Local Structural Order and Molecular Associations in Water–DMSO Mixtures. Molecular Dynamics Study

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Abstract: Pure dimethyl sulfoxide (DMSO) and water–DMSO mixtures at three concentrations (x_{DMSO} = 0.005, 0.04, and 0.2) are studied using molecular dynamics simulations. Structural properties of water in different regions of DMSO hydration are investigated by using radial distribution functions (RDF), hydrogen-bonded network parameters, and the statistical geometry approach. Reliability of RDF as indicators of structure changes at different concentrations is discussed. Enhancement of the water structure at the lowest DMSO concentration and its breakdown at x_{DMSO} = 0.04 and 0.2 is observed. Structural effects in water–DMSO mixtures are attributed to the prevailing influence of the DMSO polar group on the water structure. It is found that the complex consisting of 1 DMSO and 2 water molecules hydrogen bonded to the DMSO oxygen exists at all studied concentrations. Local order in pure DMSO is determined by dipolar forces as well as molecular association. Both components in water–DMSO mixture are tending to preserve their structural order upon dilution. All simulation results are compared with numerous experimental data. A good agreement is found in most cases.

Introduction

The interaction between components in a mixture of associated liquids often determines their behavior in a wide range of chemical and biological processes. The aqueous solutions of DMSO ($(CH_3)_2SO$) are of special interest in view of their unique biological and physicochemical properties.[1]

DMSO is a polyfunctional molecule with a highly polar S=O group and two hydrophobic CH_3 groups. Its polar site can interact with water forming strong hydrogen bonds, and its nonpolar sites can cause effects of hydrophobic hydration and hydrophobic association of DMSO molecules.

DMSO and its aqueous solutions are among the most important solvents in the organic chemistry and fine chemical technology.[2] Due to its associative character, the aqueous solution of DMSO displays a strong non-ideal behavior revealed in a number of physical properties.[3] For example, extreme deviations from additivity are observed for such properties as density,[4] viscosity,[5] adiabatic and isothermal compressibility,[6] relative dielectric permittivity,[7] surface tension,[7,8] and others.

As a solvent, the water–DMSO mixture influences microscopic dynamics of solvated ions[9,10] and dye molecules[11,12] so that these solutes exhibit a qualitatively different behavior compared to the behavior in other solvents. A distinct curvilinear dependence of the solute orientational relaxation time on the viscosity of the water–DMSO mixed solvent cannot be explained by hydrodynamic or dielectric friction mechanisms.

Biological properties of DMSO are particularly important. DMSO is a widely used cryoprotectant for biological structures such as membranes and proteins.[13] The pharmacological potential of DMSO includes but is not limited to anti-inflammation effect, nerve blockade (analgesia), anti-viral and anti-bacterial activity, radioprotection abilities, membrane penetration, and transport.[1,14] Although these effects are well-known and extensively studied, the mechanism by which they arise is still poorly understood.

In recent years DMSO and the water–DMSO system have been investigated by a wide variety of experimental techniques, including X-ray and neutron diffraction measurements[15,16] and optical,[17-21] acoustic,[6,22,23] NMR,[24-29,87] and dielectric[30-33] spectroscopies. But the computer simulation technique, which is now recognized to be among the most powerful tools used for microscopic studies of the structural and dynamical phenomena occurring in solutions, was hardly employed in the studies of systems containing DMSO.

A first attempt to perform model calculations on the solvation of alkali halides in DMSO was made by Kruus and co-workers as early as the mid-seventies.[34,35] Energy minimization was performed on a cluster of 2 ions and 16 DMSO molecules. Calculated solvent vaporization energy and ion solvation energies were in qualitative agreement with experimental data. However,

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Table I. Parameters of Molecular Geometry of DMSO[a]

	ND/L[15]	XR/L[15]	MW/L[30]	MM/G[43]	XR/L[39]	XR/S[41]	XR/S[42]	XR/L[40]
r_{SO}, nm	0.1496	0.1450	0.1485	0.1480	0.1496	0.1471	0.1531	0.1500
r_{SC}, nm	0.1800	0.1765	0.1799	0.1809	0.1805	0.1801	0.1725	0.1800
∠OSC, deg	107.2	107.0	106.7	108.1	107.0	107.2	106.7	107.7
∠CSC, deg	99.2	109.5	96.6	96.9	100.4	97.9	97.4	97.7

[a] Abbreviations for method of study and phase of substance: ND, neutron diffraction; XR, X-ray; MM, molecular mechanics; MW, microwave spectroscopy; S, solid; L, liquid; G, gaseous.

Table II. Atomic Charges in the DMSO Molecule (in es)

	ref						
	38	45	49	48	46	47	35
q_s	+0.139	+0.212	+0.596	+0.78	−0.08	−0.107	−0.099
q_o	−0.459	−0.281	−0.434		−0.30	−0.334	−0.339
q_{Me}	+0.160	+0.034	+0.136			+0.220	+0.219
q_c		−0.096				+0.35	+0.346
q_H		+0.043				−0.043	−0.042

the computer resources available at that time were not sufficient to perform extended calculations.

Conformational properties of DMSO were studied by an ab initio molecular orbital method, using various Gaussian basis sets.[36,37] The calculated asymmetric S–Me stretching potential indicates that a minor change in intermolecular interactions may cause considerable geometric distortions in the DMSO molecule, which also might be responsible for the unusual behavior of DMSO.

The first and only molecular dynamics simulation of DMSO known to us was reported recently by Rao and Singh.[38] The main goal of their work was the determination of relative differences in free energy of solvation between two different solutes in DMSO.

In the present paper, we emphasize the local structures observed in DMSO and water–DMSO mixtures, association between water and DMSO molecules, and the hydrogen bonded network properties in these systems.

Details of the Simulation

Molecular Models and Interaction Potentials. The DMSO molecule has a pyramidal shape, with an oxygen atom, a sulfur atom, and two methyl groups located at the apex positions. Geometry parameters of the DMSO molecule obtained in different studies are listed in Table I. There was a long-standing controversy in the literature[1] concerning the single or double bond nature of the S–O bond in sulfoxides and sulfones. However, as shown in Table I, the value for the S–O distance obtained from the most experiments is 0.149 ± 0.001 nm, which leads to a bond order of 1.55. The value of the S–O bond dipole moment is estimated to be 3.0 D.[44] This is lower than if the S–O bond would have a semipolar character and just slightly higher than if the bond would be covalent. Therefore, one may conclude that the doubly bonded covalent structure is the major contributor to the resonance hybrid. The correct description of the S–O bond in molecular simulation is particularly important, because this bond is mainly responsible for the intermolecular association in DMSO and its solutions. In the present work we used the molecular geometry parameters of DMSO that were obtained from the results of neutron diffraction study of liquid DMSO[15] (see column 1 in Table I).

Table III. Intermolecular Potential Parameters

	S	OD	CH_3	OW	HW
10^9A,[12] kJ/mol nm	14000	460.2	12680	2633	0
10^6C,[6] kJ/mol nm	6875	712.6	5823	2617	0
q, e	+0.139	−0.459	+0.160	−0.8476	+0.4238

Table IV. Simulation Parameters

	W	M1	M2	M3	D1	D2
n_{DMSO}		1	8	27	64	512
n_{WATER}	216	212	182	108		
ρ, g/cm^3	1.00	1.00	1.01	1.08	1.10	1.10
$r_{cut\text{-}off}$, nm	0.9	0.9	0.9	0.9	0.9	1.3

Another highly controversial issue related to the molecular model of DMSO is the distribution of atomic charges (Table II). While quantum chemical calculations that use an ab initio method with the 6-31G* basis set[38] and the CNDO/2 approximation of the SCF-LCAO-MO method[45] lead to qualitatively similar results (negative charge on the O atom, positive charge on the S atom), semiclassical calculations of charge distribution, which involve experimentally determined dipole moments and polarizabilities, lead to a small negative charge on the S atom.[35,46,47] Both types of charge distribution give reasonable values for the dipole moment. In the present simulations we use the atomic charges on DMSO that were obtained from the ab initio calculations[38] (see column 1 of Table II). In these calculations the sulfur is positively charged. This is in agreement with the only known to us experimental determination of the effective atomic charge in gaseous DMSO by means of X-ray photoelectron spectroscopy.[48] Analogous charge distribution with the positively charged sulfur atom in the disulfone molecule has been successfully tested in the MD simulation.[49] The charge on the oxygen atom (q_O = −0.46 e) is close to the one obtained in a different quantum-mechanical calculation[50] (q_O = −0.55 e) and the adequacy of this value was proved experimentally.[51] The chosen charge distribution results in the dipole moment value of 4.37 D and the angle of 21.6° between the dipole moment vector and the S–O bond. Experimental values[25] for the dipole moment and the angle are 3.96 D and 26.4°.

Intermolecular interactions in the system are described by the potential

$$V_{\alpha\beta} = A_{\alpha\beta}/r^{12} - C_{\alpha\beta}/r^6 + q_\alpha q_\beta/r \qquad (1)$$

where $A_{\alpha\alpha} = 4\epsilon_\alpha\sigma_\alpha{}^{12}$ and $C_{\alpha\alpha} = 4\epsilon_\alpha\sigma_\alpha{}^6$. The potential parameters for the DMSO–DMSO interactions were taken from the molecular mechanics force field.[43] The Lennard-Jones parameter σ for the sulfur atom is 0.356 nm, which is similar to the σ of 0.355 nm used in the Jorgensen OPLS model for disulfide molecules.[52] The

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Lennard-Jones parameter ϵ for sulfur in different force fields varies more than an order of magnitude between 0.08 and 1.05 kJ/mol. The low estimate was determined from the Slater–Kirkwood formula[53] using atomic polarizability, while the high one was obtained empirically.[52] The molecular mechanics value of 0.77 kJ/mol looks reasonable within this range. The methyl groups of DMSO are represented as united atoms in our simulation. The water–water potential is defined in terms of the SPC/E model for water.[54] Parameters for the DMSO–water interactions were obtained from the combination rules $A_{\alpha\beta} = (A_{\alpha\alpha}A_{\beta\beta})^{1/2}$ and $C_{\alpha\beta} = (C_{\alpha\alpha}C_{\beta\beta})^{1/2}$. These empirical combination rules are identical with those used by Jorgensen and his collaborators.[52] The potential parameters used in this work are listed in Table III.

Molecular Dynamics (MD) Calculations. We have carried out six MD calculations: one for pure water (W), two for pure DMSO (D1, D2), and three for water–DMSO mixtures (M1, M2, M3). All calculations were performed in a cubic box with the periodic boundary conditions in the NVT ensemble (Table IV).

The equations of motion were integrated with use of a leap-frog algorithm[55] with a time step of 2 fs. The temperature was kept constant by coupling to an external heat bath[56a] with a relaxation time constant of 0.1 ps. The SHAKE procedure[56b] was used to constrain the internal geometry of the DMSO and water molecules. A cutoff radius of 0.9 nm was applied to all interactions except in run D2 where the cutoff radius was 1.3 nm. Shifted force potential[57] has been employed to avoid truncation errors.

Run W was a standard 216 water molecules run. In run D1 the simulation box with the side length of 1.96 nm was created by placing 64 DMSO molecules at the vertices of a cubic lattice. The box length of 1.96 nm corresponds to an experimental density of DMSO at 298 K (1.1 g/cm^3). Then the system was equilibrated for 25 ps. To study the effect of the system size on the results we carried out another simulation of pure DMSO (D2). In this simulation a box of 512 DMSO molecules was created from 8 equilibrated boxes of 64 DMSO molecules. Then the system was equilibrated for another 10 ps. In runs M1, M2, and M3 the initial configurations were created by the insertion of 1 DMSO, 8 DMSO, and 27 DMSO molecules, respectively, into the box that contained the preliminary equilibrated system of 216 water molecules. In run M1 the DMSO molecule was placed in the center of the box. In runs M2 and M3 DMSO molecules were placed on the vertices of a regular cubic lattice, so that DMSO–DMSO average separation was approximately 0.9 and 0.6 nm, respectively. Water molecules at a distance less than 0.2 nm from any atom of DMSO were deleted. The resulting systems correspond to DMSO concentrations of 0.005 (M1), 0.04 (M2), and 0.2 (M3). The box size in every run was adjusted to get the experimental density of the corresponding solution. After insertion of solute molecules the system was equilibrated for 15 ps in each case. All runs were performed at $T = 298$ K and the length of each equilibrated run was 50 ps.

All systems preparations, MD runs, and data analysis were performed on IBM 3090 and Convex C-240 computers using the program package MODYS.[58]

Results

Water Structure and Association. The question about DMSO influence on water structure in water–DMSO mixtures engendered a number of different and often mutually exclusive answers.

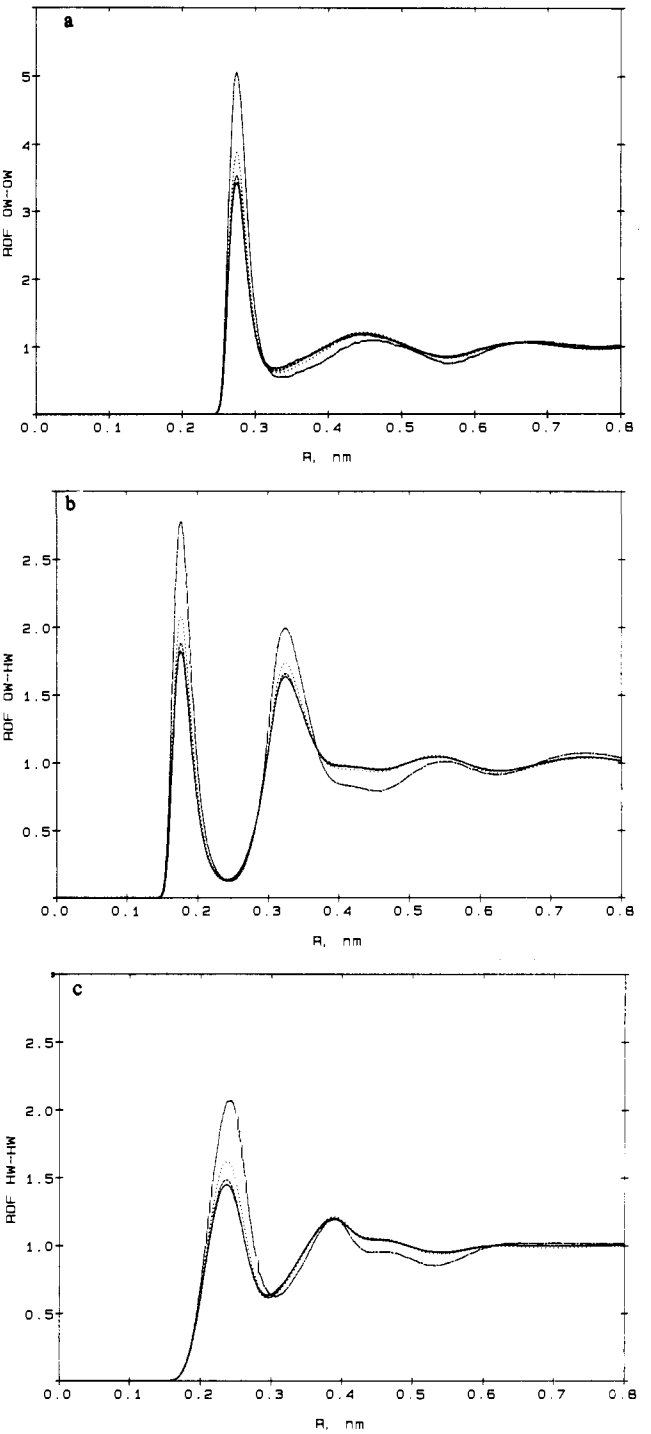

Figure 1. Plot of the water–water radial distribution functions (—, run W; - - -, run M1; ···, run M2; - · -, run M3).

Neutron inelastic scattering and X-ray diffraction studies[16] indicated that DMSO at its low concentrations produces a cooperative orientation of water molecules around each DMSO molecule, which has the effect of rigidifying the water structure. Analysis of partial molar enthalpies of solution[59] also led to the conclusion that DMSO behaves as a strong structure maker. Similar conclusions were drawn from the measurements of the spin–lattice relaxation times,[24,29] dielectric permittivities,[32] nuclear spin relaxation,[26] and proton relaxation.[28] At the same time infrared spectroscopy[17] as well as density and partial molar volume measurements[60] show that small amounts of DMSO have little

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or no effect on the water structure. Moreover, some experimental studies[20,61-63] have led to the conclusion that DMSO acts as a "structure breaker" in water.

MD simulation with its ability to determine different structural parameters directly is of great help in resolving this dispute. It is widely accepted that the best description of the liquid structure is given by the set of radial distribution functions.[64] The most important of the RDF's is the atom–atom pair correlation function $g(r)$, which in the molecular simulation is obtained from eq 2

$$g_{\alpha\beta}(r) = \frac{V_0}{N_\beta} \frac{N_\beta(r)}{4\pi r^2 \Delta r} \tag{2}$$

where N_β is the number of the β-th kind of particles in the volume V_0 of the simulation cell and $N_\beta(r)$ is the number of such particles in the spherical shell $(r, r + \Delta r)$ at distance r from a particle of type α.

Water–water RDF in both pure water and water–DMSO mixtures are displayed in Figure 1. All three atom-atom RDF of water have more pronounced peaks at higher DMSO concentrations. Exactly the same behavior of water RDF peaks as a function of the solute concentration was observed in MD simulations of aqueous solutions of significantly different species such as methanol,[65,66] *tert*-butyl alcohol,[67] acetonitrile,[68] quinuclidine,[69] acetone,[66] and ammonia.[66] In all these cases[65-69] the higher peak intensities in water–water and solute–water pair correlation functions were attributed to the enhancement of the water structure, i.e. the higher RDF peak means that water is more ordered in the respective environment. It was even suggested[68] that the extreme increase in the RDF intensity and molecular association of water could be explained partly by the fact that the water potential, having been parametrized for pure water, overestimates the molecular interactions and structural correlation in the diluted solutions. However, similar results obtained from works with various intermolecular potentials and various solutes indicate that there might be different reasons for this phenomenon.

While pair correlation function apparatus is very convenient and useful for the analysis of the liquid structure sensitivity to various physical parameters such as temperature, pressure, etc. at a permanent composition, one has to be very careful when the composition of the studied mixture is changing, especially if one or more components are associated liquids. Indeed, $g_{\alpha\beta}(r)$ which can be written as

$$g_{\alpha\beta}(r) = \rho_\beta(r)/\rho_{0_\beta} \tag{3}$$

reflects the relationship between the local density of a component β at a distance r from the central particle and the average density of a component β. Due to various types of associations between β molecules, the β component upon dilution tries to maintain the local order similar to the one in its pure liquid structure. This behavior of β molecules does not seem to be dependent on the α component. As a result when the β component content is decreasing, the fraction of β molecules which participates in the formation of the first and, sometimes, the second solvation shells around the central molecule decreases more slowly than the average fraction of β molecules in the solution. This leads to the increase of the $g(r)$ peak heights. But such an increase does not necessarily mean that the β component has a higher structural order. In fact comparing RDF in mixtures at different composition one can observe that higher RDF peaks could correspond to less ordered structures.

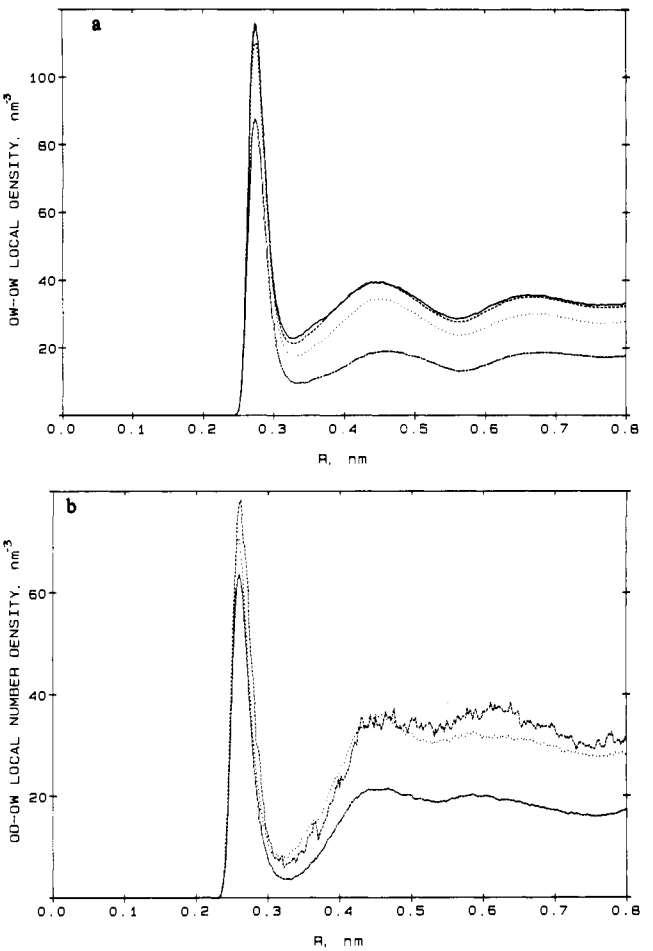

Figure 2. Plot of the oxygen local density around water oxygen (a) and DMSO oxygen (b) (lines as in Figure 1).

In order to get additional information about structural changes in the water–DMSO system we have calculated the radial distributions of atomic local densities. Water oxygen local densities around DMSO oxygen and water oxygen are shown in Figure 2. At the lowest DMSO concentration local densities of water oxygens in the first hydration shell of water are slightly higher than those in pure water. Further increase of DMSO concentration leads to the decrease of all the $\rho(r)$ peaks. This result is consistent with the observations made by Safford and co-workers.[16] In the X-ray diffraction studies, where RDF is defined as $4\pi r^2\rho(r)$, they found that a general sharpening of the water–water RDF peaks occurs on addition of small amounts of DMSO. At higher concentrations of DMSO a breakdown of the water structure was observed.[16] Similar results were obtained by Fox and Whittingham[20] using ultraviolet spectroscopy. They observed a sharp intensity maximum in the absorption spectra at 0.005 mol fraction of DMSO. This maximum arises from a relatively isolated DMSO molecule in an interstitial site and provides the evidence for hydrophobic hydration of DMSO. At concentrations higher than 0.01 mol fraction of DMSO the spectra show a breakdown of water structure.[20] A qualititatively similar picture was also produced by Werblan and Lesinski in their measurements of phase velocities of ultrasonic waves in water–DMSO mixtures.[70] They suggested that the water structure becomes more rigid up to 0.1 mol fraction of DMSO. Then they observed a slight loosening

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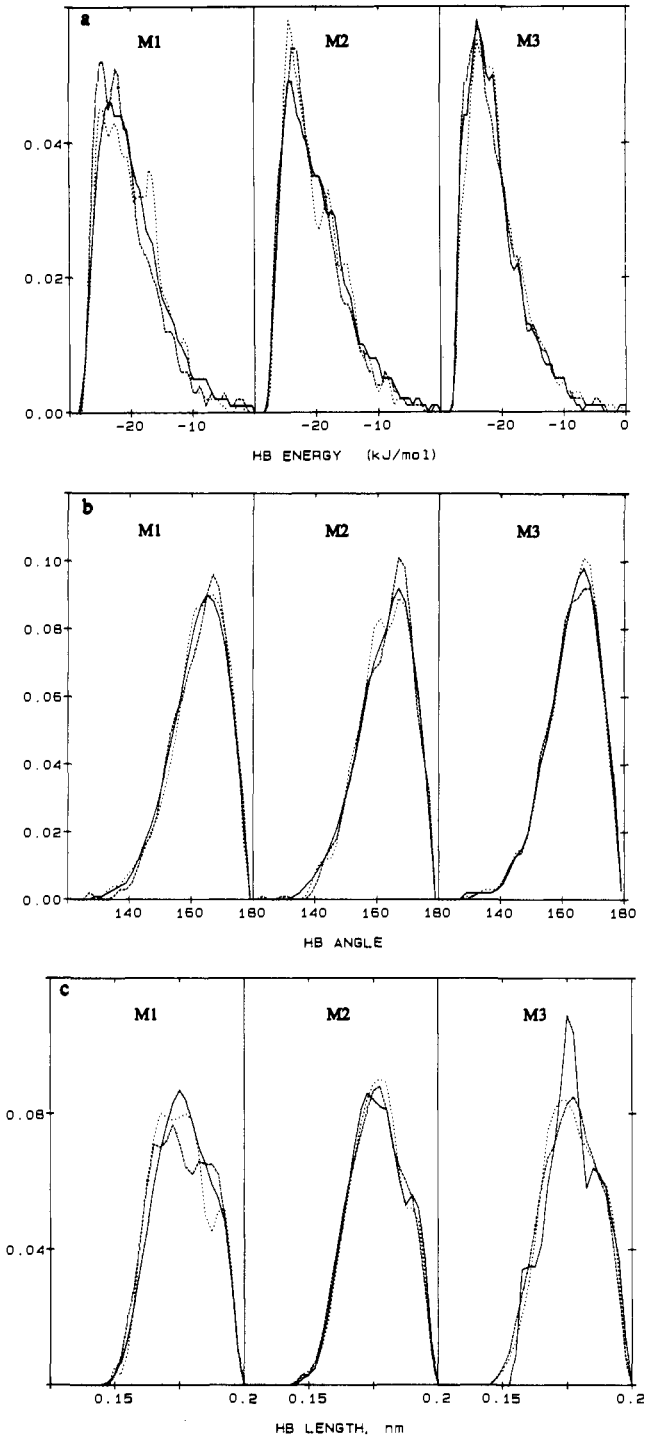

Figure 3. Plot of hydrogen bond energy (a), angle (b), and length (c) distributions from runs M1, M2, and M3 (—, bulk; - - -, nonpolar; ···, polar region).

of the water structure within the range x_{DMSO} = 0.1–0.2 and its further breaking at higher DMSO concentrations.

Additional evidence that the water structure in mixtures with DMSO is weakened can be obtained from the calculation of the coordination number of water molecules. This number decreases from 4.6 in pure water to 4.3 at x_{DMSO} = 0.04 and to 3.3 at x_{DMSO} = 0.2.

It is clear that the discussion on water structure in solutions is not particularly useful, unless an agreement about well-defined structural characteristics is reached. Since, as was shown above, RDFs do not provide unambiguous information on ordering in binary mixtures, we employed two different methods of structure evaluation: the traditional description in terms of hydrogen-bonded network parameters and the statistical geometry approach, first

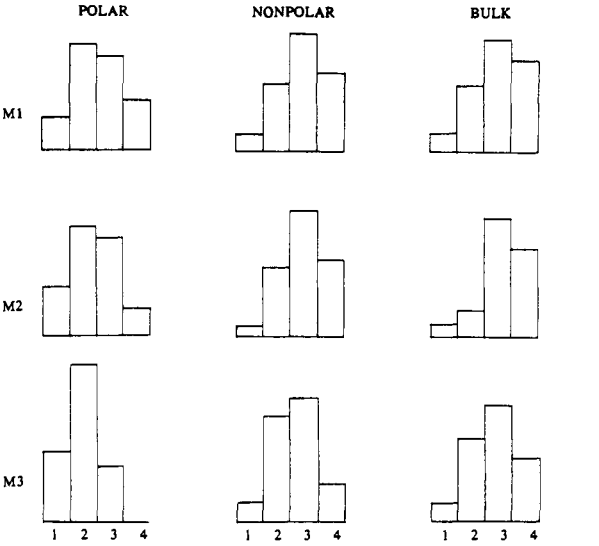

Figure 4. Distribution of the number of hydrogen bonds per water molecule.

introduced by Bernal[71] and later developed in works by Finney[72] and Medvedev and Naberukhin,[73] but scarcely used in computer simulations of liquid solutions.

In aqueous solutions of polyfunctional molecules water properties are different in the environments of different atoms and functional groups of the solute. In order to take into consideration those differences, the distribution of the number of hydrogen bonds per water molecule, hydrogen bonding energy, and angle distribution functions were calculated separately for different water regions with respect to DMSO molecules. Methods based on the proximity criterion[74] and its modification[49] were used to assign each of the water molecules to one of the following regions: polar, region of water molecules that are closest to the DMSO oxygen; nonpolar, those in the vicinity of the DMSO methyl groups; bulk, all other water molecules, which are separated from any of the DMSO atoms at a distance more than 0.36 nm. A geometric criterion for defining a hydrogen bond was applied: two molecules were considered participating in a hydrogen bond if $r_{O-H} \leq 0.20$ nm and the angle O–H···O $\geq 120°$.

Figure 3 shows that hydrogen bond energy, angle, and length distributions are nearly unchanged with the increase of DMSO concentration. This observation is in very good agreement with the measurement of the stretching vibration band profiles in the IR spectra of isotopically dilute HDO in water as a function of DMSO content.[17] From the lack of observed changes in the profiles it was concluded that the addition of DMSO did not change the distribution of hydrogen bond energies of water. This conclusion does not necessarily contradict the previous one concerning ordering of the water structure deduced from sharpening of the $g(r)$ and $\rho(r)$ peaks at low DMSO concentrations. A sharpening of the RDF indicates a general ordering in the spacial arrangement of oxygen atoms, while geometrical and energetic parameters of individual H bonds might remain almost unchanged.

The distribution of the number of water–water hydrogen bonds per molecule is shown in Figure 4. On addition of DMSO the number of water molecules involved in four hydrogen bonds decreases in all regions. Most significant changes occur in the polar region, where at x_{DMSO} = 0.2 (run M3) there are no water molecules with 4 hydrogen bonds, and just a small portion of water molecules with 3 hydrogen bonds is present. The average number of hydrogen bonds per water molecule, shown in Figure 5, decreases with the increase in DMSO concentration. So, addition

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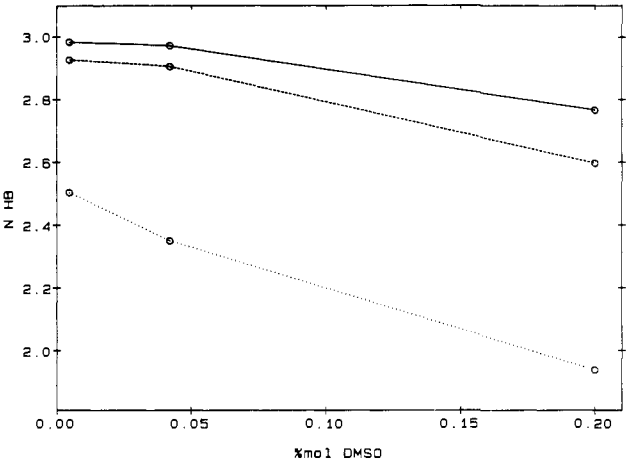

Figure 5. Plot of the average number of hydrogen bonds per water molecule as a function of DMSO concentration (lines as in Figure 3).

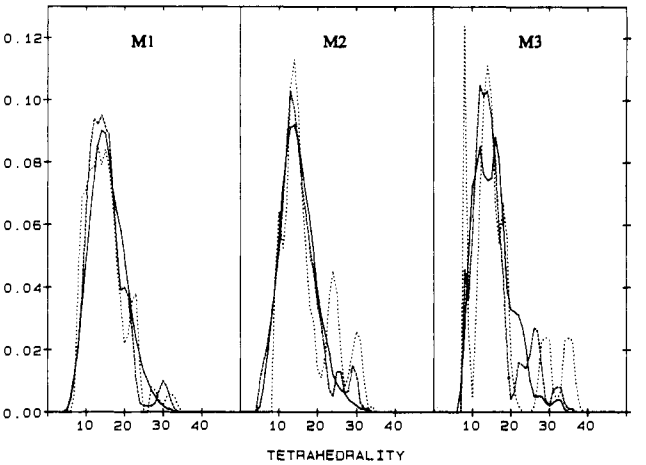

Figure 6. Plot of the distribution of tetrahedrality of the Delaunay simplexes in water (lines as in Figure 3).

of DMSO leads to the weakening of the hydrogen-bonded network of water.

Many of the properties of liquids can be most readily appreciated in terms of the packing of irregular polyhedra in what was called by Bernal the "statistical geometry" approach.[71-73] The fundamental objects of statistical geometry are Voronoi polyhedra and Delaunay simplexes. The Voronoi polyhedron is the region of space around an atom, all points of which are closer to this atom than to any other atom of the system. A group of four atoms, whose Voronoi polyhedra meet at one vertex, forms the Delaunay simplex. Although the Voronoi polyhedra and the Delaunay simplexes are completely determined by each other, Voronoi polyhedra having the same number of faces and edges may differ topologically, while the Delaunay simplexes are topologically equivalent and could be quantitatively compared. In order to describe Delaunay simplexes a quantitative measure characterizing their shape was introduced:[73]

$$T = \sum_{i>j}(l_i - l_j)^2/15\bar{l}^2 \qquad (4)$$

where T is "tetrahedrality", l_i is the length of the i-th edge, and $\bar{l}$ is the mean length of the edges of the given simplex. In the case of water, with the central molecule surrounded by four other molecules in tetrahedral arrangement, eq 4 includes one more term:[75]

$$T = \sum_{i>j}(l_i - l_j)^2/15\bar{l}^2 + \sum_{k}(r_k - \bar{r})^2/4\bar{r}^2 \qquad (5)$$

where r_k is the distance between the oxygen of the central water molecules and the oxygens at the tetrahedron vertexes, and $\bar{r}$ is the mean distance between center and vertexes.

For the ideal tetrahedron T is equal to zero and T increases with the increase of the tetrahedron distortion. The distribution of the tetrahedrality of the Delaunay simplexes in different regions of DMSO hydration is displayed in Figure 6. One can see that on addition of DMSO the number of more distorted tetrahedra increases, which is consistent with our previous observations on the changes in the hydrogen-bonded network. Most changes occur in the polar region, where significant peaks arise at T = 25–30 (run M2) and 30–35 (run M3). One could expect the decrease of distortion of the Delaunay simplexes in the nonpolar region because of the well-known ability of hydrophobic groups to promote water structure. In the case of DMSO the strong destructive influence of the molecule's polar site overrides the stabilizing effect of methyl groups. The shoulder at T = 10 in the polar region in run M1, which is transforming into a small peak in run M2 and into a very high narrow peak in run M3, probably corresponds to a rigid tetrahedral water arrangement, containing two water molecules bonded to the DMSO oxygen.

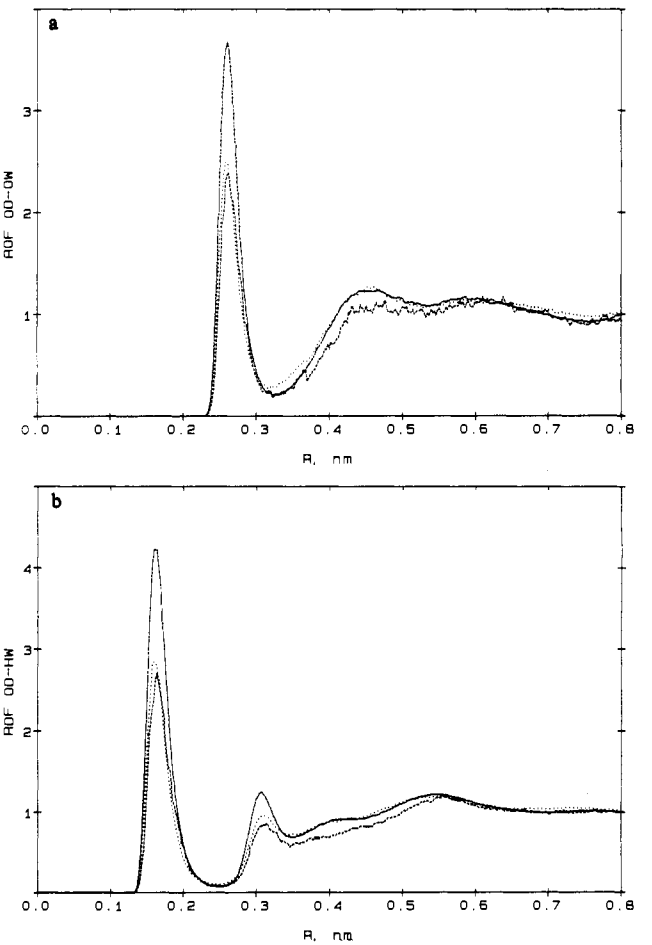

Figure 7. Plot of DMSO–water radial distribution functions (—, run M1; ---, run M2; ···, run M3).

A closer look at the water structure in the vicinity of solute molecules is possible using DMSO–water RDF (Figure 7). From the fact that OD-OW and OD-HW RDF have sharp peaks at 0.27 and 0.18 nm, respectively, it is obvious that the nearest water molecules are hydrogen bonded to the DMSO oxygen. The very existence of these hydrogen bonds and their number have been discussed for many years and there are no signs of general agreement on this problem. Various mixture properties of the water–DMSO system, obtained from viscosity,[76] ultrasonic,[22,23] and other studies, exhibit a relative maximum at about 30% mol

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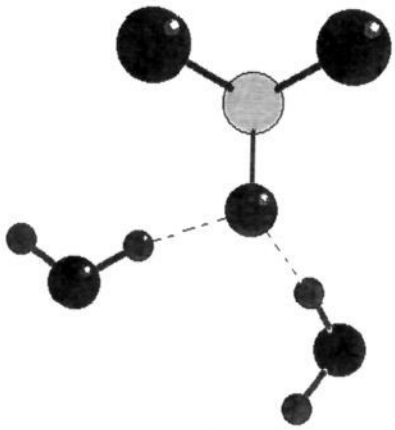

Figure 8. The snapshot of the DMSO–water complex.

fraction of DMSO. This peculiarity is an indication that a strong hydrogen-bonded complex, consisting of two water and one DMSO molecules, exists within the solution. But at the same time a eutectic point was found in water–DMSO mixture near the concentration of the viscosity maximum.[77] This fact and the absence of any observed splitting in the Raman bands of the sulfur–oxygen stretching frequencies[78] were claimed to be incompatible with the picture of DMSO–water complexes. $2DMSO{\cdot}H_2O$, $DMSO{\cdot}H_2O$, and $DMSO{\cdot}3H_2O$ complexes were observed in different experimental studies.[3,25,77] However, our simulation unambiguously confirms the formation of the one DMSO–two water complex at all studied DMSO concentrations. The snapshot of such a complex is shown in Figure 8. Similar arrangement of two water molecules bonded to an oxygen atom from the highly polar P=O group was found also in MD simulation of hexamethylphosphoric triamide aqueous solution.[80] In our simulations we observed also a $DMSO{\cdot}3H_2O$ complex with three OD···H–O hydrogen bonds, but such association occurs rarely and for a short time.

DMSO Structure. All atom–atom radial distribution functions for pure DMSO shown in Figure 9 are similar to those obtained by Rao and Singh[38] and from both X-ray and neutron diffraction experiments by Itoh and Ohtaki[40] and Bertagnolli, Schultz, and Chieux.[15] RDF obtained from both DMSO simulations (run D1 with 64 DMSO molecules and $r_{cut\text{-}off}$ = 0.9 nm, and run D2 with 512 DMSO molecules and $r_{cut\text{-}off}$ = 1.3 nm) are fairly similar.

The shortest intermolecular separation was observed for the O–C pair at 0.315 nm. Assuming the C–H bond length is 0.108 nm[15] we determine the O···H distance is slightly longer than 0.2 nm, which could be attributed to the weak C–H···O hydrogen bond. In contradiction to the conclusion drawn from the neutron[16] and infrared[81] spectra, that methyl groups are not involved in intermolecular hydrogen bonding, the presence of O···H distances in the area between 0.2 and 0.3 nm was also confirmed experimentally.[15,40] Analogous C–H···O bonding with similar C–O distances exists also in acetone[82] and dimethylformamide,[83] and probably is common for molecules with the $(CH_3)_nR{=}O$ structure.

Another controversial issue of liquid DMSO structure is the role of the dipolar forces in the local and long-range ordering. Some experimental results[1,84] lead to the conclusion that due to the dipole–dipole interactions neat DMSO forms a chain-like polymeric intermolecular association complex with alternating sulfur and oxygen atoms, while, for example, vibrational spectroscopy of crystalline DMSO[85] indicates that even at a low temperature (213 K) molecules of DMSO do not exhibit dominant dipolar interactions. Analyzing S–S and O–O RDF with well-pronounced peaks at almost similar positions (~0.55 nm) one can conclude that dipole–dipole interactions contribute significantly to the formation of the local order in liquid DMSO, but the DMSO molecules associate in the head-to-tail fashion, rather than in chains. Such arrangement of DMSO molecules was confirmed

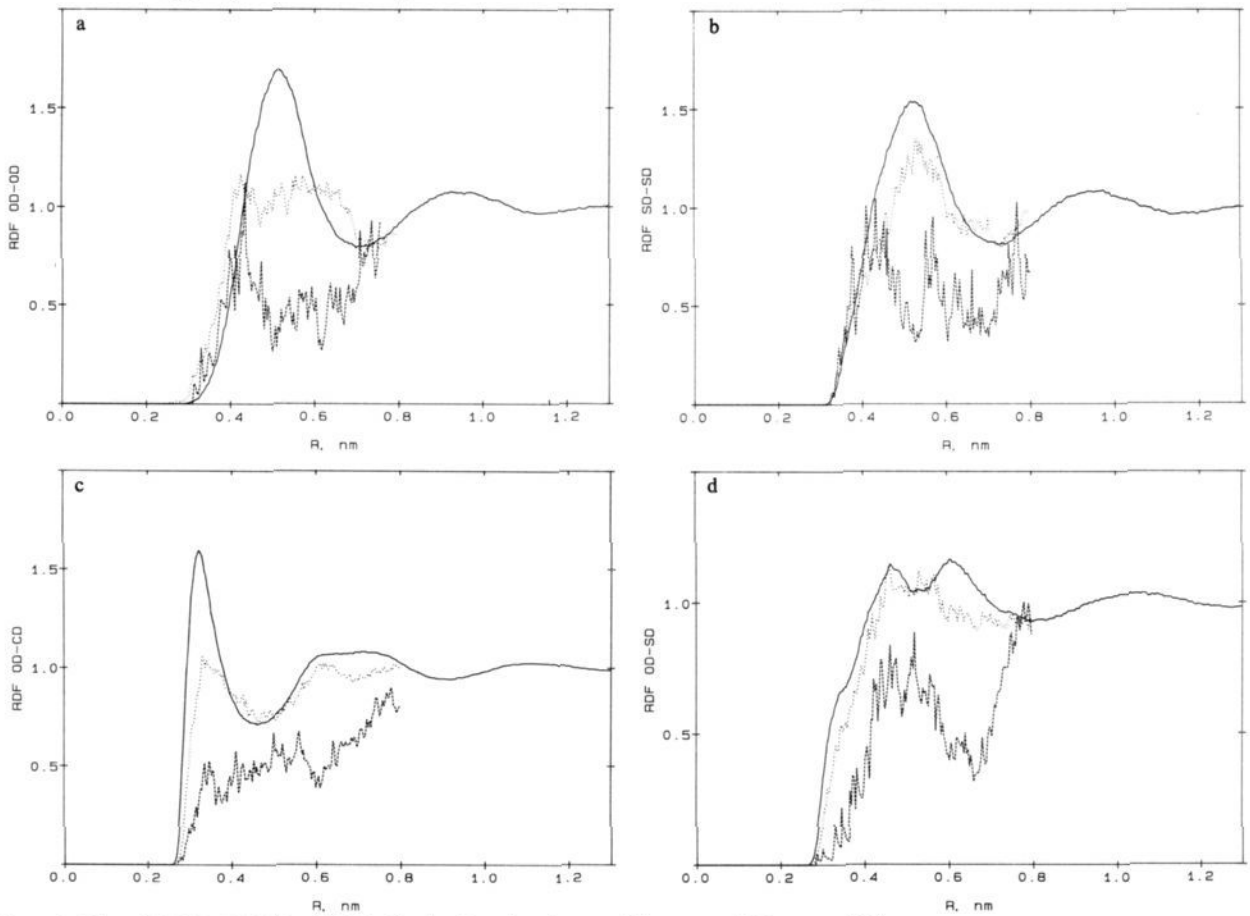

Figure 9. Plot of DMSO–DMSO radial distribution functions (—, run D2; - - -, run M2; ···, run M3).

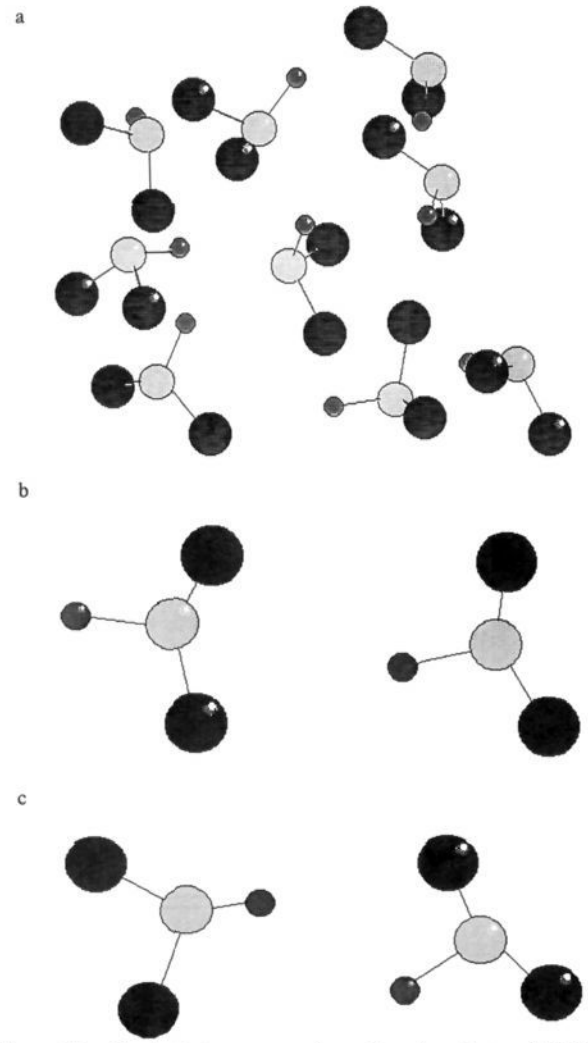

Figure 10. The instantaneous configuration of a cluster of DMSO molecules in pure DMSO (run D2; for clarity the sizes of atoms are out of scale) (a) and DMSO–DMSO dimer with parallel (b) and antiparallel (c) dipole vectors.

in experimental studies; for example, the dipole orientation correlation factor obtained from the static dielectric permittivity measurements[32] reflects some kind of antiparallel ordering of dipole moments.

A compromise to this contradiction can be inferred from the work by Bertagnolli et al.[15] On the basis of X-ray and neutron scattering intensities, they proposed a simple geometrical model of the DMSO cluster. In this model the cluster consisted of chains of DMSO molecules with parallel dipole moments, while the neighboring DMSO molecules from the adjacent chains were oriented with antiparallel dipole moments. This picture is quite consistent with the configuration of DMSO molecules obtained from our simulation. A fragment of the simulation box is displayed in Figure 10a. In this figure one can easily identify neighboring DMSO molecules, whose O–S vectors are either parallel or antiparallel. Two characteristic DMSO dimers are shown in parts b and c of Figure 10.

A broad peak with two maxima at 0.45 and 0.61 nm was observed in the O–S pair correlation function (Figure 9d). It is noteworthy that such splitting of the first peak in the O–S RDF was not obtained from Rao and Singh's simulation[38] but was observed in the X-ray diffraction study.[40]

In water–DMSO mixtures DMSO molecules initially were placed in the simulation box on vertices of a regular cubic lattice, so that DMSO–DMSO average separation was not less than 0.9 and 0.6 nm in runs M2 and M3, respectively. After 15 ps of equilibration, DMSO molecules were arranged in a pure DMSO-like structure. The peak in the O–C correlation is present at 0.33 nm as well as in pure DMSO. The first peaks in RDF OD-OD and SD-SD in solutions are shifted to the left compared with the peaks in pure DMSO. This shift can be considered as evidence of a hydrophobic association of DMSO molecules. Association of DMSO molecules in different solvents was also proved experimentally.[1,86]

Conclusions

Molecular dynamics simulation was employed to study pure DMSO and water–DMSO mixtures at three concentrations (x_{DMSO} = 0.005, 0.04, and 0.2). Structural properties of water in different regions of DMSO hydration were investigated with radial distribution functions, hydrogen-bonded network parameters, and the statistical geometry approach. The increase in RDF intensities, observed in simulations on mixtures, does not correspond to the promotion of the respective structure. This increase reflects mostly concentration changes rather than the influence of the second component. Therefore, the reliability of RDF as indicators of structure changes at different concentrations is under question. Enhancement of the water structure at the lowest DMSO concentration and its breakdown at x_{DMSO} = 0.04 and 0.2 is observed. Structural effects in water–DMSO mixtures are attributed to the prevailing influence of the DMSO polar group on water structure. The complex consisting of 1 DMSO and 2 water molecules hydrogen bonded to the DMSO oxygen exists at all studied concentrations. Local order in pure DMSO is determined by dipolar forces as well as molecular association through C–H···O bridging. Both components in water–DMSO mixture are tending to preserve their structural order upon dilution. Additional information can be drawn from the dynamical properties of DMSO and water molecules in their mixtures. This work is now in progress.

Note Added in Proof. While this paper was being prepared for publication the results from the MD simulation on DMSO as a solvent (Mierke, D. F.; Kessler, H. *J. Am. Chem. Soc.* **1991**, *113*, 9466–9470) and data from a neutron diffraction study of DMSO–water mixtures (Soper, A. K.; Luzar, A. *J. Chem. Phys.* **1992**, *97*, 1320–1331) were published. These results are in good agreement with those from the present work.

Acknowledgment. This work was supported by a grant from the Office of Naval Research. The simulations were performed on the IBM 3090 and Convex computers at UNC and on a Cray-YMP at North Carolina Supercomputing Center. Fruitful communications with Prof. Y. M. Kessler and Dr. M. G. Kiselev are greatly appreciated. We are grateful to Prof. J. J. Hermans for the careful reading of the manuscript.

Registry No. DMSO, 67-68-5; H_2O, 7732-18-5.

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