[CONTRIBUTION OF THE DEPARTMENT OF CHEMISTRY OF CLARK UNIVERSITY]

The Properties of Tetraethylammonium and Tetra-*n*-butylammonium Picrates in Anisole–Nitrobenzene Solutions[1]

BY ARNET L. POWELL[2] AND ARTHUR E. MARTELL

RECEIVED JULY 27, 1956

The effect of dielectric constant on ion association of tetraethylammonium and tetra-*n*-butylammonium picrates in mixtures of anisole (dielectric constant = 4.30) and nitrobenzene (dielectric constant = 34.9) was investigated by electrical conductance measurements. The experimental data were extrapolated to give limiting equivalent conductances and dissociation constants for a series of solvents which varied in composition from pure nitrobenzene to pure anisole. For each electrolyte, increasing steepness of the conductance curves, as anisole was added to nitrobenzene, indicated increasing formation of ion pairs. The distance of closest approach, "*a*," computed from the Bjerrum theory, varied with composition of mixed solvent, whereas application of the Sadek–Fuoss model resulted in an approximately constant value of "*a*" for each electrolyte. Insertion of the ion size, thus determined, in the Sadek–Fuoss equation gave a reaonably good reproduction of dissociation constant values as a function of dielectric constant. Variation of ion association with dielectric constant for the systems studied is similar to that reported by Fuoss and Kraus for tetraisoamylammonium nitrate in dioxane–water mixtures. The results of this research indicate that ion association is influenced by solvation as well as by ion constitution and dielectric constant.

Fuoss and co-workers[3–8] have conducted a series of investigations of electrolye–solvent interactions, using the single electrolyte, tetrabutylammonium bromide, in a variety of solvent mixtures. They found that the Bjerrum model was not satisfactory for all systems investigated, the values of the ion size "*a*" calculated from dissociation constants varying with composition of the solvent mixtures. In a number of cases, changes in ion association, observed for intermediate solvent compositions, were attributed to specific electrolyte–solvent interactions.

In this investigation, two quaternary ammonium salts—tetraethylammonium picrate and tetra-*n*-butylammonium picrate—are studied in mixtures of anisole and nitrobenzene. By variation of the solvent composition over the whole range, a variation of dielectric constant from 34.9 to 4.3 is possible. This combination of solvents offers the additional advantage of providing an opportunity of studying the effect of dielectric constant on solution conductance in a non-aqueous aprotic solvent relatively free of solute–solvent and solvent–solvent interactions. A study of conductance and ion association in such a medium would be of interest for comparison with the results of Fuoss and Kraus[9] for tetraisoamylammonium nitrate in dioxane–water mixtures.

Experimental

Apparatus.—The conductance bridge employed was a modification[10] of the design described by Foy and Martell.[11] A 0-20,000 cycle audio oscillator (General Radio No. 913-G) was used in all measurements. Temperature of the conductance cell was maintained at 25° within ±0.003° by means of a thermostatically-controlled constant-temperature oil-bath. Measurement and bath control were aided by dehumidification and regulation of room temperature in the range of 21–22°. The conductance cell was designed according to the specifications of Kraus and Fuoss,[12] and the cell constant was determined by measurement of the conductances of tetraethylammonium and tetra-*n*-propylammonium picrates in ethylene chloride, taking as standard the measurements of Tucker and Kraus.[13] The value thus determined was 0.03410. A redetermination, made after reconstruction of the cell, yielded the value 0.04163. The latter constant was used for all measurements made with tetra-*n*-butylammonium picrate.

Solvents.—Nitrobenzene and anisole were purified by vacuum distillation, using a modification of the method of Witschonke and Kraus.[14] An all-glass apparatus with ground glass joints was used with a distilling column designed to suppress entrainment. The solvent was refluxed 4-6 hours over activated alumina pellets and distilled slowly. Middle fractions were used for the conductance measurements. The best anisole obtained by this procedure had a specific conductance of about 7 × 10^{-11} mho, and the best nitrobenzene about 5 × 10^{-10} mho. Neither solvent was used for conductance measurements unless the specific conductance was less than 1 × 10^{-9} mho. The ethylene chloride used for cell calibration was purified as described by Healey and Martell[15] for ethylidene chloride. As checks on the purity of the solvents, the refractive indices at 20° were determined for ethylene chloride, anisole and nitrobenzene and the freezing point of the latter was measured. The results are summarized as follows

Solvent	$n^{20}\text{D}$ Measured	Lit.	F. p., °C. Measured	Lit.
Anisole	1.5170	1.5170[16]		
Ethylene chloride	1.4444	1.4443[17]		
Nitrobenzene	1.5524	1.5529[18]	5.82	5.72[19]
				5.50–5.85[20]

Measurements.—Densities of the solvents and solvent mixtures were determined in a 5-ml. pycnometer at 25 ± 0.01°. Doubly distilled water was used as the calibrating liquid. In the case of nitrobenzene, the best literature value of the density, 1.1987 g./ml.,[21] was used in the calculations in place of the measured value, 1.1983 g./ml. For anisole, the measured density, 0.9888 g./ml., was employed; Bien, Kraus and Fuoss[22] reported that the density of anisole at

---

[1] Abstracted from a Dissertation submitted by Arnet L. Powell to the Faculty of Clark University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1956.

[2] Office of Naval Research, Boston, Mass.

[3] H. Sadek and R. M. Fuoss, THIS JOURNAL, **72**, 301 (1950).

[4] R. C. Miller and R. M. Fuoss, *ibid.*, **75**, 3076 (1953).

[5] F. M. Sacks and R. M. Fuoss, *ibid.*, **75**, 5172 (1953).

[6] H. Sadek and R. M. Fuoss, *ibid.*, **76**, 5897 (1954).

[7] H. Sadek and R. M. Fuoss, *ibid.*, **76**, 5902 (1954).

[8] H. Sadek and R. M. Fuoss, *ibid.*, **76**, 5905 (1954).

[9] R. M. Fuoss and C. A. Kraus, *ibid.*, **55**, 1019 (1933).

[10] K. H. Stern, Ph.D. Dissertation, Clark University, 1953.

[11] W. L. Foy and A. E. Martell, *Rev. Sci. Instr.*, **19**, 628 (1948).

[12] C. A. Kraus and R. M. Fuoss, THIS JOURNAL, **55**, 21 (1933).

[13] L. M. Tucker and C. A. Kraus, *ibid.*, **69**, 454 (1947).

[14] C. R. Witschonke and C. A. Kraus, *ibid.*, **69**, 2472 (1947).

[15] F. H. Healey and A. E. Martell, *ibid.*, **73**, 3296 (1951).

[16] "International Critical Tables." Vol. I, McGraw-Hill Book Co. Inc., New York, N. Y., 1926, p. 277.

[17] Ref. 16, p. 34.

[18] Ref. 16, p. 38.

[19] R. E. Van Dyke and C. A. Kraus, THIS JOURNAL, **71**, 2694 (1949).

[20] Landolt-Bornstein, "Physikalisch-Chemische Tabellen," 5th ed., Julius Springer, Berlin, 1935, 3rd supplement, p. 342.

[21] P. Walden and E. J. Birr, *Z. physik. Chem.*, **163A**, 281 (1932).

[22] G. S. Bien, C. A. Kraus and R. M. Fuoss, THIS JOURNAL, **56**, 1860 (1934).

25° is 0.9890 g./ml. The viscosities of the two solvents and a series of intermediate mixtures were measured in an Ostwald viscosimeter at 25 ± 0.01°, using doubly distilled water as a standard. Dielectric constants of anisole, nitrobenzene and mixtures of intermediate compositions were measured at Brown University through the courtesy of Professor Robert H. Cole. The measured values of the dielectric constant for anisole (4.302) and for nitrobenzene (34.91) agree well with National Bureau of Standards measurements (D of anisole = 4.33, D of nitrobenzene = 34.82).[23] The salts used had been prepared by previous workers.[10,15] Melting points were in good agreement with the literature. The procedure used for the conductance measurements was similar to that described by Healey and Martell.[15]

Results

The results of the density, viscosity and dielectric constant measurements are given in Table I.

TABLE I

PROPERTIES OF ANISOLE-NITROBENZENE MIXTURES AT 25°

Nitrobenzene, wt. %	Nitrobenzene, mole fraction	Density, g./ml.	Viscosity, poise	Dielectric constant
0.00	0.0000	0.9888	0.01008	4.30
8.30	.0736	1.0032	.01040	5.82
19.81	.1783	1.0240	.01091	8.00
29.20	.2659	1.0418	.01145	10.04
33.34	.3052	1.0502	.01170	11.02
40.61	.3752	1.0664	.01219	12.80
42.93	.3978	1.0709	.01234	13.43
49.59	.4635	1.0842	.01279	15.27
56.85	.5364	1.0981	.01330	17.55
69.72	.6691	1.1266	.01434	21.77
80.92	.7884	1.1526	.01546	26.00
88.95	.8760	1.1710	.01646	29.59
100.00	1.0000	1.1987	.01823	34.91

The conductance data are summarized in Table II, where Λ is equivalent conductance and c is concentration in equivalents per liter. The various systems are identified by the weight % nitrobenzene above each set of data. All the solutions were sufficiently dilute so that their densities could be taken as that of the solvent without incurring appreciable error. Corrections for solvent conductance were negligible even in the most dilute solutions.

Discussion

In order to eliminate the effects of changing viscosity from mixture to mixture so that attention could be directed to the effect of variation in dielectric constant, the conductances in Table II were divided by the appropriate values of Λ_0, and Λ/Λ_0 was plotted against the square root of concentration.[6] The results are illustrated in Figs. 1 and 2.

To avoid crowding in these graphs, the curves for the 100% anisole and for the 88.95% nitrobenzene-11.05% anisole mixture in the tetraethylammonium picrate series and the curve for the 93.38% nitrobenzene-6.62% anisole mixture in the tetra-*n*-butylammonium picrate series were omitted. The limiting tangent determined from the Onsager equation is shown on each figure. As anisole is added to nitrobenzene, the dielectric constant of the mixture decreases, and an increase in ion association at a given concentration is observed (Figs. 1 and 2). In nitrobenzene, the curves are approximately straight lines and lie only a little below the limiting tangent. As the anisole content of the mixture is increased, the curves become progressively steeper at a given concentration.

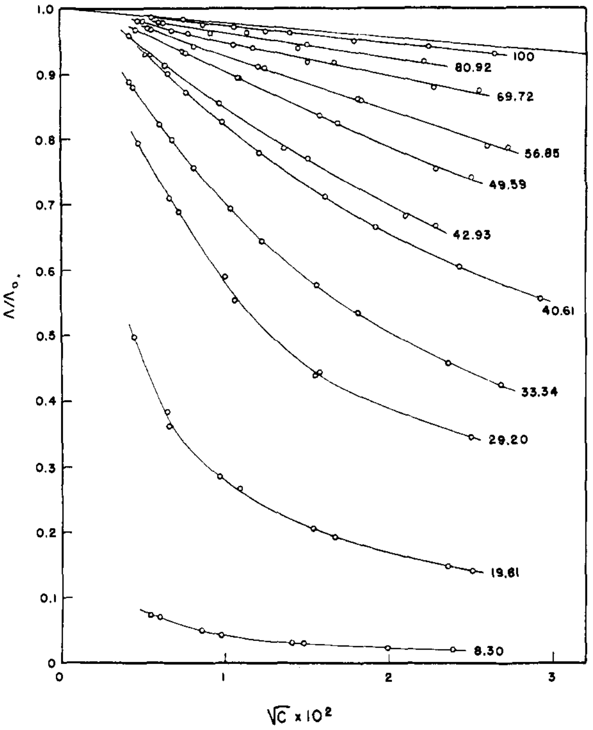

Fig. 1.—Reduced conductance curves: tetraethylammonium picrate in anisole-nitrobenzene mixtures. Figures to right of curves are weight % nitrobenzene.

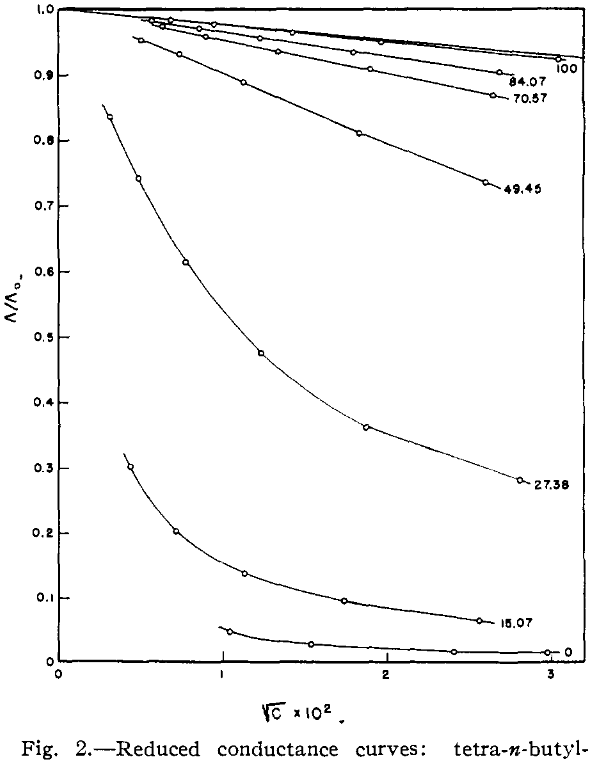

Fig. 2.—Reduced conductance curves: tetra-*n*-butylammonium picrate in anisole-nitrobenzene mixtures. Figures to right of curves are weight % nitrobenzene.

---

[23] Natl. Bur. Standards Circular No. 514, 1951, pp. 18, 23.

TABLE II

CONDUCTANCE OF QUATERNARY AMMONIUM PICRATES IN ANISOLE–NITROBENZENE MIXTURES AT 25°

A. Tetraethylammonium Picrate Series

$c \times 10^4$	Λ
0.00	
20.91	0.06675
12.78	.07275
7.839	.08374
4.521	.1025
2.699	.1219
8.30	
5.718	1.123
3.972	1.309
2.189	1.706
1.982	1.783
0.9546	2.511
.7406	2.802
.3530	4.008
.3052	4.215
19.81	
6.296	7.683
5.587	8.024
2.792	10.53
2.375	11.21
1.195	14.55
29.20	
6.263	18.06
6.194	18.09
2.496	23.42
1.063	28.86
1.006	30.82
0.5082	35.94
.4384	37.01
.2220	41.40
.1083	45.29
33.34	
7.176	21.57
5.596	23.18
3.288	27.15
2.442	29.29
1.499	32.61
1.051	35.14
0.6580	38.30
0.4584	40.49
.3640	41.71
.1945	44.64
.1729	45.13
.08464	47.62
40.61	
8.578	27.22
5.907	29.62
3.683	32.58
2.578	34.81
1.463	38.15
0.9642	40.46
.7628	42.68
.3981	44.07
.2580	45.53
42.93	
5.203	32.08
4.417	32.78
2.270	36.88
1.857	37.72
0.9286	41.05
.3938	43.83
.2905	44.60
.1767	46.08
.1135	46.58
49.59	
6.310	33.97
5.254	34.55
2.847	37.78
2.487	38.31
1.154	40.99
0.5736	42.75
.5496	42.92
.2141	44.37
56.85	
7.429	34.78
6.753	34.93
3.344	38.06
3.267	38.11
1.525	39.88
1.439	40.24
0.6537	41.71
.3018	42.89
.2816	42.90
69.72	
6.505	35.67
5.043	35.78
2.762	37.42
1.374	38.37
1.096	38.56
0.6111	39.32
.4632	39.38
.2641	40.06
.2230	40.09
80.92	
4.882	34.59
2.246	35.58
2.094	35.34
0.8901	36.28
.8496	36.20
.3906	36.83
.3679	36.92
.1733	37.41
.1532	37.60
88.95	
6.381	32.48
4.968	32.72
2.788	33.41
1.165	34.01
0.4967	34.61
0.2341	34.97
100.00	
6.941	29.91
5.028	30.36
3.214	30.56
1.955	31.00
1.559	31.06
1.118	31.33
0.7551	31.39
.5595	31.68
.3125	31.73

B. Tetra-*n*-butylammonium picrate series

0.00	
14.35	0.05606
8.838	.06567
5.772	.07698
15.07	
6.559	3.232
3.017	4.453
1.285	6.398
0.5143	9.413
.1917	14.05
27.38	
7.890	12.42
3.509	16.19
1.533	20.99
0.5886	27.15
.2352	32.79
.1010	36.97
49.45	
6.785	28.23
3.357	31.13
1.279	34.08
0.5484	35.83
.2556	36.61
.1158	37.49
70.57	
7.014	29.76
3.611	31.15
1.804	32.06
0.8095	32.87
.4010	33.35
84.07	
7.216	28.44
3.251	29.38
1.498	30.05
0.7360	30.50
.3194	30.91
93.38	
7.608	26.37
2.793	27.17
1.194	27.57
0.5442	28.16
.2251	28.55
100.00	
17.65	25.05
9.321	25.82
3.860	26.56
2.022	26.97
0.9015	27.39
.4603	27.55

The conductance data for solutions of both picrates in the solvent mixtures with $D \geqq 10$ were extrapolated by use of the Shedlovsky equation[24,25] to obtain limiting conductances and dissociation constants. The values obtained are given in Table III.

The values of Λ for anisole and for the solvent mixtures with $D < 10$ were approximated by use of Walden's rule.[26] The Walden products were computed for each quaternary ammonium picrate for all solvent mixtures with $D > 10$ and plotted *versus* mole fraction nitrobenzene.

Since approximately linear relationships were obtained for each picrate, it was possible to approximate Walden products for mixtures with lower dielectric constants by extrapolation. From these, Λ_0 was calculated for each solution by dividing by the appropriate viscosity. The values of the dissociation constant K were determined by application of the Ostwald dilution law.[9,27] The values of Λ_0 and K determined in this way are included in Table III as are Walden products $\Lambda_0\eta_0$ for all solvents and solvent mixtures investigated.

The free energy of dissociation for each solution of each picrate was computed from

$$\Delta E = 2.303RT \log K$$

The results, which are given in Table III, tend to approach the thermal energy of the solvent molecules ($\Delta E = RT = 596$ cal.) as the dielectric constant increases. The dielectric constant at the point of closest approach represents the critical value, and is in both cases beyond the highest dielec-

---

[24] T. Shedlovsky, *J. Franklin Inst.*, **225**, 739 (1938).

[25] R. M. Fuoss and T. Shedlovsky, THIS JOURNAL, **71**, 1496 (1949).

[26] C. Walden, *Z. physik. Chem.*, **55**, 207 (1906).

[27] P. A. Kraus and W. C. Bray, THIS JOURNAL, **35**, 1315 (1913).

TABLE III

PROPERTIES DERIVED FROM CONDUCTANCE DATA FOR NITROBENZENE–ANISOLE MIXTURES AT 25°

Nitrobenzene, mole fraction	Λ_0	$\Lambda_0\eta_0$	K	log D	−log K (exptl.)	−log K (calcd.)	ΔE, cal.	$a \times 10^8$, cm.
			A. Tetraethylammonium picrate					
0.0000	59.62[a]	0.6010[a]	9.40×10^{-10}	0.6335	9.025	9.025	12300	5.55
.0736	57.70[a]	.6000[a]	1.80×10^{-7}	.7649	6.745	6.530	9200	5.29
.1783	54.54[a]	.5950[a]	1.12×10^{-5}	.9031	4.951	4.947	6760	5.23
.2659	52.19	.5976	6.50×10^{-5}	1.002	4.187	4.094	5710	4.72
.3052	50.71	.5933	1.44×10^{-4}	1.042	3.842	3.820	5240	4.67
.3752	48.97	.5969	3.98×10^{-4}	1.107	3.400	3.432	4640	4.51
.3978	48.00	.5923	5.51×10^{-4}	1.128	3.259	3.315	4450	4.49
.4635	45.83	.5862	1.23×10^{-3}	1.184	2.910	3.025	3970	4.45
.5364	44.21	.5893	2.38×10^{-3}	1.244	2.623	2.745	3580	4.22
.6691	40.78	.5848	5.90×10^{-3}	1.338	2.229	2.313	3040	3.78
.7884	37.61	.5814	1.05×10^{-2}	1.415	1.979	1.956	2700	3.23
.8760	35.34	.5817	1.58×10^{-2}	1.471	1.801	1.690	2460	2.87
1.0000	32.15	.5861	3.02×10^{-2}	1.543	1.520	1.326	2070	2.65
			B. Tetra-*n*-butylammonium picrate					
0.0000	49.60[a]	0.5000[a]	1.09×10^{-9}	0.6335	8.963	8.705	12200	5.59
.1349	46.52[a]	.4970[a]	2.65×10^{-6}	0.8476	5.583	5.402	7620	5.31
.2487	44.21	.5009	4.92×10^{-5}	0.9827	4.308	4.095	5880	4.86
.4621	38.37	.4904	1.38×10^{-3}	1.183	2.860	2.929	3900	4.65
.6781	34.26	.4940	8.30×10^{-3}	1.344	2.081	2.183	2840	4.38
.8225	31.42	.4974	1.85×10^{-2}	1.438	1.733	1.742	2360	3.88
.9253	28.69	.4915	3.01×10^{-2}	1.501	1.521	1.433	2080	3.46
1.0000	27.97	.5099	7.67×10^{-2}	1.543	1.115	1.188	1520	4.67

[a] Estimated using Walden's rule.

tric constant available from the solvent system (D of nitrobenzene = 34.9).

The ion sizes "a" for each quaternary ammonium picrate were computed from the value of K for each solution by application of the Bjerrum equation.[28] The values of "a" for each salt thus obtained were not constant but varied with the composition of the solvent, as can be seen by referring to Table III. Hence, it was not possible to evaluate the mean ionic diameter by taking an average value, as was done by Fuoss and Kraus,[9] and the modified "sphere-in-continuum" theory of Sadek and Fuoss[8] was employed to obtain constant values of "a" for each solute. The relationship given by Sadek and Fuoss is

$$K = k_D/(1 + k_s)$$

where K is the ion-pair dissociation constant obtained by extrapolating the conductance data, K_D is the solvated ion pair dissociation constant calculated from the Bjerrum equation, and k_s is an empirically-derived "solvation constant" for the expulsion of the intervening solvent from an incipient ion pair. By the use of this method, "a" for tetraethylammonium picrate was found to be 5.8×10^{-8} cm., and for tetra-*n*-butylammonium picrate, 6.0×10^{-8} cm. The computed dissociation constants agree reasonably well with the experimentally-determined values, as can be seen by comparison of the −log K (exptl.) and −log K (calcd.) values in Table III. For both picrates, the average difference between the calculated and experimental values of −log K is 3.4%.

The values of the dielectric constant for each solute–solvent system corresponding to $K = 1$ and $K = \infty$ (complete dissociation) were computed from the Bjerrum theory. The values for tetraethylammonium picrate in anisole–nitrobenzene mixtures were 44 and 48, respectively; for tetra-*n*-butylammonium picrate, the corresponding values were 43 and 47.

The negative logarithms of the dissociation constants for all solutions of both quaternary ammonium salts are plotted against the logarithm of the dielectric constant in Fig. 3; the curve obtained by Fuoss and Kraus[9] for tetraisoamylammonium nitrate in dioxane–water mixtures is included for comparison (their points for solvent mixtures below D = 3.48 are omitted). Examination of the curves in Fig. 3 indicates that the two picrates investigated in the non-aqueous, aprotonic media generally exhibit the same behavior relative to changing dielectric constant as tetraisoamylammonium nitrate in the dioxane–water mixtures. Dissociation constants for the same dielectric constant are appreciably higher in the aqueous than in the non-aqueous system, an effect which probably can be ascribed to differences in the size and constitution of the ions of the electrolytes involved and to variations in solvation in the two systems. The greater dissociation observed for tetra-*n*-butylammonium picrate over that of tetraethylammonium picrate in anisole–nitrobenzene mixtures is in accord with the larger size of the former cation, the greater distance between the centers of positive and negative charge resulting in a decrease in attractive force. The values of Λ_0 for these two salts in nitrobenzene are in good agreement with the results of Taylor and Kraus.[29]

The values of the dielectric constant for $K = 1$

---

[28] N. Bjerrum, *Kgl. Danske Vidensk. Selskab, Mat.-Phys. Medd.*, **7**, No. 9 (1926).

[29] E. G. Taylor and C. A. Kraus, THIS JOURNAL, **69**, 1731 (1947).

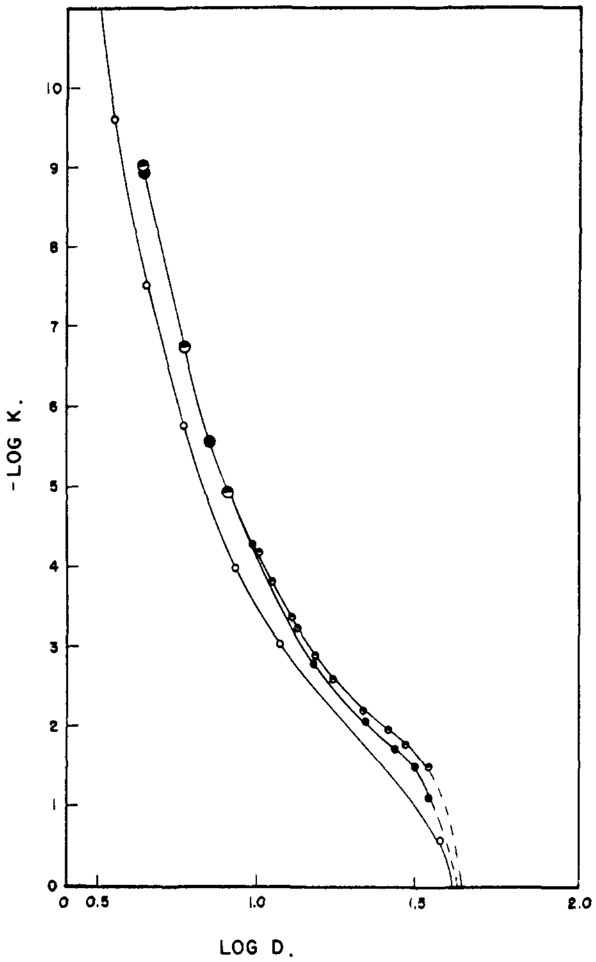

Fig. 3.—Effect of dielectric constant on dissociation of electrolytes in mixed solvents: ◓, tetraethylammonium picrate in anisole–nitrobenzene mixtures; ●, tetra-*n*-butylammonium picrate in anisole–nitrobenzene mixtures; ○, tetraisoamylammonium nitrate in dioxane–water mixtures.

for each quaternary ammonium picrate in the anisole–nitrobenzene solvent system calculated using the "*a*" values derived from the Sadek–Fuoss model[8] appear to be reasonably close to the results which would be obtained by extrapolating the $-\log K$ *vs.* $\log D$ curves. In any event, these D values and the corresponding critical dielectric constants are only approximate, being limited by the uncertainties in the larger values of K as well as the validity of the assumptions underlying the Sadek–Fuoss model. Fuoss[6,8] and Kraus[30,31] have pointed out that reliable values of dissociation constants from conductance measurements cannot be obtained for $K > 0.01$ because of uncertainties in the magnitudes of the c and $c \log c$ terms in the Onsager equation.

Densities and molar volumes of the solvent mixtures change smoothly from anisole to nitrobenzene, and deviations from volume additivity are small, the maximum being about 0.16%. The values of dielectric constant also vary smoothly with composition of the solvent mixtures. The viscosities of the solvent mixtures change continuously from the less viscous anisole to nitrobenzene and the curve shows little structure. There is no evidence of specific interactions leading to sharp changes in ion association at intermediate solvent composition of the type observed by Fuoss, *et al.*,[3–8] and by Kortum and co-workers.[32,33] Since the conductance–viscosity products are approximately constant for both systems investigated (Table III), it could be expected that Stokes' law would hold and that, at least hydrodynamically, the "sphere-in-continuum" model would be a good representation of the physical facts. Constancy of the Walden products requires that the effective ionic volumes should be constant: that is, the ion size "*a*" should not change for that particular system. However, the values of "*a*" calculated from the experimentally determined dissociation constants are not the same but vary continuously, decreasing with increasing nitrobenzene content.

There are two possible explanations which may be advanced to account for this situation. The first of these is that a solvation effect is involved. The observed increase of effective ion size with rising anisole content is consistent with an increase in solvation. Kraus[34] has shown that even large ions, such as quaternary ammonium ions, show specific differences in going from solvent to solvent and that frequently Stokes' law does not apply. Fuoss[8] has raised a possible objection to an explanation on a solvation basis in that this would require that the solvate shall remain intact in the ion pair. Regardless of the validity of this argument, the constancy of the $\Lambda_0\eta_0$ values for the systems investigated indicated that approximately constant ion sizes were to be expected.

The second explanation involves the assumption that the Bjerrum model does not apply to this system. When an anion and a cation are separated by appreciable distances, it seems reasonable to assume that the macroscopic dielectric constant of the medium is a good approximation for calculating the potential energy of the two ions approaching to form a pair. However, upon closer approach of the two ions, it is likely that such an approximation can no longer hold since the solvent molecules will be polarized by the intense electric fields of the ions. The Sadek–Fuoss model is an attempt, on an empirical basis, to solve this problem. It apparently works very well for tetrabutylammonium bromide in nitrobenzene–carbon tetrachloride mixtures[8] and reasonably well in this case for tetraethylammonium picrate and tetra-*n*-butylammonium picrate in anisole–nitrobenzene mixtures.

The results of this research confirm Kraus'[31] conclusion that the variation in ion size with changing dielectric constant cannot be attributed to experimental error. It is much more likely that the mean diameter of the solvated ions cannot be expressed precisely by the Bjerrum theory, and that some additional concept is required for the interpretation of experimentally-derived ion-pair dis-

---

(30) C. A. Kraus, *J. Phys. Chem.*, **58**, 673 (1954).

(31) C. A. Kraus, *ibid.*, **60**, 129 (1956).

(32) G. Kortum, S. D. Gorkhale and H. Wilski, *Z. physik. Chem.*, *Neue Folge*, **4**, 286 (1955).

(33) G. Kortum and H. Wilski, *ibid.*, **5**, 333 (1955).

(34) C. A. Kraus, *Ann. N. Y. Acad. Sci.*, **51**, 789 (1949).

sociation constants. Indeed, Azzari and Kraus[35] have shown recently that the Bjerrum equation fails completely in solutions of higher dielectric constant.

Acknowledgments.—The authors are indebted to Dr. C. A. Kraus of Brown University for suggesting this research topic and for valuable discussions and advice. Thanks are also due to Professor Robert H. Cole of Brown University for the use of his apparatus to measure dielectric constants of the solvent mixtures. Appreciation is expressed for solvents to The Dow Chemical Company for ethylene chloride, and the Calco Chemical Company for nitrobenzene.

WORCESTER, MASS.

[35] M. Azzari and C. A. Kraus, *Proc. Natl. Acad. Sci.*, **42**, 590 (1956).

[CONTRIBUTION FROM THE BIOLOGICAL LABORATORIES, HARVARD UNIVERSITY, AND THE DEPARTMENT OF BIOLOGICAL CHEMISTRY, HARVARD MEDICAL SCHOOL]

The Association of 4-Methylimidazole with the Ions of Cupric Copper and Zinc; with Some Observations on 2,4-Dimethylimidazole

BY YASUHIKO NOZAKI,[1] FRANK R. N. GURD, RAYMOND F. CHEN AND JOHN T. EDSALL[2,3]

RECEIVED DECEMBER 7, 1956

The 4-methyl and the 2,4-dimethyl derivatives of imidazole have been studied in their interactions with hydrogen, cupric and zinc ions, at different temperatures. The *p*H titrations, in the absence of Cu or Zn ions, gave pK' values which were extrapolated to zero ionic strength. Heats of reaction and standard entropies associated with these pK values were also determined. (ΔH° is in the range 8.5 ± 0.7 kcal./mole and ΔS° in the range -6.5 ± 0.8 cal. deg.$^{-1}$ mole^{-1}.) Similar titrations, in the presence of Cu(II) and Zn(II), showed that the number of molecules of both imidazole derivatives, bound to either of these ions, approached an upper limit of 4, at high imidazole concentrations. This number is the same as for unsubstituted imidazole. The intrinsic association constants log $\kappa_i (i = 1,2,3,4)$ at 25° were found for 4-methylimidazole to be 3.53, 3.31, 3.05 and 2.56, respectively, for combination with Cu(II), and 1.84, 2.35, 2.82 and 2.98 for combination with Zn(II). Approximate values for ΔH° in the combination of 4-methylimidazole with these ions have been estimated. Incomplete studies on the binding of 2,4-dimethylimidazole to copper indicated association constants of the same order of magnitude, but somewhat smaller, than those for 4-methylimidazole. A discussion is given of the stereochemistry of the copper and zinc complexes, and of some of the structural implications of the observed association constants.

The reactivity of the imidazole group of the histidyl residue in proteins has assumed great importance for the understanding of interactions between proteins and several metallic ions.[4–6] A previous report described the application of a method suggested by Scatchard to the interpretation of the equilibria between the parent imidazole and Cu(II) and Zn(II) ions.[7] A similar study has now been made of the corresponding equilibria of the 4-methyl derivative of imidazole, chosen because it is substituted in the same position as the imidazole ring in the histidyl residue, and thus represents a step toward the study of the metal-binding behavior of the histidyl residue in peptide chains. A fragmentary study has also been made of 2,4-dimethylimidazole, in order to determine whether the additional methyl group, attached to the carbon atom between the two nitrogens of the imidazole ring, would significantly alter the binding of the imidazole molecule to the metallic ions.

Materials and Methods

4-Methylimidazole was prepared as the crystalline salt, 4-methylimidazolium nitrate, by a modification of the method of Weidenhagen and Herrmann.[8] The free base was prepared, in the manner described by them, from acetol acetate, aqueous ammonia and formaldehyde in the presence of cupric acetate. The resulting copper complex of 4-methylimidazole was decomposed, and the copper precipitated as sulfide, by treatment with hydrogen sulfide at 50°. After removal of the precipitate, and cooling, dilute nitric acid was added cautiously to the solution, with constant stirring, until a *p*H between 2 and 3 was attained. (Further addition of nitric acid decreases both the yield and the purity of the product.) The solution was concentrated by evaporation to a small volume, *in vacuo* at 45–55°, filtered with charcoal and dried in a desiccator. The resulting crude product was recrystallized two or three times from acetone. The material was colorless and melted at 110.5–111.5°. Dedichen[9] reported a melting point of 110°. The purity of the material obtained by us was confirmed also by the constancy of the value of pK' obtained in the *p*H titrations (see below) for widely varying ratios of the concentration of free base to that of the conjugate imidazolium ion.

2,4-Dimethylimidazole also was prepared by the method of Weidenhagen and Herrmann[8]; the base released on removal of Cu(I) by sulfide was converted directly to the nitrate and the product was obtained by evaporation to dryness at low temperature. Recrystallization was from acetone or acetone–ether mixtures. Thrice recrystallized 2,4-dimethylimidazolium nitrate melted at 133-134°. The purity of the product was confirmed by the *p*H titrations discussed below.

The preparation of mixtures of methylimidazolium nitrates and Cu(II) or Zn(II) nitrates and their titration with NaOH were carried out as previously described.[7] The *p*H of each mixture was determined with a Beckman

---

[1] Overseas Research Fellow, sponsored by the Japanese Government under exchange Visitor Program at Harvard University, 1954–1955.

[2] Support for this research was provided by a grant to John T. Edsall (NSF-G621) from the National Science Foundation, and by a special fellowship granted to him by the John Simon Guggenheim Memorial Foundation.

[3] Requests for reprints and inquiries concerning this paper should be addressed to Dr. J. T. Edsall, Biological Laboratories, Harvard University, Cambridge 38, Massachusetts.

[4] F. R. N. Gurd and D. S. Goodman, THIS JOURNAL, **74**, 670 (1952).

[5] C. Tanford, *ibid.*, **74**, 211 (1952).

[6] F. R. N. Gurd and P. E. Wilcox, *Advances in Protein Chem.*, 11, 311 (1956).

[7] J. T. Edsall, G. Felsenfeld, D. S. Goodman and F. R. N. Gurd, THIS JOURNAL, **76**, 3054 (1954).

[8] R. Weidenhagen and R. Herrmann, *Ber.*, **68**, 1953 (1935). See also K. Hofmann, "Imidazole and its Derivatives" Part I. Interscience Publishers, Inc., New York, N. Y., 1953, Chapter II.

[9] G. Dedichen, *Ber.*, **39**, 1831 (1906).