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Bipyrrole-Strapped Calix[4]pyrroles: Strong Anion Receptors That Extract the Sulfate Anion

Sung Kuk Kim,[†] Juhoon Lee,[†] Neil J. Williams,[‡,§] Vincent M. Lynch,[†] Benjamin P. Hay,[∥] Bruce A. Moyer,*[,‡] and Jonathan L. Sessler*[,†]

[†]Department of Chemistry, The University of Texas at Austin, 105 E. 24th Street, Stop A5300, Austin, Texas 78712-1224, United States

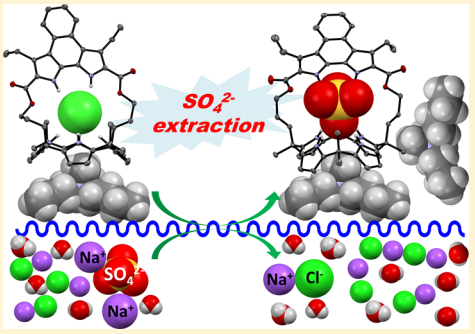
[§]Department of Chemistry, The University of Tennessee, Knoxville, Tennessee 37996-1600, United States

[‡]Chemical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37830-6119, United States

[∥]Supramolecular Design Institute, Oak Ridge, Tennessee 37830-7185, United States

Supporting Information

ABSTRACT: Cage-type calix[4]pyrroles **2** and **3** bearing two additional pyrrole groups on the strap have been synthesized. Compared with the parent calix[4]pyrrole (**1**), they were found to exhibit remarkably enhanced affinities for anions, including the sulfate anion (TBA^+ salts), in organic media (CD_2Cl_2). This increase is ascribed to participation of the bipyrrole units in anion binding. Receptors **2** and **3** extract the hydrophilic sulfate anion (as the methyltrialkyl-(C_{8-10})ammonium ($A336^+$) salt) from aqueous media into a chloroform phase with significantly improved efficiency (>10-fold relative to calix[4]pyrrole **1**). These two receptors also solubilize into chloroform the otherwise insoluble sulfate salt, $(TMA)_2SO_4$ (tetramethylammonium sulfate).



INTRODUCTION

The selective recognition and extraction of sulfate (SO_4^{2-}) is a particular challenge because this anion has a very high hydration energy (−1080 kJ/mol) and is far down the Hofmeister series.[1,2] From an application point of view, the sulfate anion is a target of interest in connection with disposing of millions of gallons of sulfate-containing high-level liquid waste (HLLW) stored at the Hanford site, involving pretreatment and vitrification prior to long-term storage.[3,4] Sulfate interferes with vitrification, primarily due to the inability to immobilize it in borosilicate glass.[5,6] In addition, SO_4^{2-} decreases the durability of glass logs while increasing the mobility and leach rates of stored actinides.[5,7] Sulfate can engender other problems. For instance, it promotes corrosion of the glass smelter, the constituent electrodes, and the superstructure components. This not only reduces performance, but it can also create a safety hazard (e.g., the explosive release of steam).[4] One potential means of removing sulfate from tank waste is via liquid−liquid extraction (LLE) using anion or ion pair receptors.[4,8,9] In 2008, we demonstrated that *β*-fluorinated calix[4]pyrrole and calix[5]pyrrole are able to extract the sulfate anion from aqueous solution.[10] More recently, it was found that the use of a methyltrialkylammonium cation allows simple, unfunctionalized calix[4]pyrrole (**1**) to function as a sulfate anion extractant.[11] This success was rationalized in terms of ion pairing effects, specifically, the concurrent binding of the sulfate anion and the methyltrialkylammonium cation to the cone-conformation of the calix[4]-pyrrole.[11] More recently, Wu and co-workers reported a tren-based tripodal hexaurea receptor capable of extracting the sulfate anion from an aqueous solution to a chloroform organic phase in the presence of tetrabutylammonium chloride (TBACl).[9] Several anion receptors have also been synthesized in the context of recognizing or transporting the sulfate anion through lipid bilayers.[12] However, relatively little progress has been made overall in the area of sulfate anion extraction. This may reflect the intrinsic difficulties associated with the design and synthesis of receptors that bind the sulfate anion with sufficient affinity to overcome the high hydration energy associated with this particular hydrophilic tetrahedral oxoanion. With such considerations in mind and as a test of the underlying hypothesis, we have now designed and synthesized the two calix[4]pyrrole-based anion receptors **2** and **3**. These two systems contain rigid or flexible bipyrrole units, respectively, that serve to span the top of what is an overall strapped calix[4]pyrrole core. Compared with the parent calix[4]pyrrole (**1**),[13] receptors **2** and **3** possess two additional relatively acidic hydrogen-bonding donors within what are effectively well-defined three-dimensional structures. As detailed below, receptors **2** and **3** display relatively high affinities for anions, including tetrahedral oxo anions. This increase in affinity is ascribed to the presence of the additional hydrogen-bond donors provided by the bipyrrole units, as well as to anion

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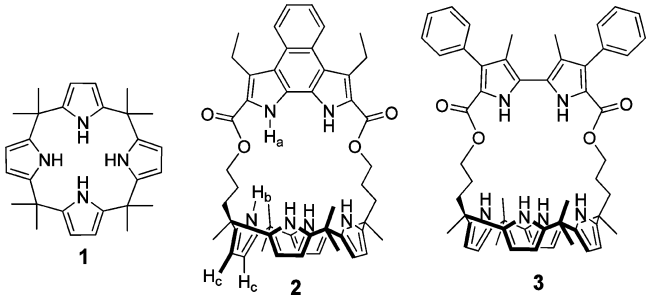
encapsulation. Consistent with their increased anion affinities, the bipyrrole-strapped calix[4]pyrroles **2** and **3** were found to extract the sulfate anion (as the methyltrialkyl(C_{8-10})-ammonium ($A336^+$) salt) from aqueous solutions into organic media with considerably greater efficiency than the parent system **1**. Receptors **2** and **3**, but not **1**, were also found to solubilize into chloroform the otherwise insoluble sulfate salt, $(TMA)_2SO_4$ (tetramethylammonium sulfate).



RESULTS AND DISCUSSION

The synthesis of receptors **2** and **3** is summarized in the Supporting Information, Schemes S1 and S2. Briefly, the dicarboxyl functionalized naphthobpyrrole **4**[14] and bipyrrole **7**[15] were coupled with 5-(3-hydroxypropyl)-5-methyl dipyrromethane (**5**) in the presence of EDCI (1-ethyl-3-(3-(dimethylamino)propyl)carbodiimide) and DMAP (4-dimethylaminopyridine) in dichloromethane. This afforded the corresponding esters **6** and **8** in 52% and 49% yield, respectively. A subsequent condensation with acetone in the presence of $BF_3{\cdot}OEt_2$ (~1.0 equiv) produced the desired compounds (**2** and **3**) in 17% and 18% yield, respectively.

Initial evidence that receptors **2** and **3** could bind the sulfate anion with significantly enhanced affinity relative to the unsubstituted calix[4]pyrrole (**1**) in solution came from ^{1}H NMR spectroscopic analyses carried out in CD_2Cl_2. As shown in the Supporting Information, Figures S1 and S2, when exposed to the sulfate anion (added in excess as the tetrabutylammonium (TBA^+) salt), the NH protons of both the calix[4]pyrrole framework and bipyrrole units of the strap undergo a remarked downfield shift ($\Delta\delta_{Ha}$ = 1.36 and 1.49 ppm; $\Delta\delta_{Hb}$ = 2.00 and 1.43 ppm for **2** and **3**, respectively) while the peaks for the β-pyrrolic proton resonances shift to higher field. These changes in the chemical shifts are ascribed to hydrogen bonding between the pyrrolic NHs and the sulfate anion. When the naphthobipyrrole−strapped calix[4]pyrrole **2** was titrated with increasing quantities of $(TBA)_2SO_4$, two sets of distinguishable resonances for the NH proton signals of both pyrrole and bipyrrole units were seen in the ^{1}H NMR spectra recorded before a full molar equivalent of the sulfate anion had been added (Supporting Information, Figure S1). The observed signals correspond to the free ligand and sulfate-complexed forms of receptor **2**, respectively. The observation of two sets of peaks in the ^{1}H NMR spectra recorded before saturation is reached is consistent with the binding/release equilibrium between receptor **2** and the sulfate anion being slow on the NMR time scale. It is also consistent with the formation of a strong 1:1 complex between the sulfate anion and receptor **2**, presumably reflecting the fact that all six NH protons of this receptor participate in hydrogen bonding with the bound sulfate anion.

In contrast to the above, in the case of receptor **3**, the NH proton signals were observed to shift to lower field as the amount of the sulfate anion increased, with saturation being reached after the addition of 1 mol equiv of $(TBA)_2SO_4$ (Figure S2). These changes in the chemical shifts are consistent with the formation of a strong, 1:1 complex, albeit with a fast binding/release equilibrium. This observation stands in sharp contrast to what was seen with calix[4]pyrrole **1**, which displays no appreciable chemical shift change in the presence of excess sulfate anion (Figure S3).

On the basis of the above findings, we conclude that receptors **2** and **3** both bind the sulfate anion with high affinity. An indication of their relative binding affinities for sulfate was gleaned from molecular mechanics calculations carried out using the MMFF94 force field model. The intrinsic binding energy for each receptor (including calix[4]pyrrole **1**), defined as $E_{(receptor\text{-}sulfate)} - E_{(sulfate)} - E_{(receptor)}$, was computed to be −59.5 kcal/mol, −104.5 kcal/mol, and −99.9 kcal/mol for receptors **1**, **2**, and **3**, respectively. Optimized structures are shown in Figure 1 (see Supporting Information for coordinates of all structures). It is noteworthy that the interaction between the bipyrrolic NH protons and the bound sulfate are different in the case of receptors **2** and **3**. Specifically, in the case of **2** a single sulfate oxygen atom is bound by the bipyrrole subunit, whereas in the case of **3** the bipyrrole NH protons with interact with two different sulfate oxygen atoms.

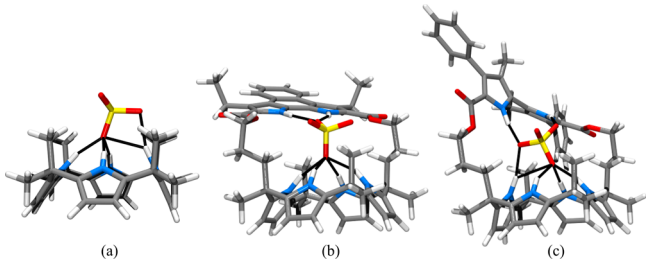


Figure 1. Optimized geometry for (a) $\mathbf{1}{\cdot}SO_4^{2-}$, (b) $\mathbf{2}{\cdot}SO_4^{2-}$, and (c) $\mathbf{3}{\cdot}SO_4^{2-}$.

To quantify the binding affinities of receptors **2** and **3** for sulfate, UV−vis spectroscopic analyses were performed in dichloromethane. When solutions of receptor **2** were titrated with $(TBA)_2SO_4$, a hypsochromic shift in the main absorption band was observed. In contrast, a bathochromic shift was observed for receptor **3** (cf. Supporting Information, Figures S4 and S5). The absorption band shift of receptor **3** to a longer wavelength is rationalized in terms of an enhancement in the planarity of the bipyrrole unit as the result of sulfate binding. Such conformational motions were expected to be less pronounced in the case of **2**.

By fitting the UV−vis spectroscopic titration curves to a standard 1:1 binding profile, association constants (K_a) corresponding to the interactions between receptors **2** and **3** and sulfate could be determined; the values were found to be 1.67×10^5 M^{-1} and 1.37×10^5 M^{-1}, respectively (Figures S4 and S5). In contrast, no evidence of sulfate binding was seen in the case of the parent calix[4]pyrrole (**1**) under identical experimental conditions (i.e., titration with $(TBA)_2SO_4$, in CH_2Cl_2) (Figure S3).

The strong sulfate anion binding inferred in the case of receptor **2** was further supported by a solid−liquid extraction experiment using tetramethylammonium sulfate ($(TMA)_2SO_4$).

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This latter salt is essentially insoluble in chloroform. The extraction test thus consisted of subjecting a $CDCl_3$ solution of a mixture of **2** and tetramethylammonium sulfate (2 molar equiv) to sonication for 10 min, followed by filtration. This produced a clear filtrate that was analyzed by ^{1}H NMR spectroscopy. This analysis revealed that the NH protons of both the calix[4]pyrrole and the naphthobipyrrole groups were shifted to lower field as compared to a corresponding solution of **2** ($\Delta\delta_{Ha}$ = 3.44 ppm and $\Delta\delta_{Hb}$ = 4.58 ppm). Likewise, the β-pyrrolic proton signals were seen to shift to higher field ($\Delta\delta_{Hc}$ = −0.45 ppm) (Figure 2). Such findings are consistent with

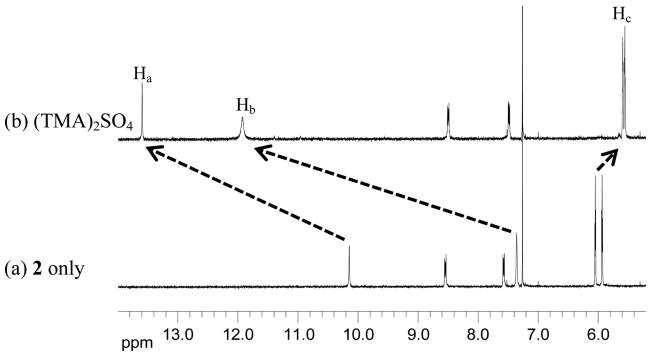

Figure 2. Partial ^{1}H NMR spectra of **2** recorded at room temperature in $CDCl_3$ (a) before and (b) after the addition of $(TMA)_2SO_4$ (as a solid, 2 equiv), followed by sonication for 10 min and filtration. The spectrum is of the filtrate.

strong complexation between **2** and tetramethylammonium sulfate. Analogously, when receptor **3** was exposed to solid $(TMA)_2SO_4$ in $CDCl_3$, all of its NH protons underwent slight downfield shifts; presumably these shifts reflect complexation and solubilization of the sulfate anion by **3** (Supporting Information, Figure S6). This presumption was further supported by the observation of a proton signal ascribable to TMA^+ at 3.24 ppm (Figure S6). The chemical shift changes seen for **2** and **3** stand in contrast to what was seen with compound **1**. In the case of the latter receptor, no appreciable chemical shift changes and no signal corresponding to TMA^+ were observed upon exposure to $(TMA)_2SO_4$ in $CDCl_3$ (Figure S7).

Further evidence that receptor **2** can interact with sulfate came from a single crystal X-ray diffraction analysis. Suitable single crystals of the $(TMA)_2SO_4$ complex were obtained by subjecting a chloroform/methanol mixture of receptor **2** to slow evaporation in the presence of $(TMA)_2SO_4$ (5 equiv). The resulting crystal structure revealed that, as predicted by the calculation (see Figure 1), receptor **2** forms a 1:1 complex with $(TMA)_2SO_4$ in the solid state where two oxygen atoms of the SO_4^{2-} guest are bound to the calix[4]pyrrole and the naphthobipyrrole, respectively, via six hydrogen-bonding interactions with distances of 2.79−2.99 Å for the O···N interactions (Figure 3). One of the TMA^+ countercation is bound to the cone-shaped calix[4]pyrrole cavity via CH-π interactions between one of its methyl groups and the π-faces of the pyrroles (Figure 3). This TMA^+ cation also interacts directly with another sulfate anion from a different complex to form a contact ion pair. The second TMA^+ cation was found to be coordinated to the outside of the calix[4]pyrrole cavity via apparent CH-π interactions (Figure 3). Overall, the structure resembles closely the optimized structure calculated for the

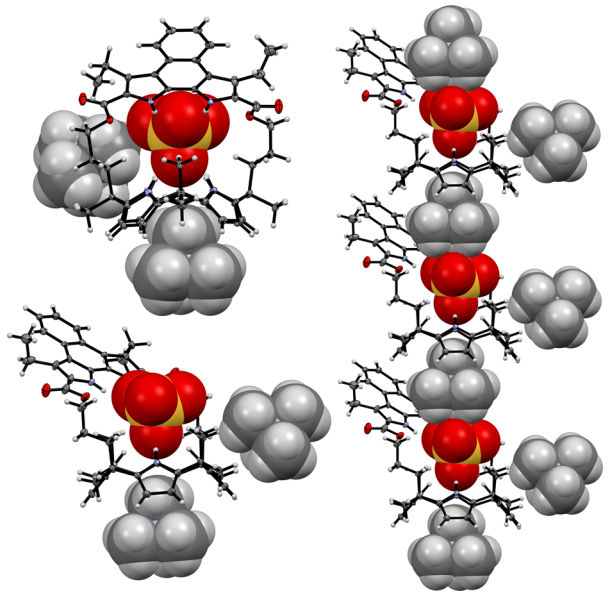

Figure 3. Left: Two different views of the single-crystal structure of the $(TMA)_2SO_4$ complex of receptor **2** (**2**·$(TMA)_2SO_4$). Right: Partial view of the extended structure seen in the crystal lattice. Thermal ellipsoids are scaled to the 50% probability level. Solvent molecules have been removed for clarity.

sulfate complex of **2**. The concordance between the calculated structure and that obtained via a single X-ray diffraction analysis was also observed in the case of the sulfate complex of **1** (cf. Supporting Information, Figure S8 and accompanying discussion).

The ability of receptors **2** and **3** to extract the sulfate in competition with the chloride anion was investigated using ^{35}S-labeled sulfate and beta liquid scintillation to monitor the exchange of sulfate. The exchange was effected from an aqueous solution containing sodium sulfate (0.1 mM) and excess sodium chloride (10 mM) into an organic layer (chloroform) that contained varying concentrations of the receptor in question and Aliquat 336-chloride (methyltrialkyl-(C_{8-10})ammonium chloride; A336Cl). The use of A336Cl reflects previous findings that tetraalkylammonium cations having at least one methyl group can synergize sulfate extraction in the case of the parent **1** by forming an ion pair complex wherein the methyl group is included in the cone-shaped calix[4]pyrrole cavity.[11] Figure 4 shows the distribution ratio of the sulfate anion ($D_{sulfate}$ = $[SO_4^{2-}]_{org}/[SO_4^{2-}]_{aq}$) measured for varying concentrations of compounds **1**−**3** with A336Cl in the organic phase. Under these conditions, the bipyrrole strapped calix[4]pyrroles **2** and **3** proved capable of extracting the sulfate anion much more effectively than the parent calix[4]pyrrole (**1**) ($D_{sulfate}$ = 0.00055, 0.00614, and 0.013 for compounds **1**, **2**, and **3** at 10 mM concentrations, respectively, in the presence of equimolar A336Cl) (cf. Figure 4 and Supporting Information, Table S1). The increase of $D_{sulfate}$ by a factor of 11 for **2** and a factor of 24 for **3** relative to **1** under identical experimental conditions is ascribed to the relatively strong interactions between the sulfate anion and receptors **2** and **3** in competition with chloride ion in the organic phase. While receptor **2** binds sulfate more strongly than **3** in the absence of chloride, as shown in the titration experiments and molecular mechanics calculations presented above, the extraction results shown in Figure 4 and Table S1

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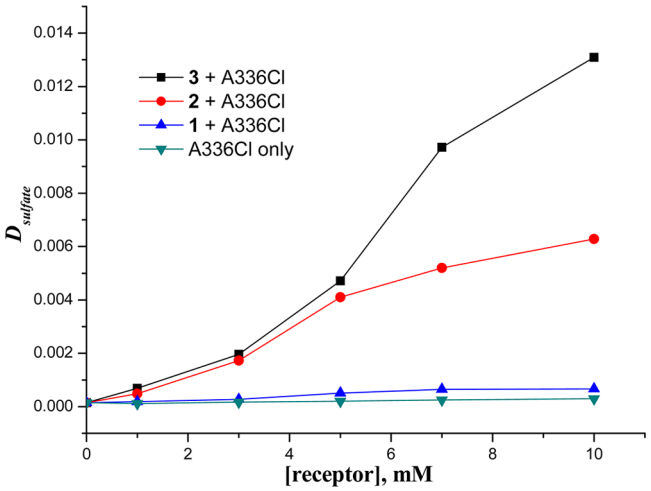

Figure 4. The distribution ratio for the extraction of the sulfate ion (as Na_2SO_4 in the aqueous phase) from water using a chloroform solution containing varying concentrations of 1:1 mixtures of receptors **1**–**3** with A336Cl. The aqueous phase consisted of 10 mM NaCl and 0.1 mM Na_2SO_4 in Milli-Q water.

further reveal that **3** is the more selective of the two receptors for sulfate versus chloride in the liquid–liquid exchange system. The sulfate selectivity may arise in part from the divergent NH vectors of the bipyrrole in **3**, which can accommodate binding two oxygen atoms of the sulfate guest but would not be expected to be efficient for spherical chloride.

An analysis of the formal synergistic factors [e.g., $S_{3+A336Cl} = D_{sulfate,3+A336Cl}/(D_{sulfate,3} + D_{sulfate,A336Cl})$] revealed evidence for classical synergism, namely, that performance of the whole exceeds that of the sum of its parts. The values of $S_{1+A336Cl}$ and $S_{3+A336Cl}$ were found to be 2.3 and 12.5 (Supporting Information, Table S2), respectively, for **1** and **3** at 5 mM in combination with 5 mM A336Cl in chloroform. It was not possible to obtain the synergistic factor for **2** + A336Cl because of the formation of a precipitate when **2** was used alone. The observed synergistic factors exceed unity, indicating a high level synergism for the strapped calixpyrrole. It was also observed that substitution of the symmetrical long-chain anion exchanger tetraheptylammonium chloride (THACl) for A336Cl greatly reduces the synergistic factor (cf. 12.5 for A336Cl vs 1.6 for THACl, Supporting Information, Table S2). Such a reduction is consistent with our previously expressed hypothesis that the methyl group of the quaternary ammonium cation A336 resides in the cup of the calix[4]pyrrole.[11]

To obtain deeper insights into the extraction process, continuous-variation experiments with receptors **2** and **3** were carried out. This was accomplished by changing the mole fraction (X) of each of these receptors relative to the A336Cl additive (X = [receptor]/([receptor] + [A336Cl]) under the condition [receptor] + [A336Cl] = 10 mM). On the basis of these studies, it was found that receptors **2** and **3** extract the sulfate anion with maximum efficiency at X = 0.30 and 0.25, respectively (Figure 5). Such findings are consistent with the notion that the extraction process is aided via the formation of higher order species, wherein more than one A336Cl ion pair interacts with the sulfate–receptor complex in the organic phase. Such aggregation effects are expected to improve the stability of the sulfate anion complex (or complexes) in the organic phase, thus enhancing the extraction process. We suggest a model exchange reaction stoichiometry as follows, where Q is the quaternary ammonium cation and R is the receptor:

$$\mathrm{QRCl(org)} + n\mathrm{QCl(org)} + \mathrm{SO_4^{2-}(aq)} \rightleftharpoons \mathrm{Q_2RSO_4}\cdot(n-1)\mathrm{QCl(org)} + 2\mathrm{Cl^-(aq)} \quad (1)$$

which is valid for the condition $n \geq 1$. On the basis of our previous equilibrium analysis of sulfate extraction by **1** and other receptors in combination with A336 salts,[16,17] we expect that all organic-phase species will be neutral with the receptor initially in the form of a complex with A336Cl when A336Cl is in excess. Binding constants of **2** and **3** with TBACl in excess of 10^5 M^{-1} (vide infra) imply that more than 99% of the receptor is bound to A336Cl in the form of the QRCl complex over most of the range of the continuous-variation experiments. In the context of eq 1, the sharp continuous-variation maxima (X_{max}) at 0.30 and 0.25 seen in Figure 5 are consistent with n = 0.7 and n = 1 for receptors **2** and **3**, respectively, on deriving X_{max} as a function of n (see Supporting Information). It thus appears probable that an A336Cl ion pair plays a role in stabilizing the sulfate complex, even though the resolution of the experiment precludes a definitive assignment of stoichiometry.

The unusual sharpness of the maxima in the continuous-variation experiments provides additional insight into the extraction stoichiometry. Equation 1 is defined only for $n \geq 1$, covering only the range $0 < X \leq 0.33$. The condition $X > 0.33$ implies a deficiency of QCl to support the anion exchange. We

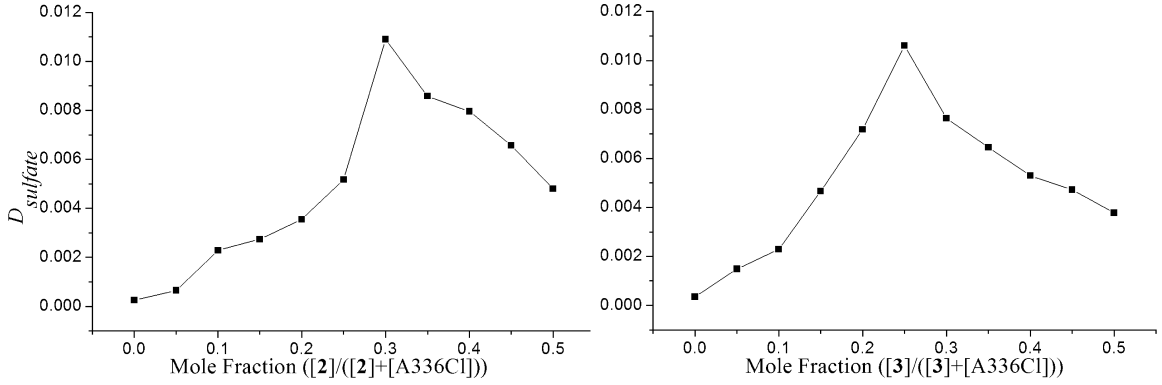

Figure 5. Distribution ratios of sulfate resulting from continuous-variation experiments involving Aliquat 336Cl (A336Cl) and receptors **2** (left) and **3** (right).

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therefore consider that extraction under these conditions occurs as follows:

$$2\mathrm{QRCl(org)} + \mathrm{SO_4^{2-}(aq)} \rightleftharpoons \mathrm{Q_2RSO_4(org)} + \mathrm{R(org)} + 2\mathrm{Cl^-(aq)} \quad (2)$$

The sharp downturn occurring at $X \geq 0.33$ in Figure 5 is consistent with the process of eq 2 being markedly less favorable than that given by eq 1. The unfavorable nature of eq 2 makes sense in that one receptor molecule must be decomplexed from a QRCl species. This represents a large energy penalty given that the binding constants for chloride recorded in organic media were found to be larger than 10^5 M^{-1} (vide infra). In addition, free QCl ion pairs are not available to interact with, and stabilize, the Q_2RSO_4 complex. Thus, Figure 5 provides empirical support for the conclusion that the maximum level synergism occurs in the approximate range $0.25 \leq X \leq 0.33$. We likewise conclude that above this range, the extraction mechanism abruptly changes, reflecting a process that is much less efficient in terms of receptor utilization.

The ability of receptors **2** and **3** to interact with other anions, such as the halides, nitrate, phosphate, and pyrophosphate anions (as the TBA^+ salts) was also analyzed via ^{1}H NMR and UV−vis spectroscopy in CD_2Cl_2. As compared with calix[4]-pyrrole **1**, the association constants (K_a) of receptors **2** and **3** are significantly enhanced (by at least 3 orders of magnitude) in the case of all anions tested except for F^- (Table 1). As inferred from the ^{1}H NMR and UV−vis spectral changes induced by anion addition, this enhancement in the K_a values is attributable to two additional hydrogen-bonding interactions provided by the bipyrrole units. Interestingly, and in contrast to what was seen with **1**, a receptor that is highly selective for fluoride over other anions in CD_2Cl_2 (K_a for F^-/K_a for X^- ($S_{F/X}$) = 49, 1720, and >1720 for Cl^-, Br^-, and I^-, respectively),[18] the selectivity of **2** and **3** for other anions is enhanced relative to F^-. For example, the $S_{F/X}$ values of receptor **2** were calculated to be 0.50, 0.56, and 7.32 for Cl^-, Br^-, and I^-, respectively, while those of receptor **3** were 0.62, 2.18, and 33.8 for Cl^-, Br^-, and I^-, respectively. The reversed selectivity of both of receptors **2** and **3**, that is, favoring chloride relative to fluoride, is consistent with the notion that the bipyrrole units, which provide more hydrogen-bonding donors but with constrained geometry, help stabilize complexation of this and other larger anions.

Table 1. Association Constants (K_a, M^{-1})[a] of Receptors 1−3 for Anions As Determined by UV−Visible Spectroscopic Titrations in CH_2Cl_2 at Room Temperature

	stability constant (M^{-1})		
anion added	**1**[b,c]	**2**	**3**
F^-	1.72×10^4	3.26×10^5	6.53×10^5
Cl^-	3.50×10^2	6.50×10^5	1.05×10^6
Br^-	10	5.72×10^5	3.00×10^5
I^-	<10	4.45×10^4	1.93×10^4
$H_2PO_4^-$	97	3.18×10^5	2.90×10^5
$HP_2O_7^{3-}$	N.D.	1.41×10^6	1.00×10^6
SO_4^{2-}	N.D.	1.67×10^5	1.37×10^5
NO_3^-	N.D.	1.08×10^6	9.07×10^4

[a]All anions were used in the form of their respective tetrabutylammonium (TBA) salts. [b]Values obtained from ^{1}H NMR titrations in CH_2Cl_2 at room temperature. [c]From ref 18; N.D., not determined.

Another selectivity reversal to be noted from Table 1 relates to an apparent difference in binding selectivity versus extraction selectivity. The extraction results displayed in Figure 4, for example, show that both **2** and **3** enhance sulfate extraction selectivity versus chloride when these receptors are combined with the anion exchanger A336Cl. Alternately, Table 1 demonstrates that both receptors bind chloride more strongly than sulfate in homogeneous solution (albeit in CH_2Cl_2 vs $CHCl_3$ used in the extraction). Moreover, **2** binds sulfate more selectively versus chloride than does **3** (Table 1), whereas **3** extracts sulfate more selectively versus chloride than does **2** (Figure 4). Notwithstanding the difference in diluents used in the binding and extraction studies, the fundamental chemistry involved in binding and extraction differs in several key ways that bear strongly upon the net selectivity observed in each case. While binding and extraction can be exactly related in special cases,[17] the effects of anion-partitioning and aggregation behavior are often more pronounced under conditions of extraction than in the homogeneous media typically used for binding studies. Unfortunately, in the present case the effects of these nonlinear phenomena cannot be evaluated quantitatively, precluding a more detailed interpretation. It is clear, however, that the aggregation behavior exemplified in eq 1 has an influence on the selectivity obtained to the extent that it can reverse the order of receptors with respect to their sulfate versus chloride selectivity seen under the conditions of the binding studies.

Evidence for hydrogen-bonding interactions involving the bipyrrole and their role in stabilizing complexes with larger anions came from ^{1}H NMR spectroscopic analyses. For instance, upon exposure of receptors **2** and **3** to the fluoride anion, a relatively small downfield shift in the NH proton signal of the bipyrrole units ($\Delta\delta_{Ha}$ = 2.48 and 2.05 ppm for **2** and **3**, respectively) relative to that of the calix[4]pyrrole framework ($\Delta\delta_{Hb}$ = 5.00 and 4.50 ppm for **2** and **3**, respectively) was seen (Supporting Information, Figures S9 and S10). Moreover, the NH proton resonance of the bipyrrole unit remained a singlet while that of the calix[4]pyrrole unit was split into a doublet, an effect ascribed to the coupling between the pyrrolic NH and the fluoride anion (Figures S9 and S10).[19] Such findings are consistent with the notion that the fluoride anion is more strongly hydrogen-bonded to the calix[4]pyrrole moiety than to the bipyrrole units. Presumably, this reflects the fact that cavities of receptors **2** and **3** are too big for all six NH protons to contribute strongly to fluoride anion binding. In contrast, shifts in NH signals of both the bipyrrole and the calix[4]-pyrrole moiety were seen when chloride (TBA^+ salt) was added to CD_2Cl_2 solutions of **2** and **3** ($\Delta\delta_{Ha}$ = 1.80 and 1.68 ppm and $\Delta\delta_{Hb}$ = 3.26 and 3.12 ppm for **2** and **3**, respectively).

Single-crystal X-ray diffraction analyses were used to obtain further insights into the binding modes of the fluoride and chloride anions with receptor **2**. The resulting crystal structure revealed that only the NH protons of the calix[4]pyrrole moiety are directly hydrogen bonded to the fluoride anion, while those of the naphthobipyrrole units interact with the anion via a solvent (methanol) bridge (Figure 6). The relevant N···F^- distances were found to be 2.81−2.86 Å and 4.70−4.77 Å for the calix[4]pyrrole and the naphthobipyrrole, respectively. In contrast, and in analogy to what was seen with the sulfate complex, all six NH protons of receptor **2** are in contact with the chloride anion via direct hydrogen bonds. In the solid state, the N···Cl^- distances are 3.34−3.45 Å and 3.33−3.46 Å for the calix[4]pyrrole and the naphthobipyrrole, respectively

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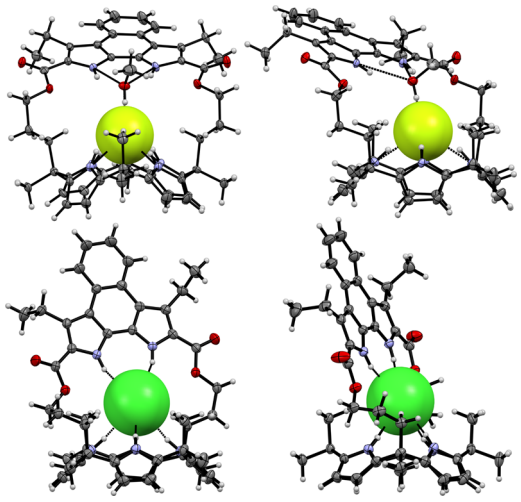

Figure 6. Top: Two different views of the single-crystal structures of the CsF complex of receptor **2** (**2**·CsF·CH_3OH). A methanol molecule is bridged between the F^- anion and the NHs of the naphtobipyrrole group. Bottom: Two different views of the single-crystal structures of the TEACl (tetraethylammonium chloride) complex of receptor **2** (**2**·TEACl). Dashed lines indicate hydrogen bonds. Thermal ellipsoids are scaled to the 50% probability level. The Cs^+ and TEA^+ cations sitting in the bowl-shaped calix[4]pyrrole cavities have been omitted for clarity.

(Figure 6). Taken in concert, the combination of solution phase and solid state data leads us to conclude that the interaction of the bipyrrole NH protons with anions plays a crucial role in determining both the anion binding affinities and selectivities of receptors **2** and **3**.

In the context of a potentially practical separation of sulfate from other anions, we regard the present results as promising. However, there remains considerable work to be done. For experimental reasons, the anion receptor concentrations have been limited in this study to ≤10 mM. This is adequate for observing the desired binding behavior but not sufficient to produce, for example, large extraction distribution ratios. Practical solvent-extraction systems typically employ organic-phase reagent concentrations exceeding 0.1 M to achieve useful loading. On the basis of eq 1, one would expect a 100-fold increase in extraction strength upon a 10-fold increase each in the A336Cl and anion receptor concentrations to 0.1 M. Extrapolating from the distribution peak values in Figure 5, one would therefore expect to obtain practical distribution ratios in excess of unity. While this is highly encouraging, additional advances are needed, for example, in making the anion receptors compatible with (i.e., soluble in) hydrocarbon diluents and in adding additional hydrogen-bond donor groups to increase the complementarity of the receptors for the tetrahedral oxoanion geometry. Work is ongoing in an effort to meet these challenges.

In summary, cryptand-like bipyrrole-strapped calix[4]-pyrroles **2** and **3** have been synthesized. Compared with the parent calix[4]pyrrole (**1**), they exhibit significantly enhanced anion binding affinities and improved selectivities for other anions relative to fluoride. The strong binding interactions between receptors **2** and **3** and sulfate are thought to account for the ability to extract this highly hydrophilic species into an organic solvent from aqueous solutions relative to the simple calix[4]pyrrole **1** when A336Cl was used as a coextractant. Strong receptor-sulfate anion interactions are also thought to underlie the solid–liquid extraction of $(TMA)_2SO_4$ seen in the case of **2** and **3**.

■ ASSOCIATED CONTENT

Supporting Information

Synthetic details, NMR and UV–vis spectroscopic data, procedure and additional data for extraction, calculation data for optimized geometry of the sulfate complexes with receptors **1**–**3**, and X-ray structural data for **2**·$(TMA)_2SO_4$·$CHCl_3$·$(CH_3OH)_3$·H_2O (CCDC 1017884), **2**·CsF·CH_3OH (CCDC 1017883), and **2**·TEACl (CCDC 1017885). This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

sessler@cm.utexas.edu

moyerba@ornl.gov

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Hofmeister, F. *Arch. Exp. Pathol. Pharmakol.* **1888**, *24*, 247–260.

(2) Custelcean, R.; Moyer, B. A. *Eur. J. Inorg. Chem.* **2007**, *10*, 1321–1340.

(3) *Report to Congress: Status of Enviornmental Management Initiatives to Accelerate the Reduction of Environmental Risks and Challenges Posed by the Legacy of the Cold War*; Report DOE/EM-0001; U. S. Department of Energy, Office of Environmental Management: Washington, DC, Jan. 2009.

(4) Moyer, B. A.; Custelcean, R.; Hay, B. O.; Sessler, J. L.; Bowman-James, K.; Day, V. W.; Kang, S. *Inorg. Chem.* **2013**, *52*, 3473–3490.

(5) Ojovan, M. I.; Lee, W. E. *An Introduction to Nuclear Waste Immobilisation*; Elsevier: Amsterdam, Netherlands, 2005; Chapter 17.

(6) Manara, D.; Grandjean, A.; Pinet, O.; Dussossoy, J. L.; Neuville, D. R. *J. Non-Cryst. Solids* **2007**, *353*, 12–23.

(7) Pirlet, V. J. *J. Nucl. Mater.* **2001**, *298*, 47–54.

(8) Ravikumar, I.; Ghosh, P. *Chem. Soc. Rev.* **2012**, *41*, 3077–3098.

(9) Jia, C.; Wu, B.; Li, S.; Huang, X.; Zhao, Q.; Li, Q. S.; Yang, X. J. *Angew. Chem., Int. Ed.* **2011**, *50*, 486–490.

(10) Fowler, C. J.; Haverlock, T. J.; Moyer, B. A.; Shriver, J. A.; Gross, D. E.; Marquez, M.; Sessler, J. L.; Hossain, M. A.; Bowman-James, K. *J. Am. Chem. Soc.* **2008**, *130*, 14386–14387.

(11) Borman, C. J.; Custelcean, R.; Hay, B. P.; Bill, N. L.; Sessler, J. L.; Moyer, B. A. *Chem. Commun.* **2011**, 7611–7613.

(12) (a) Kubik, S.; Kirchner, R.; Nolting, D.; Seidel, J. *J. Am. Chem. Soc.* **2002**, *124*, 12752–12760. (b) Kim, J.-i.; Juwarker, H.; Liu, X.; Lah, M. S.; Jeong, K.-S. *Chem. Commun.* **2010**, *46*, 764–766. (c) Young, P. G.; Clegg, J. K.; Bhadbhade, M.; Jolliffe, K. A. *Chem. Commun.* **2011**, *47*, 463–465. (d) Busschaert, N.; Karagiannidis, L. E.; Wenzel, M.; Haynes, C. J. E.; Wells, N. J.; Young, P. G.; Makuc, D.; Plavec, J.; Jolliffe, K. A.; Gale, P. A. *Chem. Sci.* **2014**, *5*, 1118–1127.

(13) Gale, P. A.; Sessler, J. L.; Král, V. *Chem. Commun.* **1998**, 1–8.

(14) Roznyatovskiy, V. V.; Roznyatovskaya, N. V.; Weyrauch, H.; Pinkwart, K.; Tübke, J.; Sessler, J. L. *J. Org. Chem.* **2010**, *75*, 8355–8362.

(15) Boev, N. V.; Ustynyuk, Y. A. *Russ. J. Org. Chem.* **2007**, *43*, 297–304.

(16) Moyer, B. A.; Sloop, F. V., Jr.; Fowler, C. J.; Haverlock, T. J.; Kang, H.-A.; Delmau, L. H.; Bau, D. M.; Hossain, A.; Bowman-James, K.; Shriver, J. A.; Bill, N.; Gross, D. E.; Marquez, M.; Sessler, J. L. *Supramol. Chem.* **2010**, *22*, 653−671.
(17) Borman, C. J.; Bonnesen, P. V.; Moyer, B. A. *Anal. Chem.* **2012**, *84*, 8214−8221.
(18) Gale, P. A.; Sessler, J. L.; Král, V.; Lynch, V. *J. Am. Chem. Soc.* **1996**, *118*, 5140−5141.
(19) Sato, W.; Miyaji, H.; Sessler, J. L. *Tetrahedron Lett.* **2000**, *41*, 6731−6736.