Synthesis of Benzofused 1,4-Azaborinols via [4+2] Annulation Strategy and its Application in Indole Synthesis

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Supporting Information

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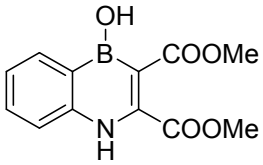
General Remarks:

All reactions were carried out under nitrogen atmosphere using a Pre-assembled screw top, 7 ml/15ml supelco vials purchased from sigma Aldrich. Microwave reactions were performed in Biotage instrument using 10 ml Biotage microwave vials. 2-amino phenylboronic acid/boronates were purchased from Combi-blocks and diethyl but-2-ynedioate, dimethyl but-2-ynedioate were purchased from Alfa Aesar. Palladium acetate, Dichloromethane, Dichloroethane were purchased from sigma Aldrich. All anhydrous solvents, reagent grade solvents for chromatography were purchased from Sigma Aldrich Chemical, Spectochem or Merck. 2-amino-5-(trifluoromethyl)phenylboronic acid was prepared according to the literature procedure for 2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethyl)aniline[1] followed by boronate ester hydrolysis using reported method.[2] Water was distilled and purified through a Milli-Q water system (Millipore Corp., Bedford, MA). General methods of purification of compounds involved the use of silica cartridges purchased from Grace Purification systems. The reactions were monitored by TLC on precoated Merck 60 F254 silica gel plates and visualized using UV light (254 nm). ^{1}H NMR and ^{13}C NMR were recorded using Bruker 300 MHz and Bruker 500 MHz NMR spectrometers respectively. Chemical shifts are reported in ppm (δ) relative to the residual solvent peak in the corresponding spectra; chloroform δ 7.26, methanol δ 3.31, DMSO-d6 δ 3.33 and coupling constants (*J*) are reported in hertz (Hz) (where s = singlet, bs = broad singlet, d = doublet, dd = double doublet, bd = broad doublet, ddd = double doublet of doublet, t = triplet, tt – triple triplet, q = quartet, m = multiplet) and analyzed using ACD NMR data processing software. ^{11}B NMR spectra were recorded on a Bruker 300 MHz spectrometer at ambient temperature. Mass spectra values are reported as *m/z*. Melting point range was determined by BUCHI Melting Point B-545 apparatus and are uncorrected. All reactions were conducted under Nitrogen and monitored using LCMS unless otherwise noted. Solvents were removed *in vacuo* on a rotary evaporator.

Experimental section

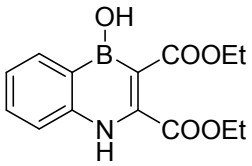
Dimethyl 4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate (3aa)



3aa

Typical procedure: To a 7 mL supelco vial**, 2**-aminophenylboronic acid **1a** (50 mg, 0.36 mmol), dimethyl but-2-ynedioate **2a** (47 µL, 0.38 mmol) and 2.5 ml of DCM were added under nitrogen atmosphere. The mixture was heated to 80°C and stirred for 30 minutes as monitored by LCMS. The reaction mixture was diluted with DCM (10 mL) and washed with water (2x 5 ml), dried over sodium sulphate and evaporated under vacuum. The crude product was purified by combiflash (eluent: hexane/ ethylacetate = 3:1) to afford 84 mg (88%) of **3aa**: Pale yellow solid; Mp: 126-128°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.77 (br. s., 1H), 8.03 (d, *J*=7.54 Hz, 1H), 7.78 (s, 1H), 7.62 (t, *J*=7.32 Hz, 1H), 7.52 (d, *J*=8.17 Hz, 1H), 7.27 (t, *J*=7.19 Hz, 1H), 3.89 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.9, 165.3, 149.9, 143.5, 131.6, 130.9, 124.3, 122.9, 118.1, 101.1, 52.9, 51.4; ^{11}B NMR (96 MHz, DMSO-d_6) δ 37.8; HRMS m/z calc'd for $C_{12}H_{12}BNO_5$ $[M+H]^+$ 262.0881, found: 262.08842; IR (cm^{-1}): 3607, 3109, 1697, 1626, 1568, 1385, 1196, 1128, 1086, 762.

Diethyl 4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate (3ab)

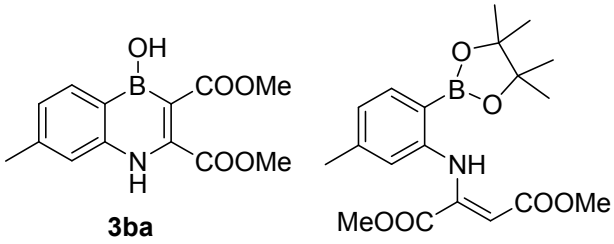


3ab

The reaction of **1a** (50 mg, 0.36 mmol), **2b** (61 µL, 0.38 mmol) in DCM (2.5 mL) afforded 89 mg (84%) of **3ab**: Light yellow solid; Mp: 104-106°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.72 (br. s., 1H), 8.02 (d, *J*=7.54 Hz, 1H), 7.79 (s, 1H), 7.58-7.67 (m, 1H), 7.46-7.58 (m, 1H), 7.27 (t, *J*=7.25 Hz, 1H), 4.35 (q, *J*=7.16 Hz, 2H), 4.06-4.25 (m, 2H), 1.33 (t, *J*=7.16 Hz, 3H), 1.25 (t, *J*=7.06 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.5, 164.6, 149.7, 143.4, 131.5, 130.7, 123.9, 122.8, 118.0, 100.9, 61.9, 59.8, 14.1, 13.6; ^{11}B NMR (96 MHz, DMSO-d_6) δ 40.0; HRMS

m/z calc'd for $C_{14}H_{16}BNO_5[M+H]^+$ 290.1194, found: 290.12052. IR (cm^{-1}): 3478, 3150, 1726, 1689, 1651, 1383, 1030, 825.

Dimethyl 4-hydroxy-7-methyl-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate (3ba) & dimethyl 2-(5-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenylamino) fumarate (3ba-i)



3ba **3ba-i**

The reaction of 5-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine (**1b)** (75 mg, 0.32 mmol), **2a** (42 µL, 0.34 mmol) in DCM (2.5 mL) afforded 31 mg (35%) of **3b** and 63mg (52%) of **3ba-i.**

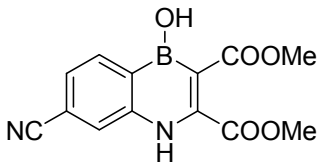
Typical procedure (Microwave): To a Biotage Microwave vial**, 1b** (75 mg, 0.32 mmol), **2a** (42 µL, 0.38 mmol) and 3 ml of DCE were added under nitrogen atmosphere. The mixture was heated to 110°C under microwaves and stirred for 30 minutes. The reaction mixture was diluted with DCM (10 mL) and washed with water (2x 5 ml), dried over sodium sulphate and evaporated under vacuum. The crude product was purified by combiflash (eluent: hexane/ ethylacetate = 3:1) to afford 66 mg (75%) of **3ba.**

Compound **3ba:** pale yellow solid; Melting point: 127-129°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.65 (br. s., 1H), 7.92 (d, *J*=7.72 Hz, 1H), 7.68 (s, 1H), 7.30 (s, 1H), 7.10 (d, *J*=7.91 Hz, 1H), 3.88 (s, 3H), 3.71 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.8, 165.2, 149.7, 143.7, 141.4, 130.8, 124.4, 121.5, 117.6, 100.8, 52.9, 51.3, 21.4; ^{11}B NMR (96 MHz, DMSO-d_6) δ 41.1; HRMS m/z calc'd for $C_{13}H_{14}BNO_5$ $[M+H]^+$ 276.10375, found: 276.10383. IR (cm^{-1}): 3500, 3155, 1742, 1694, 1632, 1562, 1383, 1246, 818.

Compound **3ba-i:** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.27 (br. s., 1H), 7.51 (d, *J*=7.54 Hz, 1H), 6.86 (d, *J*=7.54 Hz, 1H), 6.37 (s, 1H), 5.27 (s, 1H), 3.69 (s, 3H), 3.67 (s, 3H), 2.25 (s, 3H), 1.32 (s, 12H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.6, 164.9, 145.9, 145.6, 142.3, 136.3, 123.2,

118.0, 113.9, 94.6, 83.8, 53.0, 51.0, 24.6, 21.3; HRMS m/z calc'd for $C_{19}H_{26}BNO_6[M+H]^+$ 376.19257, found: 376.19275.

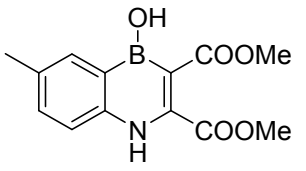
Dimethyl 7-cyano-4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate (3ca)



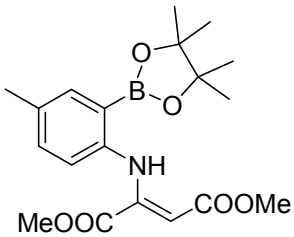
3ca

The reaction of 2-amino-4-cyanophenylboronic acid.HCl **1c** (50 mg, 0.25 mmol), DIPEA (44 µL, 0.25 mmol), **2a** (33 µL, 0.27 mmol) in DCM (2.5 mL) for 1 hr afforded 47 mg (65%) of **3ca:** White solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.96 (br. s., 1H), 8.29 (s, 1H), 8.21 (d, *J*=7.91 Hz, 1H), 7.95 (s, 1H), 7.61 (dd, *J*=1.32, 7.91 Hz, 1H), 3.90 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.4, 164.6, 149.0, 143.0, 132.4, 127.7, 124.3, 122.2, 118.5, 113.5, 104.7, 53.1, 51.5; ^{11}B NMR (96 MHz, DMSO-d_6) δ 42.8; HRMS m/z calc'd for $C_{13}H_{11}BN_2O_5$ $[M+H]^+$ 287.08335, found: 287.08362; IR (cm^{-1}): 3580, 3100, 2235, 1740, 1690, 1385, 1257, 1138, 1084, 835.

Dimethyl 4-hydroxy-6-methyl-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate (3da) & dimethyl 2-(4-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenylamino) fumarate (3da-i)



3da



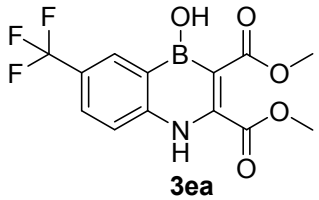
3da-i

The reaction of 4-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine (**1d)** (75 mg, 0.32 mmol), **2a** (42 µL, 0.34 mmol) in DCM (2.5 mL) afforded 40 mg (45%) of **3da** and 51mg (42%) of **3da-i.**

Microwave procedure: To a 10 ml Biotage Microwave vial**, 1b** (75 mg, 0.32 mmol), **2a** (42 µL, 0.38 mmol) and 3 ml of DCE were added under nitrogen atmosphere. The mixture was heated to 110°C under microwaves and stirred for 30 minutes. The reaction mixture was diluted with DCM (10 mL) and washed with water (2x 5 ml), dried over sodium sulphate and evaporated under vacuum. The crude product was purified by combiflash (eluent: hexane/ ethylacetate = 3:1) to afford 69 mg (78%) of **3da.**

Compound **3da:** Light yellow solid; Melting point: 145-146°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.73 (br. s., 1H), 7.82 (s, 1H), 7.69 (s, 1H), 7.38-7.46 (m, 2H), 3.88 (s, 3H), 3.72 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.9, 165.3, 149.7, 141.4, 132.7, 131.8, 130.4, 124.2, 118.0, 100.2, 52.9, 51.3, 20.7; ^{11}B NMR (96 MHz, DMSO-d_6) δ 36.4; HRMS m/z calc'd for $C_{13}H_{14}BNO_5$ $[M+H]^+$ 276.10375, found: 276.10373. IR (cm^{-1}): 3514, 3150, 1728, 1682, 1533, 1385, 1202, 1022, 825.
Compound **3da-i:** ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.26 (br. s., 1H), 7.43 (s, 1H), 7.20 (d, *J*=8.48 Hz, 1H), 6.50 (d, *J*=8.10 Hz, 1H), 5.23 (s, 1H), 3.68 (s, 3H), 3.67 (s, 3H), 2.24 (s, 3H), 1.33 (s, 12H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.7, 164.8, 146.2, 143.0, 136.5, 132.9, 131.3, 117.7, 117.1, 93.7, 84.0, 53.0, 51.0, 24.5, 20.0; HRMS m/z calc'd for $C_{19}H_{26}BNO_6[M+H]^+$ 376.19257, found: 376.19254.

Dimethyl 4-hydroxy-6-(trifluoromethyl)-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate (3ea)

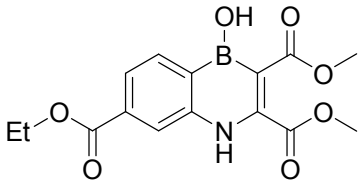


3ea

The reaction of 2-amino-5-(trifluoromethyl)phenylboronic acid (**1e)** (50 mg, 0.25 mmol), **2a** (42 µL, 0.26 mmol) in DCM (2.5 mL) for 1 hr afforded 55 mg (68%) of **3ea.** Cream-white solid; Melting point: 118-120°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.93 (br. s., 1H), 8.39 (s, 1H), 8.30 (s, 1H), 7.91 (dd, *J*=1.88, 8.67 Hz, 1H), 7.74 (d, *J*=8.67 Hz, 1H), 3.90 (s, 3H), 3.73 (s, 3H);

^{13}C NMR (126 MHz, DMSO-d_6) δ 169.7, 164.9, 149.0, 146.0, 128.6 (q, *J* = 3.8 Hz), 127.9 (q, *J* = 3.8 Hz), 125.8 (q, *J* = 271 Hz), 123.6, 123.0 (q, J = 31.5), 119.4, 105.6, 53.3, 51.7; ^{11}B NMR (96 MHz, DMSO-d_6) δ 41.1; HRMS m/z calc'd for $C_{13}H_{11}BF_3NO_5[M+H]^+$ 330.07549, found: 330.07578.

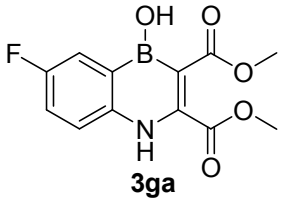
7-ethyl 2,3-dimethyl 4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3,7-tricarboxylate (3fa)



3fa

The reaction of 4-(ethoxycarbonyl)-2-aminophenylboronic acid.HCl **1f** (50 mg, 0.20 mmol), DIPEA (35 µL, 0.20 mmol), **2a** (27 µL, 0.21 mmol) in DCM (2.5 mL) for 1 hr afforded 46 mg (68%) of **3fa:** Cream-white solid; Melting point: 140-142°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.97 (br. s., 1H), 8.21 (s, 1H), 8.17 (d, *J*=7.88 Hz, 1H), 8.07 (s, 1H), 7.78 (d, *J*=7.88 Hz, 1H), 4.36 (q, *J*=7.25 Hz, 2H), 3.89 (s, 3H), 3.72 (s, 3H), 1.35 (t, *J*=7.09 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 168.5, 164.2, 163.8, 148.8, 142.2, 131.3, 130.5, 126.8, 121.0, 118.2, 101.8, 60.0, 51.9, 50.3, 13.0; ^{11}B NMR (96 MHz, DMSO-d_6) δ 39.9; HRMS m/z calc'd for $C_{15}H_{16}BNO_7[M+H]^+$ 334.10923, found: 334.10936; IR (cm^{-1}): 3524, 3300, 1703, 1630, 1587, 1383, 1136, 1014, 839.

Dimethyl 6-fluoro-4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate (3ga)

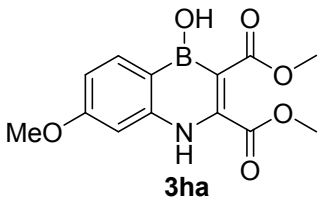


3ga

The reaction of 2-amino-5-fluorophenylboronic acid (**1g)** (50 mg, 0.32 mmol), **2a** (42 µL, 0.34 mmol) in DCM (2.5 mL) afforded 69 mg (77%) of **3ga.** Cream-white solid; Melting point: 165-167°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.86 (br. s., 1H), 7.94 (s, 1H), 7.70 (dd, *J*=2.92, 8.95 Hz, 1H), 7.57-7.65 (m, 1H), 7.45-7.54 (m, 1H), 3.88 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.7, 165.0, 157.8 (d, *J* = 243.2 Hz), 149.3, 140.0, 126.0, 120.7 (d, *J* = 7.6 Hz),

120.4 (d, *J* = 25.2 Hz), 114.7 (d, J = 20.2 Hz), 101.1, 53.0, 51.3; ^{11}B NMR (96 MHz, DMSO-d_6) δ 39.9; HRMS m/z calc'd for $C_{12}H_{11}BFNO_5[M+H]^+$ 280.07868, found: 280.07867; IR (cm^{-1}): 3502, 3283, 1740, 1709, 1385, 1217, 1016, 827.

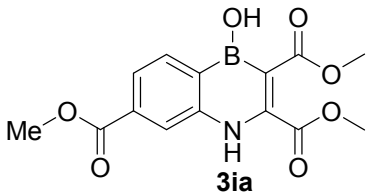
Dimethyl 4-hydroxy-7-methoxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate (3ha)



3ha

The reaction of 2-amino-4-methoxyphenylboronic acid (**1h)** (50 mg, 0.30 mmol), **2a** (39 µL, 0.32 mmol) in DCM (2.5 mL) afforded 70 mg (80%) of **3ha**. Cream-white solid; Melting point: 144-146°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.56 (br. s., 1H), 7.93 (d, *J*=8.48 Hz, 1H), 7.65 (s, 1H), 7.01 (d, *J*=2.07 Hz, 1H), 6.88 (dd, *J*=2.07, 8.48 Hz, 1H), 3.88 (s, 3H), 3.82 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.9, 165.1, 161.8, 149.0, 145.2, 132.4, 117.1, 112.0, 102.0, 100.3, 55.0, 52.9, 51.3; ^{11}B NMR (96 MHz, DMSO-d_6) δ 41.2; HRMS m/z calc'd for $C_{13}H_{14}BNO_6[M+H]^+$ 292.09867, found: 292.09235; IR (cm^{-1}): 3500, 3157, 1742, 1628, 1383, 1213, 1084, 837.

Trimethyl 4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3,7-tricarboxylate (3ia)



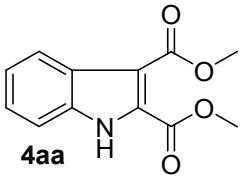
3ia

The reaction of 4-(methoxycarbonyl)-2-aminophenylboronic acid.HCl (**1i)** (50 mg, 0.22 mmol), DIPEA (38 µL, 0.22 mmol), **2a** (29 µL, 0.23 mmol) in DCM (2.5 mL) for 1 hr afforded 46 mg (66%) of **3ia:** Cream-white solid; Melting point: 161-163°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.96 (br. s., 1H), 8.13-8.24 (m, 2H), 8.07 (s, 1H), 7.78 (dd, *J*=1.32, 7.91 Hz, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.6, 165.8, 164.9, 149.8, 143.2, 132.1, 131.6, 128.0, 122.1, 119.3, 102.9, 53.0, 52.4, 51.4; ^{11}B NMR (96 MHz, DMSO-d_6) δ 40.8;

HRMS m/z calc'd for $C_{14}H_{14}BNO_7$ $[M+H]^+$; 320.09358, found: 320.09385; IR (cm^{-1}): 3491, 3314, 1740, 1707, 1662, 1521, 1384, 1118, 1009, 794.

Dimethyl *1H*-indole-2,3-dicarboxylate (4aa)[3]

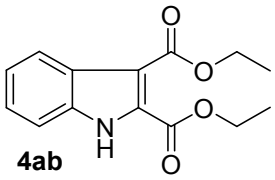
Typical procedure:



4aa

To a 7 mL supelco vial**,** Dimethyl 4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate **3aa**(50 mg, 0.19 mmol), Palladium acetate (43 mg, 0.19 mmol) and 1.5 mL of DCE were added under nitrogen atmosphere. The mixture was heated to 80°C and stirred for 30 minutes as monitored by LCMS. The reaction mixture was diluted with Ethylacetate (25 mL) and filtered through sintered funnel. The obtained filtrate was washed with water (2x 10 ml), dried over sodium sulphate and evaporated under vacuum. The crude product was purified by combiflash (eluent: hexane/ ethylacetate = 5:1) to afford 35 mg (78%) of **4aa.** Light yellow solid; Mp: 104 – 106°C; ^{1}H NMR (DMSO-d_6, 300MHz): δ (ppm) 12.59 (br. s., 1H), 7.91 (d, *J*=8.1 Hz, 1H), 7.52 (d, *J*=8.1 Hz, 1H), 7.34 (t, *J*=7.5 Hz, 1H), 7.11-7.29 (m, 1H), 3.91 (s, 3H), 3.85 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.0, 161.4, 135.2, 129.8, 125.6, 124.9, 122.1, 121.4, 112.9, 109.1, 52.5, 51.5; HRMS for $C_{13}H_{10}N_2O_4$ $(M+Na)^+$ 256.05857, found 256.05795.

Diethyl 1H-indole-2,3-dicarboxylate (4ab)[3]

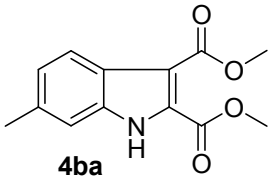


4ab

The reaction of Diethyl 4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate **3ab** (50 mg, 0.17 mmol), Palladium acetate (39 mg, 0.17 mmol) in DCE (1.5 mL) afforded 34 mg (75%) of **4ab.** Yellow solid; ^{1}H NMR (DMSO-d_6, 300MHz): δ (ppm) 12.52 (br. s., 1H), 7.91 (d, *J*=8.1 Hz, 1H), 7.51 (d, *J*=8.1 Hz, 1H), 7.33 (t, *J*=7.5 Hz, 1H), 7.18-7.27 (m, 1H), 4.41- 4.28 (m,

4H), 1.37 - 1.31 (m, 6H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.5, 161.0, 135.1, 130.0, 125.6, 124.7, 122.0, 121.2, 112.7, 109.0, 61.3, 59.9, 14.1, 13.9; HRMS for $C_{14}H_{15}NO_4$ $(M+Na)^+$ 284.08987, found 284.08905.

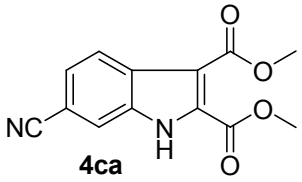
Dimethyl 6-methyl-1H-indole-2,3-dicarboxylate (4ba)[3]



4ba

The reaction of Dimethyl 4-hydroxy-7-methyl-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate **3ba** (50 mg, 0.18 mmol), Palladium acetate (41 mg, 0.18 mmol) in DCE (1.5 mL) afforded 34 mg (76%) of **4ba:** Light yellow solid; Melting point: 124 -126°C; ^{1}H NMR (DMSO-d_6, 300MHz): δ (ppm) 12.43 (br. s., 1H), 7.77 (d, *J*=8.3 Hz, 1H), 7.29 (s, 1H), 7.07 (d, *J*=8.3 Hz, 1H), 3. 90 (s, 3H), 3.84 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.9, 160.2, 134.5, 133.4, 127.8, 122.9, 122.5, 119.9, 111.1, 108.1, 51.3, 50.3, 20.2; HRMS for $C_{13}H_{13}NO_4$ $(M+H)^+$ 248.09171, found 248.09119.

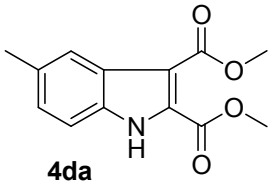
Dimethyl 6-cyano-1H-indole-2,3-dicarboxylate (4ca)



4ca

The reaction of Dimethyl 7-cyano-4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate **3ca** (50 mg, 0.17 mmol), Palladium acetate (39 mg, 0.17 mmol) in DCE (1.5 mL) afforded 32 mg (70%) of **4ca.** Pale yellow solid; ^{1}H NMR (DMSO-d_6, 300MHz): δ (ppm) 13.18 (br. s., 1H), 8.09 (d, *J*=8.5 Hz, 1H), 8.02 (s, 1H), 7.59 (d, *J*=8.3 Hz, 1H), 3.94 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.2, 160.9, 133.9, 133.7, 128.3, 124.4, 122.6, 119.4, 118.1, 108.8, 106.4, 52.9, 51.7; HRMS for $C_{13}H_{10}N_2O_4$ $(M+Na)^+$ 281.05382, found 281.05311.

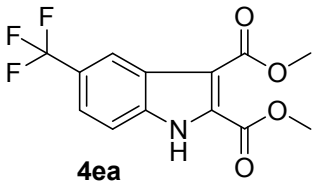
Dimethyl 5-methyl-1H-indole-2,3-dicarboxylate (4da)[3]



4da

The reaction of Dimethyl 4-hydroxy-6-methyl-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate **3da** (50 mg, 0.18 mmol), Palladium acetate (41 mg, 0.18 mmol) in DCE (1.5 mL) afforded 36 mg (80%) of **4da:** Yellow solid**;** Melting point: 114 -116°C; 1H NMR (DMSO-d_6, 300MHz): δ (ppm) 12.47 (br. s., 1H), 7.69 (s, 1H), 7.40 (d, *J*=8.3 Hz, 1H), 7.16 (d, *J*=8.3 Hz, 1H), 3.90 (s, 3H), 3.84 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.0, 161.3, 133.5, 131.0, 129.5, 126.6, 125.8, 120.5, 112.5, 108.6, 52.4, 51.3, 21.2; HRMS for $C_{13}H_{13}NO_4$ $(M+H)^+$; 248.09171, found 248.0916.

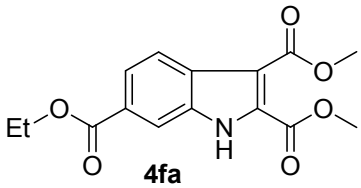
Dimethyl 5-(trifluoromethyl)-1H-indole-2,3-dicarboxylate (4ea)



4ea

The reaction of Dimethyl 4-hydroxy-6-(trifluoromethyl)-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate **3ea** (50 mg, 0.15 mmol), Palladium acetate (34 mg, 0.15 mmol) in DCE (1.5 mL) afforded 34 mg (74%) of **4ea.** Pale yellow solid**;** Mp: 135 – 138°C; ^{1}H NMR (DMSO-d_6, 300MHz): δ (ppm) 13.05 (br. s., 1H), 8.26 (s, 1H), 7.69-7.76 (m, 1H), 7.60-7.67 (m, 1H), 3.94 (s, 3H), 3.88 (s, 3H) ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.4, 161.0, 136.6, 132.2, 125.0 (q, *J* = 272.2 Hz), 124.8, 122.8 (q, *J* = 31.5 Hz), 121.1 (q, *J* = 3.8 Hz), 119.1 (q, *J* = 3.8 Hz), 114.2, 109.6, 52.9, 51.8 ESI-MS m/z 302 $[M+H]^+$ HRMS for $C_{13}H_{10}F_3NO_4$ $(M+Na)^+$ 324.04596, found 324.04602.

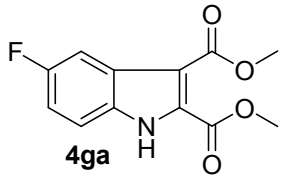
6-ethyl 2,3-dimethyl 1H-indole-2,3,6-tricarboxylate (4fa)



4fa

The reaction of 7-ethyl 2,3-dimethyl 4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3,7-tricarboxylate **3fa**(50 mg, 0.15 mmol), Palladium acetate (34 mg, 0.15 mmol) in DCE (1.5 mL) afforded 33 mg (72%) of **4fa:** Pale yellow solid**;** Mp: 120 – 122°C; ^{1}H NMR (DMSO-d_6, 300MHz): δ (ppm) 12.98 (br. s., 1H), 8.15 (s, 1H), 8.02 (d, *J*=8.5 Hz, 1H), 7.82 (d, *J*=8.5 Hz, 1H), 4.35 (q, *J*=7.0 Hz, 2H), 3.94 (s, 3H), 3.87 (s, 3H), 1.35 (t, *J*=7.2 Hz, 3H) ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.2, 162.9, 160.5, 133.8, 132.3, 128.1, 125.4, 121.6, 120.8, 114.1, 108.3, 60.1, 52.2, 51.0, 13.6 HRMS for $C_{15}H_{15}NO_6$ $(M+H)^+$ 306.09719, found 306.09753.

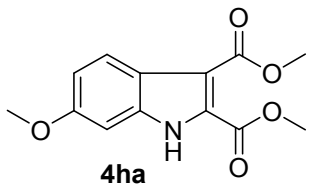
Dimethyl 5-fluoro-1H-indole-2,3-dicarboxylate (4ga)[3]



4ga

The reaction of Dimethyl 6-fluoro-4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate **3ga** (50 mg, 0.18 mmol), Palladium acetate (41mg, 0.18 mmol) in DCE (1.5 mL) afforded 34 mg (76%) of **4ga:** Pale yellow solid; ^{1}H NMR (DMSO-d_6, 300MHz): δ (ppm) 12.76 (br. s., 1H), 7.62 (dd, *J*=9.8, 2.4 Hz, 1H), 7.54 (dd, *J*=8.9, 4.6 Hz, 1H), 7.22 (td, *J*=9.2, 2.5 Hz, 1H), 3.92 (s, 3H), 3.85 (s, 3H) ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.5, 161.0, 159.3 (d, *J* = 237 Hz), 131.8, 131.6, 126.0 (d, *J* = 11.3 Hz), 114.5 (d, *J* = 10.1 Hz), 113.8 (d, *J* = 26.5 Hz), 108.7 (d, *J* = 5.0 Hz), 105.9 (d, *J* = 25.2 Hz), 52.6, 51.4 HRMS for $C_{12}H_{10}FNO_4$ $(M+H)^+$ 252.06664, found 252.06646.

Dimethyl 6-methoxy-1H-indole-2,3-dicarboxylate (4ha)[3]

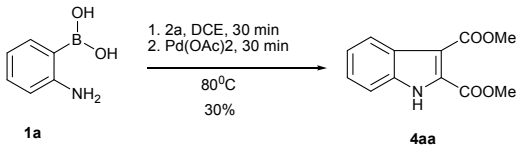


4ha

The reaction of Dimethyl 6-fluoro-4-hydroxy-1,4-dihydrobenzo[b][1,4]azaborinine-2,3-dicarboxylate **3ha** (50 mg, 0.17 mmol), Palladium acetate (39mg, 0.17 mmol) in DCE (1.5 mL) afforded 35 mg (78%) of **4ha:** Pale yellow solid**;** Mp: 134 – 137°C; ^{1}H NMR (DMSO-d_6, 300MHz): δ (ppm) 12.36 (br. s., 1H), 7.75 (d, *J*=8.9 Hz, 1H), 6.84-6.95 (m, 2H), 3.88 (s, 3H), 3.83 (s, 3H), 3.80 (s, 3H) ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.0, 161.0, 157.8, 136.2, 127.7,

122.2, 120.0, 113.4, 109.9, 94.1, 55.1, 52.2, 51.4 HRMS for $C_{13}H_{13}NO_5$ $(M+H)^+$ 264.08662, found 264.08645

Scheme 1: One pot synthesis of indoles



1a 4aa

To a 7 mL supelco vial**, 2**-aminophenylboronic acid **1a** (50 mg, 0.36 mmol), dimethyl but-2-ynedioate **2a** (47µL, 0.38 mmol) and 2.5 ml of DCE were added under nitrogen atmosphere. The mixture was heated to 80°C and stirred for 30 minutes. The reaction mixture was brought to room temperature and then Palladium acetate (82 mg, 0.36 mmol) was added. The mixture was heated to 80°C and stirred for another 30 minutes as monitored by LCMS. The reaction mixture was diluted with Ethylacetate (25 mL) and filtered through sintered funnel. The obtained filtrate was washed with water (2x 10 ml), dried over sodium sulphate and evaporated under vacuum. The crude product was purified by combiflash (eluent: hexane/ ethylacetate = 5:1) to afford 25 mg (30%) of **4aa.**

Reference

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2. C. C. Tzschucke, J.M. Murphy and J. F. Hartwig, *Org. Lett.*, 2007, **9**, 761-764.
3. (a) E. H. Huntress, T. E. Lesslie and W. M. Hearon, *J. Am. Chem. Soc.*, 1956, **78**, 419-423; (b) H. Suzuki, H. Gyoutoku, H. Yokoo, M. Shinba, Y. Sato, H. Yamada and Y. Murakami, *Synlett,* 2000, 1196-1198; (c) (d) K. Masateru, S. Kenji, T. Hiroko and N. Taiji, *Heterocycles,* 2000, **53**, 2809-2819; (d) Y. Tomioka, C. Nagahiro, Y. Nomura and H. Maruoka, *J. Heterocycl. Chem.*, 2003, **40**, 121-127; (e) Z. Shi, C. Zhang, S. Li, D. Pan, S, Ding, Y. Cui, and N. Jiao, *Angew. Chem. Int. Ed*., 2009, **48**, 4572-4576.