

# Distinctive thermodynamic properties of solute–solvent hydrogen bonds in self-associated solvents

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**Solute–solvent hydrogen bonding affects reactivity and other properties of dissolved species. In self-associated media, because of cooperativity and solvent reorganization, the thermodynamic functions of solute bonding with bulk solvent can be different from those of bimolecular solute–solvent complexes. Using available experimental data on the Gibbs free energies of solvation in aliphatic alcohols and water, we have determined the energies of solute–solvent hydrogen bonding for various proton accepting solutes. We show that the increase in the strength of hydrogen bonds because of the cooperative effect is strong for bonding with bulk water and significantly less so with bulk aliphatic alcohols. The hydrogen bonding Gibbs free energies for the same solute with bulk water and alcohol are correlated, but they correlate poorly with the energies of formation of the corresponding bimolecular solute–solvent complexes. Thus, the traditional hydrogen bond basicity scales, based on data for bimolecular complexes, do not correctly describe the thermodynamics of hydrogen bonding with self-associated solvents. Our results may help to define a separate solute basicity scale for associated media. Copyright © 2012 John Wiley & Sons, Ltd.**

**Keywords:** cooperativity; Gibbs free energy; hydrogen bond; self-association; solute–solvent interactions; solvophobic effects

## INTRODUCTION

For chemistry and biochemistry, hydrogen bonding is an ultimately important type of intermolecular interactions. Many current fundamental scientific problems are in some way connected with the hydrogen bonds. We can mention protein folding and DNA stability, the structure of liquid water, molecular recognition by enzymes and receptors as the examples.

Over the past 70 years, there have been many thousands of studies dedicated to the determination of thermodynamic functions of hydrogen bonding. Such methods as infrared and nuclear magnetic resonance spectroscopy have provided us with plenty of experimental data,<sup>[1,2]</sup> mostly for the hydrogen bonds between two molecules diluted in an inert solvent. The data have been analyzed to deduce the connection between hydrogen bond thermodynamics and the structure of interacting molecules. Several relatively general empirical relationships have been discovered. These are equations suggested by Drago *et al.*,<sup>[3]</sup> Abraham,<sup>[4]</sup> and Raevsky *et al.*<sup>[5]</sup> The predictive ability of empirical equations is quite good. These results have promoted the development of a statistical approach to predict different physical, chemical, and biological properties of chemical substances known as QSAR (quantitative structure–activity relationships) and QSPR (quantitative structure–property relationships).<sup>[6]</sup> A number of scales of proton-accepting and proton-donating ability have been suggested and used in structure–property correlations, such as  $\alpha$  and  $\beta$  scale,<sup>[4]</sup> Catalán SA and SB scales,<sup>[7]</sup> and the Gutman acceptor and donor numbers (AN and DN).<sup>[8]</sup> The above-mentioned equations and parameters of hydrogen bond acidity and basicity used in them have become the basis for the description of the influence of hydrogen bonding on various physico-chemical processes.<sup>[9,10]</sup>

The empirical equations have been derived for bimolecular hydrogen-bonded complexes in inert solvent media, primarily tetrachloromethane. For applications, it is more important to consider hydrogen bonds between a solute and solvent, which have a large impact on solute reactivity and other physico-chemical properties. We have shown<sup>[11,12]</sup> that the values of thermodynamic functions for equimolar complexes with solvents having a single basic or acidic center are close to those for the same complex in inert medium. However, the equations and data obtained for bimolecular complexes in inert medium may become useless when one considers the complexes formed by solutes with hydrogen-bonded multimers of self-associated solvents.

Self-associated solvents — from water to monohydric and polyhydric aliphatic alcohols, amides, aminoalcohols — are outstandingly important from both theoretical and practical points of view. At the same time, the thermodynamics of solute–solvent hydrogen bonding in such solvents is not well-studied. A direct experimental measurement of the complexation constants in the bulk associated solvents using vibrational or nuclear magnetic resonance spectroscopy is a very difficult task. In several works,<sup>[13,14]</sup> spectroscopic techniques have been used to obtain the value of the fraction of solute involved in H-complexes with water at different solute concentrations, but for infinitely diluted solutions it appeared to be close to unity. This fact makes it impossible for us to calculate

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the constant or the standard Gibbs free energy of hydrogen bonding with satisfactory precision. The degrees of bonding with water in diluted solutions were also estimated for a few solutes from molecular dynamics simulations and neutron diffraction data.<sup>[15]</sup> These results are quite different from those obtained using spectroscopy and depend on the chosen geometric criteria of existence of a hydrogen bond. We believe that a more fruitful approach is the use of extrathermodynamic models to analyze the thermodynamic functions of solvation in associated solvents, which include a contribution of solute–solvent hydrogen-bonding processes.

## METHODOLOGY

### The importance of the solute–solvent specific interactions energy term

For a given chemical reaction, the solvent effect on its standard thermodynamic functions is determined by the difference between the thermodynamic functions of solvation of products and reagents. The change of the energy of solute–solvent hydrogen bonds during the reaction can be a major contribution to the solvent effect, especially if the reaction goes without significant rearrangements of the structure of reagents (e.g., creation of new functional groups). A striking example is the reaction where only new hydrogen bonds between two dissolved compounds are formed. Such processes of noncovalent binding are very important for supramolecular chemistry and biological systems. The solvent effect on the constant of complexation will be determined by the Gibbs free energies of specific hydrogen bonding interactions with the solvent of those donor and acceptor centers of two solutes that are involved in mutual binding. Also, if the solvent is self-associated, the values of the Gibbs free energies of H-bonding with solvent cannot be approximated with the Gibbs free energies of 1 : 1 solute–solvent complexation.

Cooperative effects influence the energy of hydrogen bonds formed between solute and solvent multimers. For example, the internal energies and enthalpies of formation for complexes of proton accepting molecules with dimers of alcohols are more negative than for complexes with a single alcohol molecule.<sup>[16]</sup> The magnitude of the energy change because of the cooperative effect is, in general, dependent on the nature of a proton acceptor.<sup>[17]</sup>

Moreover, the concentration of free proton-donating groups and lone pair electrons in self-associated solvents is always lower than the concentration of solvent molecules, because the majority of them are involved in solvent–solvent hydrogen bonds. For example, in liquid water only about 10% of hydrogen atoms in O–H groups are not involved in O–H...O bonds.<sup>[18]</sup> Thus, breaking of some solvent–solvent bonds is required to bind a dissolved proton-accepting molecule. The number of solvent–solvent bonds that are cleaved upon dissolution can be different for different solvents and solutes.

The contribution of dissociation of solvent–solvent hydrogen bonds into the Gibbs free energy and enthalpy of specific interactions is positive by sign. The enthalpies of specific interactions of proton acceptors with alcohols are less negative than the enthalpies of formation of corresponding 1 : 1 complexes in inert solvent.<sup>[19]</sup> However, the Gibbs free energies of specific interactions of amines and pyridines with water were found to be more negative than those of 1 : 1 complexation in tetrachloromethane<sup>[20]</sup> because of cooperative effects.

The present work is devoted to the determination of the Gibbs free energies of specific interactions of various solutes with monohydric alcohols and liquid water and subsequent analysis of these data to study the peculiarities of bonding with solvent polymers.

### Terminology and procedure of calculation

We consider the solvation process of solute A from gas phase into solvent S at 298K at 1 bar standard pressure and using unit molar fraction standard state for solutions, the standard Gibbs free energy of solvation is denoted as  $\Delta_{\text{solv}}G^{A/S}$ .

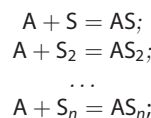
In our works<sup>[20–22]</sup> we have shown that the Gibbs free energy of solvation in water and aliphatic alcohols can be represented as a sum of three contributions: because of nonspecific (van der Waals) solvation effects  $\Delta_{\text{solv(nonsp)}}G^{A/S}$ , because of the solvophobic (or hydrophobic in the case of water) effect  $\Delta_{\text{s.e.}}G^A$ , and the specific interactions term  $\Delta_{\text{int(sp)}}G^{A/S}$  because of hydrogen bonding between solute A and solvent S (if a solute cannot form hydrogen bonds with a solvent, this term is zero)

$$\Delta_{\text{solv}}G^{A/S} = \Delta_{\text{solv(nonsp)}}G^{A/S} + \Delta_{\text{s.e.}}G^A + \Delta_{\text{int(sp)}}G^{A/S}. \quad (1)$$

The magnitude  $\Delta_{\text{int(sp)}}G^{A/S}$  is the difference in the Gibbs free energies of a mixture of solute–solvent complexes in solution and a non-hydrogen-bonded state of a dissolved molecule. It is related to the fraction of non-hydrogen-bonded molecules of solute in solution among all solute molecules  $\alpha^{A/S}$  and to the effective constant  $K^{A/S}$  of complexation with the multimers of bulk solvent through the following expressions:

$$\Delta_{\text{int(sp)}}G^{A/S} = RT \ln \alpha^{A/S} = -RT \ln \left( 1 + K^{A/S} \right), \quad (2)$$

where the effective constant for all possible solute–solvent association processes:



is defined as  $K^{A/S} = \frac{\sum [A \dots S_n]}{[A]}$  (the concentration of solvent or any of its multimers  $S_n$  cannot be changed, thus the constant is not dependent on them), and  $\alpha^{A/S} = \frac{[A]}{[A] + \sum [A \dots S_n]}$ .

Below we compare the processes of bonding with bulk solvent S and with a monomer of S in inert solvent. The Gibbs free energies of hydrogen bonding between two molecules A and S in inert solvents (let us denote it  $\Delta_{\text{HB}}G^{A \dots S}$ ) are given by  $\Delta_{\text{HB}}G^{A \dots S} = -RT \ln K^{A \dots S}$ , where  $K^{A \dots S}$  is the constant of A–S binary complex formation in molar fraction scale. To characterize the affinity of solute to the bulk solvent, it is reasonable to use the standard Gibbs free energy of solute–solvent hydrogen bonding  $\Delta_{\text{HB}}G^{A/S} = -RT \ln K^{A/S}$ . This magnitude can be assumed to be equal to the solute–solvent specific interaction Gibbs free energy  $\Delta_{\text{int(sp)}}G^{A/S}$  only for strong complexes, if about 100% of A is bonded with S. For the general case

$$\Delta_{\text{HB}}G^{A/S} = -RT \ln \left( e^{-\frac{\Delta_{\text{int(sp)}}G^{A/S}}{RT}} - 1 \right). \quad (3)$$

For strong complexes (large values of  $K^{A/S}$ ) this correction for complexation degree could be neglected. For example, if

$\Delta_{\text{int(sp)}}G^{A/S} = -8 \text{ kJ}\cdot\text{mol}^{-1}$ , then  $\Delta_{\text{HB}}G^{A/S} = -7.9 \text{ kJ}\cdot\text{mol}^{-1}$  — only  $0.1 \text{ kJ}\cdot\text{mol}^{-1}$  difference ( $K^{A/S} = 24$ , or 96% of solute is bonded). On the other hand, if  $\Delta_{\text{int(sp)}}G^{A/S} = -1.7 \text{ kJ}\cdot\text{mol}^{-1}$ , then  $\Delta_{\text{HB}}G^{A/S} = 0 \text{ kJ}\cdot\text{mol}^{-1}$ , and the difference is  $1.7 \text{ kJ}\cdot\text{mol}^{-1}$  ( $K^{A/S} = 1$ , or 50% of solute is bonded). It should be noted that, when we convert the values of  $\Delta_{\text{int(sp)}}G^{A/S}$  into  $\Delta_{\text{HB}}G^{A/S}$  using (3), there are large uncertainties in the values of  $\Delta_{\text{HB}}G^{A/S}$  if they are positive or close to zero.

The contributions of nonspecific solvation to the Gibbs free energy of solvation for various solutes A in various solvents S have been shown<sup>[23,24]</sup> to follow the empirical equation

$$\begin{aligned} \Delta_{\text{solv(nonsp)}}G^{A/S} = & \Delta_{\text{solv}}G^{A/S_0} + (\delta g^S - \delta g^{S_0}) \cdot V_x^A + \\ & + \left[ a + b\sqrt{\delta g^S} \right] \cdot \left( \Delta_{\text{solv}}G^{A/S_R} - \Delta_{\text{solv}}G^{A/S_0} \right) \\ & - (\delta g^{S_R} - \delta g^{S_0}) \cdot V_x^A; a = -\sqrt{\delta g^{S_0}} / \left( \sqrt{\delta g^{S_R}} \right. \\ & \left. - \sqrt{\delta g^{S_0}} \right); b = 1 / \left( \sqrt{\delta g^{S_R}} - \sqrt{\delta g^{S_0}} \right). \end{aligned} \quad (4)$$

Here,  $\Delta_{\text{solv}}G^{A/S_0}$ ,  $\Delta_{\text{solv}}G^{A/S_R}$  are the Gibbs free energies of solvation of solute A in the standard solvents  $S_0$  and  $S_R$  (in the present work hexadecane and benzene respectively),  $V_x^A$  is the characteristic volume<sup>[25]</sup> of solute A calculated by an atom-additivity scheme,  $\delta g^S$ ,  $\delta g^{S_R}$ ,  $\delta g^{S_0}$  are the relative cavity formation Gibbs free energies for each solvent.  $\delta g^S$  is given by the following equation:

$$\delta g^S = \left( \Delta_{\text{solv}}G^{C_8H_{18}/S} - \Delta_{\text{solv}}G^{C_8H_{18}/C_{16}H_{34}} \right) / V_x^{C_8H_{18}}, \quad (5)$$

where  $C_8H_{18}$  is *n*-octane, and  $C_{16}H_{34}$  is *n*-hexadecane. This parameter reflects the propensity of solvent molecules to the nonspecific interactions with both other solvent molecules and solute molecules. In the case of associated solvents, we have also made a correction for the solvophobic effect of octane, what has been described in detail in our previous paper.<sup>[21]</sup>

The contribution because of the solvophobic effect reflects the difference in behaviour of solutions in associated solvents from solutions in other solvents, which leads to more positive Gibbs free energies of solvation in associated solvents. We have shown that the Gibbs free energies of hydrophobic effect and solvophobic effects in aliphatic alcohols are linearly dependent on the characteristic molecular volume of the solute<sup>[21]</sup>

$$\Delta_{\text{s.e.}}G^{A/S} = k^S V_x^A + b^S. \quad (6)$$

Solvent–solvent intermolecular interactions in self-associated solvents appear to be stronger than could be predicted using  $\delta g^S$  parameter describing the strength of solute–solvent nonspecific interactions. Any molecule being dissolved in water or alcohols has an extra chemical potential depending only on its volume. The values of  $k$  and  $b$  coefficients in Eqn (6) for different solvents are given in Table 1. It can be pointed out that such well-known hydrophobicity parameter as octanol–water partition coefficient  $\log P$  cannot be used to describe the contribution of the hydrophobic effect to the Gibbs free energy of solvation, because it is also dependent on the energies of nonspecific interactions of a solute with both water and octanol, and of the solvophobic effect in octanol.

**Table 1.** Parameters of solvents used in Eqns (4) and (6) (at 298 K)

Alcohol (ROH)	$k^a$	$b^a$	$\delta g / \text{kJ}\cdot\text{cm}^{-3}\cdot 10^2 \text{ }^a$
Water	22.02	3.65	5.75
Methanol	5.17	0.23	2.60
Ethanol	3.98	0.83	1.11
Propanol	3.94	0.36	0.94
Butanol	3.06	0.50	0.65
Octanol	1.78	0.60	0.20

<sup>a</sup>Taken from <sup>[21]</sup>.

Thus, the Gibbs free energy of solute–solvent specific interactions can be determined by Eqn (1) rewritten as  $\Delta_{\text{int(sp)}}G^{A/S} = \Delta_{\text{solv}}G^{A/S} - \Delta_{\text{solv(nonsp)}}G^{A/S} - \Delta_{\text{s.e.}}G^A$  using a number of experimental thermodynamic data and molecular parameters for Eqns (3)–(5). In our previous works<sup>[20,22]</sup> we have calculated the values of  $\Delta_{\text{int(sp)}}G^{A/S}$  for a number of proton acceptors in water. Here we extend the number of considered solutes and report their values of  $\Delta_{\text{int(sp)}}G^{A/S}$  in several monohydric alcohols along with novel and previously published data for their aqueous solutions.

## RESULTS AND DISCUSSION

The calculated values of the Gibbs free energies of nonspecific solvation, solvophobic effect, and specific interactions with water and alcohols are given in Table 2. The values of the Gibbs free energies of solvation in alcohols, water, and in other solvents that are necessary to calculate  $\Delta_{\text{solv(nonsp)}}G^{A/S}$  are taken from literature.<sup>[26–28]</sup> A general schematic representation of the relationship between these three terms is shown in Fig. 1. The difference between solvation Gibbs free energy and nonspecific solvation Gibbs free energy in water is plotted against characteristic molecular volumes of solutes  $V_x^A$ . The deviation of data points from the straight line representing the correlation between the hydrophobic effect energy and  $V_x^A$  is the Gibbs specific interactions energy. It can be seen from Table 1 and Fig. 1 that the Gibbs free energies of hydrogen bonding for molecules having the same functional group and different alkyl chain length are usually almost the same. A replacement of alkyl substituent with aryl can also have little or no effect on the  $\Delta_{\text{int(sp)}}G^{A/S}$  value: the examples are acetonitrile and benzonitrile, acetone and acetophenone, nitroethane and nitrobenzene.

The values of  $\Delta_{\text{int(sp)}}G^{A/S}$  for all solutes and solvents are negative. An important point here is the necessity to take the solvophobic effects into account. In calculations of the Gibbs free energies of specific interactions with alcohols without modification of  $\delta g^S$  parameter we obtain positive values for most of the solutes, which is an unphysical result inconsistent with the second law of thermodynamics.

Now let us consider the magnitude of  $\Delta_{\text{int(sp)}}G^{A/S}$  for the same solute in different alcohols. The difference between their values for any solute from Table 2 in any two different alcohols usually fall to the bounds of uncertainties of Eqns (4)–(6) and of the experiment, which can be up to  $1\text{--}1.5 \text{ kJ}\cdot\text{mol}^{-1}$ . The root mean square deviation  $s$  for 17 Gibbs free energies of hydrogen bonding for the same solute with methanol and octanol is

**Table 2.** The Gibbs free energies of nonspecific solvation, solvophobic effect, and specific interactions in diluted aqueous and alcoholic solutions of various proton accepting solutes (at 298 K in  $\text{kJ}\cdot\text{mol}^{-1}$ )

Solute (A)	Solvent(S)	$\Delta_{\text{solv}}G^{A/S}$	$\Delta_{\text{solv(nonsp)}}G^{A/S}$	$\Delta_{\text{s.e.}}G^A$	$\Delta_{\text{int(sp)}}G^{A/S}$
Acetone	Methanol	-0.6	-2.4	3.1	-1.2
2-Butanone	Methanol	-3.2	-5.0	3.8	-1.9
2-pentanone	Methanol	-4.5	-7.8	4.5	-1.2
2-Hexanone	Methanol	-5.9	-10.3	5.2	-0.9
2-Heptanone	Methanol	-9.1	-12.6	6.0	-2.5
Dimethylamine	Methanol	1.2	2.2	2.8	-3.8
Diethylamine	Methanol	-5.4	-2.3	4.2	-7.3
Triethylamine	Methanol	-6.0	-6.1	5.7	-5.6
Acetonitrile	Methanol	-1.0	-2.8	2.3	-0.5
Methyl acetate	Methanol	-0.8	-3.3	3.4	-0.8
Propyl acetate	Methanol	-4.2	-8.0	4.8	-1.1
Butyl acetate	Methanol	-6.5	-10.2	5.5	-1.9
Methyl propanoate	Methanol	-2.2	-5.4	4.1	-0.9
Methyl hexanoate	Methanol	-8.5	-12.9	6.3	-1.9
Methyl pentanoate	Methanol	-6.4	-10.4	5.5	-1.6
1,4-Dioxane	Methanol	-4.8	-8.2	3.8	-0.3
Butyl ether	Methanol	-4.9	-9.5	6.9	-2.3
Dimethyl formamide	Methanol	-13.9	-11.5	3.6	-6.0
Dimethyl sulfoxide	Methanol	-21.0	-14.7	3.4	-9.6
Methyl tert-butyl ether	Methanol	0.1	-1.7	4.7	-2.9
Tetrahydrofuran	Methanol	-2.6	-4.0	3.4	-2.1
Acetone	Ethanol	-0.8	-1.5	3.0	-2.4
2-Butanone	Ethanol	-3.0	-4.4	3.6	-2.2
Dimethylamine	Ethanol	1.3	1.8	2.8	-3.3
Trimethylamine	Ethanol	-0.2	1.9	3.3	-5.5
Triethylamine	Ethanol	-5.4	-6.9	5.0	-3.5
Pyridine	Ethanol	-8.9	-7.8	3.5	-4.5
Acetonitrile	Ethanol	-1.6	-1.7	2.4	-2.3
Ethyl acetate	Ethanol	-2.0	-4.7	3.8	-1.0
Methyl propanoate	Ethanol	-2.4	-5.0	3.8	-1.2
1,4-dioxane	Ethanol	-4.6	-7.5	3.5	-0.7
Dimethyl formamide	Ethanol	-12.1	-10.4	3.4	-5.1
Tetrahydrofuran	Ethanol	-2.4	-4.4	3.3	-1.3
2-Butanone	Propanol	-3.1	-4.3	3.1	-1.9
Dimethylamine	Propanol	1.9	1.8	2.3	-2.2
Trimethylamine	Propanol	-0.2	1.9	2.8	-4.9
Triethylamine	Propanol	-5.6	-6.9	4.5	-3.2
Pyridine	Propanol	-8.4	-7.8	3.0	-3.6
3-Methylpyridine	Propanol	-12.2	-11.4	3.6	-4.3
Methyl propanoate	Propanol	-1.9	-4.9	3.3	-0.3
1,4-dioxane	Propanol	-4.3	-7.3	3.0	0.0
Tetrahydrofuran	Propanol	-2.2	-4.4	2.8	-0.6
Acetone	Butanol	-0.8	-0.9	2.2	-2.1
2-Butanone	Butanol	-3.4	-4.0	2.6	-2.0
Methylamine	Butanol	1.8	3.6	1.6	-3.4
Ethylamine	Butanol	-5.0	1.9	2.0	-8.9
Propylamine	Butanol	-7.2	-1.6	2.4	-8.1
Trimethylamine	Butanol	1.7	1.8	2.4	-2.5
Butylamine	Butanol	-9.2	-4.0	2.9	-8.0
Diethylamine	Butanol	-7.7	-3.0	2.9	-7.5
Triethylamine	Butanol	-6.4	-7.0	3.7	-3.1
Pyridine	Butanol	-8.7	-7.6	2.6	-3.6
3-Methylpyridine	Butanol	-12.9	-11.2	3.0	-4.7
Acetonitrile	Butanol	-1.0	-1.1	1.7	-1.6
Ethyl acetate	Butanol	-2.7	-4.4	2.8	-1.1

(Continues)

Table 2. (Continued)

Solute (A)	Solvent(S)	$\Delta_{\text{solv}}G^{A/S}$	$\Delta_{\text{solv(nonsp)}}G^{A/S}$	$\Delta_{\text{s.e.}}G^A$	$\Delta_{\text{int(sp)}}G^{A/S}$
1,4-Dioxane	Butanol	-5.2	-7.0	2.6	-0.8
Butyl ether	Butanol	-8.5	-11.3	4.5	-1.7
Acetone	Pentanol	-0.7	-0.6	2.0	-2.2
2-Butanone	Pentanol	-2.8	-3.7	2.4	-1.4
Methylamine	Pentanol	-3.1	3.6	1.5	-8.1
Ethylamine	Pentanol	-4.4	1.8	1.8	-8.1
Propylamine	Pentanol	-7.0	-1.6	2.2	-7.6
Butylamine	Pentanol	-9.5	-4.1	2.6	-8.0
Diethylamine	Pentanol	-8.7	-3.0	2.6	-8.3
Triethylamine	Pentanol	-7.3	-7.0	3.3	-3.6
Ethyl acetate	Pentanol	-2.7	-4.1	2.5	-1.1
Propyl acetate	Pentanol	-4.6	-7.1	2.9	-0.4
Acetone	Octanol	-0.6	0.0	1.6	-2.2
2-Butanone	Octanol	-3.3	-3.2	1.8	-1.9
2-Pentanone	Octanol	-5.7	-6.0	2.1	-1.7
2-Hexanone	Octanol	-8.5	-8.8	2.3	-1.9
2-Heptanone	Octanol	-11.1	-11.6	2.6	-2.1
2-Octanone	Octanol	-14.2	-14.5	2.8	-2.5
Acetophenone	Octanol	-15.7	-15.7	2.4	-2.4
Methylamine	Octanol	1.7	3.5	1.2	-3.1
Ethylamine	Octanol	-4.6	1.6	1.5	-7.7
Dimethylamine	Octanol	1.1	1.7	1.5	-2.1
Propylamine	Octanol	-7.4	-1.5	1.7	-7.6
Trimethylamine	Octanol	1.5	1.7	1.7	-1.9
Butylamine	Octanol	-8.1	-4.1	2.0	-5.9
Diethylamine	Octanol	-7.3	-3.0	2.0	-6.3
Dipropylamine	Octanol	-8.0	-8.7	2.5	-1.7
Pyridine	Octanol	-9.8	-7.1	1.8	-4.5
2-Picoline	Octanol	-13.2	-9.6	2.1	-5.6
3-Methylpyridine	Octanol	-14.2	-10.6	2.1	-5.7
4-Methylpyridine	Octanol	-15.1	-10.8	2.1	-6.3
Acetonitrile	Octanol	-0.6	-0.2	1.3	-1.7
Propionitrile	Octanol	-2.8	-2.0	1.6	-2.4
Benzonitrile	Octanol	-12.9	-13.6	2.2	-1.4
Nitroethane	Octanol	-3.9	-4.5	1.6	-1.0
Nitrobenzene	Octanol	-15.2	-16.3	2.2	-1.1
Methyl acetate	Octanol	-0.6	-1.4	1.7	-1.0
Ethyl acetate	Octanol	-2.9	-3.7	1.9	-1.1
Propyl acetate	Octanol	-5.6	-6.6	2.2	-1.1
Butyl acetate	Octanol	-8.3	-9.4	2.4	-1.4
Pentyl acetate	Octanol	-11.0	-12.1	2.7	-1.6
Methyl propanoate	Octanol	-4.5	-4.0	1.9	-2.4
Methyl pentanoate	Octanol	-8.9	-9.7	2.4	-1.7
Methyl benzoate	Octanol	-17.8	-14.7	2.5	-5.6
1,4-Dioxane	Octanol	-5.6	-6.2	1.8	-1.1
3,3-Dimethylbutan-2-one	Octanol	-6.4	-7.4	2.3	-1.4
Benzaldehyde	Octanol	-13.1	-13.2	2.2	-2.1
Butyl ether	Octanol	-9.7	-11.5	2.9	-1.0
Dimethyl formamide	Octanol	-12.5	-8.7	1.8	-5.5
Dimethyl sulfoxide	Octanol	-15.8	-10.6	1.7	-6.8
Methyl tert-butyl ether	Octanol	-2.2	-2.8	2.2	-1.6
Tetrahydrofuran	Octanol	-3.8	-4.4	1.7	-1.1
Triethyl phosphate	Octanol	-24.6	-18.7	3.1	-9.0
Acetone	Water	2.0	-3.3	15.7	-10.4
2-Butanone	Water	2.9	-5.1	18.8	-10.7
2-Pentanone	Water	3.8	-7.8	21.9	-10.3
2-Hexanone	Water	4.1	-9.7	25.0	-11.2

(Continues)

**Table 2.** (Continued)

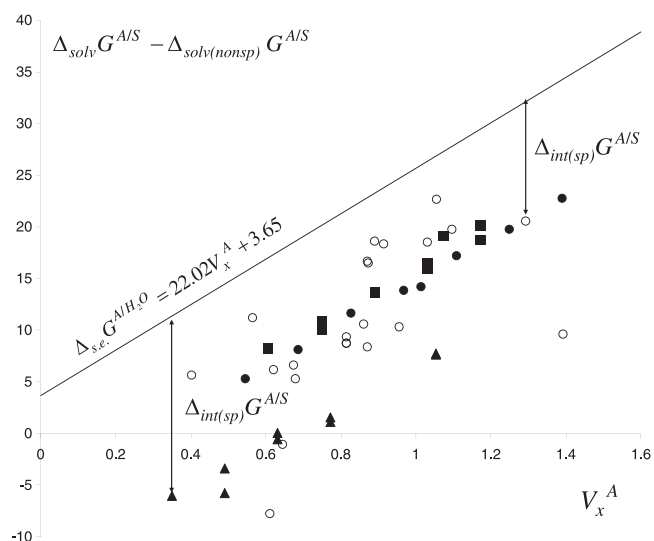
Solute (A)	Solvent(S)	$\Delta_{\text{solv}}G^{A/S}$	$\Delta_{\text{solv(nonsp)}}G^{A/S}$	$\Delta_{\text{s.e.}}G^A$	$\Delta_{\text{int(sp)}}G^{A/S}$
2-Heptanone	Water	5.6	-11.6	28.1	-11.0
2-Octanone	Water	5.9	-13.9	31.2	-11.5
2-Nonanone	Water	7.5	-15.3	34.3	-11.6
Acetophenone	Water	-1.3	-15.5	26.0	-11.8
Methylamine	Water	-1.0	5.0	11.3	-17.4
Ethylamine	Water	-0.9	4.9	14.4	-20.2
Dimethylamine	Water	0.0	3.4	14.4	-17.8
Propylamine	Water	-0.4	0.2	17.5	-18.1
Trimethylamine	Water	4.3	4.2	17.5	-17.5
Butylamine	Water	-0.1	-1.2	20.6	-19.5
Diethylamine	Water	1.0	-0.6	20.6	-19.0
Dipropylamine	Water	1.2	-6.5	26.8	-19.2
Triethylamine	Water	3.9	-3.9	26.8	-19.1
Pyridine	Water	-1.2	-7.8	18.5	-11.9
2-Picoline	Water	-1.4	-10.1	21.6	-12.9
3-Methylpyridine	Water	-2.1	-11.4	21.6	-12.3
4-Methylpyridine	Water	-2.8	-11.4	21.6	-12.9
2,6-Lutidine	Water	-1.3	-11.6	24.7	-14.4
Acetonitrile	Water	1.6	-3.9	12.5	-7.0
Benzonitrile	Water	0.3	-16.3	22.8	-6.2
Nitroethane	Water	2.4	-8.8	16.1	-4.9
Nitrobenzene	Water	0.7	-17.9	23.2	-4.6
2-nitrotoluene	Water	2.9	-15.6	26.3	-7.8
Methyl acetate	Water	4.6	-3.7	17.0	-8.7
Ethyl acetate	Water	5.0	-5.1	20.1	-10.0
Propyl acetate	Water	6.2	-7.6	23.2	-9.4
Butyl acetate	Water	6.8	-9.2	26.3	-10.3
Pentyl acetate	Water	7.6	-12.5	29.4	-9.2
Methyl propanoate	Water	5.6	-5.2	20.1	-9.2
Methyl hexanoate	Water	7.5	-11.3	29.4	-10.6
Methyl pentanoate	Water	7.2	-9.3	26.3	-9.8
Methyl benzoate	Water	1.5	-17.7	27.2	-8.0
1,4-Dioxane	Water	-3.3	-8.5	18.6	-13.4
Benzaldehyde	Water	1.1	-15.4	22.9	-6.4
Butyl ether	Water	14.4	-6.1	32.1	-11.6
Cyclohexanone	Water	-1.7	-12.2	22.6	-12.0
Dimethyl formamide	Water	-13.6	-12.5	17.9	-19.0
Dimethyl sulfoxide	Water	-24.4	-16.6	17.1	-24.9
Ethoxybenzene	Water	8.6	-14.1	26.9	-4.2
Methoxybenzene	Water	7.6	-10.7	23.8	-5.5
Methyl tert-butyl ether	Water	8.6	0.3	22.8	-14.5
N,N-dimethylaniline	Water	3.5	-16.2	27.8	-8.1
Tetrahydrofuran	Water	3.4	-2.8	17.3	-11.2
Triethyl phosphate	Water	-13.7	-23.2	34.3	-24.7

$s = 0.87 \text{ kJ}\cdot\text{mol}^{-1}$ , and for all 125 possible pairs of two Gibbs free energies of hydrogen bonding of the same compound with two different alcohols from Table 2  $s = 1.1 \text{ kJ}\cdot\text{mol}^{-1}$ . We can conclude that the hydrogen bond donating ability of bulk aliphatic alcohols with different alkyl chain length is nearly the same, and more detailed consideration is not possible because of the uncertainties.

One of the few available results from other works that can be used for comparison with our values is the fraction of nonbonded acetone in methanolic solutions reported by Max and Chapados<sup>[29]</sup> who used Attenuated total reflection Fourier transform infrared spectroscopy. The solution they considered was not infinitely diluted and was supposed to contain acetone dimers, but from

the ratio of bonded and nonbonded monomers of acetone the value of  $\Delta_{\text{int(sp)}}G^{A/S}$  can be estimated to be  $-2.9 \text{ kJ}\cdot\text{mol}^{-1}$ , which is in agreement with our findings.

In contrast, water forms much stronger complexes with all considered proton acceptors. For most of the considered solutes the degree of H-bonding with water related to  $\Delta_{\text{int(sp)}}G^{A/S}$  through Eqn (2) will be close to unity. This fact is supported by the infrared spectra of diluted aqueous solutions, where we do not observe the stretch bands of free carbonyl, carboxyl or other strong proton accepting groups that are quite intensive in the spectra of alcoholic solutions of compounds with such groups. Moreover, the analysis of infrared spectrum of moderately basic



**Figure 1.** Relationship between the contributions from nonspecific solvation, solvophobic effect, and specific interactions with water into the Gibbs free energy of hydration (at 298 K in  $\text{kJ}\cdot\text{mol}^{-1}$ ). The solutes marked with squares are esters, triangles are amines, filled circles are ketones, empty circles are other solutes from Table 1

molecule of acetonitrile diluted in water<sup>[13]</sup> gave the fraction of H-bonded solute to be more than 90%, which also corresponds with our results.

To see the influence of the cooperative effect on hydrogen-bonding strength for the complexes with bulk water and alcohols, it is necessary to know the Gibbs free energies of bonding of proton acceptors with monomers of water and alcohols. The Gibbs free energies of formation of complexes with water have never been determined experimentally, but can be estimated from empirical correlation relationships for the binding constants in inert medium (tetrachloromethane). For complexes with alcohols, there are also some experimental data. According to the scale of acidities and basicities of hydrogen bonds,<sup>[4]</sup> the values of acidity parameters of methanol and water  $\alpha_2^H$  are respectively 0.37 and 0.35. Other linear saturated alcohols are supposed to have slightly lower  $\alpha_2^H$  (0.33) than methanol.

Parameters  $\alpha_2^H$  reflecting the acidity of H-bond donor and  $\beta_2^H$  reflecting the basicity of H-bond acceptor are based on experimental data for the 1:1 complexation constants  $K^{A\cdots B}$  in tetrachloromethane, and are correlated with them through the equation

$$\lg K^{A\cdots B} = 7.354\alpha_2^H\beta_2^H - 1.094. \quad (7)$$

Here, the constant  $K^{A\cdots B}$  is expressed in molarity scale. We can go to the molar fraction scale by dividing by the molar volume of solvent,  $\text{CCl}_4$ , and then converting the constant to the standard Gibbs free energy of bonding (using the fact that  $\ln K^{A\cdots B} = \ln 10 \cdot \lg K^{A\cdots B}$ ):

$$\Delta_{\text{HB}}G^{A\cdots B} = -RT \ln 10 \cdot (\lg K^{A\cdots B} - \lg V_m(\text{CCl}_4)). \quad (8)$$

The comparison of the values for 1:1 complexes calculated by Eqn (8) with the Gibbs free energies of hydrogen bonding with the bulk solvent is given in Table 3. It can be seen that the complexes with bulk alcohols are weaker than those with a single

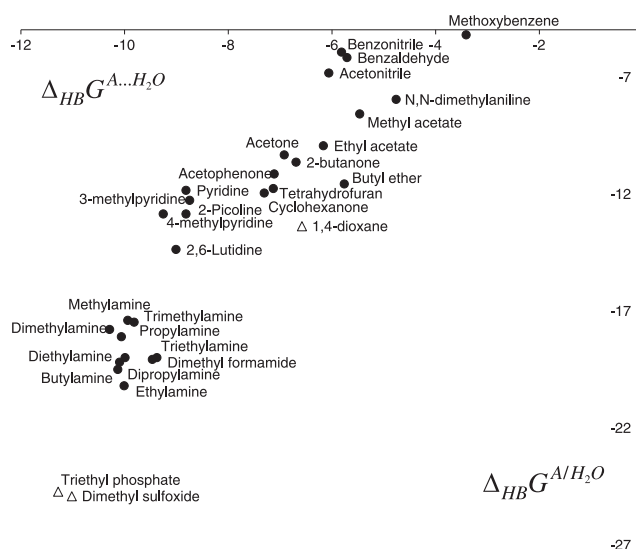
**Table 3.** The standard Gibbs free energies of hydrogen bonding with methanol into 1:1 complex  $\Delta_{\text{HB}}G^{A\cdots S}$  calculated by Eqn (8) and with bulk methanol  $\Delta_{\text{HB}}G^{A/S}$  calculated by Eqn (3) (at 298 K in  $\text{kJ}\cdot\text{mol}^{-1}$ )

Solute (A)	$\Delta_{\text{HB}}G^{A/S}$	$\Delta_{\text{HB}}G^{A\cdots S}$
1,4-Dioxane	5.1	-6.9
Acetonitrile	3.7	-6.3
2-Butanone	-0.4	-7.0
Butyl ether	-1.1	-6.0
Diethylamine	-7.2	-10.4
Dimethyl sulfoxide	-9.5	-11.5
Dimethylamine	-3.2	-10.7
Methyl acetate	2.4	-5.7
Dimethyl formamide	-5.8	-9.8
Acetone	1.2	-7.2
Tetrahydrofuran	-0.7	-7.4
Triethylamine	-5.3	-9.9

alcohol molecule, which is caused by the need to break some solvent-solvent hydrogen bonds to form a new solute-solvent H-bond. Only the strongest proton acceptors, like amines, dimethyl formamide, and dimethyl sulfoxide (which is likely to form more than one bond with methanol), have the values of  $\Delta_{\text{HB}}G^{A/S}$  more negative than  $-5 \text{ kJ}\cdot\text{mol}^{-1}$ .

The comparison of the standard Gibbs free energies of formation of complexes with water monomer and bulk water is given in Fig. 2.

In general, stronger proton acceptors as measured by the Gibbs free energy of bonding with a single proton donating molecule form stronger bonds with bulk water (e.g., amines form stronger bonds than esters and ketones, and they all form stronger bonds than nitriles). However, this rule cannot be described in strict quantitative terms. There is no single good correlation even for solutes



**Figure 2.** Standard Gibbs free energy of hydrogen bonding with bulk water versus that with water monomer estimated using Eqn (8) for different solutes at 298 K in  $\text{kJ}\cdot\text{mol}^{-1}$

that are likely to form 1 : 1 complex in aqueous solutions (marked by black circles). A rough relationship between  $\Delta_{\text{HB}}G^{\text{A}/\text{H}_2\text{O}}$  and  $\Delta_{\text{HB}}G^{\text{A}\dots\text{H}_2\text{O}}$  is  $\Delta_{\text{HB}}G^{\text{A}/\text{H}_2\text{O}} = 2.2\Delta_{\text{HB}}G^{\text{A}\dots\text{H}_2\text{O}} + 4.2$  with  $s = 1.8$   $\text{kJ}\cdot\text{mol}^{-1}$ ,  $r^2 = 0.873$ .

The correlation between the Gibbs free energies of hydrogen bonding with bulk water and those with bulk methanol for the same solute is much better. It is given by

$$\Delta_{\text{HB}}G^{\text{A}/\text{H}_2\text{O}} = 1.22\Delta_{\text{HB}}G^{\text{A}/\text{CH}_3\text{OH}} - 11.0 \quad (9)$$

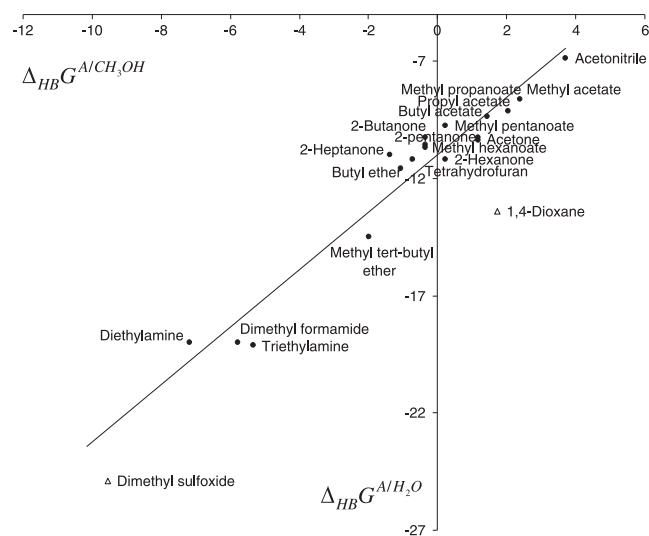
with  $s = 0.9$   $\text{kJ}\cdot\text{mol}^{-1}$ ,  $r^2 = 0.935$  (Fig. 3).

Two points plotted with triangles in Fig. 3 correspond to the solutes forming more than one hydrogen bond at least in aqueous solutions. It is important to note that if we suppose 1,4-dioxane to form two H-bonds of the same strength with water, then the Gibbs free energy of formation of such bonds will fall to the same line as for other proton acceptors. For dimethyl sulfoxide, it is difficult to make any guess on the strength of each of two H-bonds with one S=O group.

The above results can be interpreted as the following. Cooperative effects lead to a large increase of the strength (measured in terms of Gibbs free energies) of hydrogen bonds with water polymers in comparison with those with water monomer. The exact magnitude of increase is sensitive to the structure of solute; the same has been observed for the enthalpies of cooperative H-bonds of proton acceptors with alcohols. In alcoholic solutions, a cooperative increase of the bond strength is less pronounced and is often compensated by the cost of breaking alcohol–alcohol H-bonds, so that a significant fraction of solute molecules is not bonded to the solvent, except for the strongest proton acceptors like amines. However, the standard Gibbs free energies related to the formation of one bond in standard conditions are intercorrelated in methanol and water.

For the compounds with multiple proton accepting centers there will be no single correlation between the  $\Delta_{\text{HB}}G^{\text{A}/\text{S}}$  values in aqueous and alcoholic solutions. Thus, their total effective basicities will not be the same in water and in methanol or other alcohols.

In our previous works,<sup>[30,31]</sup> we also considered the thermodynamics of hydrogen bonding of normal monohydric alcohols with



**Figure 3.** Standard Gibbs free energy of hydrogen bonding with bulk water versus that with bulk methanol for different solutes at 298 K in  $\text{kJ}\cdot\text{mol}^{-1}$

water and self-association of these alcohols. Alcohols in their solutions act simultaneously as proton donors and acceptors. The Gibbs free energies of specific interactions with water for alcohols from methanol to octanol fall in the range  $-18.2 \pm 0.3$   $\text{kJ}\cdot\text{mol}^{-1}$ ,<sup>[31]</sup> while their Gibbs free energies of self-association are in the range  $-10.8 \pm 0.7$   $\text{kJ}\cdot\text{mol}^{-1}$ .<sup>[30]</sup> Again, we observe close values of  $\Delta_{\text{int}(\text{sp})}G^{\text{A}/\text{S}}$  for a homologous series of normal alcohols dissolved in water. At the same time, solutions in water behave very differently from the solutions in alcohols and exhibit much stronger solute–solvent hydrogen bonding. It is worth mentioning that alcohols do not fit the correlation (9) for proton acceptors.

There are very few purely proton donating species without proton accepting ability, which could also be very interesting to consider. One of them is chloroform. Our calculations show that in water the value of  $\Delta_{\text{HB}}G^{\text{CHCl}_3/\text{H}_2\text{O}}$  is about  $-2.1$   $\text{kJ}\cdot\text{mol}^{-1}$ , and in alcohols the values of  $\Delta_{\text{HB}}G^{\text{CHCl}_3/\text{ROH}}$  fall in the range  $-2.9 \pm 0.3$   $\text{kJ}\cdot\text{mol}^{-1}$ . The typical value of standard hydrogen bonding Gibbs free energy of chloroform with an oxygen base (ether) into an equimolar complex is about  $-3$   $\text{kJ}\cdot\text{mol}^{-1}$ . For chloroform, cooperative effects in complexes with bulk water are less pronounced than for proton acceptors. Hydrogen bonding with bulk water is even less energetically favorable than with bulk alcohols.

## CONCLUSION

The results presented and discussed above show that hydrogen bonding with self-associated solvents has its peculiarities that could not be neglected when one describes the solvent effect on solute reactivity or any other properties. The basicity scales constructed from the data for equimolar complexes cannot be directly applied for description of solute–water or solute–alcohol hydrogen bonding. The Gibbs free energies of hydrogen bonding with bulk water and alcohols are intercorrelated, which can be used to construct a separate scale of basicity for the species dissolved in associated solvents. This scale could help us to predict solvation properties and reactivities in solvents other than well-studied water and alcohols. However, H-bonding properties of molecules with multiple proton accepting centers and/or proton donating centers cannot be described using one total basicity and one total acidity parameter for all associated solvents. Each center can be taken into account separately, but another problem is that the second and subsequent bonds with solvent will not have the same energy as the first one even if the bonding sites are identical.

Thermodynamic analysis is a tool that allows to determine the Gibbs free energy of specific interactions for solutes and solvents with an arbitrary number of basic and acidic centers from experimental Gibbs free energy of solvation, without making any assumptions about the structure and energies of complexes formed in solutions. However, it cannot provide any additional information about hydrogen bonds, and further detailed experimental and theoretical studies of hydrogen bonding in associated solvents are necessary.

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## REFERENCES

- [1] M. D. Joesten, L. J. Schaad, Hydrogen bonding, Marcel Dekker, New York, **1974**.
- [2] C. Laurence, M. Berthelot, *Perspect. Drug Discov. Des.* **2000**, *18*, 3960.
- [3] R. S. Drago, N. O'Bryan, G. C. Vogel, *J. Am. Chem. Soc.* **1970**, *92*, 3924–3929.
- [4] M. H. Abraham, *Chem. Soc. Rev.* **1993**, *22*, 73–83.
- [5] O. A. Raevsky, V. Y. Grigor'ev, D. B. Kireev, N. S. Zefirov, *Quant. Struct.-Act. Relat.* **1992**, *11*, 49–63.
- [6] J. C. Dearden, T. Ghafourian, *J. Chem. Inf. Comput. Sci.* **1998**, *39*, 231–235.
- [7] J. Catala;Bn, *J. Phys. Chem. B* **2009**, *113*, 5951–5960.
- [8] G. Viktor, *Coord. Chem. Rev.* **1976**, *18*, 225–255.
- [9] J. L. M. Abboud, R. Notario, *Pure Appl. Chem.* **1999**, *71*, 645–718.
- [10] A. A. Oliferenko, P. V. Oliferenko, J. G. Huddleston, R. D. Rogers, V. A. Palyulin, N. S. Zefirov, A. R. Katritzky, *J. Chem. Inf. Comput. Sci.* **2004**, *44*, 1042–1055.
- [11] I. A. Sedov, B. N. Solomonov, *Fluid Phase Equilib.* **2009**, *276*, 108–115.
- [12] B. N. Solomonov, V. B. Novikov, M. A. Varfolomeev, N. M. Milesenko, *J. Phys. Org. Chem.* **2005**, *18*, 49–61.
- [13] J. E. Bertie, Z. Lan, *J. Phys. Chem. B* **1997**, *101*, 4111–4119.
- [14] N. Bilickov, G. Baranovic, *J. Mol. Liq.* **2009**, *144*, 155–162.
- [15] D. S. Venables, C. A. Schmuttenmaer, *J. Chem. Phys.* **2000**, *113*, 11222–11236.
- [16] H. Kleeberg, D. Klein, W. A. P. Luck, *J. Phys. Chem.* **1987**, *91*, 3200–3203.
- [17] B. N. Solomonov, M. A. Varfolomeev, V. B. Novikov, A. E. Klimovitskii, *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2006**, *64*, 405–411.
- [18] W. A. P. Luck, *Angew. Chem. Int. Ed Engl.* **1980**, *19*, 28–41.
- [19] B. N. Solomonov, M. A. Varfolomeev, V. B. Novikov, *J. Phys. Org. Chem.* **2006**, *19*, 263–268.
- [20] B. N. Solomonov, I. A. Sedov, A. A. Akhmediyarov, *J. Phys. Org. Chem.* **2009**.
- [21] I. A. Sedov, M. A. Stolov, B. N. Solomonov, *J. Phys. Org. Chem.* **2011**, *24*, 1088–1094.
- [22] I. A. Sedov, B. N. Solomonov, *J. Chem. Eng. Data* **2011**, *56*, 1438–1442.
- [23] B. N. Solomonov, I. A. Sedov, *J. Mol. Liq.* **2008**, *139*, 89–97.
- [24] I. A. Sedov, B. N. Solomonov, *Russ. J. Phys. Chem. A* **2008**, *82*, 704–708.
- [25] M. H. Abraham, J. C. McGowan, *Chromatographia* **1987**, *23*, 243–246.
- [26] J. Li, T. Zhu, G. D. Hawkins, P. Winget, D. A. Liotard, C. J. Cramer, D. G. Truhlar, *Theor. Chem. Acc.* **1999**, *103*, 9–63.
- [27] A. R. Katritzky, A. A. Oliferenko, P. V. Oliferenko, R. Petrukhin, D. B. Tatham, U. Maran, A. Lomaka, J. Acree, *J. Chem. Inf. Comput. Sci.* **2003**, *43*, 1794–1805.
- [28] C. Mintz, T. Ladlie, K. Burton, M. Clark, W. Acree, M. Abraham, *QSAR Comb. Sci.* **2008**, *27*, 627–635.
- [29] J. J. Max, C. Chapados, *J. Chem. Phys.* **2005**, *122*, 1–18.
- [30] I. A. Sedov, B. N. Solomonov, *J. Mol. Liq.* **2012**, *167*, 47–51.
- [31] I. A. Sedov, B. N. Solomonov, *Fluid Phase Equilib.* **2012**, *315*, 16–20.