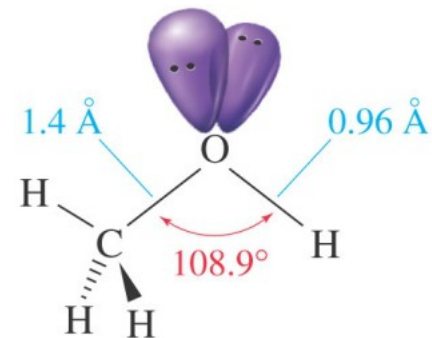


*Organic Chemistry*, 7<sup>th</sup> Edition  
L. G. Wade, Jr.

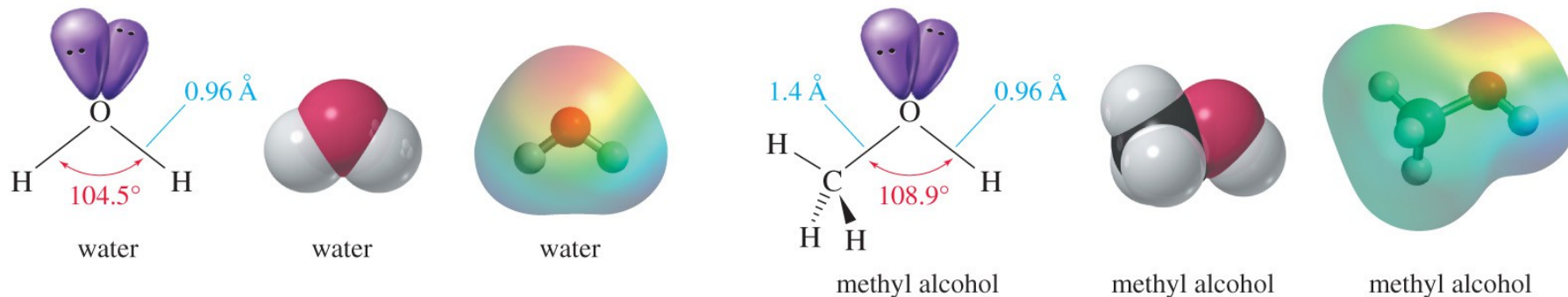


# Chapter 10

## Structure and Synthesis of Alcohols

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# Structure of Water and Methanol



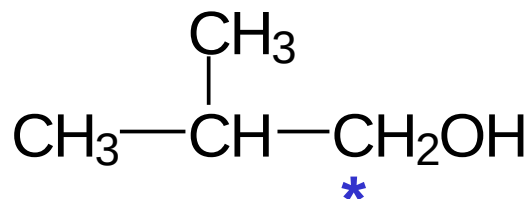
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- Oxygen is  $sp^3$  hybridized and tetrahedral.
- The H—O—H angle in water is  $104.5^\circ$ .
- The C—O—H angle in methyl alcohol is  $108.9^\circ$ .

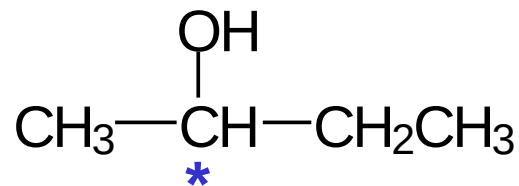
# Classification of Alcohols

- Primary: carbon with —OH is bonded to one other carbon.
- Secondary: carbon with —OH is bonded to two other carbons.
- Tertiary: carbon with —OH is bonded to three other carbons.
- Aromatic (phenol): —OH is bonded to a benzene ring.

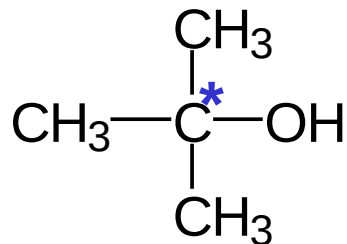
# Examples of Classifications



Primary alcohol



Secondary alcohol

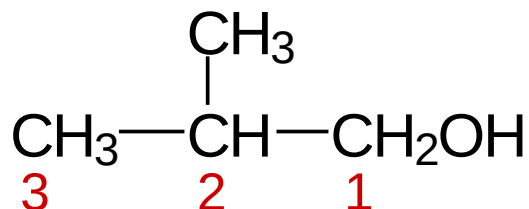


Tertiary alcohol

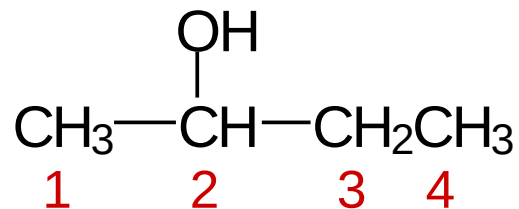
# IUPAC Nomenclature

- Find the longest carbon chain containing the carbon with the —OH group.
- Drop the -e from the alkane name, add -ol.
- Number the chain giving the —OH group the lowest number possible.
- Number and name all substituents and write them in alphabetical order.

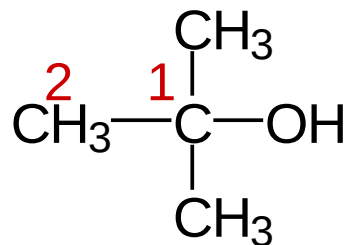
# Examples of Nomenclature



2-methyl-1-propanol  
2-methylpropan-1-ol



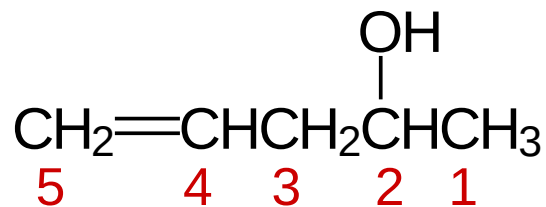
2-butanol  
butan-2-ol



2-methyl-2-propanol  
2-methylpropan-2-ol

# Alkenols (Enols)

- Hydroxyl group takes precedence. Assign the carbon with the —OH the lowest number.
- End the name in *-ol*, but also specify that there is a double bond by using the ending *-ene* before *-ol*



4-penten-2-ol

pent-4-ene-2-ol

# Naming Priority

*Highest ranking*



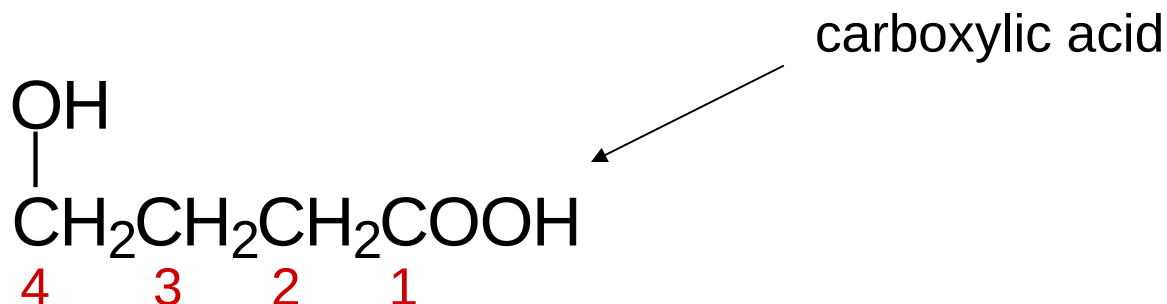
*Lowest ranking*

1. Acids
2. Esters
3. Aldehydes
4. Ketones
5. Alcohols
6. Amines
7. Alkenes
8. Alkynes
9. Alkanes
10. Ethers
11. Halides



# Hydroxy Substituent

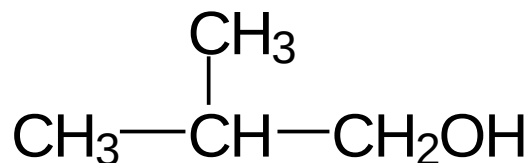
- When —OH is part of a higher priority class of compound, it is named as hydroxy.



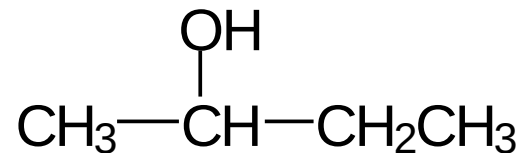
4-hydroxybutanoic acid  
*also known as -hydroxybutyric acid (GHB)*

# Common Names

- Alcohol can be named as alkyl alcohol.
- Useful only for small alkyl groups.



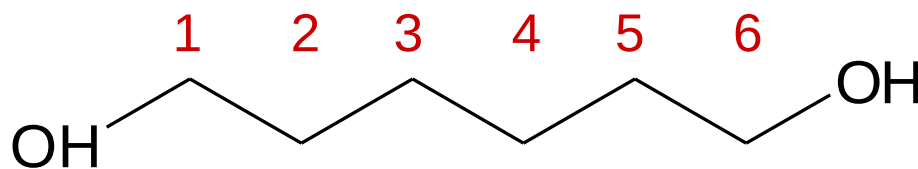
isobutyl alcohol



sec-butyl alcohol

# Naming Diols

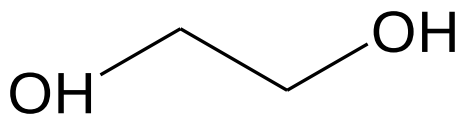
- Two numbers are needed to locate the two —OH groups.
- Use -diol as suffix instead of -ol.



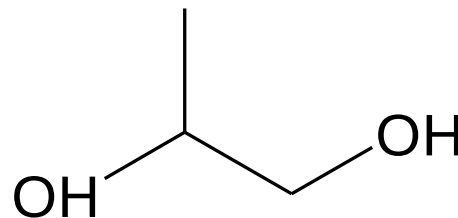
hexane-1,6- diol

# Glycols

- 1, 2-diols (vicinal diols) are called glycols.
- Common names for glycols use the name of the alkene from which they were made.



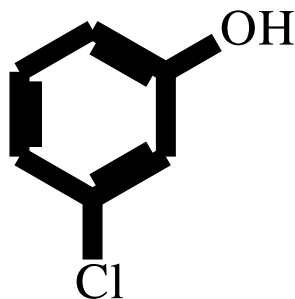
ethane-1,2- diol  
*ethylene glycol*



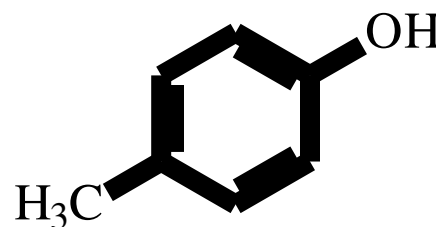
propane-1,2- diol  
*propylene glycol*

# Phenol Nomenclature

- —OH group is assumed to be on carbon 1.
- For common names of disubstituted phenols, use *ortho-* for 1,2; *meta-* for 1,3; and *para-* for 1,4.
- Methyl phenols are cresols.



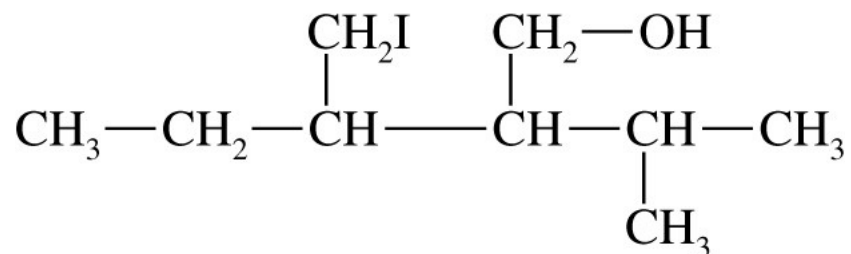
3-chlorophenol  
(*meta*-chlorophenol)



4-methylphenol  
(*para*-cresol)

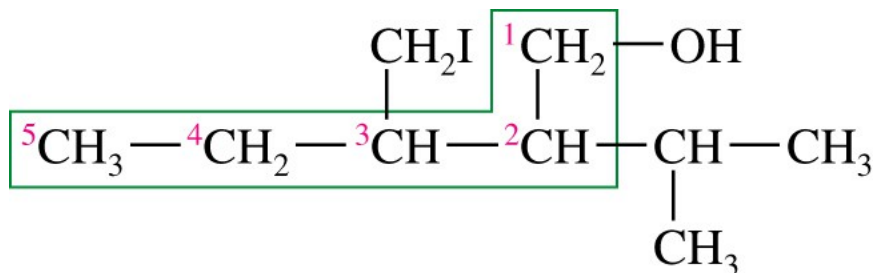
# Solved Problem 1

Give the systematic (IUPAC) name for the following alcohol.



## Solution

The longest chain contains six carbon atoms, but it does not contain the carbon bonded to the hydroxyl group. The longest chain containing the carbon bonded to the —OH group is the one outlined by the green box, containing five carbon atoms. This chain is numbered from right to left in order to give the hydroxyl-bearing carbon atom the lowest possible number.

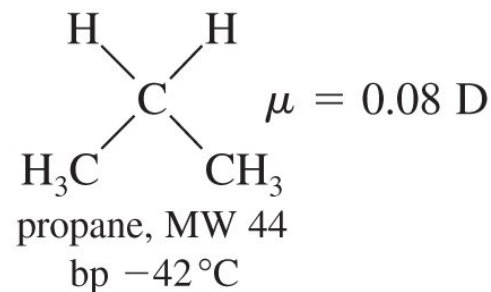
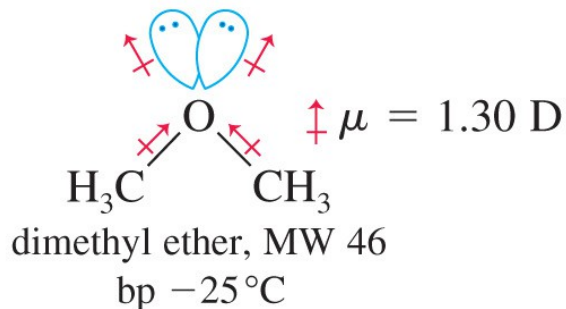
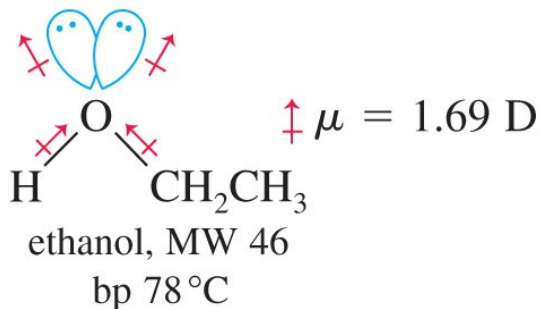


The correct name for this compound is 3-(iodomethyl)-2-isopropylpentan-1-ol.

# Physical Properties

- Alcohols have high boiling points due to hydrogen bonding between molecules.
- Small alcohols are miscible in water, but solubility decreases as the size of the alkyl group increases.

# Boiling Points of alcohols



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- Alcohols have higher boiling points than ethers and alkanes because alcohols can form hydrogen bonds.
- The stronger interaction between alcohol molecules will require more energy to break them resulting in a higher boiling point.

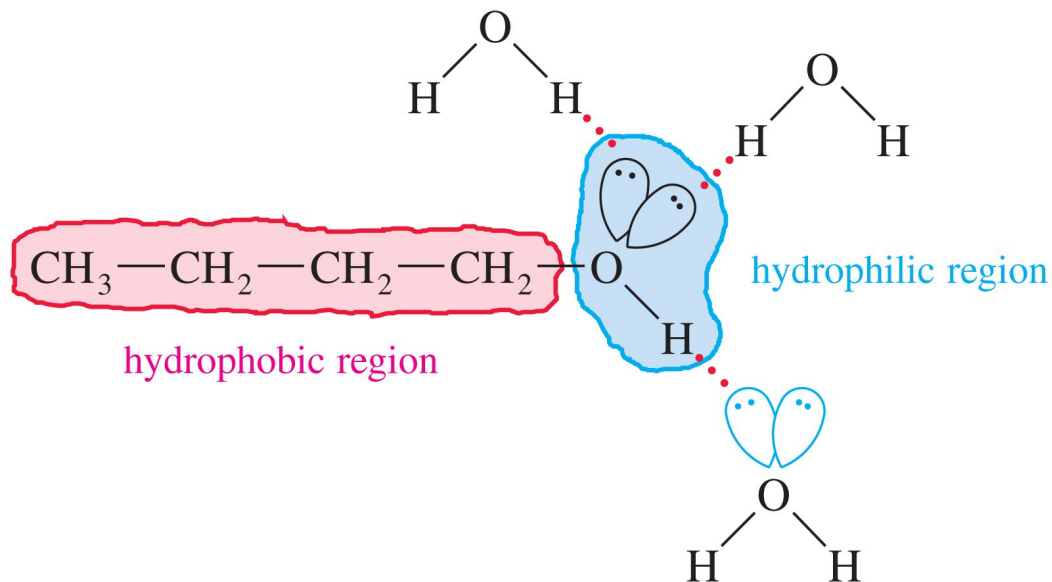


# Solubility in Water

**TABLE 10-3**

Solubility of Alcohols in Water  
(at 25 °C)

Alcohol	Solubility in Water
methyl	miscible
ethyl	miscible
<i>n</i> -propyl	miscible
<i>t</i> -butyl	miscible
isobutyl	10.0%
<i>n</i> -butyl	9.1%
<i>n</i> -pentyl	2.7%
cyclohexyl	3.6%
<i>n</i> -hexyl	0.6%
phenol	9.3%
hexane-1,6-diol	miscible



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Small alcohols are miscible in water, but solubility decreases as the size of the alkyl group increases.

# Methanol

- “Wood alcohol”
- Industrial production from synthesis gas
- Common industrial solvent
- Toxic Dose: 100 mL methanol
- Used as fuel at Indianapolis 500
  - Fire can be extinguished with water
  - High octane rating
  - Low emissions
  - Lower energy content
  - Invisible flame

# Ethanol

- Fermentation of sugar and starches in grains
- 12–15% alcohol, then yeast cells die
- Distillation produces “hard” liquors
- Azeotrope: 95% ethanol, constant boiling
- Denatured alcohol used as solvent
- Gasahol: 10% ethanol in gasoline
- Toxic dose: 200 mL

# Acidity of Alcohols

- $pK_a$  range: 15.5–18.0 (water: 15.7)
- Acidity decreases as the number of carbons increase.
- Halogens and other electron withdrawing groups increase the acidity.
- Phenol is 100 million times more acidic than cyclohexanol!

# Table of $K_a$ Values

**TABLE 10-4**

Acid-Dissociation Constants of Representative Alcohols

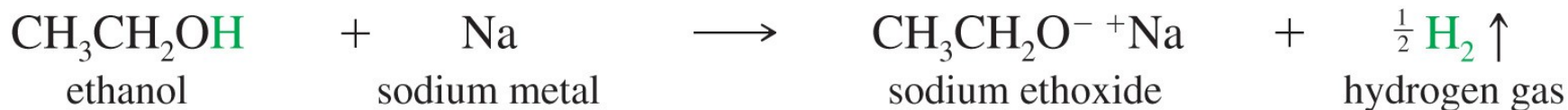
Alcohol	Structure	$K_a$	$pK_a$
methanol	$\text{CH}_3\text{—OH}$	$3.2 \times 10^{-16}$	15.5
ethanol	$\text{CH}_3\text{CH}_2\text{—OH}$	$1.3 \times 10^{-16}$	15.9
2-chloroethanol	$\text{Cl—CH}_2\text{CH}_2\text{—OH}$	$5.0 \times 10^{-15}$	14.3
2,2,2-trichloroethanol	$\text{Cl}_3\text{C—CH}_2\text{—OH}$	$6.3 \times 10^{-13}$	12.2
isopropyl alcohol	$(\text{CH}_3)_2\text{CH—OH}$	$3.2 \times 10^{-17}$	16.5
<i>tert</i> -butyl alcohol	$(\text{CH}_3)_3\text{C—OH}$	$1.0 \times 10^{-18}$	18.0
cyclohexanol	$\text{C}_6\text{H}_{11}\text{—OH}$	$1.0 \times 10^{-18}$	18.0
phenol	$\text{C}_6\text{H}_5\text{—OH}$	$1.0 \times 10^{-10}$	10.0
<i>Comparison with Other Acids</i>			
water	$\text{H}_2\text{O}$	$1.8 \times 10^{-16}$	15.7
acetic acid	$\text{CH}_3\text{COOH}$	$1.6 \times 10^{-5}$	4.8
hydrochloric acid	$\text{HCl}$	$1 \times 10^{+7}$	-7

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# Formation of Alkoxide Ions



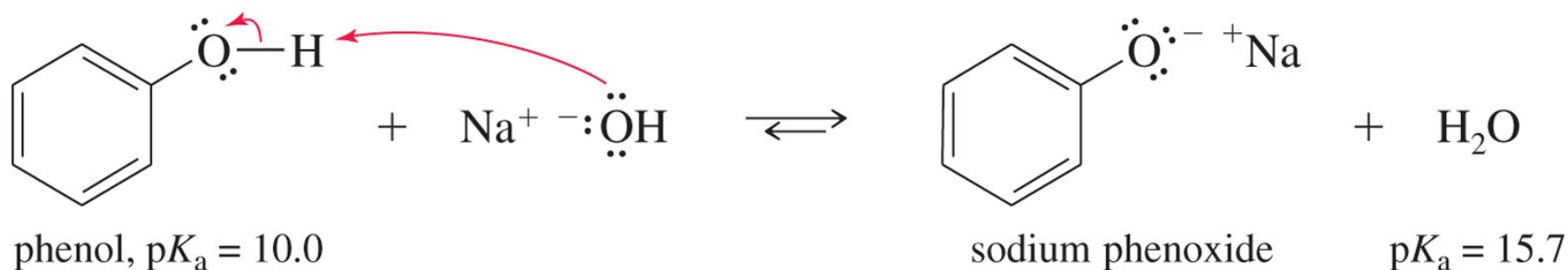
## Example



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- Ethanol reacts with sodium metal to form sodium ethoxide ( $\text{NaOCH}_2\text{CH}_3$ ), a strong base commonly used for elimination reactions.
- More hindered alcohols like 2-propanol or *tert*-butanol react faster with potassium than with sodium.

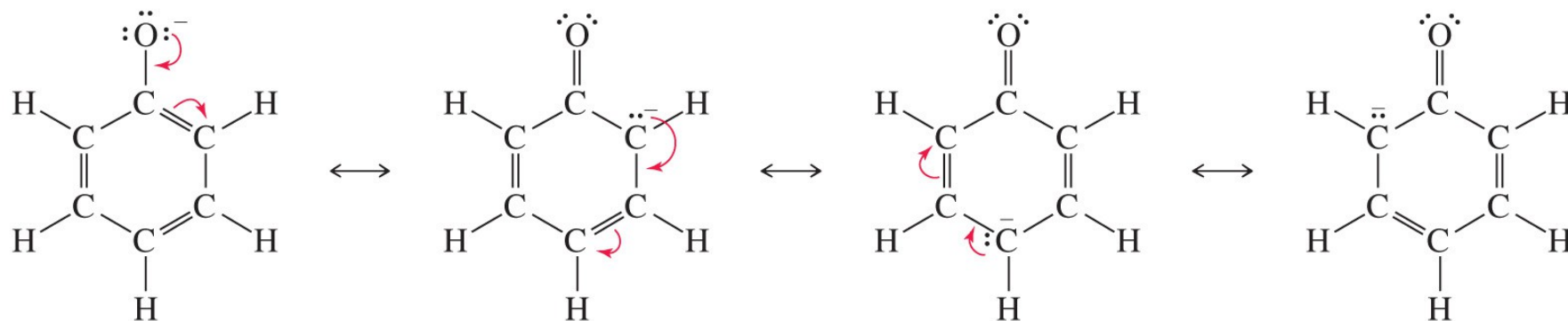
# Formation of Phenoxide Ion



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The aromatic alcohol phenol is more acidic than aliphatic alcohols due to the ability of aromatic rings to delocalize the negative charge of the oxygen within the carbons of the ring.

# Charge Delocalization on the Phenoxide Ion



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- The negative charge of the oxygen can be delocalized over four atoms of the phenoxide ion.
- There are three other resonance structures that can localize the charge in three different carbons of the ring.
- The true structure is a hybrid between the four resonance forms.



# Synthesis of Alcohols (Review)

- Alcohols can be synthesized by nucleophilic substitution of alkyl halide.
- Hydration of alkenes also produce alcohols:
  - Water in acid solution (suffers from rearrangements)
  - Oxymercuration–demercuration
  - Hydroboration–oxidation

# Synthesis of Vicinal Diols

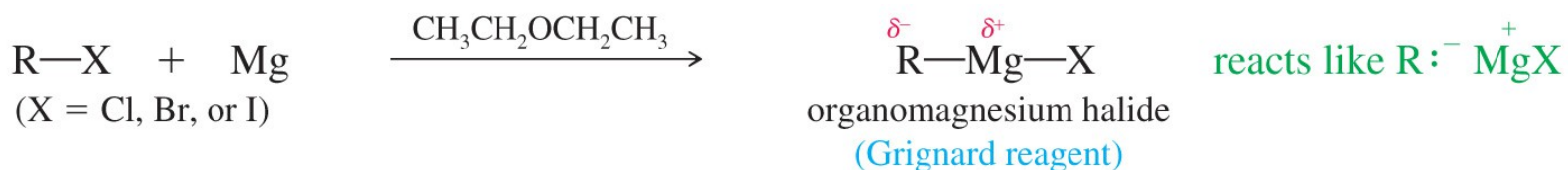
Vicinal diols can be synthesized by two different methods:

- Syn hydroxylation of alkenes
  - Osmium tetroxide, hydrogen peroxide
  - Cold, dilute, basic potassium permanganate
- Anti hydroxylation of alkenes
  - Peroxyacids followed by hydrolysis

# Organometallic Reagents

- Carbon is negatively charged so it is bonded to a metal (usually Mg or Li).
- It will attack a partially positive carbon.
  - $\text{C—X}$
  - $\text{C=O}$
- Good for forming carbon–carbon bonds.

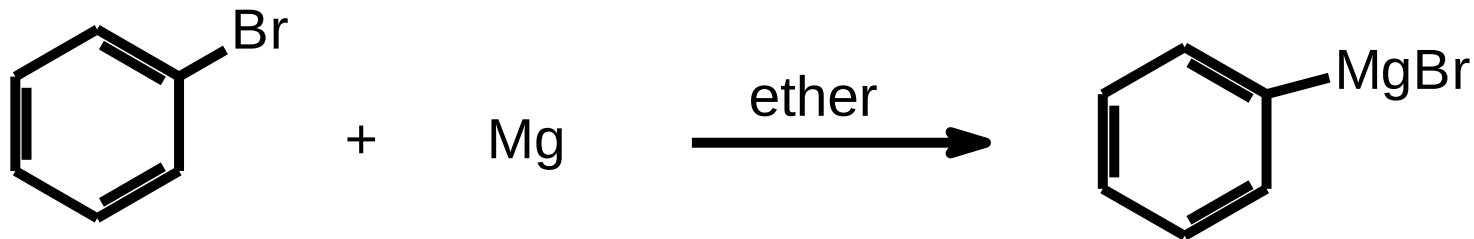
# Grignard Reagents



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- Formula  $\text{R-Mg-X}$  (reacts like  $\text{R:}^- + \text{MgX}$ ).
- Ethers are used as solvents to stabilize the complex.
- Iodides are most reactive.
- May be formed from any halide.

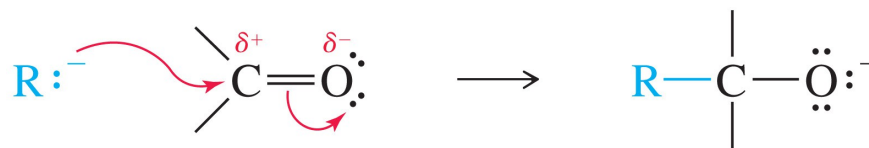
# Reactions with Grignards



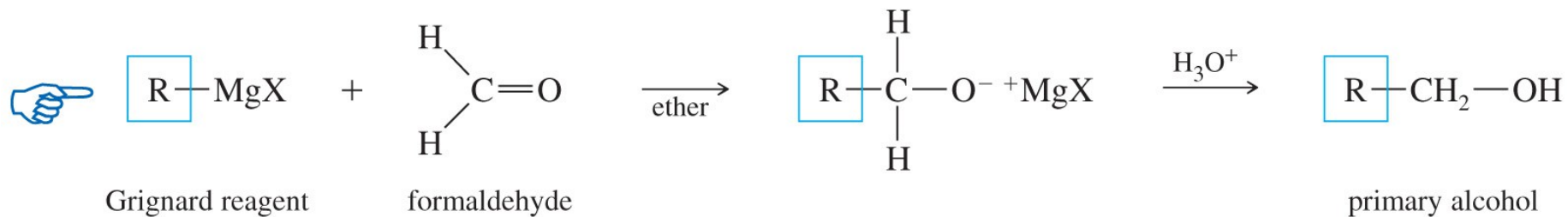
# Organolithium Reagents

- Formula  $R-Li$  (reacts like  $R:^- +Li$ )
- Can be produced from alkyl, vinyl, or aryl halides, just like Grignard reagents.
- Ether not necessary, wide variety of solvents can be used.

# Reaction with Carbonyl

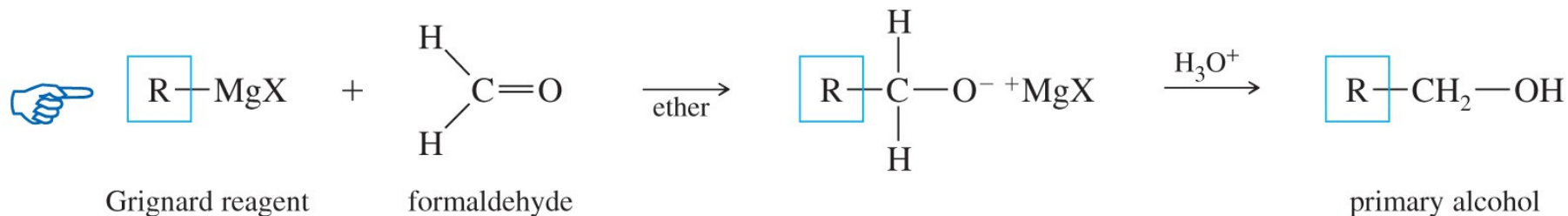


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# Formation of Primary Alcohols Using Grignard Reagents

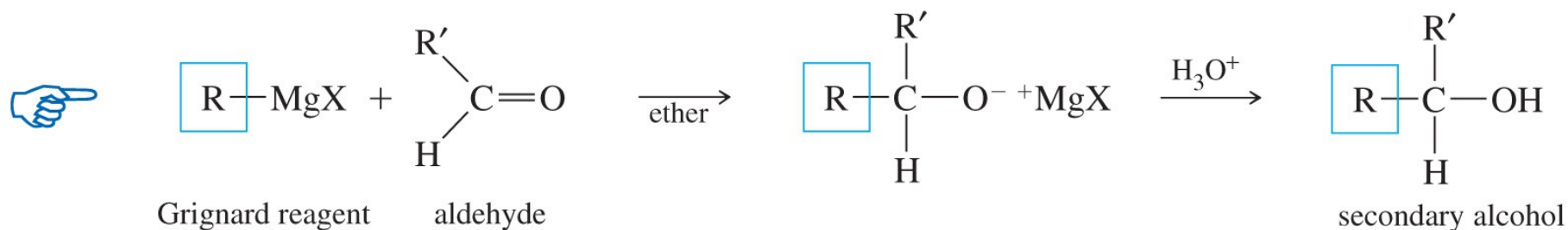


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- Reaction of a Grignard with formaldehyde will produce a primary alcohol after protonation.



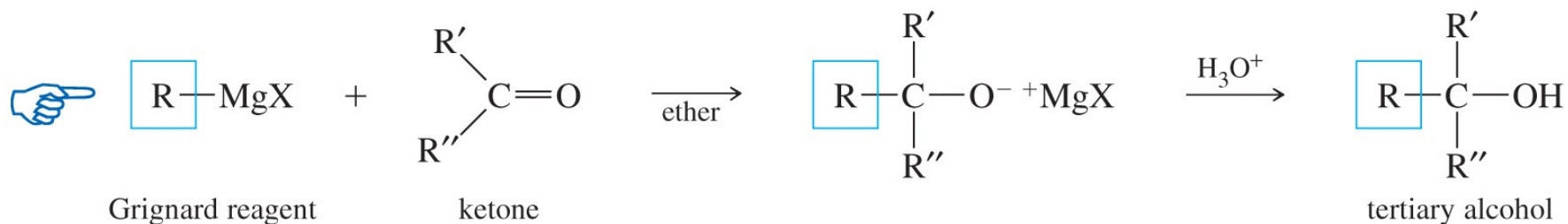
# Synthesis of 2° Alcohols



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- Addition of a Grignard reagent to an aldehyde followed by protonation will produce a secondary alcohol.

# Synthesis of 3° Alcohols

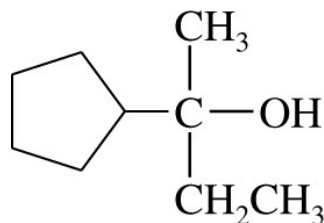


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- Tertiary alcohols can be easily obtained by addition of a Grignard to a ketone followed by protonation with dilute acid.

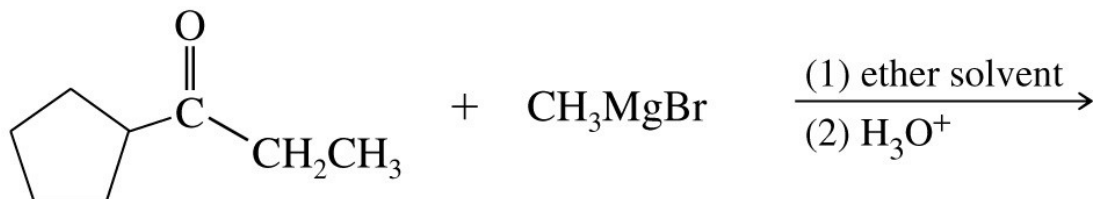
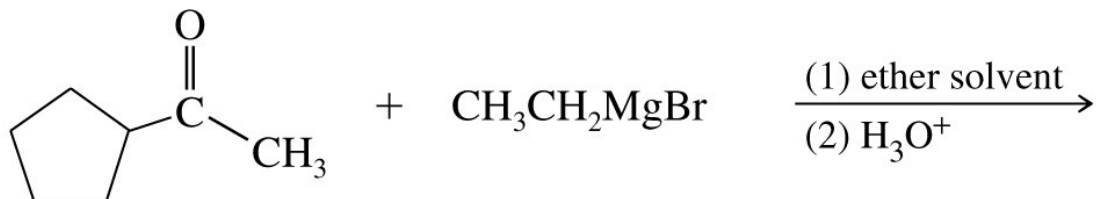
# Solved Problem 2

Show how you would synthesize the following alcohol from compounds containing no more than five carbon atoms.



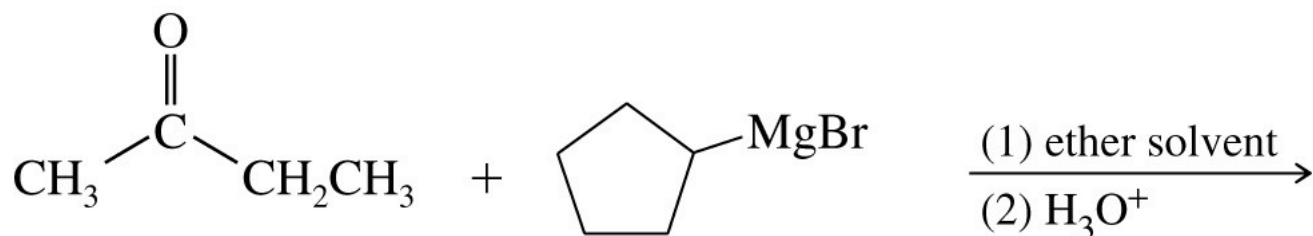
## Solution

This is a tertiary alcohol; any one of the three alkyl groups might be added in the form of a Grignard reagent. We can propose three combinations of Grignard reagents with ketones:



# Solved Problem 2 (Continued)

## Solution (Continued)

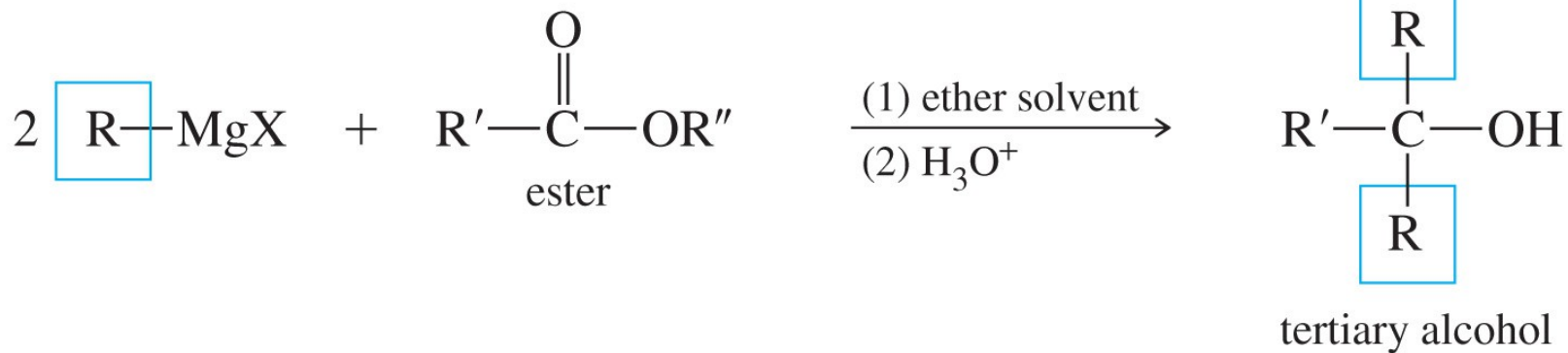
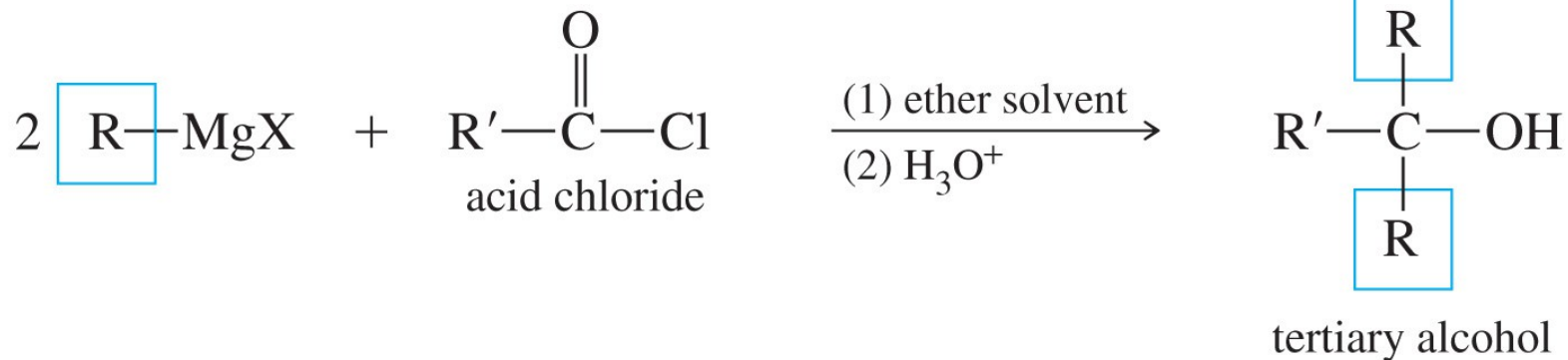


Any of these three syntheses would probably work, but only the third begins with fragments containing no more than five carbon atoms. The other two syntheses would require further steps to generate the ketones from compounds containing no more than five carbon atoms.

# 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.

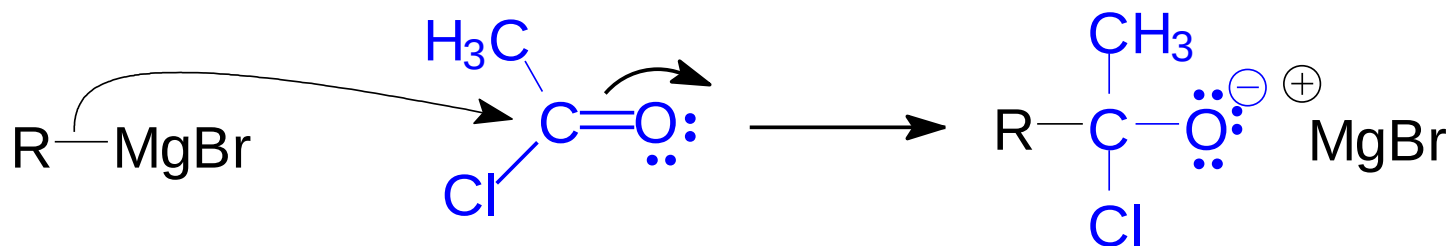
# Reaction of Grignards with Carboxylic Acid Derivatives



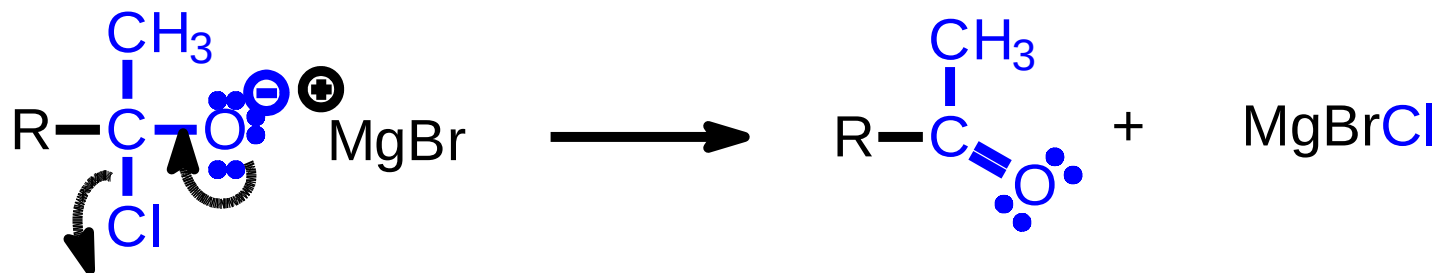
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# Mechanism

Step 1: Grignard attacks the carbonyl forming the tetrahedral intermediate.

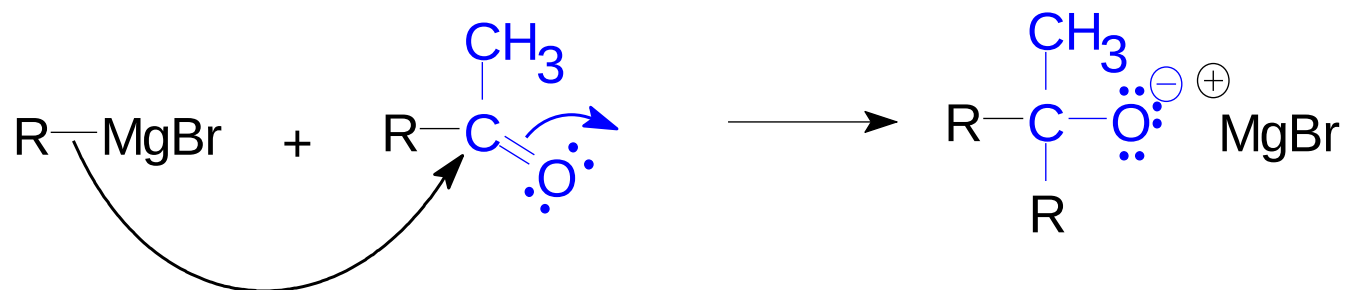


Step 2: The tetrahedral intermediate will reform the carbonyl and form a ketone intermediate.

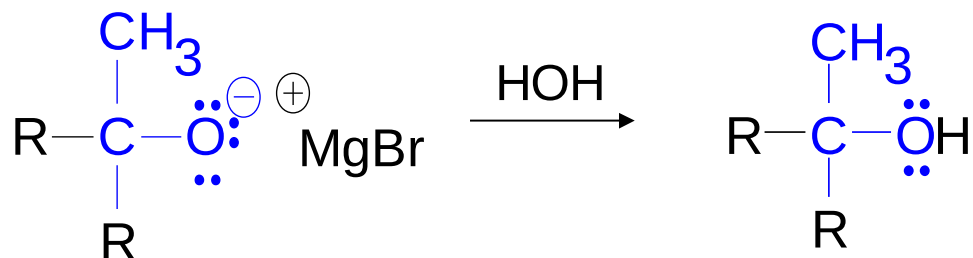


# Mechanism continued

Step 3: A second molecule of Grignard attacks the carbonyl of the ketone.

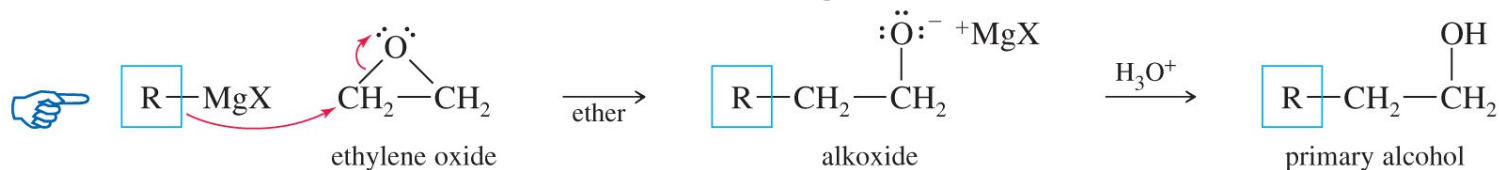


Step 4: Protonation of the alkoxide to form the alcohol as the product.

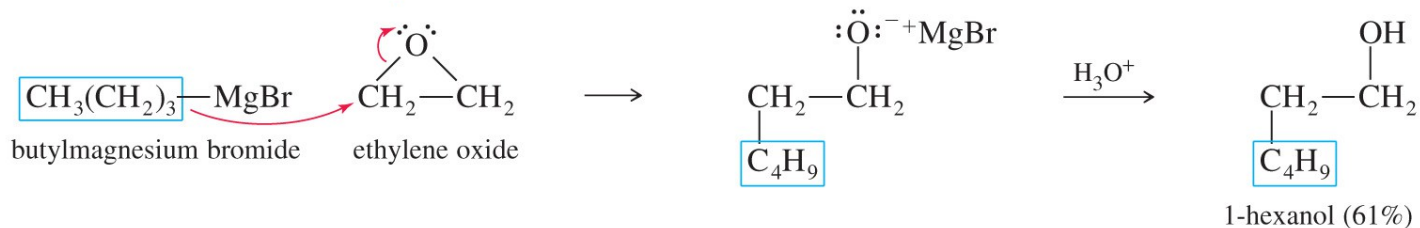




# Addition to Ethylene Oxide



## Example



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- Grignard and lithium reagents will attack epoxides (also called oxiranes) and open them to form alcohols.
- This reaction is favored because the ring strain present in the epoxide is relieved by the opening.
- The reaction is commonly used to extend the length of the carbon chain by two carbons.

# Limitations of Grignard

- Grignards are good nucleophiles but in the presence of acidic protons it will act as a strong base.
- No water or other acidic protons like O—H, N—H, S—H, or terminal alkynes.
- No other electrophilic multiple bonds, like C=N, C≡N, S=O, or N=O.

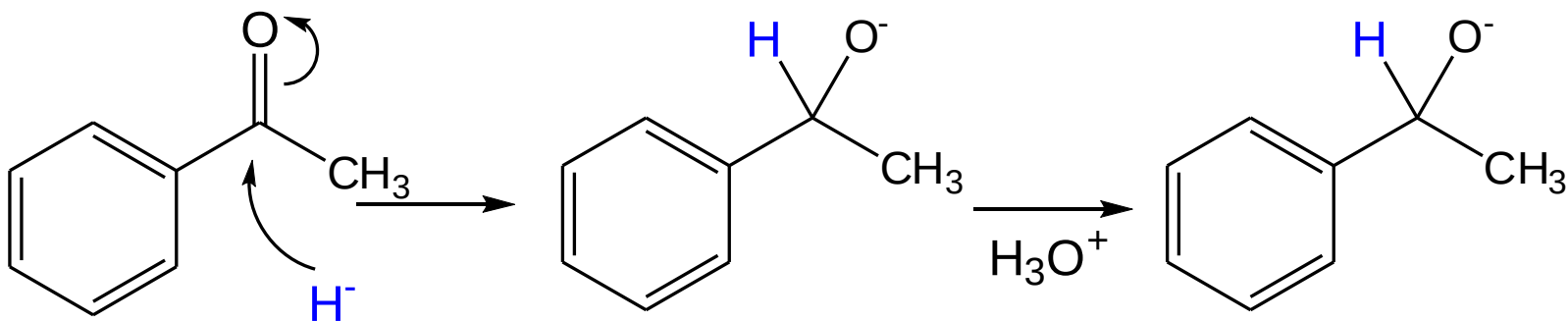
# Reduction of Carbonyl

- Reduction of aldehyde yields 1° alcohol.
- Reduction of ketone yields 2° alcohol.
- Reagents:
  - Sodium borohydride,  $\text{NaBH}_4$
  - Lithium aluminum hydride,  $\text{LiAlH}_4$
  - Raney nickel

# Sodium Borohydride

- $\text{NaBH}_4$  is a source of hydrides ( $\text{H}^-$ )
- Hydride attacks the carbonyl carbon, forming an alkoxide ion.
- Then the alkoxide ion is protonated by dilute acid.
- Only reacts with carbonyl of aldehyde or ketone, not with carbonyls of esters or carboxylic acids.

# Mechanism of Hydride Reduction

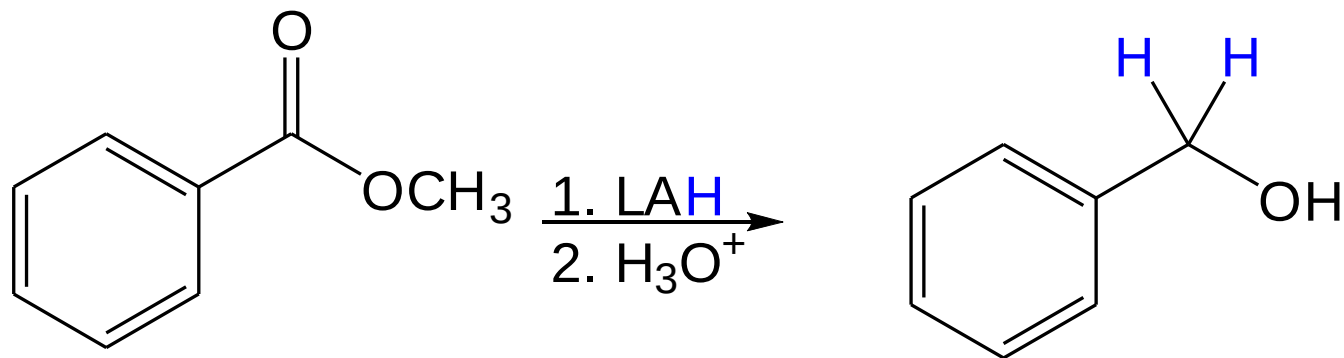


- The hydride attacks the carbonyl of the aldehyde or the ketone.
- A tetrahedral intermediate forms.
- Protonation of the intermediate forms the alcohols.

# Lithium Aluminum Hydride

- $\text{LiAlH}_4$  is source of hydrides ( $\text{H}^-$ )
- Stronger reducing agent than sodium borohydride, but dangerous to work with.
- Reduces ketones and aldehydes into the corresponding alcohol.
- Converts esters and carboxylic acids to  $1^\circ$  alcohols.

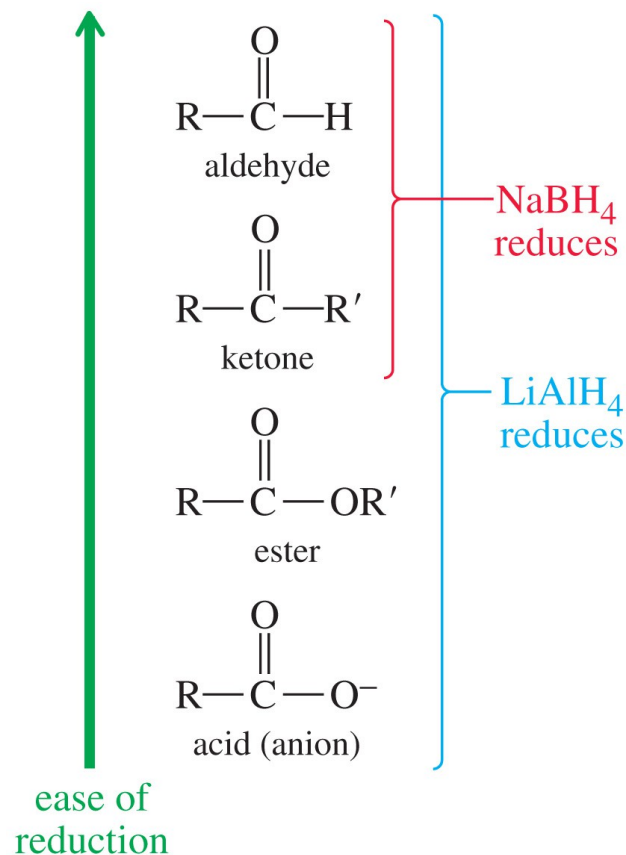
# Reduction with $\text{LiAlH}_4$



- The  $\text{LiAlH}_4$  (or LAH) will add two hydrides to the ester to form the primary alkyl halide.
- The mechanism is similar to the attack of Grignards on esters.

# Reducing Agents

- $\text{NaBH}_4$  can reduce aldehydes and ketones but not esters and carboxylic acids.
- $\text{LiAlH}_4$  is a stronger reducing agent and will reduce all carbonyls.



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# Catalytic Hydrogenation



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- Raney nickel is a hydrogen rich nickel powder that is more reactive than Pd or Pt catalysts.
- This reaction is not commonly used because it will also reduce double and triple bonds that may be present in the molecule.
- Hydride reagents are more selective so they are used more frequently for carbonyl reductions.

# Thiols (Mercaptans)

- Sulfur analogues of alcohols are called thiols.
- The —SH group is called a *mercapto* group.
- Named by adding the suffix *-thiol* to the alkane name.
- They are commonly made by an  $S_N2$  reaction so primary alkyl halides work better.

# Synthesis of Thiols

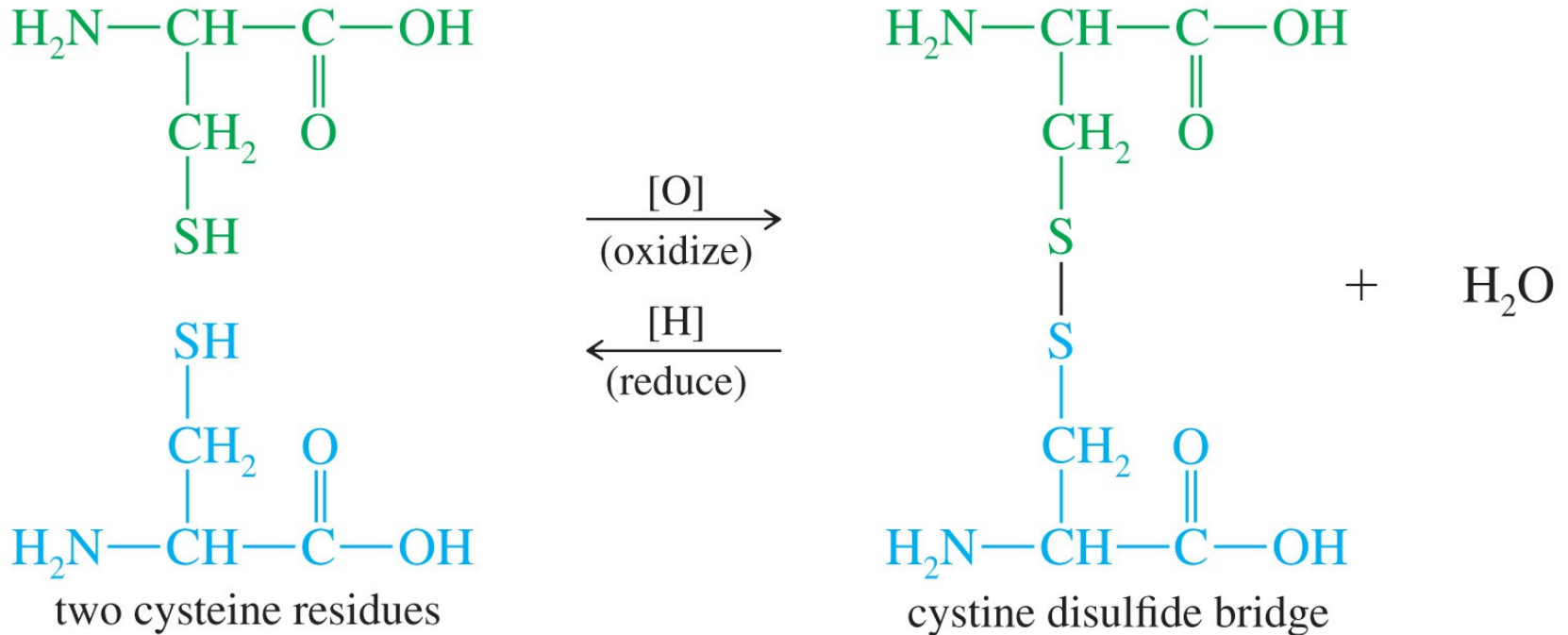


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- The thiolate will attack the carbon displacing the halide.
- This is an  $\text{S}_{\text{N}}2$  reaction so methyl halides will react faster than primary alkyl halides.
- To prevent dialylation use a large excess of sodium hydrosulfide with the alkyl halide.

# Thiol Oxidation

*Example*



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Thiols can be oxidized to form disulfides. The disulfide bond can be reduced back to the thiols with a reducing agent.