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Enthalpy of dilution of aliphatic amides in aqueous solutions at temperatures between 293.15 K and 308.15 K

Carmen M. Romero[a,*], María E. González[a], Ingolf Lamprecht[b]

[a] Departamento de Química, Universidad Nacional de Colombia, Bogotá, Colombia
[b] Institut für Biologie, Freie Universität Berlin, Berlin, Germany

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ABSTRACT

The enthalpies of dilution of aqueous solutions of acetamide, propionamide and butyramide were determined as a function of the molar fraction at 293.15 K, 298.15 K, 303.15 K and 308.15 K by flow microcalorimetric measurements. The enthalpies of dilution of amides are compared with literature data when available and the results are discussed in terms of solute–solvent interactions. The enthalpic interaction coefficients were obtained according to the McMillan–Mayer theory. The addition of a CH_2 group causes an important change in the interaction coefficients. The pairwise coefficients increase as the number of CH_2 groups increase. Two additivity approaches are used in this work: the Savage–Wood principle and a simple methylene additivity approach. The results obtained by both methods are presented and compared with literature data.

1. Introduction

Thermodynamic properties of dilute aqueous solutions of polar solutes are important as they provide useful information in the elucidation of the nature of the interactions between polar or nonpolar groups and water involved in solute hydration. At higher concentrations, the studies give information about solute-solute interactions that are important for several phenomena in biological systems.

Proteins have a complex structure and show some intricate effects on their structure. As a result it is very difficult to study the group interactions between protein molecules in aqueous solution or between proteins and water. One useful approach for a better understanding of these interactions is to study small molecules such as amino acids, amides and small peptides in water, using additivity schemes to estimate the thermodynamic behavior of more complex systems. Among these systems, aqueous solutions of amides are important because amides are nonionic uncharged molecules that constitute the structural units of polypeptide chains and proteins. For this reason the thermodynamic properties of their aqueous solutions are useful for modeling the fragments of biological molecules using additivity principles [1–3].

The behavior of excess thermodynamic properties as function of molality has been used in solution theories to determine molecular interaction coefficients of binary systems and obtain information about solute–solute interactions between hydrated molecules. The McMillan–Mayer solution theory relates the experimental thermodynamic excess properties with molality using a virial expansion to obtain interaction parameters that reflect the effects that arise from molecular pair, triplet and higher order interactions between solute molecules [4]. The contribution of three-body interactions is small compared to that of two-body interactions, and higher order interactions are usually negligible [4–8].

In this work we report the enthalpies of dilution ΔH_{dil} of acetamide, propionamide and butyramide in water at temperatures between 293.15 K and 308.15 K. Enthalpies of solution and dilution of amides in water and in aqueous mixed solvents at 298.15 K have been found in literature [1–3,9–18], however, studies at different temperatures are very scarce. The McMillan–Mayer theory was employed to obtain the pairwise interaction coefficients of amides in water from dilution enthalpies. The results are compared with literature data at 298.15 K. The interaction coefficients are discussed in terms of interactions of hydrated amide molecules.

2. Experimental

The materials used in this work were acetamide Merck 99%, propionamide Aldrich 97% and butyramide Fluka 98%. The amides were kept in desiccators before use, water was doubly distilled, degassed and treated according to literature [19]. All solutions were prepared by weight using a Mettler balance AT-261 dual range with sensitivity of 10^{-5} g in the lower range.

Measurements of heats of dilution were carried out at 293.15 K, 298.15 K, 303.15 K and 308.15 K ± 0.01 K. A LKB Flow Microcalorimeter, model 10700-1 was used in the mixing mode following

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[*] Corresponding author. Tel.: +57 1 3165032; fax: +57 1 3165344.
E-mail address: cmromeroi@unal.edu.co (C.M. Romero).

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Table 1
Enthalpies of dilution of amides in water at 293.15 K.

m_i (mol kg^{-1})	m_f (mol kg^{-1})	ΔH_{dil} (J mol^{-1})	m_i (mol kg^{-1})	m_f (mol kg^{-1})	ΔH_{dil} (J mol^{-1})
Acetamide					
0.59992	0.27356	6.0	1.59813	0.70684	30.8
0.79615	0.36084	9.9	1.79948	0.79110	37.7
1.00067	0.45070	17.0	1.99879	0.87352	43.7
1.19891	0.53672	21.0	2.50144	1.07708	58.1
1.39910	0.62254	25.4	2.99647	1.27179	78.6
Propionamide					
0.19881	0.09166	9.3	1.40036	0.61687	217.3
0.39565	0.18104	51.7	1.59868	0.69908	246.7
0.59944	0.27214	85.3	1.86498	0.80761	290.6
0.79914	0.36006	119.9	1.99808	0.86107	312.0
1.00087	0.44752	146.9	2.49729	1.05705	395.9
1.20091	0.53295	176.0	2.99731	1.24648	484.8
Butyramide					
0.19966	0.09192	63.7	1.39878	0.61013	517.8
0.40225	0.18346	102.1	1.59992	0.69177	597.4
0.60003	0.27121	184.2	1.79434	0.76934	649.8
0.80005	0.35837	275.9	1.99506	0.84807	726.5
1.00205	0.44481	349.2	2.50067	1.04055	943.6
1.19966	0.52788	411.6	2.99953	1.22265	1157.2

the procedure described in a previous paper [20]. It was prethermostated by a cryothermostat (Colora Kryo-Thermostat WK5) set to 5° below the working temperature of the instrument. The liquids were pumped by two peristaltic pumps: Pharmacia LKB P-2 and Biotech LP 80-A. The flow rates were determined by weighing the masses of liquids passing through the pumps in a given time. The sensitivity of the microcalorimeter amounted to 100 μV mW^{-1}. The calorimetric signal was registered by a Hewlett Packard multimeter 34401A, which measures up to 1000 V with 6.5 digits resolution and accuracy in the order of 0.002%.

3. Results and discussion

The measured enthalpies of dilution of acetamide, propionamide, and butyramide in water at 293.15 K, 298.15 K, 303.15 K and 308.15 K, respectively, as well as the initial and final molalities m_i and m_f are given in Tables 1–4. In all cases the relative standard deviation is less than 1 J mol^{-1}.

The dilution process for aqueous solutions of acetamide, propionamide and butyramide at different temperatures is endothermic and the enthalpies of dilution increase with concentration. The results show that at constant temperature, they increase as the apolar chain becomes larger and an increase in temperature produces a decrease of the dilution enthalpy.

The enthalpies of dilution were used to determine the enthalpic pair interaction coefficients derived from the McMillan–Mayer theory. In this approach, the excess enthalpies H^E are related to the dilution enthalpies ΔH_{dil}. The enthalpies are expressed as a virial expansion of solute molalities using Eq. (1), and the interaction coefficients are obtained fitting the experimental data by least squares to a polynomial expression [20–24].

$$\Delta H_{dil} = H^E(m_f) - H^E(m_i) = h_{xx}(m_f - m_i) + h_{xxx}(m_f^2 - m_i^2) + h_{xxxx}(m_f^3 - m_i^3) + \cdots \quad (1)$$

In Eq. (1), m_i and m_f represent the initial and final solute molalities, h_{xx}, h_{xxx} and h_{xxxx} are the interaction coefficients that represent the contribution of solute–solute interactions between pairs, triplets and higher order interactions of solvated solute molecules in a binary solution. Experimental data were adjusted using three parameters to obtain the best fitting, but due to the large uncer-

Table 2
Enthalpies of dilution of amides in water at 298.15 K.

m_i (mol kg^{-1})	m_f (mol kg^{-1})	ΔH_{dil} (J mol^{-1})	m_i (mol kg^{-1})	m_f (mol kg^{-1})	ΔH_{dil} (J mol^{-1})
Acetamide					
0.59183	0.28804	5.8	1.59206	0.75278	28.2
0.79994	0.39515	9.7	1.79159	0.84234	34.0
0.99890	0.48042	13.0	2.01114	0.96026	37.1
1.12499	0.53910	18.0	2.50367	1.17941	51.5
1.39703	0.66425	23.2	2.99868	1.36329	67.6
Propionamide					
0.19999	0.09833	17.7	1.39703	0.67228	189.0
0.39498	0.19281	47.2	1.58879	0.75955	217.0
0.59987	0.29067	70.9	1.79515	0.85219	249.3
0.79946	0.38461	113.1	2.00072	0.94320	282.0
0.97441	0.46585	125.1	2.50644	1.16180	359.6
1.18564	0.56261	157.0	3.00045	1.36838	433.8
Butyramide					
0.20002	0.09208	39.0	1.39796	0.60979	501.4
0.40310	0.18384	115.5	1.59985	0.69174	583.1
0.60040	0.27138	187.8	1.80011	0.84067	625.0
0.80021	0.35843	272.3	1.99916	0.84967	731.5
0.99926	0.44363	342.3	2.49596	1.03880	945.8
1.19455	0.57177	396.8	2.99875	1.22238	1141.7

Table 3
Enthalpies of dilution of amides in water at 303.15 K.

m_i (mol kg^{-1})	m_f (mol kg^{-1})	ΔH_{dil} (J mol^{-1})	m_i (mol kg^{-1})	m_f (mol kg^{-1})	ΔH_{dil} (J mol^{-1})
Acetamide					
0.60589	0.30096	3.9	1.60083	0.77310	23.3
0.79609	0.39330	4.1	1.80351	0.86609	27.5
1.00286	0.49254	7.8	1.99429	0.95266	33.4
1.21021	0.59090	13.7	2.49475	1.17549	48.5
1.40561	0.68254	16.3	3.00170	1.39511	62.3
Propionamide					
0.20127	0.10101	17.6	1.39984	0.67357	170.7
0.40466	0.20162	42.5	1.59787	0.76365	208.8
0.54210	0.26878	60.9	1.79662	0.85285	238.6
0.79523	0.39077	96.3	2.00190	0.94371	264.9
1.01228	0.49367	121.2	2.50329	1.16046	337.8
1.19568	0.57940	150.8	2.92680	1.33801	396.5
Butyramide					
0.20019	0.10042	45.7	1.40279	0.66929	445.8
0.39478	0.19640	102.6	1.60044	0.75751	516.1
0.59961	0.29573	166.0	1.80114	0.84566	588.7
0.80364	0.39300	233.2	1.99933	0.93134	660.2
0.99731	0.48380	298.4	2.43853	1.11648	805.2
1.20321	0.57876	373.0	2.99873	1.34362	990.5

tainty in the higher order coefficients the analysis is restricted to the first pairwise coefficients h_{xx}.

The interaction coefficients obtained in this work at four temperatures, the concentration range and literature data when available are presented in Table 5.

Table 5 shows that the pair enthalpic interaction coefficients, h_{xx}, are positive for all systems studied in water at 293.15 K and negative for acetamide at 303.15 K and 308.15 K. The value of h_{xx} increases as chain length increases and its magnitude decreases as temperature increases. The enthalpic triplet interaction coefficients are positive and smaller than the pair interaction coefficient. Since there are difficulties in the interpretation of the higher order coefficients due to the large uncertainty in their values, the analysis is restricted to the first pairwise coefficients h_{xx}.

The values for h_{xx} are in agreement with the results presented by other authors who have studied these systems at 298.15 K. Kresheck reported enthalpies of dilution of acetamide at 298.15 K; however, the results are given only as a graph [25]. Wood and Hiltzik [2] found an enthalpic interaction coefficient for acetamide at 298.15 K ($h_{xx} \approx 11.5$ J kg mol^{-2}) which compares well with the results obtained in this work. No results were found in literature for acetamide, propionamide and butyramide at different temperatures.

The pairwise coefficients describe solute–solute interactions between solvated molecules, and their values reflect the effect of apolar side-chains and the number of CH_2 groups. Our results show, that the addition of a CH_2 group causes an important change in the interaction coefficients. The h_{xx} values increase as the number of CH_2 groups increase.

For the polar non-electrolyte molecules with alkyl groups such as amides, the global effects among the solvated solutes can be interpreted as the result of different contributions [20]: (i) the hydrophobic interactions involving apolar chains are characterized by a positive contribution to h_{xx}; (ii) the polar–polar interaction between amide groups strongly hydrated with water can participate in hydrogen-bonding interactions and have a negative contribution to h_{xx}; (iii) the partial dehydration of the solvation layers is characterized by a positive contribution to h_{xx} increasing the endothermic effect. The results for the enthalpic coefficient show that butyramide is the solute that presents the most hydrophobic

Table 4
Enthalpies of dilution of amides in water at 308.15 K.

m_i (mol kg^{-1})	m_f (mol kg^{-1})	ΔH_{dil} (J mol^{-1})	m_i (mol kg^{-1})	m_f (mol kg^{-1})	ΔH_{dil} (J mol^{-1})
Acetamide					
0.59999	0.27359	1.0	1.59891	0.70717	20.8
0.80300	0.36387	2.2	1.79755	0.79030	28.6
1.00238	0.45144	5.8	1.98135	0.86634	31.1
1.19761	0.53616	10.7	2.50057	1.07674	45.6
1.40467	0.62492	16.6	3.01075	1.27732	60.0
Propionamide					
0.20020	0.09230	11.0	1.39410	0.61425	171.1
0.39954	0.18279	43.3	1.59908	0.69925	202.9
0.60036	0.27255	63.3	1.79970	0.78120	234.3
0.79921	0.36009	96.7	1.99634	0.86037	263.3
1.00102	0.44759	110.9	2.49617	1.05662	338.1
1.19950	0.53235	144.4	2.99494	1.24560	424.7
Butyramide					
0.19962	0.09190	44.2	1.40013	0.61068	460.0
0.40081	0.18282	100.1	1.60028	0.69192	532.3
0.60133	0.27178	173.7	1.79931	0.77131	603.8
0.80096	0.35876	248.7	1.99751	0.84903	667.9
0.99908	0.44355	311.9	2.49889	1.03989	848.5
1.19734	0.52691	385.6	2.99060	1.21946	996.4

Table 5
Virial enthalpic interaction coefficients for aliphatic amides in water.

T (K)	Amide	h_{xx} (J kg mol^{-2})	h_{xxx} (J kg^2 mol^{-3})	h_{xxxx} (J kg^3 mol^{-4})	Molality range
293.15	Acetamide	14 ± 3	11 ± 2	-1 ± 1	0.59992–2.99647
293.15	Propionamide	240 ± 18	21 ± 13	-4 ± 3	0.19881–2.99731
293.15	Butyramide	553 ± 42	54 ± 30	-9 ± 6	0.19966–2.99953
298.15	Acetamide	13 ± 3	11 ± 2	-1 ± 0	0.59183–2.99868
		11.5	10.35		[2]
298.15	Propionamide	222 ± 13 249.3	25 ± 9	-4 ± 3	0.19999–3.00045
			45.89		[2]
298.15	Butyramide	527 ± 28	75 ± 20	-14 ± 4	0.20002–2.99875
303.15	Acetamide	-8 ± 3	19 ± 2	-3 ± 0	0.60589–3.00170
303.15	Propionamide	199 ± 10	31 ± 7	-6 ± 2	0.20127–2.92680
303.15	Butyramide	488 ± 11	83 ± 8	-17 ± 2	0.20019–2.99873
308.15	Acetamide	-17 ± 4	24 ± 3	-4 ± 1	0.59999–3.01075
308.15	Propionamide	166 ± 16	38 ± 13	-7 ± 3	0.20020–2.99494
308.15	Butyramide	470 ± 18	83 ± 13	-18 ± 3	0.19962–2.99060

Table 6
Contribution of the interacting groups to the enthalpic interaction coefficient.

T (K)	$h_{xx\,\mathrm{CH_2-CH_2}}$ (J kg mol^{-2})	$h_{xx\,\mathrm{CH_2-CONH_2}}$ (J kg mol^{-2})	$h_{xx\ \mathrm{CONH_2-CONH_2}}$ (J kg mol^{-2})	Reference
293.15	44	26	−162	This work
298.15	48	9	−121	This work
298.15	14	95	−311	[28]
298.15	40	41	−252	[2]
303.15	41	22	−165	This work
308.15	61	−30	−65	This work

Table 7
Group contribution to the enthalpic interaction coefficients for aliphatic amides in water.

T/K	$h_{xx\,\mathrm{CH_2}}$ (J kg mol^{-2})	$h_{xx\,\mathrm{CONH_2}}$ (J kg mol^{-2})
293.15	270	−270
298.15	257	−260
303.15	248	−269
308.15	243	−280

behavior due to the combined effect of partial dehydration of solvation layers and apolar chain interactions, followed by propionamide and acetamide.

The pairwise coefficients between solutes can be described in terms of group contributions according different additivity models. When the Savage–Wood (SWAG) additivity principle [1,2,21,26,27] is used and assuming that each group can interact independently, the enthalpy of interaction may be calculated as the sum of contributions of all possible interactions that are present. Table 6 shows the contribution of the interacting groups to the enthalpic interaction coefficient calculated from Savage–Wood approach and compared with those reported in the literature.

The other group contribution scheme frequently used to predict thermodynamic properties, is a simple methylene additivity approach based on the dependence of the property on the number of carbon atoms or the number of methylene groups [29–31]. This method has been used specially to determine volumetric, heterotactic enthalpic coefficients and heat capacity contributions of methylene and functional groups but no group contributions to the homotactic enthalpic coefficient in water have been found in literature. When the enthalpic interaction coefficients are plotted as a function of the number of carbon atoms in the alkyl chain, the contribution of the methylene group considered as the basic apolar residue can be determined.

Table 7 shows the contributions of the methylene and amide groups to the enthalpic interaction coefficient at temperatures between 293.15 K and 308.15 K. At each temperature, the contribution of the methylene group to the interaction coefficient is positive as expected for a hydrophobic moiety. The contribution of the polar amide group is negative and does not show a clear trend as temperature increases.

The results reflect well the effect of increasing the alkyl chain length on the behavior of hydrophobic hydration. They show that hydrophobic interactions are enhanced and the methylene group contribution is additive.

Table 8 shows the enthalpic interaction coefficients obtained experimentally and they are compared with those calculated from literature data and with the results obtained in this work. Only group contributions data are available from the literature at 298.15 K; therefore, the table is given at that temperature.

The results obtained in this work are consistent with those reported by Blackburn et al. [28], despite the differences in the contribution of the interacting groups. The small differences can be attributed to the different solutes used in both works; Blackburn et al. worked with small peptides in aqueous solution and Wood et al. also calculated group contributions from a wide variety of compounds containing hydrocarbon, amide, and hydroxyl groups [2]. Their values do not agree with the results presented in this work and the difference can be attributed to the large standard deviation of the adjustment reported by the authors (±220 J kg mol^{-2}).

The two methods of group contribution used in this work present a good fit. However, the data adjusted by the SWAG additivity principle show better results because this model takes into account all possible interactions that are present between pairs of groups of solvated solute molecules in solution.

Table 8
Comparison between experimental and calculated values of enthalpic interaction coefficients for amides in water at 298.15 K.

Amide	h_{xx}[a] (J kg mol^{-2})	h_{xx}[b] (J kg mol^{-2})	h_{xx}[c] (J kg mol^{-2})	h_{xx} [28] (J kg mol^{-2})	h_{xx} [2] (J kg mol^{-2})
Acetamide	13	14	−3	6	−39
Propionamide	222	224	254	252	203
Butyramide	527	530	511	526	525

[a] Experimental data.
[b] Data calculated by SWAG.
[c] Data calculated by the methylene additivity approach.

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