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Thermodynamic Characteristics of Protolytic Equilibria of β-Alanylglycine in Aqueous Solution

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Abstract — Previously unknown thermal effects of stepwise dissociation of β-alanylglycine in aqueous solution were determined by direct calorimetry. The standard thermodynamic characteristics of these equilibria were calculated. The results obtained were compared with the corresponding data for related compounds.
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Acid dissociation constants of β-alanylglycine (HL) were determined in a number of papers [1–4]. These studies, on the whole, were made on a high experimental level. The pK values obtained are well consistent. The following values can be accepted as the most probable thermodynamic constants of stepwise dissociation of β-alanylglycine: pK^0(H_2L^+) 3.24 ± 0.03; pK^0(HL) 9.62 ± 0.08. At the same time, the thermal effects of the corresponding reactions are unknown. The lack of this important information makes it necessary to examine the protolytic equilibria of β-alanylglycine by direct calorimetry.

Significant difference in the constants of stepwise dissociation of β-alanylglycine allows independent determination of the thermal effects of reactions (1) and (2):

$$H_2L^+ \rightleftarrows H^+ + HL, \quad (1)$$

$$HL \rightleftarrows H^+ + L. \quad (2)$$

It is seen from the speciation diagram (see figure) that the thermal effects of dissociation of H_2L^+ and HL can be found as differences between the corresponding heats of mixing and dilution:

$$\Delta_{dis}H = -(\Delta_{mix}H - \Delta_{dil}H)/\alpha, \quad (3)$$

where $\Delta_{mix}H$ is the thermal effect of mixing of an HNO_3 solution with a solution of β-alanylglycine in the presence of a supporting electrolyte in the corresponding pH range; $\Delta_{dil}H$ is the thermal effect of dilution of HNO_3 in the supporting electrolyte at the same ionic strength; and α is the degree of protonation of HL and L^-. The obtained thermal effects of stepwise dissociation of β-alanylglycine at 298.15 K and I = 0.1, 0.5, and 1.0 (KNO_3) are given in Table 1.

The quantities $\Delta_{dis}H$ at fixed ionic strengths allow calculation of the standard thermodynamic characteristics of the equilibria under consideration. To extrapolate the concentration thermal effects to zero ionic strength, we used an equation with one individual parameter [5]:

$$\Delta_{dis}H - \Delta z^2\Psi(I) = \Delta_{dis}H^0 + b, \quad (4)$$

where $\Delta_{dis}H$ and $\Delta_{dis}H^0$ are the enthalpies of dissociation at given and zero ionic strength, respectively; b is an empirical coefficient; Δz^2, difference between the squared charges of the reaction products and reactants; $\Psi(I)$, theoretically calculated function of the ionic strength [5]. The standard thermodynamic characteristics of the dissociation of β-alanylglycine are given in Table 2, together with the results of calorimetric studies of glycylglycine [6] and β-alanyl-β-alanine [7], obtained previously in our laboratory.

The reactions of stepwise dissociation of these dipeptides are characterized by close thermal effects; the variation of $\Delta_{dis}H^0$(HL) in going from glycylglycine to β-alanylglycine and β-alanyl-β-alanine is well consistent with that observed in going from glycine (44.19 kJ mol^{-1} [8]) to β-alanine (47.16 kJ mol^{-1} [9]). Replacement of the glycine fragments of dipeptides by β-alanine fragments leads to a decrease in $\Delta_{dis}S^0$ of the corresponding dissociation reactions by 10–16 J mol^{-1} K^{-1}. Such a behavior is apparently caused by an increase in the degree of hydration of the dipeptides in the series glycylglycine–β-alanylglycine–β-alanyl-β-alanine due to increasing distance between

Table 1. Thermodynamic characteristics of stepwise dissociation of β-alanylglycine at 298.15 K and I = 0.1, 0.5, and 1.0 (KNO_3)

I (KNO_3)	pK	$\Delta_{dis}G$, kJ mol^{-1}	$\Delta_{dis}H$, kJ mol^{-1}	$-\Delta_{dis}S$, J mol^{-1} K^{-1}
		$H_2L^+ \rightleftarrows H^+ + HL$		
0.1	3.24 ± 0.03	18.49 ± 0.15	1.30 ± 0.14	57.7 ± 0.7
0.5	3.26 ± 0.03	18.61 ± 0.15	1.72 ± 0.13	56.6 ± 0.7
1.0	3.29 ± 0.03	18.78 ± 0.15	2.09 ± 0.15	56.0 ± 0.7
		$HL \rightleftarrows H^+ + L$		
0.1	9.42 ± 0.08	53.77 ± 0.46	48.37 ± 0.20	18.1 ± 1.7
0.5	9.33 ± 0.08	53.26 ± 0.46	48.97 ± 0.21	14.4 ± 1.7
1.0	9.33 ± 0.08	53.26 ± 0.46	49.68 ± 0.18	12.0 ± 1.7

Table 2. Standard thermodynamic characteristics of dissociation of glycylglycine, β-alanylglycine, and β-alanyl-β-alanine in aqueous solution

Dipeptide	pK^0	$\Delta_{dis}G^0$, kJ mol^{-1}	$\Delta_{dis}H^0$, kJ mol^{-1}	$-\Delta_{dis}S^0$, J mol^{-1} K^{-1}
		$H_2L^+ \rightleftarrows H^+ + HL$		
Glycylglycine	3.16 ± 0.01	18.04 ± 0.06	0.61 ± 0.14	58.5 ± 0.5
β-Alanylglycine	3.24 ± 0.03	18.49 ± 0.15	1.24 ± 0.15	57.9 ± 0.7
β-Alanyl-β-alanine	4.02 ± 0.02	22.93 ± 0.11	2.42 ± 0.28	68.8 ± 1.0
		$HL \rightleftarrows H^+ + L$		
Glycylglycine	8.31 ± 0.01	47.43 ± 0.06	44.19 ± 0.33	10.9 ± 1.1
β-Alanylglycine	9.62 ± 0.08	54.91 ± 0.46	47.83 ± 0.21	23.7 ± 1.7
β-Alanyl-β-alanine	9.59 ± 0.03	54.74 ± 0.15	46.70 ± 0.28	27.0 ± 1.3
		$H_2L^+ \rightleftarrows 2H^+ + L^-$		
Glycylglycine	11.47 ± 0.01	65.47 ± 0.09	44.80 ± 0.36	69.4 ± 1.2
β-Alanylglycine	12.86 ± 0.09	73.41 ± 0.48	49.07 ± 0.26	81.6 ± 1.8
β-Alanyl-β-alanine	13.61 ± 0.04	77.69 ± 0.19	49.12 ± 0.40	95.8 ± 1.5

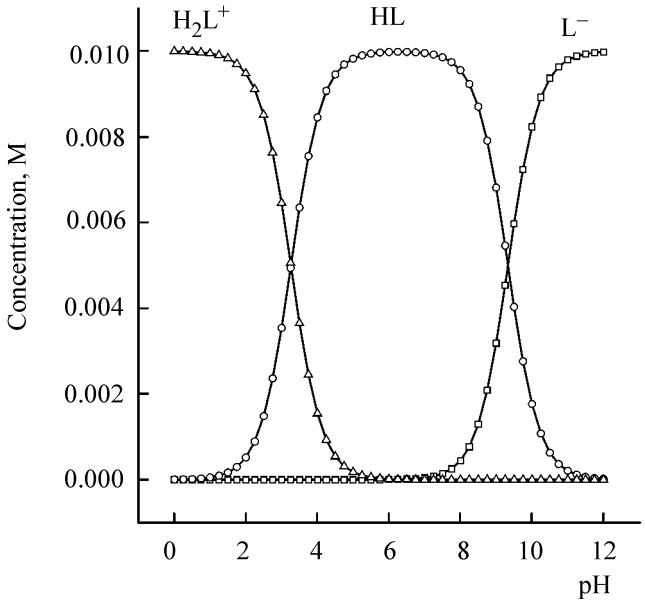

Diagram of the protolytic equilibria of β-alanylglycine in aqueous solution at 298.15 K and I 0.5 (KNO_3).

the sites of localization of the positive and negative charges.

EXPERIMENTAL

β-Alanylglycine (chemically pure grade) was purchased from Reanal (Hungary). Solutions of the dipeptide were prepared by dissolving its weighed portions in freshly double-distilled water just before experiments. Solutions of KOH and HNO_3 were prepared from chemically pure grade chemicals. The concentrations of working solutions were determined by common titration methods. Potassium nitrate (analytically pure grade) was recrystallized twice from double-distilled water before using for ionic strength adjustment.

Calorimetric measurements were performed in an ampule calorimeter with an isothermal shell, equipped with a thermistor temperature sensor and a device for automatic recording of the temperature variation in

time. The thermal effects of mixing of an HNO_3 solution (0.9470 mol kg^{-1} solution) with a 0.01 M solution of the dipeptide were measured in pH ranges 3.7–2.6 and 9.4–8.6 at 298.15 K and ionic strengths of 0.1, 0.5, and 1.0 (KNO_3). To make the required corrections, the heats of dilution of HNO_3 in a supporting electrolyte solution at the above-indicated ionic strengths were also measured.

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