[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TEXAS]

Application of the Glass Electrode to the Determination of the Thermodynamic Ionization Constants of *p*-Aminobenzoic Acid

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The thermodynamic ionization constants of *p*-aminobenzoic acid have been determined in water at 25° by use of cells without liquid junction using the commercial Beckman "General-Purpose" glass electrode. The values of pK_{A_1} and pK_{A_2} obtained were, respectively, 2.50_1 and 4.87_4.

In this investigation a method was developed for determining the first and second dissociation constants of *p*-aminobenzoic acid by the electromotive force method, using cells without liquid junction. The Beckman "General-Purpose" glass electrode was employed in measuring the hydrogen ion activity because the application of the hydrogen electrode or the quinhydrone electrode was found not to be practicable in this case. This is an extension of previous work in this Laboratory on the dissociation of weak electrolytes, which includes studies on propionic acid,[3,4] *n*-butyric acid[5] and β-alanine.[6]

Experimental

***p*-Aminobenzoic Acid Buffer Solutions.**—The K_{A1} buffer solutions were prepared from *p*-aminobenzoic acid, repurified hydrochloric acid and conductivity water; the K_{A2} buffer solutions were prepared from potassium *p*-aminobenzoate, repurified hydrochloric acid and conductivity water. The *p*-aminobenzoic acid, twice recrystallized Eastman Kodak Company White Label grade, melted sharply at 187° in agreement with the best value from the literature[7]; it was not hygroscopic. The potassium *p*-aminobenzoate, prepared from *p*-aminobenzoic acid and potassium hydroxide, was carefully purified; it was found to be free of carbonate and non-hygroscopic.

A stock solution was prepared in the highest concentration possible (about 0.035 *M* in *p*-aminobenzoic acid); and the various solutions for measurement were prepared by weight dilution, with the same buffer ratio being maintained. All solutions were deaerated immediately after preparation with solvent-saturated, high-purity nitrogen. The repurified hydrochloric acid, 0.1 to 0.3 *N*, was standardized gravimetrically.

Glass Electrode Standardization Solutions.—Three different reference buffer solutions, prepared, respectively, from reagent grade glycine, potassium tetraborate and propionic acid, were used for the standardization of the glass electrodes against hydrogen electrodes. The solutions were deoxygenated and stored under repurified electrolytic hydrogen.

Electromotive Force Measurements.—The measuring circuit consisted of a Leeds and Northrup Type K2 potentiometer (recently calibrated by the manufacturer); a Leeds and Northrup thermionic amplifier, modified internally to make it sensitive to ±0.01 millivolt; and a Leeds and Northrup Type R moving-coil galvanometer. Three standard cells were used, all recently calibrated by the Bureau of Standards. Temperature control was maintained to ±0.01° in a kerosene thermostat.

The preparation of the hydrogen electrodes and the thermal decomposition type silver–silver chloride electrodes has been previously described.[8] Each "General-Purpose" glass electrode selected for use was tested for several days to ensure a minimum drift in asymmetry potential. All glass electrode measurements were made in triplicate.

The electromotive force cells were of special design and contained four side arms. Presaturators with sintered-glass cylinders were used whenever the hydrogen electrode was employed. The cells were filled with the appropriate solutions by employing an oxygen-excluding vacuum technique. A special sweep system (for hydrogen or nitrogen) built into the cell allowed removal of any air which entered during the insertion of the glass electrodes, after the vacuum loading procedure.

The actual procedure of measurement consisted of standardization by measuring the potential of the three glass electrodes against duplicate hydrogen electrodes for at least two hours, followed by transfer of the glass electrodes to the *p*-aminobenzoic acid–buffer cell and measurement of its potential until equilibrium was reached. The glass electrodes were then transferred back to the standardization cell for recheck of their calibration. Agreement was almost always obtained to ±0.10 millivolt for the six glass electrode calibration readings, and similar agreement was obtained between the three glass electrodes in *p*-aminobenzoic acid–buffer solutions.

Calculations

The first and second dissociation reactions of *p*-aminobenzoic acid may be written $HQH^+ \rightleftarrows H^+ + HQ$ and $HQ \rightleftarrows H^+ + Q^-$, where HQ represents the neutral-molecule structure of *p*-aminobenzoic acid. Although aliphatic amino acids are usually 99.99% or more in the zwitterion form, Klotz and Gruen[9] have shown that *p*-aminobenzoic acid exists in solution predominantly (91–97%) in the neutral molecule form. pK_{A1} as determined in this investigation really represents a mixture, in the structural sense, of the predominant neutral-molecule species with a small portion of the dipolar species; the same is true in the case of pK_{A2}. Although the simultaneous presence of both species affects the kinetics of the ionization of *p*-aminobenzoic acid by introducing a second dissociation mechanism, it does not affect the final equilibrium or thermodynamic properties of the solution.[10]

From cells of the type

Glass electrode | *p*-Aminobenzoic acid (m_1), Hydrochloride of *p*-aminobenzoic acid (m_2) | AgCl | Ag

the first thermodynamic ionization constant, K_{A1}, is given by

$$-\log K_{A1} = \frac{E + E^0_{\mathrm{Ag,Cl^-,AgCl}} - E_g(1\ \mathrm{atm.})}{2.303(RT/F)} + \log \frac{m_{HQH}m_{Cl}}{m_{HQ}} + \log \frac{\gamma_{HQH}\gamma_{Cl}}{\gamma_{HQ}} \quad (1)$$

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[1] (a) This paper represents part of a dissertation submitted by Marvin L. Deviney, Jr., in partial fulfillment of the requirements for the Ph.D. degree at the University of Texas, June, 1956. (b) Holder of the Humble Oil and Refining Company Fellowship in Chemistry, 1953–1954.

[2] Deceased October 5, 1952.

[3] A. Patterson, Jr., with W. A. Felsing, THIS JOURNAL, **64**, 1480 (1942).

[4] R. L. Moore and W. A. Felsing, *ibid.*, **69**, 2420 (1947).

[5] W. A. Felsing and M. May, *ibid.*, **70**, 2904 (1948).

[6] M. May and W. A. Felsing, *ibid.*, **73**, 406 (1951).

[7] C. J. Kern, T. Antoshkiw and M. R. Maiese, *Anal. Chem.*, **20**, 19 (1949).

[8] R. L. Moore and W. A. Felsing, THIS JOURNAL, **69**, 1076 (1947).

[9] I. M. Klotz and D. M. Gruen, *ibid.*, **67**, 843 (1945).

[10] L. Michaelis, "Techniques of Organic Chemistry, Vol. I. Physical Methods of Organic Chemistry," Part II, edited by A. Weissberger, Interscience Publishers, Inc., New York, N. Y., 1949, p. 1747.

where E is the measured voltage of the cell, $E^0_{\mathrm{Ag,Cl^-,AgCl}}$ is the molal potential of the silver-silver chloride electrode at 25°,[11] E_g(1 atm) is the glass electrode constant as measured directly against a platinum-black hydrogen electrode (corrected to 1 atmosphere hydrogen pressure) immediately before and after each measurement of E, m is the weight molality and γ is the activity coefficient. The physical constants used in this investigation were the latest and most accurate values available.

The treatment of data used in this Laboratory for the evaluation of the thermodynamic ionization constants of amino acids has been previously described in detail.[6] In the case of *p*-amino-benzoic acid, however, additional calculations were necessary in order to correct for slight concentration changes caused by the overlap of the K_{A1} and K_{A2} ionization reactions. This overlap phenomenon occurs for dibasic-type acids whenever the ratio $K_{A1}/K_{A2} < 10^3$ ($pK_{A2} - pK_{A1} < 3$).[12] Equations were derived to correct for this overlap effect following the principles used by Hamer, Pinching and Acree[13,14] for a dicarboxylic acid (*o*-phthalic acid) and by Smith and Smith[15] for a dicarboxylic amino acid (aspartic acid).

K_{A2} may be determined from cells of the type

$$\begin{array}{l|l|l|l} \text{Glass} & p\text{-Aminobenzoic acid } (m_3) & & \\ \text{electrode} & \text{Potassium } p\text{-aminobenzoate } (m_4) & \text{AgCl} & \text{Ag} \\ & \text{Potassium chloride } (m_5) & & \end{array}$$

and the pK_{A2} expression is

$$-\log K_{A2} = \frac{E + E^0_{\mathrm{Ag,Cl^-,AgCl}} - E_g(1\text{ atm.})}{2.303(RT/F)} + \log\frac{m_{\mathrm{Cl}}m_{\mathrm{HQ}}}{m_{\mathrm{Q}}} + \log\frac{\gamma_{\mathrm{Cl}}\gamma_{\mathrm{HQ}}}{\gamma_{\mathrm{Q}}} \quad (2)$$

The evaluation of K_{A2} was made following the methods referred to in the preceding paragraph.

Results

The data from which the thermodynamic ionization constants of *p*-aminobenzoic acid were calculated were obtained using Beckman "General-Purpose" glass electrodes. It was found in preliminary tests that both the platinized platinum and palladiumized platinum (prepared as recommended by Hamer and Acree[16]) electrodes failed to reach equilibrium in buffer solutions of *p*-aminobenzoic acid and its hydrochloride and in buffer solutions of *p*-aminobenzoic acid and its potassium salt. It was not definitely established in this investigation whether catalytic hydrogenation of *p*-aminobenzoic acid or adsorption on the platinum black and palladium black electrodes was responsible for the instability of the hydrogen electrode. Yoshimura[17] has shown that it is not possible to make accurate electromotive force measurements with the quinhydrone electrode in amino acid solutions because of a condensation reaction between quinone and the amino acid. The mechanism of this reaction has been reported by Posner[18] and Fuson.[19] Although MacInnes and Dole[20] thin-membrane glass electrodes were successfully prepared and tested, it proved to be very difficult to use them because of the extreme fragility of the membrane (on the order of 0.001 mm. thick).

In Tables I and II are given the experimental data obtained with the Beckman electrodes for the K_{A1} and K_{A2} determinations, respectively. The E_g (1 atm.) term and the E term represent the average of six and three separate electrode readings, respectively, for the given solution.

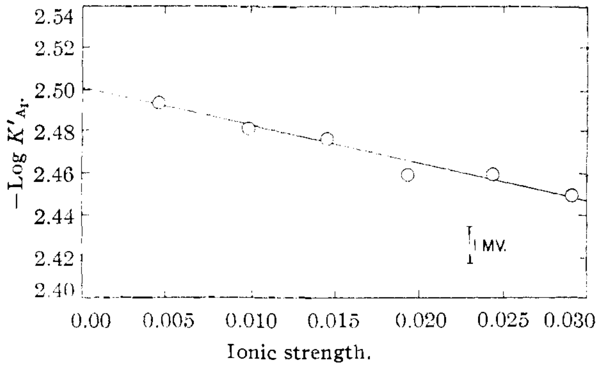

Fig. 1.—Determination of the first ionization constant of *p*-aminobenzoic acid in water at 25°.

Table I

Experimental Data for K_{A1} Determination

Point	m_1	m_2	$E - E_g$(1 atm.)
1	0.029324	0.028928	0.47113
2	.024417	.024089	.47667
3	.019528	.019266	.48267
4	.014463	.014269	.49237
5	.009882	.009750	.50404
6	.004623	.004561	.52996

Table II

Experimental Data for K_{A2} Determination

Point	$m_1 = m_3$	m_2	$E - E_g$(1 atm.)
1	0.028115	0.030664	0.60631
2	.023416	.025539	.61080
3	.018608	.020295	.61659
4	.013754	.015001	.62392
5	.009381	.010231	.63363
6	.007523	.008205	.63936
7	.004722	.005150	.65129
8	.004592	.005008	.65158

The least-squares extrapolation to infinite dilution to determine K_{A1} and K_{A2}, based on the data in the tables, is illustrated in Figs. 1 and 2. The circles in Fig. 2, the K_{A2} determination, are drawn with a radius of ± 0.10 millivolt (or ± 0.002 pK unit, which represents an error in K of 0.4%), and the circles in Fig. 1, the K_{A1} determination, are

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[11] R. G. Bates and V. E. Bower, *J. Research Natl. Bur. Standards*, **53**, 283 (1954).

[12] S. Glasstone, "An Introduction of Electrochemistry," D. Van Nostrand Co., Inc., New York, N. Y., 1942, p. 322.

[13] W. J. Hamer and S. F. Acree, *J. Research Natl. Bur. Standards*, **35**, 381 (1945).

[14] W. J. Hamer, G. D. Pinching and S. F. Acree, *ibid.*, **35**, 539 (1945).

[15] E. R. B. Smith and P. K. Smith, *J. Biol. Chem.*, **146**, 187 (1942).

[16] W. J. Hamer and S. F. Acree, *J. Research Natl. Bur. Standards* **33**, 87 (1944).

[17] H. Yoshimura, *J. Biochem.* (*Japan*), **23**, 187 (1936).

[18] T. Posner, *Ann. Chem.*, **336**, 85 (1904).

[19] R. C. Fuson, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 497.

[20] D. A. MacInnes and M. Dole, *Ind. Eng. Chem.*, *Anal Ed.*, **1**, 57 (1929); This Journal, **52**, 29 (1930).

drawn with a radius of ± 0.20 millivolt; these are believed to be the respective accuracies in the two determinations. The values of pK_{A1} and pK_{A2} obtained were, respectively, 2.50_1 (corresponding to $K_{A1} = 3.15_7 \times 10^{-3}$) and 4.87_4 (corresponding to $K_{A2} = 1.33_7 \times 10^{-5}$).

The following comparison of the values of the two ionization constants in water at 25°, as determined in this investigation, can be made with values already reported

	pK_{A1}	pK_{A2}	Method
This investigation	2.50_1	4.87_4	Galvanic cells without liquid junction
Klotz and Gruen (1945)[9]	2.504	...	Spectrophotometric
Albert and Goldacre (1942)[21]	2.49	4.83	Potentiometric titration
Kilpi and Harjanne (1948)[22]	2.38	4.89	Buffer capacity min. (liquid junction involved)
Johnston (1906)[23]	2.32	4.92	Catalytic method involving hydrolysis of methyl acetate
Winkelblech (1901)[24] and Walker (1904)[25]	2.32	4.92	Conductance

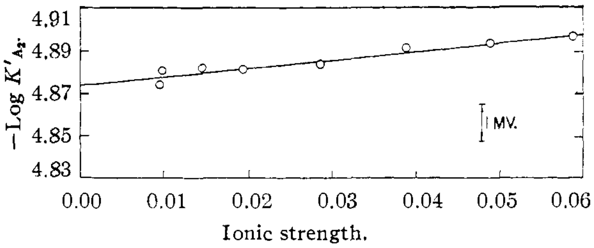

Fig. 2.—Determination of the second ionization constant of *p*-aminobenzoic acid in water at 25°.

The only previous completely thermodynamic method which has been applied to *p*-aminobenzoic acid is the spectrophotometric method, and excellent agreement was obtained between this investigation and the optical method for K_{A1}. The present investigation is apparently the only one in which corrections for the overlap of the dissociation reactions have been applied.

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AUSTIN, TEXAS

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[21] A. Albert and R. Goldacre, *Nature*, **149**, 245 (1942).

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[23] J. Johnston, *Proc. Roy. Soc. (London)*, **A18**, 82 (1906).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CINCINNATI]

Inter- and Intramolecular Hydrogen Bonds[1]

BY H. H. JAFFÉ

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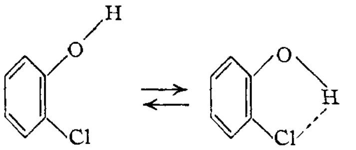
The differences in energies of intra- and intermolecular H-bonds are discussed in terms of the entropy changes accompanying H-bond formation.

Since the early work on hydrogen bonds[2] it has generally been accepted that they are usually associated with bond energies in the range of 3 to 7 kcal./mole. These estimates were based almost exclusively on intermolecular hydrogen bonds. In recent years, however, hydrogen bonds have been demonstrated to exist, or at least proposed, for which one would expect appreciably smaller bond energies.[3,4] Most of these cases involve *intra*-molecular hydrogen bonds, many of which could even be demonstrated in solution in polar media,[3] where one might have expected that hydrogen bonding with the solvent might be energetically preferred. It is the purpose of the present paper to call attention to a fundamental thermodynamic difference between *intra*- and *inter*molecular hydrogen bonds which can explain readily why intramolecular H-bonds of much smaller energy than intermolecular ones can be observed.

For the purpose of this discussion, we shall define the process of H-bond formation as the process in which this bond is formed, leaving the molecule (or molecules) otherwise effectively unchanged. For intermolecular H-bonds, this process then is equivalent to association; in case of H-bonds between atoms of the same kind, polymerization or dimerization; in this paper we shall not be concerned with association of more than two molecules, although the arguments presented will hold equally well for more extensive association. For intramolecular H-bonds, the process is represented by reaction 1 (using *o*-chlorophenol as an example) in the forward direction.



(1)

Accordingly, we may consider the process of H-bond formation as an equilibrium reaction, and we wish to examine the thermodynamics of this reaction.

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[1] This work was sponsored by the Office of Ordnance Research, U. S. Army.

[2] L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 2nd Ed., 1948, Chapter 9.

[3] D. H. McDaniel and H. C. Brown, *Science*, **118**, 370 (1953).

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