

Chemistry 210 -- Winter Semester 1997

Chapter 9

Derivatives of Alcohols

Alkoxides

Deprotonation with Strong Bases

The simple hydrides all are strong bases: LiH, NaH, KH

LDA = lithium diisopropylamide $\text{LiN}(i\text{-Pro})_2$

BuLi = butyl lithium (comes as *n*- and *t*-BuLi)

The reaction of any of these strong bases with alcohols yields complete alkoxide formation.

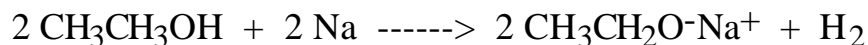
Deprotonation with Alkalimetals

Alcohols react with alkalimetals to form alkoxides and H_2 .

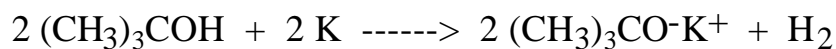
The rate of reaction depends on R in ROH and decreases in the order



Example 1: Fast formation of the ethoxide



Example 2: Slow reaction with 2-methyl-2-propanol even with K (used to destroy K in lab)

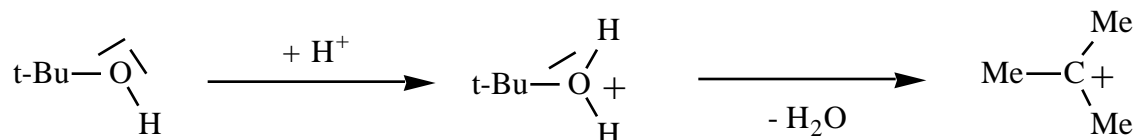


Acid-Catalyzed S_N and E Reactions of Alcohols: Alkyloxonium Ions

Principle

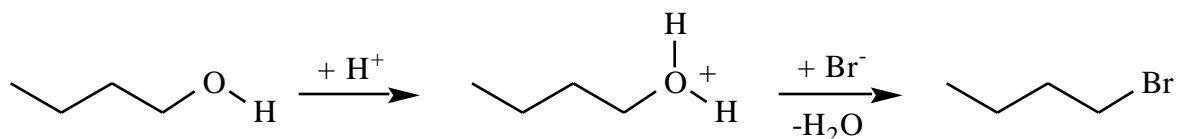
The hydroxyl group is a poor leaving group.

Protonate the hydroxyl group — that is form the alkyloxonium ion — and use water as a very good leaving group. This step is used in substitution and elimination reactions and in both types (uni- end bimolecular).



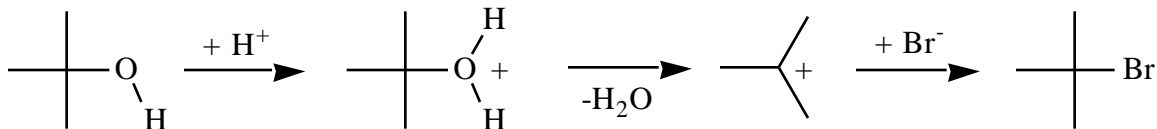
Application 1: Primary Halides from Alcohols

Why is this important? Remember that the primary halides are hard to make by radical chain halogenation. So, now we make the primary alcohol (e.g. from an aldehyde by reduction) and then do a clean S_N2 with Hbr.



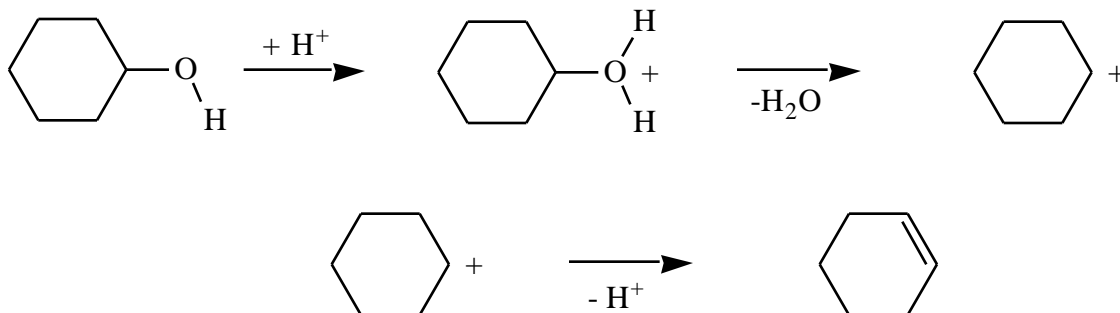
Application 2: Tertiary Halides from Alcohol

Use HBr as the acid. The proton catalyzes the water elimination. The bromide is a good nucleophile and does the substitution. In this case, the reaction is S_N1.



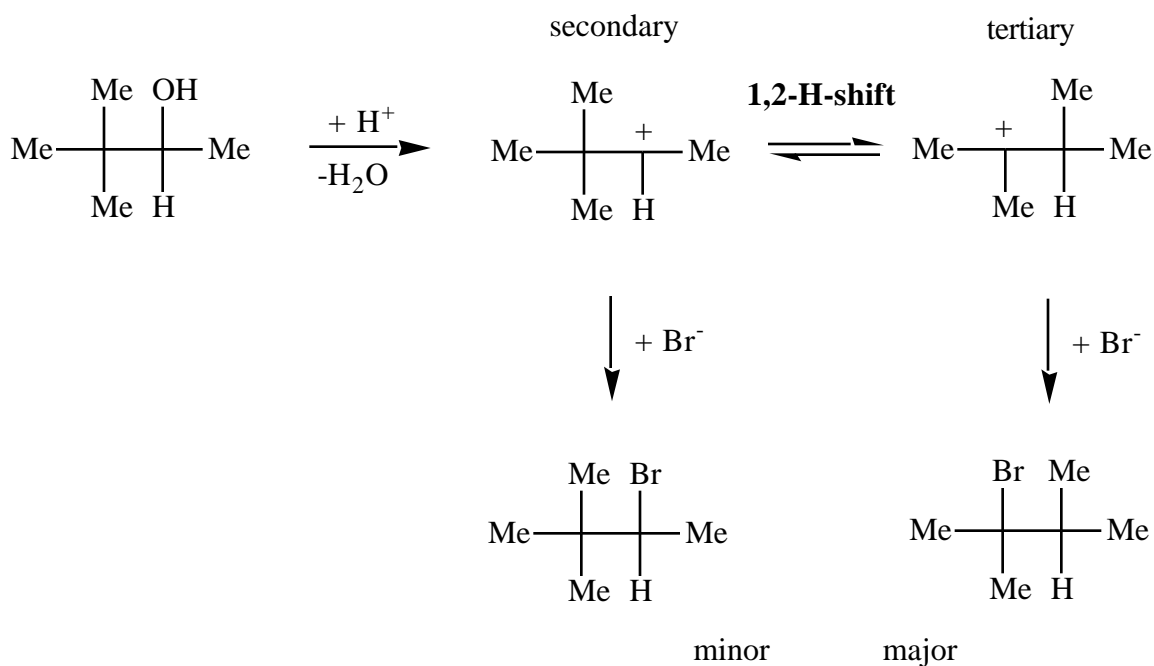
Application 3: Acid-Catalyzed Elimination

Use H_2SO_4 as the acid at 130 C. The proton catalyzes the water elimination. The sulfate is not such a good nucleophile and does not do the substitution. In this case, the reaction is E1.



The Classical Example for Alkyl Shift: Secondary to Tertiary in S_N1

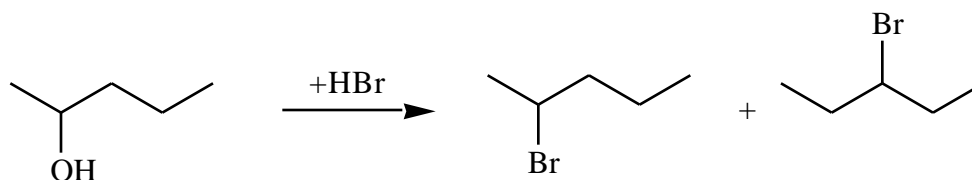
The acid-catalyzed dehydration of 3,3-dimethyl-2-butanol leads to a secondary carbocation. This cation **cannot** undergo a **hydride shift** but it **can** undergo a **alkyl shift** to form the thermodynamically more stable tertiary carbocation. Hence, the reaction of HBr with 3,3-dimethyl-2-butanol yields two products and the major product is the one that was generated by the rearrangement.



This is very much the same as the previous H-shift example. The alkyl shifts happen when the H-shifts can't help.

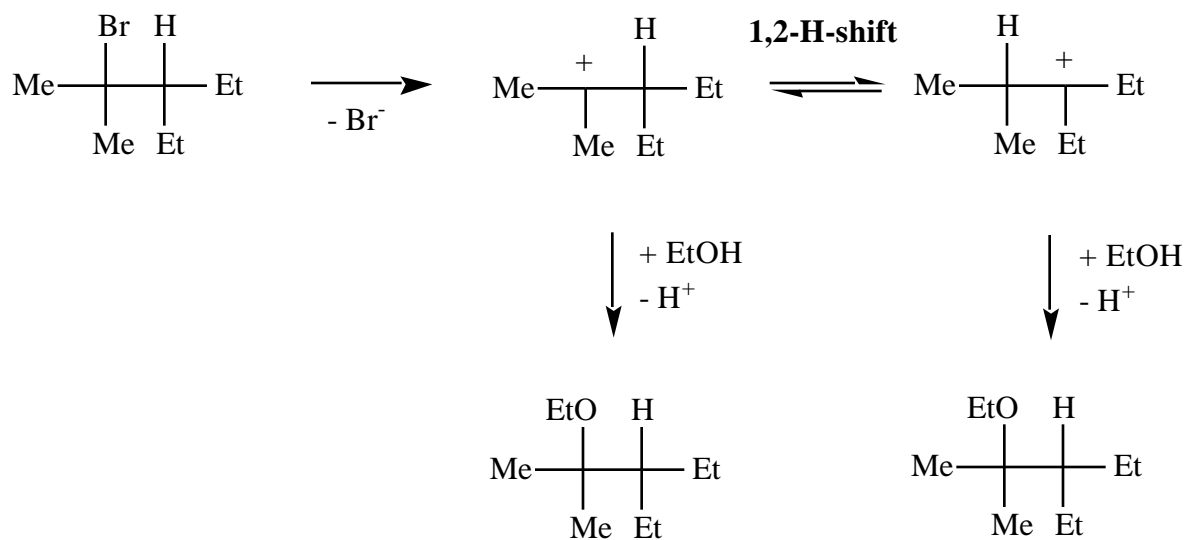
Secondary to Secondary Rearrangements in S_N1

Equilibrium may form between several secondary carbenium ion.



Note that alkyl shifts won't work in such a case because they would have to produce a primary carbocation and nothing would be gained!

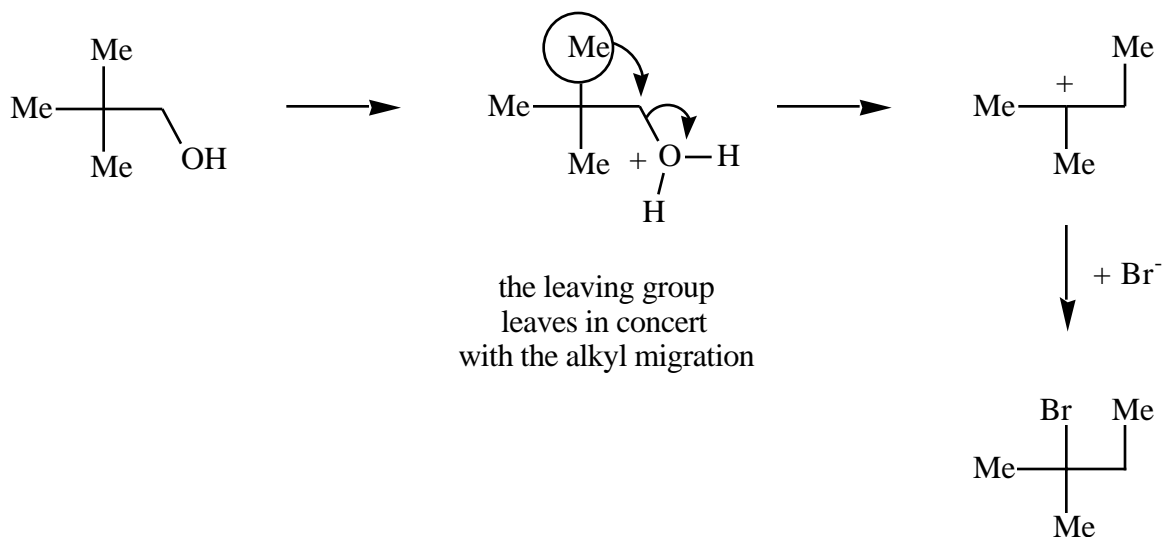
Tertiary to Tertiary Rearrangements in S_N1: Solvolysis of an alkylbromide



About Rearrangements Involving Primary Carbocations

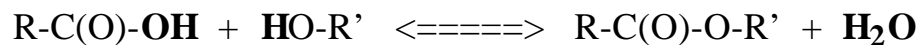
This is very rare and it is not expected to happen! The primary substrates do not react via a unimolecular reaction. So we do not expect a cation to be formed in the first place. And this is right. There is however way for such substrates to realize *de facto* rearrangements.

The rearranging alkyl group acts as the nucleophile in the S_N2 reaction that kicks out the leaving group. The product of that S_N2 reaction is the rearranged carbenium ion which then adds a nucleophile.



Organic and Inorganic Esters of Alcohols

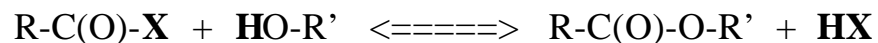
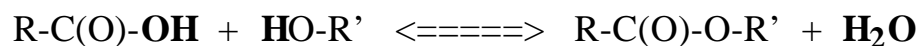
Ester = Condensation product between an acid and an alcohol.



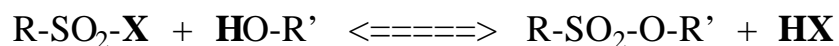
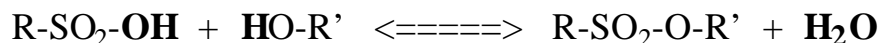
Organic Ester = Formed between carboxylic acid and alcohol

Inorganic Ester = Formed between an inorganic acid and alcohol

Often the ester is made not directly from the acid but with the use of an **acid halide**. An acid halide is the derivative of the acid in which an OH group has been replaced by a halogen.



Inorganic acids have OH groups and can formally react just like the organic acids (e.g. replace the OH by the OR). Again, most usually the inorganic ester is made not directly from the acid but with the use of an **acid halide**. The example shows sulfonates.



Examples of Inorganic Acids:

Chromic acid make chromates.

Phosphoric acid make phosphates.

Sulfuric acid makes sulfates.

Sulfonic acids make sulfonates.

Formation of Organic Esters via "Esterification"

Acid-catalyzed reaction of alcohol with carboxylic acid. The mechanism is illustrated for acetic acid and ethanol. The reaction will be discussed in very much detail later on in Chemistry 212.

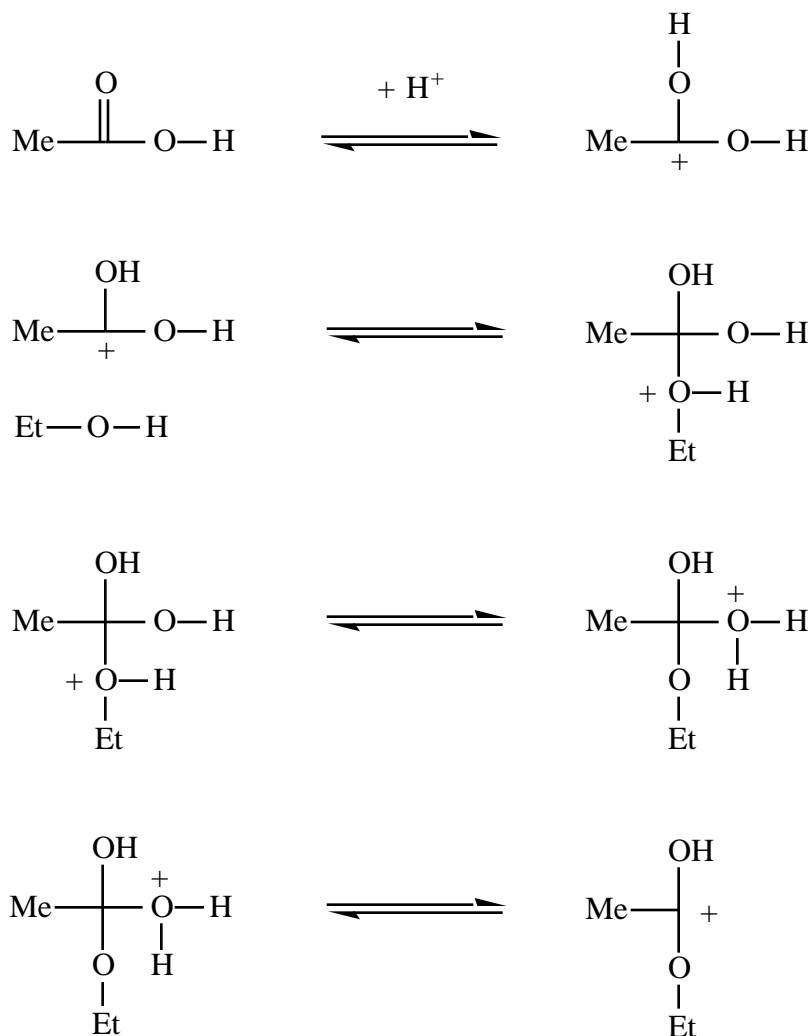
Step 1: Protonate the carbonyl-O of acetic acid.

Step 2: Add the alcohol-O and make an alkyloxonium ion.

Step 3: Proton transfer to one of the hydroxyl-O.

Step 4: Eliminate the hydroxyl group as water.

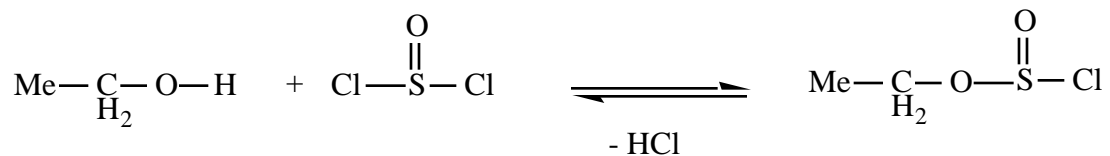
Step 5: Deprotonate at OH. (not shown)



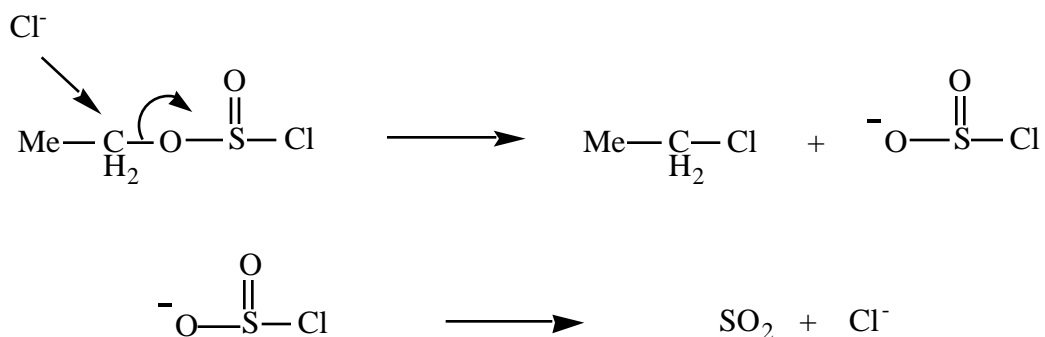
Thionyl Chloride in Chloroalkane Synthesis

Thionyl chloride is $\text{O}=\text{S}\text{Cl}_2$. The dichloride of **sulfurous** acid $\text{O}=\text{S}(\text{OH})_2$ (note the contrast to sulfuric acid which is H_2SO_4).

Thionyl chloride reacts with alcohols to form an inorganic ester under HCl elimination.



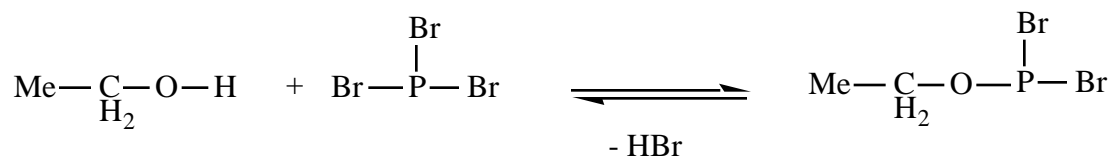
The HCl generated then initiates a bimolecular nucleophilic substitution of the inorganic ester. This ester is a very good leaving group because it forms SO_2 and HCl.



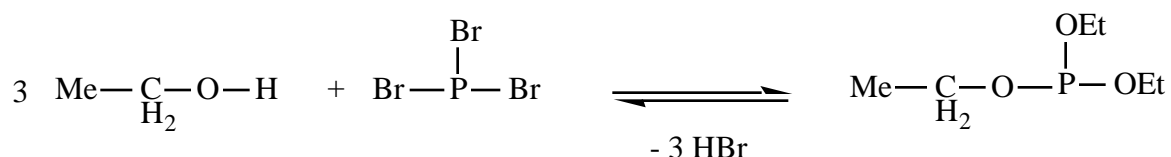
Phosphorus Tribromide in Bromoalkane Synthesis

Phosphorous tribromide is PBr_3 . The tribromide of **hypophosphorous** acid $\text{P}(\text{OH})_3$ or $\text{HP}(\text{O})(\text{OH})_2$.

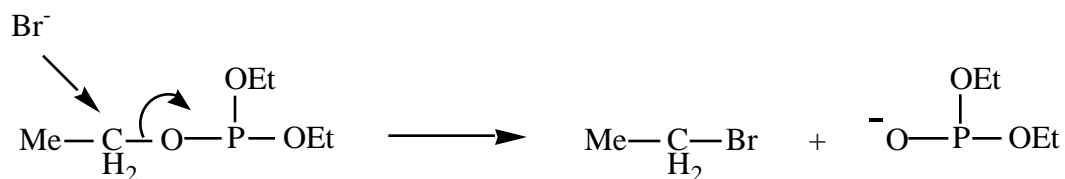
Phosphorous tribromide reacts with alcohols to form an inorganic ester under HBr elimination.



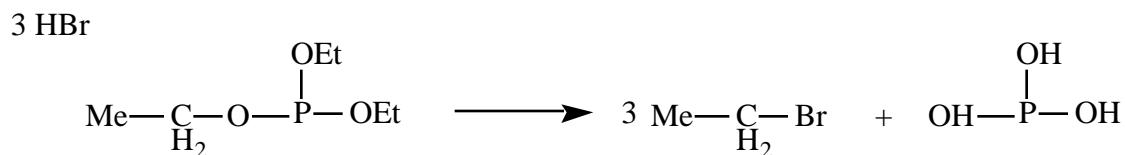
This reaction can be repeated until all P-Br bonds are replaced by the bonds to the alcohol. This leads to the **triester**.



The HBr generated then initiates a bimolecular nucleophilic substitution of the inorganic ester. This ester is a very good leaving group. Only the first nucleophilic attack is shown. The other two esters groups can be attacked in the same way and the overall reaction is shown below.



Overall reaction:



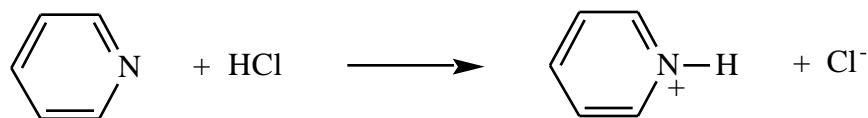
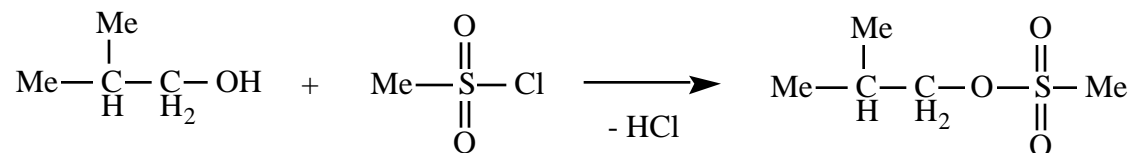
Alkylsulfonates in Substitution Reactions

Sulfonates are very good leaving groups in S_N (and E) reactions.

Sulfonates are best prepared by reaction of an alcohol with a **sulfonyl chloride**.

The reaction generates HCl and pyridine is used to capture the HCl before it can do an S_N (and E) reactions. The pyridine binds the HCl forming pyridinium chloride.

Example: 2-methyl-1-propanol and Mesyl chloride (methanesulfonyl chloride)



The sulfonates are very well suited for the preparation of **iodides** and of **mercaptanes**.

Example 1: Mesylate of 1-propanol reacts with iodide

Example 2: Tosylate of 2-propanol reacts with EtS^-

Ethers

Nomenclature and Properties

Symmetrical ethers are R-O-R and unsymmetrical ethers are R-O-R'

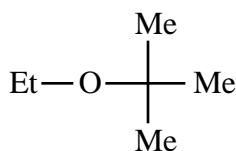
Trivial names are based on naming the alkyl groups before the word “ether”

Example: Diethyl ether

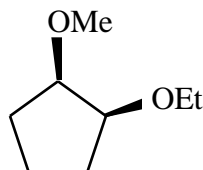
IUPAC nomenclature names the RO as a substituent with the name “alkoxy”.

Example 1: Ethoxyethane is EtOEt

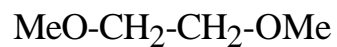
Example 2: 2-ethoxy-2-methylpropane



Example 3: *cis* 1-ethoxy-2-methoxycyclopentane

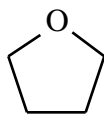


Example 4: 1,2-dimethoxyethane; aka glycol dimethyl ester or glyme

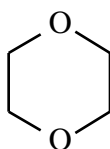


Cyclic ethers are named after the respective cycloalkane and the replacement of CH_2 by O is indicated by the suffix “oxa”.

Example 1: THF (Tetrahydrofuran) is oxacyclopentane

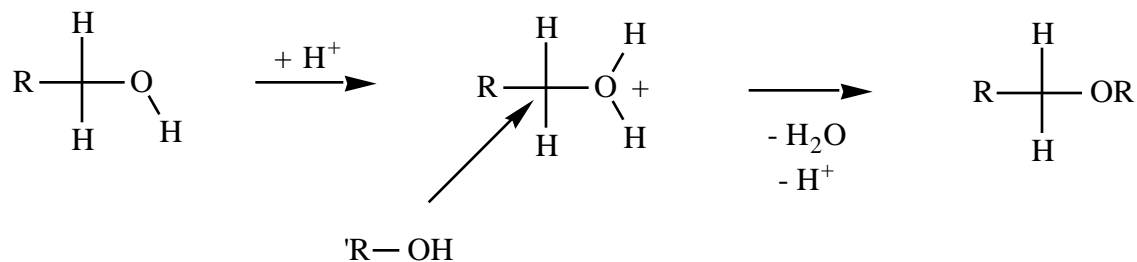


Example 2: 1,4-Dioxane is 1,4-dioxacyclohexane

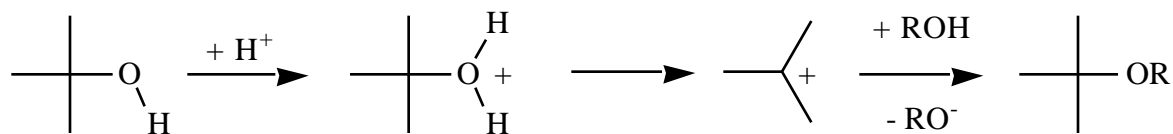


Ether Synthesis by Acid-Catalyzed Alcohol Dimerization

We have learned that we can use alcohols to make bromides, for example, by addition of HBr to alcohols. We have also learned that alcohols react with other acids with more delocalized anions under elimination. There is, however, also a possibility to form ethers if a **nonnucleophilic acid is used at high temperature**. If the temperature gets too high, then ether formation is no longer observed but instead alkenes are formed.



For secondary and tertiary alcohols, the carbenium ion is made which then catches an alcohol to form the ether.

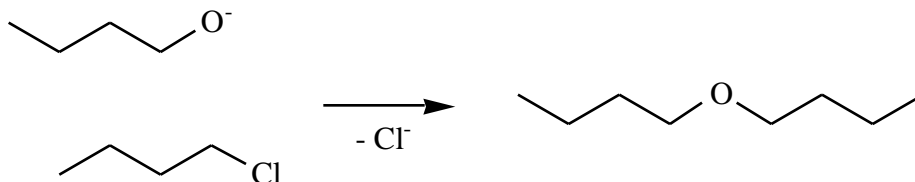


Mixed ethers can be made well if one of the alcohols is tertiary and the other one is primary. The tertiary alcohol will form the carbenium ion fast and the primary alcohol will be fast at the trapping the carbenium ion made.

Williamson Ether Synthesis

An alkoxide is reacted with a primary alkylhalide in a bimolecular nucleophilic substitution. The alcohol can be used as the solvent. Other suitable solvents are DMSO or HMPA.

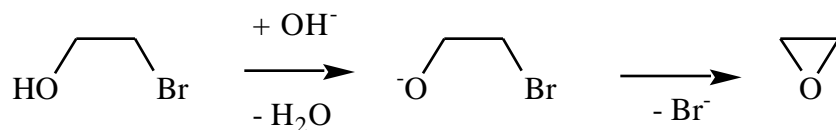
Example: 1-Butoxybutane from $n\text{-BuO}^-\text{Na}^+$ and Cl-Bu in DMSO as solvent.



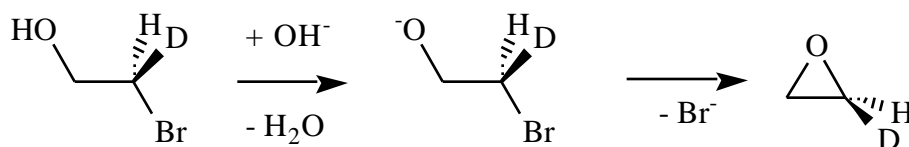
Intramolecular reaction of haloalcohols leads to cyclic ethers.

This reaction uses hydroxide to form the alkoxide which then undergoes intramolecular reaction.

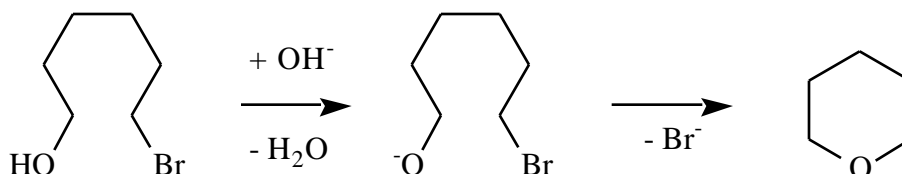
Example: Ethyleneoxide formation from beta-bromoethanol.



This reaction is stereospecific and involves inversion of configuration at the C-atom that carries the bromide.



Example: Oxacyclohexane.

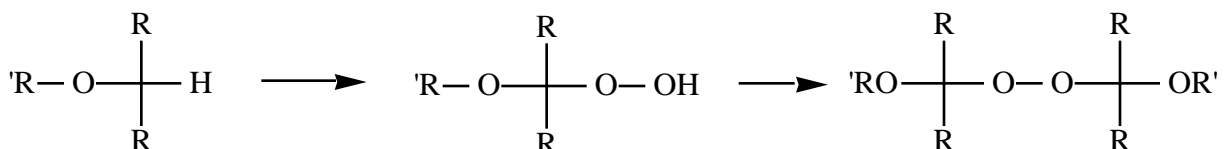


Reactions of Ethers

Autoxidation of Ethers

WARNING: Ethers can turn into explosives when exposed to air. This is what happens.

Ether hydroperoxides are formed in a radical reaction. The reaction may go on to form an ether peroxide as shown.



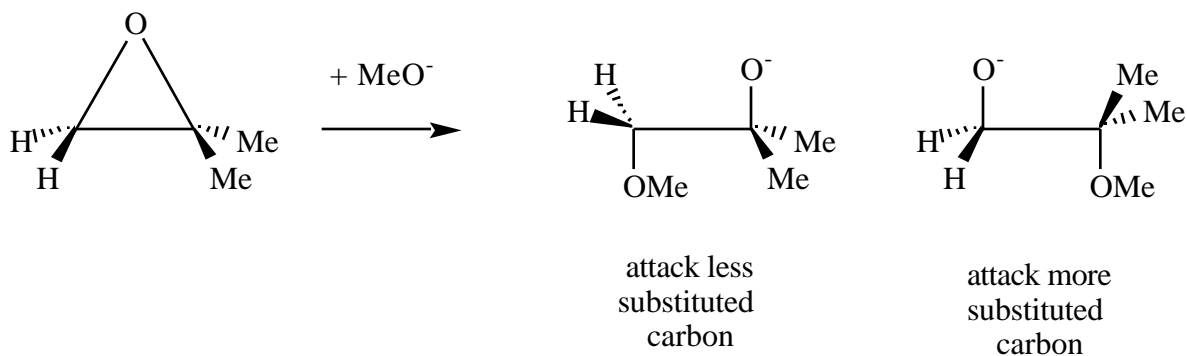
Alkyloxonium Ion Formation and Ether Cleavage

Ethers can be protonated to form alkyloxonium ions. The nucleophile (from the acid) then comes in and kicks the alcohol out (the group leaving group generated by protonation).

Not so important.

Ring-Opening Reactions of Ethyleneoxides

Interesting regiochemistry! Two products are possible and the reaction can be manipulated so that either one can be obtained.



Under basic conditions (e.g. methoxide ions in methanol), the nucleophile attacks the less substituted carbon.

==> $\text{S}_{\text{N}}2$ occurs at the less substituted carbon faster.

Under acidic conditions (e.g. H_2SO_4 in methanol), the nucleophile attacks the more substituted carbon.

==> Protonation causes O-C bond polarization and the more substituted carbon carries more of the positive charge. That is where the nucleophile attacks in the more $\text{S}_{\text{N}}1$ like reaction.