Organic Letters

3-(Dicyanomethylidene)indan-1-one-Functionalized Calix[4]arene−Calix[4]pyrrole Hybrid: An Ion-Pair Sensor for Cesium Salts

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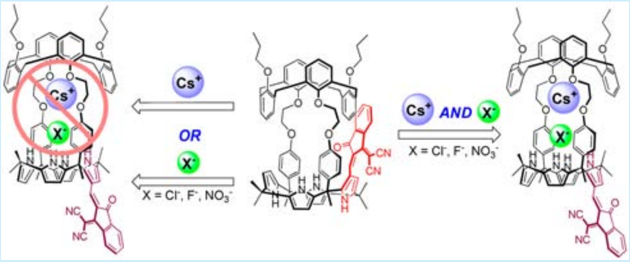
Ⓢ *Supporting Information*

ABSTRACT: A chromogenic calix[4]arene−calix[4]pyrrole hybrid ion pair receptor bearing an indane substituent at a *β*-pyrrolic position has been prepared. On the basis of solution-phase UV−vis spectroscopic analysis and ^1H NMR spectroscopic studies carried out in 10% methanol in chloroform, receptor **1** is able to bind only cesium ion pairs (e.g., CsF, CsCl, and $CsNO_3$) but not the constituent cesium cation (as its perchlorate salt) or the F^-, Cl^-, or NO_3^- anions (as the tetrabutylammonium salts). It thus displays rudimentary AND logic gate behavior. Receptor **1** shows a colorimetric response to cesium ion pairs under conditions of solid−liquid (nitrobenzene) and liquid−liquid (D_2O−nitrobenzene-d_5) extraction.



The detection and remediation of radioactive materials are topical areas of research whose importance is underscored by current events, such as the 2011 Daiichi nuclear disaster. Of the isotopes released during the associated reactor breach, ^{137}Cs (half-life, 30.2 years), produced during the nuclear fission of uranium-235, is particularly insidious. This isotope of cesium is able to replace potassium in muscles and red blood cells and, after ingestion, typically spreads out throughout the body. As a result, there is a critical need for chemosensors that can be used to detect the cesium cation with high selectivity relative to other metal cations, particular Na^+ as found in seawater.[1,2] Here, we report a modified calix[4]pyrrole−calix[4]arene hybrid that acts as a chemosensor for cesium-containing ion pairs. It functions both in organic solution and under conditions of solid−liquid and aqueous−organic extraction.

In recent years, Sessler and co-workers reported several hybrid ion-pair receptors containing both calix[4]arene and calix[4]pyrrole subunits.[3] These systems are attractive as ion-pair receptors. In general, ion-pair receptors display significantly enhanced binding affinities for specific ions as compared with simple ion receptors.[4] This improvement, which often translates to increased selectivity, can generally be rationalized in terms of favorable electrostatic interactions between cobound ions. To date, considerable success has been encountered using a calix[4]arene−calix[4]pyrrole hybrid system for cesium salt recognition. Unfortunately, the systems studied to date lack well-defined optical absorbance or emission features that could be used to monitor the binding events via color or fluorescence changes. While several chromophore- and fluorophore-containing motifs are known that respond to the cesium cation,[5] to the best of our knowledge, chromogenic or colorimetric chemical sensors capable of recognizing cesium-containing ion pairs are still lacking. An ability to sense cesium ion pairs could, however, offer potential benefits under conditions of actual use where the counteranion is likely to play a critical role in determining the chemical form of the species involved. To address this need, we have appended a chromogenic subunit to a previously studied, cesium salt-selective calix[4]arene−calix[4]pyrrole hybrid system to produce the colorimetric sensor **1**. As detailed below, this new system responds to cesium ion pairs under several limiting conditions.

System **1** relies on a merocyanine-type donor−*π*−acceptor (D−*π*−A), specifically a 3-(dicyanomethylidene)indan-1-one subunit. This class of chromophores is frequently used to create pull−push systems with useful spectral properties.[6,7] It was appended to a *β*-formylated calix[4]pyrrole in analogy to what was done previously by Anzenbacher and co-workers to produce calix[4]pyrrole based anion sensors.[8] Exposure to a cesium ion-pair source induces a conformational change in **1** and results in a modest, but detectable, change in color.

The synthesis of receptor **1** is shown in Scheme 1. It starts with the calix[4]arene−calix[4]pyrrole **2**, which was synthesized using known procedures.[3] Vilsmeier−Hack formylation then gave **3**.[9] Although two *β*-monoformylated regioisomeric products might be expected from this reaction,[10] in fact, it was regioisomer **3**, involving formylation at the more hindered *β*-position, that proved dominant. Reaction of **3** with 3-(dicyanomethylidene)indan-1-one in a 1:1 mixture of THF

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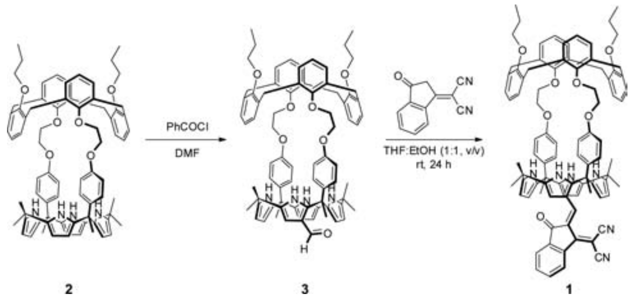
Scheme 1. Synthesis of Chromogenic Receptor 1



and EtOH (v/v) at room temperature for 24 h in the absence of an added base then gave target **1** in high yield. Receptor **1** was fully characterized by standard spectroscopic means as well as by single-crystal X-ray diffraction analysis (CCDC 1440484) (Figure 1).

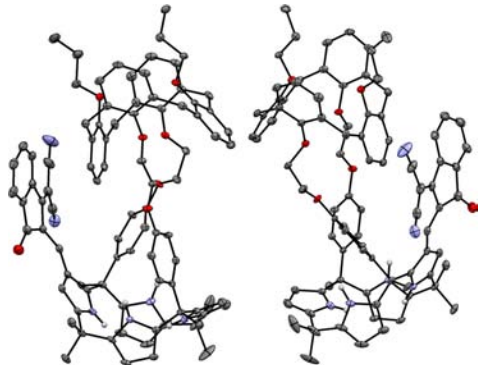


Figure 1. Two different views of the single-crystal X-ray diffraction structure of **1**. Thermal ellipsoids are scaled to the 30% probability level. Solvent molecules and most hydrogen atoms have been omitted for clarity.

On the basis of prior studies,[3] it was anticipated that receptor **1** would possess structural features that would favor the binding of cesium ion pairs but not those of closely related cations, including Rb^+. On this basis, it was expected that the Cs^+ cations would be bound to the ethylene glycol moieties between the calix[4]pyrrole and calix[4]arene subunits. Likewise, it was anticipated that the counteranions, if appropriately sized, would be bound by the calix[4]pyrrole unit. These proposed interactions were expected to give rise to a change in the calix[4]pyrrole conformation and a partial change in the electronic overlap with the dicyanoindaneone chromophore unit. The net result would be a readily detectable color change.

The ability of receptor **1** to act as a cesium selective ion-pair receptor was investigated using various cesium and tetrabutylammonium (TBA^+) salts via UV−vis spectroscopic and ^1H NMR spectroscopic analyses. In fact, discernible spectral changes were seen for **1** upon exposure to CsF, CsCl, and $CsNO_3$ in mixed organic media (10% CH_3OH in $CHCl_3$; Figure 2). These color changes proved anion dependent. In analogy to what is true for receptor **2** (studied previously), receptor **1** lacks a strong cation recognition site (e.g., a crown ether subunit). As a result, it fails to interact with individual ions, such as Cs^+, F^-, or Cl^-, when exposed to these ions in the form of noncoordinating salts (e.g., ClO_4^- for Cs^+ and TBA^+ for F^- and Cl^-, respectively). Thus, only slight changes in the absorbance intensity and no appreciable shift in the absorption maximum were observed in the UV−vis absorption spectrum when these salts were added to organic solutions of **1** in 10% CH_3OH in $CHCl_3$ (Figure 2A).

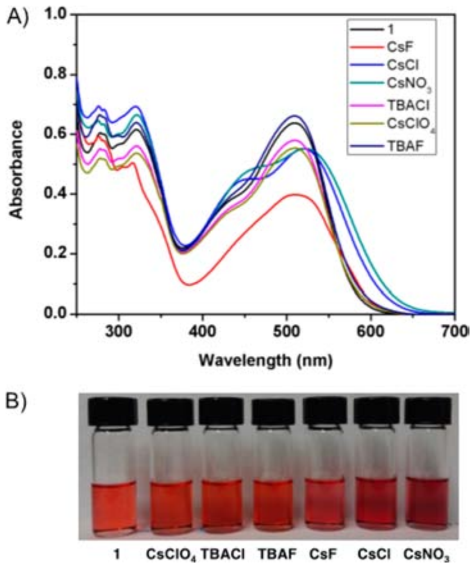


Figure 2. (A) UV−vis absorption spectra of receptor **1** (50 μM) in MeOH/$CHCl_3$ (1/9, v/v) recorded in the absence and presence of 5 equiv of various salts. (B) Solutions of receptor **1** (50 μM) in MeOH/$CHCl_3$ (1/9, v/v) photographed in the absence and presence of 5 equiv of the indicated ion pairs.

Support for the above findings came from ^1H NMR spectroscopic studies. In contrast to what is seen with $CsClO_4$, TBAF, and TBACl, the addition of CsF, CsCl, and $CsNO_3$ to a solution of receptor **1** in 10% CD_3OD in $CDCl_3$ (v/v) caused significant chemical shift changes in the ^1H NMR spectrum of **1** (Figure S1). After exposure to these latter salts, the proton signal of the allylic proton shifts to lower field, with the degree of this shift being dependent on the cesium salts in question. The pyrrolic NH proton signals were also found to shift to lower field in the case of the coordinating cesium salts. On this basis, it is inferred that CsF, CsCl, and $CsNO_3$ form ion-pair complexes with receptor **1**.

No evidence of substantial shifts is seen unless both a strongly coordinating cation (i.e., Cs^+ rather than TBA^+) and anion (e.g., F^-, Cl^-, or NO_3^-) are present. This effect was studied further using CsF and its constituent ions. It was found that neither TBAF (poorly coordination cation; strongly binding anion) nor $CsClO_4$ (strongly binding cation; weakly binding anion), when added individually, gives rise to appreciable changes in the ^1H NMR or UV−vis spectra of **1** in 10% methanol−chloroform solution. However, when mixed together with **1**, spectral features are seen that are very similar to those produced upon the addition of CsF to solutions of **1** (Figure S2). On this basis, we propose that this system functions as a rudimentary AND logic device as shown in Figure 3. A response is only seen if there is a source of both Cs^+ cations and F^- anions.

Further evidence that receptor **1** forms strong complexes with Cs^+ salts came from UV−vis spectroscopic titrations carried out with CsF in 10% CH_3OH in $CHCl_3$. Several binding models were tested, and it was found that the data could be fit to a 1:1 binding profile to give a K_a value of 1.1×10^4 M^{-1}, although relatively large residuals were seen (Figure S3). Unfortunately, binding constants corresponding to the

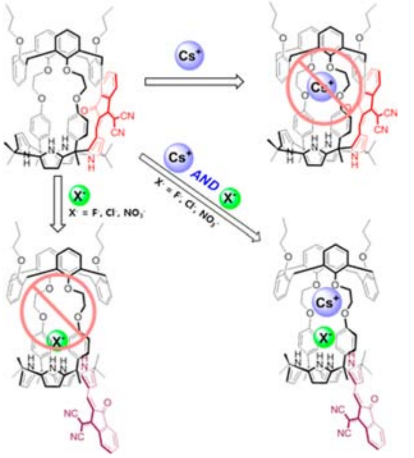


Figure 3. Proposed AND logic gate behavior displayed by the ion pair receptor **1** when exposed to different cesium salts in 10% CD_3OD–$CDCl_3$.

interaction of **1** for CsCl and $CsNO_3$ could not be determined by UV–vis or ^1H NMR spectroscopic titration methods because of the poor solubility of these salts in 10% CH_3OH in $CHCl_3$ or other readily accessible solvent systems.

In order to test the cesium ion selectivity of receptor **1**, it was exposed to other alkali metal chloride anion salts in this solvent system (i.e., 10% CH_3OH in $CHCl_3$). The resulting UV–vis spectra revealed greater changes in the absorption features of **1** in the case of CsCl as compared to the other alkali metal salts (Figure 4). These findings lead us to suggest that receptor **1** binds the cesium chloride ion pair with high selectivity over other alkali metal chloride anion salts.

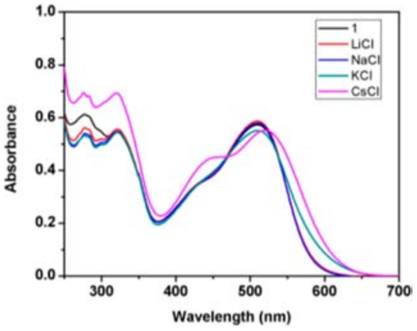


Figure 4. UV–vis absorption spectra of receptor **1** (50 μM) in MeOH/$CHCl_3$ (1/9, v/v) recorded in the absence and 5 equiv of various solid salts, namely LiCl, NaCl, KCl, and CsCl. The spectra were recorded after subjecting to sonication for 30 min.

The maximum absorption (λ_{max}) of ion-free receptor **1** appears around 520 nm. In the presence of 5 equiv of LiCl, NaCl, or KCl, no discernible change in the λ_{max} of **1** is seen. This finding is taken as evidence of a relatively weak interaction between receptor **1** and these three ion pair salts. In contrast, exposure to CsCl causes the absorption band at 520 nm to be split into two bands with λ_{max} at 440 and 540 nm, respectively. This spectral change is fully consistent with the suggestion made above, namely, that the chloride anion is bound to the calix[4]pyrrole unit while the cesium cation is concurrently bound to the ethylene glycol subunits.

The high selectively of **1** for CsCl inferred from the UV–vis spectral studies is also supported by ^1H NMR spectroscopic analyses carried out in 10% CD_3OD in $CDCl_3$ (Figure S4). For instance, upon exposure to CsCl, the vinyl proton resonance shifted from 8.7 to 9.0 ppm. In addition, the β-proton signals of pyrroles undergo upfield shifts, while those of pyrrolic NHs were shifted to lower field, presumably as a result of hydrogen-bonding interactions between the chloride anion and the pyrrolic NHs. In contrast, the aromatic proton signals of the calix[4]arene subunit undergo a downfield shift. This finding is attributable to complexation of the cesium cation by the calix[4]arene moiety.[3] In contrast, when LiCl or NaCl was added to the original solution of receptor **1**, no discernible shifts were observed. The addition of KCl to solutions **1** in 10% CD_3OD in $CDCl_3$ at stoichiometric ratios where CsCl was inferred to be fully bound gives rise to relatively minor changes in the ^1H NMR spectrum. This provides support for the contention that this ion pair is weakly bound.

The ability of receptor **1** to recognize the alkali cation salts in solid form was probed by monitoring the changes (if any) in the optical features of nitrobenzene solutions of this proposed colorimetric sensor as well as by following the chemical shift changes in the associated ^1H NMR spectra (Figures 5 and S5).

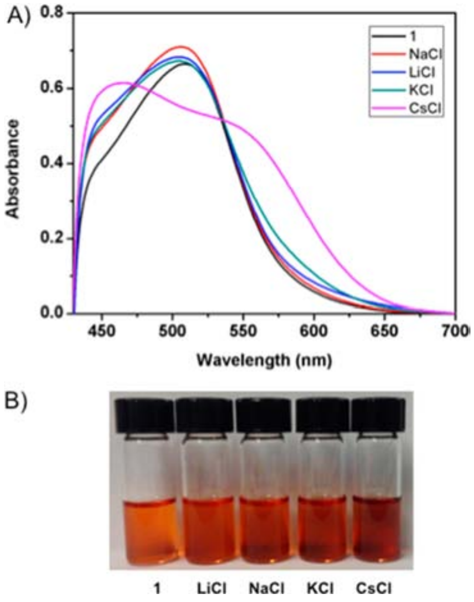


Figure 5. (A) UV–vis absorption spectra of receptor **1** (50 μM) in nitrobenzene, as obtained in the absence and presence of LiCl, NaCl, KCl, and CsCl added in excess in solid form. (B) Solutions of receptor **1** (50 μM) in nitrobenzene, photographed in the absence and presence of 5 equiv of alkali metal salts.

The experiments involved contacting nitrobenzene solutions of **1** with various solid alkali metal salts, including LiCl, KCl, NaCl, and CsCl. With CsCl, noteworthy spectral changes in both the UV–vis and ^1H NMR spectra are seen, with this effect being selective for CsCl as compared to the other alkali salts under these solid–liquid extraction conditions (Figure 5).

The ability of the indanone-functionalized hybrid system **1** to function as a selective receptor for cesium salts was also tested under liquid–liquid extraction conditions. These studies were carried out by contacting a nitrobenzene-d_5 ($C_6D_5NO_2$) solution of **1** with aqueous (D_2O) solutions containing various cesium salts, including CsF, CsCl, CsBr, $CsNO_3$, and $CsClO_4$. When receptor **1** in nitrobenzene-d_5 was contacted with an aqueous $CsNO_3$ solution, significant changes were seen in the color of the organic phase (Figure 6) as well as the ^{1}H NMR spectrum of the organic phase containing receptor **1** (cf. Figure S6). We thus infer that receptor **1** is able to extract $CsNO_3$ from an aqueous layer into the nitrobenzene phase.

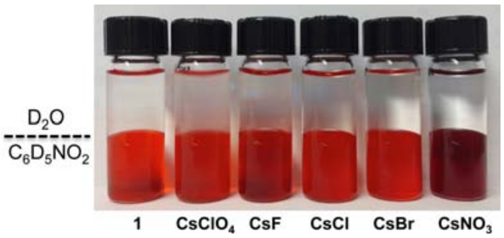


Figure 6. Photographs of solutions of **1** (30 mM) in nitrobenzene-d_5 photographed after contact with 5 equiv of various cesium salts, namely CsF, CsCl, CsBr, $CsNO_3$, and $CsClO_4$, contained in an aqueous (D_2O) layer. A salt-free control is also shown.

Related ^{1}H NMR spectral studies served to reveal that receptor **1** can also extract other cesium salts, in particular, CsF, CsCl, and CsBr, albeit with relatively low efficiencies compared to $CsNO_3$. No spectral change was observed when the nitrobenzene solution of **1** was contacted with cesium cation salts containing noncoordinating counteranions, such as ClO_4^-. In aggregate, these findings support the conclusion that receptor **1** is capable of functioning as an extractant as well as a colorimetric sensor for cesium salts dissolved in water.

In summary, a chromogenic ion-pair sensor **1** for cesium ion pairs was successfully synthesized via the condensation of a formyl functionalized calix[4]arene−calix[4]pyrrole pseudodimer with 3-(dicyanomethylidene)indan-1-one. UV−vis and ^{1}H NMR spectroscopic analyses provided support for the conclusion that receptor **1** has the ability to bind, extract, and detect cesium ion salts with high selectivity relative to other simple salts and to do so under a variety of conditions. For example, in 10% methanol−chloroform (1/9, v/v), noticeable color changes were seen upon exposure to various cesium salts, including CsF, CsCl, and $CsNO_3$. Changes in the corresponding ^{1}H NMR spectra were also seen. Control studies revealed that receptor **1** does not recognize effectively either $CsClO_4$ or simple TBA^+ anion salts (i.e., those of Cl^- and F^-). The solution-phase binding selectivity of receptor **1** thus mimics that of an AND logic gate. Receptor **1** was found to be capable of acting as a colorimetric ion-pair sensor under conditions of solid−liquid extraction. It was also effective in extracting certain Cs^+ salts, notably $CsNO_3$, from an aqueous source phase into nitrobenzene. This extraction may be followed by the naked eye.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b02155.

X-ray data for compound **1** (CIF)
Synthesis details, NMR spectroscopic data, and X-ray structural data for **1** (PDF)

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Notes

The authors declare no competing financial interest.

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