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Short communication

Calorimetric determination of enthalpy changes for the proton ionization of glycine, *N*,*N*-bis(2-hyroxyethyl)glycine (“bicine”) and *N*-tris(hydroxymethyl)methylglycine (“tricine”) in water–methanol mixtures

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Abstract

Enthalpies for the two proton ionizations of glycine, *N*,*N*-bis(2-hyroxyethyl)glycine (“bicine”) and *N*-tris(hydroxymethyl)methylglycine (“tricine”) were obtained in water–methanol mixtures with methanol mole fraction (X_m) from 0 to 0.360. With increasing methanol the ionization enthalpy for the first proton (ΔH_1) of glycine increased from 4.4 to 9.4 kJ mol^{-1} with a minimum of 4.1 kJ mol^{-1} at $X_m = 0.059$. The ionization enthalpy of the second proton (ΔH_2) for glycine decreased from 46.3 to 38.1 kJ mol^{-1}. ΔH_1 of bicine increased from 3.5 to 7.6 kJ mol^{-1} at $X_m = 0.273$ before dropping to 4.1 kJ mol^{-1} at $X_m = 0.360$. ΔH_2 of bicine increased from 24.9 to 29.4 kJ mol^{-1}. For tricine, ΔH_1 increased from 6.7 to 9.8 kJ mol^{-1} at $X_m = 0.194$ then dropped to 7.4 kJ mol^{-1} at $X_m = 0.360$. ΔH_2 for tricine first dropped from 30.8 to 28.5 kJ mol^{-1} at $X_m = 0.059$ before increasing to 33.3 kJ mol^{-1} at $X_m = 0.273$. The solvent composition was selected so as to include the region of maximum structure enhancement of water by methanol. The results were interpreted in terms of solvent–solvent and solvent–solute interactions.

Keywords: Glycine; Bicine; Tricine; Proton ionization; Calorimetry

1. Introduction

A previous communication from this laboratory [1] reported on the enthalpies of proton ionization in water–methanol solutions of *N*,*N*-bis[2-hydroxyethyl]-2-aminoethanesulfonic acid (BES) and *N*-tris[hydroxymethyl] methyl-2-amino-ethansulfonic acid (TES). A second communication [2] dealt with *N*-[2-hyroxyethyl] piperazine-*N*′-[2-ethane sulfonic acid] (HEPES) and *N*-[2-hyroxyethyl] piperazine-*N*′-[2-hydroxyropane sulfonic acid] (HEPPSO). All four compounds are zwitterionic *N*-substituted amino sulfonic acid buffers used in biochemistry. This paper reports on similar studies of glycine and two derivatives containing strongly hydrophilic groups: *N*,*N*-bis(2-hyroxyethyl)glycine (“bicine”) and tris(hydroxymethyl)methylglycine (“tricine”). Reported pK_{a2} values of these buffers at 25 °C ($I = 0$) are 9.78 for glycine [3,4], 8.33 for bicine [5] and 8.13 for tricine [5]. Bicine and tricine are thus more suited than glycine as buffers for the physiologically important pH range. Measurements were made in water–methanol mixtures containing up to 50% (w/w) methanol, corresponding to a methanol mole fraction (X_m) of 0.360. As stated earlier [1], most thermodynamic measurements on buffers in mixed solvents have determined free energies of ionization. ΔH values have been obtained from potentiometric and spectrophotometric measurements [6–11].

2. Experimental

The procedure involving the operation and calibration of the Parr 1455 solution calorimeter has already been described [1] together with the method of data analysis. Glycine, bicine and tricine were Sigma chemicals, dried before use. The initial solution temperature was ca. 21 °C. ΔT varied in the range 0–0.2 °C for the addition of glycine, bicine and tricine to the various solutions and was precise to ±0.002 °C. The ionic strength of all solutions was maintained at 0.300 M by addition of NaCl. The

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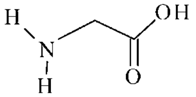
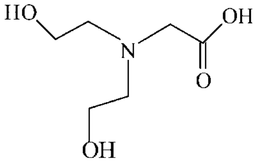
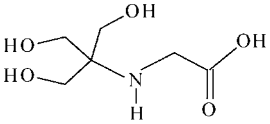
method followed was similar to that described by Ramette [12] for enthalpy determinations of the proton ionizations of glycine in water.

The starting materials were the zwitterionic forms ($HB^{\pm}$) of glycine, bicine and tricine:


glycine


bicine


tricine

Enthalpy changes were measured for:

$$HB^{\pm}(c) + H^{+} \rightarrow H_2B^{+}\,(soln.) \qquad \Delta H_A \tag{1}$$

$$HB^{\pm}(c) \rightarrow HB^{\pm}\,(soln.) \qquad \Delta H_B \tag{2}$$

and,

$$HB^{\pm}(c) + OH^{-} \rightarrow B^{-}\,(soln.) + H_2O \qquad \Delta H_C \tag{3}$$

The enthalpy of ionization of the first proton is given by:

$$H_2B^{+}\,(soln.) \rightarrow H^{+} + HB^{\pm}\,(soln.) \qquad \Delta H_1 = \Delta H_B - \Delta H_A \tag{4}$$

and ΔH_2 for the ionization of the second proton is given by:

$$\Delta H_2 = \Delta H_C - \Delta H_B - \Delta H_N \tag{5}$$

where ΔH_N is the enthalpy change for the neutralization reaction $H^{+} + OH^{-} \rightarrow H_2O$ (soln.). Values for ΔH_N at each solvent composition and ionic strength of 0.300 M have been reported earlier [1].

3. Results and discussion

Table 1 lists values of ΔH_A, ΔH_B, ΔH_c, ΔH_1 and ΔH_2 for glycine, bicine and tricine. With the exception of ΔH_A and ΔH_2 for glycine, a general trend of increase in enthalpy with methanol addition is noted. The trend is similar to that observed for the four sulphonate buffers already investigated [1,2] and has been attributed to less favorable solvation of H_2B^{+}, $HB^{\pm}$ and B^{-} as the dielectric constant of the medium is decreased by methanol addition ($\varepsilon_{H_2O} = 78.3$; $\varepsilon_{methanol} = 32.6$, at 25 °C). It is noteworthy that the increase is much more pronounced for ΔH_C. ΔH_C for glycine rose from 2.9 to 17.7 kJ mol^{-1}, for bicine from −9.2 to17.8 kJ mol^{-1} and for tricine from −3.8 to 20.7 kJ mol^{-1}. This observation is consistent with the view that the zwitterion dissociation, accompanied by ion creation, becomes increasingly unfavorable with methanol addition.

With methanol addition, ΔH_1 for glycine increases steadily from 4.4 to 9.4 kJ mol^{-1}. For bicine the change from 3.5 to 4.1 kJ mol^{-1} has a maximum of 7.6 kJ mol^{-1} at $X_m = 0.273$. For tricine the change from 6.7 to 7.4 kJ mol^{-1} has a maximum of 9.8 kJ mol^{-1} at $X_m = 0.194$. Reported values for ΔH_1 in water are 4.4 kJ mol^{-1} ($I = 0.2$ M) for glycine [13] and 5.88 ($I = 0$) for tricine [6]. It was not possible to obtain a reliable value for ΔH_1 of bicine from tabulated [14] pK_{a1} values at several temperatures, due to the large disagreements between data from various

Table 1
ΔH_A, ΔH_B, ΔH_c, ΔH_1 and ΔH_2 for glycine, bicine and tricine in water-methanol mixtures

X_m	ΔH_A (±0.2 kJ mol^{-1})	ΔH_B (±0.2 kJ mol^{-1})	ΔH_C (±0.2 kJ mol^{-1})	ΔH_1 (±0.2 kJ mol^{-1})	ΔH_2 (±0.2 kJ mol^{-1})
Glycine					
0	9.9	14.3	2.9	4.4	46.3
0.059	10.3	14.4	8.0	4.1	45.5
0.123	9.6	16.0	11.3	6.4	42.5
0.194	8.7	16.5	14.8	7.8	42.2
0.273	9.7	17.7	16.1	8.0	39.7
0.360	9.1	18.5	17.7	9.4	38.1
Bicine					
0	20.1	23.6	−9.2	3.5	24.9
0.059	20.4	26.3	−0.8	5.9	24.8
0.123	21.7	28.3	7.1	6.6	26.0
0.194	22.6	28.5	12.6	5.9	28.0
0.273	22.2	29.8	15.8	7.6	27.4
0.360	23.3	27.4	17.8	4.1	29.4
Tricine					
0	16.4	23.1	−3.8	6.7	30.8
0.059	17.4	26.3	2.9	8.9	28.5
0.123	18.5	27.7	9.7	9.2	29.2
0.194	19.0	28.8	15.2	9.8	30.3
0.273	20.0	27.9	19.8	7.9	33.3
0.360	21.6	29.0	20.7	7.4	30.7

sources. It is useful to compare the trend in ΔH_1 with that in pK_{a1}. At 25 °C ($I = 0$) pK_{a1} is 2.33 for glycine [15], 2.23 for bicine [16] and 2.02 for tricine [6]. A number of observations and compilations indicate that, within a given class of acids, an increase in pK is associated with an increase in proton ionization enthalpy [14,15,17]. Tricine, however, appears to deviate from this pattern, since among the three buffers investigated it has the lowest pK_{a1} but the highest ΔH_1. The apparent anomaly may be due to large negative entropy of ionization of the second proton. Furthermore, high negative entropy would result from high solvent orientation of the B^- ion [4]. In the case of tricine, solvent orientation is likely to be enhanced by the presence of three hydroxyl groups. The appearance of maxima may be rationalized on the basis of two competing effects within the solvent [18]. These are (a) higher zwitterion stabilization in water than water + methanol and (b) better solubilization of protons in water + methanol than in water. Notwithstanding the low value of pK_{a1}, reaction (1) can be considered essentially complete because of the large excess of HCl used (0.300 M HCl versus ~0.02 M for the three buffers).

Table 1 lists the following ΔH_2 changes, starting from water: for glycine, a decrease from 46.3 to 38.1 kJ mol^{-1}; for bicine, an increase from 24.9 to 29.4 kJ mol^{-1}; for tricine, an increase from 30.8 to 33.3 kJ mol^{-1} at $X_m = 0.273$ followed by a drop to 30.7 kJ mol^{-1}. It is noteworthy that ΔH_2 for glycine decreases with methanol addition. This is contrary to the behavior observed with BES and TES [1], HEPES and HEPPSO [2], bicine and tricine. A possible explanation is that the conjugate base of glycine, by virtue of its relatively small size, is more highly oriented in water than in water–methanol. A high entropic contribution to changes in ΔH_2 of glycine with methanol addition is supported by the observation that pK_{a2} for glycine is relatively not very sensitive to methanol (at 25 °C and $I = 0$ pK_{a2} is 9.78 in water and 9.58 in 50% methanol [4]).

It is instructive to compare the trends in ΔH_2 and pK_{a2}. At 25 °C and $I = 0$ pKa_2 is 9.78 for glycine [3,4], 8.33 for bicine [5] and 8.13 for tricine [5]. The higher ΔH_2 for glycine is thus as would be expected from its higher pKa_2 [14,15,17]. However, ΔH_2 values for bicine are significantly lower than those for tricine. This apparent anomaly can be attributed to entropic contributions. Reported ΔS of ionization values are −71.1 and −50.6 J K^{-1} mol^{-1} for bicine and tricine [19]. The smaller ΔS of tricine may be partially due to its relatively large size. The smaller ΔH_2 may be explained, as in the case of ΔH_1, by higher solvation of the conjugate base. Such a process would be similarly enhanced by the three hydroxyl groups. As has been stated in the previous communications [1,2], it is important to note trends in ΔH trends are much more difficult to interpret than those in ΔG. Enthalpy changes arise from electrostatic contributions [20] as well as structural and steric factors. It is often difficult to assess the relative contributions of these factors [21]. On the other hand, free energy changes can be understood in purely electrostatic and nonelectrostatic terms. It is hoped that additional data on proton ionization enthalpies in amphiprotic solvents such as water–methanol could lead to improved understanding of the factors involved in the ionization and solvation processes.

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