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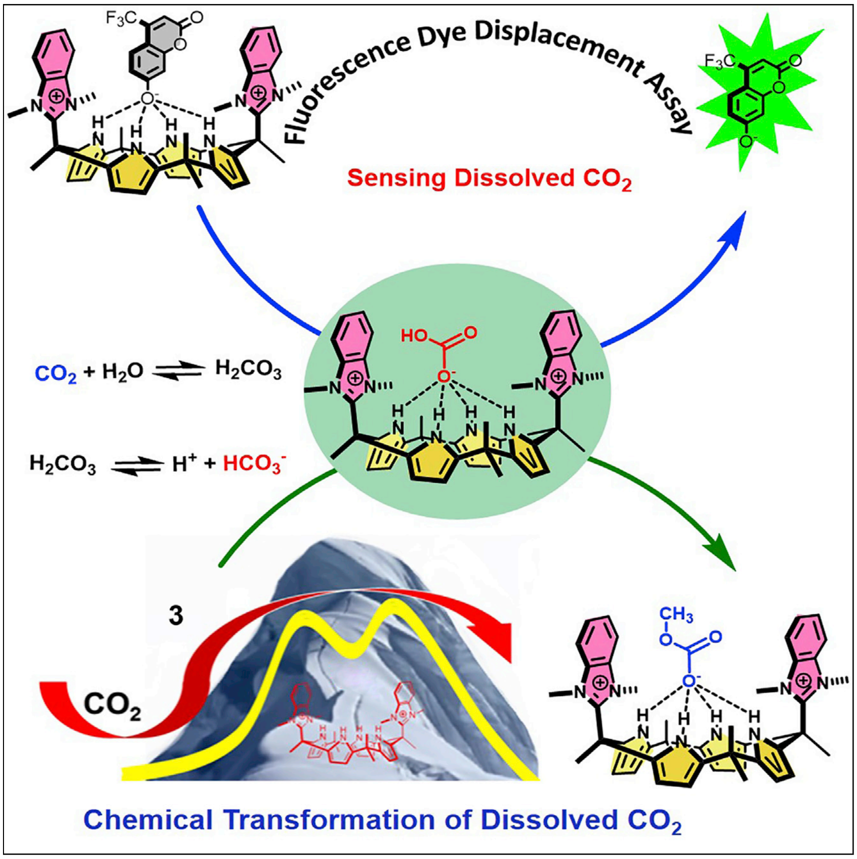
Recognition, Sensing, and Trapping of Bicarbonate Anions with a Dicationic *meso*-bis(Benzimidazolium) Calix[4]pyrrole



A synthetic dicationic *meso*-bis(benzimidazolium) calix[4]pyrrole permits the sensing and chemical capture of CO_2 in its hydrated forms.

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HIGHLIGHTS

A dicationic receptor for sensing and capturing hydrated CO_2 was prepared

The sensor can sense HCO_3^- (≥4 nM) and detect dissolved CO_2 in carbonated beverages

The receptors can transform hydrated CO_2 into normally unstable alkyl carbonate esters

3 GOOD HEALTH AND WELL-BEING

13 CLIMATE ACTION

Mulugeta et al., Chem *3*, 1–13
December 14, 2017 © 2017 Elsevier Inc.
https://doi.org/10.1016/j.chempr.2017.10.007

Please cite this article in press as: Mulugeta et al., Recognition, Sensing, and Trapping of Bicarbonate Anions with a Dicationic *meso*-bis(Benzimidazolium) Calix[4]pyrrole, Chem (2017), https://doi.org/10.1016/j.chempr.2017.10.007

Article

Recognition, Sensing, and Trapping of Bicarbonate Anions with a Dicationic *meso*-bis(Benzimidazolium) Calix[4]pyrrole

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SUMMARY

A *meso*-aryl calix[4]pyrrole derivative bearing benzimidazolium groups at the two diametrical *meso* positions was synthesized. The receptor acts as an effective host for the bicarbonate anion at concentrations as low as 4 nM. A change in fluorescence response was observed under conditions of fluorescence dye displacement when this functionalized calix[4]pyrrole was exposed to the HCO_3^- anion. Tests with various carbonated drinks revealed its ability to function as an easy-to-use sensor for dissolved CO_2, as monitored through the bicarbonate anion concentration. Depending on the specific choice of conditions, recrystallization of the calix[4]pyrrole receptor in the presence of Cs_2CO_3 and methanol yielded crystals of either the HCO_3^- anion complex or methyl carbonate ($CH_3OCO_2^-$), a normally difficult-to-access species whose formation under non-forcing equilibrium conditions is ascribed to trapping by the calix[4]pyrrole receptor. The present system thus provides a recognition-based approach to the chemical capture of hydrated, anionic forms of CO_2.

INTRODUCTION

Physiological acid-base homeostasis is essential to maintaining both intracellular and extracellular pH.[1–4] It is a key feature of healthy life and is predicated on a controlled equilibrium between carbon dioxide (CO_2), carbonic acid (H_2CO_3), and bicarbonate ions (HCO_3^-). Variations in any of these three species typically result in changes in the concentrations of the other two. Thus, HCO_3^- can function to trap excess CO_2 in a dissolved form within cells, and expired CO_2 can serve as a means to remove H_2CO_3 and HCO_3^- from an organism. Deviations in the levels of carbon dioxide and its hydrated forms, including blood pH, are classic indicators of metabolic distress and respirational disorders. Alterations in the HCO_3^-/CO_2 ratio are also known to affect vesicle-mediated calcification, with the latter increasing as the ratio increases.[5] In addition, HCO_3^- acts as a cofactor in carboxylation reactions, aids in intracellular signal transduction, and helps maintain the ionic composition of gastrointestinal and small-intestinal luminal fluids.[6,7] The HCO_3^-/CO_2 balance also has serious implications in the environmental arena. Natural water resources often serve as sinks for atmospheric CO_2, solubilizing it in the form of HCO_3^- and lowering the pH.[8–10] Regulation of dissolved CO_2 is indispensable for optimal aquatic life and ultimately critical to conservation efforts involving both flora and fauna.[11,12] Separate from its physiological and environmental importance, CO_2 has a time-honored role in the food and beverage industry, being a mainstay of carbonated drinks as well as a potential indicator of food spoilage.[13]

The Bigger Picture

CO_2 is intimately associated with life, both as a building block for carbohydrate synthesis and as the end product of aerobic respiration. It is also key to maintaining the pH of waterways and remains a topic of intense ongoing debate involving climate change. The central nature of CO_2 in the chemical world and beyond provides an incentive to develop easy-to-use "tools" to capture, sense, and chemically "fix" CO_2 and its hydrated forms (e.g., HCO_3^-). Here, we report a dicationic *meso*-bis(benzimidazolium) calix[4]pyrrole that works to capture CO_2 by modulating the HCO_3^-/CO_2 balance (including in carbonated beverages) and acts as a HCO_3^- sensor (at concentrations as low as 4 nM) under solution-phase indicator displacement assay conditions. It also promotes the conversion of hydrated CO_2 into methyl carbonate ($CH_3OCO_2^-$) under near-neutral conditions by stabilizing this normally unstable mono-ester species in bound form. The chemistry appears generalizable to other related host systems.

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The ubiquity and importance of CO_2 provides an incentive to develop methods to detect, capture, and activate chemically its hydrated forms, including the bicarbonate anion. In addition to carbonic anhydrase, long recognized for its role in removing dissolved CO_2 under conditions of respiration,[14] mammals have multiple sensory systems that allow them to detect CO_2-related species. For instance, it is now appreciated that soluble adenylyl cyclase (sAC) plays a major role in terms of monitoring physiological pH via HCO_3^- sensing.[15] sAC is directly stimulated by the bicarbonate anion and is linked with carbonic anhydrase activity.[16] Under laboratory conditions, a wide variety of techniques are available to monitor HCO_3^-/CO_2 concentrations, including chromatography,[17] near-IR/IR spectrometry,[18] potentiometry,[19,20] and coulometry.[21] Nevertheless, potential benefits, including ease of use and economy, could accrue from the development of molecular receptors that enable effective "on-site" visual analyses of dissolved CO_2 and the bicarbonate anion. Equally important would be the development of systems that allow the cost-effective capture of either CO_2 or bicarbonate and their transformation to other carbon-containing products. Recently, important progress toward achieving these individual goals has been made on the basis of supramolecular or receptor-based approaches.[22–29] However, there remains a need for a simple receptor that permits the combined capture, sensing, and chemical transformation of CO_2 and its hydrated forms. Here, we report a *meso*-bis(benzimidazolium) calix[4]pyrrole. This dicationic receptor acts as a bicarbonate anion sensor under solution-phase indicator displacement assay conditions and promotes the conversion of the bicarbonate anion (produced from Cs_2CO_3 in the presence of methanol) into methyl carbonate ($CH_3OCO_2^-$) by stabilizing the resulting anionic product in bound form. Similar transformations to the mono-alkyl esters of carbonate were observed in the case of a non-charged strapped calix[4]pyrrole under near-neutral pH conditions. The trapped mono-ester products were observed in solution and structurally characterized in the solid state. The ability to promote the formation of normally unstable carbonate esters from hydrated forms of CO_2 (e.g., HCO_3^- or CO_3^{2-}) under near-neutral, equilibrium conditions could in due course provide an attractive alternative to direct CO_2 sequestration and functionalization strategies.

RESULTS AND DISCUSSION

Synthesis and Characterization

Calix[4]pyrroles are versatile macrocyclic hosts frequently used for anion recognition,[30,31] especially for the halide ions. Structural modifications to the basic tetrapyrrolic core have been used extensively as a means of modulating the inherent substrate selectivities of calix[4]pyrroles.[32–35] In the context of this latter effort, we sought to prepare a dicationic system that might display relatively enhanced anion affinities. This led to the design of calix[4]pyrrole **3**. This "two-walled" calix[4]pyrrole bears cationic benzimidazolium moieties at the diametrically opposed *meso* positions and, as detailed below, displays high selectivity for the bicarbonate anion. Receptor **3** was synthesized as the iodide-bound, hexafluorophosphate salt in good yield by methylation of the parent *cis*-calix[4]pyrrole **2** followed by anion exchange (Scheme 1). The intermediate calix[4]pyrrole **2** was itself obtained as a mixture of *cis* and *trans* isomers via the [2 + 2] condensation of the corresponding *meso*-benzimidazolyl dipyrromethane **1** under conditions of acid catalysis. The two isomers of **2** were separated by column chromatography and the desired *cis* isomer was collected. The requisite *meso*-benzimidazolyl dipyrromethane **1** was prepared, in turn, from the acid-catalyzed condensation of 2-acetyl benzimidazole with pyrrole. All new compounds were characterized by standard

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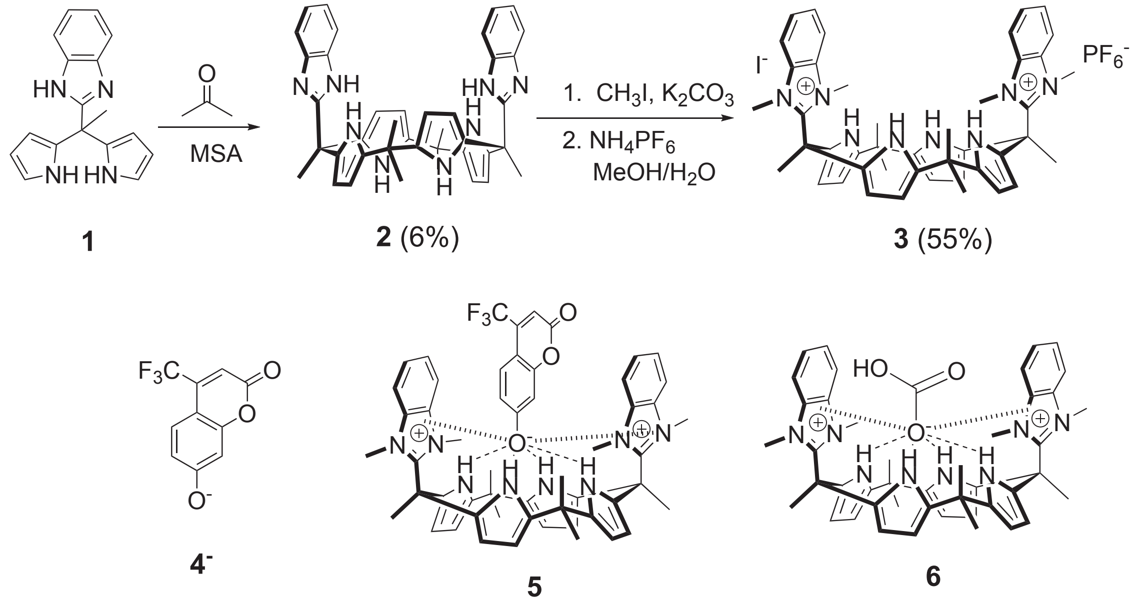
https://doi.org/10.1016/j.chempr.2017.10.007



Scheme 1. Synthesis of the Dicationic Calix[4]pyrrole 3 from Precursors 1 and 2

Also shown are the chromenolate anion 4^-, its complex with **3** (shown as **5**), and the bicarbonate anion complex of **3** (shown as **6**).

spectroscopic and analytical methods (see Figures S1–S11 and Schemes S1 and S2).

A diffraction-grade single crystal of the mixed iodide PF_6^- complex of receptor **3** was obtained via slow evaporation of a solution of **3** in acetonitrile/methanol. The structure revealed that the receptor **3** adopts a cone-like conformation with the bound iodide anion stabilized by four hydrogen-bonding interactions involving the pyrrolic NH protons (Figure 1). The receptor-bound I^- to H–N nitrogen distances range from 3.60 to 3.62 Å. The distance between the complexed iodide anion and the center of the imidazolium ''walls'' varies from 3.78 to 3.80 Å. The two benzimidazolium moieties are not completely parallel to one another. The one adjacent to PF_6^- is tilted significantly in comparison with that opposing the benzimidazolium group. Presumably, this reflects an electrostatic effect of the counter anion.

Fluorescence Dye Displacement Assay

We have previously reported that modified calix[4]pyrroles can function as sensors for simple anions by exploiting the so-called fluorescence dye displacement assay (FDDA) technique.[36,37] Using this approach, and exploiting the chromenolate anion (**4**$^-$) as a fluorescent probe, we were able to establish that receptor **3** displays a high absolute and relative affinity for the bicarbonate anion. As detailed further below, we found specifically that an FDDA sensor system consisting of **3** and **4**$^-$ displayed characteristic off-on-off behavior when first combined and then treated sequentially with HCO_3^- (as its tetraethylammonium salt) and Na^+ (as its perchlorate salt) in acetonitrile. A schematic representation of the sensing sequence is given in Scheme 2.

The initial off state results from quenching of the excited state emission of the normally highly fluorescent anion **4**$^-$ upon interacting with the calixpyrrole, as seen previously for related systems.[36–38] Specifically, as shown in Figure 2, quenching

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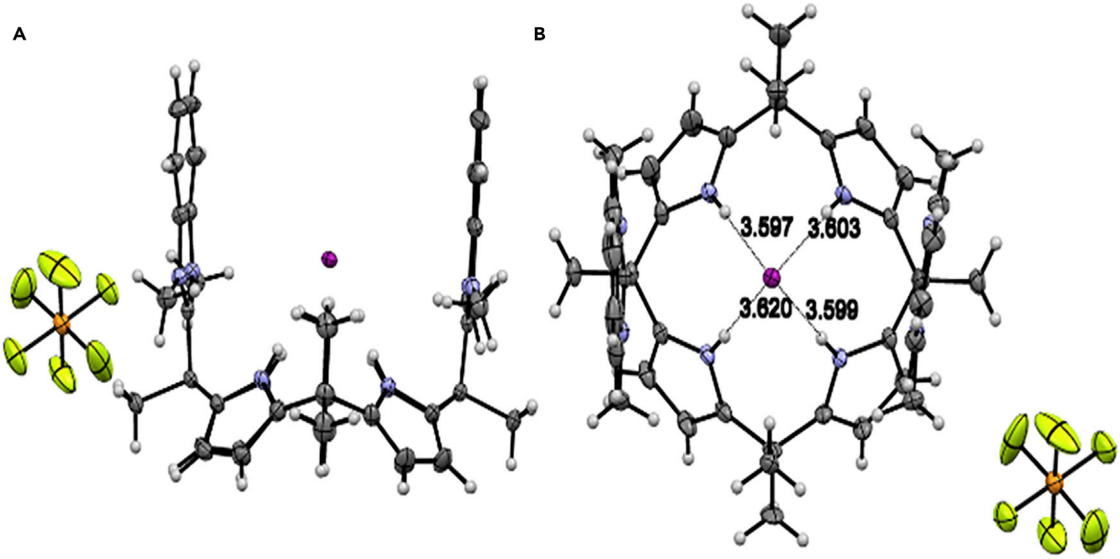


Figure 1. ORTEP Representation of the Mixed Iodide Hexafluorophosphate Complex of Receptor 3

(A) Front view as obtained from single-crystal X-ray analysis.

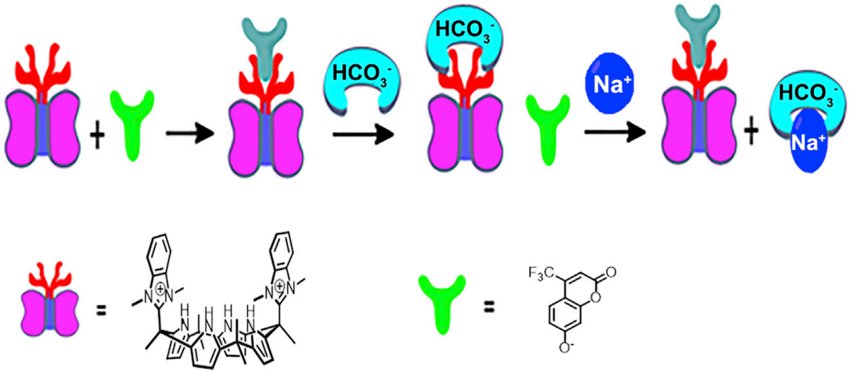
(B) Top view as obtained from single-crystal X-ray analysis. The selected pyrrolic N(H)…I$^-$ distances are 3.579, 3.603, 3.599, and 3.620 Å, respectively. MeCN and water molecules have been omitted for clarity. The displacement ellipsoids have been scaled to the 50% probability level.

in the fluorescence intensity of **4**$^-$ (2.0 μM) (λ_{max} = 501 nm) is seen upon titration with **3** (0–2.0 μM) in acetonitrile (λ_{ex} = 390 nm). The quenching was essentially complete after the addition of one molar equivalent of receptor **3**. Reasonable Stern-Volmer behavior was seen, which allowed a K_{SV} value of 1.0×10^7 M^{-1} to be calculated for the formation of the presumed 1:1 complex, **5**. Changes in the absorption spectrum were also observed upon formation of the putative chromenolate complex **5** (Figure S12). Specifically, a blue shift of the original absorption band of free **4**$^-$ from 436 to 376 nm upon complexation is seen. This is thought to reflect a reduction in intramolecular charge transfer (ICT) as the result of binding.

The proposed formation of complex **5** from **4**$^-$ and **3** was further substantiated via ^{1}H nuclear magnetic resonance (NMR) spectroscopic titration (Figure 3). As expected, the pyrrole NH protons experience a significant downfield shift. An upfield shift in the Ar–H proton signals of the benzimidazolium subunits and the *N*-methyl protons was also seen. These latter changes are consistent with the existence of stabilizing electrostatic effects as well as possible anion-π interactions. The β-pyrrolic protons signals were shifted to higher field as expected for the formation of a complex stabilized via anion-pyrrole NH hydrogen bonding.

Recognition, Sensing, and Trapping of Bicarbonate

Addition of HCO_3^- to the supramolecular ensemble **5** results in restoration of the initial fluorescence as a result of anion **4**$^-$ being competitively displaced from the binding pocket to give what is presumed to be the bicarbonate anion complex **6** and free **4**$^-$. Further evidence for the formation of complex **6** came from solid-state structural analyses (see below). Incremental addition of a solution of tetraethylammonium bicarbonate in acetonitrile to ensemble **5** gives rise to a steady increase in the fluorescence emission, with essentially full recovery of the original fluorescence of **4**$^-$ at 501 nm being observed upon the addition of one molar equivalent of HCO_3^- (Figure 4). A plot of HCO_3^- concentration versus the respective emission



Scheme 2. Graphical Representation of Bicarbonate Sensing by a “Turn-On” Mechanism and Subsequent Cation-Induced Displacement

enhancements at 501 nm revealed reasonable linearity through the nanomolar range. On this basis, the minimum detection limit for the bicarbonate indicator system consisting of **3** + **4**$^-$ was calculated to be approximately 4 nM (Figure 4, inset).

A UV-visible (UV-vis) spectral titration was also carried out. As above, the features characteristic of **4**$^-$, namely an absorption band at 436 nm, were restored upon the addition of HCO_3^- (Figure S13). To provide further support for the proposed displacement process, a CD_3CN solution of ensemble **5** was titrated with a CD_3CN solution of tetraethylammonium bicarbonate, and the ^1H NMR spectrum was recorded (Figure 3). As anticipated, the spectral changes paralleled those obtained when **3** was independently titrated with HCO_3^-. Signals corresponding to free **4**$^-$ were also seen. Hence, this experiment was taken as further confirmation that a bicarbonate complex is being formed under the conditions of the FDDA discussed above.

The final off portion of the off-on-off system was produced by treating complex **6** with Na^+ ions (as the perchlorate salt) in acetonitrile (Figure S23). This treatment leaches away the HCO_3^- anion in the form of its relatively tightly bound sodium salt thus restoring the non-fluorescent species **5**. This sodium cation-induced pseudo-reversibility is viewed as a particular advantage as it enables effective scavenging of the dissolved CO_2 by virtue of the formation of an electrostatically stabilized carbonate salt after initial binding. Importantly, it also serves to regenerate the sensor system for reuse.

The selectivity of the FDDA indicator system **5** was further probed by monitoring its preference for HCO_3^- in the presence of other anions (as their tetraalkylammonium salts), including ones of physiological importance or encountered routinely in the broader environment (Figure S24). No other anion elicited an appreciable fluorescent response when mixed with **5** in acetonitrile under conditions where HCO_3^- produced a substantial response. This latter response was maintained even in the presence of the other anions.

NMR spectral titrations of **3** with each of the possible competitive anions were carried out. No appreciable significant changes were observed under conditions where **4**$^-$ and HCO_3^- produced readily discernable shifts (Figures S17–S21). This differential binding bias in favor of bicarbonate was further corroborated by carrying out UV-vis spectral titrations wherein calix[4]pyrrole **3** was titrated

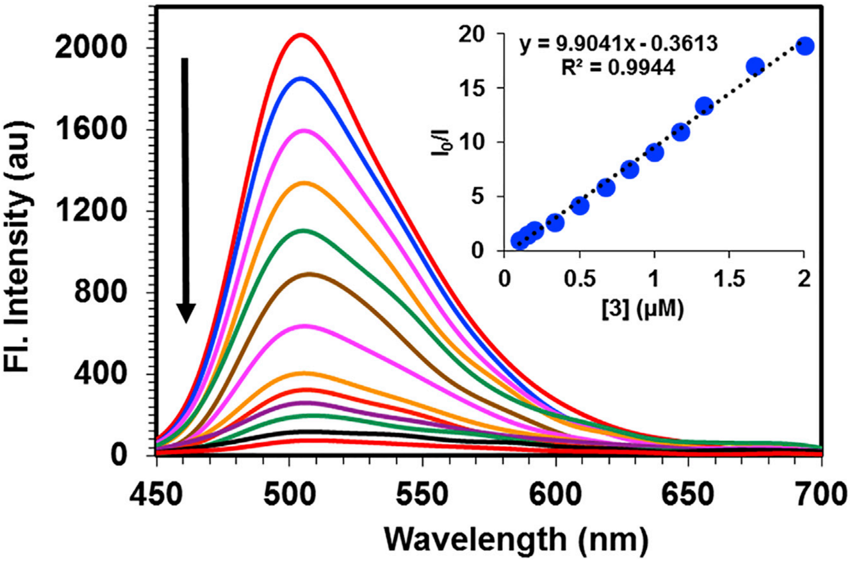


Figure 2. Changes in Fluorescence Intensity Seen upon Titration of 4^- (2.0 μM) with Receptor 3 (0–2.0 μM) in Acetonitrile (λ_{ex} = 390 nm)

Inset: Stern-Volmer plot. Relative intensities were calculated at 501 nm.

separately with **4**$^-$, HCO_3^-, and all other test anions. Fitting the data to a 1:1 binding model (Figure S25) allowed the corresponding binding constant values (K_a) to be calculated (Figures S26–S32); they are shown in Table S1. Inspection of Table S1 reveals that the dicationic receptor **3** shows the highest binding affinity for HCO_3^- among the various test anions, followed by **4**$^-$. In contrast, all other test anions gave rise to either relatively small K_a values or failed to produce detectable spectral changes. These quantitative findings are consistent with both the observed selectivity for bicarbonate and the finding that it can displace **4**$^-$ from **3**.

Given its selectivity, we felt that receptor **3**, in the form of ensemble **5**, would have a role to play as a "naked-eye" signaling probe for qualitative on-site monitoring of CO_2 and its hydrated anionic forms. As noted above, treatment of probe **5** with the bicarbonate anion gives rise to discrete color changes that are visible by the naked eye (Figure S33). To test the broader utility of ensemble **5**, it was analyzed for its ability to measure the CO_2 content in commercially available carbonated drinks, presumably through detection of equilibrated HCO_3^-.[39] Toward this end, different brands of soda were purchased commercially. Small samples were taken from each and diluted and tested with **5**, and the fluorescence recovery was determined. Considerable emission enhancements were observed in each case, as would be expected given the proposed binding with bicarbonate produced from dissolved CO_2. The emission data obtained were quantified and used to estimate the quantity of dissolved CO_2 present in each sample. This was done by use of a calibration curve constructed with known bicarbonate concentrations (Supplemental Information, Section S4; Figure S34 and Table S2). The values obtained (74, 134, and 209 mM for Sunkist, Coke, and Sprite, respectively) proved consistent with those given for the beverage in question on the internet (78, 140, and 220 mM for these three beverages, respectively).[40]

Recrystallizing receptor **3** in the presence of Cs_2CO_3 in $CH_2Cl_2/CH_3CN/MeOH$ (1:1:1, v/v/v) afforded a set of diffraction-grade single crystals. Structural analysis

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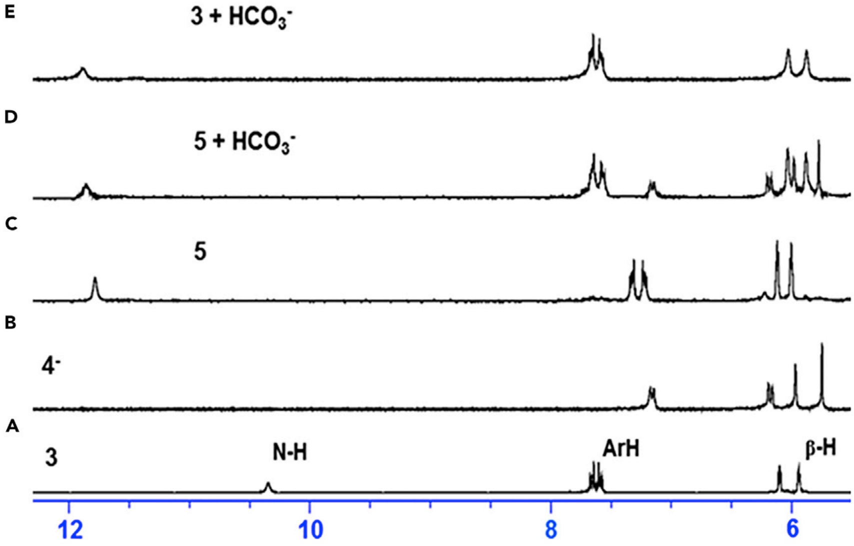

Figure 3. Partial ^{1}H NMR (300 MHz; CD_3CN) Spectra
(A) **3** only (4.1 mM).
(B) **4**$^-$ only (4.66 mM).
(C) **3** + **4**$^-$ = **5** (1:1 equiv).
(D) **5** + HCO_3^- (1:1.5 equiv as the tetraethylammonium salt).
(E) **3** + HCO_3^- (1:1.5 equiv).
The corresponding complete NMR spectra are given in the Figures S14–S16.

led to the tentative conclusion that, although the dataset was less than fully satisfactory, these crystals consist of a host-bicarbonate complex **6** in which the substrate and "walls" adopt a face-to-face geometry, as well as a host-methyl carbonate complex **7** (Figures 5A, 5B, and S35). In both structures, the calix[4]pyrroles adopt a cone-like conformation with the four pyrrole units. Presumably, under the conditions of recrystallization, protonation of the carbonate anion occurs to produce the bicarbonate anion that is trapped within receptor **3** (to produce complex **6**). The unexpected observation of methyl carbonate complex formation led us to perform further studies that would provide insights into the chemical fate of dissolved CO_2 in the presence of receptor **3**.

Promoting the Chemical Transformation of Dissolved CO_2

When recrystallization of **3** was carried out with Cs_2CO_3 in $CH_2Cl_2/CH_3CN/MeOH$ (10/1/10, v/v/v), single crystals were obtained. Although the resulting dataset was nonideal, refinement provided evidence for the presence of two methyl carbonate anion complexes within the crystals. These complexes differ in that the methyl carbonate anions are bound in different orientations (edge-to-face [ETF] versus face-to-face [FTF]) within the pockets of two separate molecules of host **3** (Figures 5C, 5D, and S36). In both structures, the calix[4]pyrrole unit adopts a cone-like conformation with the four pyrrole N–H protons involved in hydrogen bonding with only one oxygen atom of the methyl carbonate anion.

We carried out density functional theory (DFT) calculations to understand the energetic origins of the two crystal structures in greater detail, namely the complex with a perpendicular methyl carbonate (ETF) and the other complex with a parallel methyl carbonate (FTF). These two complexes were calculated to be energetically stable as discussed further below. The coordinates used for the single-point calculations were

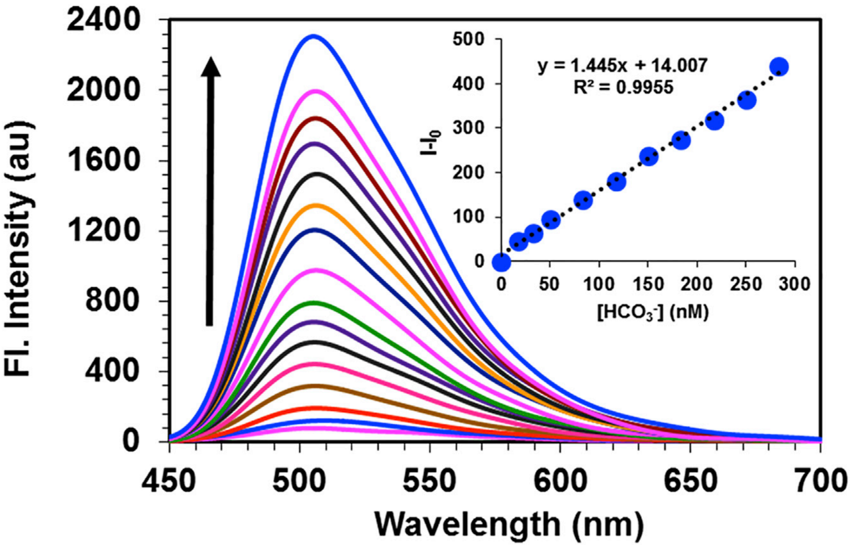

Figure 4. Restoration of Fluorescence Intensity Seen upon Titration of Receptor-Chromenolate Complex 5 with HCO_3^- (0–1.0 equiv) in Acetonitrile (λ_{ex} = 390 nm)

Inset: plot of intensity enhancement versus the HCO_3^- concentration used for determining the lowest limits of detection. Intensity differences are plotted at 501 nm.

taken from the single-crystal structures. The binding energies, calculated at the X3LYP/6–31++g** level of theory,[41] were corrected for the basis set superposition error by the Boys-Bernardi counterpoise technique.[42] All theoretical calculations were performed with the Gaussian 09 program and the Gauss-View molecular visualization program package run on a personal computer.[43,44] The resulting binding energies were calculated to be −171.03 kcal/mol for the ETF methyl carbonate complex and −172.46 kcal/mol for the FTF methyl carbonate complex, respectively. The comparable binding energies seen for these two complexes help rationalize why both structures were observed in the same set of single crystals. Nevertheless, the parallel complex was calculated to be slightly more stable. The FTF methyl carbonate complex **7** was calculated to be more stable than the corresponding bicarbonate complex **6** (binding energy = −168.75 kcal/mol) (Figure S49).

Methyl hydrogen carbonate ($CH_3OCO(OH)$), like carbonic acid (H_2CO_3), is quite labile at room temperature.[45] It was first prepared in pure form at low temperature (−50°C) by Gattow and Behrendt.[46] It and other alkyl carbonates have, however, been proposed as key intermediates in the high temperature, high pressure reactions of alcohols with CO_2 in the presence of Lewis acid catalysts used to prepare organic carbonates.[47] Above its melting temperature (−36°C), methyl hydrogen carbonate decomposes readily. In contrast, methyl carbonate salts have been known for a long time and are typically stable compounds under basic conditions. Nucleophilic attack of alkoxide anions on the CO_2 carbon atom under highly basic conditions represents a classic approach to producing alkyl carbonates.[48–50] Methyl carbonate salts have also been seen in the course of direct methylation of alkyl amines or phosphines with dimethyl carbonate.[51,52] Organocatalytic transformations of CO_2 to methyl carbonate were reported by the Cantat and Heldebrant groups in 2012 and 2014, respectively.[53,54] The present approach, involving the complexation-based transformation of hydrated anionic forms of CO_2 (e.g., HCO_3^-) to methyl carbonate under near-neutral conditions, could provide an important complement to these latter efforts.

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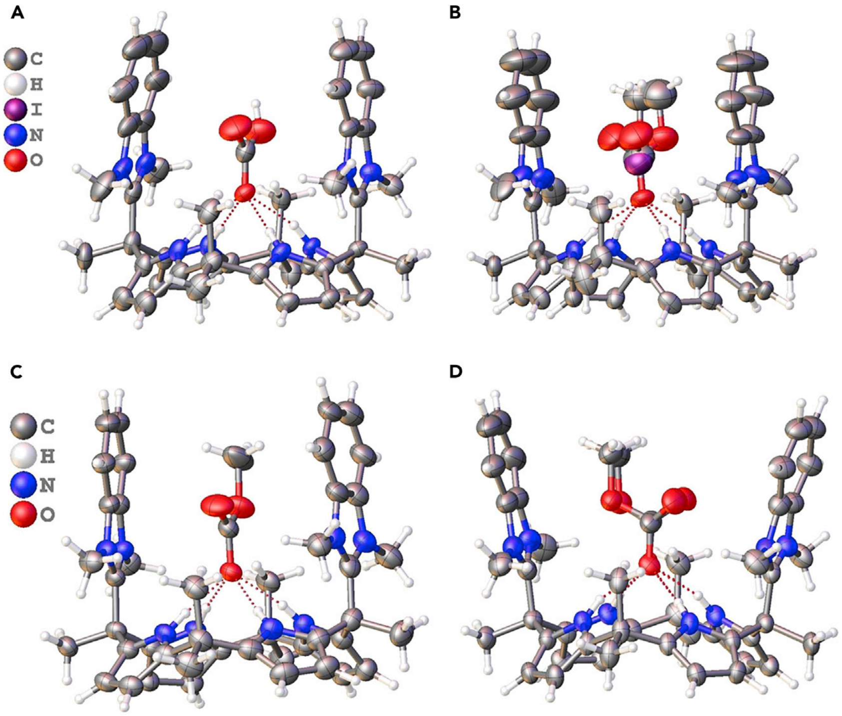

Figure 5. Crystal Structure of 6-Mixture and 7-Methylcarbonate

(A) The host-bicarbonate complex in **6**-mixture.

(B) The host-methyl carbonate complex in **6**-mixture (containing some co-crystallized iodide complex impurity).

(C) The face-to-face host-methyl carbonate complex seen in single crystals of **7**-methylcarbonate.

(D) The edge-to-face host-methyl carbonate complex seen in single crystals of **7**-methylcarbonate.

The displacement ellipsoids have been scaled to the 50% probability level. Solvent molecules and counter PF_6^- anions have been removed for clarity. For more details, see Figures S35 and S36.

Evidence that the relevant chemistry occurs under typical laboratory conditions (as opposed to those associated with crystallization) came from quantitative ^1H NMR spectroscopic studies. Specifically, titration and incubation of dicationic host **3** with Cs_2CO_3 in a 9:1 (v/v) mixture of CD_3CN and CH_3OH revealed a new signal at δ 3.45 ppm corresponding to the methyl group of the bound methyl carbonate. In addition, new pyrrole NH proton signals at δ 11.42 and 14.22 ppm are observed, which are ascribed to the bound anionic methyl carbonate and dianionic carbonate complexes of receptor **3**, respectively (Figure S22).[55] In contrast, control experiments carried out in the absence of receptor **3** revealed no changes in the ^1H NMR spectrum over the course of 24 hr (Figure S38). More importantly, the same chemical transformation induced by receptor **3** (i.e., the trapping of methyl carbonate in the form of complex **7**) was also observed when the less basic salt, tetraethylammonium bicarbonate was used (Figure S37). Thus, we conclude that receptor **3** drives the formation of complex **7** and stabilizes what would otherwise be an unstable species (methyl carbonate) (Scheme 3). This allows the trapping of dissolved CO_2 under near-neutral equilibrium conditions.[56]

Further support for the notion that functionalized calix[4]pyrrole receptors are capable of promoting the chemical transformation of dissolved CO_2 came from X-ray crystallographic analyses of the non-charged, pyridine-strapped calix[4]pyrrole **8** (Figure 6). Satisfyingly, single crystals of the methyl and ethyl carbonate complexes of receptor **8**[57] suitable for X-ray diffraction analysis were grown by subjecting

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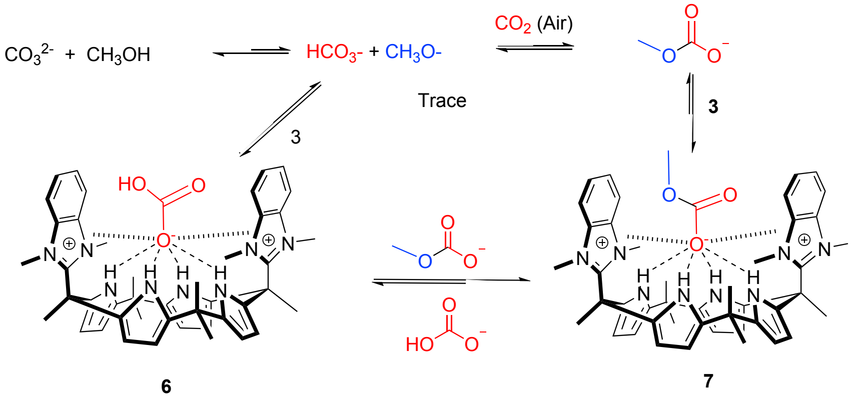

Scheme 3. Proposed Mechanism for the Formation of the Methyl Carbonate Complex 7

methanol/chloroform and ethanol/chloroform solutions of **8** to slow evaporation in the presence of excess tetraethylammonium (TEA) bicarbonate, respectively. The resulting single-crystal structures revealed that a methyl or ethyl carbonate anion sits above the cone-like calix[4]pyrrole with four pyrrole N–H protons involved in hydrogen bonding with only one oxygen atom in the carbonate. The receptor-bound O-to-N distances range from 2.93 to 3.04 Å in the methyl carbonate complex and from 2.95 to 3.01 Å in the ethyl carbonate complex. The amide NH protons in the host are also involved in the stabilization of the alkyl carbonate anions as inferred from the observed O-to-N distances of 2.96–2.97 and 2.93–2.96 Å for the methyl and ethyl carbonate complexes, respectively. These are analogous to that obtained with the dicationic receptor **3** described above. In further analogy to what has been seen for receptor **3**, receptor **8** was found to bind the bicarbonate with high affinity ($K_a = 6.8 \times 10^6$ M^{-1}), as inferred from isothermal titration calorimetry and ^1H NMR spectral titration experiments carried out in (deuterated) chloroform (Figures S40 and S41). In the presence of 5% methanol or 5% ethanol in $CDCl_3$, two new sets of pyrrole NH peaks and pyridine CH peaks are seen in the low field spectral region that we assign to the bound bicarbonate and (m)ethyl carbonate anion complexes, respectively (Figures S42 and S43). Taken together, these observations provide further support for the suggestion that, in the presence of an alcoholic solvent, dissolved CO_2 will be converted into a mono-alkyl carbonate ester with the aid of an appropriately chosen calix[4]pyrrole anion receptor under near-neutral conditions. This allows the trapping of mono-carbonate esters under conditions where they would be otherwise unstable.

Conclusion

The dicationic calix[4]pyrrole described here provides an effective receptor for the bicarbonate anion. Used in conjunction with a fluorescent probe, **4**$^-$, the present "two-walled" calixpyrrole derivative acts as an effective sensor for the bicarbonate anion in that it shows selectively in relation to other test anions. Under conditions of fluorescence displacement, the lowest limit of detection was found to be ca. 4 nM. The sensor system is easily regenerated upon treatment with sodium ions, paving the way for its reuse. Receptor **3** also acts to promote the conversion of the HCO_3^- anion to a bound mono-carbonate ester in the presence of alcoholic solvents. This conversion is not one that can normally be carried out under ambient conditions. The ability to promote the formation of a normally unstable species could represent an important step forward in the activation and trapping of CO_2. Support for the generality of this finding comes from the observation that similar chemistry is

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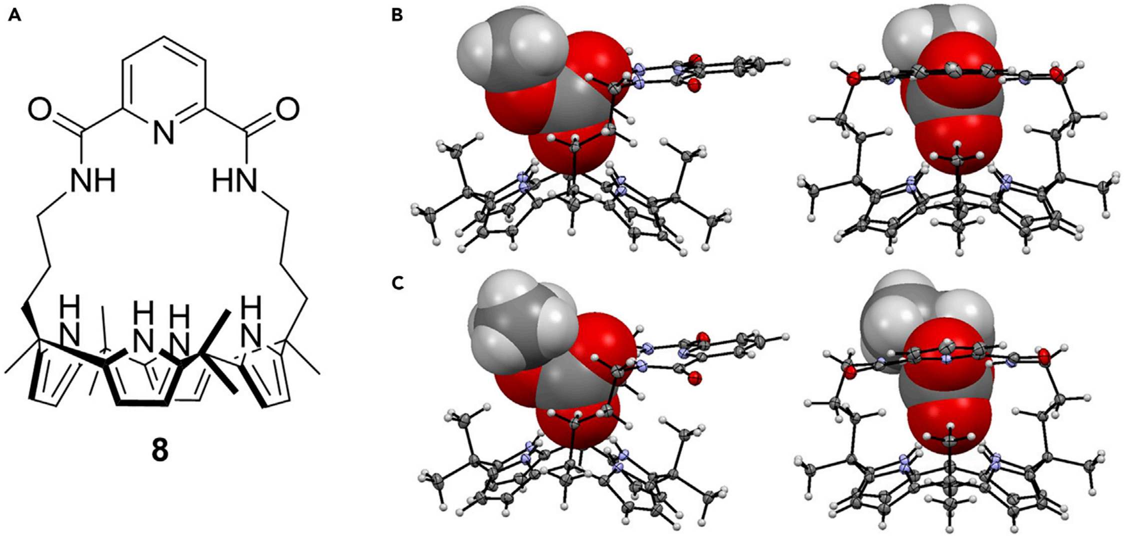

Figure 6. Molecular Structure of 8 and Solid-State Structures of Its Methyl Carbonate and Ethyl Carbonate Complexes as Inferred from Single-Crystal X-Ray Diffraction Analyses

(A) Molecular structure of compound **8**.

(B) Front view and side view of the crystal structure of **8**-methylcarbonate complex.

(C) Front view and side view of the crystal structure of **8**-ethylcarbonate complex.

Displacement ellipsoids are scaled to the 50% probability level. Solvent molecules and the counter cation, TEA^+, sitting in the calix[4]pyrrole cavity, are omitted for clarity.

promoted when a non-charged calix[4]pyrrole system, receptor **8**, is substituted for **3**. The present work could thus point the way to a new approach for capturing and functionalizing dissolved CO_2 under near-neutral conditions. Further explorations of this possibility are currently underway.

EXPERIMENTAL PROCEDURES

Full experimental procedures are provided in the Supplemental Information.

DATA AND SOFTWARE AVAILABILITY

The accession numbers for **3**-receptor, **6**-mixture, **7**-methylcarbonate, **8**-methylcarbonate, and **8**-ethylcarbonate are CCDC: 1524707, 1524050, 1533115, 1576121, and 1576122, respectively.

SUPPLEMENTAL INFORMATION

Supplemental Information includes Supplemental Experimental Procedures, 49 figures, 2 schemes, 7 tables, and 5 data files and can be found with this article online at https://doi.org/10.1016/j.chempr.2017.10.007.

AUTHOR CONTRIBUTIONS

E.M., Q.H., and D.S. contributed equally to this work (co-first authors). Synthesis and Characterization: E.M., D.S., and J.H.O.; Titration and Sensing Experiments: E.M., D.S., S.-J.H., and J.H.O.; Single-Crystal XRD Data Collection and Analysis: Q.H. and V.M.L.; DFT Calculations: Q.H.; Supervision: C.-H.L., J.L.S., and S.K.K.; Writing – Original Draft: E.M., C.-H.L., and J.L.S.; Writing – Review & Editing: Q.H., D.S., S.K.K., C.-H.L., and J.L.S.; Funding Acquisition: S.K.K., C.-H.L., and J.L.S. All authors proofread, commented on, and approved the final version of this manuscript.

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ACKNOWLEDGMENTS

Support is acknowledged from the Basic Science Research Program (2015R1A2A1A10052586 to C.-H.L.; 2017R1A4A1014595 to S.K.K.) funded by the National Research Foundation under the Korean Ministry of Science, ICT, & Future Planning. The work in Austin was supported by the US Department of Energy Office of Basic Energy Sciences (DE-FG02-01ER15186 to J.L.S.) and the Robert A. Welch Foundation (F-0018 to J.L.S.). The Central Laboratory at Kangwon National University is also acknowledged.

Received: May 3, 2017
Revised: June 19, 2017
Accepted: October 17, 2017
Published: November 9, 2017

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