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Thermodynamic Parameters for the Ionization of Some Amino Acids, Benzoic Acid, Aminobenzoic Acids, and Organic Nitrogen Compounds in Ethanol + Water at 25 °C

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Enthalpies of ionization of glycine, *dl*-α- and *dl*-β-alanines, nicotinic, picolinic, benzoic, and *o*-, *m*-, and *p*-aminobenzoic acids, aniline, pyridine, trigonelline, and ethyl nicotinate have been measured in 0−47.5 mol % ethanol in ethanol + water at 25 °C. The results are coupled with previously reported thermodynamic dissociation constant values, and the values of the entropy changes have been calculated. The findings are discussed in terms of the solvent effect on the ionization of these compounds.

Introduction

The thermodynamic parameters regarding dissociation of organic acids/bases in mixed solvent systems are relatively few (*1−4*). Despite the great importance of amino acids and pyridinecarboxylic acids, there have been few studies on the thermodynamics of ionization in aquo−organic binary solvent systems (*5−7*). Further, the zwitterionic or dipolar nature of these acids makes them a distinct class of organic acids as compared to simple aliphatic or aromatic acids. These compounds could play a role in biological synthesis or decay. Generally such acids dissociate in aqueous or mixed solvents according to equilibria 1 and 2,

$$RH_2^+ + S \overset{K_1}{\rightleftharpoons} (H^+S) + RH^\pm \qquad (1)$$

$$RH^\pm + S \overset{K_2}{\rightleftharpoons} (H^+S) + R^- \qquad (2)$$

where $R^\pm$, RH_2^+, and R^- are the carboxylic acid and its cationic and anionic forms, respectively, and S refers to water or another solvent (mixture). The thermodynamic dissociation constant values for benzoic, picolinic, nicotinic, and *o*-, *m*-, and *p*-aminobenzoic acids, glycine, *dl*-α- and *dl*-β-alanines, aniline, pyridine, trigonelline, and ethyl nicotinate in some ethanol + water mixtures have been reported previously (*8*), at 25 °C. The present paper reports the enthalpies of ionization of these acids ($\Delta H_1°$ and $\Delta H_2°$ with respect to processes 1 and 2) which were measured calorimetrically in the same solvent mixtures and at the same temperature. These results are coupled with values of the standard free energy changes ($\Delta G_1°$ and $\Delta G_2°$), and the values of the entropy changes (ΔS_1 and ΔS_2) have been calculated and are reported. The changes in the thermodynamic parameters for the ionization of these acids are discussed on the basis of changes in the solvent mixture compositions.

Experimental Section

(a) Chemicals. All the acids and bases used were of analytical grade purity from E. Merck. The purity of the substances was checked from their melting point and elemental analysis. Absolute ethanol (99.5 mass %) from E. Merck was used as such without further purification. Doubly distilled water was used as the aqueous medium or as a component of the ethanol + water mixtures.

(b) Procedure. The enthalpies of ionization of the acids and anilinium and pyridinium ions and other compounds were determined calorimetrically, using a calorimeter designed by Brandstetr *et al.* (*9*) and following the procedure of Christensen *et al.* (*10*). The calorimeter consists of a glass vessel placed in a Dewar flask of about 250 cm^3 volume, kept of 25 ± 0.01 °C in a water bath. A volume of 100 cm^3 of 0.01 M solution of each acid (in water or mixture) was taken in the vessel and thermostated for at least 4 h. A 5 mass % NaOH or $HClO_4$ solution (in the same solvent medium) was added to the acidic solution. The contents of the calorimeter were stirred mechanically, and changes in temperature were recorded on a millivoltmeter EZ4 (Laboratory Apparatus, Praha). Two thermistors were used for the determination of energy changes. One was kept in the vessel, and the other was for calibration purposes. The calorimeter was calibrated using an electric heater. Two different sets of measurements were made in order to assess the precision and accuracy of the calorimeter. The enthalpies were measured at 0.05, 0.1, 0.2, and 0.3 M ionic strengths maintained with $NaClO_4$ or tetramethylammonium perchlorate (Me_4NClO_4), both from Merck. NaOH solutions were standardized with potassium hydrogen phthalate which were further used to standardize the $HClO_4$ solutions in the same solvent.

The method for the determination of thermodynamic dissociation constants for these compounds has been described elsewhere (*8*).

Results and Discussion

The values of the standard Gibb's free energy changes ($\Delta G_1°$ and $\Delta G_2°$) listed in Table 1 were calculated from the pK_a (thermodynamic dissociation constants) values (reported elsewhere (*8*)), using the relationship

$$\Delta G° = -RT \ln K_a \qquad (3)$$

$$= 5.707 pK_a \text{ kJ·mol}^{-1} \qquad (4)$$

at 25 °C. The pK_a values were obtained at zero ionic strength, from the pK_a vs $I^{1/2}$ (where I = ionic strength) plots. The enthalpic changes for reactions 1 and 2 were

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[§] Deceased. This paper is dedicated to Professor J. Mollin with respect and affection by M. S. K. Niazi.

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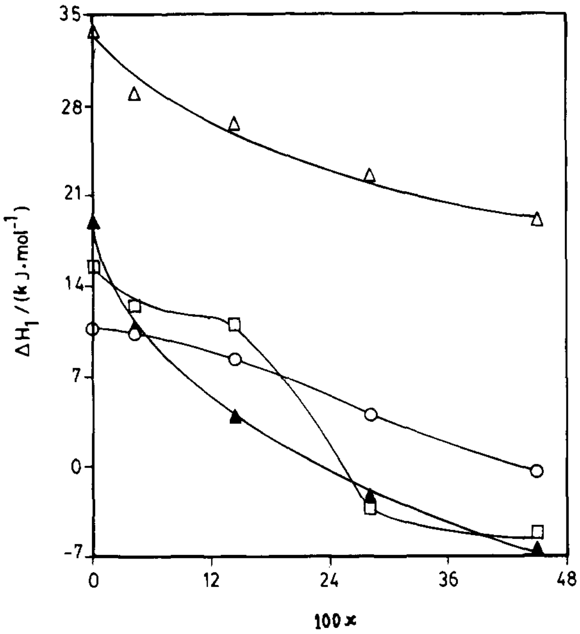

Figure 1. Dependence of enthalpy of ionization values (ΔH_1) for acids on the composition of x ethanol + $(1 - x)$ water at 25 °C: (△) anilinium ion; (□) 2-aminobenzoic acid; (○) 3-aminobenzoic acid; (▲) 4-aminobenzoic acid.

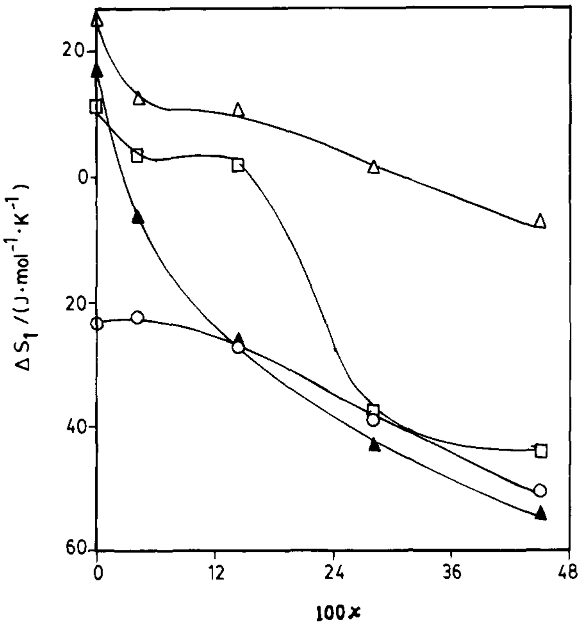

Figure 2. Dependence of entropy of ionization values ($\Delta S_1°$) for acids on the composition of x ethanol + $(1 - x)$ water at 25 °C: same acids as in Figure 1.

calculated from the expression

$$\Delta H°_{\mathrm{obs}} = Q/1000X \qquad (5)$$

at different ionic strengths, where Q is the energy liberated when X mols of acid/base is neutralized by NaOH or $HClO_4$. These values relate the ionic strength through the relationship

$$\Delta H = f(I^{1/2}/(1 + I^{1/2})) \qquad (6)$$

and extrapolate to zero ionic strength. The values of the enthalpy changes ($\Delta H_1°$ and $\Delta H_2°$) given in Table 1 (at zero ionic strength) were calculated as

$$\Delta H°_{H_2O} + \Delta H°_{\mathrm{ioniz}} = \Delta H°_{\mathrm{obs}} \qquad (7)$$

The values of neutralization of $HClO_4$ with NaOH in

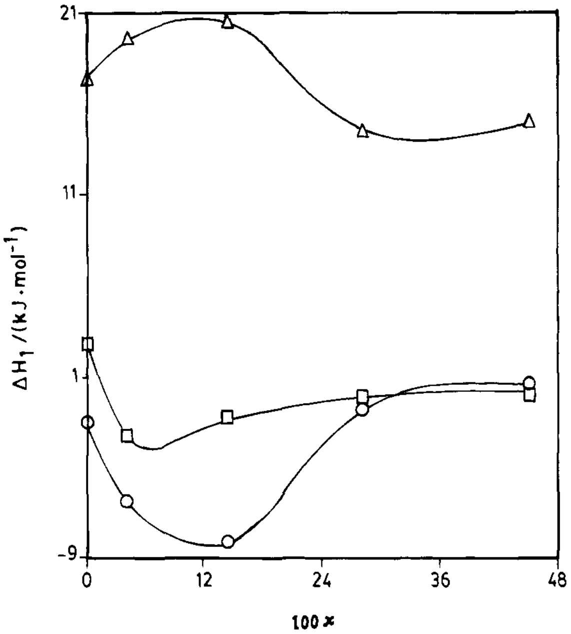

Figure 3. Dependence of enthalpy of ionization values ($\Delta H_1°$) on the composition of x ethanol + $(1 - x)$ water at 25 °C: (△) pyridinium ion; (□) nicotinic acid; (○) picolinic acid.

solvent mixtures were also measured and are 56.54, 57.52, 56.54, 49.64, and 42.40 kJ·mol^{-1} in 0, 10, 30, 50, and 71.5 mass % ethanol + water mixtures, respectively. These values are in very close agreement with those reported by Avedikian *et al.* (*3*). The values of the entropy change ($\Delta S°$) on ionization of acids were calculated from the thermodynamic relationship

$$\Delta G° = \Delta H° - T\delta S° \qquad (8)$$

The thermodynamic parameters are collected in Table 1. The errors in the values of $\Delta H°$ and $\Delta S°$ as calculated from the uncertainties associated with experimental measurements are ±0.5–1 kJ·mol^{-1} and ±10–30 J·mol^{-1}·K^{-1}, respectively. No heats of dilution were measured, and therefore, no contribution of this factor is added in the reported values for $\Delta H°$.

(a) Comparison with the Literature Values. A number of values for the enthalpy of ionization for benzoic acid have been reported by many researchers in aqueous media (*10–16*). These values for $\Delta H°$ vary from −1.758 to +0.707 kJ·mol^{-1}. Christensen and co-workers have reported the thermodynamic parameters for ionization of a number of acids and bases in aqueous media in a series of papers (*10–13*). Comparing the present values with their values for the acids/bases, it is found that two sets of values in terms of the parameters $\Delta G°$, $\Delta H°$, and $\Delta S°$ agree within less than 5% for benzoic and aminobenzoic acids, pyridine, and aniline, and differ for nicotinic and picolinic acids, glycine, and α- and β-alanines for $\Delta H_1°$ values and consequently for $\Delta S_1°$. Chakravorty *et al.* (*5*) have reported thermodynamic parameters for the ionization of glycine and α-alanine in some methanol + water mixtures. It is not possible to compare our values with the values reported by them due to different solvent systems, but the values in aqueous media are in agreement within ±1–2%. Avedikian and Dollet (*3*) have measured $\Delta H°$ values for benzoic acid in different ethanol + water mixtures. These values are 0.42, −0.25, 1.96, 4.2, and 1.33 kJ·mol^{-1} in 0, 10, 30, 50, and 70 mass % ethanol + water mixtures at 25 °C. The values reported here for $\Delta H°_{\mathrm{ioniz}}$ for benzoic acid are 0.4, −0.2, 2.0, 4.1, and 1.3, respectively, in 0, 10, 30, 50, and 70 mass % ethanol + water mixtures which are in good

Table 1. Thermodynamic Parameters for Ionization of Acids in x Ethanol + $(1 - x)$ Water at 25 °C

x	$\Delta G_{\mathrm{i}}^\circ$/ (kJ·mol^{-1})	$\Delta H_{\mathrm{i}}^\circ$/ (kJ·mol^{-1})	$\Delta S_{\mathrm{i}}^\circ$/ (J·mol^{-1}·K^{-1})	ΔG_2°/ (kJ·mol^{-1})	ΔH_2°/ (kJ·mol^{-1})	ΔS_2°/ (kJ·mol^{-1}·K^{-1})
		Anilinium Ion			Benzoic Acid	
0	26.2	33.7	25.2	23.9	0.4	−78.8
0.042	25.2	28.9	12.4	24.5	−0.2	−82.8
0.143	23.9	26.9	10.1	29.9	2.0	−93.6
0.281	22.0	22.3	1.0	32.4	4.1	−94.9
0.475	21.3	19.0	−7.7	35.6	1.3	−115.0
			2-Aminobenzoic Acid			
0	12.2	15.6	11.4	28.4	11.7	−56.0
0.042	11.7	12.7	3.4	28.7	11.2	−58.7
0.143	10.4	11.0	2.0	31.0	10.9	−67.4
0.281	8.2	−3.1	−37.9	35.1	4.1	−104.0
0.475	7.8	−5.2	−43.6	38.5	−0.7	−131.5
			3-Aminobenzoic Acid			
0	17.7	10.7	−23.5	27.3	17.6	−32.5
0.042	17.2	10.5	−22.5	27.9	16.4	−38.6
0.143	16.3	8.3	−26.8	29.3	10.4	−62.4
0.281	15.5	4.0	−38.6	31.4	4.3	−90.9
0.475	14.5	−0.5	−50.3	35.3	2.0	−111.7
			4-Aminobenzoic Acid			
0	13.8	18.9	17.1	28.0	2.9	−84.2
0.042	12.6	10.5	−7.0	29.0	4.3	−82.8
0.143	11.7	3.8	−26.5	32.2	11.7	−68.8
0.281	10.3	−2.6	−43.3	36.9	6.2	−102.9
0.475	9.6	−6.5	−54.0	40.2	3.3	−123.8
			Nicotinic Acid			
0	11.9	3.0	−29.9	27.6	8.0	−65.7
0.042	11.3	−2.2	−45.3	26.1	10.9	−51.0
0.143	10.8	−1.2	−40.2	24.9	6.7	−61.0
0.281	10.1	−0.2	−34.5	26.3	1.0	−84.9
0.475	9.7	0.2	−31.9	28.7	−4.2	−110.3
			Picolinic Acid			
0	10.4	−1.5	−39.9	31.2	7.0	−81.2
0.042	9.9	−5.8	−52.7	30.2	14.2	−53.7
0.143	9.3	−8.1	−58.4	28.9	11.2	−59.4
0.281	8.8	−0.7	−31.9	29.9	6.9	−43.6
0.475	9.2	0.5	−29.2	30.9	0.1	−103.3
		Pyridinium Ion			Ethyl Nicotinate	
0	29.3	17.4	−39.9	18.1	7.7	−34.9
0.042	27.9	19.5	−28.2	16.7	8.9	−26.2
0.143	24.9	20.5	−14.8	15.1	5.1	−33.5
0.281	22.4	14.5	−26.5	10.2	1.6	−28.8
0.475	20.2	15.0	−17.4	9.6	0.5	−30.5
		Trigonelline				
0	16.7	−7.3	−80.5			
0.042	16.9	−8.9	−86.5			
0.143	17.1	−10.2	−91.6			
0.281	17.1	−10.1	−91.2			
0.475	17.1	−7.3	−81.8			
			Glycine			
0	13.6	−1.2	−49.6	55.8	42.5	−44.6
0.042	14.1	−4.8	−63.4	55.0	47.3	−25.8
0.143	15.2	−3.6	−63.0	53.5	45.9	−25.5
0.281	17.4	−0.7	−60.7	53.7	37.3	−55.0
0.475	18.3	1.3	−57.0	54.7	33.4	−71.4
			α-Alanine			
0	13.6	−0.8	−48.3	56.3	48.0	−27.8
0.042	14.2	−4.9	−64.1	55.5	55.4	−0.3
0.143	15.7	−2.6	−61.4	54.5	50.0	−15.1
0.281	17.8	−1.1	−63.4	54.9	44.0	−36.6
0.475	19.6	2.0	−59.0	55.8	37.9	−60.0
			β-Alanine			
0	20.4	2.5	−60.0	58.4	47.1	−37.9
0.042	20.8	−5.2	−87.2	57.2	55.2	−6.7
0.143	22.8	−1.1	−78.2	56.2	50.4	−19.5
0.281	23.5	1.2	−74.8	55.9	44.8	−37.2
0.475	25.7	3.8	−73.5	57.0	40.6	−55.0

agreement with those reported by Avedekin *et al.* Ashton *et al.* (*17*) have reported $\Delta H_1°$ and $\Delta H_2°$ values for nicotinic acid in water as -11.7 ± 1.0 and -3.3 kJ·mol^{-1}, respectively. Our values are 3 and 8 kJ·mol^{-1}. Their values have been obtained from the temperature coefficient of pK_a values and also differ from those of Christensen *et al.* (*10–13*). Our values agree with those of Christensen *et al.* (13) which are 3.13 and 9.45, respectively. Further, we could

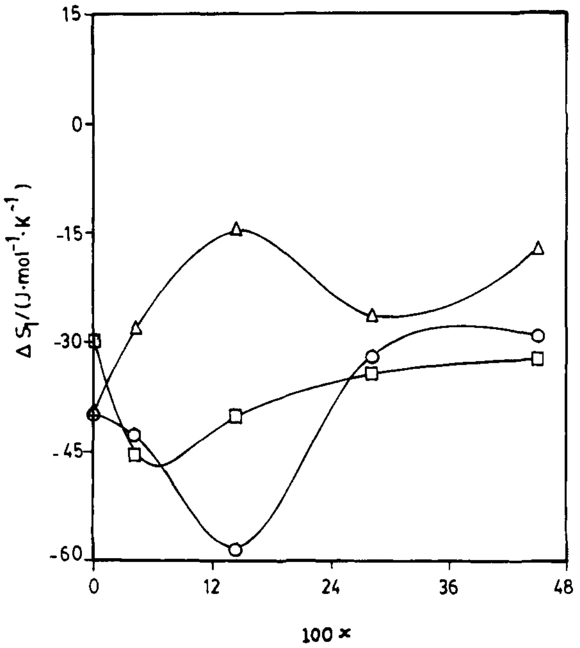

Figure 4. Dependence of entropy of ionization values ($\Delta S_1°$) on the composition of x ethanol + $(1 - x)$ water at 25 °C: same acids as in Figure 3.

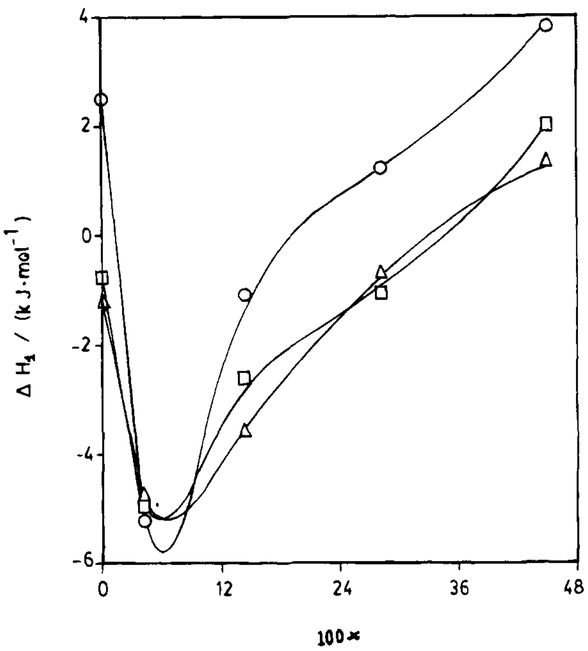

Figure 5. Dependence of enthalpy of ionization ($\Delta H_1°$) values for acids on the composition of x ethanol + $(1 - x)$ water at 25 °C: (△) glycine; (□) α-alanine; (○) β-alanine.

not find literature values for other compounds in these solvent mixtures; therefore, a comparison could not be made.

(b) Solvent Effect. The variation of the thermodynamic parameters for the ionization for different compounds with the composition of ethanol + water listed in Table 1 can be shown graphically. Figures 1–3 are plots showing the dependence of $\Delta H_1°$ and $\Delta S_1°$ values for the acids on the composition of ethanol + water. Similar plots can be shown for second ionization values. These figures indicate that there are structural changes in the amino acids and pyridinecarboxylic acids as they transfer from aqueous to ethanolic water mixtures. There are differences in the specific solvation of the acids with solvent mixtures; hence, the dependence on the composition is not regular but sigmoidal, and extrema in these plots are seen for some acids. These plots indicate that there is a distinct difference in the nature of interaction between the protonation of COO^- and NH_2 groups. Due to the more zwitterionic nature of the amino acids and pyridinecarboxylic acids as compared to the aminobenzoic acids, differences in these plots are seen.

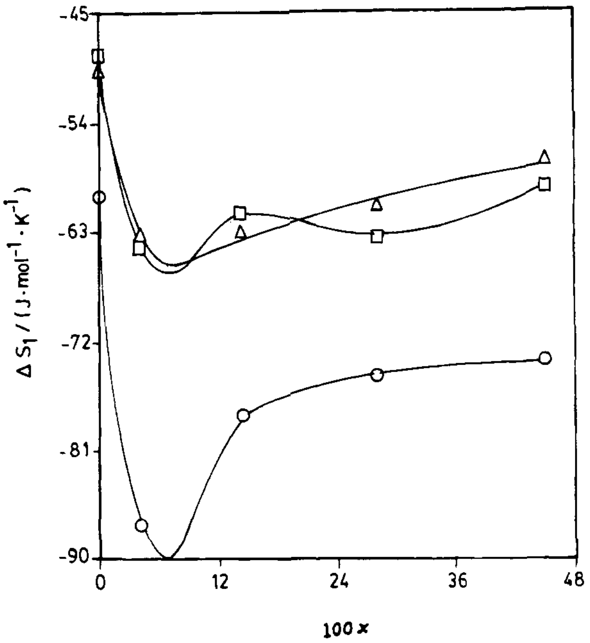

Figure 6. Dependence of entropy of ionization ($\Delta S_1°$) values for acids on the composition of x ethanol + $(1 - x)$ water at 25 °C: same acids as in Figure 5.

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