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Heat capacity effects associated with urea and tetramethylurea hydration: insight from computer simulation

Mikhail A. Krestyaninov and Andrey V. Kustov

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1S. Molecular dynamic simulations

The main goal of this work was to study the net effect of the solute on the H-bond distribution for surrounding water molecules, to compute and compare various contributions to the heat capacity of hydration of hydrophilic urea (U) and hydrophobic tetramethylurea (TMU) in terms of combination of MD simulations and the random network model of liquid water (see refs.[12-15] in the main text). We have performed molecular dynamic simulations using the DL_POLY Classic package. The NPT-ensemble and a cubic box with periodic boundary conditions contained 1000 water molecules or 999 waters and one solute molecule were applied. The pressure was 1 atm and the temperature was chosen to be equal to 288, 298 or 308 K. The Berendsen isotropic NPT thermostat and barostat with the relaxation time of 0.05 ps were applied. Each simulation step was 0.5 fs. The overall simulation time was usually 4 ns, the equilibration time was equal to 3 ns and then 1 ns was used for a data collection. The real space cut off of 10 Å and the Ewald summation with precision of 1×10^{-6} were applied.

The instantaneous snapshot for each system was analyzed every 1000 steps. The g_{OO}, g_{OH} and g_{HH} distribution functions for water and corresponding solute-water atom-atom radial distribution functions, g_r, were computed from the configurations obtained and shown in Figure 1S a-e. The g_{OO} function for SPCE water was found to be very similar to that reported elsewhere.[1S] The calculated enthalpy of vaporization equaled to 10.52±0.05 kcal mol^{-1} was in an excellent agreement with the experimental value.[1S] The average number of water molecules in the first hydration shell obtained from distribution functions was 16.4 and 33.9 for U and TMU, respectively.

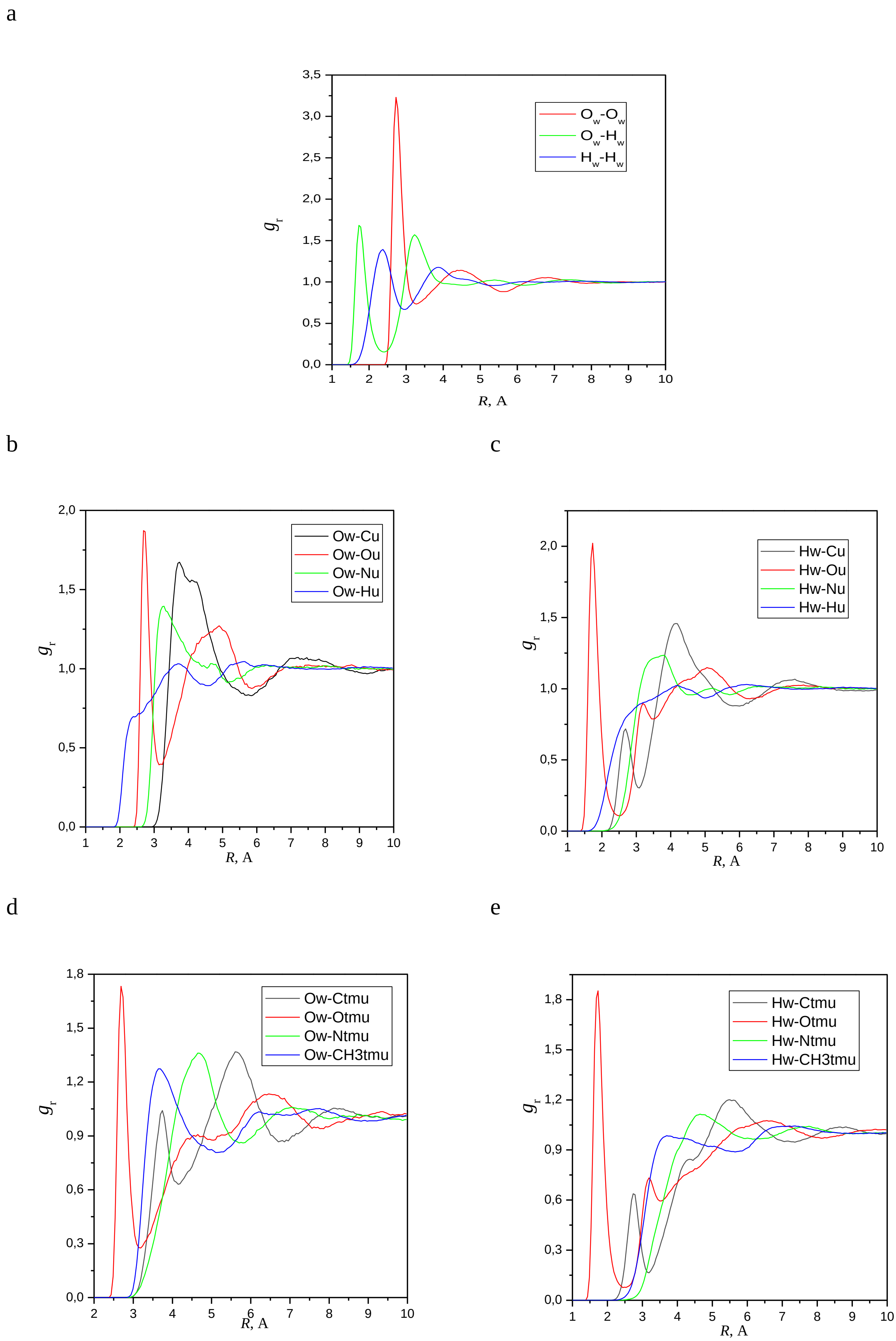

Figure S1 (a) Corresponding distribution functions for pure water (a) (SPC/E) and aqueous solutions (OPLS) of U (b, c) and TMU (d, e) at 298 K. For details see inserts in each figure.

2S. Heat capacity calculations

The calculation of individual contributions to the heat capacity of hydration was performed using equations (7-14, 16) given in the original paper of Madan and Sharp (see ref.[12] in the main text). The average oxygen-oxygen distance ($<r>$), the root-mean-squared (rms) deviation in an oxygen-oxygen distance (σ_r) and the rms H-bond angle (Θ) were obtained from the simulations and corrected with eq (16) to obtain necessary changes of these parameters compared to pure water in the presence of solute molecules. Then these corrected quantities were used to calculate bending, stretching, vibration *etc.* contributions to the heat capacity of water in terms of the RN model (see Table 1 in the main text). Figure 2S compares the angle distribution of H-bonds in pure water at 288-308 K for SPC/E and TIP3P potential functions. We see that the curves are very similar in both cases. This water behavior is consistent with the previous simulations for the TIP4P potential (see refs.[12-14] in the main text).

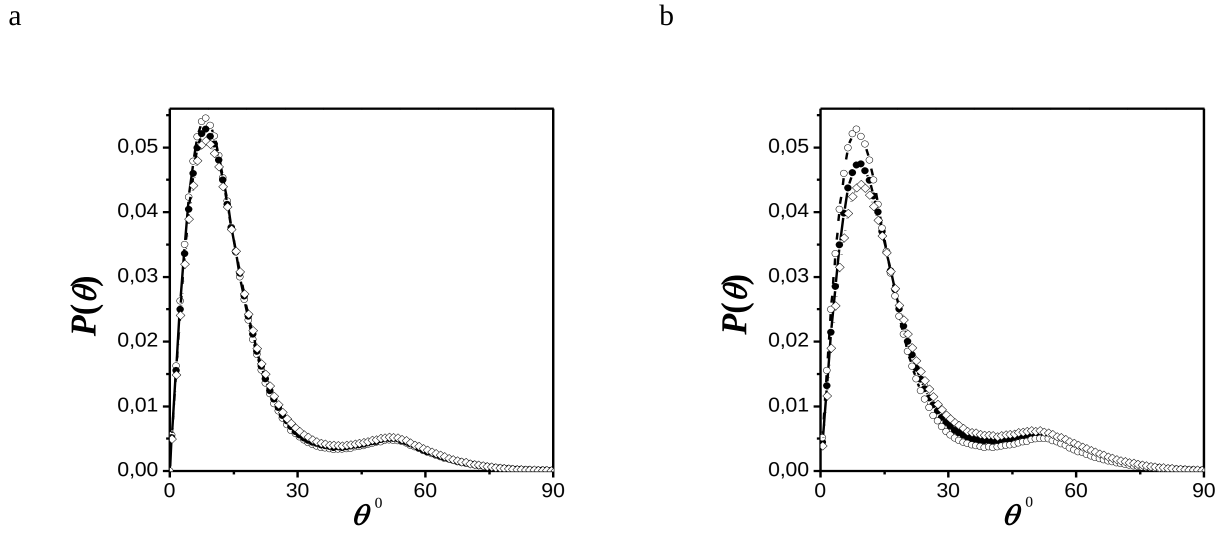

Figure S2 Probabilities of a H-bond angle distribution for SPC/E water (a) and TIP3P water (b) at 288 (○), 298 (●) and 308 (◇) K.

Table S1 Energies of U-water and TMU-water interactions (in kcal mol^{-1}) at various temperatures.[a]

System / Potential	Temperature, K		
	288	298	308
Water/SPC/E, U/OPLS	-33.37[a]	-33.25	-33.41
Water/SPC/E, U/KBFF	-27.27	-27.47	-27.37
Water/SPC/E, TMU/OPLS	-21.20	-20.84	-20.65

[a] The uncertainty of the energy values is estimated to be within 1 %.

The contribution of the solute-solvent interaction to the heat capacity of hydration was obtained from the simulations using potential functions for site-site interactions for each solute group with water molecules. We see from Table 1S that for U this value approaches zero for both potential functions, but for TMU it is significant. The corresponding energy values have been approximated *via* the following linear function: E=-29.09(2)+0.0275(0.005), R=0.985, S_d= 0.07 kcal mol^{-1}, where values in brackets are standard errors. This gives the heat capacity of TMU-water interaction equals to 27.5±5 cal mol^{-1} K^{-1}.

References

S1. S. Izadi and A. V. Onufriev. *J. Chem. Phys*., 2016, **145**, 074501.