Enthalpic Interaction Coefficients of *N*,*N*′-Hexamethylenebisacetamide with Glycine in Aqueous Glucose and Sucrose Solutions at 298.15 K

Min Liu,* Guangqian Li, Lili Wang, Dezhi Sun, and Youying Di

College of Chemistry and Chemical Engineering, Liaocheng University, Liaocheng 252059, People's Republic of China

The mixing enthalpies of *N*,*N*′-hexamethylenebisacetamide (HMBA) with glycine in aqueous glucose and sucrose solutions have been determined by means of mixing-flow isothermal microcalorimetry at the temperature of 298.15 K. The heterotactic enthalpic interaction coefficients (h_{xy}, h_{xxy}, and h_{xyy}) in the range of the saccharide molality, (0 to 1.5) mol·kg^{-1}, have been calculated according to the McMillan−Mayer theory. It has been found that the heterotactic enthalpic pairwise interaction coefficients h_{xy} between HMBA and glycine in aqueous glucose and sucrose solutions are all positive and pass through a maximum, respectively, at about 0.3 mol·kg^{-1} of glucose molality and about 0.6 mol·kg^{-1} of sucrose molality. In the meantime, the value of h_{xy} in aqueous glucose solutions is larger than that in aqueous sucrose solutions of the same molality. The variations of the heterotactic enthalpic pairwise interaction coefficients with the molality of sugar in mixtures are interpreted in terms of solute−solute and solute−solvent interactions.

Introduction

Although cancer has been described in early medical libers from antiquity, it remains one of the most serious diseases that make people terror-stricken at the name of it. Research on various cancers and antitumor drugs has been ongoing for years.[1−3] Among various kinds of antitumor drugs, *N*,*N*′-hexamethylenebisacetamide (HMBA), a small polar molecule compound, arouses people's attention. At present, people have done a series of research projects on the revulsive function of HMBA.[4−7] However, so far the induced differentiation mechanism of HMBA is still not demonstrated clearly.

It has been shown that the distribution, free concentration, and the metabolism of various drugs may be strongly affected by drug−protein interactions in the blood system. However, because of the complex conformational and configurational three-dimensional structures of proteins, it is difficult to study the drug−protein interactions directly. So, amino acids, oligopeptides, and acylamides[8−10] have been used as model compounds in the research of proteins, and among of them glycine is the simplest one. In addition, glucose and sucrose are important biological substances in the bodies of animals and plants, which can increase the thermal stability of proteins or reduce the extent of their denaturation by other reagents.[11] Although there have been many reports about the thermodynamic properties of saccharide solutions and glycine,[12−14] there are no reports on the thermodynamic properties of HMBA with glycine in the above saccharide solutions to our knowledge.

To understand the induced differentiation mechanism of HMBA in the human body, we have studied the enthalpies of dilution of HMBA in aqueous glucose and sucrose solutions.[15] As an extension to our previous studies, the present work is aimed at measuring the mixing enthalpies of HMBA with glycine in aqueous glucose and sucrose solutions by means of flow microcalorimetry. After analyzing the data, the heterotactic enthalpic pairwise interaction coefficients have been obtained. These important thermodynamic parameters reflect the sum of the enthalpic effects of interactions among the investigated species.[16−18]

* Corresponding author. E-mail: panpanliumin@163.com. Fax: +86-635-8239196.

Experimental Section

Reagents. *N*,*N*′-Hexamethylenebisacetamide (HMBA) and glycine were both purchased from Acros, and the purities are better than 0.98 and 0.99, respectively; glucose and sucrose were analytical reagents with mass fraction > 0.99 which were respectively gained from Tianjin Chemical Reagent Co. and Tianjin Damao Reagent Co., Ltd. All of the reagents were stored over P_2O_5 in a vacuum desiccator for 72 h at room temperature prior to use.

Preparation of Solution. Twice-distilled water was deionized by passing through a quartz sub-boiling purifier before use in the preparation of solutions. All of the solutions were prepared by weight using a Mettler Toledo AG 135 analytical balance with a precision of ± 0.00001 g. The molality ranges of the aqueous glucose/sucrose and HMBA/glycine solutions are (0 to 1.5) mol·kg^{-1} and (0.05 to 0.32) mol·kg^{-1},respectively. All of the solutions were degassed with ultrasonic waves and used within 12 h after preparation.

Calorimetric Measurements. The mixing enthalpies of HMBA with glycine and their respective dilution enthalpies in aqueous glucose and sucrose solutions at 298.15 K were measured with a 2277-204 measuring cylinder and a Thermometric 2277 thermal activity monitor (Thermometric, Sweden). The solutions were pumped through the mixing-flow vessel of a calorimeter using VS2-10R MIDI dual-channel pumps. The flow rates were obtained from the mass of the samples delivered in 6 min. The variation in the flow rates was less than 0.1 % both before and after a complete mixing/dilution experiment. The relative mean deviation of the mass weighed and the thermal power determined were 0.01 % and 0.3 %, respectively. According to the error propagation, the relative mean deviation of the enthalpies of dilution and mixing was less than 1 %. Further information about this apparatus, associated equipment, and the experimental procedure has been reported already.[19,20]

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Table 1. Mixing Enthalpies of HMBA (x) and Glycine (y) along with Their Corresponding Dilution Enthalpies in Water and Aqueous Glucose Solutions at 298.15 K

m (glucose) / mol·kg^{-1}	$m_{x,i}$ / mol·kg^{-1}	$m_{y,i}$ / mol·kg^{-1}	m_x / mol·kg^{-1}	m_y / mol·kg^{-1}	$\Delta H_{dil(x)}$ / J·kg^{-1}	$\Delta H_{dil(y)}$ / J·kg^{-1}	ΔH_{mix} / J·kg^{-1}	ΔH^* / J·kg^{-1}
0.0000	0.0500	0.0500	0.0263	0.0237	−1.09	0.25	0.07	0.91
	0.0800	0.0800	0.0422	0.0378	−3.08	0.67	0.14	2.55
	0.1000	0.1000	0.0525	0.0472	−5.04	1.05	0.15	4.14
	0.1200	0.1200	0.0631	0.0566	−7.45	1.52	0.11	6.04
	0.1500	0.1500	0.0784	0.0705	−11.92	2.39	−0.15	9.39
	0.1800	0.1800	0.0941	0.0842	−17.26	3.43	−0.21	13.62
	0.2000	0.2000	0.1048	0.0934	−21.43	4.24	−0.31	16.89
	0.2200	0.2200	0.1148	0.1028	−26.17	5.11	−0.60	20.46
	0.2500	0.2500	0.1300	0.1177	−34.10	6.57	−1.12	26.41
	0.2800	0.2800	0.1454	0.1311	−42.90	8.25	−1.59	33.07
	0.3000	0.3000	0.1554	0.1407	−49.53	9.45	−2.05	38.02
	0.3200	0.3200	0.1650	0.1506	−56.29	10.72	−2.54	43.03
0.1000	0.0500	0.0500	0.0243	0.0239	−1.17	0.25	0.07	0.99
	0.0800	0.0800	0.0389	0.0380	−3.23	0.65	0.17	2.75
	0.1000	0.1000	0.0485	0.0475	−5.18	1.01	0.22	4.39
	0.1200	0.1200	0.0581	0.0570	−7.57	1.46	0.26	6.37
	0.1500	0.1500	0.0724	0.0712	−12.00	2.27	0.31	10.04
	0.1800	0.1800	0.0866	0.0852	−17.46	3.26	0.29	14.49
	0.2000	0.2000	0.0959	0.0948	−21.65	4.01	0.21	17.85
	0.2200	0.2200	0.1054	0.1047	−26.26	4.84	0.19	21.61
	0.2500	0.2500	0.1194	0.1183	−34.06	6.23	0.09	27.92
	0.2800	0.2800	0.1333	0.1326	−42.85	7.80	−0.10	34.95
	0.3000	0.3000	0.1427	0.1422	−49.22	8.95	−0.16	40.11
	0.3200	0.3200	0.1520	0.1514	−56.12	10.18	−0.33	45.61
0.3000	0.0500	0.0500	0.0243	0.0236	−1.01	0.34	0.10	0.77
	0.0800	0.0800	0.0386	0.0379	−2.92	0.79	0.46	2.59
	0.1000	0.1000	0.0485	0.0471	−4.75	1.19	0.73	4.29
	0.1200	0.1200	0.0580	0.0566	−7.05	1.66	0.97	6.36
	0.1500	0.1500	0.0725	0.0710	−11.38	2.51	1.32	10.19
	0.1800	0.1800	0.0863	0.0850	−16.76	3.53	1.46	14.68
	0.2000	0.2000	0.0968	0.0942	−20.93	4.31	1.61	18.23
	0.2200	0.2200	0.1050	0.1037	−25.55	5.15	1.52	21.91
	0.2500	0.2500	0.1190	0.1174	−33.35	6.56	1.36	28.16
	0.2800	0.2800	0.1329	0.1318	−42.08	8.13	1.33	35.28
	0.3000	0.3000	0.1432	0.1408	−48.43	9.25	1.30	40.48
	0.3200	0.3200	0.1508	0.1497	−55.15	10.46	0.76	45.45
0.6000	0.0500	0.0500	0.0251	0.0237	−0.79	0.40	−0.05	0.34
	0.0800	0.0800	0.0402	0.0379	−2.35	0.85	0.74	2.23
	0.1000	0.1000	0.0501	0.0473	−3.87	1.23	1.23	3.87
	0.1200	0.1200	0.0601	0.0570	−5.81	1.67	1.79	5.93
	0.1500	0.1500	0.0750	0.0712	−9.54	2.43	2.54	9.65
	0.1800	0.1800	0.0900	0.0849	−14.29	3.36	3.20	14.13
	0.2000	0.2000	0.0988	0.0942	−18.05	4.06	3.28	17.27
	0.2200	0.2200	0.1093	0.1035	−22.29	4.80	3.68	21.16
	0.2500	0.2500	0.1235	0.1175	−29.54	6.04	3.79	27.29
	0.2800	0.2800	0.1378	0.1317	−37.96	7.42	3.72	34.26
	0.3000	0.3000	0.1467	0.1411	−44.21	8.43	3.43	39.21
	0.3200	0.3200	0.1564	0.1520	−50.97	9.51	3.41	44.87
0.9000	0.0500	0.0500	0.0250	0.0237	−0.52	0.41	0.10	0.21
	0.0800	0.0800	0.0398	0.0378	−1.81	0.84	0.93	1.89
	0.1000	0.1000	0.0497	0.0471	−3.12	1.20	1.59	3.51
	0.1200	0.1200	0.0598	0.0566	−4.82	1.62	2.29	5.49
	0.1500	0.1500	0.0739	0.0707	−8.15	2.35	3.21	9.01
	0.1800	0.1800	0.0887	0.0848	−12.43	3.21	4.13	13.35
	0.2000	0.2000	0.0983	0.0941	−15.83	3.85	4.69	16.66
	0.2200	0.2200	0.1077	0.1036	−19.66	4.55	5.25	20.35
	0.2500	0.2500	0.1224	0.1172	−26.23	5.71	5.90	26.42
	0.2800	0.2800	0.1357	0.1313	−33.80	7.01	6.52	33.31
	0.3000	0.3000	0.1455	0.1408	−39.36	7.96	7.03	38.43
	0.3200	0.3200	0.1549	0.1494	−45.33	8.98	7.10	43.45
1.2000	0.0500	0.0500	0.0241	0.0240	−0.44	0.33	0.69	0.80
	0.0800	0.0800	0.0385	0.0383	−1.54	0.69	1.58	2.43
	0.1000	0.1000	0.0477	0.0478	−2.68	0.99	2.20	3.89
	0.1200	0.1200	0.0576	0.0573	−4.19	1.36	2.93	5.75
	0.1500	0.1500	0.0712	0.0716	−7.14	1.99	3.91	9.06
	0.1800	0.1800	0.0853	0.0859	−10.94	2.74	4.95	13.15
	0.2000	0.2000	0.0954	0.0955	−13.96	3.32	5.78	16.42
	0.2200	0.2200	0.1042	0.1048	−17.54	3.95	6.18	19.78
	0.2500	0.2500	0.1175	0.1193	−23.53	4.97	6.95	25.51
	0.2800	0.2800	0.1322	0.1336	−30.45	6.11	7.96	32.31
	0.3000	0.3000	0.1411	0.1430	−35.57	6.93	8.42	37.05
	0.3200	0.3200	0.1495	0.1557	−40.98	7.74	9.54	42.77

Table 1. Continued

m (glucose) / mol·kg^{-1}	$m_{x,i}$ / mol·kg^{-1}	$m_{y,i}$ / mol·kg^{-1}	m_x / mol·kg^{-1}	m_y / mol·kg^{-1}	$\Delta H_{dil(x)}$ / J·kg^{-1}	$\Delta H_{dil(y)}$ / J·kg^{-1}	ΔH_{mix} / J·kg^{-1}	ΔH^* / J·kg^{-1}
1.5000	0.0500	0.0500	0.0245	0.0239	−0.22	0.31	0.92	0.82
	0.0800	0.0800	0.0390	0.0383	−1.06	0.64	1.89	2.31
	0.1000	0.1000	0.0480	0.0477	−1.98	0.93	2.60	3.65
	0.1200	0.1200	0.0576	0.0573	−3.21	1.25	3.36	5.32
	0.1500	0.1500	0.0722	0.0717	−5.65	1.82	4.63	8.45
	0.1800	0.1800	0.0867	0.0860	−8.87	2.49	5.86	12.23
	0.2000	0.2000	0.0957	0.0953	−11.44	2.99	6.58	15.03
	0.2200	0.2200	0.1057	0.1048	−14.37	3.53	7.40	18.24
	0.2500	0.2500	0.1184	0.1189	−19.38	4.44	8.31	23.25
	0.2800	0.2800	0.1331	0.1333	−25.27	5.47	9.52	29.31
	0.3000	0.3000	0.1423	0.1428	−29.58	6.20	10.19	33.56
	0.3200	0.3200	0.1519	0.1525	−34.13	7.04	11.14	38.23

According to the McMillian−Mayer theory,[21,22] an excess thermodynamic property can be expressed as a virial expansion of pair and triplet interaction coefficients. The excess enthalpy of a solution is defined as

$$H^E(m_x,m_y) = H(m_x,m_y) - H^* - H^{\infty}_{x,m} - H^{\infty}_{y,m} = h_{xx}m_x^2 + 2h_{xy}m_xm_y + h_{yy}m_y^2 + h_{xxx}m_x^3 + 3h_{xxy}m_x^2m_y + 3h_{xyy}m_xm_y^2 + h_{yyy}m_y^3 + ... \quad (1)$$

where $H^E(m_x, m_y)$ and $H(m_x, m_y)$ represent the excess and the absolute enthalpy of a solution containing 1 kg solvent, m_x mol of solute x, and m_y mol of solute y, respectively; m_x and m_y are the molalities of the solutes x and y, respectively. H^* is the standard enthalpy of 1 kg of pure solvent, and $H^{\infty}_{x,m}$ and $H^{\infty}_{y,m}$ are the limiting partial molar enthalpies of species x and y, respectively. The h_{ij} and h_{ijk} terms are the enthalpic virial coefficients representing the pairwise and triplet interactions between the subscripted species.

To facilitate the calculation, we introduce an auxiliary function ΔH^*:

$$\Delta H^* = \Delta H_{mix} - \Delta H_{dil(x)} - \Delta H_{dil(y)} = H^E(m_x,m_y) - H^E(m_x) - H^E(m_y) \quad (2)$$

Then, the eq 1 can be rewritten as:

$$\Delta H^* = 2h_{xy}m_xm_y + 3h_{xxy}m_x^2m_y + 3h_{xyy}m_xm_y^2 + ... \quad (3)$$

The enthalpies of dilution $\Delta H_{dil(x)}$ can be obtained from the following equation

$$\Delta H_{dil(x)} = P_x/(f_x + f_s - m_{x,i}M_xf_x) \quad (4)$$

where P_x is the dilution thermal power of solute x; $m_{x,i}$ is the initial molality of the solution x before dilution; M_x is the molar mass of the solute x; and f_x and f_s are the flow rates of solution x and the solvent, respectively. The dilution enthalpies $\Delta H_{dil(y)}$ of solution y can be calculated from eq 4 as long as subscript x in eq 4 is replaced by y.

The final molality m_x can be calculated from the following equation

$$m_x = m_{x,i}f_x/[f_s(1 + m_{x,i}M_x) + f_x] \quad (5)$$

The enthalpy of mixing ΔH_{mix} of an aqueous x solution and an aqueous y solution can be calculated from the equation

$$\Delta H_{mix} = P_{mix}/(f_x + f_y - m_{x,i}M_xf_x - m_{y,i}M_yf_y) \quad (6)$$

The uncertainties of the thermal power (P_x or P_{mix}), the initial molalities of solutes ($m_{x,i}$ or $m_{y,i}$), and the flow rates (f_x, f_y, or f_s) were ± 0.2 μW, ± 0.0001 mol·kg^{-1}, and ± 0.002 mg·s^{-1}, respectively. According to the law of propagation of uncertainty and the above uncertainties of the measured variables, the combined standard uncertainties of the final molalities m_x, the enthalpy changes ($\Delta H_{dil(x)}$ or ΔH_{mix}), and the auxiliary functions ΔH^* at a confidence level of 0.95 ($k = 2$) were estimated to be within ± 0.0001 mol·kg^{-1}, ± 0.03 J·mol^{-1}, and ± 0.05 J·mol^{-1}, respectively.

Results and Discussion

The experimental values of ΔH_{mix} and ΔH_{dil} for HMBA with glycine in different aqueous glucose and sucrose solutions are given in Tables 1 and 2, respectively, together with those of ΔH^*. Tables 3 and 4 give the heterotactic enthalpic interaction coefficients of eq 3, which are obtained from the least-squares analysis of experimental results (Tables 3 and 4 for HMBA + glycine + glucose and HMBA + glycine + sucrose systems, respectively).

Because of the complexities of the interaction among three or four solute molecules, it is difficult to display their regularities with increasing molalities of aqueous saccharide solutions. So only the enthalpic pairwise coefficients h_{xy} are discussed here. Tables 3 and 4 and the corresponding plots in the Supporting Information show the h_{xy} of HMBA with glycine versus the molality of glucose or sucrose in aqueous solutions. From them, we can see that the values of pairwise enthalpic coefficients h_{xy} for HMBA with glycine in both the saccharide solutions are positive, and the values of h_{xy} for HMBA with glycine in aqueous glucose solutions are always larger than that in aqueous sucrose solutions of the same molalities. This can be explained from the solvent mediated solute−solute interactions: (i) the direct interaction between HMBA and glycine molecules, which can be classed into two types, (a) hydrophobic−hydrophilic interaction between the hexamethylenes of the HMBA molecules and the zwitterionic parts of the glycine molecules (positive contribution to h_{xy}) and (b) hydrophilic−hydrophilic interaction between the acylamino groups of the HMBA molecules and the zwitterionic parts of the glycine molecules (negative contribution to h_{xy}); (ii) formation of intermolecular hydrogen bonds caused by the interaction of the carbonyl oxygen in HMBA/glycine molecules and the hydroxyl groups in the saccharide molecules (negative contribution to h_{xy}); (iii)

Table 2. Mixing Enthalpies of HMBA (x) and Glycine (y) along with Their Corresponding Dilution Enthalpies in Aqueous Sucrose Solutions at 298.15 K

m (sucrose) / mol·kg^{-1}	$m_{x,i}$ / mol·kg^{-1}	$m_{y,i}$ / mol·kg^{-1}	m_x / mol·kg^{-1}	m_y / mol·kg^{-1}	$\Delta H_{dil(x)}$ / J·kg^{-1}	$\Delta H_{dil(y)}$ / J·kg^{-1}	ΔH_{mix} / J·kg^{-1}	ΔH^* / J·kg^{-1}
0.1000	0.0500	0.0500	0.0242	0.0238	−1.12	0.25	0.42	1.29
	0.0800	0.0800	0.0388	0.0380	−3.15	0.69	0.44	2.90
	0.1000	0.1000	0.0485	0.0463	−5.08	1.06	0.46	4.48
	0.1200	0.1200	0.0580	0.0568	−7.47	1.50	0.48	6.46
	0.1500	0.1500	0.0720	0.0707	−11.91	2.30	0.50	10.11
	0.1800	0.1800	0.0863	0.0855	−17.40	3.26	0.52	14.66
	0.2000	0.2000	0.0966	0.0942	−21.62	4.01	0.55	18.15
	0.2200	0.2200	0.1053	0.1033	−26.33	4.83	0.58	22.08
	0.2500	0.2500	0.1194	0.1219	−34.25	6.01	1.41	29.65
	0.2800	0.2800	0.1341	0.1318	−43.06	7.72	1.31	36.65
	0.3000	0.3000	0.1426	0.1409	−49.75	8.84	1.28	42.19
	0.3200	0.3200	0.1515	0.1501	−56.72	10.03	1.25	47.95
0.3000	0.0500	0.0500	0.0267	0.0248	−0.84	0.49	−0.13	0.22
	0.0800	0.0800	0.0430	0.0397	−2.53	0.99	0.59	2.13
	0.1000	0.1000	0.0530	0.0496	−4.25	1.42	0.98	3.82
	0.1200	0.1200	0.0635	0.0594	−6.38	1.90	1.43	5.91
	0.1500	0.1500	0.0792	0.0741	−10.45	2.75	2.09	9.78
	0.1800	0.1800	0.0947	0.0890	−15.58	3.75	2.66	14.49
	0.2000	0.2000	0.1052	0.0989	−19.59	4.47	3.04	18.16
	0.2200	0.2200	0.1154	0.1086	−24.12	5.30	3.32	22.14
	0.2500	0.2500	0.1306	0.1236	−31.87	6.64	3.72	28.95
	0.2800	0.2800	0.1459	0.1384	−40.76	8.17	4.04	36.63
	0.3000	0.3000	0.1561	0.1481	−47.30	9.24	4.10	42.16
	0.3200	0.3200	0.1670	0.1578	−54.02	10.46	4.56	48.12
0.6000	0.0500	0.0500	0.0237	0.0247	−0.59	0.47	0.44	0.56
	0.0800	0.0800	0.0378	0.0396	−1.94	0.93	1.33	2.34
	0.1000	0.1000	0.0470	0.0494	−3.30	1.31	1.96	3.95
	0.1200	0.1200	0.0566	0.0592	−5.07	1.75	2.62	5.94
	0.1500	0.1500	0.0698	0.0741	−8.47	2.51	3.58	9.54
	0.1800	0.1800	0.0845	0.0890	−12.85	3.39	4.70	14.16
	0.2000	0.2000	0.0935	0.0988	−16.32	4.03	5.30	17.59
	0.2200	0.2200	0.1028	0.1085	−20.20	4.75	5.97	21.41
	0.2500	0.2500	0.1155	0.1232	−26.93	5.93	6.64	27.64
	0.2800	0.2800	0.1299	0.1379	−34.70	7.26	7.64	35.09
	0.3000	0.3000	0.1416	0.1476	−39.42	8.22	8.94	40.14
	0.3200	0.3200	0.1476	0.1575	−46.57	9.28	9.16	46.45
0.9000	0.0500	0.0500	0.0235	0.0250	−0.44	0.32	0.88	1.00
	0.0800	0.0800	0.0375	0.0400	−1.49	0.68	1.86	2.67
	0.1000	0.1000	0.0469	0.0500	−2.59	0.98	2.61	4.22
	0.1200	0.1200	0.0562	0.0599	−4.06	1.33	3.38	6.10
	0.1500	0.1500	0.0699	0.0749	−6.90	1.95	4.60	9.55
	0.1800	0.1800	0.0839	0.0899	−10.58	2.69	5.93	13.82
	0.2000	0.2000	0.0923	0.0998	−13.49	3.23	6.66	16.92
	0.2200	0.2200	0.1016	0.1097	−16.74	3.84	7.59	20.49
	0.2500	0.2500	0.1148	0.1245	−22.40	4.84	8.83	26.38
	0.2800	0.2800	0.1270	0.1394	−28.80	5.97	9.90	32.73
	0.3000	0.3000	0.1370	0.1490	−33.55	6.79	11.03	37.79
	0.3200	0.3200	0.1463	0.1588	−38.59	7.70	12.16	43.05
1.2000	0.0500	0.0500	0.0239	0.0250	−0.28	0.22	1.18	1.24
	0.0800	0.0800	0.0384	0.0400	−1.11	0.50	2.18	2.79
	0.1000	0.1000	0.0476	0.0499	−2.01	0.75	2.90	4.16
	0.1200	0.1200	0.0567	0.0599	−3.19	1.05	3.69	5.83
	0.1500	0.1500	0.0707	0.0749	−5.56	1.59	4.94	8.91
	0.1800	0.1800	0.0846	0.0896	−8.66	2.23	6.15	12.58
	0.2000	0.2000	0.0938	0.0996	−11.15	2.72	6.97	15.41
	0.2200	0.2200	0.1032	0.1096	−14.00	3.26	7.80	18.54
	0.2500	0.2500	0.1165	0.1245	−18.87	4.15	9.12	23.84
	0.2800	0.2800	0.1300	0.1392	−24.44	5.16	10.42	29.71
	0.3000	0.3000	0.1386	0.1490	−28.53	5.89	11.48	34.11
	0.3200	0.3200	0.1475	0.1587	−32.91	6.69	12.39	38.61
1.5000	0.0500	0.0500	0.0241	0.0246	−0.12	0.17	1.39	1.34
	0.0800	0.0800	0.0380	0.0395	−0.76	0.40	2.48	2.84
	0.1000	0.1000	0.0476	0.0492	−1.49	0.61	3.31	4.18
	0.1200	0.1200	0.0569	0.0590	−2.47	0.87	4.19	5.79
	0.1500	0.1500	0.0712	0.0746	−4.46	1.32	5.69	8.83
	0.1800	0.1800	0.0850	0.0885	−7.08	1.88	7.32	12.52
	0.2000	0.2000	0.0938	0.0983	−9.18	2.31	8.44	15.32
	0.2200	0.2200	0.1030	0.1079	−11.56	2.78	9.74	18.53
	0.2500	0.2500	0.1160	0.1229	−15.65	3.55	11.46	23.56
	0.2800	0.2800	0.1301	0.1373	−20.30	4.42	13.40	29.27
	0.3000	0.3000	0.1395	0.1470	−23.67	5.06	14.64	33.25
	0.3200	0.3200	0.1479	0.1566	−27.16	5.74	16.25	37.66

Table 3. Enthalpic Interaction Coefficients of HMBA and Glycine in Water and Aqueous Glucose Solutions at 298.15 K

m (glucose)	h_{xy}	h_{xxy}	h_{xyy}	SD[a]
mol·kg^{-1}	J·kg·mol^{-2}	J·kg^2·mol^{-3}	J·kg^2·mol^{-3}	J·kg^{-1}
0.0000	854 ± 6	2400 ± 499	−2564 ± 528	0.03
0.1000	954 ± 3	7955 ± 755	−7807 ± 746	0.01
0.3000	1056 ± 3	−2013 ± 287	1853 ± 285	0.02
0.6000	983 ± 10	673 ± 538	−789 ± 524	0.05
0.9000	948 ± 4	−3033 ± 536	3197 ± 547	0.03
1.2000	897 ± 1	283 ± 49	−156 ± 44	0.01
1.5000	844 ± 3	−857 ± 462	789 ± 452	0.01

[a] SD = standard deviation, and it is defined as the following equation:

$$SD = \sqrt{\frac{\sum_{i=1}^{n} (\Delta H^* - (2h_{xy}m_x m_y + 3h_{xxy}m_x{}^2 m_y + 3h_{xyy}m_x m_y{}^2 + ...))^2}{n-4}}$$

where n is the number of experimental data.

Table 4. Enthalpic Interaction Coefficients of HMBA and Glycine in Aqueous Sucrose Solutions at 298.15 K

m (sucrose)	h_{xy}	h_{xxy}	h_{xyy}	SD
mol·kg^{-1}	J·kg·mol^{-2}	J·kg^2·mol^{-3}	J·kg^2·mol^{-3}	J·kg^{-1}
0.1000	883 ± 12	1399 ± 468	−668 ± 476	0.08
0.3000	908 ± 1	−2884 ± 103	3151 ± 108	0.00
0.6000	951 ± 10	−6593 ± 472	6425 ± 444	0.08
0.9000	911 ± 1	−150 ± 63	211 ± 57	0.00
1.2000	846 ± 5	−9731 ± 701	8930 ± 634	0.01
1.5000	785 ± 3	6129 ± 385	−5683 ± 353	0.01

hydrophobic−hydrophilic interaction between the apolar group and the hydroxyl group (positive contribution to h_{xy}); and (iv) the partial dehydration of the hydration shell of the HMBA and the saccharide molecule (positive contribution to h_{xy}).

The overall effect on h_{xy} reflects the competitive equilibrium among the above effects. The positive values of h_{xy} testify that the hydrophobic−hydrophilic interaction and the partial desolvation predominate over the hydrophilic−hydrophilic interaction and the hydrogen-bond interaction. In addition, the values of h_{xy} in aqueous glucose solutions are larger than those in aqueous sucrose solutions of the same molalities. This may be due to the fact that, for solutions of the same molality, aqueous sucrose solutions contain about twice the number of OH groups compared to aqueous glucose solutions, which leads to stronger hydrogen-bond interactions in sucrose solutions than those in glucose solutions.

The data in Tables 3 and 4 also show that the value of h_{xy} passes through a maximum, respectively, at about 0.3 mol·kg^{-1} of glucose molality and about 0.6 mol·kg^{-1} of sucrose molality. This maybe due to the fact that polyhydroxy compounds have a structure-breaking effect in water.[23−25] Taylor and Rowlinson found that a strong hydrogen bonding exists between sugar and surrounding water molecules, which is stronger than the hydrogen bonding within the water molecule itself.[26,27] Using the above descriptions, the partial dehydrations of the hydration shell of HMBA and glycine are more difficult in sugar solution than in water, which give a more positive contribution to h_{xy}. But, with the increasing of the saccharide molality, the hydrogen bonds between the carbonyl oxygen in the HMBA/glycine molecule and the hydroxyl groups in the saccharide molecule increase significantly and cancel part of the partial dehydration of the solute interactions, which leads to the maximum value of h_{xy} at $m = 0.3$ mol·kg^{-1} of glucose and at $m = 0.6$ mol·kg^{-1} of sucrose in mixed solvents, respectively.

Conclusion

The mixing enthalpies of HMBA with glycine in aqueous glucose and sucrose solutions have been measured by using a mixing-flow microcalorimeter at 298.15 K. Experimental enthalpies of mixing varying with the molality of HMBA were correlated with the virial expansion equation. The heterotactic enthalpic interaction coefficients (h_{xy}, h_{xxy}, and h_{xyy}) in the equations were obtained, and the values of the enthalpic pairwise interaction coefficient h_{xy} have been discussed.

(1) The heterotactic enthalpic pairwise interaction coefficients h_{xy} between HMBA and glycine in water and aqueous glucose/sucrose solutions of different molalities are all positive, which shows that the hydrophobic−hydrophilic interaction and the partial desolvation predominate over the hydrophilic−hydrophilic interaction and the hydrogen-bond interaction.

(2) The value of h_{xy} in aqueous glucose solution is larger than that in aqueous sucrose solution of the same molality. This discrepancy is mainly attributed to the aqueous sucrose solutions containing twice the number of OH groups compared to the aqueous glucose solutions.

(3) The value of h_{xy} has a maximum with the increasing concentrations of glucose and sucrose, respectively. This is mainly due to the competition among the increasing of partial dehydration of the solutes caused by the structure-breaking effect and the increasing of the hydrogen bonds between the carbonyl oxygen in HMBA or glycine molecules with the hydroxyl groups in the saccharide molecules.

Supporting Information Available:

Plots of enthalpic pairwise interaction coefficients h_{xy} of HMBA with glycine versus the molality m of glucose and sucrose in aqueous solutions at 298.15 K. This material is available free of charge via the Internet at http://pubs.acs.org.

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