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The role of preferential interactions between similar domains in determining the behavior of aqueous solutions of aminoalkanols. A microcalorimetric study

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Abstract

Enthalpies of dilution of binary aqueous solutions containing 1 mol kg^{-1} NaOH as cosolvent and the homologous series of α,ω-aminoalkanols and 2-amino-1-alkanols as solutes have been determined by flow microcalorimetry at 298 K. Enthalpic self and cross interaction coefficients of the virial expansion of the excess enthalpies were evaluated. These coefficients are positive and increase at increasing alkyl chain length. The difference between the coefficients of positional isomers of aminoalkanols resembles that shown by the corresponding diols in water. The cross interaction coefficient relative to the ternary system containing hexane-1,6-diamine and hexane-1,6-diol is smaller than those relative to the respective binary solutions. The coefficients were interpreted using the "preferential configuration" model: it is inferred that interactions between like hydrophilic groups are preferred when compared to the like–unlike ones. © 1998 Elsevier Science B.V.

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1. Introduction

Among the weak, nonbonding interactions in aqueous solutions, the hydrophobic interaction has been the most widely studied, especially in relation to protein stability [1]. However, in the last years, it has been shown that hydrophilic interactions are strong and highly dependent on orientation and on the properties of the solvent. Thus, they are probably as important as hydrophobic ones in highly specific processes such as protein folding and molecular recognition [2–5].

Information about the mechanism through which two hydrated molecules interact in solution can be inferred from the pairwise interaction coefficients of the virial expansion of the excess thermodynamic properties. These parameters account for the variation of a thermodynamic property when two hydrated molecules are brought from an infinite to a finite distance where their hydration cospheres are perturbed. Enthalpic interaction coefficients have proved to be very useful to explain the behaviour of hydroxylated substances [6–11], α-aminoacids [12–15], carboxylic acids [16], amines [16] and mixture of these solutes. On the basis of these thermodynamic, and also spectroscopic [7], studies an interaction model has been proposed which postulates that two hydrated molecules interact through a preferential configuration stabilized by interactions between hydrophilic groups. It is just this interaction that allows the juxtaposition of hydro-

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phobic groups and, thus, makes their interaction more effective.

In the present paper, we extend calorimetric investigations to aqueous solutions containing aminoalkanols, which are solutes bearing simultaneously two different hydrophilic functional groups, namely the amino and hydroxyl groups. The aim is to verify whether a preferential configuration occurs and to gain information on the different role played by the interactions between like hydrophilic groups as respect to those between unlike ones.

2. Experimental

The solutes employed were Sigma product and they were of the highest commercially available purity. Solutions were prepared by weight, using a 1 mol kg^{-1} NaOH aqueous solution as solvent to avoid the protonation of the amino group. Protection against carbon dioxide was obtained by means of suitable traps. Water was bidistilled and filtered on a Millipore membrane. Measurements of the heats of dilution were carried out using an LKB flow microcalorimeter and a Thermal Activity Monitor from Thermometric. Calorimeters were equipped with GP 10 gradient programmer, a 500 μl mixing chamber, a PSV 50 electrovalve and a P3 peristaltic pump (all from Pharmacia) for the automatic preparation and for the pumping of solutions into the cells of the calorimeters. The method has been tested through known systems. Enthalpies of dilution in water of urea and hexane-1,2-diol have been determined, and the evaluated pairwise enthalpic interaction coefficients (h_{xx}=−331±3 J kg mol^{-2} for urea and h_{xx}=2999±46 J kg mol^{-2} for hexane-1,2-diol) were in a very good agreement with the literature values (h_{xx}=−350±13 J kg mol^{-2} for urea [17] and h_{xx}=2955±46 J kg mol^{-2} for hexane-1,2-diol [6]). The values of the dilution enthalpies, ΔH_{dil}, were obtained from:

$$\Delta H_{\mathrm{dil}}(m_{\mathrm{x}}^{\mathrm{i}} \rightarrow m_{\mathrm{x}}^{\mathrm{f}}) = -(\mathrm{d}Q/\mathrm{d}t)/P_{\mathrm{w}}$$

where (dQ/dt) is the heat evolved per unit time, P_{w} is the total mass flow-rate of water for unit time, and $m_{\mathrm{x}}^{\mathrm{i}}$ and $m_{\mathrm{x}}^{\mathrm{f}}$ are the initial and final molalities, respectively. ΔH_{dil} is given in J kg^{-1} of solvent in the final solution.

3. Results

An excess function is defined as the difference between the values of that function referred to a real and an ideal solution. Then, the excess enthalpy is obtained by:

$$H^{\mathrm{E}} = H - H^{\mathrm{id}} = H(m) - H_{\mathrm{w}}^{\circ} - \sum m_{\mathrm{x}}\bar{H}_{\mathrm{x}}^{\circ} \tag{1}$$

where H and H^{E}, the absolute and the excess enthalpy, respectively, both refer to 1 kg of solvent and m_{x} mol of each solute; H_{w}° is the enthalpy of 1 kg of water and $\bar{H}_{\mathrm{x}}^{\circ}$ is the limiting partial molal enthalpy of each solute. According to the treatment of solution properties originally proposed by McMillan-Mayer [18] and specifically applied to those of aqueous solutions of nonelectrolytes by Kauzmann [1] and other authors [19,20], an excess thermodynamic property can be expressed as a virial expansion as a function of molalities of pair and higher order interaction coefficients:

$$J^{\mathrm{E}} = \sum_{\mathrm{x}}\sum_{\mathrm{y}} J_{\mathrm{xy}} m_{\mathrm{x}} m_{\mathrm{y}} + \text{higher terms} \tag{2}$$

For three component solutions, virial coefficients of the power series of the excess enthalpies as a function of molalities can be easily derived from the enthalpies of dilution as follows:

$$\Delta H_{\mathrm{dil}}(m_{\mathrm{x}}^{\mathrm{i}}, m_{\mathrm{y}}^{\mathrm{i}} \rightarrow m_{\mathrm{x}}^{\mathrm{f}}, m_{\mathrm{y}}^{\mathrm{f}}) = \sum_{\mathrm{x}}\sum_{\mathrm{y}} h_{\mathrm{xy}} m_{\mathrm{x}}^{\mathrm{f}} m_{\mathrm{y}}^{\mathrm{f}} - (m_{\mathrm{x}}^{\mathrm{f}}/m_{\mathrm{x}}^{\mathrm{i}})\left[\sum_{\mathrm{x}}\sum_{\mathrm{y}} h_{\mathrm{xy}} m_{\mathrm{x}}^{i} m_{y}^{i}\right] + \cdots \tag{3}$$

where $m_{\mathrm{x}}^{\mathrm{i}}$, $m_{\mathrm{y}}^{\mathrm{i}}$, $m_{\mathrm{x}}^{\mathrm{f}}$, $m_{\mathrm{y}}^{\mathrm{f}}$ are the molalities of the x and y solutes before and after the dilution process, respectively. According to the McMillan-Mayer approach [18], the h coefficients represent the enthalpic contributions to the Gibbs free energy coefficients characterizing the interaction between pairs, triplets, or higher order coefficients. They implicitly account also for all variations of solvent–solvent and solute–solvent interactions. The values of the self coefficients for each solute are obtained by dilution of binary solutions. Then, the cross coefficients, h_{xy}, characterizing a ternary solution, containing the x and y solutes, can be evaluated by means of an auxiliary function ΔH^{**}:

$$\begin{aligned}\Delta H^{**} &= \Delta H_{\mathrm{dil}}(m_{\mathrm{x}}^{\mathrm{i}}, m_{\mathrm{y}}^{\mathrm{i}} \rightarrow m_{\mathrm{x}}^{\mathrm{f}}, m_{\mathrm{y}}^{\mathrm{f}}) \\ &\quad - \Delta H_{\mathrm{dil}}(m_{\mathrm{x}}^{\mathrm{i}} \rightarrow m_{\mathrm{x}}^{\mathrm{f}}) - \Delta H_{\mathrm{dil}}(m_{\mathrm{y}}^{\mathrm{i}} \rightarrow m_{\mathrm{y}}^{\mathrm{f}}) \\ &= 2h_{\mathrm{xy}} m_{\mathrm{x}}^{\mathrm{f}}(m_{\mathrm{y}}^{\mathrm{f}} - m_{\mathrm{y}}^{\mathrm{i}}) + \text{higher terms} \qquad (4)\end{aligned}$$

which depends only on the cross interaction coefficients. To determine the 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.

Aminoalkanols were studied in 1 mol kg^{-1} NaOH aqueous solution, used as solvent, to avoid the protonation of the amino group during the dilution process. To prove that the presence of Na^{+} and OH^{-} ions does not influence the labile hydration of hydrophobic domains, alkan-α,ω-diols were precedingly studied in the same solvent. The evaluated interaction coefficients are not appreciably different from those determined in pure water [16]. It can be inferred, then, that hydrophobic interactions do not change appreciably in the mixed solvent.

Dilution of all solutions investigated in the present work is an exothermic process and consequently, the derived enthalpic interaction coefficients are positive. In Table 1 the enthalpic self interaction coefficients are reported for binary aqueous solutions of the following amino-alkanols: 2-amino-1-ethanol, 3-amino-1-propanol, 5-amino-1-pentanol, 6-amino-1-hexanol, 2-amino-1-propanol, 2-amino-1-butanol, 2-amino-1-pentanol, 2-amino-1-hexanol. The enthalpic interaction coefficients increase at increasing alkyl chain length. α,ω-Isomers are characterized by coefficients smaller than those relative to 1,2-isomers, thus behaving qualitatively as the corresponding α,ω-diols with respect to 1,2-diols [6], whose data are also reported in Table 1. The comparison with the corresponding diamines is possible only with α,ω-diamines [16], because 1,2-diamines are not available. The variation of the coefficients of the aminoalkanols per every added CH_2 group, namely the cooperativity of hydrophobic interactions, is intermediate between that relative to diols and diamines.

In Table 2, enthalpic self and cross interaction coefficients are reported for the following binary and ternary systems: hexane-1,6-diol, 6-amino-1-hexanol, hexane-1,6-diamine, hexane-1,6-diol/hexane-1,6-diamine. The coefficient referring to the ternary mixture is the lowest, while the one characterizing binary solutions of hexane-1,6-diamine is the highest.

4. Discussion

A clear, though qualitative, understanding of nonbonding interactions in aqueous solutions of nonelectrolytes has been reached from the analysis of the

Table 1

Pairwise enthalpic interaction coefficients for binary aqueous solutions of amino-alkanols (x) and α,ω-diamines [a] (y) in 1 mol Kg^{-1} NaOH, 1,2-diols [b] (z) and α,ω-diols [b] in water (z), at 298.15 K

Substances	h_{xx} [c]	n [d]	c.r. [e]	Substances	h_{yy} [c]	Substances	h_{zz} [c]	h_{xx} from Eq. (6)
2-Amino-1-ethanol	299±8	24	1.2–0.25			Ethane-1,2-diol	415±30	
3-Amino-1-propanol	301±3	12	0.72–0.49	Propane-1,3-diamino	339±4	Propane-1,3-diol	523±9	421
5-Amino-1-pentanol	1296±12	24	0.16–0.070	Pentane-1,5-diamino	1522±24	Pentane-1,5-diol	1335±25	1425
6-Amino-1-hexanol	3073±24	43	0.16–0.012	Hexane-1,6-diamino	3986±18	Hexane-1,6-diol	2402±35	3094
2-Amino-1-propanol	356±5	25	0.16–0.10			Propane-1,2-diol	589±1	
2-Amino-1-butanol	547±13	24	0.20–0.13			Butane-1,2-diol	923±5	
2-Amino-1-pentanol	1548±42	23	0.16–0.080			Pentane-1,2-diol	1777±30	
2-Amino-1-hexanol	3615±17	25	0.020–0.0060			Hexane-1,2-diol	2955±55	

[a] [16].

[b] [10].

[c] Units: J kg mol^{-2}. Errors reported represent the 95% confidence limits.

[d] Number of experimental data.

[e] Concentration range, mol kg^{-1}.

Table 2
Pairwise enthalpic interaction coefficients [a] for binary and ternary solutions of hexane-1,6-diol, 6-amino-1-hexanol and hexane-1,6-diamine in 1 mol kg^{-1} NaOH, at 298.15 K

	Hexane-1,6-diol	6-Amino-1-hexanol	Hexane-1,6-diamine
Hexane-1,6-diol	2481±28 [b]		
6-Amino-1-hexanol		3073±24	
Hexane-1,6-diamine	2071±94 [c]		3986±18 [b]

[a] Units: J kg mol^{-2}.
[b] [16].
[c] 25 experimental data. Concentration range: 0.070–0.020 mol kg^{-1}.

excess thermodynamic properties using a group additivity approach proposed by Savage and Wood [17]. The analysis of the self and cross pair enthalpic coefficients, relative to the binary and ternary aqueous solutions of alkan-1,2-diols studied in this laboratory, indicated that mixed CHOH–CH_2 contributions are negligible and that only the CHOH–CHOH and CH_2–CH_2 contributions are necessary to get a good agreement between the experimental and calculated enthalpic coefficients [7]. Such a procedure is obviously in contrast with the simple additivity postulated by the group contribution approach, which assigns the same probability to all interactions occurring in solution. On the other hand, it is reported in the literature that the group contribution to the overall pairwise coefficient of the virial expansion of the Gibbs free energy is negative for interactions between groups having the same effect on the structure of water, and positive for mixed interactions ($G_{\text{hydrophilic–hydrophilic}}<0$, $G_{\text{hydrophobic–hydrophobic}}<0$, $G_{\text{hydrophilic–hydrophobic}}>0$) [21,22]. Thus, two interacting molecules prefer to be oriented in a configuration where favorable interactions between like groups are maximized. Mixed interactions are less probable because of the positive contribution to the Gibbs free energy. In the attempt to rationalize the pair enthalpic interaction coefficients relative to binary aqueous solutions of mono and polyhydroxylated substances and on the basis of the results on free energy contributions, in recent years, we proposed a model which postulates some more probable configurations in solution between two hydrated, interacting molecules [6,10]. For mono and polyhydroxylated substances, a "side on", preferential configuration was hypothesized, which allows the simultaneous juxtaposition of the maximum number of hydrophilic and hydrophobic domains. Other configurations, in which hydrophilic–hydrophobic interactions could occur, cannot be excluded but are less probable. The validity of this model was verified by the good linear correlation obtained when the enthalpic coefficients were reported as a function of an abscissa function that takes into account the number of hydrophobic groups that can actually be placed next to one another and are, therefore, available for hydrophobic interactions with another hydrated molecule [6,10]. α,ω-Diols are characterized by coefficients smaller than those for 1,2-diols, thus, indicating a reduced overlap of the hydrophobic residues depending on the mutual position of the two hydroxyl groups on the isomeric substances.

The comparison between the α,ω-aminoalkanols and 2-amino-1-alkanols reported in the present study shows that the coefficients for the α,ω isomers are lower: thus, the difference in the self-interaction follows the same direction as that occurring for the corresponding isomers of diols. This can be considered a strong indication that the side-on model holds also for these homologous series. However, for aminoalkanols only a rough linear trend was found when coefficients were plotted against the same abscissa function, thus underlining a behavior similar to that of diols, but more complex. Recent studies on alkyl-α,ω-difunctional derivatives, namely diols, dicarboxylic acids, diamines and aminoacids, show a very large difference in the capability of promoting hydrophobic interactions and, consequently, in their cooperativity in dependence of the different functional groups [16]. The order of cooperativity of hydrophobic interactions for these α,ω-derivatives was shown to be the following:

$$\mathrm{NH_3^+, COO^-} < \mathrm{OH, OH} < \mathrm{COOH, COOH} < \mathrm{NH_2, NH_2}$$

Namely, the amino group seems to be the most effective promoter of hydrophobic interactions. It is the presence of this group that probably determines the higher cooperativity of α,ω- and 2-amino-1-alkanols with respect to the corresponding diols, as detected by the higher values of the coefficients reported in Table 1.

Comparing self and cross coefficients of the α,ω-diol, α,ω-diamine and, α,ω-amino-alkanol containing six carbon atoms (see Table 2), it comes out that hexane-1,6-diol/hexane-1,6-diamine ternary system is characterized by a coefficient (h_{xy}= 2071 J kg mol^{-2}) that falls below the range of the coefficients relative to the binary solutions of the corresponding diol and diamine. Interactions in the binary solutions obviously depend on like–like hydrophilic interactions, while in the ternary system like–like hydrophilic interactions cannot occur, the only possible interactions being those between the unlike amino and hydroxyl groups. The smallest coefficient characterizing the ternary system underlines the reduced capability of unlike hydrophilic interactions in promoting hydrophobic interactions when compared with the like ones. For the binary system containing 6-amino-1-hexanol, both like–like and like–unlike hydrophilic interactions could occur, owing to the presence of the two different hydrophilic groups on the same molecule. The value of the coefficient (h_{xx}=3073 kg mol^{-2}) falls within the range of the self coefficients relative to the binary solutions of hexane-1,6-diol and hexane-1,6-diamine. That implicitly means or the absence of the mixed OH–NH$_2$ interaction or its reduced influence on the overall coefficient. This is possible only admitting the presence of a side-on preferential configuration juxtaposing prevailingly like–like, OH–OH and NH$_2$–NH$_2$, hydrophilic groups. The occurrence of mixed interactions would be detected by a lower value of the coefficient, closer to that characterizing the ternary system, as a consequence of a reduced ability in promoting hydrophobic interactions. The higher probability assigned to the presence of like–like interactions, in particular to the NH$_2$–NH$_2$ interactions, is supported also by solid-state studies [23]. From the crystal structures of oligonucleotides, it has been found that the close contacts between neighboring base pairs mostly involve the amino groups of the bases [20]. The experimentally determined values of the mutual amino group distances are smaller than the sum of the amino group van der Waals radii. Therefore, there must be a strong attractive interaction which constrains the exocyclic amino groups of DNA bases. Even though comparisons between substances in solution and in the solid state must be considered with care, this behavior of the amino groups is certainly peculiar and different from that of other functional groups.

It is possible to predict the coefficient for α,ω-amino-alkanols through a phenomenological rule, reported in the literature, that allows the enthalpic cross coefficient of a ternary solution to be evaluated, knowing the pairwise coefficients relative to the binary solutions, as follows [24–26]:

$$h_{xy} = (h_{xx}h_{yy})^{1/2} \tag{5}$$

The phenomenological relation, applied to pairs of homologous substances in water, simply means the absence of specific interactions. It is usually employed to calculate the cross coefficient for the interaction between two different solutes. In the present case, it is used to evaluate the enthalpic self-interaction coefficient of an aminoalkanol, namely a substance containing two different functional groups, starting from the self coefficients of the diamine and diol bearing the same alkyl chain, as follows:

$$h_{\alpha,\omega\text{-aminoalkanol}/\alpha,\omega\text{-aminoalkanol}} = (h_{\alpha,\omega\text{-diamine}/\alpha,\omega\text{-diamine}}h_{\alpha,\omega\text{-diol}/\alpha,\omega\text{-diol}})^{1/2} \tag{6}$$

The value of the self coefficient obtained through Eq. (6) for the aminoalkanol containing six carbon atoms, 3094 J kg mol^{-2}, is very similar to the experimental one (3073 J kg mol^{-2}). That reinforces the hypothesis that in the binary solutions of 6-amino-1-hexanol mixed interactions are absent or negligible. In fact, when only mixed interaction between functional groups are possible, as in the case of the ternary system containing both diamine and diol, the experimental coefficient is much lower (2071 J kg mol^{-2}), underlining that contributions are not additive. Then, all approaches relying on additivity, as the square root rule or the group additivity approach proposed by Savage and Wood [17], cannot predict the different values of the coefficients relative to the binary system containing the α,ω-aminoalkanol and to the ternary one involving the corresponding diamine and diol.

As a conclusion, hydrophilic interactions are an important factor in determining the strength of hydrophobic interactions. The pair interaction in aminoalkanols can be supposed to occur through a preferred side-on configuration stabilized by the simultaneous juxtaposition of hydrophilic and hydrophobic domains. The two different functional groups juxtapose so that like–like hydrophilic interactions are preferred: they work as better promoters of hydrophobic interactions than like–unlike ones.

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