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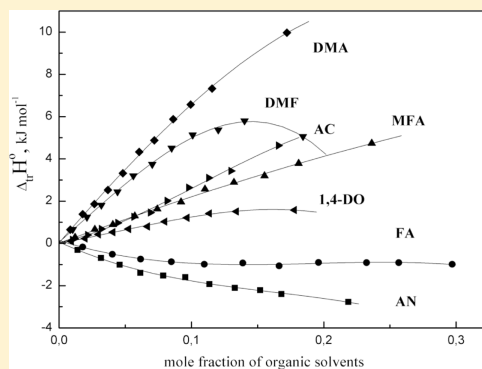
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Enthalpies of β -Alanine Dissolution in Some Water + Organic Mixtures at 298.15 K

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ABSTRACT: The enthalpies of solution ($\Delta_{\text{sol}}H^m$) of β -alanine in aqueous solutions of acetonitrile (AN), 1,4-dioxane (1,4-DO), acetone (AC), formamide (FA), *N*-methylformamide (MFA), *N,N*-dimethylformamide (DMFA), *N,N*-dimethylacetamide (DMA), and dimethyl sulfoxide (DMSO) have been determined by calorimetric method as a function of organic solvent concentration at 298.15 K. Enthalpies of transfer ($\Delta_{\text{tr}}H^\circ$) of β -alanine from water to aqueous organic mixtures as well as the enthalpy coefficients of pairwise interaction (h_{xy}) were calculated from these data. The interrelation between enthalpy characteristics of β -alanine dissolution (transfer) and the composition of water–organic solvent binary mixtures has been ascertained. By means of a modified Kamlet–Taft equation the contributions of different physicochemical properties of organic cosolvents to the energy of β -alanine–cosolvent intermolecular interactions have been estimated quantitatively.



INTRODUCTION

The study of the nature of intermolecular interactions in the solutions of biomolecules is an important task since the special features of the solvation (hydration) of simple structural elements in many respects determine solvation and biological activity of more complex biosystems. The greater part of scientific research is devoted to the study of the properties of amino acids in aqueous solutions and in solutions of simple salts (KCl, NaCl, and others).^{1–5} Considerably less attention is given to a study of the processes of interaction of amino acids and peptide in the water–organic solvents. Although many organic solvents under study are not found in living organisms (or they are present in very small quantities), they find wide application in medicine, pharmacology, various industries, and cosmetics. Dimethyl sulfoxide possesses the ability to penetrate through the biological membranes and the skin barriers. It also strengthens penetration of a number of medicinal substances through the skin. Acetone is the natural metabolite produced by the human organism. Acetonitrile, formamide, and dioxane appear to be the raw materials for the pharmaceutical industry. Alcohols and urea are widely used in the processes of protein denaturation (amino acids and peptides are protein components). Amides can serve as model substances with studies of the properties of peptides in aqueous solutions since their molecules contain the functional (peptide) CONH-group, the latter being a fragment of protein systems too. Therefore, the analysis of different physicochemical properties of the water–organic solutions of amino acids and peptides represents a significant scientific and practical interest. In attempts to explain the effects of interparticle interactions in the solutions of amino acid + water + organic solvent, there arise some questions that require a deeper insight into the problem. To detect different mechanisms of interactions for these types of

solutes, we carry on the calorimetric studies that enable the dissolution enthalpy of amino acids in different water–organic mixtures to be determined. So far, a large number of studies have been focused mainly on the thermochemistry of α -amino acids dissolution in aqueous and mixed solvents. For β -amino acids, the situation is considerably worse.^{6–8} The purpose of this work is to estimate the influence of the composition of water–organic mixtures and physicochemical properties of organic cosolvents on the thermodynamic characteristics of the dissolution of β -alanine and to assess basic differences and similarities of the thermodynamic characteristics of the dissolution of β - and α -isomers of alanine in the aqueous solutions of organic solvents. As the continuation of previous thermochemical research of the processes of β -alanine dissolving in water solutions of alcohols,⁹ we represent in this work for the first time the investigation of the processes of β -alanine dissolution in aqueous solutions of acetonitrile (AN), 1,4-dioxane (1,4-DO), acetone (AC), formamide (FA), *N*-methylformamide (MFA), *N,N*-dimethylformamide (DMFA), *N,N*-dimethylacetamide (DMA), and dimethyl sulfoxide (DMSO) at 298.15 K and mole fraction of organic solvent: $x_2 = 0$ to 0.35. The experimental data on the enthalpies of solution $\Delta_{\text{sol}}H^m$ have been used to calculate the standard values of dissolution enthalpies, $\Delta_{\text{sol}}H^\circ$ and those of transfer $\Delta_{\text{tr}}H^\circ$, of β -alanine from water to binary solvent, and also enthalpic coefficients of pairwise interactions, h_{xy} , of β -alanine with molecules of organic solvents. To quantitatively assess the energy contributions caused by polarity, polarizability, basicity, and acidity of organic solvent to the coefficients of β -alanine–

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Table 1. List of Chemicals, Their Suppliers, and Purity Values

| chemical | formula | M^a | CAS No. ^b | supplier | purity ^c |
|-------------------------------|---|-------|----------------------|---------------------|---------------------|
| β -alanine | C ₃ H ₇ NO ₂ | 89.09 | 107-95-9 | Reanal Co. | > 0.980 |
| acetonitrile | C ₂ H ₃ N | 41.05 | 75-05-8 | Sigma-Aldrich Fluka | ≥ 0.998 (anhydrous) |
| 1,4-dioxane | C ₄ H ₈ O ₂ | 88.11 | 123-91-1 | Fluka | ≥ 0.998 (anhydrous) |
| acetone | C ₃ H ₆ O | 58.08 | 67-64-1 | Fluka | ≥ 0.998 (GC) |
| formamide | CH ₃ NO | 45.04 | 75-12-7 | Aldrich | ≥ 0.998 |
| <i>N</i> -methylformamide | C ₂ H ₆ NO | 59.07 | 123-39-7 | Sigma-Aldrich | ≥ 0.990 |
| <i>N,N</i> -dimethylformamide | C ₃ H ₇ NO | 73.09 | 68-12-2 | Sigma-Aldrich Sigma | ≥ 0.990 (anhydrous) |
| <i>N,N</i> -dimethylacetamide | C ₄ H ₉ NO | 87.12 | 127-19-5 | | ≥ 0.998 (anhydrous) |
| dimethyl sulfoxide | C ₂ H ₆ SO | 78.13 | 67-68-5 | | ≥ 0.995 (GC) |

^aMolecular mass, (g·mol⁻¹). ^bChemical Abstract Service registry number. ^cMass fraction

Table 2. Standard Enthalpies of Dissolution, $\Delta_{\text{sol}}H^\circ$, of β -Alanine in Aqueous Solution of Formamide (FA), *N*-Methylformamide (MFA), *N,N*-Dimethylformamide (DMFA), *N,N*-Dimethylacetamide (DMA), Acetonitrile (AN), 1,4-Dioxane (1,4-DO), Acetone (AC), and Dimethyl Sulfoxide (DMSO) at 298.15 K.

| m_2^a | FA | m_2^a | MFA | m_2^a | DMFA | m_2^a | DMA |
|---------|------|---------|--------|---------|-------|---------|-------|
| 1.005 | 9.43 | 0.677 | 9.84 | 0.579 | 10.21 | 0.474 | 10.20 |
| 2.326 | 9.03 | 1.539 | 10.22 | 1.192 | 10.79 | 1.009 | 10.93 |
| 3.644 | 8.81 | 2.352 | 10.44 | 1.833 | 11.36 | 1.523 | 11.41 |
| 5.146 | 8.68 | 3.365 | 10.85 | 2.560 | 11.99 | 2.129 | 12.08 |
| 6.845 | 8.63 | 4.450 | 11.18 | 3.303 | 12.75 | 2.810 | 12.87 |
| 8.944 | 8.62 | 5.632 | 11.51 | 4.202 | 13.29 | 3.581 | 13.88 |
| 11.067 | 8.62 | 6.875 | 12.12 | 5.158 | 14.06 | 4.303 | 14.43 |
| 13.540 | 8.62 | 8.451 | 12.44 | 6.233 | 14.68 | 5.237 | 15.43 |
| 16.794 | 8.63 | 10.200 | 12.75 | 7.590 | 14.92 | 6.135 | 16.12 |
| 19.168 | 8.64 | 12.267 | 13.34 | 9.044 | 15.35 | 7.256 | 16.88 |
| 23.450 | 8.65 | 17.167 | 14.29 | 12.536 | 14.61 | 11.547 | 19.52 |
| m_2^a | AN | m_2^a | 1,4-DO | m_2^a | AC | m_2^a | DMSO |
| 0.787 | 9.24 | 0.518 | 9.65 | 0.569 | 9.72 | 0.591 | 9.76 |
| 1.810 | 8.86 | 1.111 | 9.78 | 1.219 | 9.95 | 1.255 | 10.17 |
| 2.661 | 8.54 | 1.698 | 9.98 | 1.828 | 10.23 | 2.034 | 10.64 |
| 3.634 | 8.27 | 2.352 | 10.08 | 2.572 | 10.52 | 2.854 | 11.02 |
| 4.737 | 8.03 | 3.074 | 10.23 | 3.324 | 10.81 | 3.812 | 11.67 |
| 5.856 | 7.81 | 3.970 | 10.35 | 4.113 | 11.01 | 4.830 | 12.07 |
| 7.112 | 7.62 | 4.817 | 10.58 | 4.927 | 11.56 | 6.023 | 12.66 |
| 8.499 | 7.45 | 5.938 | 10.76 | 6.028 | 12.19 | 7.367 | 13.56 |
| 9.941 | 7.34 | 7.109 | 10.97 | 7.072 | 12.65 | 8.888 | 14.05 |
| 11.210 | 7.15 | 8.579 | 11.06 | 8.283 | 12.98 | 10.764 | 15.38 |
| 15.519 | 6.98 | 11.995 | 11.13 | 11.023 | 14.18 | 15.496 | 16.66 |

^aThe molal concentration of organic solvent in water, m_2 , mol·kg⁻¹. Units: $\Delta_{\text{sol}}H^\circ$, kJ·mol⁻¹ at infinite dilution. Standard uncertainties (u) are $u(m_2) = 0.001$ and $u(\Delta_{\text{sol}}H^\circ) = 0.02$.

cosolvent pairwise interactions, we used a modified Kamlet–Taft correlation equation.¹⁰ The standard values of $\Delta_{\text{tr}}H^\circ$ and the values of h_{xy} of β -alanine were used for comparative analysis with similar characteristics of D,L- α -alanine in the studied mixtures.^{11,12}

EXPERIMENTAL SECTION

Materials. Before the experiments chromatographically homogeneous β -alanine (Reanal Co., Budapest, Hungary; assay, ≥ 98%) was recrystallized twice from the (H₂O + EtOH) mixture, dried in a vacuum chamber at 333 K for 48 h, and then kept over P₂O₅ in a desiccator. The molal concentration (m) of β -alanine varied within the range from 5·10⁻³ mol·kg⁻¹ to 1.5·10⁻² mol·kg⁻¹ of a mixed solvent. The data characterizing the solvents under study are listed in Table 1. The water content of the organic cosolvent determined by titration by Karl Fisher's method¹³ did not exceed 0.04 % of mass. The water was purified by distillation (a specific

conductivity of ca. 1.0·10⁻⁵ S·m⁻¹). All weighings were done on an analytic balance VLR-200 ("Gosmetr", St. Petersburg, Russia) within the accuracy of ± 5·10⁻⁵ g.

Calorimetric Measurement. Calorimetric measurements of the enthalpies of solution $\Delta_{\text{sol}}H^m$ for β -alanine have been performed in an isoperibol ampule-type hermetic calorimeter fitted with a 60 cm³ reaction vessel and electrical calibration at $T = 298.15 \pm 0.005$ K. A measuring vessel is equipped with a heater for calibration, an electrical stirrer, a thermistor, a holder of glass ampule with a sample of β -alanine, and a device for crushing it. To measure the values of $\Delta_{\text{sol}}H^m$, a comparable method was used: after each experiment the system was calibrated with an electric current. Thermometric and thermal sensitivities of the apparatus were up to 10⁻⁵ K and 2·10⁻³ J·mm⁻¹ of a scale of the recording device. A scheme of the experimental setup and description of the experimental procedure have been described earlier.¹⁴ The relative random error of measurements did not exceed 0.5 %. The calorimeter

was tested by measuring (10 experiments) the enthalpy of a solution of potassium chloride (KCl) in water at 298.15 K according to refs 15–18. Our values of $\Delta_{\text{sol}}H^m$ ($m = 0.111 \text{ mol} \cdot \text{kg}^{-1} (\text{H}_2\text{O})$) = $17.60 \pm 0.04 \text{ kJ} \cdot \text{mol}^{-1}$ and $\Delta_{\text{sol}}H^\circ = 17.23 \pm 0.07 \text{ kJ} \cdot \text{mol}^{-1}$ at infinite dilution) agree with the recommended literature values ($17.56 \pm 0.02^{16} \text{ kJ} \cdot \text{mol}^{-1}$ / $17.58 \pm 0.02^{17} \text{ kJ} \cdot \text{mol}^{-1}$ and $17.22 \pm 0.04^{18} \text{ kJ} \cdot \text{mol}^{-1}$, respectively).

RESULTS AND DISCUSSION

The standard enthalpies of β -alanine dissolution ($\Delta_{\text{sol}}H^\circ$) were defined as an average value of five measurements of $\Delta_{\text{sol}}H^m$ for each composition of a water–organic solvent (the dependence of $\Delta_{\text{sol}}H^m$ vs m) was not observed in the investigated range of β -alanine concentrations, $m = 5 \cdot 10^{-3} \text{ mol} \cdot \text{kg}^{-1}$ to $1.5 \cdot 10^{-2} \text{ mol} \cdot \text{kg}^{-1}$ of a mixed solvent). The values of $\Delta_{\text{sol}}H^\circ$ obtained for β -alanine in the investigated systems and their standard deviations are given in Table 2.

The transfer enthalpy $\Delta_{\text{tr}}H^\circ$ is calculated from

$$\Delta_{\text{tr}}H^\circ = \Delta_{\text{sol}}H^\circ(w + y) - \Delta_{\text{sol}}H^\circ(w) \quad (1)$$

where $\Delta_{\text{sol}}H^\circ(w + y)$ is the enthalpy of β -alanine dissolution in each aqueous water–organic solvent and $\Delta_{\text{sol}}H^\circ(w)$, the enthalpy of β -alanine solution in pure water (enthalpy of β -alanine dissolution in pure H_2O measured by us is $\Delta_{\text{sol}}H^\circ(w) = 9.55 \pm 0.03 \text{ kJ} \cdot \text{mol}^{-1}$ at infinite dilution). The changes in $\Delta_{\text{tr}}H^\circ$ for β -alanine against the mole fraction of organic solvent are shown in Figures 1 and 2.

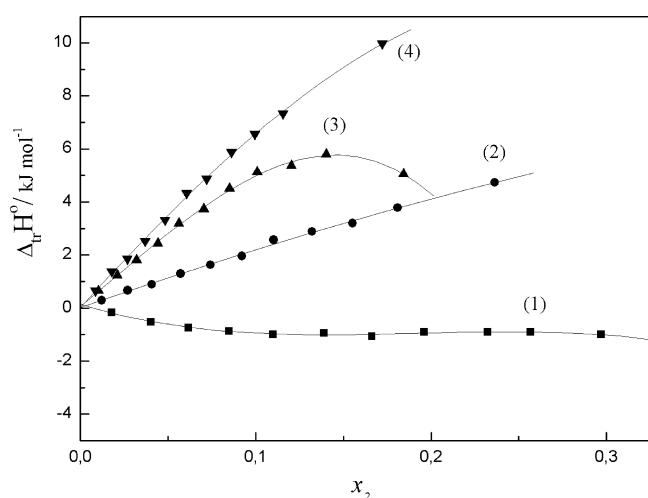


Figure 1. Enthalpies of transfer, $\Delta_{\text{tr}}H^\circ$, of β -alanine from water into ($\text{H}_2\text{O} + \text{FA}$) (1), ($\text{H}_2\text{O} + \text{MFA}$) (2), ($\text{H}_2\text{O} + \text{DMFA}$) (3), and ($\text{H}_2\text{O} + \text{DMA}$) (4) mixed solvents as functions of the amide mole fraction (x_2) at 298.15 K.

From Figures 1 and 2 one can see that a change in enthalpy of the transfer of for β -alanine from the H_2O into the ($\text{H}_2\text{O} + \text{organic solvent}$) mixtures depends both on the structure of organic solvent and on its content in the mixture as well. The values of the β -alanine transfer enthalpies can be negative in sign (in ($\text{H}_2\text{O} + \text{AN}$) and ($\text{H}_2\text{O} + \text{FA}$) mixtures) or positive (in ($\text{H}_2\text{O} + \text{MFA}$), ($\text{H}_2\text{O} + \text{DMFA}$), ($\text{H}_2\text{O} + \text{DMA}$), ($\text{H}_2\text{O} + 1,4\text{-DO}$), ($\text{H}_2\text{O} + \text{AC}$), and ($\text{H}_2\text{O} + \text{DMSO}$) mixtures) in all studied mole fraction ranges of organic cosolvent. The negative values of $\Delta_{\text{tr}}H^\circ$ of β -alanine in ($\text{H}_2\text{O} + \text{FA}$) and ($\text{H}_2\text{O} + \text{AN}$) mixtures are due to the fact that FA and AN form with H_2O molecules the weakest bonds out of all the solvents studied (the

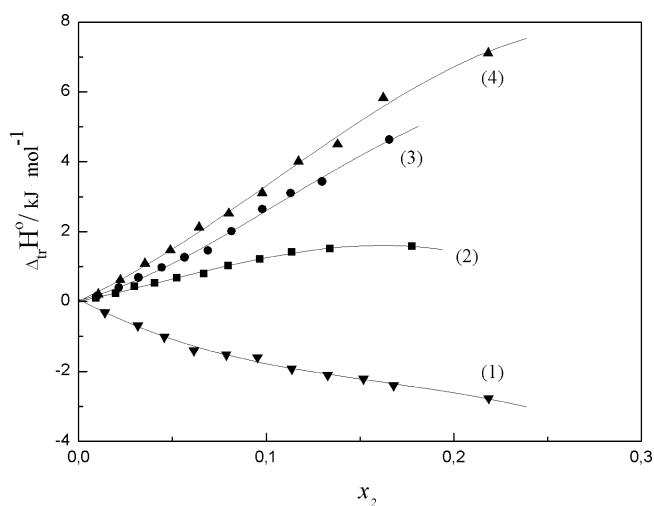


Figure 2. Enthalpies of transfer, $\Delta_{\text{tr}}H^\circ$, of β -alanine from water into ($\text{H}_2\text{O} + \text{AN}$) (1), ($\text{H}_2\text{O} + 1,4\text{-DO}$) (2), ($\text{H}_2\text{O} + \text{AC}$) (3), and ($\text{H}_2\text{O} + \text{DMSO}$) (4) mixed solvents as functions of the mole fraction of organic component (x_2) at 298.15 K.

enthalpies of ($\text{H}_2\text{O} + \text{FA}$) and ($\text{H}_2\text{O} + \text{AN}$) mixing have low positive values).^{19,20} As a consequence, the energy consumption for the dehydration of FA and molecules will be the smallest. The lower exothermic values of the transfer enthalpy of FA relative to AN can be attributed to the additional energy consumption on the destruction of self-associates of FA. In these two mixtures the exothermic enthalpy contributions from direct β -alanine–cosolvent interactions prevail over endothermic enthalpy contributions from dehydration of β -alanine and cosolvent molecules in all studied concentration ranges of FA(AN). In the case of ($\text{H}_2\text{O} + 1,4\text{-DO}$), ($\text{H}_2\text{O} + \text{AC}$), ($\text{H}_2\text{O} + \text{DMSO}$), ($\text{H}_2\text{O} + \text{MFA}$), ($\text{H}_2\text{O} + \text{DMFA}$), and ($\text{H}_2\text{O} + \text{DMA}$) mixtures the values of $\Delta_{\text{tr}}H^\circ$ for β -alanine are endothermic and increase with the increase in the organic solvent concentration. In all studied cosolvent concentration ranges, the dissolved substances are well hydrated and endothermic enthalpy contributions from the dehydration of β -alanine and cosolvent molecules prevail over exothermic contributions from the direct β -alanine–cosolvent interactions. The endothermicity of transfer of β -alanine from water into the ($\text{H}_2\text{O} + 1,4\text{-DO}$), ($\text{H}_2\text{O} + \text{AC}$), ($\text{H}_2\text{O} + \text{DMSO}$), ($\text{H}_2\text{O} + \text{MFA}$), ($\text{H}_2\text{O} + \text{DMFA}$), and ($\text{H}_2\text{O} + \text{DMA}$) mixtures increases in magnitude on going from MFA to DMFA and DMA as well on going from 1,4-DO to AC and DMSO. It is associated with the increase in the hydrophobic and polarity properties of organic solvents in the same sequences. The increase in the concentration of DMFA and 1,4-DO cosolvents to $x_2 \sim 0.15$ in an aqueous solution usually stabilizes the process of the dissolution of β -alanine. Here, the energy consumption on the restructuring of a mixed solvent and placing β -alanine molecules into it, as well as on the dehydration of the molecules of β -alanine and cosolvent, is compensated for by the energy of direct interactions between β -alanine and cosolvent molecules.

The comparison of the $\Delta_{\text{tr}}H^\circ = f(x_2)$ dependences of β -alanine and D,L- α -alanine (Figure 3) in aqueous mixtures with FA, AN, 1,4-DO, AC, and DMSO shows that β -alanine molecules undergo a stronger solvation than those of D,L- α -alanine. It is connected with hydrophobic effect of the CH_3 -group and results in intensification of the hydration of the polar

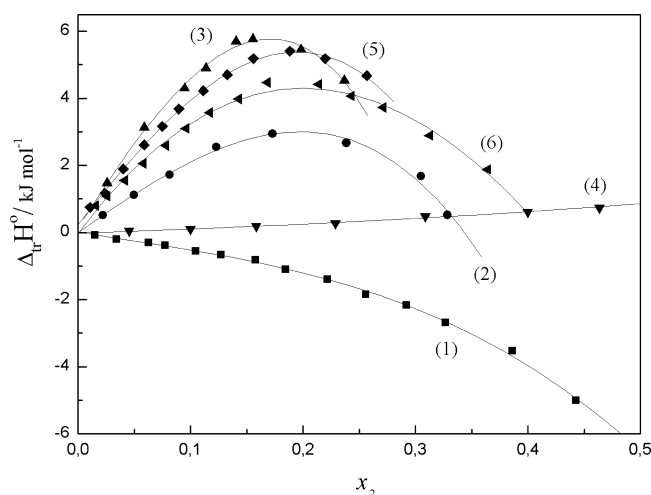


Figure 3. Enthalpies of transfer, $\Delta_{tr}H^\circ$, of D,L- α -alanine from water into the (H₂O + AN) (1), (H₂O + 1,4-DO) (2), (H₂O + AC) (3), (H₂O + FA) (4), (H₂O + DMFA) (5), and (H₂O + DMSO) (6) mixed solvents as functions of the mole fraction of the organic component (x_2) at 298.15 K.¹²

groups in a molecule of D,L- α -alanine. This, in turn, increases consumption of energy on D,L- α -alanine dehydration. It should also be noted that the dependences of $\Delta_{tr}H^\circ = f(x_2)$ of D,L- α -alanine in the aqueous mixtures with 1,4-DO, AC, DMFA, and DMSO have pronounced maximums in the concentration range of the cosolvent: $x_2 = 0.18$ to 0.20 . In the case of β -alanine, an explicit maximum is observed only for the $\Delta_{tr}H^\circ = f(x_2)$ dependence in the (H₂O + DMFA) mixture at $x_2 \sim 0.15$ and the weakly expressed maximums in (H₂O + 1,4-DO) and (H₂O + DMSO) mixtures at $x_2 \sim 0.18$ to 0.22 . This fact signals a stronger impact of the nature of the aqueous organic mixtures on the solvation of D,L- α -alanine as compared to that of β -alanine. The position of maximums (with the small displacement to the side of the larger water content) corresponds practically to the position of maximums on the curve of H₂O mixing with the organic solvent, but with the opposite sign.²¹ The increase in the concentration of the organic solvent in the mixture of more than $x_2 > 0.2$ changes the dependence of $\Delta_{tr}H^\circ = f(x_2)$ of D,L- α -alanine to the opposite in direction, while $\Delta_{tr}H^\circ = f(x_2)$ dependences of β -alanine continue to vary monotonically (with the exception of the (H₂O + DMFA) mixture).

It is known that the interparticle interactions in the tertiary systems (amino acid + H₂O + cosolvent) with a small concentration of cosolvent can be described in terms of McMillan–Mayer theory²² adapted by Kauzmann et al.^{23–25} by enthalpy coefficients of pairwise interactions h_{xy} . To calculate them, we used the data presented in Table 1 and the third-order polynomial equation

$$\Delta_{sol}H^\circ = a_0 + a_1m_2 + a_2m_2^2 + a_3m_2^3 \quad (2)$$

where m_2 is the molal concentration of the organic solvent and a_i are coefficients calculated by a least-squares method. The correlation coefficient, R , and Student criterion value, t_α , were in the range from 0.996 to 0.999 and from 0.036 to 0.096, respectively. The h_{xy} value was calculated from a_1 coefficient related to the coefficient of pairwise interactions as $h_{xy} = a_1/2$.²⁶ The calculated h_{xy} values for all of the systems in question are collected in Table 3.

Table 3. Enthalpic Coefficients of Pairwise Interactions, h_{xy} , between β -Alanine and Formamide (FA), Acetonitrile (AN), 1,4-Dioxane (1,4-DO), Acetone (AC), Dimethyl Sulfoxide (DMSO), *N*-Methylformamide (MFA), *N,N*-Dimethylformamide (DMFA), Ethanol (EtOH), 1-Propanol (1-PrOH), and 2-Propanol (2-PrOH) in Aqueous Solutions at 298.15 K and Parameters of Organic Solvents^{27,28}

| solvent | h_{xy} | $(\delta^2/1000)_1(V_2/100)$ | π^* | α | β |
|------------------|-------------------|------------------------------|---------|----------|---------|
| FA | −228 | 0.912 | 0.97 | 0.71 | 0.55 |
| AN | −127 | 1.203 | 0.75 | 0.19 | 0.31 |
| 1,4-DO | 116 | 1.955 | 0.55 | 0.00 | 0.37 |
| AC | 148 | 1.684 | 0.71 | 0.08 | 0.48 |
| DMSO | 238 | 1.627 | 1.00 | 0.00 | 0.76 |
| MFA | 220 | 1.340 | 0.90 | 0.62 | 0.80 |
| DMFA | 592 | 1.775 | 0.88 | 0.00 | 0.69 |
| EtOH | 800 ⁹ | 1.339 | 0.54 | 0.83 | 0.77 |
| 1-PrOH | 1051 ⁹ | 1.714 | 0.52 | 0.78 | 0.82 |
| 2-PrOH | 1195 ⁹ | 1.756 | 0.48 | 0.76 | 0.95 |
| H ₂ O | | | 1.09 | 1.17 | 0.18 |

Units: h_{xy} , J·kg·mol^{−2}; $(\delta^2/1000)_1(V_2/100)$, J·mol^{−1}. Standard uncertainties ($\pm u$) are $u(\Delta_{sol}H^\circ) = 25$ (FA), 15 (AN), 15 (1,4-DO), 42 (AC), 45 (DMSO), 25 (MFA), 35 (DMFA).

The data obtained earlier for the interactions of β -alanine with EtOH, 1-PrOH, and 2-PrOH⁹ are presented in Table 3 too. The values of h_{xy} are a measure of interactions occurring between the hydrated molecules of β -alanine and hydrated molecules of the organic solvents. The magnitude and the sign of h_{xy} will be determined mainly by the balance between the two processes: an exothermic process of the direct interaction between these molecules and endothermic processes of the partial dehydration of β -alanine and of organic solvent molecules. The negative value of h_{xy} for (H₂O + AN) and (H₂O + FA) mixtures suggests that the interactions between AN (FA) and β -alanine molecules prevail over the effects of their dehydration. On the contrary, a positive sign of h_{xy} values for aqueous solutions of (AC, 1, 4-DO, MFA, DMFA, DMA, and DMSO) shows that the solutes are strongly hydrated by H₂O molecules, while the interaction between hydrated β -alanine and cosolvent molecules is a weak one. The values of h_{xy} show that the endothermicity of interparticle interaction between β -alanine and amides increases in the series FA < MFA < DMFA < DMA. Such a sequence can be associated both with increasing hydrophobicity of amides²⁹ and with increasing energy of intermolecular interactions between components of the mixtures studied.¹⁹

A close-to-linear dependence depicted in Figure 4 shows that there exists an obvious interrelation between h_{xy} of β -alanine and the formamide molecules and the enthalpic coefficients of pairwise interaction between the molecules of H₂O and those of formamides. The intensification of the pairwise interaction between formamide and H₂O molecules in the mixtures leads to the increase in the endothermic contribution to h_{xy} of β -alanine–formamide interactions. The comparison of h_{xy} of β -alanine with the coefficients of pairwise interactions, h_{xy} , D,L-alanine (see Figure 5) allows asserting that the intermolecular interactions of α - and β -isomers of alanine in similar aqueous organic mixtures with a low content of organic solvent are of a comparable character.

Interesting observations can be provided by the comparison of the enthalpic coefficients of pairwise interaction of β -alanine with the functions characterizing polarity/polarizability, acidity,

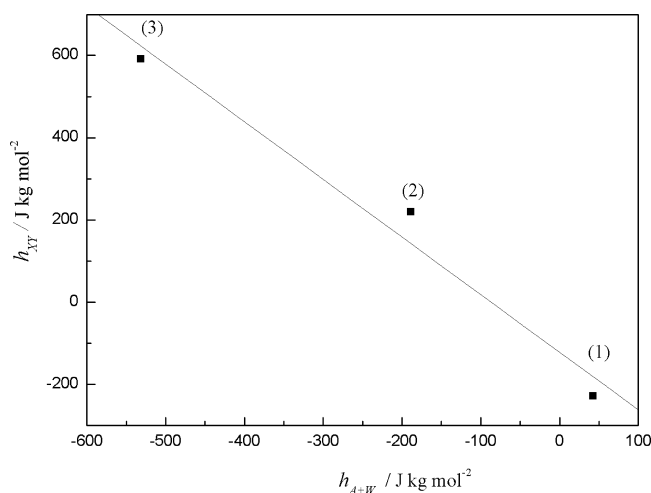


Figure 4. Correlation between the enthalpy coefficients of pairwise interactions, h_{xy} , of β -alanine with formamides and the enthalpy coefficients of pairwise interactions, h_{A+W} , of H_2O with the following: (1) FA, (2) MFA, and (3) DMFA.

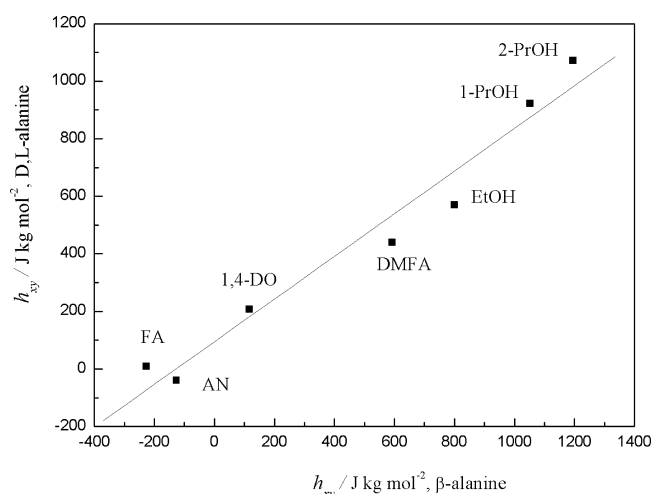


Figure 5. Correlation between the enthalpic coefficients of pairwise interaction, h_{xy} , of β -alanine and h_{xy} of D,L - α -alanine in some (water + organic) mixtures.

and basicity properties of the organic cosolvents used. In the previous works,^{30–33} we have ascertained that contributions to the energy of pairwise interactions can be quantitatively estimated by means of the modified Kamlet–Taft³⁴ equation

$$h_{xy} = A_0 + A_1((\delta^2_1/1000)(V_2/100) + A_2(\pi_1^* \pi_2^*) + A_3(\alpha_1 \beta_2) + A_4(\beta_1 \alpha_2) \quad (3)$$

where $\delta^2/1000$ and $V_2/100$ are the structural contributions of both water and the organic cosolvent to the formation of cavities (these parameters are reduced respectively by factors of 1000 and 100 to simplify the estimation of the relative contributions of various parameters to h_{xy}); δ^2 is the solubility parameter according to the Hildebrandt conception (δ^2 is proportional to the cohesion energy density), and V_2 is the molar volume of the organic solvent, being the tradeoff between its molecular weight and density; π_1^* and π_2^* are the parameters characterizing the dipolarity/polarizability of H_2O and an organic solvent, respectively; α_1 , α_2 and β_1 , β_2 are the parameters corresponding to the solvent acidity and basicity,

respectively. The solvent parameters were taken from the works of refs 27 and 28, and the calculations were performed according to the IUPAC recommendations in the field of correlation analysis in chemistry. As a result of the computation of the system of linear equations, we arrived at

$$h_{xy} = 1016.28 + 2953.31(\delta^2_1/1000)(V_2/100) - 2389.83(\pi_1^* \pi_2^*) - 5258.29(\alpha_1 \beta_2) + 1755.34(\beta_1 \alpha_2), \\ R = 0.964, \quad N = 8, \quad SD = 154.16 \quad (4)$$

As predicted by eq 4, the increases in polarity, polarizability, and basicity of the organic solvent will cause the energy of pairwise interactions of β -alanine–organic solvent to increase, while the increases of molar volume and the acidity of an organic solvent augmentation will weaken pairwise interactions. One can draw similar conclusions when analyzing eq 5 calculated for D,L - α -alanine.

$$h_{xy} = 2442.18 + 8788.24(\delta^2_1/1000)(V_2/100) - 4191.67(\pi_1^* \pi_2^*) - 10618.13(\alpha_1 \beta_2) + 1318.12(\beta_1 \alpha_2), \\ R = 0.967, \quad N = 7, \quad SD = 131.84 \quad (5)$$

So, the enthalpy coefficient of pairwise interaction of β -alanine changes just as the enthalpy coefficient does for pairwise interaction of D,L - α -alanine with a change in similar properties of organic solvents (see Figure 6).

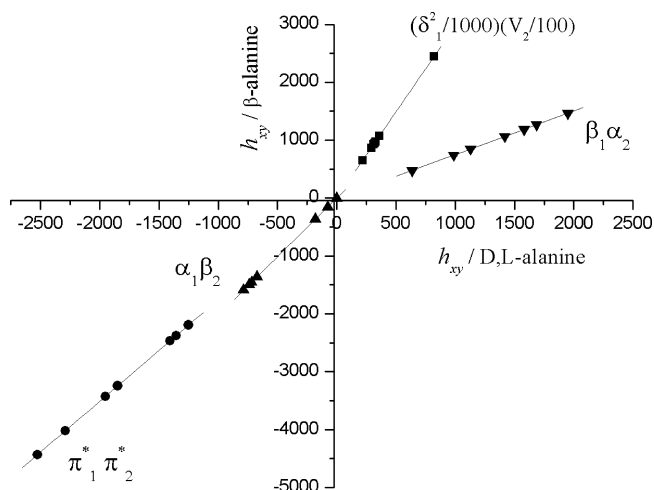


Figure 6. Energy contributions to enthalpic coefficients of pairwise interactions, h_{xy} , of β -alanine and D,L - α -alanine caused by the structural parameters $\{(\delta^2_1/1000)(V_2/100)\}$, dipolarity/polarizability $(\pi_1^* \pi_2^*)$, acidity $(\alpha_1 \alpha_2)$, and basicity $(\beta_1 \beta_2)$ of H_2O and organic cosolvents calculated by eqs 4,5.

Figure 6 illustrates a change in the contributions of different properties of seven organic solvents (FA, AN, 1,4-DO, DMFA, EtOH, 1-PrOH, and 2-PrOH) to the value of the enthalpy coefficient of pairwise interactions of β -alanine and D,L - α -alanine. The values of contributions are obtained by the multiplication of coefficients at variables $\{(\delta^2_1/1000)(V_2/100)\}$, $(\pi_1^* \pi_2^*)$, $(\alpha_1 \beta_2)$, $(\beta_1 \alpha_2)\}$ in eqs 4 and 5 and the values of variables from Table 3. Although the signs of the coefficients at variables in eqs 4 and 5 coincide, similar coefficients differ in size. Their values evidently depend not only on the properties of organic solvent but also on the type of isomerization of alanine molecules as well. The quantitative analysis of the

contributions caused by various physicochemical properties of organic solvents shows that the cohesion energy (molar volume) and the absolute terms (h_{xy})₀ of eqs 4 and 5, which quantitatively characterize the partial dehydration²⁶ of the α - and β -isomers of alanine, are primary contributions to the h_{xy} of α - and β -isomers of alanine. The increase in these parameters weakens the interaction between organic solvents and the molecules of α - and β -isomers of alanine (especially of D,L- α -alanine). At the same time, strengthening of polarity/polarizability and basicity of the molecules of the organic solvent contributes to intermolecular interactions with the molecules of alanine isomers.

CONCLUSION

The analysis of the experimental and calculated data shows that the energy of intermolecular interactions of β -alanine with of the organic solvent molecules in aqueous solution depends not only on the mixture composition and the structure of the organic solvent but also on their physicochemical properties. The comparison of the enthalpic characteristics of dissolution and transfer of α - and β -isomers of alanine in the identical aqueous organic mixtures made it possible to establish that the change in the concentration range of the organic solvents up to $x_2 \sim 0.15$ is similar. Within this range of organic solvent concentration β -alanine undergoes stronger solvation than D,L- α -alanine. A noticeable difference in the dynamics of a change in enthalpy of the transfer of α - and β -alanine is observed only with the increase in the concentration of the organic solvent in the mixture with $x_2 > 0.2$. Here, D,L- α -alanine solvation is stronger than that of β -alanine in the majority of similar mixed solvents.

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Notes

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