Chapter 23
1. What is the most and least acidic ammonium ion?

\[ \begin{align*}
1 & : \text{H}_2\text{N(CH}_2\text{CH}_3)_2^+ \\
2 & : \text{NH}_4^+ \\
3 & : \text{O}_2\text{N} \quad \text{NH}_3 \\
4 & : \text{C}_6\text{H}_4\text{NH}_3^+ 
\end{align*} \]

1 is the least acidic ammonium ion. It has the least stable conjugate base due to it being electron rich (the N has a lone pair) and there are no electron withdrawing groups.

3 is the most acidic because it forms the most stable conjugate base. There are many different resonance structures that can be formed and NO\textsubscript{2} is a very strong electron withdrawing group.

2. The following structure is histamine. Rank the three nitrogens in order of decreasing basicity by putting a number next to each (1=most basic)

\[ \begin{align*}
1 & : \text{H}_2\text{N} \\
2 & : \text{N} \\
3 & : \text{NH} 
\end{align*} \]

1 is the most basic (or least acidic) because it is sp\textsubscript{3}. 2 is sp\textsubscript{2}, making it more acidic. The “3” nitrogen will not act as a base because it is aromatic, meaning its lone pair is in a p-orbital and will be unable to attack a hydrogen.

3. Draw the mechanism and product for the following Henry Reaction.
4. Draw the mechanism and product for the following Mannich Reaction.

\[
\begin{array}{c}
\text{CH}_3 \text{C} \equiv \text{O} \rightarrow \text{CH}_2 \text{NO}_2 \\
\text{CH}_3 \text{C} \equiv \text{O} \rightarrow \text{CH}_2 \text{NO}_2 \\
\end{array}
\]

5. Draw the products for the following reactions

a. \[ \text{H}_2\text{C} \equiv \text{O}, (\text{CH}_3)_2\text{NH} \]

b. \[ \text{HCl/EtOH} \]

c. \[ \text{NaOH} \]
b. Gabriel Synthesis

\[
\begin{align*}
\text{A} & \xrightarrow{\text{HO}^-, \text{H}_2\text{O}} \text{A} \\
\text{B} & \xrightarrow{\text{H}_2\text{C}^-\text{Br}} \text{B} \\
\text{C} & \xrightarrow{\text{HCl, H}_2\text{O, }\Delta} \text{C} \\
\text{D} & \xrightarrow{\text{HO}^-} \text{D}
\end{align*}
\]

\[
\begin{array}{c}
\text{A} \\
\text{B} \\
\text{C} \\
\text{D}
\end{array}
\]

b. Gabriel Synthesis

\[
\begin{align*}
\text{A} & \xrightarrow{\text{HO}^-, \text{H}_2\text{O}} \text{A} \\
\text{B} & \xrightarrow{\text{H}_2\text{C}^-\text{Br}} \text{B} \\
\text{C} & \xrightarrow{\text{HCl, H}_2\text{O, }\Delta} \text{C} \\
\text{D} & \xrightarrow{\text{HO}^-} \text{D}
\end{align*}
\]

\[
\begin{array}{c}
\text{A} \\
\text{B} \\
\text{C} \\
\text{D}
\end{array}
\]

c. Reduction of a nitrile

\[
\begin{align*}
\text{R} & \xrightarrow{1. \text{LiAlH}_4} \text{R} \\
\text{C} & \xrightarrow{2. \text{H}_2\text{O}} \text{R}\text{NH}_2
\end{align*}
\]

d. Reduction of an amide

\[
\begin{align*}
\text{R} & \xrightarrow{1. \text{LiAlH}_4} \text{R} \\
\text{C} & \xrightarrow{2. \text{H}_2\text{O}} \text{R}\text{N}\text{R}_1\text{R}_2
\end{align*}
\]
5. Provide the reagents for the following synthesis reactions. (Includes review from ch. 16 and 17)

a.

\[ \text{Cyclohexene} \xrightarrow{?} \text{Cyclohexanol} \quad \text{NH}_2 \]

1. Cl \text{AlCl}_3
2. NBS, ROOR, hv
3. KOC(CH_3)_3
4. mCPBA
5. NaN_3, H_2O
6. H_2, Pd

b.

\[ \text{Benzene} \xrightarrow{\text{Br}, \text{Pd}} \text{Benzene} \]

1. HNO_3, H_2SO_4
2. H_2, Pd
3. Br_2 (2 eq) - don't need FeBr_3 since NH_2 is a strong activator
4. NaNO_2, H_2SO_4
5. H_3PO_4

c.

\[ \text{Benzene} \xrightarrow{?} \text{Benzene} \]

1. HNO_3, H_2SO_4
2. Br_2, FeBr_3
3. H_2, Pd
4. NaNO_2, HCl, H_2O
5. KI

d.
e.

**First Step**
1. Br₂, FeBr₃
2. HNO₃, H₂SO₄
3. Zn(Hg), HCl
4. pyridine

**Second Step**
H₂NNH₂, NaOH
or
1. LiAlH₄
2. H₂O

f.

1. NBS, ROOR, hv
2. KOC(CH₃)₃
3. (CH₃)₃CuLi
4. H₂O
5. HNO₃, H₂SO₄
6. H₂, Pd
7. NaNO₂, HCl, H₂O
8. HBF₄ Δ

Review (Ch. 18/19/20)
1. Fill in the boxes with the appropriate product, starting material, or reagent.

a. 

\[
\begin{align*}
\text{H}_2\text{C} & \quad \text{PhNH}_2 \\
\text{\text{acetonitrile, cat. AcOH}} & \quad \text{H}_3\text{C} - \text{N} - \text{Ph}
\end{align*}
\]

b. 

\[
\begin{align*}
\text{cyclopentanone} & \quad \text{HN} \\
\text{\text{acetonitrile, cat. AcOH}} & \quad \text{cyclopentenimine}
\end{align*}
\]

c. 

\[
\begin{align*}
\text{2-bromo-2-methylpropanal} & \quad \text{TsOH} \\
\text{\text{glycerol}} & \quad \text{2,3-dimethyl-2,3-dihydroxypropanoic acid}
\end{align*}
\]

d. 

\[
\begin{align*}
\text{4-hydroxy-4-oxocyclohexylamine} & \quad \text{HCl} \\
\text{H}_2\text{O} & \quad \text{2,3-diaminocyclohexanecarboxylic acid}
\end{align*}
\]
2. Complete the multistep synthesis.

a.

b.
c.

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\[ \text{\textbf{3. Suggest a plausible arrow-pushing mechanism for the following reaction.}} \]

\[ \text{\textbf{4. Fill in the boxes with the appropriate product, starting material, or reagent.}} \]

\[ \text{\textbf{a.}} \]

\[ \text{\textbf{b.}} \]

\[ \text{\textbf{i}) \text{ LiAlH}_4 \]
\[ \text{\textbf{ii}) \text{ H}_2\text{O Workup}} \]

\[ \text{\textbf{Et}_3\text{N}} \]
b.

\[
\begin{align*}
\text{bromobenzene} & \xrightarrow{\text{Mg, ether}} \text{aryl magnesium bromide} \\
\text{aryl magnesium bromide} & \xrightarrow{\text{H}_2\text{O}} \text{phenol}
\end{align*}
\]

C.

\[
\begin{align*}
\text{2-hexanone (OCH}_3\text{)} & \xrightarrow{i) \text{DIBAL-H}} \text{2-hexanone} \\
\text{2-hexanone} & \xrightarrow{\text{H}_2\text{O}} \text{2-hexanone}
\end{align*}
\]
Chapter 21

1. Determine the starting material or product for each of the following reactions

A.

\[
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A. \[
\text{Br}_2 \quad \text{AcOH} \quad \rightarrow \quad \text{product}
\]

B. \[
\text{KOC(CH}_3\text{)}_2 \quad \rightarrow \quad \text{product}
\]

C. \[
\text{Ph} \quad \text{LDA} \quad \text{THF, -78°C} \quad \rightarrow \quad \text{product}
\]
D.

\[
\begin{align*}
\text{NaOH} & \quad \Delta \\
\text{[structure]} & \rightarrow \\
\text{[product]} & 
\end{align*}
\]

E.

\[
\begin{align*}
\text{NaOEt} & \\
\text{[structure]} & \rightarrow \\
\text{[product]} & 
\end{align*}
\]

F.

\[
\begin{align*}
\text{NaOH} & \\
\text{[structure]} & \rightarrow \\
\text{[product]} & 
\end{align*}
\]
2. Determine the reagents needed for the following synthesis reaction

![Chemical Reaction Diagram]
Chapter 22:
3. Determine the starting material or major product for each of the following reactions

A.

\[
\begin{align*}
\text{MeO} & \quad + \quad \text{CH}_2\text{CH}_2\text{CO}_2\text{Et} \\
\text{O} & \quad 1. \text{NaOEt} \\
& \quad \text{2. HCl}
\end{align*}
\]

B.

\[
\begin{align*}
\text{Ph} & \quad + \quad \text{CH}_2\text{CH}_2\text{CO}_2\text{Et} \\
\text{O} & \quad 1. \text{NaOEt} \\
& \quad \text{2. HCl}
\end{align*}
\]

C.

\[
\begin{align*}
\text{CO}_2\text{CH}_3 & \quad 1. \text{NaOCH}_3 \\
\text{O} & \quad \text{2. HCl}
\end{align*}
\]
4. Determine the reagents needed for the following synthesis reaction
monosaccharides with aldehyde at C1 → Aldose
monosaccharides with ketone at C2 → Ketose

Fischer projections
- Carbon atom is located at the intersection of the two lines of the cross
- Horizontal bonds come forward → wedges
- Vertical bonds go back → dashes

D-sugar: OH group on the stereogenic center farthest from the carbonyl on the right
L-sugar: OH group on the stereogenic center farthest from the carbonyl on the left

Fischer → Haworth  (For Monosaccharides)
1. Determine D or L sugar
   - D sugar → CH₂OH group is up
   - L sugar → CH₂OH group is down

2. Place C4 or C5 oxygen (depending on 5 or 6 membered ring) in top right corner of ring
   - Create bond to carbon containing CH₂OH group

3. Go in clockwise direction, place anomeric carbon (carbonyl carbon)
   - Creating a α anomer: OH is down in D-sugar (trans to CH₂OH)
   - Creating a β anomer: OH is up in D-sugar (cis to CH₂OH)

4. Add remaining groups
   - Groups on right side of Fischer: down
   - Groups on left side of Fischer: up

Ex  Draw the β anomer using a Haworth projection
Haworth → Fischer
1. label carbons in clockwise manner, starting from anomeric carbon
2. Create Fischer skeleton (carbon #1 is the anomeric carbon)
3. Determine D or L sugar by looking at if the alcohol is up or down
   up → D-sugar
   down → L-sugar
4. Go counterclockwise and place remaining groups
   - Up = left
   - Down = right

Ex. Convert Haworth projection to Fischer projection

Treating monosaccharide with alcohol + HCl turns hemiacetal into acetal

All OH groups converted to ethers using Ag₂O + Alkyl Halide
The acetal ether can be hydrolyzed with acid

OH groups can be converted to esters

Carbonyl group Reduction

Oxidation

- Aldehyde $\rightarrow$ carboxylic acids use $\text{Ag}_2\text{O}, \text{NH}_4\text{OH}$

Tollen's
- Aldehyde + 1° alcohol → both turn into carboxylic acid use HNO₃, H₂O

Disaccharides
- Two monosaccharides joined by a glycosidic linkage
  - linkage formed from the anomeric carbon of one monosaccharide
    to any OH group on the other monosaccharide

example of 1,4 glycosidic linkage

know maltose, lactose, sucrose structures