213. *Electrometric Titrations of Weak Acids and Bases in Aqueous Solution.*

By D. O. Jordan and H. F. W. Taylor.

A method is described for the determination of the amount of alkali bound by water during the electrometric titration of a weak acid with alkali. The method is demonstrated by the determination of the pK_a' values of *p*-aminobenzenesulphonamide and of benziminazole and is equally applicable to the titration of weak bases with acid.

The determination of non-thermodynamic dissociation constants in aqueous solution by electrometric titration presents few difficulties provided that the region in which the titration is carried out falls within the limits pH 4·0—10·0. Outside this range complications arise and corrections must be applied to the pH titration curves for the volumes of acid or alkali which fail to react.

The necessity for such a correction was recognised by Cohn, Gross, and Johnson (*J. Gen. Physiol.*, 1919—1920, **2**, 145) and more clearly by Tague (*J. Amer. Chem. Soc.*, 1920, **42**, 173); they determined the volume of alkali required to bring a solution of a weak acid to a given pH and deducted therefrom the volume of alkali needed to bring an equal quantity of water to the same pH, as determined experimentally by a blank titration. This method has been used extensively (see, *e.g.*, Kirk and Schmidt, *J. Biol. Chem.*, 1929, **81**, 237; Albert and Goldacre, *Nature*, 1942, **149**, 245; Fletcher, Gulland, and Jordan, *J.*, 1944, 33) but, as pointed out by Cohn and Berggren (*J. Gen. Physiol.*, 1924—1925, **7**, 45), the correction so obtained is too small, since at any given pH the ionic strength is greater in the titration of the weak acid than in the blank, by virtue of the alkali bound by the weak acid.

Other workers have used conductance ratios (Harris, *J.*, 1923, **123**, 3294; *Proc. Roy. Soc.*, 1923—1924, *B*, **95**, 440; *Nature*, 1925, **115**, 119) or activity coefficients (see, *e.g.*, Greenstein, *J. Biol. Chem.*, 1931, **93**, 479; Cohn, Green, and Blanchard, *J. Amer. Chem. Soc.*, 1937, **59**, 509) to calculate, from the pH of the solution being titrated, the volume of alkali to be deducted. This procedure introduces a further error unless the cell employed involves no liquid junction. The liquid-junction potential existing between the dilute solution being titrated and a saturated potassium chloride bridge is greater at the extremes of pH than in neutral solution (Burton, Hamer, and Acree, *J. Res. Nat. Bur. Stand.*, 1936, **16**, 575; Hamer and Acree, *ibid.*, 1936, **17**, 605; and confirmed in this paper). The ensuing variation in the titration curve is not allowed for in the calculation, and gives rise to considerable errors when applying the correction.

It was concluded by Schmidt ("The Chemistry of the Amino-acids and Proteins," Baillière, Tindall and Cox, 1938, p. 605) and by Cannan (*Chem. Revs.*, 1942, **30**, 395) that an experimental determination of the correction is to be preferred and that it should be carried out under as nearly as possible the same experimental conditions, as regards ionic strength, as in the actual titration. This procedure is tedious since it involves the performance of a large number of blank experiments, and the following method was therefore evolved in which corrections for a series of titrations can be obtained from a single experimentally determined blank titration curve.

The Correction for the Titration of Weak Acids.—(For brevity, this discussion is restricted to the titration of weak acids; it applies equally to that of weak bases.) A solution of the weak acid, of volume V_s, is titrated with standard alkali. The titration is repeated, the same quantity of pure water being used, and the volume of alkali plotted against pH. At any given pH above 10·0, let the volumes of alkali in the two titrations be V and V_b (the latter being obtained from the curve), and the ionic strengths I and I_b respectively. Owing to the different volumes $(V_s + V)$ and $(V_s + V_b)$ respectively, and the different ionic strengths of the two solutions, a volume and an activity correction must be made to V_b before it is deducted from V to give the quantity of alkali, v, used to neutralise the acid. Hence

$$V'_b = \frac{V_b(V_s + V)f_b}{(V_s + V_b)f} \text{ and } v = V - V_b'$$

where f and f_b are the activity coefficients of the hydroxyl ion in the solution of the weak acid and the blank, respectively, and V_b' is the desired corrected value of V_b. By introducing the Debye–Hückel equation $(-\log f_{OH} = 0{\cdot}5\sqrt{I})$ we obtain $\log f_b - \log f = 0{\cdot}5\ (\sqrt{I} - \sqrt{I_b})$ or

$$\frac{f_b}{f} = \text{antilog } [0{\cdot}5(\sqrt{I} - \sqrt{I_b})]$$

and hence

$$V'_b = V_b \frac{V_s + V}{V_s + V_b} \text{antilog } [0{\cdot}5(\sqrt{I} - \sqrt{I_b})] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1$$

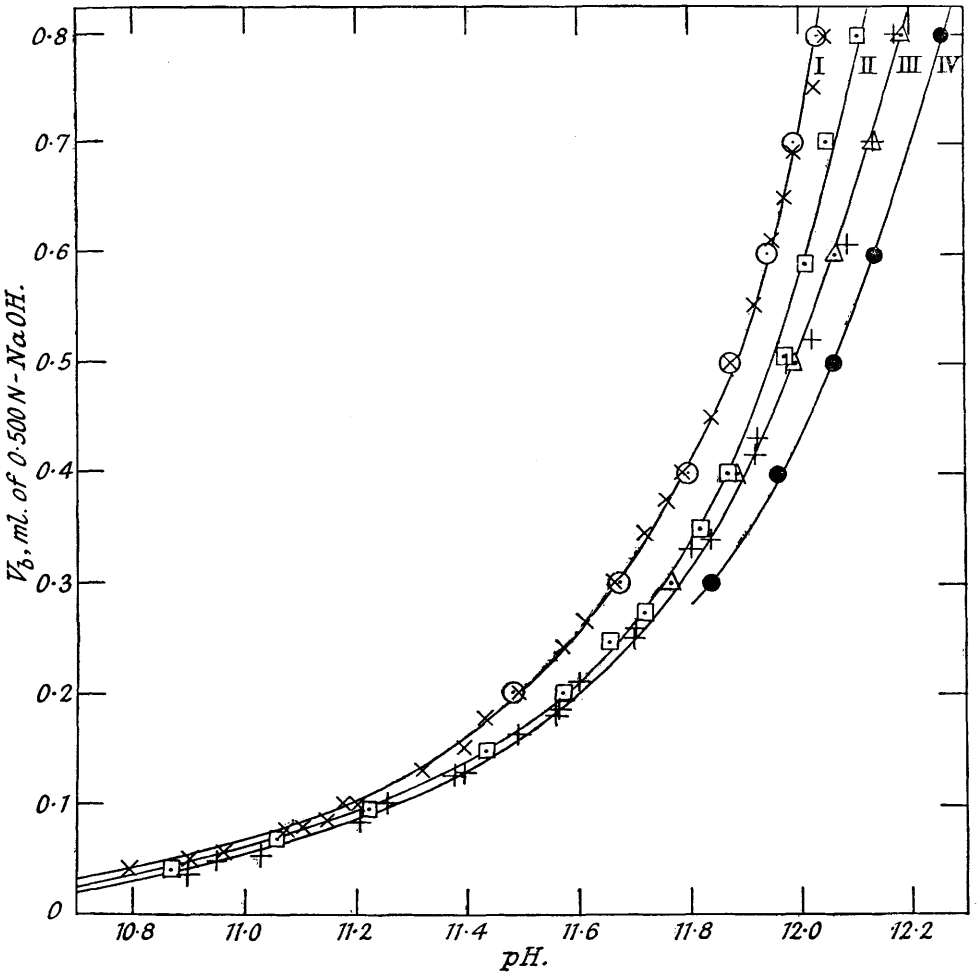
Discussion.—Experimental justification for the introduction of the Debye–Hückel equation has been obtained by using the cell $H_2Pt|NaOH, H_2O||KCl$ (satd.) in agar$||KCl(M), Hg_2Cl_2$(satd.)$|Hg$ (I) at 25°, by titrating pure water (20·0 ml.) and a solution of sodium chloride (0·0293 g. in 22·0 ml.) with 0·5M-sodium hydroxide. The results are shown in Fig. 1, curves II and I, respectively. The latter curve has also been calculated from the former by using the equation

$$-\Delta \text{pH} = \log \frac{(22 + V_b)}{(20 + V_b)} + 0{\cdot}5(\sqrt{I_I} - \sqrt{I_{II}}) \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

which has been derived on the same basis as equation (1). I_{I} and I_{II} are the ionic strengths in the solution with and without sodium chloride respectively. It will be seen that the experimental and the calculated curve are in excellent agreement. The use of extended forms of the Debye–Hückel limiting equation makes no significant difference in the calculated values.

The value of 282 mv. for the potential of the normal calomel electrode was obtained at 25° by using 0·05M-potassium hydrogen phthalate (pH 3·97; Clark, " The Determination of Hydrogen Ions," The Williams and Wilkins Co., Baltimore, 1928, p. 485). This potential includes the two liquid-junction potentials existing in cell I, of which that between the saturated potassium chloride bridge and the solution being titrated will vary with the pH. In alkaline solution this liquid-junction potential opposes that of the cell, thus reducing the

FIG. 1.



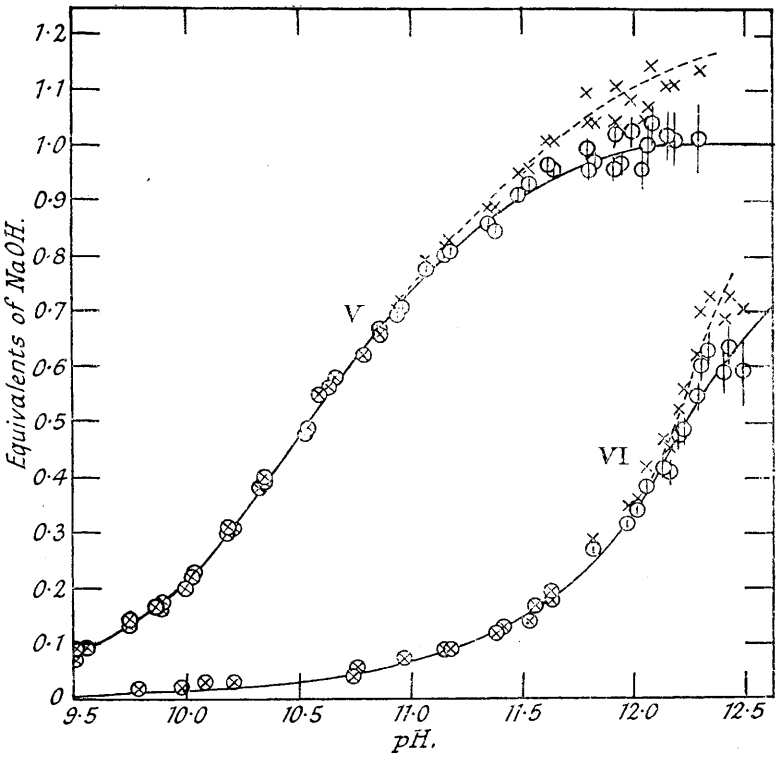
Titration curves for : I, 22·0 *ml. of water containing* 0·0293 *g. of* NaCl *using agar–calomel half-cell, experimental values* ×, *values calculated by equation* (2) *from curve* II ⊙ ; II, 20·0 *ml. of water, using agar–calomel half-cell, experimental values* ⊡ ; III, 22·0 *ml. of water containing* 0·0293 *g. of* NaCl, *using* Ag|AgCl *half-cell, experimental values* + ; *values calculated by equation* (2) *from curve* IV △ ; IV, 20·0 *ml. of water, calculated values* ●.

apparent pH, whereas in acid solution it augments the cell potential and the apparent pH is increased. The extent of the variation in alkaline solutions is seen by comparing curves II and IV (Fig. 1), the latter having been calculated from the equation $\mathrm{pH} = \mathrm{p}K_w + \log M_{\mathrm{NaOH}} f_{\mathrm{OH'}}$, on the assumption that $\mathrm{pH} = -\log a_{\mathrm{H_3O^+}}$ and that $f_{\mathrm{OH'}} = f_{\mathrm{NaOH}}$. In order to show that the discrepancy between curves II and IV could not be due either wholly or in part to a peculiarity of the agar bridge, the titration of water by use of cell I has been repeated, an aqueous saturated potassium chloride bridge being used with two reproducible liquid junctions. The results of this titration were identical with those given in curve II. This variation has also been confirmed by repeating the titration of water (22·0 ml.) in the presence of sodium chloride (0·0293 g.) with 0·5M-sodium hydroxide and using the cell $\mathrm{H_2Pt|NaOH, NaCl, H_2O, AgCl}$ (satd.)|Ag (II) at 25°, which contains no liquid junction. The results are given in curve III, Fig. 1 [also calculated from curve IV by using equation (2)], and the discrepancy between this curve and curve I, as between curves IV and II, is attributed to variations

in the liquid-junction potential and to the different assumptions on which the pH scales of curves I and II, III and IV have been based.

The Use of the Correction Method.—To demonstrate the method of correction, two weak acids, *p*-aminobenzenesulphonamide and benziminazole, have been titrated with alkali. The results of these experiments are shown in Fig. 2. It will be seen that the relation between v and pH is in good agreement with Henderson's equation, and that the use of $V_b(V_s + V)/V_s + V_b)$ in place of V'_b above pH 11·0 leads to appreciable errors. The result for *p*-aminobenzenesulphonamide (curve V) shows that the inadequately corrected curve does not tend to a limit at 1·0 equivalent, a fact of considerable importance in the interpretation of the dissociation curve of a complex substance showing an unknown number of overlapping dissociations. The result for benziminazole (curve VI) shows that an error in pK'_a may also result.

FIG. 2.



Titration curves of: V, p-*aminobenzenesulphonamide* ($pK'_{a_2} = 10{\cdot}58$); VI, *benziminazole* ($pK'_{a_2} = 12{\cdot}30$). *Smooth curves calculated from the Henderson equation;* ⊙, *equivalents calculated from* $V - V_b'$ [*the vertical lines through these points represent the error (in equivalents) produced by a variation of* ±0·01 *pH unit when applying the correction*]; ×, *equivalents calculated from* $V - \left[V_b \frac{V_s + V}{V_s + V_b}\right]$, *a broken line being drawn through these points.*

The pK'_a values obtained at 25° are: for *p*-aminobenzenesulphonamide $pK'_{a_2} = 10{\cdot}58$ (in 0·0227M-solution) [cf. Albert and Goldacre (*loc. cit.*) who give $pK'_{a_2} = 10{\cdot}20$ (in 0·025M-solution); Bell and Roblin (*J. Amer. Chem. Soc.*, 1942, **64**, 2905), 10·43; Fox and Rose (*Proc. Soc. Exp. Biol. Med.*, 1942, **50**, 142), 10·5; Cook, Heilbron, Reed, and Strachan (*J.*, 1945, 861), 10·65], and for benziminazole $pK'_{a_2} = 12{\cdot}3$ (in 0·0385M-solution).

EXPERIMENTAL.

The experimental procedure was similar to that described by Fletcher, Gulland, and Jordan (*loc. cit.*). The saturated potassium chloride in agar bridges were prepared in narrow glass tubing, a 3% agar solution being used. The aqueous potassium chloride bridge contained two liquid junctions of the type described by Coates (*J.*, 1945, 489).

The silver–silver chloride electrodes were prepared according to Brown (*J. Amer. Chem. Soc.*, 1934, **56**, 646), with the additional precaution of plating the platinum wires with gold before the silver was deposited in order to avoid the possibility of error due to the adsorption of hydrogen gas or ions. The standard potential was taken as 223 mv., a value confirmed by measuring the e.m.f. of the cell, H_2Pt|HCl (0·5M), AgCl (satd.)||Ag at 25°. The activity coefficient of 0·5M-hydrochloric acid was taken as 0·77 (MacInnes, "The Principles of Electrochemistry," Reinhold Publishing Corporation, New York, 1939, p. 185). Two electrodes were used in all titrations.

For the calculation of curve IV (Fig. 1) the following data were used: $pK_w = 14{\cdot}01$ at 25° (Harned and Hamer, *J. Amer. Chem. Soc.*, 1933, **55**, 2194), f_{NaOH} at 25° = 0·899 at 0·00997M, 0·858 at 0·0201M, 0·803 at 0·0525M (MacInnes, *op. cit.*, p. 155).

The water used was laboratory distilled water, redistilled in an all-"Pyrex" apparatus from dilute phosphoric acid, and

condensed in a counter stream of carbon dioxide-free air. The *p*-aminobenzenesulphonamide was obtained from British Drug Houses Limited, and was twice recrystallised from aqueous alcohol; m. p. 165—166°. The benziminazole was prepared as described in *Organic Syntheses* (1939, **19**, 12) and was twice recrystallised from water; m. p. 171—172°.

It is a pleasure to record our thanks to Professor J. M. Gulland, F.R.S., for his interest and encouragement, and to Imperial Chemical Industries Limited for the loan of apparatus.

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