SUPPORTING INFORMATION

Synthesis of β - and γ -Carbolines by the Palladium-Catalyzed Iminoannulation of Alkynes

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1-Benzyl-3-iodoindole-2-carboxaldehyde. This aldehyde was prepared as a white solid in 100% yield by the method used to prepare 3-iodo-1-(methoxymethyl)indole-2-carboxaldehyde,¹ only employing 3-iodo-1*H*-indole-2-carboxaldehyde and benzyl iodide: mp 114-115 °C; ¹H NMR (CDCl₃) δ 5.84 (s, 2H), 7.08 (d, *J* = 6.8 Hz, 2H), 7.20-7.27 (m, 4H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.43 (dt, *J* = 8.0, 0.4 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 10.00 (s, 1H); ¹³C NMR (CDCl₃) δ 48.0, 111.4, 122.1, 123.9, 126.6, 127.6, 128.5, 128.7, 130.0, 131.1, 137.4, 140.4, 184.5.

3-Iodo-1-tosylindole-2-carboxaldehyde. This aldehyde was prepared as a yellow solid in 73% yield by the method used to prepare 3-iodo-1-(methoxymethyl)indole-2-carboxaldehyde,¹ only employing 3-iodo-1*H*-indole-2-carboxaldehyde and tosyl chloride: mp 155-156 °C; ¹H NMR (CDCl₃) δ 2.34 (s, 3H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.39 (m, 1H), 7.53-7.60 (m, 2H), 7.66 (d, *J* = 7.8 Hz, 2H), 8.21 (d, *J* = 8.4 Hz, 1H), 10.42 (s, 1H); ¹³C NMR (CDCl₃) δ 21.9, 81.7, 115.8, 125.0, 125.6, 127.1, 130.1, 130.2, 132.5, 134.5, 134.7, 137.9, 146.1, 183.3.

5-Benzyloxy-3-iodo-1*H*-indole-2-carboxaldehyde. This aldehyde was prepared as a yellow solid in an overall 38% yield by the reaction sequence used to prepare 3-iodo-1*H*-indole-2-carboxaldehyde,¹ only starting with ethyl 5-benzyloxy-1*H*-indole-2-carboxylate:² mp 160-162 °C; ¹H NMR (acetone-*d*₆) δ 5.19 (s, 2H), 7.05 (d, *J* = 2.4 Hz, 1H), 7.16 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.31 (t, *J* =

7.2 Hz, 1H), 7.39 (t, J = 7.2 Hz, 2H), 7.47 (d, J = 8.8 Hz, 1H), 7.52 (d, J = 7.2 Hz, 2H), 9.80 (s, 1H); ^{13}C NMR (acetone- d_6) δ 70.2, 103.6, 114.5, 114.6, 120.4, 127.7, 127.8, 128.4, 130.9, 133.3, 134.2, 137.5, 154.9, 182.1.

5-Benzyloxy-3-iodo-1-(methoxymethyl)indole-2-carboxaldehyde. This aldehyde was prepared as a yellow solid in 83% yield by the method used to prepare 3-iodo-1-(methoxymethyl)indole-2-carboxaldehyde,¹ only employing 5-benzyloxy-3-iodo-1*H*-indole-2-carboxaldehyde and methoxymethyl chloride: mp 110-112 °C; ^1H NMR (CDCl_3) δ 3.28 (s, 3H), 5.15 (s, 2H), 5.94 (s, 2H), 7.03 (d, J = 2.4 Hz, 1H), 7.23 (dd, J = 9.0, 2.4 Hz, 1H), 7.35-7.52 (m, 6H), 9.98 (s, 1H); ^{13}C NMR (CDCl_3) δ 56.3, 70.9, 74.9, 78.1, 104.7, 113.2, 121.5, 128.0, 128.4, 128.9, 130.9, 131.9, 136.0, 136.9, 155.5, 184.5.

2-Iodo-1*H*-indole-3-carboxaldehyde. POCl_3 (0.9 mL, 9.6 mmol) was added slowly by a syringe to ice-cooled dry DMF (10 mL). The solution, protected from moisture with a drying tube, was stirred for 15 min at room temperature and then recooled to around 0 °C. A solution of 2-iodoindole³ (2.13 g, 8.76 mmol) in DMF (10 mL) was then added over 5 min. The mixture was stirred at room temperature for 3 h and then poured into ice water (50 mL). The yellow mixture was made alkaline with NaOH (1.5 g) in water (10 mL). The mixture was quickly boiled for 1 min and extracted with ether. The organic phase was washed with water and dried over Na_2SO_4 . The solvent was removed under vacuum and the residue was chromatographed using 3:1 hexanes:EtOAc to afford a yellow solid (1.66 g, 70%): mp 218-219 °C (decomp); ^1H NMR (acetone- d_6) δ 7.24-7.32 (m, 2H), 7.45-7.48 (m, 1H), 8.17-8.19 (m, 1H), 10.11 (s, 1H), 11.75 (s, 1H); ^{13}C NMR (acetone- d_6) δ 90.0, 112.3, 113.7, 121.4, 123.7, 124.9, 125.7, 135.8, 183.9.

2-Iodo-1-(methoxymethyl)indole-3-carboxaldehyde. This aldehyde was prepared as a yellow oil in 67% yield by the method used to prepare 3-iodo-1-(methoxymethyl)indole-2-carboxaldehyde,¹ only employing 2-iodo-1*H*-indole-3-carboxaldehyde and methoxymethyl chloride: ^1H NMR (CDCl_3) δ 3.30 (s, 3H), 5.50 (s, 2H), 7.27-7.34 (m, 2H), 7.38-7.45 (m, 1H), 8.21-8.28 (m, 1H), 10.10 (s,

1H); ^{13}C NMR (CDCl_3) δ 56.8, 74.4, 110.5, 114.0, 121.5, 124.1, 124.6, 124.8, 136.0, 136.5, 184.6.

Ethyl 4-methoxy-2-butynoate (64). A hexane solution of *n*-BuLi (2.5 M, 3.6 mL) was added to a THF (20 mL) solution of methyl propargyl ether (0.526 g, 7.5 mmol) at -78°C under Ar and the mixture was stirred for 30 min. Ethyl chloroformate (0.977 g, 1.2 equiv) in THF (10 mL) was added. After stirring at -78°C for 1 h, the reaction was quenched by satd. aq. NH_4Cl and extracted by EtOAc. The organic phase was washed with brine, dried over Na_2SO_4 and evaporated. The residue was chromatographed using 7:1 hexanes/EtOAc to afford a colorless oil (0.876 g, 82%): ^1H NMR (CDCl_3) δ 1.32 (t, $J = 7.2$ Hz, 3H), 3.42 (s, 3H), 4.24 (m, 4H); ^{13}C NMR (CDCl_3) δ 14.0, 58.1, 59.4, 62.1, 78.2, 83.0, 153.1.

Isopropyl 4-methoxy-2-butynoate (65). This ester was prepared as a colorless oil in 52% yield by the method used to prepare ethyl 4-methoxy-2-butynoate (64), only employing methyl propargyl ether and isopropyl chloroformate: ^1H NMR (CDCl_3) δ 1.30 (d, $J = 6.4$ Hz, 6H), 3.42 (s, 3H), 4.23 (s, 2H), 5.10 (m, 1H); ^{13}C NMR (CDCl_3) δ 21.6, 58.1, 59.4, 70.1, 78.6, 82.6, 152.7.

Imines Prepared

3-Iodo-1-tosylindole-2-methylene-*tert*-butylamine (28). This imine was prepared by the method used to prepare imine 1,⁴ only employing 3-iodo-1-tosylindole-2-carboxaldehyde (212 mg, 0.5 mmol). Removal of the solvent afforded 240 mg (100%) of the imine as a yellow viscous oil: ^1H NMR (CDCl_3) δ 1.44 (s, 9H), 2.30 (s, 3H), 7.15 (d, $J = 8.0$ Hz, 2H), 7.31 (t, $J = 7.6$ Hz, 1H), 7.37-7.43 (m, 2H), 7.60 (d, $J = 8.0$ Hz, 2H), 8.10 (d, $J = 8.0$ Hz, 1H), 8.59 (s, 1H); ^{13}C NMR (CDCl_3) δ 21.6, 29.6, 59.2, 73.9, 114.8, 123.3, 124.6, 126.8, 126.9, 129.9, 132.8, 134.6, 135.7, 136.2, 145.3, 148.7; IR (neat, cm^{-1}) 3022, 2964; HRMS calcd for $\text{C}_{20}\text{H}_{21}\text{IN}_2\text{O}_2\text{S}$: 480.0369. Found: 480.0375.

5-Benzyloxy-3-iodo-1-(methoxymethyl)indole-2-methylene-*tert*-butylamine (30). This imine was prepared by the method used to prepare imine

1,⁴ only employing 5-benzyloxy-3-iodo-1-(methoxymethyl)indole-2-carboxaldehyde (463 mg, 1.1 mmol). Removal of the solvent afforded 524 mg (100%) of the imine as a yellow solid: mp 97-98 °C; ¹H NMR (CDCl₃) δ 1.33 (s, 9H), 3.27 (s, 3H), 5.14 (s, 2H), 6.21 (s, 2H), 7.00 (d, *J* = 2.4 Hz, 1H), 7.08 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.33-7.52 (m, 6H), 8.48 (s, 1H); ¹³C NMR (CDCl₃) δ 29.8, 55.8, 58.7, 70.3, 71.0, 74.7, 104.6, 112.5, 117.1, 128.0, 128.2, 128.8, 131.0, 133.9, 135.1, 137.4, 149.3, 154.9; IR (neat, cm⁻¹) 3017, 2969, 2927; HRMS calcd for C₂₂H₂₅IN₂O₂: 476.0961. Found: 476.0971.

2-Iodo-1-(methoxymethyl)indole-3-methylene-*tert*-butylamine (38).

This imine was prepared by the method used to prepare imine **1**,⁴ only employing 2-iodo-1-(methoxymethyl)indole-3-carboxaldehyde (157 mg, 0.5 mmol).

Removal of the solvent afforded 185 mg (100%) of the imine as a pale yellow solid: mp 108-110 °C; ¹H NMR (CDCl₃) δ 1.34 (s, 9H), 3.29 (s, 3H), 5.55 (s, 2H), 7.22-7.30 (m, 2H), 7.40-7.43 (m, 1H), 8.50-8.54 (m, 2H); ¹³C NMR (CDCl₃) δ 30.0, 56.1, 57.4, 73.9, 109.5, 112.0, 122.3, 122.4, 123.6, 125.4, 128.9, 136.2, 148.3; IR (neat, cm⁻¹) 3054, 2964; HRMS calcd for C₁₅H₁₉IN₂O: 370.0542. Found: 370.0547.

2-Iodo-1*H*-indole-3-methylene-*tert*-butylamine (40). This imine was prepared by the method used to prepare imine **1**,⁴ only employing 2-iodo-1*H*-indole-3-carboxaldehyde (215 mg, 0.79 mmol) for 6 h. Removal of the solvent afforded 260 mg (100%) of the imine as a pale yellow solid: mp 155-157 °C; ¹H NMR (CDCl₃) δ 1.49 (s, 9H), 7.16-7.26 (m, 2H), 7.40 (d, *J* = 6.8 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.76 (s, 1H); ¹³C NMR (CDCl₃) δ 30.1, 54.7, 117.8 (broad), 119.6 (broad), 123.0, 124.3 (broad), 144.0 (broad). The ¹³C NMR spectrum of compound **40** gives incomplete (four sp² carbons missing) and unusually broad peaks for the indole ring, even when the background noise is very low; IR (neat, cm⁻¹) 3184, 3052, 2974, 1635; HRMS calcd for C₁₃H₁₅IN₂: 326.0280. Found: 326.0286.

2-Bromo-1*H*-indole-3-methylene-*tert*-butylamine (42). This imine was prepared by the method used to prepare imine **1**,⁴ only employing 2-bromo-1-*H*-

indole-3-carboxaldehyde (223 mg, 1.0 mmol) for 6 h. Removal of the solvent afforded 278 mg (100%) of the imine as a yellow solid: mp 152-153 °C; ^1H NMR (CDCl_3) δ 1.49, 7.15-7.26 (m, 2H), 7.44 (d, J = 6.9 Hz, 1H), 7.58-7.61 (m, 1H), 7.75 (s, 1H); ^{13}C NMR (CDCl_3) δ 30.3, 55.0, 117.6 (broad), 119.6, 123.2, 124.4, 145.3 (broad), 145.9 (broad). The ^{13}C NMR spectrum of compound **42** gives incomplete (three sp^2 carbons missing) and unusually broad peaks for the indole ring, even when the background noise is very low, which is very similar to compound **40**; IR (neat, cm^{-1}) 3181, 3054, 2971, 1633; HRMS calcd for $\text{C}_{13}\text{H}_{15}\text{BrN}_2$: 278.0419. Found: 278.0423.

Carbolines Prepared

4,9-Dimethyl-3-phenyl-9H-pyrido[3,4-*b*]indole (7). The reaction mixture was chromatographed using 1:1 hexanes/EtOAc to afford 34 mg (49%) of the indicated compound as a white solid: mp 179-180 °C; ^1H NMR (acetone- d_6) δ 2.89 (s, 3H), 4.06 (s, 3H), 7.30-7.42 (m, 2H), 7.45-7.51 (m, 2H), 7.60-7.71 (m, 4H), 8.33 (d, J = 7.8 Hz, 1H), 8.92 (s, 1H); ^{13}C NMR (acetone- d_6) δ 17.8, 110.4, 120.4, 122.8, 124.7, 124.9, 127.7, 128.3, 128.4, 128.6, 130.3, 131.0, 136.9, 142.6, 143.0, 149.3 (one sp^3 carbon missing due to overlap); IR (neat, cm^{-1}) 3058, 2924; HRMS calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2$: 272.1314. Found: 272.1318.

3,9-Dimethyl-4-phenyl-9H-pyrido[3,4-*b*]indole (8). The reaction mixture was chromatographed using EtOAc to afford 29 mg (42%) of the indicated compound as a white solid: mp 117-119 °C; ^1H NMR (acetone- d_6) δ 2.42 (s, 3H), 4.02 (s, 3H), 6.85-6.95 (m, 2H), 7.40-7.85 (m, 7H), 8.89 (s, 1H); ^{13}C NMR (acetone- d_6) δ 22.3, 29.5, 110.2, 119.7, 121.7, 123.7, 127.7, 128.5, 128.6, 129.5, 129.9, 130.0, 131.2, 132.7, 139.9, 143.1, 145.2; IR (neat, cm^{-1}) 3053, 2924; HRMS calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2$: 272.1314. Found: 272.1318. The regiochemistry of carbolines **7** and **8** was determined by comparison of the spectral data for these compounds with those of carboline **4**.² Compared to the chemical shift of 5-H in carboline **7**, the chemical shift of 5-H in carboline **8** is shifted to higher field by 0.7 ppm, which is due to the phenyl group present in the 4-position of carboline **8**.

4-Hydroxymethyl-9-methyl-3-phenyl-9H-pyrido[3,4-*b*]indole (9). The reaction mixture was chromatographed using 1:3 hexanes/EtOAc to afford 26 mg (36%) of the indicated compound as a white solid: mp 193-195 °C; ¹H NMR (DMSO-*d*₆) δ 3.98 (s, 3H), 4.93 (s, 1H), 5.40 (s, 1H), 7.28 (t, *J* = 7.2 Hz, 1H), 7.35-7.47 (m, 3H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 3H), 8.41 (d, *J* = 7.6 Hz, 1H), 9.02 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 29.8, 59.4, 110.3, 120.0, 120.9, 125.4, 126.7, 127.7, 128.2, 128.3, 128.4, 130.4, 132.0, 136.5, 141.1, 142.3, 148.2; IR (neat, cm⁻¹) 3214, 3056, 2925; HRMS calcd for C₁₉H₁₆N₂O: 288.1263. Found: 288.1268.

3-Hydroxymethyl-9-methyl-4-phenyl-9H-pyrido[3,4-*b*]indole (10). The reaction mixture was chromatographed using 1:1 EtOAc/acetone to afford 31 mg (43%) of the indicated compound as a white solid: mp 278-280 °C; ¹H NMR (acetone-*d*₆) δ 4.08 (s, 3H), 4.44 (s, 1H), 4.53 (s, 2H), 6.95-7.01 (m, 2H), 7.47-7.50 (m, 2H), 7.52-7.56 (m, 1H), 7.59-7.66 (m, 4H), 9.01 (s, 1H); ¹³C NMR (acetone-*d*₆) δ 62.5, 110.4, 120.1, 121.8, 124.0, 128.3, 129.0, 129.1, 129.2, 129.9, 130.1, 130.6, 137.8, 143.7, 146.6 (one sp³ and one sp² carbon missing due to overlap); IR (neat, cm⁻¹) 3195, 3056, 2922; HRMS calcd for C₁₉H₁₆N₂O: 288.1263. Found: 288.1268. The regiochemistry of carboline **9** and **10** was determined by comparison of the spectral data for these compounds with those of carboline **4**.² Compared to the chemical shift of 5-H in carboline **9**, the chemical shift of 5-H in carboline **10** is shifted to higher field by 0.7 ppm, which is due to the phenyl group present in the 4-position of carboline **10**.

Ethyl 3,9-dimethyl-9H-pyrido[3,4-*b*]indole-4-carboxylate (12) and ethyl 4,9-dimethyl-9H-pyrido[3,4-*b*]indole-3-carboxylate (13). The reaction mixture was chromatographed using 1:3 hexanes/EtOAc to afford 49 mg (73%) of the indicated compounds as a yellow solid (1:1 inseparable mixture of isomers). ¹H NMR (acetone-*d*₆) δ 1.41 (t, *J* = 7.2 Hz, 3H), 1.46 (t, *J* = 7.2 Hz, 3H), 2.68 (s, 3H), 3.03 (s, 3H), 4.02 (s, 3H), 4.05 (s, 3H), 4.40 (q, *J* = 7.2 Hz, 2H), 4.61 (q, *J* = 7.2 Hz, 2H), 7.25 (m, 1H), 7.35 (m, 1H), 7.65 (m, 4H), 8.09 (d, *J* = 8.1 Hz, 1H), 8.35 (d, *J* = 8.1 Hz, 1H), 8.86 (s, 1H), 8.96 (s, 1H); ¹³C NMR (acetone-

δ 14.5, 14.7, 16.5, 22.6, 29.7, 61.3, 62.2, 110.6, 110.8, 120.1, 120.4, 121.0, 121.2, 122.6, 124.1, 124.7, 125.9, 127.7, 128.7, 129.5, 130.1, 132.7, 133.6, 136.3, 138.0, 142.9, 143.3, 144.7, 168.3, 169.4; IR (neat, cm^{-1}) 3055, 2927, 1717; HRMS calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_2$: 268.1212. Found: 268.1217.

4-Hydroxymethyl-3,9-dimethyl-9H-pyrido[3,4-*b*]indole (14) and 3-hydroxymethyl-4,9-dimethyl-9H-pyrido[3,4-*b*]indole (15). The reaction mixture was chromatographed using acetone to afford 68 mg (100%) of a 1:1 inseparable mixture of the indicated compounds as an off-white solid. ^1H NMR ($\text{DMSO-}d_6$) δ 2.70 (s, 3H), 2.82 (s, 3H), 3.92 (s, 3H), 3.94 (s, 3H), 4.79 (s, 2H), 5.04 (s, 2H), 5.05 (s, 1H), 5.23 (s, 1H), 7.23-7.31 (m, 2H), 7.55-7.70 (m, 4H), 8.28 (d, $J = 8.0$ Hz, 1H), 8.33 (d, $J = 8.0$ Hz, 1H), 8.78 (s, 1H), 8.81 (s, 1H); ^{13}C NMR ($\text{DMSO-}d_6$) δ 15.3, 21.7, 29.6, 29.7, 58.4, 63.8, 110.1, 110.3, 119.6, 119.9, 120.6, 121.5, 124.1, 125.1, 125.5, 127.3, 127.5, 128.1, 128.2, 128.6, 130.9, 136.4, 136.6, 142.1, 142.2, 145.5, 147.6; IR (neat, cm^{-1}) 3350, 3012, 2924; HRMS calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}$: 226.1106. Found: 226.1111.

9-Methyl-3-phenyl-4-trimethylsilyl-9H-pyrido[3,4-*b*]indole (18). The reaction mixture was chromatographed using 1.5:1 hexanes/EtOAc to afford 28 mg (34%) of the indicated compound as a yellow solid: mp 138-140 $^{\circ}\text{C}$; ^1H NMR ($\text{acetone-}d_6$) δ 0.21 (s, 9H), 4.06 (s, 3H), 7.31 (m, 1H), 7.40-7.49 (m, 3H), 7.55-7.70 (m, 4H), 8.32 (dd, $J = 8.1, 0.9$ Hz, 1H), 9.01 (s, 1H); ^{13}C NMR ($\text{acetone-}d_6$) δ 1.0, 28.8, 110.0, 118.9, 121.9, 124.6, 125.8, 127.6, 127.87, 127.9, 130.7, 132.2, 134.0, 135.3, 142.6, 146.1, 156.3; IR (neat, cm^{-1}) 3057, 2932; HRMS calcd for $\text{C}_{21}\text{H}_{22}\text{N}_2\text{Si}$: 330.1552. Found: 330.1557.

9-Methyl-4-phenyl-3-trimethylsilyl-9H-pyrido[3,4-*b*]indole (19). The reaction mixture was chromatographed using 2:1 hexanes/EtOAc to afford 21 mg (25%) of the indicated compound as a yellow oil: ^1H NMR ($\text{acetone-}d_6$) δ 0.04 (s, 9H), 4.05 (s, 3H), 6.83 (d, $J = 7.8$ Hz, 1H), 6.94 (dt, $J = 7.8, 0.9$ Hz, 1H), 7.42-7.46 (m, 2H), 7.51 (dd, $J = 7.2, 1.2$ Hz, 1H), 7.58-7.63 (m, 4H), 9.17 (s, 1H); ^{13}C NMR ($\text{acetone-}d_6$) δ -0.04, 28.9, 109.6, 119.4, 121.2, 123.1, 125.2, 127.8, 128.2, 128.6, 130.1, 132.1, 136.3, 138.2, 139.9, 141.8, 151.5; IR (neat, cm^{-1}) 3055,

2953; HRMS calcd for $C_{21}H_{22}N_2Si$: 330.1552. Found: 330.1557. The regiochemistry of carboline **18** and **19** was determined by comparison of the spectral data for these compounds with those of carboline **4**.² Compared to the chemical shift of 5-H in carboline **18**, the chemical shift of 5-H in carboline **19** is shifted to higher field by 0.7 ppm, which is due to the phenyl group present in the 4-position of carboline **19**.

3,9-Dimethyl-4-trimethylsilyl-9H-pyrido[3,4-*b*]indole (20). The reaction mixture was chromatographed using 1:3 hexanes/EtOAc to afford 21 mg (31%) of the indicated compound as a yellow solid: mp 186-187 °C; 1H NMR (acetone- d_6) δ 0.61 (s, 9H), 2.80 (s, 3H), 3.99 (s, 3H), 7.22-7.28 (m, 1H), 7.56-7.64 (m, 2H), 8.27 (d, J = 8.4 Hz, 1H), 8.87 (s, 1H); ^{13}C NMR (acetone- d_6) δ 1.9, 27.4, 28.6, 109.7, 118.5, 121.3, 124.0, 126.2, 127.6, 132.3, 133.1, 135.1, 142.5, 151.6; IR (neat, cm^{-1}) 3027, 2922; HRMS calcd for $C_{16}H_{20}N_2Si$: 268.1396. Found: 268.1400.

4,9-Dimethyl-3-trimethylsilyl-9H-pyrido[3,4-*b*]indole (21). The reaction mixture was chromatographed using 1:1.5 hexanes/EtOAc to afford 15 mg (22%) of the indicated compound as a yellow oil: 1H NMR (acetone- d_6) δ 0.43 (s, 9H), 2.97 (s, 3H), 3.99 (s, 3H), 7.28-7.32 (m, 1H), 7.58-7.65 (m, 2H), 8.27 (d, J = 8.0 Hz, 1H), 8.99 (s, 1H); ^{13}C NMR (acetone- d_6) δ -0.2, 17.8, 109.4, 119.5, 121.7, 123.7, 125.4, 127.3, 130.5, 133.3, 136.5, 141.4, 151.8 (one sp^3 carbon missing due to overlap); IR (neat, cm^{-1}) 3030, 2924; HRMS calcd for $C_{16}H_{20}N_2Si$: 268.1396. Found: 268.1400. The regiochemistry of carboline **21** was determined from its NOESY spectrum.

4-*tert*-Butyl-9-methyl-3-phenyl-9H-pyrido[3,4-*b*]indole (22). The reaction mixture was chromatographed using 1:2 hexanes/EtOAc to afford 25 mg (32%) of the indicated compound as a yellow solid: mp 152-154 °C; 1H NMR ($CDCl_3$) δ 1.55 (s, 9H), 3.99 (s, 3H), 7.33-7.42 (m, 6H), 7.54 (d, J = 8.0 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 8.48 (d, J = 8.4 Hz, 1H), 8.82 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 29.4, 32.6, 36.1, 109.3, 119.0, 121.2, 126.9, 127.2, 127.6, 127.7, 128.5, 128.9, 129.8, 136.6, 137.8, 142.1, 146.2, 148.4. The regiochemistry of carboline **22**

was determined from its NOESY spectrum. IR (neat, cm^{-1}) 3010, 2926; HRMS calcd for $\text{C}_{22}\text{H}_{22}\text{N}_2$: 314.1783. Found: 314.1787.

9-Benzyl-3,4-diphenyl-9H-pyrido[3,4-*b*]indole (27). The reaction mixture was chromatographed using 3:1 hexanes/EtOAc to afford 103 mg (100%) of the indicated compound as a yellow solid: mp 200-201 $^{\circ}\text{C}$; ^1H NMR (acetone- d_6) δ 5.86 (s, 2H), 6.95-7.05 (m, 2H), 7.16 (m, 3H), 7.25-7.35 (m, 5H), 7.40 (m, 4H), 7.45-7.55 (m, 4H), 7.71 (d, J = 8.4 Hz, 1H), 9.12 (s, 1H); ^{13}C NMR (acetone- d_6) δ 46.3, 110.1, 119.5, 121.5, 123.3, 126.4, 126.9, 127.2, 127.5, 127.6, 127.7, 128.1, 128.7, 128.8, 129.4, 130.3, 130.4, 131.5, 135.8, 137.5, 138.7, 141.4, 142.0, 147.1; IR (neat, cm^{-1}) 3057, 2922; HRMS calcd for $\text{C}_{30}\text{H}_{22}\text{N}_2$: 410.1783. Found: 410.1787.

3,4-Diphenyl-9-tosyl-9H-pyrido[3,4-*b*]indole (29). The reaction mixture was chromatographed using 6:1 hexanes/EtOAc to afford 37 mg (32%) of the indicated compound as a white solid: mp 238-239 $^{\circ}\text{C}$; ^1H NMR (acetone- d_6) δ 2.35 (s, 3H), 6.77 (d, J = 7.8 Hz, 1H), 7.16 (t, J = 8.4 Hz, 1H), 7.19-7.23 (m, 3H), 7.30-7.35 (m, 2H), 7.35-7.43 (m, 4H), 7.43-7.50 (m, 3H), 7.64 (m, 1H), 7.98 (d, J = 8.4 Hz, 2H), 8.43 (d, J = 8.7 Hz, 1H), 9.70 (s, 1H); ^{13}C NMR (acetone- d_6) δ 21.5, 115.6, 124.4, 124.9, 125.4, 127.7, 128.0, 128.2, 129.0, 129.8, 130.5, 130.6, 130.9, 131.0, 131.2, 132.2, 134.4, 135.4, 136.2, 138.0, 140.0, 141.1, 147.2, 152.7; IR (neat, cm^{-1}) 3061, 2923; HRMS calcd for $\text{C}_{30}\text{H}_{22}\text{N}_2\text{O}_2\text{S}$: 474.1402. Found: 474.1409.

6-Benzyloxy-9-methoxymethyl-3,4-diphenyl-9H-pyrido[3,4-*b*]indole (31). The reaction mixture was chromatographed using 1:1 hexanes/EtOAc to afford 92 mg (79%) of the indicated compound as a white solid: mp 163-164 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 3.37 (s, 3H), 4.75 (s, 2H), 5.77 (s, 2H), 6.57 (d, J = 2.4 Hz, 1H), 7.15-7.41 (m, 16H), 7.50 (d, J = 8.8 Hz, 1H), 9.07 (s, 1H); ^{13}C NMR (CDCl_3) δ 56.5, 70.2, 74.6, 106.8, 110.7, 119.2, 122.4, 126.7, 127.6 (2), 127.7, 127.9, 128.3, 128.5, 128.6, 129.7, 130.2, 130.4, 131.3, 136.3, 136.9, 137.0, 138.0, 140.7, 147.8, 153.1; IR (neat, cm^{-1}) 3040, 2976, 2871; HRMS calcd for $\text{C}_{32}\text{H}_{26}\text{N}_2\text{O}_2$: 470.1994. Found: 470.2000.

Ethyl 3,5-dimethyl-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (36) and ethyl 4,5-dimethyl-5*H*-pyrido[4,3-*b*]indole-3-carboxylate (37). The reaction mixture was chromatographed using 1:1.5 hexanes/EtOAc to afford 56 mg (84%) of a 1:2.4 inseparable mixture of the indicated compounds as a yellow solid.

Ethyl 3,5-dimethyl-5*H*-pyrido[4,3-*b*]indole-4-carboxylate (minor isomer): ^1H NMR (CDCl_3) δ 1.49 (t, $J = 7.2$ Hz), 2.78 (s), 3.81 (s), 4.56 (q, $J = 7.2$ Hz), 8.11 (d); all other peaks overlap with the peaks of the major isomer. **Ethyl 4,5-dimethyl-5*H*-pyrido[4,3-*b*]indole-3-carboxylate** (major isomer): ^1H NMR (CDCl_3) δ 1.48 (t, $J = 7.2$ Hz, 3H), 2.99 (s, 3H), 4.19 (s, 3H), 4.51 (q, $J = 7.2$ Hz, 2H), 7.37 (m, 1H), 7.46 (d, $J = 8.4$ Hz, 1H), 7.58 (m, 1H), 9.20 (s, 1H). Additional spectral data from the mixture: ^{13}C NMR (CDCl_3) δ 14.3, 14.4, 15.3, 22.8, 30.7, 32.8, 61.8, 61.9, 109.2, 109.3, 111.9, 117.0, 118.7, 120.3, 120.6, 120.8, 121.0, 127.0, 127.4, 140.1, 141.6, 141.9, 142.2, 142.4, 144.2, 145.4, 151.0, 167.9, 168.7. The regiochemistry of carbolines **36** and **37** was determined from the NOESY spectrum of the mixture. IR (neat, cm^{-1}) 2980, 1722; HRMS calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_2$: 268.1212. Found: 268.1217.

3,4-Diphenyl-5*H*-pyrido[4,3-*b*]indole (41). The reaction mixture was chromatographed using 3:1 hexanes/EtOAc to afford 54 mg (68%) of the indicated compound as a white solid: mp 316-317 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 7.22 (m, 3H), 7.32-7.50 (m, 10H), 8.19 (d, $J = 7.6$ Hz, 1H), 8.37 (s, 1H), 9.36 (s, 1H); ^{13}C NMR (CDCl_3) δ 111.0, 118.8, 119.1, 120.9, 121.1, 122.0, 126.9, 127.3, 127.7, 127.8, 129.2, 130.1, 130.3, 136.0, 139.8, 140.4, 141.3, 144.0 (one sp^2 carbon missing due to overlap); IR (neat, cm^{-1}) 3054, 1595; HRMS calcd for $\text{C}_{23}\text{H}_{16}\text{N}_2$: 320.1314. Found: 320.1317.

4,5-Dimethyl-3-phenyl-5*H*-pyrido[4,3-*b*]indole (47). The reaction mixture was chromatographed using 1:1 hexanes/EtOAc to afford 33.5 mg (49%) of the indicated compound as a white solid: mp 180-182 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 2.74 (s, 3H), 4.10 (s, 3H), 7.31 (t, $J = 7.6$ Hz, 1H), 7.35-7.42 (m, 2H), 7.43-7.58 (m, 5H), 8.13 (d, $J = 7.6$ Hz, 1H), 9.19 (s, 1H); ^{13}C NMR (CDCl_3) δ 16.7, 32.6, 109.1, 113.1, 118.9, 120.3, 120.6, 121.2, 126.6, 127.5, 128.1, 129.9, 140.1,

141.5, 142.1, 145.1, 155.7. The regiochemistry of carboline **47** was determined from its NOESY spectrum. IR (neat, cm^{-1}) 3054, 1582; HRMS calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2$: 272.1314. Found: 272.1318.

3,5-Dimethyl-4-phenyl-5H-pyrido[4,3-*b*]indole (48). The reaction mixture was chromatographed using 1:2 hexanes/EtOAc to afford 34.5 mg (51%) of the indicated compound as a yellow oil: ^1H NMR (CDCl_3) δ 2.43 (s, 3H), 3.17 (s, 3H), 7.30 (m, 2H), 7.34-7.38 (m, 2H), 7.44-7.53 (m, 4H), 8.14 (m, 1H), 9.20 (s, 1H); ^{13}C NMR (CDCl_3) δ 23.2, 31.5, 109.1, 118.5, 119.4, 120.2, 120.5, 121.1, 126.4, 128.0, 128.6, 130.6, 137.3, 140.9, 141.8, 143.2, 152.3; IR (neat, cm^{-1}) 3054, 2928, 1587; HRMS calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2$: 272.1314. Found: 272.1318.

5-Methyl-3-phenyl-4-trimethylsilyl-5H-pyrido[4,3-*b*]indole (49) and 5-methyl-3-phenyl-5H-pyrido[4,3-*b*]indole (50). The reaction mixture was chromatographed using 3:1 hexanes/EtOAc to afford 25 mg (38%) of a 1:5 inseparable mixture of the indicated compounds as a yellow oil. **5-Methyl-3-phenyl-4-trimethylsilyl-5H-pyrido[4,3-*b*]indole** (minor compound): ^1H NMR (CDCl_3) δ 0.12 (s), 3.98 (s), 9.27 (s); all other peaks overlap with the peaks from compound **50**. Fifty mg of the above mixture (collected from two runs) was dissolved in 2 mL of methanol and 10 mg of KOH was added. The mixture was stirred at room temperature for 20 h and checked by TLC, which showed only one spot. The solvent was removed by vacuum and the residue was chromatographed using 3:1 hexanes/EtOAc to afford 36 mg of compound **50** as a yellow solid. **5-Methyl-3-phenyl-5H-pyrido[4,3-*b*]indole**: mp 106-107 °C (lit.⁵ mp 106-107 °C); ^1H NMR (CDCl_3) δ 3.89 (s, 3H), 7.34 (t, $J = 7.6$ Hz, 1H), 7.40-7.46 (m, 2H), 7.49-7.56 (m, 3H), 7.69 (s, 1H), 8.11 (d, $J = 8.0$ Hz, 2H), 8.17 (d, $J = 8.0$ Hz, 1H), 9.36 (s, 1H); ^{13}C NMR (CDCl_3) δ 29.1, 100.6, 108.9, 118.7, 120.6, 120.7, 121.3, 126.7, 127.3, 128.5, 128.8, 140.6, 141.5, 142.3, 146.1, 153.6; IR (neat, cm^{-1}) 3054, 1594; HRMS calcd for $\text{C}_{18}\text{H}_{14}\text{N}_2$: 258.1157. Found: 258.1161.

Ethyl 5-methyl-5H-pyrido[4,3-*b*]indole-3-carboxylate (59). The reaction mixture was chromatographed using 1:2 hexanes/EtOAc to afford 45 mg (71%) of the indicated compound as a yellow solid: mp 150-151 °C; ^1H NMR

(acetone- d_6) δ 1.42 (t, J = 7.2 Hz, 3H), 4.04 (s, 3H), 4.43 (q, J = 7.2 Hz, 2H), 7.38 (dt, J = 0.9, 7.2 Hz, 1H), 7.63 (dt, J = 0.9, 7.2 Hz, 1H), 7.71 (d, J = 8.4 Hz, 1H), 8.29 (s, 1H), 8.34 (d, J = 8.4 Hz, 1H), 9.41 (s, 1H); ^{13}C NMR (acetone- d_6) δ 13.9, 60.8, 106.4, 109.9, 120.6, 120.9, 121.2, 121.4, 127.8, 142.1, 142.3, 144.1, 144.8, 165.9 (one sp^3 carbon missing due to overlap); IR (neat, cm^{-1}) 3059, 2979, 1713; HRMS calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_2$: 254.1055. Found: 254.1058.

5-Methoxymethyl-3-*n*-octyl-5*H*-pyrido[4,3-*b*]indole (61). The reaction mixture was chromatographed using 1:1 hexanes/EtOAc to afford 75 mg (92%) of the indicated compound as a yellow oil: ^1H NMR (CDCl_3) δ 0.87 (t, J = 8.8 Hz, 3H), 1.20-1.43 (m, 11H), 1.82 (quintet, J = 9.2 Hz, 2H), 3.29 (s, 3H), 5.63 (s, 2H), 7.26 (s, 1H), 7.30 (t, J = 10.0 Hz, 1H), 7.50 (m, 2H), 8.10 (d, J = 10.0 Hz, 1H), 9.21 (s, 1H); ^{13}C NMR (CDCl_3) δ 14.3, 22.9, 29.5, 29.7, 29.8, 30.7, 32.1, 39.3, 56.6, 74.3, 103.1, 109.8, 118.5, 120.7, 121.5, 122.2, 126.8, 140.8, 142.3, 146.3, 159.1; IR (neat, cm^{-1}) 3027, 2986; HRMS calcd for $\text{C}_{21}\text{H}_{28}\text{N}_2\text{O}$: 324.2202. Found: 324.2206.

Ethyl 6-benzyloxy-4,9-bis(methoxymethyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (66). The reaction mixture was chromatographed using 1:2 hexanes/EtOAc to afford 67 mg (62%) of the indicated compound as a pale yellow solid: mp 105-107 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 1.49 (t, J = 7.2 Hz, 3H), 3.27 (s, 3H), 3.47 (s, 3H), 4.53 (q, J = 7.2 Hz, 2H), 5.22 (s, 2H), 5.32 (s, 2H), 5.74 (s, 2H), 7.30-7.45 (m, 4H), 7.51 (d, J = 6.9 Hz, 2H), 7.56 (d, J = 9.0 Hz, 1H), 7.90 (d, J = 2.4 Hz, 1H), 8.99 (s, 1H); ^{13}C NMR (CDCl_3) δ 14.7, 56.6, 58.4, 62.0, 67.8, 71.2, 74.7, 109.3, 111.1, 119.6, 122.3, 127.8, 128.3, 128.9, 129.0, 129.3, 131.9, 137.0, 137.3, 138.2, 139.2, 154.5, 167.2. The regiochemistry of carboline **66** was determined from its NOESY spectrum in which the correlation signal between the 4-methoxymethyl group and 5-H was observed. IR (neat, cm^{-1}) 3032, 2928, 1724; HRMS calcd for $\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}_5$: 434.1842. Found: 434.1850.

Ethyl 6-benzyloxy-3,9-bis(methoxymethyl)-9*H*-pyrido[3,4-*b*]indole-4-carboxylate (67). The reaction mixture was chromatographed using 1:2 hexanes/EtOAc to afford 26 mg (24%) of the indicated compound as a yellow oil:

^1H NMR (CDCl_3) δ 1.46 (t, J = 7.2 Hz, 3H), 3.26 (s, 3H), 3.40 (s, 3H), 4.53 (q, J = 7.2 Hz, 2H), 4.88 (s, 2H), 5.16 (s, 2H), 5.70 (s, 2H), 7.30-7.53 (m, 7H), 7.68 (d, J = 2.4 Hz, 1H), 8.95 (s, 1H); ^{13}C NMR (CDCl_3) δ 14.4, 56.5, 58.6, 62.1, 71.1, 74.6, 75.0, 107.5, 111.1, 120.3, 120.7, 121.4, 126.8, 127.8, 128.2, 128.8, 132.6, 136.8, 137.3, 137.4, 145.6, 154.0, 168.4; IR (neat, cm^{-1}) 3032, 2980, 1728; HRMS calcd for $\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}_5$: 434.1842. Found: 434.1850.

Isopropyl 6-benzyloxy-4,9-bis(methoxymethyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate (68). The reaction mixture was chromatographed using 1:1.5 hexanes/EtOAc to afford 64 mg (57%) of the indicated compound as a pale yellow solid: mp 90-92 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 1.48 (d, J = 6.4 Hz, 6H), 3.26 (s, 3H), 3.45 (s, 3H), 5.22 (s, 2H), 5.26 (s, 2H), 5.40 (m, 1H), 5.73 (s, 2H), 7.31-7.43 (m, 4H), 7.51 (d, J = 7.2 Hz, 2H), 7.55 (d, J = 9.2 Hz, 1H), 7.90 (d, J = 2.4 Hz, 1H), 8.99 (s, 1H); ^{13}C NMR (CDCl_3) δ 22.0, 56.4, 58.1, 67.8, 69.4, 71.0, 74.5, 109.1, 110.9, 119.4, 122.1, 127.7, 128.0, 128.1, 128.7, 129.0, 131.9, 136.8, 137.1, 137.9, 140.0, 154.2, 166.9. The regiochemistry of carboline **68** was determined from its NOESY spectrum in which the correlation signal between the 4-methoxymethyl group and 5-H was observed. IR (neat, cm^{-1}) 2925, 1717; HRMS calcd for $\text{C}_{26}\text{H}_{28}\text{N}_2\text{O}_5$: 448.1998. Found: 448.2003.

Isopropyl 6-benzyloxy-3,9-bis(methoxymethyl)-9H-pyrido[3,4-*b*]indole-4-carboxylate (69). The reaction mixture was chromatographed using 1:1.5 hexanes/EtOAc to afford 41 mg (37%) of the indicated compound as a yellow oil: ^1H NMR (CDCl_3) δ 1.48 (d, J = 6.0 Hz, 6H), 3.25 (s, 3H), 3.39 (s, 3H), 4.87 (s, 2H), 5.15 (s, 2H), 5.47 (m, 1H), 5.70 (s, 2H), 7.31-7.36 (m, 2H), 7.40 (t, J = 7.2 Hz, 2H), 7.50 (m, 3H), 7.74 (d, J = 2.4 Hz, 1H), 8.94 (s, 1H); ^{13}C NMR (CDCl_3) δ 22.0, 56.5, 58.4, 69.9, 71.1, 74.6, 74.9, 107.5, 111.1, 120.1, 120.8, 121.9, 126.6, 127.8, 128.2, 128.8, 132.6, 136.8, 137.2, 145.3, 154.0, 168.0; IR (neat, cm^{-1}) 2980, 1717; HRMS calcd for $\text{C}_{26}\text{H}_{28}\text{N}_2\text{O}_5$: 448.1998. Found: 448.2003.

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8.474
7.644
7.625
7.606
7.549
7.529
7.410
7.403
7.400
7.386
7.378
7.364
7.346
7.326
7.274

3.992

1.545

Table 2, Compound 22

Table 2, Compound 31

Table 3. Compound 40

Table 3. Compound 41

Table 3, Compound 42