Unique guest inclusion within multi-component, extended-cavity resorcin[4]arenes

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Co-crystals involving *C*-methylcalix[4]resorcinarene 1 and substituted pyridines obtained from $MeNO_2$–benzene and MeCN–benzene yields multi-component complexes 1·4(4-picoline)·$MeNO_2$ 2 and 1·4(1,10-phenanthroline)·MeCN·benzene 3 in which the cavity of 1 is extended by four pyridines supramolecularly and the included solvent serves as a guest.

There is currently a great deal of interest in utilizing noncovalent forces for the construction of multi-component host frameworks (*e.g.* molecular capsules) that display recognition properties analogous to their monomolecular predecessors (*e.g.* carcerands).[1–3] These frameworks typically involve replacing covalent bonds with supramolecular synthons that retain the structural integrity of the parent host molecule. Notably, in addition to providing access to systems which are difficult to obtain using conventional molecular synthesis,[3] such frameworks can display properties not found in the molecular analog (*e.g.* reversible formation)[4] which, in some instances, can bear relevance in understanding related biological phenomena (*e.g.* virus formation).[5]

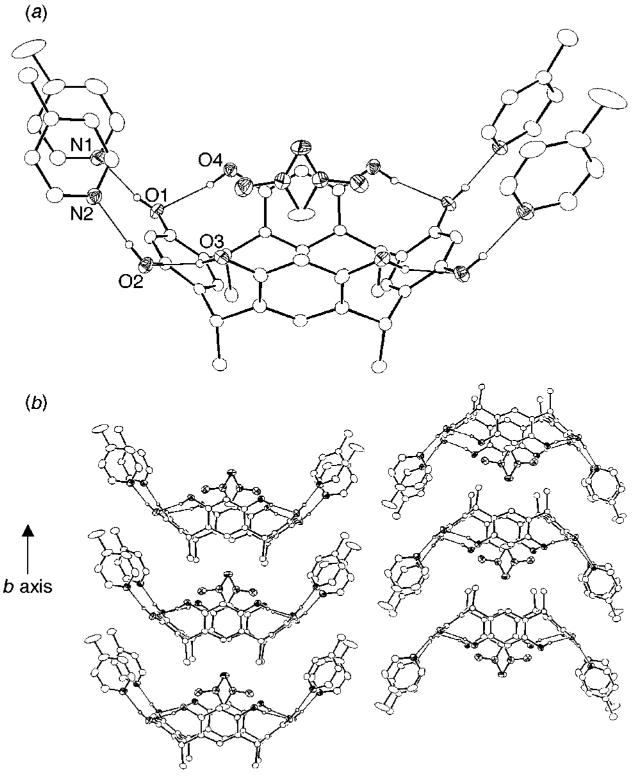

Fig. 1 ORTEP perspective of (*a*) the six-component assembly **2**, and (*b*) self-inclusion displayed by **2**. Selected interatomic distances (Å): O(1)···O(4) 2.840(3), O(1)···N(1) 2.740(3), O(2)···O(3) 2.806(3), O(2)···N(2) 2.704(3).

Along these lines, we have recently shown that it is possible to extend the cavities of resorcin[4]arenes (*e.g. C*-methylcalix[4]resorcinarene **1**) supramolecularly using aromatic-based hydrogen bond acceptors.[2] Our initial attempt at a discrete system, **1**·4(py)·py (py = pyridine), consisted of six molecules comprised of two different components in which four molecules of py participate in four O–H···N hydrogen bonds, as two stacked dimers, along the upper rim of **1**, to form a cavity large enough to host a fifth py. Here, we now demonstrate that it is possible to isolate a guest within a discrete supramolecular cavity based upon **1**, in **1**·4(4-pic)·$MeNO_2$ **2** (4-pic = 4-picoline), which is different than that of the 'substituents' hydrogen bonded to the upper rim of the macrocycle. By employing similar conditions used to form **2**, we also demonstrate that is possible to expand the chemistry of these systems to a chelating agent, 1,10-phenanthroline (1,10-phen), in **1**·4(1,10-phen)·MeCN·benzene **3**, which assembles to form both conventional and bifurcated O–H···N hydrogen bonds along the upper rim of **1**. Such observations are important since, in addition to showing that it is possible to fully mimic host–guest properties of monomolecular calix[4]arenes supramolecularly, they confirm generality in this approach with respect to both upper rim substitution and guest inclusion.

Addition of **1** (0.020 g) to a boiling aliquot of 4-pic (2 ml) yielded a yellow precipitate. Attempts to grow crystals of this material suitable for single crystal X-ray analysis failed. The precipitate was then heated and $MeNO_2$ (3 ml) followed by benzene (2 ml) were added dropwise, with continuous heating, according to eqn. (1), until the solid dissolved. Yellow crystals of **2** suitable for X-ray analysis formed, upon cooling, within a day. The formulation of **2** was confirmed by single crystal X-ray analysis† and ^1H NMR spectroscopy.

$$\mathbf{1} + \text{4-pic (excess)} + MeNO_2\ \text{(excess)} + \text{benzene (excess)} \rightarrow \mathbf{1}\cdot 4(\text{4-pic})\cdot MeNO_2\ \mathbf{2} \qquad (1)$$

A view of the six-component complex **2** is shown in Fig. 1(*a*). In a similar way to **1**·4(py)·py,[2] four molecules of 4-pic have assembled along the upper rim of **1** such that they form stacked dimers and participate in four O–H···N hydrogen bonds with two opposite resorcinol units of **1** [O···N separations (Å): O(1)···N(1) 2.740(4), O(2)···N(2) 2.704(4)]. Unlike **1**·4(py)·py, however, the cavity created by the five molecules is occupied by a guest which is different than the walls of the host. Specifically, a molecule of $MeNO_2$, which lies disordered across a crystallographic two-fold rotation axis, has assembled within **1** and interacts with **1** *via* C–H···π-arene interactions. Thus, by selecting a guest with an appropriate size, shape, and chemical exterior to assemble within **1**·4(4-pic), full structural mimicry, in a single step and virtually quantitative yield, of those host–guest properties displayed by upper rim substituted monomolecular calix[4]arenes has been achieved.[9] In other words, this approach to discrete, extended cavity frameworks based upon **1** is not limited to two component **1**·4(pyr)·pyr (where pyr = pyridine, substituted monopyridines) systems.[2]

A view of the crystal structure of **2** is shown in Fig. 1(*b*). Unlike **1**·4(py)·py, **2** self-assembles in the solid state such that the complexes self-include and lie in an antiparallel fashion along the crystallographic *b* axis. Indeed, the ability of **2** to exhibit self-inclusion may be attributed to the small size the $MeNO_2$ guest which, unlike **1**·4(py)·py, allows neighbouring molecules of **1** to assemble within the cavities created by the 4-pic moieties.‡

That this approach to discrete extended cavity frameworks based upon **1** may be expanded to a system involving a bifurcated hydrogen bond and a different guest is demonstrated by **3**. When **1** (0.020 g) was added to a boiling aliquot of MeCN (4 ml) in the presence of 1,10-phen (0.027 g) a white microcrystalline solid formed. Attempts to grow single crystals of this material suitable for single crystal X-ray analysis failed. Colorless crystals of **3** suitable for X-ray analysis were obtained by redissolving the solid, by heating, in the presence of benzene (2 ml), according to eqn. (2), and allowing the solution to slowly cool. The formulation of **3** was confirmed by single crystal X-ray analysis§ and ^1H NMR spectroscopy.

$$\mathbf{1} + 4(1,10\text{-phen}) + \text{MeCN (excess)} + \text{benzene (excess)} \rightarrow \mathbf{1}\cdot 4(1,10\text{-phen})\cdot\text{MeCN}\cdot\text{benzene}\,\mathbf{3} \qquad (2)$$

A view of the seven-component complex **3** is shown in Fig. 2. In a similar way to **2**, four molecules of 1,10-phen have assembled along the upper rim of **1** and lie approximately orthogonal to two opposite resorcinol units of the macrocycle. Unlike **2**, however, in addition to conventional O–H···N forces, the phenanthroline moiety interacts with **1** *via* a bifurcated hydrogen bond. In particular, three phenanthroline units participate in conventional O–H···N hydrogen bonds [O···N separations (Å): O(1)···N(1,2) 2.77(1), 3.20(1); O(2)···N(3,4) 2.67(1), 3.38(1); O(5)···N(5,6) 2.73(1), 3.40(1)] while a fourth participates in a bifurcated interaction [O···N separations (Å): O(6)···N(7,8) 2.77(1), 3.00(1)]. Interestingly, in the case of the former, the longest O···N separations are associated with the 'outer' region of the upper rim of **1** while, in the case of the latter, the longest distance is associated with the 'inner' region. As a consequence of these forces, a cavity has formed, inside which a molecule of MeCN is located, interacting with **1**, in a similar way to the $MeNO_2$ guest of **2**, *via* C–H···π-arene interactions.¶ The molecule of benzene, which completes **3**, is then observed to lie sandwiched between two opposite phenanthroline moieties, in a region above a resorcinol unit of **1**, such that the aromatic participates in two edge-to-face π–π interactions with the bipyridines.[10] To the best of our knowledge, in addition to **3**, an assembly involving 'resorcinol' and a chelating agent such as 1,10-phen has not been observed.

In a similar way to **1**·4(py)·py,[2] **3** self-assembles in the solid state such that the cavities of **1** lie at approximately right angles to each other. Thus, in a similar way to the guest of **1**·4(py)·py, the 1,10-phen moieties, owing to their size and location above **1**, preclude self-inclusion of **1** as observed in **2**.

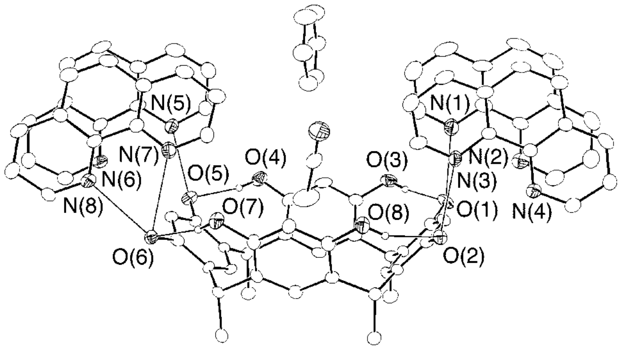

Fig. 2 ORTEP perspective of the seven-component assembly **3**. Selected interatomic distances (Å): O(1)···O(3) 2.73(1), O(1)···N(1) 2.77(1), O(1)···N(2) 3.20(1), O(2)···O(8) 2.76(1), O(2)···N(3) 2.67(1), O(2)···N(4) 3.38(1), O(4)···O(5) 2.75(1), O(5)···N(5) 2.73(1), O(5)···N(6) 3.40(1), O(6)···O(7) 2.78(1), O(6)···N(8) 2.77(1), O(6)···N(7) 3.00(1).

The results reported herein demonstrate that by using appropriately functionalized molecular components, it is possible to mimic host–guest properties of calix[4]arenes supramolecularly with respect to both upper rim substitution and guest inclusion. With these observations realized, focus can be placed upon determining if mimicry of those methods that involve sterochemical control to extending the cavity of **1** (*e.g.* C_4 *vs.* C_{2v}) can be achieved.[11] If one also considers that this approach stemmed from a crystal engineering design strategy,[12] such observations attest to the utility in using a supramolecular synthon, such as the resorcinol-based system[13] employed here, for rational solid state design.

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Notes and references

† *Crystal data* for **2**: monoclinic, space group $P2/c$, $a = 11.481(1)$, $b = 7.566(1)$, $c = 29.501(2)$ Å, $\beta = 96.434(1)°$, $U = 2546.5(3)$ Å^3, $D_c = 1.28$ g cm^{-3}, Mo-Kα radiation ($\lambda = 0.71070$ Å) for $Z = 2$. Least-squares refinement based on 2523 reflections with $I_{net} > 2.0\sigma(I_{net})$ (out of 3304 unique reflections) led to a final value of $R = 0.048$. 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. 6) and refinement was conducted using SHELXL93 (ref. 7) locally implemented on a pentium-based IBM compatible computer. Structure refinements and production of the figures were accomplished with the aide of RES2INS (ref. 8).

‡ We also note an O4···O4′ (O-4′ $-x + 1$, $+y$, $-z + 1.5$) separation of 3.025(3) Å between self-included strands of adjacent layers which suggests a weak hydrogen bond involving a disordered hydroxy hydrogen atom.

§ *Crystal data* for **3**: orthorhombic, space group $P2_12_12_1$, $a = 14.504(1)$, $b = 15.752(1)$, $c = 31.097(2)$ Å, $U = 7104.3(6)$ Å^3, $D_c = 1.29$ g cm^{-3}, Mo-Kα radiation ($\lambda = 0.71070$ Å) for $Z = 4$. Least-squares refinement based on 6469 reflections with $I_{net} > 2.0\sigma(I_{net})$ (out of 9237 unique reflections) led to a final value of $R = 0.068$. Aromatic 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 and refinement was conducted as described for **2**. CCDC 182/1117.

¶ We note that the included MeCN lies slightly tilted towards one of the resorcinol units of **1** such that the positioning of the molecule conforms to the cavity defined by the 1,10-phen moieties.

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