Supplementary Material (ESI) for Chemical Communications

A facile aminocyclization for the synthesis of pyrrolidine and piperidine derivatives

Zhihui Shao, Jingbo Chen, Yongqiang Tu, Liang Li, and Hongbin Zhang*

General Experimental: Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on a Bruker Avance 300 spectrometer at 300 MHz. Carbon-13 nuclear magnetic resonance (^{13}C-NMR) was recorded on Bruker Avance 300 spectrometer at 75.5 MHz. Chemical shifts are reported as δ values in parts per million (ppm) relative to tetramethylsilane (TMS) for all recorded NMR spectra. Low resolution Mass spectra were recorded on Finnigan Trace 2000 GC-MS spectrometer. Optical rotations were recorded on HORIBA SEPA-300 digital Polarimeter at 24ºC. Starting materials and reagents used in reactions were obtained commercially from Acros, Aldrich, Fluka and were used without purification, unless otherwise indicated.

General method for aminocyclization: The secondary amine (2 mmol) in dichloromethane (5 mL) were stirred at –78°C under air for 5 minutes. Dry bromine (2.4 mmol, pre-washed with concentrated sulfuric acid) was added dropwise during a period of 10 minutes. The mixture was then stirred at room temperature for 30 minutes. The dichloromethane was removed under vacuum and acetone (10 mL) or DMF (10 mL) was then added together with K_2CO_3 (4 mmol). The resulting mixture was heated to 75°C (oil bath) under air. The reaction was monitored by thin-layer chromatography. After removal of the solvent, the residue was diluted with water (50mL) and extracted with ethyl ether (3X 15mL). The organic phases were combined and washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvents, the residue was chromatographied on silica gel to afford the pure products. All compounds were characterized by ^{1}H-NMR, ^{13}C-NMR and GC-MS.

For Table 1:

1-[(6-Bromo-1,3-benzodioxol-5-yl)methyl]-2,3,5,6,7,7a-hexahydro-1*H*-indole: **^{1}H-NMR** (300MHz, $CDCl_3$): δ 6.92 (1H, s), 6.89 (1H, s), 5.85 (2H, s), 5.35 (1H, br s), 3.88 (1H, d, *J* = 13.8 Hz), 3.27 (1H, d, *J* = 13.8 Hz), 2.95 (1H, m), 2.62 (1H, m), 2.32-2.15 (2H, m), 2.14-1.90 (4H, m), 1.75 (1H, m), 1.40 (1H, m), 1.10 (1H, m). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 146.24, 146.04, 139.26, 130.81, 117.52, 113.17, 111.34, 109.51, 100.52, 63.46, 56.75, 51.30, 27.12, 27.08, 24.09, 19.44. **MS** (m/z): 337 (M^++2, 10%), 335 (M^+, 11%), 309 (17), 307 (19), 215 (98), 213 (100), 157 (9), 135 (17), 95 (14).

Ethyl 2,3,5,6,7,7a-hexahydro-1*H*-indol-1-ylacetate: **^{1}H-NMR** (300MHz, $CDCl_3$): δ 5.41 (1H, br s), 4.17 (2H, q, *J* = 7.1 Hz), 3.55 (1H, d, *J* = 16.2 Hz), 3.28 (1H, m), 3.09 (1H, d, *J* = 16.2 Hz), 2.69 (1H, m), 2.42 (1H, m), 2.28 (1H, dd, *J* = 8.2, *J* = 16.3 Hz), 2.10-1.90 (4H, m), 1.82 (1H, m), 1.40 (1H, m), 1.25 (3H, t, *J* = 7.1 Hz), 1.12 (1H, m). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 170.99, 139.49, 118.90, 63.78, 60.62, 55.31, 52.51, 28.26, 27.64, 25.03, 20.48, 14.36. **MS** (m/z): 209 (M^+, 2%), 181 (4), 136 (73), 122 (44), 108 (92), 91 (19), 79 (40), 53 (19), 44 (45), 42 (100).

1-(1,3-Benzodioxol-5-ylmethyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole: **^{1}H-NMR** (300MHz, $CDCl_3$): δ 6.86 (1H, s), 6.77 (1H, d, *J* = 7.8 Hz), 6.72 (1H, d, *J* = 7.8 Hz), 5.95 (2H, s), 5.43 (1H, br s), 3.96 (1H, d, *J* = 12.6 Hz), 3.14 (1H, d, *J* = 12.6 Hz), 2.95 (1H, m), 2.62 (1H, m), 2.41-2.28 (2H, m), 2.12-1.94 (4H, m), 1.85 (1H, m), 1.46 (1H, m), 1.19 (1H, m). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 147.90, 146.84, 140.67, 133.23, 122.48, 119.05, 110.02, 108.21, 101.22, 64.70, 58.97, 52.35, 28.45, 28.27, 25.51, 20.87. **MS** (m/z): 257 (M^+, 4%), 229 (15), 135 (100), 122 (20), 77 (19).

1-(1,3-Dimethylbutyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole: **^{1}H-NMR** (300MHz, $CDCl_3$): δ 5.39 (1H, br s), 3.05 (1H, m), 2.92-2.74 (2H, m), 2.44 (1H, dd, *J* = 8.3, *J* = 16.4 Hz), 2.40-2.30 (2H, m), 2.11-2.00 (3H, m), 1.85 (1H, m), 1.72 (1H, m), 1.55-1.12 (3H, m), 1.05 (1H, m), 0.97-0.85 (9H, m). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 141.00, 118.00, 59.02, 48.72, 45.23, 42.14, 28.27, 27.95, 25.47, 24.93, 23.03, 22.72, 20.69, 10.52. **MS** (m/z): 207 (M^+, 1%), 206 (3), 192 (17), 179 (21), 150 (100), 122 (93), 79 (14), 56 (28).

1-(1-Phenylethyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole: **^{1}H-NMR** (300MHz, $CDCl_3$): δ 7.29 (2H, dd, *J* = 1.5, *J* = 8.3 Hz), 7.20 (2H, ddd, *J* = 1.5, *J* = 8.1, *J* = 8.3 Hz), 7.15 (1H, dd, *J* = 1.5, *J* = 8.1 Hz), 5.32 (1H, br s), 3.57 (1H, q, *J* = 6.7 Hz), 2.98 (1H, m), 2.63 (1H, m), 2.40-2.25 (3H, m), 1.86 (2H, m), 1.57 (1H, m), 1.31 (3H, d, *J* = 6.7 Hz), 1.31-1.10 (3H, m). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 144.56, 139.89, 127.01, 126.66, 125.73, 117.60, 62.73, 61.19, 47.59, 28.61, 26.71, 23.93, 19.86, 17.70. **MS** (m/z): 227 (M^+, 15%), 212 (17), 199 (52), 122 (25), 105 (100), 95 (84), 91 (23), 77 (31).

1-(2-Furylmethyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole: **^{1}H-NMR** (300MHz, $CDCl_3$): δ 7.36 (1H, d, *J* = 2.0 Hz), 6.30 (1H, dd, *J* = 2.0, *J* = 3.1 Hz), 6.18 (1H, d, *J* = 3.1 Hz), 5.41 (1H, br s), 3.94 (1H, d, *J* = 14.1 Hz), 3.46 (1H, d, *J* = 14.1 Hz), 3.03 (1H, m), 2.56 (1H, m), 2.41-2.30 (2H, m), 2.22 (1H, dd, *J* = 8.0, *J* = 16.1 Hz), 2.12- 1.95 (3H, m), 1.82 (1H, m), 1.41 (1H, m), 1.22-1.02 (1H, m). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 152.74, 142.22, 140.36, 119.10, 110.41, 108.50, 63.94, 52.29, 50.17, 28.25, 28.05, 25.43, 20.87. **MS** (m/z): 203 (M^+, 18%), 175 (28), 81 (100), 53 (19).

1-Benzyl-2-methyl-1,2,3,4,6,7,8,8a-octahydroquinoline: **^{1}H-NMR** (300MHz, $CDCl_3$): δ 7.32 (2H, d, *J* = 7.5 Hz), 7.22 (2H, dd, *J* = 7.2, *J* = 7.5 Hz), 7.13 (1H, d, *J* = 7.2 Hz), 5.43 (1H, br s), 3.74 (1H, d, *J* = 12.6 Hz), 3.72 (1H, d, *J* = 12.6 Hz), 2.96 (1H, m), 2.57 (1H, m), 2.20-1.80 (5H, m), 1.55 (1H, m), 1.40-1.10 (4H, m), 1.01 (3H, d, *J* = 6.2 Hz). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 142.75, 137.00, 128.07, 127.86, 126.14, 122.44, 61.40, 58.05, 54.50, 34.69, 33.93, 29.86, 25.60, 22.38, 21.69. **MS** (m/z): 241 (M^+, 23%), 226 (15), 213 (91), 198 (44), 91 (100), 65 (16).

1-(1-Phenylethyl)-1,2,3,4,6,7,8,8a-octahydroquinoline: **^{1}H-NMR** (300MHz, $CDCl_3$): δ 7.39 (2H, d, *J* = 7.5 Hz), 7.22 (2H, dd, *J* = 7.1, *J* = 7.5 Hz), 7.13 (1H, d, *J* = 7.1 Hz), 5.41 (1H, br s), 4.32 (1H, q, *J* = 6.7 Hz), 3.01 (1H, m), 2.40 (1H, d, *J* = 11.2 Hz), 2.25-1.85 (6H, m), 1.75 (1H, m), 1.65-1.20 (4H, m), 1.20 (3H, d, *J* = 6.7 Hz). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 144.88, 137.88, 128.05, 127.93, 126.29, 121.78, 57.79, 53.92, 45.25, 34.85, 29.18, 26.85, 25.66, 21.82, 7.80. **MS** (m/z): 241 (M^+, 2%), 213 (26), 136 (13), 109 (98), 105 (100), 94 (10), 91 (25), 79 (47), 77 (44), 67 (16), 53 (10), 41 (20).

1-(1-Phenylethyl)-2,3,4,6,7,7a-hexahydro-1*H*-cyclopenta[*b*]pyridine: **^{1}H-NMR** (300MHz, $CDCl_3$): δ 7.39 (2H, d, *J* = 7.2 Hz), 7.23 (2H, dd, *J* = 7.0, *J* = 7.2 Hz), 7.16 (1H, d, *J* = 7.0 Hz), 5.32 (1H, br s), 3.99 (1H, q, *J* = 6.7 Hz), 3.43 (1H, m), 2.54-2.05 (6H, m), 1.90-1.22 (4H, m), 1.26 (3H, d, *J* = 6.7 Hz). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 143.32, 142.01, 126.80, 126.79, 125.28, 121.13, 64.78, 55.08, 43.52, 30.14, 28.71, 26.33, 24.94, 7.52. **MS** (m/z): 227(M^+, 47%), 226 (24), 212 (38), 123 (35), 122 (74), 108 (24), 105 (100), 95 (23), 91 (21), 79 (47), 77 (37).

For Table 2:

1-[1-(*R*)-Phenylethyl]-1,2,3,4,6,7,8,8a-octahydroquinoline: $[\alpha]_D = -23.67^\circ$ (c = 0.0017g/mL , $CHCl_3$). **^{1}H-NMR** (300MHz, $CDCl_3$): δ 7.39 (2H, d, *J* = 7.5 Hz), 7.22 (2H, dd, *J* = 7.1, *J* = 7.5 Hz), 7.13 (1H, d, *J* = 7.1 Hz), 5.41 (1H, br s), 4.32 (1H, q, *J* = 6.7 Hz), 3.01 (1H, m), 2.40 (1H, d, *J* = 11.2 Hz), 2.25-1.85 (6H, m), 1.75 (1H, m), 1.65-1.20 (4H, m), 1.20 (3H, d, *J* = 6.7 Hz). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 144.88, 137.88, 128.05, 127.93, 126.29, 121.78, 57.79, 53.92, 45.25, 34.85, 29.18, 26.85, 25.66, 21.82, 7.80. **MS** (m/z): 241 (M^+, 2%), 213 (26), 136 (13), 109 (98), 105 (100), 94 (10), 91 (25), 79 (47), 77 (44), 67 (16), 53 (10), 41 (20).

1-[1-(*S*)-Phenylethyl]-1,2,3,4,6,7,8,8a-octahydroquinoline: $[\alpha]_D = +26.79^\circ$ (c = 0.0028g/mL , $CHCl_3$). **^{1}H-NMR** (300MHz, $CDCl_3$): δ 7.39 (2H, d, *J* = 7.5 Hz), 7.22 (2H, dd, *J* = 7.1, *J* = 7.5 Hz), 7.13 (1H, d, *J* = 7.1 Hz), 5.41 (1H, br s), 4.32 (1H, q, *J* = 6.7 Hz), 3.01 (1H, m), 2.40 (1H, d, *J* = 11.2 Hz), 2.25-1.85 (6H, m), 1.75

(1H, m), 1.65-1.20 (4H, m), 1.20 (3H, d, *J* = 6.7 Hz). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 144.88, 137.88, 128.05, 127.93, 126.29, 121.78, 57.79, 53.92, 45.25, 34.85, 29.18, 26.85, 25.66, 21.82, 7.80. **MS** (m/z): 241 (M^+, 2%), 213 (26), 136 (13), 109 (98), 105 (100), 94 (10), 91 (25), 79 (47), 77 (44), 67 (16), 53 (10), 41 (20).

1-[1-(*S*)-Phenylethyl]-2,3,5,6,7,7a-hexahydro-1*H*-indole: $[\alpha]_D$ = – 6.73˚(c = 0.0052g/mL , $CHCl_3$). **^{1}H-NMR** (300MHz, $CDCl_3$): δ 7.29 (2H, dd, *J* = 1.5, *J* = 8.3 Hz), 7.20 (2H, ddd, *J* = 1.5, *J* = 8.1, *J* = 8.3 Hz), 7.15 (1H, dd, *J* = 1.5, *J* = 8.1 Hz), 5.32 (1H, br s), 3.57 (1H, q, *J* = 6.7 Hz), 2.98 (1H, m), 2.63 (1H, m), 2.40-2.25 (3H, m), 1.86 (2H, m), 1.57 (1H, m), 1.31 (3H, d, *J* = 6.7 Hz), 1.31-1.10 (3H, m). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 144.56, 139.89, 127.01, 126.66, 125.73, 117.60, 62.73, 61.19, 47.59, 28.61, 26.71, 23.93, 19.86, 17.70. **MS** (m/z): 227 (M^+, 15%), 212 (17), 199 (52), 122 (25), 105 (100), 95 (84), 91 (23), 77 (31).

1-(1-(*S*)-Phenylethyl)-2,3,4,6,7,7a-hexahydro-1*H*-cyclopenta[*b*]pyridine: $[\alpha]_D$ = – 9.77˚(c = 0.0062g/mL , $CHCl_3$). **^{1}H-NMR** (300MHz, $CDCl_3$): δ 7.39 (2H, d, *J* = 7.2 Hz), 7.23 (2H, dd, *J* = 7.0, *J* = 7.2 Hz), 7.16 (1H, d, *J* = 7.0 Hz), 5.32 (1H, br s), 3.99 (1H, q, *J* = 6.7 Hz), 3.43 (1H, m), 2.54-2.05 (6H, m), 1.90-1.22 (4H, m), 1.26 (3H, d, *J* = 6.7 Hz). **^{13}C-NMR** (75MHz, $CDCl_3$): δ 143.32, 142.01, 126.80, 126.79, 125.28, 121.13, 64.78, 55.08, 43.52, 30.14, 28.71, 26.33, 24.94, 7.52. **MS** (m/z): 227(M^+, 47%), 226 (24), 212 (38), 123 (35), 122 (74), 108 (24), 105 (100), 95 (23), 91 (21), 79 (47), 77 (37).