Structural relationship between a host included chain of spirocyclic water hexamers and bulk water – the role of water clusters in self assembly and crystallization processes†

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Infinite chains of spirocyclic water hexamers are included in the crystal lattice of a tin complex with a curved, hydrophobic surface and only weak intermolecular bonding interactions between the host molecules, so that the enclosed water clusters might be reminiscent of the solvation sphere in solution.

Since water is nature's solvent, the scientific community requires profound knowledge on the structural composition of gaseous, liquid and solid water assemblies.[1–5] In particular, medium-sized and larger water clusters have important attributes, since they are (i) surrounding and solvating solutes and biologically active molecules such as sugars, proteins, DNA, vitamins, etc., (ii) filling discrete voids and channels in molecular and supramolecular assemblies including the reactive sites in enzymes, (iii) interpenetrating into the interfacial region of hydrophobic surfaces, and (iv) involved in dynamic processes such as proton transport, protein folding, membrane formation, micellar assembly, etc.[5c,5e,6,7]

In the self-assembly processes of host–guest systems water molecules may play different roles: either they just fill the voids left by the host-aggregate[6] or they play an active role in the assembly of the host structure in form of the water clusters present in bulk liquid water.[8] Creating knowledge on both situations is important, in the first case because the microscopic organization of the water molecules in the bulk liquid phase is revealed, and in the second case because the structural flexibility and adaptability of water clusters comes to light.

In a continuation of our efforts to structurally elucidate supramolecular systems containing hydrogen bonding interactions with water molecules,[6g,9] we have now discovered a host with a high affinity to water molecules, but apparently a very low potential to form intermolecular host···host interactions. There is a certain probability that this system contains intact cluster fragments from bulk water.

Compound **1** is a tin complex with three sites available for regular hydrogen bonding interactions, one N–H donor group and two phenolic oxygen atoms as acceptor groups.[10] The remaining

functional groups are capable to participate only in weaker intramolecular bonding like C–H···X, π–π and van der Waals interactions.
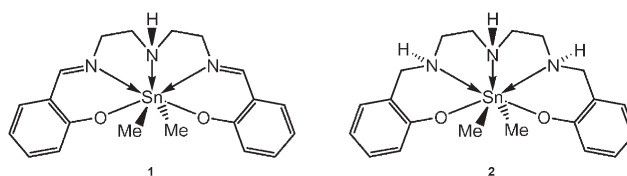
In the solid state this molecule adopts a very particular curved conformation (Fig. 1), having a hydrophobic outer sphere that is only partially interrupted by the presence of the N–H donor and O_{Ph} acceptor sites. This spatial distribution of the electron density inhibits the formation of stronger intermolecular interactions between molecules of compound **1**, but allows for the simultaneous interaction with one or more guest molecules. Upon crystallization of **1** from a solution of ethanol–water a hydrate of the composition **1**·2.5H_2O is formed that has been characterized by X-ray crystallography at 100 K.‡

In accordance with the space group determined for the crystals of **1**·2.5H_2O, $P4_2bc$, in the crystal lattice molecule pairs of **1** are organized along the 4_2 axis in mutual perpendicular orientations, thus giving rise to channels that are filled by chains of spirocyclic water hexamers. The perspective views shown in Fig. 2 demonstrate that units of four host molecules resemble the conformation of calixarenes or cyclodextrins. These cone-shaped assemblies are packed in a head-to-tail arrangement along axis c.

Within the chain the hexameric water rings are orthogonal to each other and are joined in a spiro-type way at the 1,4 positions. This chain can be also described as crossed double helix formed from two polymeric water chains.
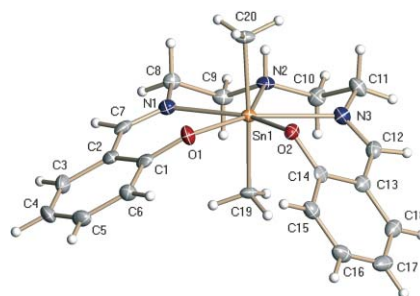
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[b] Programa de Ingeniería Molecular, Instituto Mexicano del Petróleo, Eje Central Lázaro Cárdenas 152, Col. San Bartolo Atepehuacan, México D.F., México

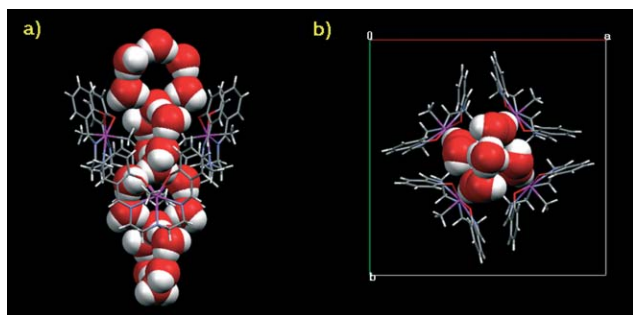**Fig. 1** Perspective view of the molecular structure of compound **1**.

Fig. 2 Two views of the host–guest complexes present in the crystal lattice of **1**·2.5H$_2$O, showing the encapsulation of the water chains by the hydrophobic host molecules that are arranged in a cone-like conformation.

The complete cluster structure is built up from only three crystallographically independent water molecules W1, W2 and W3, of which one is located on the 4$_2$ axis (Fig. 3). The $O_W \cdots O_W$ distances vary from 2.717(4)–2.883(4) Å† and cover the range found for ice (2.76 Å for ice I_h at 90 K)[11] and bulk liquid water (2.85 Å).[1a] The $O_W \cdots O_W \cdots O_W$ bond angles vary from 112.5 to 126.9° and are significantly larger than the tetrahedral angle found in ice I_h and I_c. The $O_W \cdots O_W \cdots O_W \cdots O_W$ torsion angles have values of 12.8, 13.9 and −24.7°, indicating a twisted, but on the other hand an almost planar conformation of the hexameric cycles. It is important to mention that planar conformations for the cyclic water hexamer (H$_2$O)$_6$ have been characterized previously by experimental and theoretical methods.[1c,1d]

Interestingly, such a tape of hexameric water clusters is inherent in both the hexagonal and cubic ice modifications,[6g] however, with the difference that the hexameric water units within the tapes described above do not adopt chair- or boat-conformations. In order to answer the question, whether the most stable conformation of the hexameric rings within water clusters similar to that shown in Fig. 3 is planar, chair, boat, twisted, *etc.*, further studies will be necessary, but it may be supposed that the energy differences are small.

For **1**·2.5H$_2$O all hydrogen atoms could be localized by difference Fourier maps. Unlike in other water systems, disorder was not observed in this case. Within the hexameric rings of the water clusters two water molecules (W3) form only interactions to further water molecules, one acting as twofold hydrogen donor and the other one as twofold acceptor; the remaining four water molecules function as onefold donor and acceptor to neighboring water molecules each and participate furthermore in hydrogen bonding interactions with the host-system (W1 and W2). Of these, the water molecules labelled W2 in Fig. 4 are tetra-coordinate, forming one bridge to a phenolate oxygen O2 (2.79 Å, 172°) and
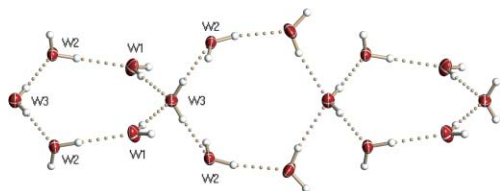

Fig. 3 Fragment of one of the infinite water chains present in the crystal lattice of **1**·2.5H$_2$O and **2**·2.5H$_2$O.

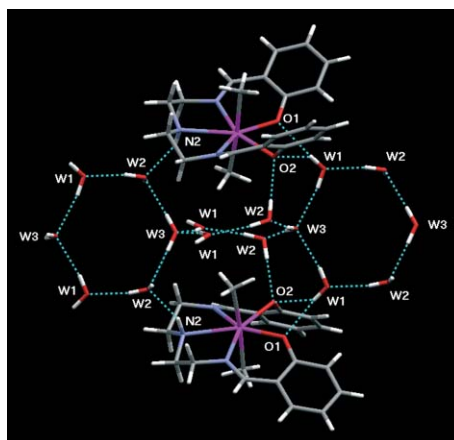**Fig. 4** Fragment of the crystal lattice of **1**·2.5H$_2$O, showing part of the hydrogen bonding interactions between the water cluster and the host molecules. For clarity only two of the four host molecules surrounding the cluster fragment are shown.

another one to a N–H group of neighboring host molecules (2.97 Å, 158°). The water molecules labelled W1 are only three-coordinate, but form a bifurcated hydrogen bridge to the two phenolic oxygen atoms of one and the same host molecule (2.90 Å, 148° and 3.12 Å, 137°; Fig. 4). This is a very interesting observation, since the occurrence of such bifurcated interactions has been predicted for bulk liquid water.[1a]

Because the above described water cluster has a structural relationship to the water aggregates present in the most important ice modifications I_c and I_h, and those existing in bulk liquid water,[1a,6g] it is probable that part of the water cluster has been included as it is found as such within the solvent surrounding the solute. It is known that water clusters play an active role during self assembly and crystallization processes.[8] Although this is a complicated phenomenon due to the dynamics involved, a closer look at the final products may help to improve understanding, especially if part of the participating clusters are trapped in the interior of the resulting crystal lattice.

In order to elucidate the role of water clusters in the crystallization process of **1** further, two strategies have been applied. Firstly, we have crystallized compound **1** from solvents other than water in order to examine, whether the structure of the host molecules is maintained or changed. Secondly, we modified the structure of compound **1** in order to enhance the number of sites available for hydrogen bonding interactions and to evaluate the strength and flexibility of the guest water cluster. With respect to the first experiment, crystals suitable for X-ray crystallography could be grown from MeOH and DMSO, giving **1**-MeOH and **1**-DMSO. Interestingly, in both cases hydrogen bonding interactions are present between the host and the guest molecules,† however, in comparison to **1**·2.5H$_2$O two completely different supramolecular arrangements have been identified.§ In this respect it is important to note that the organic backbone of methanol would be small enough to fit in the channels formed by compound **1** in **1**·2.5H$_2$O. Although the methanol molecules present in **1**-MeOH show the same bifurcated hydrogen bonding interaction as water W1 in **1**·2.5H$_2$O, the supramolecular arrangement is different, which clearly demonstrates that water-clusters play an active role during the crystallization of **1**·2.5H$_2$O, and do not just

fill empty cavities. With respect to the second strategy complex **2** has been prepared by reduction of the imine functions in compound **1**, giving a complex with three N–H donor groups instead of one. Although there is a strong similarity in the overall configurations of compounds **1** and **2**,† the enhanced number of hydrogen bonding sites should permit a different organization of the host–guest complex, if the water clusters found in **1**·2.5H$_2$O would not have an extraordinary stability or play a central role during the crystallization process. It was indeed somewhat surprising for us to find that the unit cell dimensions for crystals obtained from a solution of **2** in ethanol–water were very similar to those of **1**·2.5H$_2$O, especially with respect to axis c, the main axis of the included water aggregate.¶ The hydrogen bonding system found in **2**·2.5H$_2$O is practically identical to that of **1**·2.5H$_2$O, however, there are variations in the geometric parameters: $O_W \cdots O_W = 2.735(6)–2.925(7)$ Å, $O_W \cdots O_W \cdots O_W = 107.3–130.5°$ and $O_W \cdots O_W \cdots O_W \cdots O_W = -13.7, -16.8$ and $28.2°$. These variations in the bonding geometry may be attributed to the flexibility of water clusters, however, the fact that almost identical water clusters are found in the two crystal lattices shows that this cluster possesses enhanced stability and may play an important role in the activity of liquid water.

In conclusion, this contribution has shown that careful X-ray crystallographic studies of organic and inorganic hydrates can contribute important findings to the understanding of water cluster chemistry. This is because fragments of these assemblies may be trapped by appropriate supramolecular hosts that possess functional groups with the proper spatial distribution to stabilize the cluster when it is removed from its natal medium. It should be noticed that the functional groups in compounds **1** and **2**, which are interacting with the water assembly described herein (NH, O), are very common also in biologically active molecules like amino-acids, peptides, *etc.*, so that this and similar systems may function as models to study composition, structure, thermodynamics and dynamics of aggregates formed between these molecules and larger water clusters, in particular within the ion channels present in cell membranes.

Notes and references

‡ *Crystal data* for **1**·2.5H$_2$O: C$_{20}$H$_{25}$SnN$_3$O$_2$·2.5H$_2$O, $M_r = 503.16$ g mol^{-1}, $0.16 \times 0.18 \times 0.52$ mm^3, tetragonal, space group $P4_2bc$, $a = 20.3573(11)$, $c = 10.4631(9)$ Å, $V = 4336.1(5)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.542$, $2\theta_{max} = 25$, 3833 independent reflections, $R_1 = 0.033$ for 3672 reflections with $I > 2\sigma(I)$ and w$R_2 = 0.083$ for all data, 303 parameters. CCDC 273789. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b509787h

§ *Crystal data* for **1**·MeOH: C$_{20}$H$_{25}$SnN$_3$O$_2$·MeOH, $M_r = 490.16$ g mol^{-1}, $0.11 \times 0.11 \times 0.41$ mm^3, orthorhombic, space group $P2_12_12_1$, $a = 12.1196(8)$, $b = 12.5833(8)$, $c = 13.8292(9)$ Å, $V = 2109.0(2)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.544$, $2\theta_{max} = 25$, 3717 independent reflections, $R_1 = 0.029$ for 3641 reflections with $I > 2\sigma(I)$ and w$R_2 = 0.064$ for all data, 262 parameters. CCDC 273788. *Crystal data* for **1**·DMSO: C$_{20}$H$_{25}$SnN$_3$O$_2$·DMSO, $M_r = 536.25$, $0.20 \times 0.25 \times 0.38$ mm^3, orthorhombic, space group $Pnna$, $a = 20.362(2)$, $b = 15.5806(19)$, $c = 7.5321(9)$ Å, $V = 2389.6(5)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.491$, $2\theta_{max} = 25$, 2184 independent reflections, $R_1 = 0.032$ for 1941 reflections with $I > 2 \sigma(I)$ and w$R_2 = 0.079$ for all data, 150 parameters. CCDC 273791. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b509787h

¶ *Crystal data* for **2**·2.5H$_2$O: C$_{20}$H$_{29}$SnN$_3$O$_2$·2.5H$_2$O, $M_r = 507.19$, $0.08 \times 0.09 \times 0.42$ mm^3, tetragonal, space group $P4_2bc$, $a = 20.8481(12)$, $c = 10.4021(9)$ Å, $V = 4521.2(5)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.490$, $2\theta_{max} = 25$,

3958 independent reflections, $R_1 = 0.043$ for 3416 reflections with $I > 2\sigma(I)$ and w$R_2 = 0.091$ for all data, 310 parameters. CCDC 273790. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b509787h

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