ELSEVIER

Thermochimica Acta 291 (1997) 21–26

thermochimica acta

Hydrophilic groups determine preferential configurations in aqueous solutions. A calorimetric study of monocarboxylic acids and monoalkylamines at 298.15 K

Giuseppina Castronuovo*, Vittorio Elia, Filomena Velleca

Department of Chemistry, University Federico II of Naples, via Mezzocannone, Naples 4-80134, Italy

Received 10 June 1996; received in revised form 24 July 1996; accepted 9 September 1996

Abstract

Enthalpies of dilution of binary aqueous solutions containing monocarboxylic acids and monoalkylamines have been determined by microcalorimetry at 298.15 K. Pairwise self-interaction coefficients of the virial expansion of the excess enthalpies were evaluated and compared with those obtained for alkan-1-ols. The values of the coefficients are positive and increase differently with increasing number of carbon atoms on the alkyl chain, depending on the nature of the functional groups. For all series, starting with the terms containing five methylene groups, the coefficients tend to attain a constant value. Attempting to explain this behaviour, the attention was focused on the nature of the hydration of the alkyl chain. © 1997 Elsevier Science B.V.

Keywords: Calorimetry; Excess enthalpies; Monoamines; Monocarboxylic acids; Preferential configuration

1. Introduction

Hydrophobic interactions have long been invoked as the major driving forces in many biochemical processes, while a minor role has been usually assigned to hydrophilic interactions. Recently, the latter interactions have received due attention and have been demonstrated to be important in highly specific processes such as protein folding and molecular recognition [1–4].

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. The analysis of the magnitudes and signs of the enthalpic interaction coefficients for a variety of compounds has shown that these coefficients depend on the number, position, stereochemistry and nature of the functional groups [5–9]. However, a group additivity approach reported in the literature has failed in distinguishing positional isomers and in reproducing self-consistent values of the contribution of groups to the pair enthalpic coefficients of a homologous series [10]. This has led us 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 most probable

*Corresponding author. Fax: ++ 815527771.

PII S0040-6031(96)03089-4

configuration between interacting hydrated molecules ('side on' model) [11–17]. This configuration is responsible for the failure of the cited statistical approach and for the different cooperativity of hydrophobic interactions found for alkanols, alkylureas [18], dicarboxylic acids [19], diamines [19] and aminoacids [13–16]. Also the study of interactions in ternary aqueous solutions containing hydrophobic structure makers and hydrophilic structure breakers has yielded evidence for the occurrence of a preferential configuration stabilized by the juxtaposition of hydrophilic domains [20].

In the present paper, we report a calorimetric study of binary aqueous systems containing monocarboxylic acids and monoalkylamines. The aim is to verify whether a preferential configuration also exists in solution for these substances and to reveal the effects of the nature of the carboxyl and amino groups on the cooperativity of hydrophobic interactions.

2. Experimental

Monocarboxylic acids and monoalkylamines were Sigma or Aldrich products. They were of the highest commercially available purity. Solutions were prepared by weight, employing 0.01 m HCl and 1 M NaOH aqueous solutions as solvents. 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 a 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 the pumping of solutions into the vessels of the calorimeters. The method has been tested through known systems, and the results were in agreement with those reported in the literature. The values of the dilution enthalpies, $\Delta_{dil}H$, were obtained from:

$$\Delta_{dil}H(m_x^i \rightarrow m_x^f) = -(dQ/dt)/P_w$$

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_x^i and m_x^f are the initial and final molalities, respectively. $\Delta_{dil}H$ is given in J kg^{-1} of water 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. It can be expressed as a virial expansion as a function of molalities, m_i, of pair and higher order coefficients, j_i:

$$J^E = \sum_x \sum_y j_{xy} m_x m_y + \text{higher terms.} \quad (1)$$

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 the respective binary and ternary solutions. The enthalpy change that occurs upon the dilution of a solution containing n solutes, $\Delta_{dil}H$, is related to the corresponding excess enthalpy, H^E, as follows:

$$\Delta_{dil}H = H^E(m_x^f, m_y^f, \ldots) - (m_x^f/m_x^i)H^E(m_x^i, m_y^i, \ldots) \quad (2)$$

where x is anyone of the solutes, and m_x^f and m_x^i are the molalities of each solute after and before the dilution process, respectively.

Substituting relations between excess enthalpies and virial coefficients into Eq. (2), the following relation is obtained:

$$\Delta_{dil}H = \sum_x \sum_y h_{xy} m_x^f m_y^f - (m_x^f/m_x^i) \times \left(\sum_x \sum_y h_{xy} m_x^i m_y^i \right) + \ldots \quad (3)$$

From this equation it is possible to deduce simultaneously self- and cross-enthalpic coefficients. According to the McMillan–Mayer approach, these coefficients are the enthalpic contributions to the free-energy coefficients characterizing the interactions among pair, triplet or higher number of solute particles [21]. These coefficients implicitly account for solute–solvent and solvent–solvent interactions.

For a two-component system Eq. (3) reduces to:

$$\Delta_{dil} = h_{xx} m_x^f (m_x^f - m_x^i) + \text{higher terms.} \quad (4)$$

To determine the h_{xx} coefficients, a least squares procedure was used. Owing to the limited range of concentrations explored, only pairwise coefficients

Table 1
Pairwise enthalpic interaction coefficients [a] for alkan-1-ols [b], monocarboxylic acids [c] and monoalkylamines [d] at 298 K

	R=CH_2OH	R=COOH	R=NH_2
CH_3R	243±10 [e]	—	—
CH_3CH_2R	559±14 [f]	653±10	—
$CH_3(CH_2)_2R$	1003±15 [f]	1261±20	801±18
$CH_3(CH_2)_3R$	1766±68 [f]	1984±82	1083±59
$CH_3(CH_2)_4R$	2401±70 [g]	3062±60	1360±62
$CH_3(CH_2)_5R$	2183±160 [g]	2464±92	1296±32

[a] Units: J kg mol^{-2}. Errors reported are the 95% confidence limits. [b] Values obtained in water. [c] Values obtained in HCl aqueous solutions. [d] Values obtained in NaOH aqueous solutions. [e] [22]. [f] [23]. [g] [17].

were found to be necessary for the best fit of experimental data.

The enthalpic self-interaction coefficients for the homologous series of monocarboxylic acids in 0.01 m HCl and of monoalkylamines in 1 M NaOH are reported in Table 1 and compared with the values for alkan-1-ols in water. The dilution of these binary solutions is an exothermic process, and then the derived coefficients are positive. In Fig. 1 the enthalpic-interaction coefficients are reported as a function of n_C, the number of carbon atoms in the alkyl chain, for monocarboxylic acids, monoamines and alkan-1-ols. The coefficients increase differently at increasing alkyl chain lengths depending on the nature of the functional group. They tend to attain a plateau when the alkyl chain becomes sufficiently long, namely for n_C=5. Monocarboxylic acids were studied in 0.01 m HCl, while monoalkylamines in 1 M NaOH, to avoid the dissociation of the carboxyl and the protonation of the amino groups during the dilution process. To prove that the presence of H^+, Cl^-, OH^- and Na^+ ions does not influence the labile hydration of hydrophobic domains, alkan-α, ω-diols were previously studied in 0.01 m HCl and in 1 M NaOH aqueous solutions. The evaluated interaction coefficients are not significantly different from those determined in water [24]. It can be inferred, then, that hydrophobic interactions do not change appreciably in the mixed solvent.

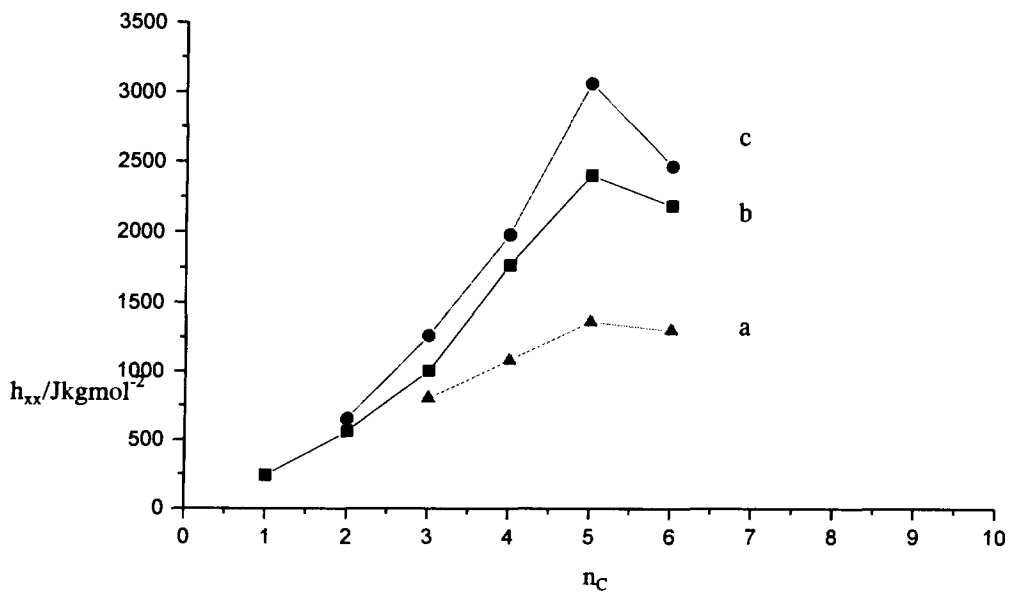

Fig. 1. Enthalpic pairwise interaction coefficients, h_{xx}, vs. the total number of carbon atoms, n_C: (a) for monoamines in NaOH aqueous solutions; (b) for alkan-1-ols in water; and (c) for monocarboxylic acids in HCl aqueous solutions, at 298 K.

4. Discussion

Thermodynamic studies concerning aqueous solutions of hydroxylated substances have demonstrated the importance of the functional group in improving hydrophobic interactions. Hydrophilic interactions, acting synergetically with the hydrophobic ones, determine preferential configurations through which interactions between two hydrated molecules occur. These preferential configurations are considered more probable as against other possible ones in that they can maximize the interaction between similar domains, simultaneously minimizing the mixed ones [5–9]. Two similar domains are characterized by the same effect on water structure and the interaction occurring between them is thermodynamically favourable: on the contrary, interactions between unlike domains are unfavourable [25]. That is clearly inferred from the analysis of the excess Gibbs free energy treated through a group additivity approach [10]. This statistical approach, however, does not account for the large differences in the thermodynamic parameters concerning positional isomers or stereoisomers, or for the enhanced cooperativity of hydrophobic interactions of hydroxylated compounds, α, ω dicarboxylic acids and diamines [19]. On the contrary, the preferential configuration model has allowed to explain the very high differences in the values of the pairwise enthalpic coefficients of positional isomers for mono- and polydihydroxylated compounds [5–9]. For these substances the following unifying linear correlation is obtained:

$$h_{xx} = a + bN.$$

This equation describes very well the enthalpic self- and cross- interaction coefficients of all cited compounds, including positional isomers. Notwithstanding its roughness, it works as a powerful predictive method through the abscissa N, that takes into account steric differences existing between the groups when the interacting molecules assume the most probable configuration. N is a function of the third power of the number of equivalent CH_2 groups, as follows:

$$N = n_{CH_2}(n_{CH_2} - n_{\alpha CH_2})(n_{CH_2} - n_{CH_2OH})$$

where n_{CH_2} is the total number of equivalent CH_2 groups ($CH_3 \equiv 1.5CH_2$, $CH \equiv 0.5CH_2$), $n_{\alpha CH_2}$ is the number of equivalent CH_2 groups in the α position of a carbon atom bearing a functional OH group, and n_{CH_2OH} is the number of equivalent CH_2 groups bearing hydroxyl functional groups. $n_\alpha CH_2$ and n_{CH_2OH} are subtracted from the total number of CH_2 groups since the model used considers them as remote and then less effective towards the overlap of their hydration cospheres. Then, the parameter N is a measure of the role of hydrated hydrophobic groups which can actually juxtapose and are available for hydrophobic interactions with another molecule.

Hexane-1-ol and heptane-1-ol are characterized by the similarity of their enthalpic coefficients, thus demonstrating a reduced hydrophobic interaction between the alkyl chains [17]. Thus, up to pentane-1-ol, the functional group is able to force hydrophobic interactions. At increasing chain lengths, the interactions between the last methylene groups become less effective, probably because of their distance from the functional group which is now unable to force hydrophobic interactions. As a conclusion, beyond a certain length of the alkyl chain, the hydrophobic interaction is not influenced by the promoting hydrophilic interaction and the enthalpic coefficients become almost invariant. The decrease of hydrophobic interactions could be explained simply in terms of an effect of the alkyl chain length [17]. For instance, starting with hexane-1-ol, folding of the alkyl chain could occur, generating hydrophobic intramolecular interactions that could make an increased number of hydrophobic hydrogen atoms to be remote [17].

The present study shows that this behaviour represents a general rule for monofunctional molecules. In fact, for the homologous series presented here, namely monocarboxylic acids and monoalkylamines, the enthalpic self-coefficients as a function of the number of carbon atoms on the alkyl chain present a trend characterized by the attainment of a plateau. Then, this behaviour, common to all series studied, is independent of the nature of the functional group and probably related to the nature of hydrophobic hydration of the alkyl chain. Studies reported in the literature about volumetric properties of aqueous solutions of various homologous series of solutes reveal that hydrophobic hydration is not uniform because of the different influence of the hydrophilic functional group on the hydration of methylene groups in the alkyl chain [7,26]. A major influence is undergone by the methylene groups nearest to the functional group. The

influence of an uncharged functional group, as a hydroxyl group, on the hydrophobic hydration can be supposed to be effective up to the fourth methylene group in the alkyl chain. In fact, starting from this last one the contribution to the limiting partial molal volumes of a methylene group tends to attain a constant value of 16 cm^3 mol^{-1} [27]. This contribution remains invariant at increasing chain lengths showing that processes of folding of the alkyl chains are scarcely probable, at least up to heptane-1-ol. On the basis of the existence of a preferential configuration through which two hydrated monofunctional molecules interact, namely the side-on configuration, it is possible to explain the observed behaviour. The functional group makes different the hydrophobic hydration of methylene groups and consequently the self interactions that these can establish in a side-on configuration. For the homologous series of alkan-1-ols up to butane-1-ol the self-interaction coefficients do not increase linearly with the number of carbon atoms of the alkyl chain, but it is very difficult to establish whether the dependence is quadratic or cubic. Only adding pentane-1-ol alone makes it possible to affirm that this dependence is cubic. This could be explained admitting that the pure hydrophobic methylene groups present in pentane-1-ol interact between themselves better than those nearest to the functional group. For hexane-1-ol and heptane-1-ol, the invariance of the coefficients [17] indicates that the interaction of the last methylene groups is less effective. Probably, their distance from the functional group is such that this cannot exert its forcing action on hydrophobic interactions. Starting from εCH_2, hydrophobic interactions are not influenced by the promoting hydrophilic interactions. The same could be invoked for monocarboxylic acids and monoalkylamines: in both cases the attainment of a plateau occurs at the same number of carbon atoms on the alkyl chain. The coefficients increase with the alkyl chain length in a different manner depending on the nature of the functional groups. The carboxyl group improves hydrophobic interactions better than the hydroxyl or amino groups, as already demonstrated for dicarboxylic acids [19] and *N*-acetylaminoacids [24] in HCl 0.01 m. The increase of the coefficients for monoalkylamines is linear with the number of carbon atoms on the alkyl chain suggesting that the amino group does not improve hydrophobic interactions between the alkyl chains. This is in contrast with the behaviour shown by α, ω-diamines that, compared with the α, ω-dicarboxylic acids and α, ω-alkandiols, are characterised by the largest increase of the coefficients at increasing lengths of the alkyl chain [19].

The analysis of the enthalpic self-interaction coefficients in terms of the influence of the functional groups on the hydration cospheres of the alkyl groups in the chain helps in understanding the complex behaviour of the examined substances when they interact with another hydrated molecule. The model postulating preferential configurations between interacting molecules is based on the hypothesis that interactions between like domains are maximized. The side-on configuration is the only one allowing the juxtaposition of groups similarly hydrated. It should be stressed that this model has also been successful in explaining data concerning chiral recognition shown by cycloalkandiols [17] and α-aminoacids in the zwitterionic form. For the latter systems the configuration 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 suppressed [11–16].

Acknowledgements

This work was financially supported by the Ministry of University and Scientific Research (MURST), Rome.

References

[1] M. Mezei and A. Ben-Naim, J. Chem. Phys. 92 (1990) 1359.
[2] A. Ben-Naim, Biopolymers 29 (1990) 567.
[3] A. Ben-Naim, J. Chem. Phys. 93 (1990) 8196.
[4] S.T. Durell, B.R. Brooks and A. Ben-Naim, J. Phys. Chem. 98 (1994) 2198.
[5] G. Castronuovo, R.P. Dario and V. Elia, Thermochim. Acta 181 (1991) 305.
[6] C. Cascella, G. Castronuovo, V. Elia, R. Sartorio and S. Wurzburger, J. Chem. Soc. Faraday Trans. I 86 (1990) 85.
[7] S. Wurzburger, R. Sartorio, V. Elia and C. Cascella, J. Chem. Soc. Faraday Trans. I 86 (1990) 3891.
[8] S. Andini, G. Castronuovo, V. Elia and L. Fasano, J, Chem. Soc. Faraday Trans. I 86 (1990) 3567.

[9] L. Ambrosone, S. Andini, G. Castronuovo, V. Elia and G. Guarino, J. Chem. Soc. Faraday Trans. I 87 (1991) 2989.
[10] J.J. Savage and R.H. Wood, J. Solution Chem. 5 (1976) 731.
[11] G. Barone, G. Castronuovo, P. del Vecchio, V. Elia and S. Puzziello, J. Solution Chem. 18 (1989) 1105.
[12] G. Castronuovo, V. Elia, C. Giancola and S. Puzziello, J. Solution Chem. 19 (1990) 855.
[13] G. Castronuovo, V. Elia and M. Magliulo, Can. J. Chem. 69 (1991) 794.
[14] S. Andini, G. Castronuovo, V. Elia and F. Velleca, J. Solution Chem. 24 (1995) 485.
[15] G. Castronuovo, V. Elia and F. Velleca, J. Solution Chem. 24 (1995) 1211.
[16] G. Castronuovo, V. Elia and F. Velleca, J. Solution Chem. 25 (1996) 51.
[17] G. Castronuovo, V. Elia and F. Velleca, J. Chem. Soc. Faraday Trans. I 92 (1996) 1149.
[18] G. Castronuovo, V. Elia and F. Velleca, J. Molecular liquids 68 (1996) 55.
[19] G. Castronuovo, V. Elia and F. Velleca, J. Chem. Soc. Faraday Trans. I 92 (1996) 3093.
[20] G. Castronuovo, V. Elia, G. Petrone and F. Velleca, Thermochim. Acta 247 (1994) 273.
[21] W.G. McMillan Jr. and J.E. Mayer, J. Chem. Phys. 13 (1945) 276.
[22] F. Franks, M. Pedley and S. Reid, J. Chem. Soc., Faraday Trans. I 72 (1976) 359.
[23] H.L. Friedman and C.V. Krishnan, J. Solution Chem. 2 (1973) 119.
[24] G. Castronuovo, V. Elia and F. Velleca, J. Solution Chem., in press.
[25] B. Okamoto, R.H. Wood and P.T. Thompson, J. Chem. Soc. Faraday Trans. 1 74 (1978) 1990.
[26] M. Abbate, G. Castronuovo, V. Elia and S. Puzziello, Can. J. Chem. 71 (1993) 2150.
[27] A.K. Mishra and J.C. Ahluwalia, J. Phys. Chem. 88 (1984) 86.