Supporting Information

Ready synthesis of free $N$-$H$ 2-arylindoles via copper-catalyzed amination of 2-bromo-arylacetylenes with aqueous ammonia and sequential intramolecular cyclization

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I General information

All reagents unless otherwise noted were obtained from commercial source (>99%) and used without further purification. The reactions were carried out under argon atmosphere and the products were isolated by column chromatography on silica gel (200-300 mesh) using petroleum ether (60-90°C) and ethyl acetate as eluate. Compounds described in the literature were characterized by comparison of their $^1$H NMR and $^{13}$C NMR spectra to the reported data. $^1$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra were recorded in CDCl$_3$ or DMSO-$d_6$ and chemical shifts were reported in parts per million relative to TMS. MS data were performed on HP1100. High resolution mass spectrometric data (HRMS) were performed on HPLC-Q-Tof MS. HPLC analyses were tested on Waters 2695-2996.
II Experimental procedures for all compounds

The 2-bromo-anilines were obtained from commercial source or can conveniently be prepared by NBS bromination of anilines along with a catalytic amount of ammonium acetate (NH₄OAc) in CH₃CN as described in the literature.¹

The 2-bromo-iodides were prepared based the Sandmeyer reaction as described in the literature.²

The 2-arylhaloarenes were prepared based the Sonogashira coupling as described in the literature.³

General Procedure for the synthesis of 2-arylindoles

Amination: A flame-dried test tube with a magnetic stirring bar was charged with 2-arylhaloarenes (0.4 mmol), Cu(OTf)₂ (0.04 mmol), picolinaldehyde oxime (0.08 mmol), K₂CO₃ (0.5 mmol), NH₃-H₂O (1.0 mL) in DMSO (1.5 mL) and stirred at 100 ºC under argon. The mixture reacted at the indicated temperature for 18 h and cooled to room temperature. The resulting mixture was extracted with ethyl acetate (3×25 mL). The combined organic layers were dried over Na₂SO₄ and then concentrated under vacuum.

Cyclization: The residue was direct treated with ZnBr₂ (0.2 mmol) and toluene (4 mL) and reflux under 110 ºC for 6 h or 15 h. After cyclization completion detected by HPLC, the toluene was removed under vacuum and then purified by column chromatography on silica gel with an eluent of petroleum ether and ethyl acetate. All the physical data of the known compounds were in agreement with those reported in the literatures.

2-phenyl-1H-indole (3a)⁴

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a white solid. Yield: 67 mg, 87%.

¹H NMR (400 MHz, CDCl₃): δ= 8.34 (br, 1H), 7.67 (d, J = 7.2 Hz, 2H), 7.63 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.40 (d, J = 8.0 Hz, 1H), 7.32 (t, J = 7.2 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 6.83 (d, J = 1.6 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ= 137.9, 136.8, 132.4, 129.2, 129.0, 127.7, 125.2, 122.3, 120.6, 120.3, 110.9, 100.0. MS (API, m/z): 194.1 [M+H]⁺. M.p.: 186-187

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a white solid. Yield: 70 mg, 85%.

1H NMR (400 MHz, CDCl3): δ = 8.28 (br, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 8.0 Hz, 2H), 7.18 (t, J = 7.6 Hz, 1H), 7.11 (t, J = 7.6 Hz, 1H), 6.78 (s, 1H), 2.39 (s, 1H). 13C NMR (100 MHz, CDCl3) δ = 138.0, 137.6, 136.6, 129.7, 129.5, 129.3, 125.0, 122.1, 120.5, 120.2, 110.8, 99.4, 21.2. MS (API, m/z): 208.1 [M+H]+. M.p.: 212-213 °C.

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a pale orange solid. Yield: 76 mg, 84%.

1H NMR (400 MHz, CDCl3): δ = 8.27 (br, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.4 Hz, 2H), 7.42-7.38 (m, 3H), 7.20 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 6.80 (s, 1H). 13C NMR (100 MHz, CDCl3) δ = 136.9, 136.7, 133.5, 130.9, 129.23, 129.20, 126.3, 122.7, 120.8, 120.5, 120.9, 100.5. MS (API, m/z): 228.1 [M+H]+. M.p.: 196-197 °C.

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5-1/2) giving a white solid. Yield: 77 mg, 87%.

1H NMR (400 MHz, CDCl3): δ = 8.26 (br, 1H), 7.61-7.58 (m, 3H), 7.38 (d, J = 8.0 Hz, 1H), 7.17 (t, J = 7.2 Hz, 1H), 7.10 (t, J = 7.2 Hz, 1H), 6.98 (d, J = 8.8 Hz, 2H), 6.71 (s, 1H), 3.86 (s, 3H). 13C NMR (100 MHz, CDCl3) δ = 159.4, 138.0, 136.6, 129.4, 125.4, 121.9, 120.3, 120.2, 114.5, 110.9, 45.6. MS (API, m/z): 244.1 [M+H]+. M.p.: 227-228 °C.

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5-1/1) giving a pale orange solid. Yield: 83 mg, 83%.

1H NMR (400 MHz, CDCl3): δ = 8.36 (br, 1H), 7.62 (d, J = 7.6, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 8.0 Hz, 1H), 6.81-6.80 (m, 3H), 6.4 (s, 1H), 3.86 (s, 6H). 13C NMR (100 MHz, CDCl3) δ = 161.2, 137.8, 136.7, 134.3, 129.1, 122.4, 120.7, 120.3, 110.9, 103.6, 100.4, 99.7, 55.5.
HR-ESI-MS: [M-H]⁻ m/z calcd for C₁₆H₁₄NO₂ 252.1025, found: 252.1023. GC-MS (EI) m/z: 253 (M⁺, 100%). M.p.: 127-128 °C.

2-(naphthalen-1-yl)-1H-indole (3f)

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a white solid. Yield: 81 mg, 83%.

1H NMR (400 MHz, CDCl₃): δ=8.32-8.31 (m, 2H), 7.91-7.87 (m, 2H), 7.70 (d, J = 7.6 Hz, 1H), 7.63 (d, J = 7.2 Hz, 1H), 7.55-7.49 (m, 3H), 7.44 (d, J = 8.0 Hz, 1H), 7.24 (t, J = 8.4 Hz, 1H), 7.12 (t, J = 8.0 Hz, 1H), 6.80 (s, 1H). 13C NMR (100 MHz, CDCl₃) δ=136.7, 136.3, 133.9, 131.5, 131.1, 128.8, 128.6, 128.5, 127.2, 126.7, 126.2, 125.7, 125.3, 122.2, 120.6, 120.2, 110.8, 103.7. MS (API, m/z): 244.1 [M+H⁺]. M.p.: 102-103 °C.

1-(4-(1H-indol-2-yl)phenyl)ethanone (3g)

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5-1/1) giving a orange solid. Yield: 64 mg, 68%.

1H NMR (400 MHz, CDCl₃) δ=8.48 (br, 1H), 8.03 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H), 7.65 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 73 Hz, 1H), 6.97 (s, H), 2.63 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ=197.4, 137.3, 136.3, 135.8, 129.2, 129.1, 124.8, 123.3, 121.1, 120.6, 111.1, 102.0, 26.6. MS (API, m/z): 236.1 [M+H⁺]. M.p.: 212-213 °C.

2-(4-fluorophenyl)-1H-indole (3h)

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a white solid. Yield: 74 mg, 88%.

1H NMR (400 MHz, CDCl₃) δ=8.22 (br, 1H), 7.63-7.59 (m, 3H), 7.38 (d, J = 8.0 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 7.15-7.11 (m, 3H), 6.75 (s, H); 13C NMR (100 MHz, CDCl₃) δ=163.64 (d, J = 246 Hz, 1C), 137.01, 136.81, 129.24, 128.72 (d, J = 3.0 Hz, 1C), 126.88 (d, J = 8.0 Hz, 1C), 122.42, 120.64, 120.39, 116.15 (d, J = 21 Hz, 1C), 110.88, 99.94. 19F NMR (400 MHz, CDCl₃) δ=-113.9 Hz. MS (API, m/z): 212.1 [M+H⁺]. M.p.: 185-186 °C.

2-(4-(trifluoromethyl)phenyl)-1H-indole (3i)

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a white solid. Yield: 74 mg, 88%.

1H NMR (400 MHz, CDCl₃) δ=8.22 (br, 1H), 7.63-7.59 (m, 3H), 7.38 (d, J = 8.0 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 7.15-7.11 (m, 3H), 6.75 (s, H); 13C NMR (100 MHz, CDCl₃) δ=163.64 (d, J = 246 Hz, 1C), 137.01, 136.81, 129.24, 128.72 (d, J = 3.0 Hz, 1C), 126.88 (d, J = 8.0 Hz, 1C), 122.42, 120.64, 120.39, 116.15 (d, J = 21 Hz, 1C), 110.88, 99.94. 19F NMR (400 MHz, CDCl₃) δ=-113.9 Hz. MS (API, m/z): 212.1 [M+H⁺]. M.p.: 185-186 °C.

2-(4-(trifluoromethyl)phenyl)-1H-indole (3i)

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a white solid. Yield: 87 mg, 83%.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$=8.37 (br, 1H), 7.76 (d, $J$ = 8.4 Hz, 2H), 7.67 (d, $J$ = 8.4 Hz, 2H), 7.65 (d, $J$ = 8.0 Hz, 1H), 7.04 (d, $J$ = 8.0 Hz, 1H), 7.12 (t, $J$ = 7.6 Hz, 1H), 6.92 (s, H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$=137.15, 136.11, 135.71, 129.03, 126.03 (q, $J$ = 32 Hz, 1C), 125.45, 125.12, 123.21, 121.05, 120.66, 111.09, 101.73. $^{19}$F NMR (400 MHz, CDCl$_3$) $\delta$=-63.0 Hz. MS (API, m/z): 262.1 [M+H]$^+$. M.p.: 251-252 °C.

2-(thiophen-2-yl)-1H-indole (3j)$^6$

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a white solid. Yield: 45 mg, 57%.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$=8.21 (br, 1H), 7.59 (d, $J$ = 8.0 Hz, 1H), 7.37 (d, $J$ = 7.6 Hz, 1H), 7.29-7.25 (m, 1H), 7.19 (t, $J$ = 7.6 Hz, 1H), 7.13-7.08 (m, 2H), 6.73 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$=136.5, 135.6, 132.3, 129.1, 127.9, 124.6, 122.9, 122.6, 120.5, 110.8, 100.4. MS (API, m/z): 200.1 [M+H]$^+$. M.p.: 186-187 °C.

6-methyl-2-phenyl-1H-indole (4a)$^6$

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a pale orange solid. Yield: 66 mg, 80%.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$=8.20 (br, 1H), 7.64 (d, $J$ = 7.6 Hz, 2H), 7.50 (d, $J$ = 8.0 Hz, 1H), 7.42 (t, $J$ = 7.6 Hz, 2H), 7.30 (t, $J$ = 7.6 Hz, 1H), 7.18 (s, 1H), 6.95 (d, $J$ = 8.0 Hz, 1H), 6.77 (s, 1H), 2.46 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$=137.3, 137.2, 132.5, 132.2, 129.0, 127.4, 127.1, 125.0, 122.0, 120.3, 110.9, 99.8, 21.8. MS (API, m/z): 208.1 [M+H]$^+$. M.p.: 189-190 °C.

5-methyl-2-phenyl-1H-indole (4b)$^7$


Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a pale orange solid. Yield: 74 mg, 90%.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$=8.22 (br, 1H), 7.64 (d, J = 7.6 Hz, 2H), 7.45-7.41 (m, 3H), 7.33-7.27 (m, 2H), 7.02 (d, J = 8.4 Hz, 1H), 6.75 (s, 1H), 2.45 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$=137.9, 135.2, 132.5, 129.54, 129.48, 129.0, 127.6, 125.1, 124.0, 120.3, 110.5, 99.6, 21.5. MS (API, m/z): 208.1 [M+H]$^+$. M.p.: 220-221 °C.

6-chloro-2-phenyl-1H-indole (4c)$^8$

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a pale orange solid. Yield: 74 mg, 82%.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$=8.30 (br, 1H), 7.64 (d, J = 7.6 Hz, 2H), 7.51 (d, J = 8.4 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.38 (s, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.09 (d, J = 8.4 Hz, 1H), 6.79 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$=138.6, 137.1, 131.9, 129.1, 128.0, 127.8, 125.1, 121.5, 121.0, 110.8, 99.9. MS (API, m/z): 228.1 [M+H]$^+$. M.p.: 182-183 °C.

4,6-dichloro-2-phenyl-1H-indole (4d)$^9$

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a white solid. Yield: 84 mg, 80%.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$=8.34 (br, 1H), 7.59 (d, J = 7.6 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.34 (t, J = 7.2 Hz, 1H), 7.21 (s, 1H), 7.11 (s, 1H), 6.83 (d, J = 1.2 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$=139.1, 137.1, 131.2, 129.2, 128.4, 127.7, 126.9, 126.2, 125.2, 120.5, 109.6, 98.4. MS (API, m/z): 262.0 [M+H]$^+$. M.p.: 109-110 °C.

6-nitro-2-phenyl-1H-indole (4e)$^{10}$

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5-1/1) giving a red solid. Yield: 66 mg, 69%.

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1H NMR (400 MHz, DMSO-d6) δ=12.36 (s, 1H), 8.30 (s, 1H), 7.96-7.91 (m, 3H), 7.73 (d, J = 8.8 Hz, 1H), 7.55 (t, J = 7.6 Hz, 2H), 7.44 (t, J = 7.2 Hz, 1H), 7.16 (s, 1H); 13C NMR (100 MHz, DMSO-d6) δ=144.2, 141.9, 135.4, 133.7, 130.8, 129.1, 128.9, 125.7, 120.1, 114.8, 107.7, 99.8. MS (EI, m/z): 238 [M]+, 165, 208, 192. M.p.: 219-220 °C.

1-(2-phenyl-1H-indol-6-yl)ethanone (4f)

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5-1/1) giving a orange solid. Yield: 65 mg, 69%.

1H NMR (400 MHz, CDCl3) δ=8.84 (br, 1H), 8.14 (s, 1H), 7.76-7.72 (m, 3H), 7.65 (d, J = 8.4 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.38 (t, J = 7.6 Hz, 1H), 6.87 (s, 1H), 2.68 (s, 1H); 13C NMR (101 MHz, CDCl3) δ=198.3, 141.8, 136.3, 133.2, 131.6, 131.5, 129.2, 128.6, 125.5, 120.8, 111.9, 100.2, 26.84. HR-ESI-MS: [M+Na]+ m/z calcd for C16H14NO2 258.0895, found: 258.0897. GC-MS (EI) m/z: 220 (100%), 235 (M+, 70%). M.p.:212-213 °C.

6-fluoro-2-phenyl-1H-indole (4g)

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a white solid. Yield: 68 mg, 80%.

1H NMR (400 MHz, DMSO-d6) δ=11.66 (br, 1H), 7.85 (d, J = 8.0 Hz, 2H), 7.76-7.72 (m, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.38 (t, J = 7.6 Hz, 1H), 7.32 (t, J = 7.2 Hz, 1H), 7.15 (d, J = 6.0 Hz, 1H), 6.92-6.85 (m, 2H); 13C NMR (100 MHz, DMSO-d6) δ=159.62 (d, J = 234 Hz, 1C), 139.04 (d, J = 4 Hz, 1C), 137.65 (d, J = 13 Hz, 1C), 132.62, 129.56, 128.08, 126.07, 125.49, 121.70 (d, J = 11 Hz, 1C), 108.50 (d, J = 24 Hz, 1C), 108.38, 99.34 (d, J = 3.0 Hz, 1C), 97.87 (d, J = 25 Hz, 1C). 19F NMR (400 MHz, DMSO-d6) δ=-121.5. MS (API, m/z): 212.1 [M+H]+. M.p.: 171-172 °C.

2-phenyl-6-(trifluoromethoxy)-1H-indole (4h)

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/3) giving a white solid. Yield: 85 mg, 77%.

1H NMR (400 MHz, CDCl3) δ=8.36 (br, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 8.4 Hz, 1H), 7.44 (t,
J = 8.0 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.26 (s, 1H), 7.00 (dd, J1=8.0 Hz, J2=1.0 Hz, 1H), 6.80 (d, J = 1.2 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ=145.15, 139.43, 136.36, 131.88, 129.14, 128.12, 127.97, 125.19, 124.62, 121.88 (q, J = 255 Hz, 1C), 114.39, 103.96, 99.87. 19F NMR (400 MHz, CDCl3) δ=-57.9. MS (API, m/z): 278.0 [M+H]+. HR-ESI-MS: [M+Na]+ m/z calcd for C16H14NO2 258.0895, found: 258.0897. M.p.: 167-168 °C.

2-phenyl-6-(trifluoromethyl)-1H-indole (4i)

Following the general procedure, the crude product was purified over a silica gel column using ethyl acetate / petroleum ether (1/5) giving a white solid. Yield: 73 mg, 70%.

1H NMR (400 MHz, CDCl3) δ=8.51 (br, 1H), 7.70-7.67 (m, 4H), 7.47 (t, J = 8.4 Hz, 2H), 7.40-7.35 (m, 2H), 6.87 (s, 1H); 13C NMR (101 MHz, CDCl3) δ=140.58, 135.60, 131.61, 129.21, 128.49, 125.16 (q, J = 269 Hz, 1C), 125.43, 124.23 (q, J = 32 Hz, 1C), 120.92, 117.04 (q, J = 4 Hz, 1C), 117.00, 108.39 (q, J = 4 Hz, 1C), 100.07; 19F NMR (400 MHz, CDCl3) δ=-60.6. MS (API, m/z): 262.1 [M+H]+. M.p.: 181-182 °C.

III Copies for $^1$HNMR and $^{13}$CNMR.
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$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
**1H NMR (400 MHz, CDCl₃)**

**13C NMR (100 MHz, CDCl₃)**