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Supporting Information

Visible-Light-Induced Radical Isocyanide Insertion Protocol for Synthesis of Difluoromethylated Spiro[indole-3,3'-quinoline] Derivatives

Jingjing Zhang[a,b,‡], Wentao Xu,[a,‡] Yi Qu,[a] Yuxiu Liu,[a] Yongqiang Li,[a] Hongjian Song,[a,*] and Qingmin Wang[a,*]

[a] State Key Laboratory of Elemento-Organic Chemistry, College of Chemistry, Collaborative Innovation Center of Chemical Science and Engineering (Tianjin), Nankai University, Tianjin 300071, People's Republic of China

[b] Tianjin Agricultural University, Tianjin 300384, People's Republic of China

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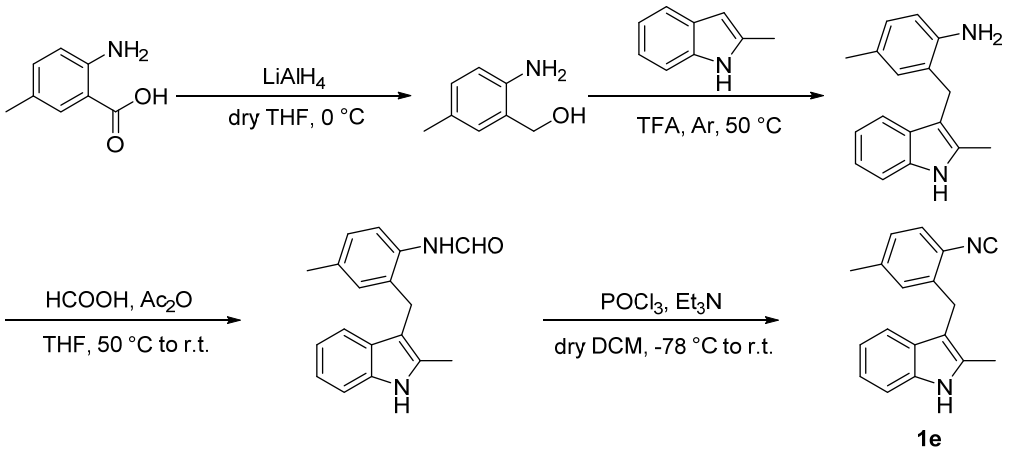
1. General information

Reagents were purchased from commercial sources and were used as received. ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded on Bruker Avance 400 Ultrashield NMR spectrometers. ^{19}F NMR spectra were recorded on a Varian 400 instrument spectrometer. 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). The melting points were determined on an X-4 microscope melting point apparatus and are uncorrected. Conversion was monitored by thin layer chromatography (TLC). Flash column chromatography was performed over silica gel (100-200 mesh). Blue LED (3 W, λ_{max} = 470 nm) purchased from JIADENG (LS) was used for blue light irradiation. A fan attached to the apparatus was used to maintain the reaction temperature at room temperature.

2. Synthesis of compounds 1 (1e was selected as example)



Scheme 1S. Synthesis of **1e**

To a solution of $LiAlH_4$ (15 mmol) in anhydrous THF (20 mL) was added 2-amino-5-methylbenzoic acid (10 mmol) dropwise at 0 °C. Then, the mixture was gradually warmed to room temperature. When the reaction was complete as monitored by TLC, water was added to quench the reaction, and the mixture was extracted with ethyl acetate three times. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated to afford the desired product (2-amino-5-methylphenyl)methanol 1.339 g, 98% yield.

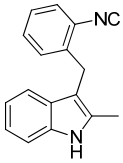
To a solution of (2-amino-5-methylphenyl)methanol (9.8 mmol) and 2-methyl-1*H*-indole (12.74 mmol) in 1,2-dichloroethane (40 mL). After degassing with argon and four evacuation/backfill cycles with argon, trifluoroacetic acid (3.92 mmol) was added dropwise, then the mixture was heated with heating mantle and stirred at 50 °C. When the reaction was complete as monitored by TLC, aqueous solution of saturated Na_2CO_3 was added, concentrated under reduced pressure, dilute hydrochloric acid was added, and the mixture was extracted with dichloromethane three times. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated, and the resulting mixture was purified by column chromatography on silica gel to afford the product 4-methyl-2-((2-methyl-1*H*-indol-3-yl)methyl)aniline 1.528 g, 62% yield.

To a 50 mL flask were added formic acid (27.5 mmol) and acetic anhydride (25 mmol). The reaction mixture was heated with heating mantle and stirred at 50 °C for 2 h, then a solution of 4-methyl-2-((2-methyl-1*H*-indol-3-yl)methyl)aniline in THF was added. When the reaction was complete as monitored by TLC, the mixture was adjusted to pH 7 with NaOH solution (1M), extracted with ethyl acetate three times. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated, and the resulting mixture was purified by column chromatography on silica gel to afford the product *N*-(4-methyl-2-((2-methyl-1H-indol-3-yl)methyl)phenyl)formamide 1.32 g, 82% yield.

To a 100 mL flask were added *N*-(4-methyl-2-((2-methyl-1*H*-indol-3-yl)methyl)phenyl)formamide (4 mmol) and 20 mL anhydrous THF. After degassing with argon and four evacuation/backfill cycles with argon, triethylamine (20 mmol) was added, then the mixture was cooled to −78 °C，and phosphorus oxychloride (12 mmol) was added to the solution. When the reaction was complete as monitored by TLC, aqueous solution of saturated Na_2CO_3 was added, extracted with ethyl acetate three times. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated, and the resulting mixture was purified by column chromatography on silica gel to afford the product **1e** 0.78g, 74%

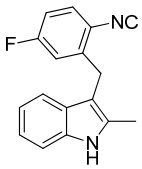
yield.

3-(2-isocyanobenzyl)-2-methyl-1H-indole (1a)



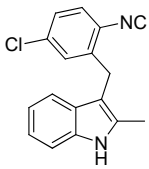
White solid, mp 91-92°C, 82% yield; R_f = 0.40 (DCM/EtOAc, 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.37 (s, 1H), 7.29 (d, J = 7.6 Hz, 2H), 7.20 – 7.06 (m, 3H), 7.06 – 6.97 (m, 2H), 4.18 (s, 2H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.2, 137.9, 135.4, 132.6, 129.5, 129.4, 129.3, 128.7, 126.8, 121.3, 119.5, 118.2, 110.4, 110.3, 107.9, 26.4, 11.9. HRMS (ESI) calcd for $C_{17}H_{14}N_2$ $[M+H]^+$ 247.1230, found 247.1235

3-(5-fluoro-2-isocyanobenzyl)-2-methyl-1H-indole (1b)



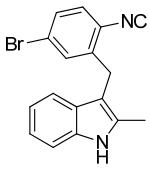
Brown solid, mp 123-124°C, 72% yield; R_f = 0.30 (DCM/EtOAc, 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.35 (dd, J = 8.4, 5.2 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.17 – 7.10 (m, 1H), 7.09 – 7.00 (m, 1H), 6.85 (td, J = 8.4, 2.8 Hz, 1H), 6.69 (dd, J = 9.6, 2.8 Hz, 1H), 4.14 (s, 1H), 2.36 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) 166.6, 162.6 (d, J = 250 Hz), 141.1, 135.4, 132.7, 128.5, 128.4, 121.5, 119.7, 118.0, 116.5(d, J = 24.0 Hz), 114.1 (d, J = 24.0 Hz), 110.5, 107.1, 26.5, 11.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.1 (td, J = 9.5, 4.3 Hz). HRMS (ESI) calcd for $C_{17}H_{13}FN_2$ $[M+H]^+$ 265.1136, found 265.1135.

3-(5-chloro-2-isocyanobenzyl)-2-methyl-1H-indole (1c)



Brown oil, 73% yield; R_f = 0.40 (DCM/EtOAc, 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.36 – 7.27 (m, 3H), 7.21 – 7.12 (m, 2H), 7.09 – 7.02 (m, 1H), 6.99 (s, 1H), 4.15 (s, 2H), 2.41 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.6, 140.0, 135.5, 132.9, 129.6, 127.9, 127.2, 121.4, 119.6, 117.9, 110.6, 106.9, 26.4, 11.9. HRMS (ESI) calcd for $C_{17}H_{13}ClN_2$ $[M+H]^+$ 281.0840, found 281.0836.

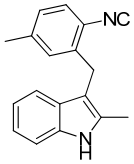
3-(5-bromo-2-isocyanobenzyl)-2-methyl-1H-indole (1d)



Brown oil, 63% yield; R_f = 0.50 (DCM/EtOAc, 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.31 (s, 2H), 7.24 – 7.19 (m, 1H), 7.14 – 7.09 (m, 2H), 7.04 – 6.96 (m, 2H), 4.14 (s, 2H), 2.29 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.3, 138.0, 135.5, 132.0, 129.6, 129.5, 128.7, 126.8, 126.7, 121.3, 119.5, 118.2, 110.5, 107.8, 26.5, 11.9. HRMS (ESI) calcd for

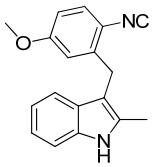
$C_{17}H_{13}BrN_2$ $[M+H]^+$ 325.0335, found 325.0314

3-(2-isocyano-5-methylbenzyl)-2-methyl-1H-indole (1e)



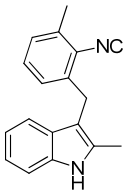
Brown solid, mp 102-103°C, 66% yield; R_f = 0.40 (DCM/EtOAc, 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.35 – 7.28 (m, 2H), 7.25 (d, J = 2.2 Hz, 1H), 7.15 – 7.07 (m, 1H), 7.06 – 7.00 (m, 1H), 6.97 (d, J = 8.1 Hz, 1H), 6.84 (s, 1H), 4.13 (s, 2H), 2.39 (s, 3H), 2.18 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 139.7, 137.6, 135.4, 132.4, 130.0, 128.8, 127.4, 126.6, 121.2, 119.5, 118.2, 110.3, 108.1, 26.3, 21.5, 11.9. HRMS (ESI) calcd for $C_{18}H_{16}N_2$ $[M+H]^+$ 261.1386, found 261.1390.

3-(2-isocyano-5-methoxybenzyl)-2-methyl-1H-indole (1f)



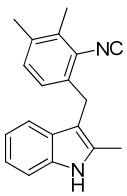
White solid, mp 120-121°C, 85% yield; R_f = 0.50 (DCM/EtOAc, 6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.35 – 7.26 (m, 3H), 7.16 – 7.06 (m, 1H), 7.06 – 6.97 (m, 1H), 6.67 (dd, J = 8.7, 2.8 Hz, 1H), 6.55 (d, J = 2.7 Hz, 1H), 4.13 (s, 2H), 3.62 (s, 3H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.0, 139.7, 135.4, 132.5, 128.7, 128.0, 121.3, 119.5, 118.2, 115.3, 111.4, 110.3, 110.0, 107.8, 55.4, 26.6, 11.9. HRMS (ESI) calcd for $C_{18}H_{16}N_2O$ $[M+H]^+$ 277.1335, found 277.1339.

3-(2-isocyano-3-methylbenzyl)-2-methyl-1H-indole (1g)



White solid, mp 154-155°C, 58% yield; R_f = 0.40 (DCM/EtOAc, 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.30 (dd, J = 8.0, 0.7 Hz, 2H), 7.18 – 6.98 (m, 5H), 6.86 (t, J = 4.5 Hz, 1H), 4.17 (s, 3H), 2.46 (s, 4H), 2.40 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.3, 137.8, 135.4, 135.0, 132.4, 128.7, 127.9, 126.8, 121.2, 119.4, 118.3, 110.3, 108.1, 26.8, 19.0, 11.9. HRMS(ESI) calcd for $C_{18}H_{16}N_2$ $[M+H]^+$ 261.1386, found 261.1386.

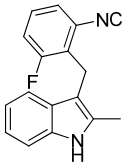
3-(2-isocyano-3,4-dimethylbenzyl)-2-methyl-1H-indole (1h)



White solid, mp 112-113°C, 48% yield; R_f = 0.40 (DCM/EtOAc, 5:1);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.35 – 7.26 (m, 2H), 7.14 – 7.06 (m, 1H), 7.04 – 6.98 (m, 1H), 6.96 (d, J = 8.0 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 4.13 (s, 2H), 2.38 (s, 6H), 2.23 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.7, 135.4, 135.2, 135.1, 133.2, 132.4, 130.2, 128.8, 126.2, 121.2, 119.4,

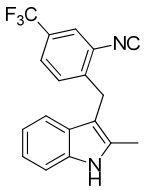
118.3, 110.3, 108.2, 26.8, 20.1, 15.6, 11.9. HRMS (ESI) calcd for $C_{19}H_{18}N_2$ $[M+H]^+$ 275.1543, found 275.1547.

3-(2-fluoro-6-isocyanobenzyl)-2-methyl-1H-indole (1i)



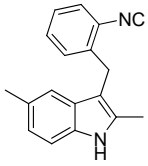
White solid, mp 130-131°C, 66% yield; R_f = 0.40 (DCM/EtOAc, 6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.42 (d, J = 7.6 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.19 – 7.14 (m, 2H), 7.12 – 7.04 (m, 2H), 7.03 – 6.96 (m, 1H), 4.16 (s, 3H), 2.48 (s, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.6, 161.1 (d, J =197.0 Hz), 135.1, 132.3, 128.3, 128.0, 127.9, 126.3, 123.4, 121.1, 119.4, 118.1, 117.0, 116.7, 110.2, 107.5, 21.0, 12.3. ^{19}F NMR (376 MHz, CDCl3) δ -122.2 (td, J = 10.0, 4.6 Hz). HRMS (ESI) calcd for $C_{17}H_{13}FN_2$ $[M+H]^+$ 265.1136, found 265.1138.

3-(2-isocyano-4-(trifluoromethyl)benzyl)-2-methyl-1H-indole (1j)



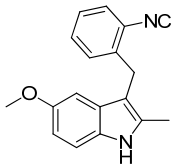
Yellow solid, mp 114-115°C, 82% yield; R_f = 0.50 (DCM/EtOAc, 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.66 (s, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.25 (s, 1H), 7.20 – 7.10 (m, 2H), 7.04 (t, J = 7.6 Hz, 1H), 4.22 (s, 2H), 2.40 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.7, 142.0, 135.4, 132.7, 130.3, 128.9, 127.4 (d, J = 245.7 Hz), 126.0, 123.8, 121.6, 119.4, 117.9, 110.5, 106.9, 26.6, 11.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.7 (s, 3F). HRMS (ESI) calcd for $C_{18}H_{13}F_3N_2$ $[M+H]^+$ 315.1114, found 315.1119

3-(2-isocyanobenzyl)-2,5-dimethyl-1H-indole (1k)



White solid, mp 145-146°C, 87% yield; R_f = 0.40 (DCM/EtOAc, 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.37 (dd, J = 5.2, 3.8 Hz, 1H), 7.19 – 7.12 (m, 1H), 7.09 (s, 1H), 7.04 – 6.98 (m, 1H), 6.94 (d, J = 8.2 Hz, 1H), 4.14 (s, 1H), 2.37 (s, 1H), 2.33 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.3, 138.0, 133.7, 132.7, 129.5, 129.4, 129.0, 128.7, 126.7, 122.8, 117.9, 110.0, 107.4, 26.3, 21.6, 11.9. HRMS (ESI) calcd for $C_{18}H_{16}N_2$ $[M+H]^+$ 261.1386, found 261.1389

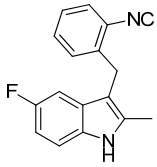
3-(2-isocyanobenzyl)-5-methoxy-1H-indole (1l)



White solid, mp 119-120 °C, 84% yield; R_f = 0.60 (DCM/EtOAc, 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.42 – 7.34 (m, 1H), 7.22 – 7.14 (m, 3H), 7.08 – 7.01 (m, 1H), 6.84 – 6.73 (m, 2H), 4.14 (s, 2H),

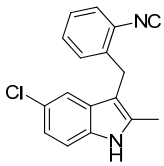
3.76 (s, 3H), 2.37 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 154.0, 137.7, 133.3, 130.4, 129.5, 129.4, 129.2, 126.7, 126.6, 110.9, 110.8, 107.8, 100.6, 55.9, 26.4, 12.0. HRMS (ESI) calcd for $C_{18}H_{16}N_2O$ $[M+H]^+$ 277.1335, found 277.1337.

5-fluoro-3-(2-isocyanobenzyl)-2-methyl-1H-indole (1m)



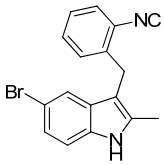
White solid, mp 156-157 °C, 65% yield; R_f = 0.40 (DCM/EtOAc, 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.56 – 7.33 (m, 1H), 7.25 – 7.18 (m, 4H), 7.07 (dd, J = 8.8, 2.0 Hz, 1H), 7.03 – 6.97 (m, 1H), 4.13 (s, 2H), 2.39 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 166.4, 157.9 (d, J = 232.7 Hz), 137.4, 134.5, 131.8, 129.4 (d, J = 4.1 Hz), 129.1 (d, J = 9.8 Hz), 126.9, 126.8, 110.8 (d, J = 9.6 Hz), 109.4, 109.2(d, J = 26.1 Hz), 108.2, 103.3 (d, J = 23.5 Hz), 26.5, 12.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.5 (td, J = 9.5, 4.3 Hz). HRMS (ESI) calcd for $C_{17}H_{13}FN_2$ $[M+H]^+$ 265.1136, found 265.1134.

5-chloro-3-(2-isocyanobenzyl)-2-methyl-1H-indole (1n)



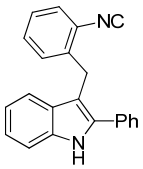
White solid, mp 140-141°C, 80% yield; R_f = 0.40 (DCM/EtOAc, 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.45 – 7.35 (m, 1H), 7.29 – 7.07 (m, 4H), 7.06 – 6.99 (m, 1H), 7.02 – 6.77 (m, 2H), 4.13 (s, 2H), 2.39 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 137.3, 134.2, 133.7, 129.8, 129.5, 129.3, 127.0, 126.8, 125.2, 121.5, 118.7, 117.7, 111.3, 107.7, 26.4, 12.0. HRMS (ESI) calcd for $C_{17}H_{13}ClN_2$ $[M+H]^+$ 281.0840, found 281.0843.

5-bromo-3-(2-isocyanobenzyl)-2-methyl-1H-indole (1o)



White solid, mp 171-172°C, 82% yield; R_f = 0.40 (DCM/EtOAc, 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.45 – 7.34 (m, 1H), 7.24 – 7.13 (m, 1H), 7.04 – 6.84 (m, 1H), 4.13 (s, 1H), 2.38 (s, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 137.3, 134.0, 133.9, 130.5, 129.5, 129.3, 127.0, 126.8, 124.1, 120.7, 112.8, 111.8, 107.6, 26.3, 12.0. HRMS (ESI) calcd for $C_{17}H_{13}BrN_2$ $[M+H]^+$ 325.0335, found 325.0330.

3-(2-isocyanobenzyl)-2-phenyl-1H-indole (1p)



White solid, mp 124-125°C, 77% yield; R_f = 0.40 (DCM/EtOAc, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.49 – 7.40 (m, 2H), 7.40 – 7.31 (m, 1H), 7.25 – 7.13 (m, 1H), 7.13 – 6.97 (m, 1H), 4.38 (s, 1H).

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 166.6, 137.7, 136.2, 136.1, 132.5, 129.5, 129.3, 129.2, 129.1, 128.1, 127.8, 126.8, 126.7, 122.7, 120.1, 119.3, 111.0, 108.6, 26.9. HRMS (ESI) calcd for $C_{22}H_{16}N_2$ $[M+H]^+$ 309.1386, found 309.1387.

3. Synthesis of compounds 2 (2c and 2f were selected as examples)

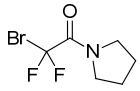
Method 1： To a Shrek tube were added bromodifluoroacetate (10 mmol), cyclohexylamine (10 mmol), and the mixture was reacted at room temperature. When the reaction was complete as monitored by TLC, diluted hydrochloric acid (1M) was added, extracted with ethyl acetate three times. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated, and the resulting mixture was purified by column chromatography on silica gel to afford **2c** as a colorless oil 2.401 g, 99% yield.

2d-2e were synthesized using the similar method as **2c**.

Method 2： To a 100 mL flask were added N-methyl piperazine (5 mmol), $La(OTf)_3$ (0.25 mmol), and anhydrous THF (20 mL), bromodifluoroacetate (6 mmol) was added to the mixture dropwise under agon atmosphere. Then, the reaction mixture was heated with heating mantle. When the reaction was complete as monitored by TLC, diluted hydrochloric acid (1M) was added, extracted with ethyl acetate three times. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated, and the resulting mixture was purified by column chromatography on silica gel to afford **2f** as a colorless oil 0.6975g, 55% yield.

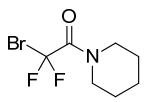
2g-2k were synthesized using the similar method as **2f**.

2-bromo-2,2-difluoro-1-(pyrrolidin-1-yl)ethan-1-one (2b)



Colorless oil, 36% yield; R_f = 0.40 (petroleum ether/EtOAc, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 – 3.27 (m, 2H), 2.50 – 1.48 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 157.8 (t, J = 27.2 Hz), 111.4 (t, J = 315.1 Hz), 47.9, 47.6 (t, J = 4.3 Hz), 26.4, 23.3.^{19}F NMR (376 MHz, $CDCl_3$) δ -56.9. HRMS (ESI) calcd for $C_6H_8BrF_2NO$ $[M+H]^+$ 227.9830, found 227.9826

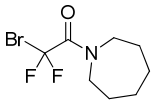
2-bromo-2,2-difluoro-1-(piperidin-1-yl)ethan-1-one (2c)



Colorless oil, 99% yield; R_f = 0.50 (petroleum ether/EtOAc, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 – 3.19 (m, 4H), 2.33 – 1.39 (m, 6H).

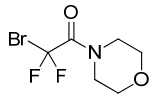
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 157.6 (t, J = 30.8 Hz), 110.8 (t, J = 314.5 Hz), 47.7, 45.0, 25.8, 25.4, 24.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -53.9. HRMS (ESI) calcd for $C_7H_{10}BrF_2NO$ $[M+H]^+$ 241.9987, found 241.9984.

1-(azepan-1-yl)-2-bromo-2,2-difluoroethan-1-one (2d)



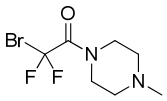
Colorless oil, 49% yield; R_f = 0.60 (petroleum ether/EtOAc, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (t, J = 6.0 Hz, 2H), 3.57 (t, J = 6.0 Hz, 2H), 1.90 – 1.70 (m, 4H), 1.62 – 1.59 (m, 4H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.0, 111.2 (t, J = 314.7 Hz), 48.5 (t, J = 3.7 Hz), 48.4, 29.0, 27.5, 26.4, 25.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -53.6. HRMS (ESI) calcd for $C_8H_{12}BrF_2NO$ $[M+H]^+$ 256.0143, found 256.0144.

2-bromo-2,2-difluoro-1-morpholinoethan-1-one (2e)



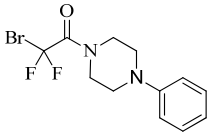
Colorless oil, 99% yield; R_f = 0.50 (petroleum ether/EtOAc, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 – 3.40 (m, 8H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 157.9 (t, J = 26.5 Hz), 110.5 (t, J = 314.4 Hz), 66.5, 66.1, 47.3, 43.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -54.5. HRMS (ESI) calcd for $C_6H_8BrF_2NO_2$ $[M+H]^+$ 243.9769, found 243.9764.

2-bromo-2,2-difluoro-1-(4-methylpiperazin-1-yl)ethan-1-one (2f)



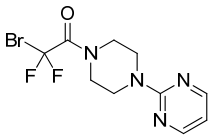
Colorless oil, 55% yield; R_f = 0.60 (petroleum ether/EtOAc, 15:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 – 3.63 (m, 4H), 2.55 – 2.42 (m, 4H), 2.34 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 157.6 (t, J = 26.3 Hz), 110.5 (t, J = 314.3 Hz), 54.3, 54.2, 46.4 (t, J = 3.9 Hz), 45.7, 43.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -54.3. HRMS (ESI) calcd for $C_7H_{11}BrF_2N_2O$ $[M+H]^+$ 257.0096, found 257.0099.

2-bromo-2,2-difluoro-1-(4-phenylpiperazin-1-yl)ethan-1-one (2g)



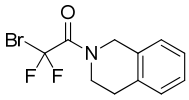
White solid, mp 47-48°C, 53% yield; R_f = 0.50 (petroleum ether/EtOAc, 15:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, J = 8.0 Hz, 2H), 7.13 – 6.88 (m, 3H), 3.99 – 3.74 (m, 4H), 3.35 – 3.07 (m, 4H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 157.8 (t, J = 26.4 Hz), 150.6, 129.4, 120.9, 116.8, 110.7 (t, J = 314.5 Hz), 49.2, 49.1, 46.6 (t, J = 3.8 Hz), 43.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -53.6. HRMS (ESI) calcd for $C_{12}H_{13}BrF_2N_2O$ $[M+H]^+$ 319.0252, found 319.0253.

2-bromo-2,2-difluoro-1-(4-(pyrimidin-2-yl)piperazin-1-yl)ethan-1-one(2h)



White solid, mp 107-108°C, 51% yield; R_f = 0.50 (petroleum ether/EtOAc, 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 4.8 Hz, 2H), 6.59 (t, J = 4.8 Hz, 1H), 4.15 – 3.83 (m, 4H), 3.83 – 3.55 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.4, 157.9, 110.9, 110.6(t, J = 312.5 Hz), 46.5, 43.7, 43.3, 43.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -54.2. HRMS (ESI) calcd for $C_{10}H_{11}BrF_2N_4O$ $[M+H]^+$ 321.0157, found 321.0157.

2-bromo-1-(3,4-dihydroisoquinolin-2(1H)-yl)-2,2-difluoroethan-1-one (2i)

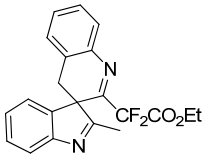


White solid, mp 30-31°C, 54% yield; R_f = 0.50 (petroleum ether/EtOAc, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (s, 1H), 5.22 – 4.60 (m, 1H), 4.02 – 3.47 (m, 1H), 3.28 – 2.40 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ(major) 158.4 , 133.4, 131.6, 128.6, 127.1, 126.9, 126.6, 110.8 (t, J = 312.1 Hz), 46.0, 44.2 (t, J = 4.1 Hz), 28.9. δ(minor) = 158.3 , 134.2, 131.6, 128.8, 127.5, 126.8, 126.1, 110.9 (t, J= 312.6 Hz), 48.1 (t, J= 4.5 Hz), 42.54, 27.8.^{19}F NMR (376 MHz, $CDCl_3$) δ (major) -54.1, δ (minor) -54.2. HRMS (ESI) calcd for $C_{11}H_{10}BrF_2NO$ $[M+H]^+$ 289.9987, found 289.9983.

4. Sythesis of compounds 3

To Shrek tube were added **1** (0.20 mmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (0.002 mmol), $NaHCO_3$ (0.4 mmol, 2.0 equiv), and dimethyl sulfoxide (2 mL). After degassing with argon and four evacuation/backfill cycles with argon, **2** (0.30 mmol, 1.5 equiv) was added, The reaction mixture was irradiated by a 3W blue LED bulb (approximately 2 cm away from the reaction vessel) at room temperature for 24 h before concentrating in vacuo. The reaction mixture was quenched with water and then extracted with EtOAc. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography to give the desired compound **3**.

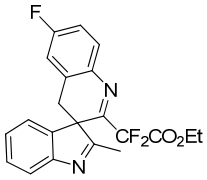
ethyl 2,2-difluoro-2-(2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)acetate (3a)



Colorless oil, 86% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.6 Hz, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.41 (dd, J = 13.7, 7.2 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H),

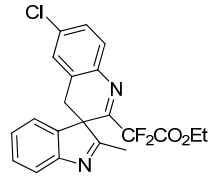
7.18 – 7.13 (m, 2H), 7.09 (d, J = 7.6 Hz, 1H), 4.34 (q, J = 7.2 Hz, 2H), 3.18 – 3.05 (m, 2H), 2.27 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 179.7, 162.3, 158.4, 154.9, 140.9, 139.1, 130.1, 129.3, 128.6, 128.5, 128.1, 125.9, 125.2, 122.9, 120.6, 112.9(t, J = 253.2 Hz), 63.0, 59.0, 34.5, 17.7, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.6 (d, J = 283.0 Hz), -107.0 (d, J = 282.6 Hz). HRMS (ESI) calcd for $C_{21}H_{18}F_2N_2O_2$ $[M+H]^+$ 369.1409, found 369.1407.

2-ethyl-2,2-difluoro-2-(6'-fluoro-2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)acetate (3b)



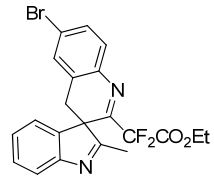
Colorless oil, 44% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.47 (m, 2H), 7.41 (t, J = 7.6 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.14 (d, J = 7.2 Hz, 1H), 7.10 – 7.01 (m, 1H), 6.75 (d, J = 7.6 Hz, 1H), 4.34 (q, J = 7.2 Hz, 2H), 3.25 – 2.96 (m, 2H), 2.22 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 179.6, 162.2, 158.7(d, J = 222.9 Hz), 151.0, 140.8, 140.7, 130.3, 128.7, 128.1, 124.7, 121.3, 121.2, 116.1, 115.8, 115.4, 112.9(t, J = 254.1 Hz), 110.3, 63.1, 59.3, 34.4, 17.7, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.2 (d, J = 283.8 Hz), -107.3 (d, J = 283.8 Hz), -116.2 (dd, J = 13.2, 8.7 Hz). HRMS (ESI) calcd for $C_{21}H_{17}F_3N_2O_2$ $[M+H]^+$ 387.1315, found 387.1310.

2-ethyl-2-(6'-chloro-2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-2,2-difluoroacetate (3c)



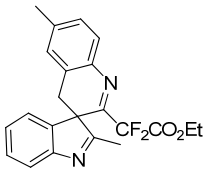
Colorless oil, 67% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.6 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.43 – 7.34 (m, 2H), 7.18 – 7.11 (m, 2H), 7.05 (d, J = 7.4 Hz, 1H), 4.30 (q, J = 7.2 Hz, 2H), 3.06 (q, J = 16.8 Hz, 2H), 2.22 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 179.2, 162.1, 158.9, 154.9, 139.5, 138.7, 135.6, 129.8, 129.5, 128.8, 128.2, 127.0, 126.0, 122.8, 120.7, 112.7(t, J = 255.1 Hz), 63.1, 58.7, 34.2, 17.7, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.1 (d, J = 283.8 Hz), -107.3 (d, J = 283.8 Hz). HRMS (ESI) calcd for $C_{21}H_{17}ClF_2N_2O_2$ $[M+H]^+$ 403.1019, found403.1015..

2-ethyl-2-(6'-bromo-2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-2,2-difluoroa cetate (3d)



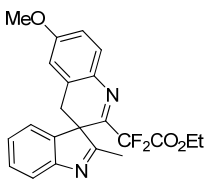
Colorless oil, 72% yield; R_f = 0.20 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.6 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.44 – 7.35 (m, 2H), 7.32 (d, J = 1.2 Hz, 1H), 7.17 – 7.10 (m, 2H), 7.07 (s, 1H), 4.31 (q, J = 7.2 Hz, 2H), 3.09 (d, J = 5.2 Hz, 2H), 2.24 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 179.7, 162.3, 158.4, 154.9, 140.9, 139.1, 130.1, 129.3, 128.6, 128.5, 128.1, 125.9, 125.2, 122.9, 120.6, 113.0(t, J = 254.9 Hz), 63.0, 59.0, 34.5, 17.7, 13.9.^{19}F NMR (376 MHz, $CDCl_3$) δ -105.6 (d, J = 283.5 Hz), -106.9 (d, J = 283.6 Hz). HRMS (ESI) calcd for $C_{21}H_{17}BrF_2N_2O_2$ $[M+H]^+$447.0514, found 447.0508.

2-ethyl-2-(2,6'-dimethyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-2,2-difluoroacetate (3e)



Colorless oil, 87% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.6 Hz, 1H), 7.38 (t, J = 7.6 Hz, 2H), 7.22 – 7.04 (m, 3H), 6.93 (s, 1H), 4.31 (q, J = 7.2 Hz, 2H), 3.04 (s, 2H), 2.37 (s, 3H), 2.24 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.0, 162.4, 157.0, 154.9, 140.5, 139.3, 138.8, 129.2, 129.1, 128.8, 128.5, 125.8, 124.9, 122.9, 120.5, 110.5(t, J = 252.6 Hz), 62.9, 59.1, 34.6, 21.5, 17.7, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.2 (d, J = 282.8 Hz), -106.7 (d, J = 282.4 Hz). HRMS (ESI) calcd for $C_{22}H_{20}F_2N_2O_2$ $[M+H]^+$ 383.1566, found 383.1562.

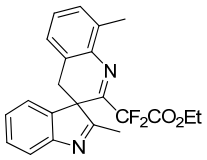
2-ethyl-2,2-difluoro-2-(6'-methoxy-2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl) acetate (3f)



Colorless oil, 91% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.6 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 7.18 – 7.03 (m, 2H), 6.93 – 6.83 (m, 1H), 6.64 (s, 1H), 4.30 (q, J = 7.2 Hz, 2H), 3.82 (s, 3H), 3.03 (s, 2H), 2.24 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.0, 162.5(t, J = 31.3 Hz), 160.7, 155.0 (t, J = 29.4 Hz), 154.9, 139.4, 134.7, 130.1, 129.2, 127.0, 125.8, 122.9, 120.5, 114.0, 113.1(t, J = 253.0 Hz), 112.9, 110.6, 62.9, 58.8,

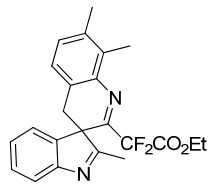
55.5, 34.9, 17.7, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.8 (d, J = 281.6 Hz), -108.4 (d, J = 281.6 Hz). HRMS (ESI) calcd for $C_{22}H_{20}F_2N_2O_3$ $[M+H]^+$ 399.1515, found 399.1516.

2-ethyl-2-(2,8'-dimethyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-2,2-difluoroacetate (3g)



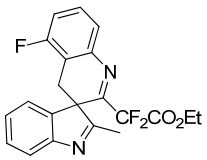
Colorless oil, 84% yield; R_f = 0.40 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.6 Hz, 1H), 7.43 – 7.32 (m, 1H), 7.25 – 7.04 (m, 4H), 6.94 (d, J = 6.8 Hz, 1H), 4.40 – 4.22 (m, 2H), 3.06 (s, 2H), 2.46 (s, 3H), 2.23 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 179.8, 162.6 (t, J = 31.1 Hz), 156.8 (t, J = 30.2 Hz), 154.9, 139.3, 139.0, 137.0, 130.2, 129.7, 129.1, 125. 8, 125.7, 125.1, 122.9, 120.5, 113.4 (t, J = 255.0 Hz), 62.9, 58.7, 34.8, 17.7, 17.1, 14.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.7 (d, J = 284.1 Hz), -108.9 (d, J = 284.1 Hz). HRMS (ESI) calcd for $C_{22}H_{20}F_2N_2O_2$ $[M+H]^+$ 383.1566, found 383.1566.

2-ethyl-2,2-difluoro-2-(2,7',8'-trimethyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)acetate (3h)



Colorless oil, 88% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.6 Hz, 1H), 7.41 – 7.31 (m, 1H), 7.20 – 7.02 (m, 3H), 6.84 (d, J = 7.6 Hz, 1H), 4.42 – 4.24 (m, 2H), 3.03 (s, 2H), 2.40 (s, 3H), 2.33 (s, 3H), 2.22 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.0, 162.7, 156.6, 154.9, 139.4, 138.8, 137.5, 135.9, 130.9, 129.1, 125.8, 125.0, 122.9, 122.4, 120.4, 113.5(t, J = 250.4 Hz), 62.9, 58.7, 34.9, 20.1, 17.8, 14.0, 13.2.^{19}F NMR (376 MHz, $CDCl_3$) δ 141.6 (d, J = 283.5 Hz), 139.4 (d, J = 283.9 Hz). HRMS (ESI) calcd for $C_{23}H_{22}F_2N_2O_2$ $[M+H]^+$ 397.1722, found 397.1723.

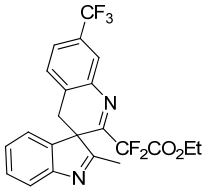
2-ethyl-2,2-difluoro-2-(5'-fluoro-2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)acetate (3i)



Colorless oil, 42% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.6 Hz, 1H), 7.49 – 7.30 (m, 3H), 7.22 – 7.00 (m, 3H), 4.31 (dd, J = 13.6, 6.8 Hz, 2H), 3.11 (d, J

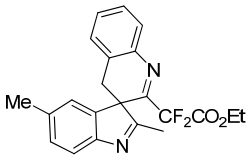
= 4.8 Hz, 2H), 2.25 (s, 3H), 1.31 (t, J = 7.2 Hz, 4H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 180.3, 162.1, 157.3, 153.5, 140.8, 140.6, 131.5, 130.4, 129.5, 128.8, 128.1, 126.9 (t, J = 238 Hz), 125.1,, 123.3, 121.4, 63.1, 59.3, 34.3, 17.7, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -107.17 (d, J = 284.3 Hz), -108.8 (d, J = 284.2 Hz), -120.8. HRMS (ESI) calcd for $C_{21}H_{17}F_3N_2O_2$ $[M+H]^+$ 387.1315, found 387.1322.

2-ethyl-2,2-difluoro-2-(2-methyl-7'-(trifluoromethyl)-4'H-spiro[indole-3,3'-quinolin]-2'-yl)acetate (3j)



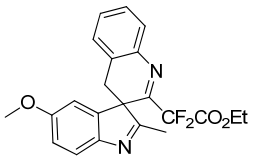
Colorless oil, 34% yield; R_f = 0.30 (petroleum ether/EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.63 – 7.55 (m, 2H), 7.40 (t, J = 7.6 Hz, 1H), 7.28 (d, J = 8.8 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 7.03 (d, J = 7.6 Hz, 1H), 4.32 (q, J = 7.2 Hz, 2H), 3.24 – 3.05 (m, 2H), 2.27 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 178.9, 162.0, 160.6, 154.9, 141.1, 138.5, 131.3, 129.6, 129.3, 129.2, 128.7, 126.6, 126.1, 125.4, 122.8, 120.8, 120.6, 116.8(q, , J = 331.2 Hz), 112.6（d, J = 255.7 Hz）, 63.2, 58.7, 34.2, 17.7, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.1 (s), -106.1 (d, J = 284.6 Hz), -107.2 (d, J = 284.6 Hz). HRMS (ESI) calcd for $C_{22}H_{17}F_5N_2O_2$ $[M+H]^+$ 437.1283, found 437.1285.

2-ethyl-2-(2,5-dimethyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-2,2-difluoroacetate (3k)



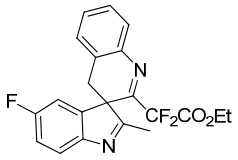
Colorless oil, 81% yield; R_f = 0.40 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 7.6 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.39 (t, J = 7.2 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.17 (d, J = 7.2 Hz, 1H), 7.12 (d, J = 7.2 Hz, 1H) 6.89 (s, 1H), 4.31 (dd, J = 14.0, 7.2 Hz, 2H), 3.07 (s, 2H), 2.29 (s, 3H), 2.19 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 178.6, 162.4, 158.5, 152.8, 140.9, 139.4, 135.8, 130.1, 129.9, 128.6, 128.5, 128.1, 126.6, 125.2, 122.7, 120.1, 115.5(t, J = 254.7 Hz) 63.0, 58.9, 34.6, 21.4, 17.6, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.2 (d, J = 283.1 Hz), -107.3 (d, J = 283.3 Hz). HRMS (ESI) calcd for $C_{22}H_{20}F_2N_2O_2$ $[M+H]^+$ 383.1566, found 383.1570.

2-ethyl-2,2-difluoro-2-(5-methoxy-2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl) acetate (3l)



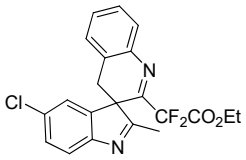
Colorless oil, 80% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (t, J = 8.0 Hz, 2H), 7.38 (t, J = 7.2 Hz, 1H), 7.33 – 7.27 (m, 1H), 7.12 (d, J = 7.2 Hz, 1H), 6.88 (dd, J = 8.4, 2.0 Hz, 1H), 6.65 (s, 1H), 4.32 (q, J = 7.2 Hz, 2H), 3.71 (s, 3H), 3.07 (s, 2H), 2.18 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 177.2, 162.3 (t, J = 31.1 Hz), 158.4 (t, J = 29.0 Hz), 158.2, 148.7, 140.9, 140.3, 130.1, 128.5, 128.1, 125.1, 120.7, 113.7, 112.9 (t, J = 252.9 Hz), 109.7, 63.0, 59.1, 55.6, 34.7, 17.5, 17.5, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.7 (d, J = 283.6 Hz), -107.6 (d, J = 283.6 Hz). HRMS (ESI) calcd for $C_{22}H_{20}F_2N_2O_3$ $[M+H]^+$ 399.1515, found 399.1516.

2-ethyl-2,2-difluoro-2-(5-fluoro-2,8'-dimethyl-4'H-spiro[indole-3,3'-quinolin]-2'-y l)acetate (3m)



Colorless oil, 77% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.48 (m, 2H), 7.42 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.3Hz, 1H), 7.16 (d, J = 7.2 Hz, 1H), 7.08 (td, J = 8.8, 2.0 Hz, 1H), 6.77 (dd, J = 8.0, 2.0 Hz, 1H), 4.36 (q, J = 7.2 Hz, 2H), 3.18 – 3.03 (m, 2H), 2.24 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 179.6, 162.3, 158.7(d, J = 223.0 Hz), 157.6, 151.0, 140.9, 140.8, 130.3, 128.8, 128.7, 128.1, 124.7, 121.2, 116.1, 115.4, 112.9(t, J = 253.2 Hz), 110.8, 63.1, 59.4, 34.4, 17.7, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -107.4 (d, J = 283.7 Hz), -108.5 (d, J = 283.8 Hz), -117.40. HRMS (ESI) calcd for $C_{21}H_{17}F_3N_2O_2$ $[M+H]^+$ 387.1315, found 387.1322.

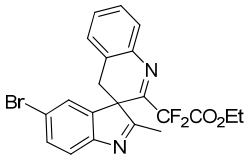
2-ethyl-2-(5-chloro-2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-2,2-difluoroac etate (3n)



Colorless oil, 78% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (t, J = 7.6 Hz, 2H), 7.44 – 7.31 (m, 3H), 7.18 – 7.10 (m, 1H), 7.03 (s, 1H), 4.34 (q, J = 7.2 Hz, 2H), 3.08 (dd, J = 24.8, 16.4 Hz, 2H), 2.22 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H).

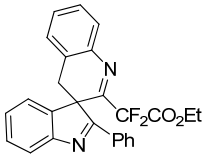
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 180.3, 162.1, 157.3, 153.5, 140.8, 140.6, 131.5, 130.4, 129.5, 128.8, 128.1, 126.8, 124.6, 123.3, 121.4, 112.9(t, J =253.7 Hz), 63.1, 59.3, 34.3, 17.7, 13.9.^{19}F NMR (376 MHz, $CDCl_3$) δ -107.3 (d, J = 283.4 Hz), -108.5 (d, J = 283.5 Hz). HRMS(ESI) calcd for $C_{21}H_{17}ClF_2N_2O_2$ $[M+H]^+$ 403.1019, found 403.1027.

2-ethyl-2-(5-bromo-2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-2,2-difluoroacetate (3o)



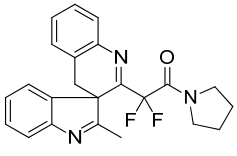
Colorless oil, 82% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.49 (m, 2H), 7.49 – 7.32 (m, 3H), 7.26 – 7.12 (m, 2H), 4.44 – 4.26 (m, 2H), 3.09 (s, 2H), 2.21 (s, 3H), 1.42 – 1.27 (m, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 180.4, 162.2, 157.2, 153.9, 141.2, 140.6, 132.4, 130.4, 128.8, 128.1, 126.2, 124.5, 121.9, 119.4, 112.8(t, J = 252.3 Hz), 63.2, 59.3, 34.3, 17.7, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.6 (d, J = 283.5 Hz), -106.9 (d, J = 283.6 Hz). HRMS (ESI) calcd for $C_{21}H_{17}BrF_2N_2O_2$ $[M+H]^+$447.0514, found 447.0511.

2-ethyl-2,2-difluoro-2-(2-phenyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)acetate (3p)



Colorless oil, 74% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, J = 6.4, 1.6Hz, 2H), 7.76 (d, J = 7.6 Hz, 1H), 7.58 (d, J = 7.6 Hz, 1H), 7.51 – 7.38 (m, 6H), 7.35 – 7.26 (m, 1H), 7.08 – 6.99 (m, 2H), 6.84 (d, J = 7.2 Hz, 1H), 4.37 – 4.15 (m, 2H), 3.80 (d, J = 16.8 Hz, 1H), 2.60 (d, J = 16.8 Hz, 1H), 1.27 (t, J = 7.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 178.0, 162.4, 159.5, 154.0, 140.7, 139.3, 131.6, 131.2, 130.2, 129.7, 129.5, 129.0, 128.6, 128.5, 128.4, 127.8, 126.2, 124.8, 121.9, 121.7, 112.7(t, J =252.7 Hz), 63.0, 57.4, 35.6, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -103.5 (d, J = 276.0 Hz), -108.7 (d, J = 275.7 Hz). HRMS (ESI) calcd for $C_{21}H_{17}F_2N_2O_2$ $[M+H]^+$431.1566, found 431.1561.

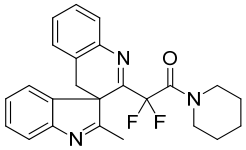
2,2-difluoro-2-(2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-1-(pyrrolidin-1-yl)ethanone (3q)



Colorless oil, 71% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.50 (m, 2H), 7.44 – 7.30

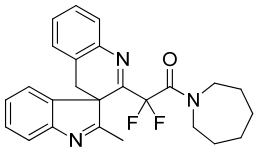
(m, 3H), 7.15 – 6.99 (m, 3H), 3.60 – 3.40 (m, 2H), 3.31 – 3.17 (m, 2H), 3.15 – 2.99 (m, 2H), 2.27 (s, 3H), 1.89 – 1.73 (m, 4H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 180.5, 162.8, 160.7, 155.2, 141.3, 139.0, 129.8, 129.2, 128.5, 128.4, 128.1, 125.5, 125.4, 123.1, 120.5, 114.1(t, J =256.5 Hz), 59.2, 47.5, 46.6, 34.4, 26.4, 23.3, 17.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.5 (d, J = 284.7 Hz), -104.3 (d, J = 286.0 Hz). HRMS (ESI) calcd for $C_{23}H_{21}F_2N_3O$ $[M+H]^+$394.1725, found 394.1719.

2,2-difluoro-2-(2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-1-(piperidin-1-yl)ethan-1-one (3r)



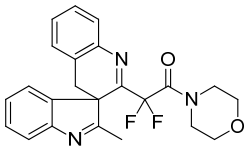
Colorless oil, 71% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, J = 13.6, 7.6 Hz, 2H), 7.45 – 7.29 (m, 3H), 7.14 (d, J = 7.2 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 7.2 Hz, 1H), 3.74 (m, 1H), 3.43 – 3.32 (m, 1H), 3.28 (d, J = 16.4 Hz, 1H), 3.03 (m, 2H), 2.91 (d, J = 16.4 Hz, 1H), 2.34 (s, 3H), 1.69 – 1.49 (m, 4H), 1.32 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 179.4, 159.3, 157.5, 153.8, 140.3, 137.7, 128.8, 128.3, 127.6, 127.4, 127.3, 124.4, 124.3, 121.7, 119.6, 113.9(t, J =250.6 Hz), 57.9, 45.8, 45.7, 43.3, 33.1, 24.8, 23.3, 16.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -96.1 (d, J = 289.1 Hz), -103.7 (d, J = 289.1 Hz). HRMS (ESI) calcd for $C_{24}H_{23}F_2N_3O$ $[M+H]^+$408.1882, found 408.1885.

1-(azepan-1-yl)-2,2-difluoro-2-(2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)ethanone (3s)



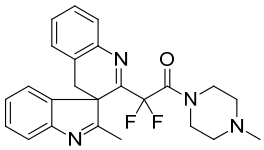
Colorless oil, 72% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.52 (m, 2H), 7.45 – 7.29 (m, 3H), 7.14 (d, J = 7.6 Hz, 1H), 7.06 (t, J = 7.6 Hz , 1H), 6.98 (d, J = 7.6 Hz, 1H), 3.66 – 3.52 (m, 1H), 3.45 – 3.32 (m, 1H), 3.25 – 2.96 (m, 4H), 2.31 (s, 3H), 1.75 (d, J = 4.4 Hz, 2H), 1.58 – 1.31 (m, 6H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 180.5, 161.7, 158.8, 155.0, 141.3, 138.9, 129.8, 129.2, 128.5, 128.4, 128.2, 125.5, 125.4, 123.1, 120.6, 114.8(t, J =255.7 Hz), 59.0, 47.3, 34.4, 31.0, 28.9, 27.8, 26.7, 25.8, 17.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -96.8 (d, J = 287.0 Hz), -104.5 (d, J = 287.1 Hz). HRMS (ESI) calcd for $C_{25}H_{25}F_2N_3O$ $[M+H]^+$422.2038, found 422.2044.

2,2-difluoro-2-(2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-1-morpholinoetha n-1-one (3t)



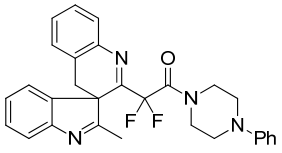
Colorless oil, 74% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, J = 14.4, 7.6 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.27 (q, J = 16.0, 8.0 Hz, 2H), 7.07 (d, J = 7.2 Hz, 1H), 6.94 (t, J = 7.6 Hz, 1H), 6.76 (d, J = 7.6 Hz, 1H), 3.74 – 3.60 (m, 3H), 3.51 – 3.33 (m, 3H), 3.24 (d, J = 16.4 Hz, 1H), 3.08 (s, 2H), 2.82 (d, J = 16.4 Hz, 1H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.3, 154.9, 141.1, 138.5, 138.2, 130.2, 129.6, 128.7, 128.4, 125.5, 125.3, 122.4, 120.8, 120.0, 112.5(t, J =246.5 Hz), 66.4, 58.9, 46.5, 43.4, 34.0, 29.3, 17.9.^{19}F NMR (376 MHz, $CDCl_3$) δ -104.3 (d, J = 290.1 Hz), -111.4 (d, J = 290.1 Hz). HRMS (ESI) calcd for $C_{23}H_{21}F_2N_3O_2$ $[M+H]^+$410.1675, found 410.1671.

2,2-difluoro-2-(2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-1-(4-methylpipera zin-1-yl)ethan-1-one (3u)



Yellow oil, 58% yield; R_f = 0.40 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, J = 16.8, 8.0 Hz, 2H), 7.48 – 7.29 (m, 3H), 7.14 (d, J = 7.2 Hz, 1H), 7.02 (t, J = 7.2 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 3.84 – 3.69 (m, 1H), 3.61 – 3.50 (m, 1H), 3.31 (d, J = 16.4 Hz, 1H), 3.20 – 3.08 (m, 2H), 2.90 (d, J = 16.4 Hz, 1H), 2.43 (s, 2H), 2.36 (s, 3H), 2.26 (s, 3H), 2.22 – 2.08 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.3, 160.6, 158.5, 154.9, 141.2, 138.6, 130.0, 129.5, 128.6, 128.4, 128.3, 125.5, 125.4, 122.5, 120.8, 114.8(t, J =252.5 Hz), 58.9, 54.5, 46.0, 45.7, 43.0, 41.0, 34.1, 18.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -98.3 (d, J = 290.1 Hz), -105.6 (d, J = 290.0 Hz). HRMS (ESI) calcd for $C_{24}H_{24}F_2N_4O$ $[M+H]^+$423.1991, found 423.1987.

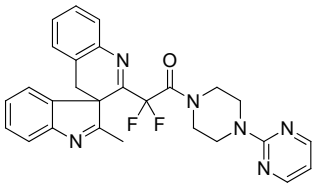
2,2-difluoro-2-(2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-1-(4-phenylpipera zin-1-yl)ethanone (3v)



Yellow oil, 51% yield; R_f = 0.30 (petroleum ether/EtOAc, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.8 Hz, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.42 – 7.26 (m, 5H), 7.14 (d, J = 7.2 Hz, 1H), 7.04 (t, J = 7.2 Hz, 1H), 6.96 – 6.83 (m, 4H), 4.05 – 3.57 (m, 3H), 3.34 –

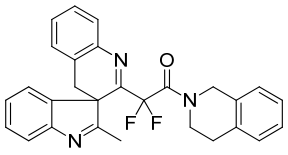
3.27 (m, 2H), 3.25 – 2.83 (m, 5H), 2.37 (s, 2H), 2.17 (s, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 180.3, 154.9, 150.8, 141.1, 138.7, 130.1, 129.6, 129.3, 128.7, 128.5, 128.4, 125.5, 125.3, 122.5, 120.8, 120.7, 119.5(t, J =248.6 Hz), 116.8, 59.0, 49.3, 45.8, 43.1, 34.1, 29.3, 17.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -97.1 (d, J = 290.0 Hz), -104.2 (d, J = 289.9 Hz). HRMS (ESI) calcd for $C_{29}H_{26}F_2N_4O$ $[M+H]^+$485.2147, found 485.2146.

2,2-difluoro-2-(2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-1-(4-(pyrimidin-2-yl)piperazin-1-yl)ethan-1-one (3w)



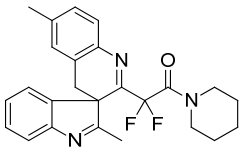
Yellow oil, 52% yield; R_f = 0.30 (petroleum ether/EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 4.7 Hz, 2H), 7.57 (dd, J = 33.9, 7.7 Hz, 2H), 7.42 – 7.19 (m, 3H), 7.19 – 7.00 (m, 2H), 6.90 (d, J = 7.5 Hz, 1H), 6.54 (t, J = 4.7 Hz, 1H), 4.07 – 3.43 (m, 7H), 3.38 – 2.83 (m, 4H), 2.38 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 180.2, 161.3, 157.8, 154.9, 141.1, 138.6, 130.1, 129.6, 128.7, 128.5, 128.4, 125.6, 125.4, 122.4, 120.8, 114.8(t, J =250.4 Hz), 110.6, 59.0, 43.3, 43.2, 43.1, 34.0, 18.0, 17.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -97.1 (d, J = 290.4 Hz), -104.3 (d, J = 290.4 Hz). HRMS (ESI) calcd for $C_{27}H_{24}F_2N_6O$ $[M+H]^+$487.2052, found 487.2055.

1-(3,4-dihydroisoquinolin-2(1H)-yl)-2,2-difluoro-2-(2-methyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)ethan-1-one (3x)



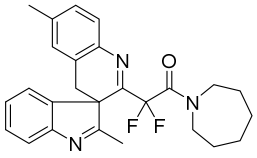
Colorless oil (rotamer, ratio 1:1), 69% yield; R_f = 0.20 (petroleum ether/EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.58 (m, 1H), 7.55 – 7.45 (m, 1H), 7.42 – 7.28 m, 3H), 7.23 – 6.90 (m, 6H), 6.81 – 6.69 (dd, J = 13.6, 7.4 Hz, 1H), 4.85 – 4.57 (m, 1H), 4.29 (s, 1H), 3.44 – 3.21 (m, 2H), 3.08 – 2.50 (m, 4H), 2.41 and 2.35 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 180.5, 161.5, 154.8, 141.2, 138.7, 134.6, 132.3, 130.0, 129.5, 128.9, 128.5, 128.4, 128.2, 126.9, 126.6, 126.3, 125.6, 125.4, 122.7, 120.8, 114.8 (t, J =238.8 Hz), 59.0, 47.7, 45.6, 34.2, 30.9, 29.0, 18.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -91.9 (d, J = 288.0 Hz), -98.6 (d, J = 288.0 Hz). HRMS (ESI) calcd for $C_{28}H_{23}F_2N_3O$ $[M+H]^+$456.1882, found 456.1878.

2-(2,6'-dimethyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-2,2-difluoro-1-(piperidin-1-yl)ethan-1-one (3y)



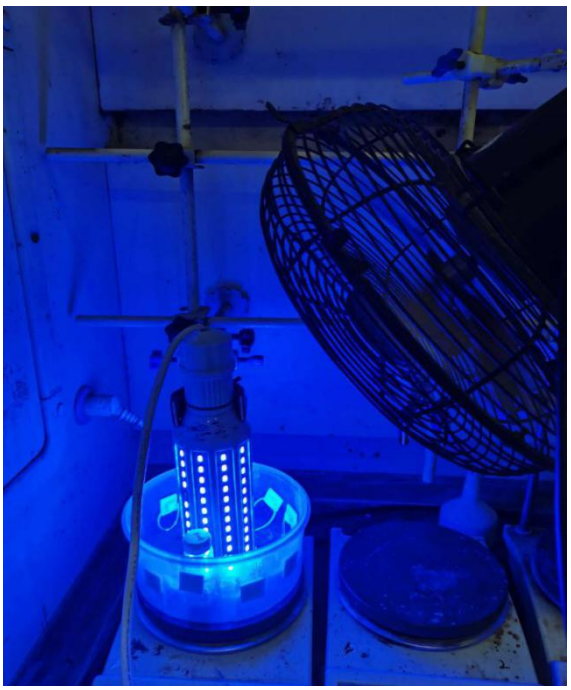
Colorless oil, 77% yield; R_f = 0.30 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.6 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.96 – 6.87 (m, 2H), 3.79 – 3.65 (m, 1H), 3.41 – 3.31 (m, 1H), 3.25 (d, J = 16.0 Hz, 1H), 3.10 – 2.94 (m, 2H), 2.84 (d, J = 16.0 Hz, 1H), 2.36 (d, J = 6.0 Hz, 6H), 2.17 (s, 2H), 1.69 – 1.47 (m, 4H), 1.36 – 1.28 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.6, 160.1, 157.2, 154.8, 140.2, 139.2, 139.0, 129.2, 129.1, 129.0, 128.3, 125.4, 125.2, 122.7, 120.6, 115.0(t, J =249.6 Hz), 59.0, 46.8, 44.3, 34.3, 30.9, 25.8, 25.3, 24.3, 21.4, 17.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -96.7 (d, J = 288.9 Hz), -104.4 (d, J = 288.8 Hz). HRMS (ESI) calcd for $C_{25}H_{25}F_2N_3O$ $[M+H]^+$422.2038, found 422.2044.

2-(2,6'-dimethyl-4'H-spiro[indole-3,3'-quinolin]-2'-yl)-2,2-difluoro-1-(piperidin-1-yl)ethan-1-one (3z)

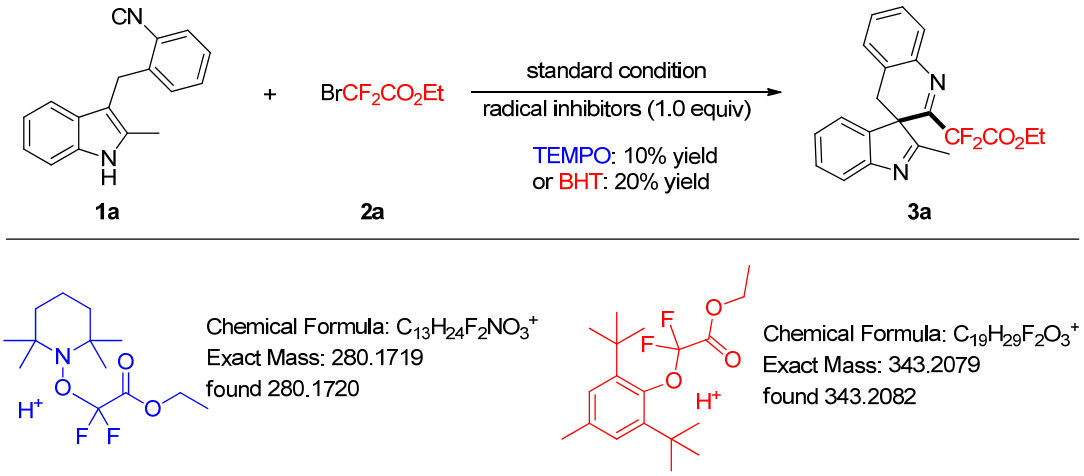


Colorless oil, 72% yield; R_f = 0.40 (petroleum ether/EtOAc, 3:1);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.6 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.19 (d, J = 7.6 Hz, 1H), 7.04 (t, J = 7.2 Hz, 1H), 7.00 – 6.88 (m, 2H), 3.62 – 3.51 (m, 1H), 3.46 – 3.32 (m, 1H), 3.11 (dt, J = 18.8, 15.6 Hz, 3H), 2.92 (d, J = 16.4 Hz, 1H), 2.37 (s, 3H), 2.32 (s, 3H), 1.74 (d, J = 4.4 Hz, 2H), 1.62 – 1.36 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.7, 161.8, 157.5, 154.9, 140.1, 139.2, 139.1, 129.1, 128.9, 128.3, 125.4, 125.2, 123.0, 120.5, 114.9(t, J =255.2 Hz), 59.1, 47.3, 34.4, 28.8, 27.9, 26.7, 25.8, 21.4, 18.0, 17.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -95.8 (d, J = 287.1 Hz), -103.8 (d, J = 287.0 Hz). HRMS (ESI) calcd for $C_{26}H_{27}F_2N_3O$ $[M+H]^+$436.2195, found 436.2195.

5. Reaction set-up for irradiation of mixture with blue LEDs



6. Free Radical Capture Experiments



Scheme 2S. Free radical capture experiments

Based on the general procedure, TEMPO or BHT (0.20 mmol, 1.0 equiv) were added before the inert gas protecting step. When one equivalent free radical inhibitor BHT (2,6-di-*tert*-butyl-4-methylphenol) was added to the reaction system, the yield of product **3a** was decreased dramatically to 20%. When TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) was added to the reaction system, the yield of product **3a** was reduced to 10%. Furthermore, BHT and TEMPO adducts of ethyl 2-fluoroacetate radical (generated in situ) were detected by LC−MS.

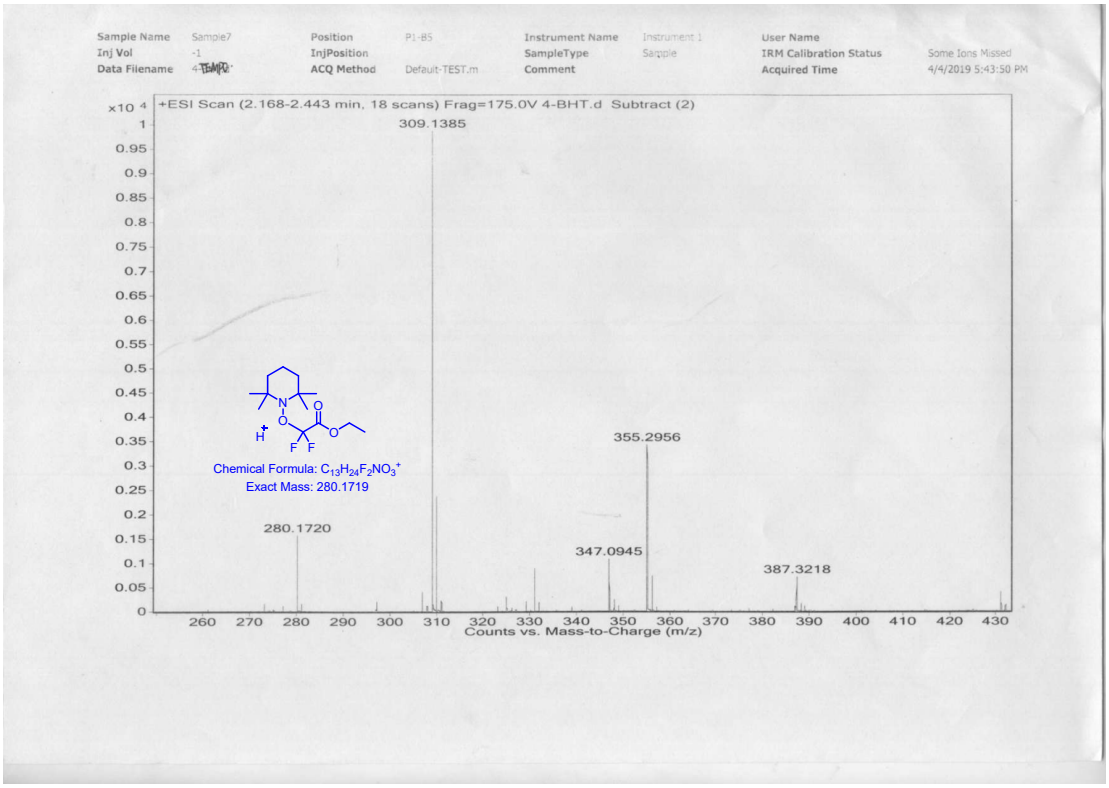


Figure 1S. LC-MS spectrum of adduct of TEMPO and CF_2CO_2Et

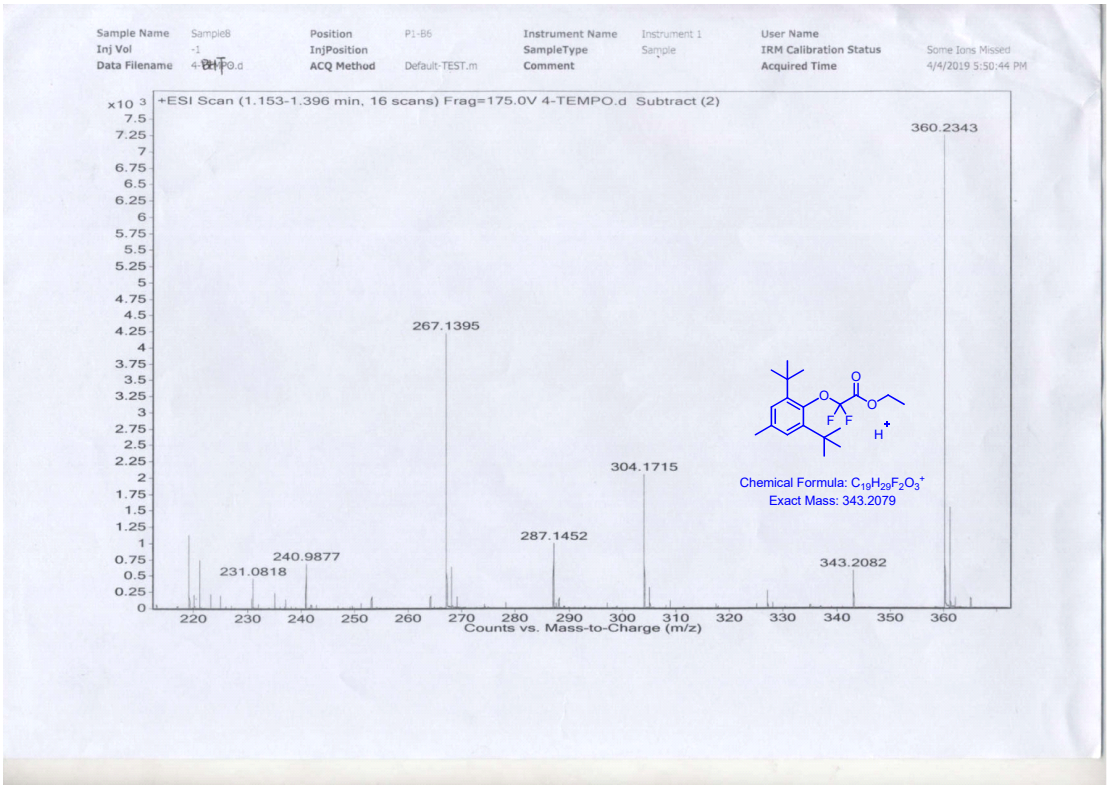
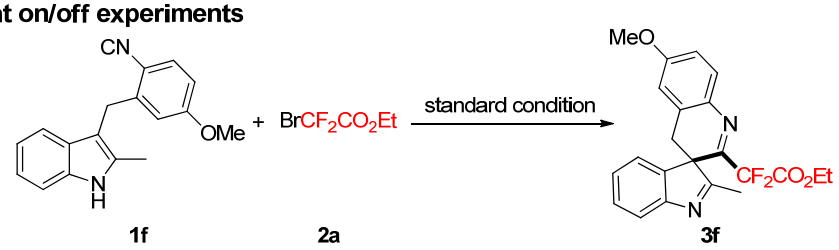


Figure 2S. LC-MS spectrum of adduct of BHT and CF_2CO_2Et

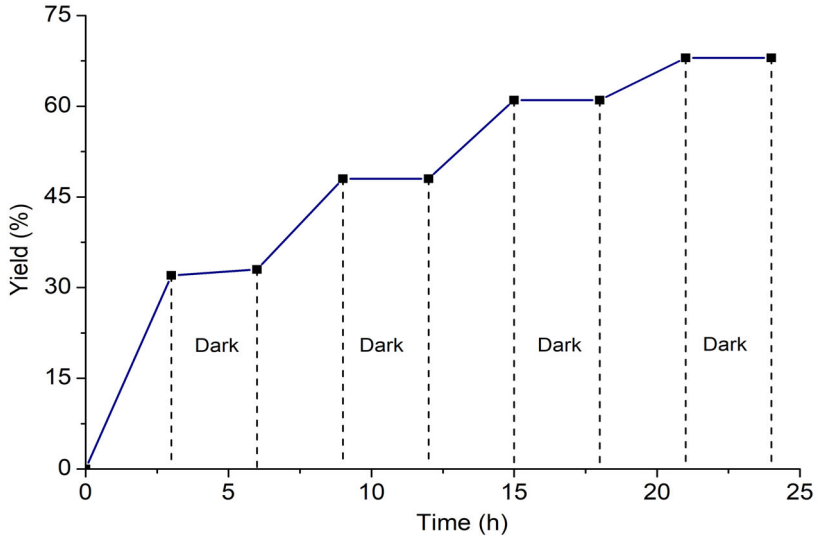
7. Light on/off experiments

Eight standard reaction mixtures in 10 mL Shrek tube were equipped with a magnetic stir bar, added **1f** (0.2 mmol, 1.0 equiv), ethyl bromodifluoroacetate (0.3 mmol, 1.5 equiv) and *fac*-Ir(ppy)$_3$ (0.002 mmol) in DMSO (2.0 mL). Then the mixture was stirred and irradiated by 3W blue LEDs at room temperature. After 3 h, the blue LEDs were turned off, and one Shrek tube was removed from the irradiation setup for analysis. The remaining seven Shrek tubes were stirred in the absence of light for an additional 3 h. Then, one Shrek tube was removed for analysis, and the blue LEDs were turned back on to irradiate the remaining six reaction mixtures. After an additional 3 h of irradiation, the blue LEDs were turned off, and one Shrek tube was removed for analysis. The remaining five Shrek tubes were stirred in the absence of light for an additional 3 h. Then, Shrek tube was removed for analysis, and the blue LED s were turned back on to irradiate the remaining four reaction mixtures. After 3 h, the blue LEDs were turned off, and one Shrek tube was removed for analysis. The remaining three Shrek tubes were stirred in the absence of light for an additional 3 h, then, a Shrek tube was removed for analysis and the green LEDs were turned back on to 8 irradiate the remaining two reaction mixtures. After 3 h, the blue LEDs were turned off, and one Shrek tube was removed for analysis. The last Shrek tube was stirred in the absence of light for an additional 3 h, and then it was analyzed. The yield was determined by ^{1}H NMR spectroscopy.

light on/off experiments



1f **2a** **3f**

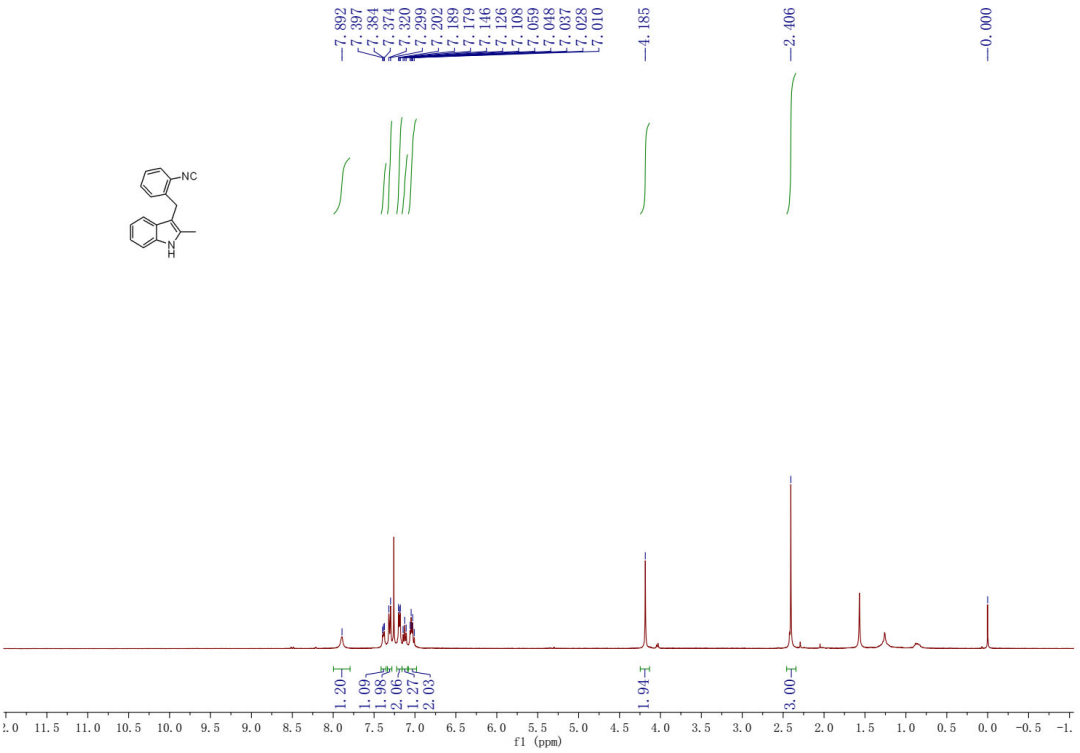


Entry	Time(h)								Yield(%)[a]
	3	6	9	12	15	18	21	24	
1	On	—	—	—	—	—	—	—	32
2	On	Off	—	—	—	—	—	—	33
3	On	Off	On	—	—	—	—	—	48
4	On	Off	On	Off	—	—	—	—	48
5	On	Off	On	Off	On	—	—	—	62
6	On	Off	On	Off	On	Off	—	—	62
7	On	Off	On	Off	On	Off	On	—	68
8	On	Off	On	Off	On	Off	On	Off	68

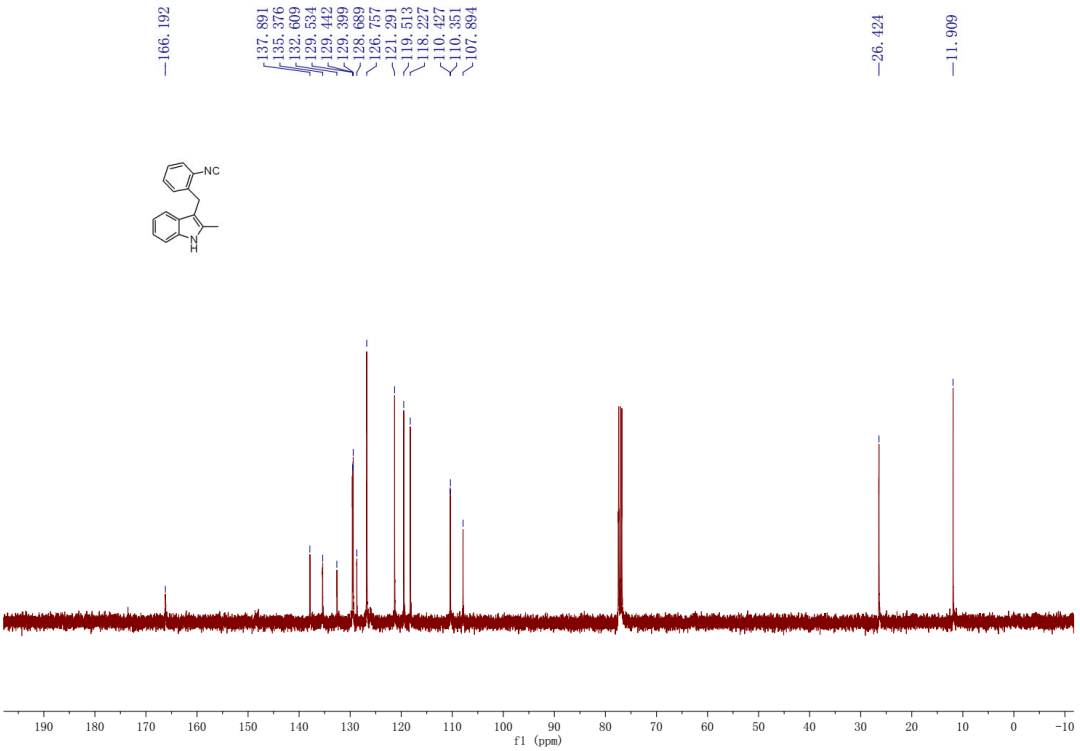
Determined by ^{1}H NMR analysis.

8. NMR spectra of 1, 2, and 3

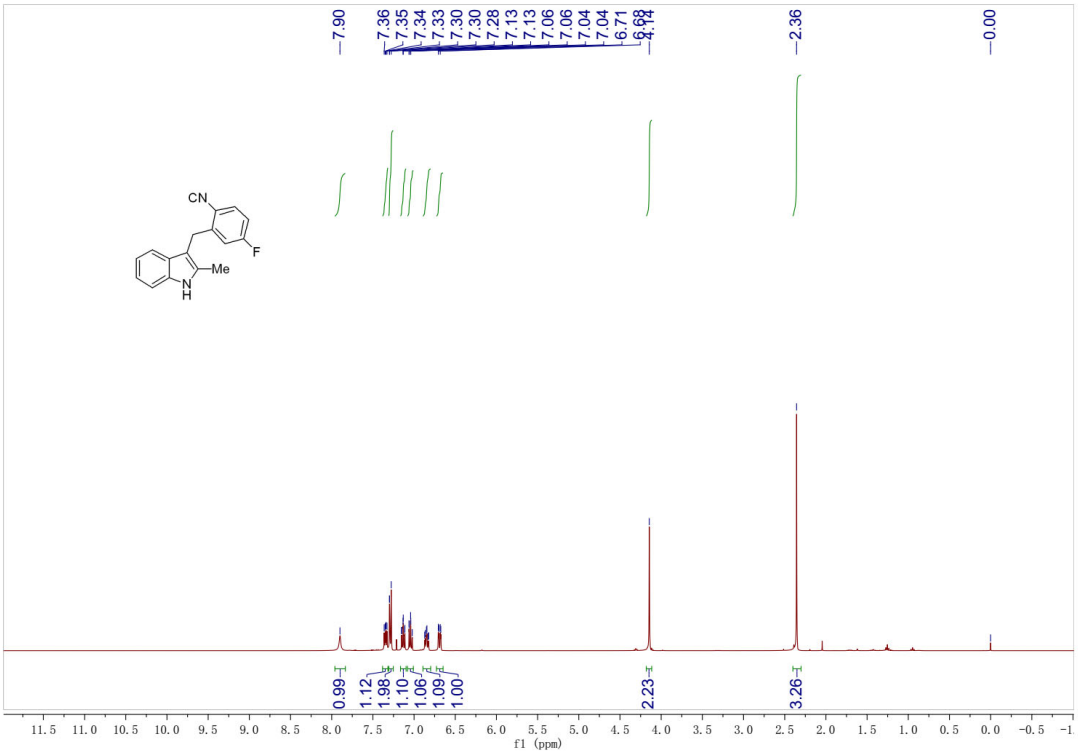
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1a



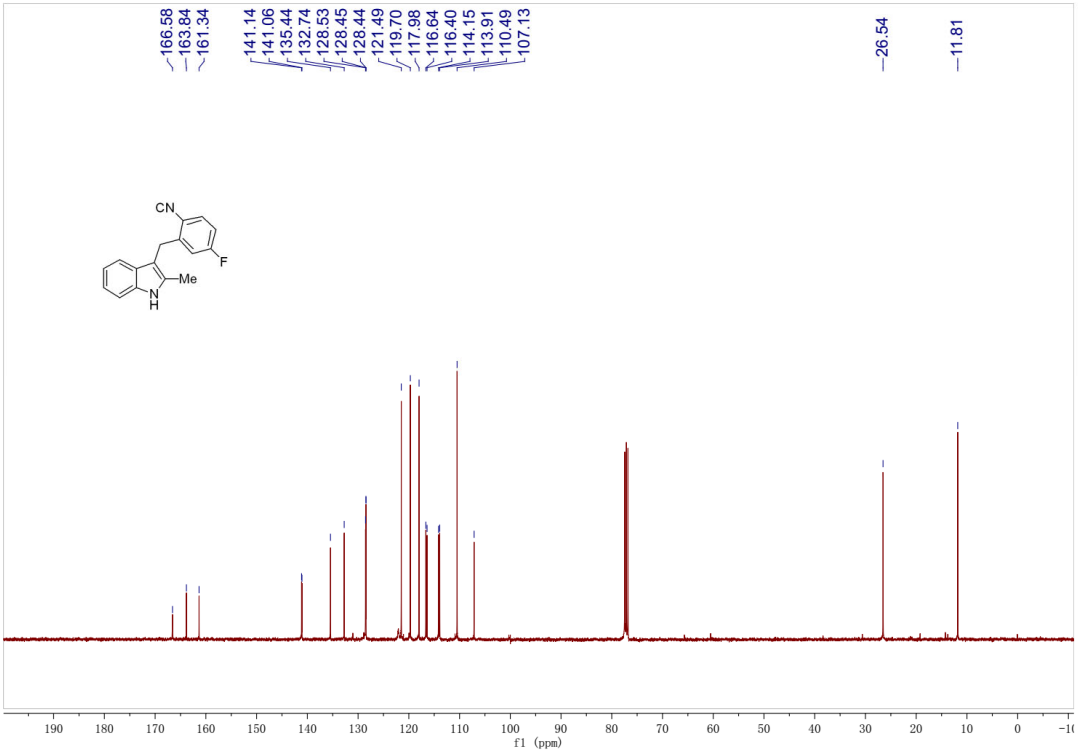
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1a



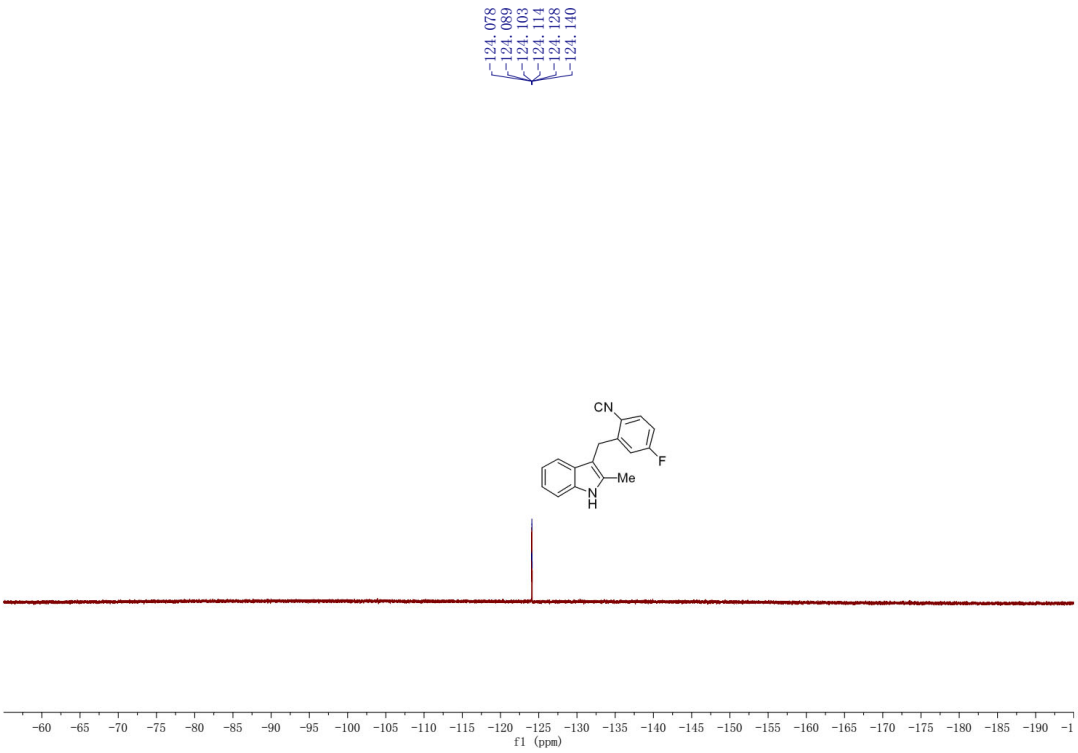
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1b



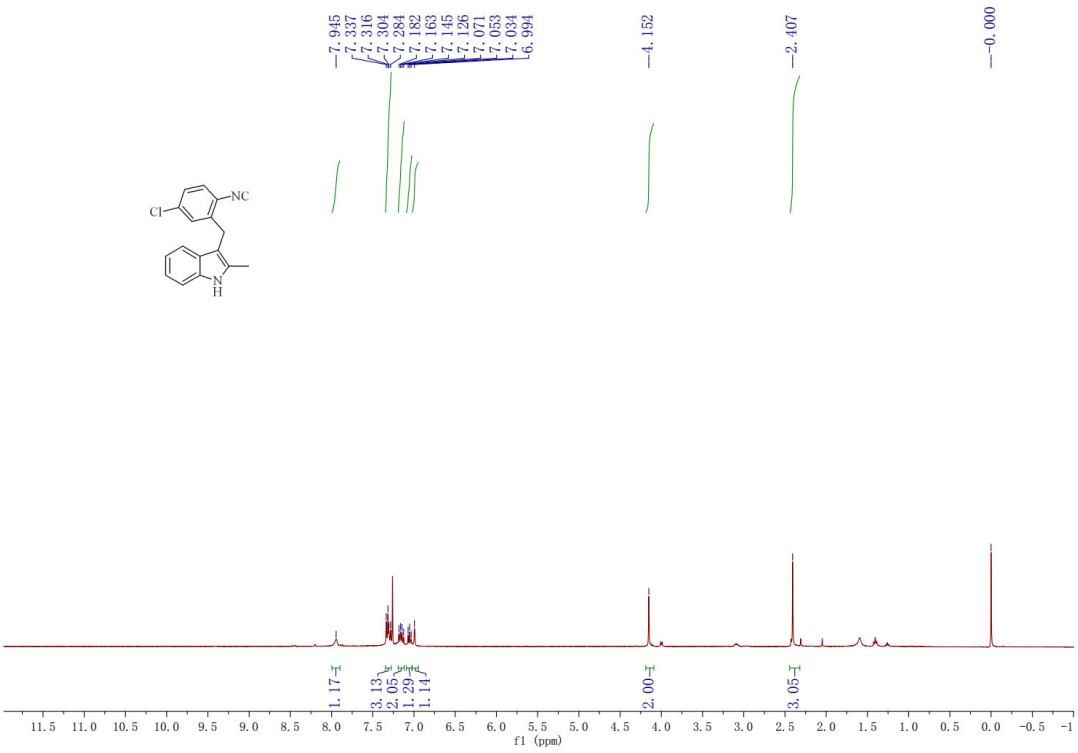
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1b



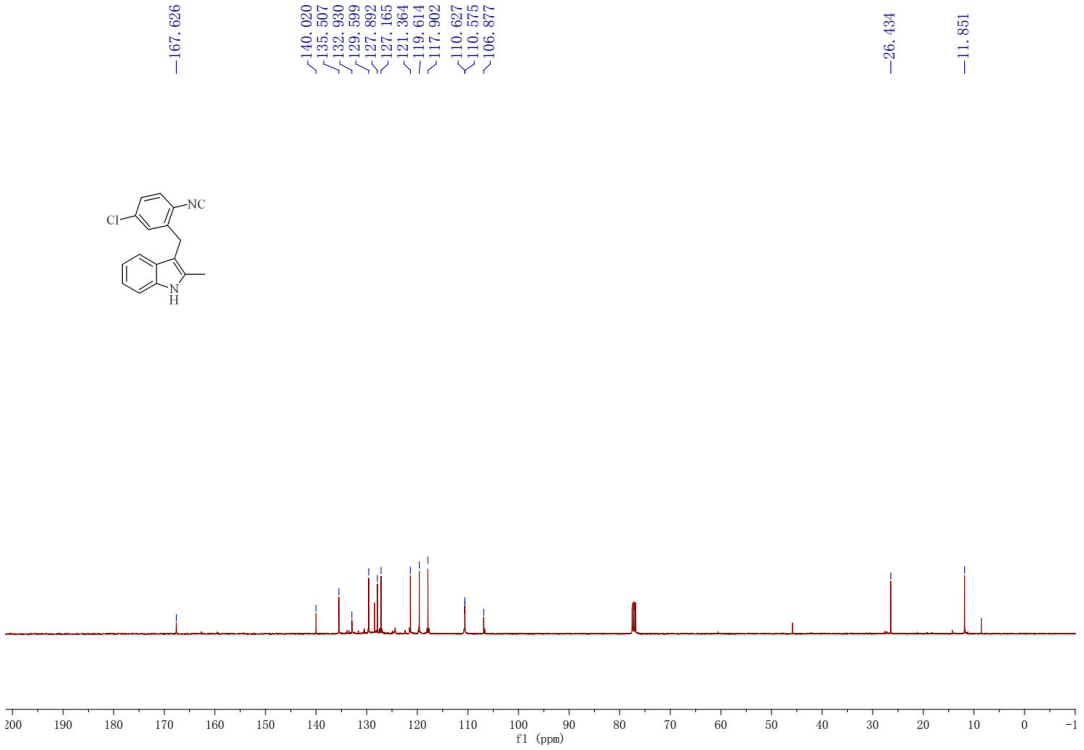
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 1b



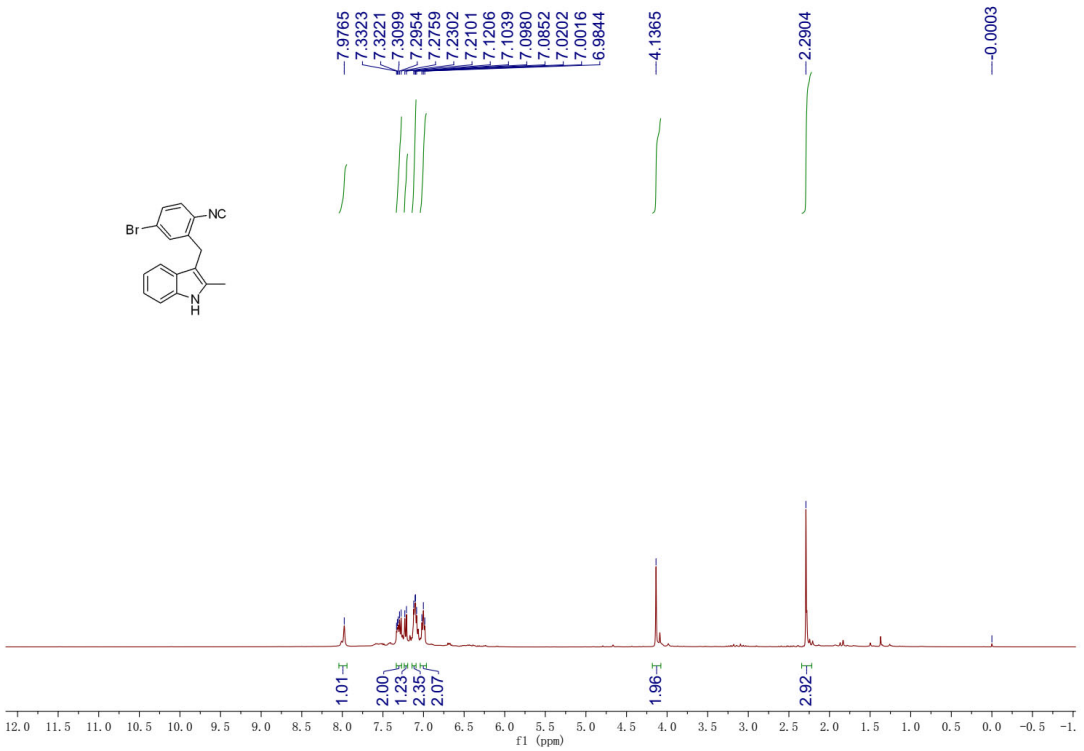
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1c



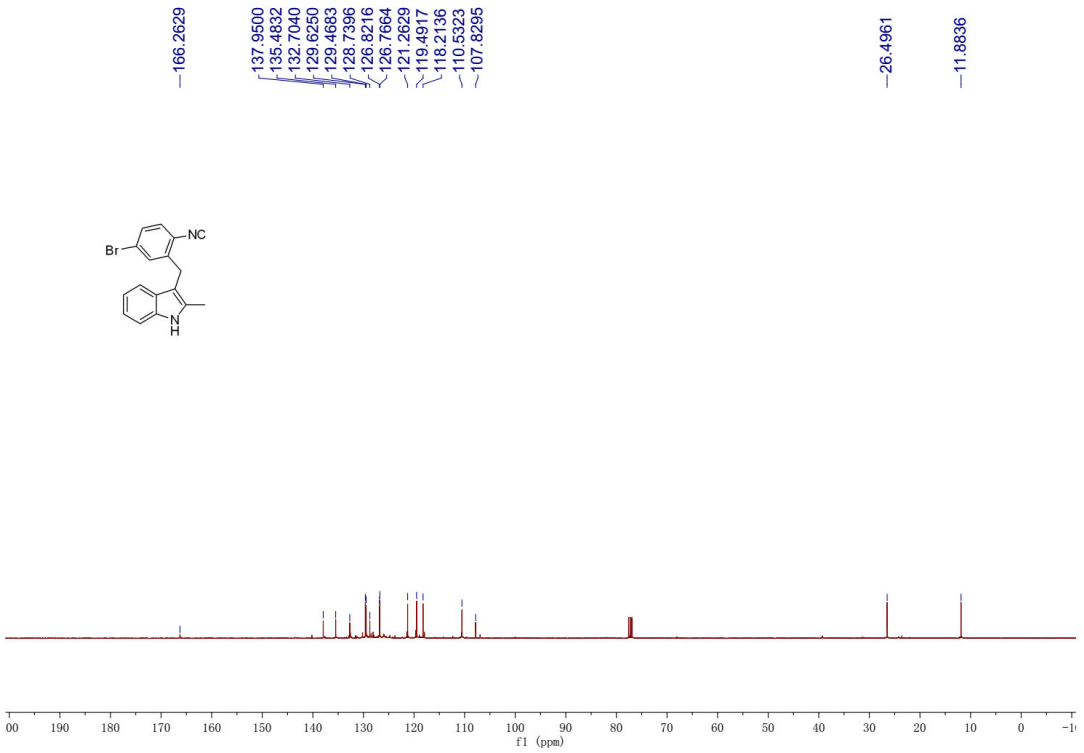
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1c



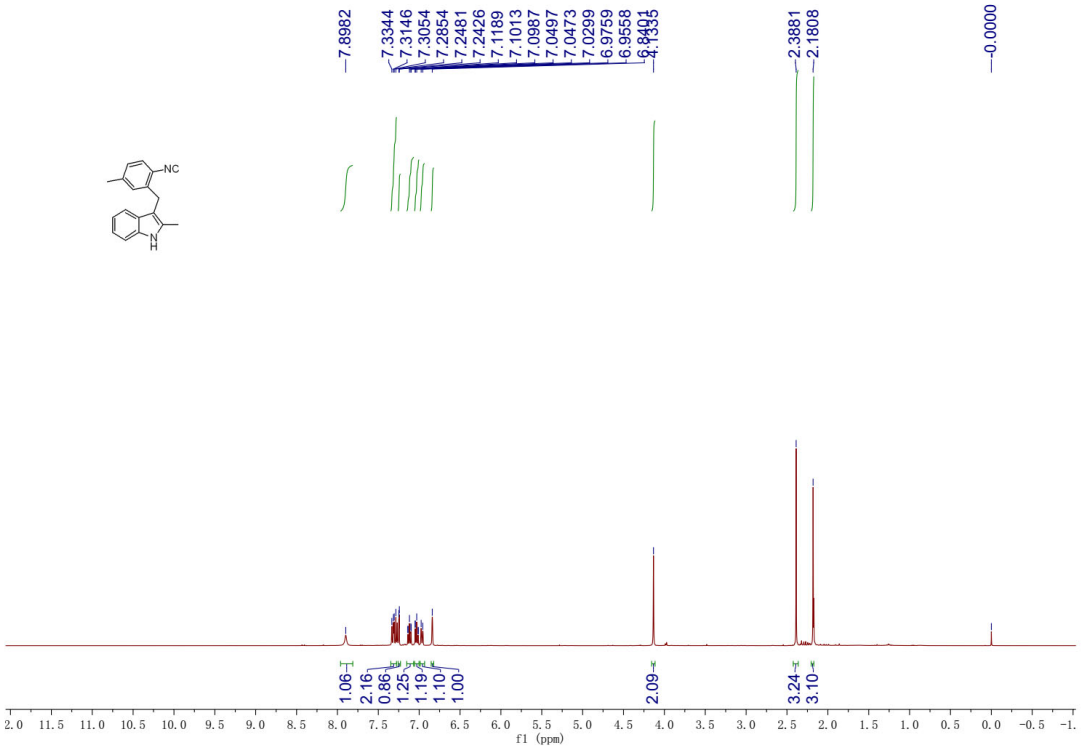
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1d



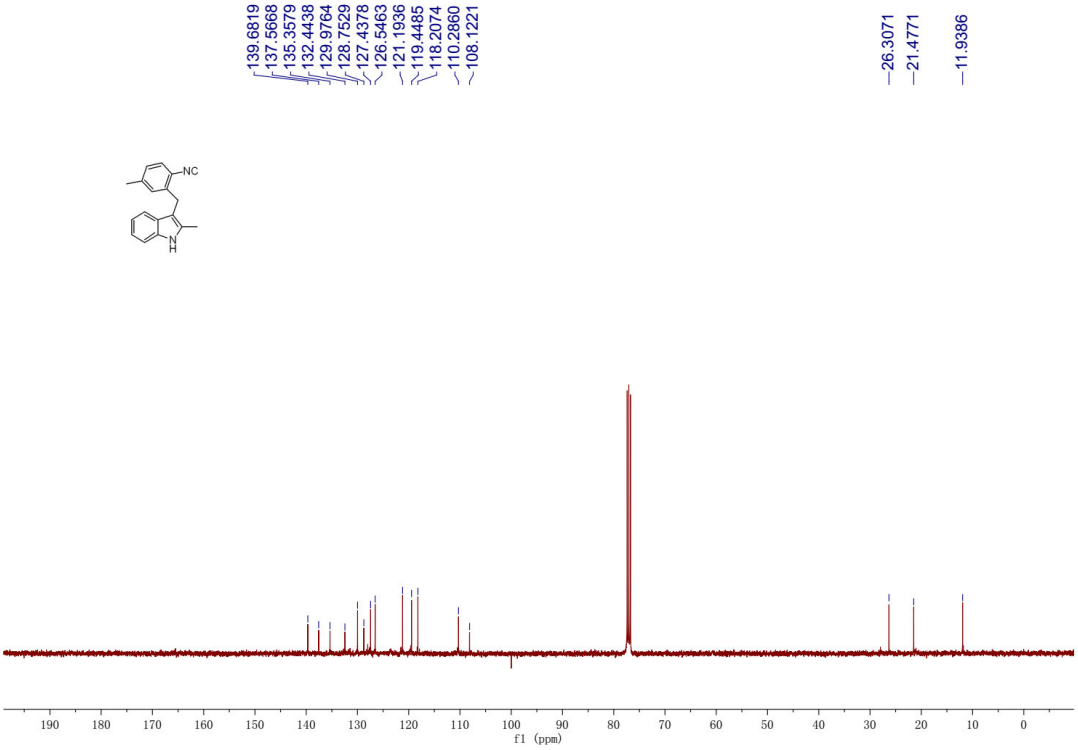
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1d



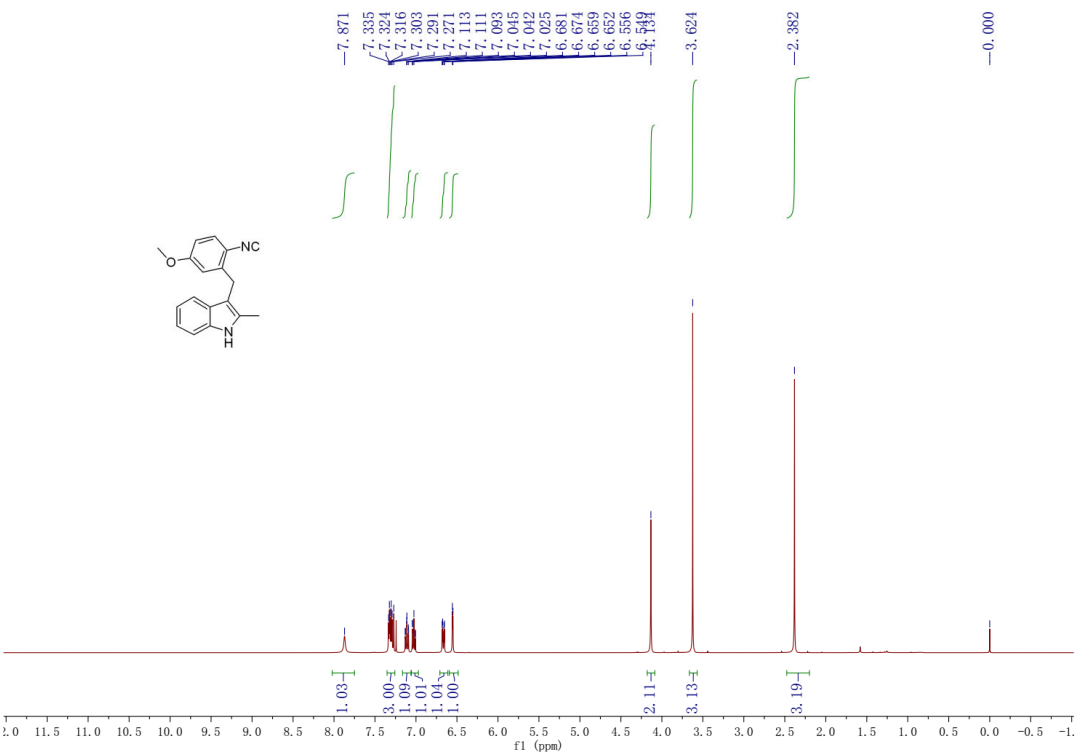
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1e



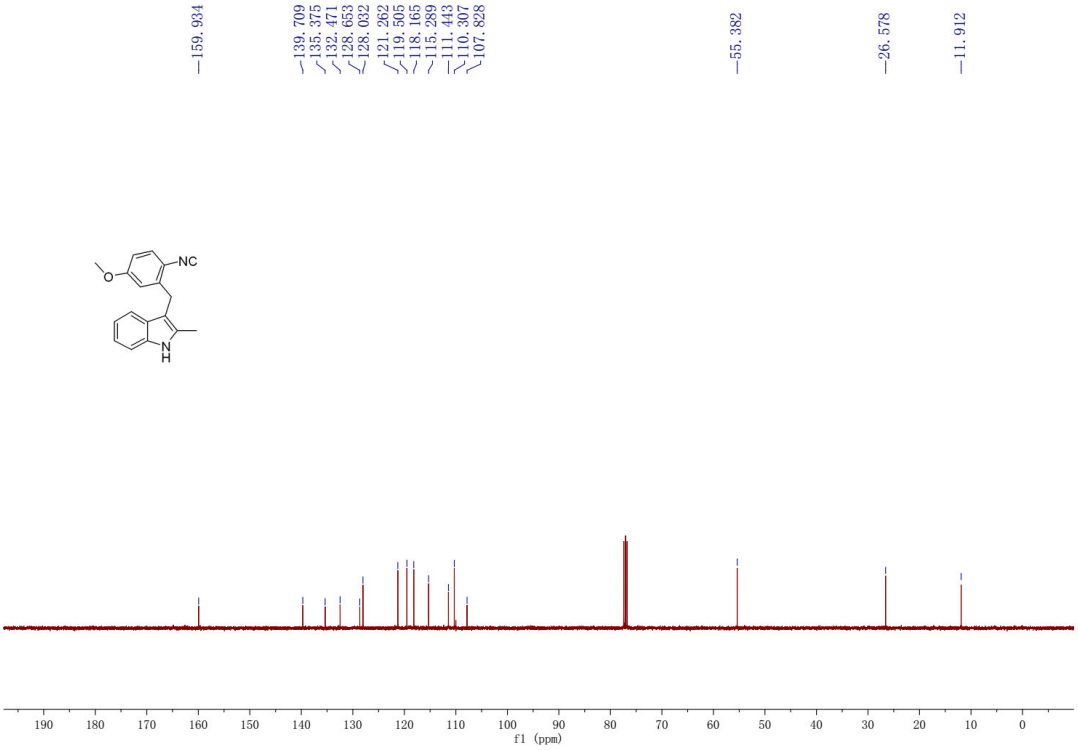
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1e



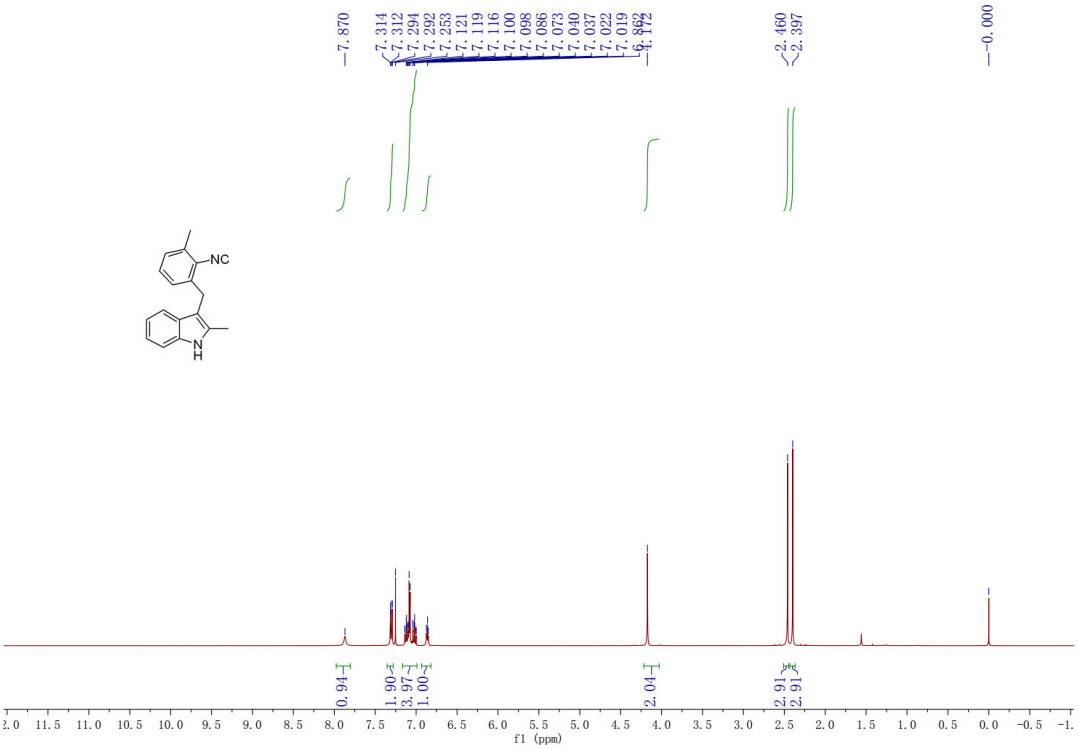
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1f



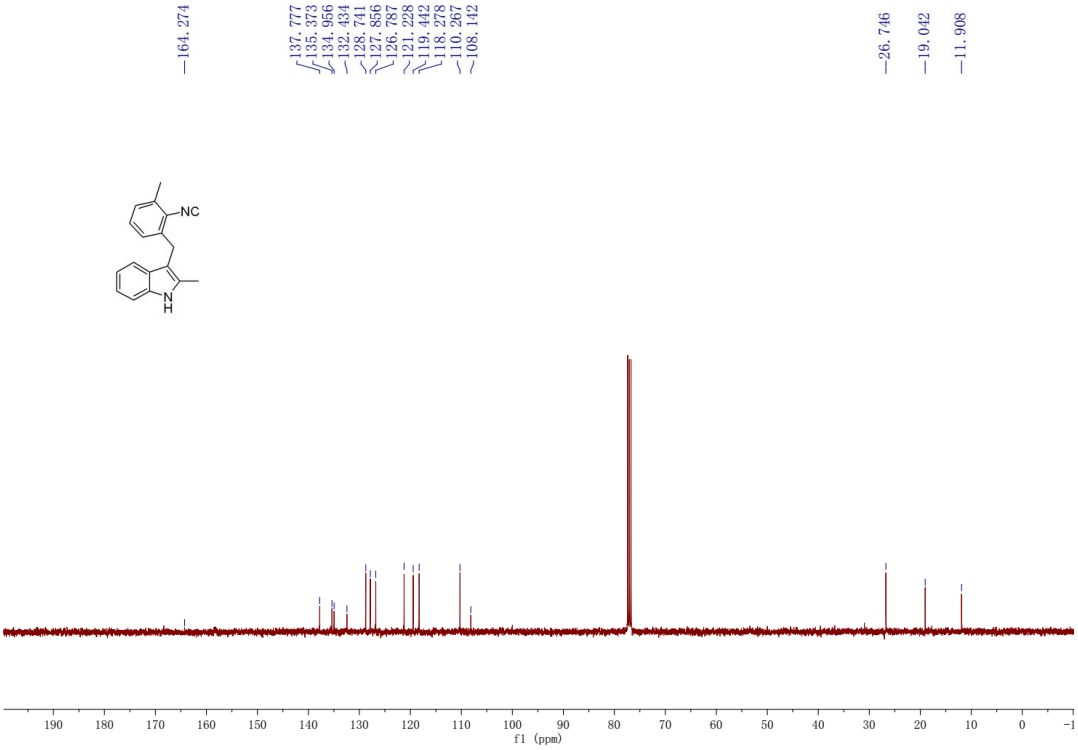
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1f



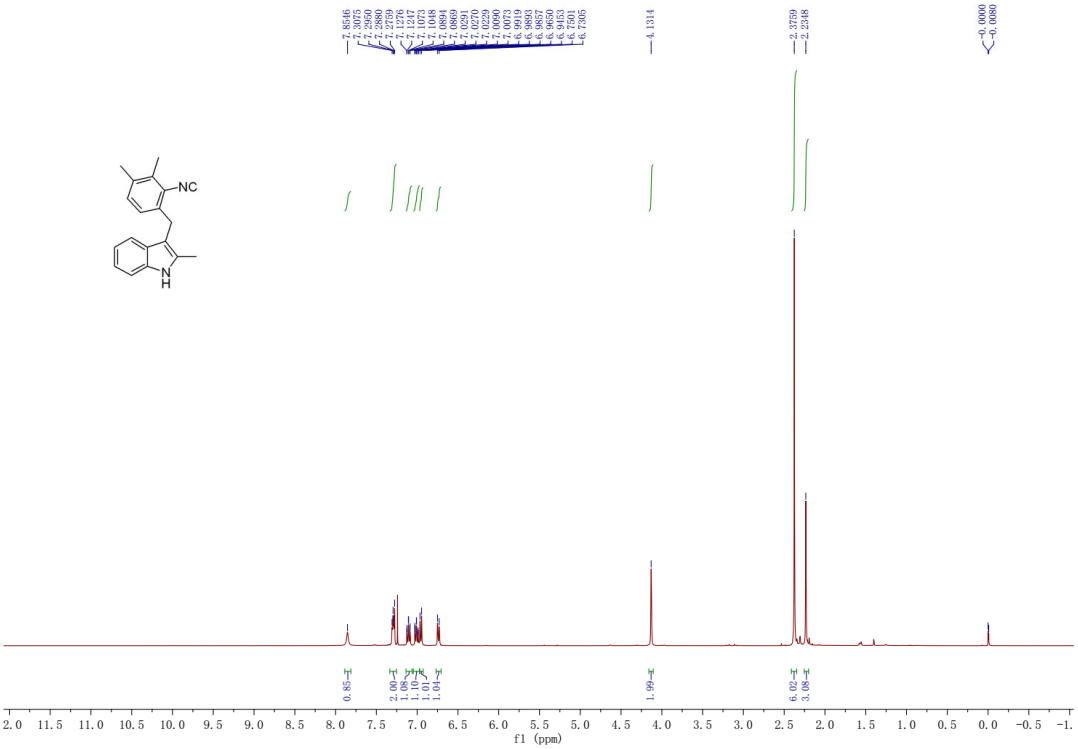
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1g



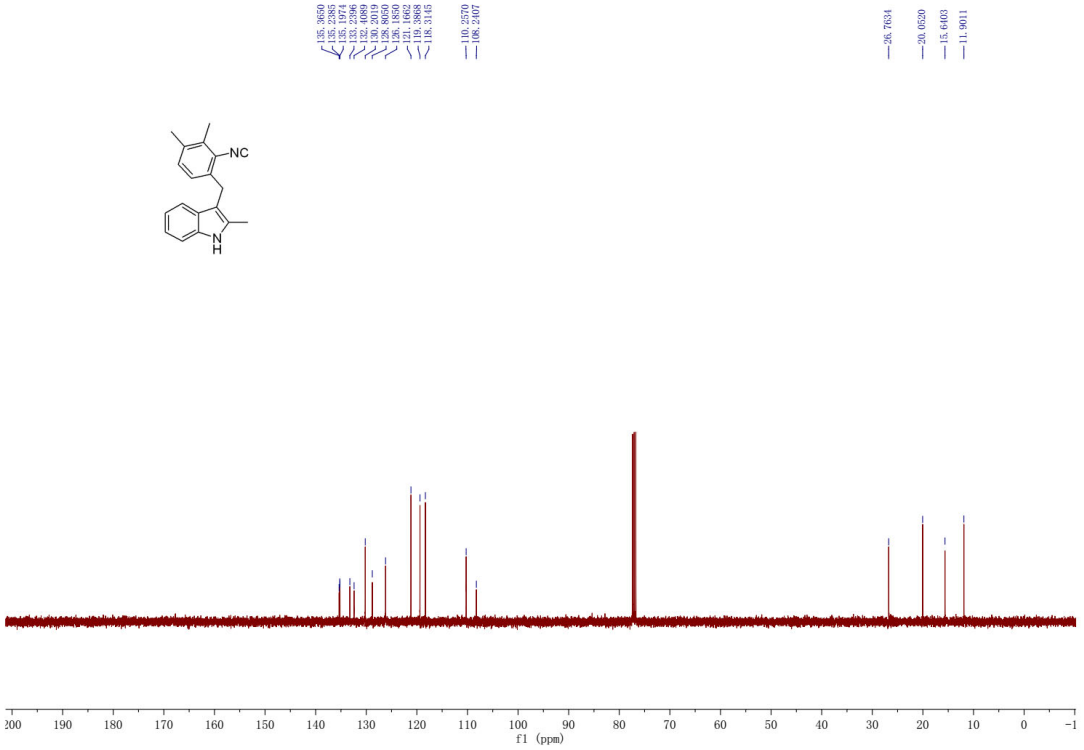
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1g



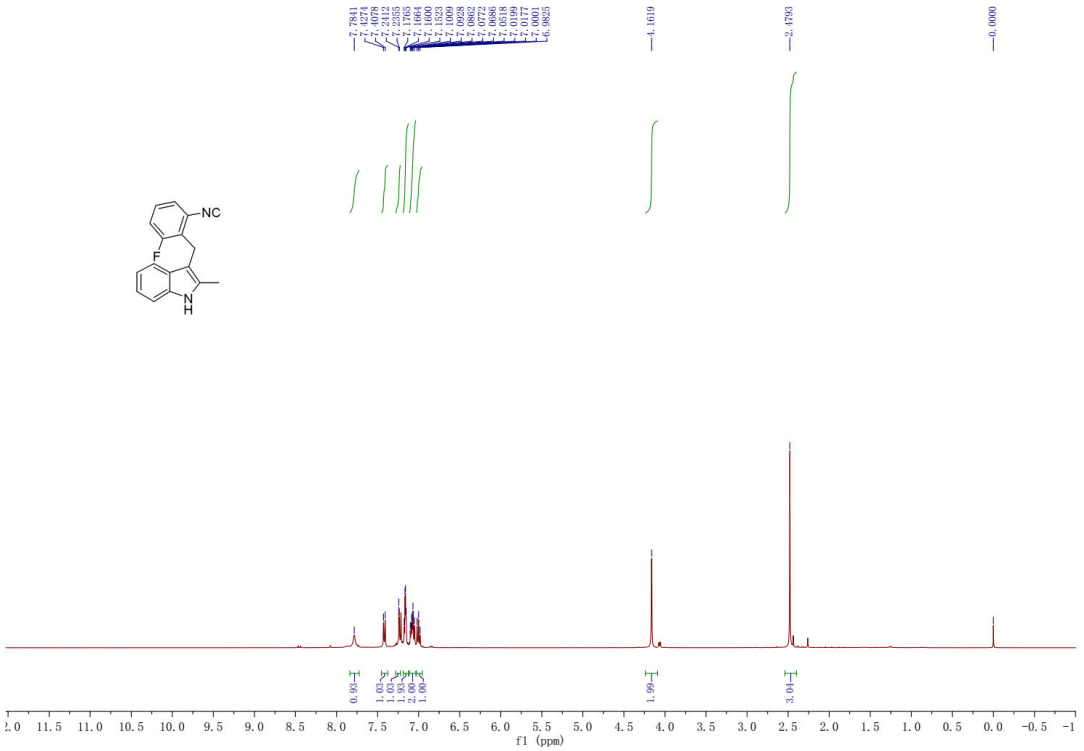
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1h



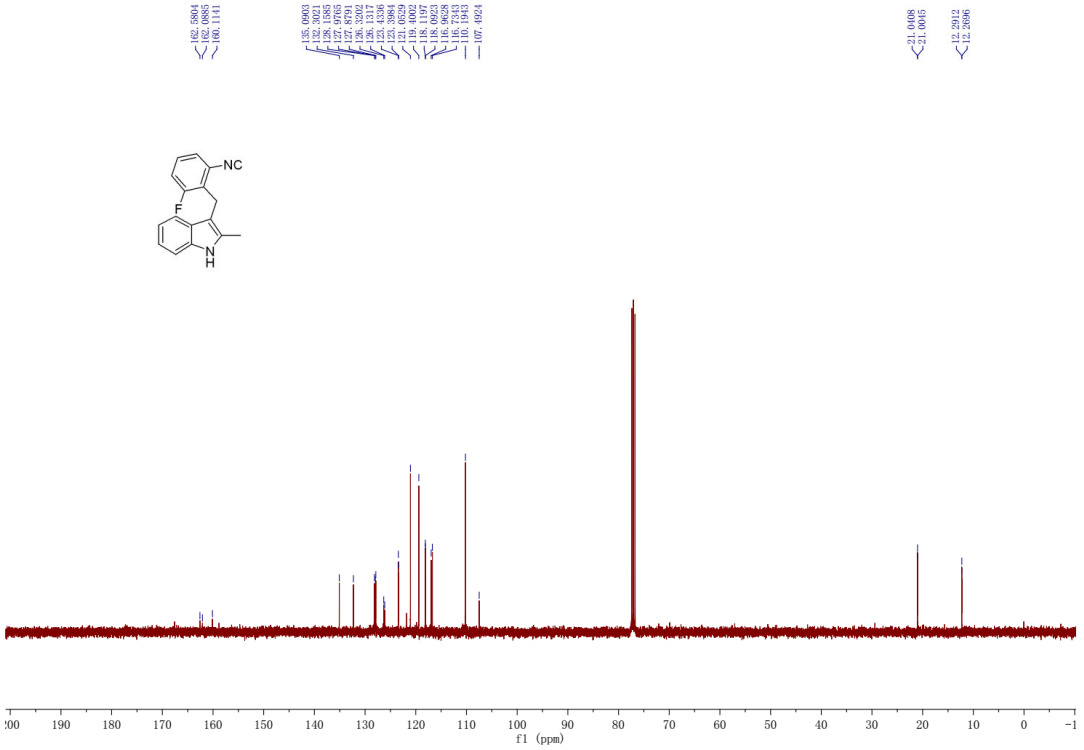
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1h



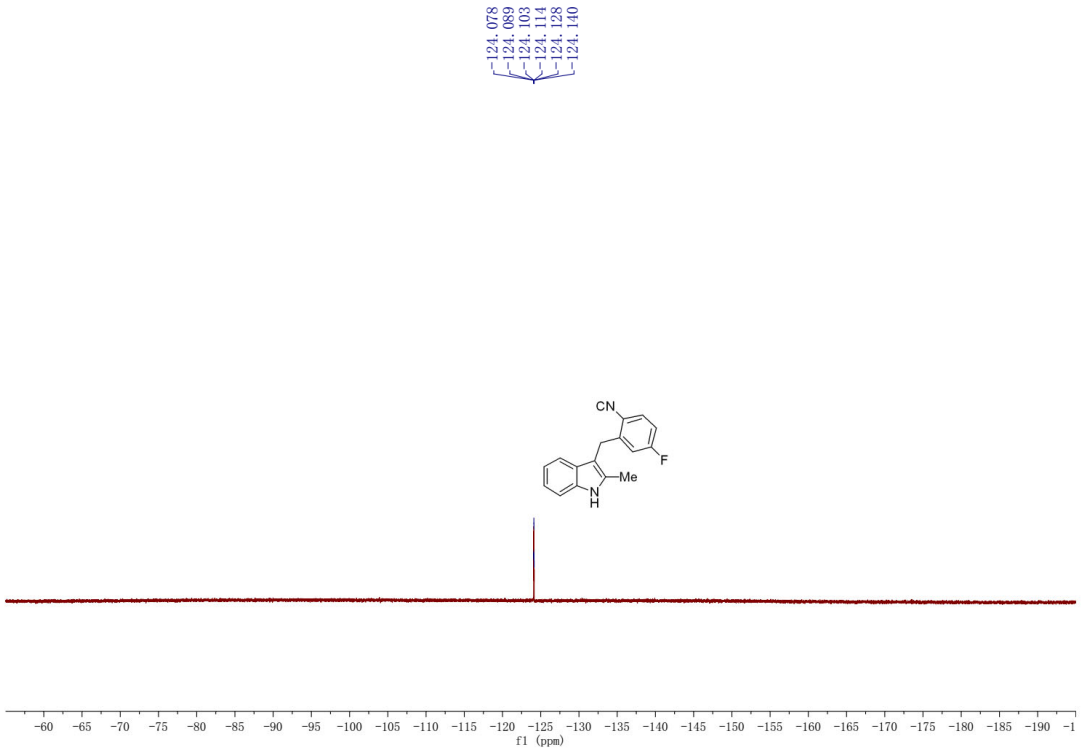
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1i



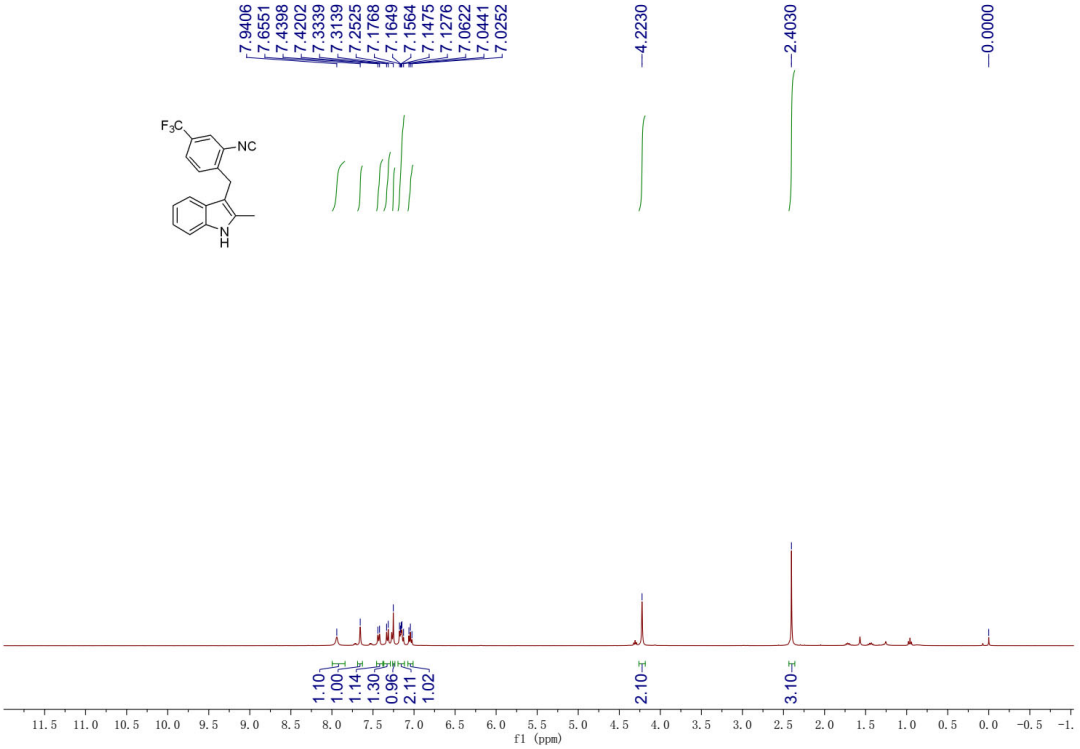
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1i



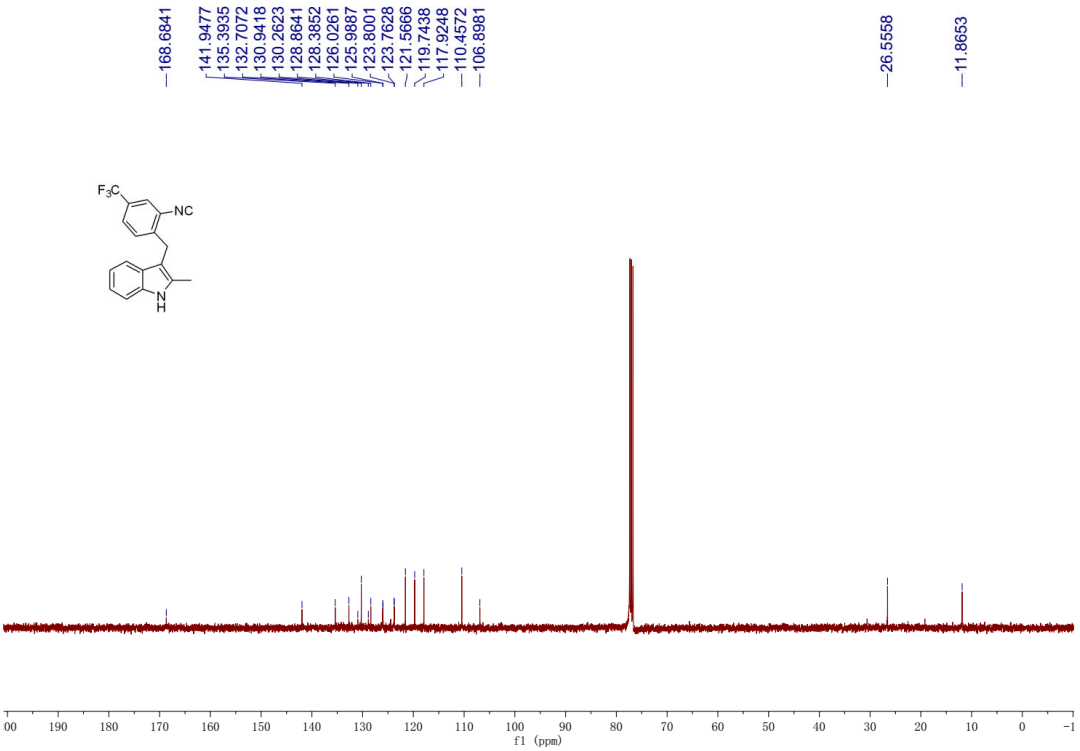
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 1i



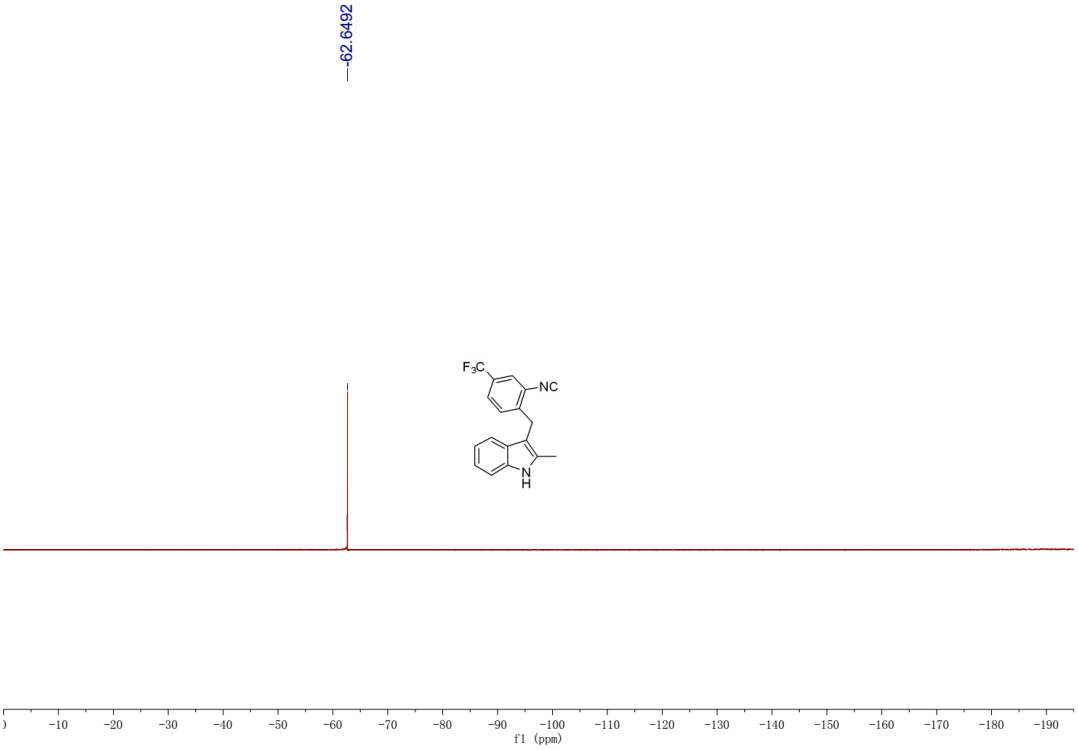
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1j



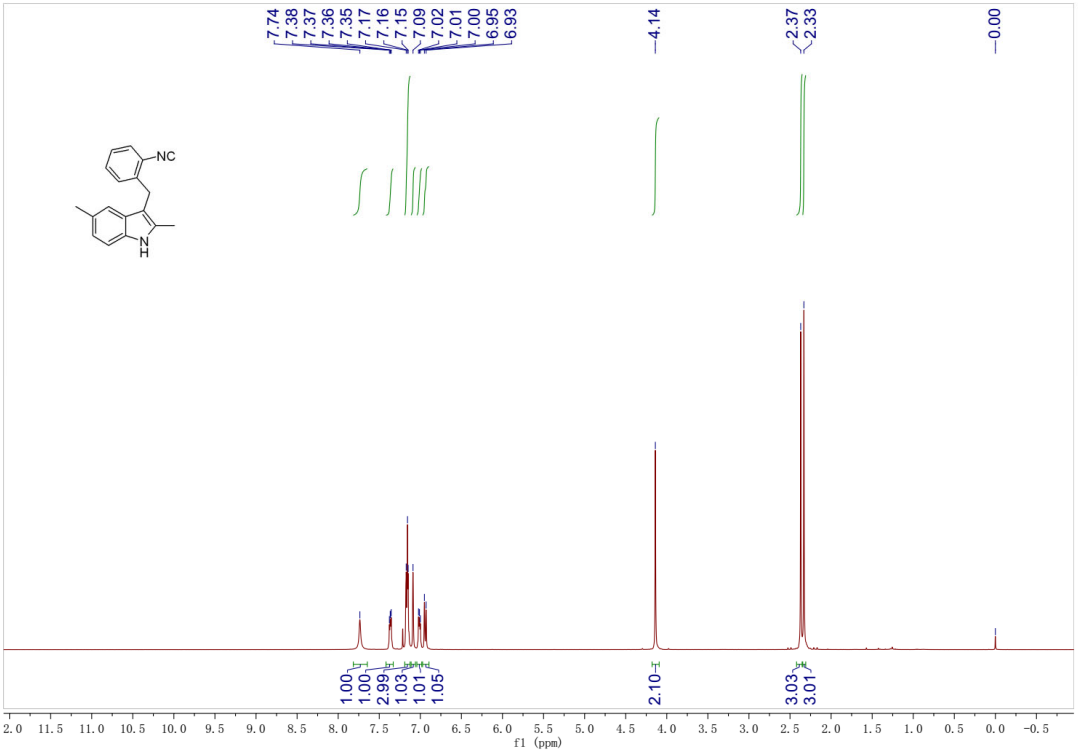
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1j



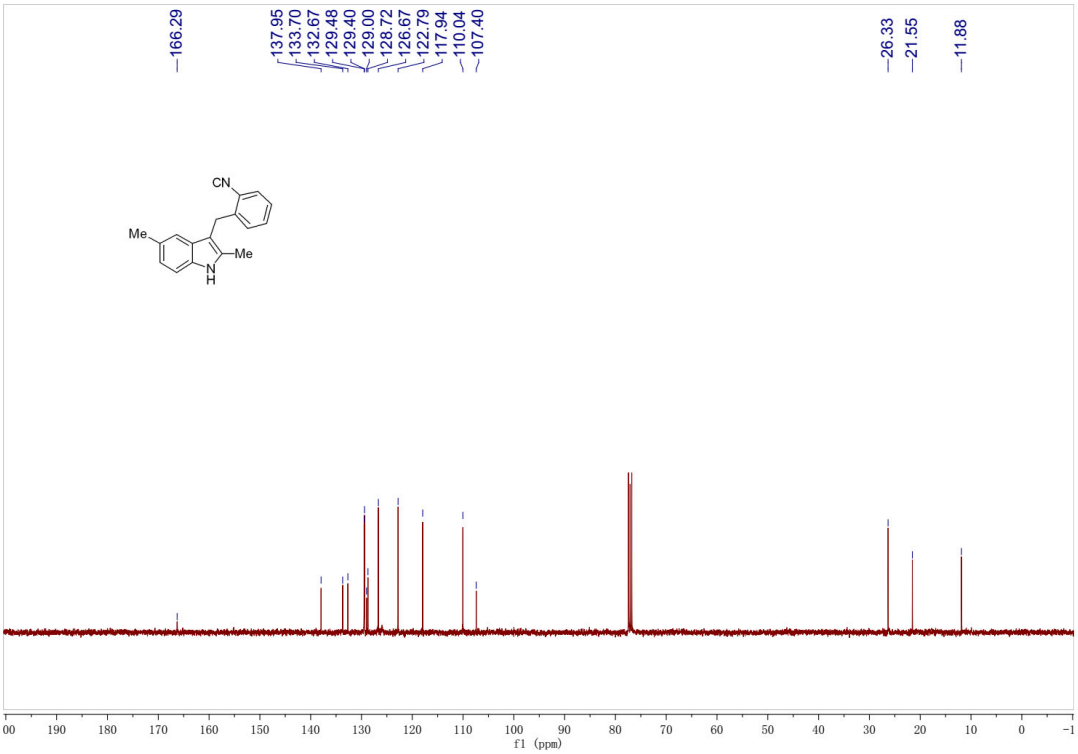
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 1j



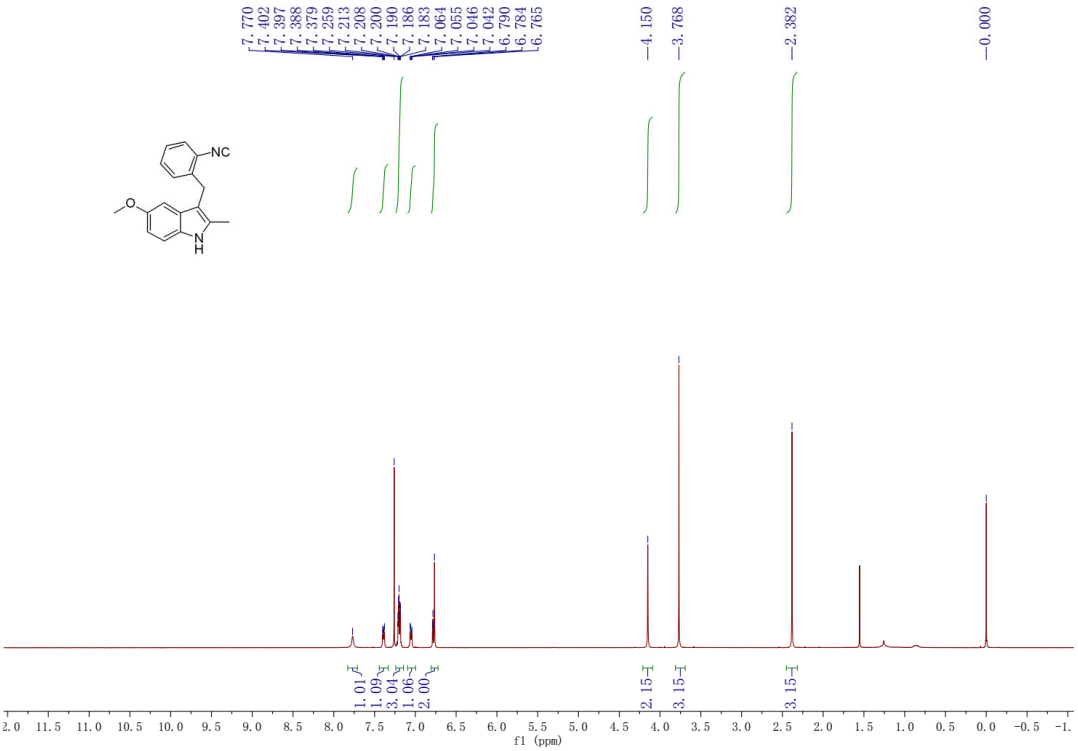
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1k



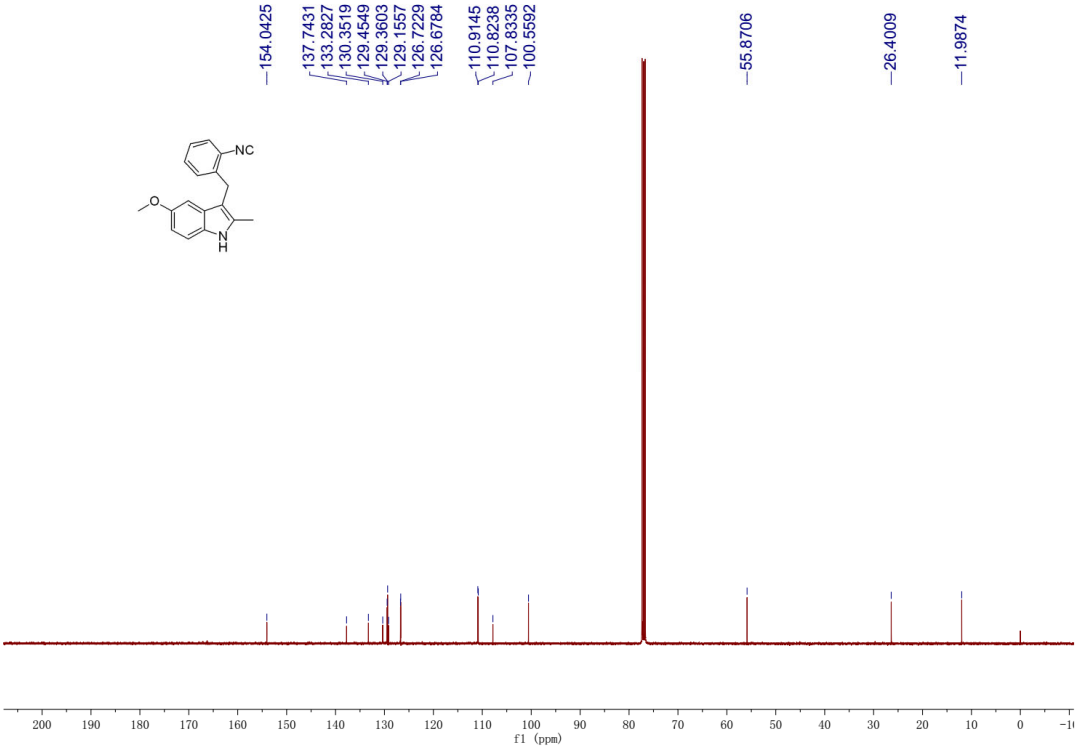
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1k



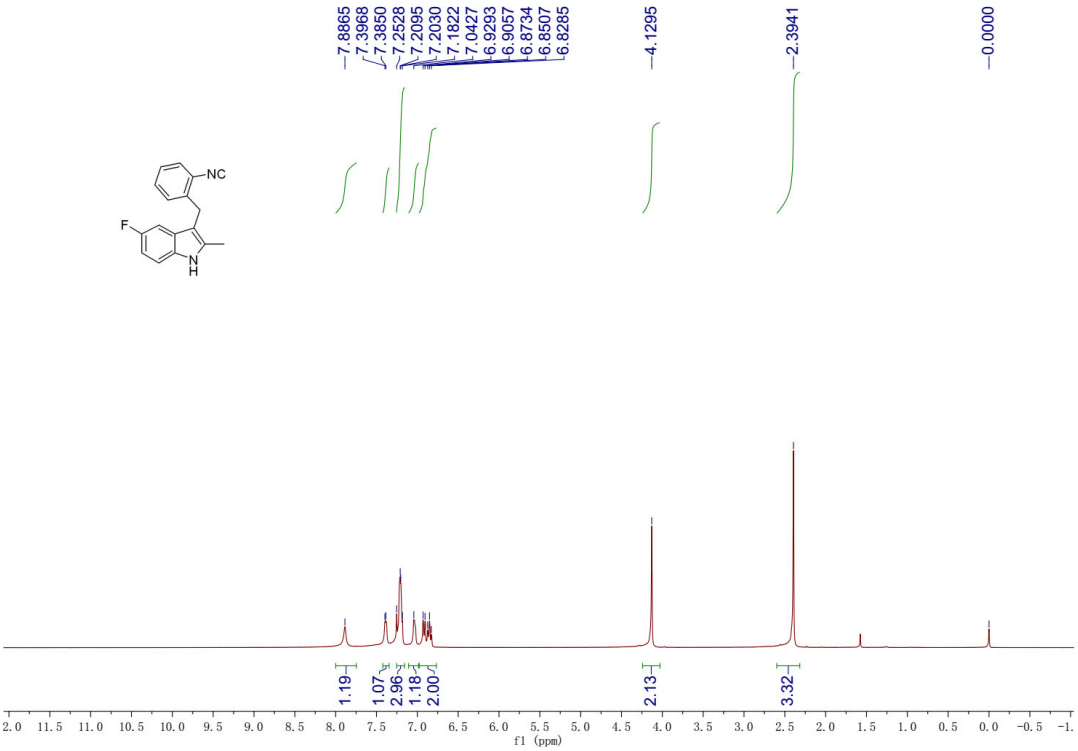
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1l



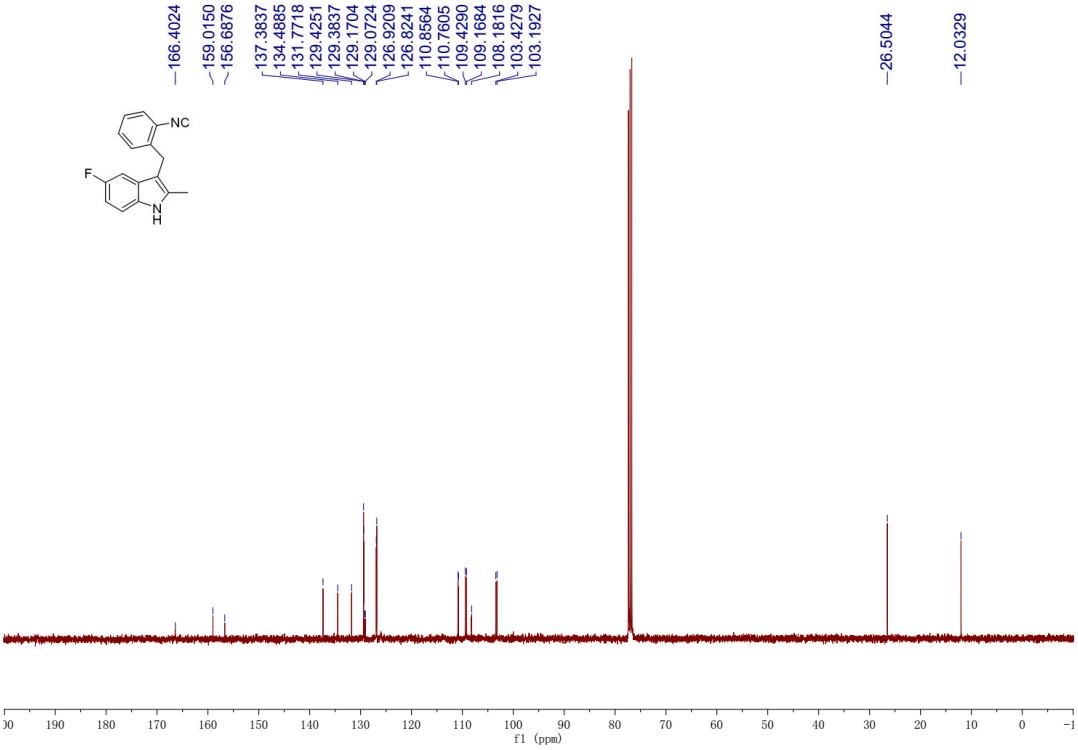
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1l



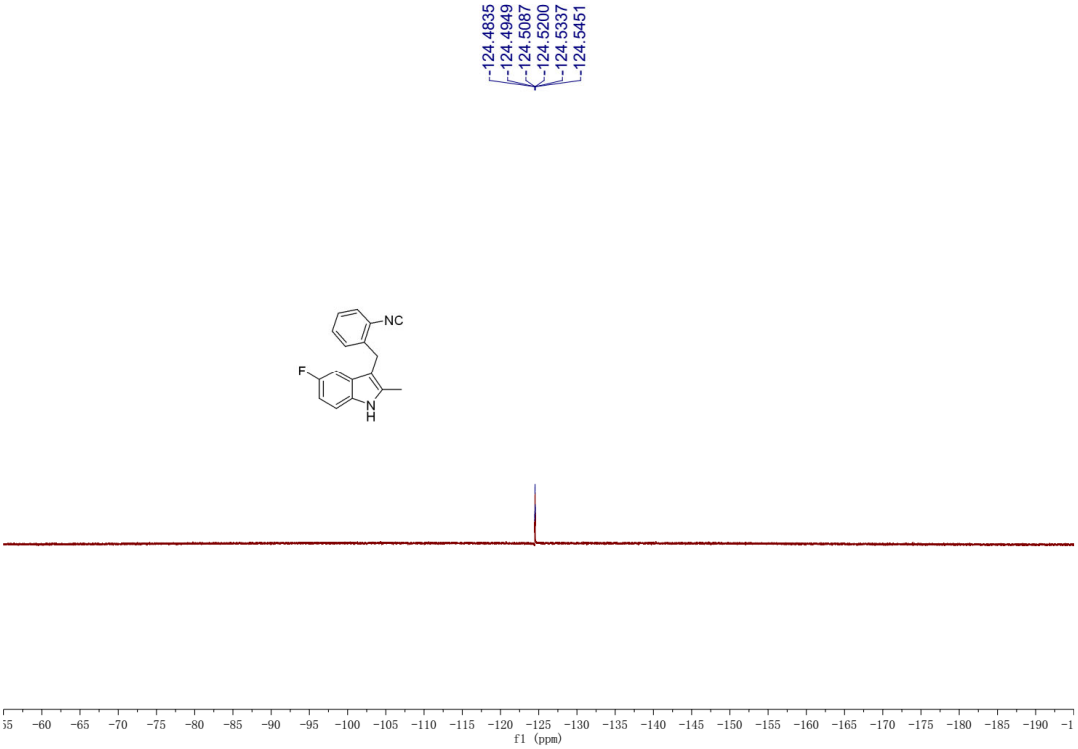
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1m



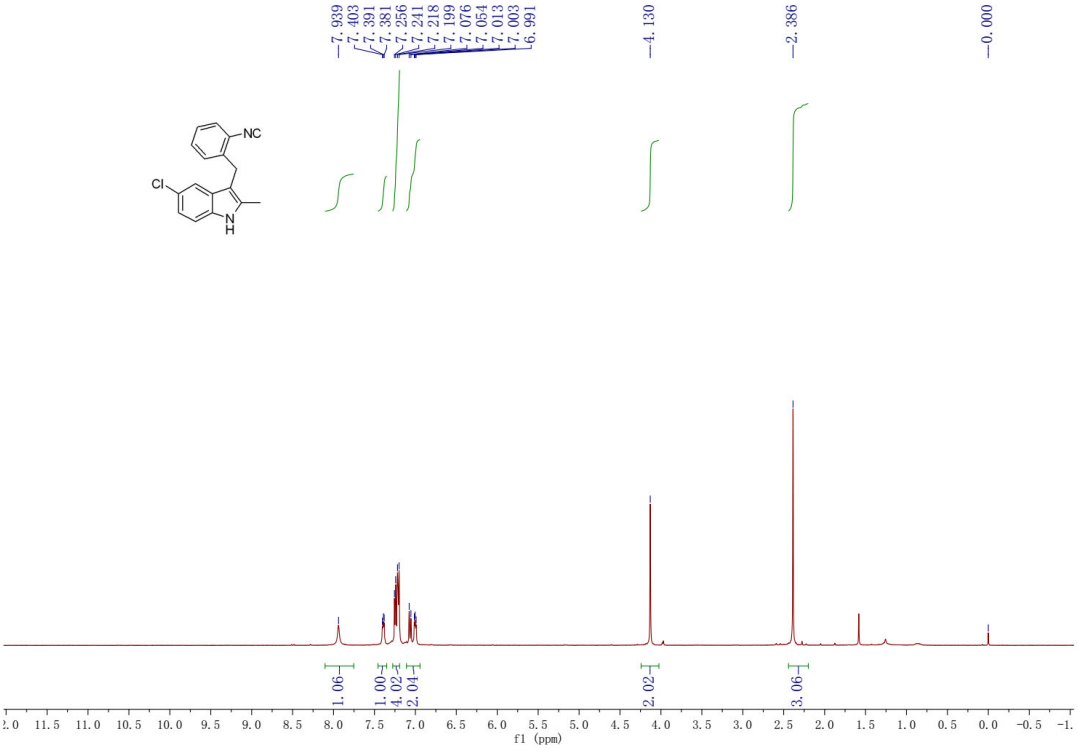
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1m



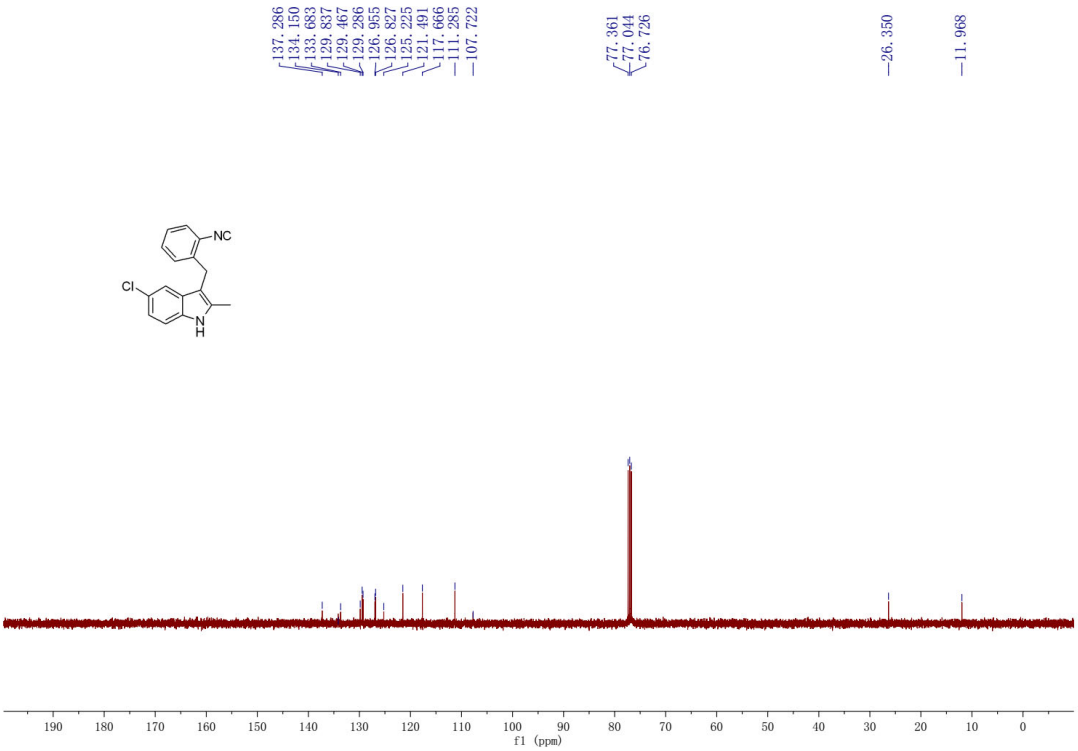
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 1m



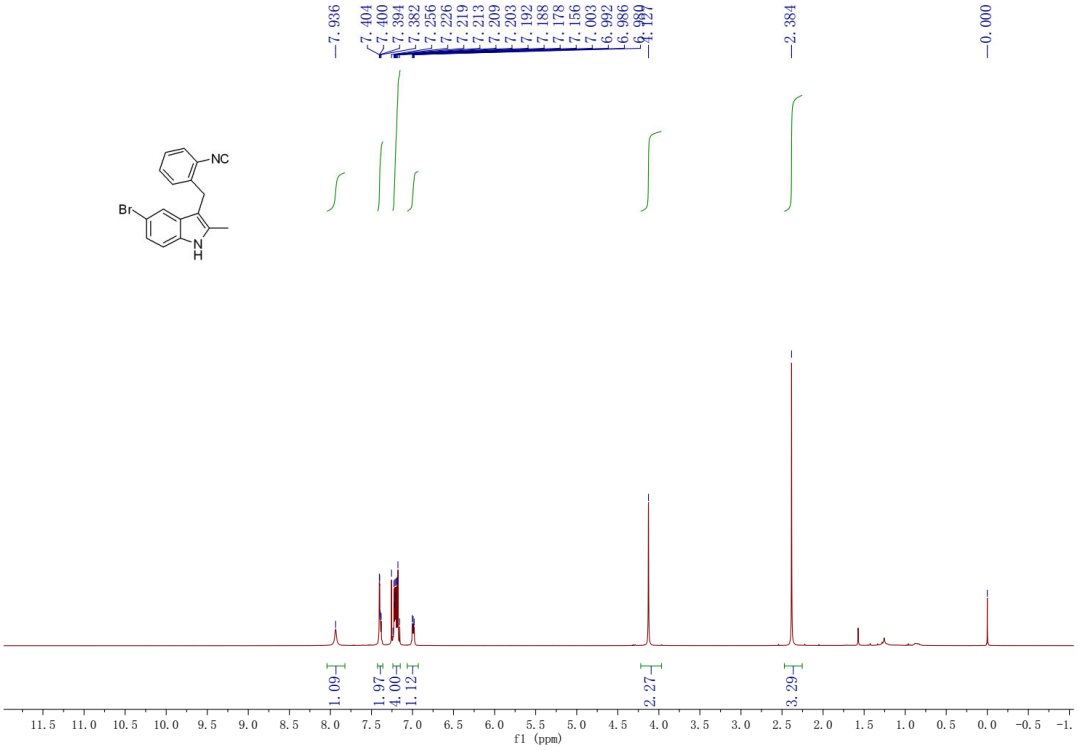
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1n



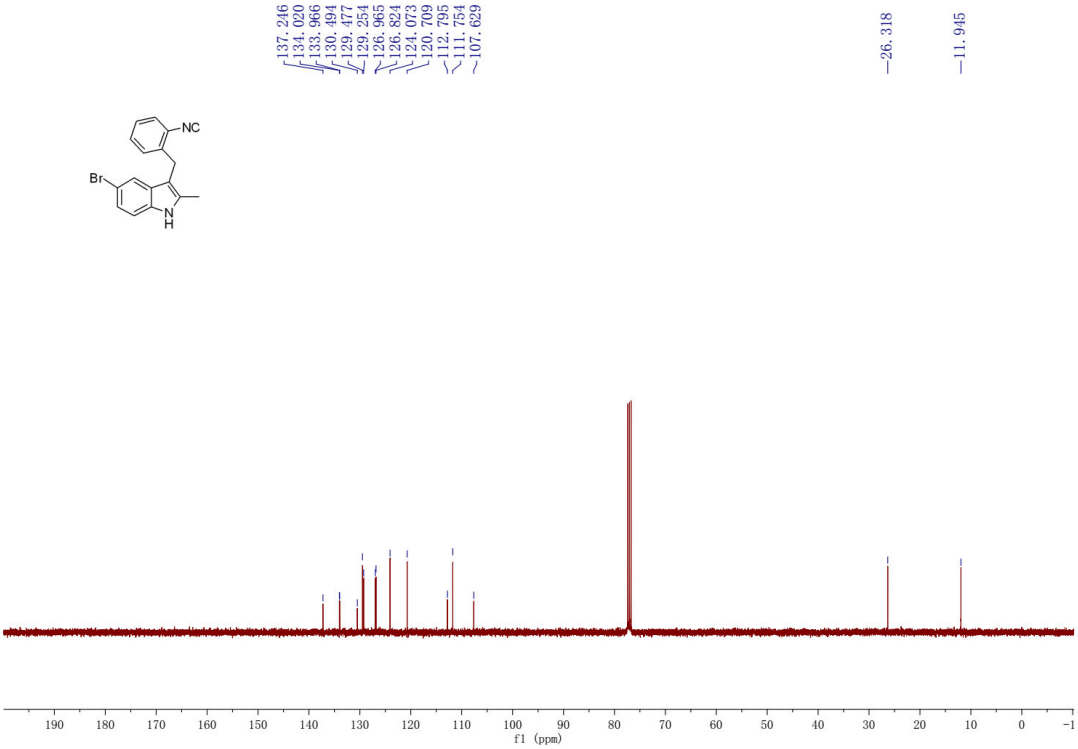
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1n



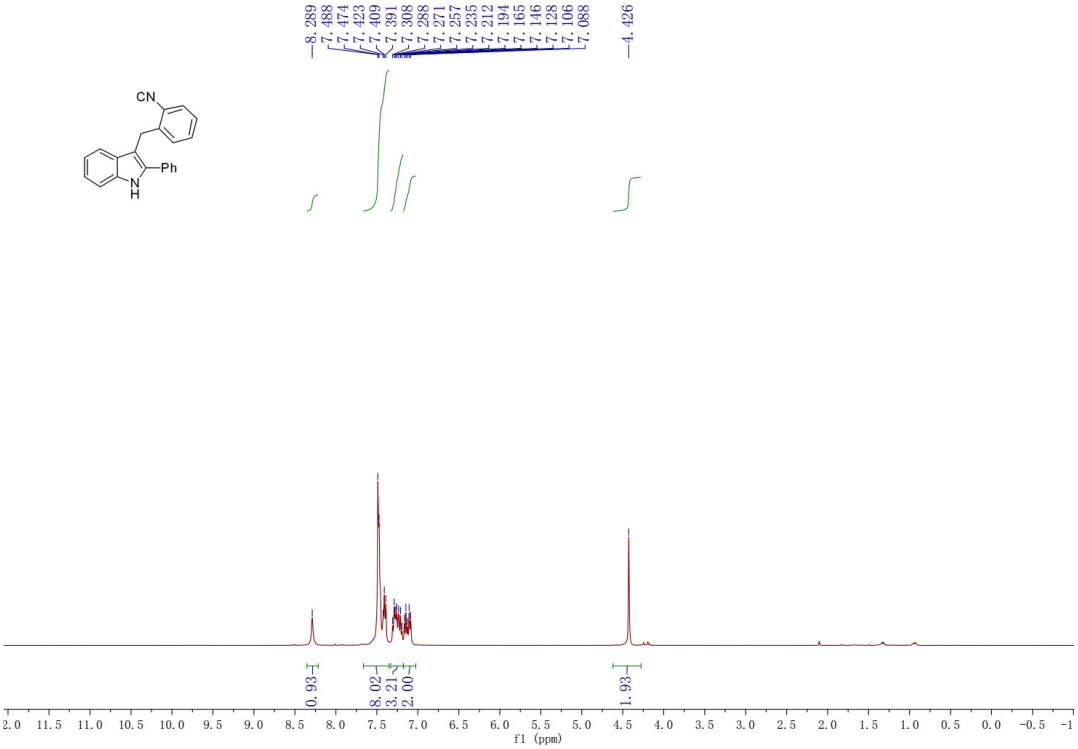
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1o



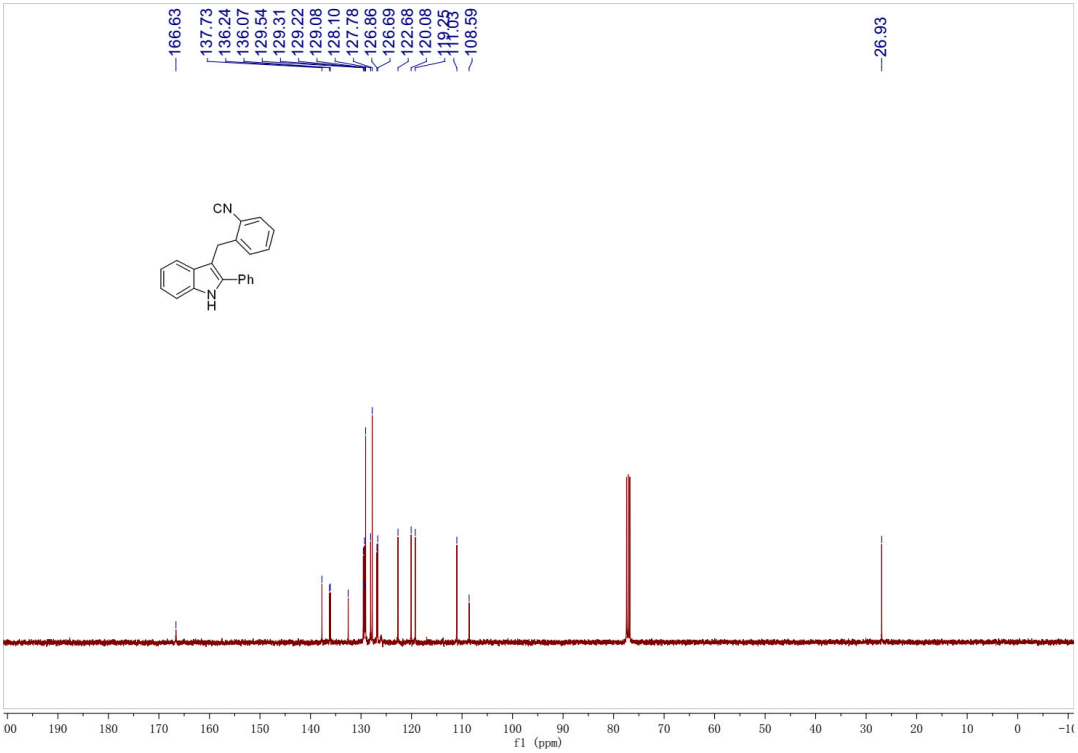
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1o



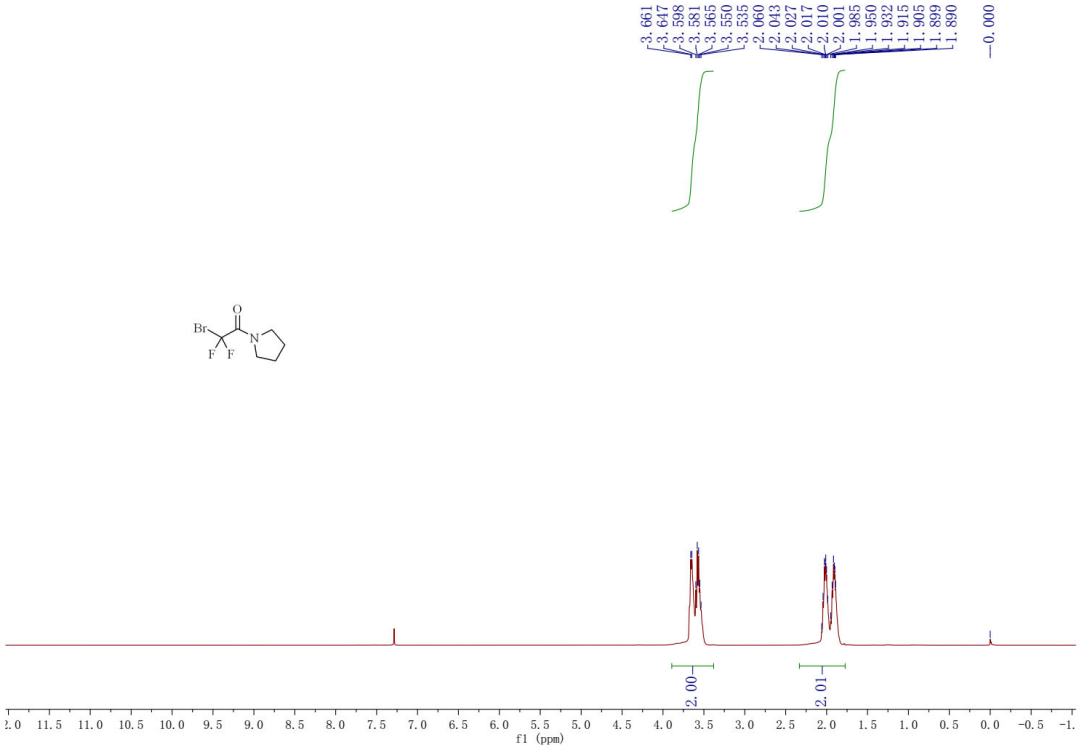
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1p



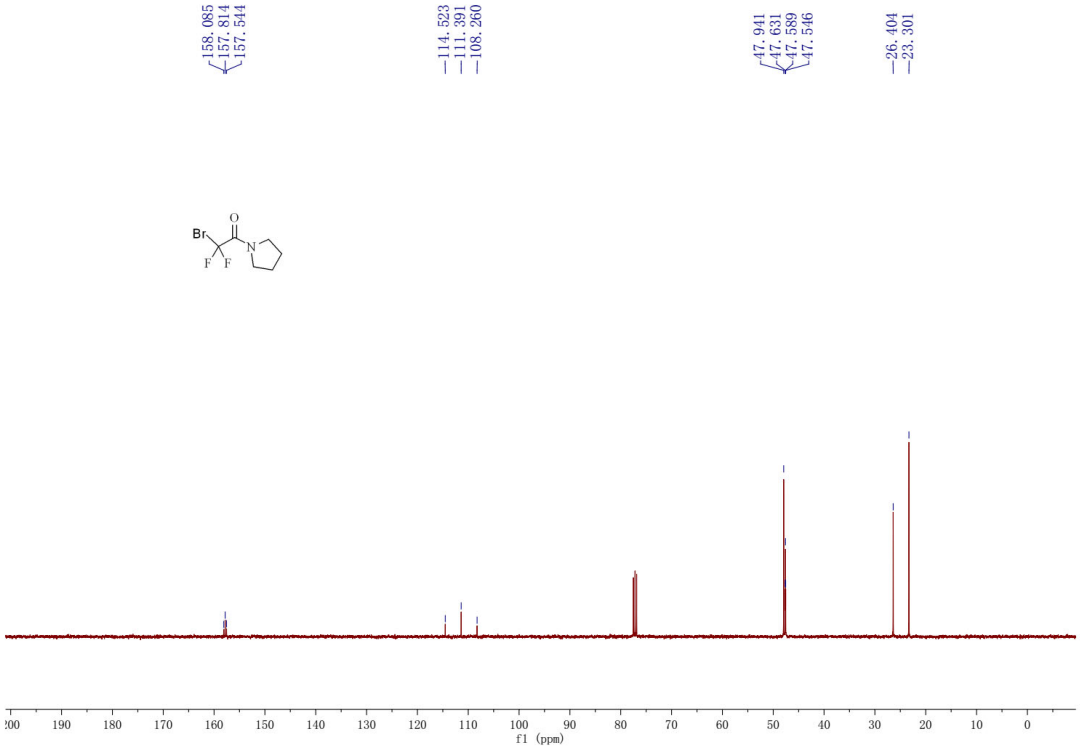
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1p



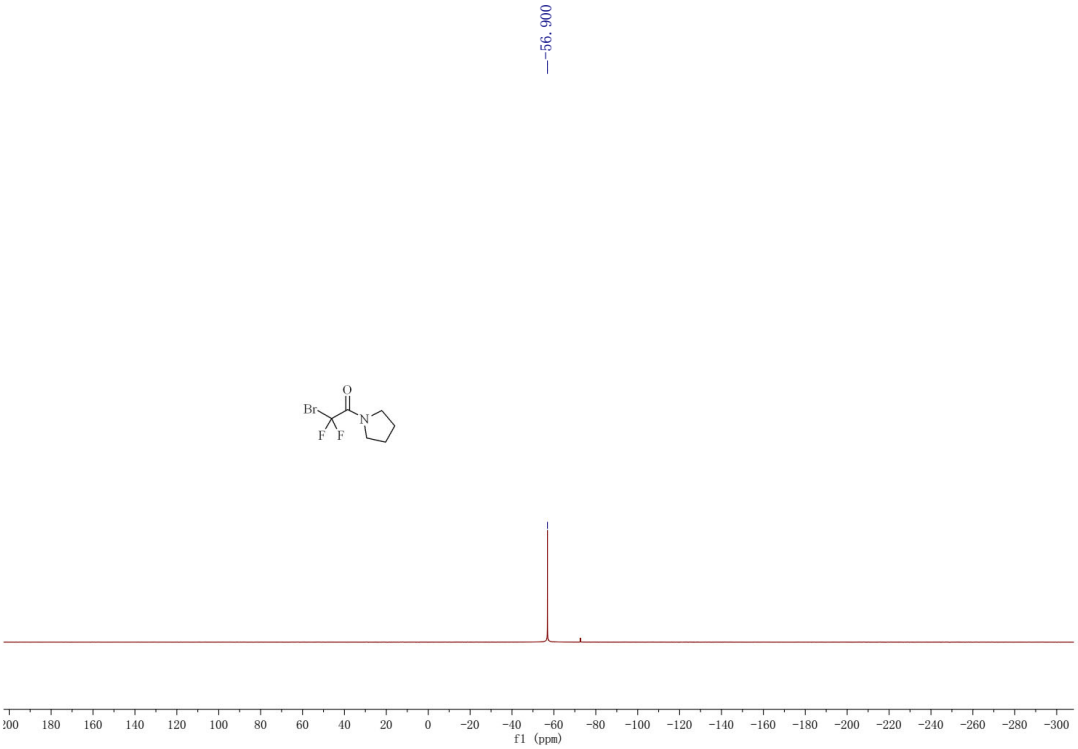
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 2b



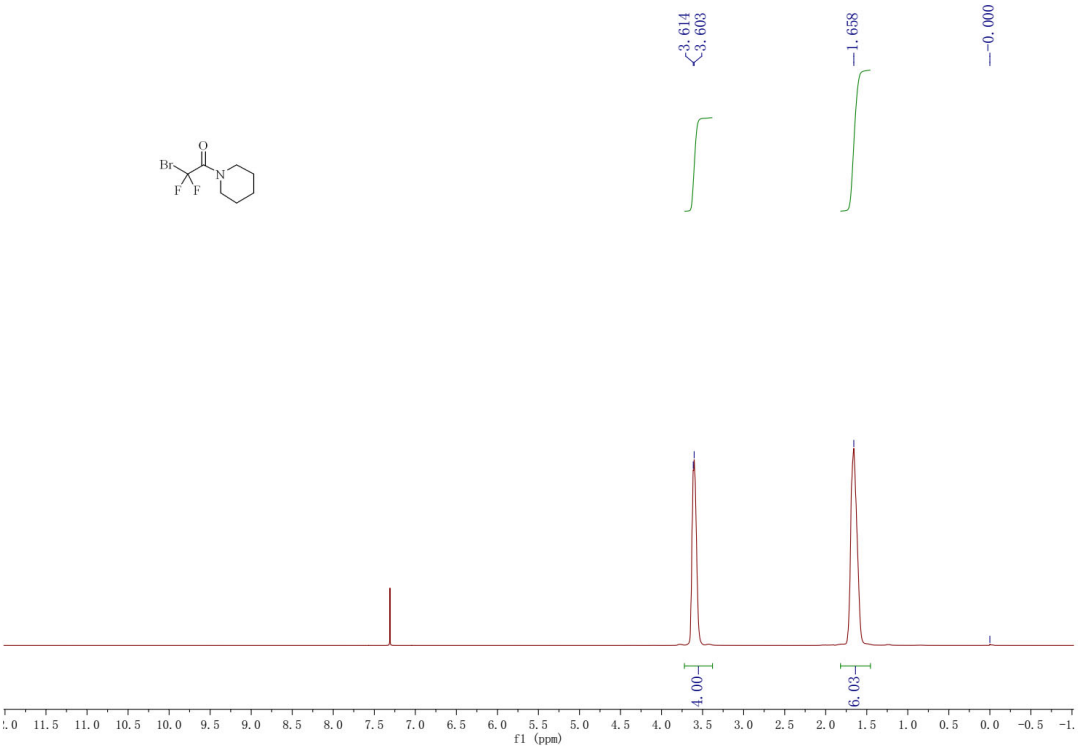
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 2b



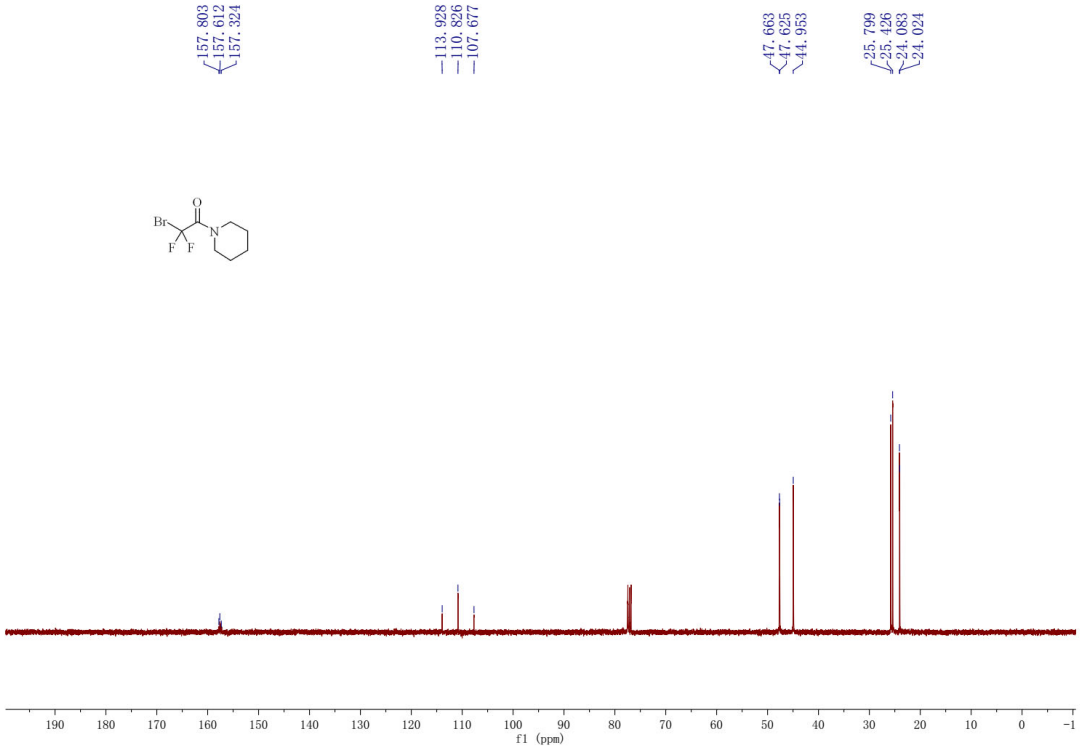
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 2b



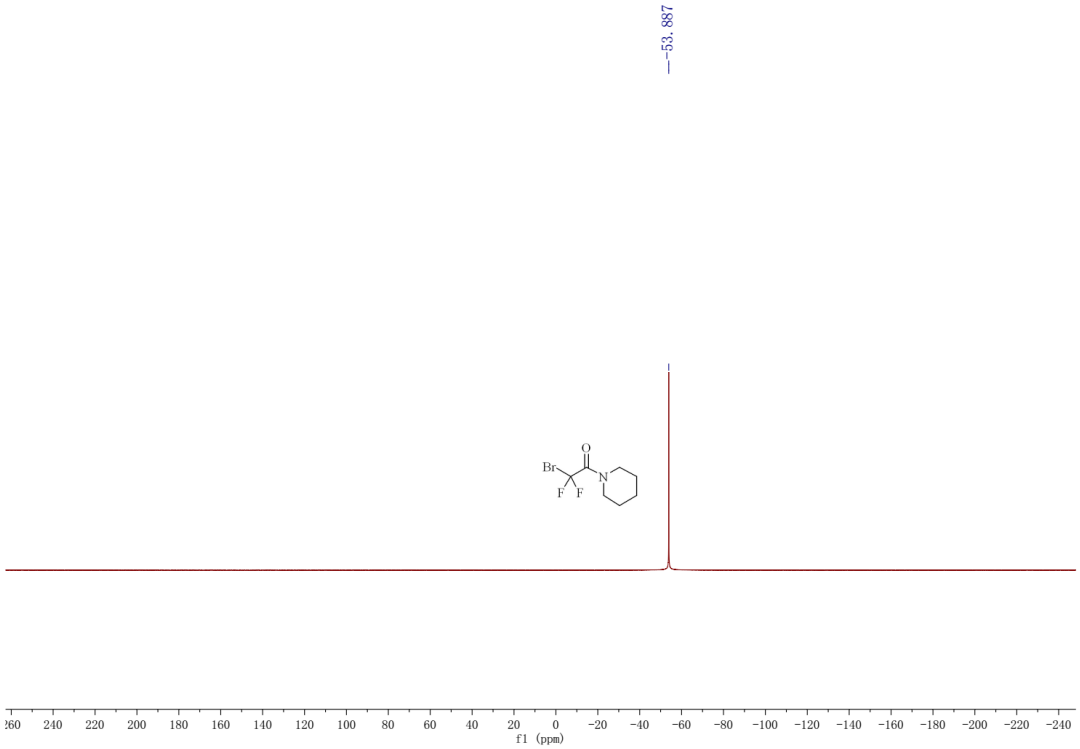
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 2c



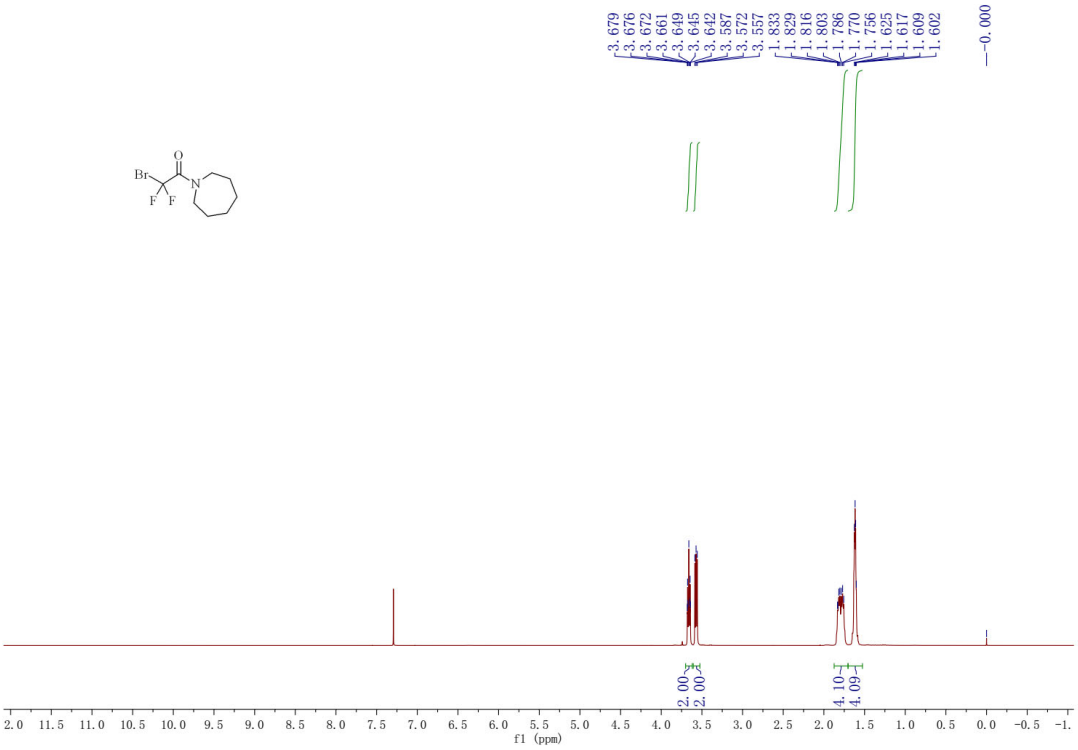
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 2c



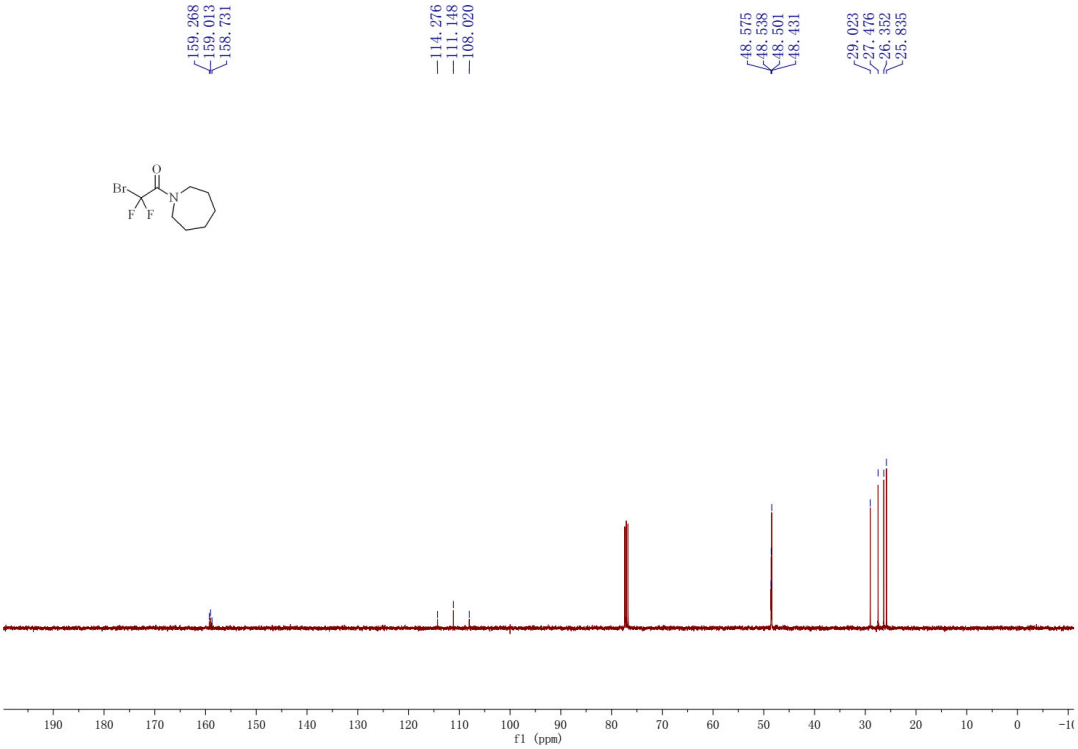
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 2c



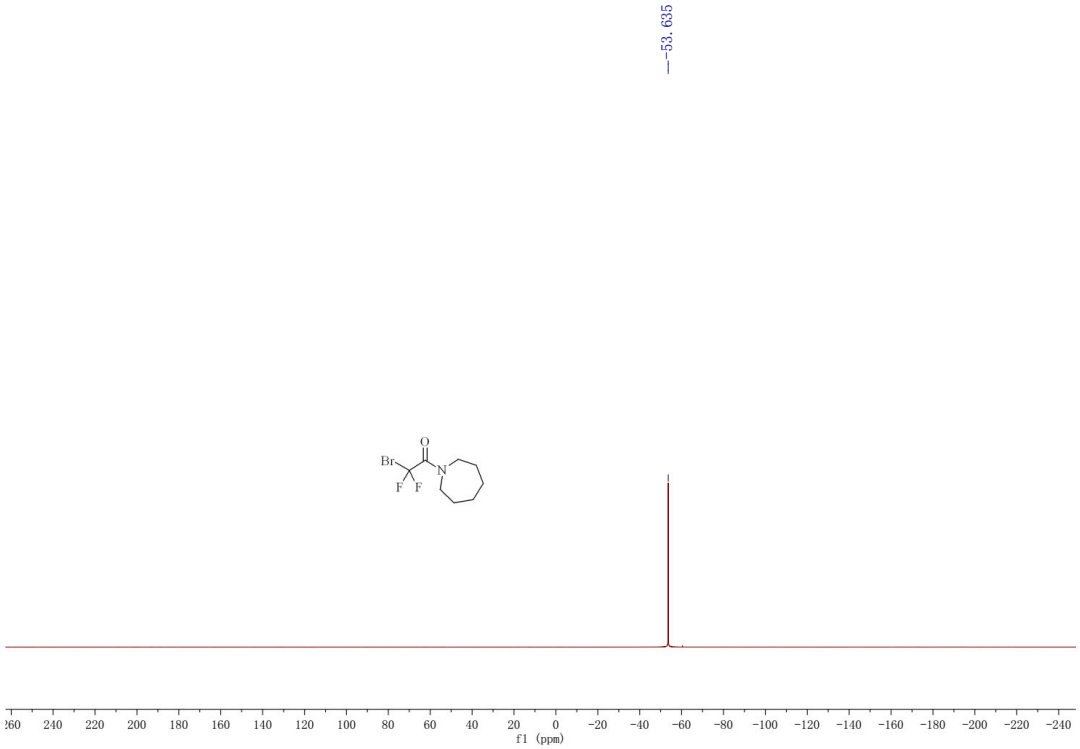
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 2d



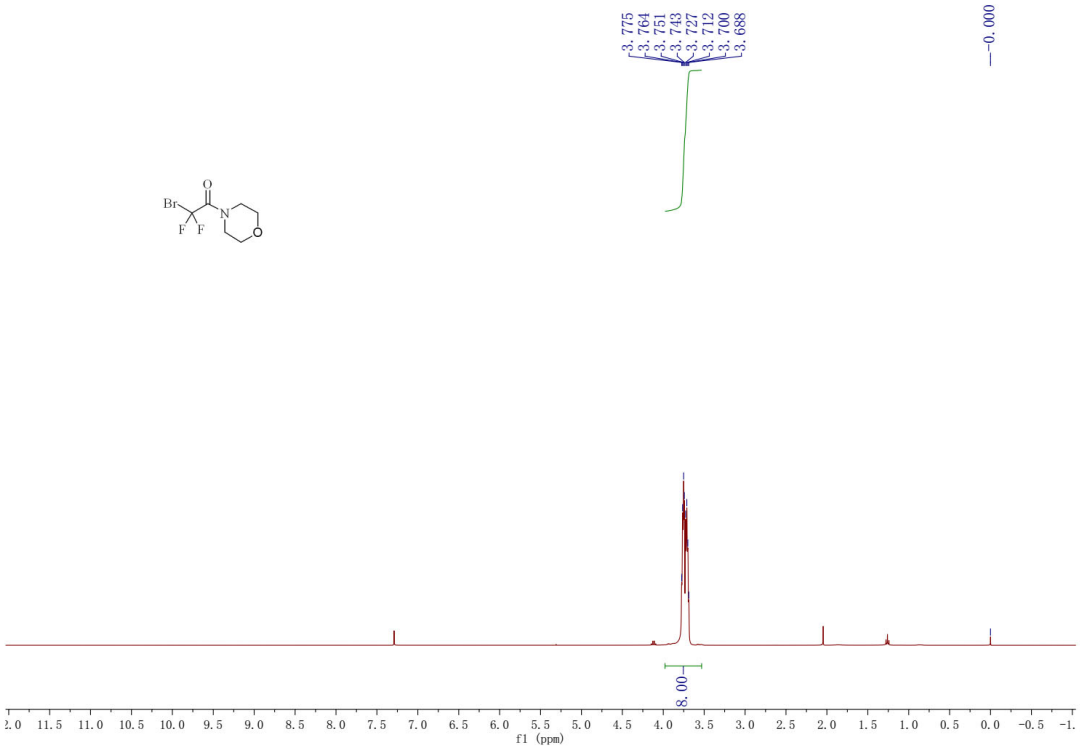
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 2d



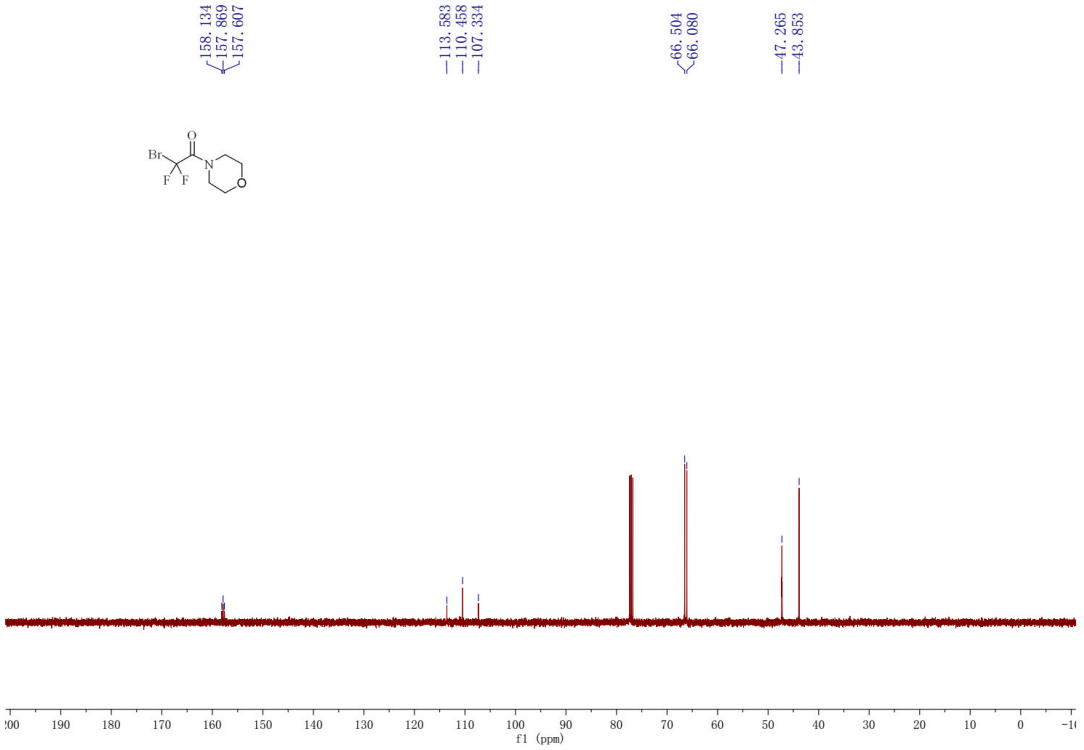
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 2d



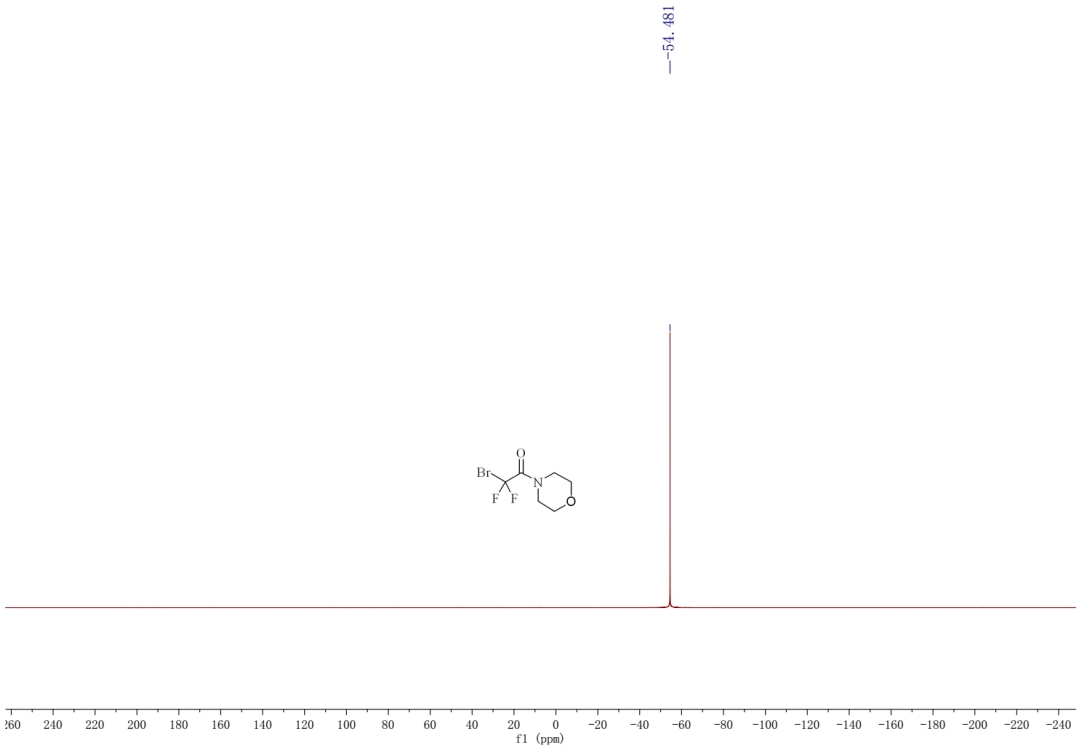
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 2e



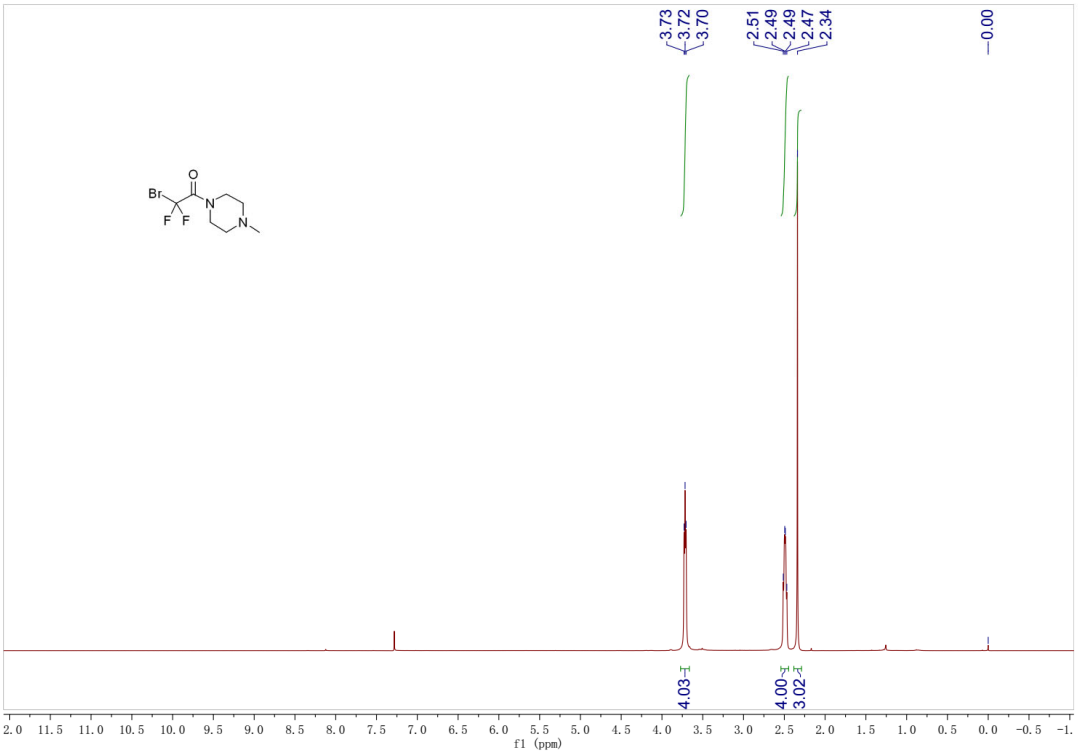
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 2e



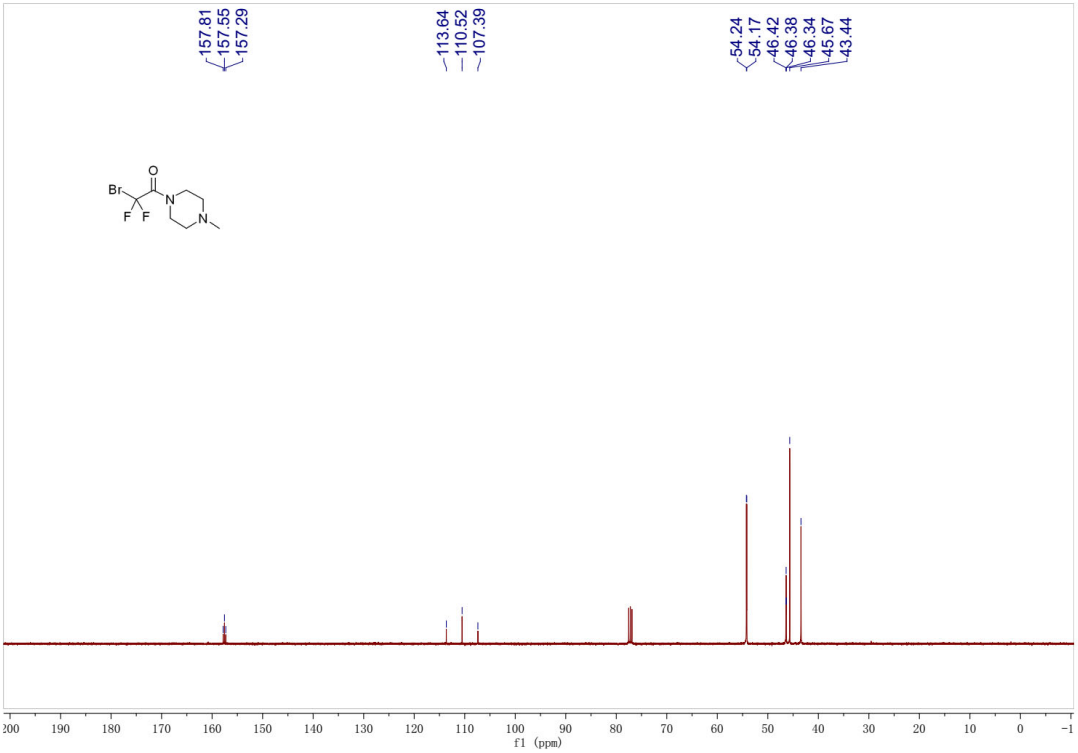
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 2e



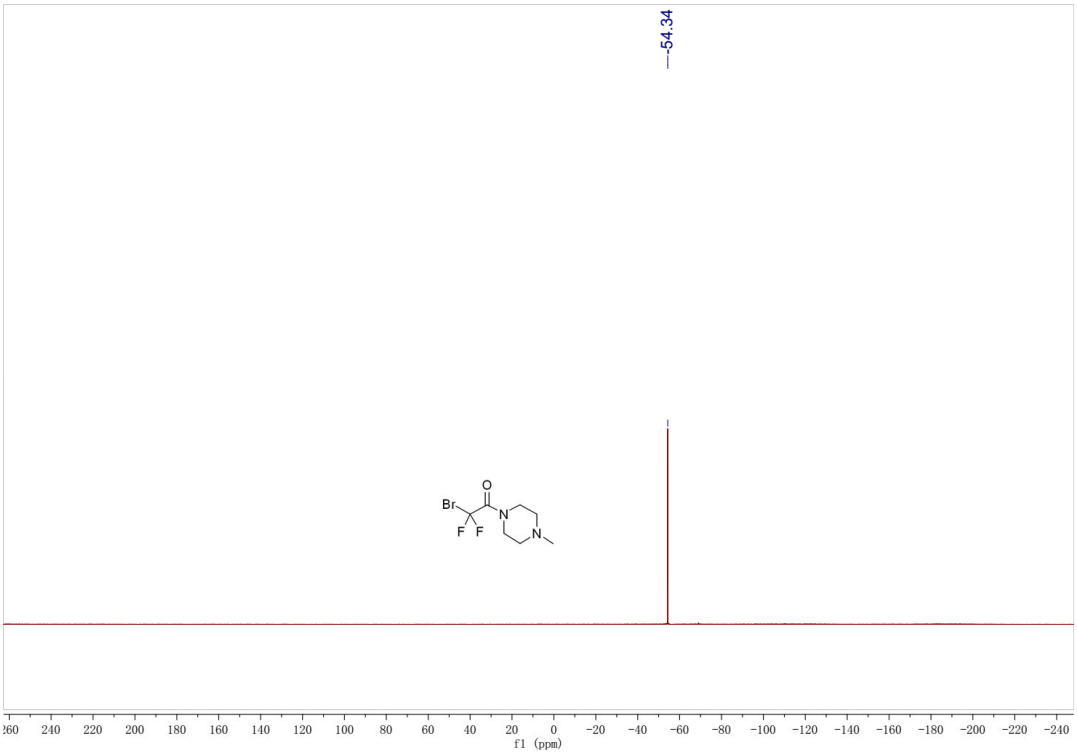
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 2f



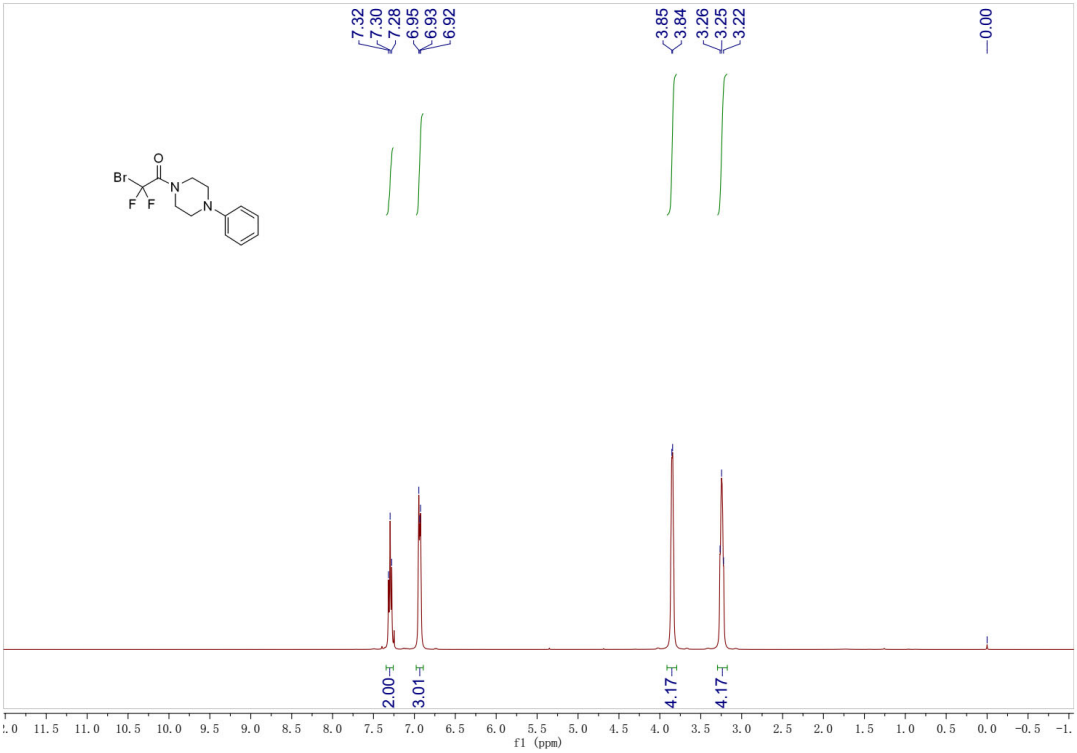
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 2f



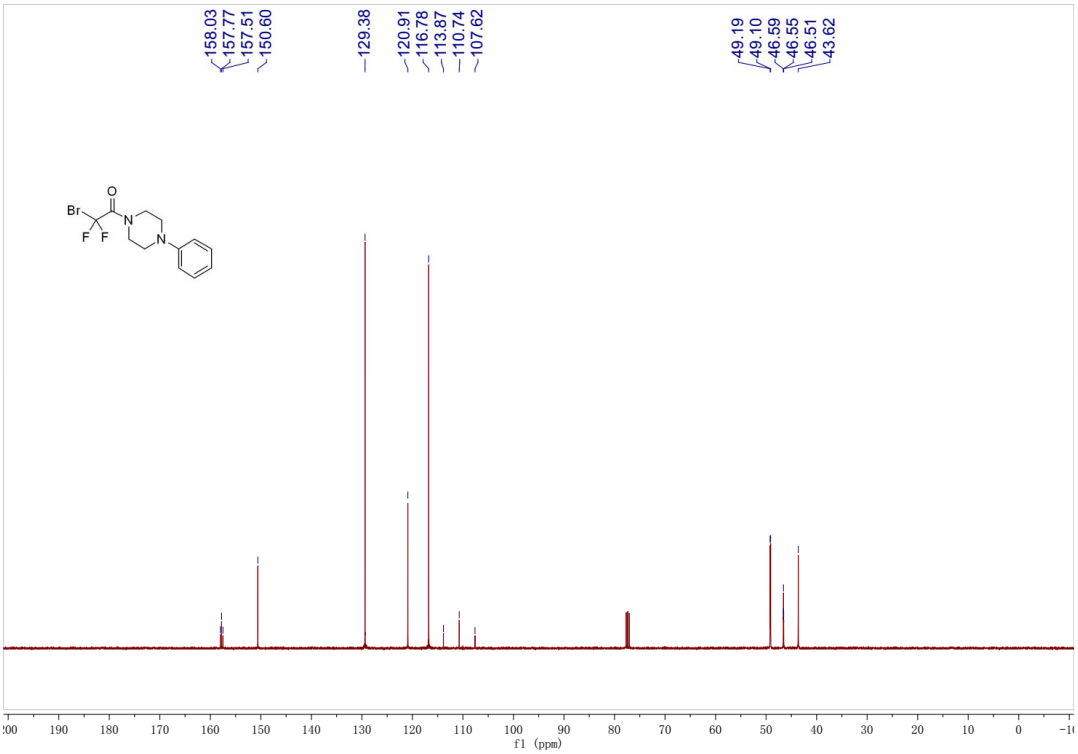
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 2f



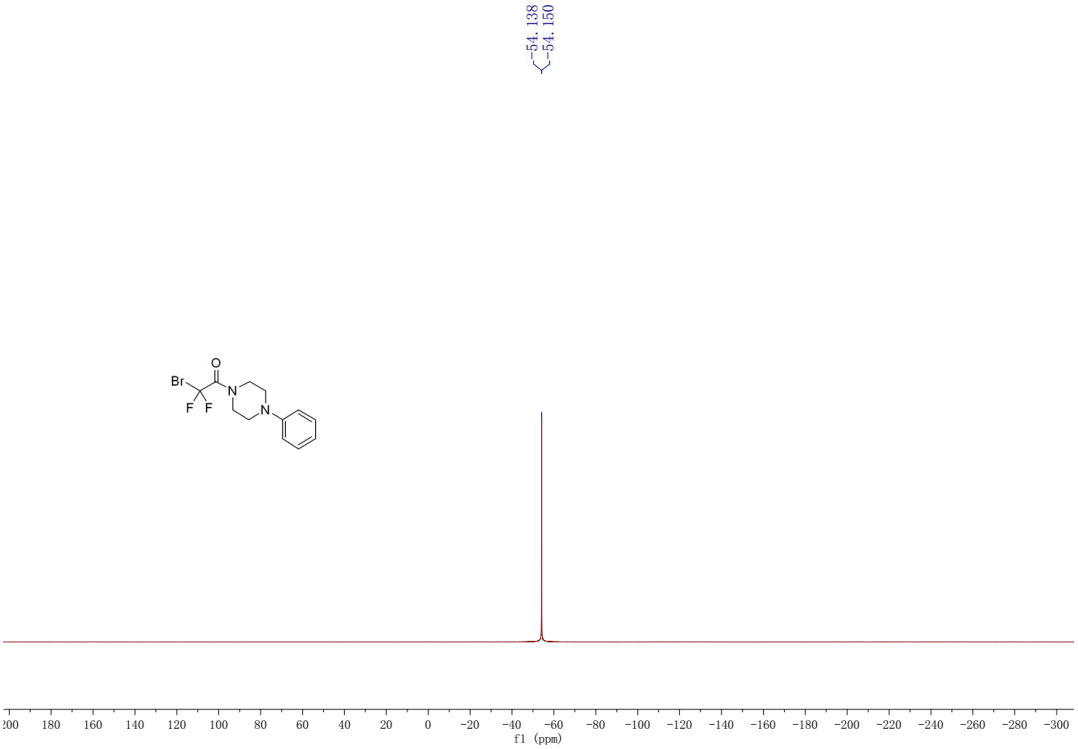
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 2g



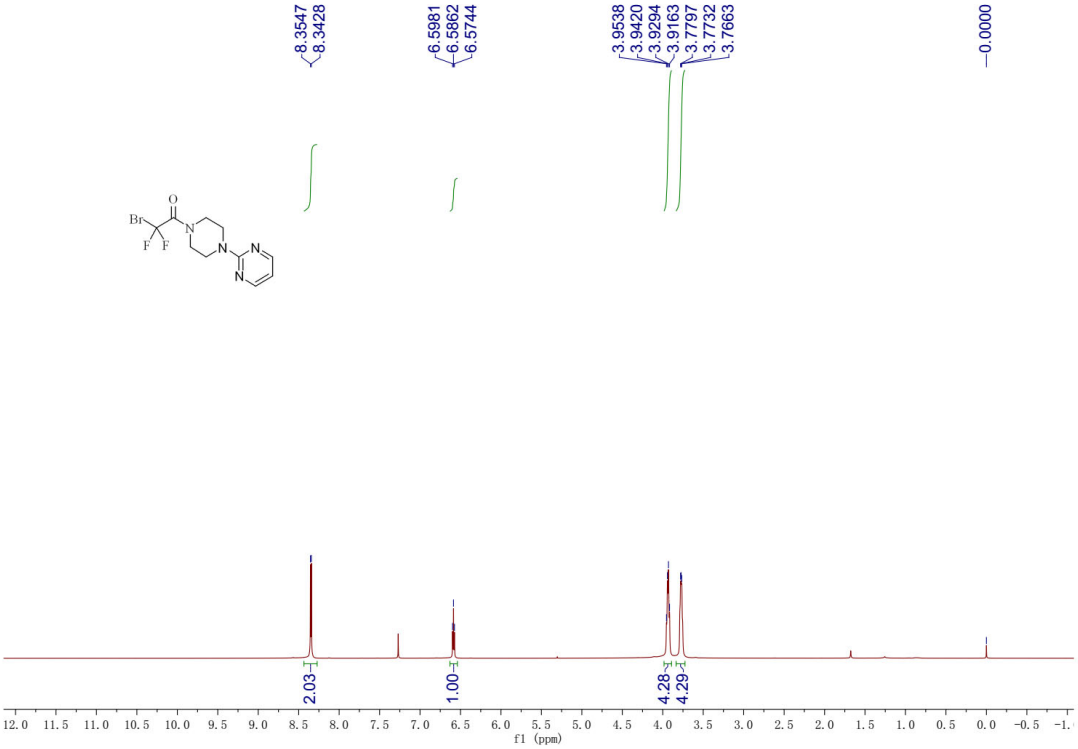
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 2g



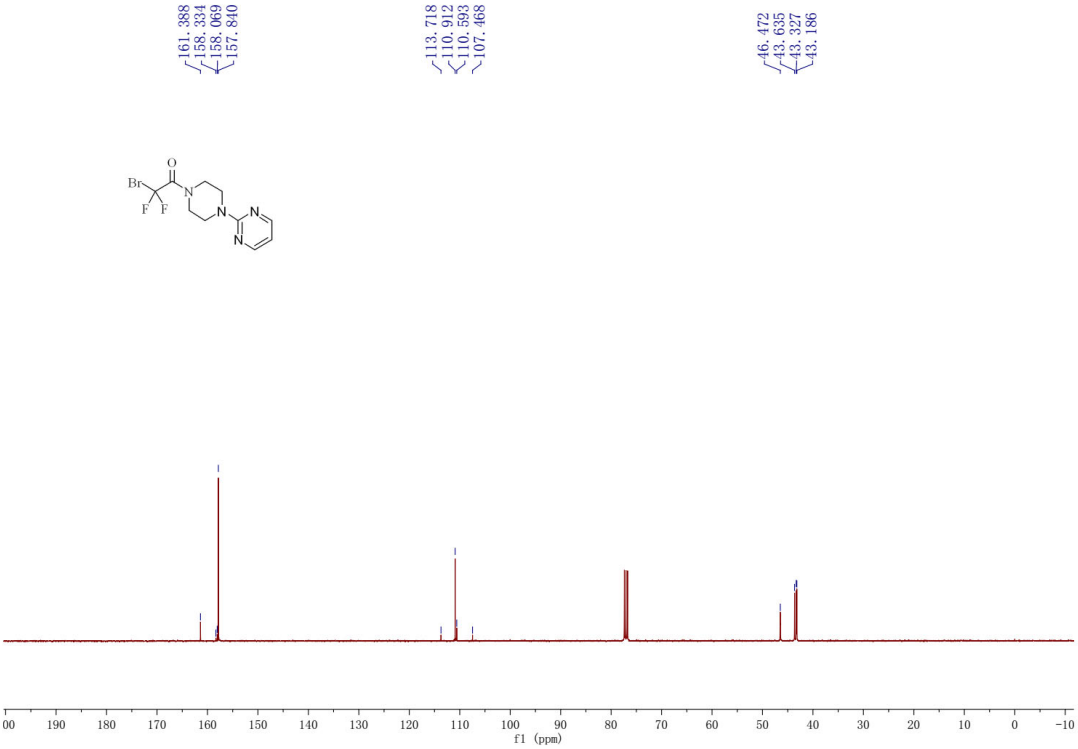
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 2g



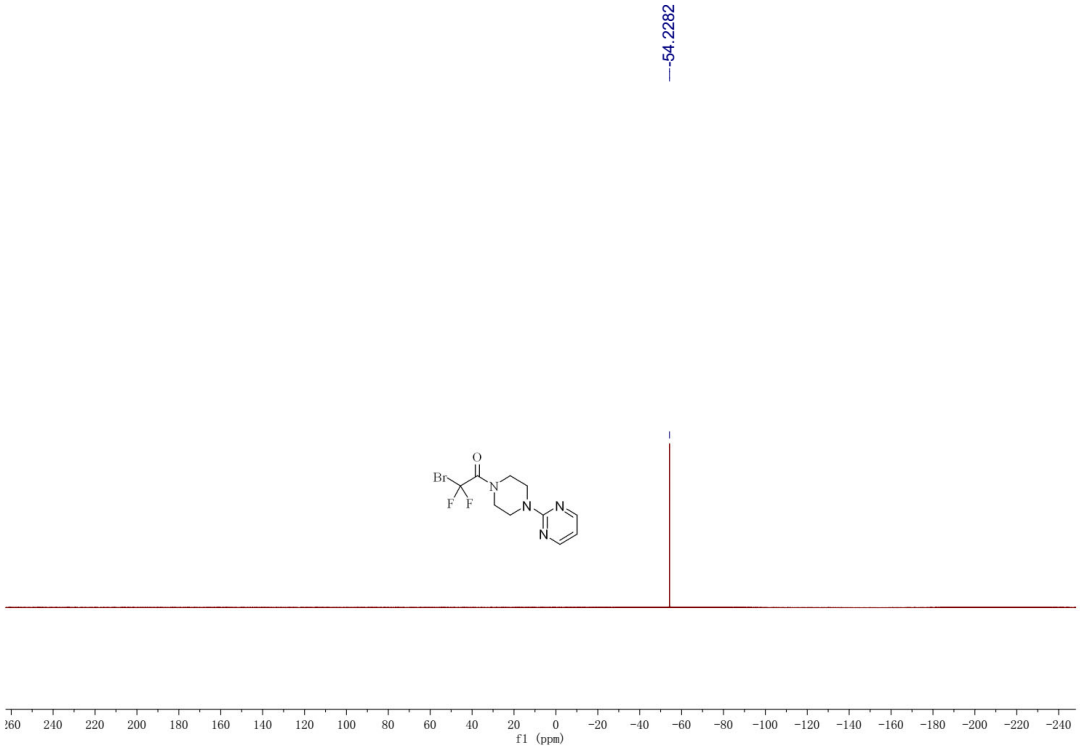
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 2h



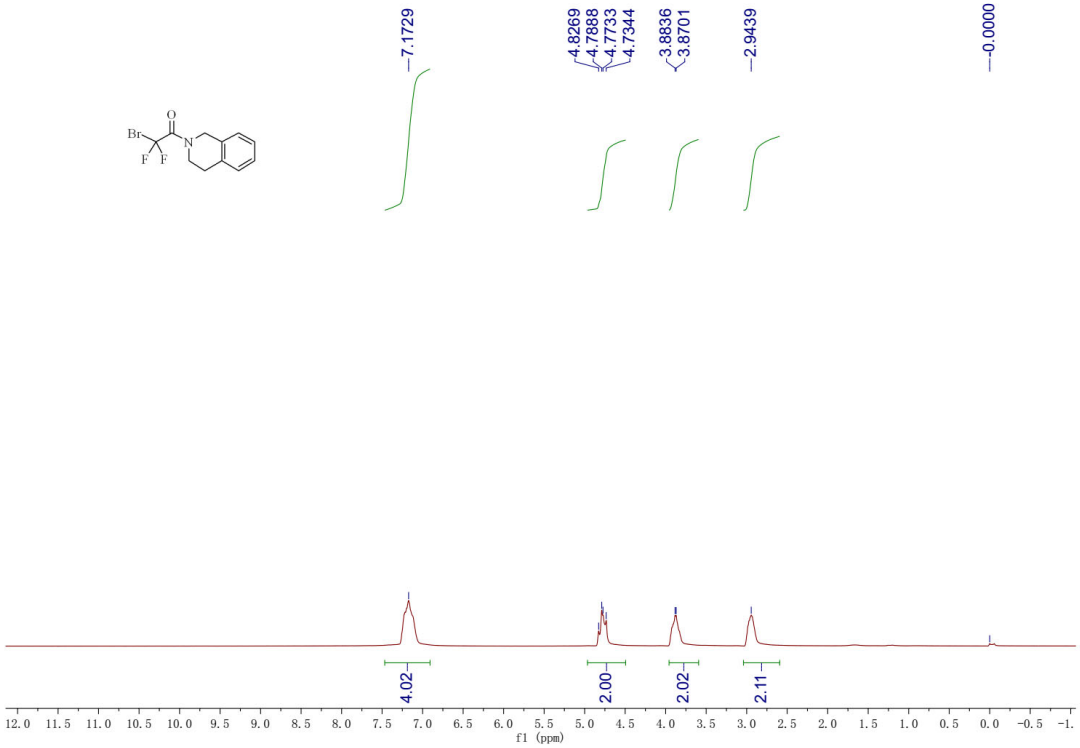
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 2h



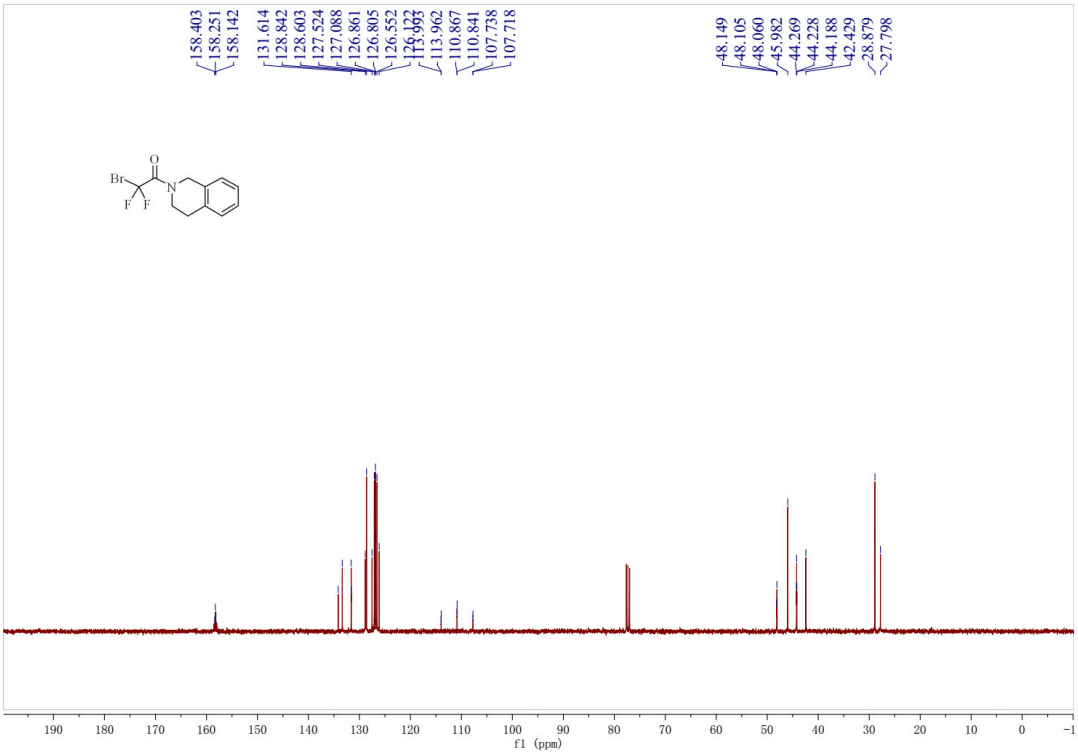
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 2h



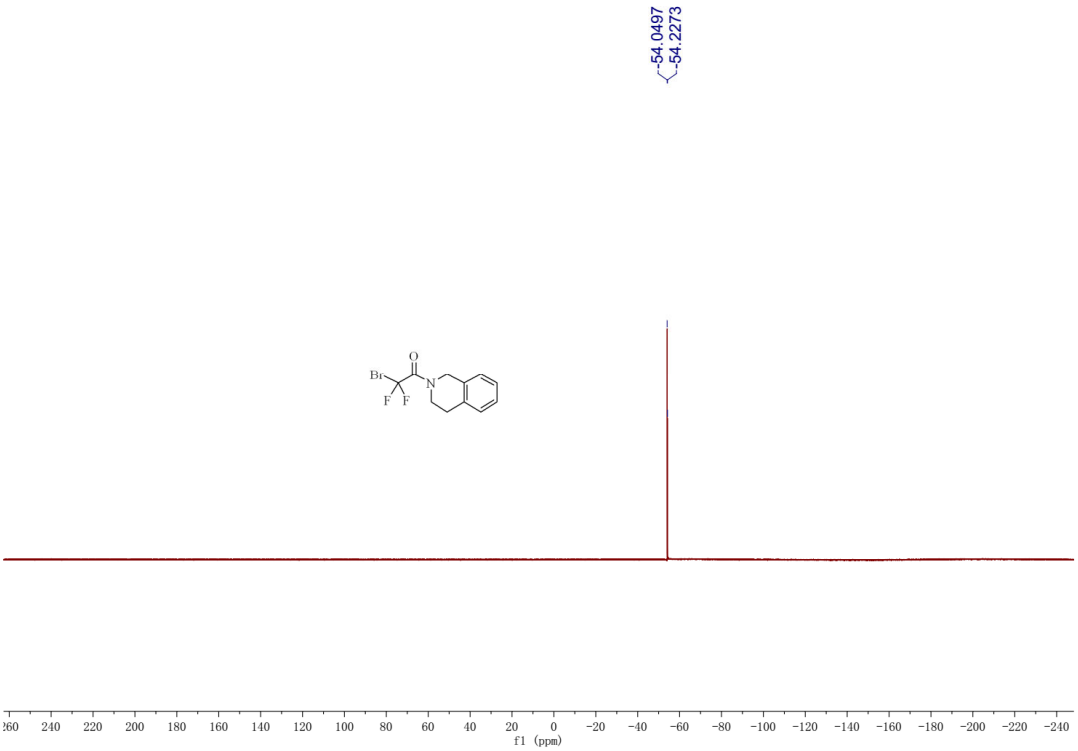
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 2i



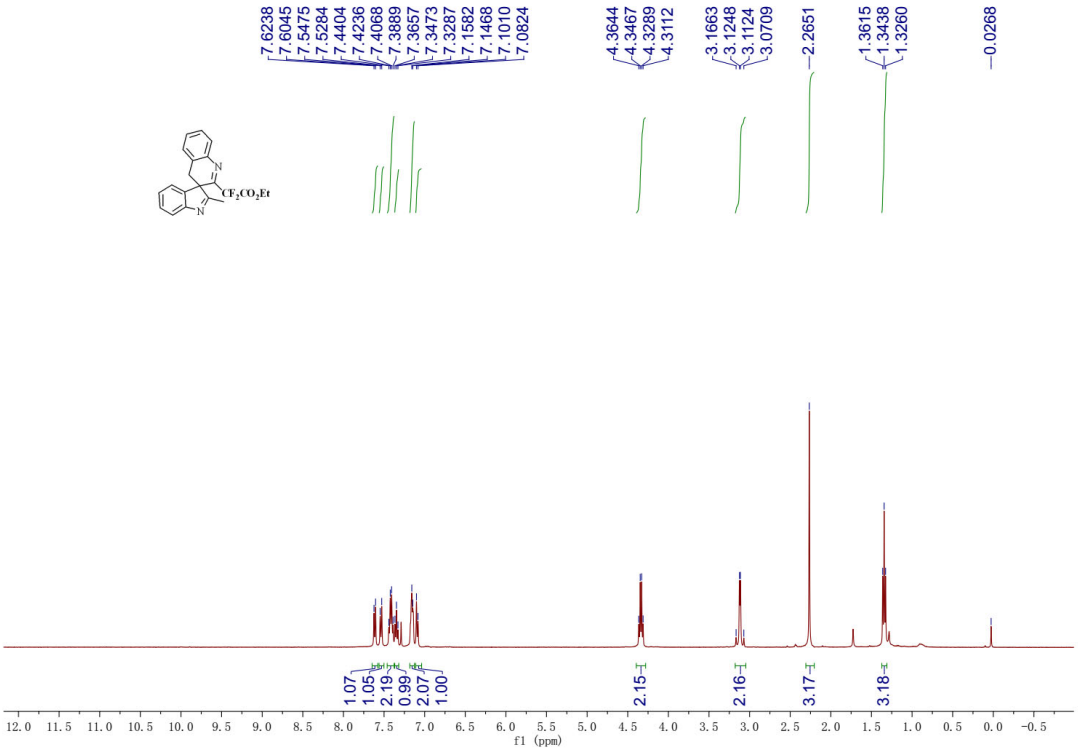
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 2i



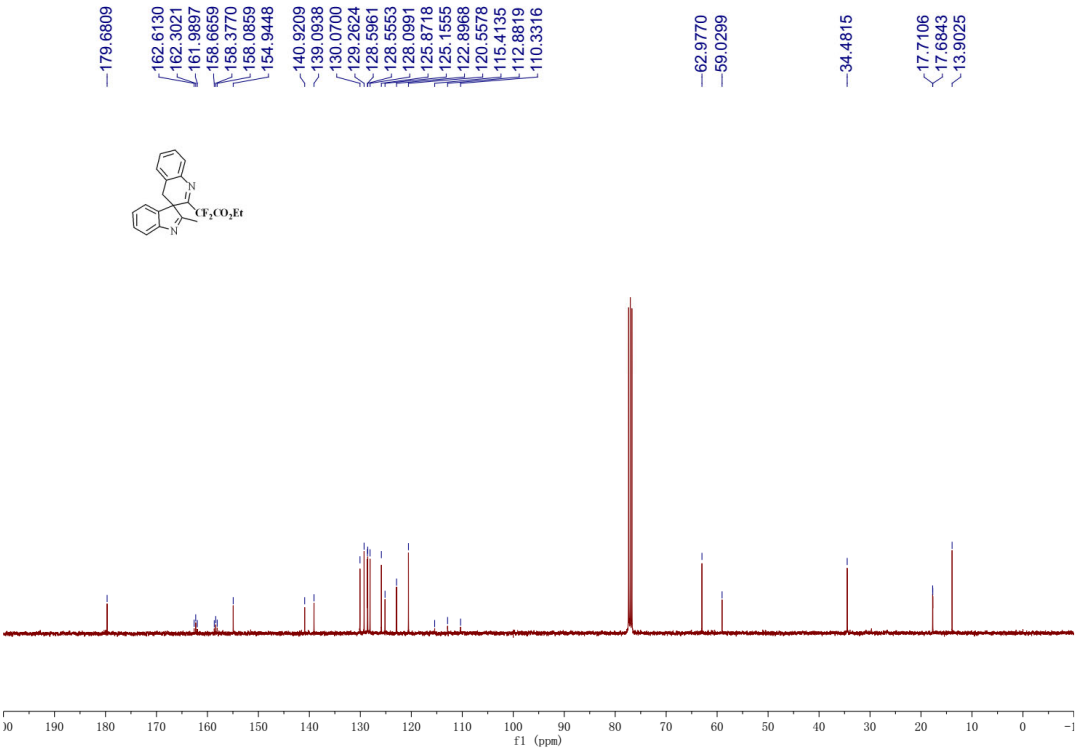
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 2i



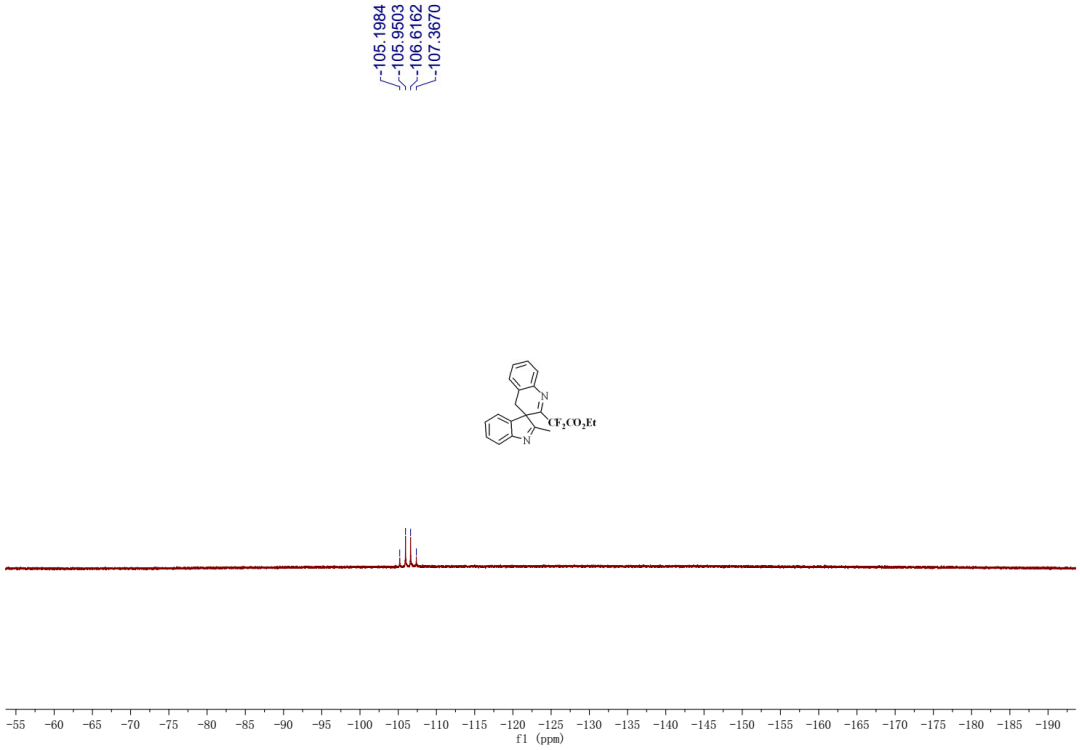
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3a



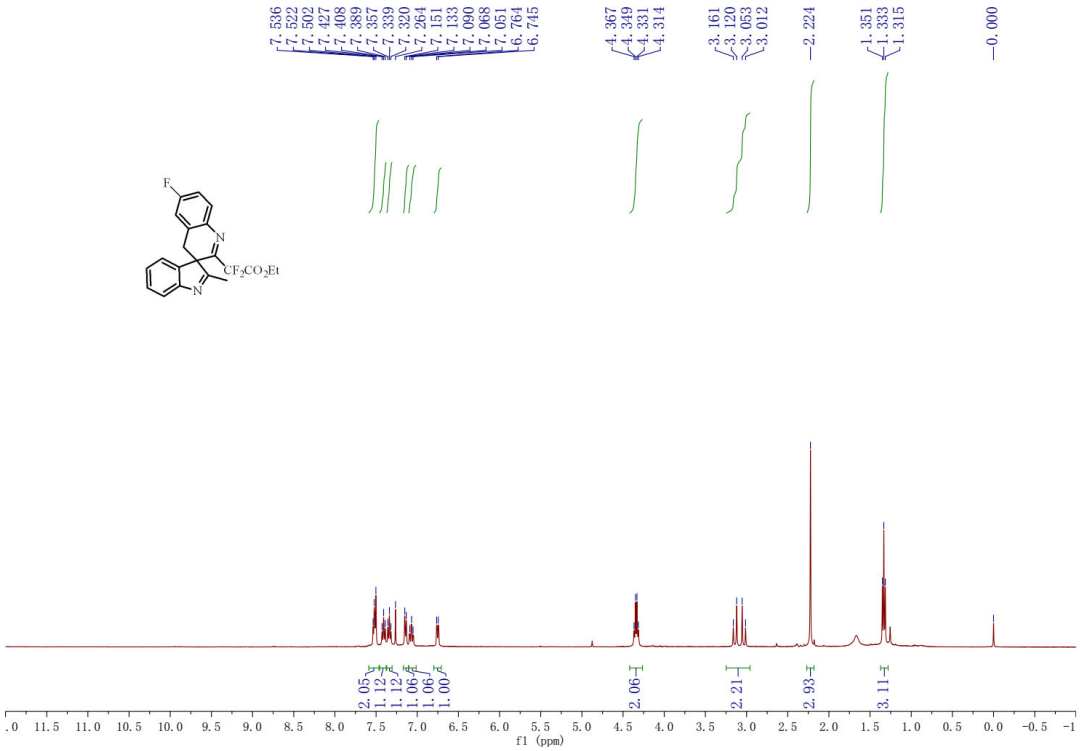
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3a



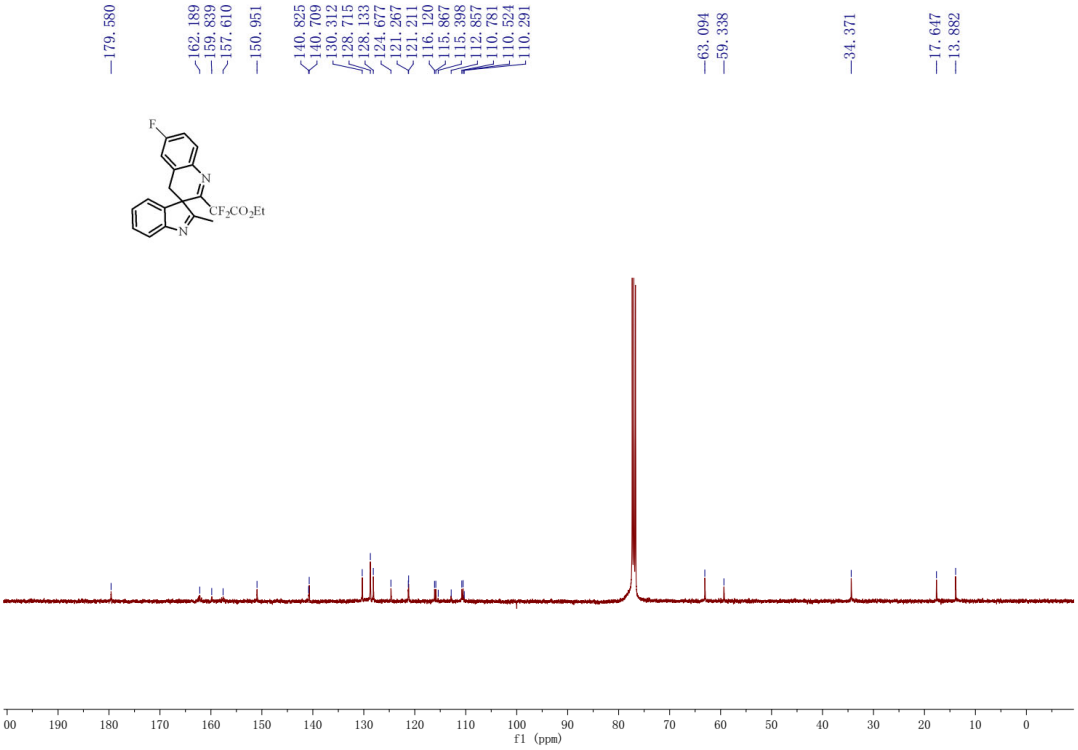
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3a



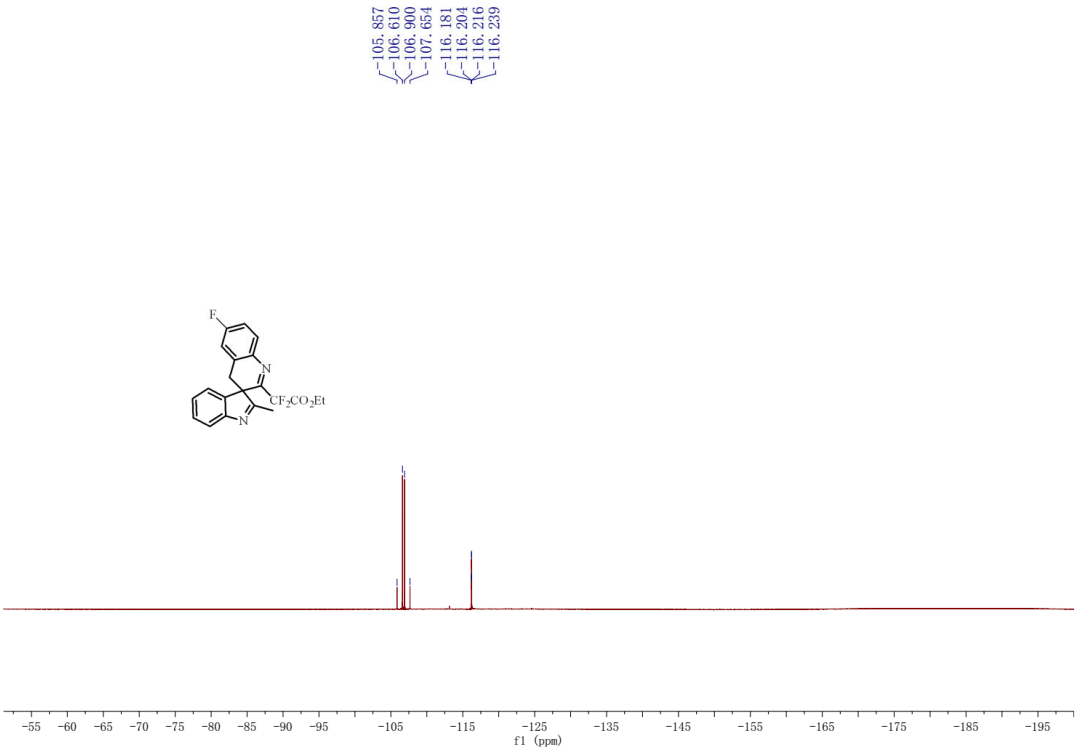
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3b



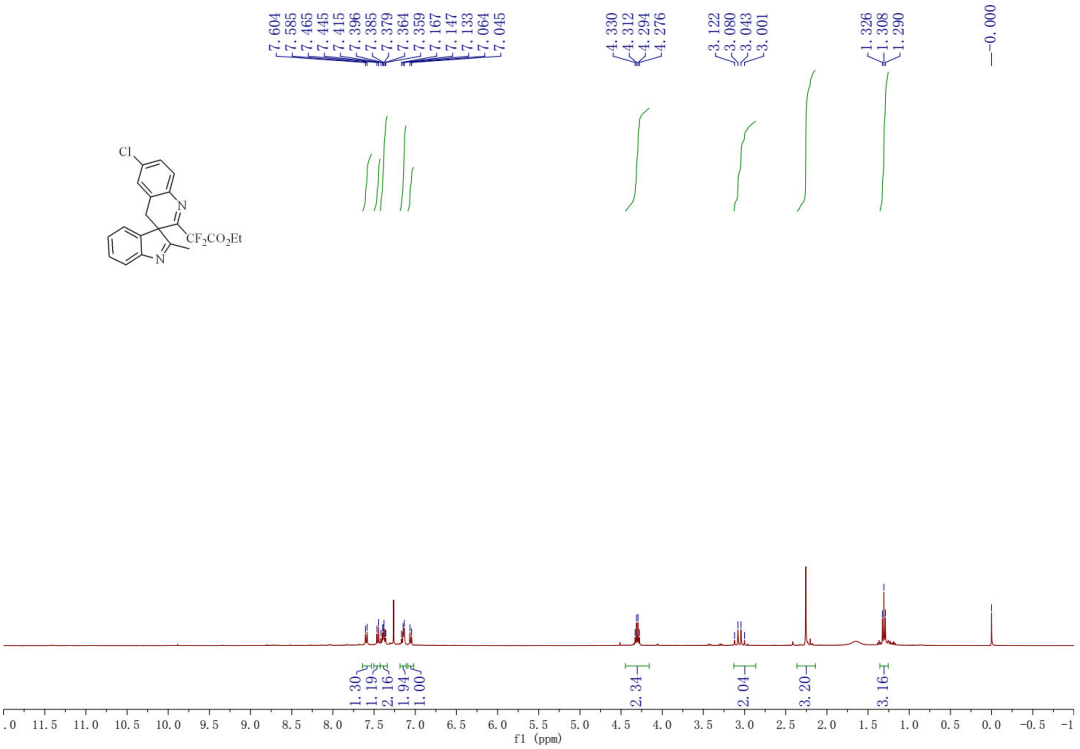
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3b



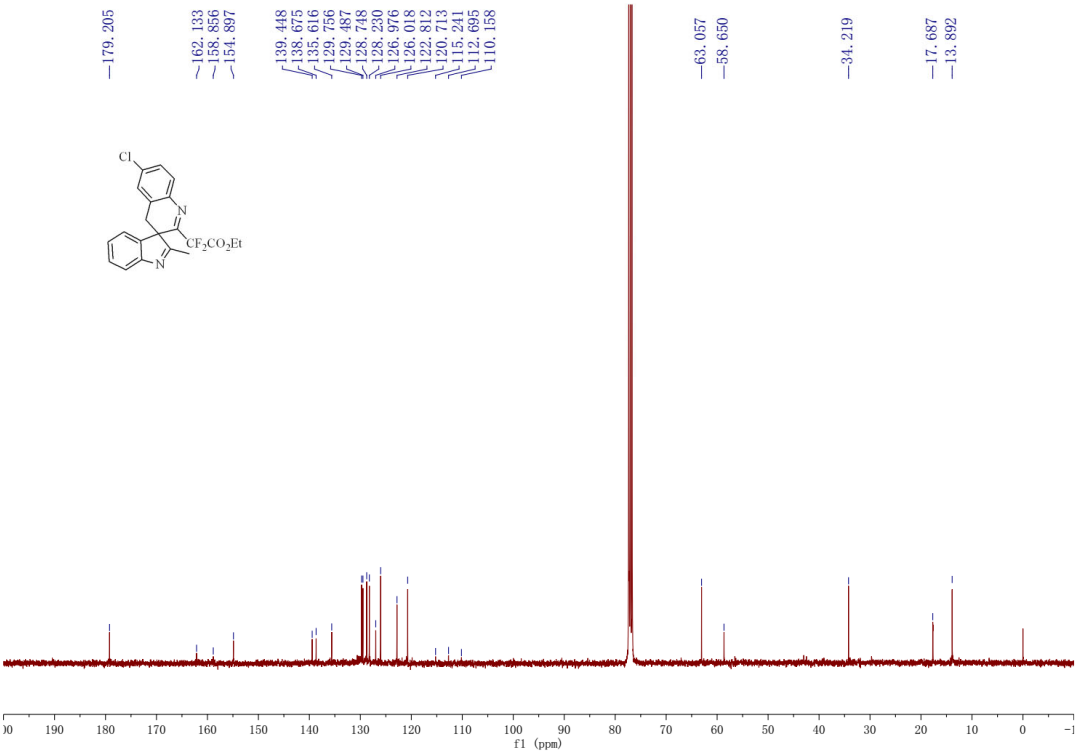
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3b



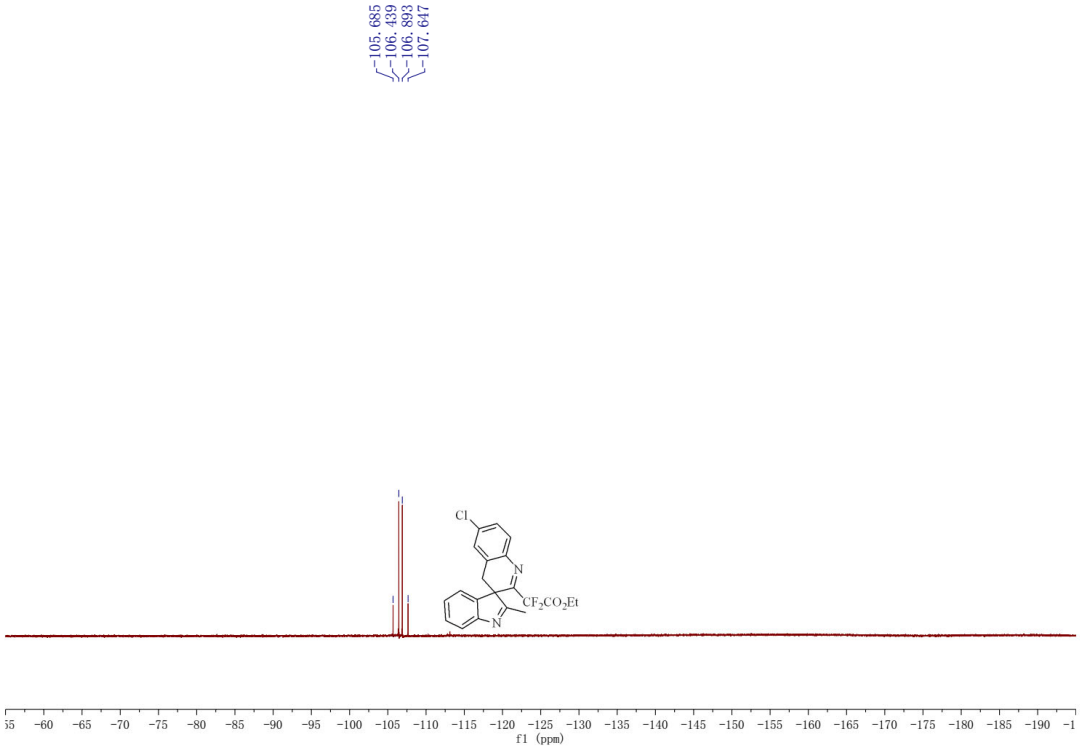
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3c



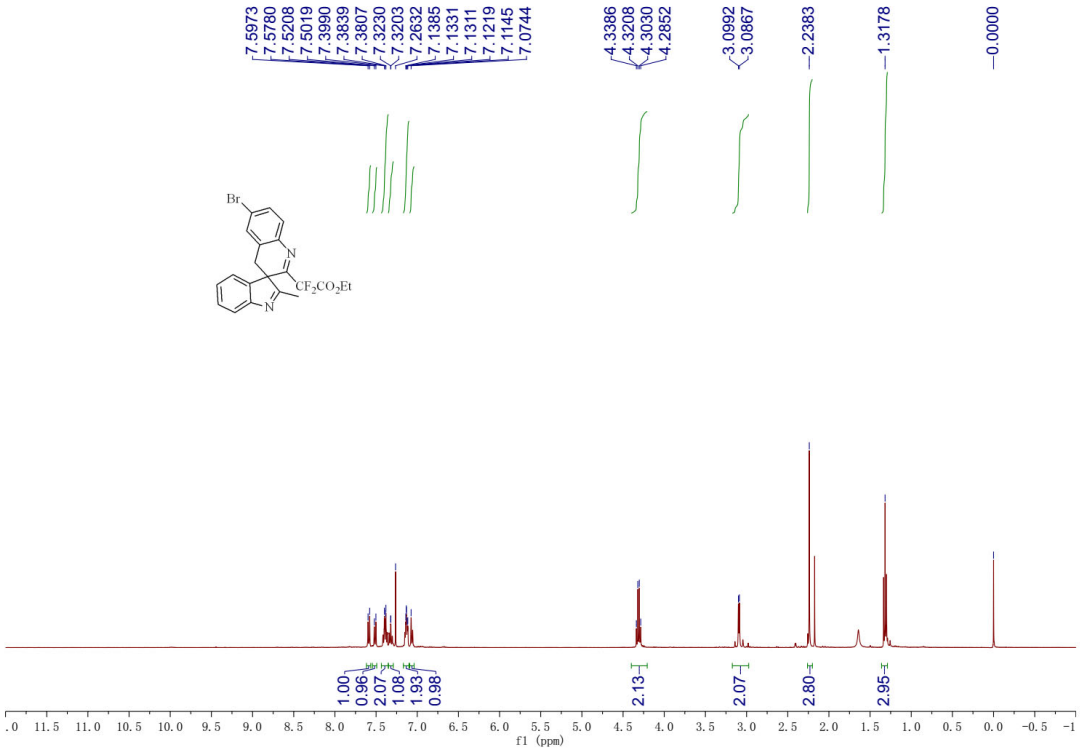
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3c



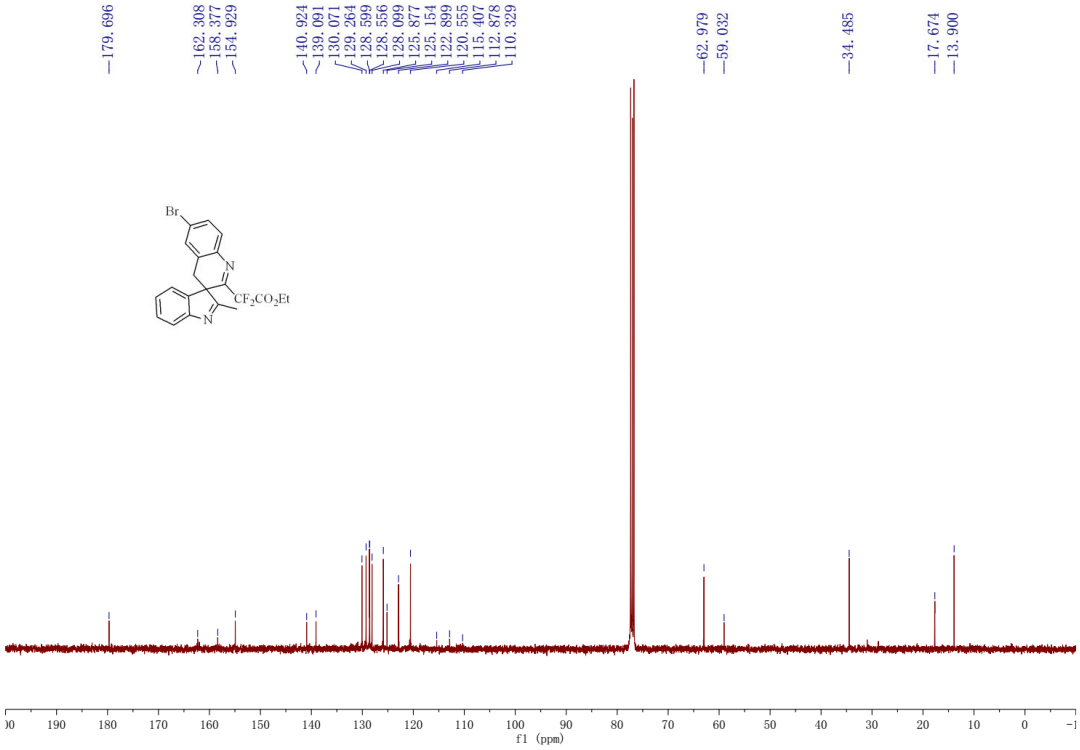
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3c



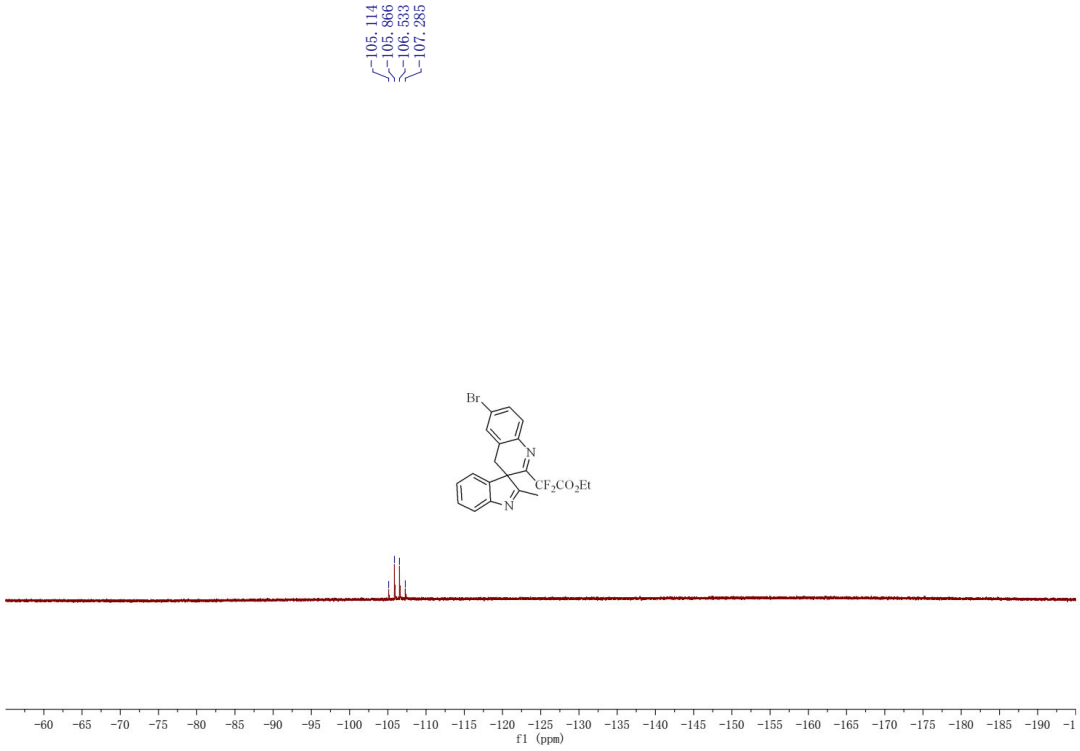
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3d



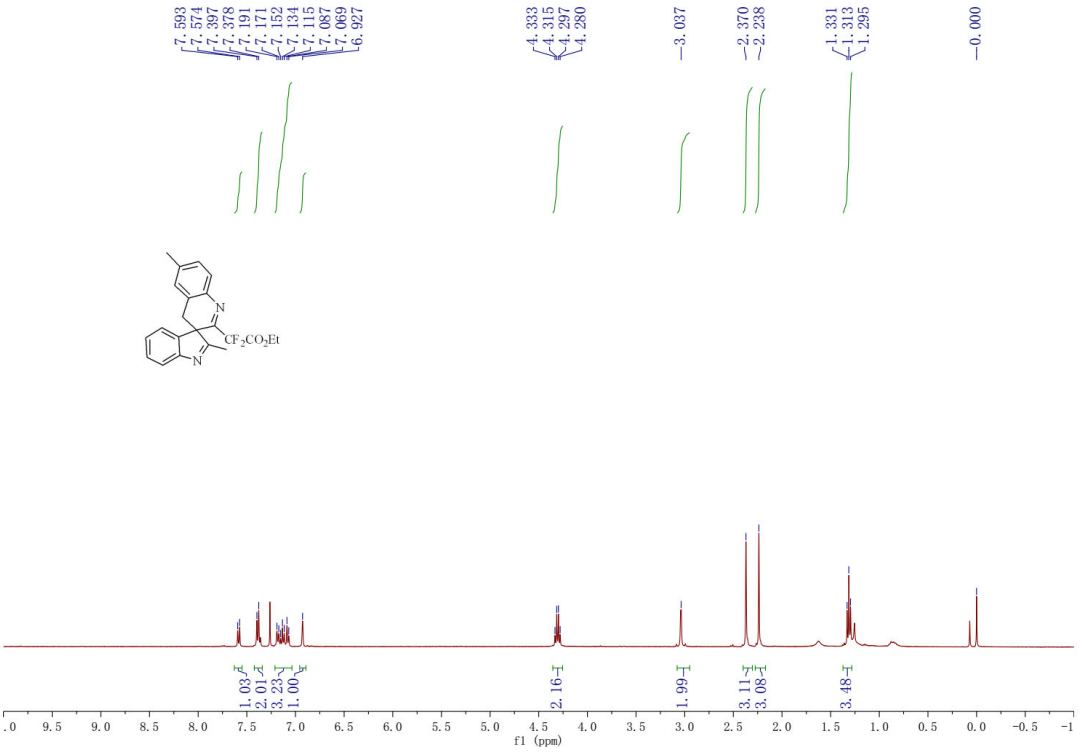
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3d



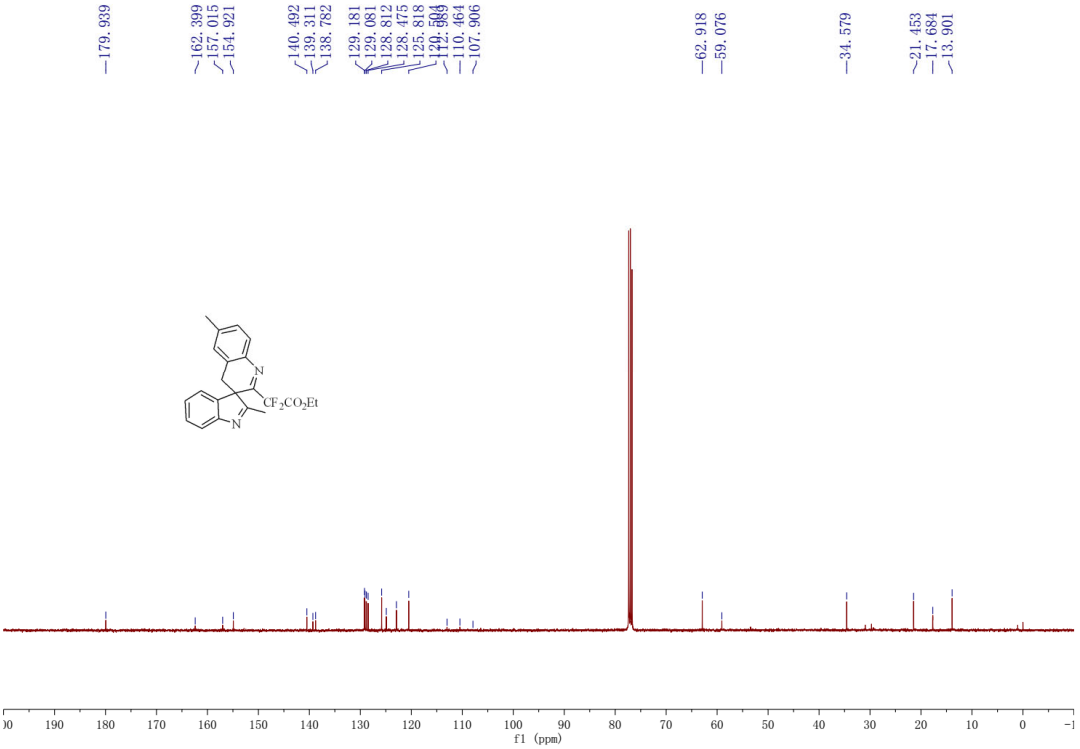
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3d



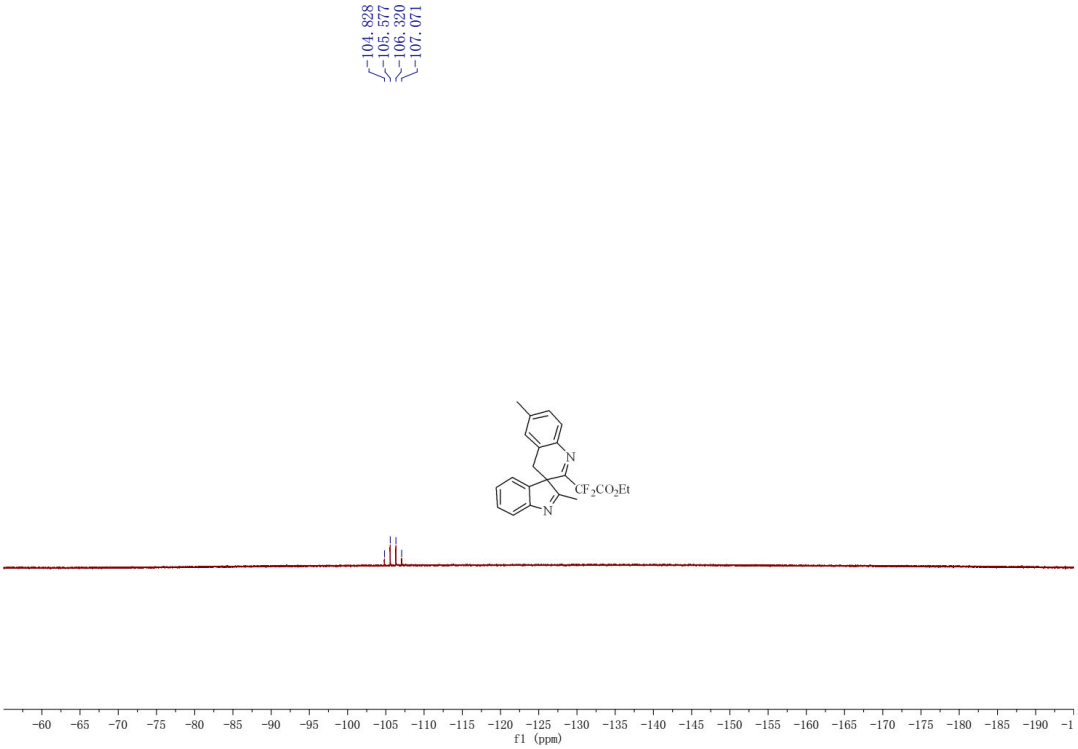
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3e



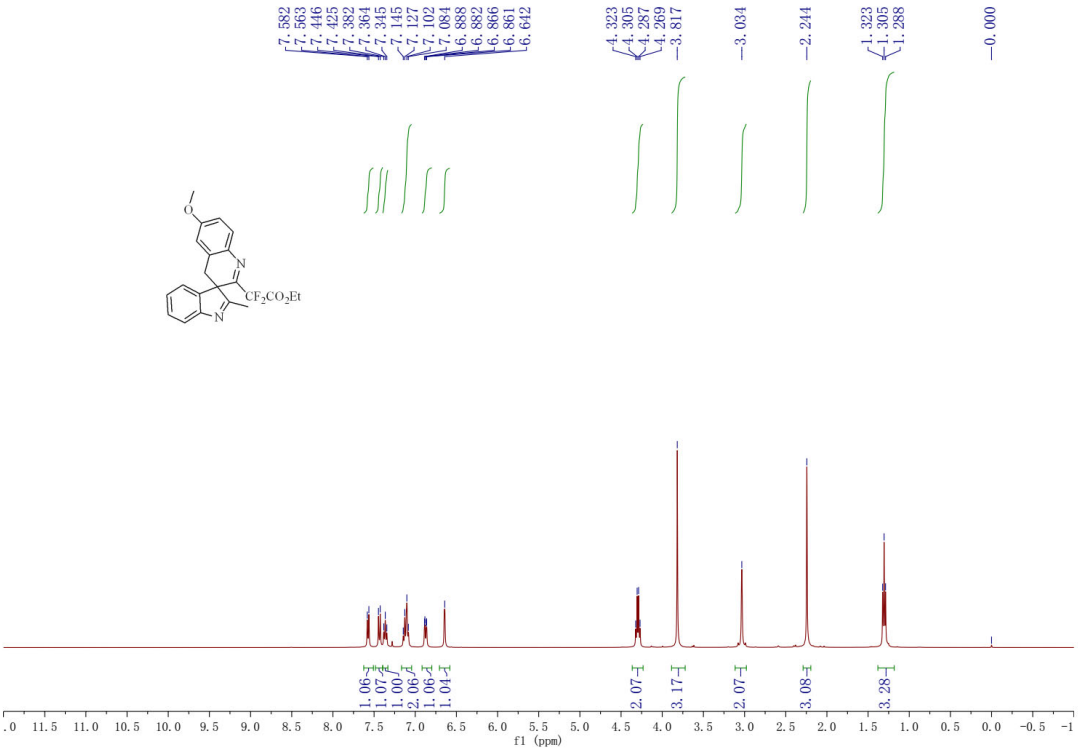
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3e



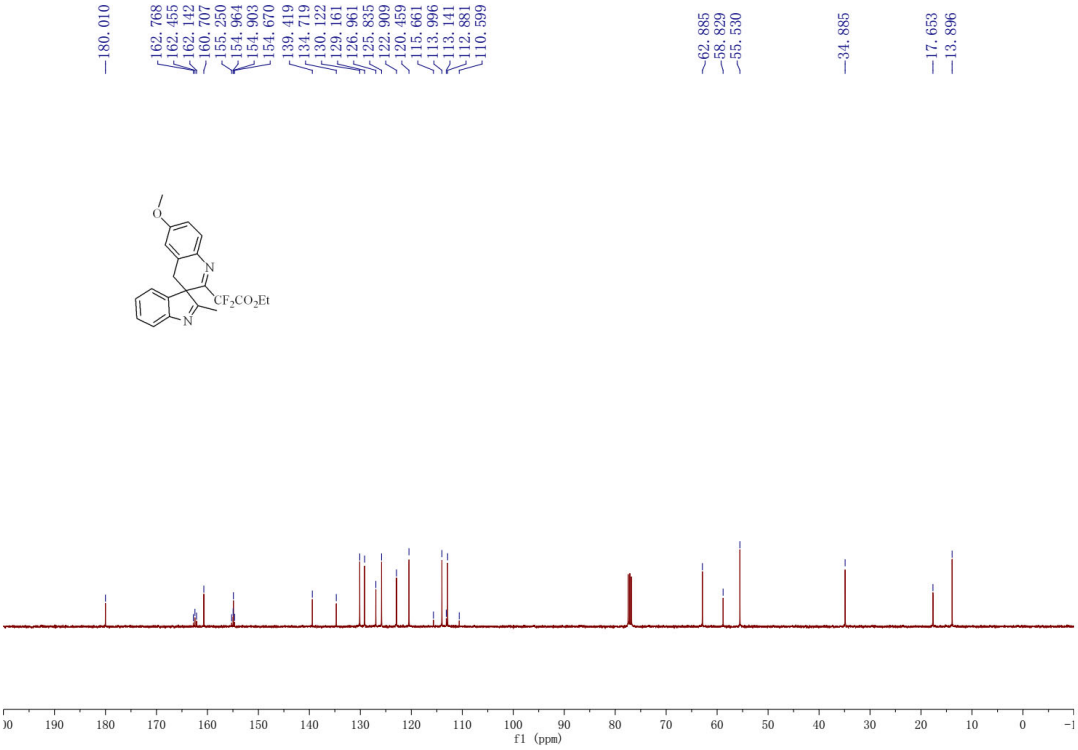
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3e



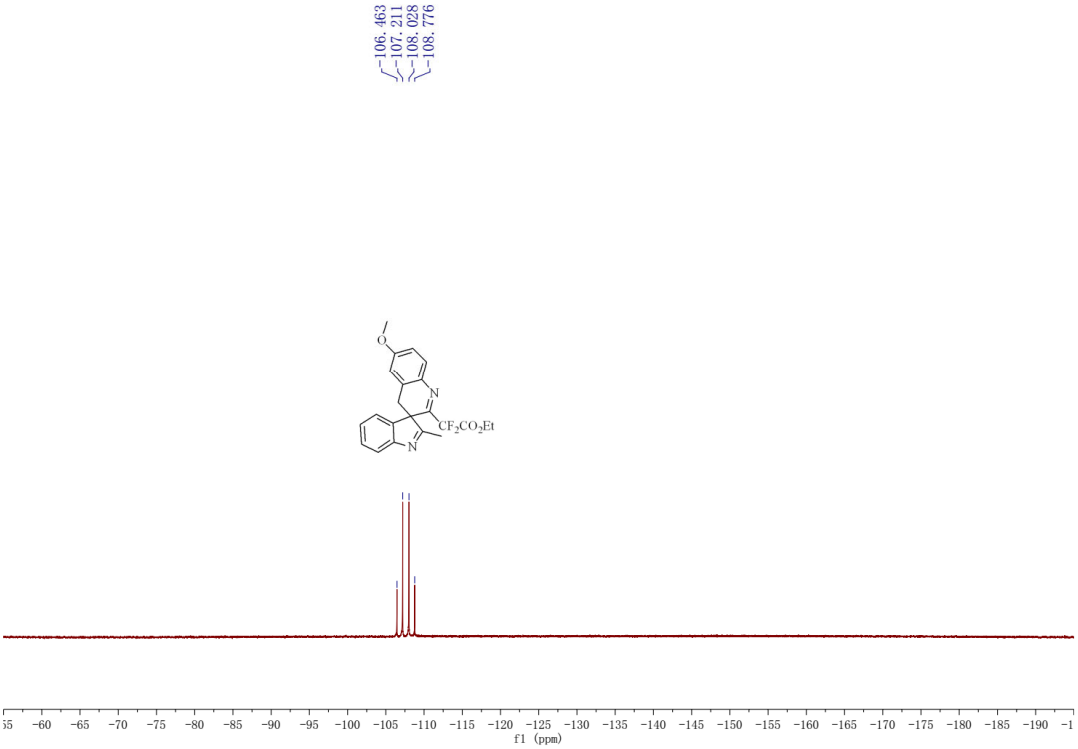
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3f



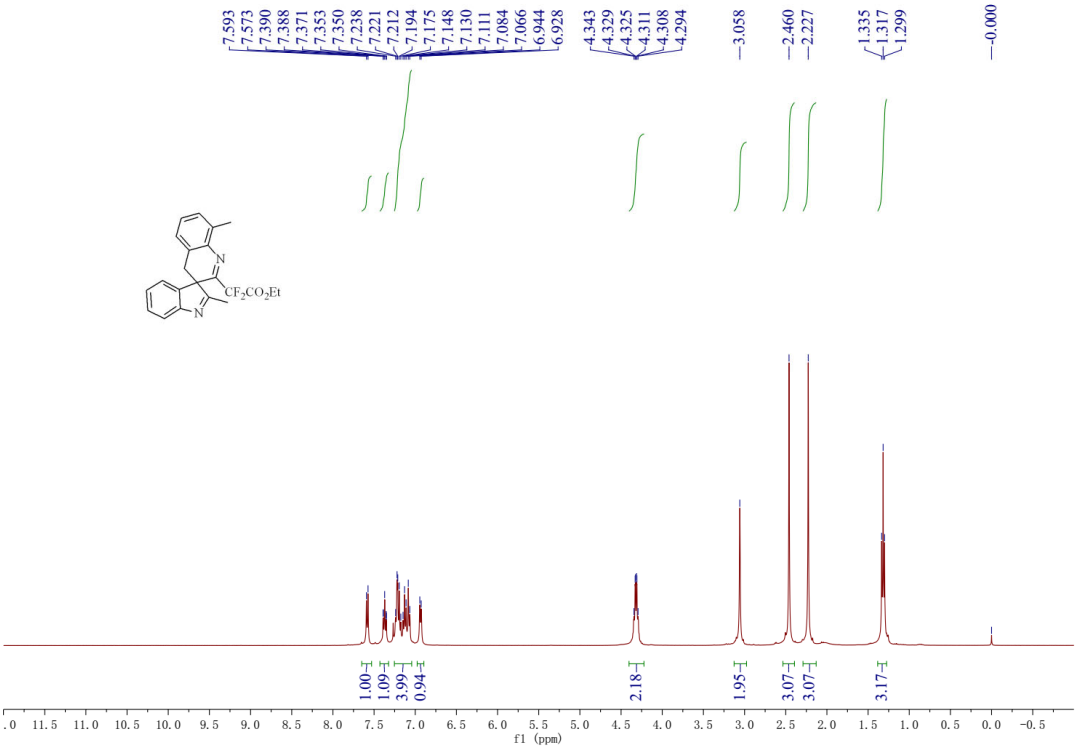
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3f



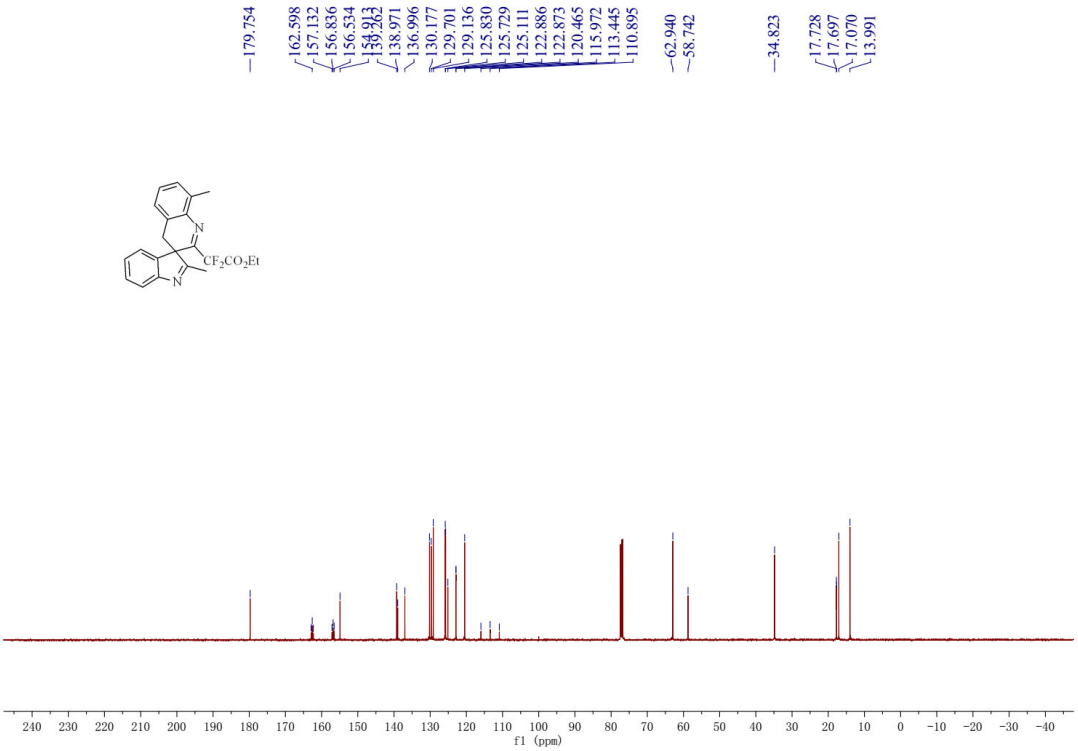
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3f



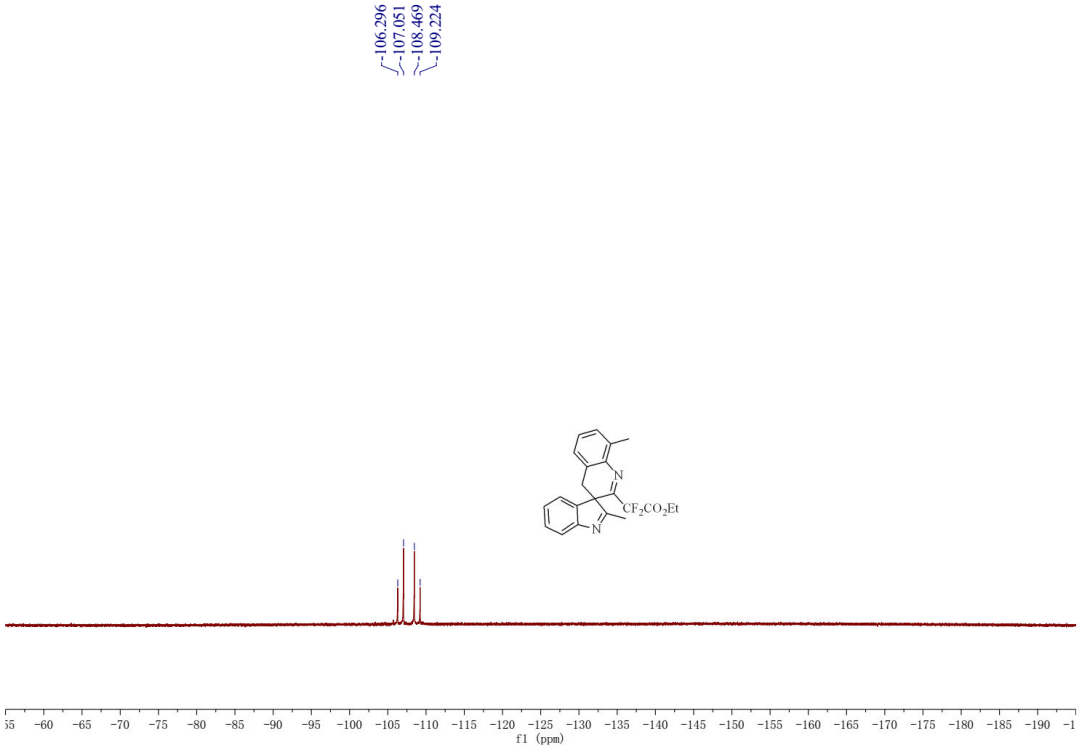
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3g



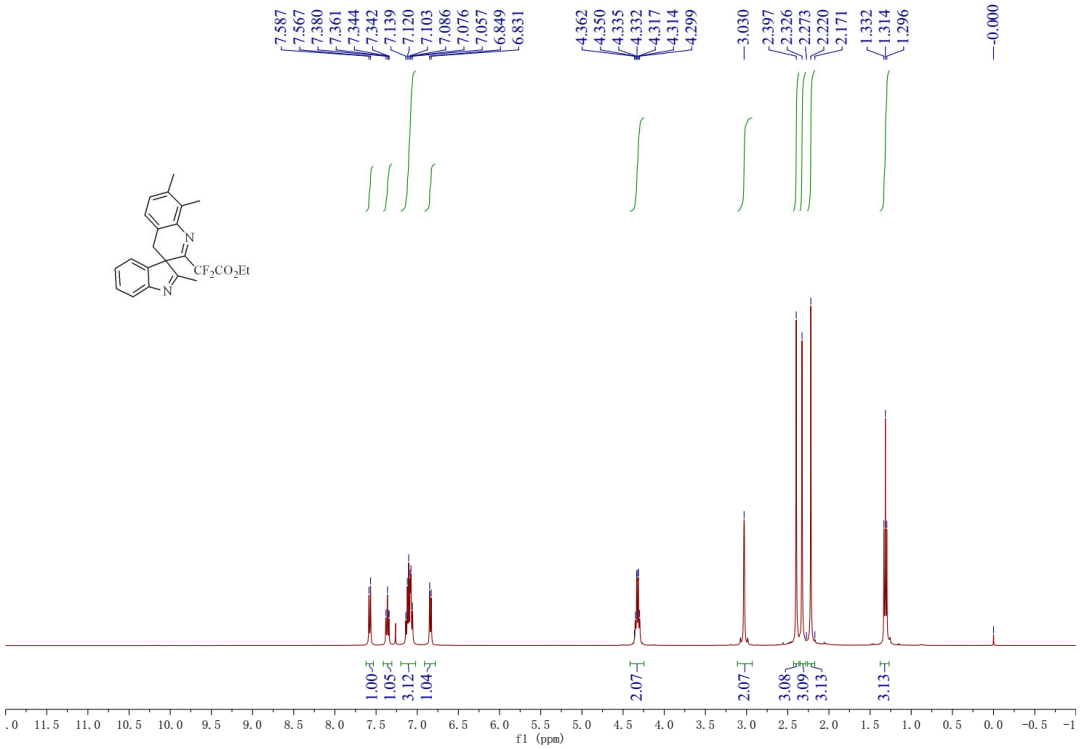
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3g



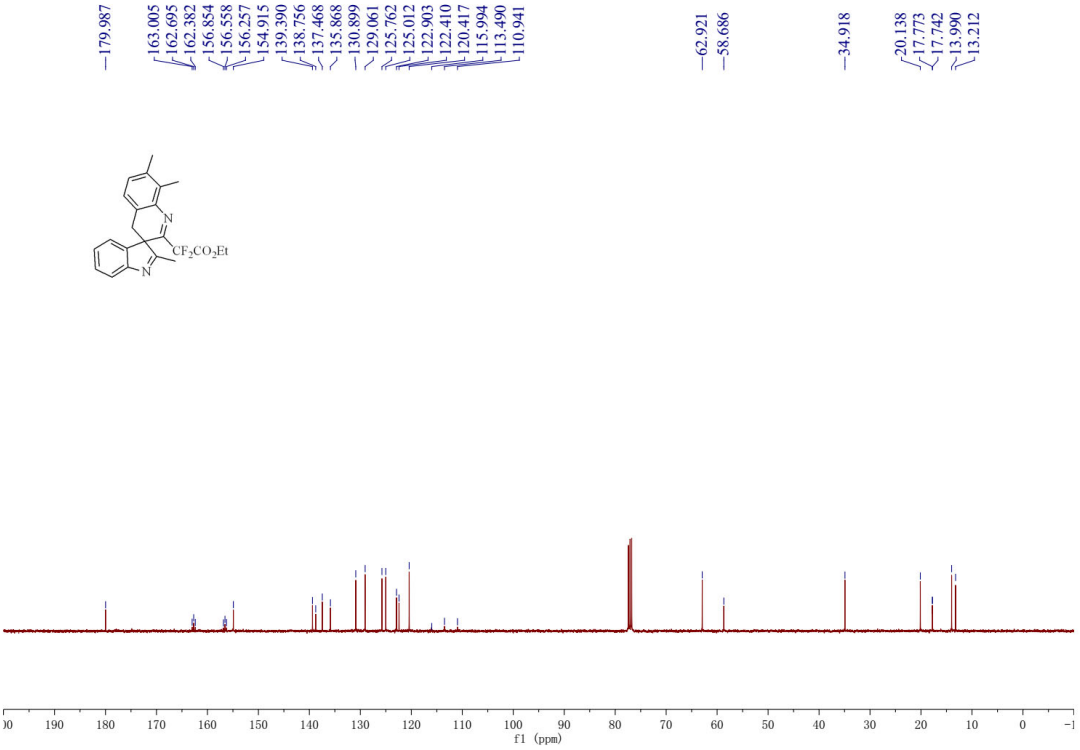
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3g



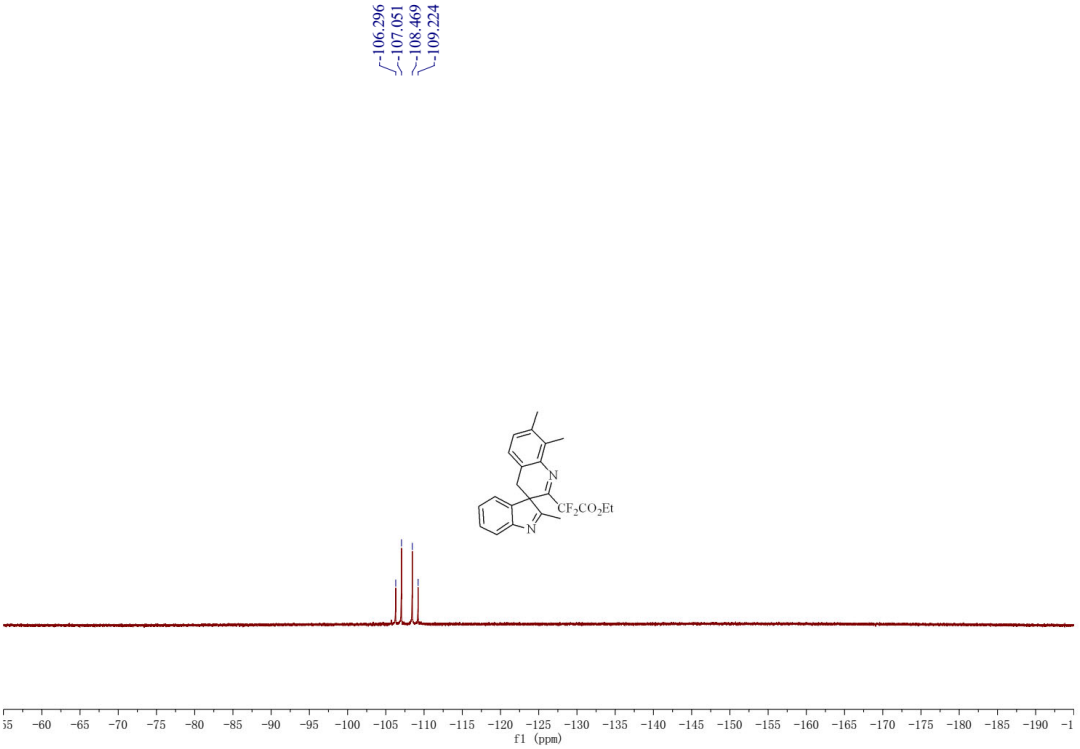
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3h



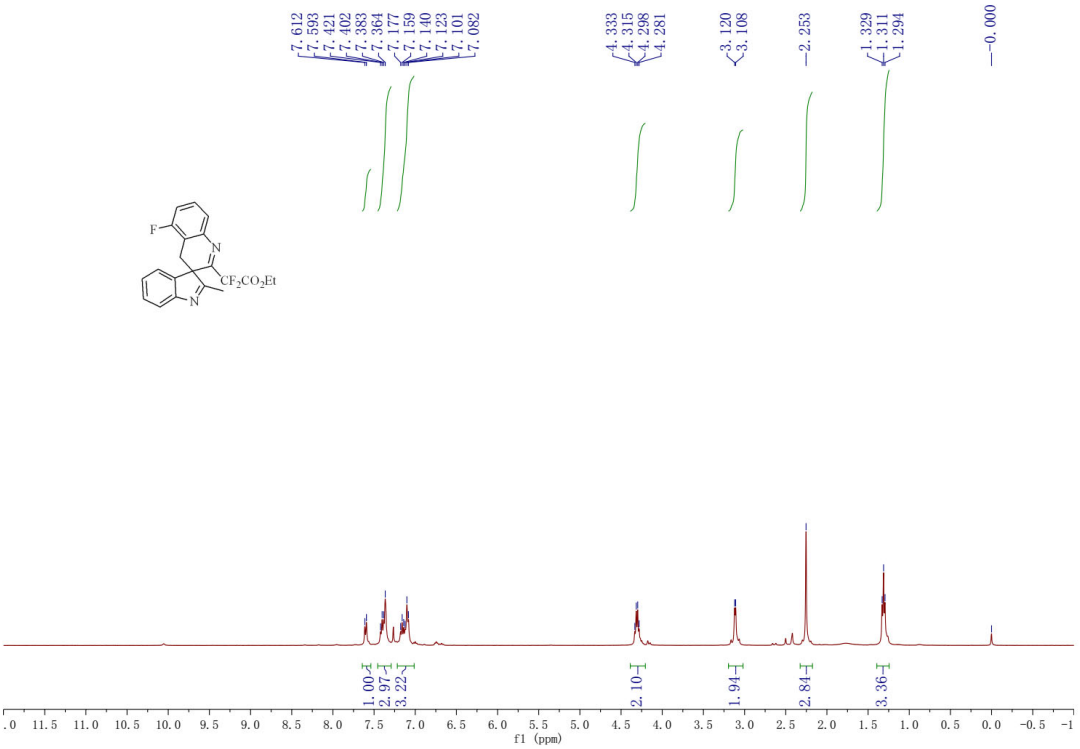
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3h



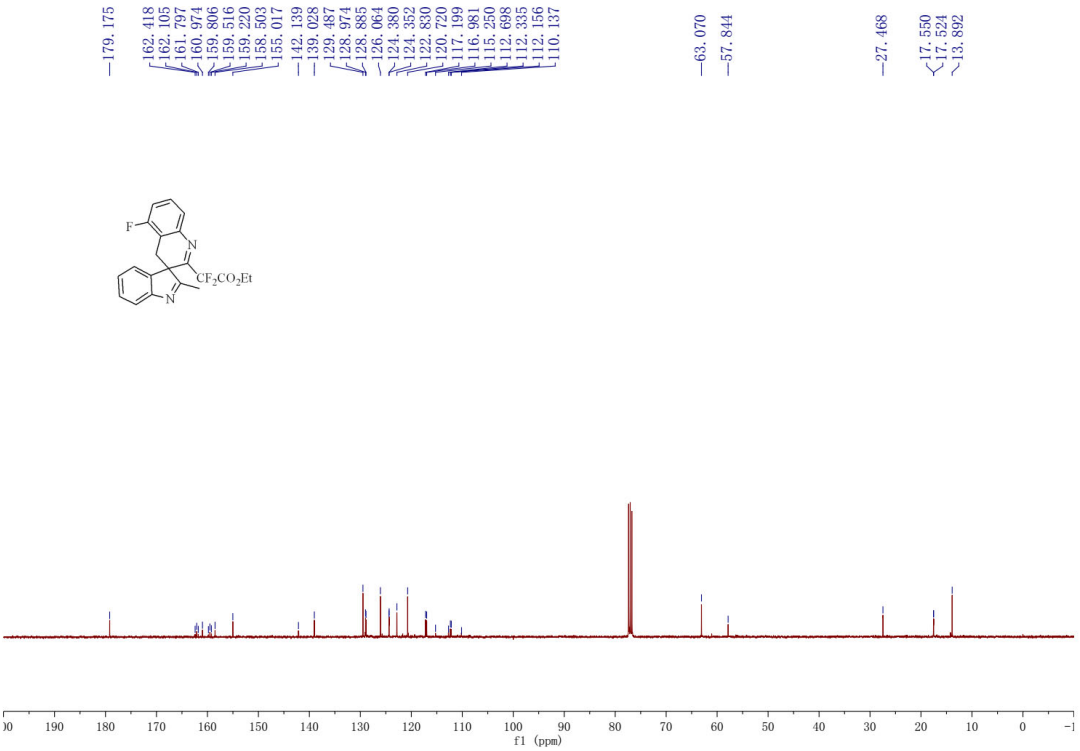
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3h



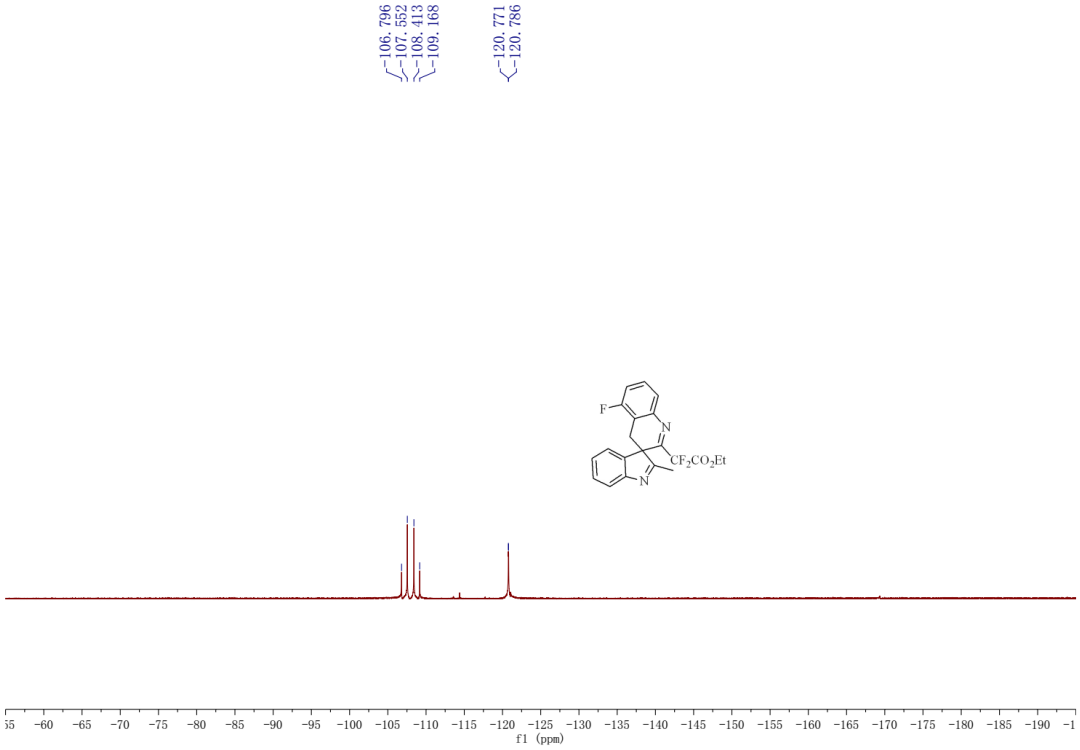
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3i



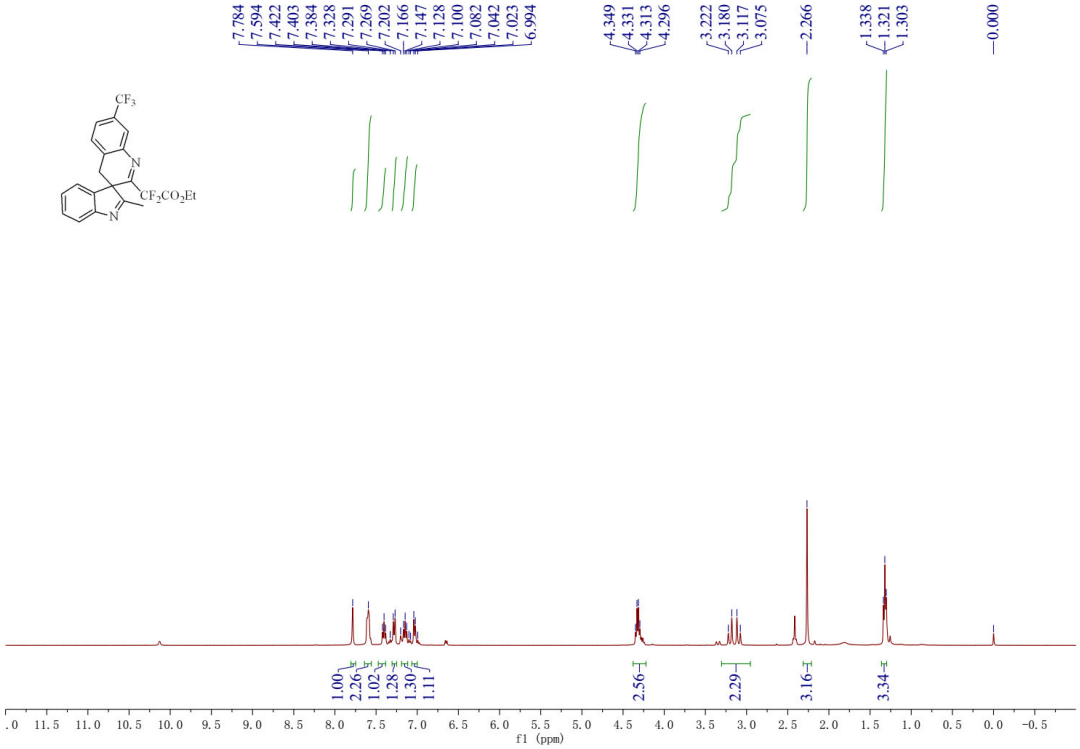
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3i



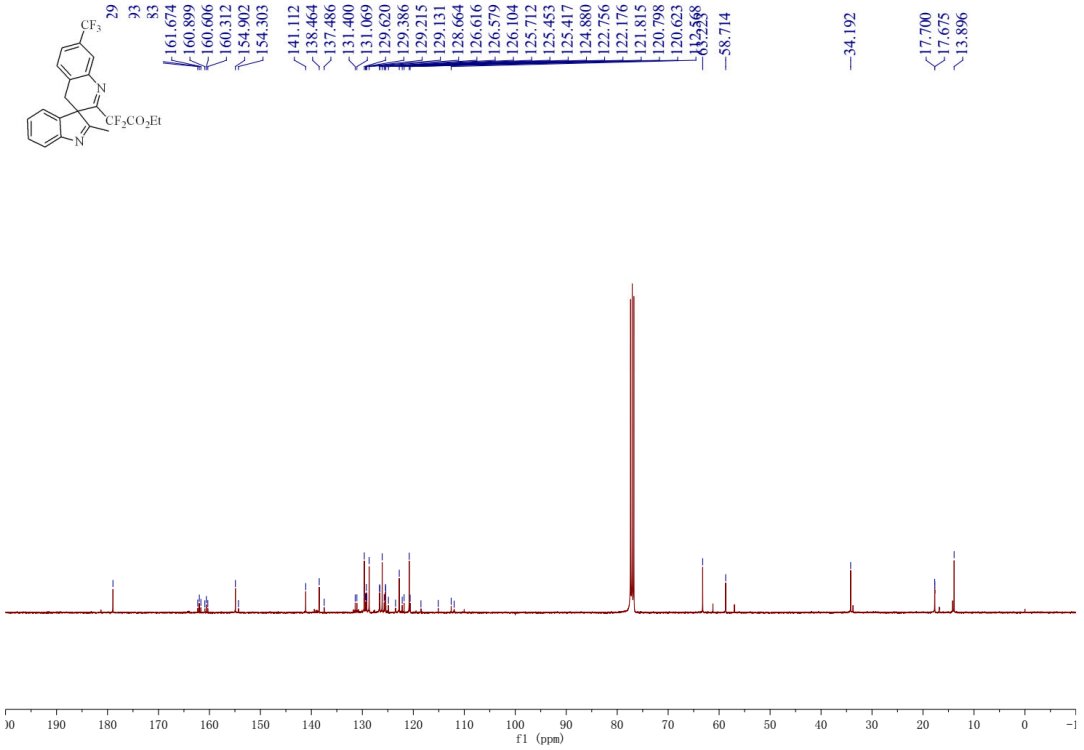
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3i



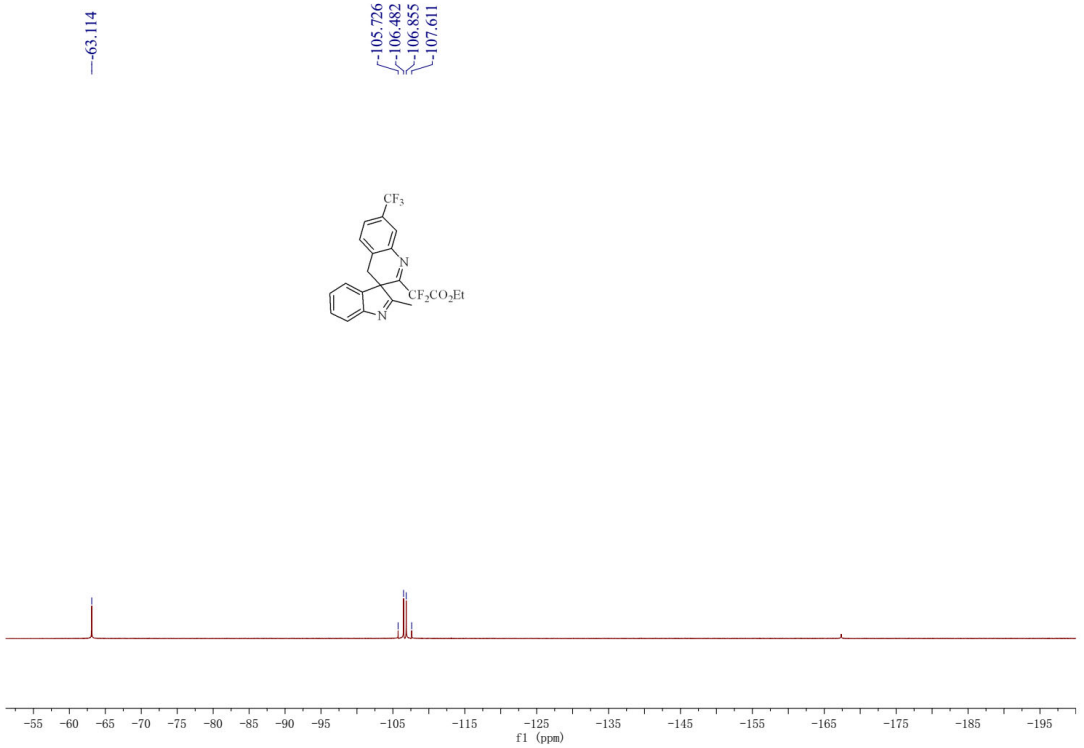
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3j



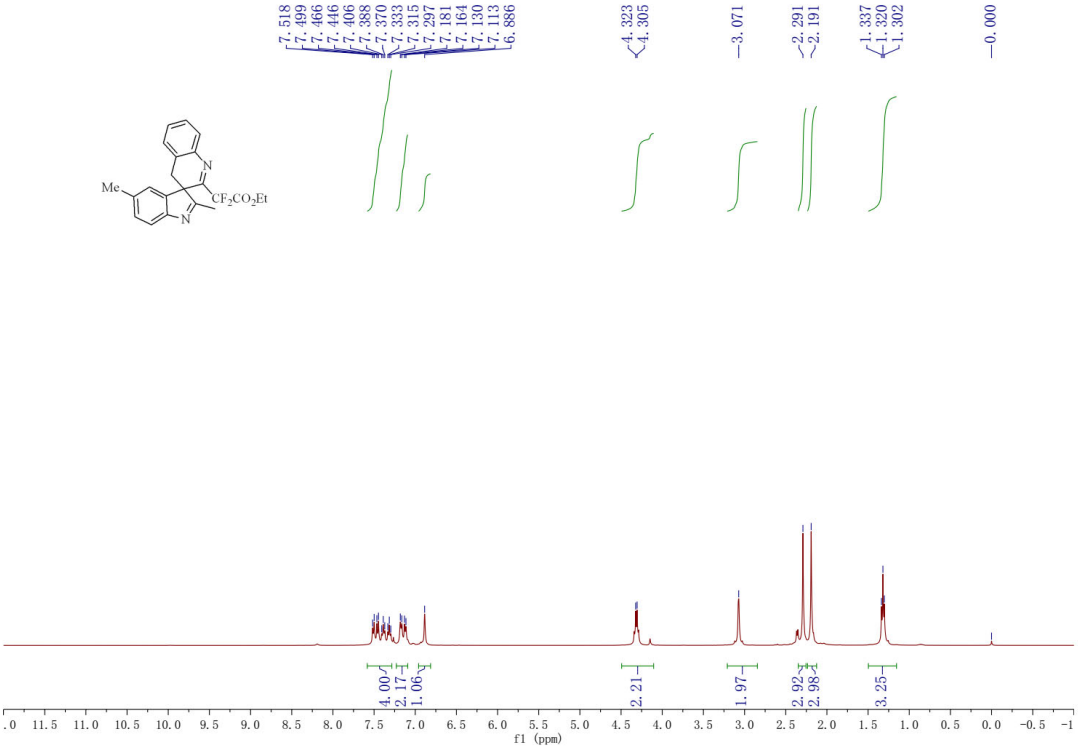
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3j



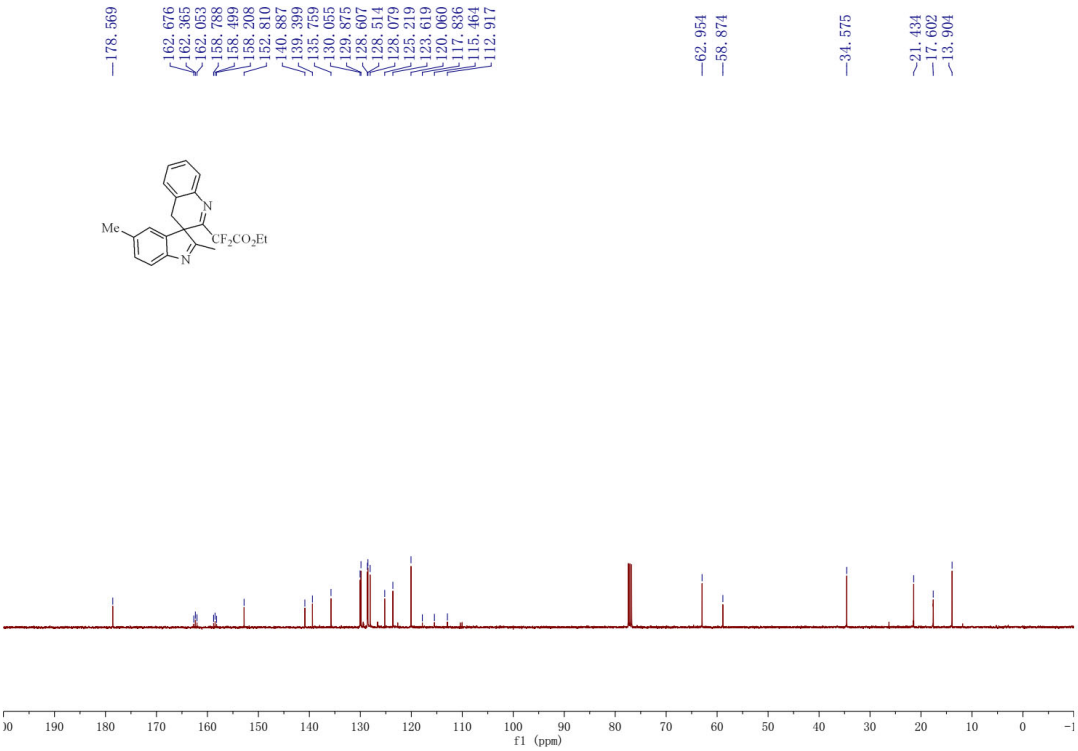
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3j



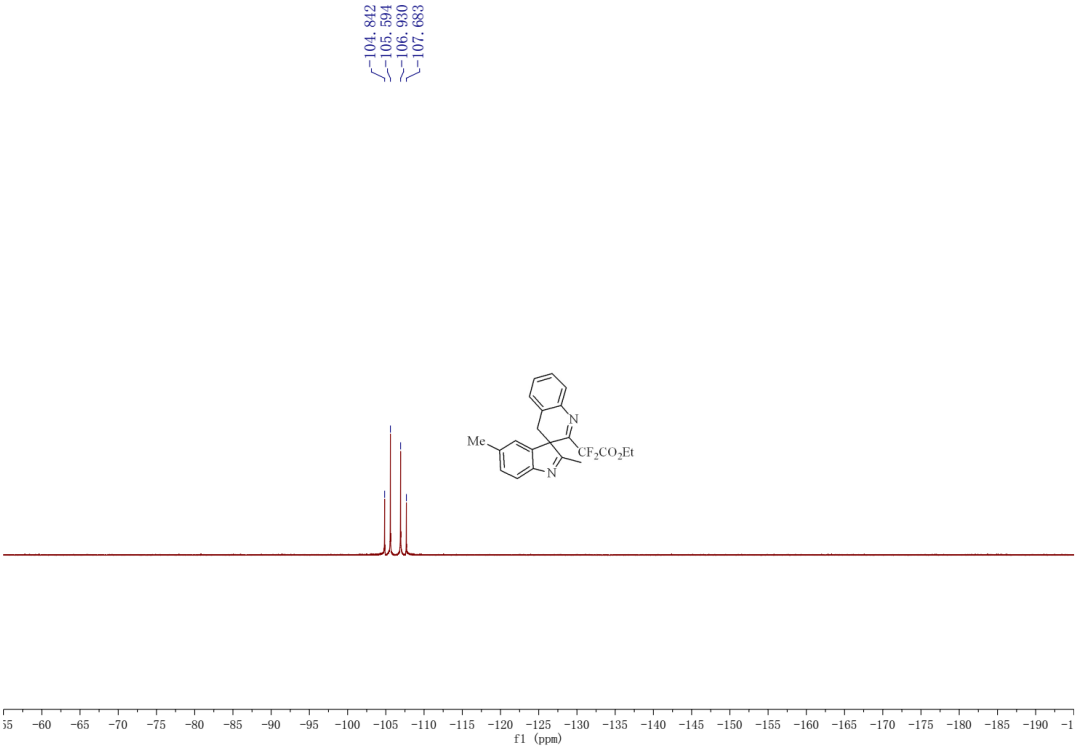
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3k



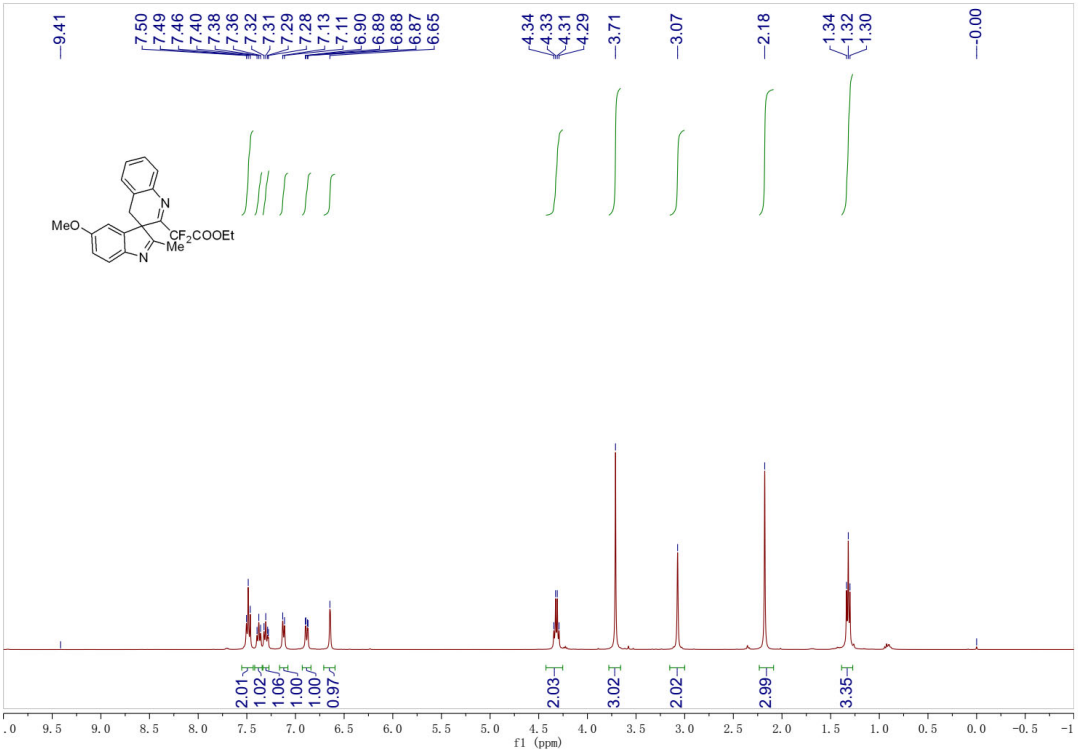
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3k



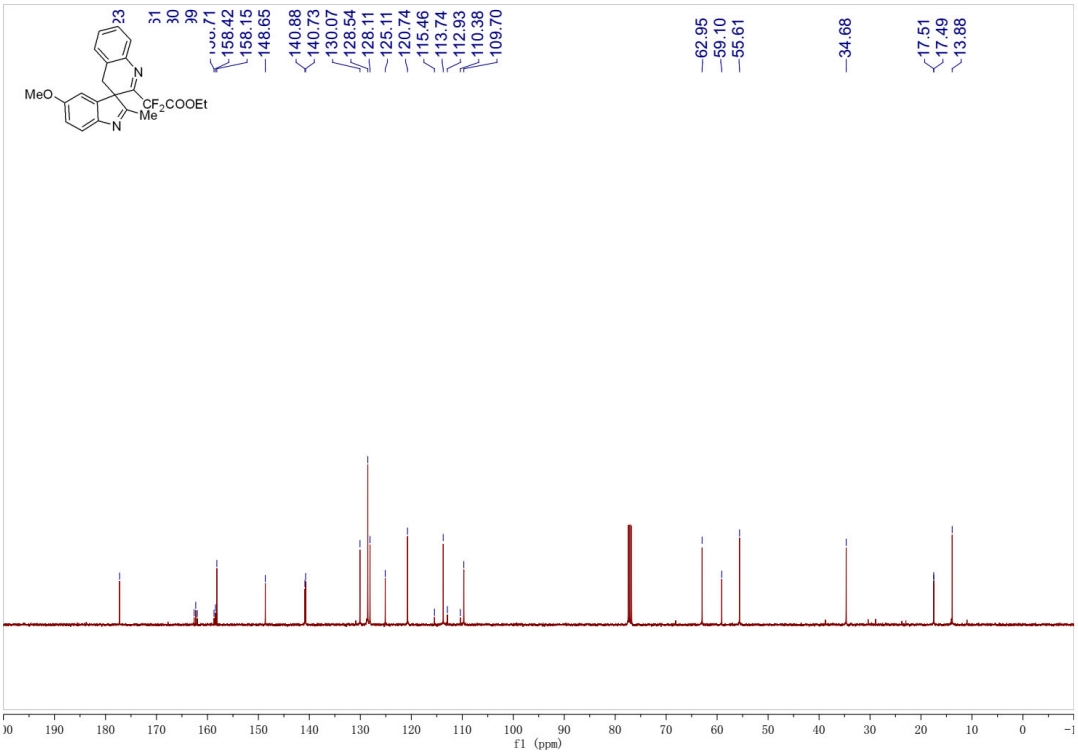
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3k



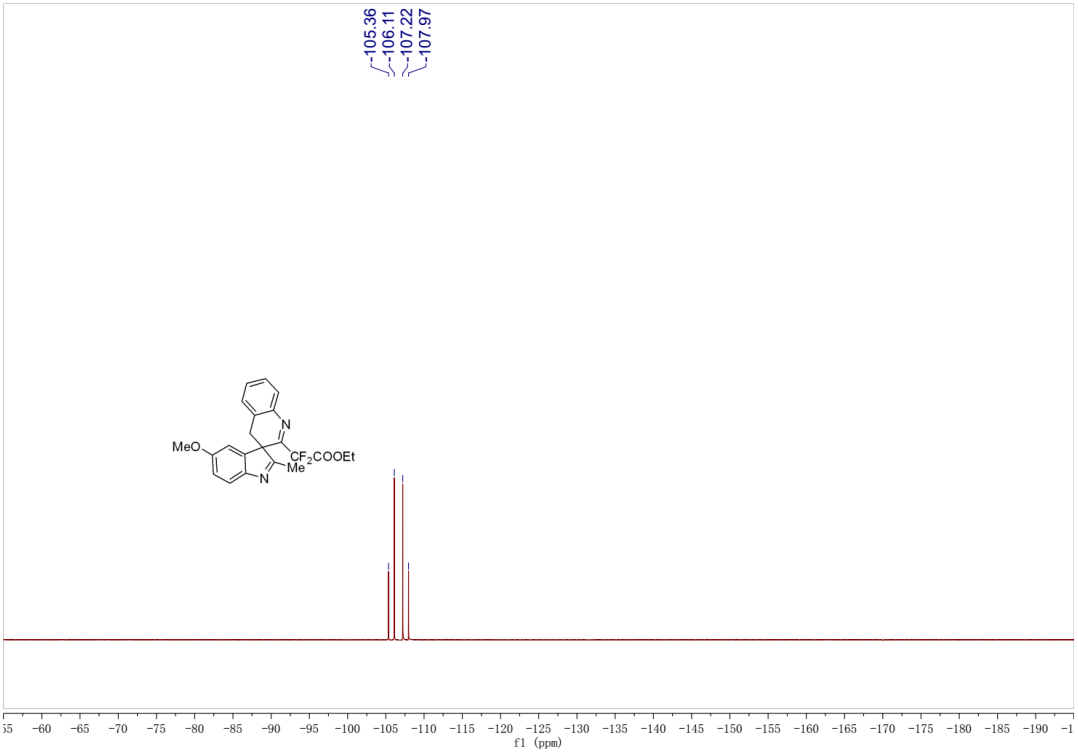
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3l



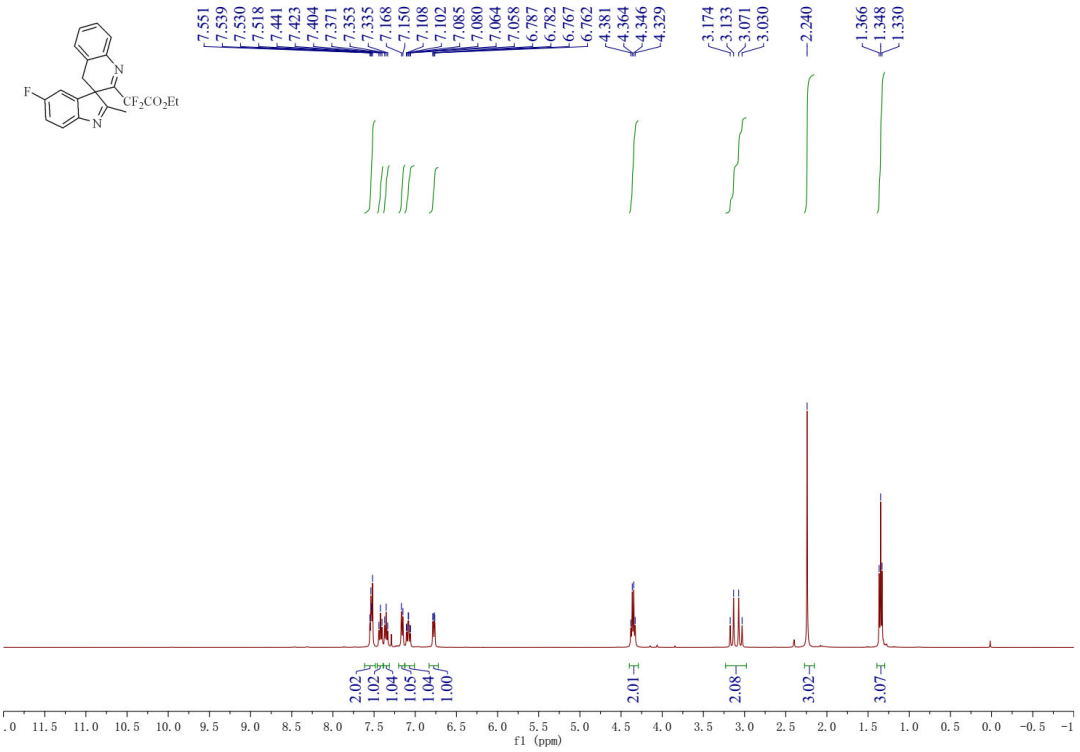
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3l



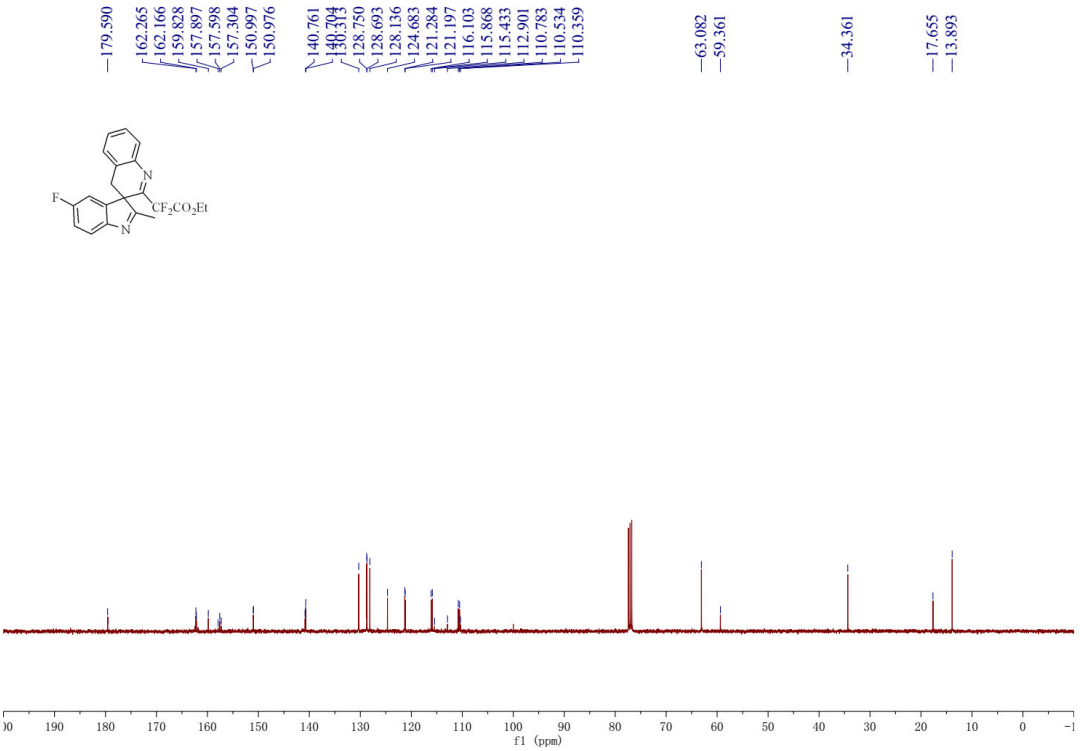
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3l



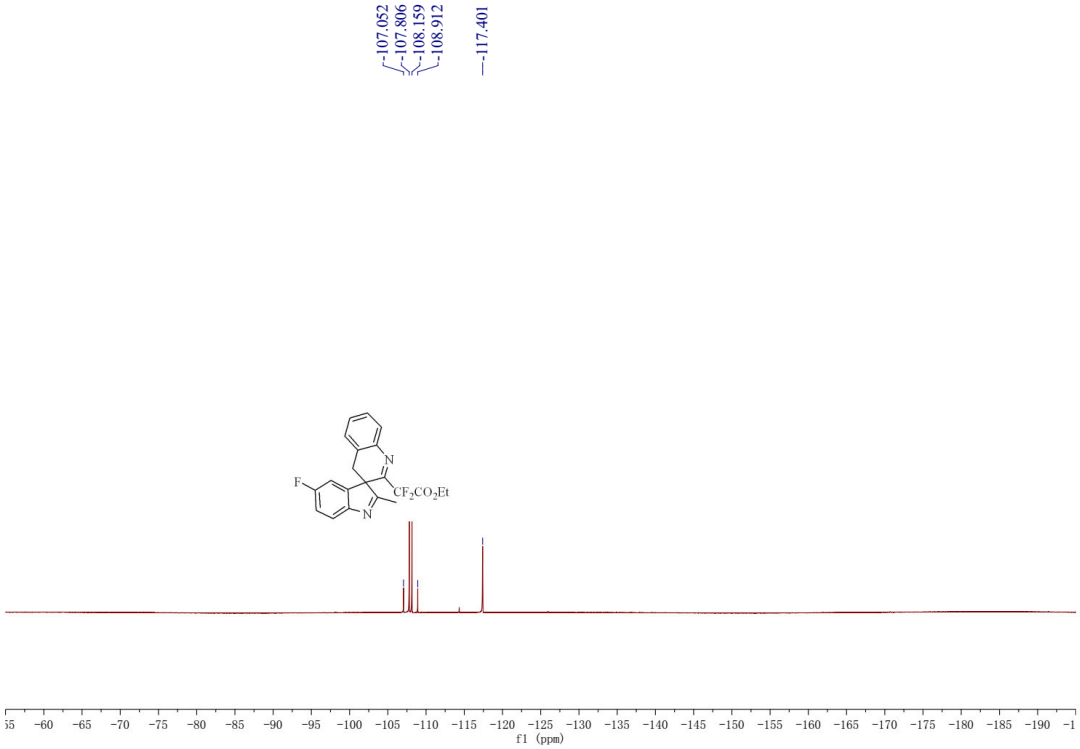
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3m



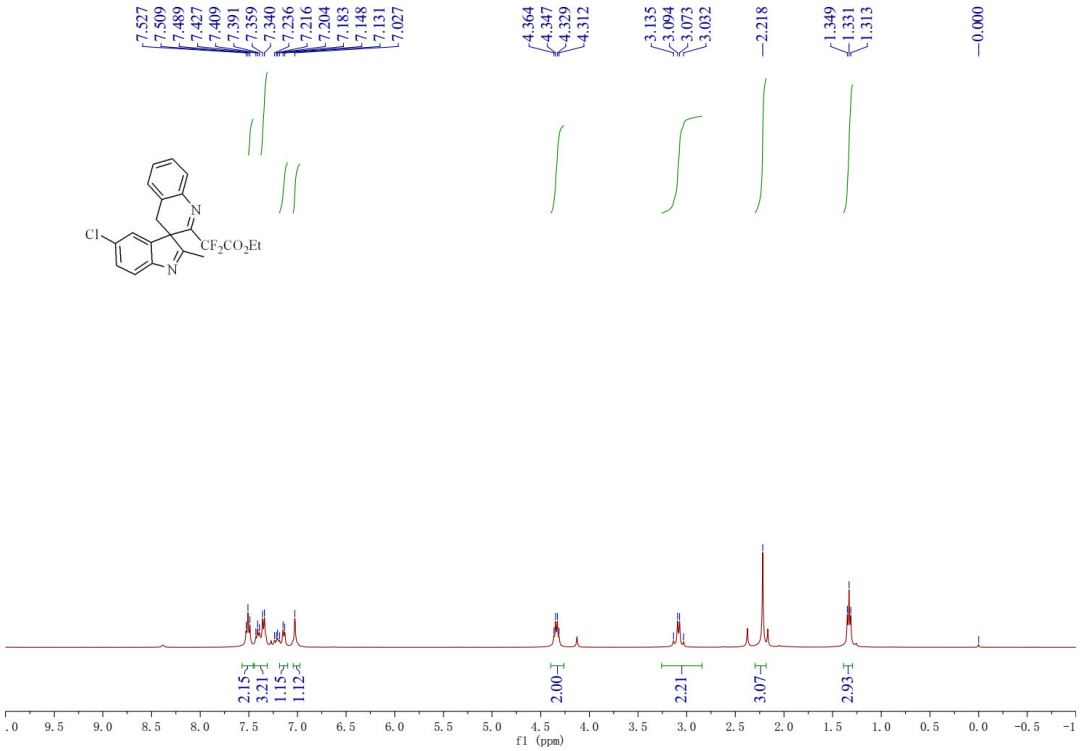
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3m



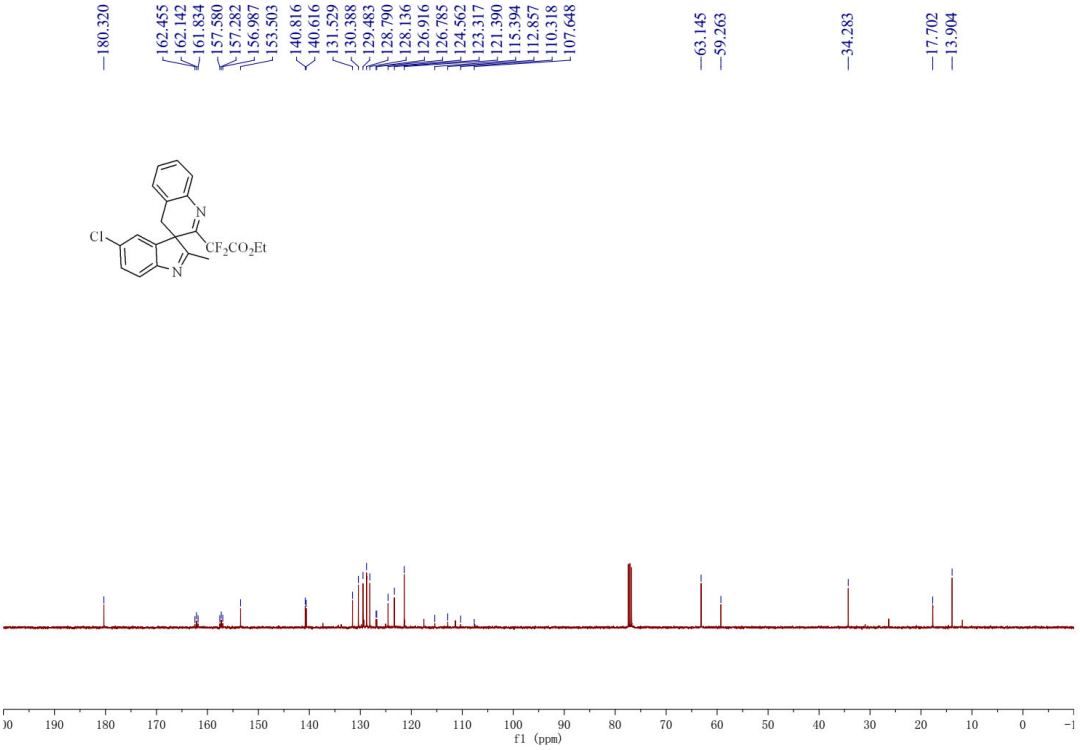
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3m



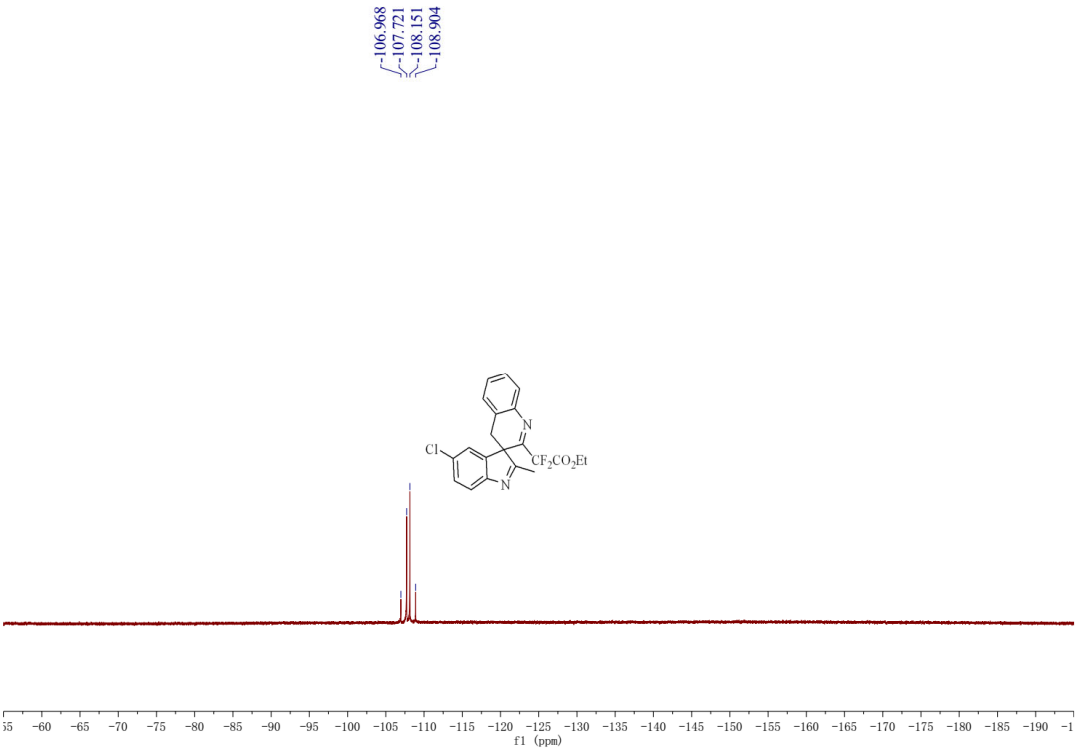
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3n



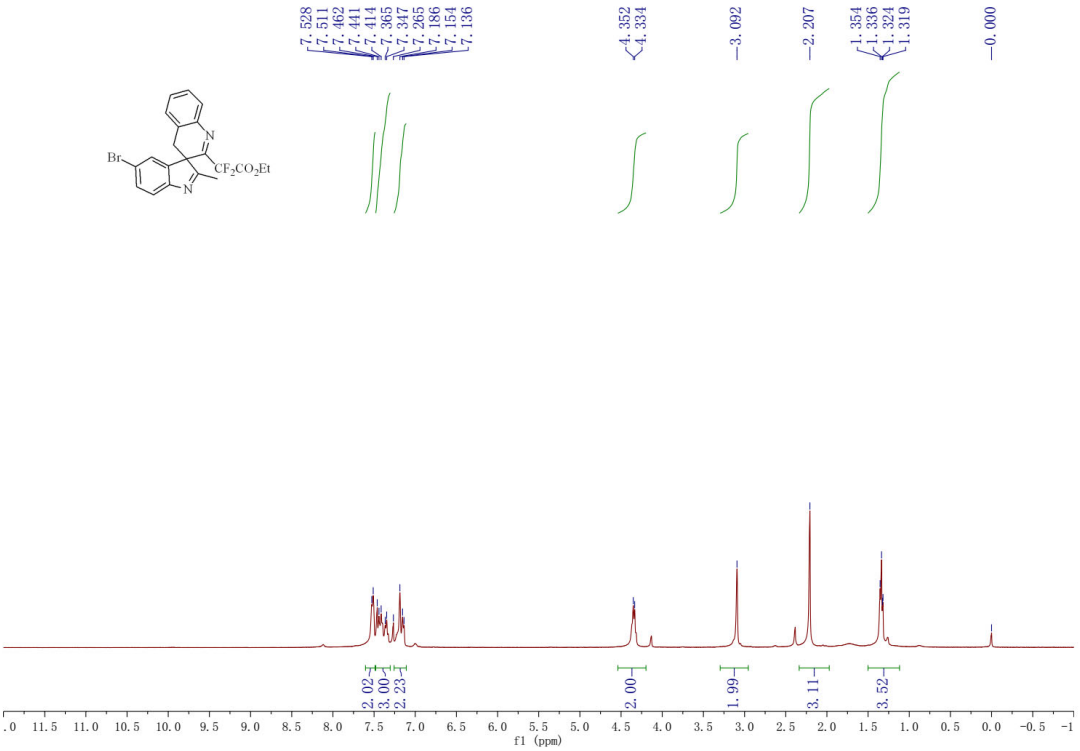
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3n



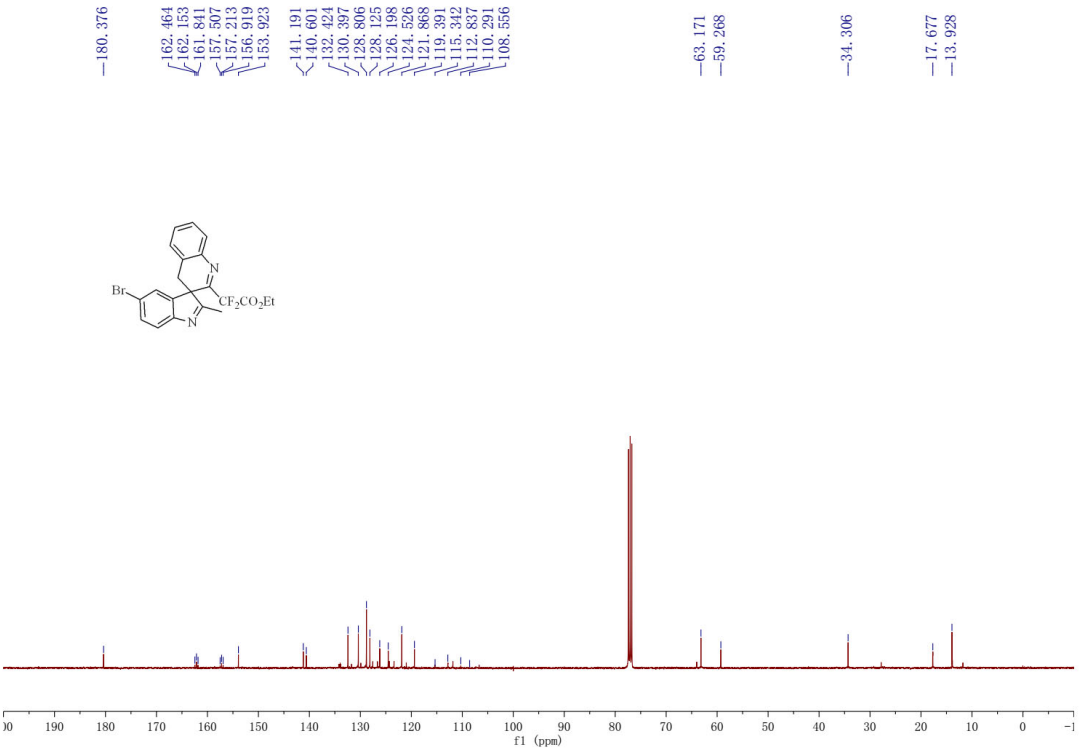
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3n



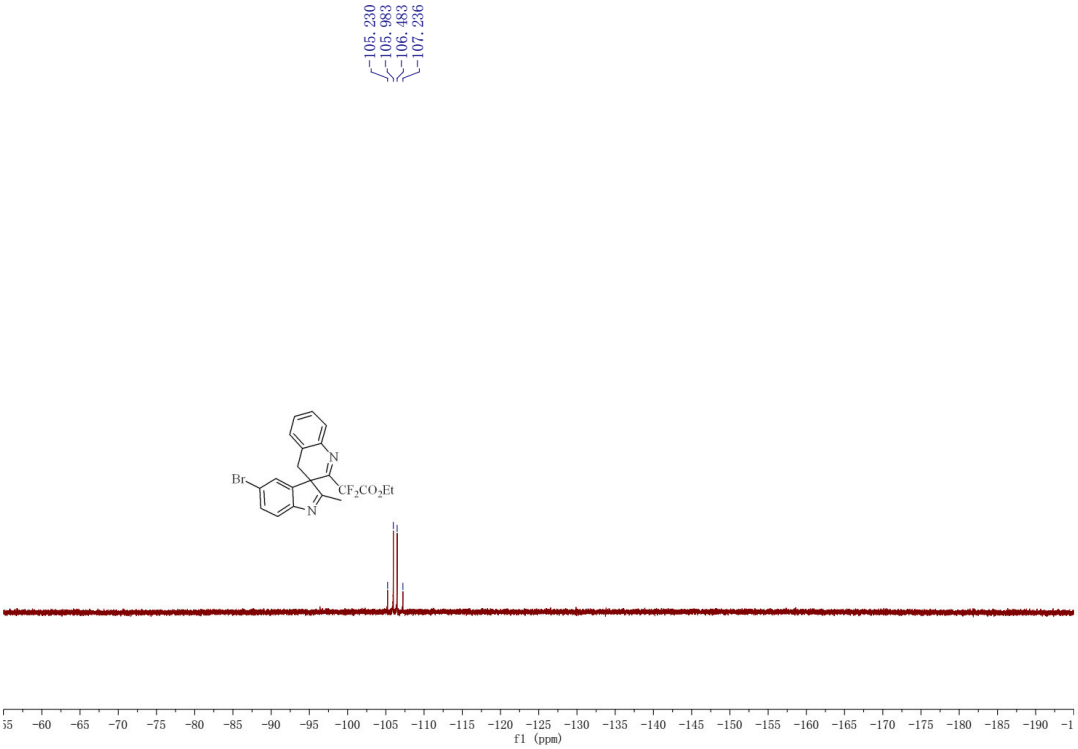
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3o



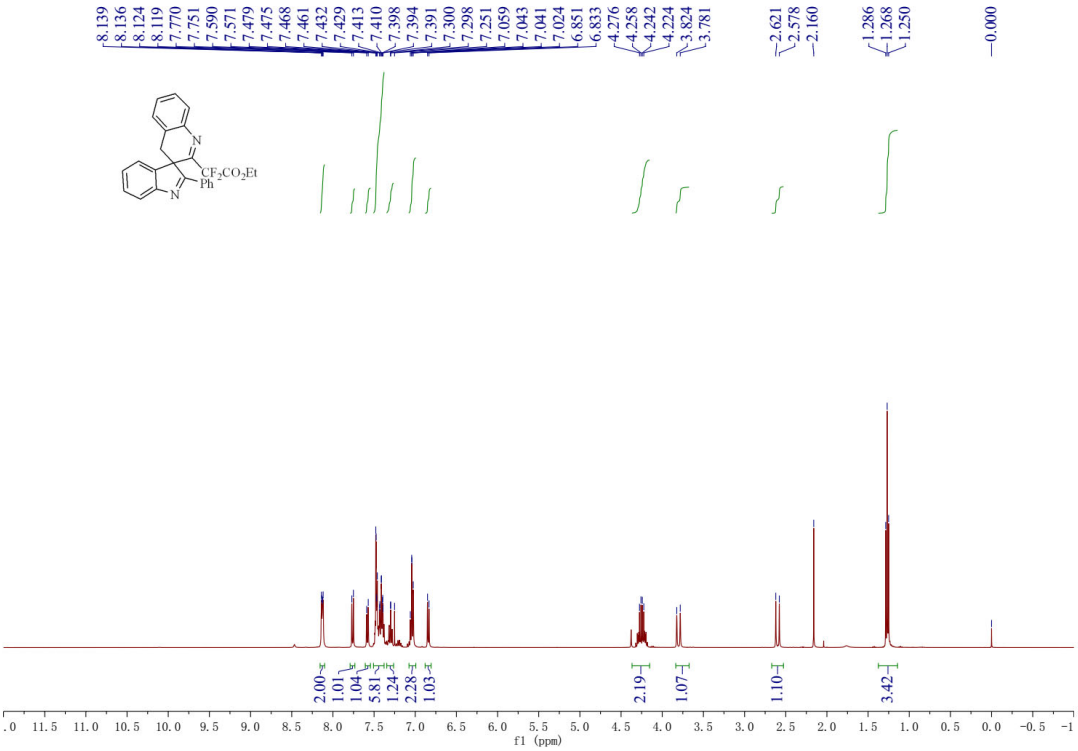
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3o



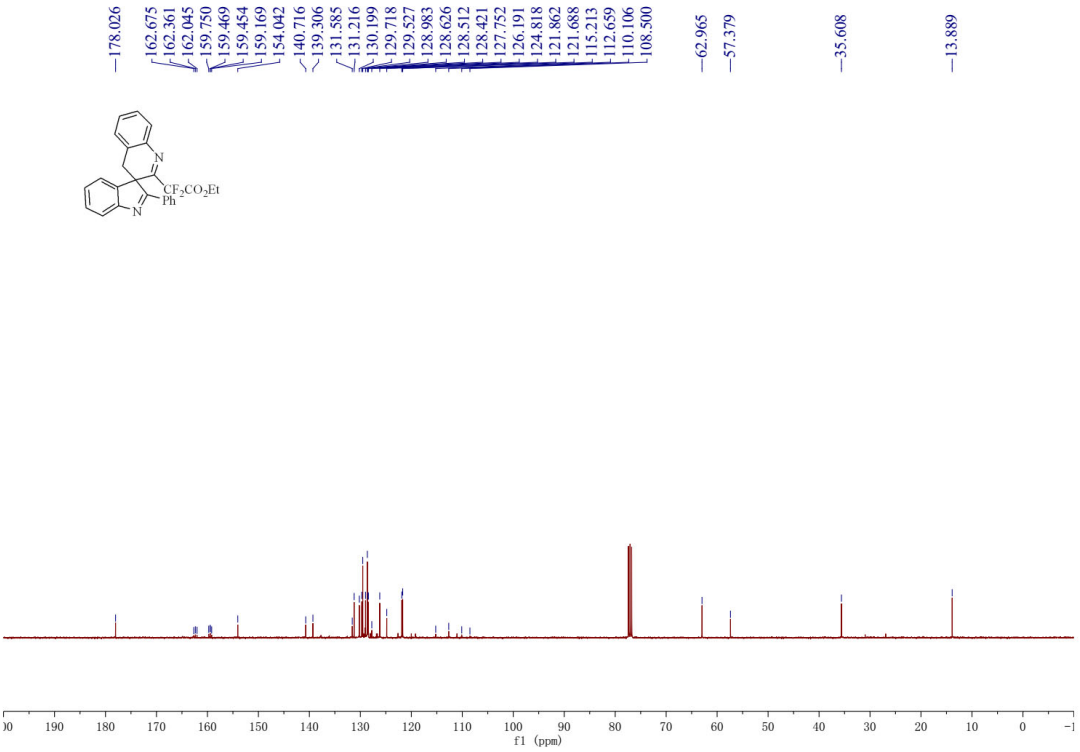
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3o



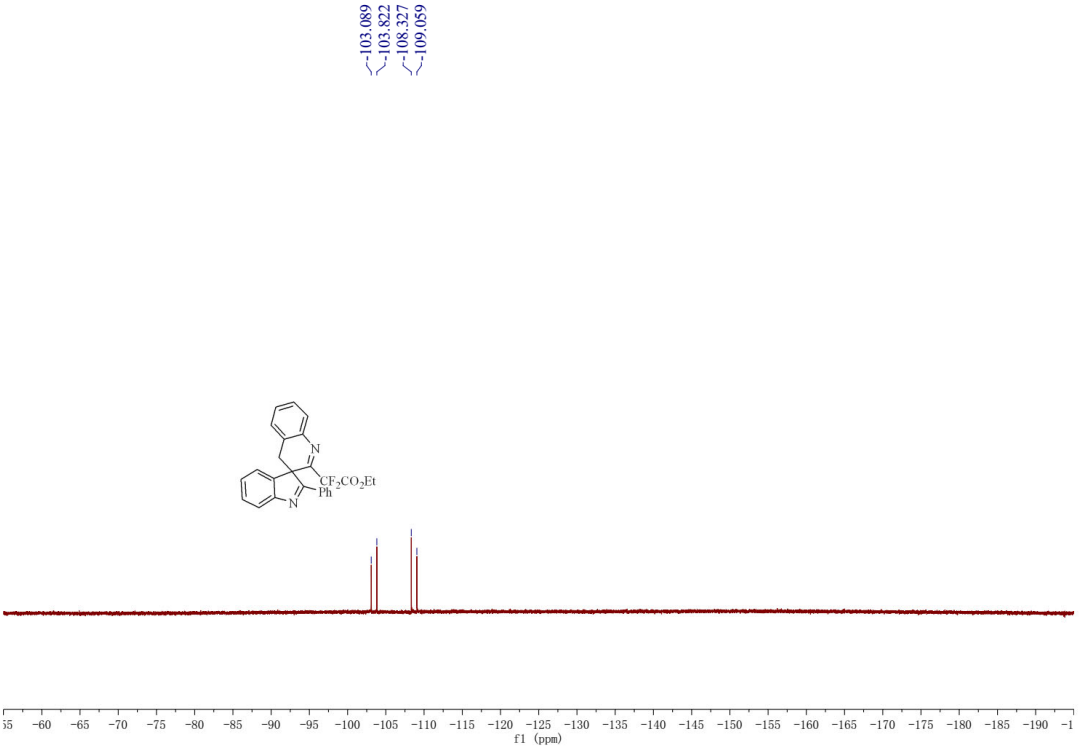
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3p



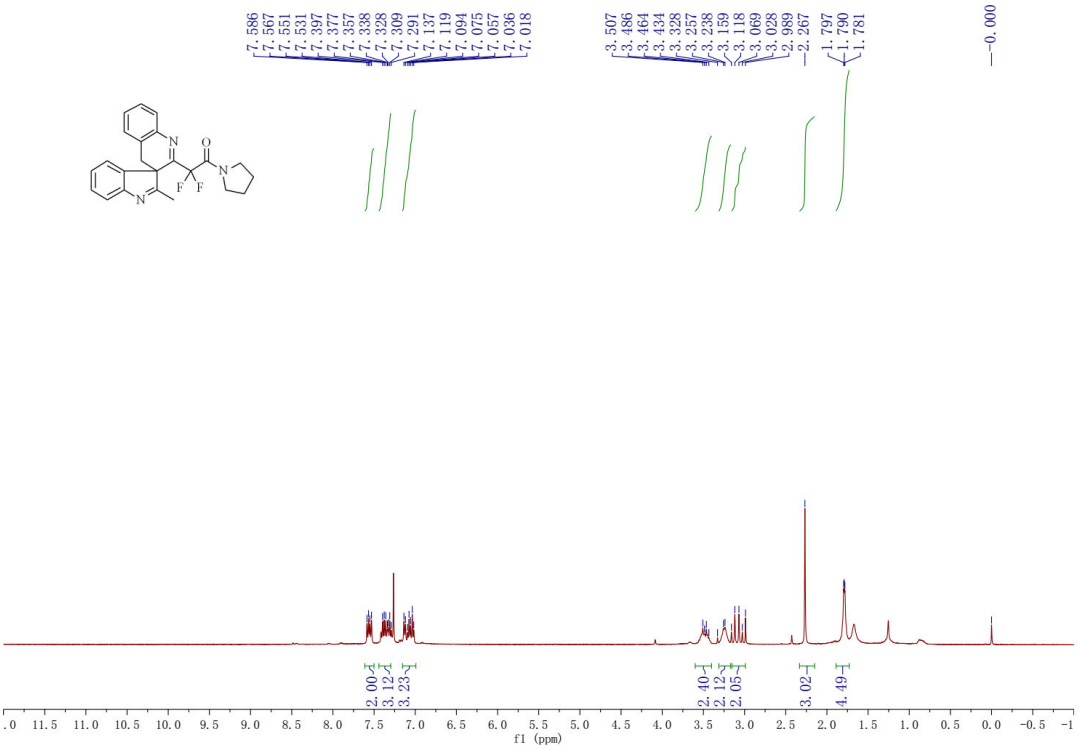
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3p



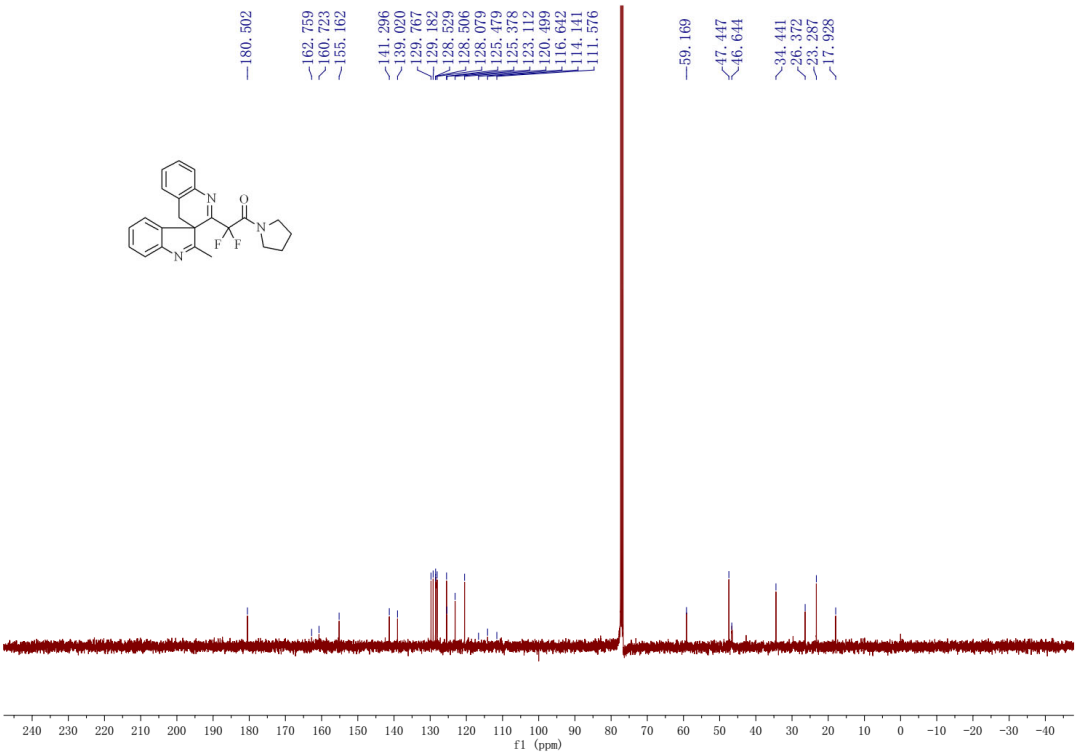
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3p



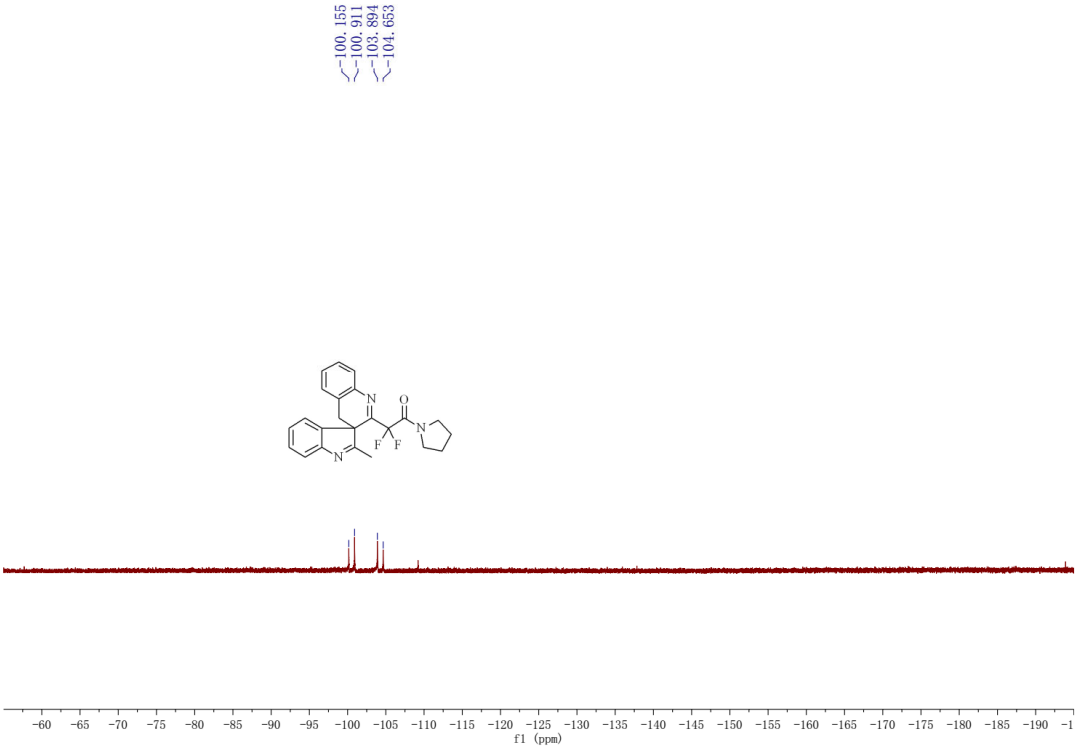
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3q



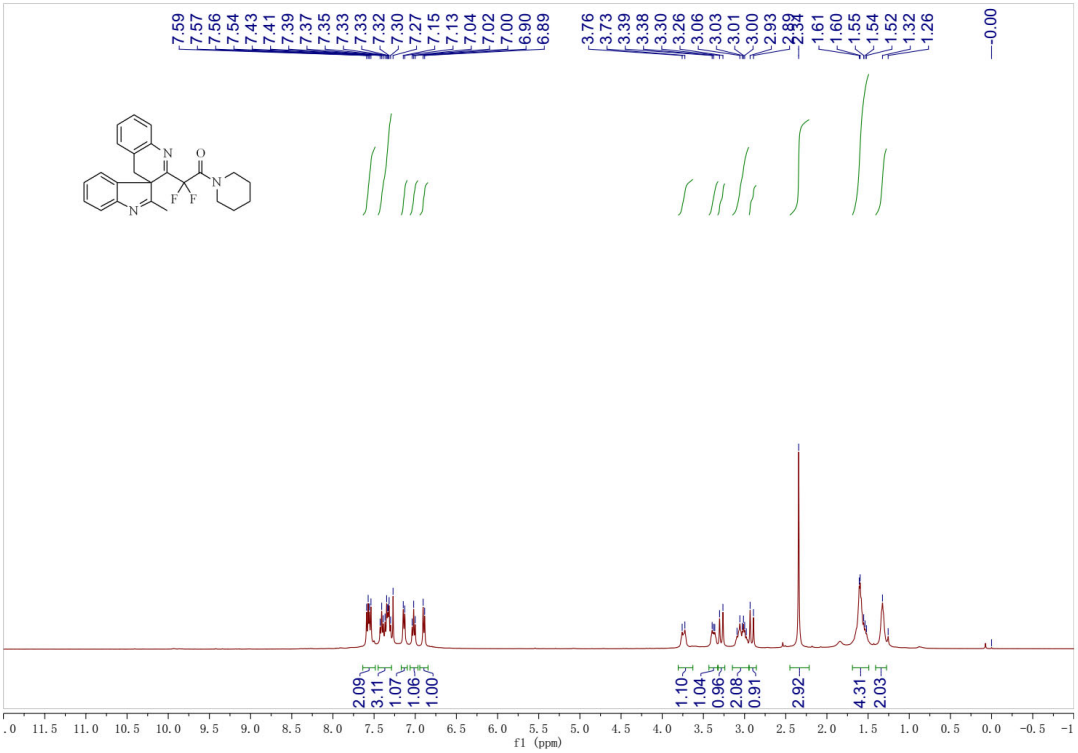
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3q



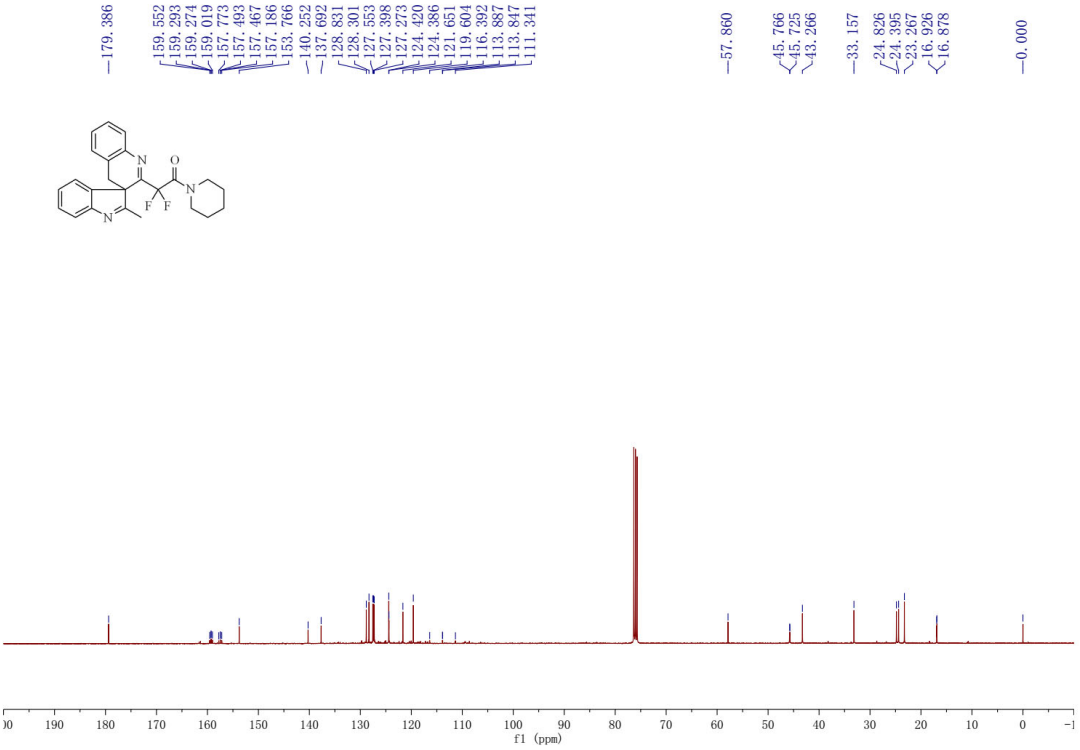
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3q



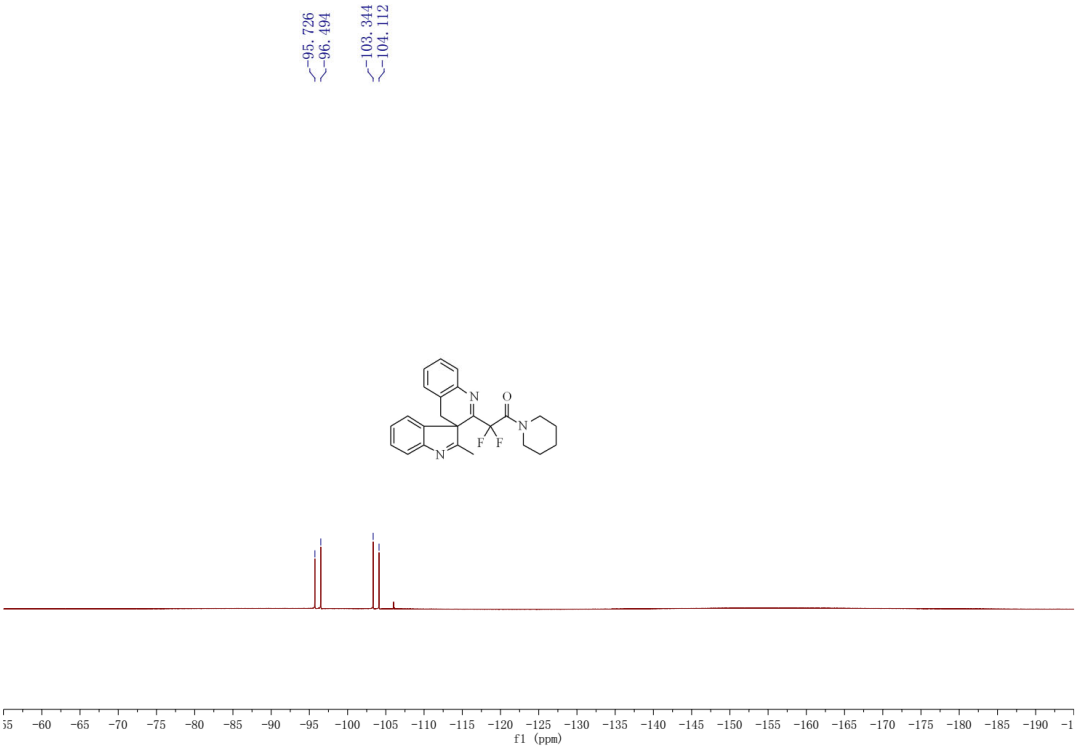
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3r



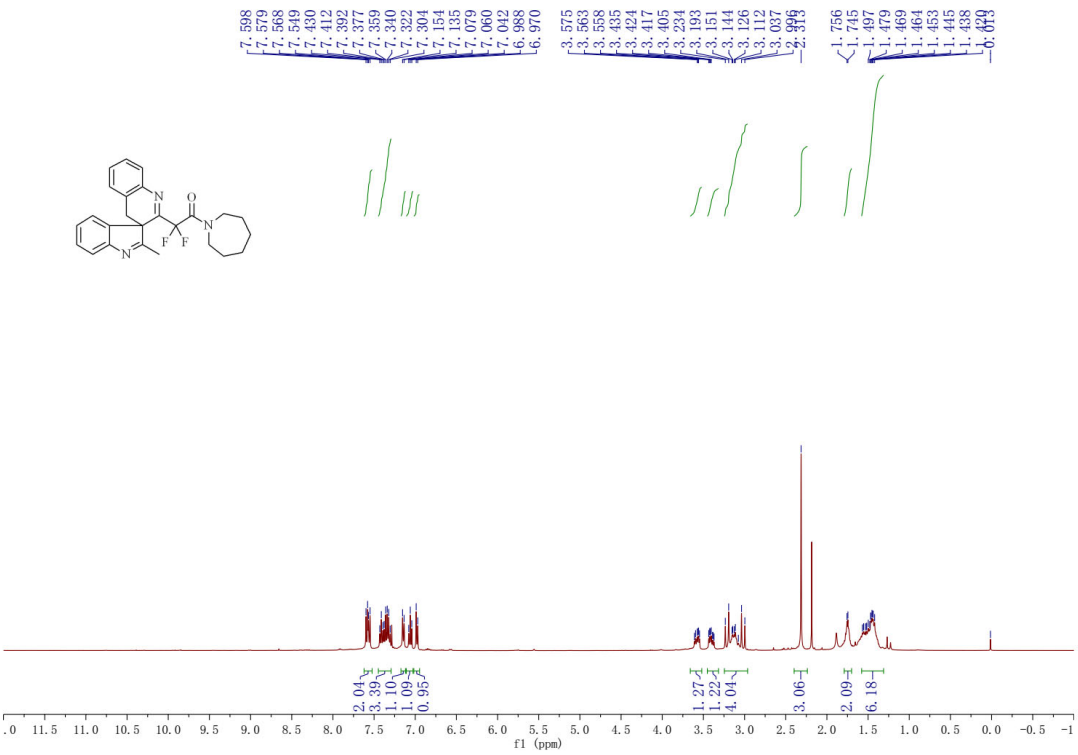
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3r



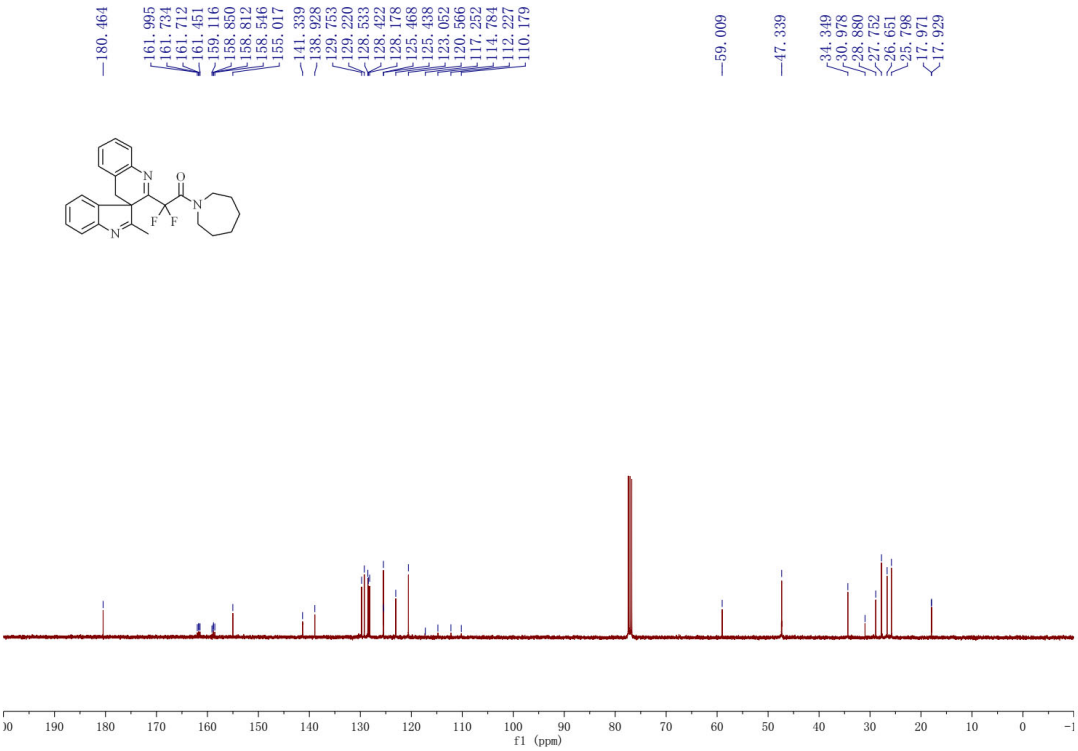
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3r



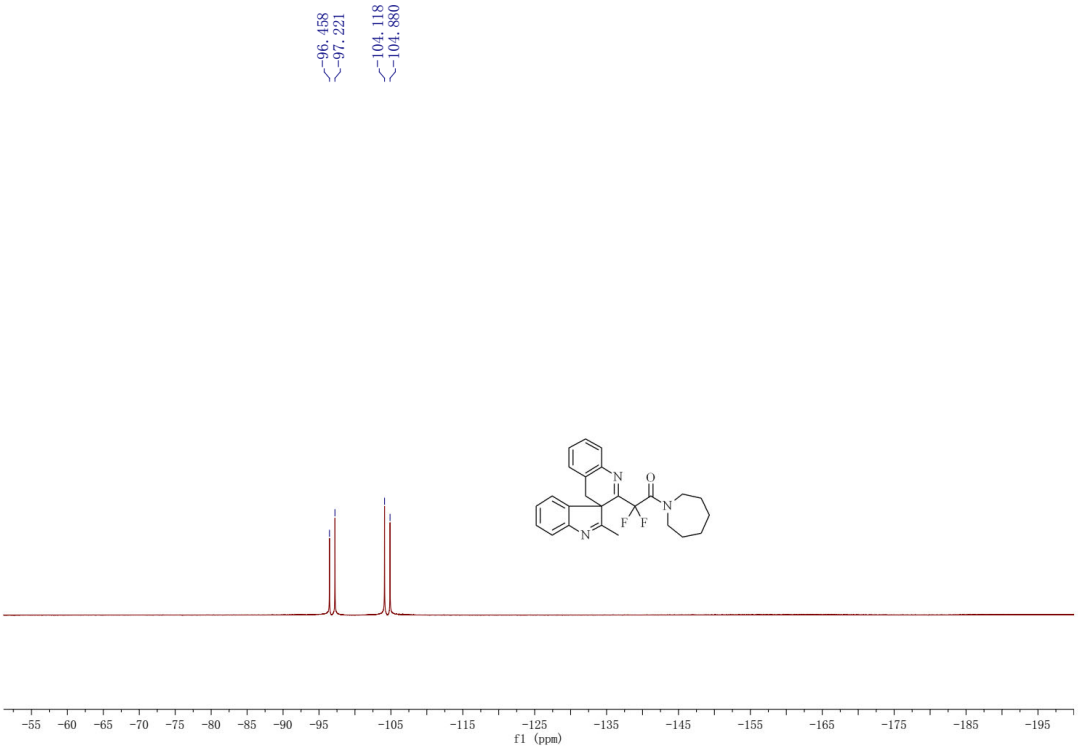
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3s



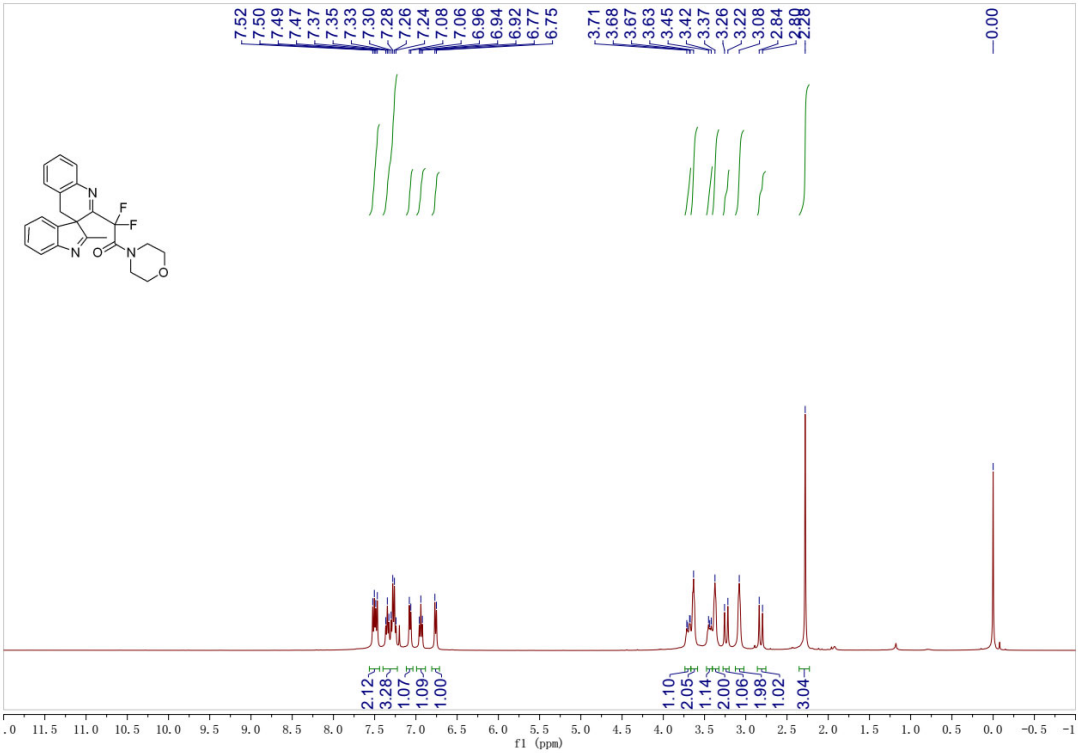
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3s



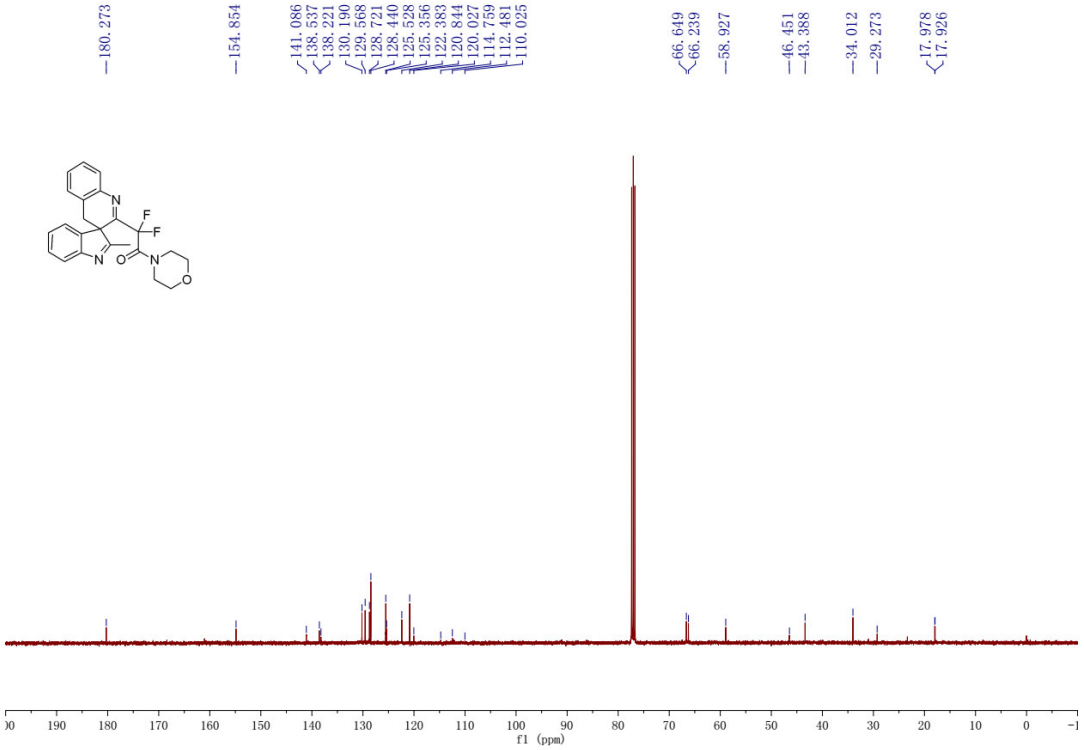
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3s



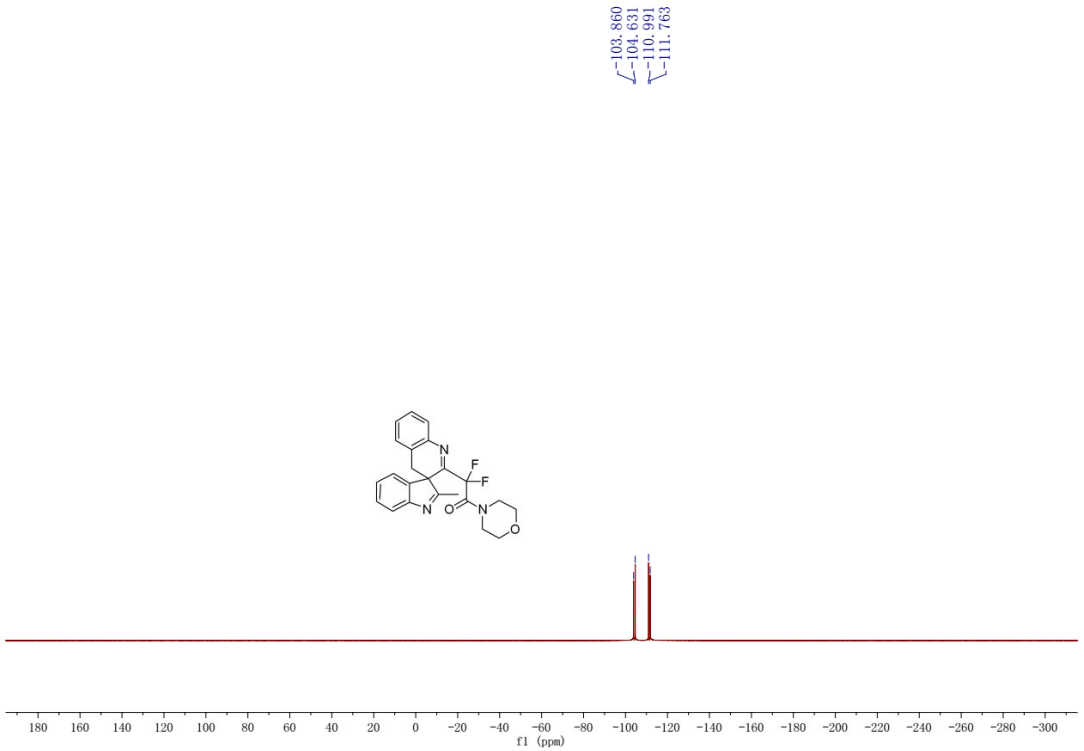
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3t



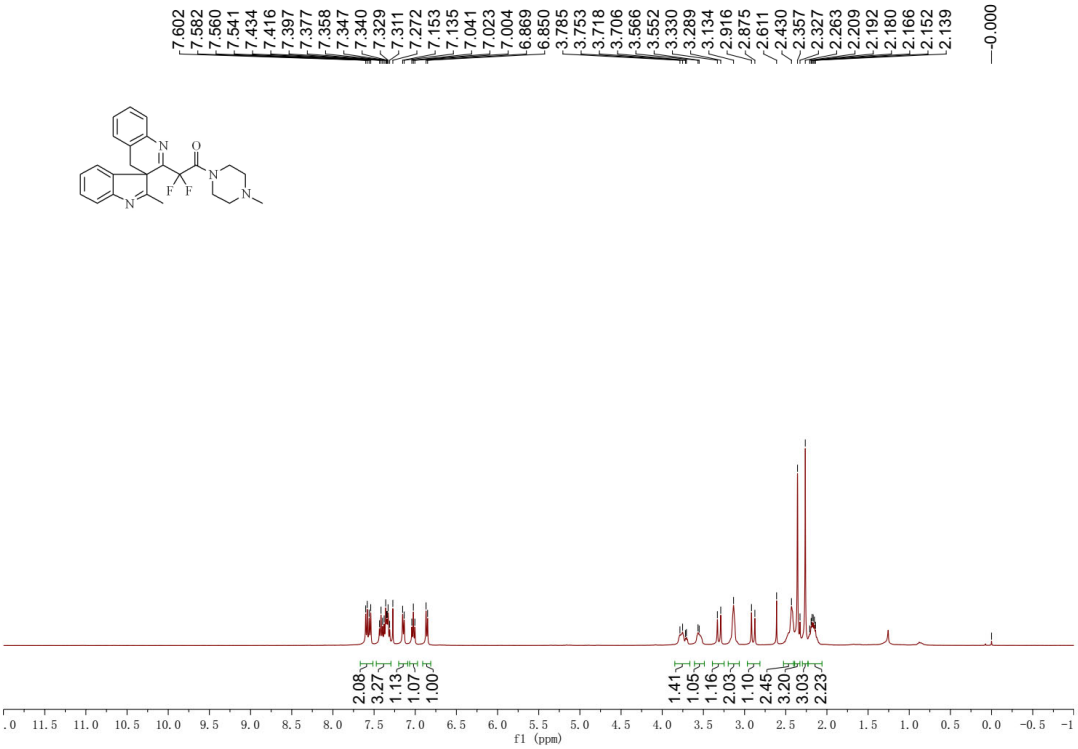
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3t



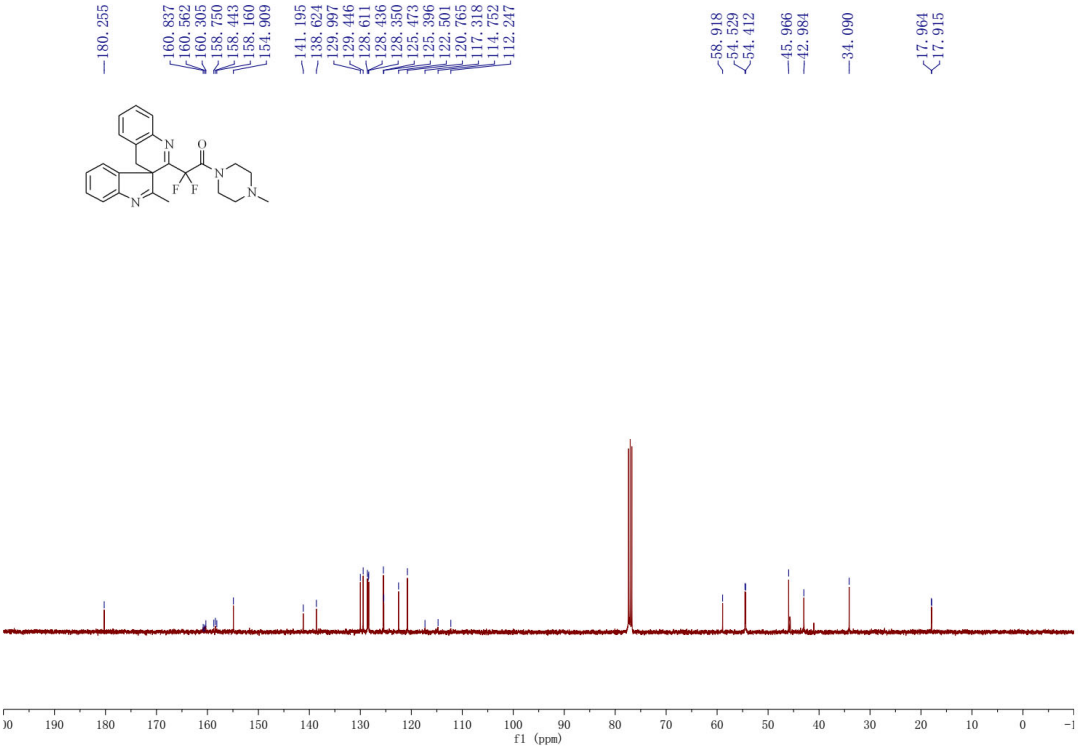
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3t



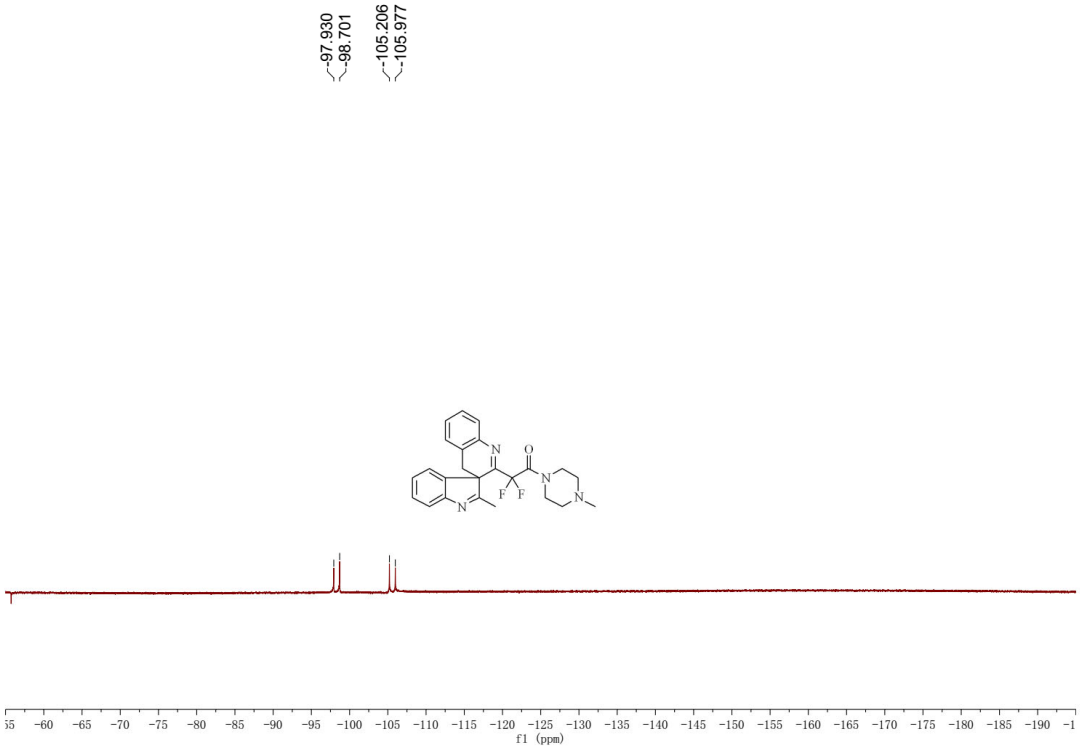
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3u



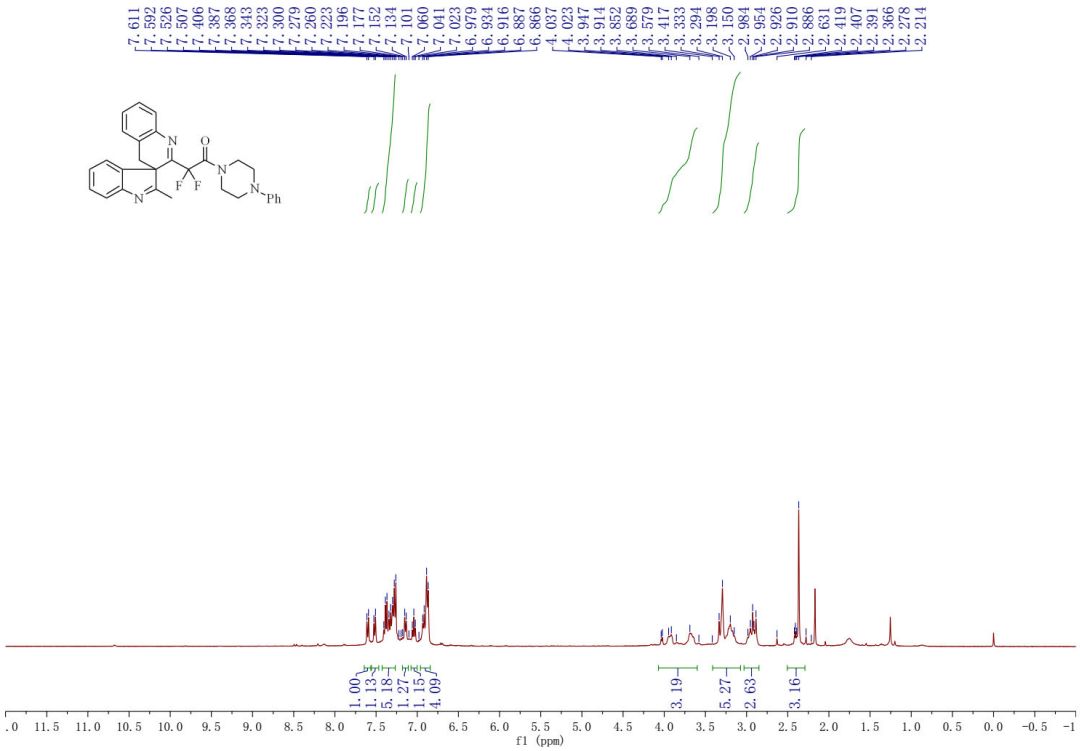
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3u



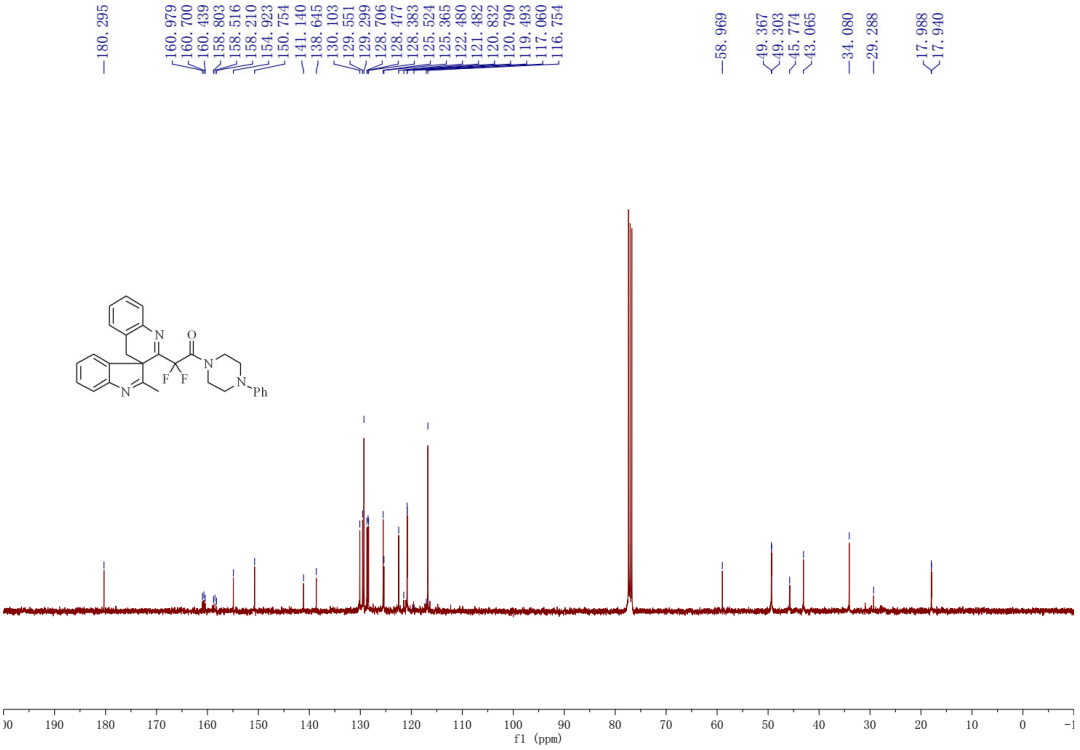
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3u



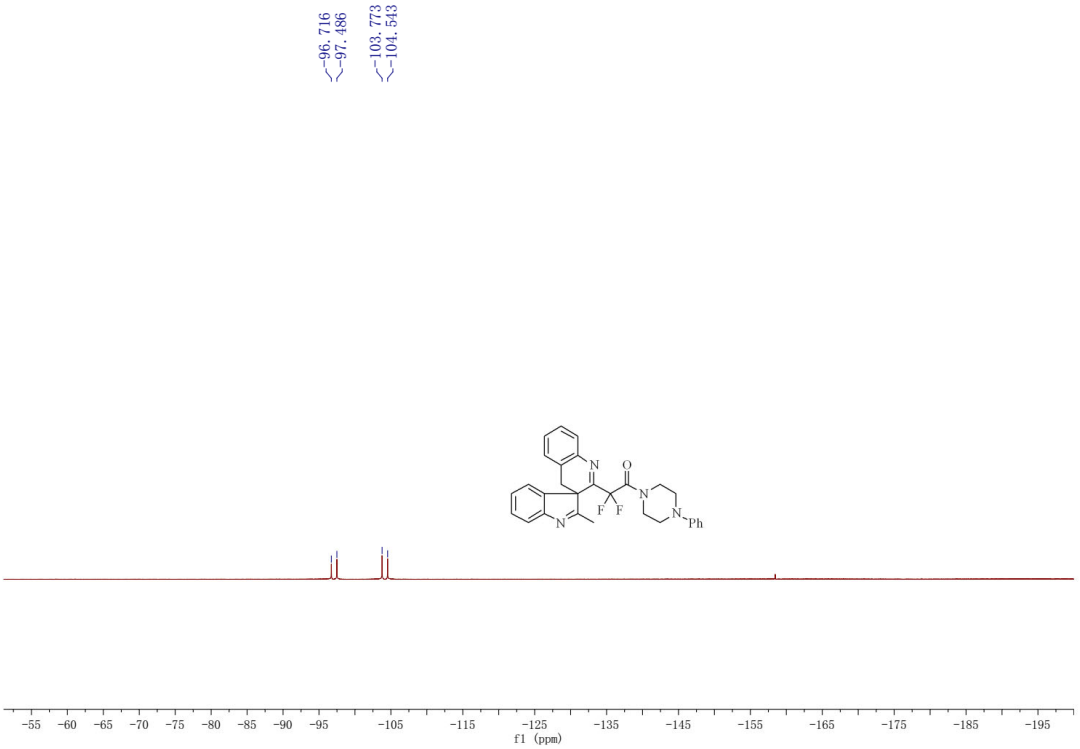
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3v



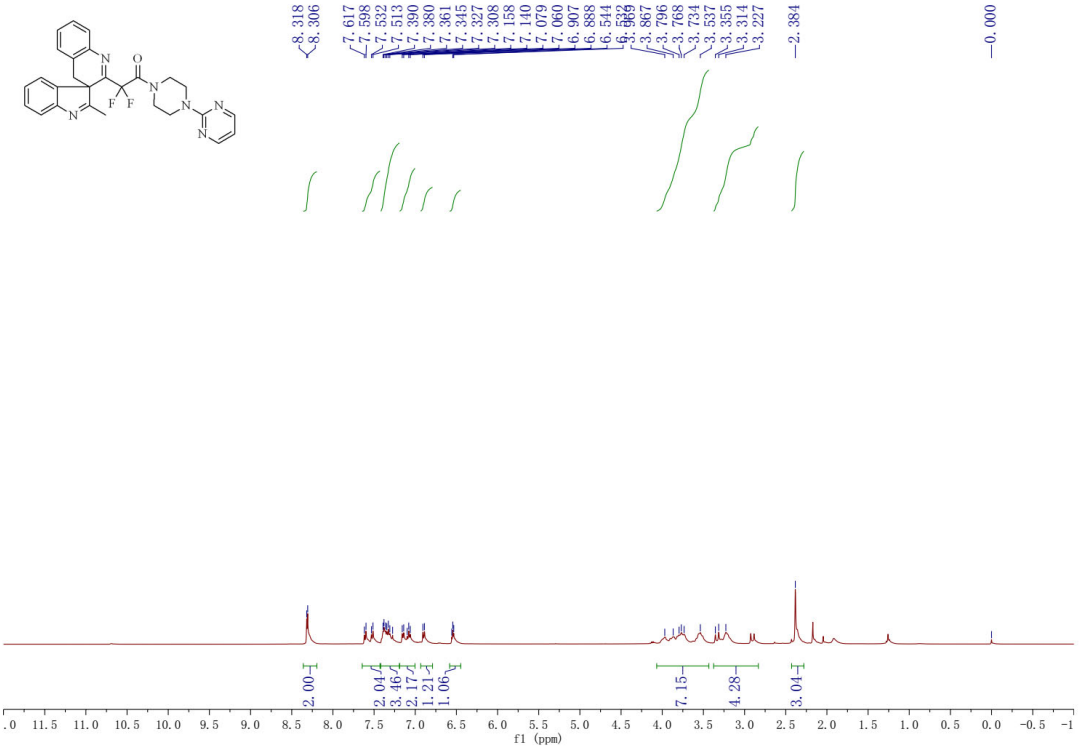
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3v



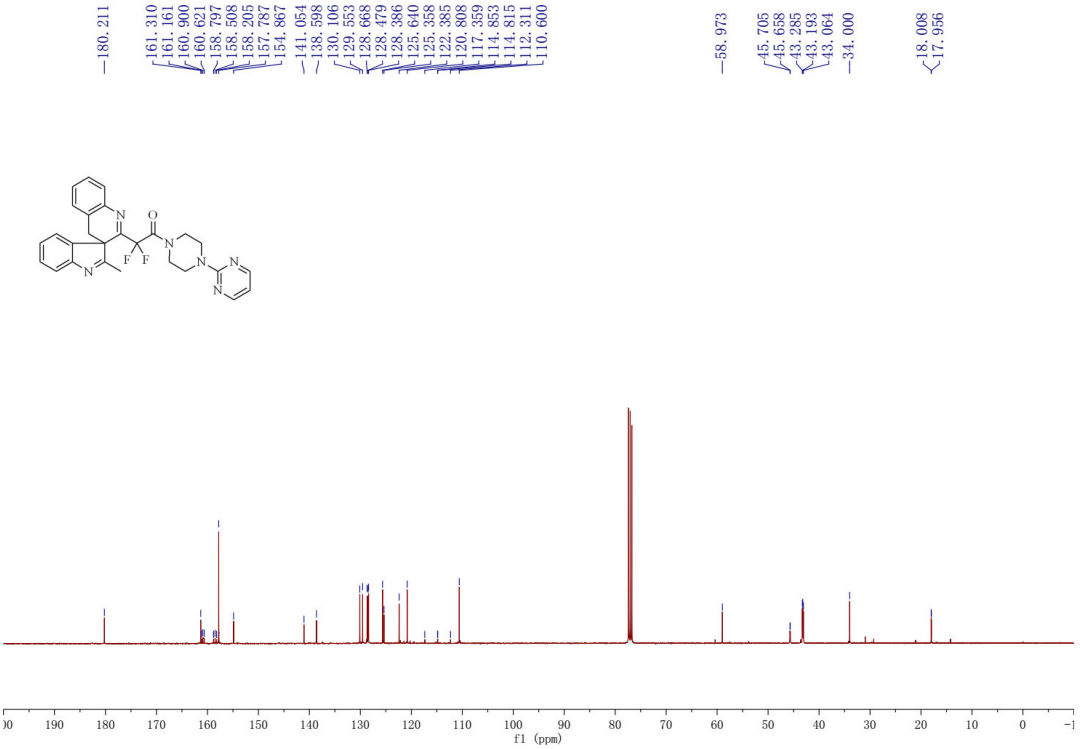
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3w



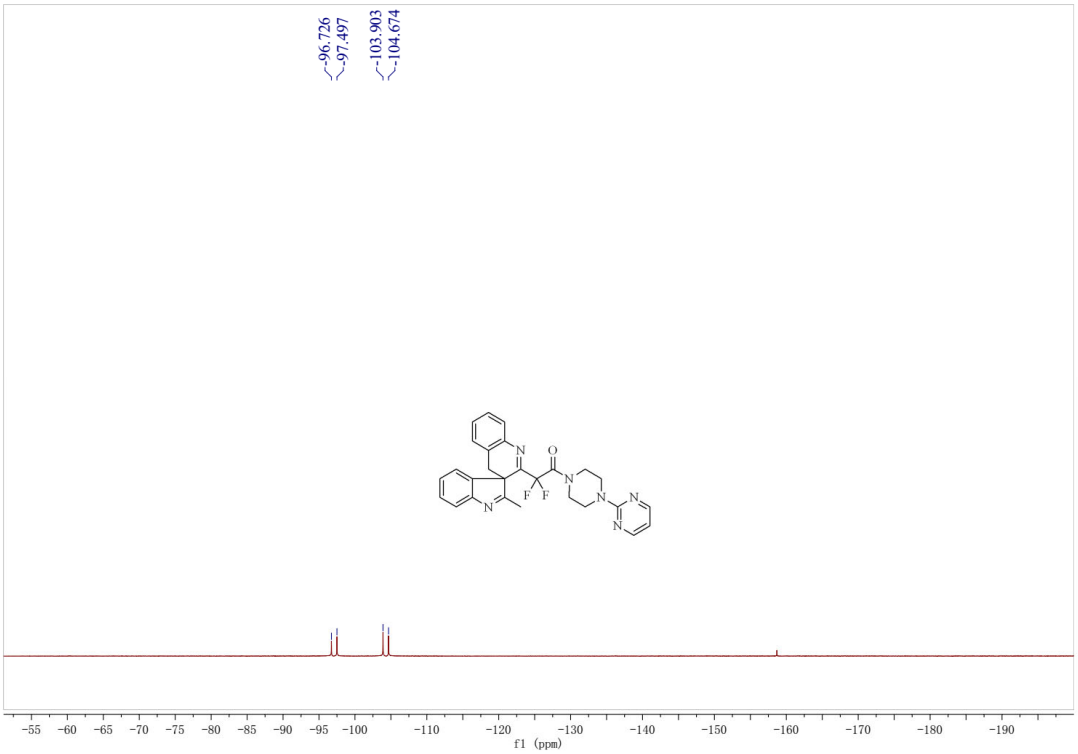
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3w



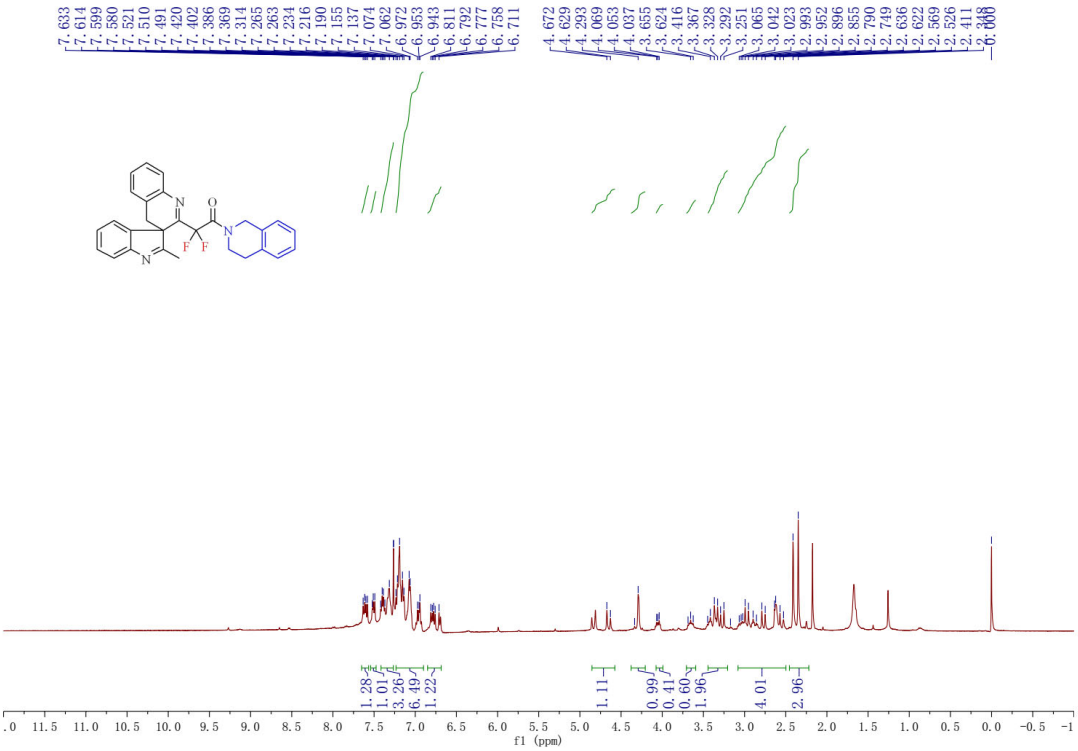
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3w



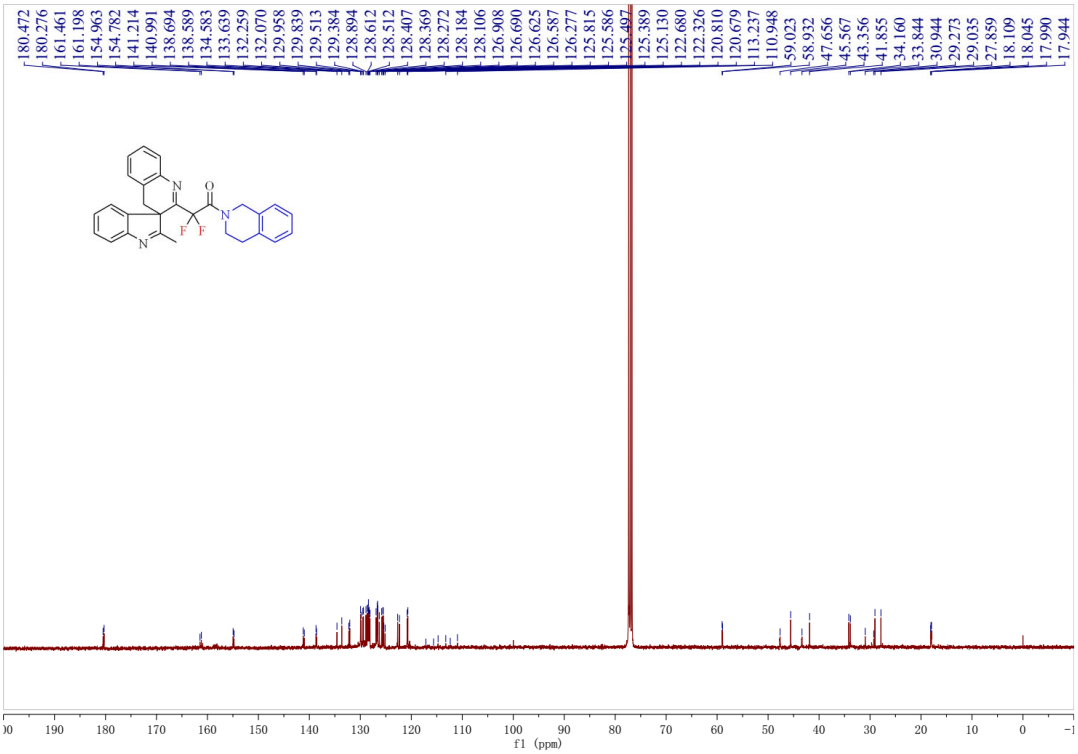
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3w



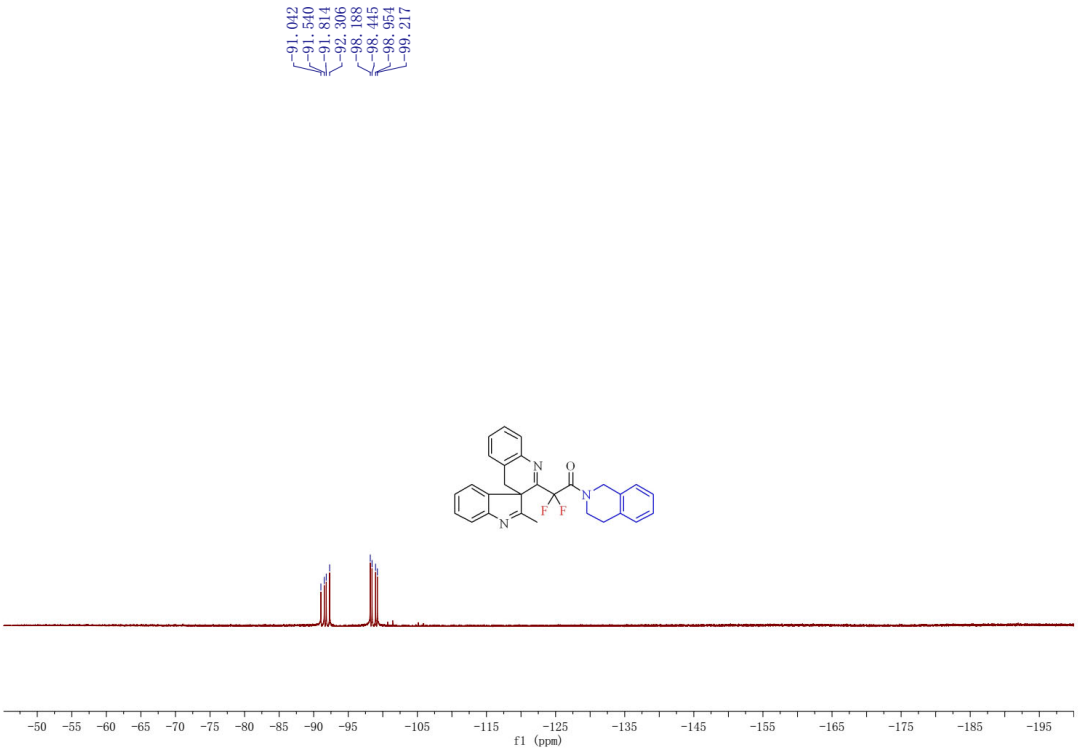
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3x



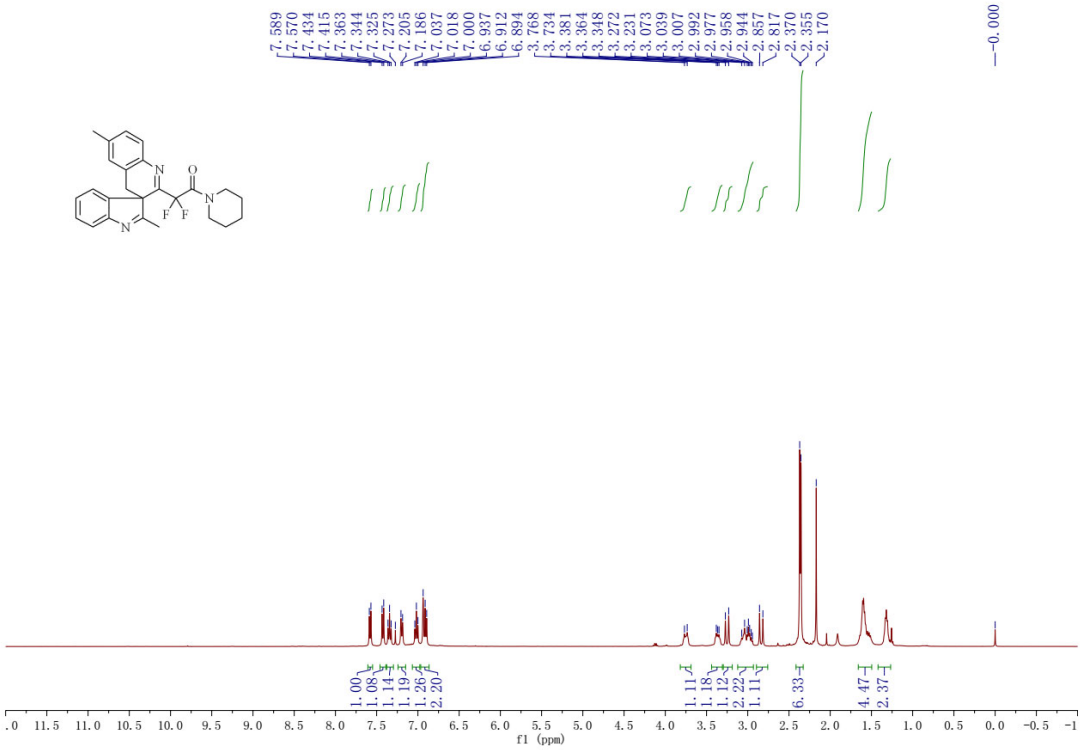
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3x



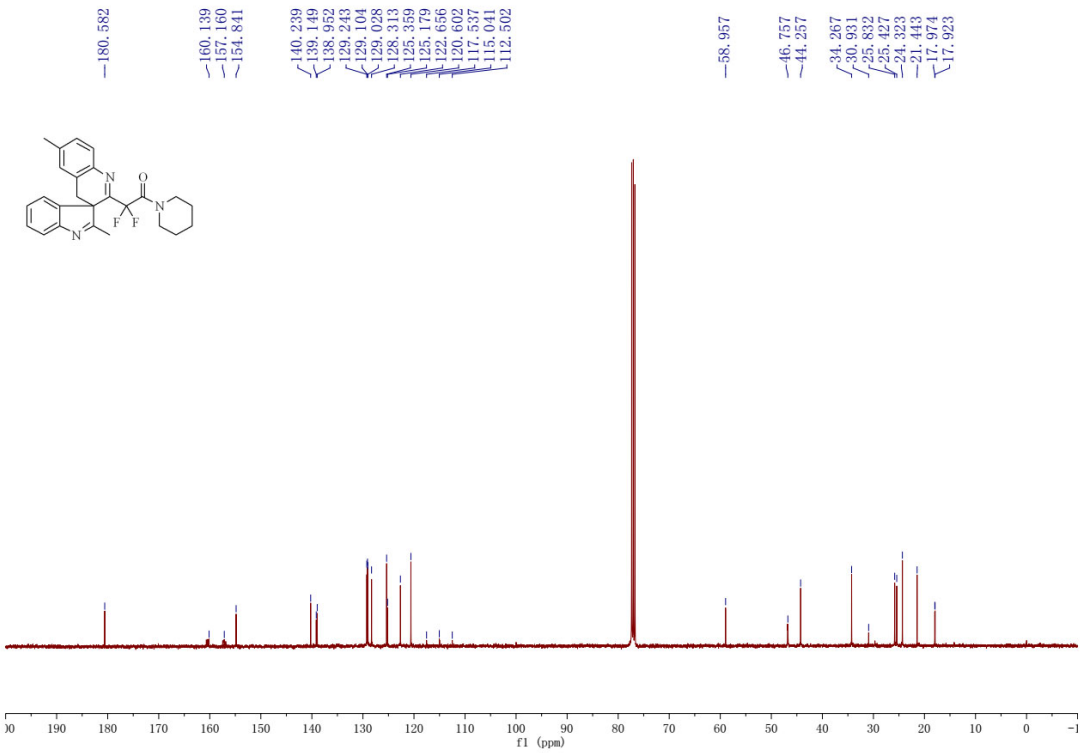
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3x



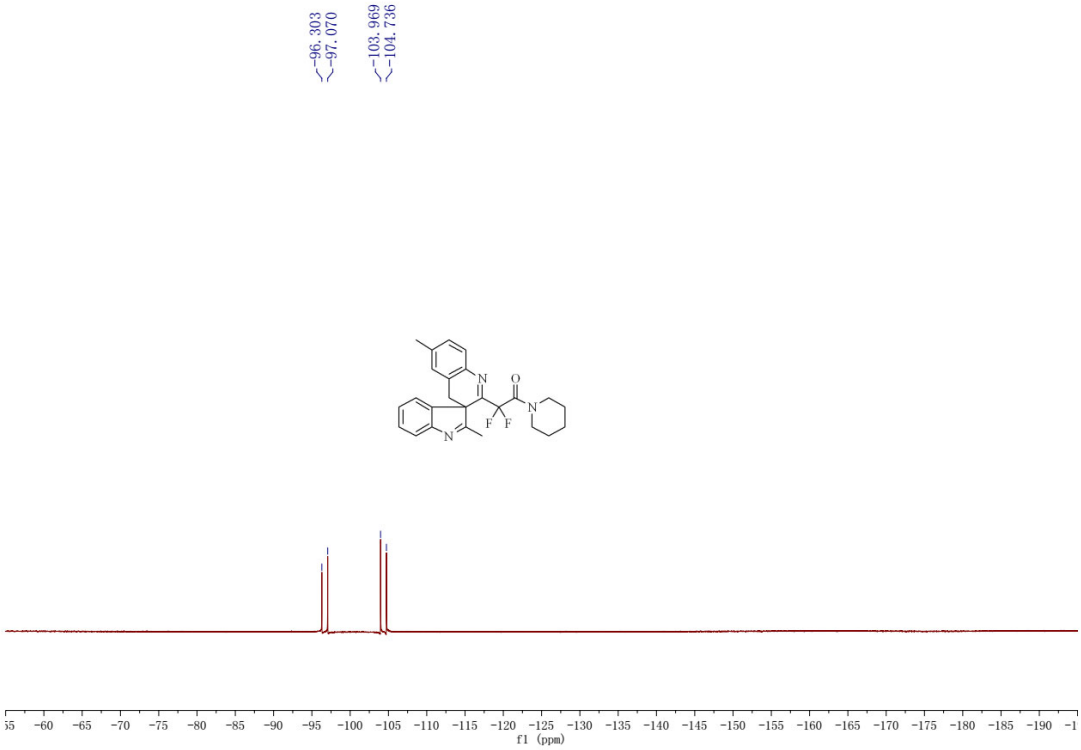
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3y



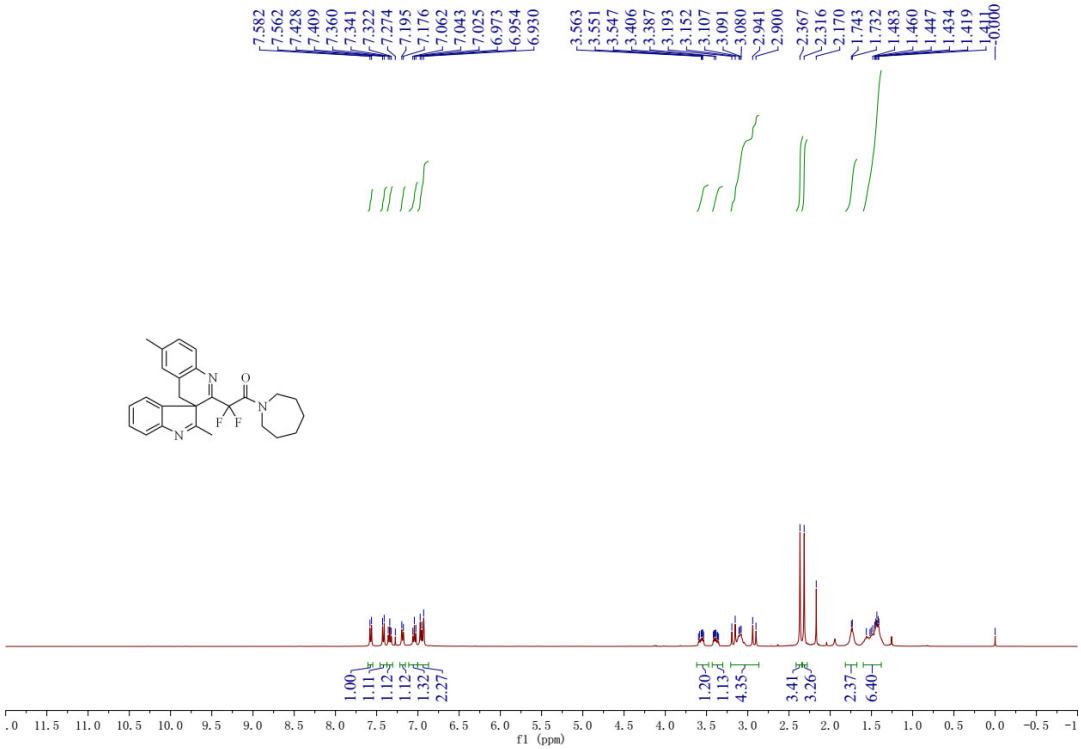
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3y



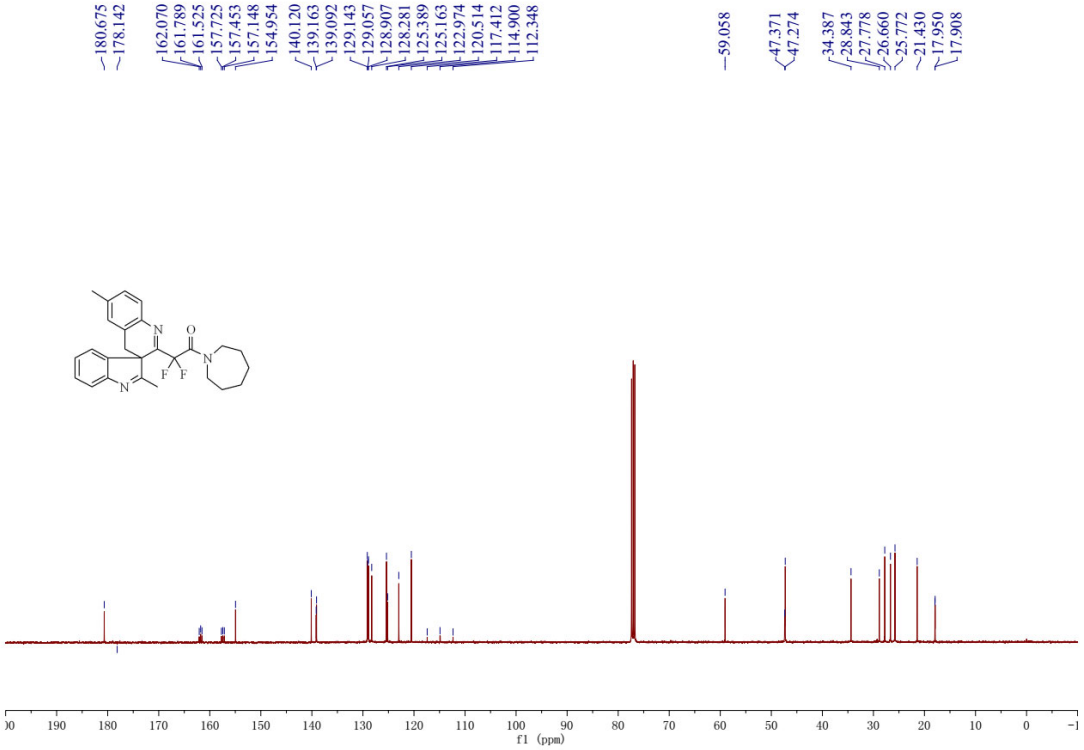
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3y



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3z



^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3z



^{19}F NMR (376 MHz, $CDCl_3$) spectrum of 3z