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A Flexible and Catalytic One-Pot Procedure for the Synthesis of Indoles

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General Remarks: All reactions were performed under an inert atmosphere of argon in flame dried Duran glassware (e.g. Schlenk tubes equipped with Teflon stopcocks). Toluene was distilled from molten sodium under argon. 1,4-Dioxane was dried with molecular sieves (3 Å). [Cp_2TiMe_2] was synthesized according to ref. [4a] Aminoalkynes **23-30** were synthesized according to ref. [8] 1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride was synthesized according to a literature procedure (A. J. Arduengo, III, R. Krafczyk, R. Schmutzler, H. A. Craig, J. R. Goerlich, W. J. Marshall, M. Unverzagt, *Tetrahedron* **1999**, *55*, 14523-14534). All other reagents were purchased from commercial sources and were used without further purification. Unless otherwise noted, yields refer to isolated yields of pure compounds as gauged by TLC and ^{1}H and ^{13}C NMR. All products were characterized by ^{1}H NMR, ^{13}C NMR, and infrared (IR) spectroscopy, and mass spectrometry (MS). New compounds were further characterized by high-resolution mass spectrometry (HRMS) or CHN elemental analysis. NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer. All ^{1}H NMR spectra are reported in δ units ppm downfield from tetramethylsilane internal standard. All ^{13}C NMR spectra are reported in δ units ppm relative to the central line of the triplet for

$CDCl_3$ at 77.0 ppm. Infrared spectra were recorded on a Bruker Vector 22 spectrometer using an attenuated total reflection (ATR) method. Mass spectra were recorded on a Finnigan MAT 312 or a VG Autospec (EI) with an ionization potential of 70 eV or a Micromass LCT (ESI). Elemental analysis were carried out on an Elementar Vario EL machine. PE: light petroleum ether, b.p. 40-60°C.

Synthesis of Indoles. General Procedure A: A Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was charged with amine (2.0 mmol), alkyne (2.0 mmol), and a solution of [Cp_2TiMe_2] (0.21 mL, *c* = 0.48 mol/L in toluene, 0.1 mmol, 5.0 mol %). The mixture was heated to 110°C for 24 h (TLC monitoring). After the obtained brown liquid had been allowed to reach room temperature, [$Pd_2(dba)_3$] (92 mg, 0.1 mmol, 5.0 mol %), 1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride (68 mg, 0.2 mmol, 10.0 mol %), KO*t*Bu (337 mg, 3.0 mmol), and 1,4-dioxane (5.0 mL) were added. The mixture was heated to 110°C for further 12 h (TLC monitoring). Then, the reaction mixture was filtered through SiO_2. After the SiO_2 had been washed with CH_2Cl_2, the organic layer was concentrated under vacuum. The residue was purified by flash chromatography (SiO_2).

Indole 11: General Procedure A was used to synthesize indole **11** from alkyne **1** and (*rac*)-1-phenylethylamine. 10.0 mol % [Cp_2TiMe_2] and 3.0 mmol amine were used for the hydroamination step. After purification by flash chromatography (PE/EtOAc, 50:1), compound **11** (344 mg, 1.31 mmol, 65 %) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 7.3 Hz, 3 H), 1.69-1.79 (m, 2 H), 1.93 (d, *J* = 7.2 Hz, 3 H), 2.67 (ddd, *J* = 15.5, 7.8, 7.7 Hz, 1 H), 2.74 (ddd, *J* = 15.6, 7.7, 7.6 Hz, 1 H), 5.72 (q, *J* = 7.2 Hz, 1 H), 6.31 (s, 1 H), 6.91 (d, *J* = 3.5 Hz, 2 H), 6.97-7.01 (m, 1 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 7.20-7.30 (m, 3 H), 7.53 (d, *J* = 7.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.0 (CH_3), 18.5 (CH_3), 22.1 (CH_2), 29.7 (CH_2), 52.2 (CH), 99.8 (CH), 111.6 (CH), 119.0 (CH), 119.8 (CH), 120.1 (CH), 126.2 (CH), 127.0 (CH), 128.5 (CH), 128.8 (C), 135.4 (C), 141.1 (C), 141.5 (C) ppm. IR: ν = 3029, 2959, 2932, 2871, 1604, 1544, 1456, 1403, 1376, 1309, 747, 732, 695 cm^{-1}. HRMS (ESI, CH_3CN): calcd.

($C_{19}H_{21}N$+H) 264.1752; found 264.1764. $C_{19}H_{21}N$ (263.4): calcd. C 86.65, H 8.04, N 5.32; found C 86.26, H 8.00, N 5.26.

Indole 12: General Procedure A was used to synthesize indole **12** from alkyne **2** and 4-methoxyaniline. After purification by flash chromatography (PE/EtOAc, 10:1), compound **12** (436 mg, 1.56 mmol, 78 %) was isolated as a brown solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7.4 Hz, 3 H), 1.31 (sex, *J* = 7.5 Hz, 2 H), 1.56 (quin, *J* = 7.2 Hz, 2 H), 2.58 (t, *J* = 7.5 Hz, 2 H), 3.87 (s, 3 H), 6.38 (d, *J* = 0.6 Hz, 1 H), 7.01 (d, *J* = 8.9 Hz, 2 H), 6.99-7.10 (m, 3 H), 7.23 (d, *J* = 8.9 Hz, 2 H), 7.57 (dd, *J* = 6.6, 2.2 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 13.8 (CH_3), 22.3 (CH_2), 26.7 (CH_2), 30.7 (CH_2), 55.5 (CH_3), 99.6 (CH), 109.9 (CH), 114.5 (CH), 119.5 (CH), 119.7 (CH), 120.8 (CH), 128.0 (C), 129.4 (CH), 130.7 (C), 138.6 (C), 142.2 (C), 159.0 (C) ppm. IR: ν = 3048, 2954, 2930, 2860, 1610, 1547, 1510, 1456, 1245, 1034, 829, 745 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{19}H_{21}NO$+H) 280.1701; found 280.1715. $C_{19}H_{21}NO$ (279.4): calcd. C 81.68, H 7.58, N 5.01; found C 81.64, H 7.69, N 5.45.

Indole 13: General Procedure A was used to synthesize indole **13** from alkyne **3** and 4-methylaniline. After purification by flash chromatography (PE), compound **13** (383 mg, 1.55 mmol, 77 %) was isolated as a grey solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.74-0.78 (m, 2 H), 0.80-0.87 (m, 2 H), 1.64-1.71 (m, 1 H), 2.44 (s, 3 H), 6.17 (s, 1 H), 7.04-7.11 (m, 3 H), 7.30 (d, *J* = 8.8 Hz, 2 H), 7.33 (d, *J* = 8.8 Hz, 2 H), 7.51-7.55 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 8.3 (CH_2), 8.3 (CH), 21.2 (CH_3), 96.9 (CH), 109.9 (CH), 119.7 (CH), 119.9 (CH), 121.0 (CH), 127.9 (CH), 127.9 (C), 129.9 (CH), 135.5 (C), 137.3 (C), 138.3 (C), 144.1 (C) ppm. IR: ν = 3043, 3010,1550, 1515, 1456, 1397, 1309, 1298, 1211, 881, 839, 747, 733 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{18}H_{17}N$+H) 248.1439; found 248.1446. $C_{18}H_{17}N$ (247.3): calcd. C 87.41, H 6.93, N 5.66; found C 87.38, H 6.93, N 5.51.

Indole 14: General Procedure A was used to synthesize indole **14** from alkyne **4** and *tert*-butylamine. After purification by flash chromatography (PE), compound **14** (197 mg, 0.78 mmol, 39 %) was isolated as a brown solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ =

1.65-1.82 (m, 4 H), 1.77 (s, 9 H), 2.15-2.19 (m, 2 H), 2.25-2.27 (m, 2 H), 5.79 (quin, *J* = 1.9 Hz, 1 H), 6.16 (d, *J* = 0.6 Hz, 1 H), 7.03 (td, *J* = 7.5, 0.7 Hz, 1 H), 7.09 (td, *J* = 8.4, 1.4 Hz, 1 H), 7.51 (dd, *J* = 7.7, 0.7 Hz, 1 H), 7.63 (dd, *J* = 8.4, 0.6 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 21.9 (CH_2), 22.8 (CH_2), 25.5 (CH_2), 30.9 (CH_3), 32.6 (CH_2), 58.4 (C), 103.4 (CH), 114.7 (CH), 118.9 (CH), 120.0 (CH), 120.2 (CH), 128.1 (CH), 129.2 (C), 134.7 (C), 136.9 (C), 144.6 (C) ppm. IR: ν = 2992, 2934, 2836, 1530, 1473, 1455, 1397, 1370, 1319, 1291, 1199, 784, 752, 735 cm^{-1}. MS (25°C): *m/z* (%) = 254 (87) [M^+], 197 (100), 169 (60), 154 (16), 130 (21), 117 (38), 103 (2), 79 (8). HRMS: calcd. ($C_{18}H_{23}N$) 253.1831; found 253.1828. $C_{18}H_{23}N$ (253.4): calcd. C 85.32, H 9.15, N 5.53; found C 84.75, H 8.79, N 5.01.

Indole 15: General Procedure A was used to synthesize indole **15** from alkyne **5** and *tert*-butylamine. After purification by flash chromatography (PE/EtOAc, 10:1), compound **15** (470 mg, 1.40 mmol, 70 %) was isolated as a grey solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.66-1.88 (m, 4 H), 1.82 (s, 9 H), 2.97 (t, *J* = 6.2 Hz, 2 H), 3.52 (t, *J* = 6.2 Hz, 2 H), 4.50 (s, 2 H), 6.28 (s, 1 H), 7.01 (td, *J* = 7.3, 1.0 Hz, 1 H), 7.06 (td, *J* = 8.3, 1.5 Hz, 1 H), 7.25-7.34 (m, 5 H), 7.48 (dd, *J* = 7.5, 1.1 Hz, 1 H), 7.66 (dd, *J* = 8.3, 0.3 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 21.2 (CH_2), 29.7 (CH_2), 31.3 (CH_2), 31.5 (CH_3), 58.8 (C), 70.1 (CH_2), 72.9 (CH_2), 102.8 (CH), 114.5 (CH), 118.6 (CH), 119.8 (CH), 127.5 (CH), 127.6 (CH), 128.3 (CH), 129.1 (C), 137.2 (C), 138.6 (C), 142.6 (C) ppm. IR: ν = 2932, 2857, 1604, 1538, 1454, 1400, 1368, 1288, 1202, 1103, 777, 732, 696 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{23}H_{29}NO$+H) 336.2327; found 336.2312. $C_{23}H_{29}NO$ (335.5): calcd. C 82.34, H 8.71, N 4.18; found C 82.44, H 8.59, N 4.65.

Indole 16: General Procedure A was used to synthesize indole **16** from alkyne **6** and *tert*-butylamine. After purification by flash chromatography (PE), compound **16** (320 mg, 1.30 mmol, 65 %) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03 (t, *J* = 7.3 Hz, 3 H), 1.74 (sex, *J* = 7.5 Hz, 2 H), 1.81 (s, 9 H), 2.90 (t, *J* = 7.5 Hz, 2 H), 3.82 (s, 3 H), 6.20 (d, *J* = 0.5 Hz, 1 H), 6.71 (dd, *J* = 9.2, 2.6 Hz, 1 H), 6.96 (d, *J* = 2.6 Hz, 1 H), 7.54 (d, *J* = 9.2 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$):

δ = 14.2 (CH_3), 23.7 (CH_2), 31.5 (CH_3), 33.7 (CH_2), 55.7 (CH_3), 58.6 (C), 101.5 (CH), 102.4 (CH), 109.5 (CH), 115.1 (CH), 129.6 (C), 132.3 (C), 143.5 (C), 153.1 (C) ppm. IR: ν = 2958, 2872, 2829, 1615, 1577, 1472, 1434, 1368, 1210, 1176, 1130, 1040, 833 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{16}H_{23}NO$+H) 246.1858; found 246.1869. $C_{16}H_{23}NO$ (245.4): calcd. C 78.32, H 9.45, N 5.71; found C 78.13, H 9.14, N 6.03.

Indole 17: General Procedure A was used to synthesize indole **17** from alkyne **7** and 4-methoxyaniline. After purification by flash chromatography (PE/EtOAc, 10:1), compound **17** (674 mg, 1.62 mmol, 81 %) was isolated as a brown solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.57-1.70 (m, 4 H), 2.59 (t, *J* = 7.3 Hz, 2 H), 3.41 (t, *J* = 6.2 Hz, 2 H), 3.84 (s, 3 H), 3.85 (s, 3 H), 4.44 (s, 2 H), 6.31 (s, 1 H), 6.72 (dd, *J* = 8.9, 2.5 Hz, 1 H), 6.90 (d, *J* = 8.9 Hz, 1 H), 6.98 (d, *J* = 8.9 Hz, 2 H), 7.04 (d, *J* = 2.4 Hz, 1 H), 7.20 (d, *J* = 8.9 Hz, 2 H), 7.24-7.35 (m, 5 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 25.4 (CH_2), 26.8 (CH_2), 29.3 (CH_2), 55.5 (CH_3), 55.9 (CH_3), 70.0 (CH_2), 72.8 (CH_2), 99.6 (CH), 101.8 (CH), 110.6 (CH), 110.7 (CH), 114.5 (CH), 127.4 (CH), 127.5 (CH), 128.2 (C), 128.3 (CH), 129.3 (CH), 130.7 (C), 133.9 (C), 138.6 (C), 142.4 (C), 154.3 (C), 158.9 (C) ppm. IR: ν = 3011, 2937, 2867, 2799, 1614, 1578, 1511, 1477, 1448, 1247, 1212, 1166, 1099, 1084, 1033, 836, 802, 759, 703 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{27}H_{29}NO_3$+H) 416.2226; found 416.2245. $C_{27}H_{29}NO_3$ (415.5): calcd. C 78.04, H 7.03, N 3.37; found C 77.94, H 6.93, N 3.18.

Indole 18: General Procedure A was used to synthesize indole **18** from alkyne **8** and 4-methylaniline. After purification by flash chromatography (PE/EtOAc, 40:1), compound **18** (428 mg, 1.36 mmol, 68 %) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.76-0.80 (m, 2 H), 0.82-0.91 (m, 2 H), 1.63-1.70 (m, 1 H), 2.46 (s, 3 H), 6.23 (s, 1 H), 7.12 (d, *J* = 8.5 Hz, 1 H), 7.27-7.35 (m, 5 H), 7.82 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 8.3 (CH), 8.5 (CH_2), 21.2 (CH_3), 97.6 (CH), 110.0 (CH), 117.3 (CH, q, *J* = 4 Hz), 117.7 (CH, q, *J* = 4 Hz), 122.3 (C, q, *J* = 32 Hz), 125.5 (CF_3, q, *J* = 271 Hz), 127.3 (C), 127.8 (CH), 130.1 (CH), 134.8 (C), 138.1 (C), 139.6 (C), 146.2 (C) ppm. IR: ν = 3012, 2925, 1613, 1557, 1515, 1452, 1328, 1275, 1151, 1106, 1054, 806 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{19}H_{16}NF_3$+H) 316.1313; found

316.1321. $C_{19}H_{16}NF_3$ (315.3): calcd. C 72.37, H 5.11, N 4.44; found C 72.47, H 5.00, N 4.32.

Indole 19: General Procedure A was used to synthesize indole **19** from alkyne **9** and 4-methylaniline. After purification by flash chromatography (PE/EtOAc, 20:1), compound **19** (640 mg, 1.50 mmol, 75 %) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.70-0.83 (m, 4 H), 1.59-1.66 (m, 1 H), 2.40 (s, 3 H), 6.05 (s, 1 H), 6.46 (d, *J* = 1.8 Hz, 1 H), 6.64 (dd, *J* = 8.2, 1.8 Hz, 1 H), 7.06 (d, *J* = 8.3 Hz, 2 H), 7.11 (dd, *J* = 7.8, 1.6 Hz, 2 H), 7.19-7.42 (m, 9 H), 7.68-7.70 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 8.2 (CH_2), 8.4 (CH), 21.1 (CH_3), 96.9 (CH), 103.2 (CH), 115.9 (CH), 119.3 (CH), 124.4 (C), 127.6 (CH), 127.9 (CH), 128.0 (CH), 128.1 (CH), 129.1 (CH), 130.2 (CH), 135.4 (C), 137.0 (C), 137.2 (C), 138.4 (C), 140.4 (C), 143.8 (C), 145.4 (C), 166.9 (C) ppm. IR: ν = 3024, 1659, 1595, 1567, 1514, 1444, 1296, 811, 693 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{31}H_{26}N_2$+H) 427.2174; found 427.2190.

Indole 20: General Procedure A was used to synthesize indole **20** from alkyne **10** and 4-methoxyaniline. After purification by flash chromatography (PE/EtOAc, 10:1), compound **20** (586 mg, 1.28 mmol, 64 %) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 7.3 Hz, 3 H), 1.25-1.34 (m, 2H), 1.49-1.57 (m, 2 H), 2.52 (t, *J* = 7.5 Hz, 2 H), 3.84 (s, 3 H), 6.25 (d, *J* = 0.6 Hz, 1 H), 6.40 (d, *J* = 1.6 Hz, 1 H), 6.62 (dd, *J* = 8.3, 1.9 Hz, 1 H), 6.91 (d, *J* = 8.9 Hz, 2 H), 6.99 (d, *J* = 8.9 Hz, 2 H), 7.08-7.13 (m, 2 H), 7.21-7.29 (m, 3 H), 7.32 (d, *J* = 8.2 Hz, 1 H), 7.34-7.41 (m, 3 H), 7.69 (dd, *J* = 8.3, 1.3 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 13.8 (CH_3), 22.4 (CH_2), 26.7 (CH_2), 30.6 (CH_2), 55.5 (CH_3), 99.3 (CH), 103.4 (CH), 114.4 (CH), 115.7 (CH), 119.1 (CH), 124.5 (C), 127.9 (CH), 128.0 (CH), 128.1 (CH), 129.1 (CH), 129.1 (CH), 129.6 (CH), 130.2 (CH), 130.5 (C), 137.1 (C), 138.7 (C), 140.4 (C), 142.0 (C), 145.1 (C), 158.7 (C), 166.8 (C) ppm. IR: ν = 3056, 2954, 2929, 2859, 1607, 1511, 1444, 1244, 1032, 833, 815, 766, 693 cm^{-1}. MS (180°C): *m/z* (%) = 458 (100) [M^+], 415 (24), 287 (16), 272 (12), 210 (9), 204 (9), 91 (9). HRMS: calcd. ($C_{32}H_{30}N_2O$) 458.2358; found 458.2356.

Cleavage of the Benzophenone Imine. General Procedure B: A round-bottomed flask equipped with a magnetic stirring bar was charged with indole (1.0 mmol), THF (3.5 mL), and HCl (2 N, 0.35 mL). After this had stirred at 25°C for 30 min (TLC monitoring), KOH (2 N) and *tert*-butyl methyl ether were added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3×). The combined organic layers were dried with Na_2SO_4 and concentrated under vacuum. The residue was purified by flash chromatography (SiO_2).

Indole 21: General Procedure B was used to synthesize indole **21** from indole **19**. After purification by flash chromatography (PE/EtOAc, 3:1), compound **21** (226 mg, 0.86 mmol, 86 %) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.67-0.83 (m, 4 H), 1.58-1.65 (m, 1 H), 2.44 (s, 3 H), 3.47 (br. s, 2 H), 6.06 (br. s, 1 H), 6.42 (d, *J* = 1.8 Hz, 1 H), 6.52 (dd, *J* = 8.3, 2.0 Hz, 1 H), 7.30 (d, *J* = 7.3 Hz, 1 H), 7.31 (br. s, 4 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 7.9 (CH_2), 8.3 (CH), 21.2 (CH_3), 95.9 (CH), 97.1 (CH), 110.5 (CH), 120.3 (CH), 121.1 (C), 127.9 (CH), 129.8 (CH), 135.8 (C), 137.1 (C), 139.4 (C), 141.5 (C), 142.1 (C) ppm. IR: ν = 3429, 3351, 3006, 2919, 1623, 1513, 1492, 1453, 1399, 1241, 1124, 1020, 804 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{18}H_{18}N_2$+H) 263.1548; found 263.1546.

Indole 22: General Procedure B was used to synthesize indole **22** from indole **20**. After purification by flash chromatography (PE/EtOAc, 1:1), compound **22** (250 mg, 0.85 mmol, 85 %) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 7.3 Hz, 3 H), 1.23-1.34 (m, 2 H), 1.52 (quin, *J* = 7.6 Hz, 2 H), 2.51 (t, *J* = 7.4 Hz, 2 H), 3.43 (br. s, 2 H), 3.86 (s, 3 H), 6.24 (d, *J* = 0.8 Hz, 1 H), 6.32 (d, *J* = 2.0 Hz, 1 H), 6.52 (dd, *J* = 8.3, 2.0 Hz, 1 H), 7.00 (d, *J* = 8.9 Hz, 2 H), 7.21 (d, *J* = 8.8 Hz, 2 H), 7.32 (d, *J* = 8.3 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 13.8 (CH_3), 22.3 (CH_2), 26.6 (CH_2), 30.7 (CH_2), 55.4 (CH_3), 96.0 (CH), 99.4 (CH), 110.3 (CH), 114.5 (CH), 120.1 (CH), 121.2 (C), 129.4 (CH), 130.9 (C), 139.7 (C), 140.1 (C), 141.3 (C), 158.8 (C) ppm. IR: ν = 3435, 3353, 2954, 2929, 2859, 1622, 1510, 1493, 1455, 1243, 1032, 805 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{19}H_{22}N_2O$+H+CH_3CN) 336.2076; found

336.2073. $C_{19}H_{22}N_2O$ (294.4): calcd. C 77.52, H 7.53, N 9.52; found C 76.98, H 7.43, N 9.89.

Synthesis of Indoles. General Procedure C: A Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was charged with aminoalkyne (1.0 mmol) and a solution of [Cp_2TiMe_2] (0.10 mL, *c* = 0.48 mol/L in toluene, 0.05 mmol, 5.0 mol %). The mixture was heated to 110°C for 4-48 h (TLC monitoring). After the obtained brown liquid had been allowed to reach room temperature, [$Pd_2(dba)_3$] (46 mg, 0.05 mmol, 5.0 mol %), 1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride (34 mg, 0.1 mmol, 10.0 mol %), KO*t*Bu (168 mg, 1.5 mmol), and 1,4-dioxane (2.5 mL) were added. After this had stirred at 110°C for 12 h (TLC monitoring), water and *tert*-butyl methyl ether were added. The organic layer was separated and the aqueous layer was extracted with *tert*-butyl methyl ether (3×). The combined organic layers were dried with Na_2SO_4 and concentrated under vacuum. The residue was purified by flash chromatography (SiO_2).

Indole 31: General Procedure C was used to synthesize indole **31** from aminoalkyne **23**. The reaction time of the hydroamination step was 6 h. After purification by flash chromatography (PE/EtOAc, 20:1), compound **31** (116 mg, 0.68 mmol, 68 %) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.81-1.90 (m, 2 H), 2.01-2.10 (m, 2 H), 2.95 (t, *J* = 6.2 Hz, 2 H), 4.00 (t, *J* = 6.2 Hz, 2 H), 6.17 (s, 1 H), 7.06 (td, *J* = 7.0, 1.1 Hz, 1 H), 7.11 (td, *J* = 7.2, 1.2 Hz, 1 H), 7.23 (d, *J* = 8.2 Hz, 1 H), 7.51 (d, *J* = 7.4 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 21.2 (CH_2), 23.4 (CH_2), 24.2 (CH_2), 42.3 (CH_2), 97.5 (CH), 108.5 (CH), 119.5 (CH), 119.5 (CH), 120.1 (CH), 128.2 (C), 136.3 (C), 137.1 (C) ppm. IR: ν = 3044, 2945, 2861, 2835, 1609, 1574, 1476, 1454, 1414, 1360, 1329, 1317, 1303, 1269, 1250, 1229, 1162, 1132, 1109, 1088, 1065, 1011, 992, 962, 918, 901, 866, 822, 767, 742, 729, 701, 667 cm^{-1}. MS (25°C): *m/z* (%) = 171 (100) [M^+], 154 (20), 143 (36), 130 (17), 128 (15), 117 (18), 115 (22), 90 (14). HRMS: calcd. ($C_{12}H_{13}N$) 171.1048; found 171.1048. $C_{12}H_{13}N$ (171.2): calcd. C 84.17, H 7.65, N 8.18; found C 84.35, H 7.28, N 8.10.

Indole 32: General Procedure C was used to synthesize indole **32** from aminoalkyne **24**. The reaction time of the hydroamination step was 48 h. After purification by flash chromatography (PE/EtOAc, 20:1), compound **32** (98 mg, 0.53 mmol, 53 %) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.82-1.90 (m, 2 H), 2.02-2.10 (m, 2 H), 2.50 (s, 3 H), 2.97 (t, *J* = 6.3 Hz, 2 H), 4.01 (t, *J* = 6.1 Hz, 2 H), 6.19 (d, *J* = 0.8 Hz, 1 H), 6.87 (d, *J* = 6.9 Hz, 1 H), 7.04 (t, *J* = 7.0 Hz, 1 H), 7.10 (d, *J* = 8.0 Hz, 1 H) ppm; ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 18.7 (CH_3), 21.3 (CH_2), 23.5 (CH_2), 24.3 (CH_2), 42.4 (CH_2), 96.0 (CH), 106.2 (CH), 119.8 (CH), 120.3 (CH), 127.9 (C), 128.9 (C), 135.9 (C), 136.5 (C) ppm. IR: ν = 3047, 2938, 2863, 1584, 1538, 1493, 1476, 1427, 1414, 1363, 1319, 1286, 1255, 1236, 1193, 1153, 1135, 1090, 1078, 1065, 959, 939, 862, 827, 787, 745, 713 cm^{-1}. MS (25°C): *m/z* (%) = 185 (100) [M^+], 184 (91), 177 (14), 170 (22), 157 (24), 156 (31), 149 (18), 142 (37), 128 (19), 115 (32), 77 (9). HRMS: calcd. ($C_{13}H_{15}N$) 185.1204; found 185.1204. $C_{13}H_{15}N$ (185.3): calcd. C 84.28, H 8.16, N 7.56; found C 83.89, H 7.91, N 7.27.

Indole 33: General Procedure C was used to synthesize indole **33** from aminoalkyne **25**. The reaction time of the hydroamination step was 6 h. After purification by flash chromatography (PE/EtOAc, 20:1), compound **33** (151 mg, 0.75 mmol, 75 %) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.82-1.90 (m, 2 H), 2.02-2.06 (m, 2 H), 2.93 (t, *J* = 6.3 Hz, 2 H), 3.83 (s, 3 H), 3.97 (t, *J* = 6.2 Hz, 2 H), 6.10 (s, 1 H), 6.77 (dd, *J* = 8.6, 2.4 Hz, 1 H), 7.00 (d, *J* = 2.4 Hz, 1 H), 7.11 (d, *J* = 8.6 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 21.2 (CH_2), 23.4 (CH_2), 24.2 (CH_2), 42.3 (CH_2), 55.9 (CH_3), 97.2 (CH), 102.0 (CH), 109.1 (CH), 109.9 (CH), 128.6 (C), 131.7 (C), 137.8 (C), 154.3 (C) ppm. IR: ν = 2958, 2929, 2830, 1613, 1578, 1483, 1474, 1437, 1419, 1364, 1346, 1327, 1316, 1285, 1268, 1237, 1204, 1157, 1129, 1110, 1035, 992, 961, 940, 884, 842, 822, 795, 767, 739, 688 cm^{-1}. MS (80°C): *m/z* (%) = 201 (100) [M^+], 186 (54), 170 (15), 158 (39), 156 (16), 143 (9), 130 (52), 116 (17), 101 (6), 91 (7), 77 (7), 65 (4). HRMS: calcd. ($C_{13}H_{15}NO$) 201.1153; found 201.1153. $C_{12}H_{15}NO$ (201.1): calcd. C 77.58, H 7.51, N 6.96; found C 77.05, H 7.07, N 7.80.

Indole 34: General Procedure C was used to synthesize indole **34** from aminoalkyne **26**. The reaction time of the hydroamination step was 6 h. After purification by flash chromatography (PE/EtOAc, 20:1), compound **34** (185 mg, 0.77 mmol, 77 %) was isolated as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.82-1.92 (m, 2 H), 2.02-2.11 (m, 2 H), 3.00 (t, *J* = 6.3 Hz, 2 H), 4.03 (t, *J* = 6.1 Hz, 2 H), 6.25 (s, 1 H), 7.27 (d, *J* = 8.6 Hz, 1 H), 7.34 (d, *J* = 8.6 Hz, 1 H), 7.80 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 20.9 (CH_2), 23.2 (CH_2), 24.2 (CH_2), 42.5 (CH_2), 98.5 (CH), 108.6 (CH), 116.8 (CH, q, *J* = 4 Hz), 117.1 (CH, q, *J* = 4 Hz), 121.9 (C, q, *J* = 32 Hz), 125.6 (CF_3, q, *J* = 270 Hz), 127.5 (C), 137.5 (C), 139.0 (C) ppm. IR: ν = 2958, 2875, 1618, 1543, 1450, 1412, 1373, 1343, 1319, 1265, 1220, 1153, 1133, 1098, 1052, 963, 920, 896, 885, 844, 824, 805, 781, 750, 712, 679, 657 cm^{-1}; MS (25°C): *m/z* (%) = 239 (91) [M^+], 238 (64), 220 (34), 221 (41), 198 (38), 171 (61), 170 (100), 143 (48), 142 (45), 115 (41). HRMS: calcd. ($C_{13}H_{12}NF_3$) 239.0921; found 239.0921. $C_{13}H_{12}NF_3$ (239.2): calcd. C 65.27, H 5.06, N 5.85; found C 65.85, H 4.94, N 5.62.

Indole 36: General Procedure C was used to synthesize indole **36** from aminoalkyne **28**. The reaction time of the hydroamination step was 4 h. After purification by flash chromatography (PE/EtOAc, 30:1), compound **36** (90 mg, 0.53 mmol, 53 %) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.51 (s, 3 H), 2.57 (quin, *J* = 7.2 Hz, 2 H), 3.00 (t, *J* = 7.3 Hz, 2 H), 4.02 (t, *J* = 7.0 Hz, 2 H), 6.16 (d, *J* = 0.9 Hz, 1 H), 6.85 (d, *J* = 6.6 Hz, 1 H), 7.02 (t, *J* = 6.9 Hz, 1 H), 7.07 (d, *J* = 8.0 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 18.8 (CH_3), 24.3 (CH_2), 27.8 (CH_2), 43.6 (CH_2), 90.7 (CH), 107.0 (CH), 119.3 (CH), 120.2 (CH), 129.6 (C), 132.3 (C), 133.0 (C), 143.8 (C) ppm. IR: ν = 3048, 2975, 2899, 1605, 1575, 1542, 1494, 1454, 1429, 1407, 1369, 1346, 1299, 1280, 1233, 1164, 1148, 1116, 1071, 1034, 998, 975, 938, 745 cm^{-1}. MS (25°C): *m/z* (%) = 171 (100) [M^+], 156 (22), 142 (28), 128 (25), 115 (29), 77 (17). HRMS: calcd. ($C_{12}H_{13}N$) 171.1048; found 171.1048. $C_{12}H_{13}N$ (171.2): calcd. C 84.17, H 7.65, N 8.18; found C 84.04, H 8.00, N 8.21.