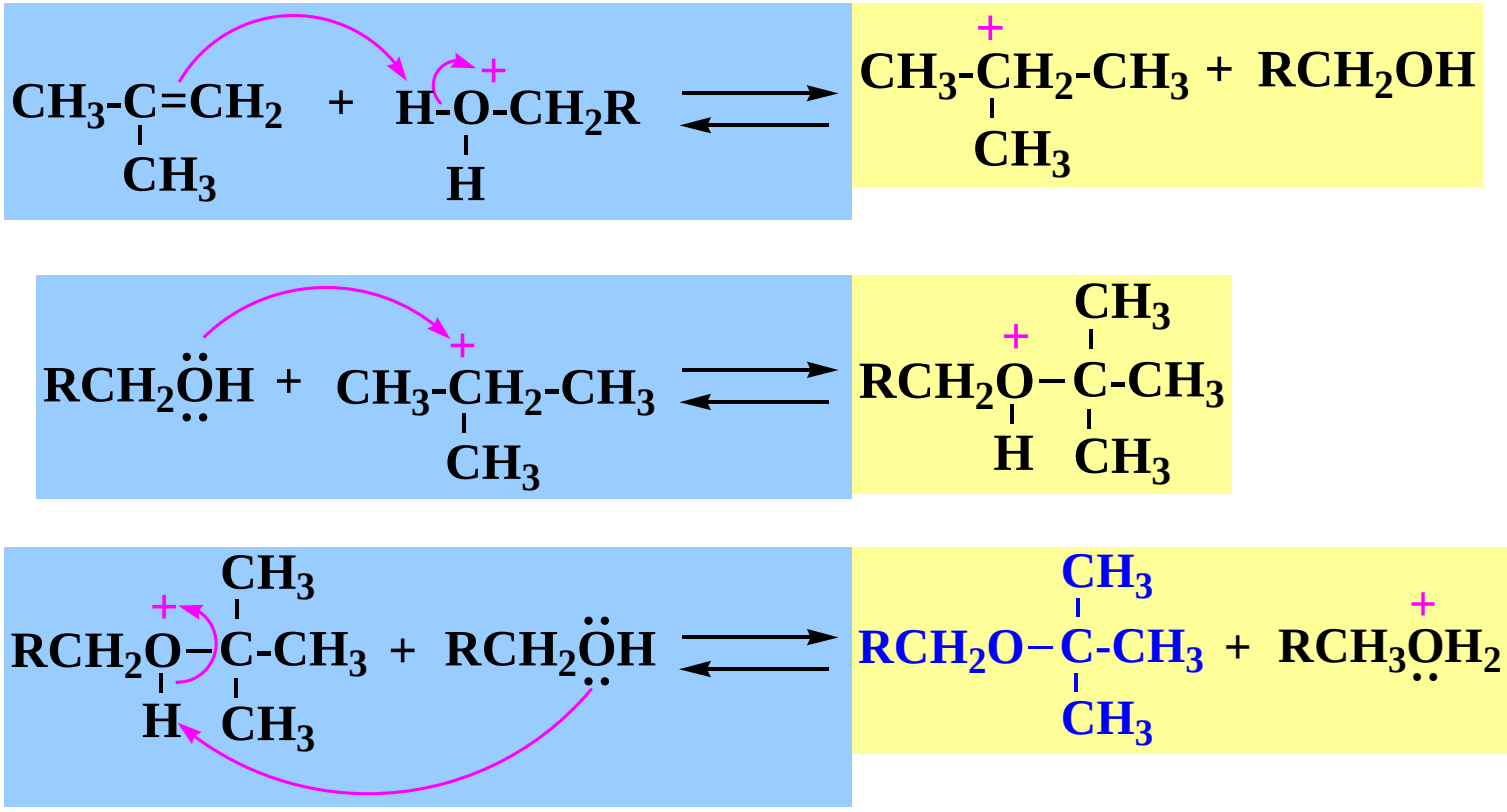
Primary alcohols may be protected by converting them into **tert-butyl ethers**.



Protected Primary Alcohols

Primary alcohols may be protected as tert-butyl ethers by dissolving the alcohols in strong acids, such as sulfuric acid and slowly adding isobutene. Slow addition is required to prevent the dimerization and polymerization of isobutene.

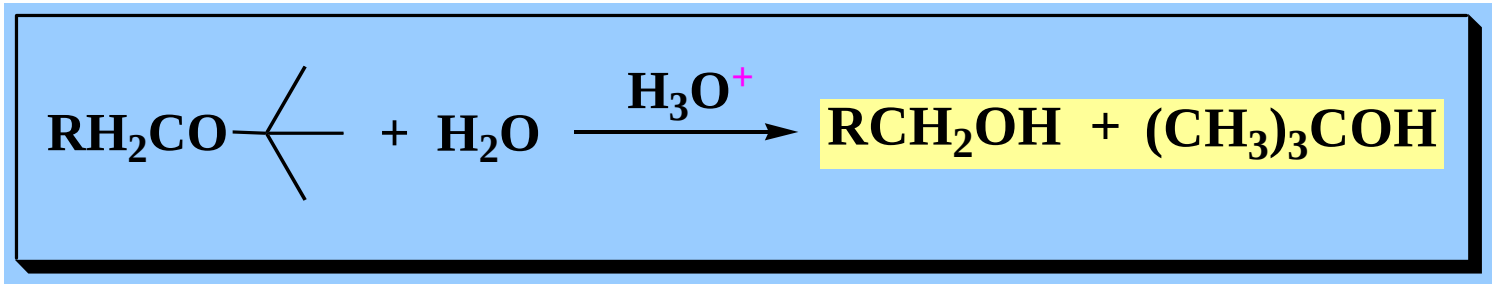
Mechanism



Removal of the Protecting Group

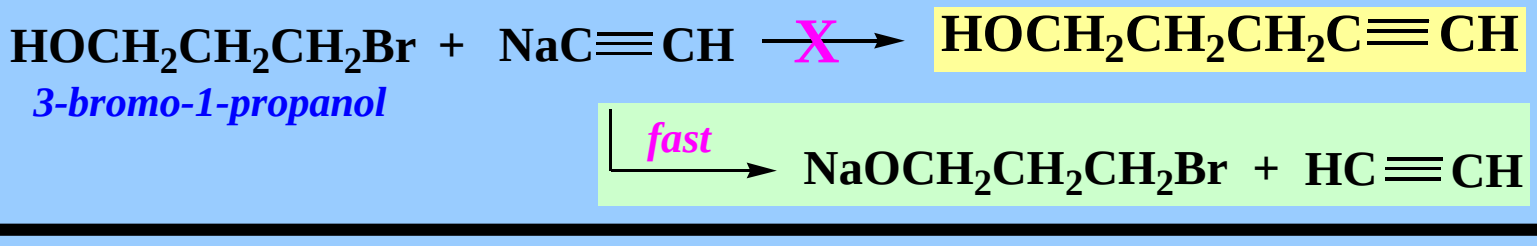
Protecting groups must be easy to put on and easy to take off.

The tert-butyl ether protecting group of primary alcohols is removed in aqueous acid:

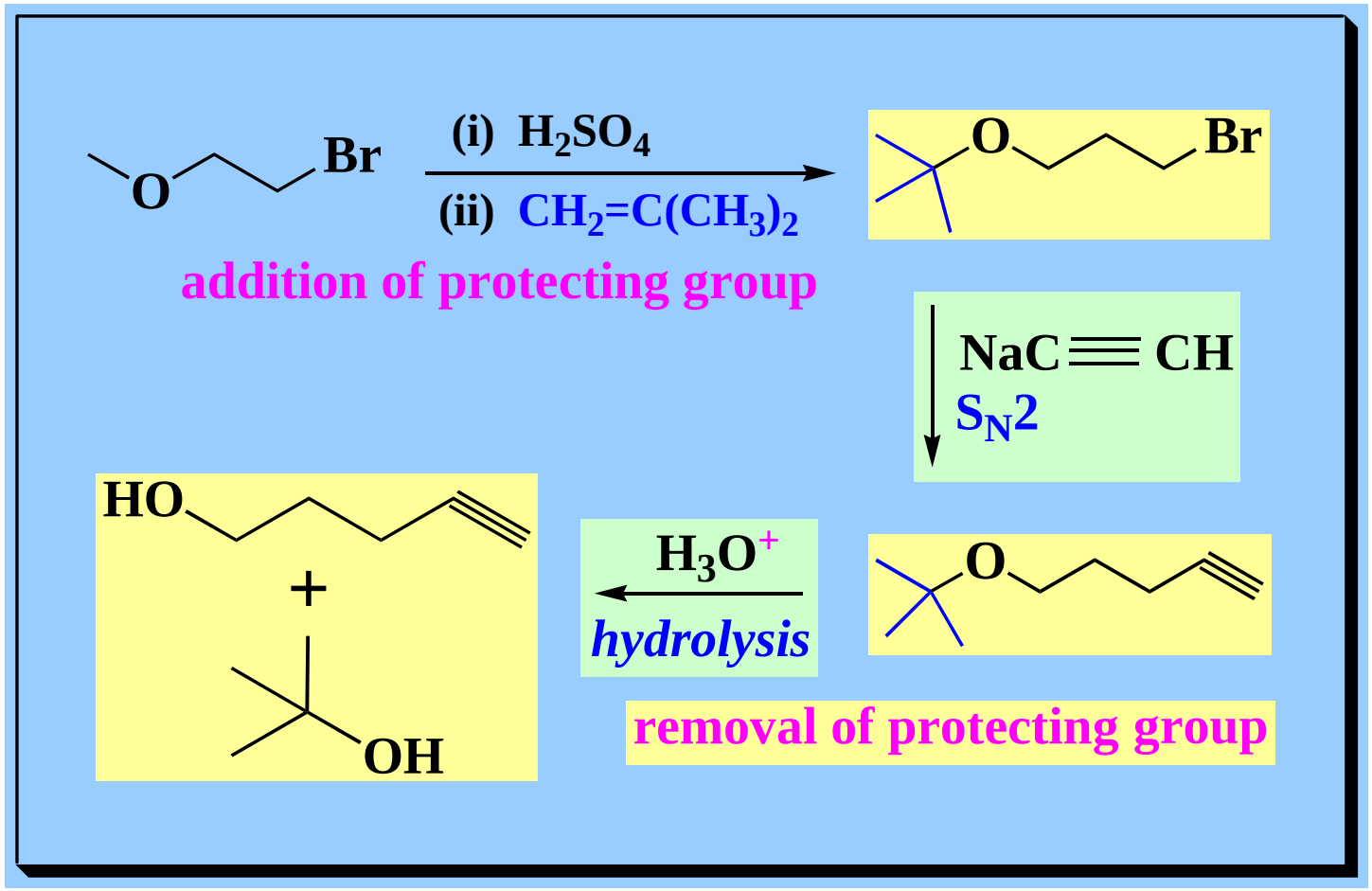


Example

This S_N2 reaction will not occur:

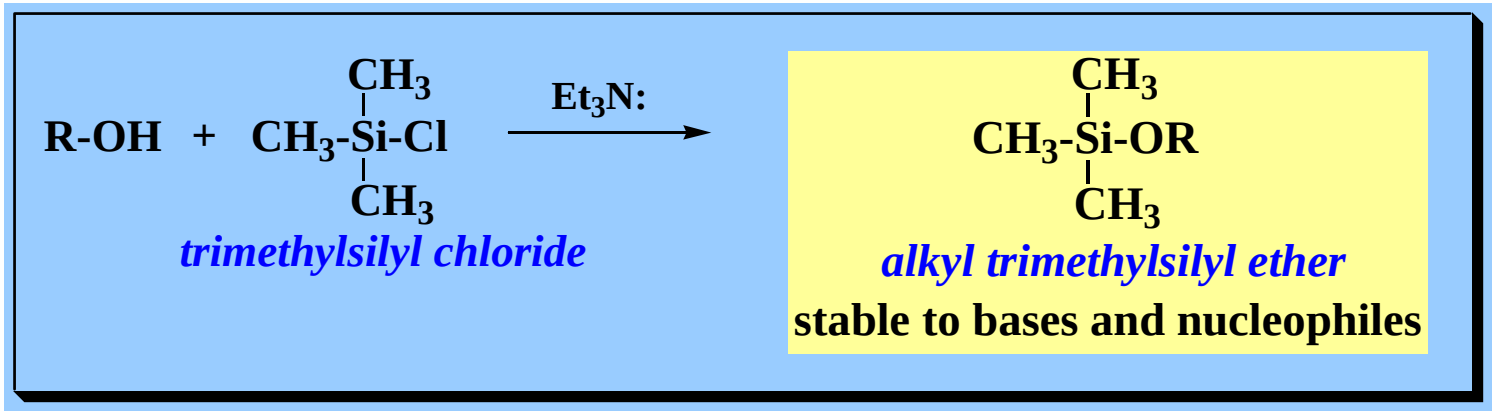


Solution


O
Br
(i) H2SO4
(ii) CH2=C(CH3)2
O
Br
addition of protecting group
NaC≡CH
SN2
HO
+
OH
H3O+
hydrolysis
O
removal of protecting group

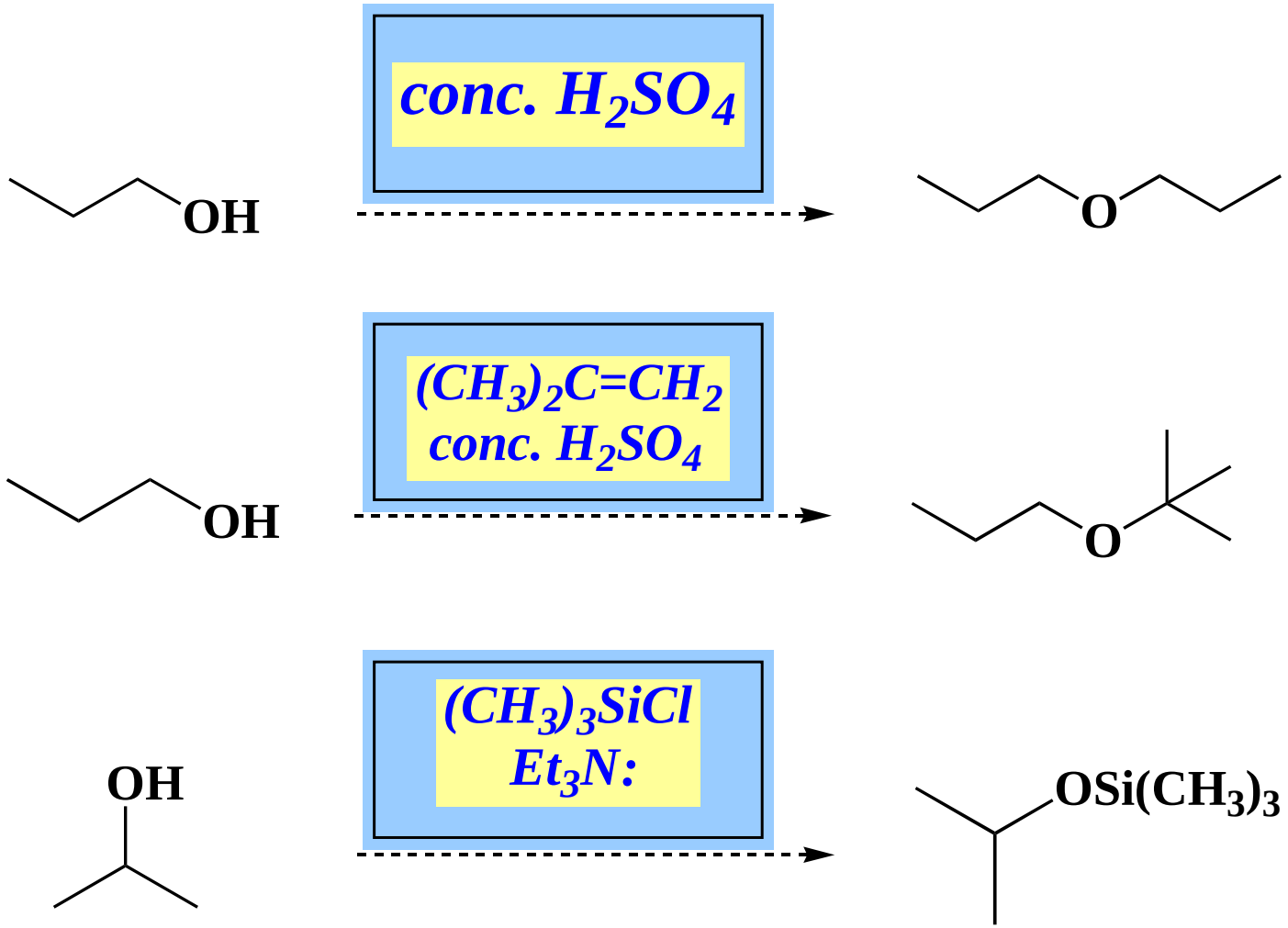
The Trimethylsilyl Protecting Group

A widely used protecting group for all alcohols is the trimethylsilyl ether that is easily prepared from the alcohol and trimethylsilyl chloride in the presence of an amine base:



Quiz Chapter 11 Section 11

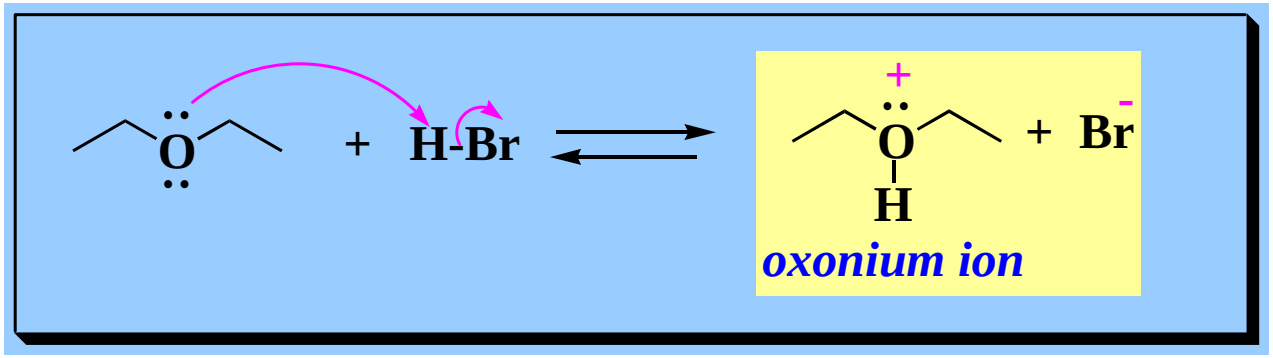
Indicated the reagents and other materials needed to prepare the products below from the designated starting compound.



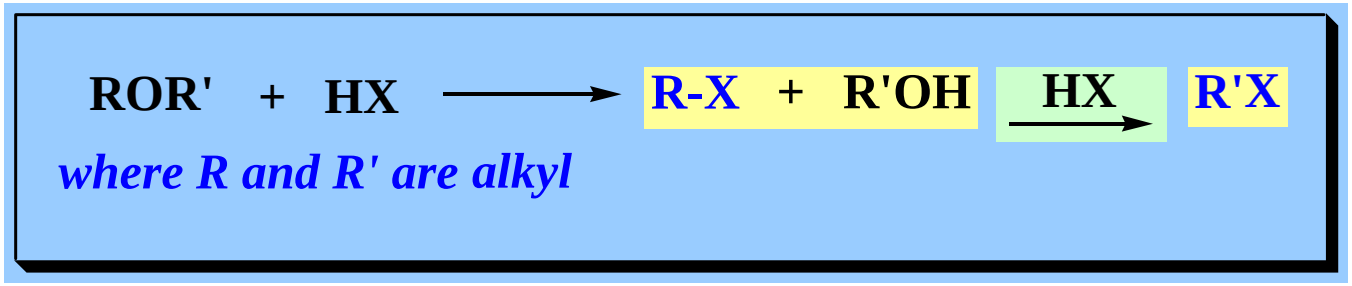
Section 12--Reactions of Ethers

Cleavage of Ethers by Acids

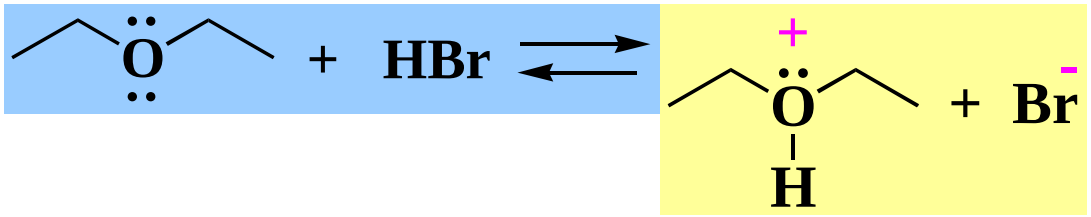
Ethers are Lewis bases and react with acids to form oxonium ions:

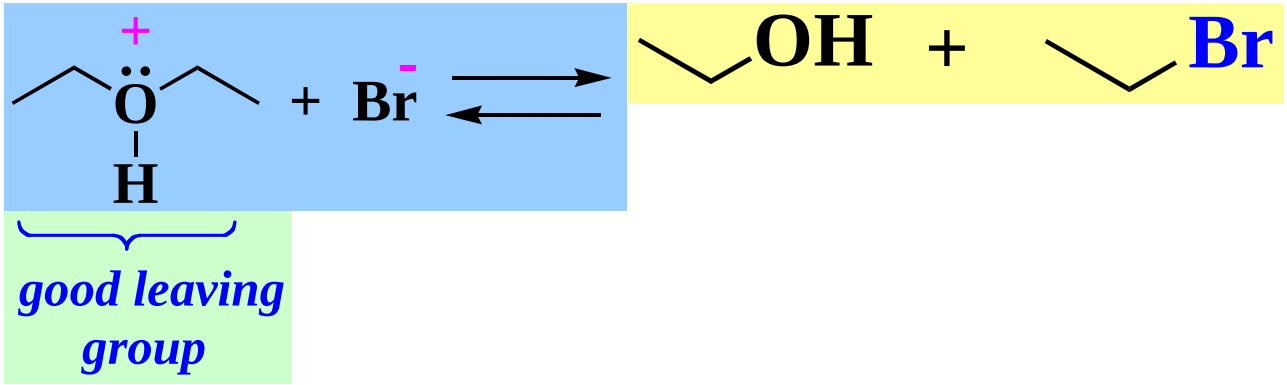


Strong acids (HI, HBr, H_2SO_4) cleave dialkyl ethers:

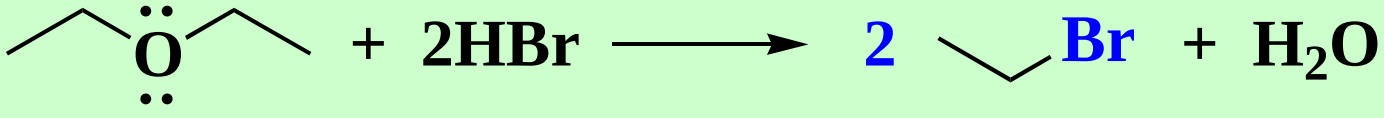


Example

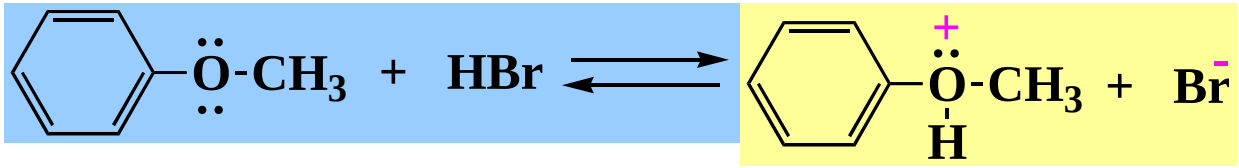


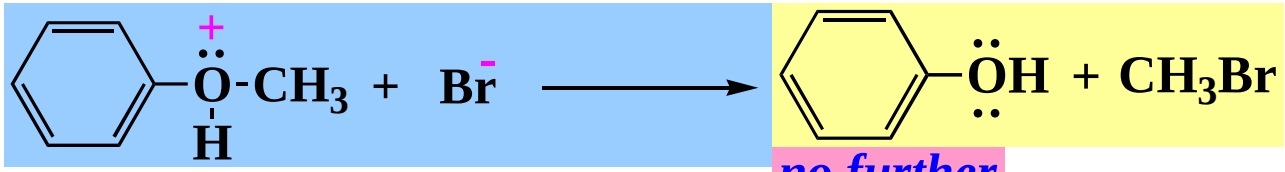


overall



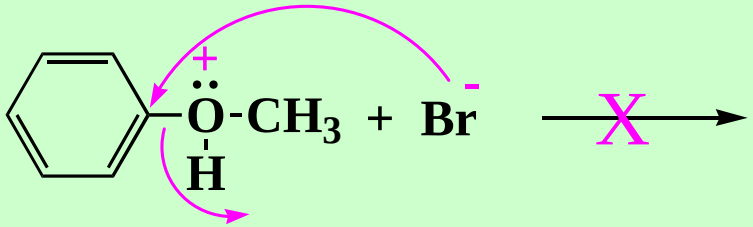
Cleavage of Aryl Alkyl Ethers





no further reaction

alternative nucleophilic substitution reaction does not occur:



Quiz Chapter 11 Section 12

Provide all the organic products of the following reaction.