Enthalpic Interaction Coefficients of Several L-α-Amino Acids in Aqueous Sodium Chloride Solutions at 298.15 K

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The enthalpies of solution of L-α-isoleucine, L-α-cysteine, L-α-aspartic acid, and L-α-glutamic acid have been measured in aqueous sodium chloride solutions at 298.15 K. From the obtained experimental results the standard dissolution enthalpies of amino acids in aqueous NaCl solutions have been determined. These data were used to calculate of the heterogeneous enthalpic pair interaction coefficients based on McMillan−Mayer's theory. These values were interpreted in the terms of the hydrophobic or hydrophilic effects of the side chains of amino acids on their interactions with dissociated sodium chloride in water.

Introduction

There is pool of free L-α-amino acids in the biological fluids which are essential for proper functioning of organisms. These fluids contain also a specified quantity of ions, especially sodium, potassium, and chloride ions, indispensable for the metabolic processes of living organisms to proceed. The aim of the present investigation is to study in detail interactions between natural amino acids and sodium and chloride ions of biological fluids. In this paper, we have determined the interactions of amino acids zwitterions and ions of sodium chloride taking place in water. Therefore, we estimated the enthalpies of solution of several L-α-amino acids in aqueous solutions of sodium chloride. The obtained results were used to calculate the heterogeneous enthalpic pair interaction coefficients according to McMillan−Mayer's theory,[1] modified by Friedman and Krishnan[2] and Franks et al.[3] These parameters describe the global effects of interactions between two heterogeneous molecules or ions in aqueous solutions.

Experimental Section

Materials. L-α-Isoleucine (Ile), L-α-cysteine (Cys), L-α-aspartic acid (Asp), and L-α-glutamic acid (Glu) (all Fluka > 99 %) were crystallized from ethanol solutions and dried under reduced pressure at 333 K for 72 h. NaCl (Fluka > 99.5 %) was dried under reduced pressure at 373 K. The water used in the experiments was deionized and distilled twice.

Calorimetric Measurements. The enthalpies of solution of amino acids were measured in water and in aqueous solutions of sodium chloride using an "isoperibol" calorimeter.[4] The temperature stability of the thermostat was better than 0.002 K. The uncertainties in the measured enthalpies did not exceed ± 0.5 % of the measured value. The examined aqueous solutions containing from (0 to 3.00) mol of NaCl (E) in 1 kg of water and the aqueous solutions of L-α-amino acids (A) (0.001 to 0.005) mol(A)·kg^{-1}(solvent) were prepared by mass with an accuracy of ± 0.00002 g using a Mettler AE240 balance. The standard enthalpies of solution of L-α-amino acids in aqueous solutions of sodium chloride were determined by the linear extrapolation to zero concentration of the results obtained for seven to eight measured enthalpies within the investigated range of the amino acid concentration.

Table 1. Standard Enthalpies of Solution of L-α-Amino Acids in the Mixtures of Sodium Chloride (E) with Water (W) at 298.15 K

m	$\Delta_{sol}H^0_m(W + E)$ (kJ·mol^{-1})			
mol(E)·kg^{-1}(W)	Ile	Cys	Asp	Glu
0	3.06 ± 0.01[a]	11.15 ± 0.03[a]	25.82[b]	27.85[b]
0.5	3.38 ± 0.04	10.81 ± 0.05	24.64 ± 0.12	26.76 ± 0.13
1.0	3.64 ± 0.05	10.55 ± 0.04	23.69 ± 0.12	25.97 ± 0.14
1.5	3.74 ± 0.06	10.26 ± 0.05	22.82 ± 0.11	25.47 ± 0.13
2.0	3.88 ± 0.05	10.04 ± 0.04	22.32 ± 0.11	25.04 ± 0.12
2.5	3.96 ± 0.05	9.82 ± 0.05	21.72 ± 0.11	24.60 ± 0.11
3.0	3.98 ± 0.05	9.62 ± 0.04	21.32 ± 0.11	24.41 ± 0.12

[a] Ref 5. [b] Ref 6.

Results and Discussion

The standard enthalpies of solution of the L-α-amino acids (A) in water (W) $\Delta_{sol}H^0_m(W)^{5,6}$ and in aqueous solutions of sodium chloride (E) $\Delta_{sol}H^0_m(W + E)$ are presented in Table 1. These values we used to calculate the enthalpic heterogeneous pair interaction coefficients between L-α-amino acids zwitterions and dissociated sodium chloride in water, by the equation proposed by Desnoyers et al.:[7]

$$\Delta_{sol}H^0_m(W + E) - \Delta_{sol}H^0_m(W) = 2h_{AE}m_E + 3h_{AEE}m_E^{\,2} + \ldots \qquad (1)$$

where h_{AE} is the heterogeneous enthalpic pair interaction coefficient, h_{AEE} is the enthalpic triplet interaction coefficient, and m_E denotes the molal concentration of electrolyte [mol(NaCl)·kg^{-1}(water)]. The enthalpic pair and triplet interaction coefficients determined in this work are listed in Table 2.

The values of h_{AE} are the sum of the effect of interaction between the L-α-amino acid zwitterion with the cation (M^+) and the anion (X^-) of NaCl in aqueous solutions:

$$h_{AE} = h(A - M^+X^-) = h_{AM^+} + h_{AX^-} \qquad (2)$$

The interpretation of the triplet interaction coefficient is obscured by the fact that they also contain some contributions

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Table 2. Values of the Heterogeneous Pair and Triplet Interaction Coefficients for L-α-Amino Acids (A) with Sodium Chloride (E) in Water at 298.15 K

amino acids	h_{AE} $J \cdot kg \cdot mol^{-2}$	h_{AEE} $J \cdot kg^2 \cdot mol^{-3}$	CH_2
Gly[a]	−480.0 ± 6.3	33.10 ± 5.41	0.5
Ala[b]	−89.0 ± 3.7	15.6 ± 1.0	1.5
Aba[b]	162.8 ± 7.6	−20.7 ± 2.0	2.5
Val[b]	257.7 ± 10.3	−31.2 ± 2.7	3.5
Leu[b]	295.2 ± 11.9	−34.3 ± 3.10	4.5
Ser[b]	−535.8 ± 19.9	46.9 ± 5.2	
Thr[b]	−167.3 ± 7.8	19.9 ± 3.1	
Ile	301.5 ± 37.5	−34.6 ± 0.4	
Cys	−332 ± 24	17.4 ± 1.2	
Asp	−1215 ± 45	105 ± 9	
Glu	−1057 ± 61	109 ± 13	

[a] Ref 8. [b] Ref 9.

Table 3. Homogeneous Enthalpic Pair Interaction Coefficients for Amino Acids in Water (h_{AA}),[11,12] Heterogeneous Enthalpic Pair Interaction Coefficients for Amino Acids with Urea in Water (h_{AU}),[6] and the Free Energy Transfer of Amino Acids (ΔG_R)[13]

amino acids	h_{AA} $J \cdot kg \cdot mol^{-2}$	h_{AU} $J \cdot kg \cdot mol^{-3}$	ΔG_R $kJ \cdot mol^{-1}$
Gly	−424	−390.2	0.00
Ala	206	−238.2	0.67
Val	871	−116	1.50
Leu	1243	−98	1.90
Ile	1319	−95	1.90
Ser	−709	−511	0.01
Thr	−99	−350	0.52
Cys	−130	−358	0.38
Asp		−831	−1.2
Glu	−2165	−820.8	−0.76
Aba	514	−185	

from the pairwise interaction terms, and they are not discussed in this paper.

The values of the enthalpic heterogenic pair interaction coefficients, h_{AE}, describe the total energetic interactions between the hydrated zwitterions of the amino acid and the hydrated pair of the cation and the anion of sodium chloride including the contribution of the solvent molecules surrounding the interacting solute molecules.

The mentioned effect is a sum of:

(a) An exothermic effect of the interactions between the zwitterion "head" of amino acid ($-CHNH_3^+COO^-$) and its polar side groups ($-SH$ group in L-α-cysteine or $-COO^-$ in aspartic acid or glutamic acid) with the dissociated electrolyte (as the sum of contributions of the cation and the anion).

(b) Endothermic effects of partial dehydrations of the hydration sheaths of ionic or polar groups of amino acids and ions (Na^+, Cl^-). The latter effect for amino acids with alkyl side chains is superimposed by an additional effect of hydrophobic hydration. The process of hydration causes the reinforcement of the hydrogen bonds between the water molecules surrounding these alkyl groups. This effect of intensified interactions between water molecules surrounding the nonpolar amino acid groups is transferred to water molecules hydrating the zwitterion's head ($- CHNH_3^+COO^-$), and it reinforces the interaction between the water molecules and the amino acid polar head. Consequently, the effect of partial dehydration of the reinforced hydration layers of the zwitterions of the amino acid becomes more endothermic, and the total effect of investigated interaction between L-α-amino acids and ions (Na^+, Cl^-) becomes more endothermic.

The obtained values of enthalpic heterogeneous pair interaction coefficients (h_{AE}) for the amino acids with alkyl side chains[9] increase according to the number of carbon atoms in the side substituent in the following sequence: Gly < Ala < Aba < Val < Leu ≤ Ile (Table 2). Probably the phenomena of hydrophobic hydration that reinforce the interactions between water molecules surrounding the more remote alkyl groups are transferred to a lesser extent onto water molecules that hydrate the zwitterion's "head" of the amino acid.

Thus, the endothermic effect of partial dehydration of the solvation sheath in the polar portion of amino acid does not increase proportionally to the number of carbon atoms in the side chain, similarly to in aqueous solutions of amino acids and the urea molecule.[5]

The replacement of the hydrogen atom in the side chain of L-α-alanine[9] by a polar thiol group, $-SH$, brings about a decrease in the enthalpic pair interaction coefficient of dissociated electrolyte and zwitterions of L-α-cysteine ($h_{Ala-NaCl} > h_{Cys-NaCl}$; see Table 2). Analyzing the values of enthalpic pair interaction coefficients of dissociated sodium chloride and zwitterions of L-α-alanine,[9] L-α-cysteine, and L-α-seryne,[9] one can observe a decrease in the value of enthalpic coefficients h_{AE} with the substitution of the alanine side chain with polar groups such as $-SH$ and $-OH$ (see Table 2). The values of enthalpic heterogeneous pair interaction coefficients of alanine and its derivatives change in the following sequence: $h_{(Ala-NaCl)} > h_{(Cys-NaCl)} > h_{(Ser-NaCl)}$. The replacement of $-SH$ with $-OH$ brings about an increase in direct exothermic interactions between the deionized sodium chloride and the amino acid zwitterions, which seems to be caused by the greater ability of the $-OH$ group of serine to form donor−acceptor bonds in comparison with the $-SH$ group of cysteine.[10]

An examination of the values of the enthalpic pair interaction coefficient of dissociated sodium chloride and zwitterions of L-α-aspartic acid with an acidic substituent indicates a great exothermic contribution to the summary effects of h_{AE} because of the interaction of the carboxyl group in the side chain of the amino acid (Asp) with the dissociated electrolyte (see Table 2). Considering the values of enthalpic coefficients (h_{AE}) of L-α-aspartic acid and L-α-glutamic acid, one observes a hydrophobic influence of the nonpolar group CH_2 that causes the attenuation of the summary exothermic effect $h_{(Glu-NaCl)} > h_{(Asp-NaCl)}$ (Table 2).

The results of the enthalpic pair interaction coefficients between L-α-amino acid zwitterions and dissociated sodium

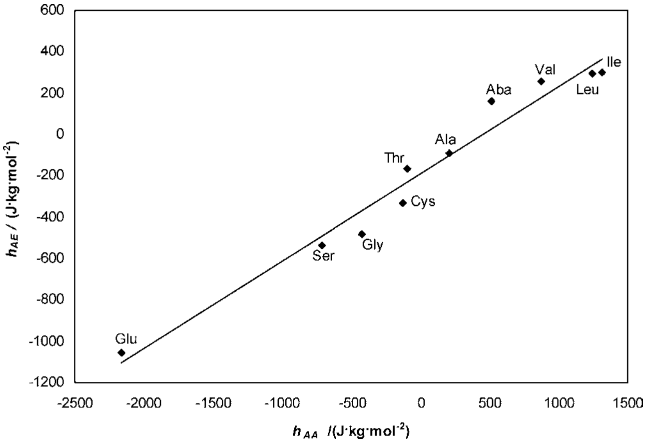

Figure 1. Relationship between the enthalpic homogeneous pair interaction coefficients h_{AA} of amino acid zwitterions in water and the enthalpic pair interaction coefficients h_{AE} of amino acid zwitterions−sodium chloride in water.

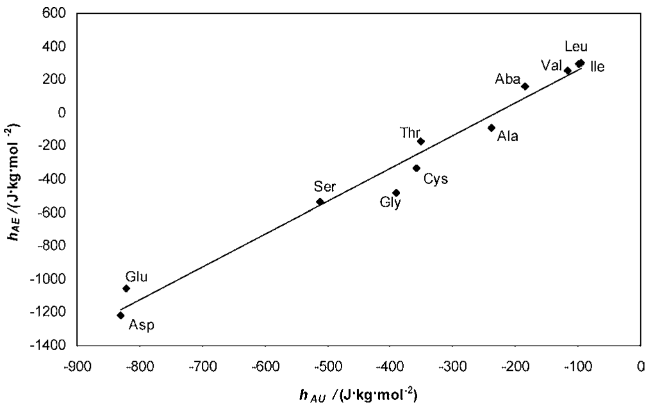

Figure 2. Relationship between the enthalpic pair interaction coefficients h_{AU} of amino acid zwitterions−urea molecule in water and the enthalpic pair interaction coefficients h_{AE} of amino acid zwitterions−sodium chloride in water.

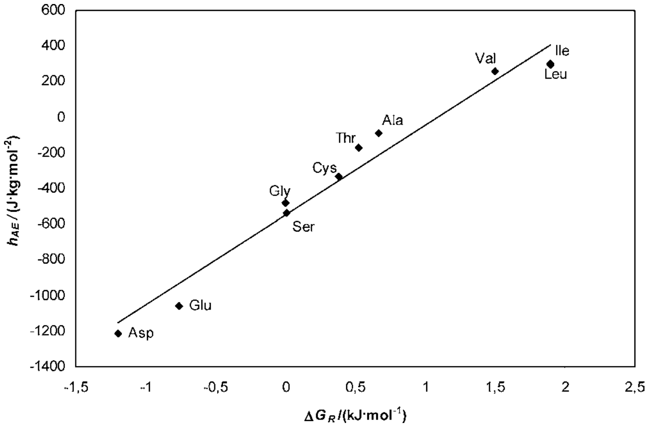

Figure 3. Relationship between the hydrophobicity parameters of amino acids ΔG_R and the enthalpic heterogeneous pair interaction coefficients h_{AE} of the amino acid zwitterions−sodium chloride in water.

chloride in water, h_{AE}, were compared with the values of the enthalpic homogeneous pair interaction coefficients (Table 3) between L-α-amino acid zwitterions in water, h_{AA}[11,12] (Figure 1). Figure 1 shows the linear relation for which $R^2 = 0.9666$. Similarly, the obtained results of enthalpic coefficients h_{AE} were confronted with the enthalpic pair interaction coefficients h_{AU}[6] (Table 3) between urea molecules and zwitterions of L-α-amino acids in aqueous solutions (Figure 2). The above relationships are described by the equation of straight line, for which $R^2 = 0.9765$. These linear relations indicate similar contributions of the functional groups of the L-α-amino acid side chain to the summary effects described by the enthalpic pairs interaction coefficients h_{AA}, h_{AU}, and h_{AE}.

The values of the enthalpic pairs coefficients h_{AE} were also compared with lipophilicity scale of amino acids calculated by Eisenberg and McLachlan.[13] The obtained graph (Figure 3) displays the linear dependence ($R^2 = 0.9687$) between the lipophilicity parameters ΔG_R and the enthalpic pair interaction coefficients of amino acids and dissociated sodium chloride h_{AE}.

Conclusions

The above dependencies indicate that heterogeneous enthalpic pair interaction coefficients between zwitterions of amino acids and dissociated sodium chloride, examined on the basis of calorimetric measurement, describe quite well the hydrophobic−hydrophilic properties of L-α-amino acids.

Literature Cited

(1) McMillan, W. G.; Mayer, J. E. The statistical thermodynamics of multicomponent systems. *J. Chem. Phys.* **1945**, *13*, 276–305.
(2) Friedman, H. L.; Krishnan, C. V. Studies of hydrophobic bonding in aqueous alcohols: enthalpy measurements and model calculations. *J. Solution Chem.* **1976**, *2*, 119–140.
(3) Franks, F.; Padley, M.; Ried, D. S. Solute interactions in dilute aqueous solutions. *J. Chem. Soc., Faraday Trans. 1* **1976**, *72*, 359–367.
(4) Waliszewski, D.; Stepniak, I.; Piekarski, H.; Lewandowski, A. Heat capacities of liquids and their heats of solution in molecular liquids. *Thermochim. Acta* **2005**, *433*, 149–152.
(5) Palecz, B. The enthalpies of interactions of some L-α-amino acids with urea molecule in aqueous solutions at 298.15 K. *Amino Acids* **2004**, *27*, 299–303.
(6) Palecz, B. Enthalpic pair interaction coefficient between zwitterions of L-α-amino acids and urea molecule as a hydrophobicity parameter of amino acid side chains. *J. Am. Chem. Soc.* **2005**, *127*, 17768–17771.
(7) Desnoyers, J. E.; Perron, G.; Avedikian, L.; Morel, J.-P. Enthalpies of the urea-*tert*-butanol-water system at 25 °C. *J. Solution Chem.* **1976**, *5*, 631–644.
(8) Palecz, B. Enthalpies of solution of glycine in aqueous electrolyte solutions at 298.15 K. *Thermochim. Acta* **1991**, *180*, 199–202.
(9) Palecz, B. Thermochemical properties of L-α-amino acids in electrolyte-water mixtures. *Fluid Phase Equilib.* **2000**, *167*, 253–261.
(10) Pillai, L.; Boss, R. D.; Greenberg, M. S. On the role of solvent in complexation equlibria. II. The acid-base chemistry of some sulfhydryl and ammonium-containing amino acids in water-acetonitrile mixed solvents. *J. Solution Chem.* **1979**, *8*, 635–646.
(11) Palecz, B.; Piekarski, H.; Romanowski, S. Studies on homogeneous interactions between zwitterions of several L-α-amino acids in water at a temperature 298.15 K. *J. Mol. Liq.* **2000**, *84*, 279–288.
(12) Palecz, B. Enthalpic homogeneous pair interaction coefficients of L-α-amino acids as a hydrophobicity parameter of amino acid side chains. *J. Am. Chem. Soc.* **2002**, *124*, 6003–6008.
(13) Eisenberg, D.; McLachlan, A. D. Solvation energy in protein folding and binding. *Nature* **1986**, *319*, 199–203.

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