Carboxylic acid Derivatives

Part A

B. Pharm. Semester-1

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Learning Outcomes

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

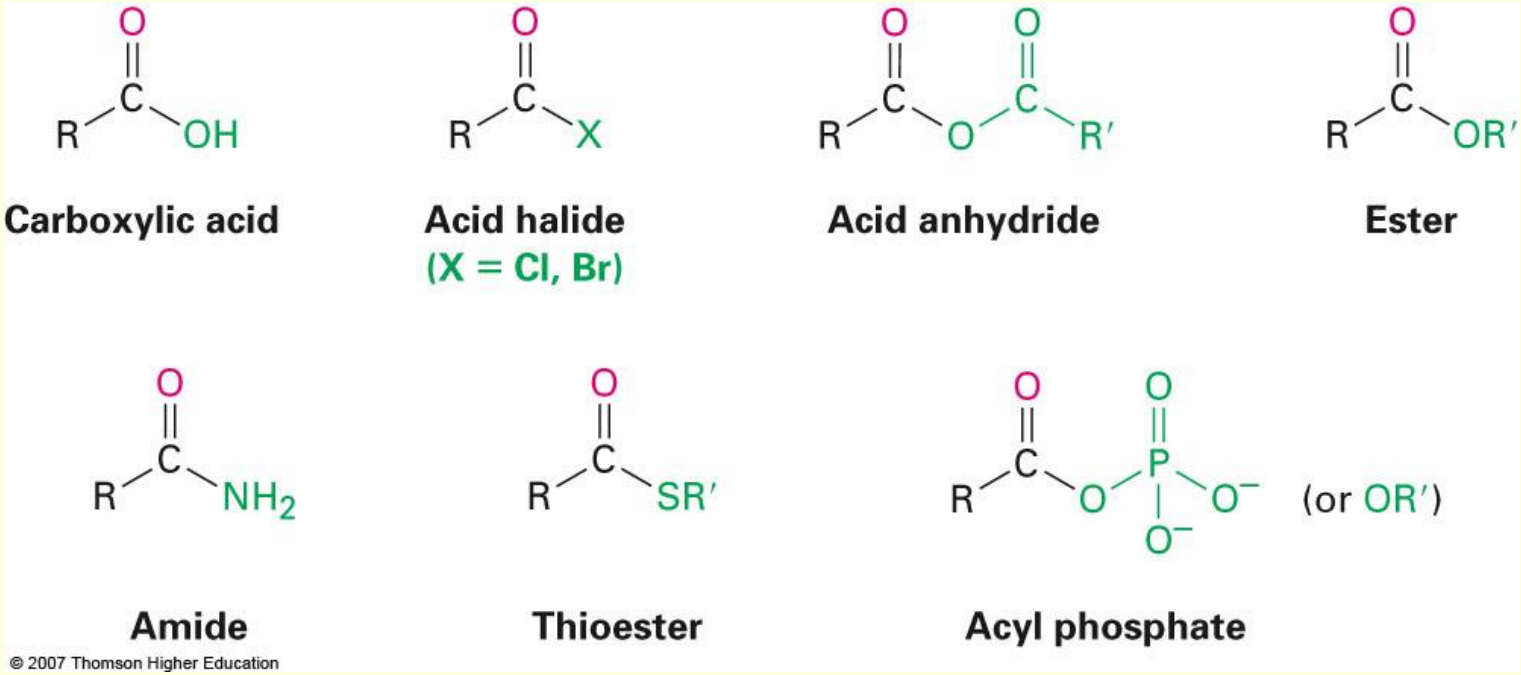
- **Naming of Carboxylic acid derivatives**
- **Nucleophilic Acyl Substitution on Carboxylic acids**

Objective

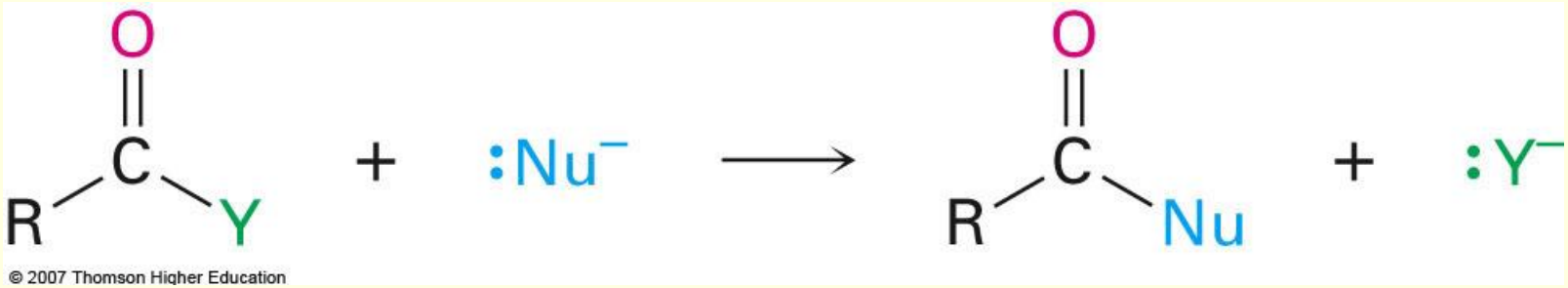
The objective of this course is to give to the students of pharmacy the basic knowledge about the organic chemistry.

Carboxylic acid Derivatives

- Acyl group bonded to X, an electronegative atom or a leaving group.
- X = halide (acid halides), acyloxy (anhydrides), alkoxy (esters), amine (amides), thiolate (thioesters), phosphate (acyl phosphates).



Nucleophilic acyl substitution



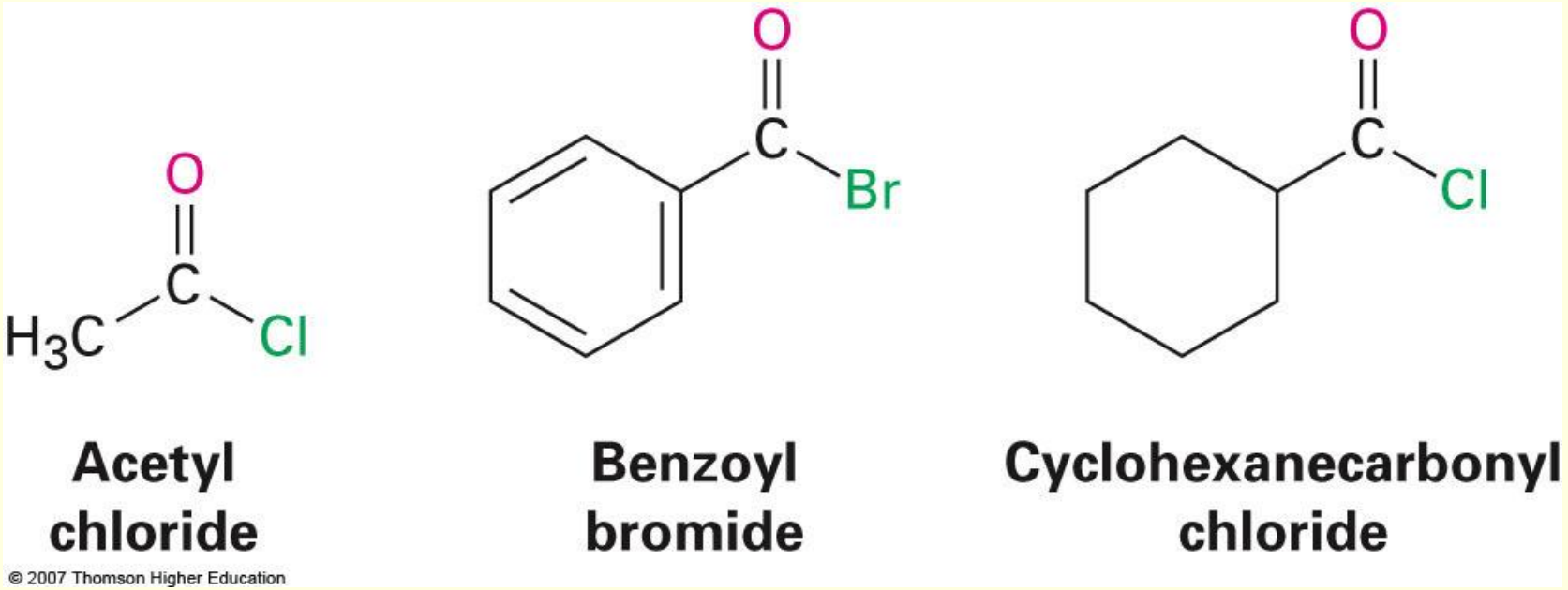
Why this Chapter?

- Carboxylic acids are among the most widespread of molecules.
- A study of them and their primary reaction "nucleophilic acyl substitution" is fundamental to understanding organic chemistry.

Naming Carboxylic Acid Derivatives: Acid halides (R-CO-X)

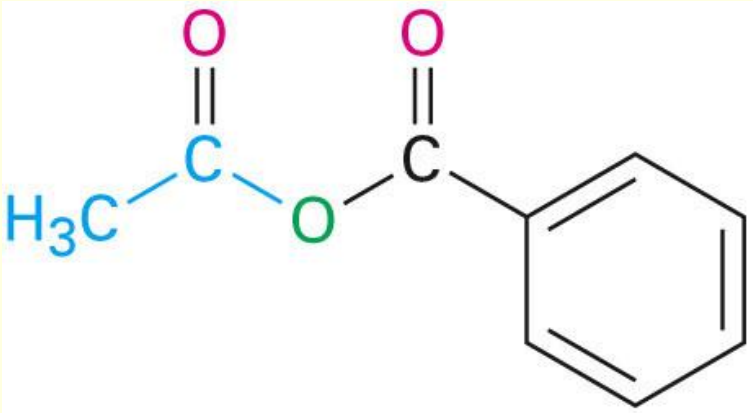
Acid Halides, RCOX

They are derived from the carboxylic acid name by replacing the -ic acid ending with -yl or the -carboxylic acid ending with –carbonyl and specifying the halide.



Naming Carboxylic Acid Derivatives: Acid Anhydrides (RCO_2COR')

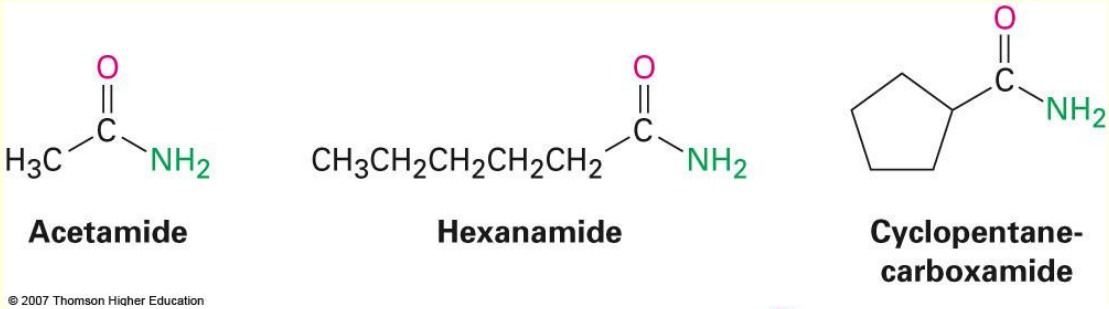
- ✓ If symmetrical replace "acid" with "anhydride" based on the related carboxylic acid.
- ✓ From substituted monocarboxylic acids: use bis- ahead of the acid name
- ✓ Unsymmetrical anhydrides- cite the two acids alphabetically.

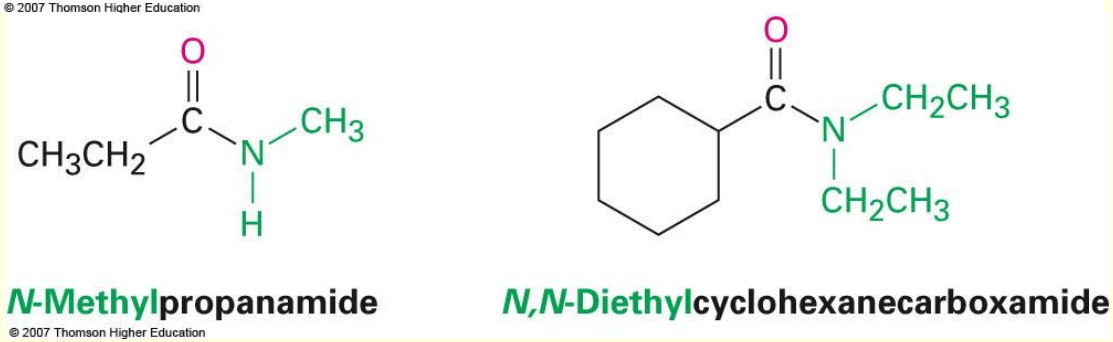


Acetic benzoic anhydride

Naming Carboxylic Acid Derivatives: Amides ($RCONH_2$)

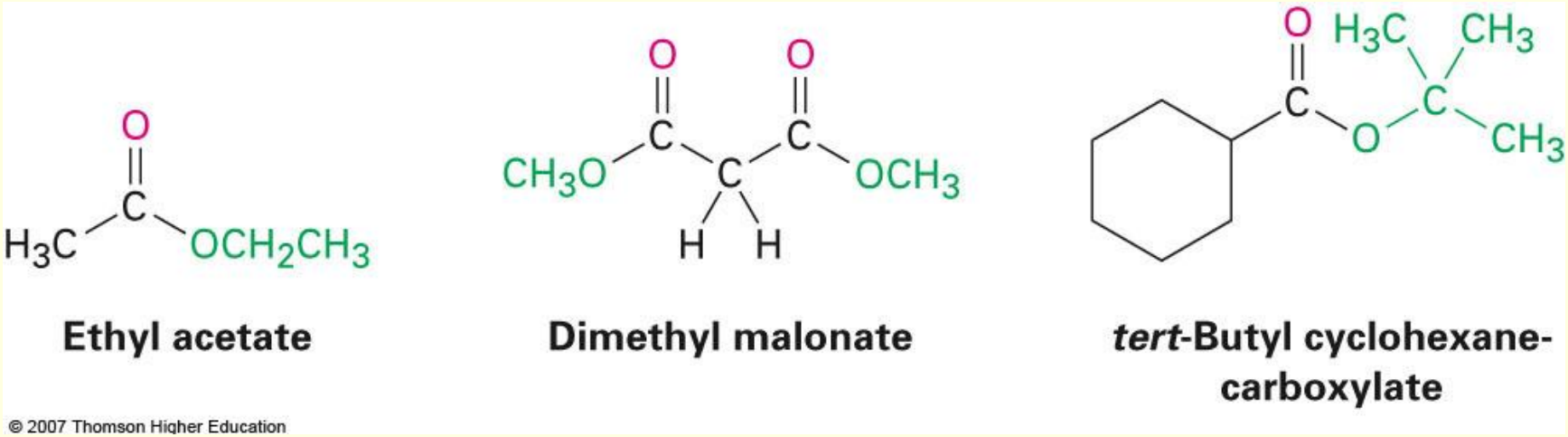
- With unsubstituted -NH_2 group. replace -oic acid or -ic acid with -amide, or by replacing the -carboxylic acid ending with –carboxamide.
- If the N is further substituted, identify the substituent groups (preceded by "N") and then the parent amide.





Naming Carboxylic Acid Derivatives: Esters (RCO_2R')

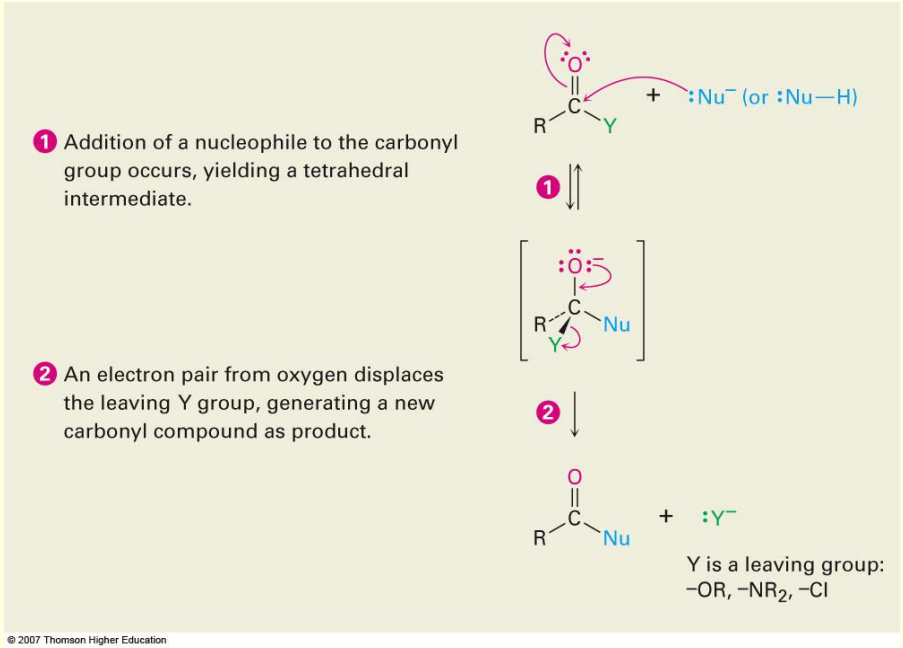
Name R' and then, after a space, the carboxylic acid (RCOOH), with the "-ic acid" ending replaced by "-ate"



Nucleophilic acyl substitution

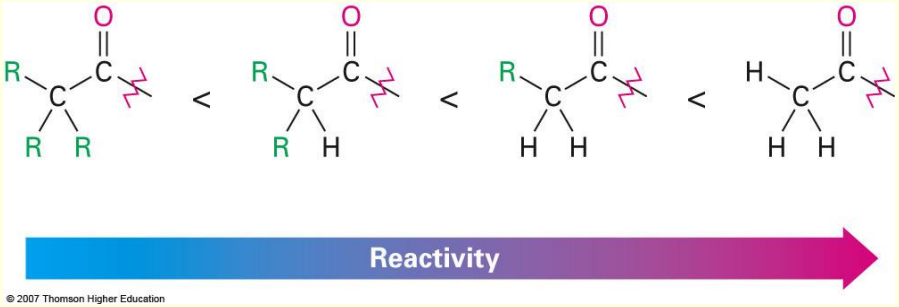
Carboxylic acid derivatives have an acyl carbon bonded to a group -Y that can leave.

A tetrahedral intermediate is formed and the leaving group is expelled to generate a new carbonyl compound, leading to the substitution.

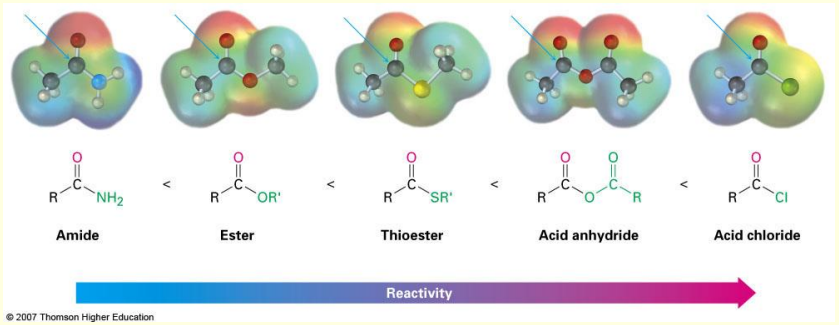


Relative Reactivity of Carboxylic Acid Derivatives

Nucleophiles react more readily with unhindered carbonyl groups



More electrophilic carbonyl groups are more reactive to addition (acyl halides are most reactive, amides are least)

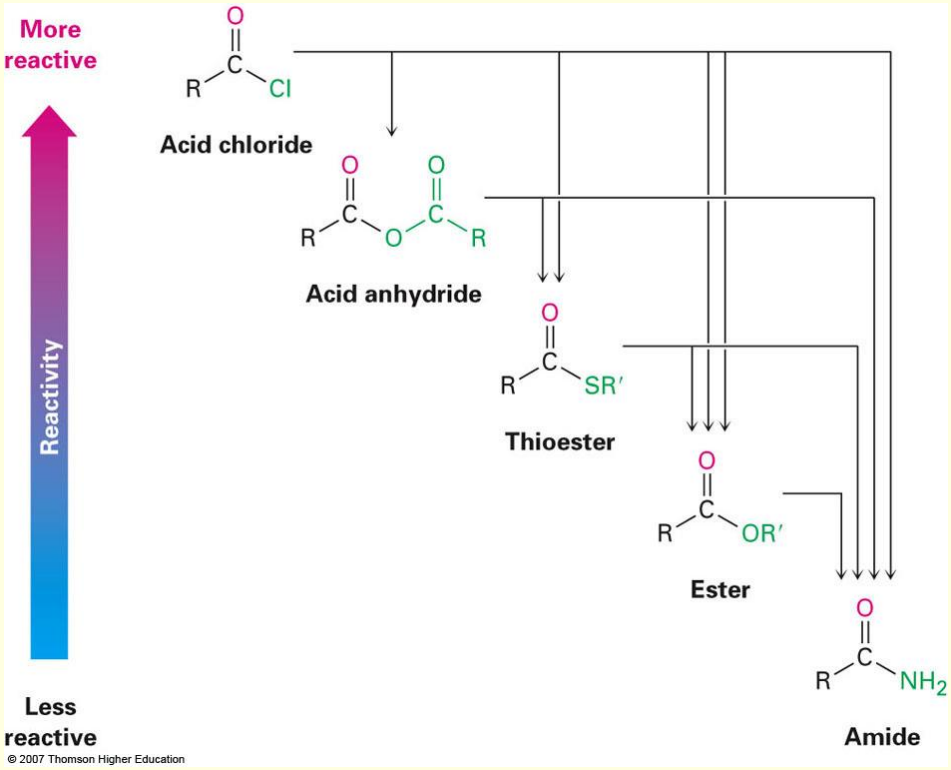


The intermediate with the best leaving group decomposes fastest

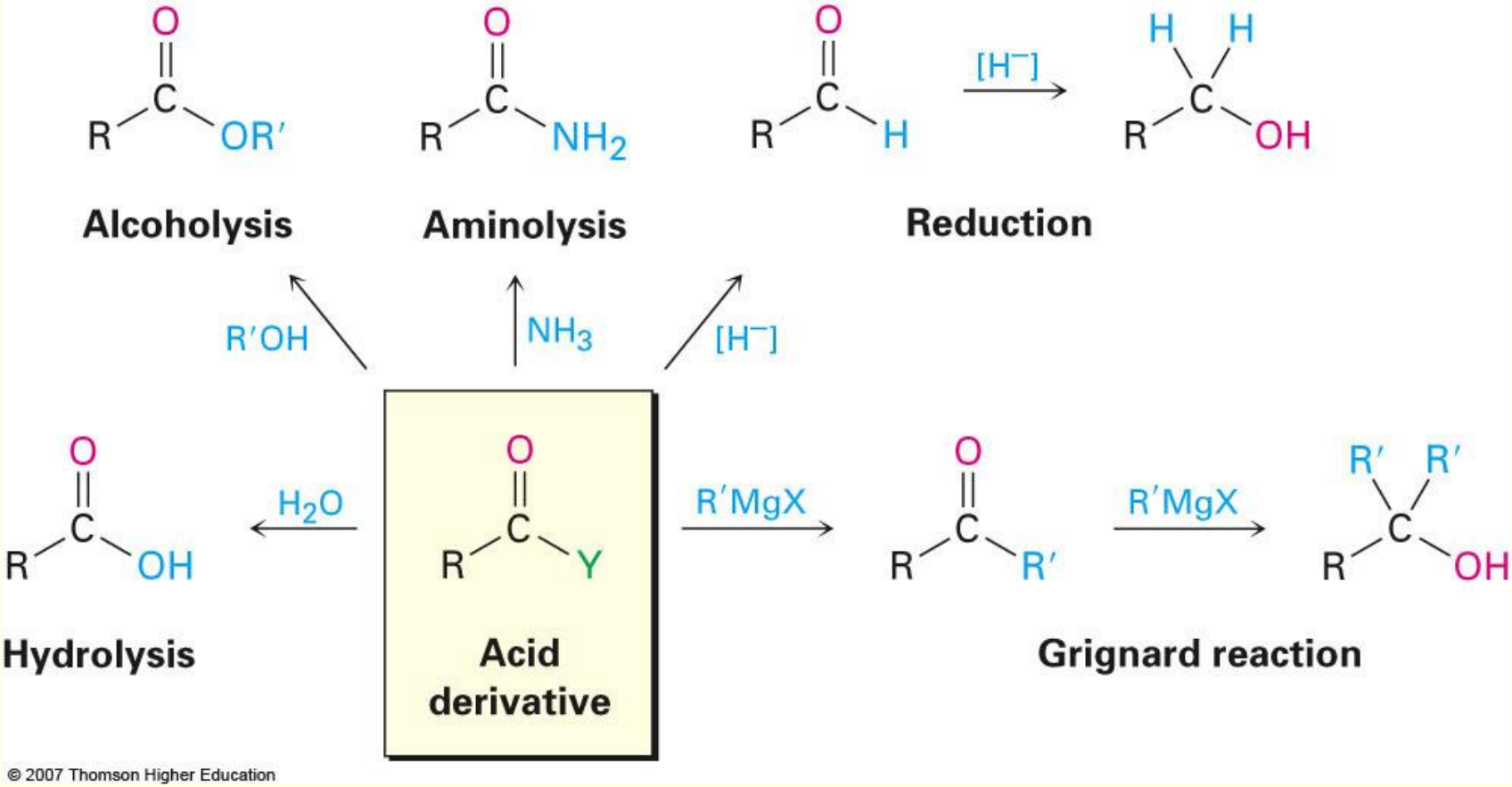
Substitution in Synthesis

❖We can readily convert a more reactive acid derivative into a less reactive one.

❖Reactions in the opposite sense are possible but require more complex approaches.

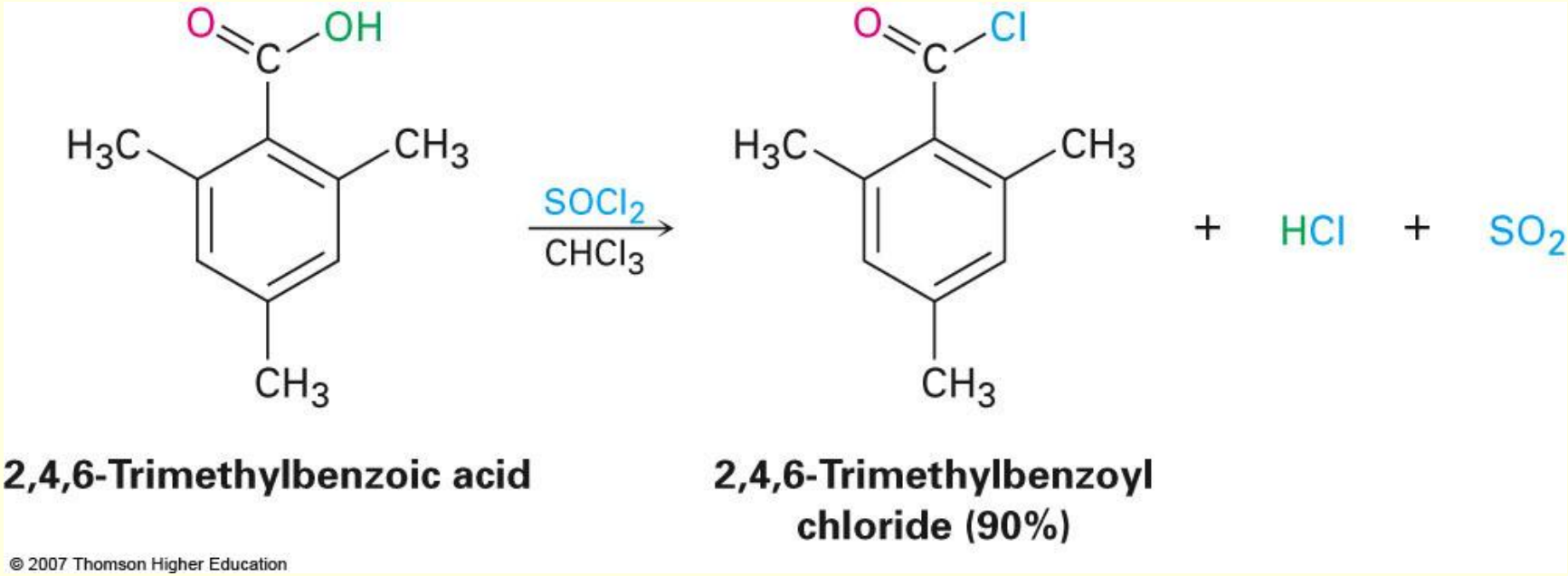


General Reactions of Carboxylic Acid Derivatives



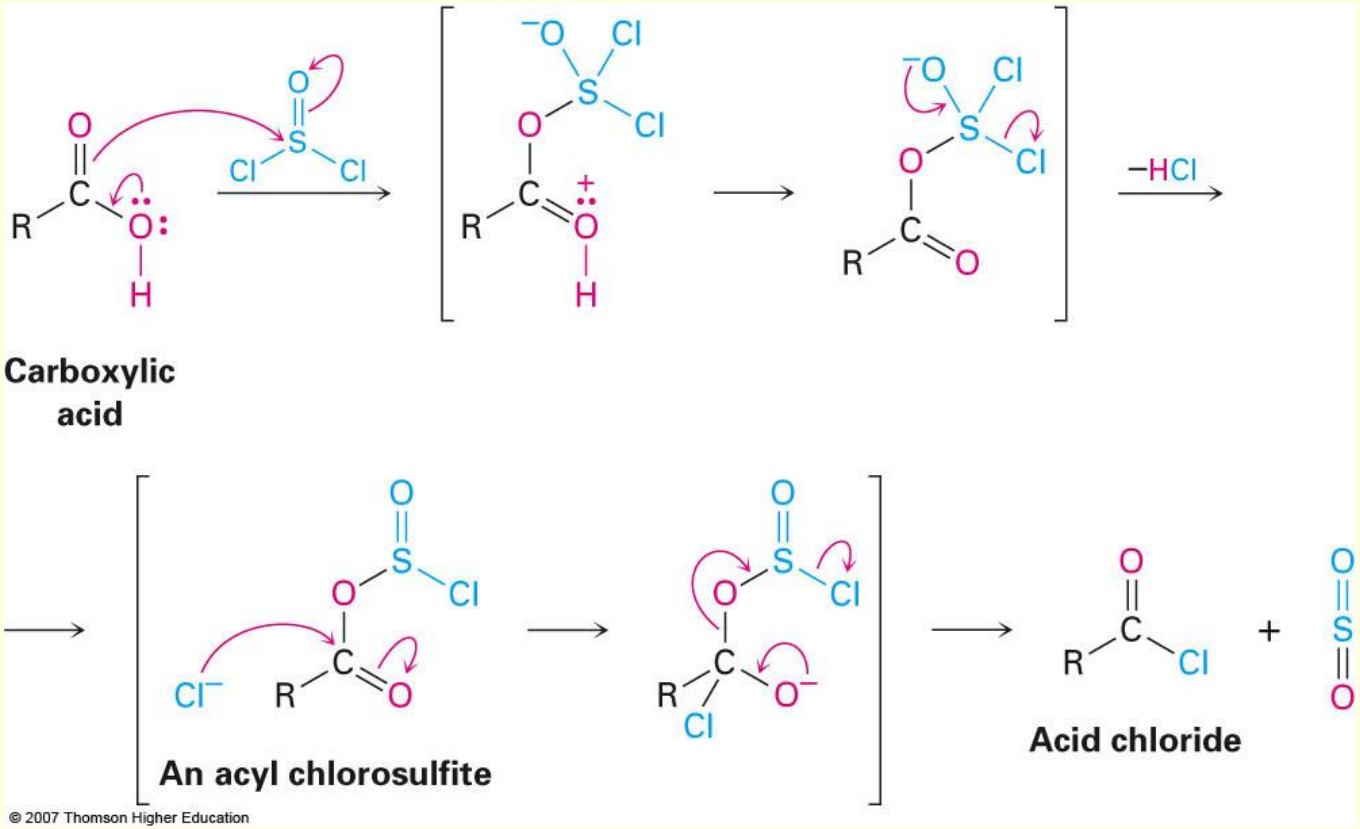
Conversion of Carboxylic Acids into Acid Chlorides

- Reaction with thionyl chloride, $SOCl_2$



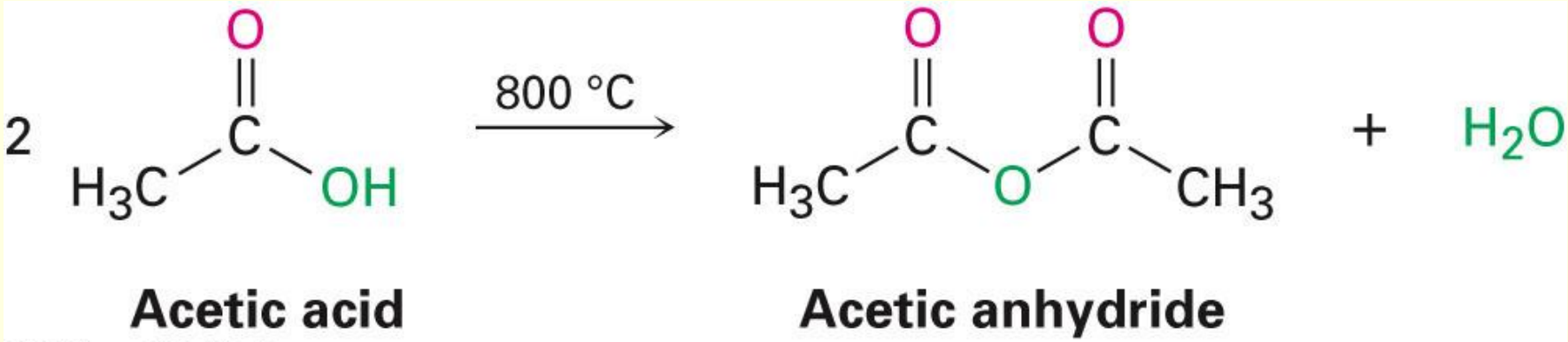
Mechanism of Thionyl Chloride Reaction

- Nucleophilic acyl substitution pathway
- Carboxylic acid is converted into a chlorosulphite which then reacts with chloride



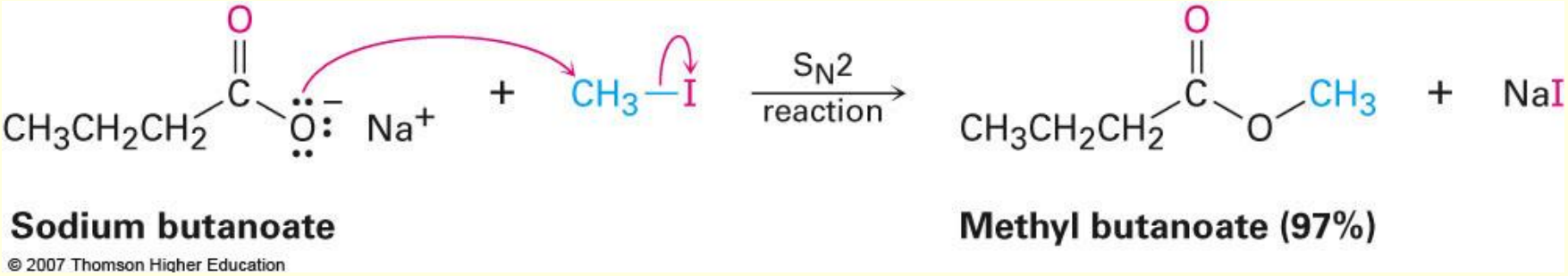
Conversion of Carboxylic Acids into Acid Anhydrides

Acid anhydrides can be derived from two molecules of carboxylic acid by strong heating to remove water.



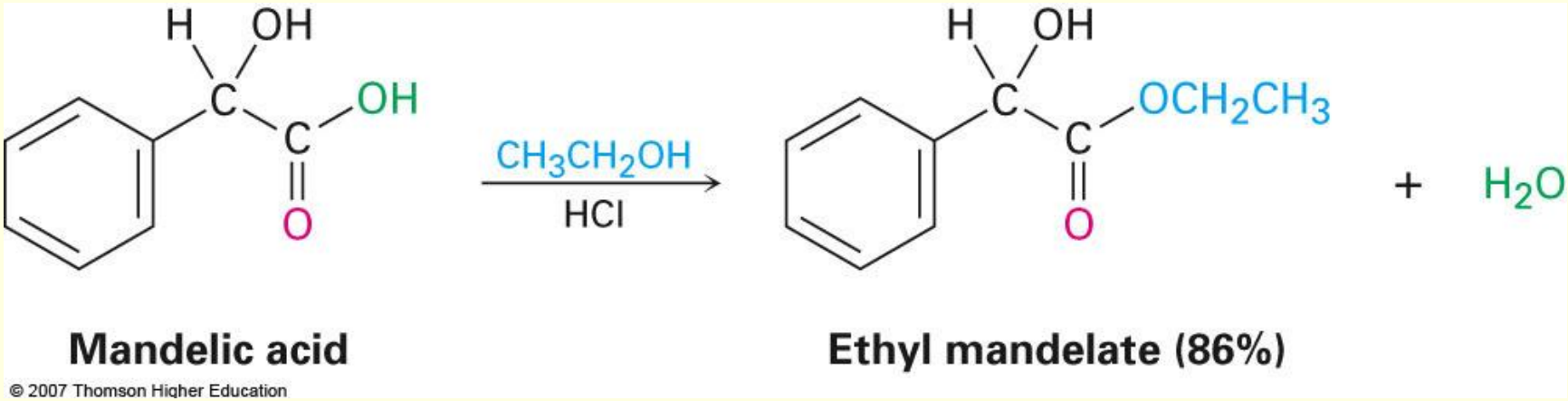
Conversion of Carboxylic Acids into Esters

Methods include reaction of a carboxylate anion with a primary alkyl halide.



Fischer Esterification

Heating a carboxylic acid in an alcohol solvent containing a small amount of strong acid produces an ester from the alcohol and acid.



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3. **Textbook of Organic Chemistry, 22nd Edition, 2022, Authors: Arun Bahl & B S Bahl, Publisher: S Chand, ISBN: 978-9352531967.**

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