Unlocking the Water Trimer Loop: Isotopic Study of Benzophenone-(H$_2$O)$_{1-3}$ Clusters with Rotational Spectroscopy

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Abstract: The synergistic interplay between different kinds of noncovalent interactions is crucial to explain the structures of molecular clusters. In this study, we examined the structures of complexes of benzophenone microsolvated with up to three water molecules by using broadband rotational spectroscopy and the cold conditions of a molecular jet. The analysis of the experimental structures shows that the water molecules dock sideways on benzophenone for the water monomer and dimer moieties, and they move to the top of one of the aromatic rings when the water cluster grows to the trimer. The analysis of the rotational spectra reveals that the water trimer moiety in the complex adopts an open-looped arrangement. In contrast, ab initio calculations face a dilemma of identifying the global minimum between the open loop and the closed loop, which is only solved when zero-point vibrational energy correction is applied. A noncovalent interaction analysis indicates that an OH···H bond and a Bürgi–Dunitz interaction between benzophenone and the water trimer are present in the cluster. This work throws light on the subtle balance between water-water and water-solute interactions when the solute molecule offers several different anchor sites for water molecules.

The way how molecules interact with each other to form molecular clusters is governed by the interplay between different kinds of noncovalent interactions. One important aspect of the process of aggregation is that several noncovalent interactions can operate simultaneously, and even small changes can tip the balance towards one or the other preferred binding scheme. Thus, knowledge of how noncovalent interactions manifest themselves and how they compete and cooperate with each other in small molecular clusters can be essential for a comprehension of molecular aggregation.

There is a long-lasting effort to qualitatively and quantitatively understand the intermolecular interactions of water, since it is a remarkable substance of great importance for life. Water’s chemical-physical properties and its role in biological processes arise from its outstanding capability to form interactions, and water clusters are favored model systems to investigate these inter-water interactions. Back in the 1960s, Morokuma and Pedersen and Kollman and Allen were the first to study the hydrogen bond (HB) between water molecules with ab initio Hartree–Fock calculations. Hanks and co-workers investigated the interaction potential for the water dimer and trimer in 1970. Experimentally, the structures of isolated water clusters of increasing size in the gas phase are still of interest today since the first experimental study of the water dimer. Recently, Perez et al. have employed broadband rotational spectroscopy to determine the structures of different isomers of water clusters up to the water nonamer and decamer using a pulsed molecular jet expansion. Water self-association is dominated by intermolecular HBs. However, when interacting with solute molecules, other noncovalent interactions may appear and alter the structures of water clusters. The characterization of these systems provides new insight into solvation phenomena such as the spectroscopic study of the structures of benzene-(H$_2$O)$_n$ clusters. Thus, it is important to identify the structures not only of pure water clusters, but also of solvated complexes.

Rotational spectroscopy is a method with high resolution and especially useful to determine molecular structures since rotational spectra are highly sensitive to changes in the moments of inertia and thus in the overall mass distribution of the molecules. The two main requirements for rotational spectroscopy are that the experiment needs to be performed in the gas phase and that the molecules or molecular clusters are polar. Combining rotational spectroscopy with the supersonic jet technique allows us to generate and study weakly bound complexes. Typically, the analysis of rotational spectra is supported by quantum-chemical calculations.

The smallest cyclic arrangement of water molecules, the water trimer, is not accessible with rotational spectroscopy due to the lack of a permanent dipole moment in its vibrationally averaged structure. However, when the water trimer is bound to a solute molecule, this overall cluster is usually polar and becomes visible in pure rotational spectra. A few high-resolution molecular spectroscopy studies have explored the water trimer interacting with other molecules, illustrating that the structure of the elusive water trimer is significantly affected by the environment. Resonant ion-dip infrared spectroscopy has demonstrated that the water clusters keep a cyclic structure in the C$_2$H$_6$-(H$_2$O)$_{3.5}$ clusters. Rotational spectroscopy revealed that Ar-(H$_2$O)$_{21}$ is a prolimate symmetric top with Ar located on top of the cyclic water trimer subunit. A similar arrangement was also observed for acenaphthene-(H$_2$O)$_{22}$ and CH$_3$F$_2$-(H$_2$O)$_{23}$. Interestingly, when complexing with β-propiolactone, camphor, glycolaldehyde dimer, or verbenone the water trimer adopts a chain structure. In the formamide-(H$_2$O)$_3$ complex, all molecules, including formamide, are located almost in one plane closing a sequential cycle. It was shown that formamide can act as a substitute of two water molecules, and the formamide-(H$_2$O)$_3$ complex mimics the overall structure of the cyclic water pentamer. The water trimer thus forms different configurations depending on the solute molecule that it interacts with, highlighting the crucial role of the interplay between the water-water and water-solute interactions. A comparison of these studies indicates that the water trimer prefers to form chains when it interacts with the solute molecule as a HB donor through a strong HB such as OH···O, otherwise it prefers the cyclic form. This naturally leads to the question: Which structure will the water trimer adopt when the
The synergistic interplay between different weak interactions is also a challenge for quantum-chemical calculations. Useful predictions of cluster structures require high-level calculations to provide a reliable estimation of noncovalent interactions, while, at the same time, it is important to efficiently explore the complex interaction potential energy surfaces for these clusters with many degrees of freedom. Their potential energy surface is often characterized by shallow and quasi-degenerate local minima, whose number increases with the dimensions (degrees of freedom) and the size of the molecules.\cite{23-29,33} Therefore, experiments providing an energy ranking of different structures corresponding to local minima for a given system can also be useful for benchmarking purposes.\cite{34,35}

Herein, we report the broadband rotational spectroscopy study of microsolvated benzophenone (Ph$_3$CO, Ph = C$_6$H$_5$) to explore the preferred binding positions of water in a stepwise procedure. Complexes with up to three water molecules were observed. In Ph$_3$CO, two aromatic rings are linked by a carbonyl group (Figure S1 in supporting information (SI)). The carbonyl group can interact with water via a HB, whereas any of the two π rings can act as dispersion docking sites.

To accompany the spectroscopic measurements, the initial geometries of the clusters were explored using the program CREST (conformer-rotamer ensemble sampling tool)\cite{36}. This method is efficient for searching for conformations of molecular clusters.\cite{37} The resulting geometries were used as inputs for geometry optimizations at the B3LYP-D4/def2-TZVP level\cite{38} of theory using the Orca program\cite{39}. Computational details are given in the SI. In total, five isomers for Ph$_3$CO·H$_2$O, twelve isomers for Ph$_3$CO·(H$_2$O)$_2$, and 52 isomers for Ph$_3$CO·(H$_2$O)$_3$, were predicted to be real minima. We divided the Ph$_3$CO·(H$_2$O)$_3$ isomers into three types based on their binding topologies: type 1 corresponds to structures including a cyclic water trimer; type 2 structures form a cyclic tetramer via OH···O HBs between the water molecules and the oxygen atom of Ph$_3$CO; in the type 3 structures the water molecules form an open-looped structure (Table S14).

We employed high-resolution chirped-pulse Fourier transform microwave (CP-FTMW) spectroscopy\cite{40,41} in the 2-8 GHz frequency region using the Hamburg COMPACT spectrometer.\cite{42} Details on the experiment, the analysis, and the fitting procedure are given in the supporting information. A gas mixture of benzophenone and water was supersonically expanded into the vacuum chamber to produce the molecular clusters and to cool down the rotational temperature to a few Kelvin. The inherent molecular fingerprint charater of rotational spectroscopy arises from the fact that even small changes in the moments of inertia significantly change the resulting molecular rotational spectrum. Thus, it is possible to differentiate between isomers, conformers, and isotopologues. Based on this advantage, molecular structures can be determined from the experimental dataset of different isotopologues without structural assumptions by solving the Kraitchman equations.\cite{43} This method exploits the shifts in the moments of inertia upon isotopic substitution, often in natural abundance or using enriched samples, to determine the coordinates of the isotopically substituted atom in the principal axis system, allowing building up the substitution structure ($r_s$) atom by atom. In another approach, following a nonlinear least-squares procedure, the least-square mass-dependent geometry ($r_w$) can be determined by fitting partial internal coordinates based on quantum chemical structures to the observed moments of inertia.\cite{44,45}

The rotational spectrum of the Ph$_3$CO monomer has been previously recorded in the 8-14 and 60-73 GHz frequency ranges.\cite{46,47} However, no isotopically substituted data was provided, which is crucial for experimental structure determination. The strongest rotational transition of the Ph$_3$CO monomer in our Ph$_3$CO·H$_2$O$_{18}$O spectrum within 2-8 GHz had a signal-to-noise ratio (SNR) of about 3000:1 (5.6 million free induction decay (FID) acquisitions). This high SNR allowed us to assign all the $^{13}$C mono-substituted isotopologues and even the $^{18}$O isotopologue in natural abundances of 1.1 % and 0.2 %, respectively (Figure S1). Both $r_s$ and $r_w$ structural parameters have been obtained (Table S3 and Figure S2). The torsional angle of the phenyl ring was determined to 32.3(5)$^\circ$ ($r_s$) and 31.12(9)$^\circ$ ($r_w$). No indication of internal motion was observed. This is contrary to the related diphenyl ether system,\cite{48} pointing to a significantly higher barrier than in the diphenyl ether case.

After removing the rotational transitions belonging to the Ph$_3$CO monomer and its isotopologues, a significant amount of transitions still remained in the spectrum (Figure 1). A majority of these transitions could be assigned to the water complexes Ph$_3$CO·H$_2$O, Ph$_3$CO·(H$_2$O)$_2$, and Ph$_3$CO·(H$_2$O)$_3$, using the JB95 program.\cite{49} Refined fits were obtained with the AABS suite\cite{50} employing a standard Watson-type Hamiltonian (S-reduction and $I^r$ representation)\cite{51} as implemented in Pickett’s SPFIT program.\cite{52} Their experimental and theoretical rotational constants are collected in Table 1 and in the SI (Tables S5, S10, S15) together with all observed transitions (Tables S24 - S42). No tunneling splittings arising from water motions were observed for the complexes, different to observations for other water-containing clusters.\cite{21-23,28} In order to achieve a straightforward and unequivocal identification, we performed a second set of experiments using an isotopically enriched water sample containing about 33% H$_2$O$_{18}$O (7.3 million FID acquisitions, 28.5 hours of measurement time). All the $^{16}$O/$^{18}$O water combinations were identified for Ph$_3$CO·H$_2$O and Ph$_3$CO·(H$_2$O)$_2$, providing us with the experimental structures as shown in Figure 2.

In water-containing clusters, the orientation of the OH group of the water molecule can give rise to different conformations with rather similar rotational constants, but different magnitudes of the dipole moment components. For example, the OH of the Ph$_3$CO·H$_2$O cluster can rotate out of plane and result in two minima, conformers 1 and 2 (Table S4). Interestingly, there are eight conformers for Ph$_3$CO·(H$_2$O)$_2$ with comparable rotational constants that can be interconverted by only changing the OH orientations (Table S14).

In order to identify the experimentally observed species among the isomers with similar rotational constants, we estimated the ratios of the dipole moment components by comparing the intensities of nearby rotational transitions according to the formula.\cite{50}
Here, $\mu_a$, $\mu_b$, represent the types of the dipole moment components ($\mu_\perp$, $\mu_\parallel$, $\mu_\parallel$). $I$ is the experimental peak intensity, and $\gamma$ is the simulated intensity of the considered transitions excluding the contribution of permanent dipole moment components. We used transitions with a signal-to-noise ratio better than 5 in the 4-7 GHz frequency region. The estimated ratios $\frac{\mu_a \mu_b}{\mu_c}$ are 1:1:3:0.1 for Ph$_2$CO-H$_2$O, 1:0:4:0.3 for Ph$_2$CO-(H$_2$O)$_2$, and 1:1:4:0.0 for Ph$_2$CO-(H$_2$O)$_3$.

Conformers 1 and 2 (Table S4) of Ph$_2$CO-H$_2$O match the experimentally identified Ph$_2$CO-H$_2$O complex both with respect to the rotational constants and the dipole moment components ratios (1:1:1:0.2 for both conformers 1 and 2). These two conformers only slightly differ in the orientations of the free OH group of the water molecule. The hydrogen atom of the free OH of conformer 1 rotates out of the ab plane of Ph$_2$CO (Figure 2), whereas that of conformer 2 is located in the ab plane (Table S4). Both conformers are computed to be almost isoenergetic (with and without zero-point vibrational energy (ZPVE)). The next conformer is about 4.5 kJ/mol higher in energy. To provide further information for the assignments, we calculated their planar moments of inertia $P_{cc}$, which indicate the mass distribution out of the ab inertial plane. The $P_{cc}$ value of conformer 1 (50.11 μÅ$^2$) is in agreement with that of the experimentally observed Ph$_2$CO-H$_2$O complex (51.23828(56) μÅ$^2$), while the $P_{cc}$ value of conformer 2 (47.68 μÅ$^2$) is closer to the experimental $P_{cc}$ value of the Ph$_2$CO monomer (47.56578(13) μÅ$^2$). Thus, we assign conformer 1 to the experimentally observed structure.

The structure of Ph$_2$CO-(H$_2$O)$_2$ can be assigned to the most stable conformer (conformer 1) by comparing the experimentally obtained rotational constants and the extracted ratios of the dipole moment components with the theoretical ones (Tables 1 and S9). The identified structures for Ph$_2$CO-(H$_2$O)$_2$ can be further confirmed with the experimental $r_0$ and $r_0^\delta$ structures. We searched for the other predicted Ph$_2$CO-H$_2$O and Ph$_2$CO-(H$_2$O)$_2$ structures, but the remaining rotational transitions could not be assigned to any of the predicted Ph$_2$CO-H$_2$O and Ph$_2$CO-(H$_2$O)$_2$ isomers.

Figure 1. Broadband rotational spectrum of Ph$_2$CO with water. The black upper trace corresponds to the experiment (average of 5.6 million FIDs, 22 h of acquisition time). All rotational transitions arising from the Ph$_2$CO monomer and its isotopologues have been removed. The lower traces represent simulations produced with the experimental spectroscopic parameters, a rotational temperature of 1 K, and the theoretical dipole moment components (Table 1) for Ph$_2$CO-H$_2$O (red), Ph$_2$CO-(H$_2$O)$_2$ (blue), and Ph$_2$CO-(H$_2$O)$_3$ (green), respectively. At the bottom, parts of the spectra highlight representative transitions from each of the three complexes.
The theoretical structures (B3LYP-D4/def2-TZVP) of the Ph$_2$CO–H$_2$O$_{1-3}$ complexes are shown in Figure 2, with the experimentally derived atom positions superimposed. To investigate and visualize the intermolecular interactions, we used the noncovalent interaction (NCI) approach [39] which is based on the electron density and its derivatives. It indicates where strong HBs (blue) and weak attractive interactions (green) occur. The observed clusters consist of a network of multiple noncovalent bonds. In each case, one water moiety is anchored to the carbonyl group through an O$_w$–H···O$_w$ HB (in the subscript, w denotes water, C=O is the carbonyl group). For Ph$_2$CO–H$_2$O, the water molecule almost lies in the ab symmetry plane of the Ph$_2$CO monomer, as discussed, and is locked through a secondary C–H···O$_w$ interaction, which explains the observed lack of water tunneling. For Ph$_2$CO–(H$_2$O)$_2$, the second water interacts with the first water molecule as a proton donor through an O$_w$–H···O$_w$ HB and is reinforced by two bifurcated weak C–H···O$_w$ interactions with the two adjacent hydrogen atoms of the phenyl group, with computed distances of 2.69 Å and 2.77 Å. The distances and angles defining those intermolecular interactions have been characterized experimentally by $r_s$ and $r_{el}^{(1)}$ structures. They are in good agreement with the $r_s$ structure using the DFT-D4 method (Figures 2, S3, S6, and Tables S7, S12).
The second water and the phenyl ring interact with the lowest energy complexes, with the lowest energy complex of this group being about 6.5 kJ/mol higher in energy than those of the other five type 3 isomers (vide supra). The principal axis frames of Ph$_2$CO-(H$_2$O)$_2$ and Ph$_2$CO-(H$_2$O)$_3$, respectively. The structural parameters of the hydrogen bonding network of this complex (15.1 kJ/mol) were employed to determine their relative energies (Figure S11). Most of them predict the open-looped-(I) structure as the global minimum, while the DLPNO-CCSD(T) method suggests the CW-(I) structure to be the most stable conformer. The B3LYP-D3(BJ)/def2-TZVP method energetically prefers the CCW-(I) structure. However, with the addition of ZPVE and BSSE corrections, all methods identify the open-looped-(I) as the global minimum (see its structure and partial structural information in Figure 2), except for the MP2/6-311++/g(d,p) method, which predicts the CCW-(I) and the open-looped-(I) structure to be quasi isoenergetic (within 0.2 kJ/mol (Tables S14 and S19).

For the remaining complex (15.1 kJ/mol), the two OH groups of one water molecule act as proton donors for HBs (bifurcated structure). For conciseness, only the most stable structures (open-looped-(I), (II), CW-(I), and CCW-(I)) will be discussed here (Figure 3).

Nine computational methods were employed to determine their relative energies (Figure S11). Most of them predict the open-looped-(I) structure as the global minimum, while the DLPNO-CCSD(T) method suggests the CW-(I) structure to be the most stable conformer. The B3LYP-D3(BJ)/def2-TZVP method energetically prefers the CCW-(I) structure. However, with the addition of ZPVE and BSSE corrections, all methods identify the open-looped-(I) as the global minimum (see its structure and partial structural information in Figure 2), except for the MP2/6-311++g(d,p) method, which predicts the CCW-(I) and the open-looped-(I) structure to be quasi isoenergetic (within 0.2 kJ/mol (Tables S14 and S19).

For the Ph$_2$CO-(H$_2$O)$_3$ complex, quantum-chemical calculations (B3LYP-D4/def2-TZVP level) predict eight local minima with rather similar rotational constants within a relative energy window of about 15 kJ/mol after ZPVE and basis set superposition error (BSSE) corrections (Table S14). Three of them, with corrected relative energies of 0, 4.6, and 7.3 kJ/mol, respectively, are type 3 open-looped structures (vide supra). They differ from each other in the orientation of the free OH group. In the open-looped-(I) and (II) structures, an O-H⋯π bond between the second water and the phenyl ring is formed. In the open-looped-(III) structure, the free OH group of the second water molecule points to the opposite direction of the π ring. This last arrangement could cause a higher relative energy. The other five isomers belong to the type 1 group, in which water molecules form a cyclic trimer, with the lowest energy complex of this group being about 6.5 kJ/mol higher in energy. Their structures differ in the orientation of the hydrogen bonding network of the water trimer. Two structures adopt a clockwise (CW) and the other two a counterclockwise (CCW) orientation.
Despite an intense search, only one Ph₃CO-(H₂O)₃ cluster could be identified in the spectrum. The barrier to unlock the cyclic water trimer, which means to pass from CW-(I) to open-looped-(I), is computed to be 2.1 kJ/mol (at the B3LYP-D4/def2-TZVP level, Figure S12). Most probably, this low barrier cannot prevent the cyclic water trimer from breaking its hydrogen bonding during the relaxation process upon rapid cooling in the supersonic expansion. Typically, two angles are used to characterize this unexpected O···C bond, we evaluated the presence or absence of bonds stabilizing the complexes. The bond critical points (BCPs) and bond paths illustrate the interaction O₃···C=O formed in the open-looped-(I) structure (Figure S14) but absent in the CCW-(I) and CW-(I) structures. This interaction, where the nucleophilic oxygen of the water molecule attacks the carbonyl carbon with a direction of about 90°, corresponds to the so-called Bürgi–Dunitz interaction. This kind of interaction has received great attention, partly due to its ubiquity across chemistry and biology. For instance, it has been demonstrated to play an important role in dictating protein structures. In the investigation of the thermostability of the proline-rich protein collagen these interactions led to a robust structure despite a relatively low potential for hydrogen bonding. Typically, two angles are used
to characterize the trajectory of the nucleophile, the Bürgi–Dunitz (αBD) and the Flippin–Lodge (αFL) angle. For Ph2CO-(H2O)3, αBD and αFL are experimentally determined to be around 95(1)° and 4(2)°, respectively (Figure 4(a)). These interactions have been discussed to result from electron donation. The Bürgi–Dunitz trajectory can maximize the overlap of the lone pair (nπ) of the nucleophile with the π* orbital of the acceptor carbonyl group. Natural bond orbital (NBO) analysis can provide insight into the nπ-π* interaction. As shown in Figure 4(b), the structure of Ph2CO-(H2O)3 presents a large overlap between the nπ orbital of O3 and the π* orbital of the carbonyl group with a stabilization energy of 3.6 kJ/mol (Table S17).

Figure 4. (a) Bürgi–Dunitz trajectory and (b) overlap of the nπ donor orbital of the water oxygen with the π* orbital of the carbonyl group. In panel (a), the green plane is defined by the carbonyl group and its adjacent carbon atoms, and the blue plane is defined by the oxygen atom of the third water, the carbonyl carbon atom, and the carbonyl oxygen atom. The angle between the direction of nucleophilic attack (red dashed line) and the C=O bond corresponds to αBD, which is 98.5° at the B3LYP-D4/def2-TZVP level of theory, and 95(1)° in the experimental structure (εnπ). The angle between the direction of nucleophilic attack and its projection on the plane perpendicular to the plane of the carbonyl group (green plane) corresponds to αFL, which can be expressed with the formula αFL = asin(sin(αBD)·cos(β)), where β is the dihedral angle defined by the blue and green planes, αFL = 2.7° at the B3LYP-D4/def2-TZVP level of theory, and 4(2)° in the experimental structure (εnπ). The distance of nucleophilic attack is 3.08(2) Å and 3.03 Å in the experimental and theoretical structures, respectively.

In summary, we present a rotational spectroscopy study of Ph2CO-(H2O)3 (n=1-3) clusters. The unambiguous identification and accurate structural parameters of these complexes are reported. When the cluster size grows from n=1,2 to n=3, the water bonding moieties move from the side of the phenyl group to the top of the aromatic π cloud. For the n=3 complex, a structure with the water trimer subunit forming an open-looped arrangement like an isosceles right-angled triangle was experimentally observed; in contrast, quantum-chemical calculations struggle to identify the global minimum among the cyclic and open-looped isomers. An additional OH--π bond and a Bürgi–Dunitz interaction stabilize the Ph2CO-(H2O)3 complex. Our results show the importance of the synergistic effect of different kinds of noncovalent interactions in the molecular aggregation. The cooperative use of theoretical calculations and rotational spectroscopy is powerful to determine structural information of water-solute clusters and the intermolecular interactions at play. Experimental results can be used to benchmark theoretical calculations, which in turn could facilitate the experimental analysis of new unexplored systems.

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Conflict of interest

The authors declare no conflict of interest.

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The subtle discrepancy between the experimental and theoretical structures of the Ph₂CO-(H₂O)₃ complex has been unveiled. An open-looped structure, instead of the cyclic structure, of the water trimer moiety over one of the π clouds was determined by rotational spectroscopy.

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