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## Why are the Nitro and Sulfone Groups Poor Hydrogen Bonders?

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**ABSTRACT:** The interactions of water or methanol with nitromethane and dimethyl sulfone vs. comparison molecules, e.g. dimethylsulfoxide (DMSO), are reported. For nitromethane with water, the classical (edgewise) hydrogen bonded configuration is modestly stabilizing. However, the approach of water over the face of the nitro group is preferred in AM1 calculations. Generally, molecules such as sulfones and nitro compounds have lower energy bonding orbitals than sulfoxides. The energy of the  $n \delta \sigma^*$  interaction (e.g. nitro lone pair to O-H of water) thus is larger for the nitro and sulfone cases, and this interaction is less prevalent than other cases. Since the interaction of the nitro group with water is somewhat favorable, the reason for the insolubility of nitromethane in water was investigated. It was found that the energy of segregated sets of nitromethane and of water molecules was lower than the mixed nitromethane - water state. In contrast, the energy of the mixed DMSO-water hydrogen bonded mixed state is lower than segregated molecules.

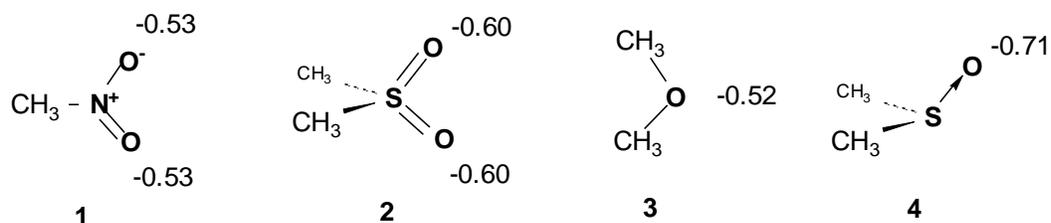
**KEYWORDS:** hydrogen bonding, nitro, sulfone, DMSO, ab initio, infrared.

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From a classical point of view, the nitro and the sulfone groups should be excellent hydrogen bond acceptors.<sup>1</sup> The nitro group has a high charge density on the two oxygens (cf. Scheme. 1), as well as several non-bonded pairs of electrons. In nitromethane (**1**), three of the four major atoms are polar, yet nitromethane is only modestly soluble in water, a strongly H bonding medium (cf. Table I).<sup>2</sup> Dimethyl ether (**3**) is much more soluble in water than nitromethane despite a smaller Mulliken charge density on its single oxygen, a lower dipole moment, fewer hydrogen bonding sites, and more hydrocarbon groups. Dimethyl sulfone (**2**)

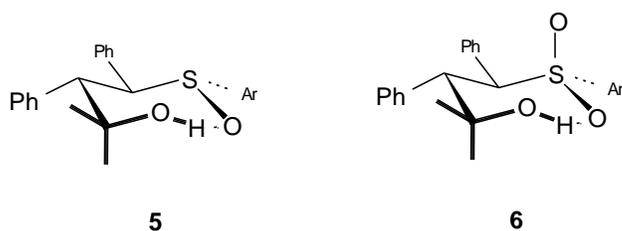
has limited solubility in water in contrast to its congener, dimethyl sulfoxide (DMSO) (**4**), which is miscible in water in all proportions. In fact, the solution gets warm when the two are mixed.<sup>3</sup> DMSO has fewer hydrogen bonding sites than the sulfone, and a smaller dipole moment, although the charge density on oxygen is somewhat larger.

Scheme I: Mulliken Charge Densities on Oxygen

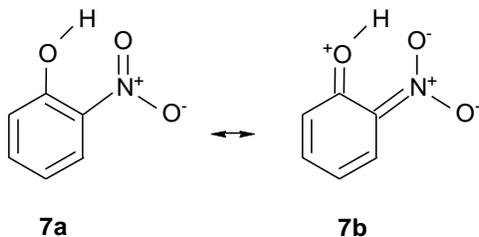


The shift in OH infrared frequency  $\Delta\nu$ , upon H bonding, is frequently taken as an index of the strength of a hydrogen bond, although the phenomena has been the source of some controversy.<sup>4,5</sup> The frequency drop,  $\Delta\nu$ , may be ascribed to the  $n_{\text{NO}_2} \delta \sigma_{\text{OH}}^*$  interaction that results in partial electron population of the antibonding (O-H)\* orbitals. The OH bond is weakened, resulting in a greater bond distance, and a lower infrared frequency. The reduction of kinetic energy as electrons move in the field of many atoms instead of a few atoms is a feature not only of chemical bonding, but quite likely of hydrogen bonding as well, which represents a partial “repayment” for the seemingly unfavorable population of high energy orbitals.

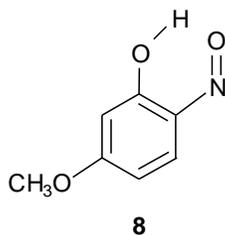
In acyclic  $\beta$ -nitroalcohols, early work seemed to support an intramolecular hydrogen bond, although the data were somewhat inconsistent.<sup>5-8</sup> Kuhn and co-workers found  $\Delta\nu$  to be  $15 \text{ cm}^{-1}$  in  $\beta$ -nitroethanol.<sup>9</sup> However, Ungnade, et al., seemed to suggest that  $\Delta\nu$  was close to zero for the  $\text{NO}_2$  --HO interaction.<sup>9</sup> Schleyer and co-workers strongly disagreed, and cited  $\Delta\nu$  values of  $10\text{-}28 \text{ cm}^{-1}$  for the intramolecular hydrogen bond.<sup>5</sup> However, the reason for the complexity of the OH absorption was never elucidated. OH- $\text{O}$  interactions were not considered until later publications.<sup>11</sup> Whichever point of view is accepted, the  $\text{NO}_2$ --HO hydrogen bond cannot be considered as strong.<sup>12</sup> In contrast,  $\gamma$ -hydroxyethers show a  $\Delta\nu$  of ca.  $86 \text{ cm}^{-1}$ .<sup>7a</sup> The sulfoxide **5** showed a much larger  $\Delta\nu$  (ca.  $245 \text{ cm}^{-1}$ ) than the corresponding sulfone **6** ( $85 \text{ cm}^{-1}$ ).<sup>13</sup>



The rigid molecule, *o*-nitrophenol (**7**), shows a strong intramolecular hydrogen bond ( $\Delta\nu$  ca 340  $\text{cm}^{-1}$ ).<sup>6</sup> This huge shift was ascribed to the importance of charged resonance structures (**7b**) by Schleyer and co-workers. In contrast, the  $\Delta\nu$  due to intermolecular association between nitrobenzene and phenol is ca. 80  $\text{cm}^{-1}$ .<sup>6</sup>



The nitroso group is the most direct congener of the nitro group. Due to a facile rearrangement of alkyl nitroso compounds to form oximes, aromatic cases must be studied.<sup>12</sup> The  $^1\text{H}$  nmr spectrum of the nitroso-phenol **8** shows a peak at ca.  $\delta 17$ , similar to other phenols with strong H bonds to *ortho* substituents. However, tautomeric structures similar to **8b** are present in other cases.<sup>14</sup> PM3 calculations predict that **8b** is 12 kcal less stable than **8a** (in vacuo) and 9 kcal less stable in an aqueous matrix. In **8a**, it is not known whether oxygen (as shown) or nitrogen is the acceptor. PM3 calculations favor the N bonded form in by 0.6 kcal whereas RHF/6-31G\* calculations favor the O bonded form by 0.7 kcal. The IR spectrum of **8** shows concentration insensitive peaks at 3687 and at 3602  $\text{cm}^{-1}$ . Thus, **8** appears to be less strongly intramolecularly H bonded than *o*-nitrophenol **7**.



Kamlet and Taft have established three linear free energy relationships for solvation, two of which are distantly relevant to the present case. Kamlet and Taft's  $\alpha$  scale (H bond acceptance) shows that nitromethane is at the very weak end of the scale (ca. 0), whereas DMSO is strong (0.76). Yalkowski and Banerjee have summarized a host of efforts to quantify group contributions to water solubility.<sup>2</sup> These range from the comparatively simple relationship of Leo, Hansch, and Elkins:  $\log K_{ow}(RG) = \log K_{ow}(RH) + \pi G$ ,<sup>16</sup> to the complex LSER (linear solvation energy relationship) of Kamlet, Taft, and coworkers in its various forms, e.g.  $\log S_w = 0.37 - 0.0530 V_I + 0.8 \pi^* + 3.89 \beta$ .<sup>15,17</sup> In the former case, the effect of replacing hydrogen by groups G (e.g. nitro) upon the octanol/water partition favors solubility in water, but the effect of nitro ( $G = -0.82$ ) less than for carbonyl (-1.2) or hydroxyl or amino (ca. -1.1). In Kamlet's relationship, the terms of interest are  $\beta$ , which refers to the hydrogen bond basicity of the group in question, and also  $\pi^*$ , a dielectric effect.<sup>17</sup> The  $\beta$  term is substantially lower for nitro than corresponding terms for ketones, nitriles, alcohols, etc. Later versions dropped  $\pi^*$  as statistically insignificant. Koppel and Palm favor a multi-parameter approach to solvent polarity:  $A = A_0 + \gamma Y + \rho P + e E + b B$ , which includes polarizability and polarization terms as well as Lewis acidity and Lewis basicity (B). The basicity term is only 58 for nitromethane, compared to 129 for diethyl ether and 193 for DMSO.<sup>18</sup>

Famini and Wilson have extended Kamlet and Taft's LSER approach by including parameters from theoretical calculations.<sup>18</sup> In particular, the terms for the HOMO and for the LUMO are included representing the tendency of the solute to serve as an electron pair donor for a H bond and also to accept the lone pair of water. Nitromethane and sulfones were not among the solvents considered

Gutmann's "donor numbers" represent the interaction of electron-pair donors with  $SbCl_5$ , as determined calorimetrically.<sup>19</sup> The donor number value is extremely low for nitromethane (2.7 kcal/mol), intermediate for sulfolane (14.8), and ethers (ca. 19), and quite high for DMSO (29.8). Clearly, DMSO

shares its non-bonded electrons more easily. In Drago's studies of H bond acceptance with phenol as OH donor, DMSO was an order of magnitude stronger than sulfolane (enthalpy of association 1.6 kcal more favorable).<sup>20</sup> A bifurcated H bond from phenol to the sulfone was tentatively suggested as the reason

Retention time in chromatography is strongly dependent upon H bond basicity of the eluent. In liquid chromatography, Tan and Carr found that nitro compounds were correlated with very low H bond basicity parameters, e.g. nitropropane,  $\Sigma\beta_2H$  of 0.31, compared to 0.45 for diethyl ether and 0.89 for DMSO, Abraham's basicity parameters from gas chromatography studies were used successfully.<sup>21</sup>

In a NMR study of the influence of various compounds on the  $\text{CHCl}_3$  chemical shift (where  $\text{CHCl}_3$  donates a H bond to the compound in question), nitromethane had the smallest effect of any oxygen containing compounds, although the effect was larger than chlorinated solvents. One compilation of data associated with Hildebrand's cohesive energy density values<sup>22</sup> placed nitromethane in the "non-polar" class of solvents.<sup>23</sup>

Dimroth and Reichardt's solvatochromic shift,  $E_T$ , is a measure of solvent polarity based on the UV transition energy for an internal electron transfer in a zwitterionic polynuclear pyridinium compound in the solvent in question. The  $E_T$  values for nitromethane, DMSO and sulfolane, ca. 44 kcal/mol, are in-between hydrocarbons (ca. 30) and water (63 kcal), and indicate similar bulk polarity.

Thus, various experimental findings in the literature are in substantial agreement that nitromethane and sulfones are weak H bond acceptors, but reasons for this behavior are seldom considered.

$^{17}\text{O}$  nmr also has been used to study H bonding. For ketones, the  $^{17}\text{O}$  resonance undergoes a 52 ppm *upfield* shift upon H bonding to OH, probably because the carbonyl  $n \rightarrow \delta \pi^*$  transition is inhibited by H bonding.<sup>x,y</sup> The  $^{17}\text{O}$  signal of neat nitromethane occurred at 608.4 ppm from external  $\text{D}_2\text{O}$ . In a 1:1(v/v) mixture with methanol, the chemical shift of nitromethane was unchanged. However, in trifluoroacetic acid, and in 1:1 sulfuric acid, an upfield shift to 607 and then to 602 ppm occurs. The dimethylsulfone  $^{17}\text{O}$  peak at 166 ppm ( $\text{CDCl}_3$ ) was unchanged in 1:1  $\text{CH}_3\text{OH}$  within experimental error. For the powerfully H bonding DMSO, the  $^{17}\text{O}$  chemical shift moves upfield from 16 ppm (neat) to 12.6 ppm (1:1 v/v,  $\text{CH}_3\text{OH}$ ). This small change may simply be due to a large HOMO/LUMO gap. For DMSO, the gap is 5.20 eV vs. 7.06 eV for dimethyl sulfone, 3.90 eV for acetone, and 3.62 eV for nitromethane. Unfortunately, since the chemical

shift changes are not directly comparable from one molecule to another and since  $^{17}\text{O}$  peaks are broad, this technique is not as revealing as other methods.

### Calculations:

In his classic studies on the water dimer problem, Coulson dissected the H bond interaction of ca. 9 kcal into the electrostatic interaction energy (ca. 6 kcal), repulsive terms (-8.4 kcal), dispersion (3 kcal), and delocalization (8 kcal). Morokuma gave the following components for the 6.6 kcal hydrogen bond energy: electrostatic (8.0 kcal); exchange (-9.86); polarization and dispersion (0.25); and charge transfer (8.16). Other prominent theoreticians gave somewhat similar data.<sup>xx</sup> In contrast, the data from extensive semiempirical calculations were considered to be somewhat erratic by Joesten and Schaad in their authoritative commentary.<sup>xx</sup>

*Ab initio* calculations (Gaussian RHF/6-31G(2d,p) and then at B3LYP/6-31G(2d,p), plus limited runs at the MP2 level were performed on **1-4** and water in an H bonded state, and as separate molecules. When overall energies of interaction with water are considered (“products” vs. “reactants”), DMSO **4** shows the highest level of stabilization, 6.2 kcal (cf. Table II). In comparison, nitromethane **1** shows a small, but nonetheless favorable energy of interaction, 1.55 kcal. This figure is in agreement with findings from very early experimental work.<sup>xx</sup> The calculated H bond geometry was the classical edgewise approach of water to  $\text{NO}_2$ . In the case of nitromethane, attempts to bring the water over the pi system resulted in a chemical reaction in which the oxygen of water became covalently bound to nitrogen. In PM3 calculations, however, approach of water to the pi orbitals of nitromethane was more favorable than the edgewise interaction, although the energy of the interaction thus calculated, 5.1 kcal, seems unrealistic. In general, the orientation of water with respect to nitro seemed rather indefinite, with a number of orientations showing similar interaction energies.

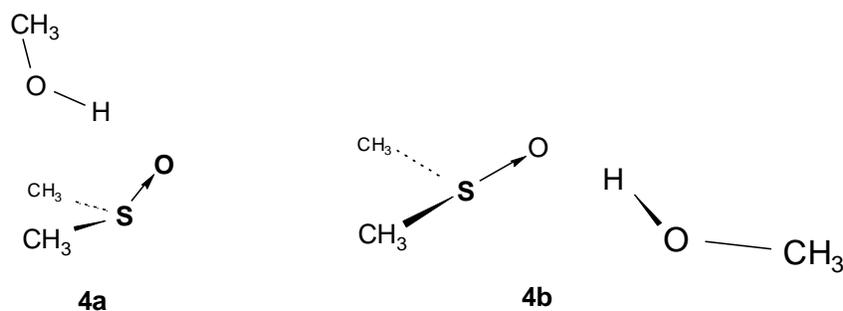
The energy of interaction of water with dimethyl sulfone **2** (2.63 kcal) is somewhat more favorable, than the nitromethane-water interaction. Dimethyl ether **3** shows a 2.54 kcal interaction. In the case of the hypothetical molecule nitrosomethane **9**, difficulty was encountered in achieving an interaction that did not show imaginary frequencies, perhaps due to multiple sites for interaction and a low barrier between states.

. At the RHF/6-31G(2d,p) level, Natural Bond Orbitals (NBO) analysis suggests that a weak interaction of the nitro group with the antibonding (O-H)\* of water (i.e.  $n_{\text{NO}_2} \delta \sigma_{\text{OH}}^*$ ) exists which populates

(O-H)\* by 0.0046 electron. This interaction is an order of magnitude less than the DMSO–H<sub>2</sub>O case (population of (O-H)\* of 0.0588). The NBO second-order perturbation analysis indicates an energy of interaction for  $n_{\text{NO}_2} \delta \sigma_{\text{OH}}^*$  of 1.79 kcal, i.e. a comparatively insignificant value not dissimilar to H-H hyperconjugative interactions in ethane. In the DMSO–H<sub>2</sub>O case,  $n_{\text{SO}} \delta \sigma_{\text{OH}}^*$  is 9.16 kcal; and, in addition, a second interaction of 6.43 kcal exists. Dimethyl ether shows the second highest value (4.63 kcal) for the  $n_{\text{O}} \delta \sigma_{\text{OH}}^*$  interaction, in addition to a second interaction of 2.10 kcal. For dimethyl sulfone, the  $n_{\text{SO}_2} \delta \sigma_{\text{OH}}^*$  interaction is 0.55 kcal (largest of a group of similar interactions). Density function calculations (B3LYP/6-31G(2d,p)) gave roughly similar trends of data, although the energies of interaction were smaller.

The separation of the donor oxygen from the H-O in the best geometry located is: 2.54 Å for nitromethane, 2.49 Å for dimethyl sulfone, 2.06 Å for dimethyl ether and 1.95 Å for DMSO. The H bonded H-O bond distance increases in the same order: 0.942 Å, 0.944 Å, 0.946 Å, and 0.951 Å, compared to 0.941 Å for a free water molecule. Thus, nitromethane barely perturbs water, and the interaction probably is best regarded as mainly electrostatic

Nitromethane shows the lowest energy HOMO (-0.4641) of the compounds of this study (cf. Table II). DMSO exhibits the highest energy HOMO (-0.3594). The parallel between HOMO energies and water solubility is striking (cf. Table I), but probably not directly significant, since many orbitals contribute to the H bond phenomenon. DMSO has the highest energy set of orbitals and also the greatest net drop in energy upon interaction with water (Table II). DMSO—HOCH<sub>3</sub> optimizations avoid the rather serious electrostatic interaction of SO with two OH's of water. These optimizations showed two rather persistent motifs: i.e. **4a** and **4b**. The latter is perhaps unexpected, as the OH lies at the side of S-O, rather than “in line”.



The interaction of DMSO with boron trifluoride was studied in order to see more of a HOMO/LUMO influence on geometry, and to minimize the very strong electrostatic effect present in the water interaction.

The O—B separation distance at the optimum geometry for 1-4 is 2.48, 2.28, 1.67 and 1.57. Only in the latter two cases was non-planarity of  $\text{BF}_3$  appreciable.

To "calibrate" the system, the interaction of dimethyl sulfoxide with hydrogen at the same separation as DMSO to water was investigated. A slight stabilization is found (cf. Table II).

The question remains as to why nitromethane is not more highly water soluble, in view of its small, but favorable, interaction energy. In these investigations, PM3 calculations were used although BSSE corrections were not possible with the software at hand. The approach was to look at larger aggregates of mixed vs. segregated sets of molecules. When "dimers"  $(\text{CH}_3\text{NO}_2\text{--H}_2\text{O})_2$  and "tetramers"  $(\text{CH}_3\text{NO}_2\text{--H}_2\text{O})_4$  are compared to the same numbers of segregated nitromethanes  $(\text{CH}_3\text{NO}_2)_4$  and waters  $(\text{H}_2\text{O})_4$ , the segregated molecules were found to be more favorable in energy. The effect increased monotonically with the numbers of molecules in question. Thus, four nitromethanes with their dipoles antiparallel (energy -2293.5 kcal) and four H bonded waters (energy -907.6) have a 12 kcal energy advantage over the "tetramer"  $(\text{CH}_3\text{NO}_2\text{--H}_2\text{O})_4$  in the best orientation found (-3198.0 kcal). Thus, it appears that the weak nitromethane-water H bond is disfavored compared to the water-water interaction.

In the case of DMSO, calculations show that the "dimer"  $(\text{DMSO--H}_2\text{O})_2$  (-2105.4 kcal) is preferred over segregated molecules (sum of energies: -2099.7 kcal) by 6 kcal. The advantage increases with increasing aggregation, with the "tetramer" 13 kcal more stable than a like number of segregated molecules. These interaction energies are probably high, since BSSE corrections were not possible.

So, why do not nitromethane and dimethyl sulfone H bond to water more forcefully? Our present view is that electrostatic forces draw the OH of water toward the potential H bonding site, where interactions of  $(\text{O--H})^*$  with an array of filled orbitals occurs. The energies of the top five occupied orbitals are listed in Table II for various substrates. For an edgewise approach of water to the nitro oxygens, the HOMO-1 nitro orbital would appear to offer the greatest chances of interaction with the LUMO of water.

Again, the energy differences are rather large. No shared contours were evident when water is present at its most favored location. Shared contours are seen in the HOMO-4 interaction with water.

For dimethylsulfone, like nitromethane, the HOMO resembles in-phase p orbitals on the two oxygens forming a rather diffuse extended molecular orbital. With HOMO-1, an approach to the side of the oxygen would be necessary. In contrast, the DMSO HOMO is highly compact orbital centered on the single oxygen.

In conclusion, a return to the question of reasons for powerful H bonding in *o*-nitrophenol vs. weak H bonding in  $\beta$ -nitroethanol is in order. One immediate difference, of course, is the lower acidity of OH in the acyclic case. The nitro and hydroxyl are merely non-interacting. If the calculation is set up in a classical six-membered H-bonded ring, this geometry is rejected.

In *o*-nitrophenol, the hydroxyl and nitro groups must be coplanar with the aromatic ring for overlap reasons, and the H bonded geometry is of lowest energy. However, the antithesis should also be considered (cf. **2c**). If the hydroxyl hydrogen were directed away from nitro, the lone pair(s) of hydroxyl would be directed toward the lone pairs of the nitro oxygen, a highly repulsive situation.

**Table I**

Comparison of Solutes

<u>Solute</u>	<u>charge on O</u>	<u>dipole moment<sup>a</sup></u>	<u>HOMO Energy</u>		<u>sol/H<sub>2</sub>O<sup>b</sup></u>
			<u>PM3<sup>c</sup></u>	<u>RHF/6-31G(2d,p)<sup>a</sup></u>	
<b>1</b> CH <sub>3</sub> NO <sub>2</sub>	-0.53	4.1 D	-11.97 eV	-0.464 au	9.5
<b>2</b> (CH <sub>3</sub> ) <sub>2</sub> SO <sub>2</sub>	-0.60	4.44 D	-11.40	-0.440	ca. 20
<b>3</b> [CH <sub>3</sub> N=O]	-0.32	2.03 D	-10.34	(-0.406)	
<b>4</b> CH <sub>3</sub> OCH <sub>3</sub>	-0.52	1.3 D	-10.61	-0.433	3700
<b>5</b> (CH <sub>3</sub> ) <sub>2</sub> SO	-0.71	4.3 D	-9.54	-0.365	infinite

- a. From 2 RHF/6-31G(2d,p) calculations with BSSE correction.. Other basis sets and density functional calculations, or semiempirical calculations give different charges, although the order is similar.
- b. Solubility in grams per 100 mL of water.
- c. Calculated by PM3 (HyperChem)

Table II

Energies of Bonding Orbitals (Before) and **After** Interaction with Water

<b>compd</b>	<b>HOMO</b>	<b>H-1</b>	<b>H-2</b>	<b>H-3</b>	<b>H-4</b>
<b>1</b> CH <sub>3</sub> NO <sub>2</sub> --H <sub>2</sub> O	<b>-0.46408</b> (H <sub>2</sub> O orbital)	<b>-0.47372</b> (-0.45426)	<b>-0.50060</b> (-0.48651)	<b>-0.50730</b> (-0.48842)	<b>-0.54847</b> largely H <sub>2</sub> O
<b>2</b> (CH <sub>3</sub> ) <sub>2</sub> SO <sub>2</sub> – H <sub>2</sub> O	<b>-0.44065</b> (-0.43590)	<b>-0.46945</b> (H <sub>2</sub> O)	<b>-0.48068</b> (-0.45915)	<b>-0.49860</b> (-0.48835)	<b>-0.50500</b> (-0.49522)
<b>3</b> CH <sub>3</sub> OCH <sub>3</sub> --H <sub>2</sub> O	<b>-0.43275</b> (-0.41722)	<b>-0.47091</b>	<b>-0.48911</b> (-0.47435)	<b>-0.53890</b> (-0.52878)	<b>-0.54795</b> (-0.55100)
<b>4</b> (CH <sub>3</sub> ) <sub>2</sub> SO--H <sub>2</sub> O rhf 6-31g (2d,p) no plus	<b>-0.36525</b> (-0.35721)	<b>-0.42078</b> (-0.41134)	<b>0.47520</b> (H <sub>2</sub> O orbital)	<b>-0.51450</b> (-0.50930)	<b>-0.54563</b> (-0.54537)
(CH <sub>3</sub> ) <sub>2</sub> SO – He	<b>-0.36450</b>	<b>-0.42028</b>	<b>-0.51852</b>	<b>-0.54977</b>	<b>-0.56798</b>
(CH <sub>3</sub> ) <sub>2</sub> SO – H-H O—H distance 2.01A	<b>-0.36883</b>	-0.42628	-0.50200	-0.55355	-0.56435
(CH <sub>3</sub> ) <sub>2</sub> SO – H-H O—H distance 2.74A, equilibrium RHF6-31+G(2D,P)	<b>-0.36650</b> (-0.36458)	<b>-0.42242</b> (-0.42025)	<b>-0.52206</b> (-0.51835)	<b>-0.55118</b> (-0.54988)	<b>-0.55844</b> (-0.56768)

### Calculation Methods

Calculations were done using Gaussian 94, with an occasional run at Gaussian 98 under identical operating conditions. In general calculations were performed to minimize basis set superposition errors, by using dummy orbitals. Thus, in the calculation of nitromethane or water by itself, the same number of orbitals were used as in the H-bonded combination. Zero point energy corrections from frequency calculations (suitably scaled) were made to the initial RHF or B3LYP calculated energies.

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