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The Role of Methyl Groups in the Formation of Hydrogen Bond in DMSO−Methanol Mixtures

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Hydrogen bonds play a vital role in various chemical/biological systems, including stabilizing biomolecular structures, modulating specificity and speed of enzymatic reactions, and constructing supramolecular structures.[1] Hydrogen bonding is usually presented in the form of R−X−H···Y−R', where X and Y are electronegative elements. While studies of hydrogen bonding are mainly focused on the atoms directly involved, namely the atoms X, Y, and H,[2] little attention has been paid to the effects of the secondary alkyl groups R and R'.

In this work, we present FTIR, NMR, and theoretical evidence to show that these alkyl groups make positive contributions to the formation of hydrogen bonds. To investigate interactions between species at molecular and submolecular level, we propose here an excess spectroscopy approach, following the idea of excess thermodynamic functions.[3] The excess spectrum, defined as the difference between the spectrum of a real solution and that of the corresponding ideal solution under the same conditions, reflects nonideality of mixtures and can be used to explain excess thermodynamic properties at the molecular level and to unveil microscopic information on molecular interactions.

The attenuated total reflection (ATR) FTIR spectra of dimethyl sulfoxide (DMSO)−methanol mixtures in the methyl rocking region are shown in Figure 1A and B, where A depicts the spectra in the form of absorption coefficient ϵ, and B, the corresponding excess spectra ϵ^E. The band at 1115 cm^{-1} arises from methanol,[4] while those at 930 and 952 cm^{-1} are from DMSO.[5] The missing part between 970 and 1070 cm^{-1} is mainly from the S=O stretching modes of DMSO. From Figure 1A the IR spectra only show the expected intensity increase with increasing concentration of the respective component. By contrast, negative and positive bands are seen in the excess spectra (Figure 1B) for the methyl groups from methanol and DMSO, respectively.

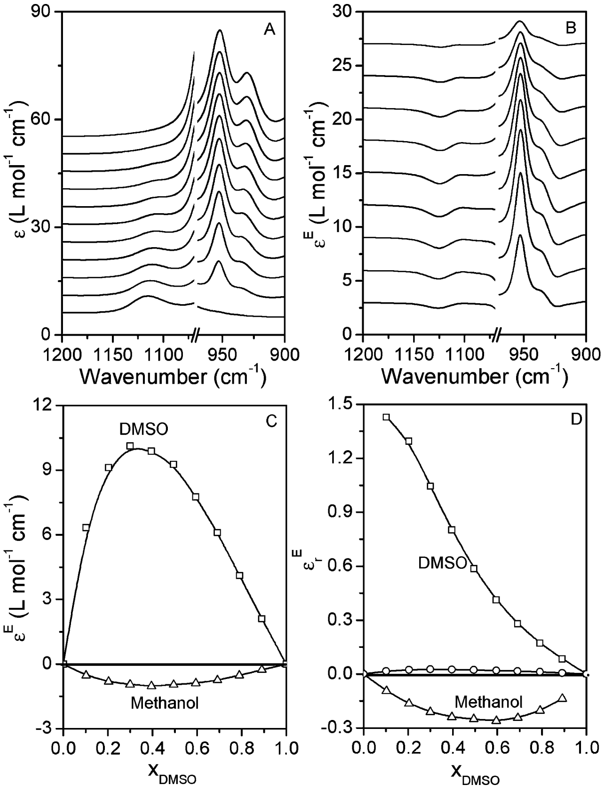

Figure 1. Partial infrared spectra (A), excess spectra (B), excess absorption coefficient at the peak points (C), and relative excess absorption coefficient (D) of DMSO−methanol binary mixtures. Mole fraction of DMSO increases from 0 to 1 with an increment of 0.1 from bottom to top in panels A and B. Open circles in panel D are results of hexane−heptane mixtures.

To further demonstrate this difference, the peak values of the excess absorbance and the relative excess absorbance ϵ_r^E of the binary mixtures are shown in Figure 1C and D, where ϵ_r^E is the normalized excess absorbance by the respective ideal absorbance at each concentration. As a comparison, results of the hexane−heptane system are also shown in Figure 1D, and the ϵ_r^E values are very close to zero, indicating this is nearly an ideal system. The results suggest unambiguously that the methyl groups in the two constituent molecules play different roles upon formation of the hydrogen bonds. Further experiments on DMSO−ethanol mixtures reveal behavior similar to that of the DMSO−methanol mixtures (see Figure S1).

The positive and negative deviations of the absorptivities from ideality can be attributed to changes in the dipolar properties of the molecules,[6] which cause changes in the charge densities on the methyl groups. Such a charge-transfer phenomenon is the molecular basis of the polarizability of molecules. Inasmuch as there is charge transfer from the electron donor to the proton donor during the formation of a hydrogen bond, as a response, the methyl groups of methanol and DMSO may respectively serve as electron-withdrawing and -donating groups to rebalance the charge distribution in the binary complexes.

To elaborate on this assessment, we calculated the total charges of the methyl groups of a model system of the DMSO−methanol binary complexes via the natural population analysis (NPA).[7] The calculations were performed on three conformers (I, II, III) at the level of MP2/6-31+G(d). Solvent effects on the natural charges were evaluated at the B3LYP/6-311++G(d,p) level.[8] Listed in Table 1 are the charges (q) of the methyl groups and hydrogen atoms in the monomers and the changes of the charges (Δq) upon formation of hydrogen bonds in three conformers of the supramolecular complexes (see Supporting Information for details of the conformers I, II, and III). In Table 1, positive (negative) Δq values indicate decrease (increase) in electron density of the respective groups and atoms. Clearly, for all the three conformers the methyl groups of DMSO have positive Δq, while the methyl group of the

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Table 1. NPA Charges (in e) of the Methyl Groups and Hydrogen Atoms in the Monomers and Their Changes upon Formation of DMSO−Methanol Supermolecules[a]

	q(monomer)	Δ*q*(I)	Δ*q*(II)	Δ*q*(III)
2CH_3 (DMSO)	−0.233	0.048	0.041	0.032
6H (DMSO)	1.505	0.050	0.035	0.023
CH_3 (Methanol)	0.323	−0.003	−0.007	−0.019
3H (Methanol)	0.569	−0.013	−0.016	−0.029

[a] I, II, and III are three conformers of the DMSO−methanol complexes.[9]

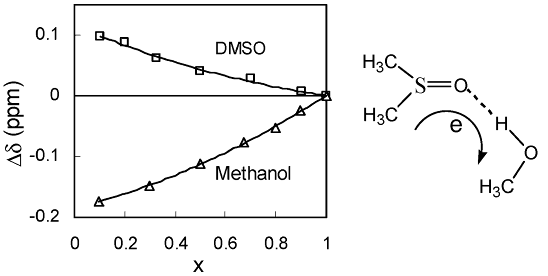

Figure 2. (Left) Chemical shift difference of methyl hydrogens in DMSO−methanol mixtures at various mole fractions of the respective components. (Right) Scheme showing the direction of charge transfer involving the methyl groups.

methanol has negative Δ*q*. The negative charge of the DMSO methyl groups in the binary complexes that is less than that in the DMSO monomer demonstrates a charge-donating effect of the DMSO methyl groups upon the formation of a hydrogen bond with methanol. Similarly, the positive charge of the methanol methyl group in all the conformers of the binary complexes less than that in pure methanol indicates a charge-withdrawing effect of the alkyl group in the alcohol. Taking conformer I as an example, which has the largest interaction energy,[10] the charge donation in DMSO−methanol system is 0.048e, whereas the corresponding charge withdrawal is 0.003e. The charge withdrawals are 0.007e and 0.019e, respectively, for the other two conformers.

On the basis of these theoretical results, ^1H NMR experiments were carried out by employing a JEOL JNM-ECA600 spectrometer to evaluate the electron-donating or -withdrawing effects, which would cause changes in chemical environments of the methyl hydrogen atoms. By defining the chemical shift difference as $\Delta\delta = \delta - \delta^0$, where δ and δ^0 are the chemical shift of hydrogen in a complex and that in its constituent molecules, concentration dependences of $\Delta\delta$ were monitored, and the results are shown in Figure 2. Interestingly, positive values for protons in DMSO and negative values for the methyl protons of methanol are observed, indicating low-field and high-field shifting, respectively. The NMR results of the solution shown in Figure 2 are consistent with the theoretical results calculated on a binary complex model, thus confirming that the electron density increases around the methyl proton in methanol and decreases around the methyl proton in DMSO upon formation of hydrogen bonds. As a further confirmation of our observation, high-field shifting of the alkyl ^1H NMR spectra of various alcohols was recently reported when solvent was changed from $CDCl_3$ to DMSO.[11] However, the shift was simply considered as a result of solvent effects. From our results, solvent effects play little role in the calculated differences of the charge density and NMR shielding of the DMSO−methanol system. We believe that charge transfer mainly accounts for such shifting.

In our theoretical calculations we selected DMSO−methanol binary complex as a model to account for the two-body interactions in the solution. In the real solution, there exist three-body or other many-body interactions as in linear and cyclic oligomers. However, because of the dominant effect of the two-body interaction over other many-body interactions, the calculated results based on the dimer model are representative. Indeed, the solvation effect evaluated via a PCM solvation model only causes a few percent of the changes of hydrogen bonding in charge transfer (see Supporting Information).

Thus, when DMSO forms a hydrogen bond with a methanol molecule, charge transfers from the oxygen lone pair in DMSO to the antibond orbital of OH group in the methanol,[12,2c] which lead to decrease of electron density on the oxygen atom in DMSO and increase of electron density on the H−O bond in methanol. The changes of charge density are compensated by the electron-donating methyl groups in DMSO and the electron-withdrawing methyl group in methanol. The hydrogen-bonded binary complexes are thus stabilized via the redistribution of charge densities. A scheme showing the direction of charge flux during the formation of the hydrogen bond is depicted in Figure 2.

In summary, using an excess spectroscopy approach we have provided evidence based on FTIR and NMR experiments and quantum chemical calculations that the alkyl groups in DMSO and alcohols play different roles in the formation of hydrogen bonds. The former is electron-donating, and the latter is electron-withdrawing, with both making constructive contributions to the hydrogen bonding. The findings reveal non-negligible effects of secondary alkyl groups in hydrogen bonding and may shed light on the understanding of other more complicated hydrogen-bonded systems in chemical and biological systems.

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Supporting Information Available: Description of the experiments, the theory of excess absorption spectroscopy, computational details, structures of the optimized conformations, and details of ref 8. This material is available free of charge via the Internet at http://pubs.acs.org.

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