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Homogeneous enthalpic interaction of amino acids in DMF–H_2O mixed solvents

Ruisen Lin*, Xingen Hu, Xiaoling Ren

Department of Chemistry, Thermodynamics & Thermochemistry Institute, Zhejiang University, Hangzhou 310027, China

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Abstract

The dilution enthalpies of glycine, L-valine and L-serine in various DMF–H_2O mixtures have been determined using LKB-2277 flow microcalorimetry at 298.15 K. The homogeneous enthalpic interaction coefficients over the whole range have been calculated according to the excess enthalpy concept. The results have been interpreted with the points of view of the structure alteration of the mixed solvents and the association interactions between solvated zwitterionic molecules of different side-chain natures. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Homogeneous enthalpic interaction; DMF–H_2O mixtures; Amino acids

1. Introduction

Mixtures of aliphatic amides and water have been the subject of many studies [1–6]. Since these amides cover a very wide range of dielectric constants and are usually miscible with water, their aqueous mixtures are often used in studies of the interrelations between the solubility of drugs and the dielectric constants of the mixed solvents [7], and of the influence of solvent structure on the solvation of the third component [8,9]. In addition, the amides can serve as model compounds for the investigations of the properties of peptides in aqueous solutions [10,11]. Among these amides, *N*,*N*-dimethylformamide (DMF) is of particular interest in view of the lack of hydrogen bonding in the pure solvent, and of the structure alteration of its aqueous mixtures [12]. Amino acids are considered to be the model compounds for specific aspects of the more complex proteins in aqueous solutions as these small solutes incorporate some of the structural features found in globular proteins. There are extensive thermodynamic studies on aqueous amino acid systems [13–20], but few in binary mixtures of organic solvent and water [6,21,22]. The energetics involved in the weak or non-bonding interactions of bio-organic molecules has attracted considerable attention for many years [23,24]. The ultimate objectives of these works are related to problems in protein chemistry and in particular to the tendency of some polypeptides to fold spontaneously into relatively well-defined structures and the ability of peptide substrates to interact with the active sites of some enzymes. As a part of our extensive research on the thermodynamics of model compounds in the biomimetic aqueous mixed solvents [6,20], the present work reports the dilution enthalpies and the calculated homogeneous enthalpic interaction coefficients of glycine, L-valine and L-serine in various DMF–H_2O mixtures.

* Corresponding author. Fax: +86-571-7951846.

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2. Experimental

Analytical reagent grade glycine, L-valine and L-serine were recrystallized from ethanol–water mixtures. They were used after drying in an infrared drier at 373 K for 12 h and then in vacuo over silica gel at room temperature for at least 2 days. Analytical reagent grade DMF was dried by storage over 4A molecular sieves for 2 days and used without further purification. Deionized water was distilled using a quartz sub-boiling purifier and then was used to prepare DMF–H_2O mixtures in 10% increments from 5 to 45% by mass. All solutions of amino acids were prepared on the molality scale.

The calorimetric measurements were performed by LKB-2277 BioActivity Monitor. All the measurements were carried out at (298.15±0.0005) K. The mixed solvents and the amino acid solutions were pumped into the mixing cell of the calorimeter by two LKB-2132 microperpex peristaltic pumps. The flow rates were determined by weighing the masses of liquids passing through pumps in a given time. The molar dilution enthalpies $\Delta_{dil}H_m$ were calculated by the equation

$$\Delta_{dil}H_m = -\frac{P(1 + m_i M \times 10^{-3})}{f_u m_i} \quad (1)$$

in which P is the thermal power (μW), m_i is the initial molality of the solution (mol kg^{-1}), M is the molar mass of amino acid (g mol^{-1}), and f_u is the flow rate of the solution (mg s^{-1}).

3. Results and discussion

The thermodynamic formalism used to treat the enthalpies of dilution is based on the excess enthalpy concept. The excess massic enthalpy h^E of a binary solution is defined by

$$h^E = h - h_w^* - mH_2' \quad (2)$$

where h is the massic enthalpy of a solution of molality m, h_w^* is the massic enthalpy of water, and H_2' is the partial molar enthalpy of the solute at infinite dilution. The excess massic enthalpy can be expressed as a power series in the solution molality.

$$h^E = h_2 m^2 + h_3 m^3 + \cdots \quad (3)$$

where h_2 is the enthalpic interaction coefficient which represents the interaction between pairs of solvated solute molecules and h_3 relates to triplet interactions. For the dilution of a solution of initial molality m_i to give a solution of final molality m_f, the molar enthalpy of dilution $\Delta_{dil}H_m$ is given by

$$\Delta_{dil}H_m = \frac{h^E(m_f)}{m_f} - \frac{h^E(m_i)}{m_i} \quad (4)$$

where $h^E(m_f)$ is the excess massic enthalpy for the solution of molality m_f and $h^E(m_i)$ is that for the solution of molality m_i. From Eqs. (3) and (4) it follows that

$$\Delta_{dil}H_m = h_2(m_f - m_i) + h_3(m_f^2 - m_i^2) + \cdots \quad (5)$$

In the present work, DMF–H_2O mixtures are treated as solvents. The experimental values of $\Delta_{dil}H_m$ for solutions of the above amino acids together with the initial and final molalities are given in Tables 1–3. The results were fitted to Eq. (5) using the least-squares procedure. As there are some difficulties in the interpretation of the higher h coefficients, only the pairwise coefficient h_2 is considered here. The values of h_2 for glycine, L-valine and L-serine in pure water are −472.40, 858.25 and −719.44 J kg mol^{-2}, respectively, which are in good agreement with those of other workers [14]. The variations of h_2 coefficients for the three amino acids with the mass percentages of DMF in the mixed solvents are illustrated in Fig. 1.

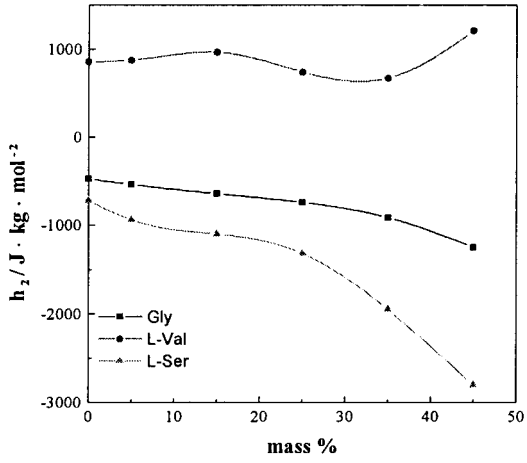

Fig. 1. Homogeneous enthalpic pair interaction parameters of glycine, L-valine and L-serine in DMF–H_2O mixtures at 298.15 K plotted against mass% of DMF.

Table 1
Molar enthalpies of dilution $\Delta_{dil}H_m$ of solutions of glycine in DMF–H_2O mixtures at 298.15 K

m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})	m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})
H_2O					
0.4001	0.1304	111.39	0.3000	0.1479	64.14
0.4001	0.1702	94.94	0.3000	0.1975	43.12
0.4001	0.1968	83.14	0.2499	0.0821	72.49
0.4001	0.2239	71.84	0.2499	0.1232	54.62
0.4001	0.2635	55.36	0.2499	0.1650	36.53
0.3500	0.1146	98.87	0.2001	0.0659	59.58
0.3500	0.1722	73.84	0.2001	0.0988	44.74
0.3500	0.2302	49.57	0.2001	0.1322	30.04
0.3500	0.0983	85.77			
5% DMF–H_2O mixtures					
0.4016	0.1975	91.55	0.2997	0.1467	71.13
0.4016	0.2640	61.07	0.2997	0.1966	47.63
0.4016	0.1302	123.30	0.2997	0.0973	95.76
0.4016	0.2240	78.85	0.2498	0.1224	60.81
0.4016	0.1695	104.41	0.2498	0.1642	40.71
0.3496	0.1710	81.77	0.2498	0.0810	81.34
0.3496	0.2296	54.54	0.2002	0.0983	50.04
0.3496	0.1132	109.68	0.2002	0.1317	33.62
0.3496	0.1948	70.14	0.2002	0.0652	66.73
0.3496	0.1475	92.32			
15% DMF–H_2O mixtures					
0.4001	0.1958	107.49	0.2999	0.0976	112.76
0.4001	0.2625	72.19	0.2502	0.1226	71.20
0.4001	0.1300	146.39	0.2502	0.1648	48.37
0.3498	0.1716	95.73	0.2502	0.0816	96.20
0.3498	0.2299	64.14	0.2000	0.0983	59.30
0.3498	0.1138	128.24	0.2000	0.1315	39.80
0.2999	0.1471	84.13	0.2000	0.0653	78.57
0.2999	0.1970	56.79			
25% DMF–H_2O mixtures					
0.3499	0.1712	112.72	0.2500	0.0813	114.97
0.3499	0.2293	77.72	0.2007	0.0984	70.97
0.3499	0.1133	155.01	0.2007	0.1320	48.10
0.2999	0.1464	100.48	0.2007	0.0652	95.16
0.2999	0.1968	68.34	0.1499	0.0735	53.99
0.2999	0.0961	136.43	0.1499	0.0986	37.32
0.2500	0.1226	85.86	0.1499	0.0491	72.02
0.2500	0.1644	57.80			
35% DMF–H_2O mixtures					
0.3000	0.1480	122.10	0.2018	0.0665	115.55
0.3000	0.1982	82.97	0.2000	0.0990	86.98
0.3000	0.0986	168.31	0.2000	0.1322	58.81
0.2508	0.1240	102.71	0.2000	0.0659	117.00
0.2508	0.1658	71.75	0.1000	0.0496	45.56
0.2508	0.0827	141.57	0.1000	0.0663	31.50
0.2018	0.0999	87.95	0.1000	0.0330	60.47
0.2018	0.1334	59.26			
45% DMF–H_2O mixtures					
0.2000	0.0992	111.68	0.1798	0.1013	86.78
0.2000	0.1326	76.73	0.1500	0.0745	88.32

Table 1 (*Continued*)

m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})	m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})
0.2000	0.0661	151.81	0.1500	0.0992	60.54
0.2000	0.1128	94.54	0.1500	0.0496	118.44
0.1798	0.0893	103.44	0.1000	0.0997	60.99
0.1798	0.1191	69.53	0.1000	0.0663	41.98
0.1798	0.0593	136.69	0.1000	0.0331	

Table 2
Molar enthalpies of dilution $\Delta_{dil}H_m$ of solutions of L-valine in DMF–H_2O mixtures at 298.15 K

m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})	m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})
H_2O					
0.4800	0.2412	−204.90	0.4014	0.2503	−129.64
0.4800	0.1906	−248.30	0.3112	0.1502	−138.14
0.4800	0.1590	−275.42	0.3112	0.1041	−177.68
0.4800	0.3201	−137.20	0.3112	0.2018	−93.86
0.4014	0.3030	−84.42	0.2032	0.1016	−87.17
0.4014	0.2002	−172.63	0.2032	0.1500	−45.64
0.4014	0.1496	−216.00			
5% DMF–H_2O mixtures					
0.3504	0.1711	−166.51	0.2501	0.0817	−153.69
0.3504	0.2296	−108.83	0.1997	0.0979	−90.72
0.3504	0.1127	−211.58	0.1997	0.1316	−61.30
0.2995	0.1469	−137.08	0.1997	0.0652	−121.47
0.2995	0.1967	−93.05	0.1495	0.0737	−67.35
0.2995	0.0976	−182.31	0.1495	0.0988	−45.66
0.2501	0.1229	−113.68	0.1495	0.0490	−89.16
0.2501	0.1645	−77.63			
15% DMF–H_2O mixtures					
0.2994	0.1467	−147.38	0.2001	0.0655	−127.47
0.2994	0.1968	−98.64	0.1501	0.0740	−72.37
0.2994	0.0972	−194.98	0.1501	0.0993	−49.05
0.2495	0.1227	−120.12	0.1501	0.0494	−95.34
0.2495	0.1644	−81.60	0.1001	0.0494	−48.61
0.2495	0.0813	−161.68	0.1001	0.0662	−32.53
0.2001	0.0986	−96.41	0.1001	0.0328	−64.23
0.2001	0.1318	−65.49			
25% DMF–H_2O mixtures					
0.2486	0.1226	−118.85	0.1806	0.0595	−111.47
0.2486	0.1641	−80.08	0.1499	0.0742	−96.66
0.2486	0.0814	−155.97	0.1499	0.0992	−46.91
0.1999	0.0988	−96.39	0.1499	0.0494	−90.29
0.1999	0.1321	−64.23	0.1002	0.0496	−46.15
0.1999	0.0657	−125.18	0.1002	0.0664	−30.79
0.1806	0.0891	−86.223	0.1002	0.0331	−58.26
0.1806	0.1194	−57.36			
35% DMF–H_2O mixtures					
0.1600	0.0792	−77.27	0.1202	0.0397	−62.03
0.1600	0.1059	−51.00	0.0999	0.0496	−39.46
0.1600	0.0528	−98.57	0.0999	0.0662	−25.85
0.1401	0.0695	−64.14	0.0999	0.0330	−49.26

Table 2 (*Continued*)

m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})	m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})
0.1401	0.0927	−42.08	0.0811	0.0403	−29.26
0.1401	0.0462	−83.00	0.0811	0.0539	−21.07
0.1202	0.0596	−47.42	0.0811	0.0268	−38.54
0.1202	0.0798	−31.39			
45% DMF–H_2O mixtures					
0.0793	0.0395	−21.03	0.0793	0.0449	−16.91
0.0793	0.0527	−14.26	0.0793	0.0341	−21.98
0.0793	0.0263	−25.46	0.0793	0.0475	−15.29
0.0997	0.0496	−27.97	0.0997	0.0660	−20.67

Table 3
Molar enthalpies of dilution $\Delta_{dil}H_m$ of solutions of L-serine in DMF–H_2O mixtures at 298.15 K

m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})	m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})
H_2O					
0.4118	0.2002	135.76	0.3125	0.2524	64.30
0.4118	0.1611	162.08	0.2514	0.1300	81.37
0.4118	0.2553	99.35	0.2514	0.1001	102.00
0.4118	0.1306	182.36	0.2514	0.2012	33.20
0.3125	0.1515	106.24	0.2028	0.1002	69.80
0.3125	0.2107	66.42	0.2028	0.1488	36.40
0.3125	0.1011	140.86			
5% DMF–H_2O mixtures					
0.4004	0.1988	153.45	0.3003	0.0992	161.30
0.4004	0.2646	100.55	0.2500	0.1241	102.01
0.4004	0.1311	206.20	0.2500	0.1656	66.82
0.3496	0.1732	136.78	0.2500	0.0827	137.09
0.3496	0.2314	88.59	0.1999	0.0993	83.92
0.3496	0.1148	180.86	0.1999	0.1324	54.17
0.3003	0.1488	119.23	0.1999	0.0661	112.16
0.3003	0.1988	78.67			
15% DMF–H_2O mixtures					
0.4001	0.2032	150.34	0.3005	0.1519	133.68
0.4001	0.2700	115.57	0.3005	0.2021	92.36
0.4001	0.1364	230.52	0.3005	0.1023	182.61
0.3500	0.1765	151.40	0.2502	0.1263	113.36
0.3500	0.2349	104.31	0.2502	0.1683	79.51
0.3500	0.0092	208.53	0.2502	0.0851	157.53
25% DMF–H_2O mixtures					
0.3500	0.1754	176.83	0.2497	0.1254	142.59
0.3500	0.2339	126.62	0.2497	0.1671	99.25
0.3500	0.1180	252.86	0.2497	0.0843	194.75
0.2988	0.1501	162.45	0.2000	0.1003	115.41
0.2988	0.2000	111.70	0.2000	0.1340	82.77
0.2988	0.1008	224.86	0.2000	0.0676	161.16
35% DMF–H_2O mixtures					
0.2999	0.1506	209.39	0.2004	0.1001	150.08
0.2999	0.2005	143.50	0.2004	0.1339	103.97
0.2999	0.1006	291.77	0.2004	0.0671	210.68
0.2503	0.1249	182.23	0.0750	0.1501	118.63

Table 3 (*Continued*)

m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})	m_i (mol kg^{-1})	m_f (mol kg^{-1})	$\Delta_{dil}H_m$ (J mol^{-1})
0.2503	0.1671	122.88	0.1501	0.1002	82.69
0.2503	0.0839	247.80	0.1501	0.0505	164.26
45% DMF–H_2O mixtures					
0.1501	0.0752	149.75	0.1501	0.1003	106.83
0.1501	0.0504	209.09	0.1021	0.0512	111.22
0.1021	0.0683	78.09	0.1021	0.0344	145.11
0.0797	0.0399	91.79	0.0797	0.0533	63.02
0.0797	0.0269	124.78			

It is generally accepted that the excess enthalpies, and hence the h coefficients, are attributable to the interactions between solvated solute molecules. For the pair-wise interaction of two hydrated amino acid molecules in aqueous solutions, the most probable configuration is that in which the positively charged amino group of one zwitterion interacts with the negatively charged carboxyl group of the second molecule. Associated with this charge–charge interaction, a contribution arising from the perturbation of the solvent cospheres is expected. Both the amino and carboxyl functional groups are structure-breaking in terms of their interaction with solvent water. Such strong dipolar interactions are expected to result in a coalescence of the hydration cospheres of the charged groups, with a subsequent relaxation of water molecules to the bulk solvent. If these effects dominate the pair-wise interaction, a negative h_2 coefficient should be observed. The h_2 value for the simplest amino acid, glycine, is indeed negative.

In the pair-wise association of other amino acids, interactions involving the side-chains will also be significant. The exact contribution depends on the nature of the side-chain involved. For amino acids with apolar side-chains, positive contributions to h_2 arise from both the interactions between hydrated hydrocarbon chains and those between the hydrated side-chains and the ionic groups. The positive value of h_2 for L-valine with an alkyl side-chain suggests that interactions involving the side-chains dominate over the zwitterion–zwitterion interactions. For amino acids with side-chain functional groups that can participate in hydrogen bonding on pair-wise interaction, the contribution to h_2 should be negative. The h_2 coefficient for L-serine, which is more negative than that for glycine, supports this view.

The variations of h_2 coefficients for the three amino acids with mass percentage of DMF (Fig. 1) should be the results of structure alteration of the mixed solvents. Hydrogen bonds between water and the carbonyl oxygen of DMF molecule are stronger than that between water molecules, and this effect is strengthened by the nitrogen atom due to the resonance structure of DMF [25]. The molecules of DMF are considered to be the structure-breakers towards water which is well known to be highly structured in its pure liquid state. The mixture goes from a very structured liquid to that where specific structure effects are absent on adding DMF. Since the h_2 coefficient relates closely to the solvent-mediated interactions between two solvated molecules [26], the energetic effect arising from changes in the solvent structure in the vicinity of the dissolved particles leads to the variations in h_2 coefficients in the mixed solvents. Further investigations are needed to explain this solvent effect.

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