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Anion-Binding Behavior of Hybrid Calixpyrroles

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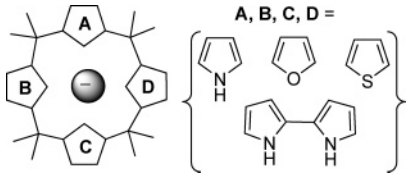

Hybrid calixpyrrole systems are calixpyrrole-like macrocycles that are based on more than one type of small molecule building block. Structurally, these "mixed-breed" macrocycles differ from calixpyrroles in that some pyrrolic units in the latter are replaced by other hetereocyclic units such as furan, thiophene, bipyrrole, and bithiophene. Although several such systems have been reported in recent years, only a few have been studied as possible anion receptors. In this paper, the results of detailed anion binding studies involving several prototypic systems are reported. Taken in concert, these results highlight the fact that some hybrid systems, including compounds **2**−**5**, display anion affinities that are considerably weaker than those of the parent system **1**. On the other hand, they also show that compounds **6**−**8** are good receptors for "Y-shaped" anions, such as carboxylates, and that they bind these species with high affinity. These findings are strongly supported by solid-state structural studies, which reveal an interesting "cross binding mode" for the binding of carboxylate anions by the bis-thiophene, bis-pyrrole system **7**.

Introduction

Anions play important roles in nature, and anion coordination chemistry has become an active area of research within the molecular recognition community over the last two decades.[1−5] However, the inherent properties of anions, such as low charge density and different inherent geometries (i.e., size and shape; orientation of charges, etc.), make the design of anion receptors a continuing challenge. Here, one area of emphasis is to generate neutral receptors for anions, a focus that is inspired in part by the fact that Nature uses neutral anion-binding motifs to recognize, bind, and transport physiologically important anions such as sulfate,[6] phosphate,[7] and chloride.[8] In recent years, calix[4]pyrroles (e.g., **1**) have been widely studied as novel neutral anion receptors. These simple-to-prepare porphyrinogen-like macrocycles bind small anions, such as fluoride and chloride, reasonably well in common aprotic

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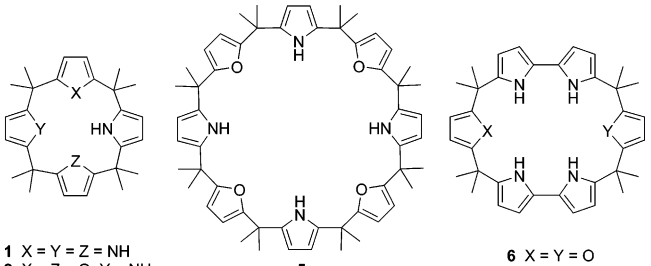
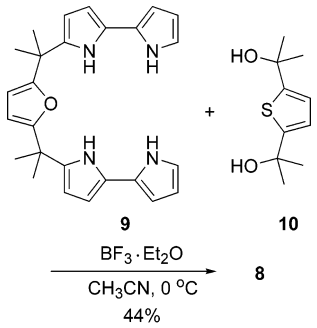
CHART 1



solvents.[9] Efforts to extend the effective binding range to larger anions has prompted the synthesis of several so-called higher order calix[*n*]pyrroles ($n \geq 4$),[10−12] as well as calix[*n*]bipyrroles ($n = 3, 4$)[13] that contain larger binding cavities than **1** (Chart 1). Work with calix[4]-pyrroles has also inspired the synthesis of "mixed breed" macrocycles, such as **2**−**7**, that rely on the use of non-pyrrolic building blocks, such as furan,[14,15] thiophene,[14,15] bithiophene,[16] phenyl,[17] and pyridine,[18] in addition to pyrrole or bipyrrole. Recently, we reported the synthesis and preliminary anion binding studies of two hybrid systems, namely calix[2]bipyrrole[2]furan **6** and calix[2]-bipyrrole[2]thiophene **7**, which display selectivity toward carboxylate anions.[15] In this paper, the results of detailed anion binding studies carried out on the hybrid systems **2**−**8** will be reported. While several of the systems studied, in particular **2**−**5**, showed little or no affinity for the test anions of interest (halides, dihydrogen phosphate, and carboxylates) when analyzed in acetonitrile (in the form of their tetrabutylammonium salts), several of the other receptor systems, namely the bipyrrole-based compounds **6**−**8**, showed good anion binding affinities and reasonable selectivity toward carboxylates. An unexpected result coming from the present study is the finding that calix[2]bipyrrole[1]furan[1]thiophene **8**, despite the structural similarity it bears to both **6** and **7**, binds chloride, benzoate, and acetate anions approximately 5−10 times more effectively than these latter two systems.

SCHEME 1. Synthesis of Calix[2]bipyrrole[1]furan[1]thiophene 8



Results and Discussion

The synthesis of compounds **2**−**7** has been reported previously.[14,15] Compound **8** was prepared using an approach analogous to that used to prepare **6** and **7**. Specifically, the bis(bipyrrolyl)furan **9** was reacted with **10** (1:1 molar ratio) in acetonitrile in the presence of a catalytic amount of $BF_3 \cdot Et_2O$ at 0 °C to give **8** in 44% yield (Scheme 1). Compound **8** was characterized by standard spectroscopic methods, as well as via single-crystal X-ray diffraction analysis.

Diffraction-grade crystals of **8** were grown by slow evaporation of a dichloromethane solution of **8** in an atmosphere saturated with hexanes. X-ray structural analysis revealed that two dichloromethane molecules are included in the unit cell and that the positions of the oxygen and sulfur atoms are disordered about the center of symmetry. This disorder is not shown in Figure 1, which gives a representation of the structure. The two pyrroles in each bipyrrole unit are orientated in opposite directions. The two pyrroles linked to the same heterocyclic linker (furan or thiophene) are orientated in the same directions, with both NH protons bound to one chlorine atom from a dichloromethane molecule via two NH- - -Cl hydrogen-bonding interactions. The nitrogen-to-chlorine distances are 3.430(2) and 3.486(2) Å, respectively; the NH proton-to-chlorine distances are 2.83(2) Å and 2.90(2) Å, respectively; and the nitrogen−hydrogen−chlorine bond angles are 128(2)° and 129(2)°, respectively. These hydrogen bond distances are within the ranges expected for effective hydrogen-bonding interactions, although the bond angles are less than ideal. Each of the pyrrole rings is also bound to one hydrogen atom present on a different dichloromethane molecule via a π- - -H−C hydrogen-bonding interaction, thus bringing the hydrogen atoms on the solvent molecule into close contact with the ring center of the pyrrole rings. The bond lengths for the proposed CH- - -π type interactions involving the solvent (CH) hydrogen and pyrrole ring of 2.55(3) and 2.53(2) Å, respectively, are also in the range of what is expected for these kinds of motifs.

Solution-phase anion-binding studies of compounds **2**−**8** were made by carrying out ^{1}H NMR spectroscopic

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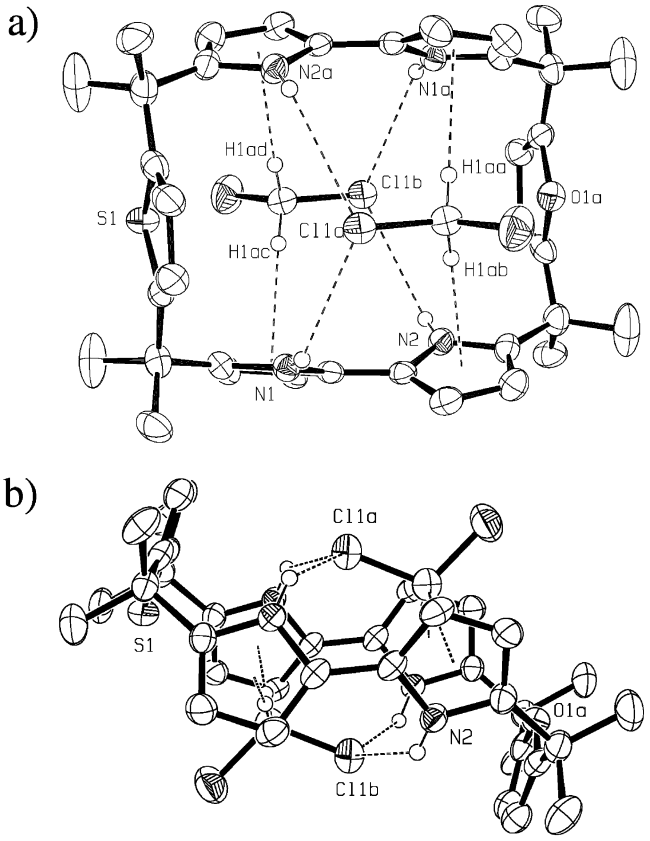

FIGURE 1. X-ray crystal structure of **8**·2CH_2Cl_2 (ORTEP, displacement ellipsoids scaled to the 50% probability level; some hydrogen atoms have been removed for clarity): (a) top view, (b) side view. Dashed lines are indicative of NH- - -Cl and CH- - -π hydrogen bonds. The positions of the oxygen and sulfur atoms are disordered about the center of symmetry. However, this disorder is not shown.

titrations in CD_3CN and ITC titrations in CH_3CN (Table 1). Compared to the parent system **1**, the hybrid calixpyrrole systems derived from pyrrole, furan, and thiophene, **2**−**5**, displayed very low affinities for the anions of interest, including F^-, Cl^-, $H_2PO_4^-$, and $PhCO_2^-$. In the case of compounds **2**−**4**, we ascribe the weak binding to a simple lack of hydrogen bond donor units within the macrocycles compared to **1** (two pyrrole subunits in **2**−**4** vs four in the case of **1**). In the case of compound **5**, the macrocycle is large and flexible, and the four pyrrole units are considered to be too far away from each other to bind anions in an effective or cooperative fashion. This leads to the poor anion affinities observed by experiment.

As shown in Table 1, standard ^1H NMR spectroscopic titrations confirmed that compounds **6**−**8** bind chloride, bromide, and hydrogen sulfate anions only weakly. Such a lack of strong binding was expected given the size and geometry mismatch between the anions and the receptor binding cavities. By contrast, the tetrahedral anion dihydrogen phosphate was found to be bound well by **7**, whereas compound **6** displays only a weak affinity for this anion. Unfortunately, no binding constant could be determined for **8** due to the loss in the NH proton signal intensity seen upon the addition of the dihydrogen phosphate anion.

We ascribe the differences in $H_2PO_4^-$ binding displayed by **6** and **7** to the different degree of geometry matching between the anion and the macrocyclic receptor in question. Specifically, the $C_{meso}-C_{meso}$ and $C_\alpha-C_\alpha$ distances in the furan case are shorter than those in the thiophene case (Figure 2). The different lengths of the linkers (furan or thiophene) in compounds **6** and **7** serve to define two different bipyrrole separations, which, in turn, regulate the possible macrocycle−anion interactions and hence the anion affinities.

Table 1 also shows that, as is true for compounds **6** and **7**, the structurally similar mixed furan−thiophene system **8** displays selectivity for carboxylates relative to other test anions (cf. Table 1). Taken in concert, these results serve to highlight how the minor structural differences associated with **6**−**8** can give rise to a rather significant change in anion binding ability. For instance, relative to **6** and **7**, compound **8** shows affinities for chloride, benzoate, and acetate anions that are enhanced by 5−10-fold while displaying comparable bromide and hydrogen sulfate anion affinities. As a consequence, compound **8** displays an enhanced selectivity for carboxylate anions over bromide and hydrogen sulfate relative to **6** and **7**, but no improvement in the carboxylate over chloride anion-binding ratio.[19]

The finding that compounds **6**−**8** selectively bind carboxylate anions over other anions revealed possible geometry matching between the hosts and the guests, since such a preference is not seen in the case of **1** (despite the greater basicity of carboxylate anions relative to, e.g., chloride anion). Based on an analysis of the geometries of both the carboxylate anions and these receptors, we propose three possible binding modes that might contribute to the host−guest interactions observed in solution (Figure 3). One such interaction involves a "one point binding" mode, in which only one oxygen atom of the carboxylate anion interacts with the macrocycles via four NH- - -O Hydrogen bonds. This kind of binding mode was seen in the crystal structure of calix[4]pyrrole carboxylate dimers.[20] The other two proposed interactions can be considered as "two point binding" modes, where both oxygen atoms of the carboxylate anion interact with the macrocycle via four NH- - -O hydrogen bonds. Here, both "cross binding" and "parallel binding" orientations can be defined. In the "cross binding" mode, the carboxylate anion plane is perpendicular to the bipyrrole plane, with each oxygen atom bound to one bipyrrole unit. By contrast, in the "parallel binding" mode, the carboxylate anion plane is parallel to the two bipyrrole subunits, with each of the latter being bound to the two carboxylate oxygen atoms simultaneously. However, other than the

(19) Currently, we rationalize the difference between **6** and **7** vs **8** to a competitive interplay between conformational and electrostatic effects. On one hand, macrocycle **6** is more conformationally flexible than **7** due to the smaller size of its constituent furan subunits relative to the thiophene present in **7**; this flexibility is helpful in accommodating bound anions and is expected to be manifest in terms of an increase in the binding affinity. On the other hand, the electrostatic repulsion effect between the furan oxygen or thiophene sulfur atom lone pairs (or between these heterocyclic subunits and the bound anion) is also expected to be bigger in the case of **6**; this electrostatic repulsion is expected to reduce the anion binding and leads to the prediction that macrocycle **7** will be a more effective anion receptor than **6**. In the case of macrocycle **8**, both a reduced level of electrostatic repulsion relative to **6** and a greater degree of flexibility relative to **7** is expected, an optimization of features that could account for its relatively enhanced anion binding affinities. Theoretical calculations designed to confirm or refute this hypothesis are currently underway.

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TABLE 1. Stability Constants (M^{-1}) for Compounds 1−8 Determined in Acetonitrile[a]

anions	1	2	3	4	5	6	7	8
F^-	N.D.	4.4[d]	7.6[d]	N.D.	34[d]	N.D.	N.D.	N.D.
Cl^-		<5[d]	N.D.	22[d]	N.D.	960[c,d]	1540[c,d]	6700[d]
	140 000[b,e]					1100[c,e]	940[c,e]	
Br^-	3400[b,e]					37[c,d]	100[c,d]	150[d]
HSO_4^-	N.D.					130[c,d]	28[c,d]	36[d]
$H_2PO_4^-$		N.D.	N.D.	N.D.	N.D.	240[d]	>10 000[d]	N.D.
$PhCO_2^-$	115 000[c,e]	13[d]	7[d]	20[d]	10[d]	63 000[c,e]	99 600[c,e]	670 000[e]
$MeCO_2^-$	351 000[c,e]					78 000[c,e]	139 000[c,e]	710 000[e]

[a] Anions used in this assay were in the form of their tetrabutylammonium salts. N.D.: not determined. [b] From ref 13. [c] From ref 15. [d] Value obtained from ^1H NMR titrations at 25 °C. [e] Value obtained from ITC titrations at 30 °C.

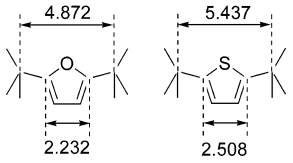


FIGURE 2. Different carbon−carbon distances (Å) as determined from the crystal structures of compounds **6** and **7**.

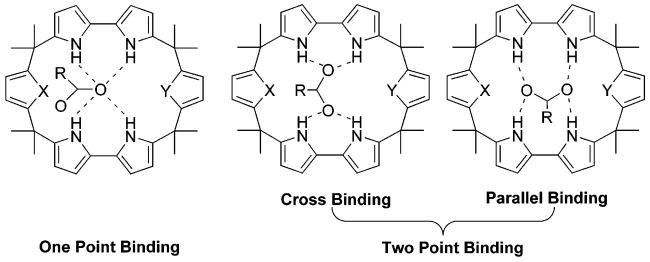


FIGURE 3. Three possible binding modes proposed for the interactions of receptors **6**−**8** with carboxylate anions.

three limiting binding modes described above, there are also a large number of intermediate binding modes that might contribute to the overall binding interactions. Unfortunately, few solution-phase methods proved effective to probe the distribution of these binding modes with the precision needed to make a distinction. Thus, we turned our attention to analyzing the binding process in the solid state.

Insights into the binding modes in the solid state came from X-ray structural analyses. Such analyses are often used to obtain useful information that can help in the interpretation of solution-phase results. Several diffraction-grade crystals of macrocycle **7**−anion complexes were successfully obtained and studied via X-ray diffraction analysis.

Diffraction grade crystals of $[\mathbf{7}\cdot PhCO_2]^-$ were grown by slow evaporation of a dichloromethane solution containing **7** and tetrabutylammonium benzoate (1:1 molar ratio) in an atmosphere saturated with hexanes. X-ray structural analysis revealed that the macrocycle adopts a cone-like conformation, with each bipyrrole unit bound to one oxygen atom of a benzoate anion via NH- - -O hydrogen- bonding interactions (Figure 4). The two thiophene planes are nearly parallel to each other, pointing toward outside from the parallel positions with small angles. The nitrogen-to-oxygen distances are in the range of 2.840(3)−2.854(4) Å, and the nitrogen−hydrogen−oxygen angles are in the range of 161(3)−172(4)°. As a result, the planar benzoate anion is perpendicular to the bipyrrole plane, bisecting the macrocycle into two mirror

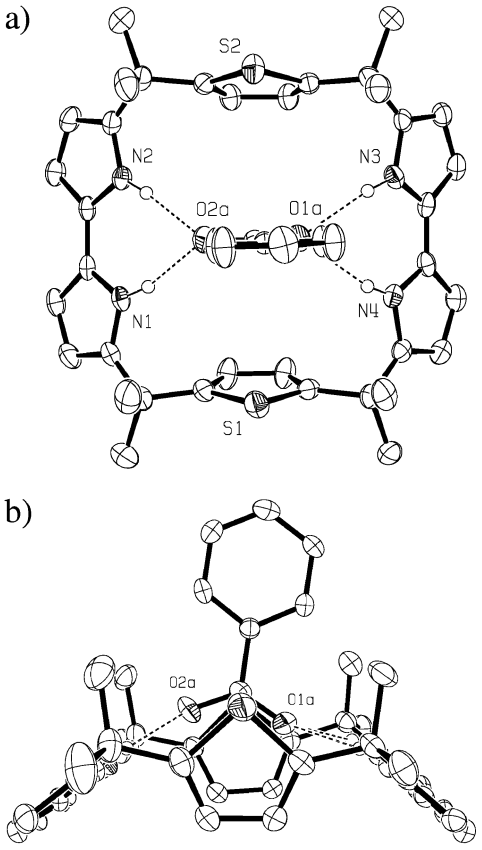


FIGURE 4. ORTEP view of the molecular structure of $[\mathbf{7}\cdot PhCO_2]^-$: (a) top view, (b) side view. Displacement ellipsoids are scaled to the 30% probability level. Most hydrogen atoms have been removed for clarity. Dashed lines are indicative of N−H- - -O hydrogen-bonding interactions.

parts across the midpoints of the two bipyrrole units. The anion is thus bound in a "cross binding", and not in a "parallel binding" or "one point binding" mode, at least in this solid-phase structure. However, a side view reveals that the axis of the benzoate anion is not perpendicular to the macrocyclic plane (defined by the N_4 root-mean-square). Rather, a small deviation is seen. As a consequence, two different sets of hydrogen bonding interactions are defined between the two bipyrrole units and the two oxygen atoms of the benzoate anion.

The cross binding mode seen in the solid-state structure of $[\mathbf{7}\cdot PhCO_2]^-$ is also seen in the crystal structure of the acetate anion complex, $[\mathbf{7}\cdot MeCO_2]^-$. X-ray structural analysis revealed a molecular structure for $[\mathbf{7}\cdot MeCO_2]^-$ that is quite similar to that of $[\mathbf{7}\cdot PhCO_2]^-$ (Figure 5). The nitrogen-to-oxygen distances are in the

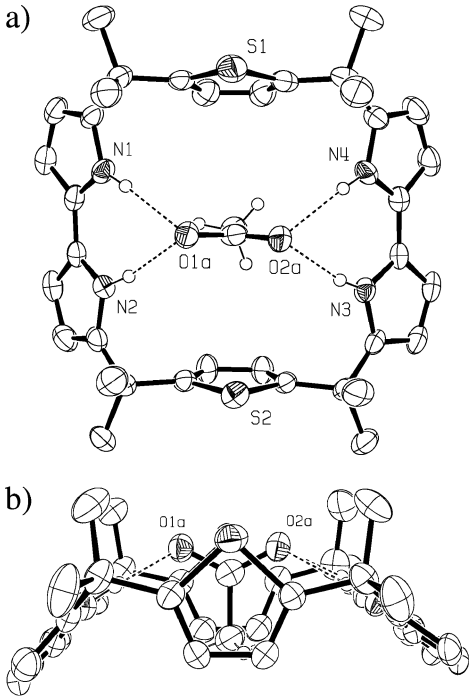
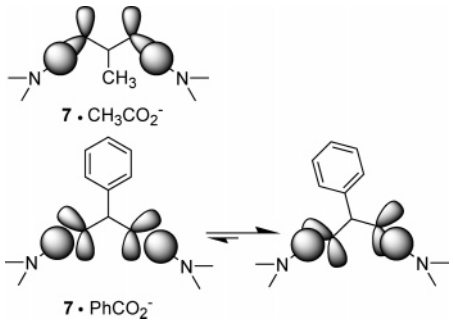


FIGURE 5. ORTEP view of the molecular structure of the $[\mathbf{7}\cdot MeCO_2]^-$: (a) top view, (b) side view. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms have been removed for clarity. Dashed lines are indicative of N−H- - -O hydrogen-bonding interactions.

range of 2.855(4)−2.869(3) Å, and the nitrogen−hydrogen−oxygen angles are in the range of 167(2)−169(3)°. One difference between the two crystal structures is that the methyl group of the acetate anion is buried within the cone-like cavity of the macrocycle, while the benzyl group of the benzoate anion resides outside the cavity. As reflected both by the more even hydrogen bond distances observed (particularly NH- - -O, see the Supporting Information) and, more dramatically, by the associated hydrogen bond angles, the crystal structure reveals more effective host−guest hydrogen-bonding interactions in the case of $[\mathbf{7}\cdot MeCO_2]^-$ complex than in $[\mathbf{7}\cdot PhCO_2]^-$. This difference in solid-state binding is also consistent with the solution-phase results summarized in Table 1.

Another difference between the two crystal structures is that the axis of the acetate anion is perpendicular to the macrocycle plane, while the axis of benzoate anion deviates from the perpendicular position to a small degree (vide supra). We rationalize these differences in terms of orbital effects. The orbitals of the oxygen atoms (carboxylate anions) are sp^2 hybridized, with the three resulting orbitals being coplanar and separated by angles that are close to 120°. When hydrogen bonding to the pyrrolic protons takes place, one orbital is expected to be oriented toward the orbital of the pyrrolic NH hydrogen-bonding donor so as to maximize the orbital overlap. In the case of $[\mathbf{7}\cdot MeCO_2]^-$, when the acetate anion is oriented perpendicular relative to the macrocycle plane, one orbital of each oxygen atom is oriented toward the largely spherical hydrogen's orbital. In the case of $[\mathbf{7}\cdot PhCO_2]^-$, with the benzoate anion oriented perpendicular to the macrocycle plane but pointed out of the cavity (as the result of steric effects), effective overlap with the hydrogen atom orbitals is precluded. Such an orientation thus does not support good orbital overlap or fully effective hydrogen bonding interactions. However, once the benzoate anion begins to deviate from its initial perpendicular position, the orbital overlap between the oxygen and the hydrogen atoms begins to improve, with the net result that the strength of the hydrogen bonding interactions is enhanced (Scheme 2).

SCHEME 2. Schematic Representation of the Orbital Overlap Expected between the Pyrrole NH Protons and the Oxygen Atoms of Two Different Carboxylate Anions when Bound by Receptor 7



Despite the above "fine-tuning" details, it is important to appreciate that both crystal structures reflect a geometric match between receptor **7** and the targeted carboxylate anions. Given this nice fit, we ascribe the poor anion affinities displayed by compound **7** (as well as **6** and **8**) toward other anions, such as chloride, to a corresponding structural mismatch between the host and guest. To provide support for this latter rationalization, efforts were made to obtain diffraction grade crystals of $[\mathbf{7}\cdot Cl]^-$.

Diffraction-grade crystals of the chloride anion complex of **7** were obtained by vapor diffusion of pentane into a dichloromethane solution containing **7** and tetrabutylammonium chloride (1:1 molar ratio). X-ray structural analysis of the resulting complex, $[\mathbf{7}\cdot Cl]^-$, revealed that one of the thiophene rings of the macrocycle was disordered by rotation about the meso carbons to which the ring is attached to the macrocycle (for the sake of clarity the disorder is removed from Figure 6, which shows the structure of $[\mathbf{7}\cdot Cl]^-$). The macrocycle adopts a 1,3-alternate conformation in the solid state, with the two bipyrrole units oriented in one direction and the two thiophene units oriented in the opposite direction. One bipyrrole unit is bound to a chloride anion via two NH- - -Cl hydrogen bonds, while another bipyrrole unit is bound to a water molecule via two NH- - -O hydrogen-bonding interactions. The bound chloride simultaneously interacts with the bound water molecule via one OH- - -Cl hydrogen bond. While such motifs have been observed previously within anion receptors,[21] such interactions help stabilize an overall dimeric structure. In particular, two adjacent macrocycles are found to dimerize through a hydrogen bond anion−water bridge. A chloride anion hydrogen bonded to one macrocycle is also hydrogen bonded to a water molecule, which is, in turn, hydrogen bonded to the adjacent macrocycle (Figure 7). The nitrogen-to-oxygen distances are 2.939(5) and 3.032(5) Å, respectively; the nitrogen-to-chloride distances are 3.207(4) and 3.330(4), respectively; and the oxygen-to-chloride

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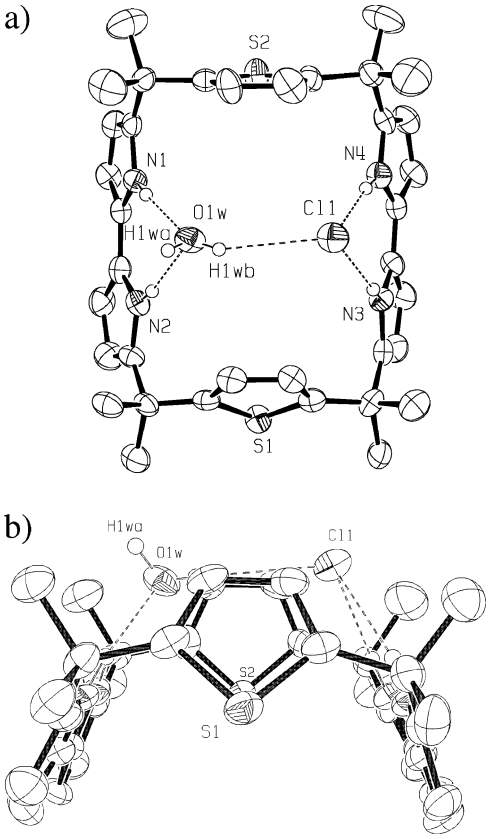

FIGURE 6. ORTEP view of the molecular structure of [**7**·Cl]$^-$: (a) top view, (b) side view. Displacement ellipsoids are scaled to the 40% probability level. Most hydrogen atoms have been removed for clarity. A disorder involving one of the thiophene rings is also not shown for clarity. Dashed lines are indicative of hydrogen-bonding interactions.

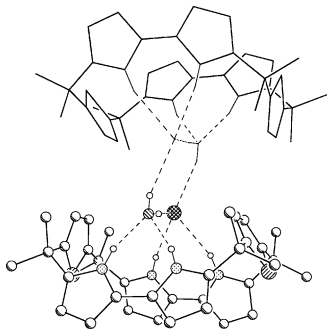

FIGURE 7. View of the molecular structure of [**7**·Cl]$^-$ illustrating the hydrogen-bonding interactions between the macrocycle, the chloride anions, and the water molecules. The hydrogen bound complex lies around a crystallographic inversion center at $^1/_2$, $^1/_2$, 0. Dashed lines are indicative of hydrogen-bonding interactions.

distances are 3.125(5) and 3.312(6). The nitrogen−hydrogen−oxygen angles are 162.8° and 164.3°; the nitrogen−hydrogen-chloride angles are 161.9° and 171.5°; and the oxygen−hydrogen-chloride angles are 143.5° and 156.8°.

Figures 6 and 7 serve to highlight the fact that, at least in the solid state, the size and geometry of **7** and chloride anion are poorly matched. This finding, together with the good match seen in the X-ray structures of [**7**·$PhCO_2$]$^-$ and [**7**·$MeCO_2$]$^-$, provides an attractive and simple first-order explanation for the selectivities seen in the solution-phase studies (cf. Table 1).

Conclusion

In conclusion, the anion-binding properties of the hybrid systems **2**−**8** were studied using a combination of solution-phase affinity measurements and solid-state X-ray diffraction analyses. Compared to **1**, compounds **2**−**4** show substantially decreased anion-binding affinities due to a reduced number of anion-binding subunits (i.e., pyrrole NH hydrogen bond donor groups). The low affinity of **5** is ascribed to its large size and inability to bind the test anions of interest in a cooperative, multitopic fashion. Compounds **6**−**8** bind carboxylate anions well in acetonitrile solution and show selectivity for such Y-shaped anions over other anions. This is ascribed to effective geometry matching, a conclusion that is supported by solid-state structural studies. Further highlighting the importance of structure, and the big effect that small deviations in receptor geometry can have on the anion-binding properties of ostensibly similar receptors, macrocycle **8** was found to display affinities for carboxylate and chloride anions that are enhanced relative to those of **6** and **7**. Current work is focused on understanding the exact determinants of these effects and to the design and synthesis of novel ditopic anion receptors based on **6**−**8** that could be used to effect the recognition of amino acids.

Experimental Section

Tetrabutylammonium fluoride trihydrate and tetrabutylammonium chloride were purchased from Fluka, Inc., and dried under high vacuum at 40 °C for 24 h before use. Acetonitrile was dried by passage through two columns of activated alumina. CD_3CN was purchased in bottles from Cambridge Isotopes, Inc., and dried over molecular sieves (4 Å) prior to use. All other reagents were obtained from commercial sources and used as received. Proton and ^{13}C NMR spectra used in the characterization of product and titration studies were recorded on 400 MHz spectrometers.

Synthesis of *meso*-Octamethylcalix[2]bipyrrole[1]furan-[1]thiophene 8. 2,5-Bis[(α-(1*H*,1′*H*-[2,2′]bipyrro-5-yl)-α,α-dimethyl)methyl]furan **9** (0.13 g, 0.3 mmol) and 2,5-bis[(α-hydroxy-α,α-dimethyl)methyl]thiophene **10** (60 mg, 0.3 mmol) were dissolved in dry acetonitrile (300 mL), and the mixture was degassed by bubbling Ar through the solution for 10 min. The mixture, kept under Ar, was then cooled to 0 °C using an ice−water bath. BF_3·Et_2O (44 mg, 0.3 mmol) was added, and the mixture was stirred at 0 °C for 2 h. The reaction was quenched with triethylamine, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, dichloromethane−hexanes 4:1 v/v) to afford **8** as a white solid (77 mg, 44%): ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.62 (s, 12H), 1.71 (s, 12H), 5.88 (t, 2H), 5.95−5.96 (m, 8H), 6.71 (s, 2H), 7.65 (s, 2H), 7.86 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 27.2, 30.1, 36.0, 37.8, 103.7. 103.9, 104.0, 104.3, 109.7, 121.3, 124.9, 137.8, 139.7, 153.4, 159.7; HR-MS (CI^+) *m/z* ($M + H^+$) calcd for $C_{36}H_{41}N_4OS$ 577.3001, found 577.2991.

X-ray Structural Analysis. The data were collected on a Nonius Kappa CCD diffractometer using a graphite monochromator with Mo Kα radiation (λ = 0.710 73 Å). The data were collected at 153 K using an Oxford Cryostream low-temperature device. Data reduction were performed using DENZO-SMN.[22] The structures were solved by direct methods using SIR97[23] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms

using SHELXL-97.[24] The hydrogen atoms on carbon were calculated in ideal positions with isotropic displacement parameters set to $1.2U_{eq}$ of the attached atom ($1.5U_{eq}$ for methyl hydrogen atoms). Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the *International Tables for X-ray Crystallography* (1992).[25]

Compound **8**: $C_{38}H_{44}Cl_4N_4OS$; crystals grew as colorless prisms by slow evaporation of a dichloromethane solution of **8** in an atmosphere saturated with hexanes. The data crystal was cut from a larger crystal and had approximate dimensions 0.24 × 0.22 × 0.20 mm: monoclinic, space group $P2_1/n$, a = 10.4748(2) Å, b = 13.6047(2) Å, c = 13.2513(2) Å, β = 92.435(1)°, V = 1886.69(5) Å^3, Z = 2, ρ_{calcd} = 1.314 g cm^{-3}, μ = 0.405 mm^{-1}, $F(000)$ = 784. A total of 418 frames of data were collected using ω-scans with a scan range of 1° and a counting time of 41 s per frame. A total of 7911 reflections were measured, 4314 unique (R_{int} = 0.0414). The structure was refined on F^2 to 0.117, with $R(F)$ equal to 0.0467 and a goodness of fit S = 1.04.

Compound [**7**·$PhCO_2$]$^-$: $C_{60}H_{83}Cl_2N_5O_2S_2$; crystals grew as clusters of colorless lathes by slow evaporation of a dichloromethane solution of **7** and tetrabutylammonium benzoate (1:1 molar ratio) in an atmosphere saturated with hexanes. The data crystal was a long lathe that had approximate dimensions 0.55 × 0.18 × 0.10 mm: monoclinic, space group $P2_1$, a = 11.5806(2) Å, b = 22.8486(4) Å, c = 12.1009(2) Å, β = 113.6230(10)°, V = 2933.59(5) Å^3, Z = 2, ρ_{calcd} = 1.179 g cm^{-3}, μ = 0.227 mm^{-1}, $F(000)$ = 1120. A total of 338 frames of data were collected using ω-scans with a scan range of 1° and a counting time of 204 s per frame. A total of 10518 reflections were measured, 10518 unique. The structure was refined on F^2 to 0.107, with $R(F)$ equal to 0.0507 and a goodness of fit S = 0.99.

Compound [**7**·$MeCO_2$]$^-$: $C_{55}H_{81}Cl_2N_5O_2S_2$; crystals grew as colorless plates by slow evaporation of a dichloromethane solution of **7** and tetrabutylammonium acetate (1:1 molar ratio) in an atmosphere saturated with hexanes. The data crystal was cut from a larger plate and had approximate dimensions 0.27 × 0.26 × 0.10 mm: triclinic, space group P-1, a = 12.0220(2) Å, b = 14.4610(2) Å, c = 17.7050(3) Å, α = 70.8010(9)°, β = 88.9990(8)°, γ = 72.4930(8)°, V = 2760.82(8) Å^3, Z = 2, ρ_{calcd} = 1.178 g cm^{-3}, μ = 0.237 mm^{-1}, $F(000)$ = 1056. A total of 461 frames of data were collected using ω-scans with a scan range of 1° and a counting time of 151 s per frame. A total of 19 709 reflections were measured, 12485 unique (R_{int} = 0.0431). The structure was refined on F^2 to 0.142, with $R(F)$ equal to 0.0754 and a goodness of fit S = 1.72.

Compound [**7**·Cl]$^-$: $C_{54}H_{82}Cl_5N_5OS_2$; crystals grew as colorless plates by vapor diffusion of pentane into a dichloromethane solution of **7** and tetrabutylammonium chloride (1:1 molar ratio). The data crystal was cut from a larger crystal and had approximate dimensions 0.36 × 0.28 × 0.15 mm: monolinic, space group $P2_1/n$, a = 15.1902(5) Å, b = 18.6941(6) Å, c = 20.9059(8) Å, β = 98.979(2)°, V = 5863.8(4) Å^3, Z = 4, ρ_{calcd} = 1.199 g cm^{-3}, μ = 0.359 mm^{-1}, $F(000)$ = 2264. A total of 365 frames of data were collected using ω-scans with a scan range of 0.8° and a counting time of 145 s per frame. A total of 17 723 reflections were measured, 10 250 unique (R_{int} = 0.0718). The structure was refined on F^2 to 0.158, with $R(F)$ equal to 0.0956 and a goodness of fit S = 1.78.

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Supporting Information Available: ^{1}H NMR spectroscopic titration, ITC titration, and X-ray crystallographic information. This material is available free of charge via the Internet at http://pubs.acs.org.

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