

Aqueous Solutions Containing Amino Acids and Peptides

Part 10.—Enthalpy of Interaction of Glycine with some Alkali Metal Chlorides at 298.15 K

BY TERENCE H. LILLEY,* EDWIN MOSES AND IAN R. TASKER†

Chemistry Department, The University, Sheffield S3 7HF

Received 1st June, 1979

The enthalpies of mixing of aqueous glycine and aqueous alkali metal chloride solutions have been investigated at 298.15 K using a microcalorimetric method. The salts investigated were LiCl, NaCl, KCl and CsCl. The experimental data have been used to determine pairwise enthalpy of interaction coefficients and from these and earlier corresponding free energy coefficients the entropy coefficients have been obtained. The results indicate that the lithium ion interacts with glycine in a markedly different way to the other cations, even though the free energy coefficients are quite similar.

NOTATION

B^*	McMillan-Mayer second virial coefficient
E_i°	Partial molar expansibility of species i in its standard state
H^{ex}	Excess specific (1 kg of solvent) enthalpy of a solution
$H_{m,\text{MX}}^{\text{ex},\circ}(m)$	Molar excess enthalpy of a solution containing only electrolyte MX at molality m
$H_{m,\text{A}}^{\text{ex},\circ}(m_{\text{A}})$	Molar excess enthalpy of a solution containing only non-electrolyte A at molality m_{A}
L	Avogadro constant
M_s	Relative molar mass of solvent
R	Gas constant
T	Temperature (in K)
V_i°	Partial molar volume of species i in its standard state
a	McMillan-Mayer free energy parameter representing the sum of the cation and anion pairwise interactions with a non-electrolyte
a_{ij}	McMillan-Mayer free energy parameter for species i with j
a', a''	Number of kilogrammes of solvent in the solution containing salt MX, on the "reaction" and "reference" sides of the calorimeter
b'	Number of kilogrammes of solvent in the solution containing non-electrolyte on the "reaction" side of the calorimeter
b''	Number of kilogrammes of solvent on the "reference" side of the calorimeter
g	Lewis-Randall free energy parameter representing the sum of the cation and anion pairwise interactions with a non-electrolyte
g_{ij}	Lewis-Randall free energy parameter for species i with j

† Present address: Chemistry Department, University of Delaware, Newark, Delaware 19711, U.S.A.

h	Lewis–Randall enthalpy parameter corresponding to g
h_{ij}	Lewis–Randall enthalpy parameter corresponding to g_{ij}
$h_A^{\text{ex}}, h_{\text{MX}}^{\text{ex}}, h_{\text{MX,W}}^{\text{ex}}, h_{\text{MX,A}}^{\text{ex}}$	Excess enthalpies of solutions containing non-electrolyte A, electrolyte MX before dilution, electrolyte MX after dilution and a mixture of MX and A, respectively
m	Molality of electrolyte
m_A	Molality of non-electrolyte
m', m''	Molality of electrolyte after dilution in the “reaction” and “reference” sides of the calorimeter
m'_A	Molality of non-electrolyte after dilution
$\Delta q, \Delta q^{\text{corr}}$	Experimental and corrected enthalpy changes
s	McMillan–Mayer or Lewis–Randall entropy coefficients representing the sum of the pairwise interactions between cation and non-electrolyte and anion and non-electrolyte
s_{ij}	McMillan–Mayer or Lewis–Randall pairwise interaction entropy coefficient for species i with j
u	McMillan–Mayer energy term corresponding to a
u_{ij}	McMillan–Mayer energy term corresponding to a_{ij}
κ	Isothermal compressibility of solvent

The thermodynamic description of the interaction of the components of proteins with ionic and non-ionic species has occupied our attention for some time.¹⁻⁹ Most of the work described hitherto has been concerned with free energy investigations of one sort or another but we have recently shown⁴ that the enthalpy of interaction of glycine with sodium chloride behaves in an unexpected way. The object of the present work was to reinvestigate this system using a more appropriate calorimetric technique and to extend the measurements to those systems for which free energy data are available.

EXPERIMENTAL

The preparation and purification of materials have been described elsewhere.⁵ Calorimetric measurements were made using a LKB batch microcalorimeter.

On the “reaction” side of the calorimeter, accompanying the mixing process there are contributions to the enthalpy change arising from: (i) the interaction of the salt (MCl) with the amino acid (A), (ii) the heat of dilution of MCl and (iii) the heat of dilution of A.

In order to investigate (i), which is our concern here, allowance must be made for contributions (ii) and (iii). Experimentally the situation is made easier by “backing off” most of the heat of dilution of the electrolyte by mixing salt solution with water in the “reference” side of the calorimeter. The experiments were performed so that $a' \approx a''$, $b' \approx b''$ and hence $m' \approx m''$. Thus most of the heat of dilution of MCl to the overall heat change on the “reaction” side of the calorimeter was cancelled and the small corrections necessary arising from the inequalities of a' and a'' and b' and b'' were made using literature¹⁰ heat of dilution data. Contribution (iii) above was calculated using previous results.^{11, 12} The molalities of the solutions investigated were in the range 0.2–1.5 mol kg⁻¹.

DATA TREATMENT AND RESULTS

Consider a solution containing 1 kg of solvent, an electrolyte MX of molality m and a non-electrolyte A of molality m_A . The excess enthalpy of such a solution is given by

$$H^{\text{ex}} = [mH_{m,\text{MX}}^{\text{ex},\circ}(m) + m_A H_{m_A}^{\text{ex},\circ}(m_A)] + 2mm_A(h_{\text{MA}} + h_{\text{XA}}) + 3m^2m_A(h_{\text{MMA}} + 2h_{\text{MXA}} + h_{\text{XXA}}) + 3mm_A^2(h_{\text{MAA}} + h_{\text{XAA}}) + \dots \quad (1)$$

where we have used the usual polynomial expansion in solute molalities. In eqn (1) $H_{m,MX}^{ex,\circ}(m)$ and $H_{m,A}^{ex,\circ}(m_A)$ are the molar excess enthalpies of single solute solutions containing MX at molality m and A at molality m_A , respectively. (These are sometimes called relative apparent molar enthalpies and given the symbol ϕ_L .) The coefficients h_{ijk} are enthalpy terms representing the interaction between the sub-scripted species. We have changed our previous terminology to bring it in line with that of others.¹³⁻¹⁵

In terms of eqn (1) the enthalpies of the various solutions before and after mixing are:

Reaction side

(i) for the starting solutions

$$h_{MX}^{ex} = ma'H_{m,MX}^{ex,\circ}(m) \quad (2)$$

$$h_A^{ex} = m_A b'H_{m,A}^{ex,\circ}(m_A) \quad (3)$$

(ii) for the mixed solution

$$\begin{aligned} h_{MX,A}^{ex} = & ma'H_{m,MX}^{ex,\circ}(m') + m_A b'H_{m,A}^{ex,\circ}(m'_A) + \\ & (a' + b')[2(h_{MA} + h_{XA}) + 3(h_{MMA} + 2h_{MXA} + h_{XXA})m' + \\ & 3(h_{MAA} + h_{XAA})m'_A + \dots]m'm'_A. \end{aligned} \quad (4)$$

Reference side

(i) for the starting solution

$$h_{MX}^{ex} = ma''H_{m,MX}^{ex,\circ}(m) \quad (5)$$

(ii) for the diluted solution

$$h_{MX,W}^{ex} = (a'' + b'')m''H_{m,MX}^{ex,\circ}(m'') = ma''H_{m,MX}^{ex,\circ}(m''). \quad (6)$$

The experimental enthalpy change (Δq) is therefore given by (4) - (2) - (3) - (6) + (5) which becomes, after a little rearrangement,

$$\begin{aligned} \Delta q = & m\{a'[H_{m,MX}^{ex,\circ}(m') - H_{m,MX}^{ex,\circ}(m)] - a''[H_{m,MX}^{ex,\circ}(m'') - H_{m,MX}^{ex,\circ}(m)]\} + \\ & m_A b'[H_{m,A}^{ex,\circ}(m'_A) - H_{m,A}^{ex,\circ}(m_A)] + \\ & (a' + b')m'm'_A[2(h_{MA} + h_{XA}) + 3(h_{MMA} + 2h_{MXA} + h_{XXA})m' + \\ & 3(h_{MAA} + h_{XAA})m'_A] + \dots \end{aligned} \quad (7)$$

The first two terms in this equation are calculable and consequently we define a term Δq^{corr} which is the experimental enthalpy corrected for electrolyte¹⁰ and non-electrolyte dilutions,^{11, 12} i.e.,

$$\begin{aligned} \Delta q^{corr} = & (a' + b')m'm'_A[2(h_{MA} + h_{XA}) + 3(h_{MMA} + 2h_{MXA} + h_{XXA})m' + \\ & 3(h_{MAA} + h_{XAA})m'_A + \dots]. \end{aligned} \quad (8)$$

In practise we prepared solutions so that the molalities of the electrolyte and non-electrolyte in the unmixed solutions were the same ($m = m_A$) and so

$$\begin{aligned} [\Delta q^{corr}(a' + b')/m^2 a' b'] = & 2(h_{MA} + h_{XA}) + 3(h_{MMA} + 2h_{MXA} + h_{XXA})m' + \\ & 3(h_{MAA} + h_{XAA})m'_A + \dots \end{aligned} \quad (9)$$

Table 1 lists some data on the NaCl + glycine system to illustrate the magnitudes of the various correction terms which must be applied to obtain the quantity of interest. The remainder of the raw experimental data are listed elsewhere^{16, 17} as are the triplet terms in eqn (9). (Terms higher than triplets were not required.)

The experimental results obtained were fitted to eqn (9) by a least-squares routine and the pairwise enthalpy parameters obtained are given in table 2.

TABLE 1.—ILLUSTRATIVE ENTHALPY DATA FOR THE SYSTEM NaCl+GLYCINE

m /mol kg ⁻¹	m_A /mol kg ⁻¹	$10^3 a'$ /kg	$10^3 b'$ /kg	$10^3 a''$ /kg	$10^3 b''$ /kg	$-\Delta q$ /J
1.4999	1.4998	1.8034	1.8661	1.7717	1.7734	1.166
1.0001	0.9996	2.0814	1.9092	1.7932	2.0912	0.550
0.7499	0.7502	2.0613	1.7028	1.8304	2.0584	0.294
0.5001	0.5000	2.1820	2.1327	2.1082	2.1003	0.148
0.2500	0.2497	1.7001	2.0021	1.9697	1.9066	0.0323
$H_{m,MX}^{ex,\circ}(m)$ /J mol ⁻¹ kg	$H_{m,MX}^{ex,\circ}(m')$ /J mol ⁻¹ kg	$H_{m,MX}^{ex,\circ}(m'')$ /J mol ⁻¹ kg	$H_{m,A}^{ex,\circ}(m_A)$ /J mol ⁻¹ kg	$H_{m,A}^{ex,\circ}(m_A')$ /J mol ⁻¹ kg		
-414.21	86.40	77.77	-521.94	-299.46		
-97.07	228.32	263.81	-377.26	-197.07		
77.56	291.64	320.07	-295.14	-143.04		
241.22	357.33	357.96	-205.17	-105.89		
358.09	356.75	361.32	-106.91	-59.03		
$ma'[H_{m,MX}^{ex,\circ}(m') - H_{m,MX}^{ex,\circ}(m)]/J$	$ma''[H_{m,MX}^{ex,\circ}(m'') - H_{m,MX}^{ex,\circ}(m)]/J$	$m_A b'[H_{m,A}^{ex,\circ}(m_A') - H_{m,A}^{ex,\circ}(m_A)]/J$	$-\Delta q^{corr}$ /J			
1.354	1.309	0.623	1.834			
0.677	0.647	0.344	0.924			
0.331	0.333	0.194	0.486			
0.127	0.123	0.106	0.258			
-0.001	0.002	0.024	0.0533			

TABLE 2.—LEWIS-RANDALL SCALE PAIRWISE INTERACTION PARAMETERS FOR ALKALI METAL CHLORIDES AND GLYCINE AT 298.15 K

salt	$g/J \text{ kg mol}^{-2}$	$h/J \text{ kg mol}^{-2}$	$Ts/J \text{ kg mol}^{-2}$
LiCl	-543 ± 15	71 ± 9	614 ± 24
NaCl	-616 ± 17	-504 ± 8 (-446^a) (-499 ± 25^b)	112 ± 25
KCl	-501 ± 7	-490 ± 10	11 ± 17
CsCl	-575 ± 45	-508 ± 3	67 ± 44

The errors correspond to the 95 % confidence limits obtained from the least-squares fitting procedure. ^a J. W. Larson and D. G. Morrison, *J. Phys. Chem.*, 1976, **80**, 1449. J. W. Larson, W. J. Plymale and A. F. Joseph, *J. Phys. Chem.*, 1977, **81**, 2074. It was difficult to estimate the possible error in the coefficient because of the way the experiments were carried out. ^b B. P. Kelley and T. H. Lilley, *J. Chem. Thermodynamics*, 1978, **10**, 703.

DISCUSSION

We have included in table 2 the free energy⁵ and entropy terms for the systems studied. These pairwise coefficients are shown in fig. 1. The free energy term does not vary monotonically with increasing ion size and, in an approximate manner at least, the free energy term is independent of the cation. This is in marked contrast to the corresponding enthalpy terms for which the lithium salt is markedly different to those of the other salts investigated. This does indicate that the lithium ion interacts with glycine in a different way to the other alkali metal ions. It is not, of course, possible to consider the absolute values of the contributions from the various cations since the chloride ion also contributes to the terms. Essentially all one can do is consider the trends within the series given that the experimental coefficients should be ion additive. Thus the enthalpy and entropy coefficients for the lithium ion are considerably greater in a more positive sense than the corresponding terms for the other alkali metal ions.

The principal contribution to the interaction between a metal ion and glycine probably occurs through the carboxylate region of the zwitterionic head of the amino acid. The qualitative conclusion which may be drawn from the experimental data

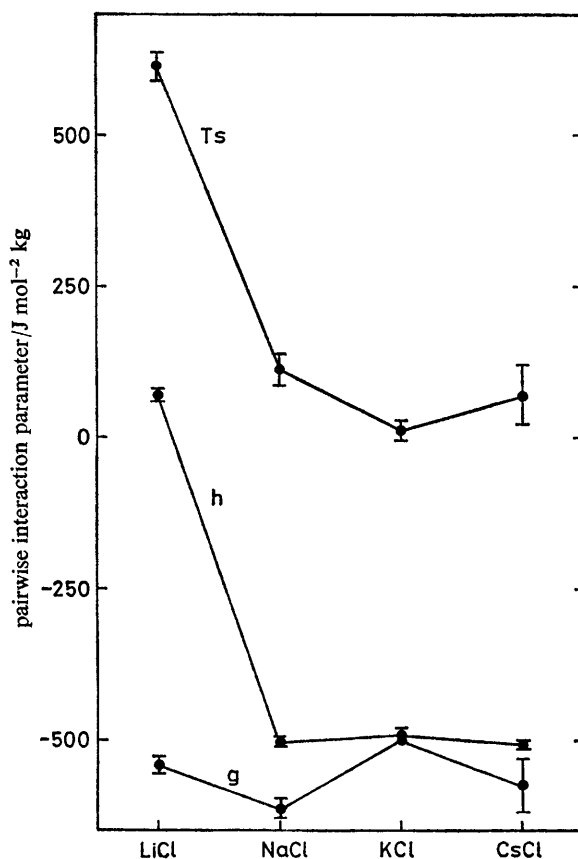


FIG. 1.—Dependence of the LR pairwise interaction terms for glycine + alkali metal chlorides on metal ion.

and in particular from the entropy series (by the use of an argument based only upon the "freedom" of solvent molecules) is that in the interaction between cation and amino acid there are water molecules in the carboxylate and ion cosphere regions which are firmly held and which are expelled from the solvation regions when the species are in proximity.¹⁸ One qualitatively imagines that the solvent peripheral to the lithium ion is held in a much more restricted way than that for the other alkali metal ions and indeed n.m.r. relaxation data indicates that this is so as too does the very high solubility of many lithium salts. The considerably higher enthalpy coefficient is also indicative of energy needing to be supplied to the system when the species approach and this energy would presumably be needed to strip off the solvent molecules from the lithium ion.

TABLE 3.—McMILLAN-MAYER SCALE PAIRWISE INTERACTION PARAMETERS FOR ALKALI METAL CHLORIDES AND GLYCINE AT 298.15 K

salt	$a/\text{J dm}^3 \text{ mol}^{-2}$	$u/\text{J dm}^3 \text{ mol}^{-2}$	$Ts/\text{J dm}^3 \text{ mol}^{-2}$
LiCl	-418 ± 15	27 ± 19	445 ± 34
NaCl	-490 ± 17	-564 ± 18	-74 ± 35
KCl	-363 ± 7	-553 ± 15	-190 ± 22
CsCl	-422 ± 45	-560 ± 13	-138 ± 58

The error limits included in this table were obtained assuming no error in the volumetric data of the compounds used, but with an error corresponding to a total of $\pm 10 \text{ J dm}^3 \text{ mol}^{-2}$ from the expansibility data.

The above representation, although superficially attractive, does need some reconsideration since part at least of the trends observed are related to the choice of standard states. In earlier papers^{2, 3, 5-9} we have discussed the use of the McMillan-Mayer (MM) standard states rather than the Lewis-Randall (LR) states.¹⁹ In the spirit of our adoption of more popular terminology, rather than continue with our earlier notation, we define the corresponding MM coefficients a , u and s for the pairwise free energy, internal energy and entropy coefficients in the MM state. The free energy term is related to our earlier terminology by

$$a = (RT LB^*/2).$$

We thus have for salt + non-electrolyte mixtures

$$(a_{\text{Mi}} + a_{\text{Xi}}) = V_s^\circ M_s^{-1}(g_{\text{Mi}} + g_{\text{Xi}}) + RT(V_{\text{MX}}^\circ + 2V_i^\circ - 2RT\kappa)/2$$

$$(u_{\text{Mi}} + u_{\text{Xi}}) = M_s^{-1}[V_s^\circ(h_{\text{Mi}} + h_{\text{Xi}}) - TE_s^\circ(g_{\text{Mi}} + g_{\text{Xi}})] -$$

$$RT^2(E_{\text{MX}}^\circ + 2E_1^\circ - 2R\kappa)/2$$

$$(s_{\text{Mi}} + s_{\text{Xi}}) = [(u_{\text{Mi}} + u_{\text{Xi}}) - (a_{\text{Mi}} + a_{\text{Xi}})]/T.$$

In table 3 we list values of the above coefficients calculated from the LR coefficients given in table 2 and appropriate volumetric data.²⁰⁻²² The general trends observed in the LR data prevail in the transposed data but the transposition does change the numerical values and also changes the sign of the entropy terms for the Na, K and Cs salts.

It is convenient to consider that a gross free energy parameter is composed of three contributions arising from excluded volume effects, electrostatic effects and a solvent reorganisation term. In our previous work we have assumed that the

excluded volume effect could be approximated by considering that the interacting molecular species could be represented as hard bodies. Attempts have been made²³ to use "softer" repulsive potential energy profiles for solute-solute interactions in aqueous solutions but even though the adoption of such an approach will be nearer molecular reality, it necessarily would introduce extra parameters in the present instances. In view of this we have continued to assume hard-body repulsions as representations of the excluded volume effect. As earlier we also assume that the electrostatic contribution is given by the Kirkwood^{24, 25} approximation, *i.e.*, the electrostatic interactions are represented by a model similar to the Debye-Hückel model for electrolytes. This is also an approximation and the solvent-reorganisation term is a catch-all which allows not only for changes in the solvent on bringing solvated species into juxtaposition but also absorbs any deficiencies in the excluded volume and electrostatic terms. These various contributions to the MM parameters are

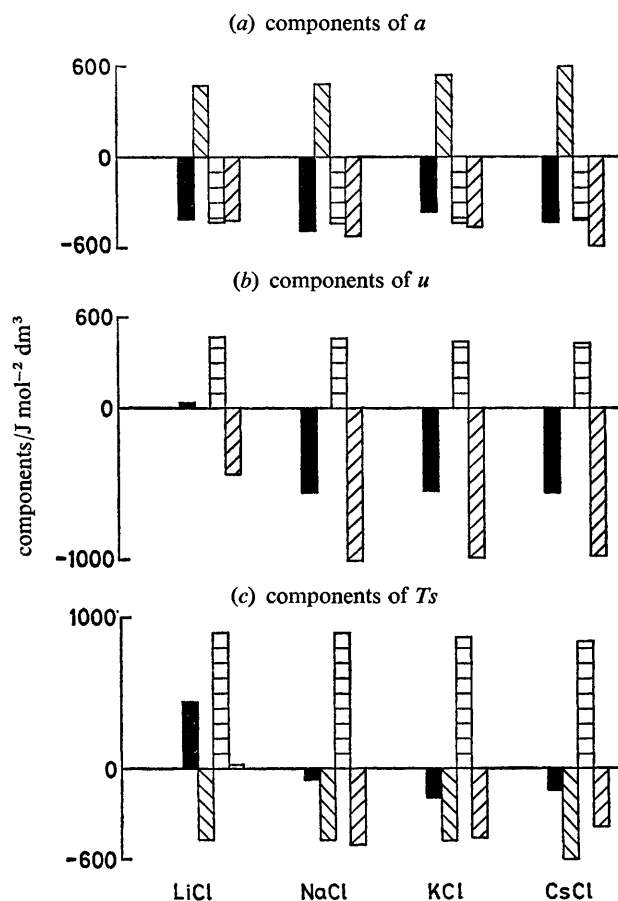
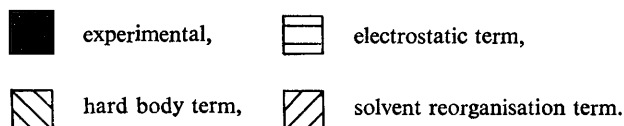


FIG. 2.—Deconvolution of the MM pairwise interaction terms for glycine+alkali metal chlorides :



shown in fig. 2. In constructing this figure the radius of the glycine was approximated from partial molar volume data after allowing for electrostriction²⁶ and the ionic radii were obtained from Robinson and Stokes' text.²⁷

As was pointed out earlier⁵ the experimental free energy coefficients are fairly well represented by the electrostatic term only, *i.e.*, the excluded volume terms and the solvent reorganisation terms are in each instance approximately equal and opposite. When the components of the free energy terms are considered [see fig. 2(b) and (c)] corresponding compensation does not occur and indeed for the internal energy term it is only for lithium chloride that the electrostatic term gives the correct sign. This seems unusual even though one expects from general chemical experience that the lithium ion would behave in a different way to the other alkali metal ions.

The general qualitative features discussed above are borne out by this deconvolution of the MM parameters in that the solvent reorganisation contribution for the lithium salt is much more positive than that for the other salts. Also, an argument based on "localised hydrolysis"²⁸ would not explain the observed features in that for such a mechanism the contribution to the entropy and the energy from the solvent would be more negative for the lithium salt than the other salts.

In conclusion within the limits imposed by the deficiencies of the deconvolution it seems that what one is seeing is a manifestation of what may be termed hydrophilic-hydrophilic interaction between the amino acid and the cation. The lithium ion apparently interacts favourably with the carboxylate group with considerable exclusion of solvent with concomitantly high entropy and energy changes. The solvent perturbation induced by the other alkali metal cations in their interaction with glycine appears to be quite different.

We acknowledge financial support from the S.R.C. to E. M. and I. R. T. and from the A.R.C. for an equipment grant. We dedicate this paper to the memory of R. A. Robinson, a scientific, gentle man.

¹ C. C. Briggs, T. H. Lilley, J. Rutherford and S. Woodhead, *J. Solution Chem.*, 1974, **3**, 649.

² T. H. Lilley and R. P. Scott, *J.C.S. Faraday I*, 1976, **72**, 184.

³ T. H. Lilley and R. P. Scott, *J.C.S. Faraday I*, 1976, **72**, 197.

⁴ B. P. Kelley and T. H. Lilley, *J. Chem. Thermodynamics*, 1978, **10**, 703.

⁵ B. P. Kelley and T. H. Lilley, *J. C. S. Faraday I*, 1978, **74**, 2771.

⁶ B. P. Kelley and T. H. Lilley, *Canad. J. Chem.*, 1980, in press.

⁷ T. H. Lilley and I. R. Tasker, *J. Chem. Thermodynamics*, 1980, in press.

⁸ B. P. Kelley and T. H. Lilley, *J.C.S. Faraday I*, 1978, **74**, 2779.

⁹ B. P. Kelley and T. H. Lilley, *J. Chem. Thermodynamics*, 1979, **11**, 513.

¹⁰ J. L. Fortier and J. E. Desnoyers, *J. Solution Chem.*, 1976, **5**, 297.

¹¹ F. T. Gaucker, H. B. Pickard and W. L. Ford, *J. Amer. Chem. Soc.*, 1940, **62**, 2698.

¹² W. E. Wallace, W. F. Offutt and A. L. Robinson, *J. Amer. Chem. Soc.*, 1943, **65**, 347.

¹³ J. J. Savage and R. H. Wood, *J. Solution Chem.*, 1976, **5**, 733.

¹⁴ F. Franks, M. Pedley and D. S. Reid, *J.C.S. Faraday I*, 1976, **72**, 359.

¹⁵ H. L. Friedman and C. V. Krishnan, *J. Solution Chem.*, 1973, **2**, 119.

¹⁶ I. R. Tasker, *Thesis* (Sheffield University, 1979).

¹⁷ E. Moses, *Thesis* (Sheffield University, 1979).

¹⁸ J. E. Prue, *Ionic Equilibria* (Pergamon, Oxford, 1966), chap. 10.

¹⁹ H. L. Friedman, *J. Solution Chem.*, 1972, **1**, 387, 413, 419.

²⁰ H. J. V. Tyrell and M. Kennerley, *J. Chem. Soc. A*, 1968, 2724.

²¹ F. J. Millero, *J. Phys. Chem.*, 1968, **72**, 4589.

²² F. J. Millero, in *Water and Aqueous Solutions*, ed. R. A. Horne (Wiley, New York, 1972), chap. 13.

²³ See H. L. Friedman and W. D. T. Dale, in *Statistical Mechanics, Part A.*, ed. B. J. Berne (Plenum Press, New York, 1977), chap. 3.

²⁴ J. G. Kirkwood, *Chem. Rev.*, 1939, **24**, 233.

- ²⁵ J. G. Kirkwood, in *Proteins, amino-acids and peptides*, ed. E. J. Cohn and J. T. Edsall (Reinhold, New York, 1943), chap. 12.
- ²⁶ E. E. Schrier and R. A. Robinson, *J. Biol. Chem.*, 1971, **246**, 2870.
- ²⁷ R. A. Robinson and R. H. Stokes, *Electrolyte Solutions* (Butterworths, London, 2nd edn, 1970), appendix 3.1.
- ²⁸ R. A. Robinson and H. S. Harned, *Chem. Rev.*, 1941, **28**, 419.

(PAPER 9/849)