

*Supporting Information***Colorimetric Detection of Cyanide with a Chromogenic Oxazine**

Massimiliano Tomasulo and Francisco M. Raymo\*

*Center for Supramolecular Science, Department of Chemistry, University of Miami  
1301 Memorial Drive, Coral Gables, FL 33146-0431*

**Materials and Methods.** Chemicals were purchased from commercial sources and used as received with the exception of CH<sub>2</sub>Cl<sub>2</sub>, which was distilled over CaH<sub>2</sub>. All reactions were monitored by thin-layer chromatography, using aluminum sheets coated with silica (60, F<sub>254</sub>). High-performance liquid chromatography (HPLC) was run with a Varian ProStar system coupled to a ProStar 330 photodiode array detector. Analytical (column dimensions = 4.6 × 250 mm, flow rate = 1.0 mL min<sup>-1</sup>, injection volume = 10 µL, sample concentration = 0.1 mM) and semi-preparative (column dimensions = 21.4 × 250 mm, flow rate = 10 mL min<sup>-1</sup>, injection volume = 10 mL, sample concentration = 0.1 mM) Varian Microsorb BDS columns were employed. The retention time (*RT*) and the peak asymmetry (*PA*) were determined at a wavelength of 254 nm. The average purity parameter (*APP*) was calculated for the peak heart in the wavelength range 215–700 nm. Melting points (mp) were determined with an Electrothermal Mel-Temp. Fast atom bombardment mass spectra (FABMS) were recorded with a VG Mass Lab Trio-2 spectrometer, using 3-nitrobenzyl alcohol as matrix. Nuclear magnetic resonance (NMR) spectra were recorded with Bruker Avance 400 or Avance 500 spectrometers. Absorption spectra were recorded with Varian Cary 100 Bio spectrometer, using quartz cells with a path length of 0.5 cm.

**2-Hydroxymethyl-4-(4'-nitrophenylazo)phenol (3).** A solution of **2** (1.12 g, 5 mmol) in H<sub>2</sub>O (15 mL) was added over 90 min to a solution of **1** (535 mg, 4.3 mmol) in aqueous NaOH (1 M, 5 mL) and H<sub>2</sub>O (10 mL) maintained at 0 °C. The mixture was stirred for a further 45 min. During this time, the temperature was allowed to raise to ambient conditions and the pH was maintained at *ca.* 8 by adding aliquots of aqueous NaOH (1 M). After the addition of aqueous HCl (1 M, 5 mL), the mixture was cooled to -5 °C and maintained at this temperature for 1 h. The resulting precipitate was filtered, dissolved in MeCO<sub>2</sub>Et (50 mL) and dried (MgSO<sub>4</sub>). After filtration, the solvent was distilled off under reduced pressure to afford **3** (1.13 g, 96%) as a bright-orange solid. mp = 178–179 °C; FABMS: *m/z* = 274 [M + H]<sup>+</sup>; <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ = 2.43 (1H, bs), 5.03 (2H, s), 7.05 (1H, d, 9 Hz), 7.73 (1H, d, 2 Hz), 7.85 (1H, dd, 2 and 9 Hz), 7.97 (2H, d, 9 Hz), 8.15 (1H, bs), 8.36 (2H, d, 9 Hz); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 60.4, 116.3, 123.3, 123.8, 125.6, 125.7, 130.4, 147.1, 149.1, 157.1, 160.4.

**2-(4'-Nitrophenylazo)-5a,6,6-trimethyl-5a,6-dihydro-12*H*-indolo[2,1-*b*][1,3]benzoxazine (5).** A solution of PBr<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub> (1:20 v/v, 360 µL) was added over 20 min to a solution of **3** (117 mg, 0.4 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (25 mL) maintained at 0 °C under N<sub>2</sub>. The mixture was stirred for a further 3 h. During this time, the temperature was allowed to raise to ambient conditions. At this point, **4** (345 µL, 2 mmol) was added and the mixture was stirred for a further 1 h. After filtration over a plug of SiO<sub>2</sub>, the solvent was distilled off under reduced pressure and the residue was purified by HPLC [semi-preparative, MeCN/H<sub>2</sub>O (95:5)] to give **5** (73 mg, 41%) as an orange-red solid. HPLC [analytical, MeCN/H<sub>2</sub>O (95:5)]: *RT* = 3.9 min, *PA* = 1.6, *APP* = 309.6 ± 0.2 nm; mp = 156 °C; FABMS: *m/z* = 415 [M + H]<sup>+</sup>; <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ = 1.25 (3H, s), 1.51 (3H, s), 1.61 (3H, s), 4.66 (2H, s), 6.59 (1H, d, 8 Hz), 6.80 (1H, d, 9 Hz), 6.82 (1H, t, 7 Hz), 7.08 (1H, td, 1 and 8 Hz), 7.13 (1H, dd, 1 and 7 Hz), 7.74 (1H, dd, 2 and 9 Hz), 7.80 (1H, d, 2 Hz), 7.96 (2H, d, 9 Hz), 8.37 (2H, d, 9 Hz); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 16.7, 19.1, 26.2, 40.5, 48.2, 103.8, 108.6, 118.8, 119.4, 120.4, 121.5, 122.4, 122.7, 123.3, 124.9, 127.7, 138.4, 146.4, 147.4, 148.6, 156.5, 158.1.