Supporting Information

Total Synthesis of (±)-Hasubanonine

Spencer B. Jones, Liwen He, and Steven L. Castle*

Department of Chemistry and Biochemistry

Brigham Young University, Provo, Utah, 84602

Table of Contents

General Experimental Details	S2
Experimental Procedures and Spectral Data	S2–S12
¹ H and ¹³ C NMR Spectra	S13–S38

General Experimental Details

Dimethyl formamide, dimethyl sulfoxide, methanol, methylene chloride, and tetrahydrofuran were dried by passage through a Glass Contour solvent drying system containing cylinders of activated alumina.¹ Flash chromatography was carried out using 60–230 mesh silica gel. ¹H NMR spectra were acquired on 300 or 500 MHz spectrometers with chloroform (7.27 ppm) or benzene (7.16 ppm) as internal reference. Signals are reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), td (triplet of doublets), br s (broad singlet), m (multiplet). Coupling constants are reported in hertz (Hz). ¹³C NMR spectra were acquired on spectrometers operating at 75 or 125 MHz with chloroform (77.23 ppm) or benzene (128.06 ppm) as internal reference. Infrared spectra were obtained on an FT-IR spectrometer. Mass spectral data were obtained using FAB or ESI techniques.

4-Benzyloxy-2,3-dimethoxy-6-nitrobenzaldehyde (8). A solution of **7**² (565 mg, 2.07 mmol) in glacial acetic acid (5 mL) at 0 °C was treated dropwise with a 1:2 v/v mixture of glacial acetic acid:fuming nitric acid (5 mL). The resulting mixture was stirred at 0 °C for 90 min, then poured into ice water (50 mL) and extracted with CH₂Cl₂ (3 × 15 mL). The combined organic layers were washed with sat aq NaHCO₃ (2 × 30 mL) and brine (10 mL), dried (Na₂SO₄), and concentrated in vacuo. Flash chromatography (SiO₂, 15% EtOAc in hexanes elution) provided **8** (627 mg, 1.98 mmol, 96%) as a yellow solid: ¹H NMR (CDCl₃, 500 MHz) δ 10.24 (s, 1H), 7.46–7.38 (m, 5H),

¹ Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

² Kurosawa, K.; Ollis, W. D.; Sutherland, I. O.; Gottlieb, O. R.; De Oliveira, A. B. *Phytochemistry* **1978**, *17*, 1389.

7.39 (s, 1H), 5.22 (s, 2H), 3.984 (s, 3H), 3.982 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 186.9, 154.7, 153.3, 147.3, 143.1, 134.9, 128.9 (2C), 128.7, 127.6 (2C), 121.3, 105.1, 71.6, 62.9, 61.3; IR (film) ν_{max} 2944, 2874, 1704, 1595, 1524, 1309, 1116, 747 cm^{-1} ; HRMS (ESI) m/z 318.09863 (MH^+ , $\text{C}_{16}\text{H}_{15}\text{NO}_6\text{H}$ requires 318.09721).

4-Benzyloxy-6-iodo-2,3-dimethoxybenzaldehyde (5). A mixture of **8** (2.30 g, 7.26 mmol), $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (20.2 g, 72.6 mmol), CH_3OH (116 mL), and H_2O (30 mL) was heated to 80 $^\circ\text{C}$ with stirring. As soon as the mixture reached this temperature, conc aq NH_4OH (25–30 wt %, 21.8 mL, 157 mmol) was added dropwise with vigorous stirring. The resultant mixture was stirred for 10 min, cooled to rt, filtered through a pad of Celite (rinsed with 200 mL EtOAc), and washed with brine (25 mL). The organic layer was dried (Na_2SO_4), and the solvent was removed in vacuo to afford the derived aniline, which was used directly in the next step.

A solution of the aniline in CH_3CN (145 mL) at 0 $^\circ\text{C}$ was treated dropwise with HBF_4 (50 wt % in H_2O , 1.2 mL, 9.6 mmol). The mixture was warmed to rt, stirred for 25 min, then cooled to 0 $^\circ\text{C}$, treated dropwise with *t*-BuONO (1.25 mL, 1.08 g, 10.5 mmol), and stirred for 60 min. The mixture was then poured into a solution of KI (60.2 g, 363 mmol) in H_2O (363 mL) at 0 $^\circ\text{C}$, stirred at 0 $^\circ\text{C}$ to rt for 16 h, and extracted with CH_2Cl_2 (3 $\times$ 50 mL). The combined organic layers were washed with sat aq $\text{Na}_2\text{S}_2\text{O}_3$ (25 mL) and brine (25 mL), dried (Na_2SO_4), and concentrated in vacuo. Flash chromatography (SiO_2 , 20% EtOAc in hexanes elution) afforded **5** (1.18 g, 3.0 mmol, 41%) as a light yellow oil: ^1H NMR (CDCl_3 , 500 MHz) δ 10.06 (s, 1H), 7.46–7.36 (m, 5H), 7.38 (s, 1H), 5.16 (s, 2H), 3.98 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 191.0, 157.5, 157.3, 143.4, 135.6, 128.9 (2C), 128.8, 127.7 (2C), 123.5, 122.3, 89.7, 71.4, 62.8, 61.3;

IR (film) $\nu_{\max}$ 2936, 2850, 1689, 1569, 1481, 1367, 1295, 1105, 743 cm^{-1} ; HRMS (ESI) m/z 399.00766 (MH^+ , $\text{C}_{16}\text{H}_{15}\text{O}_4\text{IH}$ requires 399.00878).

2-Iodo-3,4-dimethoxybenzaldehyde (10). A solution of trimethylethylenediamine (860 μL , 6.63 mmol) in anhydrous benzene (5.5 mL) at 0 $^{\circ}\text{C}$ under Ar was treated dropwise with *n*-BuLi (1.4 M in hexane, 4.60 mL, 6.44 mmol). The resultant mixture was warmed to rt and stirred for 15 min, then cooled to 0 $^{\circ}\text{C}$ and treated dropwise with a solution of 3,4-dimethoxybenzaldehyde (**9**, 988 mg, 5.95 mmol) in anhydrous benzene (4.5 mL). The resultant mixture was warmed to rt and stirred for 15 min, then cooled to 0 $^{\circ}\text{C}$ and treated dropwise with PhLi (1.8 M in *n*-Bu₂O, 10.0 mL, 18.0 mmol) over a period of 10 min. The mixture was warmed to rt and stirred under Ar for 9 h. Anhydrous THF (8.85 mL) was added, and the mixture was cooled to -78°C , then treated via cannula with a solution of 1,2-diiodoethane (7.63 g, 27.1 mmol) in anhydrous THF (11.1 mL). The resultant solution was warmed to rt and stirred for 16 h, then washed with sat aq NH_4Cl (50 mL), sat aq $\text{Na}_2\text{S}_2\text{O}_3$ (50 mL), H_2O (50 mL), and brine (50 mL). The organic layer was dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (SiO_2 , 10% EtOAc in hexanes elution) afforded **10** (1.04 g, 3.57 mmol, 60%) as a yellow oil: ^1H NMR (CDCl_3 , 300 MHz) δ 10.05 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.01 (d, J = 8.4 Hz, 1H), 3.99 (s, 3H), 3.90 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 195.2, 158.0, 149.0, 129.2, 127.6, 112.1, 100.6, 60.7, 56.5; IR (film) $\nu_{\max}$ 2936, 2846, 1674, 1577, 1019, 927 cm^{-1} ; HRMS (ESI) m/z 292.96626 (MH^+ , $\text{C}_9\text{H}_9\text{O}_3\text{IH}$ requires 292.96691).

3,4-Dimethoxy-2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzaldehyde (6). A solution of **10** (149 mg, 0.510 mmol), bis(pinacolato)diboron (143 mg, 0.561

mmol), KOAc (150 mg, 1.53 mmol), and Pd(OAc)₂ (3.5 mg, 0.015 mmol) in anhydrous DMF (2 mL) was stirred at 80 °C under Ar for 16 h. The mixture was then diluted with H₂O (2 mL) and Et₂O (3 mL), the layers were separated, and the aqueous layer was extracted with Et₂O (3 × 3 mL). The combined organic layers were washed with brine (2 × 2 mL), dried (Na₂SO₄), and concentrated in vacuo. Flash chromatography (SiO₂, 10% EtOAc in hexanes elution) afforded **6** (123 mg, 0.421 mmol, 83%) as a white solid: ¹H NMR (CDCl₃, 500 MHz) δ 9.80 (s, 1H), 7.54 (d, *J* = 8.5 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 1H), 3.93 (s, 3H), 3.86 (s, 3H), 1.46 (s, 12H); ¹³C NMR (CDCl₃, 125 MHz) δ 191.4, 157.4, 152.6, 133.5, 130.5, 112.2, 96.2, 84.4 (2C), 61.3, 55.9, 24.9 (4C); IR (film) ν_{max} 2977, 2841, 1684, 1561, 1458, 1041, 967, 849 cm⁻¹; HRMS (ESI) *m/z* 293.15617 (MH⁺, C₁₅H₂₁O₅BH requires 293.15548).

5-Benzyloxy-3,4,5',6'-tetramethoxy-biphenyl-2,2'-dicarbaldehyde (11). A solution of aryl iodide **5** (1.18 g, 2.96 mmol), arylboronic ester **6** (1.08 g, 3.70 mmol), K₂CO₃ (1.64 g, 11.8 mmol), and Pd(dppf)Cl₂·CH₂Cl₂ (362 mg, 0.44 mmol) in anhydrous DMSO (37 mL) was stirred at 80 °C under Ar for 16 h. The mixture was diluted with brine (20 mL) and EtOAc (25 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with brine (2 × 20 mL), dried (Na₂SO₄), and concentrated in vacuo. Flash chromatography, (SiO₂, 30% EtOAc in hexanes elution) afforded **11** (1.02 g, 2.34 mmol, 79%) as a yellow solid: ¹H NMR (CDCl₃, 500 MHz) δ 10.18 (s, 1H), 9.46 (s, 1H), 7.77 (d, *J* = 8.5 Hz, 1H), 7.41–7.32 (m, 5H), 7.05 (d, *J* = 9.0 Hz, 1H), 6.57 (s, 1H), 5.12 (s, 2H), 4.07 (s, 3H), 3.98 (s, 3H), 3.97 (s, 3H), 3.50 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 190.2, 189.3, 157.6, 157.5, 156.7, 145.9, 142.3, 138.5, 136.0, 132.0, 128.9 (2C), 128.6, 128.2, 127.6 (2C),

125.5, 123.1, 112.7, 111.7, 71.2, 62.7, 61.3, 60.7, 56.2; IR (film) $\nu_{\max}$ 2940, 2841, 1684, 1586, 1560, 1276, 1254, 1109 cm^{-1} ; HRMS (ESI) m/z 437.16032 (MH^+ , $\text{C}_{25}\text{H}_{24}\text{O}_7\text{H}$ requires 437.15948).

5-Benzyloxy-3,4,2',3'-tetramethoxy-2,6'-divinyl-biphenyl (12). A suspension of methyltriphenylphosphonium bromide (purified by flash chromatography with 5–15% MeOH in CH_2Cl_2 gradient elution, then dried over P_2O_5 in a vacuum desiccator for 3 d, 3.20 g, 8.96 mmol) in anhydrous THF (100 mL) was cooled to 0 °C and treated dropwise with *n*-BuLi (6.40 mL, 1.6 M in hexanes, 10.24 mmol). The solution was warmed to rt and stirred for 2 h, then cooled to –78 °C and treated dropwise over 10 min with a solution of **11** (869 mg, 1.99 mmol) in anhydrous THF (90 mL + 2 $\times$ 5 mL rinses). The resultant mixture was stirred for 10 min, then warmed to rt and stirred for 1.5 h. The reaction was quenched by the addition of 2 N HCl (9 mL, 18 mmol), diluted with brine (100 mL), and extracted with EtOAc (3 $\times$ 70 mL). The combined organic layers were dried (Na_2SO_4), and the solvent was removed in vacuo. Flash chromatography (SiO_2 , 5–15% EtOAc in hexanes gradient elution) afforded **12** (800.8 mg, 1.85 mmol, 93%) as a colorless oil: ^1H NMR (CDCl_3 , 300 MHz) δ 7.43–7.25 (m, 6H), 6.92 (d, J = 9.0 Hz, 1H), 6.49 (s, 1H), 6.33 (dd, J = 11.7, 18.0 Hz, 1H), 6.21 (dd, J = 11.1, 17.4 Hz, 1H), 5.49 (d, J = 17.4 Hz, 1H), 5.43 (d, J = 17.7 Hz, 1H), 5.13–5.03 (m, 3H), 4.96 (d, J = 11.1 Hz, 1H), 3.98 (s, 3H), 3.90 (s, 6H), 3.48 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 152.7, 152.6, 151.2, 146.4, 142.4, 137.1, 135.0, 134.7, 131.6, 131.3, 130.3, 128.7 (2C), 128.1, 127.6 (2C), 124.3, 120.6, 117.7, 113.1, 112.0, 111.8, 70.8, 61.3, 60.8, 60.6, 56.0; IR (film) $\nu_{\max}$ 2936, 2836, 1589, 1481, 1290, 1128, 912, 738 cm^{-1} ; HRMS (ESI) m/z 433.20074 (MH^+ , $\text{C}_{27}\text{H}_{28}\text{O}_5\text{H}$ requires 433.20095).

3-Benzyloxy-1,2,5,6-tetramethoxy-phenanthrene (4). A solution of **12** (367 mg, 0.849 mmol) and the Grubbs second-generation ruthenium catalyst³ (18.2 mg, 0.021 mmol) in anhydrous CH₂Cl₂ (83 mL) was stirred at 40 °C under Ar for 2 h. The solvent was removed in vacuo and the residue was purified via flash chromatography to afford **4** (340 mg, 0.841 mmol, 99%) as a white solid: ¹H NMR (CDCl₃, 300 MHz) δ 9.11 (s, 1H), 7.91 (d, *J* = 9.3 Hz, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.57–7.52 (m, 3H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.35–7.25 (m, 2H), 5.36 (s, 2H), 4.07 (s, 6H), 4.01 (s, 3H), 3.70 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 151.5, 151.2, 148.6, 146.7, 141.7, 137.4, 128.8 (2C), 128.6, 128.0, 127.3 (2C), 126.4, 125.3, 125.1, 124.3, 123.5, 118.8, 113.1, 107.0, 70.7, 61.9, 61.4, 60.1, 56.7; IR (film) $\nu_{\max}$ 2933, 2830, 1597, 1501, 1276, 1113, 742 cm⁻¹; HRMS (ESI) *m/z* 427.15077 (MNa⁺, C₂₅H₂₄O₅Na requires 427.15159).

1,2,5,6-Tetramethoxy-9,10-dihydro-phenanthren-3-ol (3). A flask containing **4** (340 mg, 0.841 mmol), 10% Pd/C (170 mg), and EtOAc (28 mL) was placed inside a Parr apparatus, pressurized to 70 psi with H₂, and stirred for 16 h. The mixture was filtered through a pad of Celite and concentrated in vacuo. Flash chromatography (SiO₂, 22% EtOAc/hexanes elution) afforded **3** (252 mg, 0.797 mmol, 95%) as a colorless oil: ¹H NMR (CDCl₃, 500 MHz) δ 7.90 (s, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 5.57 (s, 1H), 3.99 (s, 3H), 3.89 (s, 3H), 3.85 (s, 3H), 3.74 (s, 3H), 2.76–2.71 (m, 2H), 2.68–2.64 (m, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 152.3, 149.0, 147.4, 147.2, 139.1, 132.2, 129.0, 127.9, 124.8, 123.0, 111.3, 111.1, 61.1, 60.9, 60.4, 56.2, 29.7, 21.9; IR (film) $\nu_{\max}$ 3421, 2937, 2834, 1568, 1096, 760 cm⁻¹; HRMS (ESI) *m/z* 317.13840 (MH⁺, C₁₈H₂₀O₅H requires 317.13835).

³ Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953.

1,2,2,5,6-Pentamethoxy-9,10-dihydro-2H-phenanthren-3-one (13). A mixture of KHCO_3 (112.7 mg, 1.11 mmol), I,I-diacetoxiodobenzene (164.8 mg, 0.512 mmol), and anhydrous CH_3OH (5 mL) was cooled to $-10\text{ }^\circ\text{C}$ and treated dropwise over 5 min with a solution of **3** (147 mg, 0.465 mmol) in anhydrous CH_3OH (5 mL + 1 mL rinse). The resultant mixture was stirred at $-10\text{ }^\circ\text{C}$ for 20 min, then diluted with brine (10 mL) and CH_2Cl_2 (15 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 ($3 \times 5\text{ mL}$). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (SiO_2 , 2:8:90 $\text{Et}_3\text{N}/\text{EtOAc}/\text{hexanes}$ elution) afforded **13** (141.6 mg, 0.409 mmol, 88%) as a yellow oil that solidified upon standing: ^1H NMR (C_6D_6 , 500 MHz) δ 7.37 (s, 1H), 6.58 (d, $J = 8.0\text{ Hz}$, 1H), 6.48 (d, $J = 8.0\text{ Hz}$, 1H), 3.91 (s, 3H), 3.57 (s, 3H), 3.42 (s, 6H), 3.27 (s, 3H), 2.58–2.55 (m, 2H), 2.43–2.40 (m, 2H); ^{13}C NMR (C_6D_6 , 125 MHz) δ 195.1, 153.6, 152.9, 150.5, 146.3, 135.9, 128 (obscured by solvent peak), 126.9, 123.4, 120.3, 115.2, 95.0, 60.4, 59.8, 56.2, 51.2 (2C), 30.3, 23.4; IR (film) ν_{max} 2941, 2840, 1660, 1541, 1340, 1078 cm^{-1} ; HRMS (ESI) m/z 369.13084 (MNa^+ , $\text{C}_{19}\text{H}_{22}\text{O}_6\text{Na}$ requires 369.13086).

3-Allyl-1,2,2,5,6-pentamethoxy-2,3,9,10-tetrahydro-phenanthren-3-ol (14). A solution of **13** (213 mg, 0.615 mmol) in anhydrous Et_2O (21 mL) at $-78\text{ }^\circ\text{C}$ under Ar was treated dropwise with allylmagnesium chloride (2.0 M in THF, 1.69 mL, 3.38 mmol). The resulting mixture was stirred at $-78\text{ }^\circ\text{C}$ for 1 h, then treated with brine (2 mL) and allowed to warm to rt. The mixture was diluted with additional brine (20 mL) and sat aq potassium tartrate (5 mL), then extracted with EtOAc ($3 \times 20\text{ mL}$). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (SiO_2 , 2:10:88 $\text{Et}_3\text{N}/\text{EtOAc}/\text{hexanes}$ elution) afforded **14** (222 mg, 0.572 mmol, 93%) as

a colorless oil: ^1H NMR (C_6D_6 , 500 MHz) δ 7.10 (s, 1H), 6.64 (d, $J = 8.5$ Hz, 1H), 6.47 (d, $J = 8.5$ Hz, 1H), 6.31–6.22 (m, 1H), 5.12 (dd, $J = 17.0, 2.0$ Hz, 1H), 5.02 (dd, $J = 10.5, 1.0$ Hz, 1H), 3.71 (s, 3H), 3.62 (s, 3H), 3.45 (s, 3H), 3.34 (s, 3H), 3.23 (s, 3H), 3.05 (s, 1H), 2.91–2.85 (m, 1H), 2.79–2.74 (m, 1H), 2.54–2.45 (m, 3H), 2.43–2.37 (m, 1H); ^{13}C NMR (C_6D_6 , 125 MHz) δ 153.1, 149.8, 136.5, 135.9, 135.5, 132.9, 127.7, 125.7, 125.4, 123.5, 117.8, 112.5, 101.8, 80.5, 61.2, 59.9, 56.3, 51.6, 51.0, 40.0, 30.5, 24.1; IR (film) ν_{max} 3582, 2937, 2835, 1480, 1261, 1218, 1053 cm^{-1} ; HRMS (ESI) m/z 411.17711 (MNa^+ , $\text{C}_{22}\text{H}_{28}\text{O}_6\text{Na}$ requires 411.17781).

4a-Allyl-1,2,2,5,6-pentamethoxy-4,4a,9,10-tetrahydro-2H-phenanthren-3-one (15). A mixture of $\text{KO}t\text{-Bu}$ (70 mg, 0.62 mmol), 18-crown-6 (169 mg, 0.64 mmol), and anhydrous THF (5 mL) at -10 $^\circ\text{C}$ under Ar was stirred for 10 min. A solution of **14** (80 mg, 0.206 mmol) in anhydrous THF (5 mL) was added to the mixture dropwise over three min, and the resultant mixture was stirred at -10 $^\circ\text{C}$ for 10 min. The solution was treated with brine (10 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (SiO_2 , 2:5:93 $\text{Et}_3\text{N}/\text{EtOAc}/\text{hexanes}$ elution) afforded **15** (59.4 mg, 0.153 mmol, 74%) as a colorless oil: ^1H NMR (C_6D_6 , 500 MHz) δ 6.81–6.76 (m, 2H), 5.61–5.50 (m, 1H), 4.96 (d, $J = 16.0$ Hz, 1H), 4.90, (d, $J = 10.0$ Hz, 1H), 3.89 (s, 3H), 3.84 (s, 3H), 3.78 (s, 3H), 3.59 (d, $J = 14.0$ Hz, 1H), 3.43 (s, 3H), 3.24 (s, 3H), 3.12–3.07 (m, 1H), 3.01–2.86 (m, 3H), 2.77 (td, $J = 14.0, 5.0$ Hz, 1H), 2.60 (dd, $J = 14.0, 8.0$ Hz, 1H), 2.17 (td, $J = 14.0, 5.0$ Hz, 1H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 203.1, 151.8, 148.3, 145.7, 135.6, 135.0, 134.9, 130.0, 124.1, 118.1, 111.9, 97.9, 62.3, 60.7, 56.1, 52.7, 51.3, 49.0, 46.4, 44.8, 31.7,

23.0; IR (film) $\nu_{\max}$ 2939, 2836, 1731, 1483, 1275, 1089, 919, 808, 736 cm^{-1} ; HRMS (ESI) m/z 411.17711 (MNa^+ , $\text{C}_{22}\text{H}_{28}\text{O}_6\text{Na}$ requires 411.17781).

Hemiaminal 16. A solution of **15** (30.0 mg, 0.0772 mmol) in EtOAc (7.5 mL) at $-78\text{ }^{\circ}\text{C}$ was treated with O_3 (bubbled slowly through the mixture) until the starting material was consumed as indicated by TLC. The solution was then stirred for five min before being treated with Et_3N (33.0 μL , 0.232 mmol). The resultant solution was stirred at rt for 16 h, then concentrated in vacuo to afford the crude aldehyde.

The aldehyde was then dissolved in anhydrous CH_3OH (1 mL) and treated with 4 Å MS (50 mg) followed by CH_3NH_2 (1.7 M in CH_3OH , 181 μL , 0.308 mmol). The mixture was stirred at rt for 30 min, then treated with NaBH_3CN (9.7 mg, 0.154 mmol) and stirred for 5 h before being quenched with 0.1 N NaOH (0.5 mL), diluted with brine (0.5 mL), and extracted with EtOAc ($4 \times 1.5\text{ mL}$). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (SiO_2 , 2:20:78 $\text{Et}_3\text{N}/\text{EtOAc}/\text{hexanes}$ elution) afforded **16** (19.2 mg, 0.0474 mmol, 62%) as a colorless oil: ^1H NMR (C_6D_6 , 500 MHz) δ 6.64 (d, $J = 8.0\text{ Hz}$, 1H), 6.50 (d, $J = 8.0\text{ Hz}$, 1H), 3.85 (s, 3H), 3.67 (s, 3H), 3.58 (s, 3H), 3.37 (s, 3H), 3.32 (s, 3H), 3.29–3.24 (m, 1H), 3.09 (d, $J = 12.5\text{ Hz}$, 1H), 3.07–2.94 (m, 2H), 2.93 (s, 3H), 2.80–2.75 (m, 1H), 2.73–2.66 (m, 2H), 1.97 (d, $J = 11.5\text{ Hz}$, 1H), 1.81 (td, $J = 13.0, 5.5\text{ Hz}$, 1H), 1.40–1.24 (m, 1H), 1.18 (d, $J = 12.5\text{ Hz}$, 1H); ^{13}C NMR (C_6D_6 , 125 MHz) δ 152.7, 150.3, 148.6, 135.8, 131.2, 131.0, 124.2, 112.2, 100.1, 86.4, 62.9, 60.8, 56.0, 52.4, 49.2, 42.6, 41.3, 37.3, 31.9, 30.6, 29.9, 22.3; IR (film) $\nu_{\max}$ 3421, 2920, 2854, 1596, 1460, 1254, 1064 cm^{-1} ; HRMS (ESI) m/z 406.2220 (MH^+ , $\text{C}_{22}\text{H}_{31}\text{NO}_6\text{H}$ requires 406.2230).

(±) **Hasubanone (1)**. A solution of **16** (7.2 mg, 0.0178 mmol) in anhydrous CH_2Cl_2 (2.0 mL) was treated with 4Å MS (72 mg) and stirred at rt for 10 min. Trifluoroacetic acid (1.0 M in CH_2Cl_2 , 53 μL , 0.053 mmol) was added slowly, and the resultant mixture was stirred at 35 °C for 22 h. The reaction was quenched by the addition of K_3PO_4 (50 mg), stirred for 5 min, filtered, and concentrated in vacuo. Flash chromatography (SiO_2 , 2:20:78 $\text{Et}_3\text{N}/\text{EtOAc}/\text{hexanes}$ elution) afforded **1** (5.4 mg, 0.0145 mmol, 81%) as a light yellow oil that solidified on standing: ^1H NMR (CDCl_3 , 500 MHz) δ 6.82 (d, J = 8.5 Hz, 1H) 6.78 (d, J = 8.5 Hz, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 3.72 (s, 3H), 3.51 (s, 3H), 3.42–3.34 (m, 1H), 3.22 (d, J = 19 Hz, 1H), 3.01–2.95 (m, 1H), 2.95–2.88 (m, 1H), 2.84–2.77 (m, 2H), 2.65–2.58 (m, 1H), 2.41 (s, 3H), 2.33 (d, J = 19 Hz, 1H), 2.20–2.12 (m, 1H), 1.49–1.44 (m, 1H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 205.7, 152.0, 148.4, 146.2, 135.8, 129.5, 124.0, 111.2, 92.7, 61.8, 60.8, 56.1, 51.9, 49.4, 47.7, 39.4, 34.9, 30.5, 29.9, 29.5, 22.5; IR (film) ν_{max} 2925, 2849, 1724, 1660, 1601, 1483, 1272 cm^{-1} ; HRMS (ESI) m/z 374.19811 (MH^+ , $\text{C}_{21}\text{H}_{27}\text{NO}_5\text{H}$ requires 374.19620).

2D ^{13}C – ^1H HETCOR NMR (CDCl_3 , 125 MHz) 124.0/6.82, 111.2/6.78, 61.8/3.72, 60.8/3.89, 56.1/3.85, 51.9/3.51, 49.4/3.42–3.34 (C-16/H-16a), 49.4/2.95–2.88 (C-16/H-16b), 47.7/3.22 (C-5/H-5a), 47.7/2.33 (C-5/H-5b), 34.9/2.41 (N-Me), 30.5/2.84–2.77 (C-15/H-15a), 30.5/1.49–1.44 (C-15/H-15b), 29.5/2.84–2.77 (C-10/H-10a), 29.5/2.65–2.58 (C-10/H-10b), 22.5/3.01–2.95 (C-9/H-9a), 22.5/2.20–2.12 (C-9/H-9b); 2D ^1H – ^1H COSY NMR (CDCl_3 , 500 MHz) 3.42–3.34/2.95–2.88 (s, H-16a/H-16b), 3.42–3.34/2.84–2.77

(m, H-16a/H-15a), 3.42–3.34/1.49–1.44 (s, H-16a/H-15b), 3.22/2.33 (s, H-5a/H-5b), 3.01–2.95/2.84–2.77 (m, H-9a/H-10a), 3.01–2.95/2.65–2.58 (s, H-9a/H-10b), 3.01–2.95/2.20–2.12 (s, H-9a/H-9b), 2.95–2.88/2.84–2.77 (s, H-16b/H-15a), 2.84–2.77/2.65–2.58 (s, H-10a/H-10b), 2.84–2.77/2.20–2.12 (s, H-10a/H-9b), 2.84–2.77/1.49–1.44 (m, H-15a/H-15b), 2.65–2.58/2.20–2.12 (m, H-10b/H-9b).

Pulse Sequence: szpu1

/05

spencer 4-benzyloxy-2,3-dimethoxy-6-nitrobenzaldehyde file 1222-cl3-nitrobenz
Pulse Sequence: szpul

STANDARD PROTON PARAMETERS
Pulse Sequence: szpu1

CL3 of E7H-202 on ID-probe, before HMQC. 03/11/2003.

Pulse Sequence: szpul

Iodide

Pulse Sequence: zgpg30

spencer jones 2-iodo-3,4-dimethoxybenzaldehyde file 1222-cl3-2iodo
Pulse Sequence: szpul

spencer_jones_bpin_file_1222-bpin
Pulse Sequence: zgpg30

spencer spin file c13bpin
Pulse Sequence: szpul

spencer jones file 1222-diaid
Pulse Sequence: szpul

spencer_jones 4-25-06 file dia1d4-25
Pulse Sequence: szpul

diene

Pulse Sequence: zgpg30

spencer jones clean diene
Pulse Sequence: szpul

phenanthrene

Pulse Sequence: szpul

4 (CDCl₃, 300 MHz)

spencer.jones@cleauphenc13
Pulse Sequence: szpul

spencer jones dihydrophenanthreneol file 5-03-dihydro
Pulse Sequence: szpul

dihydrophenanthrenol
Pulse Sequence: szpu1

dearomatized

Pulse Sequence: szpul

dearomatized

Pulse Sequence: zgpg30

tertiary alcohol

Pulse Sequence: szpul

tertiary alcohol
Pulse Sequence: zgpg30

KATC 21-6

Pulse Sequence: s2pu1

ketone

Pulse Sequence: zgpg30

Pulse Sequence: s2pul

NAME: 1

Pulse Sequence: szpul