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The role of hydrophilic interactions in determining preferential configurations in aqueous solution: alkan-1-ols, alkan-1,2-diols, alkan-α,ω-diols, and α-aminoacids interacting with glycine and its oligomers at 298.15 K

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Abstract

Enthalpies of dilution of ternary aqueous solutions containing glycine, diglycine or triglycine and alkan-1-ols, alkan-1,2-diols, alkan-α,ω-diols, and α-aminoacids have been determined by microcalorimetry at 298.15 K. Pairwise cross interaction coefficients of the virial expansion of the excess enthalpies were evaluated. The values of these coefficients are positive, depending in a very complex manner on the number and position of the hydroxyl groups. The behaviour of these systems seems to be determined by a balance between favourable hydrophilic–hydrophilic and repulsive hydrophilic–hydrophobic interactions. The chaotropic agents employed play a major role: they are more complex than other purely hydrophilic substances, such as urea or biuret, because of the presence of hydrophobic domains on their molecules.

Keywords: Alkanol; Amino acid; Glycine; Heat of dilution; Hydrophilic; Hydrophobic; Ternary system

1. Introduction

Hydrophobic interactions [1] have long been invoked to explain many biochemical processes, while a minor role is assigned to hydrophilic interactions. Recently,

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the latter interactions have received due attention and have been demonstrated to be highly important in processes such as protein folding and molecular recognition [2–5].

Thermodynamic [6] and spectroscopic [7] studies from this laboratory concerning model molecules of biological interest have led to the hypothesis that hydrophilic interactions allow the molecules to interact in solution through preferential orientations. These orientations are such that they influence the strength and cooperativity of the hydrophobic interactions [8–11].

Very useful information about the interaction mechanism can be inferred from the pairwise interaction coefficients of the virial expansion of an excess thermodynamic property. These parameters account for the variation of a thermodynamic property when two hydrated molecules are brought from an infinite to a finite distance where the hydration cospheres are perturbed. Enthalpic interaction coefficients have proved very useful for explaining the behaviour of substances having the same action on the structure of water (mono and polyhydroxylated compounds). Therefore, we were encouraged to extend these studies to molecules having a different action on water structure. A systematic investigation of ternary aqueous solutions containing hydrophobic structure makers and hydrophilic structure breakers [12–15] is under way. On the basis of these studies, an interaction model has been proposed which relies on the occurrence of a preferential configuration stabilized by the juxtaposition of the hydrophilic domains on the two interacting molecules.

In the present paper, we extend this investigation with the calorimetric study of the ternary aqueous systems containing alkan-1-ols, alkan-1,2-diols, alkan-α,ω-diols, and α-aminoacids as structure makers, and glycine, diglycine and triglycine as prevailingly chaotropic [16] agents. The aim is to verify, in addition to the occurrence of a preferential configuration, the effects of using structure breakers that are more complex than the simpler hydrophilic substances such as urea or biuret.

2. Experimental

Glycine, diglycine and triglycine were Sigma products. Alkanols were purchased from different sources (Sigma or Aldrich): they were of the highest commercially available purity. Solutions were prepared by weight and solutes were dried in vacuum over P_2O_5. Measurements of the heats of dilution were carried out by means of an LKB flow microcalorimeter and a thermal activity monitor (TAM), following experimental details reported in the literature [6,17–21].

3. Results

Virial coefficients of the power series of the excess enthalpies as a function of molalities can easily be derived from the enthalpies of dilution of solutions

containing n solutes and from the enthalpies of dilution of the respective binary solutions. The enthalpy change that occurs upon dilution ΔH_{dil} is related to the corresponding excess enthalpy H^E

$$\Delta H_{dil}(\text{in J kg}^{-1}) = H^E(\bar{m}^f) - (m_x^f/m_x^i)H^E(\bar{m}^i) \quad (1)$$

where x is any one of the solutes, $\bar{m}^f$ and $\bar{m}^i$ are the osmolalities of the solutions after and before the dilution process, respectively, and $\bar{m} = \Sigma_x m_x$. Substituting relations between excess enthalpies and virial coefficients into Eq. (1), the following relation is obtained

$$\Delta H_{dil}(\text{in J kg}^{-1}) = \sum_x \sum_y h_{xy} m_x^f m_y^f - (m_x^f/m_x^i)\left[\sum_x \sum_y h_{xy} m_x^i m_y^i\right] + \cdots \quad (2)$$

Knowing the values of the self coefficients h_{xx} for each solute, the cross coefficients h_{xy} are evaluated by means of an auxiliary function ΔH^{n*} [22]

$$\Delta H^{n*} = \Delta H_{dil}(m^i \rightarrow \bar{m}^f) - \sum_x \Delta H_{dil}(m_x^i \rightarrow m_x^f) \quad (3)$$

which depends only on the cross interaction coefficients. In the case of a ternary solution, Eq. (3) reduces to

$$\begin{aligned} \Delta H^{**} &= \Delta H_{dil}(\bar{m}^i \rightarrow \bar{m}^f) - \Delta H_{dil}(m_x^i \rightarrow m_x^f) - \Delta H_{dil}(m_y^i \rightarrow m_y^f) \\ &= 2h_{xy} m_x^f (m_y^f - m_y^i) + \text{higher terms} \\ &= 2h_{xy} m_y^f (m_x^f - m_x^i) + \text{higher terms} \end{aligned} \quad (4)$$

To determine the h_{xy} coefficients, a least-square procedure was used. Owing to the limited range of concentration explored, only pairwise coefficients were found to be necessary for the best-fitting of experimental data.

In Tables 1–3, the enthalpic cross interaction coefficients are reported for ternary aqueous solutions containing glycine (G), diglycine (G_2) and triglycine (G_3) and alkan-1-ols, alkan-1,2-diols and alkan-α,ω-diols. The cross coefficients are positive. They vary in a very complex manner with increasing number of carbon atoms of the alkyl chain of the alkanols. The positive sign is an indication that, upon interaction of the alkanols with the destructuring agent, structured water relaxes prevailingly from the hydrophobic hydration cospheres to the bulk.

Table 1
Enthalpic interaction coefficients h_{xy} for ternary aqueous solutions containing alkan-1-ols and glycine (G), diglycine (G_2) and triglycine (G_3), at 25°C

Alkan-1-ol	h_{xy}(G) [a]	h_{xy}(G_2) [a]	h_{xy}(G_3) [a]
Methane-1-ol	377(13) [b]	465(7)	622(15)
Ethane-1-ol	553(12) [c]	696(5)	948(9)
Propane-1-ol	654(6) [c]	722(33)	1170(4)
Butane-1-ol	799(10) [c]	767(25)	1155(14)
Pentane-1-ol	810(71) [b]	725(46)	1003(69)

[a] In J kg mol^{-2}. Numbers in parentheses are the 95% confidence limits. [b] Ref. [13]. [c] Ref. [23].

Table 2
Enthalpic interaction coefficients h_{xy} for ternary aqueous solutions containing alkan-1,2-diols and glycine (G), diglycine (G_2) and triglycine (G_3), at 25°C

Alkan-1,2-diol	$h_{xy}(G)$ [a]	$h_{xy}(G_2)$ [a]	$h_{xy}(G_3)$ [a]
Ethane-1,2-diol	120(4)	149(12)	262(8)
Propane-1,2-diol	316(35)	392(22)	572(12)
Butane-1,2-diol	544(39)	476(25)	920(29)
Pentane-1,2-diol	518(20)	676(37)	951(37)
Hexane-1,2-diol	606(28)	900(52)	1303(32)

[a] In J kg mol^{-2}. Values in parentheses are the 95% confidence limits.

Table 3
Enthalpic interaction coefficients h_{xy} for ternary aqueous solutions containing alkan-α,ω-diols and glycine, diglycine and triglycine, at 25°C

Alkan-α,ω-diol	$h_{xy}(G)$ [a]	$h_{xy}(G_2)$ [a]	$h_{xy}(G_3)$ [a]
Ethane-1,2-diol	120(4)	149(12)	262(8)
Propane-1,3-diol	276(11)	383(13)	710(7)
Butane-1,4-diol	646(40)	868(20)	1070(58)
Pentane-1,5-diol	614(28)	1103(34)	1068(16)
Hexane-1,6-diol	654(18)	1007(50)	1266(13)
Hetpane-1,7-diol	879(44)	1266(54)	1549(24)

[a] In J kg mol^{-2}. Numbers in parentheses are the 95% confidence limits.

Table 4
Enthalpic interaction coefficients h_{xy} for ternary aqueous solutions containing glycine and the α-amino acids reported, at 25°C

α-amino acid	h_{xy} [a]
D-Alanine	−61(2)
D-α-Aminobutyric acid	183(10)
D-Norvaline	264(27)
D-Norleucine	319(15)

[a] In J kg mol^{-2}. Numbers in parentheses are the 95% confidence limits.

In Table 4, the enthalpic cross interaction coefficients are reported for ternary aqueous solutions containing glycine and the following α-aminoacids: alanine, aminobutyric acid, norvaline, and norleucine. The coefficients are positive, with the exception of the one referring to the alanine/glycine system.

In Table 5, the enthalpic pairwise coefficients are reported for all the substances employed. It must be stressed that the coefficients for glycine, diglycine and triglycine have been recently redetermined. They are smaller than the values already reported in the literature, obtained in different (higher) concentration ranges [24–26].

Table 5
Enthalpic interaction coefficients h_{xx} for binary aqueous solutions containing glycine, diglycine, triglycine, and the α-amino acids or alkanols employed, at 25°C

Substance	h_{xx} [a]	h_{xxx} [b]
Glycine	−367(7) [c]	
Diglycine	−620(6) [c]	
Triglycine	−1534(53) [c]	
D-Alanine	217(4) [d]	
D-α-Aminobutyric acid	536(12) [d]	
D-Norvaline	927(25) [d]	
L-Norleucine	1424(31) [d]	
Methane-1-ol	218 [e]	
Ethane-1-ol	243(10) [f]	65
Propane-1-ol	559(14) [f]	158
Butane-1-ol	1003(15) [f]	646
Pentane-1-ol	1766(68) [g]	
Ethane-1,2-diol	415(30) [h]	−21
Propane-1,2-diol	589(1) [i]	96
Butane-1,2-diol	923(5) [j]	60
Pentane-1,2-diol	1777(30) [k]	
Hexane-1,2-diol	2955(55) [k]	
Propane-1,3-diol	523(9) [i]	5
Butane-1,4-diol	787(2) [i]	−8
Pentane-1,5-diol	1335(25) [i]	−20
Hexane-1,6-diol	2402(35) [i]	−65
Heptane-1,7-diol	4017(84) [l]	

[a] In J kg mol^{-2}. [b] In J kg^2 mol^{-3}. Values in parentheses are the 95% confidence limits. [c] Values obtained at low concentrations. Literature values, obtained in higher concentration ranges, are reported in Refs. [24], [25] and [26] for glycine, diglycine and triglycine, respectively. [d] Ref. [27]. [e] Ref. [28]. [f] Ref. [19]. [g] Ref. [9]. [h] Ref. [29]. [i] Ref. [18]. [j] Ref. [30]. [k] Ref. [6]. [l] Ref. [8].

4. Discussion

The analysis of the pair enthalpic interaction coefficients relative to binary aqueous solutions of alkane-*m*,*n*-diols led to the proposal of a model which accounts for the interactions between hydrated molecules [6]. The fundamentals of this method are based on free energy parameters. The group contribution to the pairwise coefficient of the virial expansion of the excess Gibbs free energy is negative for interactions between groups having the same action on the structure of water, and positive for mixed interactions ($G_{\text{hydrophilic-hydrophilic}} < 0$, $G_{\text{hydrophobic-hydrophobic}} < 0$, $G_{\text{hydrophilic-hydrophobic}} > 0$) [31]. Thus, two interacting molecules would prefer a configuration where favourable interactions between like groups are maximized. Mixed interactions are less probable because of the positive contribution to the Gibbs free energy. On these bases, enthalpic interaction coefficients have been considered by neglecting cross interactions. Such a procedure is obviously in contrast with a simple additivity approach, which assigns the same probability to all

interactions occurring in solution [17]. Given the different premises, the results derived from the two approaches often disagree. They are markedly different in the case of homologous series of substances, for positional or stereo isomers, and for the interaction between molecules having a different action on water structure.

The preferential configuration model has proved to be very powerful in explaining the experimental data relative to polyhydric alcohols. In this case, the hypothesis holds for a preferred orientation, the "side on", which juxtaposes simultaneously the maximum number of hydrophilic and hydrophobic groups [6]. Other orientations in which hydrophilic–hydrophobic interactions could occur cannot be excluded but are less probable. Hydrophobic interactions are enhanced, as evidenced by the linearity of the coefficients vs. the third power of the number of methylene groups in the molecule. The absolute value of the cross coefficients is found to depend on the number of functional groups that can actually juxtapose [10]. It was also shown that it is possible to reproduce the enthalphic pairwise coefficients of polyhydroxylated compounds by means of a very simple, unifying relation [10].

Furthermore, it seemed worthwhile to investigate the interactions between solutes having contrasting effects on water structure. For that, interactions between hydrophobic structure makers (alkan-*m*-ols and alkan-*m*,*n*-diols) and hydrophilic structure breakers (urea, biuret) were investigated [12–15]. The enthalphic cross interaction coefficients, when reported vs. the number of carbon atoms of the alkanols, present a maximum with increasing alkyl chain length. This trend can be explained through the presence of a preferential configuration stabilized by hydrophilic interactions. When the hydroxyl group/s are not confined to one end of the molecule, the alkyl chain is differently involved in the interaction, depending on the distance between the CHOH functional groups. The necessity of minimizing mixed interactions with increasing alkyl chain length leads to the two interacting molecules being as separated as possible which causes the coefficients to decrease. In the case of alkan-1-ols, alkan-1,2-diols, and alkan-1,2,3-triols, when the hydrophilic region is confined to the end of the molecule, cross coefficients increase linearly until a plateau is attained [13].

In the present study we have gone further in the investigation of these kinds of ternary systems, studying the interactions in aqueous solution of glycine, diglycine and triglycine with alkan-1-ols, alkan-1,2-diols, and alkan-α,ω-diols, and those of glycine with several α-amino acids bearing unsubstituted alkyl chains. In Fig. 1, the cross interaction coefficients are reported vs. the number of carbon atoms in the alkanols for the alkan-1-ols interacting with the three structure breakers. The interactions with glycine resembles that with biuret or urea: in fact, the coefficients increase linearly, and then they stabilize on an invariant value beginning at $n_C = 4$. It can be supposed that the two interacting molecules orient themselves, maximizing hydrophilic interactions, so that the destructuring agent can exert its action only on the three methylene groups beyond that bearing the hydroxyl group.

The trend relative to the interaction of the same alkanols with diglycine resembles that with glycine. However, surprisingly, the invariant value begins at $n_C = 2$. Probably, the necessity of minimizing mixed interactions leads the longer structure breaker remaining as distant as possible, interacting with the alkanol through only

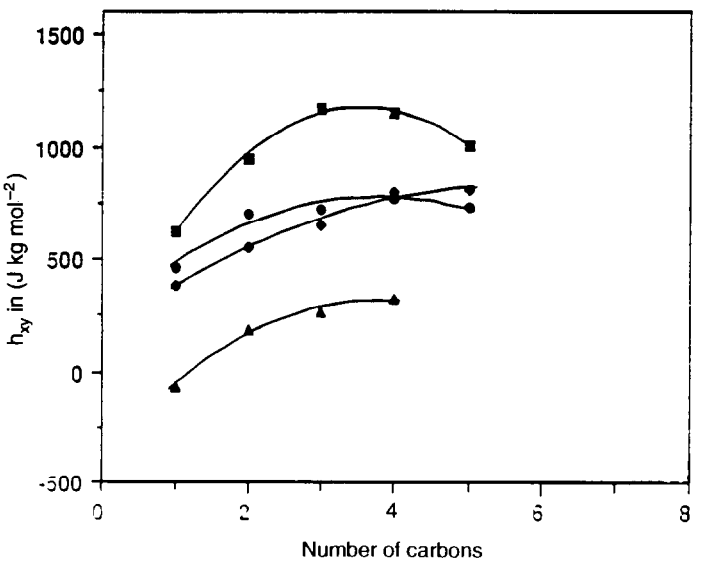

Fig. 1. Enthalpic cross interaction coefficients h_{xy} for alkan-1-ols interacting with glycine (◆), diglycine (●), and triglycine (■), and for α-amino acids (alanine, aminobutyric acid, norvaline, norleucine) interacting with glycine (▲), vs. the number of aliphatic carbon atoms n_C at 298 K.

one of its polar heads. Then, the chaotropic agent disturbs a smaller part of the alkyl chain. With increasing complexity of the structure breaker, this effect is much more pronounced. For systems containing triglycine, a maximum appears whose presence is always an indication of a balance between the contrasting effects. Up to a certain number of carbon atoms, favourable interactions prevail for the juxtaposition of the hydrophilic domains and the involvement of the whole alkyl chain. With increasing length of the alkyl chain, to minimize the unfavourable hydrophilic–hydrophobic interactions, the two molecules withdraw, making the coefficients decrease.

To test the capability of the zwitterion to "force" the interacting molecules into a preferential configuration, ternary systems containing glycine and α-amino acids with unsubstituted alkyl side chains have been investigated. The presence of a zwitterion, with its opposite electrical charges, might lead to a greater stabilization of the preferential configuration. In Fig. 1, cross coefficients are reported relative to the interaction of alanine, α-amino butyric acid, norvaline and norleucine with glycine. The trend is similar to that characterizing alkan-1-ols/glycine systems, but the curve bends at lower n_C. This could indicate a more effective interaction, which, however, is not so effective as expected, probably because of the rigidity of the ionic hydration. The cross interaction coefficients are much smaller than those referring to alkan-1-ols having an alkyl chain of comparable length. In a preceding paper, the contribution of the zwitterion–zwitterion interaction to the enthalpic coefficient was evaluated and found to be high and negative [32]. Then, the positive contribution due to the interaction between the alkyl chains is contrasted by the negative

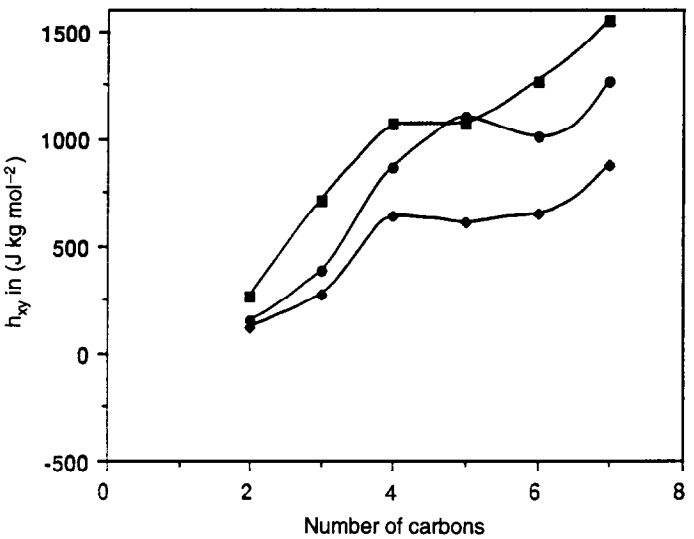

Fig. 2. Enthalpic cross interaction coefficients h_{xy} for alkan-α-ω-diols interacting with glycine (◆), diglycine (●), and triglycine (■) vs. the number of aliphatic carbon atoms n_C at 298 K.

contribution of the hydrophilic interaction, thus determining the low value of the cross coefficient. For alanine, which has the shortest alkyl chain, the negative contribution prevails.

In Fig. 2, the data are given relative to the interaction between alkan-α,ω-diols and the same struture breakers. The first part of the plots shows a behaviour similar to that of alkan-1-ols interacting with glycine and diglycine. Probably, up to $n_C = 5–6$, the interaction occurs with the involvement of only one hydroxyl group. The increase at $n_C = 6–7$ could indicate the involvement of the second hydroxyl group, i.e. the alkyl chain could be long enough to juxtapose both hydrophilic heads to the structure breaker by partial folding. In this way, a "forced" interaction between the two molecules occurs, with the subsequent release of a larger quantity of structured water from the hydrophobic hydration cosphere.

The presence of a hydrophilic head confined to one end of the molecule could support the hypothesis that the behaviour of alkan-1,2-diols is similar to that of alkan-1-ols. The plots reported in Fig. 3 indicate that this actually only occurs for the interaction with glycine. In contrast, the coefficients increase continuously for the interaction with diglycine and triglycine, with slight modulations around $n_C = 3–4$. In this case the complexity of the destructuring molecule, together with the presence of CH_2 groups, results in a more complex interaction. Something similar to a "side on" configuration could be operating, stabilized by the maximum number of hydrophilic–hydrophilic and hydrophobic–hydrophobic interactions.

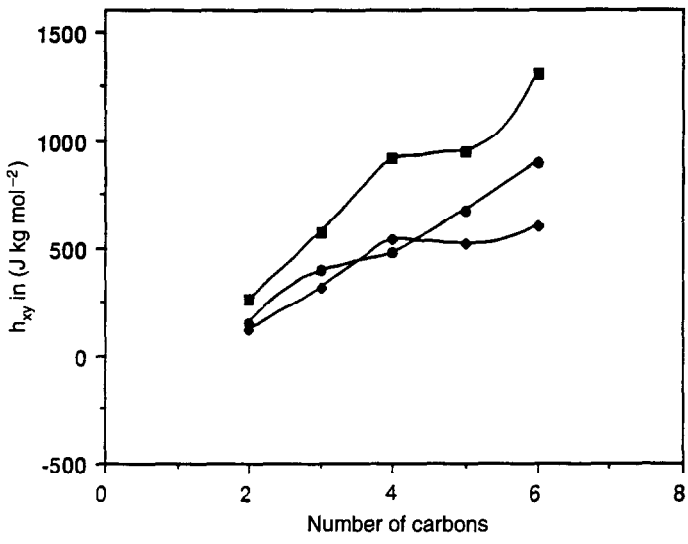

Fig. 3. Enthalpic cross interaction coefficients h_{xy} for alkan-1,2-diols interacting with glycine (◆), diglycine (●), and triglycine (■) vs. the number of aliphatic carbon atoms n_C at 298 K.

5. Conclusions

The systems discussed in this paper are much more complex than those involving urea or biuret owing to the hydrophobic regions present on the structure breakers here employed. Analysis of the cross coefficients in terms of favourable or unfavourable interactions is consistent with the model postulating preferential configurations between interacting molecules. It should be stressed that this model has also been successful in explaining data concerning chiral recognition shown by α-amino acids bearing alkyl chains [22,27]. With the α-amino acids in the zwitterionic form, the configuration which is stabilized by the interactions between the charged groups of the zwitterion is thought to prevail. This preferential configuration, enhancing steric differences between the enantiomers, leads to the detection of chiral recognition, which disappears when the zwitterion is destroyed [32].

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References

[1] J.J. Kozak, W.S. Knight and W. Kauzmann, J. Chem. Phys., 48 (1968) 675.
[2] A. Ben-Naim, J. Chem. Phys., 90 (1989) 7412.

[3] A. Ben-Naim, J. Phys. Chem., 94 (1990) 6893.
[4] M. Mezei and A. Ben-Naim, J. Chem. Phys., 92 (1990) 1359.
[5] A. Ben-Naim, Biopolymers, 29 (1990) 567.
[6] C. Cascella, G. Castronuovo, V. Elia, R. Sartorio and S. Wurzburger, J. Chem. Soc. Faraday Trans. 1, 86 (1990) 85.
[7] S. Andini, G. Castronuovo, V. Elia and L. Fasano, J. Chem. Soc. Faraday Trans. 1, 86 (1990) 3567.
[8] L. Ambrosone, S. Andini, G. Castronuovo, V. Elia and G. Guarino, J. Chem. Soc. Faraday Trans. 1, 87 (1991) 2989.
[9] G. Castronuovo, R.P. Dario and V. Elia, Thermochim. Acta, 181 (1991) 305.
[10] G. Castronuovo, C. Della Volpe, V. Elia and G. Scirè, J. Chem. Soc. Faraday Trans., 88 (1992) 2667.
[11] G. Barone, B. Bove, G. Castronuovo and V. Elia, J. Solution Chem., 10 (1981) 803.
[12] C. Cascella, G. Castronuovo, V. Elia, R. Sartorio and S. Wurzburger, J. Chem. Soc. Faraday Trans. 1, 85 (1989) 3289.
[13] G. Castronuovo, R.P. Dario, C. Della Volpe and V. Elia, Thermochim. Acta, 206 (1992) 43.
[14] S. Andini, P. Cacace, G. Castronuovo, V. Elia and F. Racioppoli, J. Chem. Soc. Faraday Trans., 89 (1993) 503.
[15] G. Castronuovo, C. Della Volpe and V. Elia, J. Chem. Soc. Faraday Trans., 89 (1993) 3061.
[16] F. Franks, Philos. Trans. R. Soc. London, Ser. B, 278 (1977) 33.
[17] J.J. Savage and R.H. Wood, J. Solution Chem., 5 (1976) 731.
[18] G. Borghesani, R. Pedriali and F. Pulidori, J. Solution Chem., 18 (1989) 289.
[19] F. Franks, M.D. Pedley and S. Reid, J. Chem. Soc. Faraday Trans. 1, 72 (1976) 1359.
[20] H.L. Friedman and C.V. Krishnan, J. Solution Chem., 2 (1972) 119.
[21] J.E. Desnoyers, G. Perron, L. Avédikian and J.P. Morel, J. Solution Chem., 5 (1976) 631.
[22] G. Castronuovo, V. Elia and M. Magliulo, Can. J. Chem., 69 (1991) 794.
[23] G. Barone, G. Castronuovo, P. Del Vecchio, and V. Elia, J. Therm. Anal., 69 (1988) 431.
[24] T.H. Lilley and R.P. Scott, J. Chem. Soc. Faraday Trans. 1, 72 (1976) 184.
[25] S.H. Dyke, G.R. Hedwig, and I.D. Watson, J. Solution Chem., 10 (1981) 321.
[26] G. Barone, P. Bonpresa, P. Cacace, G. Castronuovo, V. Elia and M.F. Fragassi, Proceedings of Journées de Calorimetrie et d'Analyse Thermique, vol. 9, 1978, p. 55.
[27] G. Barone, G. Castronuovo, P. Del Vecchio, V. Elia and S. Puzziello, J. Solution Chem., 18 (1989) 1105.
[28] J. Perron and J.E. Desnoyers, J. Chem. Thermodyn., 13 (1981) 1105.
[29] F. Franks and M.D. Pedley, J. Chem. Soc. Faraday Trans. 1, 79 (1983) 2249.
[30] G. Borghesani, R. Pedriali, F. Pulidori, and I. Scaroni, J. Solution Chem., 15 (1986) 397.
[31] B. Okamoto, R.H. Wood and P.T. Thompson, J. Chem. Soc. Faraday Trans. 1, 74 (1978) 1990.
[32] G. Castronuovo, V. Elia, C. Giancola and S. Puzziello, J. Solution Chem., 19 (1990) 855.