A C-H Borylation Approach to Suzuki-Miyaura Coupling of Typically Unstable 2-Heteroaryl and Polyfluorophenyl Boronates with Simple Catalysts

Supporting Information

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Experimental Information

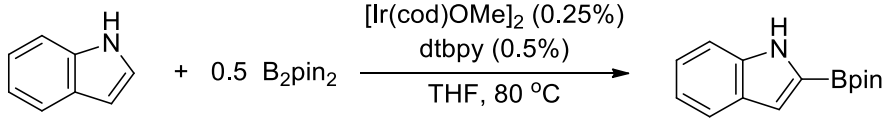
General Procedures. All reactions were conducted under a nitrogen atmosphere in flame-dried glassware or in an inert atmosphere glovebox. Dry and degassed solvents were used unless otherwise noted. The water used as co-solvent was deionized and degassed by bubbling N_2 gas for 10 minutes. Column chromatography was performed with a Teledyne Isco Combiflash® R_f system with Redi*Sep* R_f columns. Analytical thin-layer chromatography was performed on glass plates coated with silica gel (Silicycle, 60 A pore size, 40-64 um particle size) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by ultraviolet light and staining solution of *p*-anisaldehyde or KMnO4.

Materials. $[Ir(cod)OMe]_2$ and Q-phos (1,2,3,4,5-Pentaphenyl-1'-(di-*t*-butylphosphino)ferrocene) were obtained from Johnson Matthey and used as received. 4,4'-Di-*tert*-butylbipyridine was obtained from Aldrich Chemicals and used as received. Bis(pinacolato)diboron (B_2pin_2) was obtained from Allychem and used as received. Arenes, heteroarenes, aryl halides, tri-*o*-tolylphosphine, sodium carbonate, potassium phosphate, and pinacolborane were obtained from Aldrich, Alfa Aesar, Acros, Combiblocks, Oakwood Chemicals or TCI America and used as received. Heteroaryl boronic acids and boronate esters were obtained from Combi-Blocks or Aldrich and used as received. $Pd(dba)_2$ was synthesized according to published procedures.[1] Pd-hydroxide complexes were prepared according to published procedures.[2]

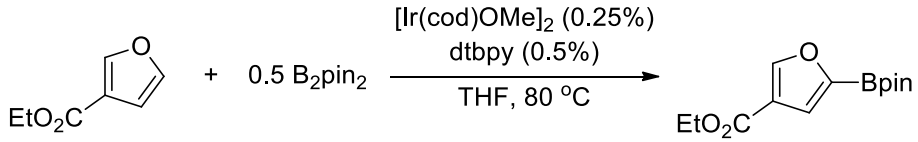
Instruments. ^1H NMR spectra were recorded on a 500 MHz Varian instrument (126 MHz for ^{13}C). Chemical shifts are reported in parts per million relative to residual protiated solvent (7.26 ppm for $CDCl_3$). The carbon bonded to boron in the arene and heteroarene borylation products were not observed via ^{13}C NMR spectroscopy. This observation is consistent with previous reports of borylated arenes and heteroarenes.[3] GC-MS data were obtained on an Agilent 6890-N GC system containing an Alltech EC-1 capillary column and an Agilent 5973 mass selective detector. GC analyses were obtained on an Agilent 6890 Gas Chromatograph equipped with an HP- 5 25 m x 0.20 mm ID x 0.33 μm capillary column (Agilent) and an FID detector.

Experimental Procedures

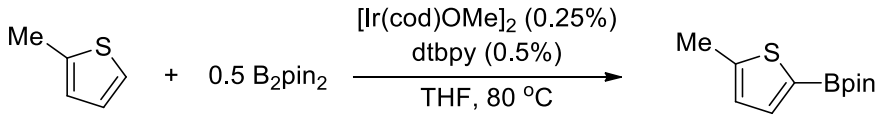
General Procedure for the Borylation of Heteroarenes. Inside a glove box, $[Ir(cod)OMe]_2$ (1.7 mg, 0.0025 mmol, 0.0025 equiv), dtbpy (1.4 mg, 0.0050 mmol, 0.0050 equiv), B_2pin_2 (127 mg, 0.500 mmol, 0.500 equiv) or HBpin (141 mg, 1.10 mmol, 1.10 equiv), the heteroarene (1.00 mmol, 1.00 equiv), and THF (2 mL) were added consecutively to a dry vial with a magnetic stir bar. The vial was sealed and heated at 80 °C for 18 h. The reaction mixture was cooled to room temperature, concentrated and purified by column chromatography to give the product.



Borylation of Indole. Prepared according to the general procedure with indole (117 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (175 mg, 72%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 8.60 (s, 1H), 7.70 (d, J = 8.1 Hz, 1H), 7.40 (m, 1H), 7.25 (m, 1H), 7.13 (m, 2H), 1.38 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.48, 128.55, 123.87, 121.85, 120.03, 114.12, 111.51, 84.40, 25.07. Anal. Calcd for $C_{14}H_{17}BNO_2$: C, 68.17; H, 7.46; N, 5.76. Found: C, 69.55; H, 7.42; N, 6.08.

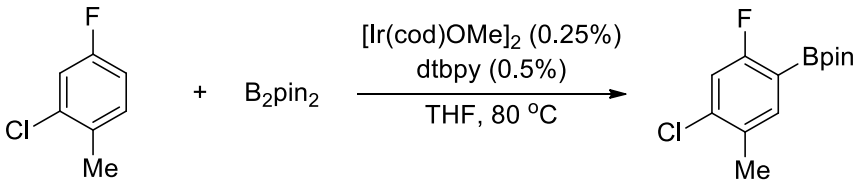


Borylation of ethyl 3-furoate. Prepared according to the general procedure with ethyl 3-furoate (140 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (172 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.31 (s, 1H), 4.22 (q, J = 6.9 Hz, 2H), 1.24 (m, 15H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.06, 151.99, 123.01, 120.45, 84.77, 60.65, 24.88, 14.43. Anal. Calcd for $C_{13}H_{19}BO_5$: C, 58.68; H, 7.20. Found: C, 58.75; H, 7.12.

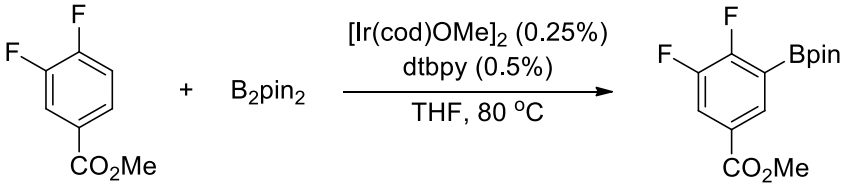


Borylation of 2-Methylthiophene. Prepared according to the general procedure with 2-methylthiophene (98 mg, 1.0 mmol, 1.0 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (166 mg, 74%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.48 (d, J = 3.4 Hz, 1H), 6.86 (d, J = 3.3 Hz, 1H), 2.55 (s, 3H), 1.35 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.73, 137.89, 127.24, 84.08, 24.99, 15.62. Anal. Calcd for $C_{11}H_{17}BO_2S$: C, 58.95; H, 7.65. Found: C, 58.71; H, 7.40.

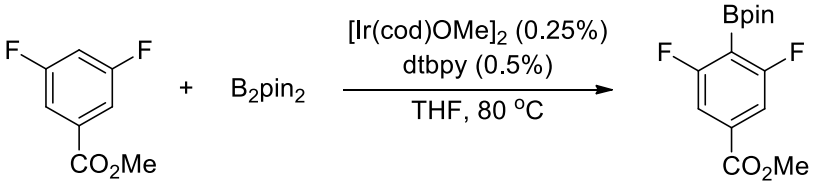
General Procedure for the Borylation of Fluoroarenes. Inside a glove box, $[Ir(cod)OMe]_2$ (1.7 mg, 0.0025 mmol, 0.0025 equiv), dtbpy (1.4 mg, 0.0050 mmol, 0.0050 equiv), B_2pin_2 (153 mg, 0.600 mmol, 0.600 equiv) or HBpin (141 mg, 1.10 mmol, 1.10 equiv), the arene (1.00 mmol, 1.00 equiv), and THF (2 mL) were added consecutively to a dry vial with a magnetic stir bar. The vial was sealed and heated at 80 °C for 18 h. The reaction mixture was cooled to room temperature and purified by column chromatography to give the product.



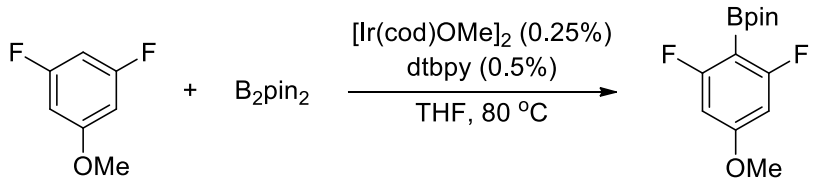
Borylation of 2-chloro-4-fluorotoluene. Prepared according to the general procedure with 2-chloro-4-fluorotoluene (144 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (223 mg, 83%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.58 (d, J = 6.3 Hz, 1H), 7.07 (d, J = 8.9 Hz, 1H), 2.33 (s, 3H), 1.37 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.46 (d, J = 252.9 Hz), 138.45 (d, J = 8.7 Hz), 131.57 (d, J = 3.7 Hz), 116.52 (d, J = 5.3 Hz), 116.30 (d, J = 5.1 Hz), 84.25 (s), 25.01 (s), 19.18 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.11 (s). Anal. Calcd for $C_{13}H_{17}BClFO_2$: C, 57.71; H, 6.33. Found: C, 58.04; H, 6.14.



Borylation of Methyl 3,4-difluorobenzoate. Prepared according to the general procedure with methyl 3,4-difluorobenzoate (172 mg, 1.0 mmol, 1.0 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (217 mg, 73%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 8.16 (dd, J = 4.1, 2.0 Hz, 1H), 7.88 (ddd, J = 10.2, 7.6, 2.2 Hz, 1H), 3.90 (s, 3H), 1.35 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.40 (d, J = 2.3 Hz), 157.71 (dd, J = 260.6, 12.0 Hz), 150.25 (dd, J = 250.5, 14.9 Hz), 133.244 (dd, J = 7.9 Hz, 3.7 Hz), 126.83 (t, J = 4.4Hz), 121.491 (dd, J = 18.8 Hz, 2.3 Hz), 84.73 (s), 52.58 (s), 24.99 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.44 (dd, J = 4.1, 21.3), -137.78 (dd, J = 10.5, 21.2). Anal. Calcd for $C_{14}H_{17}BF_2O_4$: C, 56.41; H, 5.75. Found: C, 56.30; H, 5.68.

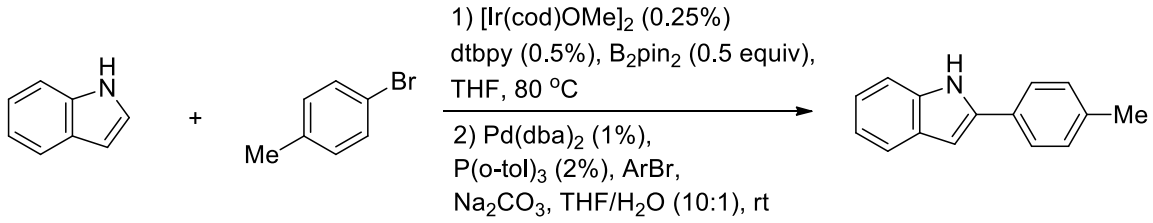


Borylation of Methyl 3,5-difluorobenzoate. Prepared according to the general procedure with methyl 3,5-difluorobenzoate (172 mg, 1.0 mmol, 1.0 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (202 mg, 68%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.48 (m, 2H), 3.91 (s, 3H), 1.37 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.36 (dd, J = 251.3, 12.8 Hz), 165.03 (t, J = 3.4 Hz), 135.25 (t, J = 9.9 Hz), 112.35 (m), 84.88 (s), 52.82 (s), 24.91 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.06 (d, J = 6.5). Anal. Calcd for $C_{14}H_{17}BF_2O_4$: C, 56.41; H, 5.75. Found: C, 56.15; H, 6.01.



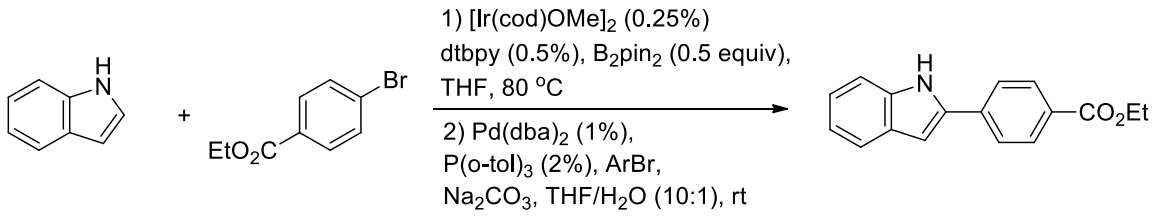
Borylation of 3,5-difluoroanisole. Prepared according to the general procedure with 3,5-difluoroanisole (144 mg, 1.0 mmol, 1.0 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (200 mg, 74%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 6.38 (d, J = 9.5 Hz, 2H), 3.78 (s, 3H), 1.35 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.19 (dd, J = 249.8, 16.6 Hz), 164.11 (t, J = 14.7 Hz), 97.92 (m), 83.94 (s), 55.94 (s), 24.94 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.53 (d, J = 8.2). Anal. Calcd for $C_{13}H_{17}BF_2O_3$: C, 57.81; H, 6.34. Found: C, 57.82; H, 6.24.

General Procedure for one-pot C-H Borylation and Suzuki-Miyaura cross-coupling of heteroarenes with aryl bromides. Inside a glove box, $[Ir(cod)OMe]_2$ (2.0 mg, 0.0030 mmol, 0.0030 equiv), dtbpy (1.6 mg, 0.0060 mmol, 0.0060 equiv), B_2pin_2 (153 mg, 0.600 mmol, 0.600 equiv), the heteroarene (1.20 mmol, 1.20 equiv), and THF (2 mL) were added consecutively to a dry vial with a magnetic stir bar. The vial was sealed and heated at 80 °C for 18 h. The reaction mixture was cooled to room temperature, and the volatile materials were removed under vacuum. $Pd(dba)_2$ (5.8 mg, 0.010 mmol, 0.010 equiv), tri-*o*-tolylphosphine (6.1 mg, 0.020 mmol, 0.020 equiv), Na_2CO_3 (424 mg, 4.00 mmol, 4.00 equiv), the aryl halide (1.00 mmol, 1.00 equiv), THF (3 mL) and degassed H_2O (0.3 mL) were added consecutively to the reaction mixture. The reaction mixture was sealed and stirred at room temperature for 18 h. The reaction mixture was filtered through silica gel, washing with EtOAc, and concentrated under vacuum. The reaction mixture was purified by column chromatography to give the product.

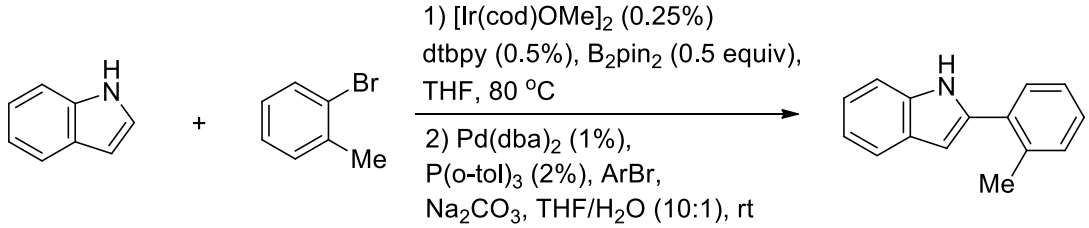


Arylation of indole with 4-bromotoluene. Prepared according to the general procedure with indole (141 mg, 1.20 mmol, 1.20 equiv) and 4-bromotoluene (171 mg, 1.00 mmol,

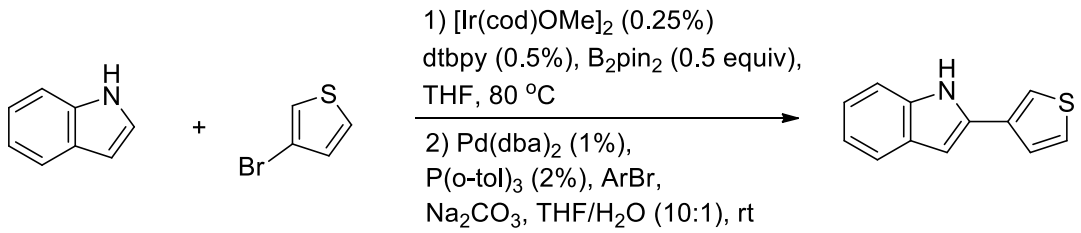
1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (174 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.66 (d, J = 7.8 Hz, 1H), 7.57 (d, J = 8.1 Hz, 2H), 7.40 (d, J = 7.8 Hz, 1H), 7.27 (d, J = 7.8 Hz, 2H), 7.22 (m, 1H), 7.16 (t, J = 7.5 Hz, 1H), 6.82 (s, 1H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.32, 137.89, 136.95, 129.96, 128.69, 125.32, 122.37, 120.77, 120.45, 111.10, 102.85, 99.64, 21.51. Anal. Calcd for $C_{15}H_{13}N$: C, 86.92; H, 6.32; N, 6.76. Found: C, 86.60; H, 6.29; N, 6.79.



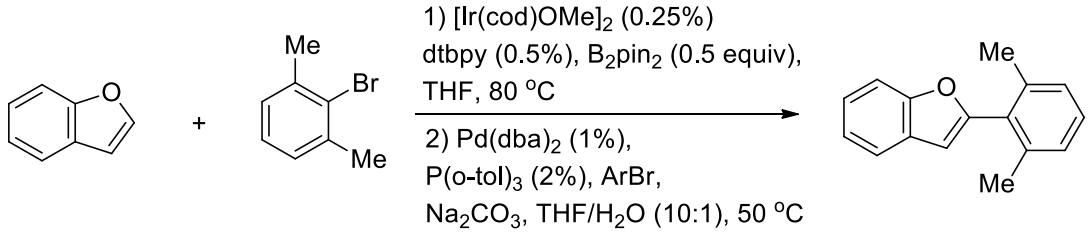
Arylation of indole with ethyl 4-bromobenzoate. Prepared according to the general procedure with indole (141 mg, 1.20 mmol, 1.20 equiv) and ethyl 4-bromobenzoate (229 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (15% EtOAc:85% hexanes) to give the product (231 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.04 (s, 1H), 8.00 (s, 1H), 7.52 (d, J = 8.5 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 7.20 (t, J = 2.8 Hz, 1H), 6.92 (s, 1H), 6.58 (s, 1H), 4.35 (q, J = 7.1 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.94, 157.04, 146.34, 135.95, 128.26, 125.55, 122.36, 121.38, 119.07, 116.88, 111.76, 103.27, 102.79, 60.79, 14.61. Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.48; H, 5.21; N, 5.47. C, 76.10; H, 5.46; N, 5.29.



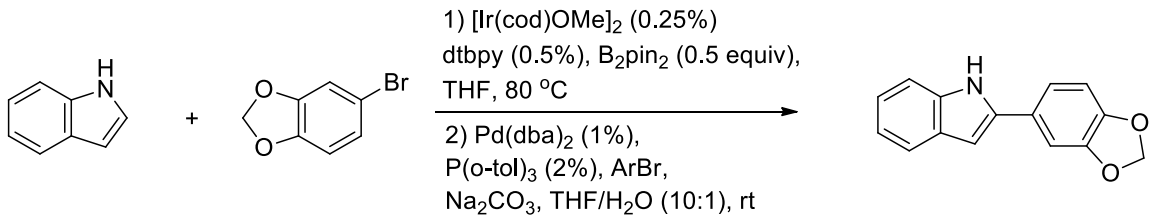
Arylation of indole with 2-bromotoluene. Prepared according to the general procedure with indole (141 mg, 1.20 mmol, 1.20 equiv) and 2-bromotoluene (171 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (151 mg, 73%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.79 (d, J = 7.7 Hz, 1H), 7.54 (m, 2H), 7.46 (d, J = 8.1 Hz, 1H), 7.41 (m, 2H), 7.34 (m, 1H), 7.29 (m, 1H), 6.74 (s, 1H), 2.60 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.79, 136.51, 136.42, 132.96, 131.40, 129.34, 129.20, 128.30, 126.41, 122.39, 120.88, 120.40, 111.16, 103.29, 21.43. Anal. Calcd for $C_{15}H_{13}N$: C, 86.92; H, 6.32; N, 6.76. Found: C, 86.76; H, 6.16; N, 6.76.



Arylation of indole with 3-bromothiophene. Prepared according to the general procedure with indole (141 mg, 1.20 mmol, 1.20 equiv) and 3-bromothiophene (163 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (148 mg, 74%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.63 (dd, J = 7.9, 1.0 Hz, 1H), 7.43 (s, 3H), 7.39 (m, 1H), 7.21 (ddd, J = 8.2, 7.1, 1.2 Hz, 1H), 7.14 (ddd, J = 8.0, 7.1, 1.0 Hz, 1H), 6.73 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.65, 134.37, 134.18, 129.33, 126.88, 125.94, 122.51, 120.81, 120.51, 119.31, 110.97, 100.21. Anal. Calcd for $C_{12}H_9NS$: C, 72.33; H, 4.55; N, 7.03. Found: C, 72.39; H, 4.56; N, 7.03.

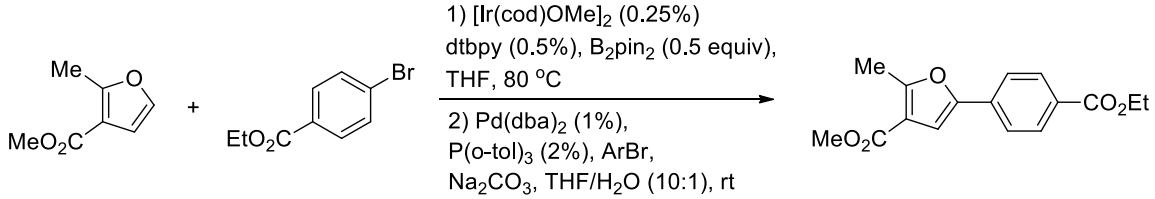


Arylation of benzofuran with 2,6-dimethylbromobenzene. Prepared according to the general procedure with benzofuran (142 mg, 1.20 mmol, 1.20 equiv) and 2,6-dimethylbromobenzene (185 mg, 1.00 mmol, 1.00 equiv) and the Suzuki coupling step at 50 °C. The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (159 mg, 72%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (m, 1H), 7.61 (m, 1H), 7.36 (m, 3H), 7.23 (m, 2H), 6.75 (s, 1H), 2.36 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.14, 155.06, 138.84, 130.91, 129.48, 129.08, 127.88, 124.11, 122.97, 121.09, 111.51, 106.42, 20.93. Anal. Calcd for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.41; H, 6.17.

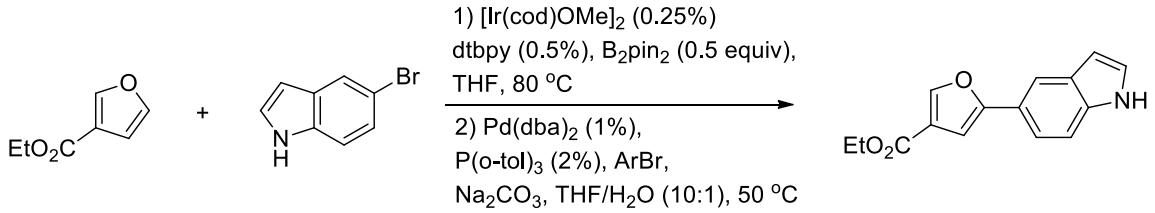


Arylation of indole with 1-Bromo-3,4-(methylenedioxy)benzene. Prepared according to the general procedure with indole (141 mg, 1.20 mmol, 1.20 equiv) and 1-Bromo-3,4-(methylenedioxy)benzene (201 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (199 mg,

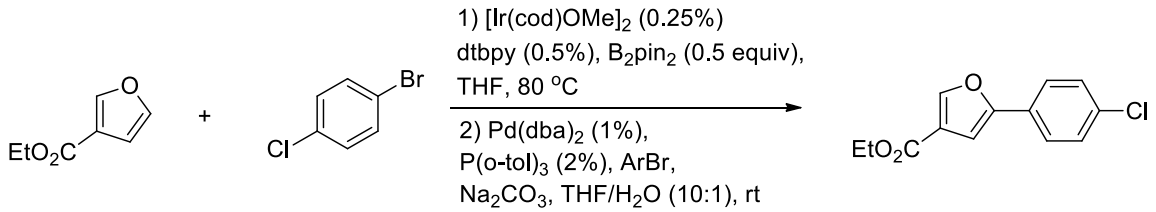
84%). ^{1}H NMR (499 MHz, Acetone-d6) δ 9.74 (s, 1H), 6.76 (dd, *J* = 7.8, 1.0 Hz, 1H), 6.59 (m, 3H), 6.30 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 6.23 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 6.15 (d, *J* = 8.5 Hz, 1H), 6.01 (m, 1H), 5.27 (s, 2H). ^{13}C NMR (126 MHz, Acetone) δ 148.63, 147.50, 138.21, 137.55, 129.63, 127.33, 121.69, 120.20, 119.75, 118.99, 111.18, 108.78, 105.84, 101.59, 98.61. Anal. Calcd for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90. Found: C, 75.68; H, 4.37; N, 5.63.



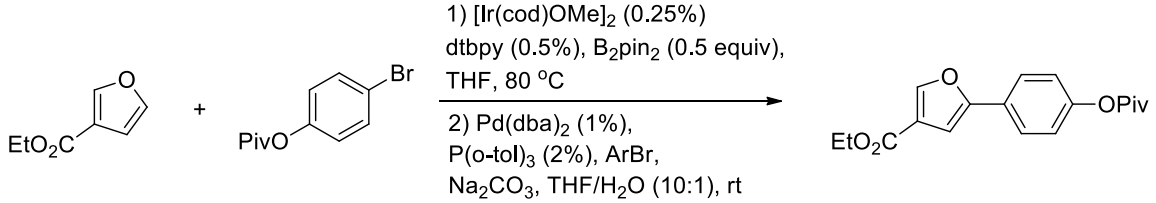
Arylation of methyl 2-methyl-3-furancarboxylate with ethyl 4-bromobenzoate. Prepared according to the general procedure with methyl 2-methyl-3-furancarboxylate (168 mg, 1.20 mmol, 1.20 equiv) and ethyl 4-bromobenzoate (229 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (15% EtOAc:85% hexanes) to give the product (280 mg, 97%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J* = 8.6 Hz, 2H), 6.91 (s, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 2.59 (s, 3H), 1.35 (t, *J* = 7.5 Hz 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.26, 164.20, 159.80, 150.84, 133.91, 130.20, 129.31, 123.30, 115.64, 107.77, 61.15, 51.60, 14.52, 14.05. Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.28; H, 5.50.



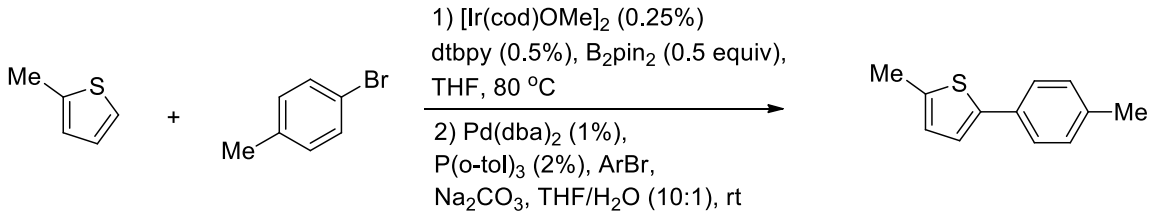
Arylation of ethyl 3-furoate with 5-bromoindole. Prepared according to the general procedure with ethyl 3-furoate (168 mg, 1.20 mmol, 1.20 equiv) and 5-bromoindole (196 mg, 1.00 mmol, 1.00 equiv) and the Suzuki coupling step at 50 °C. The mixture was purified by flash column chromatography (15% EtOAc:85% hexanes) to give the product (225 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.04 (s, 1H), 7.52 (m, 1H), 7.40 (s, 1H), 7.38 (s, 1H), 7.21 (t, *J* = 2.8 Hz, 1H), 6.93 (s, 1H), 6.59 (d, *J* = 3.0 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.94, 157.04, 146.34, 135.95, 128.26, 125.55, 122.36, 121.38, 119.07, 116.88, 111.76, 103.27, 102.79, 60.79, 14.61. Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.40; H, 5.13; N, 5.42.



Arylation of ethyl 3-furoate with 4-bromochlorobenzene. Prepared according to the general procedure with ethyl 3-furoate (168 mg, 1.20 mmol, 1.20 equiv) and 4-bromochlorobenzene (192 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (223 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 0.8 Hz, 1H), 7.58 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.6 Hz, 2H), 6.95 (s, 1H), 4.32 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.15, 154.24, 147.10, 134.12, 129.24, 128.55, 125.46, 121.65, 105.18, 60.85, 14.56. Anal. Calcd for $C_{13}H_{11}ClO_3$: C, 62.29; H, 4.42. Found: C, 61.94; H, 4.25.

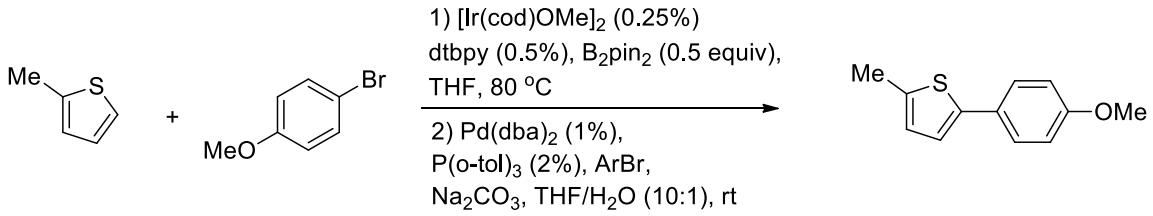


Arylation of ethyl 3-furoate with 4-bromophenyl pivalate. Prepared according to the general procedure with ethyl 3-furoate (168 mg, 1.20 mmol, 1.20 equiv) and 4-bromophenyl pivalate (257 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (253 mg, 80%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.66 (d, J = 8.6 Hz, 2H), 7.10 (d, J = 8.6 Hz, 2H), 6.94 (s, 1H), 4.32 (q, J = 7.1 Hz, 2H), 1.37 (m, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.10, 163.24, 154.68, 151.14, 146.95, 127.65, 125.31, 122.21, 121.58, 104.71, 60.77, 39.33, 27.34, 14.57. Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 67.96; H, 6.41.

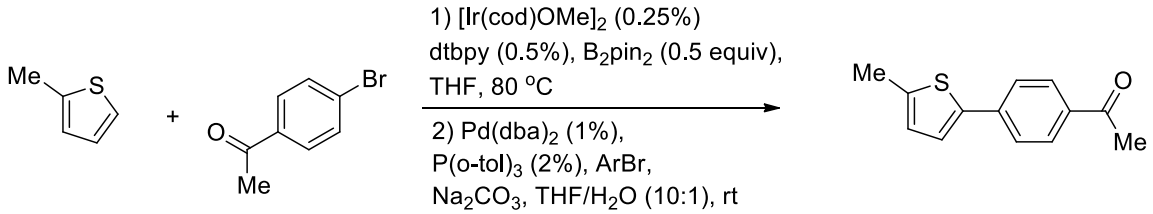


Arylation of 2-methylthiophene with 4-bromotoluene. Prepared according to the general procedure with 2-methylthiophene (118 mg, 1.20 mmol, 1.20 equiv) and 4-bromotoluene (171 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (171 mg, 91%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.57 (d, J = 8.1 Hz, 2H), 7.26 (d, J = 7.8 Hz, 2H), 7.17 (d,

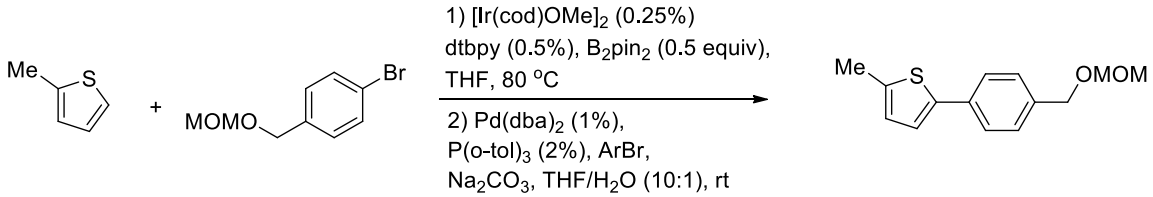
J = 3.5 Hz, 1H), 6.82 (s, 1H), 2.60 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.50, 139.18, 137.08, 132.33, 129.81, 126.43, 125.75, 122.68, 21.46, 15.73. Anal. Calcd for $C_{12}H_{12}S$: C, 76.55; H, 6.42. Found: C, 76.37; H, 6.47.



Arylation of 2-methylthiophene with 4-bromoanisole. Prepared according to the general procedure with 2-methylthiophene (118 mg, 1.20 mmol, 1.20 equiv) and 4-bromoanisole (187 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (172 mg, 84%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.7 Hz, 2H), 7.05 (d, *J* = 3.5 Hz, 1H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.76 (m, 1H), 3.86 (s, 3H), 2.55 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.15, 142.20, 138.69, 127.95, 127.03, 126.35, 122.11, 114.51, 55.57, 15.67. Anal. Calcd for $C_{12}H_{12}OS$: C, 70.55; H, 5.92. Found: C, 70.36; H, 6.00.

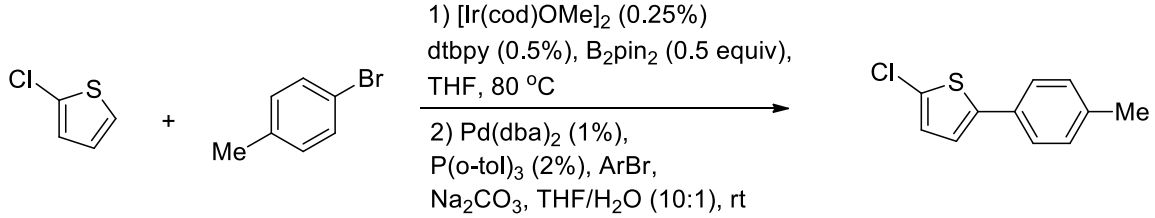


Arylation of 2-methylthiophene with 4-bromoacetophenone. Prepared according to the general procedure with 2-methylthiophene (118 mg, 1.20 mmol, 1.20 equiv) and 4-bromoacetophenone (199 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (195 mg, 90%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 3.6 Hz, 1H), 6.75 (d, *J* = 4.6 Hz, 1H), 2.58 (s, 3H), 2.51 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.48, 141.73, 140.67, 139.28, 135.46, 129.31, 126.94, 125.25, 124.86, 26.75, 15.79. Anal. Calcd for $C_{13}H_{12}OS$: C, 72.19; H, 5.59. Found: C, 72.50; H, 5.70.

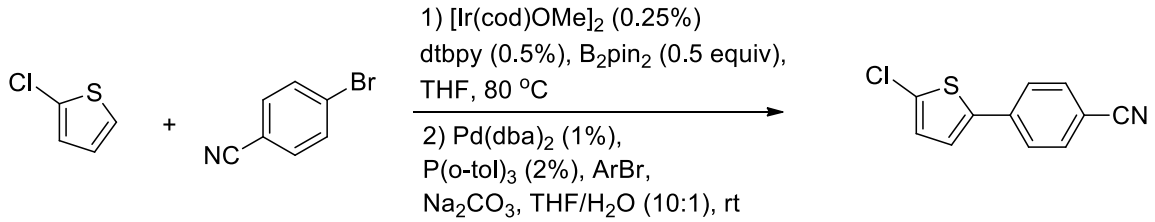


Arylation of 2-methylthiophene with 1-bromo-4-(methoxymethoxy)benzene. Prepared according to the general procedure with 2-methylthiophene (118 mg, 1.20 mmol, 1.20 equiv) and 1-bromo-4-(methoxymethoxy)benzene (217 mg, 1.00 mmol, 1.00 equiv).

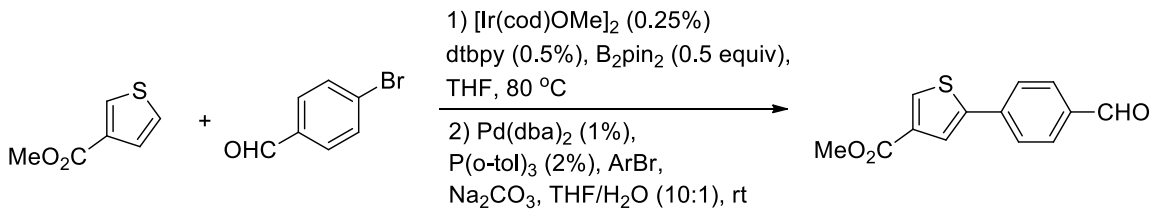
The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (197 mg, 84%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.59 (d, J = 8.3 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 3.5 Hz, 1H), 6.77 (d, J = 3.5, 1H), 4.77 (s, 2H), 4.64 (s, 2H), 3.47 (s, 3H), 2.55 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.95, 139.76, 136.91, 134.45, 128.69, 126.51, 125.75, 123.22, 95.92, 69.11, 55.62, 15.72. Anal. Calcd for $C_{14}H_{16}O_2S$: C, 67.71; H, 6.49. Found: C, 68.01; H, 6.53.



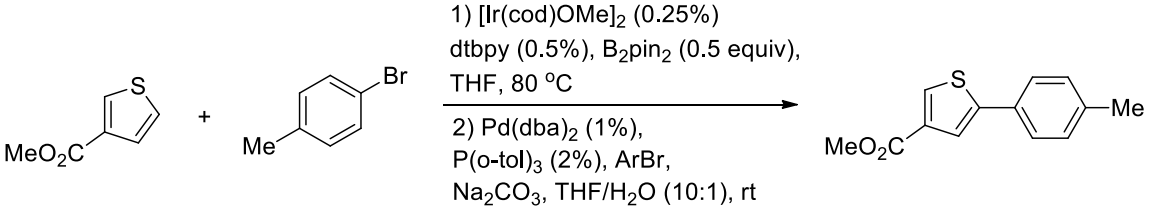
Arylation of 2-chlorothiophene with 4-bromotoluene. Prepared according to the general procedure with 2-chlorothiophene (143 mg, 1.20 mmol, 1.20 equiv) and 4-bromotoluene (171 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (192 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 3.9 Hz, 1H), 6.91 (d, J = 3.8 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.41, 138.04, 131.20, 129.95, 128.76, 127.31, 125.71, 121.96, 21.48. Anal. Calcd for $C_{11}H_9ClS$: C, 63.30; H, 4.35. Found: C, 63.35; H, 4.44.



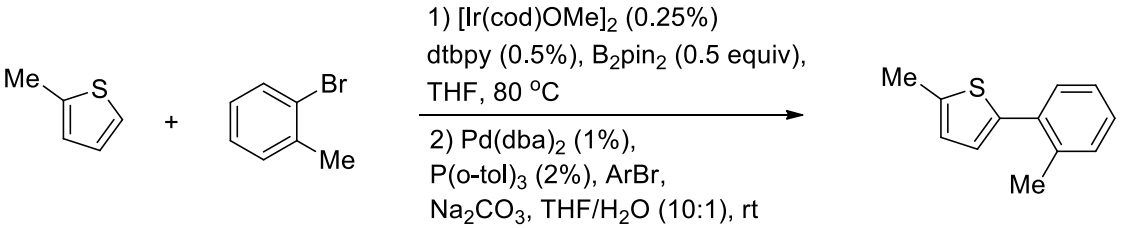
Arylation of 2-chlorothiophene with 4-bromobenzonitrile. Prepared according to the general procedure with 2-chlorothiophene (143 mg, 1.20 mmol, 1.20 equiv) and 4-bromobenzonitrile (182 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (187 mg, 85%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.63 (m, 2H), 7.56 (m, 2H), 7.18 (d, J = 3.9 Hz, 1H), 6.93 (d, J = 4.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.65, 137.95, 133.05, 131.97, 127.94, 125.84, 124.68, 118.89, 111.14. Anal. Calcd for $C_{11}H_6ClNS$: C, 60.14; H, 2.75; N, 6.38. Found: C, 59.97; H, 2.64; N, 6.14.



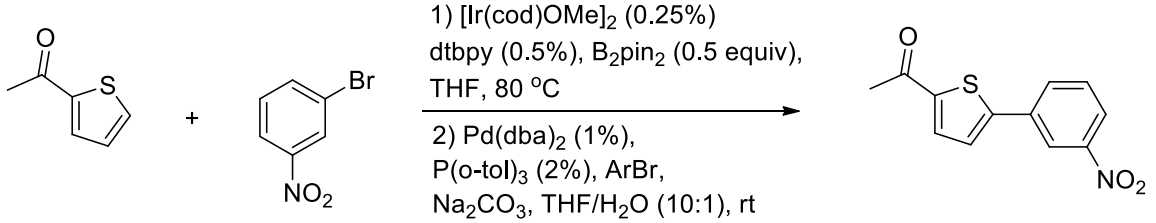
Arylation of methyl thiophene-3-carboxylate with 4-bromobenzaldehyde. Prepared according to the general procedure with methyl thiophene-3-carboxylate (171 mg, 1.20 mmol, 1.20 equiv) and 4-bromobenzaldehyde (185 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (204 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.94 (s, 1H), 8.04 (s, 1H), 7.82 (d, J = 8.3 Hz, 2H), 7.76 (s, 1H), 7.67 (d, J = 8.2 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.49, 162.96, 143.41, 139.11, 135.74, 134.75, 133.46, 130.67, 126.20, 125.44, 52.22. Anal. Calcd for $C_{13}H_{10}O_3S$: C, 63.40; H, 4.09. Found: C, 63.11; H, 3.98.



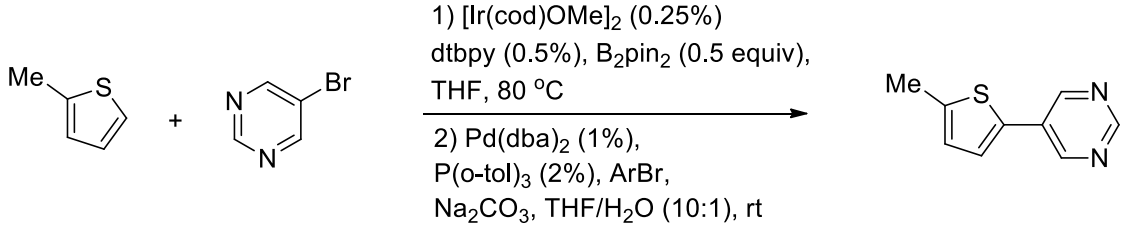
Arylation of methyl thiophene-3-carboxylate with 4-bromotoluene. Prepared according to the general procedure with methyl thiophene-3-carboxylate (171 mg, 1.20 mmol, 1.20 equiv) and 4-bromotoluene (171 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (221 mg, 95%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.69 (s, 1H), 7.50 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 7.8 Hz, 2H), 3.90 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.41, 145.46, 138.30, 134.34, 131.46, 130.96, 129.91, 126.03, 123.03, 52.03, 21.42. Anal. Calcd for $C_{13}H_{12}O_2S$: C, 67.22; H, 5.21. Found: C, 67.53; H, 5.23.



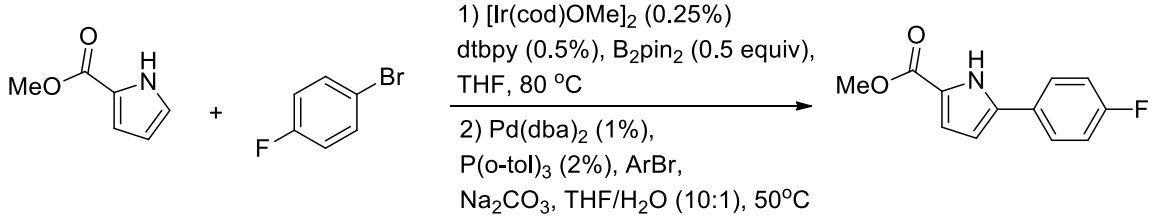
Arylation of 2-methylthiophene with 2-bromotoluene. Prepared according to the general procedure with 2-methylthiophene (118 mg, 1.20 mmol, 1.20 equiv) and 2-bromotoluene (171 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (181 mg, 96%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.51 (m, 1H), 7.33 (m, 3H), 6.97 (d, J = 3.4 Hz, 1H), 6.85 (d, J = 3.3 Hz, 1H), 2.63 (s, 3H), 2.56 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.18, 139.91, 136.21, 134.86, 131.06, 130.60, 127.80, 126.60, 126.21, 125.64, 21.57, 15.58. Anal. Calcd for $C_{12}H_{12}S$: C, 76.55; H, 6.42. Found: C, 76.87; H, 6.43.



Arylation of 2-acetylthiophene with 3-bromonitrobenzene. Prepared according to the general procedure with 2-acetylthiophene (152 mg, 1.20 mmol, 1.20 equiv) and 3-bromonitrobenzene (202 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (205 mg, 83%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.16 (m, 1H), 7.92 (m, 1H), 7.68 (d, J = 3.9 Hz, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.43 (d, J = 3.9 Hz, 1H), 2.57 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.81, 149.33, 148.91, 144.83, 135.17, 133.67, 132.12, 130.48, 125.75, 123.53, 121.00, 25.04. Anal. Calcd for $C_{12}H_9NO_3S$: C, 58.29; H, 3.67; N, 5.66. Found: C, 58.37; H, 3.83; N, 5.43.

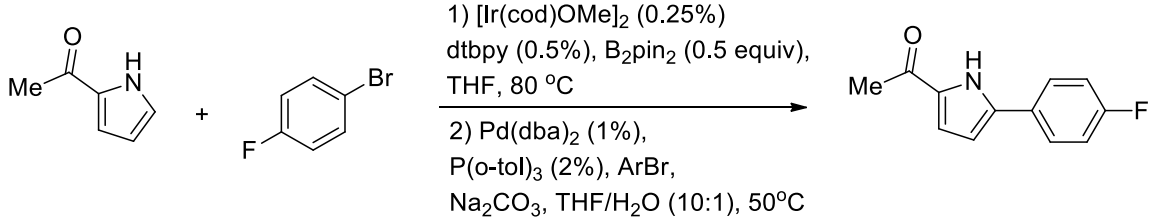


Arylation of 2-methylthiophene with 5-bromopyrimidine. Prepared according to the general procedure with 2-methylthiophene (118 mg, 1.20 mmol, 1.20 equiv) and 5-bromopyrimidine (159 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (15% EtOAc:85% hexanes) to give the product (139 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.83 (d, J = 2.2 Hz, 2H), 7.17 (t, J = 2.7 Hz, 1H), 6.76 (s, 1H), 2.50 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.95, 153.11, 142.56, 133.91, 129.05, 127.03, 125.42, 15.69. Anal. Calcd for $C_9H_8N_2S$: C, 61.34; H, 4.58; N, 15.90. Found: C, 61.24; H, 4.55; N, 15.56.

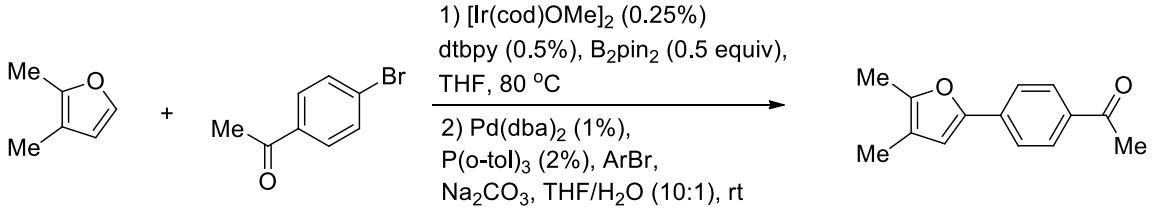


Arylation of methyl pyrrole-2-carboxylate with 4-fluorobromobenzene. Prepared according to the general procedure with methyl pyrrole-2-carboxylate (150 mg, 1.20 mmol, 1.20 equiv) and 4-fluorobromobenzene (175 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (15% EtOAc:85% hexanes) to give the product (199 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (s, 1H), 7.59 (dd, J

= 8.8, 5.2 Hz, 2H), 7.09 (t, *J* = 8.6 Hz, 2H), 6.96 (dd, *J* = 3.8, 2.4 Hz, 1H), 6.48 (dd, *J* = 3.8, 2.7 Hz, 1H), 3.87 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.58 (d, *J* = 248.5 Hz), 162.14 (s), 136.56 (s), 128.01 (d, *J* = 3.3 Hz), 126.96 (d, *J* = 8.0 Hz), 123.25 (s), 117.26 (s), 116.16 (d, *J* = 21.8 Hz), 108.17 (s), 51.88 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.20 (s). Anal. Calcd for $C_{12}H_{10}FNO_2$: C, 65.75; H, 4.60; N, 6.39. Found: C, 65.49; H, 4.40; N, 6.17.



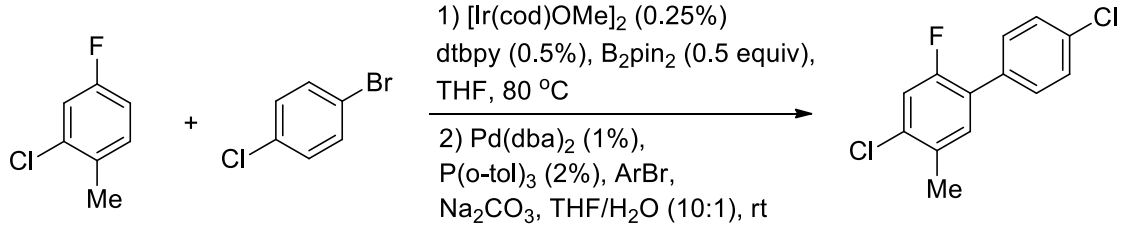
Arylation of 2-acetylpyrrole with 4-fluorobromobenzene. Prepared according to the general procedure with 2-acetylpyrrole (131 mg, 1.20 mmol, 1.20 equiv) and 4-fluorobromobenzene (175 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (15% EtOAc:85% hexanes) to give the product (152 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.47 (s, 1H), 7.69 (d, *J* = 5.4 Hz, 2H), 7.10 (m, 2H), 6.97 (d, *J* = 2.5 Hz, 1H), 6.50 (m, 1H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.10 (s), 162.81 (d, *J* = 248.2 Hz), 138.33 (s), 132.94 (s), 127.40 (d, *J* = 8.1 Hz), 119.05 (s), 116.12 (d, *J* = 21.9 Hz), 110.82 (s), 108.41 (s), 25.56 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.57 (s). Anal. Calcd for $C_{12}H_{10}FNO$: C, 70.93; H, 4.96; N, 6.89. Found: C, 70.58; H, 4.87; N, 6.83.



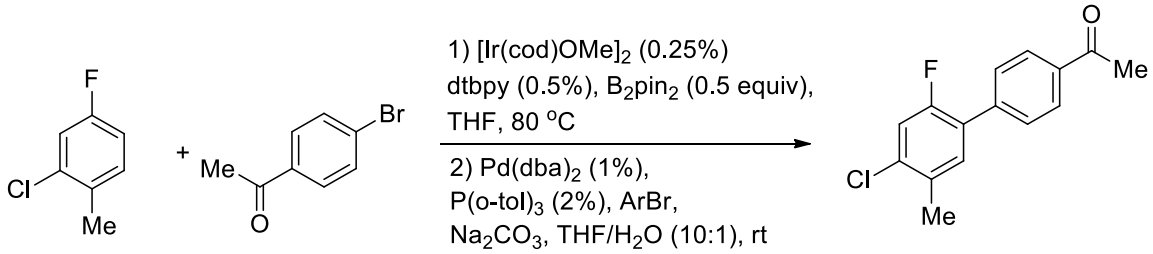
Arylation of 2,3-dimethylfuran with 4-bromoacetophenone. Prepared according to the general procedure with 2,3-dimethylfuran (116 mg, 1.20 mmol, 1.20 equiv) and 4-bromoacetophenone (199 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (204 mg, 95%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 6.56 (s, 1H), 2.55 (s, 3H), 2.26 (s, 3H), 1.96 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.62, 149.95, 149.28, 135.46, 134.95, 129.14, 122.96, 117.10, 111.37, 26.62, 11.79, 10.09. Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.48; H, 6.63.

General Procedure for one-pot C-H Borylation and Suzuki-Miyaura cross-coupling of *ortho*-fluoroarenes with aryl bromides. Inside a glove box, $[Ir(cod)OMe]_2$ (2.0 mg, 0.0030 mmol, 0.0030 equiv), dtbpy (1.6 mg, 0.0060 mmol, 0.0060 equiv), B_2pin_2 (183 mg, 0.720 mmol, 0.720 equiv), the heteroarene (1.20 mmol, 1.20 equiv), and THF (2 mL) were added consecutively to a dry vial with a magnetic stir bar. The vial was sealed and

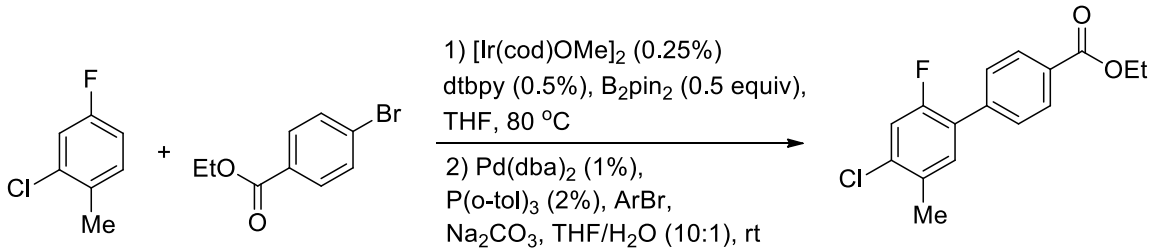
heated at 80 °C for 18 h. The reaction mixture was cooled to room temperature, and the volatile materials were removed under vacuum. $Pd(dba)_2$ (5.8 mg, 0.01 mmol, 0.01 equiv), tri-*o*-tolylphosphine (6.1 mg, 0.020 mmol, 0.02 equiv), Na_2CO_3 (424 mg, 4.00 mmol, 4.00 equiv), the aryl halide (1.00 mmol, 1.00 equiv), THF (3 mL) and degassed H_2O (0.3 mL) were added consecutively to the reaction mixture. The reaction mixture was sealed and stirred at room temperature for 18 h. The reaction mixture was filtered through silica gel, washing with EtOAc, and concentrated under vacuum. The reaction mixture was purified by column chromatography to give the product.



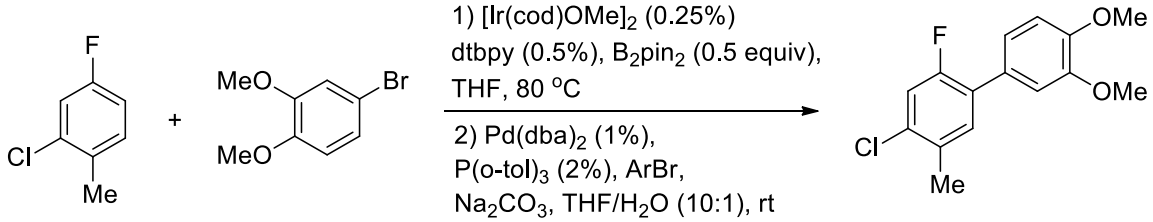
Arylation of 2-chloro-4-fluorotoluene with 4-chlorobromobenzene. Prepared according to the general procedure with 2-chloro-4-fluorotoluene (174 mg, 1.20 mmol, 1.20 equiv) and 4-chlorobromobenzene (192 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (245 mg, 96%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.44 (m, 4H), 7.27 (d, J = 8.2 Hz, 1H), 7.20 (d, J = 10.1 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.77 (d, J = 249.2 Hz), 134.22, 134.16, 133.59 (d, J = 1.7 Hz), 132.48 (d, J = 3.9 Hz), 132.17 (d, J = 3.8 Hz), 130.35 (d, J = 3.0 Hz), 128.97, 126.50 (d, J = 13.2 Hz), 117.22 (d, J = 26.2 Hz), 19.57. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.64. Anal. Calcd for $C_{13}H_9Cl_2F$: C, 61.20; H, 3.56. Found: C, 61.01; H, 3.54.



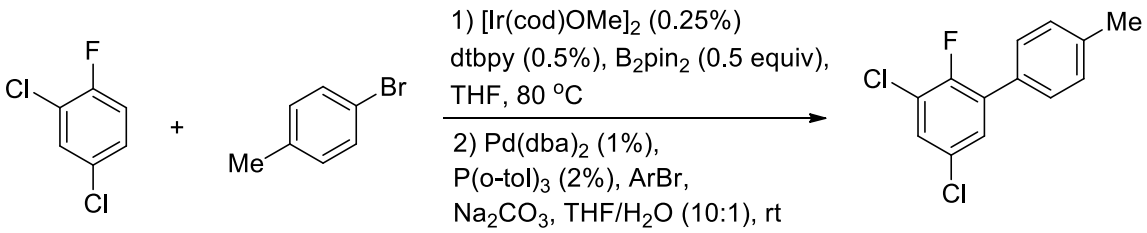
Arylation of 2-chloro-4-fluorotoluene with 4-bromoacetophenone. Prepared according to the general procedure with 2-chloro-4-fluorotoluene (174 mg, 1.20 mmol, 1.20 equiv) and 4-bromoacetophenone (199 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (222 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.1 Hz, 1H), 7.15 (d, J = 10.1 Hz, 1H), 2.60 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.74, 157.80 (d, J = 249.9 Hz), 139.79 (d, J = 1.7 Hz), 136.40, 134.76 (d, J = 10.2 Hz), 132.58 (d, J = 3.8 Hz), 132.22 (d, J = 3.6 Hz), 129.20 (d, J = 3.2 Hz), 128.72 , 126.45 (d, J = 13.1 Hz), 117.26 (d, J = 26.1 Hz), 26.85, 19.53. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.24. Anal. Calcd for $C_{15}H_{12}ClFO$: C, 68.58; H, 4.60. Found: C, 68.61; H, 4.79.



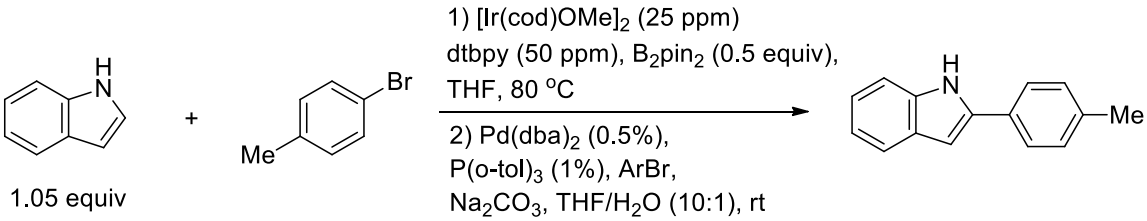
Arylation of 2-chloro-4-fluorotoluene with ethyl 4-bromobenzoate. Prepared according to the general procedure with 2-chloro-4-fluorotoluene (174 mg, 1.20 mmol, 1.20 equiv) and ethyl 4-bromobenzoate (229 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (237 mg, 81%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 8.10 (d, J = 8.4 Hz, 2H), 7.56 (dd, J = 8.4, 1.7 Hz, 2H), 7.28 (d, J = 8.2 Hz, 1H), 7.17 (d, J = 10.1 Hz, 1H), 4.41 (q, J = 7.1 Hz, 2H), 2.37 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.44, 157.84 (d, J = 249.8 Hz), 139.56 (d, J = 1.7 Hz), 134.65 (d, J = 10.2 Hz), 132.50 (d, J = 3.9 Hz), 132.27 (d, J = 3.7 Hz), 130.02, 129.91, 128.97 (d, J = 3.1 Hz), 126.66 (d, J = 13.0 Hz), 117.24 (d, J = 26.1 Hz), 61.25, 19.49, 14.56. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.26. Anal. Calcd for $C_{16}H_{14}ClFO_2$: C, 65.65; H, 4.82. Found: C, 65.51; H, 4.97.



Arylation of 2-chloro-4-fluorotoluene with 4-bromoveratrole. Prepared according to the general procedure with 2-chloro-4-fluorotoluene (174 mg, 1.20 mmol, 1.20 equiv) and 4-bromoveratrole (217 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (278 mg, 99%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.26 (dd, J = 8.2, 0.8 Hz, 1H), 7.14 (d, J = 10.2 Hz, 1H), 7.07 (t, J = 1.8 Hz, 1H), 7.05 (t, J = 1.5 Hz, 1H), 6.92 (d, J = 8.1 Hz, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.79 (d, J = 247.9 Hz), 149.08 (d, J = 7.5 Hz), 133.22 (d, J = 10.1 Hz), 132.19 (d, J = 3.8 Hz), 132.15, 127.81, 127.50 (d, J = 13.2 Hz), 121.58 (d, J = 2.9 Hz), 117.14, 116.92, 112.33 (d, J = 3.2 Hz), 111.38, 56.16, 56.11, 19.52. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.64. Anal. Calcd for $C_{15}H_{14}ClFO_2$: C, 64.18; H, 5.03. Found: C, 64.18; H, 5.16.



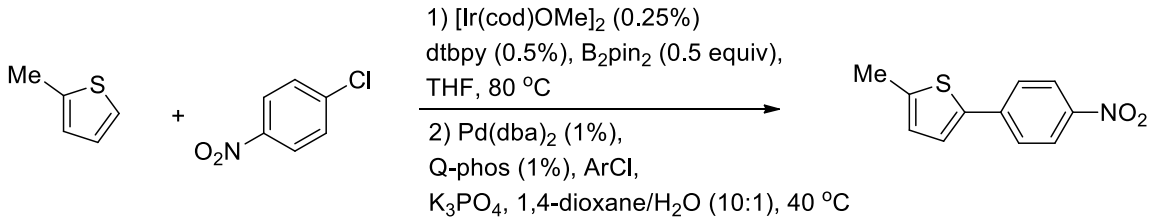
Arylation of 2,4-dichlorofluorobenzene with ethyl 4-bromobenzoate. Prepared according to the general procedure with 2,4-dichlorofluorobenzene (198 mg, 1.20 mmol, 1.20 equiv) and 4-bromotoluene (171 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (243 mg, 95%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.43 (dd, J = 8.1, 1.8 Hz, 2H), 7.39 (dd, J = 5.9, 2.6 Hz, 1H), 7.34 (dd, J = 6.0, 2.7 Hz, 1H), 7.31 (d, J = 7.9 Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.29 (d, J = 249.9 Hz), 138.95, 131.98 (d, J = 15.1 Hz), 131.10, 129.67, 129.52 (d, J = 4.5 Hz), 129.02 (d, J = 3.1 Hz), 128.97 (d, J = 3.2 Hz), 128.90, 122.95 (d, J = 20.5 Hz), 21.49. ^{19}F NMR (376 MHz, $CDCl_3$) δ -122.63. Anal. Calcd for $C_{13}H_9Cl_2F$: C, 61.20; H, 3.56. Found: C, 60.80; H, 3.44.



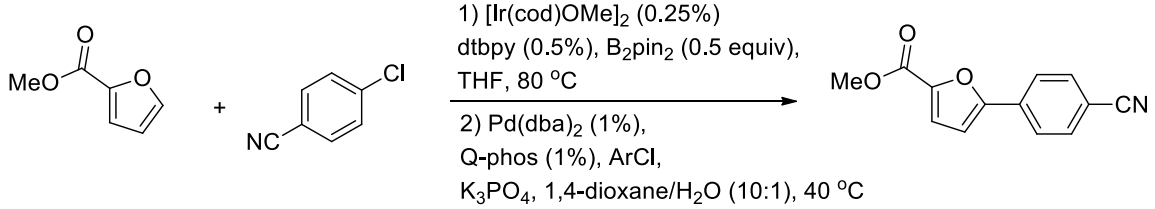
Arylation of indole with 4-bromotoluene on 5 mmol scale. Inside a glove box, $[Ir(cod)OMe]_2$ (0.9 mg, 0.001 mmol, 0.0003 equiv), dtbpy (0.8 mg, 0.002 mmol, 0.0005 equiv), B_2pin_2 (667 mg, 2.63 mmol, 0.525 equiv), indole (615 mg, 5.25 mmol, 1.05 equiv), and THF (10 mL) were added to a dry vial with a magnetic stir bar. The vial was sealed and heated at 80 °C for 18 h. The reaction mixture was cooled to room temperature and the volatile materials were removed under vacuum. $Pd(dba)_2$ (14.4 mg, 0.025 mmol, 0.0050 equiv), tri-*o*-tolylphosphine (15.2 mg, 0.050 mmol, 0.010 equiv), 4-bromotoluene (855 mg, 5.00 mmol, 1.00 equiv), Na_2CO_3 (2.12 mg, 20.0 mmol, 20.0 equiv), THF (15 mL) and degassed H_2O (1.5 mL) were added to the reaction mixture. The reaction mixture was sealed and stirred at room temperature for 18 h. The reaction mixture was filtered through silica gel washing with EtOAc, and concentrated under vacuum. The reaction mixture was purified by column chromatography (15% EtOAc:85% hexanes) to give the product (859 mg, 83%). Spectral data matched that obtained for the reaction conducted on 1 mmol scale.

General Procedure for one-pot C-H Borylation and Suzuki-Miyaura cross-coupling of heteroarenes with aryl chlorides. Inside a glove box, $[Ir(cod)OMe]_2$ (2.0 mg, 0.003 mmol, 0.003 equiv), dtbpy (1.6 mg, 0.0060 mmol, 0.0060 equiv), B_2pin_2 (153 mg, 0.600 mmol, 0.600 equiv), the heteroarene (1.20 mmol, 1.20 equiv), and THF (2 mL) were added to a dry vial with a magnetic stir bar. The vial was sealed and heated at 80 °C for

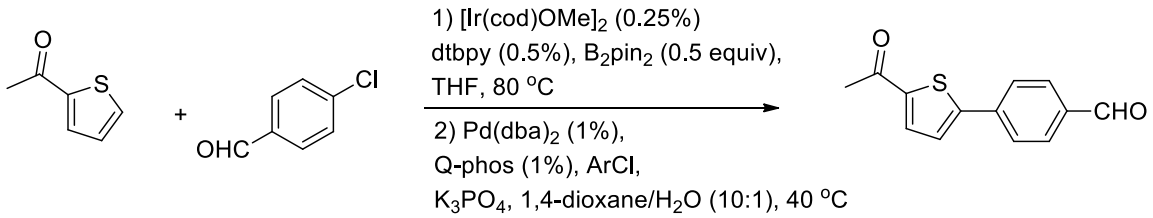
18 h. The reaction mixture was cooled to room temperature and the volatile materials were removed under vacuum. $Pd(dba)_2$ (5.8 mg, 0.01 mmol, 0.01 equiv), Q-phos (7.1 mg, 0.010 mmol, 0.010 equiv), the aryl chloride (1.00 mmol, 1.00 equiv), K_3PO_4 (849 mg, 4.00 mmol, 4.00 equiv), 1,4-dioxane (3 mL) and degassed H_2O (0.3 mL) were added to the reaction mixture. The reaction mixture was sealed and stirred at 40 °C for 18 h. The reaction mixture was filtered through silica gel washing with EtOAc, and concentrated under vacuum. The reaction mixture was purified by column chromatography to give the product.



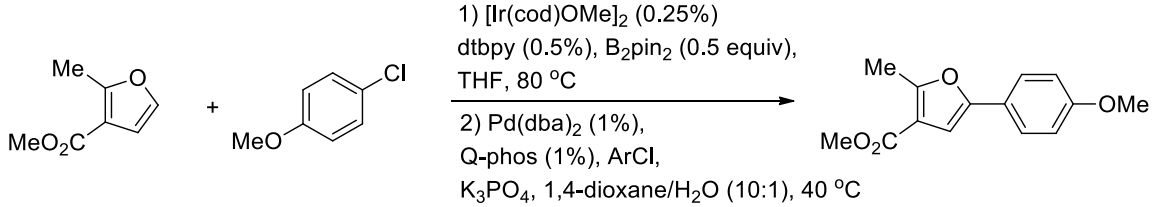
Arylation of 2-methylthiophene with 4-chloronitrobenzene. Prepared according to the general procedure with 2-methylthiophene (152 mg, 1.20 mmol, 1.20 equiv) and 4-chloronitrobenzene (158 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (178 mg, 79%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 8.17 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 8.8 Hz, 2H), 7.27 (d, J = 3.7 Hz, 1H), 6.79 (s, 1H), 2.54 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.39, 143.24, 141.07, 139.32, 127.29, 126.04, 125.53, 124.57, 15.81. Anal. Calcd for $C_{11}H_9NO_2S$: C, 60.26; H, 4.14; N, 6.39. Found: C, 60.35; H, 4.07; N, 6.52.



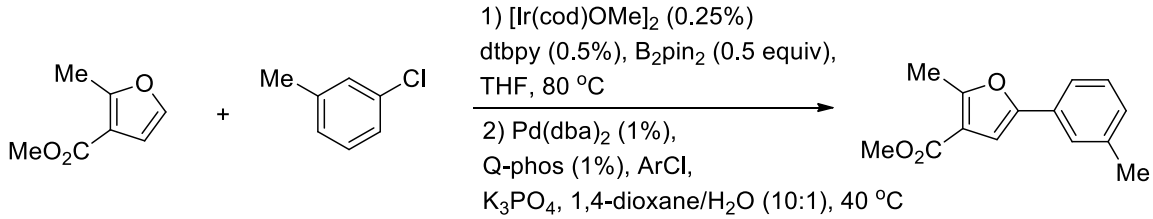
Arylation of methyl 2-furoate with 4-chlorobenzonitrile. Prepared according to the general procedure with methyl 2-furoate (151 mg, 1.20 mmol, 1.20 equiv) and 4-chlorobenzonitrile (138 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (15% EtOAc:85% hexanes) to give the product (218 mg, 96%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 3.6 Hz, 1H), 6.88 (d, J = 3.7 Hz, 1H), 3.92 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.07, 155.25, 145.08, 133.47, 132.89, 125.28, 120.08, 118.74, 112.23, 109.73, 52.34. Anal. Calcd for $C_{13}H_9NO_3$: C, 68.72; H, 3.99; N, 6.16. Found: C, 68.56; H, 3.87; N, 6.46.



Arylation of 2-acetylthiophene with 4-chlorobenzaldehyde. Prepared according to the general procedure with 2-acetylthiophene (152 mg, 1.20 mmol, 1.20 equiv) and 4-chlorobenzaldehyde (141 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (210 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.90 (d, J = 7.7 Hz, 2H), 7.76 (d, J = 7.8 Hz, 2H), 7.66 (d, J = 3.9 Hz, 1H), 7.42 (d, J = 3.8 Hz, 1H), 2.55 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.57, 190.84, 150.60, 144.90, 138.99, 136.34, 133.68, 130.71, 126.80, 125.88, 25.04. Anal. Calcd for $C_{13}H_{10}O_2S$: C, 67.80; H, 4.38. Found: C, 67.86; H, 4.38.

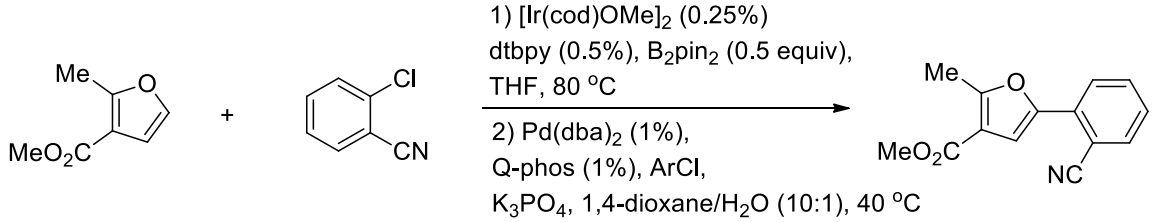


Arylation of methyl 2-methyl-3-furancarboxylate with 4-chloroanisole. Prepared according to the general procedure with methyl 2-methyl-3-furancarboxylate (168 mg, 1.20 mmol, 1.20 equiv) and 4-chloroanisole (143 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (133 mg, 54%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.57 (s, 2H), 6.91 (s, 1H), 6.74 (s, 2H), 3.85 (s, 3H), 3.82 (s, 3H), 2.64 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.78, 159.49, 158.32, 152.08, 125.34, 123.29, 115.21, 114.39, 103.96, 55.51, 51.54, 14.04. Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.64; H, 5.80.

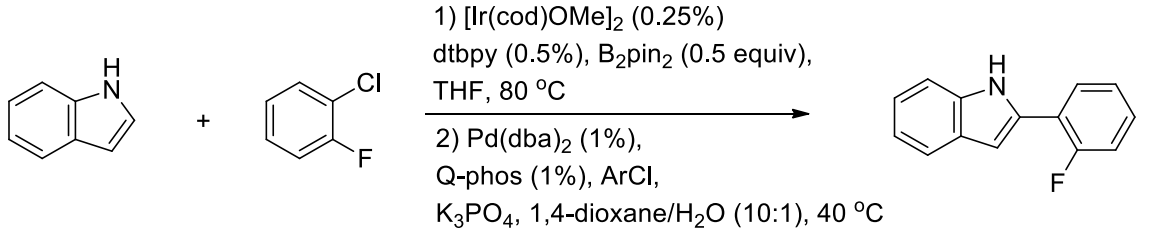


Arylation of methyl 2-methyl-3-furancarboxylate with 3-chlorotoluene. Prepared according to the general procedure with methyl 2-methyl-3-furancarboxylate (168 mg, 1.20 mmol, 1.20 equiv) and 3-chlorotoluene (127 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (133 mg, 58%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.44 (d, J = 8.1 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 7.5 Hz, 1H), 6.86 (s, 1H), 3.85 (s, 3H), 2.65 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.71, 158.85, 152.15,

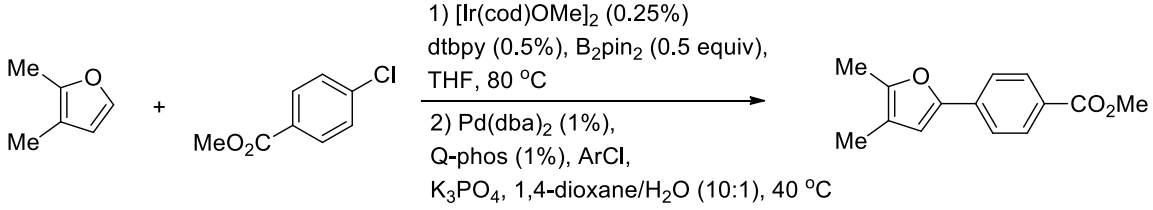
138.56, 130.15, 128.85, 128.69, 124.47, 121.04, 115.28, 105.50, 51.58, 21.69, 14.09. Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 72.79; H, 6.13.



Arylation of methyl 2-methyl-3-furancarboxylate with 2-chlorobenzonitrile. Prepared according to the general procedure with methyl 2-methyl-3-furancarboxylate (168 mg, 1.20 mmol, 1.20 equiv) and 2-chlorobenzonitrile (138 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (20% EtOAc:80% hexanes) to give the product (193 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 8.1 Hz, 1H), 7.65 (m, 1H), 7.57 (td, J = 7.8, 1.4 Hz, 1H), 7.43 (s, 1H), 7.30 (m, 1H), 3.82 (s, 3H), 2.64 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.08, 160.22, 147.70, 134.40, 133.15, 132.45, 127.64, 125.92, 118.80, 115.85, 110.95, 106.95, 51.71, 14.01. Anal. Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81. Found: C, 69.46; H, 4.47; N, 5.74.

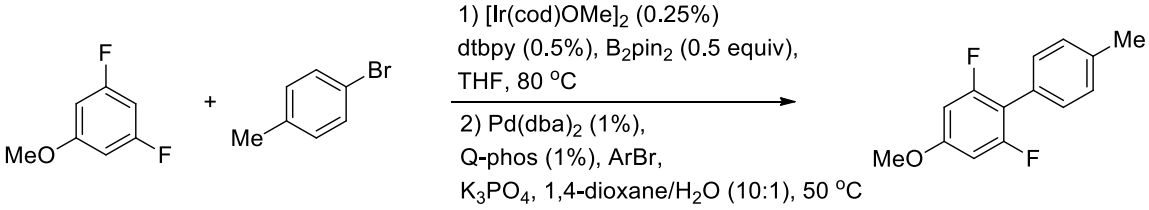


Arylation of indole with 2-fluorochlorobenzene. Prepared according to the general procedure with indole (141 mg, 1.20 mmol, 1.20 equiv) and 2-fluorochlorobenzene (131 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (15% EtOAc:85% hexanes) to give the product (127 mg, 60%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.82 (dd, J = 8.8, 6.9 Hz, 1H), 7.75 (d, J = 7.9 Hz, 1H), 7.47 (d, J = 8.1 Hz, 1H), 7.27 (m, 5H), 7.03 (d, J = 2.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.60 (d, J = 246.4 Hz), 136.93 (d, J = 1.6 Hz), 132.89 (d, J = 2.4 Hz), 129.10 (d, J = 8.9 Hz), 128.49 (s), 128.25 (d, J = 4.0 Hz), 125.09 (d, J = 3.1 Hz), 122.99 (s), 120.99 (s), 120.55 (s), 120.24 (s), 116.80 (d, J = 23.0 Hz), 111.36 (s), 101.97 (d, J = 3.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.86 (s). Anal. Calcd for $C_{14}H_{10}FN$: C, 79.60; H, 4.77; N, 6.63. Found: C, 79.22; H, 4.72; N, 6.42.

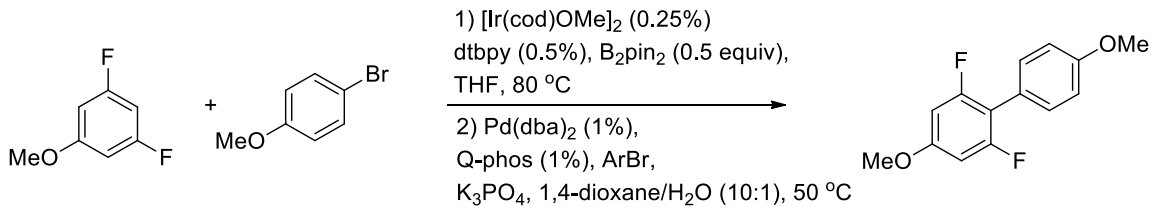


Arylation of 2,3-dimethylfuran with methyl 4-chlorobenzoate. Prepared according to the general procedure with 2,3-dimethylfuran (116 mg, 1.20 mmol, 1.20 equiv) and methyl 4-chlorobenzoate (171 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (184 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.5 Hz, 2H), 7.61 (d, *J* = 8.5 Hz, 2H), 6.55 (s, 1H), 3.89 (s, 3H), 2.27 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.16, 150.04, 149.05, 135.35, 130.25, 127.83, 122.85, 116.98, 111.06, 52.20, 11.77, 10.10. Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 72.93; H, 6.28.

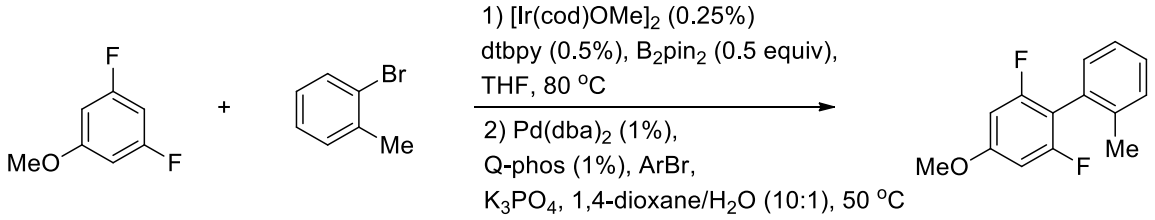
General Procedure for one-pot C-H Borylation and Suzuki-Miyaura cross-coupling of 3,5-difluoroarenes with aryl bromides. Inside a glove box, $[Ir(cod)OMe]_2$ (2.0 mg, 0.003 mmol, 0.003 equiv), dtbpy (1.6 mg, 0.0060 mmol, 0.0060 equiv), B_2pin_2 (183 mg, 0.720 mmol, 0.720 equiv), the arene (1.20 mmol, 1.20 equiv), and THF (2 mL) were added consecutively to a dry vial with a magnetic stir bar. The vial was sealed and heated at 80 °C for 18 h. The reaction mixture was cooled to room temperature and the volatile materials were removed under vacuum. $Pd(dba)_2$ (5.8 mg, 0.010 mmol, 0.010 equiv), Q-phos (7.1 mg, 0.010 mmol, 0.010 equiv), the aryl bromide (1.00 mmol, 1.00 equiv), K_3PO_4 (849 mg, 4.00 mmol, 4.00 equiv), 1,4-dioxane (3 mL) and degassed H_2O (0.3 mL) were added consecutively to the reaction mixture. The reaction mixture was sealed and stirred at 50 °C for 18 h. The reaction mixture was filtered through silica gel washing with EtOAc, and concentrated under vacuum. The reaction mixture was purified by column chromatography to give the product.



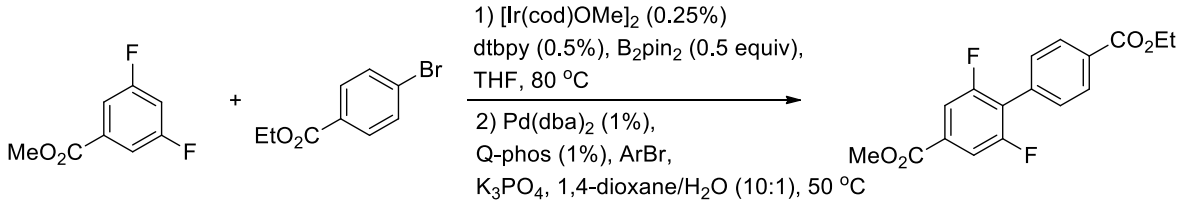
Arylation of 3,5-difluoroanisole with 4-bromotoluene. Prepared according to the general procedure with 3,5-difluoroanisole (173 mg, 1.20 mmol, 1.20 equiv) and 4-bromotoluene (171 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (180 mg, 77%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 7.7 Hz, 2H), 6.59 (d, *J* = 9.3 Hz, 2H), 3.84 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.94 (dd, J = 246.96 Hz, 10.46 Hz), 160.094 (t, *J* = 14.24 Hz), 137.85 (s), 130.45 (s), 129.24 (s), 126.57 (s), 111.21 (t, *J* = 19.6 Hz), 98.39 (m), 55.96 (s), 21.50 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.24 (s). Anal. Calcd for $C_{14}H_{12}F_2O$: C, 71.79; H, 5.16. Found: C, 71.87; H, 5.24.



Arylation of 3,5-difluoroanisole with 4-bromoanisole. Prepared according to the general procedure with 3,5-difluoroanisole (173 mg, 1.20 mmol, 1.20 equiv) and 4-bromoanisole (187 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (185 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 8.8 Hz, 2H), 7.00 (d, J = 8.8 Hz, 2H), 6.56 (d, J = 9.5 Hz, 2H), 3.86 (s, 3H), 3.82 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.91 (dd, J = 245.70 Hz, 10.46 Hz), 159.901 (t, J = 14.24 Hz), 159.42 (s), 131.70 (s), 121.71 (s), 114.00 (s), 110.88 (t, J = 19.4 Hz), 98.37 (m), 55.95 (s), 55.45 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.35 (s). Anal. Calcd for $C_{14}H_{12}F_2O_2$: C, 67.20; H, 4.83. Found: C, 67.52; H, 4.66.

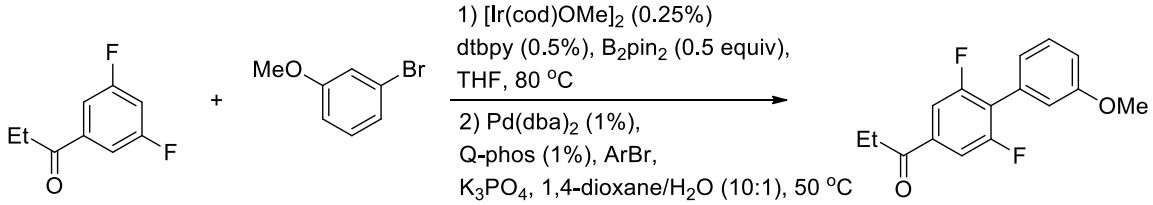


Arylation of 3,5-difluoroanisole with 2-bromotoluene. Prepared according to the general procedure with 3,5-difluoroanisole (173 mg, 1.20 mmol, 1.20 equiv) and 2-bromotoluene (171 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (5% EtOAc:95% hexanes) to give the product (164 mg, 70%). 1H NMR (500 MHz, CDCl3) δ 7.34 (s, 2H), 7.28 (m, 3H), 6.59 (d, J = 9.1 Hz, 1H), 3.85 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.87 (dd, J = 245.83, 10.96), 160.55 (t, J = 13.8 Hz), 137.96 (s), 131.27 (s), 130.29 (s), 129.17 (s), 128.66 (s), 125.79 (s), 110.63 (t, J = 22.1 Hz), 98.13 (m), 56.00 (s), 20.03 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.03 (s). Anal. Calcd for $C_{14}H_{15}F_2O$: C, 71.78; H, 5.16. Found: C, 72.00; H, 5.00.

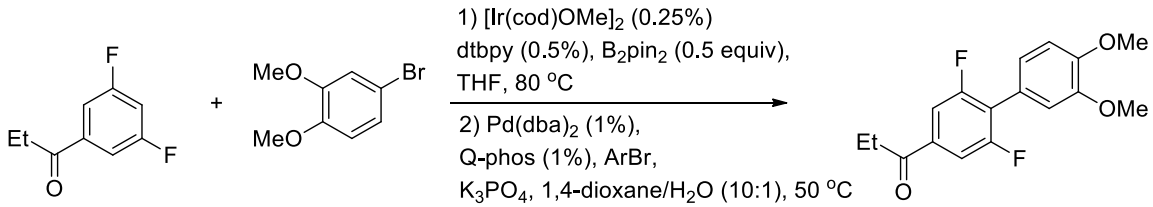


Arylation of methyl 3,5-difluorobenzoate with ethyl 4-bromobenzoate. Prepared according to the general procedure with methyl 3,5-difluorobenzoate (207 mg, 1.20 mmol, 1.20 equiv) and ethyl 4-bromobenzoate (229 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (269 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, J = 8.3 Hz, 2H), 7.63 (d,

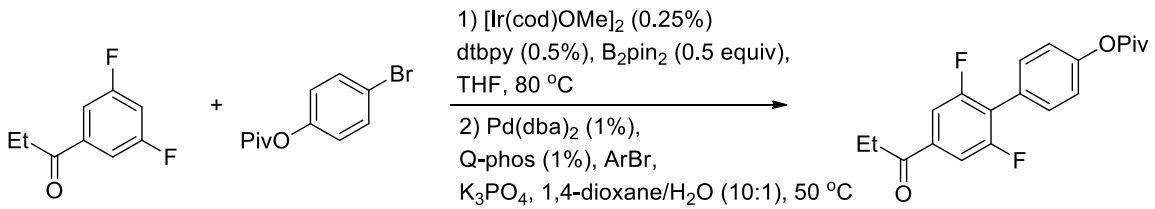
J = 7.5 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.92 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.21 (s), 164.81 (t, *J* = 3.2 Hz), 159.79 (dd, *J* = 250.8, 6.8 Hz), 132.92 (s), 131.97 (t, *J* = 9.6 Hz), 130.95 (s), 130.41 (s), 129.68 (s), 122.14 (t, *J* = 18.5 Hz), 113.26 (m), 61.36 (s), 52.91 (s), 14.51 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.08 (s). Anal. Calcd for $C_{17}H_{14}F_2O_4$: C, 63.75; H, 4.41. Found: C, 63.86; H, 4.37.



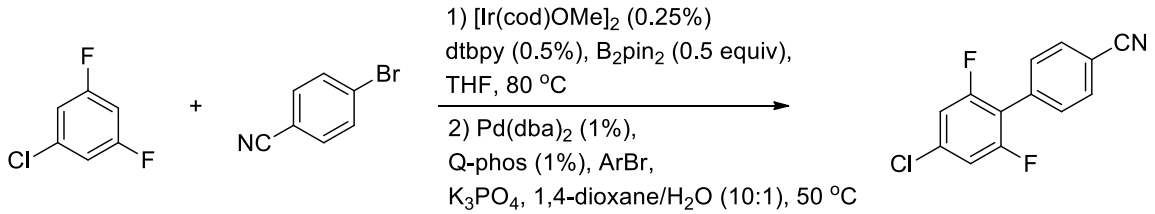
Arylation of 3,5-difluoropropiophenone with 3-bromoanisole. Prepared according to the general procedure with 3,5-difluoropropiophenone (204 mg, 1.20 mmol, 1.20 equiv) and 3-bromoanisole (187 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (199 mg, 72%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.06 (m, 1H), 7.02 (d, *J* = 1.3 Hz, 1H), 6.98 (m, 1H), 3.83 (s, 3H), 2.97 (q, *J* = 7.2 Hz, 2H), 1.24 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.07 (s), 160.23 (dd, *J* = 245.70 Hz, 6.80 Hz), 159.68 (s), 137.80 (t, *J* = 7.8 Hz), 129.63 (s), 123.05 (s), 122.90 (s), 122.72 (s), 116.03 (s), 114.67 (s), 111.51 (m), 55.51 (s), 32.13 (s), 8.23 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.67 (s). Anal. Calcd for $C_{16}H_{14}F_2O_2$: C, 69.56; H, 5.11. Found: C, 69.59; H, 5.08.



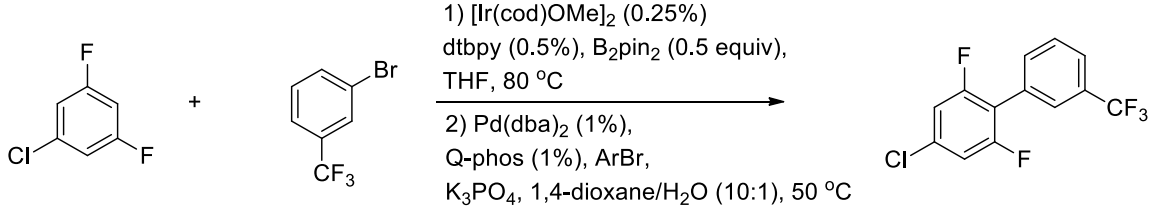
Arylation of 3,5-difluoropropiophenone with 4-bromoveratrole. Prepared according to the general procedure with 3,5-difluoropropiophenone (204 mg, 1.20 mmol, 1.20 equiv) and 4-bromoveratrole (217 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (187 mg, 61%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.7 Hz, 2H), 7.05 (d, *J* = 8.1 Hz, 1H), 6.99 (s, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 3.91 (s, 3H), 3.88 (s, 3H), 2.94 (m, 2H), 1.22 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.03 (s), 160.22 (dd, *J* = 249.8, 6.9 Hz), 149.78 (s), 148.97 (s), 137.25 (t, *J* = 7.8 Hz), 123.31 (s), 122.84 (t, *J* = 18.6 Hz), 120.70 (s), 113.54 (s), 111.50 (m), 111.21 (s), 56.18 (s), 56.08 (s), 32.06 (s), 8.23 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.05 (s). Anal. Calcd for $C_{20}H_{20}F_2O_3$: C, 69.35; H, 5.82. Found: C, 69.20; H, 5.62.



Arylation of 3,5-difluoropropiophenone with 4-bromophenyl pivalate. Prepared according to the general procedure with 3,5-difluoropropiophenone (204 mg, 1.20 mmol, 1.20 equiv) and 4-bromophenyl pivalate (257 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (194 mg, 56%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, J = 8.1 Hz, 2H), 7.51 (d, J = 8.7 Hz, 2H), 7.19 (d, J = 8.6 Hz, 2H), 3.00 (q, J = 7.2 Hz, 2H), 1.37 (s, 9H), 1.26 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.05 (s), 177.02 (s), 160.22 (dd, J = 250.8, 6.8 Hz), 151.71 (s), 137.81 (t, J = 7.8 Hz), 132.57 (s), 131.53 (s), 125.72 (s), 121.80 (s), 111.55 (m), 39.38 (s), 32.14 (s), 27.33 (s), 8.25 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.99 (s). Anal. Calcd for $C_{17}H_{16}F_2O_3$: C, 66.66; H, 5.26. Found: C, 66.45; H, 5.07.

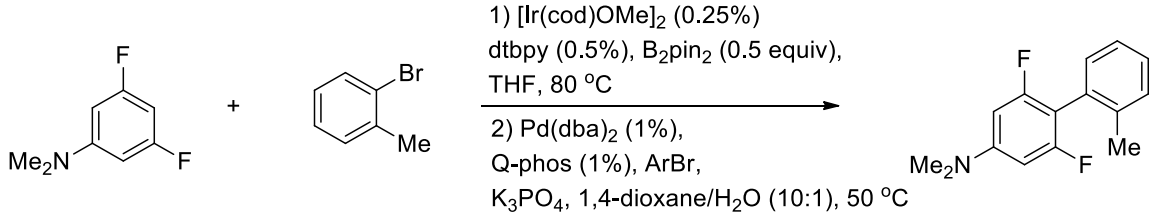


Arylation of 3,5-difluorochlorobenzene with 4-bromobenzonitrile. Prepared according to the general procedure with 3,5-difluorochlorobenzene (179 mg, 1.20 mmol, 1.20 equiv) and 4-bromobenzonitrile (182 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (192 mg, 77%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 2H), 7.57 (m, 2H), 7.07 (d, J = 7.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.85 (dd, J = 252.6, 7.9 Hz), 135.63 (t, J = 13.4 Hz), 133.28 (s), 132.30 (s), 131.19 (s), 118.58 (s), 115.82 (t, J = 18.6 Hz), 113.36 (m), 112.71 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.95 (s). Anal. Calcd for $C_{13}H_6ClF_2N$: C, 62.54; H, 2.42; N, 5.61. Found: C, 62.34; H, 2.36; N, 5.42.

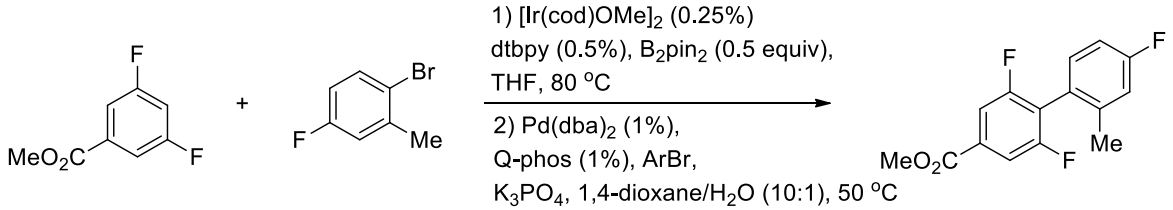


Arylation of 3,5-difluorochlorobenzene with 3-bromobenzotrifluoride. Prepared according to the general procedure with 3,5-difluorochlorobenzene (179 mg, 1.20 mmol, 1.20 equiv) and 3-bromobenzotrifluoride (225 mg, 1.00 mmol, 1.00 equiv). The mixture

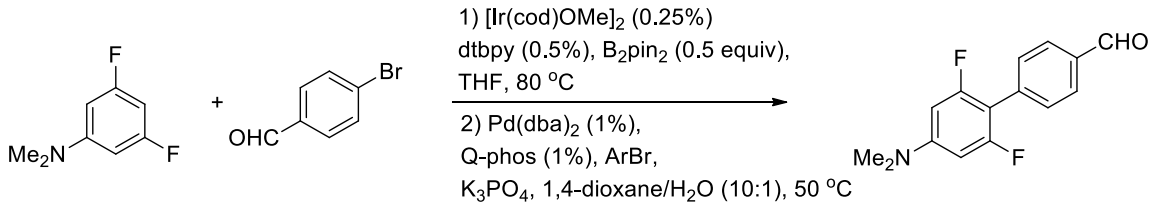
was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (196 mg, 67%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.70 (d, J = 7.0 Hz, 1H), 7.64 (m, 1H), 7.60 (m, 1H), 7.08 (d, J = 7.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.00 (dd, J = 252.1, 8.3 Hz), 135.03 (t, J = 13.4 Hz), 133.75 (s), 131.20 (q, J = 32.5 Hz), 129.29 (s), 129.14 (s), 127.24 (m), 125.56 (q, J = 3.7 Hz), 124.16 (q, J = 273 Hz), 116.19 (t, J = 18.6 Hz), 113.27 (m). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.20 (s), -113.16 (s). Anal. Calcd for $C_{13}H_6ClF_5$: C, 53.36; H, 2.07. Found: C, 53.09; H, 2.35.



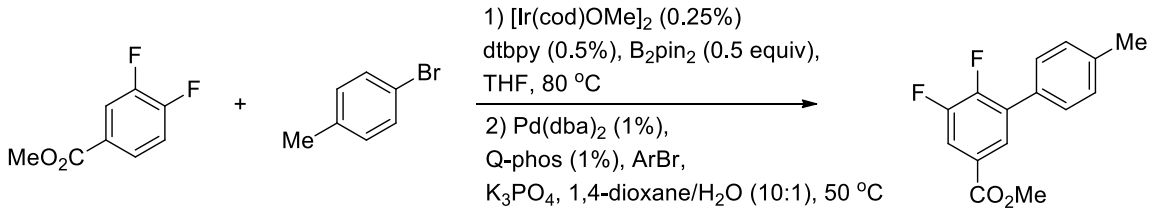
Arylation of 3,5-difluoro-*N,N*-dimethylaniline with 2-bromotoluene. Prepared according to the general procedure with 3,5-difluoro-*N,N*-dimethylaniline (189 mg, 1.20 mmol, 1.20 equiv) and 2-bromotoluene (182 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (232 mg, 94%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.38 (m, 3H), 7.34 (s, 1H), 6.37 (d, J = 10.9 Hz, 2H), 3.03 (s, 6H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.28 (dd, J = 242.3, 11.6 Hz), 151.34 (t, J = 13.4 Hz), 138.26 (s), 131.63 (s), 130.26 (s), 130.06 (s), 128.29 (s), 125.73 (s), 105.53 (t, J = 22.4 Hz), 95.20 (m), 40.44 (s), 20.21 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.47 (s). Anal. Calcd for $C_{15}H_{15}F_2N$: C, 72.86; H, 6.11; N, 5.66. Found: C, 73.06; H, 6.20; N, 5.66.



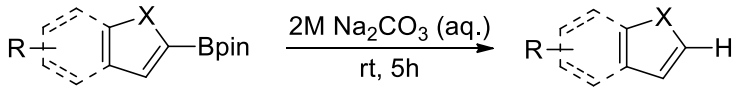
Arylation of methyl 3,5-difluorobenzoate with 2-bromo-5-fluorotoluene. Prepared according to the general procedure with methyl 3,5-difluorobenzoate (207 mg, 1.20 mmol, 1.20 equiv) and 2-bromo-5-fluorotoluene (189 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (163 mg, 58%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 7.68 (d, J = 7.4 Hz, 2H), 7.28 (m, 1H), 7.07 (td, J = 8.4, 2.8 Hz, 1H), 6.96 (dd, J = 9.0, 2.7 Hz, 1H), 3.97 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.01 (t, J = 3.4 Hz), 160.89 (d, J = 245.32 Hz), 159.92 (dd, J = 250.74 Hz, 7.2 Hz), 133.04 (d, J = 3.4 Hz), 132.29 (t, J = 9.5 Hz), 131.78 (d, J = 7.9 Hz), 129.65 (d, J = 8.2 Hz), 121.91 (t, J = 21.4 Hz), 117.28 (d, J = 22.3 Hz), 116.14 (d, J = 20.6 Hz), 113.03 (m), 52.94 (s), 19.10 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.12 (s), -118.26 (s). Anal. Calcd for $C_{15}H_{11}F_3O_2$: C, 64.29; H, 3.96. Found: C, 64.30; H, 3.82.



Arylation of 3,5-difluoro-*N,N*-dimethylaniline with 4-bromobenzaldehyde. Prepared according to the general procedure with 3,5-difluoro-*N,N*-dimethylaniline (189 mg, 1.20 mmol, 1.20 equiv) and 4-bromobenzaldehyde (185 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (186 mg, 71%). ^{1}H NMR (499 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.90 (s, 2H), 7.63 (s, 2H), 6.27 (s, 2H), 2.99 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.11 (s), 161.17 (dd, J = 244.9, 10.8 Hz), 151.60 (t, J = 13.8 Hz), 137.23 (s), 134.97 (s), 131.05 (t, J = 2.6 Hz), 129.62 (s), 104.47 (t, J = 18.7 Hz), 95.45 (m), 40.26 (s). ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.20 (s). Anal. Calcd for $C_{15}H_{13}F_2NO$: C, 68.96; H, 5.02; N, 5.36. Found: C, 68.65; H, 4.89; N, 5.09.



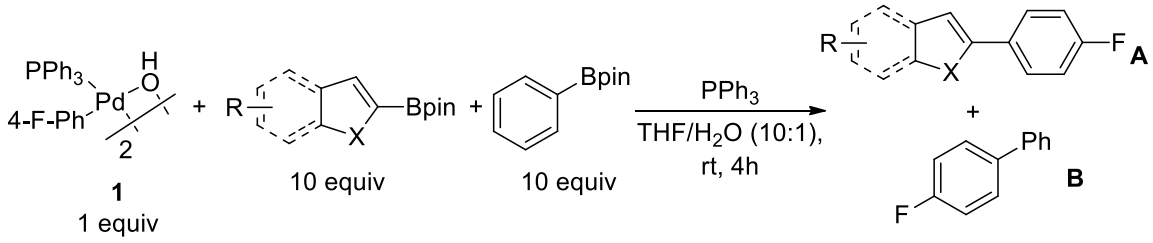
Arylation of methyl 3,4-difluorobenzoate with 4-bromotoluene. Prepared according to the general procedure with methyl 3,4-difluorobenzoate (207 mg, 1.20 mmol, 1.20 equiv) and 4-bromotoluene (171 mg, 1.00 mmol, 1.00 equiv). The mixture was purified by flash column chromatography (10% EtOAc:90% hexanes) to give the product (231 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (m, 1H), 7.80 (m, 1H), 7.46 (dd, J = 8.1, 1.6 Hz, 2H), 7.28 (m, 2H), 3.93 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.49 (d, J = 2.6 Hz), 151.20 (dd, J = 250.74, 6.43 Hz), 150.93 (dd, J = 248.72, 12.85 Hz), 138.88, 131.50 (d, J = 11.0 Hz), 131.00 (d, J = 2.6 Hz), 129.66 , 128.97 (d, J = 3.1 Hz), 127.26 (t, J = 3.2 Hz), 126.63 (dd, J = 6.6, 4.2 Hz), 117.15 (m), 52.72, 21.45. ^{19}F NMR (376 MHz, $CDCl_3$) δ -136.27 (d, J = 20.0 Hz), -136.70 (dd, J = 20.6, 10.4 Hz). Anal. Calcd for $C_{15}H_{12}F_2O_2$: C, 68.70; H, 4.61. Found: C, 68.73; H, 4.56.



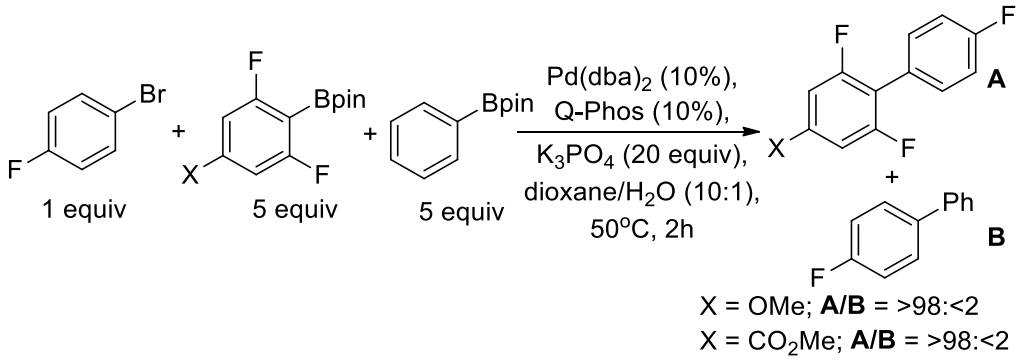
X = NH, O, S

General Procedure for (hetero)aryl Bpin stability studies. Into a vial with a magnetic stir bar were added the (hetero)aryl Bpin (0.1 mmol), THF (0.3 mL), 2M aqueous Na_2CO_3 and 1,3,5-trimethoxybenzene (10 mg). The vial was sealed and was allowed to stir at room temperature for 5 hours. At this time, a sample was removed and analyzed

using gas chromatography. The conversion of the (hetero)aryl Bpin was determined by comparison to the internal standard.



General Procedure for competition experiments between heteroaryl pinacol boronate esters and phenyl pinacol boronate. Inside a glove box, Pd complex **1** (9.6 mg, 0.010 mmol, 1.0 equiv), heteroaryl Bpin (0.100 mmol, 10.0 equiv), PhBpin (20.4 mg, 0.100 mmol, 10.0 equiv), PPh_3 (15.9 mg, 0.0600 mmol, 6.00 equiv), THF (0.25 mL), H_2O (0.025 mL), and 1,3,5-trimethoxybenzene (10 mg) were added to a dry vial equipped with a magnetic stir bar. The reaction mixture was sealed and stirred at room temperature for 5 h. At this time, a sample was removed and the yields of the 2-aryl-heteroarene and 4-fluorobiphenyl were determined using gas chromatography by comparison to the internal standard.

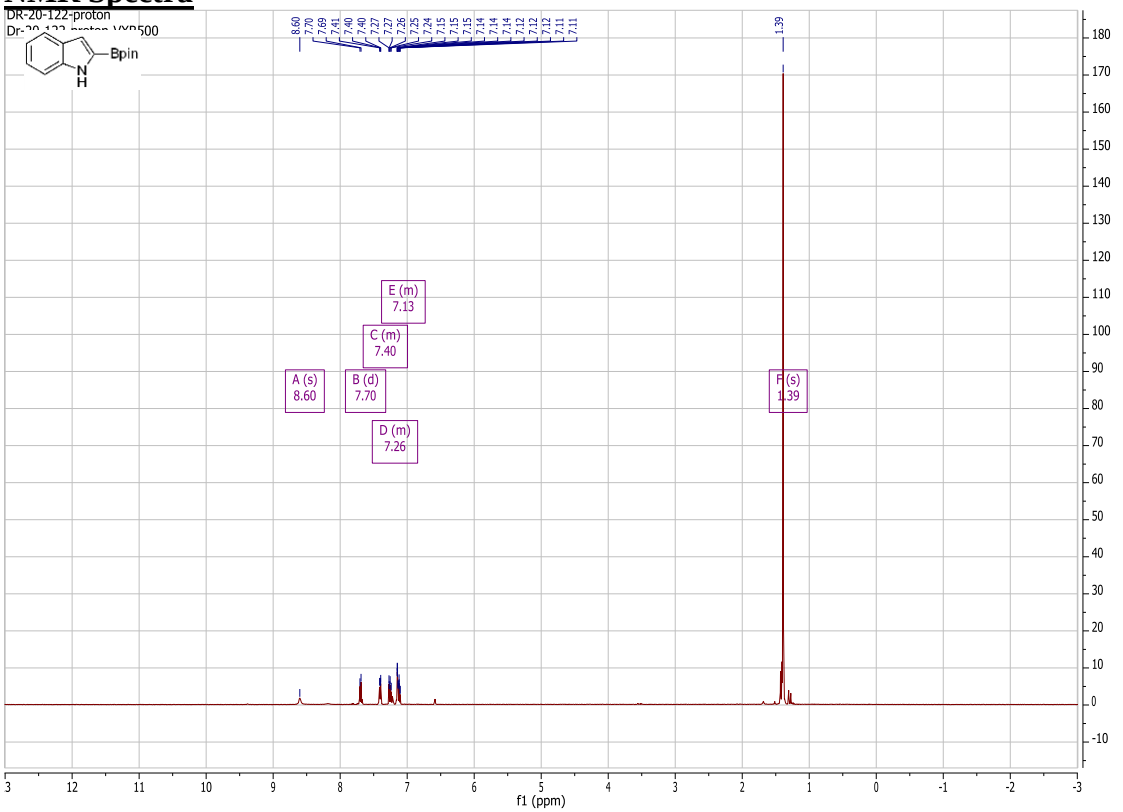


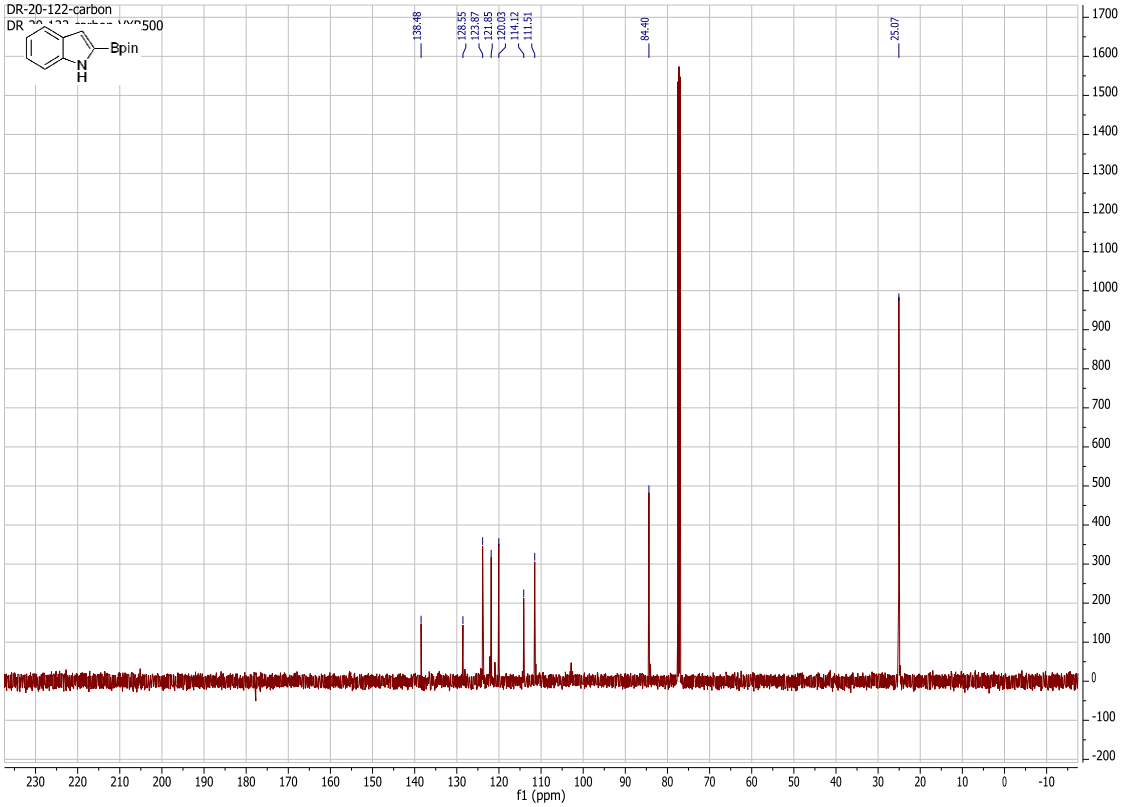
General Procedure for competition experiments between 2,6-difluoroaryl pinacol boronate esters and phenyl pinacol boronate. Inside a glove box, $Pd(dba)_2$ (2.3 mg, 0.0040 mmol, 0.10 equiv), Q-phos (2.9 mg, 0.0040, 0.10 equiv), 2,6-difluoroaryl Bpin (0.200 mmol, 5.00 equiv), PhBpin (40.8 mg, 0.200 mmol, 5.00 equiv), 1-bromo-4-fluorobenzene (7.0 mg, 0.040 mmol, 1.0 equiv), K_3PO_4 (170 mg, 0.80 mmol, 20 equiv), 1,4-dioxane (0.5 mL), H_2O (0.05 mL), and 1,3,5-trimethoxybenzene (10 mg) were added to a dry vial equipped with a magnetic stir bar. The reaction mixture was sealed and stirred at 50 °C for 2 h. At this time, a sample was removed and the yields of the 2,6-difluorobiaryl and 4-fluorobiphenyl were determined using gas chromatography by comparison to the internal standard.

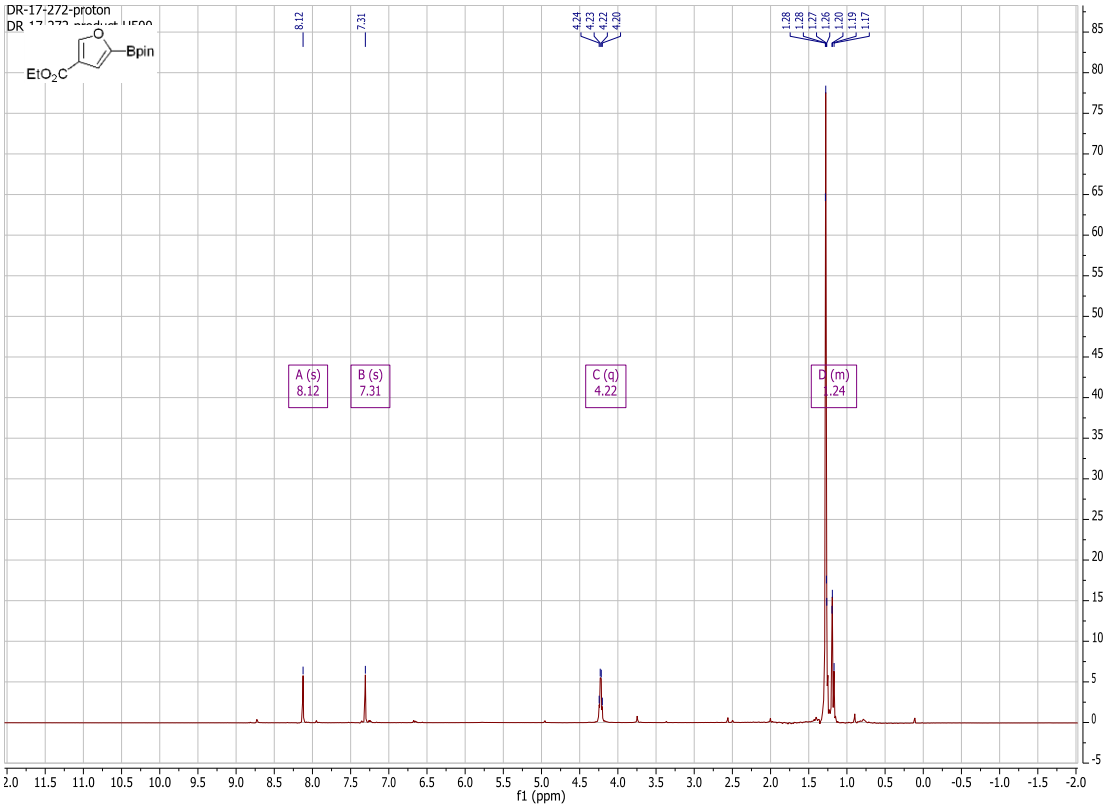
References

(1) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253.
(2) a) Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 2116; b) Driver, M. S.; Hartwig, J. F. *Organometallics* **1997**, *16*, 5706.
(3) a) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *124*, 390; b) Robbins, D. W.; Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 4068.

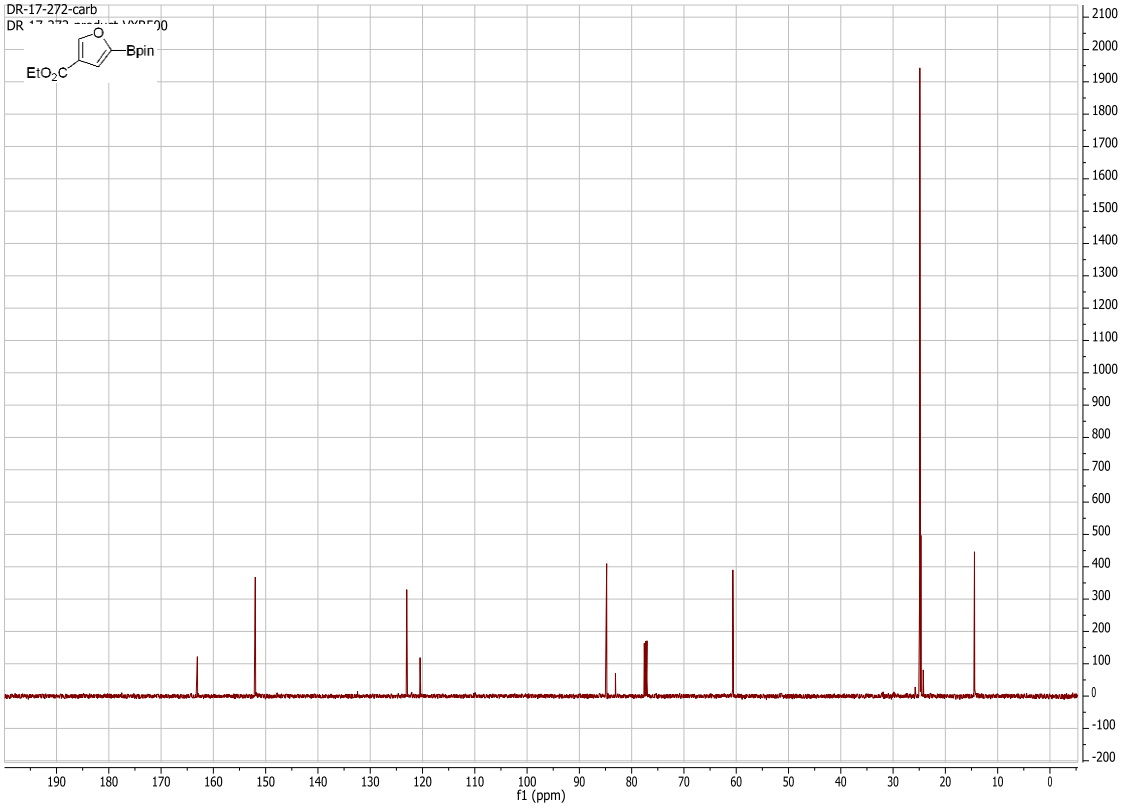
NMR Spectra

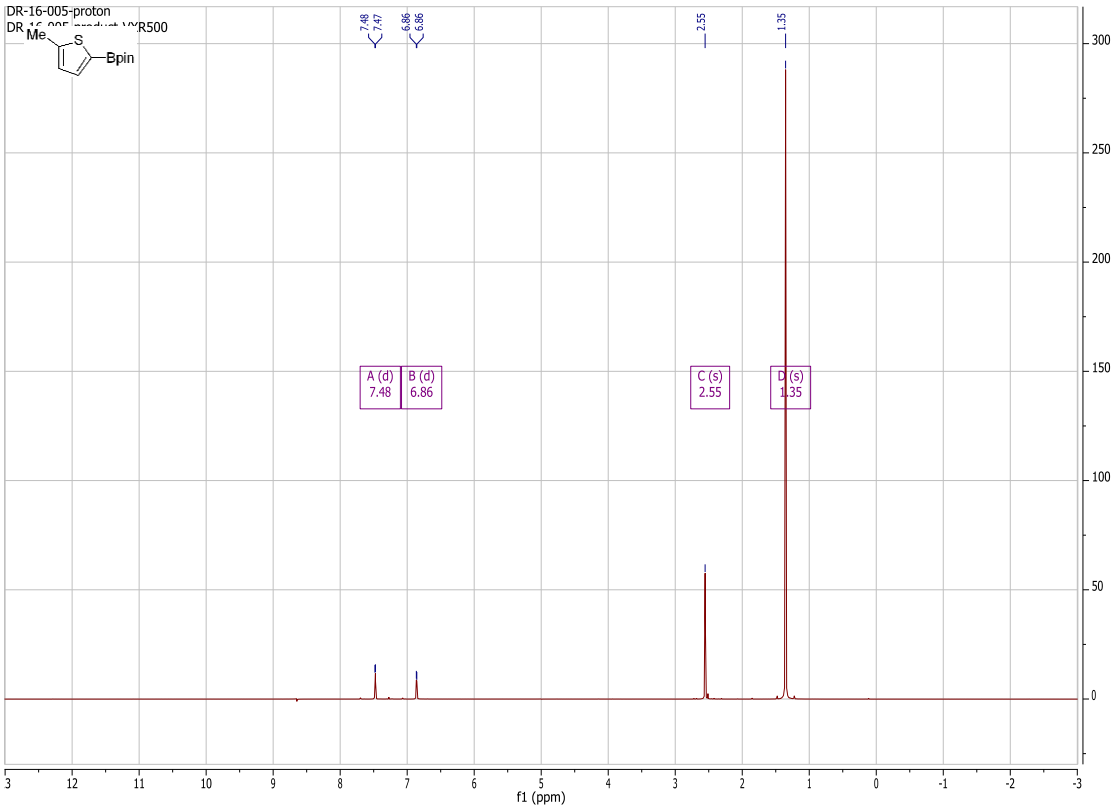

DR-20-122-proton
Bpin
N
H
8.60
7.70
7.69
7.41
7.40
7.40
7.27
7.27
7.26
7.25
7.24
7.15
7.15
7.15
7.14
7.14
7.14
7.12
7.12
7.12
7.11
7.11
1.39
E (m)
7.13
C (m)
7.40
A (s)
8.60
B (d)
7.70
D (m)
7.26
F (s)
1.39
f1 (ppm)

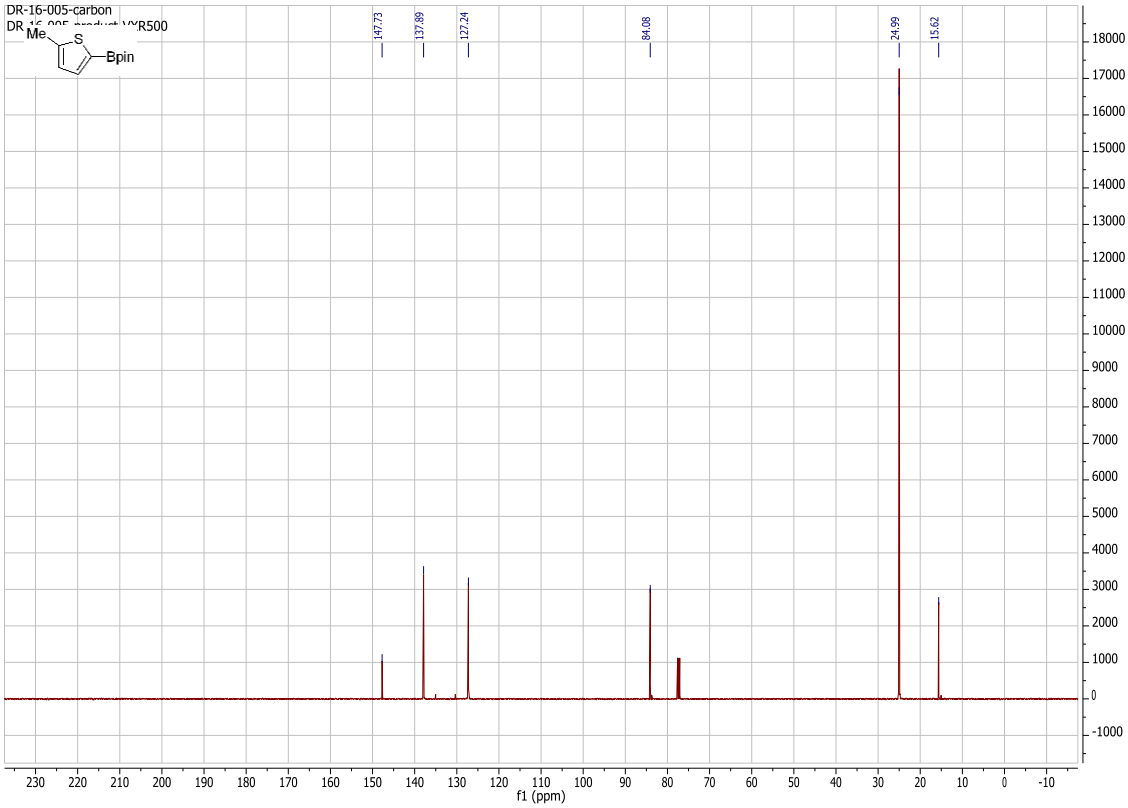

DR-20-122-carbon
Bpin
N
H
138.48
128.55
123.87
121.85
120.03
114.12
111.51
84.40
25.07
f1 (ppm)


DR-17-272-proton
Bpin
EtO2C
8.12
7.31
4.24
4.23
4.22
4.20
1.28
1.28
1.27
1.26
1.20
1.19
1.17
A (s)
8.12
B (s)
7.31
C (q)
4.22
D (m)
1.24
f1 (ppm)

;


DR-17-272-carb
Bpin
EtO2C
f1 (ppm)


DR-16-005-proton
Me
S
Bpin
7.48
7.47
6.86
6.86
2.55
1.35
A (d)
7.48
B (d)
6.86
C (s)
2.55
D (s)
1.35
300
250
200
150
100
50
0
f1 (ppm)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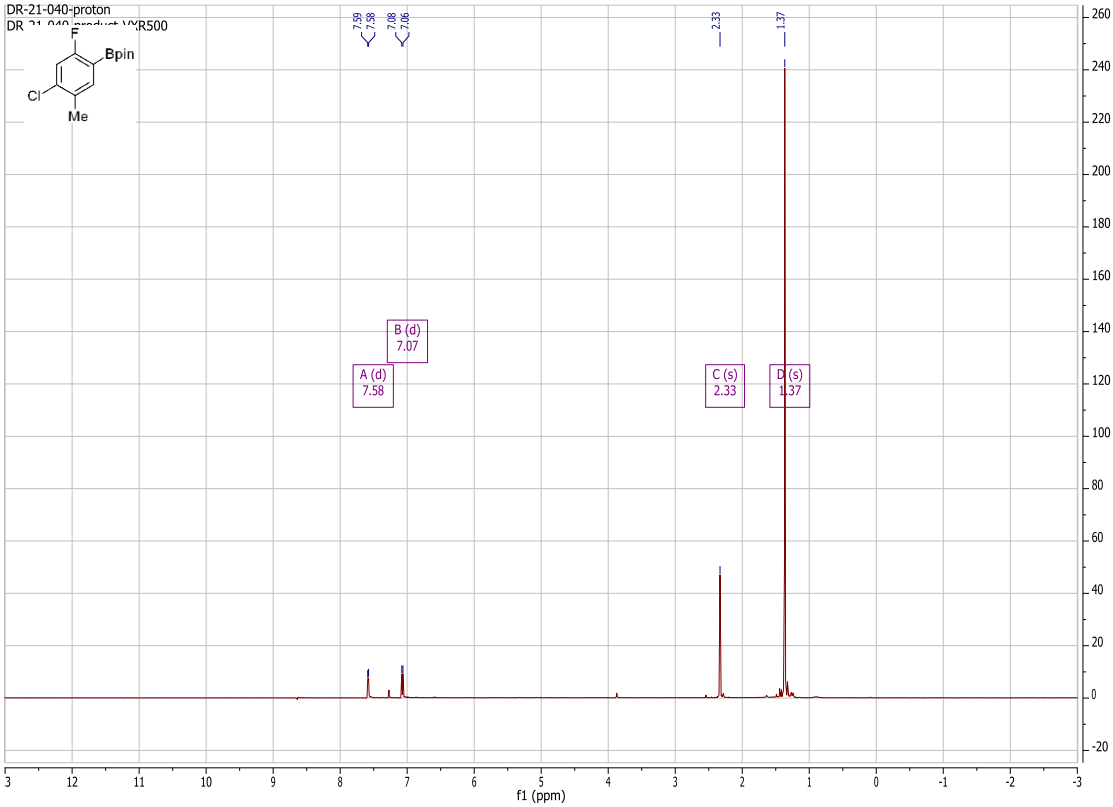
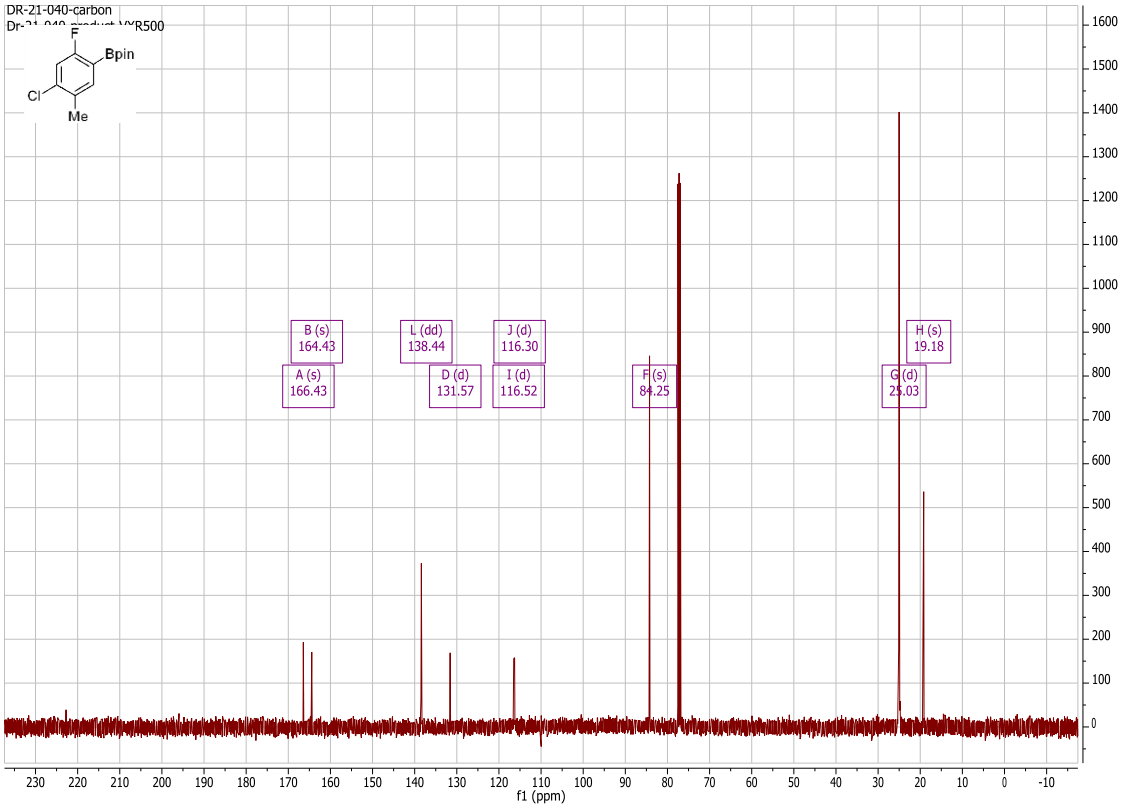
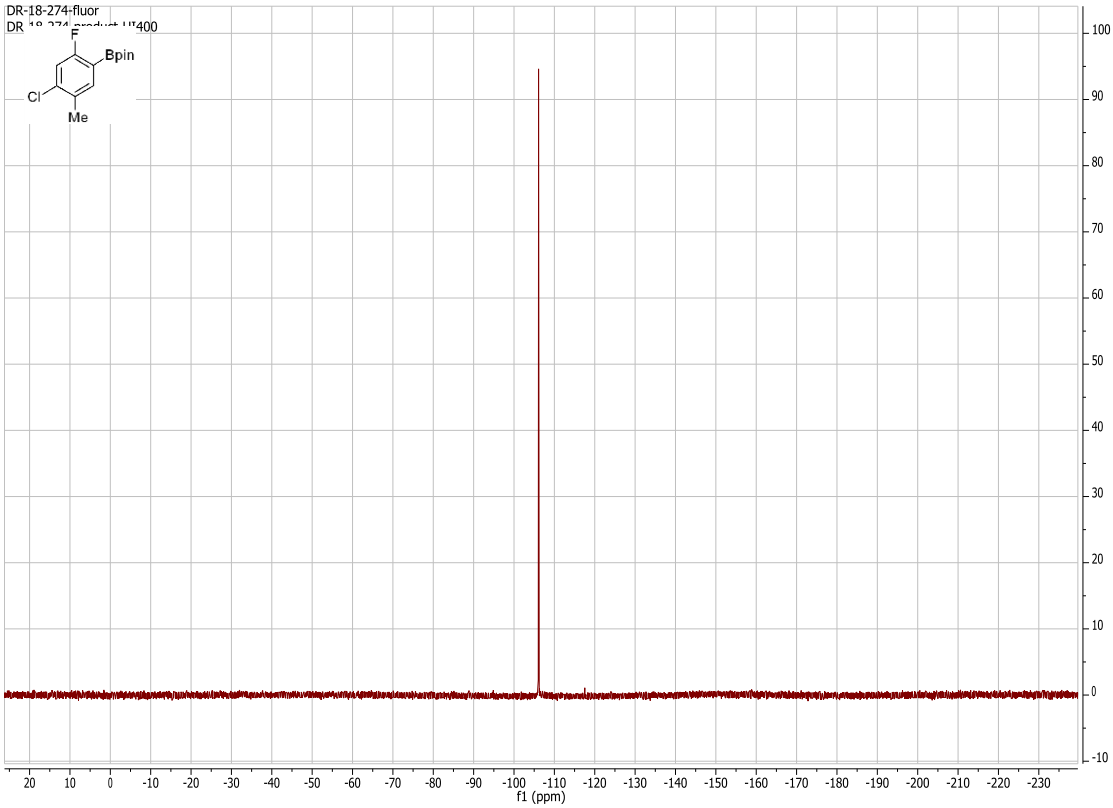
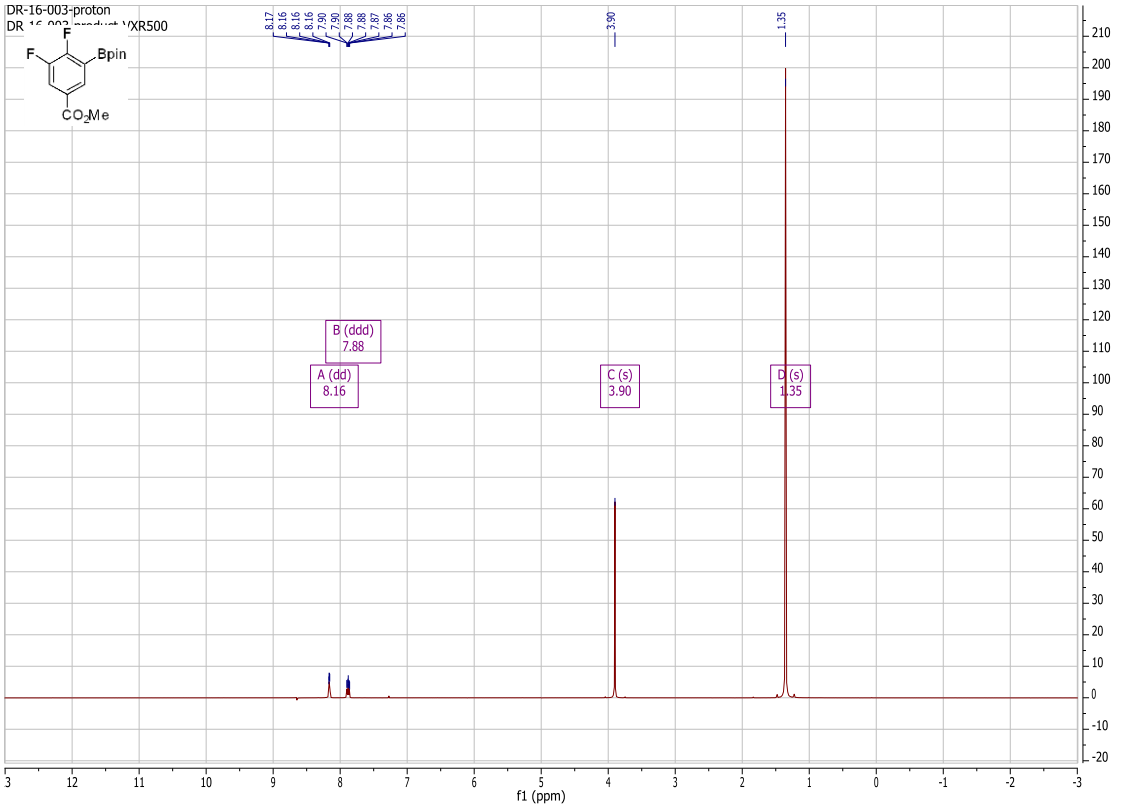
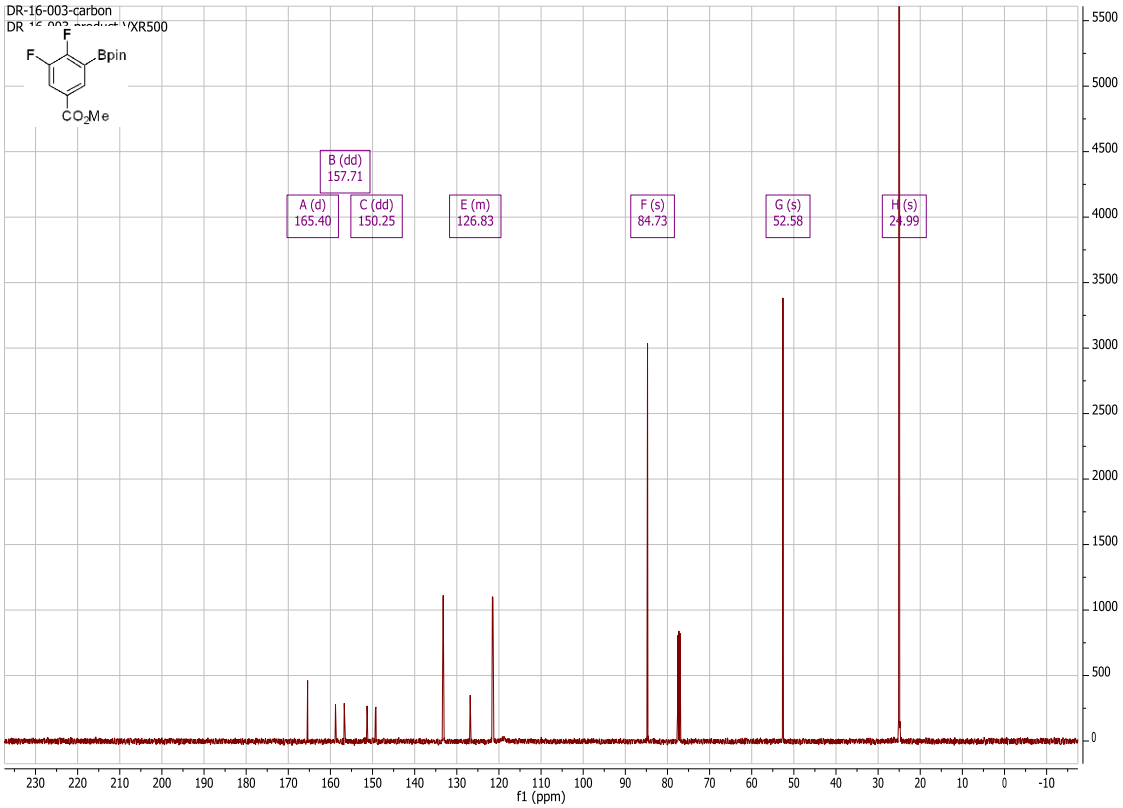
Me
S
Bpin
147.73
137.89
127.24
84.08
24.99
15.62
f1 (ppm)

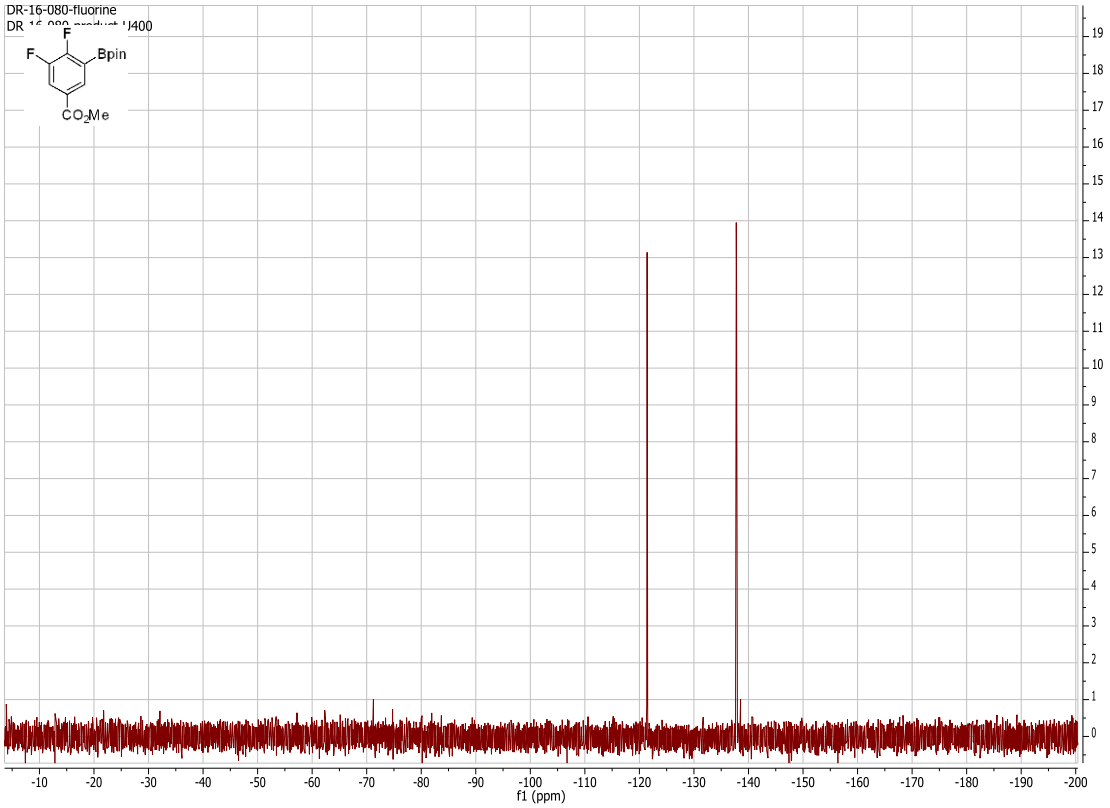

DR-21-040-proton
F
Bpin
Cl
Me
7.59
7.58
7.08
7.06
2.33
1.37
B (d)
7.07
A (d)
7.58
C (s)
2.33
D (s)
1.37
f1 (ppm)

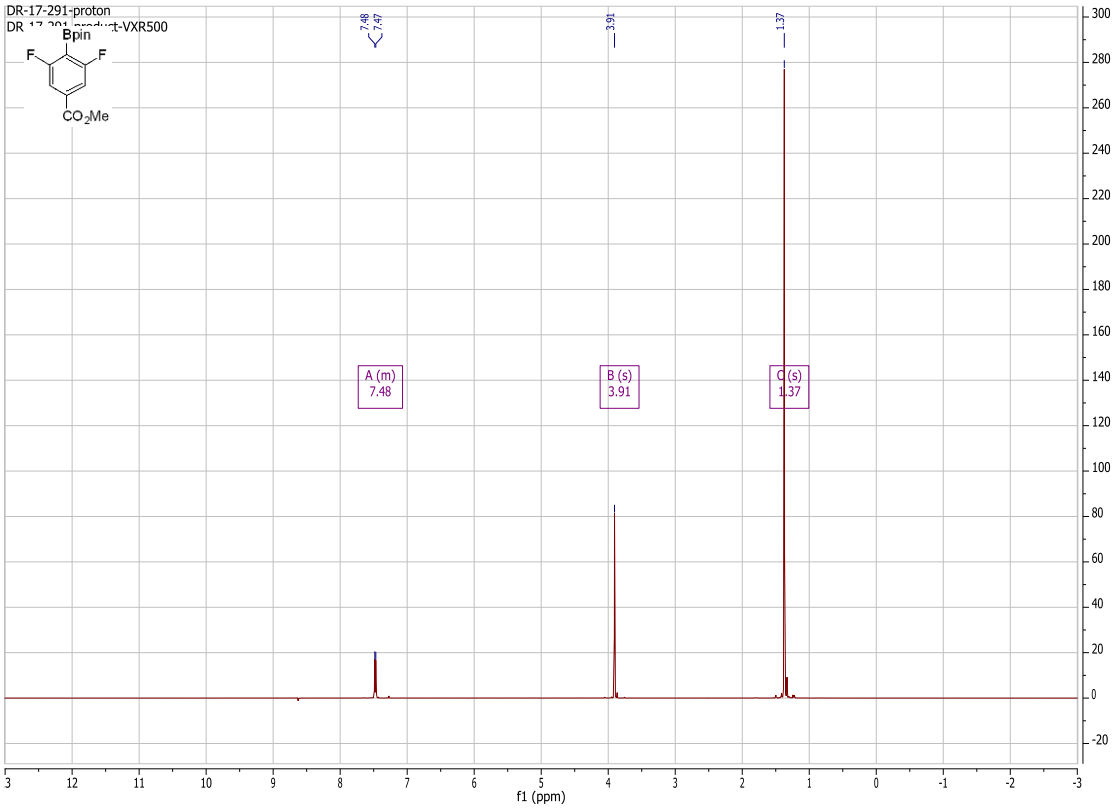

DR-21-040-carbon
F
Bpin
Cl
Me
B (s)
164.43
A (s)
166.43
L (dd)
138.44
D (d)
131.57
J (d)
116.30
I (d)
116.52
F (s)
84.25
H (s)
19.18
G (d)
25.03
f1 (ppm)

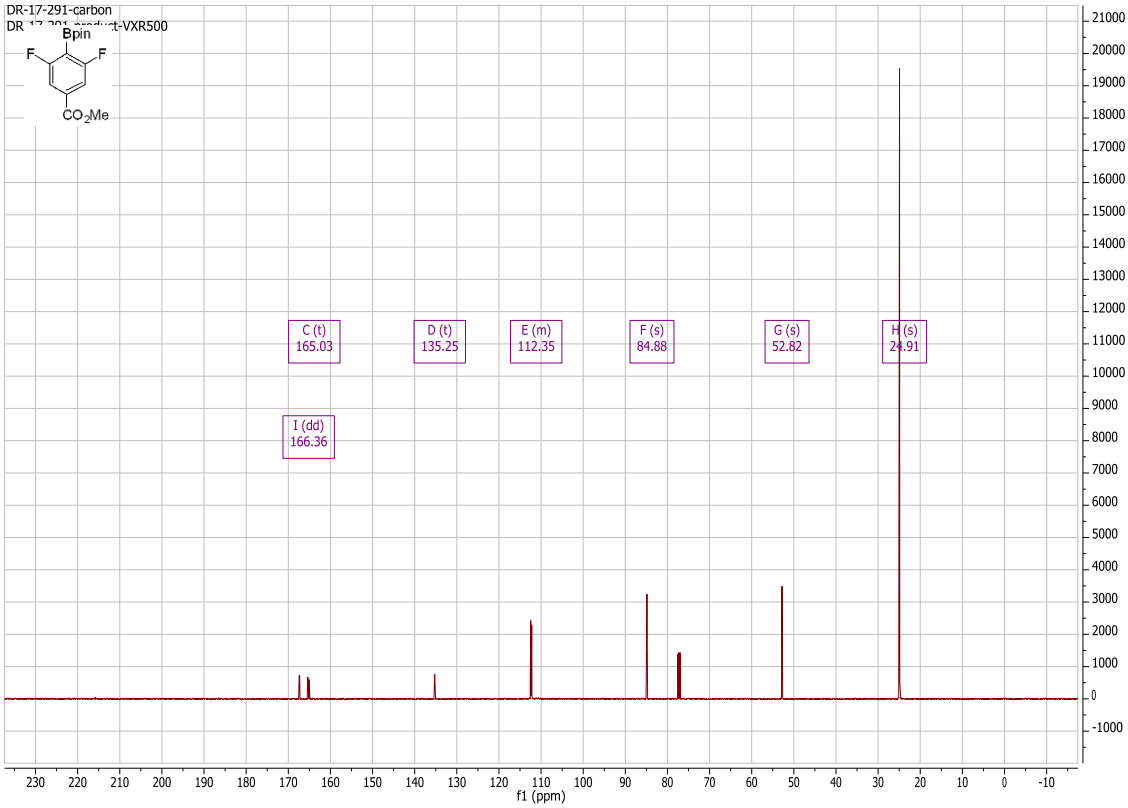

DR-18-274-fluor
F
Bpin
Cl
Me
f1 (ppm)

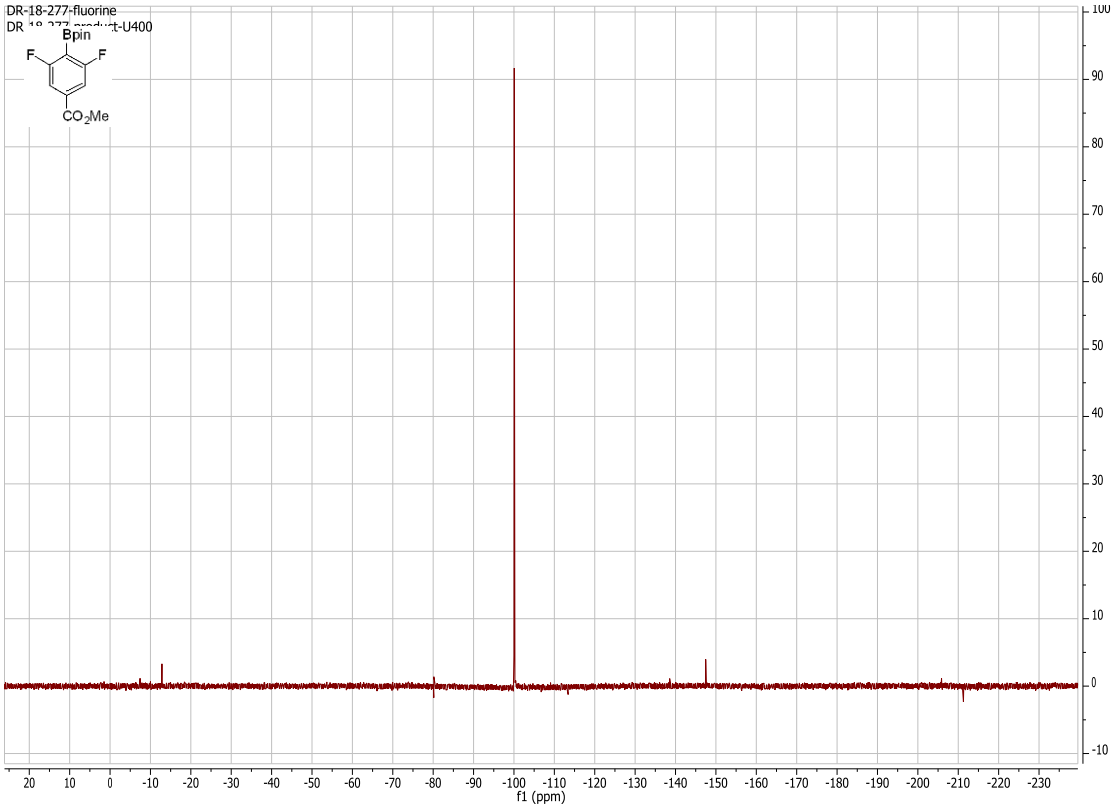

DR-16-003-proton
F
Bpin
CO2Me
8.17
8.16
8.16
8.16
7.90
7.88
7.88
7.87
7.86
7.86
3.90
1.35
B (ddd)
7.88
A (dd)
8.16
C (s)
3.90
D (s)
1.35
f1 (ppm)

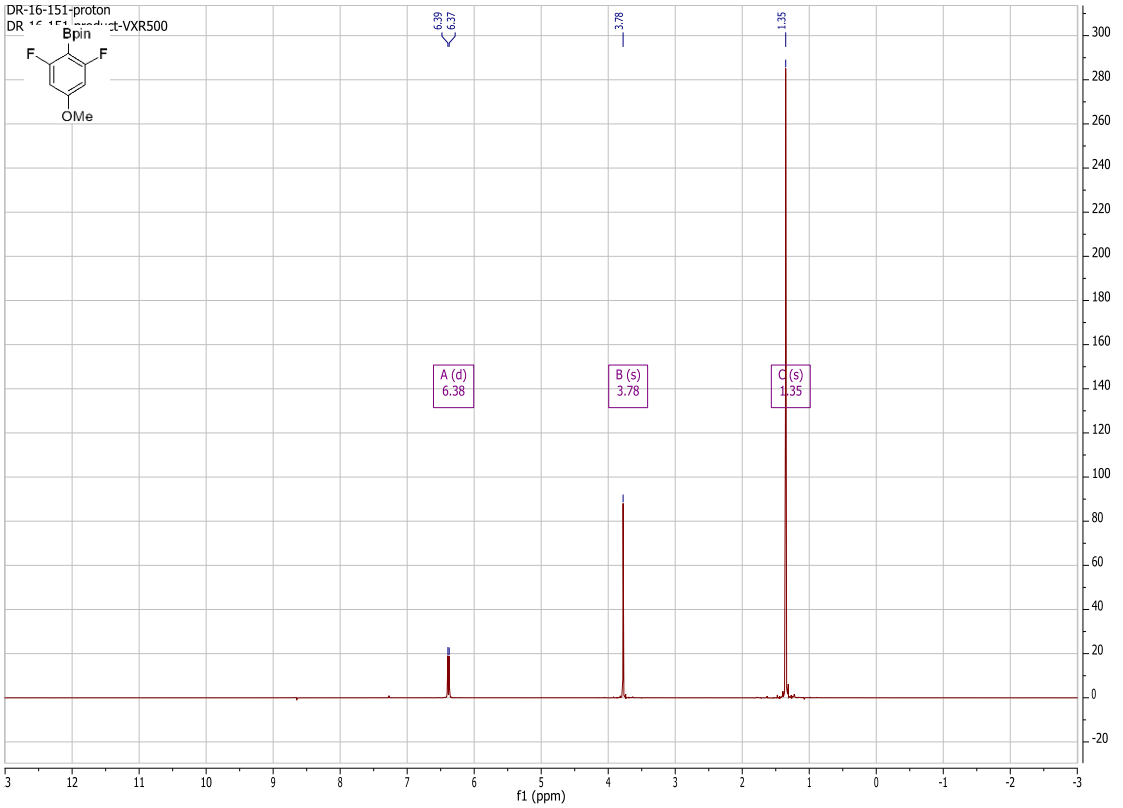

DR-16-003-carbon
F
Bpin
CO2Me
B (dd)
157.71
A (d)
165.40
C (dd)
150.25
E (m)
126.83
F (s)
84.73
G (s)
52.58
H (s)
24.99
f1 (ppm)

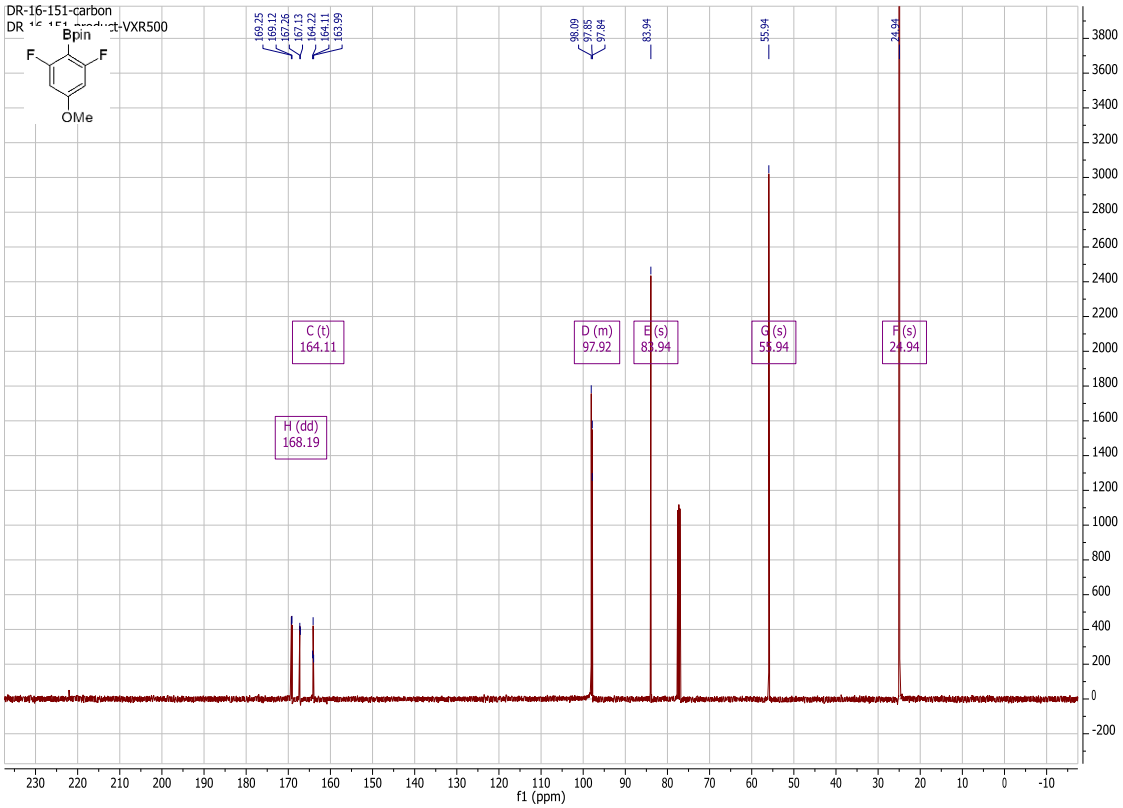

DR-16-080-fluorine
F
F
Bpin
CO2Me
f1 (ppm)

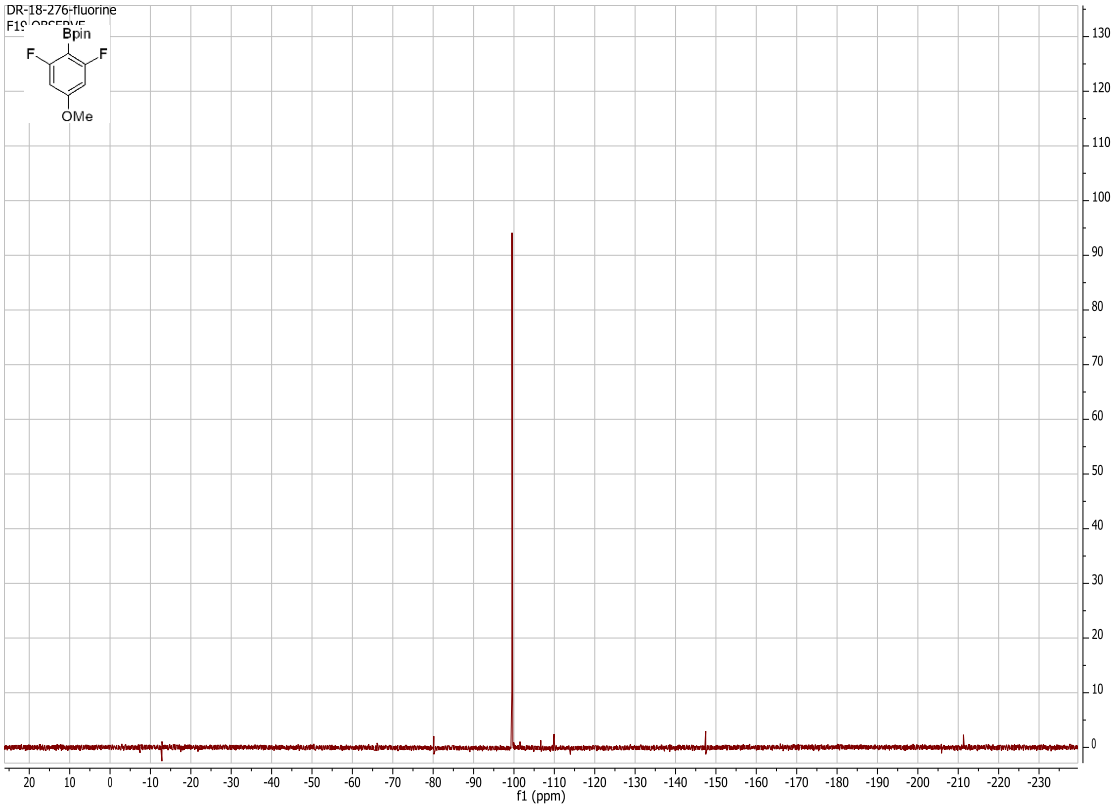

DR-17-291-proton
Bpin
F
F
CO2Me
7.48
7.47
3.91
1.37
A (m)
7.48
B (s)
3.91
C (s)
1.37
f1 (ppm)

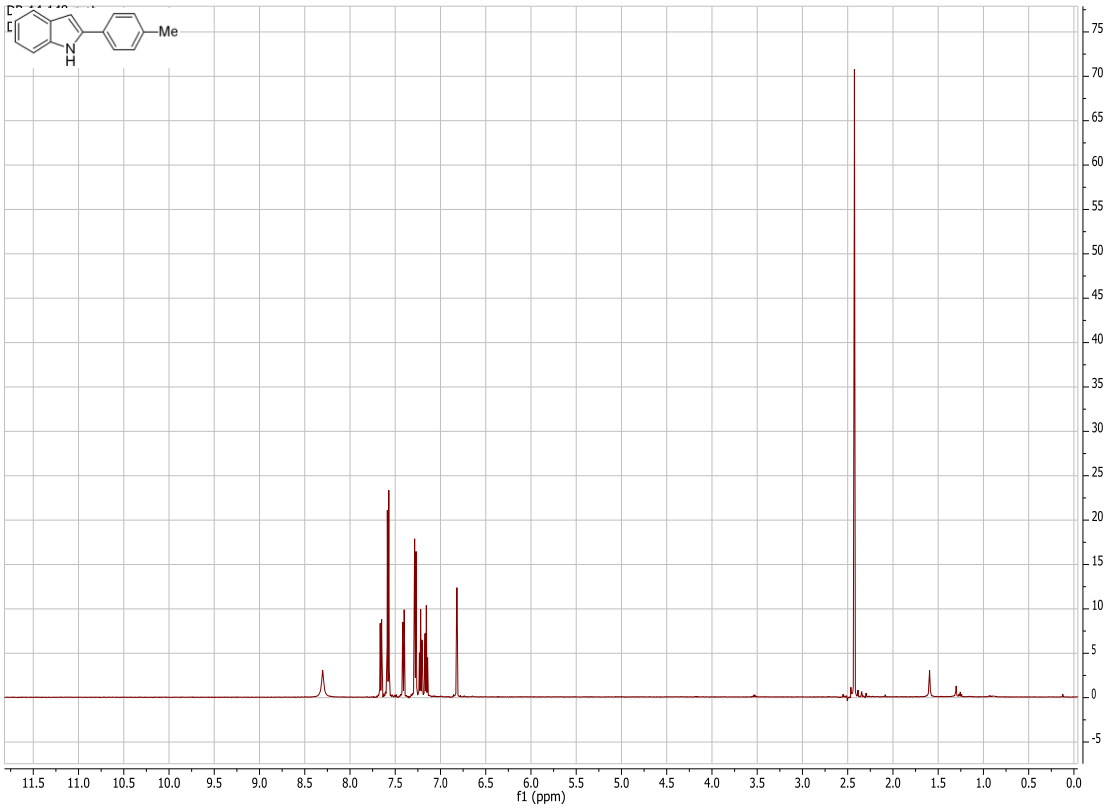

DR-17-291-carbon
Bpin
F
F
CO2Me
C (t)
165.03
D (t)
135.25
E (m)
112.35
F (s)
84.88
G (s)
52.82
H (s)
24.91
I (dd)
166.36
f1 (ppm)

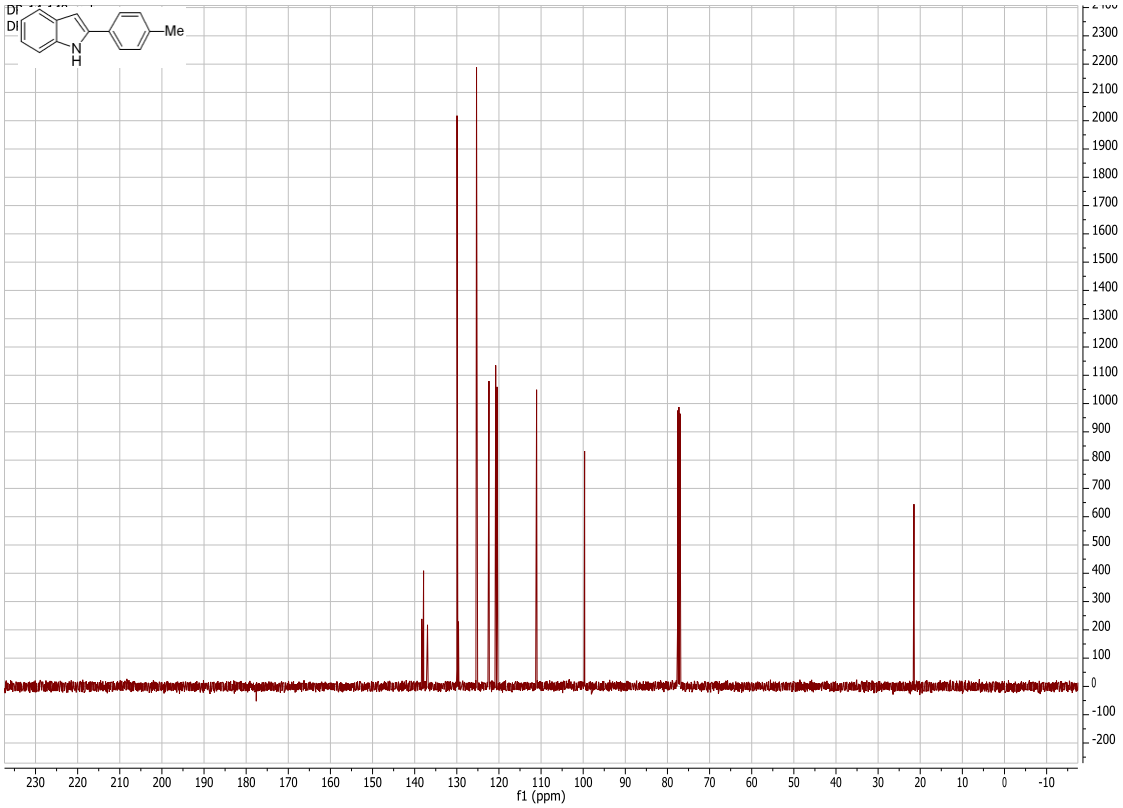

DR-18-277-fluorine
Bpin
F
F
CO2Me
f1 (ppm)

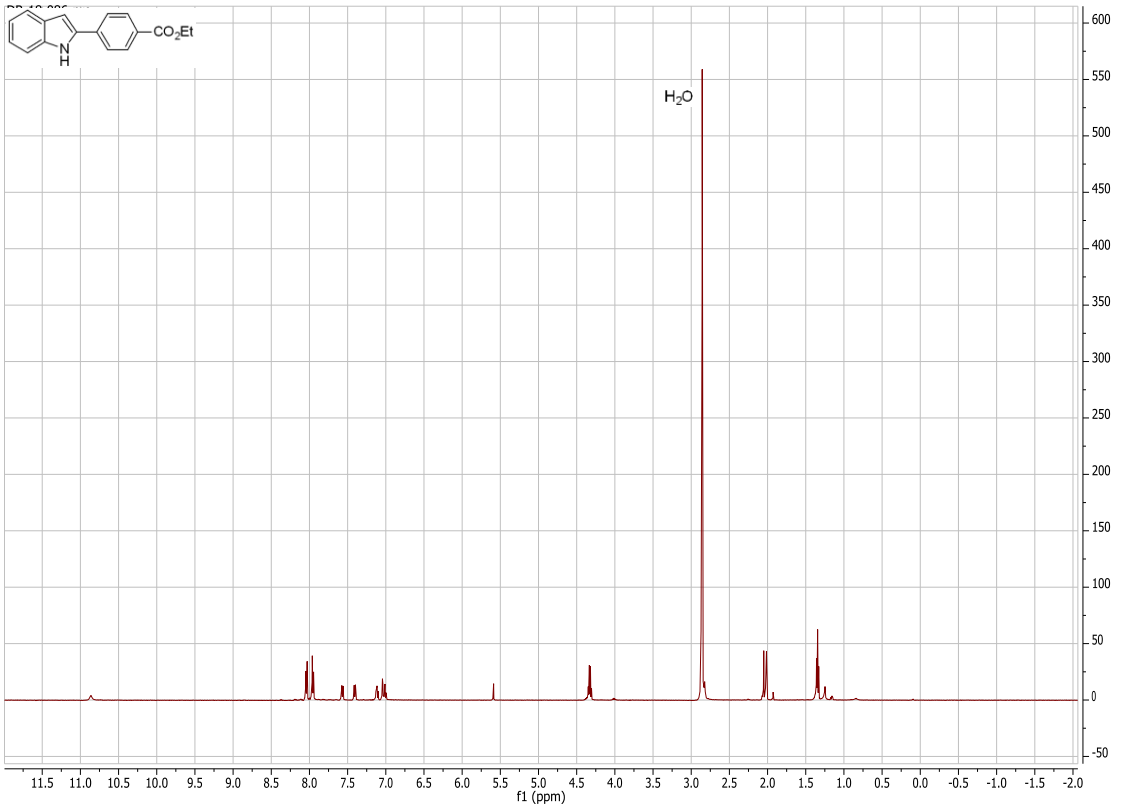

DR-16-151-proton
Bpin
F
F
OMe
6.39
6.37
3.78
1.35
A (d)
6.38
B (s)
3.78
C (s)
1.35
f1 (ppm)

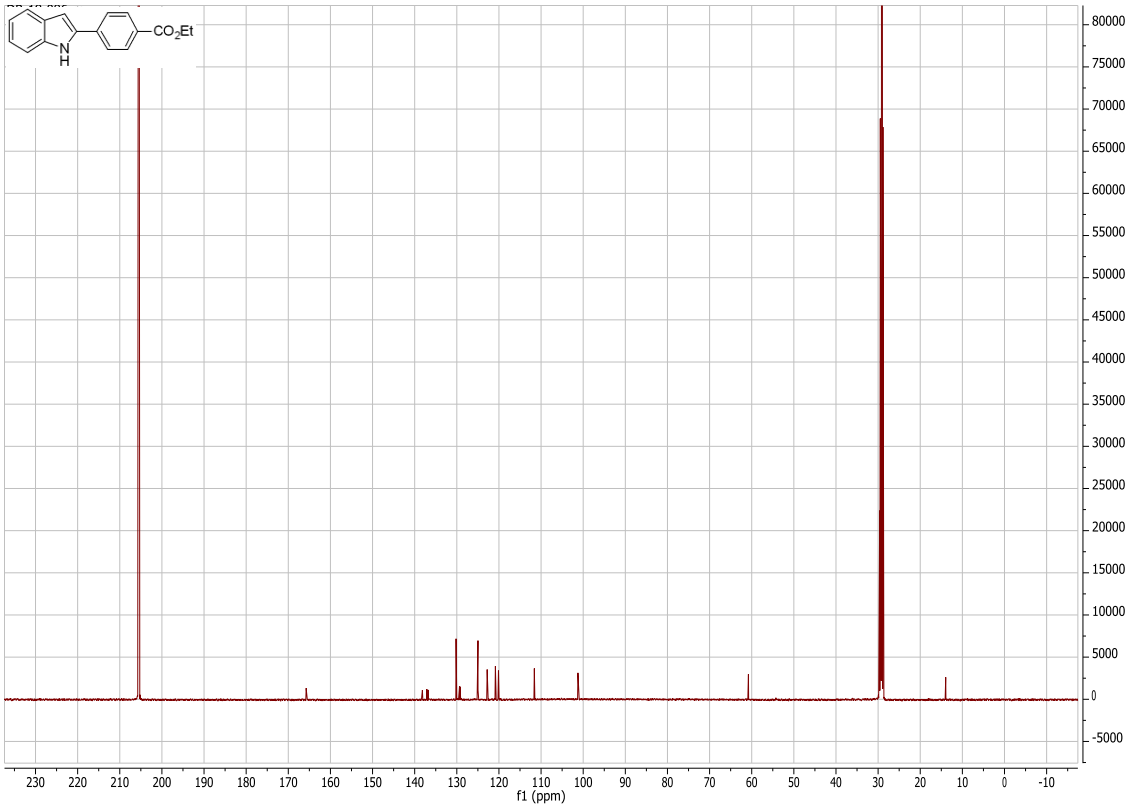

DR-16-151-carbon
Bpin
F
F
OMe
169.25
169.12
167.26
167.13
164.22
164.11
163.99
98.09
97.85
97.84
83.94
55.94
24.94
C (t)
164.11
H (dd)
168.19
D (m)
97.92
E (s)
83.94
G (s)
55.94
F (s)
24.94
f1 (ppm)

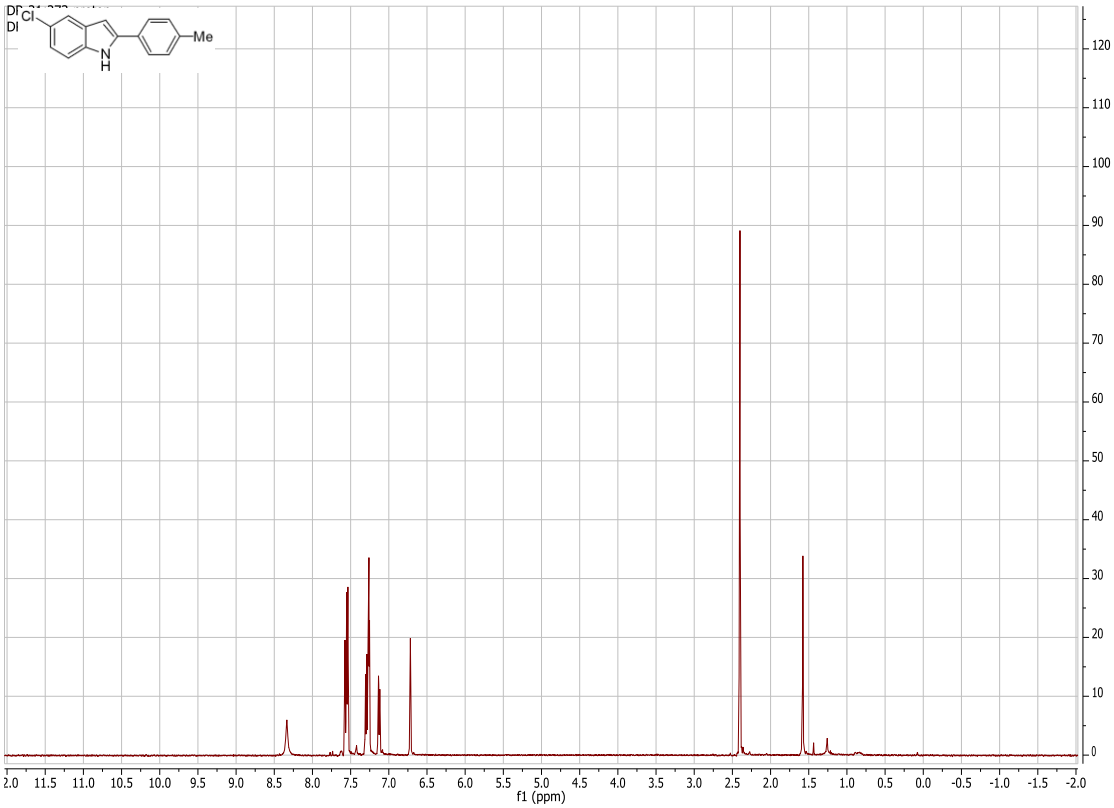

DR-18-276-fluorine
Bpin
F
F
OMe
f1 (ppm)

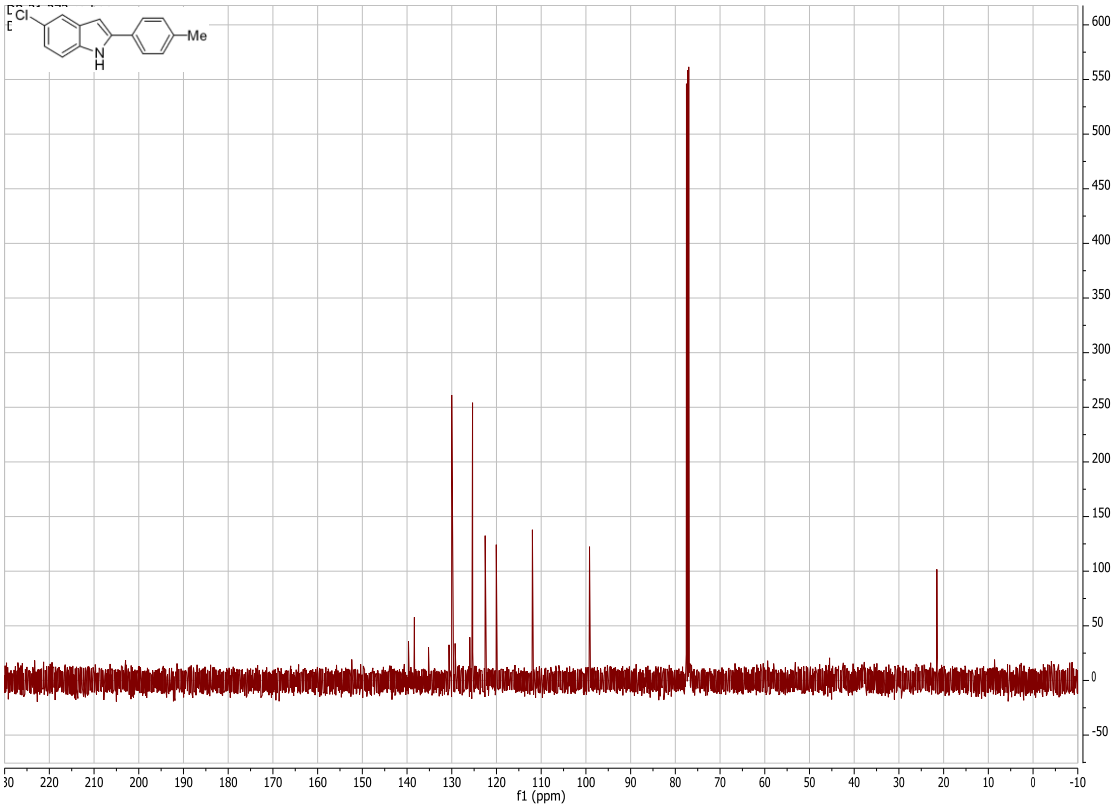

Me
N
H
f1 (ppm)

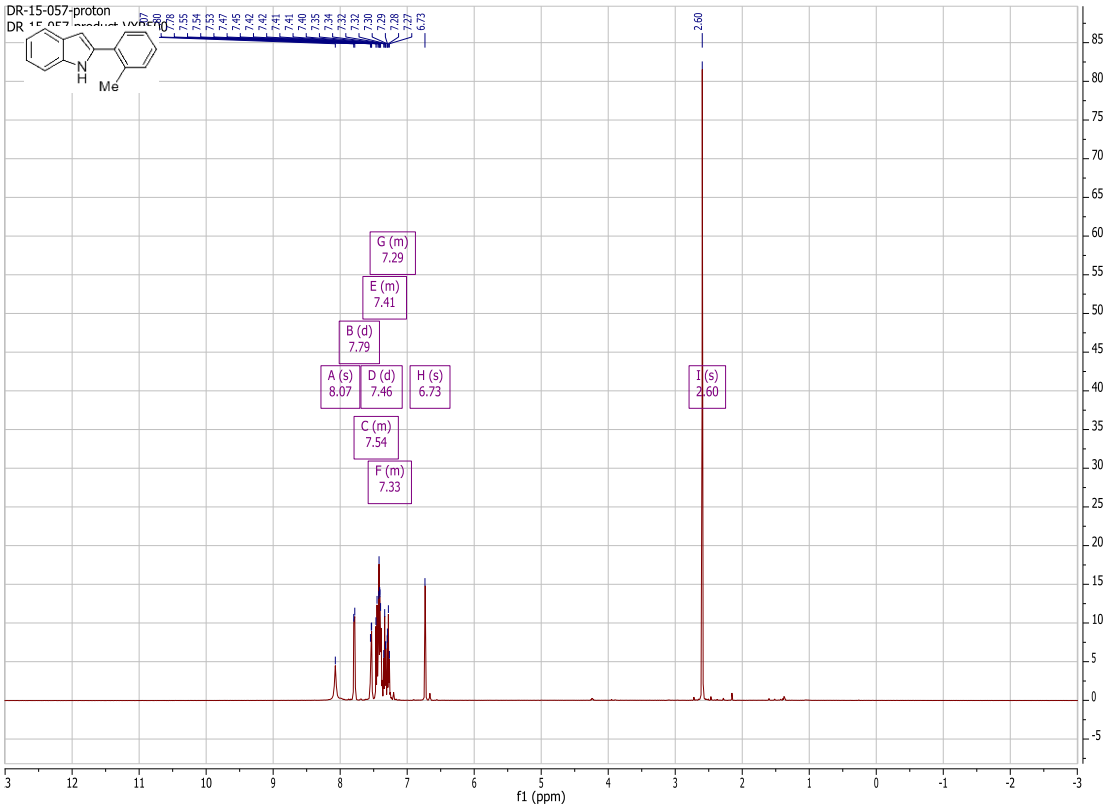

Me
N
H
f1 (ppm)

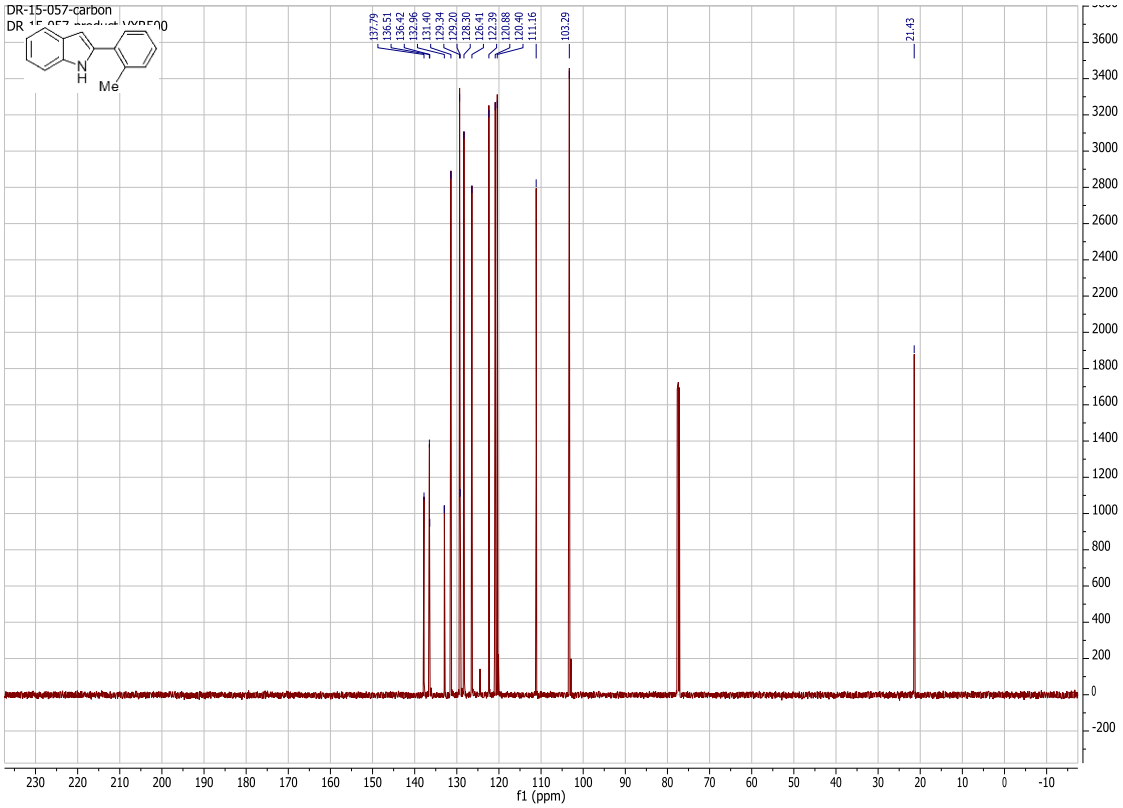

CO2Et
N
H
H2O
f1 (ppm)

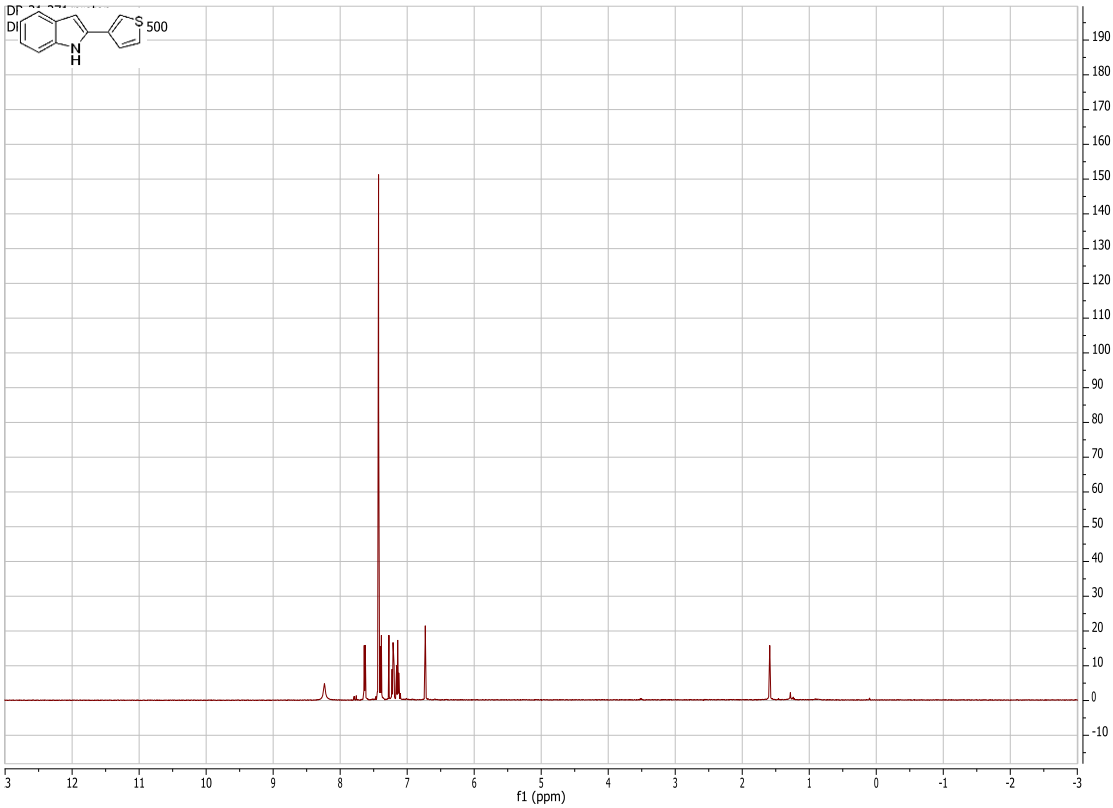

CO2Et
N
H
80000
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

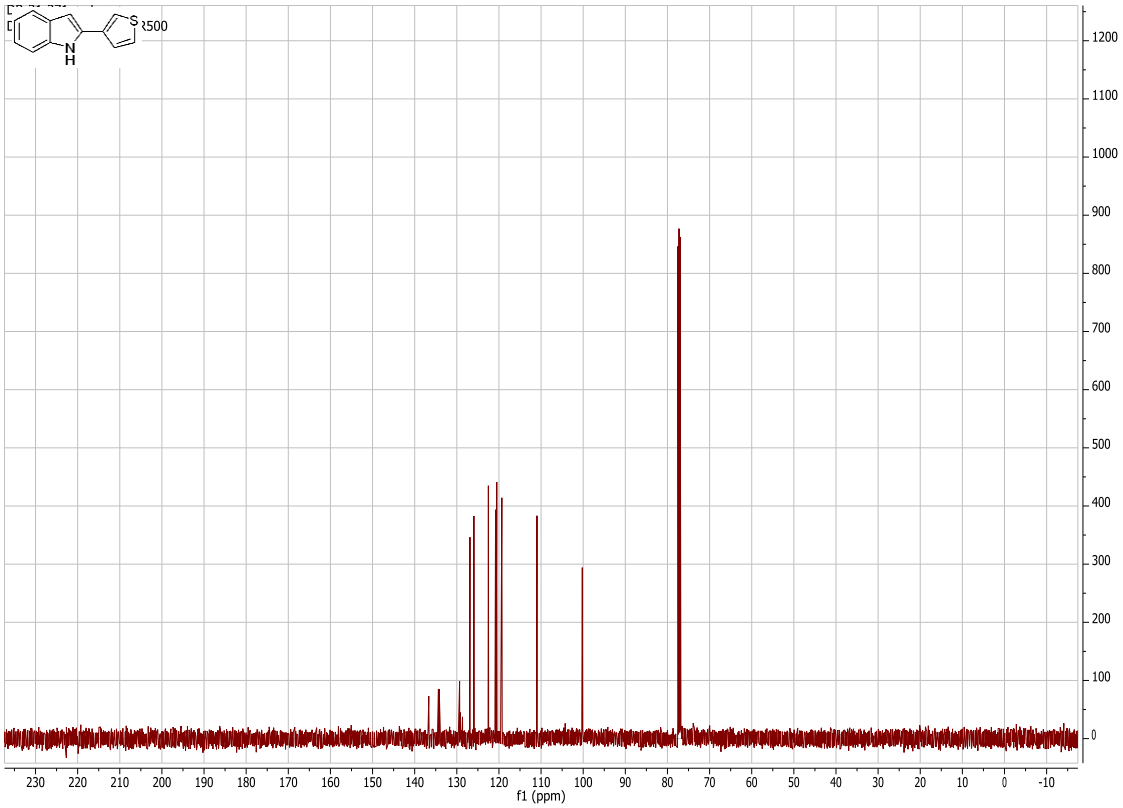

Cl
Me
N
H
120
110
100
90
80
70
60
50
40
30
20
10
0
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)

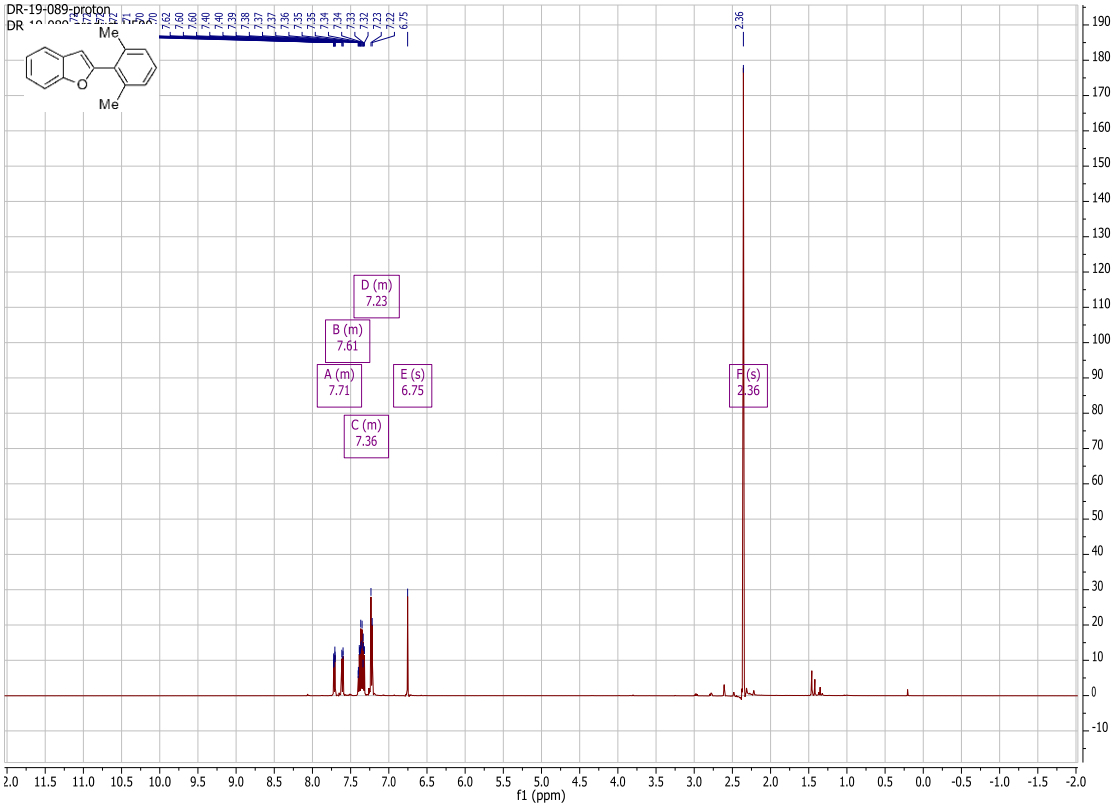

Cl
Me
N
H
f1 (ppm)

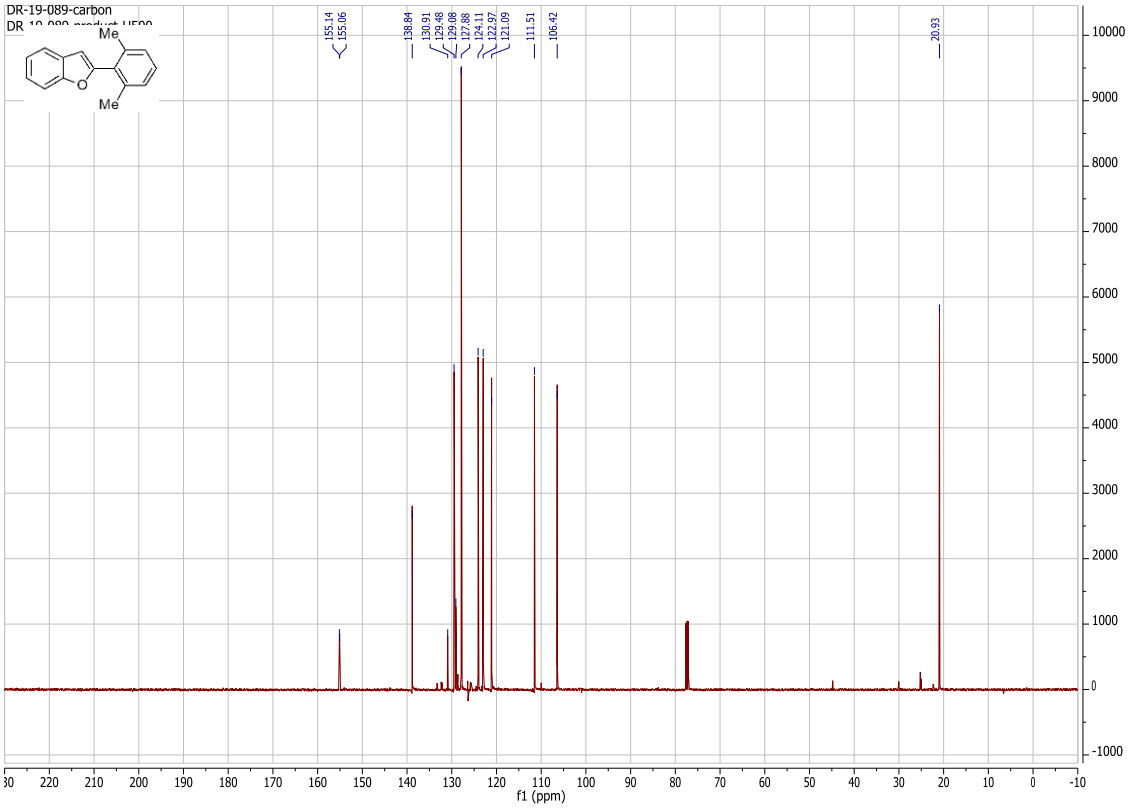

DR-15-057-proton
Me
N
H
G (m)
7.29
E (m)
7.41
B (d)
7.79
A (s)
8.07
D (d)
7.46
H (s)
6.73
C (m)
7.54
F (m)
7.33
I (s)
2.60
f1 (ppm)

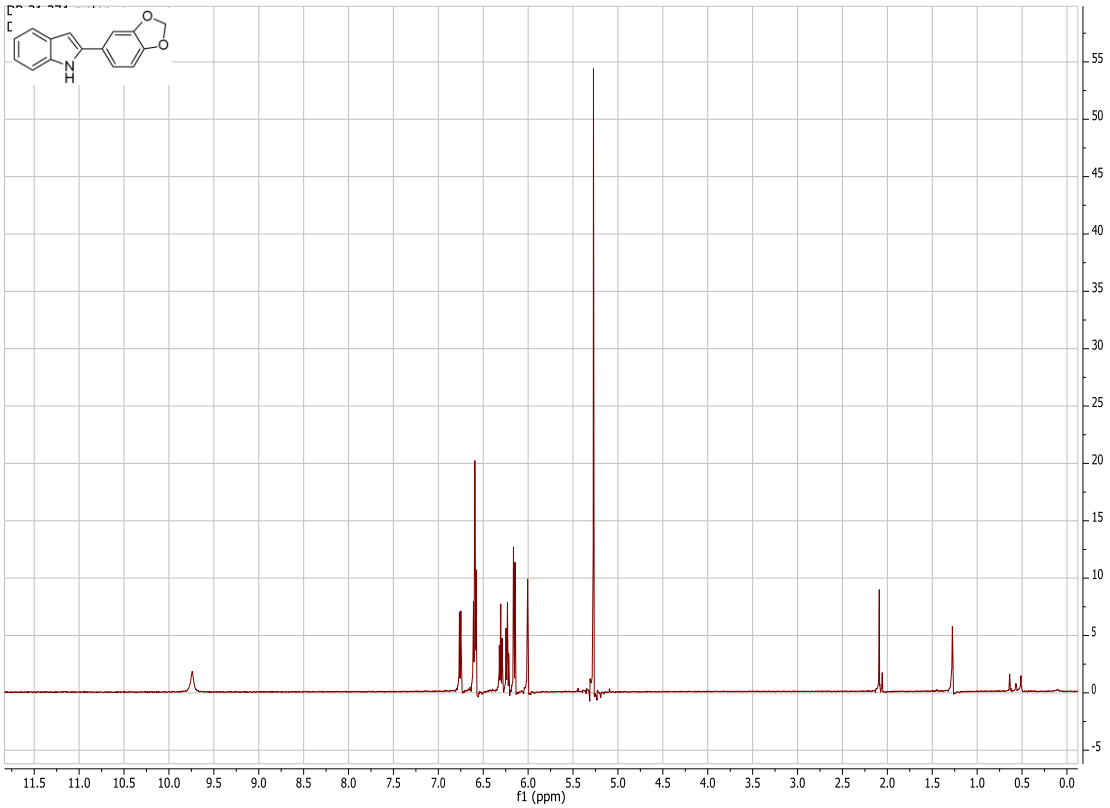

DR-15-057-carbon
137.79
136.51
136.42
132.96
131.40
129.34
129.20
128.30
126.41
122.39
121.88
120.40
111.16
103.29
21.43
Me
f1 (ppm)

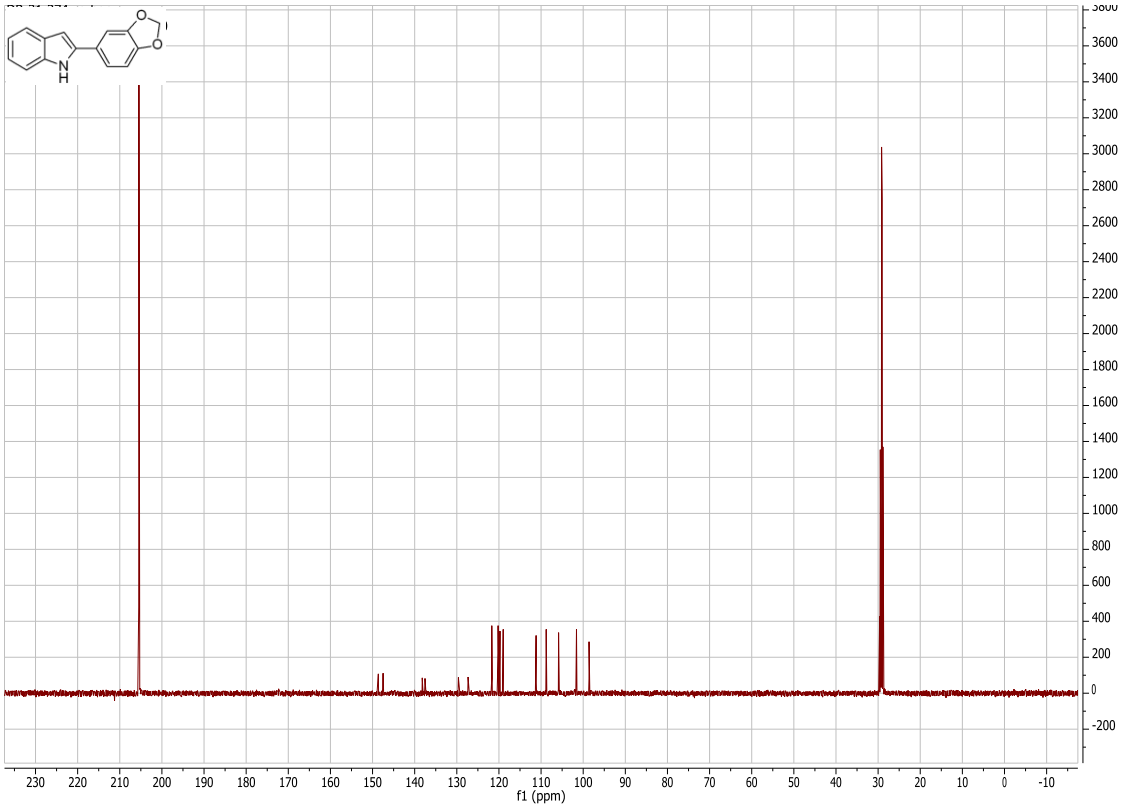

500
f1 (ppm)

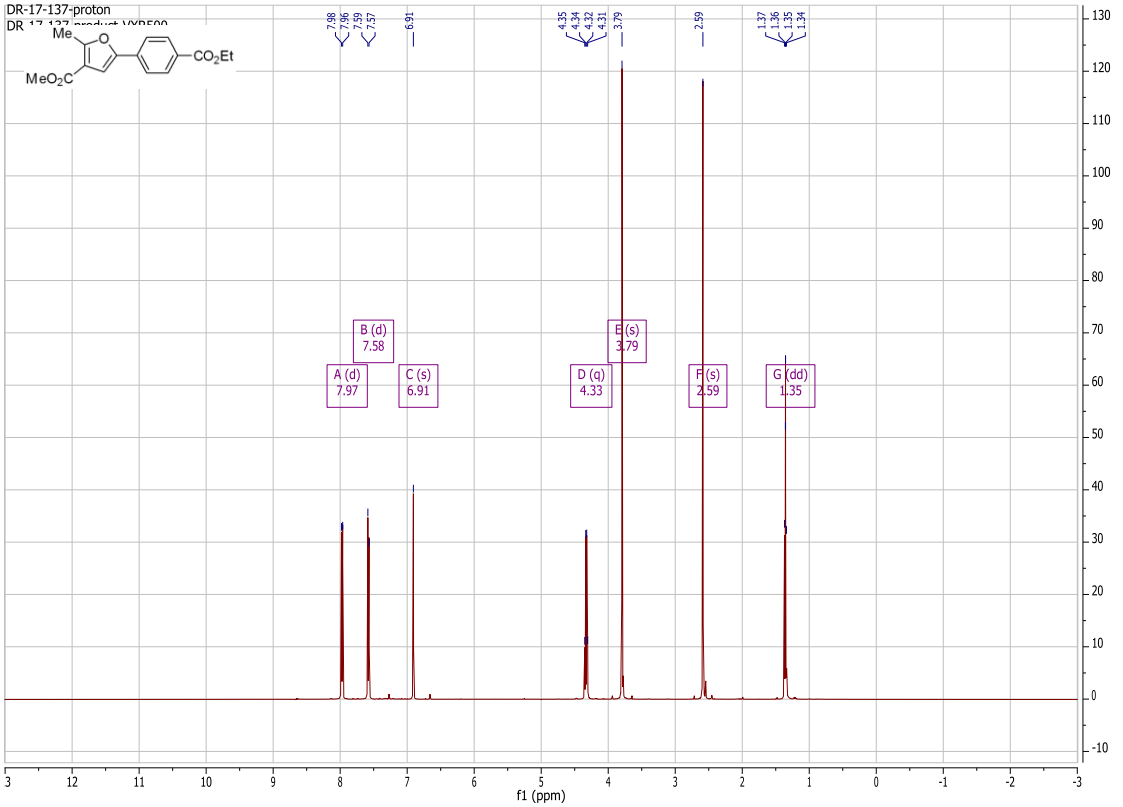

S
N
H
f1 (ppm)

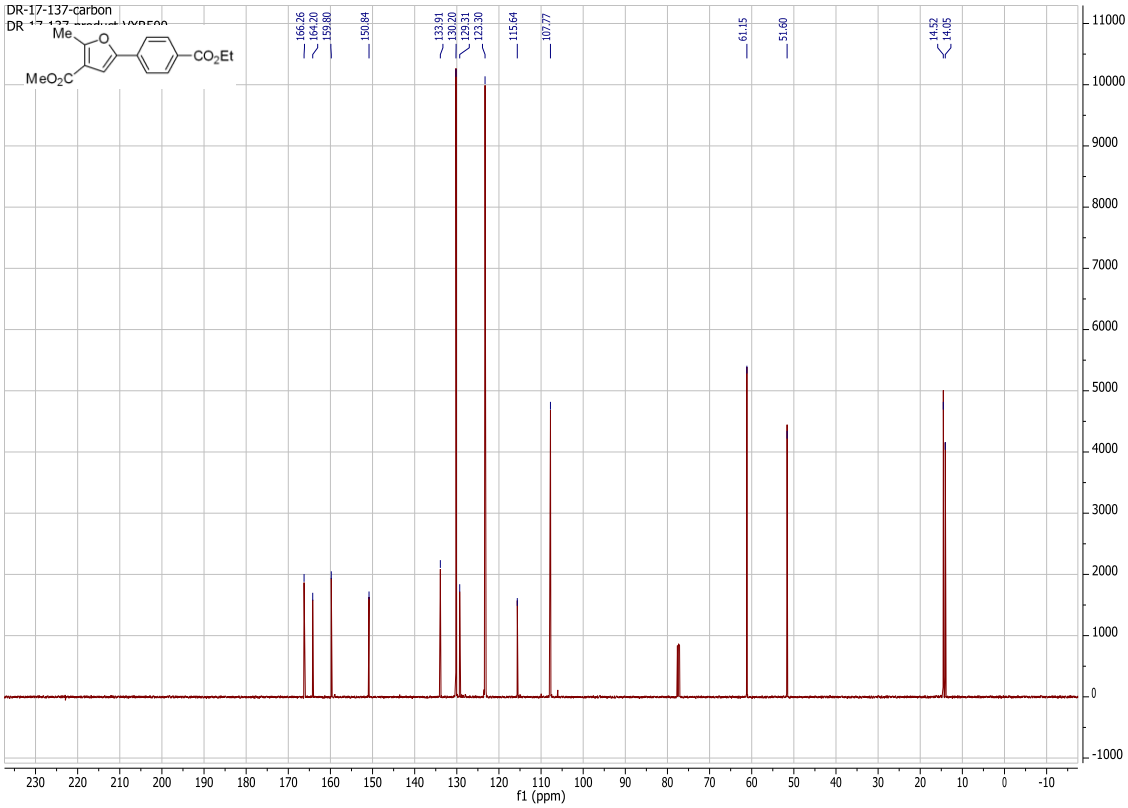

DR-19-089-proton
Me
Me
O
D (m)
7.23
B (m)
7.61
A (m)
7.71
E (s)
6.75
C (m)
7.36
F (s)
2.36
f1 (ppm)

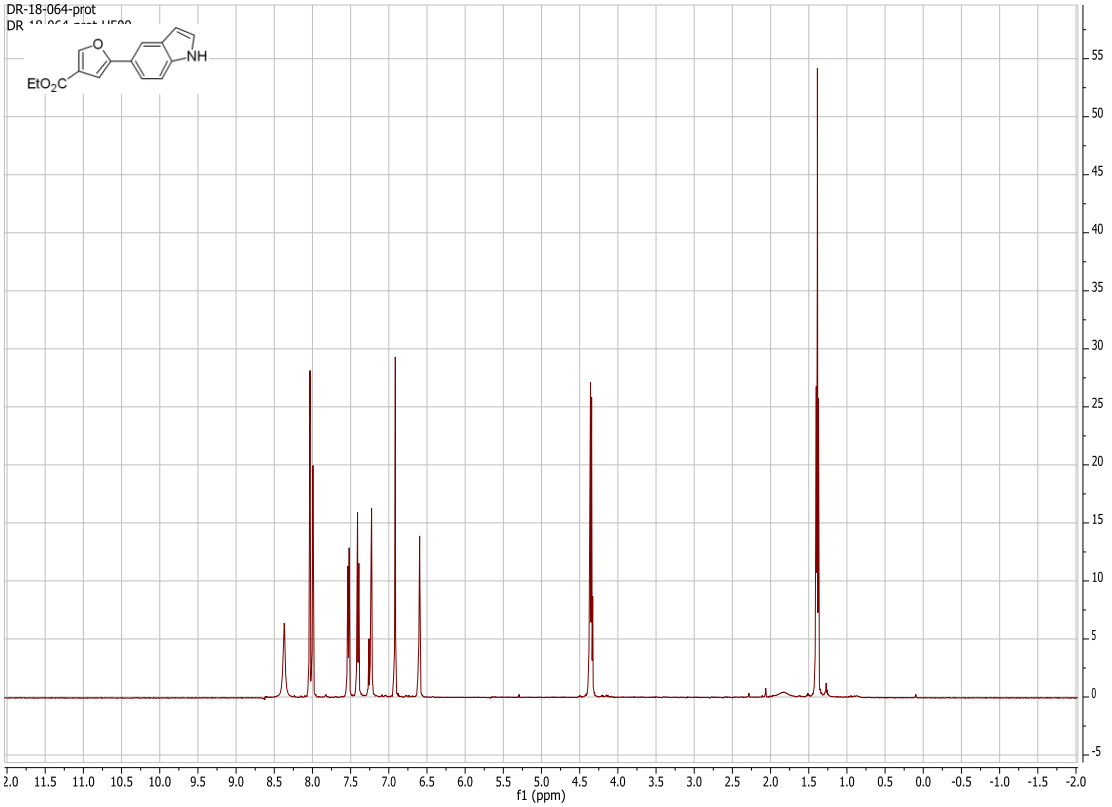

DR-19-089-carbon
Me
Me
155.14
155.06
138.84
130.91
129.48
129.08
127.88
124.11
122.37
121.09
111.51
106.42
20.93
f1 (ppm)


N
H
O
O
f1 (ppm)


f1 (ppm)


DR-17-137-proton
Me
MeO2C
CO2Et
7.98
7.96
7.59
7.57
6.91
4.35
4.34
4.32
4.31
3.79
2.59
1.37
1.36
1.35
1.34
B (d) 7.58
E (s) 3.79
A (d) 7.97
C (s) 6.91
D (q) 4.33
F (s) 2.59
G (dd) 1.35
f1 (ppm)


DR-17-137-carbon
Me
MeO2C
CO2Et
166.26
164.20
159.80
150.84
133.91
130.20
129.31
123.30
115.64
107.77
61.15
51.60
14.52
14.05
f1 (ppm)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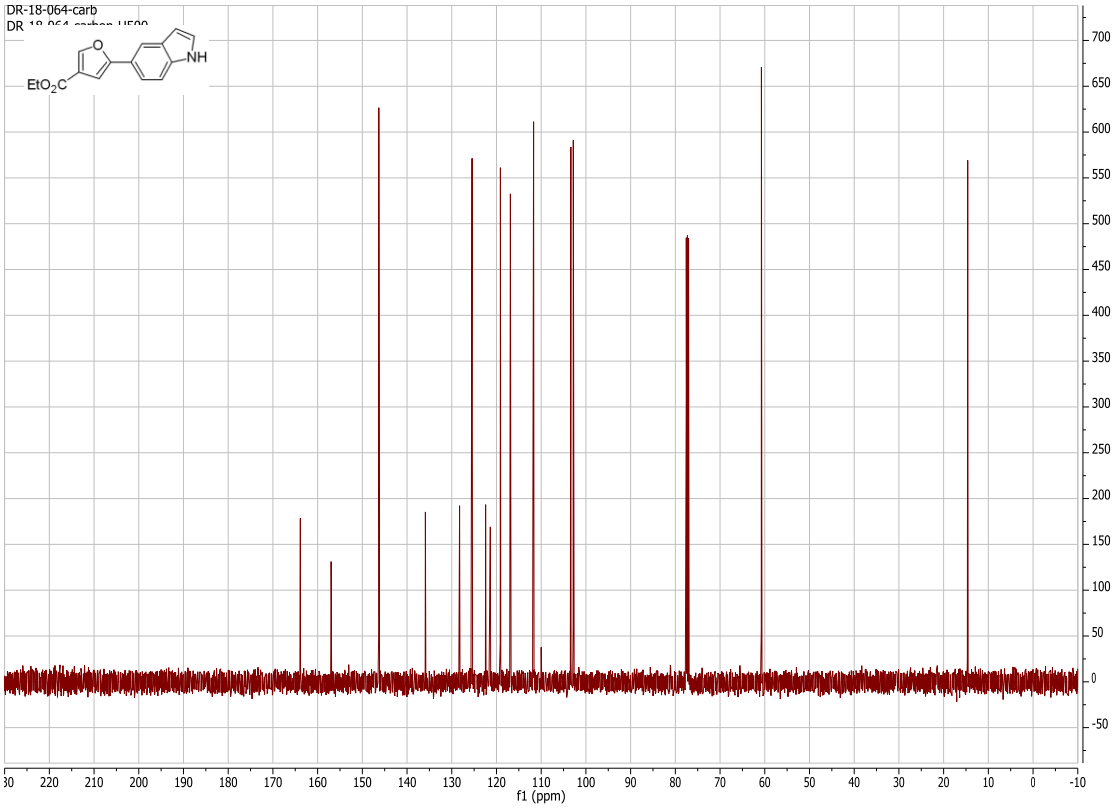
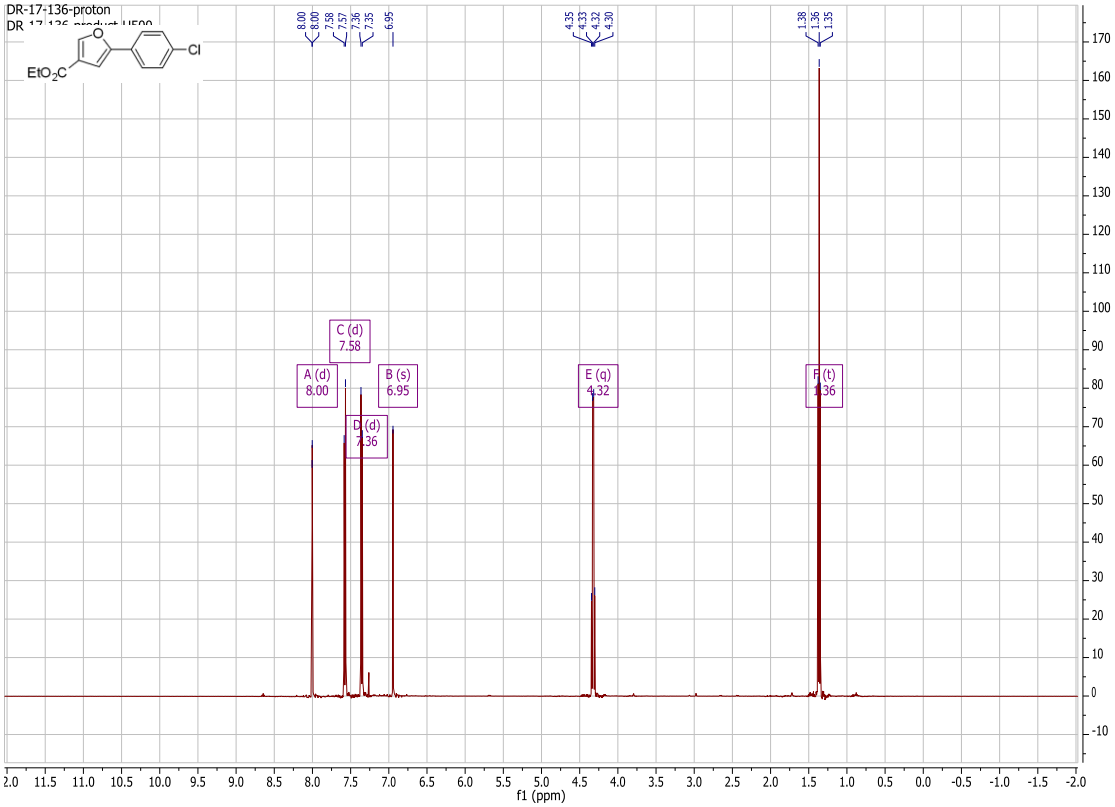
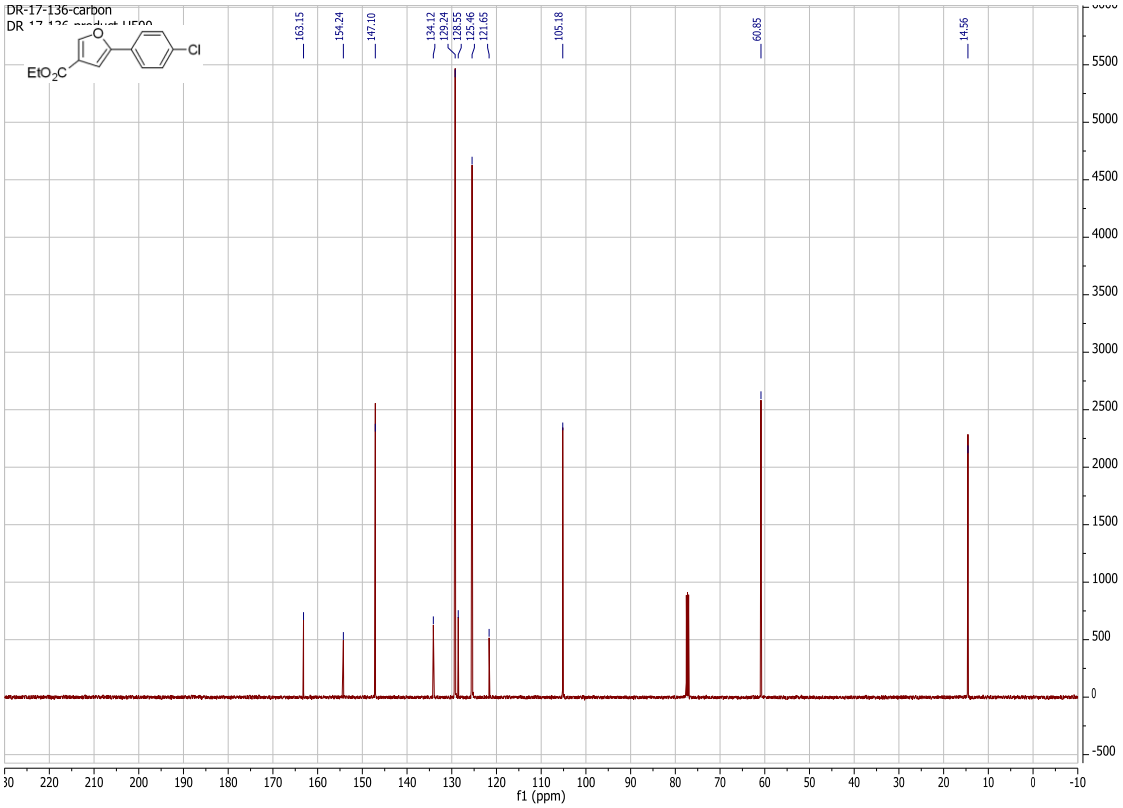
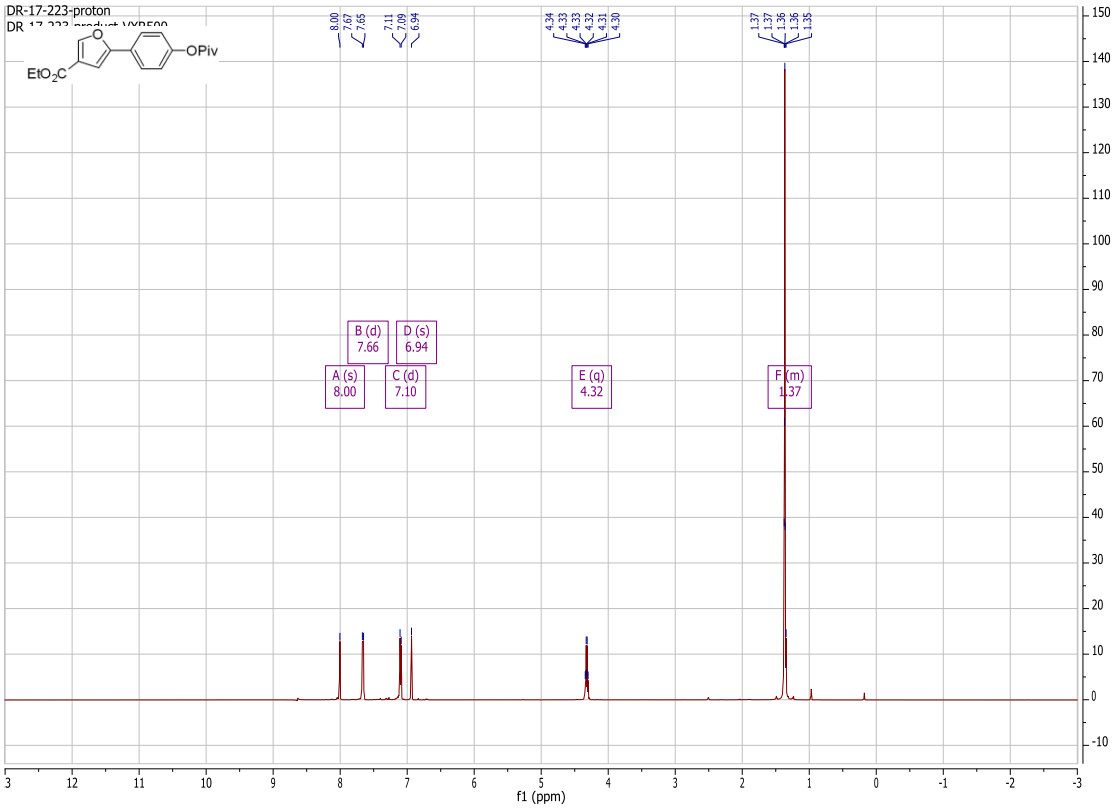
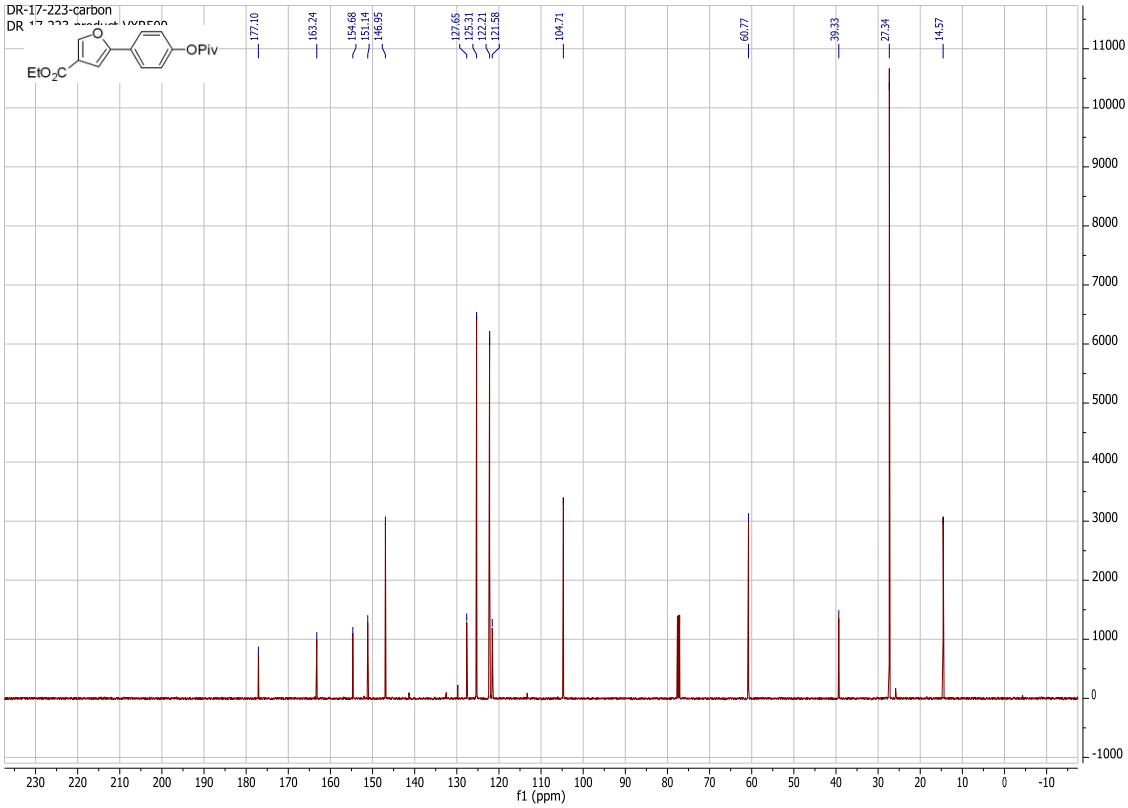
NH
EtO2C
f1 (ppm)

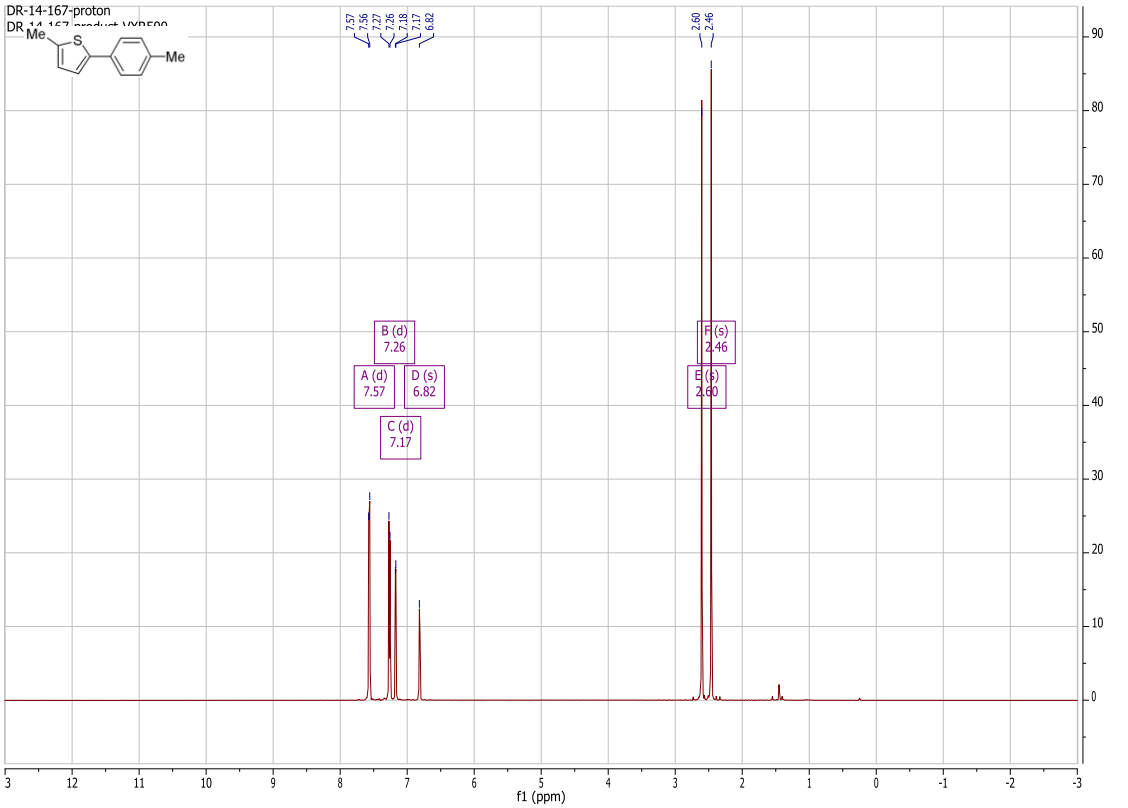

DR-18-064-carb
NH
O
EtO2C
f1 (ppm)

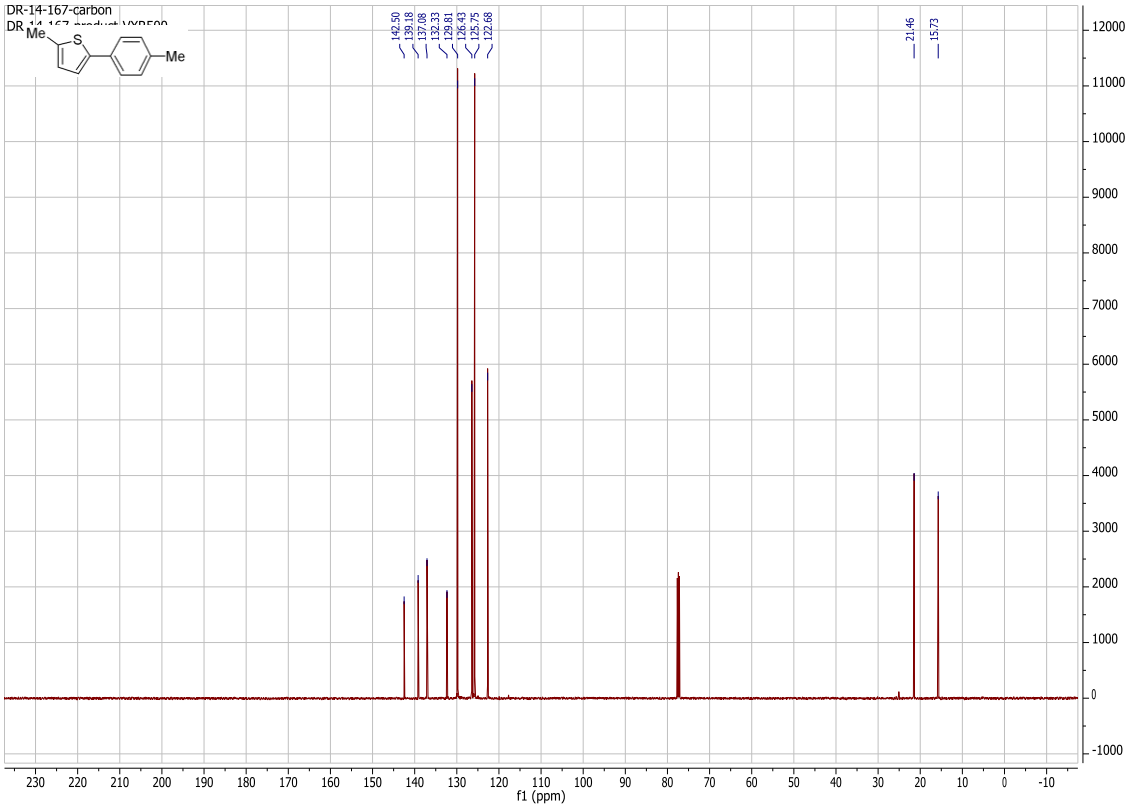

DR-17-136-proton
O
Cl
EtO2C
8.00
8.00
7.58
7.57
7.36
7.35
6.95
4.35
4.33
4.32
4.30
1.38
1.36
1.35
C (d)
7.58
A (d)
8.00
B (s)
6.95
D (d)
7.36
E (q)
4.32
F (t)
1.36
f1 (ppm)

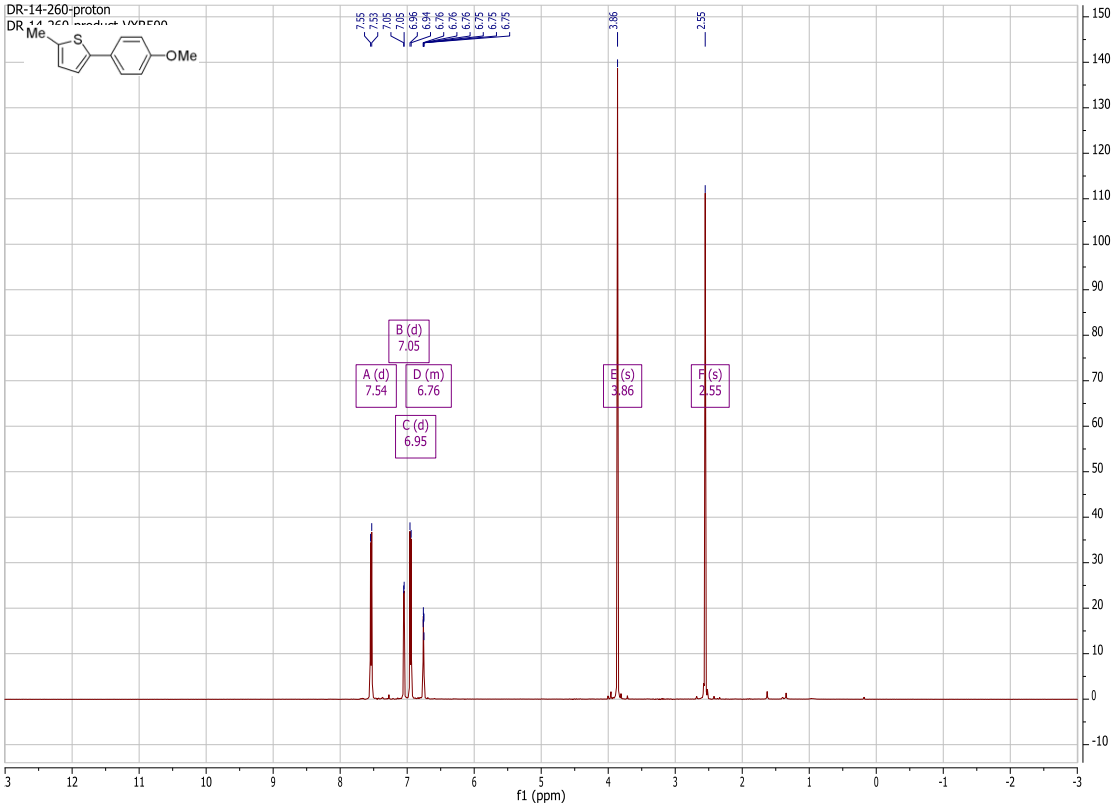

DR-17-136-carbon
163.15
154.24
147.10
134.12
129.24
128.55
125.46
121.65
105.18
60.85
14.56
Cl
EtO2C
f1 (ppm)

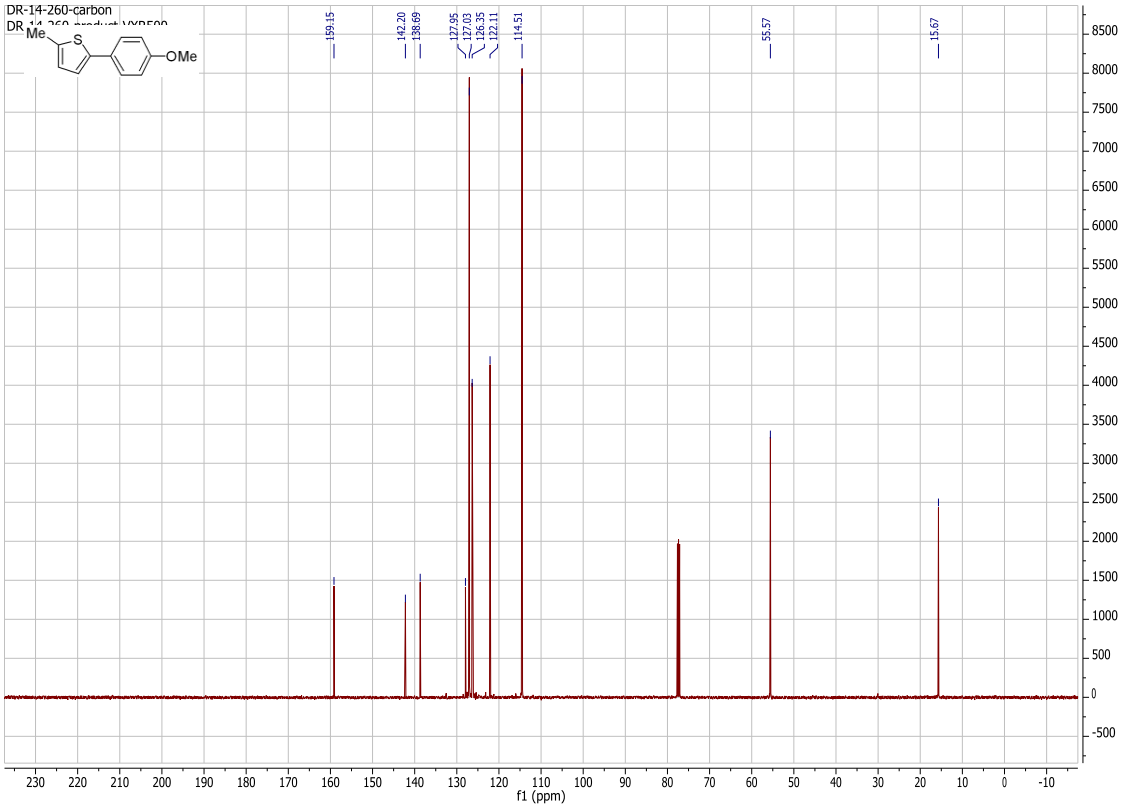

DR-17-223-proton
8.00
7.67
7.65
7.11
7.09
6.94
4.34
4.33
4.33
4.32
4.31
4.30
1.37
1.37
1.36
1.36
1.35
OPiv
EtO2C
B (d) 7.66
D (s) 6.94
A (s) 8.00
C (d) 7.10
E (q) 4.32
F (m) 1.37
f1 (ppm)

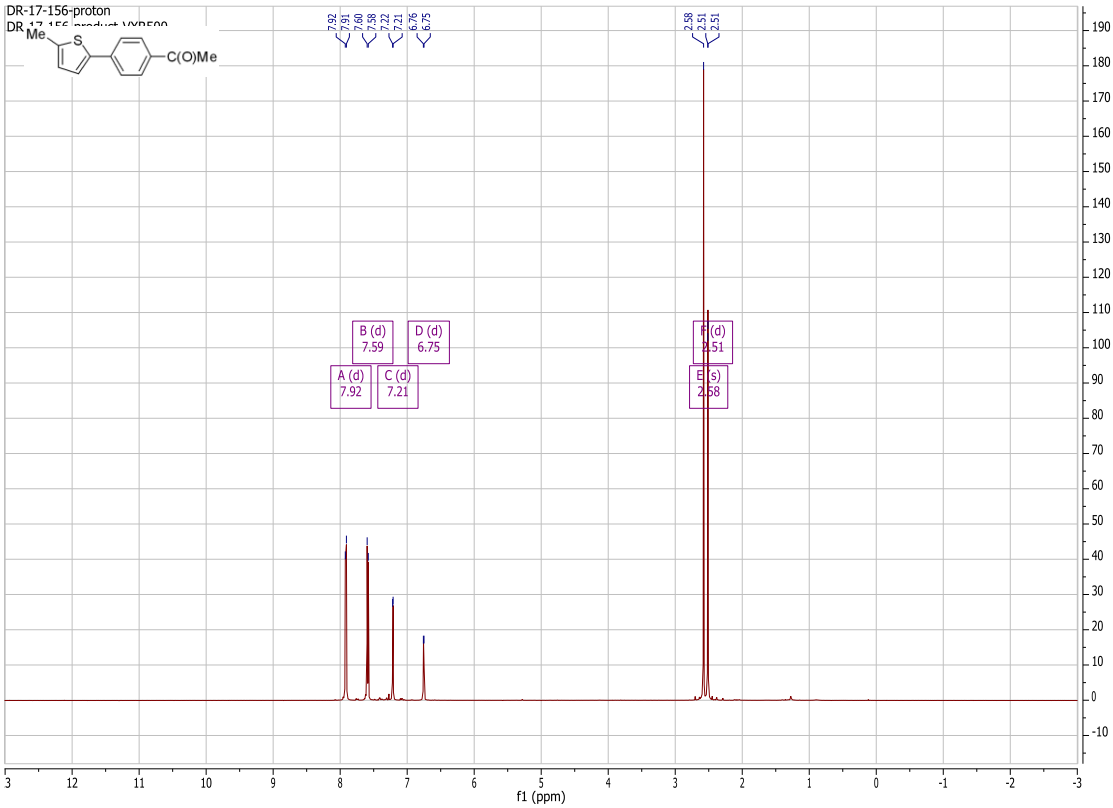

DR-17-223-carbon
EtO2C
OPiv
177.10
163.24
154.68
151.14
146.95
127.65
125.31
122.21
121.58
104.71
60.77
39.33
27.34
14.57
f1 (ppm)

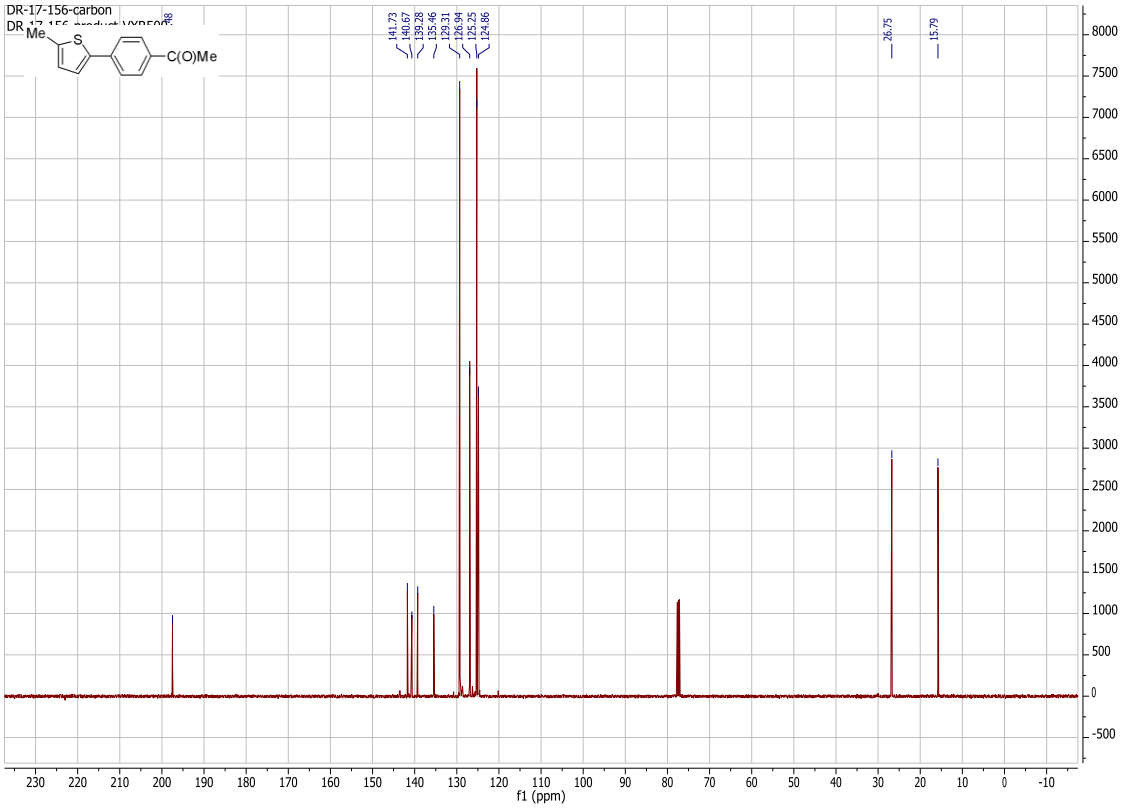

DR-14-167-proton
Me
S
Me
7.57
7.56
7.27
7.26
7.18
7.17
6.82
2.60
2.46
B (d)
7.26
A (d)
7.57
D (s)
6.82
C (d)
7.17
F (s)
2.46
E (s)
2.60
f1 (ppm)

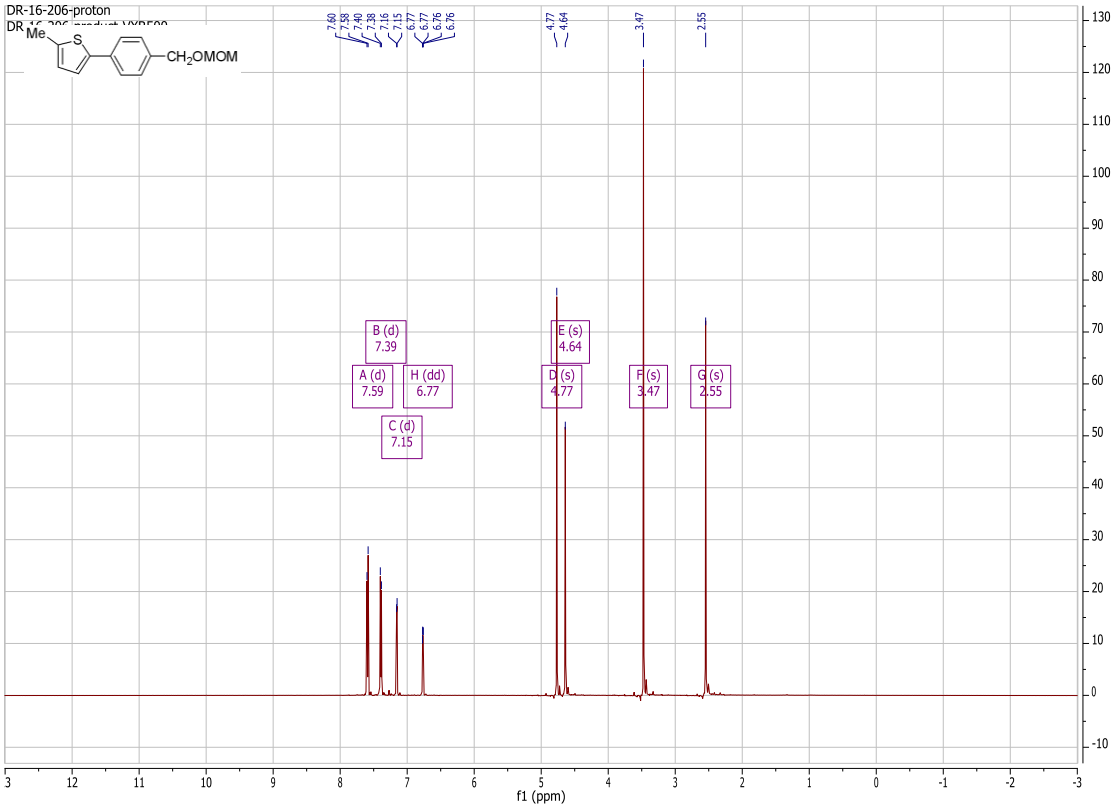

DR-14-167-carbon
Me
S
Me
142.50
139.18
137.08
132.33
129.81
126.43
125.75
122.68
21.46
15.73
f1 (ppm)

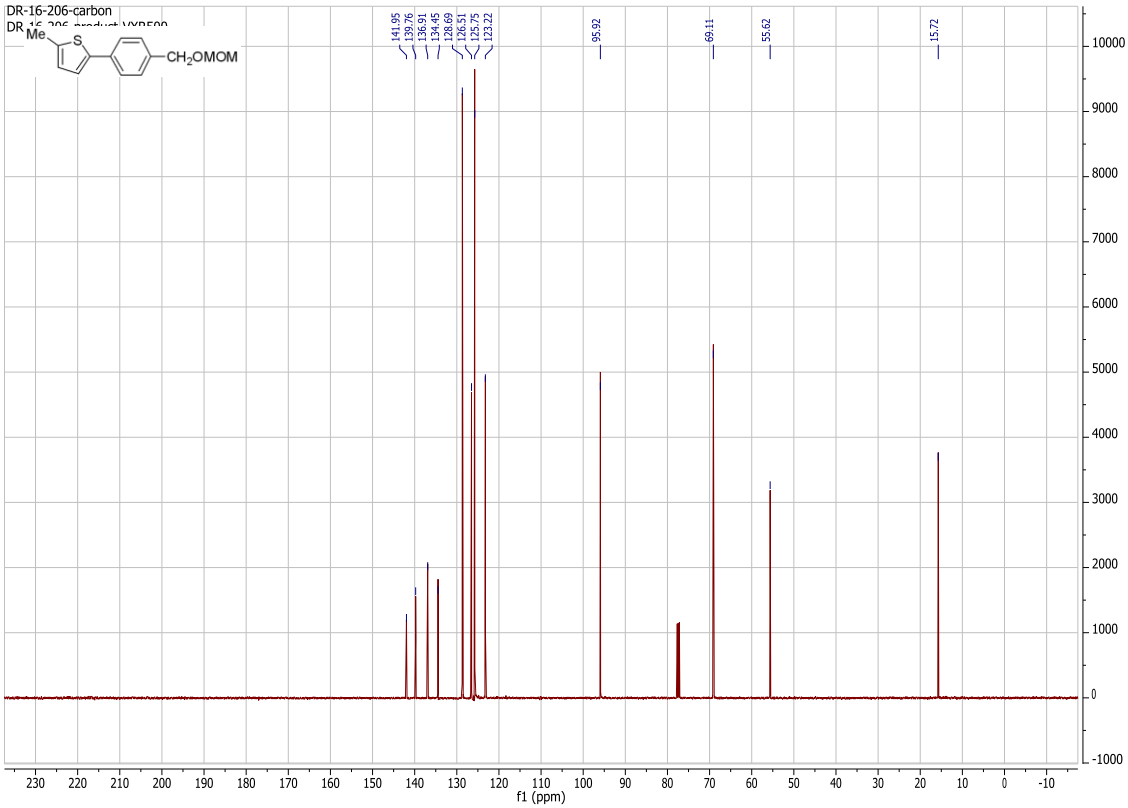

DR-14-260-proton
Me
S
OMe
7.55
7.53
7.05
7.05
6.96
6.94
6.76
6.76
6.76
6.75
6.75
6.75
3.86
2.55
B (d)
7.05
A (d)
7.54
D (m)
6.76
C (d)
6.95
E (s)
3.86
F (s)
2.55
f1 (ppm)

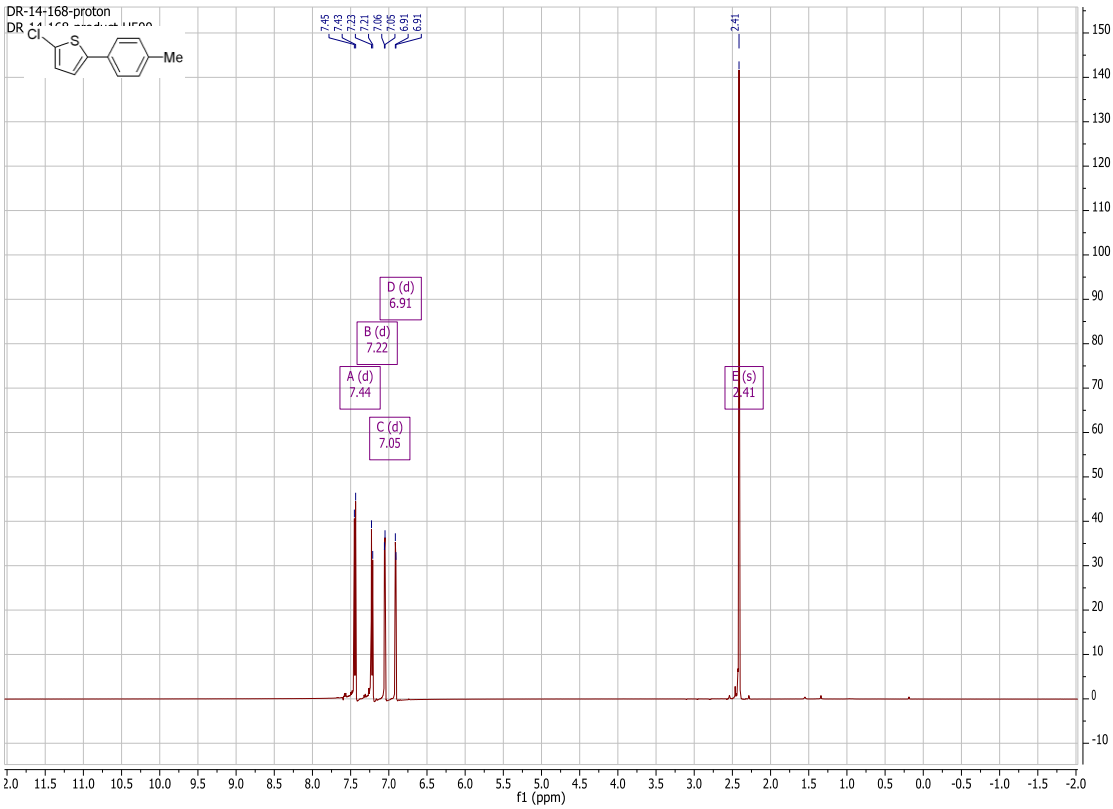

DR-14-260-carbon
Me
S
OMe
159.15
142.20
138.69
127.95
127.03
126.35
122.11
114.51
55.57
15.67
f1 (ppm)

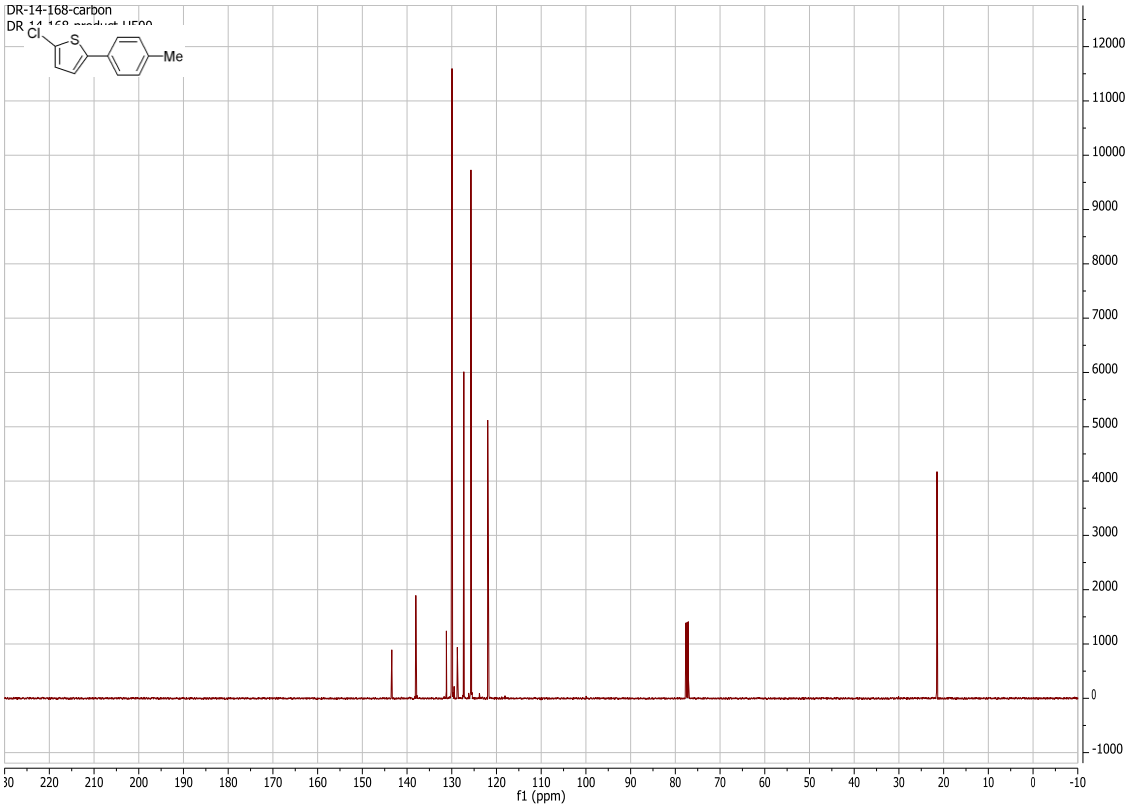

DR-17-156-proton
Me
S
C(O)Me
7.92
7.91
7.60
7.58
7.22
7.21
6.76
6.75
2.58
2.51
2.51
2.51
B (d) 7.59
D (d) 6.75
A (d) 7.92
C (d) 7.21
F (d) 2.51
E (s) 2.58
f1 (ppm)

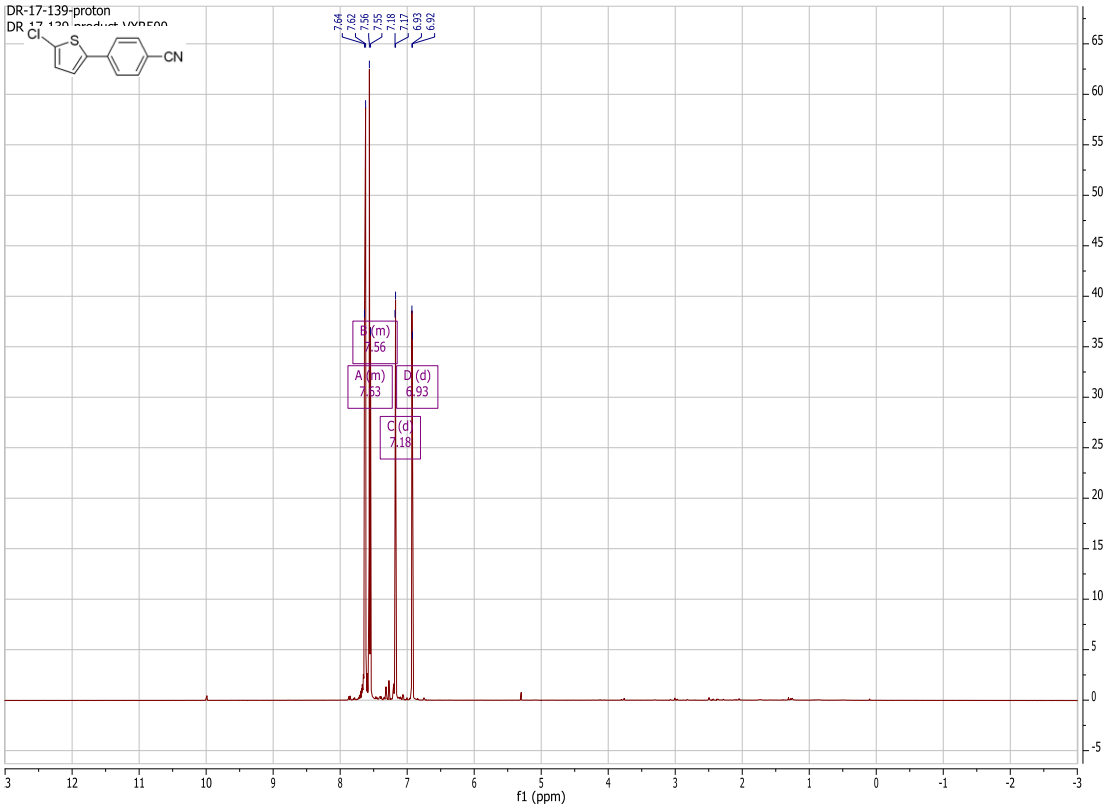

DR-17-156-carbon
Me
S
C(O)Me
141.73
140.67
139.28
135.46
129.31
126.94
125.25
124.86
26.75
15.79
f1 (ppm)

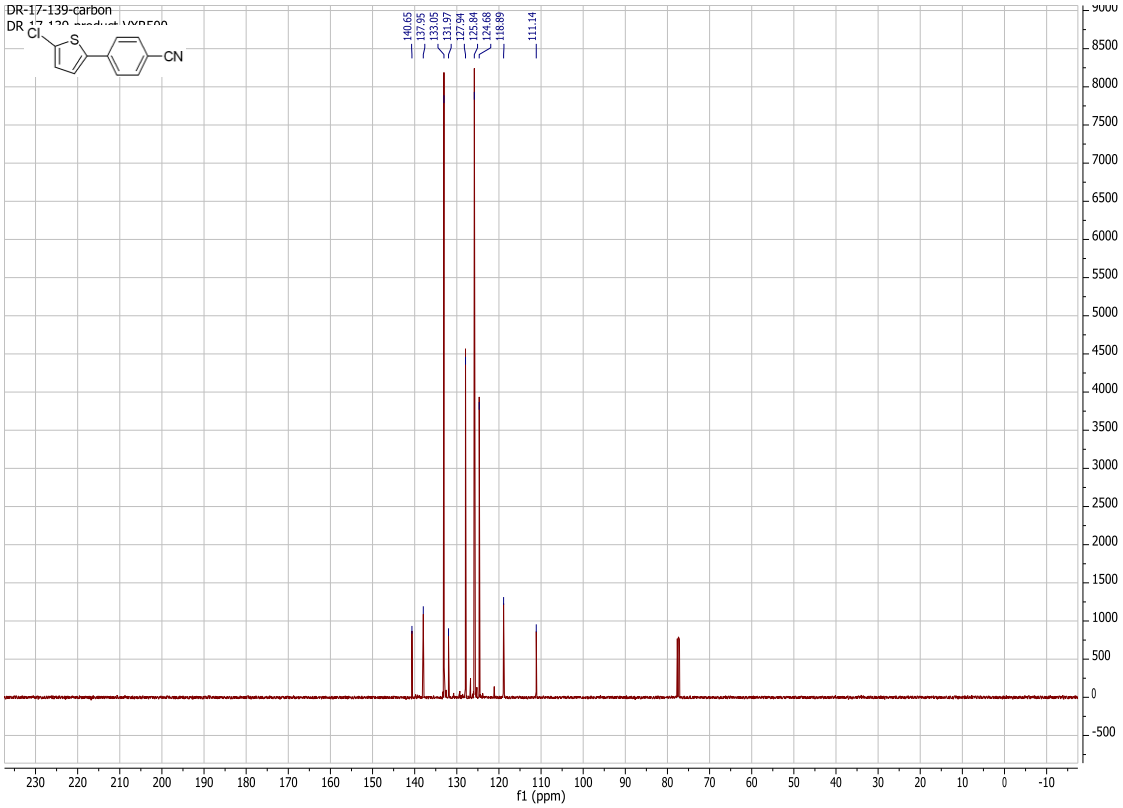

DR-16-206-proton
Me
S
CH2OMOM
7.60
7.58
7.40
7.38
7.16
7.15
6.77
6.77
6.76
6.76
4.77
4.64
3.47
2.55
B (d)
7.39
A (d)
7.59
H (dd)
6.77
C (d)
7.15
E (s)
4.64
D (s)
4.77
F (s)
3.47
G (s)
2.55
f1 (ppm)

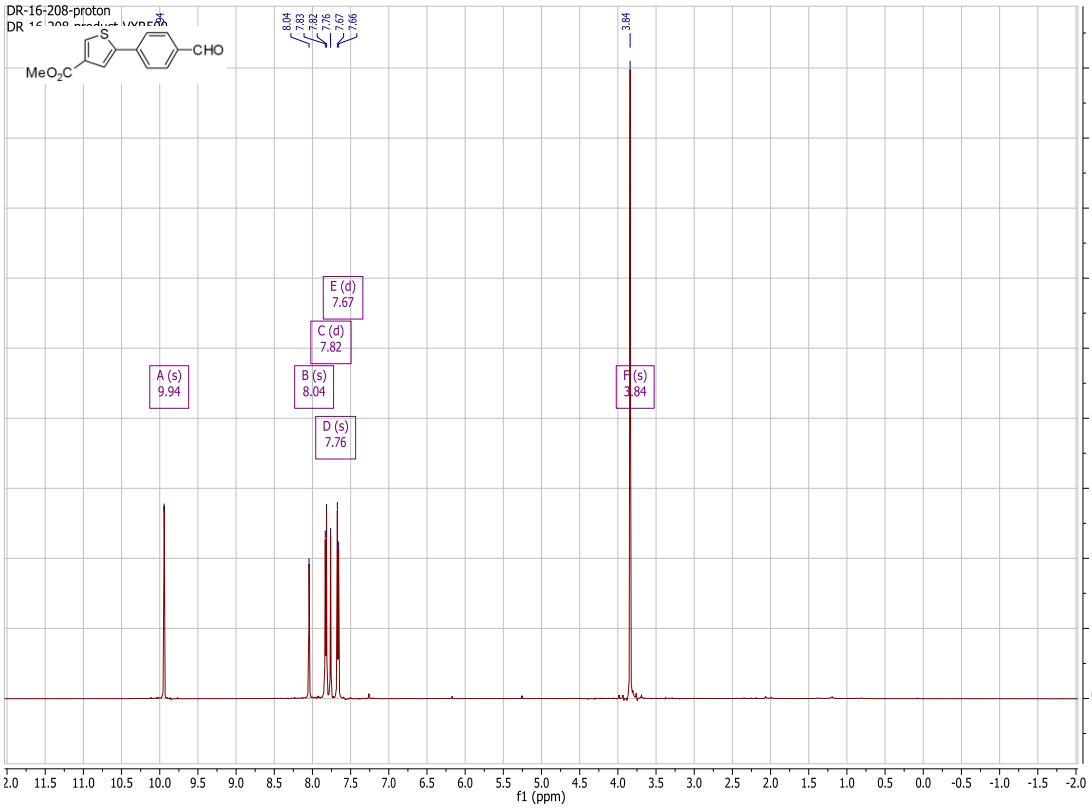

DR-16-206-carbon
Me
S
CH2OMOM
141.95
139.76
134.91
134.45
128.69
126.51
125.75
123.22
95.92
69.11
55.62
15.72
f1 (ppm)

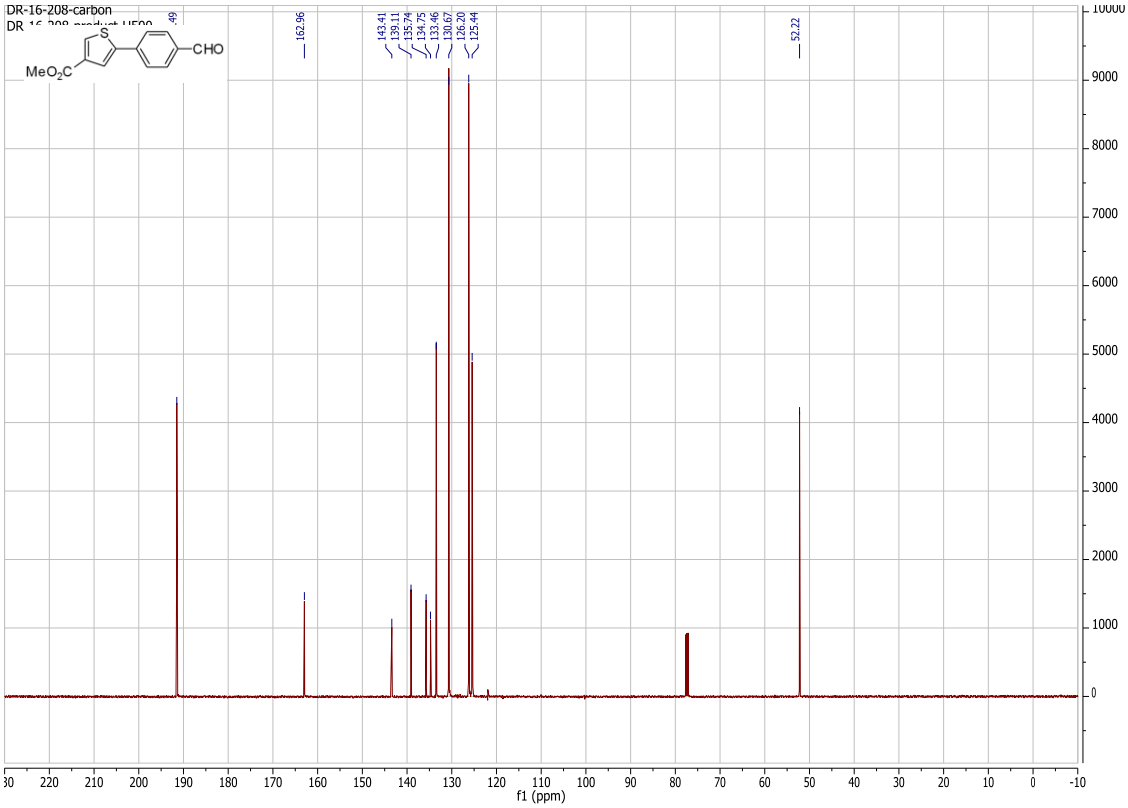

DR-14-168-proton
Cl
S
Me
7.45
7.43
7.33
7.21
7.06
7.05
6.91
6.91
2.41
D (d)
6.91
B (d)
7.22
A (d)
7.44
C (d)
7.05
E (s)
2.41
f1 (ppm)

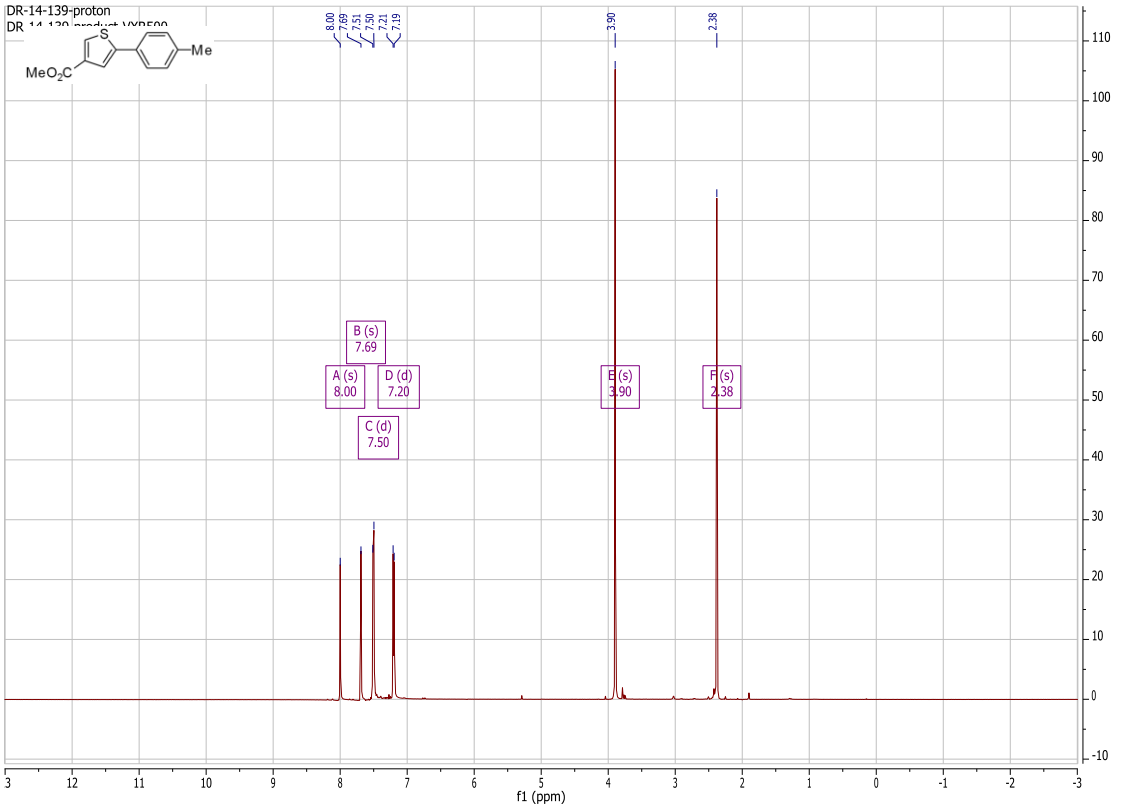

DR-14-168-carbon
Cl
S
Me
f1 (ppm)

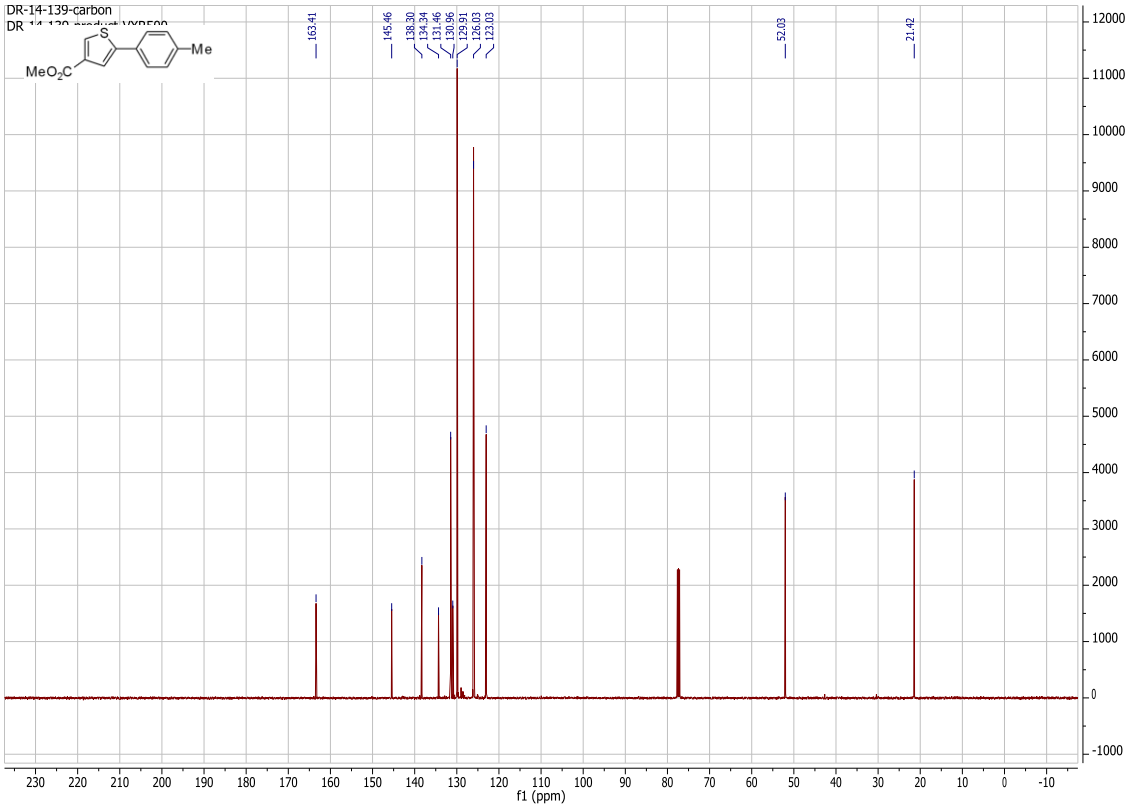

DR-17-139-proton
Cl
S
CN
7.64
7.62
7.56
7.55
7.18
7.17
6.93
6.92
B (m)
7.56
A (m)
7.53
D (d)
6.93
C (d)
7.18
f1 (ppm)

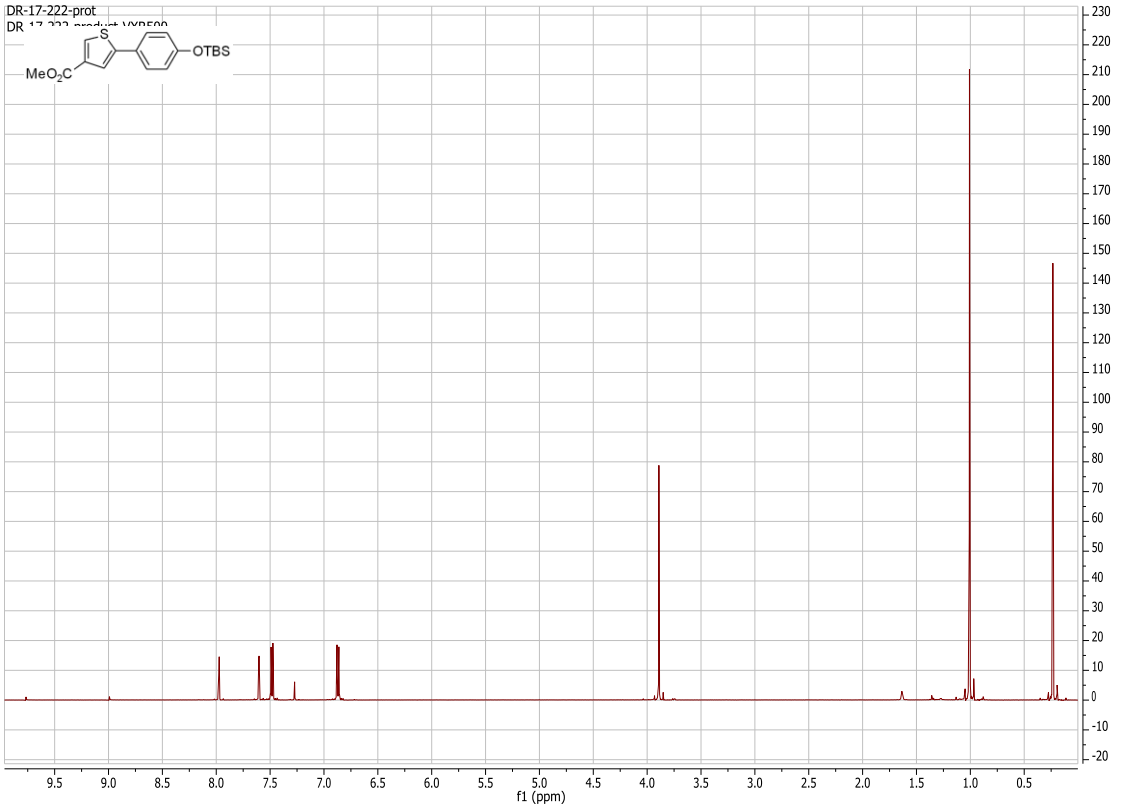

DR-17-139-carbon
Cl
S
CN
140.65
137.95
133.05
131.97
127.94
125.84
124.68
118.89
111.14
f1 (ppm)

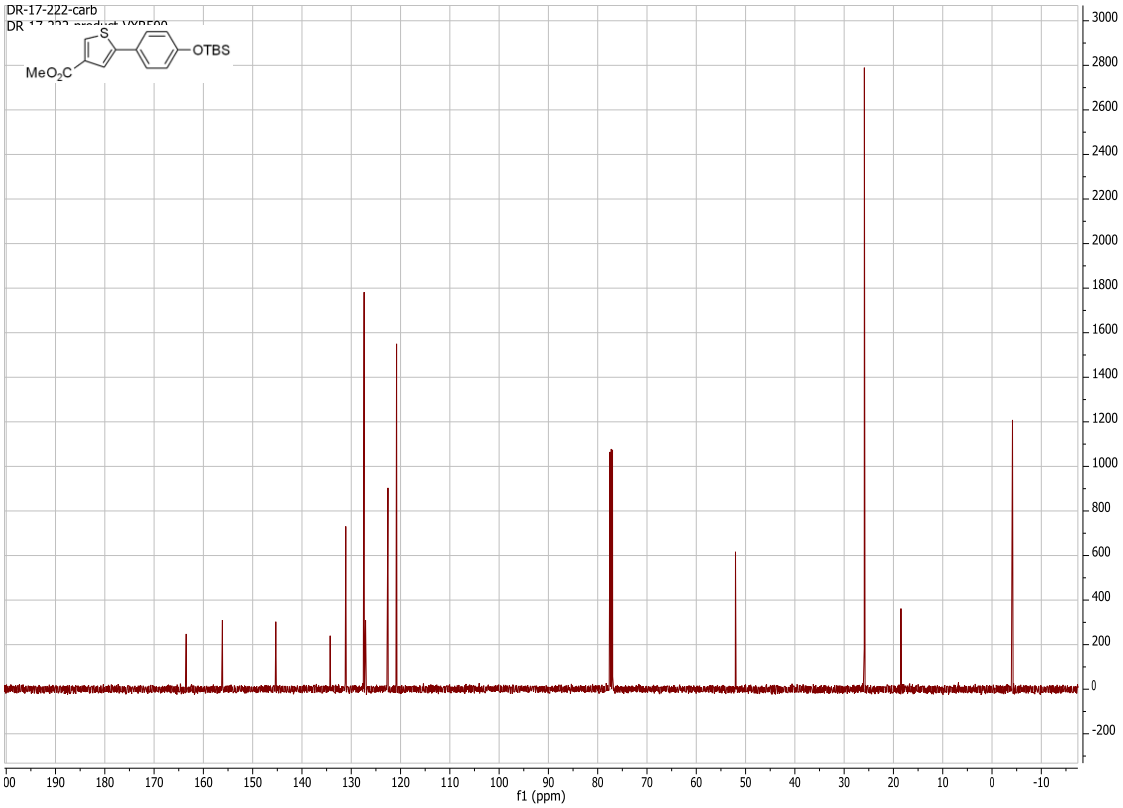

DR-16-208-proton
S
CHO
MeO2C
9.94
8.04
7.83
7.82
7.76
7.67
7.66
3.84
E (d)
7.67
C (d)
7.82
A (s)
9.94
B (s)
8.04
F (s)
3.84
D (s)
7.76
f1 (ppm)

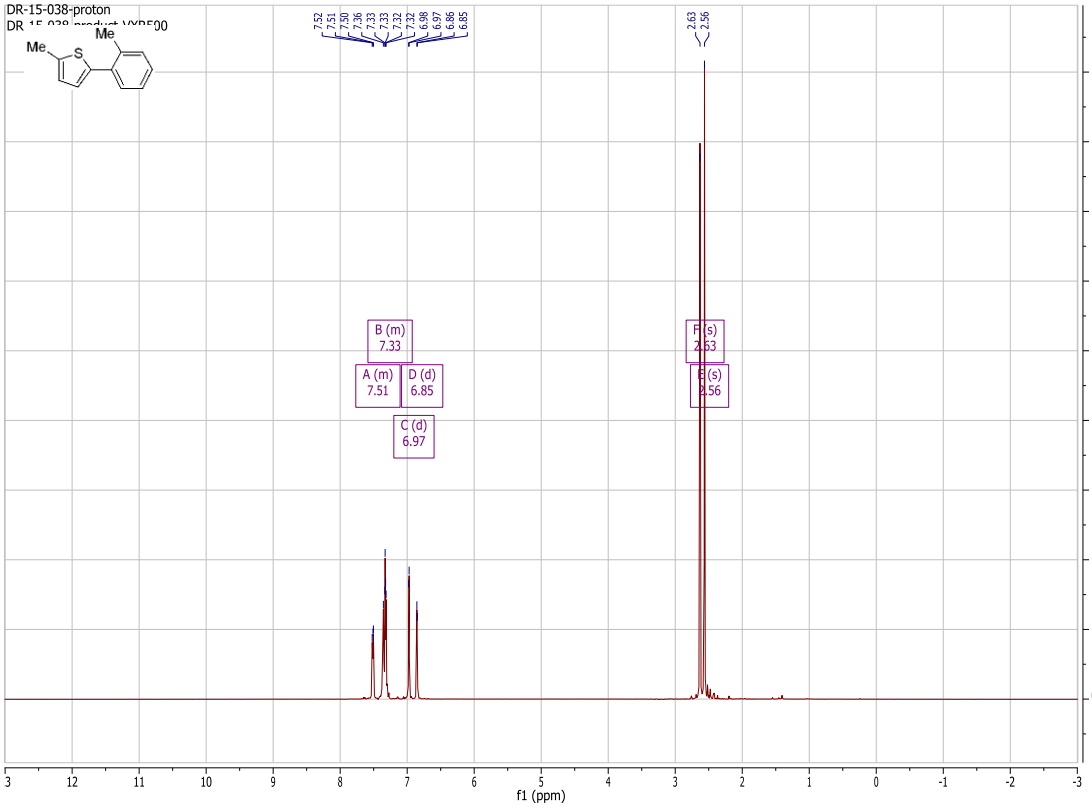

DR-16-208-carbon
MeO2C
CHO
162.96
143.41
139.11
134.75
133.46
130.67
126.20
125.44
52.22
f1 (ppm)

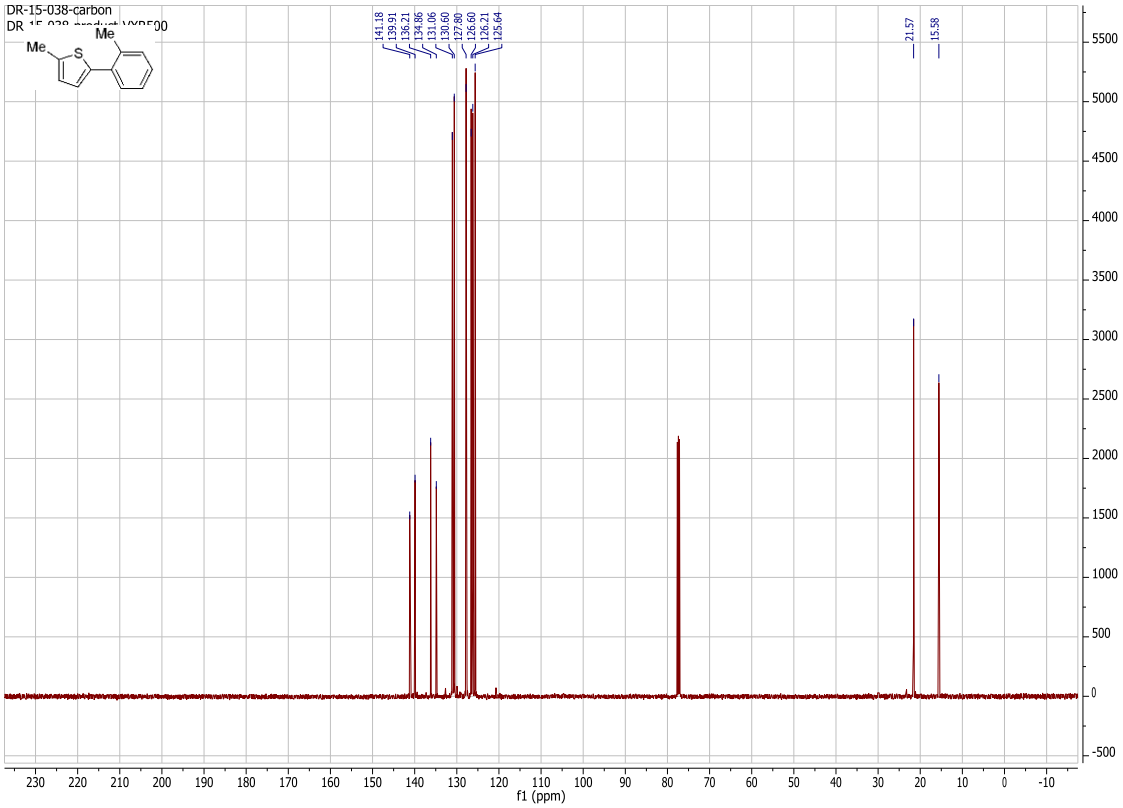

DR-14-139-proton
MeO2C
Me
8.00
7.69
7.51
7.50
7.21
7.19
3.90
2.38
B (s) 7.69
A (s) 8.00
D (d) 7.20
C (d) 7.50
E (s) 3.90
F (s) 2.38
f1 (ppm)

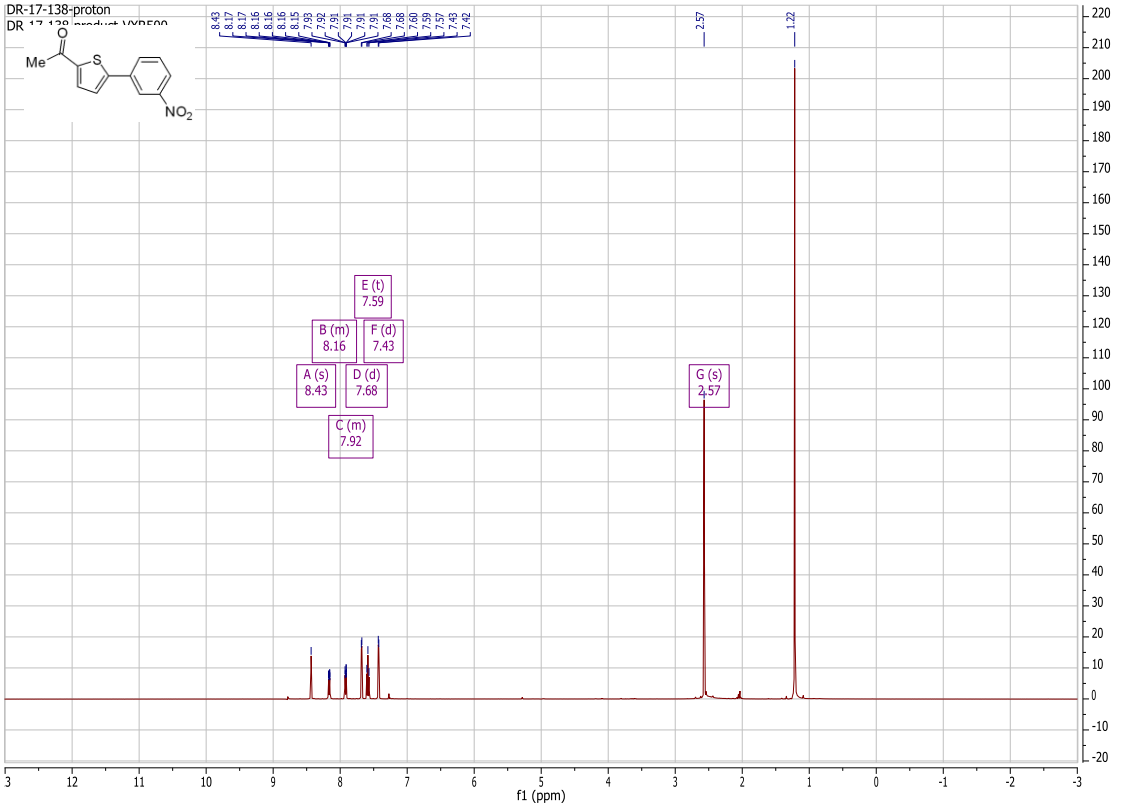

DR-14-139-carbon
MeO2C
Me
163.41
145.46
138.30
134.34
131.46
130.96
129.51
126.03
123.03
52.03
21.42
f1 (ppm)

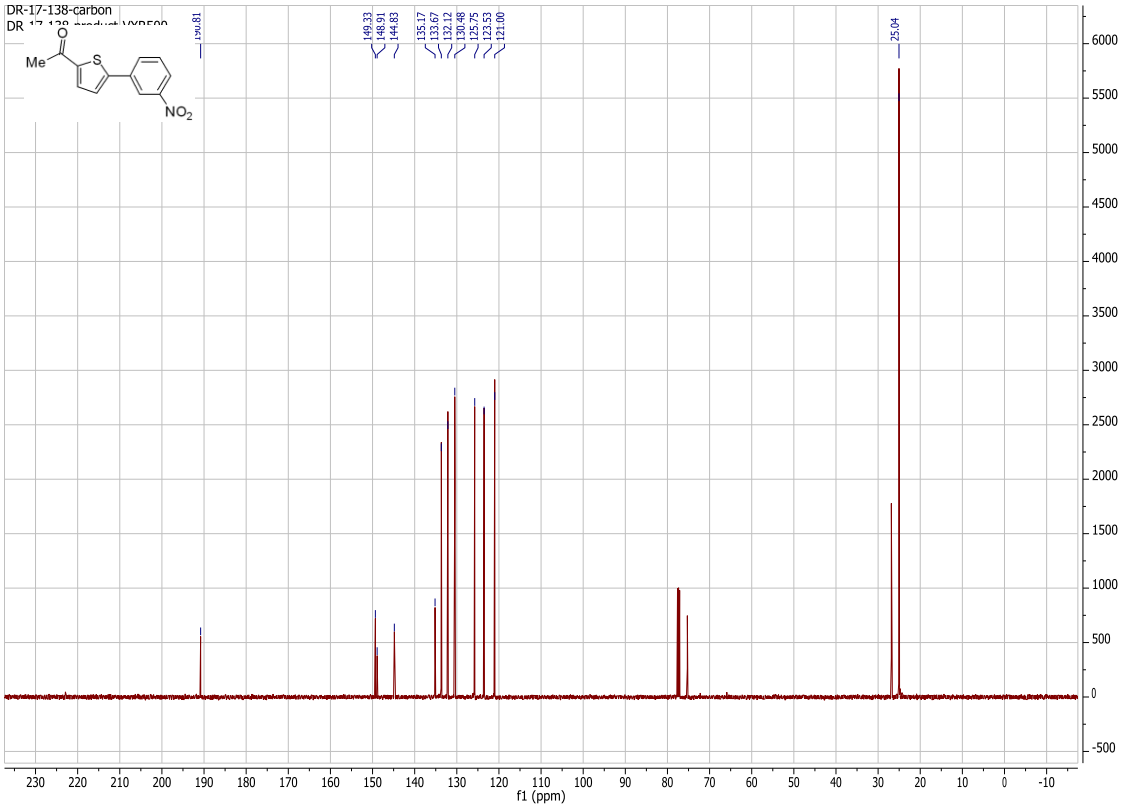

DR-17-222-prot
MeO2C
OTBS
f1 (ppm)

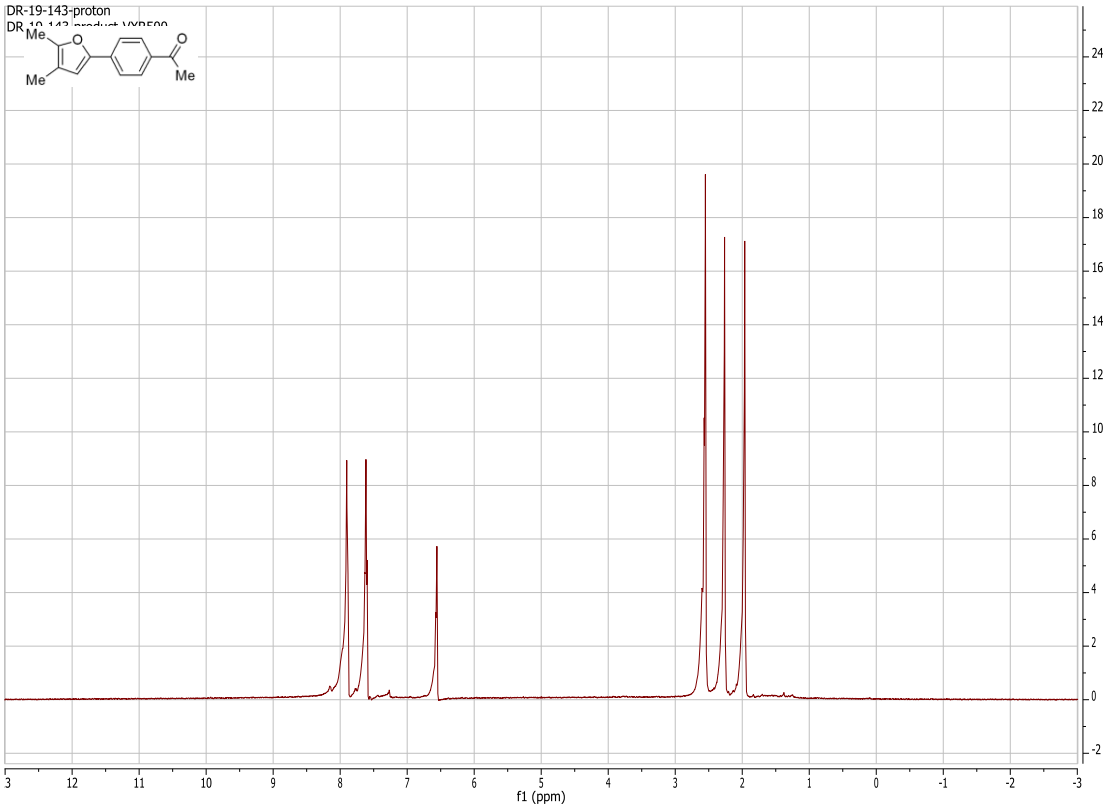

DR-17-222-carb
S
OTBS
MeO2C
f1 (ppm)

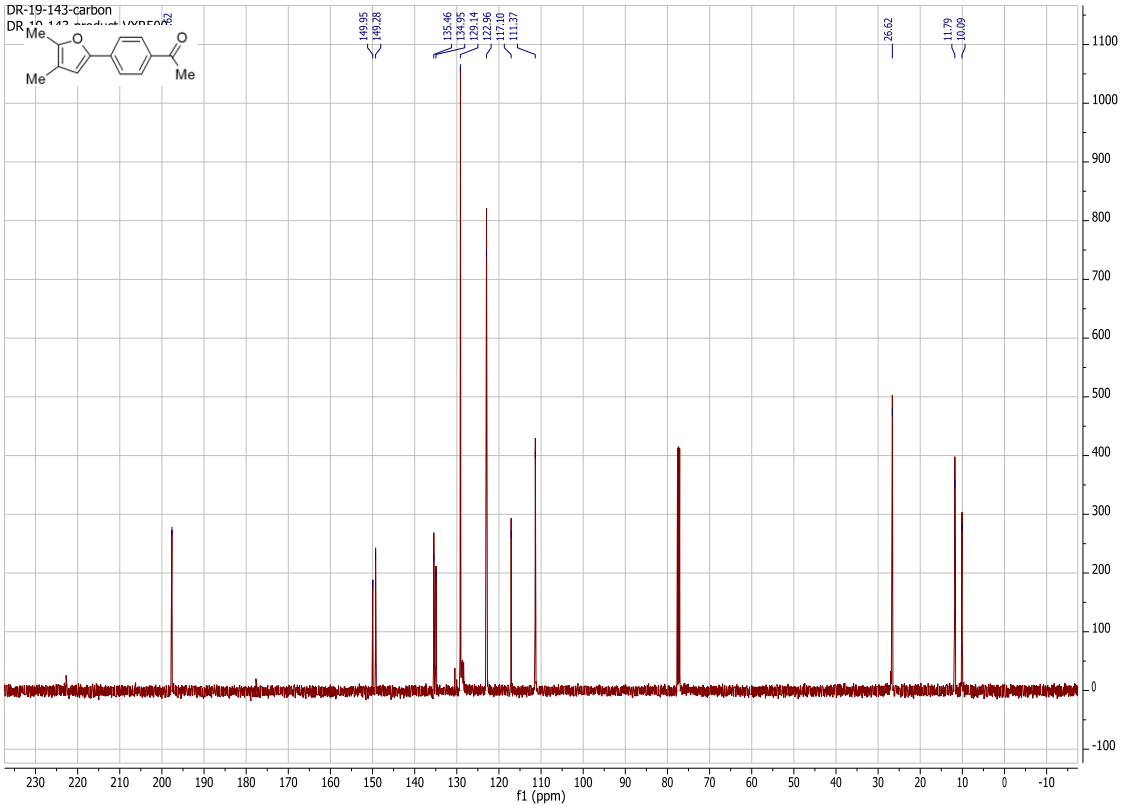

DR-15-038-proton
Me
Me
S
7.52
7.51
7.50
7.36
7.33
7.33
7.32
7.32
6.98
6.97
6.86
6.85
2.63
2.56
B (m)
7.33
A (m)
7.51
D (d)
6.85
C (d)
6.97
F (s)
2.63
E (s)
2.56
f1 (ppm)

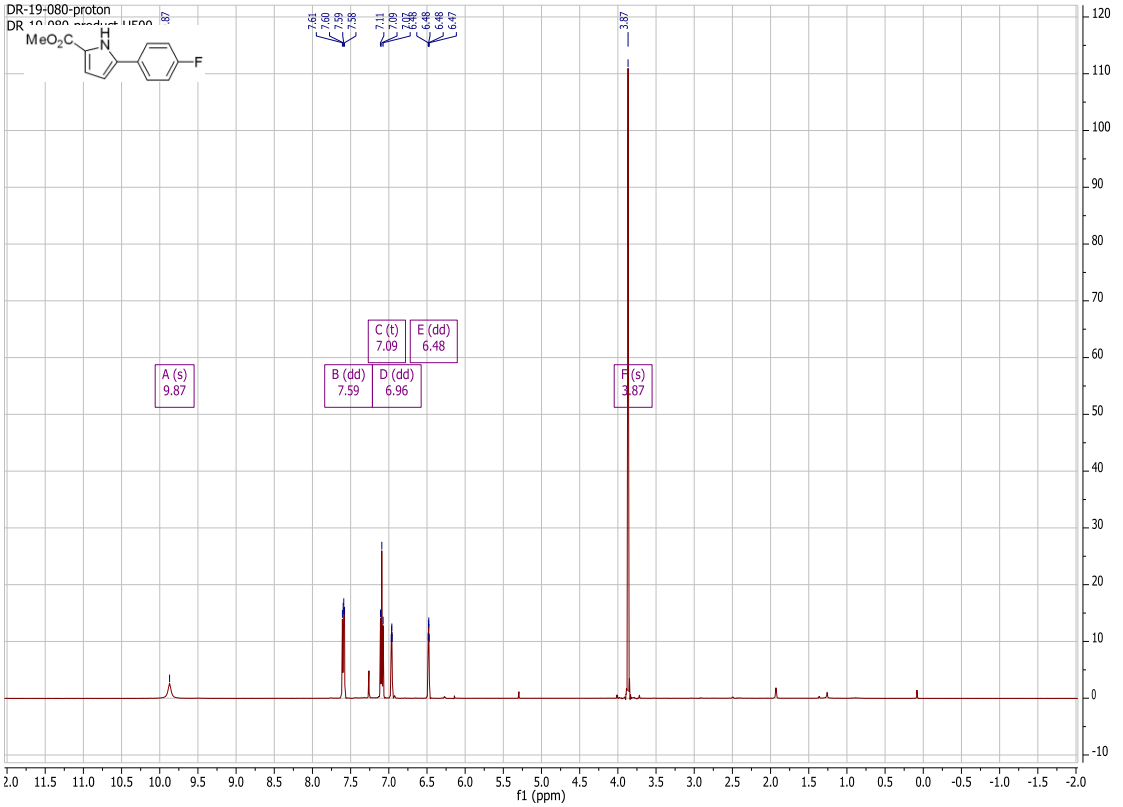

DR-15-038-carbon
Me
Me
S
141.18
139.91
136.21
134.86
131.06
130.60
127.80
126.60
126.21
125.64
21.57
15.58
f1 (ppm)

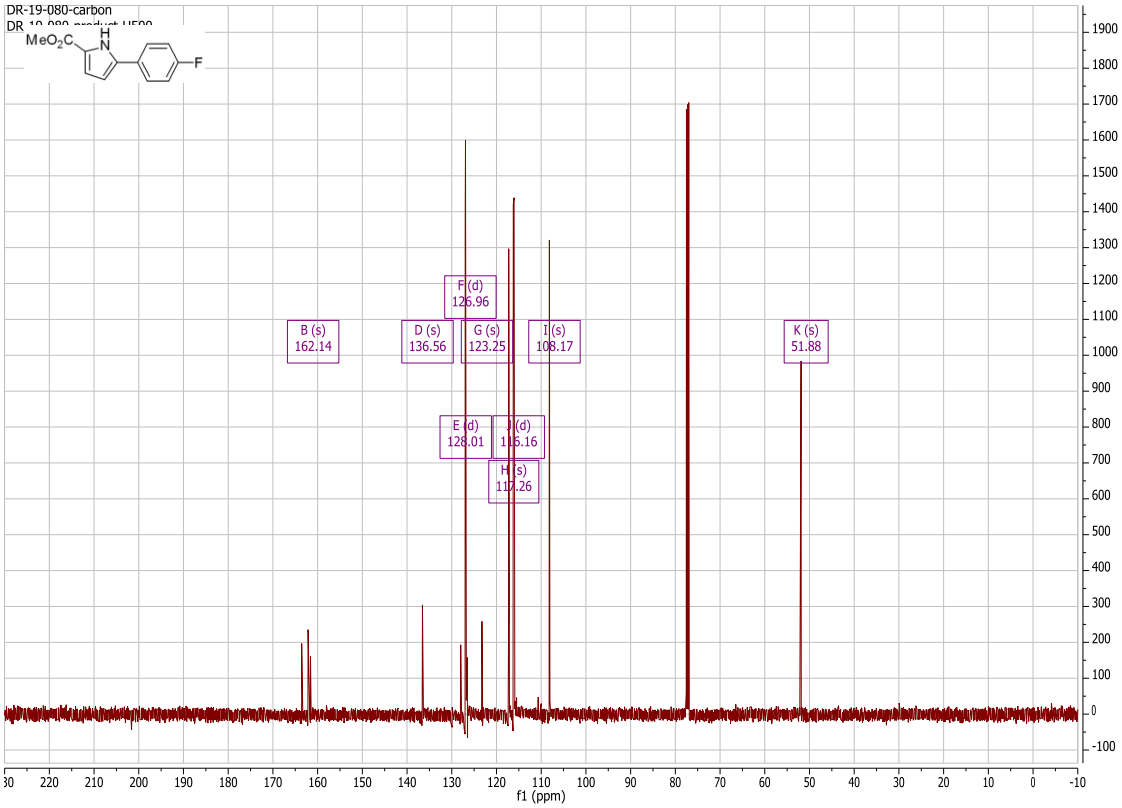

DR-17-138-proton
O
Me
S
NO2
8.43
8.17
8.16
8.15
7.93
7.92
7.91
7.68
7.60
7.59
7.57
7.43
7.42
2.57
1.22
E (t)
7.59
B (m)
8.16
F (d)
7.43
A (s)
8.43
D (d)
7.68
C (m)
7.92
G (s)
2.57
f1 (ppm)

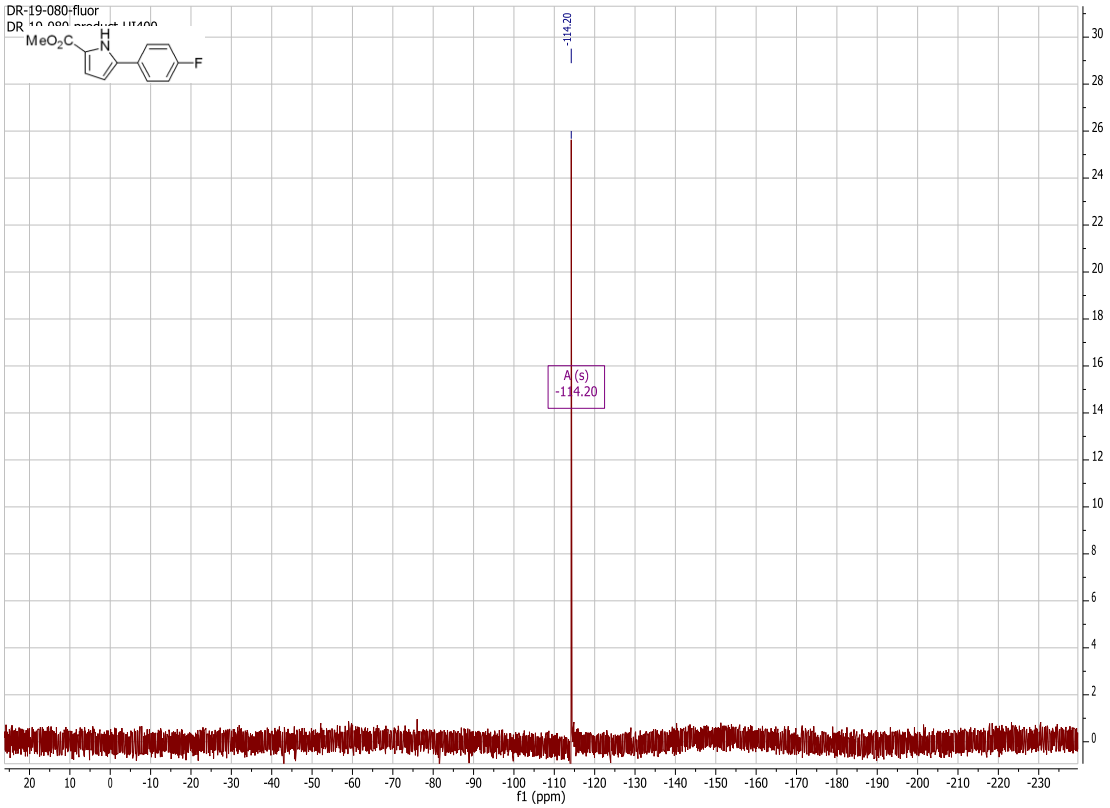

DR-17-138-carbon
190.81
149.33
148.91
144.83
135.17
133.67
132.12
130.48
125.75
123.53
121.00
25.04
Me
S
NO2
f1 (ppm)

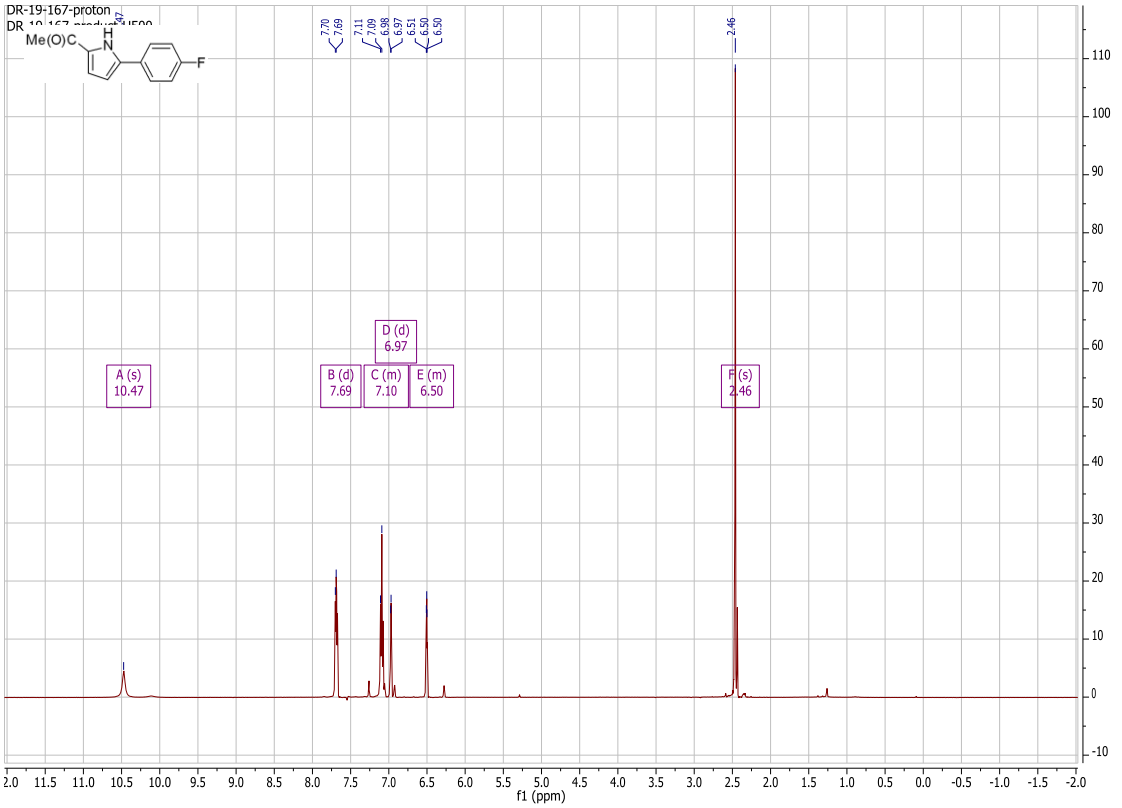

DR-19-143-proton
Me
O
Me
Me
f1 (ppm)

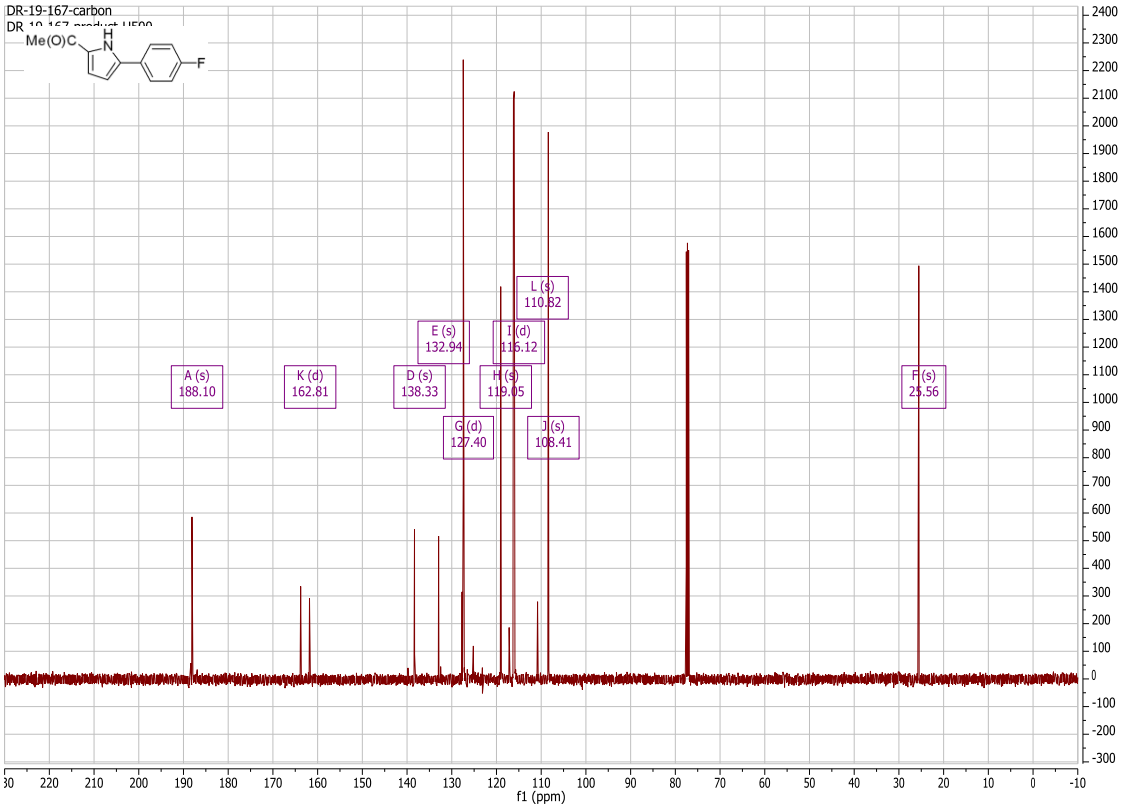

DR-19-143-carbon
Me
Me
O
Me
149.95
149.28
135.46
134.95
129.14
122.96
117.10
111.37
26.62
11.79
10.09
f1 (ppm)

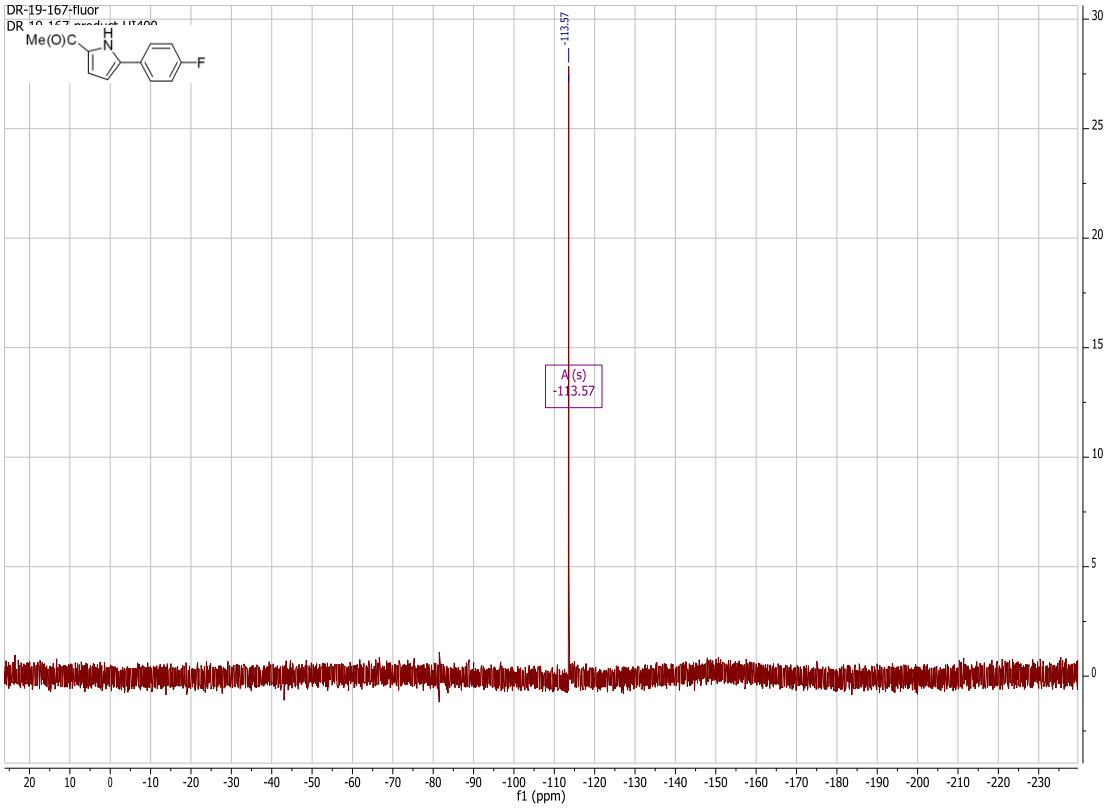

DR-19-080-proton
MeO2C
H
N
F
7.61
7.60
7.59
7.58
7.11
7.09
7.07
6.48
6.48
6.47
3.87
A (s)
9.87
B (dd)
7.59
C (t)
7.09
D (dd)
6.96
E (dd)
6.48
F (s)
3.87
f1 (ppm)

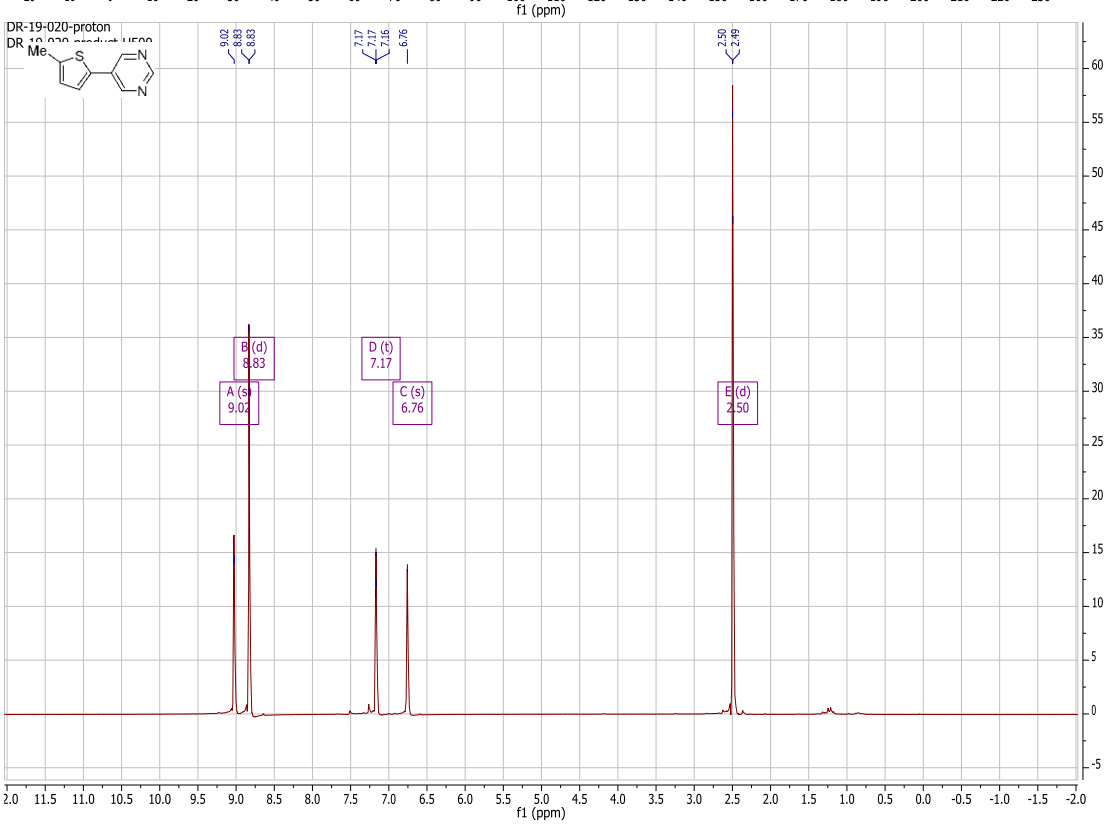

DR-19-080-carbon
MeO2C
H
N
F
F (d)
126.96
B (s)
162.14
D (s)
136.56
G (s)
123.25
I (s)
108.17
K (s)
51.88
E (d)
128.01
J (d)
115.16
H (s)
112.26
f1 (ppm)

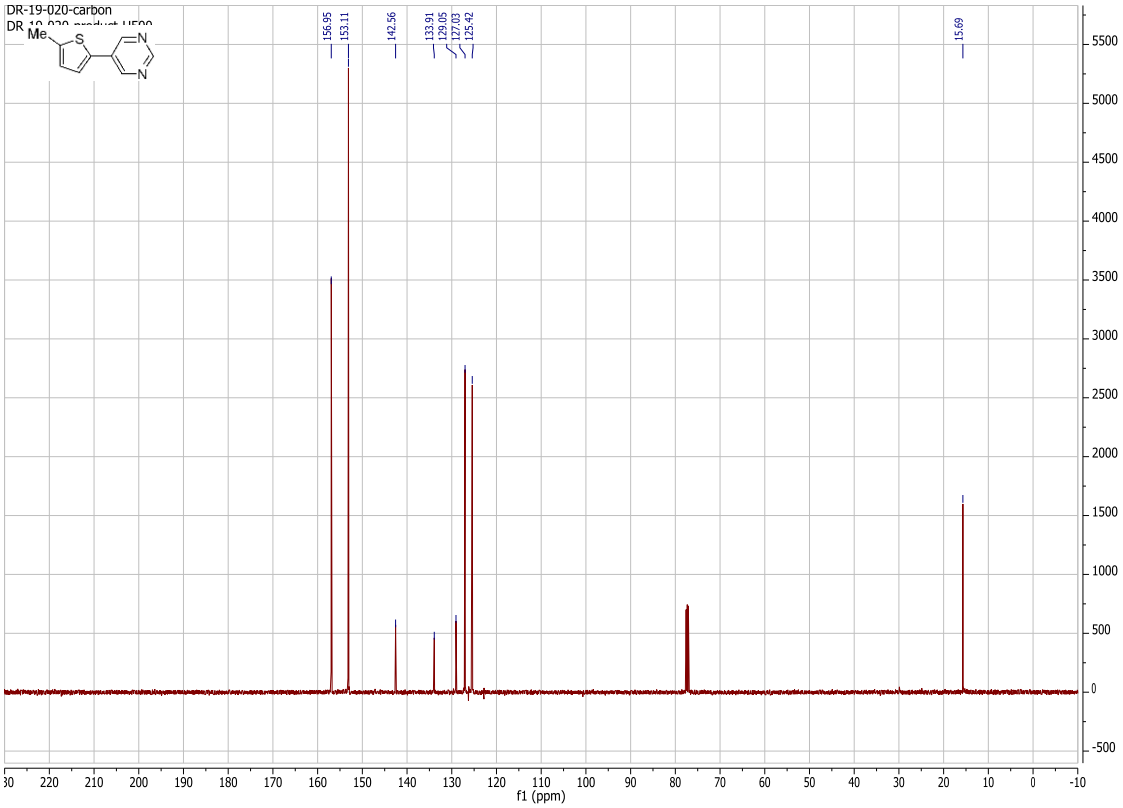

DR-19-080-fluor
MeO2C
H
N
F
-114.20
A (s)
-114.20
f1 (ppm)

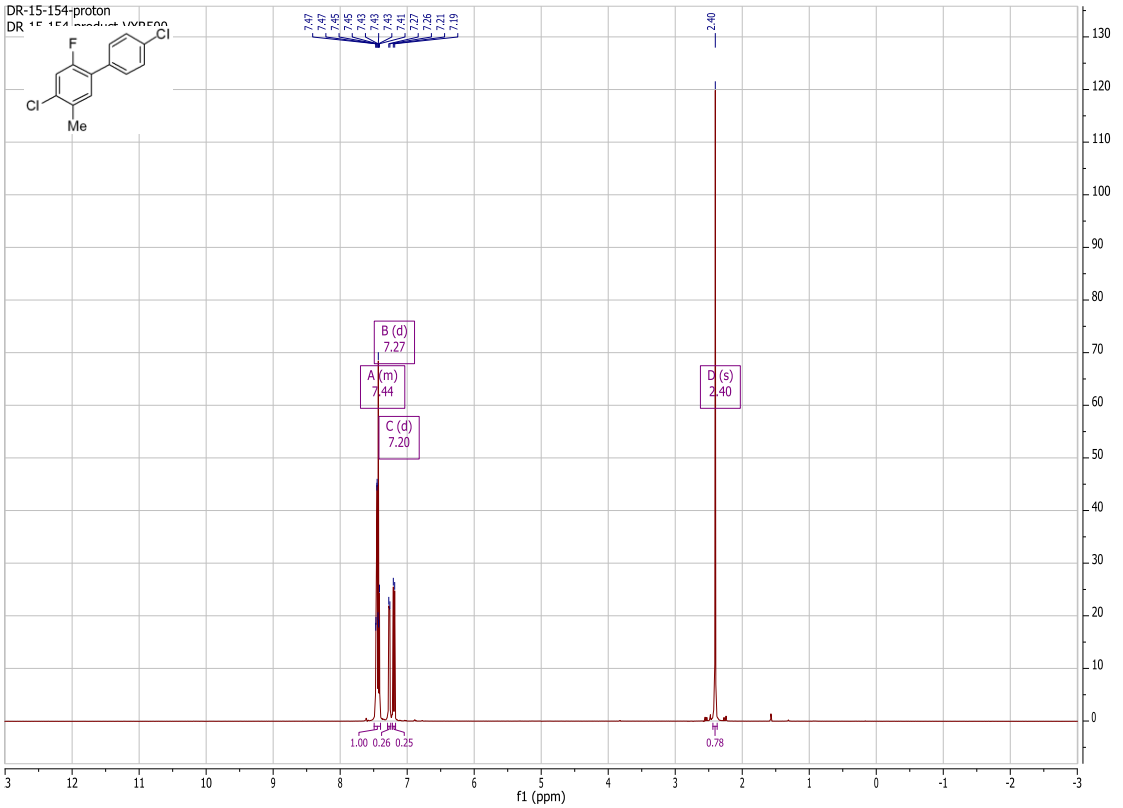

DR-19-167-proton
Me(O)C
H
N
F
7.70
7.69
7.11
7.09
6.98
6.97
6.51
6.50
6.50
2.46
A (s)
10.47
B (d)
7.69
C (m)
7.10
D (d)
6.97
E (m)
6.50
F (s)
2.46
f1 (ppm)

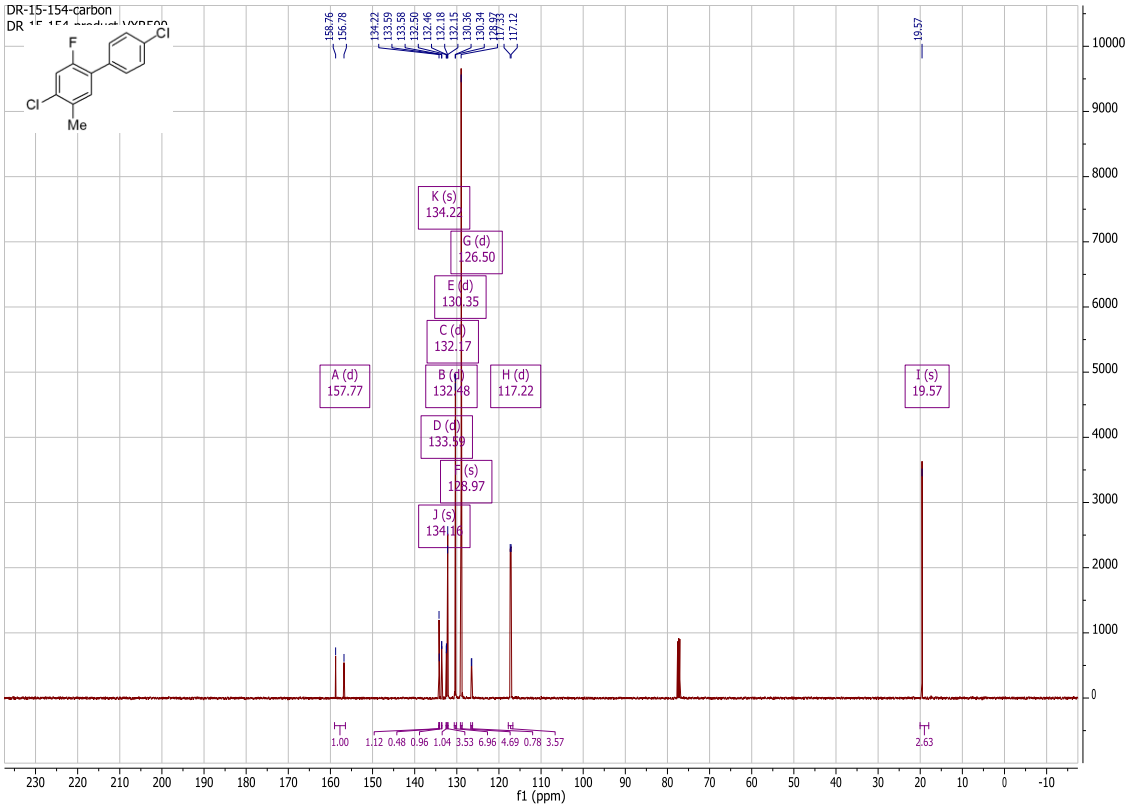

DR-19-167-carbon
Me(O)C
H
N
F
A (s)
188.10
K (d)
162.81
D (s)
138.33
E (s)
132.94
G (d)
127.40
H (s)
119.05
I (d)
116.12
L (s)
110.82
J (s)
108.41
F (s)
25.56
f1 (ppm)

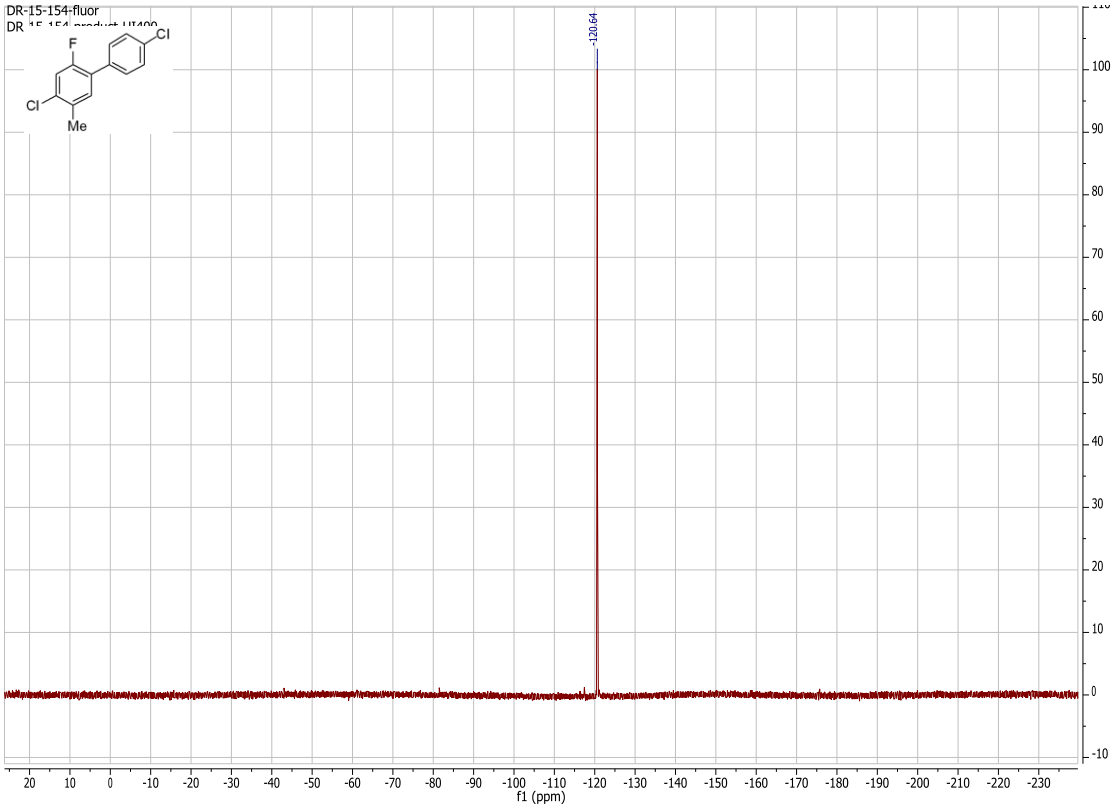

DR-19-167-fluor
Me(O)C
H
N
F
-113.57
A (s)
-113.57
f1 (ppm)

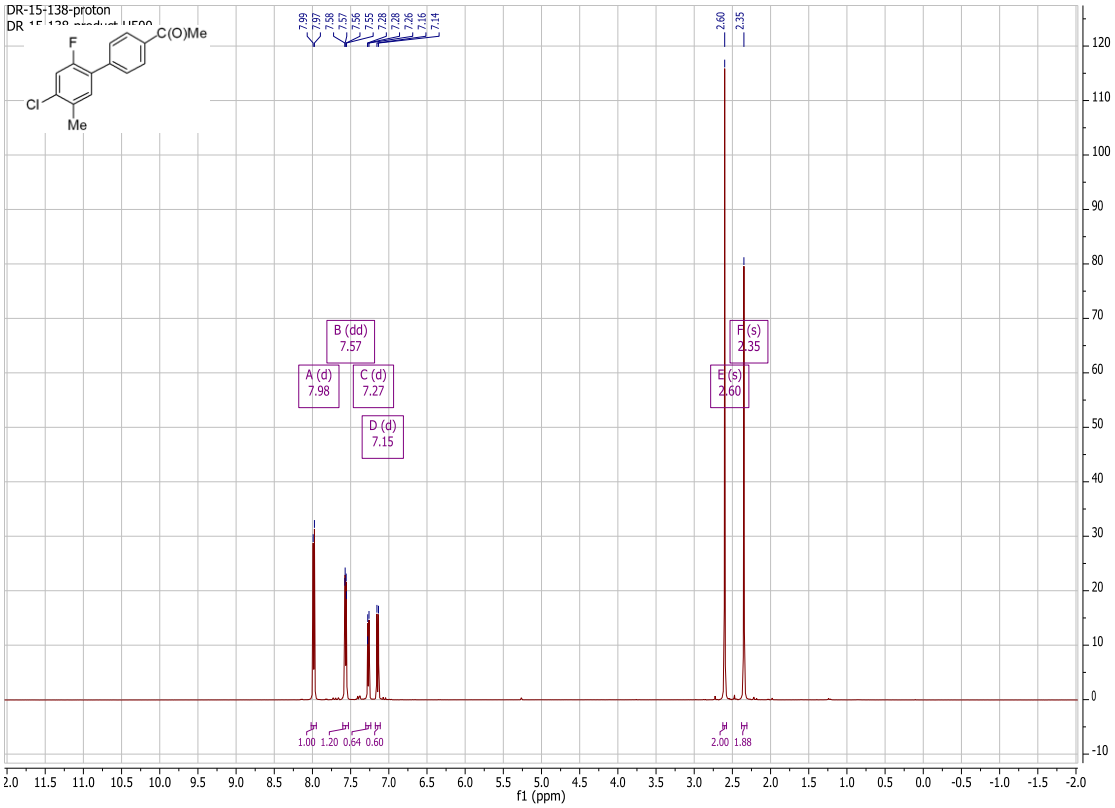

DR-19-020-proton
Me
S
N
N
9.02
8.83
8.83
7.17
7.17
7.16
6.76
2.50
2.49
B (d)
8.83
A (s)
9.02
D (t)
7.17
C (s)
6.76
E (d)
2.50
f1 (ppm)

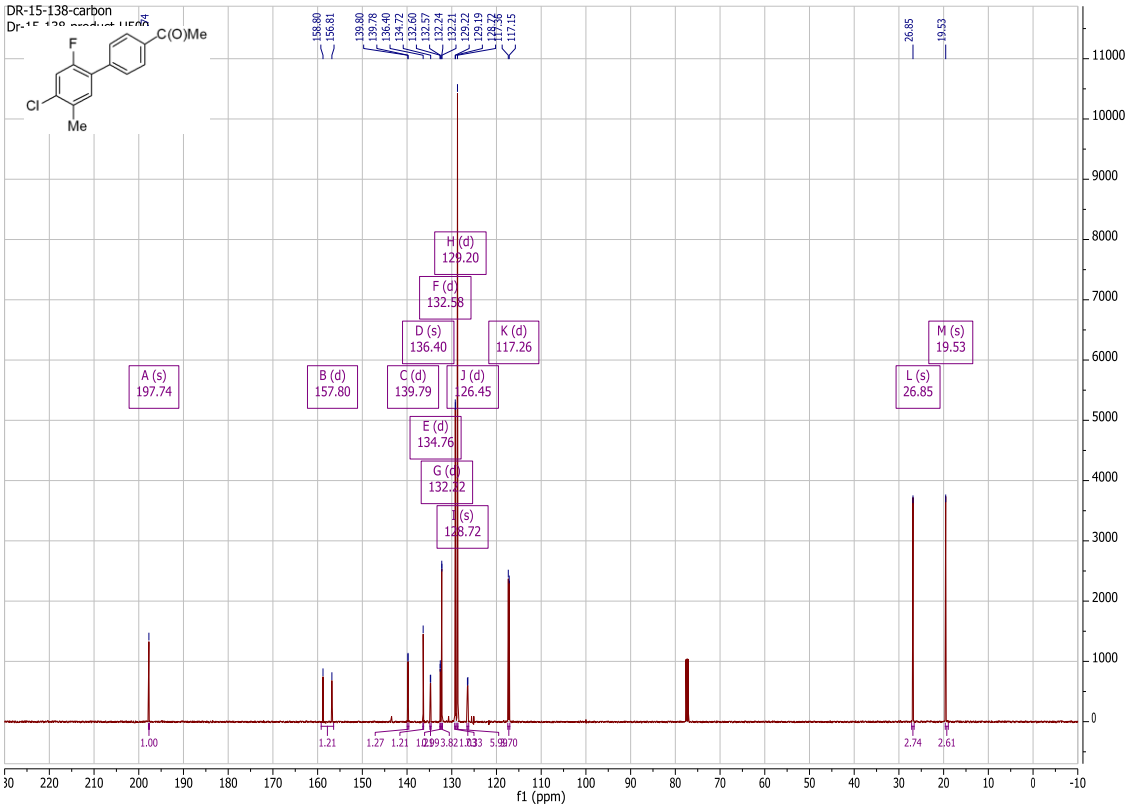

DR-19-020-carbon
Me
S
N
N
156.95
153.11
142.56
133.91
129.05
127.03
125.42
15.69
f1 (ppm)

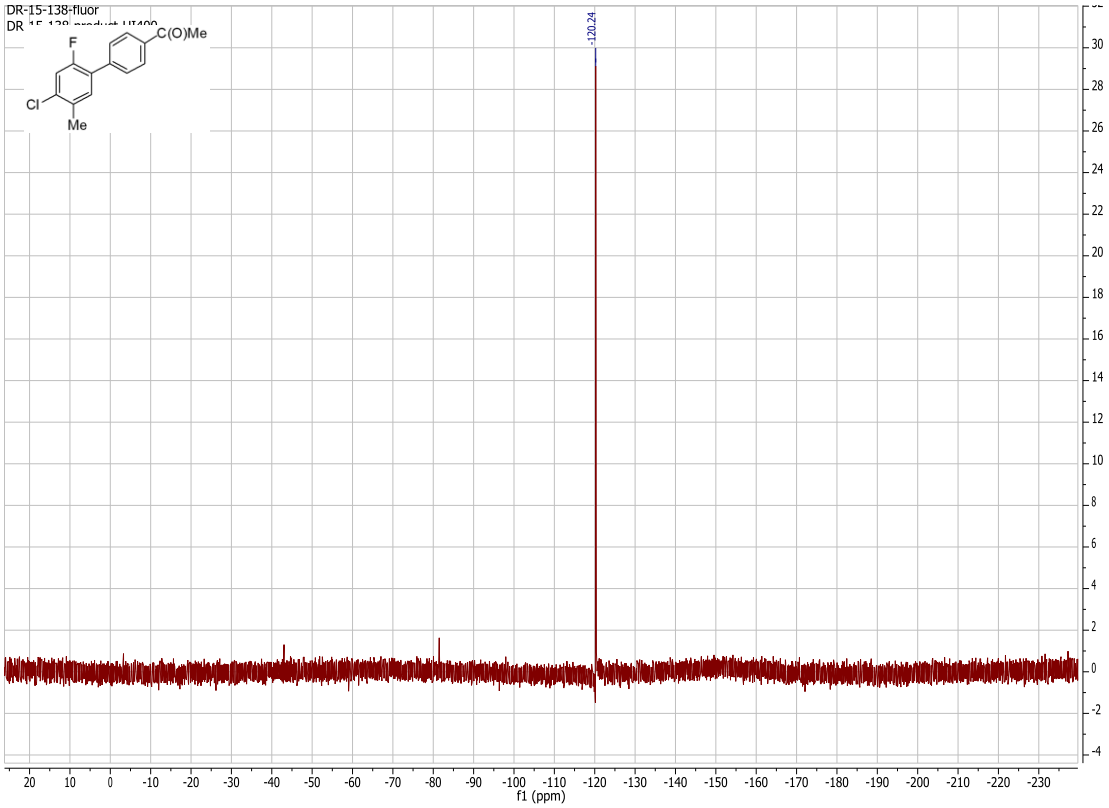

DR-15-154-proton
F
Cl
Cl
Me
7.47
7.47
7.45
7.45
7.43
7.43
7.43
7.41
7.27
7.26
7.21
7.19
2.40
B (d)
7.27
A (m)
7.44
C (d)
7.20
D (s)
2.40
1.00 0.26 0.25
0.78
f1 (ppm)

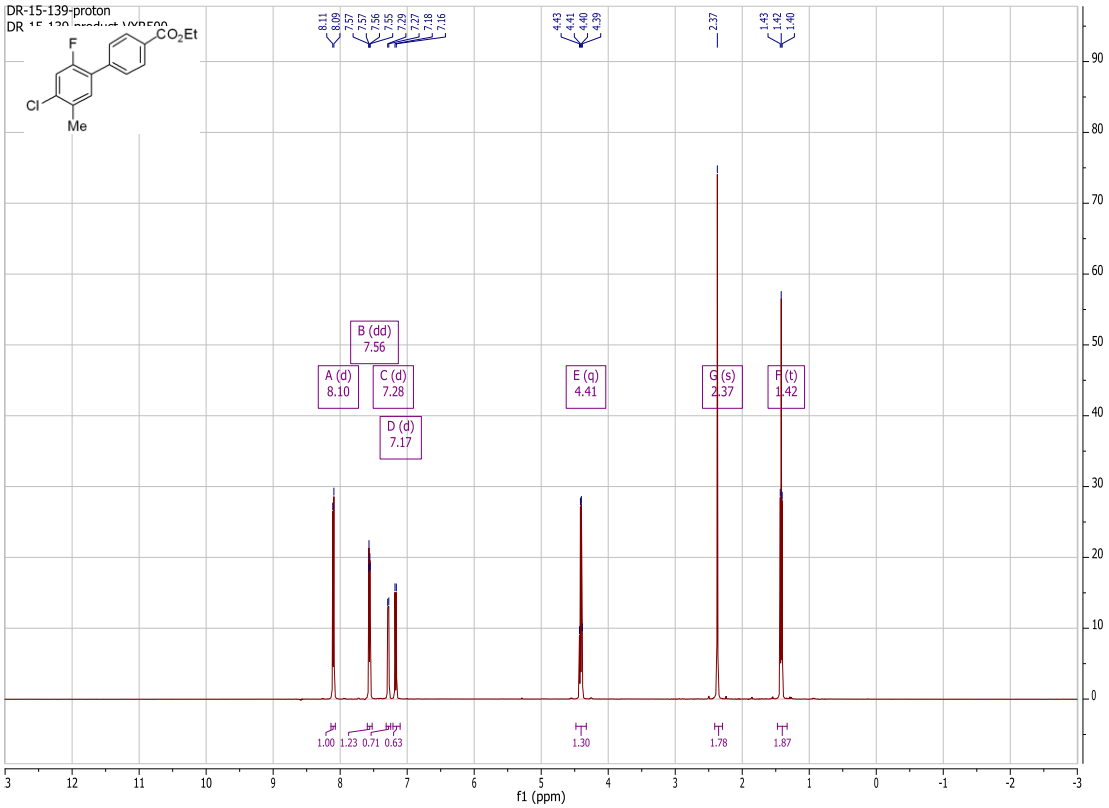

DR-15-154-carbon
F
Cl
Cl
Me
158.76
156.78
134.22
133.59
133.58
132.50
132.46
132.18
132.15
130.36
130.34
117.33
117.12
19.57
K (s)
134.22
G (d)
126.50
E (d)
130.35
C (d)
132.17
A (d)
157.77
B (d)
132.48
H (d)
117.22
D (d)
133.59
F (s)
128.97
J (s)
134.16
I (s)
19.57
1.00
1.12
0.48
0.96
1.04
3.53
6.96
4.69
0.78
3.57
2.63
f1 (ppm)

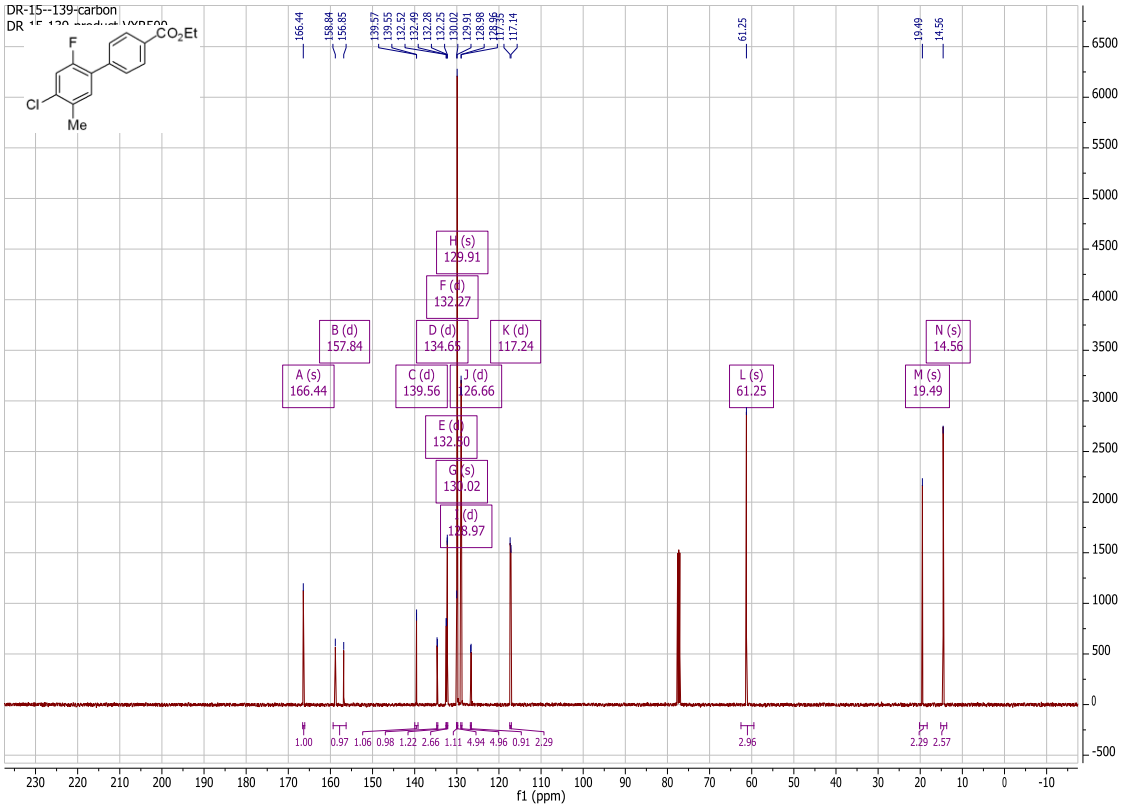

DR-15-154-fluor
F
Cl
Cl
Me
-120.64
f1 (ppm)

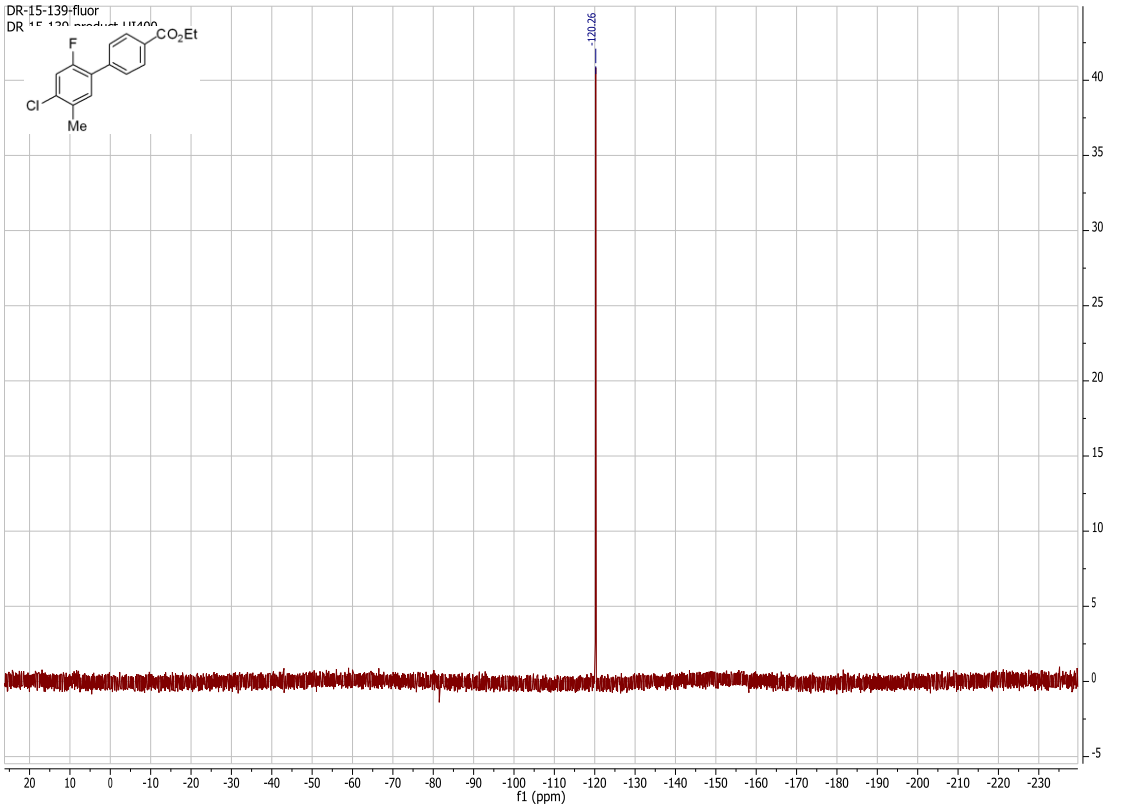

DR-15-138-proton
C(O)Me
F
Cl
Me
7.99
7.97
7.58
7.57
7.56
7.55
7.28
7.28
7.26
7.16
7.14
2.60
2.35
B (dd)
7.57
A (d)
7.98
C (d)
7.27
D (d)
7.15
F (s)
2.35
E (s)
2.60
1.00
1.20
0.64
0.60
2.00
1.88
f1 (ppm)

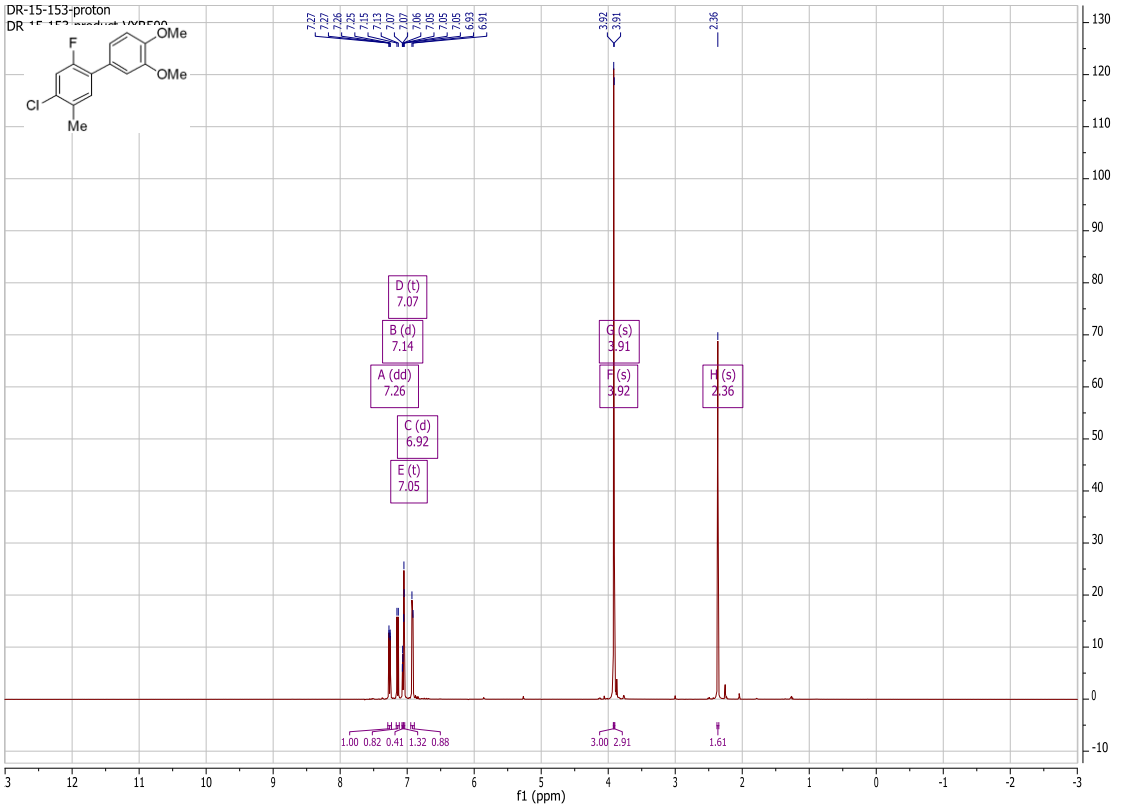

DR-15-138-carbon
C(O)Me
F
Cl
Me
158.80
156.81
139.80
139.78
136.40
134.72
132.60
132.57
132.24
132.21
129.22
129.19
117.36
117.15
26.85
19.53
H (d)
129.20
F (d)
132.58
D (s)
136.40
K (d)
117.26
M (s)
19.53
A (s)
197.74
B (d)
157.80
C (d)
139.79
J (d)
126.45
L (s)
26.85
E (d)
134.76
G (d)
132.22
I (s)
128.72
1.00
1.21
1.27
1.21
2.74
2.61
f1 (ppm)

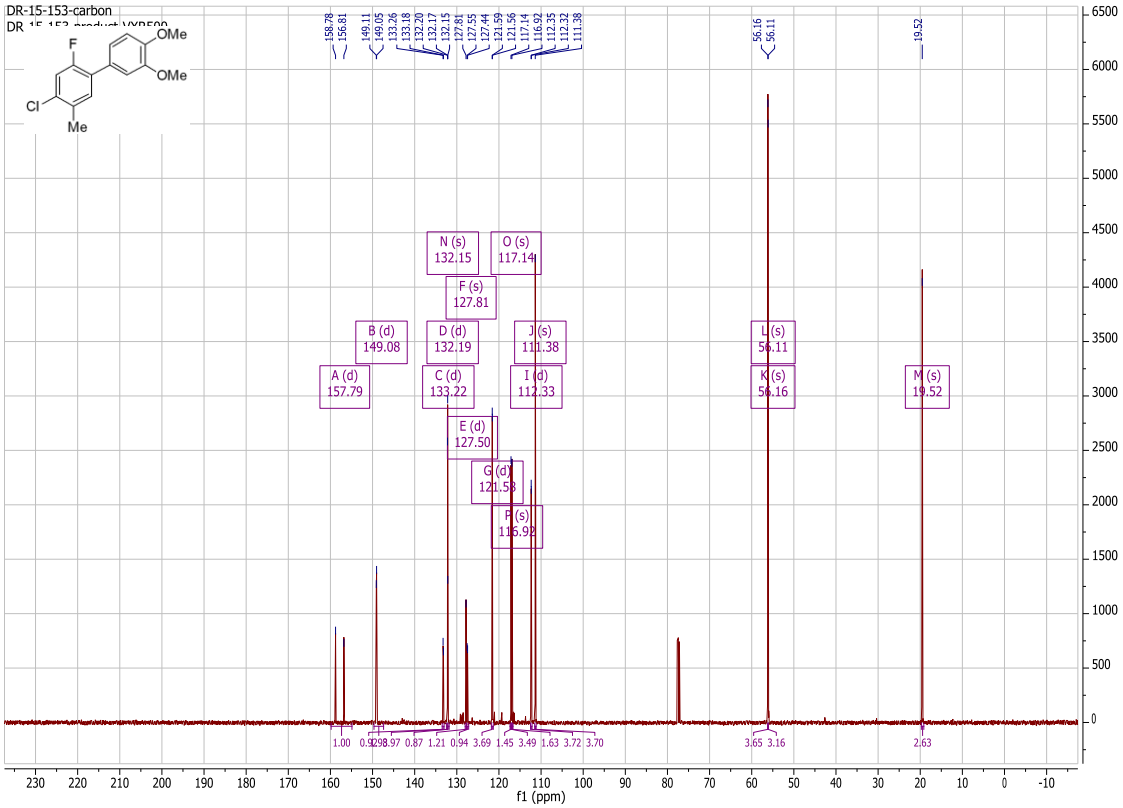

DR-15-138-fluor
C(O)Me
F
Cl
Me
-120.24
f1 (ppm)

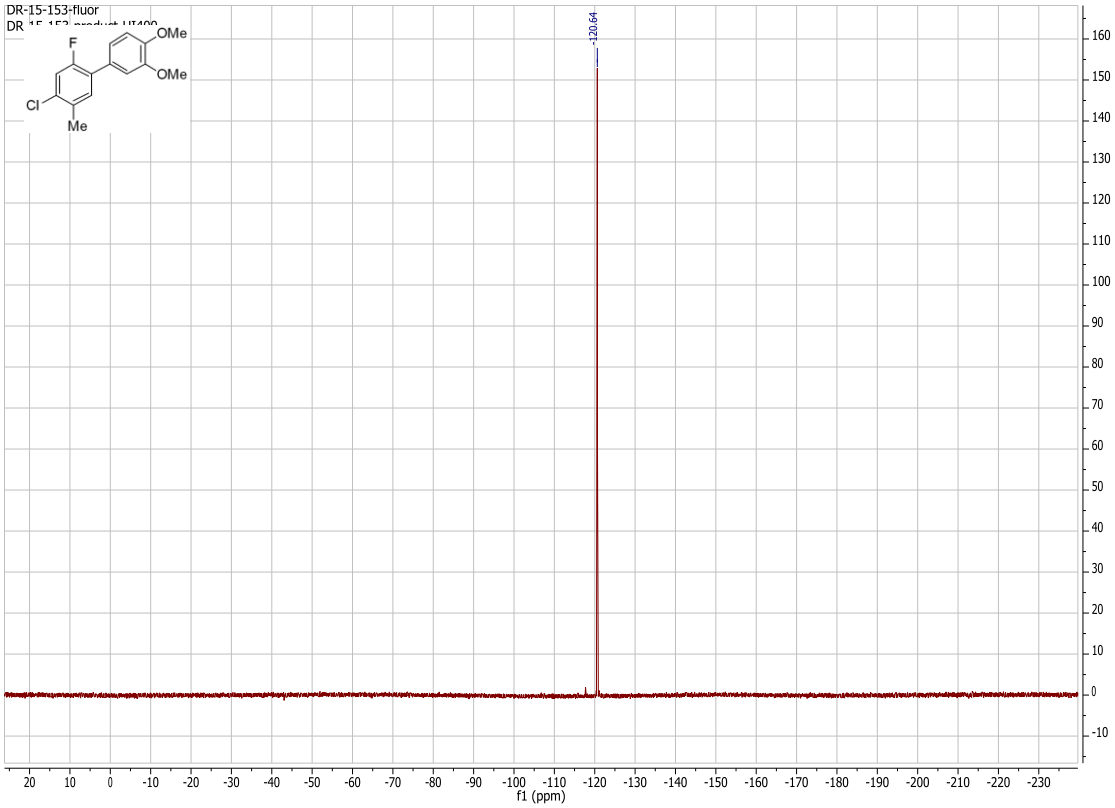

DR-15-139-proton
CO2Et
F
Cl
Me
8.11
8.09
7.57
7.57
7.56
7.55
7.29
7.27
7.18
7.16
4.43
4.41
4.40
4.39
2.37
1.43
1.42
1.40
B (dd)
7.56
A (d)
8.10
C (d)
7.28
D (d)
7.17
E (q)
4.41
G (s)
2.37
F (t)
1.42
1.00
1.23
0.71
0.63
1.30
1.78
1.87
f1 (ppm)

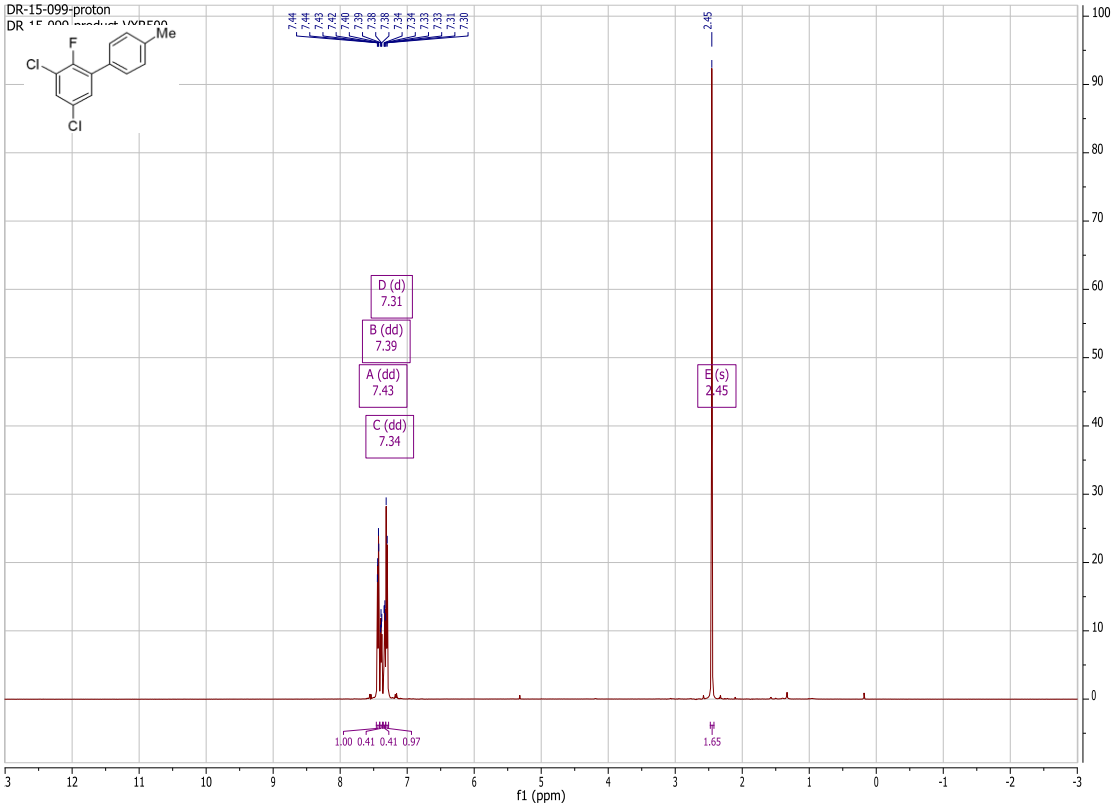

DR-15--139-carbon
F
Cl
Me
CO2Et
166.44
158.84
156.85
139.57
139.55
132.52
132.49
132.28
132.25
130.02
129.91
128.98
117.36
117.14
61.25
19.49
14.56
A (s) 166.44
B (d) 157.84
C (d) 139.56
D (d) 134.65
E (d) 132.50
F (d) 132.27
G (s) 130.02
H (s) 129.91
I (d) 128.97
J (d) 126.66
K (d) 117.24
L (s) 61.25
M (s) 19.49
N (s) 14.56
1.00 0.97 1.06 0.98 1.22 2.66 1.11 4.94 4.96 0.91 2.29
2.96
2.29 2.57
f1 (ppm)

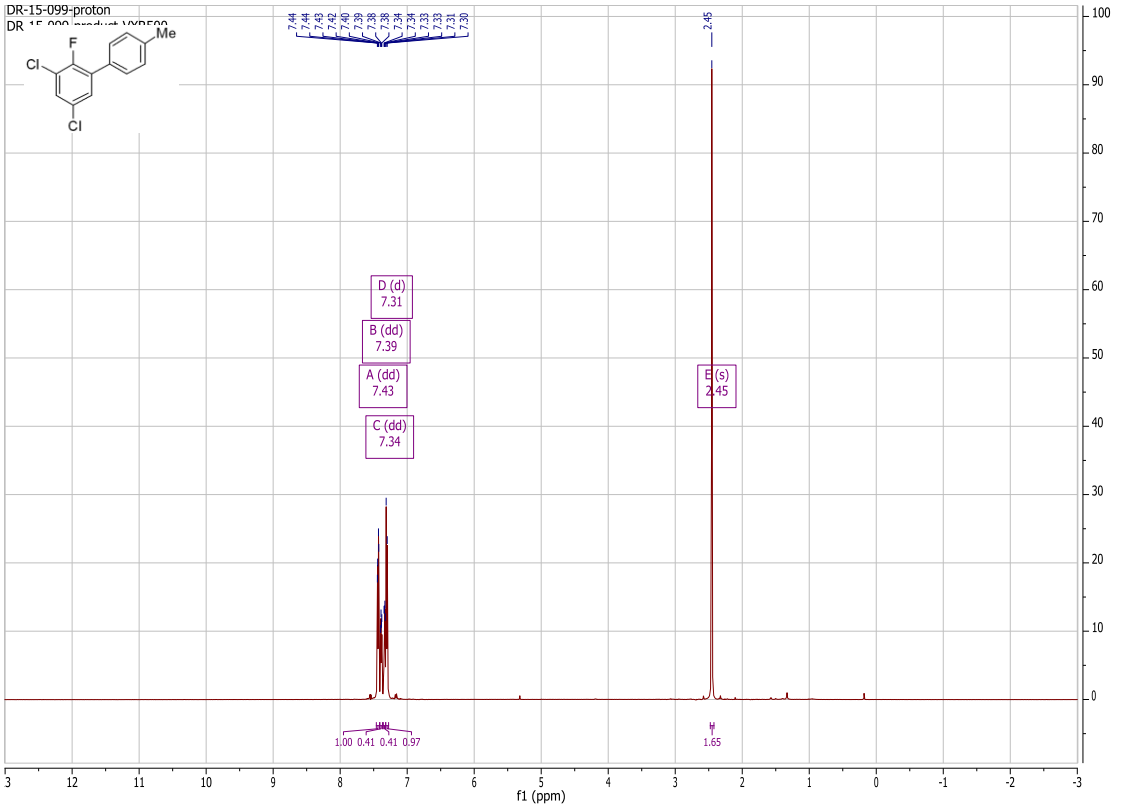

DR-15-139-fluor
F
Cl
Me
CO2Et
-120.26
f1 (ppm)

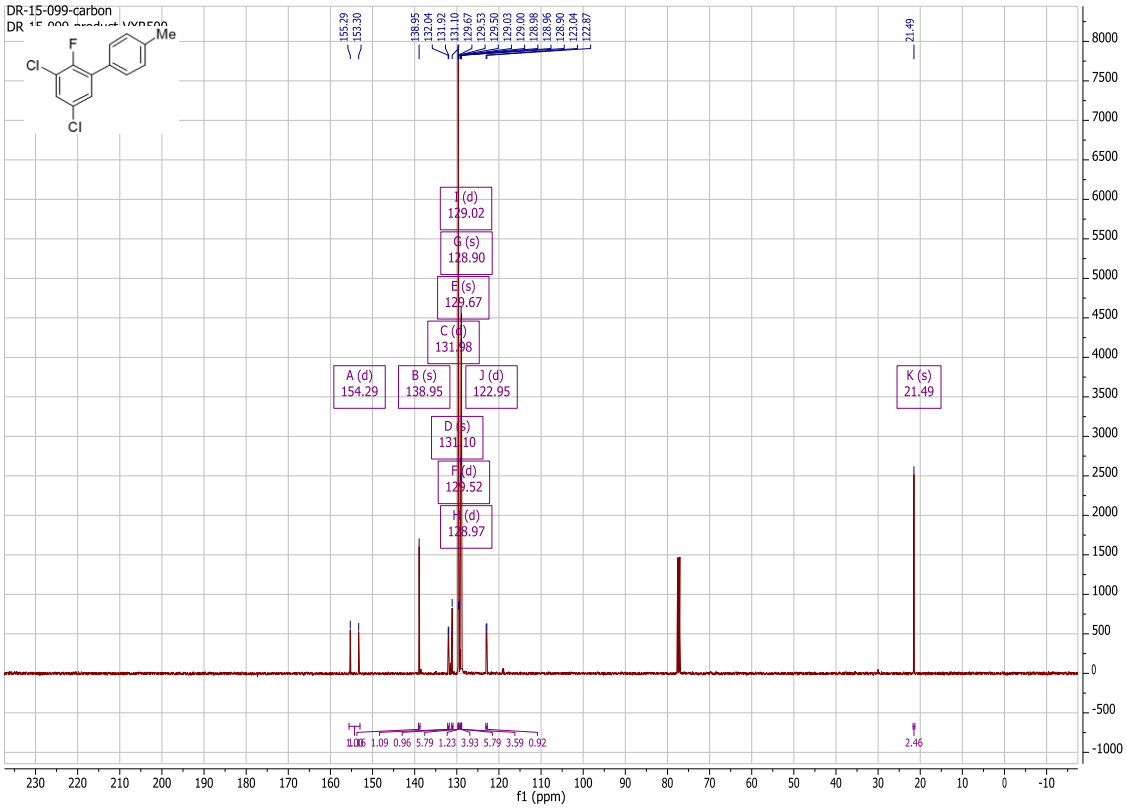

DR-15-153-proton
OMe
OMe
F
Cl
Me
D (t)
7.07
B (d)
7.14
A (dd)
7.26
C (d)
6.92
E (t)
7.05
G (s)
3.91
F (s)
3.92
H (s)
2.36
f1 (ppm)

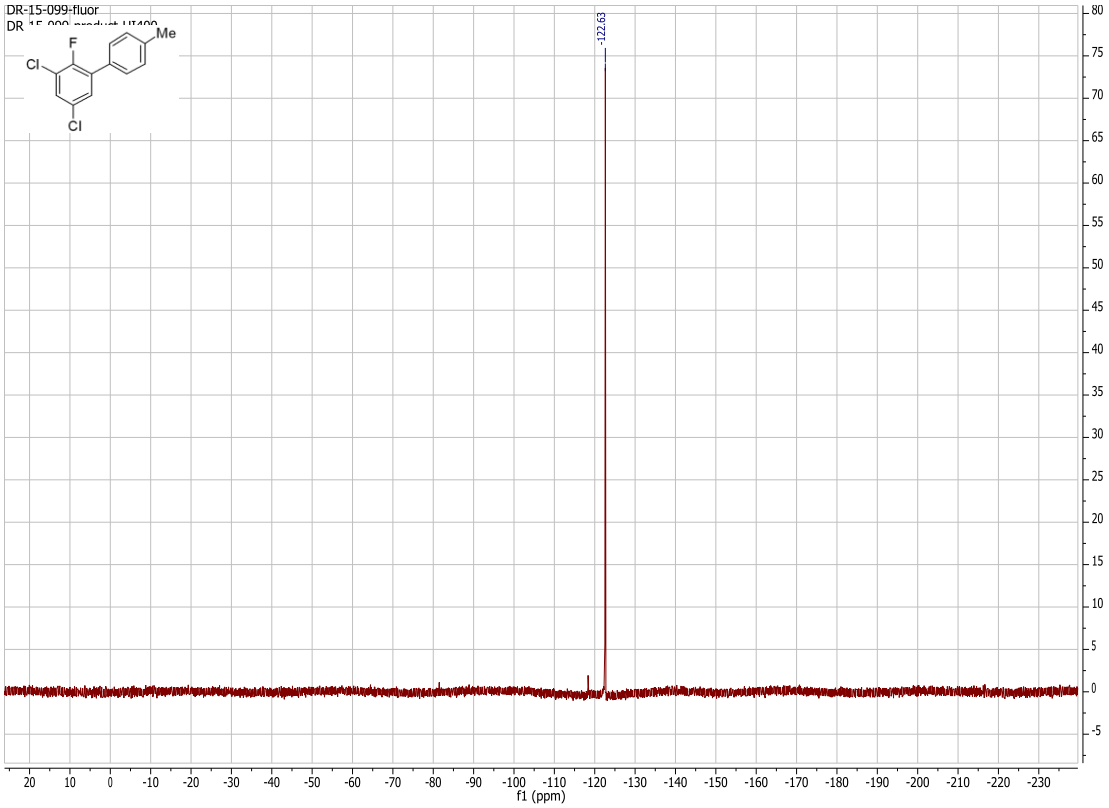

DR-15-153-carbon
OMe
OMe
F
Cl
Me
N (s)
132.15
O (s)
117.14
F (s)
127.81
B (d)
149.08
D (d)
132.19
J (s)
111.38
A (d)
157.79
C (d)
133.22
I (d)
112.33
E (d)
127.50
G (d)
121.58
P (s)
116.92
L (s)
56.11
K (s)
56.16
M (s)
19.52
f1 (ppm)

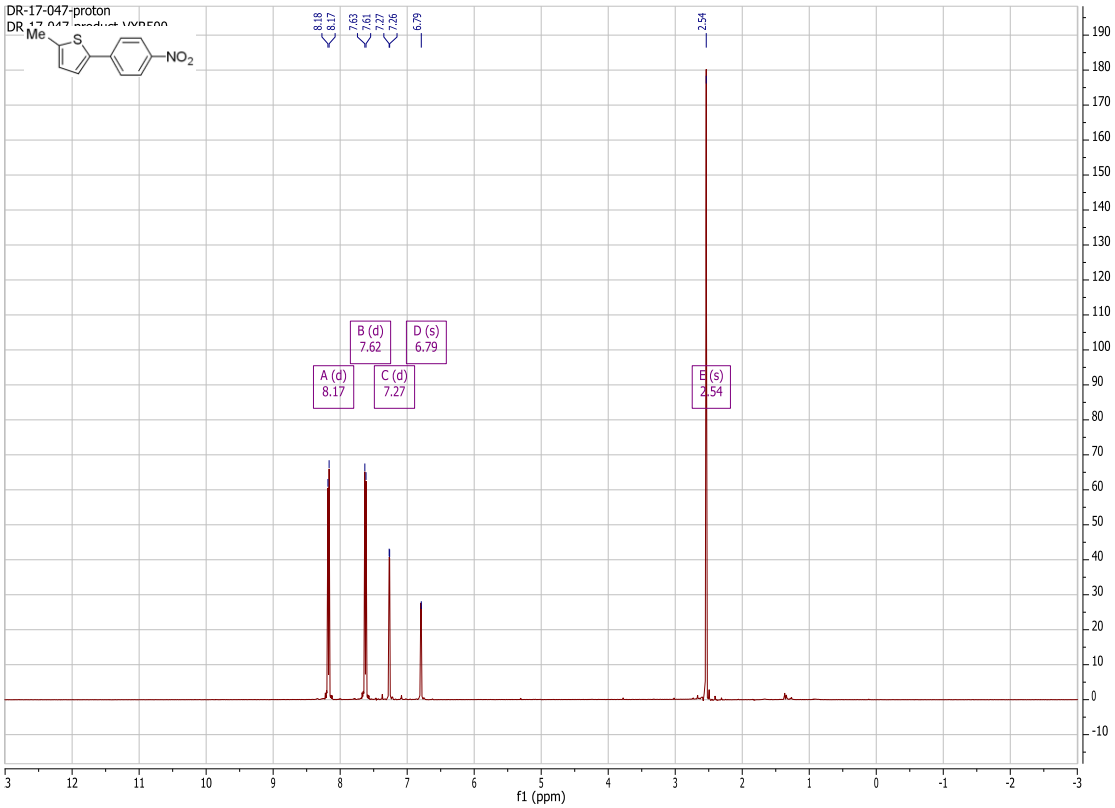

DR-15-153-fluor
F
OMe
OMe
Cl
Me
-120.64
f1 (ppm)

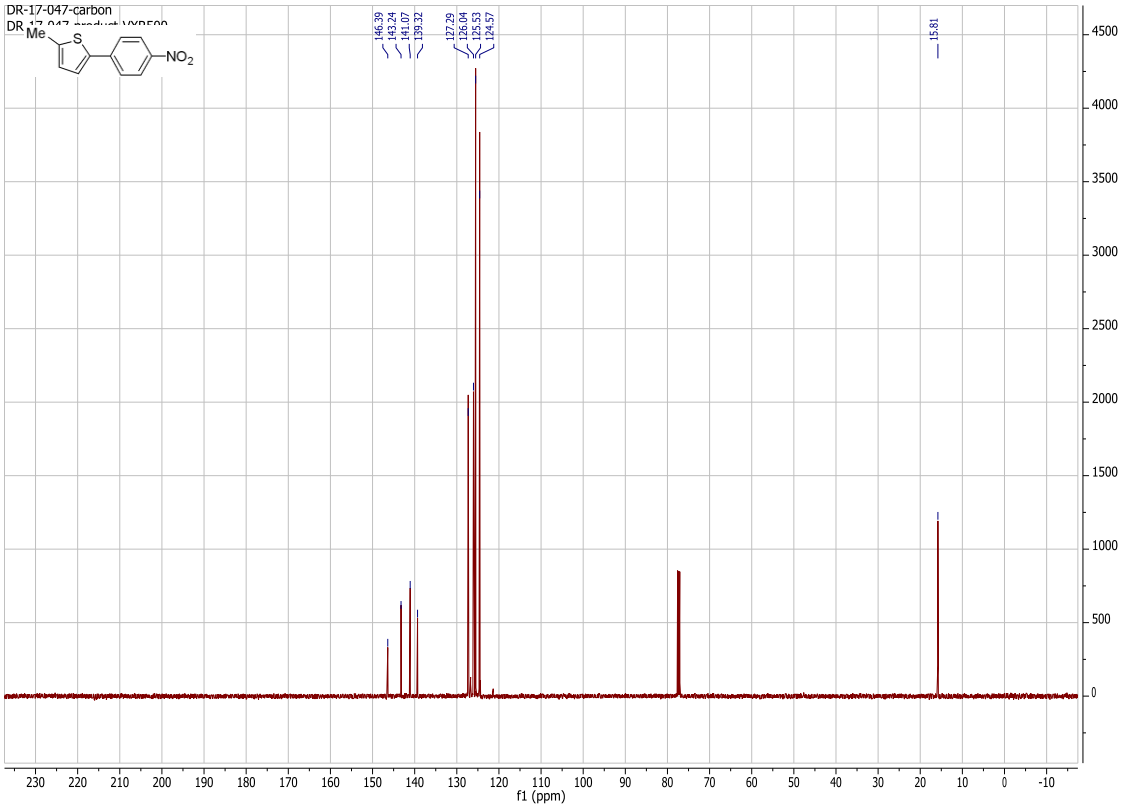

DR-15-099-proton
F
Me
Cl
Cl
7.44
7.44
7.43
7.42
7.40
7.39
7.38
7.38
7.34
7.34
7.33
7.33
7.31
7.30
2.45
D (d)
7.31
B (dd)
7.39
A (dd)
7.43
C (dd)
7.34
E (s)
2.45
1.00 0.41 0.41 0.97
1.65
f1 (ppm)

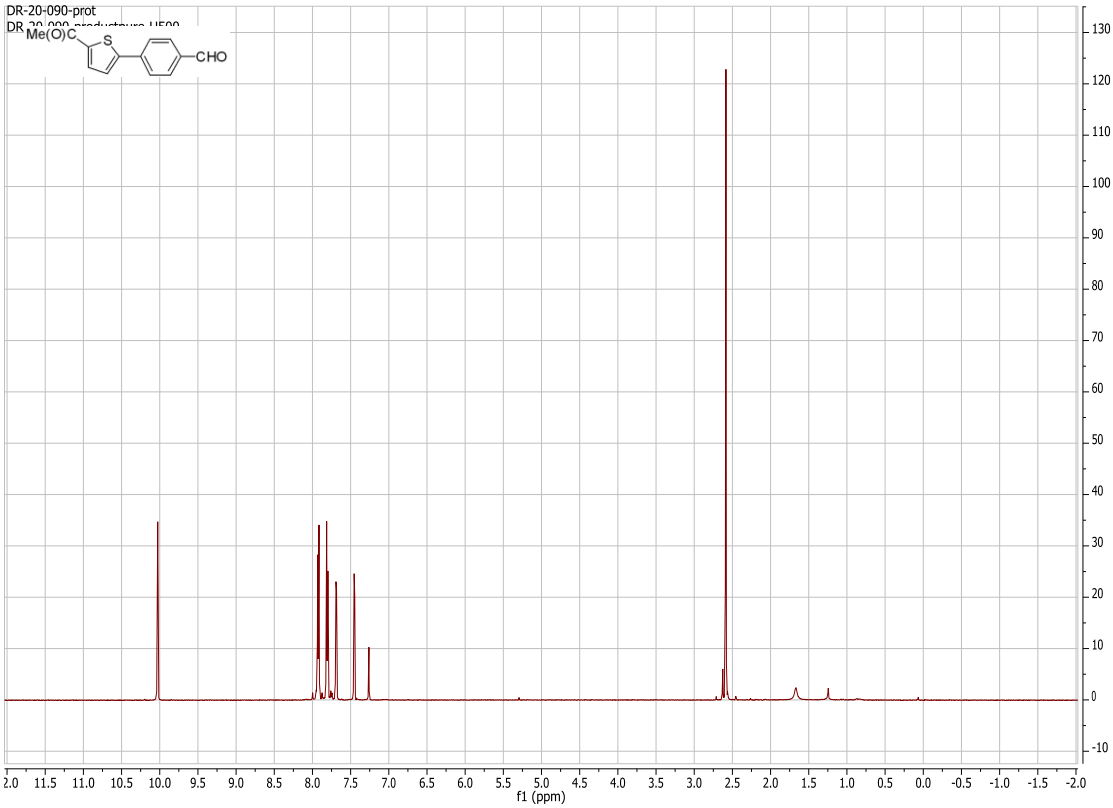

DR-15-099-proton
Me
F
Cl
Cl
D (d)
7.31
B (dd)
7.39
A (dd)
7.43
C (dd)
7.34
E (s)
2.45
1.00 0.41 0.41 0.97
1.65
f1 (ppm)

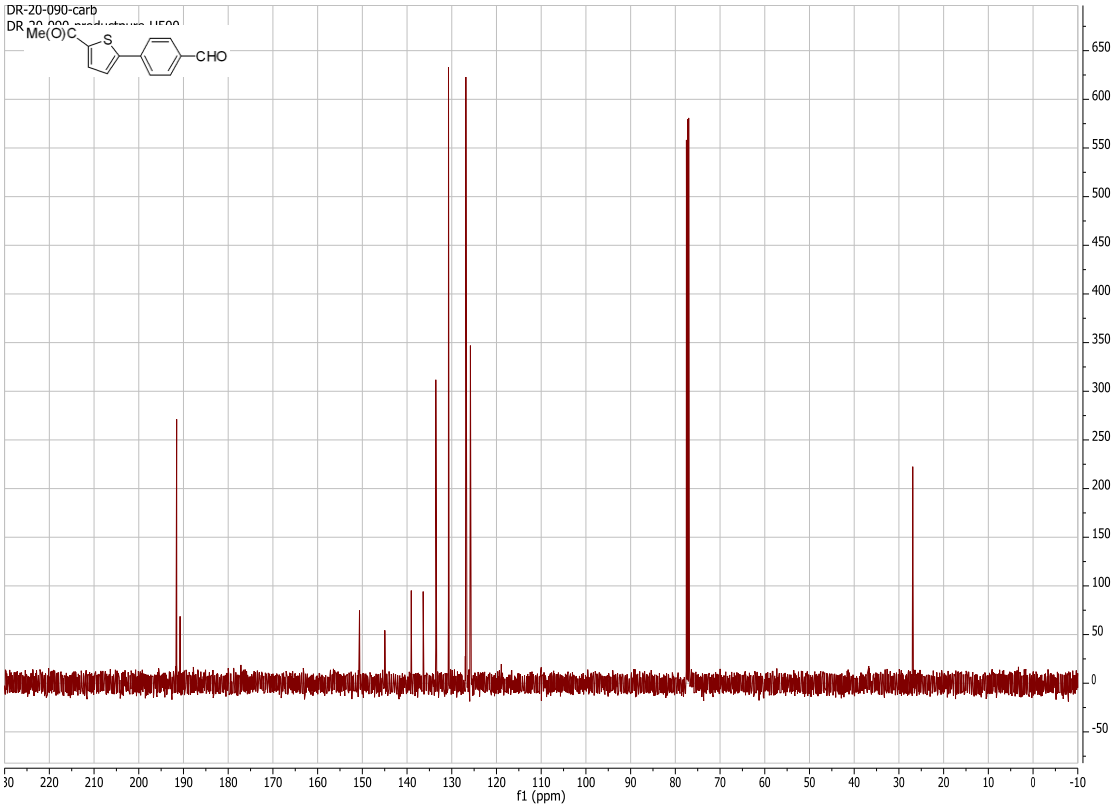

DR-15-099-carbon
Me
F
Cl
Cl
I (d)
129.02
G (s)
128.90
E (s)
129.67
C (d)
131.98
A (d)
154.29
B (s)
138.95
J (d)
122.95
D (s)
131.10
F (d)
128.52
H (d)
128.97
K (s)
21.49
2.46
f1 (ppm)

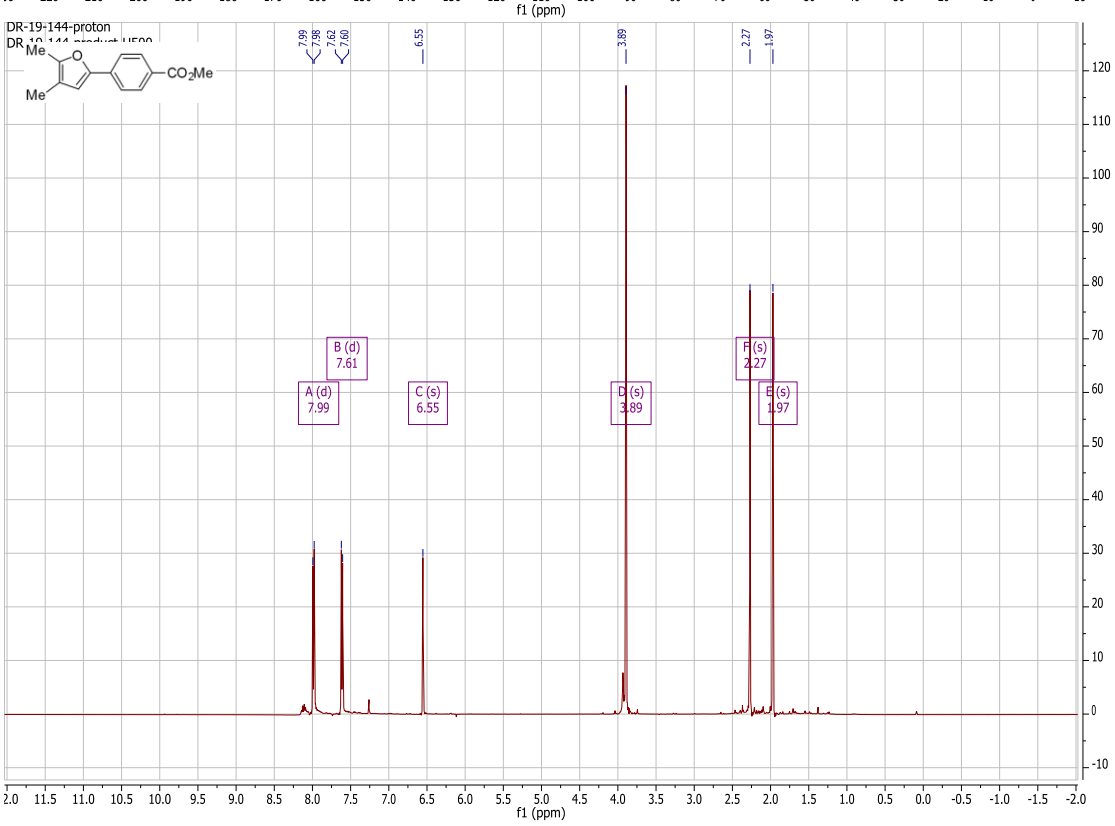

DR-15-099-fluor
F
Me
Cl
Cl
-122.63
f1 (ppm)

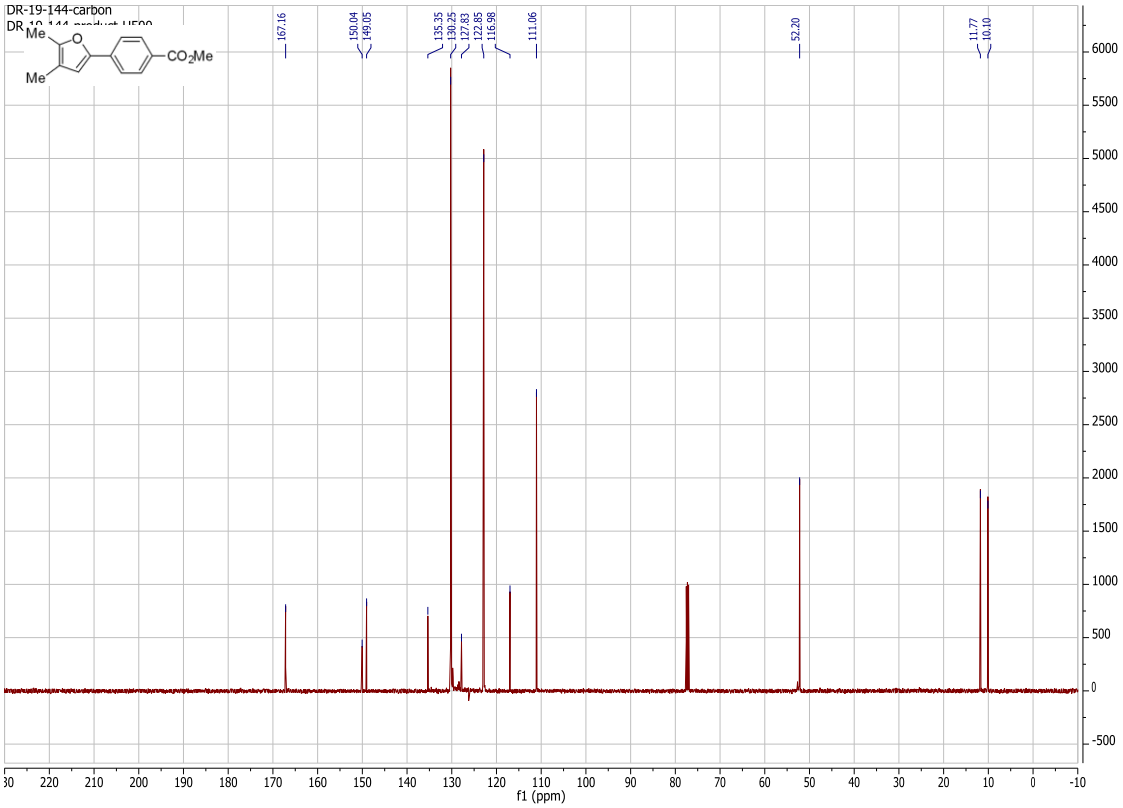

DR-17-047-proton
Me
S
NO2
8.18
8.17
7.63
7.61
7.27
7.26
6.79
2.54
B (d)
7.62
D (s)
6.79
A (d)
8.17
C (d)
7.27
E (s)
2.54
f1 (ppm)

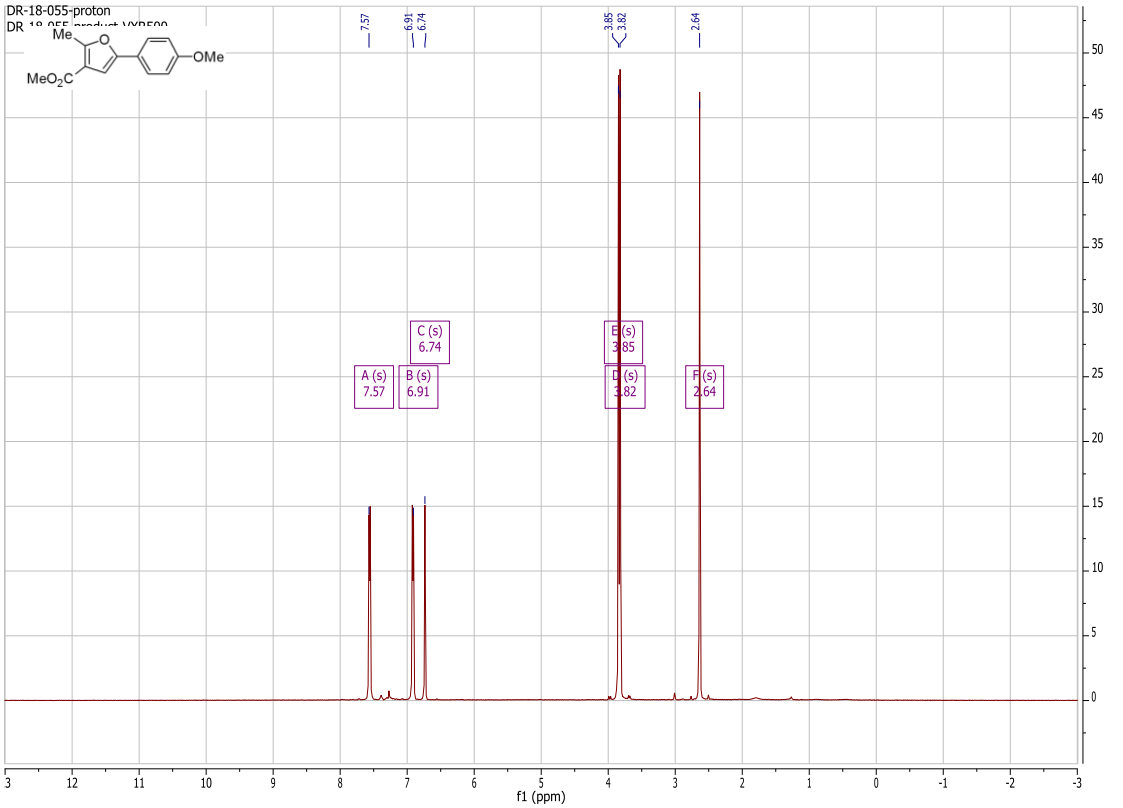

DR-17-047-carbon
Me
S
NO2
146.39
143.24
141.07
139.32
127.29
126.04
125.53
124.57
15.81
f1 (ppm)

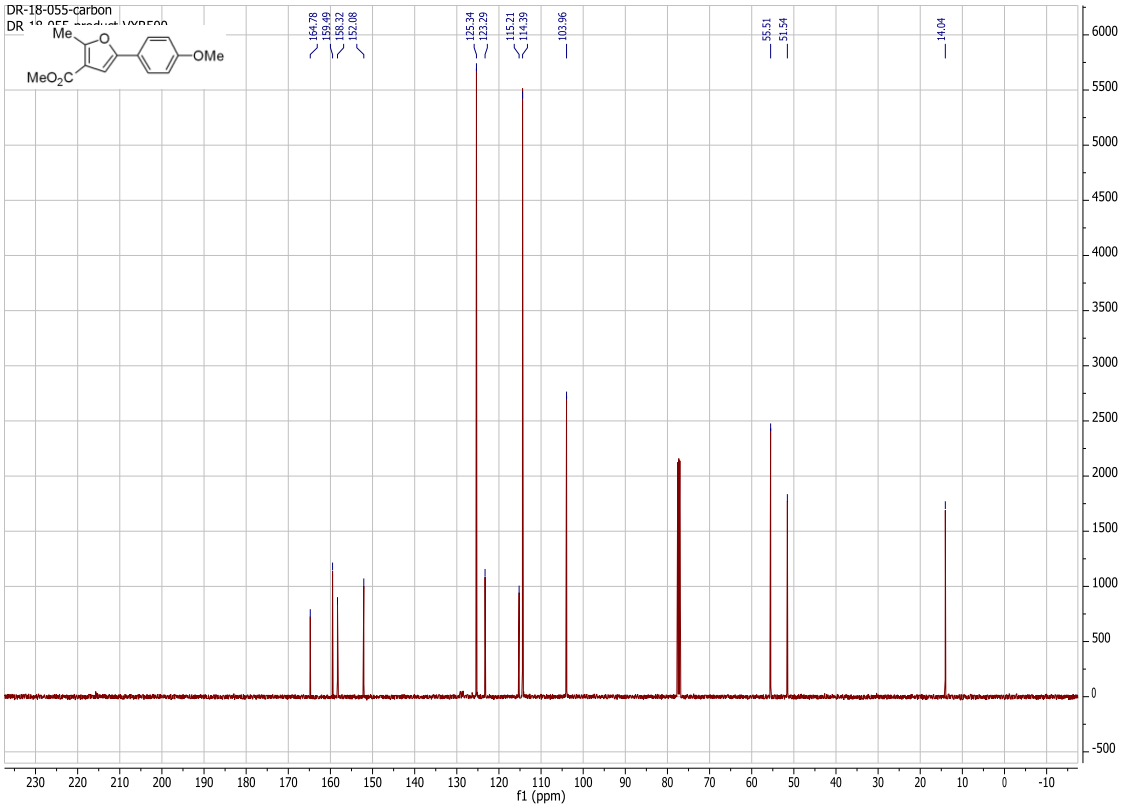

DR-20-090-prot
Me(O)C
S
CHO
f1 (ppm)

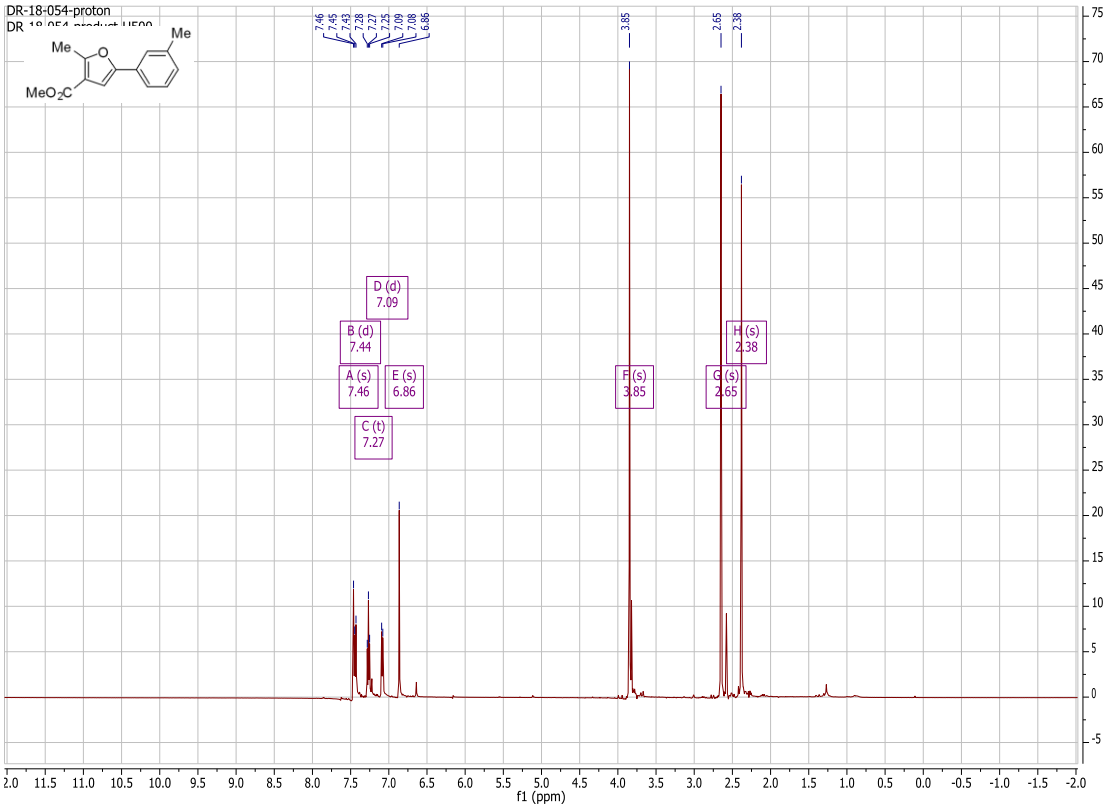

DR-20-090-carb
Me(O)C
S
CHO
f1 (ppm)

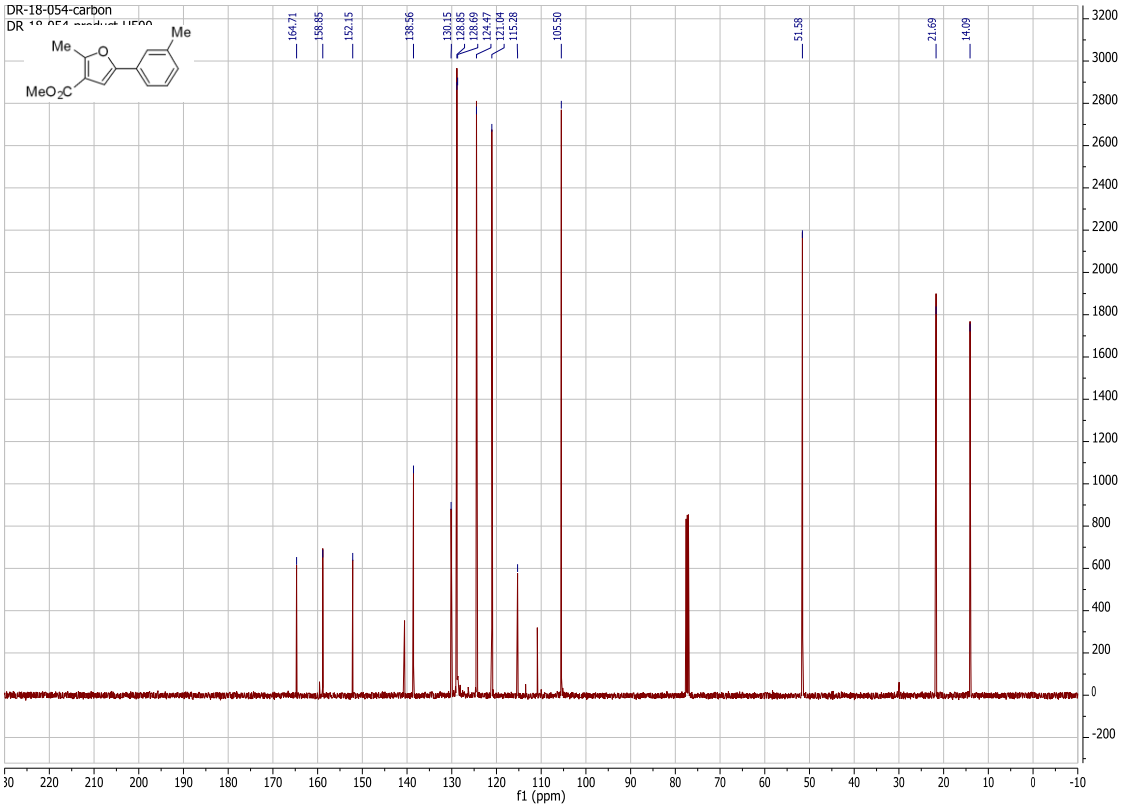

DR-19-144-proton
Me
O
CO2Me
Me
7.99
7.98
7.62
7.60
6.55
3.89
2.27
1.97
A (d) 7.99
B (d) 7.61
C (s) 6.55
D (s) 3.89
E (s) 1.97
F (s) 2.27
f1 (ppm)

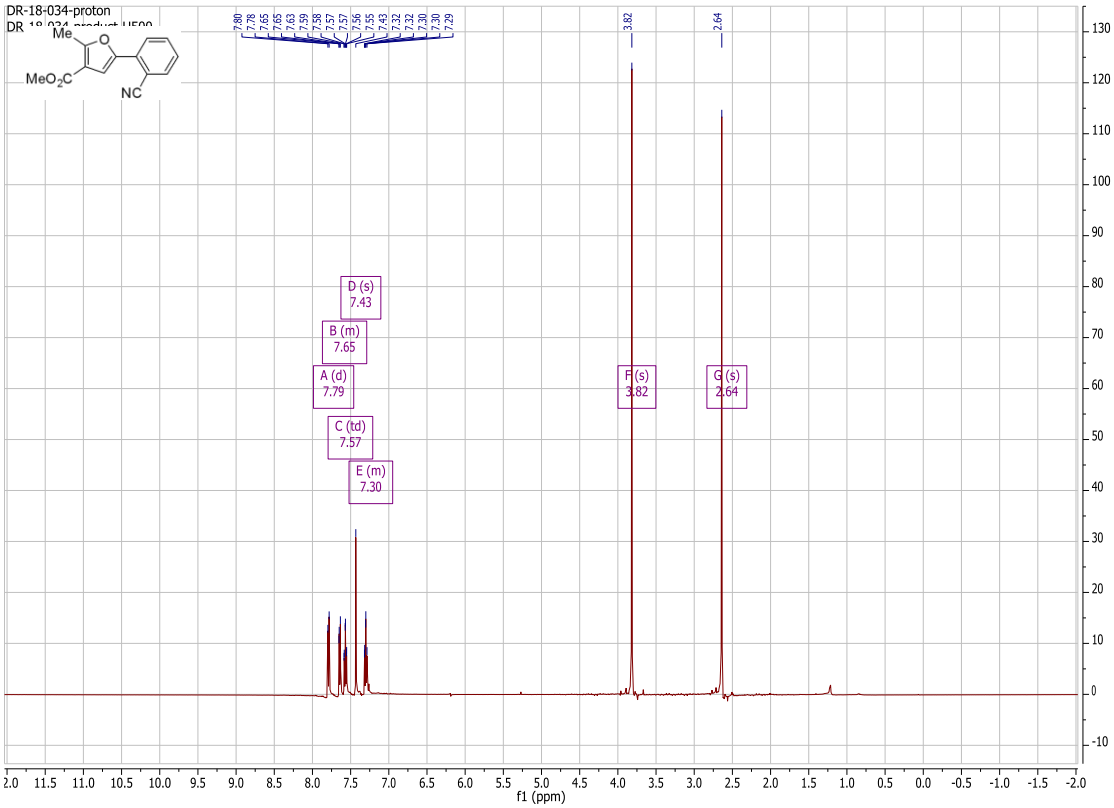

DR-19-144-carbon
Me
Me
CO2Me
167.16
150.04
149.05
135.35
130.25
127.83
123.55
116.98
111.06
52.20
11.77
10.10
f1 (ppm)

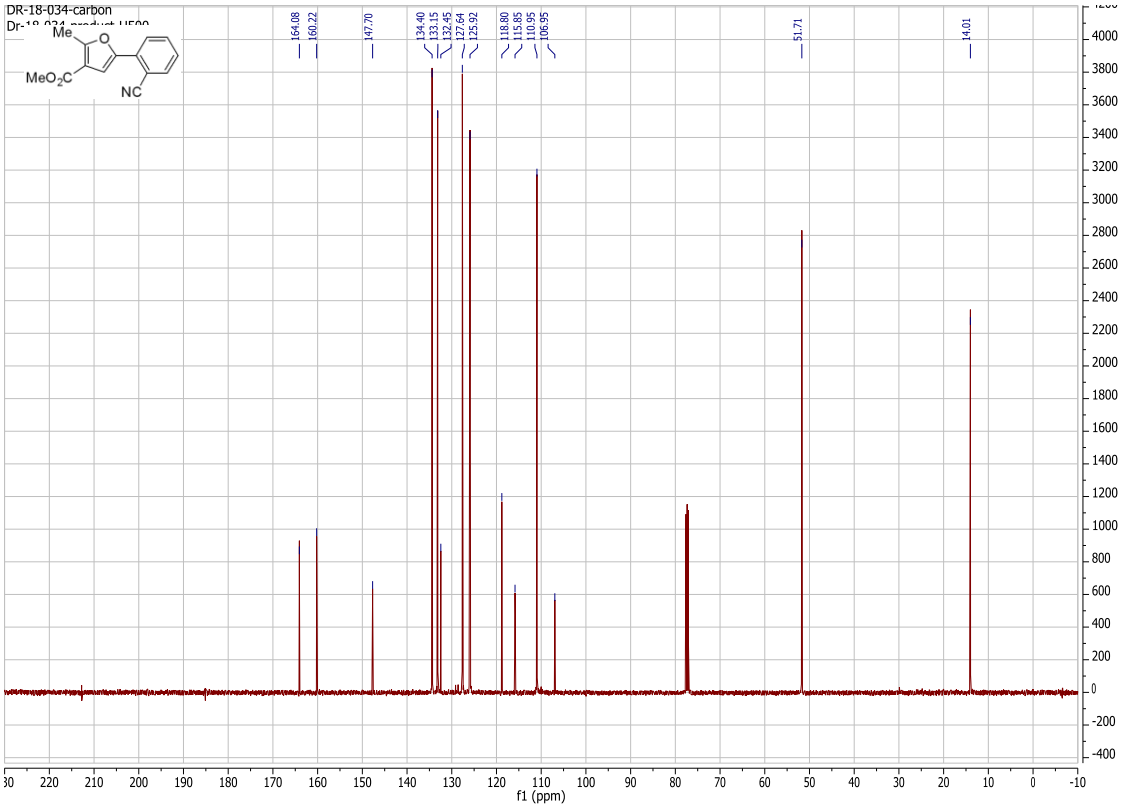

DR-18-055-proton
Me
MeO2C
OMe
7.57
6.91
6.74
3.85
3.82
2.64
C (s) 6.74
A (s) 7.57
B (s) 6.91
E (s) 3.85
D (s) 3.82
F (s) 2.64
f1 (ppm)

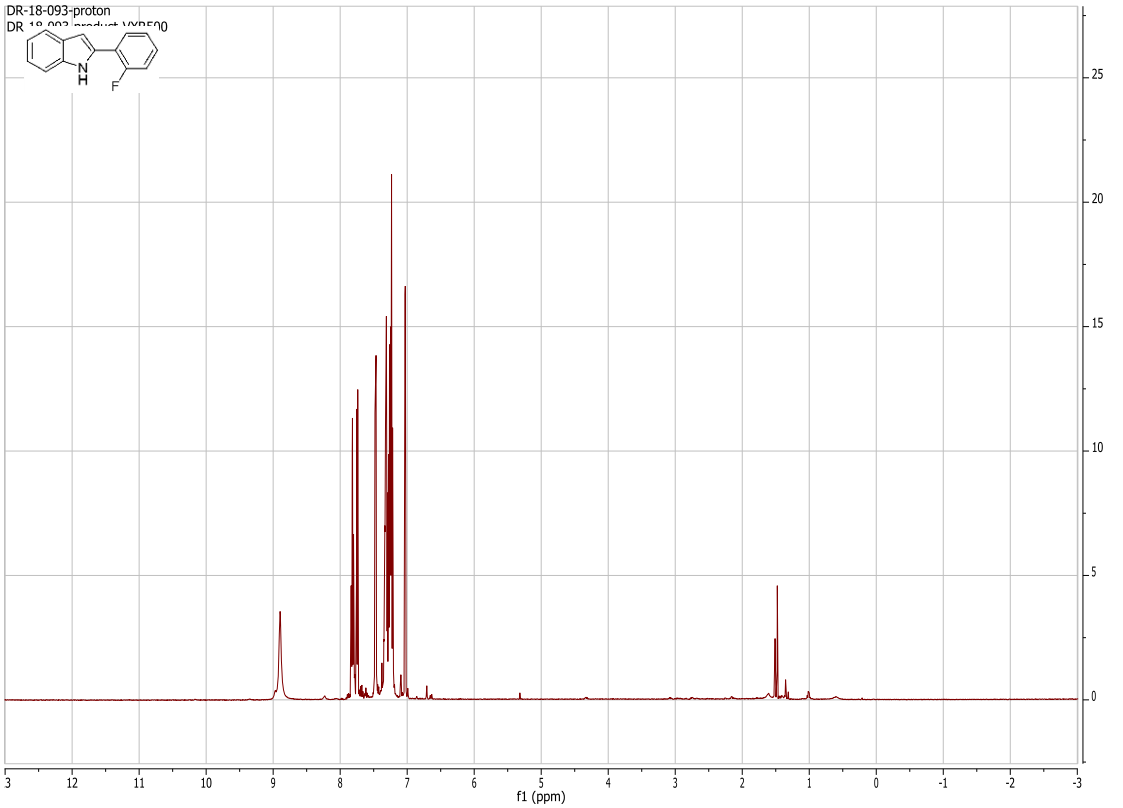

DR-18-055-carbon
Me
OMe
MeO2C
164.78
159.49
158.32
152.08
125.34
123.29
115.21
114.39
103.96
55.51
51.54
14.04
f1 (ppm)

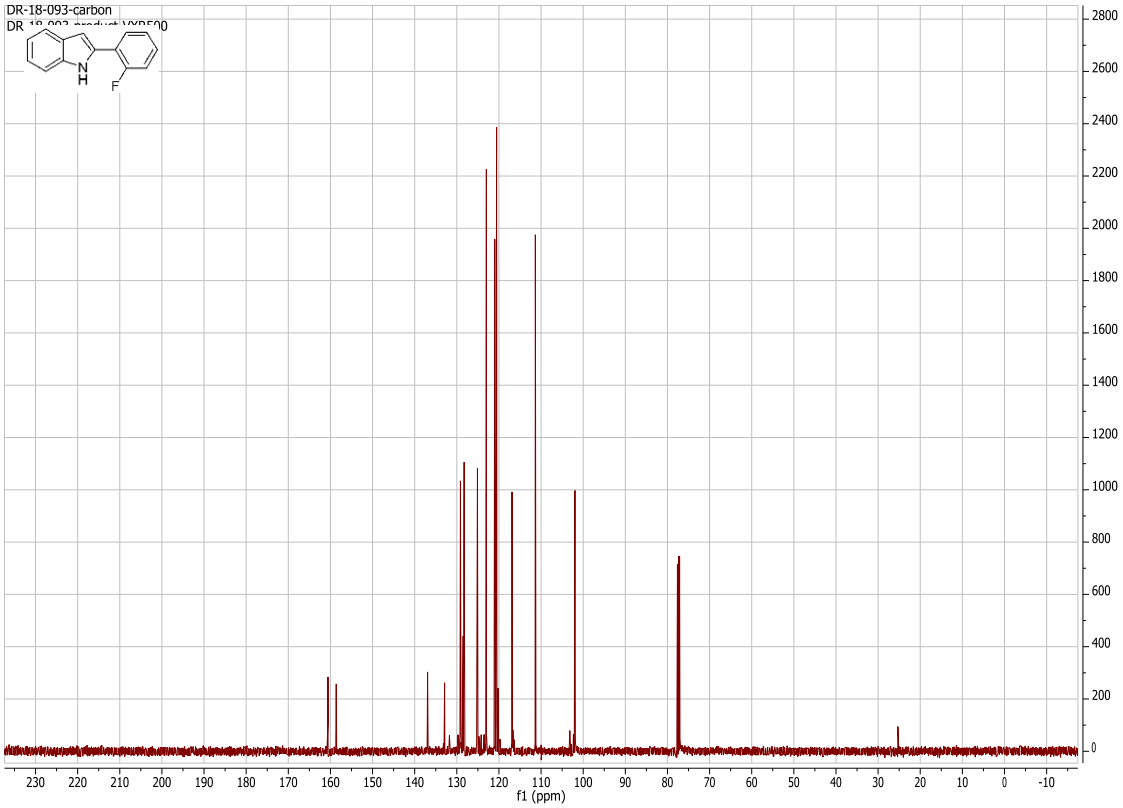

DR-18-054-proton
Me
Me
MeO2C
7.46
7.45
7.43
7.28
7.27
7.25
7.09
7.08
6.86
3.85
2.65
2.38
D (d) 7.09
B (d) 7.44
A (s) 7.46
E (s) 6.86
C (t) 7.27
F (s) 3.85
G (s) 2.65
H (s) 2.38
f1 (ppm)

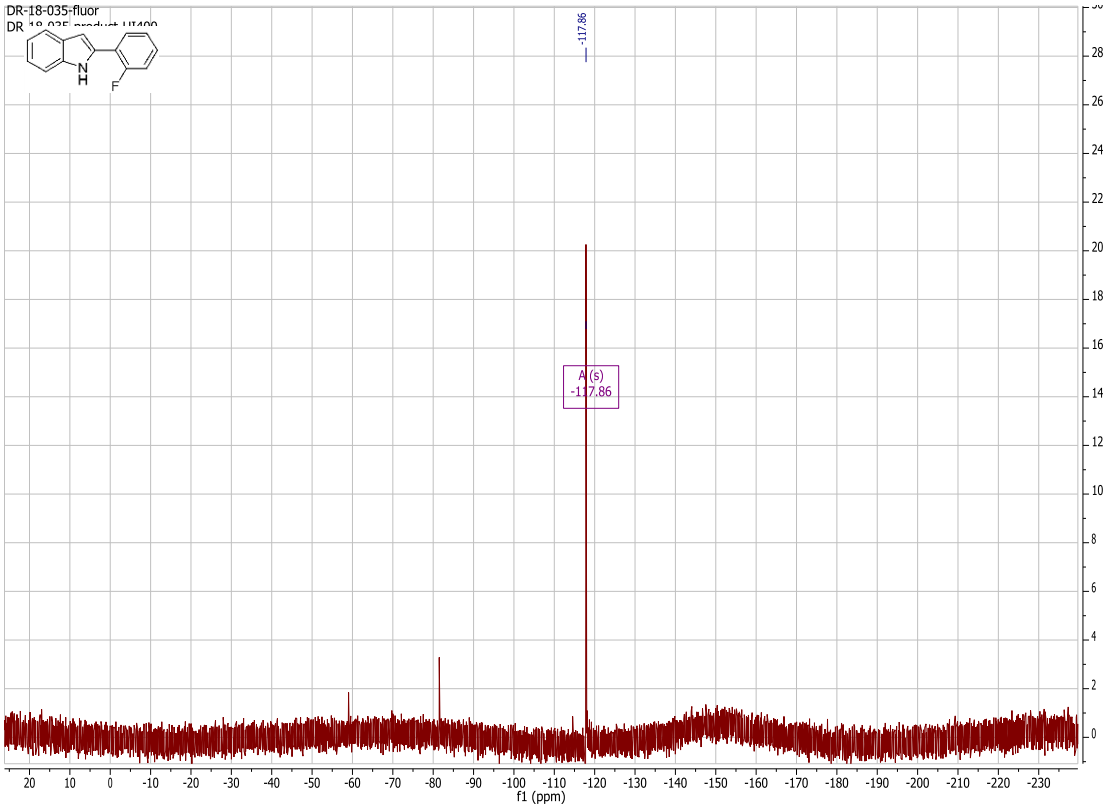

DR-18-054-carbon
Me
Me
MeO2C
164.71
158.85
152.15
138.56
130.15
128.85
128.69
124.47
121.04
115.28
105.50
51.58
21.69
14.09
f1 (ppm)

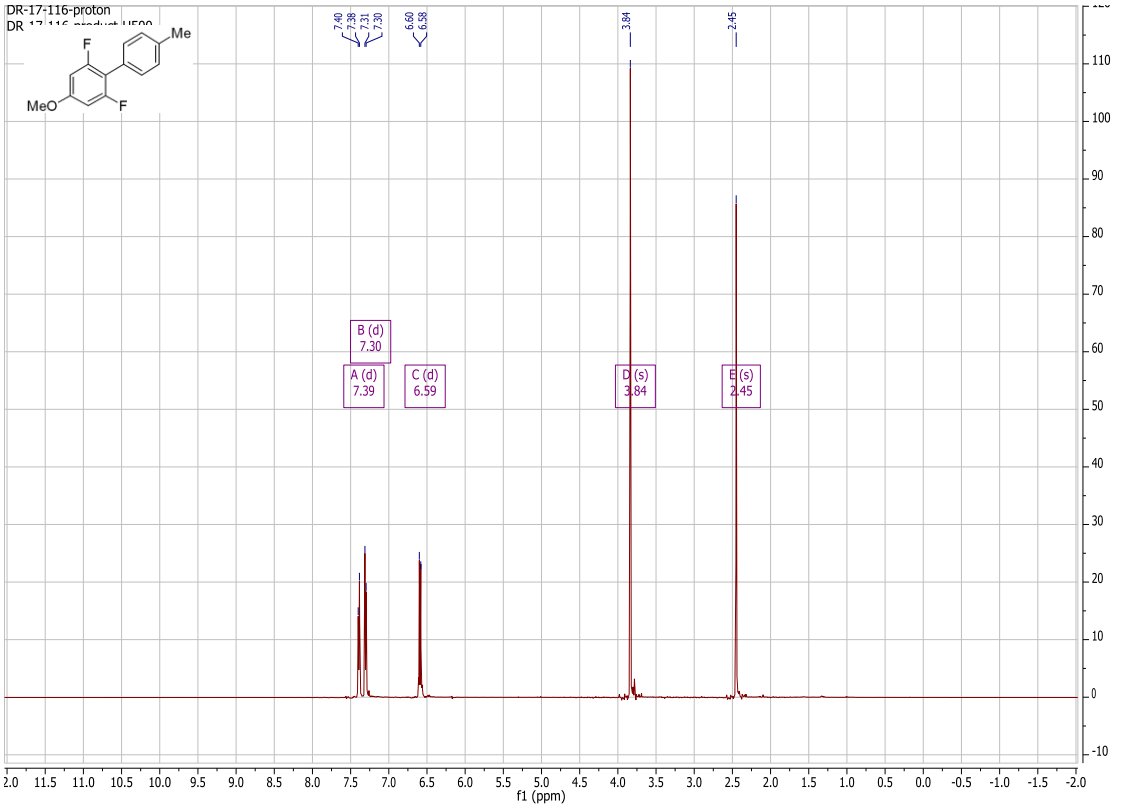

DR-18-034-proton
Me
MeO2C
NC
7.80
7.78
7.65
7.63
7.59
7.58
7.57
7.56
7.55
7.43
7.32
7.30
7.29
3.82
2.64
D (s)
7.43
B (m)
7.65
A (d)
7.79
C (td)
7.57
E (m)
7.30
F (s)
3.82
G (s)
2.64
f1 (ppm)

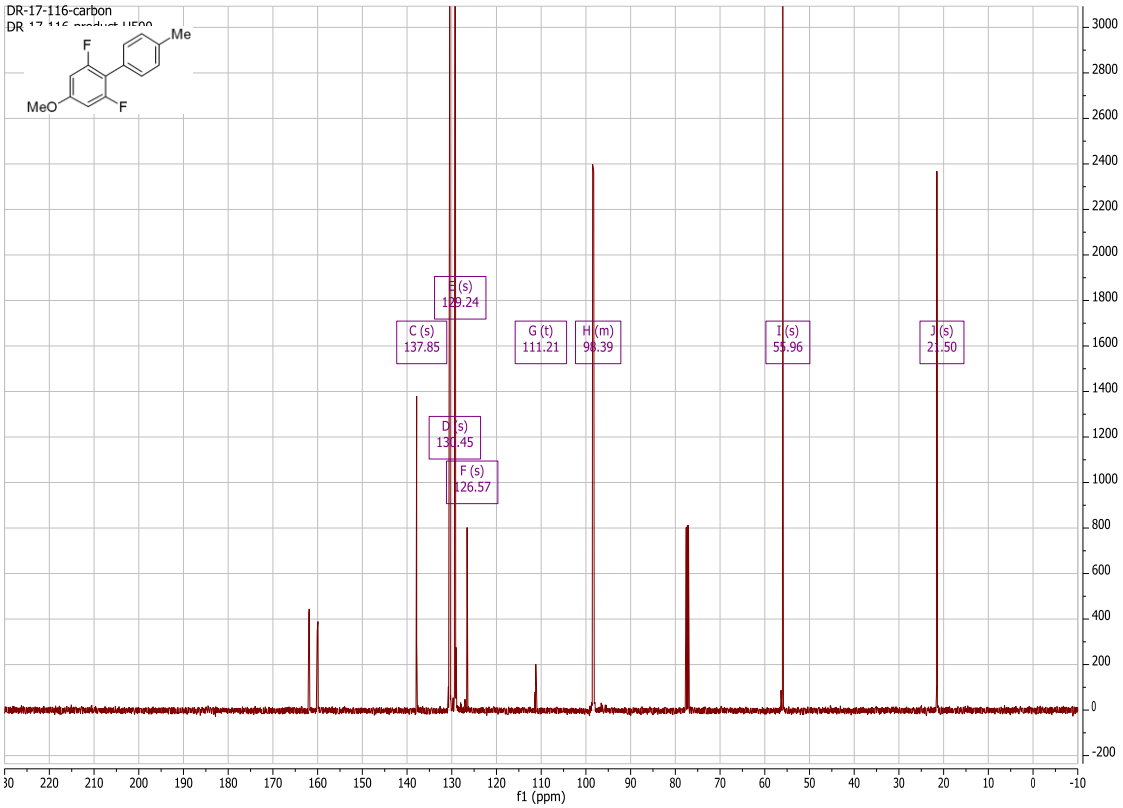

DR-18-034-carbon
Me
MeO2C
NC
164.08
160.22
147.70
134.40
133.15
132.45
127.64
125.92
118.80
115.85
110.95
106.95
51.71
14.01
f1 (ppm)

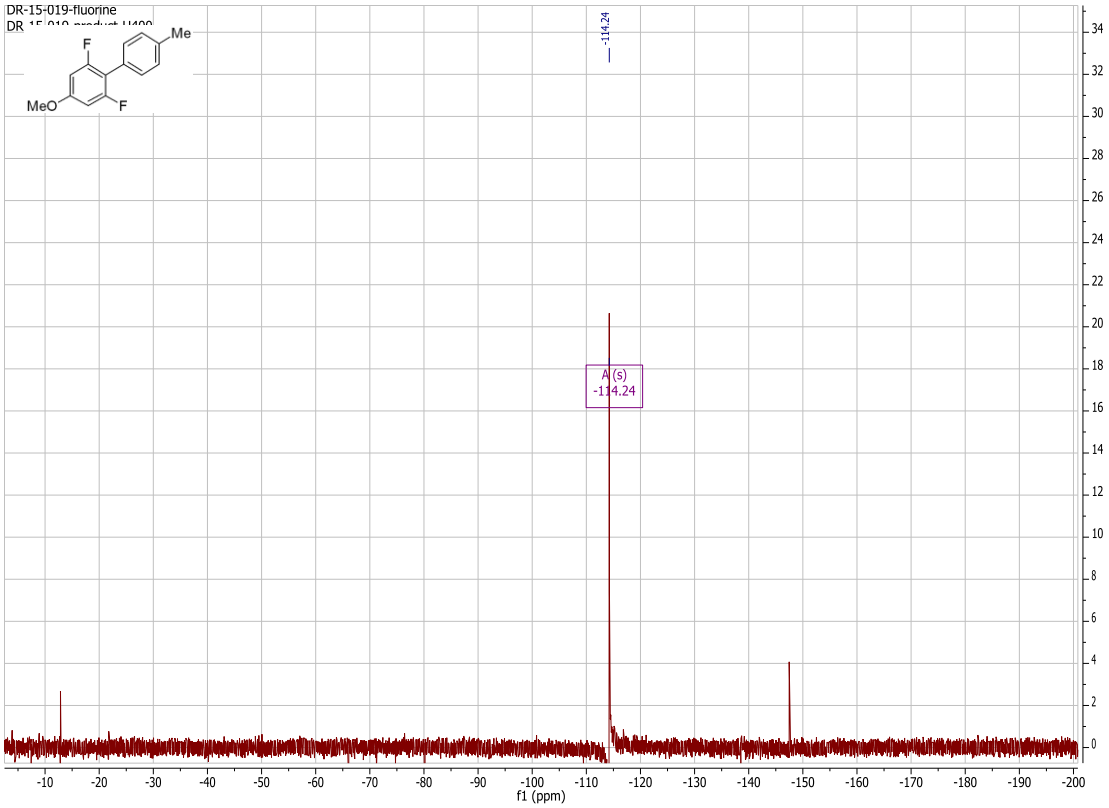

DR-18-093-proton
N
H
F
f1 (ppm)

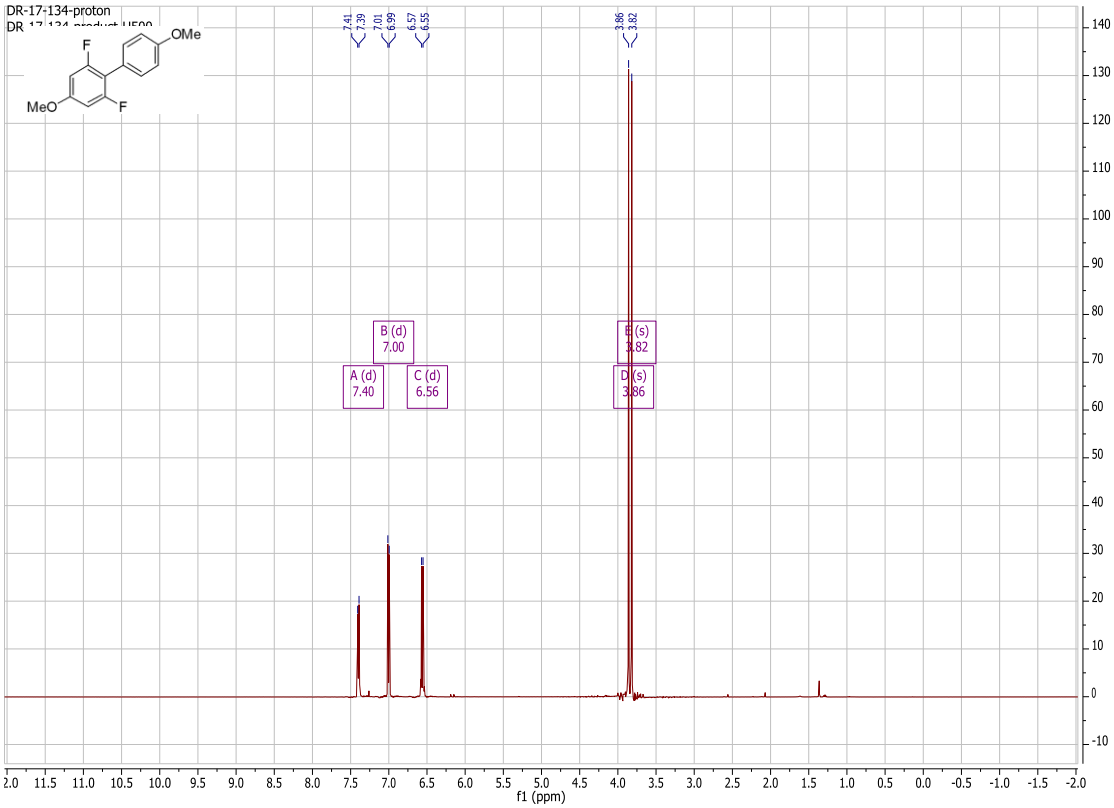

DR-18-093-carbon
f1 (ppm)

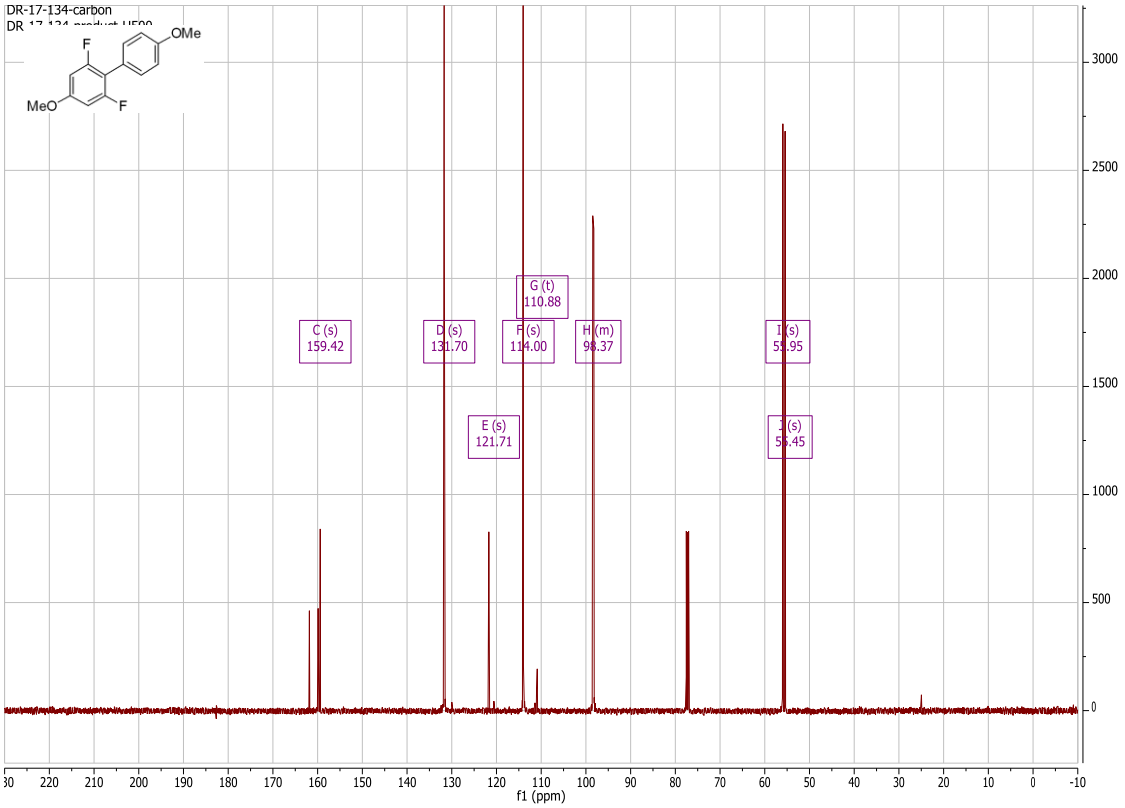

DR-18-035-fluor
-117.86
A (s)
-117.86
f1 (ppm)

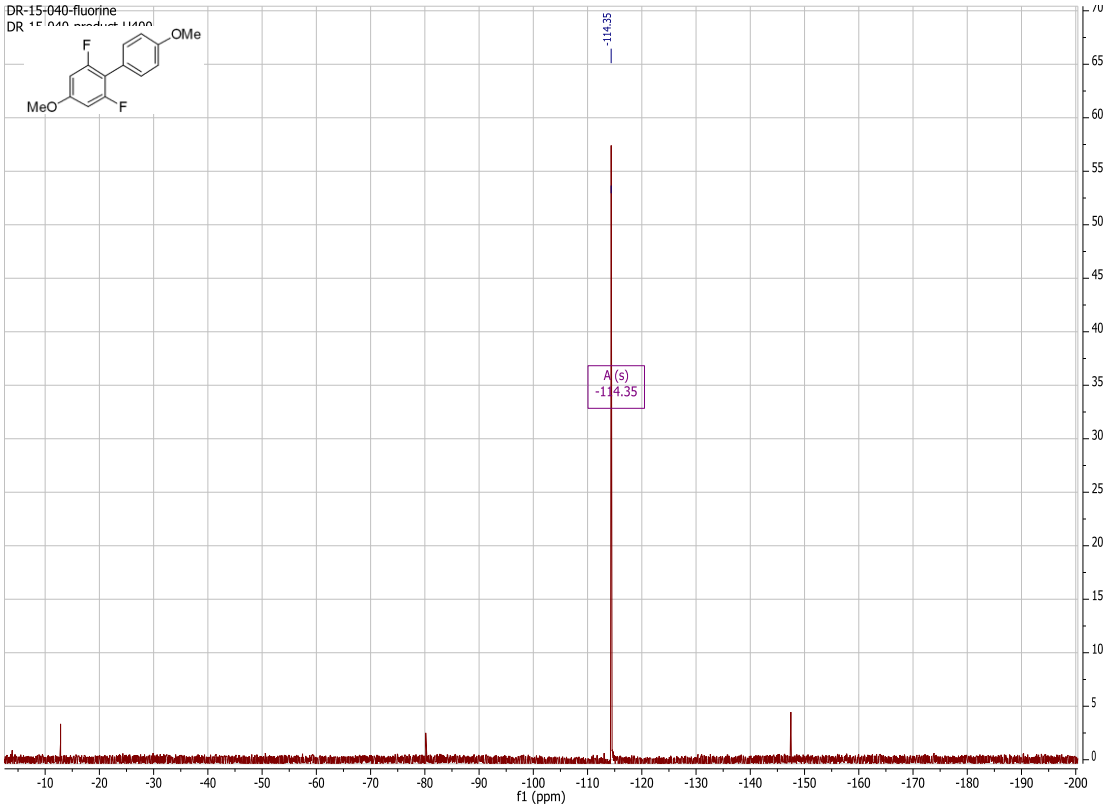

DR-17-116-proton
F
Me
MeO
F
7.40
7.38
7.31
7.30
6.60
6.58
3.84
2.45
B (d)
7.30
A (d)
7.39
C (d)
6.59
D (s)
3.84
E (s)
2.45
f1 (ppm)

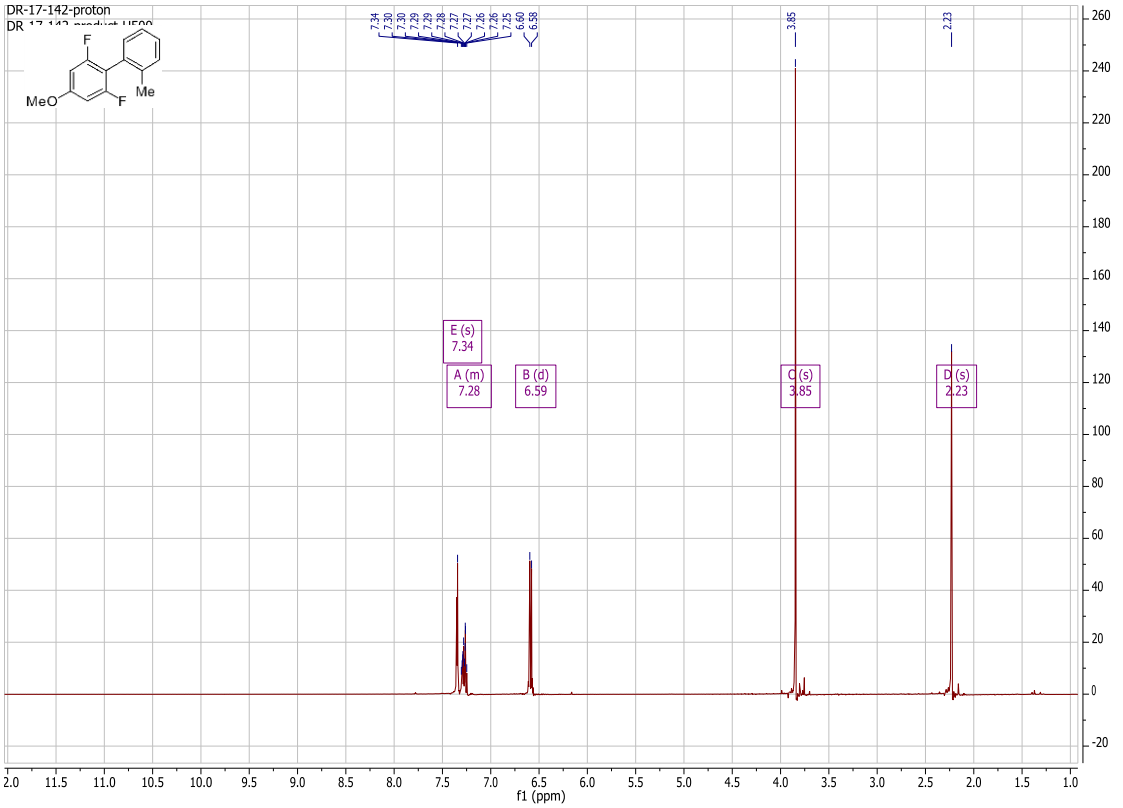

DR-17-116-carbon
F
Me
MeO
F
E (s)
129.24
C (s)
137.85
G (t)
111.21
H (m)
98.39
I (s)
55.96
J (s)
21.50
D (s)
130.45
F (s)
126.57
f1 (ppm)

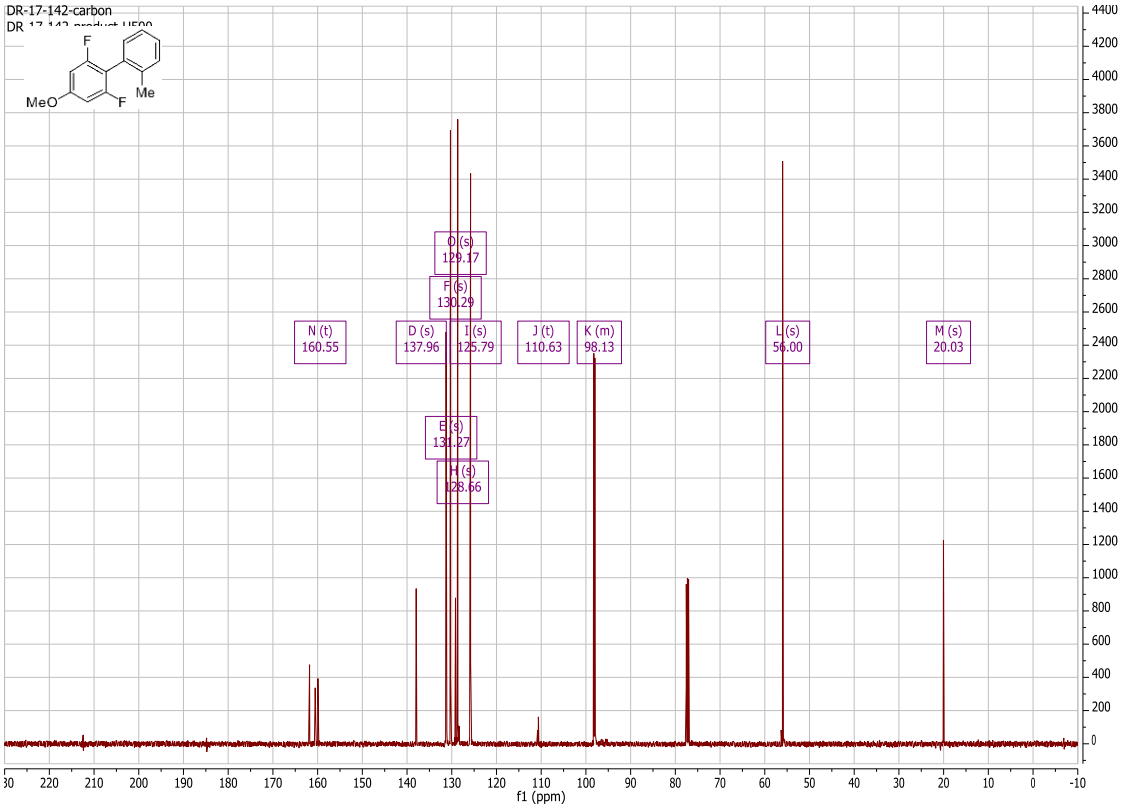

DR-15-019-fluorine
F
Me
MeO
F
-114.24
A (s)
-114.24
f1 (ppm)

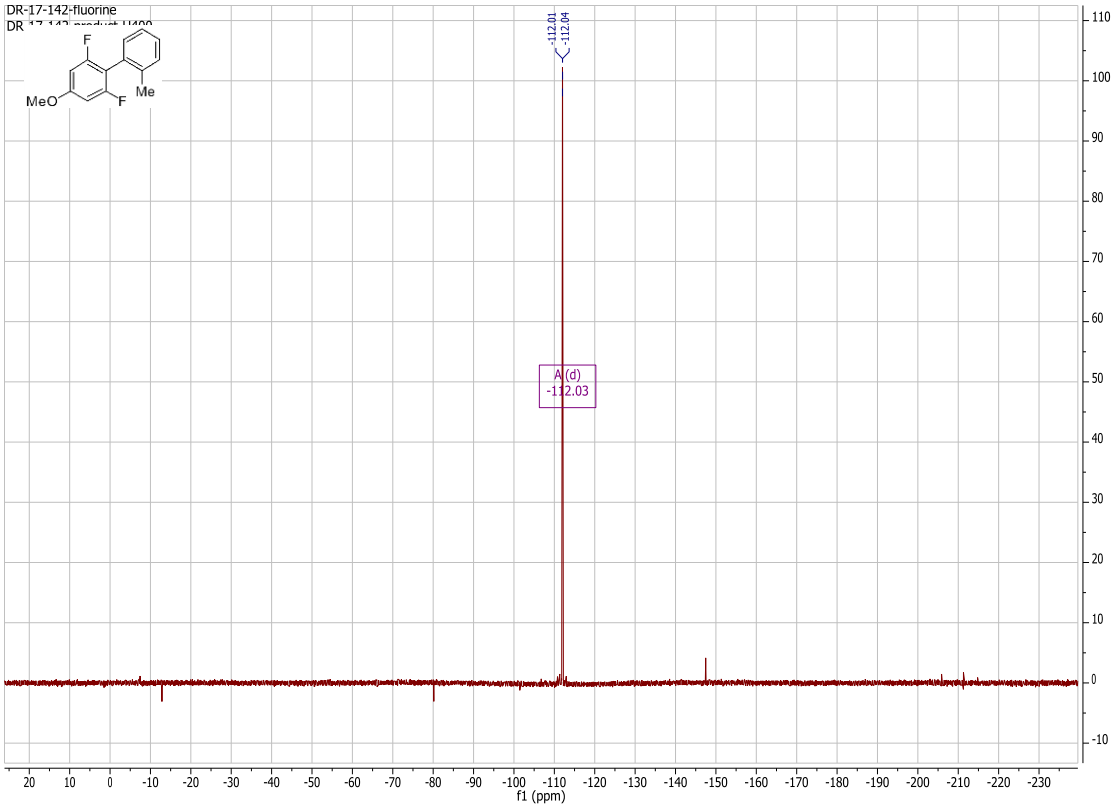

DR-17-134-proton
F
OMe
MeO
F
7.41
7.39
7.01
6.99
6.57
6.55
3.86
3.82
B (d)
7.00
A (d)
7.40
C (d)
6.56
D (s)
3.86
f1 (ppm)

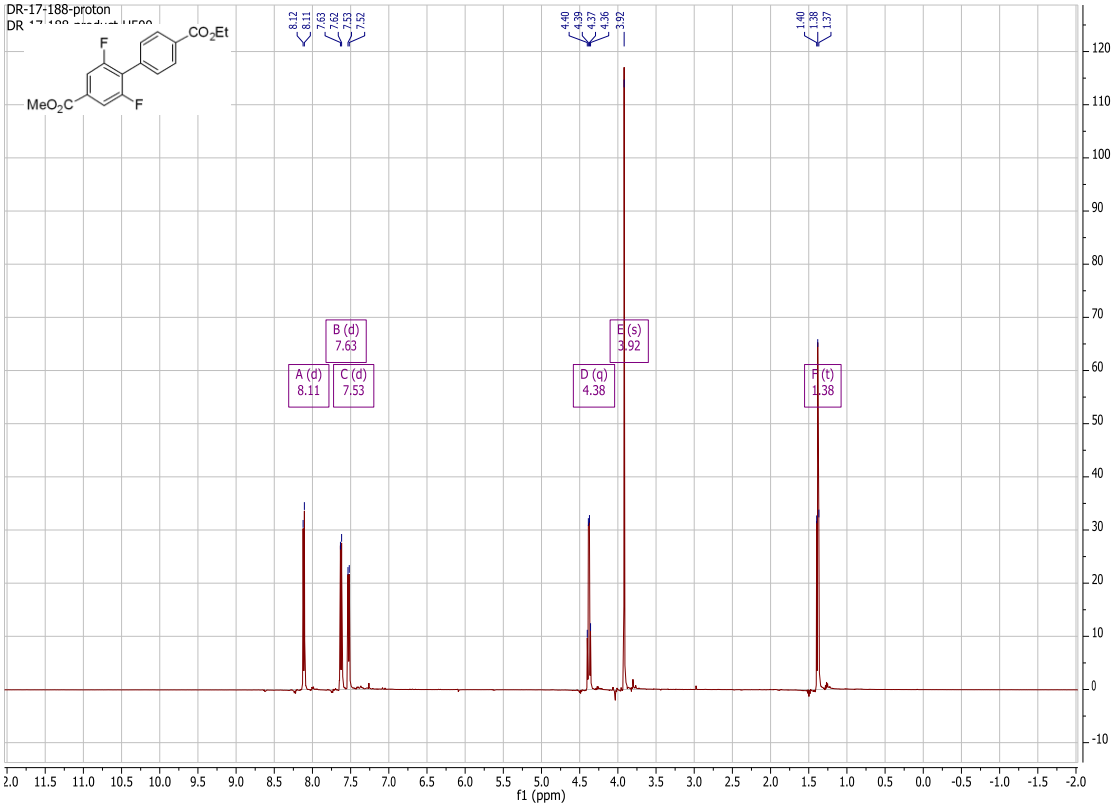

DR-17-134-carbon
OMe
F
MeO
F
C (s)
159.42
D (s)
131.70
E (s)
121.71
F (s)
114.00
G (t)
110.88
H (m)
98.37
I (s)
55.95
J (s)
55.45
f1 (ppm)

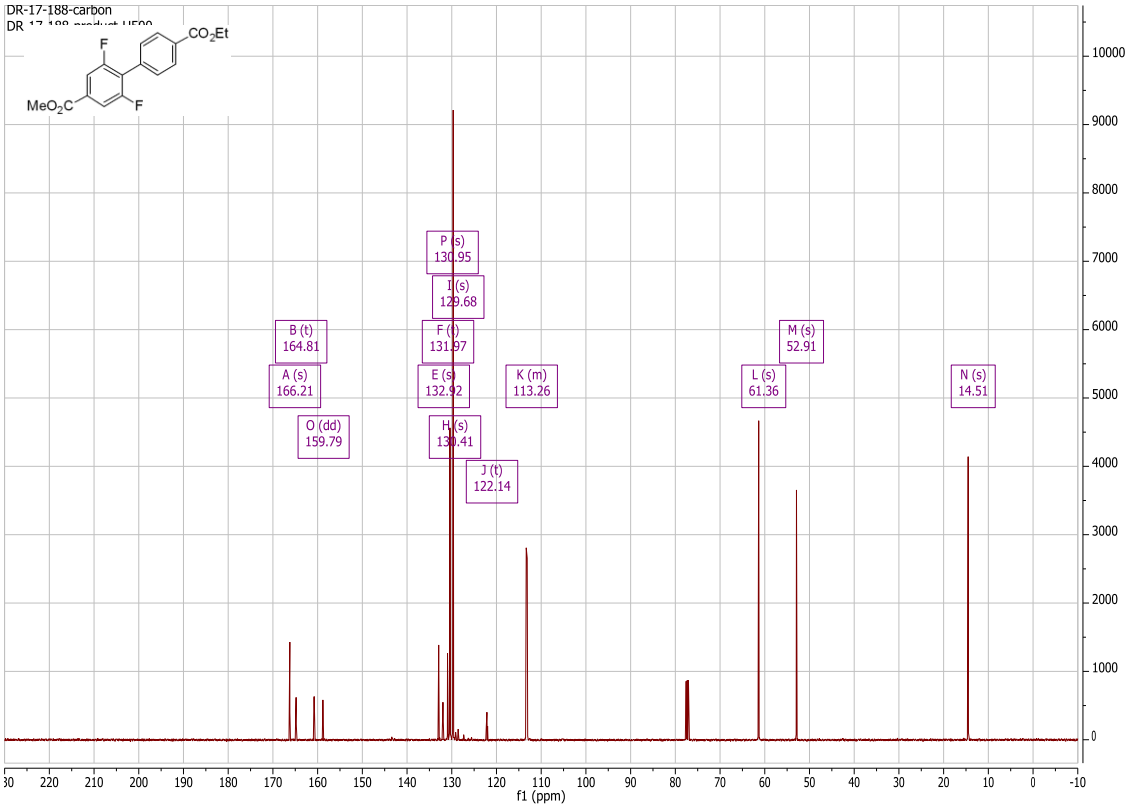

DR-15-040-fluorine
OMe
F
MeO
F
-114.35
A (s)
-114.35
f1 (ppm)

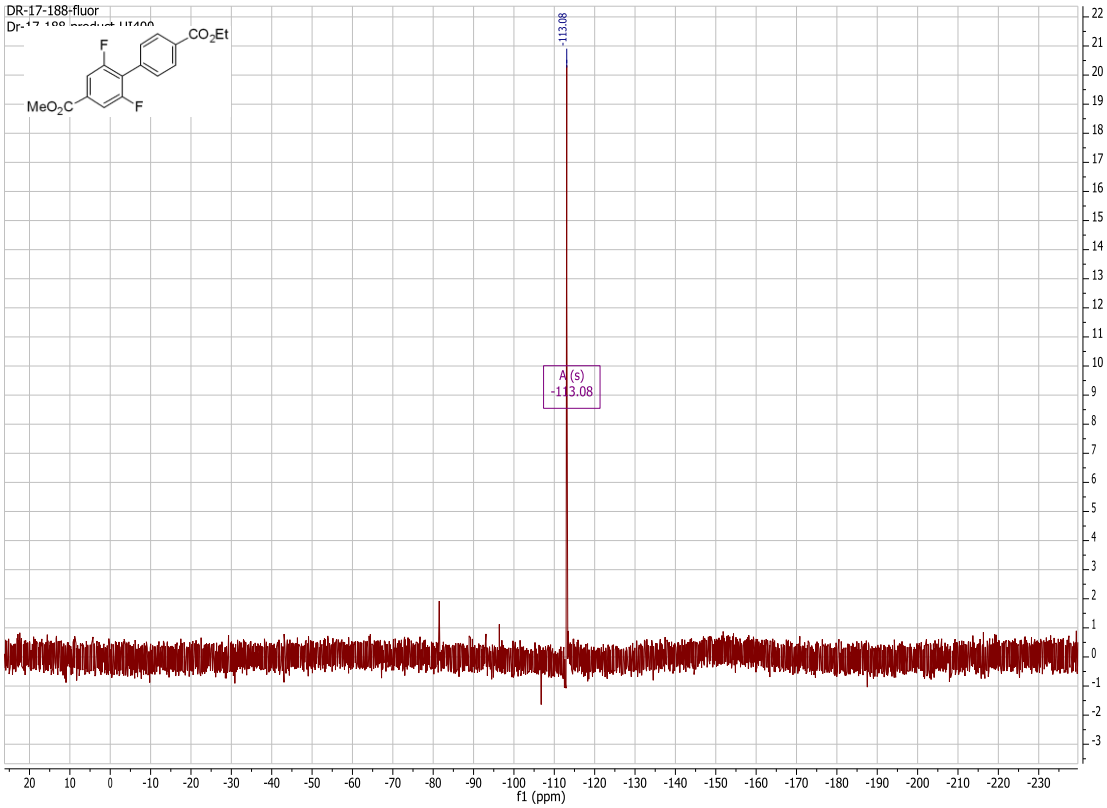

DR-17-142-proton
F
MeO
F
Me
7.34
7.30
7.30
7.29
7.29
7.28
7.27
7.27
7.26
7.26
7.25
6.60
6.58
3.85
2.23
E (s)
7.34
A (m)
7.28
B (d)
6.59
C (s)
3.85
D (s)
2.23
f1 (ppm)

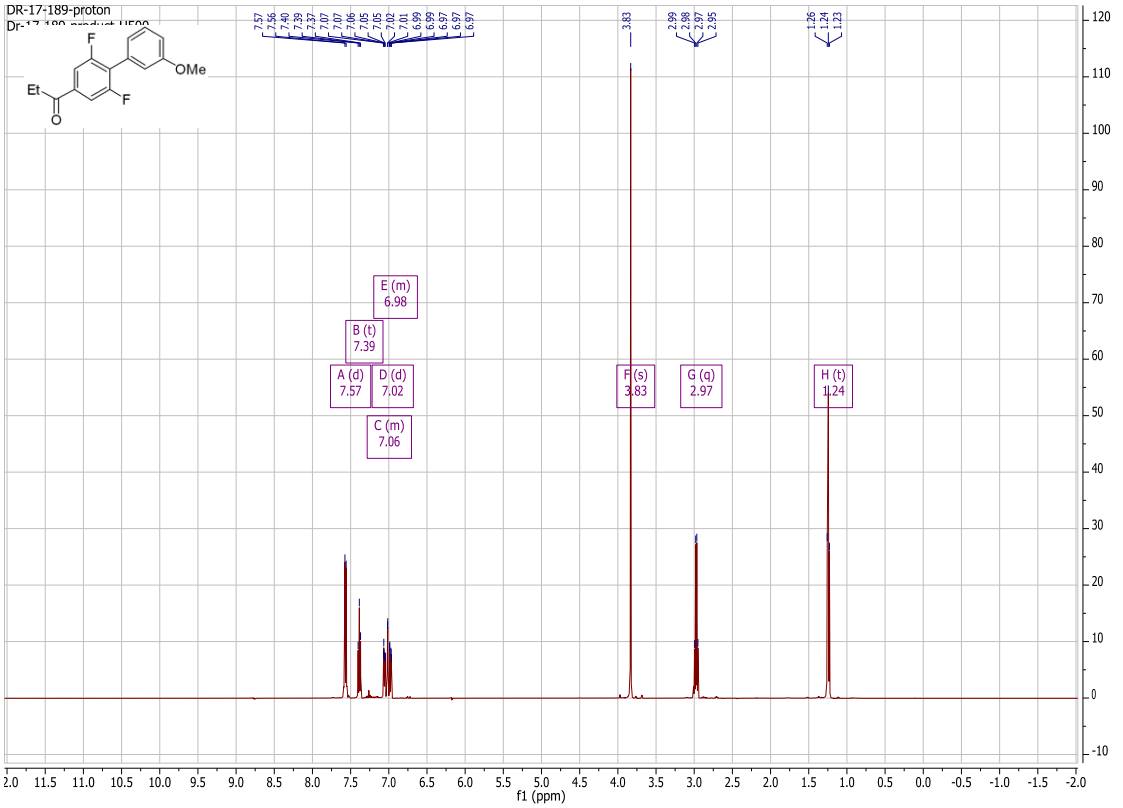

DR-17-142-carbon
F
MeO
F
Me
O (s)
129.17
F (s)
130.29
N (t)
160.55
D (s)
137.96
I (s)
125.79
J (t)
110.63
K (m)
98.13
L (s)
56.00
M (s)
20.03
E (s)
131.27
H (s)
128.66
f1 (ppm)

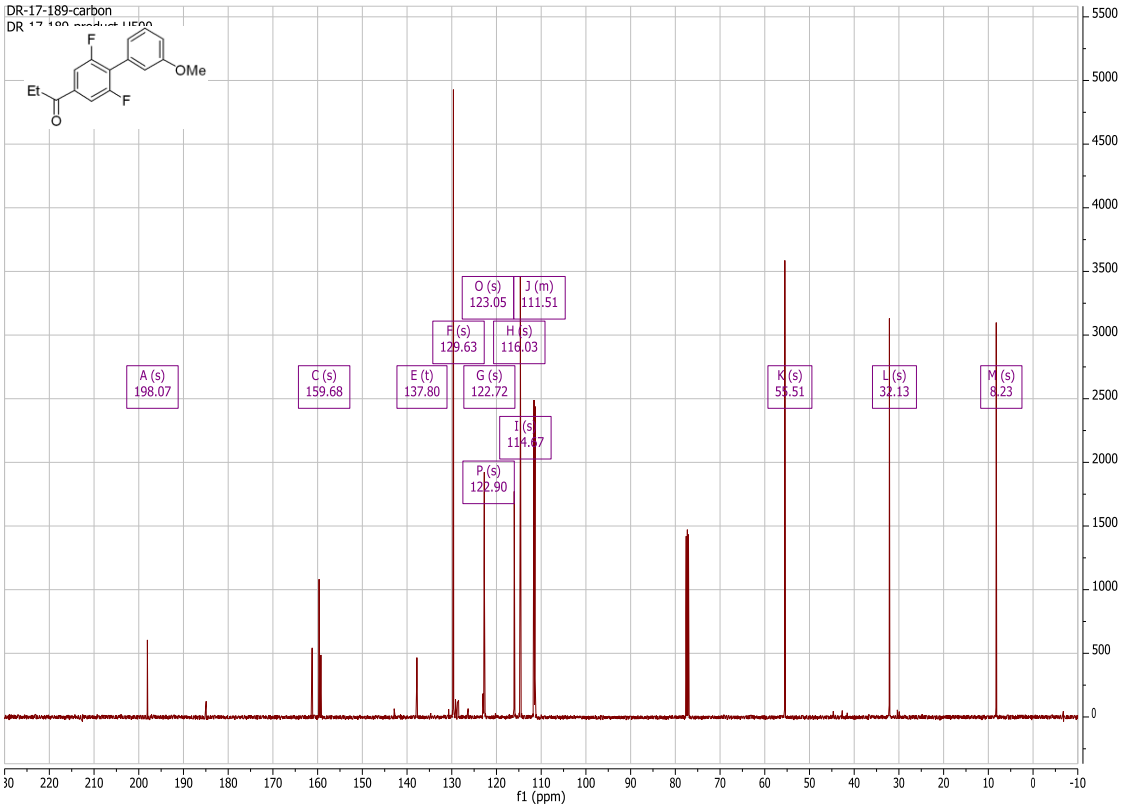

DR-17-142-fluorine
F
MeO
F
Me
-112.01
-112.04
A (d)
-112.03
f1 (ppm)

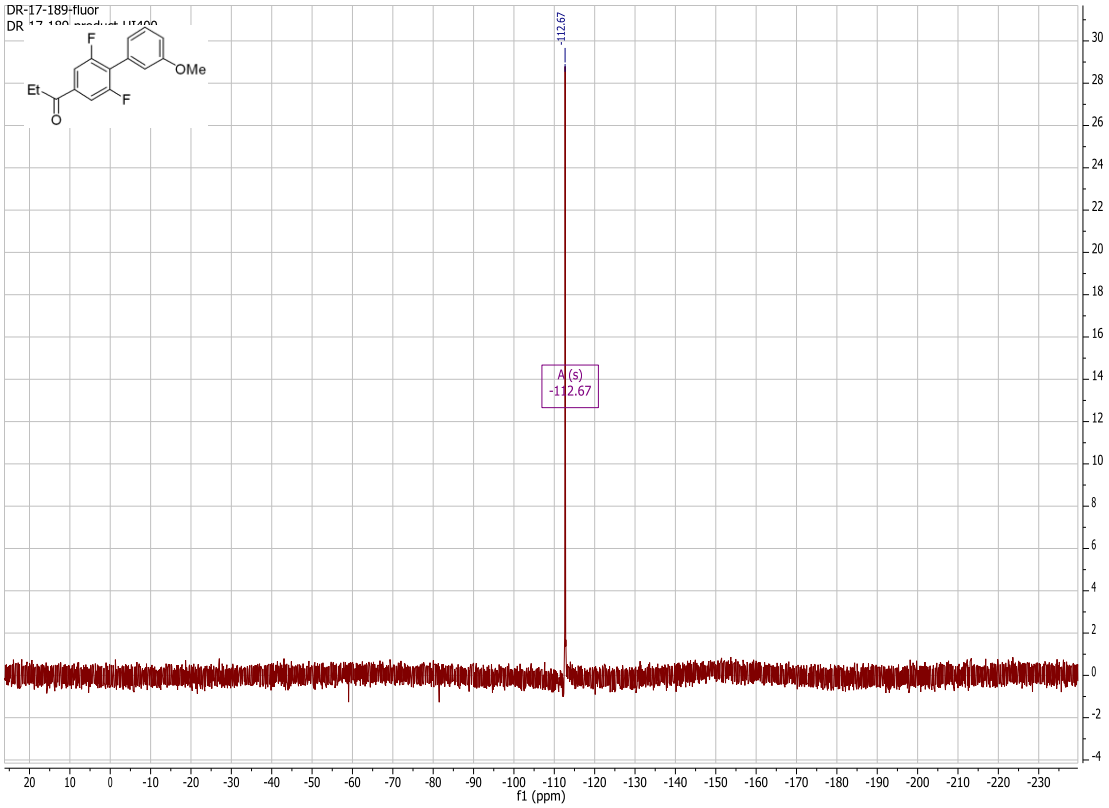

DR-17-188-proton
F
CO2Et
MeO2C
F
8.12
8.11
7.63
7.62
7.53
7.52
4.40
4.39
4.37
4.36
3.92
1.40
1.38
1.37
B (d)
7.63
A (d)
8.11
C (d)
7.53
E (s)
3.92
D (q)
4.38
F (t)
1.38
f1 (ppm)

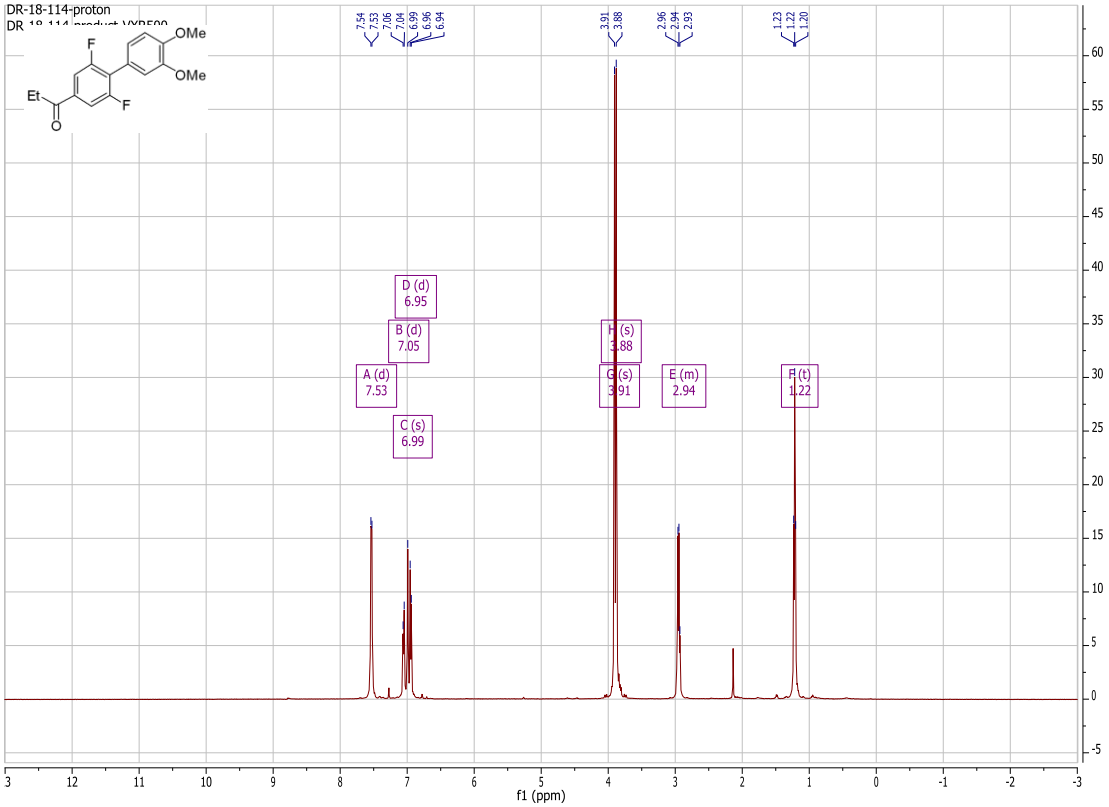

DR-17-188-carbon
F
CO2Et
MeO2C
F
P (s)
130.95
I (s)
129.68
B (t)
164.81
F (t)
131.97
M (s)
52.91
A (s)
166.21
E (s)
132.92
K (m)
113.26
L (s)
61.36
N (s)
14.51
O (dd)
159.79
H (s)
130.41
J (t)
122.14
f1 (ppm)

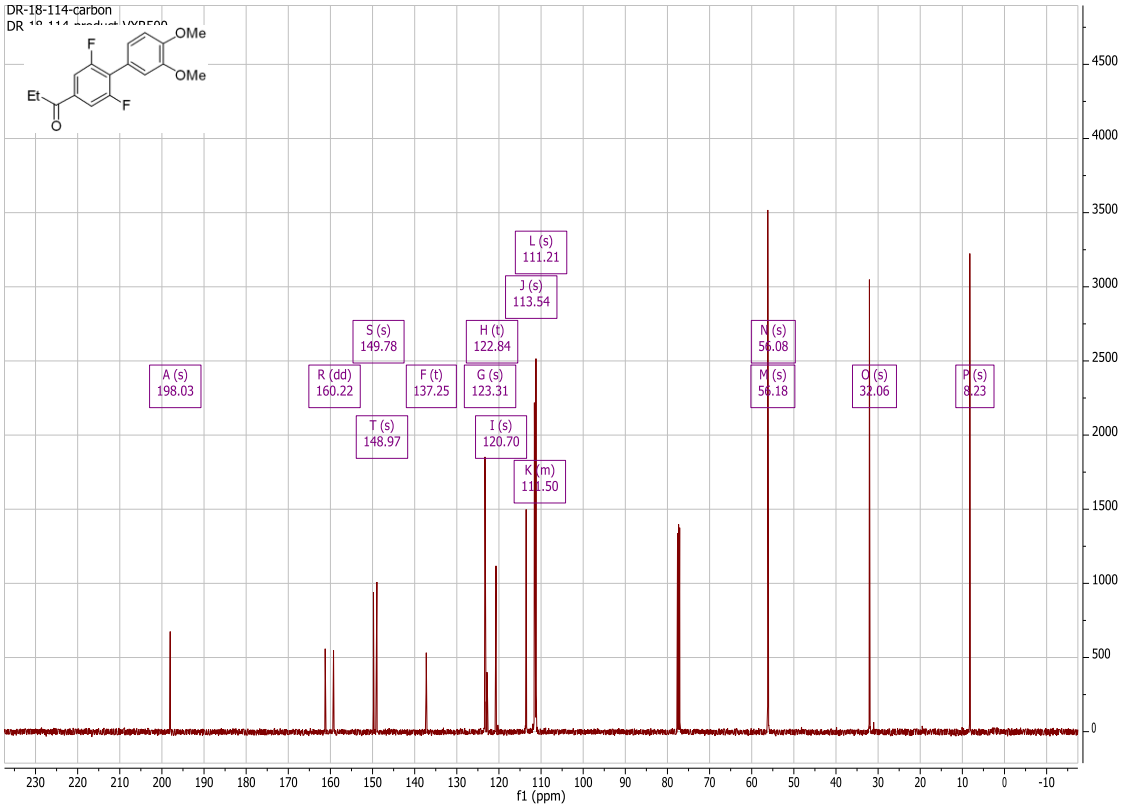

DR-17-188-fluor
F
CO2Et
MeO2C
F
-113.08
A (s)
-113.08
f1 (ppm)

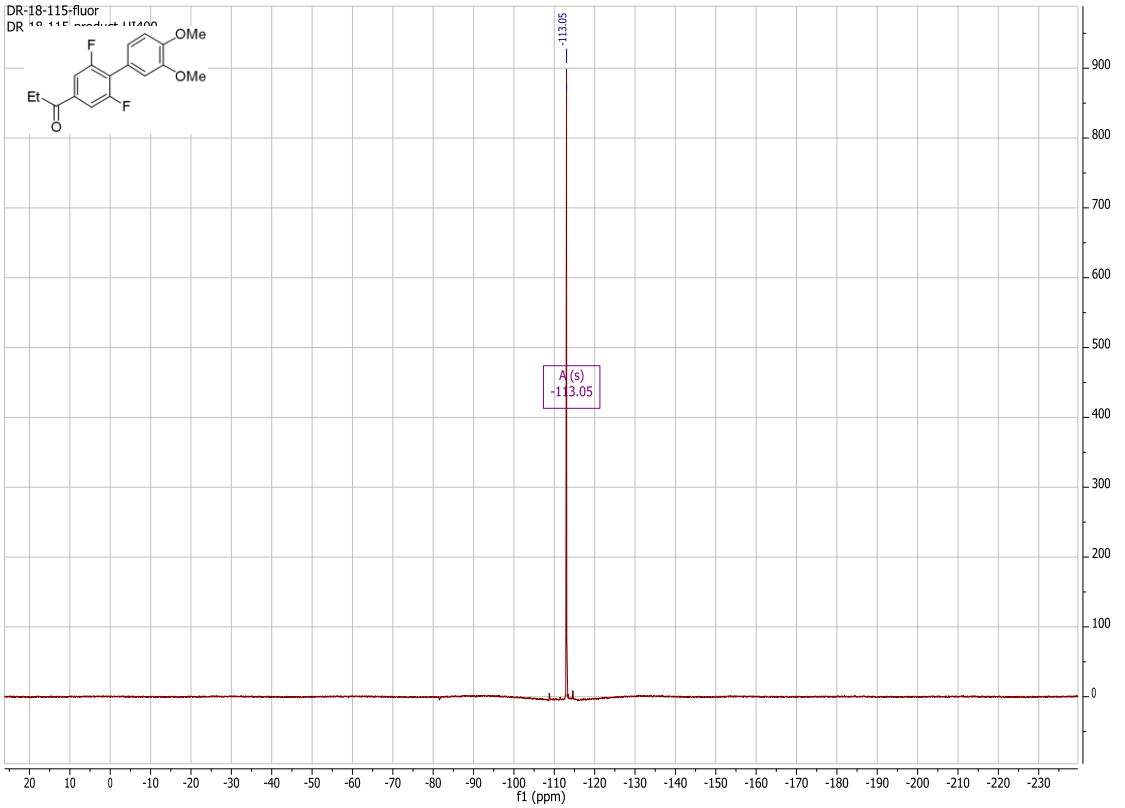

DR-17-189-proton
F
OMe
Et
F
O
E (m) 6.98
B (t) 7.39
A (d) 7.57
D (d) 7.02
C (m) 7.06
F (s) 3.83
G (q) 2.97
H (t) 1.24
f1 (ppm)

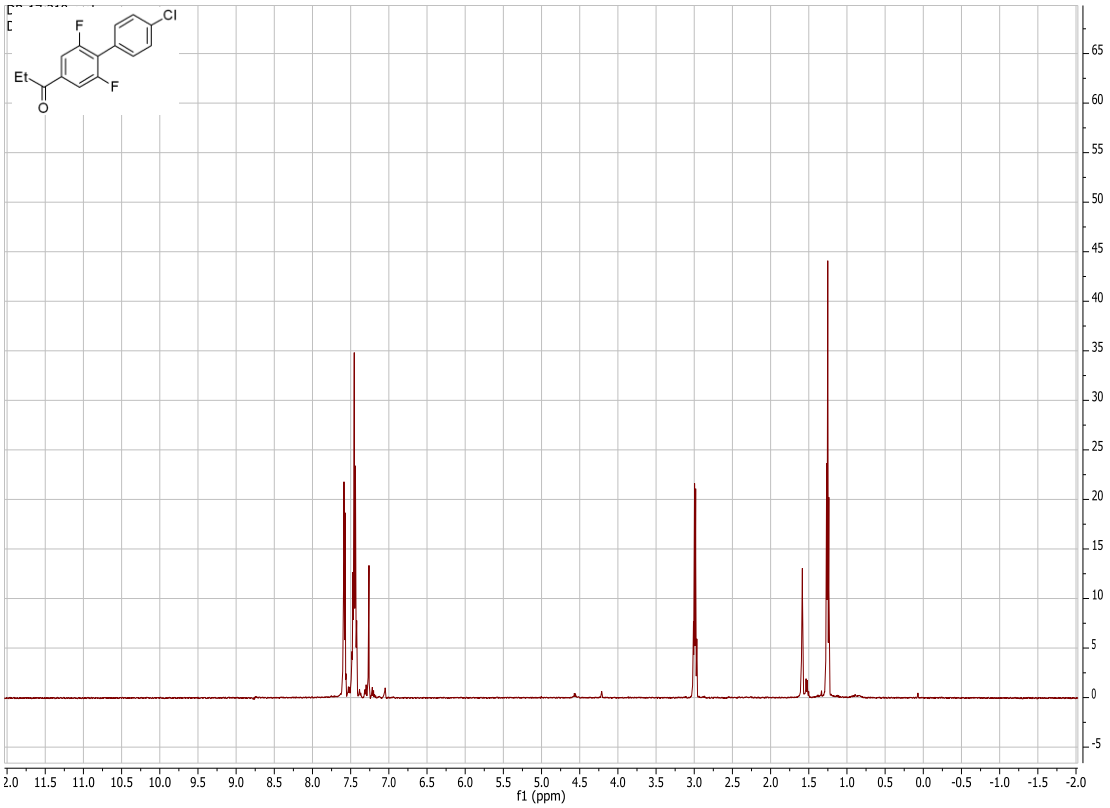

DR-17-189-carbon
F
OMe
Et
F
O
O (s) 123.05
J (m) 111.51
F (s) 129.63
H (s) 116.03
A (s) 198.07
C (s) 159.68
E (t) 137.80
G (s) 122.72
I (s) 114.67
P (s) 122.90
K (s) 55.51
L (s) 32.13
M (s) 8.23
f1 (ppm)

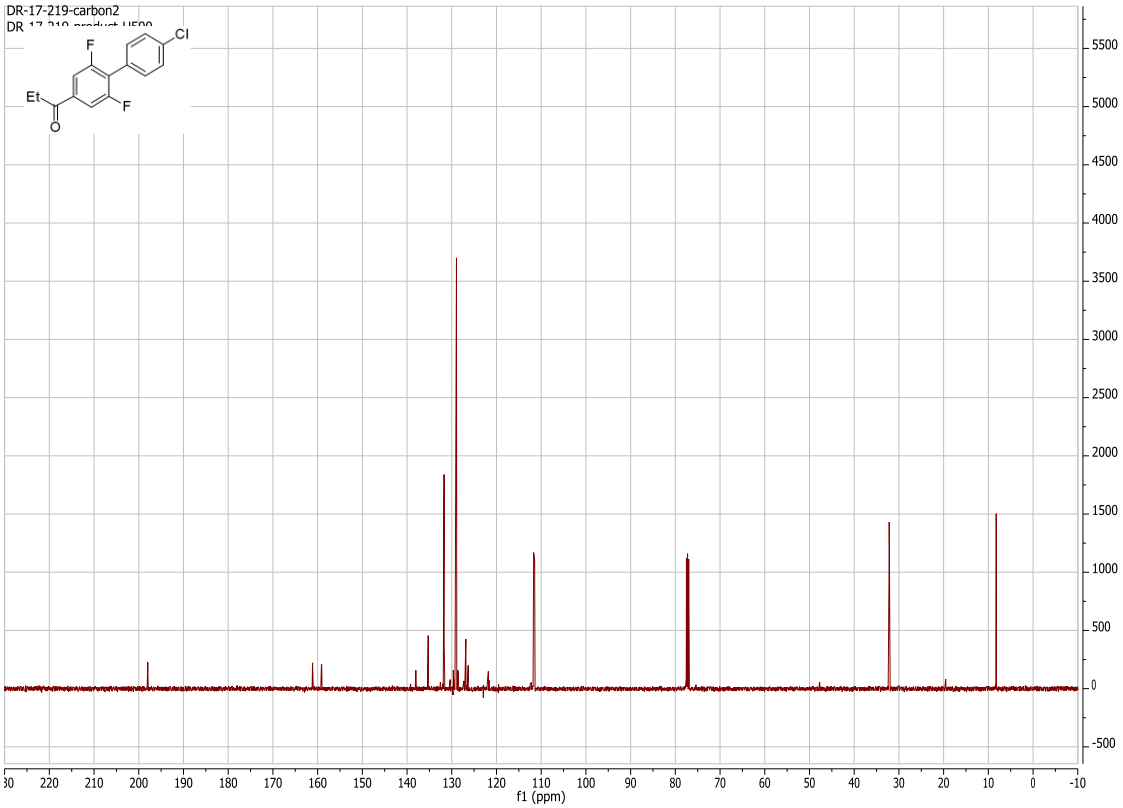

DR-17-189-fluor
F
OMe
Et
F
O
-112.67
A (s)
-112.67
f1 (ppm)

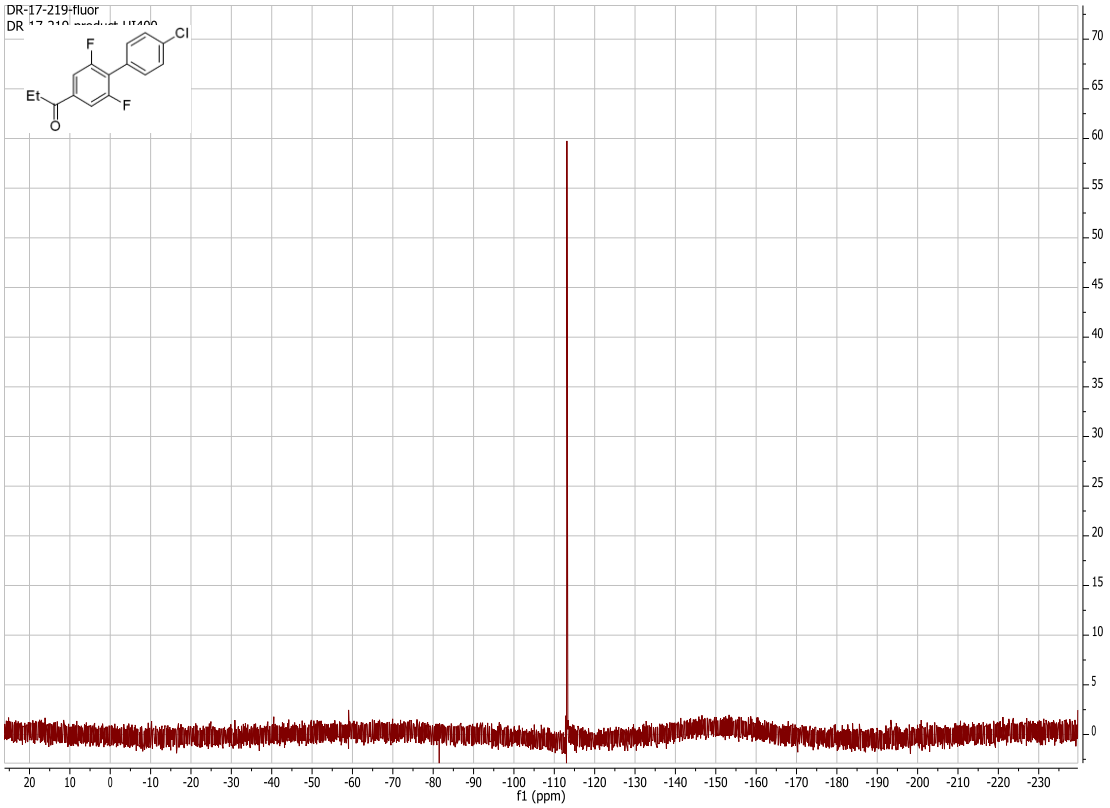

DR-18-114-proton
OMe
OMe
F
Et
F
O
7.54
7.53
7.06
7.04
6.99
6.96
6.94
3.91
3.88
2.96
2.94
2.93
1.23
1.22
1.20
D (d)
6.95
B (d)
7.05
A (d)
7.53
C (s)
6.99
H (s)
3.88
G (s)
3.91
E (m)
2.94
F (t)
1.22
f1 (ppm)

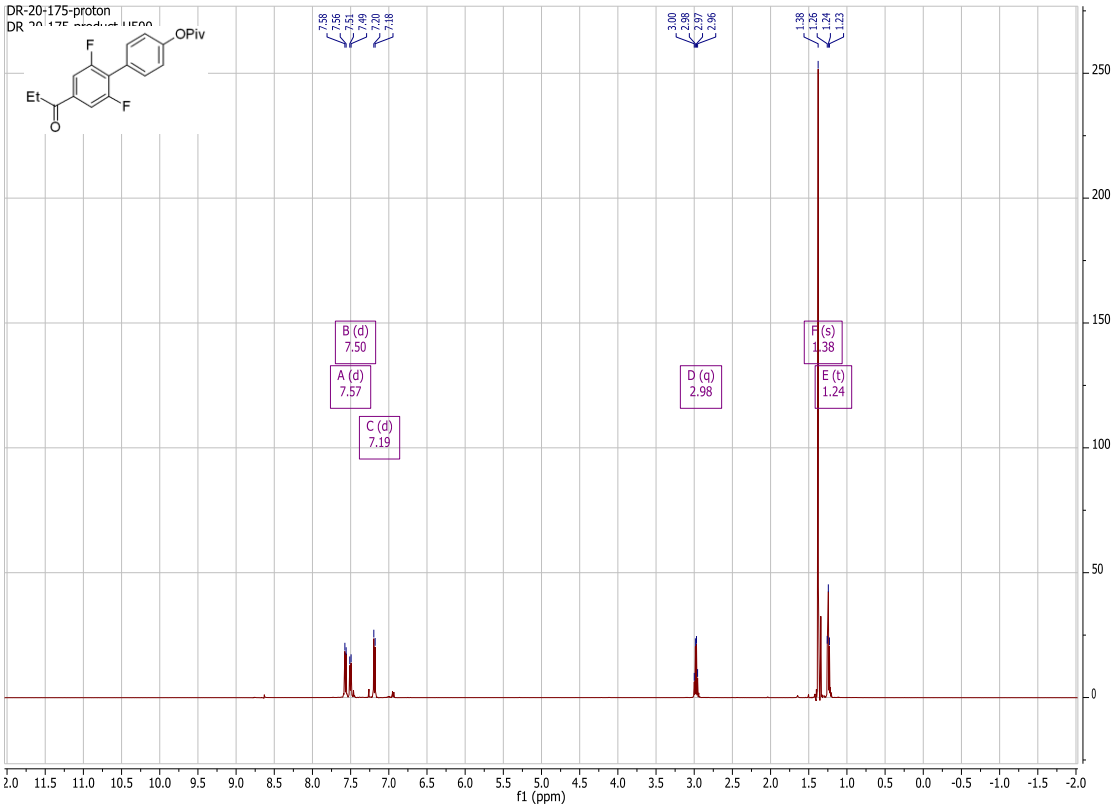

DR-18-114-carbon
OMe
OMe
F
F
Et
O
A (s)
198.03
R (dd)
160.22
S (s)
149.78
T (s)
148.97
F (t)
137.25
G (s)
123.31
H (t)
122.84
I (s)
120.70
K (m)
111.50
L (s)
111.21
J (s)
113.54
N (s)
56.08
M (s)
56.18
O (s)
32.06
P (s)
8.23
f1 (ppm)

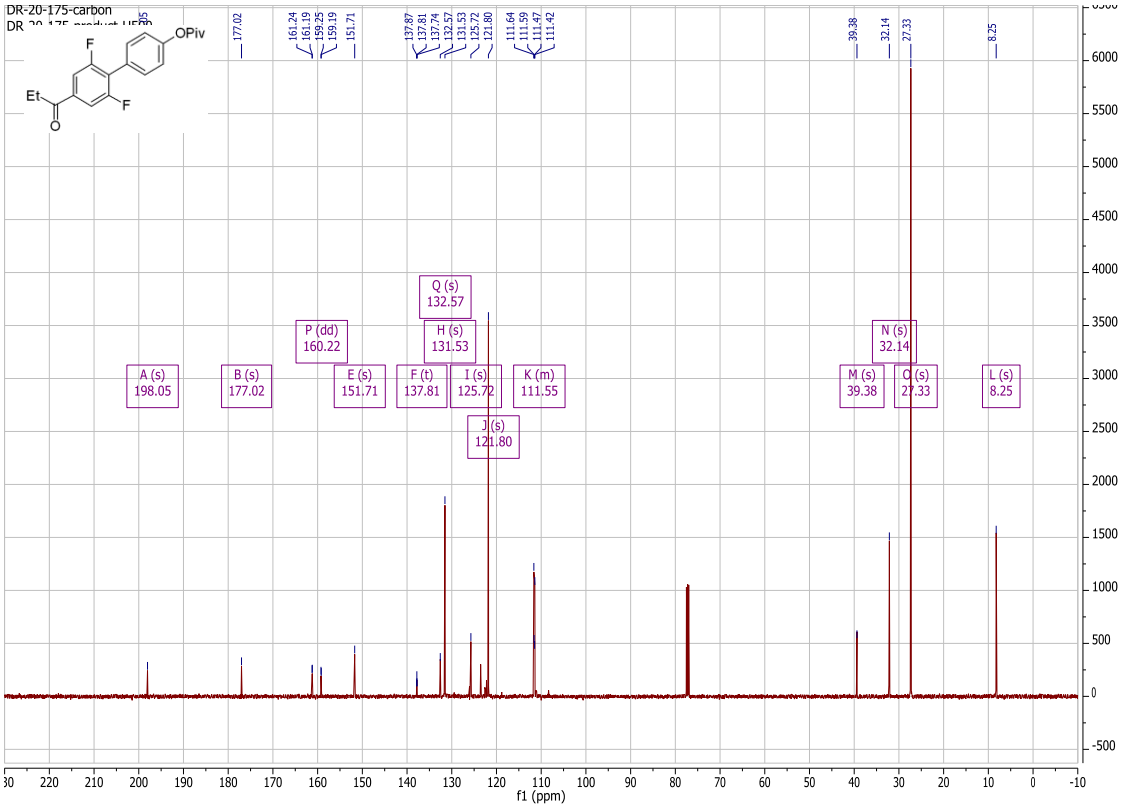

DR-18-115-fluor
OMe
OMe
F
F
Et
O
-113.05
A (s)
-113.05
f1 (ppm)

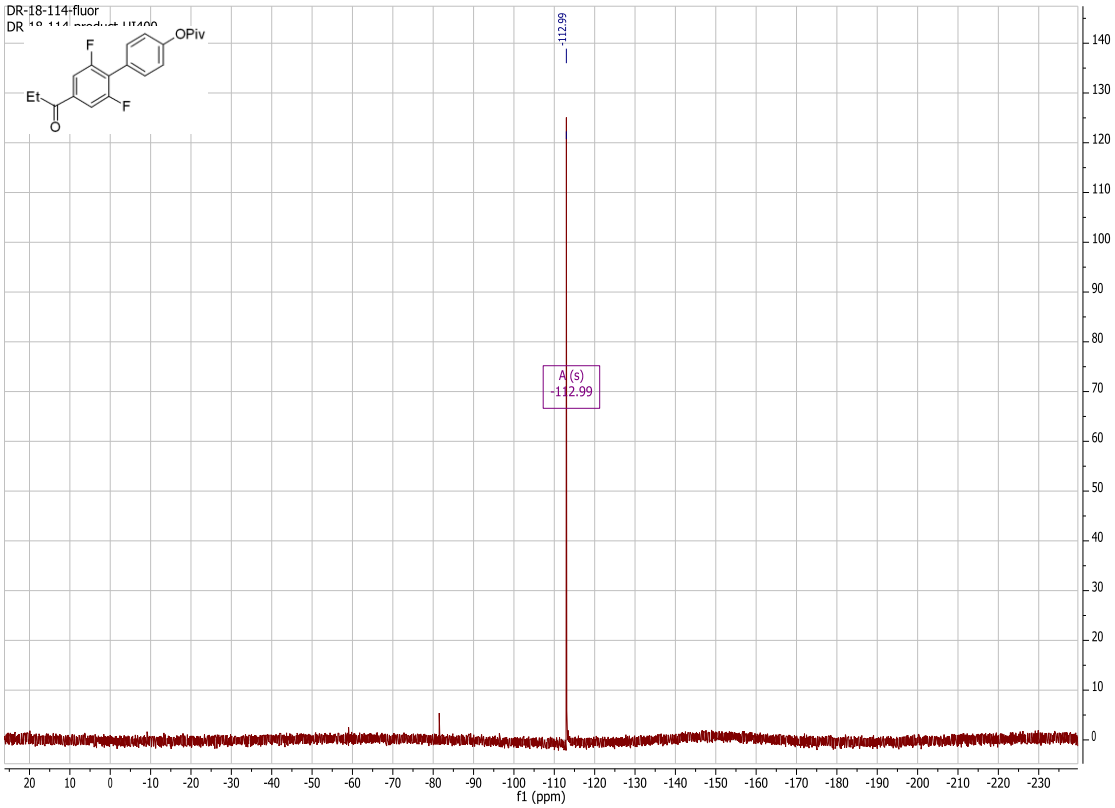

Cl
F
Et
F
O
f1 (ppm)

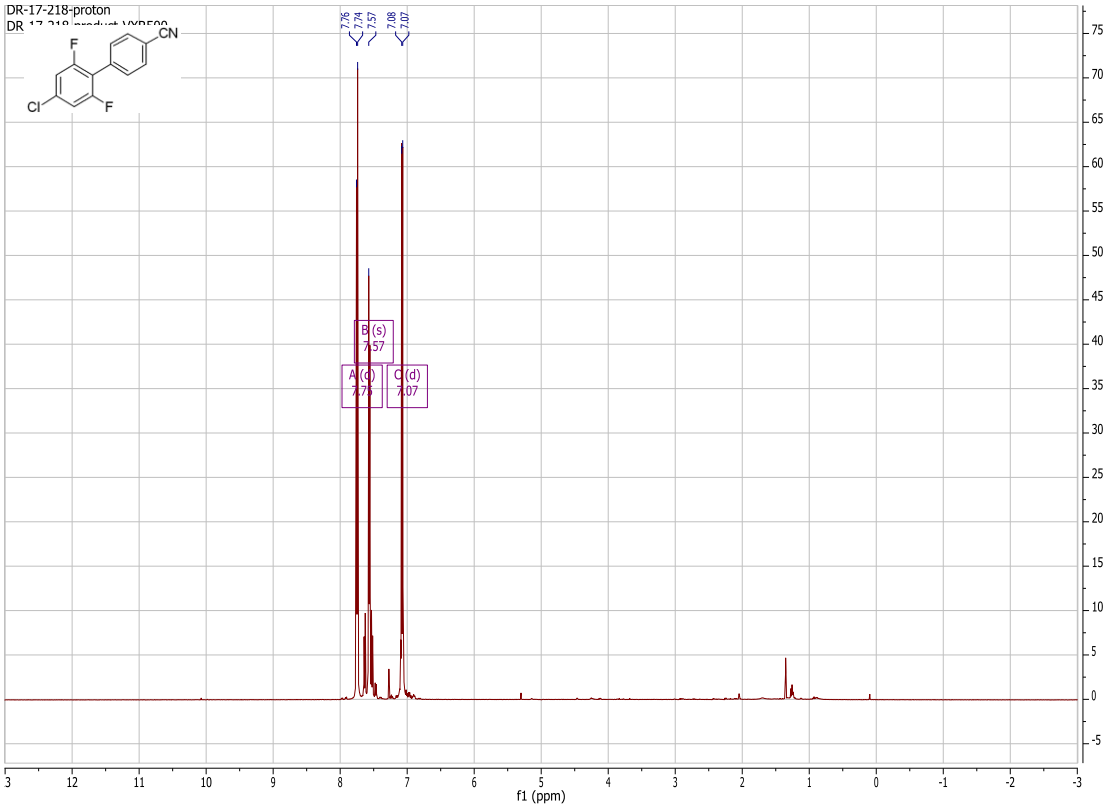

DR-17-219-carbon2
Cl
F
Et
F
O
f1 (ppm)

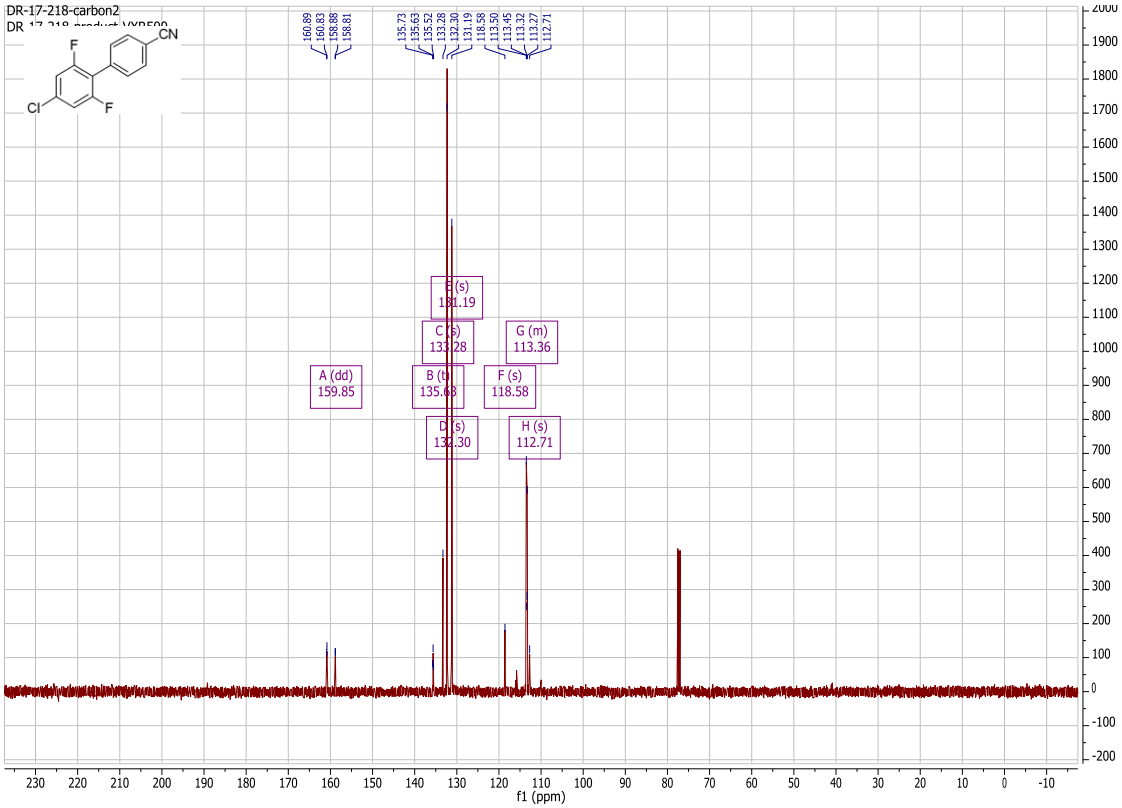

DR-17-219-fluor
Cl
F
Et
O
F
f1 (ppm)

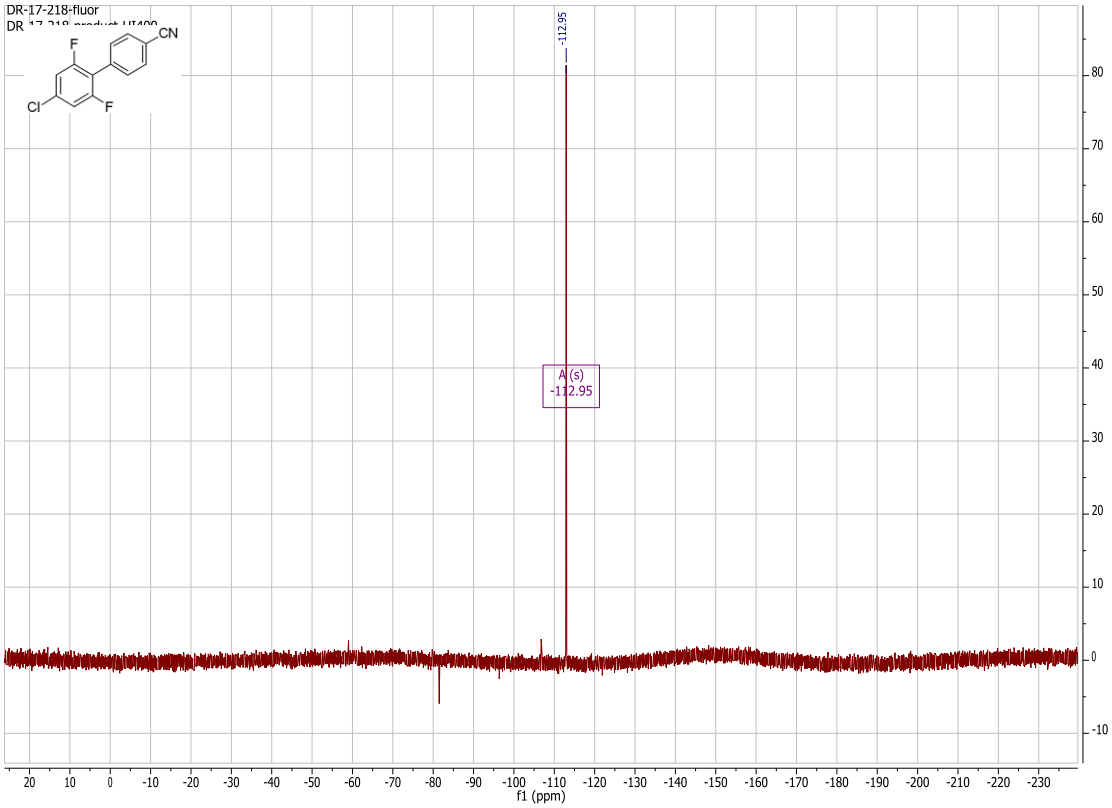

DR-20-175-proton
OPiv
F
Et
O
F
7.58
7.56
7.51
7.49
7.20
7.18
3.00
2.98
2.97
2.96
1.38
1.26
1.24
1.23
B (d)
7.50
A (d)
7.57
C (d)
7.19
D (q)
2.98
F (s)
1.38
E (t)
1.24
f1 (ppm)

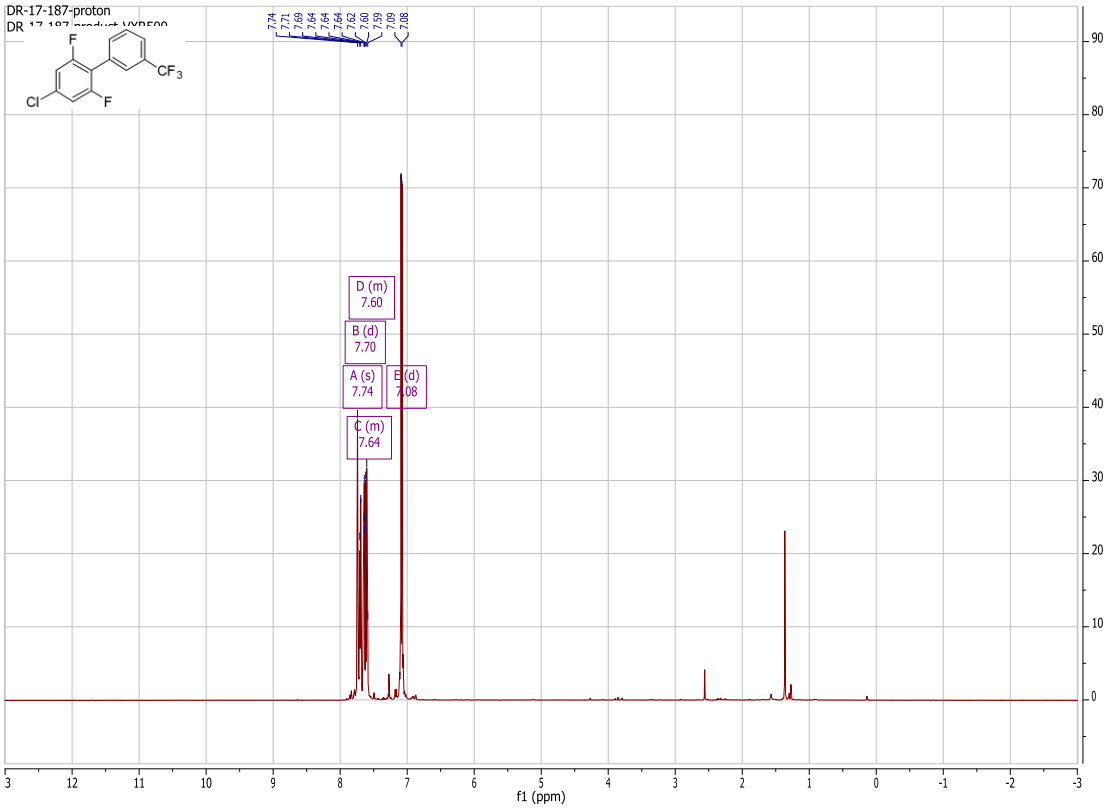

DR-20-175-carbon
OPiv
F
F
Et
O
177.02
161.24
161.19
159.25
159.19
151.71
137.87
137.81
137.74
132.57
131.53
125.72
121.80
111.64
111.59
111.47
111.42
39.38
32.14
27.33
8.25
A (s) 198.05
B (s) 177.02
P (dd) 160.22
E (s) 151.71
F (t) 137.81
Q (s) 132.57
H (s) 131.53
I (s) 125.72
J (s) 121.80
K (m) 111.55
M (s) 39.38
N (s) 32.14
O (s) 27.33
L (s) 8.25
f1 (ppm)

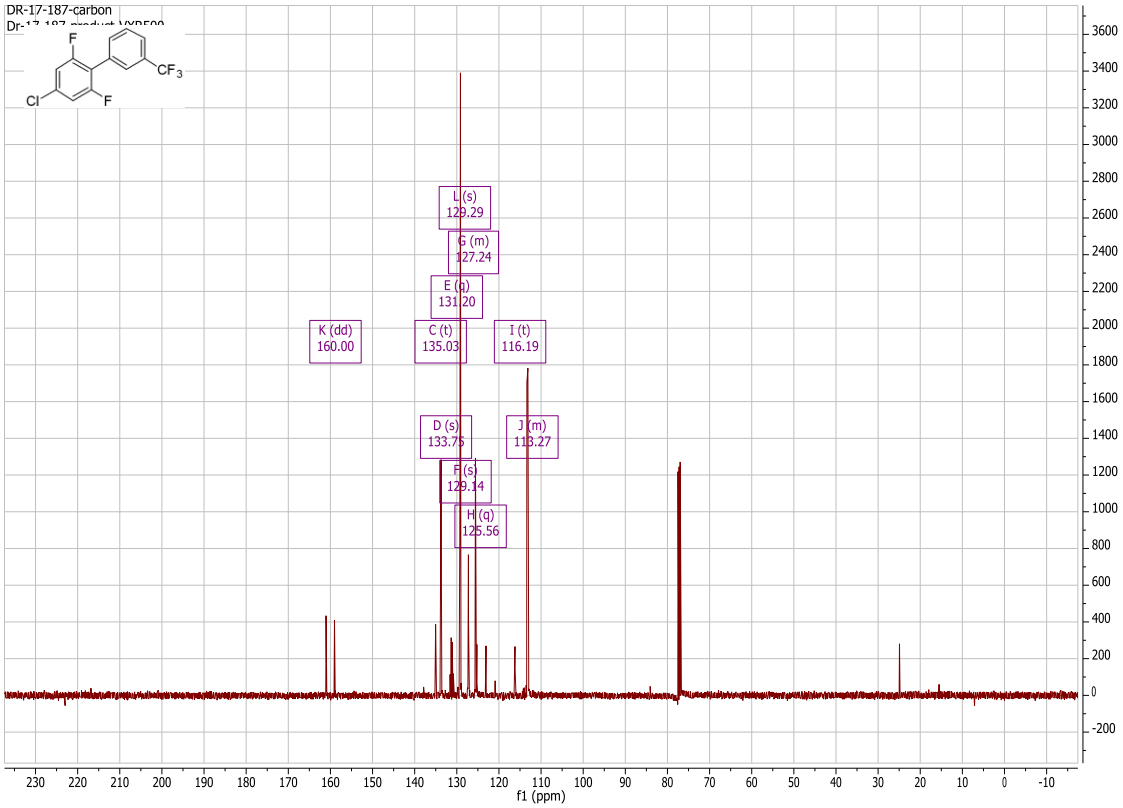

DR-18-114-fluor
OPiv
F
F
Et
O
-112.99
A (s) -112.99
f1 (ppm)

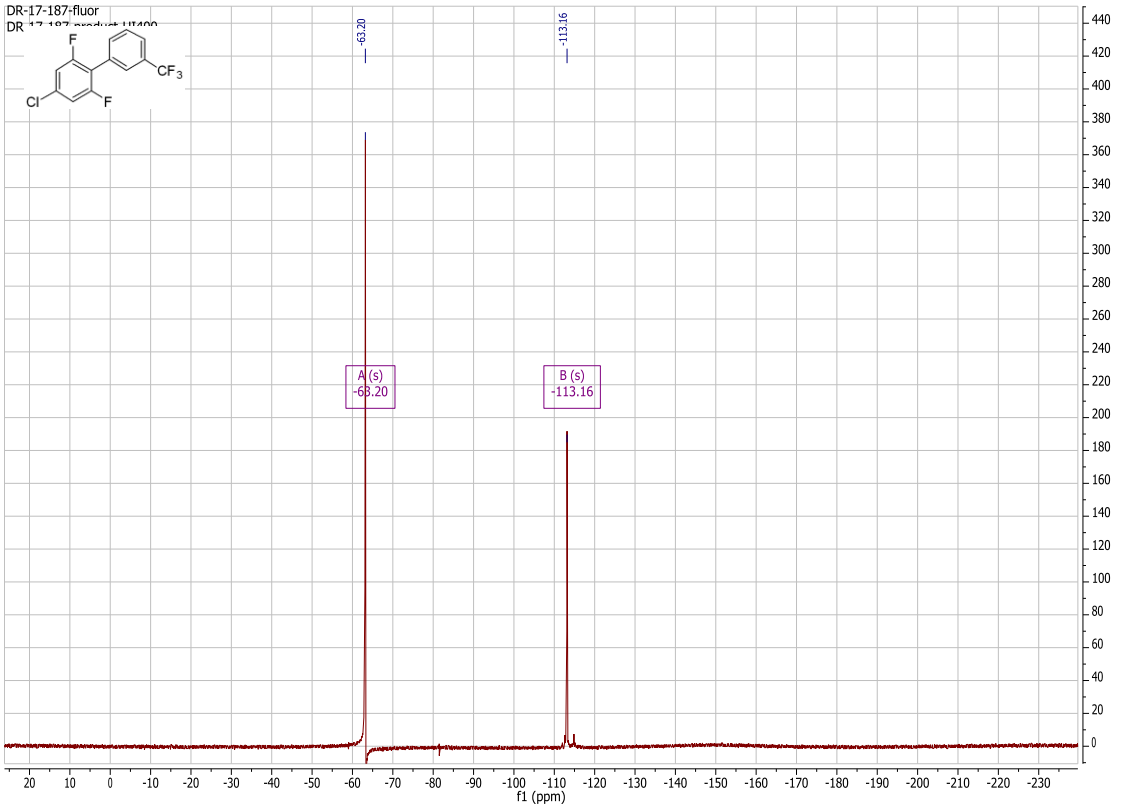

DR-17-218-proton
7.76
7.74
7.57
7.08
7.07
B (s)
7.57
A (Q)
7.75
C (d)
7.07
f1 (ppm)

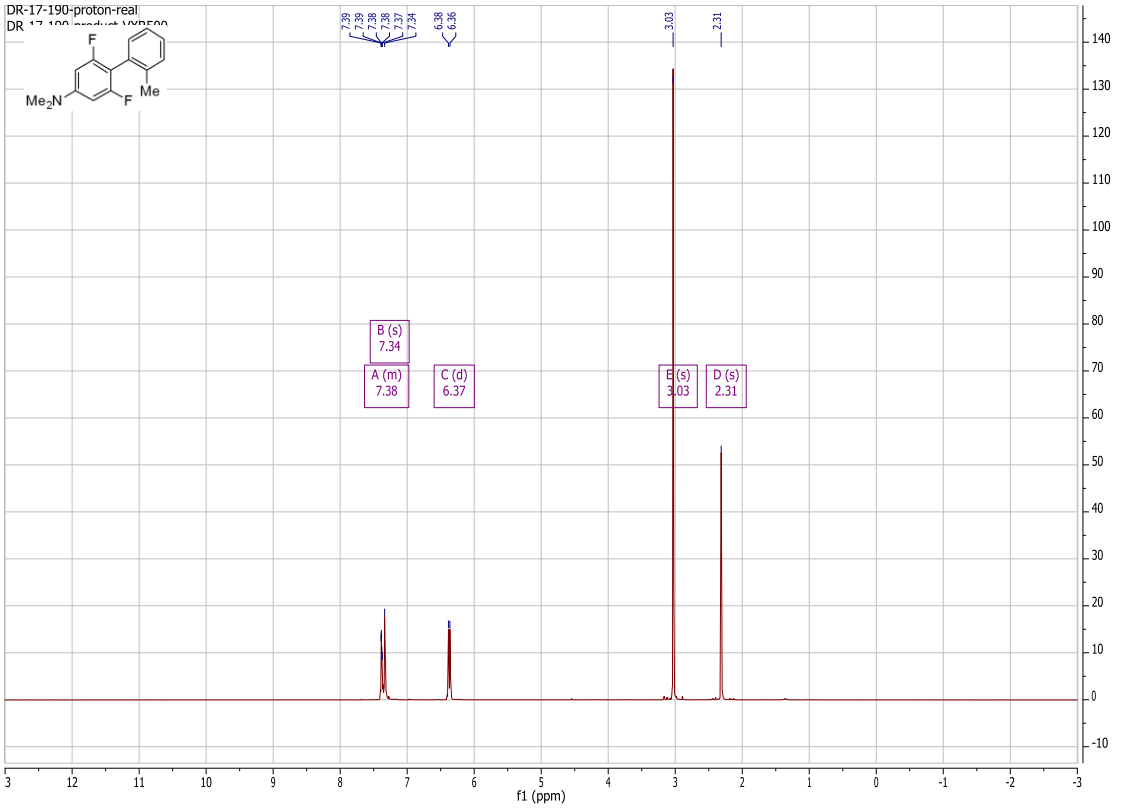

DR-17-218-carbon2
160.89
160.83
158.88
158.81
135.73
135.63
135.52
133.28
132.30
131.19
118.58
113.50
113.45
113.32
113.27
112.71
B (s)
131.19
C (s)
133.28
G (m)
113.36
A (dd)
159.85
B (t)
135.63
F (s)
118.58
D (s)
132.30
H (s)
112.71
f1 (ppm)

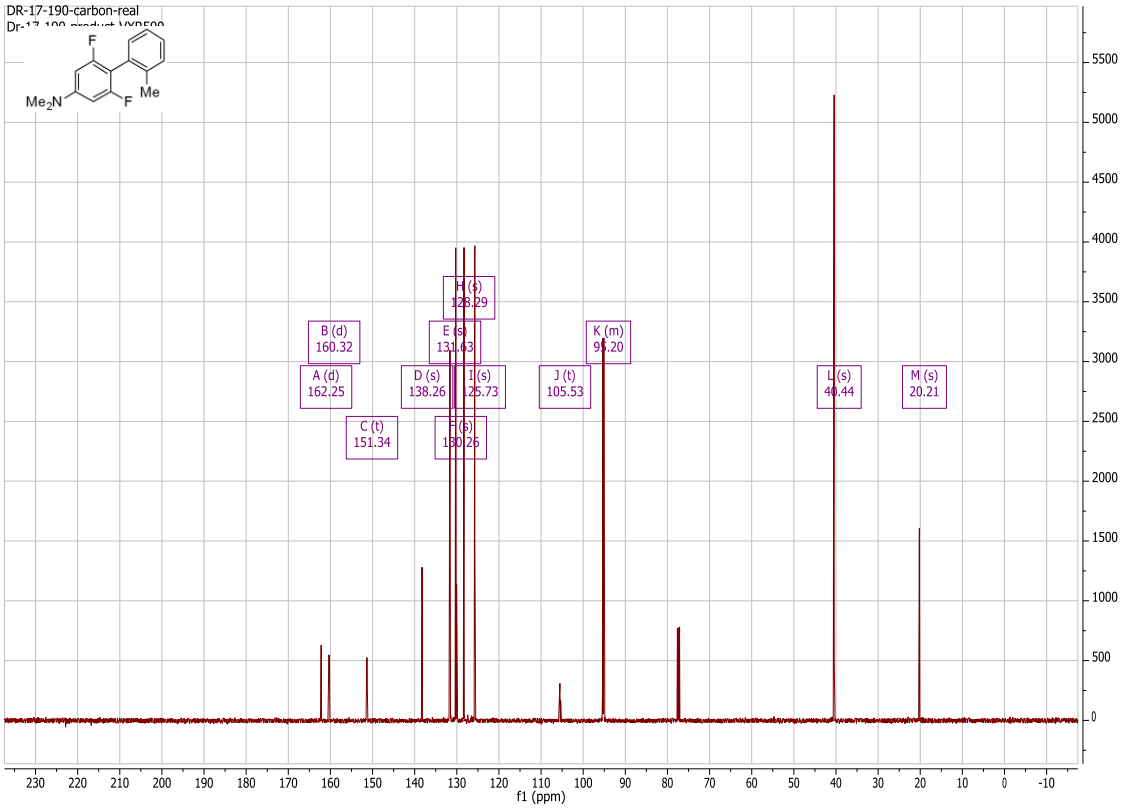

DR-17-218-fluor
F
CN
Cl
F
-112.95
A (s)
-112.95
f1 (ppm)

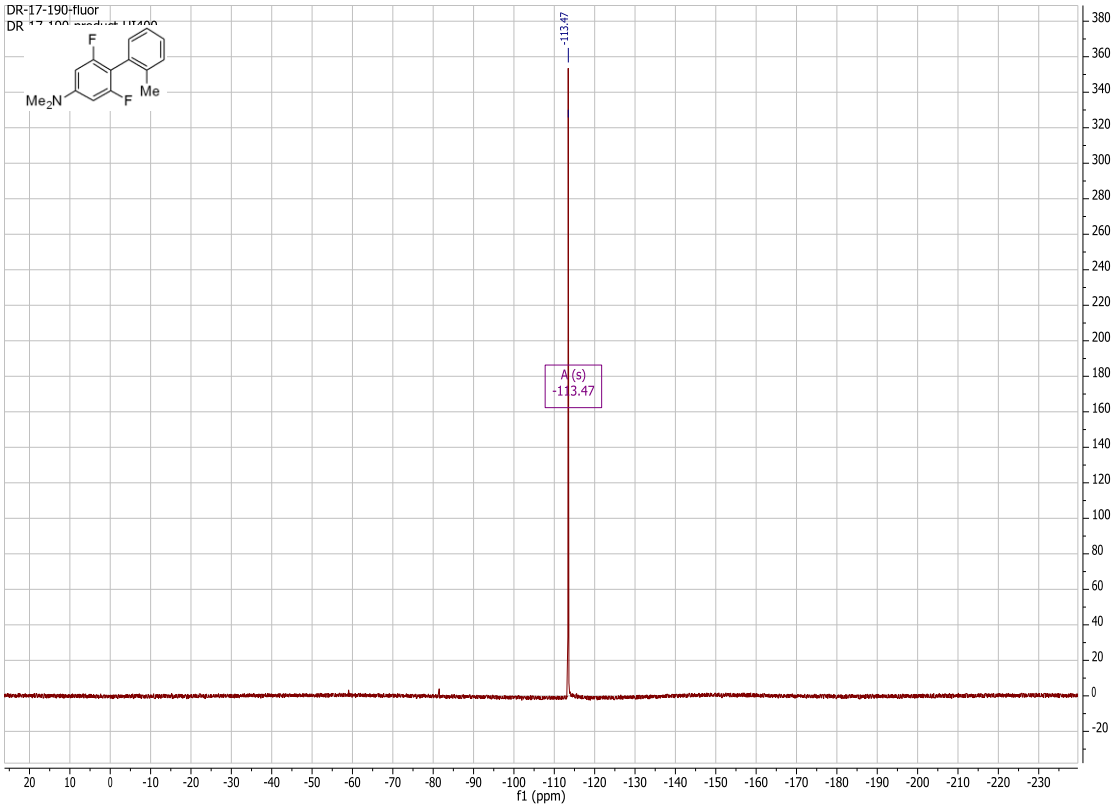

DR-17-187-proton
F
CF3
Cl
F
7.74
7.71
7.69
7.64
7.64
7.63
7.60
7.59
7.09
7.08
D (m)
7.60
B (d)
7.70
A (s)
7.74
E (d)
7.08
C (m)
7.64
f1 (ppm)

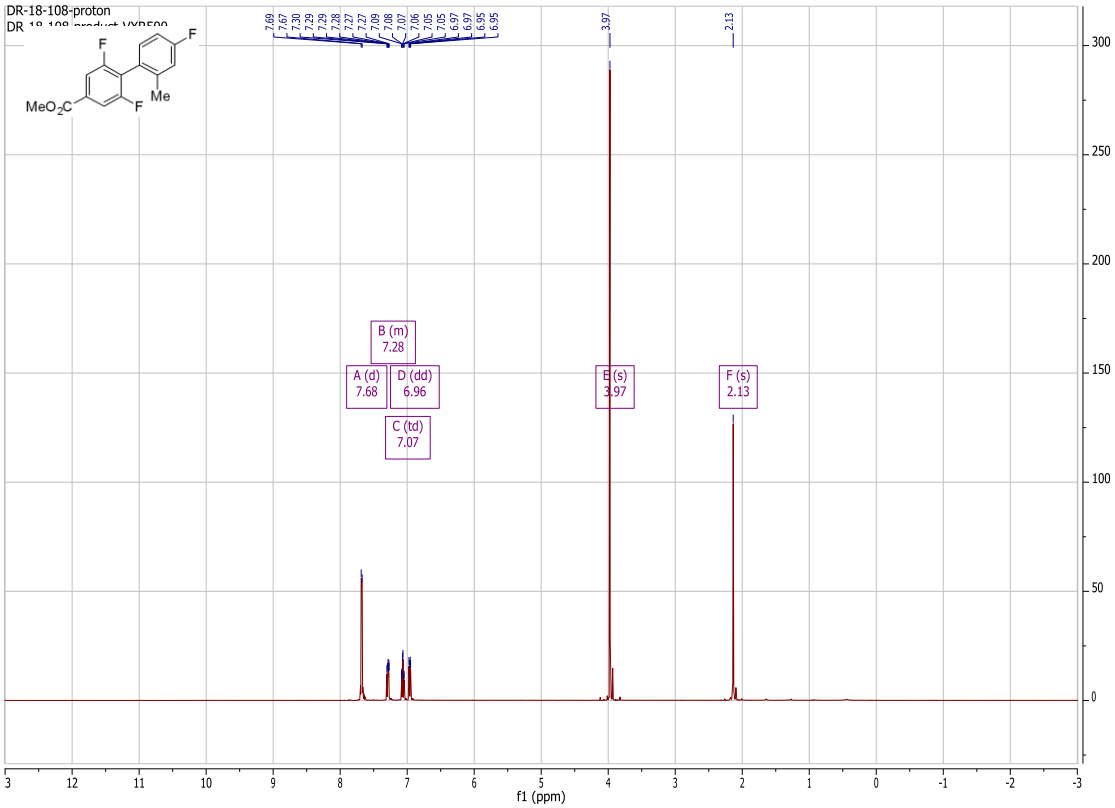

DR-17-187-carbon
L (s)
129.29
G (m)
127.24
E (q)
131.20
K (dd)
160.00
C (t)
135.03
I (t)
116.19
D (s)
133.75
J (m)
113.27
F (s)
129.14
H (q)
125.56
f1 (ppm)

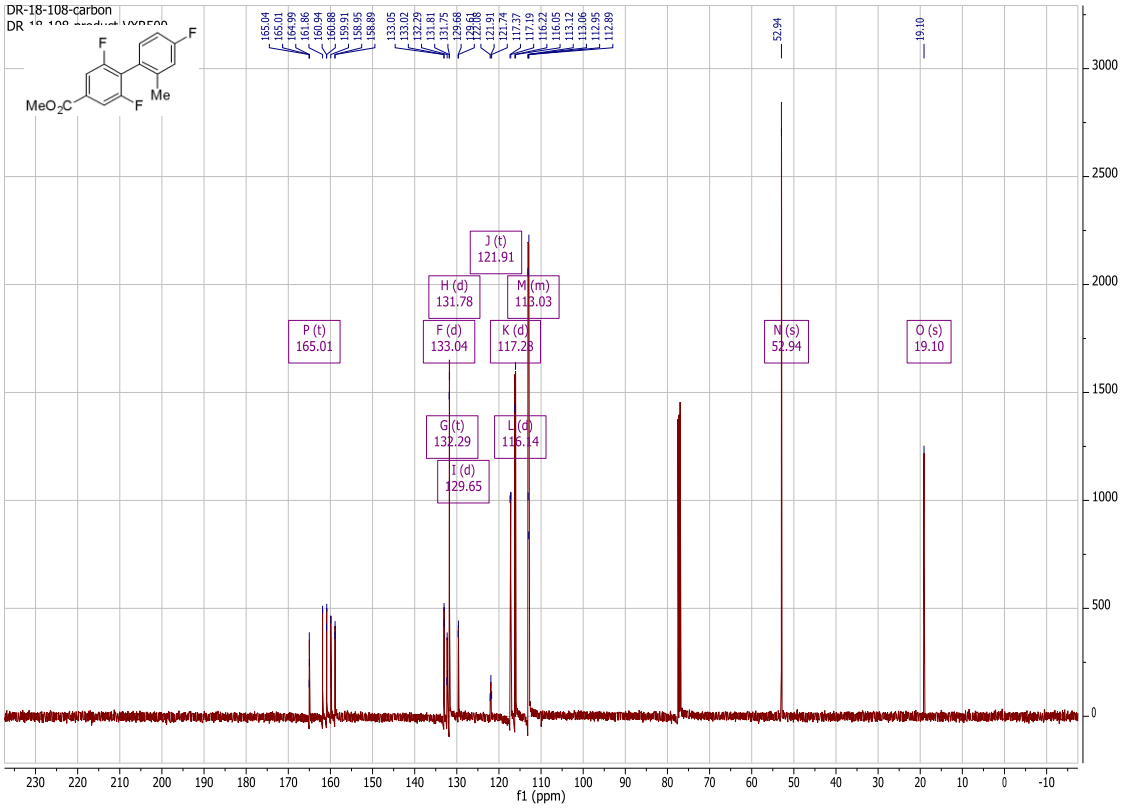

DR-17-187-fluor
-63.20
-113.16
A (s)
-63.20
B (s)
-113.16
f1 (ppm)

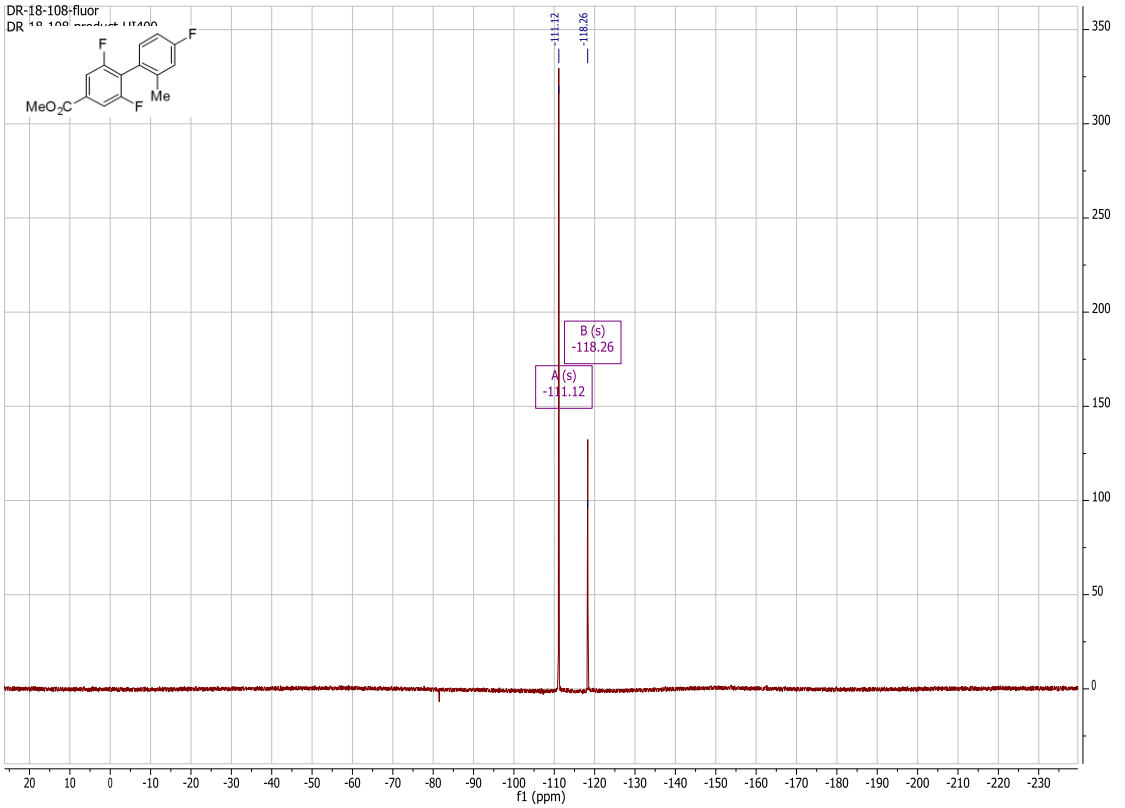

DR-17-190-proton-real
F
Me2N
F
Me
7.39
7.39
7.38
7.38
7.37
7.34
6.38
6.36
3.03
2.31
B (s)
7.34
A (m)
7.38
C (d)
6.37
E (s)
3.03
D (s)
2.31
f1 (ppm)

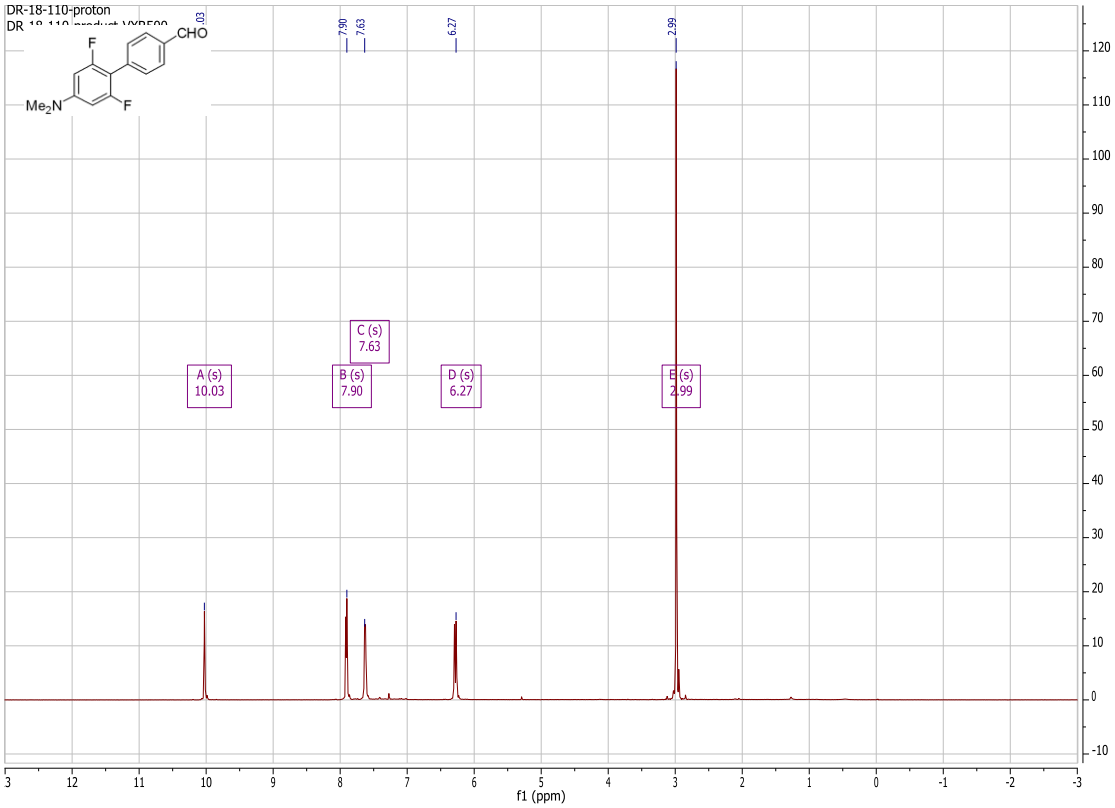

DR-17-190-carbon-real
F
Me2N
F
Me
H (s)
128.29
B (d)
160.32
E (s)
131.63
K (m)
99.20
A (d)
162.25
D (s)
138.26
I (s)
125.73
J (t)
105.53
L (s)
40.44
M (s)
20.21
C (t)
151.34
F (s)
130.26
f1 (ppm)

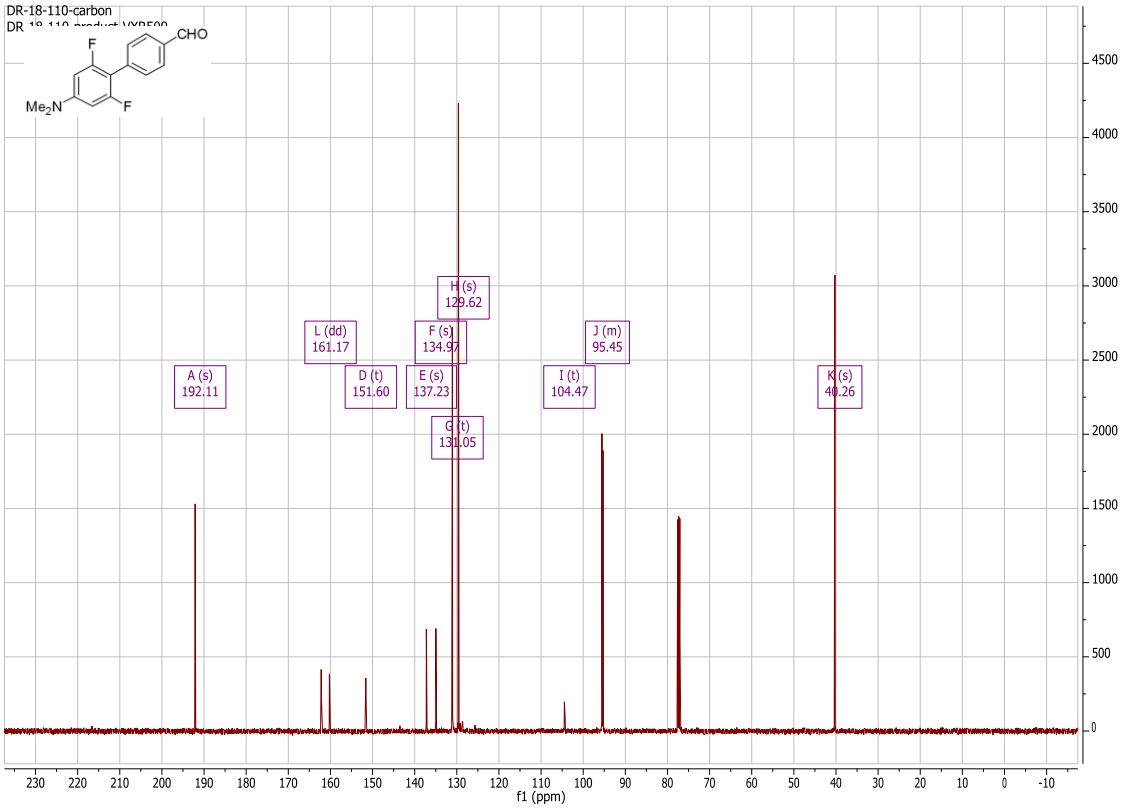

DR-17-190-fluor
F
Me
Me2N
F
-113.47
A (s)
-113.47
f1 (ppm)

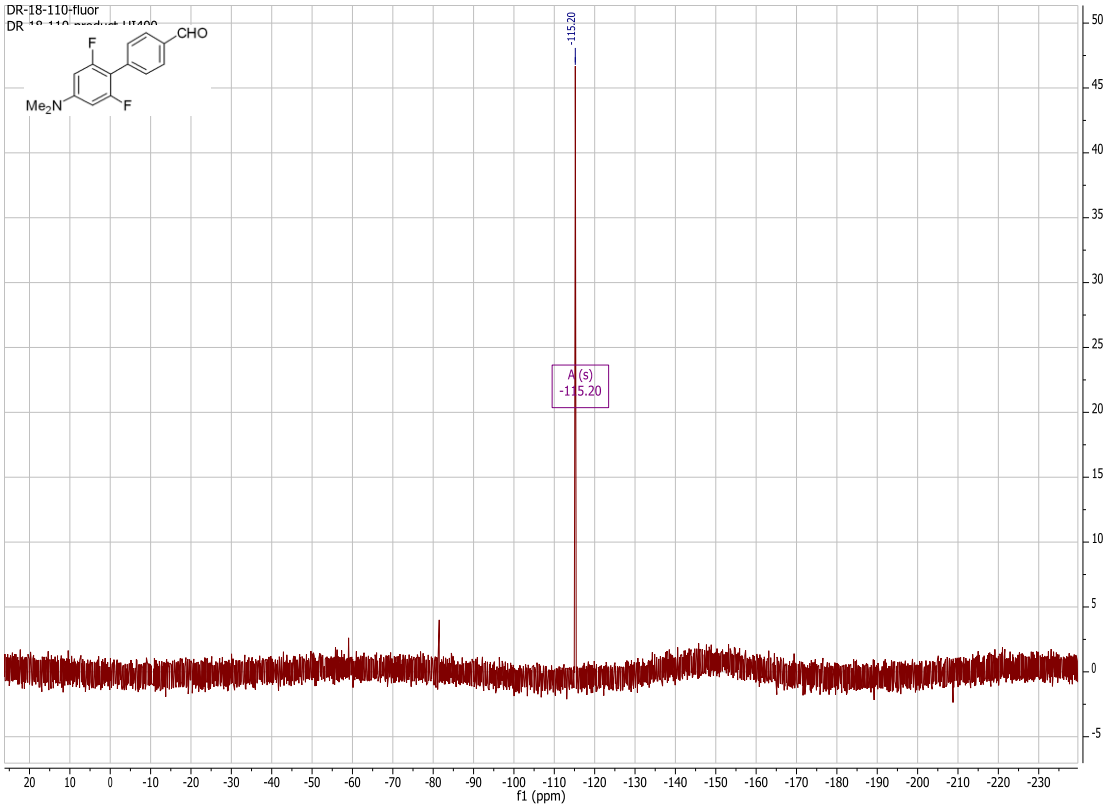

DR-18-108-proton
F
F
Me
MeO2C
F
7.69
7.67
7.30
7.29
7.28
7.27
7.27
7.09
7.08
7.07
7.06
7.05
7.05
6.97
6.97
6.95
6.95
3.97
2.13
B (m)
7.28
A (d)
7.68
D (dd)
6.96
C (td)
7.07
E (s)
3.97
F (s)
2.13
f1 (ppm)


DR-18-108-carbon
F
F
Me
MeO2C
F
165.04
165.01
164.99
161.86
160.94
160.88
159.91
158.95
158.89
133.05
133.02
132.29
131.81
131.75
129.68
121.91
121.74
117.37
117.19
116.22
116.05
113.12
113.06
112.95
112.89
52.94
19.10
J (t)
121.91
H (d)
131.78
M (m)
113.03
P (t)
165.01
F (d)
133.04
K (d)
117.28
N (s)
52.94
O (s)
19.10
G (t)
132.29
L (d)
116.14
I (d)
129.65
3000
2500
2000
1500
1000
500
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


DR-18-108-fluor
F
F
Me
MeO2C
F
-111.12
-118.26
B (s)
-118.26
A (s)
-111.12
350
300
250
200
150
100
50
0
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230
f1 (ppm)


DR-18-110-proton
CHO
F
Me2N
F
10.03
7.90
7.63
6.27
2.99
A (s)
10.03
B (s)
7.90
C (s)
7.63
D (s)
6.27
E (s)
2.99
f1 (ppm)


DR-18-110-carbon
CHO
F
Me2N
F
A (s)
192.11
L (dd)
161.17
D (t)
151.60
E (s)
137.23
H (s)
129.62
F (s)
134.97
G (t)
131.05
I (t)
104.47
J (m)
95.45
K (s)
40.26
f1 (ppm)


DR-18-110-fluor
CHO
F
Me2N
F
-115.20
A (s)
-115.20
f1 (ppm)