

## **ENTHALPIES OF INTERACTION OF GLYCINE WITH SOME AMIDES IN AQUEOUS SOLUTIONS AT 298.15 K**

*B. Pałecz*

Department of Physical Chemistry, University of Łódź, Pomorska 18, 91-416, Łódź, Poland

### **Abstract**

The dissolution enthalpies of glycine in aqueous solutions of acetamide, N-methylacetamide, N,N-dimethylacetamide, N-ethylformamide, N,N-diethylformamide and N,N-diethylacetamide were measured at 298.15 K. The enthalpic pair interaction coefficients of glycine zwitterion – amide molecules were determined by using standard solution enthalpies of glycine in water and aqueous solutions of amides. The additivity of groups concept of Savage and Wood was used to estimate the contribution of each of the functional groups of the studied amides.

**Keywords:** aqueous solutions of amides, enthalpies of solutions, glycine

### **Introduction**

The thermodynamic properties of aqueous solutions of amino acids are of current interest as a means of allowing a better understanding of complex biochemical systems. Studies on the thermodynamic interactions in aqueous solutions between amino acid molecules and model compounds containing functional groups analogous to those existing in proteins are of great interest [1–5]. The present work reports the results of calorimetric measurements of the dissolution enthalpies of glycine in aqueous solutions of amides. These results served as the basis for calculations of enthalpic coefficients of interactions between a glycine zwitterion and amides in aqueous solution [6], according to the McMillan-Mayer model. These coefficients reflect the sum of the enthalpic effects of the interactions between the two solutes in aqueous solution and also the contributions of the solvation effects of the two dissolved substances.

### **Experimental**

Liquid amides were purified by vacuum distillation from solid sodium hydroxide, acetamide was recrystallized from ethanol, and glycine was recrystallized from methanol – water and dried in vacuum over P<sub>2</sub>O<sub>5</sub> at room temperature for at least 72 h before use.

The water used in the experiments was deionized, twice distilled and degassed.

The concentrations of the solvents were determined by weight.

The calorimetric measurements of the solution enthalpies were performed with an 'isoperibol' type calorimeter. The glass calorimeter vessel, with a capacity of about 120 cm<sup>3</sup>, was equipped with a calibration heater, two thermistors and a stirrer – ampoule holder, and was closed with a 'Teflon' stopper. The thermistors (10 kohm) were connected to a Wheatstone bridge. The voltage of the unbalanced bridge was measured with a Keithley K-148 nanovoltmeter connected to a digital V-540 voltmeter (Mera-Tronik). The temperature sensitivity was about 4×10<sup>-5</sup> deg and the experimental error was ±0.5%. The standard enthalpy of solution was calculated as a mean value of 6–8 independent measurements in the concentration range 0.002–0.02 mol·kg<sup>-1</sup>. The calorimeter was calibrated on the basis of the standard enthalpy of solution at infinite dilution of urea (Calorimetric Standard US, N.B.S.) in water at 298.15 K. The value obtained in this study was 15.31±0.04 kJ·mol<sup>-1</sup> (Desnoyers *et al.* [6] 15.30 kJ·mol<sup>-1</sup>; Schrier *et al.* [7] 15.29 kJ·mol<sup>-1</sup>). The effect of breaking the ampoule was imperceptible. To prepare the exact concentrations of the samples, a Sartorius RC 210D balance was used. The calorimeter was placed in a hermetically closed brass jacket with a volume of about 1 dm<sup>3</sup>, within a water thermostat. The temperature stability of the thermostat was better than 10<sup>-3</sup> deg.

## Results and discussion

The enthalpies of dissolution of glycine (G) in aqueous solutions of amides (0.5–3.0 mol amide/kg water) in the concentration range 0.002–0.02 mol G/kg solvent were measured at 298.15 K. On the basis of the dissolution enthalpy values, the standard enthalpies of dissolution of glycine in aqueous solutions of amides were calculated (Table 1). The standard enthalpies of glycine solutions in water ( $\Delta H_{S(G \text{ in } W)}^{\circ} = 14.20 \text{ kJ}\cdot\text{mol}^{-1}$ ) [8] and aqueous solutions of amides ( $\Delta H_{S(G \text{ in } W+A)}^{\circ}$ ) were used to estimate the enthalpic pair interaction coefficients for glycine zwitterion – amide molecule  $h_{GA}$  in water (Table 2) [6].

$$\Delta H_{S(G \text{ in } W+A)}^{\circ} - \Delta H_{S(G \text{ in } W)}^{\circ} = 2h_{GA}m_A + 3h_{GAA}m_A + \dots \quad (1)$$

where  $m_A$  is the molal concentration of amide (mol amide/kg water), and the parameter  $h_{GAA}$  is related to a triplet interaction term. The interpretation of the triplet interaction coefficients is obscured by the fact that they also contain pairwise interaction terms [9, 10] and hence this is omitted from this paper.

The enthalpic pair interaction coefficient between a zwitterion of glycine and a molecule of acetamide (Table 2) has a negative value. This is indicative of a predominant, strongly exothermic effect of a direct interaction between a

zwitterion of glycine and a molecule of amide over the endothermic effect of partial dehydration of the solvation layers of glycine and amide in aqueous solution [11, 12]. The replacement of a hydrogen atom in a molecule of acetamide (or formamide [8]) by an alkyl radical, causes an increase in the enthalpic pair interaction coefficient  $h_{GA}$ , this increasing with increase in the number and size of the alkyl substituents (Table 2). This effect is due to a reduction in the interactions between the zwitterion of glycine and the alkyl-substituted amide, and hence to the prevalence of endothermic processes of dehydration of the molecules in aqueous solutions.

Table 1 Standard enthalpies of solution of glycine in aqueous amides solutions at 298.15 K

$m_A /$ $\text{mol} \cdot \text{kg}^{-1}$	$\Delta H_{\text{S}(G \text{ in } W+A)}^{\circ} / \text{kJ mol}^{-1}$					
	A	NMA	DMA	NEF	DEF	DEA
0.5	14.15	14.45	14.59	14.43	14.80	14.99
1.0	14.11	14.68	14.97	14.65	15.35	15.73
1.5	14.08	14.90	15.30	14.83	15.88	16.40
2.0	14.06	15.10	15.62	15.02	16.34	17.04
2.5	14.04	15.28	15.91	15.18	16.82	17.60
3.0	14.02	15.43	16.15	15.31	17.20	18.22

Table 2 Experimental and calculated values heterotactic enthalpic pair interaction coefficients for glycine with amides in water at 298.15 K

	$h_{GA}^{\text{exp}}$	$h_{GA}^{\text{calc}}$	$n_{\text{CH}_2}$
	$\text{J} \cdot \text{kg} \cdot \text{mol}^{-2}$		
G-F	-224(13) <sup>a</sup>	-182	0.5
G-NMF	156(8) <sup>a</sup>	76	2
G-NEF	240	247	3
G-A	-53	-10	1.5
G-NMA	259	247	3
G-DMF	370(7) <sup>a</sup>	294	3.5
G-DMA	407	466	4.5
G-DEF	617	637	5.5
G-DEA	812	809	6.5

Group additivity coefficients (in  $\text{J} \cdot \text{kg} \cdot \text{mol}^{-2}$ ) for glycine zwitterion-amide pairs in water:  
 $h_{\alpha-\text{CH}_2} = 172 \pm 19$ ;  $h_{\alpha-\text{P-pp}} = -267 \pm 46$ ;  $h_{\alpha-\text{I-pp}} = -306 \pm 98$ ; <sup>a</sup>Ref. [16]

The enthalpic pair interaction coefficients can be also correlated by means of the well-known Savage & Wood group additivity model (SWAG) [13]. According to this model, each functional group of one molecule interacts with

each functional group of another one, thereby contributing to the observed overall enthalpic effect.

In accordance with the proposal advanced by Savage and Wood [13], it is accepted that  $\text{CH}_3$  corresponds to  $1.5\text{CH}_2$ , while  $\text{CH}$  corresponds to  $0.5\text{CH}_2$ . Following Lilley *et al.* [12, 14, 15], it is assumed that the primary and secondary amides function as one defined group (denoted 'Pep'), while the tertiary amide (denoted 'iPep') functions as a distinct defined group. In the considered systems, a zwitterion of glycine has been treated as (an individual corresponding to) a single dipolar functional group, and thus the Savage & Wood formula can be written as follows:

$$h_{\text{GA}} = \sum_i n_{\text{A},i} h_{\text{G},i} \quad (2)$$

where  $n_{\text{A},i}$  is the number of type  $i$  groups in the molecule of individual amide  $A$ , while  $h_{\text{G},i}$  describes the interactions between group  $i$  of the amide and a zwitterion of glycine. Application of the multiple linear regression method to solve Eq. (2) for 9 amides (Table 2) possessing the distinguished groups in their molecules (formamide, N-methylformamide, N-ethylformamide, acetamide, N-methylacetamide, N,N-dimethylformamide, N,N-dimethylacetamide, N,N-diethylformamide and N,N-diethylacetamide) led to the estimated group contributions and values presented in Table 2.

The coefficient of interaction between glycine and the apolar  $\text{CH}_2$  group has a positive value, which reflects the 'thermochemical repulsion' between the hydrated zwitterion of glycine and the hydrophobically hydrated  $\text{CH}_2$  group. The other coefficients describing the interactions between a glycine molecule and polar groups have negative values, which is a result of predominant ion-dipole type attractive forces over the endothermic effects of partial dehydration of both a glycine zwitterion and the interacting functional group of the amide.

The latter contributions become more negative in the following sequence:  $\text{Pep} < \text{iPep}$ . The observed sequence does not mean that the energies of interaction of the glycine zwitterion with the discussed functional groups become stronger in the same order. The coefficients  $h_{\text{GA}}$  are a measure of the solvent-mediated solute-solute interactions, and their experimentally determined values should therefore be treated as a result of competition between the solute hydration and solute-solute interaction. The values of the enthalpic group interaction coefficients were used to calculate the enthalpic coefficients of interaction between a zwitterion of glycine and an amide molecule  $h_{\text{GA}}^{\text{calc}}$  (Table 2). These values differ only slightly from those obtained experimentally. The differences are due to the adopted simplified identical treatment of various functional groups of amide molecules with similar physico-chemical properties.

As mentioned above, the coefficients  $h_{GA}$  are a measure of the interactions between the components in solution in the presence of solvent. The interactions of the solvent with the dissolved substances affect the experimental values of the thermodynamic quantities to a great extent.

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**Zusammenfassung** — Messungen zur Bestimmung der Lösungsenthalpie von Glycin bei 298.15 K in wäßrigen Lösungen von Acetamid (A), N-Methylacetamid (NMA), N,N-Dimethylacetamid (DMA), N-Ethylformamid (NEF), N,N-Diethylformamid (DEF) und N,N-Diethylacetamid (DEA) wurden durchgeführt. Unter Anwendung der Standard-Lösungsenthalpien von Glycin in Wasser und wäßrigen Lösungen von Amiden wurden die Enthalpie-Paarwechselwirkungskoeffizienten von Glycinzwitterion-Amidmolekülen bestimmt. Unter Anwendung des Gruppenadditionskonzeptes von Savage und Wood (SWAG) wurde der Beitrag jeder funktionellen Gruppe der untersuchten Amide abgeschätzt.