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The structure of a self-assembled calixarene aqua-channel system

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The crystal structure of the complex 12.calix-[4]-arene dihydroxyphosphonic acid, 12.propane diammonium, 12.ethanol and 40.water molecules is based on dimeric units of the calix, assembled via trigonal units into a hexameric tube of 15 Å radius and 16 Å depth, further assemby via spanning propane diammonium cations and ethanol molecules forms a channel (40 Å), selectively containing all the water molecules.

The upsurge in nanotechnology has created growing interest in the construction of functional nanosystems.[1] Nature itself has, of course, had functioning nano-structures in place for a much longer time.[2] Of considerable interest in this area are the constructions of tubular structures. The rigid skeleton of the calixarenes has proved fruitful in the synthesis of tubular systems including the p-sulphonato-calixarene systems of Atwood *et al*.[3] and the recent work of Kim *et al*. on the calix hydroquinones.[4] Indeed Kim *et al*. noted that those systems might prove excellent biological mimics for ion and water membrane channels.

The crystallisation of calix-[4]-arene dihydroxyphosphonic acid[5,6] **1**, with propane diamine from aqueous ethanol leads to formation of a crystalline tubular system, showing strong structural analogy to the aquaporin water channel.[7–9] While both ethanol and water are present in the structure, the channel itself shows total selectivity for water.

The solid-state structure at the molecular level shows **1** to have flattened cone conformation, with ring tilt angles of 10.8° and 36.4°. Intramolecular hydrogen bonds between phenolics and the phosphonate rigidify the structure (d = 2.86(1) Å and 2.84(1) Å).

The calix-[4]-arene building block[10,11] is present as an included head to head dimer, Fig. 1. This building block is common to all analogous structures in the CSD.[12] The tight dimer, is held together by intermolecular π–π interactions (d = 4.1 Å), the molecular interpenetration is 1 Å greater than that observed in 25,27-bis(dihydroxyphosphoryloxy)calix[4]arene.[5]

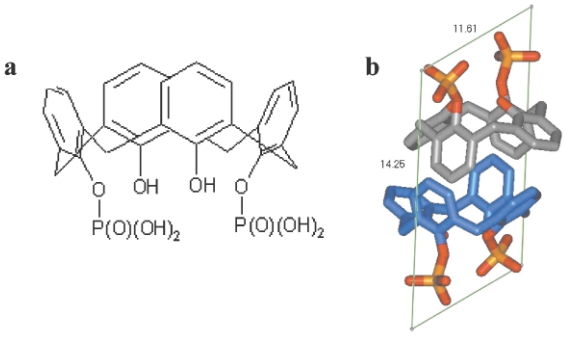

Fig. 1 (a) Molecular structure of calix-[4]-arene dihydroxyphosphonic acid, (b) Structure of the dimeric tecton of **1**, and the dimensions of tectonic parallelepiped, depth is 10.55 Å.

At each end of the long axis of the tecton, two diphosphonate groups are presented to act as hydrogen-bonding connectors. As shown in Figs. 2a and 2b, the dimeric tectons assemble, as two stacked symmetry related trimers to form a novel nanoscopic hexagonal assembly with a radius of 15 Å and an axis of 16 Å. The two triangular subunits are connected by hydrogen bonded propane diammonium cations, assuring the structural integrity of the hexameric assembly.

The diammonium cations are bonded by two hydrogen bonds to a phosphonate of one triangular unit (d = 2.87(1) Å and 2.76(1) Å) and by one hydrogen bound to a phosphonate of the other subunit (d = 2.68(1) Å). Ethanol molecules are hydrogen bonded to the phosphonate groups (d = 2.61(1) Å). The channel walls are common to the neighbouring chains forming a honeycomb arrangement, Fig. 2c. The total length of the channel formed is 40 Å.

The full structural motif is formed by the connection of one hexagonal assembly along the [111] direction to another via six propane diammonium cations and six ethanol molecules, Fig. 3.

One terminal ammonium function is bonded to two phosphonate functions of the same calix-4-arene of one assembly (Donor–Acceptor distance: 2.75(2) and 2.93(3) Å) and two different calix-4-arene molecules of another one (D–A distance: 2.73(3) and 2.73(4)) Å respectively). The alcohol solvent

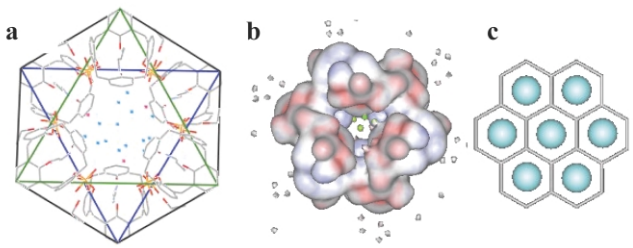

Fig. 2 (a) Top view showing the hydrophobic cavity of **1** along the [111] direction of unit cell, (b) surfaces representation of **1** showing the hydrophilic (red) and hydrophobic (blue) zones, (c) schematic of the honeycomb packing.

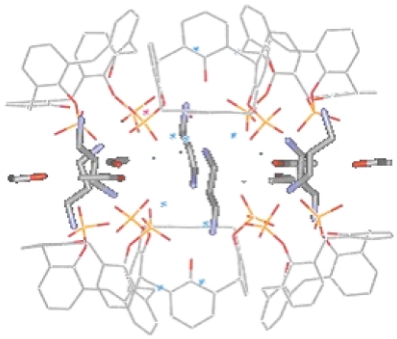

Fig. 3 Representation of the crown formed by the propane diammonium cations and ethanol molecules in the hydrophilic zone.

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contributes also to this joint (D–A distance: 2.57(3) and 2.67(3) Å).

The cavity delimited by the channel contains alternately a hydrophobic face, 10 Å diameter and 4 Å depth (van der Waals included), the hydrophobic region of the aromatic rings, 8 Å diameter and 14 Å depth, the hydrophilic zone of the phosphate ammonium interactions, 12 Å diameter and 6 Å depth and a hydrophobic zone of the alkyl chains of the propane diammonium cations of 14 Å diameter and 4 Å depth, repeated to form the 40 Å length channel. The ethanol molecules are located external to the channel and are hydrogen bonded to the phosphonate, P=O groups (D–A distance: 2.57(4) and 2.63(3) Å). The water molecules are located in disordered positions along the channel. Along the cavity the water molecules, Fig. 4, are situated in both hydrophilic and hydrophobic zones. In the hydrophobic zone, a partially occupied water trimer participates in an asymmetrical sandwich to two opposing aromatic rings (O–Ar1 = 3.18(2) Å and O–Ar2 = 3.79(2) Å). In the aquaporin structure, a short water to Phe contact (d = 3.60 Å) is present here via an edge to water interaction. The water molecules are not located above the aromatic centroid, in contrast to many water–aromatic interactions observed in proteins.[13] Numerous water–water paths, given the threefold crystallographic symmetry, can be traced along the channel, however variable short long arrangements 5.68–3.54–3.35 and 4.69 Å predominate amongst sites showing the highest occupation. Thermal gravimetric analysis of the calix-aqua-porin shows 3 zones of loss of solvent at 34 °C, 50 °C and 67 °C. These will correspond to switching of water molecules between binding sites. The total weight loss is about 8% corresponding to the total water content of the system. Further weight loss 6% corresponding to ethanol occur between 75° and 140°, and the system decompose above 150 °C.

The channel structure can be compared to two different systems; firstly the calix-hydroquinone structure of Kim *et al*.[14] and secondly the water channel structure of aquaporin 1 reported by Fujiyoshi *et al*.[15] In the case of the calix-hydroquinone structure, the channel geometry is a square nanotube of 8 × 8 Å^2. Water molecules are placed regularly on the wall of the tube along the cavity forming a longitudinal H-bond relay and are hydrogen bonded to each other and to the hydroquinone functions.

For aquaporin, the channel is formed by 6 completely spanning α-helices, and the junction of two shorter helices E and F. This junction is held together by interactions between Asn 76 and Asn 192 amino acids and forms a hydrophilic water gate responsible for the selectivity of aquaporin 1. The aquaporin channel is traversed by a hydrophilic face, a hydrophobic zone, the hydrophilic E–F core and again a hydrophobic zone and a hydrophilic face. Within the channel water molecules are situated at varying distances (4.1–2.97–3.84–5.97 and 3.1Å).

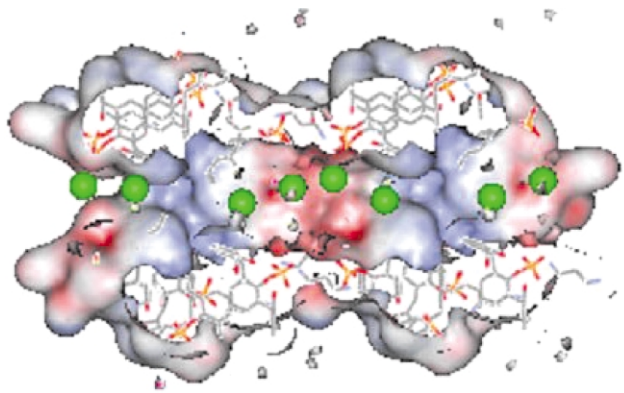

Fig. 4 Longitudinal section of *p*-H-calix-4-arene dihydroxyphosphonic acid. 1,3-diaminopropane tubular assemblies, showing only the most representative positions of water molecules.

Both the length ~40 Å and geometry of the channel formed by **1** and the combination of the variable polarity of the cavity surface and inter molecular water distances, show clearer analogies to the aquaporin 1 channel than to the calix-hydroquinone channel reported by Kim *et al*. The complex multimolecular assembly of **1** makes the structure a potent mimetic of biological membrane transport channels.

Notes and references

† CCDC 203285. See http://www.rsc.org/suppdata/cc/b3/b301460f/ for crystallographic data in .cif or other electronic format.

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12 To a solution of 1,3-diaminopropane (0.01 M) in water, a solution of *p*-H-calix-[4]-arene dihydroxyphosphonic acid (0.01 M) in ethanol is added forming a biphasic phase. Crystals were obtained by slow evaporation of solvent at room temperature after several days.
Crystal data for $(C_{28}H_{24}O_{10}P_2).(C_3H_{12}N_2).C_2H_5O.$ 3.33H_2O: Mr = 763.34; colorless, 0.50 × 0.15 × 0.10 mm, trigonal R-3, $a = b = c$ = 19.175(2) Å, $\alpha = \beta = \gamma$ = 106.039(17)°, V = 6019(1)Å^3, Z = 6, ρcalc = 1.26 g cm^{-3}, 2θmax = 49.4°, μ(Mo–Kα) = 0.173 mm^{-1}, 6671 independent reflections, 3073 with $I > 2\sigma(I)$. Intensity data were collected at 123 K on a Kappa-Nonius CAD4-CCD diffractometer using Mo–Kα radiation (λ = 0.7107 Å). Lorentz and polarisation corrections were applied and diffracted data were not corrected for absorption. The structure was solved by direct methods and Fourier techniques (SHELXS-86) and refined, on $|F|^2$, using the program SHELX-97. 3.33 water molecules were located, distributed over 12 sites, all sites with an occupation factor less than one. For the two phosphonate functions, the O atoms are disordered on two positions (0.7/0.3 and 0.8/0.2 occupancy factors respectively). One terminal ammonium function and one carbon atom of the diammonium cation is disordered over two sites (0.6 and 0.4 occupancy factors). All hydrogen atoms were placed in calculated positions and refined as riding atoms with isotropic thermal parameters based upon the corresponding ridden atom [U(H) = 1.2 Ueq]. R_1 = 0.0862, wR_2 = 0.2654. GoodF = 0.968 for all data. Residual electron density was 0.101 and −0.056 e Å^{-3}.†
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