*J. Chem. Eng. Data* **2010,** *55,* 3055–3058 **3055**

# Standard Enthalpies and Heat Capacities of Solution of Urea and Tetramethylurea in Water

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This paper presents the results of accurate measurements of the enthalpies of solution of a typical hydrophilic solute, urea, and its hydrophobic derivative, tetramethylurea, in water in the temperature range of (278.15 to 338.15) K. The standard enthalpies and heat capacities of solution are computed and compared with available literature values. Our results do indicate that the standard heat capacity of the solution of urea is very small, but it changes its sign at about the temperature minimum of the water heat capacity at constant pressure, while the heat capacity of tetramethylurea solution in water is large, positive, and independent of the temperature.

## Introduction

Urea and its alkyl derivatives are widely known protein denaturants. However, the molecular mechanism by which these solutes denature proteins in aqueous solutions is still not well understood.[1–4] This explains the existence of detailed efforts directed to studying structural and thermodynamic properties of both dilute and concentrate aqueous solutions of these solutes.[5–9] Although numerous experimental data and their critical analyses are available in literature (see refs 8 to 17 and references therein), the thermodynamic behavior of hydrophilic urea and its substituted hydrophobic derivatives in cold and hot water is not well studied. The results available are found to be very contradictory. In fact, Figure 1a clearly demonstrates that the enthalpies of urea solution at a room temperature reported in various papers[11–13] are almost identical, whereas in hot water they reveal strongly different temperature dependences, which results in different signs for standard heat capacities of urea solution in water.

The present study focuses on the experimental measurements of the enthalpies of solution of urea and tetramethylurea in both cold and hot water to compute the heat capacities of solution and partial molar heat capacities and compare the thermodynamic behavior of the hydrophilic urea and its hydrophobic substituted derivative in an aqueous solution.

## Experimental Section

Distilled water was treated with basic potassium permanganate and then redistilled in a quartz still to reach the electric conductivity of $1 \cdot 10^{-5}$ $S \cdot m^{-1}$. Urea (Harnstoff, initial mass fraction purity > 99.5 %) was dried under reduced pressure at 343 K for several days and used without further purification. Tetramethylurea (Merck, analytical grade) was distilled under reduced pressure, washed by 4 Å molecular sieves, and then distilled twice at 313 K, the middle fraction being selected. Chromatographic analysis showed that the final mass fraction purity of the product was better than 99.9 %. Karl Fisher titration indicated that the water mass fraction in liquid tetramethylurea did not exceed 0.02 %.

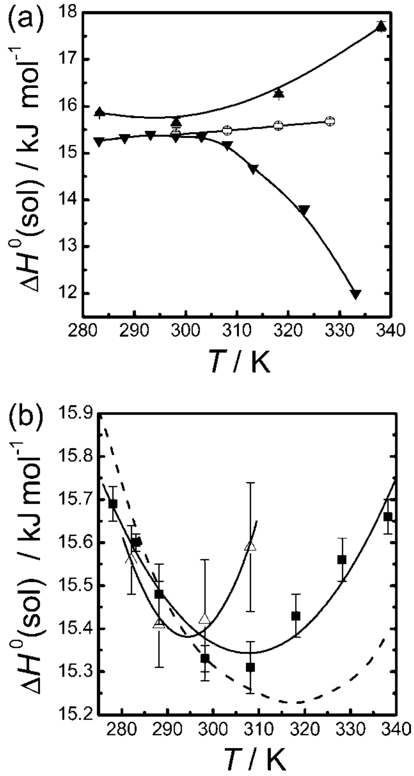

**Figure 1.** Temperature dependence of the enthalpies of urea solution in water. (a) ▲, ref 12; ○, ref 13; ▼, ref 11. Refs 12 and 13 represent the results of direct calorimetric measurements, whereas the data reported by Jakly and Van Hook[11] have been obtained from the temperature dependence of vapor pressure values. (b) ■, our results; △, ref 14; dashed curve, our calculation with the $\bar{C}_p^0$ values reported by Gucker and Ayres.[26] Solid lines represent a polynomial description.

The calorimetric measurements were carried out with a precise ampule calorimeter fitted with a 70 $cm^3$ titanium vessel.[18,19] The vessel was equipped with a calibration heater, a titanium stirrer, and a thermistor. A glass ampule containing a solute was attached to the stirrer and crushed against the vessel bottom to initiate the dissolution process. Thermistor resistance was directly measured by the standard temperature measuring

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10.1021/je9010689

**Table 1. Experimental $\Delta H^{m}(\mathrm{sol})$ and Standard Enthalpies of Solution $\Delta H^{0}(\mathrm{sol})$ for Urea in Water from $T$ = (278.153 to 328.15) K**

| $m$[a]<br>$\mathrm{mol \cdot kg^{-1}}$ | $\Delta H^{m}(\mathrm{sol})$<br>$\mathrm{kJ \cdot mol^{-1}}$ | $m$<br>$\mathrm{kJ \cdot mol^{-1} kJ \cdot mol^{-1}}$ | $\Delta H^{m}(\mathrm{sol})$<br>$\mathrm{kJ \cdot mol^{-1}}$ | $m$<br>$\mathrm{mol \cdot kg^{-1}}$ | $\Delta H^{m}(\mathrm{sol})$<br>$\mathrm{kJ \cdot mol^{-1}}$ | $m$<br>$\mathrm{mol \cdot kg^{-1}}$ | $\Delta H^{m}(\mathrm{sol})$<br>$\mathrm{kJ \cdot mol^{-1}}$ |
|---|---|---|---|---|---|---|---|
| $T$/K = 278.15 | | $T$/K = 283.15 | | $T$/K = 288.15 | | $T$/K = 298.15 | |
| 0.01596 | 15.66 | 0.01483 | 15.62 | 0.02160 | 15.41 | 0.02231 | 15.36 |
| 0.02936 | 15.67 | 0.01644 | 15.58 | 0.02583 | 15.48 | 0.02533 | 15.33 |
| 0.02945 | 15.72 | 0.01834 | 15.55 | 0.02856 | 15.49 | 0.02877 | 15.28 |
| 0.03019 | 15.75 | 0.02161 | 15.64 | 0.06849 | 15.55 | 0.03089 | 15.34 |
| 0.03582 | 15.67 | 0.03689 | 15.59 | | | 0.03598 | 15.39 |
| | | | | | | 0.03872 | 15.29 |
| | | | | | | 0.04804 | 15.32 |
| | | | | | | 0.04944 | 15.29 |
| | | | | | | 0.05257 | 15.31 |
| | | | | | | 0.05270 | 15.34 |
| $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = 15.69 ± 0.03[b] | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = 15.60 ± 0.03 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = 15.48 ± 0.06 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = 15.33 ± 0.03 | |
| $T$/K = 308.15 | | $T$/K = 318.15 | | $T$/K = 328.15 | | $T$/K = 338.15 | |
| 0.02048 | 15.33 | 0.02435 | 15.36 | 0.01547 | 15.60 | 0.03120 | 15.68 |
| 0.02197 | 15.26 | 0.02842 | 15.44 | 0.02356 | 15.59 | 0.03484 | 15.62 |
| 0.04933 | 15.35 | 0.05136 | 15.50 | 0.05128 | 15.53 | 0.03717 | 15.64 |
| 0.05279 | 15.28 | 0.08118 | 15.40 | 0.05295 | 15.50 | 0.07253 | 15.70 |
| $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = 15.31 ± 0.04 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = 15.43 ± 0.06 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = 15.56 ± 0.05 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = 15.66 ± 0.04 | |

[a] Solute molality. [b] Uncertainties from here on represent twice the standard deviation of the mean.

**Table 2. Experimental $\Delta H^{m}(\mathrm{sol})$ and Standard Enthalpies of Solution $\Delta H^{0}(\mathrm{sol})$ for Tetramethylurea in Water from $T$ = (278.153 to 328.15) K**

| $m$[a]<br>$\mathrm{mol \cdot kg^{-1}}$ | $-\Delta H^{m}(\mathrm{sol})$<br>$\mathrm{kJ \cdot mol^{-1}}$ | $m$<br>$\mathrm{mol \cdot kg^{-1}}$ | $-\Delta H^{m}(\mathrm{sol})$<br>$\mathrm{kJ \cdot mol^{-1}}$ | $m$<br>$\mathrm{mol \cdot kg^{-1}}$ | $-\Delta H^{m}(\mathrm{sol})$<br>$\mathrm{kJ \cdot mol^{-1}}$ | $m$<br>$\mathrm{mol \cdot kg^{-1}}$ | $-\Delta H^{m}(\mathrm{sol})$<br>$\mathrm{kJ \cdot mol^{-1}}$ |
|---|---|---|---|---|---|---|---|
| $T$/K = 278.15 | | $T$/K = 283.15 | | $T$/K = 288.15 | | $T$/K = 293.15 | |
| 0.02303 | 28.61 | 0.02309 | 27.50 | 0.01812 | 26.37 | 0.02265 | 25.27 |
| 0.03730 | 28.62 | 0.03418 | 27.57 | 0.02115 | 26.38 | 0.02510 | 25.31 |
| 0.03927 | 28.63 | 0.03546 | 27.51 | 0.02712 | 26.36 | 0.02612 | 25.34 |
| 0.04241 | 28.63 | 0.03686 | 27.52 | 0.02945 | 26.34 | 0.02752 | 25.34 |
| 0.04511 | 28.63 | 0.03807 | 27.56 | 0.03713 | 26.40 | 0.03225 | 25.30 |
| $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = −28.62 ± 0.01[b] | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = −27.53 ± 0.03 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = −26.37 ± 0.02 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = −25.31 ± 0.03 | |
| $T$/K = 298.15 | | $T$/K = 303.15 | | $T$/K = 308.15 | | $T$/K = 313.15 | |
| 0.01917 | 24.44 | 0.02491 | 23.43 | 0.01019 | 22.24 | 0.02918 | 21.19 |
| 0.02785 | 24.43 | 0.02614 | 23.43 | 0.02043 | 22.26 | 0.03032 | 21.16 |
| 0.02933 | 24.41 | 0.03601 | 23.47 | 0.02270 | 22.20 | 0.03051 | 21.15 |
| 0.03789 | 24.46 | 0.04424 | 23.45 | 0.05040 | 22.22 | 0.05426 | 21.14 |
| 0.06223 | 24.40 | 0.05601 | 23.45 | 0.05496 | 22.24 | 0.05797 | 21.21 |
| $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = −24.43 ± 0.02 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = −23.45 ± 0.02 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = −22.23 ± 0.02 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = −21.17 ± 0.03 | |
| $T$/K = 318.15 | | $T$/K = 328.15 | | $T$/K = 338.15 | | | |
| 0.03031 | 20.02 | 0.03079 | 18.13 | 0.02166 | 15.96 | | |
| 0.03086 | 20.04 | 0.03413 | 18.13 | 0.02838 | 15.97 | | |
| 0.03211 | 20.05 | 0.03726 | 18.14 | 0.04375 | 15.96 | | |
| 0.03490 | 20.06 | 0.03781 | 18.16 | 0.04753 | 15.93 | | |
| 0.06247 | 20.05 | 0.06897 | 18.15 | 0.08974 | 16.00 | | |
| $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = −20.04 ± 0.01 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = −18.14 ± 0.01 | | $\Delta H^{0}(\mathrm{sol})/(\mathrm{kJ \cdot mol^{-1}})$ = −15.95 ± 0.03 | | | |

[a] Solute molality.

instrument (BMC, Minsk). The signal of the instrument was converted automatically to the degrees using the International Temperature Scale of 1990. The detection limit of the apparatus was 10 μK. The temperature instability in the Thermostat A 3 bath (BMC, Minsk) was less than 1 mK in the temperature range of (275 to 350) K. The enthalpies of solution were measured by a comparative method. An electrical calibration was carried out before each experiment. The calorimeter was tested by measuring the enthalpies of solution of potassium chloride (KCl) and 1-propanol (1-PrOH) in water at 298.15 K according to recommendations given elsewhere.[20] The agreement between our results [$\Delta H^{m}(\mathrm{sol})$ ($m = 0.111\ \mathrm{mol \cdot kg^{-1}}$) = (17.61 ± 0.02) $\mathrm{kJ \cdot mol^{-1}}$ and $\Delta H^{0}(\mathrm{sol})$ = (−10.18 ± 0.03) $\mathrm{kJ \cdot mol^{-1}}$ for KCl and 1-PrOH, respectively] and recommended literature values of (17.58 ± 0.02 and −10.16 ± 0.02) $\mathrm{kJ \cdot mol^{-1}}$ for KCl and 1-PrOH, respectively)[20] was found to be excellent.[18]

## Results and Discussion

Experimental enthalpies of solution of urea and tetramethylurea in water are listed in Tables 1 and 2. As can be seen, the experimental values for both solutes do not depend on their molality for the concentration range studied. This allows us to compute the standard enthalpies of solution or enthalpies of solution at infinite dilution as the mean values in the range of the experimental results. The standard enthalpy of solution of urea in water at 298.15 K reported here (see Table 1) is in excellent agreement with known literature values of (15.26 ± 0.05,[17] 15.30 ± 0.02,[15] 15.31 ± 0.03,[16] 15.35 ± 0.2,[11] and 15.42 ± 0.14[14]) kJ·mol$^{-1}$ but slightly lower than the enthalpy of solution given elsewhere[12] (see also Figure 1). The standard enthalpy of tetramethylurea solution in water at 298.15 K given in Table 2 is found to be in good agreement with the results reported by Rouw and Somsen,[21] Batov and Ivanov,[22] and Della Gatta et al.[23] which are (−24.53 ± 0.04, −24.86 ± 0.09, and −24.38 ± 0.31) kJ·mol$^{-1}$, respectively, but significantly smaller than the $\Delta H^0$(sol) value[24] equal to (−22.07 ± 0.05) kJ·mol$^{-1}$. In our opinion, the disagreement observed may simply arise from different final purities of the product used.

The temperature dependence of the enthalpies of solution of urea in water is found to fit quite enough to the second-order polynomial:

$$\Delta H^0(\mathrm{sol})/\mathrm{kJ{\cdot}mol^{-1}} = (15.38 \pm 0.04) - (0.00743 \pm 0.002)(T/\mathrm{K} - 298.15) + 0.5(0.00078 \pm 0.0002)[(T/\mathrm{K} - 298.15)^2] \qquad s_\mathrm{f} = 0.05\ \mathrm{kJ{\cdot}mol^{-1}} \tag{1}$$

where the first term is the enthalpy of solution at the reference temperature of 298.15 K; the 0.00743 and 0.00078 values are the heat capacity of solution and its temperature derivative, respectively; the uncertainties from here on represent twice the standard deviation of the thermodynamic quantities obtained, and $s_\mathrm{f}$ is the standard deviation of the fit. The results represented in Figure 1b show that the enthalpy of urea solution slightly depends on the temperature, indicating that the heat capacity of solution is very small. However, the $\Delta C_\mathrm{p}{}^0$(sol) values are seen to be negative in cold water but positive in hot water. The similar behavior appears to reveal the experimental data reported by Subramanian et al.[14] (see Figure 1b); however, in this case the temperature range of measurements is narrow, and experimental uncertainties are large enough to confirm this fact. Using experimental heat capacities of solid urea given elsewhere[11] and our $\Delta C_\mathrm{p}{}^0$(sol) value (see eq 1), we have estimated the standard partial molar heat capacity of urea in water at 298.15 K to be equal to 86 J·mol$^{-1}$·K$^{-1}$. This value is seen to be in excellent agreement with the $\bar{C}_\mathrm{p}{}^0$ data reported by Desnoyers et al. (87.5 J·mol$^{-1}$·K$^{-1}$),[25] Gucker and Ayres (82.4 J·mol$^{-1}$·K$^{-1}$),[26] and Jakly and Van Hook (82 J·mol$^{-1}$·K$^{-1}$),[11] but larger than the value of 74 J·mol$^{-1}$·K$^{-1}$ given elsewhere.[17] Gucker and Ayres,[26] using a highly sensitive twin calorimeter, performed probably the most accurate measurements of heat capacities of urea solutions from 0.1 mol·kg$^{-1}$ to a nearly saturated region at (275 to 313) K. They, however, pointed out the deviation of the experimental results at low concentrations from extrapolating polynomials, that causes problems in obtaining reliable $\bar{C}_\mathrm{p}{}^0$ values.

We have fitted their standard partial molar heat capacities versus temperature to the third-order polynomial to reach experimental accuracy. Then, using the heat capacity of solid urea[11] and our $\Delta H^0$(sol) value at 298.15 K, we have reconstructed the $\Delta H^0(\mathrm{sol}) - f(T)$ curve in the temperature range studied with standard thermodynamic relation. Figure 1b shows a good agreement between experimental and computed $\Delta H^0$(sol) values, although the minimum in the latter case is shifted to higher temperatures.

The $\Delta H^0(\mathrm{sol}) - f(T)$ curve for tetramethylurea is found to fit very well to the following linear dependence:

$$\Delta H^0(\mathrm{sol})/\mathrm{kJ{\cdot}mol^{-1}} = -(24.36 \pm 0.06) + (0.210 \pm 0.002)\cdot 298.15\left(\frac{T/\mathrm{K}}{298.15} - 1\right) \qquad s_\mathrm{f} = 0.09\ \mathrm{kJ{\cdot}mol^{-1}} \tag{2}$$

Figure 2 demonstrates very good agreement between our and the latest reported enthalpies of solution[22] in the temperature range studied. The heat capacity of tetramethylurea solution equal to (210 ± 2) J·mol$^{-1}$·K$^{-1}$ is seen to be in good agreement with the literature values of [(218 ± 13)[14] and (219 ± 5)[22]] J·mol$^{-1}$·K$^{-1}$ but larger than the heat capacity value of (171 ± 11) J·mol$^{-1}$·K$^{-1}$, reported by Della Gatta et al.[23] The standard partial molar heat capacity of tetramethylurea in water at 298.15 can be simply estimated from our $\Delta C_\mathrm{p}{}^0$(sol) value (see eq 2) and the heat capacity of liquid solvent which has been found to be equal to 253 J·mol$^{-1}$·K$^{-1}$.[25] The value of 463 J·mol$^{-1}$·K$^{-1}$ is slightly larger than the partial molar heat capacity of 435 J·mol$^{-1}$·K$^{-1}$ reported by Desnoyers et al.[25]

Thus, enthalpies and heat capacities of solution for hydrophilic urea and its hydrophobic derivative reveal different behavior. The heat capacity of tetramethylurea solution is large, positive, and independent of the temperature as it is usually observed for hydrophobic solutes.[27–29] The heat capacity of tetramethylurea hydration estimated at 298.15 K from our data and Cabani et al. compilation[30] is large, positive, and equal to 322 J·mol$^{-1}$·K$^{-1}$. Such solute behavior is associated[6,27] with increasing the number of nearly straight and shorter water−water hydrogen bonds and decreasing the population of more bent H-bonds in the nearest vicinity of nonpolar groups. This phenomenon induces increasing energy fluctuations in the hydrophobic hydration shell that results in large and positive $\Delta C_\mathrm{p}{}^0$(sol) and $\Delta C_\mathrm{p}{}^0$(h) values for tetramethylurea. It is worthy of note that the heat capacity of urea hydration at 298.15 K is small, but positive, being 30 J·mol$^{-1}$·K$^{-1}$.[30] Since urea molecule contains no hydrophobic groups, this solute behavior appears to be surprising. However, the results of computer simulation clearly show[6] that hydrogen bonds between water molecules surrounding amine groups of urea become very similar to those around hydrophobic solutes, that is, one can observe the slight excess of shorter lengths and smaller angles in their nearest vicinity. On the contrary, the hydration of carbonyl oxygen induces deficit water pairs with low angle geometry, which induces the decrease of water heat capacity.[6] Both phenomena contribute to the heat capacity of hydration nearly canceling each other at 308 K. Since they appear to reveal different temperature behavior, we suppose that this fact may define the different signs of the $\Delta C_\mathrm{p}{}^0$(sol) values for urea in cold and hot water.

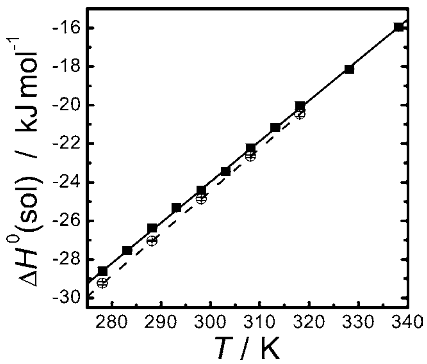

**Figure 2.** Temperature dependence of the enthalpies of tetramethylurea solution in water: ■, this work; ○, ref 22. Solid lines represent a linear description.

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Received for review December 19, 2009. Accepted April 2, 2010. This work was supported in part by the Russian Foundation for Basic Researches (Grant No. 05-03-96401) and Russian Science Support Foundation.

JE9010689