Worksheet 5, Chem 51C, Jarvo

1. a. Label each amide as 1°, 2°, or 3°

\[
\begin{align*}
\text{H}_2\text{N} & \quad \text{O} & \quad \text{N} & \quad \text{Me} \\
\text{Me} & \quad \text{H} & \quad \text{O} & \quad \text{Me} \\
\text{O} & \quad \text{N} & \quad \text{Me} & \quad \text{Me} \\
\end{align*}
\]

2°  3°  1°

b. Fill in the correct nucleophile and electrophile from the table to complete the retrosyntheses.

<table>
<thead>
<tr>
<th>Nucleophiles</th>
<th>Electrophiles</th>
</tr>
</thead>
<tbody>
<tr>
<td>A NaOH</td>
<td>E N≡CPh</td>
</tr>
<tr>
<td>B LiAlH₄</td>
<td>F N≡C</td>
</tr>
<tr>
<td>C DIBAL-H</td>
<td>G PhO</td>
</tr>
<tr>
<td>D MeMgBr</td>
<td>H PhC≡N</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>i. ( \text{OH} \quad \text{Ph-CH₂-NH₂} \rightarrow \text{B} + \text{H} ) then ( \text{H}_3\text{O}⁺ )</td>
</tr>
<tr>
<td>ii. ( \text{H} \quad \text{O} \rightarrow \text{E} + \text{F} ) then ( \text{H}_3\text{O}⁺ )</td>
</tr>
<tr>
<td>iii. ( \text{Me} \quad \text{O} \rightarrow \text{D} + \text{E} ) then ( \text{H}_3\text{O}⁺ )</td>
</tr>
</tbody>
</table>
2. Fill in the boxes with the appropriate starting material, reagent or major product. Show stereochemistry where appropriate.

a. 

b. 

1. H₂O (excess), HCl
2. SOCl₂
3. MeNH₂ (2 equivs)

1. Ph₂CuLi
2. H₂O

3. MeOH, HCl
3. Fill in the blank and provide an arrow-pushing mechanism.

a.  
\[
\text{O} \quad \xrightarrow{\text{H}_3\text{O}^+} \quad \text{Me} \quad \xrightarrow{\text{HO-} \text{(excess)}} \quad \text{O} \quad \xrightarrow{} \quad \text{Me}
\]

b.  
\[
\text{O} \quad \xrightarrow{\text{H}_2\text{O}, \text{HCl \ heat}} \quad \text{Me} \quad \xrightarrow{} \quad \text{O} \quad \xrightarrow{} \quad \text{Me}
\]

c.  
\[
\text{O} \quad \xrightarrow{\text{LiAlH}_4 \text{ (excess)}} \quad \text{Me} \quad \xrightarrow{} \quad \text{Me}
\]

d. Provide an arrow-pushing mechanism

\[
\text{NH}_2\text{OH} \quad \xrightarrow{\text{Cl}-\text{Cl \ pyridine}} \quad \text{HN} \quad \xrightarrow{} \quad \text{O}
\]
4. Show at least four different transformations of the ester below, each one generating a different functional group.

4. Show at least four different syntheses of the amine below, each one from a different starting material.
**Target A:**

\[
\text{Br} \quad \text{1. Li (4 equiv)} \quad \text{Cu}^+ \quad \text{Cl}^-
\]

\[
\text{2. CuI (1 equiv)} \quad \text{1. } \quad \text{2. } \quad \text{H}_2\text{O}
\]

\[
\text{CH}_3\text{I} \quad \text{1. PPh}_3 \quad \text{H}_2\text{C} = \text{PPh}_3
\]

\[
\text{2. nBuLi} \quad \text{H}_2\text{C} = \text{PPh}_3
\]

**Target B:**

\[
\text{OH} \quad \text{TBDMSCl} \quad \text{TBDMSO}
\]

\[
\text{pyridine} \quad \text{H}_2\text{C} = \text{OCH}_3 \quad \text{H}_2\text{O (excess)} \quad \text{TBDMSO}
\]

\[
\text{HCl} \quad \text{H}_2\text{C} = \text{OCH}_3 \quad \text{SOCl}_2
\]

\[
\text{H}_3\text{C} \quad \text{H}_3\text{C} \quad \text{H}_3\text{C}
\]

\[
\text{Br} \quad \text{1. Li (4 equiv.)} \quad \text{1. } \quad \text{2. } \quad \text{H}_2\text{O}
\]

\[
\text{OH} \quad \text{TBDMSO}
\]

\[
\text{TBAF} \quad \text{TBDMSO}
\]

\[
\text{H}_3\text{C} \quad \text{H}_3\text{C} \quad \text{H}_3\text{C}
\]
7  a. Draw a resonance structure for the enolate below and label the hybridization of each carbon and oxygen:

\[
\ce{H3C\text{O}^-\text{CH2}} \rightleftharpoons \ce{H3C\text{sp}^3\text{CH3}}\]

b. Rank the following from most to least acidic, label each with their pKa, and draw the corresponding conjugate bases:

\[
\begin{align*}
\text{pKa A} &= 24 \\
\text{pKa B} &= 20 \\
\text{pKa C} &= 9
\end{align*}
\]

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

c. Rank the following enols from most to least stable:

\[
\begin{align*}
\text{A} \\
\text{B} \\
\text{C}
\end{align*}
\]

\[
\begin{array}{c}
\text{B} > \text{C} > \text{A}
\end{array}
\]
Fill in the boxes with the appropriate starting material, reagent or major product.
Show stereochemistry where appropriate

a. 

b. 

\[ \text{Br}_2, \text{NaOH} \rightarrow \]

\[
\begin{array}{c}
\text{Br} \\
\text{Br} \\
\end{array}
\]

c. 

\[
\begin{array}{c}
\text{CH}_3 \\
\text{C}_6\text{H}_{12} \\
\end{array}
\]

\[
\begin{array}{c}
\text{CH}_3 \\
\text{C}_6\text{H}_{12} \\
\end{array}
\]

d. 

\[
\begin{array}{c}
\text{BF}_3 \\
\text{THF} \\
\text{LDA} \\
\text{THF} \\
\text{-78°C} \\
\end{array}
\]

e. 

\[
\begin{array}{c}
\text{H}_3\text{CO}_2\text{OCH}_3 \\
\end{array}
\]

\[
\begin{array}{c}
1. \text{Na}^+\text{OET}^+ \\
\text{EtOH} \\
2. \cdot \text{Br} \\
3. \text{H}_3\text{SO}_4, \Delta \\
\end{array}
\]

\[
\begin{array}{c}
\text{H}_3\text{CO}_2\text{CH}_3 \\
\end{array}
\]
9  Fill in the blank and provide an arrow-pushing mechanism.

a.  
\[
\begin{align*}
\text{Br}_2, \text{NaOH} & \rightarrow \text{Br}_2, \text{NaOH} \\
\text{Br}_2, \text{NaOH} & \rightarrow \\
\end{align*}
\]

b.  
\[
\begin{align*}
\text{Cl}_2, \text{HCl} & \rightarrow \text{Cl}_2, \text{HCl} \\
\text{Cl}_2, \text{HCl} & \rightarrow \\
\end{align*}
\]

c.  
\[
\begin{align*}
1. \text{LDA, THF, } -78^\circ \text{C} & \rightarrow 1. \text{LDA, THF, } -78^\circ \text{C} \\
2. \text{Br} & \rightarrow 2. \text{Br} \\
\end{align*}
\]

Note: for your arrow-pushing mechanism, feel free to abbreviate the starting material as \( \text{Ar} \text{CH}_3 \).
10 Draw a reaction coordinate diagram that shows formation of the kinetic and thermodynamic enolates from the ketone below. Clearly draw and label:
- kinetic enolate
- thermodynamic enolate
- $\Delta G^\ddagger$ for formation of each enolate

What conditions would you employ to favor formation of the kinetic enolate? The thermodynamic enolate?

$\text{Kinetic: LDA, THF, } -78^\circ\text{C}$

$\text{Thermodynamic: NaOEt, EtOH}$
Propose syntheses of the targets shown below.

All carbons in the product must come from the starting materials provided, you can use any reagent you wish.

**Target A.**

![Target A. structure]

(racemic)

**Target B.**

![Target B. structure]

(+ enantiomers)

**Target C.**

![Target C. structure]

(racemic)

**Target D.**

![Target D. structure]

(racemic)

**Target E.**

![Target E. structure]

(racemic)

**Target F.**

![Target F. structure]