Electronic Supplementary Information

Torsionally Restricted Tetradentate Fluorophore: A Swiveling Ligand Platform for Ratiometric Sensing of Metal Ions

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Experimental Section

General Considerations. All reagents were obtained from commercial suppliers and used as received unless otherwise noted. The solvents dichloromethane, diethyl ether, toluene, THF, and MeCN were saturated with nitrogen and purified by passage through activated Al_2O_3 columns under nitrogen (Innovative Technology SPS 400). Triethylamine, diisopropylamine and DMF were saturated with nitrogen and used without further purification. The compounds 4-*tert*-butyl-2-iodophenol[1] and 5-ethynyl-2,2'-bipyridine (**6**)[2] were prepared according to literature procedures. All air-sensitive manipulations were carried out under nitrogen atmosphere in an M.Braun drybox or by standard Schlenk-line techniques.

Physical Measurements. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a 400 MHz Varian Inova NMR Spectrometer or a 400 MHz Varian Unity NMR Spectrometer. Chemical shifts were reported versus tetramethylsilane and referenced to the residual solvent peaks. High-resolution chemical ionization (CI) (using CH_4 as CI reagent) and electrospray ionization (ESI) mass spectra were obtained on a Thermo Electron Corporation MAT 95XP-Trap. FT-IR spectra were recorded on a Nicolet 510P FT-IR Spectrometer with EZ OMNIC E.S.P. software. UV-vis spectra were recorded on a Varian Cary 5000 UV-vis-NIR spectrophotometer. Fluorescence spectra were recorded on a Photon Technology International QM-4-CW Spectrofluorometer with FeliX32 software.

4-*tert*-Butyl-2-iodophenyl trifluoromethanesulfonate (5). The synthesis of this compound has previously been reported,[3] but details of its synthesis and characterization are not available. To a solution of 4-*tert*-butyl-2-iodophenol (5.66 g, 20.5 mmol) in anhyd CH_2Cl_2 (40 mL) was added pyridine (2.98 mL, 36.9 mmol) and the mixture was cooled to 0 °C under nitrogen atmosphere. A portion of trifluoromethanesulfonic anhydride (4.03 mL, 24.6 mmol) was added dropwise over a period of 1 h and the mixture was warmed to r.t. The reaction was complete within 5 min as determined by TLC. The mixture was diluted with CH_2Cl_2 (40 mL) and quenched with aq HCl (2 M, 50 mL). The organic layer was washed with water (3 × 50 mL), dried over anhyd $MgSO_4$, filtered, and concentrated under reduced pressure to afford **5** as a pale yellow liquid (8.30 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ 7.87 (d, $J = 2.3$ Hz, 1H), 7.41 (dd, $J = 8.7, 2.3$ Hz, 1H), 7.22 (d, $J = 8.7$ Hz, 1H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ 153.4, 148.1, 137.9, 127.4, 121.5, 121.0, 88.9, 34.8, 31.3. FT-IR (thin film on NaCl, cm^{-1}): 2967, 2908, 2873, 1482, 1427, 1213, 1140, 1031, 889, 677. HRMS (CI) calcd for $C_{11}H_{12}F_3IO_3S$ $[M]^+$ 407.9498, found 407.9500.

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[1] Kometani, T.; Watt, D. S.; Ji, T. *Tetrahedron Lett.* **1985**, *26*, 2043–2046.

[2] (a) Schwab, P. F. H.; Fleischer, F.; Michl, J. *J. Org. Chem.* **2002** , *67*, 443–449. (b) Grosshenny, V.; Romero, F. M.; Ziessel, R. *J. Org. Chem.* **1997**, *62*, 1491–1500.

[3] Amano, M.; Saiga, A.; Ikegami, R.; Ogata, T.; Takagi, K. *Tetrahedron Lett.* **1998**, *39*, 8667–8668.

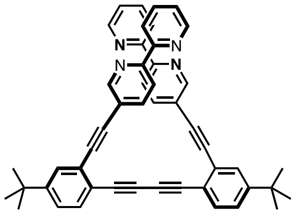
2-(2,2'-Bipyridin-5-ylethynyl)-4-tert-butylphenyl trifluoromethanesulfonate (7). A heterogeneous mixture of **5** (6.52 g, 16.0 mmol), **6** (2.61 g, 14.5 mmol), $PdCl_2(PPh_3)_2$ (225 mg, 0.32 mmol), and CuI (91 mg, 0.48 mmol) in $^iPr_2NH$/THF (60 mL, 2:1, v/v) was stirred for 12 h under nitrogen atmosphere at r.t. The crude reaction mixture was filtered through a pack of Celite and the filtrate concentrated under reduced pressure. The residual brown solid material was purified by flash column chromatography on SiO_2 (hexanes:EtOAc = 9:1 to 4:1, v/v) to afford **7** as a white solid (5.59 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ 8.87 (d, J = 2.0 Hz, 1H), 8.70 (d, J = 4.8 Hz, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.44 (d, J = 8.0 Hz, 1H), 8.00 (dd, J = 8.4, 2.0 Hz, 1H), 7.83 (td, J = 7.6, 1.6 Hz, 1H), 7.67 (d, J = 2.4 Hz, 1H), 7.45 (dd, J = 8.8, 2.4 Hz, 1H), 7.35 (m, 1H), 7.23 (d, J = 8.8 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ 155.6, 155.5, 151.9, 151.8, 149.5, 147.7, 139.7, 137.1, 130.9, 127.8, 124.2, 121.6, 121.3, 120.5, 119.5, 117.3, 117.1, 97.7, 87.2, 35.0, 31.3. FT-IR (thin film on NaCl, cm^{-1}): 2967, 1421, 1210, 1140, 878, 747, 614. HRMS (ESI) calcd for $C_{23}H_{19}F_3N_2O_3$ $[M + H]^+$ 461.1147, found 461.1128.

4-[2-(2,2'-Bipyridin-5-ylethynyl)-4-*tert*-butylphenyl]-2-methylbut-3-yn-2-ol (8). A 200-mL round bottom flask was loaded with **7** (5.59 g, 12.1 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (593 mg, 0.726 mmol), and CuI (208 mg, 1.09 mmol) under nitrogen atmosphere. A 1:1 (v/v) mixture of $^iPr_2NH$ and DMF (80 mL) was added under nitrogen, followed by 2-methylbut-3-yn-2-ol (5.91 mL, 60.5 mmol). The solution was stirred at 80 °C for 14 h under nitrogen. The crude reaction mixture was filtered through a pack of SiO_2 and the filtrate was diluted with Et_2O (300 mL) and washed with water (3 × 200 mL) and brine (200 mL). The organic layer was dried over anhyd $MgSO_4$, filtered, and concentrated under reduced pressure. The residual material was purified by flash column chromatography on SiO_2 (hexanes:EtOAc = 4:1 to 2:1, v/v) and triturated with hexanes (200 mL) to afford **8** as a yellow solid (4.51 g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ 8.84 (d, J = 1.6 Hz, 1H), 8.68 (d, J = 4.0 Hz, 1H), 8.41(d, J = 8.0 Hz, 2H), 7.97 (dd, J = 8.4, 2.4 Hz, 1H), 7.81 (td, J = 7.6, 1.6 Hz, 1H), 7.56 (d, J = 1.6 Hz, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.34 (m, 2H), 1.65(s, 6H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ 155.6, 155.0, 151.7, 151.6, 149.4, 139.5, 137.1, 131.9, 129.0, 126.1, 124.9, 122.6, 121.6, 120.6, 120.5, 97.8, 92.9, 89.5, 80.9, 65.8, 34.9, 31.8, 31.2. FT-IR (thin film on NaCl, cm^{-1}): 2968, 1459, 1364, 1163, 963, 796, 746. HRMS (ESI) calcd for $C_{27}H_{26}N_2O$ $[M + H]^+$ 395.2123, found 395.2120.

5-[(5-*tert*-Butyl-2-ethynylphenyl)ethynyl]-2,2'-bipyridine (9). A heterogeneous mixture of **8** (4.81 g, 12.1 mmol) and pulverized KOH (2.37 g, 42.4 mmol) in toluene (40mL) was heated at reflux for 5 h under nitrogen. The reaction mixture was cooled to r.t. and partitioned between Et_2O and water. The organic layer was washed with water (3 × 50 mL) and dried over anhyd $MgSO_4$, filtered, and concentrated under reduced pressure. The residual material was purified by flash column chromatography on SiO_2 (hexanes:EtOAc = 4:1, v/v) to afford **9** as a yellow solid (3.53 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ 8.86 (d, J = 2.0 Hz, 1H), 8.69 (d, J = 4.8 Hz, 1H), 8.43 (d, J = 8.0 Hz, 1H), 8.42 (d, J = 8.0 Hz, 1H), 7.97 (dd, J = 8.4, 2.0 Hz, 1H), 7.82 (td, J = 7.6, 1.6 Hz, 1H), 7.59 (d, J = 1.6 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.36 (dd, J = 8.0, 2.0 Hz, 1H), 7.31 (ddd, J = 7.6, 4.8, 2.0 Hz, 1H), 3.35 (s, 1H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ 155.6, 155.0, 152.2, 151.9, 149.4, 139.6, 137.1, 132.6, 129.0, 126.1, 125.3, 124.1, 122.1, 121.5, 120.5, 92.7, 89.9, 82.2, 80.8, 35.0, 31.2. FT-IR (thin film on NaCl, cm^{-1}): 3290, 2963, 2869, 1458, 796, 746. HRMS (ESI) calcd for $C_{24}H_{20}N_2$ $[M + H]^+$ 337.1705, found 337.1702.

1,4-Bis[2-(2,2'-bipyridin-5-ylethynyl)-4-*tert*-butylphenyl]buta-1,3-diyne (4). A 100-mL round bottom flask was loaded with **9** (3.53 g, 10.5 mmol), $PdCl_2(PPh_3)_2$ (147 mg, 0.209 mmol), and $Cu(OAc)_2$ (381 mg, 2.10 mmol) under air. A mixture of $^iPr_2NH$ (15 mL), THF (15 mL) and pyridine (6 mL) was added, followed by I_2 (1.33 g, 5.25 mmol). After the heterogeneous mixture was stirred at r.t. for 1 h under air, the reaction was complete as determined by TLC. The crude reaction mixture was filtered through a pack of SiO_2 and extracted with CH_2Cl_2 (3 × 30 mL). The organic layer was dried over anhyd $MgSO_4$, filtered, and concentrated under reduced pressure to afford **4** as a yellow solid (2.18 g, 62%). The product was recrystallized by slow diffusion of pentanes into a $CHCl_3$ solution, which produced single crystals suitable for X-ray crystallography. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ 8.84 (d, J = 2.0 Hz, 2H), 8.64 (d, J = 4.4 Hz, 2H), 8.33 (d, J = 8.0 Hz, 4H), 8.30 (d, J = 8.4 Hz, 2H), 7.97 (dd, J = 8.0, 2.0 Hz, 2H), 7.77 (m, 2H), 7.61 (d, J = 1.6 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.38 (dd, J = 8.0, 1.6 Hz, 2H), 7.28 (m, 2H), 1.36 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ 155.6, 154.9, 152.7, 151.9, 149.3, 139.7, 137.0, 132.8, 129.1, 126.3, 126.2, 123.9, 121.9, 121.5, 120.4, 120.3, 92.6, 90.7, 81.4, 77.7, 35.1, 31.1. FT-IR (KBr pellet, cm^{-1}): 2963, 2865, 1584, 1456, 890, 854, 830, 796, 750. HRMS (CI) calcd for $C_{48}H_{38}N_4$ $[M]^+$ 670.3091, found 670.3089.

[Zn(4)(OTf)$_2$]. A solution of **4** (67 mg, 0.10 mmol) in CH_2Cl_2 (10 mL) was treated with a solution of $Zn(OTf)_2$ (36 mg, 0.10 mmol) in MeCN (5 mL). The mixture was stirred for 1 h under nitrogen at r.t. Volatile fractions were removed under reduced pressure and the residual solid material was extracted into CH_2Cl_2 (10 mL), filtered through a pack of Celite, and concentrated under reduced pressure to afford [Zn(**4**)(OTf)$_2$] as a yellow solid (100 mg, 97%). Colorless crystals suitable for X-ray crystallography were grown by vapor diffusion of Et_2O into a $CHCl_3$/MeOH solution of this material. ^{1}H NMR (400 MHz, CD_2Cl_2, 298 K): δ 8.67 (s, 2H), 8.50 (d, J = 4.8 Hz, 2H), 8.40 (m, 4H), 8.35 (d, J = 8.8 Hz, 2H), 8.23 (t, J = 8.0 Hz, 2H), 7.68 (m, 2H), 7.63 (s, 2H), 7.56 (d, J = 8.4 Hz, 2H), 7.45 (dd, J = 8.4, 1.6 Hz, 2H), 1.33 (s, 18H); ^{13}C NMR (100 MHz, CD_2Cl_2, 298 K): δ 153.5, 150.6, 149.1, 148.9, 148.3, 144.2, 141.9, 133.8, 130.2, 127.7, 127.4, 124.4, 124.1, 123.1, 122.5, 121.6, 95.7, 87.2, 81.1, 77.7, 35.3, 31.0. FT-IR (KBr pellet, cm^{-1}): 2962, 2905, 2868, 2210, 1597, 1475, 1440, 1282, 1240, 1165, 1030, 749, 735, 638. HRMS (ESI) calcd for $C_{50}H_{41}N_4O_2Zn$ $[Zn(\mathbf{4})(OAc)]^+$ 793.2521, found 793.2547.



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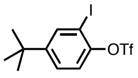

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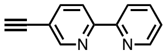

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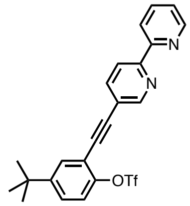

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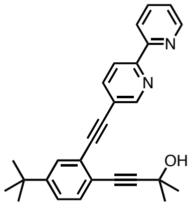

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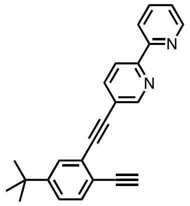

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Density Functional Theory Calculations

All calculations were carried out using Density Functional Theory (DFT). Initial Cartesian coordinates were imported from crystallographic data and optimized using Jaguar 6.0 suite[4] of ab initio quantum chemistry program at the B3LYP level of theory.[5] The structure of **4** was simplified by removing the two *tert*-butyl groups. Geometry optimization (GO) was performed employing the Los Alamos LACVP** basis set,[6] since this protocol represents a reasonable compromise between numerical accuracy and computational cost. Molecular Orbital (MO) pictures were drawn at isodensity value 0.05 a.u. as produced by the MOLDEN packages.[7]

Binding Constant Measurements

Binding constant (= K_a) was determined by non-linear regression analysis[8,9] of the absorbance data (= A) obtained with increasing concentration of the metal (= $[\mathbf{M}]_0$) with respect to a fixed concentration of the ligand (= $[\mathbf{L}]_0$) with known extinction coefficient $\epsilon_{[\mathrm{L}]}$ (eq (1)). The parameters $\epsilon_{[\mathrm{ML}]}$ (= extinction coefficient of the complex **ML**) and K_a were allowed to vary during the iterative least squares process.

$$A = \epsilon_{[\mathrm{L}]}[\mathbf{L}]_0 + \left(\epsilon_{[\mathrm{ML}]} - \epsilon_{[\mathrm{L}]}\right) \frac{\left([\mathbf{L}]_0 + [\mathbf{M}]_0 + \frac{1}{K_a}\right) - \sqrt{\left([\mathbf{L}]_0 + [\mathbf{M}]_0 + \frac{1}{K_a}\right)^2 - 4[\mathbf{L}]_0[\mathbf{M}]_0}}{2} \tag{1}$$

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[4] Jaguar; Version 6.0 ed.; Schrödinger, Inc.: Portland, Oregon, 2003.

[5] (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652. (b) Lee, C. T.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789.

[6] (a) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299–310. (b) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 270–283. (c) Wadt, W. R.; Hay, P. J. *J. Chem. Phys.* **1985**, *82*, 284–298.

[7] Schaftenaar, G.; University of Nijmegen: Nijmegen, Netherlands.

[8] K. A. Connors, *Binding Constants: The Measurement of Molecular Complex Stability*, Wiley, New York, 1987.

[9] Origin; version 8.0; OriginLab Corp.: Northampton, MA.

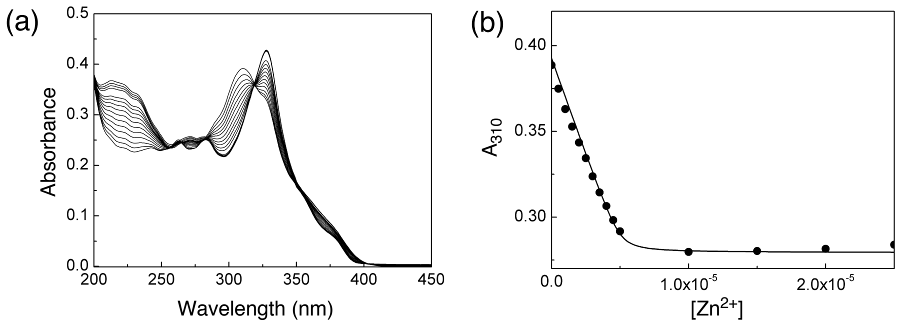

Fig. S1 (a) Changes in the electronic absorption spectra of **4** (5.0 μM) upon addition of $Zn(OTf)_2$ (0–25.0 μM) in MeCN at 298 K. (b) A plot of A_{310} (= absorbance at 310 nm) vs $[Zn^{2+}]$ fitted with a 1:1 binding isotherm of $K_a = 1.7\ (\pm\ 0.5) \times 10^7\ M^{-1}$.

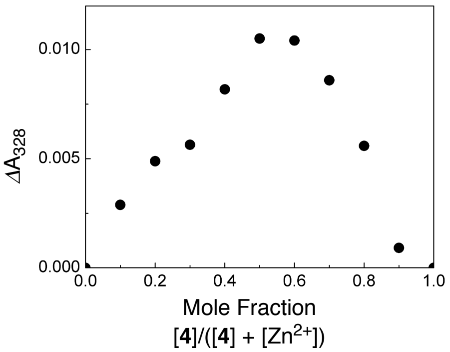

Fig. S2 Job's plot for the binding between **4** and Zn^{2+} generated by monitoring ΔA_{328} (= change in the absorbance at λ = 328 nm with respect to ligand-only value, i.e. at [**4**] = 5.0 μM) in MeCN at 298 K. [**4**] + $[Zn^{2+}]$ = 5.0 μM.

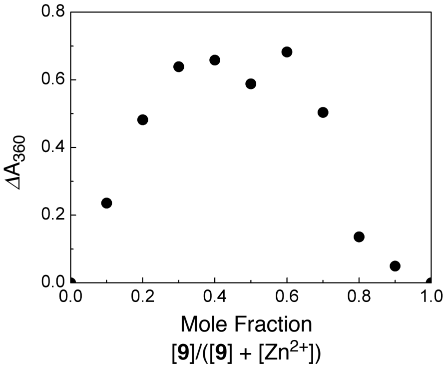

Fig. S3 Job's plot for the binding between **9** and Zn^{2+} generated by monitoring ΔA_{360} (= change in the absorbance at λ = 360 nm with respect to ligand-only value, i.e. at [**9**] = 0.10 mM) in MeCN at 298 K. [**9**] + $[Zn^{2+}]$ = 0.10 mM.

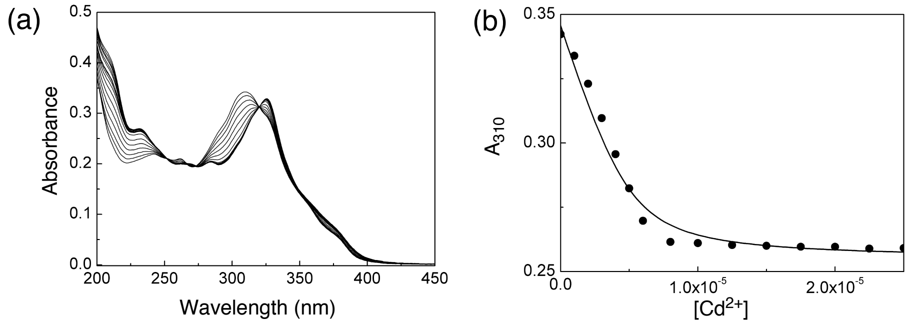

Fig. S4 (a) Changes in the electronic absorption spectra of **4** (5.0 μM) upon addition of $Cd(ClO_4)_2$ (0–25.0 μM) in MeCN at 298 K. (b) A plot of A_{310} (= absorbance at 310 nm) vs [Cd^{2+}] fitted with a 1:1 binding isotherm of $K_a = 1.5\ (\pm\ 0.5) \times 10^6\ M^{-1}$.

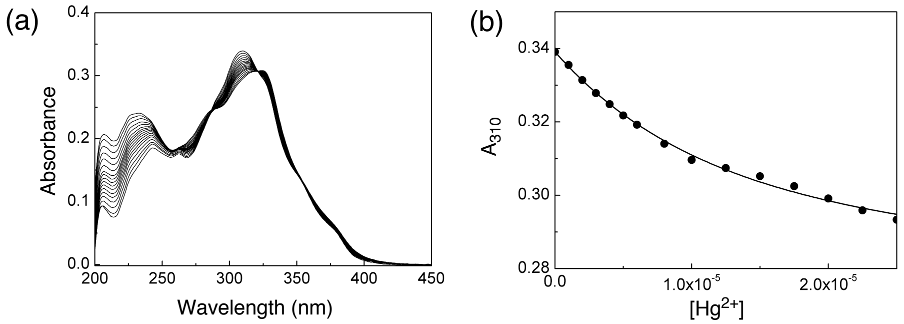

Fig. S5 (a) Changes in the electronic absorption spectra of **4** (5.0 μM) upon addition of $Hg(ClO_4)_2$ (0–25.0 μM) in MeCN at 298 K. (b) A plot of A_{310} (= absorbance at 310 nm) vs [Hg^{2+}] fitted with a 1:1 binding isotherm of $K_a = 9.4\ (\pm\ 0.9) \times 10^4\ M^{-1}$.

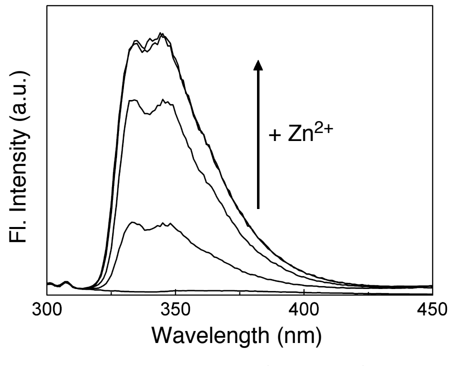

Fig. S6 Changes in the emission spectra of **6** (1.0 μM) upon addition of $Zn(OTf)_2$ (10–40 μM) in MeCN at 298 K with $\lambda_{exc} = 280$ nm. Each trace corresponds to an increment of 10 μM [Zn^{2+}] from 0 to 40 μM.