Synthesis of Fluoroalkoxy Substituted Arylboronic Esters by Iridium-Catalyzed Aromatic C–H Borylation

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Supporting Information

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General Considerations and Starting Materials:

All reactions were carried out under nitrogen atmosphere, without the use of glove box or Schlenk line. Chemicals and reagents were purchased from Sigma-Aldrich®, Combi-Blocks Inc., and Matrix Scientific, and were used without further purification unless otherwise noted. *n*-Hexane, ethyl acetate, and dichloromethane were purchased from local suppliers and were distilled before use. All the borylation reactions were carried out in air–free 25mL Schlenk flask (0-4mm Valve, 175 mm OAH) purchased from Chemglass Life Sciences. Analytical thin-layer chromatography (TLC) was carried out using 250 µm thick SiliaPlate™ TLC Plates (Aluminum (Al) Silica, indicator F–254, SiliCycle Inc.). Visualization was achieved under a UV lamp (254 nm and 365 nm). Aryl boronic esters generally showed tailing on the TLC plates. Column chromatography was carried out using SiliaFlash® (particle size: 40–63 µm, 230–400 mesh) purchased from SiliCycle Inc. All reported yields are for isolated materials. Reaction times and yields are not optimized.

Analytical Characterization:

Infrared spectra were recorded as neat using a Bruker Alpha-P FT-IR instrument in the ATR geometry with a diamond ATR unit. Melting Points were taken on Stuart® SMP3 melting point apparatus and are uncorrected.

Reactions were monitored by Thermo Scientific ISQ single quadrupole GC–MS operating in EI mode, and equipped with Trace 1300 GC and AI 1310 auto injector. Column type: Trace™ TR-5MS, 5% phenyl polysilphenylene-siloxane, 30m × 0.25mm ID × 0.25µm. GC–MS method: injector 250 °C, oven 50 °C (1 min), 50 °C to 250 °C (20 °C min^{-1}), 250 °C (10 min); carrier gas: He (1.5 mL min^{-1}).

Accurate mass determinations (HRMS) were obtained using a Thermo LTQ Velos Orbitrap mass spectrometer (ThermoFisher Scientific, Pittsburgh, PA, USA) equipped with different atmospheric pressure sources (Ion Max APCI, Syagen's Photo-Mate APPI and heated ESI ion source). The mass scan range was set 100–1000 m/z, with a resolving power of 100,000. The m/z calibration of the LTQ-Orbitrap analyzer was performed with positive ESI ionization mode using a solution containing caffeine, MRFA (met-arg-phe-ala) peptide and Ultramark 1621 according to the manufacturer's guidelines. The Orbitrap mass spectrometer was operated using the XCalibur software. The ESI source was performed with heated ion source equipped with a metal needle and operated at 4 kV. The APCI source was performed with a corona discharge operated at 5µA. For all experiments, the source vaporizer temperature was adjusted to 350 °C, the capillary temperature

was set at 250 °C, sheath and auxiliary gases were optimized and set to 40 and 20 arbitrary units, respectively.

^{1}H NMR spectra were recorded at 700.130 MHz and ^{13}C NMR spectra were recorded at 176.048 MHz at ambient temperature using AVANAC III spectrometers (Bruker BioSpin, Rheinstetten, Germany) equipped with Bruker 5-mm TCI cryoprobe. The chemical shifts in ^{1}H NMR spectra are reported using TMS as internal standard and were referenced with the residual proton resonances of the corresponding deutrated solvent ($CDCl_3$: 7.26 ppm). The chemical shifts in the ^{13}C NMR spectra are reported relative to TMS ($\delta = 0$) or the central peak of $CDCl_3$ ($\delta = 77.23$) for calibration.

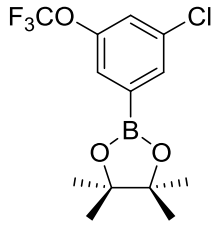
The abbreviations used for the chemical shifts are as; s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), tt (triplet of triplet), tq (triplet of quartet), ttd (triplet of triplet of doublet), m (unresolved multiplet), and br (broad). All coupling constants are apparent *J* values measured at the indicated field strengths. In ^{13}C NMR spectra of arylboronic esters, the carbon atom attached to the boron atom of BPin group is typically not observed due to broadening from and coupling with boron. Regiochemistry of the borylated product isomers, where present, was assigned by NMR spectroscopy (^{1}H & ^{13}C NMR).

General Procedure for Borylation:

In a fume hood, an oven dried Schlenk flask equipped with magnetic stirring bar was filled with nitrogen and evacuated (three cycles). Under nitrogen atmosphere $[Ir(OMe)(COD)]_2$ (13.2 mg, 0.02 mmol, 2 mol% Ir), 2,2′-bipyridyl (6.2 mg, 0.04 mmol, 2 mol%), and pinacolborane (HBPin) (435 µL, 384 mg, 3 mmol, 1.5 equiv) were added. Fluoroalkoxy arene substrate (2 mmol, 1 equiv) was added via micropipette under nitrogen atmosphere. The Schlenk flask was closed and the reaction mixture was heated at 80 °C in an oil bath. The color of the reaction mixture changed from light yellow to dark brown. The progress of reaction was monitored by GC-MS and TLC. Upon completion of reaction, the Schlenk flask was cooled to room temperature and exposed to air. The reaction mixture was taken out by dissolving in dichloromethane and the volatiles were removed under reduced pressure using rotary evaporator. The crude yield was determined. The crude product was purified by column chromatography (silica gel).

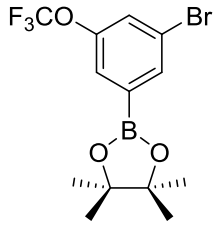
Experimental Details:

Compound 1a: 2-(3-Chloro-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



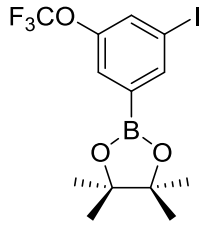
The general procedure was applied to 1-chloro-3-(trifluoromethoxy)benzene (287 µL, 393 mg, 2 mmol, 1 equiv) for 24 h. Column chromatography (DCM/*n*-hexane 1 : 9, R_f 0.50) furnished the product as colorless oil (632 mg, 98 %). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.71 (d, *J* = 1.3 Hz, 1 H), 7.52 (s, 1 H), 7.31 (s, 1 H), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 149.2 (C), 134.8 (C), 133.1 (CH), 124.9 (CH), 124.1 (CH), 120.4 (q, $^1J_{C–F}$ = 256 Hz, OCF_3), 84.6 (2 C), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 2981, 1573, 1471, 1413, 1348, 1255, 1211, 1163, 1140, 1099, 977, 959, 870, 847 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 322 (M^+, 54), 324 (M+2, 16), 307 (100), 236 (72), 223 (29), 201 (13); HRMS: *m/z* 307.05060 [(M^+–CH_3); Calcd for $C_{12}H_{12}BClF_3O_3$: 307.05146].

Compound 1b: 2-(3-Bromo-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



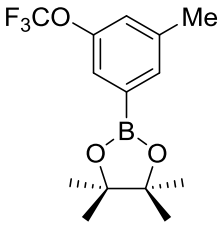
The general procedure was applied to 1-bromo-3-(trifluoromethoxy)benzene (296 µL, 482 mg, 2 mmol, 1 equiv) for 24 h. Column chromatography (DCM/*n*-hexane, 0.5 : 9.5, R_f 0.40) furnished the product as colorless oil (715 mg, 97 %). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.86 (d, *J* = 1.1 Hz, 1 H), 7.56 (s, 1 H), 7.46 (s, 1 H), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 149.2 (C), 136.0 (CH), 127.0 (C), 125.4 (CH), 122.5 (CH), 120.4 (q, $^1J_{C–F}$ = 258 Hz, OCF_3), 84.6 (2 C), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 2979, 1592, 1456, 1411, 1346, 1254, 1212, 1140, 1111, 1099, 974, 865, 847 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 366 (M^+, 35), 368 (M+2, 32), 351 (76), 280 (62), 267 (27); HRMS: *m/z* 366.02254 [(M^+); Calcd for $C_{13}H_{15}BBrF_3O_3$: 366.02442].

Compound 1c: 2-(3-Iodo-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



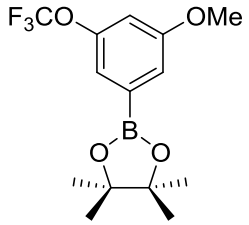
The general procedure was applied to 1-iodo-3-(trifluoromethoxy)benzene (309 µL, 576 mg, 2 mmol, 1 equiv) for 24 h. Column chromatography (DCM/*n*-hexane, 1 : 9, R_f 0.45) furnished the product as colorless oil (768 mg, 93 %). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.06 (d, J = 0.6 Hz, 1 H), 7.65 (s, 1 H), 7.59 (d, J = 0.6 Hz, 1 H), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 148.8 (C), 141.9 (CH), 132.6 (CH), 126.0 (CH), 120.3 (q, $^1J_{C–F}$ = 258 Hz, OCF_3), 93.7 (C), 84.6 (2 C), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 2979, 2932, 1561, 1451, 1407, 1371, 1252, 1211, 1161, 1138, 973, 864, 847 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 414 (M^+, 100), 399 (61), 328 (47), 314 (9); HRMS: *m/z* 414.00871 [(M^+); Calcd for $C_{13}H_{15}BIF_3O_3$: 414.01055].

Compound 1d: 4,4,5,5-Tetramethyl-2-(3-methyl-5-(trifluoromethoxy)phenyl)-1,3,2-dioxaborolane



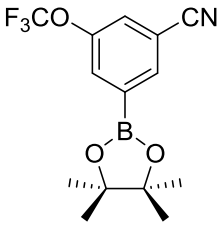
The general procedure was applied to 1-methyl-3-(trifluoromethoxy)benzene (294 µL, 352 mg, 2 mmol, 1 equiv) for 24 h. The GC-MS showed about 90% conversion of substrate after 24 h. Further heating did not improved conversion. Column chromatography (DCM/*n*-hexane 1 : 1, R_f 0.60) furnished the product as colorless oil (411 mg, 68 %). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.54 (s, 1 H), 7.43 (s, 1 H), 7.10 (s, 1 H), 2.37 (CH_3), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 149.0 (C), 139.5 (C), 133.8 (CH), 124.4 (CH), 123.8 (CH), 120.5 (q, $^1J_{C–F}$ = 256 Hz, OCF_3), 84.1 (2 C), 24.8 (4 CH_3 of BPin), 21.0 (CH_3); FT-IR (neat) ν: 2980, 2930, 1360, 1141, 965 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 302 (M^+, 29), 287 (41), 216 (100), 203 (71), 69 (100); HRMS: *m/z* 287.10535 [(M^+–CH_3); Calcd for $C_{13}H_{15}BF_3O_3$: 287.10609].

Compound 1e: 2-(3-methoxy-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



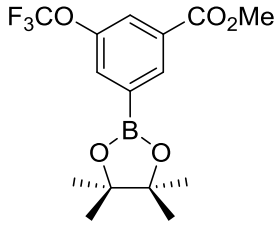
The general procedure was applied to 1-methoxy-3-(trifluoromethoxy)benzene (308 µL, 384 mg, 2 mmol, 1 equiv) for 24 h. Column chromatography (DCM/*n*-hexane 0.5 : 9.5, R_f 0.50) furnished the product as colorless oil (599 mg, 94 %). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.25 (d, *J* = 2.4 Hz, 1 H), 7.24 (br s, 1 H), 6.84 (br s, 1 H), 3.84 (OCH_3), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 160.2 (C), 149.8 (C), 120.5 (q, $^1J_{C–F}$ = 256 Hz, OCF_3), 118.9 (CH), 117.5 (CH), 110.6 (CH), 84.3 (2 C), 55.7 (OCH_3), 24.9 (4 CH_3 of BPin); FT-IR (neat) ν: 2980, 1584, 1360, 1247, 1213, 1139, 1054, 848 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 318 (M^+, 100), 303 (40), 232 (91), 218 (73); HRMS: *m/z* 318.12374 [(M^+); Calcd for $C_{14}H_{18}BF_3O_4$: 318.12448].

Compound 1f: 3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethoxy)benzonitrile



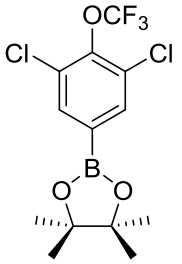
The general procedure was applied to 3-(trifluoromethoxy)benzonitrile (286 µL, 374 mg, 2 mmol, 1 equiv) for 24 h. Column chromatography (DCM/*n*-hexane, 1 : 9, R_f 0.55) furnished the product as colorless oil (576 mg, 92 %) with more than 95% purity by GC-MS. Small amounts (2-3% each) of two isomeric monoborylated products were also observed by GC-MS . ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.01 (s, 1 H), 7.84 (d, J = 0.4 Hz, 1 H), 7.56 (s, 1H), 1.35 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 148.8 (C), 136.6 (CH), 131.2 (CH), 126.6 (CH), 120.5 (q, $^1J_{C–F}$ = 259.2 Hz, OCF_3), 117.3 (C), 113.7 (C), 85.0 (2 C), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 2982, 2236, 1366, 1247, 1210, 1138, 847 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 313 (M^+, 8), 298 (30), 227 (31), 69 (100); HRMS: *m/z* 314.11623 [(M+1); Calcd for $C_{14}H_{16}BF_3NO_3$: 314.11698].

Compound 1g: Methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethoxy)benzoate



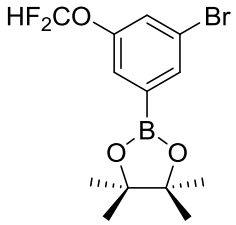
The general procedure was applied to methyl 3-(trifluoromethoxy)benzoate (305 µL, 440 mg, 2 mmol, 1 equiv) for 24 h. Column chromatography (DCM/*n*-hexane 1 : 9, R_f 0.40) furnished the product as white solid (679 mg, 98 %, mp 63-64 °C). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.38 (s, 1 H), 7.95 (s, 1 H), 7.80 (s, 1 H), 3.94 (s, 3 H), 1.35 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 165.8 (C), 148.9 (C), 134.1 (CH), 131.7 (CH), 131.2 (CH), 124.7 (C), 120.4 (q, $^1J_{C–F}$ = 256 Hz, OCF_3), 84.6 (2 C), 52.42 (CH_3), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 2984, 2957, 1728, 1371, 1142, 889 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 346 (M^+, 21), 331 (41), 303 (100), 247 (36), 215 (29), 187 (21); HRMS: *m/z* 347.12600 [(M+1); Calcd for $C_{15}H_{19}BF_3O_5$: 347.12722].

Compound 1h: 2-(3,5-dichloro-4-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



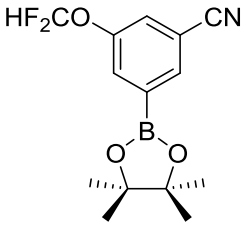
The general procedure was applied to 1,3-dichloro-2-(trifluoromethoxy)benzene (350 µL, 462 mg, 2 mmol, 1 equiv) for 12 h. The ratio of major and minor monoborylated isomers at the end of reaction was 97:3. Column chromatography (DCM/*n*-hexane 1 : 1, R_f 0.80) furnished the major monoborylated product as colorless oil (627 mg, 88 %) which was >97% pure by GC-MS. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.79 (s, 2 H), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 144.1 (C), 135.3 (CH), 130.0 (C), 120.6 (q, $^1J_{C–F}$ = 262 Hz, OCF_3), 84.8 (C), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 2981, 2934, 1382, 1350, 1247, 1184, 1124, 964, , 883, 848, 803 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 356 (M^+, 22), 358 (M+2, 14), 341 (55), 270 (100), 257 (28); HRMS: *m/z* 356.03414 [(M^+); Calcd for $C_{13}H_{14}BCl_2F_3O_3$: 356.03597].

Compound 2a: 2-(3-bromo-5-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



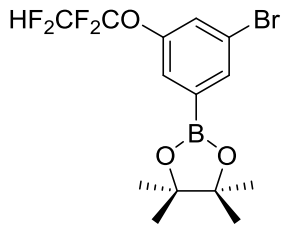
The general procedure was applied to 1-bromo-3-(difluoromethoxy)benzene (281 µL, 446 mg, 2 mmol, 1 equiv) for 16 h. Column chromatography (DCM/*n*-hexane, 0.5 : 9.5, R_f 0.45) furnished the product as colorless oil (683 mg, 98 %). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.77 (d, *J* = 1.1 Hz, 1 H), 7.45 (d, *J* = 1.9 Hz, 1 H), 7.37 (t, *J* = 1.9 Hz, 1 H), 6.51 (t, *J* = 73.5 Hz, 1 H), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 151.2 (d, $^3J_{C–F}$ = 2.2 Hz, C), 134.5 (CH), 125.8 (CH), 123.7 (CH), 122.7 (C), 115.7 (t, $^1J_{C–F}$ = 260 Hz, OCF_2H), 84.6 (2 C), 24.9 (4 CH_3 of BPin); FT-IR (neat) ν: 2979, 1564, 1341, 1118, 1044 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 348 (M^+, 63), 350 (M+2, 61), 333 (59), 262 (81), 249 (31); HRMS: *m/z* 348.03363 [(M^+); Calcd for $C_{13}H_{16}BBrF_2O_3$: 348.03385].

Compound 2b: 3-(difluoromethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile



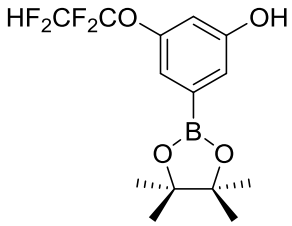
The general procedure was applied to 3-(difluoromethoxy)benzonitrile (268 µL, 338 mg, 2 mmol, 1 equiv) for 24 h. Column chromatography (DCM/*n*-hexane, 1 : 9, R_f 0.50) furnished the product as colorless oil (654 mg, 94 %). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.93 (s, 1 H), 7.74 (d, *J* = 2 Hz, 1 H), 7.48 (s, 1 H), 6.56 (t, *J* = 72.8 Hz, 1 H), 1.35 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 150.5 (d, $^3J_{C–F}$ = 2.4 Hz, C), 135.3 (CH), 129.9 (CH), 125.7 (CH), 117.6 (C), 115.3 (t, $^1J_{C–F}$ = 263 Hz, OCF_2H), 113.5 (C), 84.9 (2 C), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 2981, 2235, 1354, 1110, 1047, 847 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 295 (M^+, 10), 280 (38), 209 (40), 205 (21), 196 (22); HRMS: *m/z* 296.12659 [$(M+1)^+$; Calcd for $C_{14}H_{17}BF_2NO_3$: 296.12641].

Compound 2c: 2-(3-bromo-5-(1,1,2,2-tetrafluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



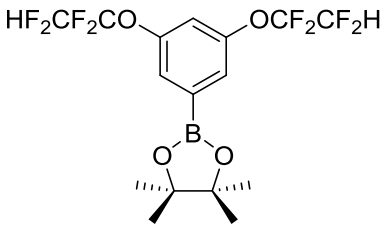
The general procedure was applied to 1-bromo-3-(1,1,2,2-tetrafluoroethoxy)benzene (337 µL, 546 mg, 2 mmol, 1 equiv) for 24 h. Gradient column chromatography (*n*-hexane → DCM/*n*-hexane, 0.5 : 9.5, R_f 0.4) furnished the product as colorless oil (789 mg, 98 %). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.85 (d, *J* = 1.1 Hz, 1 H), 7.56 (d, *J* = 1.4 Hz, 1 H), 7.47 (s, 1 H), 5.89 (tt, *J* = 53.1 Hz, *J* = 2.7 Hz, 1 H), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 148.8 (C), 135.1 (CH), 127.6 (CH), 126.2 (CH), 122.4 (C), 116.4 (tt, $^1J_{C–F}$ = 273 Hz, $^2J_{C–F}$ = 28.8 Hz, C), 107.6 (tt, $^1J_{C–F}$ = 252 Hz, $^2J_{C–F}$ = 41.3 Hz, CH), 84.6 (2 C), 24.9 (4 CH_3 of BPin); FT-IR (neat) ν: 2981, 1596, 1346, 1113 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 398 (M^+, 45), 400 (M+2, 47), 383 (73), 312 (89), 233 (17); HRMS: *m/z* 383.00580 [(M–CH_3); Calcd for $C_{13}H_{13}BBrF_4O_3$: 383.00718].

Compound 2d: 3-(1,1,2,2-tetrafluoroethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol



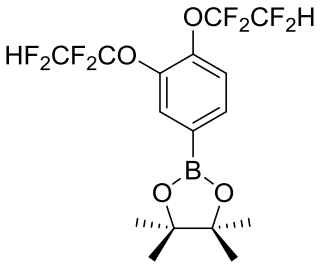
The general procedure was applied to 3-(1,1,2,2-tetrafluoroethoxy)phenol (151 µL, 210 mg, 1 mmol, 1 equiv) using 3 equivalents of pinacolborane (HBPin) (435 µL, 384 mg, 3 mmol) for 12 h.[1] Column chromatography (DCM, R_f 0.3) furnished the product as colorless oil (103 mg, 31 %). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.21 (s, 1 H), 7.15 (d, *J* = 1.9 Hz, 1 H), 6.83 (s, 1 H), 5.88 (tt, *J* = 53.1 Hz, *J* = 2.5 Hz, 1 H), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 156.1 (C), 149.4 (C), 119.7 (CH), 119.4 (CH), 116.4 (tt, $^1J_{C–F}$ = 272 Hz, $^2J_{C–F}$ = 28.6 Hz, C), 112.0 (CH), 107.6 (tt, $^1J_{C–F}$ = 252 Hz, $^2J_{C–F}$ = 41.3 Hz, CH), 84.3 (2C), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 3372 (br), 2981, 2934, 1584, 1429, 1300, 1276, 1259, 1189, 1115, 998, 984, 965, 843 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 336 (M^+, 45), 321 (24), 294 (8), 249 (100), 236 (48); HRMS: *m/z* 337.12307 [$(M+1)^+$]; Calcd for $C_{14}H_{18}BF_4O_4$: 337.12288].

Compound 2e: 2-(3,5-bis(1,1,2,2-tetrafluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



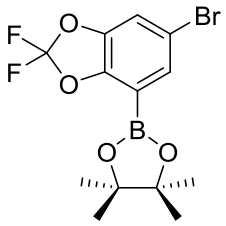
The general procedure was applied to 1,3-bis(1,1,2,2-tetrafluoroethoxy)benzene (418 µL, 620 mg, 2 mmol, 1 equiv) for 24 h. Gradient column chromatography (*n*-hexane → DCM/*n*-hexane, 1 : 9, R_f 0.45) furnished the product as colorless oil which solidified upon standing (845 mg, 97 %, mp 61 – 62 ºC). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.56 (d, *J* = 1.8 Hz, 2 H), 7.18 (br s, 1 H), 5.90 (tt, *J* = 53 Hz, *J* = 2.5 Hz, 2 H), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 148.8 (2 C), 125.6 (2 CH), 118.2 (CH), 116.4 (tt, $^1J_{C–F}$ = 273 Hz, $^2J_{C–F}$ = 28.7 Hz, 2 C), 107.6 (tt, $^1J_{C–F}$ = 252 Hz, $^2J_{C–F}$ = 41 Hz, 2 CH), 84.5 (2 C), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 2983, 1584, 1360, 1112, 844 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 436 (M^+, 27), 421 (55), 350 (100), 337 (30), 319 (15); HRMS: *m/z* 437.11485 [(M+1); Calcd for $C_{16}H_{18}BF_8O_4$: 437.11649].

Compound 2f: 2-(3,4-bis(1,1,2,2-tetrafluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



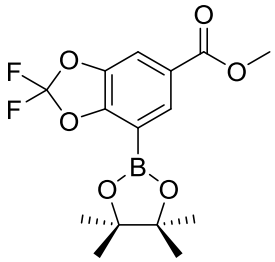
The general procedure was applied to 1,2-bis(1,1,2,2-tetrafluoroethoxy)benzene (430 µL, 620 mg, 2 mmol, 1 equiv) for 24 h. Gradient column chromatography (*n*-hexane → DCM/*n*-hexane, 1 : 9, R_f 0.45) furnished the product as a white solid (837 mg, 96 %, mp 55 °C). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.78 (br, s, 1 H), 7.74 (dd, *J* = 8.1, 1.2 Hz, 1 H), 7.38 (d, *J* = 8.1 Hz, 1 H), 5.91 (tq, *J* = 53, 2.7 Hz, 2 H), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 143.6 (C), 140.4 (C), 134.2 (CH), 129.9 (CH), 122.7 (CH), 116.4 (ttd, *J* = 274, 29, 6.1 Hz, 2 C), 107.6 (ttd, *J* = 252, 40.7, 11.8 Hz, 2 CH), 84.4 (2 C), 25.0 (4 CH_3 of BPin); FT-IR (neat) ν: 2984, 1610, 1166, 1095, 848 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 436 (M^+, 47), 421 (100), 350 (66), 337 (44); HRMS: *m/z* 421.08432 [(M–CH_3); Calcd for $C_{15}H_{14}BF_8O_4$: 421.08519].

Compound 2g: 2-(6-bromo-2,2-difluorobenzo[d][1,3]dioxol-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



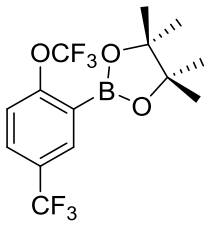
The general procedure was applied to 5-bromo-2,2-difluorobenzo[d][1,3]dioxole (273 µL, 474 mg, 2 mmol, 1 equiv) for 16 h. Gradient column chromatography (*n*-hexane → DCM/*n*-hexane, 1 : 9, R_f 0.4) furnished the product as a white solid (719 mg, 99 %, mp 109-110 °C). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.56 (d, *J* = 1.9 Hz, 1 H), 7.26 (d, *J* = 1.9 Hz, 1 H), 1.36 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 147.5 (C), 143.8 (C), 132.2 (CH), 131.6 (t, $^1J_{C–F}$ = 256 Hz, C), 115.3 (CH), 115.1 (C), 84.7 (2 C), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 2972, 1648, 1467, 1138, 849 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 362 (M^+, 70), 364 (M+2, 100), 349 (47), 298 (21), 262 (31), 254 (49); HRMS: *m/z* 362.01203 [(M^+); Calcd for $C_{13}H_{14}BBrF_2O_4$: 362.01311].

Compound 2h: Methyl 2,2-difluoro-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[d][1,3]dioxole-5-carboxylate



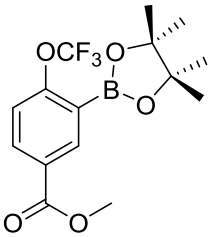
The general procedure was applied to methyl 2,2-difluorobenzo[d][1,3]dioxole-5-carboxylate (304 µL, 432 mg, 2 mmol, 1 equiv) for 1 h. Gradient column chromatography (*n*-hexane → DCM/*n*-hexane, 2 : 1, R_f 0.5) furnished the product as a white solid (649 mg, 95 %, mp 191–192 ºC). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.22 (s, 1 H), 7.81 (d, *J* = 1.2 Hz, 1 H), 3.92 (s, 3 H), 1.37 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 165.7 (C), 151.5 (C), 143.3 (C), 132.7 (CH), 131.7 (t, $^1J_{C–F}$ = 256 Hz, C), 125.7 (CH), 112.8 (C), 84.7 (2 C), 52.4 (CH_3), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 2981, 1719, 1647, 1481, 1420, 1384, 1333, 1277, 1142, 1088, 1043, 971, 896, 849 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 342 (M^+, 35), 327 (32), 311 (19), 299 (100), 211 (21); HRMS: *m/z* 343.11607 [$(M+1)^+$; Calcd for $C_{15}H_{18}BF_2O_6$: 343.11590].

Compound 3a: 4,4,5,5-tetramethyl-2-(2-(trifluoromethoxy)-5-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane



The general procedure was applied to 1-(trifluoromethoxy)-4-(trifluoromethyl)benzene (163 µL, 230 mg, 1 mmol, 1 equiv) for 4 h. GC-MS data at this stage showed a single monoborylated product isomer along with a single diborylated product isomer. GC-MS ratio of the mono-borylated product isomer to diborylated product isomer 96:4. Column chromatography (DCM/*n*-hexane 4 : 1, R_f 0.70) furnished the single mono-borylated product isomer as colorless oil (200 mg, 56 %). The regiochemistry of the single mono-borylated product is assigned based on NMR data (^{1}H, ^{13}C NMR chemicals shifts, and C-F coupling in ^{13}C NMR). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.06 (d, *J* = 1.8 Hz, 1 H), 7.74 (dd, *J* = 8.5 Hz, *J* = 1.9 Hz, 1 H), 7.35 (d, *J* = 8.5 Hz, 1 H), 1.36 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 155.5 (C), 133.9 (q, $^3J_{C–F}$ = 3.5 Hz, CH), 129.6 (q, $^3J_{C–F}$ = 3.3 Hz, CH), 128.9 (q, $^2J_{C–F}$ = 33 Hz, C), 123.7 (q, $^1J_{C–F}$ = 272 Hz, CF_3), 121.7 (s, CH), 120.2 (q, $^1J_{C–F}$ = 258 Hz, OCF_3), 84.6 (2 C), 24.7 (4 CH_3 of BPin); FT-IR (neat) ν: 2984, 2938, 1616, 1355, 1306, 1256, 1211, 1165, 1126, 1076, 963, 924, 871, 844 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 356 (M^+, 5), 341 (11), 337 (13), 297 (9), 275 (18), 271 (100), 237 (15), 231 (10), 229 (39), 217 (34), 191 (23), 171 (25); HRMS: *m/z* 337.10186 $[(M–F)]^+$; Calcd for $C_{14}H_{15}BF_5O_3$: 337.10289].

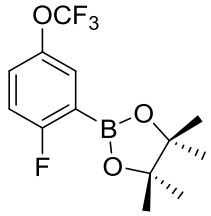
Compound 3b: methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethoxy)benzoate



The general procedure was applied to methyl 4-(trifluoromethoxy)benzoate (336 µL, 440 mg, 2 mmol, 1 equiv) for 4 h. GC-MS data at this stage showed a single monoborylated product isomer (~90%) along with two diborylated product isomers (~7% combined) in addition to unreacted starting material (~5%). Column chromatography (DCM, R_f 0.20) furnished the single mono-borylated product isomer as colorless oil which solidified upon standing (568 mg, 82 %, mp 62

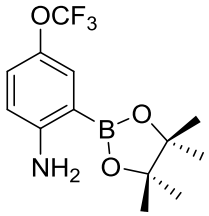
ºC). The regiochemistry of the single mono-borylated product is assigned based on the ^{1}H NMR chemicals shifts. ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.45 (d, *J* = 1.6 Hz, 1 H), 8.15 (dd, *J* = 8.5 Hz, *J* = 1.9 Hz, 1 H), 7.29 (d, *J* = 8.5 Hz, 1 H), 3.93 (s, 3 H), 1.36 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 166.0 (C), 156.5 (C), 138.2 (CH), 133.9 (CH), 128.4 (CH), 121.1 (C), 120.2 (q, $^{1}J_{C–F}$ = 258 Hz, OCF_3), 84.4 (2 C), 52.3 (OCH_3), 24.7 (4 CH_3 of BPin); FT-IR (neat) ν: 2979, 2950, 1725, 1606, 1588, 1492, 1429, 1412, 1372, 1335, 1226, 1162, 1136, 1107, 1069, 974, 923,849 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 346 (M^+, 8), 304 (10), 303 (100), 261 (27), 219 (21), 214 (16), 207 (24); HRMS: *m/z* 347.12736 [$(M+1)^+$]; Calcd for $C_{15}H_{19}BF_3O_5$: 347.12722].

Compound 3c: 2-(2-fluoro-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



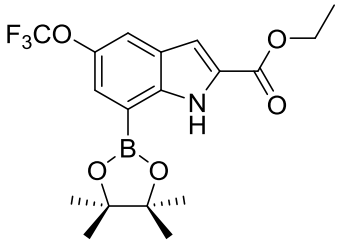
The general procedure was applied to 1-fluoro-4-(trifluoromethoxy)benzene (273 µL, 361 mg, 2 mmol, 1 equiv) for 6 h. The ratio of two mono-borylated product isomers was 97:3 by GC-MS. In addition, two di-borylated products were also observed by GC-MS. Column chromatography (DCM/*n*-hexane 1 : 9, R_f 0.40) furnished the major mono-borylated product isomer as colorless oil (331 mg, 54 %). Regiochemistry of the major mono-borylated product isomer was assigned based on NMR data (C–F coupling constant in the ^{13}C NMR). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.57 (br s, 1 H), 7.27 (dd, *J* = 8.9 Hz, $^{4}J_{H–F}$ = 4.5 Hz, 1 H), 7.05 (apparent t, *J* = 8.5 Hz, 1 H), 1.36 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 165.1 (d, $^{1}J_{C–F}$ = 251 Hz, C), 144.8 (C), 129.1 (d, $^{3}J_{C–F}$ = 9 Hz, CH), 126.0 (d, $^{3}J_{C–F}$ = 9.7 Hz, CH), 120.5 (q, $^{1}J_{C–F}$ = 257 Hz, OCF_3), 116.7 (d, $^{2}J_{C–F}$ = 26.9 Hz, CH), 84.4 (2 C), 24.8 (4 CH_3 of BPin); FT-IR (neat) ν: 2981, 1623, 1489, 1421, 1343, 1216, 1140, 1066, 966, 851, 829 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 306 (M^+, 18), 291 (25), 247 (22), 244 (19), 206 (26), 202 (40); HRMS: *m/z* 286.09704 [(M–FH)] $^{+}$; Calcd for $C_{13}H_{14}BF_3O_3$: 286.09826].

Compound 3d: 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethoxy)aniline



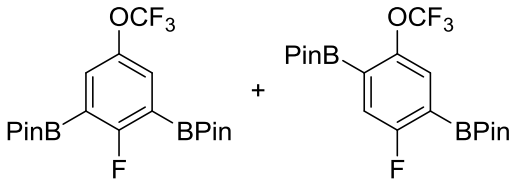
The catalytic borylation was carried out following the literature protocol.[2] In a fume hood, an oven dried Schlenk flask equipped with magnetic stirring bar was filled with nitrogen and evacuated (three cycles). Under nitrogen atmosphere, 4-(trifluoromethoxy)aniline (136 µL, 177 mg, 1 mmol, 1 equiv), and pinacolborane (HBPin) (218 µL, 192 mg, 1.5 mmol, 1.5 equiv) were added and the mixture was stirred at room temperature for 1 hr. Then $[Ir(OMe)(COD)]_2$ (6.6 mg, 0.01 mmol, 2 mol% Ir), 3,4,7,8-Tetramethyl-1,10-phenanthroline (4.7 mg, 0.02 mmol, 2 mol%), and pinacolborane (HBPin) (218 µL, 192 mg, 3 mmol, 1.5 equiv) were added in order. The Schlenk flask was closed and the reaction mixture was heated at 80 °C in an oil bath for 4 hr. At this stage, GC-MS data showed full conversion of substrate to a single monoborylated product. Trace (0.5% <) amount of single diborylate product was also observed. Column chromatography (DCM , R_f 0.30) furnished the mono-borylated product isomer as light yellow solid (185 mg, 61%, mp 74 ºC). Regiochemistry of the mono-borylated product isomer was assigned based on ^{1}H NMR data. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.43 (s, J = 2.5 Hz, 1 H), 7.05 (dd, J = 8.7 Hz, J = 2.3 Hz, 1 H), 6.56 (d, J = 8.7 Hz, 1 H), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 152.2 (C), 140.0 (C), 129.0 (CH), 126.1 (CH), 120.7 (q, $^1J_{C–F}$ = 255 Hz, OCF_3), 115.5 (CH), 84.0 (2 C), 24.9 (4 CH_3 of BPin); FT-IR (neat) ν: 3477, 3375, 2992, 2933, 1627, 1492, 1435, 1210, 1164, 1136, 965, 944, 873 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 303 (M^+, 88), 288 (7), 246 (100), 230 (32), 203 (86), 134 (30); HRMS: *m/z* 304.13264 [$(M+1)^+$]; Calcd for $C_{13}H_{18}BF_3NO_3$: 304.13264].

Compound 3e: Ethyl 7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethoxy)-1H-indole-2-carboxylate



The general procedure was applied to ethyl 5-(trifluoromethoxy)-1H-indole-2-carboxylate (136 mg, 0.5 mmol, 1 equiv) at 60 °C for 12 h. GC-MS data at this stage showed 88% conversion. Column chromatography (DCM/*n*-hexane 1 : 9 , R_f 0.70) furnished the product as colorless solid (101 mg, 51 %, mp 91– 92 ºC). 31 mg of unreacted starting indole was also recovered. Yield based on recovered starting material is 65%. ^{1}H NMR (700 MHz, $CDCl_3$) δ 9.74 (s, 1 H, NH), 7.64 (s, 1 H), 7.62 (s, 1 H), 7.20 (d, *J* = 1.9 Hz, 1 H), 4.42 (q, *J* = 7.1 Hz, 2 H), 1.43 (t, *J* = 7.1 Hz, 3 H), 1.41 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 161.7 (C=O), 143.3 (C), 139.8 (CH), 129.2 (CH), 126.8 (CH), 126.2 (CH), 120.7 (q, $^1J_{C–F}$ = 256 Hz, OCF_3), 118.1 (C), 108.1 (CH), 84.5 (2C), 61.2 (CH_2), 24.9 (4 CH_3 of BPin), 14.3 (CH_3); FT-IR (neat) ν: 3444, 29874, 2913, 1704, 1538, 1426, 1373, 1213, 1140, 1021, 972, 865, 745 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 399 (M^+, 100), 384 (13), 342 (76), 314 (19), 268 (14), 253 (74); HRMS: *m/z* 400.15408 [$(M+1)^+$; Calcd for $C_{18}H_{22}BF_3NO_5$: 400.15376].

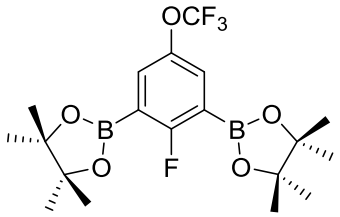
Scheme 4: Di-Borylation of 1-Fluoro-4-(trifluoromethoxy)benzene



77 : **23**

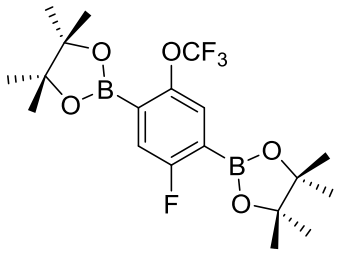
The general procedure was applied to 1-fluoro-4-(trifluoromethoxy)benzene (273 µL, 361 mg, 2 mmol, 1 equiv) and HBPin (870 µL, 768 mg, 6 mmol, 3 equiv) for 20 h. At this stage, the di-borylation was not complete as the two mono-borylated isomers were also present. The ratio of two di-borylated product isomers was 77:23 by GC-MS. Gradient column chromatography (*n*-hexane → DCM/*n*-hexane 2 : 8) was employed to isolate the two di-borylated isoemrs (Minor diborylated product = 104 mg, 12 %. Major diborylated product = 400 mg, 46%). From this reaction, major monoborylated product was also isolated (211 mg, 34%). The order of elution of these products from the column was: monoborylated, minor diborylated, major diborylated. Regiochemistry of the two di-borylated product isomers were assigned based on NMR (^{1}H & ^{13}C) data.

Compound 4a: Major Di-borylated Isomer, 2,2'-(2-fluoro-5-(trifluoromethoxy)-1,3-phenylene)bis(4,4,5,5-tetramethyl-1,3,2 dioxaborolane)



Gradient column chromatography (*n*-hexane → DCM/*n*-hexane 2 : 8) furnished the major di-borylated product isomer as a white solid (400 mg, 46 %, mp 112 – 115 °C). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.62 (d, $^{4}J_{H–F}$ = 4.1 Hz, 2 H), 1.34 (br s, 24 H, 8 CH_3 of two BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 169.3 (d, $^{1}J_{C–F}$ = 256 Hz, C), 144.5 (C), 132.2 (d, $^{3}J_{C–F}$ = 9.7 Hz, CH), 120.5 (q, $^{1}J_{C–F}$ = 257 Hz, OCF_3), 84.3 (4 C), 24.8 (8 CH_3 of two BPin); FT-IR (neat) ν: 2981, 2931, 1615, 1437, 1391, 1315, 1250, 1216, 1135, 967, 888, 846 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 432 (M^+, 63), 417 (68), 412 (94), 332 (44), 328 (56), 270 (24); HRMS: *m/z* 412.18186 [(M–FH); Calcd for $C_{19}H_{25}B_2F_3O_5$: 412.18347].

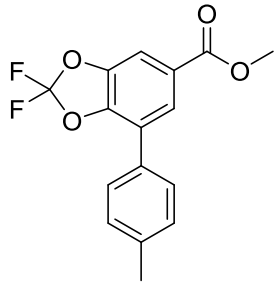
Compound 4b: Minor Di-Borylated Isomer, 2,2'-(2-fluoro-5-(trifluoromethoxy)-1,4-phenylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)



Gradient column chromatography (*n*-hexane → DCM/*n*-hexane 2 : 8) furnished the minor di-borylated product isomer as a white solid (104 mg, 12 %, mp 105 °C). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.55 (d, $^{4}J_{H–F}$ = 4.1 Hz, 1 H), 7.41 (d, $^{3}J_{H–F}$ = 8.5 Hz, 1 H), 1.36 (br s, 12 H, 4 CH_3 of BPin), 1.34 (br s, 12 H, 4 CH_3 of BPin); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 164.8 (d, $^{1}J_{C–F}$ = 252 Hz, C), 148.5 (C), 129.6 (d, $^{3}J_{C–F}$ = 8.5 Hz, CH), 122.7 (d, $^{2}J_{C–F}$ = 25.4 Hz, CH), 120.4 (q, $^{1}J_{C–F}$ = 256 Hz, OCF_3), 84.5 (2 C), 84.4 (2 C), 24.8 (4 CH_3 of BPin), 24.7 (4 CH_3 of BPin); FT-IR (neat) ν: 2979, 2931, 1501, 1402, 1336, 1298, 1255, 1211, 1137, 963, 901, 854 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 432 (M^+, 100), 417 (43), 373 (28), 351 (22), 346 (62); HRMS: *m/z* 412.18237 [(M–FH); Calcd for $C_{19}H_{25}B_2F_3O_5$: 412.18347].

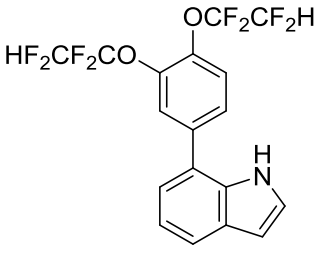
Scheme 5: Suzuki Coupling

Compound 5a: Methyl 2,2-difluoro-7-(p-tolyl)benzo[d][1,3]dioxole-5-carboxylate



In a fume hood, an oven dried Schlenk flask equipped with magnetic stirring bar was filled with nitrogen and evacuated (three cycles). Under nitrogen atmosphere boronic ester (173 mg, 0.5 mmol, 1 equiv), aryl bromide (93 µL, 128 mg, 0.75 mmol, 1.5 equiv), tetrakis(triphenylphosphine)palladium(0) (23 mg, 0.02 mmol, 4 mol% Pd), potassium phosphate tribasic (160 mg, 0.75 mmol, 1.5 equiv), and 1,2-dimethoxyethane (2 mL) were added in order. The Schlenk flask was closed and the reaction mixture was heated at 80 °C in an oil bath for 24 hr. The reaction mixture was extracted into ethyl acetate, washed with water and brine, and dried over anhydrous $MgSO_4$. Column chromatography (Hexanes/Ethyl acetate 99 : 1, R_f 0.30) furnished the product as very light yellow solid (116 mg, 76 %, mp 84 ºC). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.08 (d, *J* = 1.6 Hz, 1 H), 7.66 (d, *J* = 1.6 Hz, 1 H), 7.62 (d, *J* = 8.1 Hz, 2 H), 7.31 (d, *J* = 8.1 Hz, 2 H), 3.94 (s, 3 H), 2.42 (s, 3 H); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 165.1 (C), 144.1 (C), 143.9 (C), 139.1 (CH), 131.7 (t, $^1J_{C–F}$ = 257 Hz, OCF_2), 130.1 (C), 129.7 (2 CH), 127.8 (2 CH), 126.4 (C), 125.6 (CH), 123.8 (C), 52.5 (OCH_3), 21.3 (CH_3); FT-IR (neat) ν: 3103, 3026, 2959, 2919, 2843, 1770, 1721, 1434, 1218, 1149, 1089, 1019, 992, 898, 795 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 306 (M^+, 100), 275 (92), 247 (10), 181 (15), 153 (70); HRMS: *m/z* 307.07750 [$(M+1)^+$] ; Calcd for $C_{16}H_{13}F_2O_4$: 307.07764].

Compound 5b: 7-(3,4-Bis(1,1,2,2-tetrafluoroethoxy)phenyl)-1H-indole



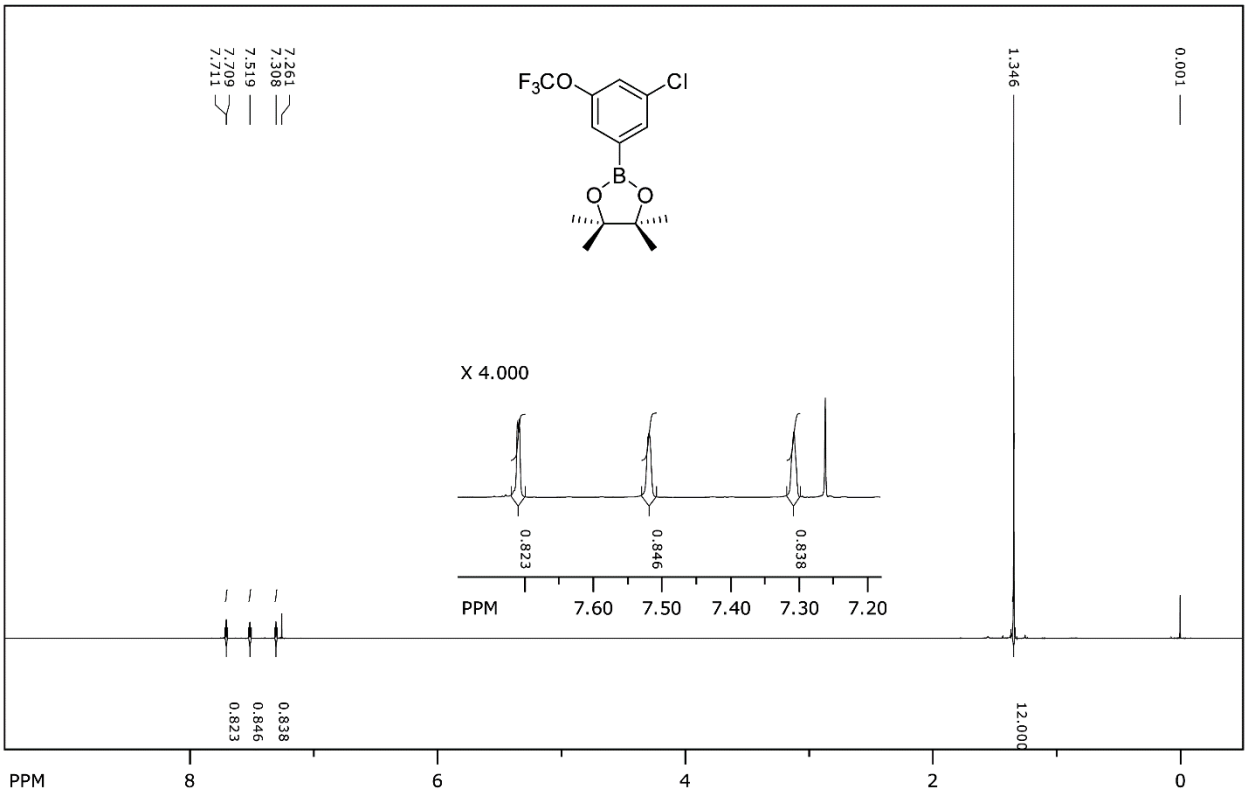
In a fume hood, an oven dried Schlenk flask equipped with magnetic stirring bar was filled with nitrogen and evacuated (three cycles). Under nitrogen atmosphere boronic ester (218 mg, 0.5 mmol, 1 equiv), aryl bromide (147 mg, 0.75 mmol, 1.5 equiv),

tetrakis(triphenylphosphine)palladium(0) (23 mg, 0.02 mmol, 4 mol% Pd), potassium phosphate tribasic (160 mg, 0.75 mmol, 1.5 equiv), and 1,2-dimethoxyethane (2 mL) were added in order. The Schlenk flask was closed and the reaction mixture was heated at 80 °C in an oil bath for 24 hr. The reaction mixture was extracted into ethyl acetate, washed with water and brine, and dried over anhydrous $MgSO_4$. Column chromatography (Hexanes/DCM 95 : 5, R_f 0.40) furnished the product as colorless oil (161 mg, 76 %). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.32 (br s, 1 H), 7.69 (d, *J* = 7.6 Hz, 1 H), 7.65 (s, 1 H), 7.56 (dd, *J* = 8.4, 1.8 Hz, 1 H), 7.51 (d, *J* = 8.4 Hz, 1 H), 7.23 – 7.18 (m, 3 H), 6.64 (apparent t, *J* = 2.3 Hz, 1 H), 5.96 (td, *J* = 53, 2.7 Hz, 2 H); ^{13}C NMR {^{1}H} (176 MHz, $CDCl_3$) δ 141. 4 (C), 140.1 (C), 139.2 (C), 133.3 (C), 128.6 (C), 127.1 (CH), 124.8 (CH), 124.4 (CH), 123.5 (CH), 123.1 (C), 122.1 (CH), 121.1 (CH), 120.4 (CH), 116.5 (tt, , *J* = 274, 29 Hz, 2 C), 107.6 (ttd, *J* = 252, 40.6, 3.9 Hz, 2 CH), 103.4 (CH); FT-IR (neat) ν: 3487, 3424, 3059, 2997, 2963, 2872, 2848, 1609, 1584, 1522, 1503, 1486, 1413, 1281, 1229, 1172, 1097, 865, 843, 794 cm^{-1}; GC-MS (EI) *m/z* (% relative intensity) 425 (M^+, 98), 405 (8), 324 (10), 240 (12), 209 (20), 178 (20), 139 (14), 101 (100); HRMS: *m/z* 426.07262 [$(M+1)^+$] ; Calcd for $C_{18}H_{12}NF_8O_2$: 426.07348].

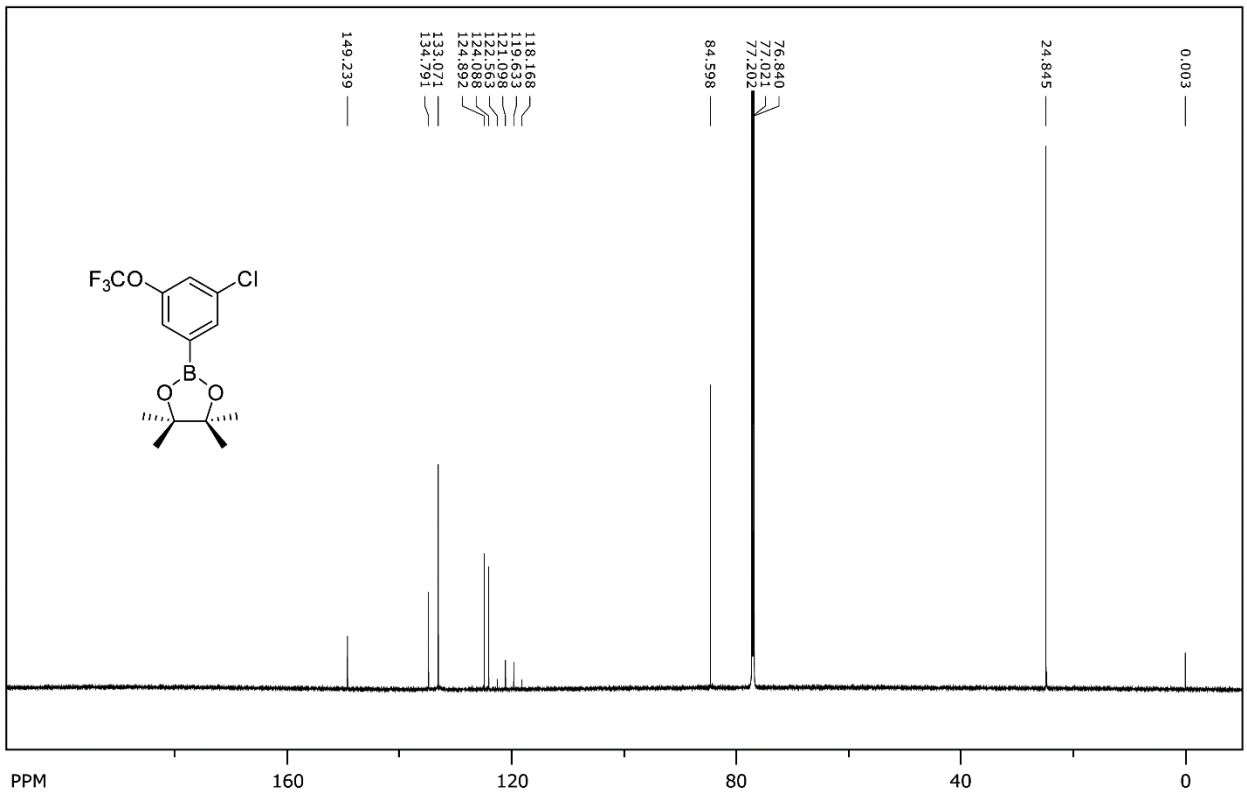
Reference

1. Roosen, P. C.; Kallepalli, V. A.; Chattopadhyay, B.; Singleton, D. A.; Maleczka, R. E.; Smith, M. R. *Journal of the American Chemical Society* **2012**, *134*, 11350.
2. Preshlock, S. M.; Plattner, D. L.; Maligres, P. E.; Krska, S. W.; Maleczka, R. E.; Smith, M. R. *Angewandte Chemie International Edition* **2013**, *52*, 12915.

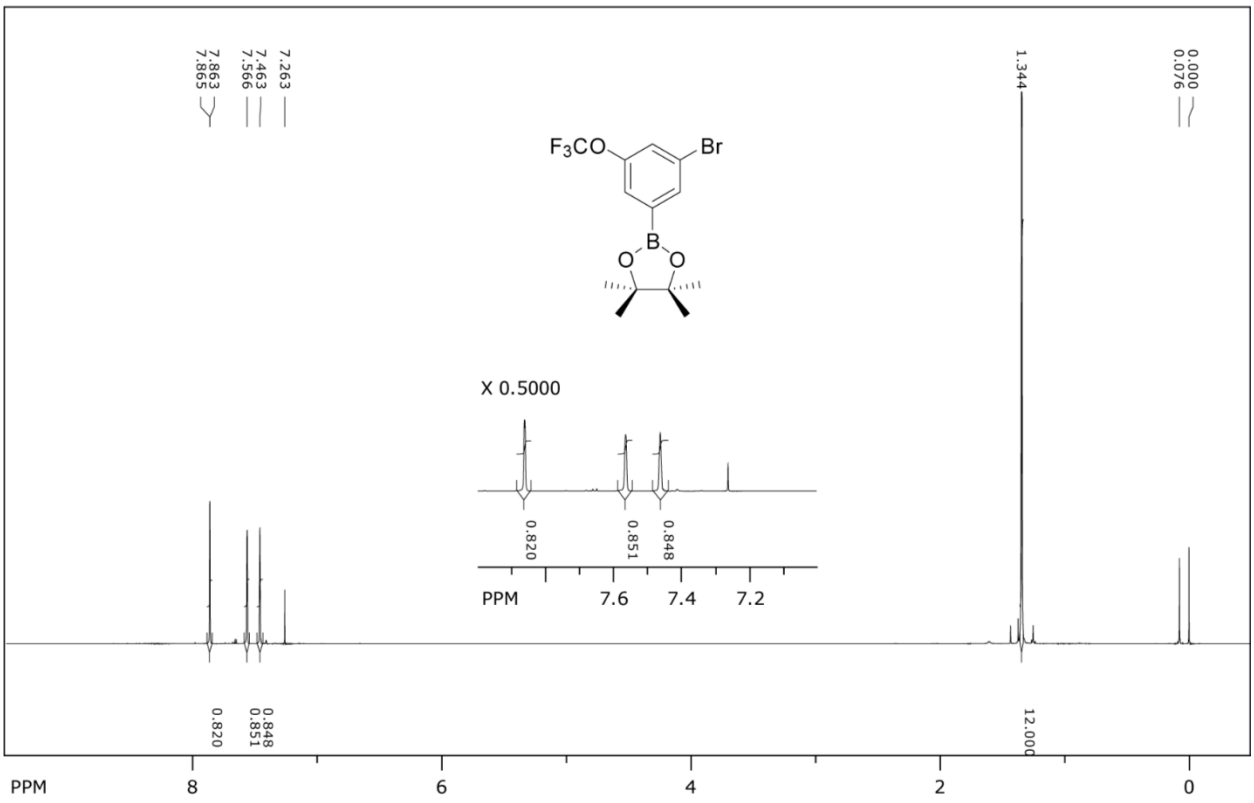
^{1}H & ^{13}C NMR Spectra



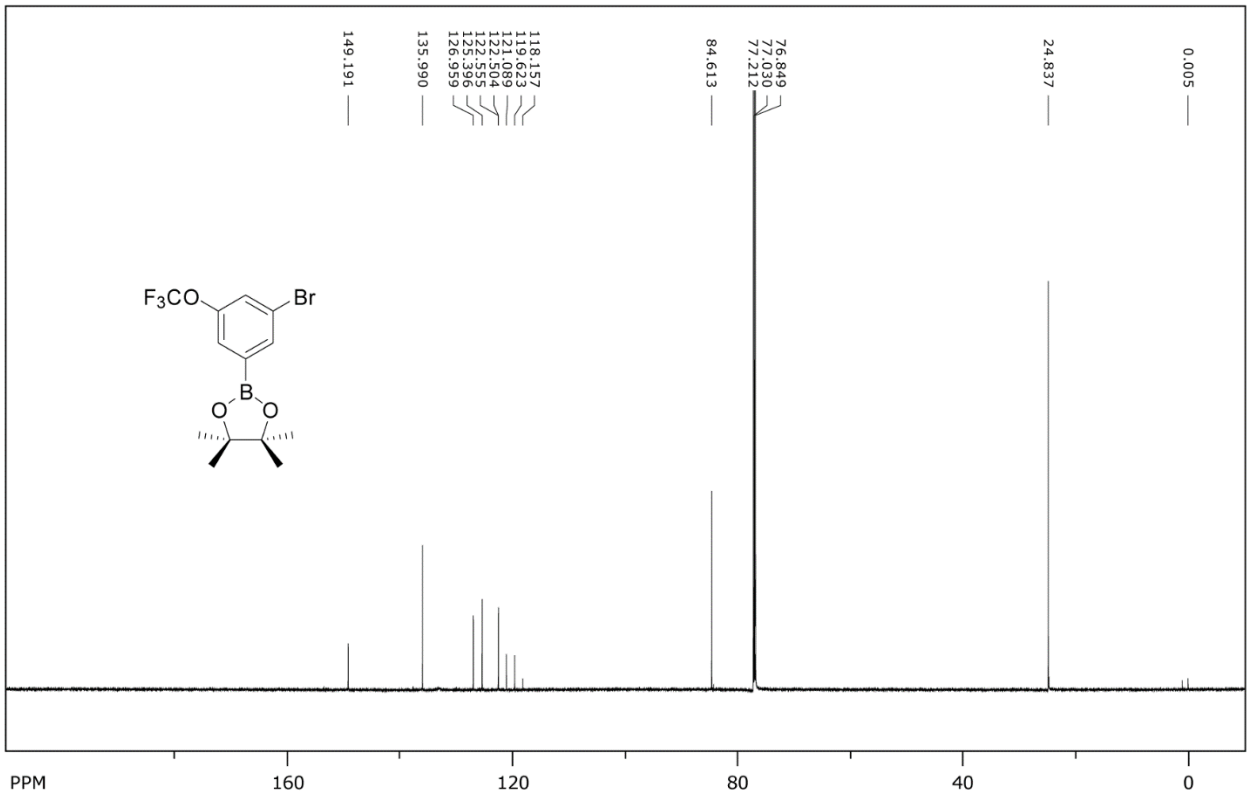
Compound 1a: ^{1}H NMR spectrum of 2-(3-chloro-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



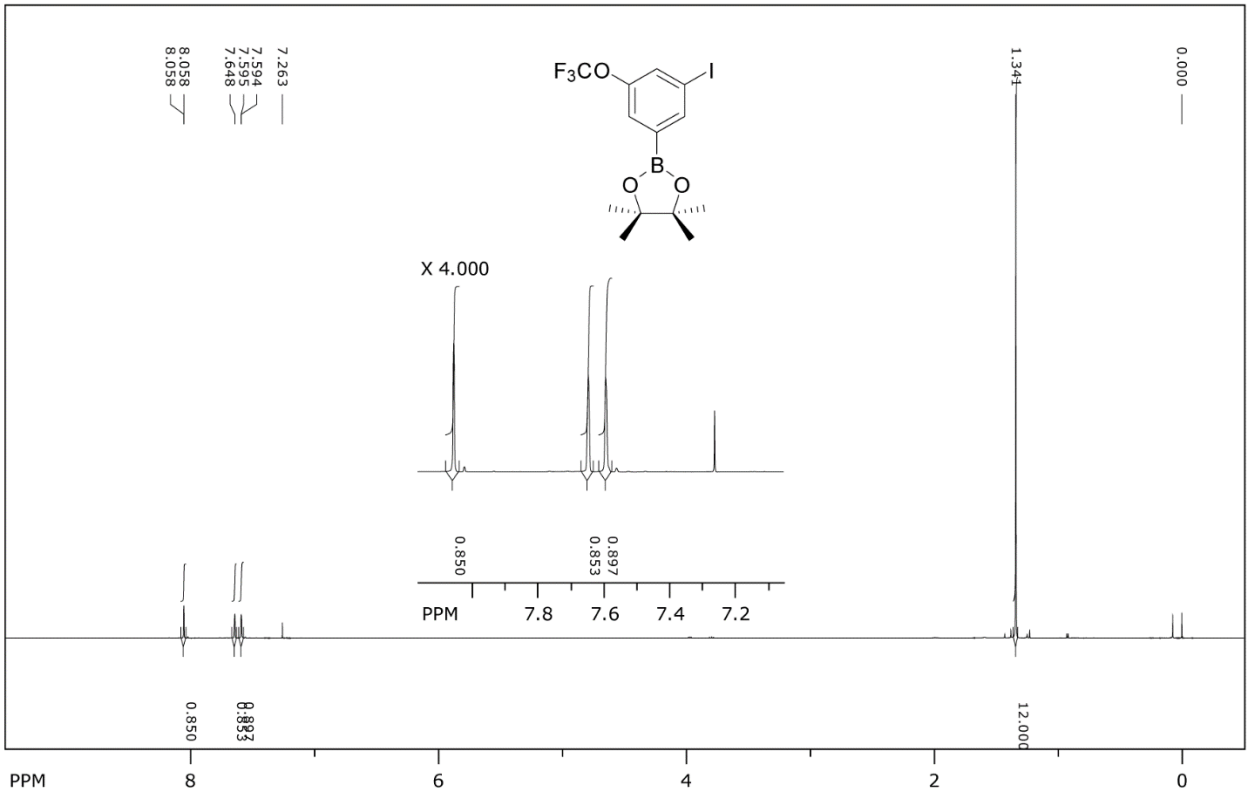
Compound 1a: ^{13}C NMR spectrum of 2-(3-chloro-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



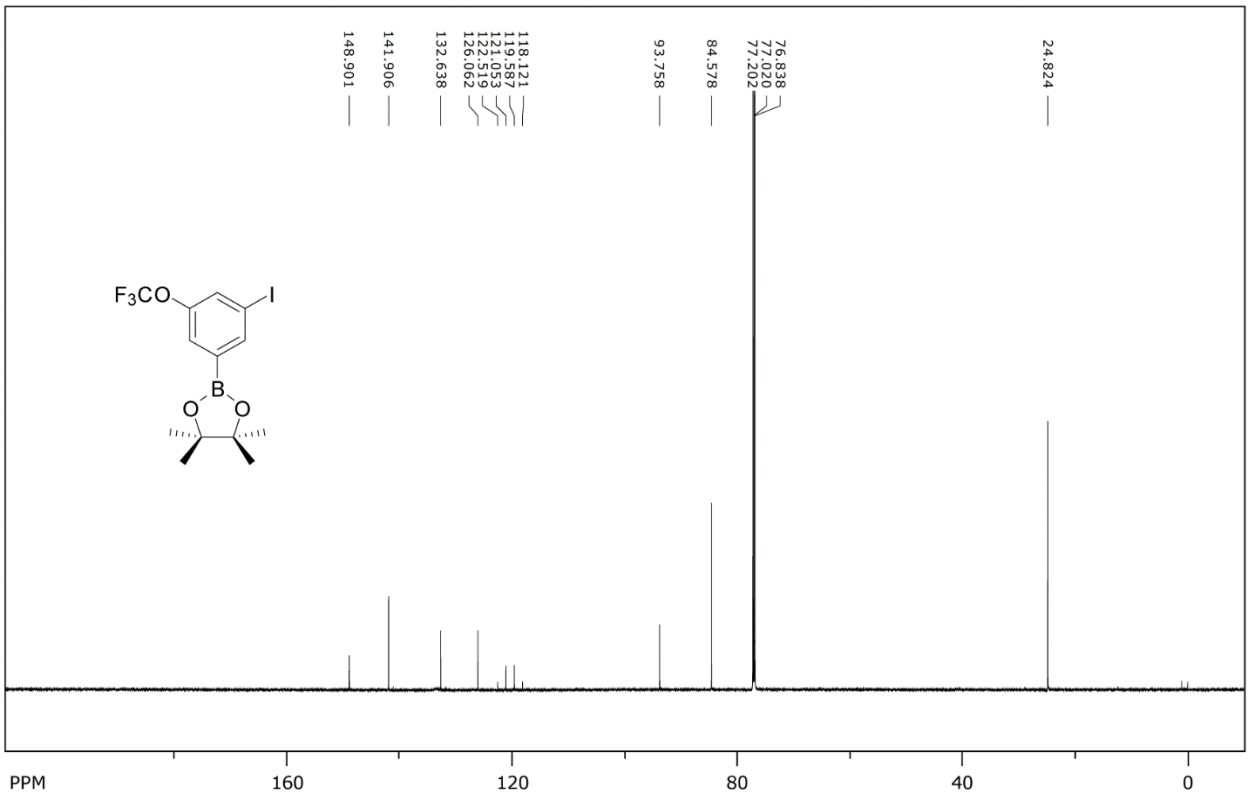
Compound 1b: ^{1}H NMR spectrum of 2-(3-bromo-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



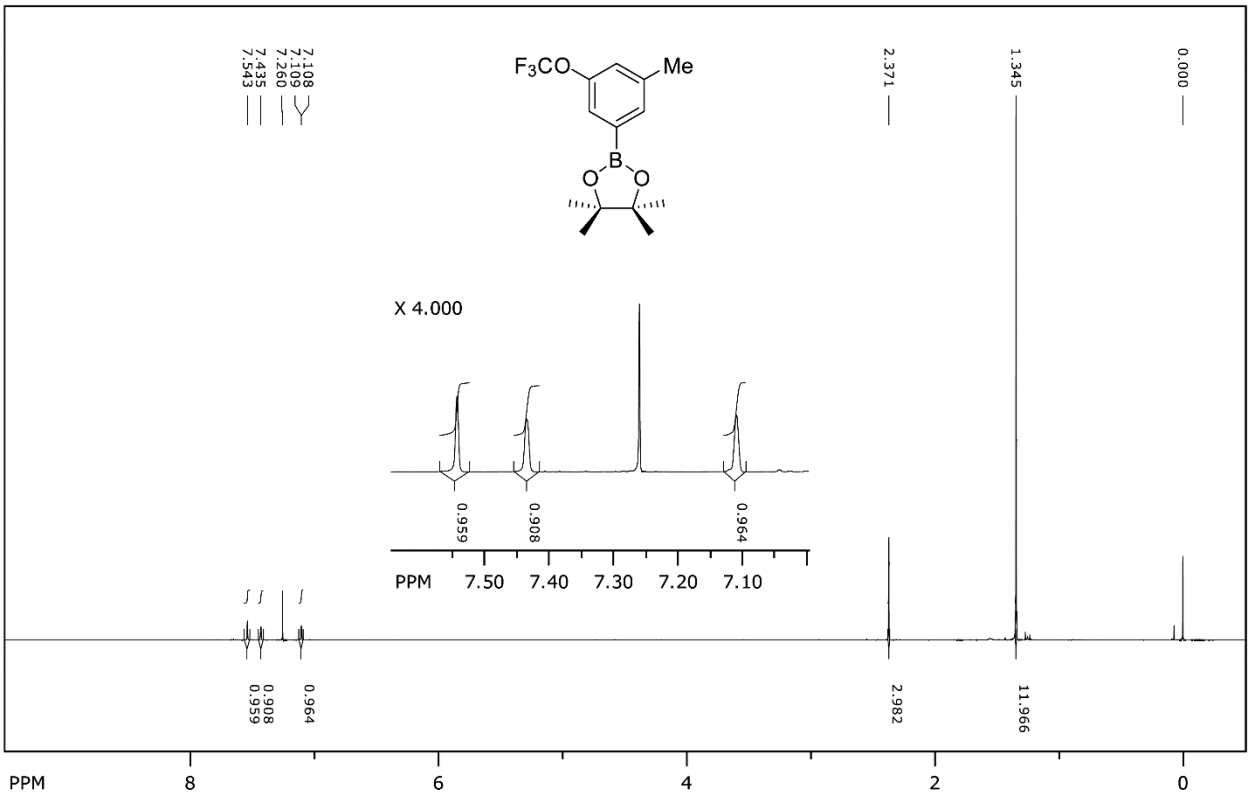
Compound 1b: ^{13}C NMR spectrum of 2-(3-bromo-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



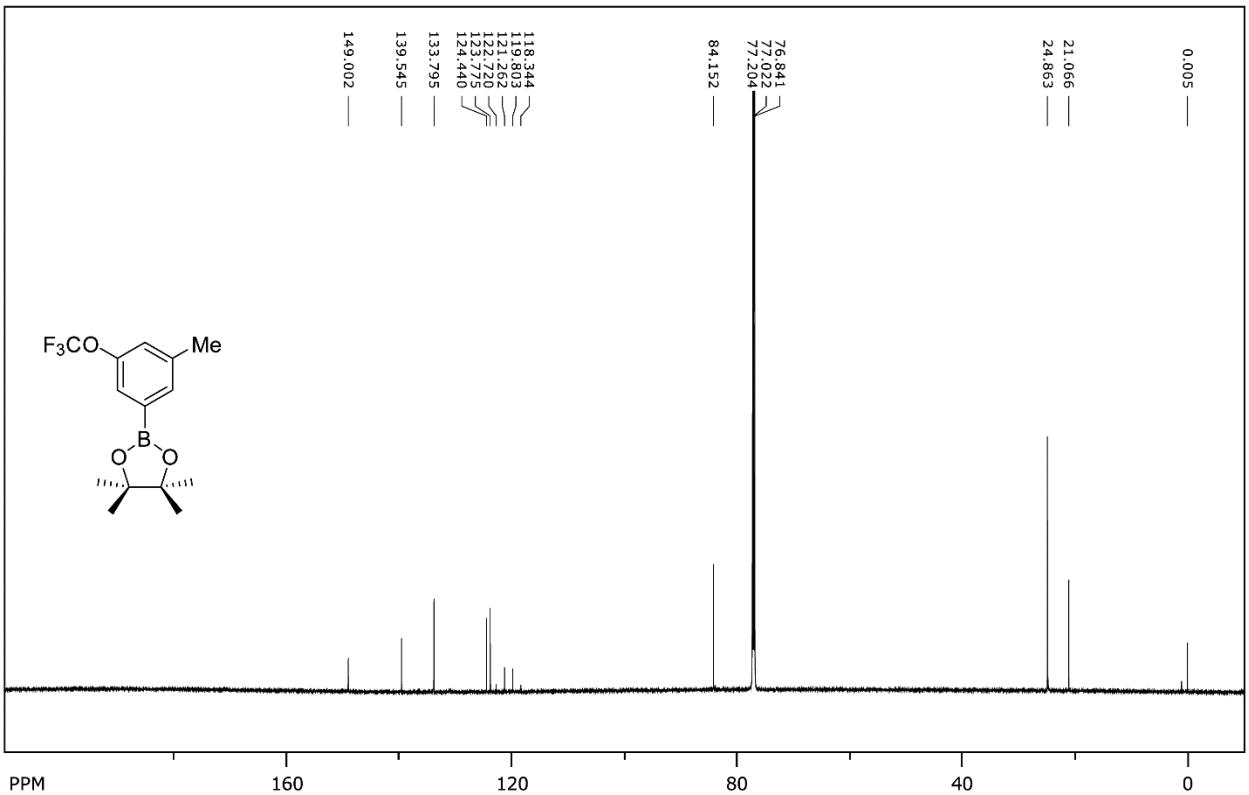
Compound 1c: ^{1}H NMR spectrum of 2-(3-iodo-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



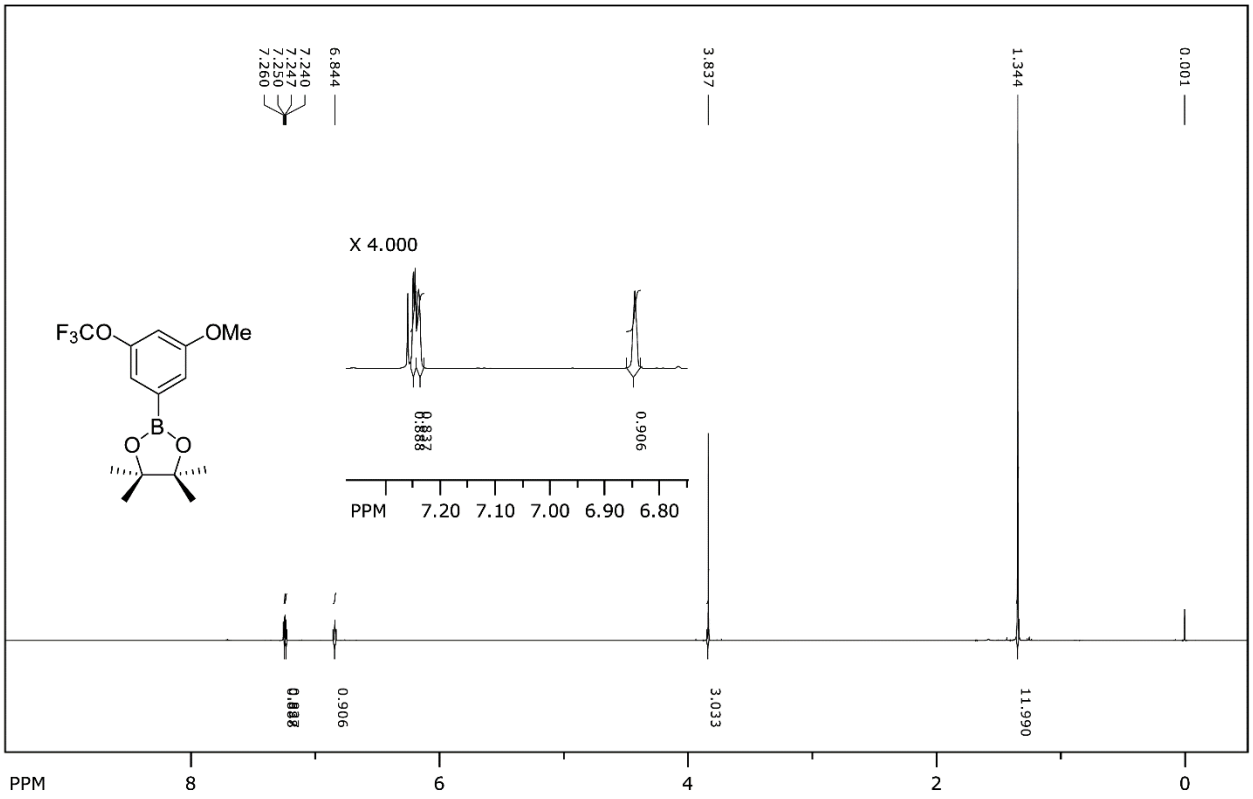
Compound 1c: ^{13}C NMR spectrum of 2-(3-iodo-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



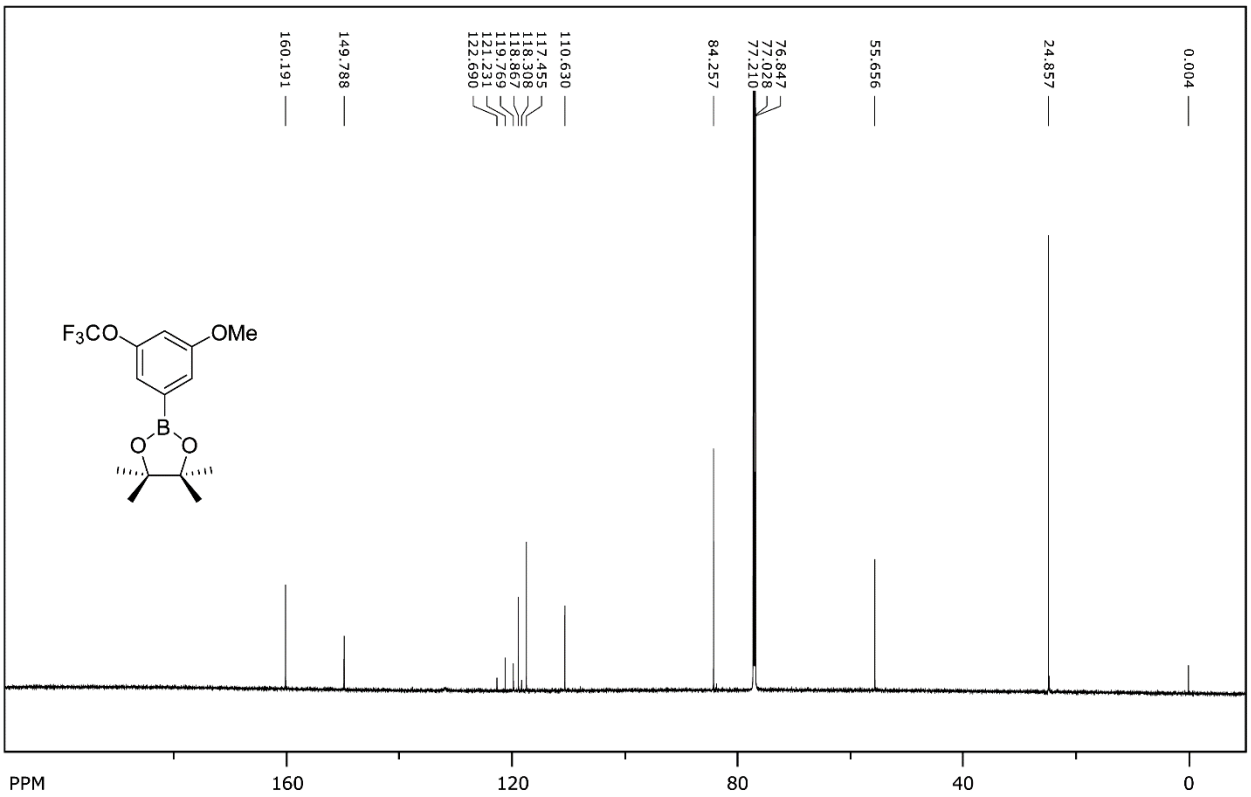
Compound 1d: ^{1}H NMR spectrum of 4,4,5,5-tetramethyl-2-(3-methyl-5-(trifluoromethoxy)phenyl)-1,3,2-dioxaborolane



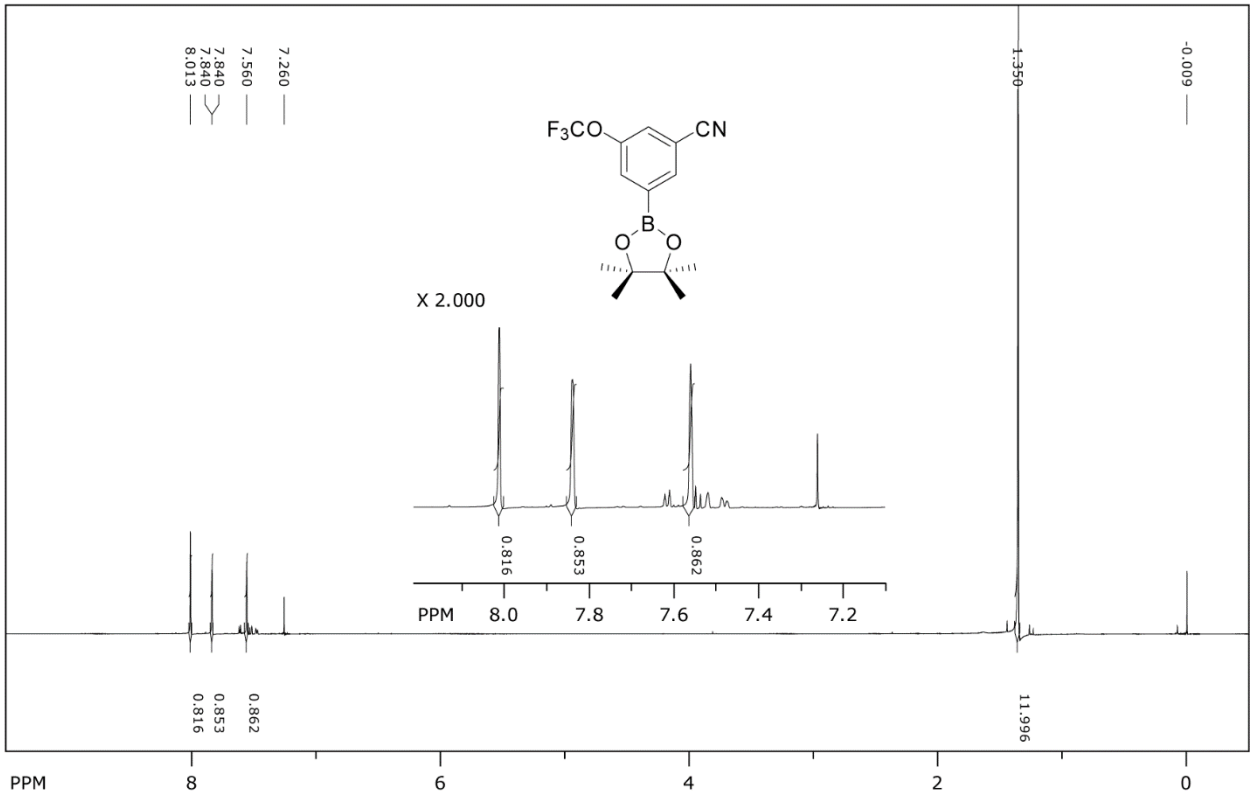
Compound 1d: ^{13}C NMR spectrum of 4,4,5,5-tetramethyl-2-(3-methyl-5-(trifluoromethoxy)phenyl)-1,3,2-dioxaborolane



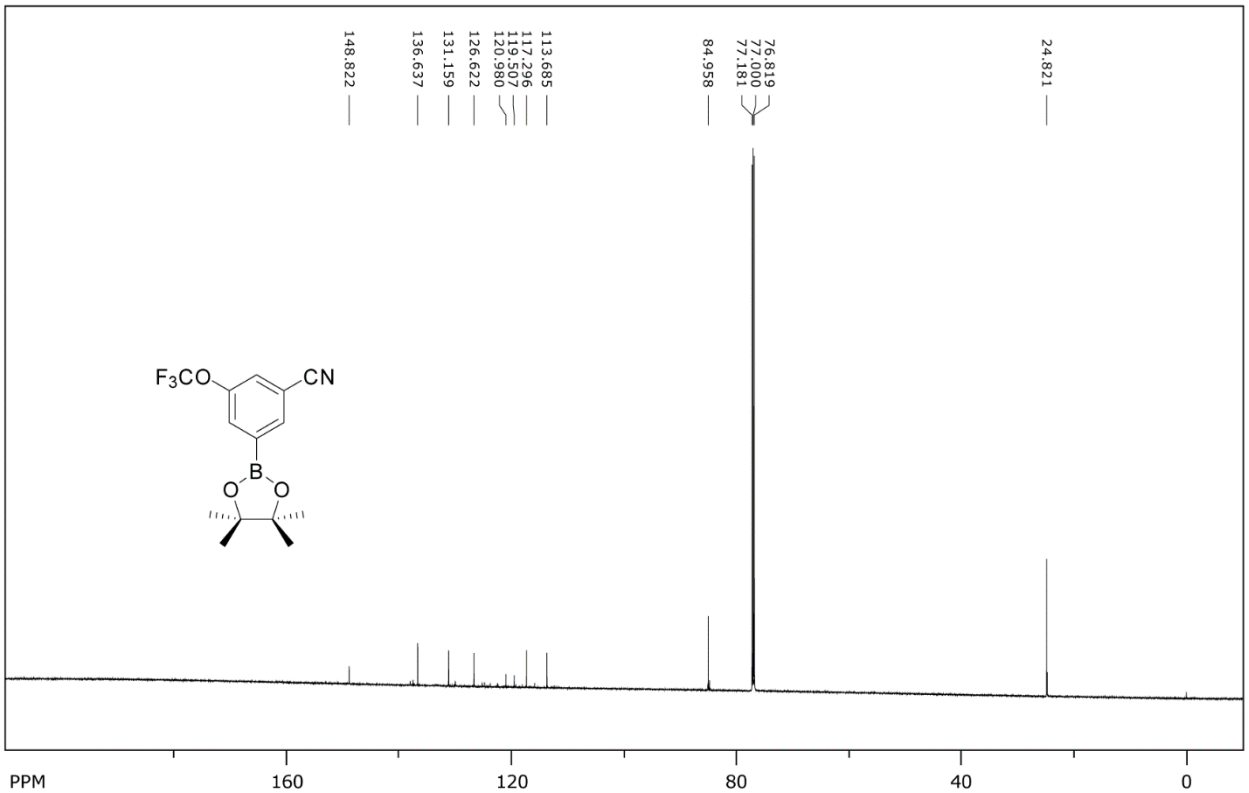
Compound 1e: ^{1}H NMR spectrum of 2-(3-methoxy-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



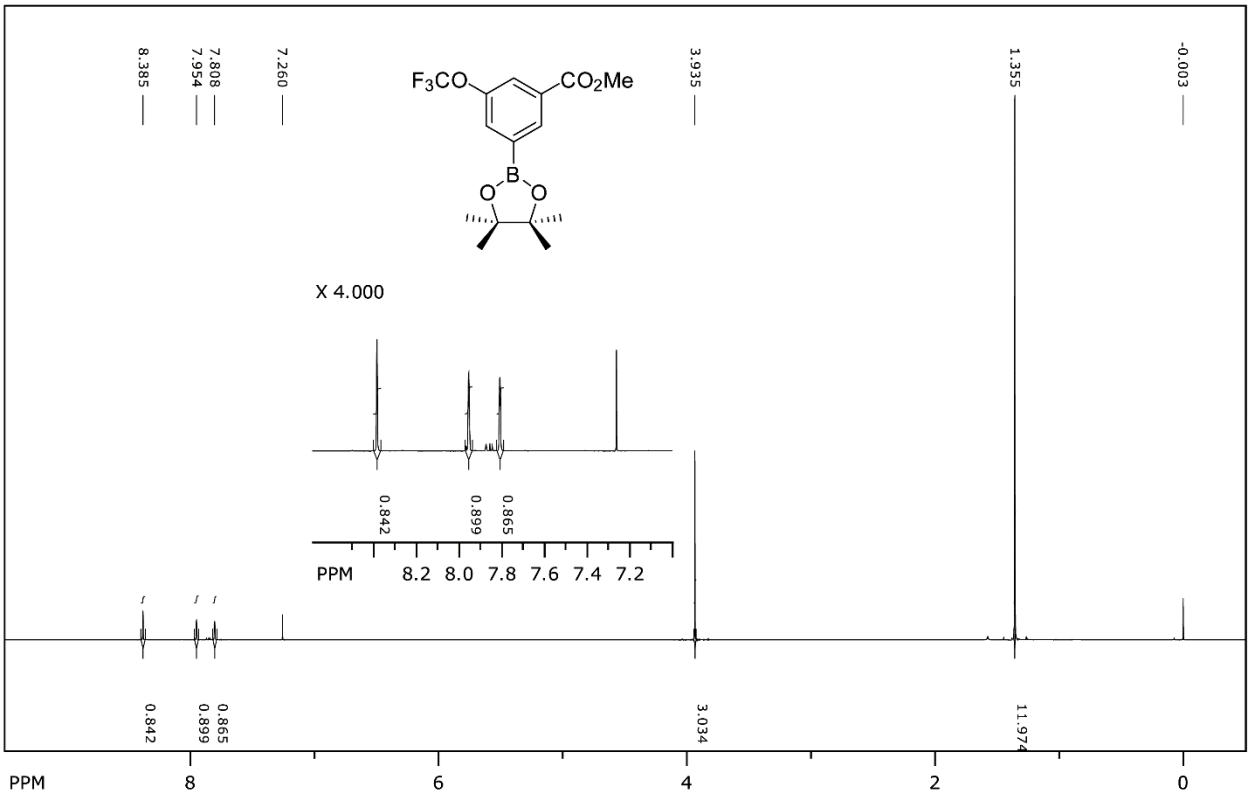
Compound 1e: ^{13}C NMR spectrum of 2-(3-methoxy-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



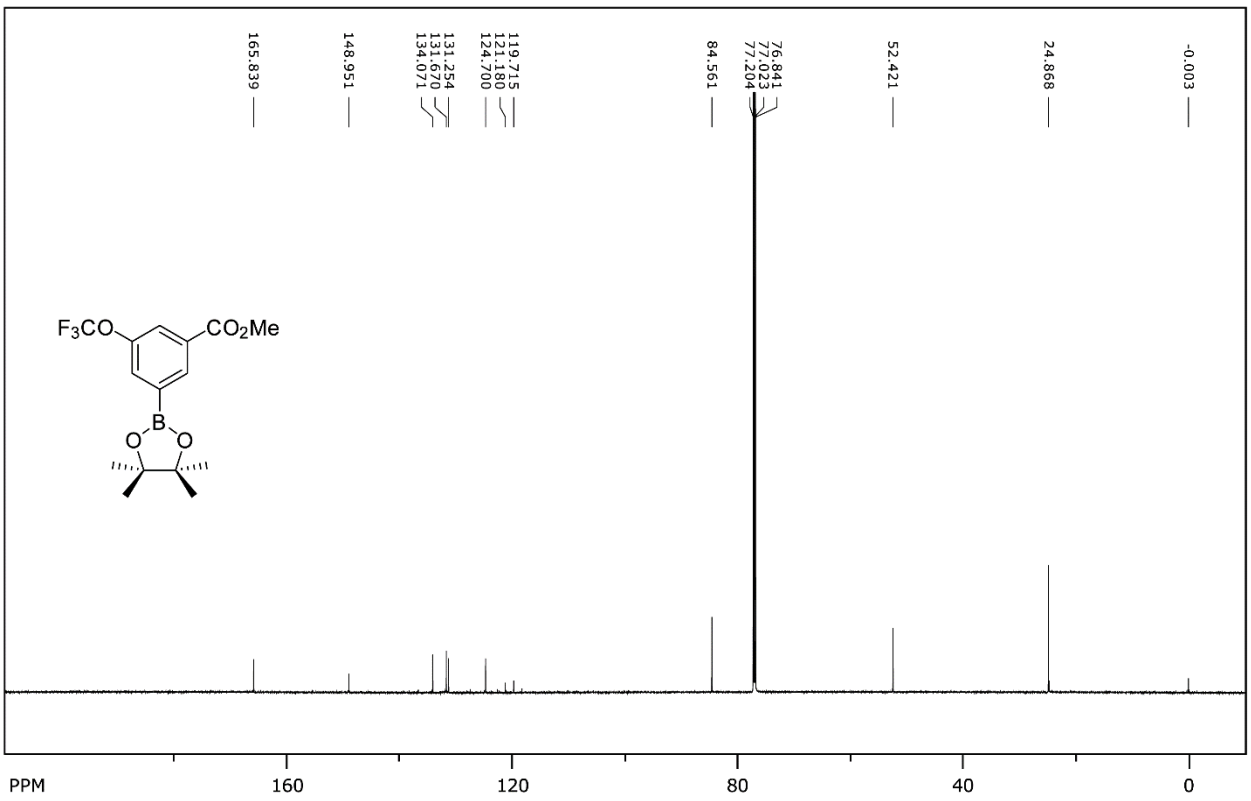
Compound 1f: ^{1}H NMR spectrum of 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethoxy)benzonitrile



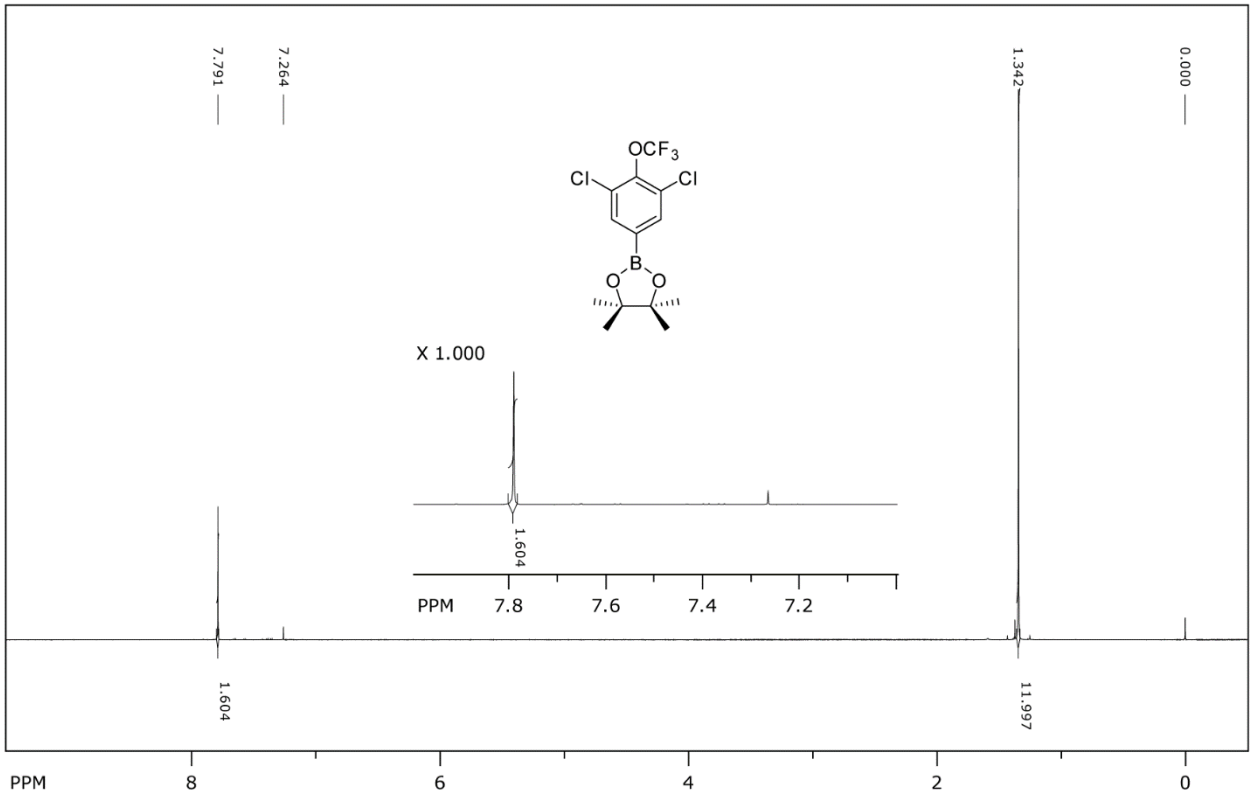
Compound 1f: ^{13}C NMR spectrum of 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethoxy)benzonitrile



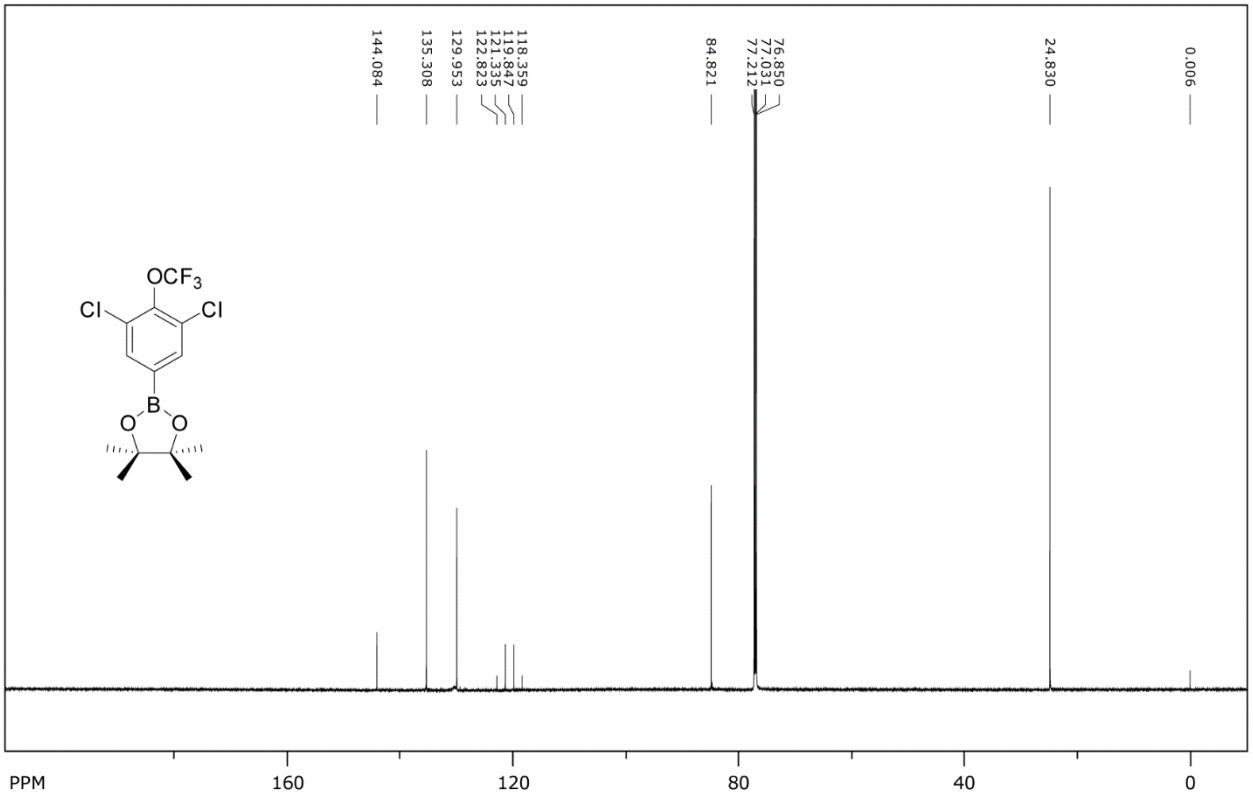
Compound 1g: ^{1}H NMR spectrum of methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethoxy)benzoate



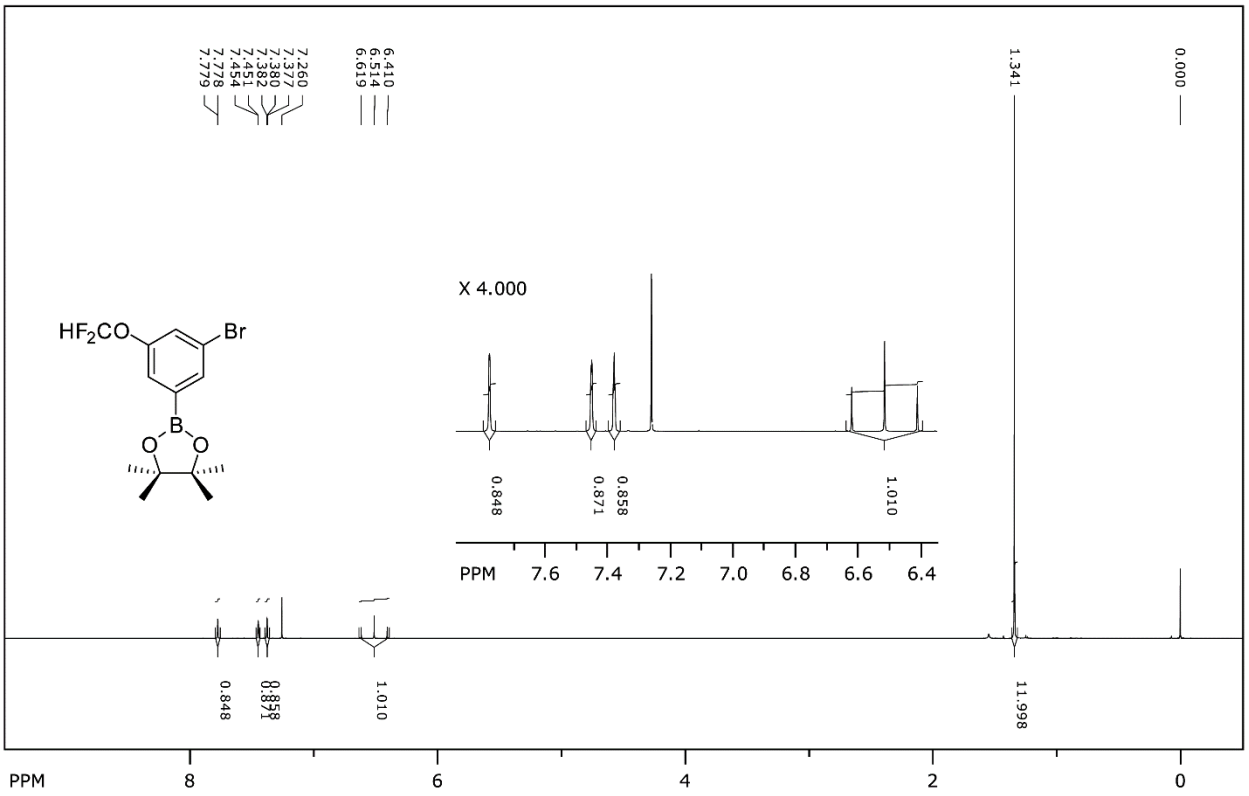
Compound 1g: ^{13}C NMR spectrum of methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethoxy)benzoate



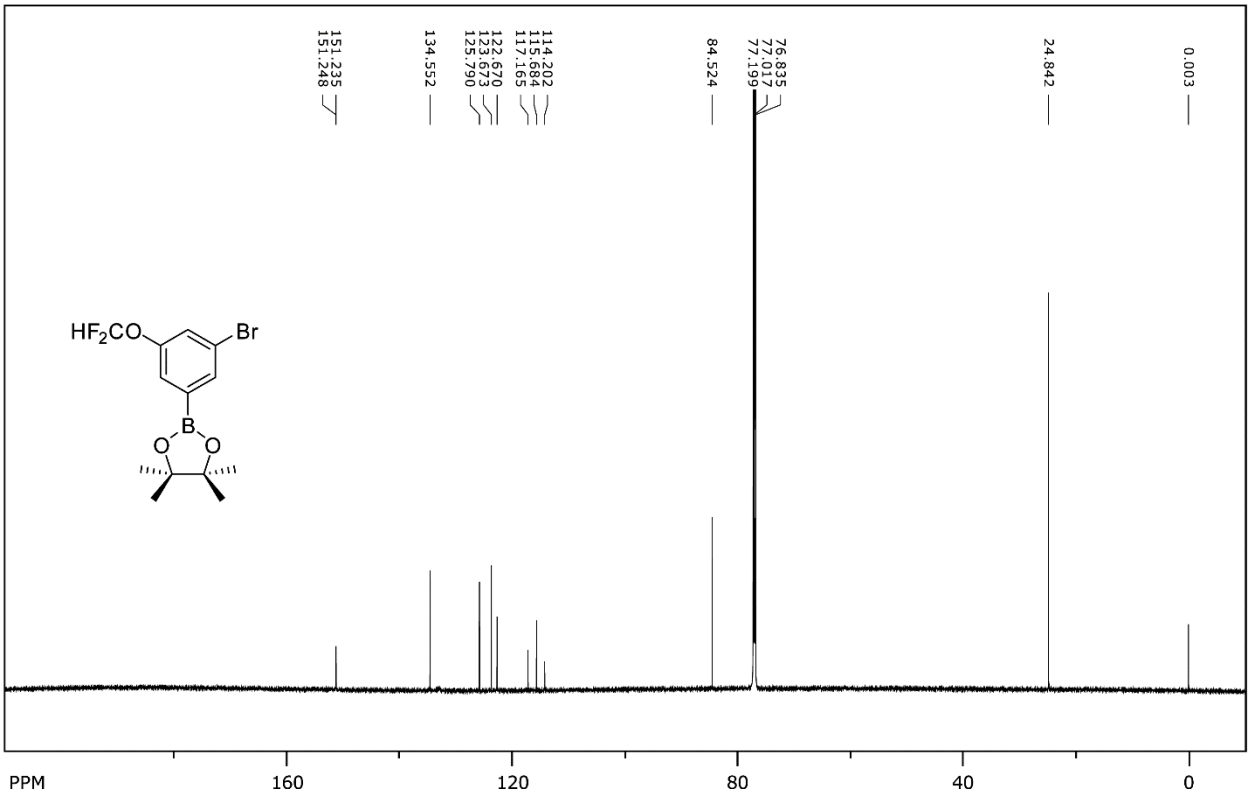
Compound 1h: ^{1}H NMR spectrum of 2-(3,5-dichloro-4-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



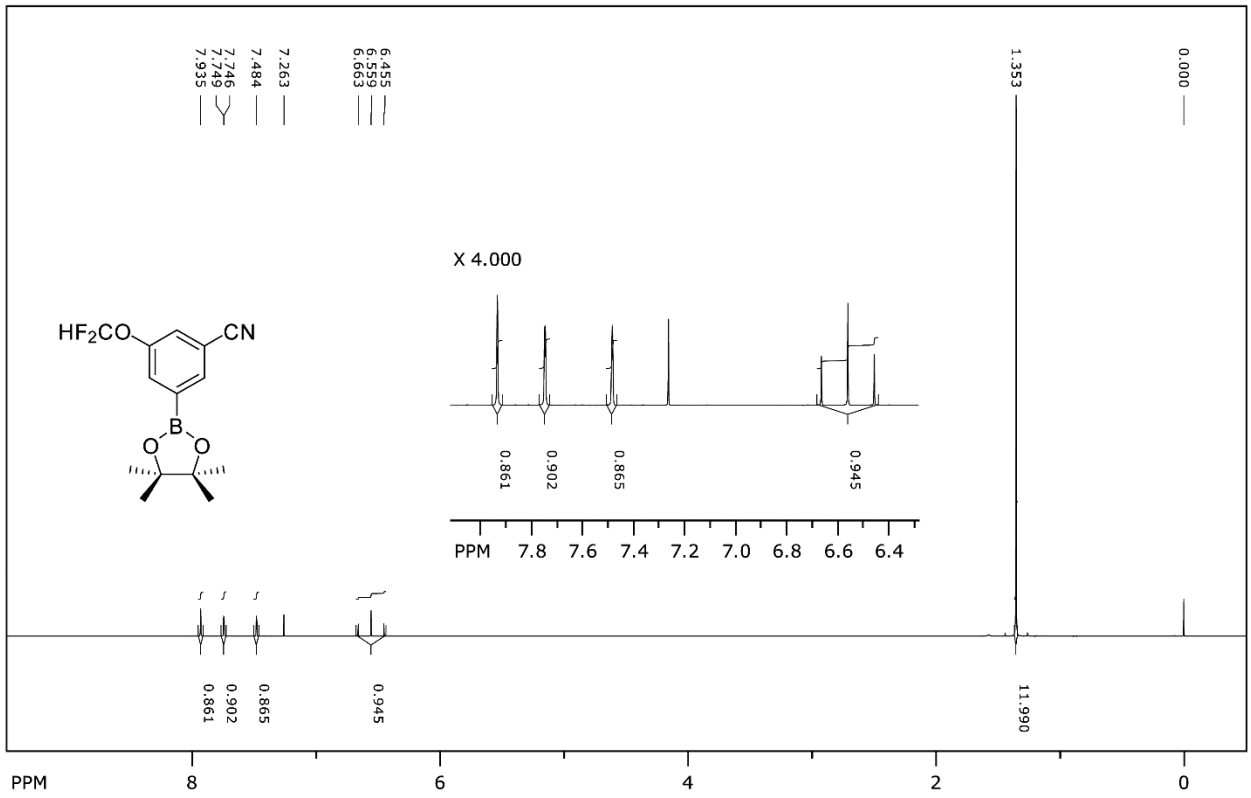
Compound 1h: ^{13}C NMR spectrum of 2-(3,5-dichloro-4-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



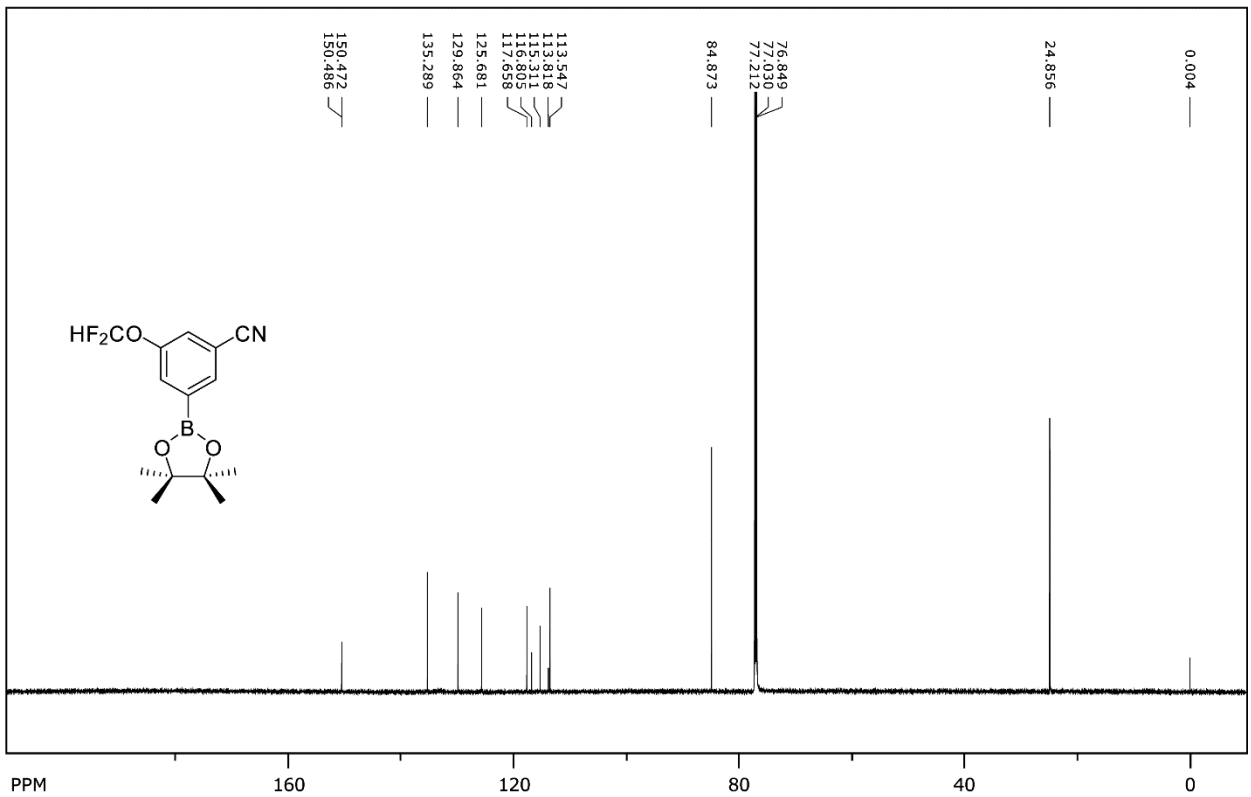
Compound 2a: ^{1}H NMR spectrum of 2-(3-bromo-5-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



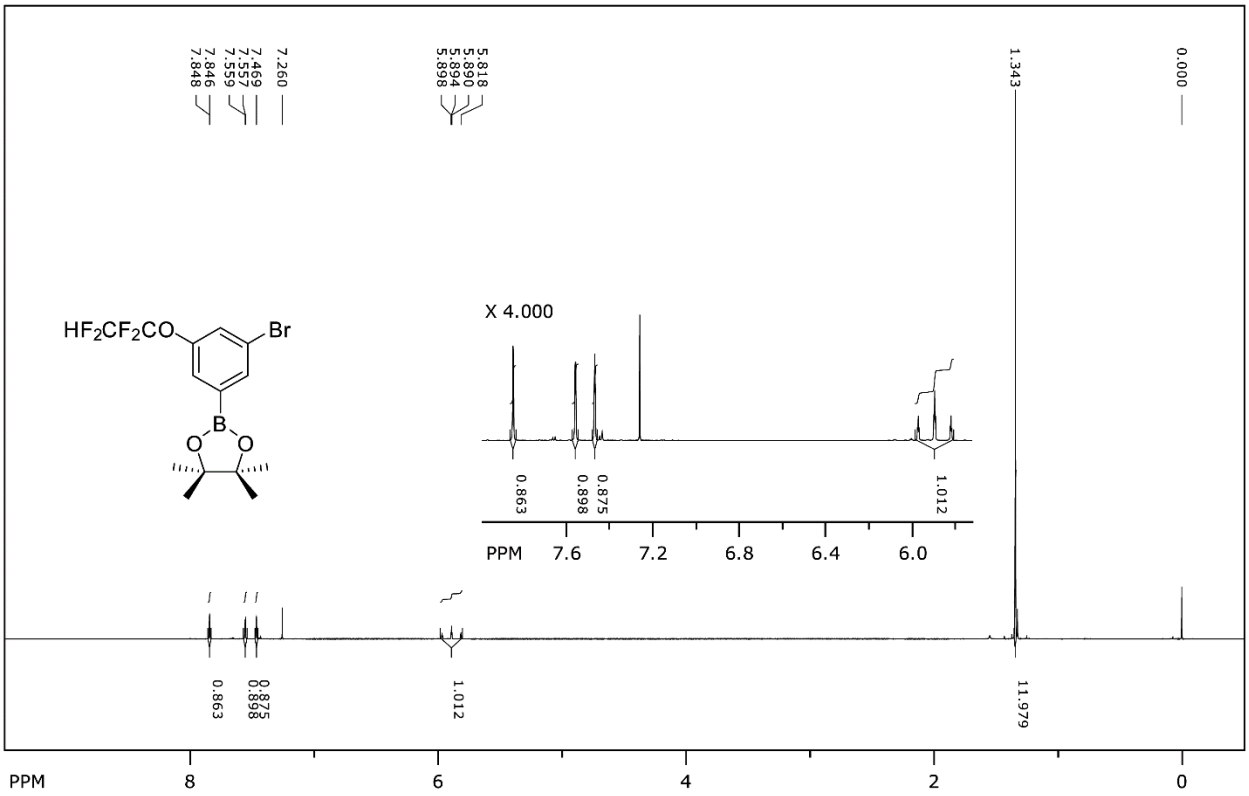
Compound 2a: ^{13}C NMR spectrum of 2-(3-bromo-5-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



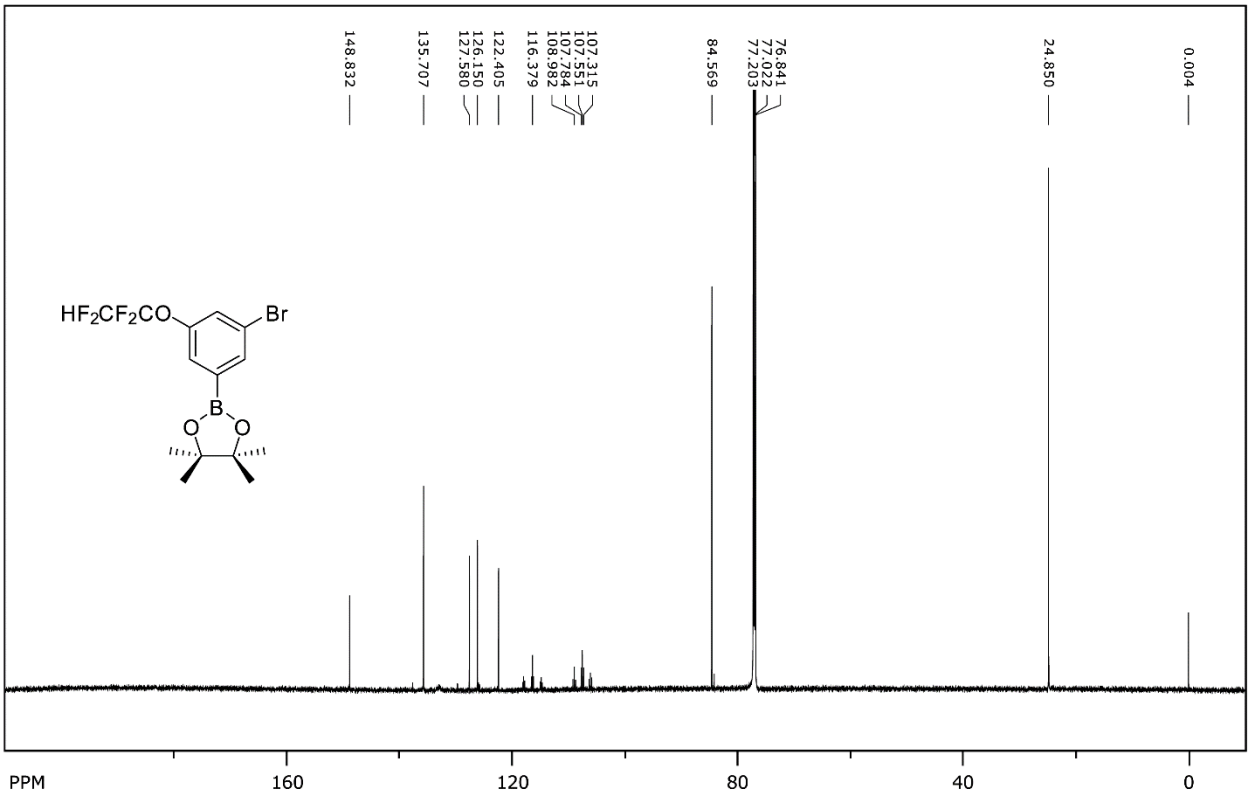
Compound 2b: ^{1}H NMR spectrum of 3-(difluoromethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile



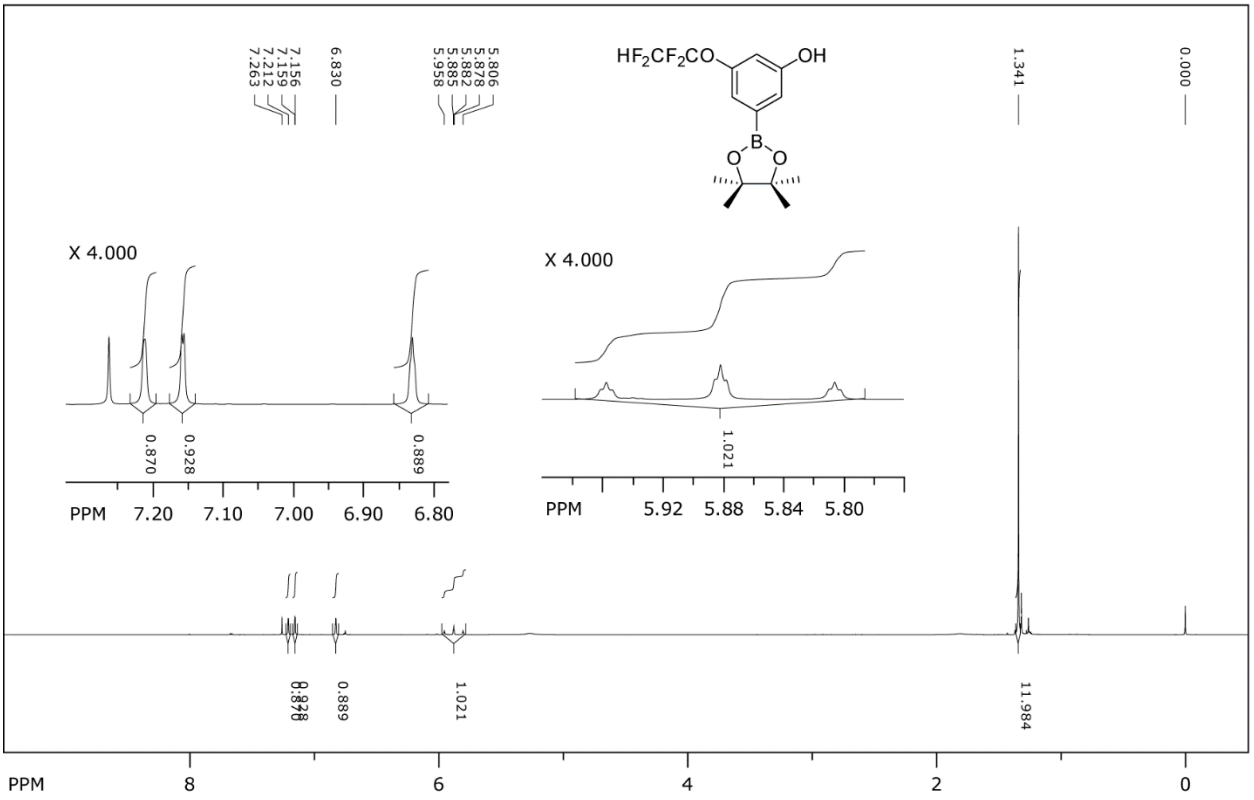
Compound 2b: ^{13}C NMR spectrum of 3-(difluoromethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile



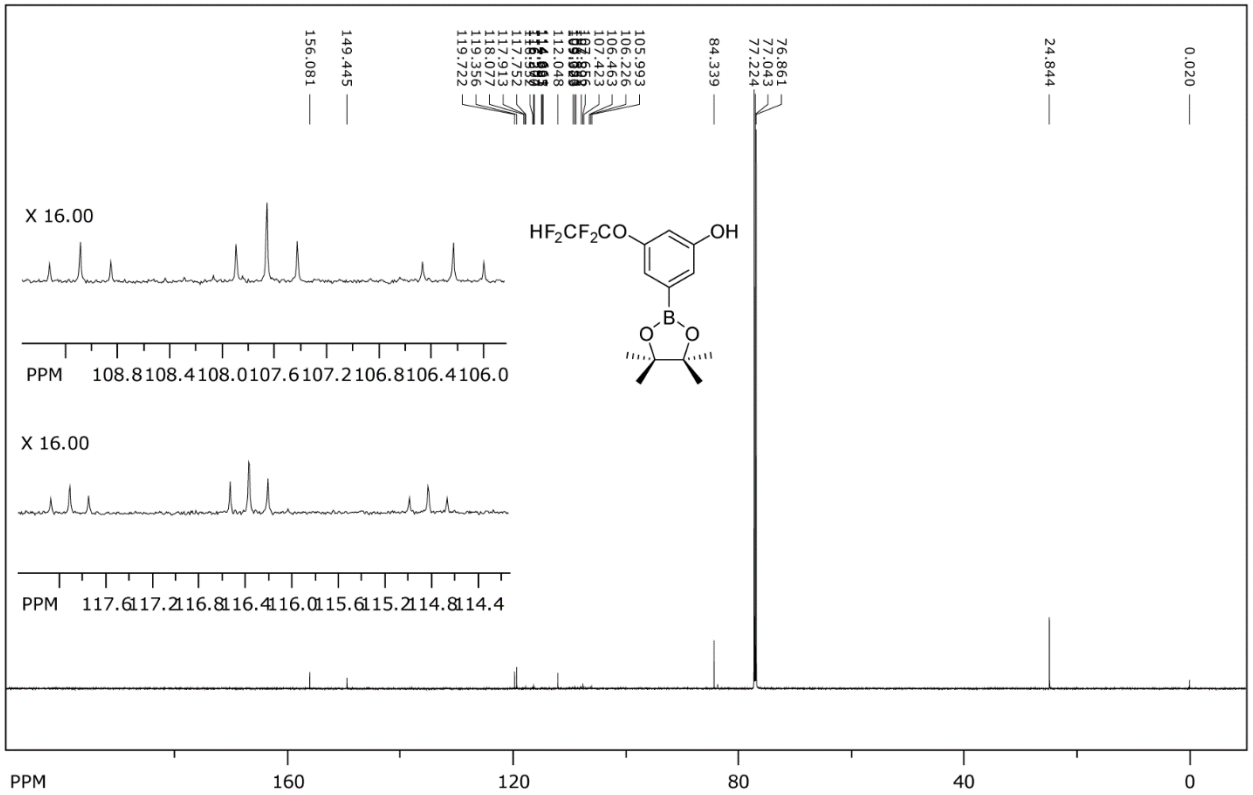
Compound 2c: ^{1}H NMR spectrum of 2-(3-bromo-5-(1,1,2,2-tetrafluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



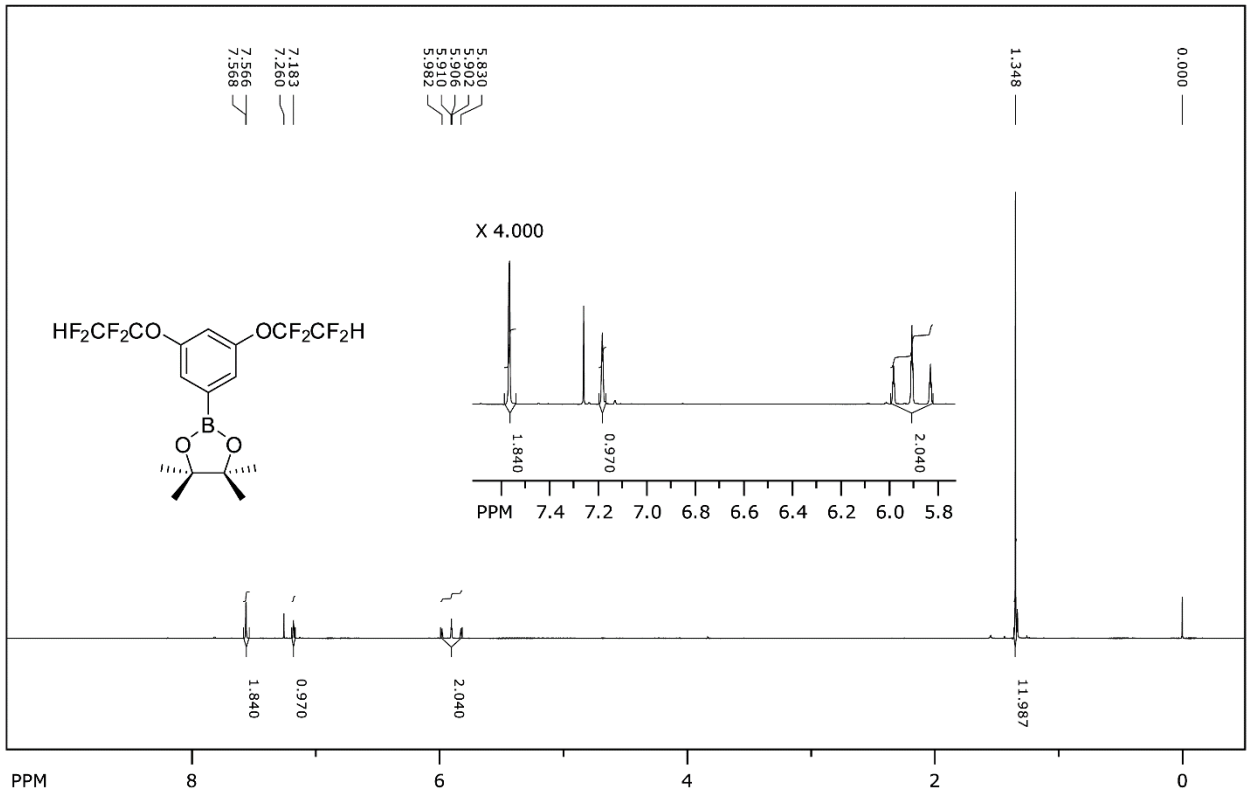
Compound 2c: ^{13}C NMR spectrum of 2-(3-bromo-5-(1,1,2,2-tetrafluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



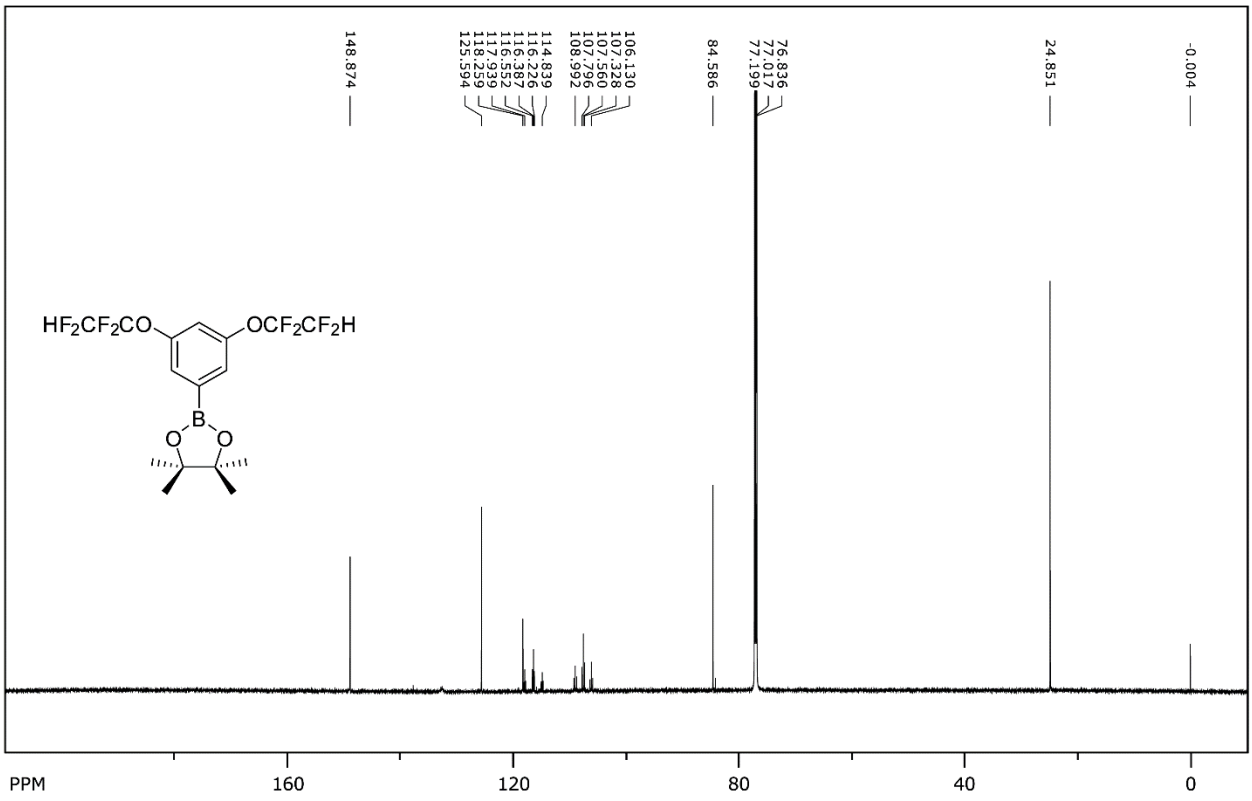
Compound 2d: ^{1}H NMR spectrum of 3-(1,1,2,2-tetrafluoroethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol



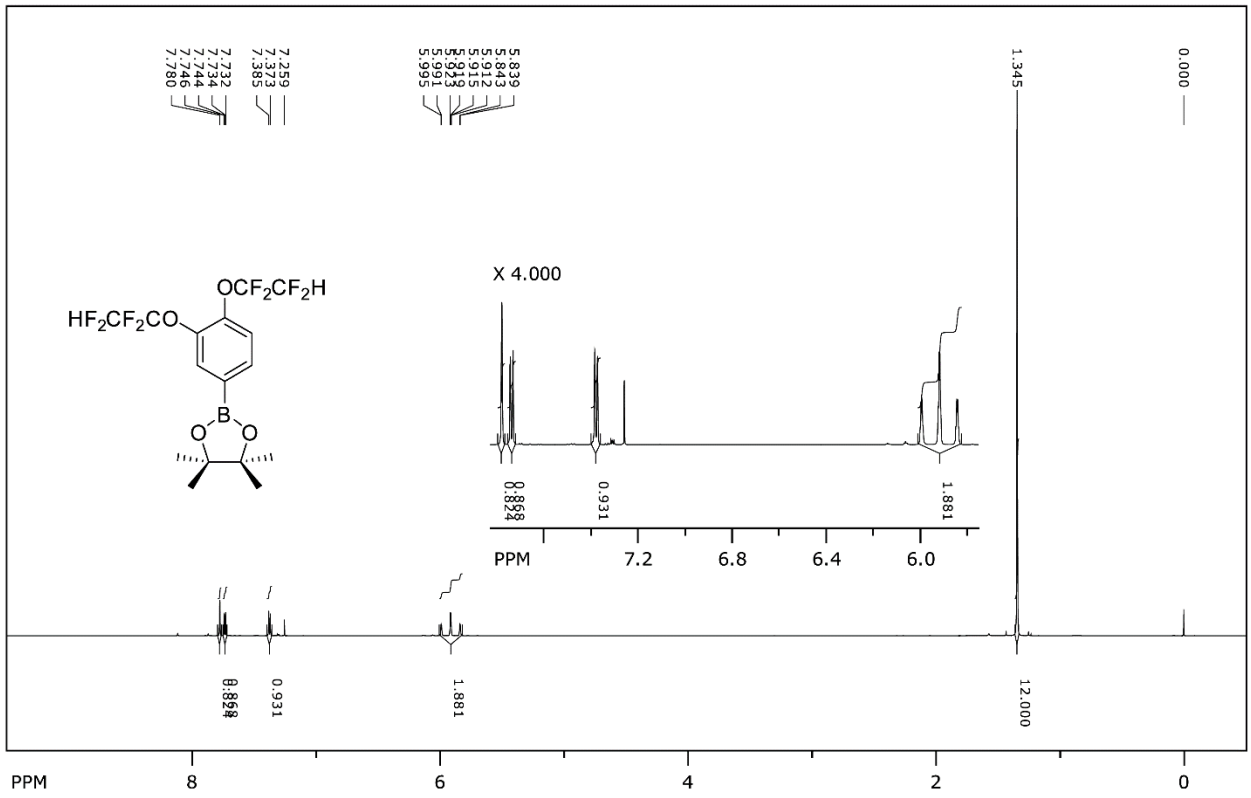
Compound 2d: ^{13}C NMR spectrum of 3-(1,1,2,2-tetrafluoroethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol



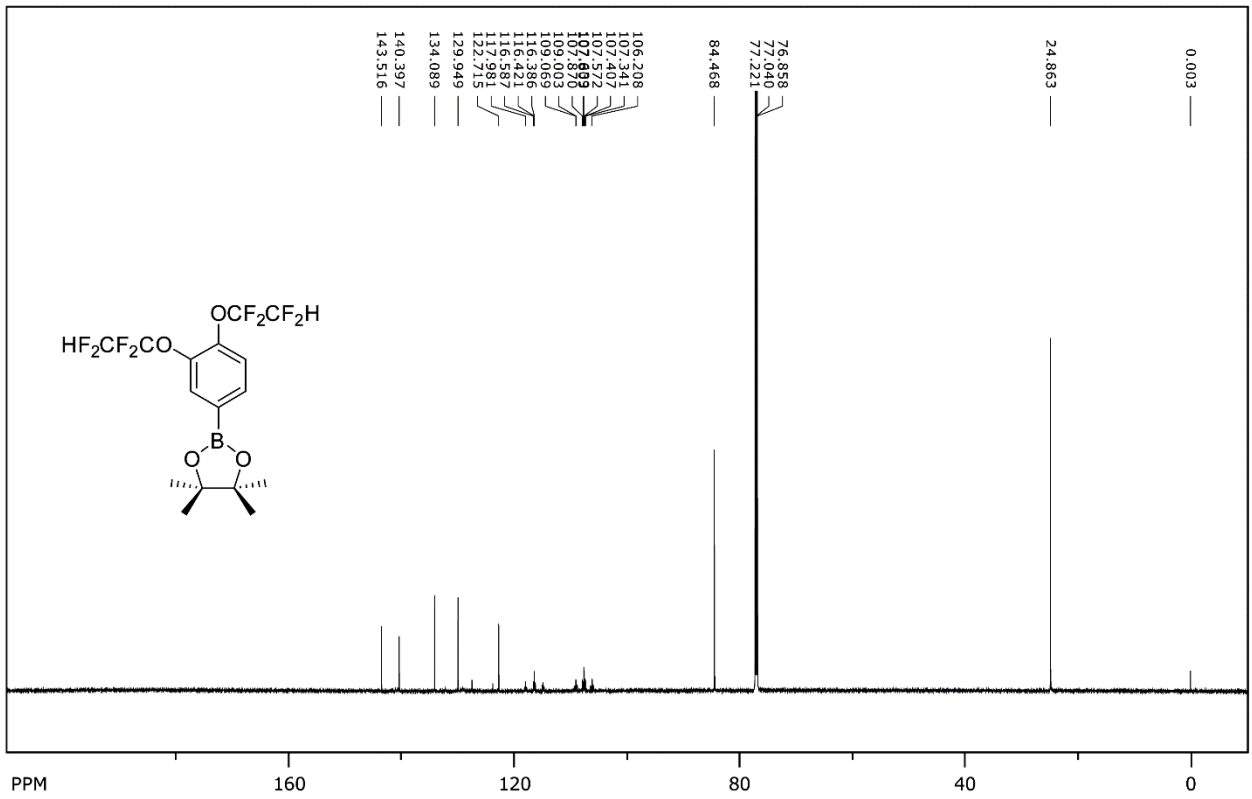
Compound 2e: ^{1}H NMR spectrum of 2-(3,5-bis(1,1,2,2-tetrafluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



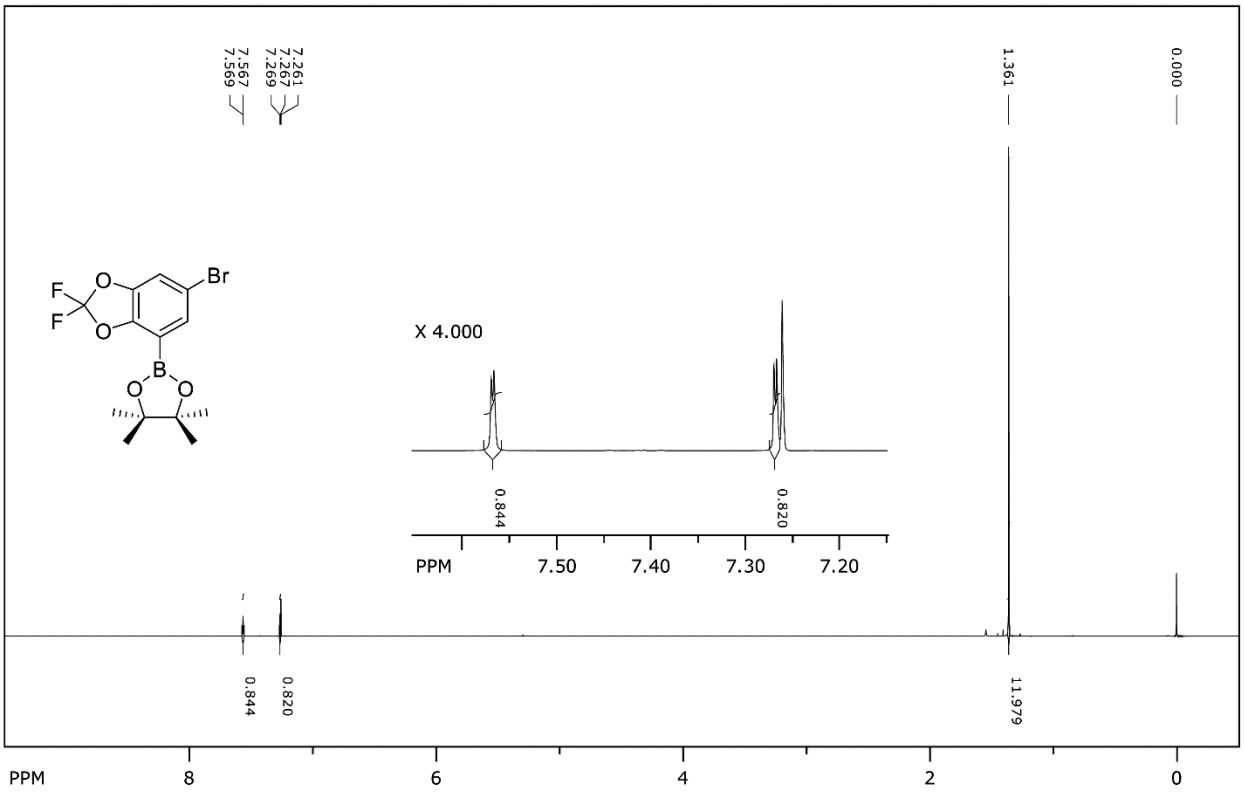
Compound 2e: ^{13}C NMR spectrum of 2-(3,5-bis(1,1,2,2-tetrafluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



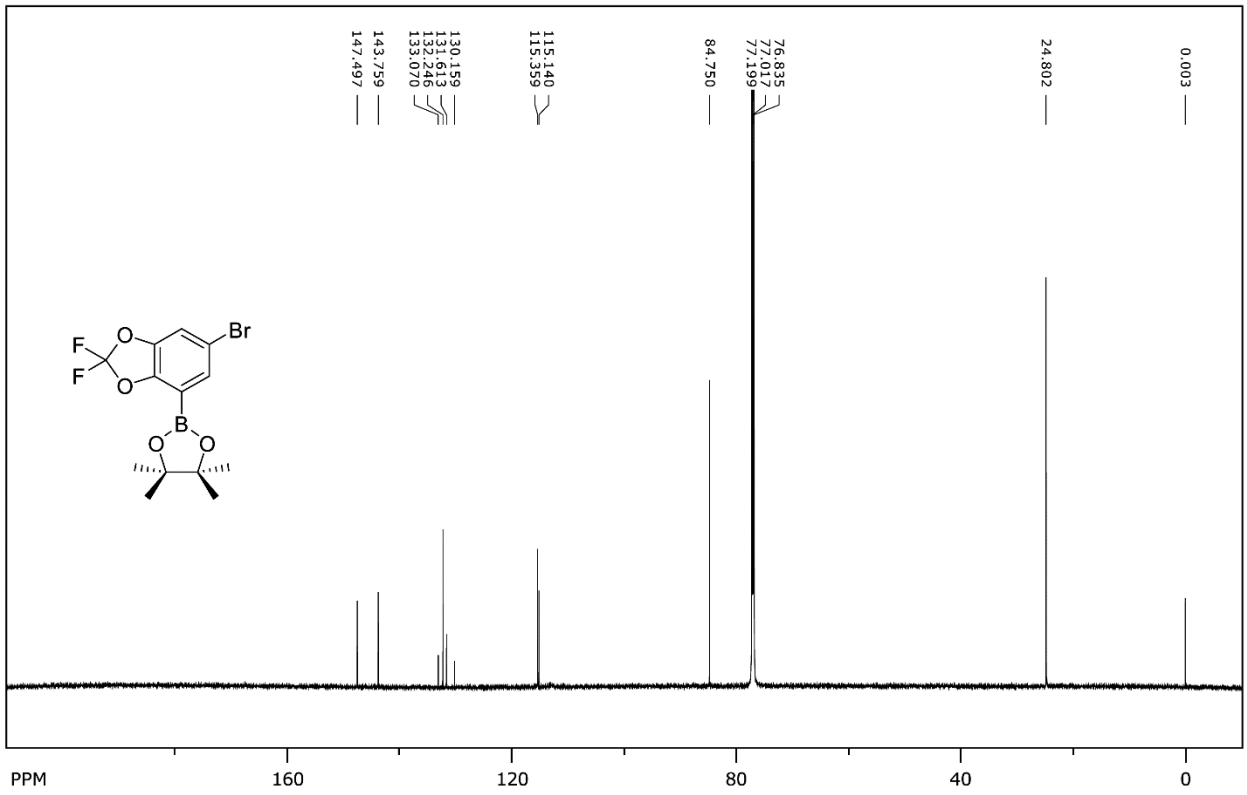
Compound 2f: ^{1}H NMR spectrum of 2-(3,4-bis(1,1,2,2-tetrafluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



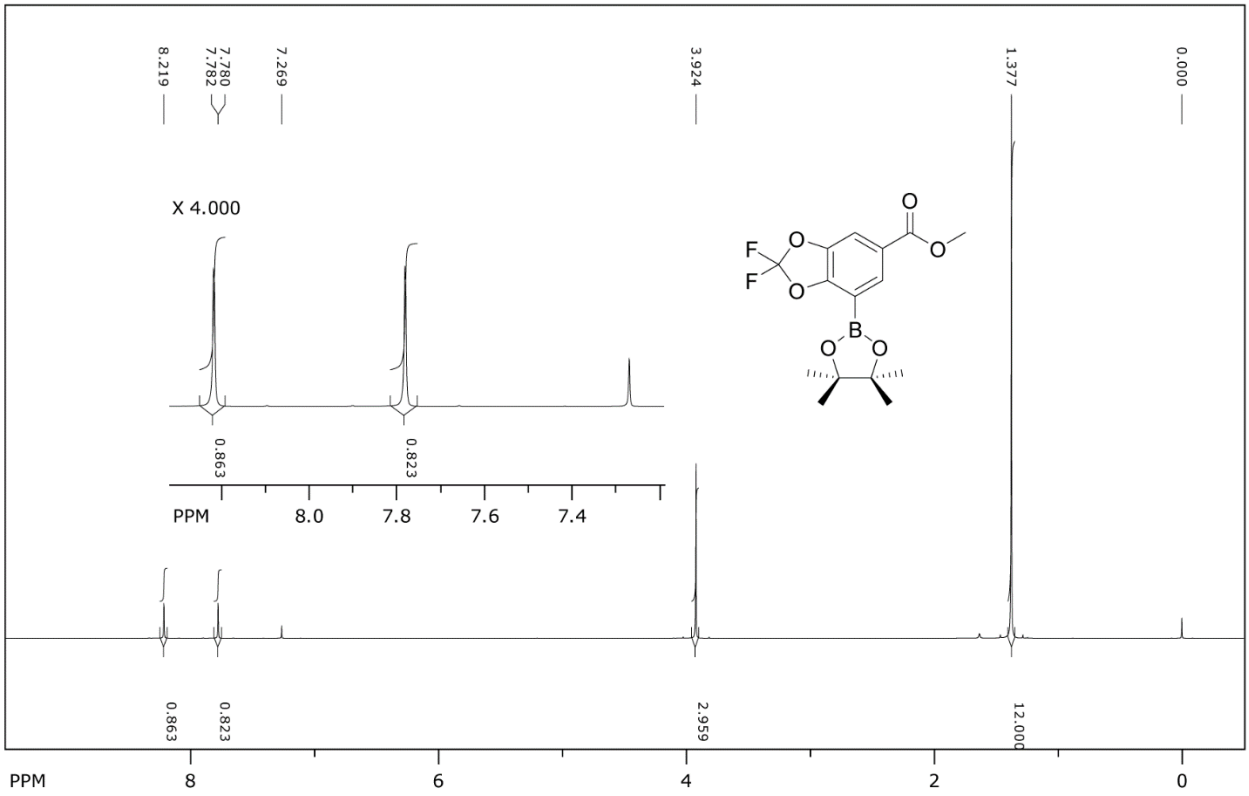
Compound 2f: ^{13}C NMR spectrum of 2-(3,4-bis(1,1,2,2-tetrafluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



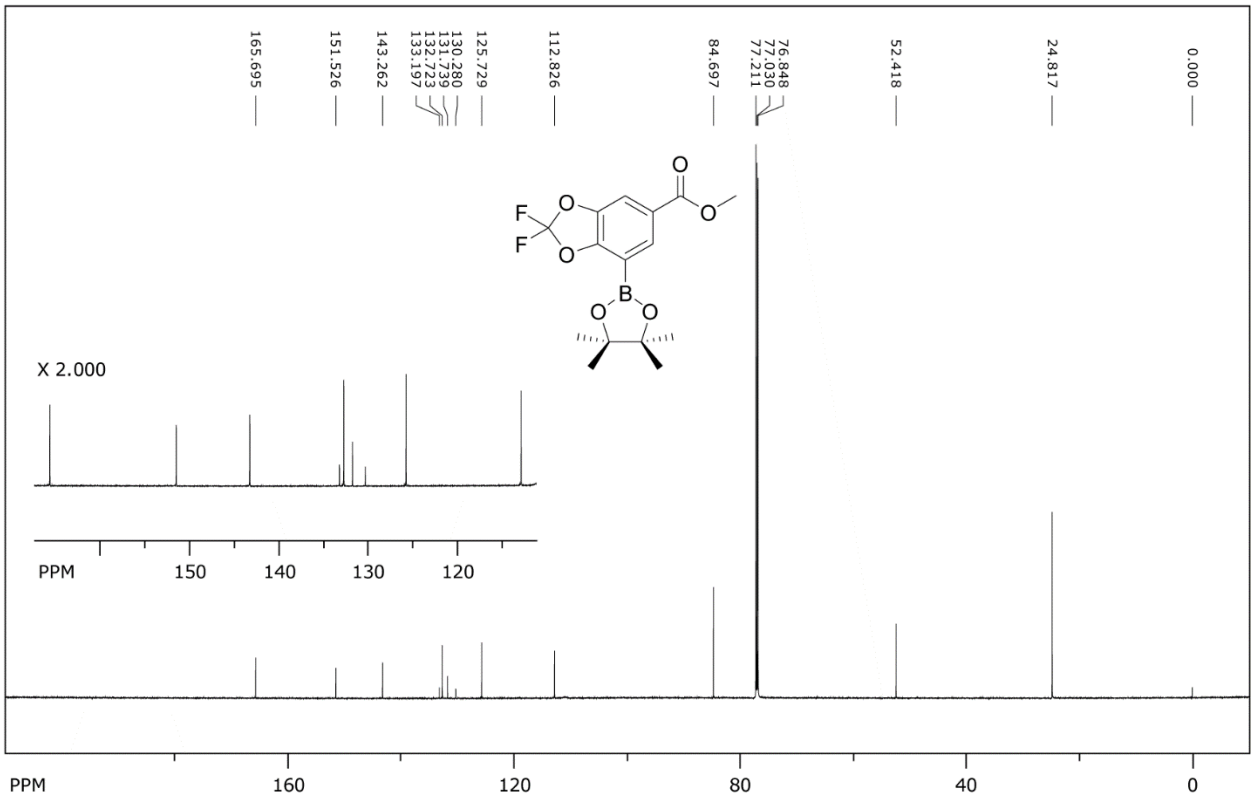
Compound 2g: ^{1}H NMR spectrum of 2-(6-bromo-2,2-difluorobenzo[d][1,3]dioxol-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



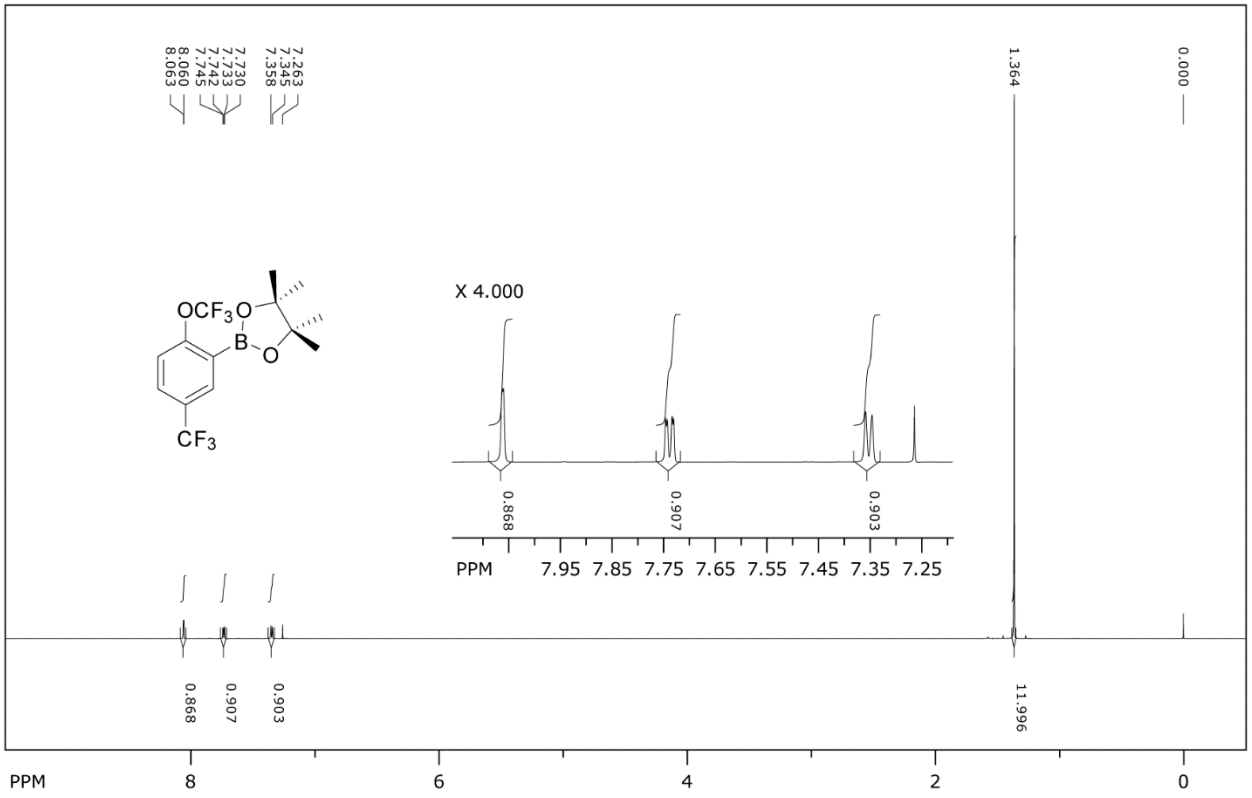
Compound 2g: ^{13}C NMR spectrum of 2-(6-bromo-2,2-difluorobenzo[d][1,3]dioxol-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



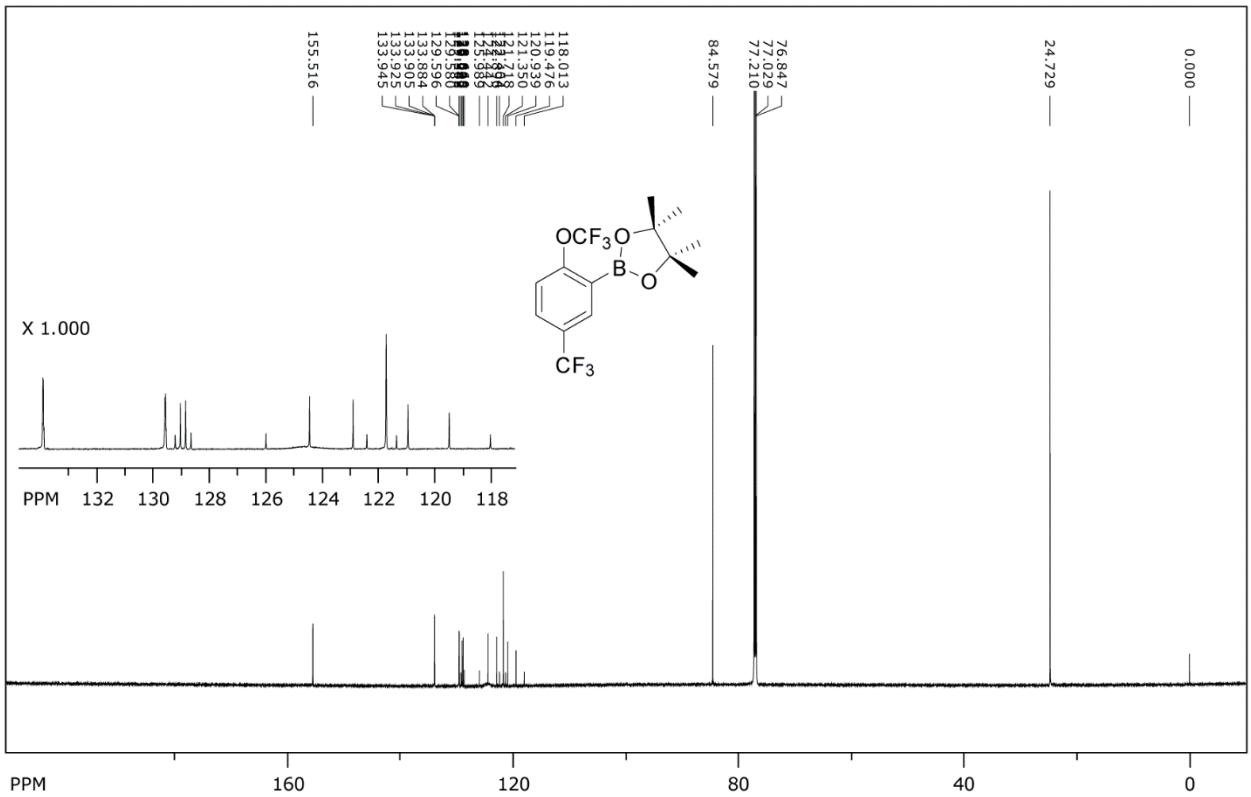
Compound 2h: ^{1}H NMR spectrum of Methyl 2,2-difluoro-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[d][1,3]dioxole-5-carboxylate



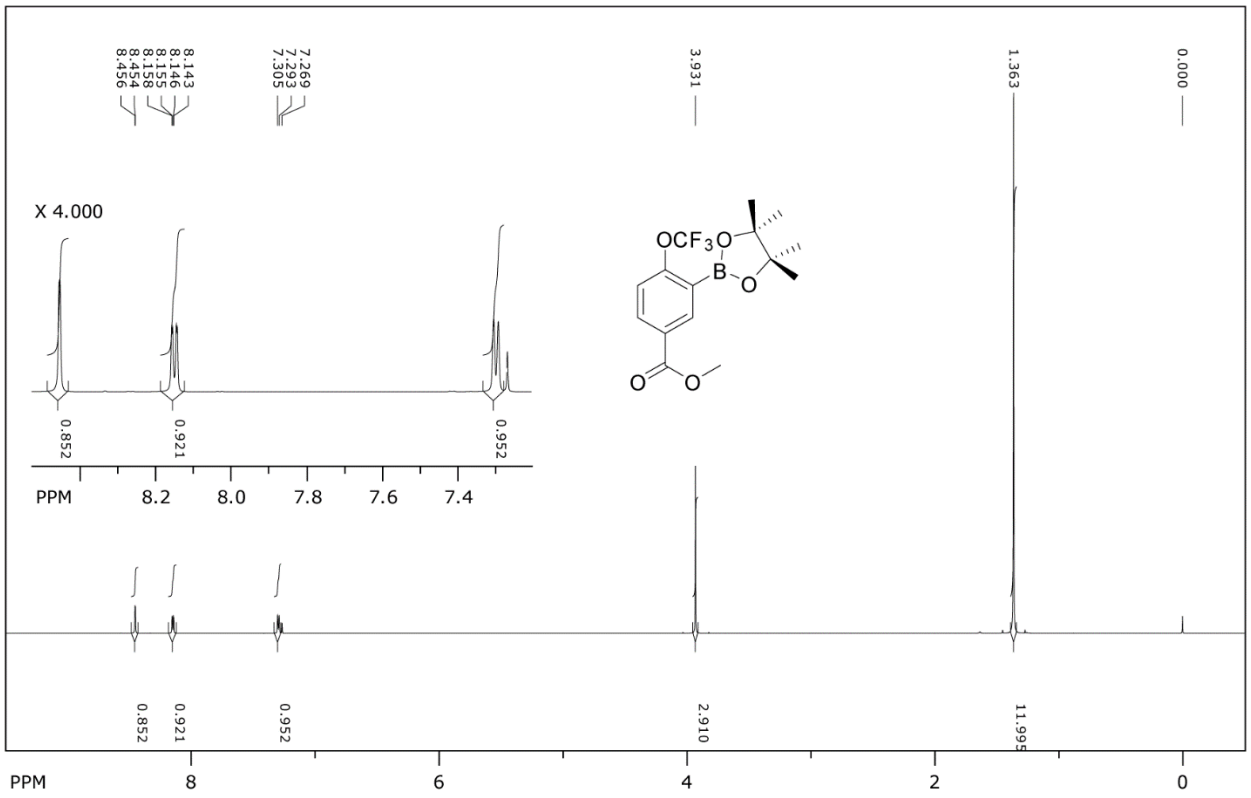
Compound 2h: ^{13}C NMR spectrum of Methyl 2,2-difluoro-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[d][1,3]dioxole-5-carboxylate



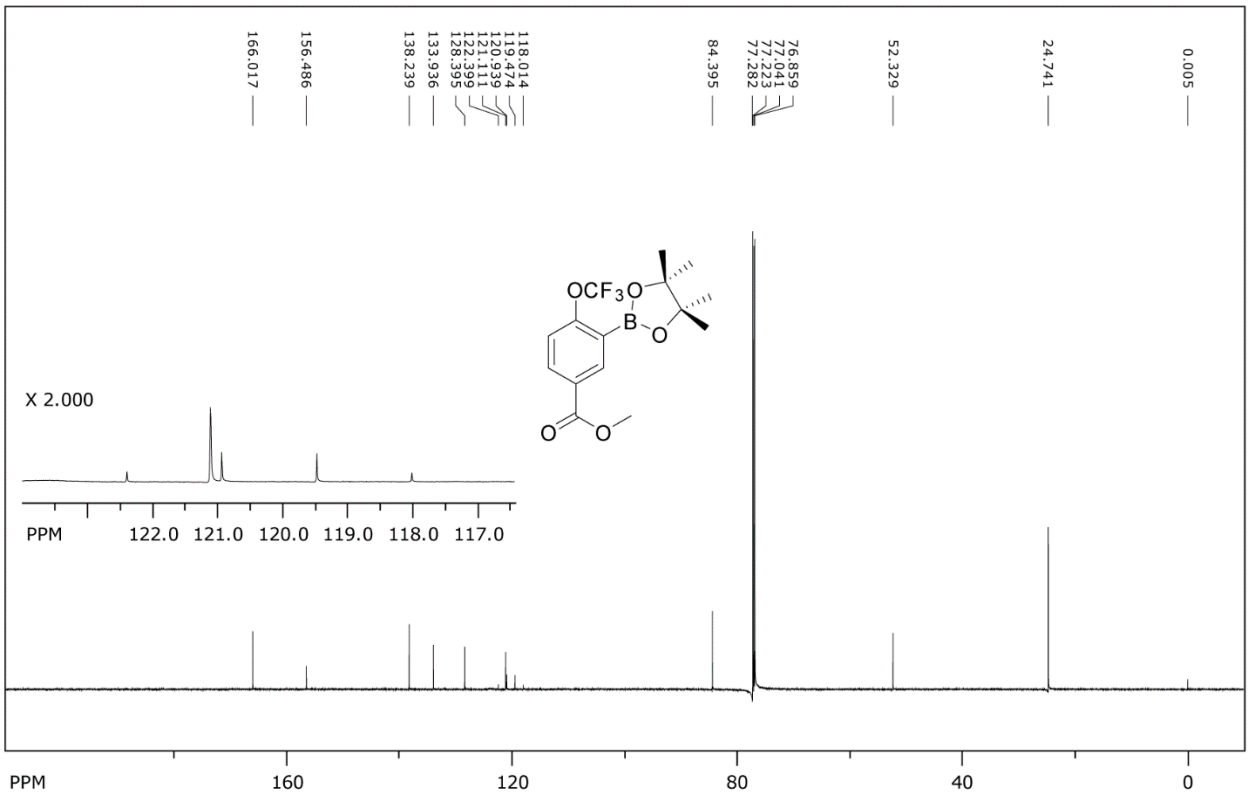
Compound 3a: ^{1}H NMR spectrum of 4,4,5,5-tetramethyl-2-(2-(trifluoromethoxy)-5-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane



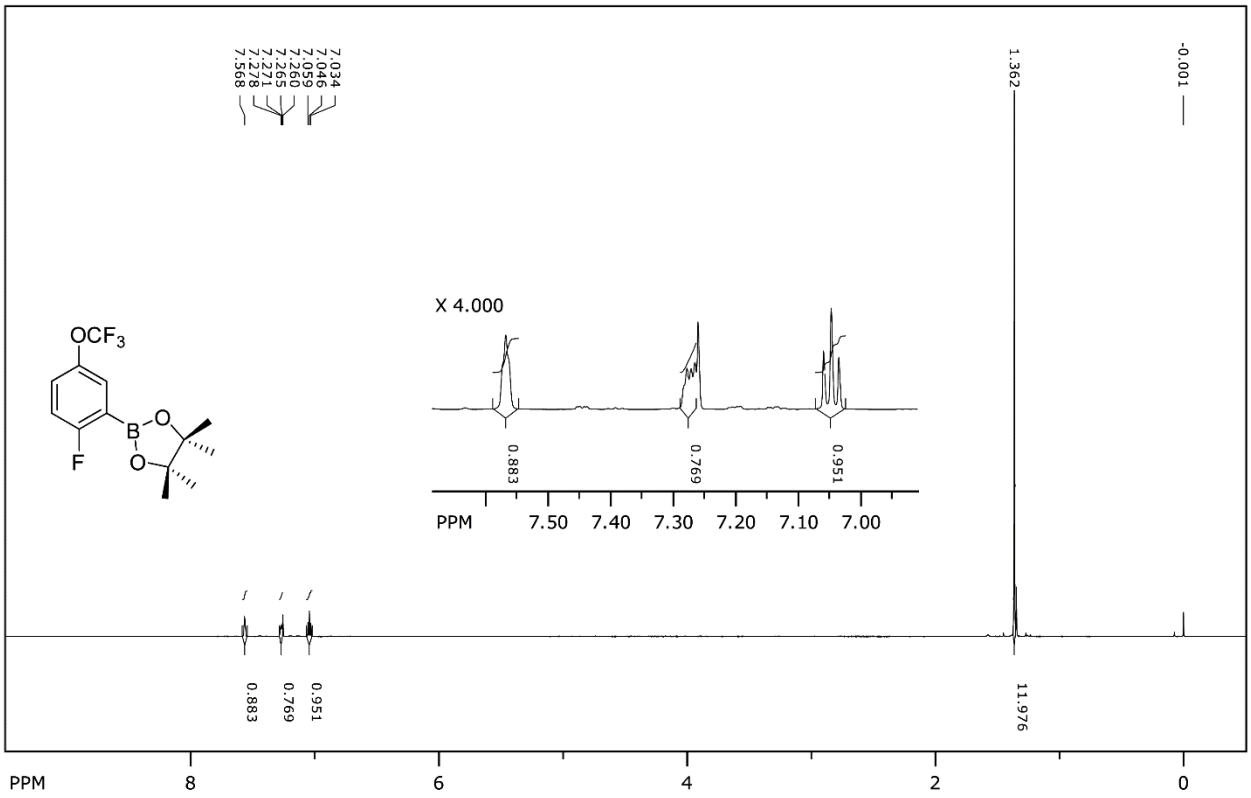
Compound 3a: ^{13}C NMR spectrum of 4,4,5,5-tetramethyl-2-(2-(trifluoromethoxy)-5-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane



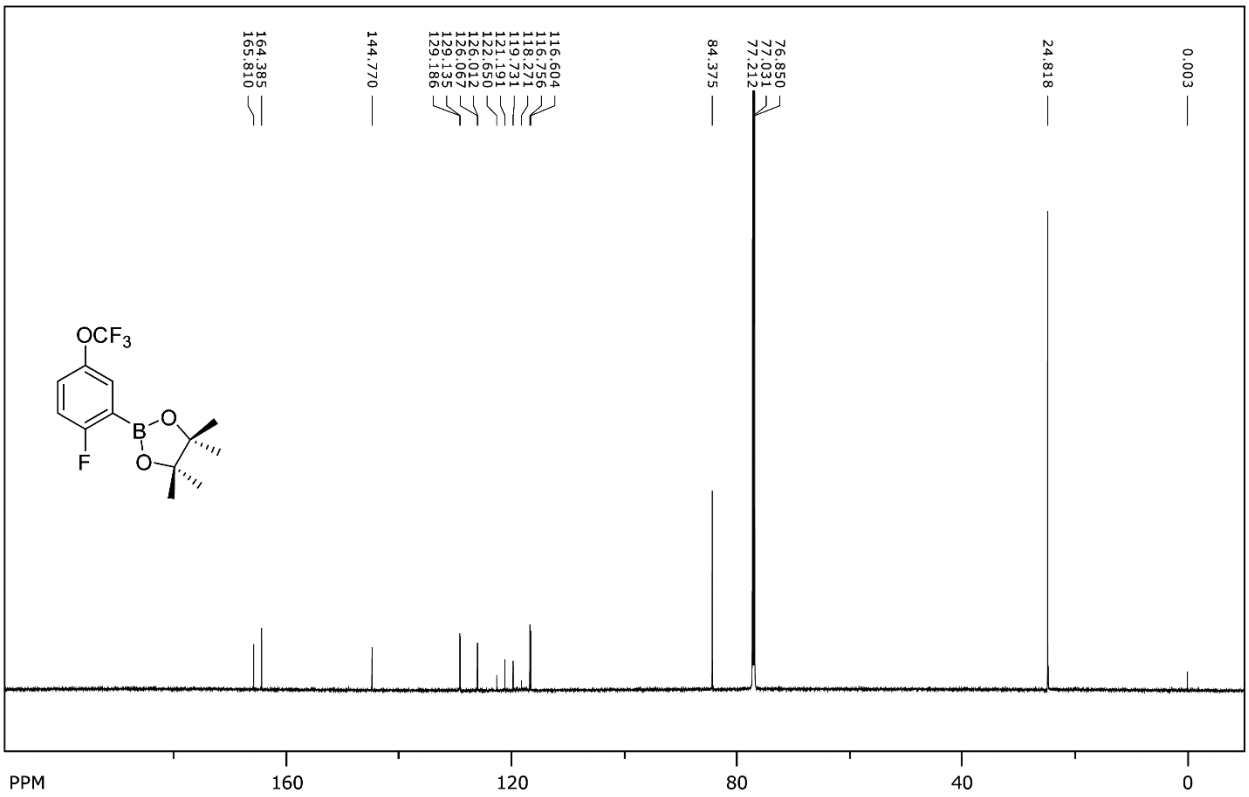
Compound 3b: ^{1}H NMR spectrum of Methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethoxy)benzoate



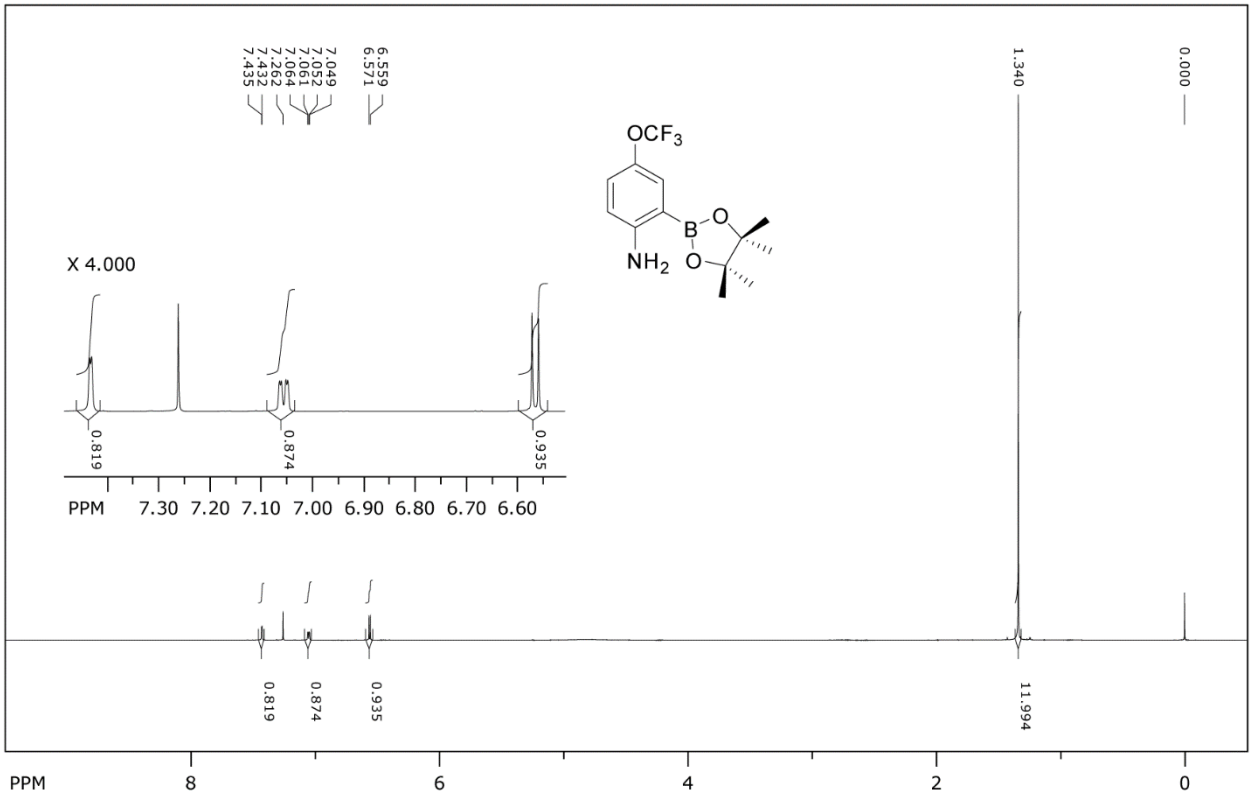
Compound 3b: ^{13}C NMR spectrum of Methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethoxy)benzoate



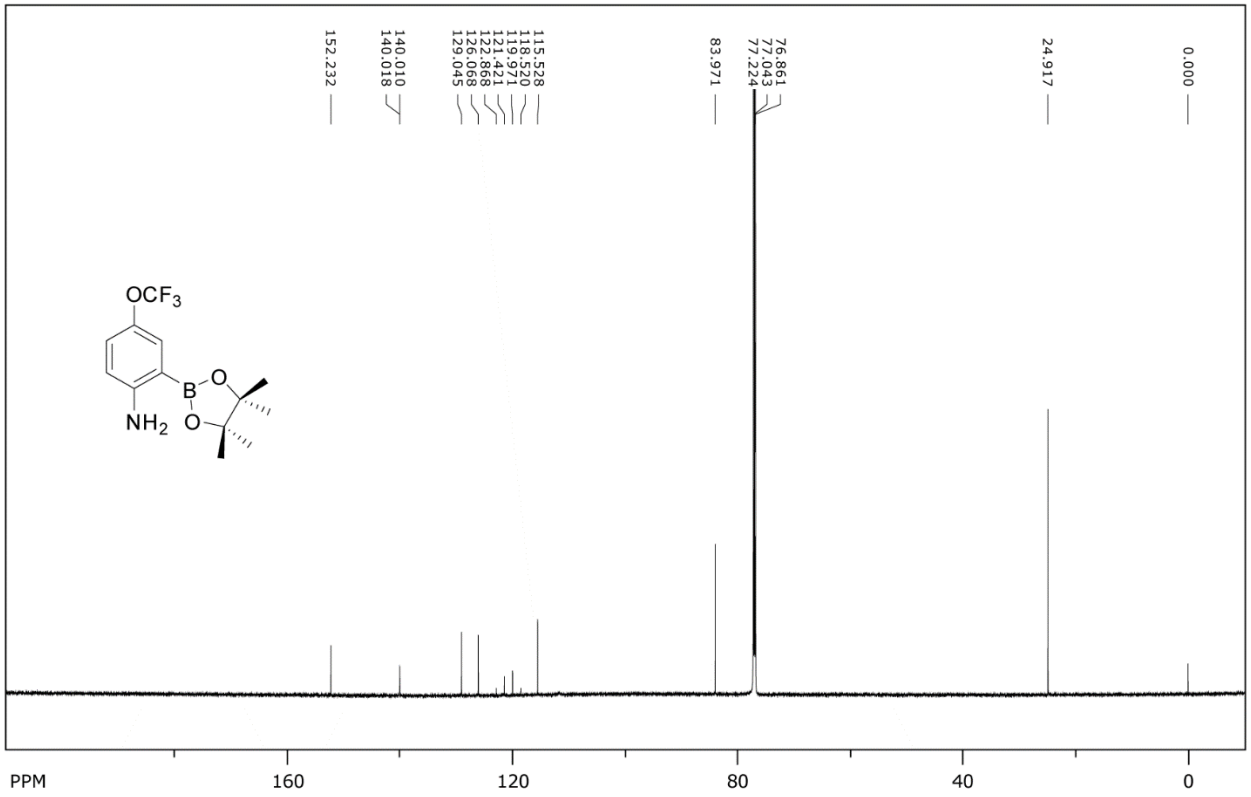
Compound 3c: ^{1}H NMR spectrum of 2-(2-fluoro-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



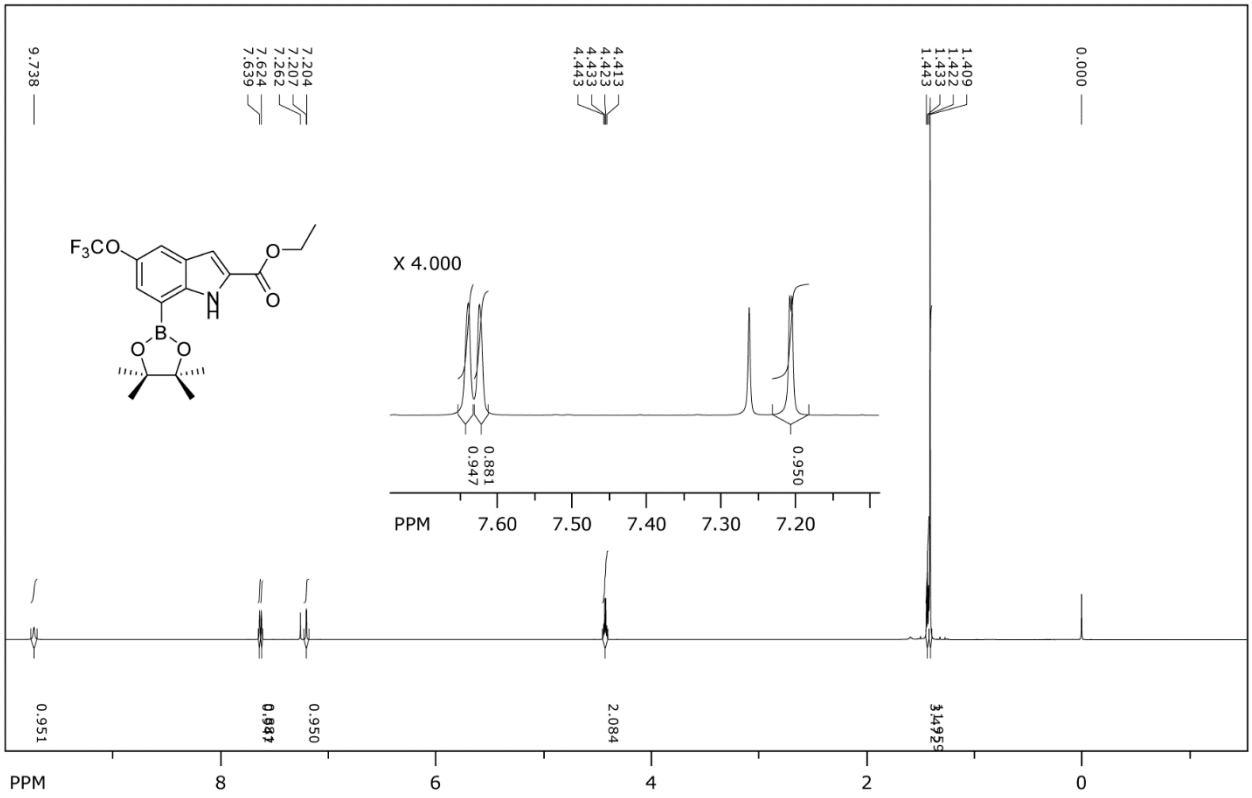
Compound 3c: ^{13}C NMR spectrum of 2-(2-fluoro-5-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



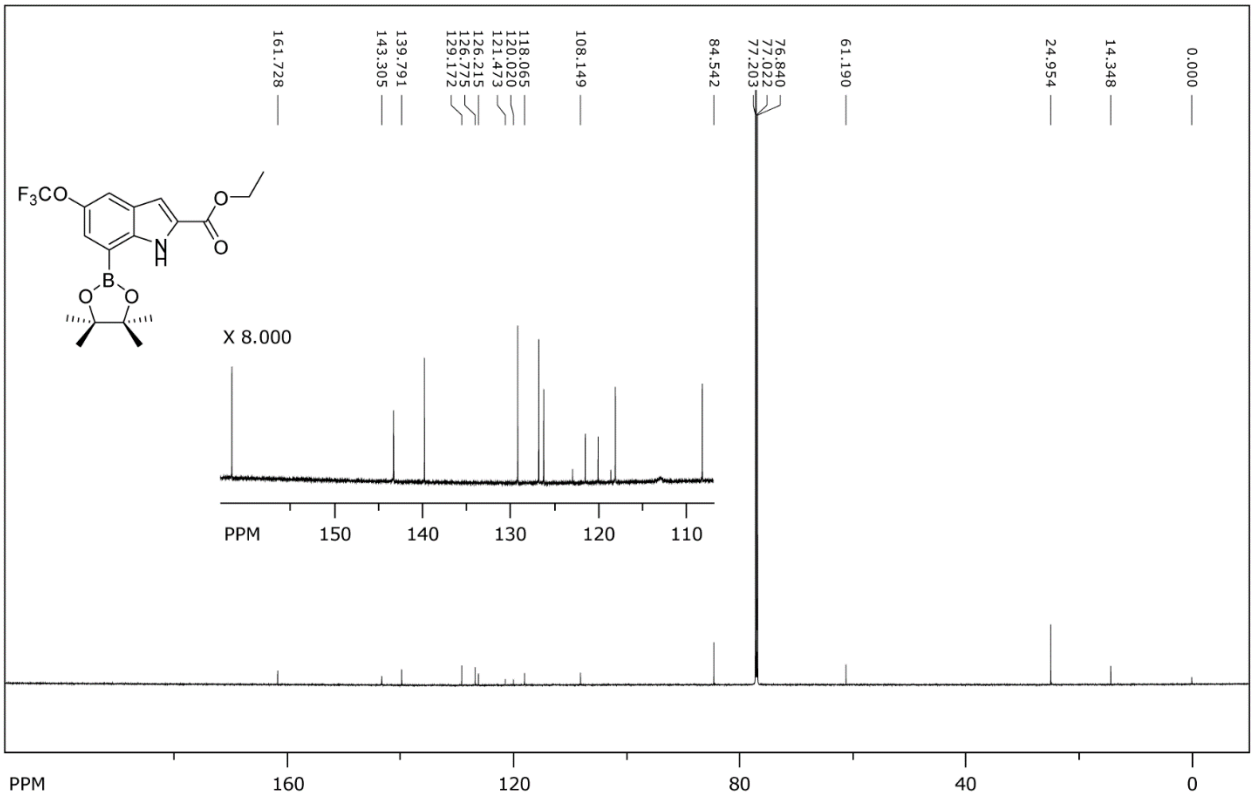
Compound 3d: ^{1}H NMR spectrum of 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethoxy)aniline



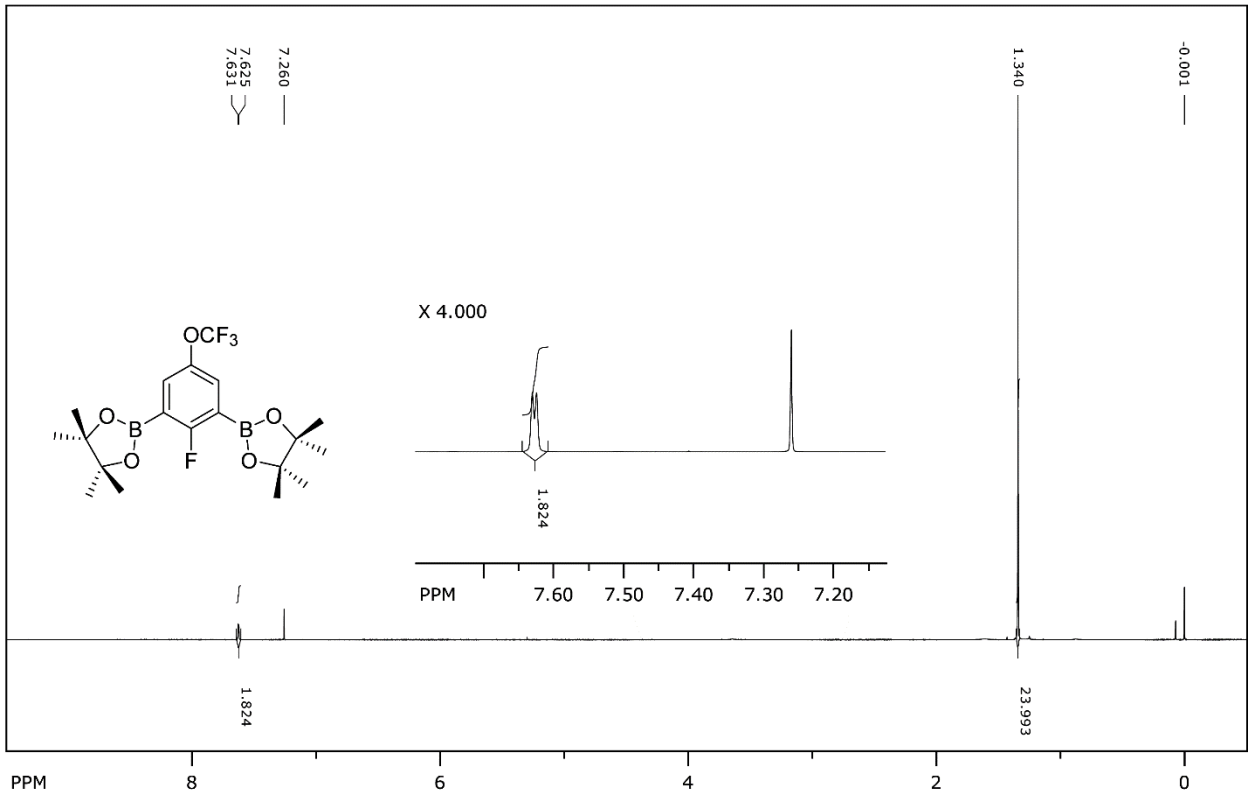
Compound 3d: ^{13}C NMR spectrum of 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethoxy)aniline



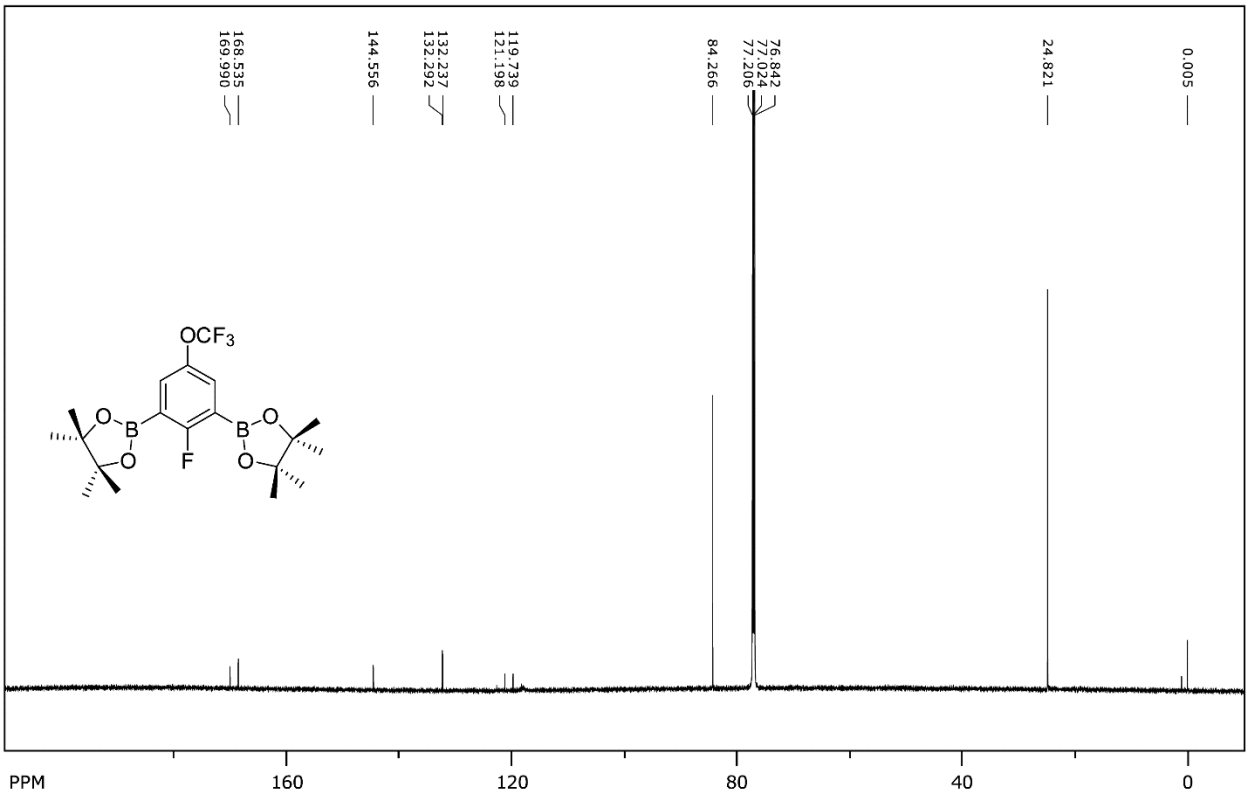
Compound 3e: ^{1}H NMR spectrum of Ethyl 7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethoxy)-1H-indole-2-carboxylate



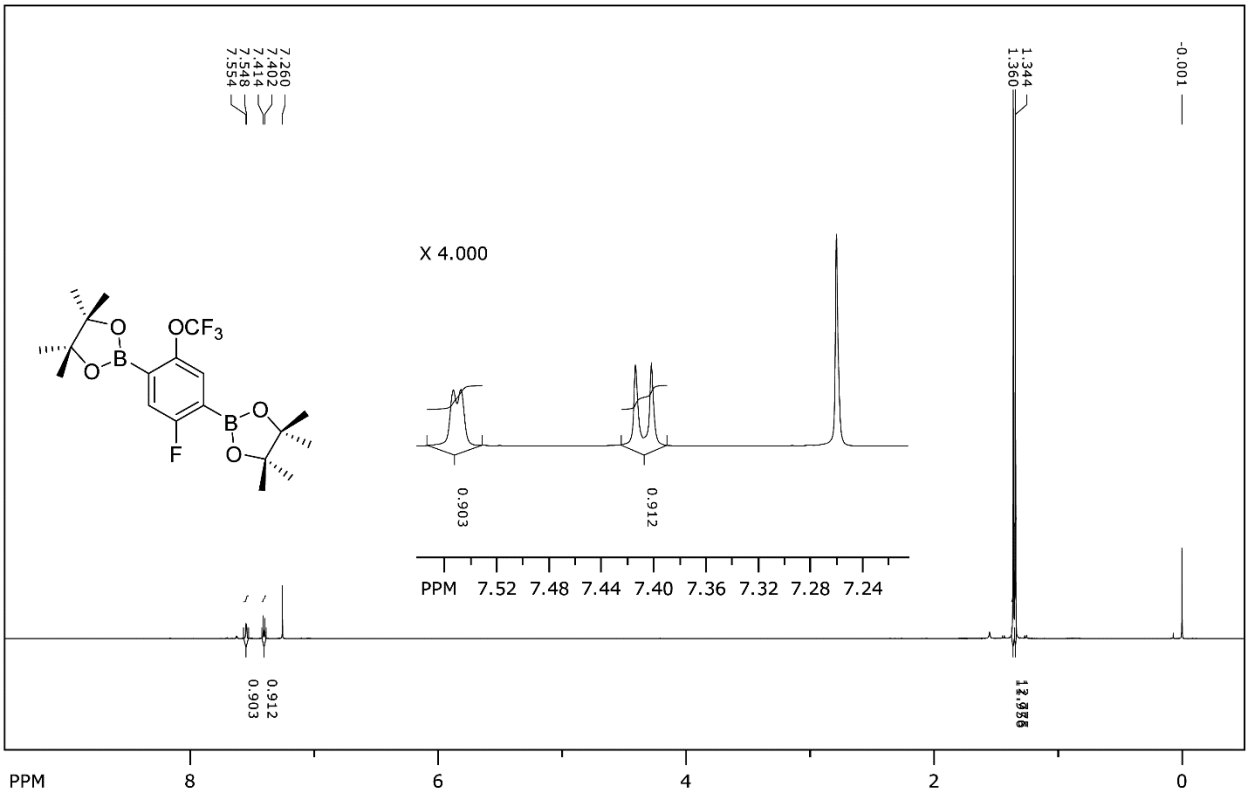
Compound 3e: ^{13}C NMR spectrum of Ethyl 7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethoxy)-1H-indole-2-carboxylate



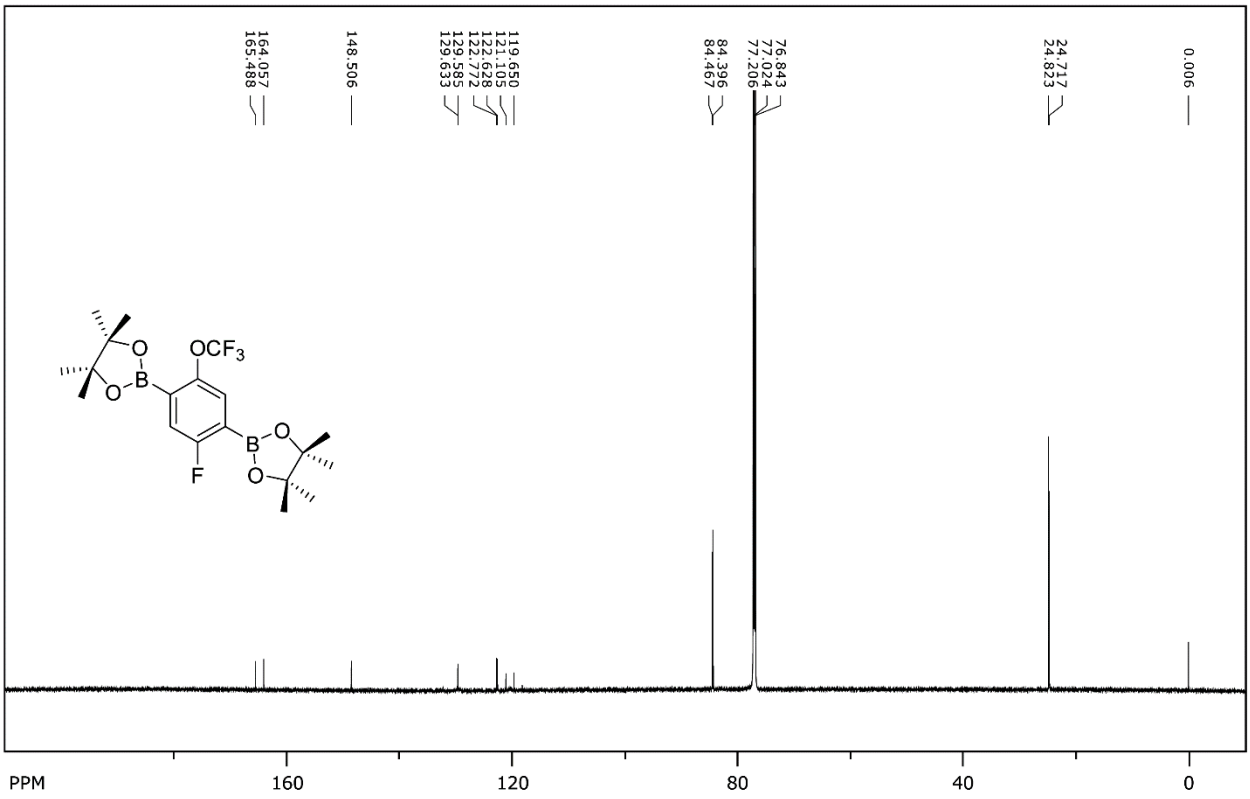
Compound 4a: ^{1}H NMR spectrum of the Major Di-borylated Isomer: 2,2'-(2-fluoro-5-(trifluoromethoxy)-1,3-phenylene)bis(4,4,5,5-tetramethyl-1,3,2 dioxaborolane)



Compound 4a: ^{13}C NMR spectrum of the Major Di-borylated Isomer: 2,2'-(2-fluoro-5-(trifluoromethoxy)-1,3-phenylene)bis(4,4,5,5-tetramethyl-1,3,2 dioxaborolane)

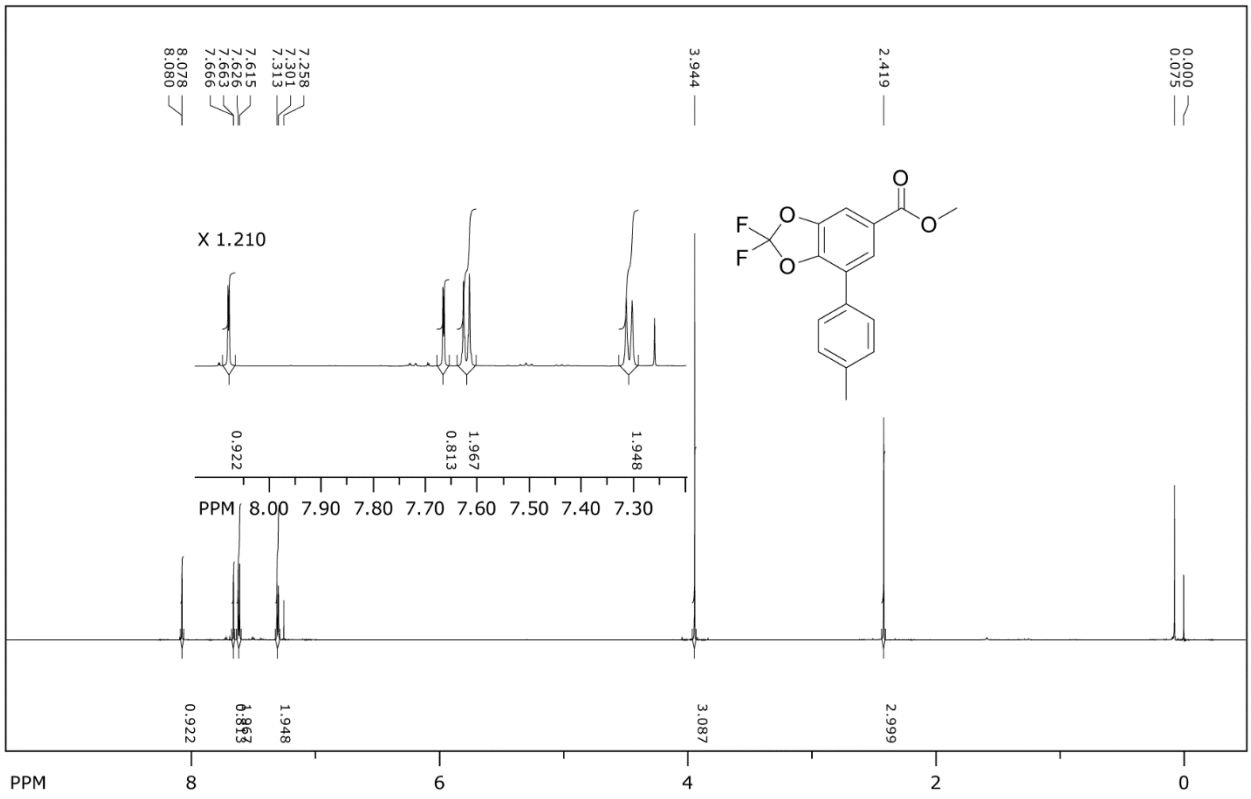


Compound 4b: ^{1}H NMR spectrum of the Minor Di-Borylated Isomer: 2,2'-(2-fluoro-5-(trifluoromethoxy)-1,4-phenylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

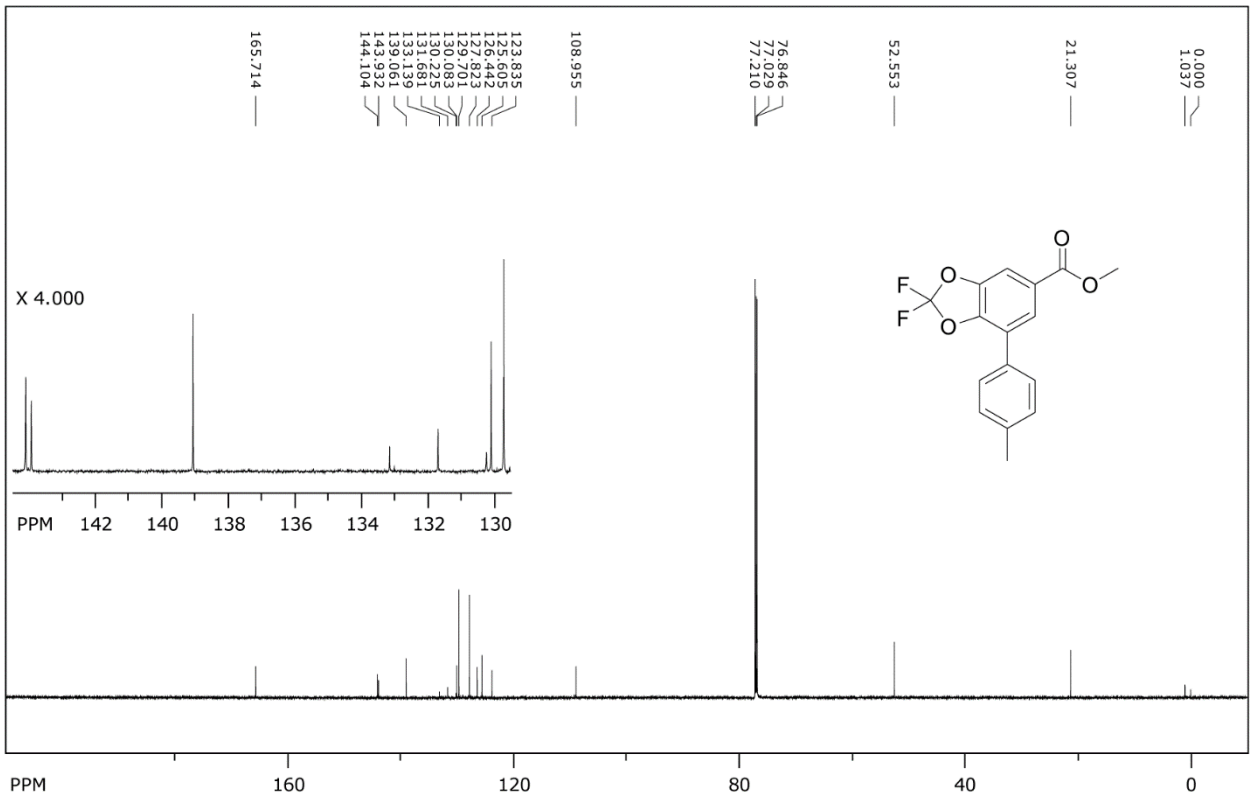


Compound 4b: ^{13}C NMR spectrum of the Minor Di-Borylated Isomer: 2,2'-(2-fluoro-5-(trifluoromethoxy)-1,4-phenylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

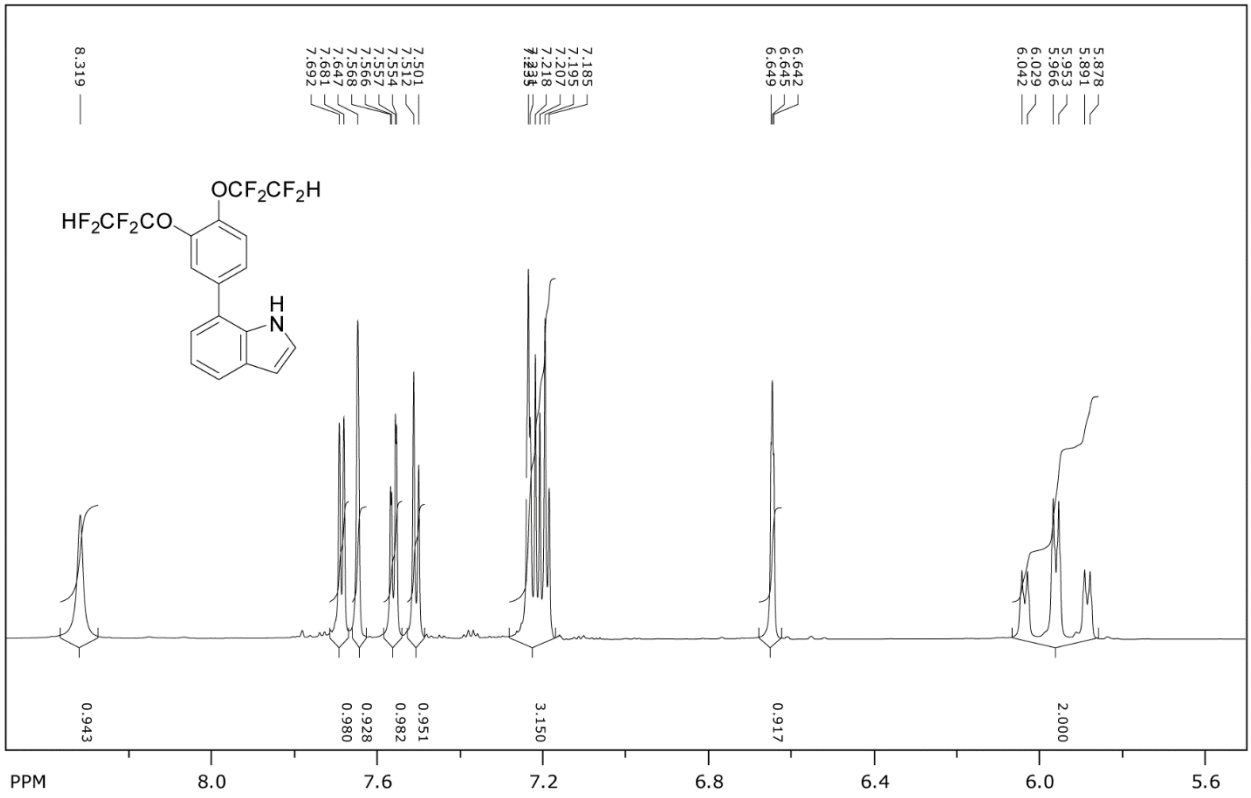
Suzuki Coupling



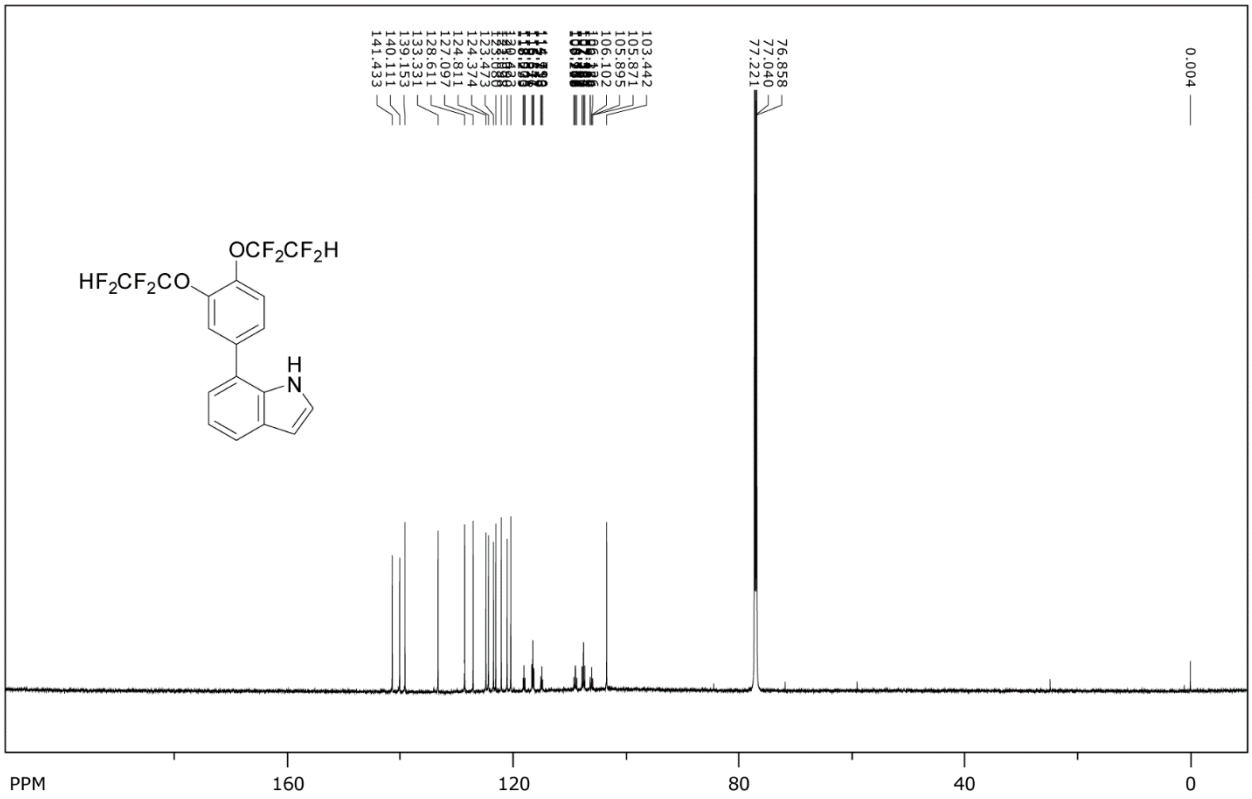
Compound 5a: ^{1}H NMR spectrum of Methyl 2,2-difluoro-7-(p-tolyl)benzo[d][1,3]dioxole-5-carboxylate



Compound 5a: ^{13}C NMR spectrum of Methyl 2,2-difluoro-7-(p-tolyl)benzo[d][1,3]dioxole-5-carboxylate



Compound 5b: ^{1}H NMR spectrum of 7-(3,4-Bis(1,1,2,2-tetrafluoroethoxy)phenyl)-1H-indole



Compound 5b: ^{13}C NMR spectrum of 7-(3,4-Bis(1,1,2,2-tetrafluoroethoxy)phenyl)-1H-indole