

105. *The Ionisation Functions of Di-isopropylcyanoacetic Acid in Relation to Hydration Equilibria and the Compensation Law.*

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Dissociation constants of di-isopropylcyanoacetic acid in aqueous solution have been measured at 5° intervals from 5 to 45° by a conductivity method of marginally improved accuracy. In combination with earlier data for cyanoacetic acid, the dependence of $\ln K$ on temperature has been examined by revised statistical methods. The results suggest that the temperature-dependence of the heat-capacity loss accompanying ionisation is different in the two cases. This inference, together with the observed effects of alkyl substitution on enthalpy and entropy of ionisation, leads to a treatment of hydrational equilibria which has a bearing on the widespread application of the Compensation Law to reactions in solution. Solute-solvent effects relevant to the extent of acidic dissociation, and to its variation with temperature, are discussed in the context of current views, and a modified treatment of the influence on the hydration of ions of steric "solvent exclusion" is proposed.

A PREVIOUS study of the thermodynamic functions of the ionisation of cyanoacetic acid in aqueous solution¹ indicated that the heat-capacity loss ($-\Delta C_P^\circ$) accompanying ionisation passes through a minimum between 25 and 30°. This behaviour was discussed in terms of the competing, incompatible ordering influences of ionic hydration and of the co-operative structure of cool liquid water. Evidence was assembled for the failure of structural co-operation in water over quite a narrow temperature range. This evidence has been supplemented^{2,3} and has a possible theoretical basis⁴ in terms of a model of the water structure consisting of hydrogen-bonded frameworks stabilised by monomeric molecules.⁵ Such a dual-structure model is supported by a recent high-resolution X-ray diffraction study of liquid water.⁶ Other theories,⁷⁻⁹ however, do not include the concept

¹ Feates and Ives, *J.*, 1956, 2798.

² Franks and Ives, *J.*, 1960, 741.

³ Franks, Gent, and Johnson, *J.*, 1963, 2716.

⁴ Frank and Quist, *J. Chem. Phys.*, 1961, **34**, 604.

⁵ Pauling, "The Nature of the Chemical Bond," 3rd edn., Oxford, 1960, p. 472.

⁶ Danford and Levy, *J. Amer. Chem. Soc.*, 1962, **84**, 3965.

⁷ Lennard-Jones and Pople, *Proc. Roy. Soc.*, 1951, *A*, **205**, 155.

⁸ Frank and Wen Yang Wen, *Discuss. Faraday Soc.*, 1957, **24**, 133.

⁹ Némethy and Scheraga, *J. Chem. Phys.*, 1962, **36**, 3382, 3401; *J. Phys. Chem.*, 1962, **66**, 1773.

of quasi-crystalline frameworks. It is contended that any theory which attributes a quasi-crystalline, structurally co-operative kind of molecular order to liquid water must allow for the occurrence of a "submerged" order-disorder transformation ("quasi-melting"), to which equilibria and processes in aqueous systems can hardly be completely indifferent. The search for effects of such a transformation therefore represents one kind of attempt to decide between theories which do, or do not, involve structural co-operation in the sense of a residual regularity of spatial geometry in the liquid state (quasi-crystallinity). The kind of co-operation intrinsic to water association, in the sense that hydrogen bonding promotes hydrogen bonding,⁸ is regarded as basic to either group of theories. There is, however, a difficulty in that no effect on the free energy functions, which are normally those most closely associated with measured quantities, is to be expected, but only, in increasing order of significance, on enthalpy (or entropy) and heat capacity and, particularly, on the dependence of the latter on temperature. The successive differentiations with respect to temperature which are involved call for very high accuracy in the original measurements if significance is not to be lost before the desired objectives are attained. It is unfortunately doubtful whether the demands have been adequately met by any electrochemical measurements; recent revision¹⁰ of some previously reported e.m.f. studies¹¹ illustrates the point.

The present work was intended to supplement the earlier investigation by using a second acid differing from the first by a factor influencing anionic hydration. Di-isopropyl substitution was chosen for this purpose because the bulky hydrocarbon groups might be expected to impose steric limitations on ionic hydration, coupled, no doubt, with other effects. Even if the net result of the substitution turned out to be quite complex, it was thought that any effect of change of water structure with temperature should be common to both the acids in aqueous solution, and should remain perceptible. The results do not confirm this view, and showed that the earlier work, although possibly not misinterpreted, was naïve in its approach, both in relation to the statistical treatment of errors, and in the discussion of the thermodynamics of ionisation. It has therefore been re-assessed by the revised methods devised for the new experiments. The combined results, although indecisive in relation to the water structure problem, lead to conclusions about hydration which are believed to be of interest and some importance in a wider field.

For the initial problem of the heat capacity of ionisation, the assessment of errors is of vital importance. The methods which have been used, under the guidance of Professor D. R. Cox, to whom the authors are greatly indebted, are of general application in situations where the significance of results depends selectively on the independent errors of more than one experimental parameter. They have not previously been applied in this field of enquiry (but cf. Please¹²), and their description is not only essential to the present account, but is considered to be a major contribution to the interest and usefulness of the work.

CALCULATIONAL METHODS AND RESULTS

The conductances of eleven very dilute aqueous solutions of di-isopropylcyanoacetic acid, determined at each of nine temperatures, are shown in Table 1.

These results have been fitted by the conductance equations¹³

$$y = \Lambda_0 - x/K \quad (1)$$

$$\text{where } y = \Lambda + aC_i^{\frac{1}{2}} \quad \text{and} \quad x = \frac{\Lambda^2 C(10^{-2}AC_i)}{\Lambda_0 - aC_i^{\frac{1}{2}}} \quad (2)$$

in which a and A are Onsager and Debye-Hückel coefficients appropriate to molar concentration C , K is the thermodynamic dissociation constant, and the other symbols have their usual

¹⁰ Gupta, Hills, and Ives, *Trans. Faraday Soc.*, 1963, **59**, 1874.

¹¹ Gupta, Hills, and Ives, *Discuss. Faraday Soc.*, 1957, **24**, 147

¹² Please, *Biochem. J.*, 1954, **56**, 196.

¹³ Ives, *J.*, 1933, 731.

TABLE I.
Equivalent conductances of di-isopropylcyanoacetic acid solutions.

10 ⁴ C (mole l. ⁻¹ at 25°)	24·8852	18·7290	15·0494	12·5803	10·5999	10·3638
Temp.						
5°	185·84	197·08	205·24	211·65	217·23	217·63
10	201·32	214·03	223·20	230·62	237·02	237·50
15	215·74	229·93	240·27	248·57	255·82	256·46
20	229·02	244·71	256·26	265·49	273·65	274·34
25	241·17	258·32	271·02	281·24	290·31	291·09
30	252·16	270·78	284·65	295·85	305·87	306·75
35	261·92	281·95	296·97	309·17	320·12	321·13
40	270·50	291·91	308·04	321·23	333·14	334·23
45	277·89	300·60	317·81	331·96	344·78	346·01
10 ⁴ C (mole l. ⁻¹ at 25°)	6·82409	5·59758	3·91818	2·16388	2·10185	
Temp.						
5°	229·76	234·68	241·81	250·20	250·81	
10	251·49	257·17	265·62	275·56	276·28	
15	272·43	278·98	288·79	300·47	301·27	
20	292·41	299·89	311·17	324·77	325·62	
25	311·36	319·82	332·65	348·34	349·28	
30	329·29	338·78	353·28	371·25	372·35	
35	345·97	356·50	372·81	393·22	394·44	
40	361·36	373·06	391·22	414·23	415·59	
45	375·57	388·30	408·39	434·18	435·65	

significance. In each case, the fitting was carried out by the iterative least-squares procedure previously described,¹³ with use of the same fundamental constants and data as in recent work of this kind.^{1,14} The 99 residuals, Δy , were tabulated and inspected with particular reference to their distributions along the sequences of x at constant T , and of T at constant x . At each value of T , the distribution of the residuals along the scale of x was satisfactorily random, indicating the adequacy of equations (1) and (2). The mean of all $|\Delta y|$ was about 0·0005 y . On the other hand, the distribution of Δy along the scale of T for various values of x was far from random, showing a marked bias in one direction or the other according to the value of x . This bias, or systematic contribution to Δy , was, however, reasonably constant over the whole range of T for each given x , and, when subtracted from the total Δy , gave a residue of satisfactory randomness, with $|\Delta y|$ averaging to about 0·00001 y . Thus, cursory inspection of this kind clearly indicated that the errors (all expressed in terms of y) arising from imperfect control of temperature were much smaller than those due to imperfect control of concentration of solution. This was to be anticipated on experimental grounds, and is a favourable circumstance in relation to the study of the temperature-dependence of the measured quantities. The following statistical treatment takes into account the independence of concentration and temperature errors.

To disregard the systematic part of Δy at constant x , a corrected sum of the squares (corr. s.s.) was calculated:

$$\text{corr. s.s.} = \Sigma(\Delta y)^2 - \frac{(\Sigma \Delta y)^2}{n} \quad (3)$$

where n is the number of temperatures. The appropriate variance, s^2 , was found by summing corr. s.s. for all x and using

$$s^2 = \frac{\Sigma(\text{corr. s.s.})}{(n-1)m} \quad (4)$$

where s is the standard deviation of y and m is the number of x values. The same procedure was applied to x at constant T , and the mean corr. s.s. of x for all temperatures was obtained, leading to the average variance of the regression coefficient, $s^2/(\text{corr. s.s. of } x)$. The mean regression coefficient for the n temperatures, $\Sigma(K^{-1})/n$, was then used in calculating the variance of \ln (regression coefficient), *i.e.*,

$$\frac{(\text{average variance of regression coefficient})}{(\text{mean regression coefficient})^2}$$

¹⁴ Ives and Pryor, *J.*, 1955, 2104.

The square-root of this variance may be regarded as the error associated with $\ln K$. The standard error in Λ_0 was calculated by means of the expression

$$s \left\{ \frac{1}{m} + \frac{(\bar{x})^2}{\text{corr. s.s. of } x} \right\}^{\frac{1}{2}}$$

which takes into account the uncertainty associated with the extrapolation to $x = 0$.

The results of the calculations based on equations (1) and (2) are shown in Table 2, in which, as in succeeding Tables, each quantity is followed by a \pm term equal to twice the standard error; this indicates the 95% confidence limit.

TABLE 2.

Dissociation constants, pK values, and Λ_0 values of di-isopropylcyanoacetic acid in aqueous solution.

Temp.	$10^5 K$ (equiv. l^{-1})	pK	Λ_0
5°	404.49 \pm 0.35	2.3931 \pm 0.0004	264.22 \pm 0.07
10	369.33 \pm 0.32	2.4326 \pm 0.0004	292.26 \pm 0.07
15	336.16 \pm 0.29	2.4734 \pm 0.0004	320.21 \pm 0.07
20	305.97 \pm 0.27	2.5143 \pm 0.0004	347.89 \pm 0.07
25	278.16 \pm 0.24	2.5557 \pm 0.0004	375.25 \pm 0.07
30	252.38 \pm 0.22	2.5980 \pm 0.0004	402.44 \pm 0.07
35	228.91 \pm 0.21	2.6403 \pm 0.0004	429.13 \pm 0.07
40	207.58 \pm 0.18	2.6828 \pm 0.0004	455.35 \pm 0.07
45	188.17 \pm 0.16	2.7255 \pm 0.0004	481.03 \pm 0.07

It is regretted that the accuracy of the earlier work¹ was over-estimated. Certain other minor errors (the authors are indebted to Dr. E. J. King for indicating them) have been rectified by complete re-computation, so that comparison can now be made between cyanoacetic acid and its di-isopropyl-substituted analogue. The first point of comparison is made in Fig. 1, which clearly shows the big difference which exists between these two acids.

The analysis of the temperature dependence of $\ln K$, required for the evaluation of the thermodynamic functions of ionisation other than ΔG° , involved the determination of the coefficients b_1, b_2, \dots which satisfy the least-squares requirement in the equation

$$-(\ln K) - C_1 = \xi_1 b_1 + \xi_2 b_2 + \xi_3 b_3 + \dots + C_2 \quad (5)$$

in which the inclusion of the two constants, C_1 and C_2 , is necessary for ease of computation. In this equation, $\xi_1 = \phi$, $\xi_2 = 3\phi^2 - 20$, $\xi_3 = \frac{5\phi^3 - 59\phi}{6}$, $\xi_4 = \frac{7}{12}\phi^4 - \frac{115}{12}\phi^2 + 18$ are orthogonal polynomials¹⁵ of degree 1, 2, 3, and 4, respectively, in ϕ ; $\phi = (t - 25)/5$, where t is temperature in °c. Equation (5) is of a form which allows the successive introduction of powers of ϕ into the polynomial without change of the coefficients already determined, and permits of a test of significance to be made for each additional term added.¹⁶ In this way, the polynomial is found which best fits the experimental results without the introduction of unnecessary powers of ϕ , with the accompanying danger of attributing significance to artefacts. The procedure may be illustrated by means of the di-isopropylcyanoacetic acid data, as follows:

Total sum of squares to be accounted for * ...	5512508502 $\times 10^{-10}$
This is accounted for by a linear contribution	5511758415 $\times 10^{-10}$
" " " " quadratic "	720038 $\times 10^{-10}$
" " " " cubic "	22886 $\times 10^{-10}$
" " " " quartic "	160 $\times 10^{-10}$
Leaving a residue	7003 $\times 10^{-10}$

* $\sum z^2 - (\sum z)^2/9$, where $z = -(\ln K) - C_1$ (cf. eqn. 5).

¹⁵ Bennett and Franklin, "Statistical Analysis in Chemistry and Chemical Industry," Wiley, New York, 1954, p. 258.

¹⁶ Fisher and Yates, "Statistical Tables for Biological, Agricultural and Medical Research," Oliver and Boyd, Edinburgh, 1953, p. 80.

The introduction of the quartic term improves the fit to an extent far smaller than the internal variance (1960×10^{-10}), and the term is therefore not justified. In less decisive cases, the addition of successive polynomial terms is examined as in the following tabulation:

	Sum of squares ($\times 10^{10}$)	Degrees of freedom	Mean square ($\times 10^{10}$)	Ratio
Gain from quadratic term	720038	1	720038	143.8
Residue from quadratic	30049	9 - 3 = 6	5008	
Gain from cubic term	22886	1	22886	15.97
Residue from cubic	7163	9 - 4 = 5	1433	
Gain from quartic term	160	1	160	0.091
Residue from quartic	7003	9 - 5 = 4	1751	

If the final ratio in the last column is appreciably greater than unity, inclusion of the corresponding term is clearly justified. To examine statistical significance, use is made of the

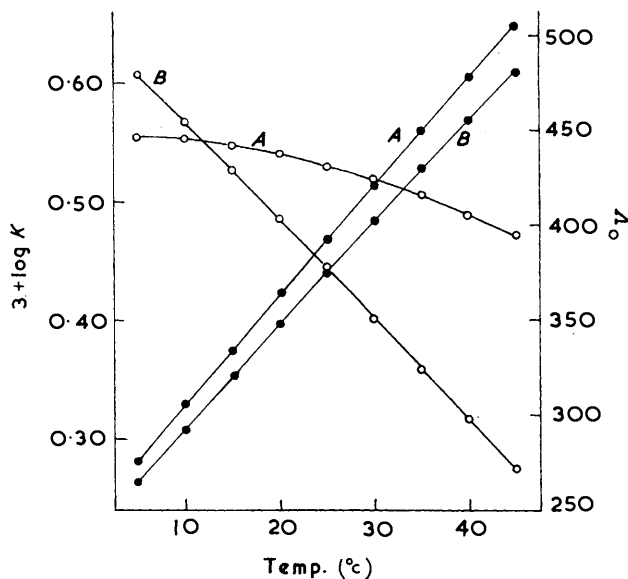


FIG. 1. Cyanoacetic and di-isopropylcyanoacetic acids in aqueous solution: $\log K$ and Δ_0 data, 5—45°.

A, Cyanoacetic acid; B, Di-isopropylcyanoacetic acid. \circ , $3 + \log K$; \bullet , Δ_0 .

table of percentage points of the F -distribution.¹⁷ Thus, for the introduction of the cubic term, above, for 1 against 5 degrees of freedom, the ratio 6.61 is tabulated at the 5% level, as compared with an observed ratio of 15.97. This means that the cubic term is statistically significant well past the 5% level. For the quartic term, however, a ratio of 7.71 is required, and comparison with 0.091 shows that this term is decisively excluded.

The same treatment has been applied to the revised data for cyanoacetic acid, and the resulting situation is best revealed by the final stage in the tabulation corresponding with that immediately above:

Gain from quartic term	11629	1	11629	7.13
Residue from quartic	6525	9 - 5 = 4	1632	

There is a difficulty here in that the residue mean square is appreciably less than the internal variance ($16,700 \times 10^{-10}$). The quartic term agrees with the variance, but its ratio to the residue is nearly significant at the 5% level. Since, in comparison with the other, similarly determined data, it is possible that the internal error is an over-estimate, this is a doubtful case,

¹⁷ Lindley and Miller, "Cambridge Elementary Statistical Tables," Cambridge, 1953, p. 8.

and we have chosen to retain the quartic term, with a degree of justification shortly to be discussed.

The standard thermodynamic functions for the ionisation of di-isopropylcyanoacetic acid were derived from the parameters of equation (5) by means of the relations

$$-\Delta G^\circ = RT \ln K \quad (6)$$

$$-\Delta H^\circ = \frac{RT^2}{5} \left[b_1 + 6b_2\phi + b_3 \left\{ \frac{15\phi - 59}{6} \right\} \right] \quad (7)$$

$$\Delta S^\circ = \frac{\Delta H^\circ - \Delta G^\circ}{T} \quad (8)$$

$$-\Delta C_P^\circ = \frac{2RT}{5} \left[b_1 + b_2 \left\{ 6\phi + \frac{3T}{5} \right\} + b_3 \left\{ \frac{15\phi^2 - 59}{6} + \frac{\phi T}{2} \right\} \right] \quad (9)$$

The variances of the coefficients b_1, b_2, \dots are statistically independent; they are given by

$$\text{var}(b_1) = \text{var}(\ln \text{ regression coefft.}) / \sum_{\phi=-4}^{+4} \xi_1^2 \quad (10)$$

and similarly for $\text{var}(b_2)$, etc. The standard errors, s , of $-\Delta H^\circ$ and $-\Delta C_P^\circ$ were then given by

$$s(-\Delta H^\circ) = \frac{RT^2}{5} \left[\text{var}(b_1) + 36\phi^2 \text{var}(b_2) + \left\{ \frac{15\phi^2 - 59}{6} \right\}^2 \text{var}(b_3) \right]^{\frac{1}{2}} \quad (11)$$

$$s(-\Delta C_P^\circ) = \frac{2RT}{5} \left[\text{var}(b_1) + \left\{ 6\phi + \frac{3T}{5} \right\}^2 \text{var}(b_2) + \left\{ \frac{15\phi^2 - 59}{6} + \frac{\phi T}{2} \right\}^2 \text{var}(b_3) \right]^{\frac{1}{2}} \quad (12)$$

In recalculations of cyanoacetic acid data retaining a quartic equation, the equations (11) and (12) included appropriate terms in $\text{var}(b_4)$. The standard errors of $-\Delta G^\circ$ and $-\Delta S^\circ$ were derived simply from $s(-\Delta G^\circ) = RT \cdot s(\ln K)$ and from $s(-\Delta S^\circ) = s(-\Delta H^\circ)/T$, the relation between the standard errors of $-\Delta G^\circ$ and of $-\Delta H^\circ$ being ignored, as a sufficient approximation. The values of the parameters of equation (5), with their variances, for the two acids are collected in Table 3, which also includes the coefficients of powers of ϕ in normal polynomial equations for $\ln K$. It may be noted that the standard errors of the observed pK values, on the basis of these equations, are 0.00017 for cyanoacetic acid, and 0.00016 for di-isopropylcyanoacetic acid. The detailed results of these calculations are assembled in Table 4.

TABLE 3.

Coefficients of interpolation equations for $\ln K$ as a function of temperature.

	Equation (5)				
	Cyanoacetic acid		Di-isopropylcyanoacetic acid		
C_1	5.6		5.5		
C_2	10268.3×10^{-5}		38841.3×10^{-5}		
	$10^5 b$	$10^{10} \text{ var}(b)$	$10^5 b$	$10^{10} \text{ var}(b)$	
b_1	2433.37	278.2	9584.50	32.615	
b_2	78.9156	6.0209	16.1169	0.7059	
b_3	-9.05353	16.86	-4.80308	1.9767	
b_4	2.41009	8.3367	—	—	
	Equation: $-\ln K = a + b\phi + c\phi^2 + d\phi^3 + e\phi^4$				
	a	$10^5 b$	$10^5 c$	$10^5 d$	$10^5 e$
Cyanoacetic acid	5.687302	2521.95	213.718	-7.5168	1.3992
Di-isopropylcyanoacetic acid	5.885190	9631.78	48.351	-4.0067	—

TABLE 4.

Standard molar thermodynamic functions for the ionisation of di-isopropylcyanoacetic acid in aqueous solution.

Temp.	5°	10°	15°	20°	25°
ΔG° (cal.).....	3044.7	3150.9	3259.8	3371.5	3485.7
	± 0.5	± 0.5	± 0.5	± 0.5	± 0.5
ΔH° (cal.)	-2783	-2941	-3098	-3252	-3402
	± 29	± 15	± 8	± 9	± 11
$T\Delta S^\circ$ (cal.)	-5827	-6092	-6358	-6623	-6887
	± 29	± 15	± 8	± 9	± 11
ΔS° (cal. deg. ⁻¹)	-20.95	-21.51	-22.06	-22.59	-23.10
	± 0.10	± 0.06	± 0.03	± 0.03	± 0.03
ΔC_P° (cal. deg. ⁻¹)	-31.9	-31.5	-31.0	-30.4	-29.6
	± 3.3	± 2.7	± 2.0	± 1.2	± 0.07
Temp.	30°	35°	40°	45°	
ΔG° (cal.).....	3602.4	3721.5	3842.8	3966.3	
	± 0.5	± 0.6	± 0.6	± 0.6	
ΔH° (cal.)	-3548	-3689	-3824	-3952	
	± 9	± 9	± 19	± 38	
$T\Delta S^\circ$ (cal.)	-7150	-7410	-7666	-7918	
	± 9	± 9	± 19	± 38	
ΔS° (cal. deg. ⁻¹)	-23.58	-24.05	-24.48	-24.89	
	± 0.03	± 0.03	± 0.06	± 0.12	
ΔC_P° (cal. deg. ⁻¹)	-28.7	-27.6	-26.3	-24.9	
	± 1.2	± 2.3	± 3.5	± 4.8	

DISCUSSION

(a) *Comparison of Cyanoacetic and Di-isopropylcyanoacetic Acids.*—(i) *The heat capacities of ionisation.* It is seen that, for the ionisation of the di-isopropyl-acid in water, $-\Delta C_P^\circ$ does not pass through a minimum with rising temperature, as previously claimed for the unsubstituted cyano-acid. The alternatives are that either this minimum was an artefact which would have been exposed by more numerous and more accurate measurements, or the tacit assumption that it would prove to be a common feature of ionisations in aqueous solution was wrong. Unfortunately, it is difficult to decide between these alternatives on the basis of existing evidence, but it is believed that the second is the more probable. This is supported by the discussion of hydrational equilibria offered later in this Paper.

The validity of the earlier finding depends on whether the quartic term in equation (5) for cyanoacetic acid is significant or not, since a cubic equation cannot lead to a minimum of the kind in question. The situation is clearly shown in Fig. 2, in which the $-\Delta C_P^\circ$ data for cyanoacetic acid (recomputed from the quartic equation included in Table 3) are plotted against temperature, between pairs of curves indicating various confidence limits within which information about $-\Delta C_P^\circ$ as a function of temperature can be accepted. It is seen that there is a little better than a 50% chance that the earlier conclusion that a minimum exists was correct.

The corresponding result for di-isopropylcyanoacetic acid is given in the same diagram; the reduction in internal error is over-emphasised by the use of a cubic equation in the latter case.

It is evident that either result would accommodate a temperature-invariant ΔC_P° , but there is a slight balance of probability in favour of the following statement. The existing results are consistent with the tentative conclusion that $-\Delta C_P^\circ$ passes through a minimum value with rising temperature in the case of cyanoacetic acid, that for the di-isopropyl-substituted acid it decreases slowly with rise of temperature, and that, therefore, the temperature variation of $-\Delta C_P^\circ$ is different in these two cases.

(ii) *Free energies, enthalpies, and entropies of ionisation.* Progress can be made, and the field of interest widened, by comparing the other thermodynamic functions for the ionisation of these two acids. Such a comparison is made in Table 5. It is seen that

TABLE 5.

Standard molar thermodynamic functions of the ionisations of cyanoacetic and di-isopropylcyanoacetic acids in aqueous solution at 25°.

	ΔG° (cal.)	ΔH° (cal.)	ΔS° (cal. deg. ⁻¹)	ΔC_P° (cal. deg. ⁻¹)
CH ₂ ·CN·CO ₂ H	3369	-891	-14.3	-36
CPr ₂ ·CN·CO ₂ H	3486	-3402	-23.1	-29.6

di-isopropyl substitution has little effect upon ΔG° at 25°. The slight weakening of acid strength observed at this temperature cannot be assigned to an inductive (+I) effect, in view of the reversal of relative acid strength that occurs at 11.97° (Fig. 1). The most striking consequences of the substitution are that ΔH° and ΔS° become more negative by

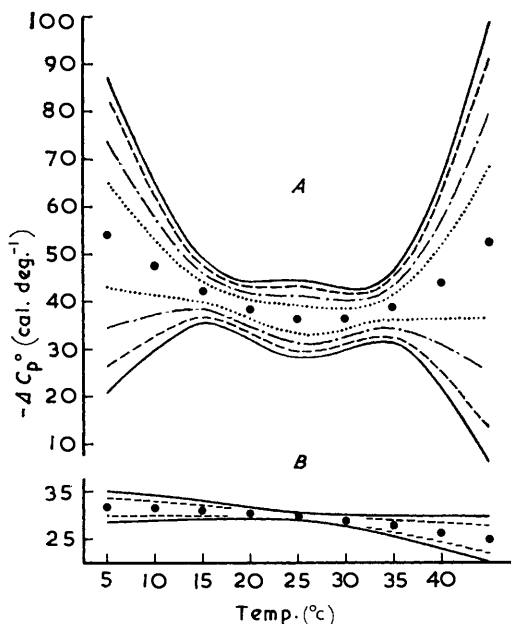


FIG. 2. Cyanoacetic and di-isopropylcyanoacetic acids in aqueous solution: $-\Delta C_P^\circ$ data from 5 to 45°, showing various confidence limits.

A, Cyanoacetic acid; B, Di-isopropylcyanoacetic acid. Confidence limits, —, 95%; ---, 90%; - · - · - ·, 75%; · · · · ·, 50%.

2.5 kcal. and by nearly 9 cal. deg.⁻¹, respectively, while ΔC_P° becomes less negative by about 6 cal. deg.⁻¹. The immediate implications would seem to be that, for the alkyl-substituted acid, ionisation is accompanied by a greater evolution of heat and by a greater enhancement of order which is, apparently, more vulnerable to thermal disruption when the temperature is raised.

The functions which are measured, however, are all differences. It was the abnormally low entropy loss accompanying the ionisation of cyanoacetic acid that emphasised the necessity of considering the hydration of molecules as well as that of the ions.¹ It is therefore clear that interpretation of such results must be attempted with caution, and must include, both for molecules and ions, intramolecular effects (such as might be concerned in a hypothetical "ideal-gas dissociation"), intermolecular effects (solute-solvent interactions), together with any temperature-dependent peculiarities of the solvent. Before making such an attempt, very likely to be both complex and uncertain, the observed effect of alkyl substitution must be considered on a wider basis.

(b) *The Effects of Alkyl Substitution and the Compensation Law.*—Table 6 shows the effects of diethyl substitution on the ionisation functions of acetic acid.¹⁸ The close analogy

¹⁸ Everett, Landsman, and Pinsent, *Proc. Roy. Soc.*, 1952, A, 215, 403.

TABLE 6.

Standard molar thermodynamic functions of the ionisations of acetic and diethylacetic acids in aqueous solution at 25°.

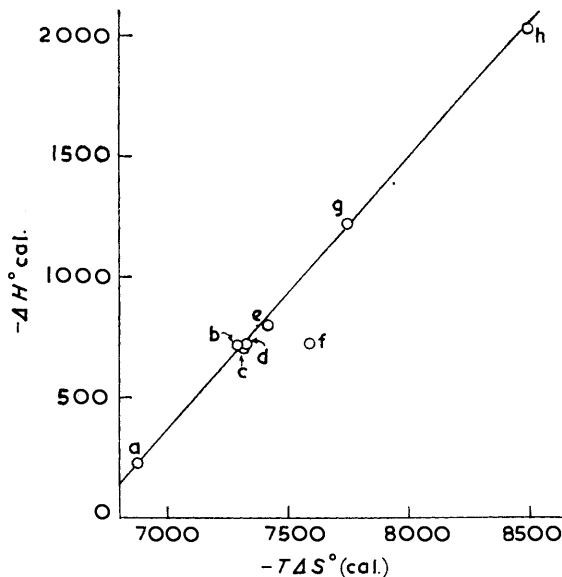
	ΔG° (cal.)	ΔH° (cal.)	ΔS° (cal. deg. ⁻¹)	ΔC_P° (cal. deg. ⁻¹)
CH ₃ CO ₂ H	6488	-105	-22.1	-37
CH ₃ CH ₂ CO ₂ H	6459	-2030	-28.5	-29

between Tables 5 and 6 is very striking; in both cases the changes in ΔH° and $T\Delta S^\circ$ produced by alkyl substitution are almost precisely self-cancelling in ΔG° . That this effect embraces a range of fatty acids¹⁸ is illustrated in Fig. 3.

It is seen that, although trimethylacetic acid deviates from the linear plot of ΔH° against $T\Delta S^\circ$ (of slope 1.12) generated by the other members, this plot forms a good

FIG. 3. $-\Delta H^\circ$ and $-T\Delta S^\circ$ for ionisation of fatty acids in aqueous solution at 25°.¹⁸

a, propionic; b, butyric; c, hexoic, d, isohexanoic and valeric; e, isobutyric; f, trimethylacetic; g, isovaleric; and h, diethylacetic acid.



example of the so-called Compensation Law, *i.e.*, the linear enthalpy-entropy effect which has recently been discussed by Leffler¹⁹ and Brown.²⁰ This linearity is very common, both in relation to equilibria and to enthalpies and entropies of activation. More often than not, it is the basis of the "linear free energy relations" which came into prominence with the Hammett equation,²¹ $\log k/k_0 = \sigma\rho$, and have been extended by Taft²² and others. Recent reviews^{23,24} indicate the width of application of these relations currently made in discussions of reactivity in organic chemistry. In so far as this depends on the status of ΔG° (or ΔG^\ddagger) as a "well-behaved function," in marked contrast to ΔH° or ΔS° , the Compensation Law must be widespread in application as well. Discussion of this matter is deferred to a later section, except for the statement that it is well understood that there is a natural tendency for ΔH and $T\Delta S$ terms, which contribute variously to ΔG over a range of reactions, to contain contributions which are of the same sign. Thus, the satisfaction of attractive forces imposes constraints (ΔH and ΔS both negative) and release from constraint confers greater freedom (ΔH and ΔS both positive). It is obvious, of

¹⁹ Leffler, *J. Org. Chem.*, 1955, **20**, 1202.

²⁰ Brown, *J. Org. Chem.*, 1962, **27**, 3015.

²¹ Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940; Jaffé, *Chem. Rev.*, 1953, **53**, 191.

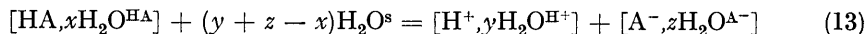
²² Taft, *J. Amer. Chem. Soc.*, 1952, **74**, 2729, 3120; 1953, **75**, 4231; "Steric Effects in Organic Chemistry," ed. Newman, Wiley, New York, 1956, ch. 13.

²³ Wells, *Chem. Rev.*, 1963, **63**, 171.

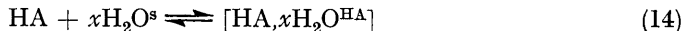
²⁴ Leffler and Grunwald, "Rates and Equilibria of Organic Reactions," Wiley, New York, 1963.

course, that ΔH and ΔS are always of the same sign for any process occurring under equilibrium conditions, because then $\Delta H = T\Delta S$, as for any reversible phase change. It is from this point of view, which appears to be relevant to any reaction in solution, that it seems profitable to discuss the ionisation of a weak acid in water as solvent.

(c) *Acidic Dissociation and Hydrational Equilibria.*—The ionisation of an acid HA in aqueous solution may be represented by the equation



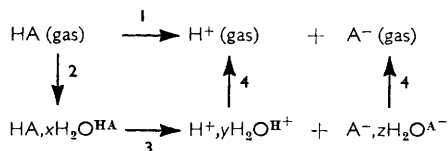
where $\text{H}_2\text{O}^{\text{HA}}$ indicates the hydration of the molecules HA, H_2O^s represents solvent water, and so on. The solvent correctly appears as an essential reactant. This reaction scheme could be split down further into contributory steps, such as



but all of these are always in equilibrium.

In considering the changes in any extensive thermodynamic property, X , which accompany reactions, ΔX for any given reaction may be analysed into additive contributions. If in this way we choose to consider that part of the reaction in which water *alone* is concerned, then the free-energy change involved is zero, because *all* the water of hydration, of whatever kind, is in continuous equilibrium with the same bulk solvent.

This may be confirmed by considering the scheme in which the upper transition (1) represents a hypothetical "ideal gas state dissociation"; the lower one (3) is a dissociation



involving the corresponding participants as they normally occur in dilute aqueous solution, and the others (2 and 4) are appropriate transfers between ideal gas and solution states. The changes in an extensive property, X , associated with these processes must satisfy the relation

$$\Delta X_1 = \Delta X_2 + \Delta X_3 + \Delta X_4 \quad (15)$$

Each of the ΔX terms on the right-hand side can be divided into a "reaction part," in which water is not *directly* concerned, and a "hydration part," in which water is *solely* concerned. Thus, one of the quantities required to define ΔX_3 can be represented by $X_{[\text{HA}, x\text{H}_2\text{O}^{\text{HA}}]}$, an extensive property of the whole hydrated complex, $[\text{HA}, x\text{H}_2\text{O}^{\text{HA}}]$. This can be divided into (1) $X_{\text{HA}(\text{aq})}$, an extensive property of HA (extensive only with respect to HA, the "anhydrous" part of the complex), *as it exists in the dissolved state*, and (2) $xX_{\text{H}_2\text{O}^{\text{HA}}}$, where $X_{\text{H}_2\text{O}^{\text{HA}}}$ is an extensive property of water in the state of hydrational association with HA.

Similar consideration can be given to all the other relevant terms, so that equation (15) can be written

$$\Delta X_1 = \Delta X_2^r + \Delta X_2^h + \Delta X_3^r + \Delta X_3^h + \Delta X_4^r + \Delta X_4^h \quad (16)$$

If the system is in equilibrium throughout, and if X is free energy, G , then

$$\begin{aligned} \Delta G_1 &= \underbrace{\Delta G_2^r + \Delta G_2^h}_{=0} + \underbrace{\Delta G_3^r + \Delta G_3^h}_{=0} + \underbrace{\Delta G_4^r + \Delta G_4^h}_{=0} \\ &= 0 \end{aligned} \quad (17)$$

A sequence of reversible processes, 2, 3, 4, may be imagined to occur in the equilibrium system. In process 2, dn mole of HA is transferred from the ideal gas phase to the solution

phase; $x \cdot dn$ mole of water comes under hydrational constraint and is modified in properties. In process 3, the constraint on $x \cdot dn$ mole of water is superseded by another kind of constraint on $(y + z)dn$ mole of water. In 4, all of the water reverts to its original state, because all of the solute that modified it in this sequence of operations has been removed. It follows, in general, that

$$\Delta X_2^h + \Delta X_3^h + \Delta X_4^h = 0 \quad (18)$$

and if $X = G$, these terms are individually equal to zero.

Equation (18) remains valid whether the reaction scheme to which it is applied is an equilibrium one or not. Thus, if it is proposed to consider, instead of the imaginably real processes in an equilibrium system, those which involve transfers from one arbitrarily standardised state to another, the standardisation operations involve only the adjustment of "cratic factors" (pressure, concentration) and those dealing with non-ideality arising from solute-solute interaction (activity coefficients). No action can sensibly be taken with regard to the solvent, unless to allow for its variation in activity from that of the pure state. If effects which may enter in concentrated solutions are excluded, such allowances are small—negligible for the dilute solutions which have vapour pressures tending to identity with that of the pure solvent. No allowance is made for solute-solvent interaction, which is tacitly assumed to be unchanged between equilibrium and standard states.

Process 3 is of present interest, and is fully expressed in equation (13), for which it can be seen that

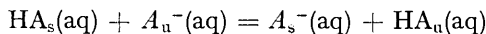
$$\Delta G_3^h = -\Delta G_2^h - \Delta G_4^h = y\mu_{\text{H}_2\text{O}^{\text{H}^+}} + z\mu_{\text{H}_2\text{O}^{\text{A}^-}} - x\mu_{\text{H}_2\text{O}^{\text{HA}}} - (y + z - x)\mu_{\text{H}_2\text{O}} \quad (19)$$

which is equal to zero because of the identity of all the chemical potential terms.

The fact of the maintenance of hydrational equilibria in general can be expressed by writing $\Delta G^h = 0$. The corresponding ΔH^h and ΔS^h terms are certainly not equal to zero, but must satisfy $\Delta H^h = T\Delta S^h$. This is the justification for thinking of hydrational changes in terms of "freezings" and "meltings," differing from ordinary freezings and meltings because they occur within a single phase and, in absence of the normal phase-rule restriction, are not confined to a single temperature. If, however, any particular kind of "freezing" involves the establishment of a degree of co-operative order, the appropriate "melting," in which this order is destroyed, could be confined to quite a narrow range of temperatures.

In contrast to ΔG^h , ΔH^h and ΔS^h make finite, perhaps major, contributions to ΔH and ΔS of the total reaction. It is this, together with the natural linking between ΔH and ΔS previously mentioned, which is believed to be the main reason why, for reactions in solution (in water or other polar solvent), ΔH is so often found, for a set of allied reactions, to be an approximately linear function of ΔS , with a slope close to T . In other words, the Compensation Law is believed to have its main application to a set of reactions which differ from each other principally in the extent of the solvational changes which accompany them; this view is amplified later.

Hepler and O'Hara²⁵ have made a similar division of ΔH° and ΔS° for acidic dissociations into "internal" and "external" contributions, corresponding with our "reaction" and "hydration" terms. For proton transfers of the type



where HA_s is the substituted analogue of the "parent," unsubstituted acid HA_u , it was assumed that $\Delta S_{\text{int}} \sim 0$, so that $\Delta S_{\text{ext}} \sim \Delta S^\circ$. On the further assumption that $\Delta H_{\text{ext}} = \beta\Delta S_{\text{ext}}$, where the constant β was assigned a value of 280° for ionisations of organic acids in water, assessments were made of ΔH_{int} for various isoelectric reactions of the above type. For the series of phenols and acetic acids studied in this way, the results appear to be highly informative, and it is believed that this new departure in the consideration of

²⁵ Hepler and O'Hara, *J. Phys. Chem.*, 1961, **65**, 811; O'Hara and Hepler, *ibid.*, 1961, **65**, 2107; Hepler, *J. Amer. Chem. Soc.*, 1963, **85**, 3089.

acid strength is very important. The present treatment of the problem differs in that β is identified with T , the absolute temperature at which the measurements are made; it is suggested that this provides an alternative basis for Hepler's treatment—it involves no change in the conclusions he has reached.

In a wider context, it is believed that the more general treatment now presented reveals the simplifying principle which operates to protect thermodynamic (and kinetic) studies of processes in solution from molecular and mechanistic complexities, particularly in the case of aqueous solutions. It follows that if any *one* thermodynamic function at a single temperature is to be used in discussing reactions in relation to molecular models (*e.g.*, polar effects of substituents) then, the zero-point energy change, ΔH_0° , being inaccessible, ΔG° is better than any other because it is far less sensitive to complications introduced by the solvent in which the reaction is performed. This is in agreement with previous conclusions,^{26,27} but it is evident that there is no thermodynamic function which can truly eliminate all the effects of "solvent participation," even if the aim to do so has any clearly identifiable meaning.

These arguments have an implication of particular importance in the context of the present problem. Since water of hydration, H_2O^h , is always in equilibrium with solvent water, there must be identity of chemical potentials:

$$\mu_{H_2O^h} = \mu_{H_2O^s} \quad (20)$$

This must be true at all temperatures, so that

$$\frac{d\mu_{H_2O^h}}{dT} = \frac{d\mu_{H_2O^s}}{dT} \quad (21)$$

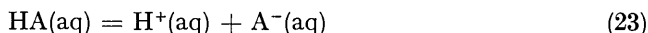
These differential coefficients must not be identified with the partial molar entropies, $\bar{S}_{H_2O^h}$ and $\bar{S}_{H_2O^s}$, which are certainly not equal. There is no paradox here, because, in particular,

$$\mu_{H_2O^h} = f(T, n^h)_P \quad (22)$$

where n^h is number of moles of water of hydration. Hydration is frequently likened to adsorption, and there must be, for each kind of hydration, an appropriate "hydration isotherm," akin to an adsorption isotherm, no doubt of a kind determined by the extreme non-ideality of highly-interacting water molecules compacted into the same hydration shell.

It follows from equations (20) to (22) that, for continuous preservation of equilibrium with the solvent, extents of solvation must change appropriately with temperature; thus x , y , and z in equation (13) must be temperature-dependent. The fact must be faced that, strictly, it is impossible to study the temperature coefficients of the parameters of a *given reaction* in solution because, as the temperature is changed, the reaction changes.

This consideration is of particular significance to the study of ΔC_P° for ionisations in solution. The experimentally accessible quantity is the sum of two terms. The first is a function of the "solute reaction proper,"



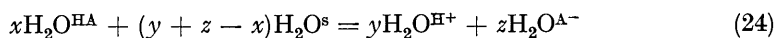
quite distinct from the hypothetical ideal-gas dissociation, because reactant and products all have the extensive properties appropriate to their dissolved state, with all of the more or less drastic modifications imposed by the influence of solvent on solute. The contribution to ΔC_P° associated with this reaction (*i.e.*, ΔC_P^r) would include, for example, any decrement of heat capacity due to loss of rotational freedom in A^- , as compared with HA .²⁸

²⁶ Evans and Polanyi, *Trans. Faraday Soc.*, 1936, **32**, 1333.

²⁷ Bell, "The Proton in Chemistry," Methuen, London, 1957, p. 70.

²⁸ Evans and Hamann, *Trans. Faraday Soc.*, 1951, **47**, 40.

The other contribution to ΔC_P° , undoubtedly by far the larger, is ΔC_P^h , attributed to the "associated solvent reaction,"



This equation, the partner to (23), expresses the fact that the extensive properties of water may be more or less drastically modified by the influence of solute on solvent, according to the situation in which it finds itself. For this hydration reaction, it is clear that

$$\Delta H^h = y\bar{H}_{\text{H}_2\text{O}^{\text{H}^+}} + z\bar{H}_{\text{H}_2\text{O}^{\text{A}^-}} - x\bar{H}_{\text{H}_2\text{O}^{\text{HA}}} - (y + z - x)\bar{H}_{\text{H}_2\text{O}^{\text{s}}} \quad (25)$$

and

$$\begin{aligned} \Delta C_P^h = & \left(\frac{\partial(\Delta H^h)}{\partial T} \right)_P = \left(\frac{\partial y}{\partial T} \right)_P \bar{H}_{\text{H}_2\text{O}^{\text{H}^+}} + y\bar{C}_{\text{P}\text{H}_2\text{O}^{\text{H}^+}} \\ & + \left(\frac{\partial z}{\partial T} \right)_P \bar{H}_{\text{H}_2\text{O}^{\text{A}^-}} + z\bar{C}_{\text{P}\text{H}_2\text{O}^{\text{A}^-}} - \left(\frac{\partial x}{\partial T} \right)_P \bar{H}_{\text{H}_2\text{O}^{\text{HA}}} - x\bar{C}_{\text{P}\text{H}_2\text{O}^{\text{HA}}} \\ & - \left\{ \left(\frac{\partial y}{\partial T} \right)_P + \left(\frac{\partial z}{\partial T} \right)_P - \left(\frac{\partial x}{\partial T} \right)_P \right\} \bar{H}_{\text{H}_2\text{O}^{\text{s}}} - (y + z - x)\bar{C}_{\text{P}\text{H}_2\text{O}^{\text{s}}} \end{aligned} \quad (26)$$

Alternatively,

$$\begin{aligned} \Delta C_P^h = & \left(\frac{\partial y}{\partial T} \right)_P (\bar{H}_{\text{H}_2\text{O}^{\text{H}^+}} - \bar{H}_{\text{H}_2\text{O}^{\text{s}}}) + \left(\frac{\partial z}{\partial T} \right)_P (\bar{H}_{\text{H}_2\text{O}^{\text{A}^-}} - \bar{H}_{\text{H}_2\text{O}^{\text{s}}}) \\ & - \left(\frac{\partial x}{\partial T} \right)_P (\bar{H}_{\text{H}_2\text{O}^{\text{HA}}} - \bar{H}_{\text{H}_2\text{O}^{\text{s}}}) + y(\bar{C}_{\text{P}\text{H}_2\text{O}^{\text{H}^+}} - \bar{C}_{\text{P}\text{H}_2\text{O}^{\text{s}}}) \\ & + z(\bar{C}_{\text{P}\text{H}_2\text{O}^{\text{A}^-}} - \bar{C}_{\text{P}\text{H}_2\text{O}^{\text{s}}}) - x(\bar{C}_{\text{P}\text{H}_2\text{O}^{\text{HA}}} - \bar{C}_{\text{P}\text{H}_2\text{O}^{\text{s}}}) \end{aligned} \quad (27)$$

Since there is no means of distinguishing the contributions of the two kinds of ions, and since in very dilute solutions $\bar{H}_{\text{H}_2\text{O}^{\text{s}}}$ and $\bar{C}_{\text{P}\text{H}_2\text{O}^{\text{s}}}$ can be equated with H° and C_P° , respectively, for pure water, this can be simplified to

$$\Delta C_P^h = \underbrace{n^h(\Delta C_P)}_{\text{Hydration of ions}} + \underbrace{\frac{\partial n^h}{\partial T}(\Delta H) - n^h(\Delta C_P) - \frac{\partial n^h}{\partial T}(\Delta H)}_{\text{Hydration of molecules}} \quad (28)$$

where the n^h terms are $(y + z)$ or x , as appropriate, and the ΔC_P and ΔH terms can be identified by reference to equation (27).

This near-obvious equation (28), indicating clearly the composite nature of ΔC_P^h , with "specific heat" (functions of state) and "latent heat" (functions of change of state) contributions, is in agreement with Kapustinskii.²⁹

Factors which determine the rate of change of hydration with temperature can be distinguished by considering the partition of water between hydrational and solvent states in a closed system. For this purpose, equation (22) must be supplemented by

$$\mu_{\text{H}_2\text{O}^{\text{s}}} = f'(T, n^{\text{s}})_P \quad (29)$$

²⁹ Kapustinskii, *J. Gen. Chem. (U.S.S.R.)*, 1942, **12**, 186.

Then, from equations (22) and (23), constancy of pressure throughout being tacitly assumed:

$$d\mu^h = \left(\frac{\partial\mu^h}{\partial T}\right)_{n^h} \cdot dT + \left(\frac{\partial\mu^h}{\partial n^h}\right)_T \cdot dn^h \quad \text{and} \quad d\mu^s = \left(\frac{\partial\mu^s}{\partial T}\right)_{n^s} \cdot dT + \left(\frac{\partial\mu^s}{\partial n^s}\right)_T \cdot dn^s \quad (30)$$

$$\frac{d\mu^h}{dT} = -\bar{S}^h + \left(\frac{\partial\mu^h}{\partial n^h}\right)_T \cdot \frac{dn^h}{dT} \quad \text{and} \quad \frac{d\mu^s}{dT} = -\bar{S}^s + \left(\frac{\partial\mu^s}{\partial n^s}\right)_T \cdot \frac{dn^s}{dT}$$

For the equilibrium state, $\mu^h = \mu^s$ at all temperatures, so that for all real situations,

$$\bar{S}^h - \bar{S}^s = \left(\frac{\partial\mu^h}{\partial n^h}\right)_T \cdot \frac{dn^h}{dT} - \left(\frac{\partial\mu^s}{\partial n^s}\right)_T \cdot \frac{dn^s}{dT}$$

This is consistent with the physical requirements that

$$\bar{S}^h < \bar{S}^s, \left(\frac{\partial\mu^h}{\partial n^h}\right)_T > \left(\frac{\partial\mu^s}{\partial n^s}\right)_T > 0$$

but, for the closed system under consideration, $\frac{dn^h}{dT} = -\frac{dn^s}{dT}$, so that

$$\bar{S}^h - \bar{S}^s = \frac{dn^h}{dT} \left[\left(\frac{\partial\mu^h}{\partial n^h}\right)_T + \left(\frac{\partial\mu^s}{\partial n^s}\right)_T \right] \quad (31)$$

If for very dilute solutions μ^s can be equated to μ° without significant error, then

$$\frac{dn^h}{dT} = \frac{\bar{S}^h - S^\circ}{\left(\frac{\partial\mu^h}{\partial n^h}\right)_T} \quad (32)$$

which shows that the (negative) rate of change of hydration with temperature is determined by the entropy loss of the water undergoing hydrational "freezing," and by the hydration isotherm.

Since $\Delta C_P^\circ = \Delta C_{P^f} + \Delta C_{P^h}$, it is clear that the interpretation of ΔC_{P° is formidably complex. It is also clear that this function is likely to be specifically variable from one ionisation to another, particularly in its dependence on temperature; certainly the form of equation (28) does not preclude the minimum in $-\Delta C_{P^\circ}$ previously found, nor the interpretation advanced for it, although the latter, if valid, is now seen to be a special case.

A "chemical-thermodynamic" treatment of this kind, emphasising the part played by temperature-sensitive solvation in reactions in solution, seems not to have been widely considered, yet the effects concerned can hardly be of minor importance within the framework of factors which are relevant in discussing such reactions. This situation, together with the inter-relation of all the mutual solute-solvent influences properly classed as solvation, calls for the following rather wide discussion.

(d) *General Discussion.*—(i) *Electrostatic theory.* The Harned and Embree equation³⁰

$$\log K = \log K_m - p(t - \theta)^2 \quad (33)$$

where K_m is the maximum value of the dissociation constant K attained at temperature θ and p is a nearly universal constant, came so close to being a generally applicable "reduced

³⁰ Harned and Embree, *J. Amer. Chem. Soc.*, 1934, **56**, 1050.

equation" as to suggest that the temperature-dependence of $\log K$ (and hence ΔH°) must be essentially determined by an electrical property of the common solvent, water, concerned in its response to the generation of ionic fields.³¹ The linearity of $\log K$ with $1/T$ (implying constancy of ΔH°) for isoelectric dissociations³² and, in some cases, the change of relative dissociation constant as a function of dielectric constant,³³ appeared to support the decisive role of electrostatic effects. Gurney^{34,35} dealt with the Harned and Embree relation by isolating a temperature-dependent, environmental contribution to the "unitary" free energy of dissociation; the electrical origin of this contribution seemed to be established by its general conformity with the Born equation. The variation of θ from one acid to another became intelligible in terms of the ratio of the temperature-independent (non-electrical) and the temperature-dependent (electrical) free-energy contributions. Baughan's demonstration³⁶ that ΔH° is in many cases linear with $(1/\epsilon)[1 + T(\delta \ln \epsilon / \delta T)]$, where ϵ is dielectric constant, as required by Born theory, was confirmed in a particularly interesting way by La Mer and Brescia,³⁷ although in each case the "ionic radii" had to be regarded as parameters which accommodated undetermined solvent effects. The Kirkwood-Westheimer theory³⁸ was effective in dealing with the influence of charged and polar substituents on dissociation constants, but the inadequacies of "cavity in dielectric" models³⁹ excluded the theory from application to the problem of temperature-dependence.⁴⁰ In the field of kinetics, limited success attended application of electrostatic theory to the influence of dielectric constant of solvent on reactions involving charged or polar reactants.⁴¹

Evidence of this kind indicated that electrostatic theory served at least as a first approximation; even although the substantial agreement with experiment turned out to be somewhat illusory, it would be unsafe to assume that long-range coulombic forces do not play a part in the ion-solvent actions which are significant to, *inter alia*, dissociation constant problems. The influence of an ion on water molecules, averaged out, can hardly decline in other than a gradual (if inflected) way with increasing distance,⁴² although this influence is able to impose restriction of translational freedom, or reduction of exchange frequency^{43,44} only on the nearest-neighbour water molecules which form the "inner shell," or primary hydration zone.* In principle, ionic field strength, falling away asymptotically with distance, will promote significant ion-solvent effects over a range no less wide than that of effective ion-ion interactions. If "solvation" is to comprehend all solute-solvent effects (no clear basis of restriction being apparent), "solvation numbers" become indefinable. The symbols x , y , z , and n^h used in the preceding equations are therefore not "hydration numbers"; they are capacity factors which, multiplied by appropriate intensive (partial molar) properties of water (under whatever kind and extent of modifying influence by the relevant solute), provide the proper contributions to the change of each extensive property for the reaction concerned. This in no way affects the overriding thermodynamic argument.

* King⁴⁵ has somewhat misinterpreted an earlier discussion relevant to this.¹

³¹ Magee, Ri, and Eyring, *J. Chem. Phys.*, 1941, **9**, 419.

³² Everett and Wynne-Jones, *Proc. Roy. Soc.*, 1938, *A*, **169**, 190.

³³ Wynne-Jones, *Proc. Roy. Soc.*, 1933, *A*, **140**, 440.

³⁴ Gurney, *J. Chem. Phys.*, 1938, **6**, 499.

³⁵ Gurney, "Ionic Processes in Solution," McGraw-Hill, New York, 1953.

³⁶ Baughan, *J. Chem. Phys.*, 1939, **7**, 951.

³⁷ La Mer and Brescia, *J. Amer. Chem. Soc.*, 1940, **62**, 617.

³⁸ Kirkwood and Westheimer, *J. Chem. Phys.*, 1938, **6**, 506.

³⁹ Wynne-Jones and Rushbrooke, *Trans. Faraday Soc.*, 1944, **40**, 99.

⁴⁰ Westheimer and Kirkwood, *Trans. Faraday Soc.*, 1947, **43**, 77.

⁴¹ Laidler and Eyring, *Ann. New York Acad. Sci.*, 1939-1940, **39**, 303.

⁴² Verwey, *Rec. Trav. chim.*, 1942, **61**, 127.

⁴³ Samoilow, *Discuss. Faraday Soc.*, 1957, **24**, 141.

⁴⁴ Samoilow, "Die Struktur von wässrigen Elektrolyt-Lösungen," B. G. Teubner Verlagsgesellschaft, Leipzig, 1961.

⁴⁵ King, *J. Amer. Chem. Soc.*, 1957, **79**, 6151.

Opinion has turned somewhat against the use of electrostatic-dielectric continuum models.⁴⁶ Failures of the Born theory,⁴⁷ sometimes spectacular,⁴⁸ undermine the status of calculations using such models, even as a basis for first approximation. This is certainly the case for ΔC_P° for the dissociation of a molecular acid in water; the representative value of -40 cal. deg.⁻¹ is of itself adequate to explain the general shape of the $\ln K$ - T curves. A revised calculation of ΔC_P° in terms of Born theory, as made by Everett and Wynne-Jones,⁴⁹ using a common ionic radius of 1 Å and more recent dielectric constant data,⁵⁰ gives values of -10.6 , -13.0 , and -15.8 cal. deg.⁻¹ for 0, 25, and 50° respectively. The indication that ΔC_P° varies with temperature carries little weight because of the gross over-all discrepancy with fact. This is, of course, the unsolved problem which the present work was designed to approach; otherwise, none of the alternative $\ln K(T)$ equations which have been proposed fitted the available data better than another so as to provide significant evidence on the possible (and likely⁵¹) temperature variation of ΔC_P° . In the circumstances, no better could be done than to assume constancy of ΔC_P° for the limited temperature range over which most measurements extended, and this was the basis of the convenient and widely used Everett and Wynne-Jones equation⁴⁹

$$\ln K = \frac{A}{T} + \frac{\Delta C_P^\circ}{R} \ln T + B \quad (34) *$$

where the significance attached to the constants A and B

$$A = \frac{-\Delta H_0^\circ}{R}; B = (\Delta S_0^\circ - \Delta C_P^\circ)/R \quad (35)$$

would probably not now be maintained. The temperature of maximum dissociation again, correctly, appears to be determined by the ratio of temperature-independent and temperature-dependent terms, since

$$\frac{-\Delta H_0^\circ}{\theta \Delta C_P^\circ} = 1 \quad (36)$$

It became clear that the thermodynamic functions of dissociation could ultimately be understood only by the application of statistical mechanics to sufficiently realistic molecular models. On these lines, Everett and Coulson⁵² succeeded in interpreting the observed magnitude of ΔC_P° by calculating typical ionic heat capacities. Their model of hydrated ions involved restricted rotations of "first shell" water molecules, but outside this shell the situation became too complex for any but Born treatment. The contribution to heat capacity from inner shell librations and that from outer "Born charging" varied oppositely with temperature, supporting the earlier assumption of constancy of ΔC_P° as a first approximation, but revealing another feature of the complexity of this function. This Paper, with others,⁵³ signposted "coulombic theory" to its proper place: inadequate for problems of condensed systems in which short-range interactions are paramount, but satisfactory for longer-range effects, or under circumstances where all but the latter cancel.

The sensitivity of the thermodynamic functions of reactions in solution to all kinds of

* It may be pointed out that our method of expressing $\ln K$ as a polynomial in temperature will accommodate this, or any other likely form of equation.

⁴⁶ Coulson, *Proc. Roy. Soc.*, 1960, *A*, **255**, 69.

⁴⁷ Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," 3rd edn., Reinhold, New York, 1958, ch. 15.

⁴⁸ Feakins and Watson, *J.*, 1963, **4686**, 4734.

⁴⁹ Everett and Wynne-Jones, *Trans. Faraday Soc.*, 1939, **35**, 1380.

⁵⁰ Malmberg and Maryott, *J. Res. Nat. Bur. Stand.*, 1956, **56**, 1.

⁵¹ Dippy and Jenkins, *Trans. Faraday Soc.*, 1941, **37**, 366.

⁵² Everett and Coulson, *Trans. Faraday Soc.*, 1940, **36**, 633.

⁵³ Eley and Evans, *Trans. Faraday Soc.*, 1938, **34**, 1093.

solvation of the ions and molecules concerned, or, more generally, to all the effects which solutes exert on solvents, is now generally recognised. When water is the solvent, the complexities are such as to exclude, as yet, the possibility of detailed interpretation; the task is rather to use the measured functions to find out what is happening, and to identify the effects which require interpretation.

(ii) *The amines; hydrogen bonding and hydrophobic hydration.* The present situation is typified by the problem of the positively charged acids. For the isoelectric dissociation of ammonium ion in aqueous solution, formally represented by $\text{NH}_4^+ + \text{H}_2\text{O} = \text{NH}_3 + \text{H}_3\text{O}^+$, ΔS° is very small at 25° and ΔC_P° at the same temperature is zero.⁵⁴ The NH_4^+ ion is said to cause little disturbance to the structure of water,⁵⁵ with which it hydrogen bonds⁵⁶ somewhat less strongly than does H_3O^+ (its standard entropy is much greater,⁵⁷ although its volume contribution is less⁵⁸). For both these ions, the hydrogen bonding is reinforced by the positive charge,⁵⁹ and is stronger than for the corresponding molecules, acting either as proton donors or acceptors. It can be seen, at least qualitatively, why ΔS° for this reaction is nearly zero, so that the equilibrium is determined by ΔH° , largely a function of the relative proton affinities of NH_3 and H_2O .⁶⁰

The unexpected acidity sequence of the successively methylated ammonium ions in water is now known to be a function of solvent action,⁶¹ but a remarkable regularity appears, in that dissociation is accompanied by an entropy loss which increases by about 5 cal. deg.⁻¹ for each methyl group.⁶² Apart from a comparatively small symmetry effect,⁶⁰ or merely the spatial exclusion of water molecules from "first shell" proximity to the site of charge,⁶³ there can be little doubt that this is due to the step-wise loss of facility to form hydrogen bonds with water molecules,⁶⁴ so that the (negative) entropy of hydration of the ammonium ions is progressively reduced. This explanation of the effects of successive substitutions is supported by Pearson's study of the interaction of the conjugate bases with nitroethane in aqueous solution.⁶⁵

On the other hand, the same substitutions cause ΔC_P° to become more positive, the successive values from ammonium to trimethylammonium being 0, 8, 23, and 44 cal. deg.⁻¹. This very remarkable effect, associated with a large heat-capacity change opposite in sign to that of entropy, can hardly be anything to do with restriction of internal rotations.⁶⁶ It strongly suggests that some other influence of solute on solvent, unique to aqueous systems, is in operation. This is now associated with the influence of hydrophobic molecules, or parts of molecules, in promoting co-operative structure in the immediately surrounding water.⁶⁷ The name "hydrophobic hydration" for this effect denotes that no bonding between solute and solvent is involved. It ostensibly gives rise to high heat capacity because, being vulnerable to rise of temperature, it "melts." If this kind of hydration (which would also contribute to the observed entropy change) is weakened or annulled by the field of a neighbouring charge, it will be largely confined to the amine molecules, as opposed to the ammonium ions, and would thus account for the increasingly positive ΔC_P° values.

It is clear that even within this group of only four simple cation acids, several effects

⁵⁴ Bates and Pinching, *J. Res. Nat. Bur. Stand.*, 1949, **42**, 419; Everett and Landsman, *Trans. Faraday Soc.*, 1954, **50**, 1221.

⁵⁵ Kaminsky, *Discuss. Faraday Soc.*, 1957, **24**, 171; Hindman, *J. Chem. Phys.*, 1962, **36**, 1000.

⁵⁶ Altshuller, *J. Amer. Chem. Soc.*, 1955, **77**, 3480.

⁵⁷ Latimer, Pitzer, and Smith, *J. Amer. Chem. Soc.*, 1938, **60**, 1829.

⁵⁸ Whalley, *Trans. Faraday Soc.*, 1959, **55**, 798.

⁵⁹ Bell and Trotman-Dickenson, *J.*, 1949, 1288.

⁶⁰ Briegleb, *Z. Elektrochem.*, 1949, **53**, 350.

⁶¹ Hall, *J. Amer. Chem. Soc.*, 1957, **79**, 5441.

⁶² Everett and Wynne-Jones, *Proc. Roy. Soc.*, 1941, *A*, **177**, 499.

⁶³ Evans and Hamann, *Trans. Faraday Soc.*, 1951, **47**, 34.

⁶⁴ Trotman-Dickenson, *J.*, 1949, 1293; Taft, *J. Amer. Chem. Soc.*, 1960, **82**, 2965.

⁶⁵ Pearson, *J. Amer. Chem. Soc.*, 1948, **70**, 204.

⁶⁶ Schaleger and Long, *Adv. Phys. Org. Chem.*, 1963, **1**, 1.

⁶⁷ Frank and Evans, *J. Chem. Phys.*, 1945, **13**, 507.

are significant in determining the dissociation equilibria, very likely reacting upon each other in ways not yet clear. Thus, no explanation offers for the volume changes involved in the dissociations; in the same order as above they are 5.5, 3.0, 3.9, and 4.7 cm.³.⁶⁸

(iii) *Alternative views on hydrophobic hydration.* The widespread incidence of hydrophobic hydration is generally agreed, even if views upon its precise nature and characteristics are not (cf. Némethy and Scheraga⁹). Thus, Ackermann and Schreiner⁶⁹ found that the calorimetrically determined partial molar heat capacities of formic, acetic, and propionic acids in aqueous solution are separated by CH₂ increments so large as to be unaccountable except in terms of a structure-promoting effect of the alkyl groups on the surrounding water. These increments, however, were just as large for the corresponding anions, and in both cases were maintained up to 120°. Signs neither of field-promoted nor temperature-induced "melting" were found, although otherwise the case to be made for the former, and the evidence for the latter⁶⁷ are strong.

An alternative view, consistent with Langmuir's,⁷⁰ directs particular attention to the formation of a cavity in the solvent to accommodate the solute.⁷¹ This involves something akin to the generation of a free water surface (the water withdrawing from the repellent, hydrophobic solute), or a water-oil interface, in which entropy defect and heat capacity excess are located. Recent evidence of the ice-likeness which may exist at the interfaces which water makes with the gas phase⁷² or with hydrocarbons,² at least at lower temperatures, may go some way to reconcile these viewpoints. It is possible, however, that two effects should be distinguished. One, peculiar to cool water, may involve the promotion of co-operative, temperature-sensitive "ice-likeness," comparable with the formation of gas hydrates. The other, a "tensile cavity" effect, might be of a more general nature, common to water at higher temperatures and other liquids, involving no greater, nor less, structure promotion than occurs in the generation of a free liquid surface.⁷³ It would vary from zero in the ideal solution case to a maximum for the case of the "hard sphere," non-interacting solute, as discussed by Rice.⁷⁴

(iv) *Restriction of intramolecular rotations by ionic fields.*—The behaviour of the series of aliphatic carboxylic acids to which reference has been made¹⁸ has been discussed not only in terms of hydrophobic hydration⁷⁵ (partially annulled by charge proximity in the case of the compact trimethylacetate ion) but also in terms of solvent exclusion and chain-stiffening. The latter effect²⁸ was first suggested by Kirkwood to Price and Hammett⁷⁶ in connection with their observation that α -methyl substitution greatly reduced the reactivity of ketones by introducing a substantially negative entropy of activation. This was interpreted in terms of the repulsion of a body of low dielectric constant (a methyl group) in a medium of high dielectric constant from the vicinity of a charge (ionic or polar transition complex). This would lead to a degree of rigidity in the complex—a stiffening associated with a "freezing out" of entropy due to intramolecular motions. Whether or not such macroscopic concepts can satisfactorily answer essentially molecular problems, the kind of entropy effect which requires explanation is of such frequent occurrence in reaction kinetics that it has been generalised by Taft;⁷⁷ the more entropy that is introduced into a reactant molecule by a substituent group close to the reaction centre, the more entropy is frozen out in the transition state. It may be justifiable to transfer this theorem from the field of reaction kinetics in which it was cultivated to equilibria in solution, but the reality of the effect for normal solutes has been questioned⁶⁹ on the grounds that

⁶⁸ Hamann and Strauss, *Trans. Faraday Soc.*, 1955, **57**, 1684.

⁶⁹ Ackermann and Schreiner, *Z. Elektrochem.*, 1958, **62**, 1143.

⁷⁰ Langmuir, *Chem. Rev.*, 1929, **6**, 451.

⁷¹ Eley, *Trans. Faraday Soc.*, 1944, **40**, 184.

⁷² Fletcher, *Phil. Mag.*, 1962, **7**, 255.

⁷³ Henniker, *Rev. Mod. Phys.*, 1949, **21**, 322.

⁷⁴ Rice, *J. Chem. Phys.*, 1947, **15**, 875.

⁷⁵ Everett, *Ind. chim. belge*, 1951, **16**, 647.

⁷⁶ Price and Hammett, *J. Amer. Chem. Soc.*, 1941, **63**, 2387.

⁷⁷ Taft, "Steric Effects in Organic Chemistry," ed. Newman, Wiley, New York, 1956, p. 669.

molecules, equally with ions, are constrained in their motions in aqueous solution by the inertial obstruction of surrounding water molecules.⁷⁸ It may be noted that methyl substitution of ammonium ion seems to have an effect opposite to that of the Price and Hammett rule. Nevertheless, this chain-stiffening has been widely discussed, and cannot be excluded in relation to dissociation equilibria.

(v) *Models of hydrated ion systems in the interpretation of dissociation functions.* Studies of, *inter alia*, amino-acids and their derivatives have enabled King^{45,79} very credibly to describe a number of factors significant to the thermodynamic functions of acidic dissociation. Recognising that changes in ΔG° from one related acid to another best reflect the inaccessible zero-point energy changes to which transmitted polar effects contribute, and that conventional entropy contributions largely cancel out between molecules and ions, he assigned the major part of ΔS° to alterations of solute-solvent effects. This involved the clear recognition of "coupling" of (or compensation between) those parts of ΔH° and $T\Delta S^\circ$ which arise from hydration effects. The influence on the aqueous medium of hydrogen bonding or polar substituents (for molecules as well as ions) was taken into account, together with that of hydrophobic hydration, which was interpreted in a very interesting way. On the basis that the influence on the structure of water of a single ionic charge extends to a distance of 5 Å,^{18,80} and that a disordered zone of high-entropy water (starting at about 2.8 Å) subtends a low-entropy primary hydration zone of monolayer thickness, it was suggested that the influence of a hydrophobic substituent group must depend critically upon its distance from the site of ionic charge. If the group is close, it will (by solvent exclusion) displace low-entropy water, increase ionic entropy, and make ΔS° less negative. If somewhat removed, it will project into the disordered zone, displace high-entropy water, reduce ionic entropy, and make ΔS° more negative. The latter effect, it was envisaged, would be reinforced by structure promotion within the otherwise disordered zone; under these circumstances, the "tensile cavity" rather than the "gas hydrate" model, was naturally preferred. If the inert group is still further removed, it will fall outside the 5 Å range and its structure-making effects, being common to molecules and ions, will influence ΔS° little, if at all. With less well-defined considerations of restricted rotation brought about by ionic charge (regarded as mainly steric, rather than electrostatic, in origin), these effects were used to explain a wide range of data with convincing self-consistency.

In spite of this success, some of King's hypotheses may be questioned, particularly in relation to the range of ionic action. The main part of the effect of the solvent on ionic standard free energy is no doubt confined to a solvent shell of limited thickness—according to Born theory, 80% within about two ionic diameters.⁸¹ This theory, however, does not allow for dielectric saturation, which increases this distance to as much as 5 Å, according to the same evidence on which King relied, cited by Everett *et al.*¹⁸ in support of their own conclusions. Since dielectric saturation is due to orientational "freezing," it represents very severe interference with the solvent; it occurs in regions where the powerful forces of inhomogeneous ionic fields are overwhelmingly predominant. It is therefore reasonable to suppose that the range of significant interference is much greater than that of dielectric saturation. Even if this may be disputed in relation to free energy, it is almost certainly true for enthalpy and entropy, the effects upon which will be "coupled," or will mutually compensate.

A similar conclusion may be reached by considering the enhanced proclivities of strongly polarised water molecules to form hydrogen bonds, and the tolerable certainty of a degree of correlation, decreasing outwards, between water molecules successively removed from the immediate vicinity of an ion. It is felt that "secondary hydration" should be retained

⁷⁸ Aranow and Witten, *J. Chem. Phys.*, 1958, **28**, 405.

⁷⁹ King, *J. Amer. Chem. Soc.*, 1956, **78**, 6020; 1960, **82**, 3575; King and King, *ibid.*, 1956, **78**, 1089.

⁸⁰ Everett and Pinsent, *Proc. Roy. Soc.*, 1952, *A*, **215**, 416.

⁸¹ Gurney, "Ions in Solution," Cambridge, 1936.

in the generalised picture of ionic hydration, in the sense in which this term was previously used,¹ namely, to denote a region in which there is appreciable loss of orientational freedom, but with no sharp demarcation from the disordered zone which subtends it. Although King's very compact model is not unsupported,⁸² its spatial expansion and "smoothing out" is not excluded by the microwave evidence⁸³ he quoted, and seems to be desirable on a number of counts.⁸⁴ Such expansion increases the range of ionic influence to more realistic distances, seems to fit better the statistical kind of order natural to fluid systems, and obviates possible difficulties (even of logical definition) associated with too narrow a zone of disorder (such as inadequate accommodation for "Frank and Evans excess entropy," or for observed fluidity effects).

Within present limitations of knowledge, there is open choice of opinion about hydrophobic hydration, except that it arises not from interaction with a solute, but rather from the absence of such interaction. One can hardly disbelieve that it is a consequence of the same kind of water-water co-operation (with altered symmetry conditions) that, in liquid water itself, prevents the average co-ordination from much exceeding that of ice. In this case, the order of hydrophobic hydration is ice-like. Ionic fields are inimical to the self-produced, ice-like order of liquid water, otherwise there could never be an entropy-raising, viscosity-lowering zone of disorder. It is therefore very likely that ionic fields are destructive to hydrophobic hydration, and there is evidence that this is so. The case of the amines, already discussed, could be quoted, and the remarkable way in which the tetra-alkyl-ammonium ions develop their astonishing properties with increasing size, and increasing distance of the periphery from the site of charge, culminating in hydrate formation. This line of thought, leaning strongly to the "gas hydrate" view of this phenomenon, excludes belief in King's model. There is no difficulty in accepting his concept of the effect of displacement of high-entropy water by an inert group, but that this group should stimulate order in the very region where the tendency to the self-production of order has been annulled is barely logical, and there is difficulty in understanding the meaning of "ice-likeness" in a region little wider than the smallest distance between oxygen atoms in ice. King does not, of course, put himself in the position of encountering these difficulties; the point to be made is that his model compels him to adopt the "tensile cavity" view of hydrophobic hydration. Disbelief in this view calls for rejection of the model.

In accepting the onus of providing a better alternative theory, we must confine attention to our own limited results, supplemented by those for the fatty acids.

If the entropy loss accompanying dissociation is essentially due to the hydration of ions, the fact that alkyl substitution increases this loss suggests, but does not prove, that it increases the hydration of the ions relative to that of the molecules. This inference is supported by the simultaneous effect of the substitution in increasing the heat evolution during ionisation, leading to the balancing of $-\Delta H^\circ$ and $-T\Delta S^\circ$ so characteristic of a freezing process. It has been pointed out that this compensation effect is widespread and has been attributed to the solvational changes involved in "associated solvent reactions" which are always in equilibrium. If this is so, it is interesting to note, from the data in Fig. 3, that hydrational changes appear to be subject to wide variations within a set of saturated fatty acid ionisations.

As a preliminary to the examination of the part that hydrophobic hydration might play, it is noted that, since the molecule HA and the ion A^- contain the same groups, it can have no effect upon heats and entropies of ionisation unless it is modified in extent or stability by juxtaposition to the site of charge in the ion. That modification is inappreciable at a sufficient distance from the charge is strongly indicated by the fact that, in the fatty acid series, extension of the hydrocarbon chain beyond the γ -carbon atom has no effect on ΔH° nor on $T\Delta S^\circ$ (Fig. 3). At lesser distances, however, it is considered that

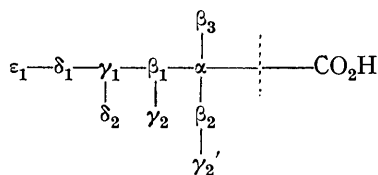
⁸² Devanathan, *J. Sci. Ind. Res.*, 1961, **20B**, 273.

⁸³ Harris and O'Konski, *J. Phys. Chem.*, 1957, **61**, 310.

⁸⁴ Benson, "The Foundations of Chemical Kinetics," McGraw-Hill, New York, 1960, pp. 518, 540.

the ionic field must act adversely on the stability of hydrophobic hydration because, to reiterate, this hydration involves a degree of contra-association which is incompatible with the alignments which the field, radiating from the centre of charge, would seek to impose. If this view is correct, ionisation would cause such hydration, near enough to the carboxyl group, to "melt." This, however, would make a positive contribution to ΔH° , *i.e.*, it would tend to make ΔH° less negative, and this would also apply to ΔS° . This is opposite to the effect observed in the case of the cyano-acids. Since, also, hydrophobic hydration is associated with high heat capacity, such "ionisational melting" would give rise to a more negative ΔC_P° for the alkyl-substituted acid: this again is not in agreement with experiment, and some other basis of explanation must be found. A similar conclusion is reached by considering the substantial lowering of the temperature of maximum dissociation caused by alkyl substitution in the cyanoacetic acid molecule ($+4.3^\circ$ to *ca.* -98°), coupled with the reduction in the value of $-\Delta C_P^\circ$. Reference to equation (36), the essence of which is not dependent on minor variation in the form of equation (34), suggests that the substitution must involve a substantial, negative contribution to the temperature-independent energy change represented by ΔH_0° . This cannot conceivably be due to an inductive effect, which would in any case work in the opposite sense.

(vi) *Reconsideration of the solvent exclusion effect.* It is clear from the results of alkyl substitution that a "first order" effect of some importance is operating. The following analysis of the fatty acid data previously used may help to identify it. If acetic acid is taken as the parent unsubstituted acid, the introduction of carbon atoms appears to have a systematic effect on ΔH° or $T\Delta S^\circ$ according to the structural situation of each atom added. In terms of the formulation



where the Greek letters represent appropriate carbon atoms, and the subscript numerals indicate first, second, and third (γ_2' represents a second γ -carbon atom not attached to the same β -atom as the first), differences of $-\Delta H^\circ$ and $-T\Delta S^\circ$ from those of acetic acid, to the nearest 5 cal., are shown in Table 7.

TABLE 7.

Differences of $-\Delta H^\circ$ and $-T\Delta S^\circ$ of ionisation in cal./mole at 25° produced by alkyl substitution in acetic acid.

	β_1	β_2	β_3	γ_1	γ_2	γ_2'	δ_1	δ_2	ϵ_1
$-(\Delta H^\circ - \Delta H_{\text{acetic}}^\circ)$	125	570	-75	485	505	745	5	-5	-20
$-T(\Delta S^\circ - \Delta S_{\text{acetic}}^\circ)$	290	535	175	410	450	665	35	0	0

These differences, with the data for acetic acid, account for all the results represented in Fig. 3 within experimental error and also fit, moderately, the cyano-acid observations.

The following interpretation is based on a suggestion by Humphreys and Hammett.⁸⁵ It resembles one aspect of Baughan's consideration³⁶ of the Born theory, and although subject to the objection of macroscopic concepts applied to molecular problems, merits consideration. In the formula above, a broken line represents a plane perpendicular to the bond between carboxyl and α -carbon atoms. The region to the right of this plane is that in which hydration can most freely occur, and it will be much the same for all the carboxylic acids. To the left, solvent exclusion will lead to a reduction of dielectric constant

⁸⁵ Humphreys and Hammett, *J. Amer. Chem. Soc.*, 1956, **78**, 521.

and a consequent redistribution of ionic field. The extent to which this occurs will depend on the size, shape, and motions of the ionic residue, and on the properties of the medium which it displaces. A revised application of the parachor to the alkanes⁸⁶ indicates that methyl groups, successively replacing the three hydrogen atoms on the same terminal carbon atom, lead to nearly equal increments of "exclusion volume" (at standard internal pressure) in the liquid phase. This suggests that the three groups are roughly stereochemically equivalent, in contrast with the " β entries" in Table 7. This evidence, however, relates to the pure liquid phase in which ideal solution conditions prevail. The problem of solvent exclusion must, on the contrary, be considered as a highly non-ideal interaction. The ionic hydrocarbon residue (which would form a separate phase if it could) will tend to carve out a cavity for itself in the foreign medium of high internal pressure. The easiest cavity to form will be a spherical one. This process presents a problem in competing molecular forces and motions which may crudely be considered in terms of intramolecular ionic motions opposed by solvent obstruction. If rotation about the α -carbon-carboxylate bond, passing through the dividing plane, be considered, it may be suggested that one β -carbon atom is relatively ineffective in displacing solvent. Two β -atoms, however, may co-operatively sweep out, and protect from the intrusion of water molecules, a much larger volume; together, the pair of them may be able to sweep out a near-spherical cavity. The more effective this is, the less will be the influence of a third β -atom, following in the path cleared by the other two. This picture is consistent with Table 7, and indicates that a substantial part of the reduction of dielectric constant may be due to an empty "co-volume."

Beyond β -atoms, each additional carbon atom may be imagined to add its own sweeping-out, solvent excluding effect, as appropriate to its location and degrees of freedom of motion. Eventually, a maximum effect must be attained, the limit of which can be regarded as such effective expulsion of water that the hypothetical plane separates regions of low and high dielectric constant. Whether in terms of field-redistribution, or of image charges of like sign to that of the carboxylate group, the field strength will be increased on the "watery side" of the plane, and this will increase the radial extent and stability of hydration. With increasing length of hydrocarbon chain, the effect will of course diminish rapidly because of weakening of field and of increasing numbers of water molecules to be excluded. Although this suggestion is contrary to the usual view of the effect of solvent exclusion on solvation, it seems to be broadly consistent with the facts.

Mention must be made of another possibility which, if not favoured, cannot be completely excluded. It is the "chelation effect" which involves, for example, the assumption of a coiled configuration by the butyrate ion, stabilised by a hydrogen bond linking the carbon atom of the terminal methyl group with a carboxylate oxygen atom. Not accessible to the acid molecule, this ion-stabilising effect would promote dissociation. Sterically possible for the higher homologues but not for the lower, this effect would explain the jump in dissociation, and in the negative values of ΔH° and ΔS° of ionisation, which occurs between propionic and butyric acids. This explanation deals with the other acids containing the necessary 4-carbon (or longer) chain,⁸⁷ including di-isopropylcyanoacetic acid, and has been discussed in a wider context.⁸⁸ It is consistent with some of the features of Table 7, but opinion about it must be reserved.

(vii) *Final comment on the ionisation of di-isopropylcyanoacetic acid.* It is thought that the solvent exclusion effect, as discussed in (vi), is predominant in differentiating the di-isopropyl-acid from its unsubstituted analogue, but that hydrophobic hydration may play a subsidiary part in the following way. Around the γ -carbon atom is regarded as the most likely "sensitive region" where, by reason of a certain balance of ordering influences, such hydration is weakened by the ionic field, and will be more than normally vulnerable

⁸⁶ Ives and Taylor, *J.*, 1957, 2551.

⁸⁷ Dippy, *J.*, 1938, 1222; *Chem. Rev.*, 1939, 25, 151.

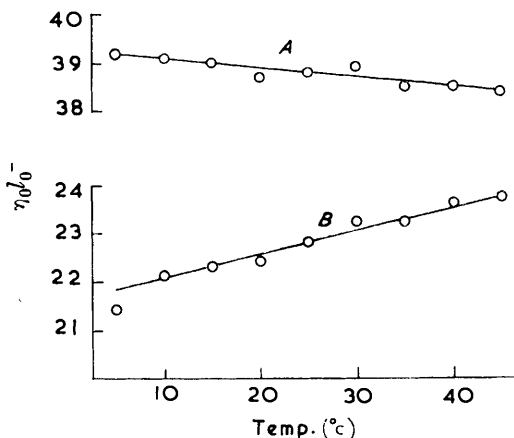
⁸⁸ Ayling, *J.*, 1938, 1014.

to rise of temperature. This, conceivably, could be the reason why $-\Delta C_P^\circ$ for the ionisation of di-isopropylcyanoacetic acid shows no tendency to increase with temperature above 30°C , as may be the case for cyanoacetic acid. The increase claimed for the latter was attributed to the collapsing "water structure opposition" to charge-induced ionic hydration. The alkylated ion might have an equally collapsing degree of hydrophobic hydration, so that opposed effects on $-\Delta C_P^\circ$ might cancel out. This conjecture receives a little support from the values of the Walden products, $\eta_0 l_0^-$, over a range of temperatures; these are shown graphically in Fig. 4, and are of self-evident significance.

FIG. 4. Walden products, $\eta_0 l_0^-$, for cyanoacetate and di-isopropylcyanoacetate ions in aqueous solution, from 5 to 45° (η_0 and l_0^+ data from Robinson and Stokes, "Electrolytic Solutions," 2nd edn., Butterworths, London, 1959).

A, Cyanoacetate ion;

B, Di-isopropylcyanoacetate ion.



(e) *Comment on the Compensation Law.*—A brief summary of the ways in which compensation may arise is necessary to show the possibly wide application of the views developed in section (c).

In considering this feature of chemical reactions in the fields of both of equilibria and reaction rates, Evans and Polanyi²⁶ used the partial derivative, β , of free energy with respect to a generalised parameter of state, χ . If χ were pressure, the significant derivatives were the volumes of reactants and products, or the intermediate volume of the transition state. The parameter χ could, however, relate to the indefinable "molecular field" at a reaction site, a function, *inter alia*, of the structure of the non-reacting molecular residue of a reactant molecule. For the members of a set (A) of mechanistically identical reactions χ took successive values $\chi^{A_1}, \chi^{A_2}, \dots$. For another set (B) of such reactions, not chemically dissimilar from the first and subject to the same structural modifications from member to member, the corresponding values of χ would be $\chi^{B_1}, \chi^{B_2}, \dots$. Then, it being assumed that $\chi^{A_1}/\chi^{B_1} = \chi^{A_2}/\chi^{B_2} = q = \text{const.}$, a basis was found for linear free energy relations then familiar in the form

$$\ln K^{A_i} = \alpha \ln K^{B_i} + \text{const.}$$

where $i = 1, 2, \dots$ and $\alpha = q \cdot (\beta_1 - \beta_2)^A / (\beta_1 - \beta_2)^B$, β_1 and β_2 relating to reactants and products, respectively.

This treatment was extended to all the possible comparisons between rate and equilibrium constants taken in pairs, with appropriate use of β_1^\ddagger or β_2 , and the conditions under which β_1^\ddagger would be expected to lie between β_1 and β_2 for a given reaction (as the evidence required) were indicated. The importance of this concept, as emphasised by Hammett,⁸⁹ lay in the fact that it was possible to represent by a continuous function the essentially discontinuous effect of the change in structure of a reactant. It seemed unlikely that the regularity in the behaviour of free energy, so strikingly emphasised in this treatment, could be preserved except by the existence of an equal regularity in the partial

⁸⁹ Hammett, *Trans. Faraday Soc.*, 1938, **34**, 156.

derivatives of enthalpy and entropy with respect to the same essentially continuous parameter of state, χ . This also implies regularity of relationship between the ΔH° and ΔS° values, varying as functions of χ , for the members of a "reaction set." Taking into account the dependence on χ of components of free energy which do, or do not, depend on temperature, Evans and Polanyi showed that the variations in ΔH° and $T\Delta S^\circ$, in contributing to ΔG° , might be in mutual support or opposition. Evidence was presented to the effect that support is likely if χ is an "external force," opposition when χ is "a force intrinsic to the reacting system." It is in the latter circumstance, therefore, that compensation is to be expected, but, arising from a generalised thermodynamic argument dealing only with functions which are "well-behaved" with respect to each other, it does not seem to be particularly noteworthy, and could well be called "the normal compensation effect." Reasons for the corresponding parallelism between frequency factors and activation energies can be found in theories of reaction kinetics;⁹⁰ they amount to a statement that the density of energy states increases with the energy.⁹¹

The present interest is in compensation of a different order which cancels out, in ΔG° , the quite wild "ill-behaviour" of ΔH° and ΔS° , in the sense of their individual lack of regular dependence on a structural parameter. Since this "abnormal compensation effect" is confined to reactions in solution, it has been considered in terms of the transfer (usually hypothetical) of reactions from the gas to the solution phase.^{41,92} This introduces the complication of non-ideality in solution systems with the associated problems of the effects of short-range forces and factors concerned with molecular shapes and sizes. Little clarification is promised were it not for the fact that the solution process is one in which well-marked compensation has been observed. If compensation occurs between ΔH° and $T\Delta S^\circ$ of transfer of reactants, transition complexes and products (some, not necessarily all) from gas to solution phases, this alone would introduce a degree of compensation between ΔH° and $T\Delta S^\circ$ for the solution reaction, even if there were none between these functions for the corresponding gas-phase reaction. It is then a short step to the proposal that compensation in solution reactions is mainly to be attributed to solvation changes. That solvation is indeed a major source of this effect has been clearly stated,⁹³ and is particularly strongly supported by examples of precise balancing, for a given reaction, of the ΔH^\ddagger and $T\Delta S^\ddagger$ variations (reasonably to be assigned to solvation changes alone) produced by increase of pressure.⁹⁴

Compensation between ΔH° and $T\Delta S^\circ$ for dissolution processes of molecular solutes, however, seems to arise in more than one way. Evans and Polanyi²⁶ assembled heats and entropies of solution for binary systems chosen from some 80 organic compounds, 15 of which appeared both as solute and solvent. The solutions concerned varied widely in type and in concentration at saturation. It was found that, for a given solute in a range of solvents, the relation $\Delta H^\circ = \alpha\Delta S^\circ + \text{const.}^*$ was followed remarkably closely, with, moreover, values of α varying only by $\pm 30\%$ for all the systems. In such cases it is very likely that the solubility of a single solute varies from one solvent to another primarily because of variation in solute-solvent interaction. Since solvation involves entropy loss, such interaction can promote dissolution only because it is exothermic; equilibria are largely determined by the negative ΔH° of solute-solvent action, with the corresponding ΔS° term playing a minor, unfavourable part. The source of this kind of compensation can be seen in the fact that the same solvation effect which makes the over-all ΔH° less positive or more negative induces changes in ΔS° in the same direction.

Evans and Polanyi²⁶ found only the most restricted correlation between ΔH° and ΔS°

* Standard states: solutes, normal states of aggregation; solutions, unspecified, but obviously uniform.

⁹⁰ Hinshelwood and Blackadder, *J.*, 1958, 2728; Fairclough and Hinshelwood, *J.*, 1937, 538.

⁹¹ Frost and Pearson, "Kinetics and Mechanism," 2nd edn., Wiley, New York, 1961, p. 108.

⁹² Wynne-Jones and Eyring, *J. Chem. Phys.*, 1935, 3, 492.

⁹³ Laidler, *Trans. Faraday Soc.*, 1959, 55, 1725.

⁹⁴ Laidler, *Discuss. Faraday Soc.*, 1956, 22, 88.

for the dissolution of a range of solutes (in standard gaseous states) in a given solvent. Yet, remarkably, it is the latter kind of correlation, and not that for a given solute in a range of solvents, which has since been most frequently encountered. The reason for this contrast probably lies in the types of system studied. The first relation (single solute, many solvents) seems to apply when "solute" cannot properly be distinguished from "solvent," except as the common component of a set of binary systems, within which behaviour is graded according to the ΔH° of inter-component action. If either component could be regarded as mainly in control, it would be the common "solute." The second relation (single solvent, many solutes) is found when there is no ambiguity in defining the solvent. This was the case for the solutions of gases, each in a selection of organic solvents, studied by Bell⁹⁵ who distinguished, in effect, between what may be called "solute-controlled" and "solvent-controlled" systems. Low molecular weights and solubilities of solutes, and low interaction energies with the solvent, are understandably favourable, but not essential, conditions for realisation of this wider enthalpy-entropy relation which has become known as the Barclay and Butler rule.⁹⁶ This rule has been incorporated into the "free volume theory" of liquids by Frank,⁹⁷ who has expressed its physical meaning in terms of the fall of a molecule (of solute or solvent) from the free state into a potential well in the liquid phase. The deeper this well, the narrower it is, the smaller the free volume, the greater the restriction of molecular motions, and the greater the loss in entropy. This picture is consistent with the concept of solvent-controlled behaviour, or with the decisive role of the "solvent reaction." This solvent reaction becomes of unique importance for the dissolution of non-polar molecules (or molecules with non-polar residues) in water. It was the well-marked enthalpy-entropy linearity observed for such dissolutions,⁹⁸ together with the excessive entropy loss, which led to the concept of hydrophobic hydration.⁶⁷ It is clear that for such aqueous systems it is the negative enthalpy and negative entropy of *solvent-solvent* interaction which are decisive in controlling solubility.

For ionic solutes, with very powerful solute-solvent interactions and complex "solvent-solvent repercussions," the problems attain their maximum complication in ways which cannot be further outlined.

In general, it is evident that the analysis of ΔG° for dissolution equilibria involves a very wide range of possibilities and can hardly be taken beyond the evaluation of ΔH° and $T\Delta S^\circ$, except by indirect inference. How these enthalpy and entropy terms are to be divided between solute-solvent and solvent-solvent effects, which of them (if either) can be regarded as determinative, and how, on a molecular basis, changes of properties are to be partitioned between effects of solvent on solute or of solute on solvent are questions with no easily accessible answers. Since these complexities apply variously to every species participating in a reaction, it is evident that the hypothetical transfer of a reaction between gas and solution phases can do little more than indicate the grounds on which compensation in solution reactions is so often to be expected.

It is in this context that the treatment used earlier in this Paper may be helpful. Overriding the obscurities associated with the total solvation of each species, there is the consideration that, for any reaction in solution which involves a net change in solvation, there must be contributions (ΔH^h and $T\Delta S^h$) to ΔH° and $T\Delta S^\circ$ (or, tacitly elsewhere, to ΔH^\ddagger and $T\Delta S^\ddagger$) which are equal to each other at all temperatures, as long as solvation equilibria are preserved. Some of the implications of this can be clearly seen.

For a set of allied reactions conforming to a linear free energy relation, it is obvious that each or any member reaction might be subject to specific solvation effects, but, however eccentric the individual values of ΔH^h and $T\Delta S^h$, there would be no disturbance of the free energy relation.

⁹⁵ Bell, *Trans. Faraday Soc.*, 1937, **33**, 496.

⁹⁶ Barclay and Butler, *Trans. Faraday Soc.*, 1938, **34**, 1445.

⁹⁷ Frank, *J. Chem. Phys.*, 1945, **13**, 493.

⁹⁸ Butler, *Trans. Faraday Soc.*, 1937, **33**, 229.

If, for a hypothetical set of reactions, ΔH^r and $T\Delta S^r$ had, separately, identical values for each member reaction, then variation of $\Delta H^h = T\Delta S^h$ between the members would lead to a linear plot of ΔH° against ΔS° of slope T , and all the reactions would have the same value of ΔG° . This precise balancing, however, could occur only at one temperature of comparison because ΔH^r and $T\Delta S^r$ are each separate and unique functions of temperature and cannot (unlike ΔH^h and $T\Delta S^h$) remain equal to each other, nor show strictly parallel variation, over a range of temperatures.

A more common situation is probably that ΔH^r is correlated with ΔS^r for a set of reactions by a "normal compensation," arising from one of the factors not directly associated with solvation. Then $\Delta H^r = \alpha\Delta S^r + \text{const.}$, where α is a constant with the dimensions of temperature. If, superimposed on this, each member of the set has its own $\Delta H^h = T\Delta S^h$, several possibilities arise. If α happens to be equal to T , the common temperature at which the reactions are compared, the original correlation is preserved, but this is regarded as a special, coincidental case. If $\alpha \neq T$, there will be various alternatives according to the effects of the parameter χ (by which the members differ from one another) on the "solute reaction proper" or on the "associated solvent reaction." Let it be supposed in the first place that these effects are independent of each other. As long as the effect on ΔH^h is small compared with that on ΔH^r , the correlation will be little disturbed. If, however, the effect on ΔH^h is large compared with that on ΔH^r , and unrelated to it, the correlation may be destroyed, with a consequent wide scatter in the plot of ΔH° against ΔS° . In the second place, it is possible that the dependences of ΔH^r and of ΔH^h on χ may be linked, when correlation will be retained, and the compensation law will operate. This could well be the case for the effects of polar substituents which, in providing a field, would influence a charge-transfer process and an ionic solvation in related ways.

In the general context of equilibria or reaction rates, the coefficient β in the expression $\Delta H^\circ = \beta\Delta S^\circ + \text{const.}$ or $\Delta H^\ddagger = \beta\Delta S^\ddagger + \text{const.}$ has been called either the isoequilibrium temperature or the isokinetic temperature.¹⁹ According to the extent to which the associated solvent reaction contributes to the compensation which is implied in these relationships, there will be a tendency for β to be "pulled" towards the temperature (or the average temperature, \bar{T}) at which the comparisons are made. This is perhaps why a rather high proportion of the reactions reviewed by Leffler¹⁹ have isokinetic temperatures not far removed from \bar{T} . If, in relation to dissolution equilibria, the distinction between solute-controlled and solvent-controlled systems is valid, a similar distinction may perhaps be useful for reactions in solution. This division may be broadly related to the division of reactions into those which are "governed" by ΔH^\ddagger rather than by ΔS^\ddagger ($\beta > \bar{T}$), or by ΔS^\ddagger rather than by ΔH^\ddagger ($\beta < \bar{T}$), since ΔH^\ddagger , involving repulsion and bond-making and -breaking energies,⁹⁹ is more intimately concerned with the solute reaction proper, whereas ΔS^\ddagger often largely depends on the associated solvent reaction. The first class of reaction, expected to be less sensitive to solvent variation, is, according to Leffler's review,¹⁹ more numerous than the second, but would become proportionally less so with rising temperature. This suggests that solvent control (and, by implication, solvation) increases in relative significance with rising temperature, or, in terms of the associated solvent reaction, that the relative contribution from a generalised term corresponding with $\Delta H^h = T\Delta S^h$ increases with temperature. Without detailed discussion, it can be seen in terms of ΔS^h that this is likely as long as solvation involves a decrease of heat capacity as well as of entropy, which is not, however, always the case.

The existence of reactions which may be regarded as very specifically solvent-controlled is supported by the interesting example of the influence of the solvent on the hydrolysis of carboxylic esters reported by Tommila and Hella.¹⁰⁰ In acetone-water mixtures covering the whole composition range, three domains were found (low, medium, and high acetone

⁹⁹ Pearson, *J. Chem. Phys.*, 1952, **20**, 1478; Frost and Pearson, "Kinetics and Mechanism," 2nd edn., Wiley, New York, 1961, p. 139.

¹⁰⁰ Tommila and Hella, *Ann. Acad. Sci. Fenn.*, 1954, *A*, **11**, 53, 3.

content), in which separate and distinct relations between \log (frequency factor) and activation energy applied. Clearly, the three main ranges of solvent structure (water-controlled, water-acetone co-operatively determined, acetone-controlled) were decisive in relation to the kinetics of an essentially solvent-controlled reaction.

Finally, a point may be made to emphasise the essential part of the free solvent in determining the thermodynamic effects of the associated solvent reaction.¹⁰¹ The entropy loss accompanying the ionisation of a weak acid in dioxan-water mixtures increases largely in the region of low water content.¹⁰² Examination of this effect in terms of the Born theory (although this does indicate that $-\Delta S^\circ$ passes through a maximum with falling dielectric constant¹⁰³) is less appropriate than consideration of the consumption of high entropy water (not self-associated in dilute solution in dioxan) involved in a net preferential hydration of ions (cf. Aksnes¹⁰⁴).

EXPERIMENTAL

The apparatus and procedure were similar to those previously employed^{1,14} except that a Sullivan standard resistance box (AC 440), in series with a shunted Cambridge resistance box, was used in the measuring bridge arm. The shunting was so arranged as to provide a nearly linear resistance scale of 0.1 ohm, divided in steps of 0.001 ohm. This has the advantage of minimising the effects of contact resistances, and the slight departure from linearity was allowed for in the careful internal calibration of the whole bridge by a standard method.

An attempt was made to improve the accuracy of the conductance measurements by use of a four-electrode cell with separate current-carrying and a.c. potential probe electrodes, which seemed to offer some advantages. This required very rigid, extremely thin electrodes, and construction of them was tried by the deposition of platinum on plane, polished Pyrex surfaces. It is of interest that satisfactorily adherent noble-metal films could be obtained by sputtering or, better, by "platinum paint" (Johnson, Matthey, "Liquid bright platinum G") fired at 680°, but only up to an inadequate limiting thickness. An attempt to thicken such films by electro-deposition of bright platinum from the complex sulphatodinitritoplatinous acid bath (Johnson, Matthey, D.N.S. platinum plating solution) failed in the most remarkable way. After a short period of smooth deposition, the film exfoliated, tearing small lenses of glass out of the underlying surface.

A mechanically unsatisfactory "mock-up" four-electrode cell was studied. It showed an apparent solution resistance which increased with rising frequency to a limiting value, an effect which was intelligible in terms of an electrical model involving a high probe electrode impedance. These attempts were therefore abandoned, and the measurements recorded in this Paper were made with the same double cell as previously, with the same systems of connection and of extrapolation to infinite frequency.^{1,14,105} Cell constants were redetermined.

Another failure in the course of this work arose from the wish to study β -cyanopropionic acid, which had been used in earlier, less accurate conductance work¹⁰⁶ with no observed difficulty. This acid,¹⁰⁶ carefully purified (m. p. 51.35–51.55°), was, however, found to hydrolyse in aqueous solution at a measurable rate, in confirmation of Wideqvist.¹⁰⁷

Di-isopropylcyanoacetic Acid.—This acid was prepared by Marshall's method¹⁰⁸ and was recrystallised five times from intensively purified and dried benzene-ligroin (b. p. 60–80°) mixtures. The product was divided into two parts, one of which was recrystallised five times again from the same solvent, desiccated in vacuum, and sublimed at 45°/10⁻⁵ mm. (sample *A*). The other part was converted into the potassium salt with cold, methanolic potassium hydroxide. The salt was crystallised, washed with methanol and ether, and dissolved in water. The aqueous solution was acidified (HCl), ether-extracted, and the ether extract was dried (CaSO₄),

¹⁰¹ Bell, *J.*, 1943, 629.

¹⁰² Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," 3rd edn., Reinhold, New York, 1958, p. 667.

¹⁰³ Frost and Pearson, "Kinetics and Mechanism," 2nd edn., Wiley, New York, 1961, p. 136.

¹⁰⁴ Aksnes, *Acta Chem. Scand.*, 1962, **16**, 1967.

¹⁰⁵ Feates, Ives, and Pryor, *J. Electrochem. Soc.*, 1956, **103**, 580.

¹⁰⁶ Ives and Sames, *J.*, 1943, 513.

¹⁰⁷ Wideqvist, *Arkiv Kemi*, 1951, **3**, 281.

¹⁰⁸ Marshall, *J.*, 1930, 2754.

filtered, and evaporated to provide the acid. The acid so obtained was recrystallised and sublimed as before (sample *B*). The constants for the two samples, determined as previously,¹ were: *A*; equiv., 169.35 ± 0.15 ; m. p. $98.25-98.55^\circ$; *B*; equiv., 169.20 ± 0.15 , m. p. $98.10-98.45^\circ$ (Calc.: equiv. 169.23). The m.p.s are higher than those previously recorded (97.5° ¹⁰⁸), and both samples gave the same conductance results within experimental error. No sign of decomposition on intensive desiccation,¹ nor of hydrolysis in aqueous solution, was observed.

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