

# Partial Molar Volumes and Isentropic Compressibilities of *N*-Acetyl Amino Acid Amides in Dilute Aqueous Solutions at (5, 15, 25, 35, and 45) °C

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The densities and sound velocities in dilute aqueous solutions of nine *N*-acetyl amino acid amides were measured at (5, 15, 25, 35, and 45) °C. The *N*-acetyl amino acid amides used were *N*-acetyl-glycinamide, *N*-acetyl-L-alaninamide, *N*-acetyl-L-valinamide, *N*-acetyl-L-leucinamide, *N*-acetyl-L-methioninamide, *N*-acetyl-L-prolinamide, *N*-acetyl-L-phenylalaninamide, *N*-acetyl-L-tryptophanamide, and *N*-acetyl-L-tyrosinamide. Partial molar volumes and partial molar isentropic compressibilities of these *N*-acetyl amino acid amides at infinite dilution were evaluated. Furthermore, the side chain contribution to the partial molar quantities of the *N*-acetyl amino acid amides can be derived using a group additivity approach. The results were compared with those of amino acids reported in our previous paper.

## Introduction

In order to obtain a better understanding of the hydration behavior of proteins, studies have been made on the volumetric properties of amino acids, considered as model compounds, in aqueous solution (Jolicœur and Boileau, 1978; Jolicœur *et al.*, 1986; Kharakoz, 1989, 1991; Millero *et al.*, 1978). However, since amino acids are zwitterions in aqueous solutions, the charged end groups may interfere with the hydration of adjacent amino acid side chains. Thus it seems that the amino acids are not necessarily the most suitable compounds to model the amino acid side chain in proteins.

Hydration effects are known to be very sensitive to temperature (Kharakoz, 1989, 1991; Sakurai *et al.*, 1994). While the temperature dependence studies of volumetric properties are useful for a more complete understanding of the solute hydration, the great majority of previous investigations of model compounds has been conducted only at 25 °C.

In view of the above fact, it is of interest to determine the volumetric properties of *N*-acetyl amino acid amides which have no ionic groups as reasonable model compounds and compare the results with those of amino acids.

Volumetric data for amino acids that can be compared have been reported in dilute aqueous solutions at (5, 15, 25, 35, and 45) °C (Kikuchi *et al.*, 1995). In the present paper we report the partial molar volumes and isentropic compressibilities of some *N*-acetyl amino acid amides in dilute aqueous solution over the same experimental temperature range as our previous investigation, (5 to 45) °C.

## Experimental Section

The *N*-acetyl amino acid amides used, *N*-acetyl-glycinamide (Ac-Gly-NH<sub>2</sub>), *N*-acetyl-L-alaninamide (Ac-Ala-NH<sub>2</sub>), *N*-acetyl-L-valinamide (Ac-Val-NH<sub>2</sub>), *N*-acetyl-L-leucinamide (Ac-Leu-NH<sub>2</sub>), *N*-acetyl-L-methioninamide (Ac-Met-NH<sub>2</sub>), *N*-acetyl-L-prolinamide (Ac-Pro-NH<sub>2</sub>), *N*-acetyl-L-phenylalaninamide (Ac-Phe-NH<sub>2</sub>), *N*-acetyl-L-tryptophanamide (Ac-Trp-NH<sub>2</sub>), and *N*-acetyl-L-tyrosinamide (Ac-Tyr-NH<sub>2</sub>), were extra pure reagents obtained commercially: *N*-acetyl-glycinamide was obtained from Aldrich Chemical Co., Inc., Milwaukee, WI; *N*-acetyl-L-tyrosinamide was obtained from Peptide Institute, Inc., Minoh, Japan. The other compounds were obtained from BACHEM Feinchemi-

kalien AG, Bubendorf, Switzerland. These samples were dried *in vacuo* before the measurements and used without further purification. All solutions were prepared by mass with deionized and distilled water. The solution densities were measured by an oscillating-tube densimeter (DMA 60/601, Anton Paar, Austria) with a precision of  $\pm (2 \times 10^{-6})$  g·cm<sup>-3</sup>. The sound velocities in the solutions were measured at a frequency of about 5 MHz using a sing-around velocimeter constructed in our laboratory. The precision of the measurements of the sound velocity was estimated to be better than 1 cm·s<sup>-1</sup> for the dilute solution range studied. The temperature of the fluid surrounding the measuring cell of the densimeter or velocimeter was maintained within  $\pm 0.002$  deg by using a laboratory-made temperature controller using Y-cut quartz. Details of the apparatus, their calibrations, and experimental procedures used have been described previously (Sakurai and Nakagawa, 1982; Sakurai *et al.*, 1994, 1995).

With the exception of Ac-Phe-NH<sub>2</sub>, Ac-Trp-NH<sub>2</sub>, and Ac-Tyr-NH<sub>2</sub>, the measurements of the densities and sound velocities of all *N*-acetyl amino acid amide solutions were carried out over the concentration range *ca.* (0.01–0.1) mol·kg<sup>-1</sup>. Because of the low solubilities of Ac-Phe-NH<sub>2</sub>, Ac-Trp-NH<sub>2</sub>, and Ac-Tyr-NH<sub>2</sub> in water, the maximum concentration of Ac-Phe-NH<sub>2</sub> was about 0.05 mol·kg<sup>-1</sup>, and those of Ac-Trp-NH<sub>2</sub> and Ac-Tyr-NH<sub>2</sub> were about 0.01 mol·kg<sup>-1</sup>. For *N*-acetyl-L-isoleucinamide, owing to the low solubility in water, it was impossible to measure the densities and sound velocities.

## Results and Discussion

The apparent molar volumes,  $V_\phi$ , and the apparent molar isentropic compressibilities,  $K_{s,\phi}$ , of the solutes were calculated from the solution densities and the isentropic compressibilities using the following equations:

$$V_\phi = M_2/\rho - (\rho - \rho_1)/(m\rho\rho_1) \quad (1)$$

and

$$K_{s,\phi} = M_2\kappa_s/\rho - (\kappa_{s,1}\rho - \kappa_s\rho_1)/(m\rho\rho_1) \quad (2)$$

In eqs 1 and 2,  $M_2$  is the solute molar mass,  $m$  is the molality,  $\rho$  is the density of the solution, and  $\rho_1$  is the density of the pure solvent. In eq 2,  $\kappa_s$  and  $\kappa_{s,1}$  are the



Table 1. (Continued)

$t/^\circ\text{C}$	$m/\text{mol}\cdot\text{kg}^{-1}$	$10^3(\rho - \rho_1)/\text{g}\cdot\text{cm}^{-3}$	$V_\phi/\text{cm}^3\cdot\text{mol}^{-1}$	$m/\text{mol}\cdot\text{kg}^{-1}$	$10^3(\rho - \rho_1)/\text{g}\cdot\text{cm}^{-3}$	$V_\phi/\text{cm}^3\cdot\text{mol}^{-1}$	$t/^\circ\text{C}$	$m/\text{mol}\cdot\text{kg}^{-1}$	$10^3(\rho - \rho_1)/\text{g}\cdot\text{cm}^{-3}$	$V_\phi/\text{cm}^3\cdot\text{mol}^{-1}$	$m/\text{mol}\cdot\text{kg}^{-1}$	$10^3(\rho - \rho_1)/\text{g}\cdot\text{cm}^{-3}$	$V_\phi/\text{cm}^3\cdot\text{mol}^{-1}$
<i>N</i> -Acetyl-L-prolinamide (156.2)													
5	0.107 20	3.425	123.82	0.053 09	1.704	123.88	35	0.107 20	3.084	127.62	0.052 50	1.519	127.67
	0.093 29	2.985	123.83	0.041 71	1.340	123.91		0.093 58	2.697	127.62	0.041 36	1.197	127.70
	0.079 62	2.550	123.85	0.032 64	1.049	123.92		0.079 61	2.297	127.64	0.032 45	0.939	127.72
	0.065 94	2.113	123.89					0.065 50	1.893	127.65			
15	0.107 20	3.292	125.16	0.052 60	1.626	125.16	45	0.107 20	3.009	128.72	0.052 90	1.494	128.74
	0.093 55	2.878	125.16	0.041 60	1.287	125.18		0.093 64	2.632	128.73	0.041 15	1.164	128.75
	0.079 56	2.451	125.16	0.032 54	1.009	125.13		0.079 67	2.245	128.71	0.032 35	0.916	128.74
	0.065 41	2.019	125.16					0.065 99	1.863	128.70			
25	0.107 20	3.183	126.39	0.052 75	1.576	126.41							
	0.093 80	2.789	126.39	0.041 64	1.246	126.39							
	0.079 53	2.369	126.39	0.032 61	0.977	126.38							
	0.065 71	1.961	126.39										
<i>N</i> -Acetyl-L-tryptophanamide (245.3)													
5	0.013 39	0.768	187.81	0.007 28	0.418	187.83	35	0.013 39	0.683	195.06	0.007 18	0.367	195.02
	0.011 88	0.681	187.81	0.005 79	0.333	187.66		0.011 91	0.608	194.99	0.005 72	0.291	195.20
	0.010 28	0.590	187.86	0.004 44	0.255	187.89		0.010 26	0.524	195.01	0.004 40	0.224	195.15
	0.008 68	0.498	187.88					0.008 62	0.440	194.98			
15	0.013 39	0.732	190.62	0.007 37	0.405	190.46	45	0.013 39	0.669	196.61	0.007 07	0.354	196.56
	0.011 83	0.648	190.57	0.005 92	0.325	190.44		0.011 82	0.592	196.50	0.005 64	0.283	196.46
	0.010 28	0.562	190.64	0.004 53	0.249	190.46		0.010 13	0.507	196.57	0.004 36	0.218	196.63
	0.008 77	0.480	190.60					0.008 51	0.427	196.54			
25	0.013 39	0.706	192.84	0.007 22	0.380	192.96							
	0.011 90	0.628	192.85	0.005 74	0.302	193.02							
	0.010 28	0.543	192.72	0.004 37	0.229	193.16							
	0.008 63	0.455	192.88										
<i>N</i> -Acetyl-L-tyrosinamide (222.24)													
5	0.011 06	0.582	169.49	0.007 01	0.369	169.55	35	0.011 06	0.520	175.89	0.006 29	0.294	176.15
	0.010 15	0.534	169.57	0.005 99	0.316	169.51		0.009 96	0.468	175.98	0.005 22	0.246	175.84
	0.009 11	0.479	169.63	0.004 81	0.254	169.50		0.008 77	0.413	175.82	0.004 19	0.197	175.99
	0.008 03	0.422	169.67					0.007 50	0.354	175.79			
15	0.011 06	0.556	171.99	0.006 98	0.350	172.14	45	0.011 06	0.507	177.58	0.007 00	0.321	177.59
	0.010 10	0.508	171.92	0.006 02	0.304	171.89		0.010 10	0.463	177.54	0.005 92	0.271	177.61
	0.009 04	0.455	171.99	0.004 84	0.244	171.89		0.009 07	0.416	177.57	0.004 79	0.219	177.71
	0.007 96	0.401	171.90					0.008 01	0.369	177.47			
25	0.011 06	0.537	173.92	0.006 91	0.337	173.88							
	0.010 16	0.495	173.82	0.005 87	0.285	173.97							
	0.009 11	0.444	173.86	0.004 71	0.229	173.85							
	0.007 99	0.388	174.02										

<sup>a</sup> Molecular masses (g/mol) are in parentheses.

isentropic compressibilities of solution and pure solvent, respectively. The isentropic compressibility was determined from the sound velocity,  $u$ , and density using the following relation:

$$\kappa_s = 1/(u^2 \rho) \quad (3)$$

The density differences between solution and pure water ( $\rho - \rho_1$ ) at (5, 15, 25, 35, and 45) °C are given in Table 1. The  $\rho_1$  values at various temperatures were taken from the table given by Kell (1975). Values of (0.999 964, 0.999 100, 0.997 045, 0.994 032, and 0.990 213) g·cm<sup>-3</sup> were used as the density of pure water at (5, 15, 25, 35, and 45) °C, respectively. These values were used to calculate the apparent molar volumes,  $V_\phi$ , of the solutes using eq 1. The calculated  $V_\phi$  values are also given in Table 1.

The sound velocity differences between solution and water ( $u - u_1$ ) at various temperatures are summarized in Table 2. The sound velocities in pure water ( $u_1$ ) were taken from the table reported by Del Grosso and Mader (1972). Values of (1426.162, 1465.931, 1496.687, 1519.808, and 1536.409) m·s<sup>-1</sup> were used as the sound velocity in pure water at (5, 15, 25, 35, and 45) °C, respectively.

The density values of the solution used for sound velocity measurements were calculated from  $V_2^\circ$  (partial molar volume at the infinite dilution) and  $S_v$  (experimental slope) values obtained by using eq 4 (see below) in the same manner reported previously (Sakurai *et al.*, 1994, 1995). These values were used to calculate the apparent molar isentropic compressibilities,  $K_{s,\phi}$ , of the solutes using eqs 2 and 3. The calculated  $K_{s,\phi}$  values are also given in Table 2.

For sufficiently dilute solutions, the variation of the apparent molar quantities,  $Q_\phi$ , with molality can be adequately represented by the linear relation

$$Q_\phi = Q_\phi^\circ + S_q m \quad (4)$$

where  $Q_\phi^\circ$  is the infinite dilution value that is equal to the partial molar quantity at infinite dilution ( $Q_2^\circ$ ) and  $S_q$  is the experimental slope.

Equation 4 was fitted to our  $V_\phi$  and  $K_{s,\phi}$  data by the least-squares method outlined earlier (Sakurai *et al.*, 1994). The  $V_2^\circ$  and  $K_{s,2}^\circ$  values together with their standard deviations are summarized in Table 3 along with the concentration dependence of these thermodynamic functions  $S_v$  and  $S_k$ . The previously available  $V_2^\circ$  values at 25 °C are (90.56, 108.06, 139.00, and 126.51) cm<sup>3</sup>·mol<sup>-1</sup> for Ac-Gly-NH<sub>2</sub>, Ac-Ala-NH<sub>2</sub>, Ac-Val-NH<sub>2</sub>, and Ac-Pro-NH<sub>2</sub>, respectively (Leslie and Lilley, 1985). The previously available  $K_{s,2}^\circ$  values at 25 °C are (-1.99 and -0.72) cm<sup>3</sup>·mol<sup>-1</sup>·GPa<sup>-1</sup> for Ac-Gly-NH<sub>2</sub> and Ac-Ala-NH<sub>2</sub>, respectively (Hedwig and Hoiland, 1995). To our knowledge, no comparable  $V_2^\circ$  and  $K_{s,2}^\circ$  data can be found in the literature, except for the above values. For  $V_2^\circ$  values, the results obtained from the present study are in good agreement with those available in the literature. However, the corresponding comparison for  $K_{s,2}^\circ$  values reveals several differences. We currently have no explanation for these discrepancies in  $K_{s,2}^\circ$  values. For Ac-Trp-NH<sub>2</sub> and Ac-Tyr-NH<sub>2</sub>, the absolute values of  $S_k$  and its standard deviations are extraordinarily large. These are because these compounds have low solubilities in water, as described in the Experimental Section, and



Table 2. (Continued)

$t/^\circ\text{C}$	$m/\text{mol}\cdot\text{kg}^{-1}$	$(u-u_1)/\text{m}\cdot\text{s}^{-1}$	$K_{s,\phi}/\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{GPa}^{-1}$	$m/\text{mol}\cdot\text{kg}^{-1}$	$(u-u_1)/\text{m}\cdot\text{s}^{-1}$	$K_{s,\phi}/\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{GPa}^{-1}$	$t/^\circ\text{C}$	$m/\text{mol}\cdot\text{kg}^{-1}$	$(u-u_1)/\text{m}\cdot\text{s}^{-1}$	$K_{s,\phi}/\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{GPa}^{-1}$	$m/\text{mol}\cdot\text{kg}^{-1}$	$(u-u_1)/\text{m}\cdot\text{s}^{-1}$	$K_{s,\phi}/\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{GPa}^{-1}$
<i>N</i> -Acetyl-L-phenylalaninamide (206.25)													
5	0.048 38	6.905	-35.96	0.027 67	3.987	-37.06	35	0.048 38	4.325	8.17	0.028 09	2.502	8.32
	0.043 59	6.243	-36.34	0.023 27	3.358	-37.26		0.043 96	3.929	8.17	0.023 53	2.085	8.60
	0.038 14	5.470	-36.51	0.020 05	2.902	-37.56		0.038 70	3.449	8.31	0.020 23	1.790	8.68
15	0.032 63	4.694	-36.87					0.033 21	2.958	8.34			
	0.048 38	6.013	-18.14	0.027 61	3.455	-18.70	45	0.048 38	3.459	19.78	0.027 76	1.974	19.93
	0.043 73	5.440	-18.22	0.023 16	2.906	-18.90		0.043 90	3.149	19.63	0.023 31	1.653	20.03
	0.038 19	4.763	-18.42	0.019 92	2.506	-19.12		0.038 45	2.745	19.80	0.020 10	1.426	20.00
0.032 62	4.077	-18.59				0.032 84		2.338	19.90				
25	0.048 38	5.092	-3.15	0.027 73	2.936	-3.49							
	0.043 78	4.619	-3.28	0.023 34	2.479	-3.68							
	0.038 33	4.045	-3.30	0.020 12	2.144	-3.88							
	0.032 75	3.468	-3.51										
<i>N</i> -Acetyl-L-prolinamide (156.2)													
5	0.107 20	12.154	-32.93	0.060 12	6.888	-33.80	35	0.107 20	7.659	1.45	0.060 26	4.313	1.45
	0.095 80	10.896	-33.19	0.050 66	5.819	-34.02		0.095 94	6.857	1.45	0.050 78	3.637	1.43
	0.083 12	9.481	-33.42	0.043 78	5.036	-34.15		0.083 22	5.948	1.47	0.043 82	3.139	1.44
	0.071 05	8.129	-33.68					0.071 18	5.090	1.47			
15	0.107 20	10.462	-18.20	0.060 14	5.927	-18.84	45	0.107 20	6.472	8.59	0.060 84	3.694	8.45
	0.095 59	9.356	-18.39	0.050 68	4.999	-18.92		0.096 22	5.815	8.56	0.051 39	3.125	8.40
	0.083 33	8.176	-18.55	0.043 73	4.316	-18.95		0.083 86	5.076	8.53	0.044 41	2.698	8.44
	0.071 08	6.984	-18.65					0.071 64	4.341	8.50			
25	0.107 20	8.798	-6.23	0.060 23	4.988	-6.66							
	0.095 76	7.880	-6.36	0.050 79	4.213	-6.74							
	0.083 42	6.881	-6.47	0.043 81	3.639	-6.81							
	0.071 19	5.883	-6.56										
<i>N</i> -Acetyl-L-tryptophanamide (245.3)													
5	0.013 63	1.933	-33.64	0.007 98	1.158	-35.95	35	0.013 63	1.181	12.41	0.007 95	0.707	11.12
	0.012 32	1.755	-34.08	0.006 78	0.990	-36.53		0.012 33	1.082	11.81	0.006 74	0.611	10.09
	0.010 85	1.562	-35.19	0.005 85	0.865	-37.76		0.010 86	0.944	12.27	0.005 82	0.527	10.15
	0.009 33	1.350	-35.60					0.009 33	0.829	11.17			
15	0.013 63	1.644	-13.44	0.007 81	0.957	-14.74	45	0.013 63	1.016	20.29	0.007 97	0.590	20.58
	0.012 23	1.476	-13.59	0.006 59	0.807	-14.73		0.012 39	0.914	20.70	0.006 76	0.508	19.93
	0.010 71	1.291	-13.50	0.005 68	0.700	-15.32		0.010 88	0.820	19.77	0.005 84	0.437	20.06
	0.009 22	1.117	-13.88					0.009 36	0.703	19.93			
25	0.013 63	1.428	-0.35	0.007 98	0.860	-2.11							
	0.012 33	1.294	-0.47	0.006 75	0.726	-1.94							
	0.010 84	1.142	-0.65	0.005 84	0.623	-1.37							
	0.009 33	1.005	-2.02										
<i>N</i> -Acetyl-L-tyrosinamide (222.24)													
5	0.011 06	1.256	-20.81	0.007 01	0.794	-20.57	35	0.011 06	0.726	17.98	0.006 48	0.413	19.14
	0.010 19	1.165	-21.32	0.006 02	0.676	-19.93		0.010 00	0.661	17.73	0.005 52	0.348	19.52
	0.009 18	1.047	-21.16	0.005 13	0.572	-19.42		0.008 79	0.581	17.73	0.004 73	0.290	20.48
	0.008 07	0.915	-20.73					0.007 58	0.497	18.05			
15	0.011 06	1.038	-3.12	0.006 88	0.640	-2.61	45	0.011 06	0.668	21.92	0.006 40	0.371	23.33
	0.010 12	0.946	-2.86	0.005 90	0.547	-2.48		0.010 02	0.605	21.92	0.005 39	0.308	23.77
	0.009 04	0.843	-2.69	0.005 05	0.466	-2.09		0.008 78	0.519	22.65	0.004 65	0.269	23.39
	0.007 93	0.740	-2.75					0.007 53	0.433	23.52			
25	0.011 06	0.901	7.03	0.006 71	0.548	6.90							
	0.010 12	0.834	6.47	0.005 74	0.467	7.11							
	0.008 97	0.730	7.08	0.004 91	0.396	7.48							
	0.007 82	0.637	7.01										

<sup>a</sup> Molecular masses (g/mol) are in parentheses.

the concentration ranges in this measurement are limited.

The temperature dependence of the partial molar volumes is equal to the partial molar expansibility  $E_2^{\circ} (= (\partial V_2^{\circ} / \partial T)_p)$ . Table 4 shows the partial molar expansibilities of *N*-acetyl amino acid amides and amino acids (Kikuchi *et al.*, 1995) in dilute aqueous solution at 25 °C. The  $E_2^{\circ}$  values were estimated by the least-squares fitting to a quadratic equation. With the exception of tyrosine and *N*-acetyltyrosinamide, Table 4 shows that  $E_2^{\circ}$  values for the *N*-acetyl amino acid amide derivative are larger than those for the amino acid derivative. The values of  $(\partial^2 V_2^{\circ} / \partial T^2)_p$  for *N*-acetyl amino acid amides are negative, similar to those of amino acids.

The  $K_{s,2}^{\circ}$  values for all the *N*-acetyl amino acid amides are small or negative within the temperature range (5 to

25) °C. *N*-Acetyl amino acid amides have two amide groups which are able to form hydrogen bonds with water. It has been considered that the hydrogen bonding leads to a decrease in the compressibility (Conway and Ayranci, 1988). Therefore, the small or negative  $K_{s,2}^{\circ}$  values of *N*-acetyl amino acid amides result from the hydrogen bonding interaction between the amide groups and water.

The  $K_{s,2}^{\circ}$  values for *N*-acetyl amino acid amides having aliphatic side chains are plotted in Figure 1 as a function of temperature. The feature of the temperature dependence of  $K_{s,2}^{\circ}$  for these compounds is as follows: with increasing side chain length, the  $K_{s,2}^{\circ}$  values decrease at lower temperatures, are practically constant between (30 and 35) °C, and increase at higher temperatures. This feature is similar to that observed for a series of amino

**Table 3. Partial Molar Volumes and Isentropic Compressibilities of *N*-Acetyl Amino Acid Amides in Dilute Aqueous Solutions at (5, 15, 25, and 45) °C**

<i>t</i> /°C	$V_2^o$ / cm <sup>3</sup> ·mol <sup>-1</sup>	$S_v$ / cm <sup>3</sup> ·kg· mol <sup>-2</sup>	$K_{s,2}^o$ / cm <sup>3</sup> ·mol <sup>-1</sup> · GPa <sup>-1</sup>	$S_k$ / cm <sup>3</sup> ·kg·mol <sup>-2</sup> · GPa <sup>-1</sup>
<i>N</i> -Acetylglycinamide				
5	88.41(0.01) <sup>a</sup>	-0.54(0.15)	-19.05(0.04)	8.06(0.53)
15	89.76(0.02)	-1.07(0.23)	-8.68(0.09)	2.63(1.12)
25	90.84(0.01)	-1.11(0.13)	-1.19(0.11)	-2.54(1.31)
35	91.87(0.01)	-2.85(0.12)	3.96(0.06)	-2.95(0.62)
45	92.70(0.01)	-1.68(0.08)	7.96(0.08)	-1.87(0.93)
<i>N</i> -Acetyl-L-alaninamide				
5	106.22(0.02)	-0.13(0.24)	-21.54(0.05)	12.43(0.60)
15	107.03(0.02)	1.31(0.27)	-10.48(0.11)	11.34(1.29)
25	108.01(0.03)	0.80(0.32)	-1.88(0.02)	7.69(0.26)
35	109.00(0.03)	0.28(0.32)	5.90(0.05)	-1.19(0.63)
45	109.65(0.03)	2.09(0.34)	10.76(0.04)	3.15(0.45)
<i>N</i> -Acetyl-L-valinamide				
5	136.45(0.01)	-1.58(0.10)	-30.81(0.03)	18.12(0.36)
15	137.74(0.01)	-1.92(0.12)	-14.75(0.05)	13.79(0.60)
25	138.96(0.01)	-1.52(0.10)	-1.93(0.03)	8.80(0.34)
35	140.07(0.02)	-0.71(0.18)	7.67(0.04)	6.73(0.48)
45	141.27(0.03)	-0.06(0.31)	15.38(0.03)	3.64(0.40)
<i>N</i> -Acetyl-L-leucinamide				
5	152.84(0.02)	-1.26(0.24)	-41.81(0.10)	30.50(1.20)
15	154.47(0.01)	-1.55(0.17)	-19.54(0.05)	21.59(0.69)
25	155.88(0.01)	-1.13(0.12)	-3.74(0.04)	15.02(0.54)
35	157.27(0.02)	-0.81(0.22)	7.87(0.03)	8.54(0.42)
45	158.75(0.04)	0.86(0.51)	17.15(0.07)	11.89(0.85)
<i>N</i> -Acetyl-L-methioninamide				
5	149.99(0.02)	-0.19(0.27)	-35.61(0.06)	30.02(0.81)
15	151.86(0.02)	0.82(0.29)	-18.61(0.08)	20.53(1.03)
25	153.73(0.01)	-0.43(0.09)	-2.84(0.04)	15.27(0.49)
35	155.36(0.01)	-0.45(0.15)	5.93(0.04)	7.93(0.48)
45	156.61(0.10)	0.94(1.40)	14.87(0.07)	9.08(0.89)
<i>N</i> -Acetyl-L-phenylalaninamide				
5	166.23(0.05)	5.10(1.33)	-38.56(0.12)	52.63(3.06)
15	168.57(0.03)	-0.04(0.71)	-19.63(0.09)	31.30(2.24)
25	170.52(0.05)	-0.15(1.19)	-4.18(0.12)	21.37(3.03)
35	172.23(0.09)	3.54(2.28)	8.87(0.13)	-14.98(3.24)
45	174.09(0.11)	5.99(2.86)	20.24(0.16)	-11.15(4.10)
<i>N</i> -Acetyl-L-prolinamide				
5	123.97(0.02)	-1.36(0.20)	-35.00(0.06)	19.1(0.66)
15	125.17(0.01)	-0.07(0.17)	-19.56(0.06)	12.4(0.67)
25	126.41(0.01)	-0.12(0.12)	-7.21(0.03)	8.93(0.31)
35	127.73(0.02)	-1.05(0.21)	1.46(0.03)	0.02(0.30)
45	128.74(0.02)	-0.19(0.24)	8.29(0.02)	2.84(0.28)
<i>N</i> -Acetyl-L-tryptophanamide				
5	187.83(0.10)	-0.55(9.07)	-39.96(0.49)	465(43.6)
15	190.39(0.10)	18.6(8.73)	-16.03(0.54)	201(48.5)
25	193.09(0.16)	-21.5(14.2)	-3.70(0.83)	250(74.1)
35	195.11(0.11)	-6.85(9.95)	8.71(0.72)	275(64.0)
45	196.50(0.10)	6.08(8.89)	19.70(0.73)	49.2(64.7)
<i>N</i> -Acetyl-L-tryosinamide				
5	169.63(0.16)	-7.26(17.2)	-18.96(0.82)	-204(88.8)
15	171.95(0.17)	1.75(18.7)	-1.63(0.23)	-129(25.4)
25	173.97(0.15)	-7.77(16.7)	7.48(0.57)	-61.3(62.4)
35	175.97(0.22)	-5.85(24.5)	20.93(1.02)	-304(112)
45	177.65(0.12)	-8.99(12.9)	25.49(0.59)	-329(64.3)

<sup>a</sup> Standard deviations are in parentheses.

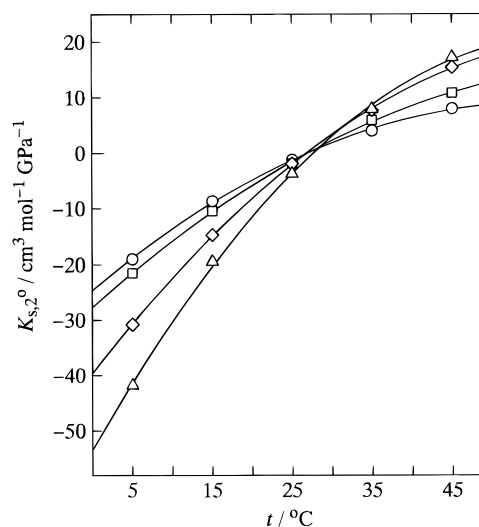
acids and *n*-alcohols (Hoiland, 1980; Kikuchi *et al.*, 1995; Nakajima *et al.*, 1975; Sakurai *et al.*, 1995). The large temperature dependence of  $K_{s,2}^o$  for the *N*-acetyl amino acid amides having more hydrophobic side chains results from the fact that the sign of a methylene or methyl group contribution to the partial molar isentropic compressibility changes with temperature: large negative at lower temperatures and positive at higher temperatures (Nakajima *et al.*, 1975; Sakurai *et al.*, 1995).

The side chain contributions to the partial molar quantity ( $Q_2^o$ ) of the various *N*-acetyl amino acid amides can be derived from the difference between the properties of each

**Table 4. Partial Molar Expansibilities of *N*-Acetyl Amino Acid Amides and Amino Acids in Dilute Aqueous Solutions at 25 °C**

side chain	$10^2 E_2^o$ /cm <sup>3</sup> ·mol <sup>-1</sup> ·K <sup>-1</sup>	
	<i>N</i> -acetyl amino acid amide derivative	amino acid derivative <sup>a</sup>
Gly	10(1) <sup>b</sup>	7(1)
Ala	8(2)	6(2)
Val	11(1)	7(1)
Leu	14(1)	9(3)
Met	16(2)	12(6)
Pro	12(2)	8(1)
Phe	19(3)	13(5)
Trp	22(4)	14(4)
Tyr	20(1)	23(11)

<sup>a</sup> Based on  $V_2^o$  data for the amino acids from Kikuchi *et al.* (1995). <sup>b</sup> Standard deviations are in parentheses.



**Figure 1.** Temperature dependence of the partial molar isentropic compressibilities of *N*-acetyl amino acid amides containing aliphatic side chains in dilute aqueous solution: (circle) *N*-acetylglycinamide; (square) *N*-acetyl-L-alaninamide; (diamond) *N*-acetyl-L-valinamide; (triangle) *N*-acetyl-L-leucinamide. The solid lines represent the results of the approximation by the second polynomial.

*N*-acetyl amino acid amide and *N*-acetylglycinamide.

$$Q_2^o(\text{Rn}) = Q_2^o(\text{N-acetyl amino acid amide}) - Q_2^o(\text{N-acetylglycinamide}) \quad (5)$$

where  $Q_2^o(\text{Rn})$  defines the side chain contribution to  $Q_2^o$  of the *N*-acetyl amino acid amide relative to the -H group of *N*-acetylglycinamide.

Values of  $V_2^o(\text{Rn})$  and  $K_{s,2}^o(\text{Rn})$  calculated using the  $V_2^o$  and  $K_{s,2}^o$  results for the *N*-acetyl amino acid amides are given in Table 5. For the purpose of comparison,  $V_2^o(\text{Ra})$  and  $K_{s,2}^o(\text{Ra})$  values, which were obtained from  $V_2^o$  and  $K_{s,2}^o$  data for amino acids (Kikuchi *et al.*, 1995) in the same manner as above, are also included in Table 5. Table 5 shows that there are differences between  $Q_2^o(\text{Rn})$  and  $Q_2^o(\text{Ra})$  values.

With the exception of the alanyl and prolyl side chains,  $Q_2^o(\text{Ra})$  values are smaller than  $Q_2^o(\text{Rn})$  values at various temperatures. It seems that these differences arise from the different interactions between the ionic groups in amino acids and the amide groups in *N*-acetyl amino acid amides with water. The amino acids in aqueous solution have two charged groups which influence electrostatically the surrounding water molecules. Electrostriction leads to a decrease in volume and compressibility (Desnoyers *et al.*, 1965; Kharakoz, 1991; Millero, 1971). Consequently, the

**Table 5. Side Chain Contributions to  $V_2^c$  and  $K_{s,2}^c$  of *N*-Acetyl Amino Acid Amides and Amino Acids in Aqueous Solution at (5, 15, 25, 35, and 45) °C**

side chain (R)	$t/^\circ\text{C}$	$V_2^c(\text{Rn})/\text{cm}^3\cdot\text{mol}^{-1}$	$V_2^c(\text{Ra})^a/\text{cm}^3\cdot\text{mol}^{-1}$	$K_{s,2}^c(\text{Rn})/\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{GPa}^{-1}$	$K_{s,2}^c(\text{Ra})^a/\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{GPa}^{-1}$
Ala	5	17.81	17.57	-2.49	-4.50
	15	17.27	17.44	-1.80	0.65
	25	17.17	17.33	-0.69	1.34
	35	17.13	17.15	1.94	2.72
	45	16.95	17.46	2.80	3.71
Val	5	48.04	47.96	-11.76	-16.50
	15	47.98	47.67	-6.07	-7.24
	25	48.12	47.62	-0.74	-3.32
	35	48.20	47.70	3.71	0.03
	45	48.57	47.93	7.42	3.33
Leu	5	64.43	64.54	-22.76	-25.97
	15	64.71	64.29	-10.86	-12.29
	25	65.04	64.57	-2.55	-5.09
	35	65.40	64.99	3.91	1.89
	45	66.05	65.37	9.19	5.21
Met	5	61.58	60.34	-16.56	-24.91
	15	62.10	61.60	-9.93	-12.49
	25	62.89	61.64	-1.65	-6.03
	35	63.49	62.04	1.97	-0.16
	45	63.91	62.51	6.91	3.42
Phe	5	77.82	77.21	-19.51	-33.01
	15	78.81	78.14	-10.95	-18.48
	25	79.68	78.31	-2.99	-8.78
	35	80.36	78.96	4.91	-0.59
	45	81.39	79.90	12.28	3.86
Pro	5	35.56	39.36	-15.95	-8.86
	15	35.41	39.28	-10.88	-1.30
	25	35.57	39.31	-6.02	2.39
	35	35.86	39.41	-2.50	5.45
	45	36.04	39.86	0.33	6.37
Trp	5	99.42	98.55	-20.91	-31.18
	15	100.63	99.09	-7.35	-16.34
	25	102.25	100.19	-2.51	-7.99
	35	103.24	100.85	4.75	-1.39
	45	103.80	101.43	11.74	6.21
Tyr	5	81.22	77.40	0.09	-37.41
	15	82.19	78.63	7.05	-15.56
	25	83.13	81.14	8.67	2.35
	35	84.10	82.82	16.97	2.93
	45	84.95	83.48	17.53	7.18

<sup>a</sup> Based on  $V_2^c$  and  $K_2^c$  data for the amino acids from Kikuchi *et al.* (1995).

results suggest that the influence of the electrostriction of the charged groups in amino acids for the hydration of adjacent amino acid side chains appears to be greater than that of hydrogen bonding interaction of amide groups in *N*-acetyl amino acid amides.

For the alanyl and prolyl side chains, contrary to the features of difference between the values of  $Q_2^c(\text{Rn})$  and  $Q_2^c(\text{Ra})$  described above,  $Q_2^c(\text{Ra})$  values are larger. In particular, the feature for the prolyl side chain is remarkable. However, at present we are unable to give a satisfactory explanation for the origin of these unique characteristics.

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