

The internal structure of binary liquid mixtures DMSO + water

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Summary:

The review of literature concerning the internal structure of dimethyl sulfoxide, water and their mixtures was presented in this paper. At the same time, results of own research connected with the analysis of intermolecular interactions in liquid mixtures of DMSO + water were discussed.

Key words: dimethyl sulfoxide, water, intermolecular interactions.

The advances in natural science follow two inseparably interrelated paths: experimental and theoretical. Accumulation of an appropriate amount of experimental data allows drawing generalized conclusions, deriving appropriate formulas and formulating laws that govern the studied phenomena. This leads to the possibility to predict and program expected effects for practical use.

Obviously, such a research cycle requires, particularly in solution chemistry, the theoretical results to be verified by experimental results.

However, in theoretical and physical chemistry, such a verification proves to be difficult.

Calculations (e.g. calculations of the internal solution structures) are based on the principles of quantum mechanics, which can be currently applied only in an approximate manner to small unit systems. It is hard to imagine a complete structural description (based on such calculations) that would take into account all possible types of intermolecular interactions, e.g. in solvent mixtures. On the other hand, experimental results are obtained for molecular systems as described above, located in actual environment, which often has a decisive effect on both the course of the observed phenomena and the properties of studied objects.

Another problem is determination of appropriate research methods. This is associated with the need to select such measurable physicochemical parameters, for which changes caused by the effects of interest might provide important information on the behavior of the entire system in the particular environment.

Such problems appear when analysis of intermolecular interactions and assessment of internal structures of liquid one-, two-, and multicomponent systems are being attempted.

The subject of analysis of intermolecular interactions and assessment of internal structures of liquid solvent mixtures is important to every chemist who carries out homophasic chemical reactions or heterophasic electrode processes in these solvents. This is due to the fact that ion-solvent molecule, ion-ion or solvate molecule-solvent molecule interactions are inseparably linked to physicochemical properties of the solvent. These properties are, in turn, a function of intermolecular interactions within the solvent. Several excellent monographs were published on the subject, such as *Intermolecular Interactions* by H. Ratajczak, published in 1982, or *Solvents and Solvent Effects in Organic Chemistry* by Ch. Reichardt, published in 1988 [1, 2].

The review of the literature data suggests that in different research sites, a wide range of spectral methods, thermochemical methods and studies of intensive macroscopic properties of solutions (such as density, viscosity, relative electric permittivity, surface tension, etc.) in different temperatures were used to analyze the internal structures of liquid solvent mixtures [3]. Obviously, when attempting to assess the structure of a two-component solvent mixture, one needs to know the properties and structure of its components. Therefore, before moving on to the attempted description of the internal structure of dimethyl sulfoxide (DMSO) – water mixtures, I am going to present a short review of data on the properties and internal structure of both components of this mixture.

The review of literature data shows that no scientific information on dimethyl sulfoxide had been available for nearly 100 years since it was discovered by Saytzeff in 1867 [4]. Only as late as in the 1960s, when the capability of this solvent to solubilize different types of chemical compounds insoluble in other solvents (among others, sulfamides) was observed, the interest in DMSO was revived. Another stimulus that greatly enhanced the interest in DMSO was the studies published in the late 1960s, suggesting a great potential for the use of this solvent in pharmacology and medicine [5-15]. Since that time, the interest in chemical and physical properties and the structure of liquid dimethylsulfoxide and its solutions has been unrelenting. This can be proved by more than ten thousand articles published to date, indicative of a great interest in this solvent in all areas of chemistry, physicochemistry, biology, pharmacology and medicine. In recent years, a large number of articles has been published regarding the use of DMSO in cryopreservation processes, more precisely regarding the replacement of 5-10% aqueous solutions of glycerol used in this process with aqueous solutions of DMSO. The mechanisms of cryopreservation are not fully studied. It is assumed that upon slow freezing, glycerol leads to cell dehydration, which prevents formation of ice crystals. Aqueous solutions of DMSO have similar properties while additionally chelating protein metals upon slow freezing, thus preventing protein denaturation.

DMSO is a very hygroscopic liquid (e.g., at a temperature of 293.15 K, under pressure of 1 atm and at a relative humidity of 65-70%, it is able to absorb the amount of water that is equal to its own mass [12]), miscible with water in any ratio and dissolving, in wide concentration ranges, lower alcohols, aldehydes, ketones, ethers, esters, heterocycles and aromatic compounds, as well as macromolecular compounds (e.g. polyacrylonitrile, nitrocellulose and cellulose acetate [16]).

From the standpoint of chemical structure, it is a very interesting feature of DMSO that while the C–S bond may be treated as a regular covalent single bond, the nature of the S–O bond has not been fully explained. An interpretation that explains well the physical properties and reactivity of DMSO is presenting DMSO molecule as a hybrid between two resonance structures:

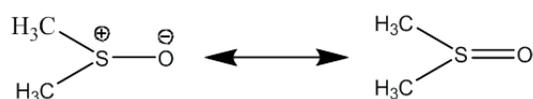


Figure 3: Resonance hybrid structures of DMSO.

The first structure is characterized by a polarized single S–O bond, while the other features a double bond [17].

DMSO is characterized by high polarity, as evidenced by relatively high values of its electric permittivity and dipole moment ($\epsilon = 48.9$, $\mu = 4.3$ D). These properties are responsible, among others, for good DMSO solubility of many types of chemicals insoluble in other solvents.

From the standpoint of structural studies, a high boiling point (189°C), evaporation entropy (123,85-J deg⁻¹·mol⁻¹) and cryoscopic studies in benzene suggest strong intermolecular associations within liquid DMSO. (DMSO)_n associates may be formed via bridge bonds [18, 19]:

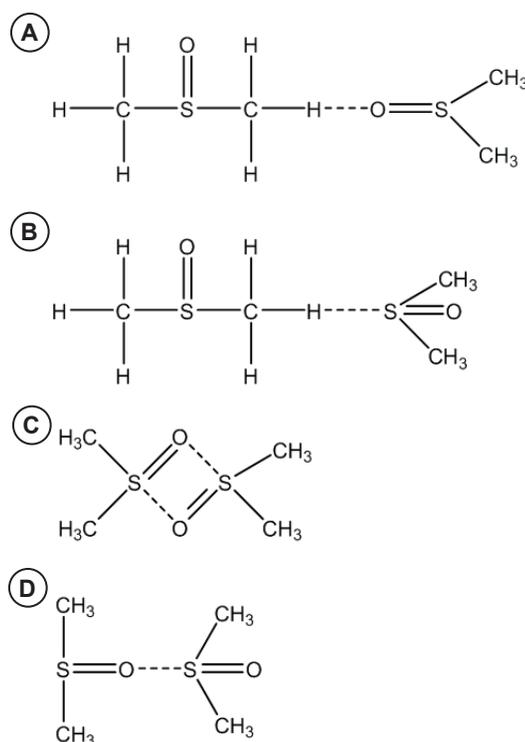


Figure 4: Example (DMSO)_n associates formed via bridge bonds.

However, most authors believe that due to low autoionization constant of DMSO ($k = 5 \cdot 10^{-18}$ [20]), the probability of formation of associates (1) or (2) is very low. According to studies conducted by Szmant *et al.*, DMSO molecules are associated by the so-called *oxygen-sulfur bridges* S–O [18]. Szmant observed, that for the absorption band of $\nu_{S-O} = 1060 \text{ cm}^{-1}$, the Lambert-Beer's law is fully met only for solutions of DMSO in CCl_4 at concentrations of less than 0.08 M. Thus, only monomers are present within this concentration range. Upon increasing the concentration of DMSO in CCl_4 from 0.08 M to 0.3 M, cyclic dimers (3) become prevalent, as evidenced by the presence of new absorption bands of $\nu_{S-O} = 1100 \text{ cm}^{-1}$. Linear dimers (4) should generate at least three distinct bands ν_{S-O} . Further increase in DMSO concentration ($c > 0.3 \text{ M}$) destroys cyclic dimers and leads to formation of macromolecular chain associates of type (4), with structures as described above.

Most researchers believe that the main reason for the lack of C–H...O bonds in liquid DMSO is the low acidity of C–H groups (as a C–H acid, DMSO is ca. 10^7 weaker than triphenylmethane), while intermolecular S...O bonds are formed in liquid DMSO or in its aqueous solutions thanks to the significant contribution of specific electron donor-acceptor (EDA) interactions, enhanced by non-specific dipole-dipole interactions. It should also be mentioned that DMSO is a strong electron donor and a weak electron acceptor (electron donor and electron acceptor numbers of 29.8 and 19.8, respectively) [21].

It might seem that in case of water, all issues regarding its properties and internal structures should be well described. However, there is nothing more erroneous.

In his wide monograph [22], containing a review of literature data on the internal structure of liquid water, Guillot states that:

“Water is the simplest compound of two most prevalent reactive compounds in the universe. Our body is composed of water in 2/3. Life or evolution would be impossible without water. Water is the most extensively studied solvent; it is therefore surprising, that its properties and behavior are still poorly understood, not only by general population, but, more importantly, by scientists who analyze its properties and internal structure.”

Experimental results suggest that water molecules may be considered as a “rigid” system, in which the precisely calculated, experimentally determined O–H bond lengths are 0.9572 Å, and the H–O–H angle is 104.5°. Water molecule is also assumed to

be an isotropic, polarizable sphere with a constant dipole moment of $6.3 \cdot 10^{-30} \text{ C}\cdot\text{m}$.

In reality, this issue is much more complicated. This may be supported by the fact that one of the recent review articles on the subject presented 46 different models of water molecule [23]. All analyzed models were the so-called “rigid” water molecule systems. They assumed that the hydrogen-oxygen bond lengths and bond angles in the molecule are constant. “Flexible” structure models, which take molecular vibrations into account, resulting in variable bond lengths and angles (such as the central force (CF) model developed by Stillinger and Rahman [24] and the BJH model developed by Bopp, Jancso and Heinzinger [25]) have also been developed.

However, one should keep in mind that liquid water is not a set of isolated, independently moving molecules. Comparing e.g. the self-diffusion coefficient of water with self-diffusion coefficients of solvents characterized by much larger molecules reveals that the process of self diffusion in water is caused not only by correlated movements of connected molecules. Based on the analysis of values of this parameter, Narten and Levy [26] assumed that intermolecular aggregates are formed in liquid water, which must affect its internal structure and properties. These aggregates and structures are formed in liquid water due to short-range interactions between neighboring water molecules and formation of intermolecular hydrogen bonds. Of course, the simplest structure of this type is a dimer consisting of two water molecules. The more linear is the hydrogen bond formed between oxygen in one molecule and hydrogen in another molecule, the stronger it is. The energy of the hydrogen bond in such cluster is ca. 20 kJ/mol and thus it is much higher than the value of the $k \cdot T$ product. Therefore, one may suspect that the lattice of hydrogen bonds in water should be energetically stable. However, one must keep in mind that the internal structure of water (and any other liquid) is a *flickering structure*. This means that the actual lattice of hydrogen bonds in water undergoes continuous rearrangement and new hydrogen bonds and, in consequence, new spatial configurations of internal structures are formed within picoseconds. This effect must have led to many different models of internal structure of liquid water being published in the literature.

In general, structural models may be divided into two categories:

- the so-called mixture models [27-29], developed from equilibrium mixtures of aggregates differing by the number of associated water molecules and the specific structural arrangement of these aggregates.

- The so-called *continuum* models [27-29], describing a continuous lattice of molecules connected by hydrogen bonds. Bending the hydrogen bonds in the lattice results in continuous distribution of hydrogen bond lengths, angles and energies.

Of course, models that constitute specific combination of bent hydrogen bond lattice with mixture model concepts are also published in the literature. This allows, among others, to interpret the experimental data describing the microscopic structure of water (diffraction analysis) using *continuum* models and the thermodynamic properties (such as compressibility or thermal capacity) by a model consisting of small internal, local structures.

It must be emphasized that all the discussed structural models assume molecular clusters of different sizes being present within liquid water. According to Walrafen [30], three structural components may be identified in liquid water: quadruply-, triply- and doubly-coordinated units of hydrogen bonds. Kim [31] postulates that water contains small water molecule clusters $(\text{H}_2\text{O})_n$, where $4 \leq n \leq 8$. Arakova [32] presents a pentamer-monomer model, based on the assumption that liquid water is an equilibrium mixture of water molecules bound in tetrahedral arrangements (pentamers) and water monomers. Luu *et al.* [33] assumed that water contains cyclic pentamers, bicyclic octamers and tricyclic octamers of the following structures:

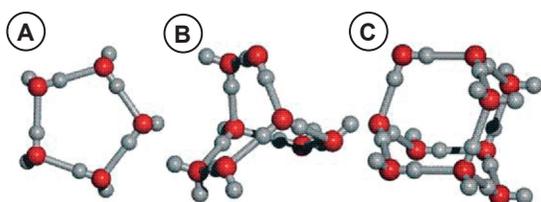


Figure 5: Spatial structure of cyclic pentamer (A), bicyclic octamer (B) and tricyclic octamer (C) [33].

These three small clusters are relatively stable and their mutual interactions lead to formation of larger clusters with icosahedral symmetry. These, in turn, bind one another to form a lattice of icosahedral $(\text{H}_2\text{O})_{280}$ clusters [22, 23, 29].

It might seem that this diversity of literature structural data makes it impossible to develop coherent interpretation of energy changes (i.e. the assessment of the energy of intermolecular interactions) in liquid water. There is nothing more erroneous. The course of changes of the intermolecular interaction energy as the function of intermolecular distance in liquid water allows interpretation of not only the structural effects, but also explanation of many abnormal properties of water (change in

density upon melting and solidification, abnormal viscosity at 4° C, specific heat or the Mpemby effect). This shows that hydrogen bonds between water molecules keep them at distances larger than in case of non-binding interactions. The conflict between these two effects and their dependence on external conditions (temperature and pressure) is responsible for the most of the aforementioned “unusual” (abnormal) properties of water [22, 23, 29].

Having at my disposal the above structural data relating to neat DMSO and water, I attempted to assess the internal structure of liquid DMSO + water molecules based on own research (densimetry, dielectrometry, viscosimetry, refractometry and ¹H-NMR and IR spectrometry [37-37]) and data published by other authors. Very important from the standpoint of issues under discussion were the spectral studies by Mierzecki *et al.* [38], consisting in Raman spectroscopic analyses of liquid DMSO-H₂O solutions. The results of these studies supported the concept of at least two intermolecular complexes being present in these liquid mixtures, i.e.: DMSO·2H₂O and DMSO·H₂O, with possibility of 2DMSO·H₂O not being excluded. However, Mierzecki did not propose a way to relate the internal association between these complexes to the internal structures of studied liquid mixtures. Analysis of Raman spectra led those authors to the conclusion that in the DMSO·H₂O complex (formed in equimolar DMSO+H₂O) mixtures, only one electron pair in DMSO oxygen is engaged in complex formation. In more water-rich solutions, both electron pairs of DMSO's oxygen atom are connected with H₂O molecules with hydrogen bonds. However, it must be mentioned that relatively stable DMSO dimers were detected by the authors even in solutions containing significant excess of water. Drawing logical conclusions from Mierzecki's work, I arrived at conviction that aqueous solutions of DMSO, formed e.g. from combining equimolar amounts of both components, contain prevalently DMSO·H₂O complexes, accompanied by more water-rich complexes (DMSO·2H₂O and DMSO·3H₂O) as well as water-deficient complexes (2DMSO·H₂O). These solutions must also contain relatively water-resistant dimers (DMSO)₂. This argumentation leads to the following conclusion: If the extreme values of several studied physicochemical processes suggest a characteristic composition of the mixture, e.g. containing ca. 50% mol DMSO, this means that the internal structure of that solution has an averaged stoichiometry $(\text{DMSO}\cdot\text{H}_2\text{O})_n$. However, one must also remember that the structure contains intermolecular complexes with more water-rich or more DMSO-rich compositions. Thus, actual internal structures of liquid bicomponent DMSO + H₂O systems are mixed structures consisting of dominant DMSO·H₂O complexes with locally included complexes of other compositions.

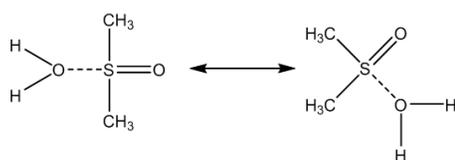


Figure 6: Spatial structures of intermolecular $\text{DMSO}\cdot\text{H}_2\text{O}$ complex proposed by Schott [39].

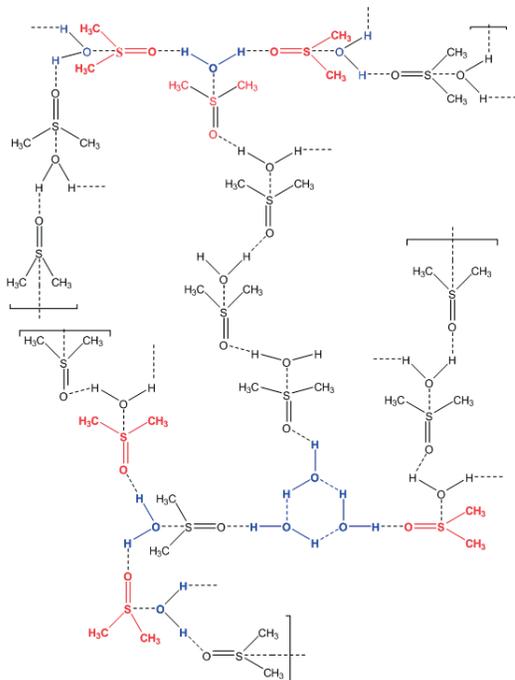


Figure 7: Proposed internal structure of liquid $\text{DMSO} + \text{H}_2\text{O}$ mixtures with predominance of $\text{DMSO}\cdot\text{H}_2\text{O}$ complexes [37].

Here, one should also mention the papers by Schott [39], in which he assumed that water may be bound to DMSO not only via the hydrogen bonds, but also via interactions between the positively charged end of dipole S–O and negatively charged end of dipole O–H. Taking this into account, Schott proposed the following spatial structures of intermolecular $\text{DMSO}\cdot\text{H}_2\text{O}$ complexes:

Taking into account the above structural considerations, the following hypothetical internal structures

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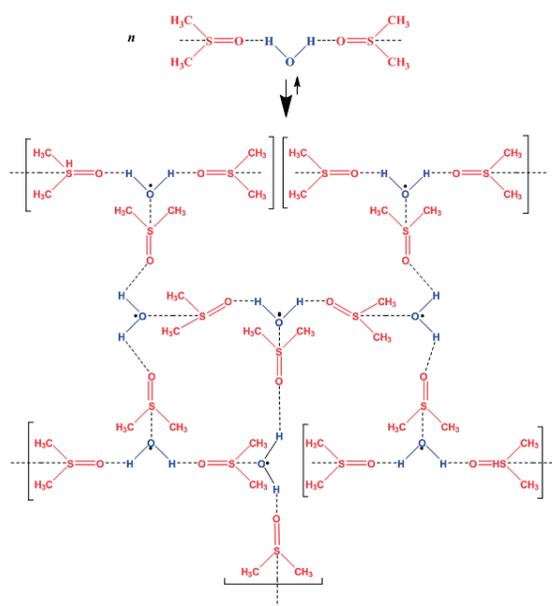


Figure 8: Proposed internal structure of liquid $\text{DMSO} + \text{H}_2\text{O}$ mixtures with predominance of $2\text{DMSO}\cdot\text{H}_2\text{O}$ complexes [37].

of liquid $\text{DMSO} + \text{H}_2\text{O}$ mixtures could be presented, containing predominant $\text{DMSO}\cdot\text{H}_2\text{O}$ complexes (Figure 5) and $2\text{DMSO}\cdot\text{H}_2\text{O}$ complexes (Figure 6).

Of course, the internal structures proposed here are purely hypothetical in nature. This is due to the fact that, as mentioned before, contrary to analogous solid structures, actual internal structures of liquid bicomponent systems are flickering structures [34–37]). This makes it impossible to determine their actual internal structure by means of semiempirical calculations or to determine the actual number n of molecules within the clusters $x\text{DMSO}\cdot y\text{H}_2\text{O}$ that form this structure at any given moment. However, one must realize that such types of studies give rise to interpretation mechanisms that allow to explain issues related to ion-ion, ion-solvent or solvent-solvent interactions in multicomponent liquid systems.

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