

Rational Design of A NIR-Emitting Pd(II) Sensor via Oxidative Cyclization to Form Benzoxazole Ring

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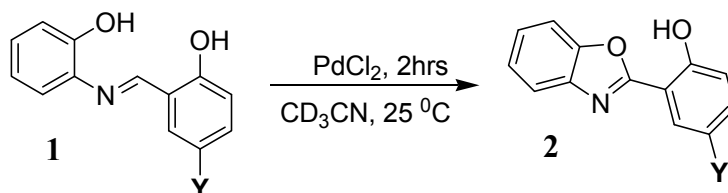
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1. General Information

Commercial reagents were purchased from Sigma Aldrich, Fisher Scientific, and Acros Organics, and used as received. NMR Spectra were collected on a Varian 300 Gemini spectrometer in CDCl₃, CD₃CN, (CD₃)₂SO (CDCl₃: ¹H 7.27 ppm, ¹³C 77.2 ppm; CD₃CN: ¹H 1.94 ppm, ¹³C 118.7 ppm; (CD₃)₂SO: ¹H 2.5 ppm, ¹³C 39.5 ppm). UV-vis spectra were acquired on a Hewlett-Packard 8453 diode-array spectrometer. Fluorescence spectra were obtained on a HORIBA Jobin Yvon NanoLog spectrometer. Mass spectra were determined on time-of-flight (TOF) mass spectrometers equipped with MALDI ion sources. Flash chromatography was performed using silica gel 60 (230-300 mesh) from Fisher.

2. Effect of substituent Y on the reaction conversion of 1 → 2



General procedure: A stock solution of the substrates (20 mM) and an internal standard in CD₃CN was prepared. The initial relative concentration of the substrate to the internal standard was determined by ¹H NMR integration. The 1mL of the stock solution was added to a vial containing 1 equiv of PdCl₂, and stirred at 25 °C for 1 hour. Cesium sulfide (1 equiv) was added to quench the reaction. The reaction mixture was filtered through a pipet packed with cotton and analyzed by ¹H NMR.

Table 1S. Conversion of 1 → 2 with different substituents determined by ¹H NMR

Y	$\delta_{\text{meta}}^{[a]}$	conversion
H	0	12
N(CH ₂ CH ₃) ₂	-0.46	4
Br	0.37	22
Me	-0.06	9.7
NO ₂	0.71	38
CN	0.62	32.6
I	0.35	19
OMe	0.1	13.8

[a] Source: H. H. Jaffe, Chem. Rev., 1953, 53, 191

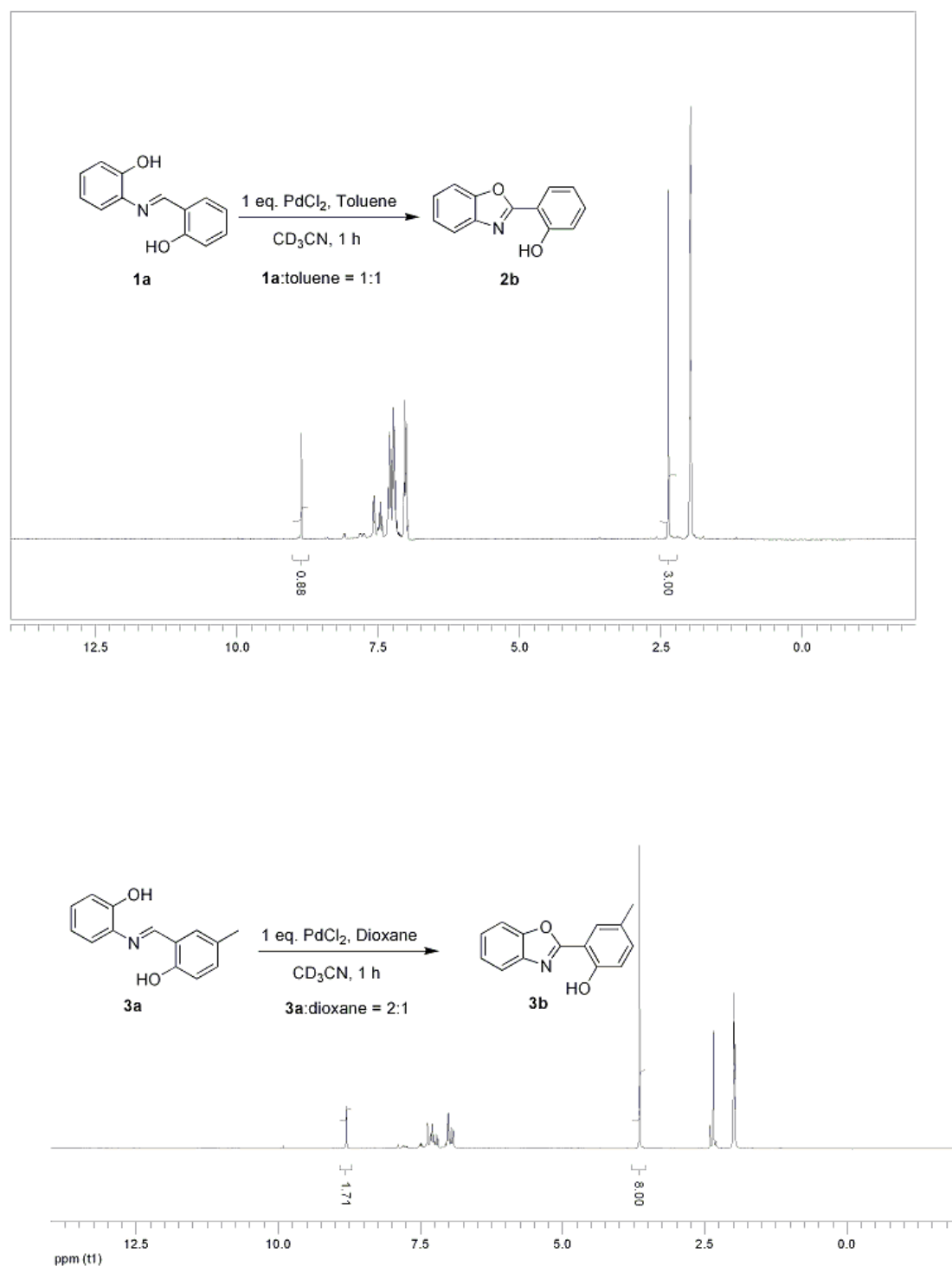
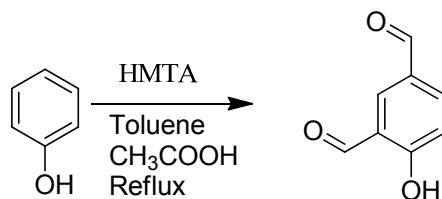
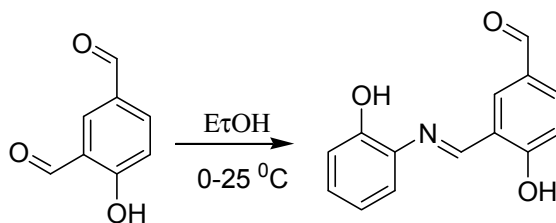


Figure 1S. Representative ¹H NMR of crude reaction mixture of the reaction 1→2. The reaction conversion was determined by the relative integration of the imine proton (H-C=N) to the internal standard (Toluene: δ_{CH₃} = 2.3, dioxane: δ_{CH₂} = 3.7).

3. Synthesis of 5 and 6

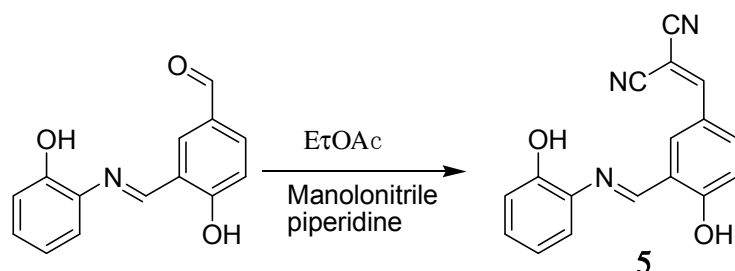


Phenol (300 mg, 3.19 mmol) was dissolved in toluene (20 mL) and acetic acid (25 mL). Hexamethylenetetramine (983 mg, 7.03 mmol) was added in one portion. The orange solution was refluxed until all the starting material was consumed (TLC monitor, ca.18 hrs); the mixture was then cooled to room temperature and poured into 6M HCl (30 mL), and the product was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with saturated brine (40 mL), then dried over Na₂SO₄. The crude product was purified by column chromatography (silica gel, ethyl acetate: hexane = 1:2) to 2,4-diformylphenol (215 mg, 45% yield) as yellow powder. ¹H NMR (300 MHz, CDCl₃): 11.54 (1H, s), 10.01 (1H, s), 9.94 (1H, s), 8.15 (1H, s), 8.07 (1H, d, *J*= 6 Hz), 7.13(1H, d, *J*=6 Hz). ¹³C NMR (75 MHz, CDCl₃): 196.1, 189.2, 166.2, 137.1, 136.4, 129.3, 120.3, 118.8. HRMS (*m/z*): [M+H]⁺ calcd for C₈H₇O₃, 151.0395 ; found, 151.0398.

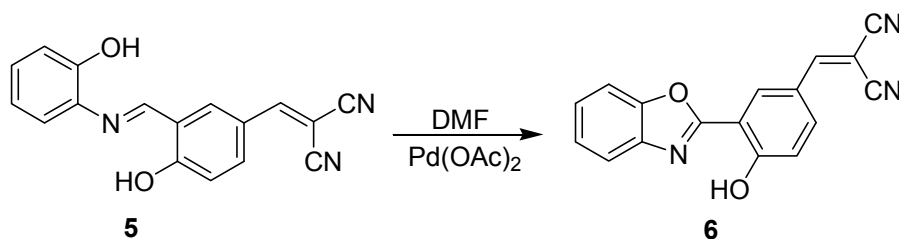


2,4-diformylphenol(200mg, 1.33mmol) and 2-aminophenol (145mg, 1.33mmol) were mixed slowly in absolute ethanol (50 mL) at 0°C. The resulting solution was stirred at room temperature for 12 hrs. The precipitate was filtered and washed with dichloromethane to give 4-hydroxy-3-((2-hydroxyphenylimino)methyl) benzaldehyde as the reddish solid. ¹H NMR (CDCl₃ 300 MHz) δ = 14.87 (br, 1H), 9.57 (s, 1H), 9.21 (br, 1H), 8.67 (s, 1H), 7.69 (s, 1H), 7.57 (d, 1H, *J*=9Hz), 7.02(d, 1H, *J*=9Hz), 6.86 (t, 1H, *J*= 7.5 Hz), 6.73 (d, 2H, *J*= 9Hz), 6.62(t, 1H, *J*=9 Hz). ¹³C NMR (75 MHz, CDCl₃):189.4, 169.2, 159.7, 150.8, 135.9, 133.2, 132.3, 128.5, 127.2, 119.8, 119.7,

119.1, 118.4, 116.8 HRMS (m/z): $[M+H]^+$ calcd for $C_{14}H_{12}NO_3$, 242.0817 ; found, 242.0813.



50 mg of 4-hydroxy-3-((2-hydroxyphenylimino)methyl) benzaldehyde (0.207 mmol) was dissolved in 5 mL of EtOAc. Then 14 mg of manolonitrile (0.212 mmol) and one drop of piperidine were added to the mixture and stirred for 12 hrs at room temperature. The solvent was removed under vacuum and the resulting residue was dissolved in ethyl acetate, washed with 50% borine. The organic layer was dried with anhydrous $MgSO_4$ and evaporated. The product was purified by silica gel column chromatography with eluent dichloromethane to afford **5** as yellow powder. (22.7 mg, 38%) 1H NMR ($CDCl_3/DMSO-d_6$ 300 MHz) δ = 14.27 (br, 1H), 8.80 (s, 1H), 8.64 (s, 1H), 8.10 (d, 1H, $d=2.7$ Hz), 7.28(d, 1H, $J=7.5$ Hz), 7.08 (m, 2H), 6.77 (d, 1H, $J=7.5$ Hz), 6.61(m, 2H) ^{13}C NMR ($CDCl_3/DMSO-d_6$ 75MHz) δ = 160.5, 156.2, 154.8, 151.6, 145.4, 144.4, 135.7, 133.8, 132.6, 129.3, 128.5, 119.7, 118.2, 116.8, 115.5, 115.2, 114.8. HRMS (m/z): $[M+H]^+$ calcd for $C_{17}H_{12}N_3O_2$, 290.0930; found, 290.0938.



To a 10mL round-bottom flask was added the Schiff base **5** (0.2 mmol), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol), and 10 mL DMF. The mixture was stirred at room temperature for 5hr, poured into 10 mL of water. The precipitate was collected by vacuum filtration and washed with 5 mL of water. The solid was redissolved in 20 mL of dichloromethane, washed with 1% EDTA aqueous solution, then washed with water. The organic layer was dried over anhydrous Na_2SO_4 . Removal of solvent afforded the desirable products **6**. 1H NMR ($CDCl_3$ 300 MHz) δ = 12.47 (br, 1H), 8.64 (d, 1H, $J=2.1$ Hz), 8.12(dd, 1H, $J= 8.7, 2.1$ Hz), 7.71 (m,3H), 7.48 (m, 2H), 7.29 (m,

¹H). ¹³C NMR (75 MHz, CDCl₃):163.8, 161.2, 158.3, 149.5, 139.5, 135.5, 131.4, 126.7, 125.9, 123.3, 119.8, 119.5, 114.4, 113.3, 112.0, 111.4, 80.2. HRMS (m/z): [M+H]⁺ calcd for C₁₇H₁₂N₃O₂, 288.0773; found, 288.0768.

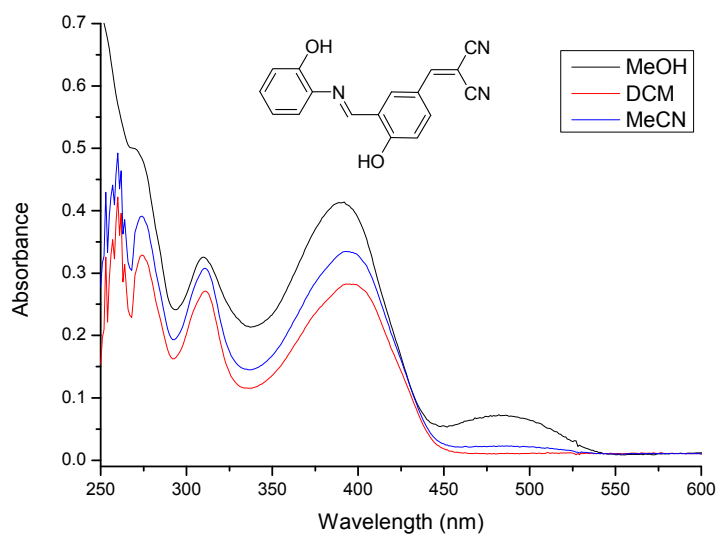


Figure 2S. UV/Vis absorption spectra for sensor **5** (2.5 μM) in different solvent, at 25 °C

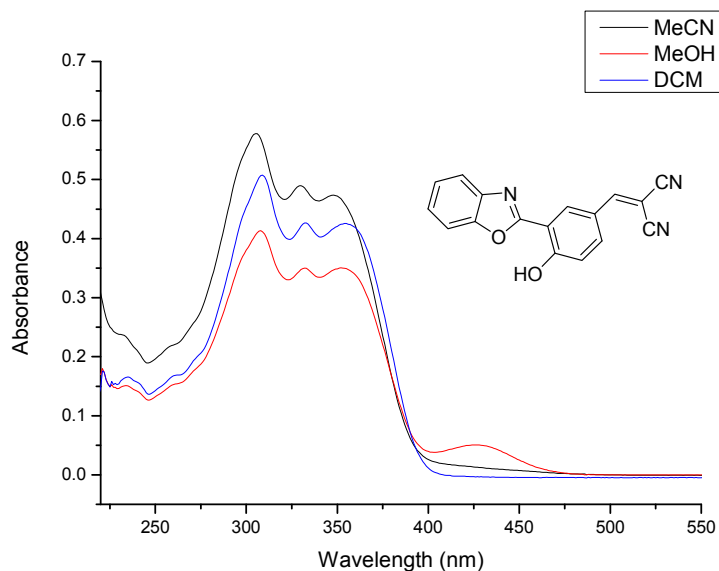


Figure 3S. UV/Vis absorption spectra for sensor **6** (2.5 μM) in different solvent, at 25 °C

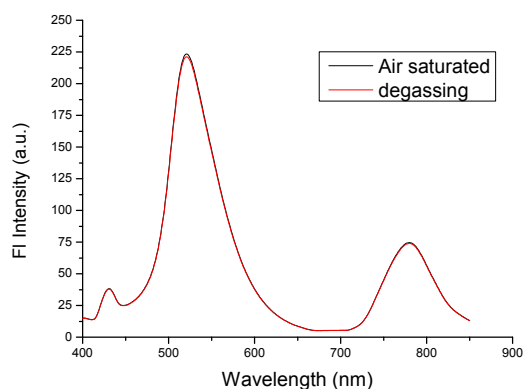


Figure 4S. Fluorescence response of **5** ($2.5 \mu\text{M}$) under degassing and air-saturated (no degassing) conditions taken 1 hour after addition of 1.0 equiv of PdCl_2 in acetonitrile with 1% (w/v) dimethylglyoxime at 25°C (excitation at 360 nm). It shows no change in fluorescent intensity

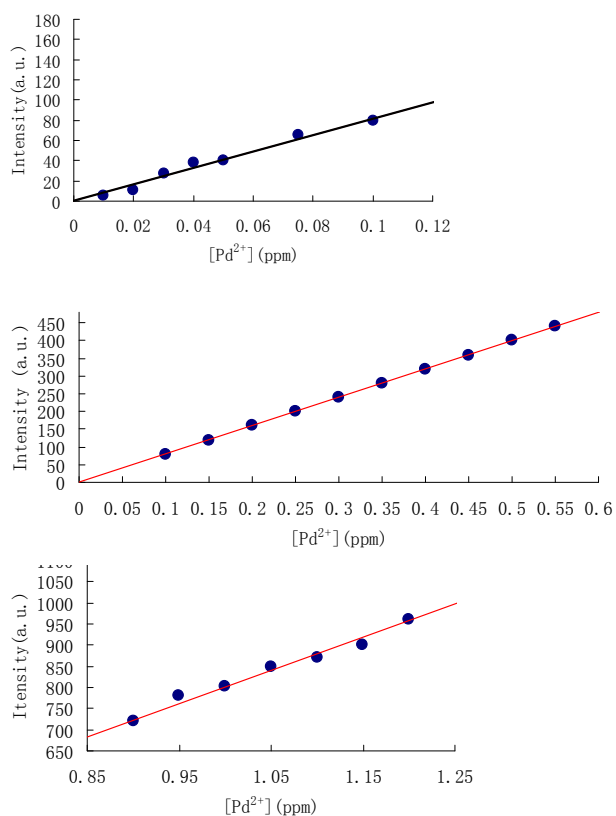


Figure 5S. Fluorescence intensity change of sensor **5** toward Pd^{2+} in the concentration range of (a) $0.01\text{--}0.1\text{ ppm}$ ($0.045\text{--}0.45 \mu\text{M}$), (b) $0.1\text{--}0.55\text{ ppm}$ ($0.45\text{--}1.56 \mu\text{M}$), and (c) $0.9\text{--}1.2\text{ ppm}$ ($4.0\text{--}5.4 \mu\text{M}$). The fluorescence intensity was measured after 60 minutes of mixing, and the intensity was taken as the peak height at 780 nm . ($1 \mu\text{M}$ of Pd^{2+} in the form of PdCl_2 is equal to 0.2234 ppm of Pd^{2+}).

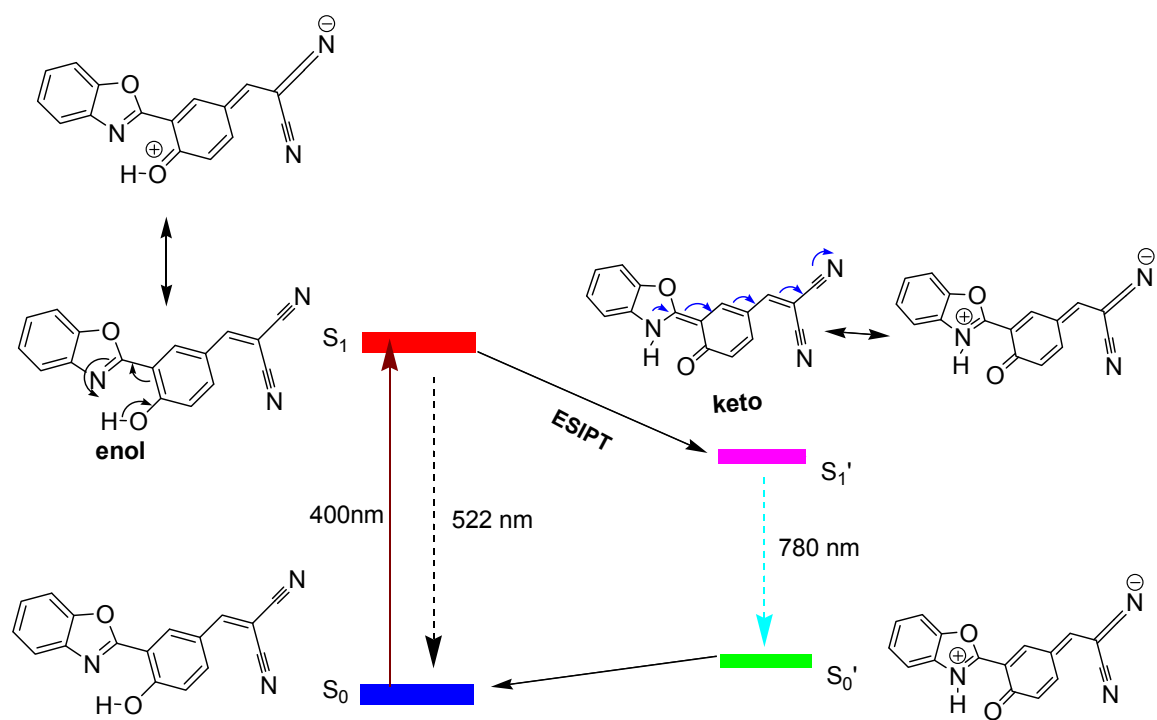


Figure 6S Hypothetical mechanism of ESIP and ICT process in **6**.

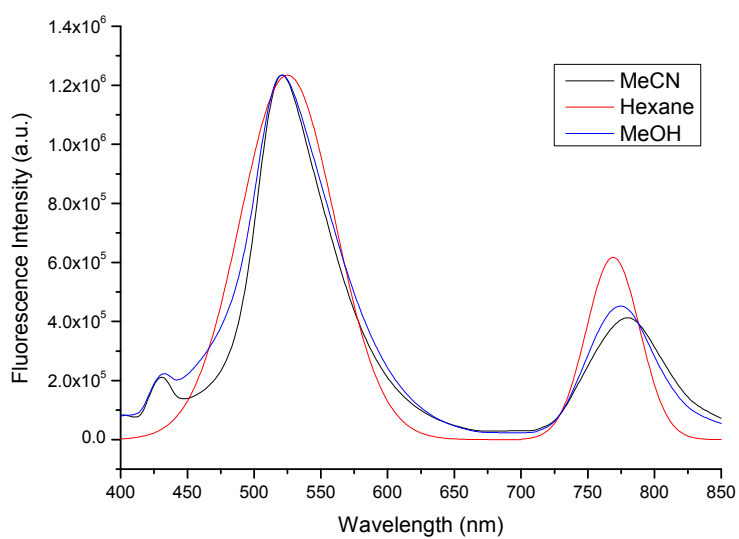


Figure 7S. Fluorescence spectra of **6** in different solvents at room temperature. The spectra are normalized at the peak of 520 nm. (excitation at 360 nm)

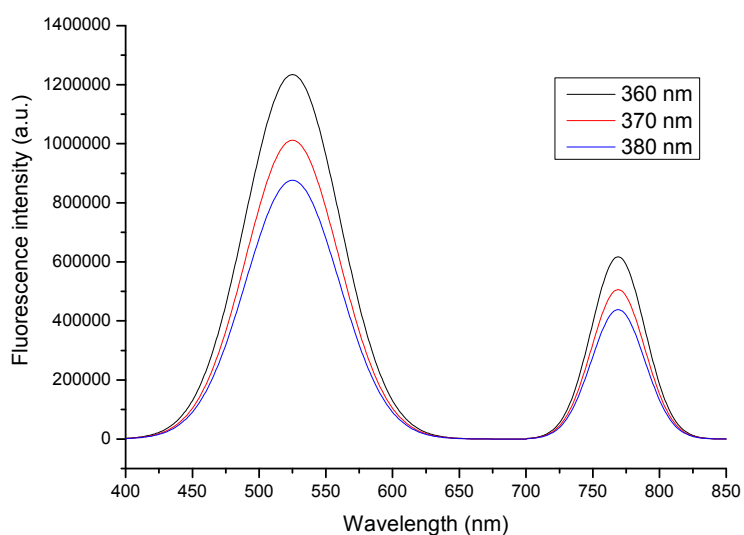


Figure 8S. Fluorescence spectra of **6** in hexane when excited at different wavelength.