Studies on the Aqueous Solutions of Guanidinium Salts. IX. Activity Coefficients of Biguanide Hydrochloride and Sucrose in Aqueous Ternary Solutions at 25 °C

Koichiro MIYAJIMA,* Shigeo NAKANISHI, and Masayuki NAKAGAKI

Faculty of Pharmaceutical Sciences, Kyoto University, Yoshida-shimoadachi-cho, Sakyo-ku, Kyoto 606

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Activity coefficients for the ternary system biguanide·HCl–sucrose–water were determined by the isopiestic vapor pressure method at 25 °C. Biguanide hydrochloride (Bg·HCl) and sucrose each decreased the activity coefficient of the other solute, showing a mutual salting-in effect. The excess free energy of mixing was negative and its magnitude was about twice as large as that of the system urea–sucrose–water. The pair interaction parameter $\{Bg\cdot HCl\text{–sucrose}\}_g$ was calculated to be -89.2 (cal mol^{-2} kg). Thermodynamic properties of this system were found to be similar to those of the system urea–sucrose–water, indicating that Bg·HCl exerted a structure breaking effect on the aqueous solutions of sucrose as urea did.

Biguanide (guanylguanidine) derivatives have been widely used as hypoglysemic agents. Though the direct interaction of the drugs with sugars is questionable, the physicochemical study of the ternary system Bg·HCl–sucrose–water seems to be important, especially concerning the denaturation of protein and the structure of water, because biguanide halides are known as strong protein denaturants and their effectiveness is known to be stronger than that of urea or guanidinium halides.[1] On the other hand, sugars and polyalcohol are known to stabilize the native conformation of protein.[2,3] In the urea–sucrose–water system, which contained two solutes with opposite effects for the denaturation of protein and the structure of water, each solute decreased the activity coefficient of the other.[4] In the mannitol–sucrose–water system, which has two solutes with similar stabilizing action for the conformational change of protein, each solute increased the activity coefficient of the other.[5] Uedaira reported that in the ternary system which contained two structure maker, mutual salting-out was observed, while in the system with a structure maker and a structure breaker, mutual salting-in was found.[6] From these points of view, we measured the activity coefficients of Bg·HCl and sucrose in mixed solutions. The results are interpreted in terms of the structural change of water.

Experimental

Materials. The free biguanide was prepared from biguanide sulfate dihydrate[7] (Aldrich Co., Ltd.). This was neutralized with hydrochloric acid solution and was concentrated under reduced pressure. The crude Bg·HCl was recrystallized twice from aqueous ethanol solution and dried *in vacuo* at room temperature. Sucrose (Wako Chemical Co., Ltd. reagent grade) was used without further purification and dried *in vacuo* at 90 °C. Analytical grade sodium chloride (Matsunaga Chemical Co., Ltd.) was dried *in vacuo* at 110 °C. These salts were dissolved in redistilled and deionized water.

Method. Osmotic and activity coefficients were determined by the isopiestic vapor pressure method.[8] About 1 ml of each sample solution was placed in a silver dish with dimensions $2\times2\times2$ cm^3. Similar quantities of the reference solutions were placed on a flat copper block containined in a vacuum desiccator, which was evacuated to a pressure of approximately 25 mmHg. The solutions were then allowed to equilibrate under reduced pressure for 3—10 d in a large thermostat bath, controlled to approximately 25 ± 0.05 °C. A total of 10 dishes were usually equilibrated together at once. The concentrations of sample and reference solutions were adjusted initially so as to be fairly close to the desired equilibrium values. The solutions were regarded to have reached the equilibria if the molalities of the two reference solutions differed by not more than 0.1%. Bacterial activity in dilute sucrose solutions was not experienced. The equilibrium concentrations were determined by weighing the dishes. Buoyancy corrections were made by using the densities of sodium chloride, sucrose and Bg·HCl: 2.165, 1.588, and 1.25 g cm^{-3}, respectively, while the corresponding molecular weight used were 58.443, 342.303, and 137.573.

After the equilibrium concentrations were measured, all solutions were diluted by adding several drops of water and reequilibrated in order to attain another equilibrium at more diluted concentrations. Several dilution treatments were carried out and then a new set of solutions was prepared.

Theory

Consider an aqueous ternary solution containing two solutes, 1 (1:1 electrolyte) and 2 (nonelectrolyte), and let m_s and ϕ_s be the molality and the osmotic coefficients of the solute s ($s=1$ and 2); then it is convenient to define a quantity[6,9]

$$\Delta = \nu_R m_R \phi_R - 2m_1\phi_1 - m_2\phi_2, \tag{1}$$

where m_R and ϕ_R are the molality and the osmotic coefficient of the reference solution which is in vapor equilibrium with the ternary solution, and ν_R is the number of moles of ions or molecules produced by the dissolution of 1 mol of the reference solute.

The value of Δ/m_1m_2 is given Eq. 2.

$$\Delta/m_1m_2 = \sum_{i=0}^{3}\sum_{j=0}^{3} A_{ij}m_1^i m_2^j \quad (i+j\leq 3) \tag{2}$$

The Δ/m_1m_2 was obtained experimentally and the coefficients A_{ij} in Eq. 2 were determined by the least-squares method.

The activity coefficients of the solute 1 and 2 in the ternary solution are given by Eqs. 3 and 4.

$$\begin{aligned}\ln\gamma_1 = \ln\gamma_1^0 &+ (1/2)A_{00}m_2 + (1/2)A_{10}m_1m_2 + (1/4)A_{01}m_2^2 \\ &+ (1/2)A_{20}m_1^2m_2 + (1/3)A_{11}m_1m_2^2 + (1/6)A_{02}m_2^3 \\ &+ (1/2)A_{30}m_1^3m_2 + (3/8)A_{21}m_1^2m_2^2 \\ &+ (1/4)A_{12}m_1m_2^3 + (1/8)A_{03}m_2^4,\end{aligned} \tag{3}$$

and

$$\ln\gamma_2 = \ln\gamma_2^0 + A_{00}m_1 + (1/2)A_{10}m_1^2 + A_{01}m_1m_2 + (1/3)A_{20}m_1^3 + (2/3)A_{11}m_1^2m_2 + A_{02}m_1m_2^2 + (1/4)A_{30}m_1^4 + (1/2)A_{21}m_1^3m_2 + (3/4)A_{12}m_1^2m_2^2 + A_{03}m_1m_2^3, \quad (4)$$

where γ_s^0 ($s=1$ or 2) are the molal activity coefficients of binary solutions containing only solute s at molality m_s. The relation among the coefficients A_{ij} in Eqs. 2, 3, and 4 was derived by using the Gibbs-Duhem equation and the cross differential relation between solute 1 and 2. Thus the concentration dependencies of γ_1 and γ_2 for the ternary systems (Eqs. 3 and 4) can be obtained if γ_1^0 and γ_2^0 have already been measured as functions of m_1 and m_2, respectively.

The excess free energy of mixing $\Delta\ \mathrm{P_m}G^{ex}$ is the sum of the contributions from each component of the ternary solution.

$$\Delta_mG^{ex} = \Delta_mG_w^{ex} + \Delta_mG_1^{ex} + \Delta_mG_2^{ex}, \quad (5)$$

where $\Delta_mG_w^{ex}$, $\Delta_mG_1^{ex}$, $\Delta_mG_2^{ex}$, are the excess free energy of mixing for water and solute 1 and 2, respectively. $\Delta_mG_w^{ex}$ is directly related to Δ as

$$\Delta_mG_w^{ex} = -RT\Delta = -RT(A_{00}m_1m_2 + A_{10}m_1^2m_2 + A_{01}m_1m_2^2 + A_{20}m_1^3m_2 + A_{11}m_1^2m_2^2 + A_{02}m_1m_2^3 + A_{30}m_1^4m_2 + A_{21}m_1^3m_2^2 + A_{12}m_1^2m_2^3 + A_{03}m_1m_m^4), \quad (5)$$

$$\Delta_mG_1^{ex} = 2m_1RT\ln(\gamma_1/\gamma_1^0) = RT(A_{00}m_1m_2 + A_{10}m_1^2m_2 + (1/2)A_{01}m_1m_2^2 + A_{20}m_1^3m_2 + (2/3)A_{11}m_1^2m_2^2 + (1/3)A_{02}m_1m_2^3 + A_{30}m_1^4m_2 + (3/4)A_{21}m_1^3m_2^2 + (1/2)A_{12}m_1^2m_2^3 + (1/4)A_{03}m_1m_2^4), \quad (6)$$

and

$$\Delta_mG_2^{ex} = m_2RT\ln(\gamma_2/\gamma_2^0) = RT(A_{00}m_1m_2 + (1/2)A_{10}m_1^2m_2 + A_{01}m_1m_2^2 + (1/3)A_{20}m_1^3m_2 + (2/3)A_{11}m_1^2m_2^2 + A_{02}m_1m_2^3 + (1/4)A_{30}m_1^4m_2 + (1/2)A_{21}m_1^3m_2^2 + (3/4)A_{12}m_1^2m_2^3 + A_{03}m_1m_2^4). \quad (7)$$

Hence Δ_mG^{ex} is expressed as

$$\Delta_mG^{ex} = RT(A_{00}m_1m_2 + (1/2)A_{10}m_1^2m_2 + (1/2)A_{01}m_1m_2^2 + (1/3)A_{20}m_1^3m_2 + (1/3)A_{11}m_1^2m_2^2 + (1/3)A_{02}m_1m_2^3 + (1/4)A_{30}m_1^4m_2 + (1/4)A_{21}m_1^3m_2^2 + (1/4)A_{12}m_1^2m_2^3 + (1/4)A_{03}m_1m_2^4). \quad (8)$$

Cassel and Wood[10] showed that Δ_mG^{ex} was related to the interaction parameters between solute molecules, as shown in Eq. 9.

$$\Delta_mG^{ex} = 2\{AB\}_gm_1m_2 + 3\{AAB\}_gm_1^2m_2 + 3\{ABB\}_gm_1m_2^2 + \cdots, \quad (9)$$

where $\{AB\}_g$ is a pair interaction parameters, and $\{AAB\}_g$ and $\{ABB\}_g$ are triplet interaction parameters. Comparing the coefficients of Eq. 8 with those of Eq. 9, we obtain

$$2\{AB\}_g = RTA_{00}, \quad (10)$$

$$3\{AAB\}_g = RTA_{10}, \quad (11)$$

$$3\{ABB\}_g = RTA_{01}. \quad (12)$$

Results

Bg·HCl–Water System. The activity coefficients of Bg·HCl in water at 25 °C are shown in Table 1. The solubility of Bg·HCl was determined to be 2.8 mol kg^{-1}, and the values of ϕ_1^0 and γ_1^0 at higher concentrations than 2.8 mol kg^{-1} were obtained from the extrapolation.

TABLE 1. OSMOTIC AND ACTIVITY COEFFICIENTS OF Bg·HCl AT 25 °C

m_1	ϕ_1^0	γ_1^0
0.1	0.919	0.760
0.2	0.891	0.693
0.3	0.871	0.647
0.4	0.855	0.613
0.5	0.843	0.585
0.6	0.831	0.561
0.7	0.821	0.541
0.8	0.813	0.523
0.9	0.804	0.508
1.0	0.797	0.493
1.2	0.783	0.468
1.4	0.770	0.446
1.6	0.758	0.427
1.8	0.748	0.411
2.0	0.739	0.396
2.5	0.722	0.367
3.0	0.701	0.341

Sucrose–Water System. Accurate isopiestic data for the sucrose–water system were reported by Robinson and Stokes[5] in the form

$$\phi_2^0 = 1 + 0.07028m_2 + 0.01847m_2^2 - 0.004045m_2^3 + 0.000228m_2^4, \quad (13)$$

$$\ln\gamma_2^0 = 0.14056m_2 + 0.02770m_2^2 - 0.00539m_2^3 + 0.000285m_2^4. \quad (14)$$

The solubility of sucrose at 25 °C is 6.053 mol kg^{-1}. In the ternary system where sucrose dissolved above this concentration, Eqs. 13 and 14 were also used for the determination of ϕ_2^0 and γ_2^0.

Bg·HCl–Sucrose–Water System. The isopiestic molalities of solute 1 (Bg·HCl) and 2 (sucrose) in the ternary solutions and of the reference solute (sucrose or sodium chloride) in reference solutions are shown in Table 2, together with the values of the experimental quantities Δ/m_1m_2. The values of osmotic coefficients for reference sodium chloride were taken from the values given by Robinson and Stokes.[12] In order to fit the experimental values of Δ/m_1m_2 to a power series of m_1 and m_2 in the form of Eq. 2, polynomials involving terms up to cubic in m_1 and m_2 were examined with a FACOM M190 computer by the least-squares method. The values of coefficients A_{ij} are shown in Table 3.

From Eqs. 3 and 4 and Table 3, we obtain

$$\ln\gamma_1 = \ln\gamma_1^0 - 0.150519m_2 + 0.057513m_1m_2 + 0.014594m_2^2 - 0.012850m_1^2m_2 - 0.005573m_1m_2^2 - 0.000844m_2^3 + 0.001518m_1^3m_2 + 0.000497m_1^2m_2^2 + 0.000166m_1m_2^3 + 0.000023m_2^4,$$

TABLE 2. ISOPIESTIC DATA FOR THE TERNARY SYSTEM Bg·HCl–SUCROSE–WATER AT 25 °C

m_1 (mol·kg^{-1})	m_2 (mol·kg^{-1})	m_R (mol·kg^{-1})	$-(\Delta/m_1m_2)$ exptl	$-(\Delta/m_1m_2)$ calcd[c]	Diff. %[d]	m_1 (mol·kg^{-1})	m_2 (mol·kg^{-1})	m_R (mol·kg^{-1})	$-(\Delta/m_1m_2)$ exptl	$-(\Delta/m_1m_2)$ calcd[c]	Diff. %[d]
0.05125	0.44633	0.52863[a]	0.3493	0.2705	0.33	1.14835	1.47217		0.1369	0.1467	−0.51
0.09410	0.37719		0.3132	0.2697	0.28	1.42212	1.15898		0.1339	0.1427	−0.45
0.16787	0.25950		0.3576	0.2683	0.71	1.74763	0.74042		0.1335	0.1398	−0.25
0.27505	0.07148		0.1352	0.2675	−0.47	1.96358	0.41759		0.1269	0.1391	−0.31
0.06692	0.48847	0.59265[a]	0.3531	0.2666	0.46	0.43102	2.28965	2.68865[a]	0.1426	0.1611	−0.54
0.11661	0.40963		0.3174	0.2657	0.40	0.80049	1.94391		0.1399	0.1505	−0.49
0.18375	0.30251		0.3152	0.2645	0.45	1.19858	1.53656		0.1338	0.1424	−0.47
0.21618	0.24627		0.2522	0.2641	−0.10	1.48711	1.21195		0.1311	0.1383	−0.39
0.26665	0.16068		0.2209	0.2636	−0.29	1.83098	0.77574		0.1306	0.1352	−0.19
0.06613	0.57591	0.67956[a]	0.2363	0.2622	−0.14	2.05814	0.43770		0.1230	0.1344	−0.30
0.12326	0.49407		0.3458	0.2606	0.72	0.43969	2.56177	2.94235[a]	0.1454	0.1520	−0.20
0.21960	0.33946		0.2733	0.2590	0.15	0.90728	2.14972		0.1393	0.1391	0.01
0.27610	0.24631		0.2520	0.2582	−0.06	1.37327	1.69596		0.1315	0.1304	0.07
0.36503	0.09487		0.1992	0.2574	−0.28	1.60576	1.44086		0.1256	0.1274	−0.11
0.08830	0.64448	0.78010[a]	0.1949	0.2564	−0.42	1.75691	1.27543		0.1285	0.1256	0.17
0.15491	0.54419		0.2022	0.2549	−0.53	1.89795	1.10968		0.1293	0.1241	0.29
0.24708	0.40679		0.2449	0.2528	−0.10	2.06525	0.89179		0.1267	0.1229	0.19
0.29134	0.33189		0.1901	0.2524	−0.73	2.19493	0.71577		0.1270	0.1220	0.21
0.36208	0.21819		0.1919	0.2514	−0.57	0.19637	2.98982	3.15484[a]	0.1503	0.1537	−0.05
0.10955	0.95406	1.10572[a]	0.1997	0.2392	−0.34	0.39316	2.82352		0.1370	0.1468	−0.27
0.20721	0.83062		0.2615	0.2359	0.36	0.59547	2.66469		0.1427	0.1404	0.09
0.37821	0.58464		0.2280	0.2321	−0.07	0.82959	2.46366		0.1354	0.1343	0.05
0.47963	0.42788		0.2055	0.2306	−0.43	1.02635	2.29264		0.1329	0.1299	0.17
0.50605	0.38406		0.1900	0.2304	−0.65	1.22738	2.10435		0.1267	0.1262	0.03
0.64511	0.16766		0.2420	0.2288	0.12	1.49757	1.84546		0.1234	0.1219	0.10
0.18358	1.33989	1.55353[a]	0.2278	0.2150	0.18	1.67646	1.66549		0.1218	0.1195	0.16
0.33136	1.16404		0.2187	0.2102	0.18	0.51537	3.00267	3.41628[a]	0.1304	0.1352	−0.16
0.54510	0.89742		0.2194	0.2046	0.41	1.07504	2.54720		0.1174	0.1216	−0.26
0.65547	0.74673		0.2140	0.2025	0.32	1.64595	2.03271		0.1122	0.1126	−0.03
0.82410	0.49919		0.2007	0.2004	0.01	1.93574	1.73695		0.1068	0.1093	−0.18
1.01030	0.21266		0.2443	0.1990	0.55	2.12656	1.54378		0.1075	0.1070	0.04
0.20127	1.60477	1.82934[a]	0.1833	0.2025	−0.29	2.30321	1.34663		0.1055	0.1051	0.03
0.38180	1.40643		0.1875	0.1963	−0.22	2.51754	1.08709		0.1029	0.1028	0.01
0.52305	1.24547		0.1891	0.1922	−0.09	2.68195	0.87456		0.1008	0.1011	−0.01
0.80741	0.89867		0.1929	0.1857	0.24	0.21395	3.25754	3.42810[a]	0.1467	0.1446	0.03
0.98600	0.65720		0.1966	0.1832	0.41	0.42925	3.08275		0.1318	0.1375	−0.17
1.15852	0.40633		0.2115	0.1817	0.66	0.65122	2.91415		0.1336	0.1309	0.11
0.19982	1.68604	1.90277[a]	0.1888	0.1993	−0.16	0.91009	2.70270		0.1271	0.1246	0.13
0.43311	1.43575		0.1925	0.1913	0.03	1.12790	2.51947		0.1235	0.1202	0.20
0.64720	1.19202		0.1933	0.1855	0.27	1.35304	2.31979		0.1172	0.1165	0.05
0.86460	0.92716		0.1966	0.1809	0.56	1.65652	2.04134		0.1131	0.1121	0.07
1.10781	0.59178		0.1967	0.1780	0.55	1.85800	1.84585		0.1120	0.1096	0.18
1.24031	0.38816		0.1963	0.1773	0.41	0.53858	3.13791	3.56127[a]	0.1267	0.1305	−0.13
0.35433	1.88226	2.23550[a]	0.1728	0.1802	−0.18	1.12650	2.66913		0.1172	0.1169	0.02
0.65058	1.57988		0.1714	0.1711	0.01	1.72993	2.13643		0.1078	0.1079	0.00
0.96128	1.23235		0.1661	0.1643	0.08	2.03788	1.82860		0.1012	0.1044	−0.25
1.18273	0.96389		0.1659	0.1607	0.22	2.24094	1.62681		0.1012	0.1020	−0.06
1.44098	0.61050		0.1654	0.1585	0.23	2.42925	1.42032		0.0991	0.0999	−0.05
1.61377	0.34319		0.1637	0.1581	0.11	2.65797	1.14773		0.0954	0.0972	−0.12
0.37646	1.99981	2.36382[a]	0.1687	0.1744	−0.15	2.83350	0.92401		0.0915	0.0950	−0.19
0.69346	1.68399		0.1642	0.1649	−0.03	0.57673	3.36020	3.79900[a]	0.1212	0.1232	−0.07
1.02946	1.31975		0.1597	0.1576	0.10	1.21143	2.87036		0.1104	0.1097	0.05
1.26958	1.03466		0.1583	0.1539	0.20	1.86966	2.30898		0.1007	0.1008	0.00
1.55189	0.65749		0.1586	0.1514	0.26	2.20873	1.98191		0.0938	0.0970	−0.27
1.73970	0.36998		0.1619	0.1509	0.25	2.43050	1.76443		0.0924	0.0943	−0.16
0.41550	2.20725	2.59749[a]	0.1475	0.1648	−0.49	2.63879	1.54283		0.0897	0.0917	−0.16
0.76993	1.86970		0.1450	0.1545	−0.42	2.88907	3.24753		0.0830	0.0882	−0.36

TABLE 2. (Continued)

m_1 (mol·kg^{-1})	m_2 (mol·kg^{-1})	m_R (mol·kg^{-1})	$-(\Delta/m_1m_2)$ exptl	$-(\Delta/m_1m_2)$ calcd[c]	Diff. %[d]	m_1 (mol·kg^{-1})	m_2 (mol·kg^{-1})	m_R (mol·kg^{-1})	$-(\Delta/m_1m_2)$ exptl	$-(\Delta/m_1m_2)$ calcd[c]	Diff. %[d]
0.62554	3.64454	4.10355[a]	0.1145	0.1146	0.00	3.50942	4.15077		0.0527	0.0499	0.42
1.32052	3.12884		0.1031	0.1014	0.12	0.97713	5.83307	4.34053[b]	0.0704	0.0709	−0.03
2.04855	2.52991		0.0921	0.0927	−0.06	1.59954	5.46115		0.0681	0.0680	0.01
2.42682	2.17760		0.0846	0.0886	−0.37	1.91644	5.26714		0.0665	0.0672	−0.06
2.67867	1.94458		0.0835	0.0851	−0.15	2.25506	5.05461		0.0640	0.0660	−0.23
2.91409	1.70379		0.0798	0.0815	−0.15	2.91370	4.61804		0.0579	0.0608	−0.38
0.28236	4.29907	4.48911[a]	0.1343	0.1147	0.37	3.09869	4.49024		0.0573	0.0582	−0.12
0.56914	4.08737		0.1097	0.1074	0.08	3.53523	4.18130		0.0520	0.0491	0.43
0.86770	3.88291		0.1057	0.1011	0.24	0.48941	6.19602	4.36719[b]	0.0827	0.0750	0.59
1.22259	3.63074		0.0992	0.0955	0.26	1.01231	5.88899		0.0797	0.0698	−0.05
1.52538	3.40736		0.0941	0.0917	0.19	1.60978	5.49608		0.0671	0.0677	−0.05
1.84334	3.16040		0.0888	0.0885	0.03	1.92893	5.30145		0.0656	0.0668	−0.13
2.27787	2.80703		0.0820	0.0841	−0.21	2.26886	5.08554		0.0626	0.0657	−0.36
2.57299	2.55616		0.0788	0.0806	−0.19	2.93066	4.64491		0.0564	0.0604	−0.54
0.70820	4.12615	4.61751[a]	0.1057	0.1017	0.18	3.13238	4.53906		0.0583	0.0574	0.14
1.50577	3.56778		0.0934	0.0898	0.29	3.55823	4.20849		0.0510	0.0484	0.39
2.35440	2.90763		0.0809	0.0814	−0.05	0.98860	5.90156	4.38777[b]	0.0691	0.0700	−0.05
2.80080	2.51318		0.0723	0.0759	−0.39	1.61896	5.52745		0.0672	0.0674	−0.01
3.09782	2.24887		0.0717	0.0708	0.09	1.94053	5.33334		0.0660	0.0665	−0.06
0.93703	4.01266	3.15085[b]	0.1001	0.0967	0.19	2.28361	5.11861		0.0634	0.0654	−0.23
1.12081	3.88576		0.0975	0.0939	0.24	2.95100	4.67715		0.0573	0.0600	−0.37
1.34149	3.72974		0.0938	0.0910	0.21	3.13739	4.54633		0.0552	0.0572	−0.29
1.60752	3.53836		0.0903	0.0881	0.18	3.58314	4.23796		0.0517	0.0476	0.62
1.81854	3.38120		0.0879	0.0861	0.17	0.49655	6.25591	4.42531[b]	0.0647	0.0741	−0.29
1.92148	3.30148		0.0861	0.0851	0.09	0.99853	5.96085		0.0697	0.0692	0.03
2.12140	3.14686		0.0835	0.0832	0.02	1.63494	5.58201		0.0671	0.0668	0.02
2.37680	2.93997		0.0812	0.0807	0.06	1.95910	5.38437		0.0652	0.0661	−0.09
1.09132	4.67339	3.64444[b]	0.0885	0.0830	0.36	2.30554	5.16754		0.0626	0.0650	−0.27
1.30777	4.53392		0.0859	0.0808	0.38	2.98094	4.72460		0.0568	0.0593	−0.35
1.56844	4.36074		0.0825	0.0787	0.33	3.16994	4.59349		0.0549	0.0564	−0.22
1.88461	4.14827		0.0796	0.0765	0.30	3.61665	4.27760		0.0506	0.0465	0.63
2.13604	3.97152		0.0762	0.0748	0.15	1.00006	5.96997	4.43227[b]	0.0694	0.0691	0.01
2.26022	3.88349		0.0747	0.0739	0.09	1.64395	5.61274		0.0715	0.0665	0.45
2.49981	3.70819		0.0718	0.0718	0.00	1.96338	5.39614		0.0656	0.0660	−0.04
2.80791	3.47319		0.0673	0.0683	−0.12	2.31920	5.19837		0.0662	0.0647	0.18
0.45303	5.70759	4.05774[b]	0.0770	0.0828	−0.16	2.98794	4.73570		0.0571	0.0592	−0.29
0.90958	5.42982		0.0791	0.0766	0.13	3.17614	4.60247		0.0549	0.0563	−0.20
1.48676	5.07608		0.0753	0.0724	0.23	3.62910	4.29232		0.0516	0.0461	0.84
1.77964	4.89116		0.0730	0.0711	0.18	1.81341	6.19400	4.83866[b]	0.0630	0.0617	0.12
2.09114	4.68785		0.0700	0.0697	0.02	2.17493	5.98008		0.0606	0.0616	−0.11
2.69805	4.27624		0.0624	0.0654	−0.39	2.56216	5.74548		0.0581	0.0603	−0.29
2.86787	4.15577		0.0618	0.0635	−0.23	3.31829	5.26135		0.0518	0.0514	0.07
3.26741	3.86453		0.0573	0.0570	0.04	3.53545	5.12522		0.0508	0.0465	0.68
0.46128	5.81154	4.12858[b]	0.0742	0.0811	−0.20	1.82277	6.22329	4.86871[b]	0.0598	0.0615	−0.17
0.92601	5.52792		0.0761	0.0751	0.05	2.18781	6.01297		0.0586	0.0613	−0.32
1.51434	5.17026		0.0731	0.0713	0.15	3.33898	5.29207		0.0504	0.0509	−0.07
1.81318	4.98333		0.0711	0.0701	0.11	3.55590	5.15277		0.0464	0.0459	0.08
2.13930	4.79515		0.0717	0.0686	0.35	2.23699	6.21949	4.99141[b]	0.0559	0.0601	−0.49
2.74990	4.35842		0.0618	0.0643	−0.32	2.70121	5.94570		0.0538	0.0583	−0.62
2.92300	4.23565		0.0596	0.0622	−0.34	3.07387	5.71521		0.0513	0.0545	−0.48
3.33362	3.94284		0.0558	0.0551	0.09	3.25850	5.59872		0.0500	0.0516	−0.24
0.48349	6.09139	4.31565[b]	0.0718	0.0766	−0.14	3.61768	5.36642		0.0476	0.0436	0.66
0.97156	5.79982		0.0737	0.0713	0.14	2.32294	6.45848	5.15367[b]	0.0574	0.0586	−0.15
1.59001	5.42859		0.0702	0.0684	0.16	2.80514	6.17446		0.0544	0.0564	−0.29
1.90488	5.23537		0.0684	0.0675	0.10	3.19428	5.93910		0.0521	0.0518	0.05
2.24050	5.02198		0.0653	0.0663	−0.11	3.38685	5.81925		0.0507	0.0482	0.40
2.89489	4.58822		0.0592	0.0612	−0.27	2.49878	6.86764	5.41611[b]	0.0576	0.0559	0.22
3.07762	4.45972		0.0571	0.0586	−0.21	2.94947	6.61109		0.0547	0.0531	0.24

a) Reference solute: sucrose. b) Reference solute: sodium chloride. c) Calculated by Eq. 2 using the values in Table 3. d) Percentage error defined by Kelly.[9]

Table 3. The values of coefficients in Eq. 2 for the system Bg·HCl–sucrose–water

Coefficient		Coefficient	
A_{00}	−0.301038	A_{02}	−0.005065
A_{10}	0.115026	A_{30}	0.003036
A_{01}	0.058376	A_{21}	0.001324
A_{20}	−0.025700	A_{12}	0.000664
A_{11}	−0.016720	A_{03}	0.000187

$$\ln \gamma_2 = \ln \gamma_2^0 - 0.301038m_1 + 0.058377m_1m_2 + 0.057513m_1^2 - 0.005065m_1m_2^2 - 0.011146m_1^2m_2 - 0.008567m_1^3 + 0.000187m_1m_2^3 + 0.000498m_1^2m_2^2 + 0.000662m_1^3m_2 + 0.000759m_1^4,$$

for the system Bg·HCl–sucrose–water.

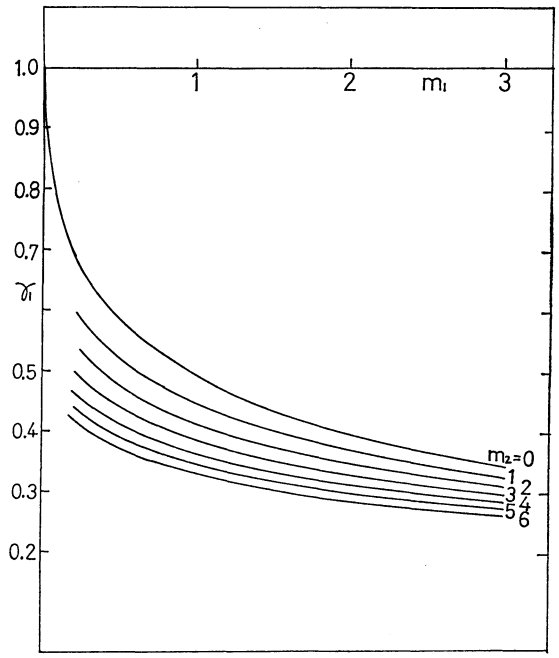

Fig. 1. Activity coefficients of Bg·HCl in sucrose solutions of various concentrations.
m_1; Molality of Bg·HCl, m_2; molality of sucrose.

The activity coefficients for Bg·HCl in binary and ternary solutions are shown in Fig. 1 and the activity coefficients of sucrose in binary and ternary solutions are given in Fig. 2. The activity coefficient of each solute decreased in the presence of the other solute.

Discussion

Bg·HCl–Water System. Biguanide is the condensed compound of two guanidine molecules and, structurally, guanidine corresponds to urea and biguanide to biuret.

Urea is known as a protein denaturant and affects the hydrophobic hydration, as in the system urea–tetrabutylammonium bromide–water,[13] and also the hydrophilic hydration, as in the system urea–sucrose–water.[4] These influences of urea on the hydrophobic and hydrophilic hydration play an important role in protein denaturation.

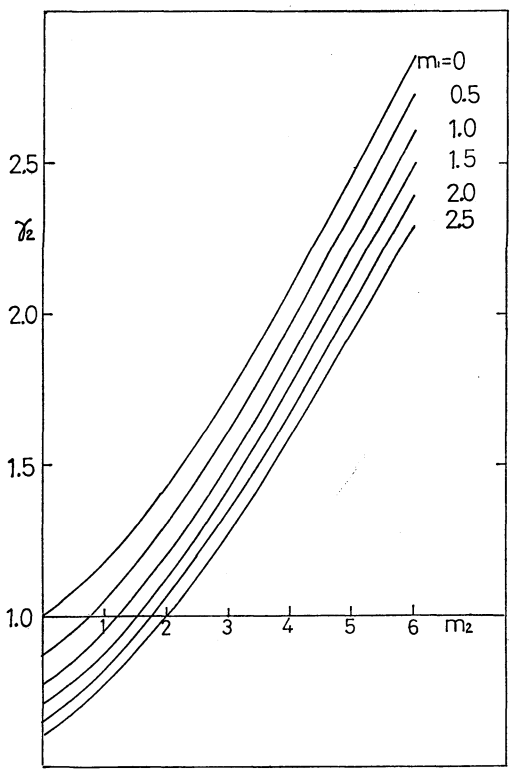

Fig. 2. Activity coefficients of sucrose in Bg·HCl solutions of various concentrations.
m_1; Molality of Bg·HCl, m_2; molality of sucrose.

Guanidinium halides are also known as protein denaturants. The properties of the guanidinium ion in aqueous solutions were studied in our laboratory and the guanidinium ion was concluded to be a strong structure breaker ion.[14–16] Biguanide halides are strong protein denaturants and their effectiveness is stronger than urea and guanidinium halides.[1] The effects of the biguanide ion on the structure of water have been studied in our laboratory. The viscosity *B*-coefficient of the biguanide ion showed no temperature dependence and the increment of the ionic *B*-coefficient arising from the change in the water structure was nearly zero, indicating the biguanide ion to be neither structure maker nor structure breaker.[17] But the temperature dependence of the Walden product obtained from the conductivity measurement was positive, indicating the biguanide ion to be a weak structure maker.[18] The activity coefficients of the biguanide salts in the aqueous solutions obtained from the isopiestic measurement were somewhat lower than those of guanidinium salts with the same counter anions. The activity coefficients of biguanide salts decreased in the order $OAc^- > Cl^- > Br^-$, as in the case of guanidinium salts, when the anion was changed.[19] These results indicate that the biguanide ion is thermodynamically a structure breaker.[15]

Bg·HCl–Sucrose–Water System. As shown in Figs. 1 and 2, the mutual salting-in was observed in this system. The free energy of transfer of trace sucrose from water to various binary solutions are shown in Fig. 3. Mannitol is regarded as a hydrophilic structure maker[5] and its structure of hydration may be similar to that of sucrose. 2-Aminobutyric acid (2-ABA) is

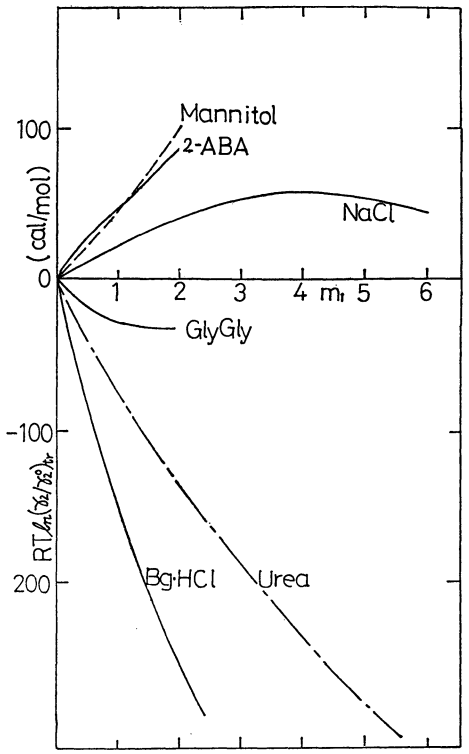

Fig. 3. Free energy of transfer of trace sucrose (solute 2) from water to aqueous solute 1 solutions at 25 °C.
m_1; Molality of solute 1 as indicated in the figure.

considered to be a weak structure maker.[6] On the other hand, glycylglycine (GlyGly)[6] and urea are regarded as structure breakers. Uedaira suggested that the mixing of two kinds of structure making solutes caused the positive free energy change of transfer, while the mixing of the structure making and the breaking solutes caused the negative free energy change of transfer for each solute in aqueous solutions.[6] As seen in Fig. 3, Bg·HCl is more structure breaking than urea and GlyGly, if Uedaira's postulation is applied to the system Bg·HCl–sucrose–water.

On the other hand, Bg·HCl is an electrolyte and its interaction with sucrose is the sum of the electrostatic and the non-electrostatic terms. Therefore it is meaningful to compare the system Bg·HCl–sucrose–water with the system NaCl–sucrose–water,[20] because the interaction involved in the system NaCl–sucrose–water may be considered to represent the electrostatic interaction for the system Bg·HCl–sucrose–water. In Fig. 4, the excess free energy of mixing for the system Bg·HCl–sucrose–water are compared with those of the system urea–sucrose–water and NaCl–sucrose–water. The excess free energy of mixing $\Delta_m G^{ex}$ is the sum of each component $\Delta_m G_w{}^{ex}$, $\Delta_m G_1{}^{ex}$, and $\Delta_m G_2{}^{ex}$. Figure 4 shows $\Delta_m G^{ex}$, $\Delta_m G_w{}^{ex}$, $\Delta_m G_1{}^{ex}$, and $\Delta_m G_2{}^{ex}$ at a total molality of 6 mol kg^{-1}. For the system urea–sucrose–water, $\Delta_m G^{ex}$, $\Delta_m G_1{}^{ex}$, and $\Delta_m G_2{}^{ex}$ are negative and $\Delta_m G_w{}^{ex}$ is positive, indicating a strong inter-

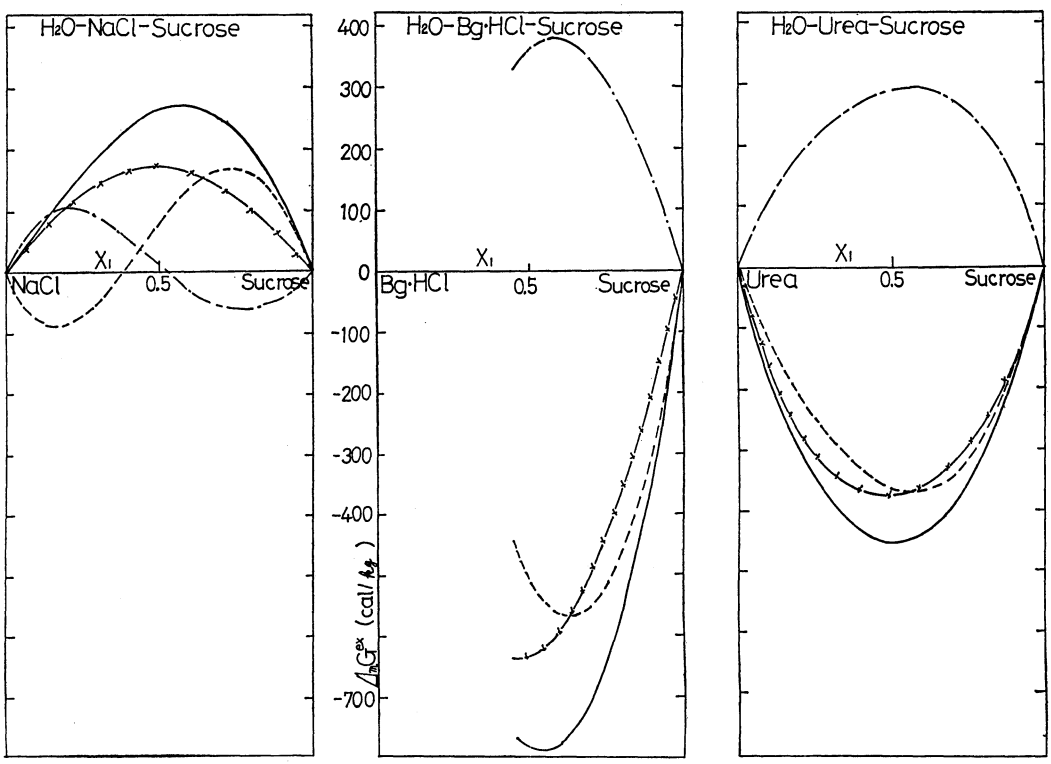

Fig. 4. Excess free energy changes of mixing for ternary systems containing sucrose as a component at 6 mol·kg^{-1} of total molality.
—·—·— $\Delta_m G_w{}^{ex}$ (excess free energy of mixing for water),
———— $\Delta_m G_1{}^{ex}$ (excess free energy of mixing for Bg·HCl or urea or NaCl),
—×—×— $\Delta_m G_2{}^{ex}$ (excess free energy of mixing for sucrose),
———— $\Delta_m G^{ex}$ (total excess free energy of mixing),
X_1; mole fraction of solute 1 (NaCl, Bg·HCl, Urea).

TABLE 4. FREE ENERGY OF TRANSFER OF Bg·HCl FROM WATER TO SUCROSE SOLUTIONS AT 25 °C (cal/mol)

m_{10} [a]	m_2 [b] 0.5	1	2	3	4	5	6
0	−74.4	−140.9	−253.2	−341.9	−411.3	−465.1	−506.3
0.2	−69.4	−131.6	−236.6	−319.9	−385.8	−437.6	−478.3
0.5	−61.9	−117.3	−211.0	−285.9	−345.9	−394.2	−433.3
1.0	−51.1	− 97.0	−175.2	−239.0	−291.8	−336.5	−375.0
1.5	−42.6	− 81.0	−147.7	−203.9	−252.6	−295.9	−335.3
2.0	−35.3	− 67.7	−126.4	−174.9	−220.1	−262.1	−301.5
2.5	−29.4	− 56.5	−105.7	−150.1	−191.7	−231.3	−269.0

a) The molality of Bg·HCl in a binary solution. The molalities in ternary solutions are slightly larger than m_{10}, as the transfer is carried out at constant mole fraction.[19] b) The molality of sucrose.

action between urea and sucrose. The system Bg·HCl–sucrose–water showed a similar tendency to that for the system urea–sucrose–water, though the values of $\Delta_m G^{ex}$, $\Delta_m G_w^{ex}$, $\Delta_m G_1^{ex}$, and $\Delta_m G_2^{ex}$ were much larger than those of the system urea–sucrose–water. There may be two kinds of interactions between sucrose and Bg·HCl, that is, the direct interaction (the formation of water soluble complex) and the interaction through the change of water structure. The free energy data do not inform us which interaction is really working. But if we take into account that both solutes are hydrophilic and that the interaction takes place in water, the possibility of the direct interaction may be small. For the system NaCl–sucrose–water, $\Delta_m G^{ex}$ and $\Delta_m G_2^{ex}$ were positive, while $\Delta_m G_1^{ex}$ changed sign as the mole fraction changed. The relation between the excess free energy changes and the mole fraction of the system Bg·HCl–sucrose–water resembled those of the system urea–sucrose–water rather than those of the system NaCl–sucrose–water. This means that a large organic salt, such as Bg·HCl, is more likely to act as a non-electrolyte like urea rather than as an inorganic electrolyte like NaCl in such a ternary system in the high concentration region. Therefore we applied Eq. 10 to the electrolyte–non-electrolyte system. The pair interaction parameter $\{AB\}_g$ of the system Bg·HCl–sucrose–water was calculated to be −89.2 and that of the system urea–sucrose–water was −37.3 in cal kg mol^{-2}.

Table 4 shows the free energy of transfer $\Delta G^t(N)$ (mole fraction scale)[21] of Bg·HCl from water to sucrose solutions of various concentrations. The trace free energy of transfer is the most negative and its magnitude is twice as large as that of urea.

As shown in Figs. 3 and 4 and Table 4, Bg·HCl exerts a more significant effect on the hydrophilic hydration than urea does. This result is consistent with the fact that Bg·HCl is a stronger denaturant than urea.

It is interesting to investigate the effect of biguanide salts on the hydrophobic hydration as observed in aqueous tetraalkylammonium salts solutions. We are currently working in this direction.

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