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pH-Controlled Molecular Switches and the Substrate-Directed Self-Assembly of Molecular Capsules with a Calix[4]pyrrole Derivative

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Abstract: 10α,20α-Bis(4-nitrophenyl)-calix[4]pyrrole (**1**) forms 1:1 complexes with anions of selected aromatic hydroxy acids in which the host orientation within the guest is controlled by a change in the pH value. Some bis-anionic guests, including those obtained from 4-hydroxybenzoic acid, 1,4- and 1,3-benzenedicarboxylic acids, induce the self-assembly of molecular capsules involving two molecules of the receptor. ^{1}H NMR data and solid-state structures of the 1:1 complex of **1** with *p*-$C_6H_4(COOH)(COO^-)^+NMe_4$ and the 2:1 capsule $[(\mathbf{1})_2 m\text{-}C_6H_4(COO^-)_2\text{-}(^+NMe_4)_2]$ provide structural details in solution and in the solid state.

Keywords: anions · calixpyrroles · capsules · hydrogen bonding · molecular recognition · self-assembly

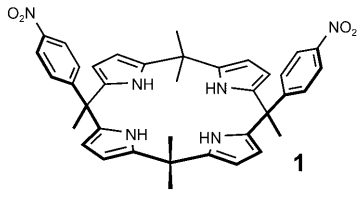
Introduction

Molecular switches and machines in which the relative positions between molecules can be modified by changing an external parameter (e.g., pH) or through a specific input (e.g., light pulses) are an extensively studied topic.[1] Molecular capsules have been investigated because of a number of interesting features.[2] Molecular encapsulation provides a means to create a microenvironment in which two or more entrapped molecules can undergo specific reactions that would not otherwise readily occur.[3] Moreover, capsules can protect an entrapped molecule from certain reactions because of the presence of other species in the outside medium,[4] or they can act as containers that can deliver entrapped guest molecules across membranes.[5]

Macrocycles based on phenols (calixarenes, resorcarenes, and pyrogallole-derived receptors) are to date among the most widely studied building units for the assembly of molecular capsules,[6] together with the glycoluril-containing building blocks extensively studied by Rebek and co-workers.[7] There are few examples in which calixpyrroles[8] are involved in capsular self-assembly. Some *meso*-aryl-substituted calix[6]pyrroles were described to form capsular structures in the solid state with neutral molecules.[9] A calix[4]-pyrrole with resorcinol units at the *meso* positions was reported to form hexameric cages.[10] A very interesting self-assembly process involving a calix[4]pyrrole derivative, chloride ions, and fullerene that led to a capsular structure has also been described.[11]

Recently, we synthesized the calix[4]pyrrole derivative **1**.[12] This compound can be viewed as a pair of molecular tweezers because the electron-deficient aromatic rings may "pinch" electron-rich substrates through π interactions, while the NH units can simultaneously be involved in the binding by acting as hydrogen-bond donors. Calixpyrroles, including **1**, have demonstrated different selectivities toward the binding of different anions.[8,12] Hence, we expected that molecules containing different functional groups that can be converted into anionic centers at different pH values could switch their position within receptor **1**.

Considering the structural features of **1**, we also expected that two molecules of this U-shaped receptor could be si-



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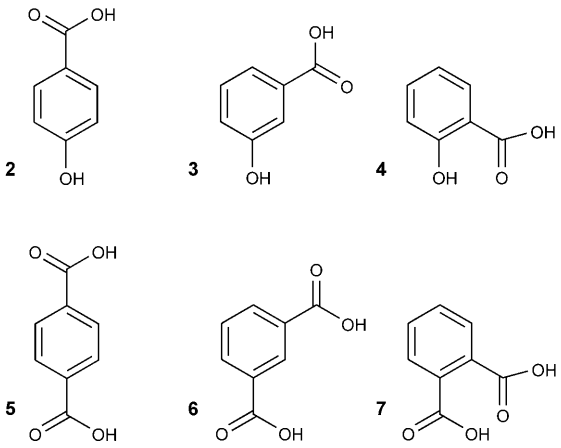
multaneously involved in the binding of selected bis-anions as interlocking pairs of horseshoes. This spatial arrangement has been described by Rebek and co-workers[7] and MacGillivray and Atwood[13] as the assembly of the two halves of a tennis ball. Herein, we report an investigation by ^{1}H NMR spectroscopic analysis (CD_3CN, 300 MHz) of the formation of a number of molecular switches and capsules from **1** with several aromatic bis-anions.

Results and Discussion

We chose to test the anions that can be generated from the hydroxybenzoic and benzenedicarboxylic acids **2–7** as potential components of pH-controlled molecular switches and/or as guests that could (as bis-anions) induce the self-assembly of molecular capsules. The various regiochemistries of the hydroxybenzoic and benzenedicarboxylic acids appeared useful to investigate the steric requirements for capsular assembly.



Solution studies: Before testing compounds **2–7**, we investigated the binding of **1** with the benzoate and phenolate anions as either $DBUH^+$ (DBU = 1,8-diazabicyclo-[5.4.0]undec-7-ene) or Cs^+ ions (from Cs_2CO_3) salts (see the Experimental Section). The ^{1}H NMR spectra indicated that 1:1 complexes were formed with complete facial selectivity (the binding occurring onto the face of the macrocycle containing the nitrophenyl units). Remarkable upfield complexation-induced shifts (CIS) were observed for the aromatic phenolate and benzoate protons in the complexes (see Figure 1) as a consequence of the shielding effect of the *p*-nitrophenyl units.[14]

Competitive-binding experiments involving benzoate and phenolate ions demonstrate that the latter displaces the benzoate ion from the receptor quantitatively (Figure 1c). The NH resonances of **1** in the phenoxy-bound complex resonate at considerably lower fields than in the carboxy-bound complex ($\delta = 12.4$ and 11.5 ppm, respectively, regardless of whether the counterion is a Cs^+ or $DBUH^+$ ion). These

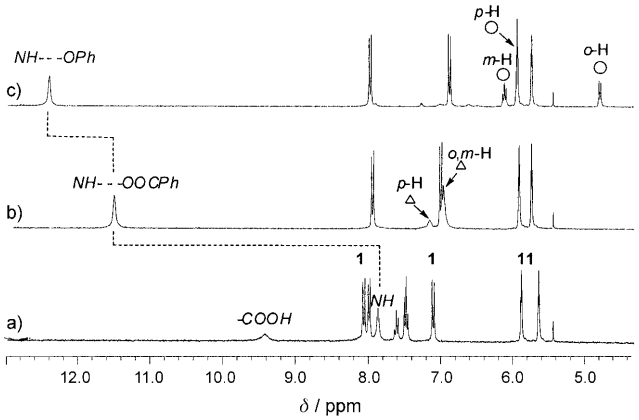


Figure 1. Partial ^{1}H NMR spectra in CD_3CN of a) **1**+PhCOOH, b) **1**+PhCOOH+Cs_2CO_3, and c) **1**+PhCOOH+Cs_2CO_3+PhOH. In (c) $PhCOO^-$ is not detected because the $PhCOO^-Cs^+$ salt, once displaced from receptor **1**, precipitates from the solution. Triangles indicate the benzoate protons and circles indicate the phenolate protons at the indicated *o*/*m*/*p* positions.

complexes are kinetically slow on the NMR timescale and the binding constants are large and beyond the limit of NMR methods for their determination. An attempt to determine binding constants by UV spectroscopic analysis was fruitless because the spectral changes upon binding of these two anions are marginal.

Under moderately basic conditions (NMe_3 or just over one equivalent of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)), all of the hydroxy acids **2–4** could be selectively deprotonated and complexed through the carboxylate unit by receptor **1**. In the presence of stronger bases, because the phenoxy anion is complexed by **1** more strongly than the carboxy anion, two evolutions of the host–guest systems can occur in theory: 1) switching of the binding mode (from the carboxy-bound monoanion to the phenoxy-bound bis-anion) or 2) the formation of a "nonsymmetric" molecular capsule involving two molecules of receptor **1**, each interacting with one of the two different anionic centers of the guests.

The carboxy-bound complex formed by the carboxylate salt of 4-hydroxybenzoic acid (**2**) with DBU with one equivalent of receptor **1** was converted into a mixture of capsule and phenoxy-bound complex (38 and 62%, respectively) upon addition of another equivalent of DBU. However, in the presence of one more equivalent of calix **1**, the capsule was quantitatively formed (Figure 2).

Although the association constants were too high to be determined by NMR spectroscopic analysis, it was evident that in the presence of the bis-anion the formation of a capsular assembly was favored over that of any of the two 1:1 complexes. The existence of a cooperative binding effect could be proved by measuring[15] the ratio of $K_{a(1:1)}/K_{a(1:2)}$, which was found to be 0.5:1, that is, well above the critical level of 0.25:1 that characterizes non-cooperativity.[16]

The 1:1 carboxy-bound complex of 3-hydroxybenzoate (**3**) with **1** was converted into the phenoxy-bound complex as a function of the added amount of DBU. This switching was

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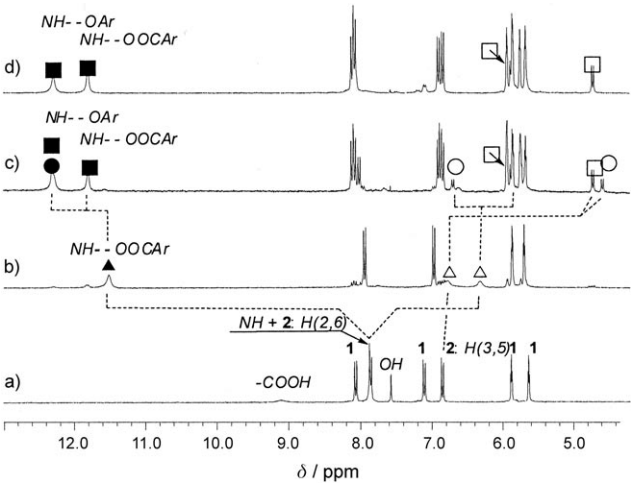

Figure 2. Partial ^{1}H NMR spectra in CD_3CN of a) **1**+**2** (1:1 molar ratio), b) **1**+**2**+DBU (1 equiv of DBU), c) **1**+**2**+DBU (2 equiv of DBU), and d) **1**+**2**+DBU (2:1:2 molar ratios, respectively). Triangles indicate the 1:1 carboxy-bound complex, circles indicate the phenoxy-bound 1:1 complex, and squares indicate the capsular assembly (black = host NH, white = guest protons).

quantitative in the presence of ten equivalents of the base (Figure 3 and Figure 4). The need for a considerable excess of the base is consistent with the lower acidity of the hydroxy unit of **3** relative to **2**. However, unlike the case of **2**, there was no evidence to support the presence of a capsular complex, even when receptor **1** was added in excess. 2-Hydroxybenzoic acid (**4**) and **1** formed only the carboxy-bound 1:1 complex, regardless of the amount of base added (Cs_2CO_3 or DBU).

Competitive binding of the two bis-anions derived from 3- and 4-hydroxybenzoic acid with **1** (i.e., 2 equiv of **1**+1 equiv of **3**+1 equiv of **2**+10 equiv of DBU) gave a mixture in which ^{1}H NMR spectroscopic analysis revealed the presence

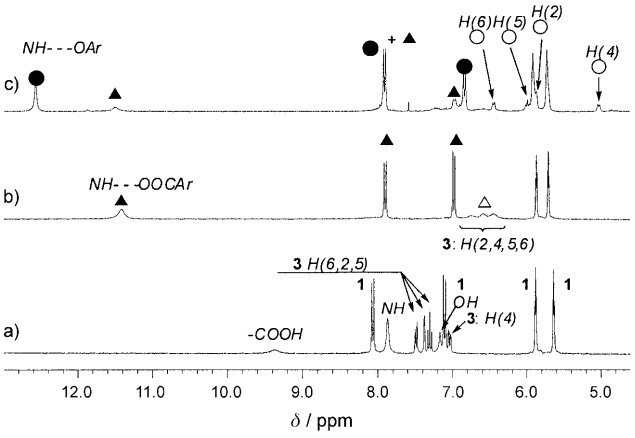

Figure 3. Partial ^{1}H NMR spectra in CD_3CN of a) **1**+**3** (1:1 molar ratio), b) **1**+**3**+DBU (1 equiv of DBU), and c) **1**+**3**+DBU (10 equiv of DBU). Triangles indicate the carboxy-bound 1:1 complex and circles indicate the phenoxy-bound complex (black = host protons, white = guest protons). The evolution of the supramolecular system corresponding to the ^{1}H NMR spectral changes from (a) to (c) is depicted in Figure 4.

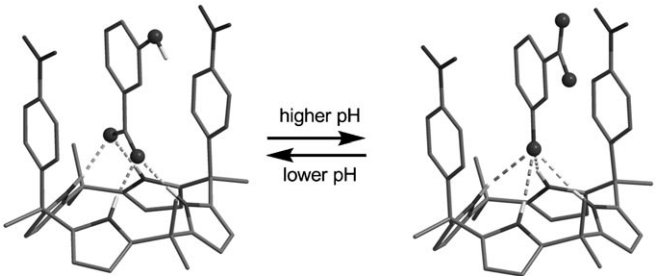

Figure 4. The topological switch for the binding of 3-hydroxybenzoic anions as a function of the amount of added base.

of 11% phenoxy-bound **3**, 29% phenoxy-bound **2**, and 60% of the encapsulated bis-anion of **2**. This composition confirmed that **1** exhibits selectivity toward the 1,4-substitution pattern and that this linear shape is best suited for the assembly of the capsular species.

1,4-Benzenedicarboxylic acid (**5**) and the Cs^+ ion were too insoluble in acetonitrile for ^{1}H NMR spectroscopic analysis (we could detect no resonance signals from these salts). However, we could explore the complexation of the bis-anion of **5** with **1** by ^{1}H NMR spectroscopic analysis by using its preformed $^+NnBu_4$ salt (Figure 5). The spectra were consistent with the binding being both strong and kinetically slow on the ^{1}H NMR timescale. The loss of symmetry for the bis-anion along the 1,4-axis in the 1:1 complex was expected to induce different chemical shifts for the two pairs of protons adjacent to each of the carboxy groups. However, we observed four and not two resonances for the protons of the bound anion. This behavior can be explained by assuming that the bis-anion is firmly held within the U-shaped cavity of **1**, with two discrete orientations (a π–π stacking interaction and an edge-to-face orientation with respect to the *p*-nitrophenyl units of **1**) and undergo slow exchange on the NMR timescale.[17] The resonance intensities for each set of the "*ortho*" protons of the 1,4-benzenedicarboxylate are identical, thus indicating that there is no substantial energy difference between the two binding modes,

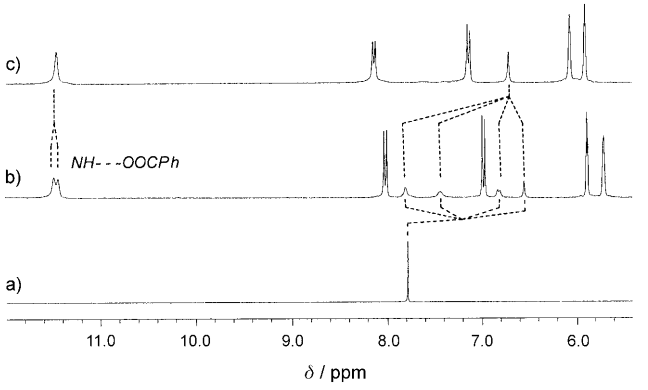

Figure 5. Partial ^{1}H NMR spectra in CD_3CN of a) p-$C_6H_4(COO^-)_2(^+NnBu_4)_2$, b) p-$C_6H_4(COO^-)_2(^+NnBu_4)_2$+**1** (1 equiv of **1**), and c) p-$C_6H_4(COO^-)_2(^+NnBu_4)_2$+**1** (2 equiv of **1**).

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although these must involve two different conformations of receptor **1.**

The origin of these four resonances was also confirmed by saturation transfer experiments. Irradiation of any of these signals resulted in the suppression of the other three signals. The NH protons of **1** appear as two signals of very similar intensity, which we ascribe to the two different modes of binding for the carbonyl oxygen atoms: 1) Each oxygen atom interacts with a pair of pyrrole NH units at either side of the *meso-p*-nitrophenyl substituent and 2) a pair of pyrrole NH units between the *p*-nitrophenyl-substituted positions.[18] This model of binding is supported by the X-ray crystal structure of the 1:1 complex of **1** with the monotetramethylammonium salt of **5** (see below).

In the presence of two equivalents of receptor **1**, the ^{1}H NMR spectrum changed dramatically (Figure 5c). The 1,4-benzenedicarboxylate and the NH signals coalesced to give single resonances. These spectral features are consistent with the formation of a molecular capsule (Figure 6). For

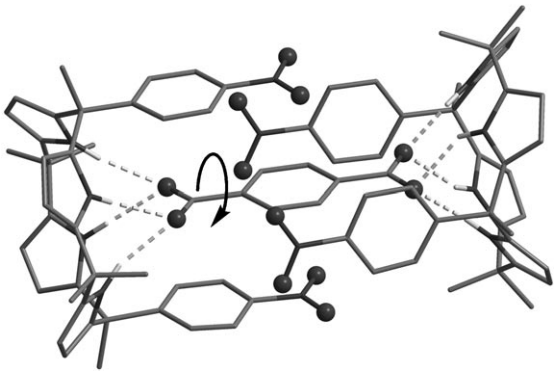

Figure 6. The structural features of the molecular capsule formed by 1,4-benzenedicarboxylate (darker shade) with two molecules of receptor **1** as suggested by its ^{1}H NMR spectrum. The arrow indicates the type of fast tumbling that averages the proton resonance signals of the guest. Only NH···O hydrogen bonds are shown, the other hydrogen atoms have been removed for clarity.

this capsule to be formed, the two macrocycles must approach with the *p*-nitropheny units "staggered" so that each of the carboxy groups of the guest can interact with one calixpyrrole moiety. In the resulting cavity, the 1,4-benzenedicarboxylate can be, at the same time, in a π–π orientation with respect to one pair of aryl rings of one molecule of **1** and in an edge-to-face orientation with the aryl rings of another molecule of **1**. We believe that this supramolecular structure allows the guest to tumble along its longer axis with an energetic pathway that only requires a slight butterfly-like motion of the aryl rings of **1**. Therefore, the two NH resonances observed in the 1:1 complex also appear as one signal in this capsule.

Variable-temperature ^{1}H NMR spectroscopic experiments on the 1:1 complex and the capsular assembly of **1** with 1,4-benzenedicarboxylate failed to provide thermodynamic parameters because of the temperature limits imposed by the solvent (see the Supporting Information), but the spectral changes were consistent with the binding modes proposed above.

Similar results were obtained by using the $DBUH^+$ salt of **5**. The 1:1 and capsular complexes were formed quantitatively depending on the amount of receptor present. However, with $DBUH^+$ as the counterion, the ^{1}H NMR spectrum of the 1:1 complex contained only two (and not four) broad resonances for the protons of 1,4-benzenedicarboxylate. We believe that this difference is consistent with previously reported studies on the role of the cationic counterpart on the binding of anions with calixpyrroles.[18] These receptors are ditopic,[19] and when they adopt the usual cone conformation, in which the NH units point toward the anion, the other side of the calix provides a conical cavity in which different cations can be accommodated. The Cs^+ ion and several "ball-shaped" ammonium ions were complexed effectively.[19]

With the cationic binding site (i.e., the conical cavity) occupied, the conformational mobility of the calixpyrrole anion complex is restricted. All these elements taken together suggest that $DBUH^+$ interacts less effectively than $^+NnBu_4$ or $^+NMe_4$ with the cation-binding site of **1.** Hence, we can qualitatively estimate that the complexes (and capsules) described here, in which $DBUH^+$ is the counterion, are weaker and more conformationally mobile than those in which the cationic components are either $^+NnBu_4$ or $^+NMe_4$. Indeed, these qualitative considerations are also supported by the encapsulation of the $^+NMe_4$ ion between two calixpyrrole units observed in the X-ray crystal structure of the 1:1 complex of **1** with the monotetramethylammonium salt of **5** and the X-ray crystal structure of the capsular complex m-$C_6H_4(COO^-)_2(^+NMe_4)_2$ (see below and Figures S4 and S6 in the Supporting Information). In solution, the
$^+NMe_4$ ion was considerably more effective than $^+NnBu_4$ and $DBUH^+$ at promoting the capsular assembly of bisanion of **5** with two molecules of **1**. In fact, in complexation studies that used this cation we could not detect any 1:1 complex (only the capsular structure was observed) regardless of the host/guest ratios used.

The addition of excess Cs_2CO_3 to a solution of 1,3-benzenedicarboxylic acid **6** and **1** (1:1 or 1:2 ratios) in CD_3CN led to the formation of a solid, whereas both the guest and the host were no longer detectable by ^{1}H NMR spectrometric analysis in solution.

However, the bis(tetramethylammonium) salt of **6** was fairly soluble in CD_3CN and the addition of **1** resulted in the formation of either a 1:1 complex or capsular assemblies in ratios that were a function of the amount of receptor present. The capsular assembly was observed only when **1** was in excess of 1:1 stoichiometry. Changes in the ^{1}H NMR spectrum could be clearly explained by the shielding effect of the nitrophenyl rings of **1** on the protons of the guest, which exhibit upfield shifts, and by taking into account the symmetry of the system (Figure 7). The most striking feature was that the 1:1 complex contained four different resonance

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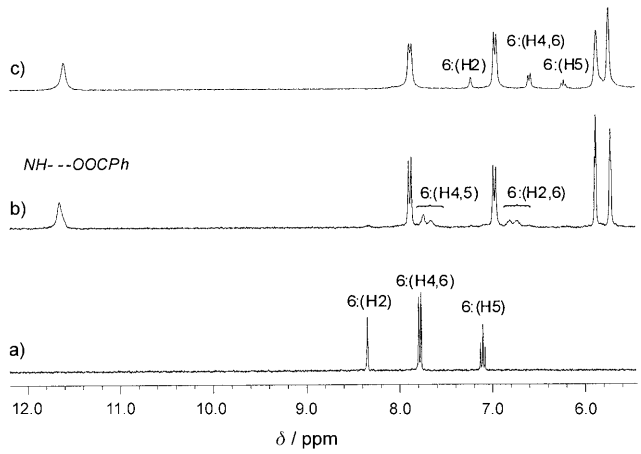

Figure 7. Partial ^{1}H NMR spectra in CD_3CN of a) *m*-$C_6H_4(COO^-)_2(N^+Me_4)_2$, b) **1**+*m*-$C_6H_4(COO^-)_2(N^+Me_4)_2$ (1:1), and c) **1**+*m*-$C_6H_4(COO^-)_2(N^+Me_4)_2$ (2:1).

signals for the bis-anion of **6**, which became three signals again in the capsule. The kinetics of the binding was slow on the NMR timescale.

Similar experiments that used $DBUH^+$ as the counterion gave very broad spectra and further investigation with this cation was not undertaken.

In a direct competition experiment, a mixture containing **1**, *m*-$C_6H_4(COO^-)_2(^+NMe_4)_2$, and *p*-$C_6H_4(COO^-)_2(^+NMe_4)_2$ in a 1.4:0.6:0.4 molar ratio, respectively, at 20 °C and with a concentration 0.008 M of **1**, contained all of the 1,4-bis-anion as the capsular complex and all of the 1,3-bis-anion as the 1:1 complex. This composition proved that although both capsules can be formed, the supramolecular capsule of **1** strictly discriminates and favors the 1,4-bis-anion as a guest. The origin of the cooperative effect in the capsular assembly formed by **1** with the 1,4-benzenedicarboxylate requires additional investigation. Although a recent study was reported on the stabilizing geometries for the interaction between the nitrobenzene units,[20] none of those described therein can be easily transferred to our case. We speculate that a stabilizing contribution in the capsule may originate from CH···O hydrogen bonds between the aromatic protons *ortho* to the nitro groups of one molecule of **1** and the oxygen atoms of the nearby nitro groups of another molecule of **1** in the capsule.

1,2-Benzenedicarboxylic acid (**7**) is soluble in CD_3CN, and the addition of DBU gives the bis salt in which the resonance signals of the protons are shifted with respect to the acid (AA′BB′ centered at $\delta = 7.59$ and 7.74 ppm in the acid shifts to $\delta = 7.44$ and 8.20 ppm in the bis-anion). When one equivalent of **1** was added, only minor perturbations of the chemical shifts were observed for the anion, the complexation was fast on the NMR timescale, and the NH signals of **1** shifted by $\Delta\delta = 1.36$ ppm, thus appearing at $\delta = 9.20$ ppm. Further addition of **1** produced only minor changes in the spectrum but no evidence for the formation of a capsular assembly. Similar results were obtained by using Cs_2CO_3.

Solid-state studies: The slow concentration of a solution of **1** and the bis(tetramethylammonium) salt of **5** in ethyl acetate gave crystals that could be analyzed by X-ray crystallographic studies. These crystals contained two independent inclusion complexes **A** and **B** of the mono(tetramethylammonium) salt of **5** (which was presumably formed by the action of adventicious carbonic acid) and the tweezer-like tetra(pyrrole) macrocyclic host **1**. (Complex **A** is shown in Figure 8 and complex **B** in Figure 9). In both complexes, the

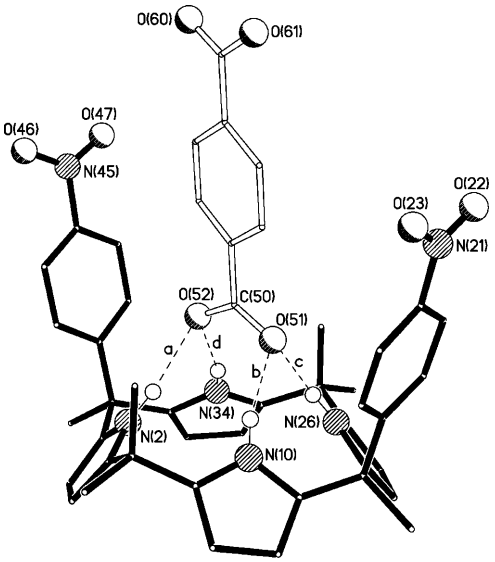

Figure 8. The molecular structure of one of the two crystallographically independent anionic inclusion complexes (**A**) present in the crystals of [**1**·*p*-$C_6H_4(COOH)(COO^-)(^+NMe_4)$]. The NH···O hydrogen-bonding geometries (N···O, H···O [Å], N–H···O [°]) are: a) 2.911(18), 2.04, 163; b) 2.798(18), 1.92, 167; c) 2.806(16), 1.93, 166; and d) 2.803(18), 1.93, 162.

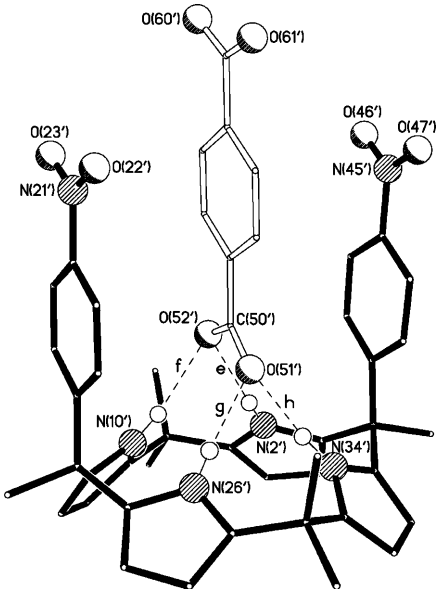

Figure 9. The molecular structure of one of the two crystallographically independent anionic inclusion complexes (**B**) present in the crystals of [**1**·*p*-$C_6H_4(COOH)(COO^-)(^+NMe_4)$]. The NH···O hydrogen bonding geometries (N···O, H···O [Å], N–H···O [°]) are: e) 2.860(19), 2.00, 161; f) 2.932(18), 2.07, 161; g) 2.796(14), 1.92, 165; and h) 2.719(12), 1.84, 166.

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presumed deprotonated carboxylate unit of the 1,4-benezenedicarboxylate anion (see the Supporting Information) is inserted into the cavity of the tweezer-shaped macrocycle[21] and forms hydrogen bonds with all four of the pyrrole NH donor atoms in a [2+2] fashion; each of the oxygen atoms accepts two hydrogen bonds (in both complexes **A** and **B** the four nitrogen atoms are coplanar to better than 0.01 Å). However, the way in which the 1,4-benzenedicarboxylate monoanion is oriented with respect to the macrocycle is different in each complex[22] and there is a corresponding difference in the conformation of the host macrocycle.

In complex **B**, the O(51′)/O(52′) carboxylate unit is oriented so that each oxygen atom accepts hydrogen bonds from the pyrrole ring NH units either side of a carbon atom bearing two methyl substituents (Figure 9). The aromatic rings of the two nitrophenyl substituents of the macrocycle are almost parallel with this CO_2 unit, the C_6 rings of the N(21′) and N(45′) nitrophenyl substituents being inclined by approximately 3 and 5°, respectively, to the C–CO_2 plane, with C(50′)···centroid separations of approximately 3.54 and 3.42 Å, respectively, indicating significant π–π stacking interactions. There are also close approaches of the N(21′) and N(45′) atoms to the centre of the 1,4-benzenedicarboxylate aromatic ring, with N···centroid separations of 3.42 and 3.68 Å, respectively. As a result, the macrocycle has a relatively closed geometry, and the centroid···centroid separation for these two nitrophenyl C_6 rings being approximately 6.92 Å.

In complex **A**, in contrast, the inserted carboxylate unit is oriented such that each oxygen atom accepts hydrogen bonds from the pyrrole ring NH units either side of a carbon atom bearing a nitrophenyl substituent (Figure 8). As a consequence, the O(51)/O(52) carboxylate group is aligned almost perpendicularly to the planes of the C_6 rings of the nitrophenyl substituents (i.e., approximately 91 and 90° for the N(21) and N(45) nitrophenyl substituents, respectively); the proximal O···centroid distances are approximately 3.47 and 3.23 Å for O(51) and O(52), respectively. Associated with these features, the macrocycle has an open conformation as the two nitrophenyl rings are bent away from the middle of the ring such that their C_6 centroid··· centroid separation is enlarged to approximately 8.90 Å (compared to approximately 6.92 Å in complex **B**). Thus, in complex **B** the insertion geometry of the 1,4-benzenedicarboxylate guest allows the two arms of the tweezer host to "grab" the guest, whereas in complex **A** the rotated insertion geometry of the guest molecule of approximately 90° "forces" the arms of the tweezer apart. These two geometries of binding are consistent with the ^{1}H NMR spectrum observed in solution (see above) in which they appear to be equally populated.

The protruding protonated $-CO_2H$ end groups of the 1,4-benzenedicarboxylate guest molecules of complexes **A** and **B** are in such proximity that it seems certain that they hydrogen bond to each other (see Figure S3 in the Supporting Information). Unfortunately, the disorder present in these anions, and the consequent geometrical optimizations, precludes any detailed analysis. The most significant inter-complex approaches to the nitrophenyl C_6 rings are a pair of C–H···π contacts from C_2-related complexes. The centroid of the N(45)-bound C_6 ring in complex **A** is approached by a CH proton from the N(21) aromatic ring of a C_2-related complex **A** with an H···π separation of approximately 2.82 Å and a CH···π angle of approximately 151°. For complex **B**, a CH proton from the N(45′) aromatic ring of one complex approaches the centroid of the N(21′) ring of a C_2-related counterpart with an H···π separation of approximately 2.89 Å and a CH···π angle of approximately 147°.

The solution of **1**+*m*-$C_6H_4(COO^-)_2(N^+Me_4)_2$ in a 2:1 ratio in CD_3CN used for the NMR spectroscopic analysis gave single crystals upon standing. Solid-state X-ray analysis revealed the expected 2:1 capsular structure with both ends of the deprotonated 1,3-benzenedicarboxylate guest species hydrogen bonding to different tetra(pyrrole) host macrocycles (Figure 10). Interestingly, although all four NH donors

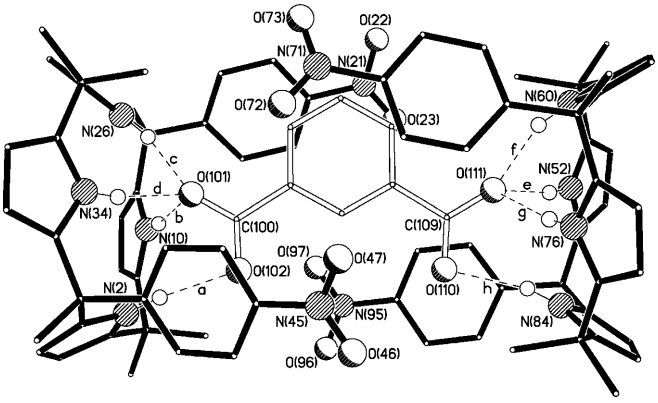

Figure 10. The molecular structure of the dianionic capsular species present in the crystals of [(**1**)$_2$·*m*-$C_6H_4(COO^-)_2(^+NMe_4)_2$]. The N–H···O hydrogen bonding geometries (N···O, H···O [Å], N–H···O [°]): a) 2.9113(13), 2.02, 173; b) 2.9875(14), 2.10, 169; c) 2.7387(13), 1.85, 167; d) 2.9335(13), 2.04, 170; e) 2.9503(13), 2.06, 170; f) 2.7500(13), 1.89, 159; g) 3.0118(14), 2.12, 171; and h) 2.9317(13), 2.05, 166.

of each host macrocycle and both of the acceptor oxygen atoms of each end of the 1,3-benzenedicarboxylate guest are involved in hydrogen bonding, the pattern is different to that seen in complexes **A** and **B** described above. Rather than the [2+2] motif seen in complexes **A** and **B**, in which each of the oxygen atoms is linked to two NH units, there is a [3+1] pattern at each end of the 1,3-benzenedicarboxylate, with one oxygen atom linked to three NH units (i.e., O(101) and O(111); interactions b–d and e–g, respectively, in Figure 10) and the other oxygen atom linked to just a single NH unit (i.e., O(102) and O(110); interactions a and h, respectively, in Figure 10). These features are presumably because the nitrophenyl arms of the tweezer-like host macrocycles need to interleave with each other for steric reasons and because of the 1,3-substitution pattern of the guest dicarboxylate molecule.

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Both of the macrocycles have relatively open geometries: the centroid···centroid separation for the two nitrophenyl C_6 rings are approximately 8.37 and 8.04 Å for the N(2) and N(52) macrocycles, respectively (compared to 6.92 and 8.90 Å for complexes **A** and **B**, respectively). The aromatic rings of the two nitrophenyl substituents of the N(52) macrocycle are inclined to the plane of the proximal C–CO_2 unit by approximately 20 and 16° for the N(71) and N(95) rings, respectively, with C(109)···centroid separations of approximately 4.23 and 3.85 Å, respectively. For the N(2) macrocycle, the aromatic rings of the two nitrophenyl substituents are inclined to the plane of the proximal C–CO_2 unit by approximately 37 and 34° for the N(21) and N(45) rings, respectively, with C(100)···centroid separations of approximately 4.49 and 3.92 Å, respectively. The aromatic ring of the 1,3-benzenedicarboxylate guest is approached by the nitro groups of two of the nitrophenyl arms (one from each macrocycle), the N(21)···centroid and N(71)···centroid separations are approximately 4.01 and 3.78 Å, indicating a degree of π–π stacking; the planes of the C–NO_2 units are inclined to the 1,3-benzenedicarboxylate C_6 ring plane by approximately 18 and 19° for the N(21) and N(71) moieties, respectively, and the two N···π vectors subtend an angle of approximately 122° at the ring centroid.

The closest inter-complex contacts to the nitrophenyl moieties are a) the approach of the O(46) atom of an adjacent complex to the centroid of the N(21)-bound C_6 ring with an O···centroid distance of approximately 3.60 Å and b) the stacking of the N(95) nitrophenyl unit with its centrosymmetrically related counterpart with mean interplanar and N(95)···centroid separations of approximately 3.31 and 3.60 Å, respectively.

Conclusion

Herein, we have demonstrated that a suitably designed calixpyrrole derivative can discriminate different anionic centers within the same molecule. This property can be exploited to control the orientation of certain guests (e.g., the anions formed by 1,3-hydoxybenzoic acid) within the receptor. This feature allows the control of the overall shape of the supramolecular aggregate by changes in pH value, and we are exploring ways of developing nanomechanical devices that exploit systems similar to the one described herein. The ability to choose which part of a guest is exposed to the outside environment and which part is instead buried within the receptor can provide a means to control the reactivity of the guest toward a given species. The formation of capsular assemblies as a function of the topological relations of bisanionic centers adds a novel dimension to the anion-recognition properties of calixpyrroles. In view of these considerations, we are therefore actively exploring the supramolecular chemistry of other variously functionalized (and expanded) calixpyrroles.

Experimental Section

General: Receptor **1** was prepared as described in reference [12]. All the chemicals were reagent grade and were used as supplied. The ^{1}H NMR spectra were recorded on a Varian Gemini 300 spectrometer at 300 MHz and 20 °C and care was taken to minimize exposure to moisture. For the complexation experiments, receptor **1** was dissolved in CD_3CN to a concentration of 2.5×10^{-3} M and one molar equivalent of the neutral putative guest was added. No CIS could be detected that would suggest interactions between the neutral compounds **2**–**7** and receptor **1**. The mixtures were treated with a base, namely, Cs_2CO_3, Et_3N, or DBU. Triethylamine formed a salt with the carboxylic groups only (but not with the phenolic OH group), and Cs_2CO_3 and DBU were strong enough bases to deprotonate both the phenolic and carboxylic units. Because Cs_2CO_3 is only sparingly soluble in CD_3CN, it had to be added as a solid and was always used in excess. Although **1** binds the carboxylate salts, as described above, we could detect no interference caused by the carbonate. DBU could be added in known amounts from stock solutions of suitable concentrations, which provided a practical means of adjusting the concentration of the base in the mixtures to achieve the stepwise deprotonation of the carboxylic and phenolic units in the guests. The *n*-tetrabutylammonium and tetramethylammonium salts of the acids were prepared by treatment with ammonium hydroxide followed by vacuum drying at 50 °C for no less than 24 h. In some cases (see below), we used NMe_4OH or $NnBu_4OH$ to prepare salts of the acids, which were used as dry, soluble solids that were added to solutions of receptor **1**.

X-ray crystallography

{[($C_{38}H_{38}N_6O_4$)·($C_8H_5O_4$)]($C_4H_{12}N$)}$_2$·$C_4H_8O_2$: $M_r=1852.12$, tetragonal, $P4/n$ (no. 85), $a=b=28.9055(2)$, $c=28.4971(5)$ Å, $V=23810.1(5)$ Å^3, $Z=8$, $\rho_{calcd}=1.033$ g cm^{-3}, $\mu(Mo_{K\alpha})=0.072$ mm^{-1}, $T=173$ K, yellow blocks, Oxford Diffraction Xcalibur 3 diffractometer; 14377 independent measured reflections, F^2 refinement, $R_1=0.137$, $wR_2=0.341$, 9771 independent observed absorption-corrected reflections ($|F_o|>4\sigma(|F_o|)$, $2\theta_{max}=49°$), 1344 parameters; CCDC-686270 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.

{[($C_{38}H_{38}N_6O_4$)$_2$·($C_8H_4O_4$)]($C_4H_{12}N$)$_2$}·2MeCN: $M_r=1680.00$, monoclinic, $P2_1/n$ (no. 14), $a=20.49098(6)$, $b=19.87053(6)$, $c=23.68069(8)$ Å, $\beta=110.6558(4)°$, $V=9022.2(2)$ Å^3, $Z=4$, $\rho_{calcd}=1.237$ g cm^{-3}, $\mu(Cu_{K\alpha})=0.670$ mm^{-1}, $T=173$ K, yellow blocks, Oxford Diffraction Xcalibur PX Ultra diffractometer; 17434 independent measured reflections, F^2 refinement, $R_1=0.036$, $wR_2=0.100$, 13495 independent observed absorption-corrected reflections ($|F_o|>4\sigma(|F_o|)$, $2\theta_{max}=143°$), 1179 parameters; CCDC-686271 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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