Noncovalent π···π-Stacked Exo-Functional Nanotubes: Subtle Control of Resorcinarene Self-Assembly**

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An exciting research challenge in supramolecular chemistry is to design, synthesize, and characterize nanosized tubular architectures with applications in biology, chemistry, and materials science.[1] Predicting and designing noncovalently bound supramolecular structures is difficult because of the weakness of the interactions involved, and the resulting superstructure is often a compromise between the geometrical constraints of the building blocks and the competing weak intermolecular interactions.[2]

Hollow tubular architectures can be constructed from radial disk-shaped or nondisk-shaped building blocks.[1] Several cyclopeptides create flat, disk-shaped supramolecular synthons that self-assemble, by stacking, into stable nanotubes.[3] Examples of nondisk-shaped building blocks include the calixarene derivatives *p*-sulfonatocalixarene[4] and calix[4]hydroquinone.[5] In the self-assembly process of calix[4]-hydroquinone nanotubes, stable ultrathin silver wires are formed in an electro-/photochemical redox reaction.[5a]

Resorcinarenes, which are structurally closely related to calixarenes, are attractive building blocks for a variety of supramolecular architectures owing to their ability to bind neutral and cationic molecules inside their electron-rich cavity and simultaneously to form multiple hydrogen bonds with the eight hydroxy groups of the upper rim of the molecule (Scheme 1).[6] Resorcinarenes are known to form dimeric and hexameric hydrogen-bonded spherical assemblies and to act as supramolecular hosts for smaller molecules.[6,7]

Our earlier work on the complexation of small molecules and self-assembly of various resorcinarenes has mostly resulted in spherical dimeric capsule-type assemblies[7b,c] or 1:1 inclusion complexes, that is, open complexes.[8] To our surprise, instead of a spherical assembly, the cocrystallization of *C*-methyl resorcinarene (**1**; Scheme 1) with a rigid diquaternary alkyl ammonium salt (**2**; 1,4-dimethyl-1,4-diazoniabicyclo[2.2.2]octane dibromide) resulted in an intriguing nano-

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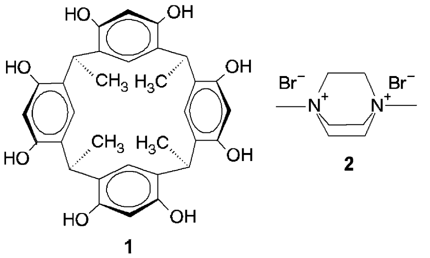

Scheme 1. Molecular structure of *C*-methyl resorcin[4]arene, **1**, and diquaternary alkyl ammonium salt **2**.

tubular structure held together by well-ordered intratubular π···π interactions.

Single crystals suitable for X-ray analysis of the nanotube structure were grown by slow evaporation of a 2:1 mixture of **1** and **2**, in aqueous *n*-propanol.[9] The asymmetric unit of the nanotube structure comprises three resorcinarene hosts, four alkyl ammonium guests, eight bromide anions, and six water molecules (Figure 1 a). All resorcinarene molecules are in crown conformation, each stabilized by four intramolecular hydrogen bonds of length 2.7–2.8 Å. Three of the four **2**$^+$ guests are present in the upright position in the resorcinarene host cavities allowing close C−H···π and cation···π interactions with the host (2.8–3.0 Å from methyl groups and 3.3–3.5 Å from methylene carbons of **2**$^+$ to the closest aromatic ring of the host). Five of the eight bromides in the asymmetric unit are disordered over two or three locations, making detailed investigation of hydrogen bonding pattern extremely difficult. Anions interact with the cations by electrostatic forces, being at a distance of 3.3–4.7 Å from the closest cationic nitrogen; at the same time they are hydrogen bonded to water molecules or free hydroxy groups of resorcinarenes ($\approx$2.7 Å for $O{-}H\cdots OH_2$ and 3.1–3.4 Å for $O{-}H\cdots Br^-$).

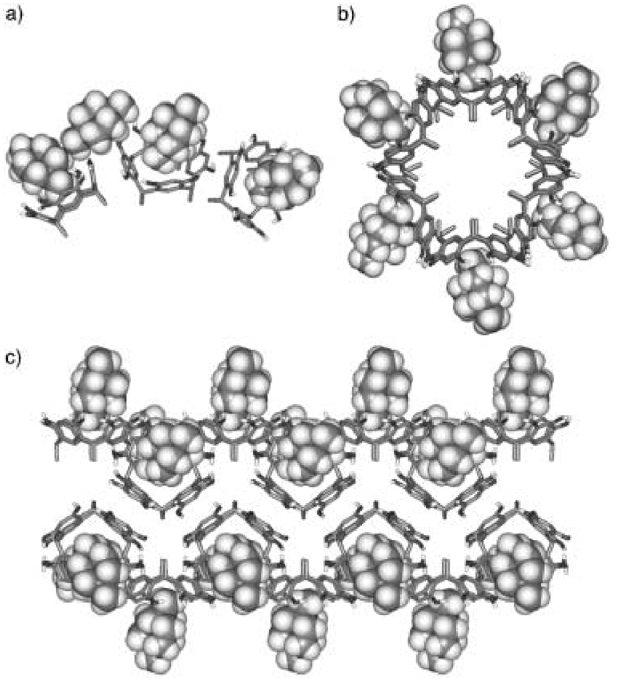

Figure 1. The structure of the nanotube showing resorcinarenes, **1**, in stick representation and diquaternary cations **2**$^+$, shown with Van der Waals radii. Anions, water molecules, non-hydrogen bonding hydrogens of resorcinarenes, and disorder of the cations are omitted for clarity. a) The asymmetric unit. b) A view of the tube along the crystallographic *a* axis. c) A perpendicular view of the tube showing the regular π···π interaction pattern.

The crystal lattice reveals a novel tubular superstructure, in which neighboring resorcinarenes are connected to each other though multiple π···π interactions (Figure 1 b and c). The nature of the interactions is offset face-to-face π···π stacking with facing aromatic rings bent by 22–28° and turned by 41–47° with respect to each other. The shortest distances between the centroids of the facing rings are 3.8–3.9 Å, while the closest individual carbon-adjacent aromatic ring distances are about 3.2 Å. The cavities and upper-rim hydroxy groups of the resorcinarenes create a hydrophilic exo-functional outer surface to the tube, which is capable of binding small guest molecules (in this case 1,4-dimethyl-1,4-diazoniabicyclo[2.2.2]octane, **2**$^+$) and of forming hydrogen bonds to surrounding hydrophilic solvent molecules and anions.

For both 1:1 inclusion complexes and spherical assemblies, the usual governing intermolecular force between the resorcinarenes is multiple hydrogen bonding, either directly or through solvent molecules or anions[7,8] In the present case, however, the distance between the hydroxy groups of adjacent resorcinarenes varies from 3.4 to 4.1 Å, thus indicating that there is no direct hydrogen bonding between them. Neither is there any obvious bridging through anions or water molecules. This means that hydrogen bonding does not govern the self-assembly. Rather, the driving force in the crystal packing is the slightly weaker and yet significant π···π interactions, supplemented by cation···π interactions and weak hydrogen bonding between the adjacent tubes through the diquaternary cation **2**$^+$.

The asymmetric unit is a curved building block which, repeated in the crystal packing, forms a chiral helical tube (Figure 2 a and b). The crystal itself, however, is a racemic mixture of antiparallel tubes. The top view (Figure 3 a), down the channel of the nanotube, shows the hexagonal outer shape of the tube, which is also repeated in the packing of the tubes. The adjacent nanotubes are linked through the **2**$^+$ ions (Figure 3 b): one methyl group of the cation is lodged in the π-basic resorcinarene cavity, while the other forms a C−H···O hydrogen bond to a hydroxy group of the resorcinarene of the adjacent tube. Interstices between the adjacent nanotubes are filled with cations, as well as bromide ions and water molecules, so that each tube is surrounded by a layer of **2** and water molecules that glues the tubes together.

Some electron density is present inside the hydrophobic tube interior, but the contents could not be reliably defined. It is nevertheless reasonable to assume from the location of the highest electron density near the lower-rim methyl groups of the resorcinarene molecules (3.8–4.4 Å) and from the X-ray structure determination of the 1:1 complex of *C*-methyl resorcinarene with 1,4-dibenzyl-1,4-diazoniabicyclo[2.2.2]octane dibromide crystallized from *n*-propanol[10] that the residual electron density inside the tube is indeed *n*-propanol. In this position the propanol hydroxy groups would point

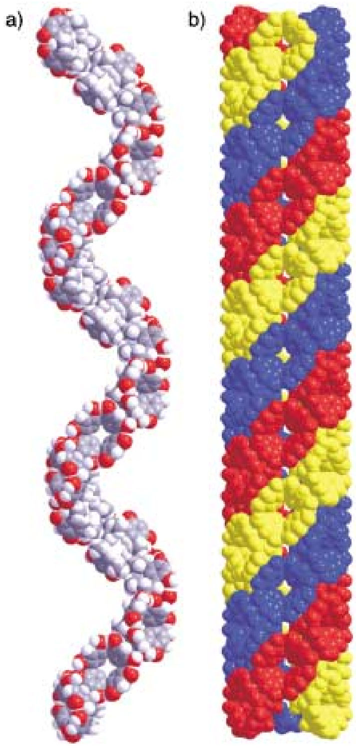

Figure 2. Tubular resorcinarene assembly shown with Van der Waals radii: a) adjacent resorcinarenes connected and rotated with respect to each other forming a single helix, b) the resorcinarene triple helix tube.

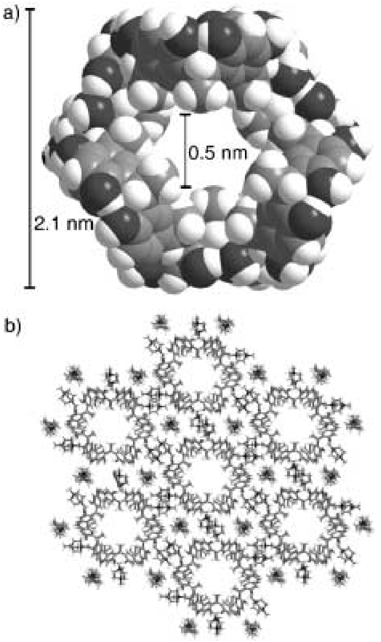

Figure 3. a) Resorcinarene nanotube shown with Van der Waals radii. b) Packing picture along the crystallographic *a* axis. Anions and water molecules are omitted for clarity.

inwards in the tube, thus allowing hydrogen bonding at the center of the tube.

The outside diameter of the nanotube is about 2.1 nm and the inner diameter about 0.5 nm, when measured as the longest Van der Waals distance between opposite resorcinarene hydroxy groups and the shortest Van der Waals distance between the centroids of opposite resorcinarene methyl groups (Figure 3a). Overall the interior of the tube is shaped like a series of stacked hourglasses, in which the narrowest point is between the resorcinarene methyl groups. The internal diameter of the nanotube, at its narrowest, is about the same as that of the widely studied and well-known α-cyclodextrin cavity (0.5 nm), which is capable of incorporating organic guests such as benzene and phenol.[11] It is reasonable to assume that similar guests may be stored and transported by the *C*-methyl resorcinarene nanotube.

Our attempts to crystallize similar tubular architectures from **1** and a corresponding diquaternary alkyl ammonium dichloride and diiodide (1,4-dimethyl-1,4-diazoniabicyclo[2.2.2]octane dichloride and diiodide) by using aqueous *n*-propanol as solvent and host-guest ratios of 2:1, 1:1, 3:4, and 1:2 have so far been unsuccessful. Only an open 1:1 complex with dichloride has been obtained[10] In this 1:1 complex the cation, as in the nanotube, is complexed inside the resorcinarene cavity, but the chloride ions are hydrogen-bonded to the resorcinarene hydroxy groups in a highly organized manner, thus mediating the facing resorcinarenes with relatively strong -O−H···Cl$^-$ ···H−O- bonds (O···Cl$^-$ separations 3.0–3.4 Å).

The role of the solvent in the formation of supramolecular structures should not be ignored or underestimated, especially if some solvent molecules are cocrystallized in the crystal lattice, as is usual in resorcinarene complexes. Earlier attempts to cocrystallize resorcin[4]arenes with **2** and tetramethyl ammonium salts from methanol or ethanol resulted in spherical complexes or open complexes in which the solvent alcohol was hydrogen-bonded to resorcin[4]arene hydroxy groups. Propanol, which is less hydrophilic and is able to interact with the resorcinarene alkyl groups through lipophilic interactions, is propably able to assist the self-assembly of *C*-methyl resorcin[4]arene towards π-stacked nanotubular structure.

We have shown that with use of a less electronegative and larger anion, that is, a weaker hydrogen bond acceptor (bromide instead of chloride) and appropriate conditions, the self-assembly process of *C*-methyl resorcinarene can be driven to favor weaker interactions such as π···π and cation···π interactions instead of hydrogen bonding. The *C*-methyl resorcinarene-based nanotube represents a new motif for nanotubular structures and opens up a wide range of possibilities for crystal engineering and nanochemical and biological research and applications. Appealing possibilities are offered by a hydrophilic and functional outer surface capable of both complexing small guest molecules and binding to hydrogen-bonding surfaces or other media. The hydrophobic interior could act as a transport channel or as storage for small lipophilic molecules. Challenges for the future include optimization of the conditions of tube formation and studies on the transport properties of the tube structure.

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[9] Crystal data for nanotube: formula $3C_{32}H_{32}O_8 \cdot 4C_8H_{18}N_2Br_2 \cdot 6H_2O$, crystal size $0.1 \times 0.1 \times 0.3$ mm, triclinic, space group $P\bar{1}$ (No.2), $a = 13.9358(2)$ Å, $b = 23.6272(2)$ Å, $c = 23.9065(3)$ Å, $\alpha = 64.617(1)°$, $\beta = 85.811(1)°$, $\gamma = 87.348(1)°$, $V = 7091.7$ Å^3, $Z = 2$, $\rho_{calcd} = 1.38\ cm^{-3}$, $Mo_{K\alpha}$ radiation, $\lambda = 0.71073$ Å, $\mu = 2.33\ mm^{-1}$, $T = 173$ K, Nonius Kappa CCD diffractometer, 85764 reflections measured, 24119 independent, 10857 used ($5.86 < 2\theta < 49.50°$), number of parameters 1680, $R_{int} = 0.121$, $R1 = 0.090$ ($I > 2\sigma I$), $wR2 = 0.227$, GOF = 1.034. Minimum and maximum peaks in the difference map -0.891 and 2.735 e Å^{-3}. CCDC-220735 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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