Chem 109 C
Bioorganic Compounds

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HFH1104

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**Chapter 21**

α-amino acid

\[ \text{R-COOH} + \text{H}_2\text{N-R} \rightarrow \text{R-CO-NH-R} - \text{H}_2\text{O} \]

peptide bond = amide bond
### Table 21.1 Examples of the Many Functions of Proteins in Biological Systems

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural proteins</td>
<td>These proteins impart strength to biological structures or protect organisms from their environment. For example, collagen is the major component of bones, muscles, and tendons; keratin is the major component of hair, hooves, feathers, fur, and the outer layer of skin.</td>
</tr>
<tr>
<td>Protective proteins</td>
<td>Snake venoms and plant toxins protect their owners from predators. Blood-clotting proteins protect the vascular system when it is injured. Antibodies and peptide antibiotics protect us from disease.</td>
</tr>
<tr>
<td>Enzymes</td>
<td>Enzymes are proteins that catalyze the reactions that occur in living systems.</td>
</tr>
<tr>
<td>Hormones</td>
<td>Some of the hormones, such as insulin, that regulate the reactions that occur in living systems are proteins.</td>
</tr>
<tr>
<td>Proteins with physiological functions</td>
<td>These proteins are responsible for physiological functions such as the transport and storage of oxygen in the body, the storage of oxygen in the muscles, and the contraction of muscles.</td>
</tr>
</tbody>
</table>
Proteins: Structural

Histone Protein Structure: DNA packaging
botulinum toxin (botox) structure
most toxic substance known
LD$_{50} = 10$ ng/kg
Amino acids, Peptides, Proteins: **Introduction**

- **α-amino acid**
- **dipeptide**
- **tripeptide**

✓ **oligopeptide**: 3 - 10 amino acids

✓ **polypeptide, or protein**: many amino acids
Proteins: Amino Acids, Configuration

natural amino acids have the L configuration (S)
Amino acids: Classification

- Hydrophobic: “water-fearing”, nonpolar side chains
  - Alkyl side chain

- Hydrophilic: “water-loving” side chains
  - Polar, neutral side chains
  - Anionic
  - Cationic

- Table 21.1 lists 20 most common natural occurring amino acids
- The structures of amino acids will be provided on the tests
nonpolar side chains
polar
neutral
(uncharged)
side chains
Amino acids: Classification

polar acidic (anionic) side chains
Amino acids: **Classification**

- **Arginine**
- **Lysine**
- **Histidine**

**polar basic (cationic) side chains**
PROBLEM 1

Explain why when the imidazole ring of histidine is protonated, the double-bonded nitrogen is the nitrogen atom that accepts the proton.

same for guanidino group in arginine.
Amino acids: Zwitterions

✓ contain the amino group

✓ contain the carboxylic acid group:

\[
\begin{align*}
\text{pH} = 0 & \quad \text{pH} = 7 & \quad \text{pH} = 11 \\
\end{align*}
\]
Amino acids: Zwitterions

$pK_a$ of amino acids:

- $\alpha$-amino: 8.84 - 10.60
- Carboxylic acid: 1.82 - 2.63

$pK_a$ of the $\alpha$-amino group is 9

$pK_a$ of the $\text{CO}_2\text{H}$ group is 2
Amino acids: Zwitterions

pKa of side-chains:

- Aspartic acid: pKa 3.86
- Glutamic acid: pKa 4.25
- Histidine: pKa 6.04
- Cysteine: pKa 8.35
- Tyrosine: pKa 10.07
- Lysine: pKa 10.79
- Arginine: pKa 12.48
Amino acids: Zwitterions

\[
\text{histidine}
\]
Amino acids: Zwitterions

PROBLEM 8

Draw the predominant form of glutamic acid in a solution with the following pH:

a. 0

b. 3

c. 6

d. 11

\[
\text{glutamic acid}
\]

\[
\begin{align*}
\text{pK}_a & = 4.25 \\
\end{align*}
\]
PROBLEM 8

Draw the predominant form of glutamic acid in a solution with the following pH:

a. 0
b. 3
c. 6
d. 11
Amino acids: Isoelectric Point (pI)

pI of amino acid is pH at which it has no net charge

\[
pI = \frac{pK_a + pK_b}{2}
\]

**Example:** Alanine

- **pK_a** of alanine: 2.34
- **pK_a** of alanine: 9.69

**Calculation:**

\[
pI = \frac{2.34 + 9.69}{2} = \frac{12.03}{2} = 6.02
\]

**Case 1: non-ionizing side chain**
Amino acids: Isoelectric Point (pI)

The pI of an amino acid is pH at which it has no net charge.

**Case 1:** Non-ionizable side chains

- **Lysine (pK_a = 10.79)**: pI = \( \frac{8.95 + 10.79}{2} = \frac{19.74}{2} = 9.87 \)
- **Glutamic acid (pK_a = 2.19)**: pI = \( \frac{2.19 + 4.25}{2} = \frac{6.44}{2} = 3.22 \)

**Case 2:** Ionizable side chain (acidic or basic)

- **Average of pK_a's of similarly ionizing groups**

\[
\begin{align*}
\text{Lysine} & : pK_a = 10.79 \\
\text{Glutamic acid} & : pK_a = 2.19
\end{align*}
\]

\[
\begin{align*}
\text{Case 2: Ionizable side chain (acidic or basic)}
\text{Average of pK_a's of similarly ionizing groups}
\end{align*}
\]
Amino acids: Separation/Purification

- Electrophoresis
  - Based on pI values of amino acids
  - Visualized with ninhydrin:

![Chemical structures](image)

- Buffer
- Paper or gel

Arginine, alanine, and aspartate separated at pH = 5
Amino acids: Separation/Purification

- paper/thin layer chromatography based on polarity
  
  visualized with ninhydrin:  

\[
\begin{align*}
\text{glutamate, alanine, and leucine}
\end{align*}
\]
Amino acids: **Separation/Purification**

- **ion-exchange chromatography**
  - based on **ions/charge**
  - used on preparative scale

Packed with insoluble resin beads

Washed with buffers of increasing pH

Fractions sequentially collected
Ion-exchange chromatography can be used to perform preparative separation of amino acids:

Negatively charged resin binds selectively to positively charged amino acids.
Amino acids: **Separation/Purification**

☑ **ion-exchange chromatography**

A typical chromatogram obtained from separation of amino acids using an automated analyzer.
Amino acid synthesis: **HVZ reaction**

**Hell-Volhardt-Zelinski reaction**, see Sections 17.5 and 9.2

Note the source of side-chains....
Amino acid synthesis: reductive amination

review Section 16.4

\[ \text{R} \text{O} \text{H} \]

1. excess \( \text{NH}_3 \)
2. \( \text{H}_2, \text{Pd/C} \)

\[ \text{R} \text{O} \text{H} \text{NH}_3^+ \]

intermediate

note the source of side-chains....
Amino acid synthesis: \( N \)-phthalimidomalonic ester

\[
\begin{align*}
\text{EtO} & \quad \text{O} \\
\text{C} \quad \text{C} & \quad \text{OEt} \\
\text{O} & \quad \text{EtO} \\
\text{Br} & \quad \text{N} \quad \text{K} \quad ^+ \quad \text{N} \\
\text{O} & \quad \text{O} \\
\text{EtO} & \quad \text{O} \\
\text{O} & \quad \text{OEt} \\
\text{O} & \quad \text{EtO} \\
\text{O} & \quad \text{O} \\
\text{N} & \quad \text{O} \\
\text{O} & \quad \text{EtO} \\
\text{H} \quad \text{CO}_2 \quad \text{H} \quad \text{CO}_2 \quad \text{H} \quad \text{CO}_2 \\
\text{N} & \quad \text{O} \\
\text{O} & \quad \text{EtO} \\
\text{O} & \quad \text{EtO} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\text{R} & \quad \text{Br} \\
\text{N} & \quad \text{O} \\
\text{O} & \quad \text{EtO} \\
\text{O} & \quad \text{EtO} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\text{R} & \quad \text{OH} \\
\text{NH}_3^+ & \quad \text{N} \\
\text{O} & \quad \text{O} \\
\text{EtO} \quad \text{O} & \quad \text{EtO} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\text{R} & \quad \text{CO}_2 \quad \text{H} \quad \text{CO}_2 \quad \text{H} \quad \text{CO}_2 \\
\end{align*}
\]

\( \alpha \)-bromomalonic ester  \quad \text{potassium phthalimide}  \quad \text{N-phthalimidomalonic ester}  \quad \text{phthalic acid}  \quad \text{CO}_2

review Sections 15.4, 17.1, and 17.17
Amino acid synthesis: **Strecker synthesis**

Review Section 15.15 for nitrile hydrolysis.