[CONTRIBUTION FROM THE NATIONAL CANCER INSTITUTE, NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE]

The Diffusion of α-Alanine in Water at 25°[1]

BY FREDERICK J. GUTTER[2] AND GERSON KEGELES[3]

RECEIVED MARCH 30, 1953

With a single lens convergent light Gouy interferometric system the differential diffusion coefficient of DL-α-alanine in water at 25° has been measured over the concentration range 0.25% to 13%, using a 0.5% concentration differential. A 6-cm. cell modeled after the Tiselius design, but having 21 mm. thick clamped-on optical flats for windows has been employed with the Polson boundary sharpening technique. The diffusion results are consistent to about 0.1%. Results obtained with D-α-alanine and L-α-alanine indicate no difference in diffusion rate from that of DL-α-alanine. The total number of fringes in the Gouy diagram plus the fractional number obtained from Rayleigh double slit interference patterns has been used to obtain values of the refractive index increments of DL-α-alanine over the concentration range studied, consistent to better than one unit in the sixth decimal place of refractive index.

The recent verification by Harned and co-workers,[4] using a conductance method, of the Nernst[5] and Onsager–Fuoss[6] theories for the diffusion of aqueous solutions of several strong electrolytes at low concentrations, and Gosting's precise agreement with these measurements for potassium chloride at higher concentration,[7] using the Gouy interference method[8] lend confidence in the accuracy as well as the precision of the Gouy method for absolute diffusion coefficient determinations.

The interpretation of the concentration dependence reported here for the diffusion coefficient in the light of recently obtained thermodynamic[9] and viscosity[10] data may be compared with similar studies for other substances.

Experimental

The apparatus employed is a modification of that described by Longsworth,[8b] most of the modifications made having been previously described in detail.[8e] The diffusion cell employed[11] is shown in Fig. 1. It has been patterned after the Tiselius electrophoresis cell[12] but has clamped-on optical flats 21 mm. thick as windows. Communication between the two side channels is made through a standard Tiselius cell bottom section and a top section with elongated arms. The entire front and back faces are ground flat after fusing. To ensure rectangularity, all the glass spacers of like size were ground together. In the center 9-mm. channel, labeled "R" in Fig. 1, the spacers at top and bottom, together with the two windows, form a completely sealed chamber. Before clamping on the second window, this chamber is nearly filled with the reference liquid, in our case water. The seal between the windows and the body of the cell is made with water-extracted and desiccated white vaseline. A diffusing boundary is formed in the column labelled "3" in Fig. 1, at the junction between bottom and center sections, and is then sharpened by siphoning through a capillary.[8e,13] This cell is so nearly perfect optically that the difference between the slit image positions obtained through the reference and diffusion channels, the so-called "δ-correction" has not exceeded 3 microns even with 13% alanine in the diffusion channel and water in the reference channel. The boundaries were sucked sharp by a four-pronged steel capillary consisting of extremely fine (0.016" outer diameter) stainless steel tubes 1 cm. long sealed into a straight bottom U-shaped loop of 1-mm. stainless steel tubing. The upper arms of the loop of 1-mm. tubing were united and sealed to a Pyrex glass stopcock with DeKhotinsky cement, as experience showed a soft rubber connection here to be extremely disadvantageous in permitting the

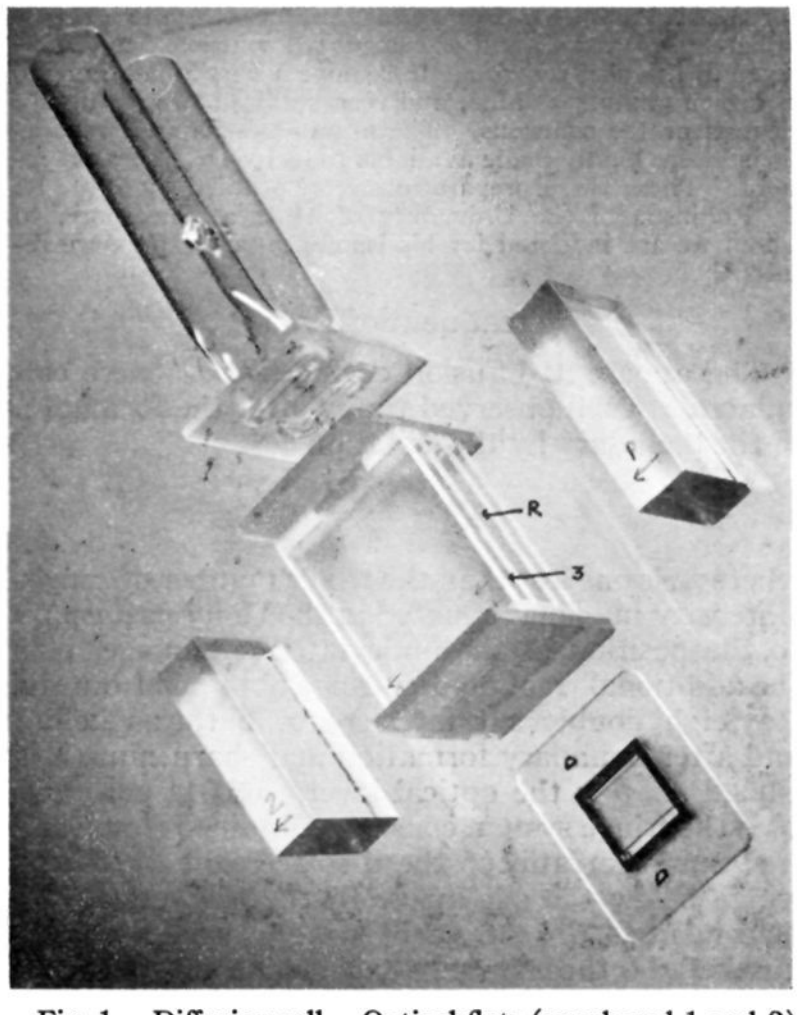

Fig. 1.—Diffusion cell. Optical flats (numbered 1 and 2) are clamped on as windows. Standard Tiselius cell bottom section is labelled D. "R" is the reference channel. "3" is the diffusion channel.

(1) Presented in part at the 122nd National Meeting, American Chemical Society, Atlantic City, N. J., September 18, 1952.

(2) Part of this material has been presented to the faculty of Georgetown University by Frederick J. Gutter in partial fulfillment of the requirements for the degree of Master of Science.

(3) Department of Chemistry, Clark University, Worcester, Mass.

(4) (a) H. S. Harned and D. M. French, *Ann. N. Y. Acad. Sci.*, **46**, 267 (1945); (b) H. S. Harned and R. L. Nuttall, THIS JOURNAL, **69**, 737 (1947); (c) H. S. Harned, *Chem. Revs.*, **40**, 462 (1947); (d) H. S. Harned and R. L. Nuttall, THIS JOURNAL, **71**, 1460 (1949); (e) H. S. Harned and R. M. Hudson, *ibid.*, **73**, 652 (1951).

(5) W. Nernst, *Z. physik. Chem.*, **2**, 613 (1888).

(6) L. Onsager and R. M. Fuoss, *J. Phys. Chem.*, **36**, 2689 (1932).

(7) L. J. Gosting, THIS JOURNAL, **72**, 4418 (1950).

(8) (a) G. L. Gouy, *Compt. rend.*, **90**, 307 (1880); (b) L. G. Longsworth, THIS JOURNAL, **69**, 2510 (1947); (c) G. Kegeles and L. J. Gosting, *ibid.*, **69**, 2516 (1947); (d) C. A. Coulson, J. T. Cox, A. G. Ogston and J. St. L. Philpot, *Proc. Roy. Soc.* (*London*), **A192**, 382 (1948); (e) L. J. Gosting, E. M. Hanson, G. Kegeles and Margaret S. Morris, *Rev. Sci. Instruments*, **20**, 209 (1949); (f) L. J. Gosting and L. Onsager, THIS JOURNAL, **74**, 6066 (1952); (g) J. M. Creeth, *Biochem. J.*, **51**, 10 (1952); (h) L. J. Gosting and D. F. Akeley, THIS JOURNAL, **74**, 2058 (1952).

(9) R. A. Robinson, *J. Biol. Chem.*, **199**, 71 (1952).

(10) L. S. Mason, R. M. Kampmeyer and A. L. Robinson, THIS JOURNAL, **74**, 1287 (1952).

(11) We are indebted to Mr. Emil Maier, Pyrocell Mfg. Co., New York, for his care in manufacturing this cell.

(12) A. Tiselius, *Trans. Faraday Soc.*, **33**, 524 (1937).

(13) D. S. Kahn and A. G. Polson, *J. Phys. Colloid Chem.*, **51**, 816 (1947).

squeezing back of cell effluent into the boundary when the stopcock is closed. Contrary to the recent findings of Trautman and Gofman,[14] careful location of the tip in our schlieren optical system and careful schlieren observational control with a horizontal knife edge of the Polson sharpening process indicated that in every experiment performed the maximum vertical refractive index gradient coincided with the horizontal level of the capillary tips, and that on prolonged sharpening the boundary became nearly symmetrical about the level of the capillary tips. The siphon was operated under a head of about three feet of water and withdrew a total of about 100 cc. of liquid through the capillaries at a rate of 3 to 7 cc. per minute. The 24-cc. capacity diffusion column was thus washed continuously, undergoing four complete changes of contents. The temperature of the water-bath was held constant to ±0.005°, and determined with a total immersion calorimeter thermometer graduated in 0.01° intervals, and calibrated to 0.001° by the National Bureau of Standards.

All solutions were made up by weight in water saturated with carbon dioxide-free air, using the same internally calibrated set of weights, and all weights were corrected to vacuum standard, using 1.424 as the density of solid alanine[15] and the densities of Gucker and Allen[16] for the alanine solutions.

Merck reagent grade DL-α-alanine was crystallized from 25% ethanol in water, recrystallized from 62.5% ethanol in water and dried to constant weight in a vacuum desiccator over phosphorus pentoxide. A readily detected lachrymatory impurity with amber color was essentially removed in one crystallization. In a preliminary series of several experiments, identity was indicated within 0.1% for the diffusion coefficients of once and twice crystallized 0.5% alanine into water. In another preliminary experiment, enough potassium chloride (6.3×10^{-5} M final concentration) was added to double the residual conductivity of the alanine, but on treatment as a one-solute system, the diffusion coefficient agreed with that of alanine to within 0.1%.[17]

At concentrations approaching saturation trouble was encountered with opalescence of solutions of the twice crystallized preparation, and the saturated solution was centrifuged in the ultracentrifuge to remove a very small amount of brown gummy residue, and recrystallized to give nearly clear saturated solutions. The D- and L-α-alanine preparations[18] were kindly made available to us by Dr. J. P. Greenstein. These three preparations were studied by Prof. R. A. Robinson of the University of Malaya, Singapore, to whom we are indebted for his isopiestic vapor pressure results.[9]

Treatment of Data

The apparent diffusion coefficients D' were calculated at each observed time t after the formation of the boundary by the equation[8b,8c]

$$D' = \frac{j_m^2 \lambda^2 b^2}{4\pi C_t^2 t} \qquad (1)$$

where j_m is one less than the whole number of fringes (intensity maxima) counted in the Gouy pattern up to the position of the undeviated slit image, plus the additional fraction of a fringe obtained from the Rayleigh double slit interference patterns before and after boundary formation and sharpening, λ is 5462.2 Å., b is the optical lever, 166.644 cm., and C_t is the fringe system constant, obtained from each fringe as the ratio of the displacement Y_j of the fringe below the slit image to the theoretical displacement $e^{-z_j^2}$. At early times, usually fringes numbered 0 through 10, 20, 25 and 30 were used to determine the C_t value for a photograph, but in a great many cases, the first 70 of about 90 fringes in late photographs produced constant C_t values to a few parts in 10,000, and after the 30th fringe in such cases, every 10th fringe was used.[8b] By use of the method of least squares, the D' values were then correlated with the corrected diffusion coefficient D and the zero time correction Δt, which reflects the initial blurring of the boundary, according to the relation[8b]

$$D' = D(1 + \Delta t/t) \qquad (2)$$

The corrected diffusion coefficients D are reported at the observed temperatures, but for the purpose of further calculations these were rounded according to the relation

$$D\eta^0/T = \text{const.} \qquad (3)$$

where η^0 is the viscosity of water at the absolute temperature T, this approximation being quite permissible over the maximum temperature interval of correction, 0.047°. The diffusion coefficients rounded to 25° were then least squared as a quadratic function of the weight per cent. w of alanine and as a quadratic function of the molarity c (moles alanine/liter solution), using 89.067 as the molecular weight of alanine, and the densities of Gucker and Allen[16] to convert from observed weight per cent. concentrations to molarities by a series of successive approximations.

The Gouy diffusion method when coupled with the Rayleigh interferometer[8d,8e] gives absolute data for refractive index increments Δn, according to the relation

$$a\Delta n/\lambda = j_m \qquad (4)$$

a being the cell thickness, λ the wave length of light 5462.2 Å. *in vacuo*, and j_m the path difference in terms of number of waves, as defined above. The specific refractive index increments Δn per unit of weight per cent. concentration, and per unit of molarity have been calculated from the data of the experiments.

Results

In Table I are shown the corrected differential diffusion coefficients of DL-α-alanine at observed temperatures, and the zero time corrections, together with the standard deviation of the diffusion coeff cient values at the twelve times in each experiment from the mean value. These results show an internal self-consistency of approximately 0.1%.

TABLE I

DIFFUSION COEFFICIENT OF DL-α-ALANINE IN WATER AS A FUNCTION OF THE CONCENTRATION, w, AT OBSERVED TEMPERATURES

w, g./100 g. soln.	$D \times 10^7$, cm.²/sec.	Temp., °C.	Δt, sec.
0.2497	91.00 ± 0.05	24.971	37.1
0.2507	91.03 ± .04	24.953	30.9
1.9821	88.28 ± .05	24.966	48.6
3.8588	85.18 ± .04	24.956	33.0
5.9472	82.78 ± .10	24.971	27.7
7.8615	80.16 ± .06	24.973	44.4
10.3267	77.11 ± .08	24.968	50.6
13.1953	73.97 ± .08	24.963	39.8

In Table II are shown the experimental values of

(14) R. Trautman and J. W. Gofman, *J. Phys. Chem.*, **56**, 464 (1952).

(15) E. J. Cohn, T. L. McMeekin, J. T. Edsall and J. H. Weare, THIS JOURNAL, **56**, 2270 (1934).

(16) F. T. Gucker and T. W. Allen, *ibid.*, **64**, 191 (1942).

(17) We wish to thank Dr. Herbert A. Sober for suggesting this experiment.

(18) S. M. Birnbaum, L. Levintow, R. B. Kingsley and J. P. Greenstein, *J. Biol. Chem.*, **194**, 455 (1952).

the diffusion coefficient rounded to 25°, and values calculated for DL-α-alanine from the equations

$$D \times 10^6 = 9.1442 - 0.16056w + 0.002186w^2 \quad (5)$$

$$D \times 10^6 = 9.1460 - 1.4277c + 0.1943c^2 \quad (6)$$

Included are a few values obtained for the D and L isomers of α-alanine.

TABLE II

COMPARISON OF EXPERIMENTAL AND LEAST SQUARE[a] DIFFUSION COEFFICIENTS—α-ALANINE IN WATER AT 25.000°

w, median wt. % alanine	$D \times 10^7$ Calcd.[a]	$D \times 10^7$ Exptl.	Remarks
0.09966	91.28	91.27	Experiment—D-α-alanine
.10083	91.28	91.18	Experiment—L-α-alanine
.3166	90.94	90.90	Experiment—L. G. Longsworth[b] using Rayleigh fringes
.2497	91.04	91.07	
.2507	91.04	91.15	
1.9821	88.35	88.36	
3.2341	86.48	86.34	Experiment—D-α-alanine
3.8588	85.57	85.28	
5.9472	82.67	82.85	
7.8287	80.21	80.22	Experiment—L-α-alanine
7.8615	80.17	80.22	
10.3267	77.20	77.18	
13.1953	74.07	74.04	

[a] $D \times 10^7 = 91.44_2 - 1.6056_3w + 0.02186w^2$. [b] L. G. Longsworth—private communication (see also ref. 28). Unless otherwise designated, all results are for DL-α-alanine.

Table III contains the observed number of fringes j_m, and the specific refractive index increments $\Delta n/\Delta w$ and $\Delta n/\Delta c$.

TABLE III

SPECIFIC REFRACTIVE INDEX INCREMENTS FOR DL-α-ALANINE

w, median wt. %	$\bar{c}$, moles/l. sol.	Δw	j_m	$\Delta n/\Delta w$	$\Delta n/\Delta c$
0.2497	0.02798	0.4993	94.28	0.001720	0.015338
0.2507	.02809	.5014	94.69	.001720	.015340
1.9821	.22331	.4844	91.98	.001729	.015254
3.8588	.43736	.4831	92.33	.001741	.015171
5.9568	.67971	.4792	91.88	.001746	.015019
7.8615	.90249	.4679	90.39	.001759	.014952
10.3267	1.19480	.4700	90.83	.001760	.014731
13.1953	1.54057	.4729	92.81	.001788	.014701

The Onsager–Fuoss theory for diffusion[5] relates the concentration dependence of the diffusion coefficient D to a mobility factor (Ω/c) and a thermodynamic factor $(1 + c\,\partial \ln y/\partial c)$, where y is the stoichiometric activity coefficient,[19] according to the relation

$$D = (\Omega/c)\{1 + c\,\partial \ln y/\partial c\} \quad (7)$$

Onsager and Fuoss calculated the concentration dependence of the mobility factor (Ω/c) for strong electrolytes at low concentrations, but in the absence of a similar theory for uncharged or dipolar molecules, Gordon[20] has suggested "as a possible convenient device for interpolation and extrapolation" the use of the relation

$$D = D_0\{1 + c\,\partial \ln y/\partial c\}(\eta^0/\eta) \quad (8)$$

where η^0 is the solvent viscosity, η the solution viscosity, and D_0 the value of the diffusion coefficient at infinite dilution. Recently, Gordon has suggested the pitfalls in applying this relation to other than very dilute solutions.[21] In the absence of a detailed microscopic theory, however, it serves a useful purpose in correlating the diffusion behavior of various substances.[8h]

Table IV shows the values of the thermodynamic factor $\{1 + c\,\partial \ln y/\partial c\}$ taken from the recent very accurate isopiestic vapor pressure data of R. A. Robinson,[8] together with the recent reciprocal relative viscosity factors of Mason, Kampmeyer and A. L. Robinson[10] calculated at the concentrations used in our experiments. If the Gordon relation held, the D_0 values in the final column, obtained by dividing the experimentally observed diffusion coefficients by the product of these factors, should be constant, and it is clear that the relation does not hold at high concentrations.

TABLE IV

THERMODYNAMIC AND VISCOSITY FACTORS FOR DL-α-ALANINE

Median concn., moles/l.	Thermodynamic factor $(1 + c\,\partial \ln y\,\partial c)$[a]	Reciprocal relative viscosity factors, η^0/η[b]	$D_0 \times 10^7$, cm.²/sec.
0.02798	1.00130	0.99250	91.64
.02809	1.00131	.99249	91.72
.22331	1.01208	.94378	92.51
.43736	1.02726	.89105	93.17
.67858	1.04858	.83371	94.77
.90249	1.07239	.78292	95.55
1.19480	1.10925	.72066	96.55
1.54057	1.16135	.65322	97.60

[a] $(1 + c\,\partial \ln y/\partial c) = 1 + 0.045513\,c + 0.038439\,c^2$. Calculated on molarity scale from data of R. A. Robinson.[5] [b] $(\eta/\eta^0) = 1 + 0.25327\,c + 0.060487\,c^2 - 7.85(10)^{-4}c^3$. Calculated on molarity scale from data of Mason, Kampmeyer and A. L. Robinson.[10]

An attempt is being made by Gosting[8h] to correlate the degree of failure to obey the Gordon relation with the permanent polarization of the solute molecule, and our data parallel the results of other workers studying sucrose,[22] glycine,[23] potassium chloride[7] and urea[8h] in finding that for charged or polar molecules the concentration dependence of the diffusion coefficient is described by something between the thermodynamic factor alone, and the product of thermodynamic and viscous factors.

Figure 2 shows the experimentally observed concentration dependence of the diffusion coefficient of DL-α-alanine as well as the concentration dependence predicted from the thermodynamic factor alone and from the Gordon relation. Also included are a few experimental points obtained with the D and L isomers of alanine.[18] It can be seen that these values agree with those obtained for DL-α-alanine. Comparison may be made with results of other workers for DL-α-alanine. The diaphragm cell measurements of Mehl and Schmidt[24] interpolated

(19) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, N. Y., 1943.

(20) A. R. Gordon, *J. Chem. Phys.*, **5**, 523 (1937).

(21) A. R. Gordon, THIS JOURNAL, **72**, 4840 (1950).

(22) L. J. Gosting and M. S. Morris, *ibid.*, **71**, 1998 (1949); A. C. English and M. Dole, *ibid.*, **72**, 3261 (1950).

(23) M. S. Lyons and J. V. Thomas, *ibid.*, **72**, 4506 (1950).

(24) J. W. Mehl and C. L. A. Schmidt, *Univ. Calif. Pub. Physiology*, **8**, No. 13, 165 (1937).

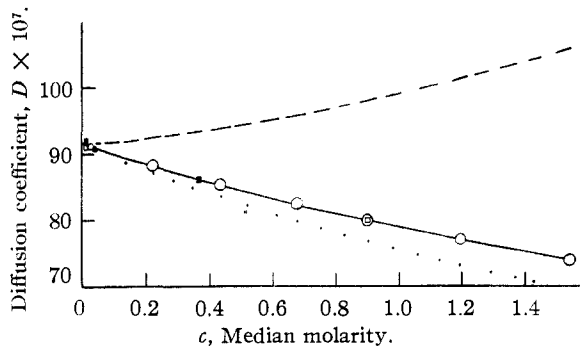

Fig. 2.—Concentration dependence of the diffusion coefficient: O, D,L-α-alanine, Gouy method, this study; □, L-α-alanine, Gouy method, this study; ■, D-α-alanine, Gouy method, this study; ▲, D,L-α-alanine, L. G. Longsworth, Rayleigh fringes; —, exptl. least square; – – – –, $D_0[1 + c\,\partial \ln y/\partial c]$; ..... $D_0\,[1 + c\,\partial \ln y/\partial c][\eta^0/\eta]$; $D_0 = 91.460 \times 10^{-7}$ (extrapolated).

to 25° are about 12% lower than ours, even after correcting their cell calibration by adjusting their 25° value for sucrose to the value obtained at the same median concentration by Gosting and Morris. The values of Polson[25] at 20° using the Lamm scale method[26] have been extrapolated to 25° using the relation $D\eta^0/T$ = const. and appear to lie a few per cent. above ours. Included in Fig. 2 is one unpublished value of Longsworth,[27] employing the vertical axis cylindrical lens type of Rayleigh interferometer,[28] in which his experimental diffusion coefficient value at 0.3166% DL-α-alanine (corrected to vacuum standard) is 9.090×10^{-6} cm.²/sec. while that calculated from our results at the same concentration using equation (5) is 9.094×10^{-6} cm.²/sec. This excellent agreement lends further confidence in the correctness of these two interference optical methods, and makes additional comparisons between them of great interest.

(25) A. G. Polson, *Biochem. J.*, **31**, 1903 (1937).
(26) O. Lamm, *Nova Acta Soc. Sci. Upsal.*, **10**, No. 6 (1937).
(27) L. G. Longsworth, private communication.
(28) H. Svensson, *Acta Chem. Scand.*, **5**, 72, 1410 (1951); G. Kegeles and H. A. Sober, *Anal. Chem.*, **24**, 654 (1952); L. G. Longsworth, THIS JOURNAL, **74**, 4155 (1952).

BETHESDA, MARYLAND
WORCESTER, MASS.

[CONTRIBUTION NO. 1157 FROM THE DEPARTMENT OF CHEMISTRY OF YALE UNIVERSITY]

A Study of the Diffusion of *n*-Butyl Alcohol in Water Using the Gouy Interference Method

BY PHILIP A. LYONS AND C. LENNART SANDQUIST

RECEIVED APRIL 10, 1953

The diffusion coefficients, densities, viscosities and specific refractive increments for solutions of *n*-butyl alcohol in water at 1 and 25° have been determined. A limiting form for expressing the diffusion coefficient as a function of concentration in relatively dilute solutions has been suggested. The temperature and concentration dependence of the diffusion coefficient and of the relative viscosity for this system are consistent with the point of view that systems with large, positive deviations from Raoult's law will have abnormally high diffusion mobilities and relative viscosities.

Precise determinations of diffusion coefficients in solutions are now possible as a result of the development of interference methods.[1-3] Using one of these methods, investigations have been made on the concentration dependence of the diffusion coefficients in dilute solutions of some non-electrolytes in water.[4-6] Among other results this work has defined the experimental limitation on the use of the change of the macroscopic relative viscosity as a measure of the change in the relative diffusion mobility. The formal limitations on this device have also been clearly outlined.[7] For the particular class of systems which exhibits large, positive deviations from Raoult's law, it has been suggested that high diffusion mobilities might be expected.[8]

Solutions of *n*-butyl alcohol and water do show large, positive deviation from Raoult's law (there is a separation of phases before the *n*-butyl alcohol concentration reaches one molar). It was the purpose of this work to see if these large deviations are reflected in the concentration and temperature dependence of the diffusion coefficients.

(1) L. G. Longsworth, THIS JOURNAL, **69**, 2510 (1947).
(2) G. Kegeles and L. J. Gosting, *ibid.*, **69**, 2516 (1947).
(3) L. G. Longsworth, *ibid.*, **74**, 4155 (1952).
(4) L. J. Gosting and M. S. Morris, *ibid.*, **71**, 1998 (1949).
(5) M. S. Lyons and J. V. Thomas, *ibid.*, **72**, 4506 (1950).
(6) L. J. Gosting and D. F. Akeley, *ibid.*, **74**, 2058 (1952).
(7) A. R. Gordon, *ibid.*, **72**, 4840 (1950).
(8) L. Onsager, *Ann. N. Y. Acad. Sci.*, **46**, 241 (1945).

Experimental Procedure

Preparation of Solutions.—Baker's C.P. *n*-butyl alcohol was dried by shaking with anhydrous $CaSO_4$ before purification. After fractionation the center cut was stored over 6-mesh anhydrous $CaSO_4$ until use. The solutions were prepared by weighing the alcohol and adding directly into calibrated volumetric flasks. Concentrations were known to about ±0.05%.

Densities and Viscosities.—Densities were determined at 1 and 25° using a twin-armed pycnometer of about a 20-ml. capacity.[9]

Flow times in an Ostwald viscometer were obtained to estimate the relative viscosities of the solutions used. All the viscosity data were corrected for kinetic energy losses.

Diffusion Data.—The equipment used to make the measurements reported is, with minor differences, the same as that already described.[10] The cell and photographic plate masking procedure of Gosting has been used.[11]

The mercury green line (5460.7 Å.) was used to produce the Gouy pattern. A Tiselius cell whose "*a*" distance, as measured by the bar and microscope method,[12] was 2.482$_7$ cm. at 25°, was used as a diffusion cell. Bath temperatures were 1 ± 0.01° and 25 ± 0.01°. The relay at 1° con-

(9) T. Shedlovsky and A. S. Brown, THIS JOURNAL, **56**, 1066 (1934).
(10) L. J. Gosting, E. M. Hanson, G. Kegeles and M. S. Morris, *Rev. Sci. Instruments*, **20**, 209 (1949).
(11) L. J. Gosting, THIS JOURNAL, **72**, 4418 (1950).
(12) L. G. Longsworth, *Ind. Eng. Chem., Anal. Ed.*, **18**, 219 (1946).