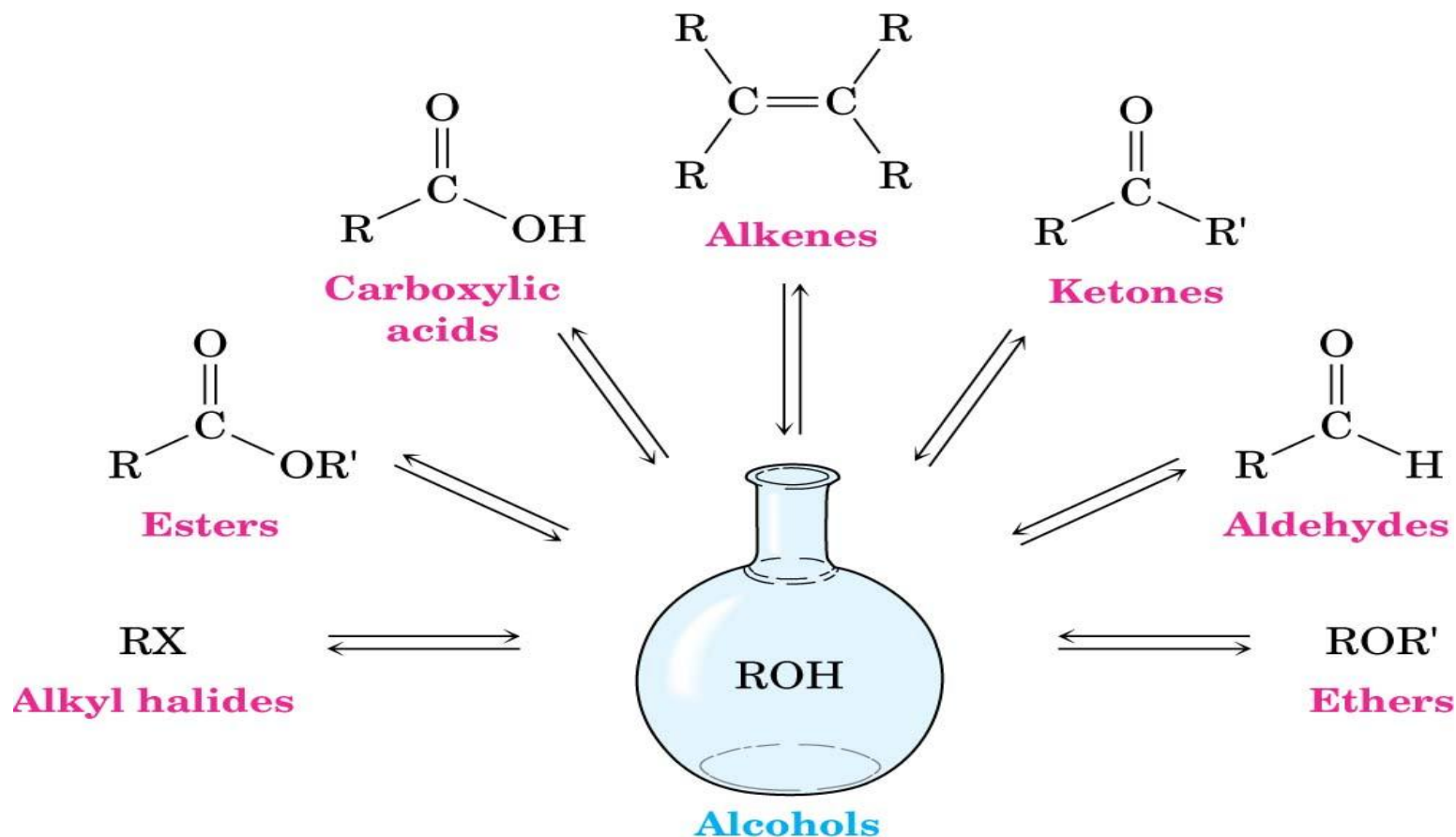


Preparation of Alcohols: an Overview

- Alcohols are derived from many types of compounds
- The alcohol hydroxyl can be converted to many other functional groups. This makes alcohols useful in synthesis



Preparation of Alcohols

- **Hydration of Alkenes**
- BH_3/THF followed by H_2O_2 in NaOH
- $\text{Hg}(\text{OAc})_2$ followed by NaBH_4
- OsO_4 followed by NaHSO_3 (cis-1,2-diols)
- RCO_3H followed by aqueous acid (trans-1,2-diols)

- **From Aldehydes and Ketones**
- Reduction with NaBH_4
 - Reduces alpha beta unsaturated carbonyls as well
- Reduction with LiAlH_4
 - Doesn't touch alpha beta unsaturated carbonyls

- **From Esters**
 - Reduction with LiAlH_4 (LAH)
 - No reaction with NaBH_4

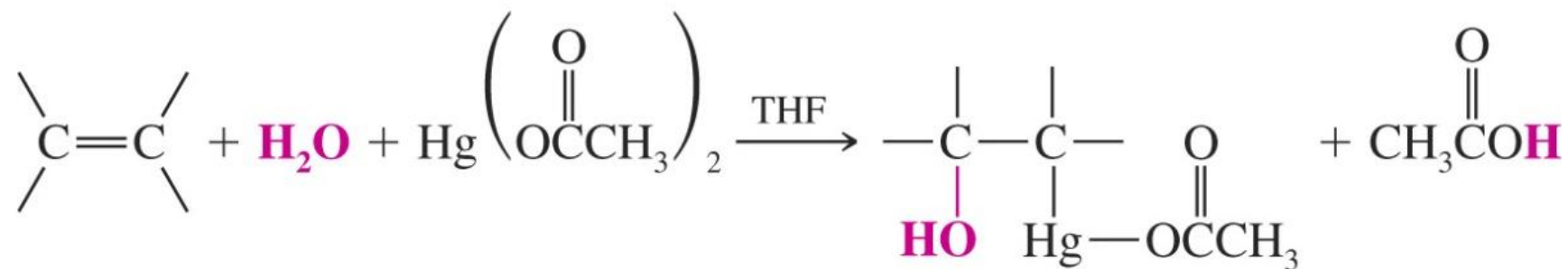
Synthesis - Hydration of alkenes

- **Acid-Catalyzed Hydration (Markovnikov)**
 - $\text{H}_3\text{O}^+/\text{H}_2\text{O}$ OR warm, dilute H_2SO_4 , H_2O
- **Oxymercuration/Demercuration (Markovnikov)**
 - 1. $\text{Hg}(\text{OAc})_2$ THF/ H_2O
 - 2. NaBH_4 , NaOH
- **Hydroboration/Oxidation (Anti-Markovnikov)**
 - 1. BH_3 : THF
 - 2. H_2O_2 , NaOH

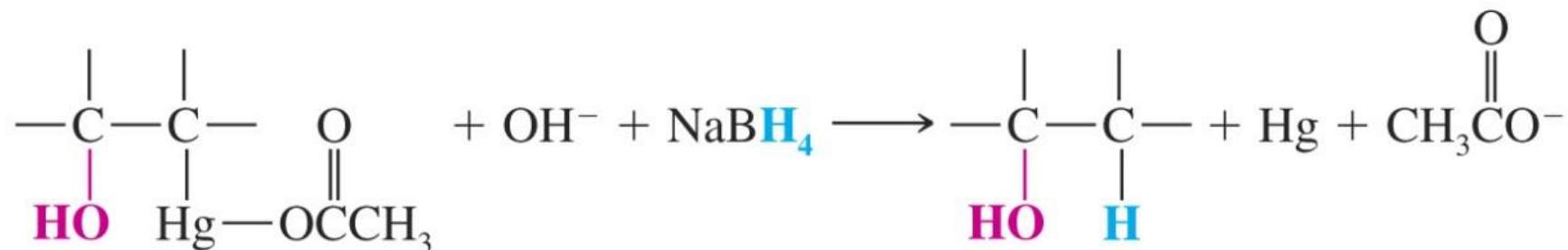
Oxymercuration-demercuration

This is a Markovnikov addition which occurs **without** rearrangement.

Oxymercuration



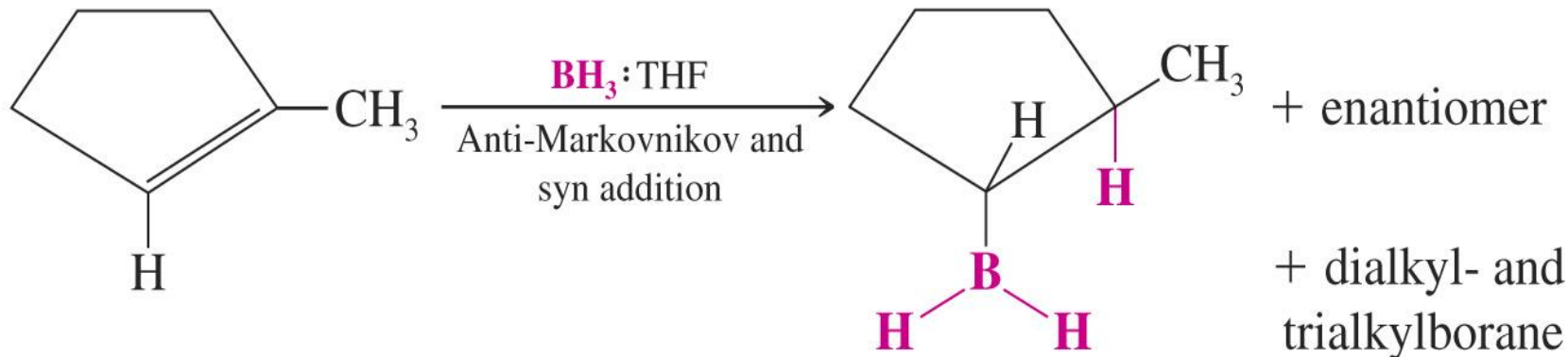
Demercuration



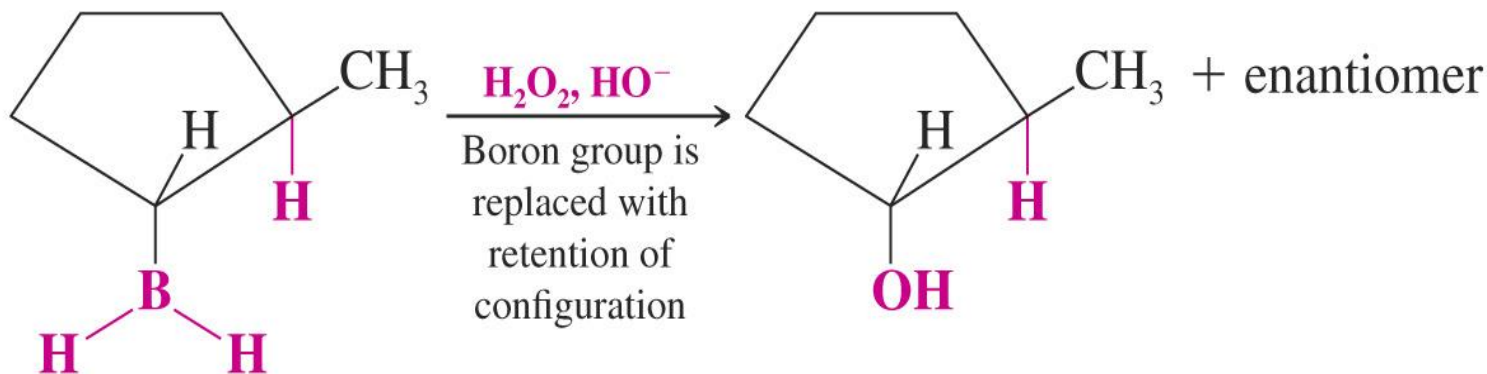
Hydroboration-Oxidation

This addition reaction occurs with anti-Markovnikov regiochemistry and syn stereochemistry

Hydroboration



Oxidation



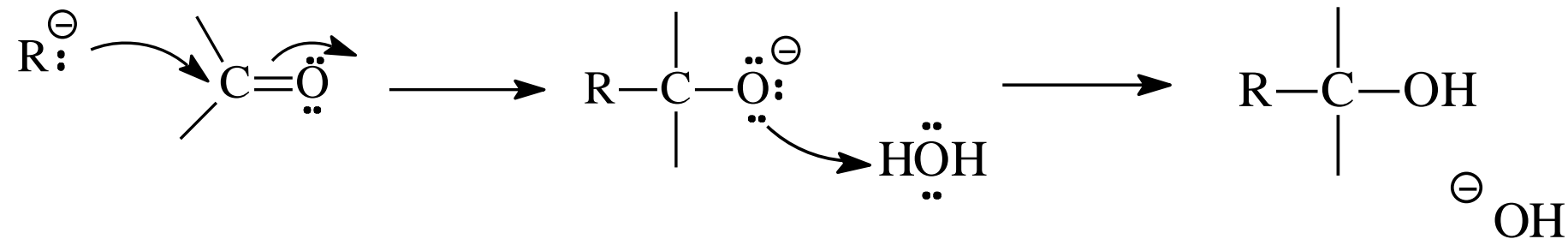
Glycols

- Syn hydroxylation of alkenes
 - osmium tetroxide, hydrogen peroxide
 - cold, dilute, basic potassium permanganate

- Anti hydroxylation of alkenes
 - peroxyacids, hydrolysis

From Carbonyl Compound

- $R:^-$ attacks the partially positive carbon in the carbonyl.
- The intermediate is an alkoxide ion.
- Addition of water or dilute acid protonates the alkoxide to produce an alcohol.



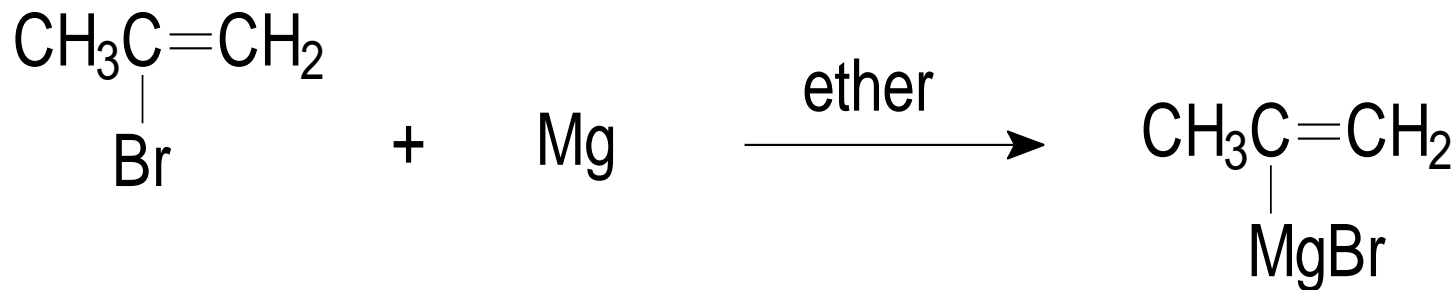
Organometallic Reagents

- Carbon is bonded to a metal (Mg or Li).
- Carbon is nucleophilic (partially negative).
- It will attack a partially positive carbon.
 - C - X
 - C = O
- A new carbon-carbon bond forms.

Grignard Reagents

- Formula R-Mg-X (reacts like $R:^- + MgX$)
- Stabilized by anhydrous ether
- May be formed from any halide
 - primary
 - secondary
 - tertiary
 - vinyl
 - aryl

Some Grignard Reagents



Organolithium Reagents

Formula R-Li (reacts like $R:^- \text{}^+Li$)

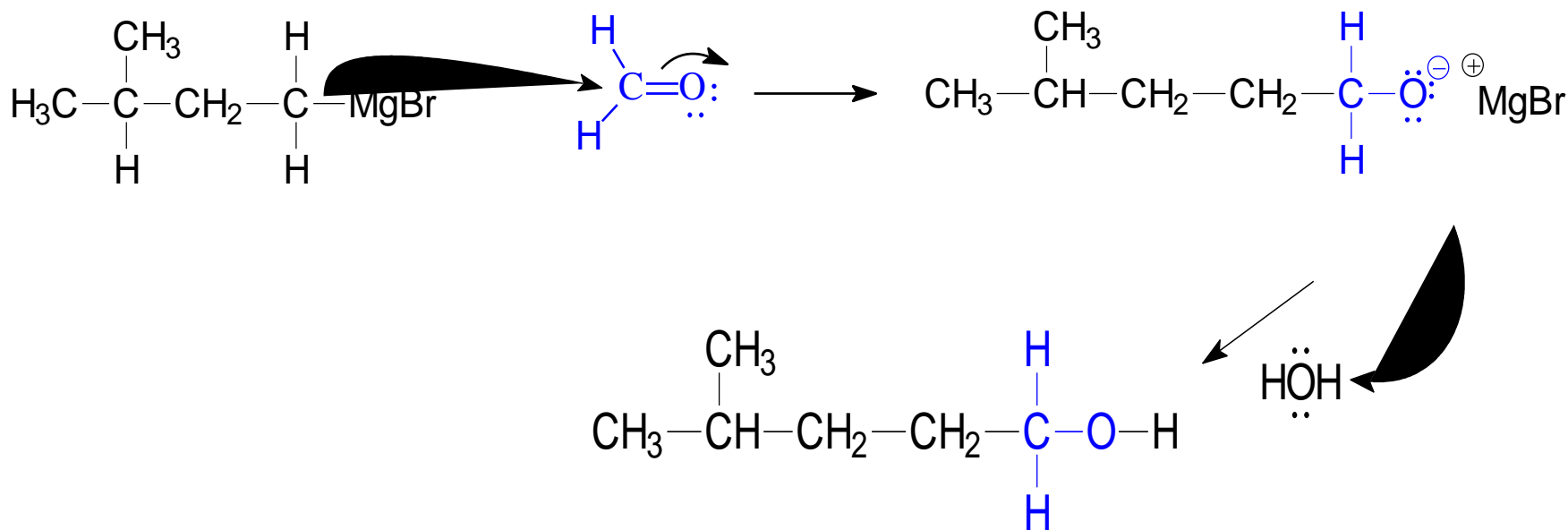
Can be produced from

- Alkyl halides
- Vinyl halides or
- aryl halides, just like Grignard reagents.

Ether not necessary, wide variety of solvents can be used.

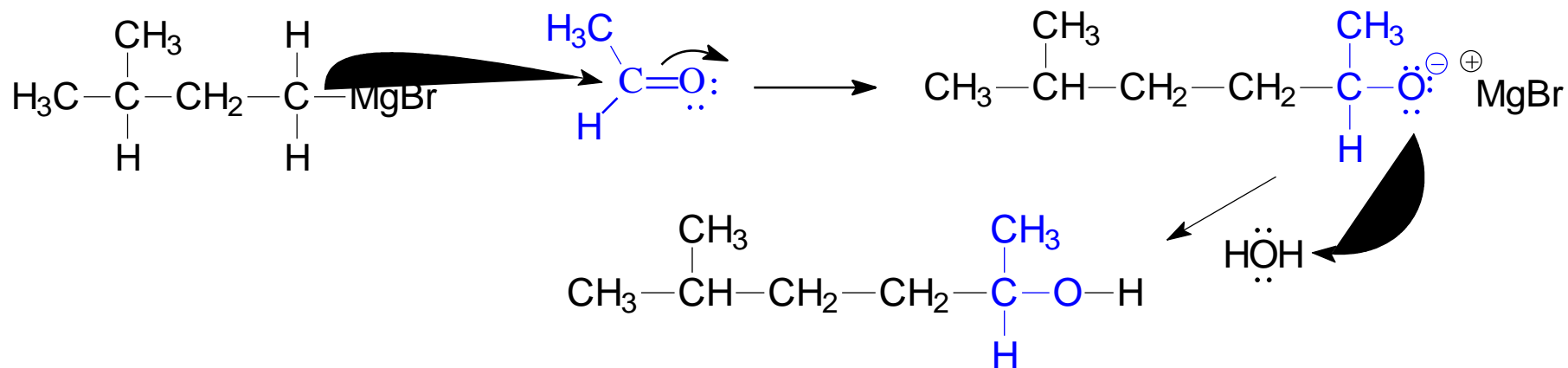
Synthesis of 1° Alcohols

Grignard + formaldehyde yields a primary alcohol with one additional carbon.



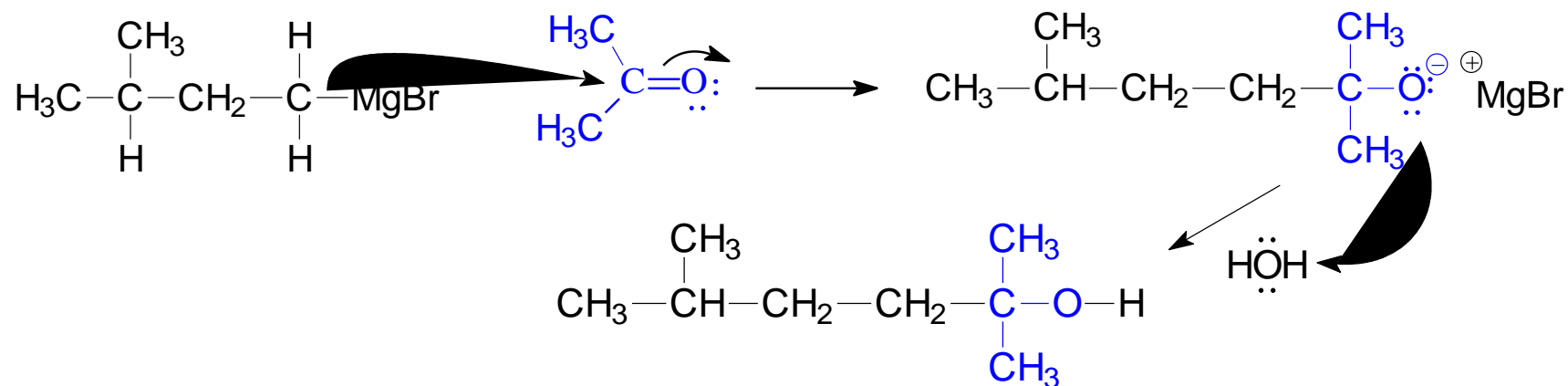
Synthesis of 2° Alcohols

Grignard + aldehyde yields a secondary alcohol.

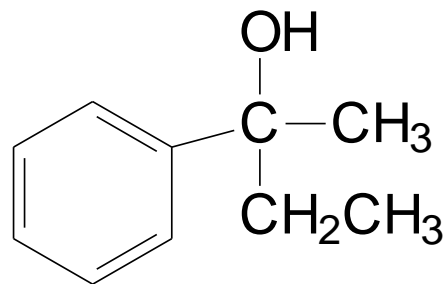
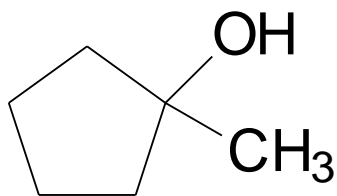
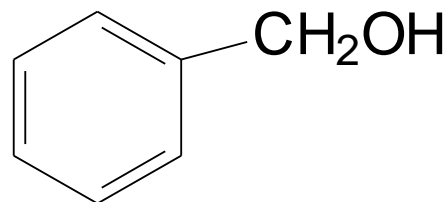
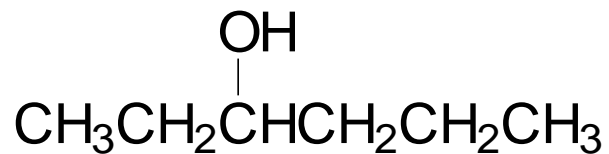


Synthesis of 3° Alcohols

Grignard + ketone yields a tertiary alcohol.



How would you synthesize...

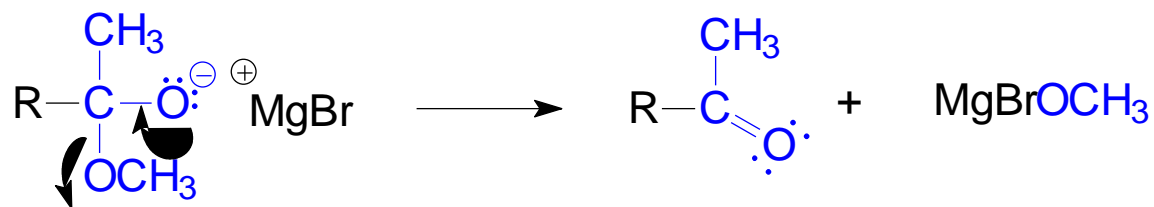
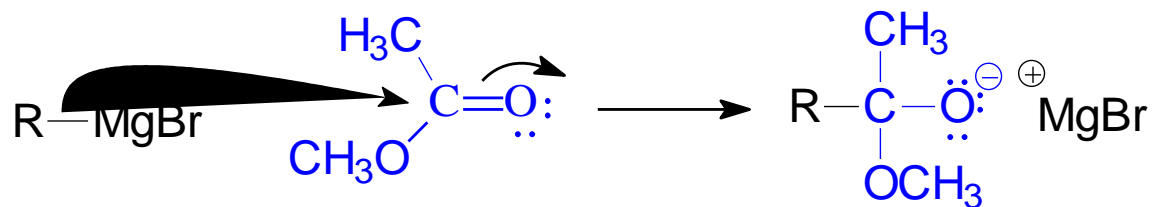
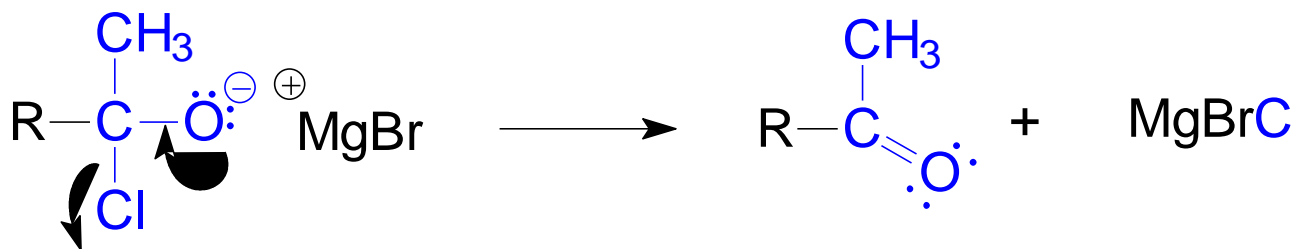
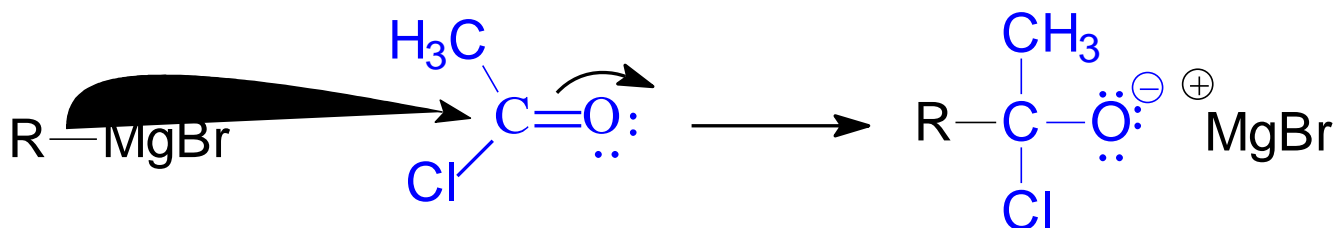


Grignard Reactions with Acid Chlorides and Esters

- Use two moles of Grignard reagent.
- The product is a tertiary alcohol with two identical alkyl groups.
- Reaction with one mole of Grignard reagent produces a ketone intermediate, which reacts with the second mole of Grignard reagent.

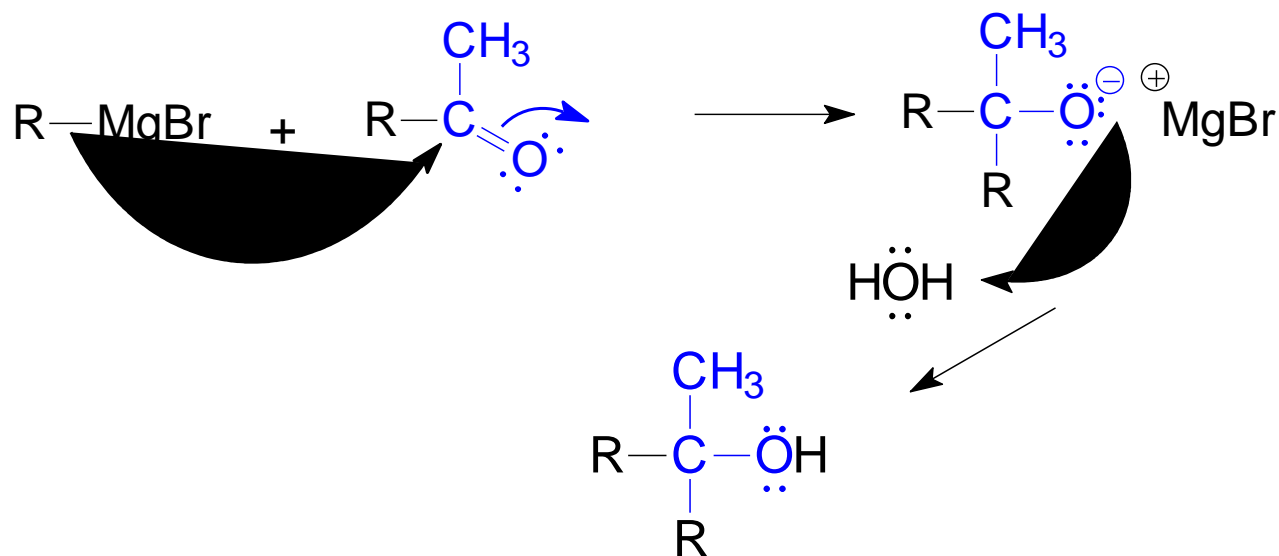
Grignard + Acid Chloride/Ester

- Grignard attacks the carbonyl.
- Chloride/ Alkoxide ion leaves.



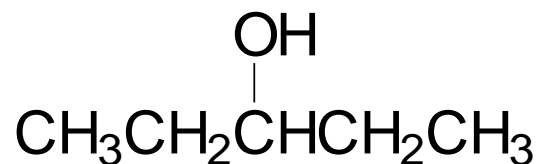
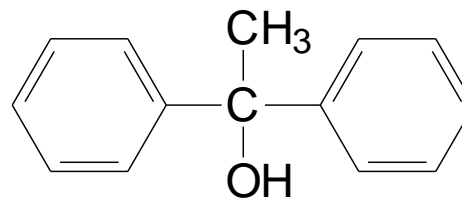
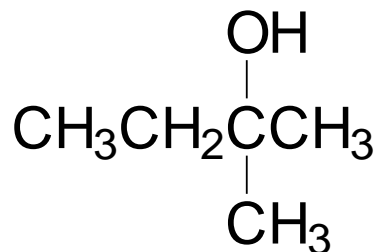
Second step of reaction

- Second mole of Grignard reacts with the ketone intermediate to form an alkoxide ion.
- Alkoxide ion is protonated with dilute acid.



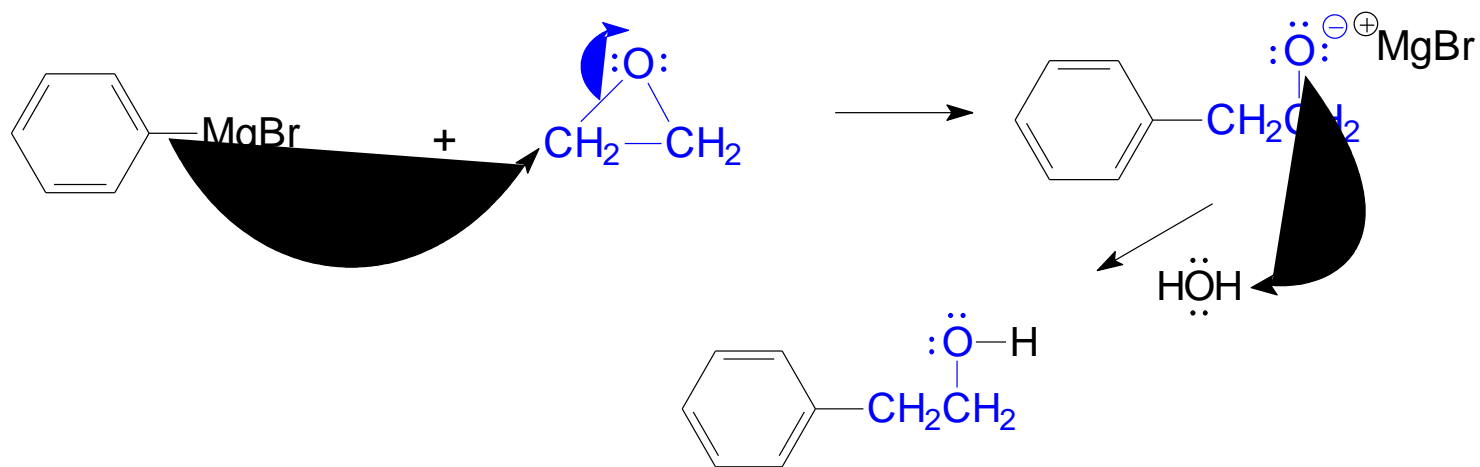
How would you synthesize...

Using an acid chloride or ester.



Grignard Reagent + Ethylene Oxide

- Epoxides are unusually reactive ethers.
- Product is a 1° alcohol with 2 additional carbons.

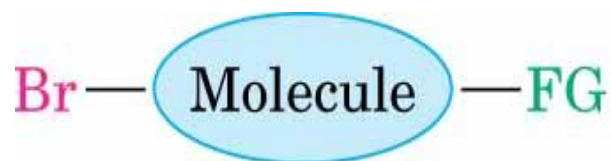


Limitations of Grignard

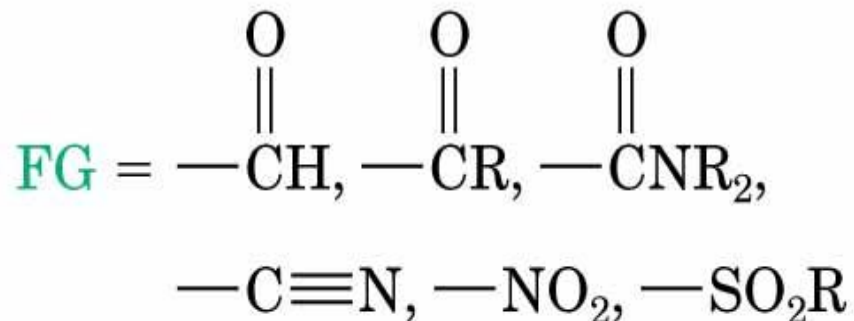
- No water
- No other acidic protons like O-H, N-H or S-H. Grignard reagent is destroyed, becomes an alkane.
- No other electrophilic multiple bonds, like C=N, C—N, S=O, or N=O.

Limitations of Grignard

- Can't be prepared if there are reactive functional groups in the same molecule, including proton donors.



The Grignard reagent is protonated by these groups.



The Grignard reagent adds to these groups.