

LETTERS

Roles of Enthalpy, Entropy, and Hydrogen Bonding in the Lower Critical Solution Temperature Behavior of Poly(ethylene oxide)/Water Solutions

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Analysis of the temperature and composition dependence of the excess thermodynamic properties for oligomers of poly(ethylene oxide) (PEO) in aqueous solution obtained from molecular dynamics simulations reveals that the lower critical solution temperature (LCST) behavior of PEO/water solutions is enthalpy-driven. At lower temperatures, the formation of ether–water hydrogen bonds results in a very favorable ΔG^{EX} consistent with the solubility of PEO and water. Increasing temperature leads to a dramatic reduction in favorable ether–water interactions due to break-up of ether–water hydrogen bonding, while relatively persistent water–water hydrogen bonding maintains the energetic penalty associated with disrupted water–water interactions upon insertion of the ether. The entropy gain associated with the break-up of ether–water hydrogen bonds and reduction in the structure of hydrating water with increasing temperature is insufficient to offset the unfavorable enthalpic effects associated with the break-up of the ether–water hydrogen bonds.

Applications of poly(ethylene oxide) (PEO) in aqueous solution are ubiquitous.¹ Many of the properties of PEO/water solutions responsible for their wide range of applications are related to their lower critical solution temperature (LCST) behavior.^{1–4} However, a molecular-level understanding of LCST behavior in PEO/water solutions is lacking. Theoretical models have been proposed with mechanisms for phase separation ranging from entropic effects induced by fitting of PEO into the liquid water structure⁵ to conformationally dependent hydrophobicity⁶ to competitive ether–water and water–water hydrogen bonding.⁷ These models, which describe the closed-loop phase behavior of PEO/water solutions with varying degrees of success, differ significantly in their treatment of entropy, enthalpy, and hydrogen bonding.

Our recent molecular dynamics (MD) simulations of aqueous solutions of 1,2-dimethoxyethane (DME), a PEO dimer, revealed that the excess free energy of mixing of DME in dilute aqueous solution is large and negative.⁸ Excess thermodynamic properties are defined as the solution value of a property relative to the

sum of the solvent and ideal gas solute (e.g., DME molecule) values, for example, $\Delta G^{\text{EX}} = G(\text{solution}) - [G(\text{solvent}) + G(\text{ideal gas solute})]$, where solvent denotes the solution minus the solute molecule and the ideal gas solute molecule is at the same concentration as in solution. The favorable ΔG^{EX} for the PEO dimer obtained from MD simulations is consistent with the solubility of PEO and water at room temperature.⁹ At the same temperature, the excess enthalpy ΔH^{EX} of the PEO dimer is favorable while the excess entropy ΔS^{EX} is unfavorable (see Table 1). The favorable excess enthalpy and unfavorable excess entropy were found to result from formation of ether–water hydrogen bonds and the structuring of the water of hydration (water comprising the first hydration shell of the ether).¹⁰

The unfavorable ΔS^{EX} for PEO/water solutions at room temperature appears to support an entropic driving force for phase separation at higher temperatures, consistent with the model of Kjellander et al.⁵ Assuming that ΔS^{EX} and ΔH^{EX} are not strongly temperature-dependent, that is, the excess heat

TABLE 1: Excess Thermodynamic Quantities for DME Solutions

T (K)	N_{ew}^b	ΔG^{EX} (kcal/mol)	ΔH^{EX} (kcal/mol)	ΔS^{EX} (kcal/(mol K))	$-T\Delta S^{\text{EX}}$ (kcal/mol)
$w_p = 0.01$					
298 ^a	1.54	-6.2	-17.1	-0.037	10.9
363	1.41	-3.5	-14.0	-0.029	10.5
$w_p = 0.52$					
298	1.13	-4.0	-9.8	-0.019	5.8
363	0.92	-3.0	-8.2	-0.015	5.3
$w_p = 0.01$ without Ether–Water Hydrogen Bonding					
298 ^b	0.13	-2.4	-12.2	-0.033	9.9
363	0.15	-1.1	-7.2	-0.017	6.3

^a From ref 8. ^b Number of ether–water hydrogen bonds per ether oxygen, defined in ref 8.

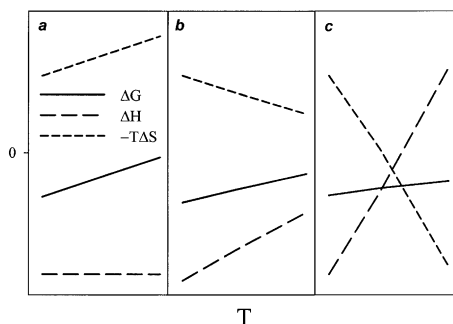


Figure 1. Schematic representation of the temperature dependence of excess thermodynamic properties of solutions with (a) zero excess heat capacity, (b) a moderately positive excess heat capacity, and (c) a large positive excess heat capacity.

capacity, ΔC_p^{EX} , is near zero, ΔG^{EX} will become increasingly less favorable with increasing temperature as the entropic contribution ($T\Delta S^{\text{EX}}$) becomes dominant, as illustrated in Figure 1a. However, our simulations have shown that ΔH^{EX} and ΔS^{EX} depend on the extent of ether–water hydrogen bonding, the structuring of water hydrating the ether, and the cohesive energy density of the solvent,¹⁰ all of which may change with temperature. Therefore, it is possible that ΔH^{EX} and ΔS^{EX} are moderately to strongly temperature-dependent in PEO/water solutions and hence a moderately positive ΔC_p^{EX} could lead to an enthalpy-driven decrease in the favorable ΔG^{EX} with increasing temperature as illustrated in Figure 1b. This behavior is predicted by the models of Karlström⁶ and Dormidontova.⁷

Recently, we have shown that the conformations, hydrogen bonding, and structure of hydrating water are nearly identical in DME and PEO solutions.¹⁰ Therefore, in this work, we have extended our recent MD simulations of DME/water solutions to address the temperature and concentration dependence of ΔG^{EX} , ΔH^{EX} , and ΔS^{EX} in aqueous PEO solutions. We have also determined the contributions of solvent–solvent (ΔE_{ss}) and ether–solvent (ΔE_{es}) interactions to ΔH^{EX} . ΔE_{ss} is the change in the interaction energy between solvent molecules in the solution relative to the solvent that results from dissolution of a DME molecule, while ΔE_{es} is the direct interaction energy of the solvent with the added ether in solution. ΔE_{es} can be determined directly from the simulations as the ensemble average solute–solvent energy, while ΔE_{ss} is given as $\Delta E_{\text{ss}} = \sigma(\text{solution}) - \sigma(\text{solvent}) - \Delta E_{\text{es}}$, where σ is the cohesive (total intermolecular nonbonded) energy of a system.

The simulation methodology and quantum chemistry based potentials employed are described fully in our recent work.^{8,10–12} Specifically, we have investigated the thermodynamics of

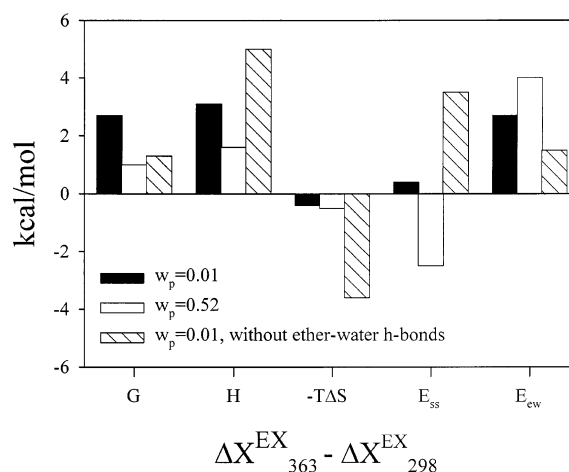


Figure 2. Temperature dependence of excess thermodynamic properties of DME/water solutions.

solvation of (a) a DME molecule in 500 water molecules ($w_p = 0.01$) at 298 K (previous work) and 363 K and (b) a DME molecule in a mixture of 128 water and 27 DME ($w_p = 0.52$) at 298 and 363 K, where w_p denotes the weight fraction of ether in the solution. The choice of compositions is motivated by our simulations of PEO/water solutions that show PEO conformations, the extent of ether–water hydrogen bonding, and the hydration of PEO to be only weakly dependent on composition for $w_p < 0.5$.^{10,12} Solvation thermodynamics in this composition range, which lies inside the miscibility gap at higher temperatures,⁹ can therefore be studied by performing simulation of dilute solutions. For $w_p > 0.5$, PEO and water are miscible at all temperatures.⁹ Here, PEO conformations, the extent of ether–water hydrogen bonding, and water clustering are strongly composition-dependent.¹²

The pertinent excess thermodynamic properties for the DME/water solutions determined from simulations are given in Table 1. The change in excess properties with increasing temperature is shown in Figure 2. ΔG^{EX} becomes less favorable with increasing temperature, consistent with the experimentally observed LCST behavior in PEO/water solutions, as well as the predictions of theoretical models.^{5–7} The effect is significantly greater for $w_p = 0.01$, representative of solutions in the miscibility gap, compared to $w_p = 0.52$. The weaker temperature dependence of ΔG^{EX} for $w_p = 0.52$ is consistent with continued miscibility of PEO/water solutions for compositions $w_p > 0.5$ at higher temperatures. Table 1 and Figure 2 reveal that $T\Delta S^{\text{EX}}$ becomes *more* favorable with increasing temperature for both compositions indicating that unfavorable entropic effects *are not* responsible for the LCST behavior of PEO/water solutions as suggested by Kjellander.⁵ This is consistent with our earlier observation that PEO is not commensurate with the structure of liquid water in any conformation¹³ as suggested in the Kjellander model.

The temperature dependence of ΔS^{EX} in dilute solution (Table 1) indicates that the entropy penalty for dissolving PEO in aqueous solution decreases significantly with increasing temperature, in qualitative agreement¹⁴ with predictions of the Karlström and Dormidontova models applied to PEO oligomer solutions. Figure 2 reveals that the increasingly unfavorable interaction of PEO with water at higher temperatures is *enthalpy*-driven. The enthalpy of solvation of DME in dilute solution is dramatically less favorable at 363 K compared to that at 298 K, again in qualitative agreement with the models of Karlström and Dormidontova. A much weaker effect is seen for $w_p = 0.52$. For both compositions, ether–water interactions become sig-

nificantly less favorable with increasing temperature, consistent with a dramatic decrease in ether–water hydrogen bonding.¹² In the model of Karlström, the increasingly unfavorable nature of ether–water interactions in PEO/water solutions with increasing temperature is associated with an increasingly large fraction of hydrophobic conformers, which also leads to an increase in configurational entropy. We have recently shown that solvation effects associated with the temperature dependence of PEO conformations and their difference in hydrophobicity are insignificant compared to effects associated with ether–water and water–water hydrogen bonding, as well as structuring of hydrating water.¹⁰ In contrast to the model of Karlström, the model of Dormidontova explicitly includes temperature-dependent ether–water hydrogen bonding, the destruction of which with increasing temperature leads to unfavorable enthalpic and favorable entropic contributions to ΔG^{EX} , in qualitative agreement with our simulations.

The solvent–solvent interactions disrupted by insertion of the ether are weaker at higher temperatures (the cohesive energy density is lower) for both compositions investigated. Countering this effect, which promotes relatively favorable solvent–solvent interactions at higher temperatures, i.e., a negative value for ΔE_{ss} , is an increase in the partial molar volume of DME with increasing temperature, resulting in perturbation of more solvent (i.e., breakup of more solvent–solvent interactions). The increase in DME partial molar volume in going from 298 to 363 K is greater for the dilute solution (18% vs 8% for $w_p = 0.52$), and the decrease in the cohesive energy density over the same temperature range is smaller for the dilute solution (14% vs 26% for $w_p = 0.52$), the latter being due to slower disruption of water–water hydrogen bonds with increasing temperature compared to ether–water hydrogen bonds.¹² As a result, the change in water–water energy upon adding DME to pure water is essentially independent of temperature (see Figure 2), while for the $w_p = 0.52$ solution the solvent–solvent interaction is less perturbed (and hence relatively favorable) upon addition of a DME molecule at 363 K compared to 298 K.

Finally, as in our previous work,¹⁰ we performed simulations of dilute DME/water solutions for a DME molecule that does not form hydrogen bonds with water as the result of introduction of a repulsive interaction between ether oxygen atoms and water hydrogen atoms. Table 1 shows that the non-hydrogen-bonding ether has a much less favorable ΔG^{EX} compared to the fully interacting ether, as expected. Figure 2 reveals that the change in ΔH^{EX} and $T\Delta S^{\text{EX}}$ with increasing temperature are much larger in the non-hydrogen-bonding DME/water solution compared to the fully interacting DME/water solution. The net result is a much smaller increase in ΔG^{EX} with increasing temperature compared to the fully interacting DME/water solution as the strongly structured (entropically unfavorable) hydrating water in the non-hydrogen-bonding solution becomes significantly less structured. This behavior corresponds to a large ΔC_p^{EX} , as illustrated in Figure 1c. Hence, while ether–water hydrogen bonds are responsible for the solubility of PEO at lower

temperatures, they also lead to a much stronger increase in ΔG^{EX} with increasing temperature than is found in the equivalent system without ether–water hydrogen bonds because of much smaller gains in entropy.

In conclusion, detailed analysis of the temperature and composition dependence of the excess thermodynamic properties of DME/water solutions obtained from MD simulations is consistent with an LCST in PEO/water solutions that is enthalpy-driven. At lower temperatures, the formation of ether–water hydrogen bonds results in a very favorable ΔG^{EX} consistent with the solubility of PEO and water. For solution compositions in the miscibility gap, increasing temperature leads to a dramatic reduction in favorable ether–water interactions due to break-up of ether–water hydrogen bonding, while relatively persistent water–water hydrogen bonding maintains the energetic penalty associated with disrupted water–water interactions upon insertion of the ether. The entropy gain associated with the break-up of ether–water hydrogen bonds and reduction in the structure of hydrating water with increasing temperature is insufficient to offset the unfavorable enthalpic effects associated with the destruction of the ether–water hydrogen bonds. In the miscible composition range, the increase in ΔG^{EX} with increasing temperature is much weaker than that in dilute solution. This is a consequence of weaker solvent–solvent interactions and a smaller increase in the partial molar volume of the ether with increasing temperature.

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