Chapter 19 Concepts: Carboxylic Acids and Nitriles
- $pK_a$ and effects of resonance, inductive effects, etc on $pK_a$
- Protonation of carbonyl $O$
- Hydrolysis of Nitriles
- Reduction of Nitriles
- Addition of Nitriles to Organometallics

- Nucleophilic Acyl Substitution
  - Acid chlorides, anhydrides, carboxylic acids, esters, amides
- Nitrile Synthesis
- More Reaction of Nitriles
  - Hydrolysis, reduction, reaction with organometallic reagents
  - Nucleophilic Acyl Substitution
  - Structure, bonding, rates
  - Carbonyl Reactivity and L.G ability
  - Acyl Chloride Reactions
    - DCC, Et$_3$N, and pyridine as solvents
    - Mechanism
  - Acid Anhydrides
  - Fischer Esterification
    - Ester Hydrolysis
  - Saponification
  - Hydrolysis of Amides
  - Multistep Synthesis

Chapter 21 Concepts: Enols and Enolates
- 21.1-4 Enol/Enolate Chemistry
  - Tautomerization
    - Acid-Catalyzed
  - 21.5 Racemization of alpha-carbon
  - 21.7 Halogenation at alpha-carbon
    - Subsequent elimination of halogen
  - 21.8 Kinetic vs Thermodynamic Enolates
  - 21.9-10 Malonic/Acetoacetic Esters
1. Draw the products of each reaction.

a. 

\[
\text{CH}_3\text{CH}_2\text{MgCl} \rightarrow \text{H}_2\text{O}
\]

b. 

\[
\text{C}_6\text{H}_5\text{Li} \rightarrow \text{H}_2\text{O}
\]

2. Rank the compounds in each group in order of increasing reactivity in nucleophilic acyl substitution.

a. 

- \(\text{CH}_3\text{NH}_2\)
- \(\text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_3\)
- \(\text{CH}_3\text{Cl}\)

b. 

- \(\text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_3\)
- \(\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_3\)
- \(\text{C}_3\text{F}_7\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_3\)

c. 

- \(\text{CH}_3\text{COOH}\)
- \(\text{CH}_3\text{COSH}\)
- \(\text{CH}_3\text{Cl}\)
3. What carboxylic acid and alcohol are needed to prepare each ester by Fischer esterification?

a. \((\text{CH}_3)_3\text{CCO}_2\text{CH}_2\text{CH}_3\)

b.

c.

d.
4. Treatment of the amino alcohol X with diethyl carbonate forms the heterocycle Y. Draw a stepwise mechanism for this process.

$$\text{NH}_2 \quad \text{OH} \quad \text{X} \quad + \quad \text{(CH}_3\text{CH}_2\text{O})_2\text{C} = \text{O} \quad \text{diethyl carbonate} \quad \rightarrow \quad \text{Y} \quad + \quad 2 \text{CH}_3\text{CH}_2\text{OH}$$

5. (a) Both monomers needed for the synthesis of nylon 6,6 can be prepared from 1,4-dichlorobutane. Write out the steps illustrating these syntheses. (b) Devise a synthesis of adipic acid from cyclohexene.
6. What two monomers are needed to prepare each polymer?

a. 

b. 
7. Explain why 5,5-dimethyl-1,3-cyclohexanedione exists predominantly in its enol form, but 2,2-dimethyl-1,3-cyclohexanedione does not.

8. Write a stepwise mechanism for this reaction. Explain why one stereogenic center changes configuration but the other does not.
9 Draw a stepwise mechanism for each reaction.

a. \[
\begin{align*}
\ce{\text{Br}_2} & \quad \ce{CH_3CO_2H} \\
\ce{O} & \quad \ce{O} \\
\ce{Br} & \quad \ce{HBr}
\end{align*}
\]

b. \[
\begin{align*}
\ce{I_2 (excess)} & \quad \ce{-OH} \\
\ce{O} & \quad \ce{O} \\
\ce{O^-} & \quad \ce{CH_3}
\end{align*}
\]
10. Devise a synthesis of valproic acid \[(\text{CH}_3\text{CH}_2\text{CH}_2)\text{CHCO}_2\text{H}\], a medicine used to treat epileptic seizures, using the malonic ester synthesis.
11. (a) Identify intermediates A–C in the following stepwise conversion of p-isobutylbenzaldehyde to the analgesic ibuprofen. (b) Direct alkylation of D by treatment with one equivalent of LDA and CH3I does not form ibuprofen. Identify the product of this reaction and explain how it is formed.

(a)
12. Treatment of ketone A with LDA followed by CH$_3$CH$_2$I did not form the desired alkylation product B. What product was formed instead? Devise a multistep method to convert A to B, a synthetic intermediate used to prepare the anticancer drug tamoxifen.
13. Draw a stepwise mechanism for this conversion in the presence of acid.