

# H<sub>2</sub>O–D<sub>2</sub>O Solvent Isotope Effects on Apparent and Partial Molar Volumes of 1,3-Dimethylurea and Tetramethylurea Solutions

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Densities of solutions of 1,3-dimethylurea and tetramethylurea in H<sub>2</sub>O and D<sub>2</sub>O have been measured at 15, 25, and 40 °C over wide concentration ranges using a vibrating tube densitometer to obtain apparent ( $V_{\phi}$ ) and partial ( $V_2$ ) molar volumes. A comparison of the data with those for urea shows interesting differences. While for urea  $V_2^E$  is positive, monotonously increases with concentration, and displays an inverse isotope effect,  $V_2^E(\text{H}) - V_2^E(\text{D}) < 0$ ,  $V_2^E$  values for the methylureas are negative, go through a minimum, and show positive solvent isotope effects which are smaller than those for typical inorganic electrolyte solutions.

## Introduction

Numerous studies on the physicochemical properties of aqueous solutions of urea and alkyl-substituted ureas have been reported (Spencer and Hovick, 1988; Bezzabotnov *et al.*, 1992; Riedl and Jolicoeur, 1984; Eagland, 1975). An important characteristic shared by many investigations is the effort to obtain information about the effect of urea and substituted ureas on the aqueous solvent structure in water and water/protein solutions. At intermediate and elevated concentrations the ureas can act as conformational perturbants; therefore, the study of the structure of their aqueous solutions should contribute to an understanding of the denaturation process (Herskovits *et al.*, 1970; Eagland, 1975). Due to the different kinds of interactions between water and urea which exist in solution, deductions concerning its influence on water structure based on different physicochemical techniques were contradictory over a long period of time (Holtzer and Emerson, 1969). Although it is now widely accepted that urea has moderate structure breaking character (Franks, 1973), the influence of the alkylureas is more complicated.

To contribute to the understanding of intermolecular interactions in urea and substituted urea solutions, we have measured H<sub>2</sub>O–D<sub>2</sub>O solvent isotope effects on thermodynamic properties of urea, 1,3-dimethylurea, and tetramethylurea solutions over wide ranges of concentration and temperature (Jakli and Van Hook, 1981, 1982, 1996). The properties investigated include excess free energies, excess enthalpies, and entropies of solution and apparent and partial molar volumes. H<sub>2</sub>O–D<sub>2</sub>O solvent isotope effects on solution thermodynamics are expected to be useful in analyzing the different components of intermolecular interactions. To begin with, 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<sub>2</sub>O are more sensitive to changes in solvent–solvent interactions induced by the presence of the solute. Therefore, in the interpretation of solvent isotope effects, it is expected that the changes in solvent–solvent interactions will

dominate, because the solute–solvent interactions, H compared to D, largely cancel.

For urea solutions our results (Jakli and Van Hook, 1981) support the conclusion that water structure is only slightly disturbed on the addition of urea. However, preliminary results we reported for activity coefficients of 1,3-dimethylurea and tetramethylurea solutions indicated that these solutes have a much stronger influence on solvent structure (Jakli and Van Hook, 1982, 1996). They did not, however, support the conclusion that changes in the properties of alkyl-substituted urea solutions are proportional to their methyl group content (Barone *et al.*, 1970). In the present paper we report detailed results on the apparent and partial molar volumes of 1,3-dimethylurea (DMU) and tetramethylurea (TMU) solutions in H<sub>2</sub>O and D<sub>2</sub>O and discuss them briefly. Earlier measurements on 1,3-dimethylurea and tetramethylurea solutions in H<sub>2</sub>O had been made only at 25 °C and below 6 *m*, and for DMU and TMU solutions in D<sub>2</sub>O only at 25 °C and high dilution (Philip *et al.*, 1974).

## Experimental Section

**Materials.** Laboratory distilled water was treated with basic potassium permanganate and redistilled two times in an all-glass apparatus. Heavy water (Merck and Co., analytical grade) was used without further purification. D/H analysis was made from density measurements with a Mettler-Paar densitometer, yielding [no. of D atoms/(no. of D atoms + no. of H atoms)] × 100 = (99.77 ± 0.01) atom % D. Tetramethylurea (Merck, analytical grade) was freshly distilled under vacuum. H<sub>2</sub>O and D<sub>2</sub>O solutions of equal aquamolality, *m* (mol of solute/55.508 mol of solvent), were prepared gravimetrically. 1,3-Dimethylurea (Merck, analytical grade) was recrystallized from ethanol and dried under vacuum to constant weight. Stock (“mother”) solutions of concentration 20 *m* were prepared in H<sub>2</sub>O and D<sub>2</sub>O and diluted gravimetrically as appropriate. For the heavy water mother solution 1,3-dimethylurea-*d*<sub>2</sub> was prepared by equilibrating 1,3-dimethylurea-*h*<sub>2</sub> with excess D<sub>2</sub>O, followed by recrystallization and vacuum drying at room temperature. The procedure was repeated several times to obtain 1,3-dimethylurea-*d*<sub>2</sub> with a D content of >99 atom %. This was checked from the density of D<sub>2</sub>O remaining after equilibration. The D content of the 20 *m* heavy water stock solution was 99.67 atom % D. On dilution with 99.77

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**Table 1. Apparent and Partial Molar Volumes of 1,3-Dimethylurea-*h* in H<sub>2</sub>O at Experimental Concentrations and Isotope Effects on Apparent and Partial Molar Volumes of 1,3-Dimethylurea<sup>a</sup>**

property	aquamolality =							
	0.5	1.00	1.50	2.00	4.00	8.00	12.00	20.00
15 °C								
$V_{\Phi}(\text{H})/(\text{cm}^3 \cdot \text{mol}^{-1})$	79.24	78.87	78.57	78.35	77.86	77.80	78.00	78.671
$\Delta V_{\Phi}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.30	0.32	0.31	0.32	0.32	0.30	0.21	0.15
$V_2(\text{H})_{\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	78.64	78.18	77.86	77.66	77.39	77.98	78.83	
$\Delta V_{2,\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.32	0.30	0.28	0.27	0.23	0.18	0.14	0.08
25 °C								
$V_{\Phi}(\text{H})/(\text{cm}^3 \cdot \text{mol}^{-1})$	79.94	79.59	79.34	79.18	78.77	78.68	78.90	79.50
$\Delta V_{\Phi}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.21	0.19	0.18	0.20	0.20	0.18	0.16	0.10
$V_2(\text{H})_{\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	79.42	78.99	78.73	78.58	78.37	78.86	79.66	
$\Delta V_{2,\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.21	0.20	0.19	0.18	0.16	0.13	0.11	0.08
40 °C								
$V_{\Phi}(\text{H})/(\text{cm}^3 \cdot \text{mol}^{-1})$	80.86	80.62	80.38	80.25	80.04	79.99	80.19	80.70
$\Delta V_{\Phi}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.10	0.11	0.11	0.11	0.12	0.11	0.09	0.08
$V_2(\text{H})_{\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	80.46	80.17	79.93	79.82	79.80	80.22	80.87	
$\Delta V_{2,\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.10	0.10	0.10	0.10	0.09	0.08	0.07	0.06

<sup>a</sup>  $V_2(\text{H})_{\text{calc}}$  calculated from eqs 3 and 5,  $\Delta V_2$  calculated from eqs 4 and 6.

atom % D D<sub>2</sub>O to the appropriate aquamolalities, corrections corresponding to the difference, (99.77 to 99.67) atom % D, were applied.

**Density Measurements.** Density data were taken using a Mettler-Paar DMA 601 HT vibrating tube densitometer. A detailed description of the apparatus and experimental procedures is given elsewhere (Dessauges et al., 1980). During the measurements the cell temperature was constant to  $\pm 0.002$  K at (15, 25 or 40) °C. The instrumental calibration constant was checked daily. The reproducibility of the densities of individual samples was  $(1 \text{ to } 2) \times 10^{-5} \text{ g} \cdot \text{cm}^{-3}$ .

## Results

The apparent molar volumes in normal and heavy water solutions,  $V_{\Phi}(\text{H})$  and  $V_{\Phi}(\text{D})$ , were calculated from the measured densities using eq 1.  $M_w$  is the molar mass of

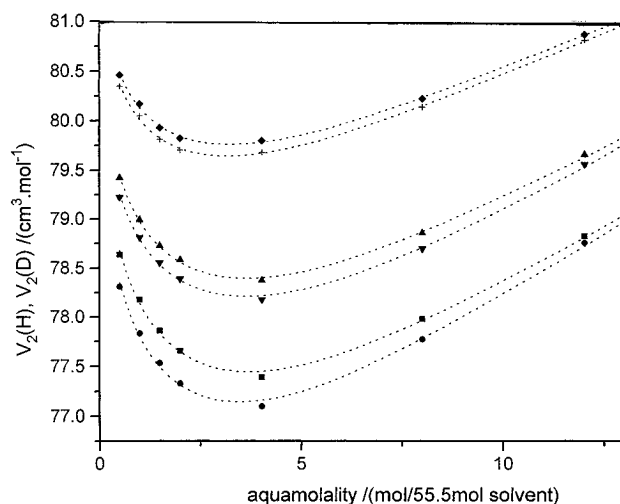
$$V_{\Phi} = M_s/d - 55.508M_w(d - d_0)/mdd_0 \quad (1)$$

normal or heavy water,  $d$  and  $d_0$  are the densities of solution and pure solvent, respectively,  $M_s$  is the molar mass of the solute, and  $m$  is the aquamolality (Millero, 1972). (For  $d_0(\text{H}_2\text{O})$  we used (999.103, 997.048, and 992.219)  $\text{kg} \cdot \text{m}^{-3}$  at (15, 25, and 40) °C, and for  $d_0(\text{D}_2\text{O})$ , 99.77 atom %) (1105.641, 1104.221, and 1099.729)  $\text{kg} \cdot \text{m}^{-3}$ , respectively.)

Partial molar volumes of the solute,  $V_2(\text{H})$  and  $V_2(\text{D})$ , were derived from the apparent molar volumes using eq 2.

$$V_2 = V_{\Phi} + m(\partial V_{\Phi}/\partial m)_P \quad (2)$$

**$V_{\Phi}$  and  $V_2$  for 1,3-Dimethylurea Solutions.** Values of  $V_{\Phi}$  and  $V_2$  for 1,3-dimethylurea obtained in this study are reported in Table 1.  $V_{\Phi}$  values come directly from experiment (*i.e.*, without smoothing); the  $V_2$  values are calculated from least squares fits of  $V_{\Phi}$  following methods outlined below. The concentration and temperature dependences of the data are illustrated for  $V_2$  in Figure 1. Comparison of the present  $V_{\Phi}(\text{H})$  values at concentrations below 6  $m$  can be made with the results of Desnoyers *et al.* (Philip *et al.*, 1970), but only at 25 °C. Agreement is within experimental error. The Canadian group also measured the H<sub>2</sub>O–D<sub>2</sub>O solvent isotope effect below 0.5 aquamolal, extrapolating the data to standard state (infinite dilution). They obtained  $V_{\Phi}^{\circ}(\text{H}) = V_2^{\circ}(\text{H}) = (80.04 \pm 0.05) \text{ cm}^3 \cdot \text{mol}^{-1}$  and  $\Delta V_{\Phi}^{\circ} = (V_{\Phi}^{\circ}(\text{H}) - V_{\Phi}^{\circ}(\text{D})) = (0.02 \pm 0.10) \text{ cm}^3 \cdot \text{mol}^{-1}$ .



**Figure 1.** Partial molar volumes,  $V_2$ , of 1,3-dimethylurea normal and heavy water solutions (dashed lines, eq 4): ■,  $V_2(\text{H})$ , 15 °C; ●,  $V_2(\text{D})$ , 15 °C; ▲,  $V_2(\text{H})$ , 25 °C; ▼,  $V_2(\text{D})$ , 25 °C; ◆,  $V_2(\text{H})$ , 40 °C; +,  $V_2(\text{D})$ , 40 °C.

Our choice of an expansion in half-integer powers of concentration (eq 3, *vide infra*) in order to fit the high

$$V_{\Phi}(\text{H}) = A_1 + A_2m^{1/2} + A_3m + A_4m^{3/2} \quad (3)$$

concentration curvature in  $V_{\Phi,m}$  plots with less statistical uncertainty than is possible with the expansion in integer powers implies misleadingly high standard state values. This is because it is well established that for polar organic molecules at low concentrations the  $V_{\Phi,m}$  curve is linear in the limit. The choice of the half-integer expansion results in a statistically superior description of the curvature at moderate and high concentration, but it is inappropriate for extrapolation to infinite dilution. We are therefore of the opinion that the  $A_1$  parameters referring to eq 3 and reported in Table 2 are best not interpreted as standard state partial molar volumes. At 25 °C the Desnoyers data extend to much lower concentration than do the present data and are to be preferred for this purpose. In any case, no matter what form is chosen for the expansion the difference in the isotope effects (*i.e.*,  $\Delta \delta V_{\Phi}^{\circ}$ ) is less than twice the combined standard errors and indicates consistency in each laboratory between the results in H<sub>2</sub>O and D<sub>2</sub>O.

The parameters reported in Table 2 result from least squares fits of the observed  $V_{\Phi}$  values to eq 3. The

**Table 2. Parameters of Eq 3 for 1,3-Dimethylurea and Tetramethylurea Solutions in H<sub>2</sub>O<sup>a</sup>**

	15 °C	25 °C	40 °C
1,3-Dimethylurea			
$A_1/(\text{cm}^3\cdot\text{mol}^{-1})$	80.77(0.15)	81.25(0.09)	81.88(0.09)
$-A_2/(\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{aquamol}^{-1/2})$	2.53(0.22)	2.19(0.14)	1.73(0.14)
$10A_3/(\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{aquamol})$	6.27(0.10)	5.41(0.58)	4.63(0.58)
$-10^2A_4/(\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{aquamol}^{-3/2})$	3.71(1.23)	3.13(0.74)	3.01(0.74)
$10^2(\sum\sigma^2)^{1/2}/(\text{cm}^3\cdot\text{mol})$	9.0	5.4	2.7
Tetramethylurea			
$A_1/(\text{cm}^3\cdot\text{mol}^{-1})$	116.6(0.25)	117.3(0.07)	118.1(0.20)
$-A_2/(\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{aquamol}^{-1/2})$	4.60(0.26)	3.82(0.07)	2.68(0.20)
$10A_3/(\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{aquamol})$	12.61(0.75)	10.7(0.21)	7.88(0.57)
$-10^2A_4/(\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{aquamol}^{-3/2})$	8.80(0.62)	7.58(0.17)	5.48(0.47)
$10^2(\sum\sigma^2)^{1/2}/(\text{cm}^3\cdot\text{mol}^{-1})$	20.7	5.8	16.3

<sup>a</sup> Values in parentheses are standard deviations of the parameters.

**Table 3. Parameters of Eq 4 for Solvent Isotope Effects of 1,3-Dimethylurea and Tetramethylurea Solutions in H<sub>2</sub>O and D<sub>2</sub>O<sup>a</sup>**

	15 °C	25 °C	40 °C
1,3-Dimethylurea			
$\Delta A_1/(\text{cm}^3\cdot\text{mol}^{-1})$	0.274(0.026)	0.179(0.018)	0.091(0.009)
$\Delta A_2/(\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{aquamol}^{-1/2})$	0.0594(0.025)	0.0281(0.017)	0.0229(0.009)
$\Delta A_3/(\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{aquamol})$	-0.0200(0.005)	-0.0101(0.003)	-0.0058(0.002)
$10^2(\sum\sigma^2)^{1/2}/(\text{cm}^3\cdot\text{mol})$	0.038	0.027	0.013
Tetramethylurea			
$\Delta A_1/(\text{cm}^3\cdot\text{mol}^{-1})$	0.738(0.050)	0.625(0.032)	0.283(0.022)
$\Delta A_2/(\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{aquamol}^{-1/2})$	-0.173(0.031)	-0.144(0.020)	-0.022(0.006)
$\Delta A_3/(\text{cm}^3\cdot\text{mol}^{-1}\cdot\text{aquamol})$	0.0127(0.004)	0.0106(0.002)	
$10^2(\sum\sigma^2)^{1/2}/(\text{cm}^3\cdot\text{mol})$	0.091	0.058	0.091

<sup>a</sup> Values in parentheses are standard deviations of the parameters.

parameters (and their standard errors) from the least square fits are collected in Table 2. Standard deviations for the fits are also reported. We regard eq 3 as a purely empirical representation of the apparent volumes of these nonelectrolyte solutions. The form of eq 3 is the same as the equation widely used to describe apparent molar properties of electrolyte solutions (Millero, 1972), but for electrolyte solutions the coefficient of the  $m^{1/2}$  term is fixed by the solvent properties according to the Debye-Huckel theory or one of its later modifications. Such is not the case for eq 3 where  $A_2$  is a purely empirical least squares parameter and has no connection to the theory of electrolyte solutions. We have also tried fits to an expansion of integer (rather than half-integer) powers of  $m$ , finding for the same number of parameters a marked increase in the residuals; this explains our choice of eq 3. (For example, for four-parameter fits of  $V_\phi(\text{H}, 25\text{ °C})$ ,  $[(\sum\sigma^2)_{\text{integer exp}}/(\sum\sigma^2)_{\text{half-int exp}}] \approx 3.5$ .)

We have chosen to represent isotope effects on  $V_\phi$  using eq 4. Once again the expansion using half-integer powers

$$\Delta V_\phi = V_\phi(\text{H}) - V_\phi(\text{D}) = \Delta A_1 + \Delta A_2 m^{1/2} + \Delta A_3 m \quad (4)$$

is better than that with integer powers. Least squares parameters of the fit of isotope effect data to eq 4 are given in Table 3.

The partial molar volumes may be approximated as

$$V_2(\text{H}) = A_1 + (3/2)A_2 m^{1/2} + 2A_3 m + (5/2)A_4 m^{3/2} \quad (5)$$

and the isotope effects as

$$\Delta V_2 = \Delta A_1 + (3/2)\Delta A_2 m^{1/2} + 2\Delta A_3 m \quad (6)$$

Calculated values of  $V_2(\text{H})$  and  $\Delta V_2$  at experimental concentrations are given in Table 1.

**$V_\phi$  and  $V_2$  for Tetramethylurea Solutions.** Experimental values of  $V_\phi$  and the  $V_2$  obtained from least squares

fits and the isotope effects are reported in Table 4. The concentration and temperature dependences for  $V_2$  are shown in Figure 2. Parameters of the least squares fits are in Tables 2 and 3. Philip *et al.* (1974) determined  $V_\phi(\text{H})$  for tetramethylurea solutions below 7 aquamolal at 25 °C, and the solvent isotope effect below 0.5 aquamolal. Their  $V_\phi(\text{H})$  values are slightly lower than the present ones (by about (0.05 to 0.1)  $\text{cm}^3\cdot\text{mol}^{-1}$ ). They report  $V_\phi^\circ(\text{H}) = V_2^\circ(\text{H}) = 115.30$  and  $V_\phi^\circ(\text{D}) = V_2^\circ(\text{D}) = 115.58$   $\text{cm}^3\cdot\text{mol}^{-1}$ . As for DMU it is inappropriate to interpret the TMU  $A_1$  parameters in Table 3 as  $V_\phi^\circ$  values.

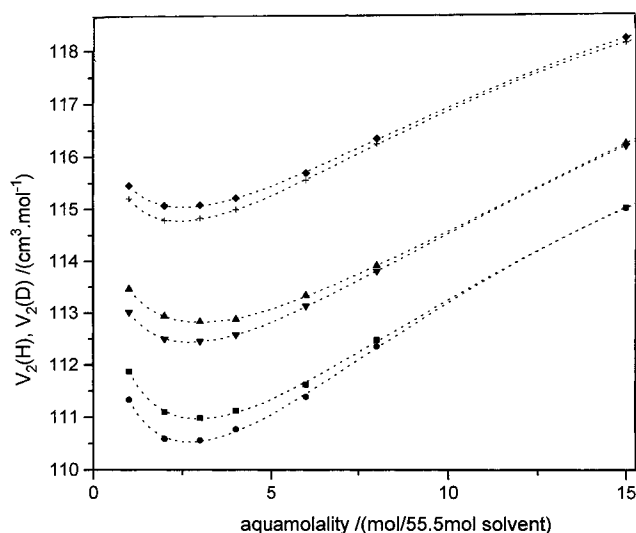
## Discussion

The dependence of DMU and TMU apparent and partial molar volumes on concentration and temperature follows the characteristic behavior of polar organic molecules in aqueous solution, showing initial negative slopes and reaching minimum values with increasing concentration. The minimum becomes more pronounced and shifts to lower concentrations with increasing hydrophobic character of the solute and with decreasing temperature. A widely accepted interpretation given by Wen and Saito (Wen and Saito, 1964) describes this kind of behavior in terms of the "interstitial" solution process, in which the alkyl chains are effectively hidden in a complete or partial solvent cage. This results in a structural rearrangement and stabilization of the solvent clusters surrounding the hydrophobic (part of the) solute molecule (hydrophobic hydration sphere). The larger the hydrophobic (part of the) solute, the higher is the number of water molecules building the cage, thus resulting in increasingly negative slopes and lower concentrations at which the hydration spheres overlap (interpreted as the concentration of the  $V_{2,m}$  minimum). The Wen and Saito ideas are based on an examination of the volumetric behavior of aqueous solutions of  $n$ -R<sub>4</sub>NBr homologues (R = methyl through butyl). In the case of  $n$ -Bu<sub>4</sub>NBr it was later shown (Jaklil and Marko, 1995) that for a given solute the caging process is stronger in D<sub>2</sub>O than

**Table 4. Apparent and Partial Molar Volumes of Tetramethylurea in H<sub>2</sub>O at Experimental Concentrations and Isotope Effects on Apparent and Partial Molar Volumes of Tetramethylurea<sup>a</sup>**

property	aquamolality =									
	1.00	2.00	3.00	4.00	6.00	8.00	15.00	25.00	50.00	
15 °C										
$V_{\Phi}(\text{H})/(\text{cm}^3 \cdot \text{mol}^{-1})$	113.20	112.30	111.90	111.70	111.50	111.70	112.70	114.00	116.00	
$\Delta V_{\Phi}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.52	0.54	0.50	0.47	0.42	0.35	0.21	0.19	0.16	
$V_2(\text{H})_{\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	112.03	111.20	111.02	111.09	111.49	112.30	115.04	(117.53)		
$\Delta V_2(\text{H})_{\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.52	0.49	0.47	0.45	0.41	0.39	0.31	0.23	0.08	
25 °C										
$V_{\Phi}(\text{H})/(\text{cm}^3 \cdot \text{mol}^{-1})$	114.44	113.80	113.50	113.30	113.24	113.30	114.20	115.50	117.10	
$\Delta V_{\Phi}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.46	0.45	0.44	0.39	0.35	0.29	0.20	0.18	0.14	
$V_2(\text{H})_{\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	113.47	112.94	112.84	112.88	113.4	113.91	116.28	(118.54)		
$\Delta V_{2,\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.44	0.42	0.40	0.39	0.35	0.33	0.27	0.20	0.08	
40 °C										
$V_{\Phi}(\text{H})/(\text{cm}^3 \cdot \text{mol}^{-1})$	116.20	115.70	115.50	115.40	115.40	115.69	116.40	117.50	119.20	
$\Delta V_{\Phi}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.22	0.27	0.26	0.25	0.21	0.28	0.16	0.15	0.14	
$V_2(\text{H})_{\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	115.54	115.12	115.10	115.20	115.63	116.26	117.29	(120.27)		
$\Delta V_{2,\text{calc}}/(\text{cm}^3 \cdot \text{mol}^{-1})$	0.26	0.2	0.24	0.24	0.23	0.22	0.19	0.17	0.12	

<sup>a</sup>  $V_2(\text{H})_{\text{calc}}$  calculated from eqs 3 and 5,  $\Delta V_2$  calculated from eqs 4 and 6.

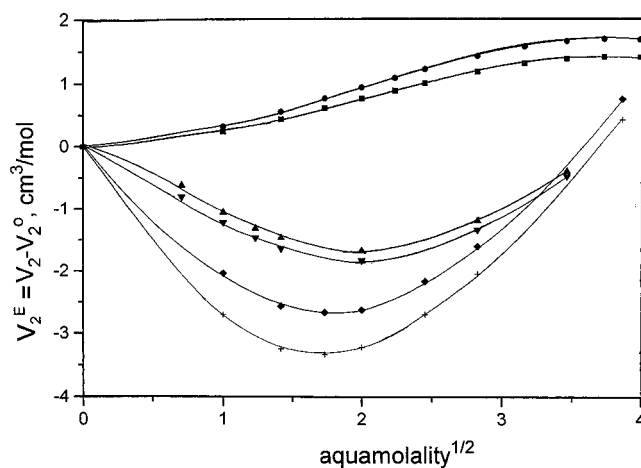


**Figure 2.** Partial molar volumes,  $V_2$ , of tetramethylurea normal and heavy water solutions (dashed lines, eq 4): ■,  $V_2(\text{H})$ , 15 °C; ●,  $V_2(\text{D})$ , 15 °C; ▲,  $V_2(\text{H})$ , 25 °C; ▼,  $V_2(\text{D})$ , 25 °C; ◆,  $V_2(\text{H})$ , 40 °C; +,  $V_2(\text{D})$ , 40 °C.

in H<sub>2</sub>O (i.e., the slope is more negative, and the  $V_2$  minimum is deeper).

To compare the volumetric characteristics of urea and substituted ureas in aqueous solution, we show the relative (or excess) partial molar volumes ( $V_2^{\text{ex}} = V_2 - V_2^\circ$ ) vs concentration at 25 °C for urea, DMU, and TMU in H<sub>2</sub>O and D<sub>2</sub>O in Figure 3. The most significant difference between urea and the methylureas is the change in sign of the  $V_2^{\text{ex}}$  solvent isotope effect on methylation (with urea  $V_2^{\text{ex}}(\text{H}) - V_2^{\text{ex}}(\text{D}) < 0$ , while with 1,3-dimethylurea and tetramethylurea it is  $> 0$ ). This is an expected consequence of the Wen–Saito model; because of the enhanced structure in heavy water (“it behaves like normal water at a lower temperature”), the substitutional solution process which dominates for urea should result in a more positive slope, while the interstitial solution process, more important for the methylureas, results in more negative slopes in D<sub>2</sub>O than in H<sub>2</sub>O. (Following the usual terminology, one can say that both the structure breaking influence of the urea and the caging process of the methylureas are stronger in the more structured heavy water.)

We caution that although in methylureas the interstitial solution (caging) process dominates over the substitutional one (up to the concentration of the minimum in  $V_2$ ), this



**Figure 3.** Relative (excess) partial molar volumes of ureas and substituted ureas in H<sub>2</sub>O and D<sub>2</sub>O at 25 °C: ■, urea-*h*; ●, urea-*d*; ▲, 1,3-dimethylurea-*h*; ▼, 1,3-dimethylurea-*d*; ◆, tetramethylurea-*h*; +, tetramethylurea-*d*.

does not mean that these solutes are overall structure makers. As is often emphasized, the overall structural influence of a solute should be deduced from entropy and/or heat capacity data. We believe the observation of a minimum in the partial molar volume vs concentration curve is a necessary, but not a sufficient, condition for an overall solvent structure enhancement.

The concentration dependence of the solvent isotope effect also shows the characteristic difference between the substitutional and interstitial solution. With urea, as for inorganic electrolytes (Dessauges *et al.*, 1980; Jakli *et al.*, 1983),  $\Delta V_{\Phi}$  and  $\Delta V_2$  decrease monotonously with increasing concentration (Jakli and Van Hook, 1981), although the effects with electrolytes are much higher. With electrolytes the negative contribution of the Coulombic hydration to the standard (limiting) molar volume is very high (Millero, 1971), while with urea a modest negative (structural) contribution must be due to filling up the void space in the solvent (Hamilton and Stokes, 1972). Both effects must be stronger at lower temperatures (or in D<sub>2</sub>O), and should decrease with increasing concentration. In the substituted ureas there is a strong competition between the substitutional and interstitial solution processes. This is especially important for 1,3-dimethylurea with its balanced polar–apolar group content and its capability to act as both a hydrogen bond donor and a hydrogen bond acceptor

(whereas tetramethylurea can act only as a hydrogen bond acceptor).

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