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Calixarenes

A Hydrogen-Bonded Hexameric Nanotoroidal Assembly**

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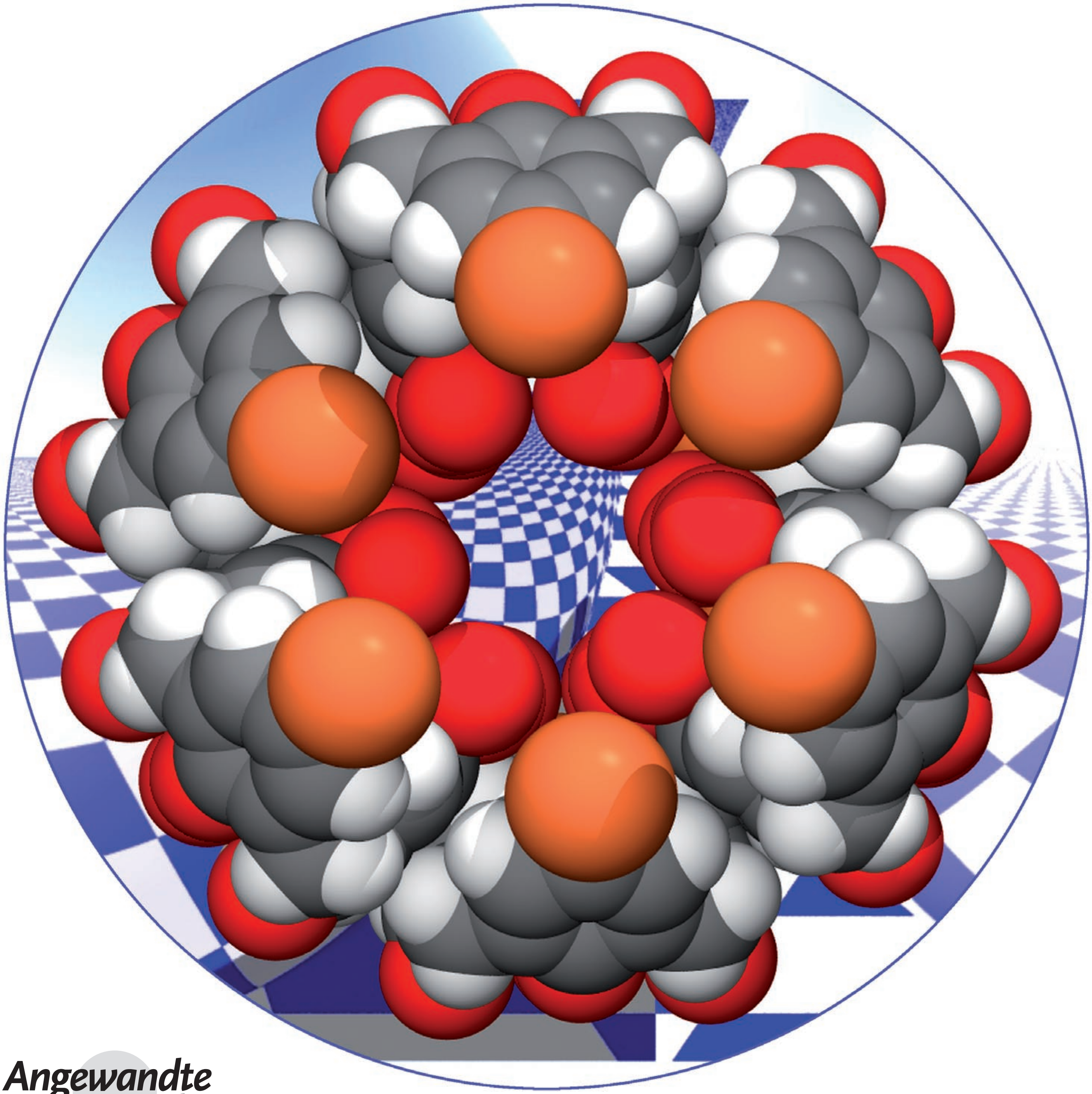
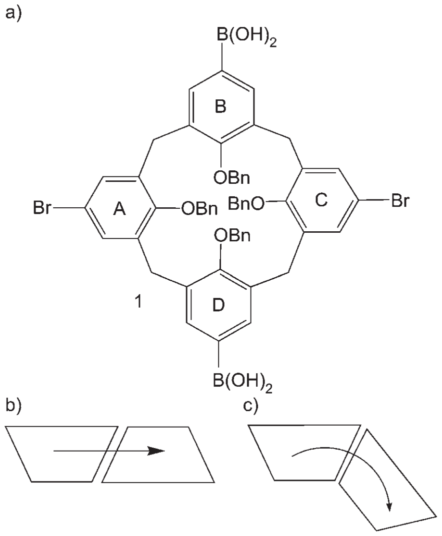


Supramolecular chemists have exploited hydrogen-bonding interactions, dynamic covalent chemistry, and metal-ion coordination to assemble a wonderful array of molecular topologies such as nanospheroids,[1–6] tubules,[7,8] and various knots.[9] In this context, any closed surface can be expressed topologically as a torus containing a finite number of holes.[10] A torus containing no holes (genus = 0) corresponds to the surface of a sphere whereas a surface with one hole (genus = 1) is topologically equivalent to a torus-shaped ring structure. The relationship between the two topologies continues to grab attention in understanding topological and chemical problems. For example, spheroid and doughnut topologies have different chemical and physical properties with the chemist taking benefit from these intrinsic differences. The multicomponent supramolecular nanospheroid assemblies have properties based upon the encapsulation of guests within their closed three-dimensional space with resultant applications in atypical regioselective guest reactions[11] to new types of stereoisomers.[12] On the other hand, the torus ring structures permit threading of various molecules through their resultant hole, which has resulted in numerous rotaxane and catenane-like assemblies with applications such as molecular-based machines.[13,14]

Given the intense focus on toroidal-shaped macrocycles such as cucurbit[*n*]uril and cyclodextrin molecules, it is surprising that less effort has been applied to developing noncovalent multicomponent toroidal equivalents which can combine the advantages of reversibility and error checking based upon self-complementary hydrogen bonding by means of the all-in-one self-assembly approach. However, the chief problem associated with this objective is achieving control over many intermolecular interactions. Despite reports on the self-assembly of concave-shaped calix[4]arene molecules into nanospheroidal assemblies,[15,16] the formation of toroidal equivalents based on the calix[4]arene building block that can be looked upon as progenitors of spheres remains elusive. Herein we report on the self-assembly of six pinched-cone tetra-O-alkylated calix[4]arene molecules into a large hexameric torus-shaped ring structure in the solid state.

Calix[4]arenes are molecules comprised of four phenolic groups bridged with methylene units and can exist in the cone, partial cone, 1,2-alternate, or the 1,3-alternate conformation.[17] However, the tetra-O-alkylated calix[4]arene macrocycles are also known to exist in solution as a mixture of two equivalent pinched-cone (C_{2v}) conformers which rapidly exchange on the NMR timescale through the cone conformer (C_{4v}).[18] The C_{2v} conformer is preferred in the solid state. The pinched-cone conformer can be described as two alternate aromatic rings within the tetrameric subunit being flipped inward toward each other in a face-to-face manner with the other two aromatic rings being pushed outward with respect to each other. Thus, the tetrameric subunit conforms to a trapezoidal shape in the solid state. Molecular packing of the corresponding trapezoidal faces in the antiparallel "up–down" or parallel "up–up" arrangement results in bilayer (noncurvature) or spherical (curvature) assemblies, respectively (Scheme 1).[15] Shape complementarity of the tetrameric subunits acting alone should result in bilayer-type structures in the solid state (Scheme 1 b). However, functional groups acting as a pivot with the capacity to form self-association interactions placed at the correct positions on the subunit should allow for the formation of supramolecular curvature (Scheme 1 c). In this context, tetra-*O*-benzyl-(A,C-dibromo-B,D-diboronic acid)-calix[4]arene **1** (see the Supporting Information for preparation) was synthesized (Scheme 1 a).



Scheme 1. a) Compound **1**; b) up–down packing of trapezoidal faces; c) up–up packing arrangement.

Single crystals of **1** suitable for X-ray diffraction studies were obtained from an acetone solution over a period of two days.[19] The crystals were of trigonal symmetry and upon structural solution, the asymmetric unit was found to comprise one tetra-O-alkylated calix[4]arene molecule **1** and various water molecules (Figure 1 a and b). The calix[4]arene subunit **1** is stabilized in its pinched-cone conformation. The two opposite B- and D-boronic acid aromatic rings are flipped inward toward each other in a face-to-face fashion (B···B 3.494 Å; Figure 1 a), whereas the remaining two A- and C-bromo aromatic rings are flipped outward with respect to each other (Br···Br 13.098 Å; Figure 1 b). The asymmetric unit of **1** viewed along the [001] plane corresponds to the tetra-O-alkylated calix[4]arene subunit representing a trapezoid face with the resultant B- and D-boronic acid hydrogen-bonding interactions being perpendicular to this trapezoid face (Figure 1 a).

Symmetry expansion reveals a hexameric circular framework in which each tetra-O-alkylated calix[4]arene trapezoi-

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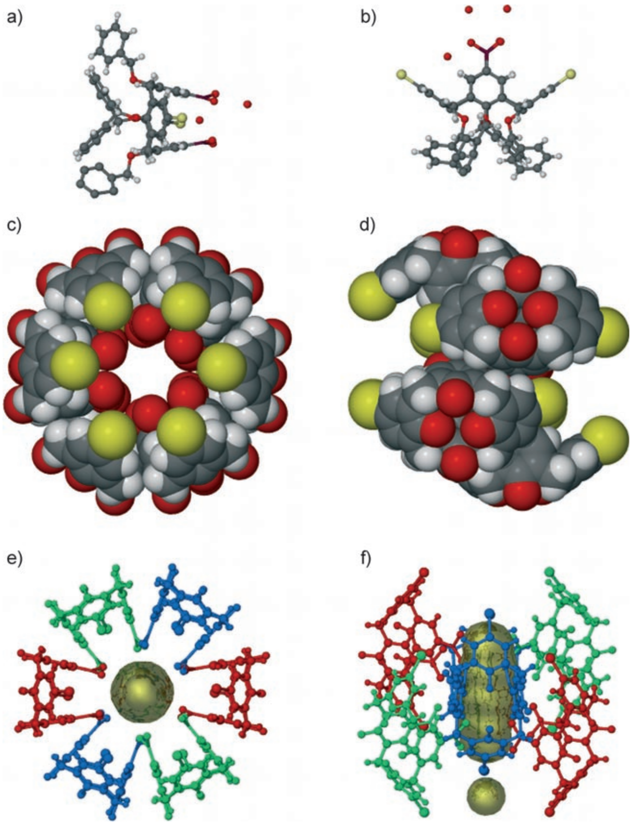


Figure 1. a) Ball-and-stick diagram showing the asymmetric unit of **1**, viewed along the [001] plane showing its trapezoidal face; b) showing the A- and C-bromo aromatic rings flipped outward. c) Space-filled representation of the hexameric torus-shaped ring structure **1**, viewed along the [001] plane; d) viewed along [100]; Br yellow, O red, C gray, H white for (a)–(d). e) Ball-and-stick diagram of the nanotoroidal structure showing the toroidal cavity space represented as a Connolly surface (gold) viewed along [001]; f) showing the tubular nature of the inner toroidal space; each calix[4]arene molecule neighbor is colored differently for clarity in (e) and (f). In (c)–(f) the benzyl groups are removed for clarity.

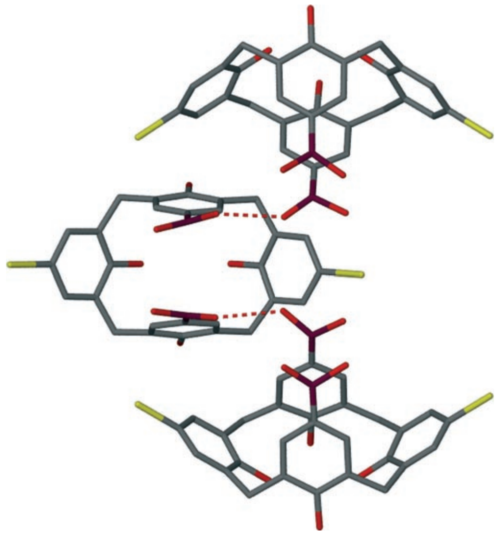
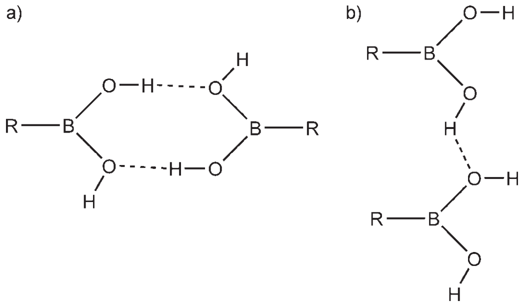


Figure 2. Stick diagram showing the intermolecular hydrogen-bonding pattern within the hexameric nanotoroidal assembly **1**, viewed along the [100] direction with three of the six calix[4]arene subunits within the hexameric structure; hydrogen atoms and benzyl groups have been removed for clarity. Dashed lines represent hydrogen-bonding interactions.



Scheme 2. a) The expected hydrogen-bonding pattern for boronic acid groups; b) the actual pattern found within the hexameric doughnut assembly **1**.

dal face is arranged in a parallel "up–up" fashion (Figure 1 c–f). The "up–up" packing arrangement of trapezoidal faces is directed by the preference of each individual $B(OH)_2$ group within each subunit **1** to form an intermolecular hydrogen bond (BO···OB 2.546 Å) to its corresponding subunit neighbor (Figure 2). The result is that only six intermolecular boronic acid hydrogen bonds BO···OB, one intermolecular hydrogen bond per subunit, hold the hexameric assembly together. Although hydrogen atoms were not located, hydrogen bonds are implied by short O···O contacts. Interestingly, boronic acid groups previously reported tend to associate into their characteristic hydrogen-bonded dimer (Scheme 2 a).[20] However, in the hexameric circular assembly **1**, each $B(OH)_2$ group forms only one boronic acid hydrogen-bonding interaction with its neighbor (Scheme 2 b).

A plausible reason for the difference in hydrogen-bonding patterns may be due to steric effects of the bromine atoms. The hexameric circular assembly **1** viewed along the [001] direction can be described as six trapezoidal subunit faces packed in the "up–up" arrangement with each subunit rotated 60° with respect to each other (Figure 1 c). The boronic acid BO···OB hydrogen-bonding interactions are perpendicular to these trapezoidal faces. As the trapezoidal subunits assemble together through hydrogen-bonding interactions, the bromine atoms are situated in such a position to prevent the formation of a second intermolecular boronic acid hydrogen bond per $B(OH)_2$ group.

The boronic acid hydrogen-bonding interactions being perpendicular to the trapezoid faces when viewed along [001] results in each calix[4]arene subunit centroid within the supramolecular hexameric assembly being positioned at the vertices of a chair conformer rather than corresponding to a hexagon shape (Figure 1 d). Furthermore, the lack of a second hydrogen bond per $B(OH)_2$ group because of steric effects from the bromine atom results in the hexameric assembly packing into an AB closed-packed arrangement rather than in a tubule arrangement (face-to-face stacking of torus structures) in the solid state. A variety of CH···π interactions between the hydrogen atoms and aromatic rings, with a

CH⋅⋅⋅centroid distance of 2.994 Å, and van der Waals interactions stabilize the subunits within the hexameric torus structure. Given the numerous benzyl groups located at the exterior of the hexameric assemblies, there were no π⋅⋅⋅π stacking interactions between the hexameric doughnut structures within the expected distances.

The trapezoidal "up–up" packing arrangement of the six subunits results in the formation of a circular structure with a hole positioned at the hexameric centroid (Figure 1 c–f). This hexameric supramolecular assembly can be regarded as a torus-shaped ring structure. The toroidal hole has a diameter of approximately 7 Å whereas the supramolecular hexameric structure has an outer diameter of approximately 26 Å when viewed along the [001] plane (Figure 1 e). Indeed, when the supramolecular hexameric assembly is viewed along the [001] plane, the nanotoroid **1** shows a remarkable structural similarity to the corresponding cucurbit[6]uril molecule, and therefore **1** may be viewed as a noncovalent analogue to cucurbit[6]uril.[21] The inner toroidal cavity volume was calculated to be approximately 150 Å^3.[22] Interestingly, a water molecule closes the entrance at both ends of the torus void. X-ray analysis revealed a single water molecule with an occupancy of one-third, positioned over three symmetry-generated sites located at the toroidal entrance. This water molecule is stabilized by forming hydrogen-bonding interactions (O⋅⋅⋅O 2.578–2.630 Å; BO⋅⋅⋅O_{water}⋅⋅⋅OB 101.68°) to the boronic acid oxygen atoms not involved in intermolecular BO⋅⋅⋅OB interactions. Within the toroidal cavity space, a single water molecule was found by X-ray analysis. A water molecule was modeled with an occupancy of one-sixth, positioned over six symmetry-generated sites.

The upper-rim boronic acid groups within the calix[4]arene subunits are situated at the toroidal hydrophilic inner surface within the nanotoroidal assembly with its corresponding intermolecular hydrogen-bonding interactions being positioned along the Connolly toroidal inner surface (Figure 1 e,f). The corresponding lower-rim benzyl groups are positioned on the exterior hydrophobic surface contrary to that found for other calix[4]arene nanospheroid assemblies where the lower-rim groups are usually found at the interior.[15,16] Thus, the hexameric torus-shaped structure **1** can be viewed as a two-dimensional inverse analogue to its three-dimensional nanospheroid cousin and a progenitor of spheres.

The results presented here demonstrate the ability of the chemist to build toroidal-shaped topologies by hydrogen bonding and shape complementarity akin to that found within the well-known nanospheroidal assemblies. In topology terms, the relationship between spheres and tori should allow the full exploitation of these two different topologies on the basis of their inherent shape. For example, our discovery that **1** assembles into a noncovalent toroidal structure could bear relevance in numerous areas similar to that found for their toroidal covalent cousins.

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[19] X-ray crystal data for **1**: $C_{84}H_{58.50}B_3Br_3O_{13.25}$, $M_r = 1551.97$, colorless block, $0.29 \times 0.21 \times 0.17$ mm^3, trigonal, space group $R\bar{3}$ (No. 148), $a = b = 27.437(2)$, $c = 34.726(4)$ Å, $V = 22639(3)$ Å^3, $Z = 12$, $\rho_{calcd} = 1.366$ g cm^{-3}, $F_{000} = 9462$, $Mo_{K\alpha}$ radiation, $\lambda = 0.71073$ Å, $T = 173(2)$ K, $2\theta_{max} = 54.4°$, 54494 reflections collected, 11142 unique ($R_{int} = 0.0449$). Final GooF = 1.023, $R1 = 0.0938$, $wR2 = 0.2814$, R indices based on 5143 reflections with $I > 2\sigma(I)$ (refinement on F^2), 640 parameters, 0 restraints, Lp and absorption corrections applied $\mu = 1.667$ mm^{-1}. One of the benzyl aromatic rings showed some disorder. All non-hydrogen atoms were refined anisotropically. Structure solved by SHELXS and refinement performed by X-Seed (G. M. Sheldrick, SHELX-97 Program, University of Göttingen, **1997** and "X-Seed program": L. J. Barbour, *J. Supramol. Chem.* **2001**, *1*, 189). CCDC-613238 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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