27.4
Synthesis of Amino Acids
From $\alpha$-Halo Carboxylic Acids

$$\text{CH}_3\text{CHCOOH} + 2\text{NH}_3 \xrightarrow{\text{H}_2\text{O}} \text{CH}_3\text{CHCOO}^- + \text{NH}_4\text{Br}$$

(65-70%)
Strecker Synthesis

\[
\begin{align*}
\text{CH}_3\text{CH} & \xrightarrow{\text{NH}_4\text{Cl}, \text{NaCN}} \text{CH}_3\text{CHC} &= \text{N} \\
\text{NH}_2 & \downarrow \quad 1. \text{H}_2\text{O}, \text{HCl}, \text{heat} \\
& \downarrow 2. \text{HO}^- \\
\text{CH}_3\text{CHCO}^- & +\text{NH}_3 \quad (52-60\%)
\end{align*}
\]
Using Diethyl Acetamidomalonate

Can be used in the same manner as diethyl malonate (Section 21.7).
Example

1. $\text{NaOCH}_2\text{CH}_3$

2. $\text{C}_6\text{H}_5\text{CH}_2\text{Cl}$

(90%)
Example

HBr, H₂O, heat

HOC₃C₅COH
H₃N⁺
CH₂C₆H₅

CH₃CH₂OC₃C₅COCH₂CH₃
CH₃C₅NH
CH₂C₆H₅
Example

HCCO

H3N+

CH2C6H5

HBr, H2O, heat

(65%)

CH3CH2OCCCOCH2CH3

CH3CNH

CH2C6H5

O
27.5
Reactions of Amino Acids
The amino nitrogen of an amino acid can be converted to an amide with the customary acylating agents.

\[
\begin{align*}
\text{H}_3\text{NCH}_2\text{CO}^- + \text{CH}_3\text{COCCCH}_3 & \rightarrow \text{CH}_3\text{CNHCH}_2\text{COH} \\
& \text{(89-92%)}
\end{align*}
\]
The carboxyl group of an amino acid can be converted to an ester. The following illustrates Fischer esterification of alanine.

\[
\begin{align*}
\text{H}_3\text{NCHCO}^- + \text{CH}_3\text{CH}_2\text{OH} & \xrightarrow{\text{HCl}} \\
\text{Cl}^- & + \text{H}_3\text{NCHCOCH}(_2\text{CH}_3) (90-95\%) 
\end{align*}
\]
Ninhydrin Test

Amino acids are detected by the formation of a purple color on treatment with *ninhydrin*.

\[
\begin{align*}
\text{RCH} + \text{CO}_2 + \text{H}_2\text{O} & \rightarrow \text{Ninhydrin} \\
\end{align*}
\]
27.6
Some Biochemical Reactions of Amino Acids
Biosynthesis of L-Glutamic Acid

This reaction is the biochemical analog of reductive amination (Section 22.11).
**Transamination via L-Glutamic Acid**

\[
\text{HO}_2\text{CCH}_2\text{CH}_2\text{CHCO}_2^- + \text{CH}_3\text{CCO}_2\text{H} + \text{NH}_3
\]

L-Glutamic acid acts as a source of the amine group in the biochemical conversion of \(\alpha\)-keto acids to other amino acids. In the example shown, pyruvic acid is converted to L-alanine.
Transamination via L-Glutamic Acid

\[
\text{HO}_2\text{CCH}_2\text{CH}_2\text{CHCO}_2^- + \text{CH}_3\text{CCO}_2\text{H} + \text{NH}_3 \xrightarrow{\text{enzymes}} \text{HO}_2\text{CCH}_2\text{CH}_2\text{CCO}_2\text{H} + \text{CH}_3\text{CHCO}_2^- + \text{NH}_3
\]
The first step is imine formation between the amino group of L-glutamic acid and pyruvic acid.
Mechanism

\[ \text{HO}_2\text{CCH}_2\text{CH}_2\text{CHCO}_2^- + \text{CH}_3\text{CCO}_2\text{H} + \text{NH}_3 \rightarrow \text{HO}_2\text{CCH}_2\text{CH}_2\text{CHCO}_2^- + \text{CH}_3\text{CCO}_2^- \]
Formation of the imine is followed by proton removal at one carbon and protonation of another carbon.
Hydrolysis of the imine function gives $\alpha$-keto glutarate and L-alanine.
Biosynthesis of L-Tyrosine

L-Tyrosine is biosynthesized from L-phenylalanine. A key step is epoxidation of the aromatic ring to give an arene oxide intermediate.

\[
\text{CH}_2\text{CHCO}_2^- + \text{NH}_3
\]
Biosynthesis of L-Tyrosine

CH₂CHCO₂⁻ + NH₃

O₂, enzyme

CH₂CHCO₂⁻ + NH₃
Biosynthesis of L-Tyrosine

\[
\text{CH}_2\text{CHCO}_2^- \quad + \text{NH}_3
\]

enzyme

\[
\text{HO} \quad \text{CH}_2\text{CHCO}_2^- \quad + \text{NH}_3
\]
Conversion to L-tyrosine is one of the major metabolic pathways of L-phenylalanine.

Individuals who lack the enzymes necessary to convert L-phenylalanine to L-tyrosine can suffer from PKU disease. In PKU disease, L-phenylalanine is diverted to a pathway leading to phenylpyruvic acid, which is toxic.

Newborns are routinely tested for PKU disease. Treatment consists of reducing their dietary intake of phenylalanine-rich proteins.
Decarboxylation is a common reaction of $\alpha$-amino acids. An example is the conversion of $L$-histidin to histamine. Antihistamines act by blocking the action of histamine.

\[ \text{Histidine} \rightarrow \text{Histamine} + \text{Ammonia} \]
Decarboxylation

\[
\text{CH}_2\text{CH}_2\text{NH}_2 \xrightarrow{\text{CO}_2, \text{enzymes}} \text{CH}_2\text{CHCO}_2^- + \text{NH}_3
\]
The chemistry of the brain and central nervous system is affected by neurotransmitters.

Several important neurotransmitters are biosynthesized from \( \text{L-tyrosine} \).
The common name of this compound is L-DOPA. It occurs naturally in the brain. It is widely prescribed to reduce the symptoms of Parkinsonism.

$L-3,4$-Dihydroxyphenylalanine
Neurotransmitters

Dopamine is formed by decarboxylation of L-DOPA.
Neurotransmitters

Norepinephrine