Carboxylic acid Derivatives

Part B

B. Pharm. Semester-1

Course Code: 0510210; Session: 2022-2023

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Learning Outcomes

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

Carboxylic acid derivatives

- **Chemistry and Reactions of acid chlorides**
- **Chemistry and Reactions of acid anhydrides**
- **Chemistry and Reactions of esters**

Objective

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

Chemistry of Acid Halides

- Acid chlorides are prepared from carboxylic acids by reaction with $SOCl_2$
- Reaction of a carboxylic acid with PBr_3 yields the acid bromide.

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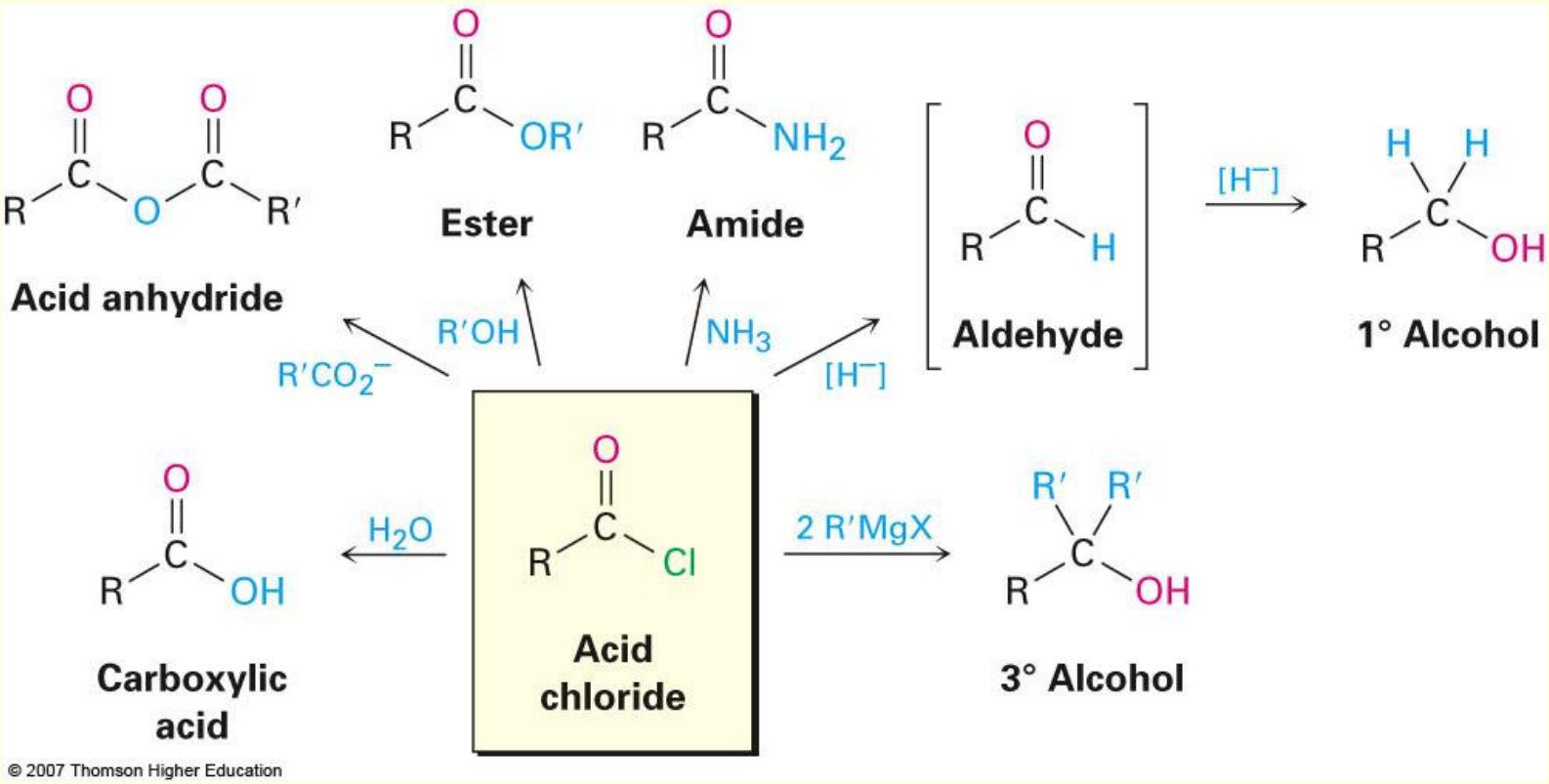
Reactions of Acid Halides

- Nucleophilic acyl substitution: Halogen replaced by -OH, by -OR, or by -NH_2
- Reduction yields a primary alcohol.



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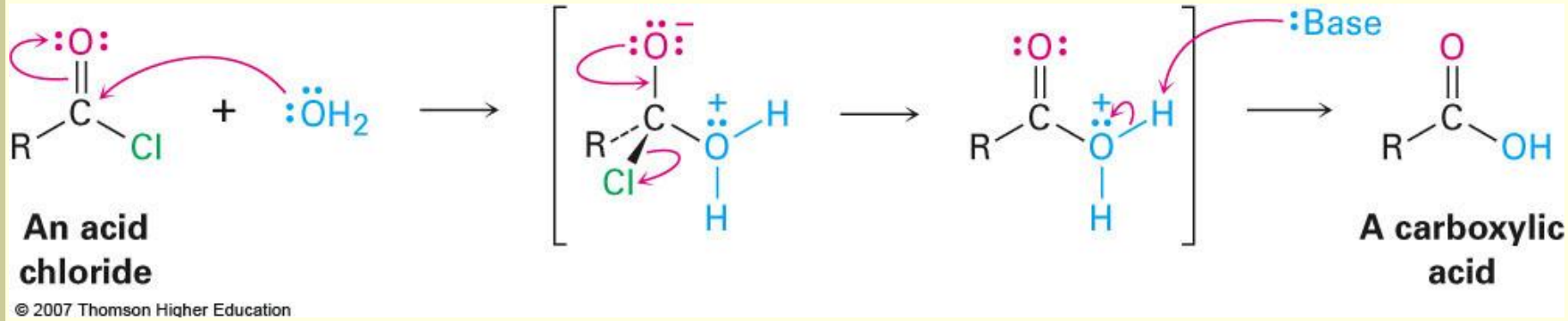
Hydrolysis: Conversion of Acid Halides into Acids

- Acid chlorides react with water to yield carboxylic acids
- HCl is generated during the hydrolysis: a base is added to remove the HCl.



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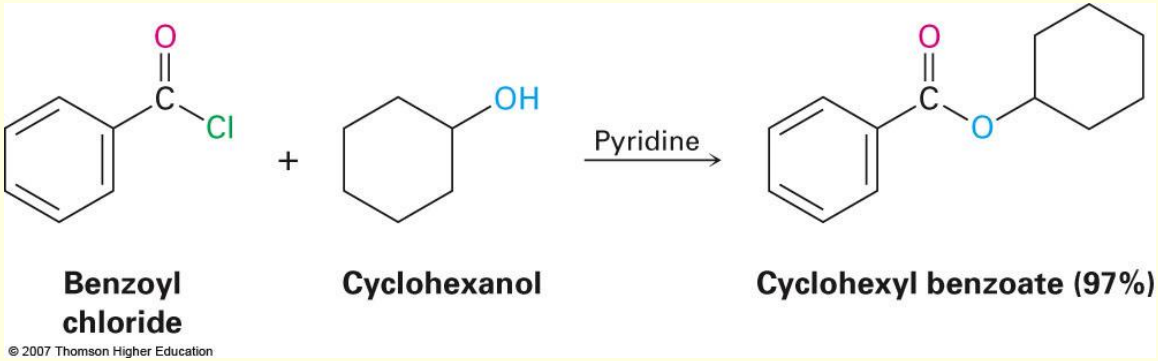
Conversion of Acid Halides into Esters

- Esters are produced in the reaction of acid chlorides with alcohols in the presence of pyridine or NaOH.
  This is called as **Alcoholysis**
- The reaction is better with less steric bulkiness.



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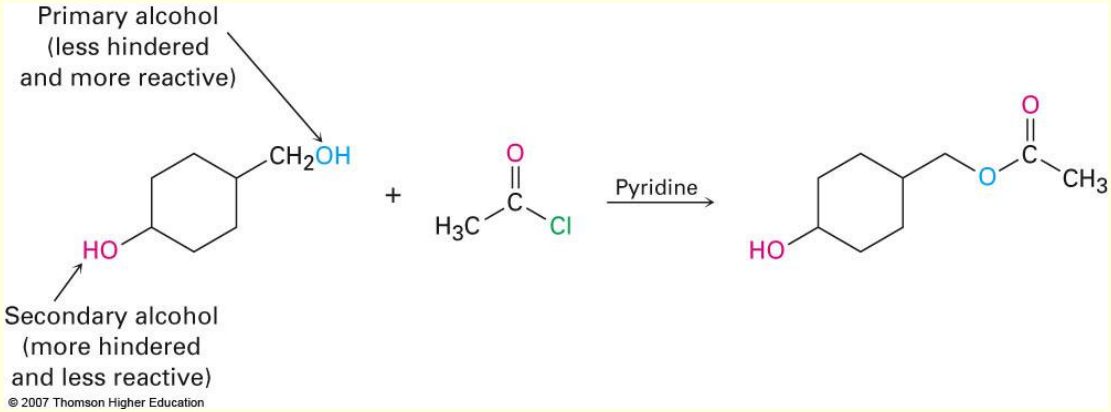

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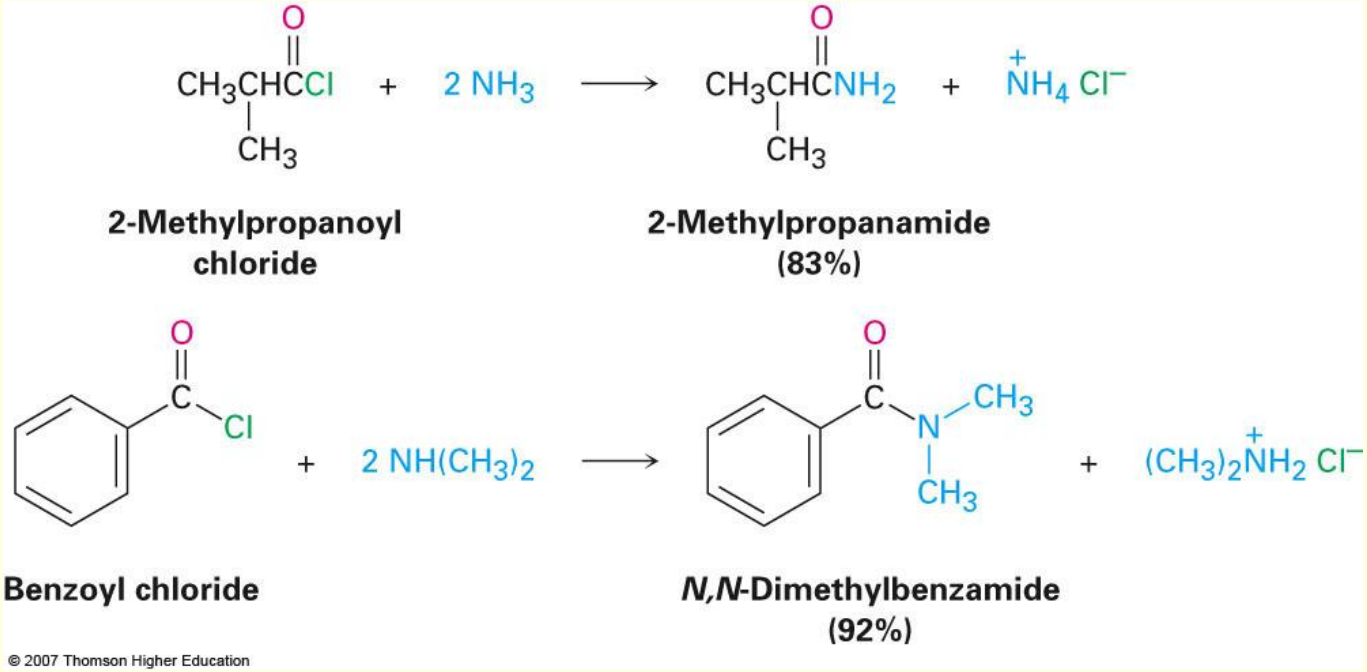
Aminolysis: Conversion of Acid Halides into Amides

- Amides result from the reaction of acid chlorides with NH_3, primary (RNH_2) and secondary amines (R_2NH).
- The reaction with tertiary amines (R_3N) gives an unstable species that cannot be isolated.
- HCl is neutralized by the amine or an added base.



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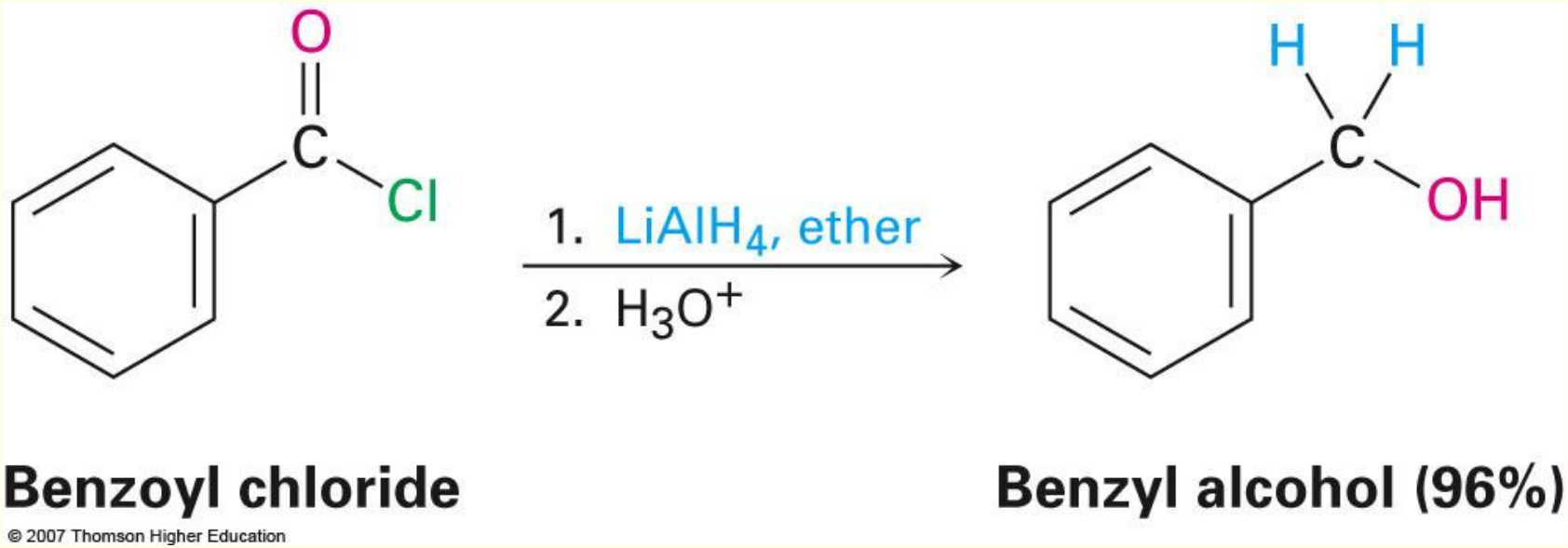
Reduction: Conversion of Acid Chlorides into Alcohols

$LiAlH_4$ reduces acid chlorides to yield aldehydes and then primary alcohols.



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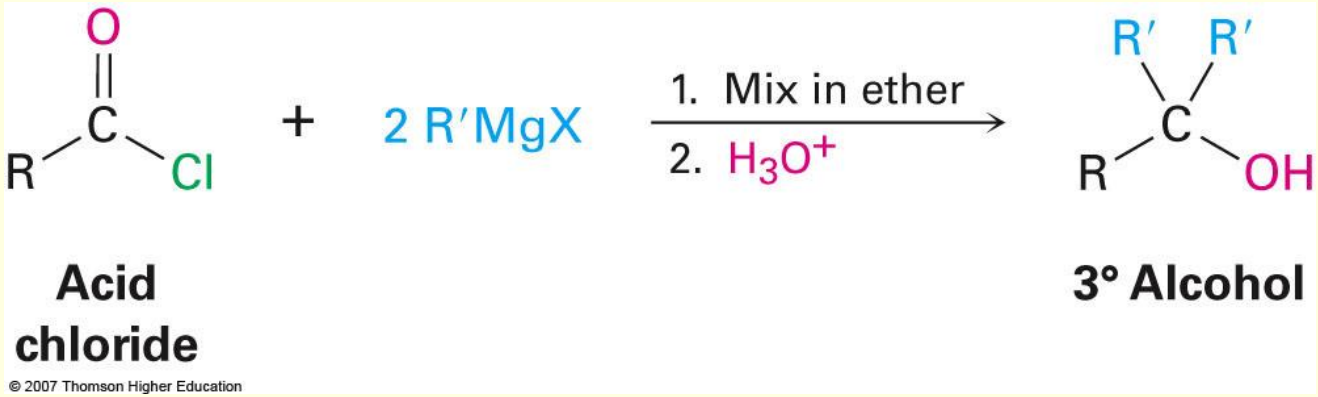
Reaction of Acid Chlorides with Organometallic Reagents

Grignard reagents react with acid chlorides to yield tertiary alcohols in which two of the substituents are the same



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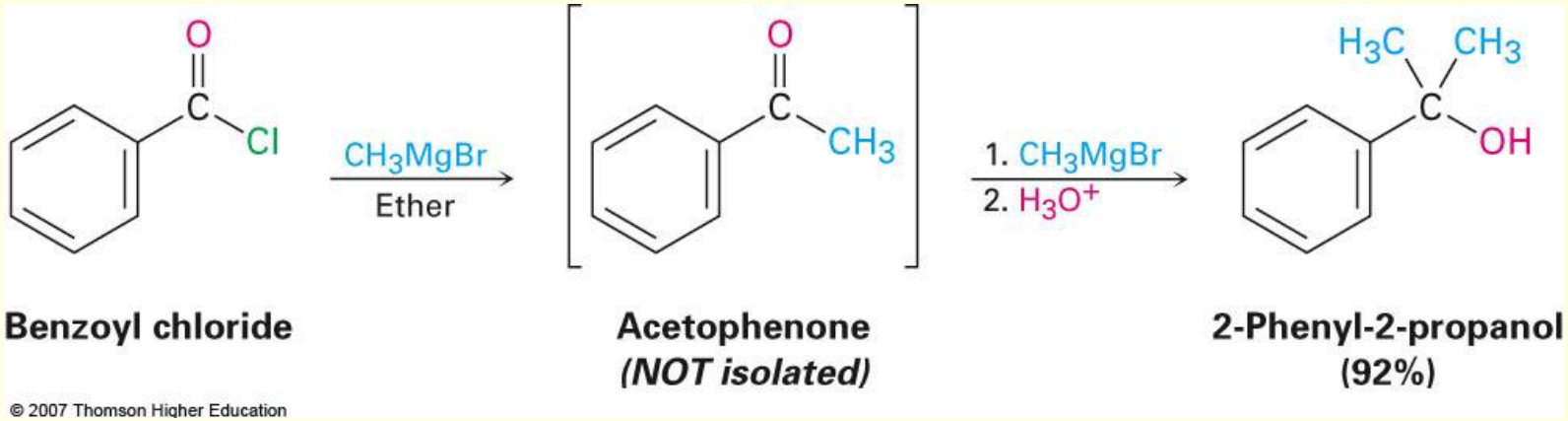

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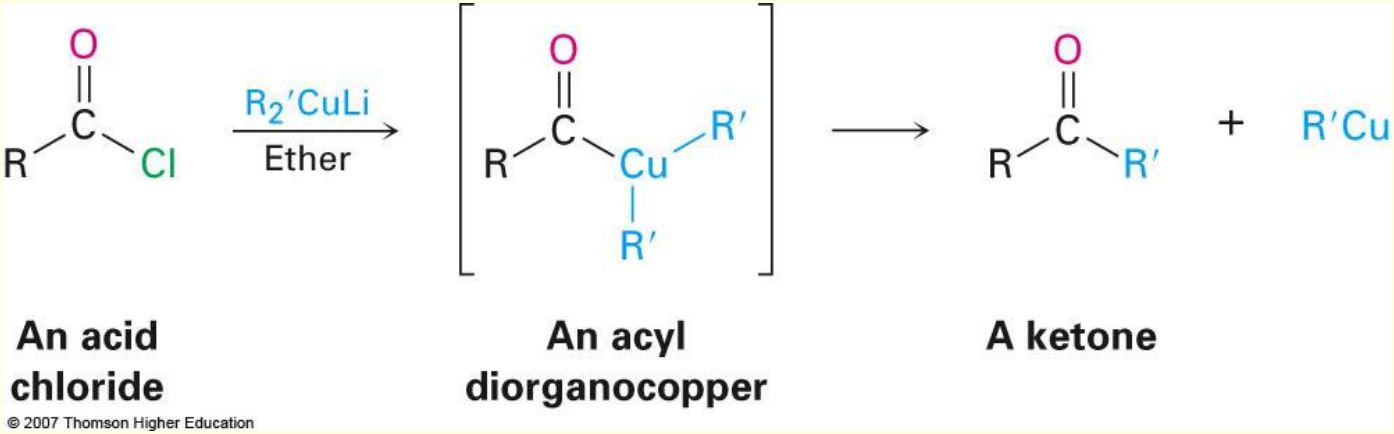
Formation of Ketones from Acid Chlorides

- Reaction of an acid chloride with a lithium diorganocopper (Gilman) reagent, Li+ R_2Cu^-
- Addition produces an acyl diorganocopper intermediate, followed by loss of R'Cu and formation of the ketone.



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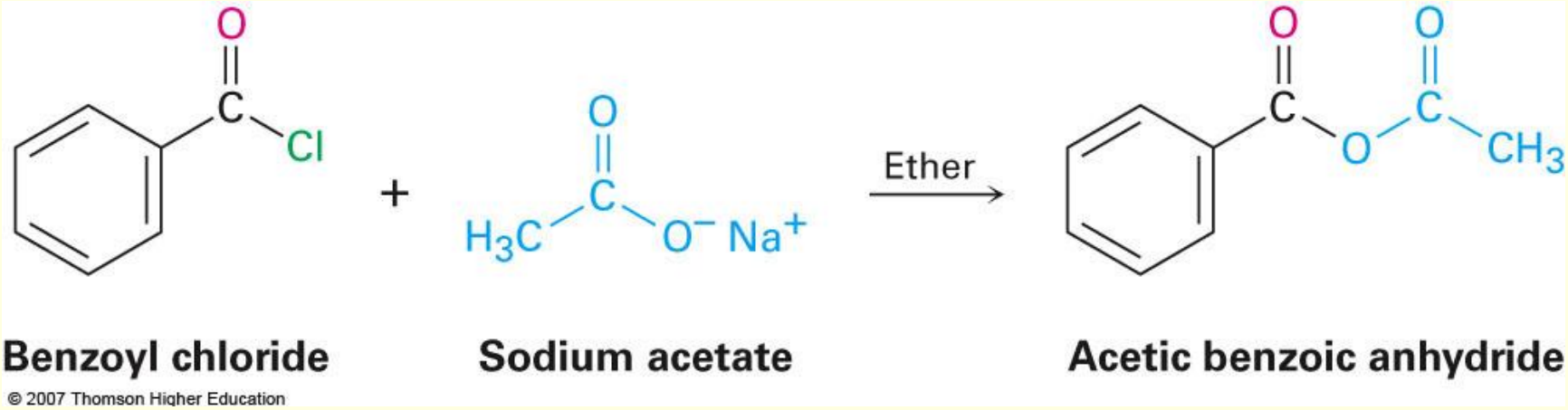
Chemistry of Acid Anhydrides

Acid anhydrides are prepared by nucleophilic acyl substitution of a carboxylate with an acid chloride.



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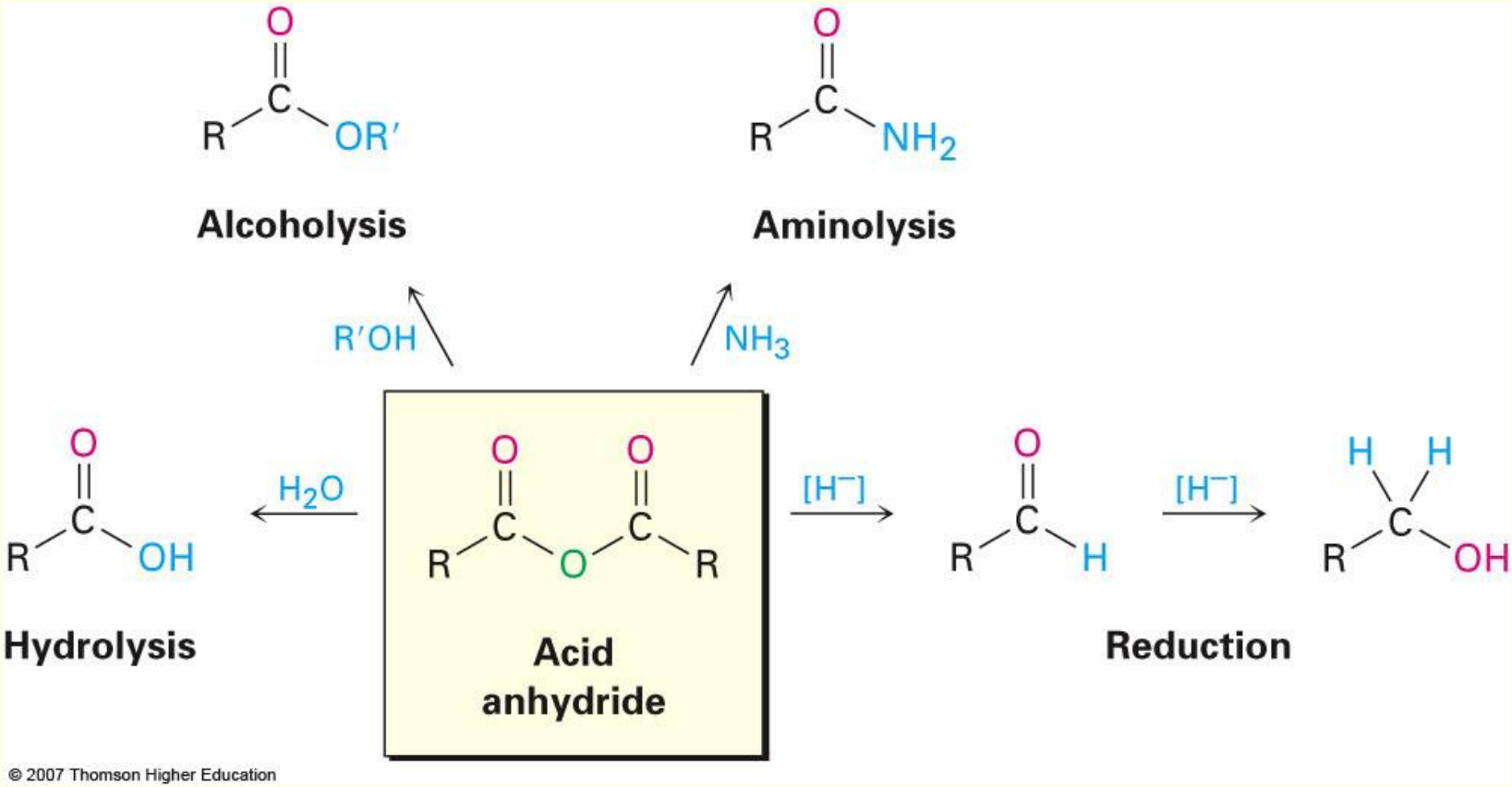
Reactions of Acid Anhydrides



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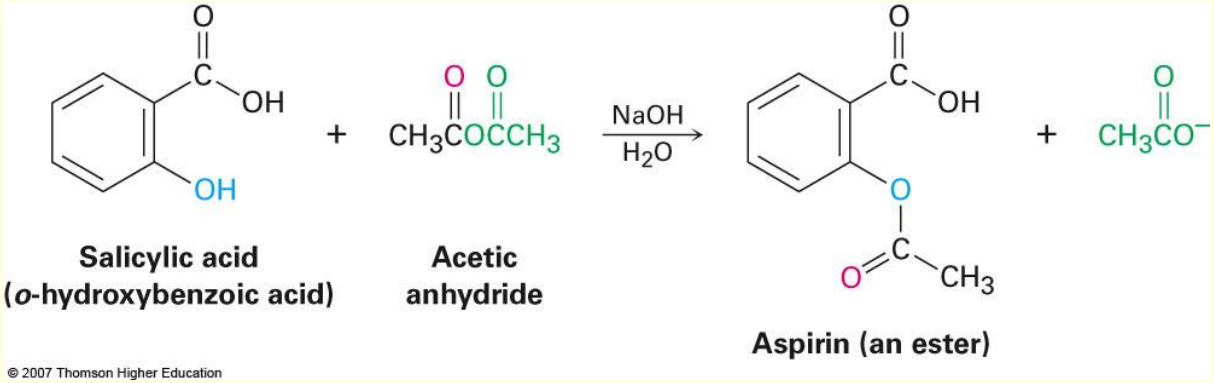
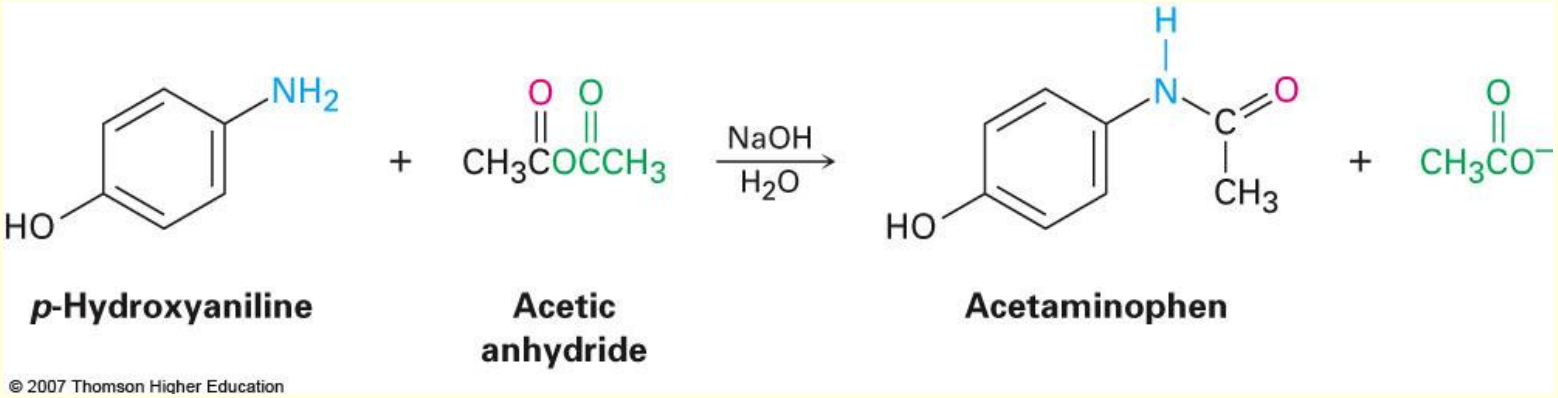
Acetylation

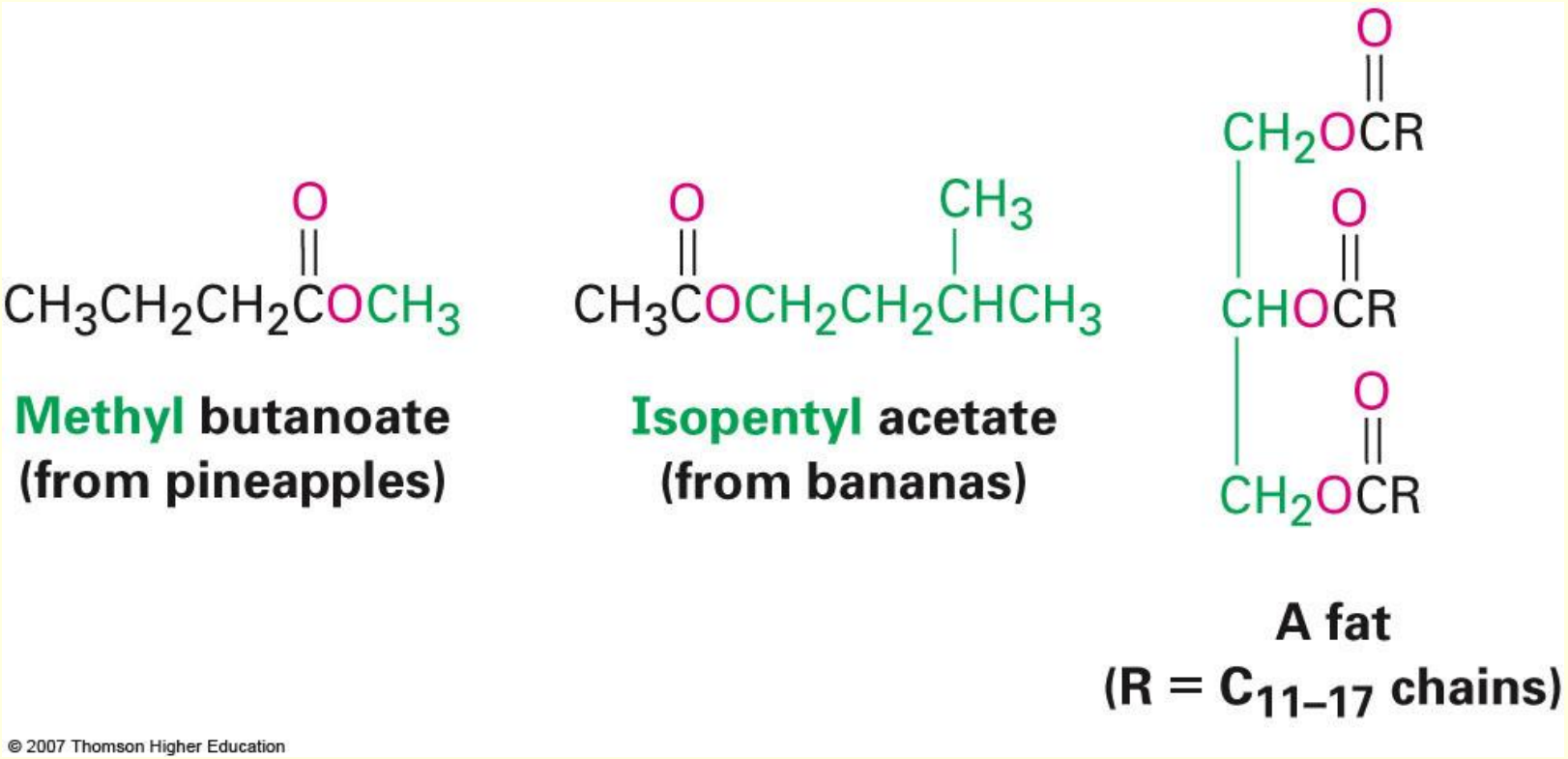
Acid anhydrides forms acetate esters from alcohols and N-substituted acetamides from amines.





Chemistry of Esters

Many esters are pleasant-smelling liquids: fragrant odors of fruits and flowers, also present in fats and vegetable oils.



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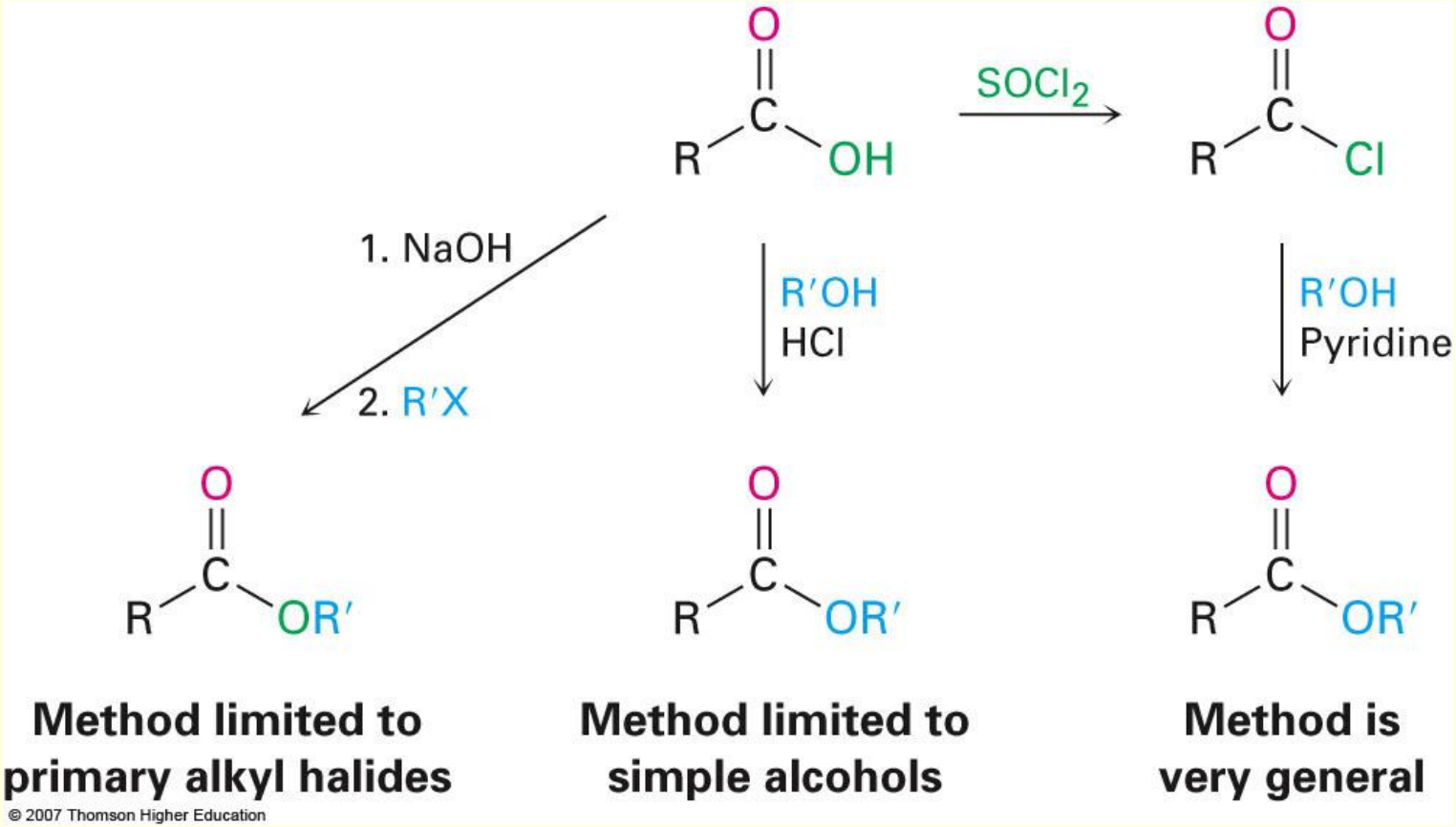
Preparation of Esters

Esters are usually prepared from carboxylic acids.



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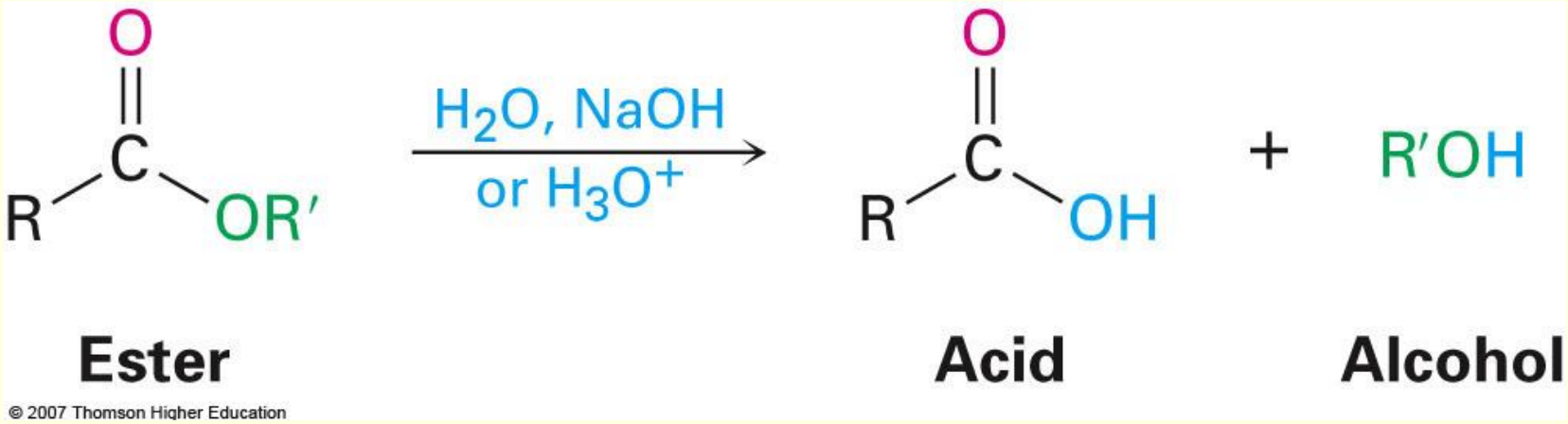
Reactions of Esters

Esters are usually less reactive toward nucleophiles than are acid chlorides or anhydrides.

Cyclic esters are called lactones and react similarly to acyclic esters

Hydrolysis: Conversion of Esters into Carboxylic Acids

An ester is hydrolyzed by aqueous base or aqueous acid to yield a carboxylic acid plus an alcohol.



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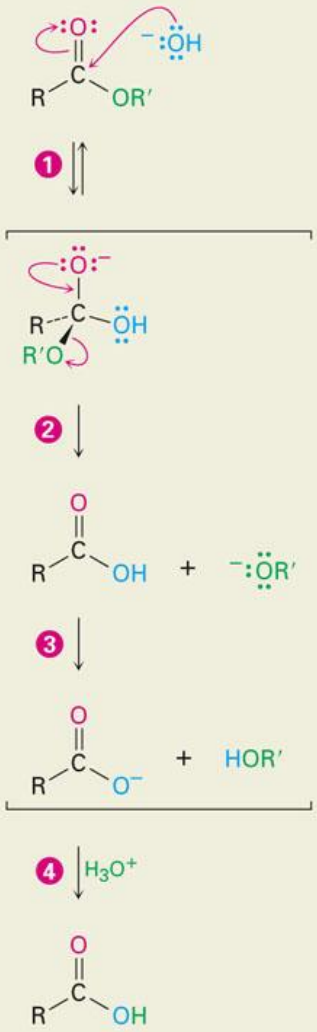
Hydrolysis of Esters: Mechanism

1. Nucleophilic addition of hydroxide ion to the ester carbonyl group gives the usual tetrahedral alkoxide intermediate.
2. Elimination of alkoxide ion then generates the carboxylic acid.
3. Alkoxide ion abstracts the acidic proton from the carboxylic acid and yields a carboxylate ion.
4. Protonation of the carboxylate ion by addition of aqueous mineral acid in a separate step then gives the free carboxylic acid.



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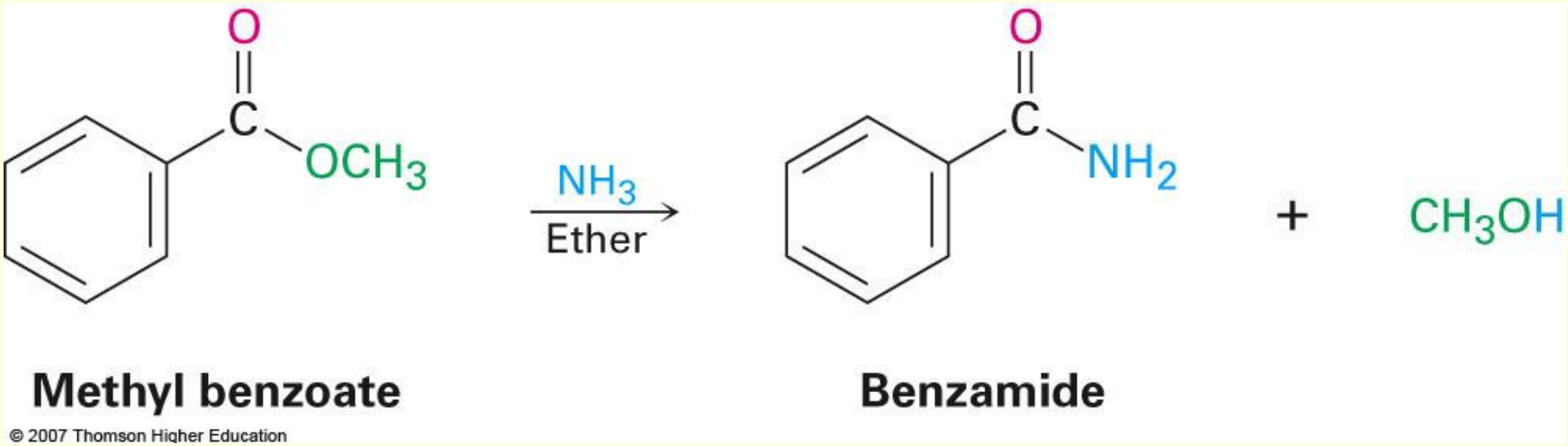
Aminolysis of Esters

Ammonia reacts with esters to form amides



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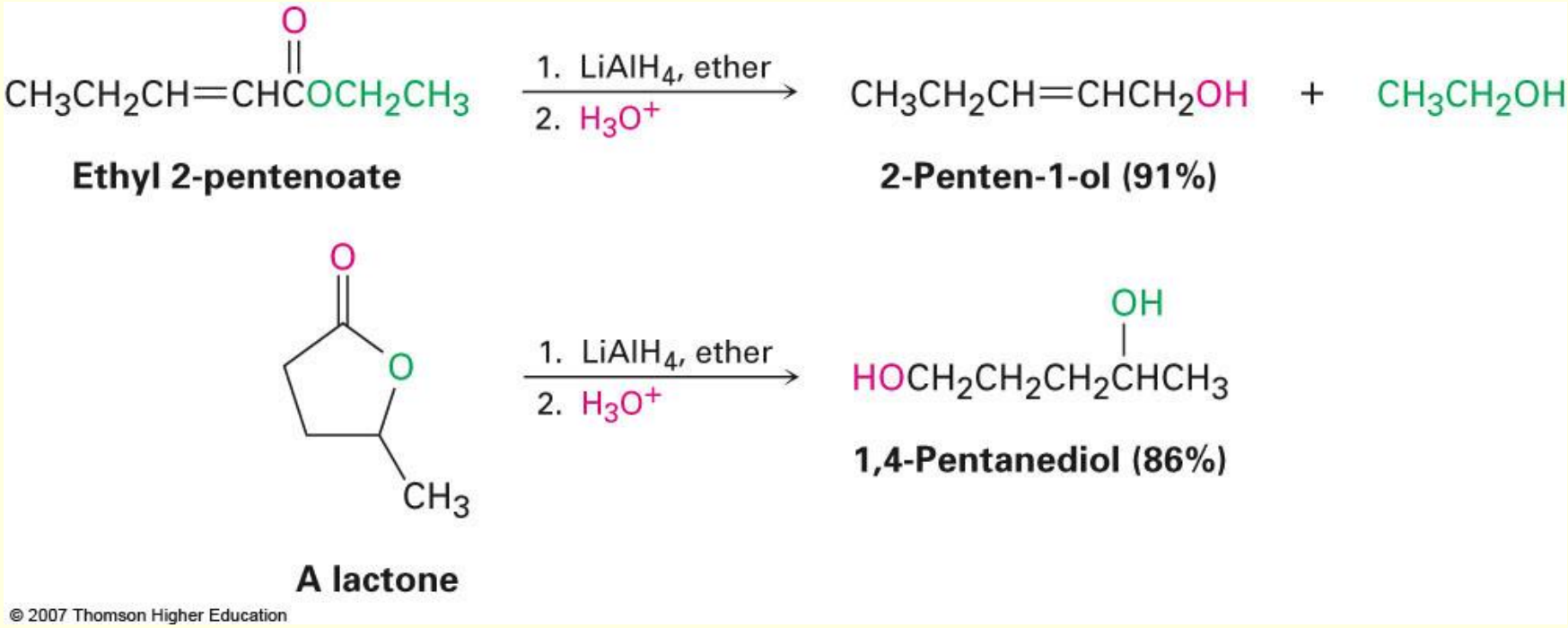
Reduction: Conversion of Esters into Alcohols

Reaction with $LiAlH_4$ yields primary alcohols



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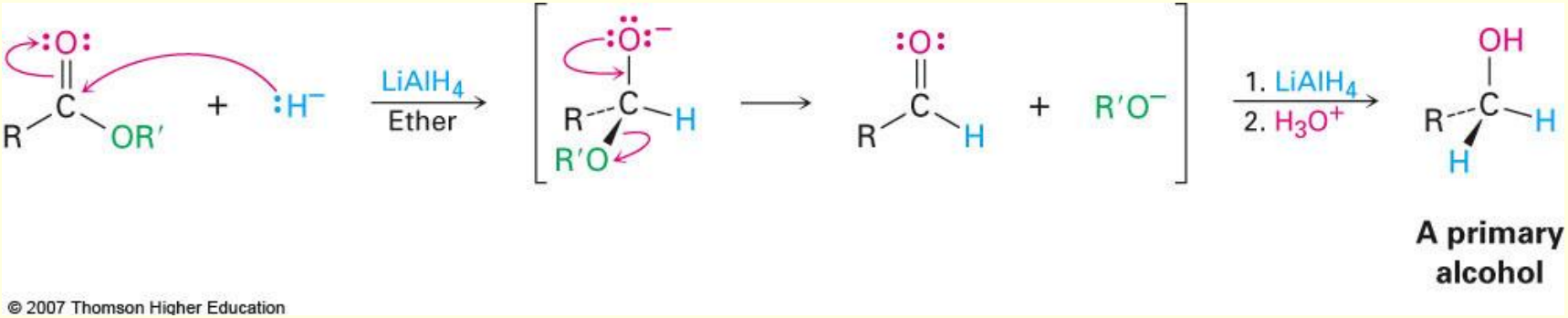
Mechanism of Reduction

- ✓Hydride ion adds to the carbonyl group, followed by elimination of alkoxide ion to yield an aldehyde.
- ✓Reduction of the aldehyde gives the primary alcohol.



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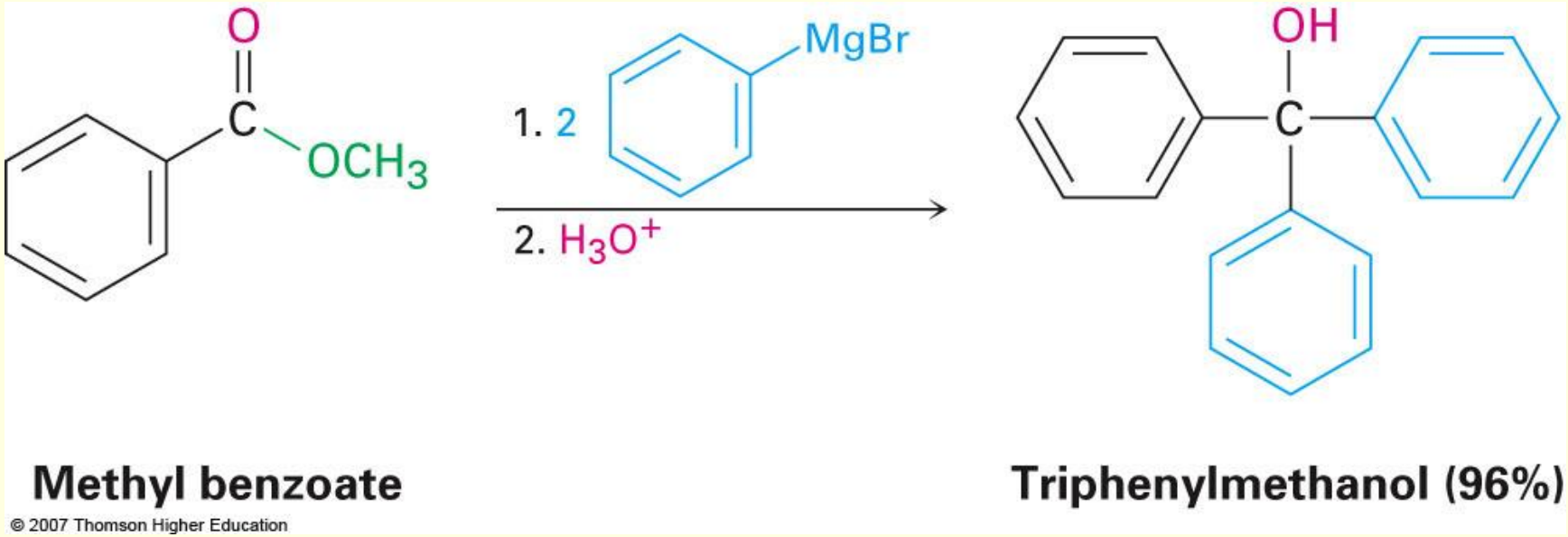
Reaction of Esters with Grignard Reagents

React with 2 equivalents of a Grignard reagent to yield a tertiary alcohol.



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