10.6. The only amino acid with significant buffering capacity at pH 6 to 8 is histidine.

5 The β-carboxyl group of aspartic acid and the γ-carboxyl group of glutamic acid, although fully ionized at pH 7.0, have pK values considerably higher than the pK' values of the α-carboxyl groups and more nearly equal to that of simple carboxylic acids such as acetic acid.

6 The thiol or sulfhydryl group (—SH) of cysteine and the p-hydroxyl group of tyrosine are only very weakly acidic. At pH 7.0, the former is about 8 percent ionized and the latter about 0.01 percent ionized.

7 The ε-amino group of lysine and the guanidinium group of arginine are strongly basic; they lose their protons only at a very high pH. At pH 7.0, these amino acids have a net positive charge.

The titration curves of amino acids with R groups that ionize, e.g., histidine, lysine, and glutamic acid, are more complex, since they are a composite of the curve corresponding to the R-group dissociation and the curves for the α-amino and α-carboxyl groups (Figure 4-9).

Formaldehyde in excess readily combines with the free, i.e., unprotonated, amino groups of amino acids to give methylol derivatives. This reaction causes an isoelectric amino acid to lose a proton from the +NH₃— group of the zwitterion form:

\[
\begin{align*}
\text{H}_2\text{NCHR}^+\text{COO}^- & \rightarrow \text{H}_2\text{NCHR}^-\text{COO}^- + \text{H}^+ \\
\text{H}_2\text{NCHR}^+\text{COO}^- + 2\text{HCHO} & \rightarrow (\text{HOCH}_2\text{NCHR}^-\text{COO})^\text{H}_2
\end{align*}
\]

Dimethylamino acid

The proton so liberated can be titrated directly with NaOH to pH 8, the end point of phenolphthalein (Figure 4-10). Titration of amino acids or amino acid mixtures in the presence of excess formaldehyde (the formol titration) is a useful analytical method for following the formation of free amino acids during hydrolysis of proteins by proteolytic enzymes.

The Stereochernistry of Amino Acids

With the single exception of glycine, all amino acids obtained from hydrolysis of proteins under sufficiently mild conditions show optical activity; they can rotate the plane of polarization of plane-polarized light when examined in a polarimeter. Optical activity is shown by all compounds capable of existing in two forms that are nonsuperimposable mirror images of each other; such compounds, which can exist in right-handed and left-handed forms, are called chiral compounds (Greek for “hand”). The phenomenon of stereoisomerism, also called chirality (“handedness”), occurs in all compounds having an asymmetric carbon atom, i.e., one with four different substituents. Because of the tetrahedral nature of the sp³ orbitals of the carbon atom, the four different substituent groups can occupy two different arrangements in space around the carbon atom to yield two different stereoisomers, or enantiomers. Glycine has no asymmetric