5-31-2019


Candace M. Lawrence
Xavier University of Louisiana, clawren2@xula.edu

Follow this and additional works at: https://digitalcommons.xula.edu/doc_cm
Part of the Organic Chemistry Commons

Recommended Citation
https://digitalcommons.xula.edu/doc_cm/73

This Organic Chemistry II is brought to you for free and open access by the Department of Chemistry at XULA Digital Commons. It has been accepted for inclusion in Course Modules by an authorized administrator of XULA Digital Commons. For more information, please contact ksiddell@xula.edu.
AMINES

A STUDENT SHOULD BE ABLE TO:

1. Give the IUPAC or common name given the structure, and draw the structure given the name of amines and common nitrogen heterocycles (pyrrole, pyridine, purine, pyrimidine, imidazole). Also, give the classification of compounds in any of the following groups, and give examples of 1º, 2º, and 3º amines, and quaternary ammonium salts.

2. From your knowledge of common nitrogen heterocycles, classify DNA/RNA subunits or similar structures as purines and pyrimidines, and identify the hydrogen bonding motifs of purine and pyrimidine pairs.

3. Predict the product(s) of reactions giving rise to amines and the reactions of amines, when given the starting materials and reaction conditions. Important reactions include:
   
   - Acid-base reactions
   - Nucleophilic substitution reactions (including the Gabriel synthesis)
   - Reduction reactions of nitro compounds, azides, amides, and nitriles
   - Reductive amination reactions
   - Reactions of amines and acid chlorides
   - Hofmann Elimination
   - Electrophilic Aromatic Substitution (EAS) reactions of nitrogen heterocycles

4. From your knowledge of the effects involved, predict or explain experimental results. Important areas include:
   
   - Physical properties (boiling points, solubility)
   - Relative acidity and basicity
   - Nucleophilic substitution (primarily S_N2)
   - Comparative reactivities
   - The extent and site of protonation as a function of pH

5. Use the reactions of #2 above, plus others learned earlier, to propose syntheses of amines, ammonium salts, and related compounds.

6. Understand and be able to draw the mechanism of acid-base reactions, nucleophilic substitution, and elimination reactions. The mechanisms will include all intermediates and proper mechanistic arrows.

7. Predict and interpret IR (2 peaks for 1º amines, 1 peak for 2º amines, and absence of a peak for 3º amines in the 3200-3600cm⁻¹ range) and NMR spectra and solubility test results to identify unknown amines. Remember that amines, unlike any other common family of organic compounds, are basic.
To best prepare for this module, please work appropriate Skill Builder problems in the textbook.

A STUDENT WHO HAS MASTERED THE OBJECTIVES FOR THIS UNIT SHOULD BE ABLE TO SOLVE THE FOLLOWING PROBLEMS AND RELATED ONES:

1.1 Provide the IUPAC or common names as appropriate for the following compounds.

a) \((\text{CH}_3\text{CH}_2)_2\text{CHCH}_2\text{NH}_2\)

b) \(\text{N} - \text{H}\)

c) \(\text{NH}_2\)

d) \(\text{NH}_2\)

e) \(\text{CH}_3\text{CICH}_2\text{CH(CH}_3\text{)CH}_2\text{NHCH}_3\)

f) \(\text{N}\)

g) \(\text{NH}_2\)

h) \(\text{HN}\)

1.2 Draw the structure of each of the following compounds.

a) diisopropylamine

b) 3-amino-1-butanol

c) \textit{para}-bromoaniline

d) \((R)\)-\textit{N}-methyl-\textit{N}-propyl-2-pentanamine

e) pyrimidine
2.1 Classify the following structures as purines or pyrimidines.

a) 
\[
\begin{array}{c}
\text{H}_2\text{N} \\
\text{HN} \\
\text{O} \\
\text{N} \\
\text{N} \\
\text{H} \\
\end{array}
\]

b) 
\[
\begin{array}{c}
\text{H}_2\text{N} \\
\text{HN} \\
\text{O} \\
\text{N} \\
\text{H} \\
\end{array}
\]

c) 
\[
\begin{array}{c}
\text{NH}_2 \\
\text{N} \\
\text{O} \\
\text{H} \\
\end{array}
\]

d) 
\[
\begin{array}{c}
\text{H} \\
\text{O} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{O} \\
\end{array}
\]

2.2 On the structures in 2.1 above, label the hydrogen bond donors with a “D” and the hydrogen bond acceptors with an “A”. It may help to add lone pairs to the structures.

3. Predict the product or products of the reactions shown (if any):

a) 
\[
\text{C}_{6}\text{H}_{4}\text{NH}_2 + \text{H}_2\text{SO}_4 \rightarrow
\]

b) 
\[
\begin{array}{c}
\text{C}_6 \text{H}_{11} \text{Br} \\
\end{array}
\]
\[
\text{NaCN} \rightarrow \text{1. LAH} \text{2. H}_2\text{O}
\]

c) 
\[
\begin{array}{c}
\text{O} \\
\text{NH} \\
\text{C} \\
\end{array}
\]
\[
\text{1. KOH} \text{2. (CH}_3\text{)}_2\text{CHCH}_2\text{CH}_2\text{Br} \text{3. H}_3\text{O}^+, \text{heat}
\]

d) 
\[
\begin{array}{c}
\text{C}_6 \text{H}_{11} \text{Br} \\
\end{array}
\]
\[
\text{NaN}_3 \rightarrow \text{1. LAH} \text{2. H}_2\text{O}
\]

e) 
\[
\begin{array}{c}
\text{OCH}_3 \\
\text{C}_6 \text{H}_4 \\
\end{array}
\]
\[
\text{HNO}_3 \rightarrow \text{H}_2, \text{Pt}
\]
3. Rank the following from most to least basic. Explain.

f) $\text{CH}_3\text{I} + \text{NH}_3 \rightarrow$

g) 

\begin{align*}
\text{cat. } \text{H}^+ \xrightarrow{\text{H}_2, \text{Pt}}
\end{align*}

h) 

\begin{align*}
excess \text{CH}_3\text{I} \xrightarrow{\text{Ag}_2\text{O}, \text{H}_2\text{O, heat}}
\end{align*}

i) 

\begin{align*}
\xrightarrow{\text{NaBH}_3\text{CN, dil. } \text{H}^+}
\end{align*}

j) 

\begin{align*}
\xrightarrow{1. \text{SOCl}_2} \xrightarrow{2. \text{CH}_3\text{NH}_2} \xrightarrow{1. \text{LAH}} \xrightarrow{2. \text{H}_2\text{O}}
\end{align*}

k) 

\begin{align*}
\xrightarrow{\text{Br}_2, 0^\circ\text{C}}
\end{align*}

4.1 Rank the following from most to least basic. Explain.

a) 

\begin{align*}
\text{I. } & \text{II. } & \text{III. } & \text{IV. }
\end{align*}

\begin{align*}
\xrightarrow{\text{most basic}} \xrightarrow{\text{least basic}}
\end{align*}

b) 

\begin{align*}
\text{I. } & \text{II. } & \text{III. } & \text{IV. }
\end{align*}

\begin{align*}
\xrightarrow{\text{most basic}} \xrightarrow{\text{least basic}}
\end{align*}
4.2 Rank the following from most to least acidic. Explain.

![Structures](image1)

most acidic _____ > _____ > _____ > _____  least acidic

4.3 Rank the following from most to least water soluble. Explain.

![Structures](image2)

most H₂O soluble _____ > _____ > _____ > _____  least H₂O soluble

4.4 Which nitrogen on purine is **least** basic? Explain.

![Structure](image3)

purine:

4.5 Rank following compounds based on boiling point. Explain.

![Structures](image4)

highest BP _____ > _____ > _____ > _____  lowest BP
4.6 For these questions, choose from the list of possible compounds at the end of the section.

a) Which is soluble in water and produces an aqueous solution that turns red litmus blue?
b) Which is insoluble in water and soluble in 5% HCl(\text{aq})?
c) Which is insoluble in water, 5% HCl(\text{aq}), and 5% NaHCO_3(\text{aq}), but soluble in 5% NaOH(\text{aq})?

The possible answers are:

I. \begin{align*}
\text{CH}_2\text{CH}_3 \\
\text{H}_2\text{C} = \text{H}
\end{align*}

II. \begin{align*}
\text{CH}_2\text{NH}_2 \\
\text{H}_2\text{C} = \text{H}
\end{align*}

III. \begin{align*}
\text{CO}_2\text{H} \\
\text{H}_2\text{C} = \text{H}
\end{align*}

IV. \begin{align*}
\text{OH} \\
\text{H}_2\text{C} = \text{H}
\end{align*}

V. CH_3CH_2NH_2

VI. CH_3CH_2OH

VII. CH_3CO_2H

4.7 Which of the following compounds reacts most rapidly with the N_3^- ion in an S_N_2 reaction? Explain.

I. CH_2Cl

II. Cl

III. \begin{align*}
\text{CH}_2\text{C} - \text{Cl}
\end{align*}

IV. \begin{align*}
\text{Cl}
\end{align*}

4.8 Based on the pKa values given, draw the dominant form of each molecule at the various pH values.

a) 4-methoxyaniline

\begin{align*}
\text{H}_3\text{CO} - \begin{array}{c}
\text{N} \\
\text{H}_2\text{C} = \text{H}
\end{array} \\
p\text{Ka of conj. acid} = 10.07
\end{align*}

\begin{align*}
p\text{H} = 5 & \quad \text{pH} = 12
\end{align*}

b) N-Butylaminoacetic acid

\begin{align*}
\text{pKa of conj. acid} = 10.07
\end{align*}

\begin{align*}
p\text{Ka} = 2.29
\end{align*}
5. Propose a synthesis of each of the following compounds, from the given starting material and any other needed reagents.

a) \( \text{from } \text{CO}_2\text{H} \)

b) \( \text{CH}_3\text{CH}_2\text{NH}_2 \text{ from } \text{CH}_3\text{CH}_2\text{OH} \)

c) \( \text{from } \text{CHO} \)

d) \( \text{from } \text{OCH}_3 \)

e) \( \text{from } \text{NH}_2 \)
5. f) Draw the complete mechanism, using proper curved arrow notation, and show all intermediates of these reactions. Add lone pairs where necessary.

6. Draw the complete mechanism, using proper curved arrow notation, and show all intermediates of these reactions. Add lone pairs where necessary.

a) \[
\begin{align*}
\text{O} & \quad + \\
\text{OH} & \quad \text{H}_2\text{N} \\
\rightarrow & \\
\text{O} & \quad + \\
\text{H}_3\text{N}
\end{align*}
\]

b) \[
\begin{align*}
\text{O} & \quad + \\
\text{Cl} & \quad \text{H}_2\text{N} \\
\rightarrow & \\
\text{O} & \quad \text{N} \\
\text{Cl} & \quad \text{H}
\end{align*}
\]
7.1 Which of these IR spectra belongs to 3-heptanamine?

a) 

b) 

c) 

d) 

7.2 Draw what you would expect the IR spectrum to look like for diethylamine.

7.3 Identify the following unknown from the given spectroscopic information.

Chemical Formula: C₅H₁₃N
IR: two peaks at 3400 cm⁻¹
¹H NMR:  
- doublet, δ 0.9, 6H
- doublet, δ 1.1, 3H
- multiplet, δ 1.6, 1H
- multiplet, δ 2.5, 1H
- broad singlet, δ 3.2, 2H
SOLUTIONS TO SAMPLE PROBLEMS:

1.1  a) 2-ethyl-1-butanamine  
     b) diethylamine  
       (N-ethyl-1-ethanamine)  
    c) cyclopentyl amine or cyclopentanamine  
    d) aniline  
     e) 4-chloro-N,2-dimethyl-1-pentanamine  
    f) pyrrole  
    g) 3-aminopentanoic acid  
    h) N,2,3-trimethylheptan-4-amine

1.2  Draw the structure of each of the following.  
     a) diisopropylamine  
     b) 3-amino-1-butanol  
     c) para-bromoaniline  
     d) (R)-N-methyl-N-propyl-2-pentanamine  
     e) pyrimidine

2.1  a)  
     b)  
     c)  
     d)  
     purine  
     pyrimidine

2.2  See the labels on the structures above.
3. Predict the product or products of the reactions shown (if any).

a) \[
\text{Ph-CH}_2\text{NH}_2 + H_2SO_4 \rightarrow \text{Ph-CH}_2\text{NH}_3^+ + HSO_4^- 
\]

b) \[
\text{Br} + \text{NaCN} \rightarrow \text{CN} \rightarrow 1. \text{LAH} \rightarrow 2. \text{H}_2\text{O} \rightarrow \text{NH}_2
\]
Note that the carbon chain was extended by one.

c) \[
\text{KOH} \rightarrow (\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{NH}_3^+ 
\]
1. \((\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{Br} \rightarrow 3. \text{H}_3\text{O}^+\), heat

Note that the number of carbons is unchanged.

d) \[
\text{Br} + \text{NaN}_3 \rightarrow \text{N}_3 \rightarrow 1. \text{LAH} \rightarrow 2. \text{H}_2\text{O} \rightarrow \text{NH}_2
\]

Note that the number of carbons is unchanged.

e) \[
\text{Ph-CH}_3 + \text{HNO}_3 \rightarrow \text{O}_2\text{N} \rightarrow \text{H}_2, \text{Pt} \rightarrow \text{H}_2\text{N} \rightarrow \text{OCH}_3 
\]

f) \[
\text{xS} \quad \text{CH}_3\text{I} + \text{NH}_3 \rightarrow (\text{CH}_3)_4\text{N}^+\text{I}^-
\]

g) \[
\text{cat. H}_3\text{O}^+ \rightarrow \text{H}_2, \text{Pt} \rightarrow \text{N}
\]

h) \[
\text{NH}_2 \quad \text{excess CH}_3\text{I} \rightarrow \text{N} \rightarrow \text{Ag}_2\text{O}, \text{H}_2\text{O} \rightarrow \text{least substituted product}
\]

i) \[
\text{N} + \text{HN(CH}_3)_2 \rightarrow \text{N(CH}_3)_2 
\]

j) \[
\text{PhCO} \rightarrow 1. \text{SOCl}_2 \rightarrow \text{PhCO} \rightarrow 1. \text{LAH} \rightarrow \text{PhC}_2\text{NHCH}_3 
\]

k) \[
\text{N} \rightarrow \text{Br}, 0^\circ \text{C}
\]

325
4.1 a) I > IV > II > III
Secondary amines are more basic than primary amines, and primary amines are more basic than delocalized aryl amines. Aryl amines with electron donating groups are more basic than aryl amines with electron withdrawing groups.

b) II > III > I > IV
Secondary amines are more basic than primary amines. Amides are weak bases (weaker than anilines) because the lone pair is delocalized onto the oxygen. The quaternary salt is not a base because it does not possess a lone pair of electrons.

4.2 III > II > IV > I
Convert all of the compounds to their conjugate bases (cb).

4.3 I > II > III > IV
Each compound contains 5 carbons. Ionic compounds are the most soluble. Alcohols form stronger hydrogen bonds than amines (OH is more polar than NH), hence alcohols are more soluble than comparable amines. Alkyl halides have polar, covalent bonds and form weaker dipole-dipole interactions with water.

4.4 The NH nitrogen in the 5-membered ring is least basic. The lone pair on this N resides in the p orbital and is part of the set of pi electrons that make the purine aromatic; aromaticity is lost if the lone pair is used as a base.

4.5 IV > I > II > III
All of the compounds have four carbons. Compound IV has hydrogen bonding with both OH and NH so it will have the highest boiling point. Alcohols form stronger hydrogen bonds than amines. Tertiary amines cannot hydrogen bond in a pure sample.

4.6 a) V b) II c) IV

4.7 S_N2 reactions proceed fastest with I, a primary alkyl halide, then II, a secondary alkyl halide. S_N2 reactions do not occur with aryl halides or tertiary alkyl halides.
4.8  a) 4-methoxyaniline  
\[ \text{H}_3\text{CO-} -\text{NH}_2 \quad \text{pH} = 5 \quad \text{pH} = 12 \]
\[ \text{pKa of conj. acid} = 10.07 \]

\[ \text{H}_3\text{CO-} -\text{NH}_3^+ \quad \text{H}_3\text{CO-} -\text{NH}_2 \]

b) \( N \)-Butylaminoacetic acid  
\[ \text{pK}_a = 2.29 \]
\[ \text{pK}_a \text{ of conj. acid} = 10.07 \]

5.  a)  
\[ \text{CO}_2\text{H} \xrightarrow{1. \text{SOCl}_2} \text{NH}_2 \xrightarrow{1. \text{LiAlH}_4} \text{NH}_2 \]
\[ \text{2. NH}_3 \quad \text{2. H}_2\text{O} \]

b) \( \text{CH}_3\text{CH}_2\text{OH} \xrightarrow{\text{HBr or PBr}_3} \text{CH}_3\text{CH}_2\text{Br} \xrightarrow{\text{NaN}_3} \text{CH}_3\text{CH}_2\text{N}_3 \xrightarrow{\text{H}_2, \text{Pt}} \text{CH}_3\text{CH}_2\text{NH}_2 \]

c)  
\[ \text{1. KMnO}_4, \quad \text{H}_2\text{O, HO}^+ \text{ heat} \quad \text{2. H}_3\text{O}^+ \]
\[ \text{1. SOCl}_2 \xrightarrow{2. \text{H}_2\text{N}} \]

d) \[ \text{OCH}_3 \xrightarrow{\text{HNO}_3} \text{O}_2\text{N} \xrightarrow{\text{Fe, HCl}} \text{H}_3\text{N}^+ \]
\[ \text{OCH}_3 \]

e) \[ \text{Br}_2 \xrightarrow{\text{hv}} \text{Br} \xrightarrow{\text{NaCN}} \text{CN} \xrightarrow{1. \text{LiAlH}_4} \text{NH}_2 \]
\[ \text{2. H}_2\text{O} \]

f) \[ \text{cat. H}^+ \xrightarrow{\text{NH}_2\text{CH}_2\text{CH}_3} \xrightarrow{\text{H}_2, \text{Pt}} \]

The synthesis can be carried out in one step with \( \text{NH}_2\text{CH}_2\text{CH}_3, \text{H}^+, \text{NaBH}_3\text{CN} \).
6.1 b) Note the characteristic double pointed absorption around $3400\text{cm}^{-1}$.

6.2 Needs a CH absorbance $\sim2900-3000\text{cm}^{-1}$ and a $2^a\text{ N-H}$ absorbance around $3400\text{cm}^{-1}$. The NH absorbance should not be as strong as an alcohol, and have a single point.

6.3 IR signal at $3400\text{cm}^{-1}$ for NH/OH; proton NMR has broad singlet for 2H, so -NH$_2$
1. Draw: isobutylamine

2. Name:

3. Draw: purine

4. Circle the letter that correctly ranks the following compounds according to basicity. (Highest basicity on the left.)

   ![Compounds](image)

   a) III > I > IV > II  
   b) I > II > IV > III  
   c) II > IV > I > III  
   d) III > IV > II > I

5. Which of these is insoluble in water and 5% NaOH\(_{(aq)}\), but soluble in 5% HCl\(_{(aq)}\)?

   ![Compounds](image)

   I.  
   II.  
   III.  
   IV.

6. Predict the product of each of the following reactions. If no reaction occurs write “N.R.”

   ![Reactions](image)
7. Propose a synthesis of each compound, from the given starting material and any other needed reagents.

a) \[ \text{from} \]

b) \[ \text{from} \]

c) \[ \text{from} \]

8. Identify the following unknown from the given spectroscopic information.

Chemical Formula: C\textsubscript{6}H\textsubscript{15}N

IR: 3300 cm\textsuperscript{-1}

\textsuperscript{1}H NMR:
- triplet, \( \delta \) 1.1, 3H
- singlet, \( \delta \) 1.2, 9H
- quartet, \( \delta \) 2.6, 2H
- broad singlet, \( \delta \) 3.3, 1H

9. Based on the pKa values given, draw the dominant form of this molecule at the various pH values.

sarcosine

pKa of conj. acid = 10.01

\( pK_a = 2.23 \)

pH = 2

pH = 13
1. Name:                  2. Draw: (S)-N,N-dimethyl-2-hexanamine  3. Name:

\[ \text{HN} \]
\[ \text{N} \]
\[ \text{NM} \]

4. Rank the following compounds according to basicity. (Highest basicity on the left.)

\[ \text{I. } \]
\[ \text{II. } \]
\[ \text{III. } \]
\[ \text{IV. } \]

a) IV > I > II > III  
   b) IV > III > I > II  
   c) I > IV > II > III  
   d) III > IV > I > II

5. Which of the following has the highest boiling point?

\[ \text{I. } \]
\[ \text{II. } \]
\[ \text{III. } \]
\[ \text{IV. } \]

6. Complete the following reactions.

a) \((\text{CH}_3)_2\text{CHCH}_2\text{CN} \rightarrow (\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{NH}_2\)

b) \[
\begin{align*}
\text{1. LiAlH}_4 & \quad \text{1. } \text{LiAlH}_4 \\
\text{2. H}_2\text{O} & \quad \text{2. H}_2\text{O}
\end{align*}
\]

\[
\text{c) } \quad \text{N} \quad \text{N}
\]

\[
\begin{align*}
\text{d) } & \quad \text{1. excess CH}_3\text{I} \\
\text{2. Ag}_2\text{O, H}_2\text{O} & \quad \text{2. Ag}_2\text{O, H}_2\text{O, heat}
\end{align*}
\]

331
7. Propose a synthesis of each compound, from the starting material given and any other needed reagents.

a) \[
\begin{align*}
\text{NH}_2
\end{align*}
\]
from

b) 1-pentanamine from pentanoic acid

8. Identify the following unknown from the given spectroscopic information.

- **Chemical Formula:** \(C_9H_{13}N\)
- **IR:** no peaks at 3300 cm\(^{-1}\)
- \(^1\)H NMR:
  - triplet, \(\delta 1.1, 3\)H
  - singlet, \(\delta 2.8, 3\)H
  - quartet, \(\delta 3.4, 2\)H
  - triplet, \(\delta 6.8, 1\)H
  - doublet, \(\delta 6.9, 2\)H
  - triplet, \(\delta 7.2, 2\)H

9. Based on the pKa values given, draw the dominant form of this molecule at the various pH values.

\[
\begin{align*}
\text{2-(4-aminophenyl)ethan-1-ol} & \quad \text{pH} = 2 \quad \text{pH} = 13 \\
pK_a \sim 15.5
\end{align*}
\]

\[
\text{pK}_a \text{ of conj. acid} \sim 5.1
\]

10. Using the purine and pyrimidine below, draw a possible hydrogen bond pairing interaction similar to DNA/RNA base pairings. Also, label the purine and pyrimidine.

\[
\begin{align*}
\text{purine} & \quad \text{pyrimidine}
\end{align*}
\]