Published in final edited form as:

Supramol Chem. 2019 ; 31(3): 203–210. doi:10.1080/10610278.2018.1535711.

Cesium Halide Ion Pair Recognition by a Pyrrole Strapped Calix[4]pyrrole

Ju Ho Yang^a, Vincent M. Lynch^b, Jonathan L. Sessler^b, Sung Kuk Kim^a

^aDepartment of Chemistry and Research Institute of Natural Science, Gyeongsang National University, Jinju, 660-701, Korea

^bDepartment of Chemistry, The University of Texas at Austin, 105 E. 24th, Street-Stop A5300, Austin, Texas 78712-1224

Abstract

The binding properties of the pyrrole-strapped calix[4]pyrrole **2** for cesium halide ion pairs were studied *via* ¹H NMR spectroscopic and single crystal X-ray diffraction analyses. Receptor **2** was found to bind CsF, CsCl, and CsBr in the solid state and in chloroform/methanol (4/1, v/v) solution with relatively high affinity as compared with the parent calix[4]pyrrole **1**. It was also revealed by solid-liquid extraction experiments that receptor **2** was capable of solubilizing CsF in CDCl₃, a medium in which this salt is otherwise insoluble. Single crystal X-ray diffraction analyses and ¹H NMR spectroscopic data recorded in 20% CD₃OD in CDCl₃ provide support for the suggestion that the strap pyrrolic NH proton of **2**, as well as those of the calix[4]pyrrole framework, contribute to anion recognition, thus increasing affinity for cesium halide salts relative to the parent system **1**. In the solid state, receptor **2** interacts with CsF to form a two dimensional coordination polymer in the presence of methanol. A linear coordination polymer is observed in the case of CsCl and CsBr. Receptor **2** was also found to form a complex with CsF in chloroform/methanol (4/1, v/v) solution, albeit with a different binding mode than is seen in the solid state.

Keywords

Ion Pair Recognition; Coordination Polymers; Calixpyrroles

Introduction

Recently, ion pair receptors, systems that have the ability to complex concurrently both an anion and a cation, have attracted increasing attention.^{1–8} Much of the interest associated with such systems reflects their generally enhanced affinity and selectivity for certain salts as compared with simple ion receptors that are designed to bind in relative isolation either a

Corresponding Authors: sessler@cm.utexas.edu, sungkukkim@gnu.ac.kr.

Disclosure Statement: The authors attest that there is no conflict of interest.

Structural Data: The reported structures have CCDC numbers 1851189-1851192.

Supporting Information Available: NMR spectroscopic binding data and X-ray structural data for **2**•CsF•CH₃OH (CCDC 1851192), **2**•CsCl (CCDC 1851190), **2**•CsBr (CCDC 1851191), and **2**•(H₂O)₃ (CCDC 1851189).

The authors declare no competing financial interest.

cation or an anion, The improved ion binding features of ion pair receptors are generally ascribed to enhanced electrostatic interactions between co-bound ions within the receptor, as well as reductions in competitive solvation effects that result from encapsulation of both target ions within the same receptor environment.^{1–4} Typically ion pair receptors contain two distinct ion binding sites, one for a cation and one for an anion. Calix[4]pyrroles, a class of non-aromatic tetrapyrrolic macrocycles, are attractive frameworks for the construction of ion pair receptors of this general class. They are relatively easy to functionalize with a variety of cation recognition motifs *via* the β -pyrrolic carbon atoms or meso carbon atoms.^{4,9,10} Moreover, the parent calix[4]pyrrole (**1**) has been recognized since 1996 for its ability to bind halide anions in apolar media *via* hydrogen bond interactions involving the pyrrolic NHs.¹¹ In 2005, the ability of calix[4]pyrrole **1** to form ion pair complexes with *inter alia* cesium halide salts, such as CsF, CsCl, and CsBr was also confirmed in solution and in the solid state.¹² In the resulting complexes, the halide anions were found hydrogen-bonded to the pyrrolic NHs while the cesium cation was bound to the bowl-shaped calix[4]pyrrole cavity *via* interactions with the π -faces of the pyrroles.¹² In follow-up studies, calix[4]pyrrole **1** was studied for its ability to effect the transmembrane transport of cesium halide ion pairs or promote their extraction under either liquid-liquid or liquid-solid conditions.^{13–15} More recently, calix[4]pyrrole-based ion pair receptors containing crown ethers and calix[4]arenes as cation binding sites were also reported and found to form complexes with various ion pairs, especially, cesium salts.^{4,16} Nevertheless, detailed binding studies involving calix[4]pyrrole **1** with cesium halide salts in solution are lacking. Herein, we report a study of the solution phase (20% CD₃OD in CDCl₃) cesium halide salt binding features of calix[4]pyrrole **1** as well as those of a strapped-calix[4]pyrrole (receptor **2**) that incorporates an additional hydrogen bond-donating pyrrole subunit.^{17,18} As compared with unfunctionalized calix[4]pyrrole **1**, receptor **2** was found to have significantly enhanced binding ability for anions, presumably as the result of participation of the strap pyrrole in anion binding.^{17,18} The improved anion affinity of **2** was expected to affect positively its capability to bind ion pairs such as cesium salts. With this expectation in mind, we now report the binding features of receptors **1** and **2** for cesium salts in solution and in the solid state. On the basis of ¹H NMR spectroscopic analyses we have determined that receptor **2** is capable of binding cesium halide salts, such as CsF, CsCl, and CsBr, in CD₃OD/CDCl₃ (4/1, v/v) solution. Moreover, as compared with the parent calix[4]pyrrole **1**, receptor **2** displays a markedly high affinity for CsF. Single crystal X-ray diffraction analyses served to confirm that receptor **2** is capable of forming complexes with cesium halide ion pairs in the solid state. The resulting structures differ from those stabilized by calix[4]pyrrole **1**.

Structures 1 and 2

Results and Discussion

Receptor **2** was synthesized following a literature procedure.¹⁷ X-ray diffraction analyses of single crystals grown in the presence of cesium halide salts provided evidence that receptor **2** is able to form complexes with CsF, CsCl and CsBr in the solid state. Single crystals of the CsF complex suitable for X-ray diffraction analysis were grown by slow evaporation of a mixture of chloroform and methanol containing **2** and excess of CsF. The resulting crystal structure revealed a 1:1 CsF-receptor complex (**2**·CsF) with two methanol molecules being coordinated to the co-bound cesium cation and fluoride anion, respectively (Figure 1). One of the two methanol molecules mediates an apparent interaction between the strap pyrrolic NH and the fluoride anion *via* hydrogen bonds with a distance of 1.74 Å (O-H---F⁻ interaction) (Figure 1). Based on the metric parameters, the fluoride anion was also found hydrogen-bonded to the pyrrolic NHs of the calix[4]pyrrole framework with distances of 2.00–2.19 Å (N-H---F⁻ interactions). In contrast, the cesium cation was bound *via* cation- π interactions within the bowl-shaped calix[4]pyrrole cavity that exists in the cone conformation as inferred from the distances between the cesium cation and the centroids of the pyrrole rings (found to vary from 3.40 to 3.53 Å). The bound cesium cation is also coordinated to a carbonyl oxygen atom present on another molecule of **2**, as well as with the oxygen atom of the methanol molecule hydrogen bonded to a different complex of **2**·CsF·CH₃OH. These two different interactions result in the formation of the 2-dimensional coordination polymer in the solid state (Figure 1). This finding stands in sharp contrast to what was observed for the complexes of **1**·CsF, **2**·CsCl, and **2**·CsBr (*vide infra*). The distance between the cesium cation and the fluoride anion within the complex **2**·CsF was found to be 4.00 Å, which is longer than what was seen in the solid state of the CsF complex of **1** (Cs-F⁻ distance = 3.69 Å).

Single crystals of the CsCl complex of **2** suitable for X-ray diffraction analysis were obtained by subjecting a mixture of chloroform and methanol containing **2** and excess of CsCl to slow evaporation.¹⁹ The resulting crystal structure revealed that the chloride anion forms a direct hydrogen bond with the strap pyrrolic NH proton, as well as with those of the calix[4]pyrrole. The distances were found to be 2.40 Å for the strap pyrrole N-H---Cl⁻ and 2.54–2.57 Å for the calix[4]pyrrole N-H---Cl interactions, respectively (Figure 2). The

cesium cation was found complexed within the bowl-shaped calix[4]pyrrole cavity *via* presumed cation- π interactions. The distances between the cation and the centroids of the pyrrole rings were found to range from 3.34 to 3.38 Å. The bound cesium cation is in close contact with the chloride anion bound to another molecule of **2** at a distance of 3.46 Å (Figure 2). As a result, a linear coordination polymer is stabilized in the solid state, which stands in contrast to what was seen for the CsF complex of **2** discussed above.

Using similar crystallization conditions, diffraction grade single crystals of the corresponding CsBr complex of **2** were obtained. In analogy to what was seen with CsCl, a linear coordination polymer is stabilized in the solid state. In addition, the bromide anion was found hydrogen bonded to both the pyrrolic NH protons of the calix[4]pyrrole framework and the pyrrole NH proton of the strap. The corresponding N-H...Br distances were found to be 2.58–2.72 Å for the calix[4]pyrrole interactions and 2.50 Å for the strap pyrrole N-H...Br[−] interaction, respectively (Figure 3). As expected, the cesium cation was bound to π -faces of the bowl-shaped calix[4]pyrrole *via* cation- π interactions. The distances between the cesium cation and the centroids of the pyrrole rings were found to range from 3.35 to 3.36 Å. Intramolecular and intermolecular Cs⁺...Br[−] distances were found to be 4.81 Å and 3.51 Å, respectively (Figure 3).

Attempts to obtain single crystals of the CsI complex of **2** under various crystallization conditions always resulted without exception in our hands in isolation of single crystals of the ion-free receptor. This observation is consistent with the low affinity for the iodide anion displayed by **1** and leads us to suggest that receptor **2** has a low affinity for CsI. The resulting crystal structure revealed the calix[4]pyrrole moiety in the 1,3-alternate conformation with three water molecules hydrogen bonded to the pyrrolic NH protons (Figure 4).

The interactions between receptor **2** for CsX (X=F[−], Cl[−], Br[−], and I[−]) were studied *via* ¹H NMR spectroscopy. For reasons of solubility, these analyses were performed using 20% methanol-*d*₄ in chloroform-*d*₁ (v/v) as the solvent. Dramatic chemical shift changes were observed in the ¹H NMR spectra when receptor **2** was treated with CsF, CsCl, and CsBr (Figure S1). In the absence of these cesium halide salts, the NH proton signals of the calix[4]pyrrole were found to resonate at 7.81 ppm, while that of the pyrrole on the strap were not observed. The failure to detect this latter signal presumably reflects H/D exchange with the CD₃OD and thus what is inferred to be the relatively high acidity of the strap pyrrolic NH compared to the calix[4]pyrrole core. Upon exposure of receptor **2** to CsF in 20% CD₃OD in CDCl₃, the singlet NH proton signal of the calix[4]pyrrole moiety in the ¹H NMR spectrum underwent a significant downfield shift to 12.05 ppm ($\delta \approx 4.24$ ppm) and was found to be split into a doublet ($J = 21.8$ Hz). The peak splitting was attributable to coupling between the bound F[−] anion and the pyrrolic NHs.²⁰

In order to elucidate the role, if any, the strap pyrrolic NH proton plays in mediating the CsF binding, deuterated methanol (CD₃OD) was replaced with normal methanol (CH₃OH). Under these conditions, ¹H NMR spectroscopic measurements of **2** alone revealed a signal ascribable to the strap pyrrolic NH proton at 10.0 ppm. This represents a substantial downfield shift compared to the resonances for the calix[4]pyrrole core ($\delta = 7.75$ ppm)

(Figure 5). In the presence of 10.0 equiv of CsF, the singlet proton signal of the strap pyrrolic NH was seen to undergo a remarkable shift towards lower field (to 13.74 ppm; $\delta \approx 3.74$ ppm) and was split into a doublet ($J = 26.7$ Hz). Presumably, these changes are the result of interacting with the fluoride anion directly and coupling to the associated ^{19}F nuclear spin.²⁰ This direct interaction stands in marked contrast to what was seen in the solid state structure of $2 \cdot \text{CsF} \cdot \text{CH}_3\text{OH}$ in the solid state where a methanol molecule is found between the pyrrole NH proton and the receptor-bound fluoride anion (*vide supra*). Downfield shifts for the calix[4]pyrrole NH protons were also seen ($\delta \approx 4.32$ ppm). In contrast, the doublet ($\delta = 5.99$ ppm) corresponding to the β -pyrrolic protons of the calix[4]pyrrole moiety experienced an upfield shift when 10 equiv of CsF were added to **2** and was split into two triplets centered at $\delta = 5.70$ ppm ($\delta \approx 0.29$ ppm). These latter spectral changes are ascribed to an increase in the electron density of the pyrrole rings resulting from the hydrogen bonding of the pyrrolic NHs with the basic fluoride anion. A slight downfield shift was seen for the proton signal (H_e) corresponding to the methylene groups directly connected to the calix[4]pyrrole *meso* carbon atoms in the presence of CsF ($\delta \approx 0.56$ ppm). Similar chemical shift changes were also observed for the methyl proton signals ($-\text{CH}_3$). On this basis it is concluded that both the methylene CH and the methyl CH protons interact with the bound fluoride anion, presumably *via* C-H---anion hydrogen bonds (Figure 5).

Further support for the strong binding interaction between receptor **2** and CsF came from an ^1H NMR spectroscopic titration of **2** with CsF carried out in $\text{CD}_3\text{OD}/\text{CDCl}_3$ (1:4, v/v) (Figure 6). When receptor **2** was subjected to titration with CsF, two distinct sets of proton signals were observed in the ^1H NMR spectra recorded before saturation was reached, which occurred upon the addition of 1.01 equiv of CsF. These spectral findings are in agreement with the coexistence of the ion-free form and the CsF-bound form of **2** at intermediate (<1 equiv) CsF stoichiometries that are in slow equilibrium on the ^1H NMR time scale. On the basis of the spectral changes observed over the course of the titration, the binding constant (K_a) corresponding to the interaction of receptor **2** with CsF was approximated to be $10,000 \text{ M}^{-1}$.²¹

An analogous ^1H NMR spectroscopic titration of **1** with CsF was also carried out. In this case, saturation was not achieved until 15.0 equiv of CsF were added to the solution of **1** (Figure S2). This finding is consistent with the parent system (**1**) being far less effective as CsF receptor than the strapped system, **2**, under these conditions. In contrast to what was seen in receptor **2**, the proton signal of the pyrrolic NHs of the calix[4]pyrrole portion remained a singlet even in the presence of excess CsF (Figures S2 and S3). Such an observation supports the inference of weaker binding and the existence of fast exchange between the bound and unbound forms.

Treatment of receptor **2** with 10 equiv of CsCl and CsBr, respectively, in $\text{CD}_3\text{OD}/\text{CDCl}_3$ (1:4, v/v) also gave rise to noticeable chemical shift changes in the corresponding ^1H NMR spectra (Figure S1). For example, the proton resonances corresponding to the pyrrolic NHs (both H_d and H_f), as well as those for the methylene and methyl CH protons, were all downfield-shifted while the β -pyrrolic protons of the calix[4]pyrrole framework underwent a slight upfield shift (Figure S1). These findings lead us to suggest that receptor **2** forms

complexes with both CsCl and CsBr *via* a similar binding mode to what was seen in the case of the CsF complex (*vide supra*). For these salts, a good correspondence was seen between the solid state structure and that inferred from the solution phase studies. No appreciable chemical shift changes were observed upon treatment with CsI. Presumably, this reflects a lack of interaction between receptor **2** and CsI under these conditions.

In light of the strong interaction between **2** and CsF inferred in solution and in the solid state, we carried out solid-liquid extraction experiments using receptor **2** and CsF. The latter salt is insoluble in chloroform. Thus, this solvent was thus chosen as the solution phase for the extraction studies. After a chloroform solution of receptor **2** was subjected to sonication in the presence of 10.0 equiv of CsF, it was filtered to remove the insoluble portion and the filtrate was analyzed by ^1H NMR spectroscopy. Sonication for 10 min produced two distinguishable sets of proton signals for **2** in the ^1H NMR spectrum. These features were assigned to the ion free receptor and its CsF complex, respectively. Comparison of the peak integral ratios for the free receptor and its corresponding CsF complex led us to suggest that approximately 10% of receptor **2** is converted to the corresponding CsF complex which is soluble in the chloroform solution. On the other hand, after sonication for 1 hr no proton signals ascribable to the ion-free form of **2** could be observed in the ^1H NMR spectrum (Figure 7). This finding was taken as evidence that under these latter conditions roughly 100% of the receptor **2** initially present in the chloroform phase is converted to the corresponding CsF ion pair complex. On this basis, we conclude that receptor **2** acts as a more effective CsF extractant than the parent calix[4]pyrrole (**1**).²²

Conclusion

In summary, the ability of the pyrrole-strapped calix[4]pyrrole (**2**) to interact with cesium halide (CsX) salts was demonstrated both in the solid state in mixed organic media. A number of ^1H NMR spectral studies were carried out in deuterated chloroform solution containing 20% deuterated as well as non-deuterated methanol. Taken in concert, these studies provide support for the suggestion that receptor **2** is able to bind CsF, CsCl, and CsBr with greater affinity than calix[4]pyrrole **1**. Single crystal X-ray diffraction analyses of the CsX complexes of **2** (X = F, Cl, and Br) revealed that the anions were bound *via* direct or indirect hydrogen bonds to both the pyrrolic NH proton of the strap and the NH protons of the calix[4]pyrrole moiety, while the cesium cation was complexed *via* cation- π interactions within the bowl-shaped calix[4]pyrrole cavity. In the solid state, receptor **2** forms a 2-dimensional coordination network in the presence of CsF whereas linear coordination polymers are observed with CsCl and CsBr. It was also found that receptor **2** binds CsF *via* a different binding mode in a methanol/chloroform mixture as compared to the solid state. For example, in solution, the fluoride anion bound to the calix[4]pyrrole moiety also forms a direct hydrogen bond with the strap pyrrolic NH. In contrast, in the solid state, the hydrogen bonding interactions between the fluoride anion and the pyrrolic NH proton on the strap were found mediated by a methanol bridge. The present work thus serves to highlight the potential utility of modified calix[4]pyrroles for ion pair recognition while calling attention to the benefits of carrying out both solution phase and solid state analyses, rather than assuming that the binding mode seen under one condition will translate to another.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgment.

This work was supported by the Basic Science Research Program (2017R1A4A1014595 to S.K.K.) funded by the National Research Foundation (NRF) under the Ministry of Science, ICT & Future Planning of Korea. The work in Austin was supported by the U.S. National Institutes of Health (grant GM103790A to J.L.S.) and the Robert A. Welch Foundation (F-0018 to J.L.S.).

References

1. Smith BD *Macrocyclic Chemistry: Current Trends and Future Prospectives In Ion-pair Recognition by Ditopic Receptors*; Gloe K, Antonioli B, Eds.; Kluwer: London, U.K., 2005; pp 137–152.
2. Kim SK; Sessler JL *Chem. Soc. Rev* 2010, 39, 3784–3809, and references cited therein. [PubMed: 20737073]
3. McConnell AJ; Beer PD *Angew. Chem., Int. Ed* 2012, 51, 5052–5061.
4. Kim SK; Sessler JL *Acc. Chem. Res* 2014, 47, 2525–2536 and references therein. [PubMed: 24977935]
5. Ciardi M; Galán A; Ballester PJ *Am. Chem. Soc* 2015, 137, 2047–2055.
6. Qiao B; Sengupta A; Liu Y; McDonald KP; Pink M; Anderson JR; Raghavachari K; Flood AH J. *Am. Chem. Soc* 2015, 137, 9746–9757. [PubMed: 26207611]
7. He Q; Zhang Z; Brewster JT; Lynch VM; Kim SK; Sessler JL J. *Am. Chem. Soc* 2016, 138, 9779–9782. [PubMed: 27442768]
8. He Q; Williams NJ; Oh JH; Lynch VM; Kim SK; Moyer BA.; Sessler JL *Angew. Chem., Int. Ed* 2018, 57, 11924–11928.
9. Gale PA; Sessler JL; Král V. *Chem. Commun* 1998, 1–8.
10. Lee C-H; Miyaji H; Yoon D-W; Sessler JL *Chem. Commun* 2008, 24–34 and references therein.
11. Gale PA; Sessler JL; Král V; Lynch VJ *Am. Chem. Soc* 1996, 118, 5140–5141.
12. Custelcean R; Delmau LH; Moyer BA; Sessler JL; Cho W-S; Gross D; Bates GW; Brooks SJ; Light ME; Gale PA *Angew. Chem., Int. Ed* 2005, 44, 2537–2542.
13. Tong CC; Quesada R; Sessler JL; Gale PA *Chem. Commun* 2008, 6321–6323.
14. Gale PA *Acc. Chem. Res* 2012, 44, 216–226.
15. Wintergerst MP; Levitskaia TG; Moyer BA; Sessler JL; Delmau LH J. *Am. Chem. Soc* 2008, 130, 4129–4139. [PubMed: 18311976]
16. Yeon Y; Leem S; Wagen C; Lynch VM; Kim SK; Sessler JL *Org. Lett* 2016, 18, 4396–4399. [PubMed: 27533478]
17. Yoon D-W; Gross DE; Lynch VM; Sessler JL; Hay BP; Lee C-H *Angew. Chem., Int. Ed* 2008, 47, 5038–5042.
18. Gross DE; Yoon D-W; Lynch VM; Lee C-H; Sessler JL J. *Incl. Phenom. Macrocycl. Chem* 2010, 66, 81–85. [PubMed: 21218134]
19. The data for the resulting crystals of the CsCl complex are poor. The data were merged from 3551 individual reflections to provide 3012 unique reflections. The Rmerge was a poor 25.9%. The Cl-complex is isostructural with the azide complex reported in the J. Org. Chem 2018, 83, 2686–2693.
20. Sato W; Miyaji H; Sessler JL *Tetrahedron Lett* 2000, 41, 6731–6736.
21. Approximate binding constant from: Connors, K, A. *Binding Constants: The Measurement of Molecular Complex Stability*; Wiley-Interscience: New York, 1987.
22. Kim SK; Gross DE; Cho D-G; Lynch VM; Sessler JL J. *Org. Chem* 2011, 76, 1005–1012. [PubMed: 21141913]

Figure 1.

Top: Two different views of the single crystal X-ray diffraction structure of $2 \cdot \text{CsF} \cdot \text{CH}_3\text{OH}$.

Bottom: 2-Dimensional cross linking coordination polymer network seen in the crystal lattice of $2 \cdot \text{CsF} \cdot (\text{CH}_3\text{OH})_2$. Displacement ellipsoids are scaled to the 50% probability level.

Figure 2.

Top: Two different views of the single crystal X-ray diffraction structure of **2**•CsCl. Bottom: Partial view of the extended structure seen in the crystal lattice. Displacement ellipsoids are scaled to the 30% probability level.

Figure 3.

Top: Two different views of the single crystal X-ray diffraction structure of **2**•CsBr. Bottom: Partial view of the extended structure seen in the crystal lattice. Displacement ellipsoids are scaled to the 50% probability level.

Figure 4.

Top: Two different views of the single crystal X-ray diffraction structure of $2 \cdot (\text{H}_2\text{O})_3$.
Bottom: Partial view of the extended structure seen in the crystal lattice. Displacement ellipsoids are scaled to the 50% probability level.

Figure 5. Partial ^1H NMR spectra of (a) **2** only and (b) **2** with 10 equiv of CsF in $\text{CH}_3\text{OH}/\text{CDCl}_3$ (1:4, v/v). * Denotes a residual NMR solvent peak.

Figure 6. Partial ¹H NMR spectra recorded during the titration of receptor **2** with CsF in CD₃OD/CDCl₃ (1/4, v/v). * Denotes a residual NMR solvent peak.

Figure 7. Proton NMR spectra of **2** recorded at room temperature in CDCl₃ (a) before, and (b) 10 minutes and (c) 60 minutes after the addition of CsF followed by sonication. *Denotes a residual NMR solvent peak.