

Molecular Dynamics Simulations of 1,2-Dimethoxyethane in Aqueous Solution: Influence of the Water Potential

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We have performed molecular dynamics simulations of aqueous solutions of 1,2-dimethoxyethane (DME), an oligomer of poly(ethylene oxide), employing several potentials for water. Specifically, we investigated the structural, conformational, and dynamic properties of DME/water solutions as a function of composition using the TIP4P, MCY, SPC, and SPC/E potentials for water. DME/DME interactions were described using our previously derived quantum-chemistry-based potential, while the DME/water potential was parametrized for each water model to best represent the energy of a DME/water complex as determined from high-level quantum chemistry calculations. For dilute (water-rich) solutions, static and dynamic properties were found to depend only weakly on the water model employed. For more concentrated solutions, important differences between the models were observed, particularly in the structure of the solutions (e.g., the size of water clusters) and the self-diffusion coefficient of water.

Introduction

The development of classical potentials that can accurately describe the structural, thermodynamic, and dynamic properties of materials remains an important and challenging task. A salient example is water. Extant water potentials usually adequately describe some properties of pure water while at the same time providing much less satisfactory descriptions of other properties. Several comparisons of the predictions of different water models for the properties of pure water can be found in the literature.^{1–3} A perhaps more important, yet much less frequently addressed, issue is the influence of the water potential on the properties of aqueous solutions. In this paper we investigate the influence of the water potential on the properties of aqueous solutions of 1,2-dimethoxyethane (DME). DME is the shortest oligomer of poly(ethylene oxide), an important hydrophilic polymer. In our previous work⁴ we developed what we believe to be an accurate atomistic force field for DME/water solutions on the basis of high-level quantum chemistry calculations. Using the TIP4P model for water,⁵ we investigated structural,⁶ conformational,⁶ and dynamic⁷ properties of the solutions as a function of composition and temperature. In this work we use the same quantum chemistry data for DME/water interactions in order to parametrize DME/water models for SPC,⁸ SPC/E,⁹ and MCY¹⁰ water potentials. We have also reparametrized the DME/water potential for the TIP4P water model, yielding a slightly different description of the DME/water interactions from those in our previous work.⁴ This allows us to investigate the sensitivity of simulation results to the description of DME/water interactions. The importance of an accurate description of DME/water interactions was clearly demonstrated in our previous work⁴ where we found that DME/water potentials obtained by applying standard combining rules to the DME/DME and water/water potentials provide a completely inadequate description of DME/water interactions. Reported here are the conformational, structural, and dynamic properties of the DME/water solutions using the above-mentioned isotropic, nonpolarizable water models for five mole fractions of DME: $X_{\text{DME}} = 0.04$,

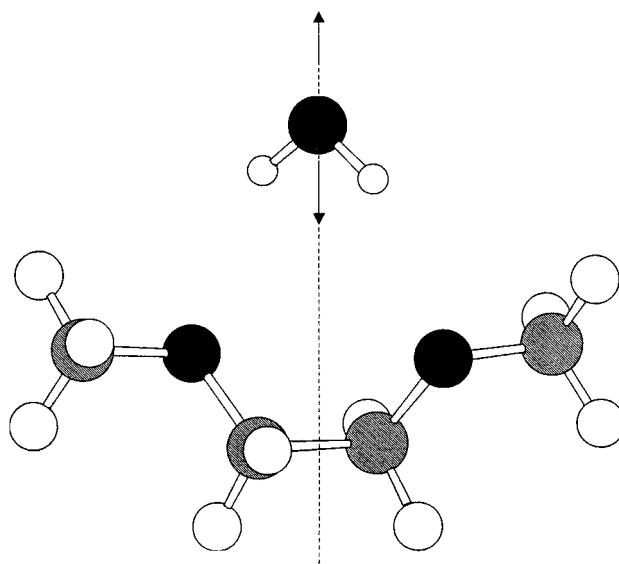


Figure 1. DME (tgt)/water complex geometry used in parametrization of the DME/water potential.

0.10, 0.18, 0.42, and 0.72 at 318 K. The influence of polarization on the solution properties will be the subject of a future manuscript.

Force Field Parametrization and Simulation Methodology. The quantum-chemistry-based intramolecular potential for DME and the DME/DME nonbonded potential are described in our earlier work.¹¹ For water/water interactions we employed the TIP4P, SPC, SPC/E, and MCY potentials as published. To parametrize the DME/water interactions, we calculated, in previous work,⁴ the MP2 level quantum chemistry binding energies of a DME/water complex, consisting of the tgt conformer of DME and a single water molecule, as a function of separation along the DME C_2 axis as illustrated in Figure 1. Details of the quantum chemistry calculations and the path description can be found in ref 4. Coulomb interactions are

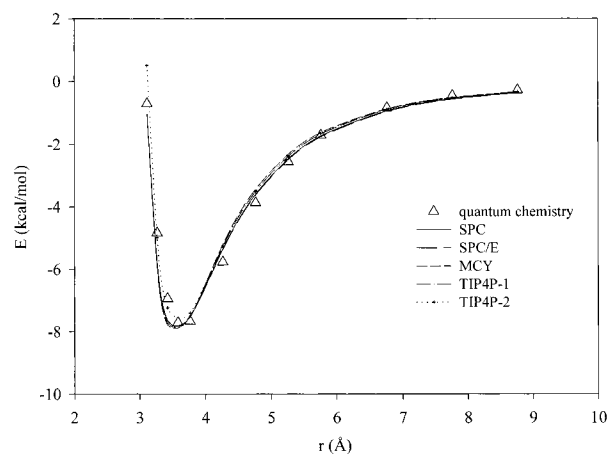


Figure 2. Binding energy of DME (tgt) and water as a function of separation along the DME C_2 axis.

TABLE 1: Lennard-Jones Parameters for DME/Water Interaction

water model	W-C		W-O		W-H	
	ϵ kcal/mol	σ Å	ϵ kcal/mol	σ Å	ϵ kcal/mol	σ Å
TIP4P-1	0.2526	3.2317	0.3665	2.9387	0.0811	3.0158
SPC	0.2335	3.2429	0.3389	2.9488	0.0750	3.0263
SPC/E	0.2065	3.2817	0.2996	2.9842	0.0663	3.0625
TIP4P-2	0.2405	3.2665	0.3490	2.9704	0.0772	3.0484

determined by the partial charges of DME and water and therefore are established for any particular water model. If we use a Lennard-Jones description for the repulsion/dispersion interactions between DME and water, we must establish the values of the six unknown nonbonded force field parameters ϵ_{C-W} , σ_{C-W} , ϵ_{O-W} , σ_{O-W} , ϵ_{H-W} , and σ_{H-W} employed in the expression

$$E_{i-w} = 4\epsilon_{i-w}[(\sigma_{i-w}/r_{i-w})^{12} - (\sigma_{i-w}/r_{i-w})^6] \quad (1)$$

where i = carbon, hydrogen, or oxygen (DME) and r_{i-w} is the separation between an atom comprising DME and the water nonbonded force center (oxygen atom). In this representation, the parameter ϵ gives the energy of maximum attraction for a given pair, and σ gives the separation at the point of zero energy. To reduce the number of unknown force field parameters, we have taken the following approach. We obtained initial values for the six parameters using standard geometric mean combining rules:

$$\epsilon_{i-w}^0 = \sqrt{\epsilon_{i-i}\epsilon_{w-w}} \quad \text{and} \quad \sigma_{i-w}^0 = \sqrt{\sigma_{i-i}\sigma_{w-w}} \quad (2)$$

We then adjusted the DME/water parameters according to

$$\epsilon_{i-w} = \alpha[\epsilon_{i-w}^0] \quad \text{and} \quad \sigma_{i-w} = \beta[\sigma_{i-w}^0] \quad (3)$$

yielding just two adjustable parameters, α and β . Values for α and β were fitted in order to reproduce the quantum chemistry binding energies. The details of the fitting procedure are described in ref 4. The resulting potentials are given in Table 1.

The description of the DME/water interaction along the quantum chemistry path is essentially indistinguishable for the four different water potentials, as can be seen in Figure 2. The DME/water potential for TIP4P water labeled TIP4P-1 differs slightly from the DME/water potential (labeled TIP4P-2) derived previously¹² and also shown in Figure 2. Note that the water/

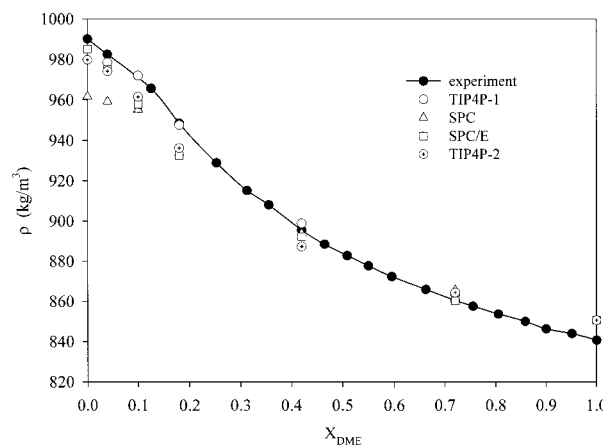


Figure 3. Density of DME/water solutions as a function of composition for various water models at 318 K.

water interaction for both TIP4P models is the same; only the interaction of water with DME differs slightly.

After parametrization of the DME/water potentials, we performed molecular dynamics (MD) simulations of DME/water solutions for five compositions with mole fractions $X_{DME} = 0.04$, 0.10, 0.18, 0.42, and 0.72 at 318 K. All systems were initially equilibrated for 1.0 ns. Constant pressure/constant temperature simulations were performed over 0.4 ns in order to establish the equilibrium density at atmospheric pressure. All reported properties were averaged over 1.5 ns at constant temperature and volume. Periodic boundary conditions were employed. The standard Shake algorithm¹³ was used to constrain the bond lengths, while all other degrees of freedom remained flexible. The Ewald summation method¹⁴ was employed to handle long-range electrostatic interactions.

Results and Discussion

Thermodynamic Properties. In Figure 3 we compare the solution densities obtained from *NPT* MD simulations with experiment¹⁵ for four water models as a function of composition. All models yield a similar description of the density, with the exception of the SPC model, which underestimates the solution density in the water-rich regime. The failure of the SPC model to accurately predict the density of liquid water is known from previous simulations.⁸ It is also known that the MCY water model does an even poorer job describing *PVT* behavior of liquid water.¹⁶ We found it impossible to obtain reasonable densities for the DME/MCY water solutions in the *NPT* ensemble. Therefore, we used densities obtained from the DME/TIP4P-1 solution simulations and performed *NVT* simulations of the DME/MCY solutions at these densities.

Figure 4 shows the excess volume for DME/water solutions as a function of composition. The excess volume is much more sensitive to the choice of water model than the solution density. By comparison of the excess volume for the TIP4P-1 and TIP4P-2 models, which have identical DME/DME and water/water interactions and differ only slightly in their description of DME/water interactions, it can be seen that the excess volume is quite sensitive to minor changes in the description of the DME/water interactions. The excess volume is also quite sensitive to the ability of the potential to describe the densities of the pure DME and water phases. Therefore, the excess volume should not be used for the *quantitative* evaluation of the accuracy of a potential unless the description of the pure phases is quite accurate. Nevertheless, a qualitative comparison

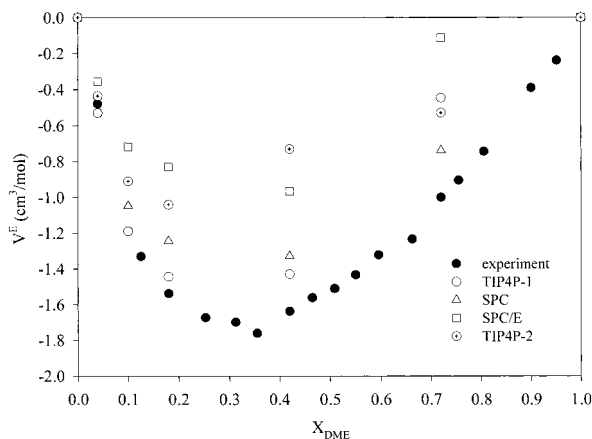


Figure 4. Excess volume of DME/water solutions as a function of composition for various water models at 318 K.

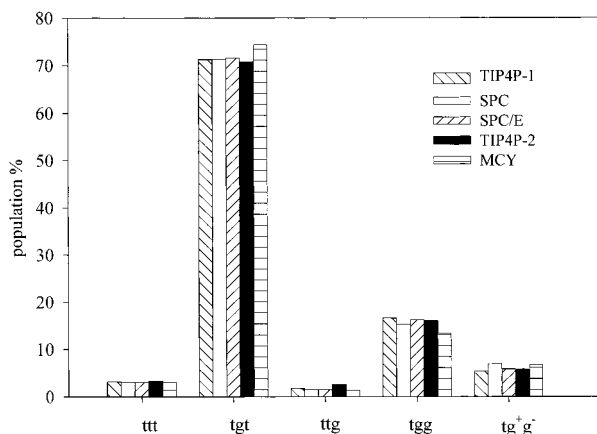


Figure 5. Population of major DME conformers for various water models at composition $X_{\text{DME}} = 0.04$.

of the excess volume obtained from simulation using various models with experimental data is quite useful. It can be seen from Figure 4 that for all water models the composition dependence of the excess volume is qualitatively consistent with experiment,¹⁵ each showing a minimum at $X_{\text{DME}} \approx 0.30$. Compared to the TIP4P-1 model, which provides the best description of the excess volume, the SPC/E and the TIP4P-2 models predict a much lower (less negative) excess volume. For the SPC/E model, this difference is due primarily to stronger water/water interactions. Evidence for stronger water/water interaction in the SPC/E model can be seen directly in the $\text{O}_w\text{--H}_w$ and $\text{O}_w\text{--O}_w$ pair distribution functions for pure water¹ and is further discussed below. For the TIP4P-2 model, the lower excess volume is the result of weaker DME/water interactions (see Figure 2).

Conformational Populations. Figures 5 and 6 show DME conformational populations for the important conformers for $X_{\text{DME}} = 0.04$ and 0.18 , respectively. For the more dilute solution ($X_{\text{DME}} = 0.04$) the conformer population distribution is almost identical for all water models employed except for the system with MCY water. We believe that in this composition range the conformer populations are determined by polar (dipole/dipole) interactions between the DME molecule and neighboring water molecules and polar interactions between the water molecules comprising the first hydration shell around the DME molecule. The importance of these interactions was emphasized in our previous work.^{6,17} As all investigated water models yield a similar local structure for pure water,¹ we would expect little dependence of the conformational populations of DME on the water model in the dilute regime, consistent with our simulation

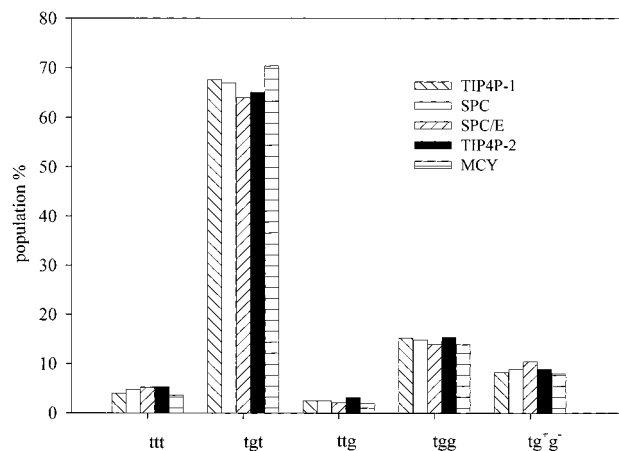


Figure 6. Population of major DME conformers for various water models at composition $X_{\text{DME}} = 0.18$.

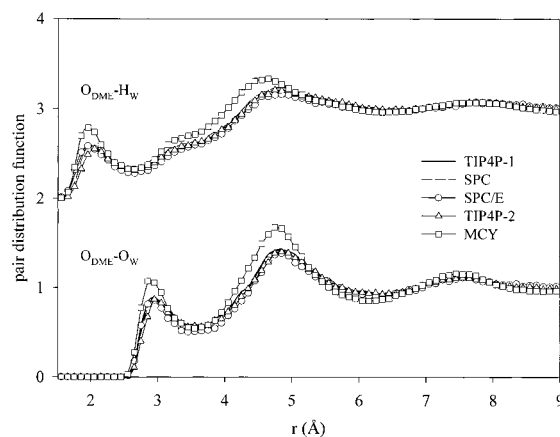


Figure 7. $\text{O}_{\text{DME}}\text{--O}_w$ and $\text{O}_{\text{DME}}\text{--H}_w$ pair distribution functions as a function of separation for various water models for composition $X_{\text{DME}} = 0.04$. The $\text{O}_{\text{DME}}\text{--H}_w$ pair distribution functions have been offset by 2.

results. The exceptional conformational populations for the DME/MCY systems are due to significant difference in the structure of local hydration of DME molecules. More pronounced differences in the conformer populations for all systems can be observed for the more concentrated solutions (Figure 6). In this composition regime individual water molecules begin to interact strongly with several DME molecules simultaneously and water no longer reacts to the DME molecules as a waterlike medium. Consequently, differences in water/water and water/DME interactions between the various models are manifested and result in DME conformer populations that are somewhat model-dependent. Specifically, compared to the other models, the SPC/E model predict a lower fraction of hydrophilic ($\text{tgt} + \text{tgg}$)⁶ conformers, consistent with the stronger water/water interactions inherent in the SPC/E model.

Structure: DME/Water Correlations. Analysis of the pair distribution functions for DME/water correlations ($\text{O}_{\text{DME}}\text{--H}_w$ and $\text{O}_{\text{DME}}\text{--O}_w$), shown in Figure 7 for $X_{\text{DME}} = 0.04$, reveals that for the more dilute solutions the local structure of water around a DME molecule is almost indistinguishable for the TIP4P-1, TIP4P-2, SPC, and SPC/E water potentials. This is consistent with the independence of the DME conformational populations on water model for dilute solutions found using these water models, as discussed above. The pair distribution functions reveal that DME/water interactions in the DME/MCY solutions are significantly stronger, *relative to water/water interactions*, in comparison to those found in other water models.

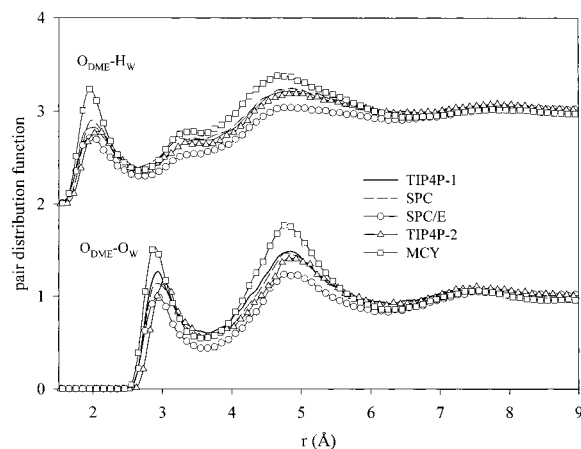


Figure 8. $O_{DME}-O_W$ and $O_{DME}-H_W$ pair distribution functions as a function of separation for various water models for composition $X_{DME} = 0.18$. The $O_{DME}-H_W$ pair distribution functions have been offset by 2.

Weak water/water interactions in the MCY potential have been noted in previous simulations using this model.¹⁸ The strength of the water/water interaction in MCY water is underestimated to such an extent that even in dilute DME/water solutions, qualitative differences between this model and the other water models investigated can be seen, including significantly enhanced DME/water hydrogen-bonding. The same radial distribution functions for the more concentrated $X_{DME} = 0.18$ solutions show more pronounced dependence on the water model employed as shown in Figure 8. The SPC/E water model in particular shows a systematically lower probability for finding a water molecule within the first hydration shell of a DME molecule (within 7 Å of a DME oxygen atom). In addition, while hydrogen bonding between DME and water is essentially independent of the water model for $X_{DME} = 0.04$, it is noticeably dependent on the water model for the more concentrated solution. For $X_{DME} = 0.18$, the SPC/E model yields 0.86 hydrogen bonds/DME oxygen while the other models yield 0.96 hydrogen bonds/DME oxygen.¹⁹ The behavior of the SPC/E model for the more concentrated solutions can be interpreted as being due to an intrinsically stronger water/water interaction than for the TIP4P and SPC models. Comparing the TIP4P-1 and TIP4P-2 models, the slightly weaker DME/water interaction in the latter model results in a shift of the first peaks in the $O_{DME}-H_W$ and $O_{DME}-O_W$ pair distribution functions to slightly greater distances. Interestingly, the number of hydrogen bonds/DME oxygen is nearly identical for the TIP4P-1 and TIP4P-2 models.

Structure: Water/Water Correlations. The tendency of water molecules to form clusters in DME/water solutions is illustrated in Figure 9, where the ratio of the local water density (water coordination number per unit volume in a sphere of radius r from a given water molecule) to the bulk solution density of water is shown for $X_{DME} = 0.72$ and $X_{DME} = 0.18$. The effect is more pronounced for the more concentrated solution.⁶ The “clusterization” of water is most pronounced for the SPC/E model and is a result of the stronger water/water interactions for this model compared to the other models investigated. The MCY water molecules show the weakest tendency to form clusters, consistent with underestimation of water/water interactions relative to DME/water interactions in this system, as discussed above. By comparison of the TIP4P-1 and TIP4P-2 models, the stronger DME/water interaction in the former model results in less clusterization of water.

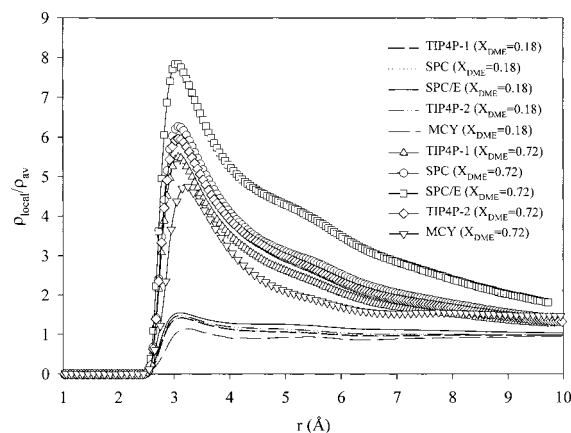


Figure 9. Ratio of the local density of water to the bulk density of water for various water models for $X_{DME} = 0.18$ and $X_{DME} = 0.72$.

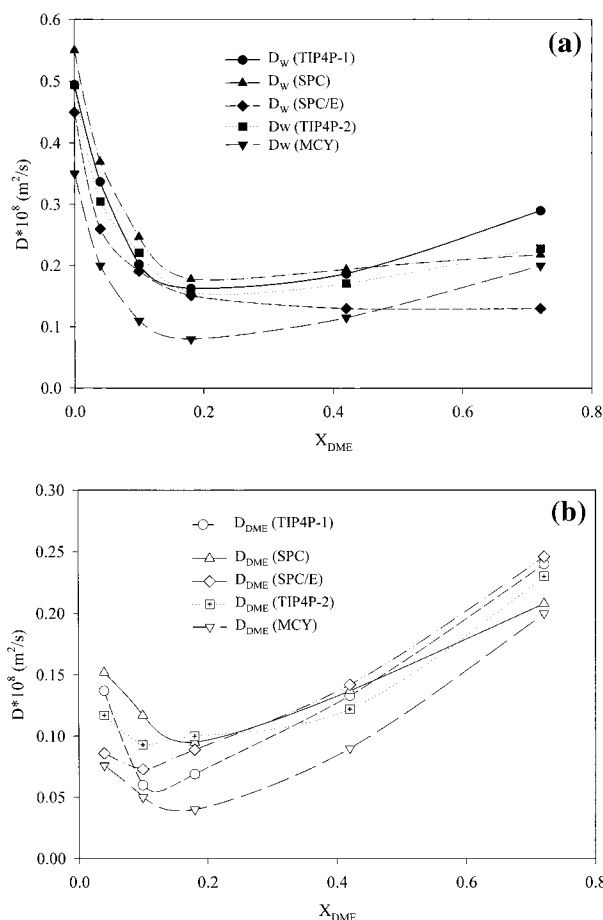


Figure 10. Self-diffusion coefficients of water (a) and DME (b) for various water models as a function of solution composition. Lines are for guiding the eye.

Self-Diffusion. We also investigated the influence of the water potential on the self-diffusion of both DME and water in DME/water solutions. In parts a and b of Figure 10 we show the diffusion coefficients for water and DME as a function of solution composition, respectively. For all models, the self-diffusion of water dramatically drops with increasing DME concentration, reaching a minimum at $X_{DME} \approx 0.20$, as reported previously.⁷ The differences in the water self-diffusion coefficient for the various water models for $X_{DME} \leq 0.20$ primarily reflect the different values for the diffusion of pure water yielded by the models. For the SPC, TIP4P-1, TIP4P-2, and MCY models, the water self-diffusion coefficient increases monotonically with increasing DME concentration.

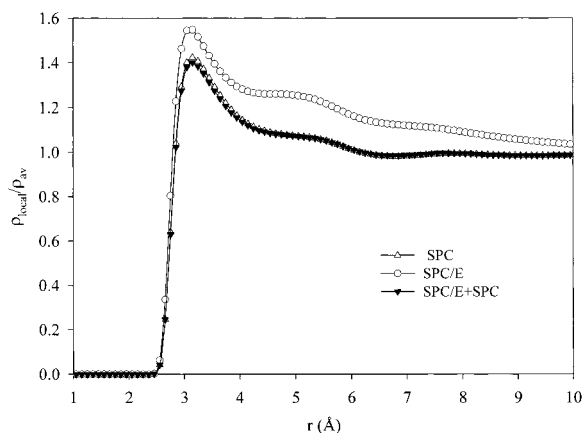


Figure 11. Ratio of the local density of water to the bulk density of water for SPC, SPC/E, and a combined SPC/E + SPC potential for $X_{\text{DME}} = 0.18$.

cally with increasing DME concentration for $X_{\text{DME}} > 0.20$. For SPC/E water, the behavior of the water self-diffusion coefficient differs qualitatively from that observed for the other models. Unlike the other models, the water self-diffusion coefficient does not increase with increasing DME concentration and therefore does not show a minimum at $X_{\text{DME}} \approx 0.20$. In the DME-rich regime the self-diffusion coefficient of water is less than that for DME for the SPC/E model. This behavior can be explained by the fact that clusters formed by SPC/E water molecules are larger than those for the SPC, TIP4P-1, TIP4P-2, and MCY water molecules in the DME-rich solutions (see Figure 9), resulting in a continued decrease in water mobility with increasing DME concentration. The changes in the DME self-diffusion coefficient with composition are less dramatic but qualitatively demonstrate the same features as seen for water with the SPC, TIP4P-1, TIP4P-2, and MCY models. There is a shallow minimum in the DME self-diffusion coefficient in the range $X_{\text{DME}} = 0.1\text{--}0.2$ and an almost linear increase for compositions $X_{\text{DME}} > 0.2$ for all models.

Influence of DME/Water Interactions. We have demonstrated that the properties of DME/water solutions investigated in this work (conformational properties, local structure, and self-diffusion) are sensitive to the water model employed. Implicit in our association of these effects with differences in water–water interactions is the assumption that the water/DME interactions are identical for the various water models employed. In Figure 2, the DME/water interaction for the different water models are indistinguishable for the DME/water configurations investigated (a single path). However, this correspondence does not unambiguously establish that the DME/water interactions are identical for all important configurations. To estimate the relative importance of differences in water/water and water/DME interactions, we have performed simulations of a system with a DME-SPC/E description of the DME/water interaction and an SPC description of water/water interactions. The SPC and SPC/E models have the same geometry and Lennard-Jones parameters and differ only by the atomic partial charges. In Figure 11 we show the ratio of local water density to average water density (as in Figure 9) for systems with SPC only, SPC/E only, and combined SPC (water/water) and SPC/E (water/DME) potentials for $X_{\text{DME}} = 0.18$. It can be clearly seen that for the combined system the formation of water clusters is nearly indistinguishable from that for the SPC potential. This supports our supposition that the description of DME/water interactions is quite similar for SPC and SPC/E water models and any differences do not significantly influence properties. Conversely,

the SPC/E model results in a much greater tendency to form water clusters than the combined potential. As the only difference in these models is the water/water interaction, this effect can with certainty be assigned to stronger water/water interactions in the SPC/E potential.

Conclusions

The dependence of the properties of DME/water solutions on the particular water model employed was found to be a function of the solution composition. In the water-rich regime (dilute solutions) structural and conformational properties were found to be nearly independent of the water model. Thermodynamic and dynamic properties showed qualitatively the same composition dependence for all water models in this regime and depend quantitatively upon the properties of pure water. We believe that in this composition range the structural properties of the solution and the conformational properties of DME are determined by the overall characteristics of the medium, which are quite similar to those of pure water and are described similarly by each of the discussed water models (excluding MCY). In the more concentrated solutions, water molecules interaction with several DME molecules simultaneously and differences in the description of water/water and water/DME interactions between the various models become important. The SPC/E model, which involves stronger water/water interactions than the other models studied, differs qualitatively in its prediction of the self-diffusion coefficient of water and in the structure of more concentrated DME/water solutions (e.g., the degree of clusterization of water) from those of other models. The TIP4P-2 model, which has weaker DME/water interactions than the TIP4P-1 model, yields a lower (less negative) excess volume and greater water clusterization in concentrated solutions than the latter model. On the basis of available experimental data, it is not possible to conclude definitively which of the studied water models provides the best description of DME/water solutions. We believe that accurate experimental measurements of the water and DME self-diffusion coefficients and the static structure factor as a function of solution composition would be invaluable in making this important determination.

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References and Notes

- (1) Watanabe, K.; Klein, M. L. *Chem. Phys.* **1989**, *131*, 157.
- (2) Wallqvist, A.; Berne, B. J. *J. Phys. Chem.* **1993**, *97*, 13841.
- (3) Kiyohara, K.; Gubbins, K. E.; Panagiotopoulos, A. Z. *Mol. Phys.* **1998**, *94*, 803.
- (4) Bedrov, D.; Pekny, M.; Smith, G. D. *J. Phys. Chem. B* **1998**, *102*, 996.
- (5) Jorgensen, W. L.; Chandrasekhar, J.; Madura, J. D.; Impey, R. W.; Klein, M. J. *Chem. Phys.* **1983**, *79*, 926.
- (6) Bedrov, D.; Borodin, O.; Smith, G. D. *J. Phys. Chem. B* **1998**, *102*, 5683.
- (7) Bedrov, D.; Borodin, O.; Smith, G. D. *J. Phys. Chem. B*, in press.
- (8) Berendsen, H. J.; Postma, J. P. M.; van Gunsteren, W. F.; Hermans, J. In *Intermolecular Forces*; Reidel: Dordrecht, 1981.
- (9) Berendsen, H. J.; Grigera, J. R.; Straatsma, T. P. *J. Phys. Chem.* **1987**, *91*, 6269.
- (10) Matsuoka, O.; Clementi, E.; Yoshimine, M. *J. Chem. Phys.* **1976**, *64*, 1351.
- (11) Jaffe, R. L.; Smith, G. D.; Yoon, D. Y. *J. Phys. Chem.* **1993**, *97*, 12752.
- (12) The TIP4P-2 potential is described in ref 4. After publication of ref 4, we discovered an error in our calculation of the excess volume for

DME/water solutions. As a consequence, we have reweighted the quantum chemistry data in fitting the DME/water potentials to give a slightly increased attraction between DME and water. This yields an improved description of the excess volume for the TIP4P-2 model as shown in Figure 4.

(13) Ryckaert, J.; Ciccotti, G.; Berendsen, H. J. C. *J. Comput. Phys.* **1977**, 23, 327.

(14) Allen, M. P.; Tildesley, D. T. *Computer Simulation of Liquids*; Oxford: New York, 1987.

(15) Das, B.; Roy, M. N.; Hazra, D. K. *Indian J. Chem. Technol.* **1994**, 1, 93.

(16) Mezei, M.; Beveridge, D. L. *J. Chem. Phys.* **1982**, 76, 593.

(17) Bedrov, D.; Smith, G. D. *J. Chem. Phys.* **1998**, 109, 8118.

(18) Lie, G. C.; Clementi, E.; Yoshimine, M. *J. Chem. Phys.* **1976**, 64, 2314.

(19) The number of hydrogen bonds per ether oxygen was determined by integrating the $\text{O}_{\text{DME}}\text{--H}_{\text{w}}$ pair distribution function from $r = 0 \text{ \AA}$ to $r = 2.7 \text{ \AA}$.