Alcohols and Phenols

Part A

B. Pharm. Semester-1
Course Code: 0510210; Session: 2022-2023

Dr. BALAKUMAR CHANDRASEKARAN
Professor-Faculty of Pharmacy
Philadelphia University-Jordan

Learning Outcomes

At the end of this lesson, students will be able to describe

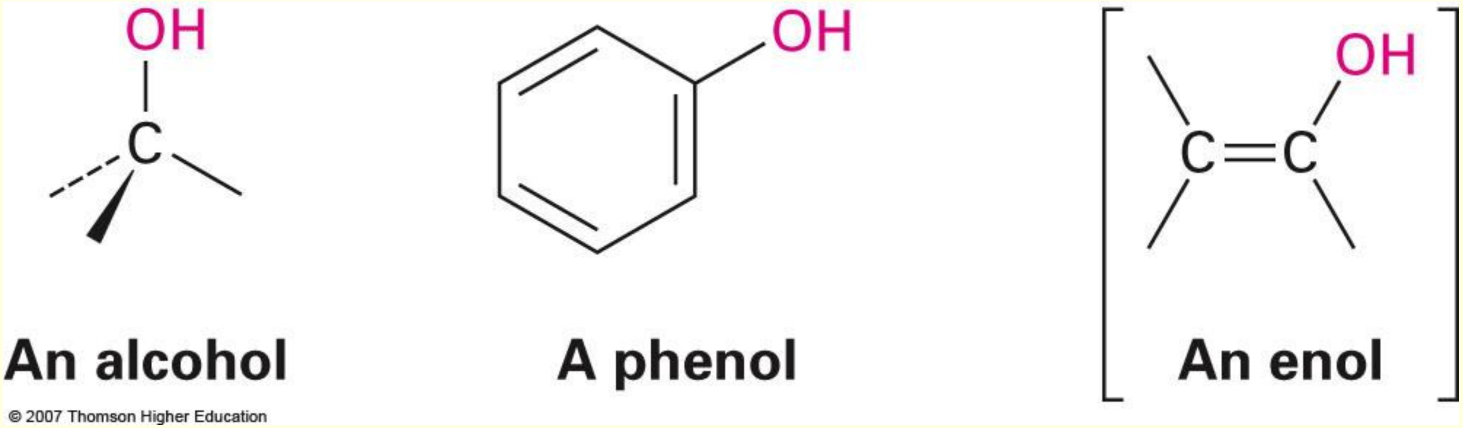
- What are Alcohols and Phenols?
- Naming Alcohols and Phenols
- Properties of Alcohols and Phenols
- Properties of Alcohols and Phenols: Acidity and Basicity
- Acidity Measurement, pKa, relative acidity
- Inductive Effects
- Acidity of Phenols
- Preparation of Alcohols

Objective

The objective of this course is to give to the students of pharmacy the basic knowledge about the organic chemistry.

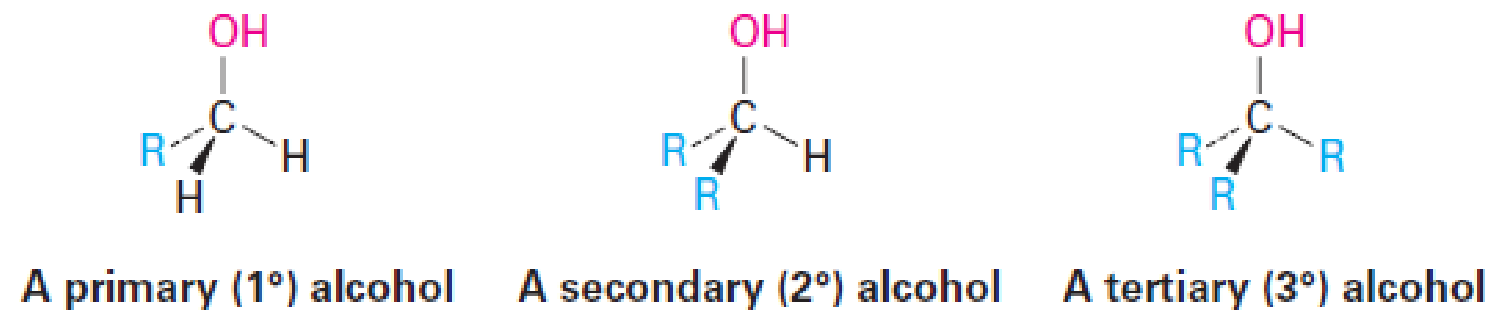
What are Alcohols and Phenols?

- Alcohols and phenols can be thought of as organic derivatives of water in which one of the water hydrogens is replaced by an organic group: H-O-H versus R-O-H and Ar-O-H.
- In practice, the group name alcohol is restricted to compounds that have their -OH group bonded to a saturated, sp3-hybridized carbon atom, while compounds with their -OH group bonded to a vinylic, sp2-hybridized carbon are called enols.



Naming Alcohols and Phenols

Alcohols are classified as primary (1°), secondary (2°), or tertiary (3°), depending on the number of organic groups bonded to the hydroxyl-bearing carbon.



A primary (1°) alcohol A secondary (2°) alcohol A tertiary (3°) alcohol

Simple alcohols are named by the IUPAC system as derivatives of the parent alkane, using the suffix -*ol*.

Naming Alcohols and Phenols

Rule 1:-

Select the longest carbon chain containing the hydroxyl group, and derive the parent name by replacing the -e ending of the corresponding alkane with -ol.

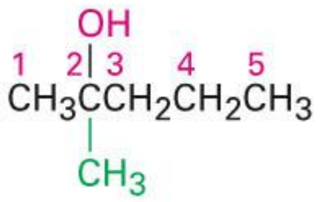
Rule 2:-

Number the alkane chain beginning at the end nearer the hydroxyl group.

Rule 3:-

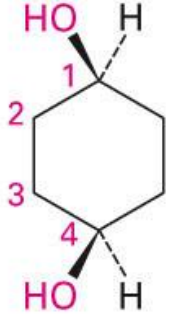
Number the substituents according to their position on the chain, and write the name, listing the substituents in alphabetical order and identifying the position to which the -OH is bonded.

Naming Alcohols and Phenols



$CH_3CCH_2CH_2CH_3$

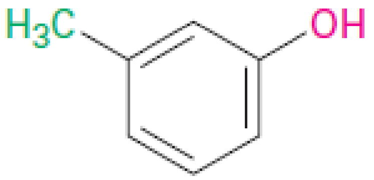
2-Methyl-2-pentanol
(New: 2-Methylpentan-2-ol)



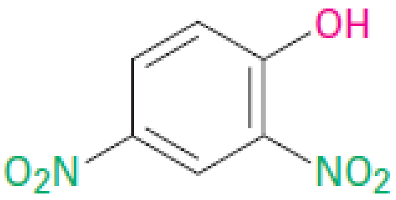
cis-1,4-Cyclohexanediol
(New: *cis*-Cyclohexane-1,4-diol)

3-Phenyl-2-butanol
(New: 3-Phenylbutan-2-ol)

Phenols



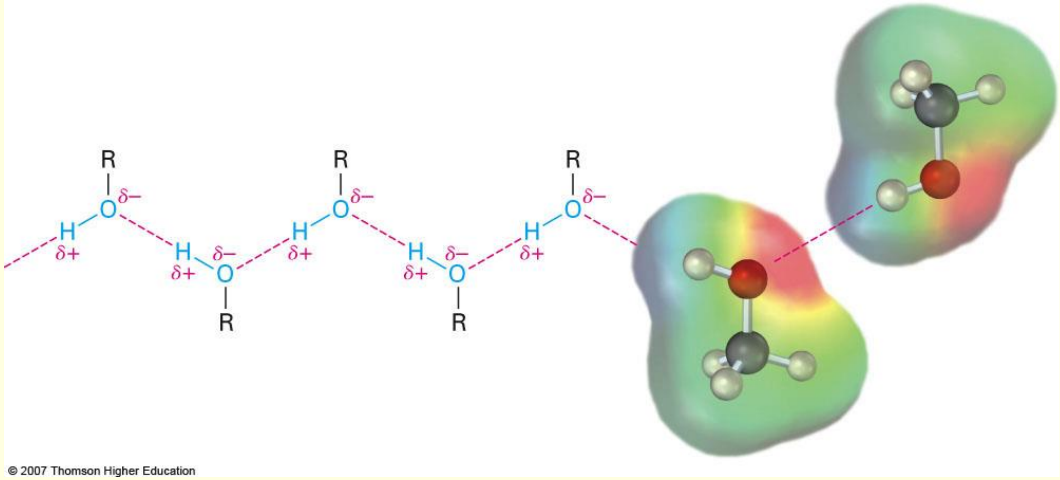
m-Methylphenol
(*m*-Cresol)



2,4-Dinitrophenol

Properties of Alcohols and Phenols

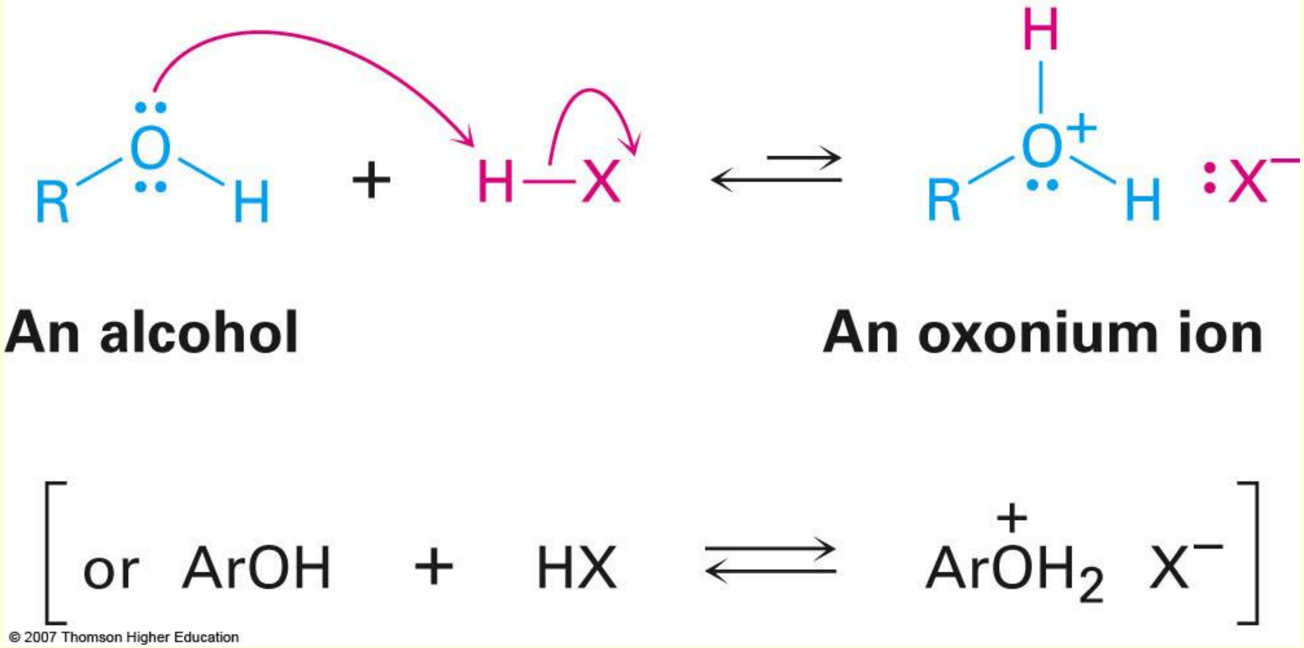
- Alcohols and phenols have nearly the same geometry around the oxygen atom as water.
- The R-O-H bond angle has an approximately tetrahedral value (108.5° in methanol, for instance), and the oxygen atom is sp^3-hybridized.
- Alcohols and phenols have higher boiling points than might be expected because of hydrogen-bonding.



© 2007 Thomson Higher Education

Properties of Alcohols and Phenols: Acidity and Basicity

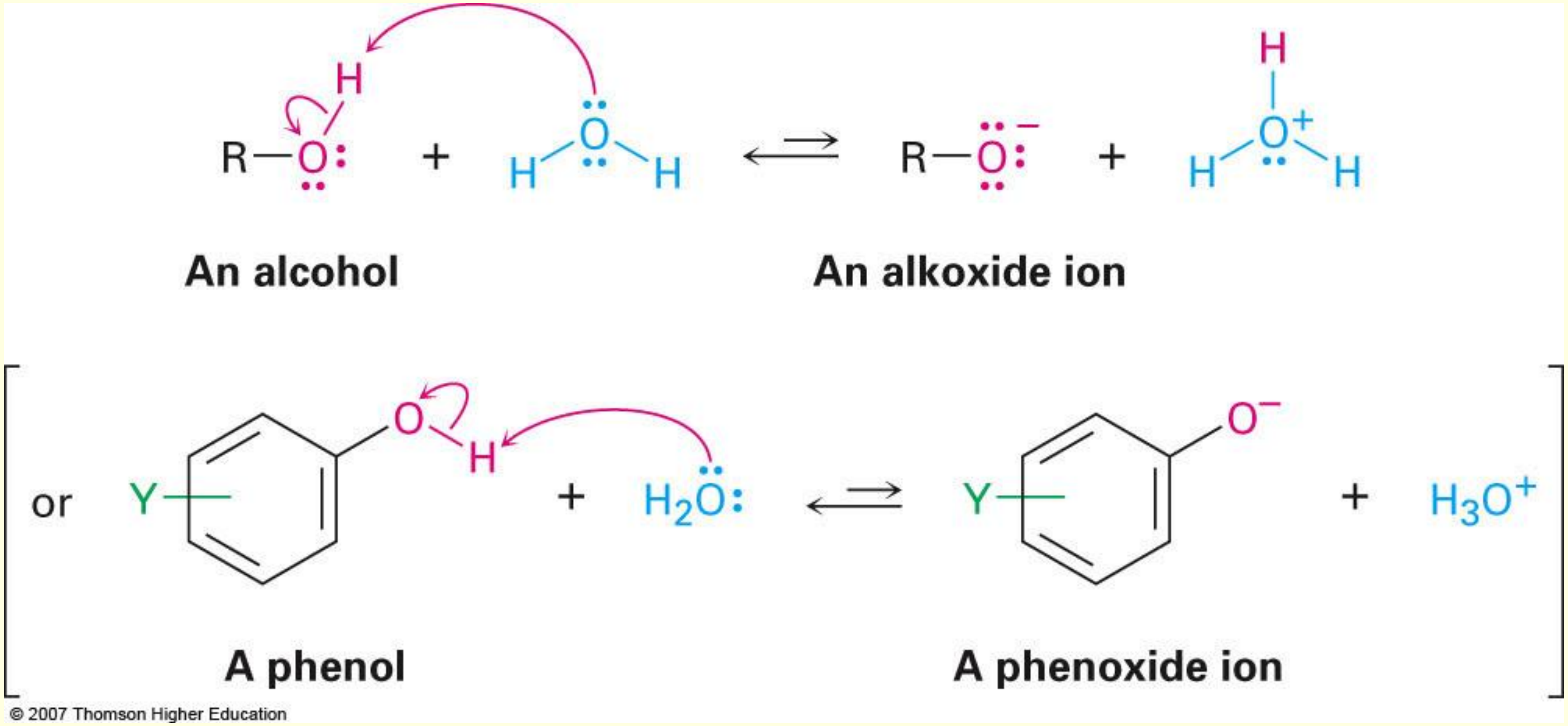
- Alcohols and phenols both weakly basic and weakly acidic.
- As weak bases, they are reversibly protonated by strong acids to yield oxonium ions, ROH_2^+.



© 2007 Thomson Higher Education

Properties of Alcohols and Phenols: Acidity and Basicity

As weak acids, they dissociate slightly in dilute aqueous solution by donating a proton to water, generating H_3O^+ and an alkoxide ion, RO^-, or a phenoxide ion, ArO^-.



© 2007 Thomson Higher Education

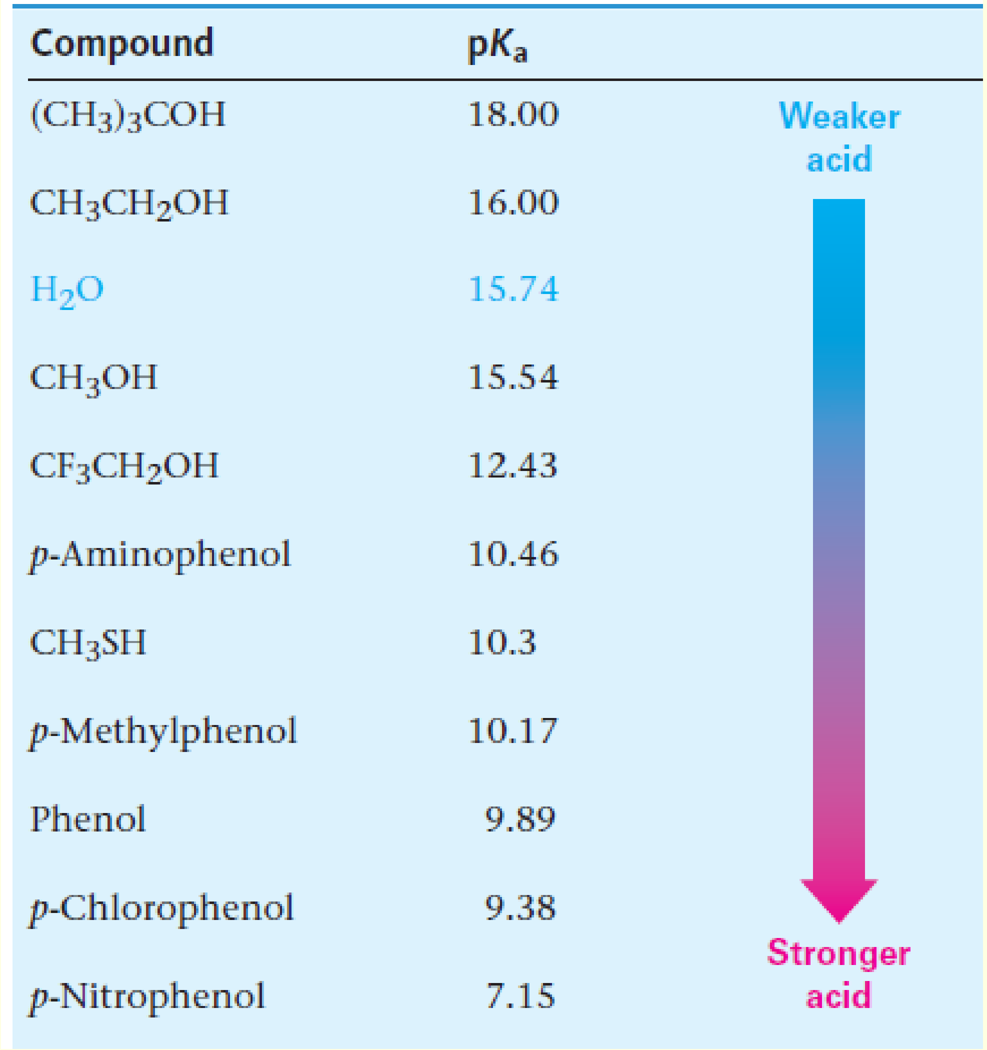
Acidity Measurement

- The acidity constant, K_a, measures the extent to which a Brønsted acid transfers a proton to water.

$$K_a = \frac{[A^-]\,[H_3O^+]}{[HA]} \quad \text{and } pK_a = -\log K_a$$

- Relative acidities are more conveniently presented on a logarithmic scale, pK_a, which is directly proportional to the free energy of the equilibrium
- Differences in pK_a correspond to differences in free energy

pKa values of some alcohols and phenols



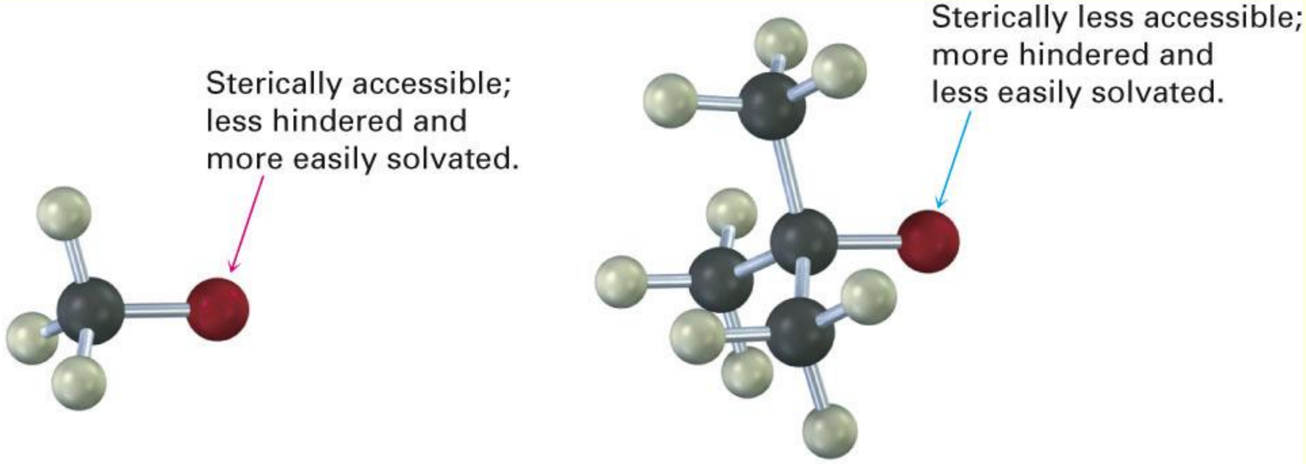
Compound	**pK_a**
$(CH_3)_3COH$	18.00
CH_3CH_2OH	16.00
H_2O	15.74
CH_3OH	15.54
CF_3CH_2OH	12.43
p-Aminophenol	10.46
CH_3SH	10.3
p-Methylphenol	10.17
Phenol	9.89
p-Chlorophenol	9.38
p-Nitrophenol	7.15

Weaker acid

Stronger acid

Relative Acidity of Alcohols

- Simple alcohols are about as acidic as water.
- Alkyl groups make an alcohol a weaker acid.
- The more easily the alkoxide ion is solvated by water the more its formation is energetically favored.
- Steric effects are important.



Sterically accessible; less hindered and more easily solvated.

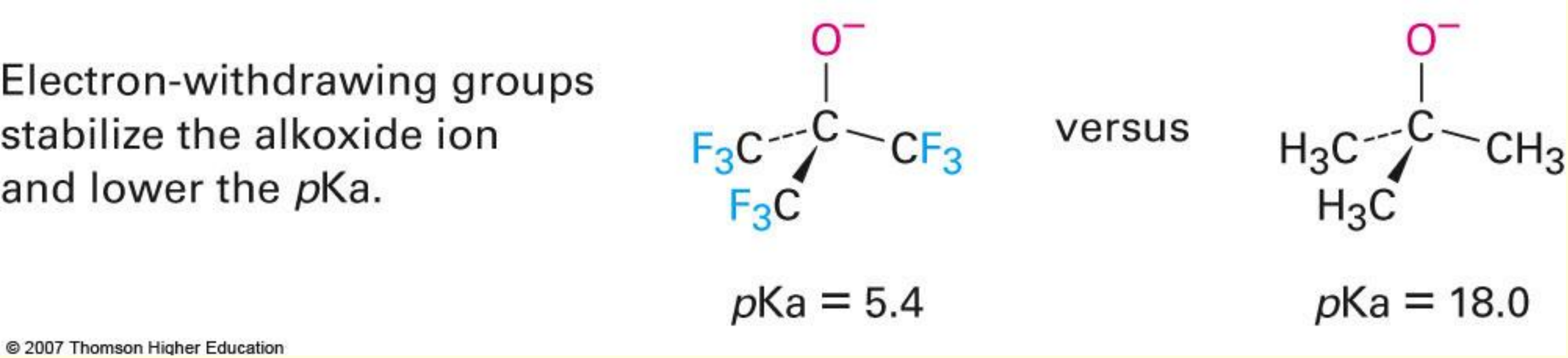
Sterically less accessible; more hindered and less easily solvated.

Methoxide ion, CH_3O^- ($pK_a = 15.54$)

***tert*-Butoxide ion, $(CH_3)_3CO^-$ ($pK_a = 18.00$)**

Inductive Effects

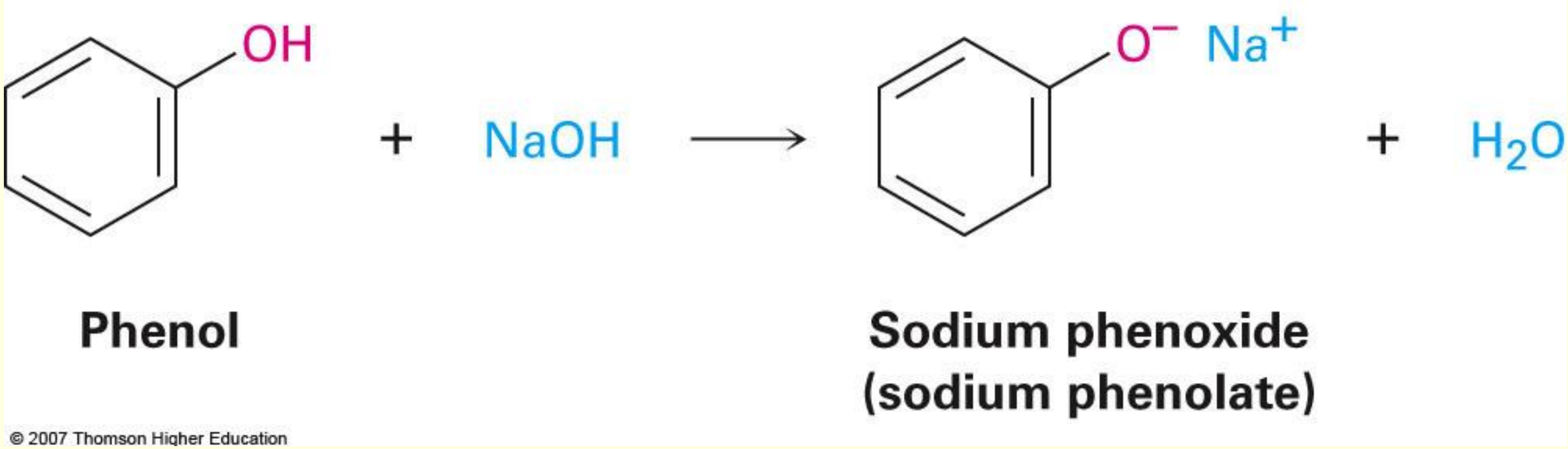
- ✓ Electron-withdrawing groups make an alcohol a stronger acid by stabilizing the conjugate base (alkoxide).
- ✓ Alcohols are weak acids – requires a strong base to form an alkoxide such as NaH, sodium amide $NaNH_2$, and Grignard reagents (RMgX).
- ✓ Alkoxides are bases used as reagents in organic chemistry.



Electron-withdrawing groups stabilize the alkoxide ion and lower the *p*Ka.

Acidity of Phenols

- Phenols are soluble in dilute aqueous NaOH and can often be separated from a mixture simply by basic extraction into aqueous solution, followed by reacidification.
- Phenols are more acidic than alcohols because the phenoxide anion is resonance-stabilized.



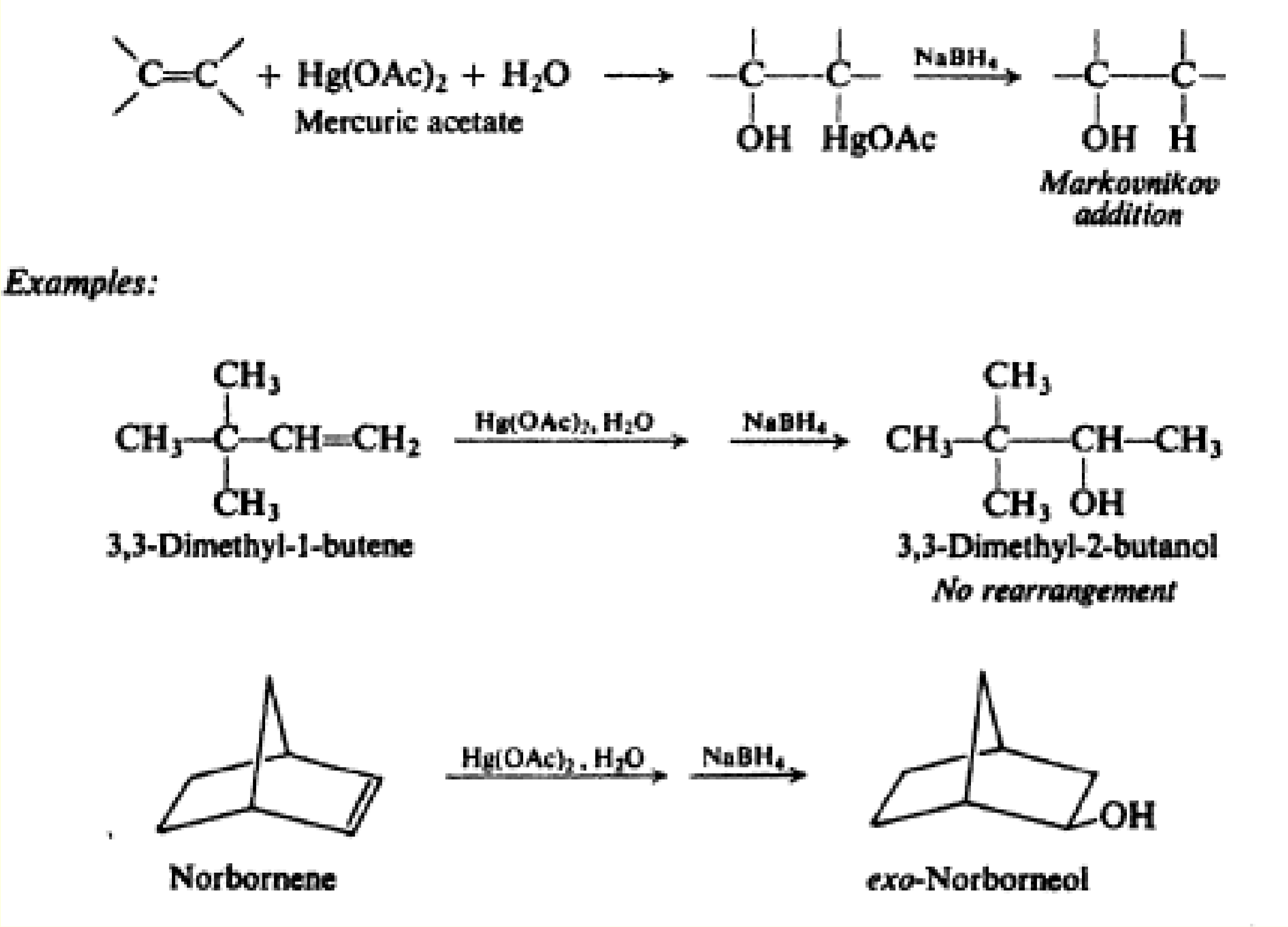
© 2007 Thomson Higher Education

Preparation of Alcohols

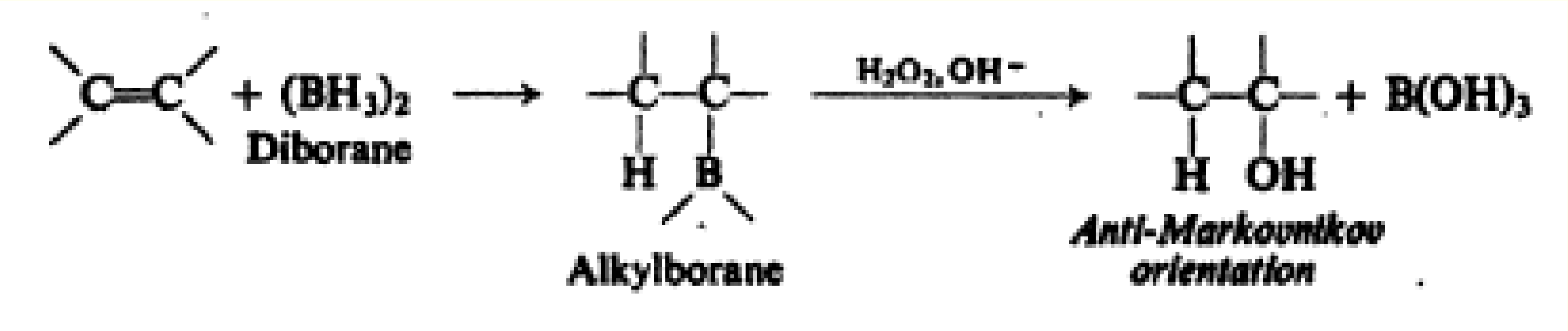
1. Oxymercuration-Demercuration
2. Hydroboration-Oxidation
3. Reduction of carbonyl compounds
4. Reduction of Carboxylic Acids and Esters
5. Reaction of Carbonyl Compounds with Grignard Reagents
6. Hydrolysis of alkyl halides
7. Aldol condensation

1. Oxymercuration-Demercuration

This reaction follows Markovnikov’s addition.



2. Hydroboration-oxidation



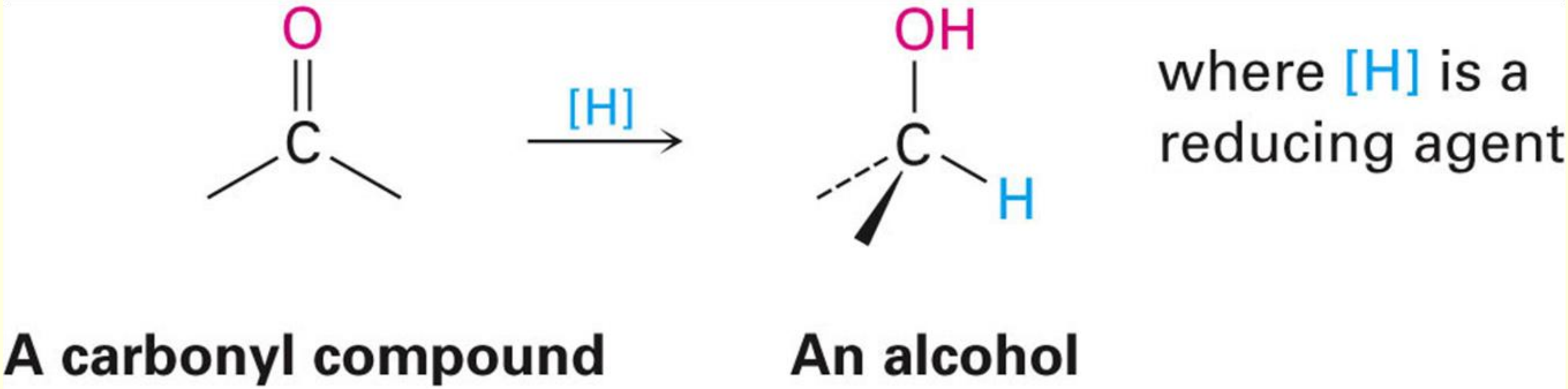
With the reagent diborane, $(BH_3)_2$, alkenes undergo hydroboration to yield alkylboranes, R_3B, which on oxidation give alcohols. This reaction follows anti-Markovnikov's addition.

$$\underset{\text{Diborane}}{(BH_3)_2} \xrightarrow{H_2C=CH_2} CH_3CH_2BH_2 \xrightarrow{H_2C=CH_2} (CH_3CH_2)_2BH \xrightarrow{H_2C=CH_2} \underset{\text{Triethylboron}}{(CH_3CH_2)_3B}$$

$$\underset{\text{Triethylboron}}{(CH_3CH_2)_3B} + \underset{\text{Hydrogen peroxide}}{3H_2O_2} \xrightarrow{OH^-} \underset{\text{Ethyl alcohol}}{3CH_3CH_2OH} + \underset{\text{Boric acid}}{3B(OH)_3}$$

3. Reduction of carbonyl compounds

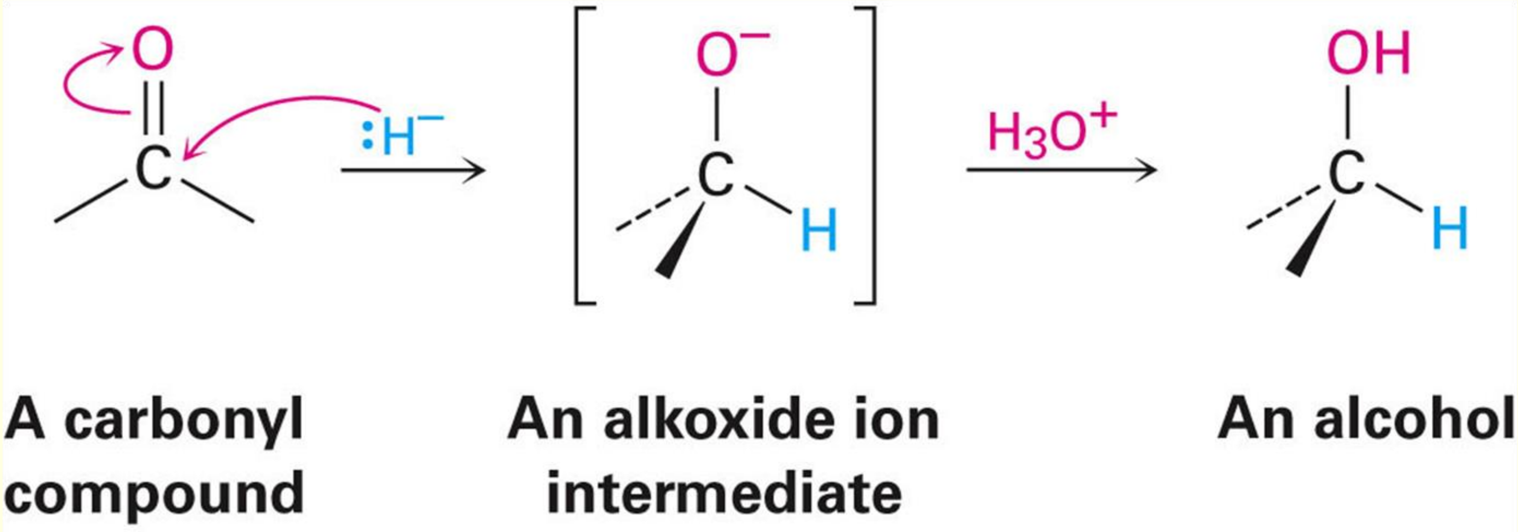
Reduction of a carbonyl compound in general gives an alcohol.



Reduction of **Aldehydes** gives **primary alcohols**.
Reduction of **Ketones** gives **secondary alcohols**.

3. Reduction of carbonyl compounds

Mechanism of Reduction

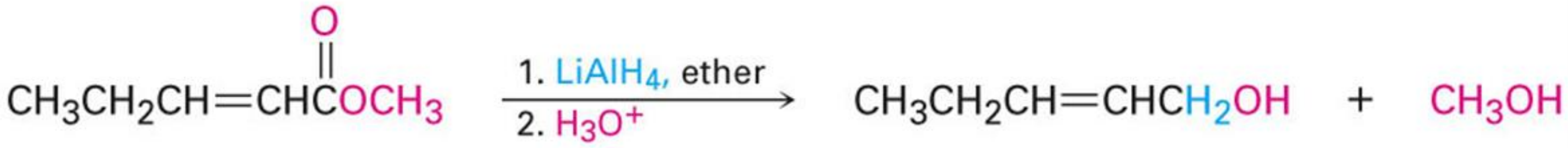


4. Reduction of Carboxylic Acids and Esters

Carboxylic acids and esters are reduced to give primary alcohols.

$$4RCOOH + 3LiAlH_4 \longrightarrow 4H_2 + 2LiAlO_2 + (RCH_2O)_4AlLi \xrightarrow{H_2O} \underset{\text{1° alcohol}}{4RCH_2OH}$$

Ester reduction



$$CH_3CH_2CH{=}CH\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow[\text{2. } H_3O^+]{\text{1. } LiAlH_4\text{, ether}} CH_3CH_2CH{=}CHCH_2OH + CH_3OH$$

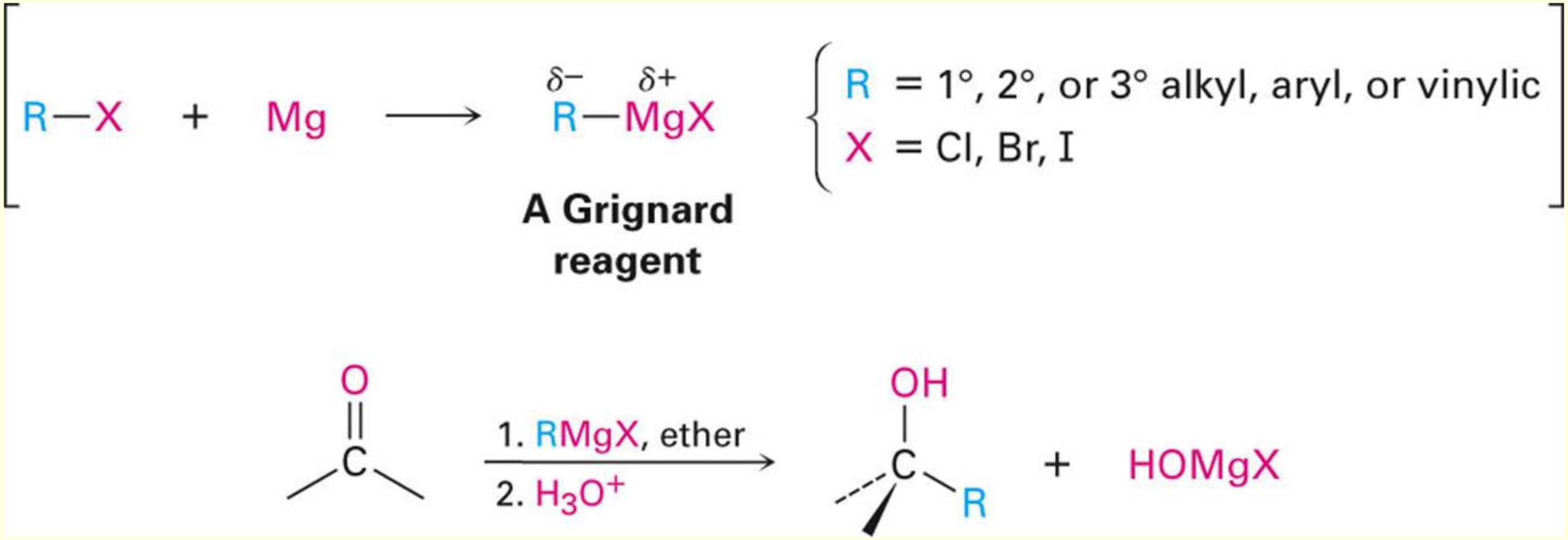
Methyl 2-pentenoate

2-Penten-1-ol (91%)

5. Reaction of Carbonyl Compounds with Grignard Reagents

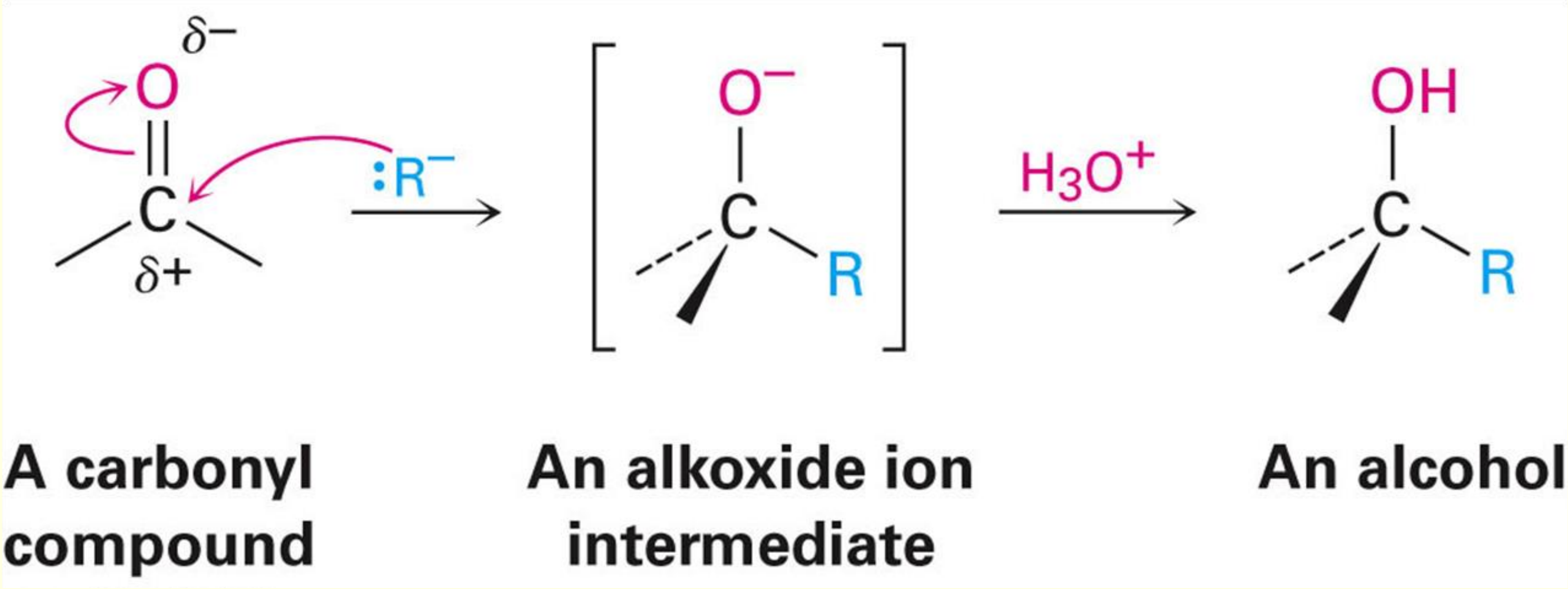
Alkyl, aryl, and vinylic halides react with magnesium in ether or tetrahydrofuran to generate Grignard reagents, RMgX.

Grignard reagents react with carbonyl compounds to yield alcohols.



Mechanism of Reaction of Carbonyl Compounds with Grignard Reagents

Grignard reagents act as nucleophilic carbon anions (carbanions, : R-) in adding to a carbonyl group.
The intermediate alkoxide is then protonated to produce the alcohol.

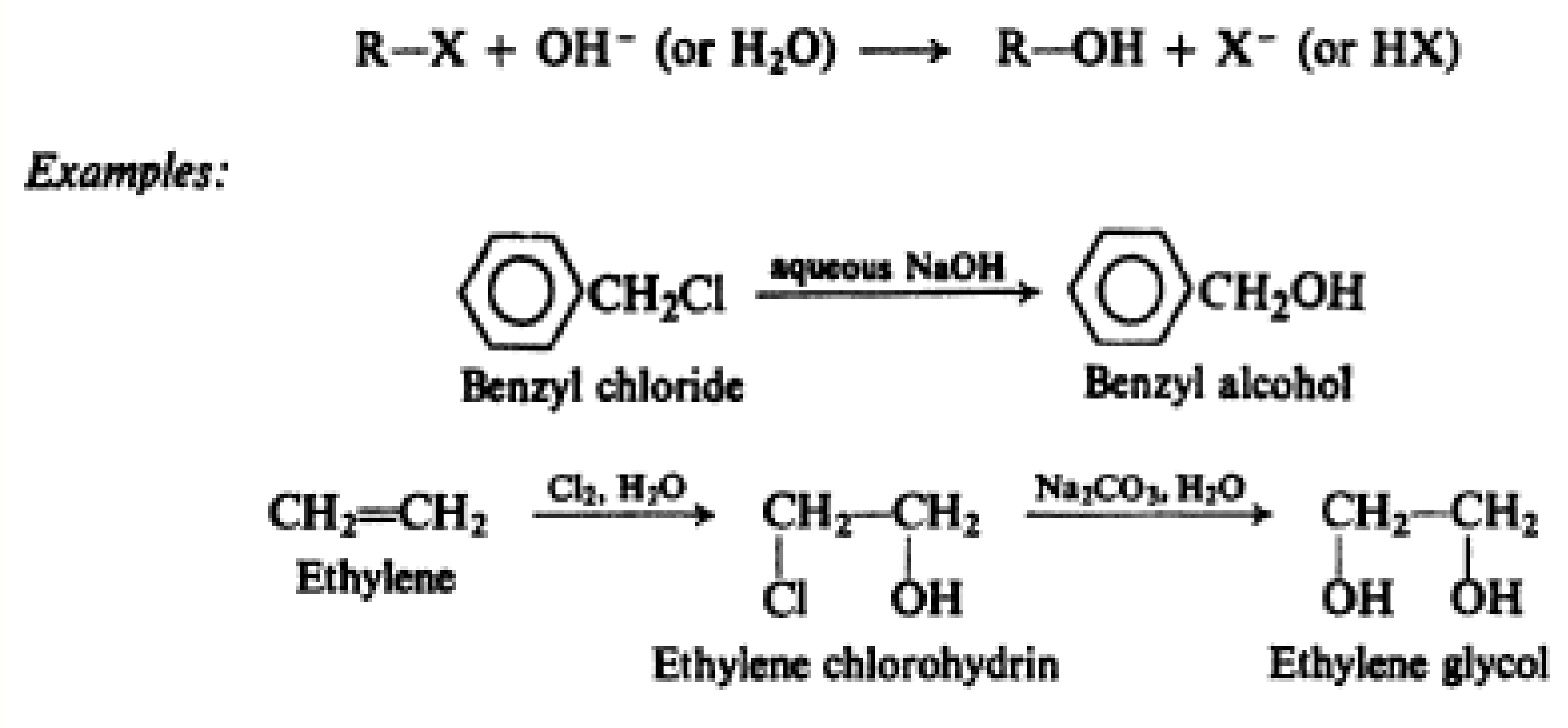


A carbonyl compound

An alkoxide ion intermediate

An alcohol

6. Hydrolysis of alkyl halides



$$R{-}X + OH^- \text{ (or } H_2O) \longrightarrow R{-}OH + X^- \text{ (or HX)}$$

Examples:

$$C_6H_5CH_2Cl \xrightarrow{\text{aqueous NaOH}} C_6H_5CH_2OH$$

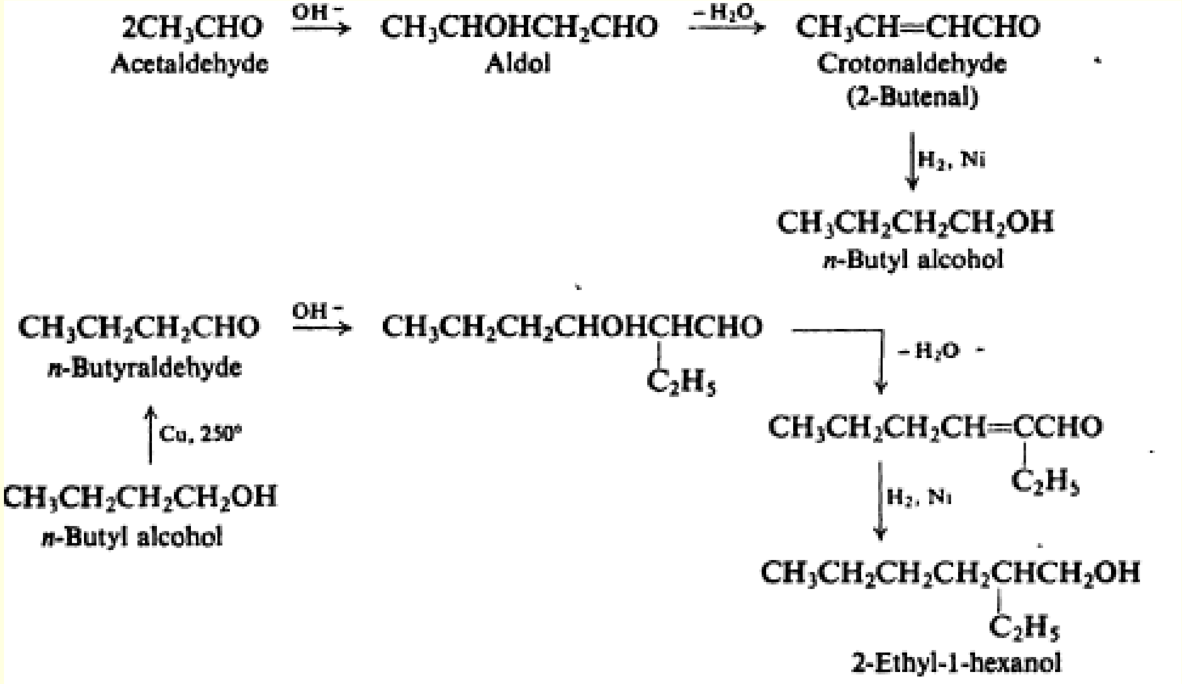
Benzyl chloride

Benzyl alcohol

$$\underset{\text{Ethylene}}{CH_2{=}CH_2} \xrightarrow{Cl_2,\ H_2O} \underset{\text{Ethylene chlorohydrin}}{\underset{Cl}{CH_2}{-}\underset{OH}{CH_2}} \xrightarrow{Na_2CO_3,\ H_2O} \underset{\text{Ethylene glycol}}{\underset{OH}{CH_2}{-}\underset{OH}{CH_2}}$$

7. Aldol condensation

Catalytic hydrogenation of α, β-unsaturated aldehydes and ketones yields saturated alcohols addition of hydrogen occurring both at carbon-carbon and at carbon-oxygen double bonds.



REFERENCES

Textbooks:

1. **Organic Chemistry, 9th Edition, 2015, Author: John E. McMurry, Publisher: Cengage Learning, ISBN: 978-1305080485.**
2. **Organic Chemistry, 7th Edition, 2010, Authors: Saibal Kanti Bhattacharjee, Robert Thornton Morrison, Robert Neilson Boyd, Publisher: Pearson India, ISBN: 978-0199270293.**
3. **Textbook of Organic Chemistry, 22nd Edition, 2022, Authors: Arun Bahl & B S Bahl, Publisher: S Chand, ISBN: 978-9352531967.**

Supplementary book:

Organic Chemistry, 11th Edition, 2015, Authors: Francis Carey Robert Giuliano Neil Allison Susan Bane, Publisher: McGraw Hill, ISBN: 978-1260148923.