Supporting Information

Combined Directed *ortho* and remote Metallation – Cross Coupling Strategies. General Method for Benzo[a]carbazoles and the Synthesis of an Unnamed Indolo[2,3-a]carbazole Alkaloid

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General Methods. Melting points are uncorrected. IR spectra were recorded neat or as thin films using BOMEM FT-IR spectrometer. ^1H 300 MHz and ^{13}C 75.43 MHz NMR spectra were obtained on a Bruker Avance-300, 400 or 500 spectrometer. Purity was measured on an Agilent GC/MS system. THF was freshly distilled from sodium benzophenone ketyl under nitrogen and CH_2Cl_2 and HN^iPr_2 were freshly distilled from CaH_2 under nitrogen. *n*-Butyllithium and *s*-butyllithium were purchased from Aldrich as solutions in hexanes, stored in resealable containers, and titrated periodically against *sec*-butanol using 1,10-phenanthroline as indicator.¹ All experiments were carried out under argon in dried glassware, using syringe-septum cap techniques. The $-78\text{ }^\circ\text{C}$ and $0\text{ }^\circ\text{C}$ external bath temperatures designated are approximate as achieved by a dry ice-acetone or ice baths, respectively. Flash column chromatography was carried out using Merck Kieselgel 60 silica gel (particle size: 32-63).

General Procedures

A. Cross Coupling Reaction of Arylboronic Acids with Aryl Halides or Triflates.

Synthesis of Heterobiaryls. A mixture of $\text{Pd}(\text{PPh}_3)_4$ (0.04 mmol), aryl boronic acid (1.4 mmol), aryl halide or vinyl triflate (1 mmol) and K_3PO_4 (3.0 mmol) in DMF (5 mL) was heated at 100°C for 12 h, cooled to rt and extracted with Et_2O ($3 \times 5\text{ mL}$). The organic extract was dried (Na_2SO_4), concentrated in vacuo, and the residue was purified by flash column chromatography (EtOAc -hexane) to afford the pure product.

B. Synthesis of Benzo[a]- and Indolo[2,3-a]carbazoles. To a solution of LDA (2.50 mmol) in THF (8 mL) was added a solution of heterobiaryl (1.00 mmol) in THF (2 mL) at $0\text{ }^\circ\text{C}$, the reaction mixture was stirred at rt for 4 h and quenched with a satd aq NH_4Cl solution (5 mL). The layers were separated and the aqueous phase was extracted with Et_2O ($3 \times 5\text{ mL}$). The combined organic phase was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc -hexane) to afford the pure product.

***N,N*-diethyl-1*H*-indole-3-carboxamide.** To a mixture of AlCl_3 (1.60 g, 12 mmol) and ClCONEt_2 (1.63 g, 12 mmol, 1.52 mL) in CH_2Cl_2 (50 mL) was added indole

(1.17 g, 10 mmol) in CH₂Cl₂ (50 mL). The reaction mixture was refluxed for 5 h, cooled, H₂O (100 mL) was added slowly and the aqueous phase was extracted with CH₂Cl₂ (2 × 100 mL). The combined organic phase was dried (Na₂SO₄) and concentrated in vacuo to give the crude product. Flash column chromatography (EtOAc-hexane 1:2 eluent) gave 2.0 g (9.2 mmol, 92%) of the product as colorless crystal, mp 147-149 °C (CH₂Cl₂), lit² mp 150.5-151.5 °C; IR (KBr) 1589 cm⁻¹; ¹H NMR (500 MHz, acetone-d₆) δ 10.62 (s, 1H), 7.84 (d, 1H, J = 8.0 Hz), 7.57 (s, 1H), 7.44 (s, 1H, J = 8.5 Hz), 7.15 (t, 1H, J = 8.0 Hz), 7.10 (t, 1H, J = 8.0 Hz), 3.57 (q, 4H, J = 7.0 Hz), 1.24 (t, 6H, J = 7.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 125.7, 122.4, 121.2, 120.4, 111.9, 41.4, 13.7; MS EI *m/z* (rel. int.) 216 (M⁺, 69), 187 (28), 144 (100).

***N,N*-diethyl-1-methyl-1*H*-indole-3-carboxamide (7).** NaH (0.96 g, 24.0 mmol, 60% dispersion in mineral oil) was washed with hexane (10 mL) twice, and added THF (50 mL). The suspension was cooled to 0 °C, and added the above carboxamide (4.36 g, 20.0 mmol) in THF (150 mL). The mixture was stirred 30 min, followed by addition of MeI (3.41 g, 24.0 mmol, 1.49 mL at 0 °C). The mixture was stirred at rt 12 h, and added aq. NH₄Cl solution (50 mL). The aqueous layer was extracted with Et₂O (100 mL × 2). The combined organic phase was dried (Na₂SO₄) and concentrated in vacuo to afford the product as a light yellow oil (4.49 g, 19.5 mmol, 98%). IR (KBr) 1610 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.78 (dd, 1H, J = 7.8, 1.2 Hz), 7.18-7.36 (m, 4H), 3.82 (s, 3H), 3.59 (q, 4H, J = 7.2 Hz), 1.24 (t, 6H, J = 7.2 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 129.8, 122.7, 121.3, 121.0, 109.9, 33.5, 14.3; MS EI *m/z* (rel. int.) 230 (M⁺, 52), 201 (23), 158 (100), 130 (53), 103 (46); HRMS *m/z* calcd for C₁₄H₁₈N₂O, 230.1419, found 230.1408.

3-(diethylcarbamoyl)-1-methyl-1*H*-indol-2-ylboronic acid (3). A solution of *s*-BuLi (1.20 mmol, 0.92 mL, 1.30 M in hexane) was added dropwise to a stirred solution of **7** (0.23 g, 1.00 mmol) in anhydr THF (10 mL) at -78 °C. The resulting mixture was stirred at -78 °C for 1 h, treated with an excess of B(OMe)₃ (0.25g, 2.40 mmol, 0.27 mL), and the mixture was warmed to ambient temperature over 8-12 h and quenched with a saturated aqueous NH₄Cl solution (5 mL). The layers were separated and the aqueous phase was extracted with Et₂O (3 × 10 mL). The combined organic phase was dried (Na₂SO₄) and concentrated in vacuo to afford product as a fluffy solid which was used in the cross coupling reactions without further purification.

***N,N*-diethyl-1-methyl-2-*o*-tolyl-1*H*-indole-3-carboxamide (8a).** Compound **8a** was prepared according to procedure **A**. Flash column chromatography (EtOAc-hexane 1:3 eluent) afforded 0.40 g (1.30 mmol, 81%) of the product as a colorless oil (purity 98.2%, by GC peak area). IR (KBr) 1621 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.65 (d, 1H, $J = 8.0$ Hz), 7.40-7.20 (m, 8H), 3.52 (s, 3H), 3.40 (s, 4H), 2.24 (s, 3H), 0.98 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 167.4, 139.0, 138.6, 137.1, 131.8, 131.0, 130.6, 129.7, 126.7, 126.6, 126.2, 122.6, 121.0, 120.2, 111.3, 110.1, 68.3, 60.8, 30.0, 30.8, 30.1, 26.8, 23.1, 20.2, 16.1, 14.6, 13.9; MS EI m/z (rel. int.) 320 (M^+ , 5), 248 (100), 203 (38); HRMS m/z calcd for $\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}$, 320.1889, found 320.1874.

2-(2-(cyanomethyl)phenyl)-*N,N*-diethyl-1-methyl-1*H*-indole-3-carboxamide (8b). Compound **8b** was prepared according to procedure **A**. Flash column chromatography (EtOAc-hexane 1:2 eluent) afforded 0.42 g (1.22 mmol, 65%) of the product as a colourless oil (purity 98.5%, by GC peak area). IR (KBr) 2245, 1614 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.60 - 7.20 (m, 8H), 3.88 (s, 2H), 3.46 (s, 3H), 3.27 (q, 4H, $J = 8$ Hz), 0.98 (s, 6H); ^{13}C (75 MHz, CDCl_3) δ 167.2, 136.9, 136.7, 132.7, 131.7, 130.9, 130.1, 129.4, 128.3, 126.9, 126.6, 125.7, 123.2, 121.4, 119.9, 118.8, 111.0, 110.6, 75.1, 32.1, 31.0, 25.2, 22.4; MS EI m/z (rel. int.) 345 (M^+ , 36), 273 (100), 232 (88), 217 (75), 203 (71), 128 (44); HRMS m/z calcd for $\text{C}_{22}\text{H}_{23}\text{N}_3\text{O}$, 345.1841, found 345.1841.

11-methyl-11*H*-benzo[*a*]carbazol-6-ol (1a). Compound **1a** was prepared according to procedure **B**. Flash column chromatography (hexane) afforded 0.58 g (2.37 mmol, 98%) of the product as colorless crystals, mp > 120 $^{\circ}\text{C}$ (decomp), IR (KBr) 3505 cm^{-1} ; ^1H NMR (300 MHz, acetone- d_6) δ 8.73 (d, 1H, $J = 2.0$ Hz), 8.48 (d, 1H, $J = 2.0$ Hz), 7.69 (d, 1H, $J = 8.0$ Hz), 7.47-7.35 (m, 3H), 4.4 (s, 3H), 2.99 (s, 1H); ^{13}C (75 MHz, acetone- d_6) δ : 127.5, 125.3, 124.5, 123.1, 122.7, 122.4, 119.8, 109.2, 101.5, 33.8; MS EI m/z (rel. int.) 247 (100), 218 (81), 201 (43), 91 (76); HRMS m/z calcd for $\text{C}_{17}\text{H}_{13}\text{NO}$, 247.0997, found: 247.0997.

6-hydroxy-11-methyl-11H-benzo[a]carbazole-5-carbonitrile (1b). Compound **1b** was prepared according to procedure **B**. Flash column chromatography (hexane) afforded 0.10 g (0.35 mmol, 92%) of the product as colorless crystals, mp > 180 °C (decomp), IR (KBr) 3231 cm⁻¹, 2207 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.70 (d, 1H, J = 5.0 Hz), 8.48 (d, 1H, J = 5.0 Hz), 8.12 (d, 1H, J = 8.0 Hz), 7.83 (d, 1H, J = 8.0 Hz), 7.67 (t, 1H, J = 9.0 Hz), 7.50 (q, 2H, J = 7.0 Hz), 7.32 (t, 1H, J = 8.0 Hz), 4.5 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 140.9, 139.6, 134.3, 127.9, 125.4, 124.4, 124.3, 123.6, 123.0, 122.6, 121.4, 119.6, 118.2, 110.7, 85.2, 46.9, 19.6; MS EI *m/z* (rel. int.) 272 (100), 243 (45), 229 (17), 100 (19); HRMS *m/z* calcd for C₁₈H₁₂N₂O, 272.0950 found 272.0949.

(R)-2-methyl-5-(prop-1-en-2-yl)cyclohex-1-enyl trifluoromethanesulfonate (9). L-Selectride (1.2 mmol, 1.2 mL) was added dropwise to a stirred solution of (+) (R)-(-)-carvone (0.15 g, 1.0 mmol, 0.16 mL) in anhydrous THF (10 mL) at -78 °C. The resulting mixture was stirred at -78 °C for 1 h, treated with an excess of PhNTf₂ (0.43 g, 1.2 mmol) in THF (2 mL), and the whole was warmed to ambient temperature over 8-12 h and quenched with a saturated aqueous NH₄Cl solution (5 mL). The layers were separated and the aqueous phase was extracted with Et₂O (3 × 10 mL). The combined organic phase was dried (Na₂SO₄) and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc-hexane 1:5 eluent) to afford 0.26 g (0.91 mmol, 91%) of the product as a colourless oil (purity 95.8%, by GC peak area). IR (KBr) 1708, 1647, 1415 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) 4.81 (s, 1H, =CH₂), 4.77 (s, 1H, =CH₂), 2.3 – 2.4 (m, 3H), 2.1 – 2.3 (m, 2H), 1.7 – 1.9 (m, 1H), 1.78 (s, 3H, CH₃), 1.76 (s, 3H, CH₃), 1.4 – 1.6 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 147.6, 142.8, 129.5, 116.8 (q, J = 317 Hz), 110.3, 42.2, 33.0, 30.2, 27.1, 20.9, 16.8; HRMS *m/z* calcd for C₁₁H₁₅F₃O₃S, 284.0694, found 284.0701.

(R)-N,N-diethyl-1-methyl-2-(2-methyl-5-(prop-1-en-2-yl)cyclohex-1-enyl)-1H-indole-3-carboxamide (10). Compound **10** was prepared according to procedure **A**. Flash column chromatography (EtOAc-hexane 1:3 eluent) afforded 0.11 g (0.30 mmol, 91%) of the product as a colourless oil (purity 99.1%, by GC peak area). IR (KBr) 1622 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.5 – 7.6 (m, 1H), 7.1 – 7.4 (m, 3H), 4.78 (s,

1H, =CH₂), 4.75 (s, 1H, =CH₂), 3.63 (m, 3H), 3.4 – 3.7 (br, 4H, NCH₂CH₃), 1.9 – 2.6 (m, 6H), 1.77 (s, 3H, CH₃), 1.5 – 1.7 (m, 1H), 1.56 (s, 3H, CH₃), 1.17 (s, 6H, NCH₂CH₃); ¹H NMR (300 MHz, CDCl₃) δ 167.8, 149.5, 141.6, 136.5, 126.5, 122.8, 121.9, 120.6, 119.9, 109.9, 109.5, 109.1, 42.0, 36.5, 32.4, 28.2, 21.3, 14.2; MS EI *m/z* (rel. int.) 364 (22), 292 (100), 211 (23), 180 (21), 100 (54), 72 (47); HRMS *m/z* calcd for C₂₄H₃₂N₂O, 364.2515, found 364.2520.

(R)-11-methyl-2-(prop-1-en-2-yl)-2,3,4,11-tetrahydro-1H-benzo[a]carbazol-6-ol (11). Compound **11** was prepared according to procedure **B**. Flash column chromatography (hexane) afforded 0.052 g (0.18 mmol, 90%) of the product as colourless crystals, mp > 185 °C (decomp), IR (KBr) 3500 cm⁻¹ (OH); ¹H NMR (500 MHz, CDCl₃) δ 8.27 (d, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 1H), 6.36 (s, 1H), 4.88 (s, 2H, =CH₂), 4.11 (s, 3H, NMe), 3.52 (dd, *J* = 15, 4.5 Hz, 1H), 3.11 (dd, *J* = 15, 4.5 Hz, 1H), 2.95 – 3.05 (m, 2H), 2.38 – 2.48 (m, 1H), 1.98 – 2.06 (m, 1H), 1.91 (s, 3H, CH₃), 1.7 – 1.8 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) 150.2, 150.1, 141.8, 135.9, 124.7, 122.7, 122.4, 119.6, 112.9, 109.8, 108.5, 106.4, 42.7, 33.6, 32.5, 31.3, 28.0, 21.3; MS EI *m/z* (rel. int.) 291 (74), 248 (16), 223 (100), 194 (18), 69 (28); HRMS *m/z* calcd for C₂₀H₂₁NO, 191.1623, found 191.1611.

2-bromo-N,N-diethyl-1-methyl-1H-3-carboxamide (12). To a solution of **7** (0.51 g, 2.2 mmol) in CH₂Cl₂ (10 mL) was added silica gel (1 g) and NBS (0.39 g, 2.2 mmol) at 0 °C. The reaction mixture was stirred for 30 min, washed with aq NaOH solution (2 M, 5 mL) and extracted with CH₂Cl₂ (2 × 10 mL). The combined organic extract was dried (Na₂SO₄), concentrated in vacuo, and the residue was to flash chromatography (EtOAc-hexane 1:3 eluent) to give **12**, 0.55 g (1.8 mmol, 81%) as colorless crystals, mp 83 – 85 °C (CH₂Cl₂), IR (neat) ν 1625 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.24 (t, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 3.77 (s, 3H), 3.2 – 3.8 (br, 4H), 1.0 – 1.4 (br, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 165.9, 136.7, 126.0, 122.9, 121.2, 119.2, 113.4, 112.8, 109.9, 43.5, 39.3, 31.8, 14.8, 13.4; HRMS calcd 308.0254 for C₁₄H₁₇BrN₂O, found 308.0250.

2-(tributylstannyl)-1H-indole-1-carboxylic acid (13). To a solution of indole (0.50 g, 4.3 mmol) in dry THF (5 mL) was added *n*-BuLi (2.3 mL, 5.1 mmol) at -78°C. The

reaction mixture was stirred for 30 min and CO₂ was blown above the solution through a needle for 10 min. The solvent was warmed to rt and evaporated to half volume in vacuo. Fresh THF (5 mL) was added and the solution was cooled to -78°C. To this mixture was added *t*-BuLi (4.2 mL, 5.12 mmol) and the whole was stirred at -78°C for 1 h, followed by addition of SnBu₃Cl (10 mL, 5.12 mmol). The whole was warmed to rt within 2 h, followed by addition of satd aq NH₄Cl solution (5 mL). The whole was extracted with Et₂O (2 × 10 mL). The combined organic extract was dried (Na₂SO₄) and concentrated in vacuo to give the crude product which was dissolved in EtOH (10 mL) and stored in the freezer at -30°C.

***N,N*-diethyl-2-(1*H*-indol-2-yl)-1-methyl-1*H*-indole-3-carboxamide (14).** A mixture of PdCl₂(PPh₃)₂ (0.035 g, 0.05 mmol), **12** (0.40 g, 1.3 mmol) in EtOH (10 mL), and **13** (0.43 M, 1.8 mmol, 4.2 mL) was heated at reflux for 2 h, cooled to rt and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc-hexane 1:3 eluent) to afford 0.35 g (1.0 mmol, 77%) of **14** as colourless crystals, mp 192 - 194 °C (CH₂Cl₂), IR (neat) ν 1605 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.6 (s, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 4.0 Hz, 1H), 7.51 (d, *J* = 3.2 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 6.8 Hz, 1H), 7.27 (t, *J* = 6.8 Hz, 1H), 7.23 (t, *J* = 6.8 Hz, 1H), 7.17 (t, *J* = 6.8 Hz, 1H), 4.0 (s, 3H), 3.0 – 4.0 (br, 4H, NCH₂CH₃), 1.34 (s, 3H, NCH₂CH₃), 0.88 (s, 3H, NCH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 169.0, 137.5, 136.5, 132.5, 128.7, 128.5, 125.6, 123.2, 123.1, 121.3, 120.8, 120.3, 119.6, 112.1, 110.9, 110.3, 103.6, 44.3, 40.0, 32.3, 14.8, 13.6; HRMS calcd 345.1841 for C₂₂H₂₃N₂O, found 345.1835.

2-(3-((dimethylamino)methyl)-1*H*-indol-2-yl)-*N,N*-diethyl-1-methyl-1*H*-indole-3-carboxamide (15). To a solution of *N,N*-dimethyliminium chloride (Eschenmoser's salt) (1.05 g, 2.6 mmol) in CH₂Cl₂ (100 mL), was added **14** (0.69 g, 2.0 mmol) in CH₂Cl₂ (5 mL). The reaction mixture was heated at reflux for 2 h, washed with aq NaHCO₃ solution (2M, 10 mL), and the layers were separated. The organic layer was dried (Na₂SO₄) and concentrated in vacuo to give 0.79 g (2.0 mmol, 98%) of the product as a yellow crystal, mp 198 - 201 °C (EtOAc), IR (neat) ν 1605 cm⁻¹; ¹H NMR (500 MHz, acetone) δ 7.88 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.15 – 7.22 (m, 2H), 7.08 (t, *J* = 8.0 Hz, 1H), 3.83 (s, 3H, NMe), 3.61 (s, 2H, CH₂NMe₂), 3.2 – 3.5 (br, 4H, NCH₂CH₃), 2.08 (s, 6H, NMe₂), 0.7 – 1.2 (br, 6H, NCH₂CH₃); ¹³C NMR (125 MHz, acetone) δ 166.5, 137.5, 137.4, 137.2, 128.7, 126.4, 126.2, 122.9, 122.8, 121.2, 121.0, 120.0, 119.4, 113.6, 111.7, 111.6, 110.6, 54.9, 45.1, 31.1, 13.5 (br); HRMS calcd 402.2420 for C₂₅H₃₀N₄O, found 402.2420.

2-(3-(cyanomethyl)-1H-indol-2-yl)-N,N-diethyl-1-methyl-1H-indole-3-carboxamide (16). To a solution of **2-(3-((dimethylamino)methyl)-1H-indol-2-yl)-N,N-diethyl-1-methyl-1H-indole-3-carboxamide** (0.20 g, 0.50 mmol) in CH₃CN (1 mL) was added MeI (0.11 g, 0.75 mmol, 0.046 mL) at rt, the reaction mixture was stirred for 10 min, and sequentially treated with KCN (0.065 g, 1.0 mmol), 18-crown-6 (0.13 g, 0.50 mmol) and DMF (1 mL). The reaction mixture was stirred at rt for 1 h, H₂O (5 mL) was added, and the whole was extracted with Et₂O (2×10 mL). The combined organic extract was dried (Na₂SO₄) and concentrated in vacuo to give the crude product which, upon flash chromatography (EtOAc-hexane 1:2 eluent), gave 0.18 g (0.46 mmol, 92%) of the product as a colorless powder, mp 259 - 261 °C, IR (neat) ν 2249 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, J = 7.6 Hz, 1H), 7.52 (t, J = 8.4 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.30 – 7.36 (m, 2H), 7.26 (d, J = 6.8 Hz, 1H), 7.22 (t, J = 8.4 Hz, 1H), 3.81 (s, 2H, CH₂CN), 3.63 (s, 3H, NMe), 3.0 – 3.7 (br, 4H, NCH₂CH₃), 1.20 (s, 3H, NCH₂CH₃), 0.84 (s, 3H, NCH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 167.0, 137.3, 136.4, 126.7, 125.8, 125.4, 123.7, 123.5, 121.4, 120.5, 119.7, 118.4, 117.3, 113.4, 112.2, 110.4, 43.6, 39.3, 31.4, 14.4, 14.2, 13.1; HRMS calcd 384.1950 for C₂₄H₂₄N₄O, found 384.1540.

6-cyano-5-hydroxy-12-methylindolo[2,3-a]carbazole. To a solution of LDA (0.4 mmol) in THF (5 mL) was added a solution of **15** (0.038 g, 0.1 mmol) in THF (2 mL) at 0 °C. The resulting mixture was stirred at rt for 30 min, quenched with a satd aq NH₄Cl solution (2 mL), and the whole was extracted with Et₂O (3 × 5 mL). The combined organic extract was dried (Na₂SO₄), concentrated in vacuo, and the residue was subjected to flash column chromatography (ⁱPrOH-hexane 1:8 eluent) to give 0.031 g (0.085 mmol, 85%) of the product as a yellow powder, mp > 300 °C (decomp); IR (neat) ν 3346 (OH), 2206 (CN) cm⁻¹; ¹H NMR (500 MHz, acetone) δ 8.56 (d, J = 8.0 Hz, 1H), 8.47 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 2H), 7.51 (t, J = 8.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.28 (t, J = 8.0 Hz, 1H), 4.40 (s, 3H, NMe); ¹³C NMR (125 MHz, acetone) δ 152.9, 141.1, 140.8, 131.8, 126.0, 125.4, 123.1, 122.8, 122.3, 120.9, 120.8, 120.5, 120.0, 119.8, 118.0, 112.3, 112.2, 111.1, 109.4, 31.6; HRMS calcd 311.1059 for C₂₀H₁₃N₃O, found 311.1050.

6-Cyano-5-methoxy-12-methylindolo[2,3-a]carbazole (5). To a solution of **6-cyano-5-hydroxy-12-methylindolo[2,3-a]carbazole** (20 mg, 0.064 mmol) in Et₂O (5 mL) was added a solution of freshly prepared CH₂N₂ (0.13 mmol) in Et₂O at rt. The reaction mixture was stirred for 30 min, and concentrated in vacuo to afford 20 mg (0.062 mmol, 97%) of the product as a yellow powder, mp > 275 °C (decomp), lit³ mp > 280 °C (decomp), IR and NMR identical to those reported.

¹ Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, 9, 165. (b) Gau, M.; House, H. O. *Org. Syn. Collective Volume VI*, 121.

² Carlock, J. T.; Bradshaw, J. S.; Stanovnik, B.; Tisler, M. *J. Org. Chem.* **1977**, 42, 1883.

³ Knubel, G.; Larsen, L. K.; Moore, R. E. *J. Antibiotics* **1990**, 43, 1236.