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KF and CsF Recognition and Extraction by a Calix[4]crown-5 Strapped Calix[4]pyrrole Multitopic Receptor

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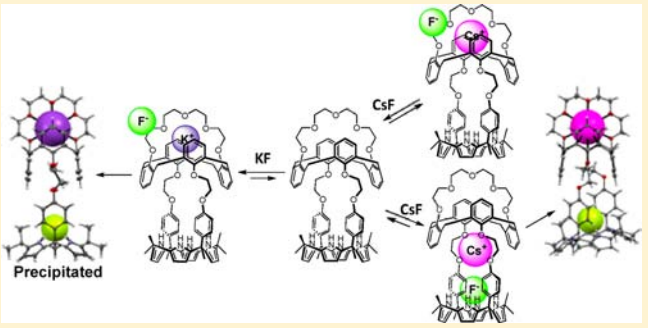
Supporting Information

ABSTRACT: On the basis of ^{1}H NMR spectroscopic analyses and single crystal X-ray crystal structural data, the ion-pair receptor **1**, bearing a calix[4]pyrrole for anion binding and calix[4]arene crown-5 for cation recognition, was found to act as a receptor for both CsF and KF ion-pairs. Both substrates are bound strongly but via different binding modes and with different complexation dynamics. Specifically, exposure to KF in 10% CD_3OD in $CDCl_3$ leads first to complexation of the K^+ cation by the calix[4]arene crown-5 moiety. As the relative concentration of KF increases, then the calix[4]pyrrole subunit binds the F^- anion. Once bound, the K^+ cation and the F^- anion give rise to a stable 1:1 ion-pair complex that generally precipitates from solution. In contrast to what is seen with KF, the CsF ion-pair interacts with receptor **1** in two different modes in 10% CD_3OD in $CDCl_3$. In the first of these, the Cs^+ cation interacts with the calix[4]arene crown-5 ring weakly. In the second interaction mode, which is thermodynamically more stable, the Cs^+ cation and the counteranion, F^-, are simultaneously bound to the receptor framework. Further proof that system **1** acts as a viable ion-pair receptor came from the finding that receptor **1** could extract KF from an aqueous phase into nitrobenzene, overcoming the high hydration energies of the K^+ and F^- ions. It was more effective in this regard than a 1:1 mixture of the constituent cation and anion receptors (**4** and **5**).



INTRODUCTION

In recent years, increasing attention has focused on so-called ditopic receptors, systems with two disparate binding sites.[1,2] Much of this interest reflects the fact that in many cases ditopic receptors containing both anion and cation binding sites display enhanced affinities for targeted ion-pairs as compared to analogous monotopic or single ion receptors.[1,2] While not established unequivocally, these enhanced recognition features are thought to result from allosteric effects and enhanced electrostatic interactions between the cobound ions present in the ion-pair complexes. More broadly, the putative improvements in affinity and selectivity that can be achieved relative to single site receptors have made ion-pair receptors attractive for use in salt solubilization, ion extraction, trans-membrane ion transport, ion sensing applications, and as logic gates.[3−8] However, despite their significant advantages, only a limited number of well-characterized ion-pair receptors are currently known. We attribute this to difficulties of molecular design and synthesis associated with incorporating two disparate binding motifs into a single framework as well as to experimental complexities associated with tracking multiple ionic species, a problem compounded by the poor solubility of many of the ion-pairs (salts) that are commonly tested.[1−8]

One of the key unresolved questions in ion-pair receptor design concerns the importance of internuclear charge separation. Examples of the cation- and anion-binding sites being proximal and remote are known.[1−8] It is perhaps most straightforward to build ion-pair receptors by linking cation receptors with anion receptors, making it a challenge to realize the internuclear distance desired for maximum stability of the ion-pair receptor complex. If charge separation is too large, then there should be no advantage of an ion-pair receptor over a simple mixture of separate molecular cation and anion receptors. The question remains as to what internuclear distances are needed for effective intramolecular cooperativity and what are the molecular-design and matrix factors that come into play for controlling cooperativity. The linked calix[4]-

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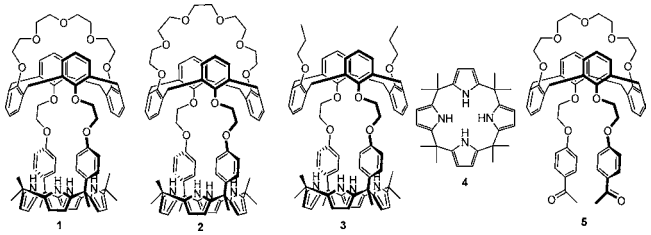
pyrrole−calix[4]crown ion-pair receptors that we have been studying represent an ideal platform for investigating this question.[8−10] Not only do they present an interesting laboratory of binding sites in the same molecule, but the strongest binding sites are at opposite ends of the molecule. They thus represent useful systems wherein the effect of various external factors, including the choice of anion, cation, and solvent, may be probed in a well-controlled manner.

In an effort to understand in greater detail the correlation between receptor structure and ion-pair binding function, we report herein the KF and CsF binding properties of ion-pair receptor **1** and provide evidence not only for site-selective binding but also for dynamic cation recognition behavior in the case of CsF. We also show that receptor **1** acts as an extractant for KF under conditions of liquid−liquid two-phase extraction and that it is more effective for this purpose than the anion receptor **4**, the cation receptor **5**, or an equimolar mixture of these two monotopic binding agents. This finding provides support for the appealing notion that effectively designed ion-pair receptors can display features that are superior to the sum of their constituent parts.



RESULTS AND DISCUSSION

In a first set of analyses, the ability of ion-pair receptor **1** to bind halide anions in $CDCl_3$ solution was investigated via ^1H NMR spectroscopy. In analogy to what was found to be true in the case of receptors **2** and **3** (studied previously), significant changes were observed in the ^1H NMR spectrum of receptor **1** when it was subjected to titration with soluble fluoride anion salts, such as tetrabutylammonium fluoride (TBAF) (Figure S1).[8,9] However, other anions tested (TBACl, TBABr, and TBAI) induced no appreciable chemical shift changes in the ^1H NMR spectra of receptor **1** in $CDCl_3$ (Figure S2). We thus conclude that, as is true for **2** and **3**, receptor **1** is highly selective for the fluoride anion under these solvent conditions.[8,9]

As shown in Figure S1, receptor **1** in its ion-free form displays a broad singlet at δ = 6.71 ppm for the NH protons and two triplets about δ = 6.04 ppm and δ = 5.95 ppm for the β-pyrrolic protons in its ^1H NMR spectrum. These peak patterns are in accord with what has been seen for compounds **2** and **3**.[8,9] The observed triplets are thought to reflect long-range couplings between the CH and NH protons. Support for this latter conclusion came from deuterium exchange experiments carried out using 10% CD_3OD in $CDCl_3$ (loss of NH signal; simplification of CH resonances into doublets).[8,9] When receptor **1** was titrated with TBAF in $CDCl_3$, two sets of distinguishable resonances for all proton signals were seen in the ^1H NMR spectra recorded before saturation was achieved. These signals were ascribed to the free form of **1** and its fluoride anion complex, respectively. This observation of two sets of peaks is consistent with the binding/release equilibrium between compound **1** and the fluoride anion being slow on the NMR time scale (Figure S1). This slow exchange kinetics presumably reflects strong complexation between the fluoride anion and receptor **1** as the result of direct anion−receptor interactions involving the calix[4]pyrrole moiety. This conclusion was further supported by the observation that over the course of the addition, the singlet ascribed to the pyrrolic NH proton resonance is shifted downfield to $\delta \approx 12.7$ ppm ($\Delta\delta \approx 6.0$ ppm) and becomes split into a doublet (J = 40.0 Hz). This latter splitting is a typical feature of calix[4]pyrrole−F^- anion complexes and is ascribed to a coupling of the bound fluoride anion with the NH protons (Figure S1).[11] The triplet peaks corresponding to the β-pyrrolic protons were likewise shifted upfield during the titration and ultimately appeared as two singlets resonating at 5.83 and 5.68 ppm, respectively (Figure S1). These latter chemical shift changes are attributed to an increase in the electron density of the pyrrole subunits resulting from the interaction between the anion and the pyrrolic NH protons.

The interactions between receptor **1** and the F^- anion (as the tetraethylammonium (TEA) salt) in acetonitrile were further probed by isothermal titration calorimetry (ITC). The resulting data revealed that the interaction between TEAF [2.97 mM] and receptor **1** [0.20 mM] is favorable in terms of both enthalpy and entropy ($K_a = 6.0 \times 10^5$ M^{-1}; ΔG = −31 kJ/mol; ΔH = −16 kJ/mol; and $T\Delta S$ = 15 kJ/mol; Table S1 and Figure S3).

Given the favorable binding observed for TEAF, an effort was made to understand the cation dependence (if any) on the recognition features of **1**. In principle, ion-pair receptor **1** can form complexes with cations via three distinct recognition motifs, the calix[4]crown-5 ring, the ethylene glycol spacers between the calix[4]arene and the calixpyrrole unit, and the π-electron-rich concave calix[4]pyrrole "cup" formed by anion complexation. As a consequence, salts could be bound to **1** via a number of binding modes.[8−10,12] Four possible limiting binding modes for the complexation of CsF are shown in Figure 1 and

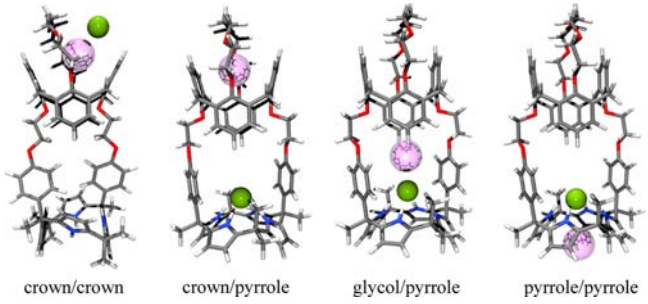


Figure 1. Views of the four limiting binding modes proposed for the interaction of receptor **1** with CsF.

are designated crown/crown, crown/pyrrole, glycol/pyrrole, and pyrrole/pyrrole, respectively. In this nomenclature, the first part of the name indicates the location of the cation, and the latter part of the name indicates the location of the anion.

Molecular mechanics calculations were performed to evaluate the relative stabilities of the binding modes shown in Figure 1 in the case of KF and CsF in the absence of solvent. The results of these calculations are summarized in Table 1.

The data in Table 1 provide some general insights into the KF and CsF recognition features of receptor **1**. First, irrespective of the binding mode, there is a strong preference for the binding of K^+ rather than Cs^+. Second, the preferred

Table 1. Calculated Gas-Phase Binding Energies for Ion-Pairs Bound to 1 via Different Limiting Binding Modes

	binding energy (kcal/mol)[a]			
ion-pair	crown/crown	crown/pyrrole	glycol/pyrrole	pyrrole/pyrrole
KF	−204.4	−186.5	−200.6	−196.6
CsF	−183.9	−165.6	−193.1	−182.5

[a] $\Delta E = E(\text{complex}) - E(\text{ligand}) - E(\text{cation}) - E(\text{anion})$.

gas-phase binding modes, crown/crown and glycol/pyrrole, are those that minimize the distance between the two cobound ions (i.e., K^+ or Cs^+ and F^-). The KF ion-pair exhibits a preference for the crown/crown mode, whereas CsF exhibits a preference for the glycol/pyrrole mode. In the absence of solvation, these preferences primarily result from maximizing the electrostatic attraction between the cation and anion.[13]

The solution-phase anion and cation binding behavior of **1** was investigated via ^{1}H NMR spectroscopy using a mixed solvent system consisting of $CDCl_3$ and CD_3OD (9/1, v/v). This particular choice of solvents was dictated by the solubility of the salts under study. A further consideration is that this solvent system was used in the case of **2** and **3**,[8,9] thus permitting direct comparisons with these previously studied systems. As shown in Figures S4 and S5, the addition of $KClO_4$ and $CsClO_4$ led to a significant change in the proton signals for the calix[4]arene crown-5 moiety but only a modest and no shift in the pyrrolic CH resonances for $KClO_4$ and $CsClO_4$, respectively. Such observations are interpreted in terms of the K^+ and Cs^+ cations being bound to the calix[4]arene crown-5 without the perchlorate anion being cobound to the calix[4]-pyrrole subunit.[10] On the basis of a quantitative analysis of chemical shifts involved, it is concluded that receptor **1** binds the K^+ cation more strongly than it does the Cs^+ cation (K_a = 6.5 × 10^6 M^{-1} for K^+ vs K_a = 3.3 × 10^4 M^{-1} for Cs^+).[10]

In contrast to the above, treatment of **1** with 5 equiv of TBAF induced no appreciable change in the ^{1}H NMR spectrum in $CDCl_3/CD_3OD$ (9/1, v/v), indicating that receptor **1** is unable to bind the F^- anion (or the large TBA^+ cation) effectively in this more polar solvent system (relative to pure $CDCl_3$; vide supra; Figure S6). Presumably, the F^- anion is strongly solvated in this mixed solvent system. This solvation may be enhanced by the fact that the TBAF used for these studies is not anhydrous. However, in the presence of coordinating cations, such as cesium and potassium, the F^- anion is bound to the receptor **1**, forming strong ion-pair complexes wherein the cation is bound to the calix[4]arene crown-5 moiety and the anion to the calix[4]pyrrole cavity (crown/pyrrole mode; cf., Figures 1, S4, and S5). Support for this conclusion comes from NMR spectral studies carried out in $CD_3OD/CDCl_3$ (1:9, v/v). For instance, as shown in Figure S5c, the addition of CsF caused all proton signals of receptor **1**, including the *β*-pyrrolic resonances of the calix[4]pyrrole moiety, to shift; this is as expected for a binding mode wherein both the calix[4]arene crown-5 and the calix[4]pyrrole moiety take part in ion-pair complexation. The presumed strong interaction between the F^- anion and receptor **1** was further evidenced by the observation that the singlet pyrrolic NH signal is split into a doublet. This splitting, which occurs upon exposure to CsF, is accompanied by a remarkable downfield shift in the NH proton signals (from 6.87 to 12.0 ppm). Changes in other spectral regions are also seen.

Under conditions where **1** is titrated with 0.72−1.38 equiv of CsF in $CD_3OD/CDCl_3$ (1:9, v/v), a new set of sharp peaks in the ^{1}H NMR spectrum, corresponding the *β*-pyrrolic protons, are seen to appear. In contrast, other peaks corresponding to the aromatic protons of the calix[4]arene moiety were merely broadened (Figure S7). This is consistent with the presence of two different kinds of binding interactions involving receptor **1** and the CsF ion-pair. In one of the modes, only the Cs^+ cation, but not the F^- anion, is weakly bound to the crown-5 ring to form a cesium complex ($[\mathbf{1}\cdot Cs^+]F^-$) wherein the F^- counter-anion is not cobound (crown/crown binding mode). This form is characterized by a general broadening of the aromatic and crown ether signals in the ^{1}H NMR spectrum, but not significant changes in the chemical shifts. This complex ($[\mathbf{1}\cdot Cs^+]F^-$) exists in fast equilibrium with the free receptor, as evidenced by the peak broadening seen for the aromatic protons of the calix[4]arene moiety. In contrast, in the other binding mode, the Cs^+ cation and the F^- anion are bound concurrently and strongly to receptor **1**. In this case, the cation and anion are stabilized by the ethylene glycol spacers and the calix[4]pyrrole moiety, respectively (glycol/pyrrole mode; cf., Figures 1 and 2). This latter complexation mode, which

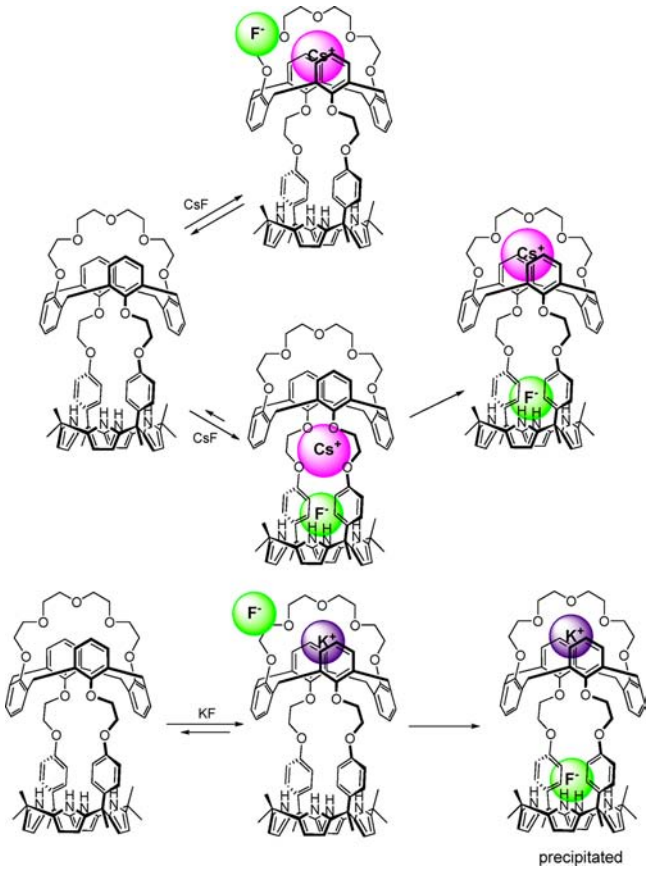


Figure 2. Proposed binding interactions involving **1** and KF and CsF in $CD_3OD/CDCl_3$ (1/9, v/v). On the basis of an analysis of the NMR spectra, a so-called pyrrole−pyrrole binding mode, wherein the Cs^+ cation is bound in the "cup" of the calix[4]pyrrole and the F^- is complexed by the pyrrole NH protons, is ruled out. See text.

involves a slow equilibrium, is similar to what was seen in the case of the CsF complex of **3** and gives rise to the new distinguishable peaks in the ^{1}H NMR spectrum.[9] After the Cs^+ cation is bound to the ethylene glycol spacer, it moves to the crown-5 ring to form a thermodynamically more stable ion-pair complex ($[\mathbf{1}\cdot CsF]$) (crown/pyrrole mode; cf., Figures 1 and 2).

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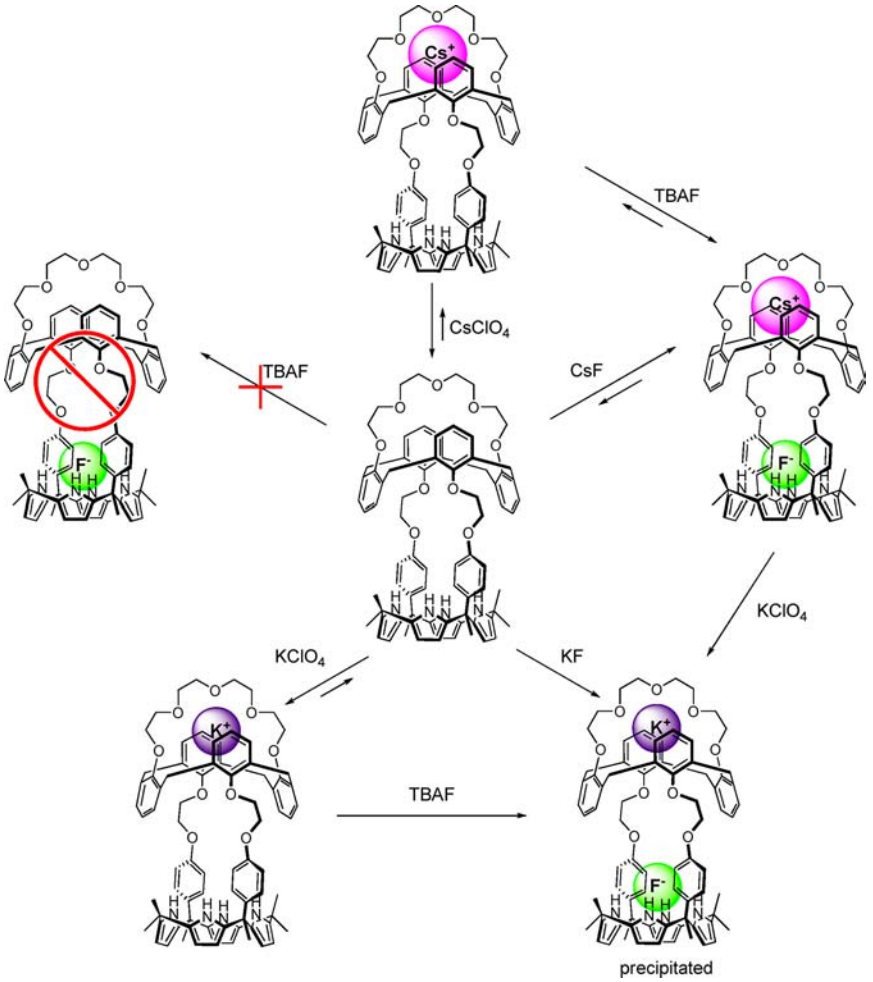

Figure 3. Proposed binding interactions involving **1** and various K^+, Cs^+, and F^- salts in $CD_3OD/CDCl_3$ (1/9, v/v). On the basis of an analysis of the ^1H NMR spectra, we rule out other possible binding modes. See text.

The affinity of receptor **1** for CsF in 10% MeOH in $CHCl_3$ was quantified by isothermal titration calorimetry (ITC). This analysis, which is subject to ≤15% error, revealed that the interaction of CsF [2.95 mM] with **1** [0.19 mM] is highly exothermic and enthalpy-driven (ΔH = −64 kJ/mol; ΔG = −26 kJ/mol; $K_a = 4.1 \times 10^4$ M^{-1}; Table S1 and Figure S8). The binding constant of receptor **1** for CsF in 10% CD_3OD in $CDCl_3$ is lower than that of **2** having the calix[4]arene crown-6 ($K_a = 3.8 \times 10^5$ M^{-1}) and higher than that of the crown-free receptor **3** ($K_a = 1.3 \times 10^4$ M^{-1}) (Table S1).[8,9] These differences are ascribed to the reduced interaction between the crown-5 ring of **1** and the Cs^+ cation relative to the corresponding crown-6 system (**2**).

Receptor **1** also forms a thermodynamically stable 1:1 ion-pair complex with KF wherein the K^+ cation is bound to the calix[4]arene crown-5 ring and the F^- anion is bound to the calix[4]pyrrole moiety (crown/pyrrole mode; cf., Figure 1). However, in terms of binding dynamics on the NMR time scale, the complexation of KF is quite different from that of CsF. Upon addition of KF to a solution of receptor **1** in 10% CD_3OD in $CDCl_3$, the proton signals of the calix[4]arene crown-5 undergo a significant shift, while those of the calix[4]pyrrole moiety remain largely unchanged (Figure S4). Such observations are consistent with receptor **1** coordinating the K^+ cation first through the calix[4]arene crown-5 ring without the F^- anion being bound to the calix[4]pyrrole moiety (crown/crown mode). This complex ([**1**·K^+]F) exists in slow equilibrium with the free receptor, as evidenced by the observation of two sets of distinguishable peaks in the proton NMR spectrum (Figure S4). Specifically, the signals are ascribable to both the K^+ complex ([**1**·K^+]F^-) and the free receptor (but no other species seen in the NMR spectrum).

Once the K^+ is bound to receptor **1**, the resulting potassium complex ([**1**·K^+]) facilitates the binding of the F^- counter-anion. In what is then a sequential process on the NMR time scale, the counteranion then binds to the calix[4]pyrrole moiety to give the KF ion-pair complex ([**1**·KF]; crown/pyrrole mode), which then precipitates from solution (Figures 1−3). As a result of the observed precipitation, the complexation of receptor **1** with KF is irreversible under these solution phase conditions. Presumably, this reflects the fact that KF is bound by **1** and that the resulting ion-pair−receptor complex is less well solvated than the ions K^+ and F^- alone.

To provide support for the above conclusion, the precipitate was collected by filtration, and its ^1H NMR spectrum was recorded in nitrobenzene-d_5 solution (in which the precipitate and putative complex are soluble). The resulting spectrum revealed proton signals ascribable to both the calix[4]arene crown-5 and the calix[4]pyrrole moieties with both sets of resonances having undergone significant chemical shift changes relative to the ion-free receptor **1**. This is consistent with the K^+ and the F^- ions being cobound in nitrobenzene to the

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calix[4]arene crown-5 and the calix[4]pyrrole subunits, respectively (Figure S9).

Precipitation was also observed when TBAF was added to a solution of the potassium complex of receptor **1** formed from potassium perchlorate ($[\mathbf{1}\cdot K^+]ClO_4^-$) in 10% CD_3OD in $CDCl_3$. This observation leads us to infer that under these conditions the KF ion-pair complex of **1** is formed as the result of counteranion exchange (Figure 3).

The stepwise binding seen for receptor **1** and KF on the NMR time scale mirrors what was seen in the case of compound **2** and CsF.[9] Therefore, it is concluded that receptors **1** and **2**, both of which have two different binding sites for specific cations (favoring K^+ and Cs^+ binding in the case of receptors **1** and **2**, respectively), display similar complexation dynamics. Specifically, the cations interact first with the receptors via the stronger cation recognition site exclusively. Only then does complexation of the counteranion occur within the calix[4]pyrrole anion binding site (Figure 2). This behavior reflects the fact that receptor **1** bears several potential cation binding sites. In this specific case, both the calix[4]arene crown-5 and the ethylene glycol spacers interact with the Cs^+ cation (cf., Figure 2).

To provide support for the inferences drawn from the ^1H NMR spectral measurements, that receptor **1** binds both KF and CsF but displays high selectivity for KF over CsF, we investigated whether cation metathesis would occur when a precomplexed CsF ion-pair complex was exposed to K^+. This study was carried out by adding $KClO_4$ to solutions of the [**1**·CsF] complex in 10% $CD_3OD/CDCl_3$ (Figures 3 and 4). When a solution of $KClO_4$ in a mixture of methanol-d_4/chloroform-d (1/9, v/v) was added to a solution of complex [**1**·CsF] in the same solvent, formation of a precipitate occurred. This phase change is ascribed to the formation of an insoluble [**1**·KF] ion-pair complex as a result of cation exchange, replacement of Cs^+ by K^+ (Figures 3 and 4). In contrast, the addition of $KClO_4$ to solutions of free receptor **1** in this same solvent mixture or to solutions of CsF alone (i.e., in the absence of receptor **1**) did not lead to precipitation. We thus conclude that adding $KClO_4$ to a solution of complex [**1**·CsF] gives rise to the corresponding KF complex, [**1**·KF] (Figures 3 and 4).

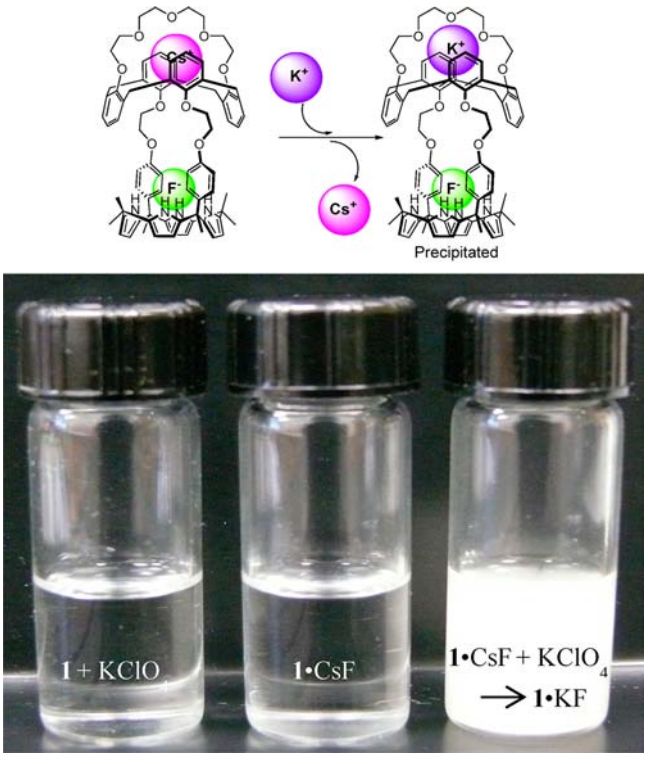

Figure 4. Precipitation induced via cation metathesis observed upon adding the K^+ cation (as $KClO_4$) to the preformed CsF complex of **1** in $CD_3OD/CDCl_3$ (1/9, v/v).

The fact that receptor **1** binds KF and CsF ion-pairs strongly led us to consider that this receptor could have use as an extractant. These fluoride salts are particularly challenging to extract from water in that the fluoride anion (ΔG_{hyd} = −465 kJ/mol for F^-) is strongly hydrated as compared to other monoanionic ions such as Cl^- (ΔG_{hyd} = −340 kJ/mol), Br^- (ΔG_{hyd} = −315 kJ/mol), I^- (ΔG_{hyd} = −275 kJ/mol), and NO_3^- (ΔG_{hyd} = −300 kJ/mol).[14] To test this possibility, ^1H NMR spectroscopy was used in conjunction with a two-phase system consisting of D_2O and nitrobenzene-d_5. Upon exposure of receptor **1** in $C_6D_5NO_2$ to aqueous (D_2O) solutions of KF, significant changes in the ^1H NMR spectrum were observed (Figure S10). The proton signals of the calix[4]pyrrole moiety, as well as those of the calix[4]arene crown-5 ring, were seen to undergo significant shifts. These changes were particularly large in the case of the NH signals ($\Delta\delta \approx 5.1$ ppm). This is consistent with the interactions between the fluoride anions and the receptor being very strong. On the basis of the absence of free receptor signals and the saturation-like behavior seen as the amount of KF in the aqueous layer increases, we conclude that to the limits of the ^1H NMR spectral analysis, 100% of receptor **1** originally present in the nitrobenzene phase exists as the KF ion-pair complex when the initial KF (in the aqueous phase) and receptor (in the organic phase) are 20 and 4.0 M, respectively. We thus conclude that it is an effective KF extractant.[15]

In contrast to what is seen with KF, exposure of the nitrobenzene solution of receptor **1** (4.0 M) to an aqueous CsF solution (20 M) leads to no discernible change in the ^1H NMR spectrum (Figure S10). This observation is taken as evidence that **1** is unable to extract CsF under these liquid−liquid extraction conditions. The selectivity for KF over CsF under conditions of extraction is noteworthy given the fact that the Cs^+ cation (ΔG_{hyd} = −250 kJ/mol) is less well hydrated than the K^+ cation (ΔG_{hyd} = −295 kJ/mol) (vide supra).[14,16]

A central question is whether receptor **1** would function more effectively than an equimolar mixture of the isolated anion and cation receptors from which it is formally derived. To address this issue, we first tested the ability of the simple cation and anion receptors (**4** and **5**) to extract KF from a water phase into a nitrobenzene phase. Upon contacting nitrobenzene-d_5 solutions of (separately) **4** and **5** (4.0 M, respectively) with D_2O solutions containing KF (20 M), no appreciable chemical shift changes were observed (Figures S12 and S13). This finding leads us to conclude that neither the anion receptor **4** nor the cation receptor **5** on their own is able to extract appreciable quantities of KF under our standard liquid−liquid extraction conditions.

We next tested an equimolar mixture of **4** and **5**. In this case, and in contrast to what was seen for the individual receptors, evidence for extraction was seen, although the level of efficacy was reduced as compared to what was observed in the case of the ion-pair receptor **1**. In particular, when an equimolecular mixture of **4** and **5** in nitrobenzene-d_5 was contacted with an

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aqueous (D_2O) solution of KF, significant chemical shift changes were observed in the ^1H NMR spectrum (Figure S14). For instance, two sets of distinguishable resonances were seen for all of the proton signals in the case of the cation receptor **5**. These signals were readily attributable to the substrate-free form of **5** and its K^+ complex, respectively. This observation led us to the inference that the binding/release equilibrium between compound **5** and the potassium cation is slow on the NMR time scale (Figure S14). In the case of calix[4]pyrrole **4**, the NH signal could not be seen in the mixture after contact with an aqueous KF solution, whereas the *β*-pyrrolic CH resonance was shifted 0.1 ppm to slightly higher field but without peak splitting. Considered in concert, these two findings provide support for the notion that under the conditions of the experiment calix[4]pyrrole **4** interacts with the fluoride anion but with binding and release both being fast on the NMR time scale (Figure S14).

Comparing the integral ratios in the ^1H NMR spectrum of the K^+ complex of compound **5** with those seen in the corresponding ion-free form revealed that ∼33% of the receptor mixture takes part in KF complexation under conditions of extraction. Because this number is ∼0% in the absence of **4**, we conclude that synergy between the anion receptor **4** and the cation receptor **5** is necessary for the effective extraction of KF. On the other hand, an equimolar mixture of **4** and **5** appears less effective for extraction than the ion-pair receptor **1**, as evidenced by the fact that, to the limits of NMR spectral analysis, ∼100% of the latter species participates in KF extraction.

Further support for the KF and CsF binding modes inferred for receptor **1** from the solution phase NMR spectroscopic studies discussed above came from single crystal X-ray diffraction analyses. Suitable single crystals of the CsF complex were obtained by subjecting a chloroform/methanol solution of receptor **1** to slow evaporation in the presence of excess cesium fluoride. The resulting crystal structure revealed that receptor **1** forms a 1:1 complex with cesium fluoride, **1**·CsF, in the solid state wherein the Cs^+ cation is bound to the calix[4]arene crown-5 moiety (Figure 5). This binding mode is observed despite the fact that the calix[4]arene crown-5 is too small to bind the Cs^+ cation strongly.[10] The Cs^+ ion is encapsulated by the calix[4]arene crown ether ring with distances of 2.84−3.03 Å for the $Cs^+\cdots O$ separations. The distances between the Cs^+ ion and the aromatic carbon atoms in the *meta*- and *para*-positions with respect to the phenoxy groups are on the order of 3.40−3.46 Å. It is thus inferred that *π*-metal interactions are playing a role in stabilizing the complex (Figure 5). As compared to the distances observed in the CsF complex of receptor **2** (3.08−3.36 Å for the $Cs^+\cdots O$ distance and 3.43−3.63 Å for the *π*-metal interaction), those observed between the bound Cs^+ cation and the calix[4]arene crown-5 of receptor **1** are much shorter. This leads us to suggest that receptor **1** holds the Cs^+ cation more tightly than does receptor **2** despite the fact that the calix[4]arene crown-6 binds the Cs^+ cation much more strongly than does the calix[4]arene crown-5.

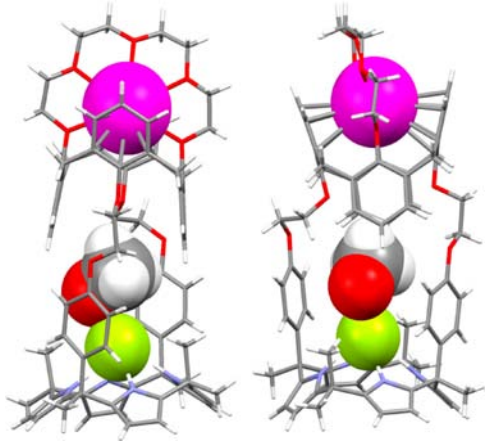

Figure 5. Two different views of the single crystal X-ray diffraction structure of **1**·CsF·CH_3OH. Solvent molecules not involved in stabilization of the ion-pair complex have been removed for clarity.

In complex **1**·CsF, the F^- ion is bound to the NH protons of the calix[4]pyrrole with the relevant $N\cdots F^-$ distances being 2.77−2.81 Å. One methanol molecule is also hydrogen bonded to the F^- anion, the $O\cdots F^-$ distance being 2.58 Å. In analogy to what was seen for the complex of compound **2** with CsF, there is no direct interaction between the Cs^+ and F^- ions bound to receptor **1**. While lattice effects may be playing a role, we take this as meaning that the stabilization energy arising from the formation of the complex, **1**·CsF, is large enough to offset the presumed Columbic energy penalty caused by what appears to be an unfavorable ion separation. The distance between the Cs^+ ion and the F^- ion in the complex was found to be 10.29 Å (Figure S11). Again, this leads us to suggest that the formation of a strong complex, **1**·CsF containing a methanol molecule, is energetically more stable than the corresponding contact ion-pair complex. This is true despite the large separation between the Cs^+ and F^- ions.

The structure of the KF complex of receptor **1** in the solid state was also determined by X-ray crystallography. Suitable single crystals were obtained by allowing a chloroform/methanol solution of the CsF complex to undergo slow evaporation in the presence of one molar equivalent of $KClO_4$. As shown in Figure 6, in the resulting structure, the K^+ cation is bound to the crown ether at $K^+\cdots O$ distances that vary between 2.77 and 2.87 Å. Evidence for a *π*-metal interaction between the aromatic rings of the calix[4]arene and the K^+ cation is seen in the $K^+\cdots C$ distances of 3.06−3.23 Å (Figure 6). The F^- anion is hydrogen bonded to the four pyrrolic NH protons with $N\cdots F^-$ distances of 2.76−2.79 Å. A methanol molecule is also bound within the receptor and interacts with the fluoride anion. The

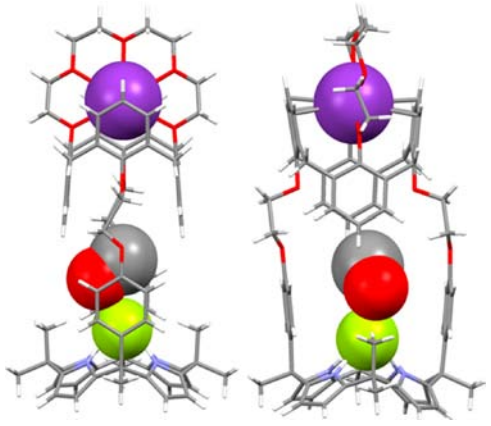

Figure 6. Two different views of the single crystal X-ray diffraction structure of **1**·KF·CH_3OH. Solvent molecules not involved in stabilization of the ion-pair complex have been removed for clarity.

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relevant O···F^- distance is 2.69 Å. The separation between the K^+ and the cobound F^- was found to be 10.74 Å (Figure S11).

CONCLUSIONS

On the basis of both ^{1}H NMR spectroscopic analyses and single crystal X-ray crystal structural data, we conclude that the ion-pair receptor **1**, which contains a calix[4]pyrrole for anion binding and calix[4]arene crown-5 for cation recognition, is able to complex both the CsF and the KF ion-pairs strongly. However, the underlying binding occurs via very different modes for these two salts. Specifically, in the case of KF, the calix[4]arene crown-5 moiety binds the K^+ cation first and then the calix[4]pyrrole subunit binds the F^- anion. This gives a stable 1:1 ion-pair complex that generally precipitates from solution. In contrast, the CsF ion-pair interacts with receptor **1** in two different ways. In one of these modes, the Cs^+ cation interacts with the calix[4]arene crown-5 ring weakly, albeit in fast equilibrium. In this case, the counteranion is not cobound. In the second interaction mode, which in 10% CD_3OD in $CDCl_3$ is thermodynamically more stable, the Cs^+ and F^- ions are simultaneously bound to the receptor framework through the ethylene glycol spacers and the calix[4]pyrrole moiety, respectively. In this case, dynamic binding behavior is seen in 10% CD_3OD in $CDCl_3$ with the Cs^+ cation being bound first to the ethylene glycol spacers and only subsequently by the calix[4]arene crown-5 subunit. While forming complexes with both CsF and KF, the present system displays ion-pair selectivity. This is manifest by the fact that addition of $KClO_4$ to the CsF complex of **1** leads to cation metathesis and formation of the more stable KF complex. The stability of the latter ion-pair complex is reflected in the ability of receptor **1** function as more effective extractant for KF in a two-phase aqueous-nitrobenzene test system than either **4** or **5**, alone or in combination. We thus conclude that suitably designed ditopic receptors, such as **1**, could offer advantages over simple mixtures of the corresponding anion and cation binding subunits.

ASSOCIATED CONTENT

Supporting Information

^{1}H NMR spectroscopic data, ITC analyses, and X-ray structural data for **1**·KF·$(CH_3OH)_3$ (CCDC 826579) and **1**·CsF·$(CH_3OH)_2$·$(CHCl_3)_2$ (CCDC 826578). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(16) Previously, we had shown that receptor **1** may be used to effect the extraction of KCl. See ref 10.