Metal ion detection by luminescent 1,3-bis(dimethylaminomethyl) phenyl receptor-modified chromophores and cruciforms†

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Chromophores ranging from simple small molecule π-conjugated systems comprised of phenylene ethynylene or fluorenylethynyl units to cross-conjugated Bunz-type cruciforms have been derivatized to include 1,3-bis(dimethylaminomethyl)phenyl moieties. The photophysical responsiveness of these diamino-substituted chromophores to metal ions has been examined. Both emission enhancement (turn-on) and ratiometric fluorescence detection of Cu^{2+} and Zn^{2+} ions have been achieved in THF.

Introduction

The interaction of metal ions with ligand-modified chromophores/fluorophores can be exploited for the formation of well-ordered, optically active coordination polymers or for spectroscopic metal ion detection. In the field of metal ion sensing, fluorophores are often modified with specialized multidentate ligands that selectively bind a target ion by specific binding site size/shape and electronics.[1–15] For example, 2,2′-bis(2-picolyl)amino derivatives are often used for Zn^{2+} sensors,[6–12] and bis(2-aminophenoxy)ethane-*N*,*N*,*N*′,*N*′-tetraacetic acid (BAPTA) is used in popular commercial Ca^{2+} biosensors.[13–15] The multi-step syntheses often required to prepare such ligand–fluorophore constructs slows sensor development and increases the cost of chemosensors. We recently reported our efforts to prepare selective sensors featuring simpler, more promiscuous ligand motifs such as 2,2′-bipyridyl (bipy).[16] In that example, a 1 : 1 ligand–metal binding was mediated by strategic placement of sterically encumbered substituents, and selectivity for Zn^{2+} was derived from its closed-shell d^{10} electronic configuration. In the current study, we continue to explore the potential utility of simpler ligand sets for metal ion sensing by preparing several 1,3-bis(dimethylaminomethyl)phenyl-modified chromophores/fluorophores (Chart 1). Dimethylaminomethyl substituents were selected to be weakly metal-binding moieties that are synthetically trivial to incorporate into various platforms. These units are also attractive because they do not exhibit an elaborate predefined binding pocket or ligand set designed for a specific metal ion. It is important to note that the amino group is insulated from the π-system by an intervening methylene, such that the N lone pair cannot participate directly with the chromophore π-system *via* n–π interactions. Ratiometric fluorescence sensors could thus be accomplished through the inductive perturbation of the π-system rather than quenching, which is often observed when a metal ion coordinates an atom that forms a part of the π-system. Selectivity for metal ions may be accomplished if different metal ions perturb the N lone pairs to different extents relative to the appended π-system and will depend on the relative energies of the π, π* and nonbonding nitrogen lone pair orbital. Turn-on fluorescent sensors, for example, could be accomplished when the orbitals are of appropriate energies for a photoinduced electron transfer (PET)-type mechanism.

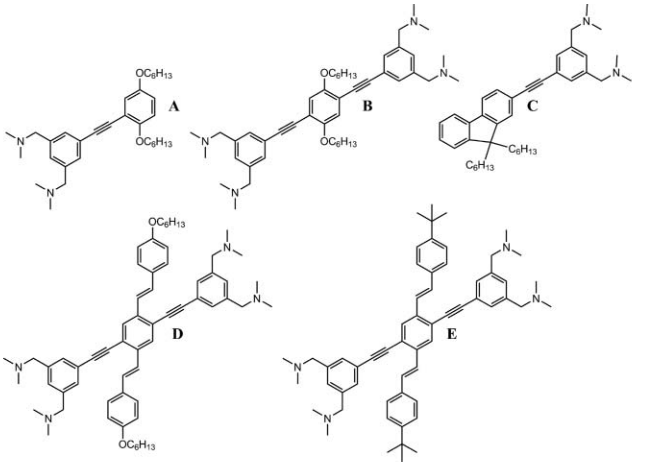

Chart 1 Structures of the 1,3-bis(dimethylaminomethyl)phenyl-substituted chromophores studied herein.

Because our group's main interests lie in π-conjugated polymer (CP) based sensors, chromophores representing small sections of common CPs were selected for initial screening (Chart 1). Both the conjugation length and the electronic properties of the chromophores were varied in order to access a wider range of π-system energies. Compound **A** is a short π-system with electron-releasing hexyloxy substituents, while the other short π-system in **C** is more electron deficient. Compound **B** was designed as an analogue of **A** with a longer effective conjugation length and an additional metal binding arm. Compounds **D**, with electron-releasing hexyloxy groups, and less electron-rich **E** are examples of cross-conjugated molecules sometimes called cruciforms. Of particular importance for sensing are the Bunz-type cruciforms comprising a 1,4-distyrylbenzene branch whose π-system overlaps that of a 1,4-di(2-arylethynyl)benzene at a shared central aryl ring (Chart 2).[17] The presence of two cross-conjugated π-systems in such molecules can lead to geometrically separate HOMO and LUMO and consequent possibility for intramolecular

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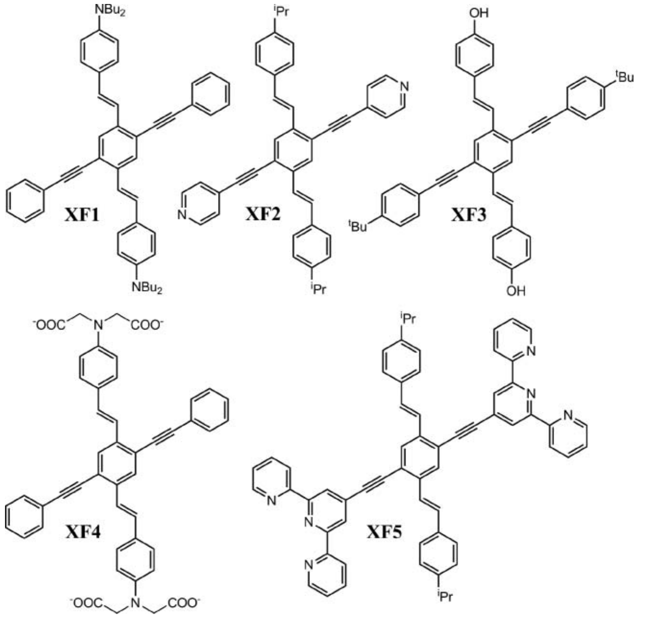


Chart 2 Some cruciforms that have been used as fluorescent sensors.

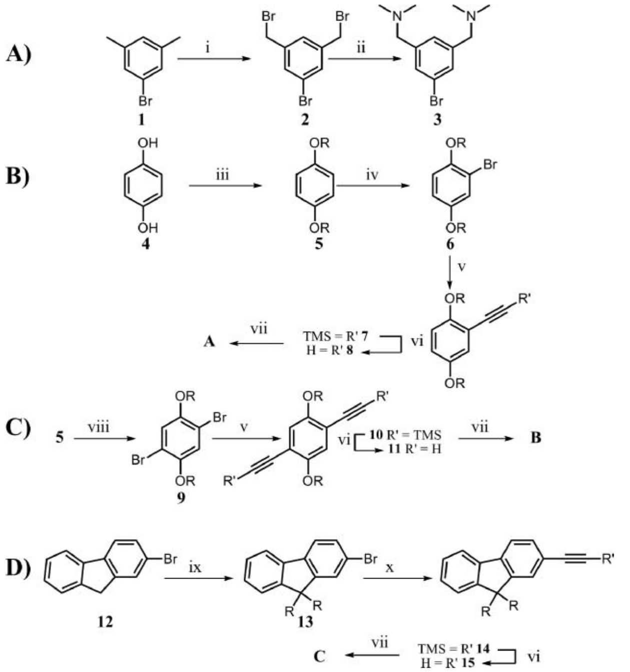
charge transfer bands in the absorption spectra. Bunz's group has demonstrated how the unique nature of these π-systems makes them outstanding candidates for metal ion sensing when modified with ligands. The two cruciforms are of interest in the current context primarily for comparison to the metal-ion sensing ability of compound **B**, which has a similar π-system to the ethynylene-containing cruciform branches, and to accomplish ratiometric fluorescence signal transduction.

The current work describes the synthesis of dimethylaminomethyl-derivatized cruciforms **D** and **E** and of single-branch compounds **A–C** with accompanying photophysical characterization, metal ion response studies and density functional theory (DFT) calculations. Ratiometric and fluorescence intensity enhancement ('turn-on') sensors for Zn^{2+} and Cu^{2+} are discussed.

Experimental

Materials and characterization methods

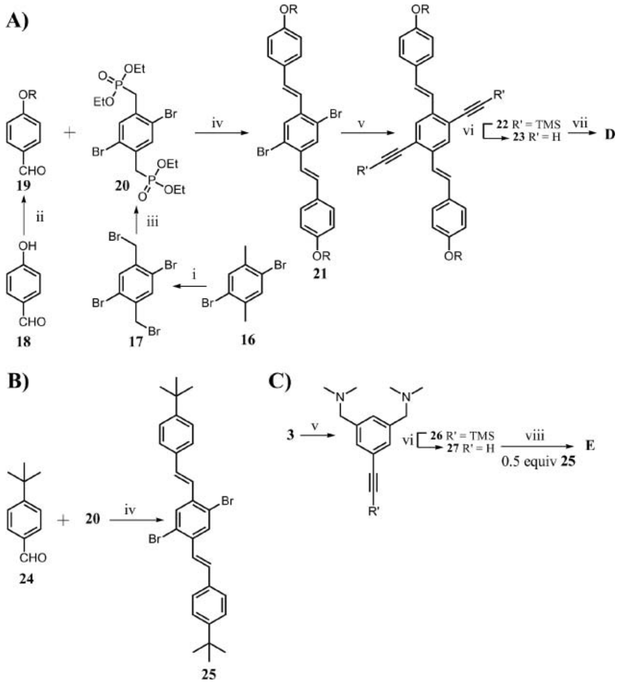
General. Reagents and solvents for extractions and chromatography were used as received from Acros, Aldrich Chemical Co., TCI America, or Alfa Aesar. Compound **2**, **3**, **26** and **27**;[18] **5** and **9**;[19] **6**;[20] **10** and **11**;[21] **13**, **14** and **15**;[22] **17**,[23] **19**,[24] **20**,[25] and [Pd(PPh$_3$)$_4$][26] were prepared as previously reported. Synthetic avenues are summarized in Schemes 1 and 2. All solvents for reactions were purified by passage through alumina columns under a N$_2$ atmosphere employing an MBraun solvent purification system. All the air sensitive reactions were performed in an MBraun dry box or using standard Schlenk techniques under a N$_2$ atmosphere. Proton, carbon-13 and phosphorus-31 NMR spectra were acquired on a Bruker Avance 300 spectrometer operating at 300, 75 and 121 MHz, respectively. All spectra were collected at 25 °C and referenced to trimethylsilane or residual solvent peak for proton and carbon-13, and to external 85% phosphoric acid for ^{31}P.



Scheme 1 A) Preparation of **3**: i. *N*-Bromosuccinimide, benzoyl peroxide, CHCl$_3$, Δ. ii. Dimethylamine, THF. B) Preparation of **A**: iii. Hexyl bromide, K$_2$CO$_3$, CH$_3$CN, Δ. iv. 1.1 equiv Br$_2$, CHCl$_3$. v. Trimethylsilylacetylene, Pd(PPh$_3$)$_4$, CuI, triethylamine, toluene, 85 °C. vi. NaOH (20% aq.), THF, MeOH. vii. **3**, Pd(PPh$_3$)$_4$, CuI, triethylamine, DMF, 85 °C. C) Preparation of **B**: viii. 2.2 equiv Br$_2$, CH$_2$Cl$_2$. D) Preparation of **C**: ix. Hexyl bromide, KOH, DMSO, Δ. x. Trimethylsilylacetylene, Pd(PPh$_3$)$_4$, CuI, diisopropylamine, 85 °C. R = *n*-hexyl in all cases.

Synthesis of (2-(2,5-bis(hexyloxy) phenyl)ethynyl) trimethylsilane (7). Under nitrogen, compound **6** (2.0 g, 5.6 mmol) was dissolved in toluene (20 mL) followed by addition of [Pd(PPh$_3$)$_4$] (0.036 g, 0.30 mmol) and copper iodide (0.064 mg, 0.30 mmol). Trimethylsilylacetylene (1.1 g, 11 mmol) was dissolved in triethylamine (20 mL) separately and added dropwise into the reaction mixture and stirred for 48 h at 85 °C. The reaction mixture was passed through silica, followed by washing with ether (70 mL). The organic layer was extracted with saturated aqueous sodium bicarbonate (4 × 100 mL), dried over sodium sulfate, and all volatiles were removed under reduced pressure. The residue was triturated with 20 mL pentane, and the pentane-soluble fraction was concentrated under reduced pressure, yielding **7** as a light yellow viscous oil (1.8 g, 86%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.27 (s, 9H; 3 × Si–CH_3), 0.90–0.95 (m, 6H; 2 × CH_3), 1.57–1.32 (m, 12H; 6 × CH_2), 1.86–1.71 (m, 4H; 2 × CH_2), 3.97 (t, 2H; J = 6.0 Hz, O–CH_2), 3.90 (t, 2H; J = 6.0 Hz, O–CH_2), 6.85–6.76 (m, 2H; Aromatic), 6.98 (d, 1H; J = 3.0 Hz, Aromatic). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 0.0, 14.0, 14.0, 22.6, 22.6, 25.7, 25.7, 29.2, 29.4, 31.5, 31.6, 68.6, 69.6, 98.1, 101.4, 113.3, 114.0, 116.9, 118.6, 152.6, 154.6.

Synthesis of 2-ethynyl-1,4-bis(hexyloxy) benzene (8). Compound **7** (0.3 g, 0.8 mmol) was dissolved in THF (20 mL) followed by the addition of methanol (10 mL) and 20% aqueous NaOH solution (10 mL) and stirred for 2 h at room temperature. Ether (30 mL) was added into the mixture, and extracted with water (4 × 50 mL). The organic layer was dried over sodium sulfate and



Scheme 2 A) Preparation of **D**: i. *N*-bromosuccinimide, benzoyl peroxide, $CHCl_3$, Δ. ii. Hexyl bromide, K_2CO_3, CH_3CN, Δ. iii. Triethyl phosphite, 90 °C, Δ. iv. Potassium *t*-butoxide, THF. v. Trimethylsilylacetylene, $Pd(PPh_3)_4$, CuI, triethylamine, toluene, 85 °C. vi. TBAF, THF. vii. **3**, $Pd(PPh_3)_4$, CuI, triethylamine, DMF, 85 °C. B–C) Preparation of **E**: viii. **25**, $Pd(PPh_3)_4$, CuI, triethylamine, DMF, 85 °C.

removed under reduced pressure, yielding a viscous oil (0.19 g, 80%). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, 6H; J = 6.0 Hz, 2 × CH_3), 1.52–1.32 (m, 12H; 6 × CH_2), 1.84–1.72 (m, 4H; 2 × CH_2), 3.26 (s, 1H; C≡CH), 3.91 (t, 2H; J = 6.0 Hz, O–CH_2), 4.00 (t, 2H; J = 6.0 Hz, O–CH_2), 6.89–6.80 (m, 2H; Aromatic), 7.01 (d, 1H; J = 3.0 Hz, Aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 22.6, 25.6, 25.7, 29.2, 29.2, 31.5, 68.7, 69.7, 80.1, 80.7, 112.3, 113.9, 117.0, 119.2, 152.6, 154.6.

Synthesis of compound A. Under nitrogen, compound **3** (0.57 g, 2.1 mmol) was dissolved in *N*,*N*-dimethylformamide (DMF, 40 mL) followed by the addition of [$Pd(PPh_3)_4$] (0.13 g, 0.13 mmol) and copper iodide (0.024 g, 0.13 mmol). Compound **8** (0.70 g, 2.3 mmol) was dissolved in triethylamine (20 mL) separately and added dropwise to the reaction mixture and stirred for 48 h at 85 °C. The reaction mixture was passed through silica, followed by washing with ether (20 mL). The organic layer was extracted with saturated sodium bicarbonate solution (4 × 100 mL) followed by extraction with 50% aqueous HCl solution (3 × 50 mL) and finally the aqueous layer was neutralized with NaOH pallets. This aqueous layer was extracted with ether (3 × 30 mL). The organic layer was dried over sodium sulfate and removed under reduced pressure. Column chromatography eluting with pentane through basic alumina (previously treated with triethylamine in ether then dried) afforded the product as a brown oil (0.12 g, 46%). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.90 (m, 6H; 2 × CH_3), 1.59 – 1.33 (m, 12H; 6 × CH_2), 1.87 – 1.75 (m, 4H; 2 × CH_2), 2.26 (s, 12H; 4 × N–CH_3), 3.42 (s, 4H; 2 × N–CH_2), 3.93 (t, 2H; J = 6.0 Hz, O–CH_2), 4.03 (t, 2H; J = 6.0 Hz, O–CH_2), 6.84 (t, 2H; J = 3.0 Hz, Aromatic), 7.02 (m, 1H; Aromatic), 7.27 (s, 1H; Aromatic), 7.40 (d, 2H; J = 3.0 Hz, Aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 14.0, 22.6, 22.6, 25.7, 25.8, 29.2, 29.4, 31.5, 31.6, 45.3, 63.9, 68.7, 69.8, 85.7, 93.3, 113.7, 114.2, 116.5, 118.3, 123.3, 129.6, 130.9, 139.1, 152.8, 154.0. HRMS $(M+H)^+$: calc'd for $C_{32}H_{49}O_2N_2$: 493.3794; found, 493.3790.

Synthesis of compound B. Under nitrogen, compound **3** (0.91 g, 3.3 mmol) was dissolved in DMF (40 mL) followed by the addition of [$Pd(PPh_3)_4$] (0.19 g, 0.20 mmol) and copper iodide (0.034 g, 0.20 mmol). Compound **11** (0.50 g, 1.5 mmol) was dissolved in triethylamine (20 mL) separately and added dropwise to the reaction mixture and stirred for 48 h at 85 °C. The reaction mixture was passed through silica followed by washing with ether (20 mL). The organic layer was extracted with saturated sodium bicarbonate solution (4 × 100 mL) followed by extraction with 50% aqueous HCl solution (3 × 50 mL) and finally the aqueous layer was neutralized with NaOH pallets. This aqueous layer was extracted with ether (3 × 30 mL). The organic layer was collected, dried over sodium sulfate and all volatiles were removed under reduced pressure. The residue was dissolved in the minimum amount of pentane and allowed to stand at room temperature overnight, leading to the formation of yellow crystals. The solid was collected by filtration and dried to afford **B** (0.46 g, 46%). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, 6H; J = 6.0 Hz, 2 × CH_3), 1.63 – 1.37 (m, 12H; 6 × CH_2), 1.88 (q, 4H; J = 6.0 Hz, 2 × CH_2), 2.27 (s, 24H; 8 × N–CH_3), 3.43 (s, 8H; 4 × N–CH_2), 4.05 (t, 4H; J = 6.0 Hz, 2 × O–CH_2), 7.02 (s, 2H; Aromatic), 7.41 (d, 4H; J = 3.0 Hz, Aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 22.6, 25.8, 29.3, 31.6, 45.4, 63.9, 69.6, 85.8, 94.9, 114.0, 117.1, 123.2, 129.8, 130.9, 139.2, 153.5. HRMS $(M+H)^+$: calc'd for $C_{46}H_{67}O_2N_4$: 707.5264; found, 707.5259.

Synthesis of compound C. Under nitrogen, compound **3** (0.40 g, 1.5 mmol) was dissolved in DMF (40 mL) followed by the addition of [$Pd(PPh_3)_4$] (0.11 g, 0.10 mmol) and copper iodide (0.019 g, 0.10 mmol). Compound **15** (0.60 g, 1.7 mmol) was dissolved in triethylamine (20 mL) separately and added into the reaction mixture dropwise and stirred for 48 h at 85 °C. The reaction mixture was passed through silica, followed by washing with ether (20 mL). The organic layer was extracted with saturated sodium bicarbonate solution (4 × 100 mL) followed by extraction with 50% aqueous HCl solution (3 × 50 mL) and finally the aqueous layer was neutralized with NaOH pallets. This aqueous layer was extracted with ether (3 × 30 mL). The organic layer was collected, dried over sodium sulfate and all volatiles were removed under reduced pressure. Column chromatography was done using pure pentane over basic alumina (previously treated with triethylamine in ether then dried) in order to get the desired dark yellow oil (0.42 g, 46%). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.81 – 0.61 (m, 10H; 2 × CH_3 and 2 × CH_2), 1.15 – 1.03 (m, 12H; 6 × CH_2), 1.98 (t, 4H; J = 9.0 Hz, 2 × CH_2), 2.28 (s, 12H; 4 × N–CH_3), 3.44 (s, 4H; 2 × N–CH_2), 7.27 (s, 1H; Aromatic), 7.39 – 7.34 (m, 3H; Aromatic), 7.46 (d, 2H; J = 3.0 Hz, Aromatic), 7.52 – 7.49 (m, 2H; Aromatic), 7.73 – 7.67 (m, 2H; Aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 22.6, 23.7, 29.7, 31.5, 40.4, 45.4, 55.1, 64.0, 89.5, 90.4, 119.6, 119.9, 121.5, 122.9, 123.2, 126.0, 126.8, 127.5, 129.7, 130.5, 130.9, 139.3, 140.4, 141.4, 150.7, 151.1. HRMS $(M+H)^+$: calc'd for $C_{39}H_{53}N_2$: 549.4209; found, 549.4200.

Synthesis of compound 21. Under nitrogen, compound **20** (3.5 g, 6.5 mmol) and 4-hexyloxy benzaldehyde (2.7 g, 13 mmol) were dissolved in dry THF (50 mL). Potassium *t*-butoxide (1.6 g, 14 mmol) was dissolved in dry THF separately and added dropwise to the reaction mixture and stirred overnight at room temperature. Methanol (100 mL) was added into the reaction mixture and all the volatiles were removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (150 mL) and extracted with water (3 × 100 mL). The organic layer was collected, dried over sodium sulfate and removed under reduced pressure, yielding a yellow solid. The crude solid was recrystallized from pure hexane (4.5 g, 54%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.94$ (b, 6H; 2 × CH_3), 1.52 – 1.34 (m, 12H; 6 × CH_2), 1.82 (q, 4H; $J = 6.0$ Hz, 2 × CH_2), 4.01 (t, 4H; $J = 6.0$ Hz, 2 × O–CH_2), 6.92 (d, 4H; $J = 9.0$ Hz, Aromatic), 7.02 (d, 2H; $J = 18$ Hz, $HC{=}CH$), 7.24 (d, 2H; $J = 18$ Hz, $HC{=}CH$), 7.50 (d, 4H; $J = 9.0$ Hz, Aromatic), 7.86 (s, 2H, Aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.0$, 22.6, 25.7, 29.2, 31.6, 68.1, 114.8, 122.8, 123.5, 128.3, 129.3, 130.0, 131.7, 137.8, 159.5. MALDI: calc'd for $C_{34}H_{40}Br_2O_2$: 638.1; found, 637.9.

Synthesis of compound 22. Under nitrogen, compound **21** (2.0 g, 3.1 mmol) was dissolved in toluene (20 mL) followed by the addition of $[Pd(PPh_3)_4]$ (0.40 g, 0.4 mmol) and copper iodide (0.070 mg, 0.4 mmol). Trimethylsilylacetylene (1.2 g, 12 mmol) was dissolved in triethylamine (30 mL) separately and added dropwise to the reaction mixture and stirred for 48 h at 85 °C. Ether (100 mL) was added to the reaction mixture and the organic layer was extracted with saturated sodium bicarbonate solution (4 × 150 mL), dried over sodium sulfate and evaporated under reduced pressure. The residue was dissolved in ether and passed through silica followed by washing with $CHCl_3$ (2 × 50 mL). The organic layer was collected and removed under reduced pressure, yielding a light yellow solid (1.1 g, 48%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.34$ (s, 18H; 6 × Si–CH_3), 0.94 (t, 6H; $J = 9.0$ Hz, 2 × CH_3), 1.52 – 1.34 (m, 12H; 6 × CH_2), 1.82 (q, 4H; $J = 6.0$ Hz, 2 × CH_2), 4.01 (t, 4H; $J = 6.0$ Hz, 2 × O–CH_2), 6.92 (d, 4H; $J = 9.0$ Hz, Aromatic), 7.17 (d, 2H; $J = 18$ Hz, $HC{=}CH$), 7.4–7.6 (m, 6H; Aromatic and $HC{=}CH$), 7.79 (s, 2H; Aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 0.0$, 14.1, 22.6, 25.7, 29.2, 31.6, 68.1, 100.7, 103.4, 114.8, 121.9, 123.3, 127.9, 128.4, 129.9, 130.0, 137.6, 159.2. MALDI: calc'd for $C_{44}H_{58}O_2Si_2$: 674.4; found, 674.3.

Synthesis of compound 23. Compound **22** (0.50 g, 0.70 mmol), was dissolved in THF (30 mL) followed by the addition of tetrabutylammonium fluoride trihydrate (2.2 g, 7.0 mmol) and stirred for 2 h at room temperature. Volatiles were removed under reduced pressure and ether (30 mL) was added into the residue followed by extraction with saturated bicarbonate solution (4 × 50 mL). The organic layer was collected, dried over sodium sulfate and evaporated under reduced pressure, yielding a yellow solid (0.35 g, 88%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.93$ (t, 6H; $J = 9.0$ Hz, 2 × CH_3), 1.52 – 1.34 (m, 12H; 6 × CH_2), 1.82 (q, 4H; $J = 6.0$ Hz, 2 × CH_2), 3.47 (s, 2H; $C{\equiv}CH$), 4.01 (t, 4H; $J = 6.0$ Hz, 2 × O–CH_2), 6.92 (d, 4H; $J = 9.0$ Hz, Aromatic), 7.15 (d, 2H; $J = 15$ Hz, $HC{=}CH$), 7.44 (d, 2H; $J = 15$ Hz, $HC{=}CH$), 7.50 (d, 4H; $J = 9$ Hz, Aromatic), 7.84 (s, 2H; Aromatic). MALDI: calc'd for $C_{38}H_{42}O_2$: 530.3; found, 530.4.

Synthesis of compound D. Under nitrogen, compound **3** (0.28 g, 0.80 mmol) was dissolved in DMF (40 mL) followed by addition of $[Pd(PPh_3)_4]$ (0.11 g, 0.10 mmol) and copper iodide (19 mg, 0.10 mmol). Compound **23** (0.20 g, 0.40 mmol) was dissolved in triethylamine (20 mL) separately and added dropwise to the reaction mixture and stirred for 48 h at 85 °C. The reaction mixture was passed through silica, followed by washing with ether (40 mL). The organic layer was extracted with saturated sodium bicarbonate solution (4 × 100 mL) followed by extraction with 50% aqueous HCl solution (3 × 50 mL) and finally the aqueous layer was neutralized with NaOH pellets. This aqueous layer was extracted with ether (3 × 30 mL). The organic layer was collected, dried over sodium sulfate and evaporated under reduced pressure. The residue was dissolved in the minimum amount of pentane and left to crystallize. The solid precipitate was filtered off as a pale yellow solid (0.30 g, 86%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.90$ – 0.96 (b, 6H; 2 × CH_3), 1.52 – 1.34 (m, 12H; 6 × CH_2), 1.82 (t, 4H; $J = 9.0$ Hz, 2 × CH_2), 2.30 (s, 24H; 8 × N–CH_3), 3.47 (s, 8H; 4 × N–CH_2), 4.01 (t, 4H; $J = 9.0$ Hz, 2 × O–CH_2), 6.94 (d, 4H; $J = 9.0$ Hz, Aromatic), 7.24 (d, 2H; $J = 15$ Hz, $HC{=}CH$), 7.32 (s, 2H; Aromatic), 7.58 – 7.49 (m, 10H; Aromatic), 7.88 (s, 2H; Aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.1$, 22.6, 25.7, 29.2, 31.6, 45.5, 64.0, 68.1, 87.9, 95.5, 114.8, 122.0, 123.0, 123.5, 128.1, 128.6, 129.9, 130.1, 130.9, 137.3, 139.4, 159.2. HRMS $(M+H)^+$: calc'd for $C_{62}H_{79}O_2N_4$: 911.6203; found, 911.6195.

Synthesis of compound 25. Under nitrogen, compound **20** (5.70 g, 10.6 mmol) and 4-*t*-butylbenzaldehyde **24** (3.45 g, 21.3 mmol) were dissolved in dry THF (50 mL). Potassium *t*-butoxide (2.62 g, 23.4 mmol) was dissolved in dry THF separately and added dropwise to the reaction mixture and stirred overnight at room temperature. Methanol (100 mL) was added into the reaction mixture and all the volatiles were removed under reduced pressure. The residue was dissolved into CH_2Cl_2 (150 mL) and extracted with water (3 × 100 mL). The organic layer was collected, dried over sodium sulfate and the solvent removed under reduced pressure, yielding a light yellow solid (3.5 g, 60%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.38$ (s, 18H; 6 × CH_3), 7.09 (d, 2H; $J = 16$ Hz, $HC{=}CH$), 7.39 (d, 2H; $J = 16$ Hz, $HC{=}CH$), 7.46 (d, 4H; $J = 8.4$ Hz, Aromatic), 7.54 (d, 4H; $J = 8.4$ Hz, Aromatic), 7.89 (s, 2H; Aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 31.2$, 34.7, 123.0, 125.1, 125.7, 126.7, 130.2, 131.9, 133.9, 137.3, 151.7. MALDI: calc'd for $C_{30}H_{32}Br_2$: 550.1; found, 550.2.

Synthesis of compound E. Under nitrogen, compound **25** was dissolved in DMF (20 mL) followed by the addition of $[Pd(PPh_3)_4]$ (44 mg, 0.040 mmol) and copper iodide (3.2 mg, 0.010 mmol). Compound **27** was dissolved in triethylamine (20 mL) separately and added dropwise to the reaction mixture and stirred for 48 h at 85 °C. Ether (20 mL) was added into the reaction mixture and washed with saturated sodium bicarbonate solution (4 × 50 mL). The organic layer was collected, dried over sodium sulfate and removed under reduced pressure. Ether (20 mL) was added to the residue and washed with concentrated 25% aq. H_2SO_4 solution (*v*:*v*) (2 × 25 mL). The aqueous layer was collected and neutralized by adding NaOH pellets (pH ~ 10). The aqueous layer was extracted with ether (3 × 20 mL). The organic layer was collected, dried over sodium sulfate and the solvent removed under reduced pressure, yielding a pale yellow solid. Finally the compound was purified over preparative TLC (CH_2Cl_2/Methanol, 200 : 1). (0.020 g, 10%) ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.37$ (s, 18H; C–CH_3), 2.23 (s, 24H; N–CH_3), 3.51 (s, 8H; N–CH_2), 7.25–7.33

(m, putatively 4H, aromatic, but overlaps $CHCl_3$), 7.40–7.45 (m, 4H; Aromatic), 7.51 (s, 4H; Aromatic), 7.58 (d, 4H; *J* = 8.4 Hz, Aromatic), 7.66 (d, 2H; *J* = 16 Hz, HC=CH), 7.91 (s, 2H; Aromatic). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 31.3$, 34.7, 45.3, 63.8, 76.6, 87.9, 95.5, 122.2, 123.0, 125.0, 125.7, 126.6, 128.7, 130.3, 130.4, 131.1, 134.6, 137.4, 138.9, 151.2. HRMS $(M+H)^+$: calc'd for $C_{58}H_{71}N_4$: 823.5679; found, 823.5684.

General spectroscopic methods

Absorption spectra were recorded on a Varian Cary 50 Bio UV-vis spectrophotometer. Photoluminescence (PL) spectra were recorded using a Varian Eclipse spectrofluorimeter. Samples for all absorption and photoluminescence spectra were prepared in HPLC grade tetrahydrofuran further purified in a MBraun Solvent Purification System. Absorption and photoluminescence spectra were recorded on samples in Spectrosil quartz cuvettes (Starna Cells, Inc.) having a path length of 1 cm. Quantum yields (Φ) for all compounds were calculated relative to quinine bisulfate in 0.1 M H_2SO_4 (aq) (Φ = 0.546).[27] Metal salts used for ion screening were $Co(NO_3)_2{\cdot}6H_2O$, $NiSO_4{\cdot}6H_2O$, $Cu(ClO_4)_2{\cdot}6H_2O$, $Zn(ClO_4)_2{\cdot}6H_2O$, $Cd(ClO_4)_2{\cdot}6H_2O$, $K(PF_6)$, $Na(PF_6)$, $Mg(SO_4)$, $CaCl_2$, $Eu(NO_3)_3$, $[Cu(NCMe)_4][BF_4]$ and $Hg(O_2CCF_3)_2$. *CAUTION*: *perchlorate salts are potentially explosive and should only be handled in small quantities by trained personnel familiar with their hazards.*

Absorption spectroscopic titrations with metal ions. A 3.0 mL aliquot of the compound of interest in THF (1.0×10^{-5} M for A, B and D; 1.6×10^{-5} M for C; 6.1×10^{-6} for E) was added to a cuvette. Aliquots of metal ion solution were added to the solutions and changes were followed by collecting an absorption spectrum after each addition.

Photoluminescence spectroscopy titrations with metal ions. As for absorption titration, but using solutions diluted by 10-fold and following titrations by photoluminescence spectroscopy with $\lambda_{ex} = \lambda_{max}$.

Results and discussion

Synthesis

The synthesis of compound **A** proceeded as shown in Scheme 1A–B. Commercial 5-bromo-*m*-xylene (**1**) underwent two-fold benzylic bromination to yield **2**[18] (27%). Condensation of **2** with aqueous dimethylamine provided key intermediate **3** (50%),[18] which eventually served as the ligand-appended subunit for all compounds **A–E**. The first step in preparing the second fragment of **A** was condensation of hydroquinone (**4**) with 1-bromohexane to give **5** (60%).[19] Although the next intermediate, **6**, was previously prepared from 1,4-dibromo-2,5-dihexyloxybenzene *via* single lithium–halogen exchange at low temperature followed by acid workup,[20] we found that **6** was more conveniently prepared in 33% yield by slow addition (over 12 h *via* syringe pump) of a solution of bromine in chloroform to **5** at room temperature. This route eliminates a step, and does not require dry ice cooling or use of a pyrophoric organolithium reagent. Sonogashira–Hagihara type coupling of trimethylsilylacetylene (TMSA) and **6** provided **7** (86%) which was deprotected by NaOH in water–THF–methanol (1 : 2 : 1) to give **8** (80%). Finally, compound **A** was prepared in 46% yield by Sonogashira–Hagihara type coupling of **3** and **8**.

Compound **B** was prepared by the sequence shown in Scheme 1C. Bromination of **5** gave **9** (80%),[19] which readily underwent double Sonogashira–Hagihara coupling with TMSA to give **10** (68%) which was subsequently deprotected by NaOH in water–THF to give **11** (90%).[21] Sonogashira–Hagihara coupling of **11** and **3** provided **B** (46%).

The first step in the preparation of fluorene derivative **C** (Scheme 1D) was alkylation of commercial 2-bromofluorene with 1-bromohexane in DMSO with KOH acting as the base to yield **13** (71%).[22] Sonogashira–Hagihara coupling of **13** and TMSA gave **14** (64%) that was subsequently deprotected by NaOH in water–methanol–THF (1 : 2 : 1) yielding **15** (95%).[22] Finally, Sonogashira–Hagihara coupling of **15** and **3** produced **C** (46%) as a yellow oil.

Cruciform **D** was prepared as outlined in Scheme 2A–B. Two-fold benzylic bromination of 2,5-dibromo-*p*-xylene (**16**) gave **17** (56%)[23] which was then subjected to a Michaelis–Arbuzov reaction with triethyl phosphite to give Horner–Wittig precursor **20** (95%).[25] Condensation of 1-bromohexane with 4-hydroxybenzaldehyde (**18**) gave **19** (96%),[24] the aldehyde required for Horner–Wittig condensation with **20** in the presence of KO^{t}Bu to install the first π-system in **21** (54%). The Horner variation of the classic Wittig condensation was selected to favour the desired all-*E* isomeric olefins,[28] as confirmed by the diagnostic coupling constant between olefinic protons in the ^1H NMR spectrum.[29] Sonogashira–Hagihara coupling of **21** and TMSA gave **22** (48%), which was readily deprotected by tetrabutylammonium fluoride (TBAF) to yield **23** (88%). Sonogashira–Hagihara coupling of **22** and **3** gave target **D** (86%) as a fluorescent, pale yellow solid.

The second cruciform, **E**, was prepared in a manner analogous to that used to prepare **D**, but employing 4-*t*-butyl benzaldehyde (**24**) in place of **19** (Scheme 2A). Proton and ^{13}C NMR spectra for all non-commercial materials **1–27** and **A–E** are provided in the ESI.†

Photophysical properties and DFT calculations

The absorption and photoluminescence spectra of **A–E** are provided in Fig. 1, with selected photophysical properties summarized in Table 1. Probes **A–E** have a good range of emission wavelengths; strong emission anywhere from ~350–500 nm is obtainable by judicious selection of one of these probes. Access to probes with specific emission wavelengths is of interest for multidye fluorescence microscopy experiments, in which each dye can be observed separately if emission maxima are well-separated. The dyes also have excellent molar absorptivities (ε, Table 1) of the order of 10^4–10^5 $M^{-1}cm^{-1}$. High molar absorptivity is a prerequisite for biosensing and environmental monitoring because it allows smaller amounts of dye to be used while retaining visual observability. Compounds **A**, **B**, **D** and **E** also have very high photoluminescence quantum yields (Φ, Table 1) of 0.48–0.64 in THF solution. Fluorene derivative **C**, on the other hand, has a rather low Φ of 0.075. The ground state HOMO and LUMO distributions for **A–E**, as determined by DFT calculations at the B3LYP/6-31G(d) level, are shown in Fig. 2. Because these are ground state calculations and are not time dependent, the most notable inference from these calculations is the geometric

Table 1 Selected photophysical properties of **A–E** and effect of metal ion binding on photoluminescence properties

	Metal-free chromophores				Metal ion response					
	Absorption		Fluorescence		Cu^{2+}			Zn^{2+}		
	λ_{abs}	$\log\varepsilon$	λ_{em}	Φ	λ_{em}	$\Delta\lambda_{em}$	I/I_0	λ_{em}	$\Delta\lambda_{em}$	I/I_0
A	329	4.56	352	0.48	411	59	0.84	410	58	0.42
B	370	4.72	400	0.58	423	23	2.0	411	11	1.6
C	341	5.02	362	0.075	373	11	9.2	373	11	8.6
D	383	5.24	454	0.57	475	21	0.77	473	19	0.84
E	375	5.19	416	0.64	451	35	0.84	443	27	0.85

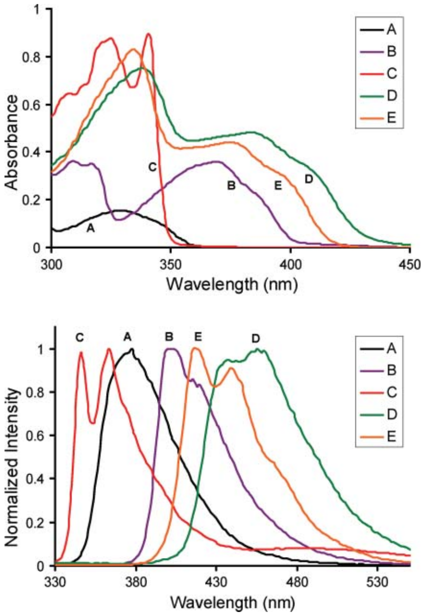


Fig. 1 Absorption (upper) and normalized fluorescence (lower) spectra for **A–E**.

separation of the HOMO and LUMO in cruciforms **D** and **E**. In both cases, the HOMO is localized to large extent on the distyrylbenzene branches, whereas the LUMO is spread more equally over both branches of the cross-conjugated core. It is also noteworthy that in all of the neutral ground state molecules **A–E** the HOMO and LUMO are π and π* in nature, respectively. The n-type nitrogen lone pair contributes primarily to the HOMO-1 (not shown in Fig. 2) in the neutral ground state.

Response to metal ions

Once the beneficial photophysical properties of **A–E** had been established, a range of metal ions were screened as potential analytes for detection by photoluminescence spectroscopy in THF. Metal salts used for ion screening were $Co(NO_3)_2{\cdot}6H_2O$, $NiSO_4{\cdot}6H_2O$, $Cu(ClO_4)_2{\cdot}6H_2O$, $Zn(ClO_4)_2{\cdot}6H_2O$, $Cd(ClO_4)_2{\cdot}6H_2O$, $K(PF_6)$, $Na(PF_6)$, $Mg(SO_4)$, $CaCl_2$, $Eu(NO_3)_3$, $[Cu(NCMe)_4][BF_4]$ and $Hg(O_2CCF_3)_2$. Of these metal ions, only Zn^{2+} and Cu^{2+} elicited notable photoluminescence changes in any of the molecules. Changes in emission intensity and maxima upon exposure to these ions are summarized in Table 1. The photoluminescence spectra shown in Fig. 3 demonstrate the progressive changes observed as up to one equiv of metal ion is added to **A–E**. None of the platforms responds strongly to metal ions in buffered aqueous solution, so all tests were done in THF. Unfortunately, all of the molecules exhibited similar responses to both Zn^{2+} and Cu^{2+}, so these sensing platforms are not able to differentiate between the two ions under the conditions employed. Interestingly, however, three distinct types of photoluminescence signal transduction were observed across the series. The first signal transduction type, exemplified by **A**, **D**, and **E**, was a ratiometric response with concomitant emission quenching. Significant shifts in photoluminescence maxima ($\Delta\lambda_{em}$) to the red were achieved for **A**, **D** and **E** ($\Delta\lambda_{em}$ = 51, 21, and 35 nm, respectively), despite the fact that the N lone pairs with which the metal ions interact are insulated from the chromophore subunit by

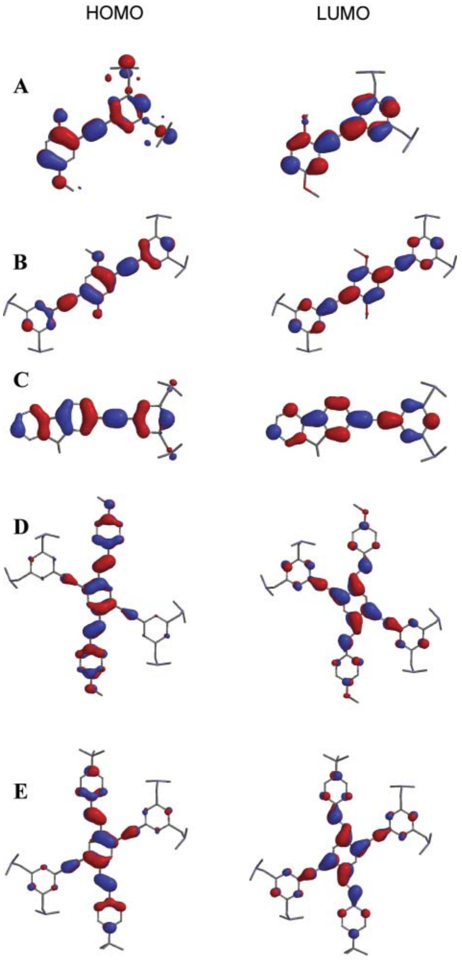


Fig. 2 HOMO and LUMO parameters from DFT calculations (B3LYP-6-31G* level) for compounds **A–E**. Hexyl groups were truncated to methyl groups for the calculations.

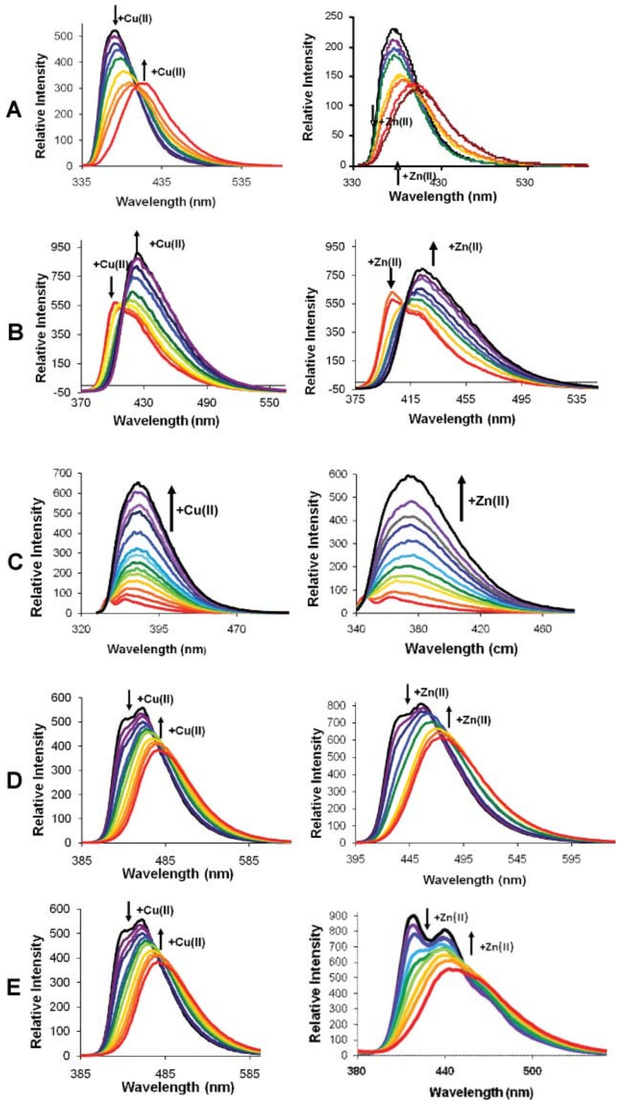


Fig. 3 Metal ion response of compounds **A–E**.

a methylene spacer. It can be inferred that the origin of the shift, then, is predominantly inductive in nature. Similar red-shifting of photoluminescence maxima was observed in phosphorus-derivatized cruciforms when appended substituents become more electron withdrawing.[30]

A second type of signal transduction is a red-shifting ratiometric response similar to that observed for **A**, **D** and **E**, but with attendant emission enhancement. This dual ratiometric/turn-on type response was only exhibited by **B**. The $\Delta\lambda_{em}$ of **B** (21 nm) is similar to that of **D** (23 nm), which also features electron donating alkoxy groups and a longer effective conjugation length than in alkoxy-substituted **A**. This qualitative observation makes sense in light of the relationship between metal–chromophore orbital energy matching and photophysical response of metal complexes of ligands appended to π-conjugated scaffolds.[31]

Compound **C** is unique among the molecules screened in that it features the least electron rich π-system, utilizing a fluorenyl moiety rather than ethynylaryl or styryl π-system constituents. This is also the only molecule screened that exhibits a notable emission enhancement without a large red shift in emission maximum upon metal binding. An approximate 9-fold increase in integrated emission intensity was observed upon binding either Zn^{2+} or Cu^{2+}. A photoinduced electron transfer (PET) mechanism, similar to that exhibited by other amine-based Zn sensors,[6–12] is likely responsible for the turn-on response of **C**.

Conclusions

We have synthesized a series of easily-prepared materials **A–E** derivatized with a robust ligating unit. Several chromophore subunits of contemporary interest have been incorporated into these molecules, including phenylenevinylene, phenylene ethynylene and fluorene moieties. Cross-conjugated cruciforms, a class of materials of escalating importance in chemical sensing, have also been examined. All of these molecules show a photoluminescence response to Zn^{2+} or Cu^{2+} over other common metal ions screened, although these two ions could not be differentiated from one another. Despite the inability of **A–E** to differentiate between Zn^{2+} and Cu^{2+}, the simple ligating units and modular approach to sensor assembly described herein should be attractive to others wishing to produce metal ion responsive materials. This simple strategy has also yielded materials capable of commercially viable ratiometric shifts in photoluminescence and emission turn-on magnitudes. The incorporation of other simplified ligand units into small molecules and extension to π-conjugated polymer analogues are currently being pursued in our laboratory.

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