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A MODEL FOR THE INTERACTIONS INVOLVING HYDROPHILIC STRUCTURE MAKER SOLUTES

A thermodynamic study of ternary aqueous solutions of glucose and hydroxylated substances

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Abstract

Enthalpies of dilution of ternary aqueous solutions containing glucose and alkan-1-ols, alkan-1,2-diols and alkan-m,n-diols were determined at 298.15 K by flow microcalorimetry. The pairwise cross interaction coefficients of the virial expansion of the excess enthalpies were evaluated: they are positive and depend in a complex manner on the length of the alkyl chain of the alkanols. The behaviour of these systems is interpreted in terms of preferential interactions between the hydrophilic groups of the alkanols and the destructured domain present on glucose.

Keywords: excess properties, glucose, preferential configuration

Introduction

Weak, non bonding interactions are important in macromolecular assembly processes, and their change or disruption may lead to the disruption of the native form of a protein. The native structure of a globular protein, in fact, is determined by a balance of the interactions between the amino acid residues with each other and with the aqueous environment. Among these weak interactions in aqueous solutions, the hydrophobic interaction has been the most widely studied, especially in relation to protein stability [1]. Correlation of the thermodynamic properties of protein folding with data on hydrophobic model compounds has allowed a better analysis of the role of non-polar interactions. Recently some authors have begun showing that intramolecular hydrophilic interactions are strong and highly dependent on orientation and on the properties of the solvent [2–5]. Thus, they are probably just as important as hydrophobic interactions in highly specific processes such as protein folding and molecular recognition.

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Non-bonding interactions can be studied through the virial coefficients of the power series of the excess thermodynamic properties expressed as a function of the molalities. These coefficients give information on the changes of the state of the solvent released upon interaction between hydrated molecules. The interaction is supposed to occur by the overlap of their hydration cospheres, with the consequent release of water molecules from these cospheres to the bulk. The sign of the thermodynamic quantity is determined by the different properties of water in the cosphere and in the bulk. A phenomenological classification of nonelectrolytes has been proposed on the basis of the signs and values of the enthalpic, entropic and Gibbs free energy coefficients as follows: [6, 7]

i) Hydrophobic structure makers: $g_{xx}<0$; $Ts_{xx}>h_{xx}>0$.
ii) Hydrophilic structure makers: $g_{xx}>0$; $h_{xx}>Ts_{xx}>0$.
iii) Hydrophilic structure breakers: $g_{xx}<0$; $h_{xx}<Ts_{xx}<0$.

The analysis of the magnitudes and signs of the enthalpic interaction coefficients for a variety of polyhydroxylated compounds has shown that these coefficients depend on the number, position and stereochemistry of the functional groups [8–14]. However, the group additivity approach proposed by Savage and Wood [15] has failed in distinguishing positional isomers and in reproducing self-consistent values of the contribution of groups to the pair enthalpic coefficients of homologous series. This has led to the proposal of an alternative approach for modelling the hydrophobic interactions between solutes bearing hydrophilic and hydrophobic groups on the same molecule. According to this approach, the juxtaposition of groups having the same effect on water structure determines the more probable configuration of the hydrated molecules ('side on' model) [8]. This configuration is responsible for the failure of the cited statistical approach and for the increased cooperativity found for polyhydroxylated compounds compared to that commonly expected for hydrophobic interactions.

The study of interactions involving hydrophobic structure makers and hydrophilic structure breakers has already led to very interesting results and has yielded evidence for the occurrence of a preferential configuration stabilized by the juxtaposition of hydrophilic domains [12]. In the present paper we report calorimetric results for the interaction between glucose, a hydrophilic structure maker, and alkan-1-ols, alkan-1,2-diols and alkan-m,n-diols, typical hydrophobic structure maker solutes. Monosaccharides are hydrophilic structuring solutes, according to the classification reported above and on the basis of spectroscopic evidences [16]. They show a complex behaviour when interacting with hydrophilic structure breaking solutes such as urea [17] and biuret [18]. The negative sign and the invariance of the enthalpic cross coefficients suggest the presence, in their hydration shells, of distorted domains, whose geometry is not compatible with the tetrahedal arrangement of water. The aim of the present paper is just to go further into the investigation of these substances and to explore how they behave in the presence of typical hydrophobic solutes such as alkanols.

Experimental

Glucose was a Sigma product. 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 vacuo over P_2O_5. Heats of dilution were measured with an LKB flow microcalorimeter, according to the experimental details reported in the literature [8, 14, 17–22].

Results

Virial coefficients of the power series of the excess enthalpies as a function of molalities can be easily 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 in a dilution process, ΔH_{dil}, is related to the corresponding excess enthalpy, H^{E}, as follows:

$$\Delta H_{\mathrm{dil}} = H^{\mathrm{E}}(m_x^{\mathrm{f}}, m_y^{\mathrm{f}}, \ldots..) + \\ - (m_x^{\mathrm{f}} / m_x^{\mathrm{i}}) H^{\mathrm{E}}(m_x^{\mathrm{i}}, m_y^{\mathrm{i}} \ldots..) \tag{1}$$

where m^{f} and m^{i} are the molalities of each solute after and before the dilution process, respectively. Substituting relations between excess enthalpies and virial coefficients into Eq. (1), the following relation is obtained:

$$\Delta H_{\mathrm{dil}} = \Sigma_x \Sigma_y h_{xy} m_x^{\mathrm{f}} m_y^{\mathrm{f}} - (m_x^{\mathrm{f}} / m_x^{\mathrm{i}}) \, [\Sigma_x \Sigma_y h_{xy} m_x^{\mathrm{i}} m_y^{\mathrm{i}}] + \ldots \tag{2}$$

Knowing the values of the self coefficients for each solute, the cross coefficients, h_{xy}, are evaluated by means of an auxiliary function ΔH^{**}, which depends on the cross interaction coefficients as follows [23]:

$$\Delta H^{**} = \Delta H_{\mathrm{dil}}(m_x^{\mathrm{i}}, m_y^{\mathrm{i}} \rightarrow m_x^{\mathrm{f}}, m_y^{\mathrm{f}}) - \Delta H_{\mathrm{dil}}(m_x^{\mathrm{i}} \rightarrow m_x^{\mathrm{f}}) \\ - \Delta H_{\mathrm{dil}}(m_y^{\mathrm{i}} \rightarrow m_y^{\mathrm{f}}) = \\ = 2h_{xy} m_x^{\mathrm{f}} (m_y^{\mathrm{f}} - m_y^{\mathrm{i}}) + \text{higher terms} = \\ = 2h_{xy} m_y^{\mathrm{f}} (m_x^{\mathrm{f}} - m_x^{\mathrm{i}}) + \text{higher terms} \tag{3}$$

To determine the coefficients h_{xy}, a least squares 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.

Table 1 Enthalpic self and cross-interaction coefficients (J·kg·mol^{-2}) for binary and ternary aqueous solutions containing alkan-1-ols and glucose at 298.15 K

Alkan-1-ol	h_{xx} ^{a}	h_{xy} ^{a,b}
Methane-1-ol	215^{c}	536±32
Ethane-1-ol	243±10^{d}	750±6^{f}
Propane-1-ol	559±14^{d}	934±9^{f}
Butane-1-ol	1003±15^{d}	1083±13^{f}
Pentane-1-ol	1766±68^{e}	1292±47

[a] Errors reported are the 95% confidence limits; [b] The self interaction coefficient for *D*-glucose is 343±10 Jkg·mol^{-2}, Ref. [15]; [c] Ref. [24]; [d] Ref.[20]; [e] Ref. [11]; [f] Ref. [25]

In Table 1 the enthalpic cross coefficients are listed for the interaction between alkan-1-ols and glucose. In Table 2 the cross coefficients are given for the interaction between alkan-1,2-diols and glucose. The same data relative to alkan-m,n-diols, different from alkan-1,2-diols, are presented in Table 3. All the coefficients are positive and they increase, in a complex manner, with increasing number of carbon atoms. The complexity of these systems is better shown in the Figure, where the cross coefficients for alkan-1-ols, alkan-1,2-diols and alkan-α,ω-diols interacting with glucose are reported as a function of the number of carbon atoms in the alkanols. In the same Figure, literature coefficients are listed for systems involving the same alkanols and triglycine [28] or biuret [12, 18, 29]. Because of their low solubility, alkan-1-ols beyond pentan-1-ol cannot be studied. The coefficients increase linearly, and they are markedly larger than those relative to diols. The trends characterizing the interactions of alkan-1,2- and alkan-α,ω-diols with glucose, biuret and triglycine are similar. However, for α,ω-diol/glucose systems the curve rises with a modula-

Table 2 Enthalpic self and cross-interaction coefficients (J·kg·mol^{-2}) for binary and ternary aqueous solutions containing alkan-1,2-diols and glucose at 298.15 K

Alkan-1,2-diol	h_{xx} ^{a}	h_{xy} ^{a,b}
Ethane-1,2-diol	415±30^{b}	391±20^{f}
Propane-1,2-diol	589±1^{c}	606±31
Butane-1,2-diol	923±5^{d}	880±46
Pentane-1,2-diol	1777±30^{e}	1003±14
Hexane-1,2-diol	2955±55^{e}	1491±113

[a] Errors reported are the 95% confidence limits; [b] Ref. [26]; [c] Ref. [19]; [d] Ref. [27]; [e] Ref. [8] [f] Ref.[15]

Table 3 Enthalpic self and cross-interaction coefficients ($J \cdot kg \cdot mol^{-2}$) for binary and ternary aqueous solutions containing alkan-m, n-diols and glucose (G) or alkan-α, ω-diols and xylose (X) at 298.15 K

Alkan-m,n-diol	h_{xx} [a]	h_{xy} (G)[a]	h_{xy} (X)[a]
Propane-1,3-diol	523±9[b]	720±24	597±13
Butane-1,3-diol	750±6[b]	983±24	
Butane-2,3-diol	837±10[b]	828±37	
Butane-1,4-diol	787±2[b]	866±46	852±49
Pentane-1,4-diol	1187±10[c]	972±20	
Pentane-2,4-diol	932±15[c]	1059±42	
Pentane-1,5-diol	1335±25[b]	1089±26	897±30
Hexane-1,5-diol	1939±68[c]	1707±61	
Hexane-2,5-diol	1796±61[c]	1346±67	
Hexane-1,6-diol	2402±35[b]	1460±63	1222±41
Heptane-1,7-diol	4017±84[d]	1460±51	1367±52

[a] Errors reported are the 95% confidence limits; [b] Ref. [19]; [c] Ref. [8]; [d] Ref. [10]

tion at $n_C=4$, and reaches an invariant value at $n_C=6$. This plateau cannot be observed for 1,2-diols, because the seven carbon atom unit is not available. In the same Figure, the data for α,ω-diol/xylose systems are also shown. The values of the coefficients are smaller, but their trend is very similar to that involving glucose.

Discussion

Saccharides are solutes whose behaviour in water is characterized by the relation $h_{xx}>g_{xx}>0$; other hydrophilic solutes, such as urea-like compounds, have an opposite behaviour: $h_{xx}<g_{xx}<0$ [16]. The McMillan-Mayer theory of solutions applied a formal separation of the excess Gibbs free energy into contributions arising from the interactions of pairs, triplets, etc. of solute particles [30]. These contributions are expressed by the second, third, etc. virial coefficients of the excess free energy as a function of the molality: these coefficients account also for the solute-solvent and solvent-solvent changes. For saccharides g_{xx} is positive, suggesting that the excess contributions to the free energy of sugar–sugar interactions are unfavourable. Probably the solute–solute interactions are screened by the more favourable sugar–water interactions. In a previous paper we have suggested that the signs and values of the second coefficients must be attributed mainly to a reversal of the hydration [16]. This process will involve little changes in the energy and degree of freedom for the water released from the more structured hydration cospheres of the saccharides to the bulk, at increasing concentration.

The interaction of monosaccharides with hydrophilic, destructuring solutes as urea [17] and biuret [18], is characterized by negative enthalpic coefficients. The little variability of the values of the cross coefficients at increasing destructuring power of urea-like solutes was rather puzzling, and led to a more complex model for the hydration of saccharides. A working hypothesis was proposed, relying on the existence of a distorted domain in the hydration cosphere of monosaccharides, besides the cage hydration stabilized by the hydroxyl groups. This domain could be due to the geometry of the hemiacetalic oxygen, which orients the water molecules in a manner not compatible with the tetrahedral arrangement. The presence of other conformations (e.g. $^1C_4$) can be another potential source of perturbation of the ordered hydration cage. In this case, the interaction of pyranoses with water can be thought of as a complex interaction in which the ordered arrangement of water molecules promoted by the hydroxyl groups is disturbed by the hydration of the other polar group. Hence, part of the cosphere fluctuates between an ordered and a distorted arrangement. The release of water from the distorted domain of the sugar cosphere should be the main factor determining the signs and values of the enthalpic cross coefficients in the presence of hydrophilic, destructuring solutes. The extension of this distorted domain should be almost the same for all the monosaccharides, given the small variability of the h_{xy} values passing from one sugar to another, and only a minor contribution would originate from the release of water from the distorted cosphere of urea-like solutes.

The interaction of *D*-glucose with ethanol, propanol and butanol has been found to be characterized by positive and very high cross interaction coefficients [25]. These coefficients are the highest among those characterizing the interaction of alkanols with hydrophilic structure breakers. Namely, *D*-glucose appears to behave not differently from these destructuring substances, and it is even more powerful than biuret. The interaction between these two classes of solutes is explained in terms of a mechanism not different from the one proposed for the urea-alkanol interaction in water. There is a prevailing release of water from the more labile hydrophobic cosphere of the alkanol, which is partially destroyed in this interaction. The same mechanism has been invoked to explain the interaction of the same alkanols with glycine and its oligomers.

A great deal of work done in our laboratory in the last few years has been interpreted by the hypothesis that a preferential configuration exists in solution between hydrated molecules bearing hydrophilic groups through which favourable interactions can be established. This interaction model permitted interpretation of the complex behaviour of positional isomers of polyhydroxylated substances, which could not be explained by a statistical group additivity approach [15]. The starting hypothesis for building this mechanism relied on the fact that interactions between domains can be characterized as follows [31]:

i) Favourable interactions between like domains:
$G_{ii}<0$.

where *i* is a hydrophilic structure maker, a hydrophilic structure breaker or a hydrophobic structure maker domain.

ii) Unfavourable interactions between unlike domains:
$G_{ij}>0$.

Here *G* is the group contribution to the pairwise coefficient of the virial expansion of the excess Gibbs energy. Then, mixed interactions occur only to a small extent because of a positive contribution to the Gibbs energy. Making use of these results, the occurrence of some more probable configurations can be hypothesized in solution between two hydrated molecules (model of preferential configuration). According to this model, two interacting molecules juxtapose simultaneously the maximum number of hydrophilic and hydrophobic groups, minimizing mixed interactions [8].

The preferential configuration model permitted interpretation of the experimental values of the pair enthalpic coefficients for the systems involving like substances. It has encouraged us to explore whether this model also holds for the cross interactions between substances having a different action on water structure. The study of the cross interactions between structure breaking solutes, such as biuret and triglycine, and alkan-1-ols, alkan-1,2-diols or alkan-1,2,3-triols has shown an unusual, common trend [12]. The cross coefficients increase linearly with increasing number of carbon atoms in the alkanols until a plateau is reached. This plateau is attained at $n_C\geq4$ for alkan-1-ols, at $n_C\geq5$ for alkan-1,2-diols, and at $n_C=6$ for alkan-1,2,3-triols. This trend has been explained in terms of the presence of a preferential configuration stabilized by hydrophilic–hydrophilic interactions between the hydroxyl groups of the alkanols and the hydrophilic groups of the destructuring agent. A critical length of the alkyl chain of the hydrophobic solute must be operating beyond which the structure breaker cannot exert its disruptive action. The behaviour of alkan-α,ω-diols is more complex: the coefficients first increase, pass through a maximum and then at $n_C=7$ increase again [29]. This increase could be due to a partial folding of heptane-1,7-diol which has an alkyl chain long enough to juxtapose both hydrophilic ends to the destructuring agent. In this configuration there is a forced interaction between the structure breaker and the hydrophobic domain of the alkanol, with the consequent release of structured water to the bulk.

In the present study the interaction of *D*-glucose with alkan-1-ols, alkan-1,2-diols and alkan-*m*,*n*-diols is investigated. The data reported in the Figure, where a comparison is shown between the interaction with glucose and that with triglycine and biuret, allow some interesting considerations. Despite the great difference in the pair enthalpic coefficients characterizing the three hydrophilic agents, the behaviour of the various classes of alkanols is surprisingly similar. Glucose behaves qualitatively and also quantitatively, as one of the most effective chaotropic agents. The coefficients relative to alkan-1-ols are more positive than those for diols, probably due to the presence of only one hydroxyl group reacting with the destructured domain of the monosaccharide. The coefficients characterizing the interaction with 1,2- and α,ω-diols are very similar, thus indicating that glucose does not discriminate between the two classes of substances. Its action is independent of the position of the hydroxyl groups in the diols. The small variability of the coefficients relative to the interaction of the various isomers of butane-, pentane-, and hexanediols with the monosaccharide further confirms this finding (Table 3). The two curves for 1,2- and α,ω-diols show an increase of the coefficients with a modulation at $n_C=4$. Beyond, for α, ω-diols this increase stops at $n_C=6$, the coefficients for hexane-1,6-diol and heptane-1,7-diol showing the same value. This plateau is an indication of the presence of a preferential configuration stabilized by the interaction of the destructured domain of glucose with the hydrophilic domain of the alkanol. In this configuration, a critical length of the alkyl chain of the alkanol must operate, above which the disruptive action of the destructuring domain of glucose has no effect. This effect is observed only for the α,ω-diols for which the seven-membered unit is available, but it is not found for the alkan-1-ol and alkan-1,2-diol series. We believe that this effect could also be observed for these series, if the higher units were available.

The complexity of the interactions occurring in these systems probably accounts for the modulations in the increase of the h_{xy} coefficients with increasing number of carbon atoms in the alkanols. It must be stressed that these modulation are present also in the curve describing the interaction of xylose with α,ω-diols (see the Figure). Beyond the interaction between the hydrophilic domain of the alkanol and the destructured domain of the monosaccharide, also the interaction between the structured domains of the saccharide and alkanol must be considered. These two structured domains are different, and a variety of mixed interactions could occur, which could be excluded for the systems previously studied. The sum of these effects can lead to a balance, and then to the presence of modulations. Moreover, it is probably their presence that makes the interaction less specific: as a consequence, the h_{xy} values for 1,2- and α,ω-diols are very similar. The coefficients characterizing the interaction with xylose are constantly smaller than those involving glucose, probably due to the absence of the CH_2OH group, namely to the absence of a hydrophobic contribution.

The h_{xy} values relative to the interaction with biuret are less positive than those referring to glucose. It can be a consequence of the larger negative contribution of the interaction between the two hydroxyl group and biuret compared with the less negative contribution of the 'soft' (destructured) domain of glucose reacting with the two OH groups. As can be seen from the Figure, for increasing number of hydroxyl groups the intercepts of the curves lower, reaching negative values, as for the interaction between propan-1,2,3-triol and biuret

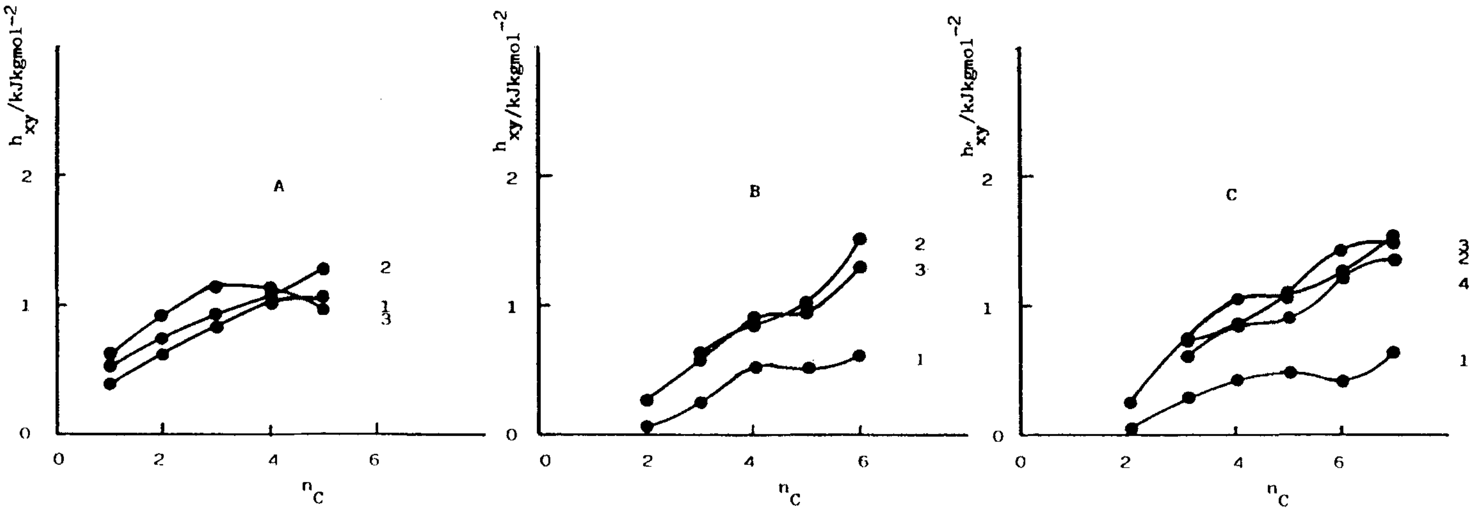

Fig. 1 Enthalpic cross interaction coefficients, h_{xy}, *vs.* the number of carbon atoms of the alkanols, n_C A: alkan-1-ols. B: alkan-1,2-diols. C: alkan-α,ω-diols. Curve 1 refers to the interaction with biuret, curve 2 to glucose, curve 3 to triglycine and curve 4 to xylose

(h_{xy} = -126 J·kg·mol^{-2}, Ref. [12]). The negative intercept, which represents the hypothetical interaction between the functional groups of diols and triols and the chaotropic agent, also underlines that glucose interacts through its destructured domain. As a conclusion, the preferential configuration model, based on the juxtaposition of domains having the same action on the structure of water, may account for the different and unexpected results.

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. I, 85 (1989) 3289.
7 G. Barone, P. Cacace, G. Castronuovo and V. Elia, J. Chem. Soc. Faraday Trans. I, 77 (1981) 1569.
8 C. Cascella, G. Castronuovo, V. Elia, R. Sartorio and S. Wurzburger, J. Chem. Soc. Faraday Trans. I, 86 (1990) 85.
9 S. Andini, G. Castronuovo, V. Elia and L. Fasano, J. Chem. Soc. Faraday Trans. I, 86 (1990) 3567.
10 L. Ambrosone, S. Andini, G. Castronuovo, V. Elia and G. Guarino, J. Chem. Soc. Faraday Trans. I, 87 (1991) 2989.
11 G. Castronuovo, R. P. Dario and V. Elia, Thermochim. Acta., 181 (1991) 305.
12 G. Castronuovo, R. P. Dario, C. Della Volpe and V. Elia, Thermochim. Acta, 206 (1992) 43.
13 G. Barone, B. Bove, G. Castronuovo and V. Elia, J. Solution Chem., 10 (1981) 803.
14 G. Castronuovo, C. Della Volpe, V. Elia and G. Scirè, J. Chem. Soc. Faraday Trans. I, 88 (1992) 2667.
15 J. J. Savage and R. H. Wood, J. Solution Chem., 5 (1976) 731.
16 G. Barone, G. Castronuovo, D. Doucas, V. Elia and C. A. Mattia, J. Phys. Chem., 87 (1983) 1931, and references therein cited.
17 V. Abate, G. Barone, G. Castronuovo, V. Elia and V. Savino, J. Chem. Soc. Faraday Trans I, 80 (1984) 759.
18 G. Barone, G. Castronuovo, P. Del Vecchio, V. Elia and M. T. Tosto, J. Solution Chem., 17 (1988) 925.
19 G. Borghesani, R. Pedriali and F. Pulidori, J. Solution Chem., 18 (1989) 289.
20 F. Franks, M. D. Pedley and S. Reid, J. Chem. Soc. Faraday Trans. I. 72 (1976) 1359.
21 H. L. Friedman and C. V. Krishnan, J. Solution Chem., 2 (1972) 119.
22 J. E. Desnoyers, G. Perron, L. Avédikian and J. P. Morel, J. Solution Chem., 5 (1976) 631.
23 G. Castronuovo, V. Elia and M. Magliulo, Can. J. Chem., 69 (1991) 794.
24 J. Perron and J. E. Desnoyers, J. Chem. Thermodyn., 13 (1981) 1105.
25 G. Barone, G. Castronuovo, P. Del Vecchio and V. Elia, J. Thermal Anal., 34 (1988) 479.
26 F. Franks and M. D. Pedley, J. Chem. Soc. Faraday Trans. I, 79 (1983) 2249.
27 G. Borghesani, R. Pedriali, F. Pulidori and I. Scaroni J. Solution Chem., 15 (1986) 397.
28 G. Castronuovo, V. Elia, G. Petrone and F. Velleca, Thermochimica Acta, 247 (1994) 273.
29 S. Andini, P. Cacace, G. Castronuovo, V. Elia and F. Racioppoli, J. Chem. Soc. Faraday Trans., 89 (1993) 503.
30 W. G. McMillan and J. E. Mayer, Jr, J. Chem. Phys., 13 (1945) 276.
31 B. Okamoto, R. H. Wood and P. T. Thompson, J. Chem. Soc. Faraday Trans. I, 74 (1978) 1990.