Linear Titration Curves of Acids and Bases

Abstract. The Henderson-Hasselbalch equation, by a simple transformation, becomes $pH - pK = pA - pB$, where pA and pB are the negative logarithms of acid and base concentrations. Sigmoid titration curves then reduce to straight lines; titration curves of polyelectrolytes, to families of straight lines. The method is applied to the titration of the dipeptide glycyl aminotricarballylic acid, with four titrable groups. Results are expressed as Cartesian and d'Ocagne nomograms. The latter is of a general form applicable to polyelectrolytes of any degree of complexity.

By means of a simple transformation, titration curves of univalent weak acids and bases may be plotted as straight lines (*1*). The Henderson-Hasselbalch equation is converted to

$$pH - pK = pA - pB \qquad (1)$$

where pA and pB are negative logarithms of the acid and base concentrations. Plotted on semilogarithmic paper, the standard curve requires no reference to logarithmic tables. A special double logarithmic paper has been designed by Druckrey for general formulations of the mass action law (*2*). This may likewise be used to obtain linear graphs.

For polyvalent electrolytes, amino acids, peptides, or polypeptides, the titration may be represented by a family of parallel straight lines. The position of each line is determined by the value of pK for the group which is represented. The general method may be illustrated by its application to a dipeptide, glycyl aminotricarballylic acid (*3*). This contains four titrable groups: three carboxylic acid groups and the amino group. At any pH the equilibrium is represented by four reactions involving hydrogen ions:

$$A_1 = B_1 + H^+$$
$$A_2 = B_2 + H^+$$
$$A_3 = B_3 + H^+$$
$$A_4 = B_4 + H^+$$

The three undissociated carboxylic acid groups are denoted A_1, A_2, and A_3, while the respective ionized forms are denoted B_1, B_2, and B_3. A_4 and B_4 represent, respectively, the positively charged and neutral forms of the amino group. Corresponding to these four reactions are four transformed mass action law equations:

$$pH - pK_1 = pA_1 - pB_1$$
$$pH - pK_2 = pA_2 - pB_2$$
$$pH - pK_3 = pA_3 - pB_3$$
$$pH - pK_4 = pA_4 - pB_4$$

The equilibrium at any pH is determined by the pK values. These are, in order: 2.70, 4.10, 5.35, and 8.32 (*3*). The state of equilibrium over any range of pH is given by the family of four parallel straight lines (Fig. 1). These constitute a linear Cartesian nomogram. This form of diagram is much simpler than a family of four sigmoid curves requiring logarithmic calculations. In addition, the diagram clearly indicates the distribution of electrical charge over the molecule as a function of pH. The graphical method is applicable to polyelectrolytes of any degree of complexity. For a protein it would illustrate the distribution of electrical charges over all titrable groups in any given pH range—for example, in the neighborhood of the isoelectric point.

Cartesian nomograms consisting of families of parallel straight lines are readily transformed to d'Ocagne nomograms (*4*). The linear form of a simple titration curve (Eq. 1) is represented by three equally spaced parallel straight lines (Fig. 2). The first line is a scale of pH over any desired range. The second is the scale of $(pA - pB)$, or log B/A. The third scale represents pK over the same range as that taken for pH. In the standard nomogram, values of pH and pK from 2 to 10 are represented. Each scale is linear, with pH and pK intervals equal. The pK scale is inverted with respect to the pH scale. The scale denoting $(pA - pB)$ is equidistant from the other two and parallel to them. It likewise is linear, with the mid-point at zero. Any value on this scale corresponds to the difference $(pH - pK)$ obtained by connecting with a straight line two points on the pH and pK scales.

The nomogram represents a generalized solution of Eq. 1. It can be used for univalent electrolytes, such as acetic acid, with only one pK value, or for polyelectrolytes of any degree of complexity. In Fig. 2, the dipeptide glycyl aminotricarballylic acid is represented. The four pK values (2.70, 4.10, 5.35, and 8.32) are indicated on the pK scale. The isoelectric point (3.41) is indicated on the pH scale. The state of ionization of each group is represented by the point of intersection with the middle scale of the line connecting pH with pK. The four connecting lines represent the distribution of charge over the four titrable groups as a function of pH. These relationships are not readily shown by the usual type of simple or compound sigmoid titration curves.

Especially in biological systems containing polyvalent titrable components is it advantageous to apply linear transformations of mass action law reactions. Redox potentials, usually described by sigmoid mass action formulations, may also be transformed to linear functions (*5*). When the redox potential depends on the pH as well as on the state of oxidation, the usual graphic formulation results in complex three-dimensional sigmoid surfaces (*6*). In biological preparations, complex polyelectrolyte systems are often coexistent with one or more oxidation-reduction systems. By means of linear transformations of all the mass action formulations, physicochemical systems of high degrees of complexity may be depicted by simple types of linear nomograms.

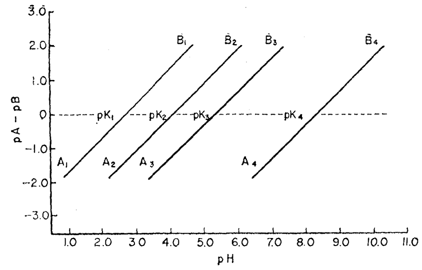

Fig. 1. Linear transformation of titration curve of glycyl aminotricarballylic acid (*3*), a Cartesian nomogram based on four pK values: 2.70, 4.10, 5.35, and 8.32.

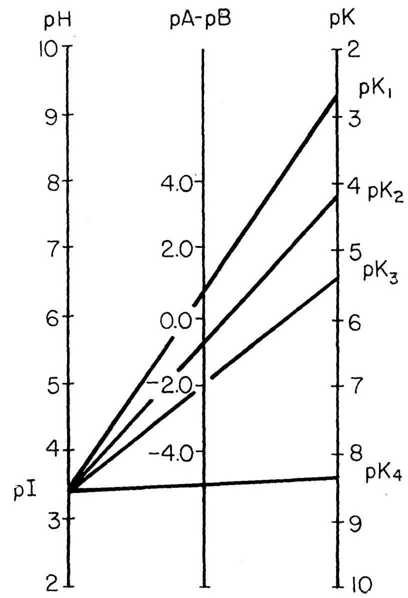

Fig. 2. Generalized d'Ocagne nomogram applicable to polyelectrolytes. Values of pK of four groups of glycyl aminotricarballylic acid are indicated on the pK scale. The value of the isoelectric point (pH 3.41) is shown on the pH scale. Simultaneous states of dissociation of the four titrable groups are indicated by the intercepts on the middle scale.

NORMAN R. JOSEPH

Department of Chemistry, College of Pharmacy, University of Illinois, Chicago

References and Notes

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