

Chapter 21 Lecture Outline

"Carboxylic Acid Derivatives and Nucleophilic Acyl Substitution"

(problems: 28, **29-30**, 32aceg, 33, **35-37**, 38, **40-41**, 42, **45-46**, 47, 50, 54, 56, 61, **64-66**)

I. Introduction - carboxylic acids, esters, amides, acid halides, acid anhydrides, thioesters, acylphosphates

II. Nomenclature of Carboxylic Acid Derivatives

- A. Acid Chlorides
- B. Acid Anhydrides
- C. Esters
- D. Amides

III. Nucleophilic Acyl Substitution

- A. General Mechanism
- B. Order of Reactivity of Carboxylic Acid Derivatives

IV. Carboxylic Acids Reactions

- A. Conversion to Acid Chlorides by thionyl chloride (SOCl_2)
- B. Conversion to Acid Anhydrides (dehydration)
- C. Conversion to Esters
 - 1. carboxylate alkylation
 - 2. diazomethane esterification
 - 3. Fischer esterification (H^+ , ROH)
- D. Conversion to Amides

V. Acid Chloride Reactions

- A. Hydrolysis to Acids (substitution by H_2O)
- B. Alcoholysis to Esters (substitution by ROH)
- C. Aminolysis to Amides (substitution by 1° or 2° amine)
- D. LiAlH_4 Reduction to 1° Alcohols by (substitution & addition of H^-)
- E. Conversion to 3° Alcohols by Grignard Reagents (substitution & addition of R^-)
- F. Conversion to Ketones by Organocuprates (substitution by R^-)

VI. Acid Anhydride Reactions

- A. Hydrolysis to Acids
- B. Alcoholysis to Esters
- C. Aminolysis to Amides
- D. LiAlH_4 Reduction to 1° Alcohols

VII. Ester Reactions

- A. Hydrolysis to Acids (acid or base catalyzed)
- B. Alcoholysis to new Esters (transesterification)
- C. Aminolysis to Amides
- D. LiAlH_4 Reduction to 1° Alcohols
- E. DIBALH Reduction to Aldehydes
- F. Conversion to 3° Alcohols by Grignard Reagents (substitution & addition of R^-)

VIII. Amide Reactions

- A. Hydrolysis to Acids (acid or base catalyzed)
- B. Reduction by LiAlH_4 to Amines
- C. Dehydration of 1° Amides by SOCl_2 to Nitriles

IX. Spectroscopy of Carboxylic Acid Derivatives

- A. IR - carbonyl stretch
- B. NMR - deshielding of α CH 's and those attached to O or N; $^{13}\text{C}=\text{O}$ signals at $\delta = 160\text{-}180\text{ppm}$