Isotope Effects in Aqueous Systems. Excess Thermodynamic Properties of 1,3-Dimethylurea Solutions in H_2O and D_2O

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The osmotic coefficients of 1,3-dimethylurea-h_2(DMUh_2)/H_2O and 1,3-dimethylurea-d_2(DMUd_2)/D_2O solutions (1, 2, 4, 12, and 20 m_{aq}, $15 < t/°C < 80$) were obtained from differential vapor pressure measurements. Excess partial molar free energies, enthalpies, and entropies for the solvent and their isotope effects were calculated from the temperature derivatives of the osmotic coefficients. New partial molar volume data are reported at 25 °C at low and intermediate concentrations. The thermodynamic properties of solution are compared with those of urea and discussed using the cage model of hydrophobic hydration. The results support the mixed (polar−apolar) character of this compound and show that its structural effect on water changes with temperature and concentration.

Introduction

Urea and its alkyl derivatives can act as conformational perturbants and denaturing agents of some polypeptides and proteins (Herskovits et al., 1970a; Barone et al., 1971), and for that reason the structure of their aqueous solutions has been systematically studied (Barone et al., 1977, 1980). Denaturing by alkylureas is usually stronger than for urea and increases with alkyl (apolar) content (Barone et al., 1978). While in many cases urea has its maximum denaturing effectiveness at 6−7 m_{aq}, the maximum is found around 5 m_{aq} for dimethylurea (DMU) and about 3 m_{aq} for tetramethylurea (TMU) (Herskovits et al., 1970b). It is useful to ask whether the denaturing action at these concentrations is caused by significant changes in solution structure induced by the ureas or is due to more direct peptide−urea interactions not directly related to solution structure. In that context we have engaged in a program measuring H_2O-D_2O solvent isotope effects on the thermodynamic properties of urea, 1,3DMU and TMU solutions over wide ranges of concentration and temperature (Jakli and Van Hook, 1981, 1982, 1995). Properties investigated include excess free energies, enthalpies, and entropies of solution and apparent and partial molar volumes.

A good deal of the qualitative and semiquantitative rationalizations of thermodynamic data for aqueous solutions of ureas, substituted ureas, and related compounds is based on ideas early articulated in the Frank−Evans (Frank and Evans, 1945) and Frank−Wen (Frank and Wen, 1957) flickering cluster models of water and its solutions and subsequent refinements. The idea is that on average each water is networked into an ever-fluctuating hydrogen-bonded network. In this model, therefore, one can speak of "substitutional" solutes—ones that can (and do) replace water in the caging network (at least on average)—and "interstitial" solutes—ones that do not participate in the caging network but rather occupy the void spaces in the loosely defined H-bonded structure. In each case, however, we choose to set the words "substitutional" and "interstitial" in quotes in order to emphasize the approximate nature of the correspondence of this model of aqueous solution structure with the rather more precise origin of these concepts in solid-state physics.

Results on aqueous solutions of urea (Jakli and Van Hook, 1981, 1996) can be rationalized using the idea that this compound slightly disturbs water structure (reducing the degree of water−water hydrogen bonding). It shows monotonous "substitutional" solution and results in no abrupt changes in any of the thermodynamic properties investigated across the range of possible concentrations. However, the volumetric properties of 1,3-DMU and TMU solutions show extrema when plotted against concentration (Jakli and Van Hook, 1996; Phillip et al., 1974), as is characteristic for the "interstitial" solution processes of polar organic compounds (Wen and Saito, 1964). Others have interpreted such behavior by supposing that different (equilibrium) solution structures dominate above and below the extrema concentrations. The partial molar volume of 1,3-DMU has its minimum ($V_{2-\min}$) at (4 ± 0.5) m_{aq} in both H_2O and D_2O (Jakli and Van Hook, 1996; Phillip et al., 1974). (In this paper we employ the symbol "m_{aq}" to represent the aquamolality. In H_2O $m_{aq} = n_{solute}/kg_{solvent}^{-1}$, which is the number of moles of solute per 55.508 mol solvent. In D_2O m_{aq} is also the number of moles of solute per 55.508 mol solute (1.104 27 kg).) The relatively large uncertainty in $V_{2-\min}$ is due to the small number of data previously available around this concentration and to the shallow character of the minimum in the (V_2, m_{aq}) projection.

D_2O solvent isotope effects in solution thermodynamics are useful in analyzing contributions from different components of intermolecular interactions. The dielectric properties of normal and heavy water are closely matched, and their ion−dipole and dipole−dipole solute−solvent interactions should be practically the same. On the other hand, at least at low temperature, heavy water is more structured than normal water, and the properties of solutions in D_2O are more sensitive to changes in solvent−solvent interactions induced by the presence of the solute. In qualitative interpretations of solvent isotope effects, it is presumed that the changes in solvent−solvent interactions dominate.

Experimental Section

Materials. Laboratory distilled water was treated with basic potassium permanganate and redistilled two times

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in an all-glass apparatus. Heavy water (Merck and Co., analytical grade) was used without further purification. D/H analysis was made using a Mettler-Paar densitometer, yielding [no. of D atoms/(no. of D atoms + no. of H atoms)] × 100 = (99.77 + 0.01) at. % D.

1,3-Dimethylurea (Merck, analytical grade) was recrystallized from ethanol and dried under vacuum at 60−70 °C to constant mass. For the heavy water mother solution, 1,3-dimethylurea-d_2 was prepared by equilibrating 1,3-dimethylurea with excess D_2O, followed by recrystallization and vacuum-drying. The procedure was repeated several times to obtain 1,3-dimethylurea-d_2 with a D content of >99 at. % checked by measuring the density of D_2O remaining after equilibration. Stock solutions of equal aquamolalitiy (mol of solute/55.508 mol of solvent) were prepared and diluted gravimetrically as appropriate. The D content of the heavy water stock solution was 99.67 at. %. On dilution with 99.77 at. % D_2O corrections corresponding to the difference (99.77 to 99.67 at. %D) were applied.

Density Measurements. The densities of the solutions were measured at (25.00 ± 0.01) °C with an Anton-Paar DMA60/602H vibrating-tube densitometer. The calibration constant was determined daily using the known densities of air and H_2O for normal water solutions or air and D_2O for heavy water solutions. The reproducibility of densities of individual samples corresponds to ($0.05 < dV_1/\mathrm{cm^3 \cdot mol^{-1}} < 0.1$).

Differential Vapor Pressure Measurements. The vapor pressure differences between pure solvent and solutions, or between normal and heavy water solutions of identical aquamolality, were measured by differential capacitance manometry as previously described (Pupezin et al., 1970; Jancso et al., 1970). The precision for aqueous systems is ∼ 0.2−0.3% in $\Delta P/P$ for ($5 < T/°\mathrm{C} < 80$).

Results

Molar Volumes. Apparent molar volumes in normal and heavy water solutions, $V_\phi(\mathrm{H})$ and $V_\phi(\mathrm{D})$, were calculated from measured densities using eq 1 (Millero 1972):

$$V_\phi = M_s/d - 55.508M_w(d - d_0)/m_{aq}dd_0 \qquad (1)$$

M_w is the molar mass of normal or heavy water, d and d_0 are the densities of solution and pure solvent, ($d_0(H_2O)$ = 997.045, $d_0(D_2O$, (99.82 at. %)) = 1104.27 kg·m^{-3}), M_s is the molar mass of solute, and m_{aq} is the aquamolality. In H_2O solutions 27 data points were obtained over the range ($0.02 < m_{aq} < 6.0$), and in D_2O 28 for ($0.05 < m_{aq} < 6.0$). Least-squares fits yield eqs 2 and 3 with standard deviations of 0.04 and 0.05 cm^3 mol^{-1}, respectively. (The expansion in half-integer powers of m_{aq} is a statistically superior fit to one in integer powers (Jakli and Van Hook 1996).) The previous data set contained insufficient points in the low to moderate concentration region prompting the volumetric part of the present study.

$$V_\phi(\mathrm{H})/(\mathrm{cm^3 \cdot mol^{-1}}) = 80.25 - 0.1395\, m_{aq}^{1/2} - 0.7198\, m_{aq} + 0.2109\, m_{aq}^{3/2} \qquad (2)$$

$$V_\phi(\mathrm{D})/(\mathrm{cm^3 \cdot mol^{-1}}) = 80.25 - 0.5115\, m_{aq}^{1/2} - 0.5754\, m_{aq} + 0.1973\, m_{aq}^{3/2} \qquad (3)$$

Partial molar volumes, $V_2(\mathrm{H})$ and $V_2(\mathrm{D})$, were obtained using eq 4 (Millero, 1972). Concentration dependences of $V_2^E = (V_2^m - V_2^\circ)$ and $\delta V_2^E = V_2^E(\mathrm{H}) - V_2^E(\mathrm{D})$ are shown in Figure 1.

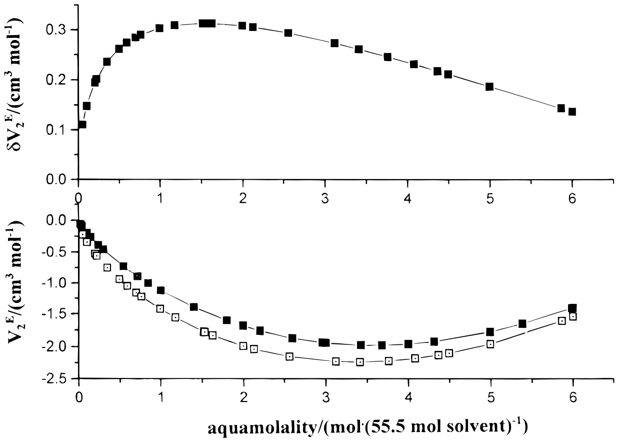

Figure 1. Volumetric properties of 1,3-DMU solutions in water and heavy water at 25.00 °C and concentrations below 6 m_{aq}. See Jakli and Van Hook (1996) for results at higher concentration. (Lower curves) Excess partial molar volumes of 1,3-DMUh_2 in H_2O (filled squares) or 1,3 DMUd_2 in D_2O (open squares). (Upper curve) Solvent isotope effect on excess partial molar volumes of 1,3 DMU, $\delta V_2^E = V_2^E(\mathrm{H}) - V_2^E(\mathrm{D})$.

$$V_2 = V_\phi + m_{aq}(\partial V_\phi/\partial m_{aq})_P \qquad (4)$$

Osmotic Coefficients. Vapor pressures of H_2O solutions (P_H^m) were obtained from differential measurements between solvent, P_H°, and solutions, P_H^m, at approximately 2° intervals ($10 < t/°\mathrm{C} < 70$). Seventy-five $\delta P = P_H^\circ - P_H^m$ data points were recorded at five concentrations (1, 2, 4, 12, and 20 m_{aq}). Parameters of least-squares fits to the Antoine equation (eq 5) are reported in Table 1.

$$\ln(P_H^m/\mathrm{kPa}) = A - B/[(C + (t/°\mathrm{C})] \qquad (5)$$

Differential vapor pressures between H_2O and D_2O solutions ($\delta P = P_H^m - P_D^m$) of identical aquamolality (67 data) were used to obtain P_D^m (here P_H^m is calculated from eq 5). Parameters of Antoine fits to P_D^m are reported in Table 1.

Osmotic coefficients of normal water solutions (ϕ_H) were obtained using eq 6

$$\phi_H = (-55.508/m_{aq})\,[\ln(P_H^m/P_H^\circ) - V_H^\circ\,(P_H^m - P_H^\circ)/RT + b_H(P_H^m - P_H^\circ)] \qquad (6)$$

and isotope effects, $\delta\phi_{H-D} = \phi_H - \phi_D$, from eq 7

$$\delta\phi_{H-D} = -\ln(a_H/a_D)55.508/m_{aq} = [\ln(P_H^\circ/P_D^\circ) - \ln(P_H^m/P_D^m)]55.508/m_{aq} \qquad (7)$$

V_H° is the molar volume of liquid water (Whalley 1958), b_H is the second virial coefficient (Eisenberg and Kauzmann 1969), and a_H or a_D is solvent activity. P_H° values were calculated from the Goff equation (Goff 1963), and the vapor pressure isotope effect of pure solvent, $\ln(P_H^\circ/P_D^\circ)$, was determined by us on the same apparatus used for the solution measurements (Jakli and Van Hook, 1981b).

The temperature and concentration dependences of ϕ_H and ϕ_D are shown in Figure 2. The lines represent least-squares fits to the empirically selected relation, eq 8

$$\phi_H = A_1 + A_2(t/°\mathrm{C}) + A_3(t/°\mathrm{C})^2 \qquad (8)$$

but a linear fit, $\delta\phi_{H-D} = A_1' + A_2'(t/°\mathrm{C})$, was sufficient to represent the temperature dependence of ϕ_{H-D}. The parameters are reported in Table 2.

Table 1. Parameters of Equation 5

m_{aq}[a]	A	B	C	$10^4\sigma$	data pts
1(H)	16.611(0.001)[b]	4017.0(0.6)	234.60(0.02)	0.24	14
1(D)	16.650(0.002)	3984.8(1.1)	229.46(0.04)	0.33	14
2(H)	16.583(0.003)	4008.4(1.8)	234.27(0.06)	0.62	14
2(D)	16.618(0.003)	3974.0(1.6)	229.04(0.05)	0.43	14
4(H)	16.520(0.005)	3984.0(3.0)	233.30(0.10)	1.25	14
4(D)	16.568(0.006)	3956.0(3.2)	228.29(0.10)	0.95	14
12(H)	16.410(0.007)	3945.2(3.6)	230.86(0.12)	1.5	17
12(D)	16.466(0.009)	3922.1(4.6)	226.07(0.15)	1.0	12
20(H)	16.281(0.017)	3901.3(9.0)	228.45(0.31)	3.5	16
20(D)	16.385(0.005)	3903.5(2.6)	224.60(0.09)	1.0	13

[a] Aquamolality (mol(55.508 mol solvent)$^{-1}$). [b] Parenthesized figures are 1 sd uncertainties.

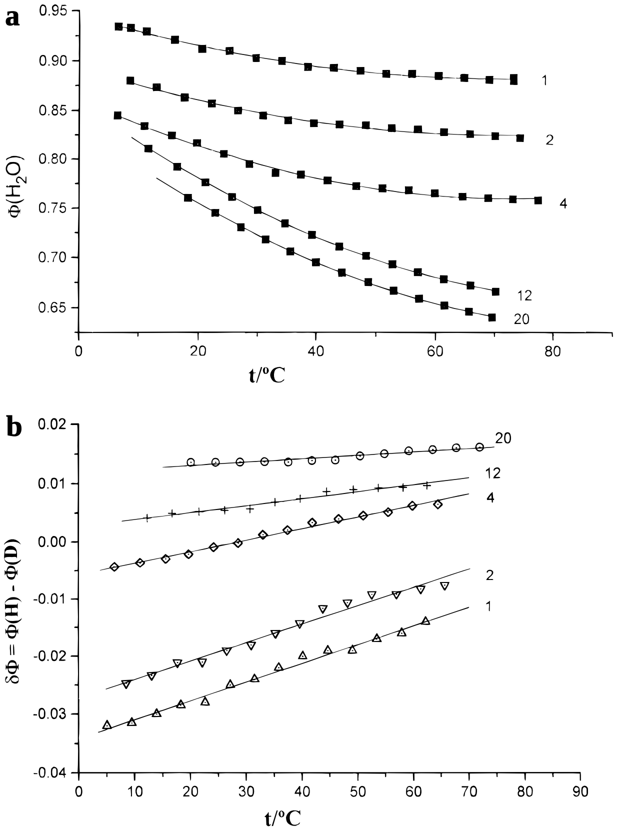

Figure 2. Osmotic coefficients of 1,3-DMUh_2/H_2O and 1,3-DMUd_2/D_2O solutions. (a) Osmotic coefficients of 1,3-DMUh_2/H_2O solutions. The numbers to the right of each curve indicate aquamolality (b) Isotopic differences between osmotic coefficients of 1,3-DMUh_2/H_2O and 1,3-DMUd_2/D_2O solutions. The numbers to the right of each curve indicate aquamolality

Table 2. Parameters of Equation 8

m_{aq}[a]	A_1	-10^2A_2	$10^5 A_3$	$10^3\sigma$
1(H)	0.946(0.001)[b]	1.787(0.07)	1.244(0.085)	1.4
1(H−D)	−0.0342(0.0004)	−0.32(0.01)		0.66
2(H)	0.894(0.002)	1.912(0.13)	1.333(0.15)	2.2
2(H−D)	−0.0273(0.0006)	−0.31(0.01)		0.88
4(H)	0.862(0.002)	2.805(0.10)	1.927(0.12)	2.0
4(H−D)	−0.0137(0.0006)	−0.27(0.02)		1.0
12(H)	0.860(0.001)	4.469(0.03)	2.452(0.05)	0.7
12(H−D)	0.0027(0.0003)	−0.12(0.01)		0.4
20(H)	0.834(0.001)	4.433(0.04)	2.384(0.06)	0.8
20(H−D)	0.0120(0.0003)	−0.06(0.01)		0.3

[a] Aquamolality (mol(55.508 mol solvent)$^{-1}$). [b] Parenthesized figures are 1 sd uncertainties.

Osmotic and activity coefficient data for normal water 1,3-DMU solutions obtained by the isopiestic gravimetric method were published earlier by the Italian group (25 °C, <3 m) (Barone et al., 1976) and Bonner and Breazeale (25 °C, 37 °C, 60 °C, <10 m_{aq}) [Bonner and Breazeale (1965)], and for heavy water solutions by Bonner (25 °C, <10 m_{aq}) (Bonner 1971). The largest deviation between present ϕ_H values and the literature is 7×10^{-3} (at 4 m_{aq}).

Excess Functions. The solvent excess free energy (ΔG_1^E), excess enthalpy (ΔH_1^E), and excess entropy (ΔS_1^E) were calculated from eqs 9−11

$$\Delta G_1^E = -55.508RT\,[m_{aq}\phi/55.508 + \ln(55.508/(m_{aq} + 55.508))] \quad (9)$$

$$\Delta H_1^E = m_{aq}RT^2\,d\phi/dT \quad (10)$$

$$\Delta S_1^E = [\Delta H_1^E - \Delta G_1^E]/T \quad (11)$$

To obtain isotope effects on the thermodynamic functions, ϕ was replaced with $\delta\phi$ in eqs 9 and 10. Values are summarized in Table 3, and plotted in Figures 3 and 4, where they are compared with excess functions for urea solutions (Jakli and Van Hook, 1981a).

Literature ϕ_H data are available below 10 m at 25, 37, and 60 °C (Barone et al., 1976; Bonner and Breazeale, 1965). ΔG_1^E calculated from these data agrees with the present values to <1.5%, while agreement of ΔH_1^E (and ΔS_1^E) is within 10 to 20%. A further check of the reliability of the ΔH_1^E (and ΔS_1^E) values derived from eq 10 can be made by comparison with the calorimetric data of Barone (Barone et al., 1976), who determined the integral heat of dilution of 1,3-DMU at 25 °C, from which the partial molal enthalpies can be evaluated (Young and Vogel, 1932). We find agreement with our ΔH_1^E data within 10%.

Discussion

Molar Volume. The characteristic behavior of aqueous solutions of polar organic compounds was established for a series of R_4N-salt homologues by Wen and Saito (Wen and Saito, 1964). Apparent or partial molar volumes plotted vs concentration show initial negative slopes and reach minimum values with increasing concentration. The minimum becomes more pronounced and shifts to lower concentration with increasing hydrophobic character of the solute and with decreasing temperature. Wen and Saito describe this behavior in terms of an "interstitial" solution process, in which the alkyl chains in time average are enclosed in a solvent cage. This results in structural stabilization of the solvent clusters surrounding the hydrophobic part of the solute molecule. The larger the hydrophobic part of the solute, the larger is the number of water molecules building the cage. This results in increasingly negative slopes and lower concentrations at which the hydration spheres of neighboring solute molecules overlap (assumed to locate $V_{2-\min}$). The present data (Figure 1) show the expected minima between 3 and 4 m. More importantly we find that the isotope effect also shows an extremum in its concentration dependence (see the upper part of Figure 1). It was because the existence of this maximum was indicated but not unequivocally supported by the older data (Phillip et al., 1974; Jakli and Van Hook, 1996) that new volumetric measurements were made in the Hungarian laboratory and are reported here.

Excess Properties. Barone et al. (1978) determined ΔG^E, ΔH^E, and $T\Delta S^E$ of 1,3-DMU/H_2O solutions at 25 °C for m_{aq} < 5. They measured calorimetric enthalpies of dilution of several alkylureas to obtain ΔH^E and obtained ΔG^E from osmotic data. The concentration dependences of the excess properties were expressed in virial form to

Table 3. Excess Properties of Solution in Aqueous 1,3-DMU

		ϕ		$(\Delta G_1^E/m_{aq})^b$		$(\Delta H_1^E/m_{aq})^b$		$(T\Delta S_1^E/m_{aq})^b$	
m_{aq}[a]	t/°C	H_2O	(H−D)	H_2O	(H−D)	H_2O	(H−D)	H_2O	(H−D)
1.0	10	0.929	−0.031	145	73	−1025	213	−1170	140
	20	0.915	−0.028	184	68	−921	229	−1106	161
	25	0.909	−0.026	203	65	−861	237	−1063	162
	30	0.904	−0.025	220	62	−795	245	−1015	182
	40	0.894	−0.021	251	56	−646	261	−897	205
	50	0.888	−0.018	277	49	−472	278	−749	229
	60	0.884	−0.015	297	42	−272	295	−569	254
2.0	10	0.876	−0.024	251	57	−1097	206	−1348	150
	20	0.861	−0.021	297	51	−985	221	−1282	170
	25	0.855	−0.019	318	48	−920	229	−1239	181
	30	0.849	−0.018	338	45	−850	237	−1188	192
	40	0.839	−0.014	375	38	−689	253	−1064	215
	50	0.832	−0.011	406	30	−502	269	−909	239
	60	0.827	−0.0081	431	22	−288	286	−719	263
4.0	10	0.836	−0.011	306	26	−1529	180	−1918	154
	20	0.814	−0.0083	371	20	−1385	193	−1824	173
	25	0.804	−0.0069	401	17	−1302	199	−1762	182
	30	0.795	−0.0056	430	14	−1210	206	−1690	192
	40	0.781	−0.0029	482	7	−1002	220	−1512	213
	50	0.770	−0.0015	526	0	−758	234	−1289	234
	60	0.763	0.0026	561	−7	−478	249	−1016	256
12.0	10	0.818	0.0039	206	−9	−2652	80	−2858	89
	20	0.781	0.0051	304	−12	−2492	86	−2796	98
	25	0.764	0.0057	351	−14	−2397	89	−2747	103
	30	0.748	0.0063	396	−16	−2290	92	−2686	107
	40	0.721	0.0075	481	−19	−2044	98	−2525	117
	50	0.698	0.0087	557	−23	−1751	104	−2308	127
	60	0.680	0.0099	623	−27	−1408	111	−2032	138
20	20	0.755	0.013	241	−32	−2486	43	−2727	75
	25	0.738	0.013	287	−33	−2395	44	−2682	78
	30	0.723	0.014	331	−35	−2294	46	−2625	80
	40	0.695	0.014	414	−37	−2059	49	−2473	86
	50	0.672	0.015	488	−40	−1779	52	−2267	92
	60	0.654	0.016	554	−43	−1451	55	−2004	98

[a] Aquamolality (mol(55.508 mol solvent)$^{-1}$). [b] Units are (J·mol^{-1}·(55.508 mol solvent)).

evaluate pair and triplet interaction coefficients. They concluded that in contrast to aqueous urea solutions the alkylureas enhance water structure; there is a driving force toward positive interaction between hydrated solute molecules. Nevertheless, the enthalpic interaction coefficients suggest the source of this effect is rearrangement of water rather than direct association of solute molecules. Strict compensation of the enthalpic and entropic effects was reported.

We expect additional information from the present data that extend over wider temperature and concentration ranges and include H_2O-D_2O solvent isotope effects. In contrast to the Barone analysis, we prefer to rationalize the effects in terms of the behavior of the solvent excess functions, ΔG_1^E, ΔH_1^E, and $T\Delta S_1^E$. These functions reflect differences relative to pure water and are a good measure of the hydrogen-bond reinforcing or weakening ability of the solute.

Excess Free Energy. The concentration dependence of the solvent excess free energy of 1,3-DMU/H_2O solutions at 25 °C is shown in Figure 3a, and the temperature dependence can be deduced from Table 3 or observed in Figure 4a. In each case the figures compare the present data with that for urea/H_2O solutions. Notice from Figure 4a that $(\partial(G_1^E/m_{aq})/\partial T) > 0$ and is of opposite sign from that observed for aqueous solutions of urea, indicating negative excess enthalpies and entropies for the alkylurea solution and structural enhancement. At lower temperatures (<40 °C), the plots of $\Delta G_1^E/m_{aq}$ vs m_{aq} for 1,3-DMU (Figure 4a) show maxima that appear at approximately the same concentration where the apparent molar volume has its minima. The differences in magnitude of ΔG_1^E between 1,3-DMU and urea are also remarkable. The stronger temperature dependence for 1,3-DMU indicates large ΔH_1^E and ΔS_1^E values, which are likely a consequence of its larger hydration number.

Excess Enthalpy and Entropy. As shown by Figure 3b, the behavior of ΔH_1^E and ΔS_1^E further supports the characterization of the hydrophobic nature of 1,3-DMU solutions. In contrast to urea, $|T\Delta S| > |\Delta H|$ in 1,3-DMU (entropy-controlled hydration). The degree of enthalpy−entropy compensation seems to characterize the hydrophobicity in solutions of polar organic molecules. Making a comparison at 25 °C and at the concentration of $V_{2-\min}$, 1,3-DMU shows 77% compensation ($\Delta H_1^E/T\Delta S_1^E = 0.77$), n-Bu_4NBr 88% (Jakli and Marko, 1995a), and n-Bu_4N-butyrate 105% (Barone et al., 1980; Jakli and Marko, 1995b). The compensation effect decays rapidly with increasing temperature, and the decrease in ΔH_1^E is more pronounced than that in ΔS_1^E (Table 3); at 10 °C $\Delta H_1^E/T\Delta S_1^E = 0.88$, at 25 °C = 0.77, at 40 °C = 0.68, and at 60 °C = 0.45, although in urea solutions $\Delta H_1^E/T\Delta S_1^E$ changes very little with temperature, remaining ~0.70 over the range $10 < t/°C < 60$.

The concentration dependence of ΔH_1^E and ΔS_1^E for 1,3-DMU solutions is significantly different than it is for solutions of more hydrophobic compounds such as n-Bu_4NBr and n-Bu_4N-butyrate. For the Bu_4N-salt solutions at the concentration where V_2 shows its minimum, the excess entropy and enthalpy indicate maximal structural enhancement of the solvent water (showing sharp minima in $\Delta H_1^E/m_{aq}$ and $\Delta S_1^E/m_{aq}$ vs m_{aq} curves), but in 1,3-DMU solutions these functions continue to decrease above $V_{2,\min}$ and become constant only above 10 m (Figure 3); the addition of solute beyond $V_{2,\min}$ results in additional

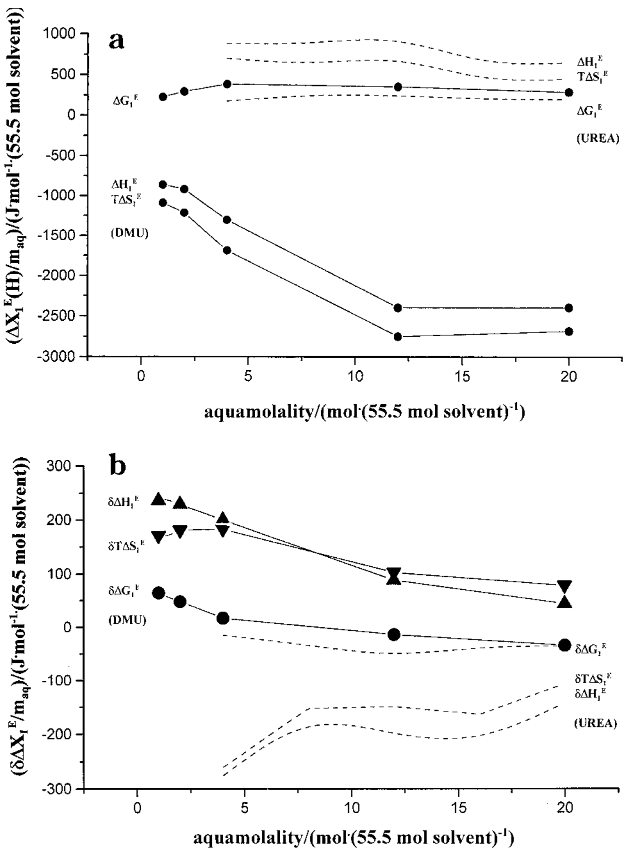

Figure 3. (a) Excess solvent partial molar free energies, entropies, and enthalpies of 1,3-DMUh_2/H$_2$O solutions at 298.15 K derived from osmotic coefficient data and compared with similar information on urea solutions (Jakli and Van Hook, 1981a). (b) Isotope effects on excess solvent free energies, entropies, and enthalpies of 1,3-DMUh_2/H$_2$O and 1,3-DMUd_2/D$_2$O solutions at 298.15 K derived from osmotic coefficient data and compared with similar information on urea solutions (Jakli and Van Hook, 1981a). $\delta\Delta X_1^E = \Delta X_1^E(H) - \Delta X_1^E(D)$.

structural enhancement, but for the apolar compounds high solute/solvent ratios result in a breakdown of the structural integrity of the water network (hydration sphere). We think the difference is a consequence of the structure of the symmetric DMU molecule, which, due to its two proton donor (N(CH$_3$)H) and two acceptor sites (CO), is capable of “substitutional” participation in hydrogen-bonded water clusters. It has been earlier argued from calorimetric (Barone et al., 1978, 1980), infrared (Barone et al., 1970), NMR (Barone et al., 1971), and diffusion (Sartorio et al., 1981) measurements that the symmetric dimethyl- and diethylurea promote additional structural enhancement over their 1,1-isomeric analogues.

In contrast to earlier interpretations, where the significance of solute–solvent dipolar interactions in the aqueous solutions of the symmetric alkyl derivatives of urea was neglected, we presume that in 1,3-DMU ($m_{aq} < 4$) the “normal” interstitial solution process (hydrophobic cage building) dominates, but above this concentration 1,3-DMU solute molecules replace (substitute) water molecules in the hydrogen-bonded water network (cage). The resulting increase in structural enhancement above 4 *m* is therefore due to solute–solvent association resulting in larger clusters that contain more solute molecules.

The H$_2$O–D$_2$O solvent isotope effects support this interpretation. The solvent isotope effects on ΔG_1^E, ΔH_1^E, and TΔS_1^E of 1,3-DMU are compared with those of the urea in Figure 3b. As expected, while for urea ΔH_1^E and TΔS_1^E values are more positive in D$_2$O than in H$_2$O, for 1,3-DMU solutions the opposite obtains. The concentration dependence of the 1,3-DMU isotope effects shows interesting characteristics. In the water-rich region (<4 m_{aq}), $\delta\Delta G_1^E$(H–D) is not “entropy controlled”, i.e., $\delta T\Delta S^E{}_{1,H-D} < \delta\Delta H^E{}_{1,H-D}$ and $(\partial(\delta\Delta H_1^E/\delta T\Delta S_1^E)/\partial m_{aq}) < 0$ This shows that the “entropy-controlled” contribution to ΔG_1^E is a consequence of the hydration of the polar part of the solute (i.e., contribution of solute–solvent interaction, largely canceled by the isotope effect). The change in isotope effects above 4 *m* supports the interpretation of a mechanistic change from “interstitial” to “substitutional” solution.

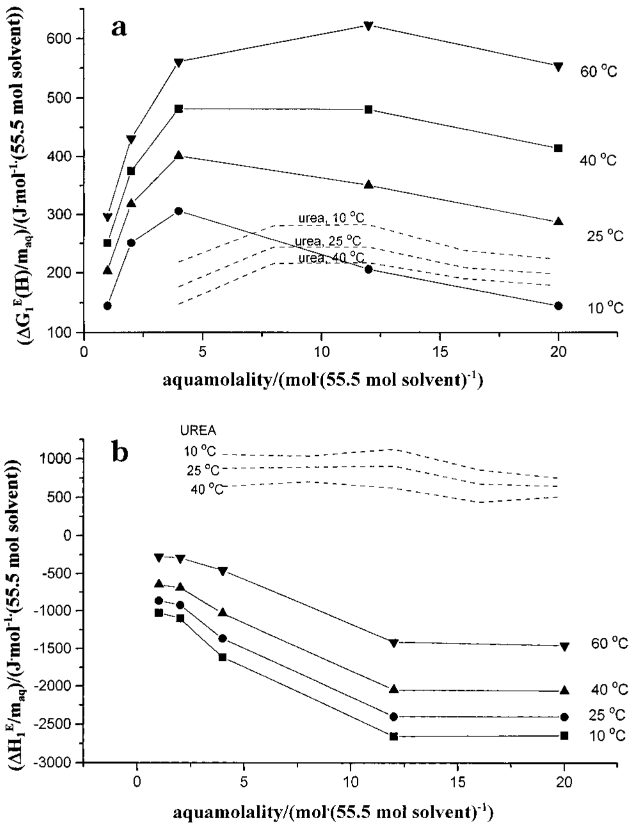

Figure 4. (a) Reduced excess solvent free energies of 1,3-DMUh_2/H$_2$O solutions compared with similar information on urea solutions at several temperatures (Jakli and Van Hook, 1981a). The corresponding isotope effects are given in Table 3. (b) Reduced excess solvent enthalpies of 1,3-DMUh_2/H$_2$O solutions compared with similar information on urea solutions at several temperatures (Jakli and Van Hook, 1981a). The corresponding isotope effects are given in Table 3.

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