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Dissociation constants of protonated methionine species in NaCl media

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Abstract

The sulfur-containing amino acid, methionine, has a role in the physiological environment because of its strong interactions with metals. To understand these interactions of metals with methionine, one needs reliable dissociation constants for the protonated methionine species ($NH_3^+CH(CH_2CH_2SCH_3)COOH$; H_2B^+). The values of stoichiometric dissociation constants, pK_i^*, for protonated methionine species ($H_2B^+ \Leftrightarrow H^+ + HB$, K_1; $HB \Leftrightarrow H^+ + B^-$, K_2) were determined from potentiometric measurements in NaCl solutions as a function of ionic strength, 0.25–6.0 mol (kg $H_2O)^{-1}$ and temperature (5–45 °C). The results were extrapolated to pure water using the Pitzer equations to estimate the activity of H^+, H_2B^+, HB and B^- as a function of ionic strength and temperature. The resulting thermodynamic values of K_1 and K_2 were fit to the equations (T/K): $\ln K_1 = 69.0013 - 3496.58/(T/K) - 10.9153 \ln (T/K)$; $\ln K_2 = 116.4162 - 10638.02/(T/K) - 18.0553 \ln (T/K)$ with standard errors of 0.003 and 0.033, respectively, for $\ln K_1^*$ and $\ln K_2^*$. Pitzer interaction parameters (λ_{HB-Na} and $\zeta_{HB-Na-Cl}$) for the neutral HB were determined from literature data. The Pitzer parameters ($\beta^0_{H_2BCl}$, $\beta^1_{H_2BCl}$ and $C^\phi_{H_2BCl}$) for the interactions of H_2B^+ with Cl^- and Na^+ with and B^{2-} (β^0_{NaB}, β^1_{NaB} and C^ϕ_{NaB}) were also determined. These coefficients can be used to make reasonable estimates of the activity coefficients of methionine species and the pK_i^* for the dissociation of methionine in physiological solutions, composed mostly of NaCl over a wide range of temperature and ionic strength.

Keywords: Dissociation constants; Protonated; Methionine species; NaCl

1. Introduction

Knowledge of thermodynamic properties of amino acids is of great interest because proteins are structurally made of amino acids [1]. The complex formation between metal ions and amino acids are, therefore, commonly used as models for metal–protein interactions. Sulfur-containing amino acids can chelate via $-NH_2$, $-COO^-$, $-S^-$ and COO^- or $-S-$ and $-NH_2$ or via all three sites [2–4]. Methionine is one of the important sulfur-contain-

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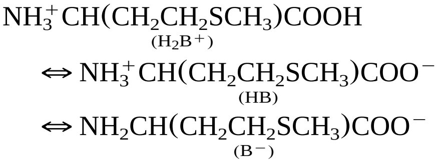
ing amino acids because it helps to initiate translation of messenger RNA by being the first amino acid incorporated into the N-terminal position of all proteins [5]. Methionine is also incorporated into proteins and enzymes. Methionine ($NH_3^+CH(CH_2CH_2SCH_3)COOH$) contains a non-polar methyl thioether group in its side chain of which the methyl group usually participates in biochemical methyl transfer reactions [5]. This process makes methionine a member of the methyl donor class of chemicals [5].

The studies of the interactions between methionine and electrolytes can be used to determine the nature of the formation of complexes with metals in physiological solution. To understand these interactions, one needs reliable dissociation constants for the protonated methionine species (Eq. (1)).



$$\begin{aligned}&\underset{(H_2B^+)}{NH_3^+CH(CH_2CH_2SCH_3)COOH}\\ &\quad\Leftrightarrow \underset{(HB)}{NH_3^+CH(CH_2CH_2SCH_3)COO^-}\\ &\quad\Leftrightarrow \underset{(B^-)}{NH_2CH(CH_2CH_2SCH_3)COO^-} \qquad (1)\end{aligned}$$

The stepwise dissociation of methionine can be presented by Eqs. (2) and (3) [6] where designation of different species of methionine as H_2B^+, HB and B^- is done for simplicity (Eq. (1)).

$$H_2B^+ \Leftrightarrow H^+ + HB \qquad (2)$$

$$HB \Leftrightarrow H^+ + B^- \qquad (3)$$

The stoichiometric (or measured) dissociation constants at a given ionic strength, K_i^*, are given by Eqs. (4) and (5).

$$K_1^* = [H^+][HB]/[H_2B^+] \qquad (4)$$

$$K_2^* = [H^+][B^-]/[HB] \qquad (5)$$

In the literature, the systematic studies on the influence of ionic strength and temperature over wide ranges on the values of $pK_i^* = -\log K_i^*$ for methionine are absent [7,8]. The values of pK_i^* over a wide range of temperature and ionic strength are needed to fully understand interactions of methionine species in electrolyte solutions.

In this paper, the potentiometric titration technique was used to determine values of pK_i^* in NaCl solutions as a function of ionic strength, 0.25–6.0 mol (kg $H_2O)^{-1}$ and temperature (5–45 °C). The measurements of pK_i^* over a wide range of ionic strengths were used to determine Pitzer parameters for the interactions of Na^+ and Cl^- ions with methionine species. These Pitzer parameters allow one to determine the activity coefficient of methionine species in physiological systems, composed mostly of NaCl.

2. Experimental

The potentiometric titrations [9,10] were carried out in a water-jacketed cell controlled at a desired temperature. The temperatures of the measurements were controlled within ±0.1 °C with a Forma circulating water bath. Thirty millilitres of the solution containing methionine ($5–10\times10^{-3}$ M), HCl ($\approx 10^{-2}$ M) and NaCl (0.5–6.0 M) was titrated with standard NaOH solution. For each experiment condition, three replicates were performed. Independent titration of a hydrochloric acid solution with standard NaOH under the same ionic strength conditions of the systems was also carried out to determine the electrode potential (E^o_{ext}) and the acidic junction potential ($E_j = j_a[H^+]$). The pH scale used in NaCl solutions was the total scale, $pH = -\log [H^+]$, where $[H^+]$ is the free proton concentration [11]. The electrodes were calibrated in the media by titrations of NaCl without the acid. The standard emf (E^0) determined in this manner was used to define the pH during a titration and determination of pH. The emf was measured with a Metrohm 605 pH meter and double junction reference electrode. The NaOH was delivered to the cell by motorized burette Metrohm model 654. The calculated accuracy was ±0.15 mV and ±0.003 cm^3 for emf and titrant volume readings, respectively. The computer program ESAB2M [10] was used to refine all the parameters related to the calibration of the elec-

Table 1
Experimental values of pK_i* (±S.D.) for the dissociation of protonated methionine species in NaCl media at different temperatures

m_{NaCl}	pK_1*	pK_2^*
	5 °C	
0.25	2.204±0.012	9.678±0.011
0.5	2.238±0.010	9.676±0.010
1.0	2.308±0.008	9.728±0.009
2.0	2.452±0.008	9.891±0.010
3.0	2.601±0.008	10.076±0.012
4.0	2.756±0.008	10.265±0.014
5.0	2.916±0.008	10.457±0.016
6.0	3.082±0.011	10.649±0.019
	5 °C	
0.25	2.164±0.006	9.105±0.003
0.5	2.193±0.006	9.099±0.003
1.0	2.251±0.007	9.146±0.005
2.0	2.370±0.010	9.296±0.007
3.0	2.495±0.012	9.467±0.008
4.0	2.626±0.012	9.645±0.009
5.0	2.762±0.011	9.825±0.010
6.0	2.903±0.012	10.004±0.013
	45 °C	
0.25	2.149±0.007	8.624±0.003
0.5	2.172±0.005	8.615±0.003
1.0	2.220±0.006	8.656±0.002
2.0	2.318±0.009	8.795±0.002
3.0	2.422±0.011	8.956±0.003
4.0	2.531±0.012	9.123±0.005
5.0	2.646±0.013	9.291±0.011
6.0	2.766±0.017	9.460±0.018

trode system and to calculate the dissociation constants.

Methionine (99%) was obtained from Sigma and was used without further purification. Sodium chloride solutions were prepared by weighing pure salt (Sigma) previously dried in an oven at 110 °C. Hydrochloric acid solution was prepared by diluting concentrated HCl (Optima, Fisher Scientific) and sodium hydroxide solutions were prepared by dissolving solid NaOH (99.99% purity, Aldrich) into water. Solutions of acid and hydroxide were standardized against sodium carbonate and potassium hydrogen phthalate, respectively. Solutions were prepared with water that had been distilled and then passed through a Milli-Q water purification system (resistivity levels 18 MΩ cm^{-1}).

3. Results and discussion

The measured values of pK_i* in NaCl solutions at different ionic strengths and temperatures are given in Table 1 and are shown as a function of the square root of ionic strength ($I^{0.5}$) in Fig. 1 and the reciprocal of the absolute temperature in Fig. 2. The results appear to be a second degree function of $I^{0.5}$ and linear function of $1/T$. A comparison of our results with literature values [12–17] at different ionic strengths at 25 °C are given in Table 2. Our pK_i* values are in good agreement with literature values (Table 2). Some of the small differences may be related to the use

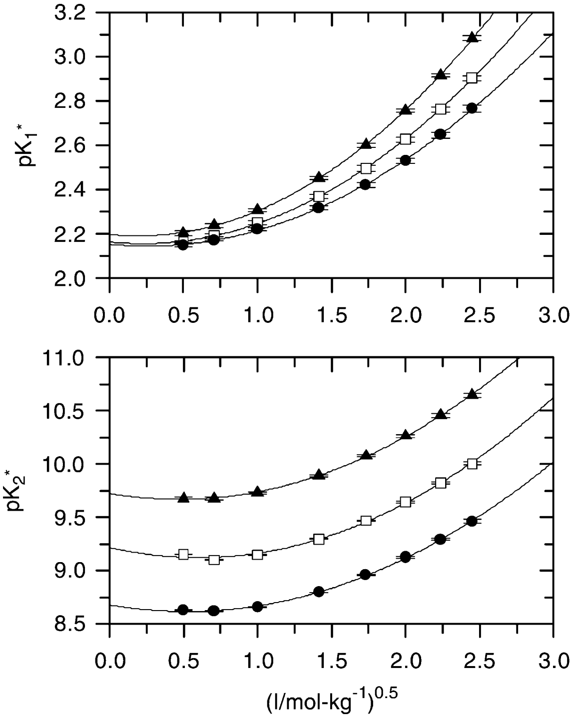


Fig. 1. Values of pK_1 and pK_2 for the dissociation of methionine in NaCl solutions as a function of molality (solid circles: 5 °C; open squares: 25 °C; closed triangles: 45 °C). The smooth curves are from the fit of the measurements to the Pitzer model.

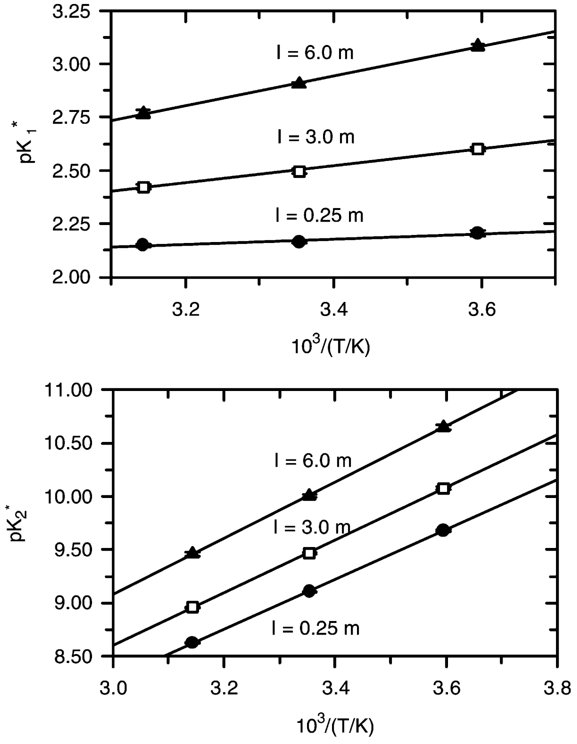


Fig. 2. Value of pK_1 and pK_2 for the dissociation of methionine in NaCl solutions as a function of temperature (T/K). (Solid circles: 5 °C; open squares: 25 °C; closed triangles: 45 °C.)

of potassium chloride in previous studies. There are also small differences in our values from pK_i^* values in the nitrate and other systems given in the IUPAC Database [18]. At high ionic strengths, the interactions between methionine and NO_3^- would be different than Cl^-, which may cause differences in pK_i^* values. The values of ΔH_i calculated from the results shown in Fig. 2 for the dissociation of protonated methionine species, H_2B^+ and HB vary from $\Delta H_1{}^* = -2.8$ to -13.4 kJ mol^{-1} and $\Delta H_2{}^* = -44.7$ to -50.4 kJ mol^{-1}, respectively, from low to high ionic strengths.

The thermodynamic values for dissociation constants for methionine (K_1 and K_2) are related to the measured values (K_1^* and K_2^*) by:

$$K_1 = K_1^* \left(\gamma_{\mathrm{H}}\, \gamma_{\mathrm{HB}}/\gamma_{\mathrm{H_2B}}\right) \tag{6}$$

$$K_2 = K_2^* \left(\gamma_{\mathrm{H}}\, \gamma_{\mathrm{B}}/\gamma_{\mathrm{HB}}\right) \tag{7}$$

where γ_i is the activity coefficient of species i. Our experimental values of K_1^* and K_2^* can be used to determine the thermodynamic constants (K_1 and K_2) and the activity coefficients of H_2B^+ and HB. This can be accomplished by using an ionic interaction model that can account for the interactions between all the species in a NaCl media. We have selected the Pitzer model to examine the effect of ionic strength and temperature on the interactions in the solution. This model has been shown to be quite reliable in accounting for the interactions of non-electrolytes and electrolytes in aqueous solutions [19].

At low concentrations of methionine, the trace activity coefficients of H^+, H_2B^+, HB and B^- in a NaCl solution can be calculated from the Pitzer equations as formulated by Millero and Pierrot [20]:

$$\ln \gamma_{\mathrm{H}} = f^{\gamma} + 2\, m_{\mathrm{Cl}}\, (B_{\mathrm{HCl}} + EC_{\mathrm{HCl}}) + R + S + m_{\mathrm{Na}}\, (2\Theta_{\mathrm{HNa}} + m_{\mathrm{Cl}}\, \Psi_{\mathrm{HNaCl}}) \tag{8}$$

$$\ln \gamma_{\mathrm{H_2B}} = f^{\gamma} + 2\, m_{\mathrm{Na}}(B_{\mathrm{H_2BCl}} + EC_{\mathrm{H_2BCl}}) + R + S \tag{9}$$

$$\ln \gamma_{\mathrm{B}} = 4f^{\gamma} + 2\, m_{\mathrm{Na}}(B_{\mathrm{NaB}} + EC_{\mathrm{NaB}}) + 2R + 4S \tag{10}$$

$$\ln \gamma_{\mathrm{HB}} = 2\, \lambda_{\mathrm{HB-Na}} m_{\mathrm{Na}} + 2\, \lambda_{\mathrm{HB-Cl}} m_{\mathrm{Cl}} + m_{\mathrm{Na}} m_{\mathrm{Cl}} \zeta_{\mathrm{HB-Na-Cl}} \tag{11}$$

Table 2
Literature values of dissociation constants of protonated methionine species in chloride salts at different ionic strength at 25 °C

I, m	Medium	pK_1^*	pK_2^*	Reference
0.00	NaCl	2.14	9.61	This study
0.10	KCl	–	9.17	[11]
0.10	KCl	2.24	9.17	[12]
0.15	NaCl	2.35	9.15	[13]
0.20	KCl	2.22	9.12	[14]
0.20	KCl	–	9.25	[15]
1.00	KCl	–	9.13	[16]
1.00	NaCl	2.25	9.15	This study

The Debye–Hückel term, f^{γ} is given by:

$$f^{\gamma} = -A^{\phi}\,[I^{1/2}/(1+1.2\,I^{0.5}) + (2/1.2)\,\ln(1+1.2\,I^{0.5})] \qquad (12)$$

where A^{ϕ} is given by Møller [21]:

$$A^{\phi} = 3.36901532\times10^{-1} - 6.32100430\times10^{-4}\,(T/K) + 9.14252359/(T/K) - 1.35143986\times10^{-2}\,\ln\,(T/K) + 2.26089488\times10^{-3}/(T/K-263) + 1.92118597\times10^{-6}\,(T/K)^{2} + 4.52586464\times10^{1}/(680-T/K) \qquad (13)$$

The medium terms R and S in Eqs. (8)–(10) in NaCl are given by Pitzer [19].

$$R = \mathrm{m_{Na}m_{Cl}B'_{NaCl}} \qquad (14)$$

$$S = \mathrm{m_{Na}m_{Cl}C_{NaCl}} \qquad (15)$$

The equivalent molality (E) and the ionic strength (I) are equal to the molality of NaCl (m) in the media.

The second (B_{MX}) and third (C_{MX}) virial coefficients are given for 1–1 and 2–1 electrolytes MX (M = Na or H) by:

$$\mathrm{B}_{MX} = \beta^{0}_{MX} + (\beta^{1}_{MX}/2I)[1-(1+2I^{0.5})\,\exp(-2I^{0.5})] \qquad (16)$$

$$\mathrm{B'}_{MX} = (\beta^{1}_{MX}/2I^{2})[-1+(1+2I^{0.5}+2I)\,\exp(-2I^{0.5})] \qquad (17)$$

$$\mathrm{C}_{MX} = \mathrm{C}^{\phi}_{MX}/(2|Z_{M}Z_{X}|^{0.5}) \qquad (18)$$

The values of β^{0}_{MX} and β^{1}_{MX} for NaCl and HCl as well as Θ_{HNa} and Ψ_{HNaCl} values at different temperatures are taken from Millero and Pierrot [20]. The parameters $\lambda_{\mathrm{HB-Na}}$, $\lambda_{\mathrm{HB-Cl}}$ and $\lambda_{\mathrm{HB-HB}}$ are for the interactions of the neutral species HB with $\mathrm{Na^{+}}$, $\mathrm{Cl^{-}}$ and itself, respectively. The value of $\lambda_{\mathrm{HB-Cl}}$ is assigned a value of zero. The $\zeta_{\mathrm{HB-Na-Cl}}$ term is for the interactions of HB with NaCl.

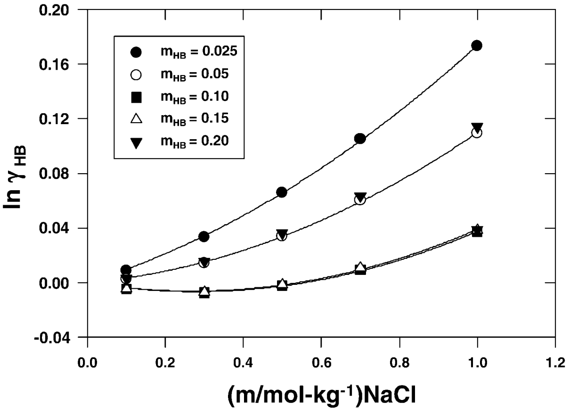


Fig. 3. Values of the activity coefficient of HB in NaCl solutions with various concentrations of HB.

The measured values of $\ln K_{1}^{*}$ and $\ln K_{2}^{*}$ are given by:

$$\ln K_{1}^{*} = \ln K_{1} + \ln\gamma_{\mathrm{H_2B}} - \ln\gamma_{\mathrm{H}} - \ln\gamma_{\mathrm{HB}} \qquad (19)$$

$$\ln K_{2}^{*} = \ln K_{2} + \ln\gamma_{\mathrm{HB}} - \ln\gamma_{\mathrm{H}} - \ln\gamma_{\mathrm{B}} \qquad (20)$$

To determine the unknown values of γ_{H2B}, γ_{HB} and γ_{B} from the measurements of $\ln K_{1}^{*}$ and $\ln K_{2}^{*}$, it is necessary to know the value of γ_{HB} or assign it a value of 1.0 over the entire range of concentration and temperature. Since the values of the γ_{HB} are known independently in NaCl solutions [22], it is possible to determine the coefficients of Eq. (11). The values of $\ln\gamma_{\mathrm{HB}}$ at 25 °C determined in the studies of Soto-Campos et al. [22] as a function of the concentration of NaCl and HB are shown in Fig. 3. As is clear from Fig. 3 the values of $\ln\gamma_{\mathrm{HB}}$ are a second degree function of the concentration of NaCl and first degree of HB. This behavior is consistent with Eq. (11). The fit of these values to Eq. (9) gives $\lambda_{\mathrm{HB-Na}} = 0.0293$, $\lambda_{\mathrm{HB-HB}} = -0.0555$ and $\zeta_{\mathrm{HB-Na-Cl}} = 0.0424$ with a $\sigma = 0.026$ in $\ln\gamma_{\mathrm{HB}}$.

The substitution of Eqs. (8)–(10) into Eqs. (19) and (20) upon rearrangement gives:

$$Y_{1} = \ln K_{1}^{*} + \ln\gamma_{\mathrm{H}} - \ln\gamma_{\mathrm{H_2B}}\,(\mathrm{Med}) + \ln\gamma_{\mathrm{HB}} = \ln K_{1} + \mathrm{m_{Cl}}\,(\mathrm{B_{H_2BCl}} + E\mathrm{C_{H_2BCl}}) \qquad (21)$$

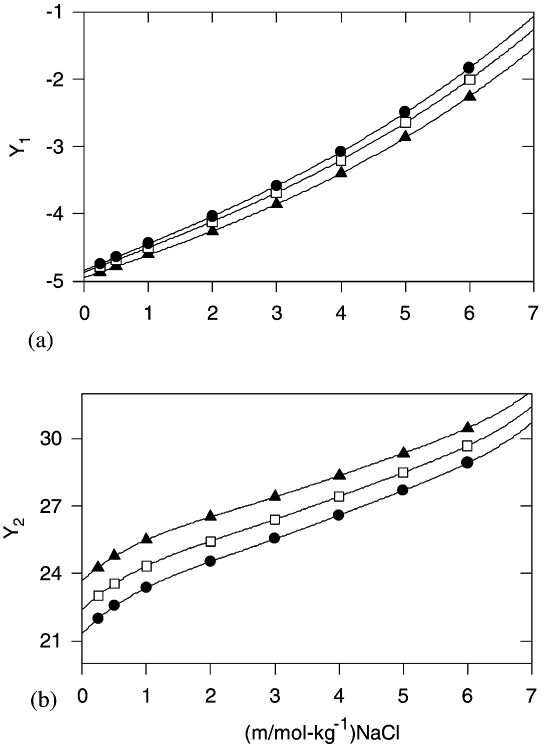


Fig. 4. Values of Y_1 and Y_2 for methionine in NaCl solutions as a function of temperature (solid circles: 5 °C; open squares: 25 °C; closed triangles: 45 °C).

$$Y_2 = -\ln K_2{}^* - \ln\gamma_H - \ln\gamma_B\ (\mathrm{Med}) + \ln\gamma_{HB} = -\ln K_2 + m_{Na}\ (B_{NaB} + EC_{NaB}) \qquad (22)$$

The media terms in NaCl are given by:

$$\ln\gamma_{H_2B}\ (\mathrm{Med}) = f^\gamma + R + S \qquad (23)$$

$$\ln\gamma_B\ (\mathrm{Med}) = 4f^\gamma + 2R + 4S \qquad (24)$$

The substitution of Eqs. (16) and (17) into Eqs. (21) and (22) gives:

$$Y_1 = \ln K_1 + 2m\ \beta^0_{H_2BCl} + 2m\ F^1\beta^1_{H_2BCl} + 2m^2\ C_{H_2BCl} \qquad (25)$$

$$Y_2 = -\ln K_2 + 2m\ \beta^0_{NaB} + 2m\ F^1\beta^1_{NaB} + 2m^2\ C_{NaB} \qquad (26)$$

where

$$F^1 = [1 - (1 + 2I^{0.5})\ \exp(-2I^{0.5})]/2I \qquad (27)$$

The values of β^0_i, β^1_i and C^ϕ_i are the Pitzer parameters for the interaction of Na^+ and Cl^- with methionine species.

Values of Y_i were determined from known parameters of Eqs. (21) and (22) and are plotted as a function of the molality at different temperatures in Fig. 4. The Pitzer parameters obtained for methionine species at different temperatures are given in Table 3. The results for all of the measurements gave temperature dependence values of K_1 and K_2 and the Pitzer parameters:

$$\ln K_1 = 69.0013 - 3496.58/(T/K) - 10.9153\ \ln(T/K) \qquad (28)$$

$$\beta^0_{H_2BCl} = 0.2954 - 57.0577/(TK) \qquad (29)$$

$$\beta^1_{H_2BCl} = 0.3011 \qquad (30)$$

$$C_{H_2BCl} = -0.0190 \qquad (31)$$

$$\ln K_2 = 116.4162 - 10638.02/(T/K) - 18.0553\ \ln(T/K) \qquad (32)$$

Table 3
Pitzer coefficients for methionine species in NaCl media at various temperatures

t (°C)	Species	lnKi	β°	β¹	C^ϕ	$\sigma(\ln K_i^*)$
5	H_2B^+	−4.9964	0.0899	0.2912	0.0192	0.0005
25	H_2B^+	−4.9177	0.1063	0.2927	0.0188	0.0008
45	H_2B^+	−4.8943	0.1142	0.3195	0.0192	0.0006
5	B^-	−23.3556	0.0901	3.1811	0.0419	0.0503
25	B^-	−22.1815	0.2315	0.6838	0.0289	0.0056
45	B^-	−21.1238	0.2472	2.7951	0.0296	0.0062

Table 4
The values of ΔH_i for some amino acids in chloride salts solutions

Amino acids	I, M	Medium	ΔH_1^* kJ mol^{-1}	ΔH_2^* kJ mol^{-1}	Reference
Glycine	0.10	KCl	–	−46.0	[21]
($NH_3^+CH_2COOH$)	0.15	NaCl	−4.3	−45.4	[8]
	0.20	KCl	−4.4	−44.3	[22]
Alanine ($NH_3^+CH(CH_3)COOH$)	0.10	KCl	−2.9	−45.0	[8]
Valine ($NH_3^+CH(CHCH_3)_2COOH$)	0.10	KCl	–	−45.3	[8]
Methionine	0.00	NaCl	−2.1	−43.8	This study
($NH_3^+CH(CH_2CH_2SCH_3)COOH$)	0.25	NaCl	−2.8	−44.7	This study

$$\beta^0_{NaB} = 20.5826 - 993.41/(T/K) - 2.9932\ \ln(T/K) \quad (33)$$

$$\beta^1_{NaB} = 4.9176 - 603.71/(T/K) \quad (34)$$

$$C_{NaB} = 0.0335 \quad (35)$$

These equations give standard errors (S.E.) of 0.003 and 0.033, respectively, in lnK_1* and lnK_2* over the entire range of concentration and temperature. It should be pointed out that the values of lnγ_{HB} at 5 and 45 °C were equated to the values at 25 °C. This assumption will cause some uncertainty in the effect of temperature on the parameters given in Eqs. (28)–(35).

Values of ΔH_i* for methionine in chloride solutions are compared with amino acids in Table 4. The small differences in ΔH_1* between glycine and alanine indicate that the $-CH_2$ does not strongly effect the enthalpy. Further additions of −S and $-CH_2$ groups in the glycine molecule do not significant effect the values of ΔH_1*. Similar effects in ΔH_1* of the $-CH_2$ groups are found in aliphatic monoamines [23–25]. The values of ΔH_2* for methionine are similar to other amino acids as shown in Table 3. These values are higher than $\Delta H = -55.7$ kJ mol^{-1} for methyamine (CH_3NH_2) [25]. This difference of ≈10 kJ mol^{-1} may be due to the presence of carboxyl group in the amino acids.

The effect of ionic strength on ΔH_i* in methionine are probably due to effect of ions on the ion–dipole and dipole–dipole interactions between carboxyl and amino groups with each other and water molecules [22,26,27]. Electrostatic interactions between Na^+ and Cl^- with the carboxyl and amino groups of methionine cause the activity coefficients to vary with ionic strengths and tem-

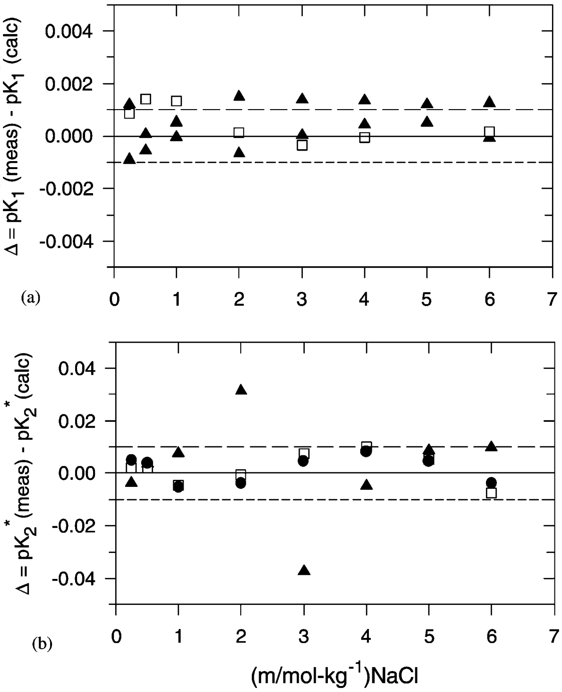


Fig. 5. Deviations between the measured and calculated values of pK_1 and pK_2 as a function of the molality and temperature (solid circles: 5 °C; open squares: 25 °C; closed triangles: 45 °C).

perature. The effect of temperature on the activity coefficients cause the variation of the values of ΔH_i* values with temperature.

The calculated values of pK_i^*, using Pitzer parameters in NaCl media at different ionic strength and temperature, are in reasonable agreement with the experimental values. This is shown in Fig. 5 where the S.E. are 0.001 and 0.014, respectively, for pK_1* and pK_2*. Our Pitzer parameters can, thus be used to make reliable estimates of pK_i^* at ionic strength, $I = 0–6$ m and from 5 to 45 °C.

In summary, the results of the present study should contribute to the understanding the effect of chelating agents such as methionine on trace element metabolism. The calculated values of pK_1^* and pK_2^* under physiological conditions of $I =$ 0.7 m at 37 °C are 2.197 and 8.828, respectively; suggesting the neutral methionine species, HB, occurs predominantly at pH 7.4. In this environment, the amino groups of the methionine molecule would be protonated. Reliable Pitzer parameters have been derived for the interactions of H_2^* and pK_2^* under physiological conditions of $I = 0.7$ m at 37 °C are 2.197 and 8.828, respectively; suggesting the neutral methionine species, HB, occurs predominantly at pH 7.4. In this environment, the amino groups of the methionine molecule would be protonated. Reliable Pitzer parameters have been derived for the interactions of H_2B^+ and B^- with Cl^- and Na^+ as a function of ionic strength and temperature. These parameters should also be useful in estimating the activity coefficients of methionine species in physiological systems.

4. Nomenclature

T: Absolute Temperature
m: Molality of solution
γ_i: Activity coefficient of species
E_j: Liquid junction potential
H: Enthalpy
K_i^*: Measured dissociation constant at a given ionic strength
K_i: Thermodynamic dissociation constant
I: Ionic strength
Z_i: Valence of ion
E: Equivalent weighing factor
M: Positive ion of the electrolyte MX
X: Negative ion of the electrolyte MX

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