

## Major Topics - Chapter 17 - Reactions at $\alpha$ -carbonyls

1. Acidity of  $\alpha$ -carbonyl hydrogens and enolate anions
2. Keto-enol tautomers and mechanism for interconversion in acid or base
3. Halogenation and haloform reaction
4. Aldol addition - mechanism and synthetic applications
  - a. Dehydration common
  - b. Reversible, especially for ketones
5. Crossed aldol, best yields when one partner has no  $\alpha$ -hydrogens
  - a. Claisen-Schmidt = simply crossed aldol with a ketone as enolate
  - b. Condensations also occur with nitriles & nitroalkanes
6. Direct formation of enolates with Lithium Diisopropyl Amide (LDA)
  - a. Kinetic control = less stable enolate formed first
  - b. Enolates can undergo aldol addition or be alkylated or acylated
  - c.  $\alpha$ -selenation of enolate, then oxidation ( $\text{H}_2\text{O}_2$ ) gives  $\alpha,\beta$ -unsaturated carbonyl
7. 1,2- vs 1,4- addition to  $\alpha,\beta$ -unsaturated carbonyls
  - a. Strong nucleophiles such as Grignards add 1,2
  - b. Weaker nucleophiles (CN, organocopper, amines, enolates) add 1,4
  - c. Michael addition = 1,4- addition of enolates
8. Robinson annelation
  - a. Michael addition followed by intramolecular crossed aldol
  - b. Useful route to six-member rings with specific functional groups

## Major Topics - Chapter 18 - Carboxylic acids and derivatives

1. Nomenclature - including common names of first 3 diacids
  - a. Lactones = cyclic esters (lactams = cyclic amides)
2. Acidity - why are COOH groups acidic and relative acidity of related compounds
3. Spectroscopy and physical properties - the most basic, not detailed
4. Preps of acid
  - a. oxidation of aldehydes and 1° alcohols
  - b. oxidative cleavage of alkenes
  - c. oxidation of aromatic side chains
  - d. oxidation of methyl ketones (haloform rxn)
  - e. hydrolysis of nitriles and cyanohydrins
  - f. carbonation of Grignard reagents
5. Nucleophilic addition substitution at COX groups
  - a. relative reactivity of acyl chlorides, anhydrides, esters and amides
  - b. prep methods for acid chlorides, esters, and amides
  - c. Mechanism of esterification, ester hydrolysis in acid or base, and similar reactions
  - d. Nitriles by dehydration of primary amides
    - i. Hydrolysis of nitriles to acids
  - e. Polyesters and polyamides

## Major Topics - Chapter 19 - $\beta$ -dicarbonyl compounds

1. Acidity of central hydrogen(s) of  $\beta$ -dicarbonyls and similar compounds
2. Claisen condensation - mechanism and products
  - a. Why reversible, and what drives to completion
  - b. Dieckmann Condensation = intramolecular Claisen
3. Crossed Claisen - best when one ester has no  $\alpha$ -hydrogens
  - a. Can use directed enolate as the nucleophile
4. Acetoacetic ester synthesis- formation of methyl ketones
  - a. Can add one alkyl group, or with stronger base, a second
  - b. Hydrolysis and decarboxylation of  $\beta$ -keto acids
  - c. Be able to apply as synthetic method and to write the mechanism
5. Malonic ester synthesis - formation of substituted acetic acids
  - a. Synthetic procedure, including stronger base for second alkyl group
  - b. Mechanism
6. Special cases for the above
  - a. Acylate instead of alkylate, gives an additional keto group
  - b. Make dianion of acetoacetic ester (need NaH or other strong base)
    - i. Alkylates the terminal C
  - c. Other e-withdrawing groups can make active  $\text{CH}_2$  - nitrile, nitro, sulfones, etc.
  - d. Can make direct enolate of esters with LDA, then alkylate
7. Alkylation of 1,3-dithianes - replaces H of  $\text{RCHO}$  with alkyl groups
  - a. Procedure, mechanism, why unique?
8. Michael addition of  $\beta$ -dicarbonyls to  $\alpha\beta$ -unsaturated carbonyls
9. Mannich reaction - adds a  $\text{CH}_2$  plus an amine to  $\alpha$ -position - Mechanism and applications
10. Enamines - formation and the Stork Enamine reaction
  - a. Alternative way to alkylate carbonyl compounds - Mechanism and procedure

## Chapter 20 - Part 1 of amines

1. Nomenclature - including common names for aniline, toluidine, pyrrole, pyridine, pyrrolidine, and piperidine and naming of amides
2. Basic structure and properties
3. Basicity and what factors enhance or reduce the basicity of amines
4. Amides, quaternary ammonium salts
5. Preparation methods for amines
  - a. Alkylation of ammonia
  - b. From azides
  - c. Gabriel synthesis - from phthalimide
  - d. Reduction of nitro groups (usually only for aromatic amines)
  - e. Reductive amination - from carbonyl via imines or iminium ions
  - f. Reduction of nitrile, oximes, or amides
  - g. Hofmann rearrangement - from primary amide
    - i. Mechanism and application
  - h. Curtius rearrangement - from carbonyl azide