Electronic Supplementary Information

A sensitive and highly selective fluorescent sensor for In$^{3+}$

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2. General Information

All reactions were performed in oven-dried flasks under a positive pressure of argon unless otherwise stated. Common reagents and materials were purchased from commercial sources and used as received. Solvents were dried by distillation under argon from the following: tetrahydrofuran (sodium/benzophenone); acetonitrile (calcium hydride). Organic extracts were, in general, dried over anhydrous sodium sulfate (Na$_2$SO$_4$). TLC plates were visualized by exposure to ultraviolet light (UV) and/or submersion in ethanolic phosphomolybdic acid (PMA), aqueous ceric ammonium molybdate solution (CAM), or solutions of ninhydrin in n-butanol, followed by brief heating on a hot plate (~200°C, 10–15 s). NMR spectra were recorded on a 300 MHz spectrometer. Chemical shifts for protons are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual proton in the NMR solvents (CHCl$_3$: δ 7.26). Chemical shifts for carbon resonances are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent (CDCl$_3$: δ 77.0). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, and coupling constant (J) in Hz. Infrared (IR) spectra were recorded on a Perkin Elmer 500 FT-IR spectrophotometer and are reported in terms of frequency of absorption (cm$^{-1}$). UV-Vis spectra were recorded on a Shimazu 2401 spectrophotometer. The fluorescence spectra were measured with a Hitachi F-4500 fluorescence spectrophotometer.
3. Experimental Procedures

3a. Synthesis of thioacetal 3

To a mixture of potassium hydroxide (82%, 68.5 g, 1.0 mol) in 250 mL of acetonitrile, ethyl cyanoacetate (2, 94%, 60.2 g, 0.5 mol) was added at room temperature. The resulting mixture was stirred at room temperature for 1 h, and carbon disulfide (38.1 g, 0.5 mol) was added at –5 °C. The mixture stirred at –5 °C for 1 h, and dimethyl sulfate (126.0 g, 1.0 mol) was added at 0 °C. The resulting mixture was stirred at 0 °C for 2 h, stirred at room temperature for 4 h, and evaporated under reduced pressure. The residue was washed with 1.0 L of water, filtered, and purified by column chromatography over silica gel (gradient elution 10% → 30% ethyl acetate in heptanes) to afford thioacetal 3 (99.8 g) in 93% yield. Pale yellow solids; mp = 58–60 °C; $^1$H NMR (300MHz, CDCl$_3$) δ 4.11 (q, 2H, J = 7.1 Hz), 2.60 (s, 3H), 2.46 (s, 3H), 1.18 (t, 3H, J = 7.1 Hz); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 180.4, 161.6, 115.5, 98.1, 61.2, 20.4, 18.5, 13.7; FTIR (film): 2981, 2930, 2210, 1700, 1460, 1425, 1248, 1142, 1024, 909, 769 cm$^{-1}$. HRMS (TOF MS ES$^+$) m/z: Calcd for C$_8$H$_{11}$NO$_2$S$_2$Na $[\text{M+Na}]^+$: 240.0129. Found: 240.0133. Anal. calcd for C$_8$H$_{11}$NO$_2$S$_2$: C, 44.22; H, 5.10; N, 6.45. Found: C, 44.17; H, 5.24; N, 6.65.

3b. Synthesis of aminopyrazole 4

To a solution of thioacetal 3 (21.7 g, 0.1 mol) in acetonitrile (30 mL) and ethanol (60 mL), aqueous hydrazine (85%, 6.1 g, 0.1 mol) was added dropwise at 0 °C. The resulting mixture was
stirred at 0 °C for 6 h, and evaporated under reduced pressure. The residue was redissolved in 100 mL of ethyl acetate, and then 50 mL of water was added. The two layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography over silica gel (gradient elution 50% → 80% ethyl acetate in heptanes) to afford aminopyrazole 4 (18.0 g) in 90% yield. Pale yellow solids; mp = 136–138 °C; 1H NMR (300MHz, CDCl3) δ 10.96 (s, br, 1H), 5.55 (s, br, 2H), 4.23 (q, 2H, J = 6.9 Hz), 2.41 (s, 3H), 1.31 (t, 3H, J = 6.9 Hz); 13C NMR (75 MHz, CDCl3) δ 164.3, 153.3, 148.6, 94.1, 59.9, 14.3, 13.7; FTIR (film): 3471, 3327, 2979, 1665, 1618, 1526, 1403, 1381, 1309, 1137, 1037, 787 cm⁻¹. HRMS (TOF MS ES⁺) m/z: Calcd for C₇H₁₁N₃O₂SNa [M+Na]⁺: 224.0470. Found: 224.0468. Anal. calcd for C₇H₁₁N₃O₂S: C, 41.78; H, 5.51; N, 20.88. Found: C, 56.65; H, 5.63; N, 20.97.

3c. Synthesis of pyrazolo[1,5-a]pyrimidine 1

To a solution of aminopyrazole 4 (2.4 g, 10.0 mmol) in 20 mL of acetic acid, pentane-2,4-dione (5, 1.2 g, 12.0 mmol) and two drops of concentrated H₂SO₄ (98%) was added. The resulting mixture was stirred at 50 °C for 10 min, and then 30 mL of water was added. The mixture was extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography over silica gel (gradient elution 30% → 50% ethyl acetate in heptanes) to afford pyrazolo[1,5-a]pyrimidine 1 (2.8 g) in 90% yield. White solids; mp = 168–170 °C; 1H NMR (300MHz, CD₃CN) δ 6.82 (s, 1H), 4.31 (q, 2H, J = 6.9 Hz), 2.67 (s, 3H), 2.58 (s, 3H), 2.55 (s, 3H), 1.35 (t, 3H, J = 6.9 Hz); 1H NMR (300MHz, CDCl₃) δ 6.56 (s, 1H), 4.37 (q, 2H, J = 7.1 Hz), 2.63 (s, 3H), 2.56 (s, 3H), 2.54 (s, 3H), 1.38 (t, 3H, J = 7.1 Hz); 13C NMR (75MHz, CDCl₃) δ 162.9,
161.9, 158.4, 149.1, 145.2, 109.1, 98.6, 60.0, 24.9, 16.7, 14.3, 13.1; FTIR (KBr) 3062, 2988, 1713, 1629, 1553, 1512, 1437, 1380, 1342, 1248, 1154, 1044, 795, 713 cm\(^{-1}\). HRMS (TOF MS ES\(^+\)) \(m/z\): Calcd for C\(_{12}\)H\(_{15}\)N\(_3\)O\(_2\)SNa [M+Na]\(^+\): 288.0783. Found: 288.0789. Anal. calcd for C\(_{12}\)H\(_{15}\)N\(_3\)O\(_2\)S: C, 54.32; H, 5.70; N, 15.84. Found: C, 54.27; H, 5.88; N, 15.72. Fluorescence quantum yield (\(\phi_\text{fl} = 0.518\) in CH\(_3\)CN).

The mixture of 5,7-dimethyl-2-(methylthio)pyrazolo[1,5-a]pyrimidine-3-carboxylate ethyl ester (1, 1 equivalent) and In(OTf)\(_3\) (1 equivalent) in CD\(_3\)CN: \(^1\)H NMR (300MHz, CD\(_3\)CN) \(\delta\) 7.28 (s, 1H), 4.51 (q, 2H, \(J = 7.1\) Hz), 2.94 (s, 3H), 2.89 (s, 3H), 2.68 (s, 3H), 1.41 (t, 3H, \(J = 6.9\) Hz).
4. $^1$H NMR and $^{13}$C NMR Spectra

4a. Thioacetal 3

$^1$H NMR (300MHz, CDCl$_3$)

$^{13}$C NMR (75MHz, CDCl$_3$)
4b. Aminopyrazole 4

$^1$H NMR (300MHz, CDCl$_3$)

$^{13}$C NMR (75MHz, CDCl$_3$)
4c1. Pyrazolo[1,5-α]pyrimidine 1

$^1$H NMR (300MHz, CDCl$_3$)

$^{13}$C NMR (75MHz, CDCl$_3$)
4c2. Pyrazolo[1,5-α]pyrimidine 1

$^1$H NMR (300MHz, CD$_3$CN)

4d. 1 in the presence of In(OTf)$_3$ (1 molar equivalent) in CD$_3$CN

$^1$H NMR (300MHz, CD$_3$CN)
5. Fluorescence Spectra

Figure 1. Fluorescence emission spectra of pyrazolo[1,5-$a$]pyrimidine 1 ($1 \times 10^{-5}$ M) in the presence of In(OTf)$_3$ in CH$_3$CN. The concentration of In(OTf)$_3$: 0, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, $1.0 \times 10^{-5}$ M; $\lambda_{ex} = 309$ nm.

Figure 2. Benesi-Hildebrand method for calculating binding constants of 1 with In$^{3+}$. Association constant (K) = $3.37 \times 10^4$ M$^{-1}$. Linear correlation coefficient (R) = 0.9988. The detection limit for In$^{3+}$ was found to be $1.9 \times 10^{-7}$ M.
Figure 3. Job plot between pyrazolo[1,5-$a$]pyrimidine 1 and In(OTf)$_3$ in CH$_3$CN. [1] + [In$^{3+}$] = 2×10$^{-5}$ M. $\lambda_{ex}$ = 309 nm.

Figure 4. Fluorescence responses of pyrazolo[1,5-$a$]pyrimidine 1 in CH$_3$CN (1 $\mu$M) upon additions of various anions (100 $\mu$M of F$^-$, Cl$^-$, Br$^-$, I$^-$, AcO$^-$, HSO$_4^-$, H$_2$PO$_4^-$, NO$_3^-$, CN$^-$, OTf$^-$). $\lambda_{ex}$ = 309 nm.
Figure 5. Fluorescence responses of 1 to representative ions in CH3CN (1 µM). The bars represent the ratio of the final fluorescence response (I) over the initial fluorescence response (I0). The black bars represent the response to the addition of the given ions [20 µM of NaCl, Mg(OTf)2, Sc(OTf)3, Hf(OTf)4, NbBr3, Cr(NO3)3, Mn(AcO)2, Fe(OTf)3, Co(AcO)2, NiSO4, Cu(OTf)2, Zn(OTf)2, Al(OTf)3, Ga(OTf)3, Pb(OAc)2, Bi(OTf)3]. The white bars represent the response to the addition of 2 µM of In3+ to the respective solution. λex = 309 nm.

Figure 6. Fluorescence responses of 1 to representative ions in CH3CN (1 µM). The bars represent the ratio of the final fluorescence response (I) over the initial fluorescence response (I0). The black bars represent the response to the addition of the given ions [100 µM of Na+(Ia), Mg2+(IIa), Sc3+(IIIb), Hf4+(IVb), Nb3+(Vb), Cr3+(VIb), Mn2+(VIIb), Fe3+(VIIIb), Co3+(VIIIb), Ni2+(VIIib), Cu2+(Ib), Zn2+(IIb), Al3+(IIIa), Ga3+(IIla), Pb2+(IVa), Bi3+(Va)]. The white bars represent the response to the addition of 10 µM of In3+(IIIa) to the respective solution. λex = 309 nm.
Figure 7. Fluorescence responses of 1 to screened ions in CH$_3$CN (1 µM). The bars represent the ratio of the final fluorescence response (I) over the initial fluorescence response (I$_0$). The black bars represent the response to the addition of the given ions (100 µM of Li$^+$, K$^+$, Rb$^+$, Cs$^+$, Ca$^{2+}$, Sr$^{2+}$, Ba$^{2+}$, Y$^{3+}$, La$^{3+}$, Ce$^{3+}$, Pr$^{3+}$, Sm$^{3+}$, Eu$^{3+}$, Gd$^{3+}$). The white bars represent the response to the addition of 10 µM of In$^{3+}$ to the respective solution. $\lambda_{ex} = 309$ nm.

Figure 8. Fluorescence responses of 1 to screened ions in CH$_3$CN (1 µM). The bars represent the ratio of the final fluorescence response (I) over the initial fluorescence response (I$_0$). The black bars represent the response to the addition of the given ions (100 µM of Ho$^{3+}$, Er$^{3+}$, Yb$^{3+}$, Ti$^{4+}$, V$^{3+}$, Ru$^{3+}$, Rh$^{3+}$, Pt$^{2+}$, Ag$^+$, Au$^{3+}$, Cd$^{2+}$, Hg$^{2+}$, Sn$^{2+}$). The white bars represent the response to the addition of 10 µM of In$^{3+}$ to the respective solution. $\lambda_{ex} = 309$ nm.
Figure 9. A photo of $\mathbf{1}$, $\mathbf{1}$ in the presence of $\text{In}^{3+}$, and $\text{In}^{3+}$ in CH$_3$CN under ultraviolet light (UV).

Figure 10. A photo of $\mathbf{1}$, $\mathbf{1}$ in the presence of $\text{In}^{3+}$, and $\text{In}^{3+}$ in CH$_3$CN under sunlight.