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# Thermodynamics of Protonation of Amino Acid Carboxylate Groups from 50 to 125°C

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*Flow calorimetry has been used to study the interaction of glycine, DL-α-alanine, DL-2-aminobutyric acid, β-alanine, 4-aminobutyric acid, and 6-aminocaproic acid with protons in aqueous solutions from 323.15 K to 398.15 K and at 1.52 MPa. LogK, $\Delta H^\circ$, $\Delta S^\circ$, and $\Delta C_p^\circ$ for the protonation of the carboxylate groups of these amino acids have been obtained at each temperature studied. Equations are given expressing these values as functions of temperature. The protonation reactions are exothermic at lower temperatures and become endothermic as temperature increases. The logK, $\Delta H^\circ$, and $\Delta S^\circ$ values are close together over the temperature range studied for the protonation of α-amino acids, i.e., glycine, DL-α-alanine, and 2-aminobutyric acid. At each temperature, the magnitudes of these thermodynamic quantities increase as the number of methylene groups between the amino group and the carboxylate group increases. The $\Delta C_p^\circ$ value for the protonation of the carboxyl group is found to lie between those of an isocoulombic reaction and a charge reduction reaction. At 323.15 K, the protonation reactions of the carboxylate groups have larger $\Delta C_p^\circ$ values which approach those associated with charge reduction reactions. As the temperature increases, $\Delta C_p^\circ$ decreases and approaches those found for isocoulombic reactions. This result is explained by considering long-range and short-range solvent effects. The trend in $\Delta H^\circ$ and $\Delta S^\circ$ with temperature and with charge separation in the zwitterions is interpreted in terms of solvent–solute interactions and the electrostatic interaction of the two oppositely charged groups within the molecule.*

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**KEY WORDS:** Protonation; amino acids; carboxylate groups; thermodynamic quantities; aqueous solutions; solvent–solute interactions; zwitterions; elevated temperatures; and calorimetry.

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# 1. INTRODUCTION

A quantitative knowledge of log*K* for proton ionization of proteins and their constituent amino acids in high temperature aqueous solutions is important in understanding biochemical reactions. Understanding the energetics of these reactions should help answer questions concerning the existence of life forms at high temperatures.(1) Recently, we have studied the protonation of the amino group for several amino acids up to 125°C.(2,3) $\Delta H^\circ$ and $\Delta S^\circ$ for these protonation reactions increase while log*K* decreases with temperature. Separation of the zwitterion charges on the carbon chain was found to be more important than the length of the carbon chain in understanding the temperature dependence of the thermodynamic properties. These results provide information valuable for an understanding of the effect of neighboring groups in biopolymers (polypeptides, proteins, enzymes, nucleic acids, *etc.*) on ion association involving various functional groups.

In the present work, log*K*, $\Delta H^\circ$, $\Delta S^\circ$, and $\Delta C_p^\circ$ for the protonation of the carboxylate group of glycine, DL-α-alanine, DL-2-aminobutyric acid, β-alanine, 4-aminobutyric acid and 6-aminocaproic acid were determined calorimetrically from 50 to 125°C (323.15 to 398.15 K) in order to learn the effect of temperature, molecular size, and zwitterion charge separation on these quantities.

The protonation reaction of the carboxylate group of an amino acid can be expressed by

$$^{+}NH_3(CH_2)_nCHR_1COO^- + H^+ = {}^{+}NH_3(CH_2)_nCHR_1COOH \qquad (1)$$

where $R_1 = H$ and $n = 0$ for glycine, $R_1 = CH_3$ and $n = 0$ for DL-α-alanine, $R_1 = CH_2CH_3$ and $n = 0$ for DL-2-aminobutyric acid; $R_1$ is H and $n = 1$ for β-alanine, $R_1 = H$ and $n = 2$ for 4-aminobutyric acid, and $R_1 = H$ and $n = 4$ for 6-aminocaproic acid. The effect of pressure on the protonation was not investigated in the present study, but is expected to be small at pressures from atmospheric up to the experimental pressure.(2,4)

Values of log*K*, $\Delta H^\circ$, $\Delta S^\circ$, and $\Delta C_p^\circ$ below 50°C for reaction 1 for the amino acids studied have been reported.(5–27) Reviews and compilations of thermodynamic quantities for interactions of protons and metal ions with amino acids are available.(5–7) Log*K* for the protonation of glycine have been reported up to 50°C.(10) No $\Delta H^\circ$, $\Delta S^\circ$, and $\Delta C_p^\circ$ values are available for reaction 1 at temperatures above 50°C for any of the amino acids studied.

# 2. EXPERIMENTAL

## 2.1. Materials

The chemicals used in this study were glycine (99+%), DL-α-alanine (99+%), β-alanine (99+%), DL-2-aminobutyric acid (99+%), 4-aminobutyric acid (97%) and 6-aminocaproic acid (98%), from Aldrich, and hydrochloric acid from Fisher (standard solution). The solutions were made using distilled, deionized water and were degassed by submersion in an ultrasonic bath for 5–10 minutes. The HCl solutions were standardized by titration using a known tris[hydroxymethyl]aminomethane solution made from Sigma 99.9% pure reagent. The molar concentrations thus obtained were converted to molalities using the density data for amino acid and HCl solutions from the literature.(28–30)

## 2.2. Method

The isothermal flow calorimeter used in this study has been described.(31) Heat of reaction data for the titration of the amino acid solutions with HCl solutions were measured at 50, 75, 100, and 125°C and at 1.52 MPa. The concentrations of the HCl and amino acid solutions for each run were approximately the same. The flow rate for each amino acid solution was set to a constant value and that of the HCl solution was varied so that the molar ratio for proton to amino acid ranged approximately from 0.25:1 to 1.6:1. No vapor phase was present in the experiments negating the need for vaporization corrections. Details of the data reduction method are available.(4)

## 2.3. Calculations

The experimental heat of reaction data were analyzed by a computer program to derive $\log K$ and $\Delta H^\circ$ values valid at zero ionic strength at each temperature. The Pitzer ion-interaction activity coefficient model(32) was used to extrapolate $\log K$ and $\Delta H^\circ$ values to zero ionic strength and to find the $\log K$ and $\Delta H^\circ$ which gave the best agreement between predicted and measured heats as has been described.(4) The temperature dependent interaction parameters for the Pitzer activity coefficient model were found by fitting heat of dilution data for the neutral amino acids (zwitterions)(3) and the amino acid chlorides to the cubic functions of temperature

$$\phi = A + B(T - 298.15) + C(T - 298.15)^2 + D(T - 298.15)^3 \quad (2)$$

where $\phi$ is $\beta^{(0)}$, $\beta^{(1)}$, $C^\phi$, or $\lambda$. The value for $A$, the parameter at 298.15 K, was taken from the literature or estimated.(32,33) Literature values were used for the parameters for HCl.(34) The parameters for zwitterion–zwitterion interactions were taken from our previous study.(3) The protonation of the amino acids and the ionization of water(35) were included in the data reduction. Associated amino acid chloride and HCl(aq)(34,36) ion pairs do not exist in significant amounts at our experimental conditions.

## 3. RESULTS AND DISCUSSION

Table I gives the calorimetric data at each temperature for the reaction of HCl(aq) with the amino acids studied. Heats of dilution for the amino acid chlorides are given in Table II. Each of the experimental runs was repeated three times and the heat data are the averages of the measured heats for the triplicate runs. The maximum standard deviation over the entire set of triplicate runs was 0.03 J-min$^{-1}$. The coefficients in Eq. (2) are listed in Table III. Table IV gives log $K$, $\Delta H^\circ$, $\Delta S^\circ$, and $\Delta C_p^\circ$ for the protonation of the six amino acids studied, together with literature values for the protonation of these amino acids at zero ionic strength at lower temperatures. The uncertainties in log$K$, $\Delta H^\circ$, $\Delta S^\circ$, and $\Delta C_p^\circ$ were estimated using a statistical analysis of the experimental data as described previously.(37) The $Q_c$ values in Tables I and II were calculated using the log$K$ and $\Delta H^\circ$ values for reaction 1 obtained from this study.

The experimental heat data for the protonation reactions were fitted well over the temperature range of this study using

$$\log K = a + \frac{b}{T} + c\ln T + d\ln \rho_w \tag{3}$$

$$\Delta H^\circ = 2.303R\left[-b+cT + dT^2\left(\frac{\partial \ln \rho_w}{\partial T}\right)\right] \tag{4}$$

where $T$ is the temperature in Kelvins, $\rho_w$ is the density of water at the experimental pressure from Haar–Gallagher–Kell equation of state for water,(38) and $a$, $b$, $c$, and $d$ are fitting parameters. The fitting parameters were adjusted to allow the calculated log$K$ and $\Delta H^\circ$ to fit those reported in the literature at 25°C as well as the measured heat values. Temperature dependent equations for $\Delta S^\circ$ and $\Delta C_p^\circ$ are derived from Eqs. (3, 4) giving

$$\Delta S^\circ = 2.303R\left\{a + c + c\ln T + d\left[\ln \rho_w + T\left(\frac{\partial \ln \rho_w}{\partial T}\right)\right]\right\} \tag{5}$$

$$\Delta C_p^\circ = 2.303R\left\{c + d\left[2T\left(\frac{\partial \ln \rho_w}{\partial T}\right) + T^2\left(\frac{\partial^2 \ln \rho_w}{\partial^2 T}\right)\right]\right\} \tag{6}$$

Table V gives the coefficients for Eqs. (3–6) for reaction (1) as a function of temperature for each of the amino acids.

In Fig. 1, the variation with temperature of $\Delta H^\circ$ of reaction (1) for the amino acids studied shows an increase as temperature increases. The protonation reactions for these amino acids are exothermic at the lower temperatures, and become endothermic as temperature increases. The general

**Table I.** Calorimetric Data for the Reaction of Amino Acids with HCl at Various Temperatures and 1.52 MPa

| Flow A[a] | $Q_m$[b] | $Q_c$[b] |
|---|---|---|
| $T$ = 323.15 K; A:0.8557$m$ HCl; B (0.4692 $gH_2O\text{-}min^{-1}$):0.9375$m$ glycine | | |
| 0.1354 | −0.3434 | −0.3727 |
| 0.2031 | −0.5047 | −0.5398 |
| 0.2708 | −0.6472 | −0.6979 |
| 0.3385 | −0.7883 | −0.8463 |
| 0.4063 | −0.9153 | −0.9822 |
| 0.4740 | −1.0161 | −1.0967 |
| 0.5417 | −1.0785 | −1.1729 |
| 0.6094 | −1.1116 | −1.2125 |
| 0.6771 | −1.1285 | −1.2341 |
| $T$ = 323.15 K; A:0.6201$m$ HCl; B (0.4759 $gH_2O\text{-}min^{-1}$):0.6884$m$ glycine | | |
| 0.1360 | −0.2294 | −0.2337 |
| 0.2041 | −0.3376 | −0.3389 |
| 0.2721 | −0.4349 | −0.4398 |
| 0.3401 | −0.5322 | −0.5357 |
| 0.4081 | −0.5989 | −0.6248 |
| 0.4762 | −0.6550 | −0.7016 |
| 0.5442 | −0.6913 | −0.7576 |
| 0.6122 | −0.7185 | −0.7918 |
| 0.6802 | −0.7414 | −0.8129 |
| $T$ = 348.15 K; A:1.0448$m$ HCl; B (0.4695 $gH_2O\text{-}min^{-1}$):1.0382$m$ glycine | | |
| 0.1355 | −0.0560 | −0.0711 |
| 0.2032 | −0.0616 | −0.0701 |
| 0.2709 | −0.0566 | −0.0644 |
| 0.3387 | −0.0498 | −0.0577 |
| 0.4064 | −0.0364 | −0.0540 |
| 0.4741 | −0.0438 | −0.0615 |
| 0.5418 | −0.0548 | −0.0835 |
| 0.6096 | −0.0782 | −0.1103 |
| 0.6773 | −0.0964 | −0.1363 |
| $T$ = 373.15 K; A:0.6713$m$ HCl; B (0.4766 $gH_2O\text{-}min^{-1}$):0.6934$m$ glycine | | |
| 0.1363 | 0.1837 | 0.1954 |
| 0.2045 | 0.2996 | 0.3310 |
| 0.2727 | 0.4114 | 0.4708 |
| 0.3408 | 0.5461 | 0.6084 |
| 0.4090 | 0.6575 | 0.7348 |
| 0.4771 | 0.7415 | 0.8310 |
| 0.5453 | 0.7953 | 0.8797 |
| 0.6135 | 0.8264 | 0.8954 |
| $T$ = 373.15 K; A:0.3303$m$ HCl; B (0.4846 $gH_2O\text{-}min^{-1}$):0.3160$m$ glycine | | |
| 0.1371 | 0.1189 | 0.1181 |
| 0.2057 | 0.1834 | 0.1914 |
| 0.2742 | 0.2570 | 0.2648 |
| 0.3428 | 0.3167 | 0.3337 |
| 0.4114 | 0.3889 | 0.3916 |
| 0.4799 | 0.4167 | 0.4313 |
| 0.5485 | 0.4465 | 0.4533 |
| 0.6170 | 0.4691 | 0.4643 |
| $T$ = 398.15 K; A:0.9040$m$ HCl; B (0.4686 $gH_2O\text{-}min^{-1}$):1.0822$m$ glycine | | |
| 0.1358 | 0.3602 | 0.3398 |
| 0.2037 | 0.6294 | 0.5958 |
| 0.2716 | 0.8836 | 0.8653 |
| 0.3395 | 1.1476 | 1.1387 |
| 0.4076 | 1.4094 | 1.4078 |
| 0.4753 | 1.6457 | 1.6583 |
| 0.5431 | 1.8326 | 1.8554 |
| 0.6110 | 1.9375 | 1.9570 |
| 0.6789 | 1.9706 | 1.9892 |
| $T$ = 398.15 K; A:0.5970$m$ HCl; B (0.4804 $gH_2O\text{-}min^{-1}$):0.5132$m$ glycine | | |
| 0.1365 | 0.3183 | 0.2749 |
| 0.2047 | 0.5087 | 0.4577 |
| 0.2730 | 0.6947 | 0.6434 |
| 0.3412 | 0.8734 | 0.8164 |
| 0.4095 | 1.0027 | 0.9447 |
| 0.4777 | 1.0699 | 1.0045 |
| 0.5460 | 1.0933 | 1.0245 |
| 0.6142 | 1.1021 | 1.0300 |
| 0.6825 | 1.1087 | 1.0302 |
| $T$ = 323.15 K; A:1.0629$m$ HCl; B (0.4617 $gH_2O\text{-}min^{-1}$):1.0668$m$ DL-α-alanine | | |
| 0.1354 | −0.1994 | −0.1458 |
| 0.2031 | −0.2890 | −0.1898 |
| 0.2708 | −0.3661 | −0.2401 |
| 0.3385 | −0.4406 | −0.2997 |
| 0.4063 | −0.5042 | −0.3670 |
| 0.4740 | −0.5581 | −0.4332 |
| 0.5417 | −0.5981 | −0.4888 |
| 0.6094 | −0.6237 | −0.5372 |
| 0.6771 | −0.6407 | −0.5815 |

**Table I.** Continued

| Flow A[a] | $Q_m$[b] | $Q_c$[b] | Flow A[a] | $Q_m$[b] | $Q_c$[b] |
|---|---|---|---|---|---|
| $T$ = 323.15 K; A:0.5782$m$ HCl; B (0.4763 $gH_2O\text{-}min^{-1}$):0.5170$m$ DL-α-alanine | | | $T$ = 398.15 K; A:1.0196$m$ HCl; B (0.4617 $gH_2O\text{-}min^{-1}$):1.0666$m$ DL-α-alanine | | |
| 0.1365 | −0.0670 | −0.0546 | 0.1355 | 0.5073 | 0.4919 |
| 0.2048 | −0.0922 | −0.0621 | 0.2033 | 0.8244 | 0.8366 |
| 0.2731 | −0.1172 | −0.0665 | 0.2710 | 1.1371 | 1.1868 |
| 0.3414 | −0.1380 | −0.0698 | 0.3388 | 1.4484 | 1.5282 |
| 0.4096 | −0.1497 | −0.0732 | 0.4066 | 1.7530 | 1.8418 |
| 0.4779 | −0.1634 | −0.0773 | 0.4743 | 1.9844 | 2.0719 |
| 0.5462 | −0.1760 | −0.0819 | 0.5421 | 2.0891 | 2.1503 |
| 0.6144 | −0.1870 | −0.0866 | 0.6098 | 2.1012 | 2.1451 |
| 0.6827 | −0.1950 | −0.0913 | 0.6776 | 2.0879 | 2.1169 |
| $T$ = 348.15 K; A:1.0649$m$ HCl; B (0.4624 $gH_2O\text{-}min^{-1}$):1.0410$m$ DL-α-alanine | | | $T$ = 398.15 K; A:0.5597$m$ HCl; B (0.4763 $gH_2O\text{-}min^{-1}$):0.5172$m$ DL-α-alanine | | |
| 0.1354 | 0.0602 | 0.0689 | 0.1365 | 0.3742 | 0.3097 |
| 0.2031 | 0.1239 | 0.1364 | 0.2048 | 0.5908 | 0.5133 |
| 0.2708 | 0.1885 | 0.2073 | 0.2730 | 0.8040 | 0.7218 |
| 0.3385 | 0.2554 | 0.2769 | 0.3412 | 0.9990 | 0.9226 |
| 0.4062 | 0.3099 | 0.3357 | 0.4095 | 1.1571 | 1.0899 |
| 0.4739 | 0.3405 | 0.3600 | 0.4777 | 1.2291 | 1.1867 |
| 0.5417 | 0.3343 | 0.3480 | 0.5460 | 1.2521 | 1.2243 |
| 0.6094 | 0.3185 | 0.3251 | 0.6142 | 1.2605 | 1.2377 |
| 0.6771 | 0.3037 | 0.3013 | 0.6825 | 1.2620 | 1.2421 |
| $T$ = 373.15 K; A:1.0219$m$ HCl; B (0.4629 $gH_2O\text{-}min^{-1}$):1.0188$m$ DL-α-alanine | | | $T$ = 323.15 K; A:0.7120$m$ HCl; B (0.4624 $gH_2O\text{-}min^{-1}$):0.8018$m$ β-alanine | | |
| 0.1355 | 0.3074 | 0.2794 | 0.1354 | −0.5231 | −0.4856 |
| 0.2033 | 0.4994 | 0.4715 | 0.2031 | −0.7622 | −0.7007 |
| 0.2710 | 0.6942 | 0.6712 | 0.2708 | −0.9766 | −0.9085 |
| 0.3388 | 0.8860 | 0.8701 | 0.3385 | −1.1846 | −1.1108 |
| 0.4065 | 1.0616 | 1.0508 | 0.4062 | −1.3877 | −1.3082 |
| 0.4743 | 1.1711 | 1.1644 | 0.4739 | −1.5282 | −1.4987 |
| 0.5420 | 1.1983 | 1.1899 | 0.5416 | −1.5726 | −1.6358 |
| 0.6098 | 1.1922 | 1.1811 | 0.6094 | −1.5960 | −1.6830 |
| 0.6775 | 1.1835 | 1.1643 | 0.6771 | −1.6120 | −1.7165 |
| $T$ = 373.15 K; A:0.5207$m$ HCl; B (0.4763 $gH_2O\text{-}min^{-1}$):0.5170$m$ DL-α-alanine | | | $T$ = 323.15 K; A:0.6420$m$ HCl; B (0.4670 $gH_2O\text{-}min^{-1}$):0.6535$m$ β-alanine | | |
| 0.1367 | 0.2181 | 0.2065 | 0.1360 | −0.3639 | −0.3834 |
| 0.2050 | 0.3417 | 0.3319 | 0.2041 | −0.5272 | −0.5556 |
| 0.2734 | 0.4711 | 0.4587 | 0.2721 | −0.6750 | −0.7232 |
| 0.3417 | 0.5925 | 0.5816 | 0.3401 | −0.8207 | −0.8873 |
| 0.4100 | 0.7102 | 0.6898 | 0.4081 | −0.9563 | −1.0473 |
| 0.4784 | 0.7880 | 0.7643 | 0.4762 | −1.0891 | −1.1855 |
| 0.5467 | 0.8339 | 0.7982 | 0.5442 | −1.2000 | −1.2374 |
| 0.6150 | 0.8558 | 0.8092 | 0.6122 | −1.2389 | −1.2679 |
| 0.6834 | 0.8676 | 0.8112 | 0.6802 | −1.2577 | −1.2932 |

**Table I.** Continued

| Flow A[a] | $Q_m$[b] | $Q_c$[b] | Flow A[a] | $Q_m$[b] | $Q_c$[b] |
|---|---|---|---|---|---|
| $T$ = 348.15 K; A:0.9310$m$ HCl; | | | $T$ = 398.15 K; A:0.3729$m$ HCl; | | |
| B (0.4642 gH$_2$O-min$^{-1}$):0.9273$m$ β-alanine | | | B (0.4753 gH$_2$O-min$^{-1}$):0.5770$m$ β-alanine | | |
| 0.1355 | −0.2290 | −0.2449 | 0.1370 | 0.1181 | 0.1263 |
| 0.2032 | −0.3023 | −0.3169 | 0.2055 | 0.2275 | 0.2299 |
| 0.2709 | −0.3565 | −0.3772 | 0.2740 | 0.3397 | 0.3370 |
| 0.3387 | −0.4043 | −0.4292 | 0.3426 | 0.4579 | 0.4458 |
| 0.4064 | −0.4494 | −0.4750 | 0.4111 | 0.5857 | 0.5556 |
| 0.4741 | −0.4833 | −0.5166 | 0.4796 | 0.7075 | 0.6657 |
| 0.5418 | −0.5205 | −0.5546 | 0.5481 | 0.8332 | 0.7756 |
| 0.6096 | −0.5494 | −0.5875 | 0.6166 | 0.9583 | 0.8841 |
| 0.6773 | −0.5657 | −0.6161 | 0.6851 | 1.0682 | 0.9865 |
| $T$ = 348.15 K; A:0.5970$m$ HCl; | | | $T$ = 398.15 K; A:0.4005$m$ HCl; | | |
| B (0.4833 gH$_2$O-min$^{-1}$):0.5004$m$ β-alanine | | | B (0.4803 gH$_2$O-min$^{-1}$):0.3899$m$ β-alanine | | |
| 0.1365 | −0.0350 | −0.0385 | 0.1370 | 0.1453 | 0.1807 |
| 0.2047 | −0.0344 | −0.0335 | 0.2054 | 0.2703 | 0.3019 |
| 0.2730 | −0.0344 | −0.0245 | 0.2739 | 0.3935 | 0.4240 |
| 0.3412 | −0.0329 | −0.0133 | 0.3424 | 0.5252 | 0.5455 |
| 0.4095 | −0.0424 | −0.0068 | 0.4109 | 0.6516 | 0.6635 |
| 0.4777 | −0.0310 | −0.0228 | 0.4793 | 0.7521 | 0.7481 |
| 0.5460 | −0.0377 | −0.0399 | 0.5478 | 0.7687 | 0.7572 |
| 0.6142 | −0.0542 | −0.0550 | 0.6163 | 0.7722 | 0.7543 |
| 0.6825 | −0.0768 | −0.0682 | 0.6848 | 0.7792 | 0.7503 |
| | | | $T$ = 323.15 K; A:0.5122$m$ HCl; | | |
| $T$ = 373.15 K; A:0.7920$m$ HCl; | | | B (0.9499 gH$_2$O-min$^{-1}$):0.5211$m$ | | |
| B (0.4670 gH$_2$O-min$^{-1}$):0.9018$m$ β-alanine | | | DL-2-aminobutyric acid | | |
| 0.1360 | 0.0358 | 0.0908 | 0.1709 | 0.0141 | −0.0166 |
| 0.2041 | 0.1152 | 0.1912 | 0.3417 | 0.0532 | −0.0063 |
| 0.2721 | 0.1986 | 0.2987 | 0.5126 | 0.1001 | 0.0089 |
| 0.3401 | 0.2976 | 0.4100 | 0.6835 | 0.1433 | 0.0246 |
| 0.4081 | 0.3969 | 0.5231 | 0.8543 | 0.1855 | 0.0362 |
| 0.4762 | 0.4979 | 0.6352 | 1.0252 | 0.2100 | 0.0378 |
| 0.5442 | 0.5835 | 0.7140 | 1.2815 | 0.2193 | 0.0259 |
| 0.6122 | 0.5879 | 0.7083 | 1.5378 | 0.2197 | 0.0110 |
| $T$ = 373.15 K; A:0.6713$m$ HCl; | | | $T$ = 323.15 K; A:0.5782$m$ HCl; | | |
| B (0.4780 gH$_2$O-min$^{-1}$):0.4743$m$ β-alanine | | | B (0.7124 gH$_2$O-min$^{-1}$):0.5211$m$ | | |
| 0.1363 | 0.1109 | 0.1838 | DL-2-aminobutyric acid | | |
| 0.2045 | 0.2049 | 0.3075 | 0.1707 | 0.0188 | −0.0158 |
| 0.2727 | 0.3000 | 0.4321 | 0.3072 | 0.0487 | −0.0088 |
| 0.3408 | 0.3932 | 0.5348 | 0.4096 | 0.0697 | −0.0021 |
| 0.4090 | 0.4001 | 0.5301 | 0.5120 | 0.0926 | 0.0035 |
| 0.4771 | 0.3868 | 0.5135 | 0.6144 | 0.1144 | 0.0050 |
| 0.5453 | 0.3766 | 0.4985 | 0.7510 | 0.1207 | −0.0023 |
| 0.6135 | 0.3715 | 0.4852 | 0.8875 | 0.1137 | −0.0142 |
| 0.6816 | 0.3670 | 0.4734 | 1.0241 | 0.1040 | −0.0259 |

**Table I.** Continued

| Flow A[a] | $Q_m$[b] | $Q_c$[b] |
|---|---|---|
| $T$ = 323.15 K; A:0.5782$m$ HCl; B (0.4726 $gH_2O$-$min^{-1}$):0.5211$m$ DL-2-aminobutyric acid | | |
| 0.1365 | 0.0087 | −0.0096 |
| 0.2048 | 0.0231 | −0.0058 |
| 0.2731 | 0.0372 | −0.0013 |
| 0.3414 | 0.0536 | 0.0024 |
| 0.4096 | 0.0640 | 0.0033 |
| 0.4779 | 0.0670 | 0.0000 |
| 0.5462 | 0.0663 | −0.0056 |
| 0.6144 | 0.0623 | −0.0117 |
| 0.6827 | 0.0576 | −0.0174 |
| $T$ = 348.15 K; A:1.0448$m$ HCl; B (0.4552 $gH_2O$-$min^{-1}$):1.0550$m$ DL-2-aminobutyric acid | | |
| 0.1355 | 0.1719 | 0.1780 |
| 0.2032 | 0.2865 | 0.3038 |
| 0.2709 | 0.4117 | 0.4342 |
| 0.3387 | 0.5320 | 0.5628 |
| 0.4064 | 0.6429 | 0.6769 |
| 0.4741 | 0.7093 | 0.7456 |
| 0.5418 | 0.7226 | 0.7588 |
| 0.6096 | 0.7132 | 0.7498 |
| 0.6773 | 0.6977 | 0.7353 |
| $T$ = 348.15 K; A:0.5970$m$ HCl; B (0.4705 $gH_2O$-$min^{-1}$):0.5850$m$ DL-2-aminobutyric acid | | |
| 0.1365 | 0.1646 | 0.1536 |
| 0.2048 | 0.2502 | 0.2482 |
| 0.2730 | 0.3527 | 0.3438 |
| 0.3412 | 0.4428 | 0.4355 |
| 0.4095 | 0.5237 | 0.5140 |
| 0.4777 | 0.5667 | 0.5642 |
| 0.5460 | 0.5946 | 0.5848 |
| 0.6142 | 0.5928 | 0.5904 |
| 0.6825 | 0.5986 | 0.5902 |
| $T$ = 373.15 K; A:0.6713$m$ HCl; B (0.4693 $gH_2O$-$min^{-1}$):0.6186$m$ DL-2-aminobutyric acid | | |
| 0.1363 | 0.3156 | 0.3194 |
| 0.2045 | 0.4945 | 0.5093 |
| 0.2727 | 0.6719 | 0.7001 |
| 0.3408 | 0.8457 | 0.8805 |
| 0.4090 | 0.9939 | 1.0248 |
| 0.4771 | 1.0774 | 1.0999 |
| 0.5453 | 1.1057 | 1.1237 |
| 0.6135 | 1.1266 | 1.1283 |
| $T$ = 373.15 K; A:0.3303$m$ HCl; B (0.4778 $gH_2O$-$min^{-1}$):0.3699$m$ DL-2-aminobutyric acid | | |
| 0.1371 | 0.1811 | 0.1799 |
| 0.2057 | 0.2921 | 0.2828 |
| 0.2742 | 0.3917 | 0.3860 |
| 0.3428 | 0.5019 | 0.4862 |
| 0.4114 | 0.5978 | 0.5786 |
| 0.4799 | 0.6798 | 0.6556 |
| 0.5485 | 0.7464 | 0.7097 |
| 0.6170 | 0.7834 | 0.7416 |
| $T$ = 398.15 K; A:1.0196$m$ HCl; B (0.4544 $gH_2O$-$min^{-1}$):1.0805$m$ DL-2-aminobutyric acid | | |
| 0.1355 | 0.5527 | 0.5542 |
| 0.2033 | 0.9012 | 0.9033 |
| 0.2710 | 1.2533 | 1.2605 |
| 0.3388 | 1.5970 | 1.6149 |
| 0.4066 | 1.9189 | 1.9467 |
| 0.4743 | 2.1750 | 2.1960 |
| 0.5421 | 2.2900 | 2.2946 |
| 0.6098 | 2.3047 | 2.3102 |
| 0.6776 | 2.2857 | 2.3024 |
| $T$ = 398.15 K; A:0.5970$m$ HCl; B (0.4705 $gH_2O$-$min^{-1}$):0.5850$m$ DL-2-aminobutyric acid | | |
| 0.1365 | 0.4143 | 0.3867 |
| 0.2048 | 0.6609 | 0.6166 |
| 0.2730 | 0.8901 | 0.8485 |
| 0.3412 | 1.1306 | 1.0726 |
| 0.4095 | 1.3213 | 1.2679 |
| 0.4777 | 1.4367 | 1.3951 |
| 0.5460 | 1.4915 | 1.4478 |
| 0.6142 | 1.5078 | 1.4647 |
| 0.6825 | 1.5185 | 1.4686 |
| $T$ = 323.15 K; A:0.4354$m$ HCl; B (0.9513 $gH_2O$-$min^{-1}$):0.4420$m$ 4-aminobutyric acid | | |
| 0.1709 | −0.0372 | −0.0638 |
| 0.3417 | −0.0606 | −0.0838 |
| 0.5126 | −0.0713 | −0.0956 |
| 0.6835 | −0.0770 | −0.1024 |
| 0.8543 | −0.0593 | −0.1059 |
| 1.0252 | −0.0677 | −0.1201 |
| 1.2815 | −0.0901 | −0.1666 |
| 1.5378 | −0.1149 | −0.2032 |

**Table I.** Continued

| Flow A[a] | $Q_m$[b] | $Q_c$[b] | Flow A[a] | $Q_m$[b] | $Q_c$[b] |
|---|---|---|---|---|---|
| $T$ = 348.15 K; A:1.0117$m$ HCl; B (0.4558 $gH_2O\text{-}min^{-1}$):1.0266$m$ 4-aminobutyric acid | | | $T$ = 398.15 K; A:0.5970$m$ HCl; B (0.4733 $gH_2O\text{-}min^{-1}$):0.5208$m$ 4-aminobutyric acid | | |
| 0.1354 | 0.0147 | 0.0105 | 01365 | 0.3211 | 0.3278 |
| 0.2031 | 0.0692 | 0.0701 | 0.2048 | 0.5461 | 0.5607 |
| 0.2708 | 0.1348 | 0.1383 | 0.2730 | 0.7764 | 0.7993 |
| 0.3385 | 0.2136 | 0.2124 | 0.3412 | 1.0147 | 1.0404 |
| 0.4062 | 0.2918 | 0.2902 | 0.4095 | 1.2394 | 1.2669 |
| 0.4739 | 0.3452 | 0.3450 | 0.4777 | 1.2625 | 1.2764 |
| 0.5416 | 0.3092 | 0.3018 | 0.5460 | 1.2463 | 1.2602 |
| 0.6094 | 0.2731 | 0.2612 | 0.6142 | 1.2362 | 1.2456 |
| 0.6771 | 0.2475 | 0.2256 | 0.6825 | 1.2245 | 1.2326 |
| $T$ = 373.15 K; A:0.1.1256$m$ HCl; B (0.4603 $gH_2O\text{-}min^{-1}$):1.1354$m$ 4-aminobutyric acid | | | $T$ = 323.15 K; A:0.4005$m$ HCl; B (0.4706 $gH_2O\text{-}min^{-1}$):0.4201$m$ 6-aminocaproic acid | | |
| 0.1356 | 0.2334 | 0.2810 | 0.1370 | 0.0596 | 0.0640 |
| 0.2034 | 0.4221 | 0.5057 | 0.2054 | 0.1505 | 0.1193 |
| 0.2712 | 0.6153 | 0.7375 | 0.2739 | 0.2593 | 0.1809 |
| 0.3391 | 0.8254 | 0.9720 | 0.3424 | 0.3820 | 0.2471 |
| 0.4069 | 1.0456 | 1.2066 | 0.4109 | 0.5192 | 0.3169 |
| 0.4747 | 1.1818 | 1.3886 | 0.4793 | 0.6100 | 0.3872 |
| 0.5425 | 1.1565 | 1.3418 | 0.5478 | 0.5688 | 0.3927 |
| 0.6103 | 1.1141 | 1.2936 | 0.6163 | 0.5299 | 0.3798 |
| | | | 0.6848 | 0.4975 | 0.3683 |
| $T$ = 373.15 K; A:0.4426$m$ HCl; B (0.4733 $gH_2O\text{-}min^{-1}$):0.4425$m$ 4-aminobutyric acid | | | $T$ = 348.15 K; A:1.0445$m$ HCl; B (0.4527 $gH_2O\text{-}min^{-1}$):1.1047$m$ 6-aminocaproic acid | | |
| 0.1367 | 0.2047 | 0.2407 | 0.1361 | 0.2456 | 0.1903 |
| 0.2050 | 0.3479 | 0.3996 | 0.2041 | 0.4823 | 0.4008 |
| 0.2734 | 0.4848 | 0.5623 | 0.2721 | 0.7301 | 0.6411 |
| 0.3417 | 0.6330 | 0.7271 | 0.3401 | 1.0046 | 0.9028 |
| 0.4100 | 0.7831 | 0.8924 | 0.4082 | 1.2908 | 1.1799 |
| 0.4784 | 0.9105 | 1.0322 | 0.4762 | 1.5661 | 1.4220 |
| 0.5467 | 0.9172 | 1.0362 | 0.5442 | 1.5369 | 1.3808 |
| 0.6150 | 0.9141 | 1.0285 | 0.6122 | 1.4892 | 1.3401 |
| 0.6834 | 0.9157 | 1.0211 | 0.6803 | 1.4499 | 1.3044 |
| $T$ = 398.15 K; A:0.9557$m$ HCl; B (0.4611 $gH_2O\text{-}min^{-1}$):1.0232$m$ 4-aminobutyric acid | | | $T$ = 348.15 K; A:0.5970$m$ HCl; B (0.4661 $gH_2O\text{-}min^{-1}$):0.5168$m$ 6-aminocaproic acid | | |
| 0.1357 | 0.3169 | 0.3046 | 0.1365 | 0.2835 | 0.3386 |
| 0.2036 | 0.6044 | 0.5689 | 0.2048 | 0.4908 | 0.5535 |
| 0.2714 | 0.9112 | 0.8444 | 0.2730 | 0.6921 | 0.7761 |
| 0.3393 | 1.2299 | 1.1254 | 0.3412 | 0.8983 | 1.0038 |
| 0.4071 | 1.5535 | 1.4087 | 0.4095 | 1.1132 | 1.2059 |
| 0.4750 | 1.8789 | 1.6879 | 0.4777 | 1.1202 | 1.1931 |
| 0.5429 | 1.9115 | 1.7420 | 0.5460 | 1.1060 | 1.1760 |
| 0.6107 | 1.8662 | 1.7078 | 0.6142 | 1.0961 | 1.1611 |
| 0.6786 | 1.8387 | 1.6761 | 0.6825 | 1.0734 | 1.1481 |

**Table I.** Continued

| Flow A[a] | $Q_{\mathrm{m}}$[b] | $Q_{\mathrm{c}}$[b] | Flow A[a] | $Q_{\mathrm{m}}$[b] | $Q_{\mathrm{c}}$[b] |
|---|---|---|---|---|---|
| $T$ = 373.15 K; A:0.5380$m$ HCl; B (0.4668 gH$_2$O-min$^{-1}$):0.5008$m$ 6-aminocaproic acid | | | $T$ = 398.15 K; A:0.9040$m$ HCl; B (0.4527 gH$_2$O-min$^{-1}$):1.0185$m$ 6-aminocaproic acid | | |
| 0.1366 | 0.3532 | 0.4381 | 0.1361 | 0.3757 | 0.2619 |
| 0.2050 | 0.6228 | 0.7344 | 0.2041 | 0.8420 | 0.6688 |
| 0.2733 | 0.8824 | 1.0416 | 0.2721 | 1.3105 | 1.1386 |
| 0.3416 | 1.1628 | 1.3559 | 0.3401 | 1.8256 | 1.6515 |
| 0.4099 | 1.4441 | 1.6729 | 0.4082 | 2.3845 | 2.1954 |
| 0.4782 | 1.5725 | 1.7813 | 0.4762 | 2.9281 | 2.7598 |
| 0.5465 | 1.5663 | 1.7697 | 0.5442 | 3.1387 | 2.9453 |
| 0.6149 | 1.5659 | 1.7586 | 0.6122 | 3.0950 | 2.9012 |
| | | | 0.6803 | 3.0602 | 2.8606 |
| $T$ = 373.15 K; A:0.3303$m$ HCl; B (0.4774 gH$_2$O-min$^{-1}$):0.2764$m$ 6-aminocaproic acid | | | $T$ = 398.15 K; A:0.5970$m$ HCl; B (0.4661 gH$_2$O-min$^{-1}$):0.5160$m$ 6-aminocaproic acid | | |
| 0.1371 | 0.2730 | 0.3151 | 0.1365 | 0.4453 | 0.4258 |
| 0.2057 | 0.4587 | 0.5156 | 0.2048 | 0.8177 | 0.7881 |
| 0.2742 | 0.6325 | 0.7208 | 0.2730 | 1.1903 | 1.1762 |
| 0.3428 | 0.8258 | 0.9287 | 0.3412 | 1.5938 | 1.5815 |
| 0.4114 | 1.0001 | 1.0965 | 0.4095 | 1.9980 | 1.9477 |
| 0.4799 | 1.0128 | 1.0952 | 0.4777 | 2.0072 | 1.9328 |
| 0.5485 | 1.0118 | 1.0899 | 0.5460 | 1.9881 | 1.9123 |
| 0.6170 | 1.0172 | 1.0851 | 0.6142 | 1.9689 | 1.8940 |
| | | | 0.6825 | 1.9517 | 1.8779 |

[a] Units: g H$_2$O-min$^{-1}$.

[b] Units: J-min$^{-1}$.

trend is that $\Delta H^{\circ}$ increases as the number of methylene groups between the amino and the carboxylate groups increases except in the case of β-alanine. $\Delta C_p^{\circ}$ for the protonation reactions decrease as temperature increases for all of the amino acids studied (Fig. 2).

Shown in Fig. 3 are the plots of $T\Delta S^{\circ}$ for reaction (1) as a function of temperature. The protonation reactions for the amino acids have large positive $T\Delta S^{\circ}$ values over the entire temperature range studied. As the temperature increases, the $T\Delta S^{\circ}$ values become larger and have increasing importance in determining the magnitudes of the log$K$ values for the protonation reaction. It can also be seen in Fig. 3 that $\Delta S^{\circ}$ of the α-amino acids are nearly the same at each temperature while those for the other amino acids increase as the number of methylene groups between the carboxylate and amino groups increases.

Each of the quantities $K$, $\Delta H^{\circ}$, $\Delta S^{\circ}$ and $\Delta C_p^{\circ}$ for the protonation reactions will now be discussed to show how they are affected by solvent–solute and intramolecular zwitterion interactions.

**Table II.** Calorimetric Data for the Dilution of the Amino Acid Chlorides at Various Temperatures and 1.52 MPa

| Flow A[a] | $Q_m$[b] | $Q_c$[b] | Flow A[a] | $Q_m$[b] | $Q_c$[b] |
|---|---|---|---|---|---|
| $T$ = 348.15 K; A:$H_2O$; | | | $T$ = 373.K; A:$H_2O$; | | |
| B (0.4695 $gH_2O\text{-}min^{-1}$): | | | B (0.4629 $gH_2O\text{-}min^{-1}$): | | |
| 1.0382*m* glycine + 1.0827*m* HCl | | | 1.0188*m* DL-α-alanine + 1.1660*m* HCl | | |
| 0.1378 | −0.0883 | −0.0664 | 0.1378 | −0.1937 | −0.1877 |
| 0.2067 | −0.0788 | −0.1014 | 0.2067 | −0.2690 | −0.2665 |
| 0.2756 | −0.1494 | −0.1354 | 0.2756 | −0.3311 | −0.3371 |
| 0.3445 | −0.1682 | −0.1678 | 0.3445 | −0.4063 | −0.4006 |
| 0.4134 | −0.2267 | −0.1984 | 0.4134 | −0.4695 | −0.4582 |
| 0.4823 | −0.1946 | −0.2273 | 0.4823 | −0.5209 | −0.5107 |
| 0.5511 | −0.2488 | −0.2545 | 0.5511 | −0.5636 | −0.5588 |
| 0.6200 | −0.2680 | −0.2801 | 0.6200 | −0.5914 | −0.6032 |
| 0.6889 | −0.3106 | −0.3042 | 0.6889 | −0.6516 | −0.6444 |
| $T$ = 373.15 K; A:$H_2O$; | | | $T$ = 398.15 K; A:$H_2O$; | | |
| B (0.4766 $gH_2O\text{-}min^{-1}$): | | | B (0.4763 $gH_2O\text{-}min^{-1}$): | | |
| 0.6934*m* glycine + 0.5661*m* HCl | | | 0.5172*m* DL-α-alanine + 0.4655*m* HCl | | |
| 0.1378 | −0.0858 | −0.0876 | 0.1378 | −0.1164 | −0.1169 |
| 0.2067 | −0.1249 | −0.1279 | 0.2067 | −0.1645 | −0.1690 |
| 0.2756 | −0.1584 | −0.1652 | 0.2756 | −0.2159 | −0.2166 |
| 0.3445 | −0.1998 | −0.1996 | 0.3445 | −0.2491 | −0.2600 |
| 0.4134 | −0.2221 | −0.2312 | 0.4134 | −0.2951 | −0.2998 |
| 0.4823 | −0.2536 | −0.2604 | 0.4823 | −0.3324 | −0.3362 |
| 0.5511 | −0.2752 | −0.2874 | 0.5511 | −0.3654 | −0.3697 |
| 0.6200 | −0.3072 | −0.3125 | 0.6200 | −0.4004 | −0.4008 |
| 0.6889 | −0.3318 | −0.3359 | 0.6889 | −0.4212 | −0.4295 |
| $T$ = 398.15 K; A:$H_2O$; | | | $T$ = 348.15 K; A:$H_2O$; | | |
| B (0.4804 $gH_2O\text{-}min^{-1}$): | | | B (0.4642 $gH_2O\text{-}min^{-1}$): | | |
| 0.5132*m* glycine + 0.5798*m* HCl | | | 1.0148*m* β-alanine + 1.0827*m* HCl | | |
| 0.1378 | −0.1450 | −0.1405 | 0.1378 | −0.0845 | −0.0656 |
| 0.2067 | −0.2002 | −0.2013 | 0.2067 | −0.1017 | −0.0886 |
| 0.2756 | −0.2580 | −0.2562 | 0.2756 | −0.0942 | −0.1080 |
| 0.3445 | −0.3048 | −0.3061 | 0.3445 | −0.1048 | −0.1248 |
| 0.4134 | −0.3444 | −0.3516 | 0.4134 | −0.1634 | −0.1398 |
| 0.4823 | −0.3952 | −0.3932 | 0.4823 | −0.1264 | −0.1534 |
| 0.5511 | −0.4336 | −0.4313 | 0.5511 | −0.1669 | −0.1658 |
| 0.6200 | −0.4677 | −0.4666 | 0.6200 | −0.1696 | −0.1774 |
| 0.6889 | −0.4990 | −0.4993 | 0.6889 | −0.2115 | −0.1881 |
| $T$ = 348.15 K; A:$H_2O$; | | | $T$ = 373.15 K; A:$H_2O$; | | |
| B (0.4624 $gH_2O\text{-}min^{-1}$): | | | B (0.4780 $gH_2O\text{-}min^{-1}$): | | |
| 1.0410*m* DL-α-alanine + 0.9714*m* HCl | | | 0.4743*m* β-alanine + 0.6125*m* HCl | | |
| 0.1378 | −0.0955 | −0.0901 | 0.1378 | −0.0858 | −0.0859 |
| 0.2067 | −0.1367 | −0.1305 | 0.2067 | −0.1199 | −0.1212 |
| 0.2756 | −0.1738 | −0.1675 | 0.2756 | −0.1604 | −0.1525 |
| 0.3445 | −0.2274 | −0.2015 | 0.3445 | −0.1837 | −0.1805 |
| 0.4134 | −0.2377 | −0.2327 | 0.4134 | −0.2069 | −0.2057 |
| 0.4823 | −0.2611 | −0.2615 | 0.4823 | −0.2319 | −0.2286 |
| 0.5511 | −0.2766 | −0.2881 | 0.5511 | −0.2589 | −0.2494 |
| 0.6200 | −0.3052 | −0.3128 | 0.6200 | −0.2779 | −0.2686 |
| 0.6889 | −0.3270 | −0.3358 | 0.6889 | −0.3014 | −0.2862 |

**Table II.** Continued

| Flow A[a] | $Q_\mathrm{m}$[b] | $Q_\mathrm{c}$[b] | Flow A[a] | $Q_\mathrm{m}$[b] | $Q_\mathrm{c}$[b] |
|---|---|---|---|---|---|
| $T$ = 373.15 K; A:H$_2$O;<br>B (0.4670 gh$_2$O-min$^{-1}$):<br>0.9018$m$ β-alanine + 1.1660$m$ HCl | | | $T$ = 348.15 K; A:H$_2$O;<br>B (0.4541 gH$_2$O-min$^{-1}$):<br>1.0812$m$ DL-2-aminobutyric acid<br>+ 1.0827$m$ HCl | | |
| 0.1378 | −0.1477 | −0.1237 | 0.1378 | −0.1484 | −0.1278 |
| 0.2067 | −0.2102 | −0.1858 | 0.2067 | −0.1645 | −0.1852 |
| 0.2756 | −0.2703 | −0.2447 | 0.2756 | −0.2848 | −0.2376 |
| 0.3445 | −0.3107 | −0.2999 | 0.3445 | −0.3140 | −0.2853 |
| 0.4134 | −0.3690 | −0.3512 | 0.4134 | −0.3417 | −0.3289 |
| 0.4823 | −0.3948 | −0.3989 | 0.4823 | −0.3587 | −0.3689 |
| 0.5511 | −0.4404 | −0.4432 | 0.5511 | −0.4153 | −0.4056 |
| 0.6200 | −0.4658 | −0.4844 | 0.6200 | −0.4710 | −0.4395 |
| 0.6889 | −0.4937 | −0.5229 | 0.6889 | −0.5147 | −0.4710 |
| $T$ = 398.15 K; A:H$_2$O;<br>B (0.4753 gH$_2$O-min$^{-1}$):<br>0.5770$m$ β-alanine + 0.5353$m$ HCl | | | $T$ = 373.15 K; A:H$_2$O;<br>B (0.4693 gH$_2$O-min$^{-1}$):<br>0.6186$m$ DL-2-aminobutyric acid<br>+ 0.5661$m$ HCl | | |
| 0.1378 | −0.0997 | −0.1061 | 0.1378 | −0.0940 | −0.1031 |
| 0.2067 | −0.1520 | −0.1538 | 0.2067 | −0.1312 | −0.1450 |
| 0.2756 | −0.1922 | −0.1975 | 0.2756 | −0.1739 | −0.1820 |
| 0.3445 | −0.2262 | −0.2374 | 0.3445 | −0.1911 | −0.2152 |
| 0.4134 | −0.2575 | −0.2738 | 0.4134 | −0.2350 | −0.2451 |
| 0.4823 | −0.2939 | −0.3071 | 0.4823 | −0.2605 | −0.2724 |
| 0.5511 | −0.3252 | −0.3377 | 0.5511 | −0.2897 | −0.2973 |
| 0.6200 | −0.3550 | −0.3660 | 0.6200 | −0.3052 | −0.3203 |
| 0.6889 | −0.3819 | −0.3921 | 0.6889 | −0.3361 | −0.3417 |
| $T$ = 323.15 K; A: H$_2$O;<br>B (0.4726 gH$_2$O-min$^{-1}$):<br>0.5216$m$ DL-2-aminobutyric acid<br>+ 0.5670$m$ HCl | | | $T$ = 398.15 K; A:H$_2$O;<br>B (0.4705 gH$_2$O-min$^{-1}$):<br>0.5850$m$ DL-2-aminobutyric acid<br>+ 0.5798$m$ HCl | | |
| 0.1378 | −0.0510 | −0.0469 | 0.1378 | −0.1287 | −0.1406 |
| 0.2067 | −0.0811 | −0.0654 | 0.2067 | −0.1925 | −0.1979 |
| 0.2756 | −0.0924 | −0.0816 | 0.2756 | −0.2341 | −0.2488 |
| 0.3445 | −0.0791 | −0.0959 | 0.3445 | −0.2823 | −0.2943 |
| 0.4134 | −0.0955 | −0.1086 | 0.4134 | −0.3305 | −0.3355 |
| 0.4823 | −0.1129 | −0.1201 | 0.4823 | −0.3749 | −0.3729 |
| 0.5511 | −0.1219 | −0.1305 | 0.5511 | −0.4151 | −0.4072 |
| 0.6200 | −0.1236 | −0.1401 | 0.6200 | −0.4461 | −0.4388 |
| 0.6889 | −0.1359 | −0.1489 | 0.6889 | −0.4794 | −0.4681 |
| $T$ = 348.15 K; A:H$_2$O;<br>B (0.4705 gH$_2$O-min$^{-1}$):<br>0.5850$m$ DL-2-aminobutyric acid<br>+ 0.5798$m$ HCl | | | $T$ = 398.15 K; A:H$_2$O;<br>B (0.4544 gH$_2$O-min$^{-1}$):<br>1.0805$m$ DL-2-aminobutyric acid<br>+ 1.0827$m$ HCl | | |
| 0.1378 | −0.0747 | −0.0741 | 0.1378 | −0.2424 | −0.2258 |
| 0.2067 | −0.1043 | −0.1041 | 0.2067 | −0.3479 | −0.3308 |
| 0.2756 | −0.1276 | −0.1306 | 0.2756 | −0.4393 | −0.4279 |
| 0.3445 | −0.1460 | −0.1543 | 0.3445 | −0.5267 | −0.5172 |
| 0.4134 | −0.1789 | −0.1757 | 0.4134 | −0.5993 | −0.5993 |
| 0.4823 | −0.2004 | −0.1952 | 0.4823 | −0.6684 | −0.6749 |
| 0.5511 | −0.2223 | −0.2130 | 0.5511 | −0.7409 | −0.7446 |
| 0.6200 | −0.2378 | −0.2294 | 0.6200 | −0.8032 | −0.8093 |
| 0.6889 | −0.2433 | −0.2446 | 0.6889 | −0.8632 | −0.8694 |

**Table II.** Continued

| Flow A[a] | $Q_\mathrm{m}$[b] | $Q_\mathrm{c}$[b] | Flow A[a] | $Q_\mathrm{m}$[b] | $Q_\mathrm{c}$[b] |
|---|---|---|---|---|---|
| $T$ = 348.15 K; A:$H_2O$; B (0.4558 g$H_2O$-min$^{-1}$): 1.0806$m$ 4-aminobutyric acid + 0.9714$m$ HCl | | | $T$ = 398.15 K; A:$H_2O$; B (0.4611 g$H_2O$-min$^{-1}$): 0.9051$m$ 4-aminobutyric acid + 1.1660$m$ HCl | | |
| 0.1378 | −0.0538 | −0.0586 | 0.1378 | −0.1871 | −0.1362 |
| 0.2067 | −0.0853 | −0.0808 | 0.2067 | −0.2609 | −0.2091 |
| 0.2756 | −0.1009 | −0.1000 | 0.2756 | −0.3206 | −0.2796 |
| 0.3445 | −0.1254 | −0.1171 | 0.3445 | −0.3719 | −0.3466 |
| 0.4134 | −0.1270 | −0.1326 | 0.4134 | −0.4244 | −0.4095 |
| 0.4823 | −0.1448 | −0.1467 | 0.4823 | −0.4627 | −0.4684 |
| 0.5511 | −0.1502 | −0.1596 | 0.5511 | −0.5003 | −0.5234 |
| 0.6200 | −0.1737 | −0.1717 | 0.6200 | −0.5327 | −0.5749 |
| 0.6889 | −0.1878 | −0.1830 | 0.6889 | −0.5617 | −0.6232 |
| $T$ = 373.15 K; A:$H_2O$; B (0.4733 g$H_2O$-min$^{-1}$): 0.5206$m$ 4-aminobutyric acid + 0.6125$m$ HCl | | | $T$ = 348.15 K; A:$H_2O$; B (0.4527 g$H_2O$-min$^{-1}$): 0.8175$m$ 6-aminocaproic acid + 0.9714$m$ HCl | | |
| 0.1378 | −0.0814 | −0.0617 | 0.1378 | −0.0297 | −0.0322 |
| 0.2067 | −0.1162 | −0.0883 | 0.2067 | −0.0459 | −0.0477 |
| 0.2756 | −0.1397 | −0.1124 | 0.2756 | −0.0591 | −0.0623 |
| 0.3445 | −0.1690 | −0.1343 | 0.3445 | −0.0866 | −0.0760 |
| 0.4134 | −0.1978 | −0.1543 | 0.4134 | −0.0941 | −0.0888 |
| 0.4823 | −0.2218 | −0.1727 | 0.4823 | −0.1036 | −0.1007 |
| 0.5511 | −0.2415 | −0.1895 | 0.5511 | −0.1054 | −0.1120 |
| 0.6200 | −0.2516 | −0.2052 | 0.6200 | −0.1190 | −0.1225 |
| 0.6889 | −0.2728 | −0.2197 | 0.6889 | −0.1299 | −0.1324 |
| $T$ = 373.15 K; A:$H_2O$; B (0.4537 g$H_2O$-min$^{-1}$): 1.0855$m$ 4-aminobutyric acid + 0.9714$m$ HCl | | | $T$ = 373.15 K; A:$H_2O$; B (0.4668 g$H_2O$-min$^{-1}$): 0.5008$m$ 6-aminocaproic acid + 0.5661$m$ HCl | | |
| 0.1378 | −0.1137 | −0.1079 | 0.1378 | −0.0374 | −0.0476 |
| 0.2067 | −0.1590 | −0.1580 | 0.2067 | −0.0825 | −0.0708 |
| 0.2756 | −0.1986 | −0.2044 | 0.2756 | −0.0913 | −0.0926 |
| 0.3445 | −0.2355 | −0.2472 | 0.3445 | −0.1113 | −0.1128 |
| 0.4134 | −0.2755 | −0.2865 | 0.4134 | −0.1321 | −0.1316 |
| 0.4823 | −0.3054 | −0.3227 | 0.4823 | −0.1408 | −0.1490 |
| 0.5511 | −0.3381 | −0.3562 | 0.5511 | −0.1785 | −0.1651 |
| 0.6200 | −0.3694 | −0.3872 | 0.6200 | −0.1743 | −0.1801 |
| 0.6889 | −0.3787 | −0.4160 | 0.6889 | −0.1929 | −0.1940 |
| $T$ = 398.15 K; A:$H_2O$; B (0.4733 g$H_2O$-min$^{-1}$): 0.5208$m$ 4-aminobutyric acid + 0.5742$m$ HCl | | | $T$ = 398.15 K; A:$H_2O$; B (0.4661 g$H_2O$-min$^{-1}$): 0.5161$m$ 6-aminocaparoic acid + 0.5742$m$ HCl | | |
| 0.1378 | −0.0999 | −0.0980 | 0.1378 | −0.0724 | −0.0597 |
| 0.2067 | −0.1387 | −0.1389 | 0.2067 | −0.1087 | −0.0891 |
| 0.2756 | −0.1797 | −0.1755 | 0.2756 | −0.1382 | −0.1168 |
| 0.3445 | −0.2176 | −0.2083 | 0.3445 | −0.1678 | −0.1426 |
| 0.4134 | −0.2489 | −0.2381 | 0.4134 | −0.1899 | −0.1667 |
| 0.4823 | −0.2788 | −0.2651 | 0.4823 | −0.2213 | −0.1890 |
| 0.5511 | −0.3058 | −0.2898 | 0.5511 | −0.2451 | −0.2096 |
| 0.6200 | −0.3362 | −0.3125 | 0.6200 | −0.2676 | −0.2289 |
| 0.6889 | −0.3565 | −0.3335 | 0.6889 | −0.2889 | −0.2468 |

**Table II.** Continued

| Flow A[a] | $Q_m$[b] | $Q_c$[b] | Flow A[a] | $Q_m$[b] | $Q_c$[b] |
|---|---|---|---|---|---|
| $T$ = 398.15 K; A:$H_2O$;<br>B (0.4527 $gH_2O\text{-}min^{-1}$):<br>0.8175*m* 6-aminocaproic acid<br>+ 0.6125*m* HCl | | | | | |
| 0.1378 | −0.0724 | −0.0883 | | | |
| 0.2067 | −0.1056 | −0.1291 | | | |
| 0.2756 | −0.1234 | −0.1668 | | | |
| 0.3445 | −0.1442 | −0.2013 | | | |
| 0.4134 | −0.1697 | −0.2329 | | | |
| 0.4823 | −0.1828 | −0.2618 | | | |
| 0.5511 | −0.1975 | −0.2883 | | | |
| 0.6200 | −0.2112 | −0.3127 | | | |
| 0.6889 | −0.2206 | −0.3353 | | | |

[a] See footnotes in Table I.

log*K* for reaction (1) for the amino acids over the temperature range studied are shown in Fig. 4. As expected, the protonation reactions for the α-amino acids have log*K* close to each other. The same trend with chain length as those for $\Delta H^\circ$ and $T\Delta S^\circ$ is observed for log*K* values among the amino acids. At each temperature, the stability of the protonated species increases as the number of methylene groups between the amino group and carboxylate group increases. This is a result of the progressively larger positive change in $\Delta S^\circ$ as the two groups become more separated (Fig. 3), and log*K* are dominated by $T\Delta S^\circ$. The protonation reaction is entropy driven. Each log*K* *vs.* *T* plot exhibits a minimum as $\Delta H^\circ$ changes from negative to positive. At temperatures higher than that at the minimum, log*K* increase with temperature.

The increase in $\Delta H^\circ$ and $T\Delta S^\circ$ as the temperature increases and the effect of charge separation on these thermodynamic quantities can be explained in terms of solvent effects. When protonation occurs, water molecules are released from the inner sphere of hydration to the bulk phase. Considerable energy is required for the newly released water molecules to attain the same energy level as that of the bulk water. As temperature increases, water molecules in the bulk phase have higher enthalpy and entropy in part due to the decrease of the hydrogen bonding.(39) The water molecules in the hydration spheres of ions are in a more ordered state than those in bulk water due to the interaction between the water dipoles and the charged ions. The result is that progressively larger positive changes in $\Delta H^\circ$ and $\Delta S^\circ$ occur as temperature increases resulting also in positive $\Delta C_p^\circ$ values.

**Table III.** Coefficients for Pitzer Parameters, Eq. (2)[a]

| Species interactions | $\phi$ | $10A$ | $10^3B$ | $10^5C$ | $10^7D$ |
|---|---|---|---|---|---|
| $^+NH_3CH_2COOH/Cl^-$ | $\beta^{(0)}$ | 0.80 | 2.4589 | −3.1916 | 0.9235 |
| | $\beta^{(1)}$ | 1.80 | 2.0303 | −2.7057 | 0.9673 |
| | $C^\phi$ | −0.162 | −8.5442 | 12.526 | −4.8707 |
| $^+NH_3CH(CH_3)COOH/Cl^-$ | $\beta^{(0)}$ | 0.80 | −3.2634 | 4.9276 | −2.7256 |
| | $\beta^{(1)}$ | 1.80 | −5.7910 | 11.4495 | −6.0393 |
| | $C^\phi$ | −0.162 | 11.0630 | −17.5215 | 9.2247 |
| $^+NH_3CH(CH_2CH_3)COOH/Cl^-$ | $\beta^{(0)}$ | 0.80 | −0.5700 | 0.0040 | −0.1067 |
| | $\beta^{(1)}$ | 1.80 | 1.3580 | −0.1454 | |
| | $C^\phi$ | −0.162 | 0.2684 | 0.2960 | |
| $^+NH_3(CH_2)_2COOH/Cl^-$ | $\beta^{(0)}$ | 0.80 | 3.4351 | −3.8680 | 1.1236 |
| | $\beta^{(1)}$ | 1.80 | 0.8911 | 0.7861 | −1.0266 |
| | $C^\phi$ | −0.162 | −0.04745 | −1.7458 | 1.9886 |
| $^+NH_3(CH_2)_3COOH/Cl^-$ | $\beta^{(0)}$ | 0.80 | 2.6048 | −2.5363 | 0.7026 |
| | $\beta^{(1)}$ | 1.80 | 2.3307 | −2.4403 | 0.8442 |
| | $C^\phi$ | −0.162 | −3.0219 | 3.6656 | −1.1870 |
| $^+NH_3(CH_2)_5COOH/Cl^-$ | $\beta^{(0)}$ | 0.80 | 3.9377 | −5.5425 | 2.1741 |
| | $\beta^{(1)}$ | 1.80 | 6.0862 | −6.1710 | 2.3434 |
| | $C^\phi$ | −0.162 | −7.5347 | 10.835 | −4.1150 |
| $^+NH_3CH_2COO^-/Cl^-$ | $\lambda$ | 0.05 | −0.3274 | −0.6245 | 0.1912 |
| $^+NH_3CH(CH_3)COO^-/Cl^-$ | $\lambda$ | 0.05 | −1.5564 | −1.1972 | 0.6167 |
| $^+NH_3CH(CH_2CH_3)COO^-/Cl^-$ | $\lambda$ | 0.05 | −1.2584 | −0.6594 | 0.3467 |
| $^+NH_3(CH_2)_2COO^-/Cl^-$ | $\lambda$ | 0.05 | −1.1271 | 0.3419 | −0.9066 |
| $^+NH_3(CH_2)_3COO^-/Cl^-$ | $\lambda$ | 0.05 | −2.1163 | 0.3343 | −0.3174 |
| $^+NH_3(CH_2)_5COO^-/Cl^-$ | $\lambda$ | 0.05 | 0.1164 | −3.5369 | 2.0736 |

[a] All parameters for ternary interactions, $\Psi'_{caa}$ and $\Psi'_{cca}$; parameters for the like charged ions, $\theta'_{aa}$, $\theta'_{cc}$; $\beta^{(0)}$, $\beta^{(1)}$, and $C^\phi$ for $OH^-/^+NH_3(CH_2)_nCHR_1COOH$ pairs; and $\lambda$ for zwitterions with other ionic species were taken to be zero. The maximum standard deviation of the fit, $\sigma_s$, is 0.031 J-min$^{-1}$ as calculated by $\sigma_s = \sqrt{\sum_{i=1}^{n} (Q_{dil,ci} - Q_{dil,mi})^2/(n - m)}$, where $Q_{dil,ci}$ and $Q_{dil,mi}$ are the calculated and measured heats of dilution, respectively, in the unit of J-min$^{-1}$, $n$ is the number of points measured in the data sets, and $m$ is the number of parameters being fitted.

The magnitudes of $\Delta H^0$ for the protonation of the carboxylate groups on the zwitterions are influenced by interactions between neighboring amino and carboxylate groups as well as solvation effects. Protonation of the carboxylate group results in the decrease (weakening) in the interaction between the positively charged amino group and the carboxylate group. This change in the interaction between the protonated and non-protonated groups is greatest for the $\alpha$-amino acids where $n$ is smallest and decreases as $n$ increases. The enthalpy of the solvent system increases upon protonation since solvent molecules influenced by the charges on the proton and carboxylate groups are released to the higher energy state of the molecules in the bulk water. This change is smallest in the case of the $\alpha$-amino acids since partial neutralization

**Table IV.** Thermodynamic Data for the Protonation of Amino Acids, Eq. (1) at Zero Ionic Strength

| $T$ | log $K$ | $\Delta H^\circ$ | $\Delta S^\circ$ | $\Delta C_p^\circ$ | Method[b] | Ref |
|---|---|---|---|---|---|---|
| Glycine | | | | | | |
| 283.15 | 2.397 | −5.90 | 24.3 | | C | 12 |
| 298.15 | 2.349 | −3.97 | 31.8 | | T | 13 |
| | 2.35 | −5.98 | 25.1 | | C | 14 |
| | 2.350 | −4.10 | 31.4 | | C | 12 |
| | 2.351 | −4.92 | 28.5 | 137.2 | T | 15 |
| | 2.35 | −3.891 | 33.5 | | C | 16 |
| | 2.347 | −4.364 | 30.3 | | T | 17 |
| | 2.348 | −4.602 | 30.5 | | T | 18 |
| | 2.358 | −4.85 | 28.9 | | T | 19 |
| | 2.352 | −4.837 | 28.9 | | T | 20 |
| | 2.352 | −3.93 | 31.9 | | C | 21 |
| 313.15 | 2.327 | −1.97 | 38.5 | | C | 12 |
| 323.15 | 2.32 | −0.9 | 41 | 119 | C | This Study[c] |
| 348.15 | 2.32 | 1.9 | 50 | 103 | C | This Study[c] |
| 373.15 | 2.35 | 4.2 | 56 | 78 | C | This Study[c] |
| 398.15 | 2.40 | 5.7 | 60 | 43 | C | This Study[c] |
| α-Alanine | | | | | | |
| 274.15 | 2.426 | −6.318 | 23.4 | | T | 22 |
| 283.15 | 2.392 | −5.23 | 27.2 | | C | 12 |
| 285.65 | 2.383 | −5.063 | 27.6 | | T | 22 |
| 293.15 | 2.350 | −3.820 | 31.8 | | T | 23 |
| 298.15 | 2.348 | −3.14 | 34.3 | | C | 12 |
| | 2.35 | −2.573 | 33.5 | | C | 24 |
| | 2.350 | −3.368 | 33.9 | 147.7 | T | 15 |
| | 2.34 | −3.012 | 34.7 | | T | 23 |
| | 2.345 | −2.43 | 36.8 | | C | 21 |
| 303.15 | 2.332 | −2.251 | 37.2 | | T | 23 |
| 308.15 | 2.327 | −1.544 | 39.3 | | T | 23 |
| 310.65 | 2.330 | −1.339 | 40.2 | | T | 22 |
| 313.15 | 2.328 | −0.96 | 41.4 | | C | 12 |
| | 2.324 | −0.900 | 41.4 | | T | 23 |
| 318.15 | 2.322 | −0.292 | 43.5 | | T | 23 |
| 323.15 | 2.332 | −1.046 | 47.7 | | T | 22 |
| | 2.33 | 0.0 | 45 | 130 | C | This Study[c] |
| 348.15 | 2.34 | 3.0 | 53 | 105 | C | This Study[c] |
| 373.15 | 2.39 | 5.1 | 59 | 65 | C | This Study[c] |
| 398.15 | 2.44 | 6.1 | 62 | 11 | C | This Study[c] |
| β-Alanine | | | | | | |
| 283.15 | 3.606 | −6.69 | 45.6 | | C | 12 |
| 298.15 | 3.551 | −4.35 | 53.6 | | C | 12 |
| | 3.55 | −4.52 | 52.7 | | C | 25 |
| | 3.55 | −4.94 | 50.2 | | T | 26 |
| 313.15 | 3.517 | −2.59 | 59.0 | | C | 12 |
| 323.15 | 3.51 | −0.9 | 65 | 139 | C | This Study[c] |

**Table IV.** Continued

| $T$ | log $K$ | $\Delta H^\circ$ | $\Delta S^\circ$ | $\Delta C_p^\circ$ | Method[b] | Ref |
|---|---|---|---|---|---|---|
| 348.15 | 3.52 | 2.3 | 74 | 114 | C | This Study[c] |
| 373.15 | 3.56 | 4.7 | 81 | 77 | C | This Study[c] |
| 398.15 | 3.61 | 6.0 | 84 | 24 | C | This Study[c] |
| DL-2-Aminobutyric Acid | | | | | | |
| 274.15 | 2.334 | −4.561 | 28.0 | | T | 22 |
| 283.15 | 2.315 | −3.22 | 32.2 | | C | 12 |
| 285.65 | 2.310 | −3.138 | 33.1 | | T | 22 |
| 298.15 | 2.286 | −1.59 | 38.5 | | C | 12 |
| | 2.288 | −1.293 | 39.3 | 161.5 | T | 15 |
| | 2.286 | −1.297 | 39.3 | | T | 22 |
| 310.65 | 2.288 | 0.920 | 46.9 | | T | 22 |
| 313.15 | 2.289 | −0.17 | 43.5 | | C | 12 |
| 323.15 | 2.297 | 3.473 | 54.8 | | T | 22 |
| | 2.29 | 1.1 | 47 | 105 | C | This Study[c] |
| 348.15 | 2.31 | 3.6 | 55 | 95 | C | This Study[c] |
| 373.15 | 2.36 | 5.8 | 61 | 80 | C | This Study[c] |
| 398.15 | 2.42 | 7.5 | 65 | 58 | C | This Study[c] |
| 4-Aminobutyric Acid | | | | | | |
| 283.15 | 4.057 | −3.14 | 66.5 | | C | 12 |
| 298.15 | 4.031 | −1.63 | 72.0 | | C | 12 |
| | 4.03 | −1.67 | 71.1 | | T | 26 |
| 313.15 | 4.027 | −0.04 | 77.4 | | C | 12 |
| 323.15 | 4.04 | 2.1 | 84 | 126 | C | This Study[c] |
| 348.15 | 4.08 | 5.0 | 93 | 104 | C | This Study[c] |
| 373.15 | 4.14 | 7.2 | 99 | 69 | C | This Study[c] |
| 398.15 | 4.21 | 8.4 | 102 | 20 | C | This Study[c] |
| 6-Aminocaproic Acid | | | | | | |
| 274.15 | 4.420 | −3.423 | 72.0 | | T | 27 |
| 283.15 | 4.392 | −0.42 | 82.8 | | C | 12 |
| 285.65 | 4.387 | −1.920 | 76.1 | | T | 27 |
| 298.15 | 4.373 | 1.34 | 88.3 | | C | 12 |
| | 4.373 | 0.033 | 83.7 | | T | 27 |
| | 4.37 | 0.0 | 83.7 | | T | 26 |
| 310.65 | 4.384 | 2.347 | 91.6 | | T | 27 |
| 313.15 | 4.388 | 3.31 | 94.6 | | C | 12 |
| 323.15 | 4.410 | 5.038 | 100.0 | | T | 27 |
| 323.15 | 4.42 | 5.0 | 100 | 127 | C | This Study[c] |
| 348.15 | 4.49 | 8.0 | 109 | 108 | C | This Study[c] |
| 373.15 | 4.58 | 10.3 | 115 | 80 | C | This Study[c] |
| 398.15 | 4.68 | 11.9 | 119 | 40 | C | This Study[c] |

[a] Units: $T$, K; $\Delta H^\circ$, kJ-mol$^{-1}$; $\Delta S^\circ$, J-mol$^{-1}$;-K$^{-1}$; and $\Delta C_p^\circ$, J-mol$^{-1}$-K$^{-1}$.

[b] The method of $\Delta H^\circ$ determination is designated by C (calorimetric) or T (temperature variation of $K$).

[c] The estimated uncertainties are ±0.03 in log $K$, ±0.4 in $\Delta H^\circ$, ±3 in $\Delta S^\circ$, and ±10 in $\Delta C_p^\circ$.

**Table V.** Coefficients for Eqs. (3–6) for Reaction (1)

| Amino Acid | *a* | *b* | *c* | *d* |
|---|---|---|---|---|
| Glycine | −86.6765 | 4000.204 | 13.27332 | 7.06975 |
| DL-α-Alanine | −116.0316 | 5201.463 | 17.71994 | 10.97738 |
| DL-2-Aminobutyric Acid | −63.88209 | 2929.324 | 9.891402 | 4.400790 |
| β-Alanine | −115.6580 | 5295.963 | 17.80919 | 10.59672 |
| 4-Aminobutyric Acid | −104.9958 | 4709.396 | 16.36708 | 9.804667 |
| 6-Aminocaproic Acid | −92.74088 | 4086.123 | 14.64205 | 8.045554 |

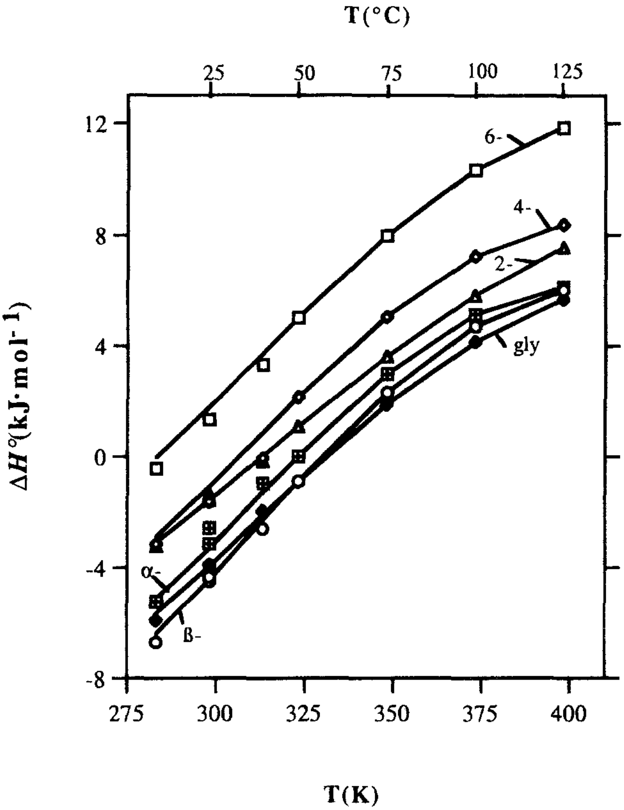

**Fig. 1.** Plot of $\Delta H^\circ$ as a function of temperature for the protonation reaction: □, 6-aminocaproic acid; ◇, 4-aminobutyric acid; △, DL-2-aminobutyric acid; ○, β-alanine; □, DL-α-alanine; ◆, glycine. The symbols at and above 323.15 K represent the results obtained in this study, all other points are taken from references listed in Table IV. The solid lines are based on Eq. (4).

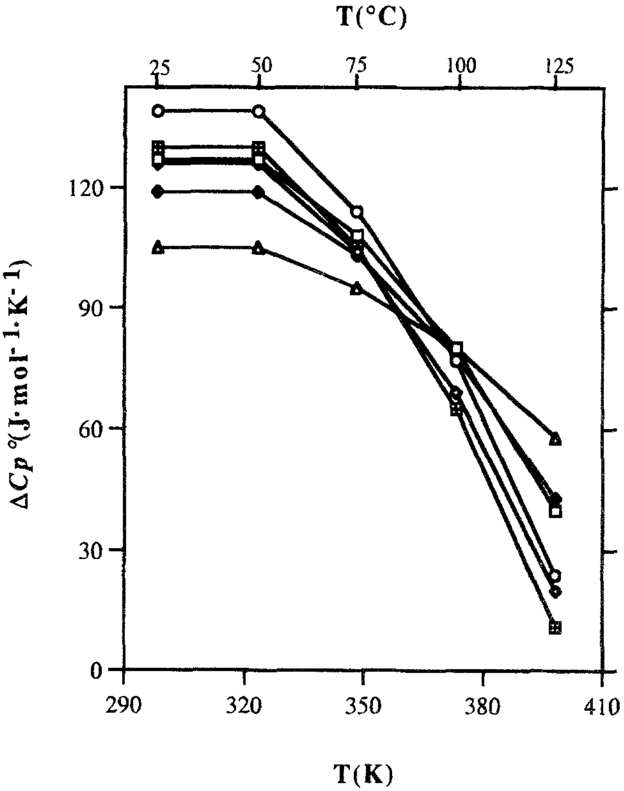

Fig. 2. Plot of $\Delta C_p^\circ$ as a function of temperature for the protonation reaction based on Eq. (6).

of the charges on the zwitterion occurs when the two groups are close together and they have less interaction with water molecules. The net change in $\Delta H^\circ$ as the number of carbon atoms between the groups changes is the result of these two effects. As $n$ increases from 0 to 1 (α-amino acids to β-alanine), $\Delta H^\circ$ at a given temperature decreases, but as $n$ increases from 1 to 2 to 4, $\Delta H^\circ$ increases as seen in Fig. 1. The reversal in trend with β-alanine ($n = 1$) is expected since the interaction between the groups drops off sharply resulting in less increase in $\Delta H^\circ$ compared to that of the α-amino acids. The solute–solvent interaction increases and becomes dominant as $n$ increases further.

The decrease in $\Delta C_p^\circ$ with temperature for the protonation reaction can be explained in terms of long-range and short-range solvation effects. The zwitterion has no net charge, however it does contain both a positively and a negatively charged site. Therefore, the long-range effects of the zwitterion are similar to those of a neutral molecule,(2) while the short-range effects are the same as those of two species containing single but opposite charges in close proximity. Viewed from the long-range perspective, the protonation of

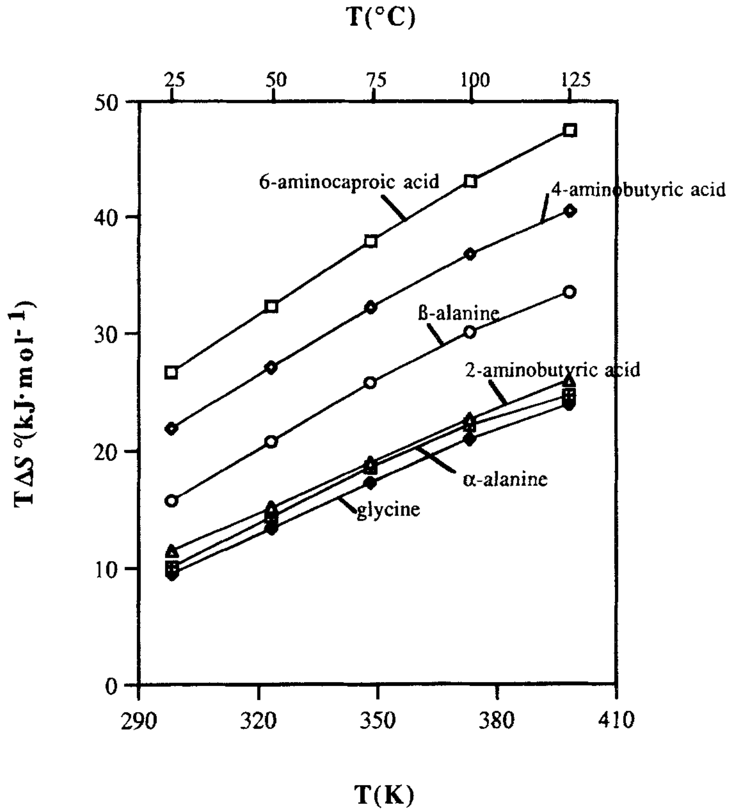

**Fig. 3.** Plot of $T\Delta S^\circ$ as a function of temperature for the protonation reaction: □, 6-aminocaproic acid; ◇, 4-aminobutyric acid; △, DL-2-aminobutyric acid; ○, β-alanine; □, DL-α-alanine; ◆, glycine. The symbols at and above 323.15 K represent the results obtained in this study. The points at 298.15 K are extrapolated based on Eq. (5).

the carboxyl group is an isocoulombic reaction with both the reactants and products containing a single positive charge. From the short-range perspective, the reaction is the same as a neutralization reaction similar to the protonation of a simple carboxylic acid. It has been shown(40) that isocoulombic reactions have small $\Delta C_p^\circ$ values resulting in relatively small, near linear changes in $\Delta H^\circ$ with temperature. On the other hand, protonation reactions which result in charge reduction have large non-linear changes in $\Delta H^\circ$ which accelerate as the temperature increases.(41,42) In the relatively lower temperature range in the study, the short-range effect dominates. Therefore, larger $\Delta C_p^\circ$ are observed due to the release of a large number of bound water molecules into the bulk phase as the carboxylate group is neutralized by a proton. As the temperature increases, the extent of hydrogen bonding decreases, causing the

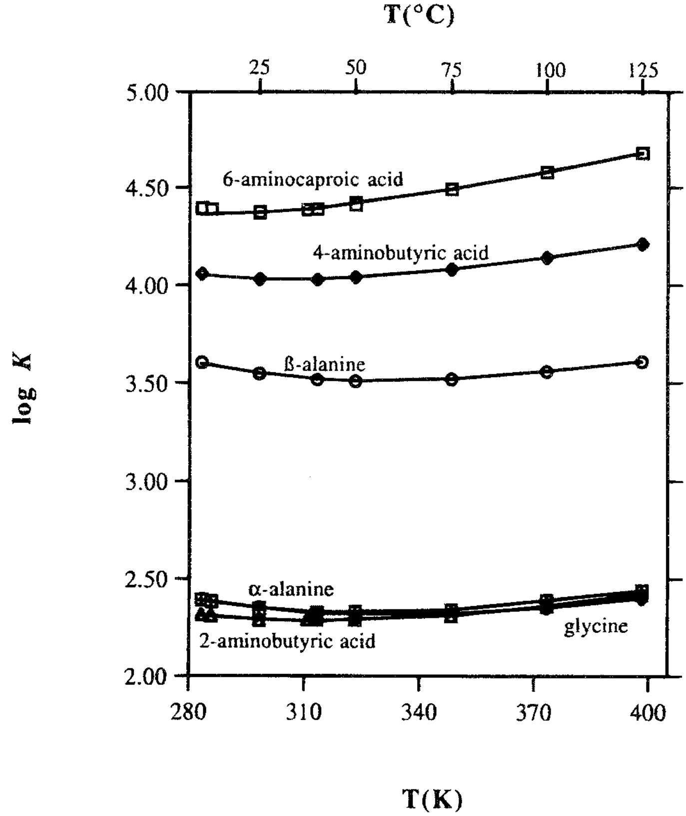

**Fig. 4.** Plot of log *K* for the protonation reaction as a function of temperature: □, 6-aminocaproic acid; ◇, 4-aminobutyric acid; △, DL-2-aminobutyric acid; ○, β-alanine; □, DL-α-alanine; ◆, glycine. The symbols at and above 323.15 K represent the results obtained in this study, all other points are taken from references listed in Table IV. The solid lines are based on Eq. (3).

dielectric constant of water to decrease and the long-range solvation effects become more important relative to short-range effects. Hence, $\Delta C_p^\circ$ decreases as a result of the domination of the long-range solvation effects and the protonation reaction behaves more like an isocoulombic reaction. The $\Delta C_p^\circ$ values for these reactions ranged from 105 to 139 J-mol$^{-1}$-K$^{-1}$ at lower temperatures ($T \leq 323.15$). These $\Delta C_p^\circ$ values are approaching that for the protonation of acetate ion (~150 J-mol$^{-1}$-K$^{-1}$, as calculated from $\Delta H^\circ$ from 273 to 333 K⁽⁵⁾), whereas $\Delta C_p^\circ$ at 398.15 K ranged from 11 to 58 J-mol$^{-1}$-K$^{-1}$, which approach those of isocoulombic reactions.

The differences in the $\Delta S^\circ$ values for the protonation reaction are primarily due to the release of solvent molecules.(3) The smaller the value of *n*, the less influence the zwitterion will have on the solvent molecules. The reaction of the amino acid zwitterion with the proton to form a positively charged species results in the smallest $\Delta S°$ when $n$ is small (Fig. 3) because fewer water molecules are released on the formation of the positively charged species from the zwitterion which has charges close together and which appear to surrounding water molecules as a 'neutral' molecule. As $n$ increases, the separated zwitterion charges influence an increasing number of water molecules. Thus, more water molecules are released to the bulk phase as the protonation of the carboxylate group occurs resulting in large $\Delta S°$. Hence, the larger the $n$ value, the larger will be $\Delta S°$ for the protonation reaction at a given temperature. This rationale is consistent with the observed trend of $T\Delta S°$ with $n$ as seen in Fig. 3. It is also seen that the difference in $T\Delta S°$ among the amino acids increases as temperature increases. This "fanning out" effect was also observed in the protonation of the amino groups.(3) The changes in the values both at a given temperature and as a function of temperature are consistent with the idea expressed earlier that the number of the released water molecules increases most with 6-aminocaproic acid and least with α-amino acids. The α-amino acids have the smallest change in $T\Delta S°$ with temperature because fewer water molecules released to the bulk water of decreasing structure and dielectric constant. Therefore, as temperature increases fewer water molecules remain 'free' with a resulting increased entropy. As $n$ increases, the charged sites have less effect on each other, more water molecules are released to the bulk solvent as the carboxylate group is protonated, and large increases in $T\Delta S°$ are observed.

The increasing $\Delta H°$ and $T\Delta S°$ with increasing chain length among the α-amino acids at a given temperature suggest that hydrophobic effects may be important in these ionization reactions. Details of the side chain effects on the thermodynamic quantities of the protonation of α-amino acids are discussed in a separate paper.(43)

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