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Solid-State Self-Assembly of a Calix[4]pyrrole−Resorcinarene Hybrid into a Hexameric Cage

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Calix[4]pyrroles are a class of tetrapyrrolic macrocycles known to be effective receptors for anions.[1] The descriptive name "calixpyrrole" was coined by Sessler and co-workers due to the conformational analogy between them and the calix[4]arenes.[2] Substitution at each of the four *meso*-carbons of the calix[4]pyrrole framework with one aryl group affords four configurational isomers containing deep aromatic cavities and fixed walls.[3] The presence and chemical modification of the aromatic rings serve to alter and tune the intrinsic anion binding selectivity of the basic calix[4]pyrrole skeleton.[4]

On the basis of these observations, we are exploring the experimental evaluation of the anion−π interaction[5] using, as a model system, calix[4]pyrroles in solution.[6] Consequently, we have designed and characterized several new *meso*-tetramethyltetraarylcalix[4]pyrroles. Here we described the molecular assembly phenomenon observed in the solid state for a two-component mixture consisting of the α,α,α,α isomer of the calix[4]pyrrole−resorcinarene hybrid **1** and tetramethylammonium chloride $\mathrm{Cl^-{\cdot}}$**2a** that is solely controlled by the relative stoichiometry of the mixture.

Compound α,α,α,α-**1** was isolated from the condensation reaction of pyrrole with methyl 3,5-dihydroxyphenylketone. The octahydroxy compound **1** possesses an array of phenolic functions reminiscent of that presented by the *C*-methylcalix[4]resorcinarene **3** upper rim (Figure 1). When viewed from the top, the X-ray structure of the acetonitrile solvate of compound **1** closely resembles that of resorcinarene **3** in the bowl or crown-like conformation (Figure 2a). Calix[4]pyrrole **1** adopts a cone conformation, stabilized by four OH···H intramolecular hydrogen bonds. The four pyrrolic NH groups are hydrogen-bonded to the nitrogen atom of an acetonitrile molecule surrounded by the aromatic cavity.[7] Compound **1** has also been crystallized from acetone, water, and acetonitrile/water, and unlike the *C*-methylresorcin[4]arene **3**, it has thus far not displayed any tendency to form solvent-mediated hexameric molecular capsules in the solid state.[8] In contrast, while resorcinarene **3** forms a simple dimeric capsule[9] in the solid state when complexed to $\mathrm{Cl^-{\cdot}}$**2a**, compound **1** assembles into a hexameric cage.

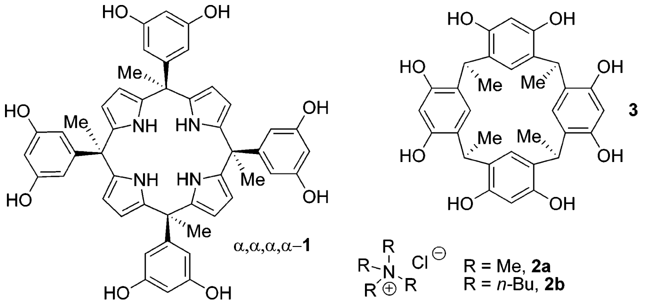

Figure 1. Structural formulas of resorcincalix[4]pyrrole **1**, resorcin[4]arene **3**, and tetralkylammonium salts **2**.

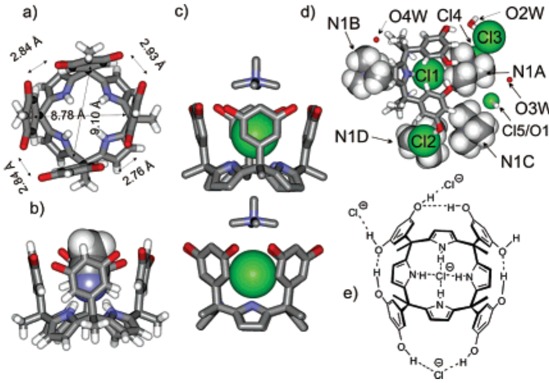

Figure 2. X-ray crystal structures of the acetonitrile complex of **1**: (a) top view (acetonitrile molecule removed for clarity) and (b) side view. (c) Packing of the *endo* cavity complex $\mathrm{Cl^-{\cdot}}$**2a**@**1**. (d) Crystallographic asymmetric unit of the hexameric assembly **4** (side view) showing calix[4]pyrrole **1** and water oxygen atoms in stick representation, while tetramethylammonium cations **2a** and chloride anions are shown with van der Waals radii. A chloride anion showing a positional alternate disorder with a water molecule (Cl5/O1W) is displayed at one-half CPK scale. (e) Observed conformation of calix[4]pyrrole **1** in hexamer **4**.

The study of the complexation properties of **1** with tetramethylammonium chloride $\mathrm{Cl^-{\cdot}}$**2a** was attempted using ^{1}H NMR titration techniques. Unexpectedly, the addition of 0.5 equiv of $\mathrm{Cl^-{\cdot}}$**2a** to an acetonitrile solution containing anion receptor **1** induced the formation of a white precipitate. To avoid the formation of the precipitate, we used the chloride anion as the tetrabutylammonium salt **2b**. The incremental addition of 5 equiv of chloride salt $\mathrm{Cl^-{\cdot}}$**2b** to an acetonitrile-d_3 solution of calix[4]pyrrole **1** produced downfield shifts of the NH ($\Delta\delta_{\mathrm{obs}} = 0.14$ ppm) and OH ($\Delta\delta_{\mathrm{obs}} = 1.42$ ppm) protons. Also, the aromatic proton at the *para* position of the resorcinol ring moved downfield, while those at the *ortho* position were shifted upfield. Under these conditions, compound **1** therefore interacts with $\mathrm{Cl^-}$ anion in the fast-exchange regime of the NMR time scale, preferentially through the hydroxyl groups of the upper rim, and forms an *exo* cavity adduct.[10] Intrigued by these findings, we turned our attention to solving the solid-state structure of the precipitate formed during the titration of **1** with $\mathrm{Cl^-{\cdot}}$**2a**.

Single crystals suitable for X-ray analysis of the structure of the complex were obtained after heating an acetonitrile suspension consisting of an equimolecular mixture of calix[4]pyrrole resorcine hybrid **1** and $\mathrm{Cl^-{\cdot}}$**2a** at 45 °C for 2 days. The X-ray structure revealed the exclusive formation of an *endo* cavity complex, $\mathrm{Cl^-{\cdot}}$**2a**@**1**. The chloride anion is symmetrically bound to the four NH groups, with a distance of 3.26 Å for the N···Cl interaction. The tetramethylammonium cation **2a** serves to bridge two calix[4]pyrrole units of **1**, forming a columnar arrangement. One methyl group is included in the middle of the electron-rich cup formed by the four pyrrole rings, and the other three $\mathrm{N{-}CH_3}$ groups are located

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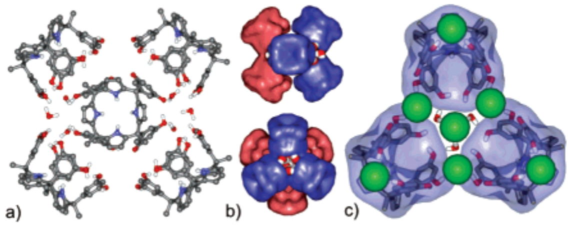

Figure 3. (a) Simplified view of the hexameric structure **4**. Tetramethylammonium cations, chloride anions, and water molecules not hydrogen bonded to **1** have been removed for clarity. The calix[4]pyrrole unit in the back of the superstructure has also been eliminated. (b) Two different views of structure **4**, in which the three calix[4]pyrrole **1** molecules, hydrogen-bonded through water molecules forming a hemisphere, are represented with identically colored surface models. (c) Cut-away view of a hemisphere of **4** along the three-fold rotation axis. Chloride anions are shown in CPK representation.

on top of the encapsulated chloride anion. Thus, it can be considered that **1** functions, in the solid state, as a ditopic cation−anion receptor (Figure 2c).[11]

We rationalized that cocrystallization of **1** with $\mathrm{Cl}^{-}\cdot$**2a** from a solution containing a high molar excess of the ammonium salt may induce the formation of solid structures in which the chloride anion will display simultaneously *endo* and *exo* cavity coordination. Colorless crystals suitable for X-ray analysis were grown from a solution of **1** in acetonitrile previously saturated with tetramethylammonium chloride $\mathrm{Cl}^{-}\cdot$**2a**.[12] Solution of the diffraction data revealed a complex asymmetric unit that comprises one calix[4]-pyrrole host **1**, four positions for tetramethylammonium cations **2a**, *five positions* for chloride anions (one *endo* and four *exo*), and four water molecules. Notably, calix[4]pyrrole−resorcine hybrid **1** now exhibits only three intramolecular hydrogen bonds which impart stability to the cone conformation attained due to binding of a chloride anion inside its deep aromatic cavity (Figure 2d,e).[7] The side of **1** that does not show an intramolecular hydrogen bond directs the two hydroxyl groups toward a chloride anion (Cl2). The crystal lattice reveals the formation of superstructure **4**, containing six calix[4]pyrroles **1**, which can be referred to as an octahedral supramolecular assembly. This supramolecular structure is closely related to that found for **3**, which together with eight water molecules self-assembles into a chiral hexameric structure stabilized by 60 hydrogen bonds.[8] Each calix[4]pyrrole **1** is hydrogen-bonded to only two of the four neighboring calix[4]pyrrole molecules through water molecules embedded along the surface of the poles of the hemisphere and through interactions with a bridged chloride anion. The water molecules also interact with a central chloride anion (Figure 3c).

The hemisphere contains enough room to accommodate six tetramethylammonium ions **2a** and three extra chloride anions, each one bound inside the aromatic cavity of **1** (see Figure S2a,b, Supporting Information). Two filled hemispheres, when tilted 60° with respect to one another, fit perfectly and yield the hexameric structure **4** detected in the solid state (Figure S2c). The two hemispheres are maintained together only through electrostatic interactions between embedded cations and anions. Furthermore, the inner space of hexamer **4** contains a fascinating arrangement of three water molecules and three chloride anions forming a hydrogen-bonded cyclic cluster (Figure S3).

To conclude, we have shown that the solid packing of the α,α,α,α isomer of calix[4]pyrrole−resorcine hybrid **1** and tetramethylammonium chloride $\mathrm{Cl}^{-}\cdot$**2a** is controlled by their relative stoichiometry in solution. On the one hand, an equimolecular mixture of calix[4]pyrrole **1** and $\mathrm{Cl}^{-}\cdot$**2a** yields crystals showing a columnar packing of the *endo* cavity complex $\mathrm{Cl}^{-}\cdot$**2a@1**. On the other hand, the use of a high molar excess of the $\mathrm{Cl}^{-}\cdot$**2a** salt induces, in the solid state, a self-assembly process of the *endo* cavity complex $\mathrm{Cl}^{-}\cdot$**2a@1** into a supramolecular hexameric structure. The self-assembly process is driven purely by hydrogen-bonding and electrostatic interactions. The hexameric structure **4** corresponds to an octahedron in which the centroid of the nitrogen atoms of the pyrroles is at each vertex.

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Supporting Information Available: Additional figures and detailed description of the solid-state structure of hexamer **4** (PDF); X-ray crystallographic files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) We have reproduced three times the crystallization protocol, and in all cases crystals of the same type were obtained.

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