Chem 109 C
Bioorganic Compounds

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Amino acids, Peptides, Proteins: Introduction

Chapter 21

α-amino acid

R

O

H

O

2

α-

aminoo acid

R

O

H

O

H

2

N

R

+  

- H₂O  

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

<table>
<thead>
<tr>
<th>Type of Protein</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>
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 ($S$)

same as

phenylalanine
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

- Asparatic Acid
- Glutamic Acid

**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 guanidine 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<sub>a</sub> of amino acids:**

\[
\begin{align*}
\text{HO}_2\text{C} & \text{R} \\
\text{NH}_2 & \\
\text{\textbf{\(\alpha\)-amino: 8.84 - 10.60\)}}
\end{align*}
\]

**pK<sub>a</sub> of the \(\alpha\)-amino group is 9**

\[
\begin{align*}
\text{HO}_2\text{C} & \text{R} \\
\text{NH}_2 & \\
\text{\textbf{carboxylic acid: 1.82 - 2.63\)}}
\end{align*}
\]

**pK<sub>a</sub> of the CO\(_2\)H group is 2**
### Amino acids: Zwitterions

#### pKa of side-chains:

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Structure</th>
<th>pKa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspartic acid</td>
<td><img src="image" alt="Aspartic acid" /></td>
<td>3.86</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td><img src="image" alt="Glutamic acid" /></td>
<td>4.25</td>
</tr>
<tr>
<td>Histidine</td>
<td><img src="image" alt="Histidine" /></td>
<td>6.04</td>
</tr>
<tr>
<td>Cysteine</td>
<td><img src="image" alt="Cysteine" /></td>
<td>8.35</td>
</tr>
<tr>
<td>Tyrosine</td>
<td><img src="image" alt="Tyrosine" /></td>
<td>10.07</td>
</tr>
<tr>
<td>Lysine</td>
<td><img src="image" alt="Lysine" /></td>
<td>10.79</td>
</tr>
<tr>
<td>Arginine</td>
<td><img src="image" alt="Arginine" /></td>
<td>12.48</td>
</tr>
</tbody>
</table>
Amino acids: Zwitterions

Histidine

\[
\begin{align*}
&\text{pH = 0} \\
&\text{pH = 4} \\
&\text{pH = 8} \\
&\text{pH = 12}
\end{align*}
\]
PROBLEM 8

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

a. 0

b. 3

c. 6

d. 11

\[
\text{glutamic acid} \quad 4.25
\]
PROBLEM 8

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

a. 0

b. 3

c. 6

d. 11

![Glutamic Acid Structure]

pK\textsubscript{a} values:

- 2.19
- 4.25
- 9.67

Note: The pH values are indicated near the structure for reference.
pI of amino acid is pH at which it has no net charge

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

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

\[
\text{pI} = \frac{pK_a + \text{pK}_a \text{of similarly ionizing groups}}{2}
\]

**Case 1**: Neutral side chain

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

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

- **Histidine**
  - **pI** = \(\frac{9.17 + 1.82}{2} = \frac{10.99}{2} = 5.495\)
  - **pK_a** of imidazole = 6.04

average of **pK_a**’s of similarly ionizing groups
PROBLEM 6

Why are the carboxylic groups of the amino acids more acidic ($pK_a \sim 2$) than in acetic acid ($pK_a 4.76$)?
Amino acids: Separation/Purification

**electrophoresis**

based on pI values of amino acids

visualized with ninhydrin:

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

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

\[
\text{GLU}
\]

glutamate, alanine, and leucine
Amino acids: Separation/Purification

☑️ Ion-exchange chromatography

Based on ions/charge – (or diff between pI and pH)

Used on preparative scale, automated

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:

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

\[
\begin{align*}
\text{R-COOH} & \xrightarrow{1. \text{Br}_2, \text{PBr}_3} \text{R-CBrOH} \\
\text{R-COOH} & \xrightarrow{2. \text{H}_2\text{O}} \text{R-CBrOH} \\
\text{NH}_3^- & + \text{NH}_4\text{Br}
\end{align*}
\]

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

review Section 16.4

1. excess NH$_3$

2. H$_2$, Pd/C

intermediate

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

\[
\begin{align*}
\text{EtO}_3\text{C} & \quad \text{EtO}_3\text{C} \\
\text{Br} & \quad \text{Br} \\
\text{K}^+ & \quad \text{K}^+ \\
\text{EtO} & \quad \text{EtO} \\
\end{align*}
\]

\(\alpha\)-bromomalonic ester  potassium phthalimide

\[
\begin{align*}
\text{EtO}_3\text{C} & \quad \text{EtO}_3\text{C} \\
\text{N} & \quad \text{N} \\
\text{EtO} & \quad \text{EtO} \\
\text{EtO} & \quad \text{EtO} \\
\end{align*}
\]

\(N\)-phthalimidomalonic ester

\[
\begin{align*}
\text{EtO}_3\text{C} & \quad \text{EtO}_3\text{C} \\
\text{R} & \quad \text{R} \\
\text{HCl}, \text{H}_2\text{O} & \quad \text{HCl}, \text{H}_2\text{O} \\
\text{heat} & \quad \text{heat} \\
\text{EtO} & \quad \text{EtO} \\
\text{CO}_2 & \quad \text{CO}_2 \\
\end{align*}
\]

phthalic acid

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

Amino acid synthesis:

\[
\begin{align*}
&\text{RCHO} + \text{NH}_3 \rightarrow \text{R} = \text{N} \rightarrow \text{RNH}_3^+ \\
&\text{NaCN, HCl} \rightarrow \text{RC} = \text{N} \\
&\text{HCl, H}_2\text{O, heat} \rightarrow \text{R} = \text{NH}_3^+ \text{CO}_2\text{H} + \text{NH}_4\text{Cl}
\end{align*}
\]

\text{an imine} \rightarrow \alpha\text{-amino nitrile}

review Section 15.15 for nitrile hydrolysis