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Supporting Information

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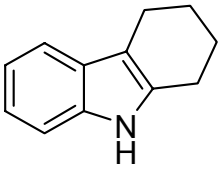
A Flexible, Palladium-catalysed Indole Synthesis by Direct Annellation of Chloroanilines with Ketones

Marc Nazaré,* Claudia Schneider, Andreas Lindenschmidt and David William Will

Aventis Pharma Deutschland GmbH, Medicinal Chemistry, DI&A Chemistry
Building G878, 65926 Frankfurt am Main, Germany

Solvents and other reagents were used as received without further purification. Column chromatography was carried out on Merck silica gel 60 (230-400 mesh). Reversed phase high pressure chromatography was conducted on a Abimed Gilson instrument using a LiChrospher 100 RP-18e (5µm) column from Merck.Thin-layer chromatography was carried out on TLC aluminium sheets with silica gel 60F254 from Merck. LC-MS analyses were performed on Agilent Series 1100 systems using a YMC J`sphere ODS H80 20x2.1 mm (4µm) column and a Merck Purosphere 55x2mm (5µm) column. Varying ratios of acetonitrile and 0.1% trifluoroacetic acid in water were used as solvent systems. NMR spectra were recorded in DMSO-d_6 either on a Bruker DRX 400 or Varian Unity Plus 300. Chemical shifts are reported as δ values from an internal tetramethylsilane standard. Mass spectral data were either obtained on a VG Bio-Q triple Quadropole mass spectrometer using electro spray ionization or a VG ZAB 2-SEQ mass spectrometer using FAB ionization. Acurate mass measurements have been conducted with a Bruker Apex III FTICR mass spectrometer. Purity and characterization of new compounds were established by a combination of LC-MS, high-resolution mass spectrometry (HRMS) and NMR analytical techniques.

Representative Synthetic Procedure: Preparation of 2,3,4,9-Tetrahydro-1H-carbazole 3

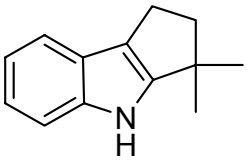


In a reaction tube, 2-chloro aniline **1** (510 mg, 4 mmol), cyclohexanone **2** (1178 mg, 12 mmol) , acetic acid (0.3 ml, 6 mmol) and $MgSO_4$ (240 mg, 2 mmol) were suspended in dimethylacetamide (12 ml). The tube was sealed with a serum cap and argon was bubbled through the solution for 10 min. K_3PO_4 (1104 mg, 5.2 mmol) and $Pd(t Bu_3P)_2$ (202 mg, 0.4 mmol) were added to the solution and argon was bubbled through the mixture for an additional 5 min. The reaction mixture was heated for 3 h at 140°C in a pre-heated parallel synthesis block (HPLC-MS reaction control). After cooling to room temperature the reaction mixture was filtered, 30 ml of water were added to the filtrate and the mixture was extracted with ethyl acetate (3x50 ml). The combined organic layers were dried over $MgSO_4$ and filtered. After removal of the solvents under reduced pressure the residue was purified by flash chromatography on silica using a heptane/ethyl acetate gradient (95% -> 50%) to yield 561 mg (3.3 mmol; 82%) of **3.**

^{1}H-NMR (400MHz, DMSO): δ= 10.5 (s, 1H), 7.5 (d, *J* = 7.6 Hz, 1H), 7.3 (t, *J* = 7.2 Hz, 1H), 7.2 (d, *J* = 7.8 Hz, 1H), 7.1 (t, *J* = 7.8 Hz, 1H), 2.65 (t, *J* = 5.4 Hz, 2H) 2.6 (t, *J* = 5.4 Hz, 2H), 1.3 (q, *J* = 4.6, *J* = 4.4, *J* = 7.7 Hz, 4H); ^{13}C-NMR (100.6MHz, DMSO): δ= 136.2 (quart. C), 135.0 (quart. C), 129.0 (CH), 127.2 (quart. C), 119.8 (CH), 117.9 (CH), 110.2 (CH), 108.1 (quart. C), 37.6 (2 CH_2), 22.8 (CH_2), 20.3 (CH_2); LCMS (ES+) = 172.2 [M+H].

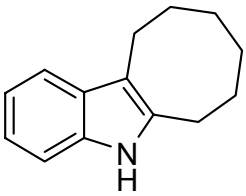
Spectroscopic data of selected compounds

3,3-Dimethyl-1,2,3,4-tetrahydro-cyclopenta[b]indole



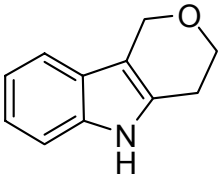
^{1}H-NMR (400MHz, DMSO): δ= 12.2 (s, 1H), 7.7 (d, *J* = 8.07 Hz, 1H), 7.2 (t, *J* = 8.3 Hz, 1H), 6.8 (d, *J* = 8.5 Hz, 1H), 6.5 (t, *J* = 8.3 Hz, 1H), 2.7 (t, *J* = 8.3 Hz, 2H), 1.8 (t, *J* = 8.3, 2H), 1.2 (s, 6H); ^{13}C-NMR (100.6MHz, DMSO): δ= 178.5 (quart. C), 151.0 (quart. C), 133.9 (CH), 131.0 (CH), 116.8 (CH), 116.2 (CH), 114.3 (CH), 108.7 (CH), 40.8 (quart. C), 34.8 (CH_2), 34.5 (CH_2), 34.8 (2 CH_3); LCMS (ES+) = 186.2 [M+H].

6,7,8,9,10,11-Hexahydro-5H-cycloocta[b]indole



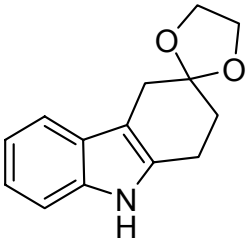
^{1}H-NMR (400MHz, DMSO): δ= 10.7 (s, *J* = 8.3, 1H), 7.4 (d, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 6.9 (t, *J* = 6.85 , *J* = 7.6 Hz, 2H), 2.8 (m, 4H), 1.7 (m, 4H), 1.4 (m, 4H); ^{13}C-NMR (100.6MHz, DMSO): δ= 135.9 (quart. C), 134.8 (quart. C), 127.8 (quart. C), 119.4 (CH), 117.7 (CH), 116.8 (CH), 110.3 (CH), 109.5 (quart. C), 29.4 (CH_2), 29.1 (CH_2), 26.5 (CH_2), 25.3 (CH_2), 25.0 (CH_2), 21.6 (CH_2); LCMS (ES+) = 200.1 [M+H]; HRMS calcd for $C_{14}H_{18}N$: 200.1434, found: 200.1442.

1,3,4,5-Tetrahydro-pyrano[4,3-b]indole



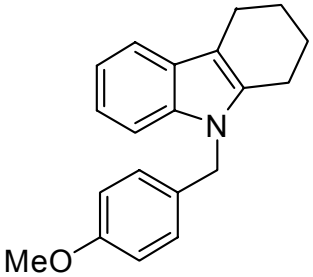
^{1}H-NMR (400 MHz, DMSO): δ= 10.8 (s, 1H), 7.3 (d, *J* = 8.1 Hz, 2H), 7.0 (t, *J* = 8.1 Hz, 1H), 6.9 (t, *J* = 8.1 Hz, 1H), 4.8 (s, 2H), 3.9 (t, *J* = 5.6 Hz, 2H), 2.8 (t, *J* = 5.6 Hz, 2H); ^{13}C-NMR (100.6MHz, DMSO): δ= 135.4 (quart. C), 131.4 (quart. C), 124.4 (quart. C), 120.2 (CH), 118.2 (CH), 117.0 (CH), 110.8 (CH), 106.8 (quart. C), 63.8 (CH_2), 63.4 (CH_2), 23.7 (CH_2); LCMS (ES+) = 174.1 [M+H]; HRMS calcd for $C_{11}H_{12}NO$: 174.0922, found: 174.0913.

5-Oxo-tetrahydrocarbazol ethylen ketal



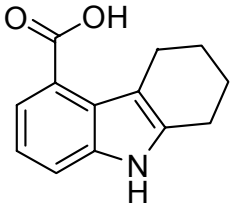
^{1}H-NMR (400MHz, DMSO): δ= 10.7 (s, 1H), 7.3 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 8.8 Hz, 1H), 6.95 (t, *J* = 7.1 Hz, 1H), 6.9 (t, *J* = 6.6 Hz, 1H), 2.8 (s, 2H), 2.3 (t, *J* = 7.1 Hz, 4H), 1.9 (t, *J* = 7.3 Hz, 4H); ^{13}C-NMR (100.6MHz, DMSO): δ= 142.8 (quart. C), 136.2 (quart. C), 132.9 (quart. C), 130.9 (CH), 129.2 (CH), 127.1 (CH), 120.1 (quart. C), 110.5 (CH), 106.5 (quart. C), 108.4 (CH), 63.8 (2 CH_2), 32.9 (CH_2), 21.0 (CH_2); LCMS (ES+) = 230.1 [M+H].

9-(4-Methoxy-benzyl)-2,3,4,9-tetrahydro-1H-carbazole



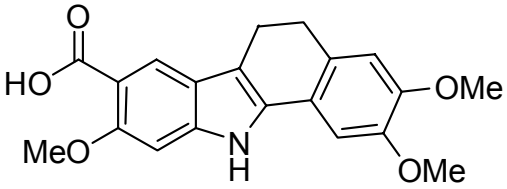
^{1}H–NMR (400MHz, DMSO): δ= 7.36 (m, 2H), 7.00 (m, 4H), 6.84 (m, 2H), 5.23 (s, 2H), 3.68 (s, 3H), 2.66 (m, 4H), 1.81 (m, 4H); ^{13}C-NMR (100.6MHz, DMSO): δ= 158.2 (quart. C), 136.0 (quart. C), 135.3 (quart. C), 130.4 (quart. C), 127.6 (2 CH), 126.9 (quart. C), 120.2 (CH), 118.3 (CH), 117.3 (CH), 113.8 (2 CH), 109.2 (CH), 108.5 (quart. C), 54.9 (CH_3), 44.8 (CH_2), 22.7 (2 CH_2), 21.6 (CH_2), 20.6 (CH_2); LCMS (ES+) = 292.4 [M+H]; HRMS calcd for $C_{20}H_{22}NO$: 292.1695, found: 292.1696.

6,7,8,9-Tetrahydro-5H-carbazole-4-carboxylic acid



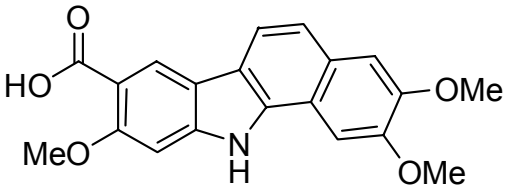
^{1}H–NMR (400MHz, DMSO): δ= 14.1 (s, 1H), 8.4 (s, 1H), 7.6 (t, *J* = 7.4 Hz, 1H), 7.2 (d, *J* = 6.4 Hz, 1H), 7.1 (d, *J* = 8.6 Hz, 1H), 1.9 (m, 6H), 1,81 (m, 2H); ^{13}C-NMR (100.6MHz, DMSO): δ= 165.7 (quart. C), 161.4 (quart. C), 137.8 (CH), 129.8 (quart. C), 119.9 (CH), 115.9 (CH), 113.5 (quart. C), 74.2 (2 CH), 37.2 (2 CH_2), 24.9 (2 CH_2); LCMS (ES+) = 216.4 [M+H]; HRMS calcd for $C_{13}H_{14}NO_2$: 216.1019, found: 216.1023.

2,3,9-Trimethoxy-5,11-dihydro-6H-benzo[a]carbazole-8-carboxylic acid



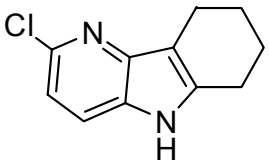
^{1}H-NMR (400MHz, DMSO): δ= 12.1 (s, 1H), 8.50 (s, 1H), 7.90 (s, 1H), 7.12 (s, 1H) 6.92 (s, 1H), 6.87 (s, 1H), 4.00 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H), 2.93 (d, *J* = 8.3 Hz, 2H), 2.83 (d, *J* = 8.6 Hz, 2H); ^{13}C-NMR (100.6MHz, DMSO): δ= 167.5 (quart. C), 155.0 (quart. C), 147.4 (2 quart. C), 139.6 (quart. C), 133.9 (quart. C), 127.9 (quart. C), 121.7 (CH), 120.5 (quart. C), 115.8 (quart. C), 113.4 (CH), 111.6 (quart. C), 109.4 (quart. C), 105.6 (CH), 94.3 (CH), 55.9 (CH_3), 55.7 (CH_3), 55.6 (CH_3), 28.3 (CH_2), 20.0 (CH_2); LCMS (ES+) = 354.2 [M+H]; HRMS calcd for $C_{20}H_{20}NO_5$: 354.1336, found: 354.1338.

2,3,9-Trimethoxy-11H-benzo[a]carbazole-8-carboxylic acid



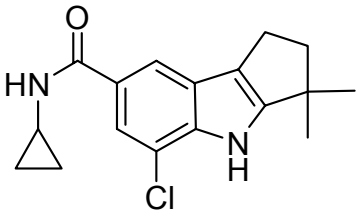
^{1}H-NMR (400MHz, DMSO): δ= 12.1 (s, 1H), 8.50 (s, 1H), 8.02 (d, *J* = 12.3 Hz, 1H), 7.92 (s, 1H), 7.52 (d, *J* = 12.6 Hz, 1H), 7.12 (s, 1H), 6.92 (s, 1H), 4.00 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H); ^{13}C-NMR (100.6MHz, DMSO): δ= 167.4 (quart. C), 157.0 (quart. C), 148.8 (2 quart. C), 148.4 (CH), 141.9 (quart. C), 135.4 (quart. C), 127.0 (quart. C), 123.3 (CH), 118.7 (CH), 116.6 (quart. C), 116.5 (quart. C), 115.8 (quart. C), 113.0 (quart. C), 108.0 (CH), 101.5 (CH), 93.9 (CH), 56.0 (CH_3), 55.5 (CH_3), 55.3 (CH_3); LCMS (ES+) = 352.1 [M+H]; HRMS calcd for $C_{20}H_{18}NO_5$: 352.1179, found: 352.1183.

2-Chloro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indole



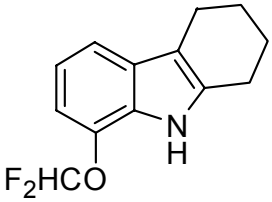
^{1}H–NMR (400MHz, DMSO): δ= 11.2 (s, 1H), 7.7 (d, *J* = 8.3 Hz, 1H), 7.0 (d, *J* = 8.3 Hz, 1H), 2.7 (t, *J* = 5.6 Hz, 2H), 2.6 (t, *J* = 6.1 Hz, 2H), 1,8 (m, 4H); ^{13}C-NMR (100.6MHz, DMSO): δ= 144.5 (quart. C), 141.2 (quart. C), 140.7 (quart. C), 127.0 (quart. C), 120.2 (CH), 114.3 (CH), 108.5 (quart. C), 22.9 (CH_2), 22.4 (CH_2), 22.3 (CH_2), 19.6 (CH_2); LCMS (ES+) = 207.2 [M+H]; HRMS calcd for $C_{11}H_{12}ClN_2$: 207.0683, found: 207.0688.

5-Chloro-3,3-dimethyl-1,2,3,4-tetrahydro-cyclopenta[b]indole-7-carboxylic acid cyclopropylamide



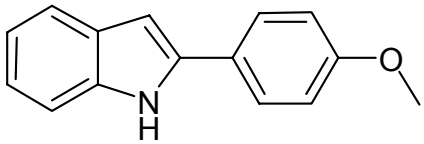
^{1}H-NMR (400MHz, DMSO): δ= 8.28 (d, *J* = 7.3 Hz, 1H), 7.83 (s, 1H), 7.57 (s, 1H), 2.92 (m, 1H), 2.75 (t, *J* = 8.8, 1H), 2.30 (t, *J* = 8.7, 2H), 1.35 (s, 6H), 0.65 (m, 2H), 0.55 (m, 2H); ^{13}C-NMR (100.6MHz, DMSO): δ= 167.1 (quart. C), 154.2 (quart. C), 138.2 (quart. C), 127.1 (CH), 126.0 (quart. C), 125.1 (quart. C), 118.3 (CH), 117.1 (CH), 115.3 (CH), 59.6 (quart. C), 45.2 (CH_2), 27.5 (2 CH_3), 23.1 (CH_2), 22.4 (CH_2), 20.6 (quart. C), 5.6 (2 CH_2); LCMS (ES+) = 303.2 [M+H].

8-Difluoromethoxy-2,3,4,9-tetrahydro-1H-carbazole



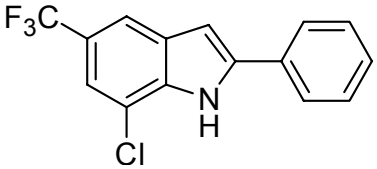
^{1}H–NMR (400MHz, DMSO): δ= 10.7 (s, 1H), 7.3 (t, *J* = 2.0 Hz, 1H), 7.25 (d, *J* = 8.6 Hz, 1H), 7.2 (d, *J* = 6.35 Hz, 1H), 2.7 (t, *J* = 5.6 Hz, 2H), 2.6 (t, *J* = 5.9 Hz, 2H), 2.0 (s, 1H), 1.8 (m, 4H); ^{13}C-NMR (100.6MHz, DMSO): δ= 136.4 (quart. C), 133.9 (quart. C), 128.3 (quart. C), 122.5 (quart. C), 119.6 (CH), 116.2 (2 CH), 111.7 (CH), 108.1 (quart. C), 22.7, (CH_2), 22.6 (CH_2), 22.5 (CH_2), 20.3 (CH_2); LCMS (ES+) = 238.3 [M+H].

2-(4-Methoxy-phenyl)-1H-indol



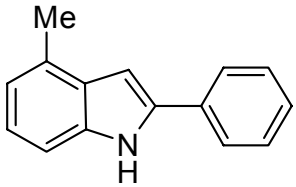
^{1}H-NMR (400MHz, DMSO): δ= 11.4 (s, 1H), 7.8 (d, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.05 (dd, *J* = 8.1, *J* = 8.8 Hz, 3H), 6.95 (t, *J* = 8.1, 1H), 6.75 (s, 1H), 3.8 (s, 3H); ^{13}C-NMR (100.6MHz, DMSO): δ= 158.0 (quart. C), 137.6 (quart. C), 136.8 (quart. C), 128.7 (quart. C), 126.2 (2 CH), 124.7 (quart. C), 120.9 (CH), 119.5 (quart. C), 119.1 (CH), 114.2 (2 CH), 110.9 (CH), 97.2 (CH), 55.1 (CH_3); LCMS (ES+) = 224.3 [M+H]; HRMS calcd for C15H14NO: 224.1070, found: 224.1072.

7-Chloro-2-phenyl-5-trifluoromethyl-1H-indole



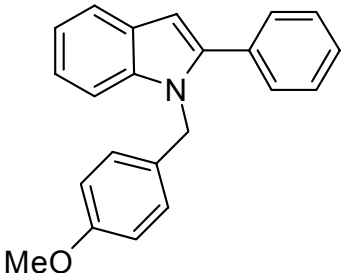
^{1}H-NMR (400MHz, DMSO): δ = 12.0 (s, 1H), 8.05 (s, 1H), 8.03 (s, 1H), 7.95 (s, 1H), 7.55 (m, 3H), 7.42 (t, *J* = 7.3 Hz, 1H), 7.18 (s, 1H); ^{13}C-NMR (100.6MHz, DMSO): δ = 141.5 (quart. C), 135.5 (quart. C), 130.9 (quart. C), 129.8 (2 CH), 128.6 (CH), 126.2 (2 CH), 125.9 (CH), 123.2 (quart. C), 121.5 (quart. C), 120.5 (CH), 117.3 (CH), 116.6 (quart. C), 101.4 (CH); LCMS (ES+) = 296.1 [M+H].

4-Methyl-2-phenyl-1H-indole



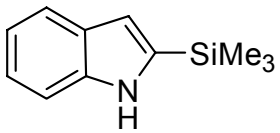
^{1}H-NMR (400MHz, DMSO): δ= 11.5 (s, 1H), 7.9 (d, *J* = 7.1 Hz, 2H), 7.4 (t, *J* = 7.6 Hz, 2H), 7.3 (t, *J* = 8.5 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 7.0 (t, *J* = 7.5 Hz, 1H), 6.9 (s, 1H), 6.8 (d, 1H), 2.5 (s, 3H); ^{13}C-NMR (100.6MHz, DMSO): δ= 136.7 (quart. C), 136.6 (quart. C), 132.2 (quart. C), 128.8 (quart. C), 128.7 (2 CH), 128.5 (quart. C), 127.1 (CH), 124.7 (2 CH), 121.5 (quart. C), 119.2 (quart. C), 108.8 (CH), 97.3 (CH), 18.4 (CH_3); LCMS (ES+) = 208.2 [M+H]; HRMS calcd for $C_{15}H_{14}N$: 208. 1121, found: 208. 1128.

1-(4-Methoxy-benzyl)-2-phenyl-1H-indole



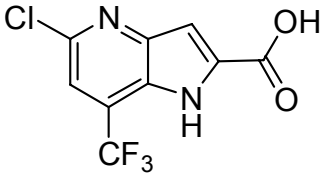
^{1}H-NMR (400MHz, DMSO): δ= 7.61 (m, 7H), 7.09 (m, 2H), 6.81 (m, 4H), 6.63 (s, 1H), 5.39 (s, 2H), 3.66 (s, 3H); ^{13}C-NMR (100.6MHz, DMSO): δ= 158.2 (quart. C), 140.9 (quart. C), 137.4 (quart. C), 132.2 (quart. C), 129.9 (quart. C), 128.8 (2 CH), 128.6 (2 CH), 128.0 (CH), 127.7 (quart. C), 127.1 (2 CH), 121.5 (CH), 120.1 (CH), 119.7 (CH), 113.8 (2 CH), 110.0 (CH), 102.0 (CH), 54.9 (CH_3), 46.1 (CH_2); LCMS (ES+) = 314.3 [M+H]; HRMS calcd for $C_{22}H_{20}NO$: 314.1535, found: 314.1539.

2-Trimethylsilanyl-1H-indole



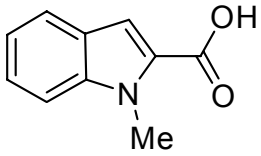
^{1}H-NMR (400MHz, DMSO): δ= 11.0 (s, 1H), 7.5 (d, *J* = 7.9 Hz, 1H), 7.4 (d, *J* = 9.1 Hz, 1H), 7.1 (t, *J* = 7.4 Hz, 1H), 6.9 (t, *J* = 7.9 Hz, 1H), 6.6 (s, 1H), 0.4 (s, 9H); ^{13}C-NMR (100.6MHz, DMSO): δ= 139.1 (quart. C), 137.9 (quart. C), 128.1 (quart. C), 121.3 (CH), 119.9 (CH), 118.5 (CH), 111.2 (CH), 110.1 (CH), -1.3 (CH_3); MS (ES+) = 190.1 [M+H].

5-Chloro-7-trifluoromethyl-1H-pyrrolo[3,2-b]pyridine-2-carboxylic acid



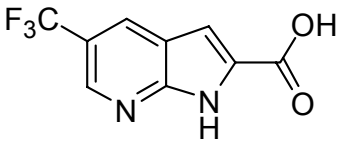
^{1}H-NMR (400MHz, DMSO): δ= 12.9 (s, 1H), 12.7 (s, 1H), 7.72 (s, 1H), 7.32 (s, 1H); ^{13}C-NMR (100.6MHz, DMSO): δ= 162.1 (quart. C), 150.2 (quart. C), 146.8 (quart. C), 143.9 (quart. C), 135.4 (CH), 124.5 (quart. C), 123.6 (CH), 115.8 (CH), 107.8 (CH); LCMS (ES+) = 265.1 [M+H]; HRMS calcd for $C_9H_5ClF_3N_2O_2$: 264.9986, found: 264.9990.

1-Methyl-1H-indole-2-carboxylic acid



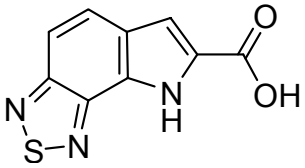
^{1}H-NMR (400MHz, DMSO): δ= 12.9 (s, 1H), 7.7 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 8.6 Hz, 1H), 7.3 (t, *J* = 8.3 Hz, 1H), 7.2 (s, 1H), 7.1 (t, *J* = 7.5 Hz, 1H), 4.1 (s, 3H); ^{13}C-NMR(100.6, DMSO): δ= 162.8 (quart. C), 139.1 (quart. C), 128.4 (quart. C), 125.2 (quart. C), 124.4 (CH), 122.0 (CH), 120.2 (CH), 110.7 (CH), 109.2 (CH), 31.3 (CH_3); LCMS (ES+) = 176.2 [M+H]; HRMS calcd for $C_{10}H_{10}NO_2$: 176.0706, found: 176.0714.

5-Trifluoromethyl-1H-pyrrolo[2,3-b]pyridine-2-carboxylic acid



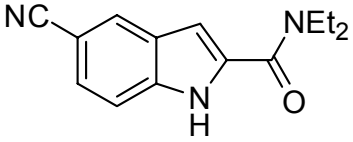
^{1}H-NMR (400MHz, DMSO): δ= 13.3 (s, 1H), 12.8 (s, 1H), 8.7 (s, 1H), 8.6 (s, 1H), 7.3 (s, 1H); ^{13}C-NMR (100.6MHz, DMSO): δ= 161.9 (quart. C), 149.8 (quart. C), 142.0 (CH), 131.4 (quart. C), 128.5 (CH), 126.1 (quart. C), 123.4 (quart. C), 118.0 (quart. C), 106.9 (CH); LCMS (ES+) = 231.1 [M+H]; HRMS calcd for $C_9H_6F_3N_2O_2$: 231.0376, found: 231.0380.

8H-Pyrrolo[2',3':3,4]benzo[1,2-c][1,2,5]thiadiazole-7-carboxylic acid



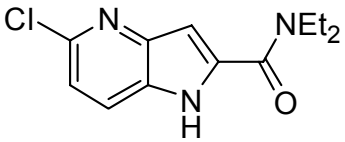
^{1}H-NMR (400MHz, DMSO): δ= 13.4 (s, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.32 (s, 1H); ^{13}C-NMR (100.6MHz, DMSO): δ= 162.3 (quart. C), 154.5 (quart. C), 144.6 (quart. C), 129.0 (quart. C), 126.8 (quart. C), 126.5 (CH), 124.8 (quart. C), 114.0 (CH), 110.3 (CH); LCMS (ES+) = 220.1 [M+H]; HRMS calcd for $C_9H_6N_3O_2S$: 220.0182, found: 220.0175.

5-Cyano-1H-indole-2-carboxylic acid diethylamide



^{1}H-NMR (400MHz, DMSO): δ= 12.1 (s, 1H), 7.7 (s, 1H), 7.4 (d, *J* = 8.6 Hz, 1H), 6.9 (d, *J* = 8.6 Hz, 1H), 6.4 (s, 1H), 1.5 (m, 10H); LCMS (ES+) = 242.3 [M+H]; HRMS calcd for $C_{14}H_{16}N_3O$: 242.1288, found: 242.1291.

5-Chloro-1H-pyrrolo[3,2-b]pyridine-2-carboxylic acid diethylamide



^{1}H-NMR (400MHz, DMSO): δ= 12.1 (s, 1H), 7.8 (d, *J* = 8.6 Hz, 1H), 7.3 (d, *J* = 8.6 Hz, 1H), 6.8 (s, 1H), 1.4 (m, 10H); ^{13}C-NMR (100.6MHz, DMSO): δ= 161.3 (quart. C), 144.2 (quart. C), 143.3 (quart. C), 134.4 (quart. C), 127.3 (quart. C), 122.7 (CH), 118.0 (CH), 101.9 (CH), 39.6 (2 CH_2), 39.2 (2 CH_3); LCMS (ES+) = 252.2 [M+H]; HRMS calcd for $C_{12}H_{15}ClN_3O$: 252.0898, found: 252.0899.