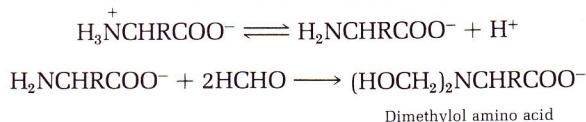


- 10.6. The only amino acid with significant buffering capacity at pH 6 to 8 is histidine.
- The  $\beta$ -carboxyl group of aspartic acid and the  $\gamma$ -carboxyl group of glutamic acid, although fully ionized at pH 7.0, have  $pK'$  values considerably higher than the  $pK'$  values of the  $\alpha$ -carboxyl groups and more nearly equal to that of simple carboxylic acids such as acetic acid.
  - The thiol or sulfhydryl group ( $-\text{SH}$ ) 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.
  - The  $\epsilon$ -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  $\alpha$ -amino and  $\alpha$ -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  $^+\text{NH}_3-$  group of the zwitterion form:



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 Stereochemistry 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  $sp^3$  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

Figure 4-9  
Titration curves of glutamic acid, lysine, and histidine. The  $pK'$  of the R group designated  $pK'_R$ .

