

# Solvophobic effects and relationships between the Gibbs energy and enthalpy for the solvation process

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An approach is suggested to describe the solvophobic effects in various solvents, qualitatively and quantitatively. We analyzed the relationships between the Gibbs energies and enthalpies of solvation of alkanes in various solvents on the basis of existing experimental data. It is shown that for a large group of solvents, there is a linear correlation between the two quantities. Other solvents, primarily self-associated, show deviations from this line. These deviations are always positive, leading to a decrease in solubility, and can be used as a measure of the strength of the solvophobic effects. It is also shown that the solvophobic effects is not the only factor determining the solubility, even for alkane solutes. The magnitudes of contributions of the solvophobic effect into the Gibbs energies of solvation of various compounds in monohydric alcohols are determined. These magnitudes are found to be linearly correlated with a characteristic molecular volume of a solute. The slope of correlation grows up with the concentration of hydrogen bonds in the liquid solvent. Copyright © 2011 John Wiley & Sons, Ltd.

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## INTRODUCTION

The concept of solvophobic effects is widely used in modern chemistry. When some species in some solvent is called solvophobic, it is usually meant that this species has little affinity to the solvent. The most important and well-studied particular case of solvophobic effects is the hydrophobic effect in water.<sup>[1]</sup>

Manifestations of the hydrophobic effect include, but are not limited to, poor solubility of apolar solutes in water. For example, aqueous solutions have anomalously large heat capacities, low entropies of formation, and many interesting structural and dynamic features.<sup>[2]</sup> These effects have been extensively studied using both experimental and theoretical methods over the past decades.

Analogous effects can take place in solvents other than water. The examples of such solvents are ethylene glycol, formamide, or glycerol. Unlike most organic solvents and similar to water, they are immiscible with alkanes. The standard thermodynamic functions of solvation of *n*-hexane from vapor phase into water, formamide, ethylene glycol, and *n*-hexane itself at 298 K are 28.3, 13.7, 12.0, and  $-4.0 \text{ kJ mol}^{-1}$  (Gibbs energies), respectively, and  $-202$ ,  $-133$ ,  $-130$ , and  $-92 \text{ J K}^{-1} \text{ mol}^{-1}$  (entropies), respectively. The different thermodynamic behavior of formamide and ethylene glycol solvents from alkanes and many other solvents can be attributed to solvophobic effects. From a structural point of view, these solvents are similar to water in the sense that their molecules have more than one acidic hydrogen and lone pair electron and are able to form a branched continuous network of hydrogen bonds. The existence of such network in a liquid phase is, however, disputed.<sup>[3]</sup>

A very important consequence of the hydrophobicity of individual apolar molecules is the so-called hydrophobic interactions, a tendency of apolar fragments of macromolecules

to stick together in aqueous medium. These interactions drive the process of micelle formation and play an important role in protein folding. Micelles assembled from amphiphilic solutes have also been observed<sup>[4]</sup> in glycerol, ethylene glycol, formamide, other 1,2-diol and 1,3-diol, 1,2-aminoalcohols, as well as mixed aqueous–organic solvents.<sup>[5]</sup> However, the critical micelle concentrations in an organic medium were substantially higher than those in water.

Although in the mentioned solvents, the solvophobic effects are pronounced and their similarity with hydrophobic effects is evident, it is not so clear whether the solvophobic effects take place in other self-associated solvents. For example, among the saturated aliphatic alcohols, only methanol is not infinitely miscible with *n*-hexane. The Gibbs energy of solvation of *n*-hexane even in methanol ( $4.2 \text{ kJ mol}^{-1}$ ) is less positive than in dimethyl sulfoxide ( $7.3 \text{ kJ mol}^{-1}$ ), which is usually considered as an aprotic solvent. Ray concluded that there are no solvophobic effects in monohydric alcohols because in these solvents, he did not observe micellization of a nonionic detergent.<sup>[4]</sup> On the other hand, Yamaguchi *et al.*<sup>[6]</sup> spoke about the solvophobic effects in monohydric alcohols on the basis of the studies of dielectric relaxation. These studies showed that, like in aqueous solutions or in formamide, the process of relaxation in monohydric alcohols is significantly slowed down in the vicinity of dissolved apolar

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molecules. This phenomenon was not observed in solvents lacking intermolecular hydrogen bonding, for example, in dimethylacetamide.

Beside the problem with the strict definition of the solvophobic effects, the question is whether we can speak about solvophobic effects only in certain solvents that have in some way a peculiar structure of the liquid phase (and then which solvents they are) or we should attribute a parameter reflecting the strength of solvophobic effects to any solvent. There are currently different views on this question.

Sinanoglu<sup>[7]</sup> was one of the first to discuss the solvophobic effects in various solvents. His "solvophobic theory" leads to a conclusion that solvent-induced association of apolar species is driven by a "solvophobic" contribution into the Gibbs energy of association, which is proportional to the surface tension of a solvent and to the change of solvent-accessible surface area during association. This solvophobic contribution remains for all solvents, but the aggregation may happen only if the surface tension is high enough.

Abraham *et al.*<sup>[8]</sup> suggested a solvophobicity parameter of solvents  $Sp$  defined by the following:

$$Sp = 1 - M(\text{solvent}) / M(n\text{-hexadecane}) \quad (1)$$

where  $M$  is a property of solvent derived from the correlations of the Gibbs energy of transfer ( $\Delta_r G^\circ$ ) of a series of solutes (noble gases and alkanes) from water:

$$\Delta_r G^\circ(\text{from water to solvent}) = M \times R_T + D \quad (2)$$

Here,  $R_T$  is a solute molecular size parameter and  $M$  and  $D$  are determined by linear regression. The  $Sp$  values can be assigned to any solvent and are scaled from unity (water) to zero ( $n$ -hexadecane). The  $Sp$  values for various solvents increase in almost the same order as the solubility of alkanes decreases in these solvents. For aprotic solvents, this scale resembles, for the order of solvents, the scales of solvent polarity or electron accepting power.<sup>[9]</sup>

On the other side, some researchers associate solvophobic effects only with solvent self-association because of intermolecular hydrogen bonding. For example, in the mobile order theory of Huyskens *et al.*,<sup>[10]</sup> the solvophobic effects are a direct consequence of self-association of a solvent. Huyskens concluded that the origin of these effects is purely entropic, and the magnitude of this additional entropy is proportional to the solute volume. However, the assumption of nonergodicity of hydrogen bonding association processes that lies in the basis of his theory is not supported by any other studies. It is also likely that at least the hydrophobic effect is not purely entropic.<sup>[11,12]</sup>

The studies of solvation of hard particles in different models of water using scaled particles theory,<sup>[11,13]</sup> Monte Carlo and molecular dynamics simulations, revealed that the low molar volume of water is primarily responsible for the large values of solvation Gibbs energies. In a model liquid without intermolecular hydrogen bonds but with the same molar volume and molecular size as water, the Gibbs energies of solvation of a hard particle were found to be approximately the same or even larger than in water models.<sup>[14,15]</sup> We can note that hydrogen bonding is still indirectly responsible for the hydrophobic effect in these models because it determines the magnitude of the molar volume of water.

## METHODOLOGY

In the present work, we suggest another view on the solvophobic effects. We give a simple thermodynamic criterion to judge whether such effects are present in the solute-solvent system and provide a method to analyze the strength of these effects quantitatively. We show that the solvophobic effects are related to the self-association of solvent but not necessarily to a branched network of solvent-solvent hydrogen bonds.

The approach suggested in the present work is based on considering the relation between the Gibbs energy and the enthalpy of solvation for a single solute in a series of solvents. It is known that for many physicochemical processes, there is a linear correlation between the entropy and enthalpy of the process in different systems, called isoequilibrium or compensation relationship.<sup>[16]</sup> The process of solvation is not an exclusion. A linear isoequilibrium relationship for this process in a number of solvents was found by Barclay and Butler<sup>[17]</sup> as early as in 1938. They pointed out that the equation of the isoequilibrium line can be different for solutions in different solvents. In their classic work, Frank and Evans<sup>[18]</sup> suggested a connection between the violation of linear isoequilibrium relationships in aqueous solutions and the hydrophobic effect, which was then underlined by Lee.<sup>[11]</sup> These notable results are a starting point for our work.

Although the term *isoequilibrium relationship* is usually used for the entropy-enthalpy compensation, linear dependence should also exist between the Gibbs energy and the enthalpy of a process, because  $\Delta G = \Delta H - T\Delta S$ . These last two quantities for the process of solvation are usually measured in two independent experiments, and the Gibbs energy values are more precise than enthalpy and entropy values. Krug<sup>[19]</sup> pointed out that  $\Delta G - \Delta H$  plots are the most useful to identify isoequilibrium correlations with minimal interference from experimental errors. In the succeeding text, we will also consider Gibbs energy versus enthalpy plots.

We study the solvophobic effects in infinitely diluted solutions of nonelectrolytes, at  $T = 298 \text{ K}$ ,  $p = 1 \text{ bar}$ . The thermodynamic functions of solvation  $\Delta_{\text{solv}} f^{A/S}$  ( $f = G, H$ ) are defined as the functions of transfer of the solute  $A$  from the gas phase into the solvent  $S$ . We are using the molar fractions-based standard state for the solutions. An advantage of this standard state is that in the case of ideal solutions, the Gibbs energy of solvation of the same solute is the same in solvents with different molar volume.

If no hydrogen bonds or any other donor-acceptor bonds can be formed between  $A$  and  $S$ , and no solvophobic or hydrophobic effects take place, only nonspecific (van der Waals) intermolecular interactions determine the values of thermodynamic functions of solvation. In such case, we say that the thermodynamic function of solvation is the same as that of nonspecific solvation  $\Delta_{\text{solv}} f^{A/S} = \Delta_{\text{solv(nonsp)}} f^{A/S}$ .

In our previous works,<sup>[12,20]</sup> we studied the hydrophobic effects in aqueous solutions of nonelectrolytes using thermodynamic analysis of experimental values of the Gibbs energies and enthalpies of hydration. We have shown that the difference in the behavior of aqueous solutions from other solvents can be described in terms of an additional contribution into the thermodynamic functions of hydration (solvation in water), which we call the thermodynamic functions of the hydrophobic effect (e.g.,  $\Delta_{\text{h.e.}} G^A$  is the Gibbs energy and  $\Delta_{\text{h.e.}} H^A$  is the enthalpy

of the hydrophobic effect). If no solute–water hydrogen bonds can be formed, one can write the following:

$$\begin{aligned}\Delta_{\text{hydr}}G^A &= \Delta_{\text{hydr(nonsp)}}G^A + \Delta_{\text{h.e.}}G^A, \\ \Delta_{\text{hydr}}H^A &= \Delta_{\text{hydr(nonsp)}}H^A + \Delta_{\text{h.e.}}H^A\end{aligned}\quad (3)$$

A similar approach is now suggested for the solvophobic effects. We divide the thermodynamic functions of solvation into the contributions from nonspecific solvation and the solvophobic effects ( $\Delta_{\text{s.e.}}G^{A/S}$ ,  $\Delta_{\text{s.e.}}H^{A/S}$ ):

$$\begin{aligned}\Delta_{\text{solv}}G^{A/S} &= \Delta_{\text{solv(nonsp)}}G^{A/S} + \Delta_{\text{s.e.}}G^{A/S}, \\ \Delta_{\text{solv}}H^{A/S} &= \Delta_{\text{solv(nonsp)}}H^{A/S} + \Delta_{\text{s.e.}}H^{A/S}\end{aligned}\quad (4)$$

It was shown<sup>[20]</sup> that the Gibbs energy of nonspecific solvation can be calculated by the following equation:

$$\begin{aligned}\Delta_{\text{solv(nonsp)}}G^{A/S} &= \Delta_{\text{solv}}G^{A/S_0} + (\delta g^S - \delta g^{S_0}) \cdot V_x^A + \\ &+ \left[ a + b\sqrt{\delta g^S} \right] \cdot \left[ (\Delta_{\text{solv}}G^{A/S_R} - \Delta_{\text{solv}}G^{A/S_0}) - (\delta g^{S_R} - \delta g^{S_0}) \cdot V_x^A \right]\end{aligned}\quad (5)$$

$$\begin{aligned}a &= -\sqrt{\delta g^{S_0}} / \left( \sqrt{\delta g^{S_R}} - \sqrt{\delta g^{S_0}} \right); \\ b &= 1 / \left( \sqrt{\delta g^{S_R}} - \sqrt{\delta g^{S_0}} \right)\end{aligned}$$

Here,  $\Delta_{\text{solv}}G^{A/S_0}$  and  $\Delta_{\text{solv}}G^{A/S_R}$  are the Gibbs energies of solvation of solute *A* in the standard solvents  $S_0$  and  $S_R$ , which should not form hydrogen bonds with the molecules of *A* (typically,  $S_0$  is *n*-hexadecane and  $S_R$  can be, for example, benzene);  $V_x^A$  is McGowan's characteristic volume of solute *A*, which can be calculated by a simple additivity scheme from atomic contributions; and  $\delta g^S$ ,  $\delta g^{S_R}$ , and  $\delta g^{S_0}$  are solvent parameters reflecting nonspecific interactions of solvent molecules with other (solvent and solute) molecules.

Parameter  $\delta g$  is determined from the Gibbs energy of solvation of *n*-octane in solvent *S*:

$$\delta g^S = \left( \Delta_{\text{solv}}G^{C_8H_{18}/S} - \Delta_{\text{solv}}G^{C_8H_{18}/C_{16}H_{34}} \right) / V_x^{C_8H_{18}}\quad (6)$$

( $C_8H_{18}$  = *n*-octane,  $C_{16}H_{34}$  = *n*-hexadecane).

For the enthalpies, the following equation has been deduced<sup>[21]</sup>:

$$\begin{aligned}\Delta_{\text{solv(nonsp)}}H^{A/S} &= \Delta_{\text{solv}}H^{A/S_0} + (\delta h^S - \delta h^{S_0}) \cdot V_x^A + \\ &+ \left[ a' + b'\sqrt{\delta h^S} \right] \cdot \left[ (\Delta_{\text{solv}}H^{A/S_R} - \Delta_{\text{solv}}H^{A/S_0}) - (\delta h^{S_R} - \delta h^{S_0}) \cdot V_x^A \right]\end{aligned}\quad (7)$$

Standard solvent  $S_0$  is cyclohexane and  $S_R$  is usually benzene or carbon tetrachloride. Here, similar enthalpic parameters of nonspecific interactions of solvent molecules ( $\delta h$ ) are used:

$$\delta h^S = \Delta_{\text{solv}}H^{C_nH_{2n+2}/S} / V_x^{C_nH_{2n+2}}\quad (8)$$

Equations (5) and (7) describe well the thermodynamic functions of solvation in various solvents that are not self-associated. When these equations are applied without any modification to solutions of nonalkanes in self-associated solvents, for example, to aqueous or alcoholic solutions, the experimental values are significantly larger than calculated. This cannot be explained by solute–solvent bonding, which always leads to a decrease in the Gibbs energy. Some examples are

**Table 1.** Experimental and calculated (Eqns (5) and (7)) values of the Gibbs energies and enthalpies of solvation of aromatic molecules in water and methanol at 298 K in  $\text{kJ mol}^{-1}$

	Naphthalene	Anthracene
$\Delta_{\text{hydr}}G^A$	7.9 (−0.6)	0.6 (−9.2)
$\Delta_{\text{hydr}}H^A$	−46.9 (−54.7)	−55.0 (−77.6)
$\Delta_{\text{solv}}G^A/\text{CH}_3\text{OH}$	−13.4 (−18.9)	−25.5 (−32.6)
$\Delta_{\text{solv}}H^A/\text{CH}_3\text{OH}$	−53.8 (−54.8)	−77.9 (−77.3)

given in Table 1. The disagreement is especially large for aqueous solutions, both for the Gibbs energy and enthalpy of hydration. For the Gibbs energies of solvation of aromatic molecules in monohydric alcohols, there is also a difference between the results from Eqn (5) and experiment. However, this difference is less in magnitude. At the same time, the enthalpies of solvation in the same systems are described by Eqn (7) with rather small errors.

Positive deviations of the experimental Gibbs energies of solvation from the results of Eqn (1) can be explained in terms of the solvophobic effect. The intermolecular interactions are not the same between solvent molecules as between solute and solvent. Thus, the nonspecific interactions between associated solvents and solutes cannot be described by a parameter that reflects the cost of cavity formation, such as  $\delta g$  or  $\delta h$ . The thermodynamic functions of solvation of *n*-octane, which are used in Eqns (6) and (8), contain a contribution of the solvophobic effect.

Thus, we should use corrected parameters  $\delta^*g$  or  $\delta^*h$ , which reflect the strength of only the nonspecific interactions between solvent and solute. They are given by the following:

$$\begin{aligned}\delta^*g^S &= \left( \Delta_{\text{solv}}G^{C_8H_{18}/S} - \Delta_{\text{s.e.}}G^{C_8H_{18}/S} - \Delta_{\text{solv}}G^{C_8H_{18}/C_{16}H_{34}} \right) / V_x^{C_8H_{18}}, \\ \delta^*h^S &= \left( \Delta_{\text{solv}}H^{C_nH_{2n+2}/S} - \Delta_{\text{s.e.}}H^{C_nH_{2n+2}/S} \right) / V_x^{C_nH_{2n+2}}\end{aligned}\quad (9)$$

In order to calculate  $\Delta_{\text{solv(nonsp)}}f^{A/S}$  correctly, one needs to substitute the modified parameters  $\delta^*g$  or  $\delta^*h$  into Eqns (5) or (7). The difference between the experimental value of  $\Delta_{\text{solv}}f^{A/S}$  and calculated  $\Delta_{\text{solv(nonsp)}}f^{A/S}$  is the thermodynamic function of the solvophobic effect:

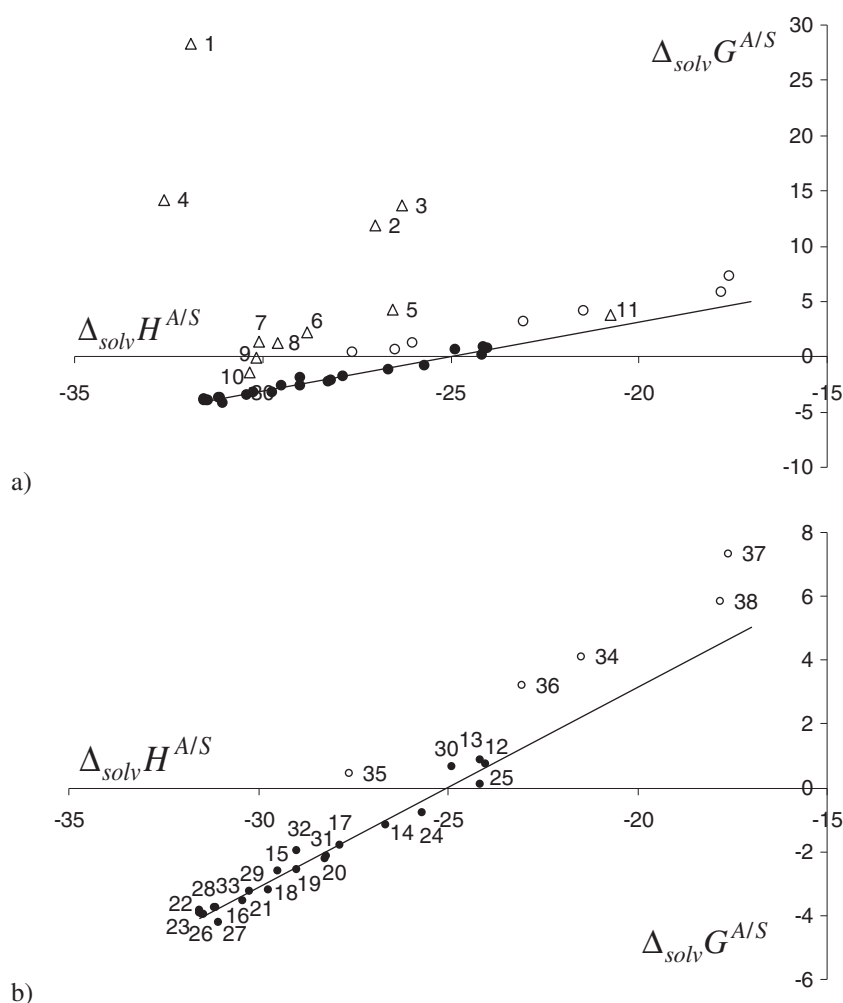
$$\Delta_{\text{s.e.}}f^{A/S} = \Delta_{\text{solv}}f^{A/S} - \Delta_{\text{solv(nonsp)}}f^{A/S}\quad (10)$$

In order to calculate  $\delta^*g$  and  $\delta^*h$ , the thermodynamic functions of the solvophobic effect must be previously found at least for a single alkane. Now, the task is to find a method that allows to say whether the solvophobic effects take place in certain solvent and to determine the thermodynamic functions of the solvophobic effect at least for alkanes. For that purpose, we will analyze the relation between the Gibbs energy and enthalpy of solvation for alkanes in various solvents.

## RESULTS AND DISCUSSION

### Relationships between the Gibbs energy and enthalpy

In Fig. 1(a, b), the Gibbs energies of solvation of *n*-hexane – an apolar molecule that is not able to form hydrogen bonds – are



**Figure 1.** A plot of the Gibbs energy versus the enthalpy of solvation of *n*-hexane in various solvents. (a) Triangles are self-associated solvents: 1, water; 2, ethylene glycol; 3, formamide; 4, glycerol; 5, methanol; 6, ethanol; 7, 1-propanol; 8, 2-propanol; 9, 1-butanol; 10, 1-octanol; 11, aniline. Filled and open circles are other solvents (see panel b). (b) Filled circles are solvents from group 1 following a linear correlation between the Gibbs energy and enthalpy of solvation: 12, 1,4-dioxane; 13, acetone; 14, benzene; 15, butyl chloride; 16, butyl ether; 17, carbon disulfide; 18, carbon tetrachloride; 19, chlorobenzene; 20, chloroform; 21, cyclohexane; 22, *n*-decane; 23, *n*-dodecane; 24, ethyl acetate; 25, ethylene chloride; 26, *n*-heptane; 27, *n*-hexadecane; 28, *n*-hexane; 29, *p*-xylene; 30, pyridine; 31, tetrahydrofuran; 32, toluene; 33, triethylamine. Open circles are as follows: 34, acetonitrile; 35, benzonitrile; 36, dimethylformamide; 37, dimethylsulfoxide; 38, nitromethane

plotted versus the enthalpies of the same process. (Experimental values and references are given in the Supporting Information section, Table S1.) There is no single dependence for all systems. However, a large group of solvents (here and in the succeeding text – group 1, filled circles in Fig. 1) follows linear dependence:

$$\Delta_{\text{solv}}G^{\text{C}_6\text{H}_{14}/\text{S}} = 0.626\Delta_{\text{solv}}H^{\text{C}_6\text{H}_{14}/\text{S}} + 15.7 \quad (11)$$

The root mean square deviation is  $0.27 \text{ kJ mol}^{-1}$  for 22 systems. Moreover, all other points in Fig. 1 are deviating to the side of larger values of the Gibbs energies of solvation.

The solvents following this dependence are not significantly self-associated. On the other hand, solvents with strong intermolecular hydrogen bonds (water, ethylene glycol, formamide, and glycerol) show maximum positive deviations from this line. It corresponds to a large reduction of solubility of *n*-hexane in these solvents. Less but still distinct deviations are present in the case of solutions in monohydric alcohols, which are also self-associated solvents.

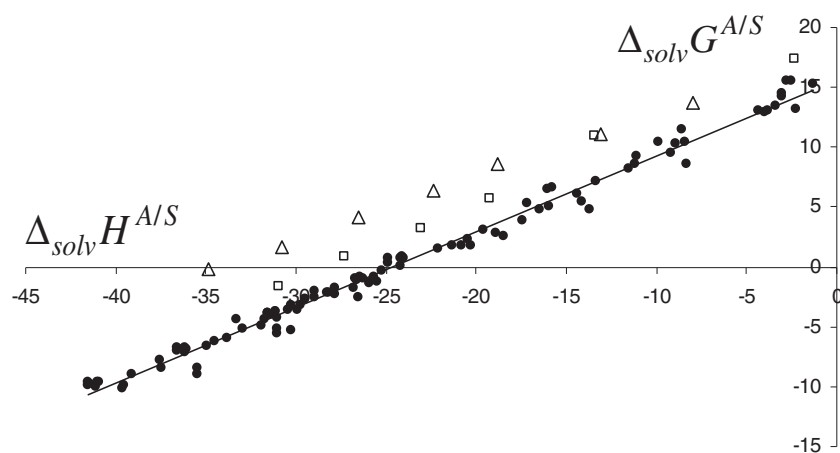
In Fig. 2, the Gibbs energy is plotted versus the enthalpy of solvation for linear alkanes with different carbon chain length (from  $\text{C}_1$  to  $\text{C}_8$ ), dissolved in solvents from group 1 (circles). (Experimental values and references are given in the Supporting Information section, Table S1.) The correlation equation is the following:

$$\Delta_{\text{solv}}G^{\text{A}/\text{S}} = 0.632\Delta_{\text{solv}}H^{\text{A}/\text{S}} + 15.6, \quad (12)$$

$$n = 101, \sigma = 0.75 \text{ kJ mol}^{-1}, R^2 = 0.9890$$

This is a good correlation, taking into account possible experimental errors, which may exceed  $1 \text{ kJ mol}^{-1}$  for the enthalpies of solvation. So, the size of alkane molecule does not influence the coefficients in the equation of correlation.

For solvents other than those of group 1, linear correlations between the Gibbs energy and enthalpy of solvation of alkanes also exist, but their equations are different from Eqn (12). Again, the points corresponding to solutions of alkanes in alcohols lie above the line (Eqn (12)). Group 1 contains solvents having



**Figure 2.** A plot of the Gibbs energy versus the enthalpy of solvation of  $C_1$ – $C_8$  linear alkanes in various solvents. Circles, solvents from group 1 (Fig. 1); squares, the solvent is dimethylformamide; triangles, the solvent is methanol

different functional groups and polarity, and different thermodynamic functions of solvation of any single alkane (e.g., *n*-hexane).

A positive deviation for a solution of alkane in some solvent from the straight line (Eqn (12)) leading to a decrease of solubility can be considered as a result of the solvophobic effects and a measure of their strength. Following this definition, we can say that the solvophobic effect is a feature of all examined self-associated solvents: aliphatic alcohols, diols, formamide, water, and aniline.

Of course, it is pointless to speak about solvophobic effects when some point deviates from this line not more than by  $1 \text{ kJ mol}^{-1}$ , which can occur because of some minor effects and/or experimental uncertainties. Larger deviations are also observed for some highly polar aprotic solvents: dimethylsulfoxide (DMSO), acetonitrile, nitromethane, and dimethylformamide. Such solvents are usually considered as slightly or even nonassociated through hydrogen bonding. The deviations from Eqn (12) could be caused by intermolecular donor–acceptor interactions rather than hydrogen bonds.

Despite the fact that the solvophobic effect always leads to a decrease in solubility and an increase of the Gibbs energy of solvation, it is clearly not the only factor determining the solubility even for alkane molecules. This can be illustrated by comparison of the values of  $\Delta_{\text{solv}}G^{A/S}$  and the deviation of the Gibbs energy of solvation from Eqn (12) for *n*-hexane in different solvents (Table 2). The order of solvents by decrease of each of two quantities is not the same. This is because the nonspecific solvation effects different from solvent to solvent also influence the value of  $\Delta_{\text{solv}}G^{A/S}$ .

The energy of nonspecific solvation of alkanes is determined by the strength of nonspecific solvent–solvent interactions described by  $\delta^*g$  parameter in Eqn (4). The solvophobic effects are governed by additional attraction between solvent molecules because of the intermolecular specific interactions. For example, DMSO lies closer to line (Eqn (12)) than methanol, but the value of  $\Delta_{\text{solv}}G^{A/S}$  is greater in DMSO than in methanol, because of the nonspecific solvation effects.

In general, the solvophobic effects can contribute to both the entropy and the enthalpy of solvation. If the enthalpic contribution due to the solvophobic effect may be neglected in some systems, the Gibbs solvophobic effect energy can be found as follows:

$$\Delta_{\text{s.e.}}G^{A/S} = \Delta_{\text{solv}}G^{A/S} - (0.632\Delta_{\text{solv}}H^{A/S} + 15.6) \quad (13)$$

**Table 2.** The Gibbs energies of solvation of *n*-hexane in various solvents at 298 K in  $\text{kJ mol}^{-1}$  and its deviation from the linear dependence given by Eqn (12)

Solvent (S)	$\Delta_{\text{solv}}G^{C_6H_{14}/S}$	$\Delta_{\text{solv}}G^{A/S} - (0.632\Delta_{\text{solv}}H^{A/S} + 15.6)$
<i>n</i> -Hexane	−3.9	0.4
Chloroform	−2.2	0.0
Benzene	−1.2	0.1
1,4-Dioxane	0.8	0.3
Nitromethane	5.8	1.5
Acetonitrile	4.1	2.0
DMF	3.2	2.2
DMSO	7.3	2.8
Methanol	4.2	5.4

DMF, dimethylformamide; DMSO, dimethylsulfoxide.

In aqueous solutions, the hydrophobic effect strongly influences both the Gibbs energy and the enthalpy of hydration.<sup>[2,12,20]</sup> On the other hand, we can show (Table 1) that the enthalpy of solvation in aliphatic monohydric alcohols satisfies the empiric Eqn (7), which was deduced for non-self-associated solvents. Hence, we assume that the Gibbs energy of the solvophobic effect of alkanes in these alcohols can be found from Eqn (13).

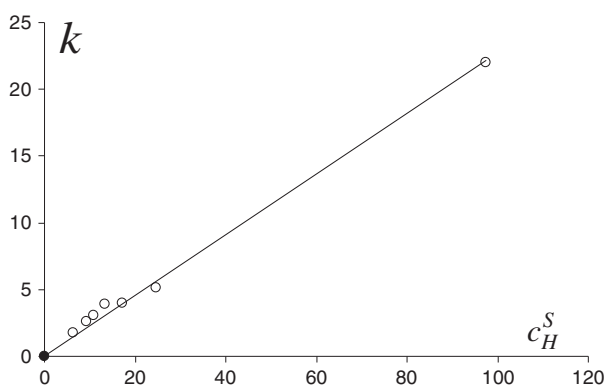
#### The Gibbs energy of solvophobic effects for various compounds in aliphatic alcohols

Combining Eqns (9) (where  $\Delta_{\text{solv}}G^{C_8H_{18}/C_6H_{34}} = 10.0 \text{ kJ mol}^{-1}$ ) and Eqns (9), we calculated the values of  $\delta^*g^S$  parameter for methanol, ethanol, 1-propanol, 1-butanol, 1-pentanol, and 1-octanol:

$$\delta^*g^S = \left(0.632\Delta_{\text{solv}}H^{C_8H_{18}/S} + 25.6\right) / V_x^{C_8H_{18}} \quad (14)$$

These values are found to be equal to  $2.60 \times 10^{-2}$ ,  $1.11 \times 10^{-2}$ ,  $0.94 \times 10^{-2}$ ,  $0.65 \times 10^{-2}$ ,  $0.45 \times 10^{-2}$ , and  $0.20 \times 10^{-2} \text{ kJ cm}^{-3}$ , respectively.

Now we can calculate the Gibbs nonspecific solvation energies of various nonelectrolytes: aromatic and unsaturated hydrocarbons, halogenated derivatives, and noble gases in



**Figure 3.** Relation between  $k$  from Eqns (15) and an average hydrogen bond concentration in solvent

alcohols by Eqn (7) and the Gibbs solvophobic effect energies by Eqn (10). Data on the solvation Gibbs energies of various apolar and slightly polar species in the reference solvents, *n*-hexadecane ( $\delta g^S = 0 \text{ kJ cm}^{-3}$ ) and benzene ( $\delta g^S = 1.66 \cdot 10^{-2} \text{ kJ cm}^{-3}$ ), are provided in the Supporting Information section, Table S2. Values of the solvation Gibbs energies in aliphatic alcohols and calculated Gibbs solvophobic effect energies are also given there.

The solvophobic effect Gibbs energy in all considered alcohols depends linearly on the solute characteristic volume:

$$\begin{aligned}
 \Delta_{\text{s.e.}} G^A / \text{CH}_3\text{OH} &= 5.17V_x^A + 0.23, \\
 n &= 37, \sigma = 0.63 \text{ kJ mol}^{-1}, R^2 = 0.9225; \\
 \Delta_{\text{s.e.}} G^A / \text{C}_2\text{H}_5\text{OH} &= 3.98V_x^A + 0.83, \\
 n &= 38, \sigma = 0.49 \text{ kJ mol}^{-1}, R^2 = 0.9418; \\
 \Delta_{\text{s.e.}} G^A / \text{C}_3\text{H}_7\text{OH} &= 3.94V_x^A + 0.36, \\
 n &= 31, \sigma = 0.34 \text{ kJ mol}^{-1}, R^2 = 0.9630; \\
 \Delta_{\text{s.e.}} G^A / \text{C}_4\text{H}_9\text{OH} &= 3.06V_x^A + 0.50, \\
 n &= 36, \sigma = 0.32 \text{ kJ mol}^{-1}, R^2 = 0.9371; \\
 \Delta_{\text{s.e.}} G^A / \text{C}_5\text{H}_{11}\text{OH} &= 2.64V_x^A + 0.55, \\
 n &= 25, \sigma = 0.31 \text{ kJ mol}^{-1}, R^2 = 0.9316; \\
 \Delta_{\text{s.e.}} G^A / \text{C}_8\text{H}_{17}\text{OH} &= 1.78V_x^A + 0.60, \\
 n &= 38, \sigma = 0.19 \text{ kJ mol}^{-1}, R^2 = 0.9276
 \end{aligned} \quad (15)$$

A similar correlation for the hydrophobic effect in aqueous solutions has been found earlier<sup>[22]</sup>:

$$\begin{aligned}
 \Delta_{\text{h.e.}} G^A &= 22.0V_x^A + 3.65, \\
 n &= 58, \sigma = 1.09 \text{ kJ mol}^{-1}, R^2 = 0.9847
 \end{aligned} \quad (16)$$

As could be seen from correlations (Eqn (15)), the contribution of the solvophobic effect into the Gibbs energy of solvation decreases with growing of the alkyl chain length in solvent molecule. It is interesting to consider which factors determine the value of the coefficient before  $V_x^A$ .

One of the characteristics of self-associated liquids is the average number of the intermolecular hydrogen bonds per volume unit or the concentration of hydrogen bonds:

$$c_H^S = \frac{n}{2V_m^S} \quad (17)$$

where  $V_m^S$  is the molar volume of solvent *S* and *n* is the average number of the intermolecular hydrogen bonds in which each solvent molecule participates. For aliphatic alcohols,  $n=2$ . The values of  $c_H^S$  for methanol, ethanol, 1-propanol, 1-butanol,

1-pentanol, and 1-octanol are 24.7, 17.1, 13.4, 10.9, 9.2, and 6.3 M, respectively. For water,  $c_H^S = 110.5$  if we assume  $n=4$ . However, simulation and spectroscopic studies give lower values of  $n$ : 3.59<sup>[23]</sup> and 3.46.<sup>[24]</sup> They correspond to  $c_H^S = 95\text{--}100 \text{ M}$ . In contrast, for alcohols, estimations give no more than 1–2% of non-H-bonded hydroxyls,<sup>[24]</sup> so the correction is unnecessary.

A plot of the slopes  $k$  of correlations (Eqn (15)) versus  $c_H^S$  is in Fig. 3. The origin point here corresponds to a solvent without intermolecular hydrogen bonds ( $k=0$  and  $c_H^S = 0$ ). There is a correlation between the two quantities ( $k = 0.227 c_H^S$ ,  $n=7$ ,  $\sigma=0.39$ ), which indicates a connection between the density of hydrogen bonds and the solvophobic effects.

## CONCLUSIONS

It is shown that the comparison of the magnitudes of the Gibbs energies and enthalpies of solvation of alkanes in various solvents allows to identify the solvophobic effects qualitatively and helps to describe them quantitatively. This can help to understand the mechanism of the solvophobic effects and the difference between these effects and other types of intermolecular interactions.

Quantification of thermodynamic functions of the solvophobic effect is important for solutes able to form hydrogen bonds with an associated solvent. It is necessary to determine the energies of solute–solvent hydrogen bonding, which determine reaction rate and equilibrium constants in solutions. The spectroscopic methods, which are traditionally used to determine the Gibbs energy and enthalpy of hydrogen bonding in inert media, are not suitable in pure H base or pure H acid media, because the concentration of solvent cannot be varied. In the case of associated solvents, we also cannot apply empiric equations describing the energies of 1:1 acid–base H complexes, because the hydrogen bonding processes are very complicated there. These processes are accompanied with the reorganization of the solvent associates, and their energy is dependent on the solute and solvent molecular structure. In addition, a solute molecule can form H bonds with solvent associates that have different size and structure, and the energy of bonding is not the same for different associates.<sup>[25]</sup> For example, H bonds with alcohol dimer are usually stronger than with monomer, what is known as the cooperative effect. The magnitude of this effect is, again, different for different solutes. Thus, we can determine solute–solvent hydrogen bonding Gibbs energy or enthalpy only from thermodynamic functions of solvation.

For the solutions of hydrogen bonding species in associated solvents, we can write the following equation instead of Eqn (4):

$$\Delta_{\text{solv}} G^{A/S} = \Delta_{\text{solv(nonsp)}} G^{A/S} + \Delta_{\text{s.e.}} G^{A/S} + \Delta_{\text{int(sp)}} G^{A/S} \quad (18)$$

Here,  $\Delta_{\text{int(sp)}} G^{A/S}$  is the contribution of specific interactions, that is, hydrogen bonding processes. In our previous work,<sup>[26]</sup> we have applied this equation for the aqueous solutions of aliphatic amines and pyridines. The results of this current work allow to extend this approach to various associated solvents. It should be noted that if we applied Eqns (10) and (5) to determine  $\Delta_{\text{int(sp)}} G^{A/S}$  without taking into account the solvophobic effect in aliphatic alcohols, the Gibbs energies of H complexation would be positive in many cases, which is impossible. This fact underlies the necessity to quantify the solvophobic effects in thermodynamic applications.

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