VIP Hydration

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Hydration of a Chiral Molecule: The Propylene Oxide···$(Water)_2$ Cluster in the Gas Phase**

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Water is one of the most abundant compounds on the surface of earth and is essential for all living organisms. Since nearly all biological molecules required for life are chiral, knowledge about the interactions between small chiral building blocks and water is a prerequisite to the understanding of chemistry of life.[1] Such knowledge is also of great importance for modeling stereoselective organic reactions in water since interactions between chiral molecules and water can significantly influence the outcome of the reactions.[2] In addition, the strong interactions between a chiral solute and water often have significant and nonintuitive effects on chiroptical measurements.[3] Interest in these interactions has intensified with the recent optical rotation studies by Vaccaro and coworkers.[4] Using a sensitive cavity ring-down polarimeter, they measured the optical rotatory dispersion spectrum of the chiral building block propylene oxide (PO) in the gas phase for the first time. Surprisingly, the gas-phase spectrum of PO resembles more closely the corresponding spectrum in water than that in benzene, in contradiction to conventional wisdom. Subsequent theoretical simulations showed that, interestingly, the optical rotation response in an aqueous environment is dominated by that of the binary PO···water complex rather than of the PO monomer itself.[5] In addition, a tentative conclusion that the water molecules bind preferentially to PO in the *anti* rather than in the *syn* position was drawn, by comparing the simulations with the experimental results.[4,5] Here, *anti* or *syn* refers to the side of PO that is opposite to or the same as the methyl group, respectively.

High-resolution spectroscopy can in principle provide a detailed description of interactions between a chiral organic molecule and water molecules. However, it can be highly challenging to achieve spectral assignments for the complexes consisting of a chiral molecule and water because of the large number of structural conformers and the resulting complex spectral patterns. Only a few investigations have been published so far.[6] Very recently, the rotational spectra of a number of PO-containing chiral molecular complexes have been studied, and detailed information about the structures of conformers and their relative stability ordering was reported.[7–9] One of the systems studied is the PO···H_2O binary complex, where both *syn* and *anti* PO···H_2O were detected experimentally.[7] While this experimental result represents a significant step towards understanding the intermolecular interactions taking place in an aqueous environment, there is still a huge gap to bridge between the isolated binary PO···H_2O complex and PO in water. In particular, *syn* PO···H_2O was found to be strongly preferred over the *anti* conformer experimentally,[7] whereas the theoretical modeling predicted *anti* to be a preferred binding position in an aqueous solution.[5] This motivated us to carry out further gas-phase studies of PO sequentially solvated by a few water molecules to bridge this gap. In this work, we report the rotational spectroscopic and high-level ab initio studies of the PO···$(H_2O)_2$ ternary cluster.

Besides pure water clusters,[10] a limited set of ternary clusters with two water molecules, such as Xe···$(H_2O)_2$,[11] HBr···$(H_2O)_2$[12] and formamide···$(H_2O)_2$,[13] have been studied using rotational spectroscopy. Based on the results of these complexes and the PO···H_2O binary complex,[7] we expect that the most stable ternary structures have two primary O–H···O hydrogen bonds since PO can act only as a proton acceptor in a classic H-bond. Specifically, the two water molecules can approach PO from *syn* and/or *anti* directions with respect to the oxirane ring. To aid the spectral search, complete geometry optimizations of the PO···$(H_2O)_2$ conformers were carried out at the level of second-order Møller–Plesset perturbation theory (MP2)[14] using the GAUSSIAN03 software package.[15] Only the basis set 6-311++G(d,p)[16] was employed in this study since it has been tested and proven to give the best agreement with experiments according to our previous studies of related systems.[7,9,17] The three most stable conformers of the PO···$(H_2O)_2$ complex, namely, *syn* PO···$(H_2O)_2$, *anti* PO···$(H_2O)_2$, and *bi* PO···$(H_2O)_2$, were located (see Figure 1). (Detailed structural coordinates from the ab initio calculations are listed in Table S1 in the Supporting Information.) Dashed and dotted/dashed lines in Figure 1 indicate the primary and secondary H-bonds, respectively. Conformers with the *S* form of PO are shown in Figure 1. For every (*S*)-PO···$(H_2O)_2$ conformer, there is a mirror-image (*R*)-PO···$(H_2O)_2$ conformer, and both give rise to the same rotational spectrum. We used (*S*)-PO throughout this study and therefore dropped *S* and *R* notations for simplicity. The minimum potential energy

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nature of the structures shown was confirmed by harmonic frequency calculations, and the corresponding zero-point energies (ZPEs) were obtained. The basis-set superposition errors (BSSEs) were calculated using the counterpoise correction method of Boys and Bernardi.[18] The predicted dissociation energies, rotational constants, and electric dipole moment components of the three conformers are summarized in Table 1. In addition to the three conformers shown in Figure 1, another group of structural isomers was also

Table 1: Calculated dissociation energies (D_e), ZPE-corrected dissociation energies (D_0), counterpoise-corrected dissociation energies (D_0+CP), rotational constants (A, B, C), and electric dipole moment components ($|\mu_{a,b,c}|$) of the three most stable conformers of PO···$(H_2O)_2$ obtained at the MP2/6-311++G(d,p) level of theory.

Parameter	*syn* PO···$(H_2O)_2$	*anti* PO···$(H_2O)_2$	*bi* PO···$(H_2O)_2$
D_e [kJ mol^{-1}]	−71.99	−70.78	−58.73
D_0 [kJ mol^{-1}]	−52.92	−52.19	−42.57
D_0+CP [kJ mol^{-1}]	−33.59	−33.29	−26.14
A [MHz]	3223	3946	3457
B [MHz]	1807	1552	1576
C [MHz]	1602	1346	1257
$\|\mu_a\|$ [D]	0.60	0.63	0.13
$\|\mu_b\|$ [D]	0.06	0.46	0.00
$\|\mu_c\|$ [D]	0.59	0.54	0.64

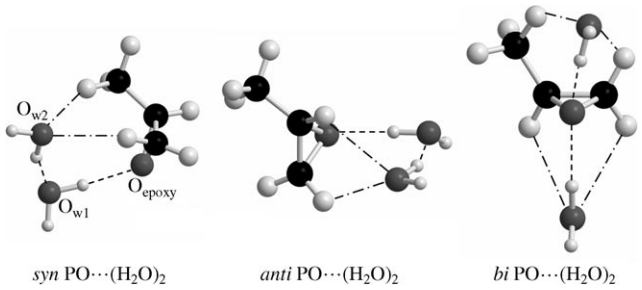

Figure 1. Optimized geometries of the three most stable conformers of PO···$(H_2O)_2$ obtained at the MP2/6-311++G(d,p) level of theory.

considered where one water molecule donates one of its H atoms to PO and the other one to the second water subunit simultaneously. Donating the first H atom reduces the electron density at the O atom and therefore significantly weakens its efficiency in donating its second H atom. Our calculations confirmed that this group of conformers are less stable than *syn* PO···$(H_2O)_2$ by more than 20 kJ mol^{-1}. They were therefore not considered further in the experimental search.

The *syn* and *anti* PO···$(H_2O)_2$ conformers were predicted to be approximately 10 kJ mol^{-1} more stable than *bi* PO···$(H_2O)_2$ by comparison of their D_0 values. The energy difference caused by the binding dissimilarity on the *syn* and the *anti* sides of PO is defined as the diastereofacial discrimination energy,[7,8] $D_0(syn)-D_0(anti)$. This value is about −0.73 kJ mol^{-1} for PO···$(H_2O)_2$. In a molecular-jet expansion, one may expect the most stable conformer, *syn* PO···$(H_2O)_2$, to be substantially more populated than the *anti* conformer, while the much less stable *bi* PO···$(H_2O)_2$ conformer may not be populated enough to be detected experimentally. On the other hand, the predicted relative energy differences depend very much on whether one includes ZPE and/or BSSE corrections. We therefore do not know a priori which conformer is more stable or if all three conformers of the PO···$(H_2O)_2$ complex will be observable experimentally.

To maximize our chance to observe all three conformers, we chose to use He as the carrier gas for initial searches, based on previous experience with the PO dimer,[9] and only used Ne in the final step to confirm the assignment. Transitions due to the PO monomer and pure water clusters were easily identified and excluded using previously measured frequencies.[10,19] Any lines not due to PO-containing clusters were identified by using a sample without PO. Nevertheless, it was still difficult to recognize the *a*-type transition patterns of PO···$(H_2O)_2$, largely because all the conformers are highly asymmetric tops; the asymmetry parameter κ is −0.75, −0.84, and −0.71 for *syn*, *anti*, and *bi* PO···$(H_2O)_2$, respectively. In addition, it was tricky to optimize the water concentration in the pre-expansion sample for the observation of the targeted molecular system. Concentration fluctuation often resulted in large changes in line intensities observed. The initial search for and assignment of the $J=3$–2 stack of the *anti* conformer was successful after substantial trial and error. In total, twenty-one *a*-type transitions were measured for *anti* PO···$(H_2O)_2$, and nineteen for *syn* PO···$(H_2O)_2$. No fine-structure splittings due to internal rotation of the methyl group or tunneling motions of the water subunits were observed for either conformer. There are only four unassigned lines, which could be ascribed to the PO + H_2O molecular systems, measured in the 8–9-GHz region in both Ne and He. None of them could be assigned satisfactorily to the *bi* PO···$(H_2O)_2$ conformer. Further efforts were made to search for this third conformer using a much longer microwave pulse width than the one optimized for *syn* or *anti* PO···$(H_2O)_2$, considering the much smaller μ_a dipole moment component predicted.[20] The search for the stronger *c*-type transitions of *bi* PO···$(H_2O)_2$ also yielded no assignment. We suspect that this higher energy conformer is only sparsely populated in the molecular expansion.

To confirm the identity of the molecular systems assigned, further experiments with an isotopically enriched $H_2{}^{18}O$ sample (70%) were performed. Because there is $H_2{}^{16}O$ in the sample, one may expect four different isotopomers with $H_2{}^{16}O$–$H_2{}^{16}O$, $H_2{}^{18}O$–$H_2{}^{18}O$, $H_2{}^{18}O$–$H_2{}^{16}O$, and $H_2{}^{16}O$–$H_2{}^{18}O$ for *anti* PO···$(H_2O)_2$ and *syn* PO···$(H_2O)_2$, respectively. The initial rotational constants for the rare isotopomers containing ^{18}O were predicted using the calculated geometries and the corresponding shifts between the experimental and calculated rotational constants of the normal isotopomers. It was relatively straightforward to locate the transitions for these rarer isotopomers. The mixed $H_2{}^{18}O$–$H_2{}^{16}O$ and $H_2{}^{16}O$–$H_2{}^{18}O$ isotopomers of the *syn* conformer were not detected as the observed intensities of the normal isotopomer of the *syn* conformer were considerably lower than the *anti* one.

A summary of all measured transition frequencies of the *syn* and *anti* conformers is given in Table S2 in the Supporting Information. They were fitted to a Watson's A-reduction

Table 2: Experimental spectroscopic constants[a] of the two PO···$(H_2O)_2$ conformers, including both normal and $H_2{}^{18}O$ isotopomers.

Conformers	*syn* ^{16}O–^{16}O	*syn* ^{18}O–^{18}O	*anti* ^{16}O–^{16}O	*anti* ^{18}O–^{18}O	*anti* ^{18}O–^{16}O	*anti* ^{16}O–^{18}O
A [MHz]	3200.394(8)[b]	3049.352(5)	3846.901(8)	3622.441(8)	3752.30(1)	3723.46(1)
B [MHz]	1744.6903(5)	1660.8805(3)	1529.8990(4)	1457.7134(4)	1490.570(1)	1492.464(1)
C [MHz]	1556.9635(4)	1461.1292(3)	1311.7199(4)	1234.3055(3)	1273.096(1)	1270.017(2)
Δ_J [kHz]	2.067(5)	1.793(3)	1.351(3)	1.201(3)	1.42(2)	1.16(2)
Δ_{JK} [kHz]	5.74(3)	5.77(2)	8.14(2)	7.81(2)	7.50(9)	7.61(9)
δ_J [kHz]	0.077(3)	0.106(2)	0.142(2)	0.128(2)	0.148(3)	0.126(3)
δ_K [kHz]	0.2(2)	−1.91(9)	−12.6(1)	−10.2(1)	−2.7(6)	−18.5(6)
N	19	24	21	23	17	17
σ [kHz]	1.6	1.8	4.8	3.1	2.3	2.4

[a] Δ_K was fixed at 0.0 in all fits. [b] Standard errors in parentheses are expressed in units of the last digits.

semirigid rotor Hamiltonian in its I^r representation.[21] The resulting spectroscopic constants of all the isotopomers are listed in Table 2. The standard deviations of the spectroscopic fits are a few kHz, in good agreement with the uncertainty of the experimental measurement. The calculated rotational constants agree reasonably well with the experimentally determined values, with the largest deviation being about 3.6%. A rough estimate for the magnitudes of the dipole moment components was obtained from the optimized microwave excitation pulse widths. μ_a was estimated to be around 0.5–1.0 Debye for both conformers, in accord with the calculations. Although *b*- and *c*-type transition frequencies were predicted fairly accurately, no *b*- or *c*-type transitions were observed for either conformer, indicating that μ_b and μ_c are much smaller than μ_a. This observation is contradictory to the ab initio predictions that μ_c of *syn* PO···$(H_2O)_2$, and μ_b and μ_c of *anti* PO···$(H_2O)_2$ are of similar magnitudes to μ_a in these two conformers.

From the good agreements between the experimental and predicted rotational constants, we can infer that the actual geometries of the PO···$(H_2O)_2$ ternary conformers are close to the calculated results. For example, the calculated distance between the O atoms in the two water molecules $R(O_{w1}$–$O_{w2})$ for *anti* PO···$(H_2O)_2$ is 2.78 Å, in reasonable agreement with the corresponding experimental value of 2.82 Å obtained using the experimental isotopic rotational constants and Kraitchman equations.[22] The important structural parameters of these two conformers are listed in Table 3, as well as the corresponding values of PO···H_2O and $(H_2O)_2$. The experimentally determined structural parameters are also included in Table 3 whenever available.[7,10] While the structural parameters of the $(H_2O)_2$ subunits in the *syn* and *anti* PO···$(H_2O)_2$ conformers are very similar, they differ noticeably from those of the pure $(H_2O)_2$. $r(O_{w1}$···H) and $R(O_{w1}$–$O_{w2})$ are about 0.1 to 0.2 Å shorter in PO···$(H_2O)_2$ than in $(H_2O)_2$, while the H-bonding angle ∢ $(O_{w1}$···H-$O_{w2})$ deviates further from linearity in PO···$(H_2O)_2$ than in $(H_2O)_2$. We suggest that these changes occur to maximize the interactions between water and PO, that is, to best solvate the PO molecule with water molecules. We also noted that $r(O_{epoxy}$···H) of the primary H-bond between PO and water is about 0.1 Å shorter in the ternary PO···$(H_2O)_2$ cluster than in the binary PO···H_2O complex. Furthermore, the secondary H-bonds O_{w2}···H–C effectively lock the O atom of the second water in a specific position, with the $r(O_{w2}$···H) values being 2.436 and 2.537 Å in *syn* PO···$(H_2O)_2$, 2.536 and 2.651 Å in *anti* PO···$(H_2O)_2$, considerably shorter than the corresponding distance of 2.71 Å in the *syn* PO···H_2O binary conformer.[7] Overall, the ternary PO···$(H_2O)_2$ cluster is more tightly packed than the corresponding binary complex.

Experimentally, line intensities of the *anti* conformer were found to be twice as high as the *syn* conformer on average. The *a*-type transitions of the two conformers in the same frequency region were used for the comparison since the corresponding dipole moment values were found to be of similar magnitude experimentally. This is very interesting since the diastereofacial discrimination favors the *syn* position in the binary PO···H_2O complex.[7] The addition of the second water molecule must have played a significant role in the diastereofacial discrimination process since the sign of diastereofacial discrimination energy is now reversed! One plausible explanation is that, as the number of water molecules grows, the secondary H-bonding contribution from the methyl group to the O atom of water, which is the deciding factor for the *syn* preference in PO···H_2O, becomes less significant. Rather, the main discriminating factors in PO···$(H_2O)_2$ are maximizing the interactions between the second H_2O and PO, and between the water molecules. The

Table 3: Important structural parameters of the two observed conformers of PO···$(H_2O)_2$ obtained at the MP2/6-311++G(d,p) level of theory, together with the corresponding values of the PO···H_2O and $(H_2O)_2$ complexes. The available experimental values are given in parentheses.

Conformer	*syn* P···$(H_2O)_2$	*anti* PO···$(H_2O)_2$	*syn* PO···H_2O[a]	*anti* PO···H_2O[a]	$(H_2O)_2$[b]
$r(O_{epoxy}$···H) [Å]	1.808	1.800	1.905 (1.908)	1.900 (1.885)	–
$r(O_{w1}$···H) [Å]	1.869	1.868	–	–	1.952
$R(O_{w1}$–$O_{w2})$ [Å]	2.789	2.784 (2.82)	–	–	2.918 (2.98)
∢ $(O_{epoxy}$···H–$O_{w1})$ [°]	168.9	166.2	158.2 (177)	153.1 (161.7)	–
∢ $(O_{w1}$···H–$O_{w2})$ [°]	157.0	156.4	–	–	178.4

[a] Ref. [7]. [b] Ref. [10].

trend observed in going from one to two water molecules is in accord with the theoretical prediction that the *anti* position is preferred for PO in aqueous solution.[5] It would be of great interest to follow the solvation process by sequentially solvating PO with more water molecules to conclusively establish the trend.

In summary, rotational spectra of two H-bonded 1:2 PO···water conformers were measured and analyzed for the first time, and their geometries and stability ordering were established. In particular, the experimental observation shows that the *anti* PO···$(H_2O)_2$ conformer is favored over the *syn* PO···$(H_2O)_2$, opposite to what was observed for the PO···H_2O complex, but in accord with what is predicted for PO in water. The current study is a step further in bridging the gap between the isolated binary PO···H_2O system and PO in water. The present report demonstrates the great potential of high-resolution spectroscopy, in combination with quantum chemistry calculations, for exploring the mechanism of solvation of chiral molecules in aqueous solutions.

Experimental Section

The gas sample mixture consisted of about 0.2% H_2O vapor and 0.09% PO (99+%, Cambridge Isotope Laboratories) in helium (Praxair) carrier gas at a stagnation pressure of about 7 atm. Isotopically enriched $H_2{}^{18}O$ (70%, Cambridge Isotope Laboratories) was used for the isotopic studies. A molecular-beam Fourier transform microwave spectrometer,[23,24] with a General Valve (Series 9) pulsed nozzle of 0.8 mm orifice diameter, was used. The uncertainty of the frequency measurements is about 2 kHz and the full line width at half height is about 18 kHz.

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