

Consider the properties of the a.a. in more detail.

Acid-dissociation equilibria of the ionizable groups of a.a. are shown in Fig. 4.3.

Relative to HCl and H₂SO₄, the ionizable groups of amino acids are all weak acids.

Weak acids are characterized by incomplete dissociation throughout a wide range of pH.

Consider the titration of a weak acid by hydroxide ion in Fig 2.3.

At low pH the conjugate acid form [HA] is the predominant form in solution.

As OH⁻ is added the pH gradually increases as [HA] decreases and the conjugate base [A⁻] increases.

An inflection point occurs in the curve when 0.5 mole OH^- per mole of HA has been added such that $[\text{HA}] = [\text{A}^-]$.

As additional OH^- is added, the $[\text{HA}]$ decreases further and $[\text{A}^-]$ becomes greater than $[\text{HA}]$.

When 1.0 mole OH^- has been added, all of the HA will be converted to A^- .

This type of behavior is characteristic of the α -amino, the α -carboxyl and ionizable R groups of a.a..

The titration of alanine is shown in Fig 4.10(a).

At very low pH, the acid forms of both the amino and carboxyl groups will predominate so that the form of the a.a. in solution is-

As the pH increases, the carboxylic acid group ionizes first because it is a stronger acid than the acid form of the amine.

At the first inflection point,

Further increases in pH lead to complete ionization of the carboxylic acid group as indicated at $\text{pH} \approx 6.0$. At this pH, the predominant form of the amino acid in solution is-

Further increases in the pH lead to ionization of the protonated amino group.

A second inflection point occurs when -

At high pH, all of the protonated amino groups are neutralized by OH^- so that the form of the a.a. in solution is-

The titration of histidine requires 3 equivalents of base and has 3 inflection points corresponding to the ionizations of the α -carboxyl, imidazole and α -amino groups.

To understand the structure and properties of proteins it is important to know whether the acidic or basic form of an R group predominates in solution at a particular pH.

The ratio of the two forms can be determined from the pK_a of the group using the Henderson-Hasselbalch equation-

Let's determine the predominant form of the ϵ -amino group of lys at pH 7.0 which is less than the pK_a -

Consider the ratio of the acidic and basic forms at a $\text{pH} = \text{pK}_a$

Consider the ratio at $\text{pH} = 13$ which is greater than the pK_a -

We observe then that if the $\text{pH} < \text{pK}_a$ the acid form predominates.

If the $\text{pH} = \text{pK}_a$, the conc. of the two forms is equal.

If the $\text{pH} > \text{pK}_a$, the basic form predominates.

Also note from the above calculations that the ratio of the acidic and basic forms will be a factor of 10 for each pH unit away from the pK_a value.

It will be necessary for you to know the pK_a values of the side chains of the amino acids shown in Table 4.2 and that the pK_a of the α -carboxyl group is ~ 2.0 and the pK_a of the α -amino group is ~ 9.5 .

As an exercise you should confirm the form of the ionizable groups shown in Table 4-1 at pH 7.0 based on the pK_a values.

