Encapsulation of two aromatics by a carcerand-like capsule of nanometre-scale dimensions†

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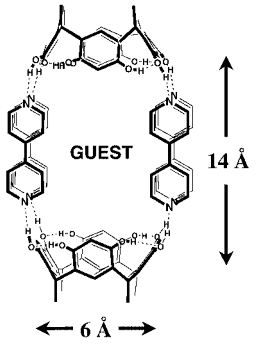
Received (in Columbia, MO, USA) 10th November 1999, Accepted 7th January 2000

Co-crystallization of *C*-methylcalix[4]resorcinarene 1 with 4,4′-bipyridine 2 in the presence of nitrobenzene 3 yields a six-component carcerand-like capsule, 2(1)·4(2), held together by 16 hydrogen bonds, in which two molecules of 3 are aligned within the interior of the complex in a head-to-head fashion.

Using a modular approach to molecular self-assembly, it has been shown that co-crystallization of *C*-methylcalix[4]resorcinarene **1** with 4,4′-bipyridine **2** typically yields a one-dimensional (1D) host–guest wave-like polymer, **1**·2(**2**), in which the cavity of **1** is deepened supramolecularly, interacting with two stacking pyridine units of **2** by way of four O–H···N hydrogen bonds.[1] The cavity created by the five molecules, which may be induced to form by way of guest template effects,[2] is remarkably flexible, being able to accommodate either single[3] or multiple guests,[4] many of which are too large to fit within the parent receptor **1**,[2] by way of a conformational change of the network.

During experiments aimed at attempts to isolate multiple guests within **1**·2(**2**), we have discovered the ability of the components of the wave-like framework to undergo a structural reorganization to form a discrete, six-component carcerand-like capsule,[5] 2(**1**)·4(**2**), held together by 16 hydrogen bonds (Fig. 1). The capsule, which is a supramolecular isomer[6] of the parent 1D material **1**·2(**2**), assembles in the solid state such that the cavity of the host, which is of nanometre-scale dimensions,[7] encapsulates two identical aromatic guests aligned within the complex in a head-to-head fashion. Whereas **1** has been shown to form multi-component capsules based upon protic solvent molecules (*e.g.* H_2O, PrOH, EtOH),[8–10] 2(**1**)·4(**2**) represents, to the best of our knowledge, the first example of a hydrogen-bonded capsule, based upon **1**, formed using an aromatic spacer as a 'bridging unit'. Our observations also confirm the ability of nano-sized capsules to accommodate more than one guest,[7] where understanding the spatial relationships displayed by the guests of such multi-guest host systems is of much current interest.[11]



2(**1**)·4(**2**)

Fig. 1 Structure of 2(**1**)·4(**2**).

Addition of **1** (0.021 g) to a boiling aliquot of THF (0.5 ml) and EtOH (1.0 ml) in the presence of **2** (0.012 g) and nitrobenzene **3** (3.0 ml) yielded, upon slow cooling, dark yellow crystals of **1**·2(**2**)·2(**3**) suitable for X-ray analysis. The formulation of **1**·2(**2**)·2(**3**) was confirmed by ^{1}H NMR spectroscopy and single-crystal X-ray diffraction.‡

An ORTEP perspective of 2(**1**)·4(**2**), along with a space-filling view, is shown in Fig. 2. As in the case of the wave-like framework **1**·2(**2**),[1–4] the components of 2(**1**)·4(**2**) have assembled in the solid state such that four pyridine units of **2**, in the form of two stacked dimers, interact with two opposite resorcinol units of **1** by way of four O–H···N hydrogen bonds [O···N separations (Å): O(1)···N(1) 2.75(1), O(2)···N(3) 2.71(1), O(5)···N(2) 2.74(1), O(6)···N(4) 2.68(1)]. The remaining hydroxy groups of **1** form four O–H···O hydrogen bonds [O···O separations (Å): O(3)···O(2) 2.76(1), O(4)···O(5) 2.79(1), O(7)···O(6) 2.79(1), O(8)···O(1) 2.71(1)] along the wider rim of **1** such that the macrocycle, as in **1**·2(**2**), adopts a bowl-like conformation with approximate C_{2v} symmetry. Unlike **1**·2(**2**), however, the four bipyridines of 2(**1**)·4(**2**), which act as bifunctional hydrogen bond acceptors, serve to bridge two, rather than three, molecules of **1**. This, in turn, gives rise to a discrete, six-component assembly held together by eight intermolecular O–H···N and eight intramolecular O–H···O hydrogen bonds, for a total of 16 structure-directing O–H···X (X = N, O) forces. In this arrangement, the cavities of **1**, which sit around a crystallographic center of inversion, are aligned in a head-to-head fashion such that the wider rims of the macrocycles, along with **2**, define a cylindrical cavity, of idealized D_{2h} symmetry, with dimensions ~ 6.0 × 14.2 Å. Indeed, the structure of 2(**1**)·4(**2**) is reminiscent of a carcerand[5] in which the eight covalent bonds that typically connect four spacer units to two molecules of **1** have been replaced by eight O–H···N forces.

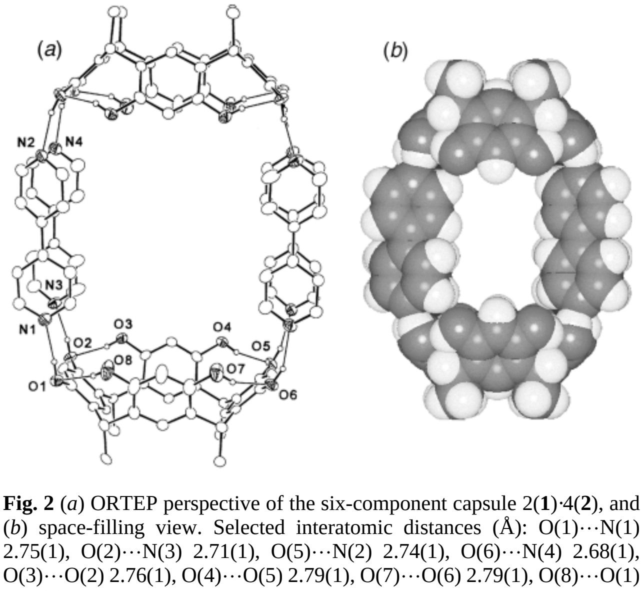


Fig. 2 (*a*) ORTEP perspective of the six-component capsule 2(**1**)·4(**2**), and (*b*) space-filling view. Selected interatomic distances (Å): O(1)···N(1) 2.75(1), O(2)···N(3) 2.71(1), O(5)···N(2) 2.74(1), O(6)···N(4) 2.68(1), O(3)···O(2) 2.76(1), O(4)···O(5) 2.79(1), O(7)···O(6) 2.79(1), O(8)···O(1) 2.71(1).

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† Published as NRCC No. 43828.

DOI: 10.1039/a909339g

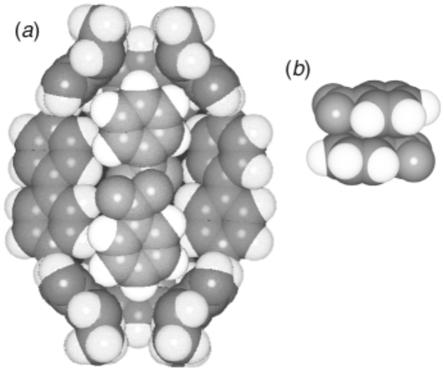

Fig. 3 Space-filling views of the guests of **1**·2(**2**)·2(**3**): (*a*) cut-away view of 2(**1**)·4(**2**)·2(**3**) displaying the two encapsulated aromatics (one occupied site is shown for clarity), and (*b*) the anti-parallel arrangement adopted by the guests exterior to 2(**1**)·4(**2**)·2(**3**).

A cut-away space-filling view depicting the guests of 2(**1**)·4(**2**) is shown in Fig. 3(*a*). Two molecules of **3**, which are disordered across two independent sites (75:25 occupancy), have assembled within the six-component complex in a head-to-head fashion such that the aromatic rings of the guests are directed into separate ends of the capsule,[7,11] each interacting with the interior of **1** by way of C–H···π interactions.[15] In these orientations, the phenyl groups of the guests of the major and minor occupied positions, in a way similar to **1**·2(**2**)·*p*-chlorotoluene,[2] lie approximately 20 and 27° off-axis to the principal rotation axis of the host and are rotated, in contrast to **1**·2(**2**)·*p*-chlorotoluene,[2] by approximately 78 and 21° along the symmetry axis of **1**, respectively.§ The nitro groups of the two encapsulated molecules are then observed to fill the center of the capsule, being separated by a distance of 3.6 Å. Interestingly, the organization displayed by the two molecules of **3** within 2(**1**)·4(**2**), in which two highly electron withdrawing substituents are oriented in close proximity,[11] contrasts that of pure **3** which self-assembles in the solid state, by way of C–H···O forces, to form antiparallel dimers.[16] Moreover, such observations confirm the ability of nano-sized capsules to encapsulate multiple guests where the cavities of such systems have been shown to impose spatial arrangements of guests not typically encountered in the free molecules.[7,11]¶

The capsule 2(**1**)·4(**2**) assembles in the solid state, in a tail-to-tail manner, to form 1D columnar arrays, which lie off-set and form a 2D layered architecture, in which two molecules of **3** are sandwiched between adjacent host–guest complexes. As shown in Fig. 3(*b*), in contrast to the two encapsulated guests, the aromatics located exterior to the host–guest complex assemble by way of face-to-face π–π interactions such that they form, in a way similar to pure **3**, antiparallel dimers (plane-to-plane separation: 3.35 Å).[16] Thus, **1**·2(**2**)·2(**3**) is an inclusion compound that possesses two different cavities, both of which accommodate two copies of the same guest in which the guests assemble in specific ways to meet the electronic and steric demands of each cavity.

In this report, we have revealed the ability of **1** to assemble with **2**, in the presence of a suitable guest, to form a six-component carcerand-like capsule, that is a supramolecular isomer of an extended 1D framework, held together by 16 hydrogen bonds.‖ The capsule, which is of nano-metre scale dimensions, features a cavity that hosts two identical aromatics as guests. With such observations realized, we are now investigating whether this system may be used to encapsulate additional guests where it may be possible to isolate two different molecules within the cavity of the assembly.[11] We are also investigating whether it is possible to lengthen 2(**1**)·4(**2**)[3] such that further analogies, in terms of structure and function, between discrete[8] and infinite[1–4] host–guest frameworks based upon **1** may be realized.

We are grateful for funding from the Natural Sciences and Engineering Research Council of Canada (graduate scholarship, J. L. R.; research grant, J. A. R.).

Notes and references

‡ *Crystal data* for **1**·2(**2**)·2(**3**): triclinic, space group $P\bar{1}$, a = 10.731(1), b = 15.075(1), c = 16.882(1) Å, α = 95.727(1), β = 94.860(1)°, γ = 93.915(2)°, U = 2699.4(3) Å^3, D_c = 1.36 g cm^{-3}, Mo-Kα radiation (λ = 0.71070 Å) for Z = 2. Least-squares refinement based on 3549 reflections with $I_{net} > 2.0\sigma(I_{net})$ (out of 6097 unique reflections) led to a final value of R = 0.071. Aromatic and hydroxy hydrogen atoms were placed by modelling the moieties as rigid groups with idealised geometry, maximising the sum of the electron density at the calculated hydrogen positions. Structure solution was accomplished using SHELXS-86 (ref. 12) and refinement was conducted using SHELXL93 (ref. 13) locally implemented on a pentium-based IBM compatible computer. Structure refinements and production of the figures were accomplished with the aide of RES2INS (ref. 14). CCDC 182/1533. See http://www.rsc.org/suppdata/cc/a9/a909339g/ for crystallographic data in .cif format.

§ For comparison, the aromatic guest of **1**·2(**2**)·*p*-chlorotoluene lies approximately 39° off-axis to the principle rotation axis of the host and is rotated by 0° along the axis of **1**.

¶ Such spatial constraints can, for example, give rise to reactivity (see ref. 11).

‖ Experiments are underway to determine if 2(**1**)·4(**2**) is maintained in solution.

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Communication a909339g