Generality of hydrophobic phenomena for aqueous solutions of amphiphiles

Katerina Zemánková, Jacobo Troncoso, Claudio A. Cerdeiriña*, Luis Romaní*

Departamento de Física Aplicada, Universidad de Vigo – Campus del Agua, As Lagoas s/n, 32004 Ourense, Spain

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ABSTRACT

With the temperature and composition dependence of the isobaric heat capacity as our experimental probe, previously reported anomalous behaviors for *tert*-butanol and 2-butoxyethanol in water are shown to belong to a general scheme for aqueous solutions of amphiphiles. As opposed to a pretransitional scenario, our results point towards aggregation of the hydrophobic moieties of solute molecules as the origin of the phenomenology. The locus in the mole fraction-temperature plane that maps anomalies for 1-pentylamine solutions extends to quite small concentrations and 330 K, thereby raising questions on the roles of hydration and aggregation in phenomena involving so-called 'molecular hydrophobic interfaces'.

1. Introduction

Amphiphilic molecules with moderately large alkyl chains reveal interesting aspects of hydrophobicity [1–5]. At sufficiently small concentrations, their aqueous solutions provide information on hydrophobic hydration, that is, the way water molecules organize around the nonpolar parts of solutes. When concentration is not small enough, either direct solute–solute contacts or effective interactions mediated by water, the latter often referred to as hydrophobic forces, become increasingly relevant. Liquid amphiphiles appear again as an important benchmark for hydrophobicity since they can be dissolved in water up to substantially higher proportions than pure hydrophobes. Notable examples are *tert*-butanol and 2-butoxyethanol. Their aqueous solutions received a great deal of attention in the past and have indeed acquired a renewed interest because they exhibit anomalous physicochemical and structural behavior in the water-rich region, say, amphiphile mole fractions up to 0.1. Experimental approaches include light scattering [6,7], small-angle X-ray scattering (SAXS) [8], neutron diffraction [9], small-angle neutron scattering (SANS) [10], Raman [11], Brillouin [12] and NMR [13] spectroscopy, or thermodynamics [14–18]. A number of computational studies have been carried out while new force fields are being developed (see, e.g., [19,20]). Despite efforts, a detailed characterization of the microscopic origins of anomalies remains an unresolved puzzle.

Hydrophobicity is relevant per se but also in light of its implications in general physical chemistry as well as in biochemical and biophysical phenomena including protein folding or ligand–protein and protein–protein binding (see [21–23] for review). Progress in our understanding of aqueous solutions of amphiphiles is therefore highly desirable. In the present context, it is tempting to inquire whether or not *tert*-butanol and 2-butoxyethanol are a rare exception within the class of small amphiphilic liquids. One should expect not.

This question is answered here by studying six selected solutes in water from the point of view of thermodynamics. As a property that has proved a useful indicator of phenomena at a molecular level, we focus on the temperature and composition dependence of the isobaric heat capacity $C_p = T(\partial S/\partial T)_p$, where S stands for the entropy. After establishing the degree of generality of anomalies, their molecular origins are analyzed. Aggregation of the hydrophobic parts of amphiphiles seems a natural microscopic scheme.

2. Experimental

All chemicals were supplied from Sigma–Aldrich with the following purities: water (>99.9%), *tert*-butanol (>99.7%), *tert*-butylamine (>99.5%), 2-butoxyethanol (>99%), 1-pentylamine (>99%), 1,4-dioxane (>99.8%) and tetrahydrofuran (>99.9%). All were degassed and dried over 4 nm molecular sieves before used. Mixtures were prepared by weighing using a Mettler AE-240 balance with an uncertainty in the mole fraction of ±0.0005.

Heat capacity measurements were performed using a Calvet-type flux calorimeter. Its operation principle is based on the detection of the differential heat flux between two experimental

* Corresponding authors.
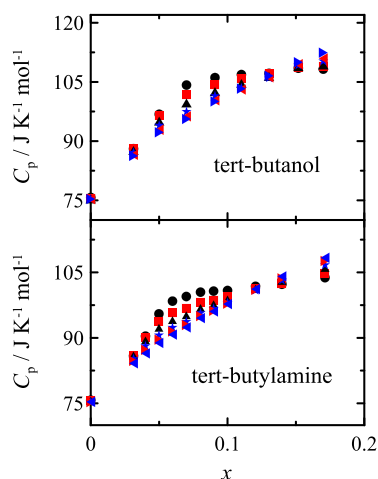 *E-mail address:* calvarez@uvigo.es (C.A. Cerdeiriña).

Figure 1. Mole fraction dependence of the isobaric heat capacity C_p of aqueous solutions of amphiphiles at atmospheric pressure and 278.15 K (circles), 288.15 K (squares), 298.15 K (black triangles), 308.15 K (stars), 318.15 K (red triangles) and 328.15 K (blue triangles). (For interpretation of reference to color in this figure legend, the reader is referred to the web version of this article.)

Figure 2. Mole fraction dependence of the isobaric heat capacity C_p of aqueous solutions of amphiphiles at atmospheric pressure and 278.15 K (circles), 288.15 K (squares), 298.15 K (black triangles), 308.15 K (stars), 318.15 K (red triangles) and 328.15 K (blue triangles). (For interpretation of reference to color in this figure legend, the reader is referred to the web version of this article.)

cells when temperature is varied at a constant, prescribed scanning rate. Cells contain the sample of unknown heat capacity and a reference liquid substance. Via the Seebeck effect, two thermopiles convert the heat flux into an electric signal which is proportional to the heat capacity per unit volume difference, thus allowing calibration to be performed using liquids of known heat capacity. In this Letter, we covered the 278.15–328.15 K range with a scanning rate of 0.25 K min^{-1}. The whole assembly is surrounded by a circulating bath of liquid undecane whose temperature is controlled with high precision using Peltier elements while temperature measurement is performed using a Pt-100 sensor. To get the heat capacity per particle, density data for the sample are required. They were determined using an Anton-Paar DMA-5000 vibrating-tube densimeter. The uncertainty of the resulting heat capacity data is ± 0.05 J mol^{-1} K^{-1}.

To operate at higher pressures, an additional set-up is needed. A pump driven by a stepping motor is employed for pressurizing the liquids while appropriate valves and tubing for purging/cleaning the system are built in. Pressure was measured using a quartz sensor with an uncertainty of ± 0.01 MPa, densities are now determined using an Anton-Paar DMA 512P apparatus, and the uncertainty of heat capacity data is estimated to be ± 0.10 J mol^{-1} K^{-1}. More detailed information on the whole experimental equipment and procedures can be found elsewhere [24–26].

3. Generality and hydrophobic character

Figure 1 shows data at atmospheric pressure along various isotherms for *tert*-butanol and *tert*-butylamine solutions. As can be seen, C_p varies nonregularly with x in a narrow range of the studied water-rich region, this behavior being more marked at low temperatures. The appealing close resemblance between these two homologous systems makes plausible to assert that the nature of the hydrophilic group of the amphiphile plays no primary role.

While, to the best of our knowledge, little work for the series of amines has been reported, these amphiphiles are quite interesting in that they allow solubilization of larger hydrophobic chains than alcohols do: in contrast to aqueous solutions of primary and secondary butanols as well as higher alcohols [27], 1-pentylamine mixes with water in all proportions, thereby opening an interesting window for experimental testing. Data for its solutions in water, shown in Figure 2, reveal the same pattern of behavior as that
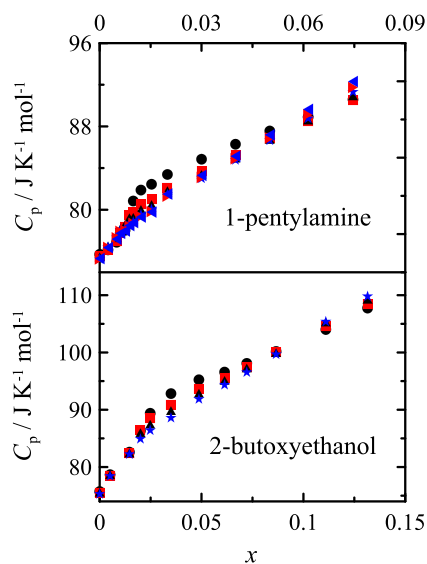
observed for *tert*-butanol and *tert*-butylamine. As a characteristic composition x^*, we choose that corresponding to the maximal variation of C_p with temperature. This is $x^* \approx 0.015$ for 1-pentylamine, significantly lower than that for *tert*-butanol and *tert*-butylamine, $x^* \approx 0.07$. Figure 2 also shows that $x^* \approx 0.04$ for 2-butoxyethanol, which, like 1-pentylamine, offers moderately large hydrophobic chains that are soluble in water. Clearly, the greater the size of the hydrophobic domain of the molecule is, the lower the concentration of the amphiphile species that marks the onset of the phenomenon.

Before going further, we may note that caution must be taken when analyzing the 'degree of hydrophobicity' of amphiphiles. Because of electronegativity, the presence of functional groups like OH and NH$_2$ distorts the electronic charge distribution in molecules. Specifically, O and N atoms effectively accumulate a negative net charge that is mostly but not fully compensated by the attached H atoms, implying that neighboring functional groups of the hydrocarbon chain acquire a positive charge. Thus, for the same reason that OH and NH$_2$ are regarded hydrophilic, CH$_2$ and CH$_3$ functional groups attached to them are, say, less hydrophobic than those that are far apart, the latter being conventional hydrophobic units. While this 'proximity effect' is known to extend up to four hydrocarbon groups, it is particularly noticeable for the nearest-neighbor (see, e.g., [28]).

With these premises, one may anticipate a quite modest degree of hydrophobicity for a solute like 1,4-dioxane, as the four CH$_2$ groups attached to the electronegative O atoms of this cyclic molecule necessarily have a compensating positive charge. To the extent that hydrophobicity drives anomalies in C_p, they should be small for these solutions. Such expectation is confirmed by data in Figure 3, which, in contrast to those for amphiphiles with harder hydrophobic parts, displays a picture free of anomalies. Tetrahydrofuran represents an intermediate case: since now we have a cyclic molecule with four CH$_2$ groups but just an O atom, it sounds reasonable to find the behavior of its aqueous solutions in between the two contrasting ones described above while closer to that exhibited by 1,4-dioxane mixtures (see Figure 3). This is consistent with the recent statement [29] that, as thermodynamic response is concerned, the degree of hydrophobicity of tetrahydrofuran compares