Supporting Information for

Synthesis of an Orange Anthrathiophene Pigment Isolated from a Japanese Bryozoan

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8-Hydroxy-5-*p*-tosyloxy-1,4-naphthoquinone (8). To a stirred mixture of naphthazarin (1.90 g; 10.0 mmol) and K_2CO_3 (2.21 g; 16.0 mmol; freshly roasted over a Meeker burner) in anhydrous THF (250 mL) under N_2 was added dropwise over 15 min a solution of *p*-TsCl (2.10 g; 11.0 mmol) in dry THF (50 mL). The reaction was monitored by TLC (silica; 1:2 EtOAc/hexanes). On silica, the top spot (R_f = 0.40) corresponding to the starting material appears red, the middle spot (R_f = 0.26) corresponding to product appears yellow and the unwanted ditosylate (R_f = 0.14) appears light brown. Upon exposing the developed TLC plate to conc. NH_4OH fumes,[4] the red spot turns blue-purple, the yellow spot turns red and the ditosylate spot turns brown. Immediately after TLC indicated that ditosylate was beginning to form (ca 8 h), the reaction was poured into saturated aqueous ammonium chloride (150 mL). The THF was then removed under house vacuum (ca 50 torr) without heating and the resulting aqueous suspension was poured into CH_2Cl_2 (150 mL). The layers were separated and the aqueous layer was extracted with fresh CH_2Cl_2 (2 × 100 mL). The organic layers were combined and, to recover the excess unreacted naphathazarin, the combined organic layers were then extracted with 0.1 M aqueous Na_2CO_3 (4 × 100 mL) until the aqueous layer became colorless (no longer blue). The organic phase was washed with water and then with brine. Afterwards, it was dried over sodium sulfate, and concentrated using a rotary evaporator. The resulting mixture was pre-adsorbed on 4 g of silica gel, placed on the top of a silica gel flash chromatography column (5.5 × 15 cm), and eluted with a solvent gradient ranging from 95:5 hexanes/EtOAc to 80:20 hexanes/EtOAc, affording 1.2 g (35%, 51% based on unrecovered **7**) of the title compound as a yellow solid. Recrystallization from MeOH afforded analytically pure material as bright orange needles: mp 160-

180 ˚C (dec.); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.47 (s, 3H), 6.80 (d, 1H, *J* = 10.2 Hz), 6.89 (d, 1H, *J* = 10.2 Hz), 7.25 (d, 1H, *J* = 9.0 Hz), 7.36 (d, 2H, *J* = 8.0 Hz), 7.42 (d, 1H, *J* = 9.0 Hz), 7.87 (d, 2H, *J* = 8.0 Hz), 12.40 (s, 1H); ^{13}C ($CDCl_3$, 125 MHz) δ: 190.15, 182.09, 160.79, 145.96, 140.91, 140.17, 137.23, 133.57, 132.74, 129.94, 128.99, 125.84, 123.65, 115.11, 21.97; MS (EI) m/z found (rel intensity): 28 (69.9), 32 (19.9), 91 (25.7), 155 (22.5), 189 (37.6), 190 (100.0), 191 (18.3), 344 (16.4); HRMS (EI): Calcd for $C_{17}H_{12}O_6S$: 344.0355. Found: 344.0357. Anal. Calcd for $C_{17}H_{12}O_6S$: C, 59.30; H, 3.51. Found: C, 59.10; H, 3.59.

Recovery of unreacted naphthazarin. The aqueous Na_2CO_3 extracts were combined and 200 mL of CH_2Cl_2 was added. Then 2 N HCl was used to neutralize the mixture to pH ~ 6 (caution: foaming). The aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined extracts were dried over Na_2SO_4, and solvent was evaporated to leave almost pure naphthazarin (**7**). Recrystallization from EtOAc/hexanes produced pure naphthazarin (0.60 g, 32%).

1,8-Dihydroxy-4-*p*-tosyloxy-9,10-anthraquinone (11). Tosylate **8** (0.250 g; 0.727 mmol) was dried under high vacuum in a 50-mL flame-dried flask with a magnetic stirring bar under P_2O_5 overnight. The flask was then put under Ar and anhydrous CH_2Cl_2 (25 mL) was added. The solution was stirred and neat diene **9** (1.38 g; 8.00 mmol) was added dropwise over a period of 20 min. After almost one hour, TLC showed the absence of the yellow starting material **8** (R_f = 0.42; 1:2 EtOAc/hexanes). The solvent was evaporated under house vacuum and the excess diene was evaporated under high vacuum for 2 hours. The residue was dissolved in MeOH (30 mL) and was opened to the air. Aqueous 1 M NaOH (~ 5 mL) was added dropwise over 10 min and the reaction was left to stir open to the air for one more hour. The solution was acidified with aqueous 1 N HCl (6 mL). The reaction mixture was poured into CH_2Cl_2 (100 mL) and water (100 mL). The organic layer was separated and the aqueous layer was further extracted with CH_2Cl_2 (2 × 100 mL). All the organic fractions were combined, dried over sodium sulfate and concentrated on a rotary evaporator. The resulting residue was put on three preparative TLC plates (silica, 20 cm × 20 cm × 1000 micron, Analtech # 81013, tapered with pre-adsorbant area) and eluted with 1:4 EtOAc/hexanes. The yellow band was scraped off and EtOAc was used to extract the silica to yield 60 mg (20 %) of **11** as a yellow solid: mp 233 - 255 ˚C (dec.); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.41 (s, 3H), 7.25 (d, 1H, *J* = 8.8 Hz),

7.27 (dd, 1H, *J* = 4.8, 4.8 Hz), 7.32 (d, 2H, *J* = 8.8 Hz), 7.42 (d, 1H, *J* = 8.8 Hz), 7.68 (d, 2H, *J* = 4.8 Hz) 7.85 (d, 2H, *J* = 8.8 Hz), 11.83 (s, 1H), 12.51 (s, 1H); ^{13}C ($CDCl_3$, 125 MHz) δ: 192.70, 179.75, 162.46, 161.88, 145.85, 141.04, 137.86, 134.41, 134.27, 132.83, 129.93, 129.10, 125.92, 125.71, 124.36, 120.35, 116.18, 115.34, 21.94. MS (EI) m/z found (rel intensity): 117 (28.5), 256 (80.4), 257 (100.0), 411 (58.1). HRMS (EI): Calcd for $C_{21}H_{14}O_7S$: 410.0460. Found: 410.0463. Anal. Calcd for $C_{21}H_{14}O_7S$: C, 61.46; H, 3.44. Found: C, 61.30; H, 3.54.

1,8-Dihydroxy-4-(methoxycarbonylmethylthio)-9,10-anthraquinone (6). A. From tosylate 11. To a 100-mL round-bottomed flask containing 140 mg of K_2CO_3 (1.01 mmol; which had been freshly roasted over a Meeker burner) and 15 mL of anhydrous THF, was added 0.10 mL of methyl mercaptoacetate (~**12**, 1.12 mmol) in one portion. The mixture was kept, with stirring and under Ar, at reflux temperature for about 20 min. Then dry tosylate **11** (82 mg; 0.20 mmol) in 20 mL of THF was added dropwise to the flask over 20 min. When TLC indicated that all tosylate (R_f = 0.47; 1:2 EtOAc/hexanes) was consumed (ca 2 h), the reaction was cooled to room temperature and then all the solvent was removed on a rotary evaporator. The resulting residue was subjected to flash column chromatography on silica gel (2.5 cm × 14 cm; 1:8 EtOAc/hexanes to 1:2 EtOAc/hexanes) to provide 45 mg (65%) of **6** as a reddish solid. **B. From nitroanthraquinone 14.** To a 100-mL round-bottomed flask containing 140 mg K_2CO_3 (1.01 mmol; which had been freshly roasted over a Meeker burner) and 15 mL of anhydrous THF, was added 0.65 mL of methyl mercaptoacetate (~**12**, 5.20 mmol) in one portion. With stirring and under Ar, the mixture was kept at 50 ˚C for about 20 min. Then a solution of dry nitro compound **14** (300 mg, 1.05 mmol) in 20 mL of anhydrous THF was added dropwise over 20 min. The stirred reaction mixture was kept at a temperature of ca 55˚C. When TLC indicated that all the nitro compound **14** (R_f = 0.46; 1:2 EtOAc/hexanes) was consumed (ca 3 h), the reaction was cooled to room temperature and then all the solvent was removed on a rotary evaporator; the excess methyl mercaptoacetate was evaporated using high vacuum. The resulting residue was subjected to flash column chromatography on NH_3-treated silica gel [4 cm × 12 cm column; column prepared from a slurry of 60 g of silica gel in a mixture of 200 mL each of EtOAc and hexanes and 20 mL of conc (30%) aq NH_4OH]. A mixture of 1:1 EtOAc/hexanes was used to elute undesired compounds; finally, a mixture of acetic acid and EtOAc (1/9 ratio) was used to elute the

desired compound to provide 185 mg (51%) of **6** as a reddish solid identical to the material prepared above. Recrystallization from EtOAc/hexanes afforded analytically pure **6**: mp 198-202 ˚C (dec.); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.77 (s, 3H), 3.78 (s, 2H), 7.29 (dd, 1H, *J* = 8.4, 0.8 Hz), 7.32 (d, 1H, *J* = 9.4 Hz), 7.71 (dd, *J* = 8.4, 8.0 Hz), 7.76 (d, 1H, *J* = 9.4 Hz), 7.87 (dd. 1H, *J* = 8.0, 0.8 Hz), 12.00 (s, 1H), 12.57 (s, 1H); ^{13}C ($CDCl_3$, 125 MHz) δ: 192.62, 182.05, 170.08, 162.47, 161.20, 137.70, 136.14, 134.08, 133.92, 127.98, 125.51, 124.09, 120.31, 116.67, 115.60, 53.07, 34.75; MS (EI) m/z found (rel intensity): 25 (100), 30 (25.7), 271 (53.2), 284 (18.3), 312 (22.1), 344 (16.1); HRMS (EI): Calcd for $C_{17}H_{12}O_6S$: 344.0355. Found: 344.0352. Anal. Calcd for $C_{17}H_{12}O_6S$: C, 59.30; H, 3.51. Found: C, 59.20; H, 3.51.

Methyl 5,7-dihydroxy-6-oxo-6*H*-anthra[1,9-*bc*]thiophene-1-carboxylate (1). A 100-mL round-bottomed flask equipped with a condenser and a Teflon-coated magnetic stir bar, under Ar, was charged with 100 mg (0.291 mmol) of **6**, 30 mL of anhydrous MeOH and 1.5 mL of 1 M NaOMe/MeOH. The mixture was refluxed for about 3 hours until TLC indicated the disappearance of starting material (R_f = 0.42; 1:2 EtOAc/hexanes). After cooling to room temperature, the reaction mixture was treated with 2.0 mL of 1 N HCl in 50 mL of H_2O and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified on a 2.5 cm × 20 cm silica gel flash chromatography column using 2:1 hexanes/EtOAc to give the final product **1** (71 mg, 75%) as a reddish solid. Recrystallization from EtOAc/hexanes produced analytically pure material: mp 233-238 ˚C (dec.), lit.[1] mp 230-235 ˚C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.05 (s, 3H), 7.12 (dd, 1H, *J* = 8.2, 0.8 Hz), 7.28 (d, 1H, *J* = 8.8 Hz), 7.68 (t, 1H, *J* = 8.2 Hz), 8.02 (d, 1H, *J* = 8.8 Hz) 8.88 (dd, 1H, *J* = 8.2, 0.8 Hz), 12.36 (s, 1H), 13.13♦ (s, 1H); ^{13}C ($CDCl_3$, 125 MHz) δ: 191.03, 164.19, 163.53, 163.45, 137.43, 136.76, 134.29, 133.03, 131.25, 130.20, 128.92, 120.33, 119.67, 119.00, 115.42, 111.53, 53.50; IR [ν_{max} cm^{-1} ($CHCl_3$)] 2358, 2339, 1721, 1626, 1610, 1488, 1446, 1224; UV♦ [λ_{max} nm (ε, EtOH)] 228 (22000), 336 (4700), 377 (2900), 398 (4500), 446 (5900), 460 (5900); MS (EI) m/z found (rel intensity): 267 (13.1), 268 (19.4), 295

♦ The authors of ref 1 reported the ^{1}H chemical shift of the most downfield peak as δ 13.21 but in the original spectrum it is at δ 13.12, in agreement with our value of 13.13. In the UV/Vis spectrum of **1**, our sample gives peaks whose positions (λ_{max}) are in agreement with those reported, but our reproducible extinction coefficients are uniformly ~70% of those reported. The difference is presumably due either to instrument malfunction or misweighing.

(31.7), 326 (100); HRMS (EI): Calcd for $C_{17}H_{10}O_5S$: 326.0249. Found: 326.0253. Anal. Calcd for $C_{17}H_{10}O_5S$: C, 62.57; H, 3.09. Found: C, 62.60; H, 3.04.

4,5-Dihydroxy-1-nitro-9,10-anthraquinone (14). (This procedure is a modification of that of ref 6.) A mixture of 1,8-dihydroxy-9,10-anthraquinone (6.20 g; 25.8 mmol), KNO_3 (4.20 g, 41.5 mmol) and glacial acetic acid (350 mL) was refluxed for one hour, then the mixture was left overnight at room temperature. Cold water (250 mL) was added in one portion and a yellow precipitate formed. The precipitate was collected by vacuum filtration and the filtrate was extracted with CH_2Cl_2 (3 × 100 mL). The CH_2Cl_2 extracts were combined and dried over Na_2SO_4. Removal of the solvent also led to a yellow solid. The crude yellow solids were combined and flash chromatographed on a 5.5 cm × 30 cm silica gel column using a hexanes/EtOAc gradient (95/5 to 2/1). The desired product (R_f = 0.46; 1:2 EtOAc/hexanes) is the second compound to elute (1.54 g, 21%). Recrystallization from xylene afforded analytically pure **14**: mp 242-245 °C, lit.[6] mp 244 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.36 (dd, 1H, *J* = 8.0, 1.2 Hz), 7.38 (d, 1H, *J* = 8.8 Hz), 7.68 (d, 1H, *J* = 8.8 Hz), 7.75 (t, 1H, *J* = 8.0), 7.80 (dd, 1H, *J* = 8.0, 1.2 Hz), 11.76 (s, 1H), 12.50 (s, 1H); ^{13}C ($CDCl_3$, 125 MHz) δ: 191.92, 179.04, 163.87, 163.03, 142.81, 138.53, 133.30, 131.37, 125.64, 125.22, 121.16, 115.48, 115.15, 109.36; HRMS (EI): Calcd for $C_{14}H_7NO_6$: 285.0273. Found: 285.0275.