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A theoretical study of hydration number of TMAO

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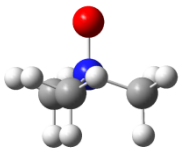


Figure 1.

TMAO, trimethylamine *N*-oxide (Figure 1), is one of the well-known osmolytes. We study the specific interaction between TMAO and water molecules to understand the origin of the osmotic pressure control of TMAO.

First, we performed Monte Carlo (MC) simulation to obtain the water distribution around TMAO. We put 500 water molecules in a cavity with a radius of 15.3 Å, such that the density was 1 g cm^{-3}. We used TIP3P potential set for water, and NPA charges for TMAO. We performed MC calculations at 300K of 2×10^5 MC steps for the equilibration and then 4×10^7 steps for the analysis, from which we calculated oxygen and hydrogen number densities of water molecules around TMAO.

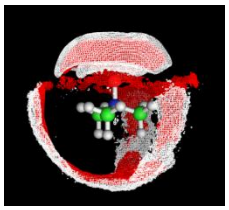


Figure 2.

The water distribution around TMAO is shown in Figure 2, where O number density (red) is larger than 0.09 atoms/$Å^3$ and H number density (white) is larger than 0.12 atoms/$Å^3$. The number of water molecules in the distribution is 11.8. Based on the water distribution (Figure 2), we constructed several kinds of structures of TMAO-$n$$H_2O$ complexes (n=3~12) and optimized the geometries at the theoretical level of MP2/aug-cc-pVDZ. One of them (n=12) is shown in Figure 3. We calculated the interaction energies between TMAO and each or cluster of water molecules with BSSE corrected using CP method. Gaussian 09 was used for all ab initio MO calculations.

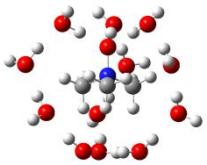
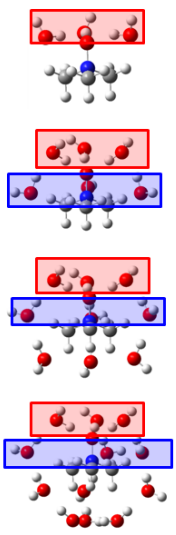


Figure 3.



MP2/aug-cc-pVDZ	kcal/mol
TMAO-h3w (C3)	
ΔE	-33.54
ΔEc2(T-h3w)	-36.18
TMAO-h6w (C3)	
ΔE	-60.93
ΔEc2(T-h6w)	-53.33
ΔEc_2(T-h3w)	-30.6
ΔEc_2(T-m3w)	-11.61
ΔEc_3(T-h3w-m3w)	-11.13
TMAO-o9w (C3)	
ΔE	-83.58
ΔEc2(T-o9w)	-63.75
ΔEc_2(T-h3w)	-32.55
ΔEc_2(T-m3w)	-9.72
ΔEc_3(T-h3w-m3w)	-9.86
TMAO-12w (C3)	
ΔE	-113.95
ΔEc2(T-12w)	-64.38
ΔEc_2(T-h3w)	-31.8
ΔEc_2(T-um3w)	-9.49
ΔEc_3(T-h3w-um3w)	-10.35

Figure 4.
Cluster interaction energies (kcal/mol) between TMAO and water molecules.

Some of the cluster interaction energies are summarized in Figure 4. Hydrogen bonds of three water molecules to the O atom of TMAO are very strong. Rather strong interactions between water molecules and methyl groups of TMAO are also found. Two-body terms are dominant, while three-body terms are also large. The hydration number may depend on the experimental technique used. Theoretically, the number of water molecules which directly surround TMAO may be regarded as ‘hydration number,’ and it is 12.