Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Synthesis of Difluoroalkylated 2-Azaspiro[4.5]decanes Derivatives via Copper-Catalyzed Difluoroalkylation/ Dearomatization of *N*-Benzylacrylamides

Chengwen Li, Yilin Zhao, Jiaxin Zhou, Xue Wang, Jingli Hou, Yuguang Song, Wenjuan Liu, Guifang Han*

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General Information

All reagents were used as received. 1,2-dichloroethane (DCE) was distilled on phosphorus pentoxide. ^{1}H, ^{13}C, and ^{19}F Nuclear Magnetic Resonance (NMR) spectra were recorded on Bruker Avance 400 Ultrashield NMR spectrometers. Chemical shifts (δ) were given in parts per million (ppm) and were measured downfield from internal tetramethylsilane. High-resolution mass spectrometry (HRMS) data were obtained on an FTICR-MS instrument (Ionspec 7.0 T). Conversion was monitored by thin layer chromatography (TLC). Flash column chromatography was performed over silica gel (200-300 mesh).

General procedure for difluoroalkylation

An oven dried reaction tube was charged with CuBr (10 mol%), substrates **1** (0.2 mmol, 1.0 equiv), base (K_2CO_3 1.5 equiv. or Cs_2CO_3 3.5 equiv.) and compound **2** (2 equiv). The vial was evacuated and backfilled with argon (this process was repeated three times) and then DCE (2 mL) was added. The reaction mixture was stirred at 85 ^{o}C for 48 h. Upon consumption of the starting material, to the mixture was added H_2O and extracted with DCM. And the organic layer was washed with saturated aqueous solution of $NaHCO_3$, and saturated brine, concentrated under in vacuo to give the crude product, which was purified by flash column chromatography (elution: PE:EA = 5:1) to give the desired compound **3**.

Procedure for compound 4a

To an Ac_2O (2 ml) solution of **3a** (50 mg, 0.14 mml), concentrated sulfuric acid (50 μl) was added. The mixture was heated to 40 ^{o}C, after stirred for 4 h cooled to room temperature, and water (2 ml) was added slowly, and then stirred for another 0.5 h at 70 ^{o}C. The reaction was quenched with water (10 ml) and the aqueous layer was extracted with DCM (10 ml*3). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give the crude material which was purified by silica gel column chromatography (PE:EA=20:1-5:1) to afford compound **4a** (39 mg, yield: 77%).

Procedure for compound 5a

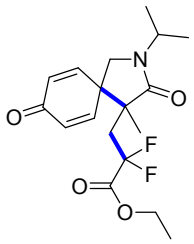
To a 10 ml reaction tube was added compound **3a** (50 mg, 0.14 mmol), EA (3 ml), Pd/C (10 mg, 10%), under the H_2. The resulting suspension was stirred at room temperature for 12 h, then filtered over a 1 cm thick pad of Celite, and the filter cake washed with EA (5 ml), and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (elution: PE:EA = 10:1-2:1) to give the desired compound **5a** (45 mg, yield: 90%).

Procedure for compound 6a

To a solution of **3a** (50 mg, 0.14 mmol) in EtOH (2 ml), NaOH (2 ml, 0.5 M in water) was added. The mixture was stirred at room temperature for 1 h, and then washed by EA (3 ml *2). HCl (3 ml, 0.5 M in water) was added into the aqueous layer, and then extracted with EA (2 ml*3). The combined organic layer was concentrated under reduced pressure to give the desired compound **6a** (41 mg, yield: 91%).

Characterization of the products

ethyl 2,2-difluoro-3-(2-isopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)propanoate (3a)



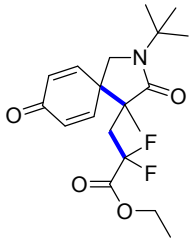
Yield: 90%. Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (dd, J = 10.3, 3.0 Hz, 1H), 6.86 (dd, J = 10.2, 3.0 Hz, 1H), 6.47 (dd, J = 10.3, 1.4 Hz, 1H), 6.41 (dd, J = 10.3, 1.6 Hz, 1H), 4.47 – 4.36 (m, 1H), 4.31 (q, J = 7.1 Hz, 2H), 3.48 (d, J = 10.4 Hz, 1H), 3.15 (d, J = 10.4 Hz, 1H), 2.71 (ddd, J = 23.1, 18.0, 16.0 Hz, 1H), 2.10 (ddd, J = 15.8, 12.4, 7.8 Hz, 1H), 1.39 (d, J = 1.9 Hz, 3H), 1.35 (t, J = 7.1 Hz, 3H), 1.19 (d, J = 6.9 Hz, 3H), 1.17 (d, J = 6.9 Hz, 3H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -96.72 (d, J = 266.2 Hz, 1F), -101.81 (d, J = 266.2 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.84, 172.98, 162.63 (t, J = 31.9 Hz), 145.96 (d, J = 0.6 Hz), 145.95, 130.79 (d, J = 1.6 Hz), 129.44, 114.73 (dd, J = 254.3, 248.0 Hz), 62.04, 50.41 (d, J = 2.0 Hz), 46.95, 46.12, 42.19, 35.89 (dd, J = 24.3, 21.6 Hz), 18.47, 18.37, 16.89 (d, J = 4.9 Hz), 12.85.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{24}F_2NO_4^+$ 356.1668; Found 356.1667.

ethyl 3-(2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2,2-difluoropropanoate (3b)



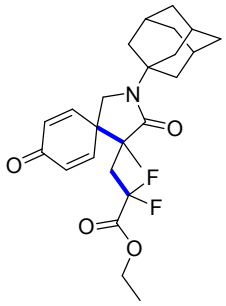
Yield: 85%. Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 – 6.87 (m, 2H), 6.50 – 6.36 (m, 2H), 4.28 (q, J = 7.1 Hz, 2H), 3.58 (d, J = 10.4 Hz, 1H), 3.22 (d, J = 10.4 Hz, 1H), 2.65 (dt, J = 24.5, 16.8 Hz, 1H), 2.07 (ddd, J = 24.7, 15.9, 8.8 Hz, 1H), 1.41 (s, 9H), 1.37 (d, J = 1.8 Hz, 3H), 1.33 (t, J = 7.1 Hz, 3H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -97.27 (d, J = 264.6 Hz, 1F), -101.78 (d, J = 264.6 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 184.94, 174.93, 163.70 (t, J = 32.2 Hz), 148.32, 146.98 (d, J = 0.8 Hz), 131.89 (d, J = 1.9 Hz), 130.27, 115.84 (dd, J = 253.7, 248.4 Hz), 63.02, 54.71, 51.89 (d, J = 0.5 Hz), 50.36, 47.34, 37.04 (dd, J = 24.0, 21.5 Hz), 27.46, 17.83 (d, J = 4.8 Hz), 13.87.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{26}F_2NO_4^+$ 370.1824; Found 370.1823.

ethyl 3-(2-(adamantan-1-yl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2,2-difluoropropanoate (3c)



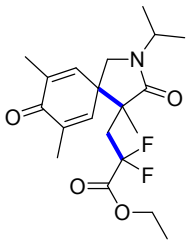
Yield: 69%. Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 – 6.89 (m, 2H), 6.48 – 6.35 (m, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.58 (d, *J* = 10.5 Hz, 1H), 3.24 (d, *J* = 10.5 Hz, 1H), 2.63 (ddd, *J* = 24.7, 17.2, 16.1 Hz, 1H), 2.16 – 2.08 (m, 9H), 2.08 – 1.99 (m, 1H), 1.70 (s, 6H), 1.36 (d, *J* = 2.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (377 MHz, $CDCl_3$) *δ* -97.39 (d, *J* = 265.0 Hz, 1F), -101.76 (d, *J* = 265.0 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 185.01, 174.89, 163.73 (t, *J* = 32.3 Hz), 148.53, 147.11, 131.85 (d, *J* = 1.8 Hz), 130.23, 115.87 (dd, *J* = 253.5, 248.4 Hz), 63.02, 55.90, 52.09, 49.41, 47.41, 39.51, 36.99 (dd, *J* = 24.1, 21.7 Hz), 36.14, 29.47, 17.91 (d, *J* = 4.6 Hz), 13.88.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{25}H_{32}F_2NO_4^+$ 448.2294; Found 448.2291.

ethyl 2,2-difluoro-3-(2-isopropyl-4,7,9-trimethyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)propanoate (3d)



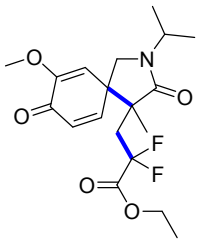
Yield: 97%. Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 6.59 (dd, *J* = 3.0, 1.4 Hz, 1H), 6.51 (dd, *J* = 3.0, 1.4 Hz, 1H), 4.37 – 4.27 (m, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.35 (d, *J* = 10.2 Hz, 1H), 3.01 (d, *J* = 10.2 Hz, 1H), 2.55 (ddd, *J* = 21.9, 19.3, 15.7 Hz, 1H), 1.97 (ddd, *J* = 22.7, 15.7, 9.7 Hz, 1H), 1.88 (d, *J* = 1.3 Hz, 3H), 1.86 (d, *J* = 1.3 Hz, 3H), 1.28 – 1.23 (m, 6H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -96.44 (d, J = 264.6 Hz, 1F), -101.83 (d, J = 264.6 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.10, 173.45, 162.76 (t, J = 32.1 Hz), 141.65, 140.75 (d, J = 0.8 Hz), 136.98 (d, J = 1.7 Hz), 135.57, 114.81 (dd, J = 254.3, 247.7 Hz), 61.91, 50.29 (d, J = 2.3 Hz), 46.23, 42.00, 35.93 (dd, J = 24.5, 21.6 Hz), 28.67, 18.49, 18.41, 16.94 (d, J = 4.8 Hz), 15.55, 15.36, 12.86.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{28}F_2NO_4^+$ 384.1981; Found 384.1980.

ethyl 2,2-difluoro-3-(2-isopropyl-7-methoxy-4-methyl-3,8-dioxo-2-azaspiro[4.5] deca-6,9-dien-4-yl)propanoate (3e)



Yield: 94%. Pale yellow oil; Isolated as an inseparatable mixture of diastereomers, *dr* =1:0.7

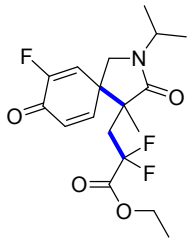
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (dd, J = 10.4, 2.8 Hz, 0.7H), 6.85 (dd, J = 10.0, 2.4 Hz, 1H), 6.47 (d, J = 10.4 Hz, 0.7H), 6.42 (d, J = 10.0 Hz, 1H), 5.75 (d, J = 2.4 Hz, 1H), 5.72 (d, J = 2.8 Hz, 0.7H), 4.46 – 4.37 (m, 1.7H), 4.33 – 4.24 (m, 3.4H), 3.73(s, 3H), 3.68(s, 2.1H), 3.50 (d, J = 10.0 Hz, 0.7H), 3.48 (d, J = 10.0 Hz, 1H), 3.18 (d, J = 10.0 Hz, 0.7H), 3.12 (d, J = 10.0 Hz, 1H), 2.77 – 2.56 (m, 1.7H), 2.26 – 1.95 (m, 1.7H), 1.40 (d, J = 1.7 Hz, 3H), 1.37 – 1.30 (m, 7.2H), 1.21 – 1.13 (m, 10.2H).

19F NMR (377 MHz, CDCl3) δ -96.20 (d, J = 264.7 Hz, 1F), -96.35 (d, J = 267.3 Hz, 0.7F), -101.38 (d, J = 264.7 Hz, 1F), -101.64 (d, J = 267.3 Hz, 0.7F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 180.10, 180.07, 174.25, 174.15, 163.73 (t, J = 32.0 Hz), 163.67 (t, J = 32.0 Hz), 153.04, 153.03, 152.34, 148.32, 147.52, 130.99, 130.97, 129.72, 115.77 (t, J = 251.25 Hz), 115.75 (t, J = 250.9 Hz), 114.32, 112.95, 63.07, 63.04, 55.08, 55.07, 51.69 (d, J = 2.5 Hz), 51.17 (d, J = 2.5 Hz), 49.01, 48.81, 48.14, 47.86, 43.11, 43.07, 37.12 (dd, J = 24.2, 16.7 Hz), 36.88 (dd, J = 24.2, 16.7 Hz), 19.51, 19.44, 18.12 (t, J = 4.6 Hz), 13.87.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{26}F_2NO_5^+$ 386.1774; Found 386.1773.

ethyl 2,2-difluoro-3-(7-fluoro-2-isopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)propanoate (3f)



Yield: 65%. Pale yellow oil; Isolated as an inseparatable mixture of diastereomers, *dr* =1:1

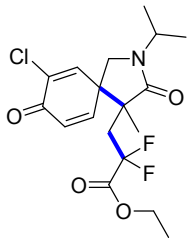
^{1}H NMR (400 MHz, CDCl3) δ 6.97 (dd, J = 10.2, 2.7 Hz, 1H), 6.87 (dd, J = 10.2, 2.7 Hz, 1H), 6.52 – 6.35 (m, 4H), 4.48 – 4.35 (m, 2H), 4.29 (q, *J* = 7.2 Hz, 4H), 3.53 (dd, *J* = 10.4, 2.2 Hz, 1H), 3.52 (d, *J* = 10.5 Hz, 1H), 3.21 (d, *J* = 10.4 Hz, 1H), 3.16 (d, *J* = 10.5 Hz, 1H), 2.79 – 2.60 (m, 2H), 2.23 – 2.01 (m, 2H), 1.40 – 1.37 (m, 6H), 1.34 (t, *J* = 7.2 Hz, 3H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.20 – 1.14 (m, 12H).

^{19}F NMR (377 MHz, $CDCl_3$) *δ* -97.53 (d, *J* = 264.8 Hz, 1F), -97.60 (d, *J* = 265.1 Hz, 1F), -101.63 (d, *J* = 265.1 Hz, 1F), -101.79 (d, *J* = 264.8 Hz, 1F), -124.91(s, 1F), -127.18(s, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 177.63, 177.41, 173.76, 173.55, 163.58 (t, *J* = 32.0Hz), 163.49 (t, *J* = 32.0Hz), 155.40 (dd, *J* = 264.4, 1.8Hz), 154.94 (d, *J* = 265.1Hz), 148.42, 147.73, 131.07 (dd, *J* = 4.2, 2.1Hz), 129.68 (d, *J* = 4.3Hz), 123.32 (d, *J* = 14.0Hz), 122.49 (d, *J* = 15.3Hz), 115.73 (dd, *J* = 252.7, 248.4Hz), 115.68 (dd, *J* = 254.0, 250.3Hz), 63.21, 63.15, 51.92, 51.45, 49.74 (d, *J* = 5.3Hz), 49.47 (d, *J* = 5.8Hz), 47.38 (d, *J* = 2.5Hz), 47.26 (d, *J* = 3.1Hz), 43.37, 43.33, 37.09 (dd, *J* = 45.9, 21.8Hz), 37.09 (dd, *J* = 43.4, 24.0Hz), 19.51 (d, *J* = 1.5Hz), 19.40, 18.06 (d, *J* = 5.1Hz), 17.97 (d, *J* = 4.8Hz), 13.87, 13.84.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{23}F_3NO_4^+$ 374.1574; Found 374.1573.

ethyl 3-(7-chloro-2-isopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2,2-difluoropropanoate (3g)



Yield: 49%. Pale yellow oil; Isolated as an inseparatable mixture of diastereomers, *dr* =1:1

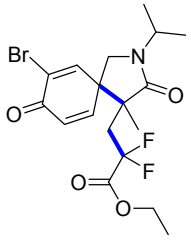
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, J = 2.9 Hz, 1H), 7.00 (d, J = 2.9 Hz, 1H), 6.96 (dd, J = 10.1, 2.9 Hz, 1H), 6.86 (dd, J = 10.1, 2.9 Hz, 1H), 6.55 (d, J = 10.1 Hz, 1H), 6.49 (d, J = 10.1 Hz, 1H), 4.44 – 4.36 (m, 2H), 4.29 (q, J = 7.2 Hz, 2H), 4.29 (q, J = 7.2 Hz, 2H), 3.51 (t, J = 10.7 Hz, 2H), 3.20 (d, J = 10.5 Hz, 1H), 3.15 (d, J = 10.5 Hz, 1H), 2.70 (dtd, J = 25.5, 16.5, 2.5 Hz, 2H), 2.20 – 2.06 (m, 2H), 1.41 (d, J = 2.4 Hz, 3H), 1.38 (d, J = 2.0 Hz, 3H), 1.34 (t, J = 7.2 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H), 1.21 – 1.14 (m, 12H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -97.58 (d, J = 264.6 Hz, 1F), -97.99 (d, J = 265.4 Hz, 1F), -101.59 (d, J = 266.2 Hz, 1F), -101.59 (d, J = 264.3 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 177.87, 177.84, 173.60, 173.57, 163.53 (q, J = 31.9 Hz), 163.48 (dd, J = 32.4, 31.4 Hz), 147.88, 147.16 (d, J = 1.4 Hz), 143.46, 142.82 (d, J = 1.3 Hz), 135.32 (d, J = 2.3 Hz), 134.58, 130.67 (d, J = 2.2 Hz), 129.27, 115.70 (t, J = 251.4Hz), 115.66 (t, J = 251.3Hz), 63.21, 63.17, 52.05, 51.75, 50.43, 50.31, 47.04, 46.95, 43.43, 43.36, 37.15 (dd, J = 24.2, 21.8Hz), 36.98 (dd, J = 24.0, 21.6Hz), 19.53 (d, J = 4.2 Hz), 19.40, 18.03 (d, J = 4.7 Hz), 13.87.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{23}ClF_2NO_4^+$ 390.1278; Found 390.1276.

ethyl 3-(7-bromo-2-isopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2,2-difluoropropanoate (3h)



Yield: 62%. Pale yellow oil; Isolated as an inseparatable mixture of diastereomers, *dr*

=1:1

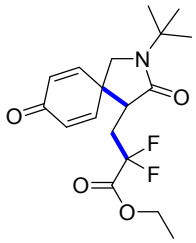
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 2.8 Hz, 1H), 7.27 (d, J = 2.8 Hz, 1H), 6.97 (dd, J = 10.2, 2.8 Hz, 1H), 6.88 (dd, J = 10.1, 2.8 Hz, 1H), 6.55 (d, J = 10.2 Hz, 1H), 6.49 (d, J = 10.1 Hz, 1H), 4.50 – 4.32 (m, 4H), 4.29 (q, J = 7.2 Hz, 2H), 4.29 (q, J = 7.1 Hz, 2H), 3.53 (d, J = 10.4 Hz, 1H), 3.49 (d, J = 10.8 Hz, 1H), 3.21 (d, J = 10.8 Hz, 1H), 3.16 (d, J = 10.4 Hz, 1H), 2.70 (dtd, J = 25.3, 16.4, 4.4 Hz, 2H), 2.23 – 2.01 (m, 2H), 1.41 (d, J = 2.2 Hz, 3H), 1.38 (d, J = 2.2 Hz, 3H), 1.34 (t, J = 7.1 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H), 1.22 – 1.14 (m, 12H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -97.57 (d, J = 264.3 Hz, 1F), -97.94 (d, J = 265.8 Hz, 1F), -101.55 (d, J = 265.8 Hz, 1F), -101.57 (d, J = 264.3 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 177.76, 177.73, 173.57, 173.53, 163.51 (t, J = 32.0 Hz), 163.46 (dd, J = 33.2, 31.5 Hz), 147.89, 147.85, 147.28 (d, J = 1.3 Hz), 147.11 (d, J = 1.4 Hz), 130.11 (d, J = 2.3 Hz), 128.72, 127.22 (d, J = 2.8 Hz), 126.40, 115.65 (t, J = 248.6 Hz), 63.21, 63.17, 51.96, 51.68, 51.33, 51.22, 46.78, 46.68, 43.42, 43.35, 37.10 (dd, J = 23.9, 21.7 Hz), 36.98 (dd, J = 24.1, 21.9 Hz), 29.70, 19.53 (d, J = 4.7 Hz), 19.40, 18.04 (d, J = 4.7 Hz), 13.89, 13.87.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{23}BrF_2NO_4^+$ 343.0073; Found 343.0074

ethyl 3-(2-(tert-butyl)-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2,2-difluoro propanoate (3i)



Yield: 90%. Pale yellow oil;

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (td, J = 11.2, 2.9 Hz, 2H), 6.45 – 6.39 (m, 2H), 4.29 (qd, J = 7.2, 1.9 Hz, 1H), 3.62 (d, J = 10.2 Hz, 1H), 3.30 (d, J = 10.2 Hz, 1H), 3.01 (dd, J = 6.5, 5.0 Hz, 1H), ^{1}H 2.71 – 2.55 (m, 1H), 1.85 – 1.68 (m, 1H), 1.42 (s, 9H), 1.33 (t, J = 7.2 Hz, 3H).

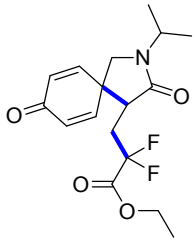
^{19}F NMR (377 MHz, $CDCl_3$) δ -101.28 (d, J = 257.5 Hz, 1F), -107.29 (d, J = 257.5

Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.13, 171.32, 163.52 (t, *J* = 32.2 Hz), 149.38, 146.28, 131.64, 131.48, 114.80 (dd, *J* = 250.0, 249.2 Hz), 63.10, 54.86, 51.54, 46.15, 46.02 (t, *J* =2.6 Hz), 30.82 (dd, *J* = 24.6, 23.5 Hz), 27.59, 13.85.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{24}F_2NO_4^+$ 356.1668; Found 356.1667.

ethyl 2,2-difluoro-3-(2-isopropyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl) propanoate (3j)



Yield: 71%. Pale yellow oil;

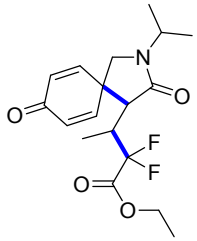
^{1}H NMR (400 MHz, $CDCl_3$) *δ* 6.89 (dd, *J* = 10.4, 3.0 Hz, 1H), 6.80 – 6.73 (m, 1H), 6.43 (d, *J* = 10.0 Hz, 2H), 4.49 – 4.37 (m, 1H), 4.31 (q, *J* = 7.2 Hz, 2H), 3.54 (d, *J* = 10.2 Hz, 1H), 3.18 (d, *J* = 10.2 Hz, 1H), 3.05 (t, *J* = 5.8 Hz, 1H), 2.77 – 2.57 (m, 1H), 1.91 – 1.73 (m, 1H), 1.34 (t, *J* = 7.2 Hz, 3H), 1.17 (d, *J* = 6.7 Hz, 6H).

^{19}F NMR (377 MHz, $CDCl_3$) *δ* -100.99 (d, *J* = 258.2 Hz, 1F), -107.51 (d, *J* = 258.2 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 185.05, 170.58, 163.49 (t, *J* = 32.1 Hz), 149.22, 145.97, 131.73, 131.46, 114.74 (t, *J* = 249.7Hz), 63.14, 48.39, 46.65, 45.25 (dd, *J* = 3.3, 2.5 Hz), 43.36, 30.71 (dd, *J* = 25.0, 23.4 Hz), 19.65, 19.60, 13.86.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{22}F_2NO_4^+$ 342.1511; Found 342.1512.

ethyl 2,2-difluoro-3-(2-isopropyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl) butanoate (3k)



Yield: 72%. *dr* =3:1, two diastereomers was obtained through flash column chromatography.

Isomer 1: Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (dd, J = 10.2, 3.0 Hz, 1H), 6.83 (dd, J = 10.0, 3.0 Hz, 1H), 6.49 (dd, J = 10.0, 1.8 Hz, 1H), 6.44 (dd, J = 10.2, 1.8 Hz, 1H), 4.41 (dt, J = 12.6, 6.3 Hz, 1H), 4.36 – 4.32 (m, 2H), 3.47 (d, J = 10.0 Hz, 1H), 3.19 (d, J = 10.0 Hz, 1H), 3.15 (s, 1H), 1.99 – 1.87 (m, 1H), 1.35 (t, J = 7.2 Hz, 3H), 1.21 (d, J = 7.3 Hz, 3H), 1.17 (d, J = 6.8 Hz, 3H), 1.14 (d, J = 6.8 Hz, 3H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -107.60 (d, J = 246.5 Hz, 1F), -109.75 (d, J = 246.5 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.10, 169.01, 163.33 (dd, J = 32.8, 31.8Hz), 149.12, 146.57, 132.35, 130.97, 116.41 (t, J = 251.9Hz), 63.21, 48.57 (dd, J = 5.0, 0.8Hz), 47.71, 47.35, 42.85, 36.19 (t, J = 23.0Hz), 19.81, 19.56, 13.94, 10.39 (t, J = 4.6Hz).

Isomer 2: Pale yellow oil;

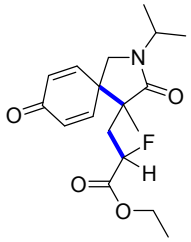
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (dd, J = 10.0, 2.8 Hz, 1H), 6.86 (dd, J = 10.0, 2.8 Hz, 1H), 6.42 (d, J = 10.0 Hz, 1H), 6.37 (dd, J = 10.0, 1.2Hz, 1H), 4.49 – 4.40 (m, 1H), 4.32 (q, J = 7.2 Hz, 2H), 3.43 (d, J = 10.0 Hz, 1H), 3.15 (d, J = 4.8 Hz, 1H), 3.13 – 3.06 (m, 1H), 3.04 (d, J = 10.0 Hz, 1H), 1.35 (t, J = 7.2 Hz, 4H), 1.17 (d, J = 6.8 Hz, 3H), 1.14 (d, J = 7.2 Hz, 3H), 1.01 (d, J = 7.2 Hz, 3H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -108.01 (d, J = 259.8 Hz, 1F), -109.35 (d, J = 259.8 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.25, 170.20, 163.61 (t, J = 32.3 Hz), 150.46, 147.44, 131.07, 129.69, 116.61 (t, J = 252.8 Hz), 62.97, 51.51, 49.57, 46.62, 43.30, 36.42 (dd, J = 23.0, 21.2 Hz), 19.73, 19.56, 13.94, 11.23 (t, J = 4.7 Hz).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{24}F_2NO_4^+$ 356.1668; Found 356.1667.

ethyl 2-fluoro-3-(2-isopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)propanoate (3l)



Yield: 65%. Pale yellow oil; Isolated as an inseparatable mixture of diastereomers, *dr* =1:0.75;

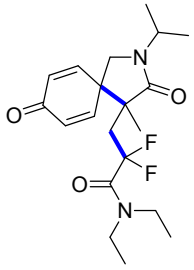
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 – 6.88 (m, 1.7H), 6.86 – 6.77 (m, 1.7H), 6.40 – 6.29 (m, 3.4H), 5.39 (dd, *J* = 49.6, 9.6 Hz, 1H), 4.81 (dd, *J* = 49.6, 9.2 Hz, 0.7H), 4.41 – 4.30 (m, 1.7H), 4.19 – 4.09 (m, 3.4H), 3.39 – 3.28 (m, 1.7H), 3.22 – 3.15 (m, 1.7H), 2.32 – 2.09 (m, 1.7H), 2.06 – 1.89 (m, 0.7H), 1.66 (ddd, *J* = 19.8, 15.3, 9.6 Hz, 1H), 1.22 – 1.19 (m, 10.2H), 1.13 – 1.08 (m, 10.2H).

^{19}F NMR (377 MHz, $CDCl_3$) *δ* -184.55(s, 1F), -185.42(s, 0.7F).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 184.77, 184.56, 174.92, 174.44, 169.62 (d, *J* = 23.5 Hz), 169.20 (d, *J* = 23.8 Hz), 148.50, 147.89, 147.79, 147.23, 131.79, 131.27, 131.18, 130.83, 85.92 (d, *J* = 183.6 Hz), 85.73 (d, *J* = 184.4 Hz), 61.86, 61.80, 50.97, 50.96, 48.29, 47.99, 46.85, 46.60, 43.09, 42.97, 37.26 (d, *J* = 20.7 Hz), 35.93 (d, *J* = 20.6 Hz), 19.55, 19.45, 19.41, 18.51 (d, *J* = 3.0 Hz), 17.52 (d, *J* = 3.0 Hz), 14.10, 14.04.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{25}FNO_4^+$ 338.1762; Found 338.1763.

***N*,*N*-diethyl-2,2-difluoro-3-(2-isopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)propanamide (3m)**



Yield: 78%. Pale yellow oil;

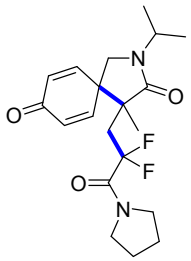
^{1}H NMR (400 MHz, $CDCl_3$) δ6.94 – 6.76 (m, 1H), 6.38 – 6.28 (m, 1H), 4.40 – 4.29 (m, 1H), 3.42 – 3.20 (m, 4H), 3.33 (d, J = 10.4 Hz, 1H), 3.11 (d, J = 10.4 Hz, 1H), 2.74 (dt, J = 27.8, 16.4 Hz, 1H), 2.38 – 2.14 (m, 1H), 1.29 (s, 3H), 1.13 – 1.03 (m, 12H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -94.19 (d, J = 277.5 Hz, 1F), -95.25 (d, J = 277.5 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 184.04, 173.20, 161.36 (t, J = 28.6 Hz), 147.14, 146.88 (d, J = 1.0 Hz), 130.14 (d, J = 1.9 Hz), 129.51, 118.57 (dd, J = 256.6, 254.7 Hz), 50.66, 47.30, 46.15, 42.15, 41.00 (t, J = 6.3 Hz), 40.81, 36.07 (t, J = 22.5 Hz), 18.48, 18.37, 17.09 (d, J = 4.2 Hz), 13.19, 11.26.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{29}F_2N_2O_3^+$ 383.2141; Found 383.2145.

4-(2,2-difluoro-3-oxo-3-(pyrrolidin-1-yl)propyl)-2-isopropyl-4-methyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3n)



Yield: 42%. Pale yellow oil;

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 – 6.89 (m, 2H), 6.42 (d, J = 10.4 Hz, 1H), 6.38 (d, J = 10.0 Hz, 1H), 4.47 – 4.34 (m, 1H), 3.64 – 3.58 (m, 2H), 3.46 (t, J = 6.8 Hz, 2H), 3.40 (d, J = 10.4 Hz, 1H), 3.19 (d, J = 10.4 Hz, 1H), 2.92 – 2.72 (m, 1H), 2.40 – 2.17 (m, 1H), 1.97 – 1.88 (m, 2H), 1.88 – 1.80 (m, 2H), 1.35 (s, 3H), 1.18 (d, J = 6.8 Hz, 3H), 1.15 (d, J = 6.8 Hz, 3H).

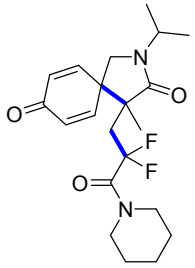
^{19}F NMR (377 MHz, $CDCl_3$) δ -96.35 (d, J = 276.3 Hz, 1F), -98.27 (d, J = 276.3 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.12, 174.15, 161.66 (t, J = 29.3 Hz), 148.13, 147.91 (d, J = 1.3 Hz), 131.15 (d, J = 2.1 Hz), 130.55, 119.00 (dd, J = 255.9, 252.3

Hz), 51.56, 48.26, 46.63 (t, *J*= 12.8 Hz), 46.63, 46.56, 43.18, 36.57 (t, *J*= 22.9 Hz), 26.49, 23.21, 19.48, 19.40, 18.07 (d, *J* = 4.6 Hz).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{27}F_2N_2O_3^+$ 381.1984; Found 381.1984.

4-(2,2-difluoro-3-oxo-3-(piperidin-1-yl)propyl)-2-isopropyl-4-methyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3o)



Yield: 51%. Pale yellow oil;

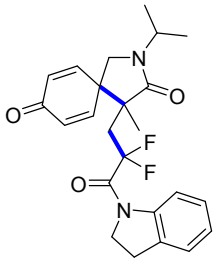
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (dd, *J* = 10.4, 3.2 Hz, 1H), 6.89 (dd, *J* = 10.4, 3.2 Hz, 1H), 6.42 (d, *J* = 10.4 Hz, 1H), 6.36 (dd, *J* = 10.0, 1.2 Hz, 1H), 4.48 – 4.35 (m, 1H), 3.61 – 3.52 (m, 2H), 3.52 – 3.44 (m, 2H), 3.43 (d, *J* = 10.4 Hz, 1H), 3.15 (d, *J* = 10.4 Hz, 1H), 2.86 – 2.68 (m, 1H), 2.44 – 2.28 (m, 1H), 1.67 – 1.60 (m, 2H), 1.59 – 1.52 (m, 4H), 1.37 (s, 3H), 1.16 (m, 6H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -93.71 (d, *J* = 277.5 Hz, 1F), -94.66 (d, *J* = 277.5 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 184.08, 173.31, 160.32 (t, *J* = 28.4 Hz), 147.26, 146.84, 130.20 (d, *J* = 1.2 Hz), 129.33, 118.52 (t, *J* = 255.5 Hz), 50.71, 47.21, 46.16, 45.90 (t, *J* = 6.6 Hz), 43.60, 42.16, 36.01 (t, *J* = 22.2 Hz), 25.39, 24.52, 23.36, 18.51, 18.35, 16.95 (d, *J* = 3.4 Hz).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{29}F_2N_2O_3^+$ 395.2141; Found 395.2141.

4-(2,2-difluoro-3-(indolin-1-yl)-3-oxopropyl)-2-isopropyl-4-methyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3p)



Yield: 44%. Pale yellow oil;

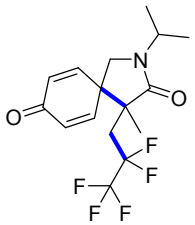
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.1 Hz, 1H), 7.24 – 7.19 (m, 2H), 7.12 – 7.05 (m, 1H), 6.98 – 6.91 (m, 2H), 6.45 – 6.38 (m, 2H), 4.45 – 4.36 (m, 1H), 4.27 (t, J = 8.1 Hz, 2H), 3.41 (d, J = 10.4 Hz, 1H), 3.23 (d, J = 10.4 Hz, 1H), 3.17 (t, J = 8.3 Hz, 2H), 2.95 (dt, J = 27.1, 16.2 Hz, 1H), 2.43 – 2.28 (m, 1H), 1.38 (s, 3H), 1.20 (d, J = 6.8 Hz, 3H), 1.15 (d, J = 6.8 Hz, 3H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -95.64 (d, J = 281.2 Hz, 1F), -98.43 (d, J = 281.2 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.03, 174.03, 160.83 (t, J = 29.6 Hz), 147.97, 147.83, 142.64, 131.71, 131.22, 130.71, 127.48, 125.08, 124.67, 119.31 (dd, J = 258.0, 252.8 Hz), 117.83, 51.53, 48.32, 48.00, 47.92 (dd, J = 9.8, 6.4 Hz), 43.20, 36.53 (t, J = 22.3 Hz), 29.70, 19.50, 19.43, 18.22 (d, J = 4.9 Hz).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{27}F_2N_2O_3^+$ 429.1984; Found 429.1983.

2-isopropyl-4-methyl-4-(2,2,3,3,3-pentafluoropropyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione(3q)



Yield: 30%. Pale yellow oil;

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (dd, J = 10.0, 2.8 Hz, 1H), 6.79 (dd, J = 10.4, 3.2 Hz, 1H), 6.46 (ddd, J = 10.4, 2.0, 1.2 Hz, 1H), 6.37 (dd, J = 10.0, 1.6 Hz, 1H), 4.49 – 4.37 (m, 1H), 3.52 (d, J = 10.4 Hz, 1H), 3.08 (d, J = 10.4 Hz, 1H), 2.67 (ddd, J = 36.4, 16.4, 9.2 Hz, 1H), 2.14 (ddd, J = 36.0, 16.4, 2.4 Hz, 1H), 1.44 (d, J = 2.7 Hz, 3H),

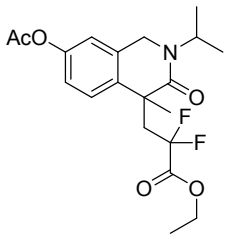
1.18 (d, J = 3.2 Hz, 3H), 1.17 (d, J = 3.2 Hz, 3H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -86.50 (s, 3F), -111.11 (d, J = 263.9 Hz, 1F), -113.97 (d, J = 263.9 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 184.62, 173.84, 147.28, 146.46 (d, J = 2.6 Hz), 132.01 (d, J = 3.7 Hz), 130.21, 118.66(q, J = 284.4 Hz), 116.26(t, J = 253.7 Hz), 51.56, 47.59, 47.45, 43.48, 33.09 (t, J = 20.7 Hz), 19.54, 19.36, 17.70(d, J = 4.9 Hz).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{19}F_5NO_2^+$ 352.1330; Found 352.1334.

ethyl 3-(7-acetoxy-2-isopropyl-4-methyl-3-oxo-1,2,3,4-tetrahydroisoquinolin-4- yl)-2,2-difluoropropanoate (4a)



Yield: 77%. Pale yellow oil;

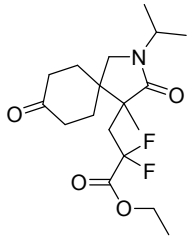
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 8.8 Hz, 1H), 7.00 (dd, J = 8.8, 2.4 Hz, 1H), 6.90 (d, J = 1.6 Hz, 1H), 5.07 – 4.95 (m, 1H), 4.47 (d, J = 16.4 Hz, 1H), 4.32 (d, J = 16.0 Hz, 1H), 4.01 – 3.84 (m, 2H), 3.15 – 3.01 (m, 1H), 2.68 – 2.54 (m, 1H), 2.30 (s, 3H), 1.62 (s, 3H), 1.26 – 1.17 (m, 9H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -99.32 (dt, J = 267.7, 13.0 Hz), -104.68 (ddd, J = 267.7, 22.8, 13.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.72, 169.31, 163.48 (t, J = 32.7 Hz), 149.41, 133.81, 131.80, 127.90, 120.59, 118.34, 115.14 (dd, J = 247.0, 244.3 Hz), 62.85, 44.83, 44.32 (t, J = 23.0 Hz), 42.78, 42.15 (d, J = 4.1 Hz), 29.18, 21.09, 19.23, 18.58, 13.71.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{26}F_2NO_5^+$ 398.1774; Found 398.1775.

ethyl 2,2-difluoro-3-(2-isopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]decan-4-yl) propanoate (5a)



Yield: 90%. Pale yellow oil;

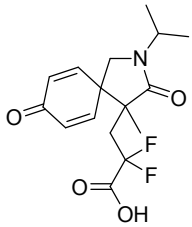
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42 – 4.35 (m, 1H), 4.32 (q, J = 7.2 Hz, 2H), 3.53 (d, J = 10.4 Hz, 1H), 3.24 (d, J = 10.4 Hz, 1H), 2.68 (dt, J = 26.0, 16.8 Hz, 1H), 2.48 – 2.41 (m, 3H), 2.38 – 2.26 (m, 1H), 2.21 – 2.05 (m, 2H), 1.99 – 1.86 (m, 2H), 1.81 – 1.74 (m, 1H), 1.36 (t, J = 7.2 Hz, 3H), 1.21 (d, J = 1.8 Hz, 3H), 1.19 – 1.14 (m, 6H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -96.42 (d, J = 259.4 Hz, 1F), -102.22 (d, J = 259.4 Hz, 1F).

^{13}C NMR (100 MHz, $CDCl_3$) δ 209.71, 175.52, 164.05 (t, J = 32.3 Hz), 116.45 (dd, J = 254.7, 246.2Hz), 63.12, 49.72 (d, J = 2.0 Hz), 45.77, 42.52, 41.67, 37.85, 37.42, 35.59 (dd, J = 23.5, 21.2 Hz), 29.78 (d, J = 5.4 Hz), 29.71 (d, J = 1.4 Hz), 19.61, 19.57, 17.24 (d, J = 5.0 Hz), 13.91.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{28}F_2NO_4^+$ 360.1981; Found 360.1983.

2,2-difluoro-3-(2-isopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)propanoic acid (6a)



Yield: 91%. Pale yellow oil;

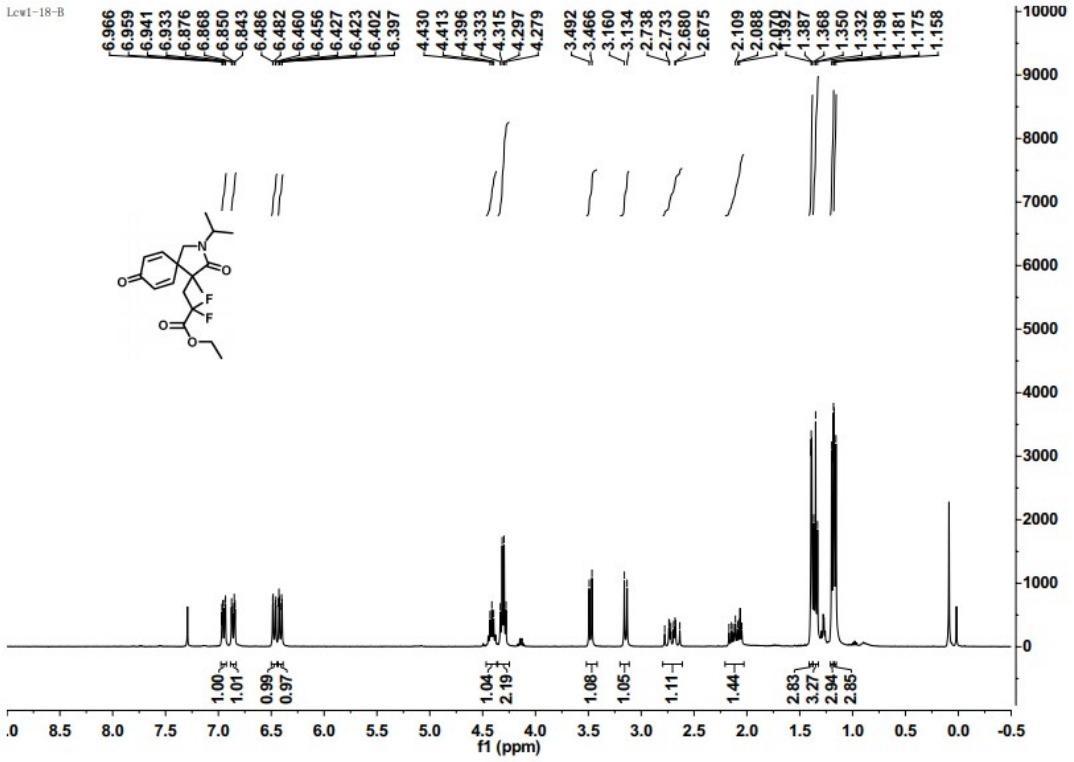
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 6.92 (dd, J = 10.0, 2.8 Hz, 1H), 6.87 (dd, J = 10.0, 2.8 Hz, 1H), 6.42 (d, J = 10.4 Hz, 1H), 6.38 (d, J = 10.8 Hz, 1H), 4.28-4.34 (m, 1H), 3.44 (d, J = 10.8 Hz, 1H), 3.13 (d, J = 10.8 Hz, 1H), 2.61 (dt, J = 22.4, 16.8 Hz, 1H), 2.13 – 1.97 (m, 1H), 1.32 (s, 3H), 1.12 – 1.07 (m, 6H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -97.67 (d, J = 263.9 Hz, 1F), -101.67 (d, J = 263.9 Hz, 1F).

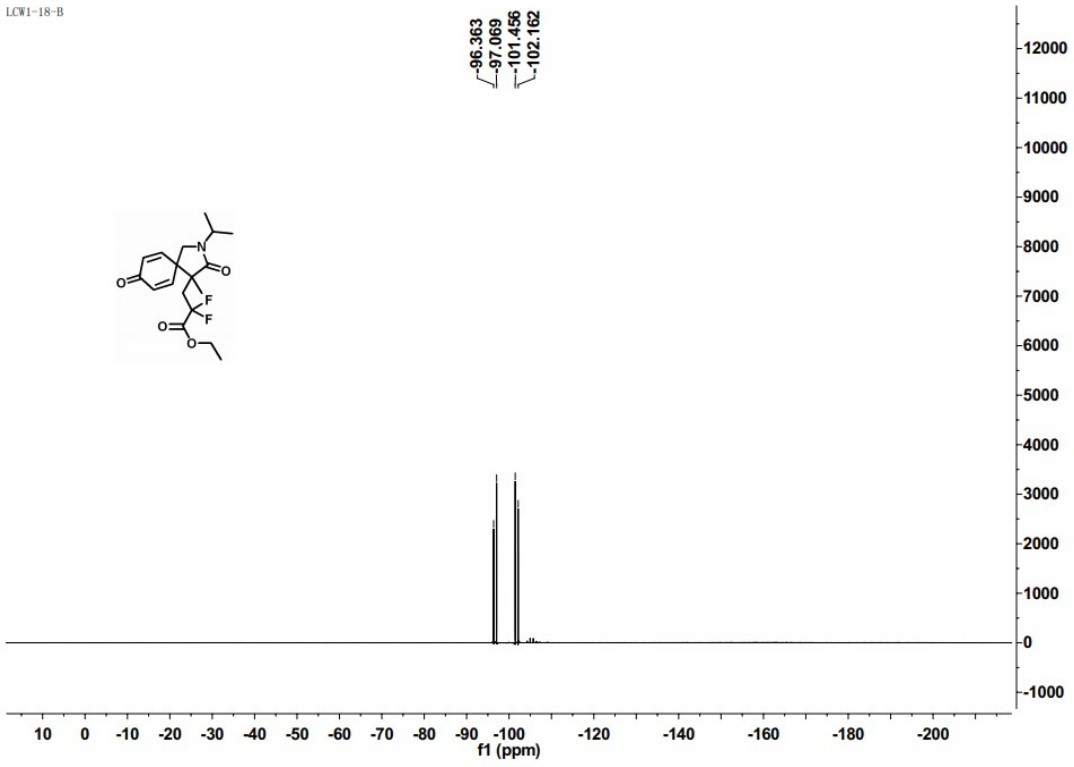
^{13}C NMR (100 MHz, $CDCl_3$) δ 185.64, 174.98, 164.93 (t, J = 31.7 Hz), 148.43, 147.73, 131.61, 130.41, 115.62 (dd, J = 253.0, 248.2 Hz), 51.83 (d, J = 2.3 Hz), 48.21, 47.27, 43.83, 36.90 (dd, J = 23.8, 22.4 Hz), 19.37, 19.30, 17.84 (d, J = 4.3 Hz).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{20}F_2NO_4^+$ 328.1355; Found 328.1355.

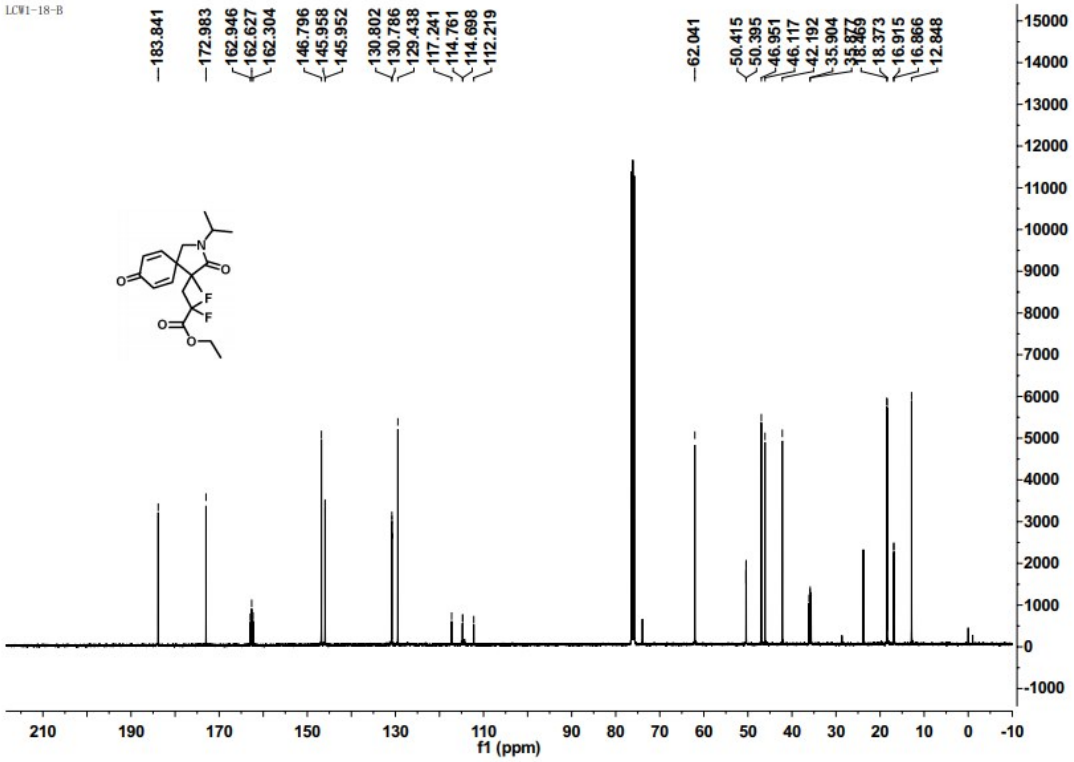
^{1}H NMR Spectra of 3a



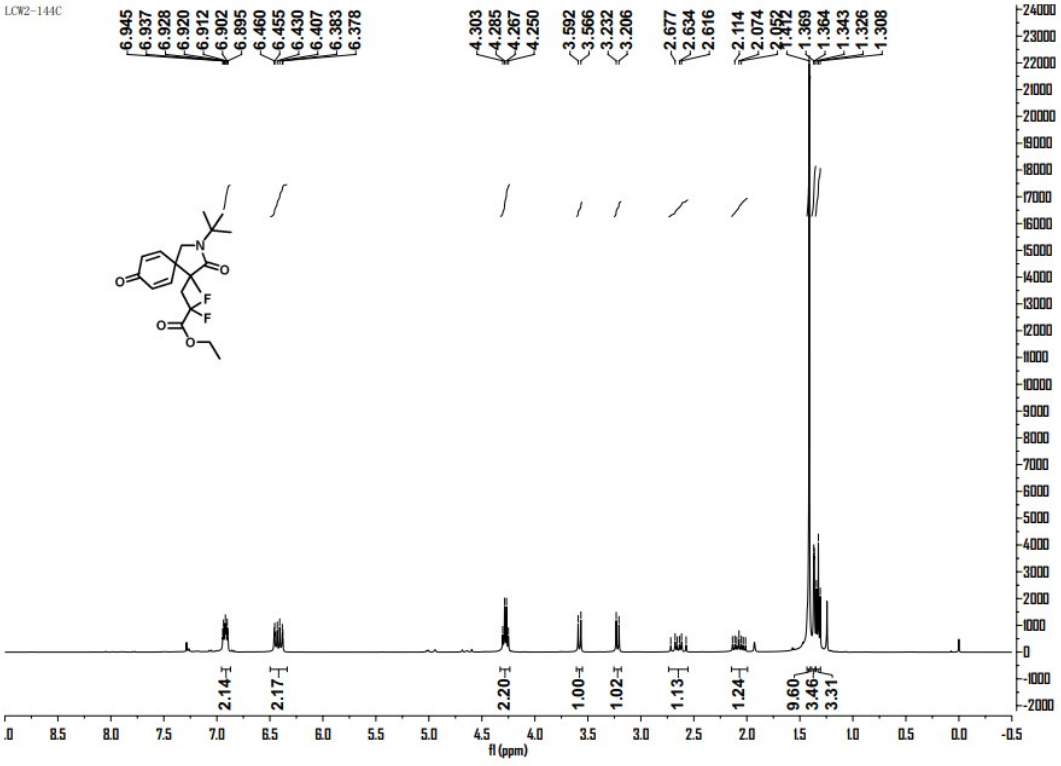
^{19}F NMR Spectra of 3a



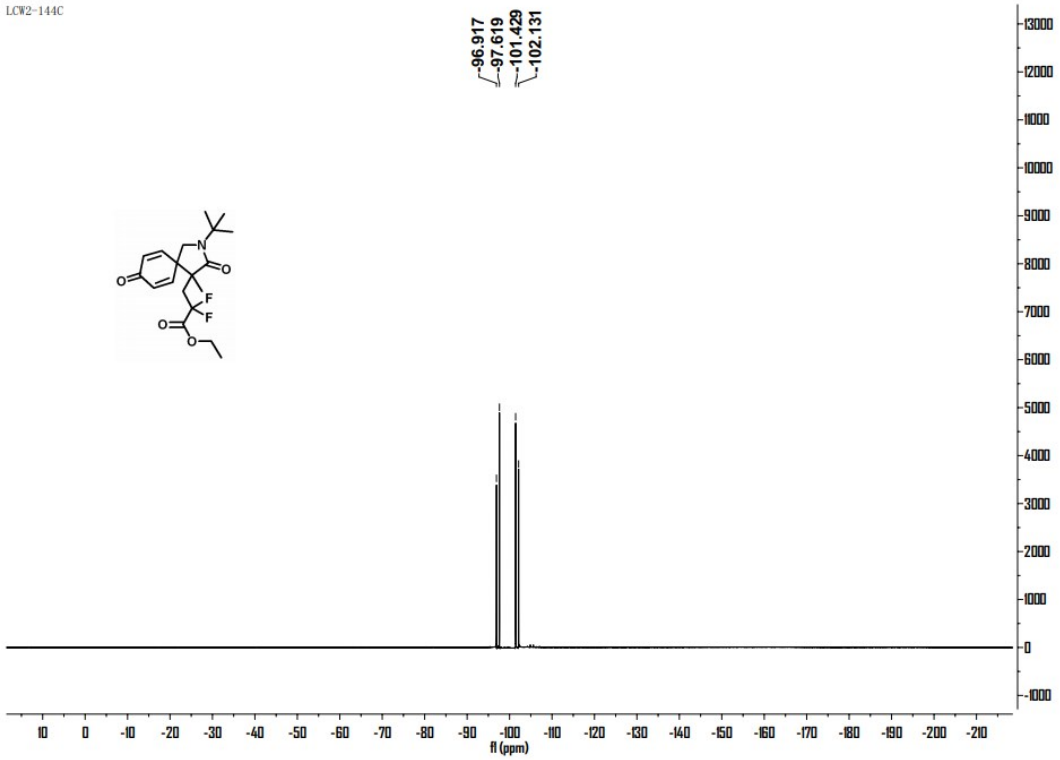
^{13}C NMR Spectra of 3a



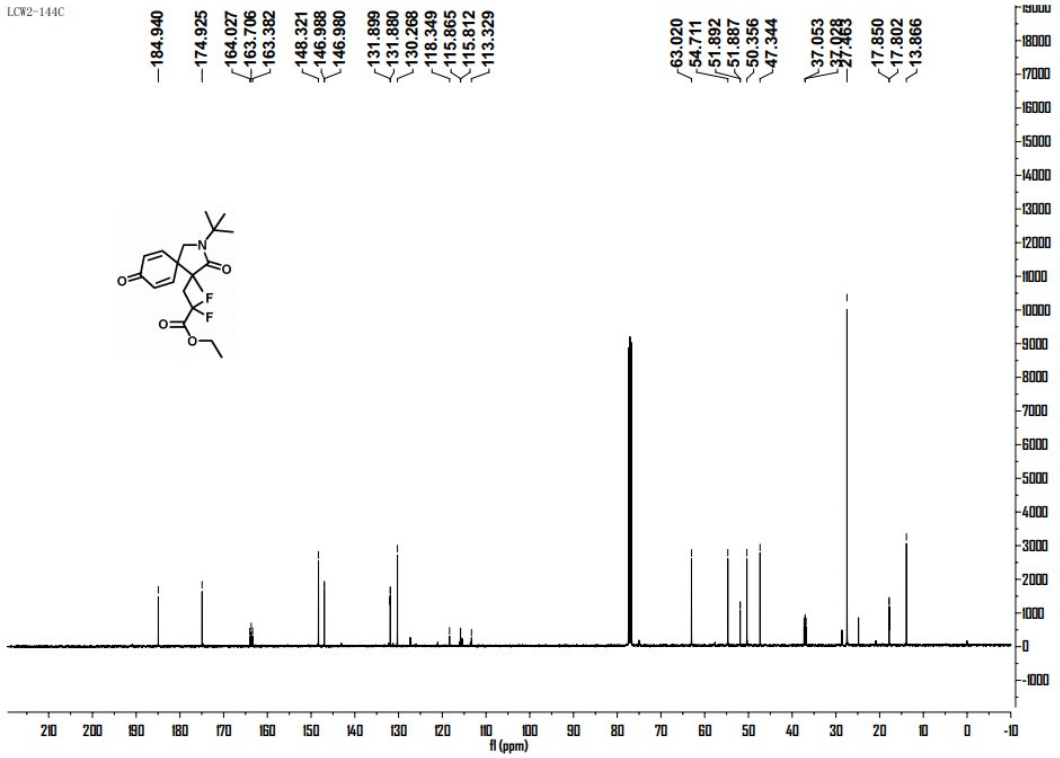
^{1}H NMR Spectra of 3b



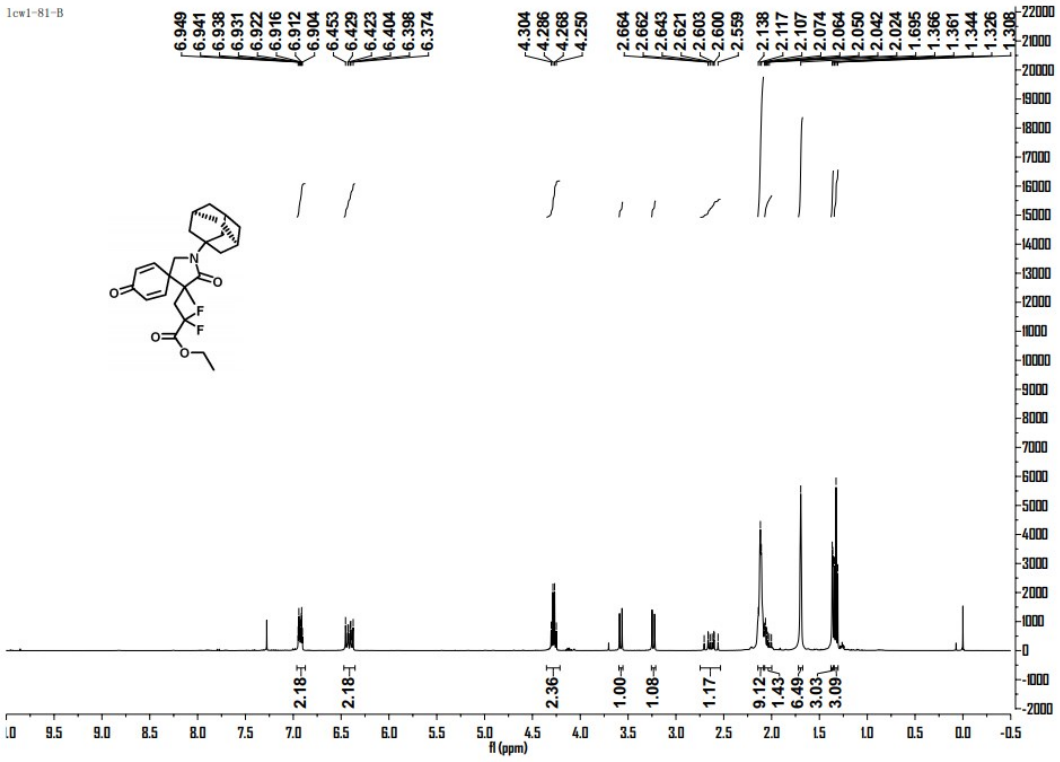
^{19}F NMR Spectra of 3b



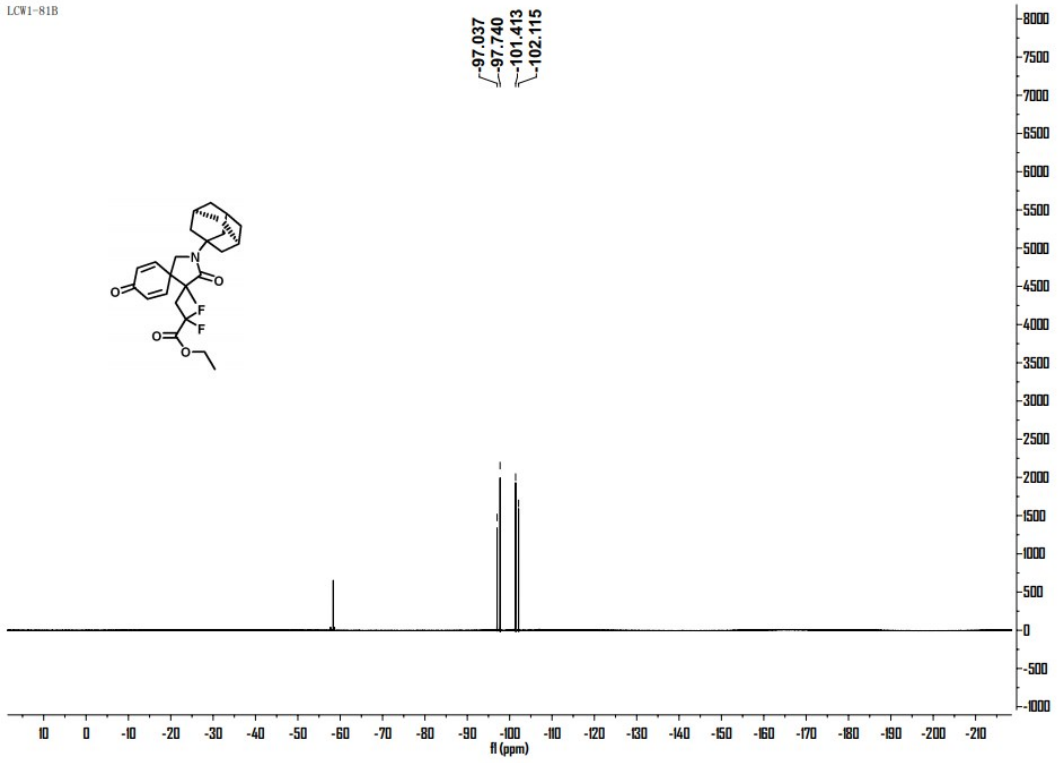
^{13}C NMR Spectra of 3b



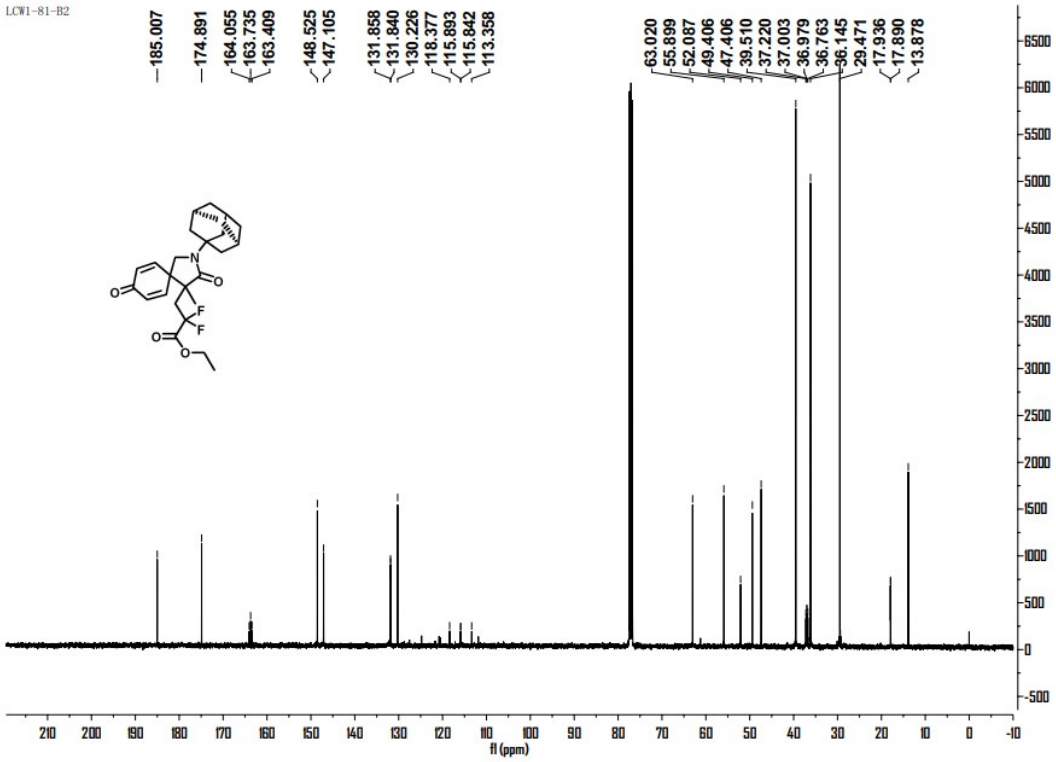
^{1}H NMR Spectra of 3c



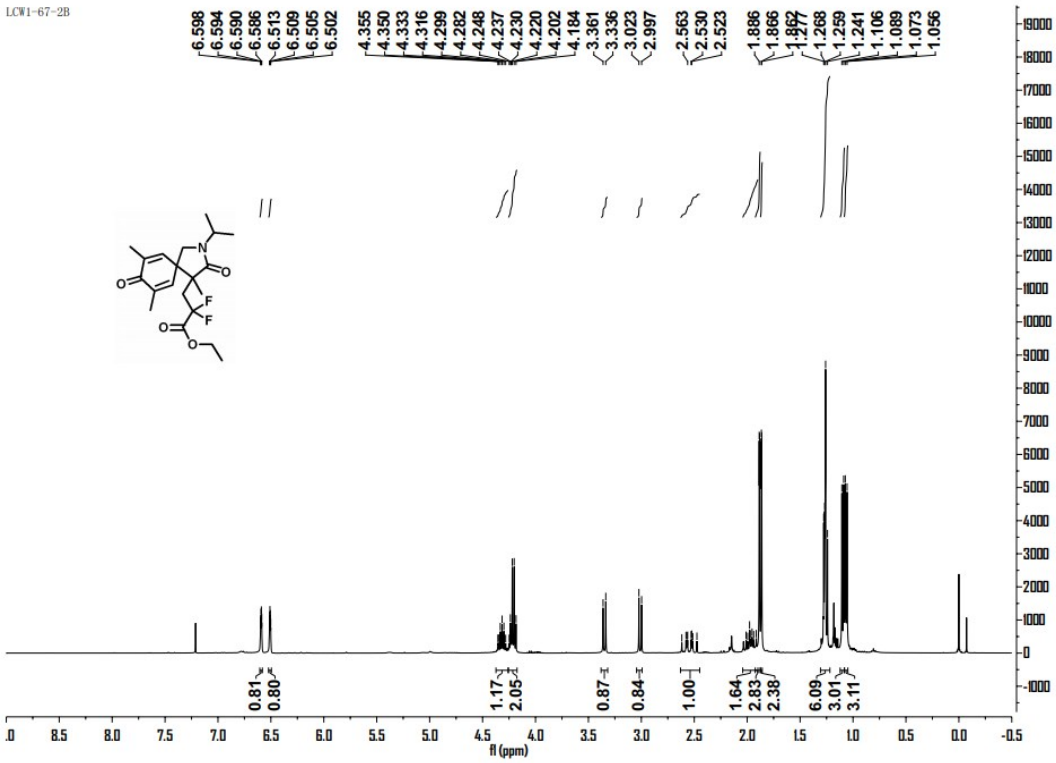
^{19}F NMR Spectra of 3c



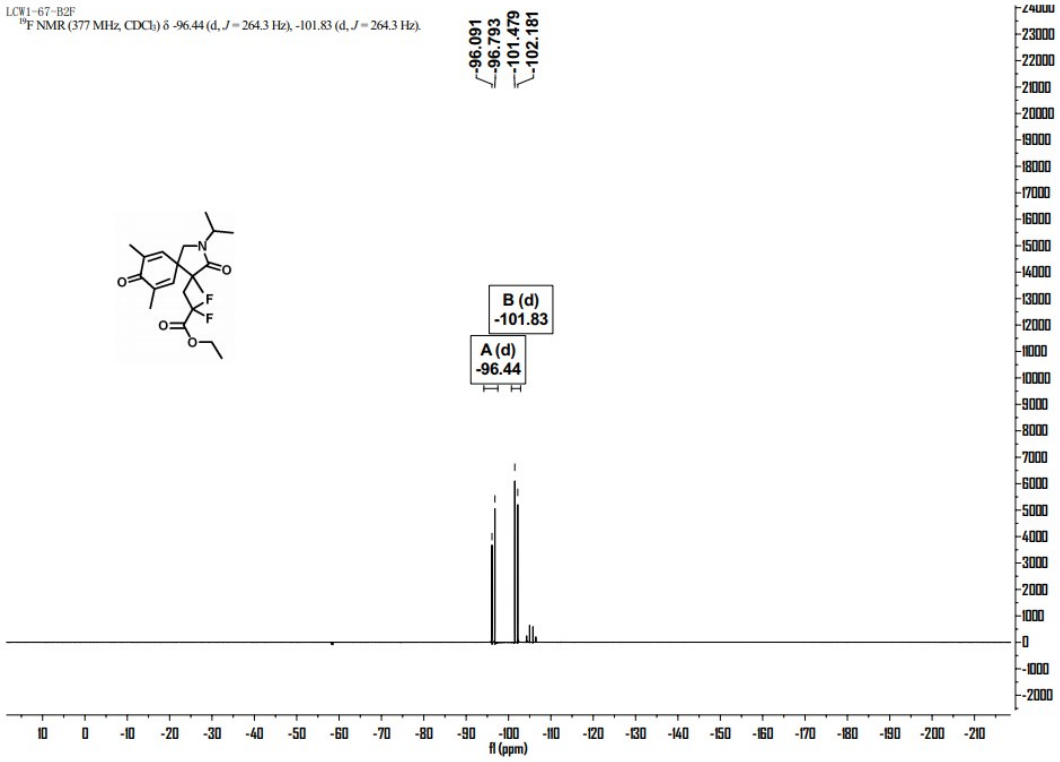
^{13}C NMR Spectra of 3c



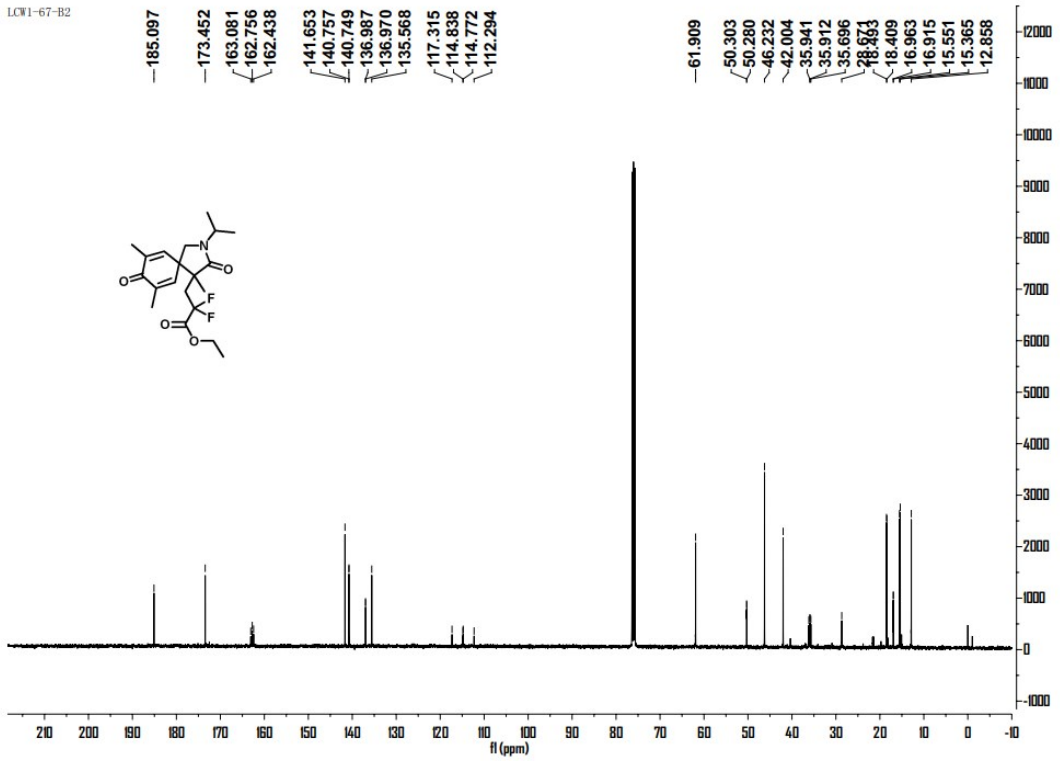
^{1}H NMR Spectra of 3d



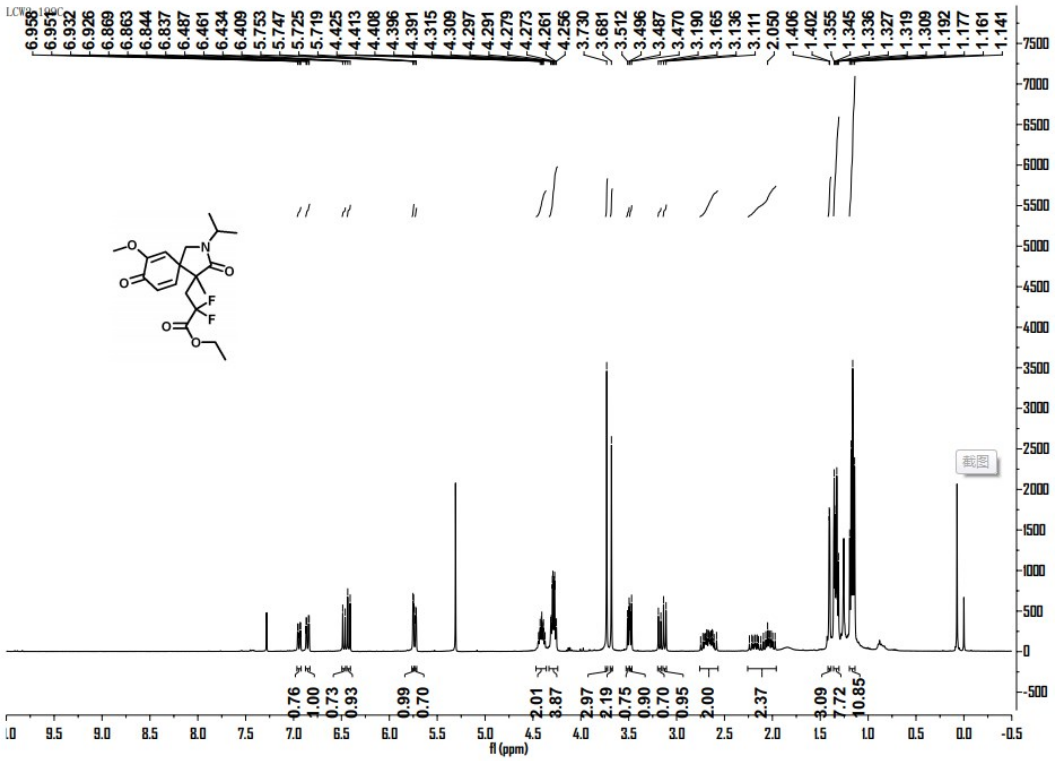
^{19}F NMR Spectra of 3d



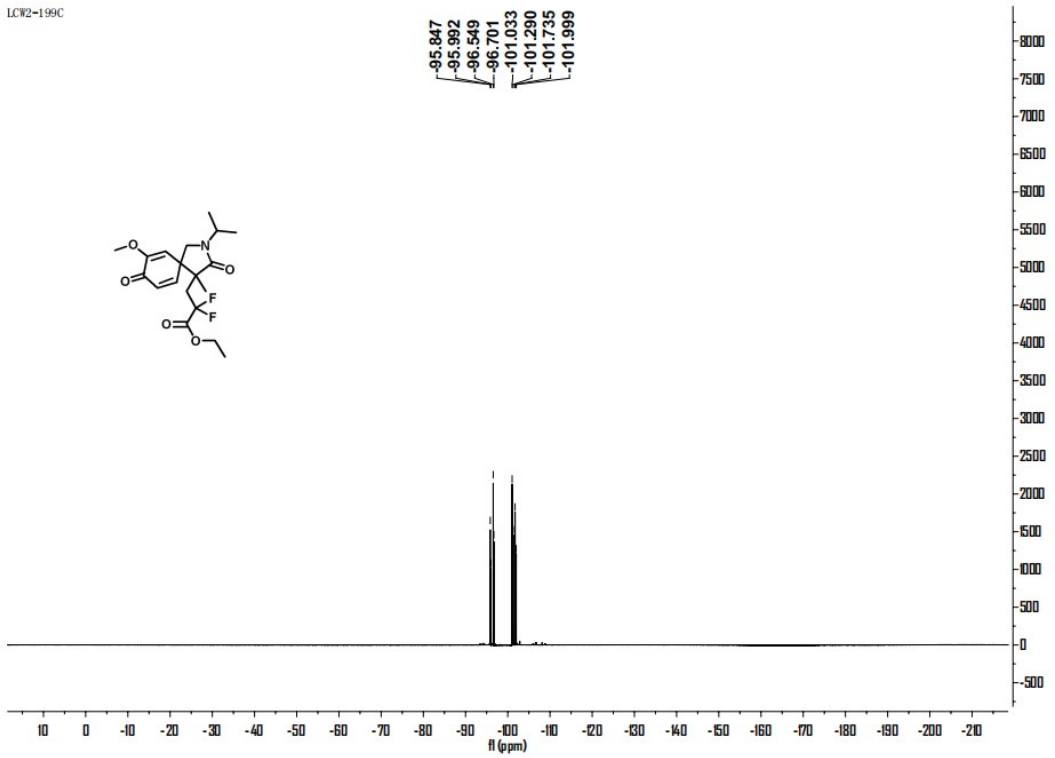
^{13}C NMR Spectra of 3d



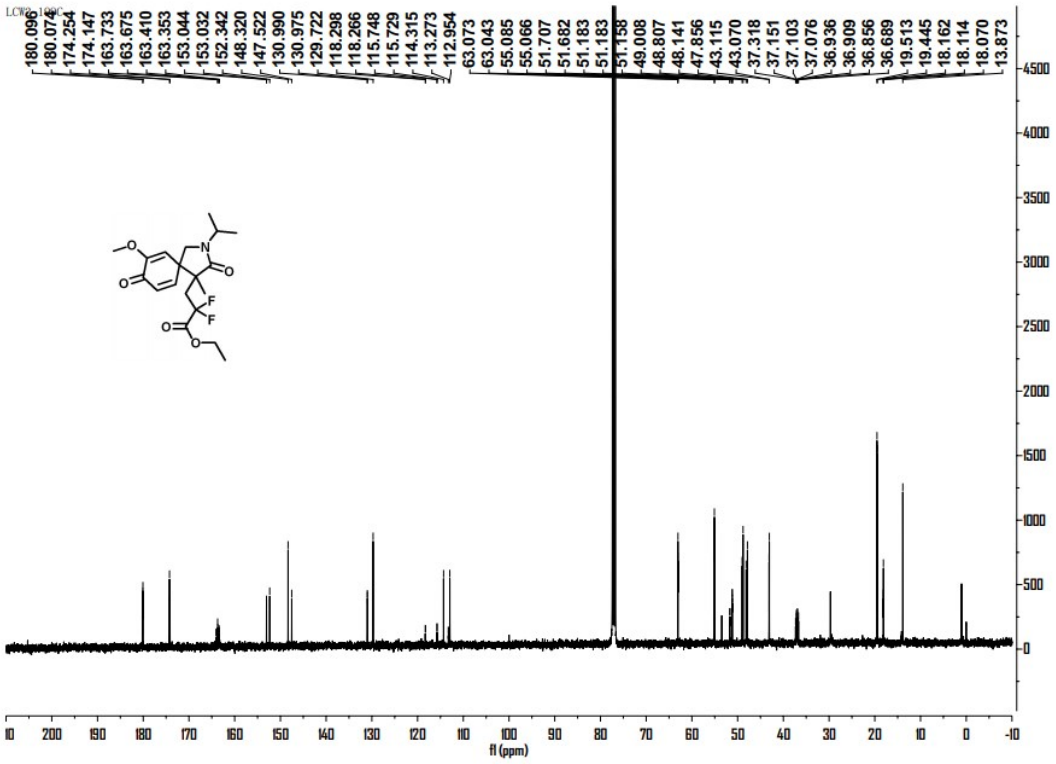
^{1}H NMR Spectra of 3e



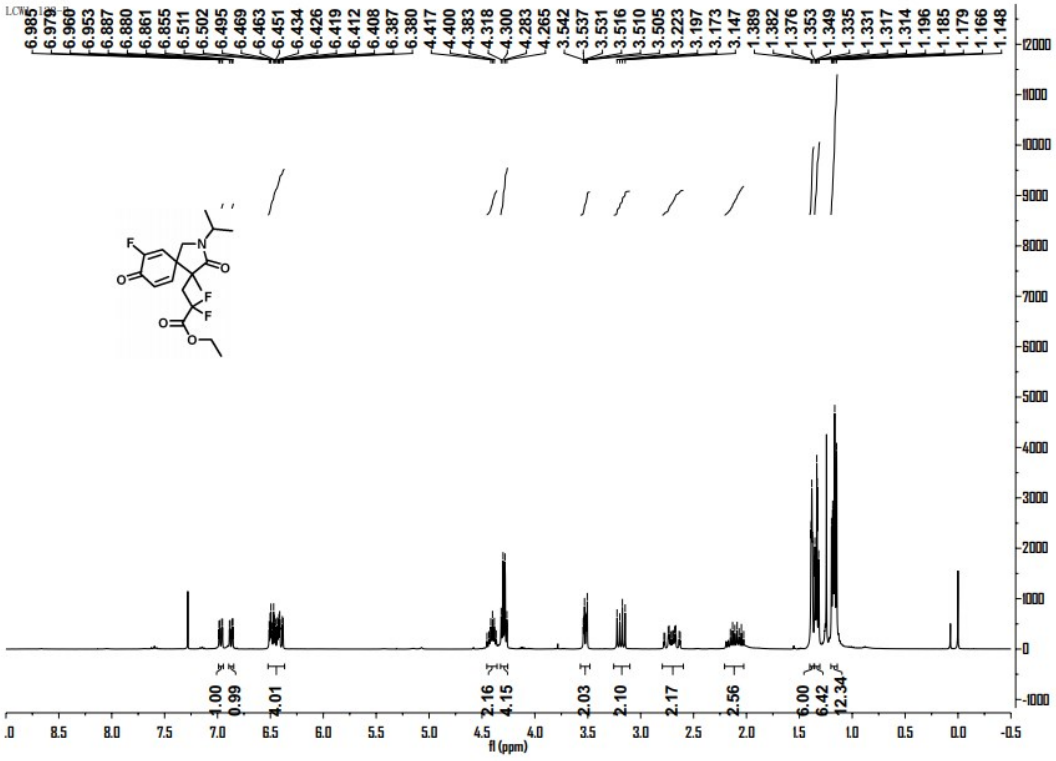
^{19}F NMR Spectra of 3e



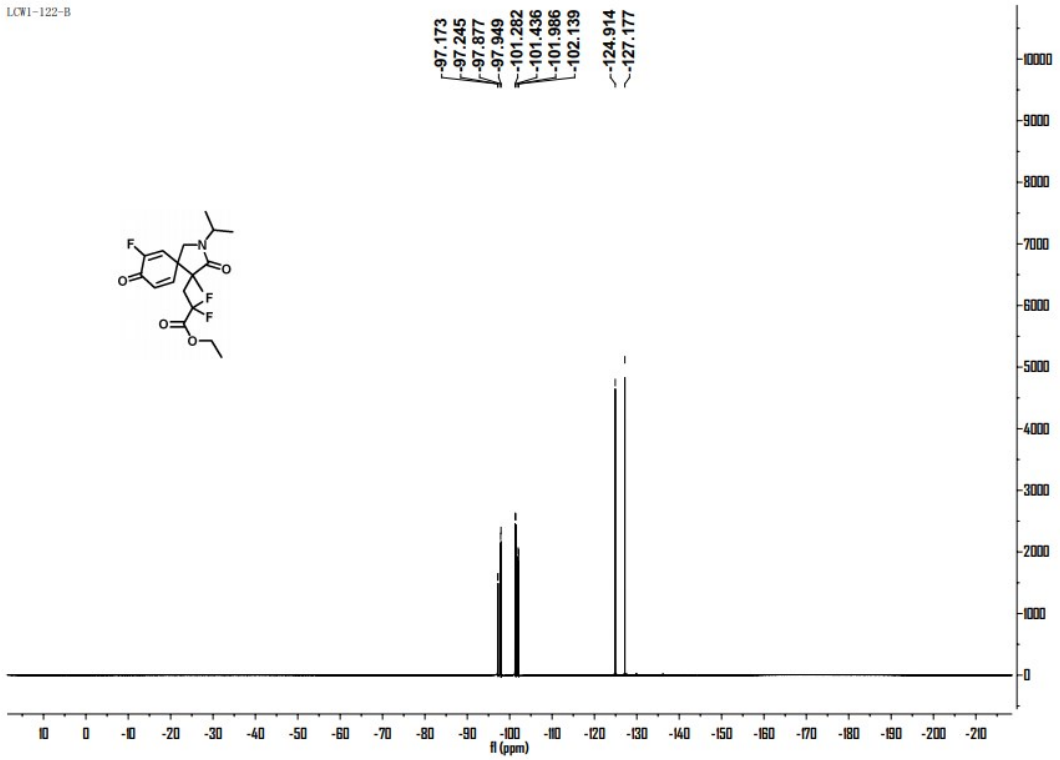
^{13}C NMR Spectra of 3e



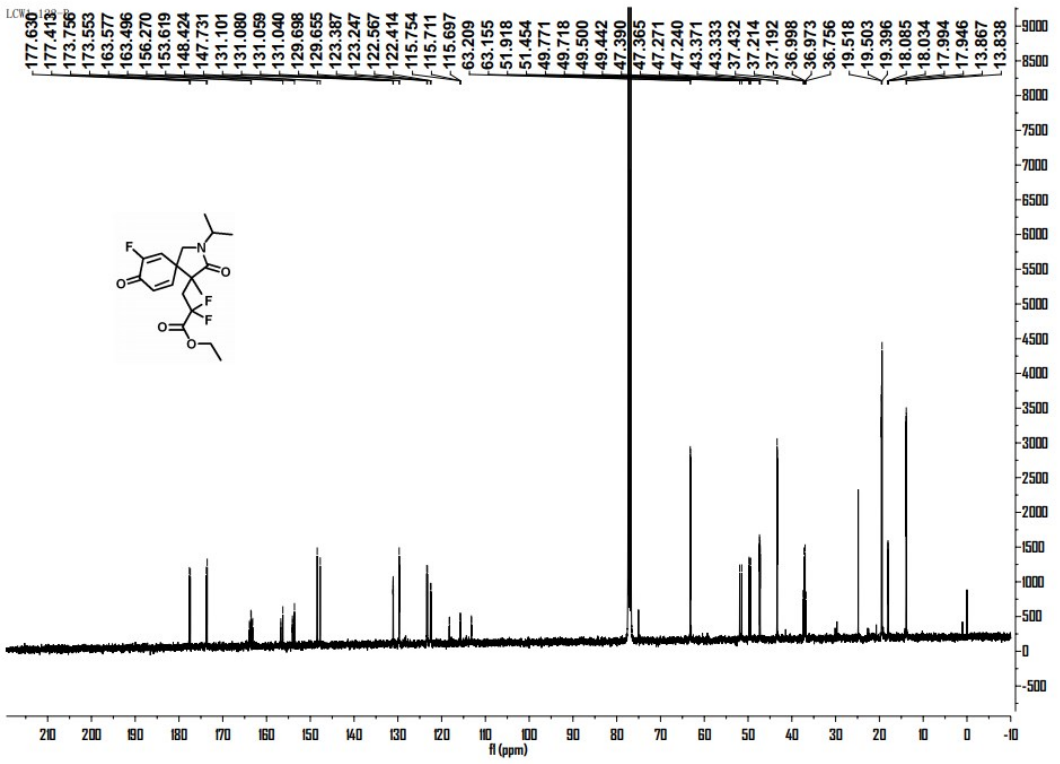
^{1}H NMR Spectra of 3f



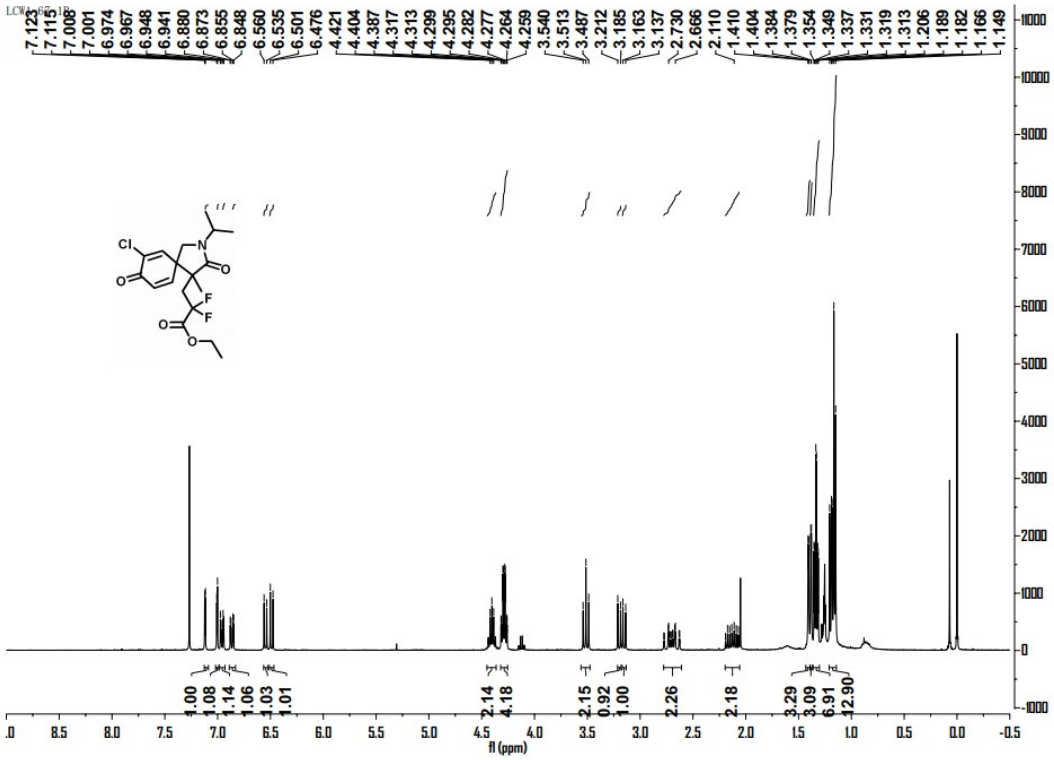
^{19}F NMR Spectra of 3f



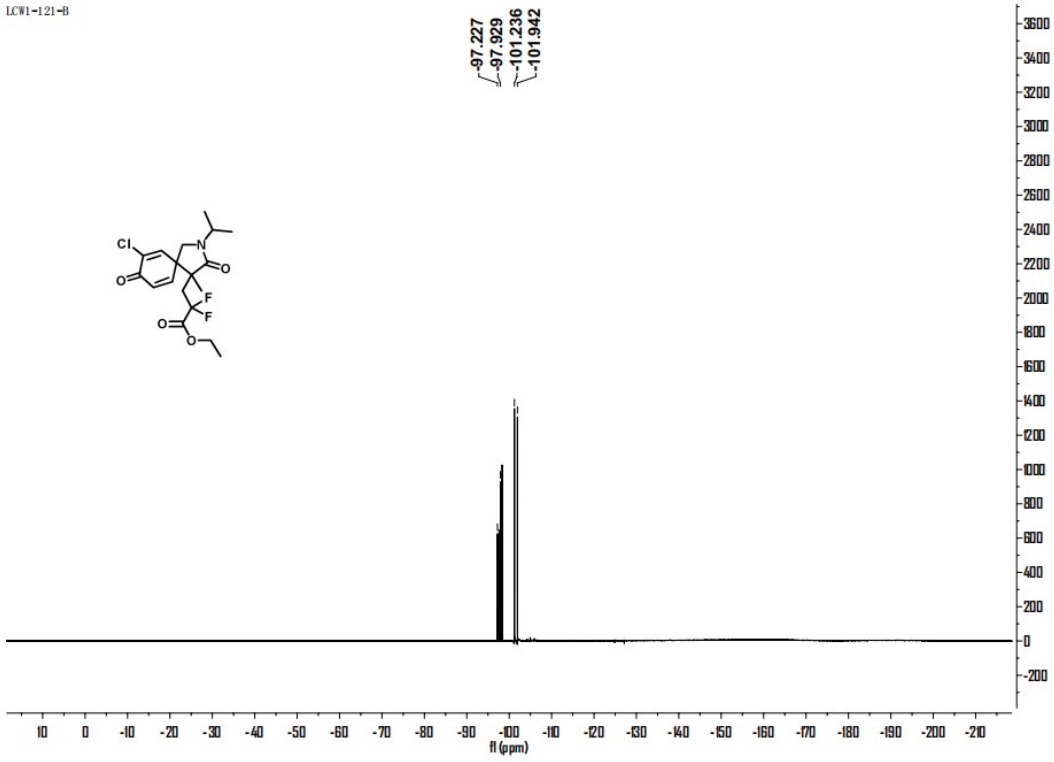
^{13}C NMR Spectra of 3f



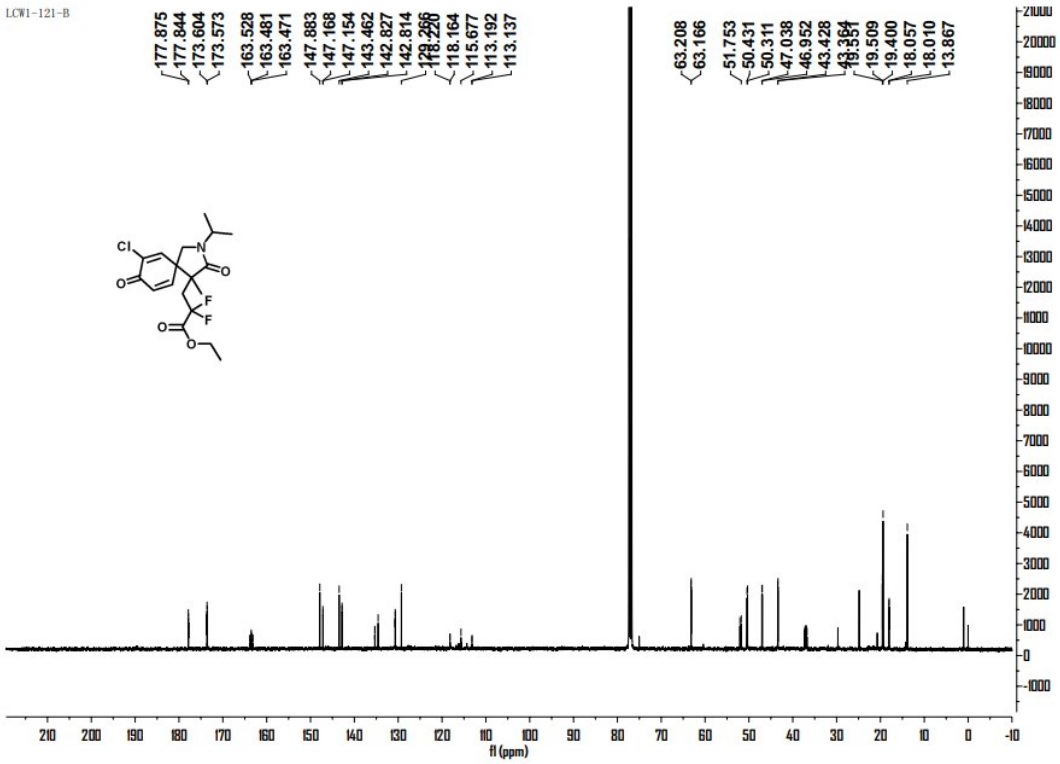
^{1}H NMR Spectra of 3g



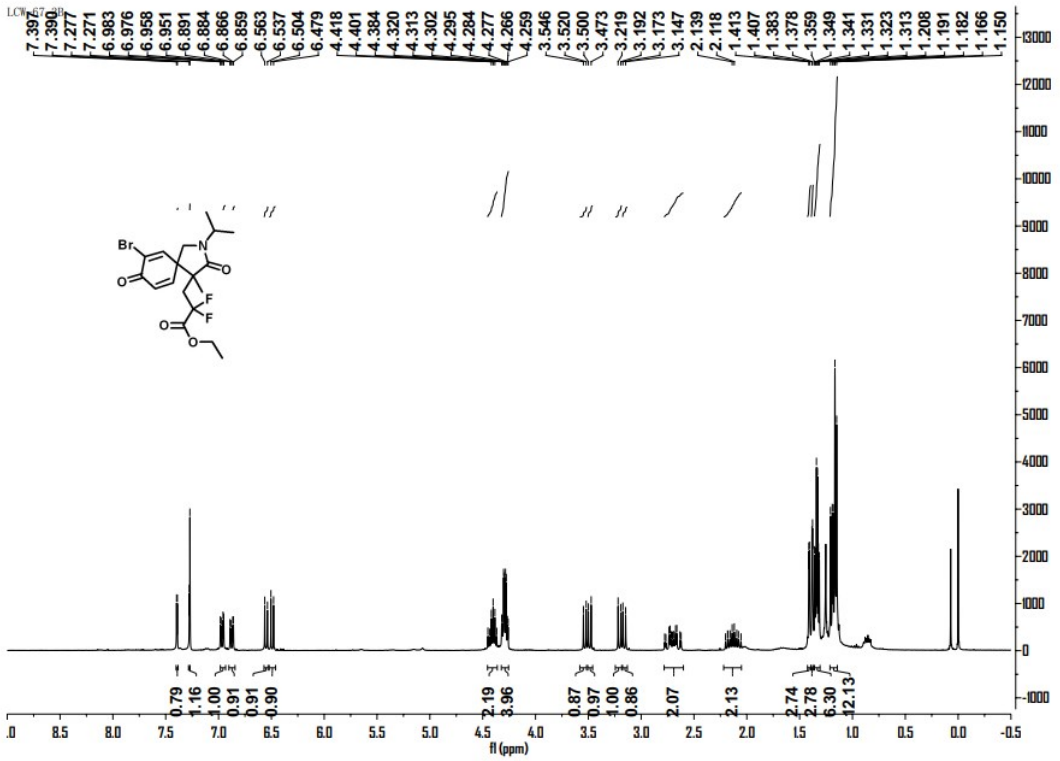
^{19}F NMR Spectra of 3g



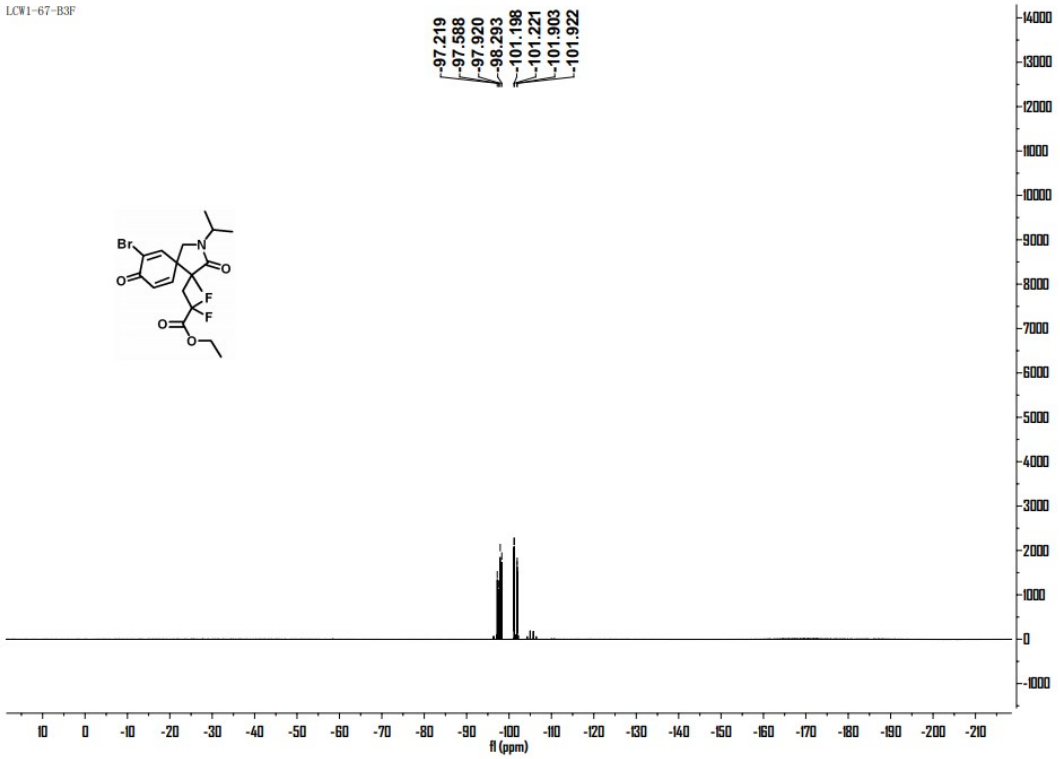
^{13}C NMR Spectra of 3g



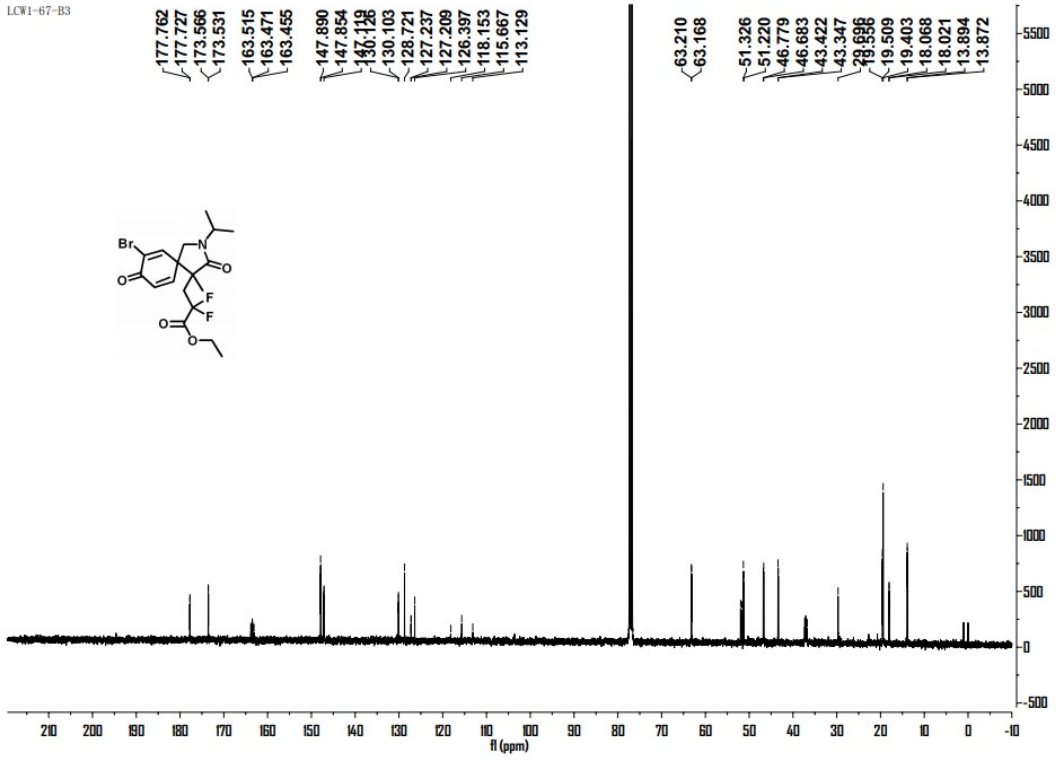
^{1}H NMR Spectra of 3h



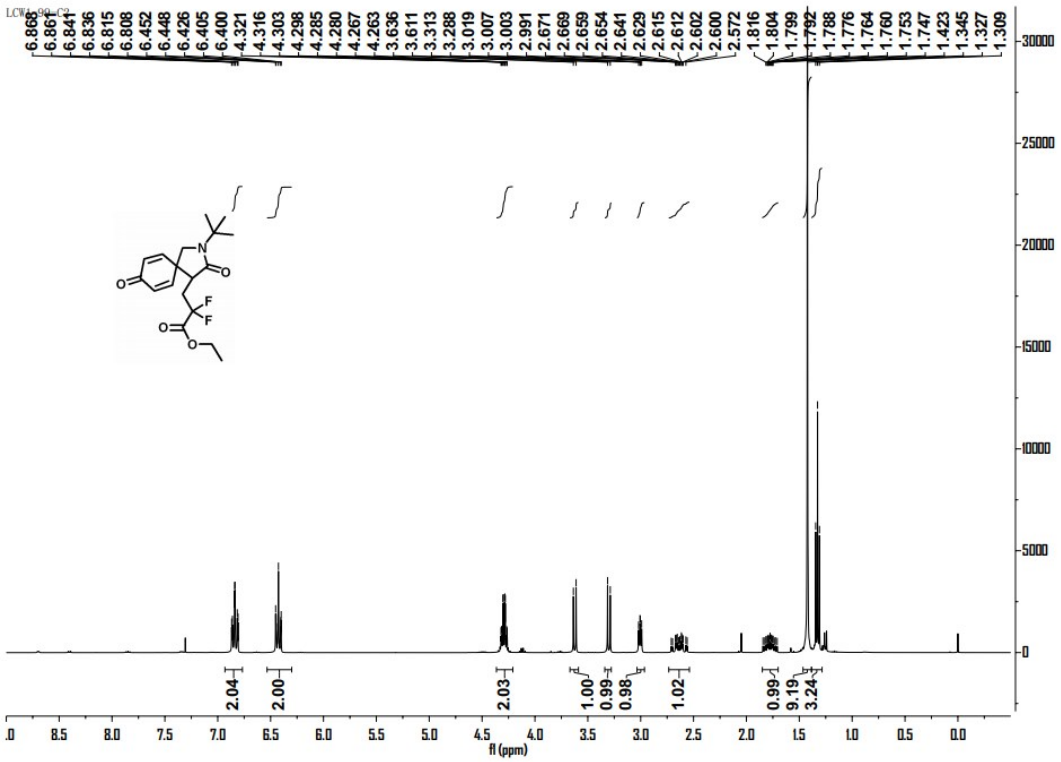
^{19}F NMR Spectra of 3h



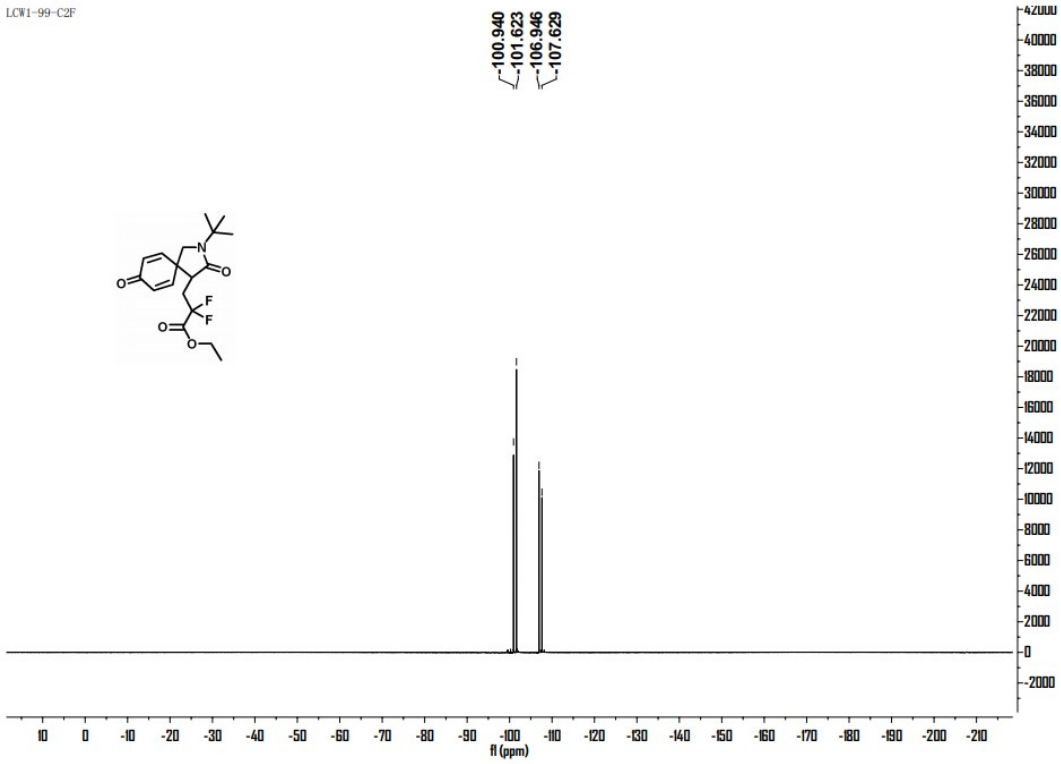
^{13}C NMR Spectra of 3h



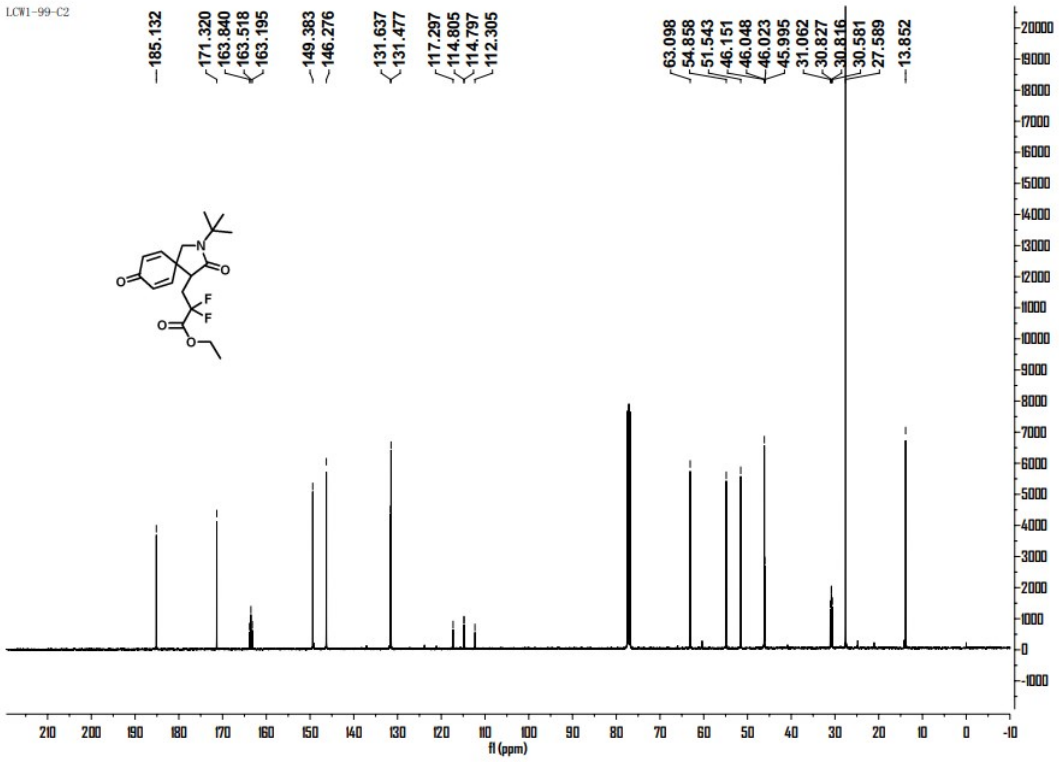
^{1}H NMR Spectra of 3i



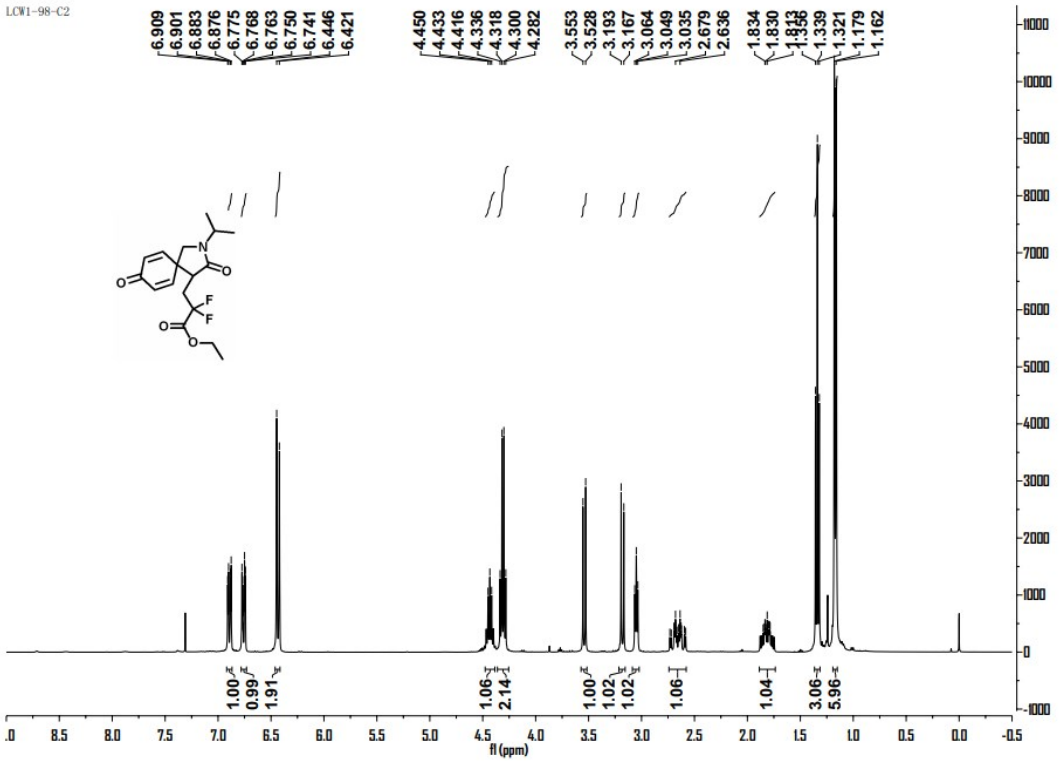
^{19}F NMR Spectra of 3i



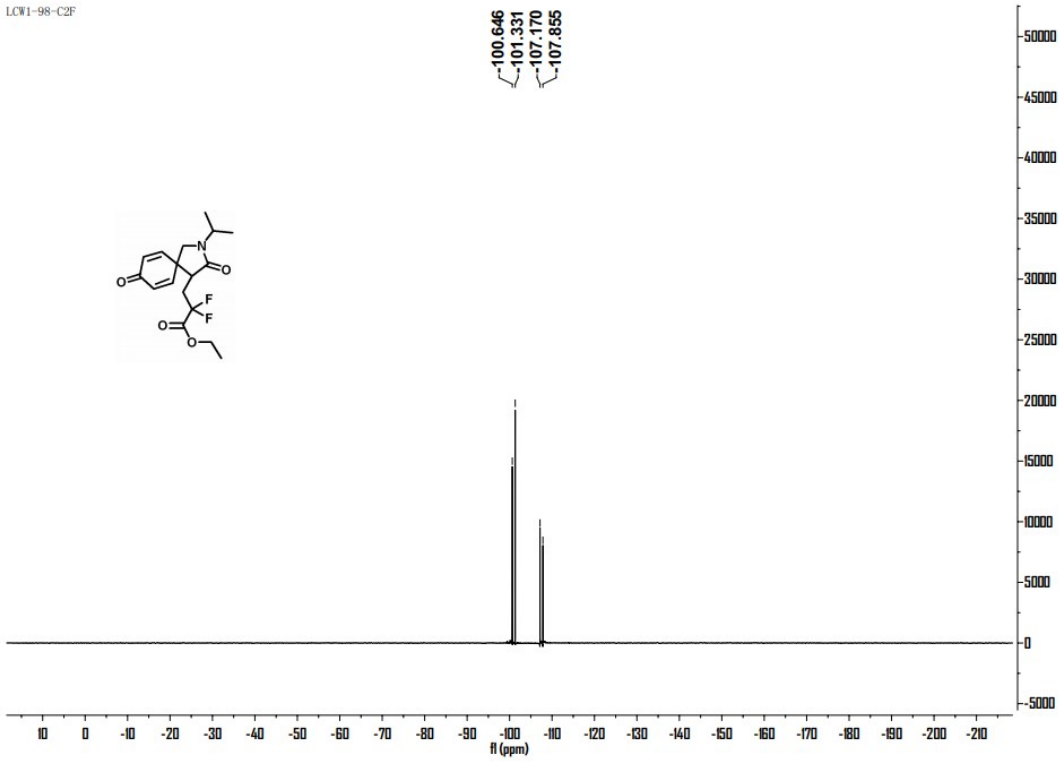
^{13}C NMR Spectra of 3i



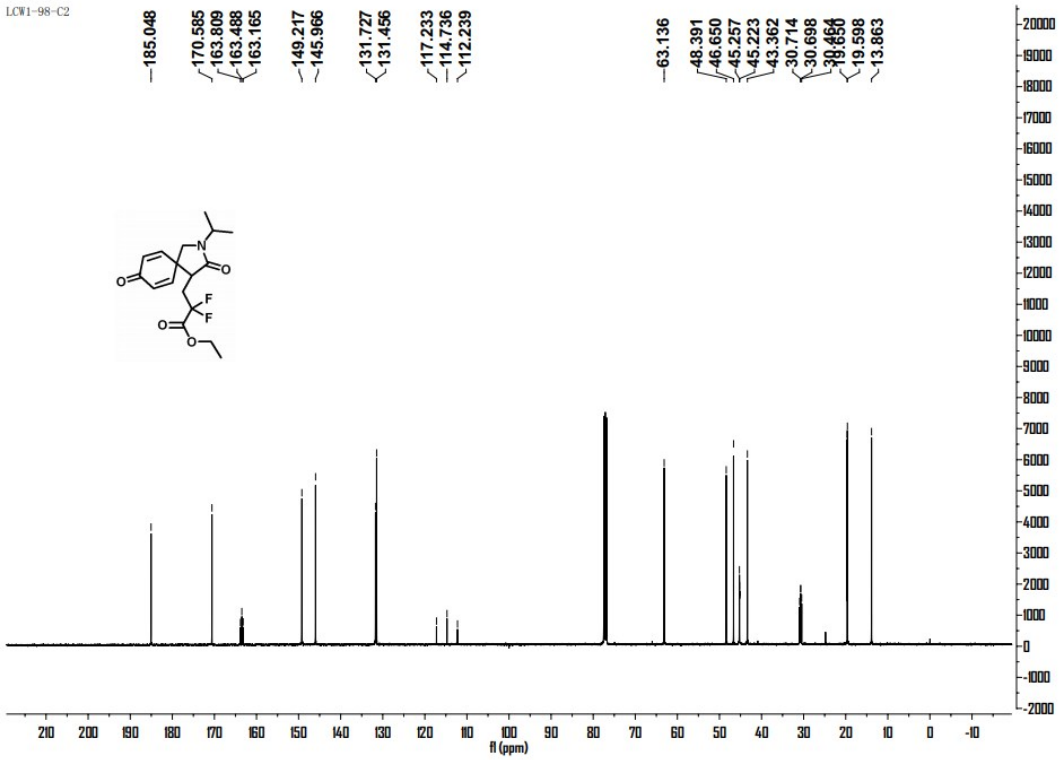
^{1}H NMR Spectra of 3j



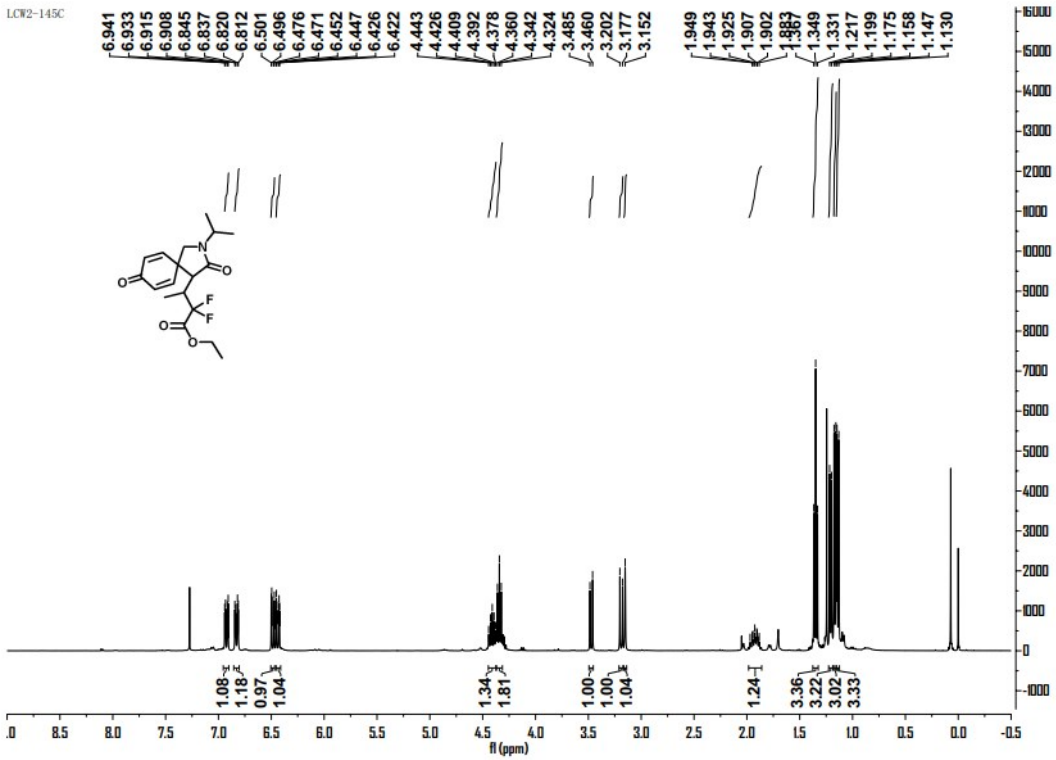
^{19}F NMR Spectra of 3j



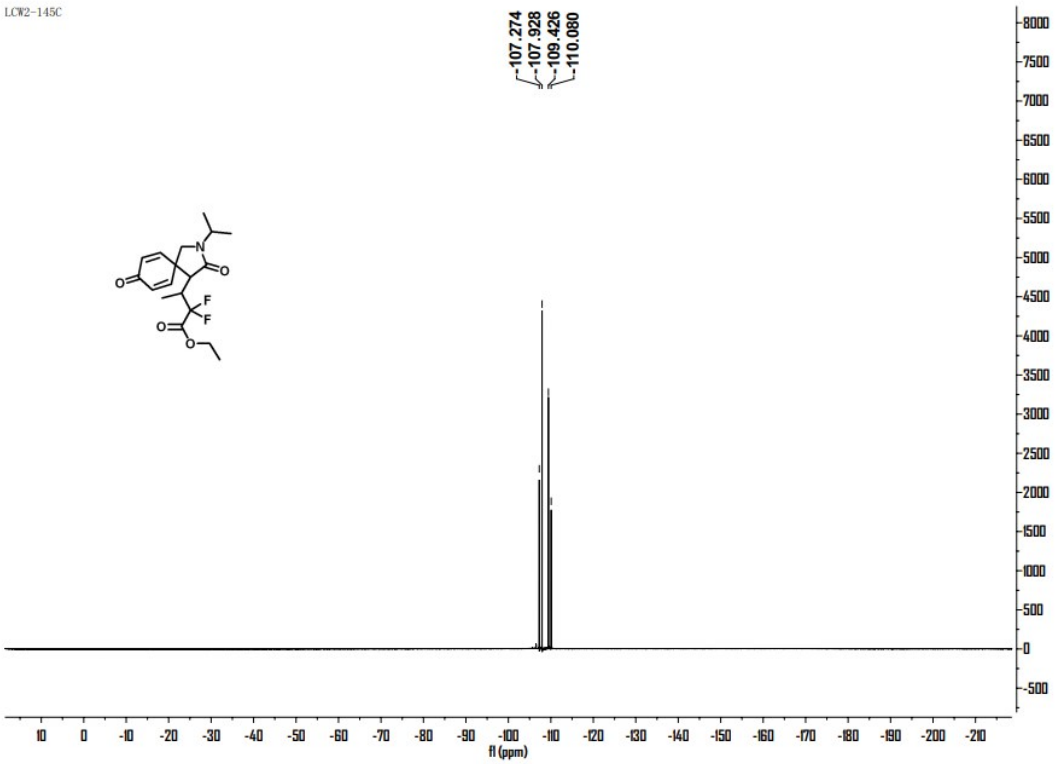
^{13}C NMR Spectra of 3j



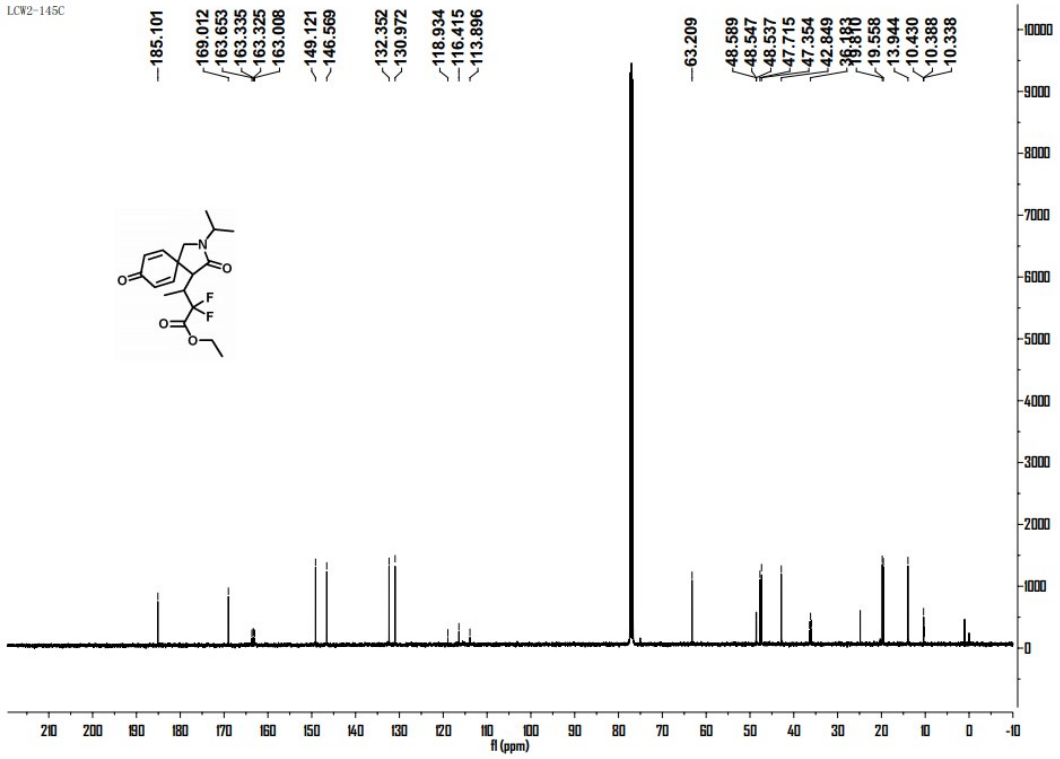
^{1}H NMR Spectra of 3k (Isomer 1)



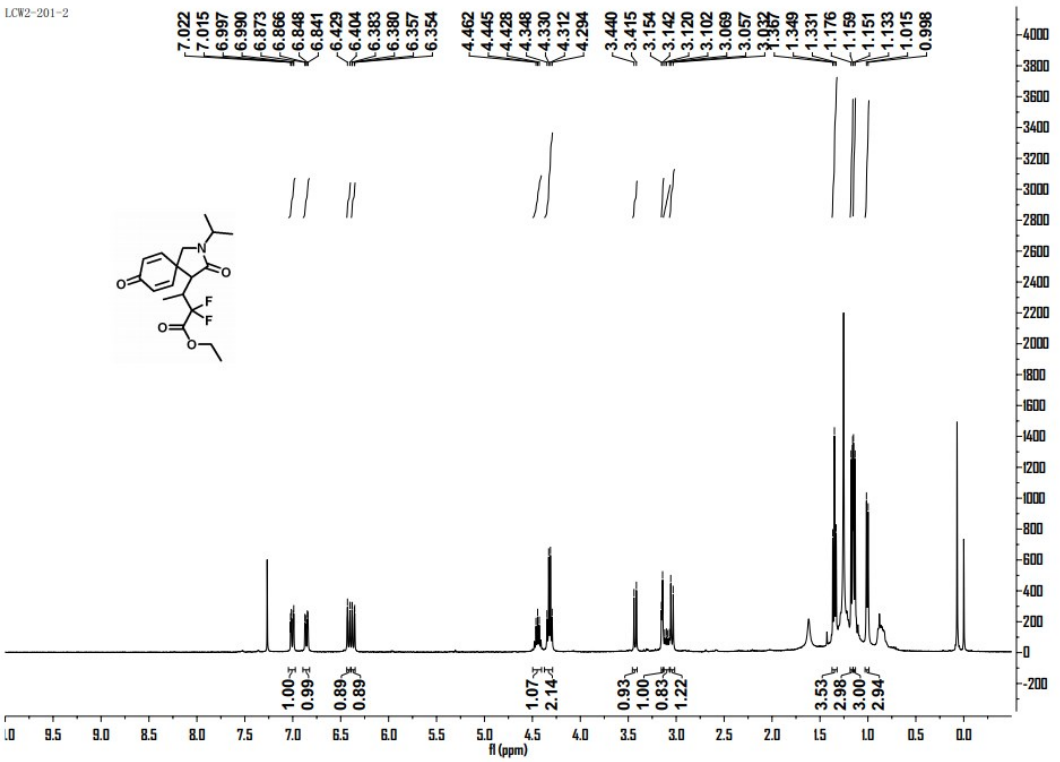
^{19}F NMR Spectra of 3k (Isomer 1)



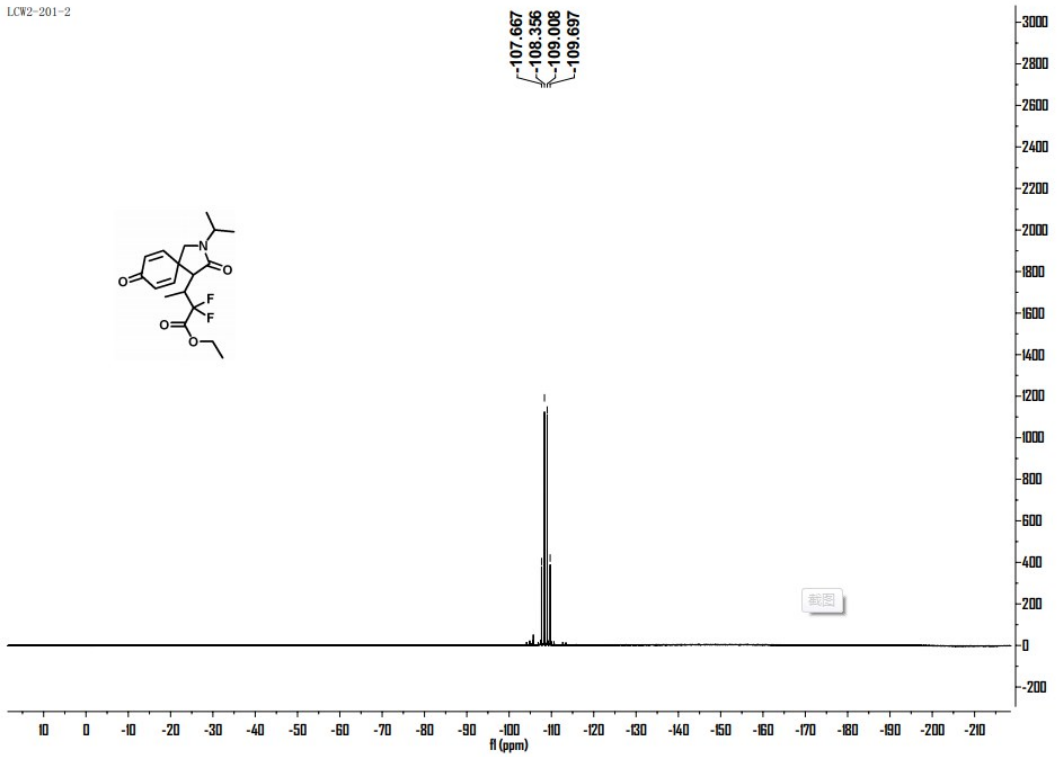
^{13}C NMR Spectra of 3k (Isomer 1)



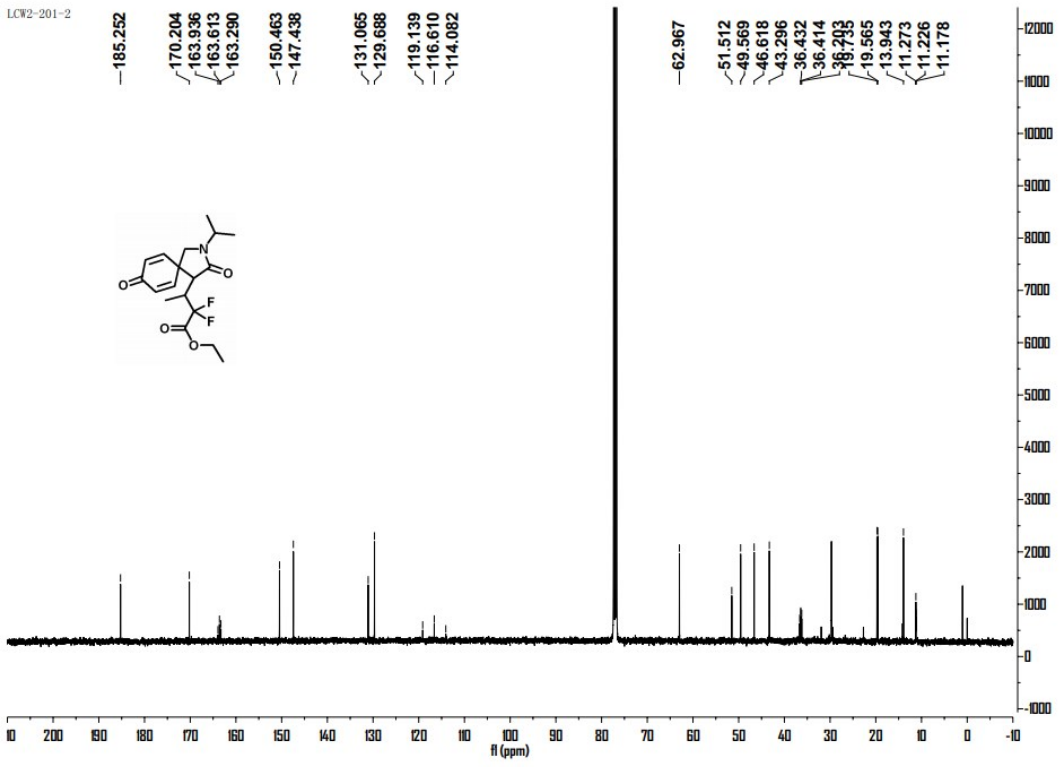
^{1}H NMR Spectra of 3k (Isomer 2)



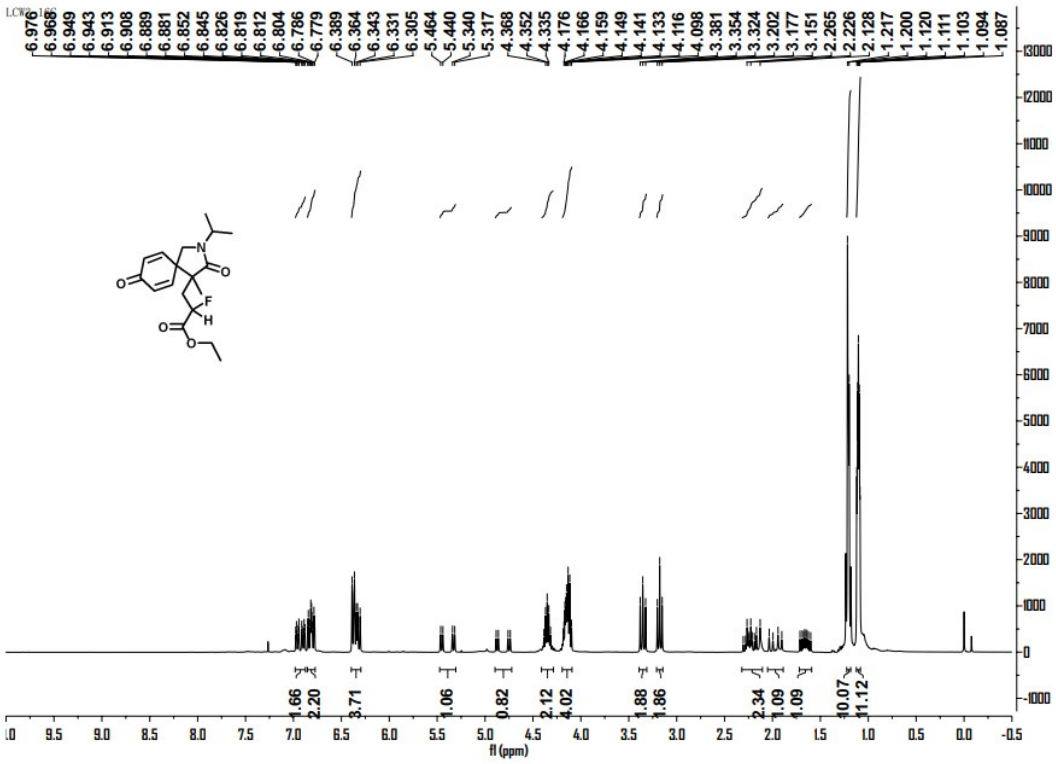
^{19}F NMR Spectra of 3k (Isomer 2)



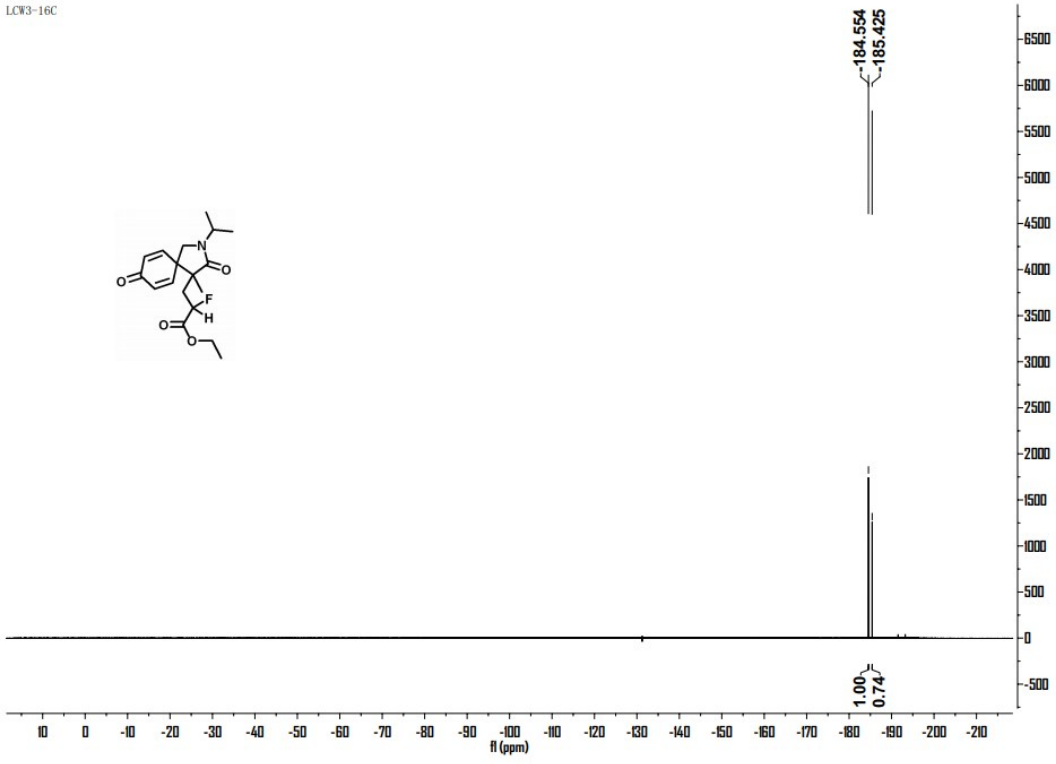
^{13}C NMR Spectra of 3k (Isomer 2)



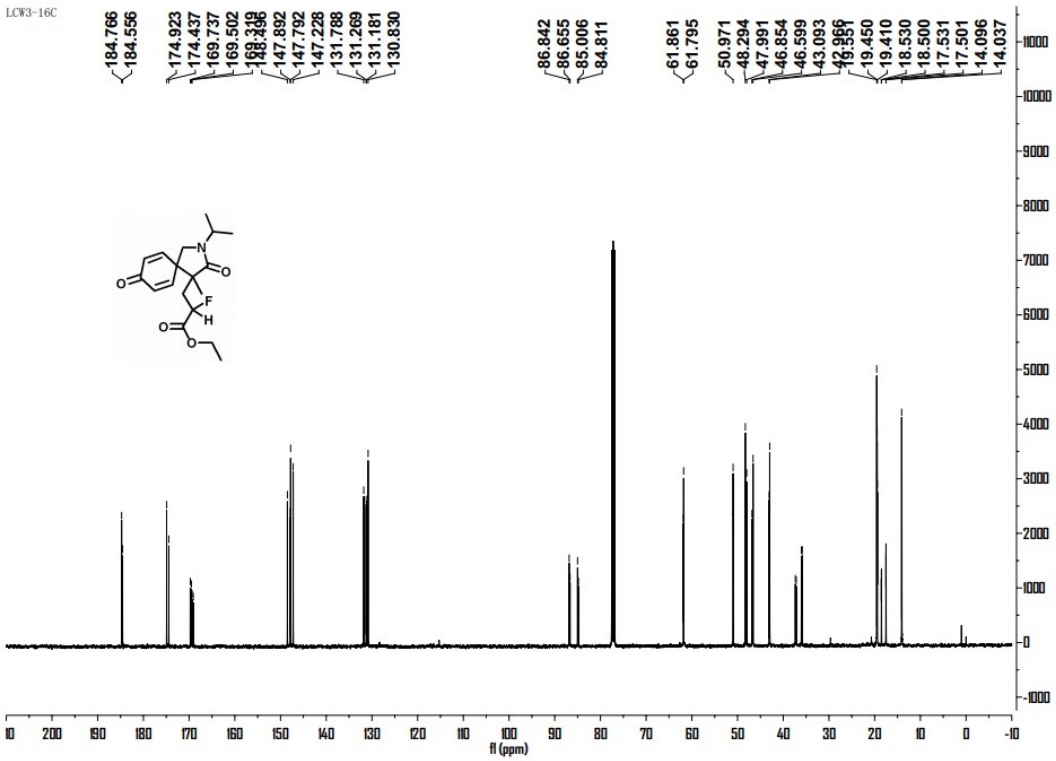
^{1}H NMR Spectra of 3l



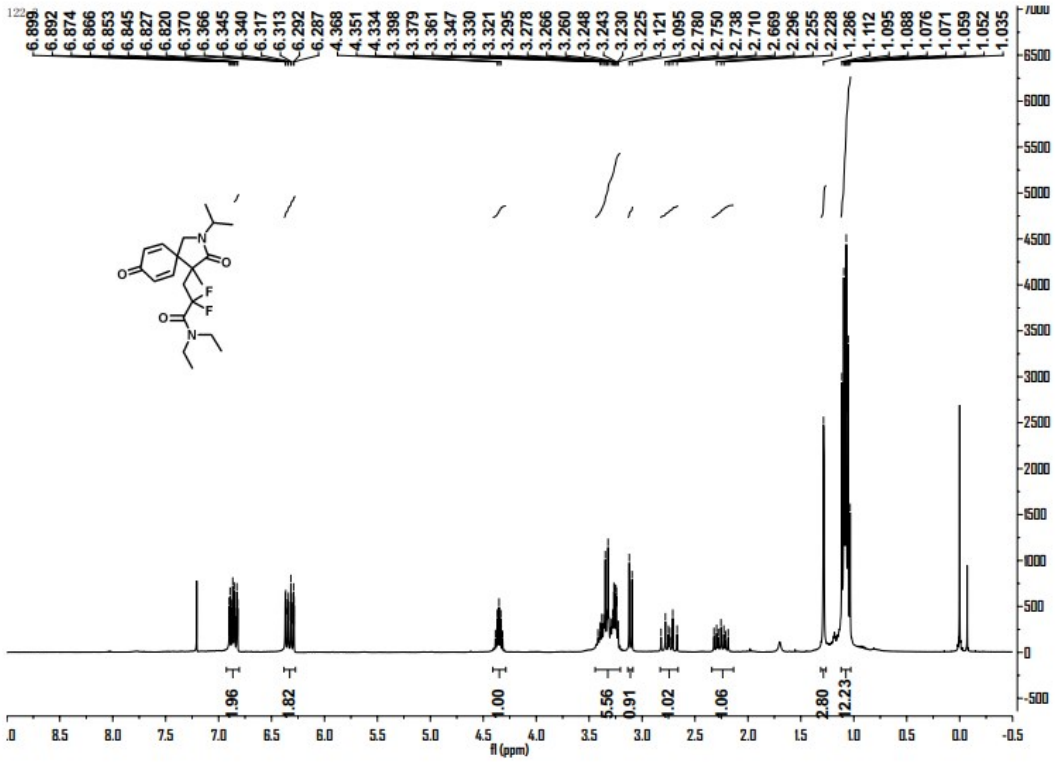
^{19}F NMR Spectra of 3l



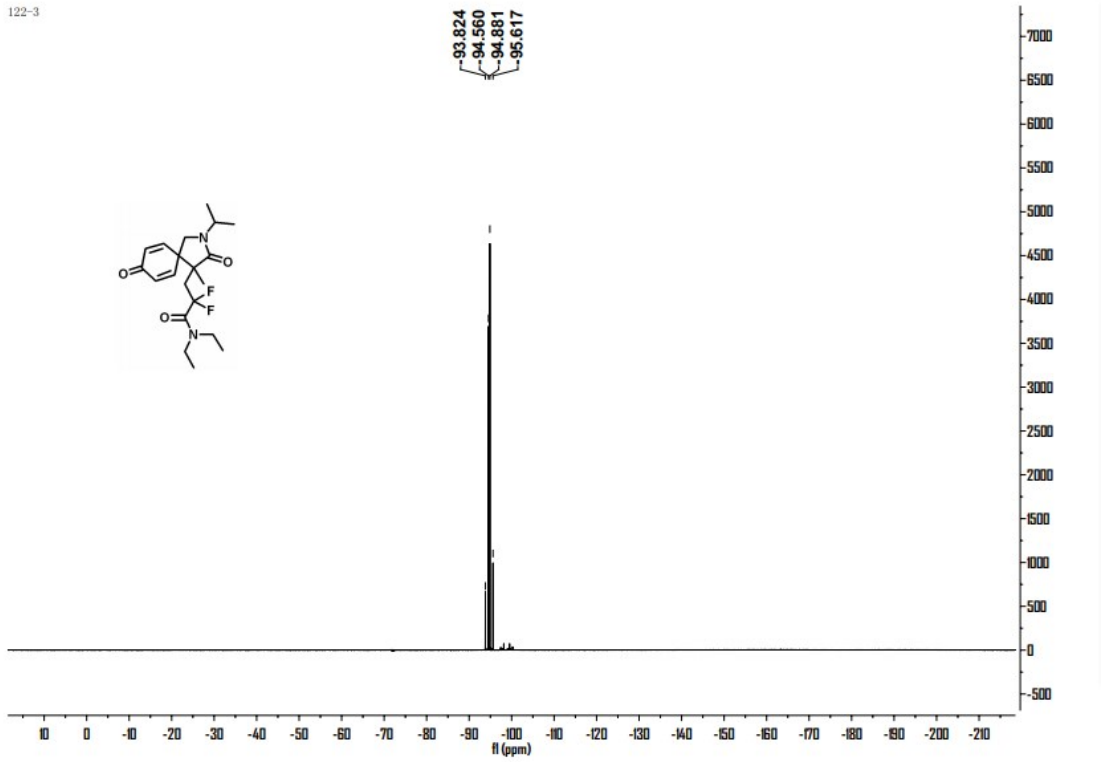
^{13}C NMR Spectra of 3l



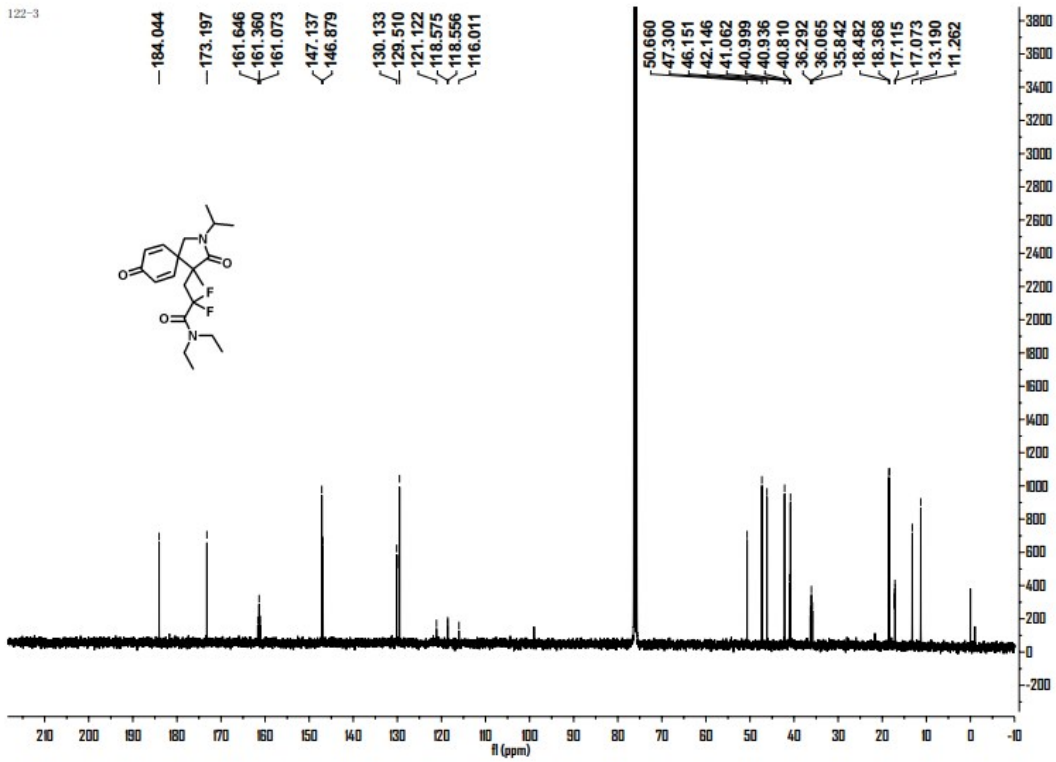
^{1}H NMR Spectra of 3m



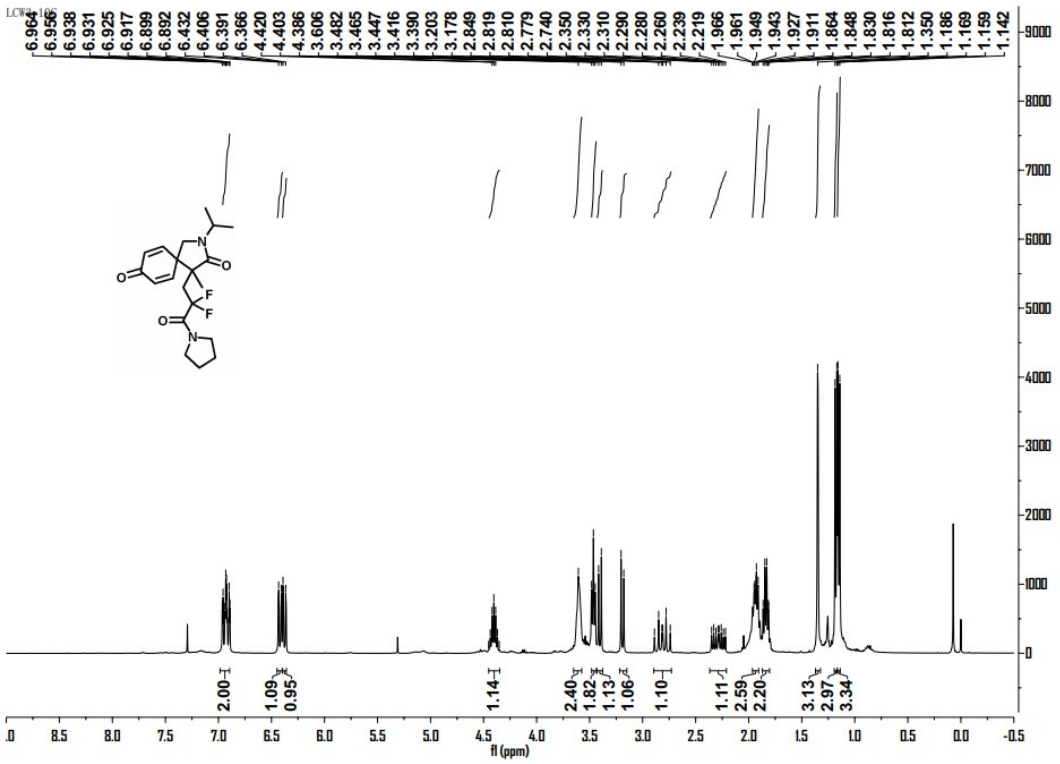
^{19}F NMR Spectra of 3m



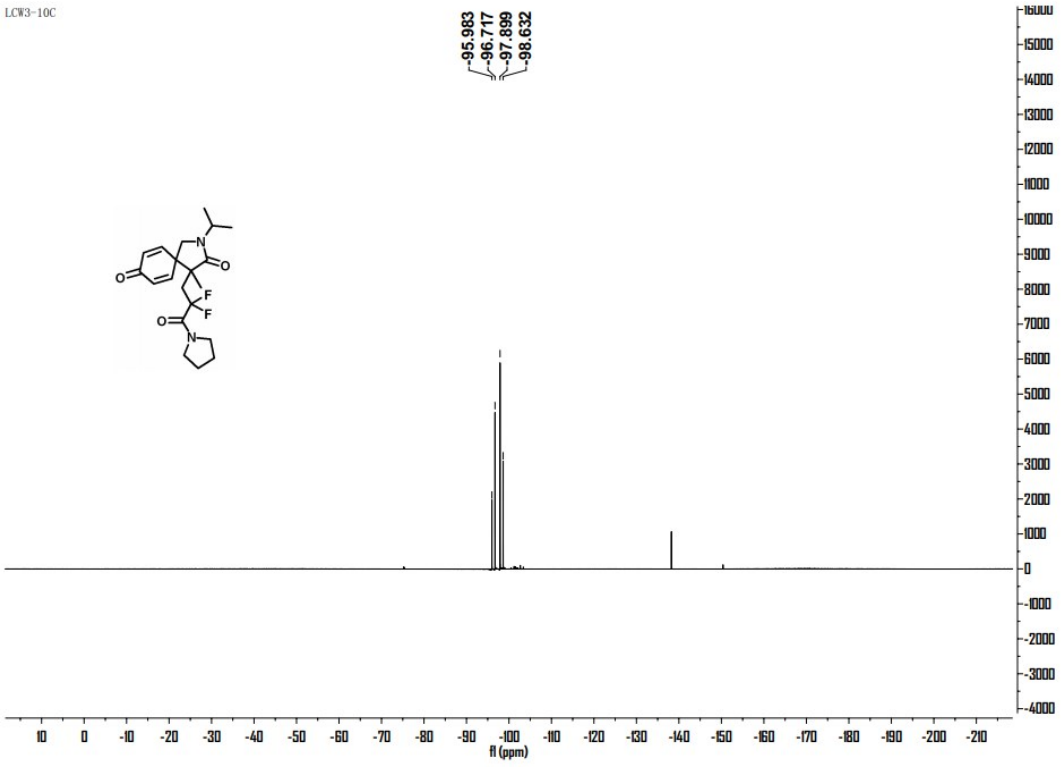
^{13}C NMR Spectra of 3m



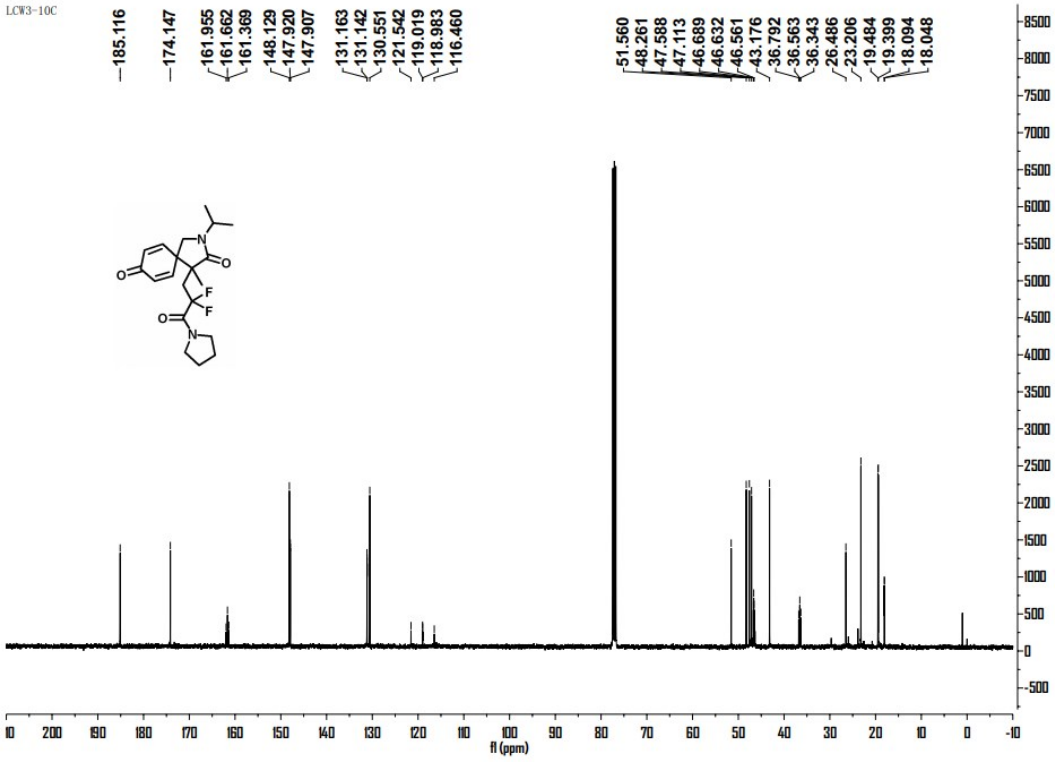
^{1}H NMR Spectra of 3n



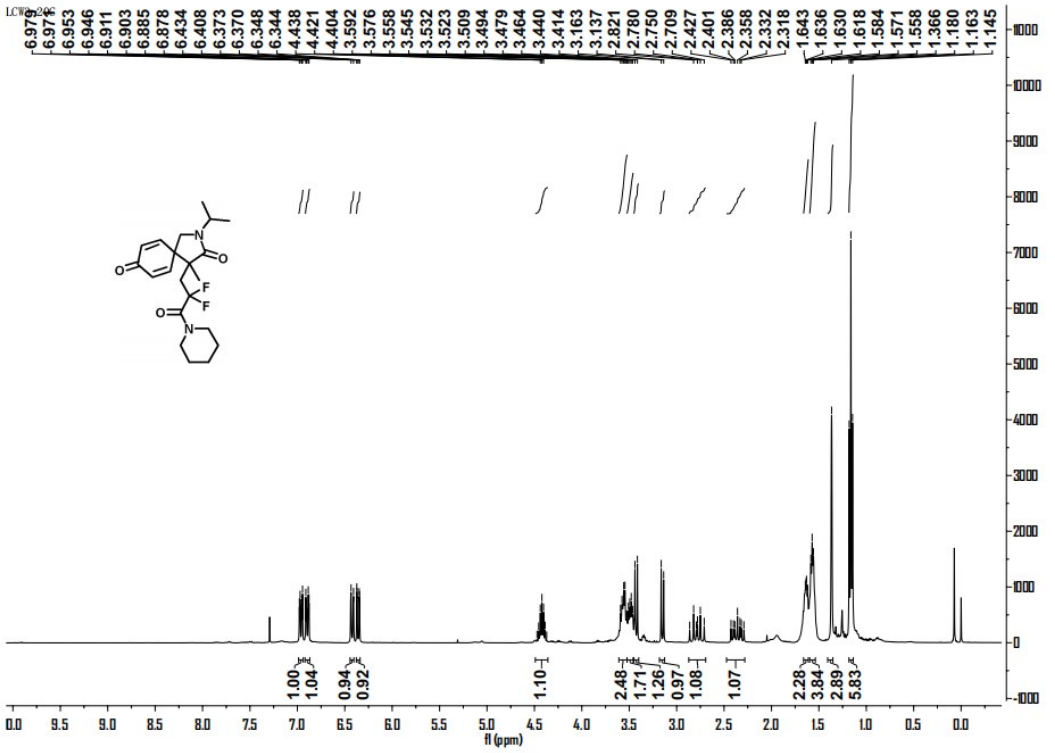
^{19}F NMR Spectra of 3n



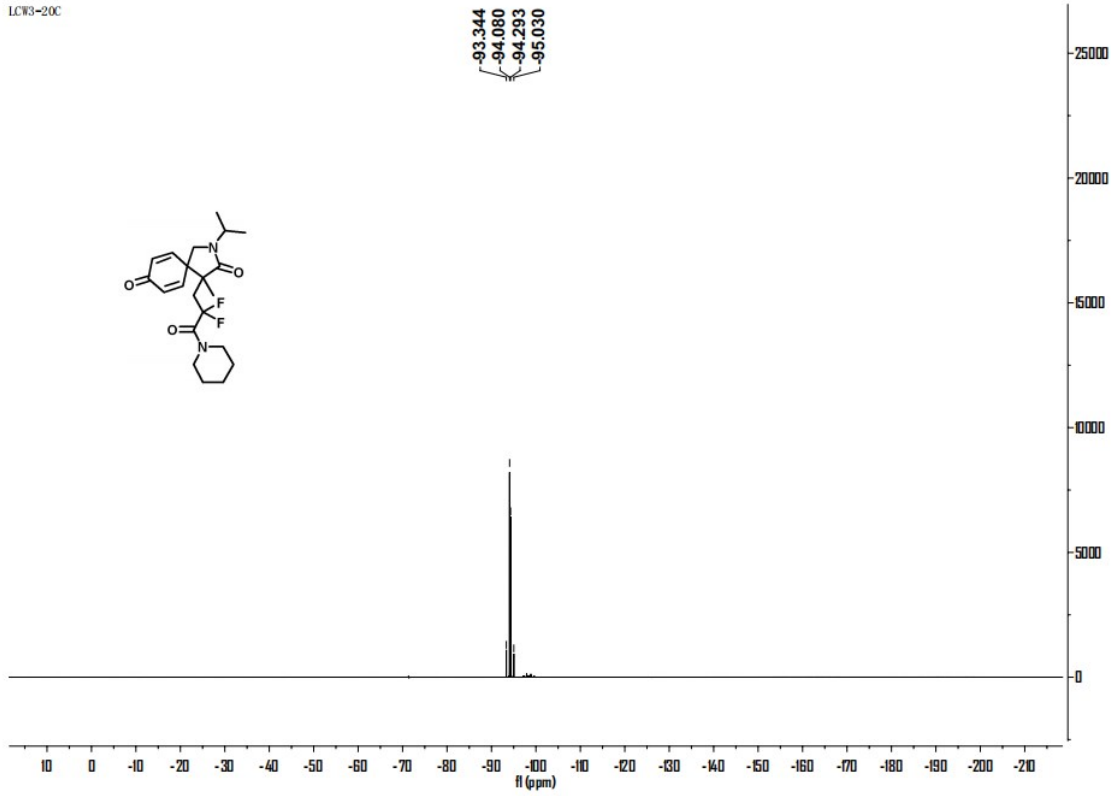
^{13}C NMR Spectra of 3n



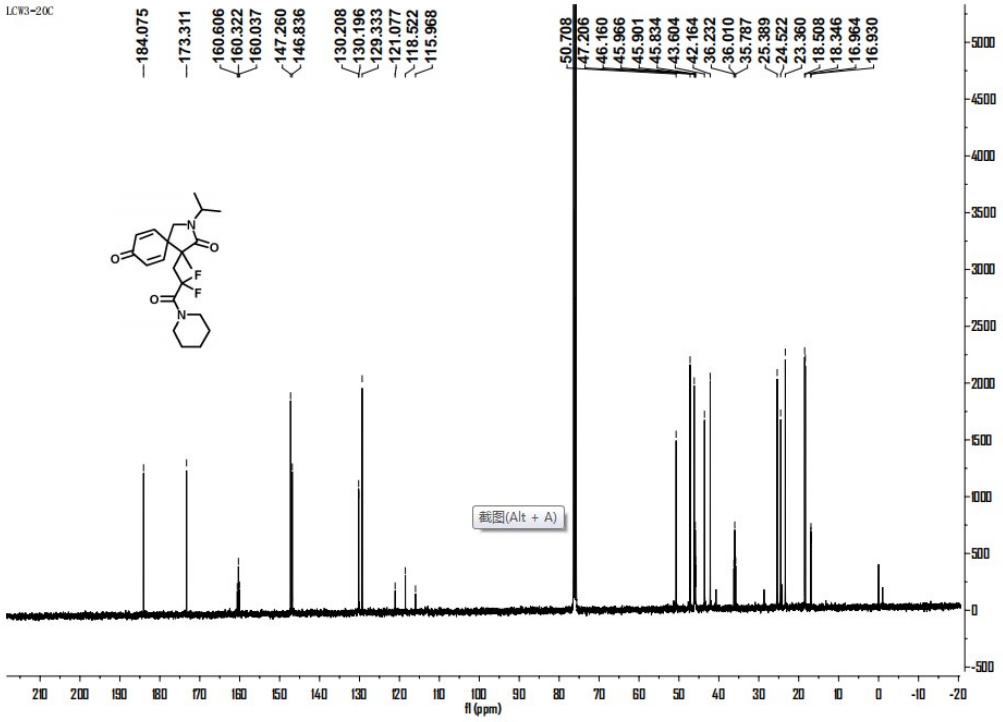
^{1}H NMR Spectra of 3o



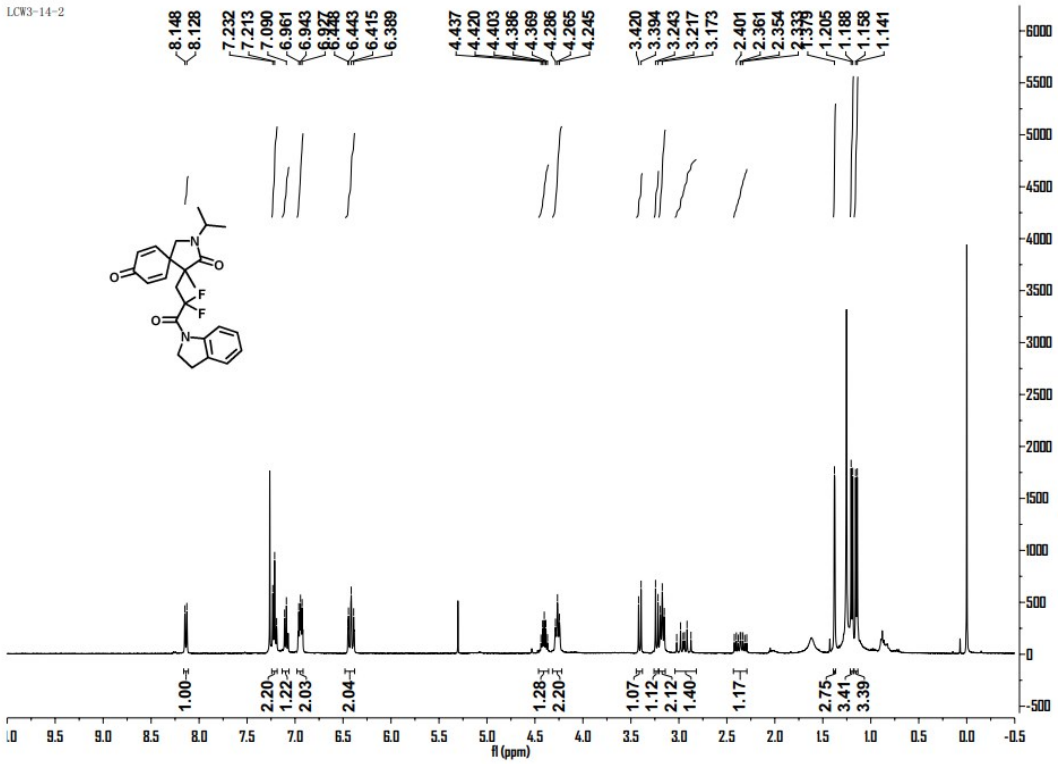
^{19}F NMR Spectra of 3o



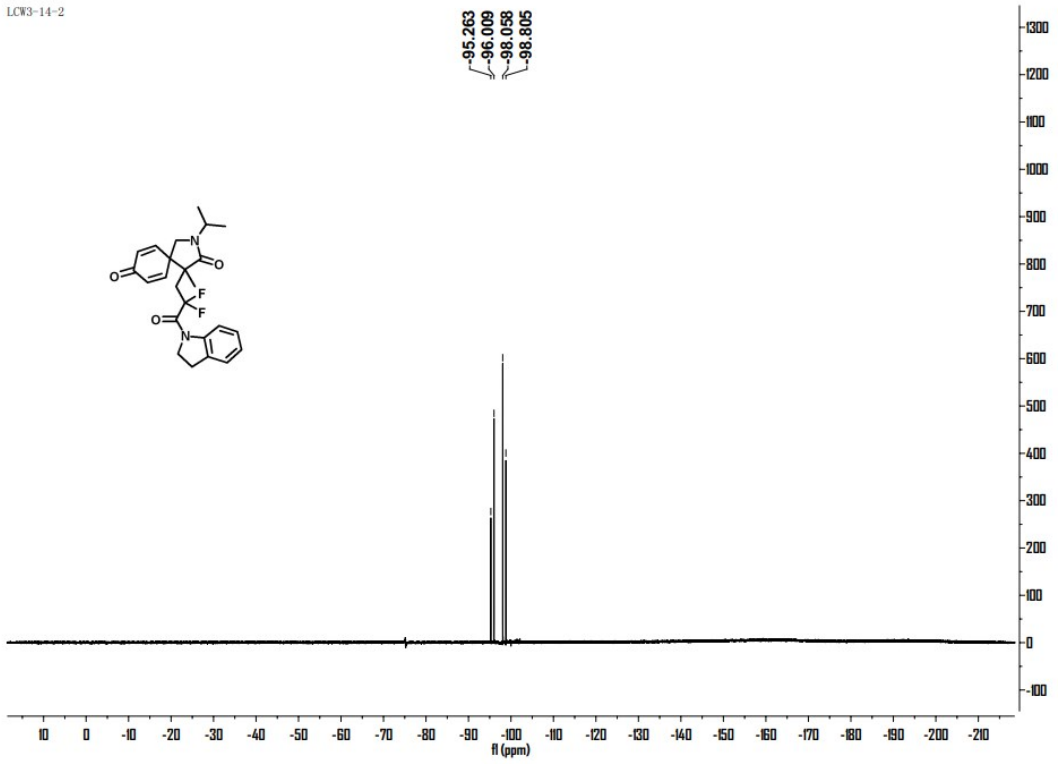
^{13}C NMR Spectra of 3o



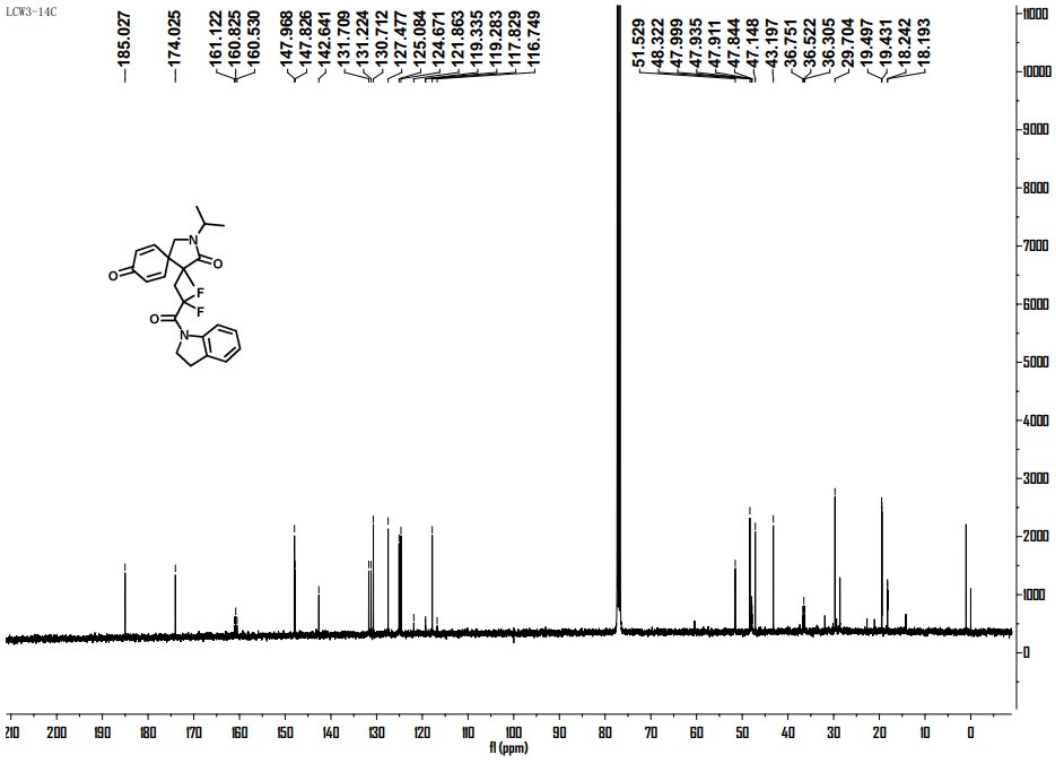
^{1}H NMR Spectra of 3p



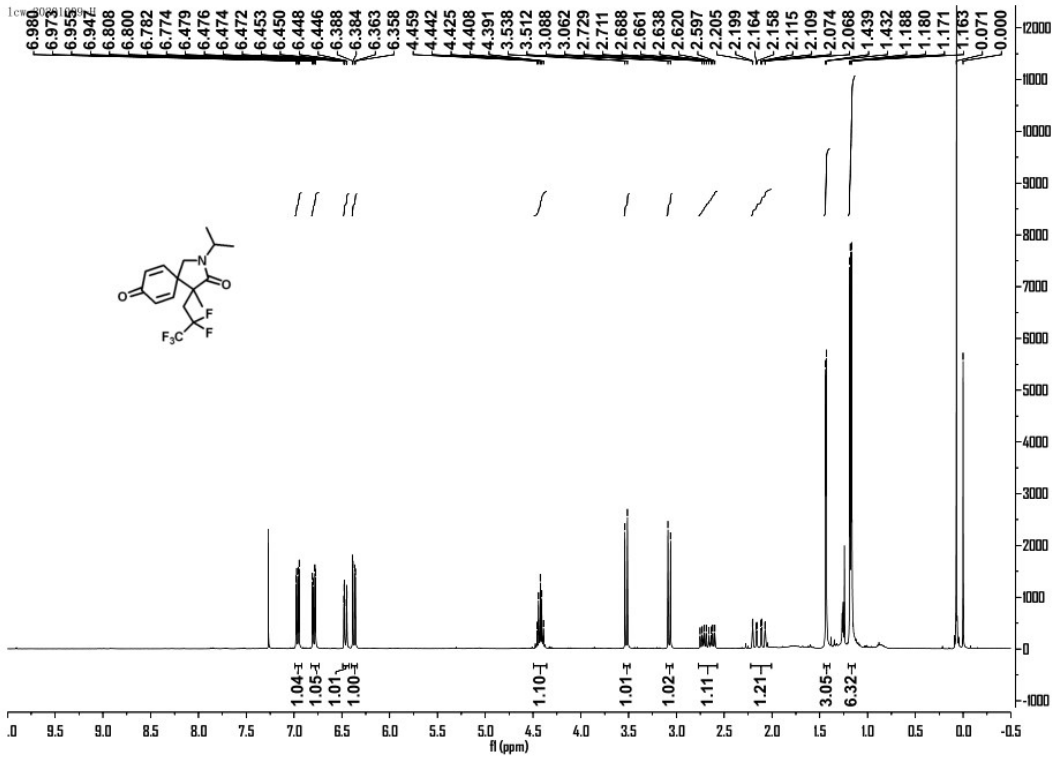
^{19}F NMR Spectra of 3p



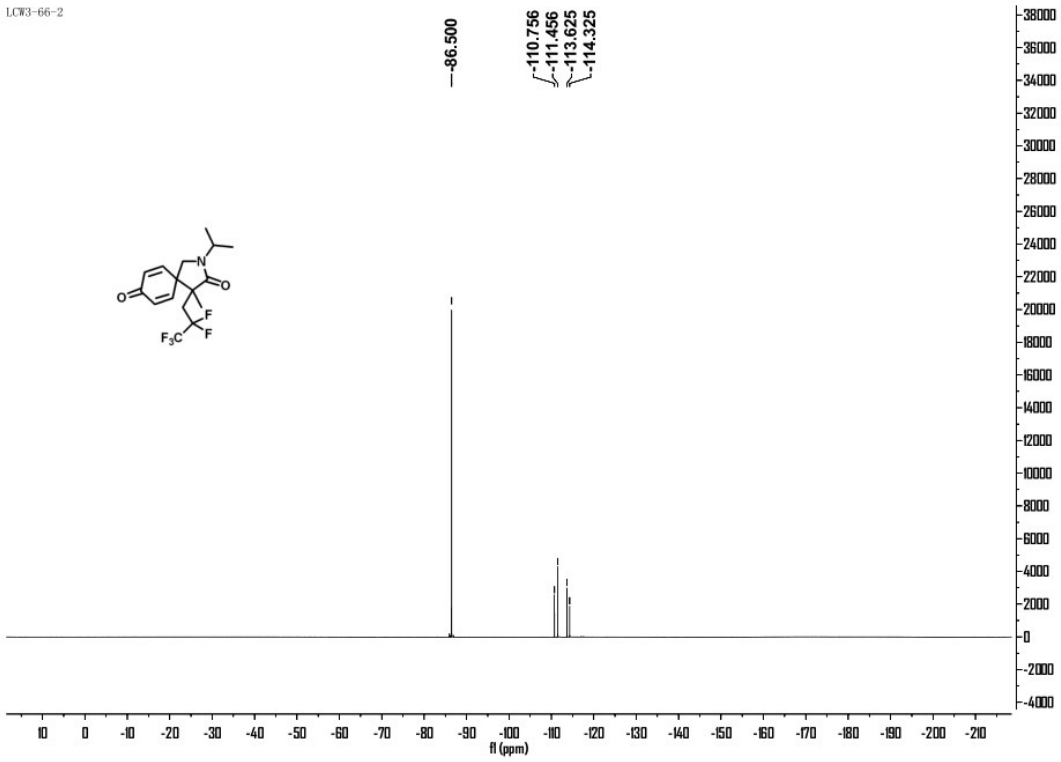
^{13}C NMR Spectra of 3p



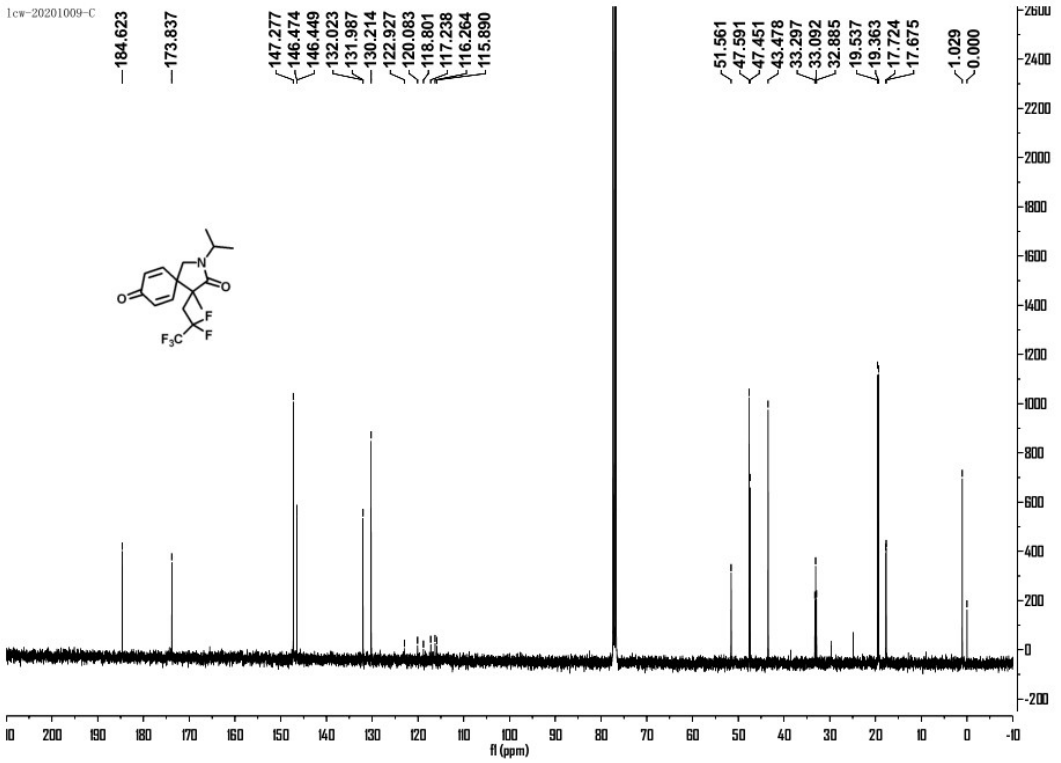
^{1}H NMR Spectra of 3q



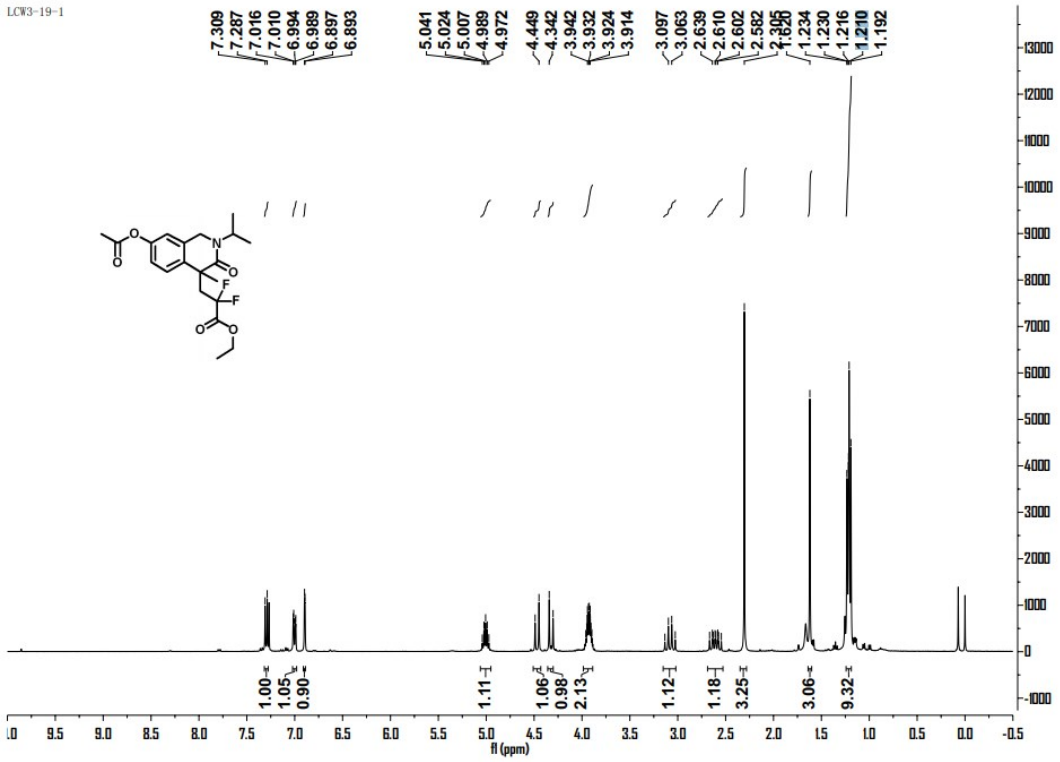
^{19}F NMR Spectra of 3q



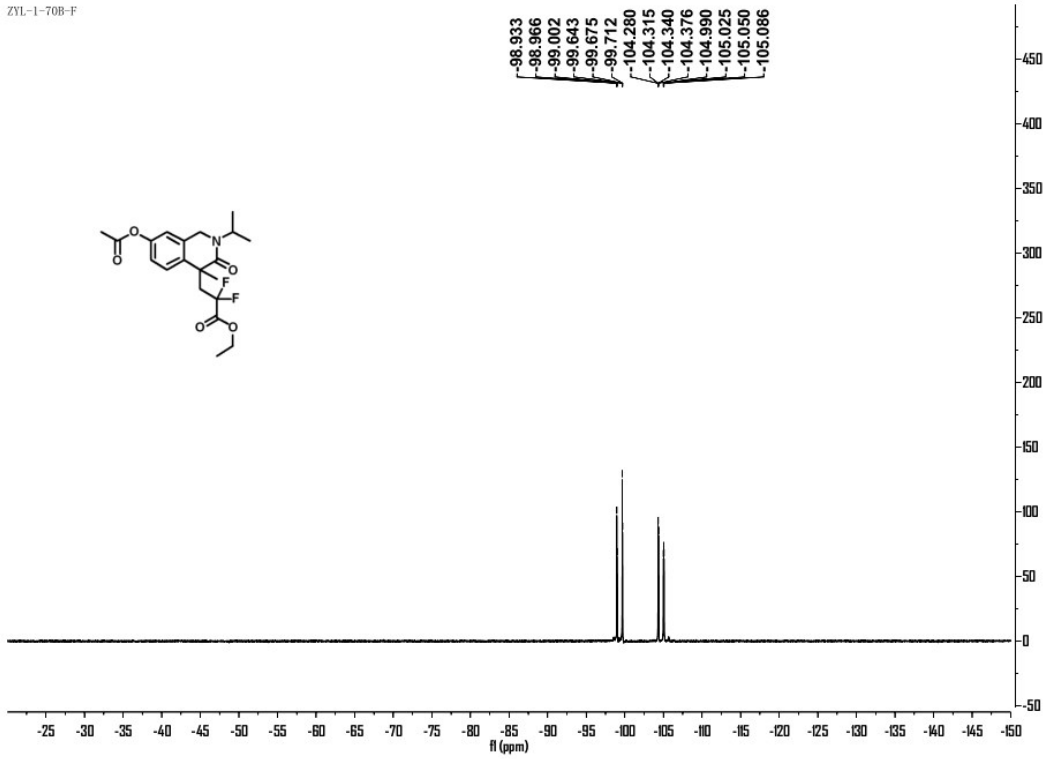
^{13}C NMR Spectra of 3q



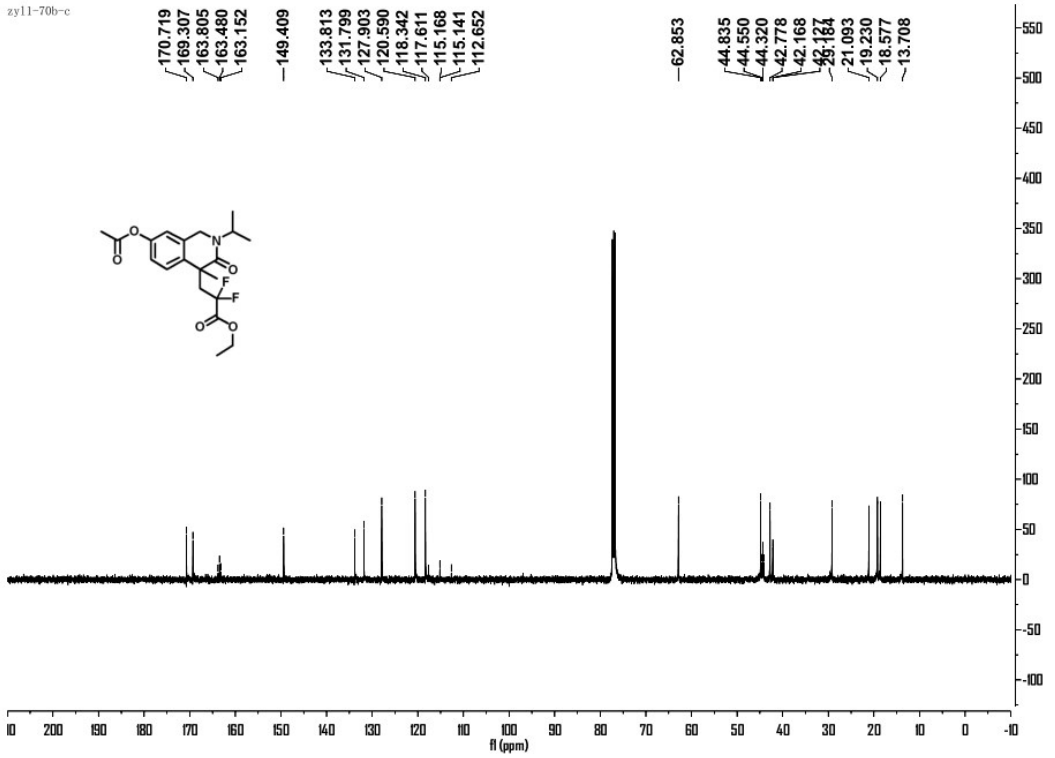
^{1}H NMR Spectra of 4a



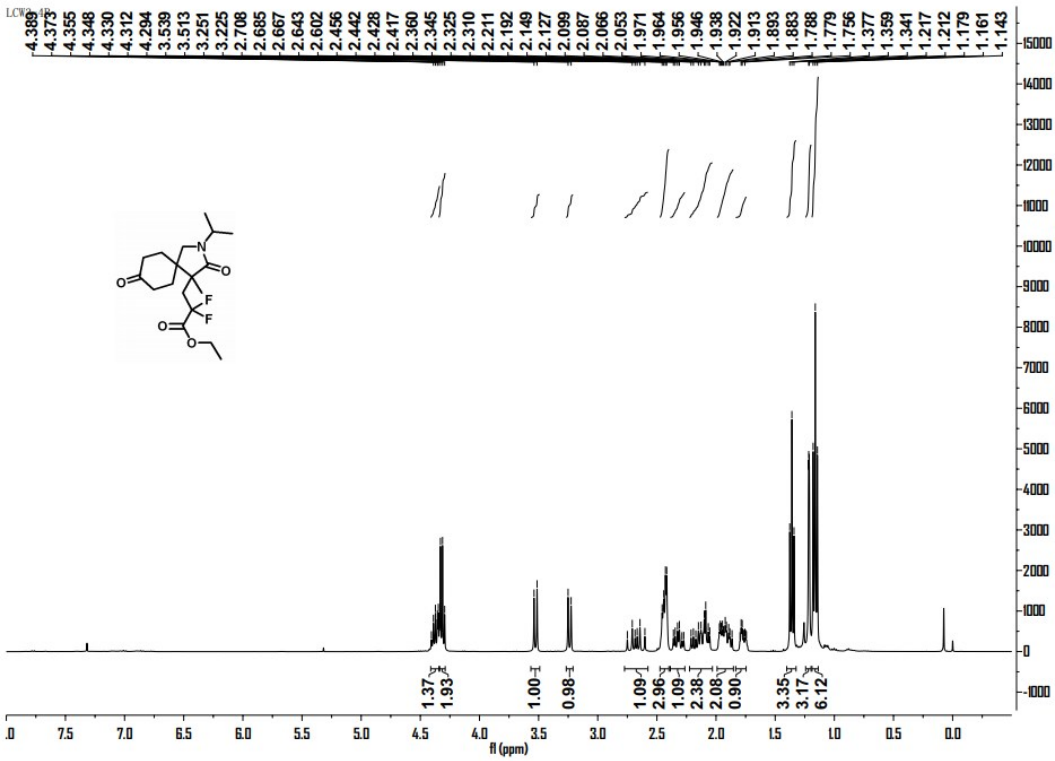
^{19}F NMR Spectra of 4a



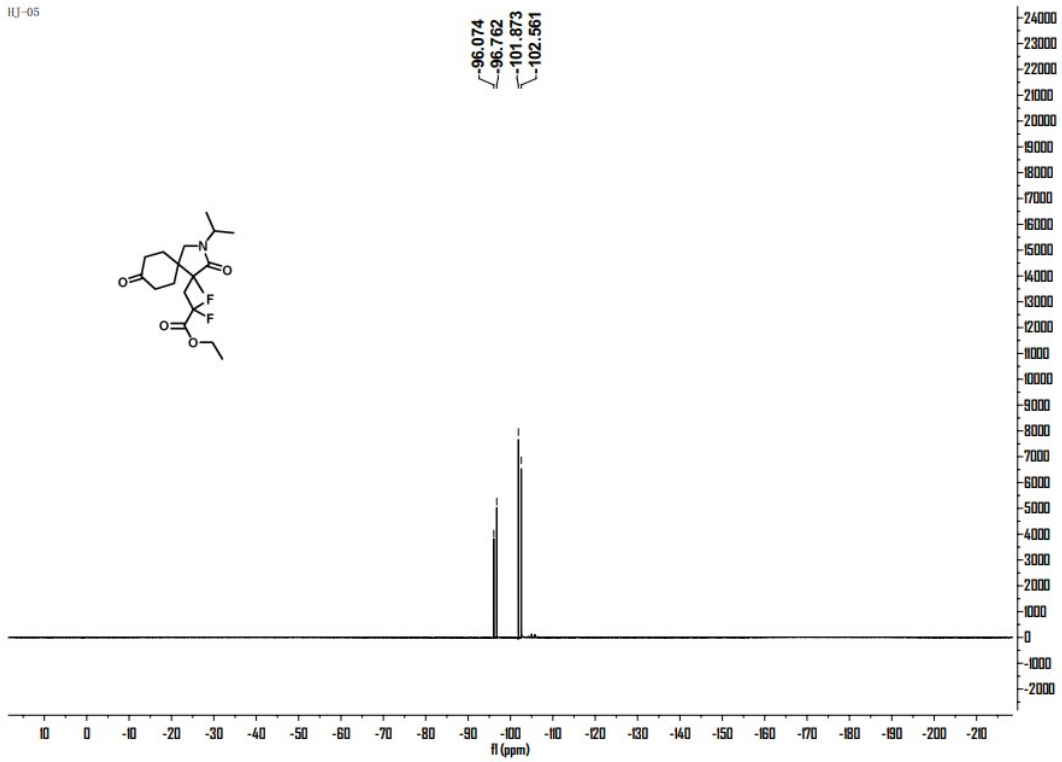
^{13}C NMR Spectra of 4a



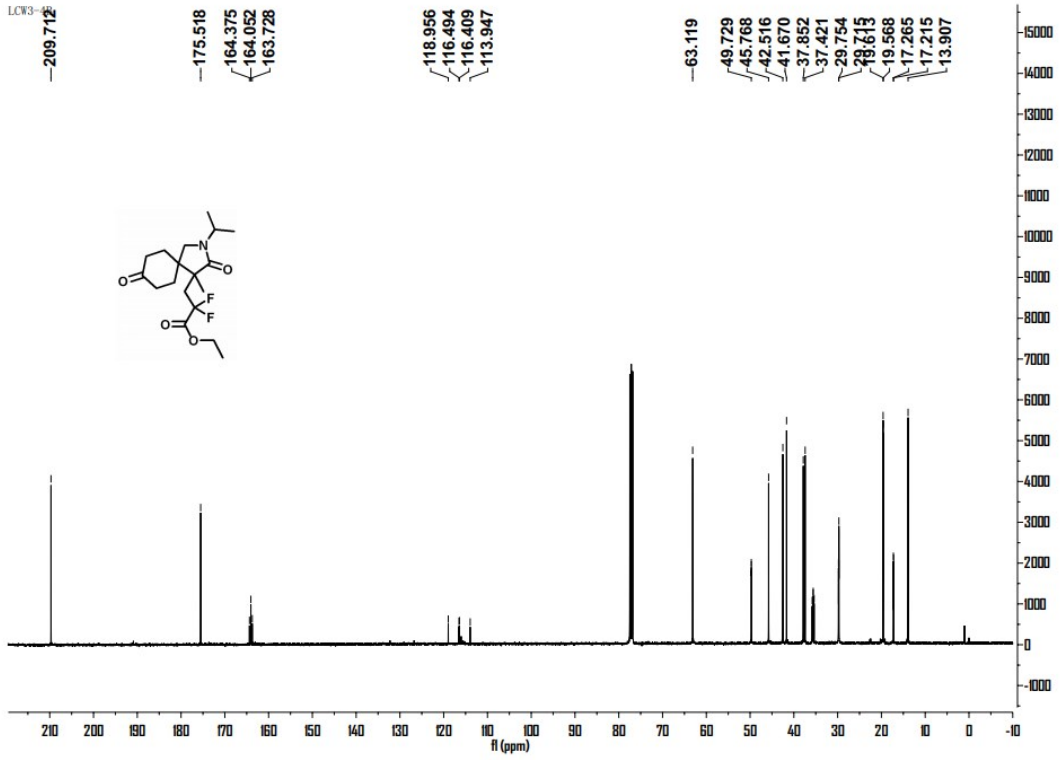
^{1}H NMR Spectra of 5a



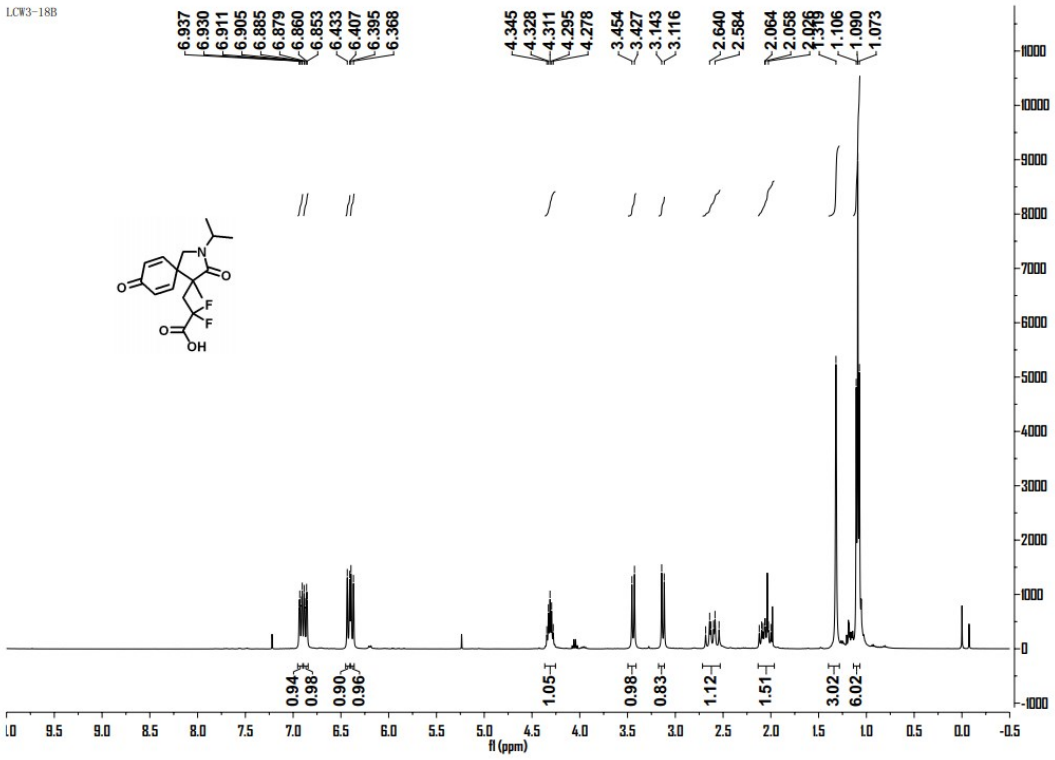
^{19}F NMR Spectra of 5a



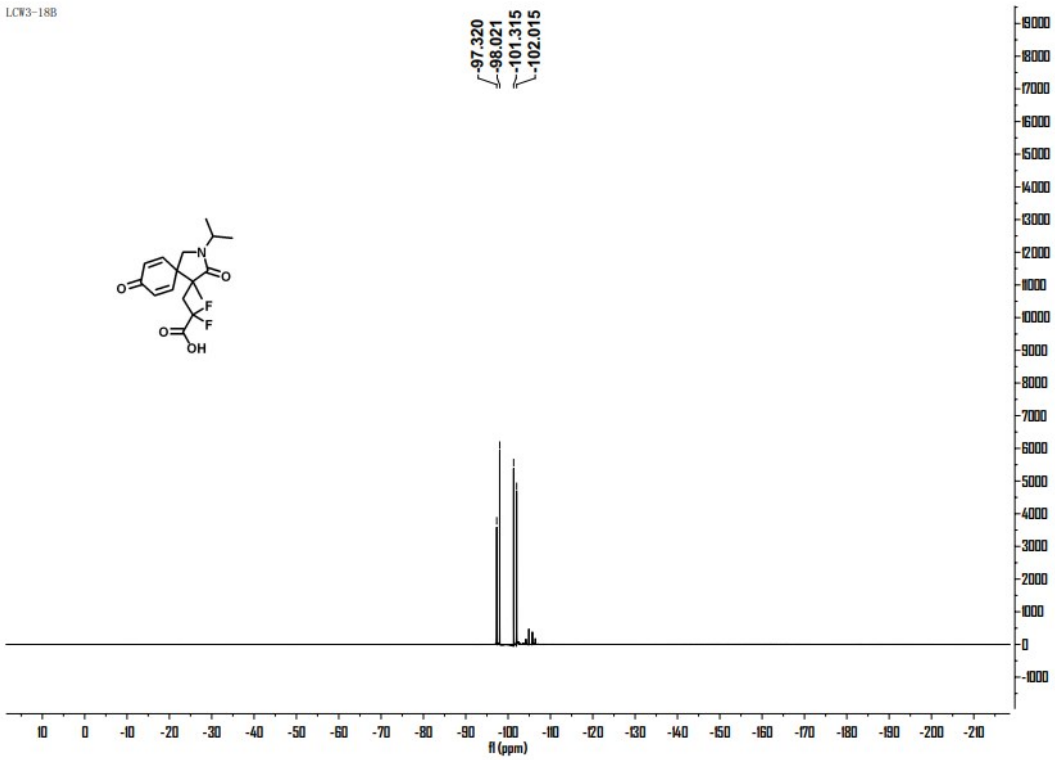
^{13}C NMR Spectra of 5a



^{1}H NMR Spectra of 6a



^{19}F NMR Spectra of 6a



^{13}C NMR Spectra of 6a