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Enthalpy of Solution of Glycine at Various pHs

V. G. Badelin, G. N. Tarasova, I. N. Mezhevoi, E. V. Kozlovskii, and A. V. Katrovtseva

Institute of Chemistry of Solutions, Russian Academy of Sciences, Ivanovo, Russia

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Abstract — A new approach to determination of the enthalpies of solution of amino acids in multicomponent solutions at various pHs is proposed. The approach allows correct estimation of the contribution of acid–base processes occurring in the system and, therefore, correct interpretation of experimental data with regard to interactions between components of the investigated systems. The approach is checked for consistency with an example of glycine.

Molecules of amino acids in solutions can occur in three different forms (zwitterions and positive and negative ions). The relationship between the zwitterionic and ionic forms, controlling the biological activity of amino acids, can be regulated by varying pH. The measured total thermodynamic effects of solution of amino acids at various pHs are composed of partial effects of solution, acid–base interactions, and specific interactions between components of the solution, including both chemical and solvation interactions. To determine the contributions of acid–base interactions to measured thermodynamic characteristics of hydration of different amino acid species, we measured the enthalpies of solution of glycine in the universal acetate–phosphate–borate buffer solution over the pH range from 4.1 to 9.6 at 298.15 K (Table 1). Acid–base interactions occurring in dissolution of glycine in the universal buffer solution can be represented by Eqs. (1)–(9).

$$CH_3COO^- + H^+ \rightleftarrows CH_3COOH, \quad (1)$$

$$B(OH)_3 + H_2O \rightleftarrows B(OH)_4^- + H^+, \quad (2)$$

$$3B(OH)_3 \rightleftarrows B_3O_3(OH)_4^- + H^+ + 2H_2O, \quad (3)$$

$$4B(OH)_3 \rightleftarrows B_4O_5(OH)_4^{2-} + 2H^+ + 3H_2O, \quad (4)$$

$$5B(OH)_3 \rightleftarrows B_5O_6(OH)_4^- + H^+ + 5H_2O, \quad (5)$$

$$PO_4^{3-} + H^+ \rightleftarrows HPO_4^{2-}, \quad (6)$$

$$HPO_4^{2-} + H^+ \rightleftarrows H_2PO_4^-, \quad (7)$$

$$H_2PO_4^- + H^+ \rightleftarrows H_3PO_4, \quad (8)$$

$$(N^+H_3CH_2COO^-) \rightleftarrows NH_2CH_2COO^- + H^+. \quad (9)$$

The contribution of reactions (1)–(9) to experimental heat effects was taken into account by introduction of the corresponding correction terms. These terms are written as $\alpha_i\Delta_{sol}H_i$, where α_i is the change in the fraction of the *i*th component of the buffer solution and $\Delta_{sol}H_i$, thermal effect of the *i*th reaction at a given ionic strength. The α_i was estimated using the RRSU software [1] intended for calculation of the equilibrium concentrations of species in systems with arbitrary number and stoichiometry of reactions using Eq. (10).

$$\alpha_i = c_{c_i} - c_{n_i}/c_{gl}. \quad (10)$$

Here c_{c_i} is the estimated (RRSU) equilibrium concentration of the *i*th component of the buffer solution in the presence of glycine (M); c_{n_i}, that without glycine (M) (RRSU); and c_{gl}, glycine concentration (M).

The equilibrium constant of reaction (1) is given in [2]. Recalculation to the corresponding ionic strength was performed by Eq. (11) [3].

$$\log \beta_c = \log \beta_0 + \Delta Z^2 A_\gamma I^{1/2}/(1 + I^{1/2} - 0.2I), \quad (11)$$

where β_c is the apparent stability constant; β_0, thermodynamic stability constant; I, ionic strength; A_γ, Debye–Hückel constant; and ΔZ^2, algebraic sum of squared charges of ions.

The heat effect of reaction (1) was taken from [4] and recalculated to the corresponding ionic strength by Eq. (12) [3].

$$\Delta H - \Delta Z^2\Psi(I) = \Delta H^0 + iI, \quad (12)$$

where Ψ is the function of the ionic strength.

The acid–base dissociation of boric acid is described by Eqs. (2)–(5). Boric acid is a monobasic acid tending to self-associate in alkaline solutions [5, 6]. The equilibrium constants of reactions (2)–(5) were taken from [6]. Our estimates showed that the contribution of reactions (3)–(5) is negligible under

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Table 1. Experimental (ΔH) and theoretical ($\Delta H'$) enthalpies of solution of glycine at various molal concentrations m (mol kg^{-1})

pH	m = 0.005		m = 0.008		m = 0.01		m = 0.012		m = 0.015	
	$\Delta_{sol}H$	$\Delta_{sol}H'$	$\Delta_{sol}H$	$\Delta_{sol}H'$	$\Delta_{sol}H$	$\Delta_{sol}H'$	$\Delta_{sol}H$	$\Delta_{sol}H'$	$\Delta_{sol}H$	$\Delta_{sol}H'$
4.1	15.85	15.88	15.75	15.77	15.74	15.76	15.87	15.89	16.32	16.34
6.1	–	–	–	–	15.36	15.36	–	–	16.44	16.44
6.8	–	–	–	–	15.99	15.89	–	–	16.68	16.59
7.0	16.55	16.39	16.69	16.54	16.72	16.57	16.75	16.60	16.68	16.53
7.2	–	–	–	–	17.50	17.26	–	–	–	–
7.9	–	–	–	–	18.25	17.04	–	–	17.77	16.58
8.9	18.27	7.67	18.38	8.16	18.38	8.40	18.36	8.56	18.38	8.90
9.6	–	–	–	–	–	–	–	–	–	–

pH	m = 0.02		m = 0.03		m = 0.04		$\Delta_{sol}H^0$	$\Delta_{sol}H^{0'}$
	$\Delta_{sol}H$	$\Delta_{sol}H'$	$\Delta_{sol}H$	$\Delta_{sol}H'$	$\Delta_{sol}H$	$\Delta_{sol}H'$		
4.1	16.77	16.79	16.33	16.35	15.95	15.97	15.80	15.8
6.1	16.59	16.59	16.28	16.28	15.55	15.55		
6.8	16.78	16.69	16.42	16.33	–	–		
7.0	16.90	16.75	16.49	16.35	16.24	16.10	16.40	16.26
7.2	–	–	–	–	–	–		
7.9	18.22	17.03	–	–	–	–		
8.9	19.40	10.36	18.10	9.81	18.29	8.64	18.20	7.07
9.6	20.48	0.26	20.04	2.24	19.02	3.32		

the experimental conditions. The heat effect of reaction (2) was taken from [7]. The equilibrium constants and heat effect were recalculated using Eqs. (11) and (12).

The equilibrium constants of reactions (6)–(8) were taken from [2] and recalculated to the corresponding ionic strengths by Eq. (11). The heat effects of these reactions were taken from [8] and recalculated by Eq. (12).

It was demonstrated that, at pH 4–8, glycine exists as the zwitterions $N^+H_3CH_2COO^-$. At pH > 8, acid dissociation by reaction (9) should be taken into consideration. The equilibrium constant and heat effect of this reaction were taken from [9] and recalculated by Eqs. (11) and (12), respectively, to the corresponding ionic strength.

The estimated α_i values for pH 4.1–9.6 and c_{gl} = 0.02 M (Table 2) show that addition of glycine shifts the acid–base equilibria realized in the buffer solution.

The heat effect of solution of glycine ($\Delta_{sol}H'$) at pH 4.1–7.0 and c_{gl} = 0.005–0.04 M was estimated by Eq. (13) taking into account the correction terms.

$$\Delta_{sol}H' = \Delta_{sol}H - (\Delta_{dis}H_{CH_3COOH}\alpha_{CH_3COOH} + \Delta_{dis}H_{Gl^-}\alpha_{Gl^-} + \Delta_{dis}H_{H_2PO_4^-}\alpha_{H_2PO_4^-} \Delta_{dis}H_{HPO_4^{2-}}\alpha_{HPO_4^{2-}}), \quad (13)$$

where $\Delta_{sol}H'$ is the theoretical heat of solution of glycine (kJ mol^{-1}) estimated taking into account the correction terms and $\Delta_{sol}H$, measured heat effect (kJ mol^{-1}).

The theoretical heats of solution of glycine are given in Table 1. Over the pH range 4.1–7.0, the heat of glycine solution was estimated to be 16.35±0.18 kJ mol^{-1} (standard deviation at a 95% confidence level). This value only slightly differs from the experimental $\Delta_{sol}H$ of glycine in water (15.79 kJ mol^{-1}) [10]. The effect of pH on solvation of the zwitterion does not contribute significantly to the heat of its solution, suggesting that no interaction of glycine with the components of the buffer solution occurs over the indicated pH range. Therefore, up to pH ~8, the differences in $\Delta_{sol}H$ are associated only with dissociation of the components of the universal buffer solution (CH_3COOH, H_3BO_3, and H_3PO_4).

As mentioned above, dissociation of the zwitterion

Table 2. Changes in the fractions (α_i) of the components of the buffer solution in the presence of glycine at various pHs (glycine concentration 0.02 M)

Component	pH						
	4.1	6.1	6.8	7.0	7.9	8.9	9.6
Gl^-	3.15×10^{-6}	3.22×10^{-4}	1.62×10^{-3}	2.52×10^{-3}	2.03×10^{-2}	1.46×10^{-1}	3.28×10^{-1}
CH_3COOH	-2.15×10^{-2}	0	5.00×10^{-5}	4.50×10^{-5}	3.40×10^{-5}	2.63×10^{-5}	2.20×10^{-5}
$B(OH)_4^-$	1.69×10^{-6}	-1.00×10^{-6}	-6.50×10^{-5}	-1.25×10^{-4}	-5.70×10^{-3}	-1.30×10^{-1}	-3.20×10^{-1}
$B_3O_3(OH)_4^-$	3.65×10^{-7}	0	-1.30×10^{-5}	-2.50×10^{-5}	-6.80×10^{-4}	4.31×10^{-3}	1.55×10^{-2}
$B_4O_5(OH)_4^{2-}$	1.71×10^{-12}	-1.00×10^{-10}	-3.30×10^{-8}	1.00×10^{-7}	-2.30×10^{-5}	-1.68×10^{-4}	1.52×10^{-3}
$B_5O_6(OH)_4^-$	8.05×10^{-10}	-5.00×10^{-10}	-3.00×10^{-8}	-5.00×10^{-8}	-7.15×10^{-7}	7.83×10^{-6}	4.08×10^{-6}
HPO_4^{2-}	6.55×10^{-5}	-5.00×10^{-5}	-1.45×10^{-3}	-2.50×10^{-3}	-1.40×10^{-2}	-1.80×10^{-2}	-6.00×10^{-3}
$H_2PO_4^-$	1.50×10^{-3}	0	1.50×10^{-3}	2.50×10^{-3}	1.38×10^{-2}	1.90×10^{-2}	1.67×10^{-2}
H_3PO_4	-1.74×10^{-3}	1.00×10^{-7}	3.00×10^{-7}	2.30×10^{-7}	9.35×10^{-8}	1.34×10^{-8}	3.32×10^{-9}

starts at pH > 8 [Eq. (9)]. The $\Delta_{sol}H'$ of glycine at pH > 8 and a glycine concentration from 0.005 to 0.04 M was estimated by Eq. (14). The results are given in Table 1.

$$\Delta_{sol}H' = \Delta_{sol}H - (\Delta_{dis}H_{Gl^-}\alpha_{Gl^-} + \Delta_{dis}H_{B(OH)_4^-}\alpha_{B(OH)_4^-} + \Delta_{dis}H_{B_3O_3(OH)_4^-}\alpha_{B_3O_3(OH)_4^-} + \Delta_{dis}H_{HPO_4^{2-}}-\alpha_{HPO_4^{2-}} + \Delta_{dis}H_{H_2PO_4^-}-\alpha_{H_2PO_4^-}). \quad (14)$$

From the concentration dependences of $\Delta_{sol}H$ and $\Delta_{sol}H'$ at pH 4.1, 7.0, and 8.9, we estimated $\Delta_{sol}H^0$ and $\Delta_{sol}H'^0$ (Table 1). As seen, $\Delta_{sol}H'^0$ decreases with increasing pH, which can be attributed to changing solvation mechanism on passing from the zwitterion $N^+H_3CH_2COO^-$ to the glycine anion $NH_2CH_2COO^-$. Another reason can be chemical interaction of the glycine anion with one of the components of the buffer mixture. Since dissociation of boric acid is significant only at pH > 8, our thought is that the key factor determining the observed decrease in $\Delta_{sol}H'^0$ of glycine with increasing pH is interaction of the glycine anion with borate. To check this assumption for consistency, we measured the heat effects of glycine dissolution in solutions of boric acid, borax ($Na_2B_4O_7\cdot10H_2O$), and also in ammonium buffer at pH ~9.6 (in the absence of boric acid dissociation products). In the borax and boric acid solutions at high pH, $\Delta_{sol}H'$ is calculated by Eq. (15).

$$\Delta_{sol}H' = \Delta_{sol}H - (\Delta_{dis}H_{Gl^-}\alpha_{Gl^-} + \Delta_{dis}H_{B(OH)_4^-}\alpha_{B(OH)_4^-}\Delta_{dis}H_{B_3O_3(OH)_4^-}\alpha_{B_3O_3(OH)_4^-}. \quad (15)$$

The experimental ΔH and estimated $\Delta H'$ values are given below.

	$\Delta_{sol}H$, kJ mol^{-1}	$\Delta_{sol}H'$, kJ mol^{-1}
H_3BO_3	19.41	3.81
$Na_2B_4O_7\cdot10H_2O$	19.91	4.31
NH_4OH	14.67	18.99

The $\Delta_{sol}H'$ of glycine considerably differs from $\Delta_{sol}H$ in water, but it is close to the value obtained in the universal buffer at pH ~9.6.

In the ammonium buffer (pH ~9.6), $\Delta_{sol}H'$ of glycine was estimated by Eq. (16).

$$\Delta_{sol}H' = \Delta_{sol}H - (\Delta_{dis}H_{Gl^-}\alpha_{Gl^-} + \Delta_{dis}H_{NH_3^+}\alpha_{NH_3^+} - \Delta_{dis}H_{H_2O}\alpha_{NH_4^+}). \quad (16)$$

In this case, the estimated $\Delta_{sol}H'$ is close to the average value obtained in the universal buffer at lower pH (<8).

We believe that these results support the assumption that glycine anion interacts with borate at high pH. It is known that H_3BO_3 forms complexes with, e.g., glycerol and mannitol, which is used to increase the acidity of boric acid. Evidently, glycine acts similarly. The approach proposed allows correct estimation of $\Delta_{sol}H'$ and $\Delta_{sol}H'^0$ for bioactive compounds of a given class in complex systems at various pHs, taking into account contributions of acid–base equilibria realized in these systems. Exact consideration of the processes occurring in the system also reveals previously unknown interactions between system components, extending our knowledge of chemical properties of these compounds in solutions.

The heat of solution of glycine was measured on an isoperibolic calorimeter [11] to within 0.6%. The

chemicals used were recrystallized twice from a water–ethanol mixture and then dried in a vacuum drying oven at 60°C to constant weight.

REFERENCES

1. Vasil'ev, V.P., Borodin, V.A., and Kozlovskii, E.V., *Primenenie EVM v khimiko-analiticheskikh raschetakh* (Computer Calculations in Chemical Research), Moscow: Vysshaya Shkola, 1993, p. 111.
2. Lur'e, Yu.Yu., *Spravochnik po analiticheskoi khimii* (Handbook of Analytical Chemistry), Moscow: Khimiya, 1989.
3. Vasil'ev, V.P., *Termodinamicheskie svoistva rastvorov elektrolitov* (Thermodynamic Properties of Electrolyte Solutions), Moscow: Vysshaya Shkola, 1982, p. 317.
4. Kochergina, L.A., *Cand. Sci. (Chem.) Dissertation*, Moscow, 1967.
5. Cotton, F.A. and Wilkinson, G., *Advanced Inorganic Chemistry*, New York, 1966. Translated under the title *Sovremennaya neorganicheskaya khimiya*, Moscow: Mir, 1969, p. 487.
6. Ingri, N., *Acta Chem. Scand.*, 1963, vol. 17, p. 581.
7. Rarres, M., Redout, J.-P., Romanetti, R.T., and Claude, H., *C. R. Acad. Sci. Paris*, 1973, vol. 276, p. 365.
8. Dushina, S.A., *Cand. Sci. (Chem.) Dissertation*, Moscow, 1994.
9. Vasil'ev, V.P. and Kochergina, L.A., *Zh. Obshch. Khim.*, 1979, vol. 49, no. 9, p. 2042.
10. Levushkin, D.A., Badelin, V.G., and Krestov, G.A., *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, 1993, vol. 36, no. 3, p. 117.
11. Korolev, V.P., Batov, D.V., Vandyshev, V.N., and Krestov, G.A., *Zh. Fiz. Khim.*, 1983, vol. 57, no. 1, p. 253.