

# Alcohols and Ethers

## Structure and Nomenclature

- The common naming names alcohols as alkyl alcohols (eg: methyl alcohol)
- The common names of ethers have the groups attached to the oxygen atom listed in alphabetical order followed by the word "ether" (eg: Ethly methyl ether)
- The RO group is called an alkoxy group (eg: OCH<sub>3</sub> is methoxy)

## Physical Properties of Alcohols and Ethers

- Ethers have boiling points that are roughly comparable with those of hydrocarbons of the same molecular weight (unlike alcohols, which have higher)
- Ethers can form hydrogen bonds with other molecules (eg: water) but not with other ethers and are, therefore, similarly soluble to those of alcohols of the same molecular weight

## Synthesis of Alcohols from Alkenes

- Well, here's where you cry yourself a river if you don't remember (or want to remember) acid-catalyzed hydration of alkenes, oxymercuration-demercuration, and hydroboration-oxidation reactions
- What's different about this chapter is that the starting reactants are alcohols, not alkenes/alkynes

## Reactions of Alcohols

- The reactions of alcohols has to do with improving the poor nature of the hydroxyl leaving group
- Protonation of the alcohol converts a poor leaving group (eg: OH) into a good one (eg: H<sub>2</sub>O)
- In H<sup>+</sup>, the hydroxyl group is protonated, becomes a good LG, and a nucleophile substitutes on
- If the nucleophile is ROH, OR substitutes on to make an ether

## Alcohols as Acids

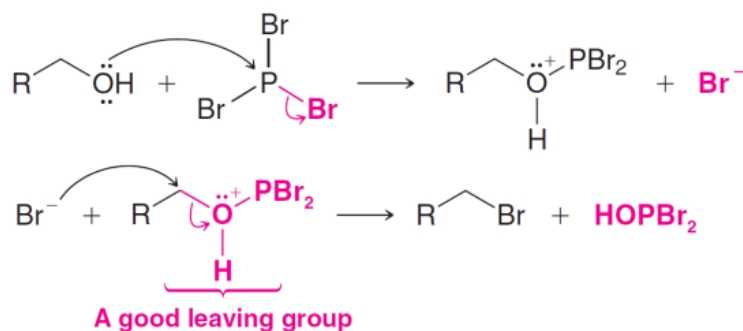
- Alcohols are about as acidic as water
- Sterically hindered alcohols are less acidic/more basic
- All alcohols are stronger acids than terminal alkynes, hydrogen, ammonia, and alkanes
- Conjugate bases of compounds with higher  $pK_a$  values than an alcohol will deprotonate it

### Alkyl Halides from the Reaction of Alcohols with Hydrogen Halides

- 2°, 3°, allylic, and benzylic alcohols go through an  $S_N1$  reaction with the protonated alcohol acting as the substrate when reacted with concentrated HX
- 1° alcohols and methanol react to form alkyl halides in concentrated HX by an  $S_N2$  mechanism where the halide anion substitutes for the water molecule LG
- Rearrangements still typically occurs here, as we've done time and time again in Chapter 8
- Racemic mixtures are produced due to the creation of the carbocation
- Elimination does not occur due to the high concentration of  $X^-$  anions in the concentrated HX solution

### Alkyl Halides from the Reaction of Alcohols with $PBr_3$ or $SOCl_2$

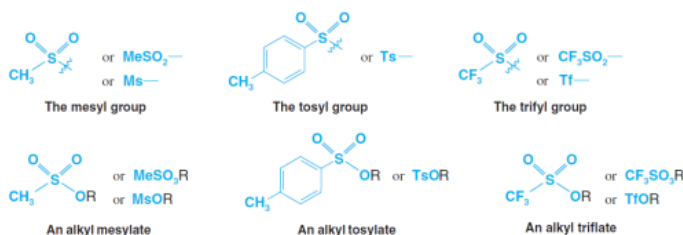
- $PBr_3$  or  $SOCl_2$  can be used to convert a 1° or 2° alcohol to a leaving group without worrying about rearrangement
- The reaction of an alcohol with  $PBr_3$  does not involve the formation of a carbocation, and, therefore, does *not* go through rearrangement
- $3ROH + PBr_3 \rightarrow 3RBr + H_3PO_3$ , only where ROH is 1° or 2°



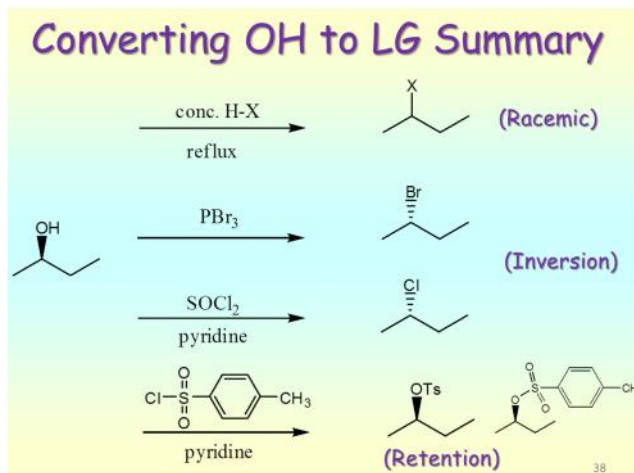
- $SOCl_2$  converts 1° and 2° alcohols to alkyl chlorides with  $C_2H_5N$  (pyridine) included to promote the reaction
- **Inversion of configuration** occurs with  $PBr_3$  and  $SOCl_2$  since it's  $S_N2$

### Tosylates, Mesylates, and Triflates: Leaving Group Derivatives of Alcohols

- The hydroxyl group of an alcohol can be converted to a good LG by conversion to a sulfonate ester derivative like the ones shown below,

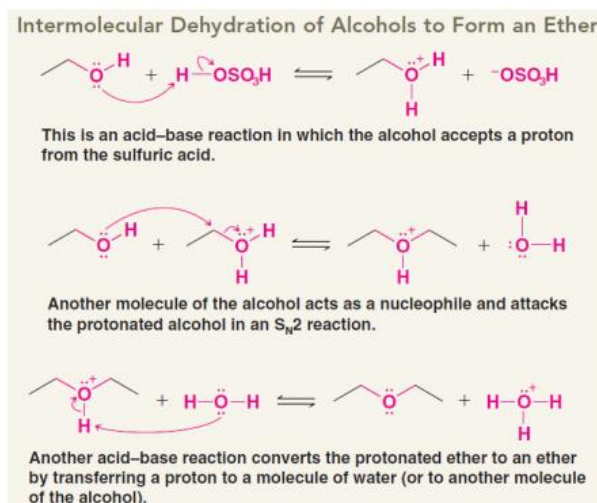


- We can prepare sulfonate esters with DMAP or pyridine and the chlorinated sulfonate derivative
- There is **retention of configuration** in the formation of a sulfonate ester because the C–O bond is not involved, as with pyridine

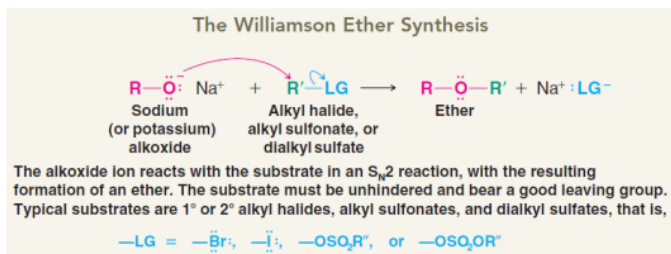


### Synthesis of Ethers

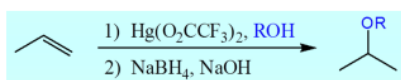
- Alcohols can dehydrate to form alkenes, as done in Chapter 7. Also,  $1^\circ$  alcohols can dehydrate to form ethers



- Alkenes form too easily for  $2^\circ$  and  $3^\circ$  alcohols to form ethers
- Acid-catalyzed dehydration is not useful for preparing unsymmetrical ethers from different  $1^\circ$  alcohols because the reaction leads to a mixture of products ( $\text{ROR}$ ,  $\text{ROR}'$ , and  $\text{R}'\text{OR}'$ )
- A **Williamson Synthesis** converts the hydroxyl group to an alkoxide ion

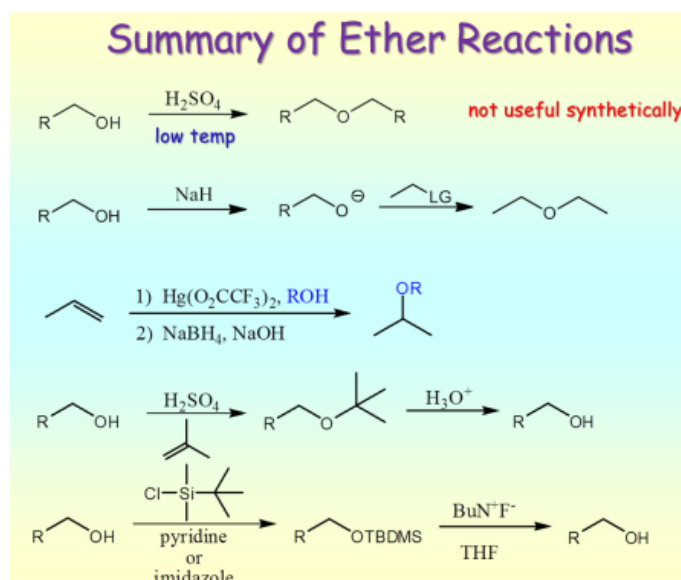


- When NaH is a reactant, the hydride anion acts as a base to form hydrogen gas thus turning the alcohol into a good nucleophile with O<sup>-</sup>
- Alkoxymercuration-demercuration is a method for synthesizing ethers directly from alkenes, like in the example below, and parallels oxymercuration-demercuration

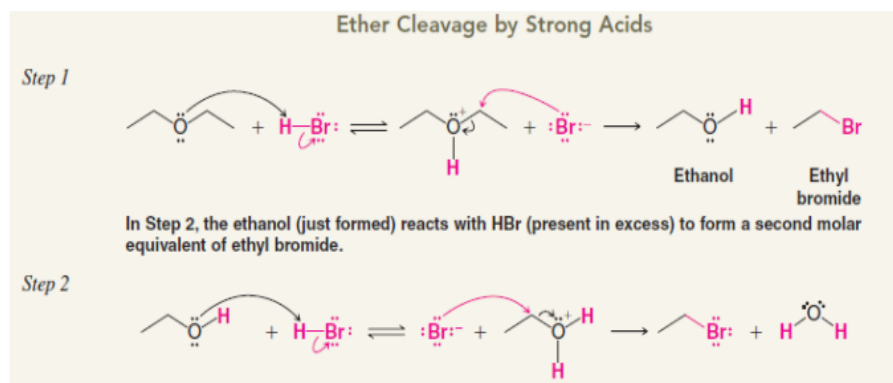


- An OH group can be protected by converting the alcohol to a temporary ether
- The reaction of 2-methylpropene and H<sub>2</sub>SO<sub>4</sub> with a primary alcohol can create a *tert*-butyl ether where the bulky substituent is a protecting group of the hydroxyl group
- Note: MTBE stands for methyl *tert*-butyl ether
- The protecting group can be removed if treated with H<sub>3</sub>O<sup>+</sup>
- A hydroxyl group can also be protected by converting it to a silyl ether group with TBDMS-Cl (chicken-footed silicon structure) as a reactant
- A fluoride anion in THF will knock out the protecting group

## Ether Summary

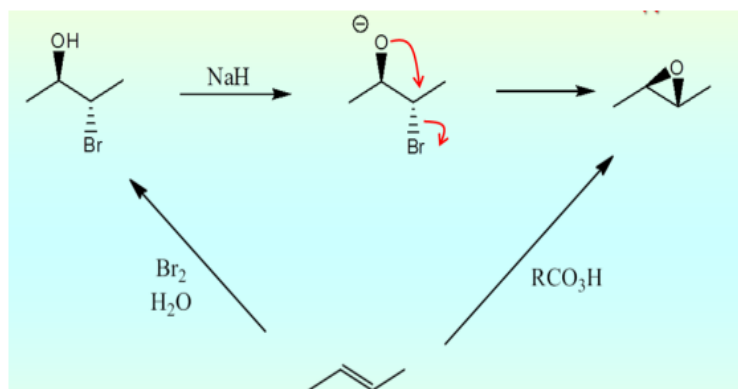


## Ether Cleavage



## Epoxides; Anti 1,2, Dihydroxylation of Alkenes Via Epoxides

- Epoxides are cyclic ethers with three-membered rings and can be prepared with an intramolecular  $S_N2$  attack



- For this reaction to occur, make sure the stereochemistry of the reactant is in a way that can allow for a center of inversion of, what was originally, the halide atom
- Epoxidation is a syn addition that is stereospecific
- $\text{RCO}_3\text{H}$  can be used to make an epoxide from an alkene (syn)

## Reactions of Epoxides

- Two Types: Acid-Catalyzed and Base-Catalyzed (both ring-opening and anti-configuration)
- BLAM: Basic = Less Substituted      Acidic = More Substituted
- The acid-catalyzed ring opening is analogous to a halohydrin reaction ( $\text{Br}_2$  in  $\text{ROH}$ )



## Alcohols from Carbonyl Compounds

### Structure of the Carbonyl Group

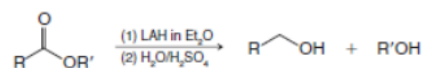
- Carbonyl compounds can go through nucleophilic addition where a pair of electrons from the C=O double bond moves up to the oxygen atom to make a negative formal charge and the nucleophile bonds to the carbon atom
- Hydride ions and carbanions are important nucleophiles in these reactions
- RedOx reactions also occur with carbonyl compounds

### Oxidation-Reduction Reactions in Organic Chemistry

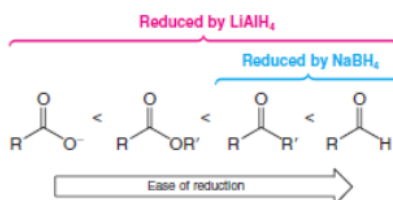
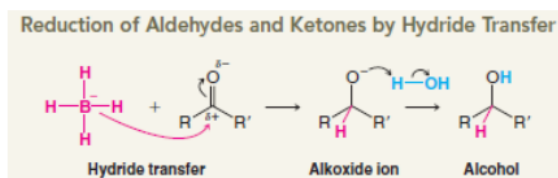
- Reduction to an organic molecule typically involves increasing hydrogen content or decreasing oxygen content
- Oxidation typically occurs with increasing oxygen content or decreasing hydrogen content
- The symbol [H] refers to reduction while [O] refers to oxidation

### Alcohols by Reduction of Carbonyl Compounds

- Reduction converts a carboxylic acid to a primary alcohol by taking off an oxygen from C=O
- Reduction converts an ester into two 1° alcohols, one derived from the carbonyl part of the ester group, and the other from the alkoxy part of the ester
- Reduction converts a ketone to a 2° alcohol and an aldehyde to a 1° alcohol



- Aldehydes and ketones are easily reduced by NaBH<sub>4</sub>

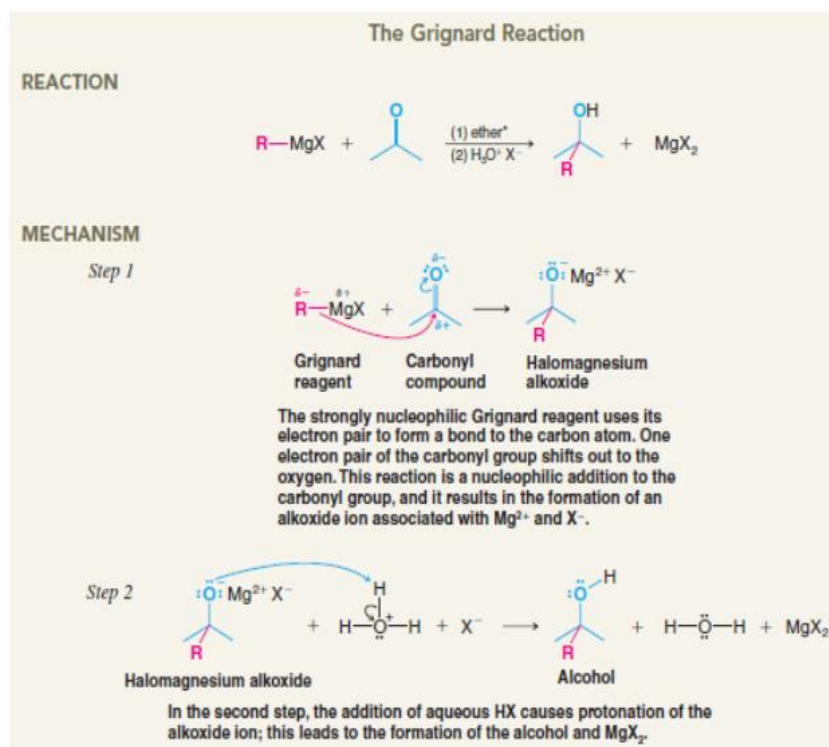


## Oxidation of Alcohols

- 1° alcohols can be oxidized to aldehydes and carboxylic acids
- PCC will convert a 1° alcohol to an aldehyde and oxidize a 2° alcohol to a ketone. NOT 3°.
- $\text{KMnO}_4$  or  $\text{H}_2\text{CrO}_4$  (Jones Reagent) can oxidize a 1° alcohol to a carboxylic acid
- Oxidizing agents based on Cr(VI) can oxidize a 2° alcohol to a ketone. One example is  $\text{H}_2\text{CrO}_4$

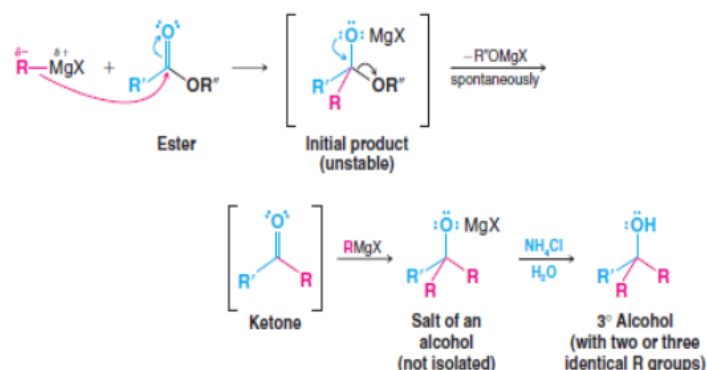
## Organometallic Compounds; Grignard Reagents

- Organometallic compounds contain carbon-metal bonds
- The general reaction to create organolithium compounds is,  $\text{RX} + 2\text{Li} \longrightarrow \text{RLi} + \text{LiX}$
- Grignard reagents are organomagnesium halides and are prepared by,  $\text{RX} + \text{Mg} \longrightarrow \text{RMgX}$
- Grignard Reagents react with any compound that has a hydrogen attached to an atom of high electronegativity (eg: oxygen, nitrogen, sulfur, etc.)
- Grignard Reagents react well with compounds that have carbonyl groups

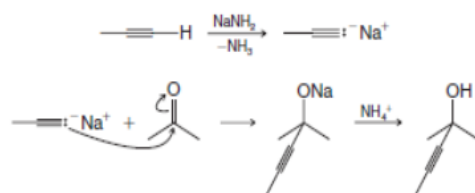


## Alcohols from Grignard Reagents

- When a Grignard reagent adds to the carbonyl group of an ester, the initial product breaks down to a ketone. Then, the ketone reacts with the excess Grignard reagent and then goes through hydrolysis to form a tertiary alcohol with two identical alkyl groups



- It is not possible to prepare a Grignard reagent from a compound that contains any hydrogen more acidic than the hydrogen atoms of an alkane or alkene
- We're essentially limited to alkyl halides or analogous organic halides containing carbon-carbon double bonds, intermolecular triple bonds, ether linkages, and NR<sub>2</sub> groups
- Acetylenic Grignard reagents can be made by allowing terminal alkynes to react with alkyl Grignard reagents (similar to what we did with NaNH<sub>2</sub>)
- Organolithium reagents react with carbonyl compounds in the same way as Grignard reagents
- Sodium alkynides react with aldehydes and ketones to yield alcohols



## Protecting Groups

- Protecting groups can be used to perform a Grignard synthesis with a compound that has a relatively acidic hydrogen by protecting that group and then taking off the protecting group with a fluoride anion