ELSEVIER

Thermochimica Acta 258 (1995) 67–76

thermochimica
acta

Hydration effect on urea–non-electrolyte enthalpic pair interaction coefficients. Dissolution enthalpies of urea in aqueous solution of alkoxyethanols at 298.15 K

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Received 18 May 1994; accepted 30 November 1994

Abstract

The dissolution enthalpies of urea in aqueous solutions of 2-methoxyethanol and 2-butoxyethanol have been measured and the relevant enthalpic pair interaction coefficients h_{xy}(urea–non-electrolyte) in water have been determined. These results, in conjunction with the data concerning urea–non-electrolyte pairs taken from our earlier reports and from the literature, were analysed with respect to the effect of non-electrolyte hydration on variations of the h_{xy} values in water. The coefficients for urea–non-electrolyte systems are linearly correlated with the heat capacity of interaction of the non-electrolyte with solvent water.

Keywords: Enthalpic interaction coefficients; Hydration; Urea–non-electrolyte

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1. Introduction

Urea is an attractive model compound for studies on multicomponent liquid mixtures that mimic naturally occurring biological systems. Its molecule, which contains the peptide group (–CONH–) without any alkyl groups, is strongly polar. Moreover, it is able to form hydrogen bonds as both a donor and an acceptor of the proton. Urea is known as a strong denaturant of globular proteins [1–3]. Despite numerous investigations, the mechanism of interactions of urea with these substances is still unclear. There is no general agreement on whether denaturation by urea results

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SSDI 0040-6031(94)02238-0

from a direct interaction of urea with the proteins or from changes in the structure of water near the surface of the protein globules [4–6]. This problem is difficult to resolve because of the complex structure of biological systems. Therefore the attention of scientists has been focused on the examination of small solutes which contain some specific functional groups characteristic of peptides, or which can be considered as models of the repeating units in natural proteins or polypeptides.

In recent years, a model of the enthalpic pair interaction coefficients h_{xy} derived from McMillan–Mayer theory [7–9] has frequently been used in studies on solute–solute interactions in dilute solutions. This model has been applied by several authors for the analysis of interactions of urea with such biologically important compounds as amides [10, 11], amino acids and small peptides [12–14], and saccharides [15]. However, in order to obtain a broader picture of urea–cosolute interactions in solution, it is necessary to examine other cosolutes having different molecular structures and properties. Such investigations have been performed also in our laboratory. We determined calorimetrically the enthalpic pair interaction coefficients for the pairs of urea with alcohols, hydrophilic urea derivatives, tetrahydrofuran, dimethyl sulphoxide and 1,2-dimethoxyethane (DME) [16–18]. Recently we have analysed the influence of non-electrolyte polarity, acidity and basicity on the h_{xy} values for urea–non-electrolyte pairs in water [18]. In this paper, we intend to discuss the effect of hydration of the non-electrolyte on the magnitude of the h_{xy} coefficients. In order to expand the amount of data for this analysis, additional h_{xy} values for urea–2-methoxyethanol (MeEtOH) and urea–2-butoxyethanol (BuEtOH) pairs have been determined. To this end, we measured the dissolution enthalpies of urea in aqueous solutions of MeEtOH and BuEtOH at 298.15 K.

2. Experimental

Urea of purissimum grade (POCh, Poland) was recrystallized from deionized, double-distilled water and dried under vacuum for several days at 330 K. 2-Methoxyethanol and 2-butoxyethanol, both from Fluka AG, were dried with 0.4 nm molecular sieves and distilled in a water-free atmosphere. The mixtures were prepared by weight using deionized, freshly distilled water.

The enthalpies of solution of urea in different solvent mixtures were measured with an isoperibol calorimeter. The glass calorimetric vessel, of capacity ca. 100 cm^3, was equipped with a calibration heater, a thermistor and a stirrer-ampoule holder. A thin-walled glass ampoule with the sample of urea to be dissolved was attached to the ampoule holder and crushed against the bottom of the calorimetric vessel during the experiment. The 10 kΩ thermistor was connected to a Wheatstone bridge. A temperature change of approximately $3 \cdot 10^{-5}$ K could be detected. The ampoule breaking-heat effect in the reaction vessel was negligible. The calorimeter was placed in a hermetically closed brass jacket with a capacity of about 1 dm^3 and immersed in a water thermostat. The temperature stability of the thermostat was better than $1 \cdot 10^{-3}$ K. The error in the calorimetric measurements was estimated to be $\pm 0.5\%$.

3. Results

Four to six independent measurements were made on each investigated mixture. The final concentration of the urea solutions ranged from 0.006 to 0.015 mol kg^{-1}. No concentration dependence (within the error limits) of the enthalpies of solution was observed and, consequently, the measured enthalpies were regarded as those at infinite dilution $\Delta_{sol}H^{\ominus}$ (standard enthalpies of solution). Values of $\Delta_{sol}H^{\ominus}$ for urea in aqueous solutions of 2-methoxyethanol and 2-butoxyethanol at 298.15 K are given in Table 1. The obtained value of the dissolution enthalpy of urea in water (15.31 ± 0.03 kJ mol^{-1}) is in very good agreement with our previous value (15.29 ± 0.03 kJ mol^{-1}) [16] and with other literature data: 15.28 kJ mol^{-1} [19], 15.29 kJ mol^{-1} [20], 15.30 kJ mol^{-1} [9] and 15.31 kJ mol^{-1} [21].

4. Discussion

4.1. Dissolution enthalpies

The enthalpies of solution of urea in mixtures of water with 2-methoxyethanol and 2-butoxyethanol are plotted in Fig. 1 as a function of the molar percentage of the 2-alkoxyethanol. For purposes of comparison the data related to 2-ethoxyethanol, taken from our earlier paper [16], are also given in the figure. The curves relating $\Delta_{sol}H^{\ominus}$ to composition for urea in water–2-alkoxyethanol mixtures exhibit maxima at low organic cosolvent content. Similar behaviour has been observed for the dissolution enthalpy of urea in mixtures of water with aliphatic alcohols [5, 16] and with tetrahydrofuran (THF) [22], and also for inorganic electrolytes in mixtures of water with alkanols [23], THF [22] and hexamethylphosphoramide (HMPA) [24]. It is generally assumed that these maxima are related to the hydrophobic hydration of organic cosolvent in the range of high water contents in the mixed water-organic solvent mixtures. As is seen from Fig. 1, the magnitude of the limiting slope of the curves

Table 1
Enthalpies of solution of urea $\Delta_{sol}H^{\ominus}$ kJ mol^{-1}, in aqueous solutions of 2-methoxyethanol (MeEtOH) and 2-butoxyethanol (BuEtOH) at 298.15 K

Mass % of non-electrolyte	$\Delta_{sol}H^{\ominus}$(MeEtOH)	$\Delta_{sol}H^{\ominus}$(BuEtOH)
0	15.34 ± 0.02	15.34 ± 0.02
2.5	15.45 ± 0.03	15.52 ± 0.03
5	15.52 ± 0.01	15.66 ± 0.03
10	15.61 ± 0.02	15.24 ± 0.03
15	15.54 ± 0.04	15.00 ± 0.01
20	15.44 ± 0.04	14.80 ± 0.01

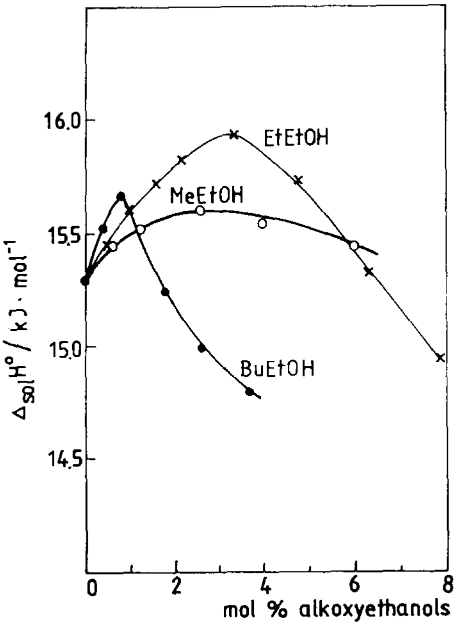

Fig. 1. Standard enthalpies of solution of urea in mixtures of water with 2-methoxyethanol (MeEtOH), 2-ethoxyethanol (EtEtOH) and 2-butoxyethanol (BuEtOH) vs. mol% of alkoxyethanol.

increases as the size of the terminal alkyl group in alkoxyethanol molecule becomes bigger. This observation confirms the suggestion concerning the origin of the extremum.

4.2. Enthalpic pair interaction coefficients

The enthalpic pair interaction coefficients, h_{xy}(urea–non-electrolyte) in water were calculated from the dissolution enthalpies of urea in water–organic mixtures by a method described previously [25].

The standard enthalpy of solution of urea in water–organic mixtures $\Delta_{sol}H^{\ominus}(U \text{ in } W+Y)$ was presented as a function

$$\Delta_{sol}H^{\ominus}(U \text{ in } W+Y) = \Delta_{sol}H^{\ominus}(U \text{ in } W) + b\omega_y + c\omega_y^2 \qquad (1)$$

where $\Delta_{sol}H^{\ominus}(U \text{ in } W)$ denotes the standard enthalpy of solution of urea in pure water, ω_y is the mass fraction of cosolvent Y and b and c are coefficients that can be determined by the least-squares method. Parameter b in Eq. (1), which represents the limiting slope of function $\Delta_{sol}H^{\ominus}(U \text{ in } W+Y)$, is connected with the McMillan–Mayer interaction coefficient h_{xy}

$$b = 2h_{xy}(\delta m_y/\delta\omega_y)_{\omega_y \to 0} \qquad (2)$$

Denoting the molar mass of the cosolvent by M_y, we have for dilute solutions

$$(\delta m_y/\delta\omega_y)_{\omega_y\to 0} = 1/M_y \tag{3}$$

Hence

$$h_{xy} = b\cdot M_y/2 \tag{4}$$

The parameter c in Eq. (1) is related to a triple interaction term, in our case to the h_{xyy} coefficient. The interpretation of the triple interaction coefficients is obscured by the fact that they also contain pairwise interaction terms [7, 25]. They will not be discussed in this paper.

The enthalpic pair interaction coefficients h_{xy}, for urea–non-electrolyte pairs determined in our laboratory and those reported in the papers of other authors are presented in Table 2. As can be seen from these data, the h_{xy} coefficients have different values depending on the kind of non-electrolyte. Generally, positive h_{xy} values are observed for the systems containing alcohols, 2-alkoxyethanols, ethers (THF, DME) and higher tertiary amides as cosolutes, which are all substances with dominant hydrophobic properties. The interactions of urea with alkanols become thermochemically more unfavourable as the apolar part of the alkanol molecule becomes larger. Thermochemically favourable interactions, characterized by negative h_{xy} values, are observed for pairs of urea with highly polar non-electrolytes which exhibit hydrophilic properties. Also in this case, the interactions are less favourable (h_{xy} becomes less negative or even positive) as the size and number of apolar groups in the non-electrolyte molecule become greater. Some authors [3] support the opinion that interactions between urea and molecules with the amide group, such as amino acids and peptides,

Table 2

Enthalpic pair interaction coefficients h_{xy} in J kg mol^{-2} for urea–non-electrolyte pairs in water

Non-electrolyte	h_{xy}	Non-electrolyte	h_{xy}
Ethanol (EtOH)	319[a]	*NN*-Dimethylformamide (DMF)	−155[h]
n-Propanol (PrOH)	424[a]	Acetamide (AA)	−142[h]
i-Propanol (iPrOH)	499[b]	*N*-Methylacetamide (NMA)	15[h]
n-Butanol (BuOH)	475[a]	*NN*-Dimethylacetamide (DMA)	−70[h]
s-Butanol (sBuOH)	623[b]	*N*-Methylpropanamide (NMPA)	180[i]
t-Butanol (tBuOH)	715[c]	*N*-Butylacetamide (NBA)	264[i]
2-Methoxyethanol (MeEtOH)	187[d]	*NN*-Diethylformamide (DEF)	36[h]
2-Ethoxyethanol (EtEtOH)	314[b]	Urea (U)	−359[i]
2-Butoxyethanol (BuEtOH)	590[d]	Thiourea (TU)	−561[j]
Acetone (ACT)	50[e]	Biuret (B)	−796[j]
Acetonitrile (AN)	149[f]	Ethylene glycol (EG)	46[i]
Dimethyl sulphoxide (DMSO)	−63[g]	1,2-Dimethoxyethane (DME)	488[g]
Tetrahydrofuran (THF)	295[e]	Glucose (Glu)	−377[i]
Formamide (FA)	−261[h]	Fructose (Fru)	−405[k]
N-Methylformamide (NMF)	−132[h]	Sucrose (Suc)	−598[i]

[a] Ref. [34]; [b] Ref. [16]; [c] Ref. [9]; [d] This paper; [e] Ref. [35]; [f] Calculated from ref. [36]; [g] Ref. [18]; [h] Ref. [10]; [i] Ref. [11]; [j] Ref. [33]; [k] Ref. [15].

occur through "bifunctional hydrogen bonding". The observed negative enthalpies of transfer of these substances from aqueous urea solutions to solutions in pure water (which result in negative h_{xy} values) illustrate, according to the opinion of the above mentioned authors, an exchange of a peptide–water H-bond for a peptide–urea H-bond. Moreover, when the non-polar moieties are attached to the peptide group, "the extent of hydrogen bond formation which is possible for the unsubstituted derivative may not be possible for the substituted ones" [3]. As a result, higher (less negative) h_{xy} values should be obtained in the latter case. However, the results of investigations of Cheek and Lilley on urea–amide interactions are at variance with the above suggestions [10].

Cheek and Lilley found that the h_{xy} coefficients for the interaction of urea with tertiary amides (*NN*-dimethylformamide, *NN*-dimethylacetamide and *NN*-diethylacetamide) have more negative values than those for the interaction with their corresponding isomers (*N*-methylacetamide, *N*-methylpropanamide and *N*-butylacetamide) having secondary amide groups. This was surprising because, contrary to chemical intuition, this would mean that the tertiary amides, which have no proton-donor capability, interact more strongly with urea than the secondary amides, which are both proton-donors and proton-acceptors. However, this inconsistency seems to be only apparent. As is known, the enthalpic pair interaction coefficients are regarded as a measure of the heat effect (i.e. the enthalpy of interaction) when two solute particles approach each other in the solution. This process is accompanied by overlap of the solvation cospheres of the solute molecules [8], resulting in a partial destruction of the solvation cospheres and a weakening of the solute–solvent interactions. This leads to an increase in enthalpy and makes an endothermic contribution to the observed h_{xy} values. Therefore the enthalpic pair interaction coefficients h_{xy} are a result of solvation effects and effects of direct solute–cosolute interactions. For the urea–non-electrolyte–water system discussed here, they can be presented as a sum of three contributions: (A) partial dehydration of the urea (endothermic effect), (B) partial dehydratation of the non-electrolyte (endothermic effect), and (C) net urea–non-electrolyte interaction (exothermic effect). Hence positive values of h_{xy} occur when the endothermic effects of dehydration predominate over the exothermic urea–non-electrolyte interaction. On the other hand, dominance of the urea–cosolute interaction effects (C) is reflected in negative values of h_{xy}. Since in our case the effect (A) can be assumed as being constant, the observed differences in the h_{xy} values are connected with the variation of effects (B) and (C). Therefore some qualitative relationships between the pairwise interaction coefficients and functions that illustrate structural features and properties of the non-electrolytes in question can be expected.

As was mentioned earlier, the influence of the polarity, acidity and basicity of the non-electrolytes on the h_{xy} coefficients under discussion was examined in our previous paper [18]. It appeared that the values of the enthalpic pair interaction coefficients decrease when the polarity of the non-electrolyte, defined by the π^* parameter [26], increases. Moreover, the analysed coefficients were found to be linearly dependent on the Dimroth–Reichardt E_T acidity parameter. However, the latter correlations concerned only groups of related compounds having a similar structure or properties (alkanols and aprotic compounds). In Figs. 2 and 3 some dependences that illustrate the

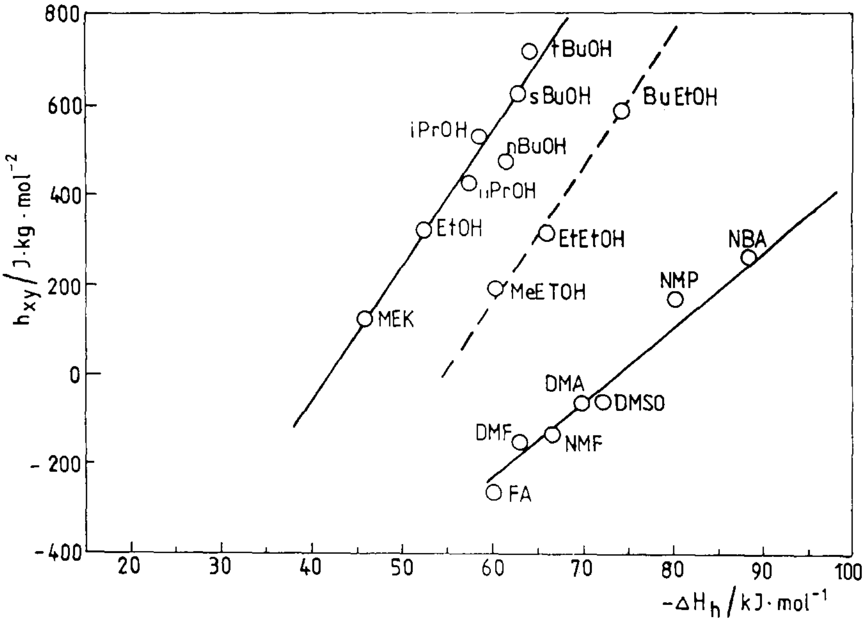

Fig. 2. Plot of the urea–non-electrolyte enthalpic pair interaction coefficients h_{xy} vs. the enthalpy of hydration of the non-electrolyte.

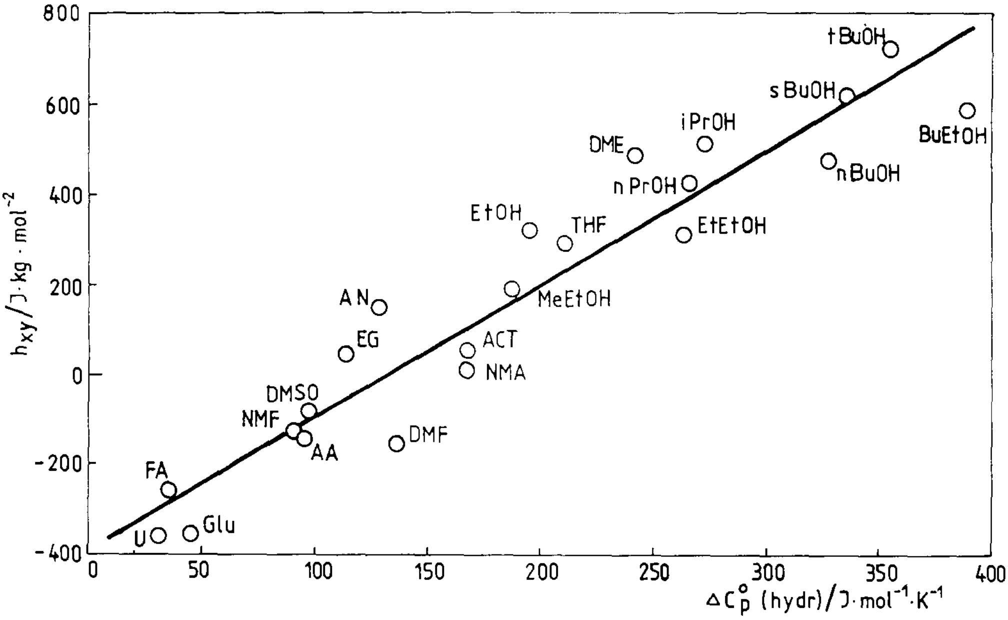

Fig. 3. Enthalpic pair interaction coefficients h_{xy} for urea–non-electrolyte pairs in water as a function of ΔC_p(hydr) of the non-electrolyte.

effect of non-electrolyte hydration on the values of the urea–non-electrolyte h_{xy} coefficients are presented. As is seen from Fig. 2, the interactions of urea with alkanols and with amides become less favourable (more positive h_{xy} values) as the enthalpy of hydration of the non-electrolyte becomes more negative (stronger hydration). Better correlations are obtained when we plot h_{xy} vs. entropy of hydration, and particularly vs. ΔC_p(hydr), which is the heat capacity of hydration of the non-electrolyte (Fig. 3). Both these functions are known to be sensitive to structural changes in solution. Therefore they reflect not only energetic but also structural effects of hydration and dehydration. The heat capacity of hydration can be presented as a sum of the heat capacity of cavity creation in water C_p(cav) and the heat capacity of interactions between the solute and water C_p(int) [27]

$$\Delta C_p^{\ominus}(\text{hydr}) = C_p(\text{cav}) + C_p(\text{int}) \tag{5}$$

The values of $\Delta C_p^{\ominus}$(hydr) can be calculated from experimental data according to the formula

$$\Delta C_p^{\ominus}(\text{hydr}) = C_{p,2}^{\ominus} - C_p^{g} - a \tag{6}$$

where $C_{p,2}^{\ominus}$ is the partial molar heat capacity of the dissolved solute at infinite dilution in water, C_p^{g} the standard molar heat capacity of the gaseous substance, and $a = R[2\alpha_p T + (\delta\alpha_p/\delta T)_p T^2 - 1]$ results from the different standard state.

If we calculate the cavity term C_p(cav) by means of SPT (Scaled Particle Theory) [27] or the method of Sinanoglu [28], and combine it with the experimentally determined heat capacity of hydration of the solute $\Delta C_p^{\ominus}$(hydr), we obtain the value of the interaction term. It seemed interesting to find out to what extent these two effects, i.e. cavity creation and solute–solvent interaction, contribute to the h_{xy} values. Therefore we tried to correlate the h_{xy} coefficients with C_p(cav) and C_p(int) of non-electrolytes for which the appropriate values could be calculated.

There is no simple correlation between the h_{xy} values for urea–non-electrolyte pairs and C_p(cav) of the non-electrolyte. However, the discussed h_{xy} coefficients are linearly correlated with the heat capacity of interaction between the dissolved non-electrolyte and the solvent water (Fig. 4). The observed dependence also encompasses non-electrolytes which are hydrophobically hydrated (e.g. higher alkanols and higher substituted amides) as well as hydrophilic ones. In terms of the model of interactions in solution presented above, the observed linear correlation suggests that in aqueous solution for a given solute X (i.e. urea in our case) the desolvation of the non-electrolyte Y(effect B) makes a major contribution to the h_{xy} values. The other possible contributions involved in effect (C) either remain constant (which is not very plausible because of the different properties of the non-electrolyte Y) or, more probably, they also change in proportion to the C_p of interaction of the non-electrolyte with water. As is known, the interaction term C_p(int) may comprise not only non-polar interactions (e.g. solute–solvent dispersion forces) and polar interactions (hydrogen bonding, dipolar and higher moment interactions) but also changes in solvent–solvent interactions (structural effects) [29]. Thus, effect (C) may contain a contribution from, e.g., the reorientation of water molecules in the hydration cosphere of the non-electrolyte Y particles under the influence of an approaching urea molecule. The differences in the "pure

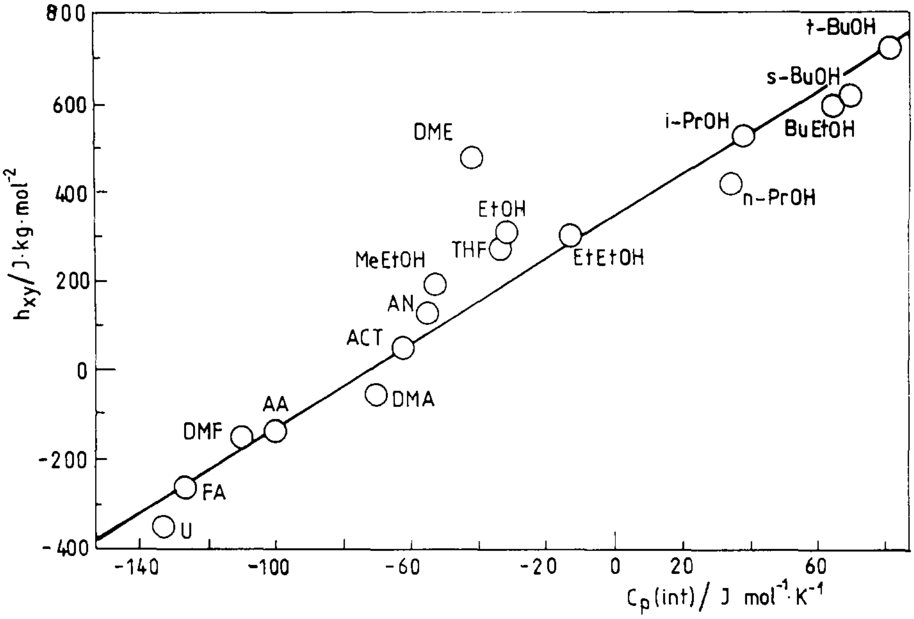

Fig. 4. Enthalpic pair interaction coefficients h_{xy} for urea–non-electrolyte pairs in water as a function of C_p(int) of the non-electrolyte.

effect" of the direct interaction of urea with the cosolute should be then relatively small not to exceed the variation in the structural–hydration effects. In some cases, this direct interaction can be more significant [30], and then deviations of the h_{xy} values from the linear relationship are observed (e.g. DME). The presented correlation enables us to accept a conclusion presented by Abate et al. [15] concerning interactions between urea and saccharides in water as a general one. According to these authors, the behaviour of the different non-electrolytes when they interact with urea molecules in water, as illustrated by the h_{xy} coefficients, is not governed by two mechanisms, one valid for the predominantly hydrophobic and the other one for hydrophilic compounds, but by only one predominant effect, i.e. a different stability of the hydration cospheres towards the action of urea. This conclusion agrees also with the observations on urea–amide systems presented by Cheek and Lilley [10].

All the correlations presented above are similar to those observed earlier for NaCl (or NaI) – non-electrolyte pairs in water [25, 31, 32]. Hence, from the viewpoint of the enthalpic pair interaction coefficients, the differences between urea–non-electrolyte and electrolyte–non-electrolyte systems are predominantly quantitative. There is probably some similarity in the hydration of urea and ionic solutes, and also in the interaction of urea and electrolytes with organic molecules in dilute aqueous solutions. This similarity suggest that the ability of the urea molecule to form hydrogen bonds with the non-electrolyte molecule does not influence decisively the behaviour of the analysed urea–non-electrolyte systems in water as illustrated by the h_{xy} coefficients.

The above conclusion is also confirmed by the observation that h_{xy} values for pairs that cannot be H-bonded (such as the urea–acetonitrile pair) correlate well with those for other urea–non-electrolyte pairs.

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