I. Electrophillic Aromatic Substitution

Give the reagents needed in each of the following reactions and indicate whether the product that forms is an ortho, para or meta director and whether or not it is an activator or a deactivator.

1. \( \text{?} \rightarrow \text{?} \rightarrow \text{?} \)

2. \( \text{?} \rightarrow \text{?} \rightarrow \text{?} \)

3. \( \text{?} \rightarrow \text{?} \rightarrow \text{?} \)

4. \( \text{?} \rightarrow \text{?} \)

5. \( \text{?} \rightarrow \text{?} \)

II. Nucleophillic Aromatic Substitution

Fill in the missing reagents.

1. \( \text{?} \rightarrow \text{?} \rightarrow \text{benzyne} \)

3. \( \text{?} \rightarrow \text{?} \)
II. Synthesis

Give the reagents necessary to accomplish the following syntheses. Careful - the order in which you add things matters.

1. \( \text{CH}_3 \quad \text{CH}_3 \quad \text{Br} \quad \text{NO}_2 \quad \text{C}_2\text{H}_4 \)

2. \( \text{C}_6\text{H}_5 \quad \text{Cl} \quad \text{NO}_2 \)

3. \( \text{C}_6\text{H}_5 \quad \text{Cl} \quad \text{NO}_2 \)

II. Mechanisms and Resonance

1. Which phenol is more acidic? Why?

\[ \text{C}_6\text{H}_5\text{OH} \quad \text{C}_6\text{H}_5\text{NO}_2 \]

2. Show mechanistically why product A is favored over product B:

\[ \text{C}_6\text{H}_5 \quad \text{FeBr}_3, \quad \text{Br}_2 \quad \text{Br} \quad + \quad \text{OCH}_3 \quad \text{C}_6\text{H}_5 \quad \text{OCH}_3 \quad \text{Br} \]

A

B
Chapter 22 Practice Problems: Introductory Level

I. Electrophillic Aromatic Substitution

Give the reagents needed in each of the following reactions and indicate whether the product that forms is an a, p, or m director:

1. \( \text{Fe}, \text{Zn} \), or \( \text{Sn with HCl} \)

2. \( \text{SO}_3 \) ? \( \text{H}_2 \text{SO}_4 \) \( \text{SO}_3 \text{H}^+ \) ? \( \text{H}_2 \text{O} ? \)

3. \( \text{FeBr}_3 \), \( \text{Br}_2 \), \( \text{AlBr}_3 \), \( \text{H}_2 \text{SO}_4 \) \( \text{HNO}_3 \)

II. Nucleophilic Aromatic Substitution

Fill in the missing reagents.

1. NH\(_3\)

2. Addition Elimination

3. Condensation with EW groups
III. Synthesis

1. Give the reagents necessary to accomplish the following syntheses. Careful! The order in which you add things matters.

1. \[ \text{Br}_2, \text{FeBr}_3 \]
   \[ \begin{array}{c}
   \text{CH}_3 \\
   \text{O} \\
   \text{Br}
   \end{array} \xrightarrow{\text{HNO}_3 \text{ ox}} \begin{array}{c}
   \text{O} \\
   \text{N} \\
   \text{H}_2\text{C}_2\text{H}
   \end{array} \xrightarrow{\text{Br}_2, \text{FeBr}_3} \begin{array}{c}
   \text{O} \\
   \text{N} \\
   \text{H}_2\text{C}_2\text{H}
   \end{array} \]

2. \[ \begin{array}{c}
   \text{Cl}_2 \\
   \text{Cl}
   \end{array} \xrightarrow{\text{HNO}_3} \begin{array}{c}
   \text{Cl} \\
   \text{O} \\
   \text{NO}_2
   \end{array} \]

3. \[ \begin{array}{c}
   \text{Cl}_2, \text{AlCl}_3 \\
   \text{Cl}
   \end{array} \xrightarrow{\text{HNO}_3} \begin{array}{c}
   \text{Cl} \\
   \text{O} \\
   \text{NO}_2
   \end{array} \]

I. Mechanisms + Resonance

1. Which phenol is more acidic? Why?
   \[ \begin{array}{c}
   \text{OH} \\
   \text{N}_2\text{O}_2
   \end{array} \quad \begin{array}{c}
   \text{OH} \\
   \text{N}_2\text{O}_2
   \end{array} \]

2. Show mechanistically why product A is favored over product B:
   \[ \begin{array}{c}
   \text{OCH}_3 \\
   \text{OCH}_3
   \end{array} \xrightarrow{\text{FeBr}_3, \text{Br}_2} \begin{array}{c}
   \text{OCH}_3 \\
   \text{OCH}_3
   \end{array} \]
   \[ \begin{array}{c}
   \text{Br} \\
   \text{Br}
   \end{array} \quad \begin{array}{c}
   \text{Br} \\
   \text{Br}
   \end{array} \]
   \[ \begin{array}{c}
   \text{Br} \\
   \text{Br}
   \end{array} \quad \begin{array}{c}
   \text{Br} \\
   \text{Br}
   \end{array} \]
   \[ \begin{array}{c}
   \text{Br} \\
   \text{Br}
   \end{array} \quad \begin{array}{c}
   \text{Br} \\
   \text{Br}
   \end{array} \]
6) [20 points] Propose a synthesis of B starting from A.

B) Circle the best nucleophile for the electrophilic aromatic substitution reaction.
6. (11 points) Provide a synthesis that will **selectively** convert A to B. Show all the key intermediates and furnish all the important reagents. This is not a one-step process.

![Chemical structures](image)

8. Synthesize the indicated compounds from the allowed starting materials shown below. All of the carbons of the target compounds should be derived from the allowed starting materials.

![Allowed starting materials](image)

Figure by MIT OCW.
Chapter 23 Practice Problems: Introductory Level

I. Fill in the missing Reagents

1. \[ \text{?} \rightarrow \text{ \( \text{NO}_2 \) ?} \rightarrow \text{ \( \text{NH}_2 \) ?} \rightarrow \text{+ \( \text{N}_2 \) ?} \]

2. \[ \text{\( \text{N}_2 \) ?} \rightarrow \text{\( \text{OH} \) ?} \rightarrow \text{\( \text{Br} \) ?} \rightarrow \text{\( \text{CN} \) ?} \]

3. \[ \text{\( \text{NH}_2 \) ?} \rightarrow \text{\( \text{Cl}^\ominus \) ?} \rightarrow \text{\( \text{N}^\oplus \) ?} \rightarrow \text{\( \text{CH}_3 \) ?} \rightarrow \text{\( \text{CH}_3 \) ?} \]
II. See questions below

\[ \text{pK}_a \approx 1 \quad \text{pK}_a \approx 2.5 \quad \text{pK}_a \approx 5 \quad \text{pK}_a \approx 11 \]

1. Which compound is the most acidic?
2. Which conjugate base is the most basic?
3. Use resonance to explain the trend in pK'a's of compounds A thru D

III. Which nitrogen is more basic? Why?

\[ \text{pK}_a \approx 7 \quad \text{(for conjugate acid)} \]

1. Draw the conjugate acid and show how resonance stabilizes the acid.
2. Which nitrogen is more basic? Why?

(hint compare \( \text{sp}^3 N \) to \( \text{sp}^2 N \))
Chapter 23 Practice Problems - Synthesis

1. Give the reagents necessary to accomplish each of the following transformations:

   1. \[
   \text{NO}_2
   \begin{array}{c}
   \text{C} \\
   \text{N}
   \end{array}
   \rightarrow
   \text{NO}_2
   \begin{array}{c}
   \text{C} \\
   \text{N}
   \end{array}
   \]

   2. \[
   \text{CH}_3
   \begin{array}{c}
   \text{C} \\
   \text{N}
   \end{array}
   \rightarrow
   \text{NO}_2
   \begin{array}{c}
   \text{C} \\
   \text{N}
   \end{array}
   \]

   3. \[
   \text{CH}_3
   \begin{array}{c}
   \text{C} \\
   \text{N}
   \end{array}
   \rightarrow
   \text{Br}
   \begin{array}{c}
   \text{C} \\
   \text{N}
   \end{array}
   \]

   4. \[
   \text{CH}_3
   \begin{array}{c}
   \text{C} \\
   \text{N}
   \end{array}
   \rightarrow
   \text{Ph}
   \begin{array}{c}
   \text{C} \\
   \text{N}
   \end{array}
   \]
Chapter 23 Practice Problems: Introductory Level

1. Fill in the missing reagents

1. HNO₃, H₂SO₄ → ? → NO₃⁻ → ? → NH₂ → HONO

Can also use LAH

2. ? → ? → Δ → OH

3. HBr, CUBr → ? → Br⁻

? / KCN, CuCN

H₃PO₂ → ?

excess CH₃-Cl

3. 2 equiv

1. CH₃⁻ → ? → NH₂

2. H₂O₂ → ? → NH₂

antipr.
II. See questions below

1. Which compound is the most acidic?
2. Which conjugate base is the most basic?
3. Use resonance to explain the trend in pKₐ's of compounds A through D (using conjugate base).

III. Which nitrogen is more basic? Why?

- pKₐ ~ 7 of conjugate acid;

- protonated here to maintain aromaticity;

- Draw the conjugate acid and show how resonance stabilizes the acid.

- Which nitrogen is more basic? Why?
  (Hint: compare sp³N to sp²N)
chapter 23 key

IV.  
\[
\begin{align*}
\text{NO}_2 & \quad \text{NH}_2 \\
\text{NH}_2 & \quad \text{N}_2 \\
\text{CH}_3 & \quad + \text{BuX} \\
\text{CO}_2\text{H} & \quad \text{Br}_2 \\
\text{C}_6\text{H}_5 & \quad \text{O}_2\text{N} \\
\end{align*}
\]
Chapter 24 Practice Problems: Introductory Level

I. Give the products:

1. 

\[\text{Br} \quad \text{Pd(OAc)}_2 \quad \text{K}_2\text{CO}_3, \text{Ph}_3\text{P}\]

2. 

\[\text{R} = \text{M}\]

3. 

\[\text{Br} \quad + \quad \text{OME} \quad \text{Pd catalyst}\]

4. 

\[\text{R} = \text{M}\]

5. 

\[\text{I} \quad + \quad \text{Cyclic} \quad \text{Pd(OAc)}_2\]

\[\text{PPh}_3, \text{K}_2\text{CO}_3\]
Chapter 24  Practice Problems Cont

II. Fill in the missing reagents or products and show mechanistic arrows:

1. \[ \text{heat} \rightarrow ? \]

2. \[ \text{heat} \]

3. \[ ? \rightarrow \]

4. \[ \text{heat} \]

5. \[ ? \]

6. \[ ? \]
Chapter 24 Practice Problems: Introductory Level

Key

1. **Intramolecular Heck**
   \[ \begin{align*}
   \text{Br} & \quad \text{Pd(OAc)}_2, \quad \text{Pd goes for less subst.} \\
   & \quad \text{K}_2\text{CO}_3, \quad \text{Ph}_3\text{P} \\
\end{align*} \]

2.

3.

4.

5.

\[ \text{Pd(OAc)}_2, \quad \text{Pd catalyst} \]

\[ \text{R} = \text{cyclohexyl} \]

\[ \text{R} \]

\[ \text{R} \]

1.
II. Fill in the missing reagents or products and show mechanistic arrows:

1. \[
\begin{array}{c}
\text{heat} \\
\end{array} \quad ? \]

2. \[
\begin{array}{c}
\text{heat} \\
\end{array} \quad \text{products} \\
\]

3. \[
\begin{array}{c}
\text{heat} \\
\end{array} \quad \text{products} \\
\]

4. \[
\begin{array}{c}
\text{products} \\
\end{array} \quad \text{products} \\
\]

5. \[
\begin{array}{c}
\text{products} \\
\end{array} \quad \text{products} \\
\]

6. \[
\begin{array}{c}
\text{products} \\
\end{array} \quad \text{products} \\
\]
1. [20 points] Propose a detailed mechanism for the following transformation.

2. Propose a synthesis of B starting from A.

3. Propose a synthesis of B starting from A. You must use the **Heck reaction** somewhere in your synthesis.

4. Give reagents to accomplish the following transformation.
5. [14 points] The following compound was formed by a Cope rearrangement. Show the substrate for the Cope rearrangement.

\[ \text{Cope rearrangement} \]

6. The following compound was formed by a Diels-Alder cycloaddition. Show the substrate for the Diels-Alder cycloaddition.

\[ \text{Diels-Alder} \]

7. Circle the product that will form in the Diels-Alder reaction between \( \text{O} \) and \( \text{O} \).
8. (22 points total) Using retrosynthetic analysis, propose a synthesis of the molecule to the right (A). You may use any reagents you wish, as long as your starting materials and any other reagent that is used to install a carbon that is found in the final product (target molecule A) have no more than 6 carbon atoms. For example, 1,3-butadiene and benzene would be acceptable, but benzyl bromide (PhCH₂Br) would not be.

Write your synthesis in the "forward" direction, showing all steps and reagents necessary. (You may include solvents, but you are not required to do so.) Draw a box around or circle your final synthesis.

Hint: Use a Diels-Alder reaction.