Supporting Information

Fluorination of 2-substituted benzo[*b*]furans with Selectfluor^{TM}

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Ⅰ. General Information

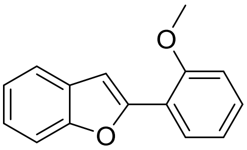
NMR spectra were obtained on a Bruker AV II-400 MHz spectrometer (^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz, and ^{19}F NMR at 376 MHz). The ^{1}H NMR chemical shifts were measured relative to $CDCl_3$ or DMSO-d_6 as the internal reference ($CDCl_3$: δ= 7.26 ppm; DMSO-d_6: δ= 2.50 ppm). The ^{13}C NMR chemical shifts were given using $CDCl_3$ or DMSO-d_6 as the internal standard ($CDCl_3$: δ= 77.16 ppm; DMSO-d_6: δ= 39.52 ppm). IR spectra were recorded on a Nicolet AVATER FTIR360 spectrometer as thin film. Absorptions were given in wave numbers (cm^{-1}). MS experiments were performed on an Agilent 5973N instrument for EI-MS and a Waters Micromass GCT Premier instrument for High-resolution mass. CH_3CN was distilled over CaH_2. Dichloromethane was distilled under argon over CaH_2. Unless otherwise noted, all reagent-grade chemicals and other solvents were obtained from commercial suppliers and were used as received. Starting materials **1a**[1]**, 1d-1f**[1]**, 1g**[2], **and 1h-1i**[1] are known compounds and were identified by comparison of their spectral data with those reported in the literature.

Ⅱ.Synthesis and characterization of the starting materials

General procedure for the synthesis of 2-substituted benzofurans by using modified procedure by Suzuki et al.[1]

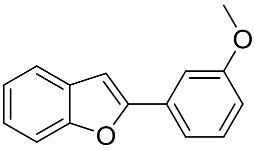
Benzo[*b*]furan-2-boronic acid (324.0 mg, 2.0 mmol), iodo-substituted derivatives (444.6 mg, 1.9 mmol), Pd $(OAc)_2$ (44.9 mg, 0.2 mmol) and Na_2CO_3 (423.2 mg, 4 mmol) were placed under Argon, and acetone (10 mL) and water (12 mL) were added. The reaction mixture was stirred at room temperature until full consumption of the starting material was indicated by TLC (c.a. 8 h). The reaction mixture was quenched with water and extracted with dichloromethane(3x10 mL).The combined organic layers were dried over anhydrous Na_2SO_4, filtrated and concentrated to dryness in vacuum. The crude compound was purified by flash chromatography (silica, pentane/EtOAc= 100:1 to 10:1) to afford 2-substituted benzo[*b*]furans.

2-(2-methoxyphenyl) benzofuran (1b)



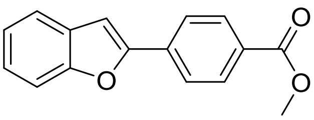
The general procedure was followed to afford the product **1b**[3] as white solid in 86% yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.09 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 8.4, 1H), 7.38 (s, 1H), 7.36-7.27 (m, 2H), 7.23 (t, *J* =7.6 Hz, 1H),7.10 (t, *J* = 7.6 Hz,1H), 7.02 (d, *J* = 8.4 Hz, 1H), 4.02 (s, 3H); ^{13}CNMR (100 MHz, CDCl$_3$): δ 156.46, 153.85, 152.13, 129.76, 129.22, 127.03, 124.07, 122.61, 121.01, 120.75, 119.34, 110.99, 110.80, 106.29, 55.44; EI: 152 (28), 181 (52), 209 (26), 224 (100).

2-(3-methoxyphenyl) benzofuran (1c)



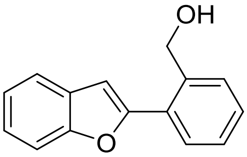
The general procedure was followed to afford the product **1c**[4] as white solid in 91% yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.60 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.49-7.43 (m, 2H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.33-7.28 (m, 1H), 7.27-7.23 (m,1H), 7.04 (s, 1H), 6.92 (dd, J_1 = 8.0 Hz, J_2 = 2.4 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 159.92, 155.72, 154.83, 131.74, 129.83, 129.15, 124.31, 122.93, 120.91, 117.50, 114.45, 111.16, 110.11, 101.61, 55.34; EI: 152 (28), 181 (32), 224 (100).

Methyl-4-(benzofuran-2-yl) benzoate (1j)



The general procedure was followed to afford the product **1j**[3] as white solid in 83% yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.12 (d, *J* = 8.4 Hz, 2H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.35-7.31 (m, 1H), 7.27-7.24 (m, 1H), 7.16 (s, 1H), 3.95 (s, 3H); ^{13}CNMR (100 MHz, CDCl$_3$): δ 166.66, 155.16, 154.64, 134.49, 130.12, 129.69, 128.90, 125.05, 124.61, 123.20, 121.27, 111.33, 103.43, 52.19; EI: 165 (32), 221 (63), 252 (100).

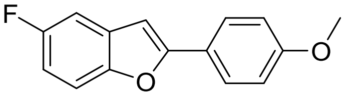
(2-(benzofuran-2-yl) phenyl) methanol (1p)



The general procedure was followed to afford the product **1p** as white solid in 81% yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.86-7.81 (m, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.59-7.56 (m, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.45-7.41 (m, 2H), 7.35-7.25 (m, 2H), 7.07 (s, 1H), 4.90 (s, 2H), 2.05 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 154.98, 154.78, 138.06, 129.54, 129.44, 129.06, 128.95, 128.68, 128.12, 124.50, 123.05, 121.15, 111.14, 105.35, 64.17; EI: 165 (41), 178 (32), 206 (89), 224 (100).

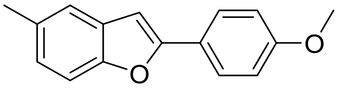
General procedure for the synthesis of 2-substituted benzofurans by using modified procedure by Miller et al.[5]

5-fluoro-2-(4-methoxyphenyl) benzofuran (1k)



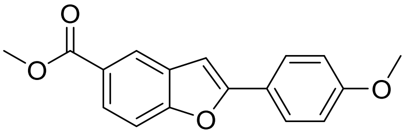
4-Fluoro-2-Iodophenol (900 mg, 3.8 mmol), 4-Methoxy-phenylacetylene (530 mg, 4.0 mmol), PdCl$_2$P (PH$_3$)$_2$ (70 mg), and CuI (50 mg) in DMF/Diethylamine (10 ml/10 ml) was heated to 60 ℃. After 1 h, the reaction was cooled and poured into water which was extracted with EtOAc. The organic layer was dried over MgSO$_4$, filtered and concentrated to give a solid which was triturated with MeOH and filtered, solid was the aim compound **1k**[5], yield: 63%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.80-7.76 (m, 2H), 7.41 (dd, J_1 = 8.8 Hz, J_2 = 4.0 Hz, 1H), 7.20 (dd, J_1 = 8.4 Hz, J_2 = 2.8 Hz, 1H), 7.00-6.93 (m, 3H), 6.84 (s, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 160.21, 159.31 (d, *J* = 236.1 Hz), 157.83, 150.89, 130.28 (d, *J* = 10.9 Hz), 126.50, 122.93, 114.27, 111.41 (t, *J* = 9.4 Hz), 111.05, 106.02 (d, *J* = 24.9 Hz), 99.78 (d, *J* = 3.6 Hz), 55.35; EI: 170 (26), 199 (42), 227 (65), 242 (100).

2-(4-methoxyphenyl)-5-methylbenzofuran (1l)



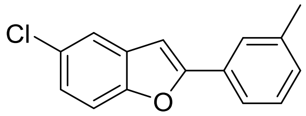
Compound **1l**[7] was synthesized following the procedure described for the preparation of 5-fluoro-2-(4-methoxyphenyl) benzofuran (1k) using 2-iodo-4-methylphenol, 1-ethynyl-3-methylbenzene was obtained as a white solid in 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 8.4 Hz, 1H), 7.34 (s, 1H), 7.07 (d, J = 8.4 Hz, 1H), 6.98 (d, J = 8.8 Hz, 2H), 6.82 (s, 1H), 3.86 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.86, 156.10, 153.11, 132.19, 129.56, 126.31, 124.95, 123.48, 120.42, 114.19, 110.44, 99.44, 55.34, 21.34; EI: 195 (27), 223 (77), 238 (100).

Methyl-2-(4-methoxyphenyl) benzofuran-5-carboxylate (1m)



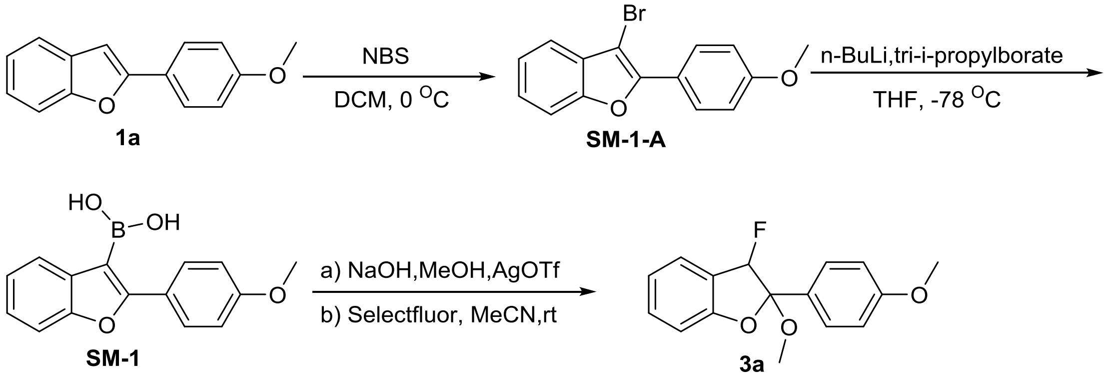
Compound **1m**[5] was synthesized following the procedure described for the preparation of 5-fluoro-2-(4-methoxyphenyl) benzofuran (1k) using methyl 4-hydroxy-3-iodobenzoate, 1-ethynyl-4-methoxybenzene was obtained as a white solid in 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, J = 1.6 Hz, 1H), 7.98 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 7.82-7.78 (m, 2H), 7.51 (d, J = 8.4 Hz, 1H), 7.01-6.97 (m, 2H), 6.93 (s, 1H), 3.95 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.36, 160.31, 157.50, 157.25, 129.52, 126.58, 125.57, 125.77, 122.90, 122.67, 114.32, 110.78, 99.82, 55.37, 52.08; EI: 165 (25), 252 (56), 282 (100).

5-chloro-2-(m-tolyl) benzofuran (1o)



Compound **1o**[6] was synthesized following the procedure described for the preparation of 5-fluoro-2-(4-methoxyphenyl) benzofuran (1k) using 4-chloro-2-iodophenol, 1-ethynyl-3-methylbenzene was obtained as a white solid in 58% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 2.0 Hz, 1H), 7.43 (d, *J* = 8.8 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.24-7.19 (m, 2H), 6.95 (s, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.58, 153.19, 138.54, 130.60, 129.85, 129.82, 128.75, 128.41, 125.63, 124.27, 122.24, 120.35, 112.05, 100.66, 21.48; EI: 172 (22), 242 (100), 244 (32).

Ⅲ. Synthesis 3a according Ritter's paper.[8]



3-bromo-2-(4-methoxyphenyl) benzofuran (**SM-1-A**)

To 3-bromo-2-(4-methoxyphenyl) benzofuran (672 mg, 3.00 mmol, 1.00 eq) in DCM (15 mL) at 0 °C was added N-Bromosuccinimide (NBS) (560 mg, 3.15 mmol, 1.05 eq). After stirring for 1.5 h at 0 °C, TLC (PE: EA=10: 1) show the reaction was completed. The solvent was removed and the residue was purified by chromatography on silica gel eluting with hexanes/EtOAc 50: 1 to 10: 1 (v/v) to afford 810 mg of the title compound as white solid (89% yield, mp: 65-68 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14-8.08 (m, 2H), 7.55-7.48 (m, 2H), 7.42-7.29 (m, 2H), 7.04-7.01 (m, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.17, 152.95, 150.47, 129.70, 128.31, 125.09, 123.35, 122.19, 119.56, 114.04, 111.09, 92.17, 55.36; MS (EI) m/z (%): 302 (M+, 100).

(2-(4-methoxyphenyl) benzofuran-3-yl) boronic acid (SM-1)

To a solution of 3-bromo-2-(4-methoxyphenyl) benzofuran (606 mg, 2.50 mmol, 1.0

eq) in THF (10 mL) at -78 °C was added a 1.6 M solution of n-butyllithium in hexane (1.72 mL, 2.75 mmol, 1.1 eq) and tri-i-propylborate (0.63 mL, 2.75 mmol, 1.1 eq), the reaction was stirred at -78 °C for 1 h, and then warmed to 25 °C for another 1 h. The reaction mixture was cooled to 0 °C and hydrolyzed with saturated aqueous ammonium chloride solution and 2 N HCl aqueous solution and stirred at 0 °C for 30 min. The aqueous layer was extracted with Et_2O (3 x 20 mL), and then the combined organic layers were extracted with 2N NaOH aqueous solution (3 x 10 mL). The combined aqueous layers were cooled to 0 °C and acidified with 2 N HCl aqueous solution to pH = 2. The precipitated boronic acid was collected by vacuum filtration, washed with cold water, and dried in vacuum to afford (2-(4-methoxyphenyl)benzofuran-3-yl)boronic acid (476 mg, 71 %, 90% purity) as a white-yellow solid (mp: 138-140 °C). ^{1}H NMR (400 MHz, d_6-DMSO): δ 7.88-7.86 (m, 2H), 7.63-7.54 (m, 2H), 7.28-7.19 (m, 2H), 7.08-7.05 (m, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO): δ 159.68, 157.73, 153.75, 132.97, 128.03, 123.90, 123.84, 122.60, 122.21, 114.22, 114.17, 110.40, 55.31; HRMS(EI): calcd. for [$C_{15}H_{13}BO_4$] 268.0907, found:268.0910.

3-fluoro-2-methoxy-2-(4-methoxyphenyl)-2, 3-dihydrobenzofuran (3a)

To NaOH (60 mg, 1.5 mmol, 1.5 eq) in MeOH (2 mL) at 23 ℃ was added (2-(4-methoxyphenyl) benzofuran-3-yl) boronic acid (268 mg, 1.0 mmol, 1.0 equiv). After stirring for 30 min at 23 ℃, the reaction mixture was cooled to 0 ℃ and to the reaction mixture was added AgOTf (514 mg, 2.0 mmol, 2.0 equiv). After stirring for 30 min at 0 ℃, the solvent was removed under reduced pressure at RT. To the residue was added MeCN (5 mL) and Selectfluor (372 mg, 1.1 mmol, 1.1 equiv) and the reaction mixture was stirred for 3 h. The solvent was removed under reduced pressure, EA (15mL) was added and washed with water, brine, dried (Na_2SO_4), the solvent was removed under reduced pressure and residue was purified by chromatography on silica gel eluting with hexanes/EtOAc 50: 1 to 10: 1 (v/v) to afford 53 mg of the title compound as clear oil which solidified upon cooling to white solid (19% yield, dr: 98: 2, mp: 87~89 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.55 (m, 2H), 7.52 (d, *J* =7.6

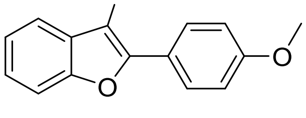
Hz, 1H), 7.45-7.40 (m, 1H), 7.09-7.04 (m, 2H), 7.01-6.98 (m, 2H), 5.62 (d, *J* =56.8 Hz, 1H), 3.86 (s, 3H), 3.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.23, 160.07 (d, *J* = 5.1 Hz), 132.06 (d, *J* = 4.2 Hz), 128.99 (d, *J* =1.3 Hz), 127.21 (d, *J* = 1.7Hz), 125.65 (d, *J* = 2 .5 Hz), 124.11 (d, *J* = 18.7 Hz), 121.87 (d, *J* = 3.3 Hz), 113.70, 113.21 (d, *J* = 27.2 Hz), 111.24 (d, *J* = 3.1 Hz), 95.00 (d, *J* = 186.4 Hz), 55.22, 50.77; ^{19}F NMR (376 MHz, $CDCl_3$): δ -166.47 (d, *J* = 56.78 Hz); IR: (KBr) ν_{max} 2931, 1618,1521, 1478, 1260, 1050, 834, 751 cm^{-1}; HRMS(EI): calcd. for [$C_{16}H_{15}FO_3$] 274.1005, found: 274.1006.

Ⅳ. Synthesis and characterization of 2a-2o

General procedure for the synthesis of 3-fluorination 2-substituted benzofurans.

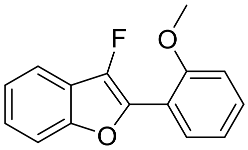
To the solution of 2-substituted benzofurans (0.5 mmol) in MeCN (8.0 mL) was added Selectfluor (195 mg, 1.1 eq) at room temperature (about 25 ^{o}C), then water (0.4 mL) was added , then the formed mixture was stirred at room temperature under air for 1h as monitored by TLC (PE: EA=10: 1), once the reaction was completed, EA (30 mL) was added, and washed with water, brine and dried (Na_2SO_4),the solvent was removed under reduce vacuum and the residue was used in the next step directly. The residue was dissolve in dry DCM (5 mL) and pyridine (0.41 mL, 5 mmol, 10 eq) was added dropwise at 0 ^{o}C, then $SOCl_2$ (0.055 mL) was added dropwise at that temperature, then the reaction was stirred at room temperature overnight as monitored by TLC, once the reaction was completed, DCM (10 mL) was added, washed with water, brine and dried (Na_2SO_4), The solvent was removed under reduce vacuum to give crude product. The crude product was purified by column chromatography on silica gel (PE: EA=100: 1 to 10: 1) to afford pure aim product.

3-fluoro-2-(4-methoxyphenyl) benzofuran (2a)



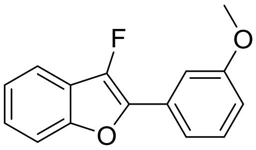
The general procedure was followed to afford the product as white-off solid in 75% yield (mp: 61-63 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.83 (m, 2H), 7.58 (dd, J_1 = 7.2 Hz, J_2 = 2.0 Hz, 1H), 7.46-7.43 (m, 1H), 7.31-7.26 (m, 2H), 7.04-7.00 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.55 (d, *J* =1.9 Hz), 150.87 (d, *J* = 9.4 Hz), 143.49 (d, *J* = 253.3 Hz), 138.33 (d, *J* = 20.6 Hz), 126.30 (d, *J* = 5.8 Hz), 124.81, 123.11, 121.50 (d, *J* = 5.3 Hz), 120.88, 117.26 (d, *J* = 7.4 Hz), 114.33, 111.60, 55.34; ^{19}F NMR (376 MHz, $CDCl_3$): δ -172.87 (d, *J* = 5.64 Hz); IR: (KBr) ν_{max} 2961, 1608, 1450, 1310, 1258, 1028, 752 cm^{-1}; HRMS(EI): calcd. for [$C_{15}H_{11}FO_2$] 242.0743, found: 242.0744.

3-fluoro-2-(2-methoxyphenyl) benzofuran (2b)



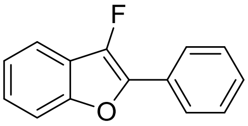
The general procedure was followed to afford the product as colorless oil in 71% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70-7.68 (m, 1H), 7.63 (d, *J* = 7.2 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.44-7.39 (m, 1H), 7.36-7.28 (m, 2H), 7.10 (t, *J* = 7.2 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.75, 151.75 (d, *J* = 8.8 Hz), 144.22 (d, *J* = 255.1 Hz), 136.29 (d, *J* = 24.1 Hz), 130.44, 129.45 (d, *J* = 2.3 Hz), 124.99, 122.88, 120.69 (d, *J* = 20.1 Hz), 120.68, 117.76 (d, *J* = 4.4 Hz), 117.68 (d, *J* = 3.0 Hz), 111.74, 111.57, 55.81; ^{19}F NMR (376 MHz, CDCl3) δ -166.06; IR: (KBr) ν_{max} 2971, 1599, 1495, 1392, 1258, 1026, 744 cm^{-1}; HRMS (EI): calcd. for [$C_{15}H_{11}FO_2$] 242.0743, found: 242.0741.

3-fluoro-2-(3-methoxyphenyl) benzofuran (2c)



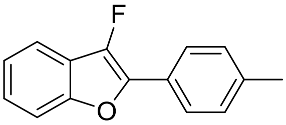
The general procedure was followed to afford the product as white solid in 62% yield (mp: 59-61 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 7.2 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.49-7.45 (m, 2H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.37-7.27 (m, 2H), 6.93-6.90 (m, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.90, 151.11 (d, *J* = 9.3 Hz), 144.74 (d, *J* = 256.2 Hz), 137.98 (d, *J* = 20.0 Hz), 129.90, 129.84, 125.47, 123.23, 120.63 (d, *J* = 19.3 Hz), 117.66, 117.37 (d, *J* = 6.2 Hz), 114.27, 111.80, 109.79, 55.34; ^{19}F NMR (376 MHz, $CDCl_3$): δ -169.48 (d, *J* = 1.88 Hz); IR: (KBr) ν_{max}3066, 1643, 1456, 1345, 1291, 1048, 750 cm^{-1}; HRMS (EI): calcd. for [$C_{15}H_{11}FO_2$] 242.0743, found: 242.0748.

3-fluoro-2-phenylbenzofuran (2d)



The general procedure was followed to afford the product as white solid in 70% yield (mp: 47-49 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 7.2 Hz, 2H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.51-7.47 (m, 3H), 7.38-7.28 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.15 (d, *J* = 9.3 Hz), 144.62 (d, *J* = 255.8 Hz), 138.11 (d, *J* = 10.2 Hz), 128.79, 128.69 (d, *J* = 5.3 Hz), 128.16 (d, *J* = 1.7 Hz), 125.39, 124.75 (d, *J* = 5.7 Hz), 123.21, 120.66 (d, *J* = 19.3 Hz), 117.63 (d, *J* = 2.1 Hz), 111.77; ^{19}F NMR (376 MHz, $CDCl_3$): δ -170.17 (d, *J* =1.88 Hz); IR: (KBr) ν_{max} 2950, 1632, 1449, 1312, 1257, 1073, 744 cm^{-1}; HRMS (EI): calcd. for [$C_{14}H_9FO$] 212.0637, found 212.0633.

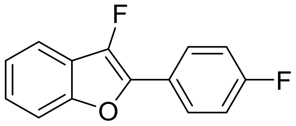
3-fluoro-2-(p-tolyl)benzofuran (2e)



The general procedure was followed to afford the product as white solid in 69% yield (mp: 61-63 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.60-7.59 (m, 1H), 7.47-7.45 (m, 1H), 7.35-7.26 (m, 4H), 2,42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.98 (d, *J* = 9.4 Hz), 144.12 (d, *J* = 254.6 Hz), 138.39 (d, *J* = 20.4 Hz), 138.21, 129.49, 125.90 (d, *J* = 5.3 Hz), 125.09, 124.69 (d, *J* = 5.6 Hz), 123.12, 120.77 (d, *J* = 22.3 Hz), 117.44, 111.70, 21.42; ^{19}F NMR (376 MHz,

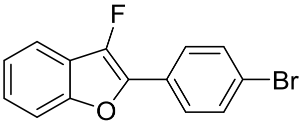
$CDCl_3$): δ -171.19 (d, *J* = 2.26 Hz); IR: (KBr) ν_{max} 2950, 1632,1512, 1450, 1257, 817, 740 cm^{-1}; HRMS (EI): calcd. For [$C_{15}H_{11}FO$] 226.0794, found 226.0789.

3-fluoro-2-(4-fluorophenyl)benzofuran (2f)



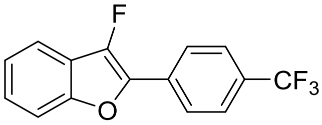
The general procedure was followed to afford the product as white solid in 58% yield (mp: 81-83 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 8.19-8.14 (m, 2H), 7.56 (d, *J* = 7.2 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.39-7.31 (m, 2H), 7.21-7.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.98 (d, *J* = 248.7 Hz), 153.09, 149.51, 129.48, 128.75 (d, *J* = 8.2 Hz), 125.79 (d, *J* = 3.3 Hz), 125.64, 123.56, 119.89, 115.74 (d, *J* = 21.7 Hz), 111.25, 93.53 (d, *J* = 1.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -112.20, -168.40; IR: (KBr) ν_{max} 2923, 1604, 1503, 1451, 1234, 1072, 831, 737 cm^{-1}; HRMS (EI): calcd. for [$C_{14}H_8F_2O$] 230.0543, found 230.0546.

2-(4-bromophenyl)-3-fluorobenzofuran (2g)



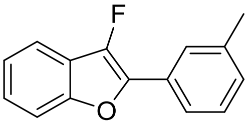
The general procedure was followed to afford the product as white solid in 51% yield (mp: 82-84 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.4 Hz, 2H), 7.64-7.60 (m, *J* = 8.8 Hz, 3H), 7.47-7.45 (m, 1H), 7.38-7.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.22 (d, *J* = 9.2 Hz), 144.90 (d, *J* = 256.8 Hz), 137.18 (d, *J* = 20.1 Hz), 132.00, 131.87, 127.62, 126.15 (d, *J* = 6.0 Hz), 125.76, 123.40, 122.10, 117.77, 111.84; ^{19}F NMR (376 MHz, $CDCl_3$): δ -168.92 (d, *J* = 2.26 Hz); IR: (KBr) ν_{max} 3016, 1631, 1490, 1389, 1074, 821, 738 cm^{-1}; HRMS (EI): calcd. for [$C_{14}H_8BrFO$] 289.9747, found 289.9749.

3-fluoro-2-(4-(trifluoromethyl)phenyl)benzofuran (2h)



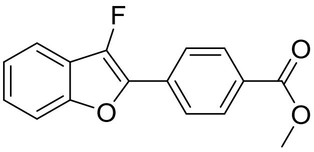
The general procedure was followed to afford the product as white solid in 61% yield (mp: 69-71 °C); ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.01 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.51-7.48 (m, 1H), 7.41-7.37 (m, 1H), 7.32 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 151.53 (d, *J* = 9.3 Hz), 145.84 (d, *J* = 258.9 Hz), 136.67 (d, *J* = 20.1 Hz), 131.94, 126.30, 125.83 (d, *J* = 21.4 Hz), 125.78, 124.72 (d, *J* = 6.1 Hz), 123.56, 120.26 (d, *J* = 19 Hz), 118.06, 111.99; ^{19}F NMR (376 MHz, CDCl$_3$): δ -62.681, -167.06 (d, *J* = 1.50 Hz); IR: (KBr) ν_{max} 2960, 1632, 1451, 1395, 1210, 1170, 837, 746 cm^{-1}; HRMS (EI): calcd. for [$C_{15}H_8F_4O$] 280.0511, found 280.0510.

3-fluoro-2-(m-tolyl)benzofuran (2i)



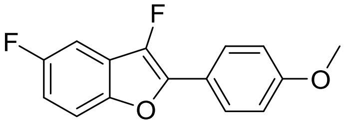
The general procedure was followed to afford the product as white solid in 71% yield (mp: 31-33 °C); ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.73 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.48-7.46 (m, 1H), 7.40-7.26 (m, 3H), 7.17 (d, *J* = 7.6 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 151.11 (d, *J* = 9.3 Hz), 144.53 (d, *J* = 255.5 Hz), 138.47, 138.29 (d, *J* = 20.2 Hz), 129.04, 128.71, 128.59 (d, *J* = 5.2 Hz), 125.31, 125.25, 123.17, 122.01, 120.71 (d, *J* = 19.3 Hz), 117.60, 111.74, 21.55; ^{19}F NMR (376 MHz, CDCl$_3$): δ -170.32 (d, *J* = 1.13 Hz); IR: (KBr) ν_{max} 2960, 1632, 1451, 1262, 1140, 867, 740 cm^{-1}; HRMS (EI): calcd. for [$C_{15}H_8F_4O$] 226.0794, found 226.0789.

Methyl 4-(3-fluorobenzofuran-2-yl) benzoate (2j)



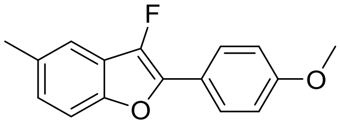
The general procedure was followed to afford the product as white solid in 43% yield (mp: 112~113 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.0 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.54-7.48 (m, 1H), 7.40-7.29 (m, 2H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.64, 151.57 (d, *J* = 9.4 Hz), 145.91 (d, *J* = 259.4 Hz), 137.12 (d, *J* = 19.9 Hz), 130.10, 129.90, 126.26, 125.86, 124.37 (d, *J* = 6.1 Hz), 123.51, 119.27, 118.03, 111.97, 52.21; ^{19}F NMR (376 MHz, $CDCl_3$): δ -166.47 (d, *J* = 1.88 Hz); IR: (KBr) ν_{max} 2953, 1728, 1608, 1437, 1279, 1108, 859, 757 cm^{-1}; HRMS (EI): calcd. for [$C_{16}H_{11}FO_3$] 270.0692, found 270.0697.

3, 5-difluoro-2-(4-methoxyphenyl) benzofuran (2k)



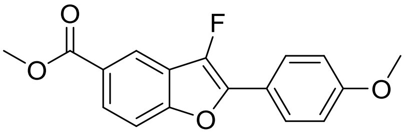
The general procedure was followed to afford the product as white solid in 68% yield (mp: 69~70 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84-7.81 (m, 2H), 7.38-7.34 (m, 1H), 7.23-7.21 (m, 1H), 7.03-6.98 (m, 3H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.82, 159.30 (d, *J* = 238.2 Hz), 147.04, 143.24 (d, *J* = 253.1 Hz), 140.30 (d, *J* = 20.1 Hz), 127.92, 126.42 (d, *J* = 5.5 Hz), 121.14, 114.38, 112.62 (d, *J* = 12.4 Hz), 112.45 (d, *J* = 6.8 Hz), 103.05 (d, *J* = 17 Hz), 55.35; ^{19}F NMR (376 MHz, $CDCl_3$): δ -119.73-119.79, -172.32 (t, *J* = 2.26 Hz); IR: (KBr) ν_{max} 2942, 1622, 1513, 1261, 1033, 830, 793 cm^{-1}; HRMS (EI): calcd. for [$C_{15}H_{10}F_2O_2$] 260.0649, found 260.0652.

3-fluoro-2-(4-methoxyphenyl)-5-methylbenzofuran (2l)



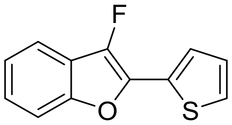
The general procedure was followed to afford the product as white solid in 70% yield (mp: 90~92 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.81 (m, 2H), 7.35 (s, 1H), 7.33-7.30 (m, 1H), 7.11-7.09 (m, 1H), 7.03-6.99 (m, 2H), 3.87 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.42, 149.38 (d, *J* = 9.5 Hz), 143.35 (d, *J* = 253.2 Hz), 138.37 (d, *J* = 20.7 Hz), 132.70, 126.22, 126.16 (d, *J* = 1.8 Hz), 121.68 (d, *J* = 5.2 Hz), 120.86 (d, *J* = 19.0 Hz), 116.96 (d, 3.0 Hz), 114.29, 111.14, 55.34, 21.32; ^{19}F NMR (376 MHz, $CDCl_3$): δ -172.86 (d, *J* = 2.26 Hz); IR: (KBr) ν_{max} 2923, 1633, 1513, 1450, 1250, 1024, 831, 801cm^{-1}; HRMS (EI): calcd. for [$C_{16}H_{13}FO_2$] 256.0900, found 256.0904.

Methyl 3-fluoro-2-(4-methoxyphenyl)benzofuran-5-carboxylate (1m)



The general procedure was followed to afford the product as white solid in 52% yield (mp: 117~119 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 1H), 8.03-8.01 (m, 1H), 7.83 (d, *J* = 8.8 Hz, 2H), 7.46 (d, *J* = 6.4 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 2H), 3.96 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.83, 159.90, 153.17 (d, *J* = 8.8 Hz), 143.24 (d, *J* = 254.6 Hz), 139.89 (d, *J* = 20.5 Hz), 126.47, 126.41, 125.58, 121.05, 120.85, 119.77, 114.39, 111.54, 55.35, 52.23; ^{19}F NMR (376 MHz, CDCl3): δ -172.29 (d, *J* = 1.88 Hz); IR: (KBr) ν_{max} 2953, 1716, 1610, 1513, 1431, 1258, 1026, 827, 764 cm^{-1}; HRMS (EI): calcd. for [$C_{17}H_{13}FO_4$] 300.0791, found 300.0793.

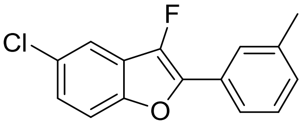
3-fluoro-2-(thiophen-2-yl)benzofuran (2n)



The general procedure was followed to afford the product as white solid in 78% yield (mp: 62~64 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 7.2 Hz, 1H), 7.53 (d, *J* = 2.8 Hz, 1H), 7.46-7.41 (m, 2H), 7.35-7.27 (m, 2H), 7.17-7.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.13 (d, *J* = 8.9 Hz), 142.98 (d, *J* = 255.9 Hz), 135.36 (d, *J* = 24.1 Hz), 129.96 (d, *J* = 7.5 Hz), 127.83, 125.88 (d, *J* = 4.2 Hz), 125.34, 124.58 (d, *J* = 5.1 Hz), 123.43, 120.27 (d, *J* = 18.3 Hz), 117.46 (d, *J* = 3.1 Hz), 111.77; ^{19}F NMR (376 MHz, $CDCl_3$): δ -170.57 (d, *J* = 1.88 Hz); IR: (KBr) ν_{max}

3025, 1634, 1451, 1203, 850, 831, 745, 694 cm^{-1}; HRMS (EI): calcd. for [$C_{12}H_7FOS$] 218.0202, found 218.0200.

5-chloro-3-fluoro-2-(m-tolyl)benzofuran (2o)



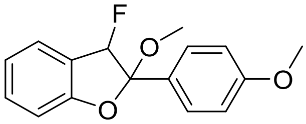
The general procedure was followed to afford the product as white solid in 52% yield (mp: 71~73 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 7.6 Hz, 2H), 7.57 (d, *J* = 2.0 Hz, 1H), 7.39-7.35 (m, 2H), 7.29-7.26 (m, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.40 (d, *J* = 8.8 Hz), 143.56 (d, *J* = 256.2 Hz), 139.90 (d, *J* = 19.7 Hz), 138.571, 129.50, 128.98, 128.77, 128.08 (d, *J* = 5.1 Hz), 125.53, 125.41 (d, *J* = 5.6 Hz), 122.12 (d, *J* = 4.9 Hz), 121.88 (d, *J* = 18.9 Hz), 117.20, 112.86, 21.53; ^{19}F NMR (376 MHz, $CDCl_3$): δ -169.86 (d, *J* = 1.88 Hz); IR: (KBr) ν_{max} 2923, 1629, 1458, 1260, 1088, 862, 740 cm^{-1}**;** HRMS (EI): calcd. for [$C_{15}H_{10}ClFO$] 260.0404, found 226.0400.

Ⅴ. Synthesis and characterization of 3a-3f and 4a-1- 4a-2

General procedure for the synthesis of 3a-3f

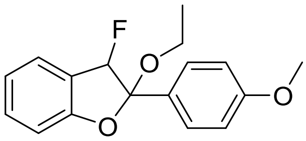
To the solution of 2-(4-methoxyphenyl)benzofuran (0.5 mmol) in MeCN (8.0 mL) was added Selectfluor (195 mg, 1.1 eq) at room temperature (about 25 °C), then nucleophiles reagent (water, methanol, ethanol et) (0.4 mL) was added , then the formed mixture was stirred at room temperature under air for 1h as monitored by TLC (PE: EA= 10: 1), once the reaction was completed, EA (30 mL) was added, and washed with water, brine and dried (Na_2SO_4),the solvent was removed under reduce vacuum and the residue was purified by silica gel column to afford aim compounds.

3-fluoro-2-methoxy-2-(4-methoxyphenyl)-2, 3-dihydrobenzofuran (3a)



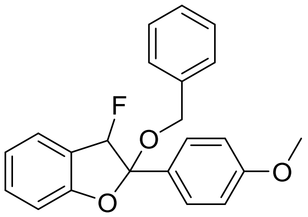
The general procedure was followed to afford the product as white solid (86% yield, dr 98: 2, mp: 87~89 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.55 (m, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.45-7.40 (m, 1H), 7.09-7.04 (m, 2H), 7.01-6.98 (m, 2H), 5.62 (d, *J* = 56.8 Hz, 1H), 3.86 (s, 3H), 3.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.23, 160.07 (d, *J* = 5.1 Hz), 132.06 (d, *J* = 4.2 Hz), 128.99 (d, *J* = 1.3 Hz), 127.21 (d, *J* = 1.7Hz), 125.65 (d, *J* = 2.5 Hz), 124.11 (d, *J* = 18.7 Hz), 121.87 (d, *J* = 3.3 Hz), 113.70, 113.21 (d, *J* = 27.2 Hz), 111.24 (d, *J* = 3.1 Hz), 95.00 (d, *J* = 186.4 Hz), 55.22, 50.77; ^{19}F NMR (376 MHz, $CDCl_3$): δ -166.47 (d, *J* = 56.78 Hz); IR: (KBr) ν_{max} 2931, 1618, 1521, 1478, 1260, 1050, 834, 751 cm^{-1}; HRMS (EI): calcd. for [$C_{16}H_{15}FO_3$] 274.1005, found 274.1006.

2-ethoxy-3-fluoro-2-(4-methoxyphenyl)-2, 3-dihydrobenzofuran (3b)



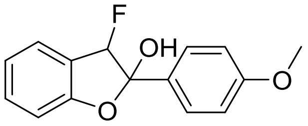
The general procedure was followed to afford the product as white solid (81% yield, dr 95: 5, mp: 101~103 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57-7.54 (m, 2H), 7.52-7.50 (m, 1H), 7.43-7.38 (m, 1H), 7.06-7.03 (m, 2H), 6.99-6.95 (m, 2H), 5.60 (d, *J* = 57.2 Hz, 1H), 3.85 (s, 3H), 3.67-3.59 (m, 1H), 3.50-3.42 (m, 1H),1.10 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.18, 160.14, 132.01 (d, *J* = 4.3 Hz), 128.85 (d, *J* = 1.3 Hz), 127.22 (d, *J* = 1.7Hz), 126.58 (d, *J* = 2.5 Hz), 124.16 (d, *J* = 18.7 Hz), 121.74 (d, *J* = 3.5 Hz), 113.63, 113.24 (d, *J* = 27.0 Hz), 111.14, 95.21 (d, *J* = 186.4 Hz), 59.25, 55.23, 15.51; ^{19}F NMR (376 MHz, CDCl3): δ -162.81 (d, *J* = 56.78 Hz); IR: (KBr) ν_{max} 2931, 1616, 1518, 1457, 1247, 1094, 834, 752 cm^{-1}; HRMS (EI): calcd. for [$C_{17}H_{17}FO_3$] 288.1162, found 288.1164.

2-(benzyloxy)-3-fluoro-2-(4-methoxyphenyl)-2, 3-dihydrobenzofuran (3c)



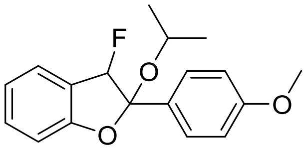
The general procedure was followed to afford the product as colorless oil (78% yield, dr 86: 14). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.68-7.56 (m, 2H), 7.54-7.52 (m, 1H), 7.45-7.38 (m, 1H), 7.32-7.19 (m, 5H), 7.09-6.93 (m, 4H), 5.74 (d, *J* = 56.4 Hz, 1H), 4.67 (d, *J* = 11.6Hz, 1H), 4.48 (d, *J* = 11.6Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 160.31, 160.03 (d, *J* = 5.1 Hz), 137.69, 132.05 (d, *J* = 4.2 Hz), 128.99 (d, *J* = 1.1 Hz), 128.25, 128.21, 127.57, 127.50, 127.23 (d, *J* = 1.7Hz), 126.14 (d, *J* = 1.5 Hz), 124.14 (d, *J* = 17.6 Hz), 121.91 (d, *J* = 3.3 Hz), 114.08, 113.79, 113.27 (d, *J* = 7.3 Hz), 111.21 (d, *J* = 2.8 Hz), 95.13 (d, *J* = 186.9 Hz), 65.61, 55.25; ^{19}F NMR (376 MHz, CDCl$_3$): δ -162.81 (d, *J* = 56.4 Hz); IR: (KBr) ν_{max} 2932, 1617, 1513, 1246, 1101, 1030, 970, 832, 752 cm^{-1}; HRMS (EI): calcd. for [$C_{22}H_{19}FO_3$] 350.1318, found 350.1321.

3-fluoro-2-(4-methoxyphenyl)-2, 3-dihydrobenzofuran-2-ol (3d)



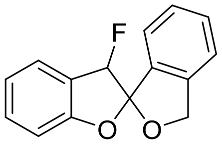
The general procedure was followed to afford the product as white solid (87% yield, dr 94: 6, mp: 110~112 °C). ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.06 (d, *J* = 8.8 Hz, 2H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.28-7.24 (m, 1H), 6.95-6.92 (m, 4H), 6.73 (d, *J* = 46.8 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 194.39 (d, *J* = 21.6 Hz), 164.66, 154.84 (d, *J* = 3.8 Hz), 131.77, 131.33, 128.53 (d, *J* = 6.5 Hz), 126.23, 120.84, 120.01 (d, *J* = 20.4 Hz), 117.87, 114.16, 90.79 (d, *J* = 183.3 Hz), 55.56; ^{19}F NMR (376 MHz, CDCl$_3$): δ -182.22 (d, *J* = 47.0 Hz); IR: (KBr) ν_{max} 3228, 2921, 1601, 1459, 1264, 1052, 862, 759 cm^{-1}; HRMS (EI): calcd. for [$C_{15}H_{13}FO_3$] 260.0849, found 260.0851.

3-fluoro-2-isopropoxy-2-(4-methoxyphenyl)-2, 3-dihydrobenzofuran (3e)



The general procedure was followed to afford the product as white solid (81% yield, dr 91: 9, mp: 104~105 °C). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.60 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.43-7.38 (m, 1H), 7.05-6.96 (m, 4H), 5.59 (d, *J* = 56.8 Hz, 1H), 4.02-3.94 (m, 1H), 3.85 (s, 3H), 1.07-1.03 (m, 6H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 160.08, 159.98 (d, *J* = 4.1 Hz), 132.04 (d, *J* = 4.3 Hz), 129.07 (d, *J* = 1.2 Hz), 127.32 (d, *J* = 2.3Hz), 127.23 (d, *J* = 1.8 Hz), 124.24 (d, *J* = 18.6 Hz), 121.66 (d, *J* = 3.4 Hz), 113.24 (d, *J* = 27.2 Hz), 113.45, 111.10 (d, *J* = 2.9 Hz), 95.30 (d, *J* = 186.5 Hz), 67.59, 55.22, 24.30, 23.73; ^{19}F NMR (376 MHz, CDCl$_3$): δ -162.84 (d, *J* = 56.78 Hz); IR: (KBr) ν_{max} 2980, 2926, 1616, 1518, 1479, 1274, 1051, 958, 832, 751 cm^{-1}; HRMS (EI): calcd. for [$C_{18}H_{19}FO_3$] 302.1318, found 302.1316.

3-fluoro-3H, 3'H-spiro [benzofuran-2, 1'-isobenzofuran] (3f)



The general procedure was followed to afford the product as white solid (75% yield, dr 93: 7, mp: 71~73 °C). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.61-7.55 (m, 2H), 7.51-7.47 (m, 1H), 7.42-7.36 (m, 3H), 7.07 (t, *J* = 7.2 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 5.85 (d, *J* = 56.4 Hz, 1H), 5.37 (d, *J* = 12.4 Hz, 1H), 5.23 (d, *J* = 12.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 160.53 (d, *J* = 5.4 Hz), 140.53, 133.74 (d, *J* = 1.5 Hz), 132.40 (d, *J* = 4.6 Hz), 130.23, 127.97, 126.84 (d, *J* = 1.9 Hz), 125.27 (d, *J* = 6.6 Hz), 123.07 (d, *J* = 18.0 Hz), 121.86 (d, *J* = 3.5 Hz), 120.907, 119.00 (d, *J* = 27.9 Hz), 110.91 (d, *J* = 3.0 Hz), 95.35 (d, *J* = 186.5 Hz), 73.25; ^{19}F NMR (376 MHz, CDCl$_3$): δ -168.61 (d, *J* = 56.4 Hz); IR: (KBr) ν_{max} 2870, 1621, 1469, 1265, 1026, 934, 888, 751 cm^{-1}; HRMS (EI): calcd. for [$C_{15}H_{11}FO_2$] 242.0743, found 242.0748.

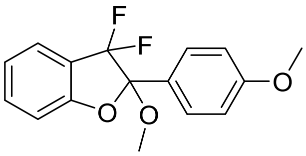
Large-scale synthesis of 3-fluoro-2-(4-methoxyphenyl) benzofuran (2a)

To the solution of 2-(4-methoxyphenyl) benzofuran (2.24 g, 10.0 mmol, 1.0 eq) in MeCN (60 mL) was added Selectfluor (3.90 g, 11.0 mmol, 1.1 eq) at room temperature (about 25 ^{o}C), then water (3 mL) was added , then the formed mixture was stirred at room temperature under air for 1h as monitored by TLC (PE: EA= 10: 1), once the reaction was completed, EA (30 mL) was added, and washed with water, brine and dried (Na_2SO_4), the solvent was removed under reduce vacuum and the residue was used in the next step directly. The residue was dissolve in dry DCM (50 mL) and pyridine (8.2 mL, 100 mmol, 10.0 eq) was added dropwise at 0 ^{o}C, then $SOCl_2$ (1.1mL) was added dropwise at that temperature, then the reaction was stirred at room temperature overnight as monitored by TLC, once the reaction was completed, DCM (150 mL) was added, washed with water, brine and dried (Na_2SO_4), The solvent was removed under reduce vacuum to give crude product. The crude product was purified by column chromatography on silica gel (PE: EA= 100: 1 to 10: 1) to afford pure aim product (1.81 g, 75% yield).

General procedure for the synthesis of 4a-1 and 4a-2

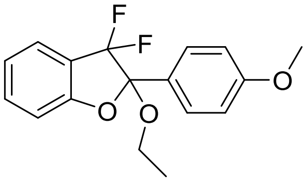
To the solution of 3-fluoro-2-(4-methoxyphenyl)benzofuran (0.5 mmol) in MeCN (8.0 mL) was added Selectfluor (195 mg, 1.1 eq) at room temperature (about 25 ^{o}C), then nucleophiles reagent (methanol, ethanol) (0.4 mL) was added , then the formed mixture was stirred at room temperature under air for 1h as monitored by TLC (PE: EA= 10: 1), once the reaction was completed, EA (30 mL) was added, and washed with water, brine and dried (Na_2SO_4),the solvent was removed under reduce vacuum and the residue was purified by silica gel column to afford aim compounds.

3, 3-difluoro-2-methoxy-2-(4-methoxyphenyl)-2, 3-dihydrobenzofuran (4a-1)



The general procedure was followed to afford the product as white solid in 72% yield (mp: 77-80 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.56 (m, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.12-7.06 (m, 2H), 7.00= 6.97 (m, 2H), 3.85 (s, 3H), 3.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.65, 158.77 (dd, J_1= 9.5 Hz, J_2= 6.3 Hz), 133.47 (d, *J* = 1.4 Hz), 128.76, 124.48, 124.32, 122.77 (d, *J* = 15.3 Hz), 122.44, 121.29 (t, *J* = 26.0 Hz), 113.83, 112.00, 109.65 (dd, J_1= 36.3 Hz, J_2= 18.3 Hz), 55.27, 51.56; ^{19}F NMR (376 MHz, $CDCl_3$): δ -84.89 (d, *J* = 248.16 Hz),-122.66 (d, *J* = 248.54 Hz); IR: (KBr) ν_{max} 2966, 1621, 1513, 1468, 1230, 1029, 834, 753 cm^{-1}; HRMS (EI): calcd. for [$C_{16}H_{14}F_2O_3$] 292.0911, found 292.0915.

2-ethoxy-3, 3-difluoro-2-(4-methoxyphenyl)-2, 3-dihydrobenzofuran (4a-2)



The general procedure was followed to afford the product as white solid in 68% yield (mp: 108~110 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 8.8Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 7.04 (d, *J* = 8.0 Hz 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 3.70-3.62 (m, 1H), 3.52-3.45 (m, 1H), 1.16 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.54, 158.85 (dd, J_1= 9.5 Hz, J_2= 6.3 Hz), 133.40 (d, *J* = 2.0 Hz), 128.62, 125.319, 124.48, 122.71 (d, *J* = 15.5 Hz), 122.49, 121.35 (t, *J* = 26.1 Hz), 113.73, 111.88, 109.71 (dd, J_1= 36.0 Hz, J_2= 18.4 Hz), 60.27, 55.26, 15.32; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.99 (d, *J* = 247.41 Hz), -122.20 (d, *J* = 247.78 Hz); IR: (KBr) ν_{max} 2989, 1612, 1515, 1469, 1225, 1040, 967, 837, 758 cm^{-1}; HRMS (EI): calcd. for [$C_{17}H_{16}F_2O_3$] 306.1068, found 306.1069.

Ⅵ.References

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(7). Ghosh, Somnath et al, *Tetrahedron Lett,* 2012, **53**, 5883.

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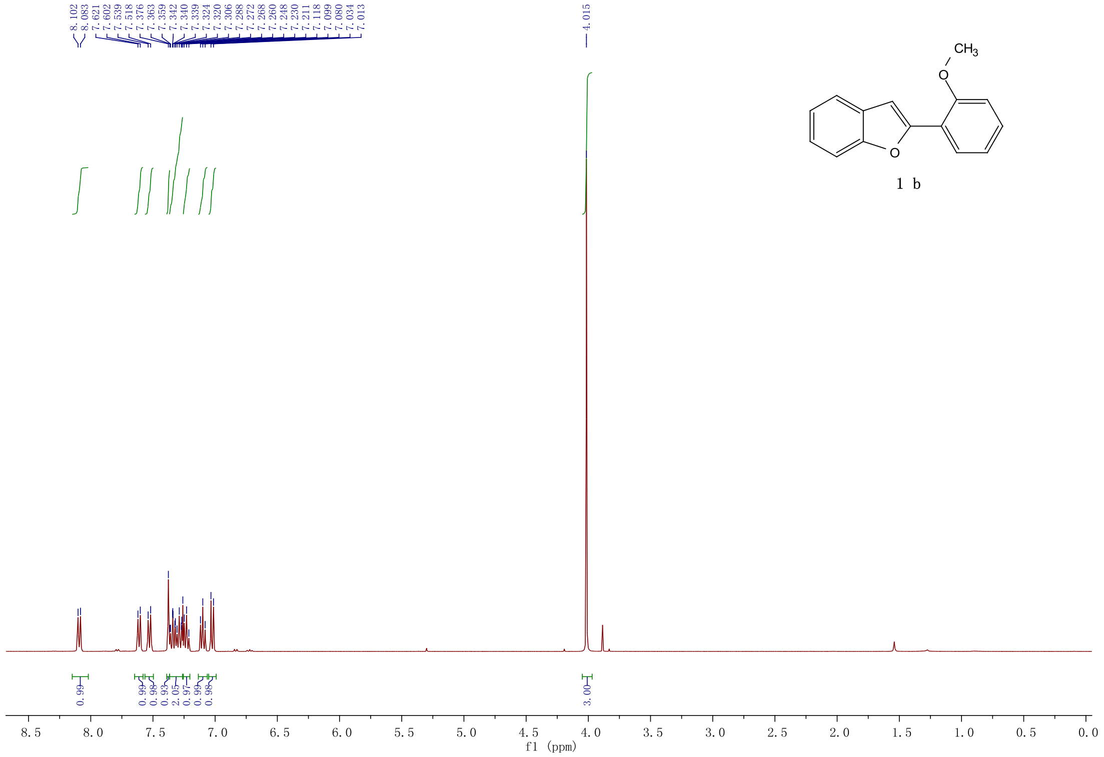
Ⅶ. ^{1}H, ^{19}F, ^{13}C NMR spectra



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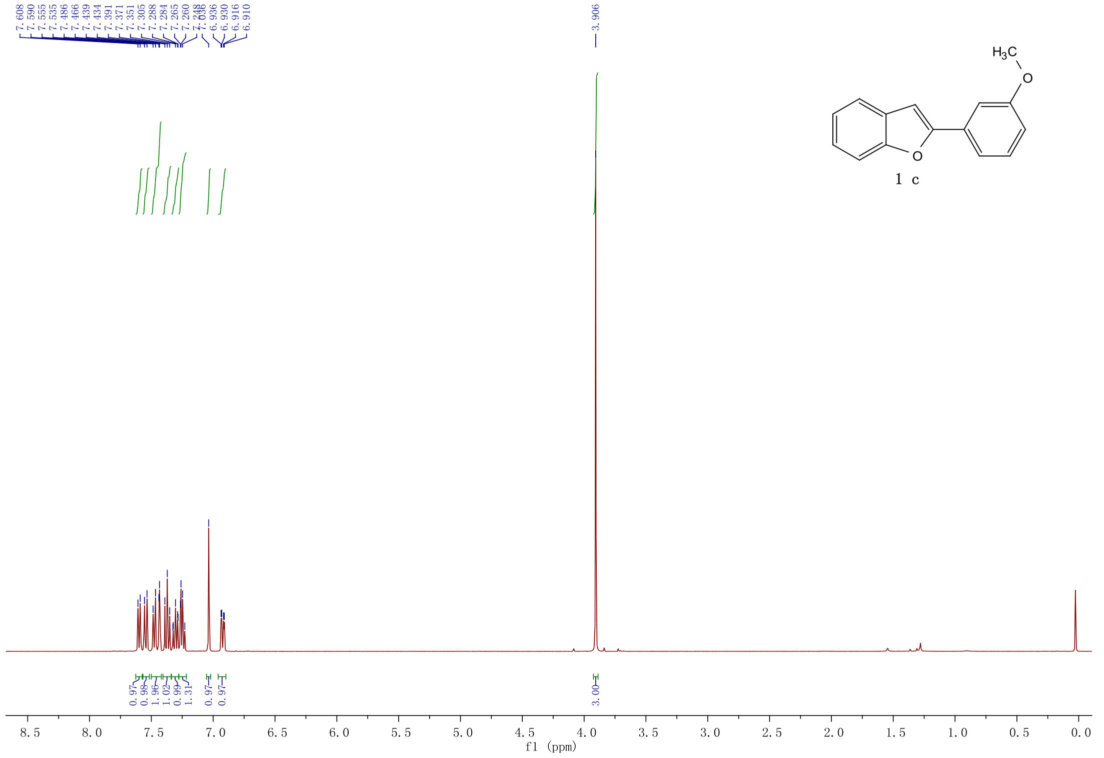

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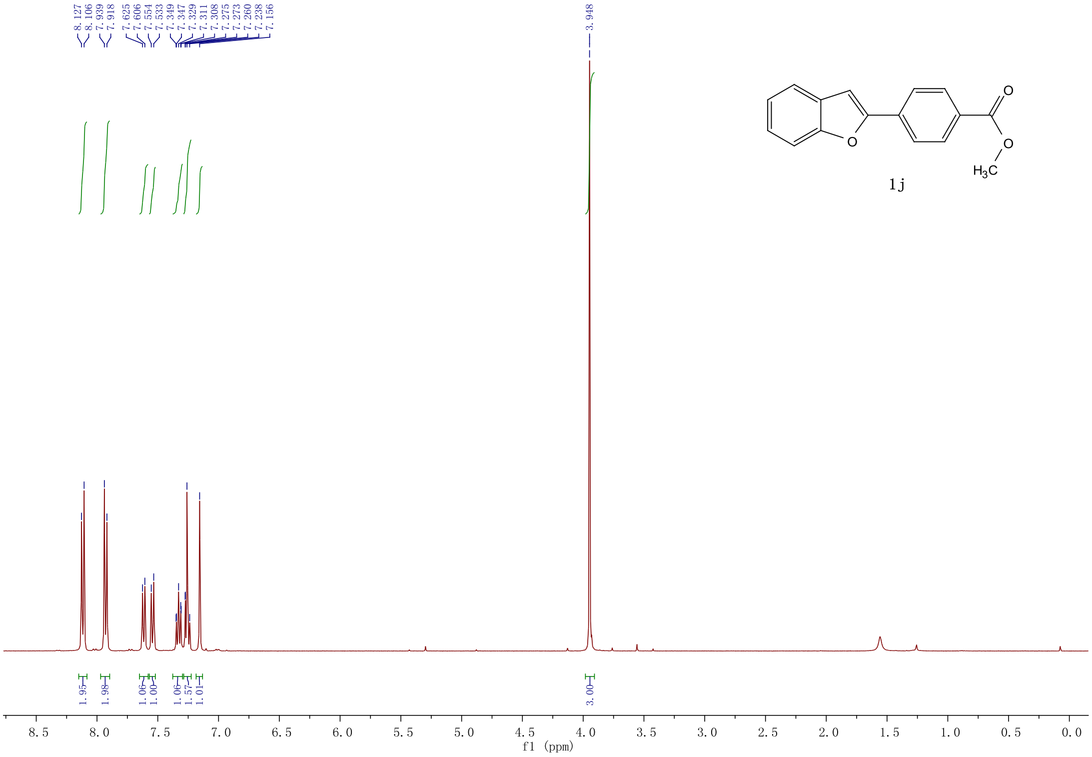
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O
O
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1j
1.95
1.98
1.06
1.00
1.06
1.57
1.01
3.00
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7.0
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6.0
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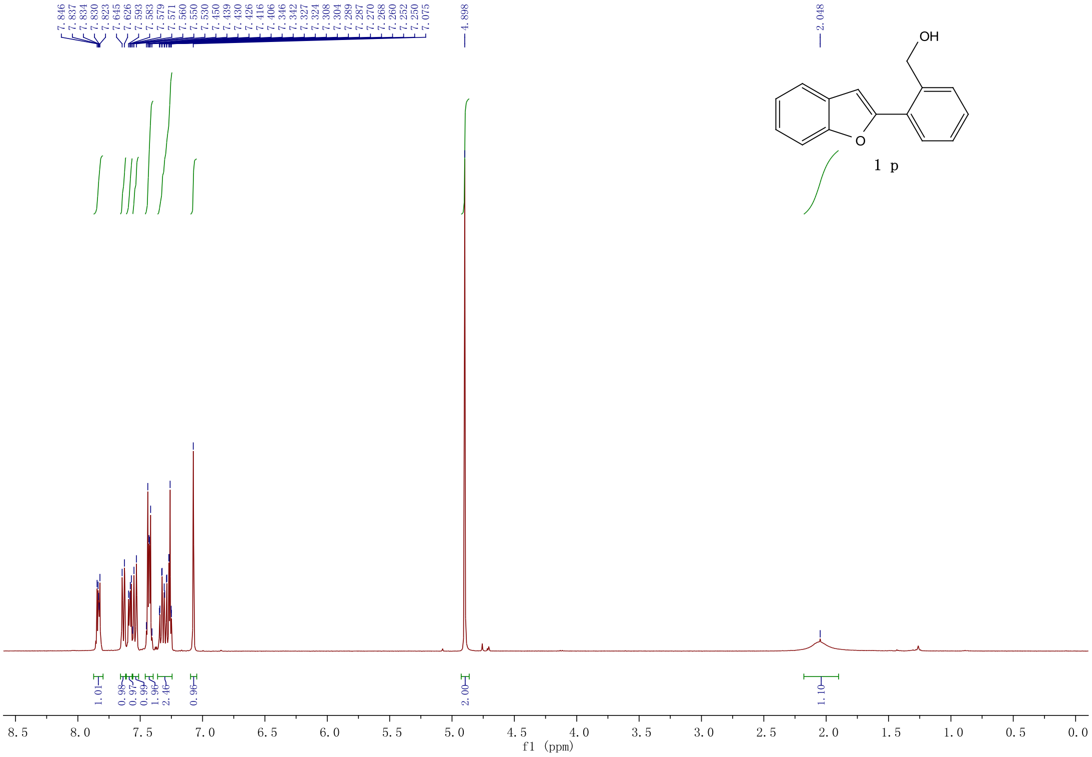
f1 (ppm)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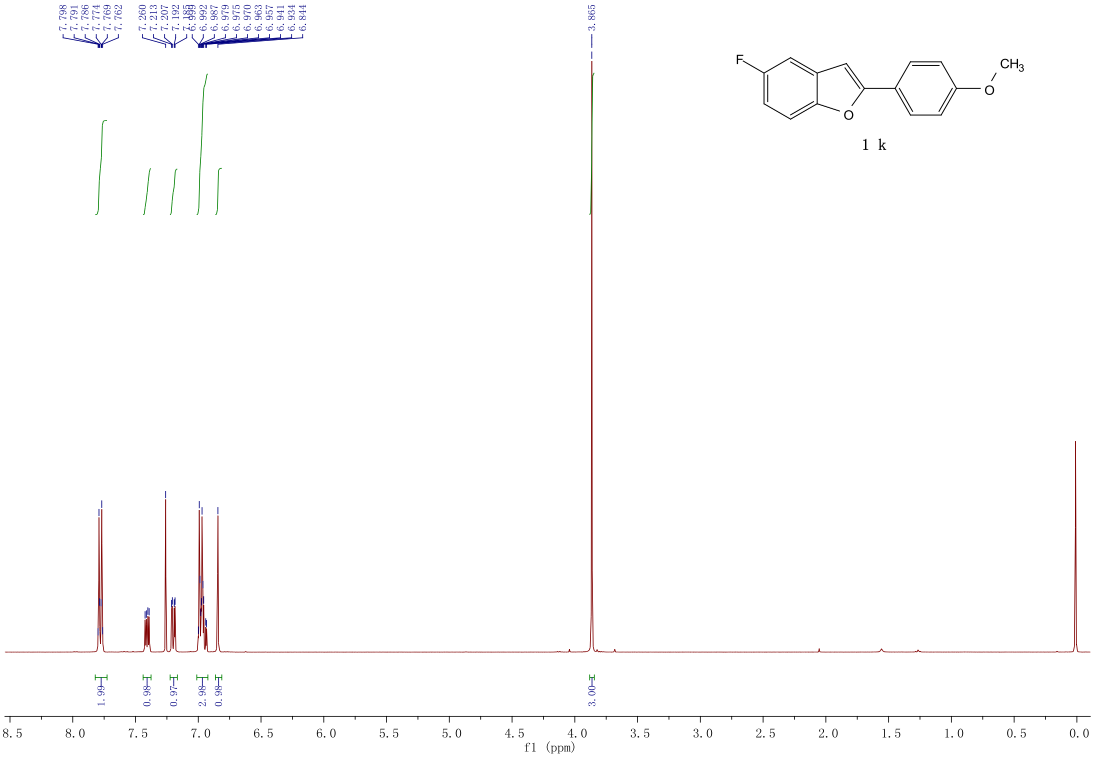
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f1 (ppm)

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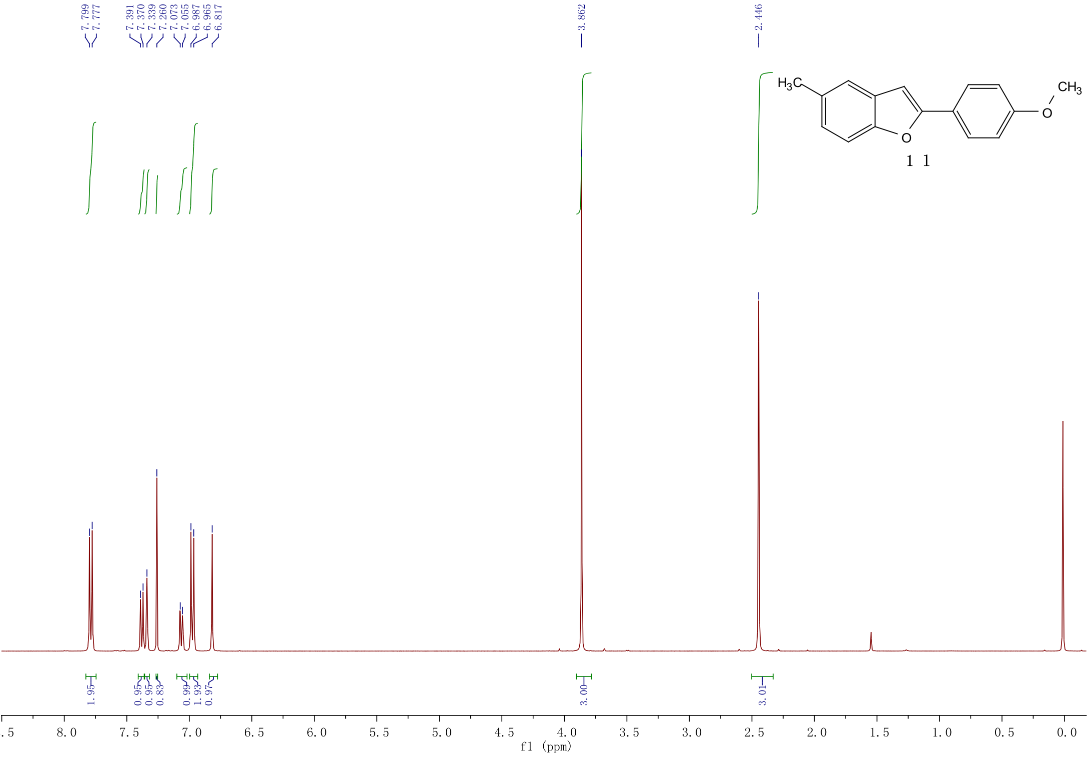
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f1 (ppm)

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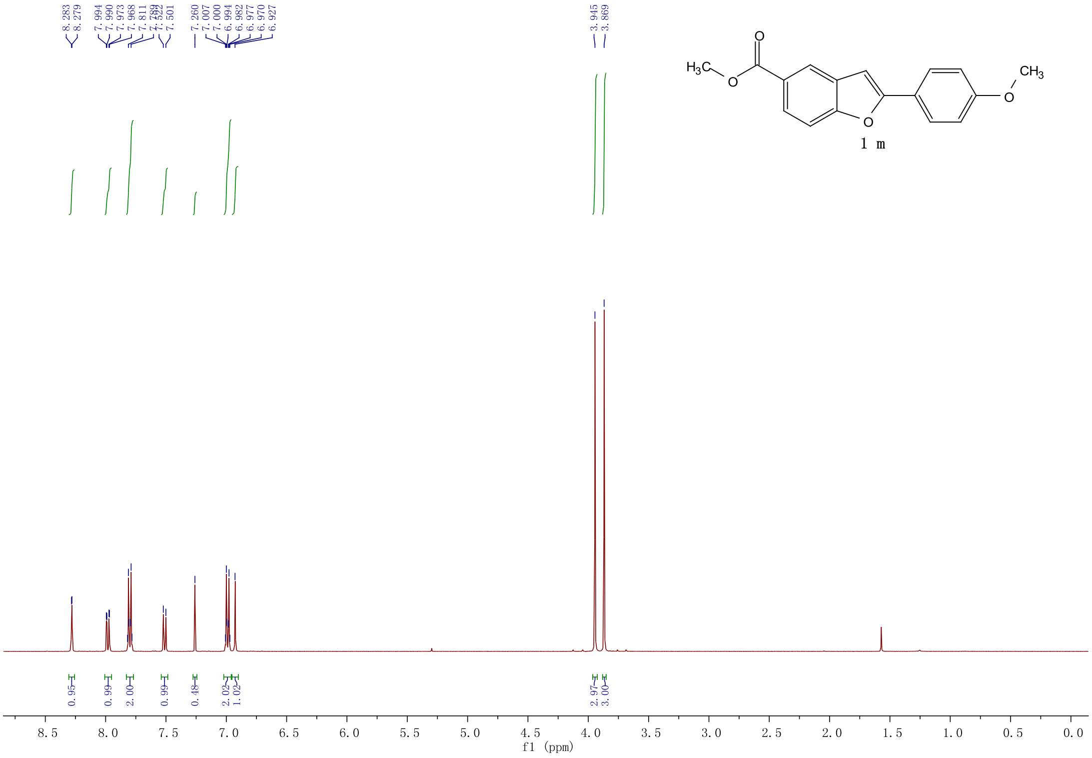
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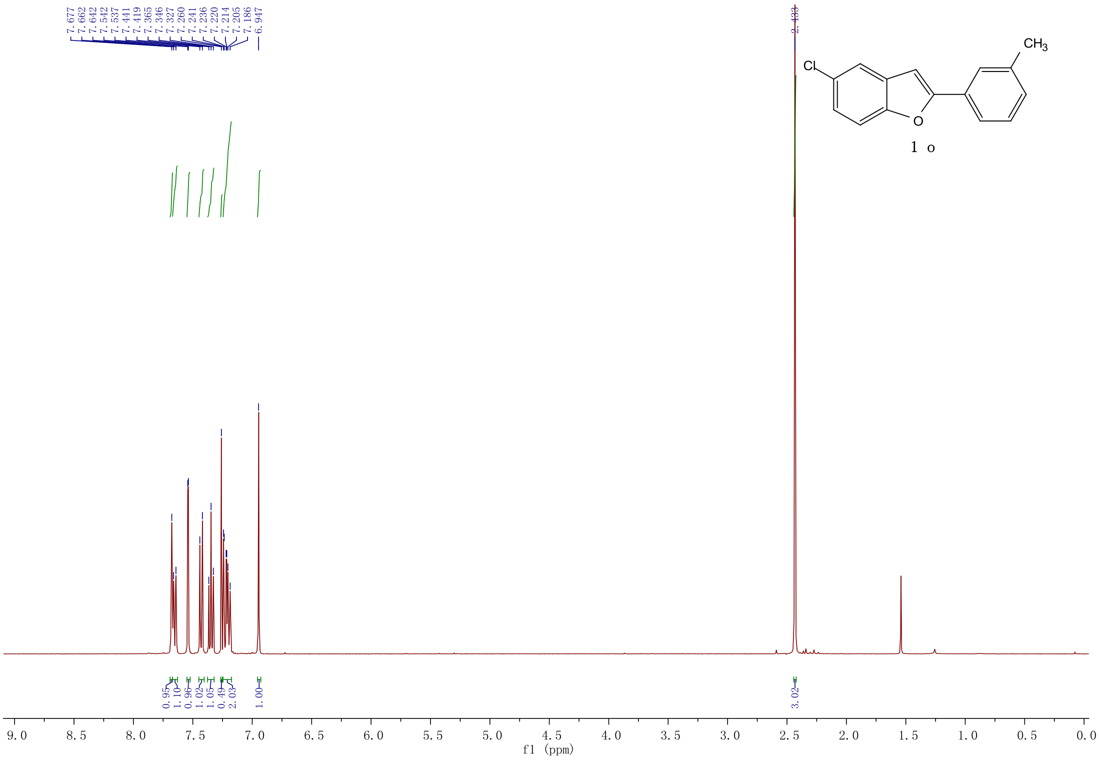
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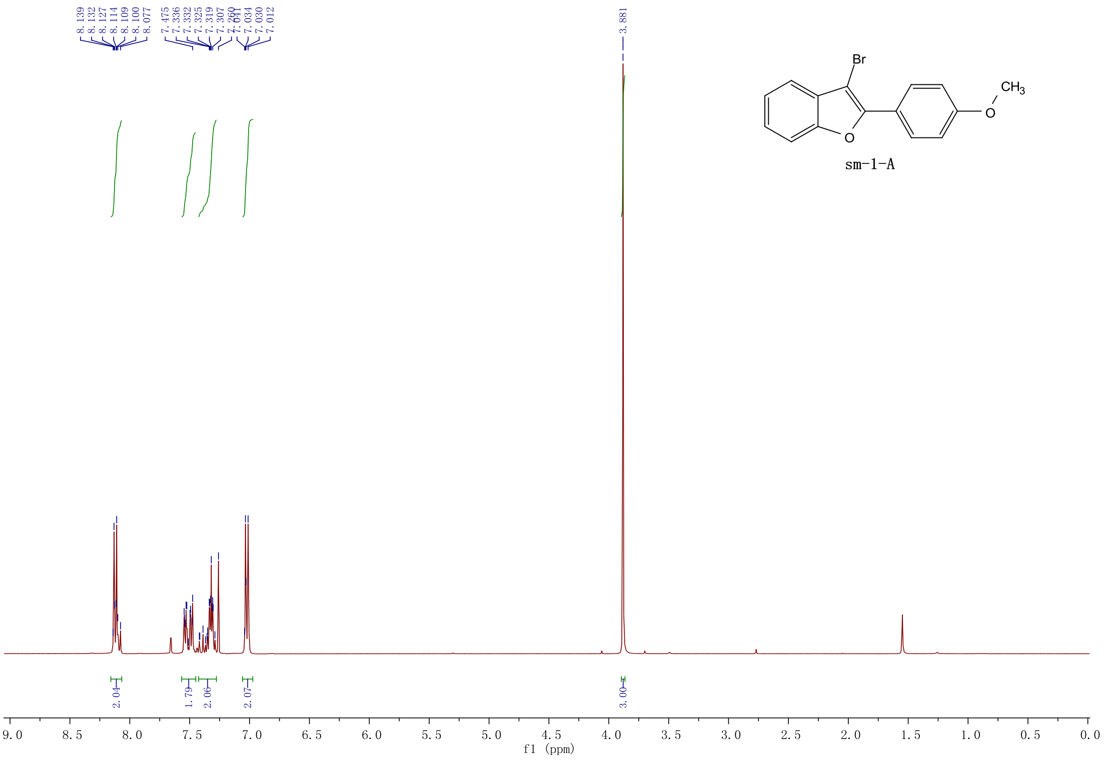
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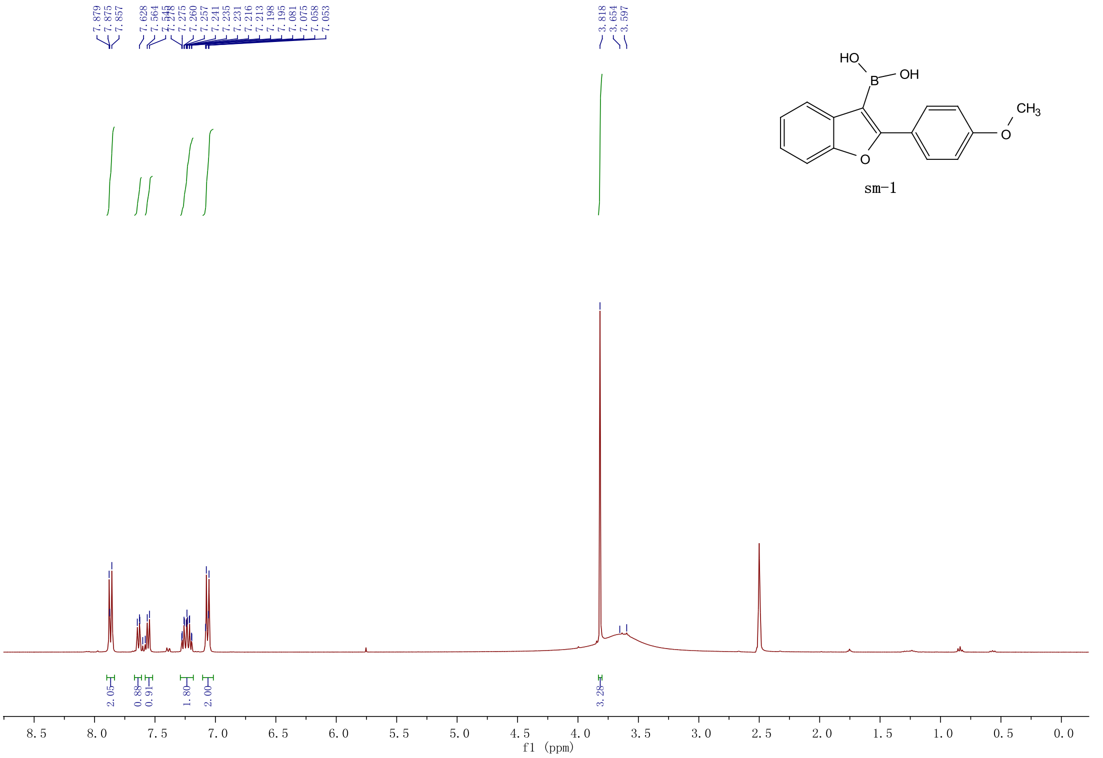
sm-1-A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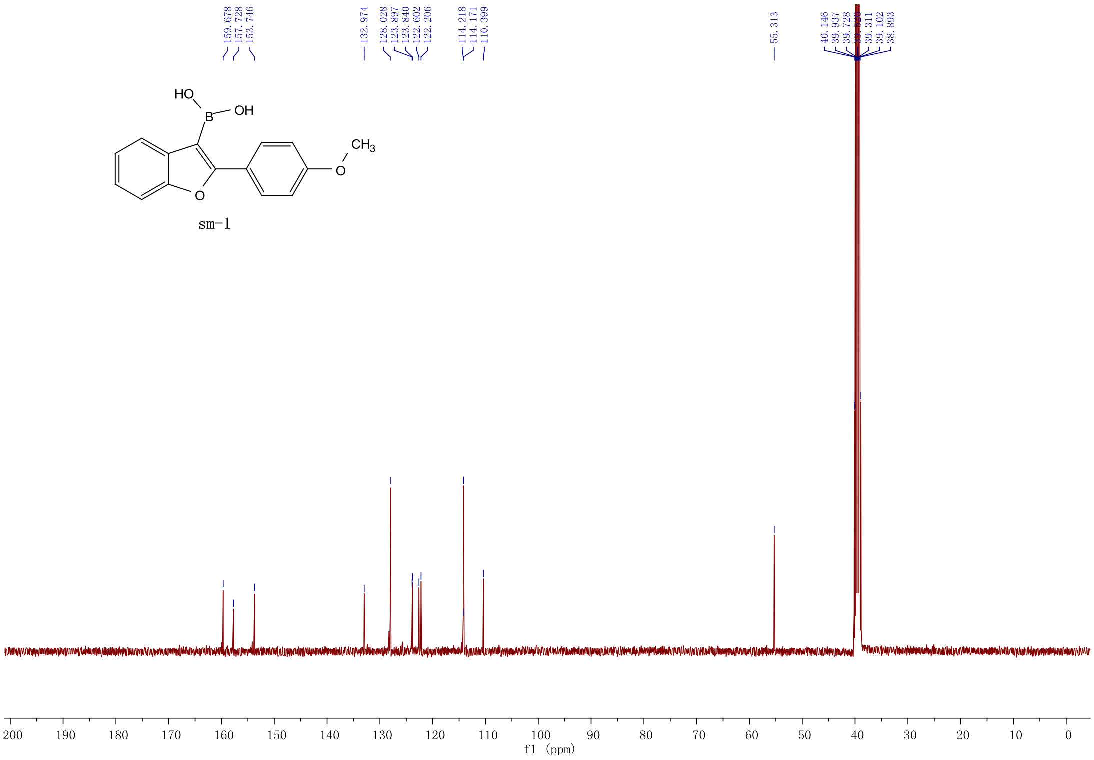
sm-1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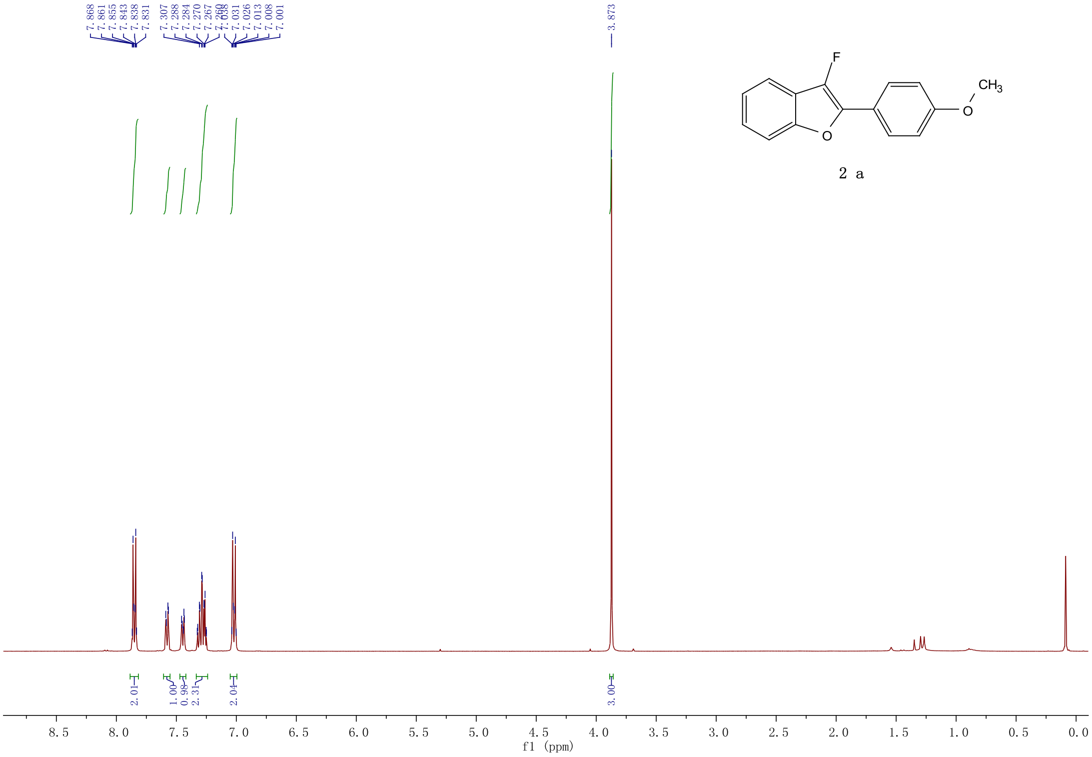
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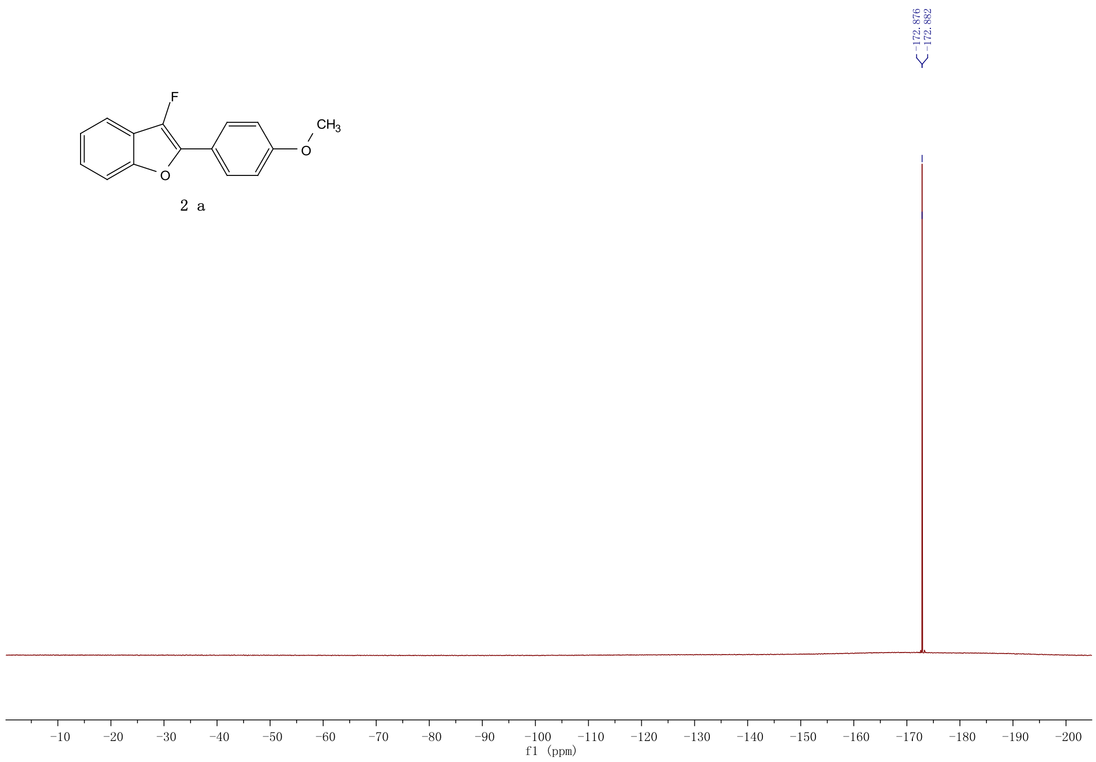
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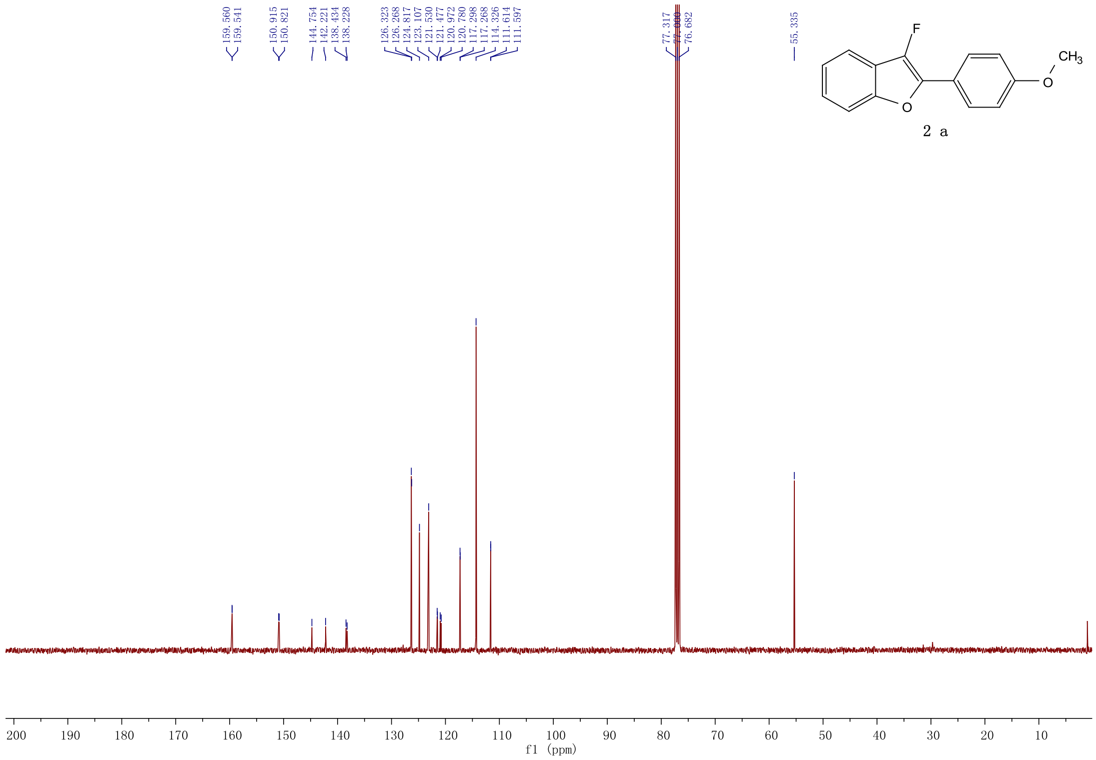
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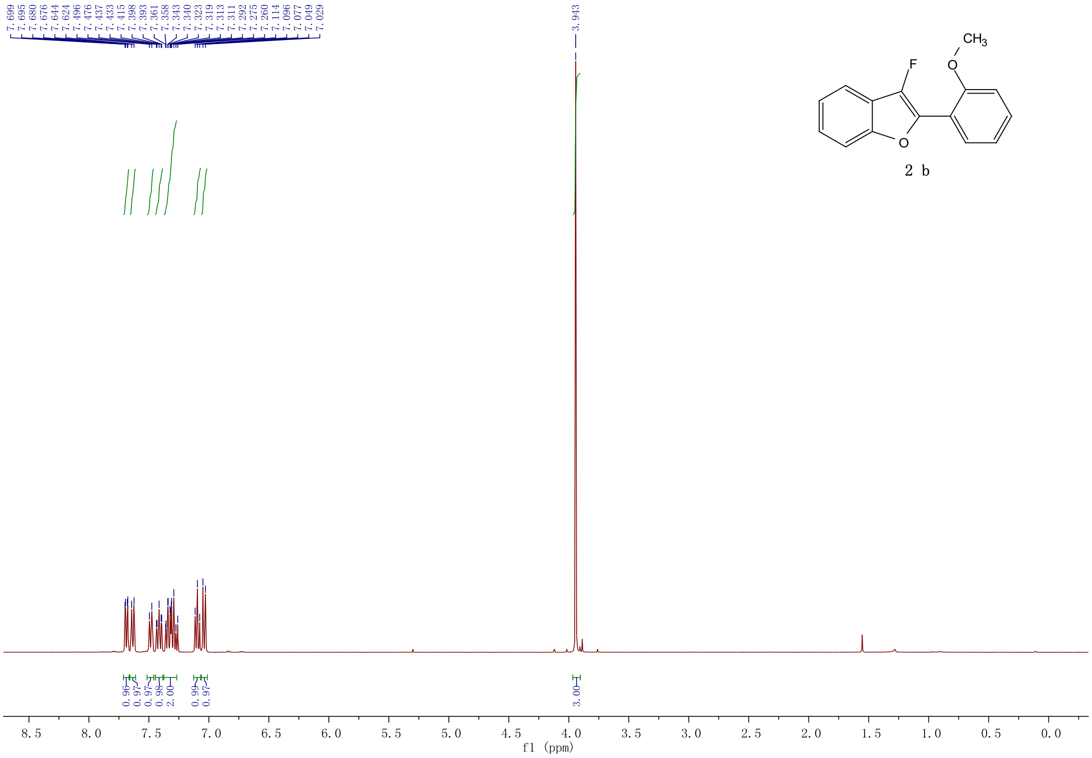
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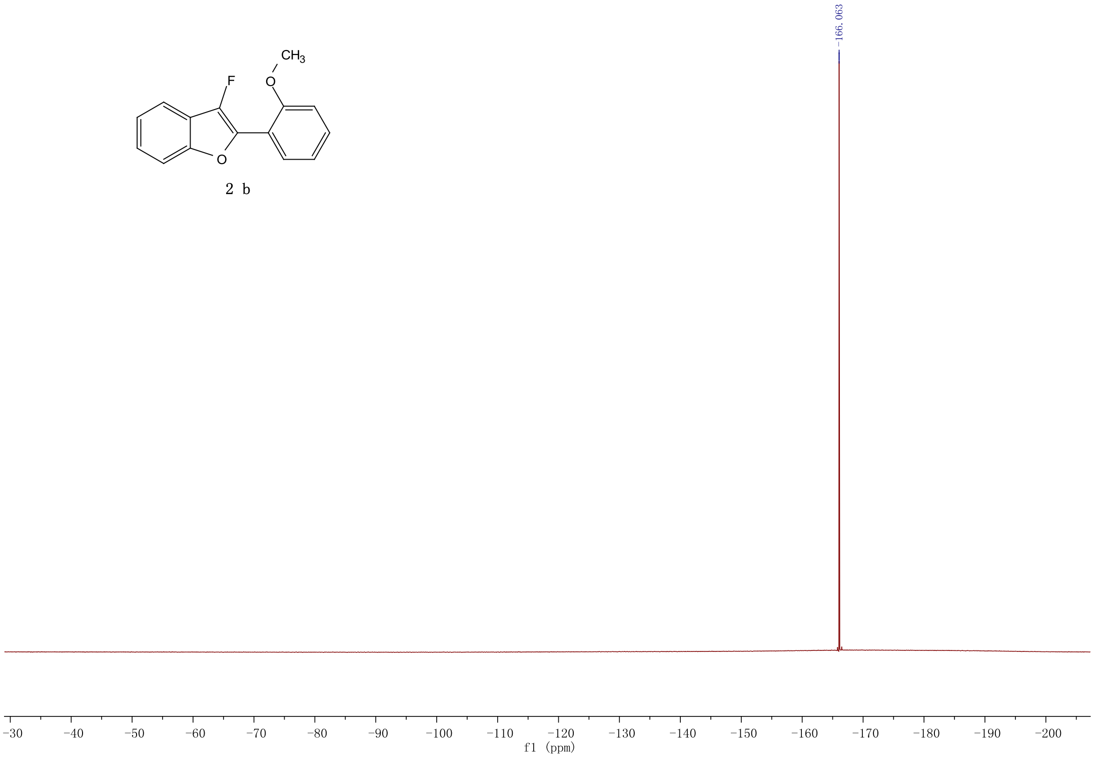
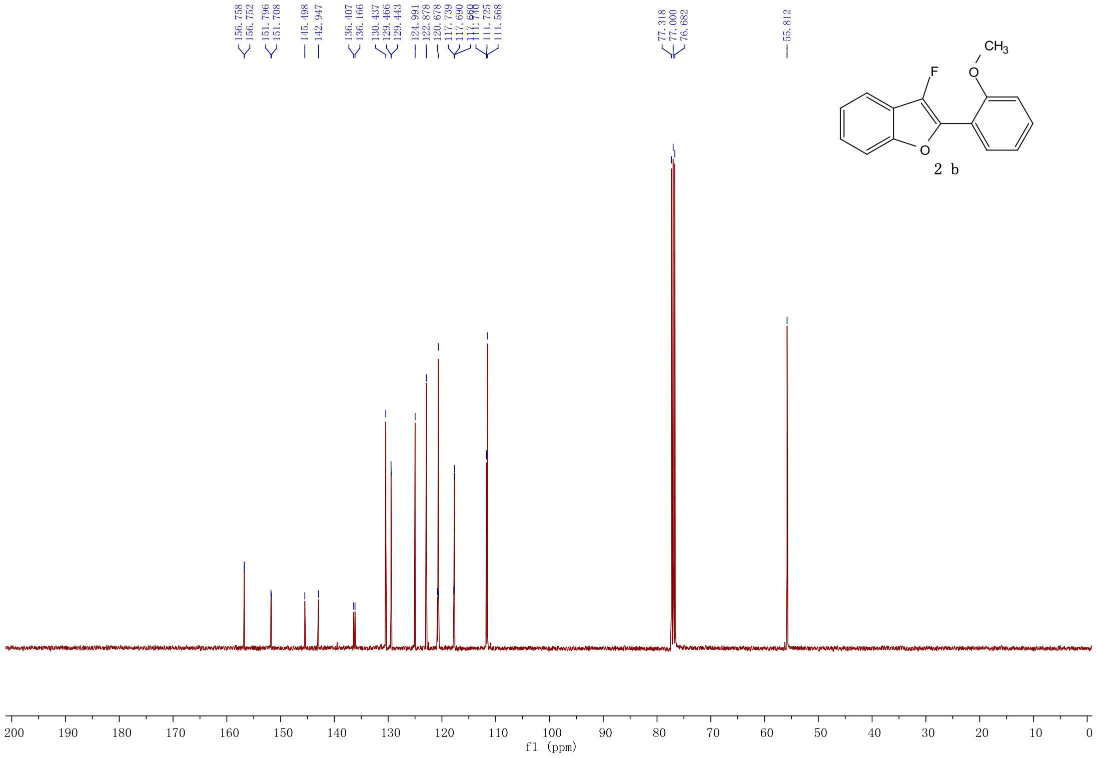
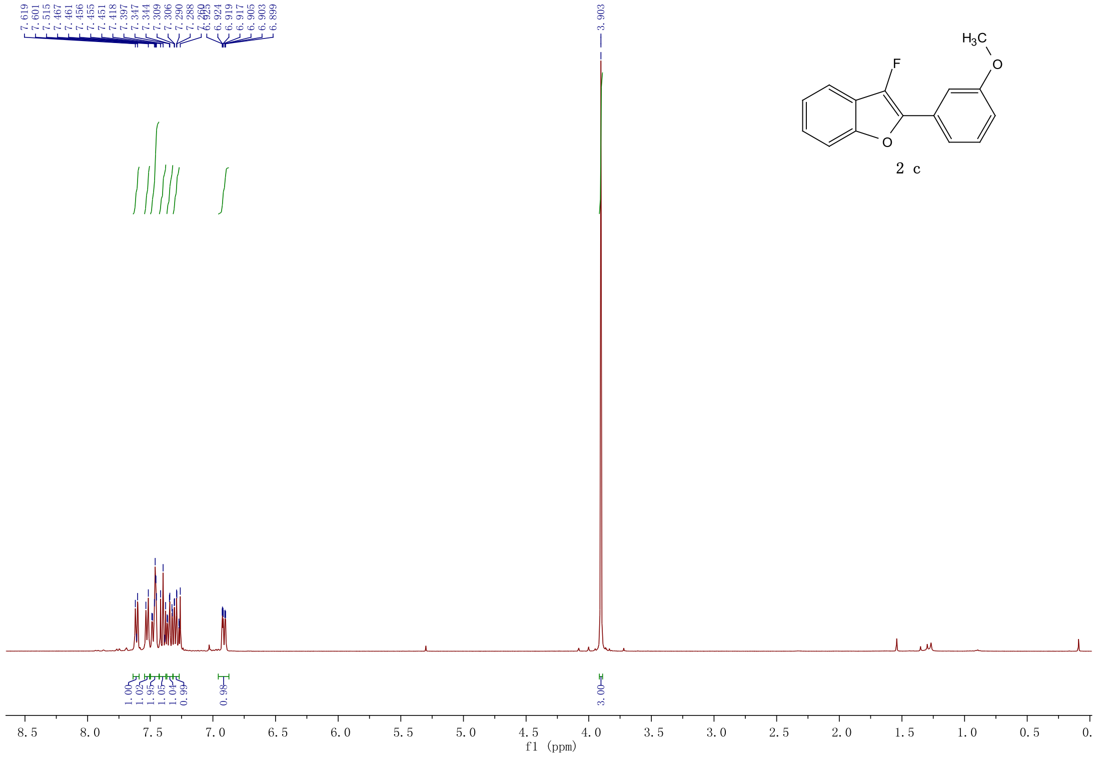
7.476
7.437
7.433
7.415
7.398
7.393
7.361
7.358
7.343
7.340
7.323
7.319
7.313
7.311
7.292
7.275
7.260
7.114
7.096
7.077
7.049
7.029
3.943
F
O
CH3
O
2 b
0.96
0.97
0.97
0.98
2.00
0.99
0.97
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

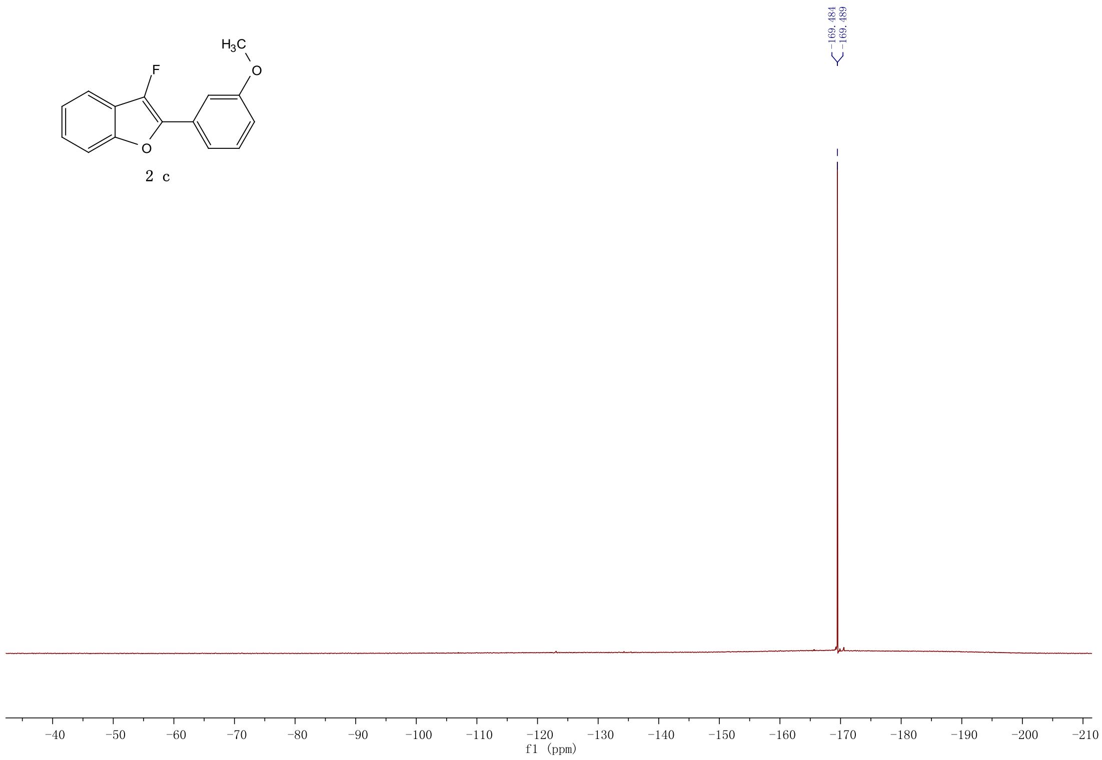

-166.063
F
O
CH3
O
2 b
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

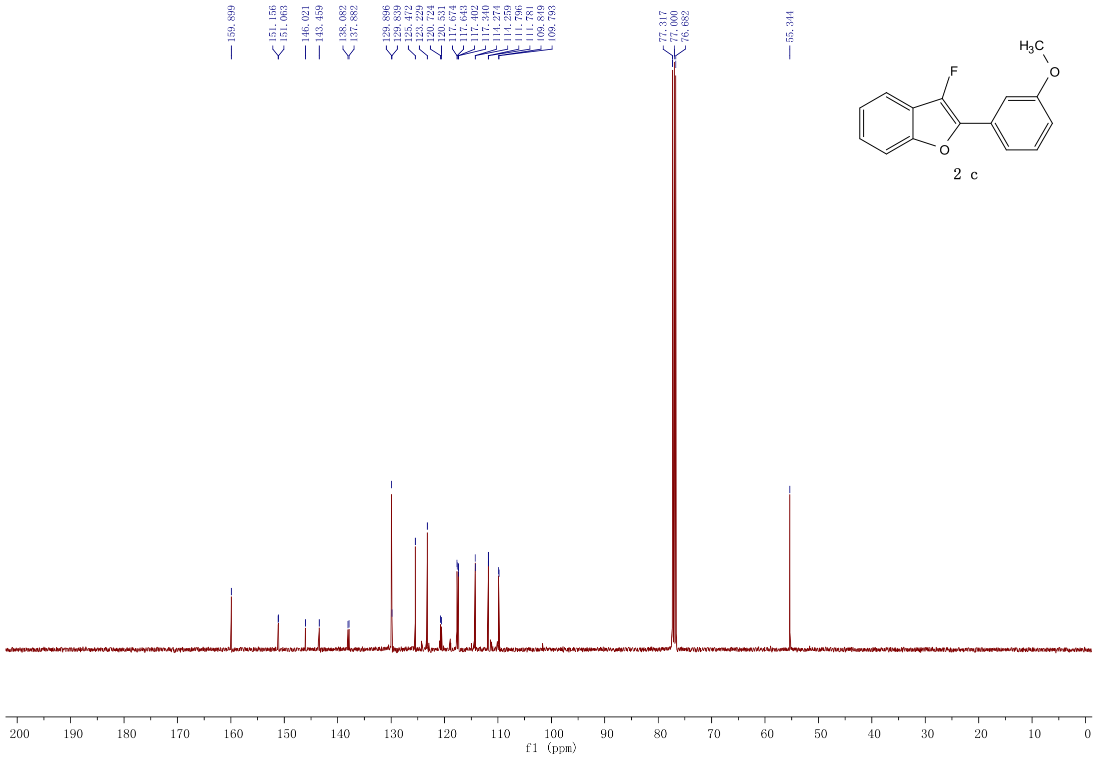

156.758
156.752
151.796
151.708
145.498
142.947
136.407
136.166
130.437
129.466
129.443
124.991
122.878
120.678
117.739
117.690
117.660
111.740
111.725
111.568
77.318
77.000
76.682
55.812
F
O
CH3
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

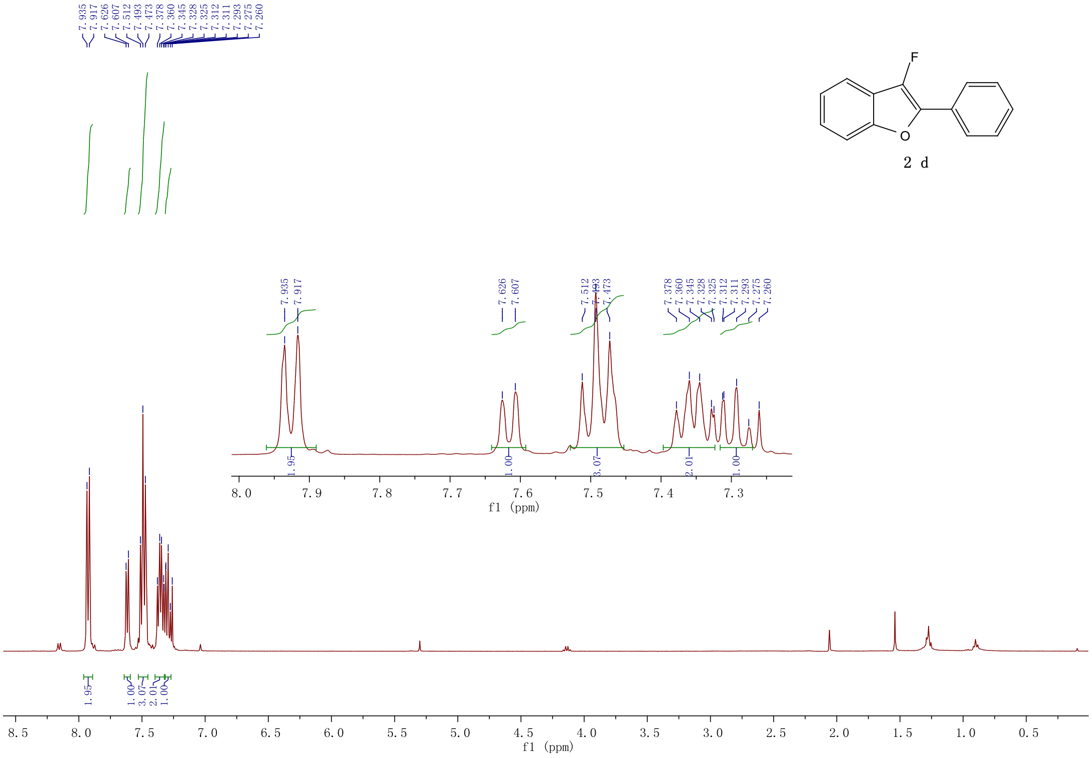
2 b

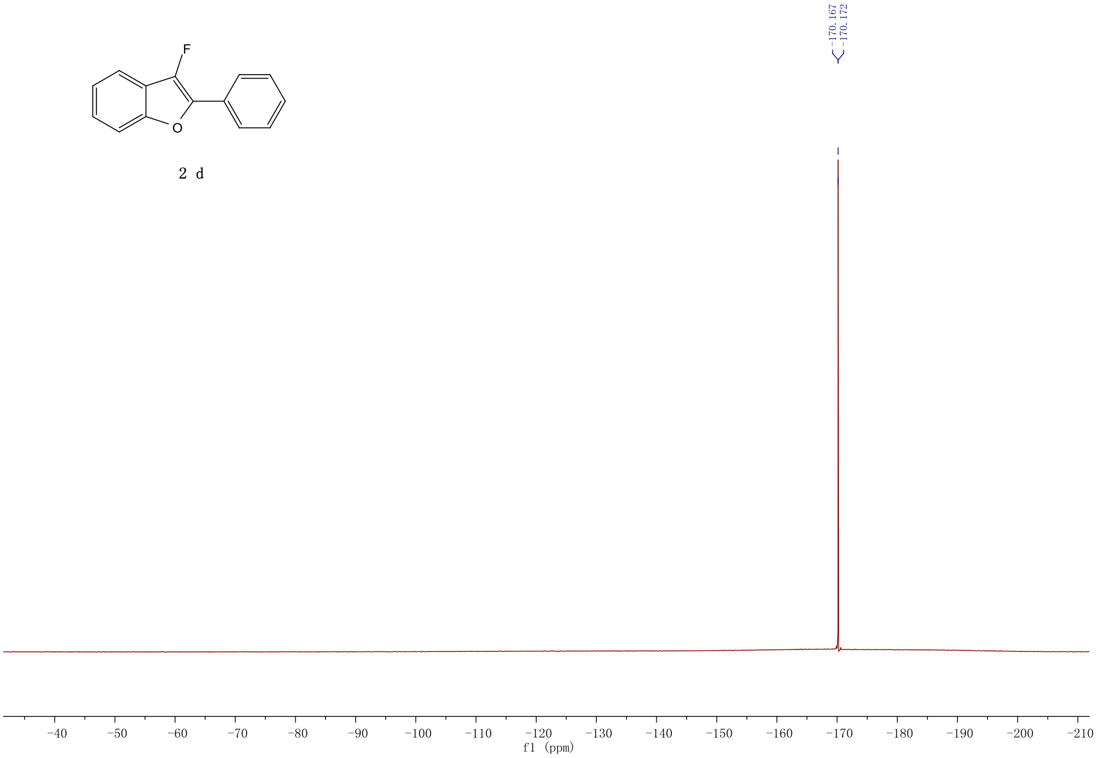

7.619
7.601
7.515
7.467
7.461
7.456
7.455
7.451
7.418
7.397
7.347
7.344
7.309
7.306
7.290
7.288
7.260
6.925
6.924
6.919
6.917
6.905
6.903
6.899
3.903
H3C
O
F
O
1.00
1.02
1.95
1.05
1.04
0.99
0.98
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

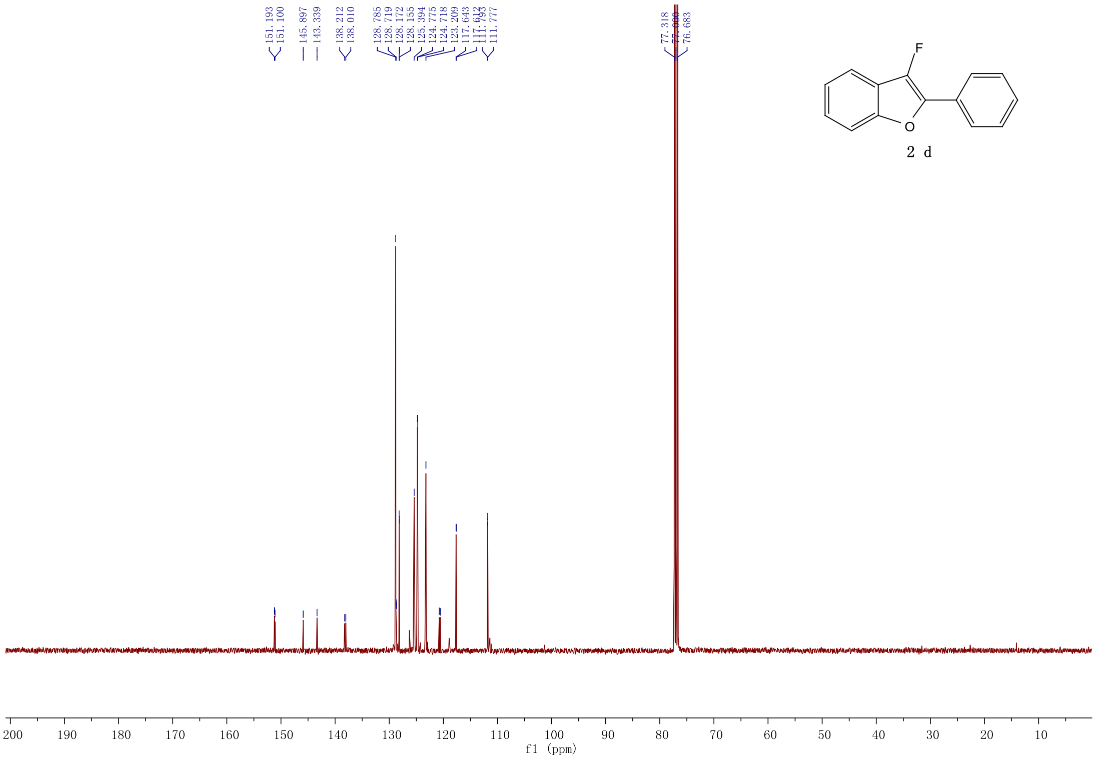
2 c


-169.484
-169.489
F
H3C
O
O
2 c
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

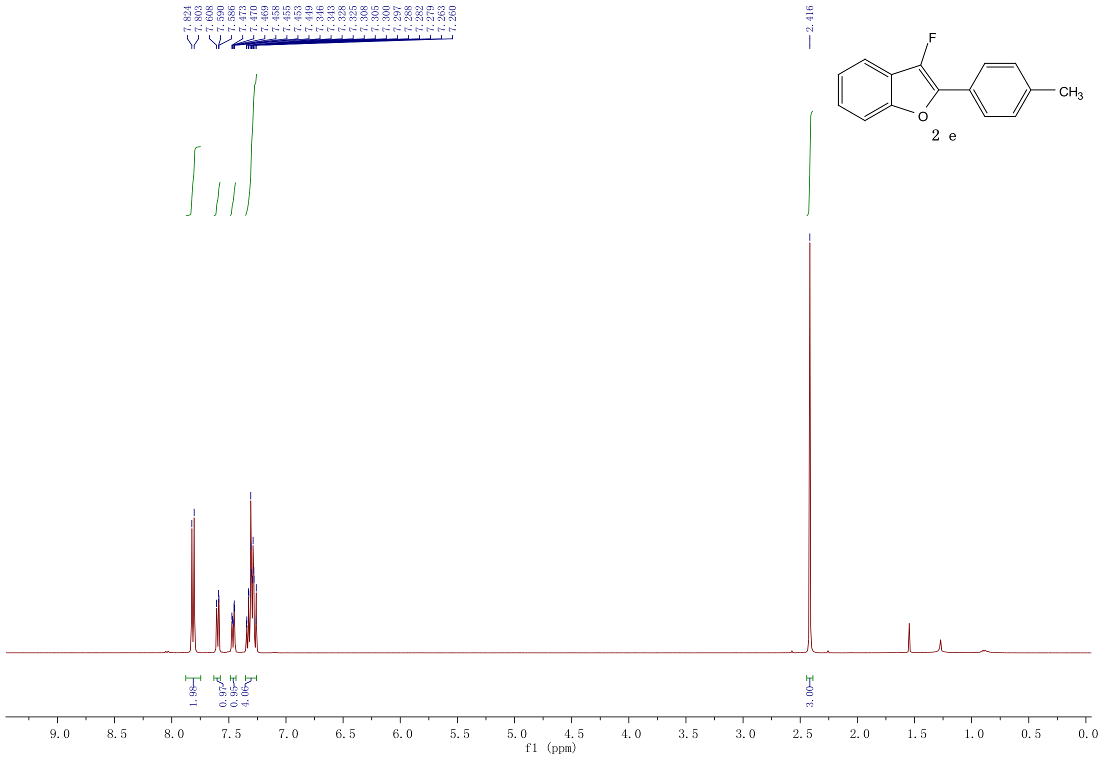

159.899
151.156
151.063
146.021
143.459
138.082
137.882
129.896
129.839
125.472
123.229
120.724
120.531
117.674
117.643
117.402
117.340
114.274
114.259
111.796
111.781
109.849
109.793
77.317
77.000
76.682
55.344
F
H3C
O
O
2 c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.935
7.917
7.626
7.607
7.512
7.493
7.473
7.378
7.360
7.345
7.328
7.325
7.312
7.311
7.293
7.275
7.260
F
O
2 d
1.95
1.00
3.07
2.01
1.00
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
f1 (ppm)
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
f1 (ppm)

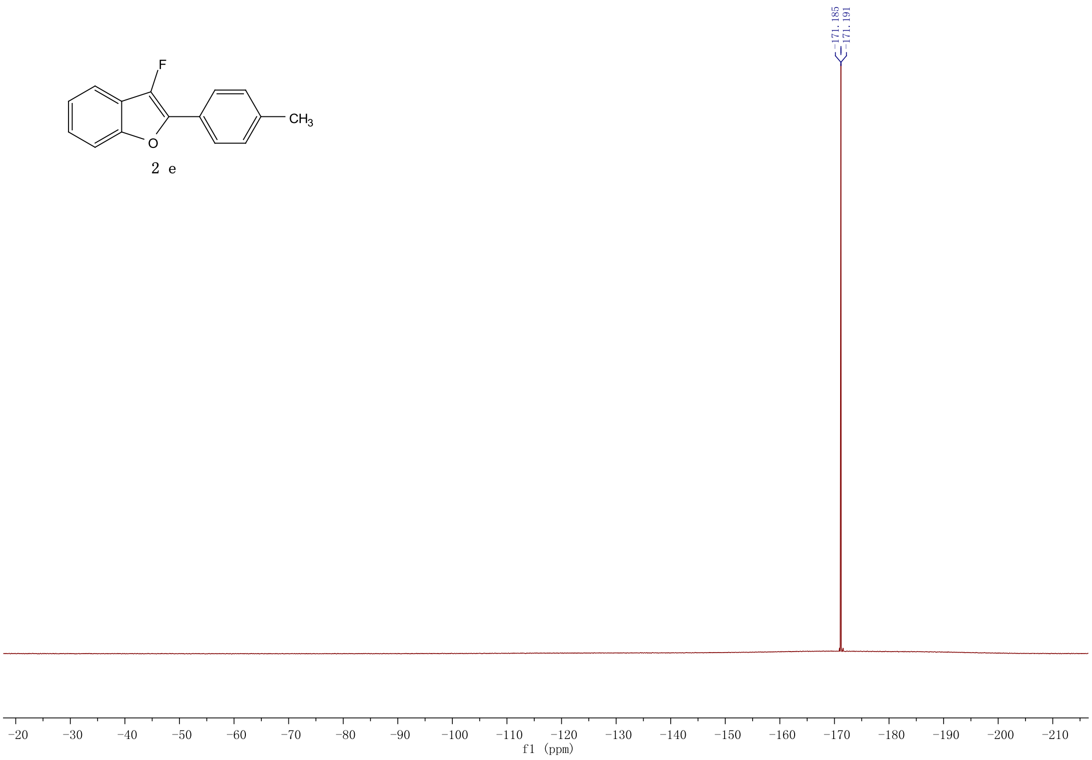

-170.167
-170.172
F
O
2 d
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

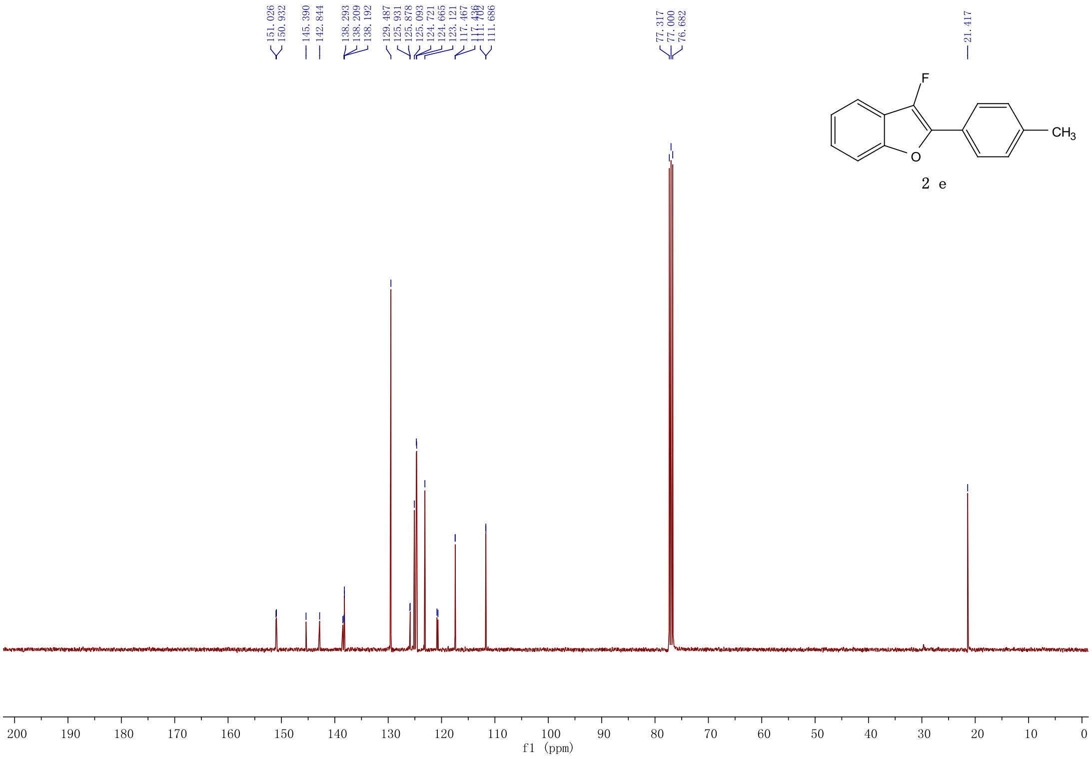

151.193
151.100
145.897
143.339
138.212
138.010
128.785
128.719
128.172
128.155
125.394
124.775
124.718
123.209
117.643
117.612
111.793
111.777
77.318
77.000
76.683
F
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

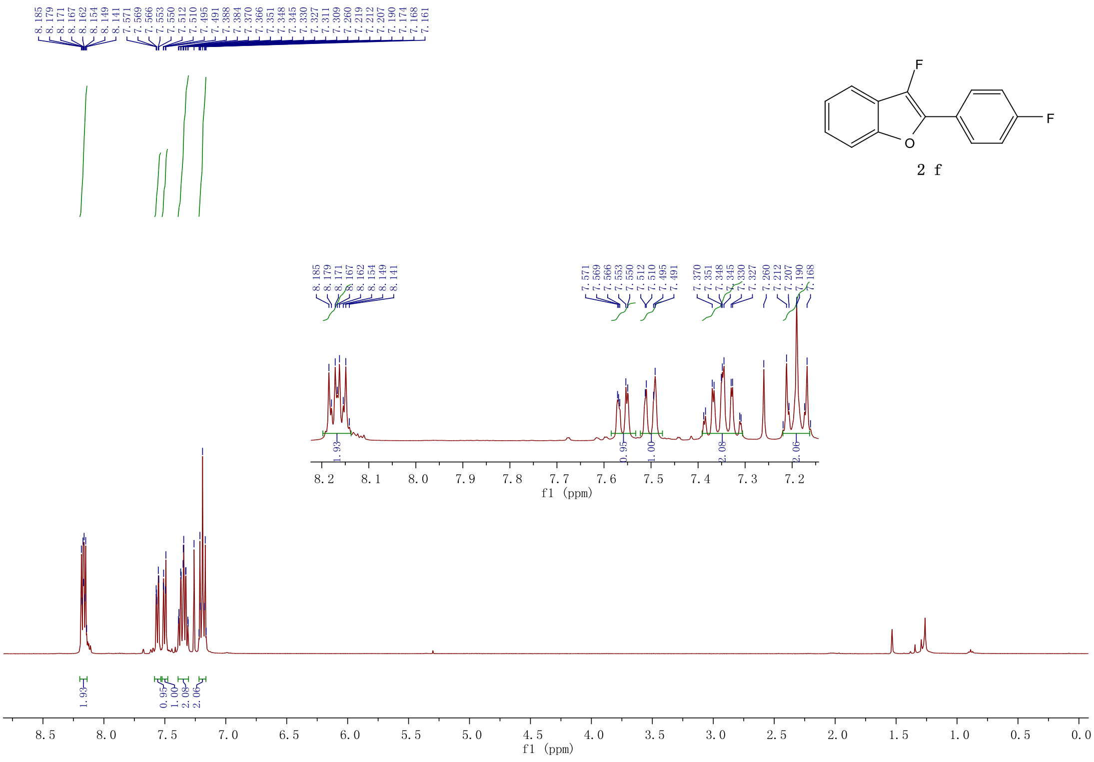
2 d

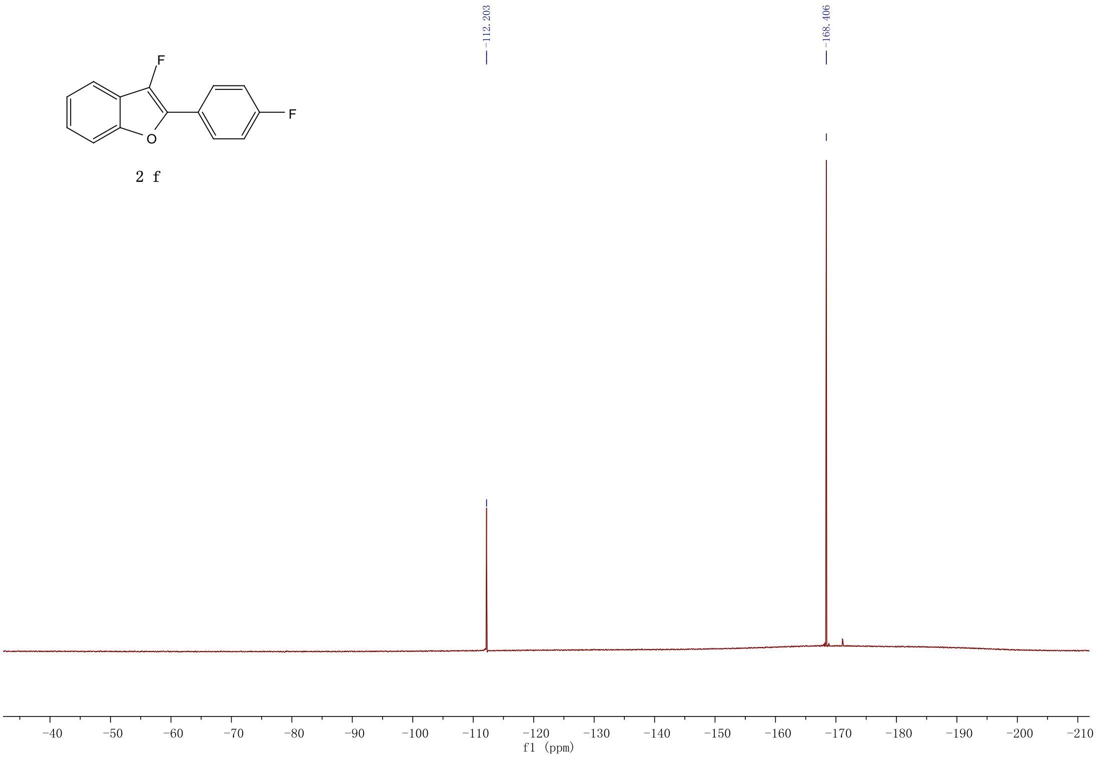

7.824
7.803
7.608
7.590
7.586
7.473
7.470
7.469
7.458
7.455
7.453
7.449
7.346
7.343
7.328
7.325
7.308
7.305
7.300
7.297
7.288
7.282
7.279
7.263
7.260
2.416
F
O
CH3
1.98
0.97
0.95
4.06
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

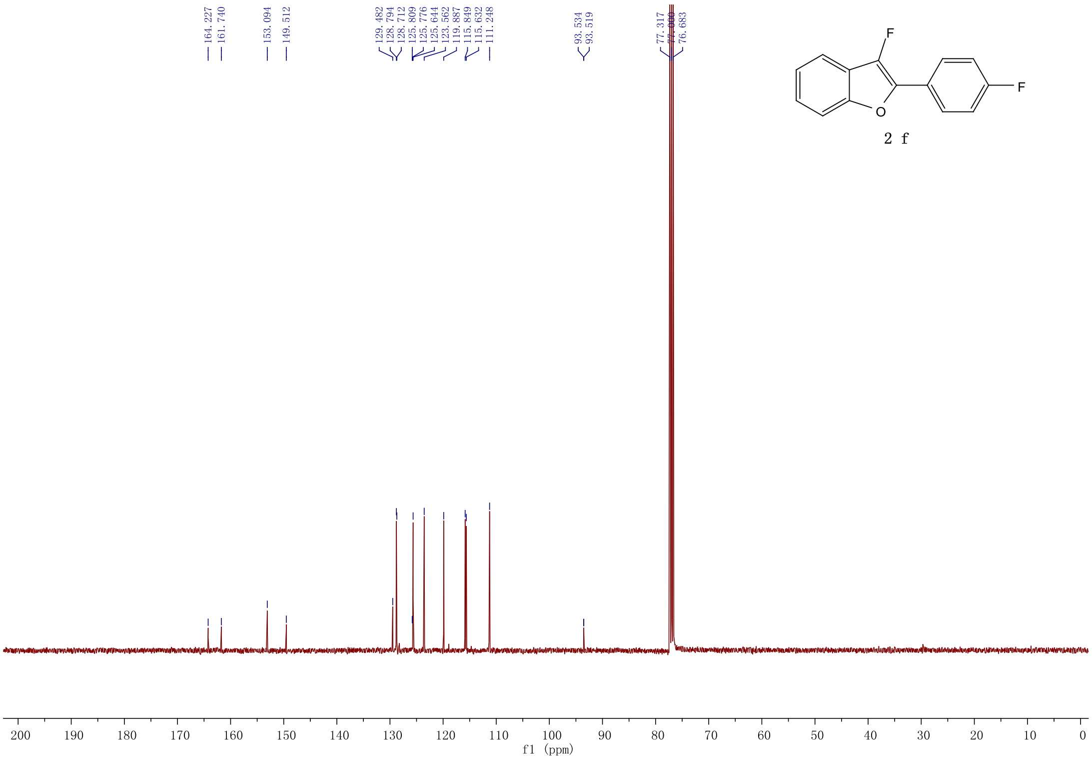
2 e


-171.185
-171.191
F
O
CH3
2 e
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

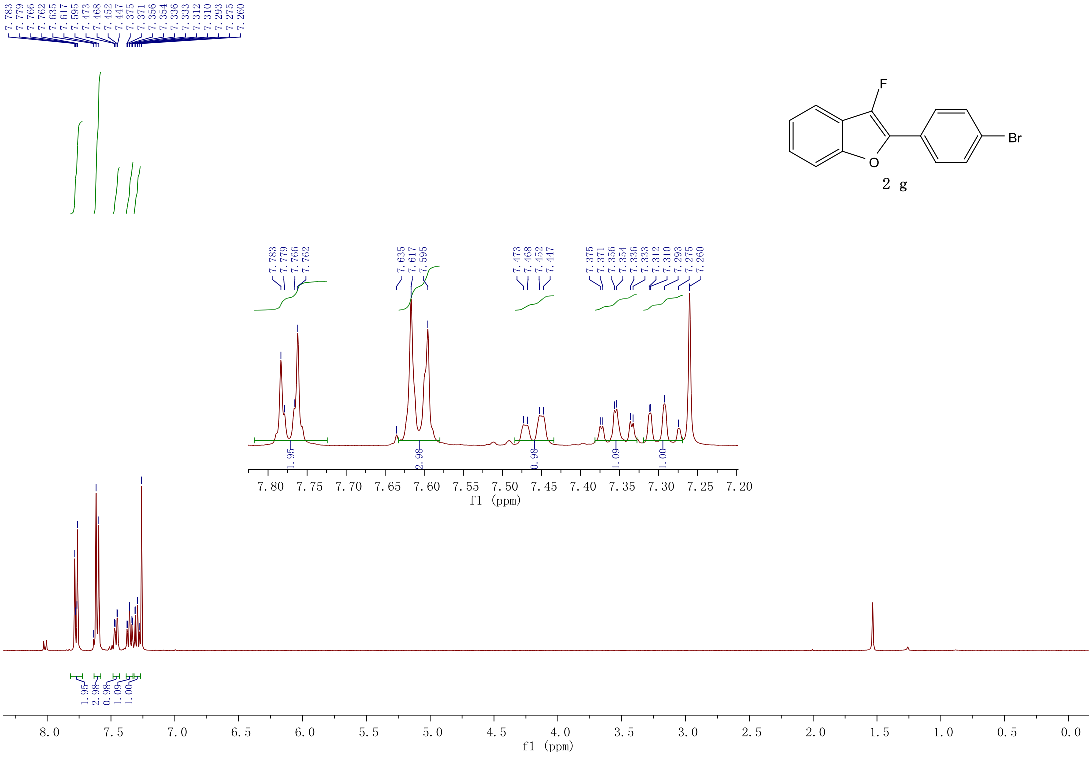

151.026
150.932
145.390
142.844
138.293
138.209
138.192
129.487
125.931
125.878
125.093
124.721
124.665
123.121
117.467
117.436
111.702
111.686
77.317
77.000
76.682
21.417
F
O
CH3
2 e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.185
8.179
8.171
8.167
8.162
8.154
8.149
8.141
7.571
7.569
7.566
7.553
7.550
7.512
7.510
7.495
7.491
7.388
7.384
7.370
7.366
7.351
7.348
7.345
7.330
7.327
7.311
7.309
7.260
7.219
7.212
7.207
7.190
7.174
7.168
7.161
F
O
F
2 f
1.93
0.95
1.00
2.08
2.06
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
f1 (ppm)
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
f1 (ppm)

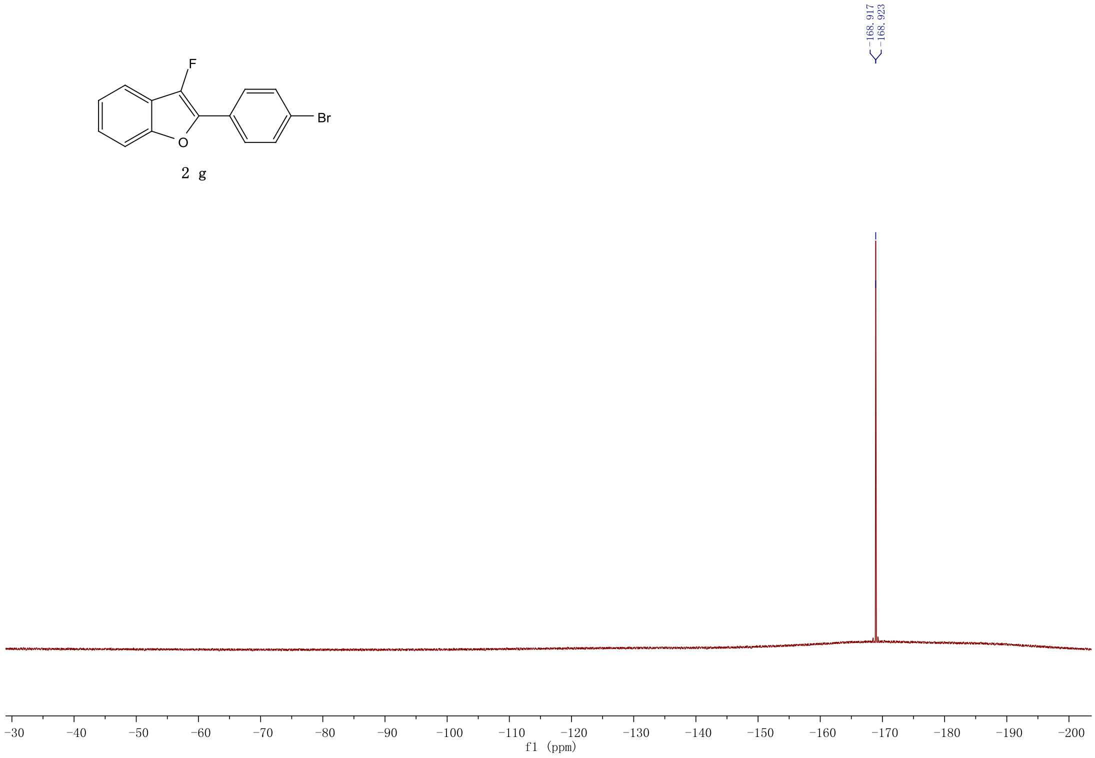

-112.203
-168.406
F
O
F
2 f
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

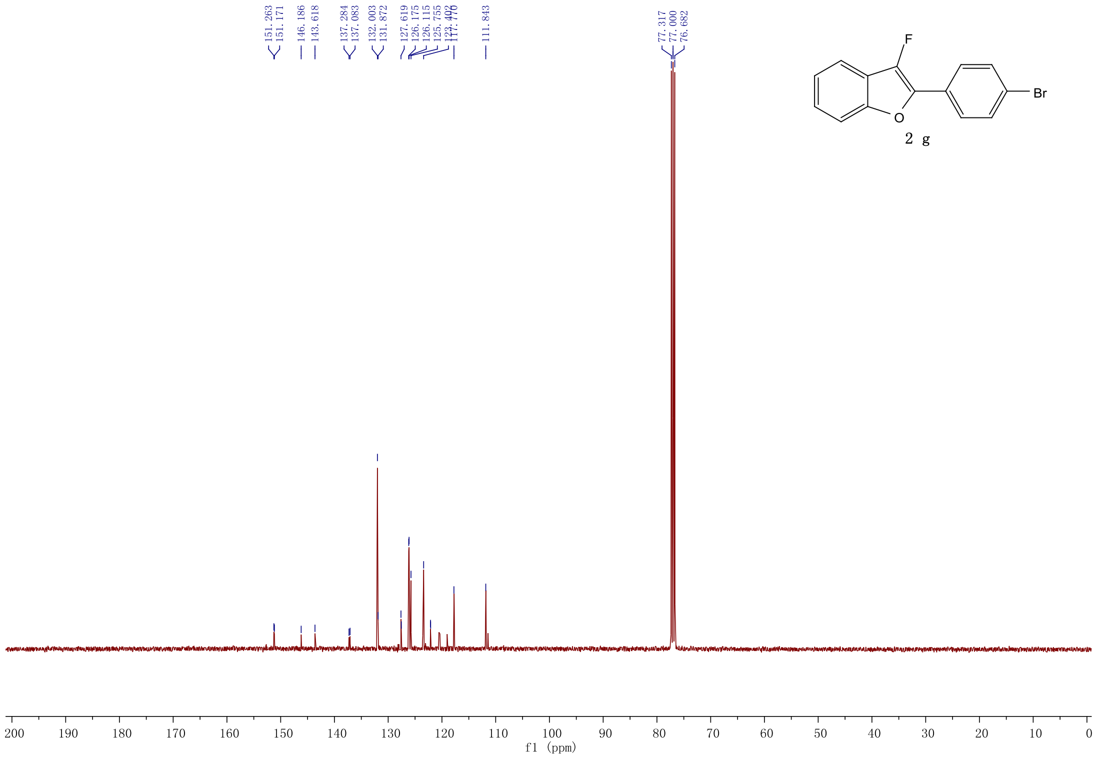

164.227
161.740
153.094
149.512
129.482
128.794
128.712
125.809
125.776
125.644
123.562
119.887
115.849
115.632
111.248
93.534
93.519
77.317
76.683
F
F
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

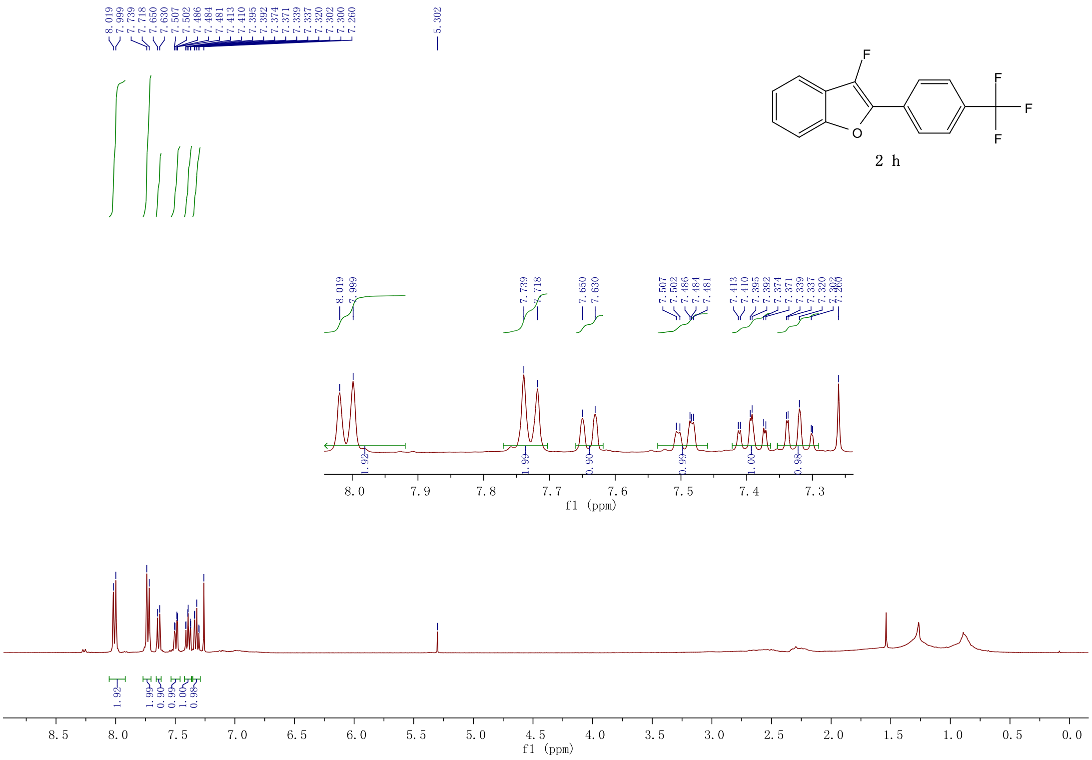
2 f

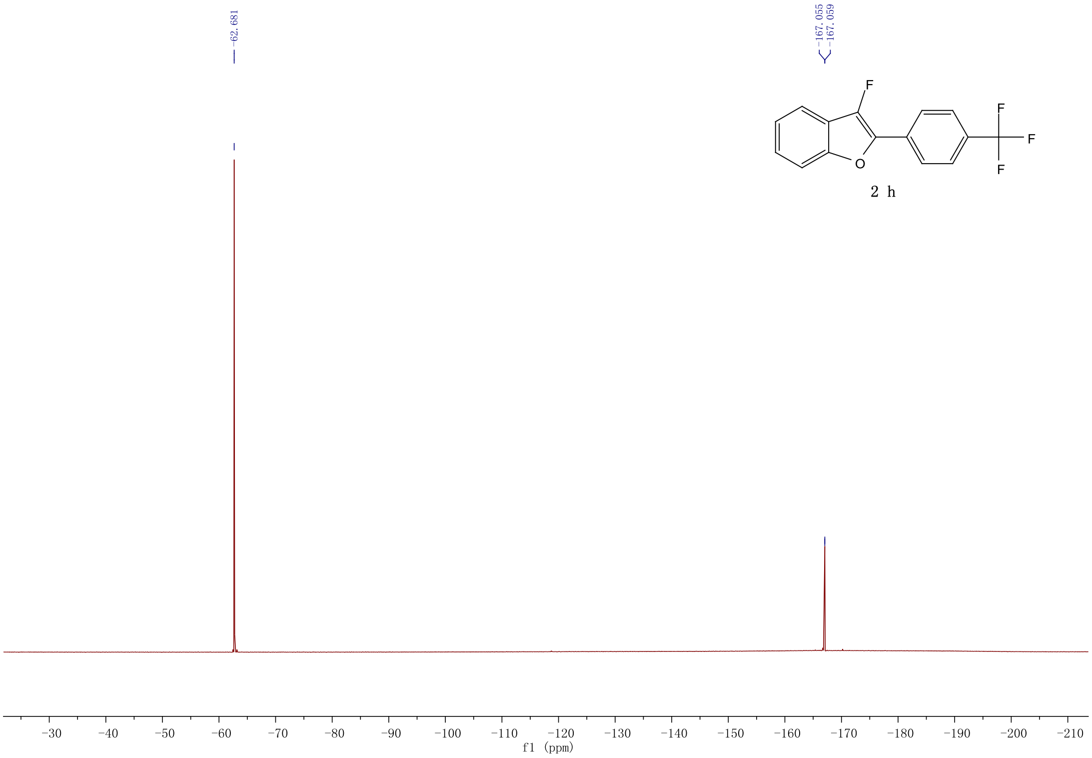

7.783
7.779
7.766
7.762
7.635
7.617
7.595
7.473
7.468
7.452
7.447
7.375
7.371
7.356
7.354
7.336
7.333
7.312
7.310
7.293
7.275
7.260
F
Br
O
1.95
2.98
0.98
1.09
1.00
7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20
f1 (ppm)
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

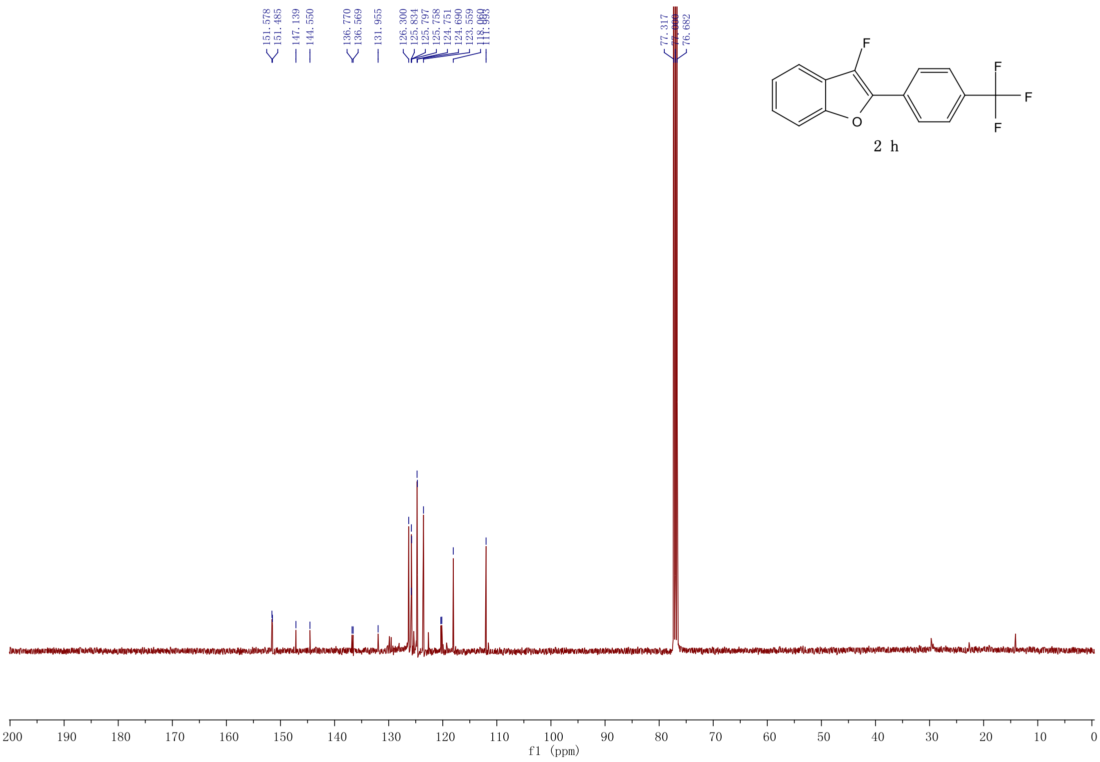
2 g

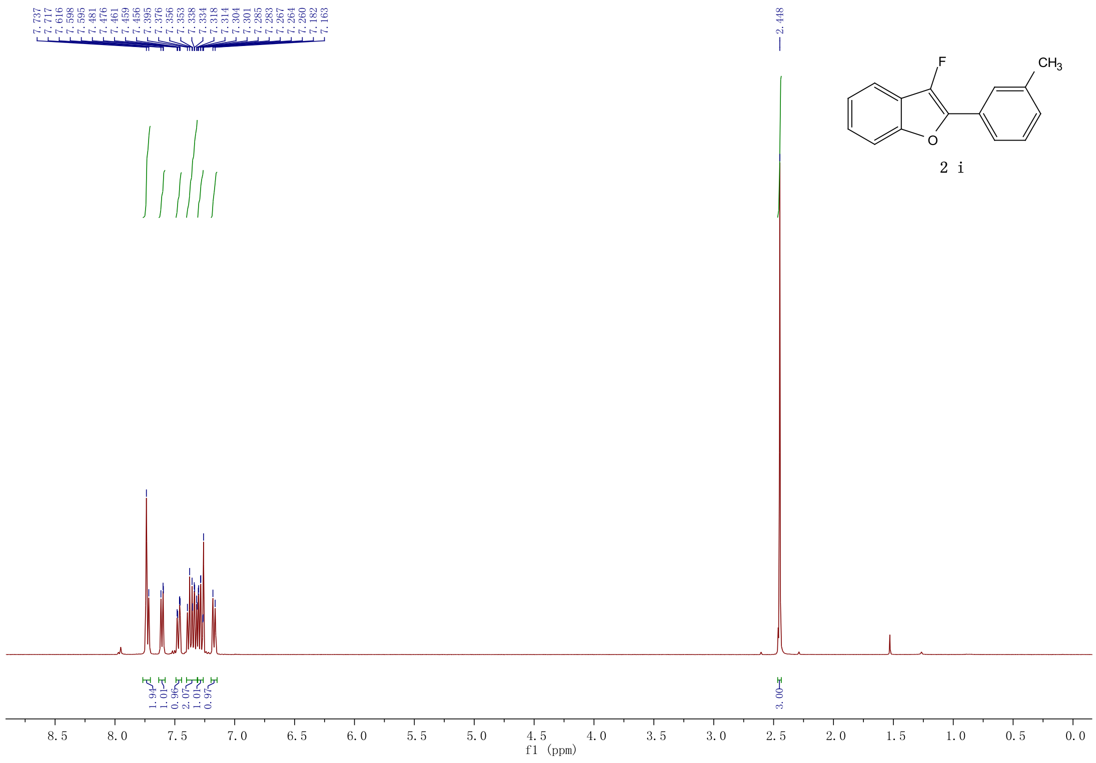

2 g
F
O
Br
-168.917
-168.923
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

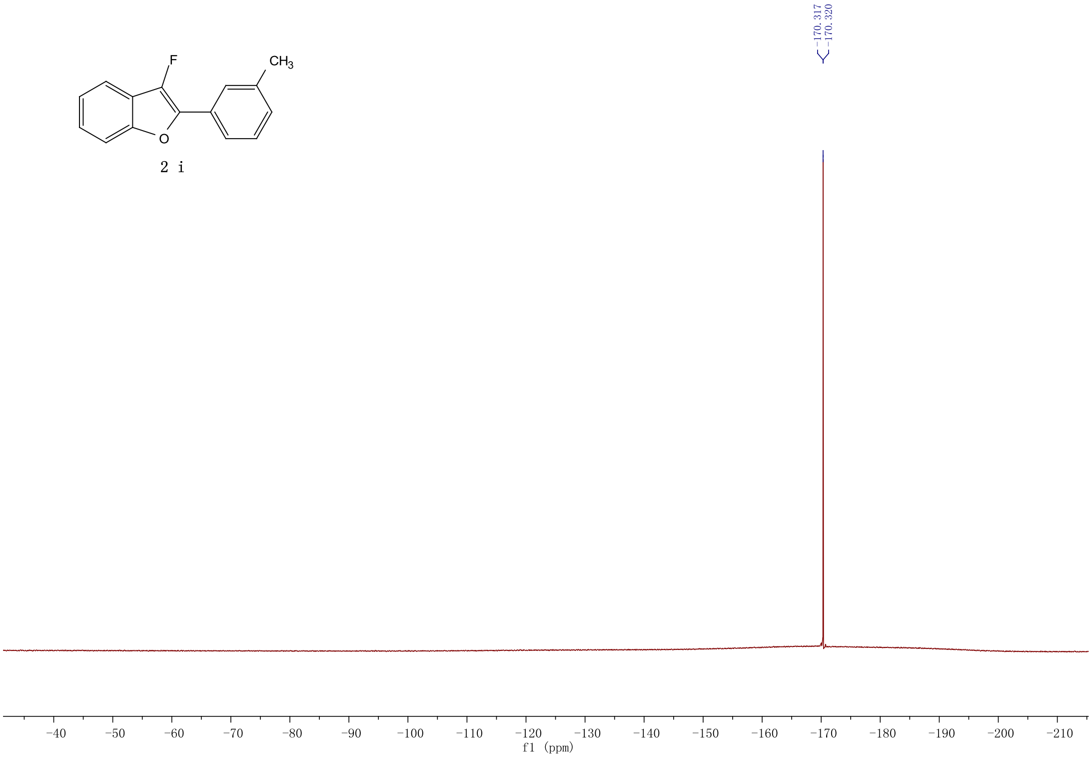

2 g
151.263
151.171
146.186
143.618
137.284
137.083
132.003
131.872
127.619
126.175
126.115
125.755
123.402
117.770
111.843
77.317
77.000
76.682
F
O
Br
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.019
7.999
7.739
7.718
7.650
7.630
7.507
7.502
7.486
7.484
7.481
7.413
7.410
7.395
7.392
7.374
7.371
7.339
7.337
7.320
7.302
7.300
7.260
5.302
F
F
F
F
O
2 h
1.92
1.99
0.90
0.99
1.00
0.98
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
f1 (ppm)
1.92
1.99
0.90
0.99
1.00
0.98
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
f1 (ppm)

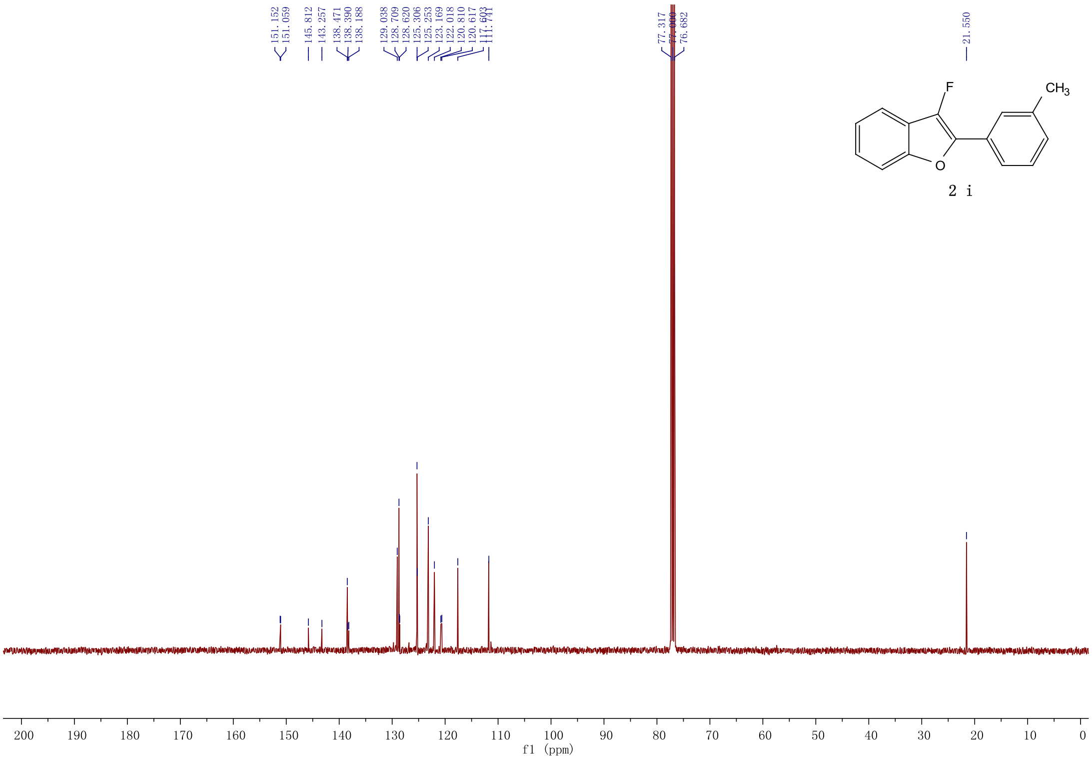

-62.681
-167.055
-167.059
F
F
F
F
O
2 h
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


151.578
151.485
147.139
144.550
136.770
136.569
131.955
126.300
125.834
125.797
125.758
124.751
124.690
123.559
118.060
111.993
77.317
77.000
76.682
F
O
F
F
F
2 h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

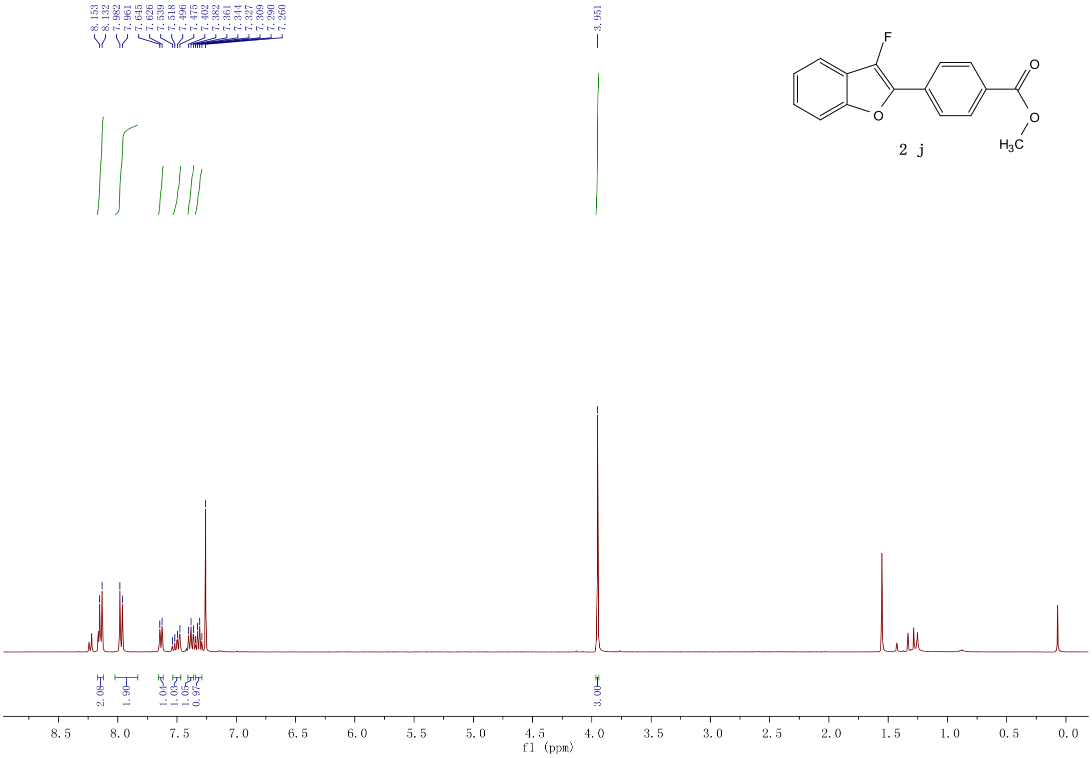

7.737
7.717
7.616
7.598
7.595
7.481
7.476
7.461
7.459
7.456
7.395
7.376
7.356
7.353
7.338
7.334
7.318
7.314
7.304
7.301
7.285
7.283
7.267
7.264
7.260
7.182
7.163
2.448
F
CH_3
O
2 i
1.94
1.01
0.96
2.07
1.01
0.97
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

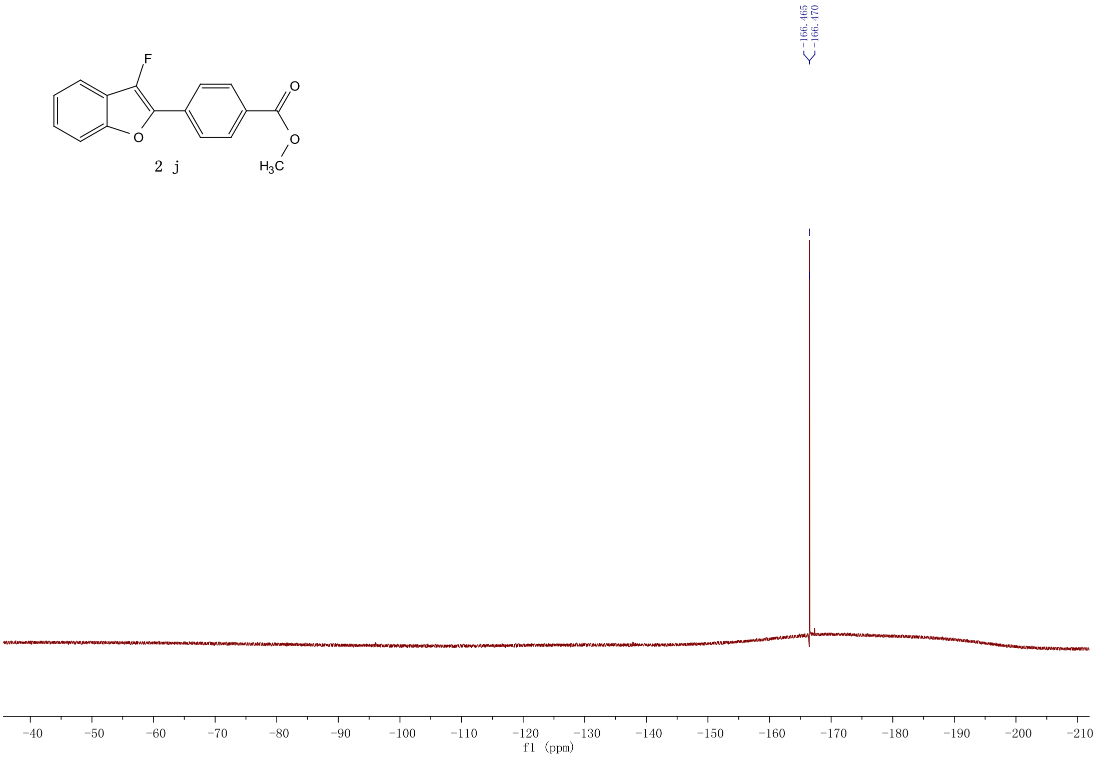


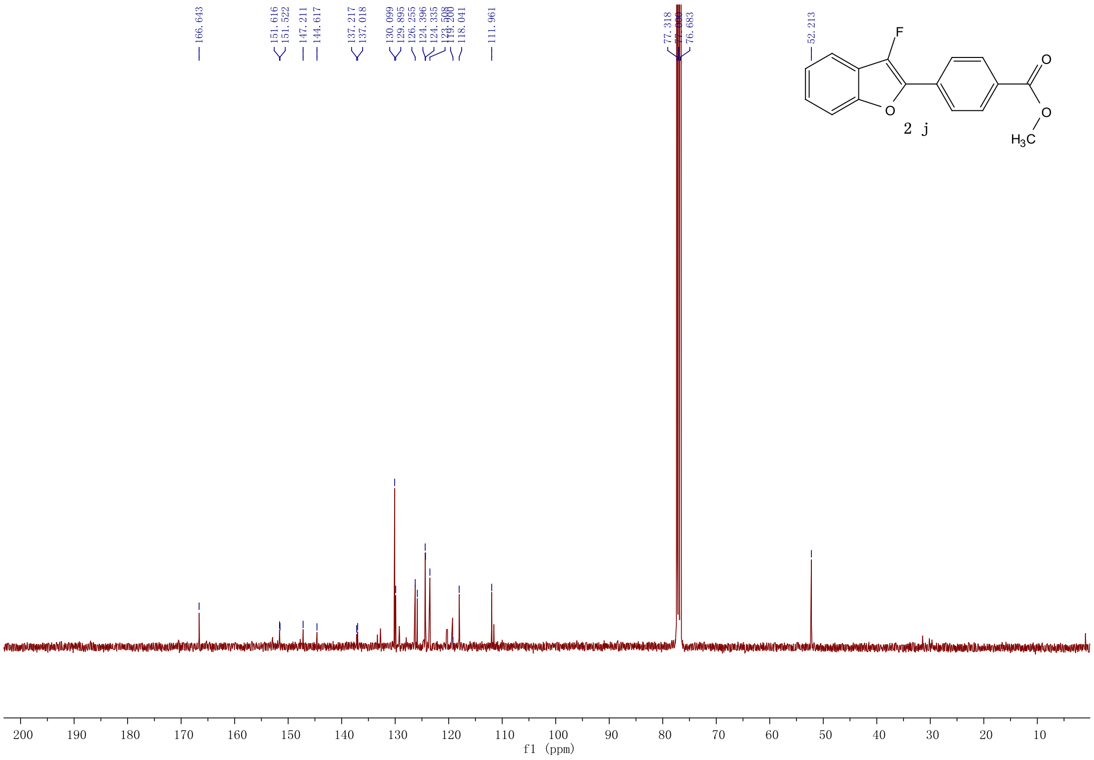
F
CH3
O
2 i
-170.317
-170.320
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)



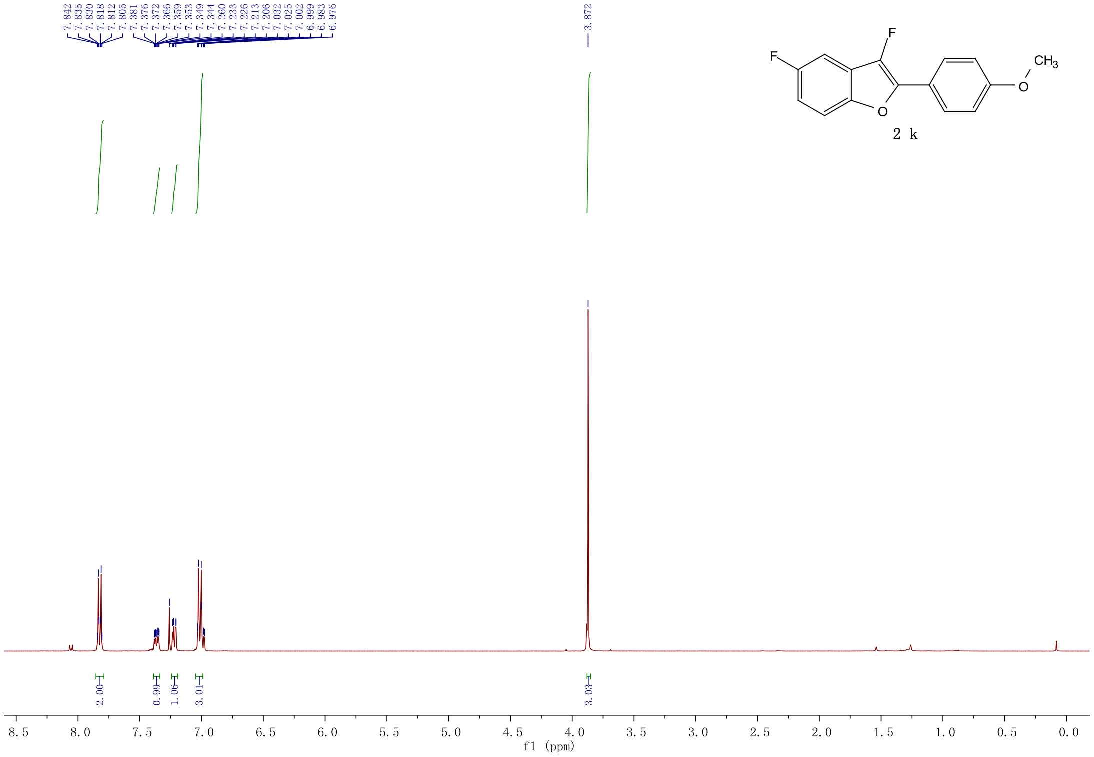
151.152
151.059
145.812
143.257
138.471
138.390
138.188
129.038
128.709
128.620
125.306
125.253
123.169
122.018
120.810
120.617
117.603
111.741
77.317
77.000
76.682
21.550
F
CH3
O
2 i
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.153
8.132
7.982
7.961
7.645
7.626
7.539
7.518
7.496
7.475
7.402
7.382
7.361
7.344
7.327
7.309
7.290
7.260
3.951
F
O
O
O
H_3C
2 j
2.08
1.90
1.04
1.03
1.05
0.97
3.00
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
f1 (ppm)

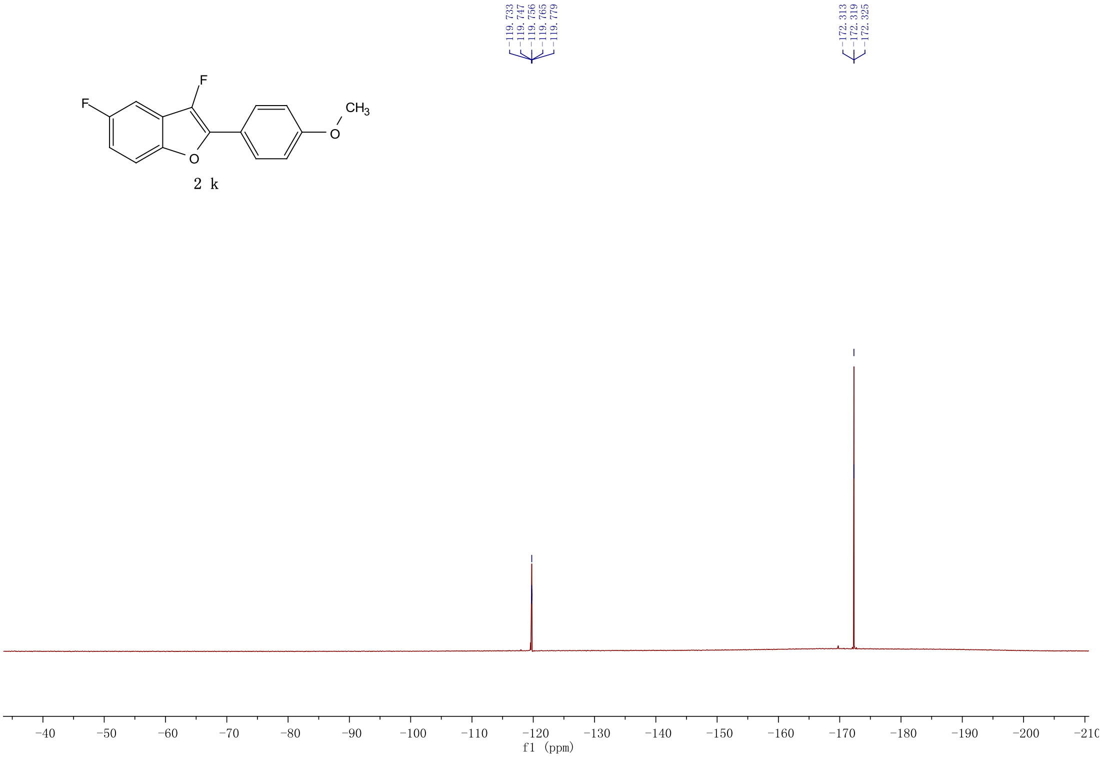

-166.465
-166.470
F
O
O
O
H_3C
2 j
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

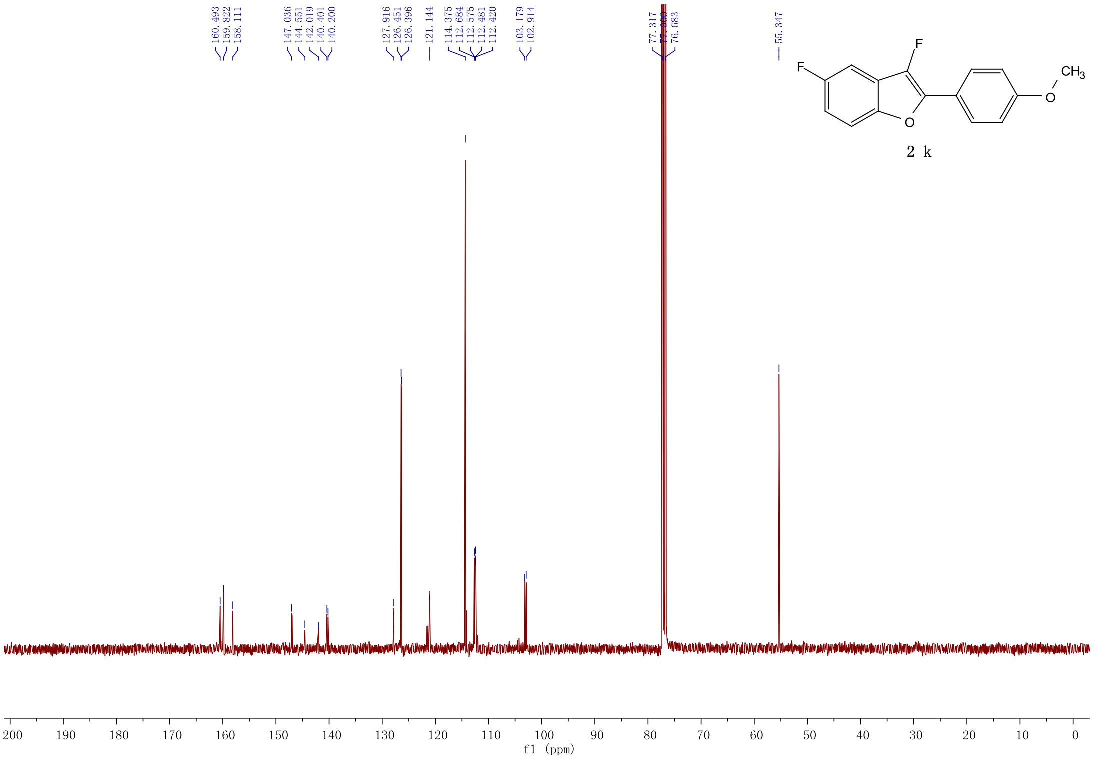

166.643
151.616
151.522
147.211
144.617
137.217
137.018
130.099
129.895
126.255
124.396
124.335
123.508
119.200
118.041
111.961
77.318
77.000
76.683
52.213
F
O
O
O
H3C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

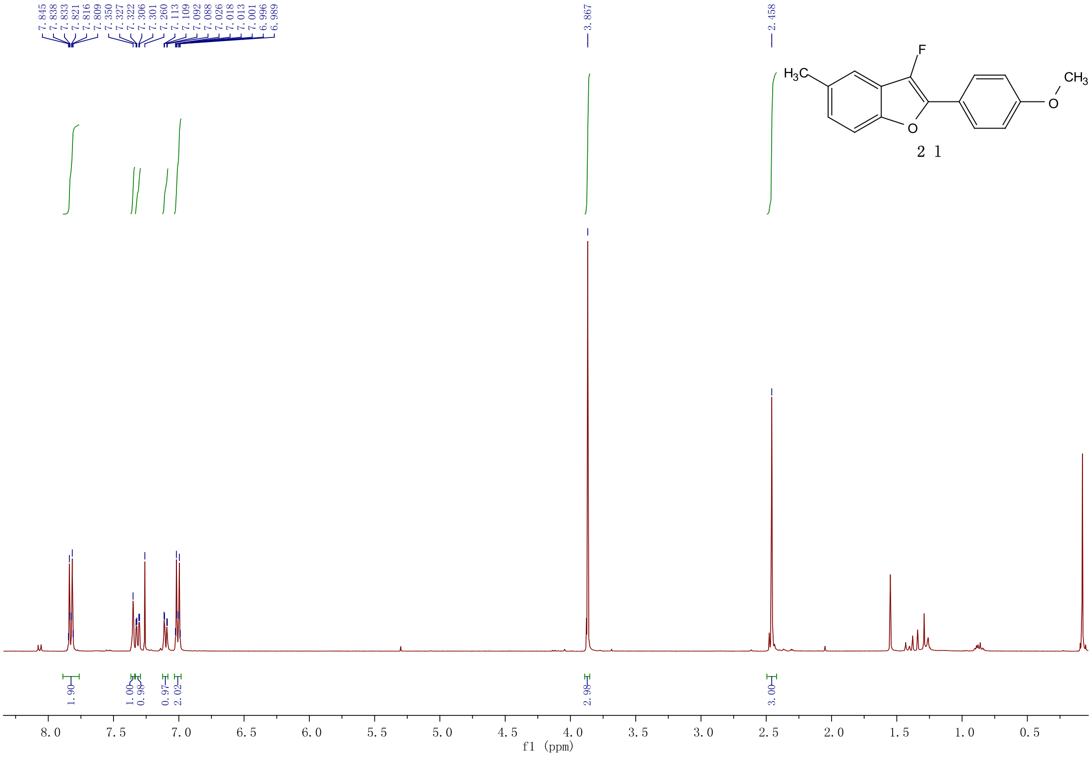
2 j

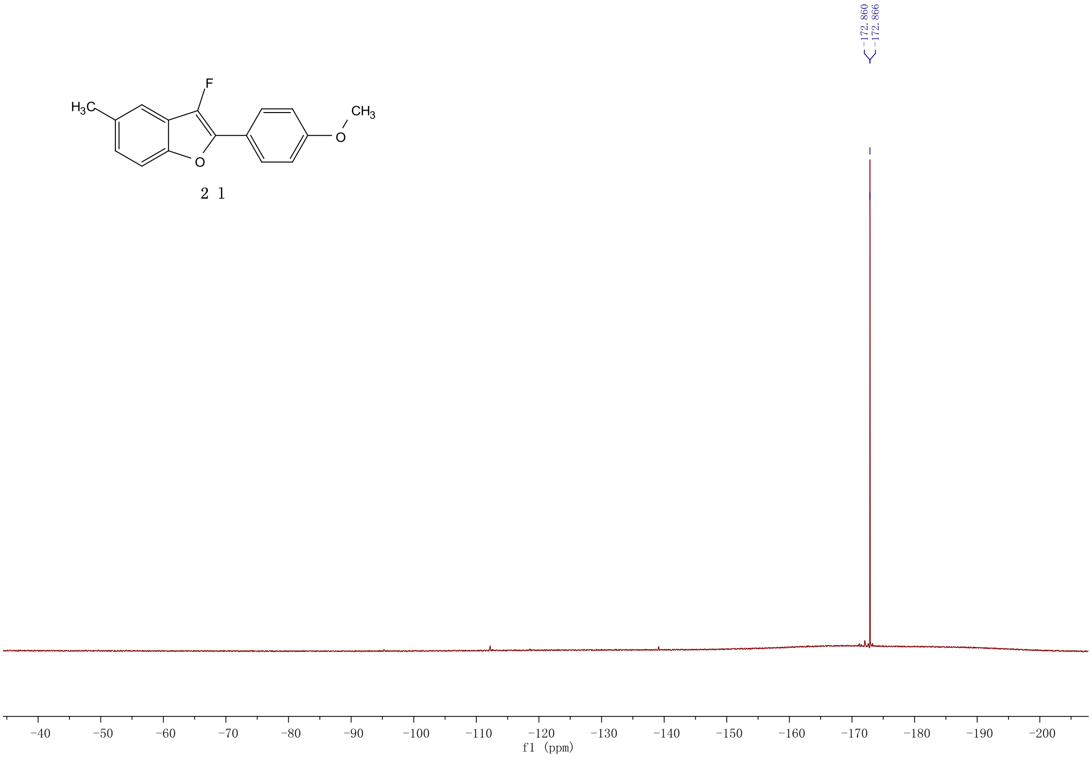

7.842
7.835
7.830
7.818
7.812
7.805
7.381
7.376
7.372
7.366
7.359
7.353
7.349
7.344
7.260
7.233
7.226
7.213
7.206
7.032
7.025
7.002
6.999
6.983
6.976
3.872
F
F
O
O
CH3
2.00
0.99
1.06
3.01
3.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

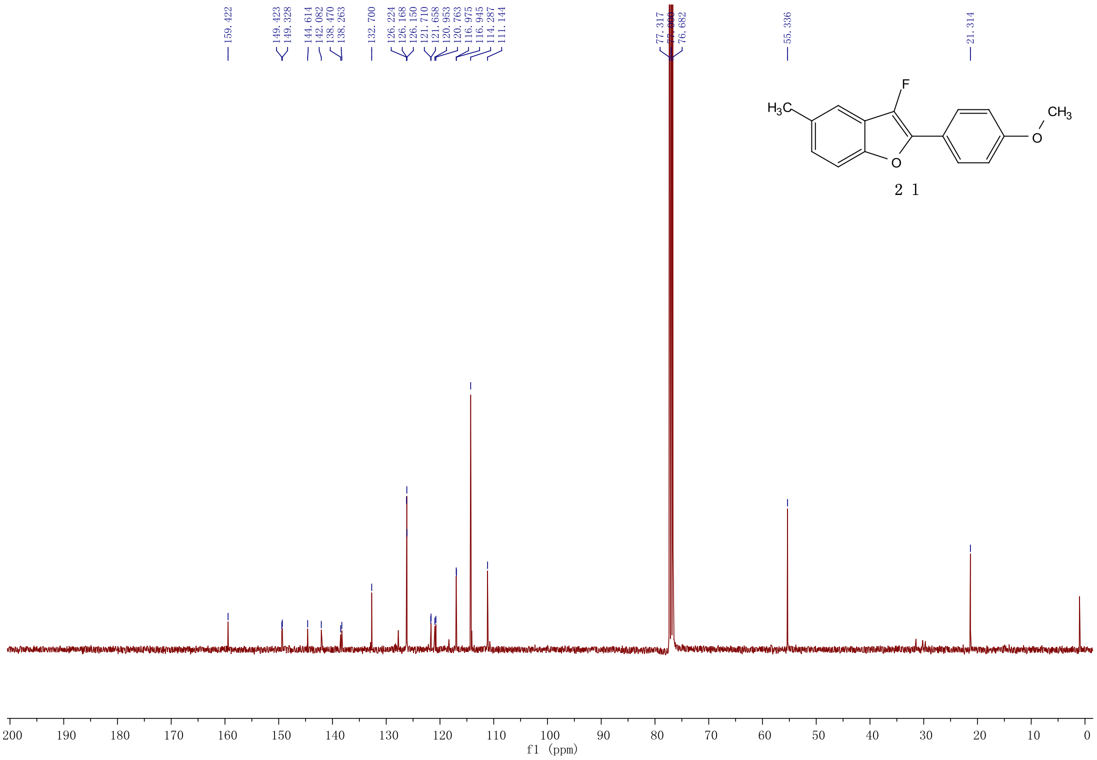
2 k


-119.733
-119.747
-119.756
-119.765
-119.779
-172.313
-172.319
-172.325
F
F
O
O
CH3
2 k
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-21
f1 (ppm)

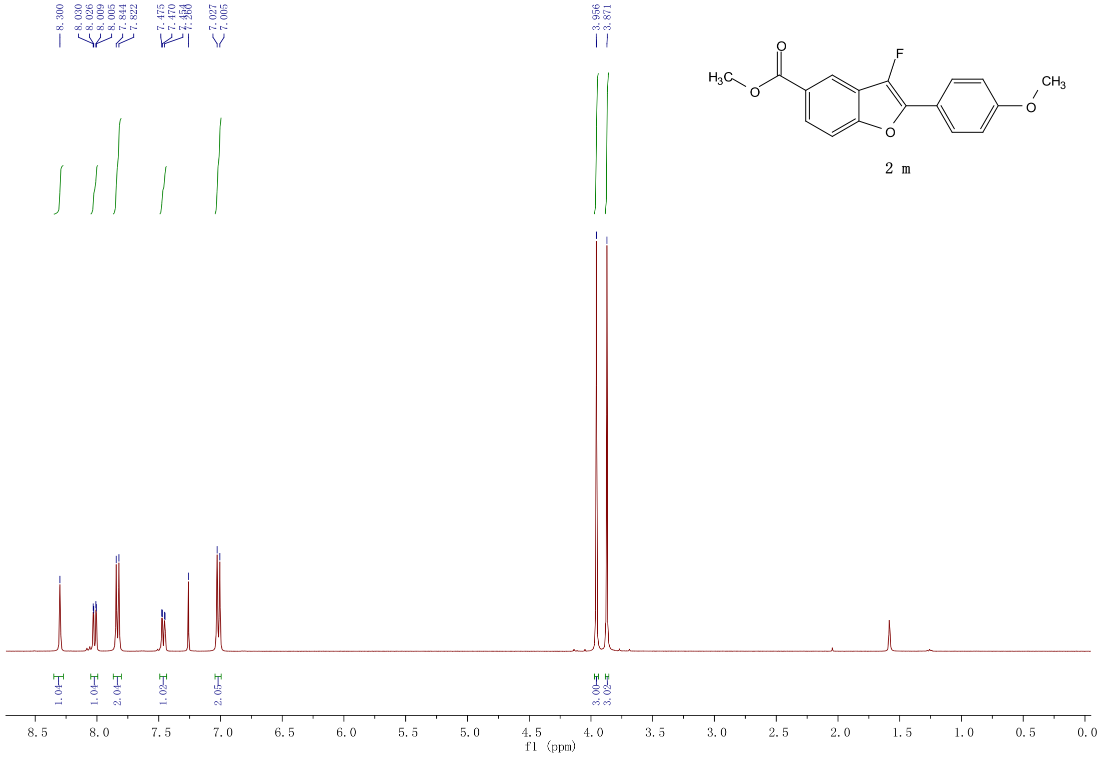

160.493
159.822
158.111
147.036
144.551
142.019
140.401
140.200
127.916
126.451
126.396
121.144
114.375
112.684
112.575
112.481
112.420
103.179
102.914
77.317
77.000
76.683
55.347
F
F
O
O
CH3
2 k
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.845
7.838
7.833
7.821
7.816
7.809
7.350
7.327
7.322
7.306
7.301
7.260
7.113
7.109
7.092
7.088
7.026
7.018
7.013
7.001
6.996
6.989
3.867
2.458
F
H_3C
O
CH_3
O
2 1
1.90
1.00
0.98
0.97
2.02
2.98
3.00
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
f1 (ppm)

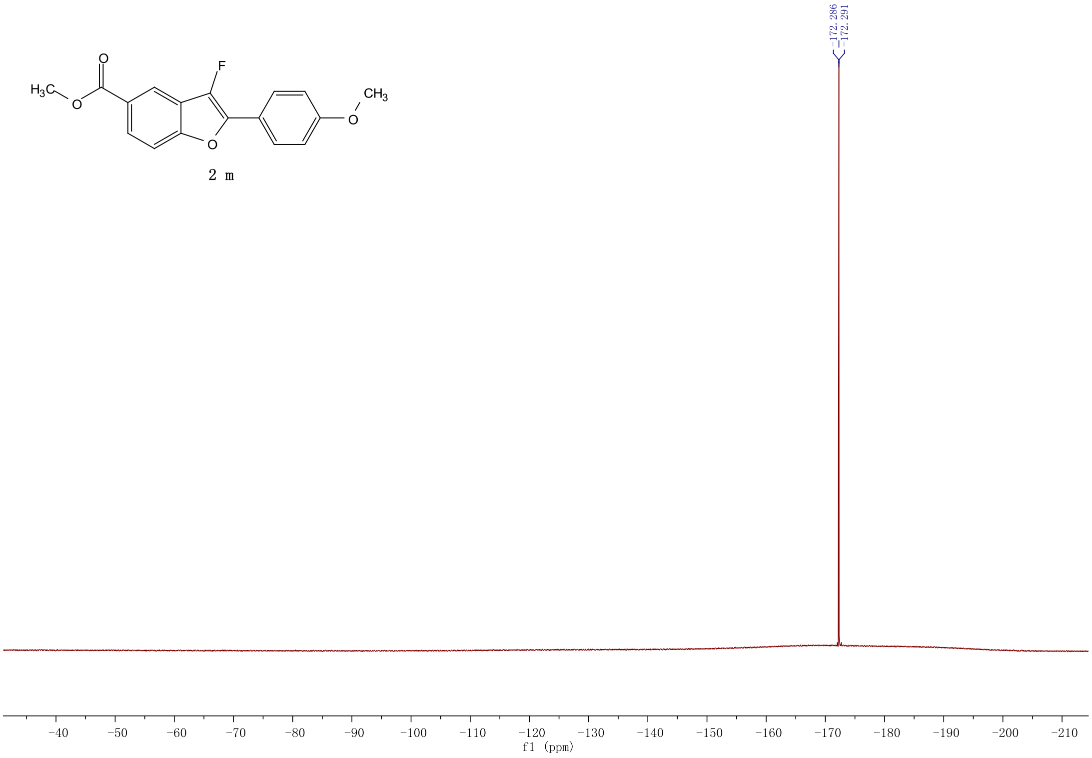

-172.860
-172.866
F
H_3C
O
CH_3
O
2 1
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

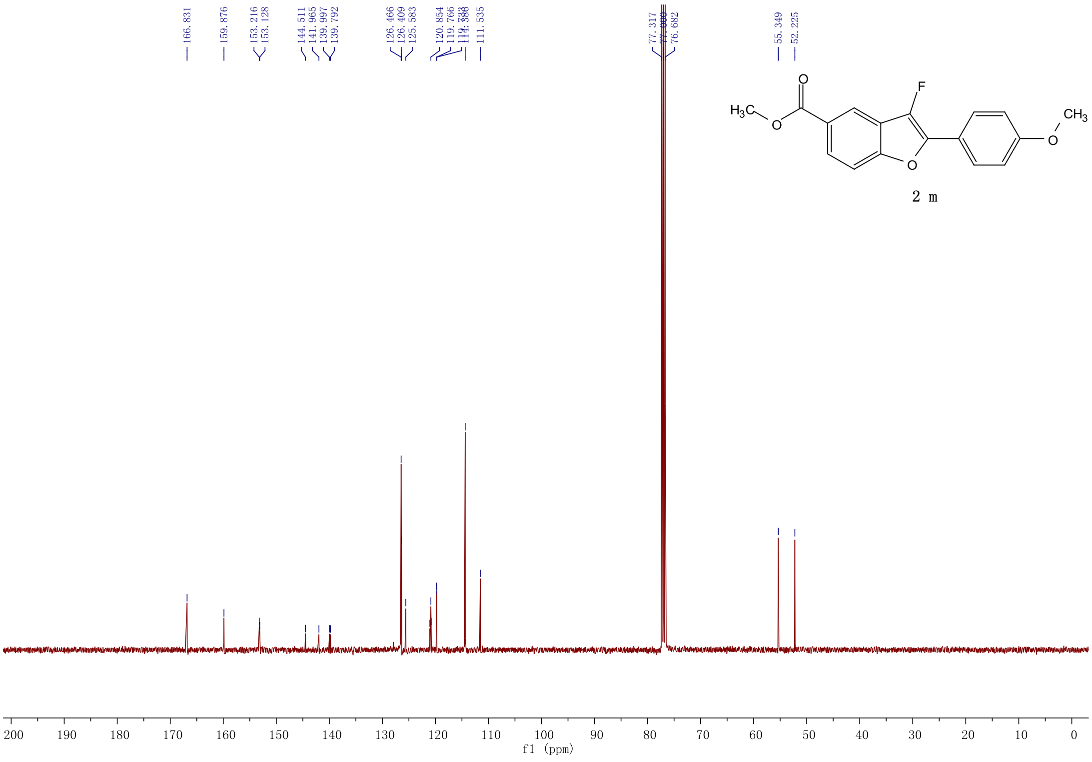

159.422
149.423
149.328
144.614
142.082
138.470
138.263
132.700
126.224
126.168
126.150
121.710
121.658
120.953
120.763
116.975
116.945
114.287
111.144
77.317
77.000
76.682
55.336
21.314
F
H3C
O
CH3
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

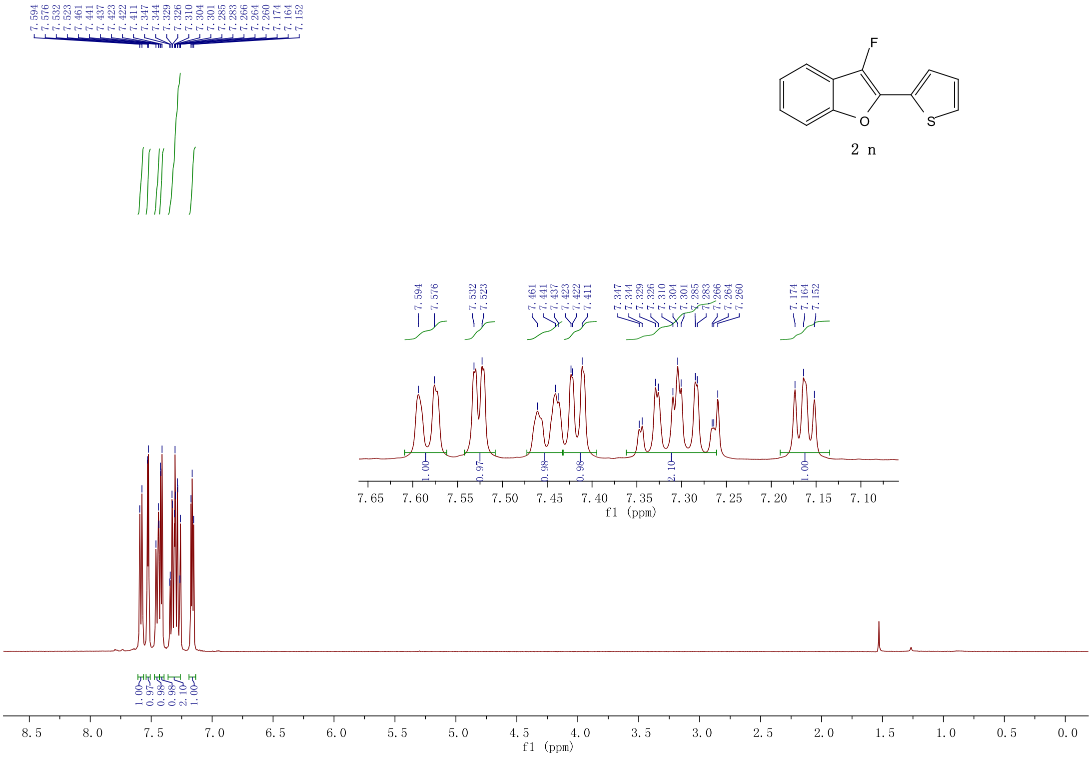
2 l

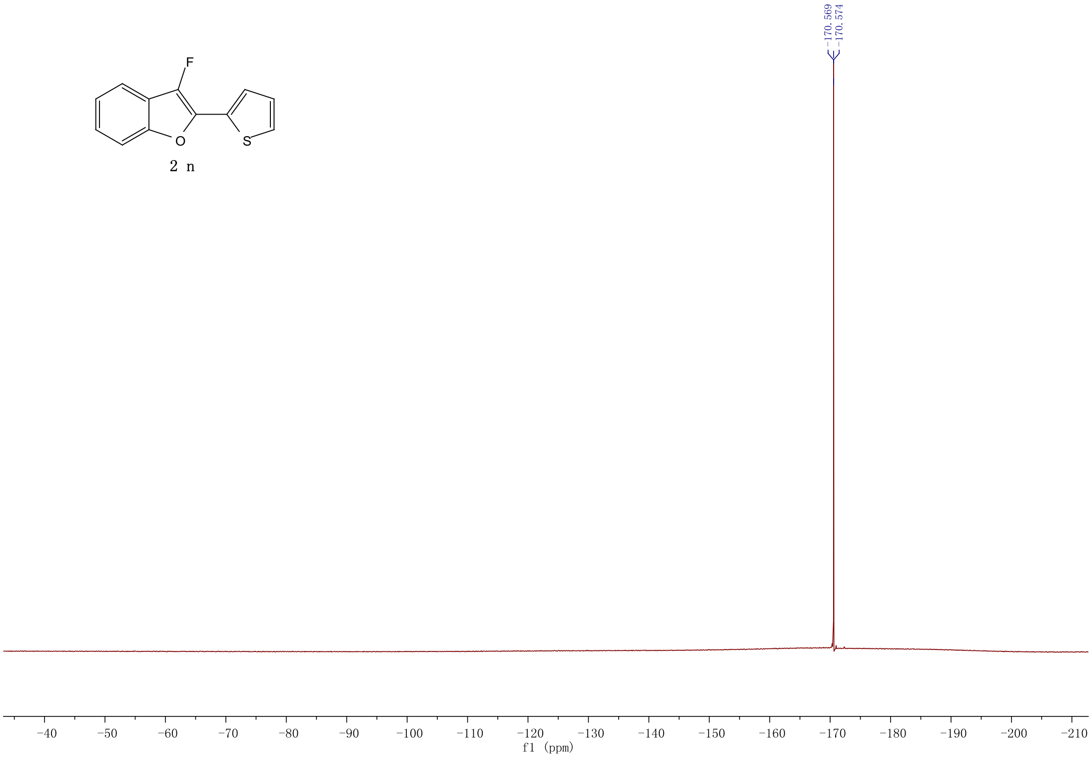

8.300
8.030
8.026
8.009
8.005
7.844
7.822
7.475
7.470
7.454
7.260
7.027
7.005
3.956
3.871
O
H3C
O
F
O
CH3
O
1.04
1.04
2.04
1.02
2.05
3.00
3.02
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

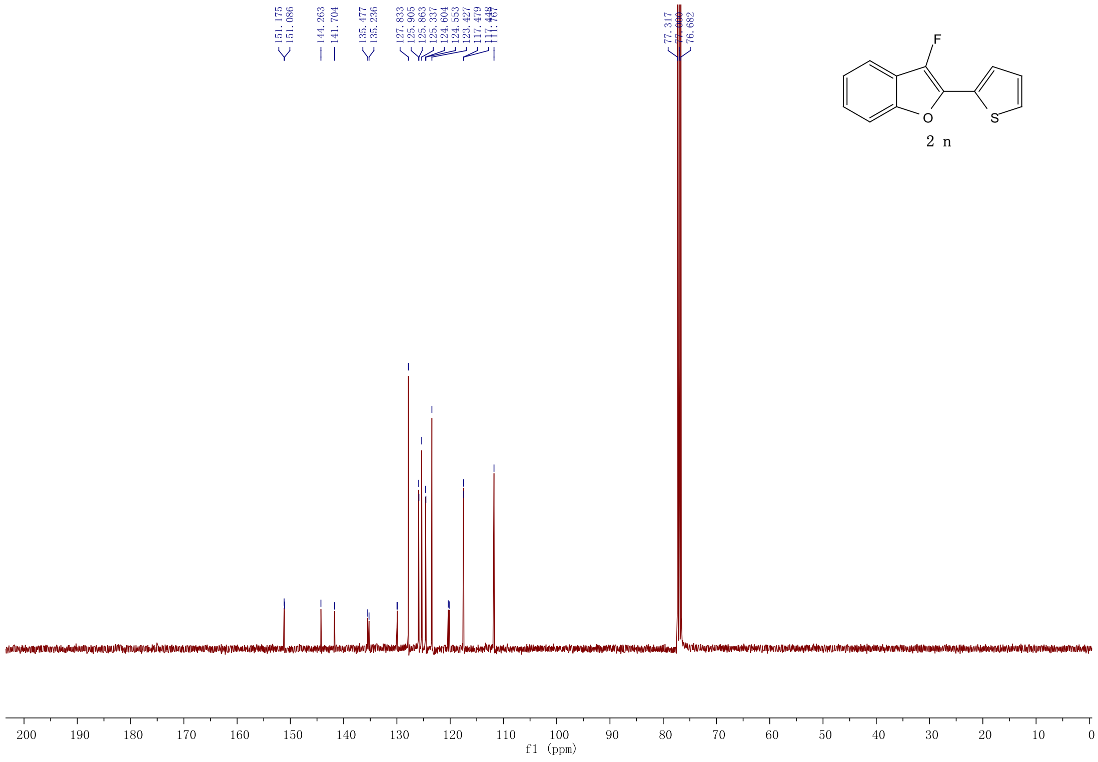
2 m

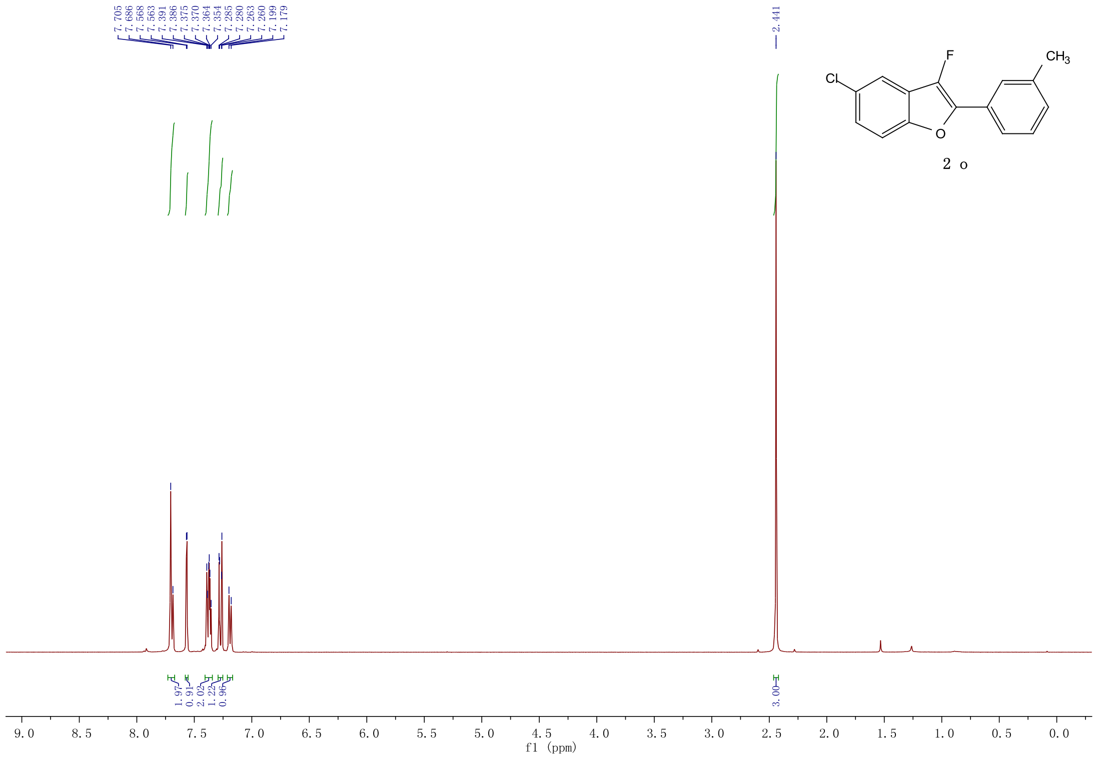

-172.286
-172.291
H3C
O
O
F
O
O
CH3
2 m
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

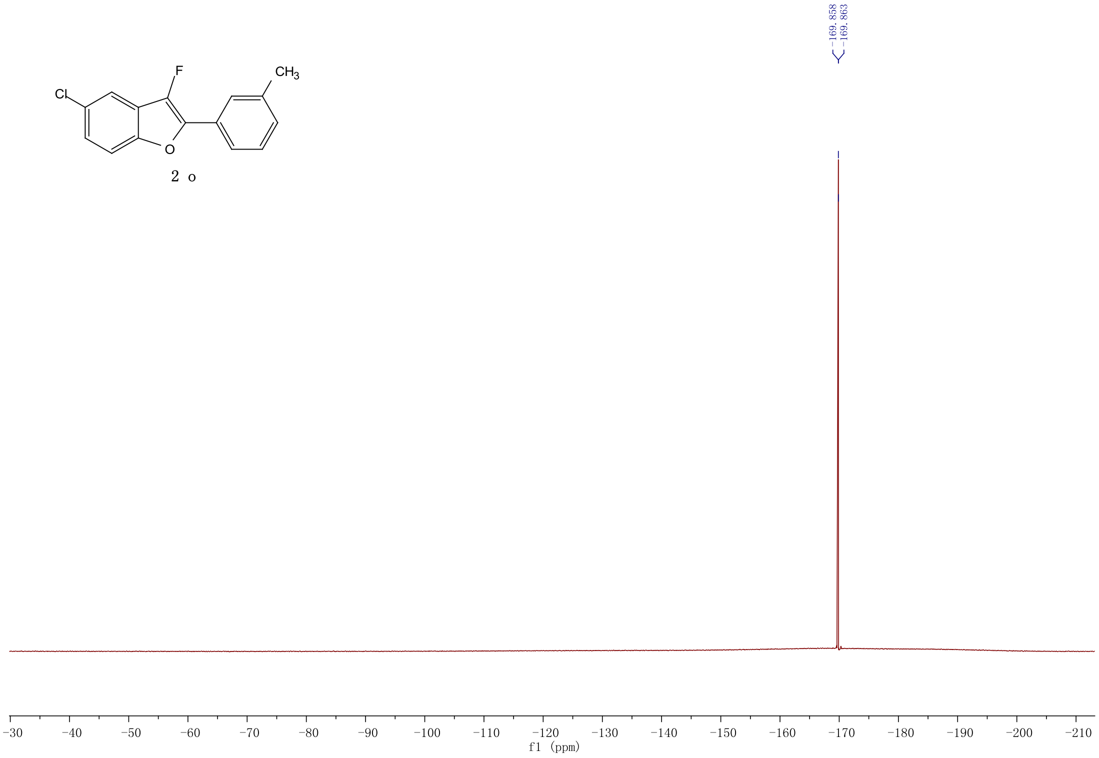

166.831
159.876
153.216
153.128
144.511
141.965
139.997
139.792
126.466
126.409
125.583
120.854
119.766
119.733
114.380
111.535
77.317
77.000
76.682
55.349
52.225
H3C
O
O
F
O
O
CH3
2 m
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.594
7.576
7.532
7.523
7.461
7.441
7.437
7.423
7.422
7.411
7.347
7.344
7.329
7.326
7.310
7.304
7.301
7.285
7.283
7.266
7.264
7.260
7.174
7.164
7.152
F
O
S
2 n
1.00
0.97
0.98
0.98
2.10
1.00
7.65
7.60
7.55
7.50
7.45
7.40
7.35
7.30
7.25
7.20
7.15
7.10
f1 (ppm)
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
f1 (ppm)

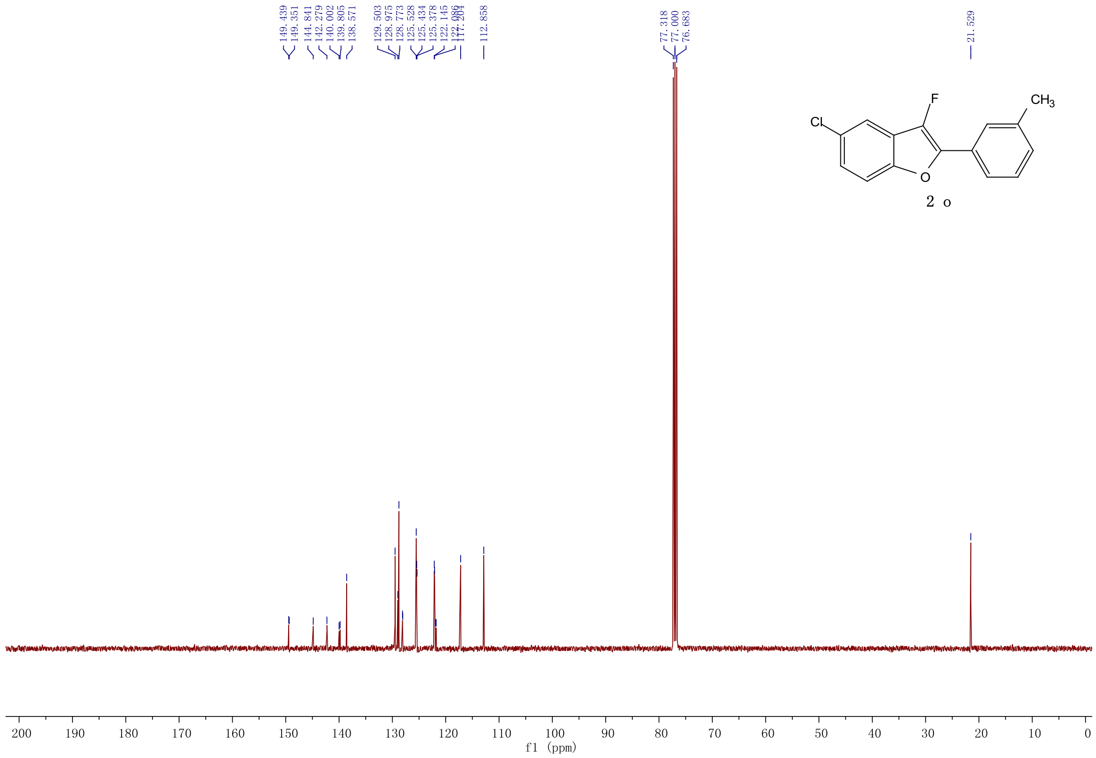

-170.569
-170.574
F
O
S
2 n
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


151.175
151.086
144.263
141.704
135.477
135.236
127.833
125.905
125.863
125.337
124.604
124.553
123.427
117.479
117.448
111.767
77.317
77.000
76.682
F
O
S
2 n
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

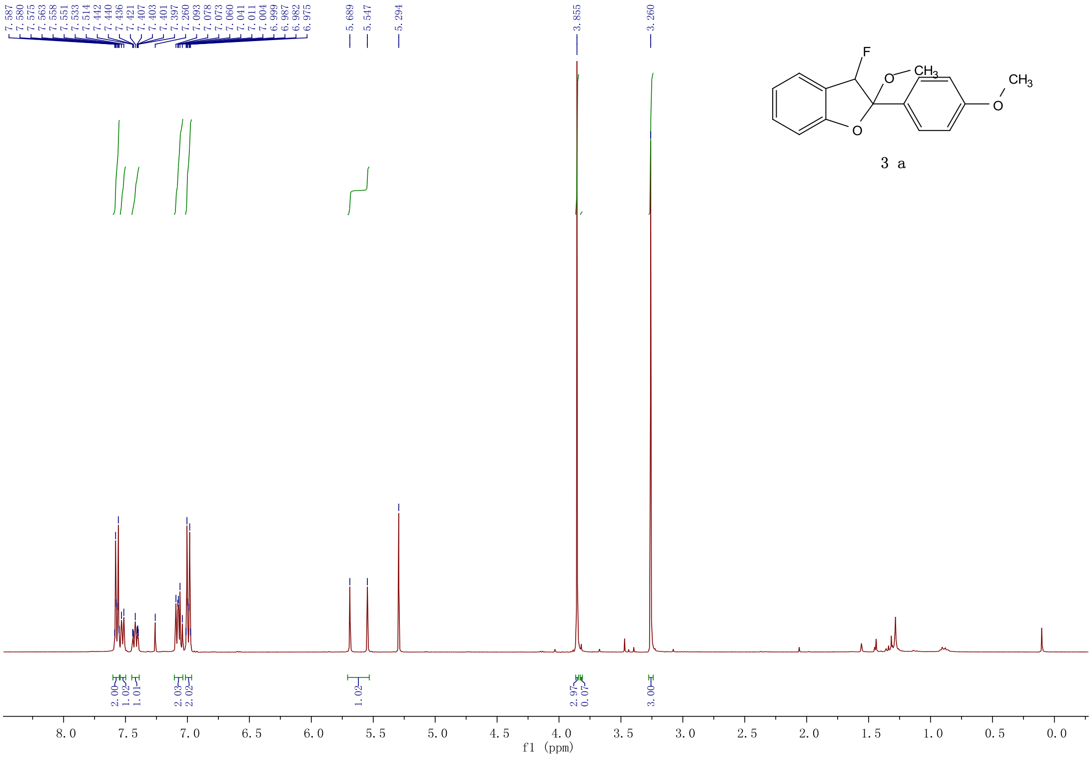

7.705
7.686
7.568
7.563
7.391
7.386
7.375
7.370
7.364
7.354
7.285
7.280
7.263
7.260
7.199
7.179
2.441
F
CH3
Cl
O
2 o
1.97
0.91
2.02
1.22
0.96
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

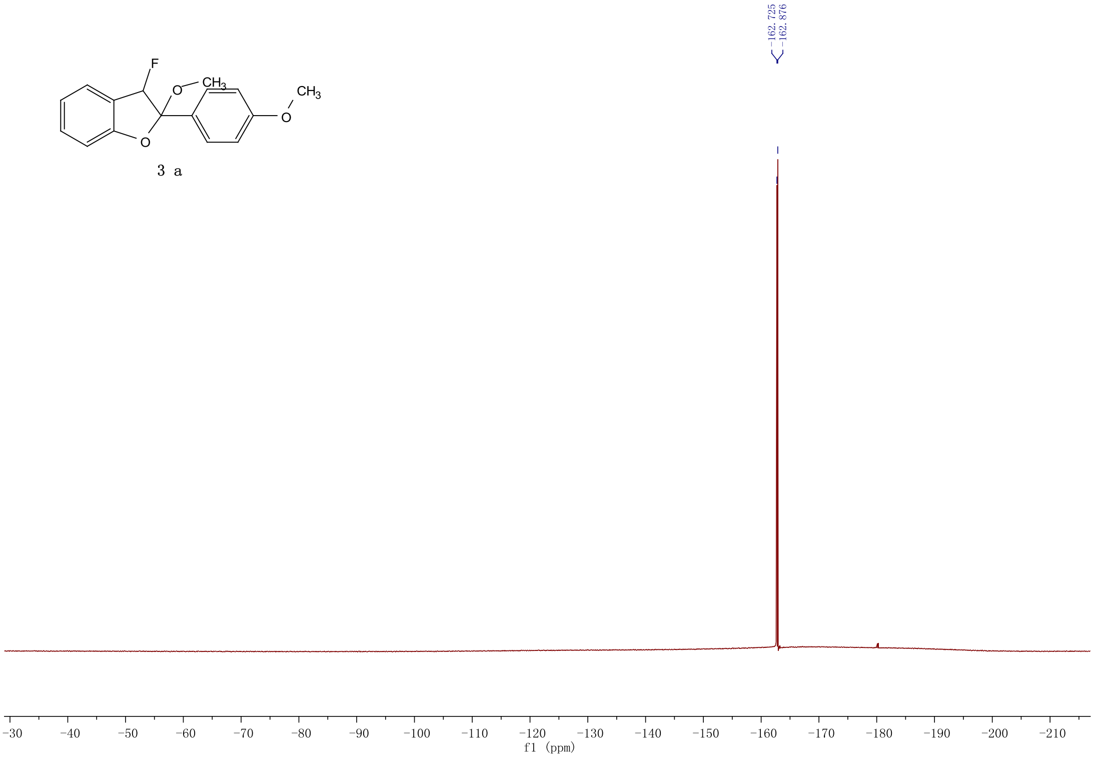

-169.858
-169.863
CH3
F
Cl
O
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

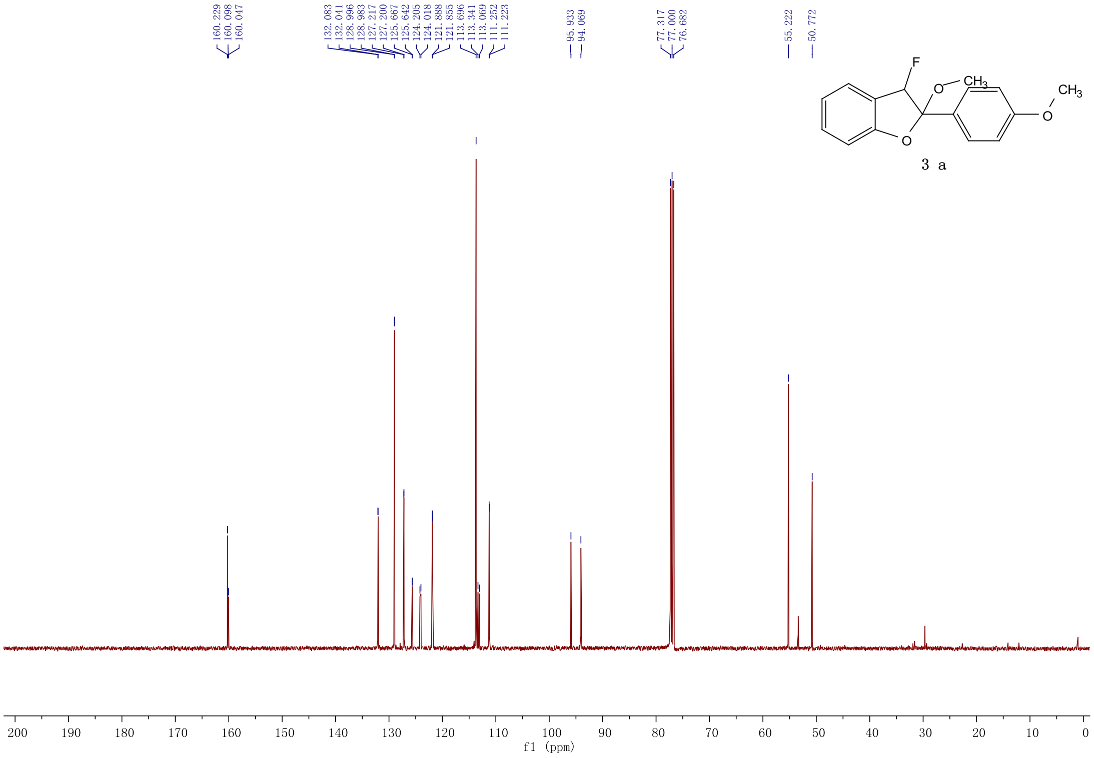
2 o

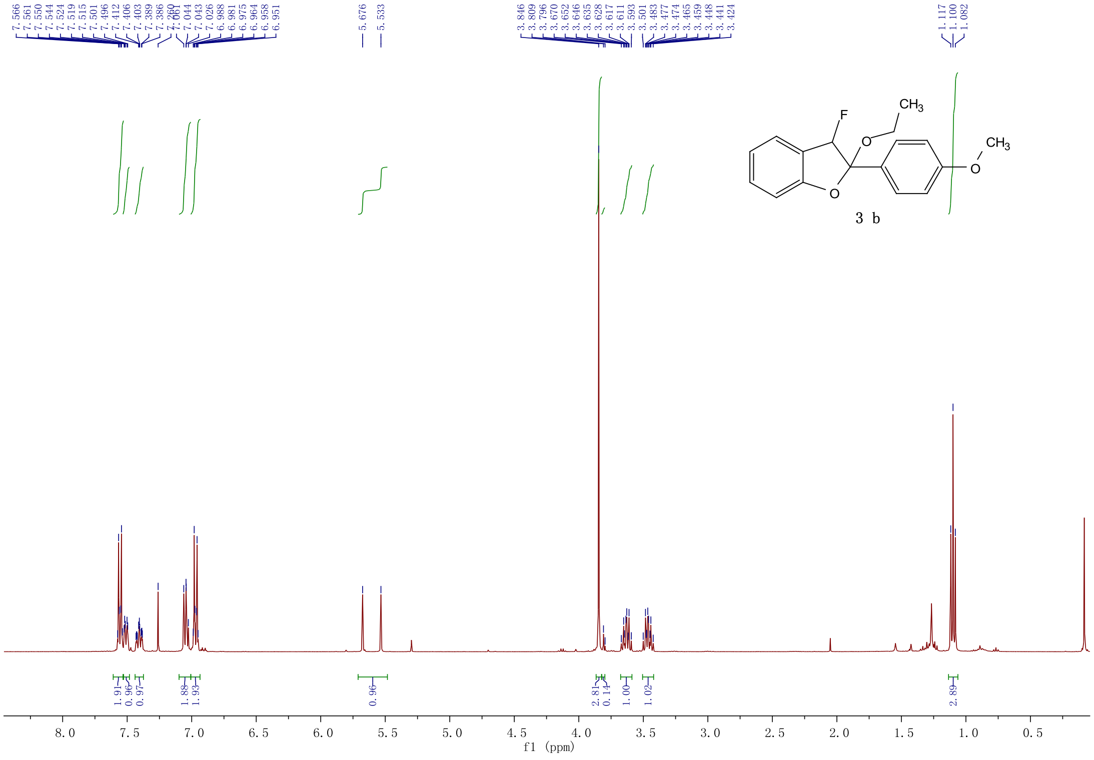

149.439
149.351
144.841
142.279
140.002
139.805
138.571
129.503
128.975
128.773
125.528
125.434
125.378
122.145
122.086
117.204
112.858
77.318
77.000
76.683
21.529
F
CH3
Cl
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

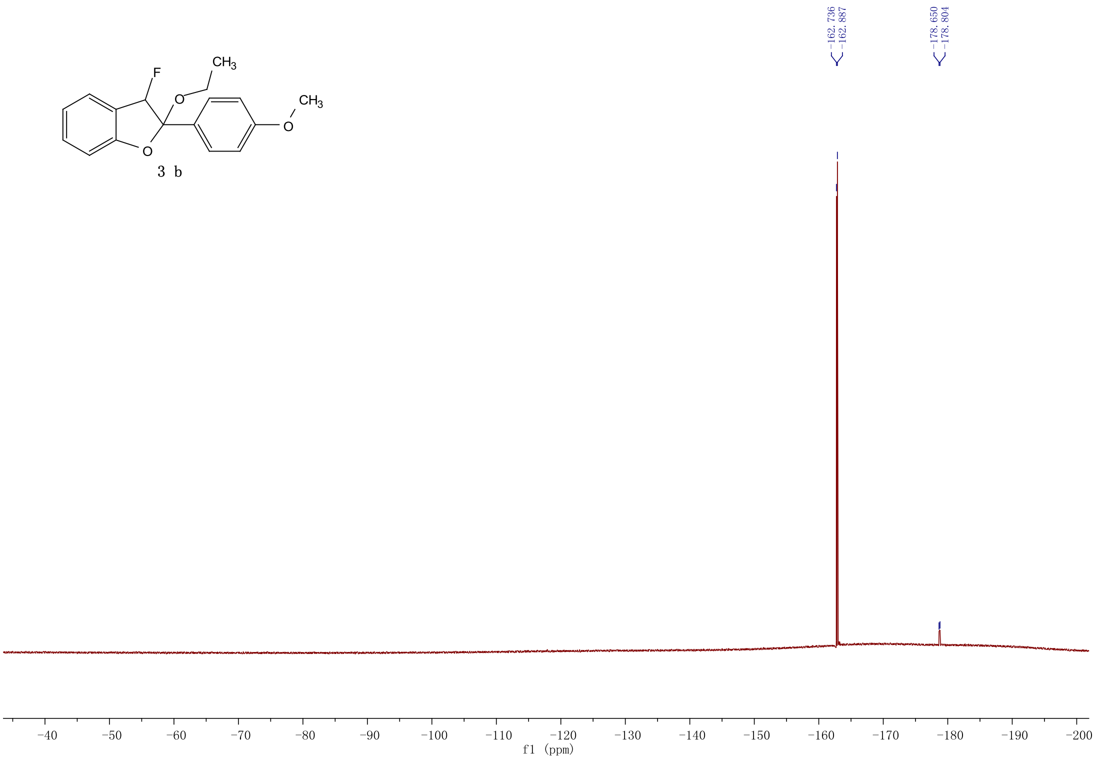
2 o

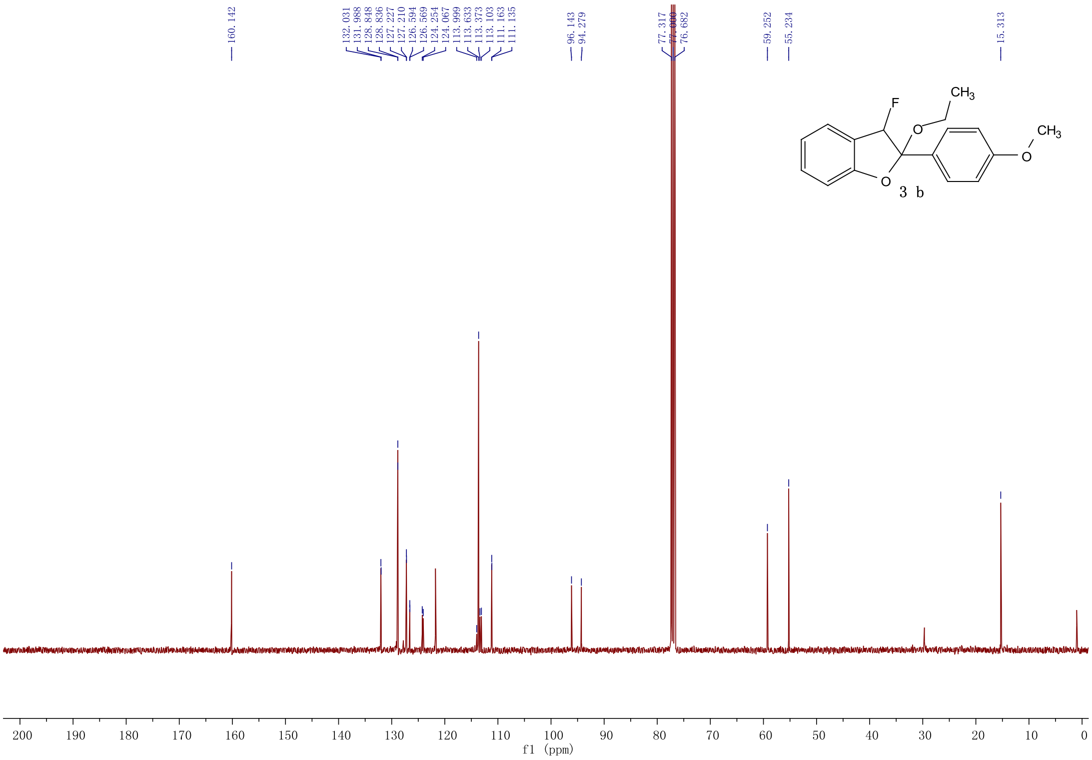

7.587
7.580
7.575
7.563
7.558
7.551
7.533
7.514
7.442
7.440
7.436
7.421
7.407
7.403
7.401
7.397
7.260
7.093
7.078
7.073
7.060
7.041
7.011
7.004
6.999
6.987
6.982
6.975
5.689
5.547
5.294
3.855
3.260
F
O
CH3
CH3
O
O
3 a
2.00
1.02
1.01
2.03
2.02
1.02
2.97
0.07
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

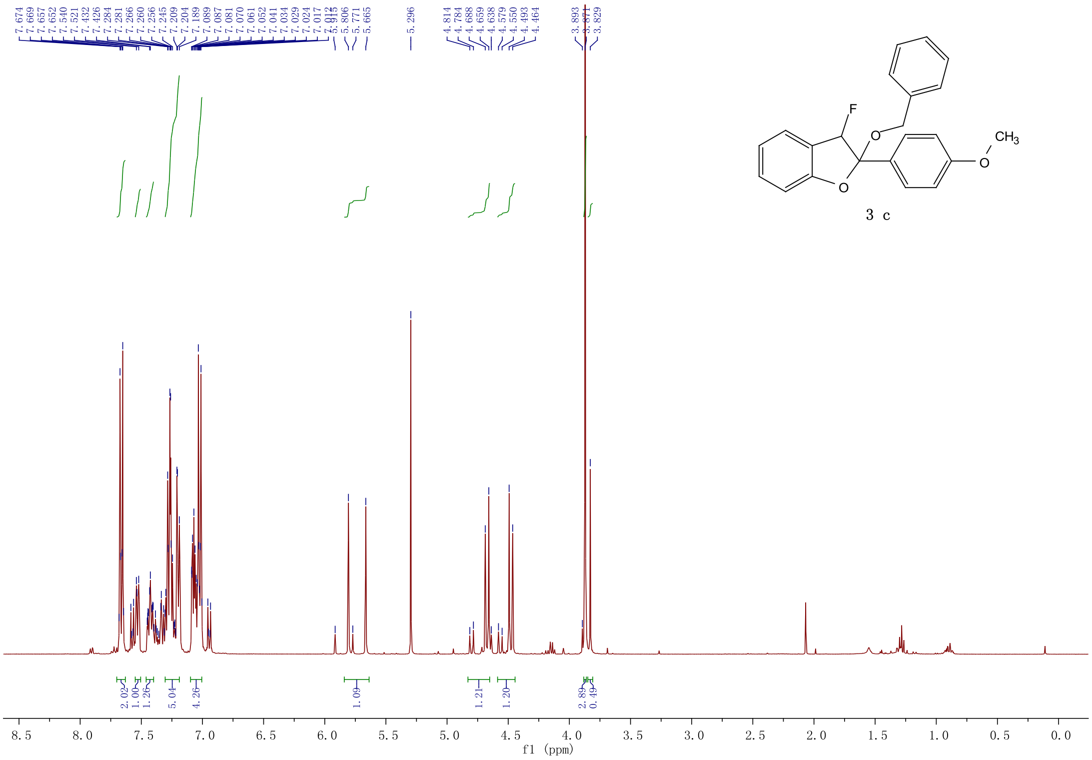

-162.725
-162.876
F
O
CH3
CH3
O
O
3 a
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

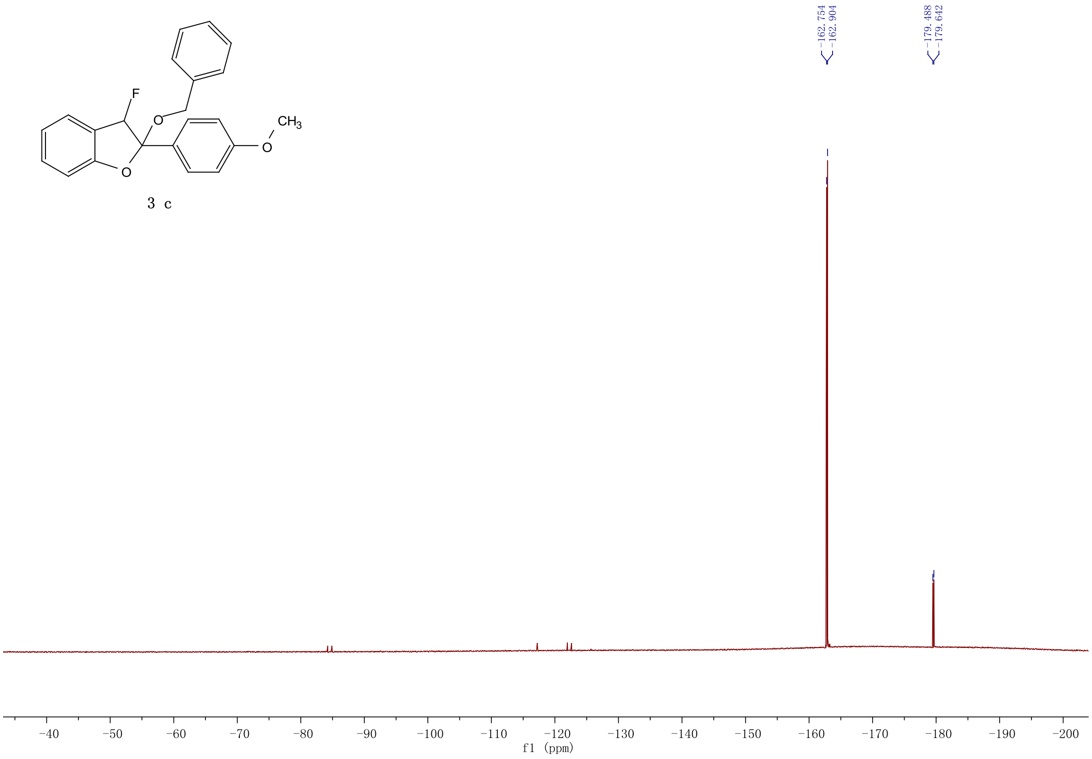

160.229
160.098
160.047
132.083
132.041
128.996
128.983
127.217
127.200
125.667
125.642
124.205
124.018
121.888
121.855
113.696
113.341
113.069
111.252
111.223
95.933
94.069
77.317
77.000
76.682
55.222
50.772
F
O
CH3
CH3
O
O
3 a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

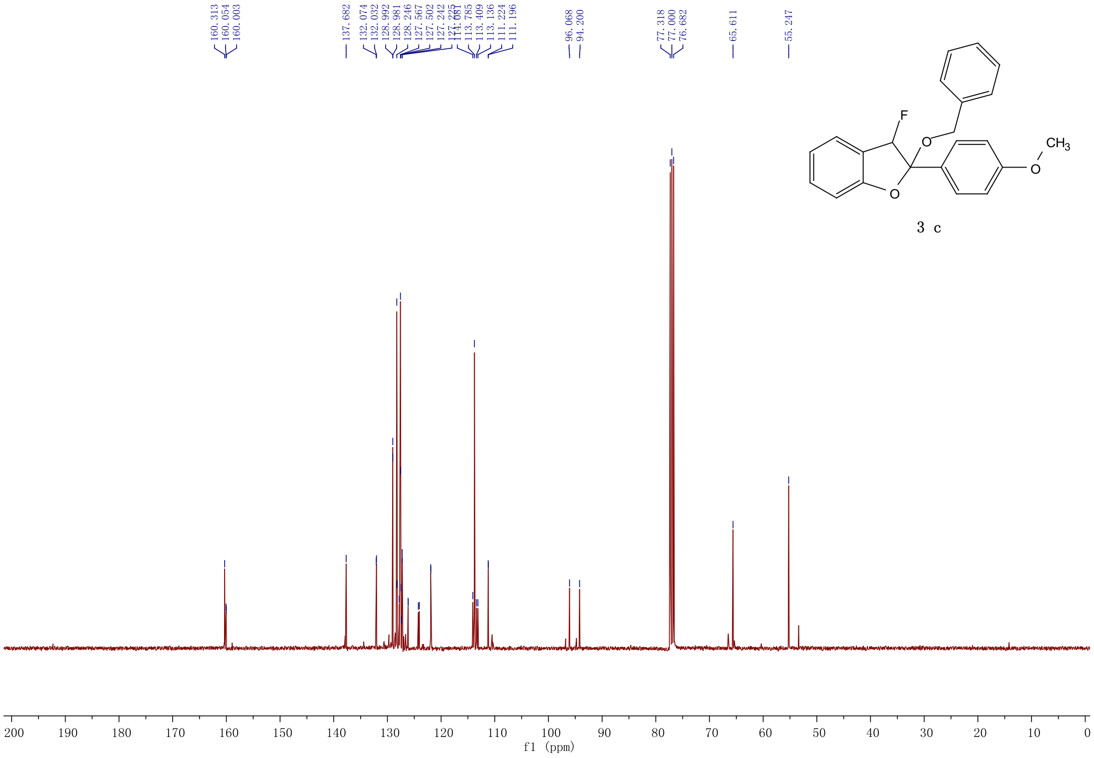

7.566
7.561
7.550
7.544
7.524
7.519
7.515
7.501
7.496
7.412
7.406
7.403
7.389
7.386
7.260
7.061
7.044
7.043
7.026
6.988
6.981
6.975
6.964
6.958
6.951
5.676
5.533
3.846
3.809
3.796
3.670
3.652
3.646
3.635
3.628
3.617
3.611
3.593
3.501
3.483
3.477
3.474
3.465
3.459
3.448
3.441
3.424
1.117
1.100
1.082
F
CH3
O
CH3
O
O
3 b
1.91
0.96
0.97
1.88
1.93
0.96
2.81
0.14
1.00
1.02
2.89
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
f1 (ppm)


-162.736
-162.887
-178.650
-178.804
F
CH3
O
O
CH3
O
3 b
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

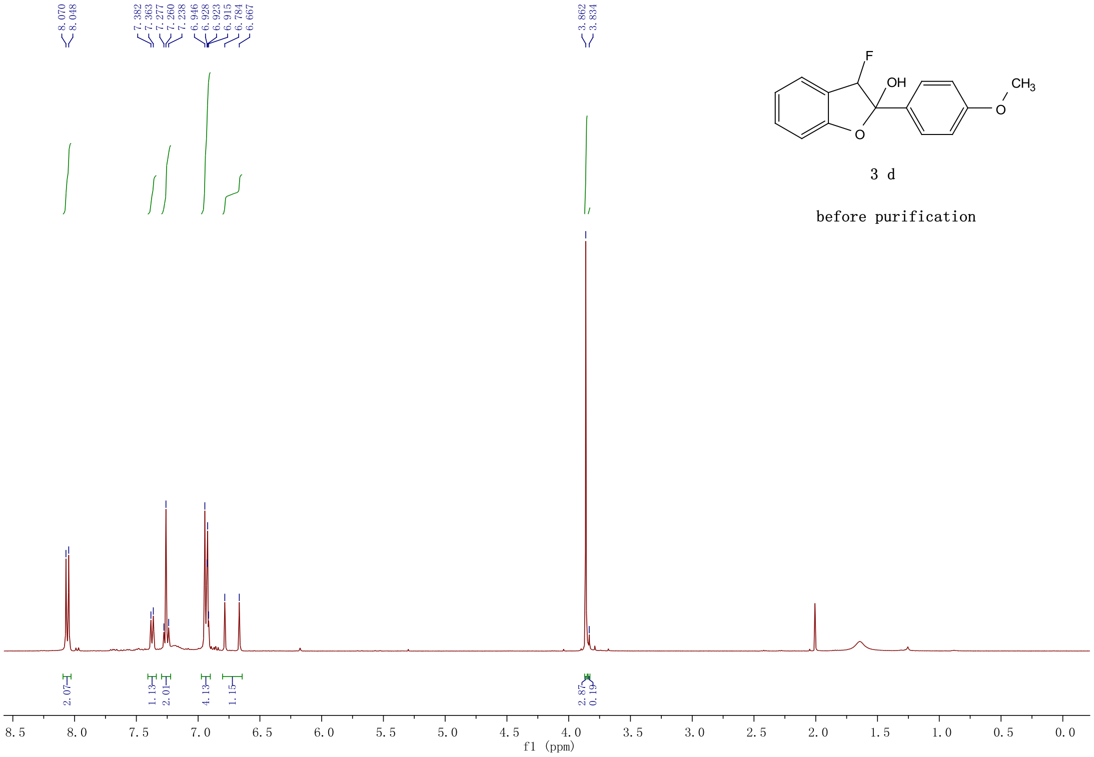

160.142
132.031
131.988
128.848
128.836
127.227
127.210
126.594
126.569
124.254
124.067
113.999
113.633
113.373
113.103
111.163
111.135
96.143
94.279
77.317
77.000
76.682
59.252
55.234
15.313
F
CH3
O
O
CH3
O
3 b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.674
7.669
7.657
7.652
7.540
7.521
7.432
7.426
7.284
7.281
7.266
7.260
7.256
7.245
7.209
7.204
7.189
7.089
7.087
7.081
7.070
7.061
7.052
7.041
7.034
7.029
7.024
7.017
7.012
5.915
5.806
5.771
5.665
5.296
4.814
4.784
4.688
4.659
4.638
4.579
4.550
4.493
4.464
3.893
3.871
3.829
F
O
O
CH3
O
3 c
2.02
1.00
1.26
5.04
4.26
1.09
1.21
1.20
2.89
0.49
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
f1 (ppm)


-162.754
-162.904
-179.488
-179.642
F
O
O
CH3
O
3 c
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

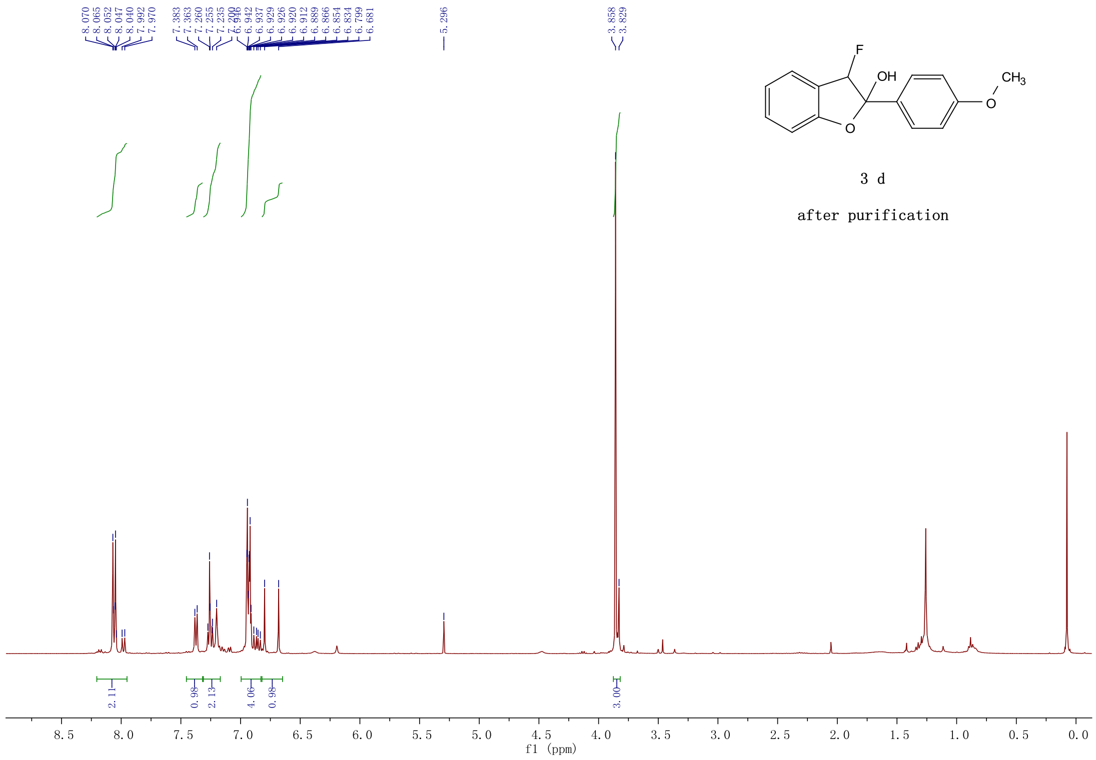


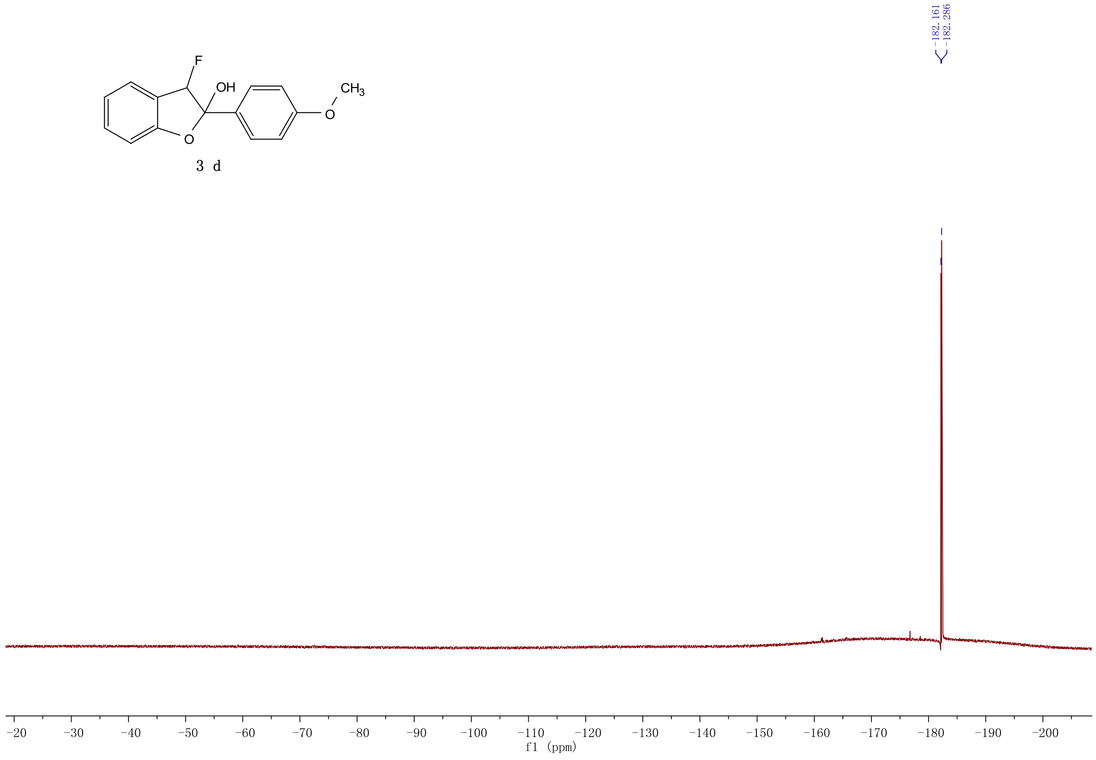
3 c

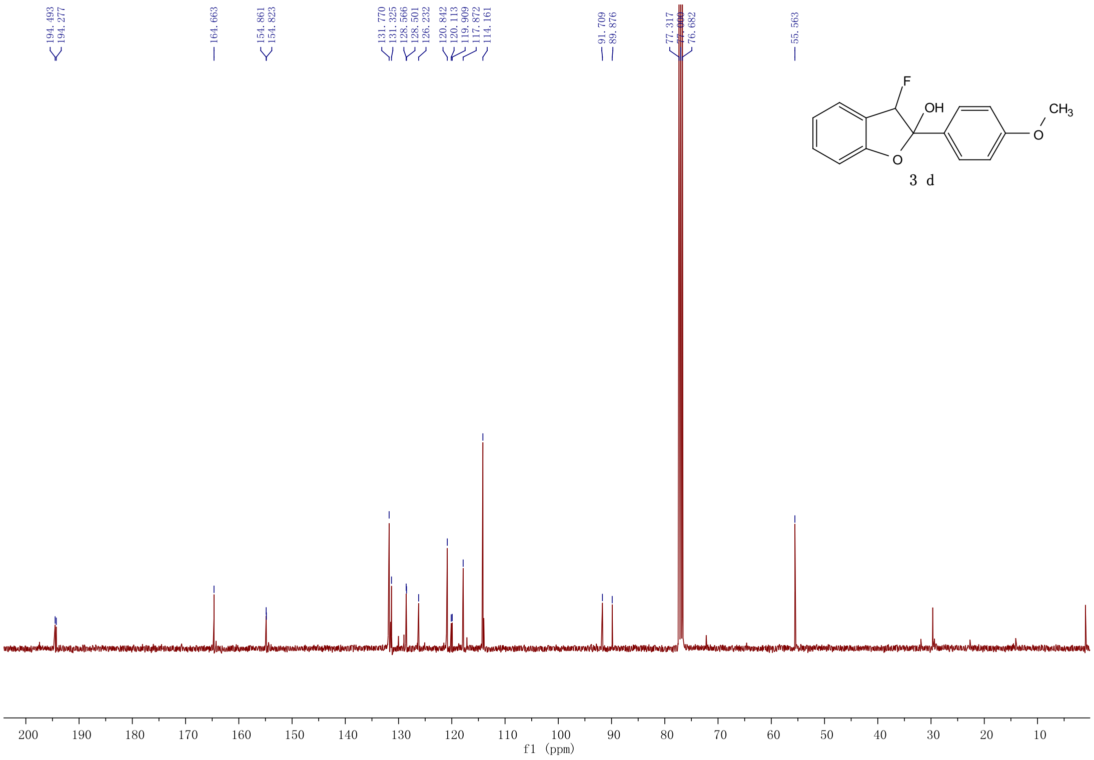


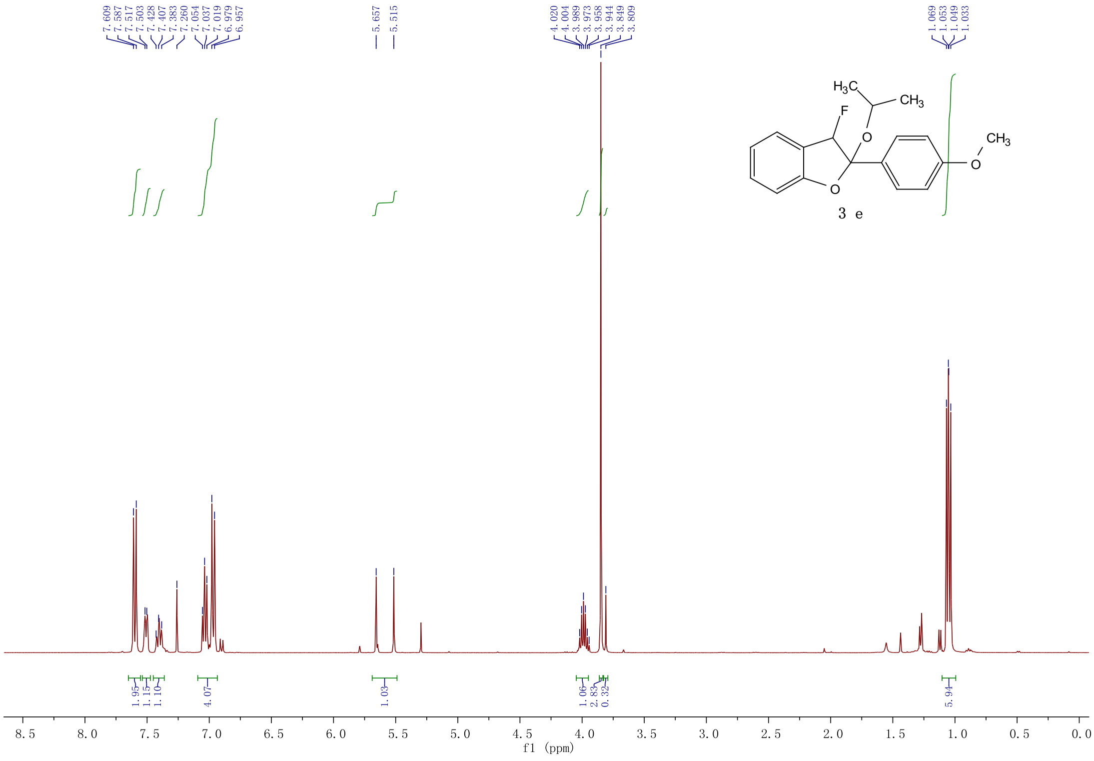
3 d

before purification


8.070
8.065
8.052
8.047
8.040
7.992
7.970
7.383
7.363
7.260
7.255
7.235
7.200
6.946
6.942
6.937
6.929
6.926
6.920
6.912
6.889
6.866
6.854
6.834
6.799
6.681
5.296
3.858
3.829
F
OH
CH3
O
O
3 d
after purification
2.11
0.98
2.13
4.06
0.98
3.00
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
f1 (ppm)


-182.161
-182.286
F
OH
CH3
O
O
3 d
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
f1 (ppm)


194.493
194.277
164.663
154.861
154.823
131.770
131.325
128.566
128.501
126.232
120.842
120.113
119.909
117.872
114.161
91.709
89.876
77.317
77.000
76.682
55.563
F
OH
CH3
O
O
3 d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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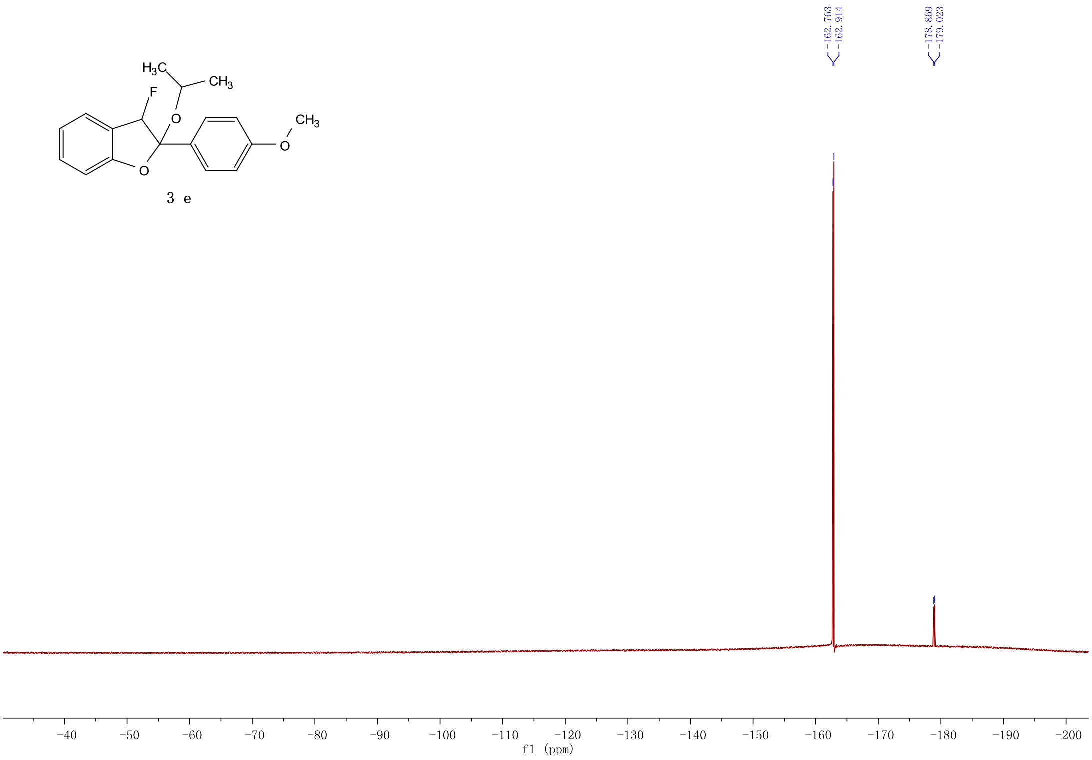
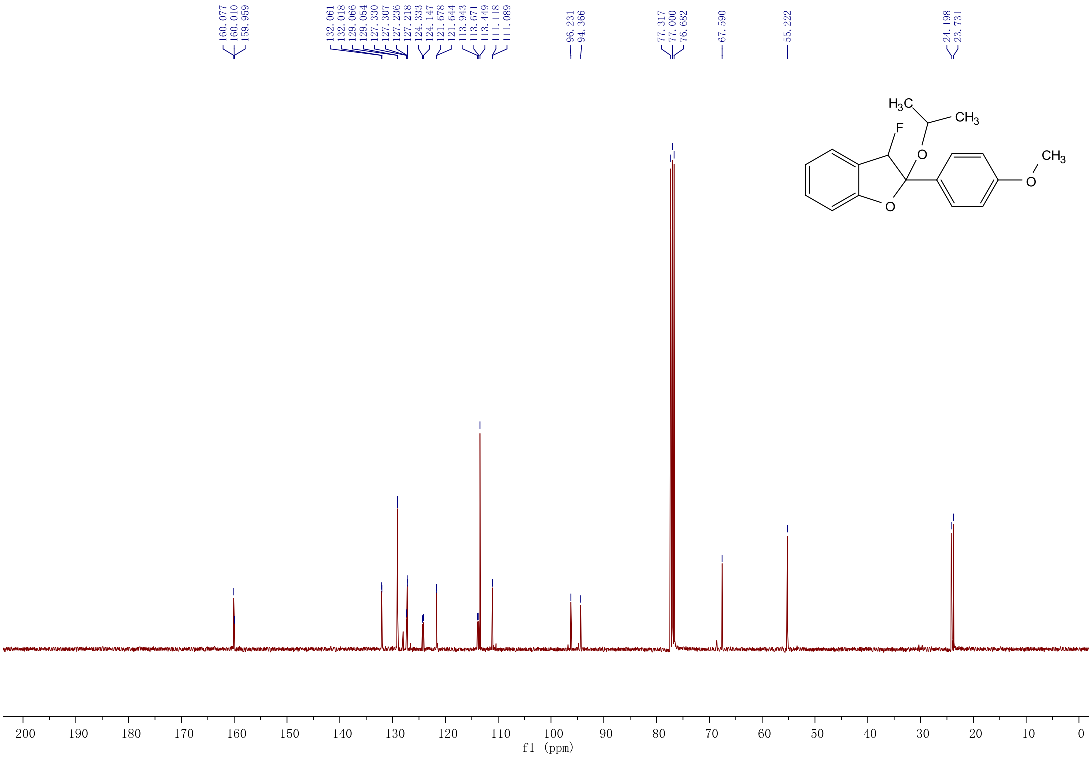
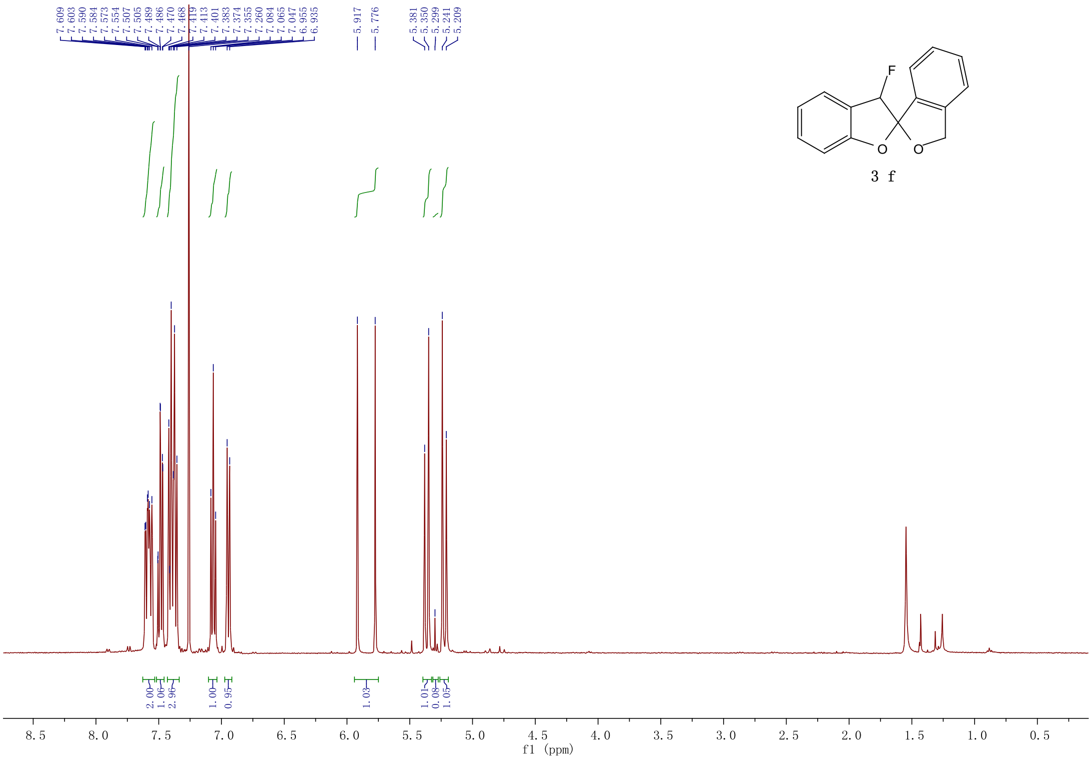
7.587
7.517
7.503
7.428
7.407
7.383
7.260
7.054
7.037
7.019
6.979
6.957
5.657
5.515
4.020
4.004
3.989
3.973
3.958
3.944
3.849
3.809
1.069
1.053
1.049
1.033
H3C
CH3
F
O
CH3
O
O
3 e
1.95
1.15
1.10
4.07
1.03
1.06
2.83
0.32
5.94
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

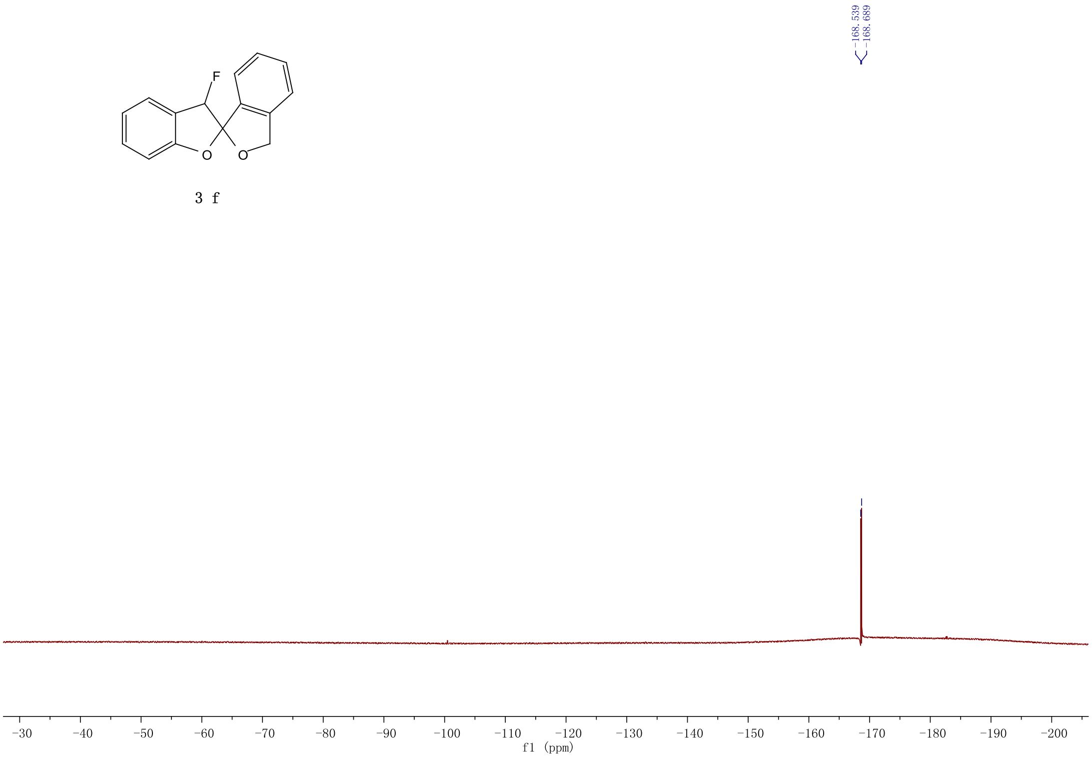

-162.763
-162.914
-178.869
-179.023
H3C
CH3
F
O
O
CH3
O
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

3 e

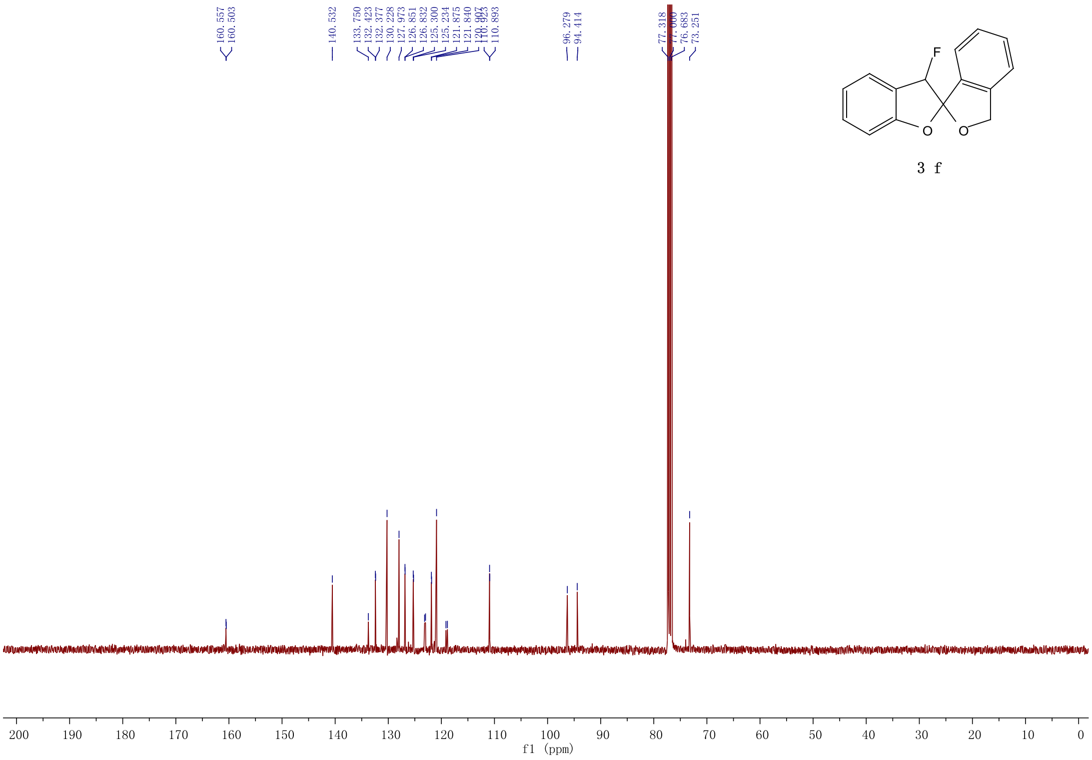

160.077
160.010
159.959
132.061
132.018
129.066
129.054
127.330
127.307
127.236
127.218
124.333
124.147
121.678
121.644
113.943
113.671
113.449
111.118
111.089
96.231
94.366
77.317
77.000
76.682
67.590
55.222
24.198
23.731
H3C
CH3
F
O
O
CH3
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.609
7.603
7.590
7.584
7.573
7.554
7.507
7.505
7.489
7.486
7.470
7.468
7.419
7.413
7.401
7.383
7.374
7.355
7.260
7.084
7.065
7.047
6.955
6.935
5.917
5.776
5.381
5.350
5.299
5.241
5.209
F
O
O
2.00
1.06
2.96
1.00
0.95
1.03
1.01
0.09
1.05
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
f1 (ppm)

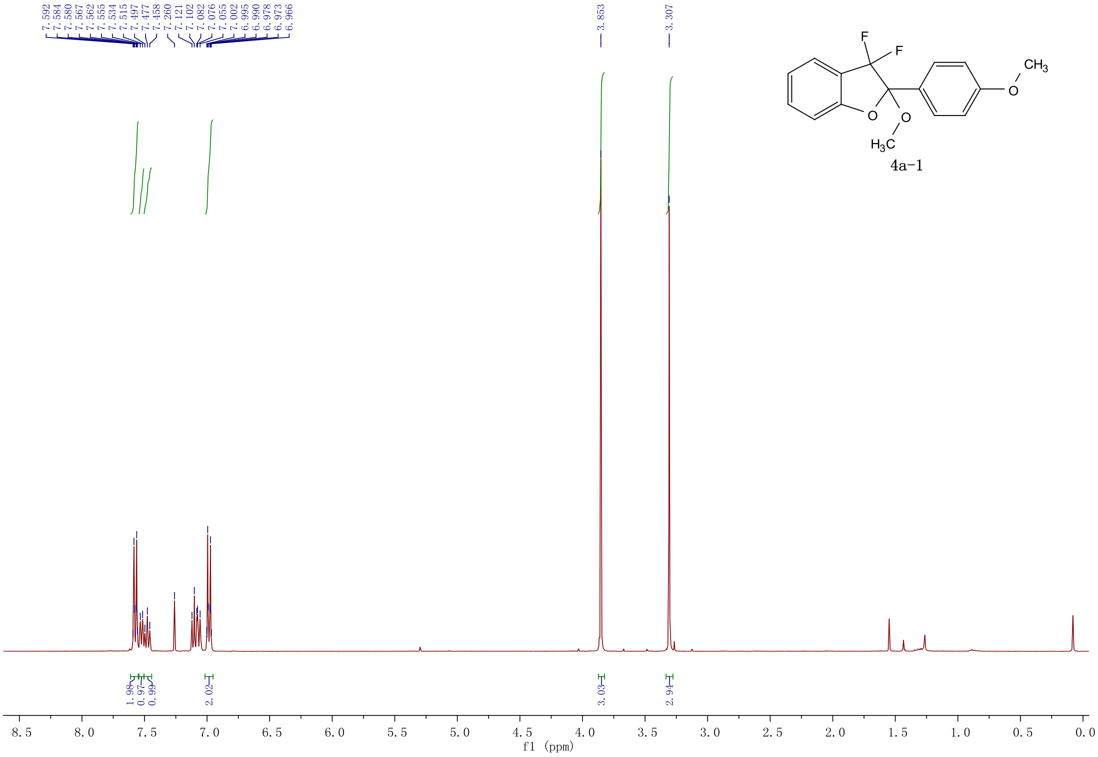
3 f


-168.539
-168.689
F
O
O
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
f1 (ppm)

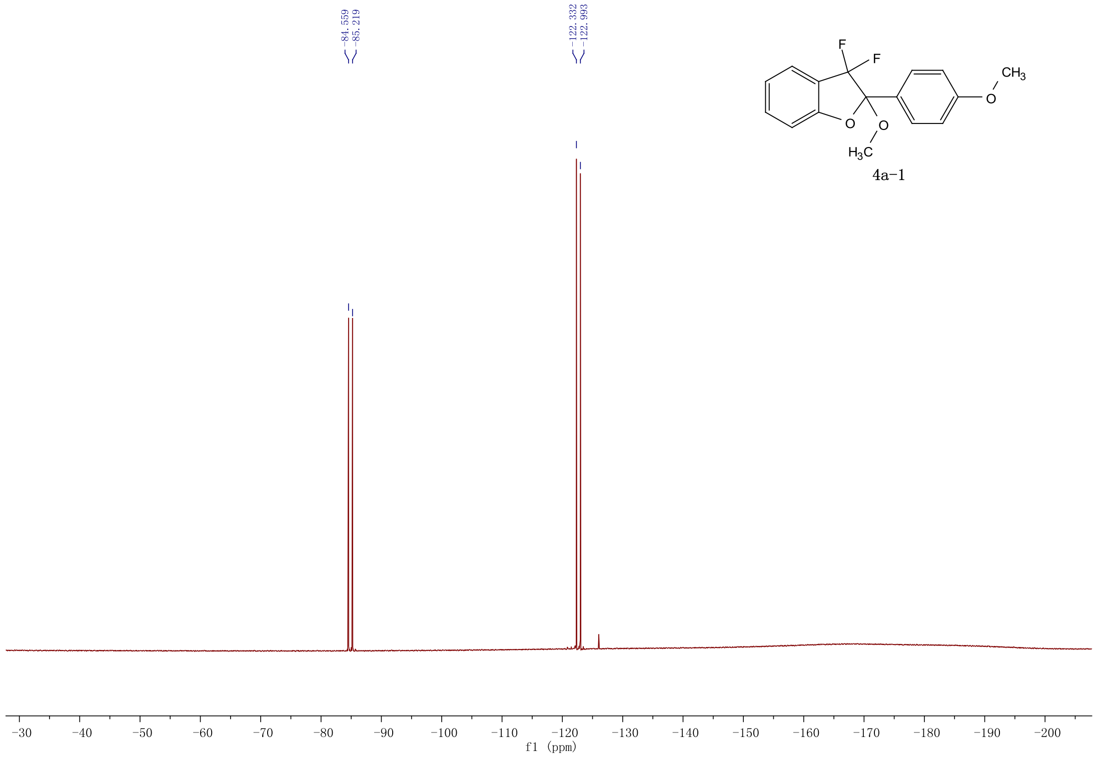
3 f

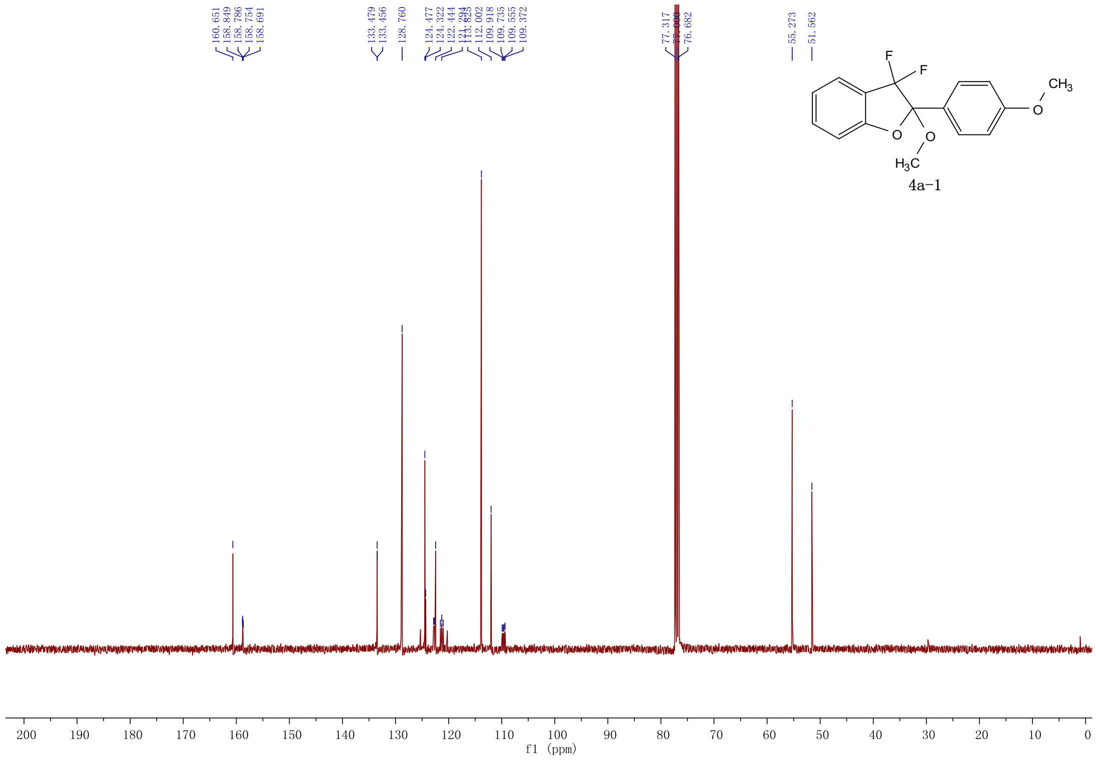

160.557
160.503
140.532
133.750
132.423
132.377
130.228
127.973
126.851
126.832
125.300
125.234
121.875
121.840
120.907
110.923
110.893
96.279
94.414
77.318
77.000
76.683
73.251
F
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

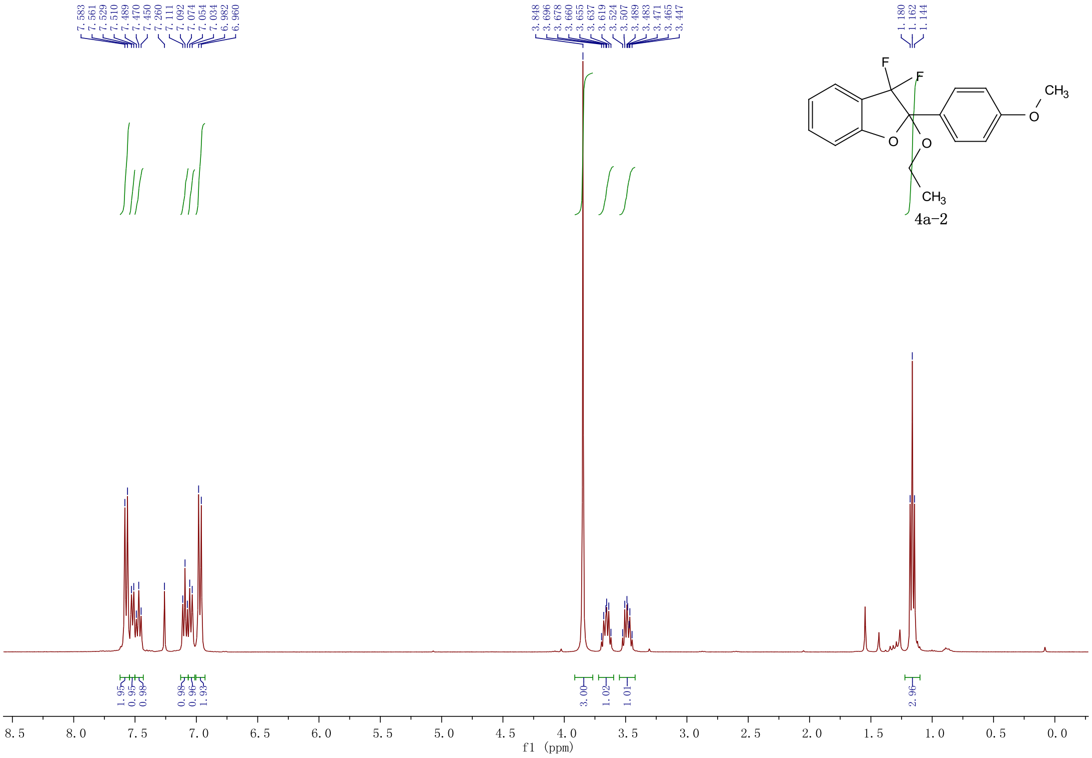
3 f

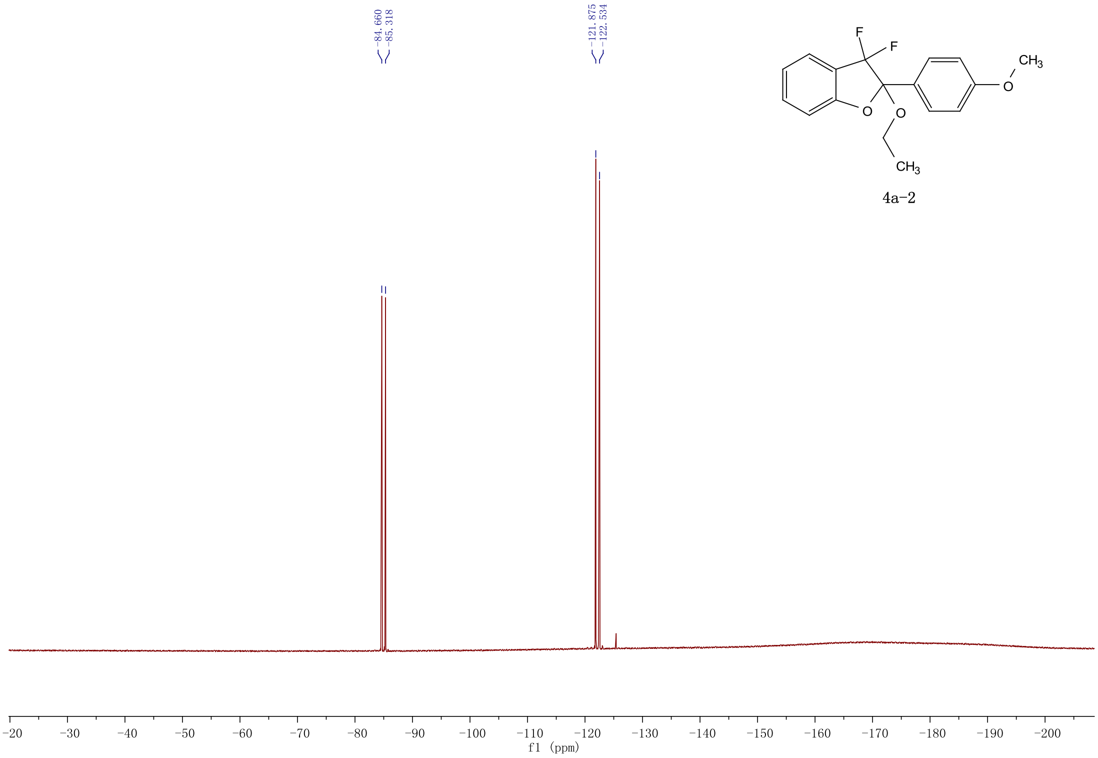

7.592
7.584
7.580
7.567
7.562
7.555
7.534
7.515
7.497
7.477
7.458
7.260
7.121
7.102
7.082
7.076
7.055
7.002
6.995
6.990
6.978
6.973
6.966
3.853
3.307
F
F
CH3
O
O
O
H3C
1.98
0.97
0.99
2.02
3.03
2.94
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

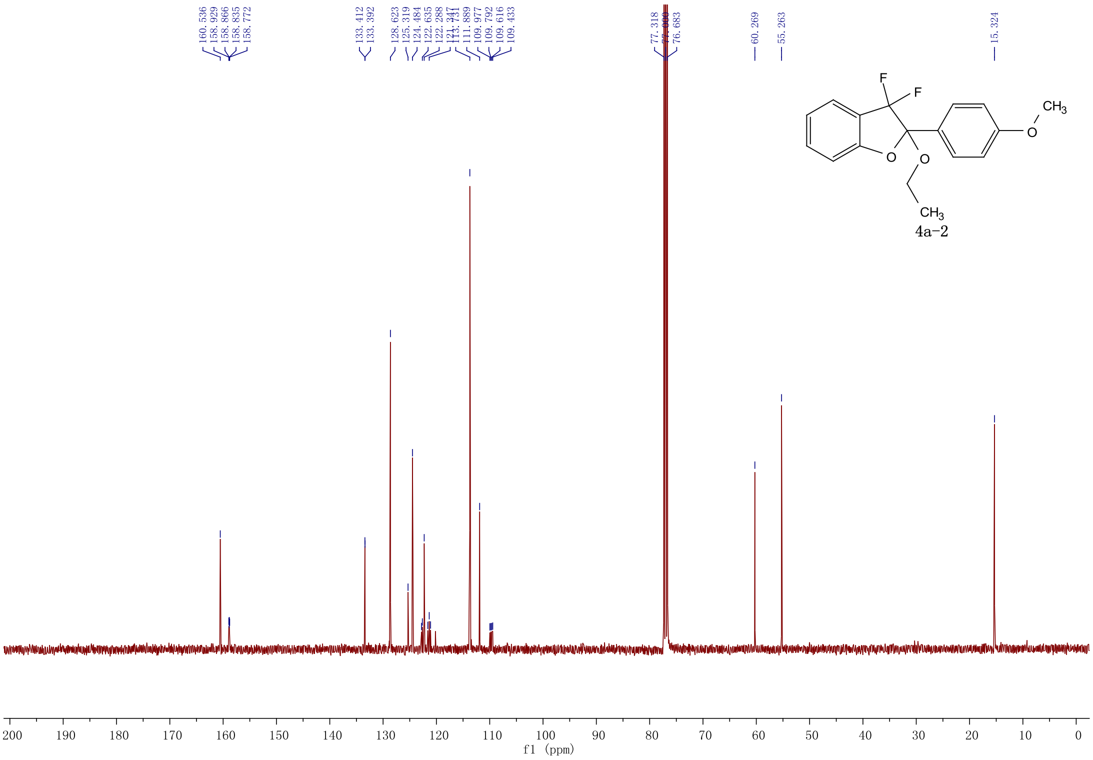
4a-1


-84.559
-85.219
-122.332
-122.993
F
F
CH3
O
O
O
H3C
4a-1
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
f1 (ppm)


160.651
158.849
158.786
158.754
158.691
133.479
133.456
128.760
124.477
124.322
122.444
121.294
113.825
112.002
109.918
109.735
109.555
109.372
77.317
77.000
76.682
55.273
51.562
F
F
CH3
O
O
O
H3C
4a-1
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.583
7.561
7.529
7.510
7.489
7.470
7.450
7.260
7.111
7.092
7.074
7.054
7.034
6.982
6.960
3.848
3.696
3.678
3.660
3.655
3.637
3.619
3.524
3.507
3.489
3.483
3.471
3.465
3.447
1.180
1.162
1.144
F
F
O
O
O
CH3
CH3
4a−2
1.95
0.95
0.98
0.98
0.96
1.93
3.00
1.02
1.01
2.96
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
f1 (ppm)


−84.660
−85.318
−121.875
−122.534
F
F
O
O
O
CH3
CH3
4a−2
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
f1 (ppm)

160.536
158.929
158.866
158.835
158.772
133.412
133.392
128.623
125.319
124.484
122.635
122.288
121.347
113.731
111.889
109.977
109.792
109.616
109.433
77.318
77.000
76.683
60.269
55.263
15.324
F
F
O
O
O
CH3
CH3
4a-2
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)