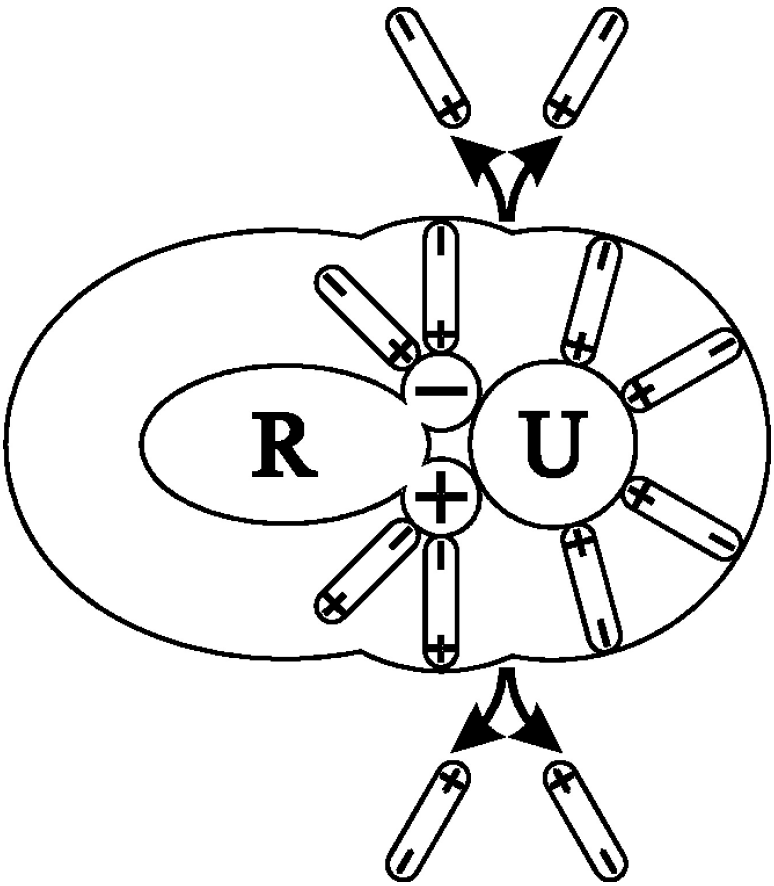
Article

Enthalpic Pair Interaction Coefficient between Zwitterions of l-α-Amino Acids and Urea Molecule as a Hydrophobicity Parameter of Amino Acid Side Chains

Bartlomiej Palecz

J. Am. Chem. Soc., **2005**, 127 (50), 17768-17771• DOI: 10.1021/ja054407l • Publication Date (Web): 24 November 2005



J|A|C|S
ARTICLES
Published on Web 11/24/2005

Enthalpic Pair Interaction Coefficient between Zwitterions of L-α-Amino Acids and Urea Molecule as a Hydrophobicity Parameter of Amino Acid Side Chains

Bartlomiej Palecz

Contribution from the Department of Physical Chemistry, University of Lodz, 90-236 Lodz, Pomorska 165, Poland

Received July 4, 2005; E-mail: paleczb@uni.lodz.pl

Abstract: Dissolution enthalpies of L-α-proline, L-α-tyrosine, L-α-tryptophan, L-α-histidyne, L-α-arginine, L-α-lysine, L-aspartic acid, and L-α-glutamic acid in aqueous solutions of urea have been measured by calorimetry at a temperature of 298.15 K. The values of dissolution enthalpy were used to determine enthalpic heterogeneous pair interaction coefficients between the zwitterions of the natural amino acids and a molecule of urea in water solution. These coefficients were interpreted in terms of the hydrophobic or hydrophilic effects of the side chains of amino acids on their interactions with a polar molecule of urea in water.

Introduction

All cells contain a permanent free amino acids pool indispensable for the proper functioning of the organism. The behaviors of free amino acids as well as those forming protein chains are influenced by the side amino acid substituent −R. Side substituents show various affinities to water and are partly responsible for the spatial structure of protein domains and subunits, and consequently for the properties and functions fulfilled by the given proteins in living organisms. Many research centers have carried out studies on the interactions of natural amino acids with molecules of nonelectrolyte[1,2] and electrolytes[3−5] in water as well as research intended to describe the hydrophobic−hydrophilic properties of amino acid side chains[10−33] responsible for their affinity to water as the medium of life. Tens of scales have been developed to determine the hydrophobicity of amino acid side substituents.[11−32] A weak correlation between these scales results from the fact that their authors have used different measuring procedures and from specific interactions between amino acids or their derivatives and the organic solvents used in measurements. Moreover, the results obtained by some authors are quite controversial. The typically ambivalent radical of tryptophan that occurs on the surface of many globular proteins[34,35] has been recognized by researchers as the most hydrophobic.[11,12,15,16,19−21,28−30] The side chain of tyrosine has been described by a team of authors as strongly hydrophobic[11,12,14,29] and as strongly hydrophilic by another group of authors.[24,25] Similarly, the side substituent of cysteine has been regarded in some presented scale even as more hydrophobic than that of alanine.[11−20,22,27,28,30]

To eliminate specific interactions connected with the use of different solvents that disturb the interpretation of experimental data, a scale has been proposed that differentiates amino acid side chains, being based on the calorimetrically determined enthalpic homogeneous pair interaction coefficients of natural amino acids.[36] However, this method did not allow one to find

(1) Gude, M. T.; van der Wielen, L. A. M.; Luyben, K. Ch. A. M. *Fluid Phase Equilib*. **1996**, *116*, 110.
(2) Lou, Y.; Lin, R. *Thermochim. Acta* **1998**, *316*, 145.
(3) Wang, J.; Yan, Z.; Zhang, H.; Lu, J. *Biophys. Chem*. **2000**, *86*, 71.
(4) Palecz, B. *J. Thermal Anal.* **1998**, *54*, 265.
(5) Palecz, B. *Amino Acids* **2004**, *27*, 299.
(6) Yu, L.; Hu, X.; Lin, R.; Shao, S.; Zhang, H. *Thermochim. Acta* **2001**, *378*, 1.
(7) Soto, A.; Arce, A.; Khoshkbarchi, M. K.; Vera, J. H. *Fluid Phase Equilib*. **1999**, *158*−*160*, 893.
(8) Yan, Z.; Wang, J.; Lu, W.; Lu, J. *Thermochim. Acta* **1999**, *334*, 17.
(9) Palecz, B.; Piekarski, H. *Fluid Phase Equlib*. **1999**, *164*, 257.
(10) Nozaki, N.; Tanford, C. J. *J. Biol. Chem*. **1971**, *246*, 2211.
(11) Levitt, M. *J. Mol. Biol.* **1976**, *104*, 59.
(12) Hopp, S.; Woods, K. S. *Proc. Natl. Acad. Sci. U.S.A.* **1981**, *78*, 3824.
(13) Kyte, J.; Doolittle, R. *J. Mol. Biol*. **1982**, *157*, 105.
(14) Sweet, R. M.; Eisenberg, D. *J. Mol. Biol.* **1983**, *171*, 479.
(15) Fauchere, J. L.; Charton, M.; Kier, L. B.; Verloop, A.; Pliska, V. *Int. J. Pept. Protein Res.* **1988**, *32*, 269.
(16) Sasagawa, T.; Eicksson, L. H.; Teller, D. C.; Titani, K.; Walsh, K. A. *J. Chromatogr*. **1984**, *29*, 307.
(17) Rose, G. D.; Geselowitz, A. R.; Lesser, G. J.; Zehfus, M. H. *Science* **1985**, *229*, 834.
(18) Miyazawa, S.; Jernigan, R. L. *Macromolecules* **1985**, *18*, 534.
(19) Kidera, A.; Konishi, Y.; Oka, M.; Ooi, T.; Scheraga, H. A. *J. Protein Chem.* **1985**, *4*, 23.
(20) Parker, J. M. R.; Guo, D.; Hodges, R. S. *Biochemistry* **1986**, *25*, 5425.
(21) Eisenberg, D.; McLachlan, A. D. *Nature* **1986**, *319*, 199.
(22) Engelman, D. M.; Steitz, T. A.; Goldman, A. *Annu. Rev. Biophys. Chem*. **1986**, *15*, 321.
(23) Hellberg, S.; Eriksson, L.; Jonsson, J.; Lindgren, F.; Sjöström, M.; Skagerberg, B.; Wold, S.; Andrews, P. *Int. J. Pept. Protein Res*. **1991**, *37*, 414.
(24) Ooi, T.; Oobatake, M.; Nemethy, G.; Scheraga, H. A. *Proc. Natl. Acad. Sci. U.S.A.* **1987**, *84*, 3086.
(25) Oobatake, M.; Ooi, T. *J. Biochem.* **1988**, *104*, 433.
(26) Radzicka, A.; Wolfenden, R. *Biochemistry* **1988**, *27*, 1664.
(27) Cowan, R.; Whittaker, R. G. *Pept. Res*. **1990**, *3*, 75.
(28) Chmelik, J.; Hudecek, J.; Putyera, K.; Makovicka, J.; Kalous, V.; Chmelikova, J. *Collect Czech. Chem. Commun.* **1991**, *56*, 2030.
(29) Norinder, U. *Peptides* **1991**, *12*, 1223.
(30) El Tayar, N.; Tsai, R.-S.; Carrupt, P.-A.; Testa, B. *J. Chem. Soc., Perkin Trans.* **1992**, *2*, 79.
(31) Van de Waterbeemd, H.; Karajiannis, H.; El Tayar, N. *Amino Acids* **1994**, *7*, 129.
(32) Yoshida, T. *J. Chromatogr. A* **1998**, *808*, 105.
(33) Yoshida, T.; Okada, T.; Hobo, T. *Bunseki Kagaku* **1999**, *48*, 917.
(34) Carter, D. C.; Ho, X. J. *Adv. Protein Chem.* **1994**, *45*, 153.
(35) Filenko, A.; Demchenko, M.; Mustafaeva, Z.; Osada, Y.; Mustafaev, M. *Biomacromolecules* **2001**, *2*, 270.
(36) Palecz, B. *J. Am. Chem. Soc*. **2002**, *124*, 6003.

10.1021/ja054407l CCC: $30.25

the enthalpic pair interaction coefficients between zwitterions of slightly water-soluble amino acids such as tyrosine or aspartic acid.

To find a parameter that would allow one to systematize all natural amino acid side chains, I have measured calorimetrically the enthalpies of solution of all natural amino acids in water and aqueous urea solution. The obtained values were used to determine the enthalpic heterogeneous pair interaction coefficients between zwitterions of amino acid and urea molecule in water. These coefficients are derived from the McMillan−Mayer theory[37] as modified by Franks at al.[38] and by Friedman and Krishman,[39] and they well describe the total effects of interactions between heterogeneous pairs taking place with the competitive participation of water molecules. The differences in the enthalpic coefficients describing the interactions between the "zwitterionic head" of a statistic amino acid (to simplify, glycine zwitterions H-C$^{\alpha}$HCO$_2^-$HN$_3^+$ was accepted) and a polar urea molecule, and the interactions of natural amino acid molecules containing various side substituents with a molecule of urea in the presence of competitive water molecules well reflect the affinity of amino acid side chains to water. Thus, they can be used as a parameter that reveals their hydrophobic−hydrophilic character. In addition, this parameter eliminates some difficulties in the interpretation of the coefficients of interactions between homogeneous pairs of amino acids possessing both strong hydrophilic (L-α-asparagine) and ionic (L-α-arginine, L-α-glutamic acid) substituents which appeared in the case of the scale based on the enthalpic coefficients of homogeneous interactions.[36] Urea selected for the experiments well fulfils the part of a differentiating model molecule. It occurs in living organisms as one of the components of metabolic urea cycle and possesses also analogical functional groups as those occurring in proteins. The obtained enthalpic interaction pair coefficients between zwitterions of all natural amino acids and urea molecule in water were analyzed applying the modified[36] equation proposed by Abraham-Kamlet−Taft.[40,41]

Experimental Section

Urea (U) (99.5% from Fluka), L-α-proline (Pro), L-α-tyrosine (Tyr), L-α-tryptophan (Trp), L-α-histidyne (His), L-α-arginine (Arg), L-α-lysine (Lys), L-aspartic acid (Asp), and L-α-glutamic acid (Glu) (all 99% from Fluka) were crystallized from water−methanol mixtures and dried under reduced pressure at 323 K (except for lysine, at room temperature). The water used in the experiments was deionized, distillated, and degassed. Water−urea mixtures 0.5−3.0 mol(U) kg^{-1}(water) were prepared by weight.

The enthalpies of solution of natural amino acids (A) in water ($\Delta H_{S(W)}$) and aqueous solution of urea ($\Delta H_{S(W+U)}$) were measured at 298.15 K with an isoperibol calorimeter.[42] The temperature sensitivity of the measuring system was about 4×10^{-5} K, and the temperature stability of the thermostat was better than 10^{-3} K. The accuracy was ±0.5%. The measurements of dissolution enthalpies of amino acids were carried out within the range from 0.001 to 0.01 mol(A) kg^{-1} (solvent). The standard enthalpies of solution of amino acids were determined by the linear extrapolation to zero amino acids concentration of the values of 8−10 independent measurements. The ampules containing the amino acids were filled in drybox and weighed with a Mettler AE 240 balance.

Table 1. Standard Enthalpies of Solution of L-α-Amino Acids in Aqueous Urea Solutions at 298.15 K

mmol(U) kg^{-1} H$_2$O	$\Delta H^0_{S(W+U)}$/kJ mol^{-1}							
	Pro	Tyr	Trp	His	Arg	Lys	Asp	Glu
0	−3.25	21.70	12.70	14.32	6.68	−15.84	25.82	27.85
0.5	−3.50	21.39	12.18	13.80	5.83	−16.56	24.95	26.98
1.0	−3.80	21.13	11.49	13.32	5.07	−17.20	24.27	26.32
1.5	−4.07	20.94	11.01	12.78	4.31	−17.70	23.48	25.42
2.0	−4.35	20.72	10.56	12.21	3.87	−18.33	22.89	24.79
2.5	−4.60	20.50	10.07	11.79	3.34	−18.75	22.30	23.93
3.0	−4.84	20.36	9.65	11.25	2.85	−19.20	21.60	23.30

Results and Discussion

The standard enthalpies of solution of amino acids in water ($\Delta H^0_{S(W)}$) and aqueous urea solutions ($\Delta H^0_{S(W+U)}$) are presented in Table 1. The standard solution enthalpies of amino acids in the aqueous solutions of urea (Table 1) show a decrease of the endothermic effect (in the event of L-α-proline and L-α-lysine an increase of the exothermic effect) with increasing urea concentration.

The obtained standard dissolution enthalpies of the examined amino acids in water and aqueous urea solutions were used to determine enthalpic pair interaction coefficients (derived from the modified McMillan−Mayer theory[37]) between zwitterions of amino acids and a molecule of urea. The standard dissolution enthalpies of amino acids in water and water−urea mixtures are described by the equation proposed by Desnoyers:[43]

$$\Delta H^0_{S(W+U)} = \Delta H^0_{S(W)} + 2h_{AU}\, m_{(U)} + 3h_{AUU}\, m_{(U)}{}^2 + \ldots \quad (1)$$

where: $m_{(U)}$ is molal concentration of urea in water mol(U) kg^{-1}(H$_2$O), h_{AU} is the enthalpic pair interaction coefficient, and h_{AUU} denotes the enthalpic triplet interaction coefficient. The enthalpic pair and triplet interaction coefficients determined in this work are listed in Table 2. The interpretation of the triplet interaction coefficients is obscured by the fact that they also contain pairwise interaction terms and for that reason are not discussed in the present paper.

The enthalpic heterogeneous pair interaction coefficients, h_{AU}, describe the effects of interactions between statistic zwitterions of the examined amino acids and a statistic molecule of urea in aqueous solutions that take place with the participation of polar molecules of water. Polar and ionic groups of the examined molecules are strongly hydrated with water molecules. To provide conditions for direct interactions between the zwitterions of amino acid and urea molecule, some water molecules of the hydration layer of those molecules must be removed, as they are a hindrance to their direct approach. The water molecules pushed out from the hydration sheaths deep into the solution assume an order typical for bulk water.

(37) McMillan, W. G.; Mayer, J. E. *J. Chem. Phys.* **1945**, *13*, 276.
(38) Franks, F.; Padley, M.; Reid, D. S. *J. Chem. Soc., Faraday Trans. 1* **1976**, *72*, 359.
(39) Friedman, H. L.; Krishnan, C. V. *J. Solution Chem.* **1973**, *2*, 119.
(40) Abraham, M. H.; Kamlet, M. J.; Taft, R. W. *J. Solution Chem.* **1982**, *2*, 923.
(41) Kamlet, M. J.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* **1983**, *48*, 2877.
(42) Palecz, B. *J. Solution Chem.* **1995**, *24*, 537.
(43) Desnoyers, J. E.; Perron, G.; Avedikian, L.; Morel, J.-P. *J. Solution Chem.* **1976**, *5*, 631.

Table 2. Heterogeneous Enthalpic Pair Interaction Coefficients for Natural L-α-Amino Acids with Urea in Water at 298.15 K and Parameters Describing Amino Acids Side Chains

amino acids	h_{AU}/J kg mol^{-2}	$\Lambda_{(norm)}$	$n_{(da)}$	V_r^{∞}/ cm^3 mol^{-1}	amino acids	h_{AU}/J kg mol^{-2}	$\Lambda_{(norm)}$	$n_{(da)}$	V_r^{∞}/ cm^3 mol^{-1}
Gly	−390.2[4]	0.0336	0	0	Cys	−358[5]	0.0858	3	30.10
Ala	−238.2[4]	0.0522	0	17.20	Asn	−819[5]	0.5075	5	34.50
Val	−116[4]	0.0933	0	47.50	Gln	−690[5]	0.4888	5	50.50
Leu	−98[4]	0.0000	0	64.40	Lys	−721.5	0.8880	3	65.42
Ile	−95[5]	0.0298	0	62.45	Arg	−892.8	1.0000	7	84.04
Phe	−97[5]	0.0634	0	78.00	His	−518.3	0.4403	2	55.70
Met	−180[5]	0.1679	0	61.90	Asp	−831	0.4478	5	30.15
Pro	−280.1	0.1604	0	39.20	Glu	−820.8	0.5784	5	47.66
Ser	−511[5]	0.1940	3	17.40	Tyr	−300.3	0.3582	3	80.70
Thr	−350[5]	0.2425	3	33.60	Trp	−610.4	0.1604	1	99.80

The determined enthalpic interaction coefficients of amino acid zwitterions with a urea molecule $h_{(A,U)}$ describe two direct effects connected with:

(a) the direct interaction between the zwitterionic "head" ($-CHCO_2^-NH_3^+$) of the examined amino acid and the polar urea molecule (exothermic process);

(b) partial dehydration of hydration sheaths of the zwiterionic "head" of amino acid and the polar urea molecule (endothermic processes).

These effects are supplemented with processes connected with the interactions between amino acid side chains and a molecule of urea in an aqueous solution.

(c) In the case of amino acids with polar or ionic substituents, the global effect is strengthened with the exothermic processes connected with the interactions of these groups with the polar urea molecule, and weakened by the endothermic effects connected with the dehydration of these polar groups.

(d) Water molecules in the direct vicinity of nonpolar side chains of amino acids strengthen hydrogen bonds between themselves[44−47] due to the hydrophobic hydration phenomenon. The effect of strengthened interaction, due to the cooperativeness of hydrogen bonds, is transferred on the water molecules surrounding polar or ionic groups, bringing about the reinforcement of the interactions between the water molecules of the hydration sheath and these groups. To remove some water molecules from hydration sheaths, constituting a hindrance to the direct interaction between polar groups (of amino acid and urea), it is necessary to supply more energy. Thus, the global effect of the interaction between the zwitterions of amino acid, possessing a nonpolar side chain, and the polar urea molecule becomes more endothermic.

The determined enthalpic coefficient of interaction between the urea molecule and the simplest amino acid, glycine, in water has a negative value (Table 2).[5] It indicates a predominant exothermic effect of direct interactions between the zwitterionic "head" of glycine (-$CHCO_2^-NH_3^+$) and the polar urea molecule over the endothermic effects of partial dehydrations of the solvation sheaths of these molecules. Some influence on this effect is exerted by the hydrophobic side substituent of glycine linked to atom C^{α}. Neglecting the weak effect caused by the presence of glycine side substituent (-H), one may assume the value of the enthalpic coefficient of interaction between the urea molecule and glycine zwitterions as a reference point to systematize the affinity of amino acid side chains to water or their hydrophobic−hydrophilic properties.

The replacement of hydrogen at C^{α} in the zwitterionic "head" with an alkyl substituent in the case of alanine (Ala), L-α-aminobutyric acid (Aba), valine (Val), leucine (Leu), and isoleucine (Ile)[5] brings about a decrease in the exothermic effects of enthalpic pair interaction coefficients, h_{AU}, with increasing number of carbon atoms in the side amino acids chains (Table 2). This indicates an increased hydrophobicity of the substituent. Similarly in the case of proline (Pro), its weak hydrophobic side substituent brings about a drop in the negative value of the enthalpic coefficient h_{AU} or an increase in the contribution of the endothermic dehydration process due to the hydrophobic hydration phenomenon.

The substitution of the benzene ring in phenylalanine (Phe) with a hydroxyl group, leading to the formation of tyrosine (Tyr), causes the negative value of enthalpic heterogeneous interaction coefficient to increase (Table 2). This is associated with the increase in the contribution of exothermic direct interactions caused by the presence of the polar hydroxyl group.

Analogously to the interactions between urea molecules and zwitterions of amino acids with polar substituents, in the case of tryptophan (Trp), the values of the determined enthalpic heterogeneous pair interaction coefficients are more exothermic than that for glycine (Table 2). The values of enthalpic pair interaction coefficients of natural amino acids with basic substituents, histidine (His), arginine (Arg), lysine (Lys), or acidic, aspartic acid (Asp) and glutamic acid (Glu), indicate a great contribution of these ionic side chains to the global effect of interactions. This is due to their strong interactions with the polar urea molecule. Considering the values of h_{AU} of aspartic acid and glutamic acid, one observes a hydrophobic influence of the nonpolar group CH_2 that causes the attenuation of the global exothermic effect $h_{Glu-U} > h_{Asp-U}$ (Table 2).

The obtained values of enthalpic heterogeneous pair interaction coefficients between the molecules of natural amino acids and the urea molecule well correlate with the values of enthalpic homogeneous pair interaction coefficients of natural amino acids[36] (Figure 1). The values of enthalpic heterogeneous pair interaction coefficients (h_{AU}) are listed with the previously developed averaged scale of hydrophobicity of amino acid side chains ($P_{hydr-pho}$)[36] in which cysteine and tryptophan were omitted. The above relationship, shown in the graph (Figure 2), is described by the equation of straight line with regression coefficient $R^2 = 0.935$ that indicates some correlation between these values.

(44) Hallenga, K.; Grigera, I. R.; Berenson, H. J. *J. Phys. Chem.* **1980**, *84*, 2381.
(45) Hechte, D.; Tadesse, F.; Walters, L. *J. Am. Chem. Soc.* **1993**, *115*, 3336−3337.
(46) Ide, M.; Maeda, Y.; Kitano, H. *J. Phys. Chem B* **1997**, *101*, 7022.
(47) Palecz, B.; Piekarski, H.; Romanowski, S. *J. Mol. Liq.* **2000**, *84*, 279.

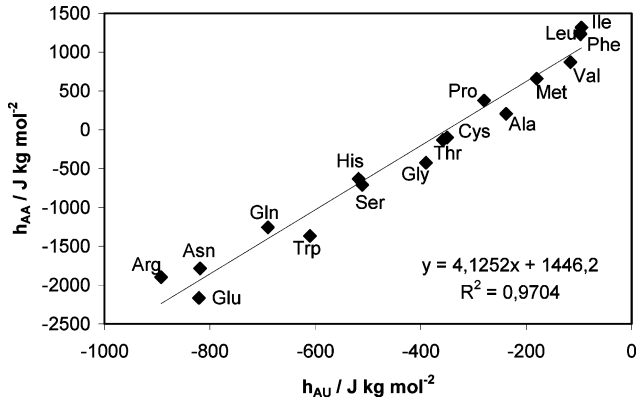


Figure 1. Relationship between the enthalpic pair coefficients of interaction between the zwitterions of natural amino acids and the urea molecule h_{AU} in water and the enthalpic homogeneous pair interaction coefficients h_{AA} of natural amino acids in water.

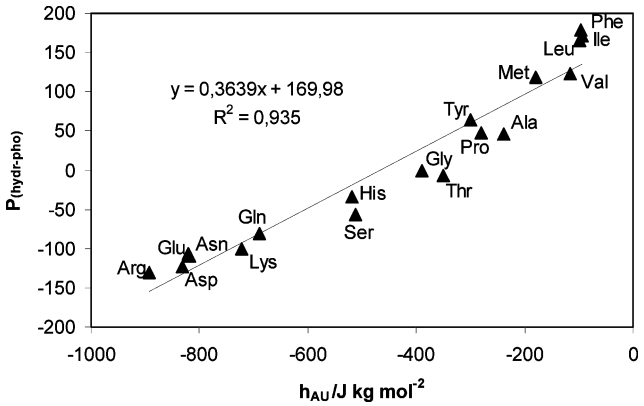


Figure 2. Relationship between the enthalpic pair coefficients h_{AU} of interaction between the zwitterions of natural amino acids and the urea molecule in water and the averaged hydrophobicity parameters $P_{(hydr-pho)}$.

To find additional information about factors that exert a considerable influence on the variability of the enthalpic coefficients of interactions between zwitterions of natural amino acids and the urea molecule in water and, at the same time, characterize the amino acid side substituents the obtained coefficients were analyzed using the modified[36] equation by Abraham−Kamlet−Taft.[40,41] Because of the lack of a parameter describing the dipolarity−polarizability of amino acid chains, it was replaced with the standardized parameter Λ[36] describing the polarity of particular amino acids as proposed by Tayar et al.[30] (Table 2). Similarly, the donor-proton and acceptor-proton properties were replaced with the value of $n_{(da)}$ (Table 2) describing the number of hydrogen bonds that can be created by the amino acid side substituent as a donor and acceptor of proton.[36,48] The values of the limiting partial molar volumes of natural amino acid side chains, V_R^{∞}, were calculated from the difference between the values concerning particular amino acids and glycine (Table 2).[36]

(48) Charton, M.; Charton, B. I. *J. Theor. Biol*. **1982**, *99*, 629.

Finally, the modified equation assumed the following form:

$$h_{AU} = (h_{A\pm,U})_0 + a\Lambda_{(norm)} + bn_{(ad)} + cV_R^{\infty} \qquad (2)$$

The modified[36] equation by Abraham−Kamlet−Taft.[40,41] allows one to correlate the parameters of the equation with the values of the enthalpic heterogeneous pair interaction coefficients of 19 natural amino acids (with the exception of tryptophan (Trp) that is described by the parameter $\Lambda_{(norm)}$[30] as strongly hydrophobic). The previously developed scale[36] contained only 15 natural amino acids.

The above parameters as independent variables are noncollinear, which allows one to make a statistically real separation of contributions in the correlation equation.

The examined enthalpic pair coefficients of interaction between zwitterions of natural amino acids and urea molecule correlated with the factors presented above are described by the following equation:

$$h_{AU} = (-275 \pm 40)_0 - (522 \pm 95)\Lambda_{(norm)} - (64.4 \pm 11.3)n_{(ad)} + (3.27 \pm 0.75)V_R^{\infty}$$

$$n = 19 \qquad R^2 = 0.95 \qquad (3)$$

This equation defines the contributions of particular parameters to the total variability of the enthalpic heterogeneous pair interaction coefficients. The free term of this equation ($h_{A\pm,U}$) is not only a selectable parameter, but it also describes direct interactions between the statistic zwitterionic "head" of amino acid and the urea molecule in water. The sign and order of magnitude of the free term is close to the value of the enthalpic coefficient of interaction between the zwitterions of glycine and urea molecule (Table 2). The term $a\Lambda_{(norm)}$ describing the main ion−dipole and dipole−dipole interactions indicates an exothermic contribution to the summary value of enthalpic coefficients (h_{AU}). The exothermic contribution to the summary effect is also described by the term $bn_{(ad)}$ that characterizes the interactions connected with the formation of hydrogen bonds between urea molecules and polar or ionic amino acid side chains. The above effects are compensated by the endothermic processes (described by cV_R^{∞}) connected with the creation of a cavity in the water structure to accommodate in it the amino acid side chain and partial dehydrations of both the polar urea molecule and amino acid polar and ionic side substituents, on which are overlaid the processes of hydrophobic hydration of nonpolar amino acid chains.

The analysis of the obtained enthalpic pair coefficients of interaction between the molecules of natural amino acids and the urea molecule in water allows one to treat the determined coefficients as a parameter for systematizing the affinity of amino acid side chains to water or their hydrophobic−hydrophilic properties.

Acknowledgment. I gratefully acknowledge the financial support of KBN within the Grant No. 4 T09A 067 25.

JA054407L