Helical water chains in aquapores of organic hexahost: remarkable halogen-substitution effect on the handedness of water helix†

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Water helices surrounding the nano-channels of trichlorophloroglucinol and tribromophloroglucinol have different handedness, *PMPMPM* and *PPPMMM* (*P* = right-handed, *M* = left-handed), depending on halogen···halogen interactions between the host molecules.

Water is the most studied and yet the least understood of chemical species.[1] Water has attracted considerable attention from structural chemists and biologists because of its importance in gas hydrates, its different topologies, and the important role of water in the structure, conformation and function of nucleotides and peptides as well as in protein–DNA binding. The helical motif is central to biology and life: apart from the structure of DNA, cooperative helical assemblies are functional in transport mechanisms, *e.g.*, as in plasma membrane of red blood cells, renal tubules, gramicidin A and aquaporin-1.[2] The inclusion of water in zeolite-like 3D network structures,[3a,b] negative thermal expansion of water helix in an organic crystal,[3c] and water conduction through the hydrophobic channel of a carbon nanotube[3d] are reported in recent papers. There is a surge of interest in applying supramolecular chemistry principles[4] to study water structures, notably the idea that the constrained microenvironment of organic and metal–organic host lattices is an excellent solid-state medium to isolate and analyze various hydrogen-bonded water clusters.[5] These "water trapped in a host matrix" structures have provided accurate and detailed information about hydrogen bonding in diverse water clusters. However, the unusual topology or architecture of hydrogen-bonded water is generally observed only in a specific host lattice. Therefore, relationship between the water topology and the host structure is difficult to delineate. Ideally, one would like to see similar water motifs (*e.g.* 1D chain, 2D layer or 3D networks) in closely related host structures. To our knowledge, there is only one such pair of structures, a $(H_2O)_{10}$ cluster of ice-like water molecules in the supramolecular complex of Cu and Co with the same ligand, reported by Atwood and coworkers.[5c,d] We report in this paper infinite 1D helical chains of water molecules in nanoporous channels of organic hexahosts trichlorophloroglucinol and tribromophloroglucinol, Cl–PHG.$(H_2O)_3$ and Br–PHG.$(H_2O)_3$. Interestingly, weak halogen···halogen interactions appear to direct the handedness of water helices surrounding a rod of Cl–PHG or Br–PHG host molecules. There are very few examples of helical water assemblies[3c,5k,5m] in the infinite water chain category.[6]

X = Cl, Cl-PHG.$(H_2O)_3$
X = Br, Br-PHG.$(H_2O)_3$
X = I, I-PHG
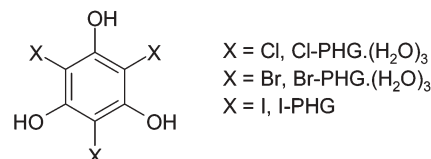
Cl–PHG crystallizes as a trihydrate from EtOAc. The X-ray crystal structure of Cl–PHG.$(H_2O)_3$ in $P2_1/n$ space group‡ has one host and three symmetry-independent water molecules. The heavy atoms are fully ordered but phenol OH and one of the water H atoms are disordered,† even at 100 K. Inversion-related molecules of Cl–PHG stack at van der Waals distance in a Piedfort Unit[7] assembly (π···π 3.28, 3.41 Å) to form a hexahost dimer with six phenol OH groups radiating outwards (Fig. 1a). Three phenol OHs (O1, O2, O3) are hydrogen-bonded to crystallographically distinct water molecules (O4, O5, O6), which are in turn H-bonded to phenol acceptor groups (O1, O3, O2; O···O 2.70–2.83 Å). The second donor hydrogen of the water molecule is used in H-bonding with itself to form a helical spine of O_w–H···O_w hydrogen bonds (helix pitch = 6.93 Å = *a*-axis; Fig. 1b). Six such helices of tetracoordinated water molecules surround a Piedfort stack of Cl-PHG host molecules. The almost flat *bc*-layer has a hexagonal arrangement of Cl–PHG molecules mediated *via* phenol groups, water molecules, and Cl···Cl contacts.[8] The trigonal nanotube containing the 1D helical water polymer along the *a*-axis has a pore of ∼4.6 Å on each side. The disorder of phenol H atoms in Cl–PHG.$(H_2O)_3$ could be due to intramolecular O–H···Cl interactions[9] with the flanking chlorine atoms.

The crystal structure of Br–PHG.$(H_2O)_3$ (crystallized from EtOAc/CHCl₃, $P2_1/c$ space group) shows similarities and differences compared to Cl–PHG trihydrate. All host and water atoms, including hydrogens, are fully ordered. The host Br–PHG molecules adopt a similar hexagonal arrangement (triangular pore size ∼4.6 Å) and are bonded to six water molecules *via* phenol OH groups (O···O 2.72–2.98 Å). However, the handedness of water helices (helix pitch = 7.11 Å = *a*-axis; Fig. 1c,d) surrounding a Piedfort stack (π···π 3.30, 3.37 Å) of Br–PHG host molecules is different (Fig. 2). The six water helices (O_w–H···O_w) encircling a rod of Cl–PHG host molecule are alternately right- and left-handed (*PMPMPM*; *P* = plus or right-handed, *M* = minus or left-handed) whereas their alignment in Br–PHG trihydrate is, surprisingly, three contiguous helices of the same chirality and the other three of opposite helicity (*PPPMMM*). The latter situation is novel among helical water chains.[5k] The water helix has homodromic chains of O_w–H···O_w hydrogen bonds (cooperative H-bonding) in the fully ordered Br–PHG.$(H_2O)_3$ structure.§ Two factors should be considered to understand these differences: (1)
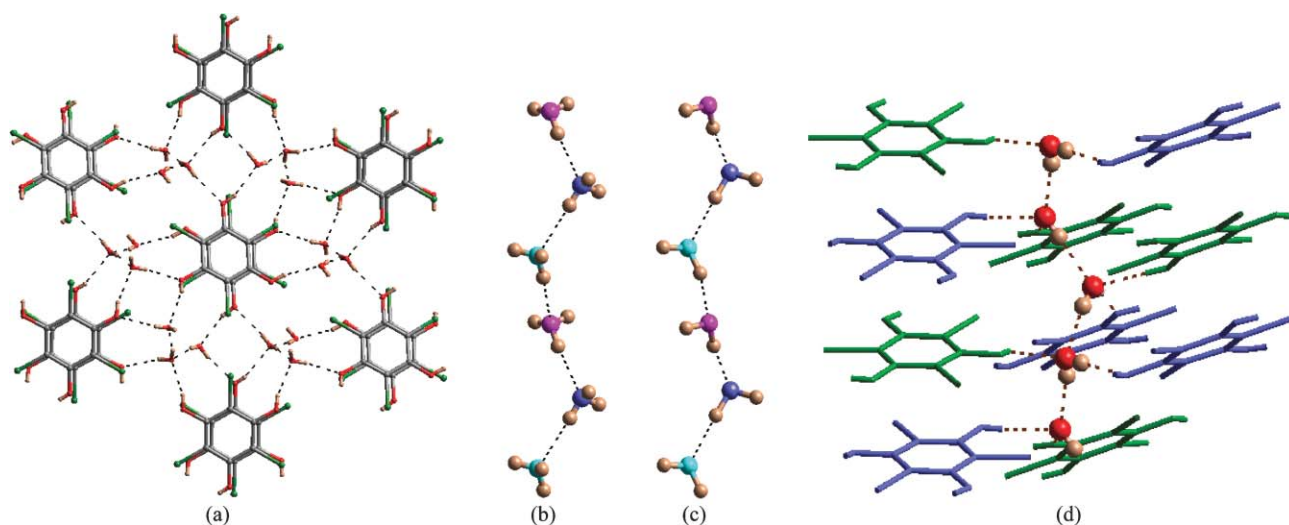

Fig. 1 (a) Piedfort Unit of π-stacked Cl–PHG molecules to show six phenol OHs extending radially. Water helices are encircled in the triangular pores of three Cl–PHG stacks. Six water helices surround a rod of host molecules when viewed down the *a*-axis. (b) O_w–H···O_w hydrogen bonding in a water helix of Cl–PHG.$(H_2O)_3$ (disordered protons are shown). (c) Homodromic H-bonds in the water helix of ordered Br–PHG.$(H_2O)_3$. (d) Spiral assembly of host molecules (green, blue) around the right-handed water helix in Br–PHG.$(H_2O)_3$. Higher occupancy disordered H-atoms are shown in (a) and symmetry-independent water oxygens are colored differently in (b) and (c).
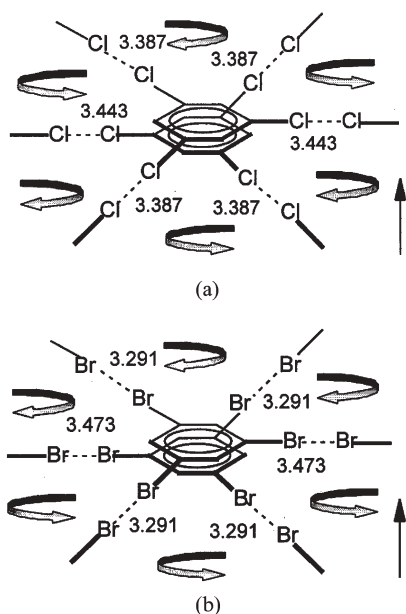

Fig. 2 Six water helices surround the Piedfort dimer of (a) Cl–PHG and (b) Br–PHG (phenol groups are omitted for clarity). The handedness of water helices across longer inter-halogen contacts of ∼3.4 Å is opposite whereas it is the same when the distance is ∼3.3 Å. This is due to the tilt of phenyl ring. See text for explanation.

The 1D water helix is the central self-assembly building unit in both hydrate host–guest structures. (2) Bromine is about 0.1 Å larger than chlorine (van der Waals radii: Cl 1.75 Å, Br 1.85 Å), and also more polarizable. There are small, yet structurally significant, differences in halogen···halogen interactions. While both Cl···Cl interactions are of about the same length (3.387, 3.443 Å) one of the Br···Br contacts is much shorter than the other (3.291, 3.473 Å).[10] Whereas Cl–PHG host molecules are arranged in an almost flat *bc*-sheet Br–PHG molecules lie in a corrugated layer because phenyl rings connected *via* the short Br···Br contact are tilted.†¶ This tilt in the phenol OH groups changes the position of hydrogen-bonded water molecules along the *a*-axis and, in turn, the helicity of the water chain. Water helices that are adjacent to the roughly coplanar host phenyl rings and lie across longer inter-halogen contacts of ∼3.4 Å are of opposite handedness (*PM*), whereas 1D water chains that are adjacent to the tilted host phenyl rings and are arranged across the short Br···Br contact of ∼3.3 Å have the same handedness (*PP* or *MM*) (Fig. 2). The present case is the first illustration on the fascinating role of weak halogen···halogen interactions in directing the helical twist of strong O_w–H···O_w chains in crystal structures.[11] The more polarizable bromine is able to participate in a shorter inter-halogen contact compared to the smaller chlorine atom. This prompted us to crystallize I-PHG but it afforded an anhydrous form whose structural details will be discussed in a full article.

Water loss in thermal gravimetric analysis (TGA, Fig. 3) matches with the trihydrate stoichiometry of Cl–PHG.$(H_2O)_3$ (obsd. 18.8%, calc. 19.0%) and Br–PHG.$(H_2O)_3$ (obsd. 12.5%, calc. 12.9%). The endotherm for water evolution from Cl–PHG is at 103 °C and from Br–PHG at 77 °C (major) and 94 °C (minor) in DSC (differential scanning calorimetry). The normalized enthalpy for water transit (−656 and −332 J g^{-1}) and strength of O–H···O hydrogen bonds in Cl–PHG.$(H_2O)_3$ and Br–PHG.$(H_2O)_3$ are 62 and 46 kJ mol^{-1} per water molecule (21
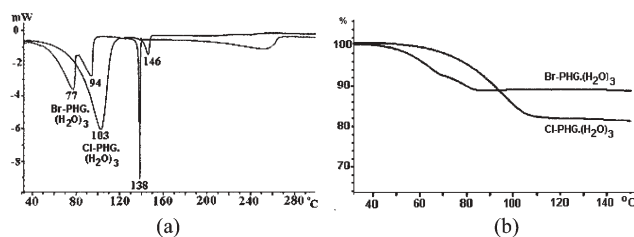

Fig. 3 DSC (a) and TGA (b) of Cl–PHG.$(H_2O)_3$ and Br–PHG.$(H_2O)_3$.

and 15 kJ per H-bond). These values are in good agreement with H-bonds in water chains and proteins[1d,12] The higher onset temperature and enthalpy for water release from Cl–PHG compared to Br–PHG channel is due to stronger (shorter) hydrogen bonds in the former structure (O···O 2.70–2.83 Å vs. 2.72–2.98 Å).

Powder X-ray diffraction (PXRD) of the hydrate and anhydrous material showed differences in dehydration/rehydration behavior. Dehydration of Cl–PHG.(H$_2$O)$_3$ at 115 °C for 2 h under vacuum afforded a material whose PXRD is identical to the original powder pattern,† showing that the host lattice is robust enough to the loss of interstitial water. The dehydrated material regained about two-third of its water from atmospheric moisture within 4 h and gained the original water stoichiometry (19% weight increase) after 24 h (TGA). Thus, Cl–PHG.(H$_2$O)$_3$ exhibits "organic zeolite"-like behavior through reversible water loss and uptake. On the other hand, PXRD trace of Br–PHG.(H$_2$O)$_3$ after dehydration is significantly different. Thus, there are structural and functional differences between these hydrate channel inclusion structures.

A strong motivation for studying hydrogen bonding in small molecule hydrated structures is that they could serve as models for the larger macromolecules, whose structures are difficult to determine to a high resolution. The hexagonal arrangement of Gly → Ala peptide rods[13] surrounding the 1D columns of water molecules in a synthetic collagen† is similar to Fig. 1a. The helical assembly of cooperative water chains supporting the spiral staircase of hexahost molecules (Fig. 1c,d) suggests another small-molecule model for studying the dynamics of water transport in aquaporin membrane proteins. Further studies on probing the influence of inter-halogen interactions on the handedness of water helix in phloroglucinols with mixed halogens is currently under way.

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Notes and references

‡ Crystal data was collected on Bruker SMART APEX CCD with Mo–Kα radiation (λ = 0.71073 Å) at 100 K. **Cl–PHG.(H$_2$O)$_3$:** C$_6$H$_9$Cl$_3$O$_6$, Mr = 283.48, monoclinic, $P2_1/n$, a = 6.9261(10), b = 16.057(2), c = 9.9510(15) Å, β = 109.923(2), V = 1040.4(3) Å^3, Z = 4, $R1$ = 0.0289, $wR2$ = 0.0698. **Br–PHG.(H$_2$O)$_3$:** C$_6$H$_9$Br$_3$O$_6$, Mr = 416.86, monoclinic, $P2_1/c$, a = 7.1076(5), b = 9.1708(7), c = 16.7599(12) Å, β = 93.9930(10), V = 1089.80(14) Å^3, Z = 4, $R1$ = 0.0193, $wR2$ = 0.0483. Intensities were corrected for absorption effects using the multi-scan technique SADABS. All non-hydrogen atoms were refined anisotropically and H atoms were located from difference electron density maps. The occupancy of disordered H atoms in Cl–PHG.(H$_2$O)$_3$ is given in ESI.† Structure solution and refinement was carried out with Bruker SHELXTL.

CCDC 257771 & 257772. See http://www.rsc.org/suppdata/cc/b5/b500284b/ for crystallographic data in CIF or other electronic format.
§ The location of water H atoms determines the homo/anti/hetero-dromic arrangement of hydrogen-bonded helices and the placement of O atoms along the *a*-axis determines their *P/M* handedness. The helicity of water chains is not affected by proton disorder in Cl–PHG.(H$_2$O)$_3$.
¶ The tilting and corrugation relieve steric congestion between these hexasubstituted benzenes.

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