OPTICAL ANION SENSORS BASED ON ALKYNE-LINKED, FUNCTIONALIZED CALIX[4]PYRROLES

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Dedicated to Professor Ivan Stibor in recognition of his accomplishments and leadership.

Linking a calix[4]pyrrole anion recognition subunit to chromophores or fluorophores via an alkynyl spacer attached to a β-pyrrolic position of a calix[4]pyrrole core produces a new class of anion sensor that permits the detection of halide and phosphate anions in organic media via direct, so-called "naked-eye" visualization or fluorescence quenching-based spectroscopic means.

Keywords: Anion complexation; Anion receptors; Sensors; Calixpyrroles; Alkynes; Pyrroles; Supramolecular chemistry; Fluorescence.

The development of sensors for specific chemical species represents an important current challenge in supramolecular chemistry[1]. In recent years, particular focus has been devoted to obtaining sensors for anionic species[2], driven in part by the importance and ubiquity of anions in biology, chemistry, and the environment. One receptor system that appears attractive in terms of anion sensor development is calix[4]pyrrole[3,4]. This class of uncharged receptors is endowed with four pyrrolic NH protons and binds anions such as F^-, Cl^-, and $H_2PO_4^-$ via directed hydrogen bonding interactions both in organic solution and in the solid state[4]. However, the calix[4]pyrroles are intrinsically colorless and must either be used in displacement-type assays[5] or functionalized in an appropriate manner to produce sensors. To

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date, such functionalization has led to the production of both electrochemical[6] and optical sensors[7,8] that have allowed for the detection of anionic analytes in various organic media, including, in the most favorable of instances, wet acetonitrile. In the context of the latter work, we recently reported that attachment of electron-deficient aromatic chromophores, specifically nitrobenzene- and anthraquinone-type moieties, to a calix[4]pyrrole skeleton through a β-pyrrole-linked acetylenic tether gives rise to so-called "naked eye" detectable sensors systems, wherein the presence of an anion is signaled through an easy-to-see color change[8]. In this report, we extend this approach and show how, by using a variety of other chromophores or fluorophores, it is possible to produce a range of colorimetric and fluorescent quenching-based anion sensors. We also provide full experimental details for work that was previously reported only in communication form[8].

EXPERIMENTAL

General

Proton and ^{13}C NMR spectra were recorded on a Varian Unity+ (500 MHz) instrument. Chemical shifts (δ, ppm) are reported relative to TMS (tetramethylsilane) as an internal standard. Coupling constants (*J*) are reported in Hz. High resolution FAB (4-nitrobenzyl alcohol matrix) and CI mass spectra were recorded using a VG ZAB2-E mass spectrometer. Low resolution FAB and CI mass spectra were obtained on a Finningan MATTSQ 70 mass spectrometer. Elemental analyses were performed by Atlantic Microlab Inc. (Norcross, Ga 30071). Fluorescence studies were carried out on an Instruments SA, Inc. Fluorolog FL3-11 spectrophotometer. UV-VIS spectra were recorded on a Beckman DU-650 spectrometer.

Tetrabutylammonium fluoride trihydrate was purchased from Fluka. Other tetrabutylammonium salts were purchased from Aldrich. All salts were used as received.

5,5,10,10,15,15,20,20-Octamethyl-2-[(trimethylsilyl)ethynyl]calix[4]pyrrole (**3**)

To a solution of iodocalix[4]pyrrole **2** [8,9] (319 mg, 0.58 mmol) in diisopropylamine (20 ml) was added (trimethylsilyl)acetylene (1.65 ml, 11.7 mmol). The reaction mixture was stirred at 80 °C for 2 h in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium(0) and copper iodide under argon. After removal of the solvent in vacuo, the residue was extracted with dichloromethane (2 × 20 ml) and the organic layer was washed with saturated ammonium chloride (30 ml) and brine. The solvent was evaporated and the residue was purified by column chromatography on silica gel (eluent: dichloromethane/hexane, 1:1) to give the [(trimethylsilyl)ethynyl]calix[4]pyrrole **3** (220 mg, 73%). Here, it is important to appreciate that both an excess of TMS-acetylene and an optimized temperature of 80 °C, were found necessary to ensure a good yield. For **3**: ^1H NMR (500 MHz, CD_2Cl_2): 7.26 (s, 1 H, NH); 7.18 (s, 1 H, NH); 6.92 (s, 1 H, NH); 6.83 (s, 1 H, NH); 5.98 (d, 1 H, J = 3.0, CH_{py}); 5.96–5.82 (m, 6 H, CH_{py}); 1.67 (s, 6 H, CH_3); 1.51 (s, 6 H, CH_3); 1.50 (s, 6 H, CH_3); 1.44 (s,

6 H, CH_3). ^{13}C NMR (125 MHz, CD_2Cl_2): 142.04, 139.52, 139.24, 138.68, 138.13, 137.90, 137.60, 137.12, 108.88, 103.97, 103.94, 103.82, 103.20, 103.03, 102.40, 99.28, 68.01, 66.03, 37.31, 35.45, 35.43, 35.38, 29.27, 28.84, 28.70, 28.26, 0.08. HRMS (CI^+): calculated for $C_{33}H_{45}N_4Si$ 525.3414; found: 525.3419.

2-Ethynyl-5,5,10,10,15,15,20,20-octamethylcalix[4]pyrrole (**4**)

To a solution of the [(trimethylsilyl)ethynyl]calix[4]pyrrole **3** (280 mg, 0.53 mmol) in THF (30 ml) was added tetrabutylammonium fluoride (1 M THF solution, 0.55 ml, 0.55 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 6 h. After removal of the solvent in vacuo, the residue was extracted with dichloromethane (2 × 15 ml) and the organic layer was washed with saturated sodium hydrogencarbonate (2 × 30 ml) and brine. The solvent was evaporated and the residue was purified by column chromatography on silica gel (eluent: ethyl acetate/hexane, 7:93) to give the ethynylcalix[4]pyrrole **4** (215 mg, 89%). ^1H NMR (500 MHz, CD_2Cl_2): 7.25 (s, 1 H, NH); 7.20 (s, 1 H, NH); 6.91 (s, 1 H, NH); 6.83 (s, 1 H, NH); 6.06 (d, 1 H, J = 3.0, CH_{py}); 5.94–5.82 (m, 6 H, CH_{py}); 3.06 (s, 1 H, CH) 1.66 (s, 6 H, CH_3); 1.50 (s, 12 H, CH_3); 1.45 (s, 12 H, CH_3). ^{13}C NMR (125 MHz, CD_2Cl_2): 141.77, 139.43, 139.16, 138.64, 138.06, 137.75, 137.44, 137.11, 109.18, 104.09, 104.05, 103.92, 103.85, 103.13, 102.32, 98.02, 80.92, 78.57, 37.19, 35.41, 35.38, 35.33, 28.28, 28.81, 28.70, 28.34. HRMS (CI^+): calculated for $C_{30}H_{37}N_4$ 453.3018; found: 453.3014.

5,5,10,10,15,15,20,20-Octamethyl-2-(*p*-tolylethynyl)calix[4]pyrrole (**5**)

To a solution of ethynylcalix[4]pyrrole **4** (60 mg, 0.13 mmol) and 4-iodotoluene (35 mg, 0.16 mmol) in diisopropylamine (4.5 ml) and DMF (2.3 ml) was added a catalytic amount of tetrakis(triphenylphosphine)palladium(0) and copper(I) iodide under Ar. The reaction mixture was stirred at room temperature for 12 h. After removal of the solvent in vacuo, the residue was extracted with dichloromethane (2 × 20 ml) and the organic layer was washed with brine. The solvent was evaporated off using a rotary evaporator and the residue was purified by column chromatography on silica gel (eluent: ethyl acetate/hexane, 3:97) to give the (*p*-tolylethynyl)calix[4]pyrrole **5** (63 mg, 87%). ^1H NMR (500 MHz, CD_2Cl_2): 7.32 (d, 2 H, J = 8.1, C_6H_4); 7.23 (s, 1 H, NH); 7.14 (s, 1 H, NH); 7.13 (d, 2 H, J = 8.1, C_6H_4); 6.94 (s, 1 H, NH); 6.91 (s, 1 H, NH); 6.89 (s, 1 H, NH); 6.83 (s, 1 H, NH); 6.06 (d, 1 H, J = 3.0, CH_{py}); 5.94–5.83 (m, 6 H, CH_{py}); 2.34 (s, 3 H, $C_6H_4CH_3$); 1.72 (s, 6 H, CH_3); 1.51 (s, 12 H, CH_3); 1.48 (s, 6 H, CH_3). ^{13}C NMR (125 MHz, CD_2Cl_2): 141.02, 139.55, 139.76, 138.21, 137.97, 137.92, 137.74, 137.45, 130.92, 129.46, 121.93, 108.58, 104.07, 104.04, 103.87, 103.22, 103.14, 102.44, 99.33, 90.55, 86.08, 37.35, 35.51, 35.43, 30.11, 29.35, 28.89, 28.56, 21.54. HRMS (CI^+): calculated for $C_{37}H_{43}N_4$ 543.3488; found: 543.3481. For $C_{37}H_{42}N_4 \cdot 0.5EtOAc$: 79.82% C, 7.90% H, 9.55% N; found: 80.11% C, 7.99% H, 9.34% N.

5,5,10,10,15,15,20,20-Octamethyl-2-[(4-nitrophenyl)ethynyl]calix[4]pyrrole (**6**)

This product was made from ethynylcalix[4]pyrrole **4** (57 mg, 0.13 mmol) and 1-iodo-4-nitrobenzene (41 mg, 0.16 mmol) in diisopropylamine (3.0 ml) using the reaction and work-up conditions described for **5**. A mixture of ethyl acetate/hexane/*i*-PrOH (6:93:1) was used, however, to effect chromatographic purification (silica gel). The yield obtained in this way was 82% (59 mg). ^1H NMR (500 MHz, CD_2Cl_2): 8.17 (d, 2 H, J = 8.8, C_6H_4); 7.55 (d, 2 H, J = 8.8, C_6H_4); 7.30 (s, 1 H, NH); 7.25 (s, 1 H, NH); 6.99 (s, 1 H, NH); 6.93 (s, 1 H, NH);

6.11 (d, 1 H, J = 3.0, CH_{py}); 5.96–5.82 (m, 6 H, CH_{py}); 1.74 (s, 6 H, CH_3); 1.51 (s, 12 H, CH_3); 1.49 (s, 6 H, CH_3). ^{13}C NMR (125 MHz, CD_2Cl_2): 146.60, 142.83, 139.74, 139.32, 138.88, 138.20, 138.11, 137.65, 137.27, 132.22, 131.38, 124.05, 108.73, 104.32, 104.30, 103.99, 103.32, 103.14, 102.33, 98.41, 93.57, 89.78, 37.49, 35.54, 35.51, 35.45, 30.11, 29.30, 28.85, 28.76, 28.66. HRMS (CI^+): calculated for $C_{36}H_{40}N_5O_2$ 574.3182; found: 574.3179. For $C_{36}H_{39}N_5O_2 \cdot 0.5i$-PrOH: 74.60% C, 7.18% H, 11.60% N; found: 75.00% C, 7.07% H, 11.71% N.

2-[(2,4-Dinitrophenyl)ethynyl]-5,5,10,10,15,15,20,20-octamethylcalix[4]pyrrole (**7**)

This product was obtained from ethynylcalix[4]pyrrole **4** (167 mg, 0.37 mmol) and 1-iodo-2,4-dinitrobenzene (109 mg, 0.37 mmol) using the same general reaction and work-up conditions described for **5**. A mixture of ethyl acetate/hexane/*i*-PrOH (8:90:2) was used, however, to effect chromatographic purification (silica gel). The yield obtained in this way was 67% (153 mg). ^{1}H NMR (500 MHz, CD_2Cl_2): 8.91 (d, 1 H, J = 2.4, C_6H_3); 8.36 (dd, 1 H, J = 8.7, 2.4, C_6H_3); 7.76 (d, 1 H, J = 8.7, C_6H_3); 7.30 (s, 1 H, NH); 7.27 (s, 1 H, NH); 7.09 (s, 1 H, NH); 6.92 (s, 1 H, NH); 6.19 (d, 1 H, J = 3.0, CH_{py}); 5.97–5.81 (m, 6 H, CH_{py}); 1.75 (s, 6 H, CH_3); 1.51 (s, 12 H, CH_3); 1.50 (s, 6 H, CH_3). ^{13}C NMR (125 MHz, CD_2Cl_2): 148.04, 145.50, 145.09, 139.91, 139.35, 138.93, 138.63, 138.08, 137.41, 136.78, 135.02, 127.26, 126.95, 121.04, 109.53, 104.60, 104.46, 104.09, 103.95, 103.39, 103.17, 102.24, 98.12, 87.76, 46.69, 37.58, 37.58, 35.58, 35.51, 35.45, 29.32, 28.84, 28.73, 28.66. HRMS (CI^+): calculated for $C_{36}H_{39}N_6O_4$ 619.3033; found: 619.3037. For $C_{36}H_{38}N_6O_4 \cdot 0.5i$-PrOH: 69.42% C, 6.53% H, 12.95% N; found: 69.22% C, 6.37% H, 12.81% N.

2-[(4-{[4-(Dimethylamino)phenyl]azo}phenyl)ethynyl]-5,5,10,10,15,15,20,20-octamethylcalix[4]pyrrole (**8**)

This product was obtained from ethynylcalix[4]pyrrole **4** (181 mg, 0.40 mmol) and 4-(dimethylamino)-4′-iodoazobenzene (169 mg, 0.48 mmol) using the same general reaction and work-up conditions described for **5**. A mixture of ethyl acetate/hexane/*i*-PrOH (7:92:1) was used to effect chromatographic purification. The yield obtained in this way was 79% (214 mg). ^{1}H NMR (500 MHz, CD_2Cl_2): 7.85 (d, 2 H, J = 9.2, C_6H_4); 7.79 (d, 2 H, J = 8.7, C_6H_4); 7.52 (d, 2 H, J = 8.7, C_6H_4); 7.31 (s, 1 H, NH); 7.25 (s, 1 H); 6.95 (s, 2 H, NH); 6.78 (d, 2 H, J = 9.2, C_6H_4); 6.10 (d, 1 H, J = 3.0, CH_{py}); 5.95–5.83 (m, 6 H, CH_{py}); 3.09 (s, 6 H, $N(CH_3)_2$); 1.75 (s, 6 H, CH_3); 1.51 (s, 12 H, CH_3); 1.49 (s, 6 H, CH_3). ^{13}C NMR (125 MHz, CD_2Cl_2): 153.11, 152.25, 143.99, 141.63, 139.64, 139.29, 138.80, 138.20, 137.92, 137.65, 137.63, 131.64, 126.02, 125.34, 122.60, 111.87, 108.69, 104.17, 104.12, 103.91, 103.23, 103.17, 102.42, 99.18, 90.88, 89.11, 40.50, 37.43, 35.54, 35.51, 35.44, 29.36, 28.90, 28.79, 28.63. HRMS (CI^+): calculated for $C_{44}H_{50}N_7$ 676.4128; found: 676.4137. For $C_{44}H_{49}N_7 \cdot i$-PrOH: 76.70% C, 7.81% H, 13.32% N; found: 76.39% C,7.42% H, 12.98% N.

2-[(1-Anthryl)ethynyl]-5,5,10,10,15,15,20,20-octamethylcalix[4]pyrrole (**9**)

This product was obtained from ethynylcalix[4]pyrrole **4** (248 mg, 0.55 mmol) and 1-iodoanthracene (167 mg, 0.55 mmol) in diisopropylamine (13 ml) using the same general reaction and work-up conditions described for **5**, with the exception that stirring was maintained for 24 h. A mixture of ethyl acetate/hexane (7:93) was used to effect chromatographic purification. The yield obtained in this way was 69% (238 mg). ^{1}H NMR (500 MHz, CD_2Cl_2): 8.06 (d, 1 H, J = 6.3); 8.01 (d, 1 H, J = 6.3); 7.95 (d, 1 H, J = 8.9); 7.67 (d, 1 H, J = 6.9); 7.67

(d, 2 H, *J* = 6.9); 7.39 (s, 1 H, NH); 7.30 (s, 1 H, NH); 6.99 (s, 1 H, NH); 6.97 (s, 1 H, NH); 6.27 (d, 1 H, *J* = 3.0, CH_{py}); 5.98–5.85 (m, 6 H, CH_{py}); 1.87 (s, 6 H, CH_3); 1.54 (s, 6 H, CH_3); 1.53 (s, 6 H, CH_3); 1.52 (s, 6 H, CH_3). ^{13}C NMR (125 MHz, CD_2Cl_2): 141.34, 139.61, 139.28, 138.82, 138.20, 137.88, 137.73, 137.57, 132.38, 132.31, 131.82, 131.46, 129.27, 128.87, 128.36, 127.13, 126.17, 126.12, 125.52, 125.30, 122.77, 108.99, 104.21, 104.19, 103.92, 103.27, 103.24, 102.42, 99.39, 92.37, 89.09, 37.46, 35.58, 35.51, 35.45, 29.38, 28.88, 28.83, 28.78. HRMS (CI^+): calculated for $C_{44}H_{45}N_4$ 629.3644; found: 629.3635. For $C_{44}H_{44}N_4 \cdot 1.5CH_3OH$: 80.73% C, 7.45% H, 8.28% N; found: 81.05% C, 7.50% H, 8.29% N.

2-[(9,10-Dioxo-9,10-dihydro-1-anthryl)ethynyl]-
5,5,10,10,15,15,20,20-octamethylcalix[4]pyrrole (**10**)

This product was obtained from ethynylcalix[4]pyrrole **4** (50 mg, 0.11 mmol) and 1-iodoanthraquinone (41 mg, 0.12 mmol) using the same general reaction and work-up conditions described for **5**. A mixture of ethyl acetate/hexane (20:80) was used to effect chromatographic purification. The yield obtained in this way was 73% (53 mg). ^{1}H NMR (500 MHz, CD_2Cl_2): 8.32 (d, 1 H, *J* = 7.0); 8.23 (t, 2 H, *J* = 7.0); 7.86 (d, 1 H, *J* = 7.8); 7.84–7.77 (m, 2 H); 7.70 (t, 1 H, *J* = 7.8); 7.35 (s, 1 H, NH); 7.32 (s, 1 H, NH); 7.00 (s, 1 H); 6.96 (s, 1 H, NH); 6.24 (d, 1 H, *J* = 3.0, CH_{py}); 5.97–5.83 (m, 6 H, CH_{py}); 1.81 (s, 6 H, CH_3); 1.52 (s, 18 H, CH_3). ^{13}C NMR (125 MHz, CD_2Cl_2): 183.31, 182.18, 142.81, 139.57, 139.34, 138.82, 138.13, 137.84, 137.54, 134.96, 134.81, 134.68, 133.99, 133.29, 133.07, 132.63, 127.67, 127.05, 126.46, 125.51, 109.22, 104.20, 104.13, 103.94, 103.27, 103.16, 102.42, 99.37, 94.44, 91.32, 37.49, 35.53, 35.45, 29.41, 28.92, 28.78, 28.73. HRMS (CI^+): calculated for $C_{44}H_{43}N_4O_2$ 659.3386; found: 659.3390. For $C_{44}H_{42}N_4O_2 \cdot 0.5CH_2Cl_2 \cdot 0.5H_2O$: 75.35% C, 6.32% H, 7.81% N; found: 75.48% C, 6.39% H, 7.64% N.

2-[(4-Hydroxy-9,10-dioxo-9,10-dihydro-1-anthryl)ethynyl]-
5,5,10,10,15,15,20,20-octamethylcalix[4]pyrrole (**11**)

This product was obtained from ethynylcalix[4]pyrrole **4** (50 mg, 0.11 mmol) and 1-hydroxy-4-iodoanthraquinone (50 mg, 0.12 mmol) using the same general reaction and work-up conditions described for **5**, with the exception that stirring was maintained for 24 h. A mixture of ethyl acetate/hexane (13:87) was used to effect chromatographic purification. The yield obtained in this way was 82% (61 mg). ^{1}H NMR (500 MHz, CD_2Cl_2): 12.37 (s, 1 H, OH); 8.28 (t, 2 H, *J* = 7.6); 7.86–7.78 (m, 2 H); 7.70 (d, 1 H, *J* = 8.8); 7.47 (s, 1 H, NH); 7.44 (s, 1 H, NH); 7.22 (d, 1 H, *J* = 8.7); 6.99 (s, 1 H, NH); 6.97 (s, 1 H); 6.15 (d, 1 H, *J* = 3.0, CH_{py}); 5.91–5.83 (m, 6 H, CH_{py}); 1.79 (s, 6 H, CH_3); 1.53 (s, 12 H, CH_3); 1.51 (s, 6 H, CH_3). ^{13}C NMR (125 MHz, CD_2Cl_2): 189.10, 181.15, 162.88, 142.64, 142.46, 139.81, 139.39, 138.85, 138.11, 137.75, 137.64, 135.25, 134.85, 134.00, 132.86, 132.10, 127.87, 126.86, 124.29, 117.93, 116.52, 109.21, 104.13, 104.02, 103.94, 103.35, 103.08, 102.41, 99.49, 93.13, 91.66, 37.51, 35.58, 35.55, 35.46, 29.28, 28.97, 28.82, 28.82, 28.73. HRMS (CI^+): calculated for $C_{44}H_{43}N_4O_3$ 675.3335; found: 675.3336. For $C_{44}H_{42}N_4O_3 \cdot 0.5i$-PrOH: 77.53% C, 6.58% H, 7.95% N; found: 77.36% C, 6.74% H, 7.59% N.

Fluorescence Titration Experiments

Quantitative fluorescence titration experiments involving compound **9** were carried out under conditions identical to those used previously to study receptors **12** and **13** (50 μM dichloromethane solutions in **9**, 25 °C, 2.5 ml initial volume, 1 cm cuvettes)[7a]. As mentioned in the text, the isosbestic point observed in the absorption spectra associated with analogous titrations was used as the excitation wavelength, with the intensity of the emission maximum then being recorded as a function of added anion concentration. Each anion in question (fluoride, chloride, bromide, dihydrogenphosphate, and hydrogensulfate), in the form of its tetrabutylammonium salt, was dissolved in dichloromethane and aliquots of the solution were added to the initial solution (the total increase in volume was less than 5%). As in the case of **12**, and **13** and other fluorescent sensors developed in our laboratory[7], data reduction was effected using Scott-type plots[10]. The goodness of fit obtained during such analyses was considered a confirmation of the proposed 1:1 binding mode, a stoichiometry that is well-established for the anions of interest in the case of calix[4]pyrrole-type receptors[4].

In these experiments, as throughout the present study, the tetrabutylammonium salts were purchased commercially and used without further purification. In the case of fluoride, such salts are known to be impure and to contain water in excess of what one would expect for a trihydrate[11]. However, this caveat noted[12], relatively reliable inter-comparisons among receptor classes may be made (e.g., **9** vs **12** and **13**).

UV-VIS Titration Experiments

UV-VIS titration experiments were carried out at 25 °C by measuring the change in absorption spectra of 50 μM dichloromethane solutions of each receptor in question (2 ml initial volume) as a function of added anion concentration. Again, each anion (fluoride, chloride, bromide, dihydrogenphosphate, and hydrogensulfate), was used in the form of its tetrabutylammonium salt, that latter being dissolved in dichloromethane to provide concentrated stock solutions whose addition caused relatively change in the total volume (i.e., less than 5%). Data reduction was effected using Benesi–Hildebrand plots[10,13] ($1/\Delta A$ vs 1/[Guest]) with good linear fits being seen in all cases (correlation coefficient $r > 0.995$).

RESULTS AND DISCUSSION

In previous communications, we reported a method for the functionalization of calix[4]pyrrole that involved first monohalogenation followed by metal mediated C–C bond formation and demonstrated its utility in the formation of colorimetric anion sensors by using it to attach various functional groups to a β-pyrrolic position of a calix[4]pyrrole anion binding core through an intervening acetylene moiety[8]. We believe this approach to optical anion sensor development is particularly advantageous, not only because of the ease and generality of the synthesis, but also because the π-conjugated acetylene moiety could act as a “molecular wire” thereby facilitating electron (or energy) transfer between the calix[4]pyrrole anion binding entity and the chromophore-derived reporting subunit as shown

in Fig. 1. In order to provide further support for this contention, we report here in full detail the synthesis of several new and previously reported acetylene-linked calix[4]pyrrole chromophore constructs and show that many of these species are effective anion sensors in organic media, permitting both colorimetric (i.e., "naked eye") and fluorescence-based anion detection.

Scheme 1 provides a summary of the synthetic approach used to prepare alkyne-linked, chromophore or fluorophore functionalized calix[4]pyrrole anion sensors. In this approach, the key intermediate is the β-pyrrole-substituted, mono-iodocalix[4]pyrrole, **2**. This species, which is a potentially useful precursor for the functionalization of calix[4]pyrrole via Pd catalyzed carbon–carbon bond forming methods, such as the Negishi, Suzuki, Stille and Sonogashira reactions[14], was obtained by subjecting calix[4]pyrrole **1** to iodination with [bis(trifluoroacetoxy)iodo]benzene and iodine in dichloromethane at room temperature. This gave a mixture of iodinated compounds including the mono-, di- (several isomers), and trace amounts of more highly substituted iodinated calix[4]pyrroles. The desired mono-iodocalix[4]pyrrole **2** was readily purified by column chromatography over silica gel (eluent: dichloromethane/hexane, 1:1) and was obtained in 20% isolated yield[8,9]. With it in hand, efforts to effect direct C–C bond forma-

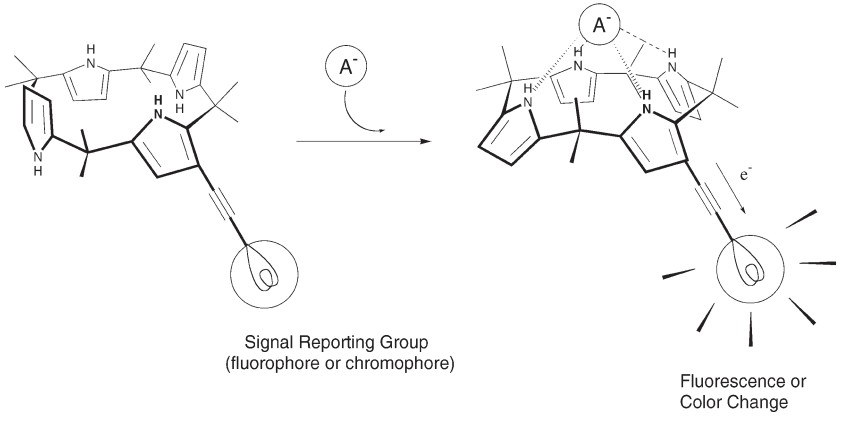
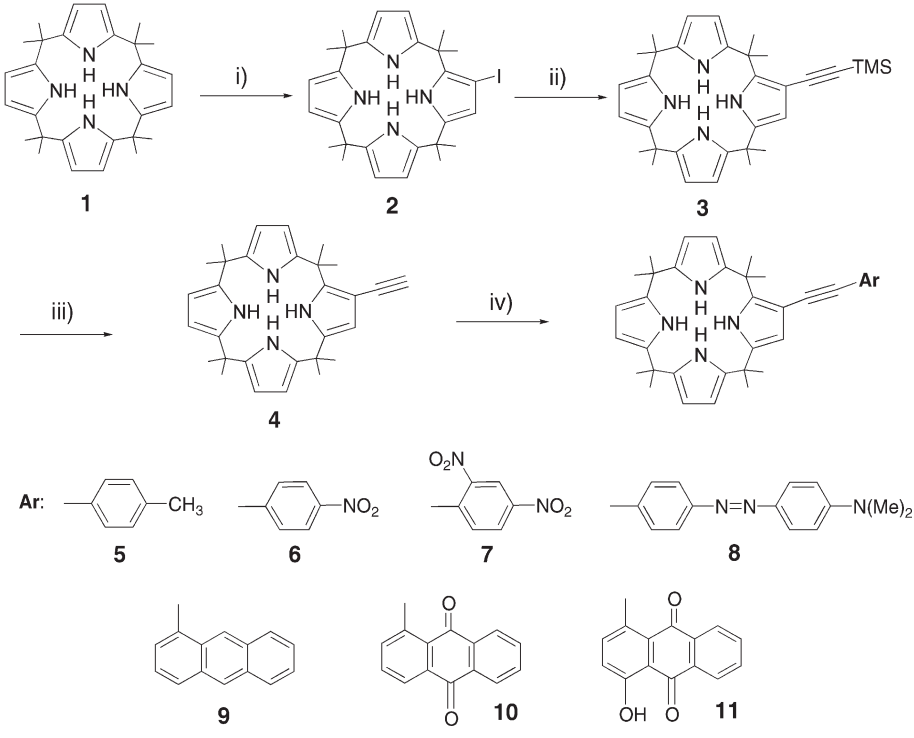


FIG. 1
Schematic representation of the present approach to anion sensor generation; it relies on the use of an acetylene linker to establish a conjugated pathway for enhanced electronic coupling between a calix[4]pyrrole anion binding subunit and a chromophore or fluorophore signaling group. In the limit, this enhanced coupling could result in full electron transfer as shown. However, attaining such a complete charge-transfer limit, shown for the sake of illustration, is expected and is not necessary to produce a strong anion-dependent optical response

tion were made. Initially, attempts were made to couple organozinc reagents and organoboronic acid derivatives to iodocalix[4]pyrrole **2**. However, under standard Negishi (or Suzuki) conditions such attempted couplings gave rise only to the deiodinated calix[4]pyrrole **1**. Considering the possibility that this failure could reflect a low reactivity as the result of steric hindrance resulting from the neighboring gem dimethyl groups, it was decided to introduce first an alkynyl "spacer" and then subsequently functionalize the terminus of this potentially reactive group. Such an approach would allow us to take advantage of Sonogashira coupling methods that we have previously used to good effect to functionalize calixpyrrole[8b,15] and other systems[16]. In accord with such thinking, intermediate **2** was carried on to the protected alkynyl derivative **3** in 73% yield by exposure to excess TMS-acetylene in diisopropylamine–DMF at 80 °C in

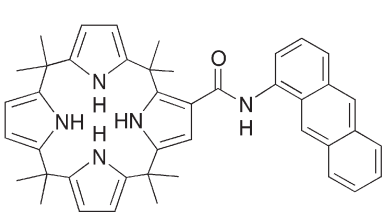


SCHEME 1

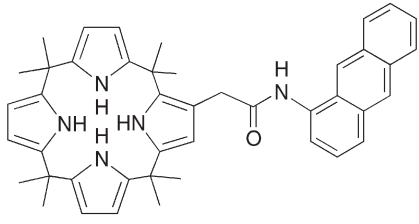
Reagents: (i) I_2-$(CF_3CO_2)_2PhI$ (20%); (ii) TMS-acetylene, $[Pd(PPh_3)_4]$ (73%), CuI; (iii) tetrabutylammonium fluoride, then $NaHCO_3$ (89%); (iv) ArI, $[Pd(PPh_3)_4]$, CuI. Yields: **5**, 87%; **6**, 82%; **7**, 67%; **8**, 79%; **9**, 69%; **10**, 73%; **11**, 82%

the presence of $[Pd(PPh_3)_4]$–CuI. Compound **3** was deprotected by exposure to tetrabutylammonium fluoride in THF at room temperature; this gave the desilylated compound **4** in 89% yield after basic work-up. Once obtained, ethynylcalix[4]pyrrole **4** was reacted with various aromatic iodides in the presence of $[Pd(PPh_3)_4]$ and CuI to give the arylalkynyl-functionalized products **5**–**11** in excellent yields as shown in Scheme 1 (cf. Experimental).

Compound **9** contains an anthracene fluorophore as its putative signaling moiety. As can be inferred from the line drawing in Scheme 1, in the case of **9**, this fluorophore is connected to a β-pyrrolic position of a calix[4]pyrrole through an acetylene bridge. Previously, we reported anthracene-functionalized calix[4]pyrroles wherein this same fluorophore is linked via amido linkages (cf. structures **12** and **13**)[7a]. Such systems were found to undergo quenching in the presence of anionic analytes (particularly fluoride anion) and were thus considered to be useful first generation sensors. Because of the presence of a direct π-conjugation pathway between the anthracene and calix[4]pyrrole moieties in **9**, it was thought that this latter system would act as a more sensitive, and hence improved anion sensor.



12



13

Here, it is important to appreciate that it is the extent of absolute quenching that establishes the sensitivity (and ultimately "real world" utility) of a potential fluorescence-based sensor, whereas it is the relative degree of quenching (i.e., as a percentage of total quenching at full saturation) that reflects the extent of binding at any given analyte concentration. Thus, it is quite possible to have a sensor that is inherently more sensitive, even though it binds its targeted substrate less well. Such potential considerations are important in the case of **9** vs **12** and **13** since the latter (especially **12**) contain linking amide moieties that could provide ancillary sites for anion recognition, even though they do not provide a direct electronic connection between the anthracene fluorophore and the calix[4]pyrrole anion binding site. As discussed below, system **9**, which was designed to provide such a direct electronic coupling connection (vide supra), was

found to be a far more sensitive sensor than either **12** or **13**, as reflected in the fact that the absolute extent of quenching at any given anionic analyte concentration was observed to be greater. However, with the exception of phosphate anion, where an increased affinity was seen for the more tightly linked amide system, **12**, as a general rule **9** and **12** displayed anion affinities that were roughly commensurate with one another.

As in previous work[7], fluorescence titration experiments were carried out by adding solutions of various anions, namely fluoride, chloride, bromide, dihydrogenphosphate, or hydrogensulfate (in the form of their commercially available tetrabutylammonium salts) to 50 μM solutions of compounds **9** in dichloromethane. Due, presumably, to the strong electric interaction between the anthracene subunit and the calix[4]pyrrole anion binding site, the absorption maximum of the anthracene moiety of compound **9** was also found to be changed, undergoing a red shift, as the result of anion binding. While these changes were not sufficiently great or in appropriate wavelength to allow for the use of compound **9** as a colorimetric sensor, they did allow for the study of this system by absorption-based methods (vide infra), they also required that care be taken in carrying out fluorescence quenching-based analyses. In particular, these spectral shifts required that the excitation wavelength (λ_{ex}) for quantitative fluorescence titration analyses be chosen so as to coincide with a region where the absorption spectrum was invariant to the presence or absence of an added anion (i.e., an isosbestic point). In the case of tetrabutylammonium fluoride, this isosbestic point appeared at 413 nm. Using this excitation wavelength, the maximum fluorescence emission ($\lambda_{em,max}$) appeared at 468 nm. As expected, the fluorescence signal was found to be substantially quenched upon the addition of tetrabutylammonium fluoride (Fig. 2), with the degree of quenching at any given fluoride anion concentration (including, of course, at full saturation) being far greater than that previously observed in the case of either **12** or **13** [7a].

Fluorescence quenching was also observed to varying degrees when other anions were added to dichloromethane solutions of receptor **9**. However, as can be seen from an inspection of Fig. 3, the extent of quenching was greatest in the case of fluoride, followed by chloride and dihydrogenphosphate. This same conclusion may be drawn from the data tabulated in Table I, which provides not only a comparison of the fluorescence quenching seen for compound **9** in the presence of various anions, but also that observed for its amide-linked congeners, **12** and **13**. A comparison with compound **12** and **13** shows the π-conjugated system **9** acts as a far more sensitive halide anion sensor in that the extent of quenching in an absolute sense is al-

ways greater at any given analyte concentration. For example, after the addition of 1 equivalent of fluoride anion, the fluorescence of **9** was decreased to 7% of its initial intensity. In contrast, the fluorescence signals for **12** and **13** were decreased to 17 and 48% of their initial values, respectively. The

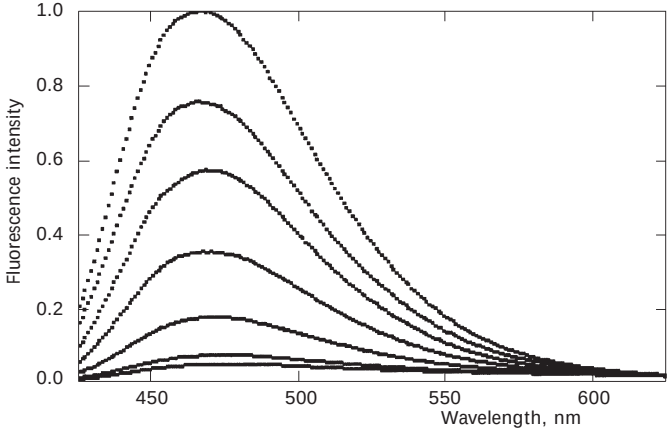


FIG. 2

Fluorescence spectra of **9** (50 μmol/l, CH_2Cl_2, 25 °C) showing the quenching induced upon treatment with, from top to bottom, 0, 0.2, 0.4, 0.6, 0.8, 1, and 1.2 equivalents of tetrabutylammonium fluoride

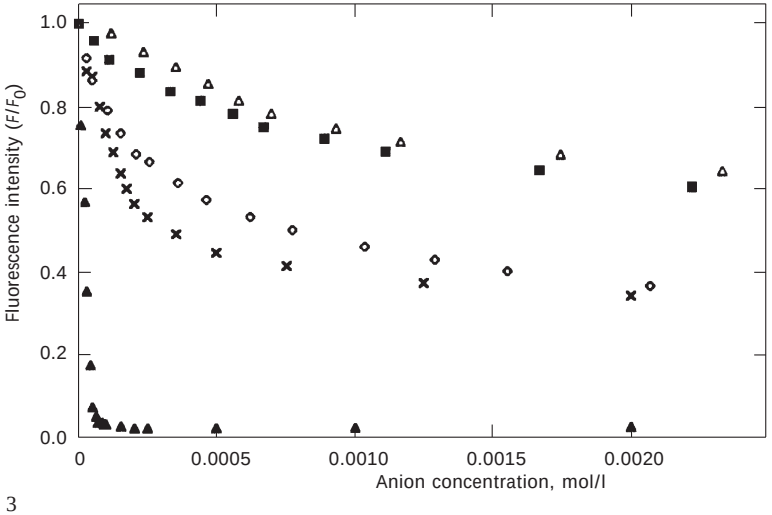


FIG. 3

Relative quenching induced by the addition of various anions to dichloromethane solutions of compound **9** (50 μmol/l, 25 °C). The observed changes were normalized to the initial fluorescence intensity and are recorded at the point of maximum fluorescence intensity, $\lambda_{em,max}$. Anions: × Cl^-, ◇ $H_2PO_4^-$, ■ Br^-, △ HSO_4^-

greater sensitivity of **9** leads us to propose that it could be applied for the quantitative analysis of fluoride anions, at least in organic media. Consistent with such a proposition, it was found that nearly complete fluoride-induced fluorescence quenching (>95%) was observed at an instrument-limited detection limit of 10 nM (concentration of **9** in dichloromethane) in the presence of 5 equivalents of tetrabutylammonium fluoride. Such near-complete quenching was not observed in the presence of the other

TABLE I

Fluorescence quenching data for compounds **9**, **12**, and **13** measured in dichloromethane. Compound **9** was excited at 413 nm and the emission intensity was recorded at $\lambda_{em,max}$ = 468 nm, compound **12** was excited at 378 nm, $\lambda_{em,max}$ = 427 nm, whereas compound **13** was excited at 393 nm, $\lambda_{em,max}$ = 429 nm

Anion		**9**	**12**	**13**
F^-	1 equiv.	0.07	0.17	0.48
	2 equiv.	0.03	0.12	0.16
	5 equiv.	0.02	0.11	0.11
	10 equiv.	0.02	0.10	0.08
Cl^-	1 equiv.	0.87	0.81	0.90
	2 equiv.	0.74	0.72	0.86
	5 equiv.	0.53	0.57	0.78
	10 equiv.	0.45	0.47	0.70
Br^-	1 equiv.	0.91	0.99	0.99
	2 equiv.	0.88	0.98	0.99
	5 equiv.	0.78	0.95	0.97
	10 equiv.	0.69	0.92	0.94
$H_2PO_4^-$	1 equiv.	0.86	0.63	0.87
	2 equiv.	0.79	0.44	0.83
	5 equiv.	0.66	0.27	0.77
	10 equiv.	0.58	0.21	0.71
HSO_4^-	1 equiv.	0.98		
	2 equiv.	0.93	No significant quenching observed	No significant quenching observed
	5 equiv.	0.81		
	10 equiv.	0.71		

anionic analytes investigated, although easily discernible quenching was observed for all the species tested. Taken together, these findings provide support for the notion that **9** is not only a potentially sensitive, but also likely a selective, fluoride anion sensor.

Association constants (K_a) for the interaction of **9**, **12**, and **13** with various anions were determined from fluorescence quenching studies using Scott-type analyses[10], as employed previously by our group[7]. The results are shown in Table II. In accord with expectations and reflecting the relative quenching values given in Table I, dihydrogenphosphate was found to be bound more strongly by the amide-linked receptor **12** than by the new, alkyne-bridged system **9**, with the K_a values for **9** and **13** being the same within error. Such findings are consistent with dihydrogenphosphate, a potentially multitopic anionic analyte, interacting not only with the calix[4]pyrrole NH-rich core, but also with the bridging amide moiety in the case of **12** and, possibly, **13**. Such ancillary interactions are likely to be less important in the case of the simple halides, fluoride, chloride, and bromide, and consistent with such thinking the affinity constants for each of these analytes were found to decrease in the order **9** > **12** > **13**. However, the effects were not large and thus to a first approximation, these two disparate receptor classes appear to bind halide anions more or less equally well.

Replacing the fluorophore present in **9** by a chromophore is of interest because it could lead to colorimetric anion sensors, wherein changes in the UV-VIS absorption spectrum or naked-eye detectable changes in color are used to signal the presence of an anion. With such an objective in mind,

TABLE II

Association constants (log K_a) for compounds **9**, **12**, and **13** with various anions as determined from fluorescence quenching studies carried out in dichloromethane[a]

Anion	**9**	**12**	**13**
F^-	>5	4.94	4.52
Cl^-	3.86	3.69	2.96
Br^-	3.14	3.01	[b]
$H_2PO_4^-$	3.56	4.20	3.56
HSO_4^-	1.52	[b]	[b]

[a] Errors are estimated to be <15%. [b] Quenching insufficient to provide an accurate stability constant value.

we prepared compounds **6**–**8**, **10**, and **11**. In all cases, a visible light-absorbing chromophore, designed to provide a read-out signal, was attached to a calix[4]pyrrole anion binding core via the same alkyne-derived, π-conjugated pathway present in **9**.

The first system prepared was the nitrobenzene conjugate **6**. It was synthesized because the absorption maximum of the nitrobenzene moiety in organic solvent lies in the UV region ($\lambda_{max} < 400$ nm) but was expected to shift into the visible region ($\lambda_{max} \geq 400$ nm) upon the addition of anions. We believed that such an anion-induced change from essentially colorless to colored, would provide an attractive "switched-off", "switched-on" type of sensor. In the event, the absorption maximum of calix[4]pyrrole **6**, coming at 391 nm in dichloromethane in the absence of an anion, was found to shift to 433 nm upon the addition of tetrabutylammonium fluoride in slight excess. As a result of this change in λ_{max}, the color of the solution changes from almost colorless (pale yellow) to an intense, easy-to-visualize yellow (cf. Fig. 4). While these color changes did not provide the complete "off-on" demarcation that was originally sought, it is noteworthy that compound **5**, synthesized as a control (absorption maximum in the UV spectral region), did not show any kind of visible color change, even when exposed to a considerable excess of fluoride anion.

The effects of various other anions were also tested in the case of **6** and the results of these experiments are also reproduced in Fig. 4. As can be

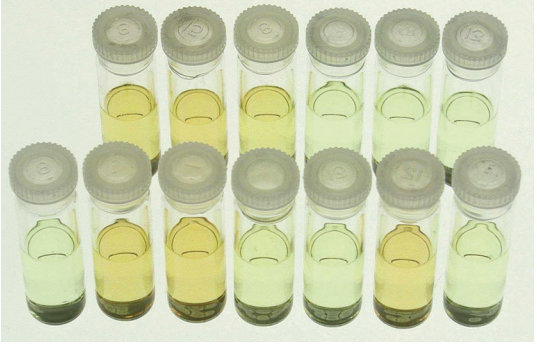


FIG. 4

Photograph showing dichloromethane solutions of **6** (5.0×10^{-5} mol/l) observed in the presence and absence of 100 molar equivalents of representative anions (studied in the form of their tetrabutylammonium salts). Front row, from left to right: **6**, **6** + F^-, **6** + Cl^-, **6** + Br^-, **6** + I^-, **6** + $H_2PO_4^-$, **6** + HSO_4^-. Back row, from left to right: **6** + AcO^-, **6** + BzO^-, **6** + CN^-, **6** + NO_3^-, **6** + SCN^-, **6** + ClO_4^-

seen by an inspection of this figure, not only fluoride anion, but also chloride, dihydrogenphosphate, acetate, benzoate, and cyanide (used in the form of their tetrabutylammonium salts) induced a naked-eye detectable change in color when added in excess (100 molar equivalents) to dichloromethane solutions of calix[4]pyrrole **6** (50 μM concentration). On the other hand, no discernible change in color was induced when the tetrabutylammonium salts of bromide, iodide, nitrate, thiocyanate (SCN^-), and perchlorate were added to solutions of **6**, again at the 100 molar equivalent level.

Even more dramatic color changes were observed when dichloromethane solutions of receptor **7**, containing a dinitrobenzene read-out moiety, were treated with various anions (Fig. 5). In particular, the color was seen to change from yellow to red (≈orange) upon the addition of fluoride, chloride, dihydrogenphosphate, acetate, benzoate, cyanide anions (again 100 molar equivalents; tetrabutylammonium salts). Presumably, these easier-to-visualize changes reflect the presence of the additional electron-withdrawing group (NO_2), which served both to shift the absorption maximum of calix[4]pyrrole **7** and its anion complexes into a region of the visible spectrum where our eyes are more sensitive and to produce a sensor that is more responsive to small changes in its overall electronics. In support of the latter supposition, the absorption maximum of **7**, appearing at 441 nm in the absence of an anion, was found to undergo a bathochromic shift to 498 nm in the presence of fluoride anion. Unfortunately, this par-

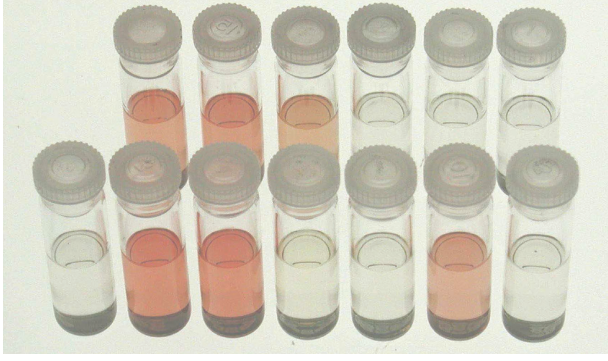


FIG. 5

Photograph showing dichloromethane solutions of **7** (5.0×10^{-5} mol/l) observed in the presence and absence of 100 molar equivalents of representative anions (studied in the form of their tetrabutylammonium salts). Front row, from left to right: **7**, **7** + F^-, **7** + Cl^-, **7** + Br^-, **7** + I^-, **7** + $H_2PO_4^-$, **7** + HSO_4^-. Back row, from left to right: **7** + AcO^-, **7** + BzO^-, **7** + CN^-, **7** + NO_3^-, **7** + SCN^-, **7** + ClO_4^-

ticular system proved less than fully stable. Thus, the use of nitroaryls was abandoned in favor of other types of chromophores.

In an initial effort to introduce a different kind of chromophore, an azo dye was connected to calix[4]pyrrole to give system **8**. In this case, the absorption maximum of the attached *N*,*N*-dimethylaminophenylazobenzene chromophore, observed at 441 nm in dichloromethane in the absence of an added anion was found to undergo only a 20 nm bathochromic shift (to 461 nm) in the presence of excess fluoride anion. As a consequence, the color of the solution was yellow both before and after the addition. These observations, in turn, led us to consider that chromophores containing electron-withdrawing groups, capable of effecting a "pull" to complement the charge-transfer "push" arising from bound calix[4]pyrrole–anion complex, would give rise to greater bathochromic shifts and hence more easily visualized anion-induced color changes.

Quinones are known to be electron-deficient compounds. We chose anthraquinones because we expected that the "push-pull" effect postulated above would be dramatic in the case of these easy-to-see chromophores. Accordingly, the anthraquinone-functionalized calix[4]pyrrole **10** was prepared. In this case, the colors of dichloromethane solutions were found to change from yellow in the absence of anions to red (or orange-red) upon

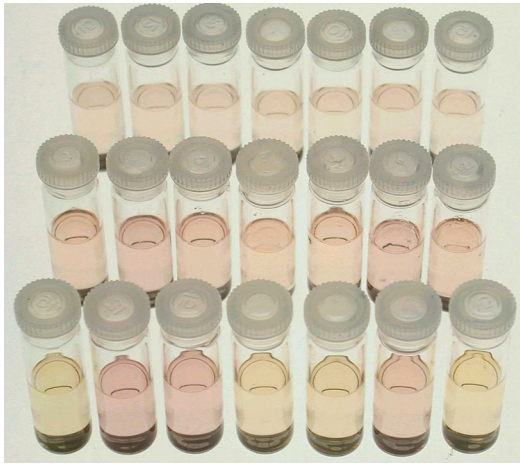


FIG. 6

Photograph showing solutions of **10** (5.0×10^{-5} mol/l) observed in the presence and absence of 100 molar equivalents of representative anions as recorded in three different solvents. Anions, from left to right: **10**, **10** + F^-, **10** + Cl^-, **10** + Br^-, **10** + I^-, **10** + $H_2PO_4^-$, **10** + HSO_4^-. Solvents, from front to back: CH_2Cl_2, DMSO, ethanol

the addition of 100 equivalents of fluoride, chloride, dihydrogenphosphate, acetate, benzoate, and cyanide anions, but not in the presence of equal quantities of bromide, iodide, sulfate, nitrate, isocyanate, or perchlorate anions (all studied in the form of the corresponding tetrabutylammonium salts). In the case of fluoride anion, where specific measurements were made, the absorption maximum of **10** was found to shift from 467 nm (yellow) to 518 nm (red) upon the addition of 100 equivalents of fluoride anion.

The strong spectral shifts seen in the case of **10** and the ease with which the anion binding process could be followed by simple naked-eye visualization, led us to study solvent and concentration effects in some detail. As illustrated in Fig. 6, moving from dichloromethane to the more polar solvent, DMSO, served to obviate in large measure the color changes induced via the addition of chloride and dihydrogenphosophate anions (100 molar equivalents). In this solvent, the extent of the fluoride-induced color change was also strongly reduced, although it remained readily discernable upon the addition of 100 molar equivalents. By contrast, in ethanol no detectable color changes were seen with any of the anions tested, at least at the studied 100 molar equivalent level used for this study. Such a result, which was anticipated on the basis of previous studies[4,17], is consistent with a strong competition between this highly polar, hydrogen bonding solvent and either the added anionic salts, or the calix[4]pyrrole receptor, or both.

The above observations provide a potential limit to the "real world" utility of sensors such as **10** and others described in this report: They will need to be applied under conditions where the polarity of the environment can be effectively controlled. However, it is important to appreciate that under appropriate conditions **10** and its congeners are potentially very sensitive sensors. This impression is underscored by dilution studies, such as those illustrated in Fig. 7. This figure shows the effect of varying concentration on the anion-dependent color changes observed for dichloromethane solutions of receptor **10**. As is readily apparent on simple inspection, the addition of 100 molar anion equivalents of fluoride, chloride, and dihydrogenphosphate serves to induce a visible change in the color of the solution, whereas under these conditions the addition of bromide, iodide, and sulfate anions do not. As the number of molar anion equivalents is reduced from 100 to 20, the color changes become less dramatic, with those induced by the addition of chloride and dihydrogenphosphate being discernable only with difficulty. Finally, at the 2 molar equivalent level, the only solution that displays a clear, anion-induced color change is the one containing fluoride. This finding, which provides another "hint" that receptors such as those described here could find use in fluoride anion detec-

tion applications, is in accord with the higher anion affinity expected for this latter anion relative to chloride and phosphate.

Quantitative analyses of the anion binding behavior of compound **10**, as well as of its congeners **5**–**9** and **11** (vide infra), were carried out by monitoring the spectral shifts as a function of added fluoride, chloride, and dihydrogenphosphate anion concentration. The use of standard Benesi–Hildebrand plots[10,13] then allowed calculation of the affinity constants (K_a). In all cases, excellent fits of the data were obtained assuming a 1:1 binding profile, as would be expected on the basis of prior work with calix[4]pyrroles[4]. Comparison of the resulting values, shown in Table III, served to confirm the anticipated trend, namely that the affinity constants, K_a, decreased in the order $F^- > Cl^- > H_2PO_4^-$. Similar comparisons also served to highlight that the nitrobenzene and in particular dinitrobenzene, and functionalized systems **6** and **7** displayed the highest anion affinities. By contrast, the hydroxyanthraquinone system, with its electron-donating, phenol-like functionality, displayed the lowest anion affinities. Finally, perhaps as expected, the anthraquinone-containing sensor **10** was found to have affinities that were essentially analogous to those of the, anthracene-derived "control" system, **9**.

Interestingly, in the case of **9**, the only system studied by both methods, the association constants (K_a) determined via fluorescence quenching (cf.

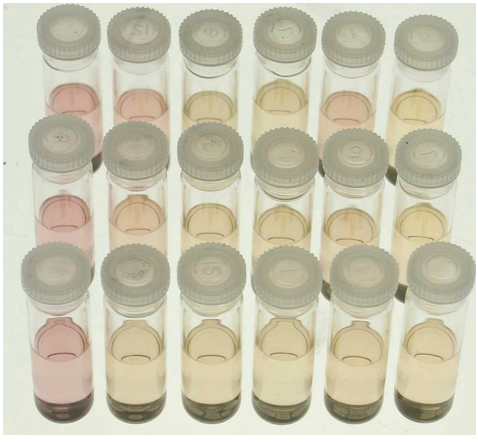
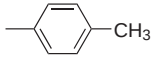
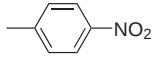
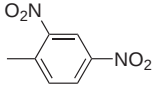
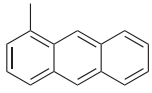
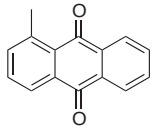
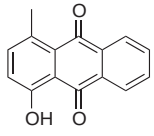


FIG. 7

Photograph showing dichloromethane solutions of **10** (5.0×10^{-5} mol/l) observed in the presence and absence of different concentrations (anion equivalents) of representative anions. Solutions, from left to right: **10** + F^-, **10** + Cl^-, **10** + Br^-, **10** + I^-, **10** + $H_2PO_4^-$, **10** + HSO_4^-. Anion equivalents for each row, from front to back: 2, 20, 100

Table II) proved to be higher than those calculated from fits to the UV-VIS data (cf. Table III). These differences, which are most substantial in the case of fluoride anion, are thought to reflect the fact that the coupling between the bound anion and the anthracene read-out moiety is enhanced in the

TABLE III
Association constants (log K_a values) for compounds **5**–**7** and **9**–**11** with anions determined from UV-VIS titrations in dichloromethane

Compounds	Ar	F^-	Cl^-	$H_2PO_4^-$
5		4.04	3.36	2.68
6		4.23	3.67	3.03
7		4.51	3.84	3.28
9		3.66	3.16	2.86
10		3.71	3.16	3.04
11		3.43	3.13	2.76

excited state relative to the ground state; this enhanced coupling, which allows for increased charge transfer, and with it fluorescence quenching, is as expected for a system bridged via a π-conjugated alkyne linker. Less clear, however, is which method (UV-VIS vs fluorescence quenching) provides a K_a value that most accurately reflects the thermodynamics of the actual anion binding process. This uncertainty notwithstanding, the key point is that both sets of studies give rise to association constants that point to the fact that system **9** (and, by inference, system **10**) binds fluoride anion extremely well in dichloromethane.

While displaying the lowest anion affinities of the various alkyne-linked systems produced to date, the hydroxyanthraquinone derivative **11** is endowed with one important attribute that makes it very attractive as a potential fluoride anion sensor, namely that it is red in the absence of an added anion and provides a purple-blue response when exposed to certain anionic analytes (viz. fluoride, chloride, dihydrogenphosphate, acetate, benzoate, and cyanide; cf. Fig. 8). This feature, which was highlighted in our initial communication[8b], is important not only for the increased sensitivity that it provides (the human eye responds more readily to color changes in the blue-green spectral region), but also because it shows that through the careful choice of read-out elements, it is possible to span, and hence exploit for use, the full range of the visible spectrum. This ability to fine-tune the response and effect sensing at more than one wavelength is likely to be particularly important in multi-analyte or array-type sensing

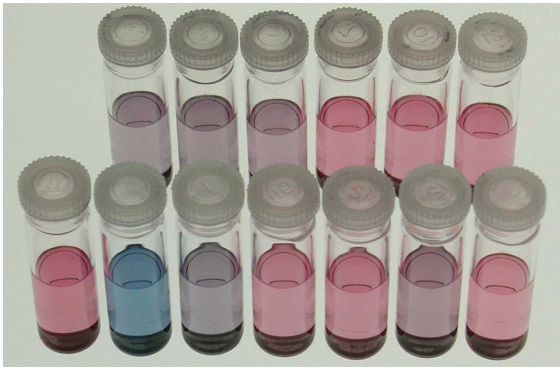


FIG. 8

Photograph showing solutions of **11** (5.0×10^{-5} mol/l) observed in the presence and absence of 100 molar equivalents of representative anions. Front row, from left to right: **11**, **11** + F^-, **11** + Cl^-, **11** + Br^-, **11** + I^-, **11** + $H_2PO_4^-$, **11** + HSO_4^-. Back row, from left to right: **11** + AcO^-, **11** + BzO^-, **11** + CN^-, **11** + NO_3^-, **11** + SCN^-, **11** + ClO_4^-

applications. On a more immediate level, it serves to underscore the versatility of the alkyne-tethered, calix[4]pyrrole-based approach described in this report.

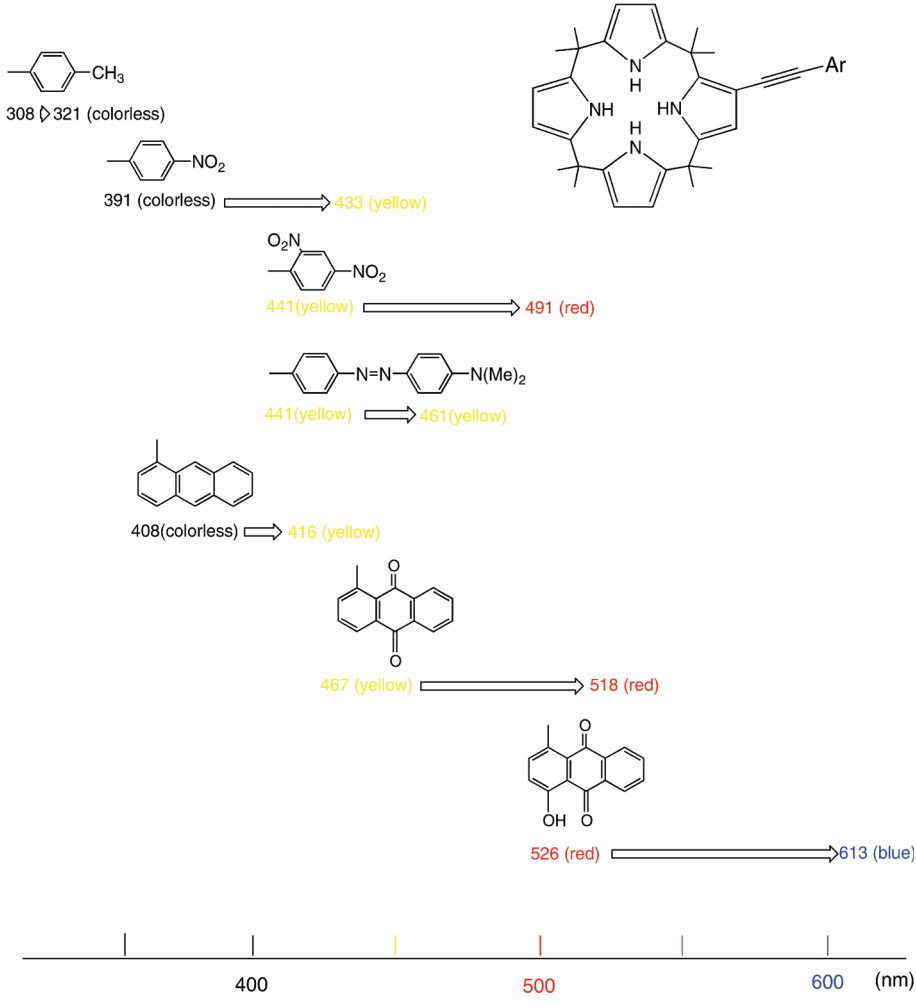


FIG. 9

Graphical representation of the color tuning that is possible in the present [4]pyrrole-based approach to colorimetric sensor development as the result of replacing the alkyne-appended chromophore. These latter optical read-out elements are represented by Ar in the line drawing at top right and are specifically shown for each individual species as part of the main graphic

CONCLUSIONS

Building on work that has been communicated previously[8], we have been able to show here that calix[4]pyrroles connected to a fluorophore (i.e., anthracene) through an acetylene linker, give rise to highly effective anion sensors (compound **9**), presumably because of the enhanced electronic interactions such a π-conjugated group provides relative to earlier, first-generation amide-based systems. The strong fluorescence quenching seen in the case of fluoride anion in dichloromethane allows this analyte to be detected at or below 50 nM concentrations, provided competing solvents are avoided.

Replacing the fluorophore present in **9** by a chromophore, such as a nitroaromatic or anthraquinone derivative, provides colorimetric sensors (e.g., **5**–**7** and **10**, **11**) that allow for the detection of various anionic analytes via simple naked-eye visualization in organic media. As with **9**, these systems are most selective for fluoride anion, however, chloride, dihydrogenphosphate, acetate, benzoate, and cyanide anions will all trigger a detectable color change (i.e., detectable response) when added in excess to dichloromethane solutions of the sensor system in question. Because the chromophore read-out element used to produce the anion-induced color change may be varied seemingly at will (as long as its linkage to the key alkynyl-substituted precursor, **4**, can be effected via Sonogashihara coupling), this generalized approach to sensor development appears quite powerful. In the present study, we have shown that it may be used to produce systems whose colors, both before and after the addition of anions, span nearly the full range of the visible spectrum as summarized graphically in Fig. 9. Current work, therefore, is being devoted to extensions of this approach that involve the use of yet additional chromophores and improved anion binding cores (e.g., modified, higher affinity calixpyrroles), as well as studying its application in situations, such as multianalyte array-based sensing, where the ability to effect an anion triggered response at multiple, independent wavelengths could be beneficial.

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