Electronic Supplementary Information

Metal-Free Synthesis of Difluoro/Trifluoromethyl Carbinol-Containing Chromones *via* Tandem Cyclization of *o*-Hydroxyaryl Enaminones

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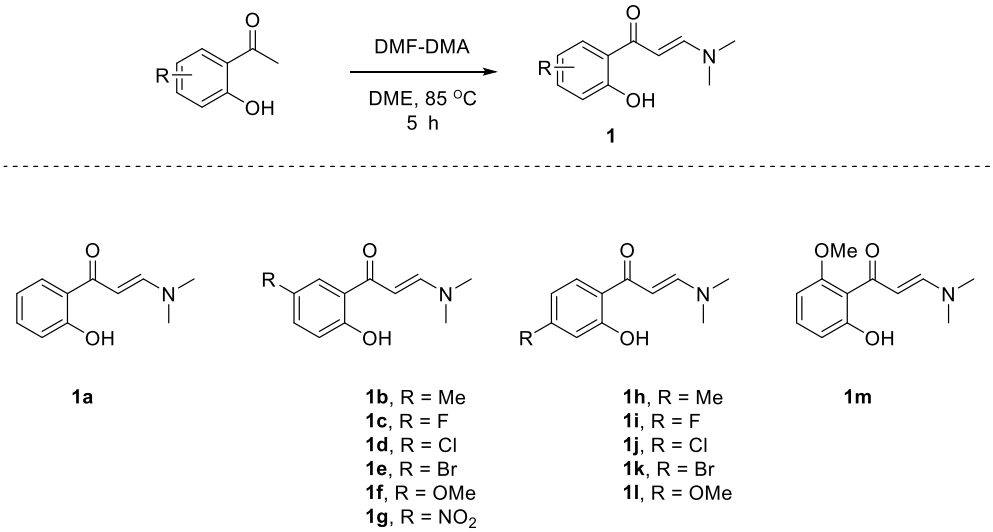
Table of Contents

General Information

Melting point (m.p.) was performed on a Büchi Melting Point B-545 instrument without correcting. ^{1}H, ^{13}C and ^{19}F NMR spectra were collected on a BRUKER DRX-400 spectrometer in $CDCl_3$ (or DMSO-d6/CD_3OD) using tetramethylsilane (TMS) as an internal standard.High-resolution mass spectra (HRMS) were obtained with a LCMS-IT-TOF mass spectrometer. Single-crystal X-ray analysis was obtained using Bruker APEX2 Smart CCD. TLC was performed by using commercially prepared 100-400 mesh silica gel plates (GF254) and visualization was detected at 254 or 365 nm. All reagents and solvents were purchased from commercial sources and used without further purification. (2*E*)-3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-ones **1** were synthesized from 2'-hydroxyacetophenone and *N*,*N*-dimethylformamide dimethyl acetal (see the following for details).

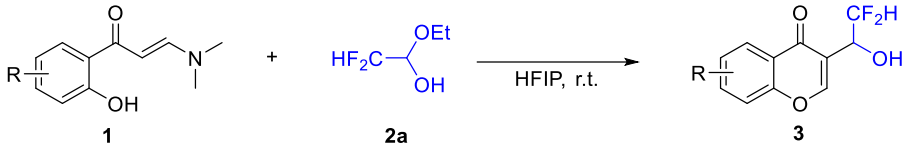
Experimental Procedure for Compounds 1a-1m



Scheme S1

According to the reported procedure[1, 2], compounds **1a-1m** were synthesized. 2'-Hydroxyacetophenone (20.0 mmol, 1.0 equiv) and *N*,*N*-Dimethylformamide dimethyl acetal (60.0 mmol, 3.0 equiv) in DMA (30.0 mL) was refluxed for 5 h. After monitoring the end of the reaction on TLC, the mixture was cooled to room temperature. Upon completion of the reaction, the resulting mixture was concentrated in vacuo. The crude product is recrystallized in petroleum ether to obtain the required compound **1a-1m**.

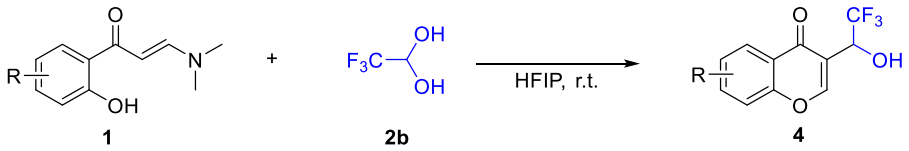
Experimental Procedure for Compounds 3a-3m



Scheme S2

Hydroxyaryl enaminone (0.2 mmol, 1.0 equiv.) and difluoroacetaldehyde ethyl hemiacetal (0.24 mmol, 1.2 equiv.) were stirred in HFIP (1.0 mL) at room temperature for 12 h. After monitoring the end of the reaction on TLC, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 5:1) to give the pure product **3a-3m**.

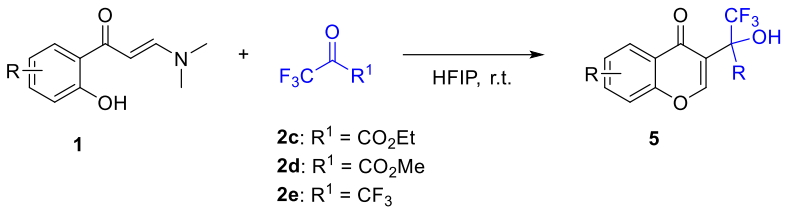
Experimental Procedure for Compounds 4a-4l



Scheme S3

Hydroxyaryl enaminone (0.2 mmol, 1.0 equiv.) and trifluoroacetaldehyde hydrate (0.4 mmol, 2.0 equiv.) were stirred in HFIP (1.0 mL) at room temperature for 12 h. After monitoring the end of the reaction on TLC, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 5:1) to give the pure product **4a**-**4l**.

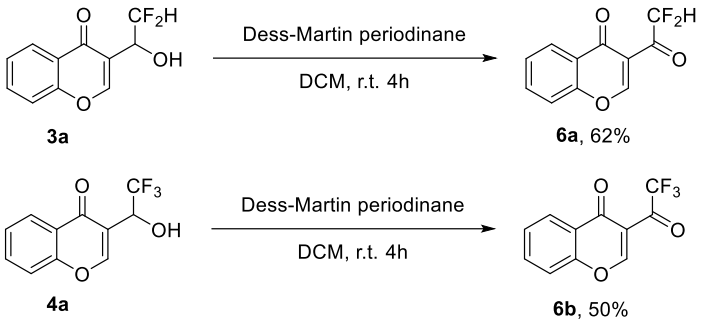
Experimental Procedure for Compounds 5a-5q



Scheme S4

Hydroxyaryl enaminones (0.2 mmol, 1.0 equiv.) and methyl trifluoropyruvate (0.24 mmol, 1.2 equiv.)/ethyl trifluoropyruvate (0.24 mmol, 1.2 equiv.)/hexafluoroacetone trihydrate (0.6 mmol, 3.0 equiv.) were stirred in HFIP (1.0 mL) at room temperature for 12 h. After monitoring the end of the reaction on TLC, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 5:1) to give the pure product **5a**-**5q**.

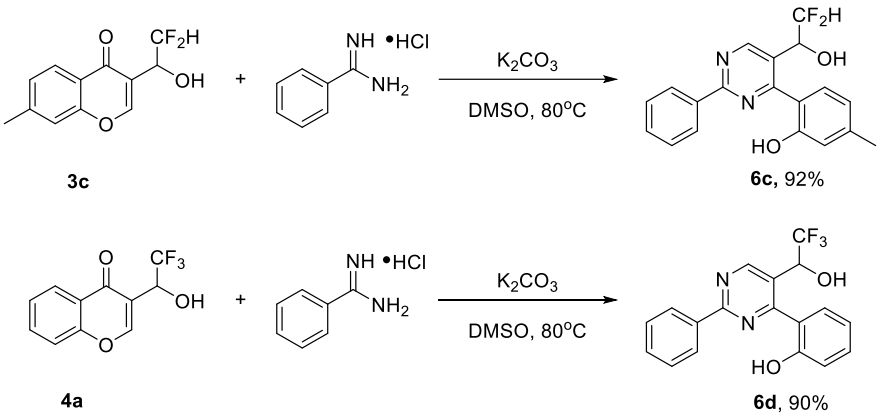
Experimental Procedure for Compounds 6a and 6b



Scheme S5

Compounds **3a** (0.1 mmol, 1.0 equiv.) or compounds **4a** (0.1 mmol, 1.0 equiv.), Dess-Martin periodinane (0.37 mmol, 3.7 equiv.) in DCM (1.0mL), white were stirred in a ground glass test tube at room temperature for 4 h. After monitoring the end of the reaction on TLC, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 5:1) to give the pure product **6a** and **6b**.

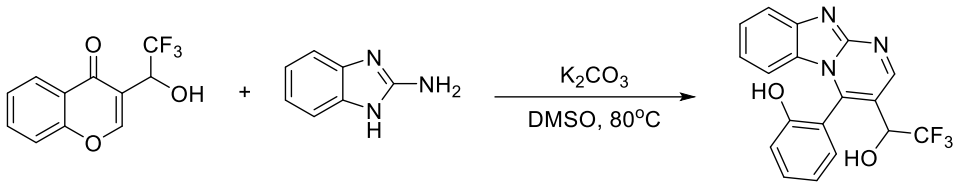
Experimental Procedure for Compounds 6c and 6d



Scheme S6

Compounds **3c** (0.2 mmol, 1.0 equiv.) or compounds **4a** (0.2 mmol, 1.0 equiv.), benzamidine hydrochloride (0.4 mmol, 2.0 equiv.), K_2CO_3(0.4 mmol, 2.0 equiv.) in DMSO (1.0 mL), which were stirred in a ground glass test tube at 80 °C for 4 h. After monitoring the end of the reaction on TLC, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the pure product **6c** and **6d**.

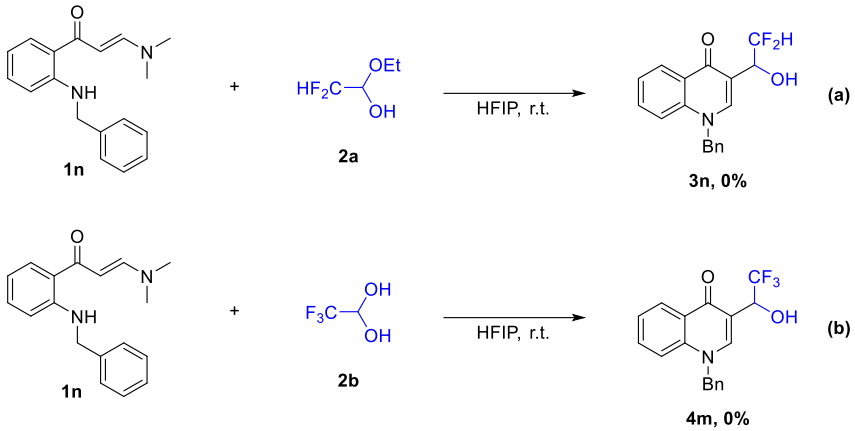
Experimental Procedure for Compound 6e



Scheme S7

Compound **4a** (0.2 mmol, 1.0 equiv.), 2-aminobenzimidazole (0.24 mmol, 1.2 equiv.), K_2CO_3 (0.24 mmol, 1.2 equiv.) in DMSO (1.0 mL), reacted at 80 ºC for 12 h. After monitoring the end of the reaction on TLC, the resulting mixture was extracted with ethyl acetate, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified with silica gel chromatography (petroleum ether/ethyl acetate = 1:2) to give the correcting product **6e**.

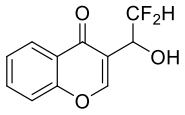
Reaction of *o*-aminophenyl enaminone with 2a or 2b.



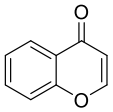
Scheme S8

(*E*)-1-(2-(benzylamino)phenyl)-3-(dimethylamino)prop-2-en-1-one **1n** (0.2 mmol, 1.0 equiv.) and trifluoroacetaldehyde hydrate **2a** (0.24 mmol, 1.2 equiv.) or trifluoroacetaldehyde hydrate **2b** (0.4 mmol, 2.0 equiv.) were stirred in HFIP (1.0 mL) at room temperature for 12 h. Unfortunately, the expected difluoro/trifluoromethylated carbinols **3n** or **4m** could not be obtained.

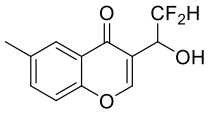
Characterization Data for the Products 3a-3m



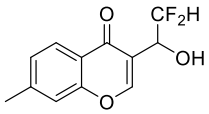
3-(2,2-Difluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**3a**): white solid, 45 mg, 99% yield; m.p. 145-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 4.27 (*br*, 1H), 4.71-4.86 (*m*, 1H), 6.13 (*td*, *J* = 55.8, 3.8 Hz, 1H), 7.45-7.53 (*m*, 2H), 7.72-7.79 (*m*, 1H), 8.04 (*s*, 1H), 8.21 (*dd*, *J* = 8.0, 1.2 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -127.1 (*d*, *J* = 282.3 Hz, 1F), -130.1 (*d*, *J* = 281.8 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 69.8 (*t*, *J* = 25.2 Hz), 114.1 (*t*, *J* = 245.1Hz), 118.35, 118.44, 123.6, 125.6, 125.8, 134.6, 154.9, 156.3, 178.1; ESI-HRMS, *m/z*: Calcd for $C_{11}H_9F_2O_3^+$ $[M+H]^+$: 227.0514, found: 227.0534.



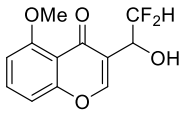
4*H*-Chromen-4-one (**3a'**): white solid, 8 mg, 26% yield; m.p. 53-54 °C (51-52 °C[3]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 6.35 (*dd*, *J* = 6.0, 1.5 Hz, 1H), 7.39-7.47 (*m*, 2H), 7.65-7.70 (*m*, 1H), 7.87 (*d, J* = 6.0 Hz, 1H), 8.20 (*d, J* = 8.0 Hz, 1H).



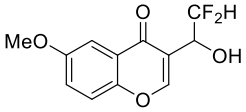
3-(2,2-Difluoro-1-hydroxyethyl)-6-methyl-4*H*-chromen-4-one (**3b**): white solid, 52 mg, 98% yield; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 2.37 (*s*, 3H), 4.51 (*br*, 1H), 4.71-4.78 (*m*, 1H), 6.04 (*td*, *J* = 56.1, 3.7 Hz, 1H), 7.30 (*d*, *J* = 8.6 Hz, 1H), 7.43-7.45 (*m*, 1H), 7.87 (*s*, 1H), 7.95 (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -126.7 (*d*, *J* = 281.2 Hz, 1F), -130.4 (*d*, *J* = 281.2 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 21.0, 69.4 (*t*, *J* = 30.6Hz), 114.2 (*t*, *J* = 244.7 Hz), 116.6, 118.0, 118.4 (*t*, *J* = 3.3Hz), 123.2, 124.8, 135.8, 155.0, 178.1; ESI-HRMS, *m/z*: Calcd for $C_{12}H_{11}F_2O_3^+$ $[M+H]^+$: 241.0671, found: 241.0680.



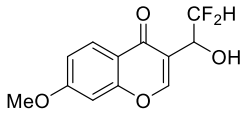
3-(2,2-Difluoro-1-hydroxyethyl)-7-methyl-4*H*-chromen-4-one (**3c**): white solid, 49 mg, 91% yield; m.p. 114-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 2.41 (*s*, 3H), 4.52 (*br*, 1H), 4.69-4.76 (*m*, 1H), 6.04 (*td*, *J* = 55.9, 3.8 Hz, 1H), 7.16-7.19 (*m*, 2H), 7.92 (*s*, 1H), 7.97 (*d*, *J* = 8.1 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -127.10 (*d*, *J* = 282.4 Hz, 1F), -130.31 (*d*, *J* = 282.4 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 21.9, 69.4 (*t*, *J* = 25.3 Hz), 114.2 (*t*, *J* = 244.6 Hz), 118.0, 118.4 (*t*, *J* = 3.2 Hz)， 121.3, 125.3, 127.3, 146.1, 154.8, 156.4, 177.9; ESI-HRMS, *m/z*: Calcd for $C_{12}H_{11}F_2O_3^+$ $[M+H]^+$: 241.0671, found: 241.0680.



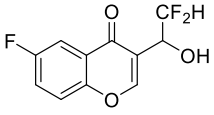
3-(2,2-Difluoro-1-hydroxyethyl)-5-methoxy-4*H*-chromen-4-one (**3d**): white solid, 50 mg, 97% yield; m.p. 104-106 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 4.00 (*s*, 3H), 4.53 (*br*, 1H), 4.67-4.71 (*m*, 1H), 6.14 (*td*, *J* = 56.3, 4.2 Hz, 1H), 6.85 (*d*, *J* = 8.3 Hz, 1H), 7.05 (*d*, *J* = 8.5 Hz, 1H), 7.61 (*t*, *J* = 8.4 Hz, 1H), 7.89 (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -126.0 (*d*, *J* = 282.9 Hz, 1F), -130.0 (*d*, *J* = 282.3 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 56.5, 69.9 (*t*, *J* = 28.5 Hz), 106.7, 110.3, 114.2 (*t*, *J* = 244.8 Hz), 116.5, 119.7, 134.7, 153.3, 158.2, 159.9, 178.2; ESI-HRMS, *m/z*: Calcd for $C_{12}H_{11}F_2O_4^+$ $[M+H]^+$: 257.0620, found: 257.0610.



3-(2,2-Difluoro-1-hydroxyethyl)-6-methoxy-4*H*-chromen-4-one (**3e**): yellow solid, 50 mg, 95% yield; m.p. 101-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 3.82 (*s*, 3H), 4.50 (*br*, 1H), 4.73-4.79 (*m*, 1H), 6.04 (*td*, *J* = 55.9, 3.7 Hz, 1H), 7.22 (*dd*, *J* = 9.1, 3.1 Hz, 1H), 7.35 (*d*, *J* = 9.2 Hz, 1H), 7.44 (*d*, *J* = 3.0 Hz, 1H), 7.96 (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -127.18 (*d*, *J* = 282.2 Hz, 1F), -130.35 (*d*, *J* = 281.5 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 56.0, 69.4 (*t*, *J* = 24.5 Hz), 104.4, 114.2 (*t*, *J* = 244.7 Hz), 117.8 (*t*, *J* = 3.3 Hz), 119.7, 124.2, 124.7, 151.2, 154.8, 157.3, 177.8; ESI-HRMS, *m/z*: Calcd for $C_{12}H_{11}F_2O_4^+$ $[M+H]^+$: 257.0620, found: 257.0610.

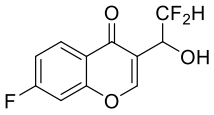


(2,2-Difluoro-1-hydroxyethyl)-7-methoxy-4*H*-chromen-4-one (**3f**): white solid, 48 mg, 99% yield; m.p. 101-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 3.84 (*s*, 3H), 4.45 (*br*, 1H), 4.66-4.72 (*m*, 1H), 6.04 (*td*, *J* = 56.0, 3.8 Hz, 1H), 6.78 (*d*, *J* = 2.4 Hz, 1H), 6.93 (*dd*, *J* = 9.0, 2.4 Hz, 1H), 7.88 (*s*, 1H), 8.00 (*d*, *J* = 9.0 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -126.99 (*d*, *J* = 281.7 Hz, 1F), -130.14 (*d*, *J* = 281.4 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 56.0, 69.6 (*t*, *J* = 24.8 Hz), 100.2, 114.2 (*t*, *J* = 244.8 Hz), 115.4, 117.4, 118.4 (*t*, *J* = 3.1 Hz), 126.9, 154.5, 158.2, 164.7, 177.4; ESI-HRMS, *m/z*: Calcd for $C_{12}H_{11}F_2O_4^+$ $[M+H]^+$: 257.0620, found: 257.0610.

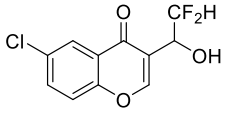


3-(2,2-Difluoro-1-hydroxyethyl)-6-fluoro-4*H*-chromen-4-one (**3g**): white solid, 46 mg, 94% yield; m.p. 138-140 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 4.80-4.87 (*m*, 1H), 6.12 (*td*, *J* = 55.8, 3.6 Hz, 1H), 7.44-7.49 (*m*, 1H), 7.53-7.56 (*m*, 1H), 7.84 (*dd*, *J* = 8.0, 3.0 Hz, 1H), 8.07 (*s*,

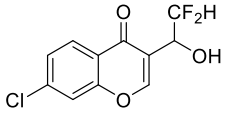
1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -113.78 (*s*, 1F), -127.49 (*d*, *J* = 281.7 Hz, 1F), -130.60 (*d*, *J* = 282.5 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 69.3 (*t*, *J* = 25.0 Hz), 110.5 (*d*, *J* = 24.0 Hz), 114.0 (*t*, *J* = 244.9 Hz), 118.0 (*t*, *J* = 3.0 Hz), 120.5 (*d*, *J* = 8.0 Hz), 122.9 (*d*, *J* = 26.0 Hz), 124.7 (*d*, *J* = 7.0 Hz), 152.6, 155.2, 159.8 (*d*, *J* = 253.0 Hz), 177.2; ESI-HRMS, *m/z*: Calcd for $C_{11}H_8F_3O_3^+$ $[M+H]^+$: 245.0420, found: 245.0413.



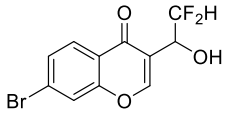
3-(2,2-Difluoro-1-hydroxyethyl)-7-fluoro-4*H*-chromen-4-one (**3h**): white solid, 49 mg, 99% yield; m.p. 107 -109 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 4.42 (*br*, 1H), 4.84-4.91 (*m*, 1H), 6.12 (*td*, *J* = 55.7, 3.4 Hz, 1H), 7.16-7.21 (*m*, 2H), 8.06 (*s*, 1H), 8.22 (*dd*, *J* = 9.6, 6.2 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -100.99 (*s*, 1F), -127.55 (*d*, *J* = 281.3 Hz, 1F), -130.87 (*d*, *J* = 282.2 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 68.8 (*t*, *J* = 25.0 Hz), 104.9 (*d*, *J* = 25.3 Hz), 114.0 (*t*, *J* = 244.6 Hz), 114.7 (*d*, *J* = 22.8 Hz), 119.0 (*t*, *J* = 3.4 Hz), 120.4, 128.3 (*d*, *J* = 10.8 Hz), 155.3, 157.3 (*d*, *J* = 13.4 Hz), 166.0 (*d*, *J* = 255.1 Hz), 176.9; ESI-HRMS, *m/z*: Calcd for $C_{11}H_8F_3O_3^+$ $[M+H]^+$: 245.0420, found: 245.0413.



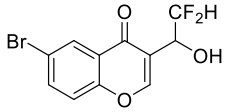
6-Chloro-3-(2,2-difluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**3i**): white solid, 49 mg, 94% yield; m.p. 97-99 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 4.27 (*br*, 1H), 4.76-4.83 (*m*, 1H), 6.04 (*td, J* = 55.7, 3.4 Hz, 1H), 7.33 (*dd*, *J* = 8.6, 1.9 Hz, 1H), 7.44 (*d*, *J* = 1.9 Hz, 1H), 7.97 (*s*, 1H), 8.04 (*d*, *J* = 8.6 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -127.59 (*d*, *J* = 282.3 Hz, 1F), -130.87 (*d*, *J* = 281.8 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 68.8 (*t, J* = 25.0 Hz), 114.0 (*t, J* = 243.0 Hz), 118.4, 119.2 (*t, J* = 3.1 Hz), 122.1, 126.7, 127.0, 140.7, 155.2, 156.3, 177.0; ESI-HRMS, *m/z*: Calcd for $C_{11}H_8ClF_2O_3^+$ $[M+H]^+$: 261.0125, found: 261.0147.



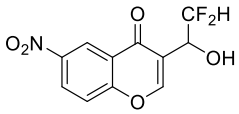
7-Chloro-3-(2,2-difluoro-1-hydroxyethyl)-4*H*-chromen-4-one(**3j**): white solid, 47 mg, 90% yield; m.p. 133-135 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 4.05 (*br*, 1H), 4.80-4.85 (*m*, 1H), 6.12 (*td, J* = 55.9, 3.4 Hz, 1H), 7.49 (*d*, *J* = 9.0 Hz, 1H), 7.68 (*dd*, *J* = 8.9, 2.5 Hz, 1H), 8.05 (*s*, 1H), 8.16 (*d*, *J* = 2.4 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -127.53 (*d*, *J* = 281.5 Hz, 1F), -130.69 (*d*, *J* = 282.4 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 69.3 (*t, J* = 24.5 Hz), 114.0 (*t, J* = 244.3 Hz), 118.7, 120.1, 124.5, 125.1, 131.8, 134.8, 154.6, 155.1, 176.8; ESI-HRMS, *m/z*: Calcd for $C_{11}H_8ClF_2O_3^+$ $[M+H]^+$: 261.0125, found: 261.0147.



Bromo-3-(2,2-difluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**3k**): white solid, 48 mg, 80% yield; m.p. 113-115 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 4.85-4.91 (*m*, 1H), 6.02 (*td*, *J* = 55.8, 3.4 Hz, 1H), 7.49 (*dd*, *J* = 8.6, 1.7 Hz, 1H), 7.63 (*d*, *J* = 1.7 Hz, 1H), 7.97 (*d*, *J* = 8.0 Hz, 1H), 8.02 (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), *δ*, ppm: -127.60 (*d*, *J* = 282.1 Hz, 1F), -130.75 (*d*, *J* = 281.8 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 69.1 (*t*, *J* = 24.6 Hz), 114.0 (*t*, *J* = 244.9 Hz), 119.1 (*t, J* = 3.1 Hz), 121.4, 122.4, 127.0, 128.9, 129.5, 155.0, 156.3, 177.2; ESI-HRMS, *m/z*: Calcd for $C_{11}H_8BrF_2O_3^+$ $[M+H]^+$: 304.9619, found: 304.9629.

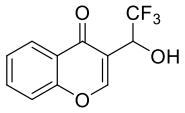


6-Bromo-3-(2,2-difluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**3l**): white solid, 61 mg, 99% yield; m.p. 116-118 °C; ^{1}H NMR (400 MHz, $CDCl_3$), *δ*, ppm: 4.09 (*br*, 1H), 4.75-4.82 (*m*, 1H), 6.04 (*td, J* = 55.6, 3.4 Hz, 1H), 7.34 (*d*, *J* = 9.0 Hz, 1H), 7.73 (*dd*, *J* = 8.9, 2.4 Hz, 1H), 7.99 (*s*, 1H), 8.23 (*d*, *J* = 2.4 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), *δ*, ppm: -127.61 (*d*, *J* = 282.0 Hz, 1F), -130.83 (*d*, *J* = 282.3 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 69.0 (*t, J* = 24.8 Hz), 114.0 (*t, J* = 243.1 Hz), 119.0 (*t, J* = 3.3 Hz), 119.3, 120.3, 124.8, 128.3, 137.5, 155.0, 155.2, 176.5; ESI-HRMS, *m/z*: Calcd for $C_{11}H_8BrF_2O_3^+$ $[M+H]^+$: 304.9619, found: 304.9629.

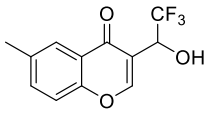


3-(2,2-Difluoro-1-hydroxyethyl)-6-nitro-4*H*-chromen-4-one (**3m**): yellow oil, 27 mg, 50% yield; ^{1}H NMR (400 MHz, $CDCl_3$), *δ*, ppm: 3.80 (*br*, 1H), 4.87-4.93 (*m*, 1H), 6.07 (*td, J* = 55.5, 3.0 Hz, 1H), 7.63 (*d*, *J* = 9.2 Hz, 1H), 8.09 (*s*, 1H), 8.48 (*dd*, *J* = 9.2, 2.8 Hz, 1H), 9.00 (*d*, *J* = 2.8 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), *δ*, ppm: -128.17 (*d*, *J* = 282.5 Hz, 1F), -131.53 (*d*, *J* = 282.3 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 67.3 (*t, J* = 24.8 Hz), 112.7 (*t, J* = 243.3 Hz), 118.8 (*t, J* = 3.2 Hz), 119.2, 121.5, 122.6, 127.6, 144.0, 154.5, 157.9, 175.1; ESI-HRMS, *m/z*: Calcd for $C_{11}H_8F_2NO_5^+$ $[M+H]^+$: 272.0365, found: 272.0371.

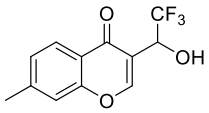
Characterization Data for the Products 4a-4l



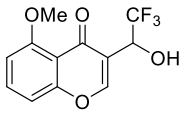
3-(2,2,2-Trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4a**): white solid, 48 mg, 99% yield; m.p. 78-80 °C (82.5-84.0 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 5.12-5.26 (*m*, 1H), 5.62 (*d*, *J* = 4.8 Hz, 1H), 7.44-7.51 (*m*, 2H), 7.71-7.76 (*m*, 1H), 8.10 (*s*, 1H), 8.19 (*dd*, *J* = 8.0, 1.6 Hz, 1H).



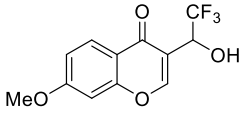
6-Methyl-3-(2,2,2-trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4b**): white solid, 51 mg, 99% yield; m.p. 101-103 °C (98.1-100.4°C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 2.47 (*s*, 3H), 5.02-5.09 (*m*, 1H), 5.61 (*d*, *J* = 8.4 Hz, 1H), 7.41 (*d*, *J* = 8.6 Hz, 1H), 7.55 (*dd*, *J* = 8.6, 2.0 Hz, 1H), 7.99 (*d*, *J* = 0.9 Hz, 1H), 8.02 (*s*, 1H).



7-Methyl-3-(2,2,2-trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4c**): white solid, 51 mg, 99% yield; m.p. 106-107 °C (101.0-103.0 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 2.51 (*s*, 3H), 4.98-5.06 (*m*, 1H), 5.62 (*d*, *J* = 8.6 Hz, 1H), 7.27-7.30 (*m*, 2H), 7.98 (*s*, 1H), 8.09 (*d*, *J* = 8.0 Hz, 1H).

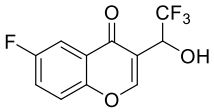


5-Methoxy-3-(2,2,2-trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4d**): white solid, 46 mg, 84% yield; m.p. 115-117 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 3.99 (*s*, 3H), 5.09-5.15 (*m*, 1H), 5.75 (*br*, 1H), 6.85 (*d*, *J* = 8.3 Hz, 1H), 7.02 (*dd*, *J* = 8.5, 0.8 Hz, 1H), 7.58-7.62 (*m*, 1H), 7.91 (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -78.40 (*s*, 3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 56.5, 67.7 (*q*, *J* = 33.4 Hz), 107.0, 110.1, 114.1, 118.2, 124.4 (*q*, *J* = 281.1 Hz), 134.8, 154.2, 158.0, 159.9, 177.6; ESI-HRMS, *m/z*: Calcd for $C_{12}H_{10}F_3O_4^+$ $[M+H]^+$: 275.0526, found:275.0514.

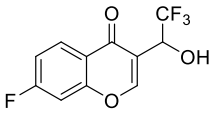


7-Methoxy-3-(2,2,2-trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4e**): white solid, 52 mg, 95% yield; m.p. 122-124 °C (128.6-130.5 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 3.92 (*s*, 3H), 5.02-5.06 (*m*, 1H), 5.74 (*d*, *J* = 8.2 Hz, 1H), 6.87 (*d*, *J* = 2.2 Hz, 1H), 7.02 (*dd*, *J* = 9.0, 2.2

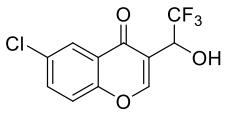
Hz, 1H), 7.96 (*s*, 1H), 8.10 (*d*, *J* = 9.0 Hz, 1H).



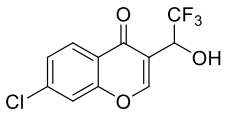
6-Fluoro-3-(2,2,2-trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4f**): white solid, 52 mg, 99% yield; m.p. 111-113 °C (108.3-110.3 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), *δ*, ppm: 5.17-5.18 (*m*, 1H), 5.28-5.31 (*m*, 1H), 7.45-7.50 (*m*, 1H), 7.55 (*dd*, *J* = 9.2, 4.2 Hz, 1H), 7.83 (*dd*, *J* = 8.0, 3.0 Hz, 1H), 8.11 (*s*, 1H).



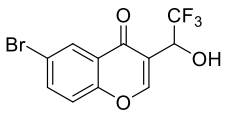
7-Fluoro-3-(2,2,2-trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4g**): white solid, 69 mg, 99% yield; m.p. 99-100 °C (96.4-98.2 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), *δ*, ppm: 5.06-5.14 (*m*, 1H), 5.27 (*d*, *J* = 8.3 Hz, 1H), 7.19-7.24 (*m*, 2H), 8.05 (*s*, 1H), 8.25 (*dd*, *J* = 9.6, 6.2 Hz, 1H).



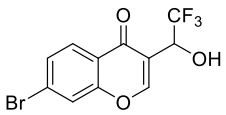
6-Chloro-3-(2,2,2-trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4h**): white solid, 53 mg, 95% yield; m.p. 100-102 °C (102.9-104.5 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), *δ*, ppm: 5.02-5.15 (*m*, 2H), 7.49 (*d*, *J* = 8.0 Hz, 1H), 7.79 (*dd*, *J* = 8.0, 2.4 Hz, 1H), 8.07 (*s*, 1H), 8.18 (*d*, *J* = 2.4 Hz, 1H).



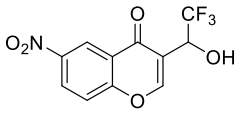
7-Chloro-3-(2,2,2-trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4i**): white solid, 52 mg, 94% yield; m.p. 119-121 °C (115.7-117.0 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), *δ*, ppm: 5.13-5.19 (*m*, 1H), 5.31 (*d*, *J* = 7.8 Hz, 1H), 7.43 (*dd*, *J* = 8.6, 1.8 Hz, 1H), 7.53 (*d*, *J* = 1.8 Hz, 1H), 8.07 (*s*, 1H), 8.18 (*d*, *J* = 8.6 Hz, 1H).



6-Bromo-3-(2,2,2-trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4j**): white solid, 63 mg, 99% yield; m.p. 99-101 °C (97.0-98.4 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), *δ*, ppm: 5.07-5.35 (*m*, 2H), 7.41 (*d*, *J* = 8.9 Hz, 1H), 7.81 (*dd*, *J* = 8.9, 2.4 Hz, 1H), 8.11 (*s*, 1H), 8.30 (*d*, *J* = 2.4 Hz, 1H).

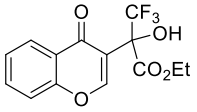


7-Bromo-3-(2,2,2-trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4k**): white solid, 57 mg, 88% yield; m.p. 132-134 °C (128.5-130.5 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 5.14-5.19 (*m*, 1H), 5.30 (*br*, 1H), 7.57 (*dd*, *J* = 8.6, 1.8 Hz, 1H), 7.70 (*d*, *J* = 1.8 Hz, 1H), 8.04-8.06 (*m*, 2H).

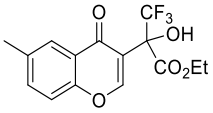


6-Nitro-3-(2,2,2-trifluoro-1-hydroxyethyl)-4*H*-chromen-4-one (**4l**): yellow oil, 40 mg, 65% yield; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 4.77 (*s*, 1H), 5.18-5.21 (*m*, 1H), 7.64 (*d*, *J* = 9.2 Hz, 1H), 8.13 (*s*, 1H), 8.49 (*dd*, *J* = 9.2, 2.8 Hz, 1H), 8.99 (*d*, *J* = 2.8 Hz, 1H).

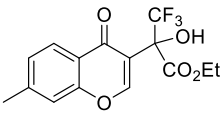
Characterization Data for the Products 5a-5l



Ethyl 3,3,3-trifluoro-2-hydroxy-2-(4-oxo-4*H*-chromen-3-yl)propanoate (**5a**): white solid, 62 mg, 99% yield; m.p. 77-79 °C (75.1-77.0 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 1.31 (*t*, *J* = 8.0 Hz, 3H), 4.34-4.44 (*m*, 2H), 5.98 (*br*, 1H), 7.46-7.53 (*m*, 2H), 7.73-7.77 (*m*, 1H), 8.19 (*dd*, *J* = 8.0, 1.4 Hz, 1H), 8,32 (*s*, 1H); ^{19}F NMR(376 MHz, $CDCl_3$), δ, ppm: -74.94 (*s*, 3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.9, 64.0, 76.3 (*q*, *J* = 30.2 Hz), 118.1, 118.2, 123.0 (*q*, *J* = 285.2 Hz), 123.5, 125.9, 126.1, 134.8, 155.4 (*q*, *J* = 3.4 Hz), 155.9, 167.6, 176.9.

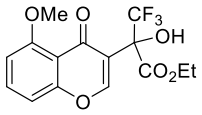


Ethyl 3,3,3-trifluoro-2-hydroxy-2-(6-methyl-4-oxo-4*H*-chromen-3-yl)-propanoate (**5b**): white solid, 61 mg, 92% yield; m.p. 79-81 °C (86.4-88.2 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 1.23 (*t*, *J* = 8.0 Hz, 3H), 2.38 (*s*, 3H), 4.25-4.35 (*m*, 2H), 6.07 (*s*, 1H), 7.33 (*d*, *J* = 8.6 Hz, 1H), 7.46 (*dd*, *J* = 8.6, 1.9 Hz, 1H), 7.87 (*s*, 1H), 8.21 (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -75.11 (*s*, 3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.8, 21.0, 63.9, 73.4 (*q*, *J* = 30.0 Hz), 117.6, 117.9, 123.0 (*q*, *J* = 285.3 Hz), 123.2, 125.1, 136.1, 136.2, 154.2, 155.3 (*q*, *J* = 3.3 Hz), 167.6, 177.1.

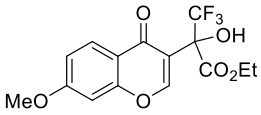


Ethyl 3,3,3-trifluoro-2-hydroxy-2-(7-methyl-4-oxo-4*H*-chromen-3-yl)propanoate (**5c**): white solid, 63 mg, 96% yield; m.p. 83-84 °C (86.6-87.9 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 1.22 (*t*, *J* = 8.0 Hz, 3H), 2.42 (*s*, 3H), 4.25-4.35 (*m*, 2H), 6.12 (*br*, 1H), 7.17-7.22 (*m*, 2H), 7.97 (*d*, *J* = 8.0 Hz, 1H), 8.19 (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -75.15 (*s*,

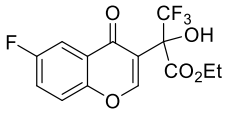
3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.8, 21.9, 63.8, 73.4 (*q*, *J* = 30.0 Hz), 117.6, 117.8, 121.2, 123.0 (*q*, *J* = 285.2 Hz), 125.5, 127.6, 146.5, 155.2 (*q*, *J* = 3.5 Hz), 156.0, 167.6, 177.0.



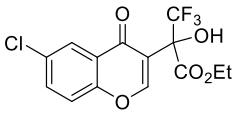
Ethyl 3,3,3-trifluoro-2-hydroxy-2-(5-methoxy-4-oxo-4*H*-chromen-3-yl)propanoate (**5d**): white solid, 69 mg, 99% yield; m.p. 86-89 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 1.30 (*t*, *J* = 8.0 Hz, 3H), 3.97 (*s*, 3H), 4.31-4.44 (*m*, 2H), 5.87 (*br*, 1H), 6.85 (*d*, *J* = 8.4 Hz, 1H), 7.05 (*d*, *J* = 8.4 Hz, 1H), 7.62 (*t*, *J* = 8.0 Hz, 1H), 8.13 • (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -74.69 (*s*, 3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.9, 56.5, 63.8, 76.5 (*q*, *J* = 30.0 Hz), 107.0, 109.9, 114.1, 119.4, 123.0 (*q*, *J* = 285.2 Hz), 135.0, 153.2 (*q*, *J* = 3.7 Hz), 157.8, 160.0, 167.5, 176.6; ESI-HRMS, *m/z*: Calcd for $C_{15}H_{14}F_3O_6^+$ $[M+H]^+$: 347.0737, found: 347.0732.



Ethyl 3,3,3-trifluoro-2-hydroxy-2-(7-methoxy-4-oxo-4*H*-chromen-3-yl)propanoate (**5e**): white solid, 57 mg, 82% yield; m.p. 107-109 °C (106.8-108.1 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 1.31 (*t*, *J* = 8.0 Hz, 3H), 3.93 (*s*, 3H), 4.33-4.42 (*m*, 2H), 6.34 (*s*, 1H), 6.88 (*d*, *J* = 2.4 Hz, 1H), 7.02 (*dd*, *J* = 9.0, 2.4 Hz, 1H), 8.08 (*d*, *J* = 9.0 Hz, 1H), 8.24 (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -75.26 (*s*, 3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.9, 56.0, 63.8, 76.5 (*q*, *J* = 30.0 Hz), 100.1, 115.6, 117.3, 117.4, 123.0 (*q*, *J* = 285.2 Hz), 127.2, 154.9 (*q*, *J* = 3.4 Hz), 157.8, 164.9, 167.6, 176.4.

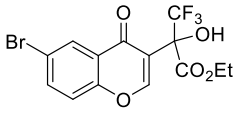


Ethyl 3,3,3-trifluoro-2-(6-fluoro-4-oxo-4*H*-chromen-3-yl)-2-hy-droxypropanoate (**5f**): white solid, 66 mg, 99% yield; m.p. 90-92 °C (90.3-91.6 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 1.31 (*t*, *J* = 8.0 Hz, 3H), 4.35-4.43 (*m*, 2H), 5.69 (*s*, 1H), 7.45-7.50 (*m*, 1H), 7.55 (*dd*, *J* = 9.2, 4.2 Hz, 1H), 7.81 (*dd*, *J* = 8.0, 3.0 Hz, 1H), 8.32 (*s*, 1H); ^{19}F NMR(376 MHz, $CDCl_3$), δ, ppm: -74.72 (*s*, 3F), -113.33 (*s*, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.8, 64.1, 76.1 (*q*, *J* = 30.3 Hz), 110.8 (*d*, *J* = 23.8 Hz), 117.9, 120.5 (*d*, *J* = 8.2 Hz), 122.9 (*q*, *J* = 285.3 Hz), 123.1 (*d*, *J* = 25.3 Hz), 124.7 (*d*, *J* = 7.6 Hz), 152.1 (*d*, *J* = 1.3 Hz), 155.4 (*q*, *J* = 3.6 Hz), 159.9 (*d*, *J* = 247.0 Hz), 167.5, 176.0 (*d*, *J* = 2.3 Hz).

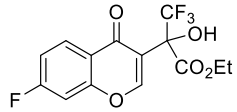


Ethyl 2-(6-chloro-4-oxo-4*H*-chromen-3-yl)-3,3,3-trifluoro-2-hy-droxypropanoate (**5g**): white solid, 64 mg, 92% yield; m.p. 119-121 °C (111.5-112.6 °C[4]); ^{1}H NMR (400 MHz,

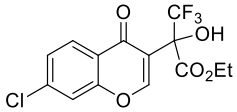
$CDCl_3$), δ, ppm: 1.31 (*t*, *J* = 8.0 Hz, 3H), 4.34-4.42 (*m*, 2H), 5.63 (*br*, 1H), 7.49 (*d*, *J* = 8.9 Hz, 1H), 7.68 (*dd*, *J* = 9.0, 2.6 Hz, 1H), 8.13 (*d*, *J* = 2.6 Hz, 1H), 8.30 (*s*, 1H); ^{19}F NMR(376 MHz, $CDCl_3$), δ, ppm: -74.66 (*s*, 3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.8, 64.1, 75.9 (*q*, *J* = 30.3 Hz), 118.6, 120.0, 122.9 (*q*, *J* = 285.3 Hz), 124.4, 125.3, 132.1, 135.0, 154.2, 155.4 (*q*, *J* = 3.5 Hz), 167.5, 175.5.



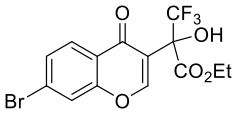
Ethyl 2-(6-bromo-4-oxo-4*H*-chromen-3-yl)-3,3,3-trifluoro-2-hy-droxypropanoate (**5h**): white solid, 69 mg, 88% yield; m.p. 127-128 °C (124.6-125.8 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 1.31 (*t*, *J* = 8.0 Hz, 3H), 4.33-4.44 (*m*, 2H), 5.60 (*s*, 1H), 7.43 (*d*, *J* = 8.8 Hz, 1H), 7.82 (*dd*, *J* = 8.9, 2.4 Hz, 1H), 8.30 (*s*, 2H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -74.64 (*s*, 3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.8, 64.1, 76.0 (*q*, *J* = 30.0 Hz), 118.8, 119.5, 120.2, 122.9 (*q*, *J* = 285.3 Hz), 124.8, 128.5, 137.8, 154.6, 155.4 (*q*, *J* = 3.6 Hz), 167.5, 175.3.



Ethyl 3,3,3-trifluoro-2-(7-fluoro-4-oxo-4*H*-chromen-3-yl)-2-hy-droxypropanoate (**5i**): white solid, 64 mg, 99% yield; m.p. 85-87 °C (80.7-82.2 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 1.22 (*t*, *J* = 8.0 Hz, 3H), 4.26-4.35 (*m*, 2H), 5.68 (*s*, 1H), 7.10-7.14 (*m*, 2H), 8.11-8.15 (*m*, 1H), 8.20 (*s*, 1H); ^{19}F NMR(376 MHz, $CDCl_3$) δ -74.82 (*s*, 3F), -100.38 (*s*, 1F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.8, 64.0, 76.0(*q*, *J* = 30.0 Hz), 104.9 (*d*, *J* = 25.4 Hz), 115.0 (*d*, *J* = 27.3 Hz), 118.6, 120.4 (*d*, *J* = 2.1 Hz), 122.9 (*q*, *J* = 285.4 Hz), 128.6 (*d*, *J* = 10.7 Hz), 155.4 (*q*, *J* = 3.1 Hz), 156.9 (*d*, *J* = 13.6 Hz), 166.1 (*d*, *J* = 255.8 Hz), 167.5, 175,8.

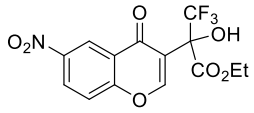


Ethyl 2-(7-chloro-4-oxo-4*H*-chromen-3-yl)-3,3,3-trifluoro-2-hy-droxypropanoate(**5j**): white solid, 62 mg, 89% yield; m.p. 104-106 °C (103.6-106.1 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 1.30 (*t*, *J* = 8.0 Hz, 3H), 4.34-4.44 (*m*, 2H), 5.68 (*s*, 1H), 7.42 (*dd*, *J* = 8.6, 1.9 Hz, 1H), 7.54 (*d*, *J* = 1.8 Hz, 1H), 8.11 (*d*, *J* = 8.6 Hz, 1H), 8.27 (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -74.71 (*s*, 3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.8, 64.1, 76.0 (*q*, *J* = 30.3Hz), 118.3, 118.8, 122.0, 122.9 (*q*, *J* = 285.3 Hz), 127.0, 127.3, 141.0, 155.3 (*q*, *J* = 3.6 Hz), 155.9, 167.5, 175.9.

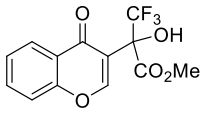


Ethyl 2-(7-bromo-4-oxo-4*H*-chromen-3-yl)-3,3,3-trifluoro-2-hy-droxypropanoate (**5k**):

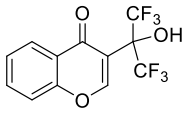
white solid, 77 mg, 97% yield; m.p. 106-108 °C (114.4-115.9 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 1.30 (*t*, *J* = 8.0 Hz, 3H), 4.33-4.44 (*m*, 2H), 5.66 (*br*, 1H), 7.58 (*dd*, *J* = 8.6, 1.8 Hz, 1H), 7.71 (*d*, *J* = 1.7 Hz, 1H), 8.03 (*d*, *J* = 8.6 Hz, 1H), 8.27 (*s*, 1H); ^{19}F NMR(376 MHz, $CDCl_3$), δ, ppm: -74.69 (*s*, 3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.8, 64.1, 76.0 (*q*, *J* = 30.4 Hz), 118.8, 121.3, 122.4, 122.9 (*q*, *J* = 285.3 Hz), 127.3, 129.2, 129.7, 155.2 (*q*, *J* = 3.6 Hz), 155.8, 167.5, 176.0.



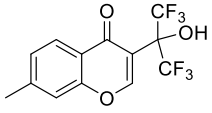
Ethyl 3,3,3-trifluoro-2-hydroxy-2-(6-nitro-4-oxo-4*H*-chromen-3-yl)-propanoate (**5l**): yellow solid, 51.0 mg, 71% yield; m.p. 129-131 °C (124.6-126.1 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 1.31 (*t*, *J* = 8.0 Hz, 3H), 4.36-4.45 (*m*, 2H), 5.24 (*s*, 1H), 7.72 (*d*, *J* = 9.2 Hz, 1H), 8.35 (*d*, *J* = 0.6 Hz, 1H), 8.59 (*dd*, *J* = 9.2, 2.8 Hz, 1H), 9.06 (*d*, *J* = 2.8 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -74.29 (*s*, 3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 13.8, 64.4, 76.0 (*q*, *J* = 30.6 Hz), 119.9, 120.2, 122.68，122.73 (*q*, *J* = 285.3 Hz), 123.7, 128.9, 145.2, 155.6 (*q*, *J* = 3.8 Hz), 158.6, 167.3, 174.9.



Methyl 3,3,3-trifluoro-2-hydroxy-2-(4-oxo-4*H*-chromen-3-yl)propanoate (**5b**): white solid, 51 mg, 85% yield; m.p. 83-85 °C (78.5-79.9 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 3.92 (*s*, 3H), 6.12 (*s*, 1H), 7.45-7.53 (*m*, 2H), 7.73-7.78 (*m*, 1H), 8.19 (*dd*, *J* = 8.0, 1.6 Hz, 1H), 8.32 (*d*, *J* = 1.6 Hz, 1H); ^{19}F NMR(376 MHz, $CDCl_3$), δ, ppm: -75.21 (*s*, 3F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 54.4, 76.4 (*q*, *J* = 30.5 Hz), 117.8, 118.2, 123.0 (*q*, *J* = 285.3 Hz), 123.5, 125.9, 126.1, 134.9, 155.5 (*q*, *J* = 3.4 Hz), 155.9, 168.2, 177.1.

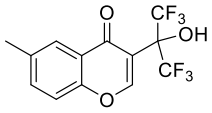


3-(1,1,1,3,3,3-Hexafluoro-2-hydroxypropan-2-yl)-4*H*-chromen-4-one (**5n**): white solid, 40 mg, 64% yield; m.p. 106-108 °C (99.6-101.6 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 7.46-7.52 (*m*, 2H), 7.75-7.79 (*m*, 1H), 8.18 (*dd*, *J* = 8.0, 1.6 Hz, 1H), 8.25 (*s*, 1H), 9.91 (*s*, 1H).

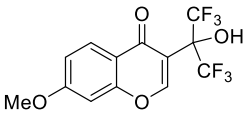


3-(1,1,1,3,3,3-Hexafluoro-2-hydroxypropan-2-yl)-7-methyl-4*H*-chromen-4-one (**5o**):

white solid, 40 mg, 62% yield; m.p. 95-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 2.50 (*s*, 3H), 7.47 (*d*, *J* = 8.8 Hz, 1H), 7.63 (*dd*, *J* = 8.8, 2.4 Hz, 2H), 8.02 (*m*, 1H), 8.29 (*s*, 1H), 10.08 (*s*, 1H); ^{19}F NMR(376 MHz, $CDCl_3$), δ, ppm: -77.28 (*s*, 6F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 21.1, 78.14 (*q*, *J* = 31.0 Hz), 110.1, 118.0, 122.46 (*q*, *J* = 287.0 Hz), 122.82, 125.08, 137.0, 137.2, 154.0, 156.5-156.7 (*m*), 180.5; ESI-HRMS, *m/z*: Calcd for $C_{13}H_9F_6O_3^+$ $[M+H]^+$: 327.0450, found: 327.0435.

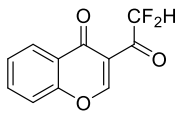


3-(1,1,1,3,3,3-Hexafluoro-2-hydroxypropan-2-yl)-6-methyl-4*H*-chromen-4-one (**5p**): white solid, 36 mg, 52% yield; m.p. 97-99 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 2.55 (*s*, 3H), 7.34-7.36 (*m*, 2H), 8.12 (*d*, *J* = 8.2 Hz, 1H), 8.27 (*s*, 1H), 10.11 (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -77.30 (*s*, 6F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 22.1, 78.14 (*q*, *J* = 31.0 Hz), 110.1, 117.9, 120.9, 122.46 (*q*, *J* = 287.0 Hz), 125.6, 128.4, 147.7, 155.8, 156.4-156.6 (*m*), 180.3; ESI-HRMS, *m/z*: Calcd for $C_{13}H_9F_6O_3^+$ $[M+H]^+$: 327.0450, found: 327.0435.

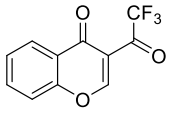


3-(1,1,1,3,3,3-Hexafluoro-2-hydroxypropan-2-yl)-7-methoxy-4*H*-chromen-4-one (**5q**): white solid, 35 mg, 51% yield; m.p. 114-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 3.95 (*s*, 3H), 7.09 (*dd*, *J* = 9.2, 2.4 Hz, 1H), 7.27 (*s*, 1H), 8.13 (*d*, *J* = 9.2 Hz, 1H), 8.22 (*s*, 1H), 10.24 (*s*, 1H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -77.33 (*s*, 6F); ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 56.2, 78.14 (*q*, *J* = 31.0 Hz), 100.0, 110.0, 116.5, 116.8, 122.47 (*q*, *J* = 285.0 Hz), 127.3, 156.0-156.2 (*m*), 157.6, 165.7, 179.6; ESI-HRMS, *m/z*: Calcd for $C_{13}H_9F_6O_4^+$ $[M+H]^+$: 343.0400, found: 343.0403.

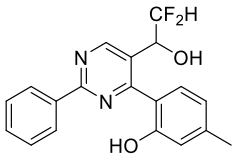
Characterization Data for the Products 6a-6d.



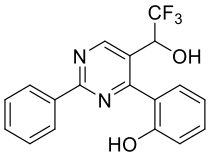
3-(2,2-Difluoroacetyl)-4*H*-chromen-4-one (**6a**): white solid, 14 mg, 62% yield; m.p. 160-161 °C (165-166 °C[5]); ^{1}H NMR (400 MHz, CD_3OD), δ, ppm: 6.10-6.39 (*m*, 1H), 7.49-7.53 (*m*, 1H), 7.63 (*d*, *J* = 8.0 Hz, 1H), 7.80-7.84 (*m*, 1H), 8.16 (*dd*, *J* = 8.0, 1.5 Hz, 1H), 8.46 (*s*, 1H); ^{19}F NMR (376 MHz, CD_3OD), δ, ppm: -131.66 (*d*, *J* = 282.2 Hz, 1F), -140.75 (*d*, *J* = 281.7 Hz, 1F);^{13}C NMR (100 MHz, CD_3OD), δ, ppm: 113.23, 113,27 (*t*, *J* = 243.0 Hz), 117.7, 118.2, 123.5, 125.1, 125.8, 134.6, 156.4, 158.8, 177.1.



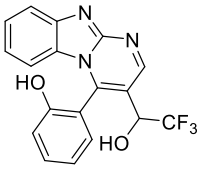
3-(2,2,2-Trifluoroacetyl)-4*H*-chromen-4-one (**6b**): white solid, 12 mg, 50% yield; m.p. 148-149 °C (145 °C[6]); ^{1}H NMR (400 MHz, CD_3OD), δ, ppm:7.53-7.57 (*m*, 1H), 7.66 (*d*, *J* = 8.4 Hz, 1H), 7.84-7.88 (*m*, 1H), 8.19 (*dd*, *J* = 8.4, 1.6 Hz, 1H), 8.49 (*s*, 1H); ^{19}F NMR (376 MHz, CD_3OD), δ, ppm: -86.51 (*s*, 3F); ^{13}C NMR (100 MHz, DMSO-d6), δ, ppm: 92.6 (*q*, *J* = 33.0 Hz), 119.0, 119.1, 123.3, 123.7 (*q*, *J* = 287.7 Hz), 125.6, 127.0, 135.9, 156.2, 159.8, 177.8.



2-(5-(2,2-Difluoro-1-hydroxyethyl)-2-phenylpyrimidin-4-yl)-5-methylphenol (**6c**): yellow solid, 63 mg, 92% yield; m.p. 68-70 °C; ^{1}H NMR (400 MHz, CD_3OD), δ, ppm: 2.34 (s, 3H), 5.01-5.07 (*m*, 1H), 5.92 (*td*, *J* = 55.3, 2.4 Hz, 1H), 6.80 (*s*, 1H), 6.83 (*d*, *J* = 7.8 Hz, 1H), 7.26 (*d*, *J* = 7.8 Hz, 1H), 7.45-7.47 (*m*, 3H), 8.38-8.41 (*m*, 1H), 9.03 (*s*, 1H); ^{19}F NMR (376 MHz, CD_3OD), δ, ppm: -128.88 (*d*, *J* = 282.3 Hz, 1F), -132.73 (*d*, *J* = 282.2 Hz, 1F); ^{13}C NMR (100 MHz, CD_3OD), δ, ppm: 20.1, 68.1 (*t*, *J* = 22.7 Hz), 115.5 (*t*, *J* = 243.3 Hz), 116.0, 120.6, 121.6, 127.9, 128.0, 128.3, 130.59, 130.62, 137.1, 141.6, 154.0, 157.1, 163.8, 164.5; ESI-HRMS, m/z: Calcd for $C_{19}H_{17}F_2N_2O_2^+$ $[M+H]^+$: 343.1253, found: 343.1236.



2-(2-Phenyl-5-(2,2,2-trifluoro-1-hydroxyethyl) pyrimidin-4-yl) phenol (**6d**): yellow oil[4], 62 mg, 90% yield; ^{1}H NMR (400 MHz, CD_3OD), δ, ppm: 5.33 (*q*, *J* = 6.8 Hz, 1H), 6.97-7.03 (*m*, 2H), 7.34-7.37 (*m*, 2H), 7.46-7.48 (*m*, 3H), 7.41-7.44 (*m*, 2H), 9.09 (*s*, 1H).



2-(3-(2,2,2-Trifluoro-1-hydroxyethyl)benzo[4,5]imidazo[1,2-a]pyrimidin-4-yl)phenol (**6e**): yellow solid, 30 mg, 42% yield; m.p. 91-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 4.98-5.03 (*m*, 1H), 6.22 (*d*, *J* = 8.0 Hz, 1H), 6.92-6.96 (*m*, 1H), 7.05-7.09 (*m*, 2H), 7.15 (*d*, *J* = 6.8 Hz, 1H), 7.24-7.28 (*m*, 1H), 7.44-7.54 (*m*, 2H); ^{19}F NMR (376 MHz, $CDCl_3$), δ, ppm: -77.02; ^{13}C NMR (100 MHz, $CDCl_3$), δ, ppm: 65.16 (*q*, *J* = 32.0 Hz), 113.3, 115.53, 116.47, 118.37, 118.68, 119.97, 121.48, 124.18 (*q*, *J* = 246.0 Hz), 125.30, 126.67, 129.28, 132.22, 142.56, 146.28, 149.16, 154.08, 154.95; ESI-HRMS, m/z: Calcd for $C_{18}H_{13}F_3N_3O_2^+$ $[M+H]^+$:

360.0954, found: 360.0941.

Data of Single-crystal X-ray Analysis

Table S1. Crystal data and structure refinement for **3k**

Compound	**3k**
Empirical formula	$C_{11}H_7BrF_2O_3$
Formula weight	305.08
Crystal system	Monoclinic
Space group	$P2_1/c$
a (Å)	11.4857(15)
b (Å)	9.7788(14)
c (Å)	9.6329(11)
α (°)	90.00
β (°)	101.874(12)
γ (°)	90.00
Volume(Å^3)	1058.8(2)
Z	4
D_{calc} (g cm^{-3})	1.914
F (000)	600.0
Reflections collected	3446
Independent reflections	1976
R_{int}	0.052
Goodness-of-fit on F^2	1.017
R_1, wR_2 [$I >= 2\sigma(I)$]	0.0679, 0.1727
R_1, wR_2[all data]	0.0867, 0.2021

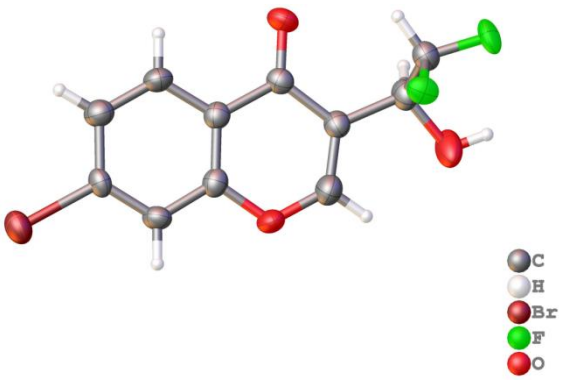


Fig. S1. The molecular structure of **3k**

NMR Spectra for All Compounds 3a-3m, 4a- 4l, 5a-5q and 6a-6e.

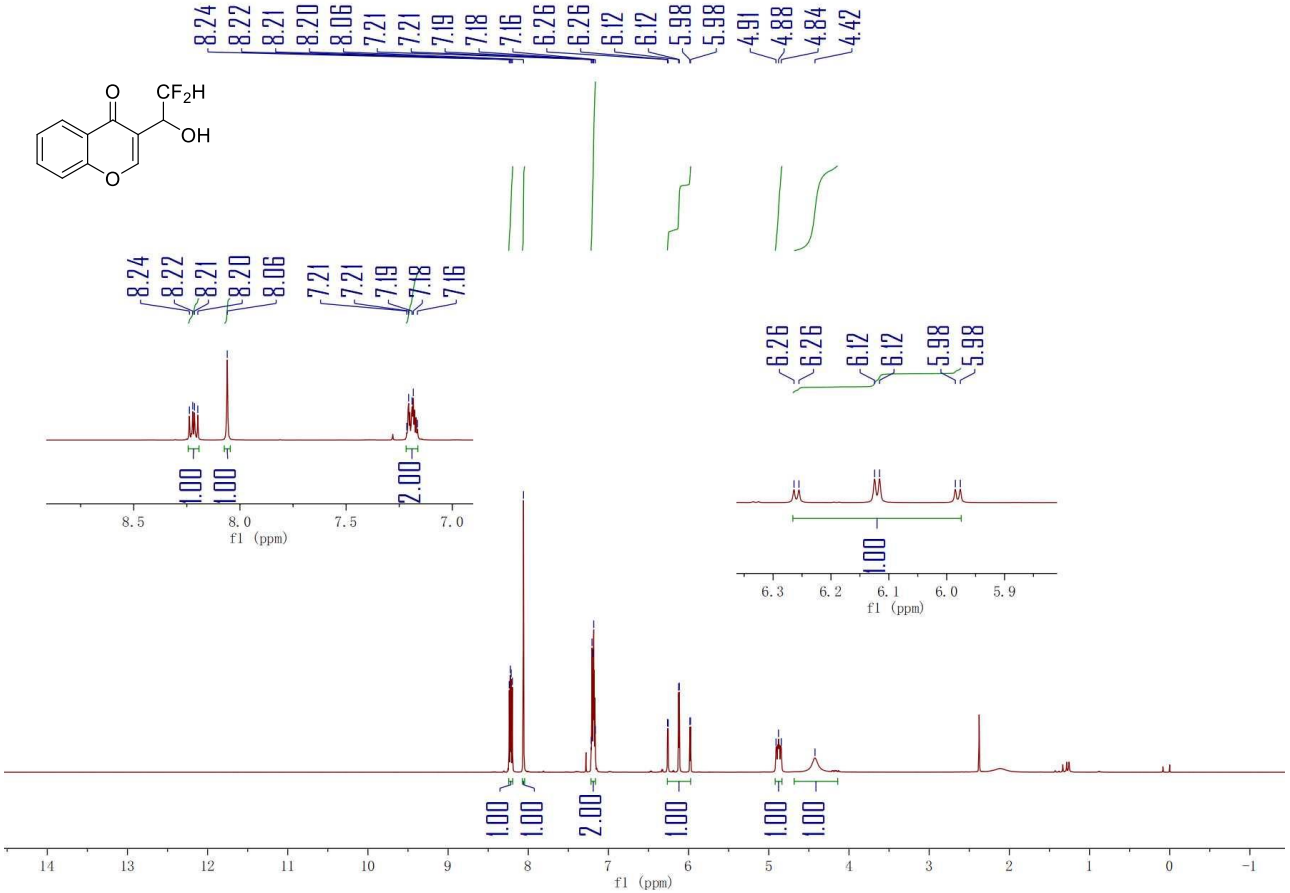


Fig. S2. ^{1}H NMR spectrum of compound **3a**

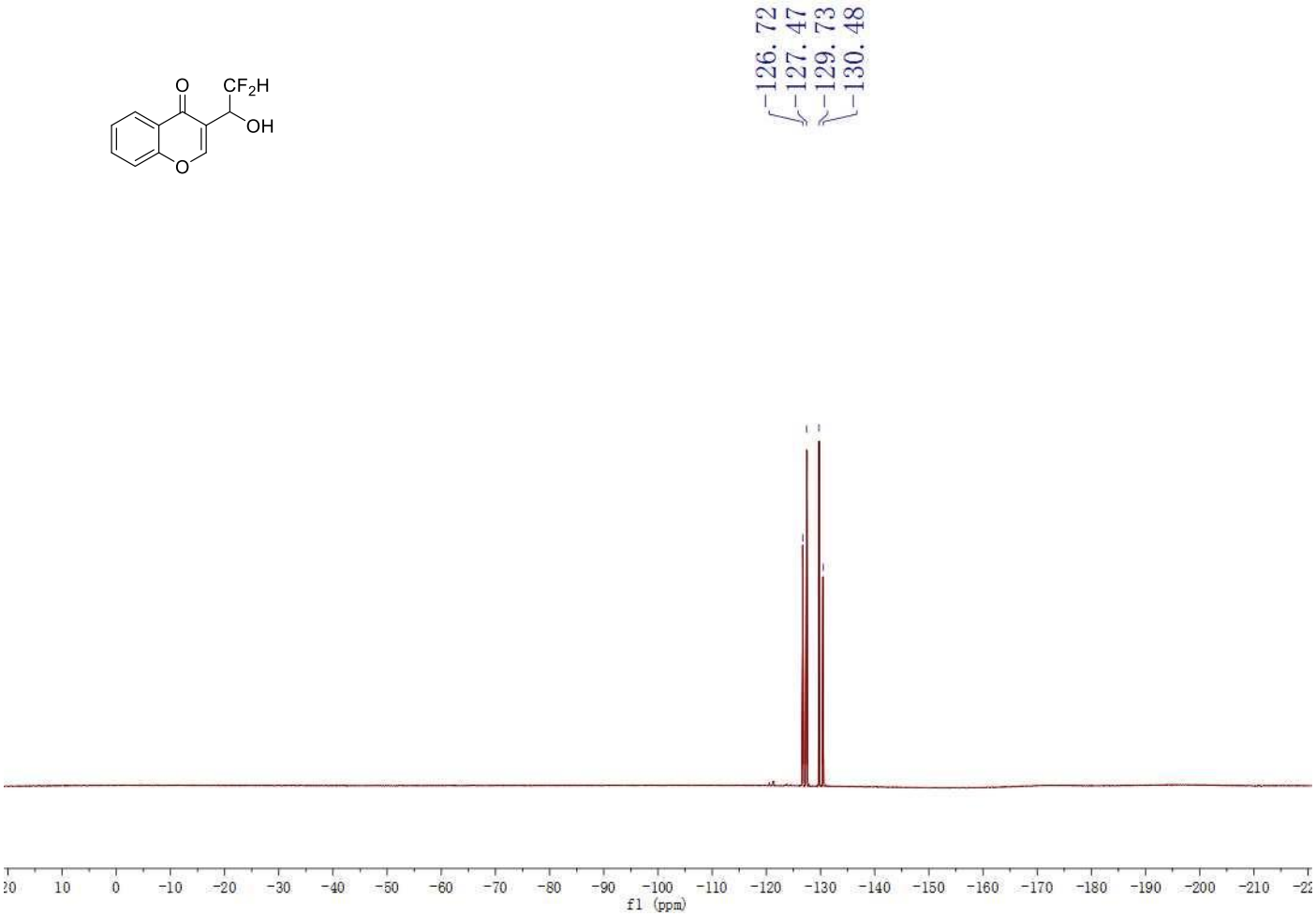


Fig. S3. ^{19}F NMR spectrum of compound **3a**

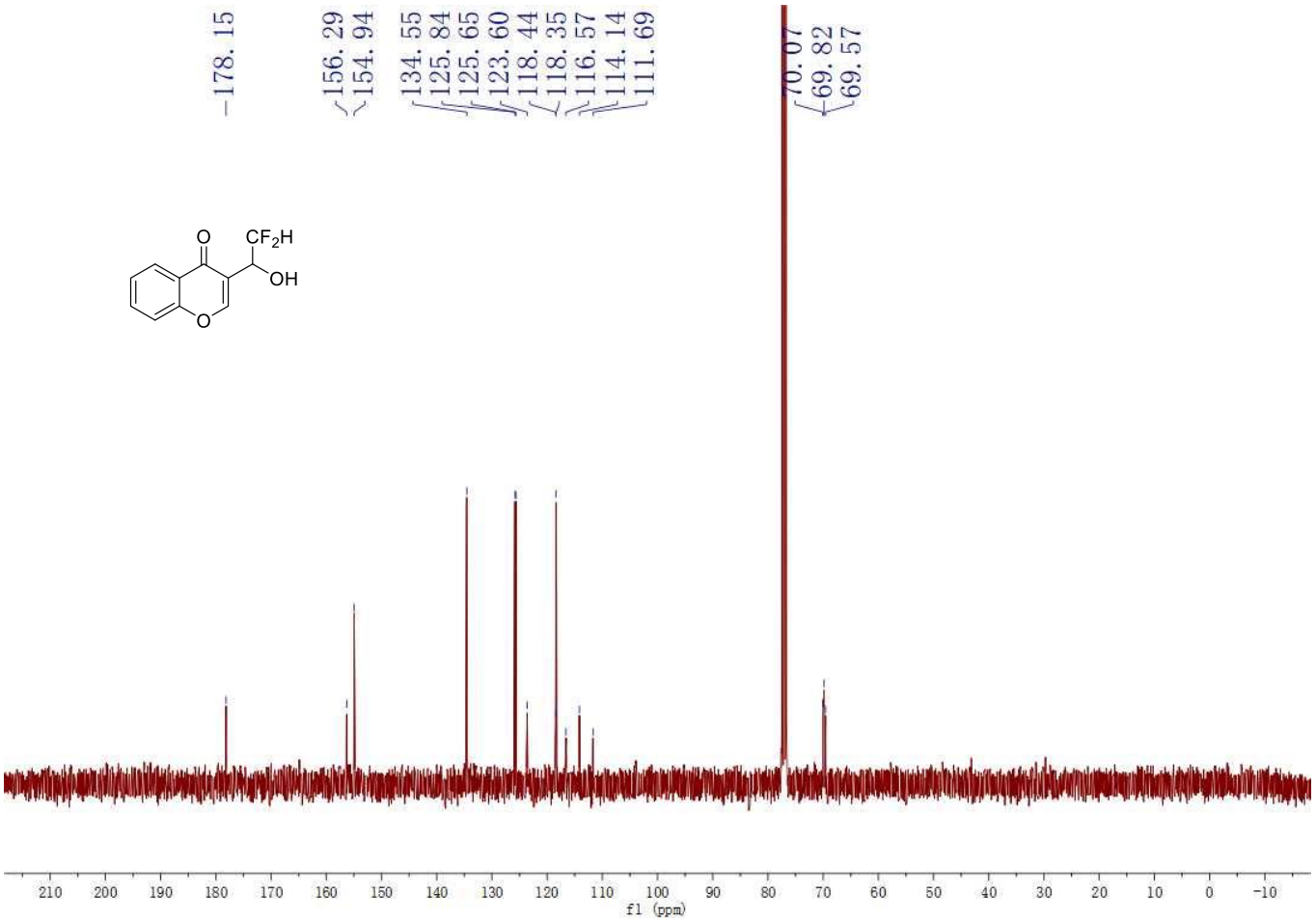


Fig. S4. ^{13}C NMR spectrum of compound **3a**

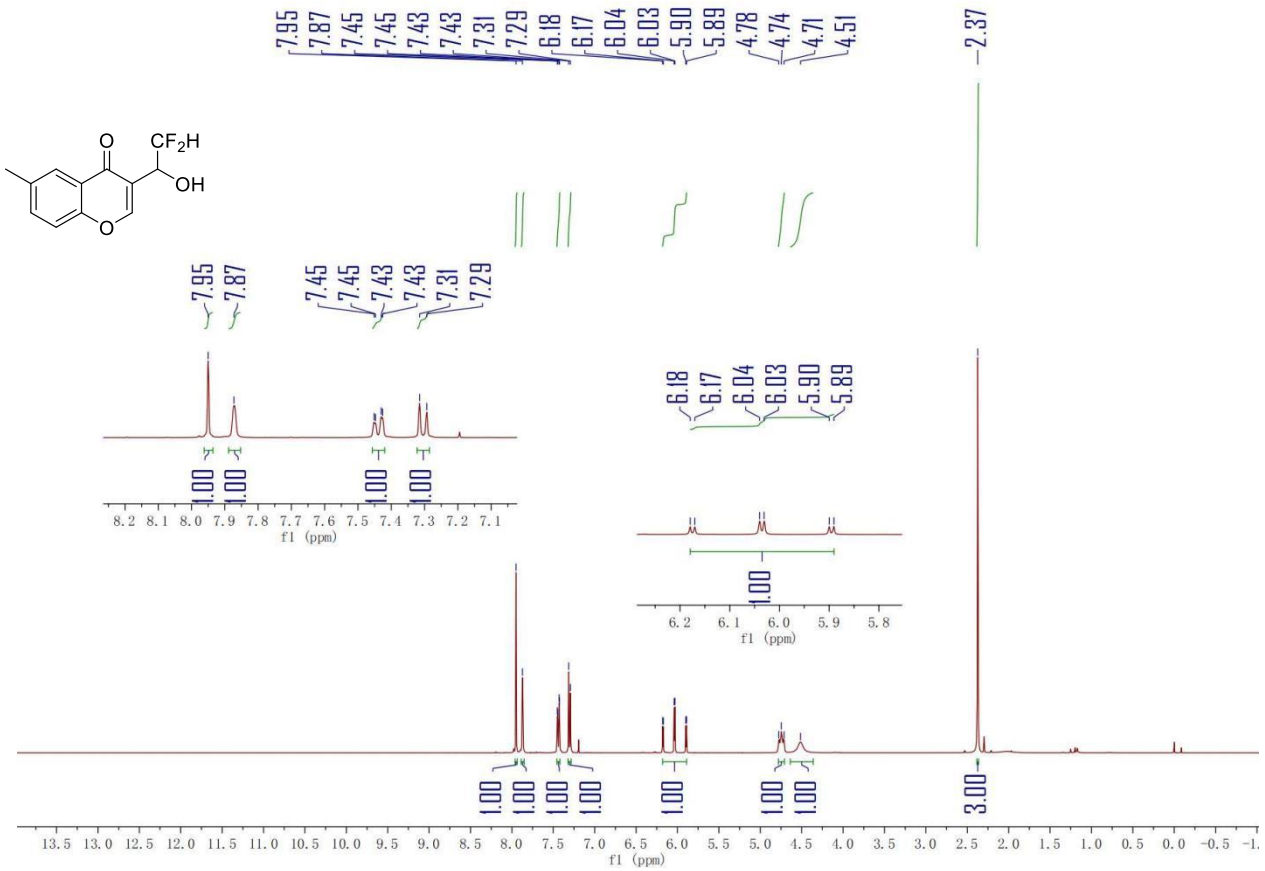


Fig. S5. ^{1}H NMR spectrum of compound **3b**

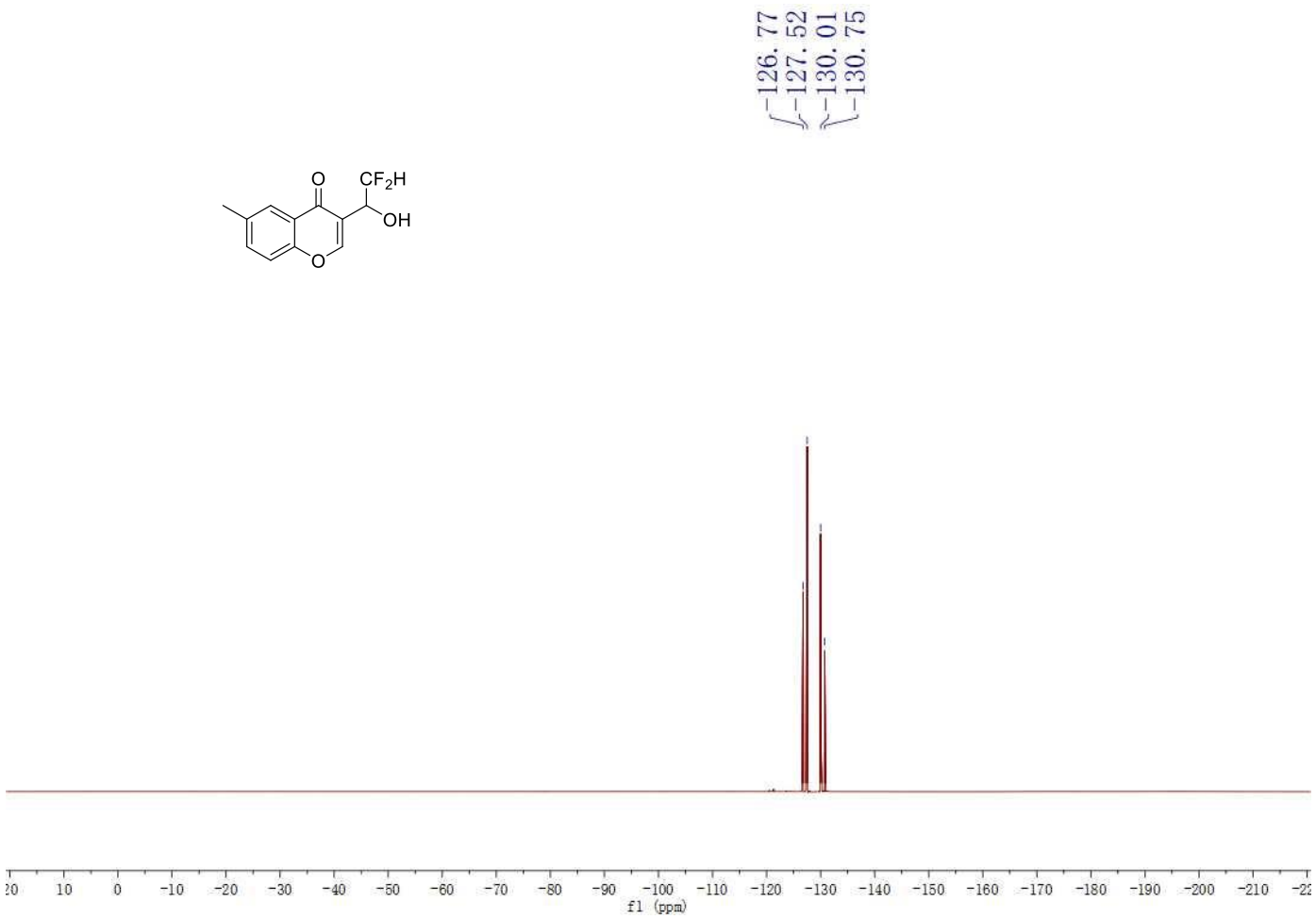


Fig. S6. ^{19}F NMR spectrum of compound **3b**

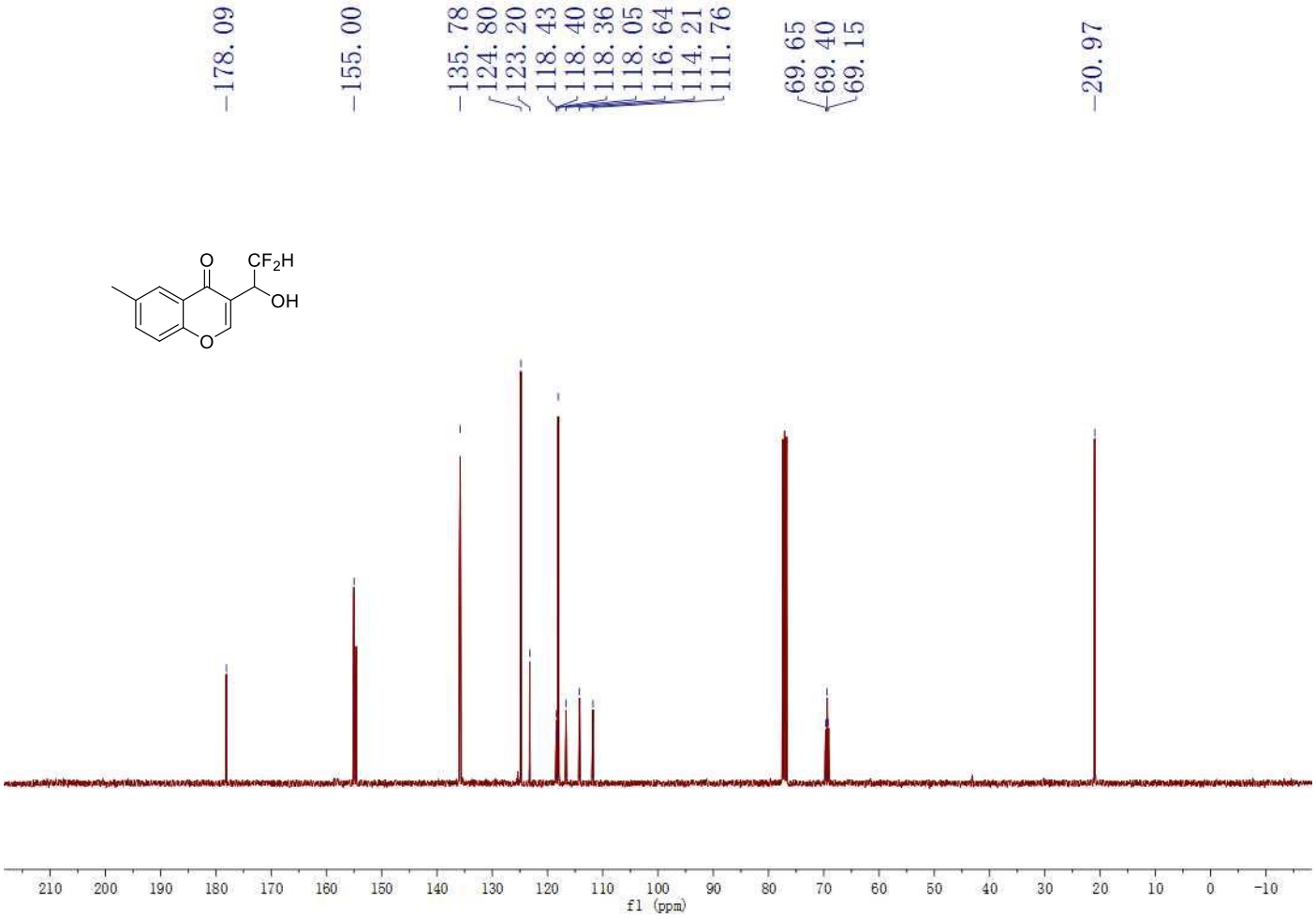


Fig. S7. ^{13}C NMR spectrum of compound **3b**

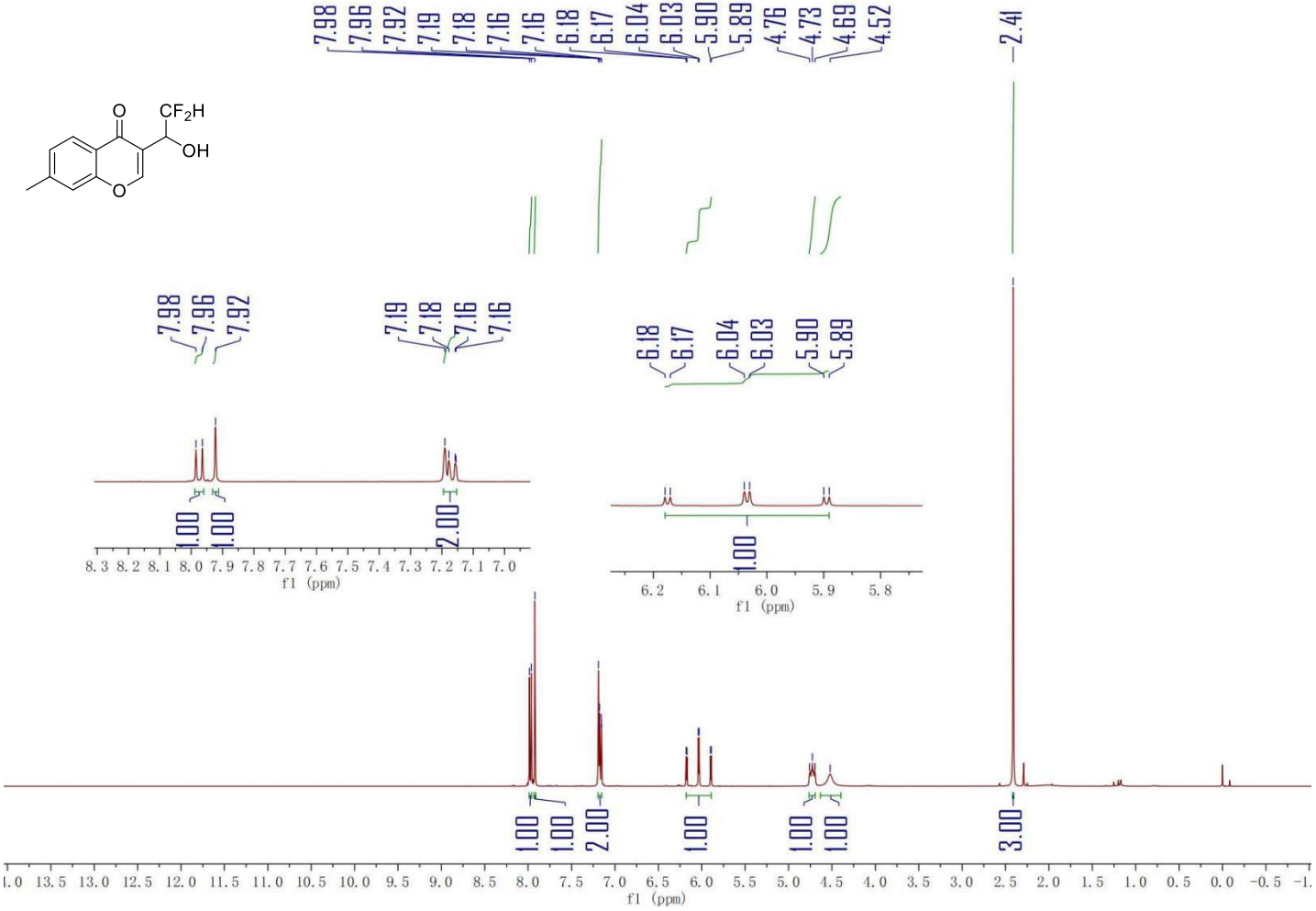


Fig. S8. ^{1}H NMR spectrum of compound **3c**

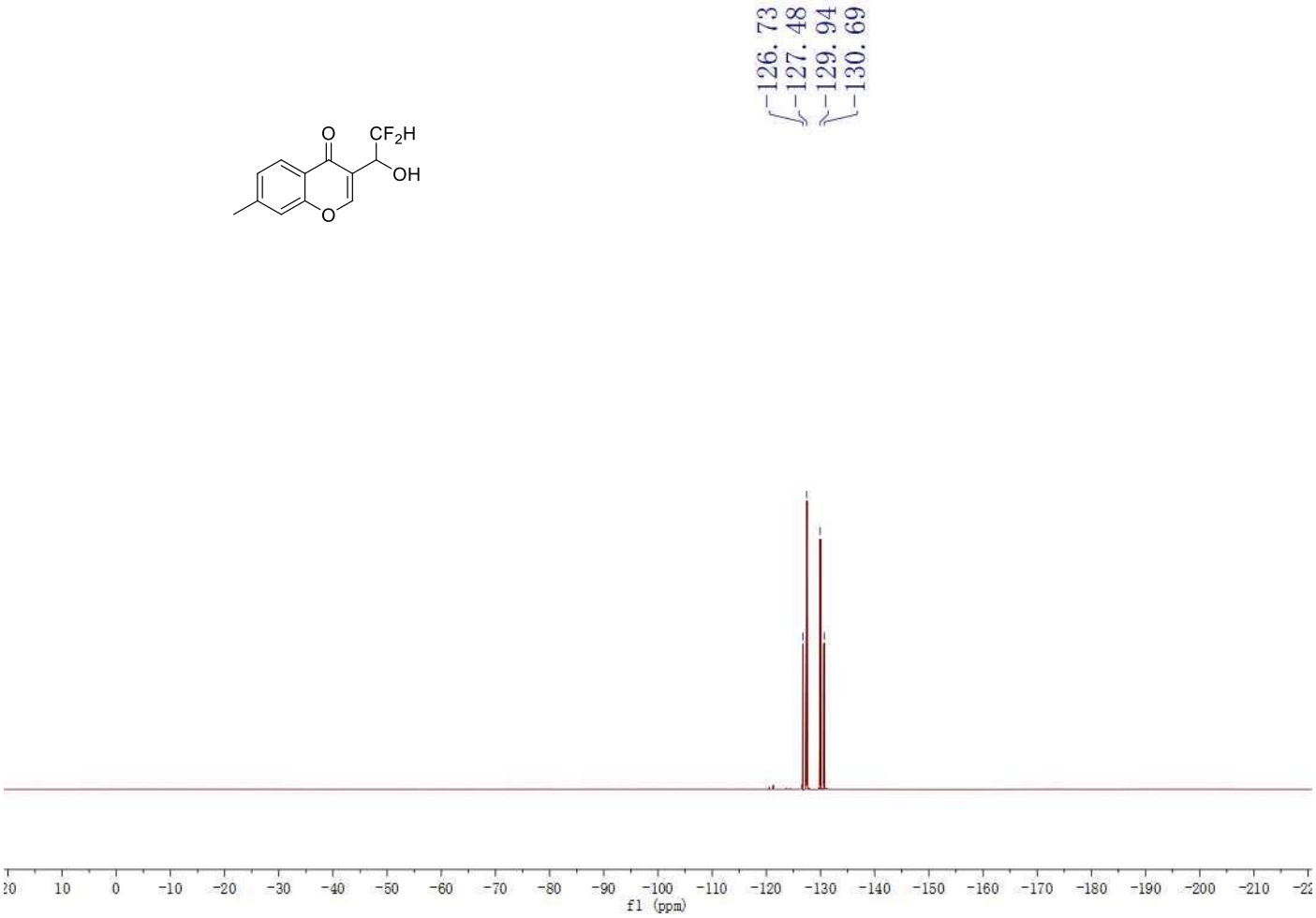


Fig. S9. ^{19}F NMR spectrum of compound **3c**

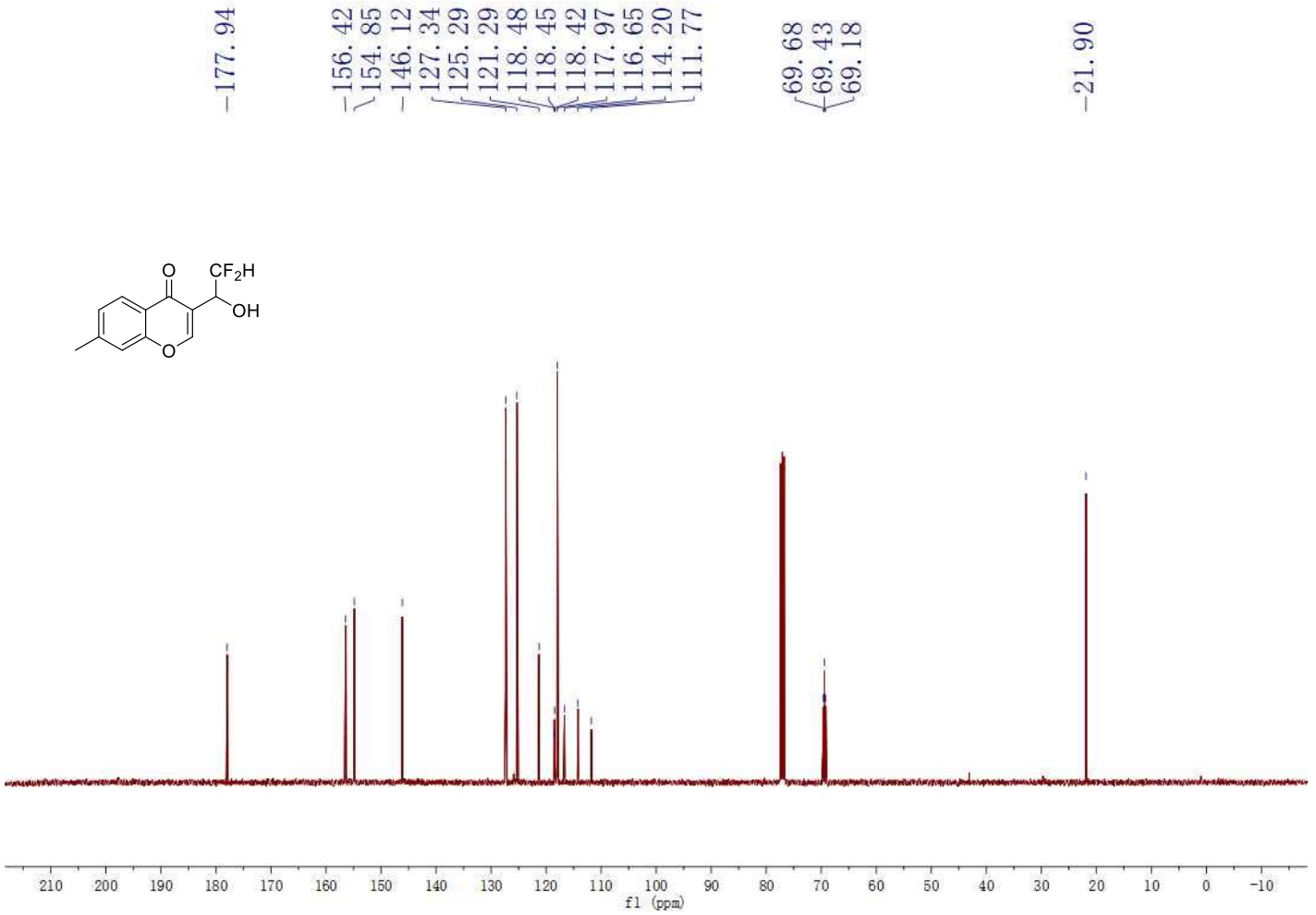


Fig. S10. ^{13}C NMR spectrum of compound **3c**

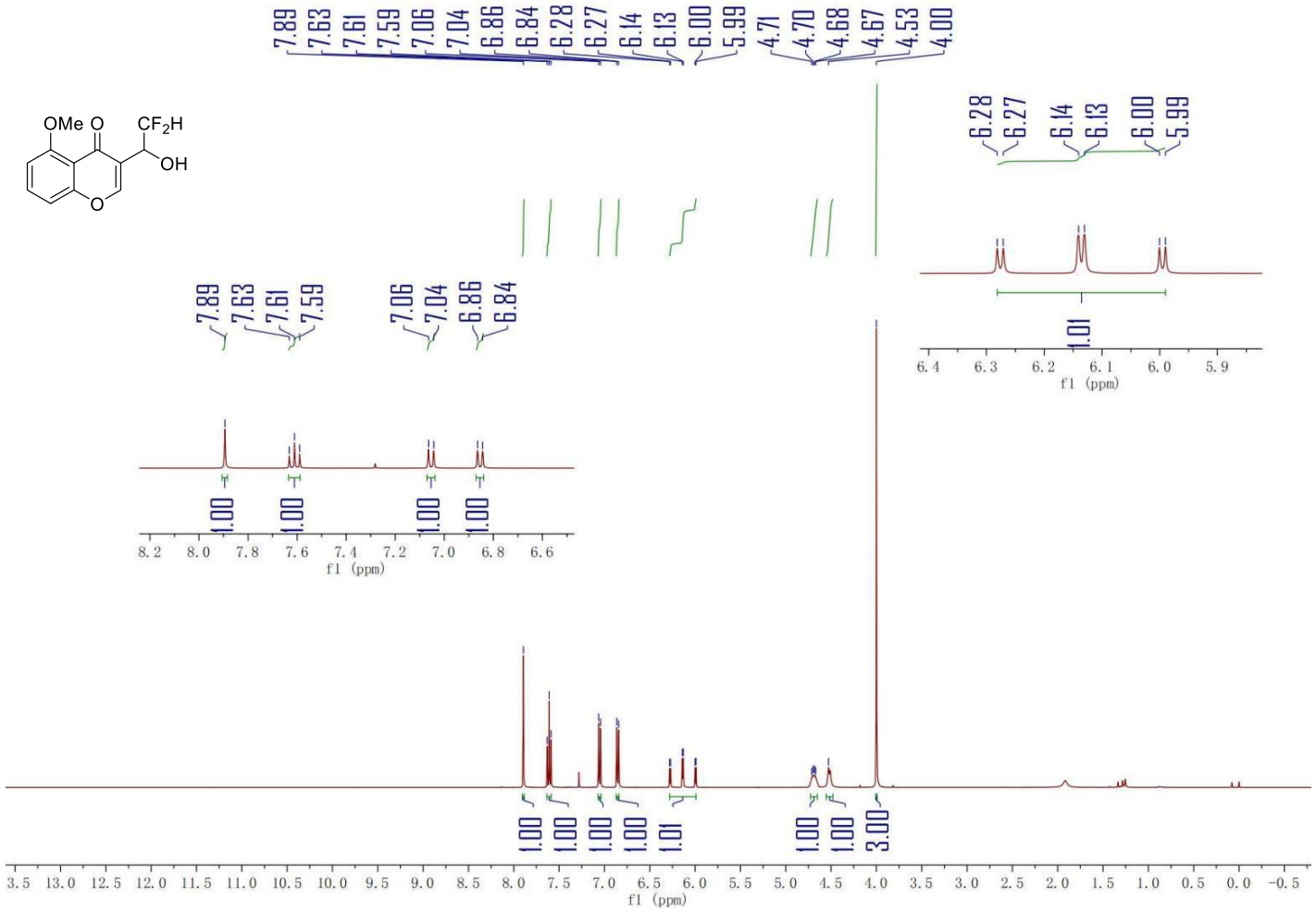


Fig. S11. ^{1}H NMR spectrum of compound **3d**

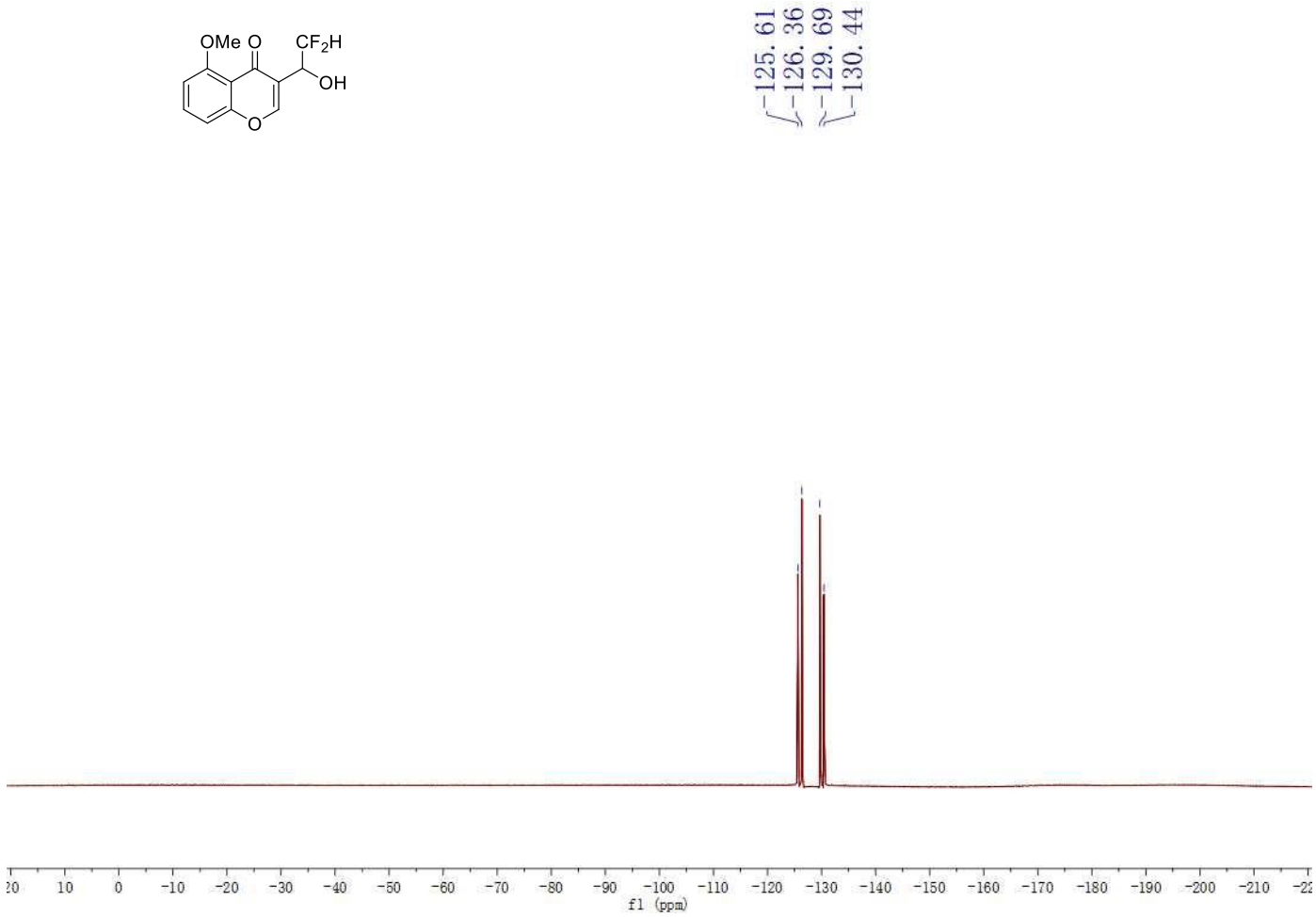


Fig. S12. ^{19}F NMR spectrum of compound **3d**

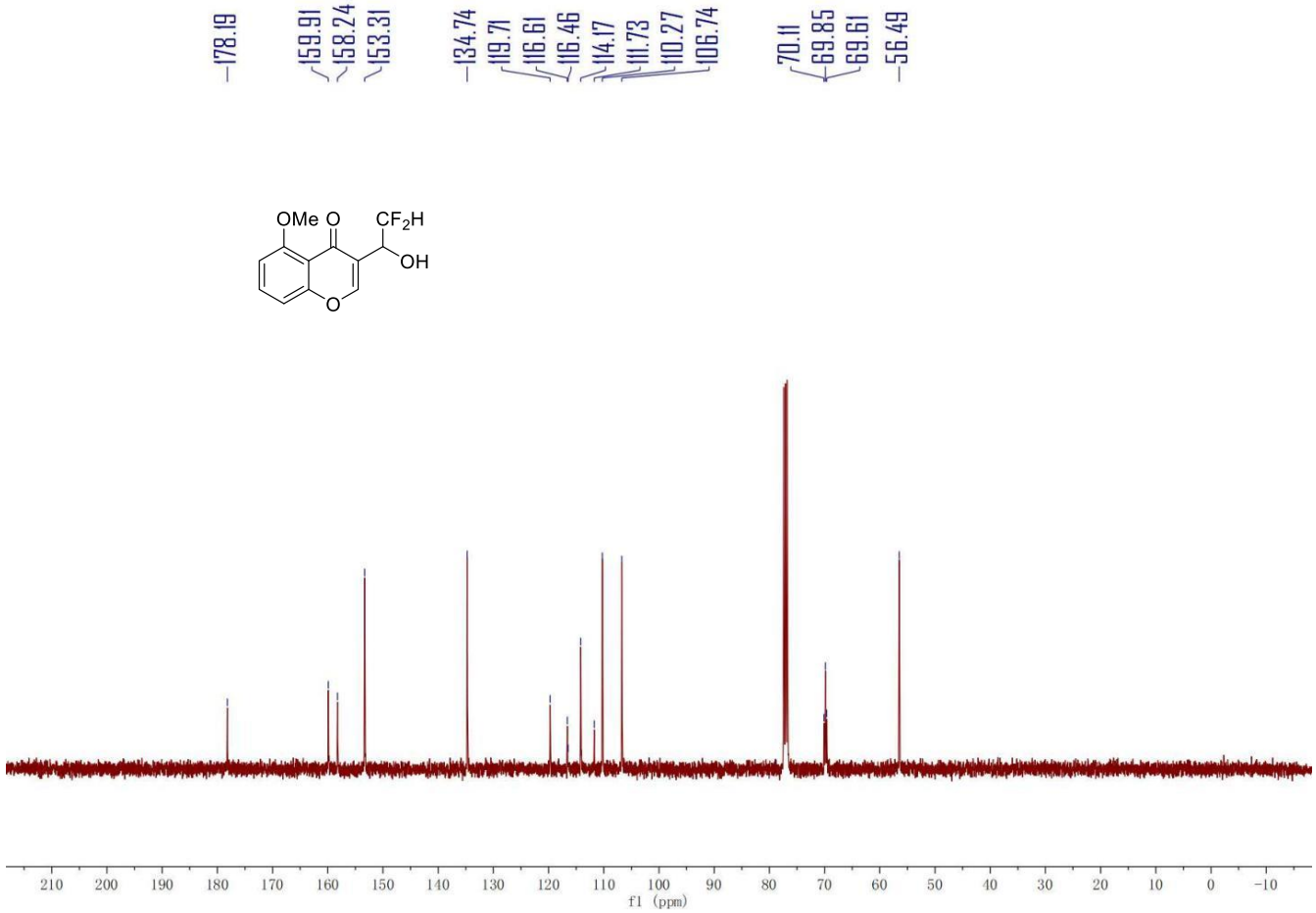


Fig. S13. ^{13}C NMR spectrum of compound **3d**

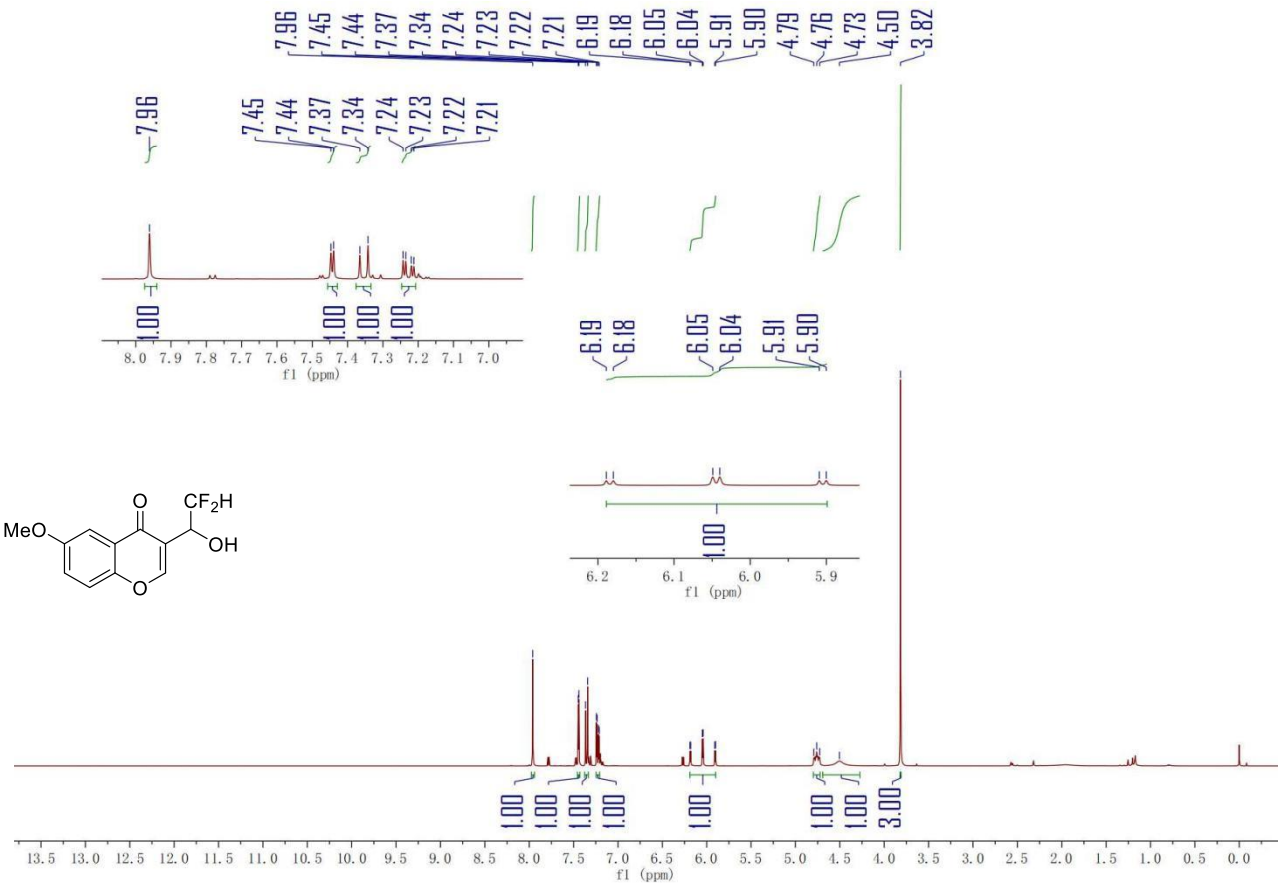


Fig. S14. ^{1}H NMR spectrum of compound **3e**

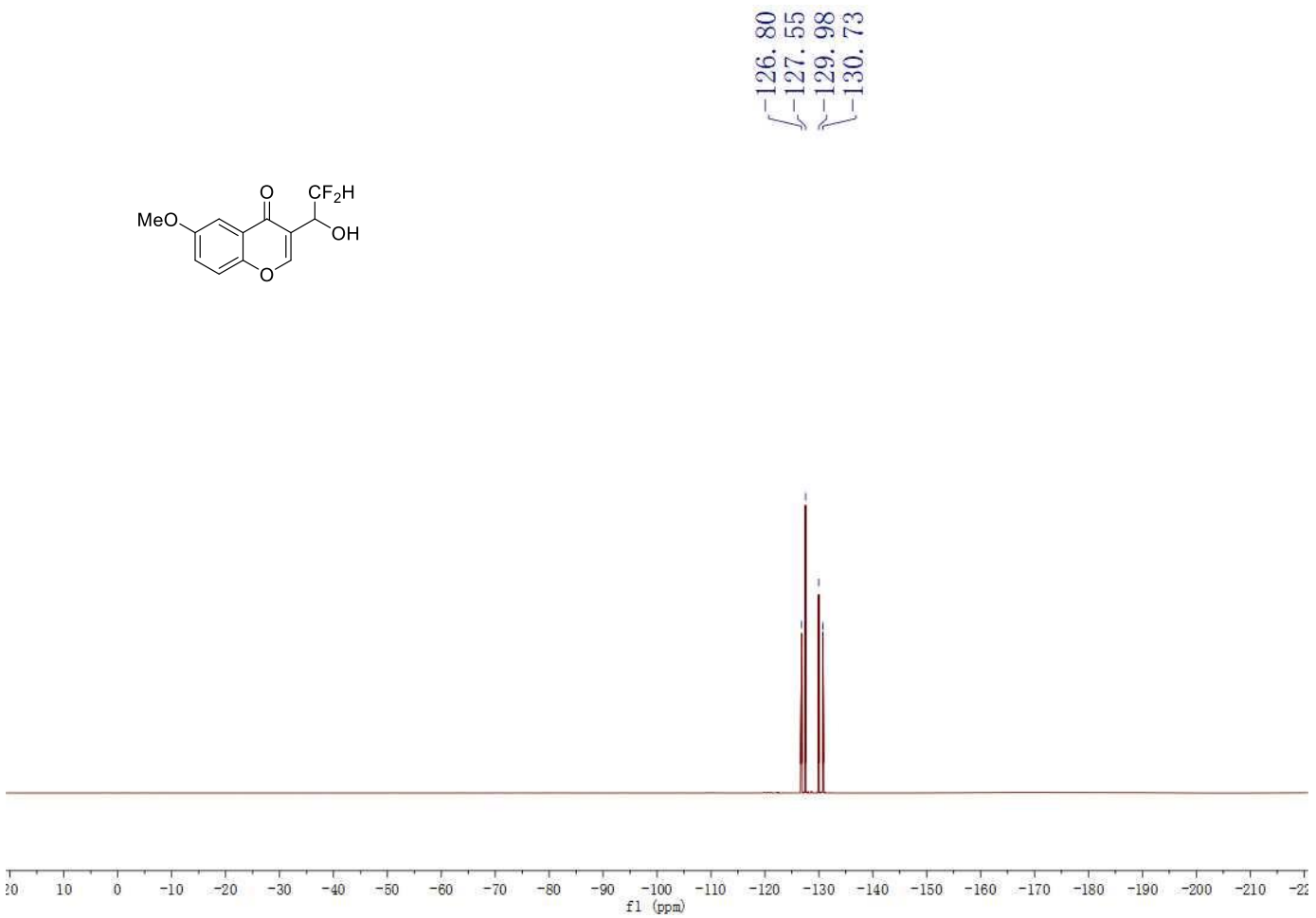


Fig. S15. ^{19}F NMR spectrum of compound **3e**

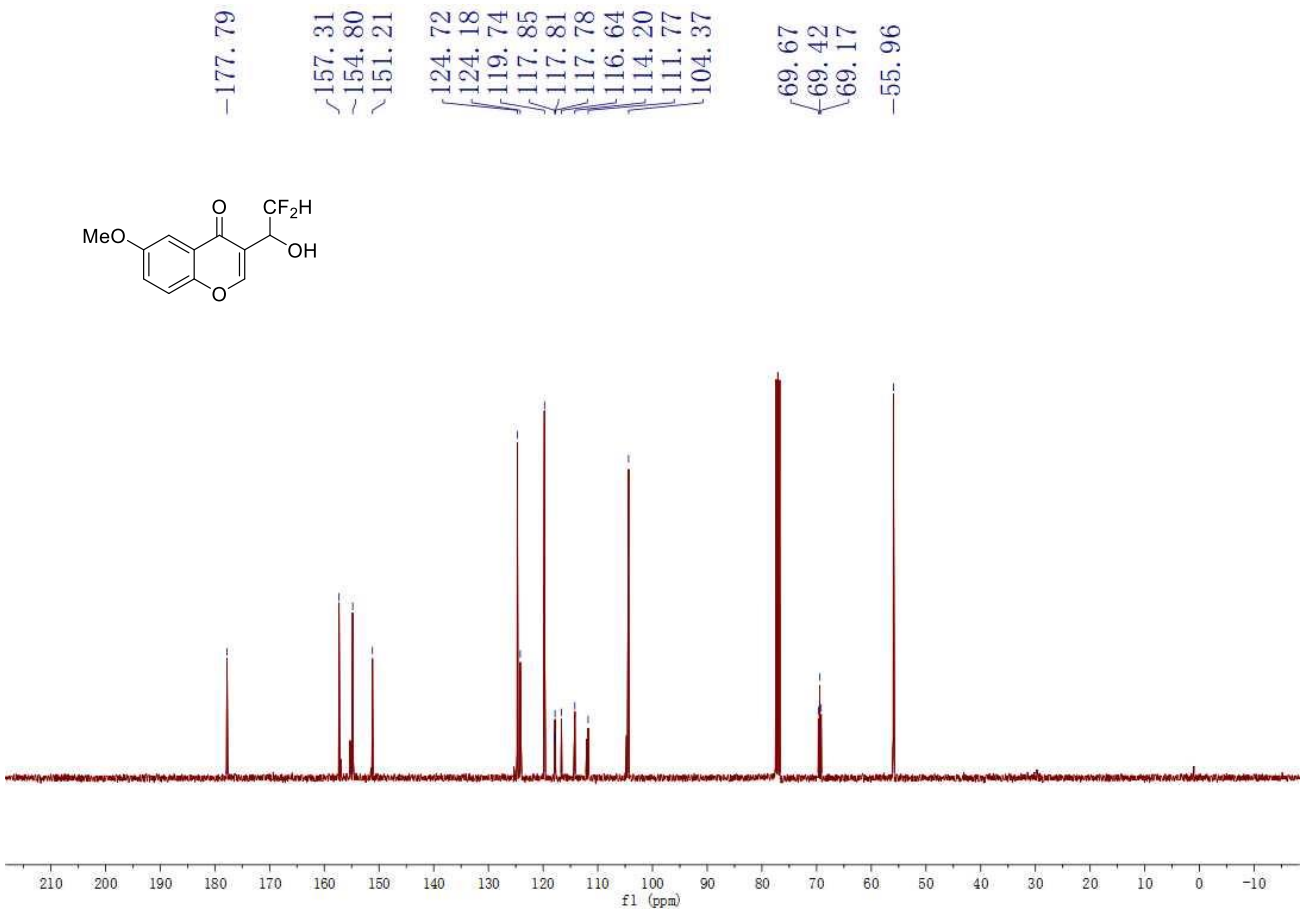


Fig. S16. ^{13}C NMR spectrum of compound **3e**

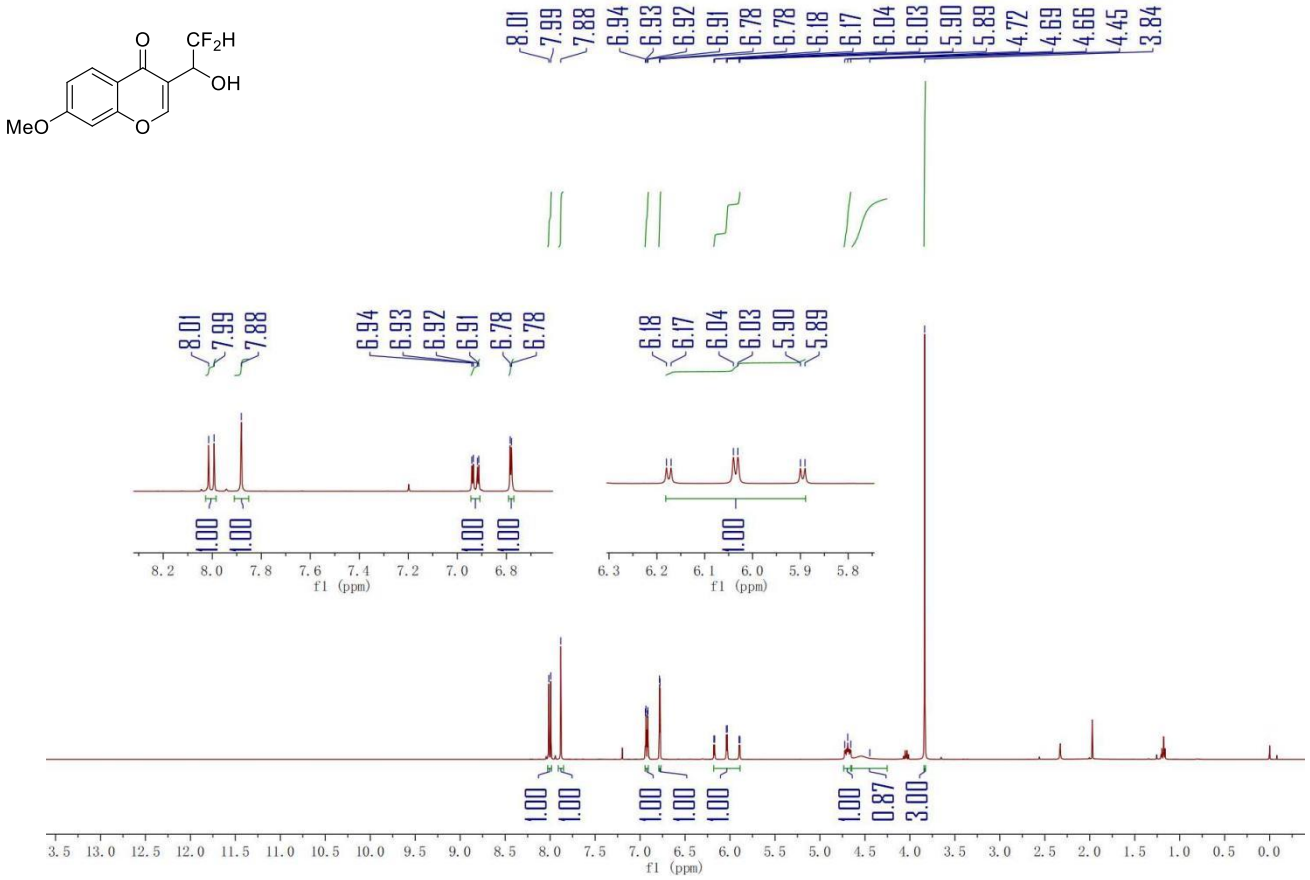


Fig. S17. ^{1}H NMR spectrum of compound **3f**

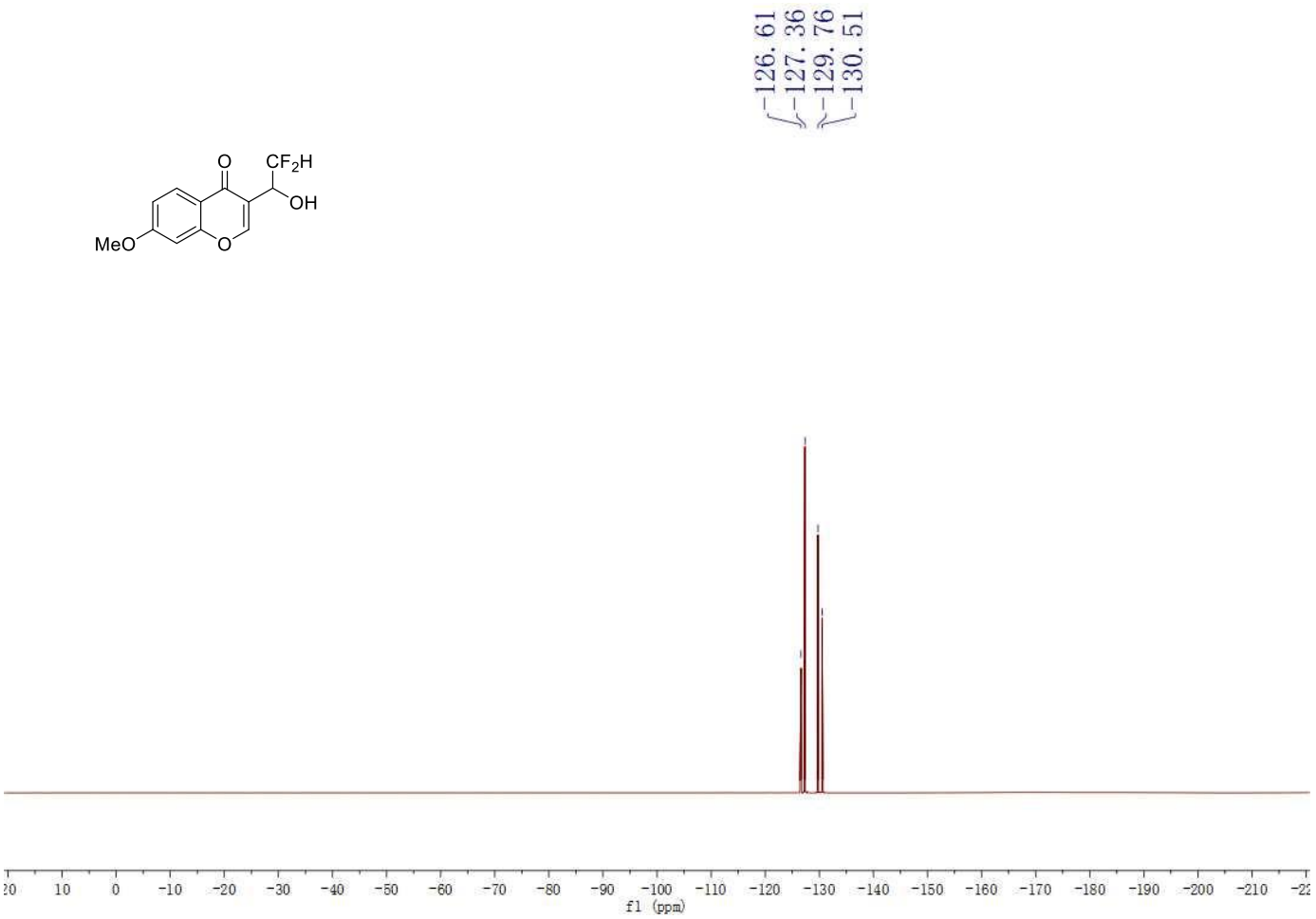


Fig. S18. ^{19}F NMR spectrum of compound **3f**

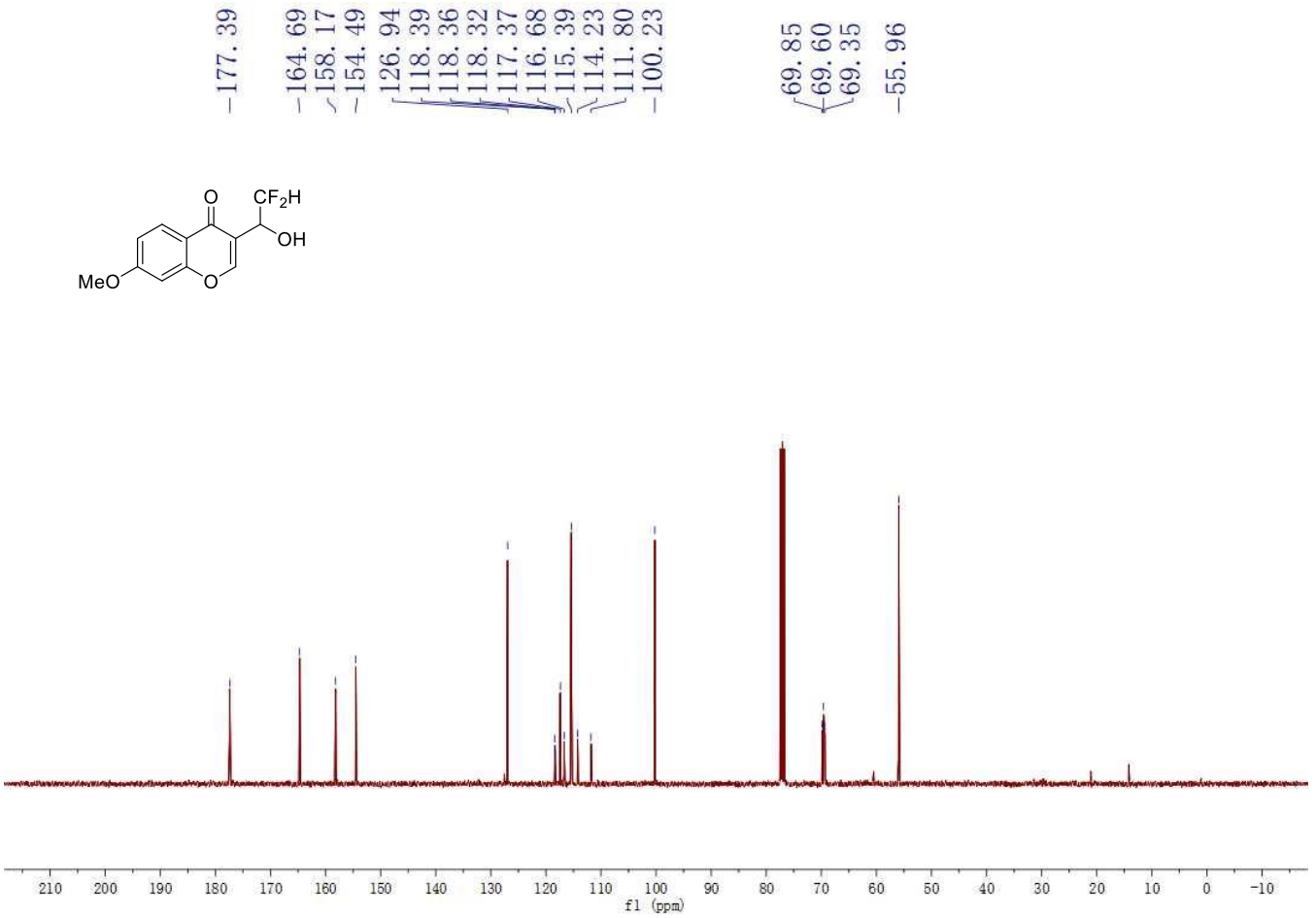


Fig. S19. ^{13}C NMR spectrum of compound **3f**

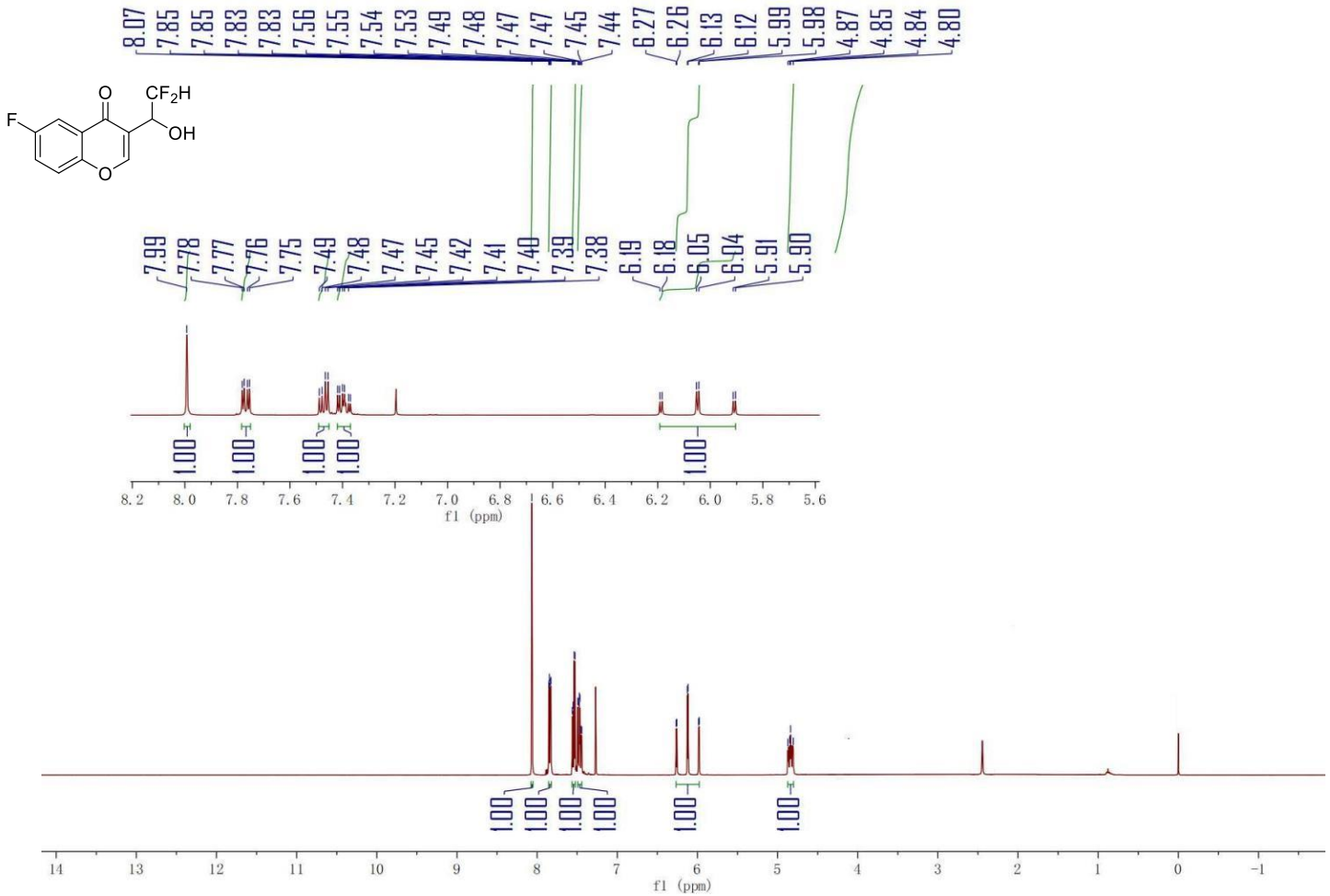


Fig. S20. ^{1}H NMR spectrum of compound **3g**

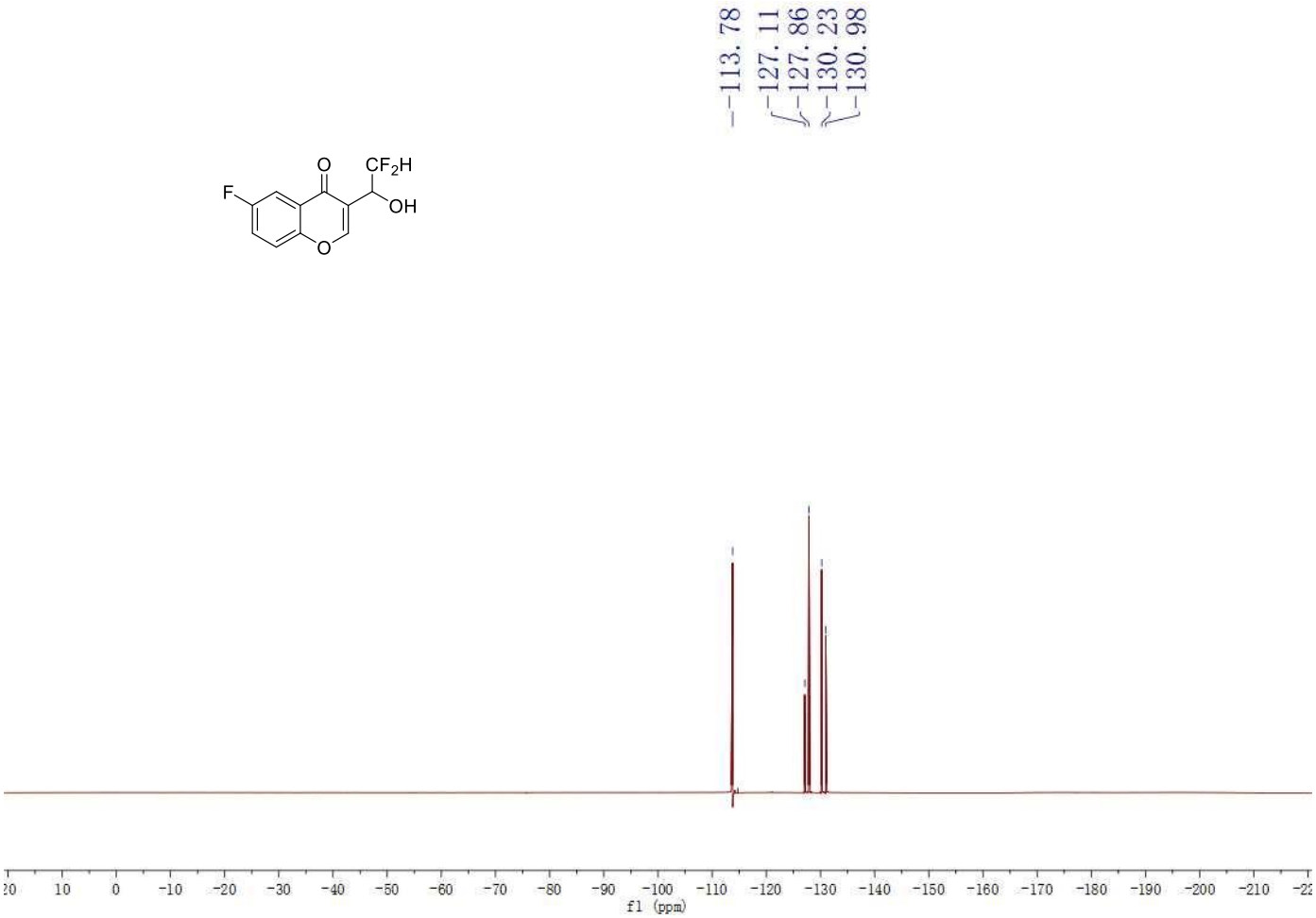


Fig. S21. ^{19}F NMR spectrum of compound **3g**

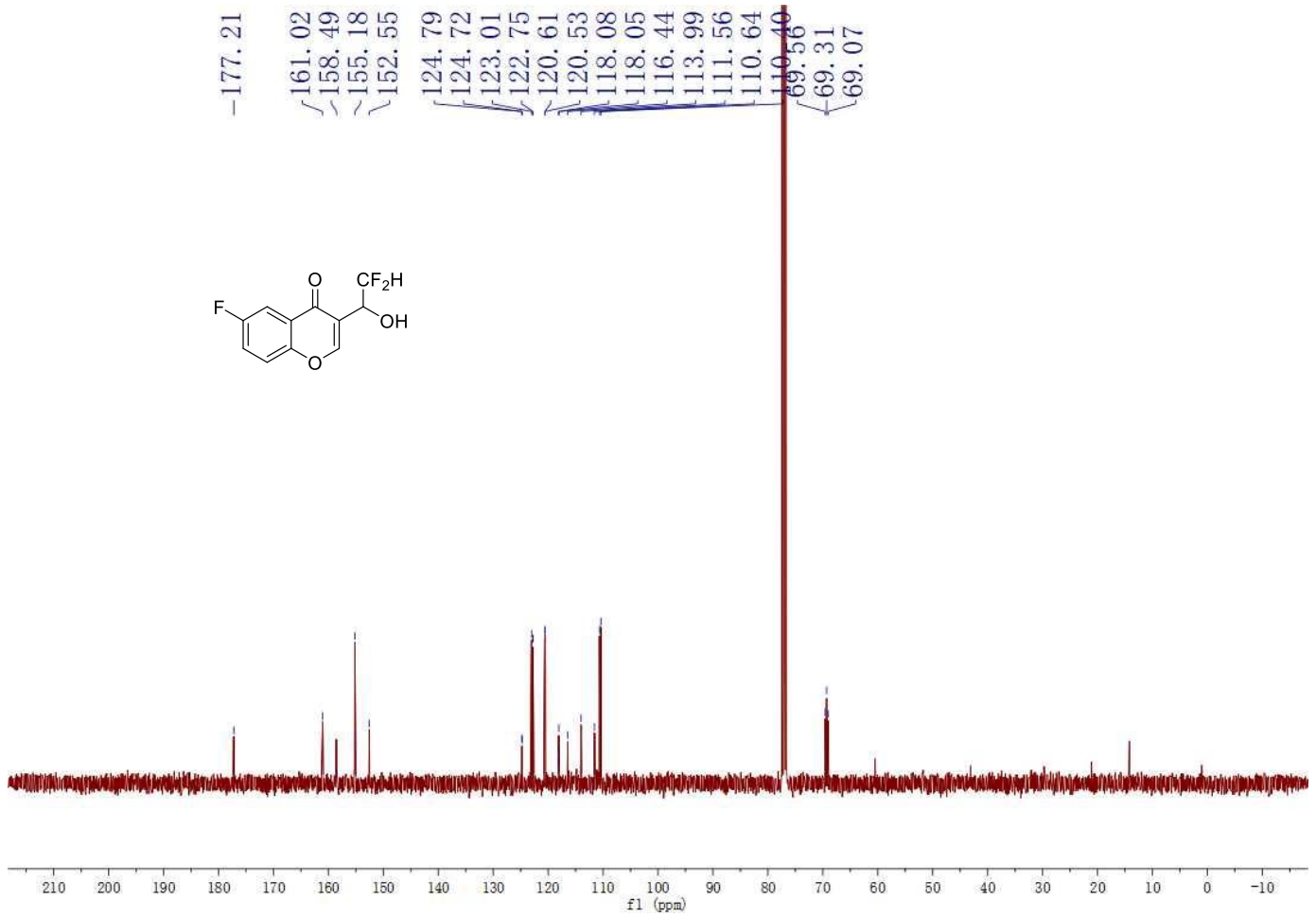


Fig. S22. ^{13}C NMR spectrum of compound **3g**

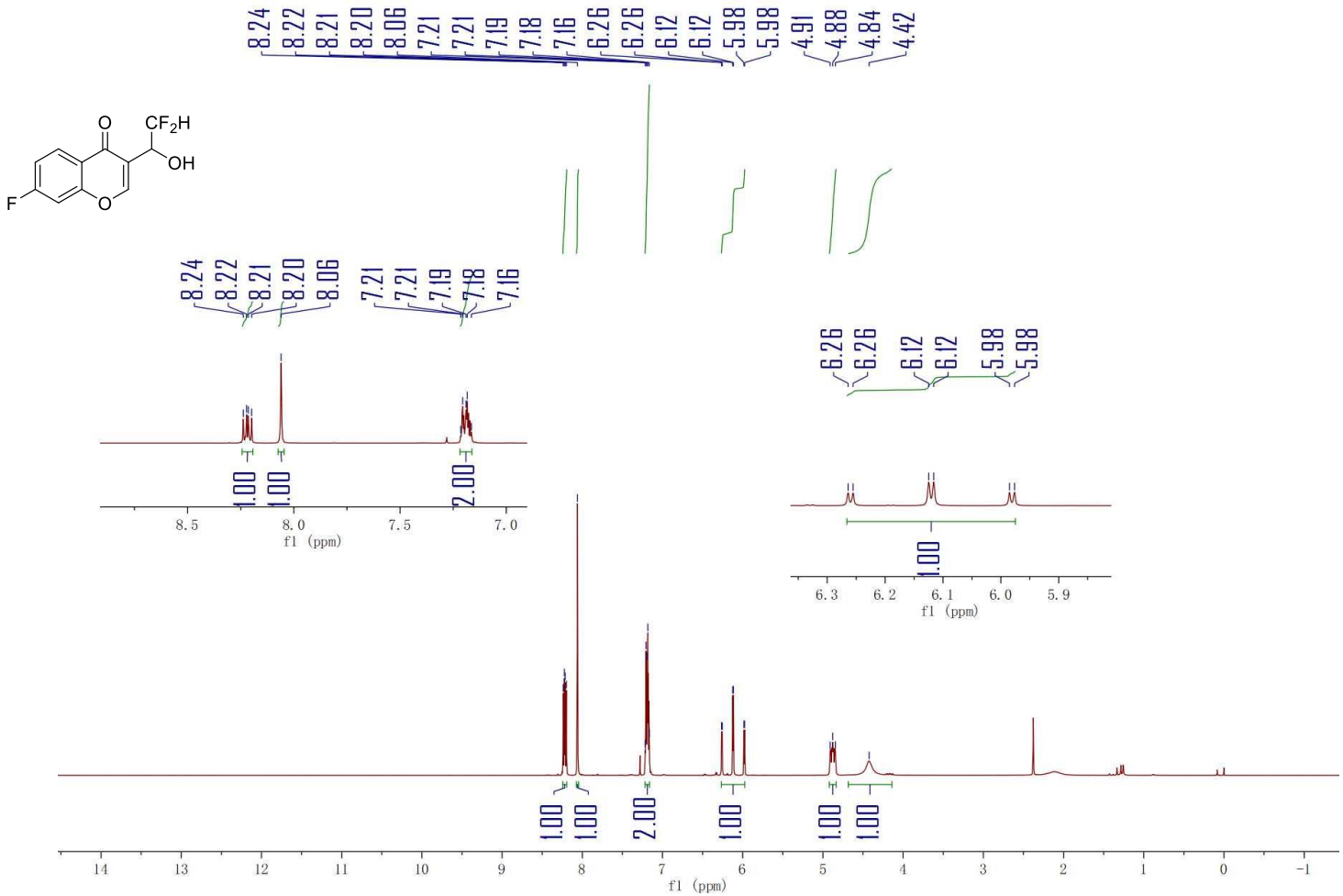


Fig. S23. ^{1}H NMR spectrum of compound **3h**

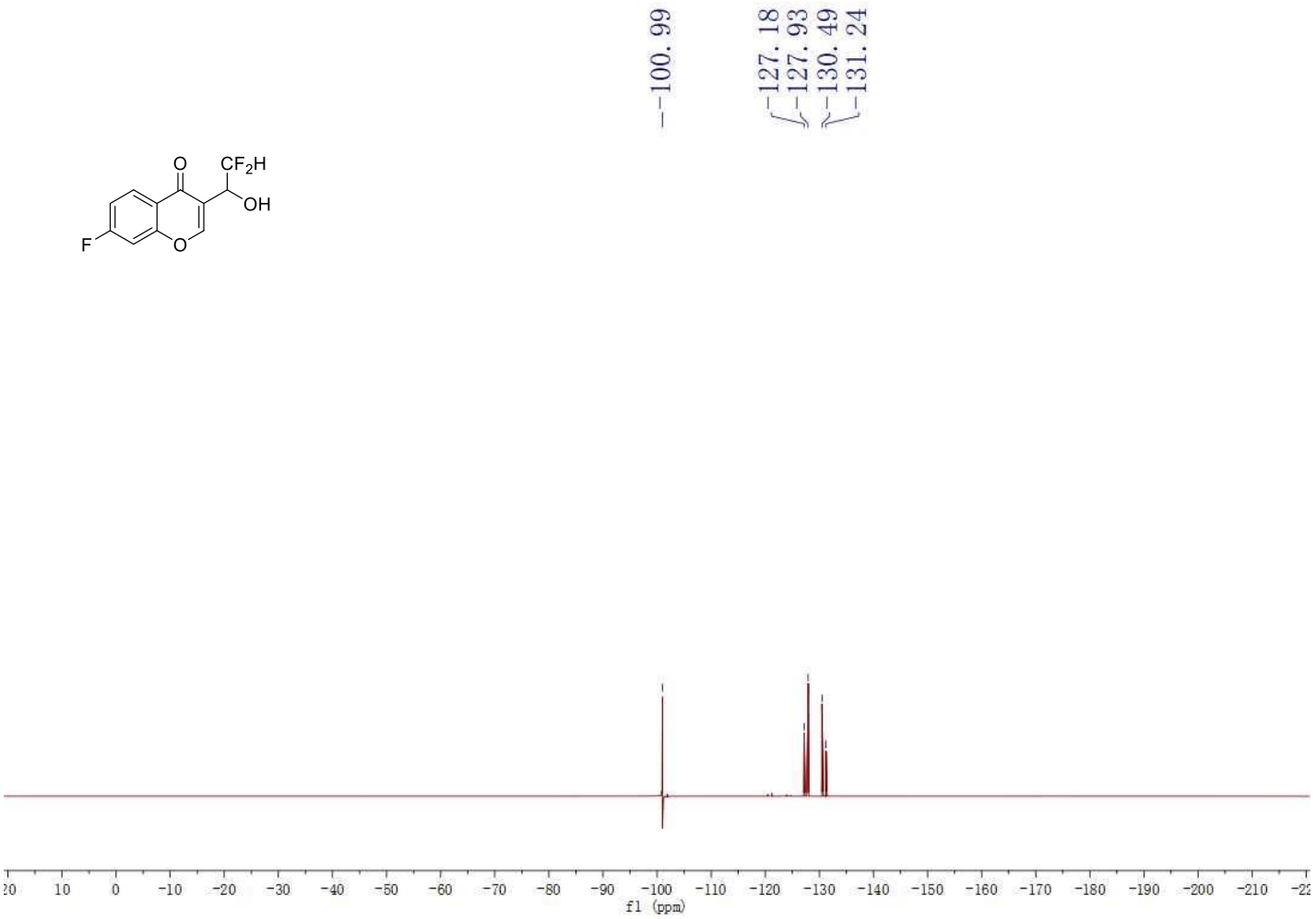


Fig. S24. ^{19}F NMR spectrum of compound **3h**

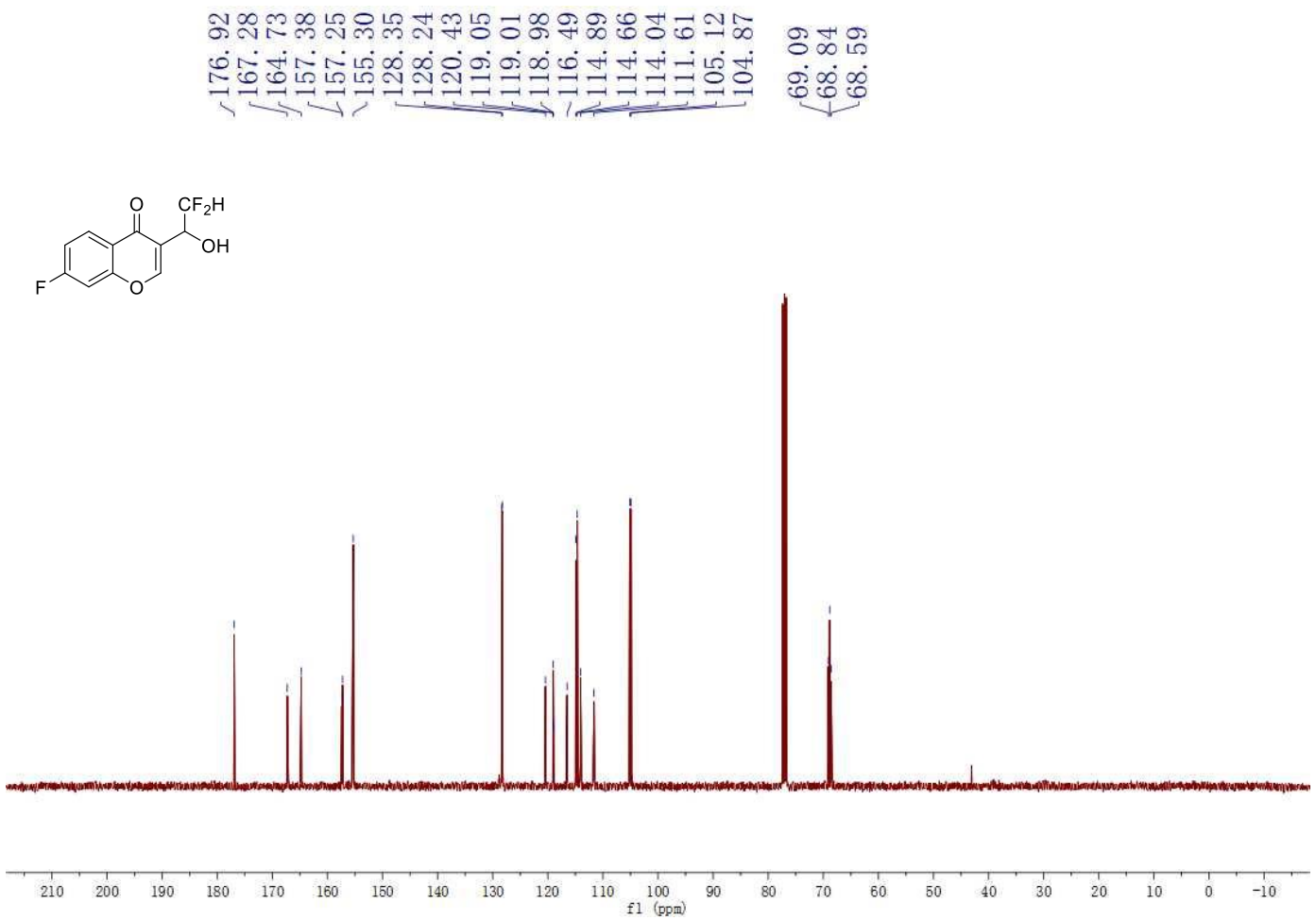


Fig. S25. ^{13}C NMR spectrum of compound **3h**

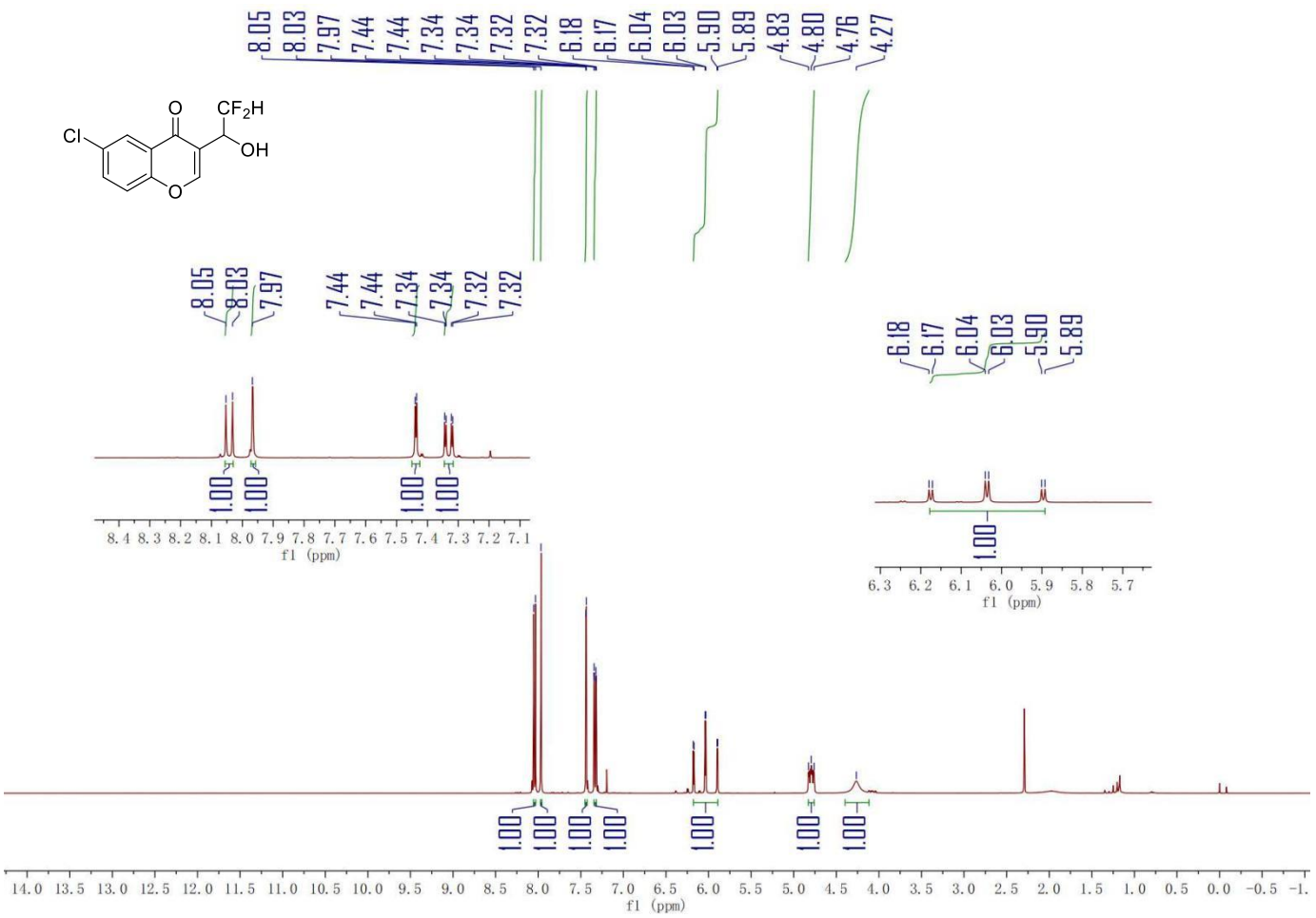


Fig. S26. ^{1}H NMR spectrum of compound **3i**

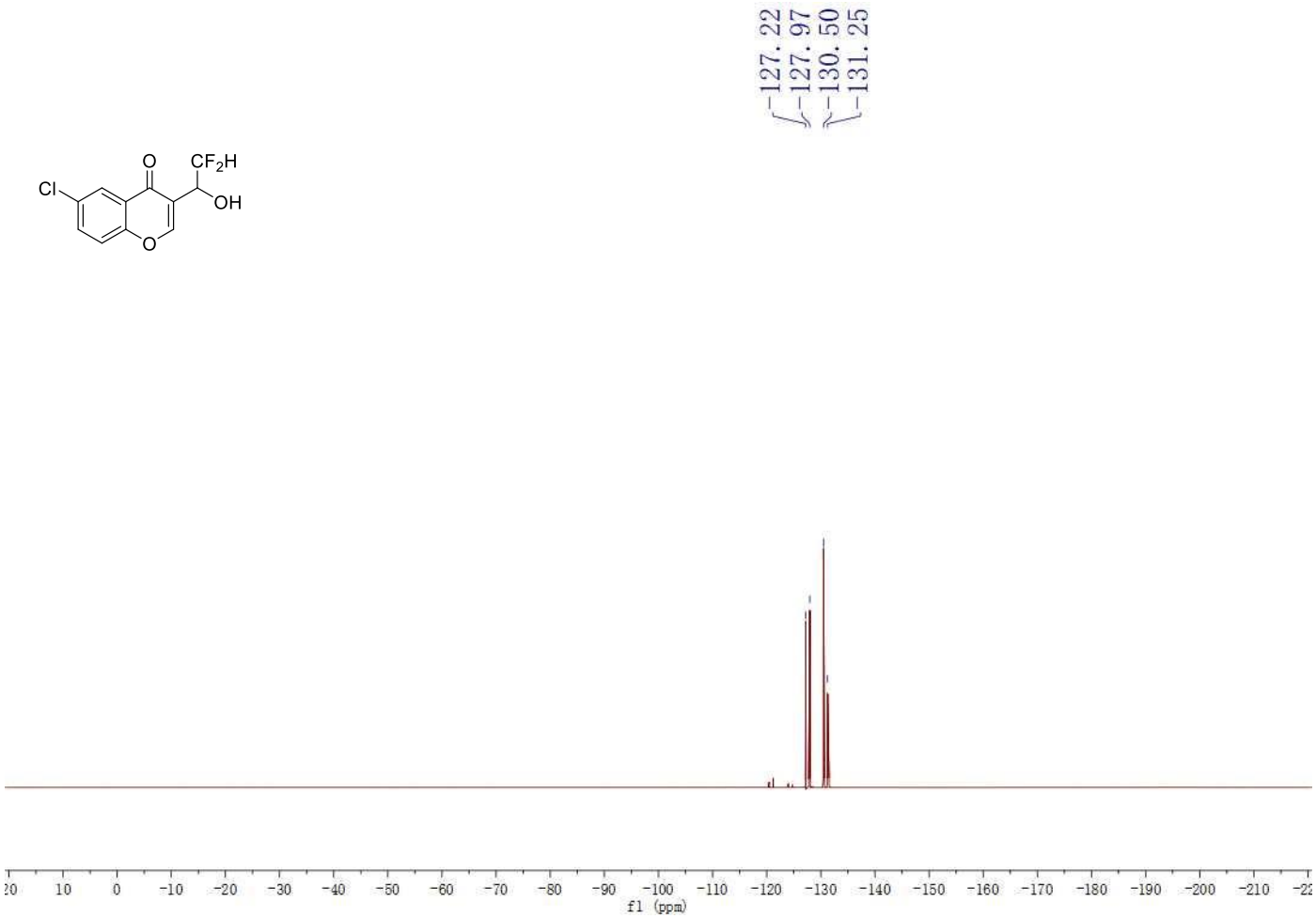


Fig. S27. ^{19}F NMR spectrum of compound **3i**

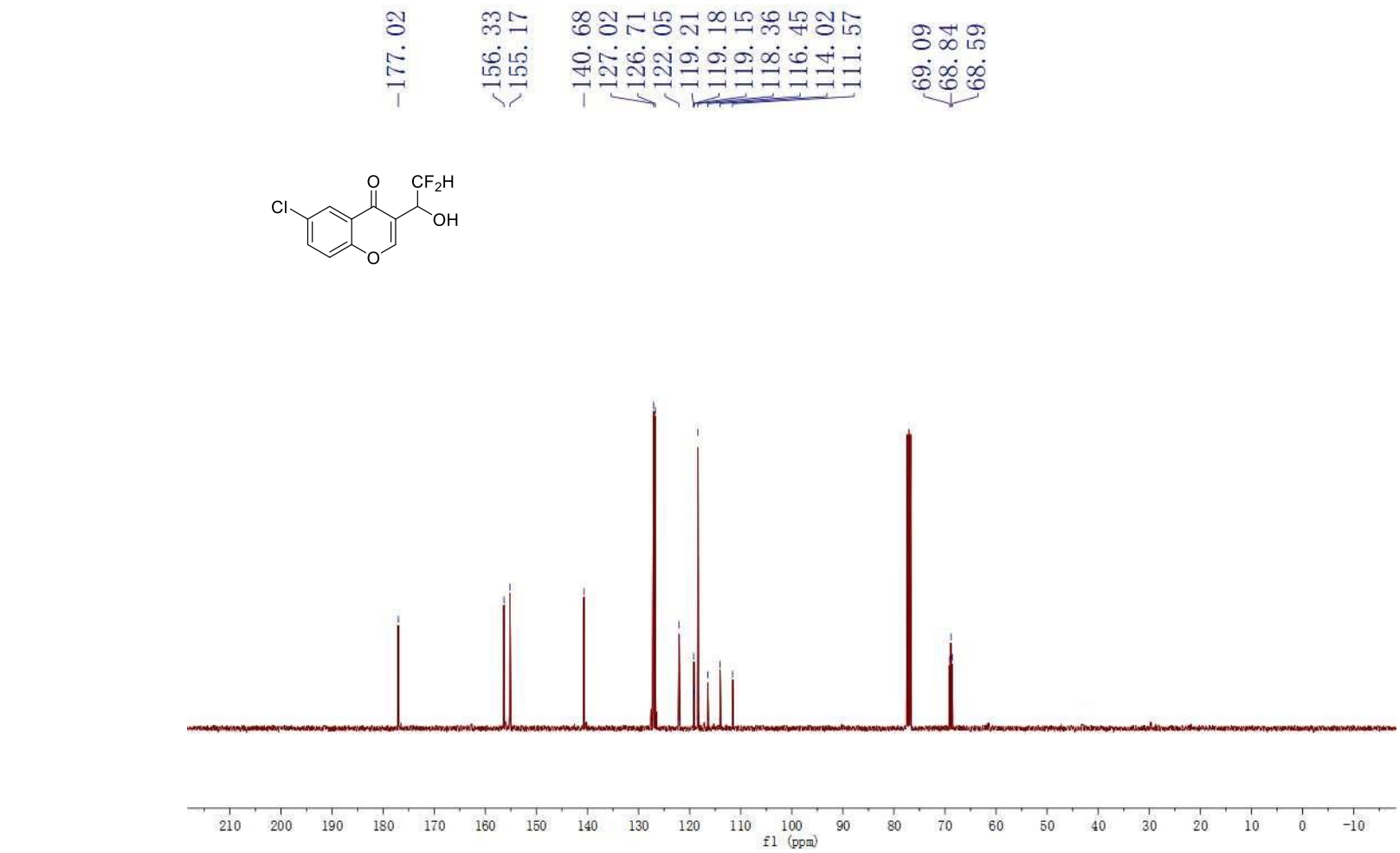


Fig. S28. ^{13}C NMR spectrum of compound **3i**

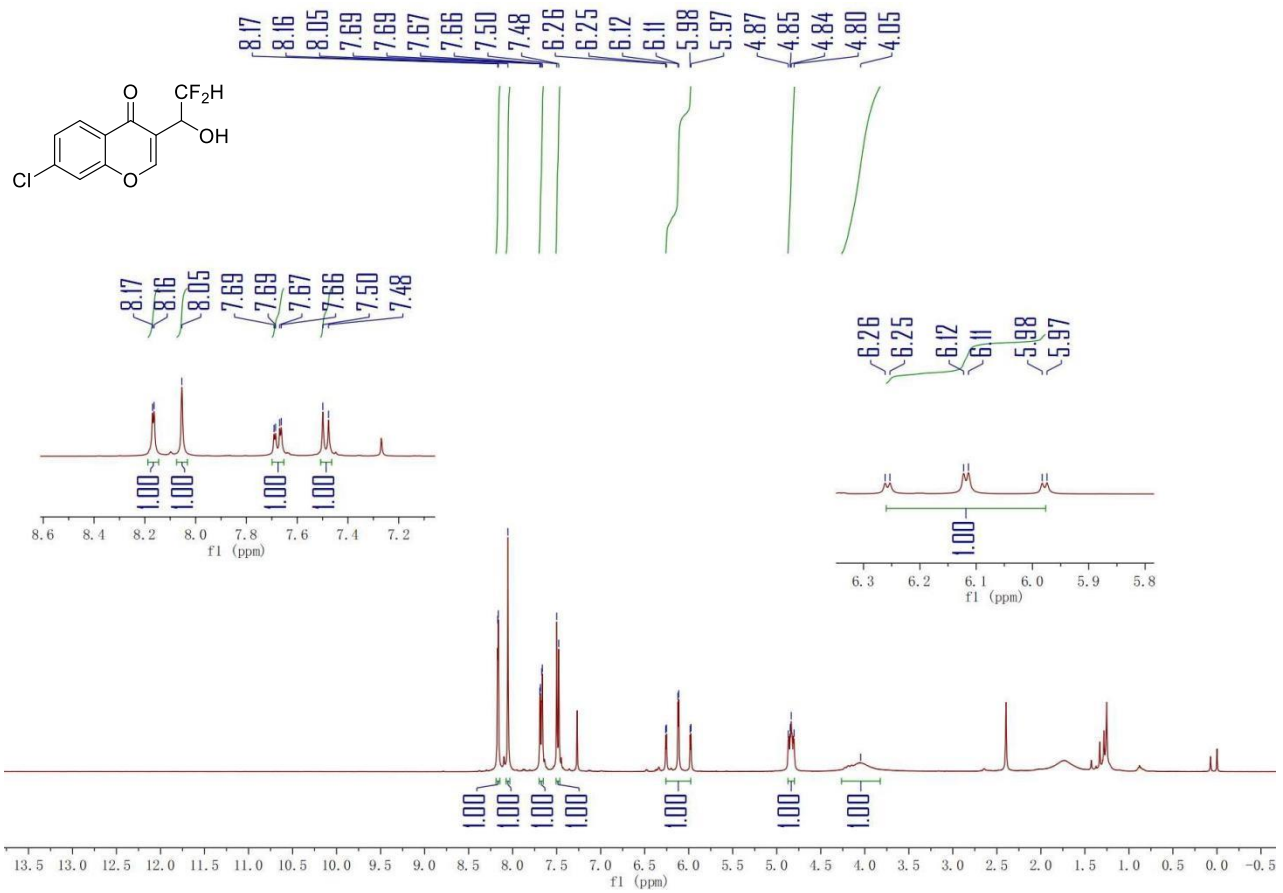


Fig. S29. ^{1}H NMR spectrum of compound **3j**

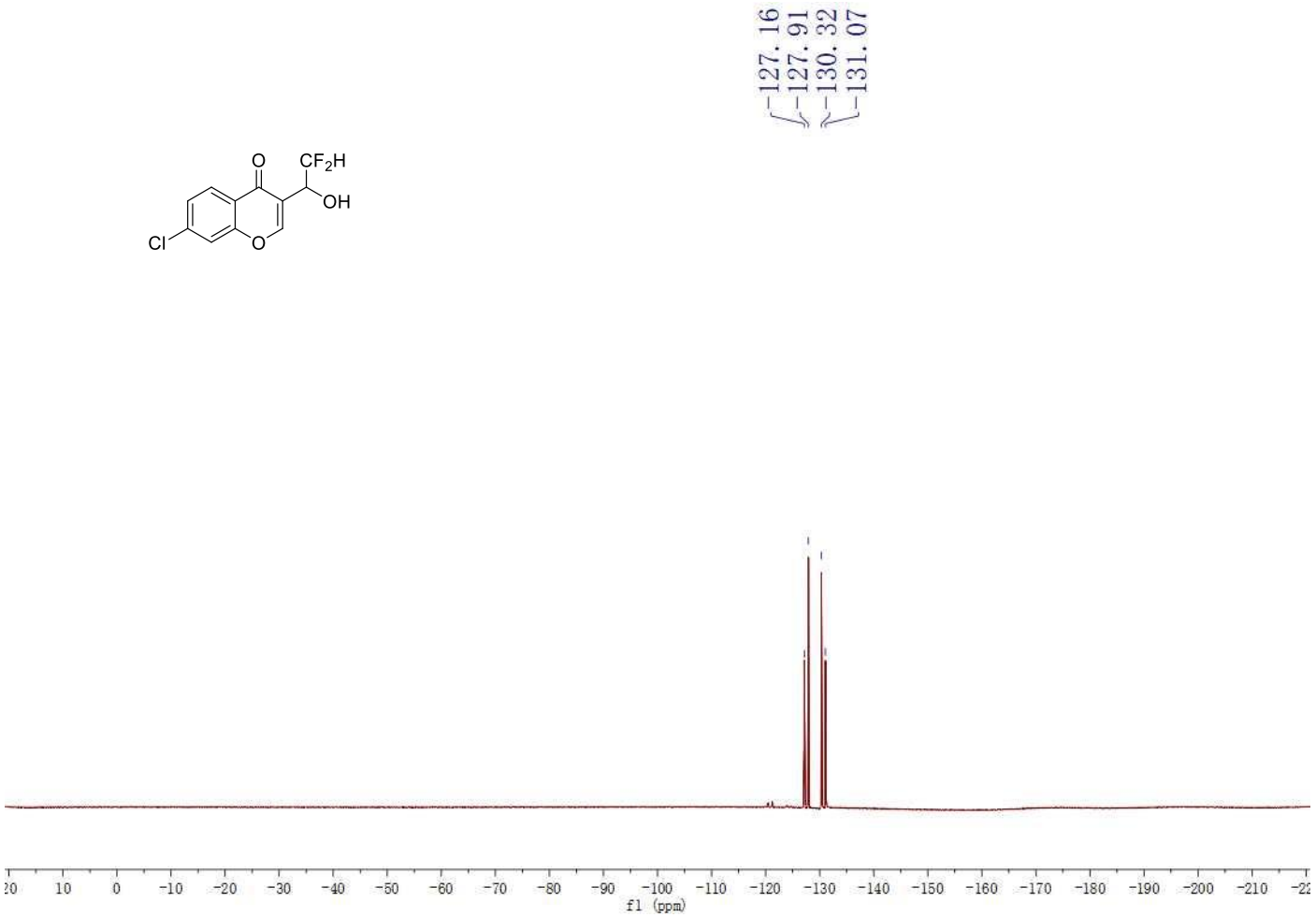


Fig. S30. ^{19}F NMR spectrum of compound **3j**

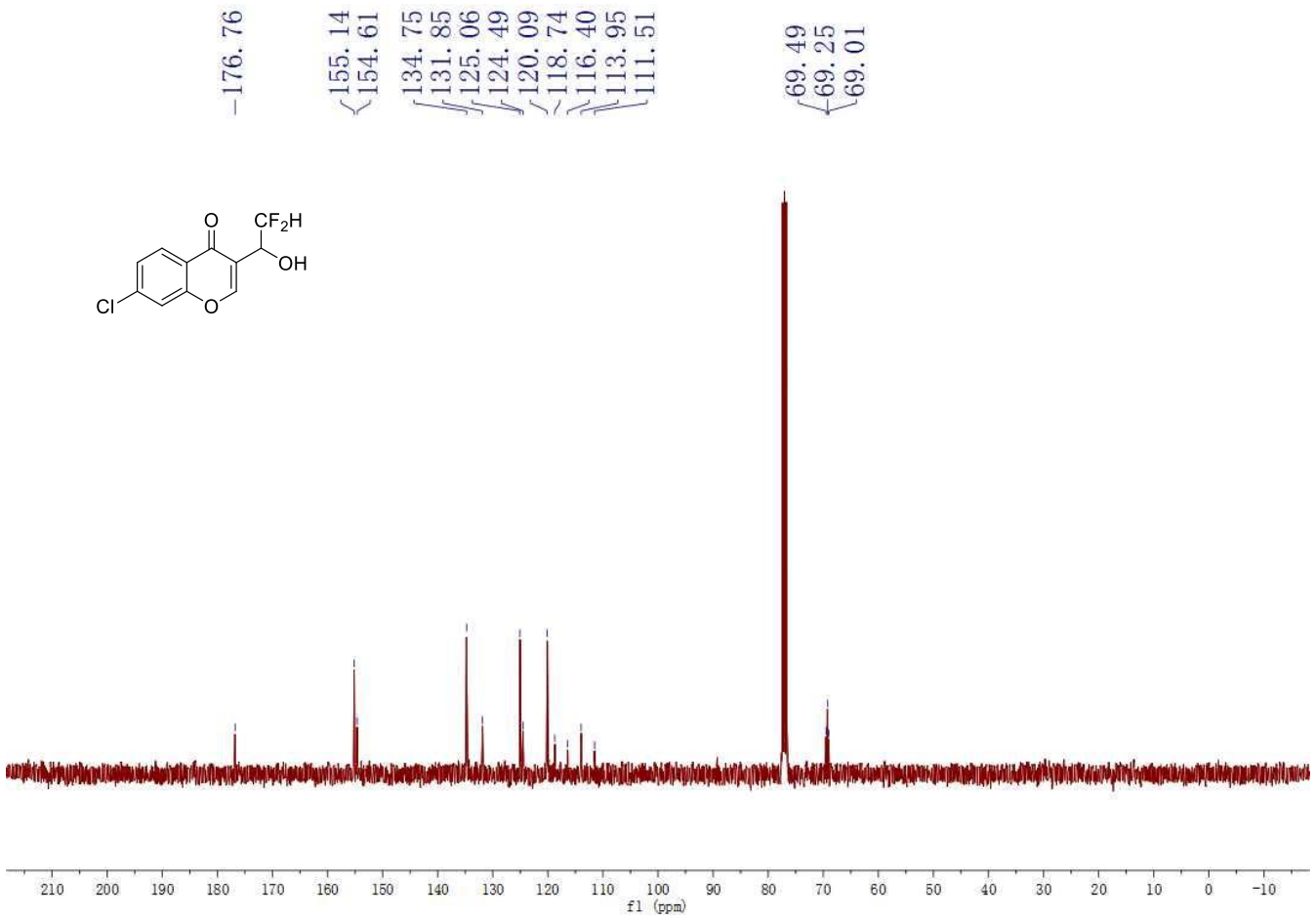


Fig. S31. ^{13}C NMR spectrum of compound **3j**

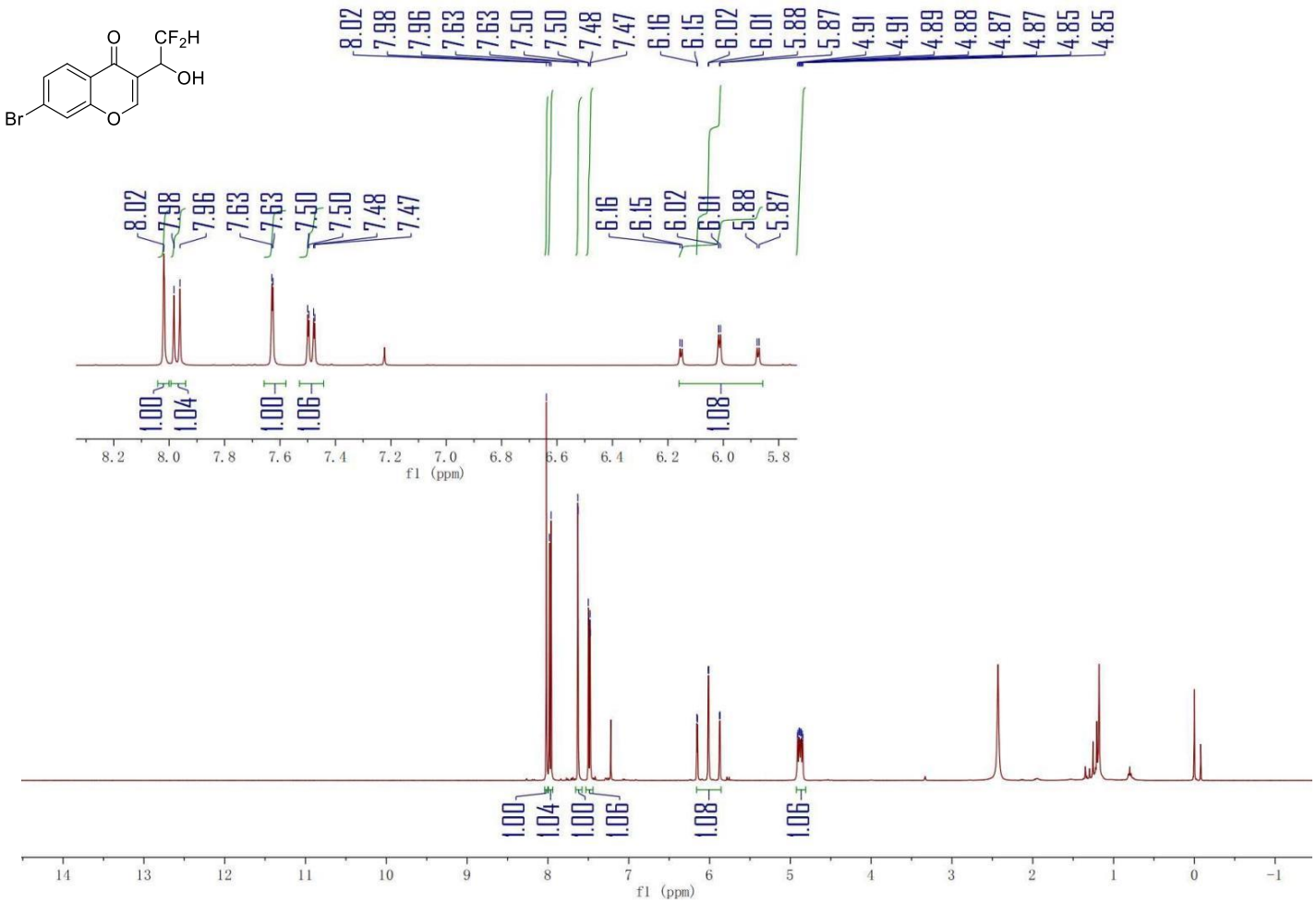


Fig. S32. ^{1}H NMR spectrum of compound **3k**

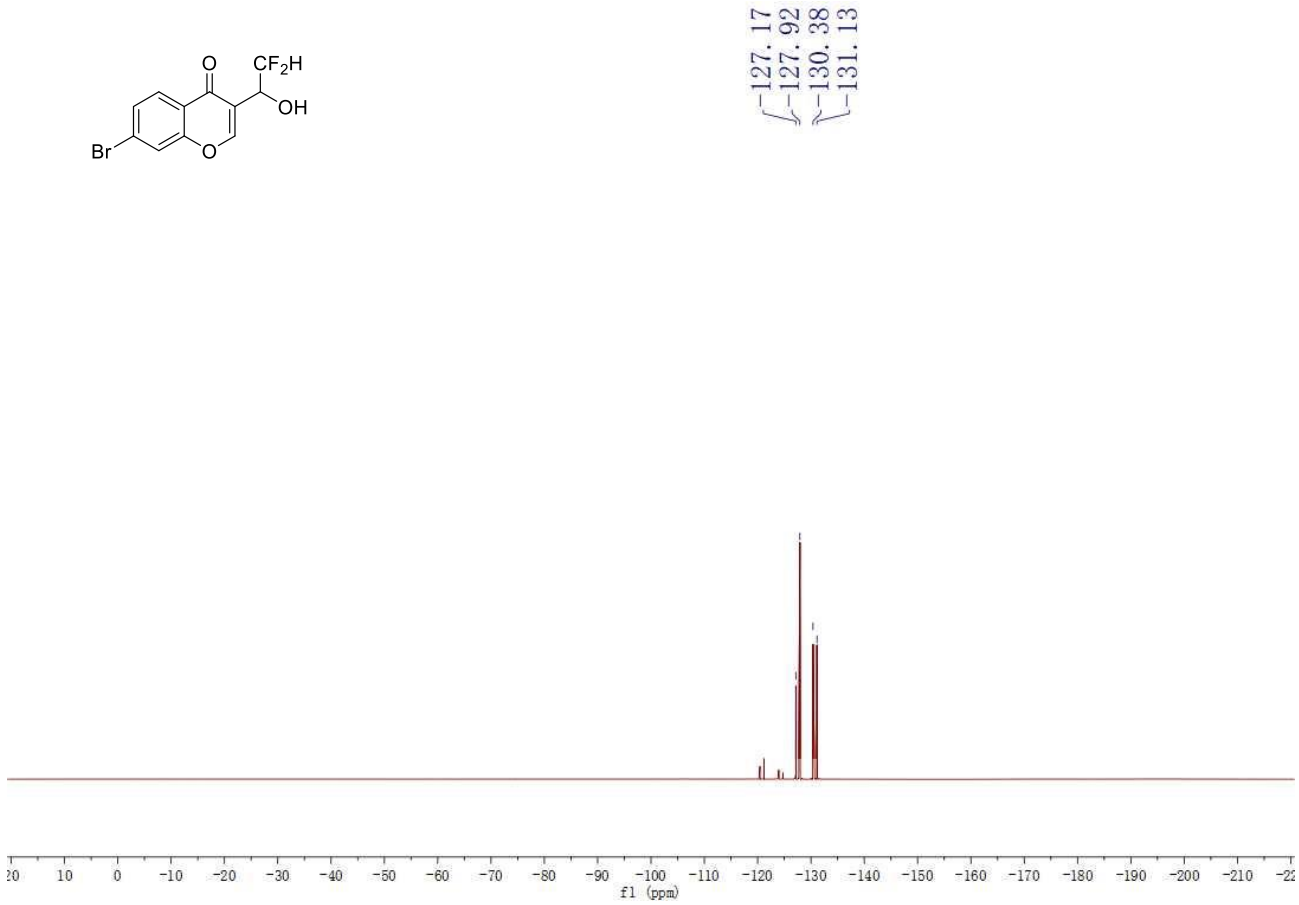


Fig. S33. ^{19}F NMR spectrum of compound **3k**

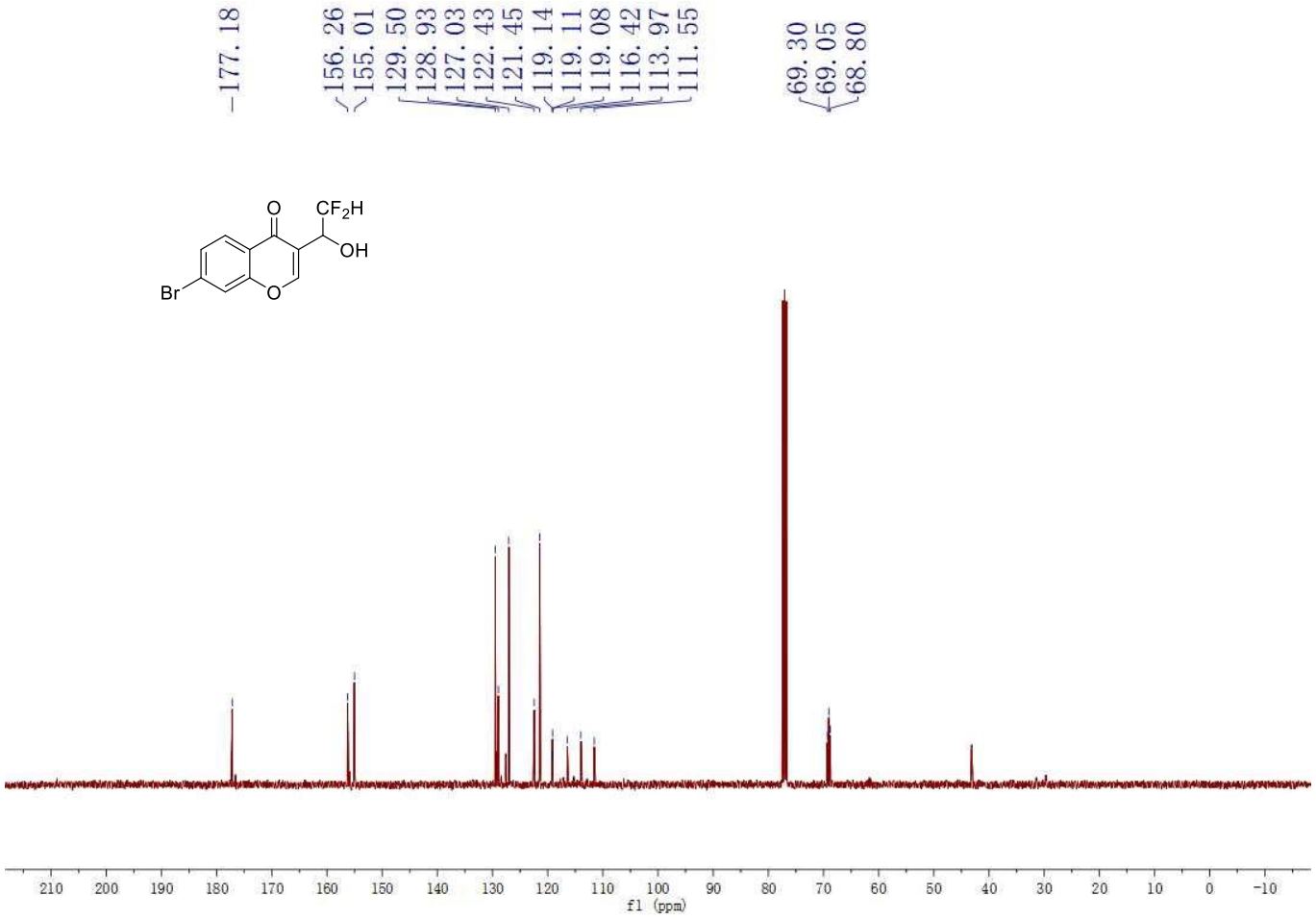


Fig. S34. ^{1}H NMR spectrum of compound **3k**

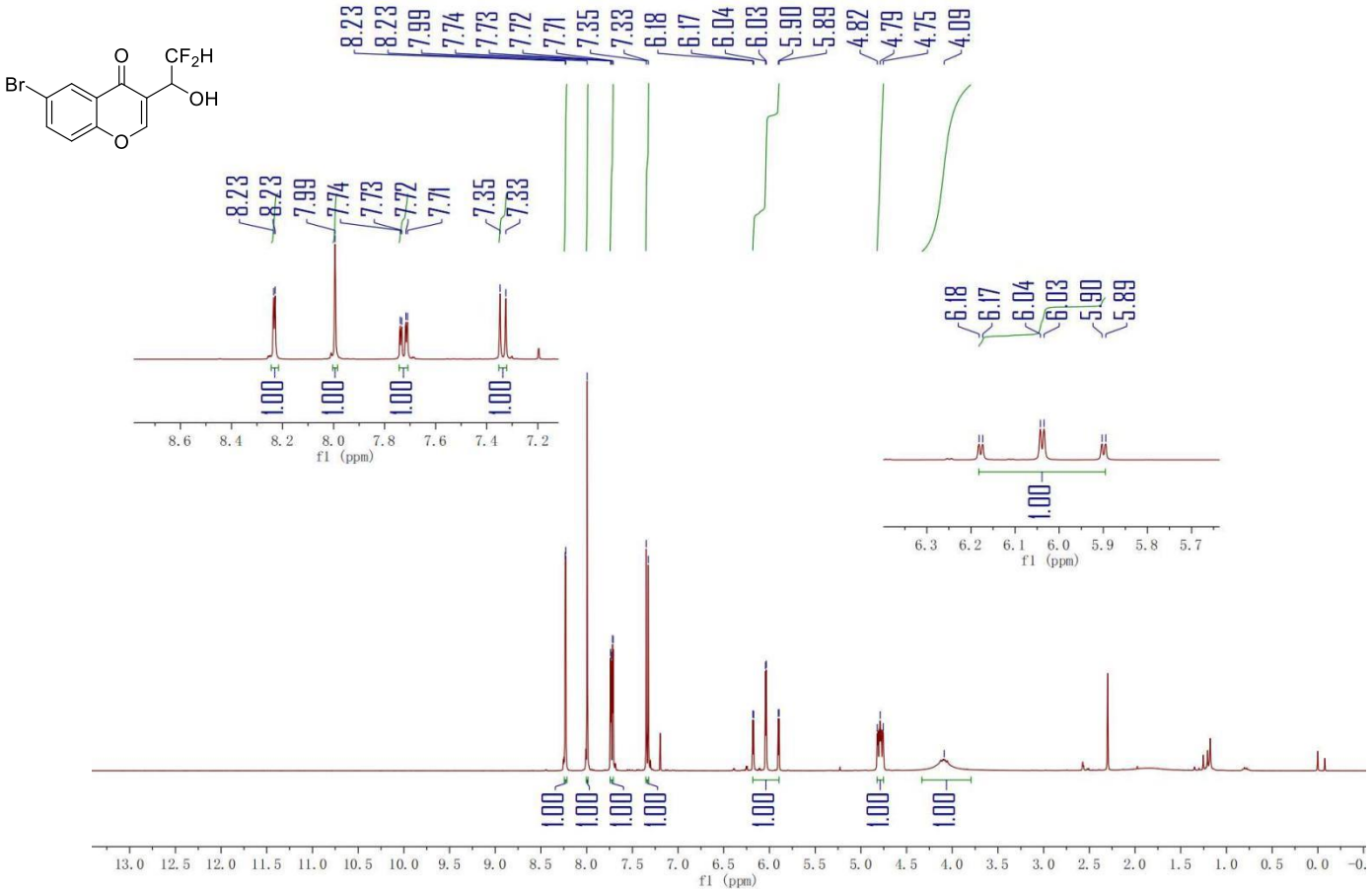


Fig. S35. ^{19}F NMR spectrum of compound **3l**

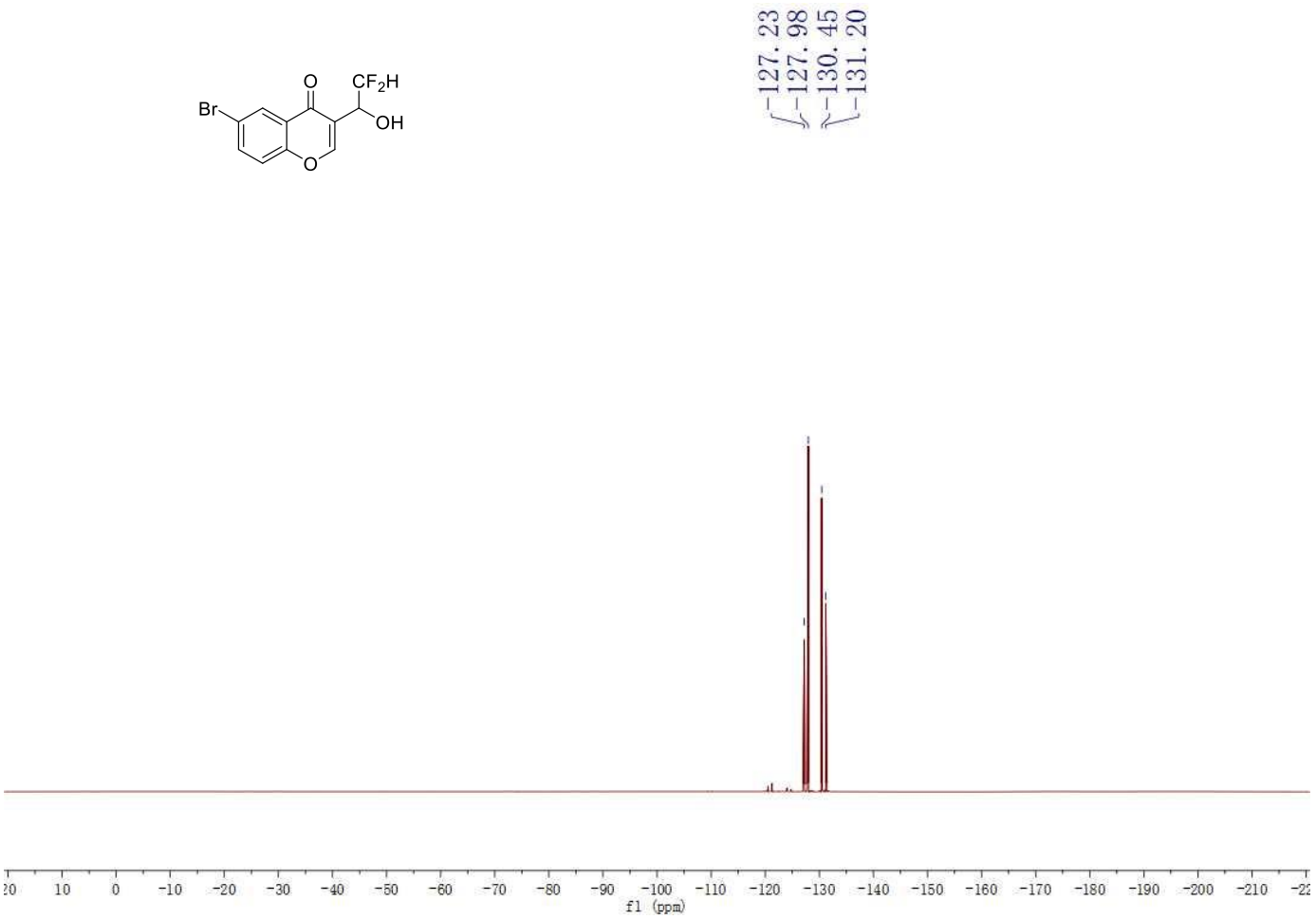


Fig. S36. ^{1}H NMR spectrum of compound **3l**

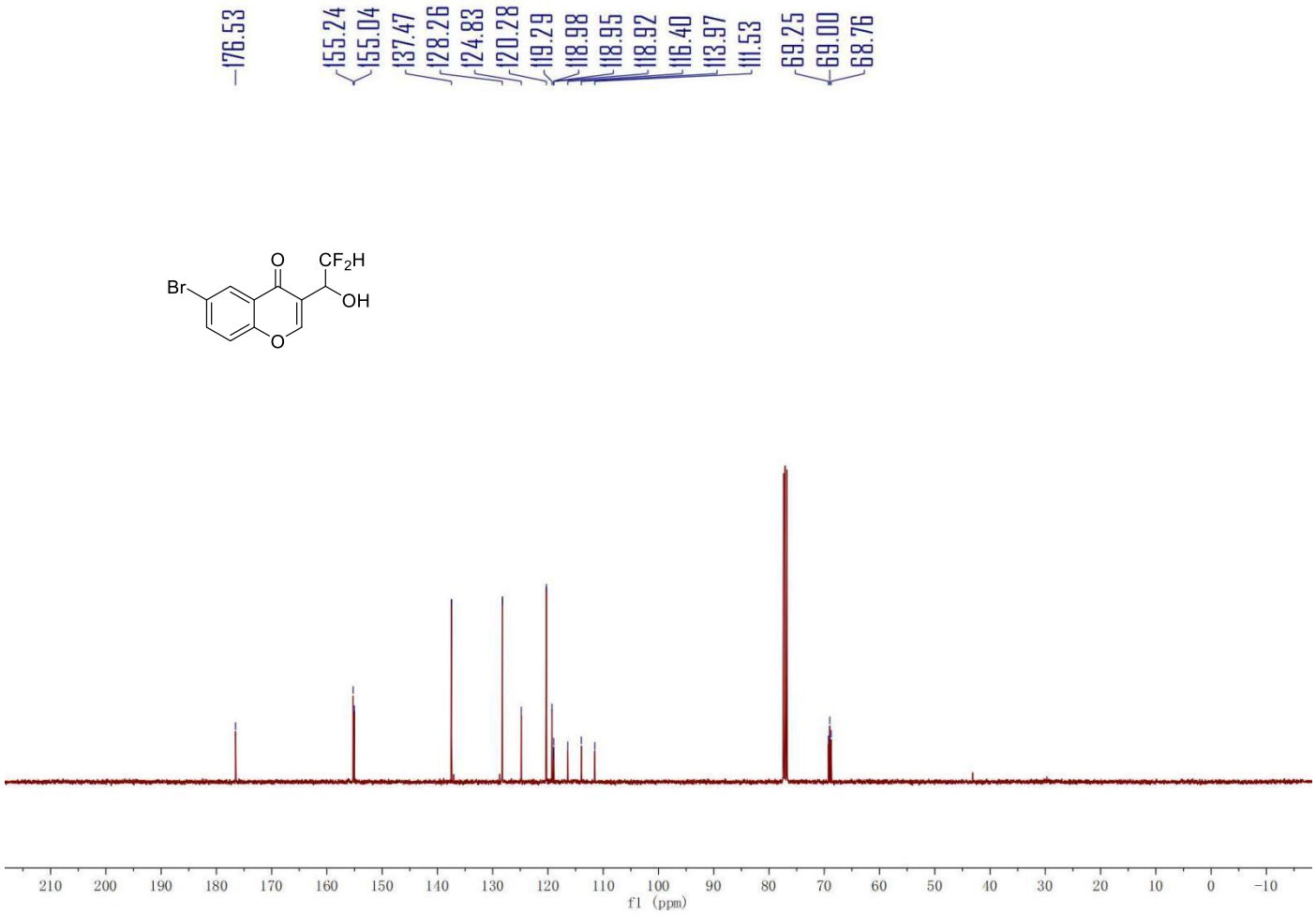


Fig. S37. ^{19}F NMR spectrum of compound **3l**

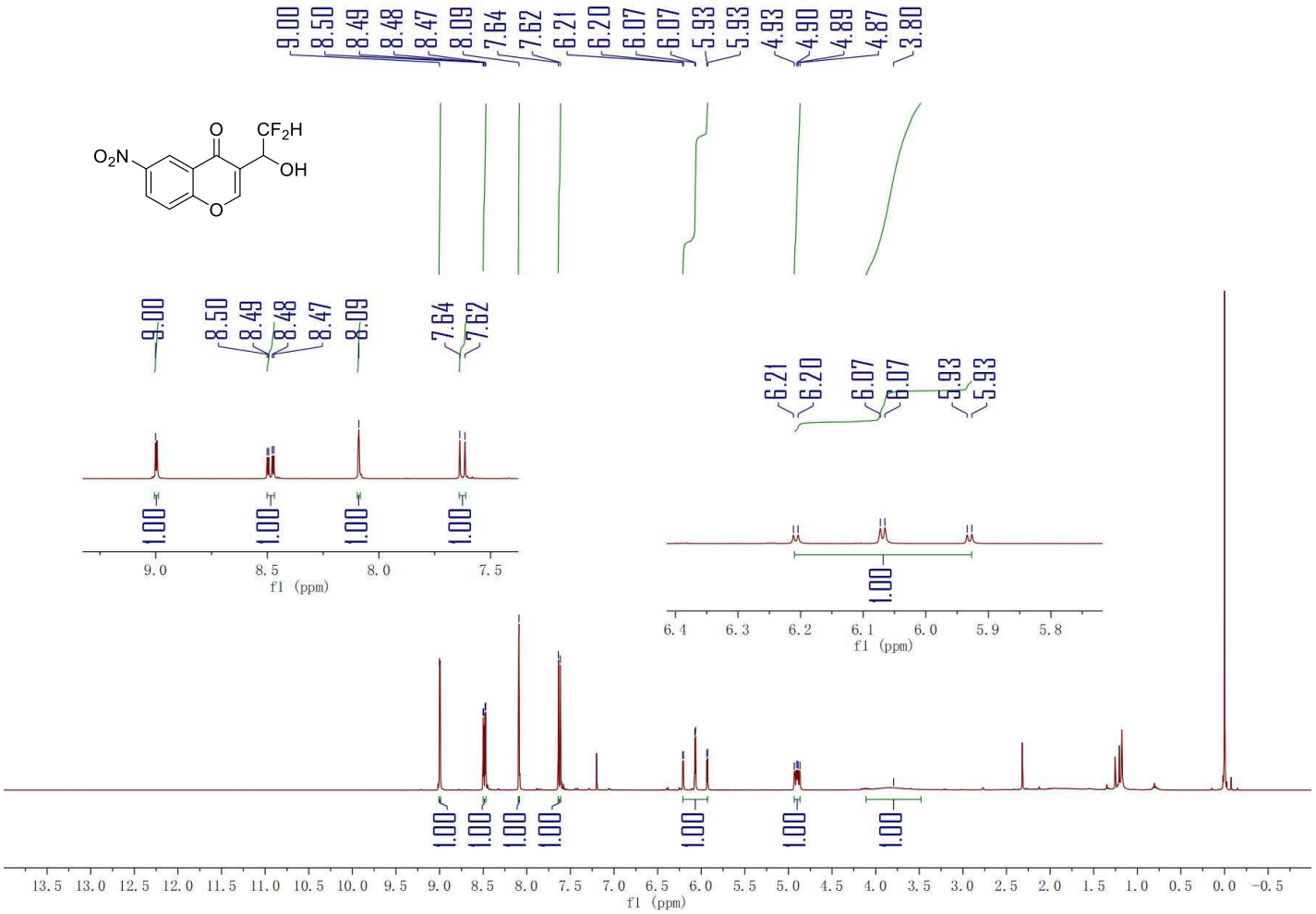


Fig. S38. ^{13}C NMR spectrum of compound **3m**

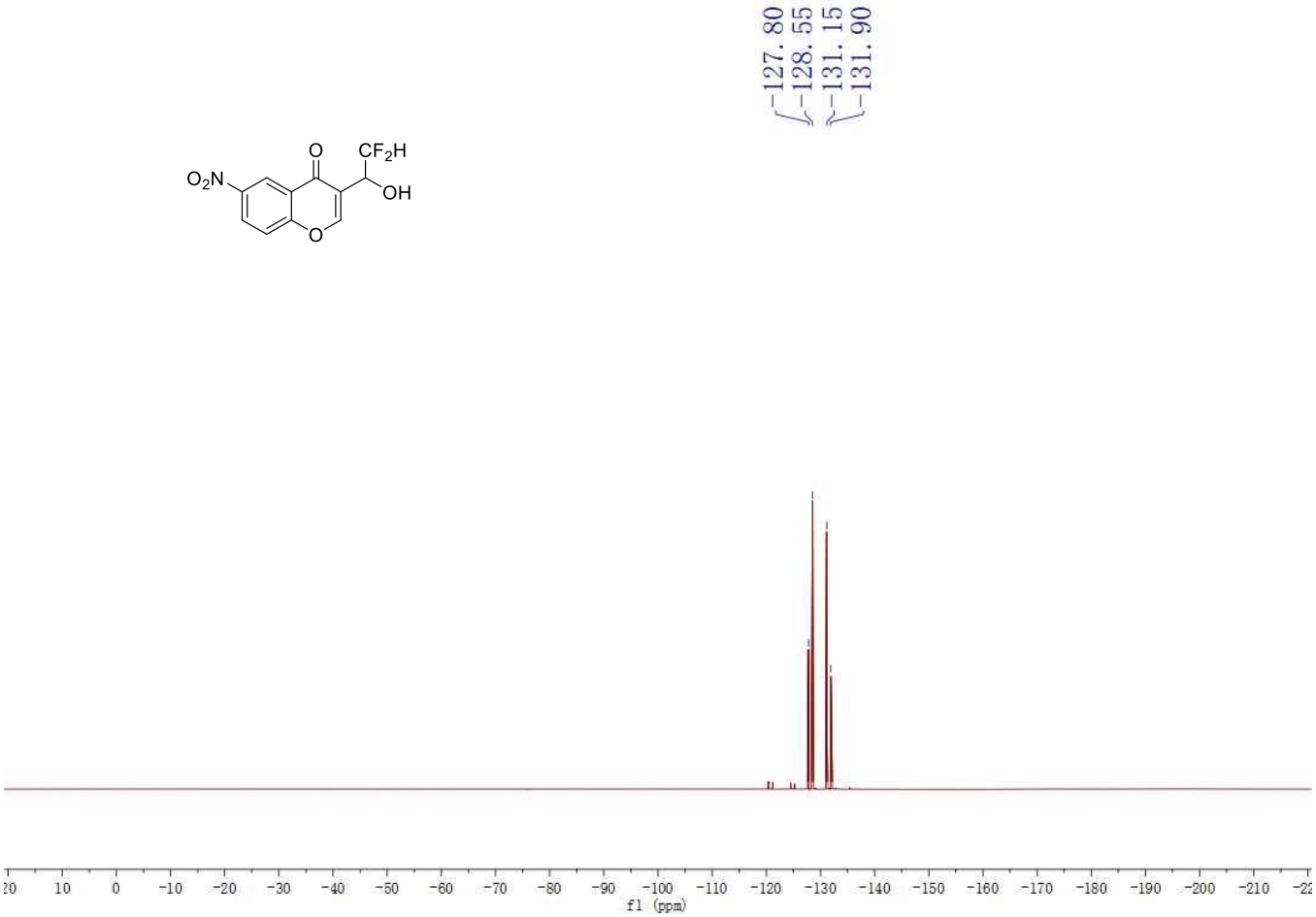


Fig. S39. ^{1}H NMR spectrum of compound **3m**

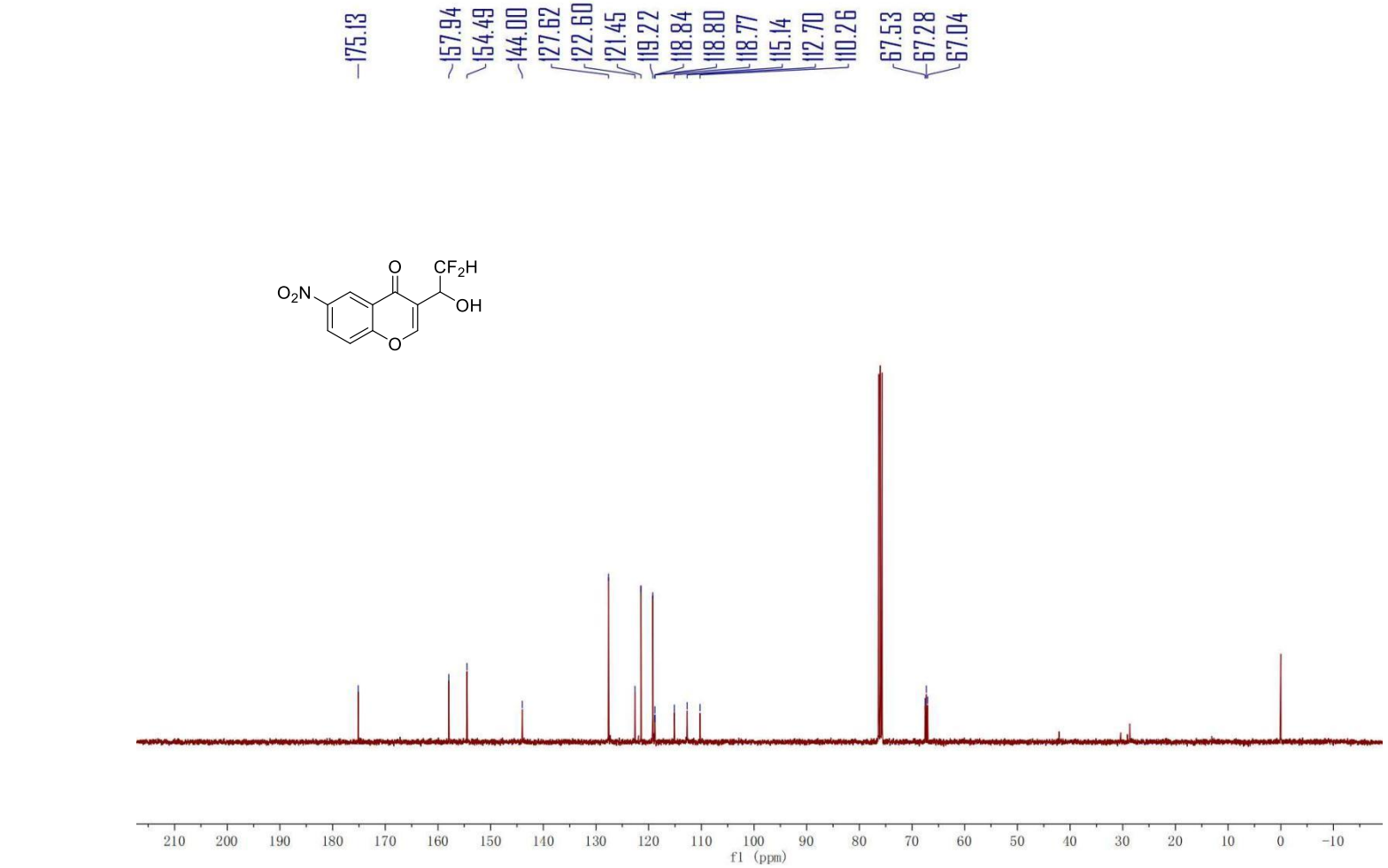


Fig. S40. ^{19}F NMR spectrum of compound **3m**

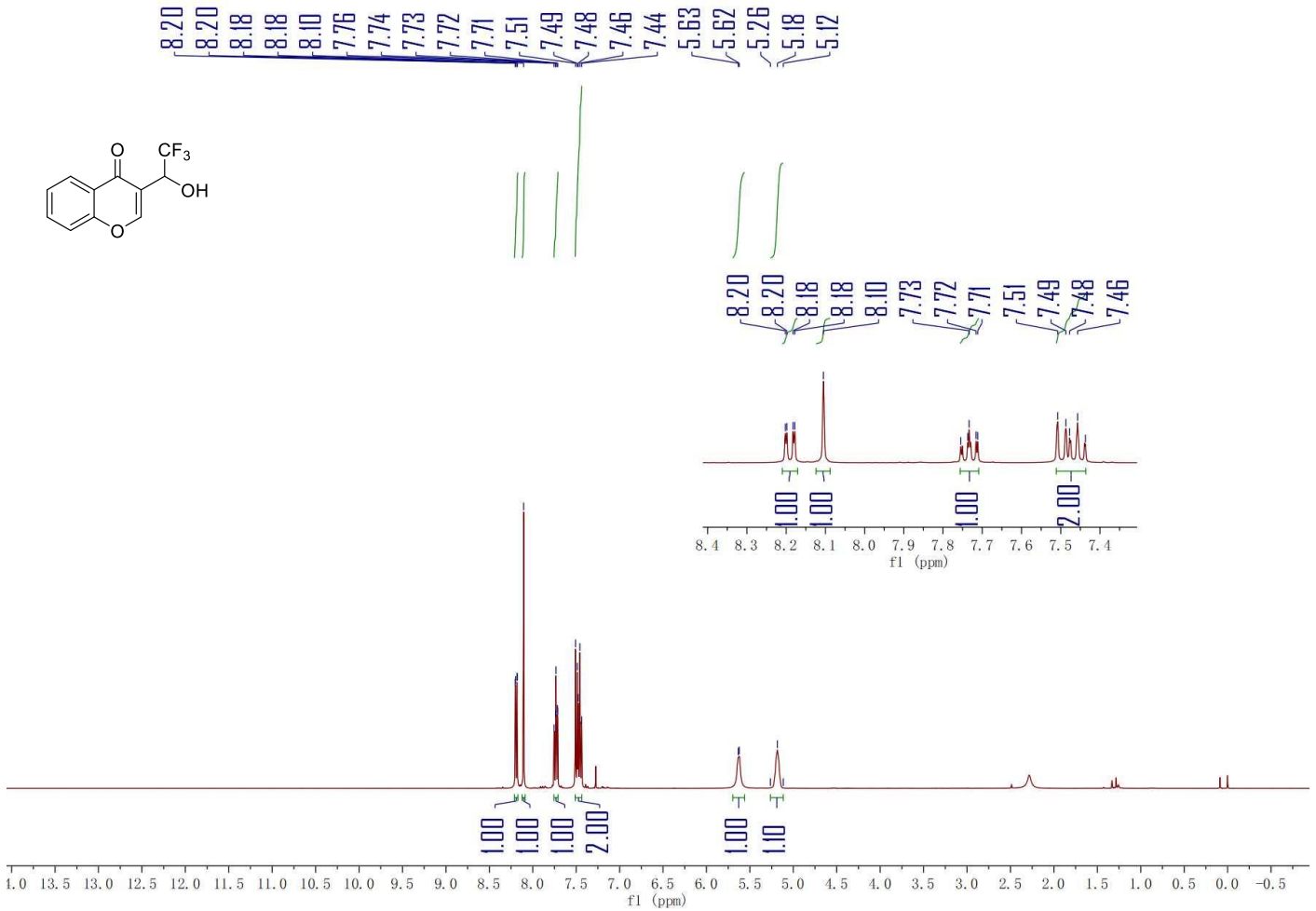


Fig. S41. ^{1}H NMR spectrum of compound **4a**

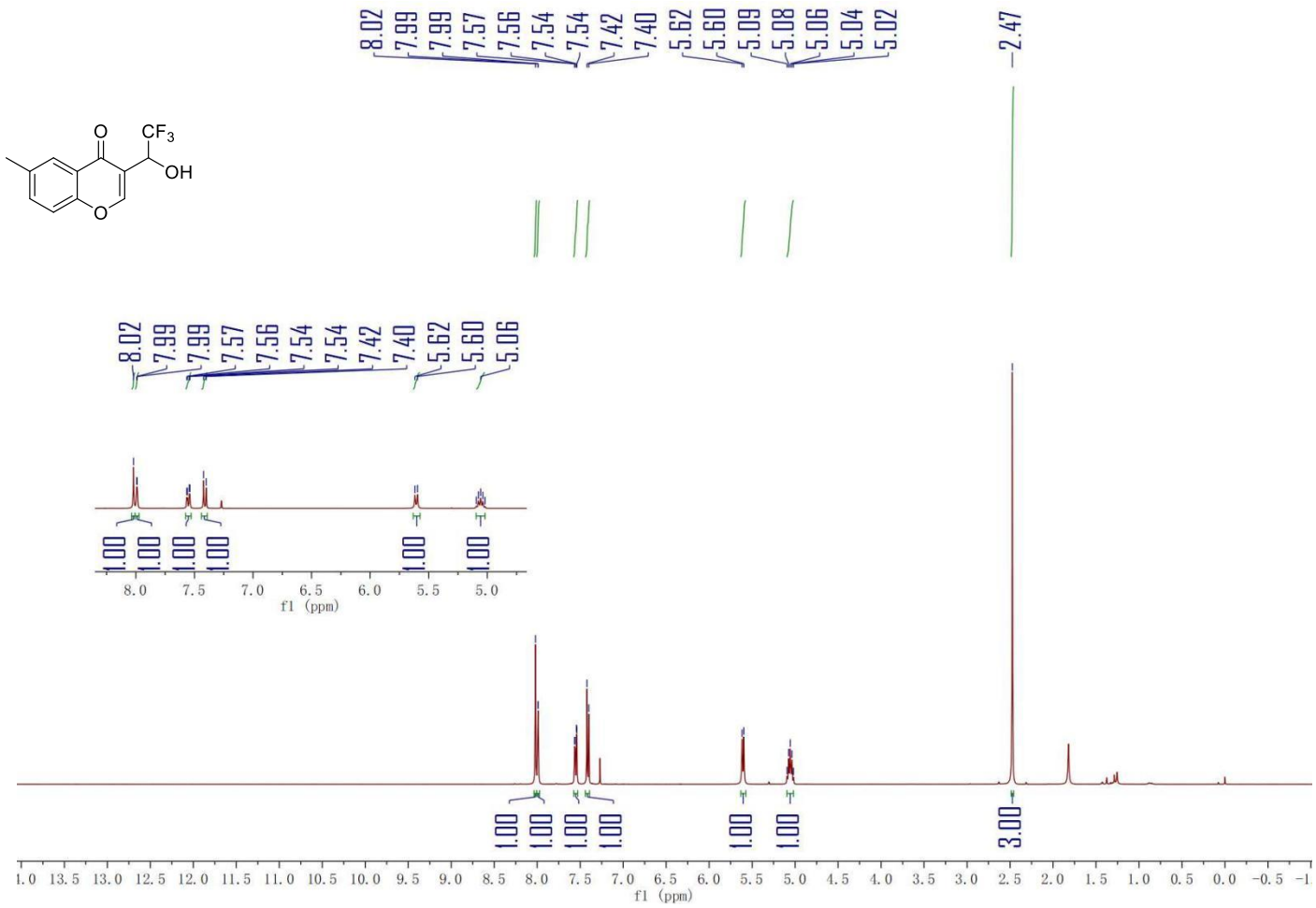


Fig. S42. ^{1}H NMR spectrum of compound **4b**

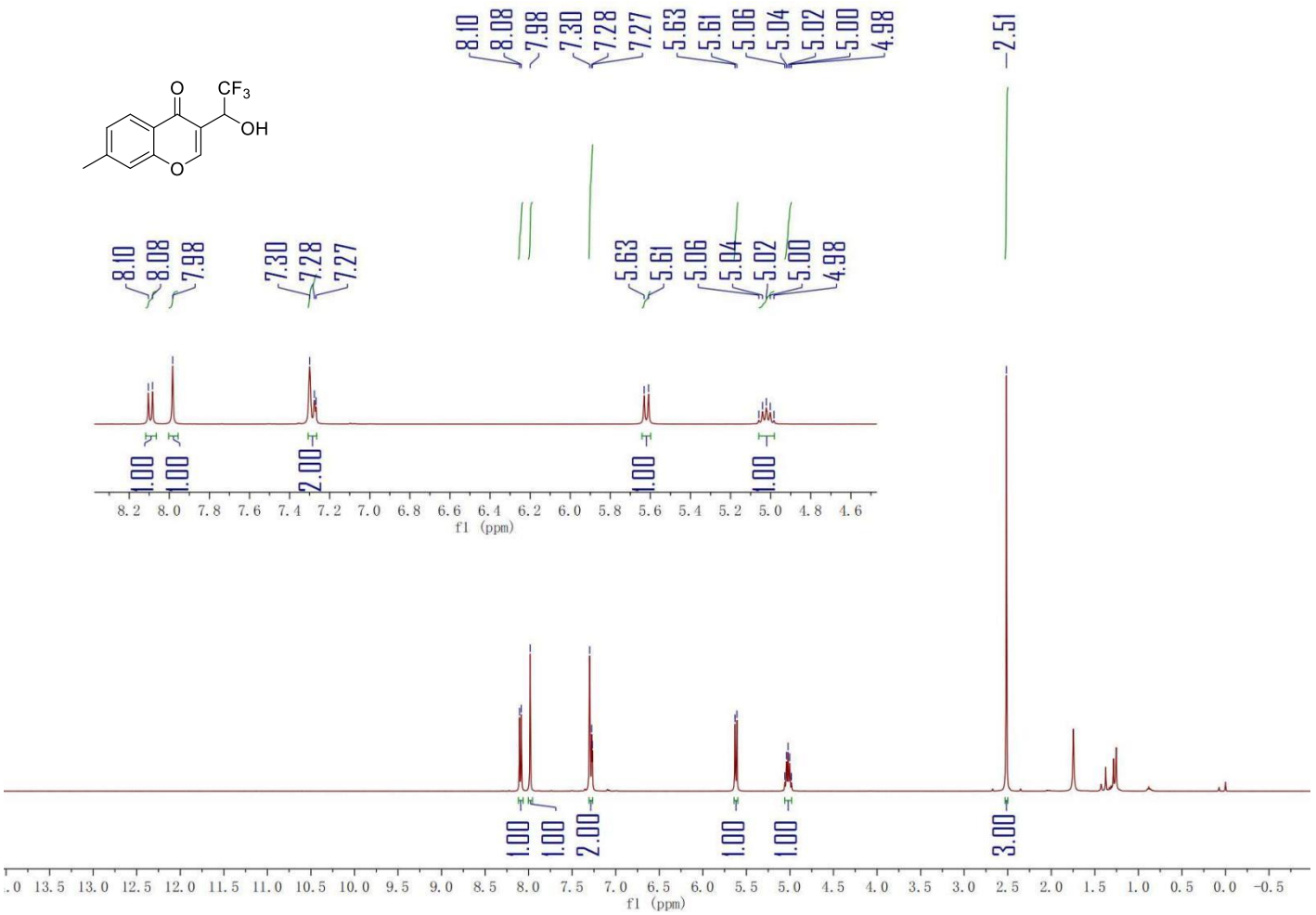


Fig. S43. ^{1}H NMR spectrum of compound **4c**

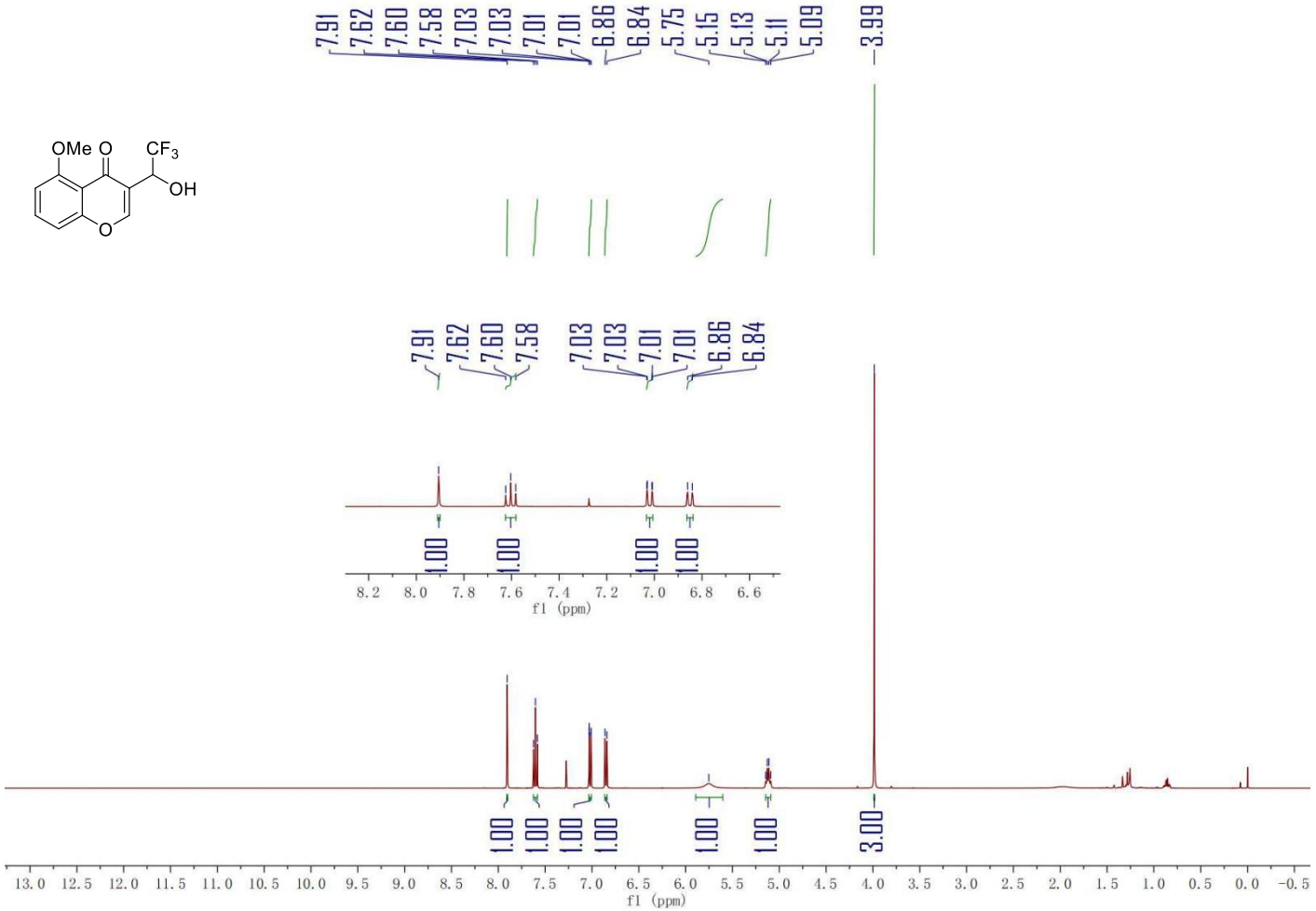


Fig. S44. ^{1}H NMR spectrum of compound **4d**

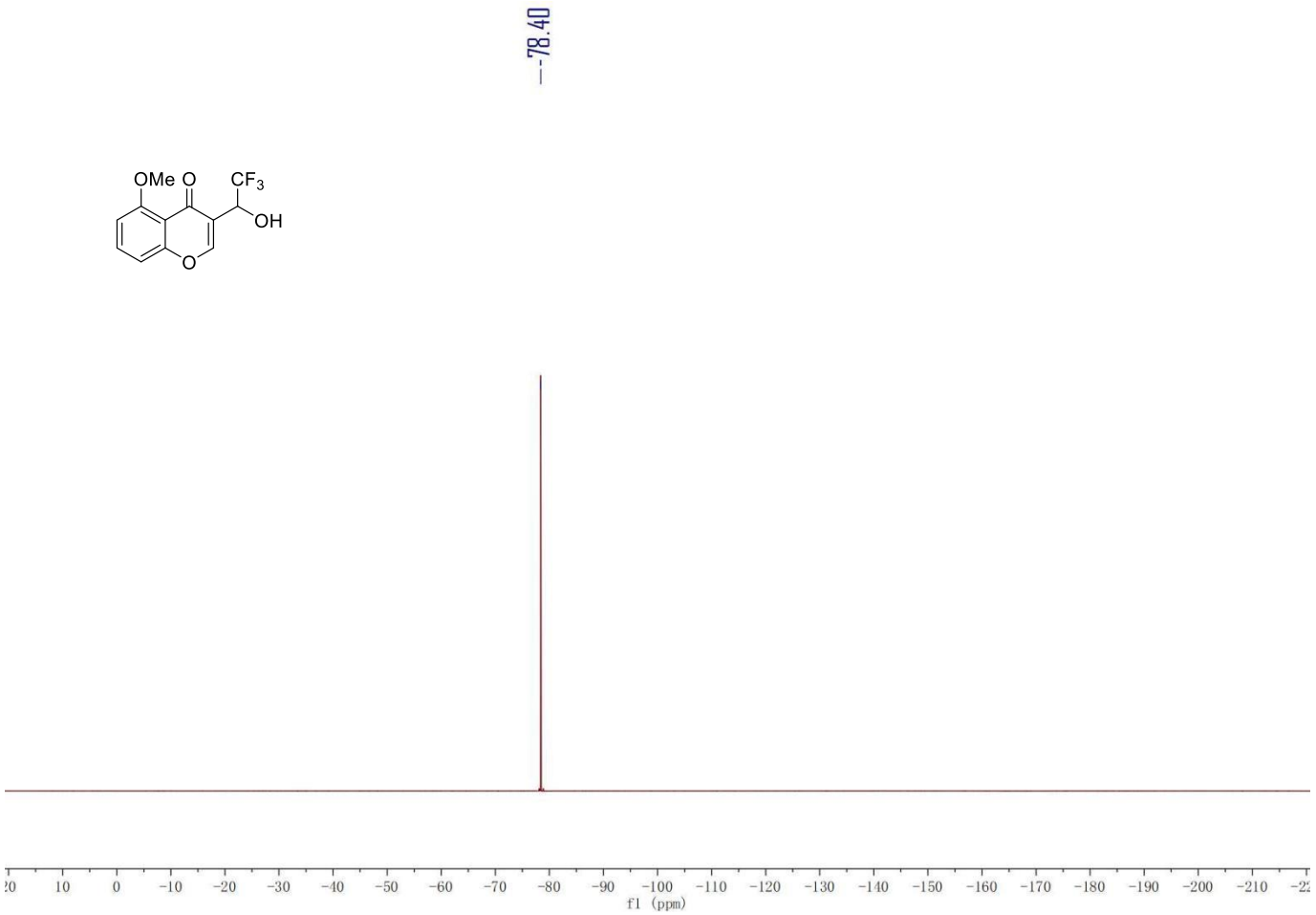


Fig. S45. ^{19}F NMR spectrum of compound **4d**

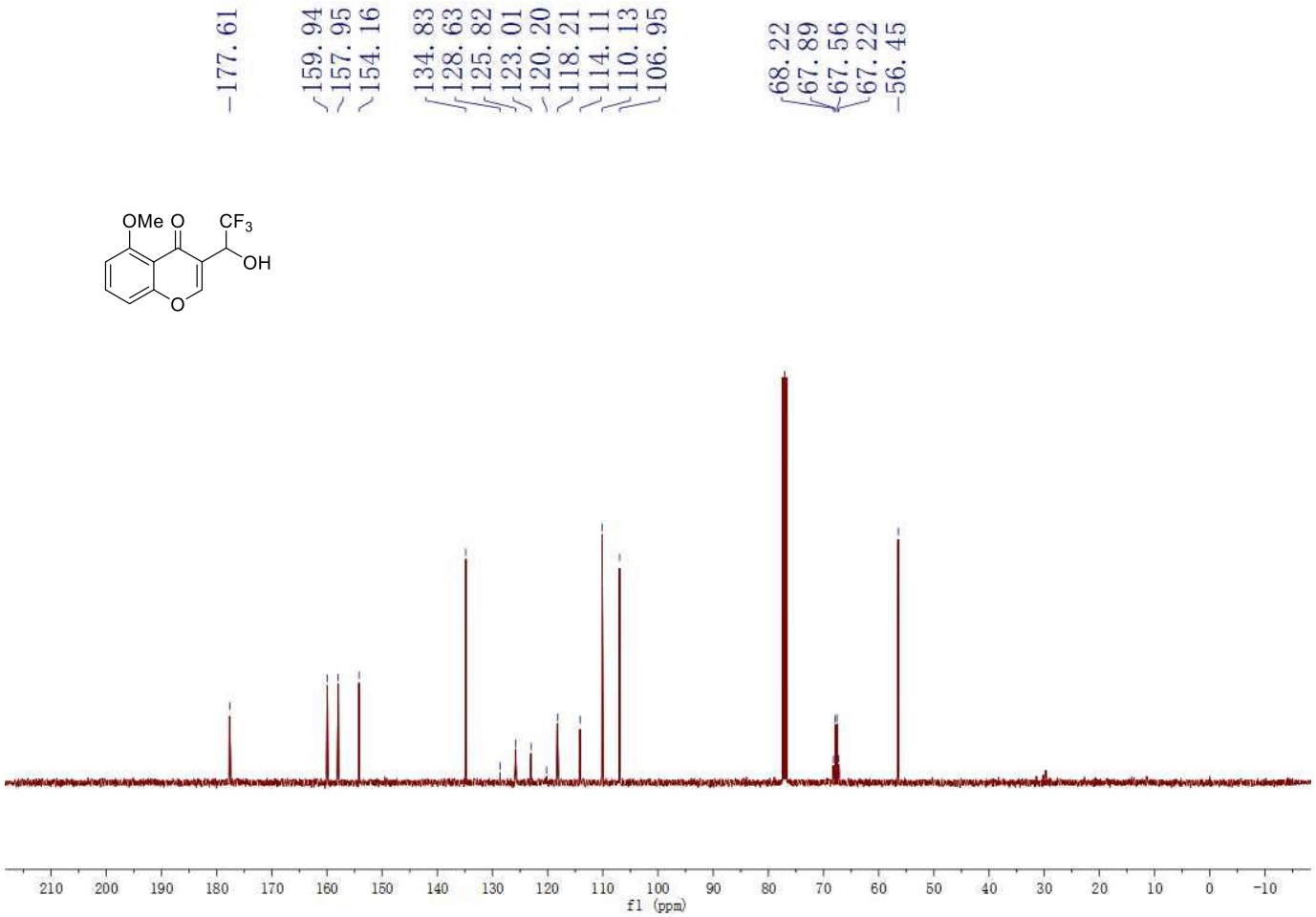


Fig. S46. ^{13}C NMR spectrum of compound **4d**

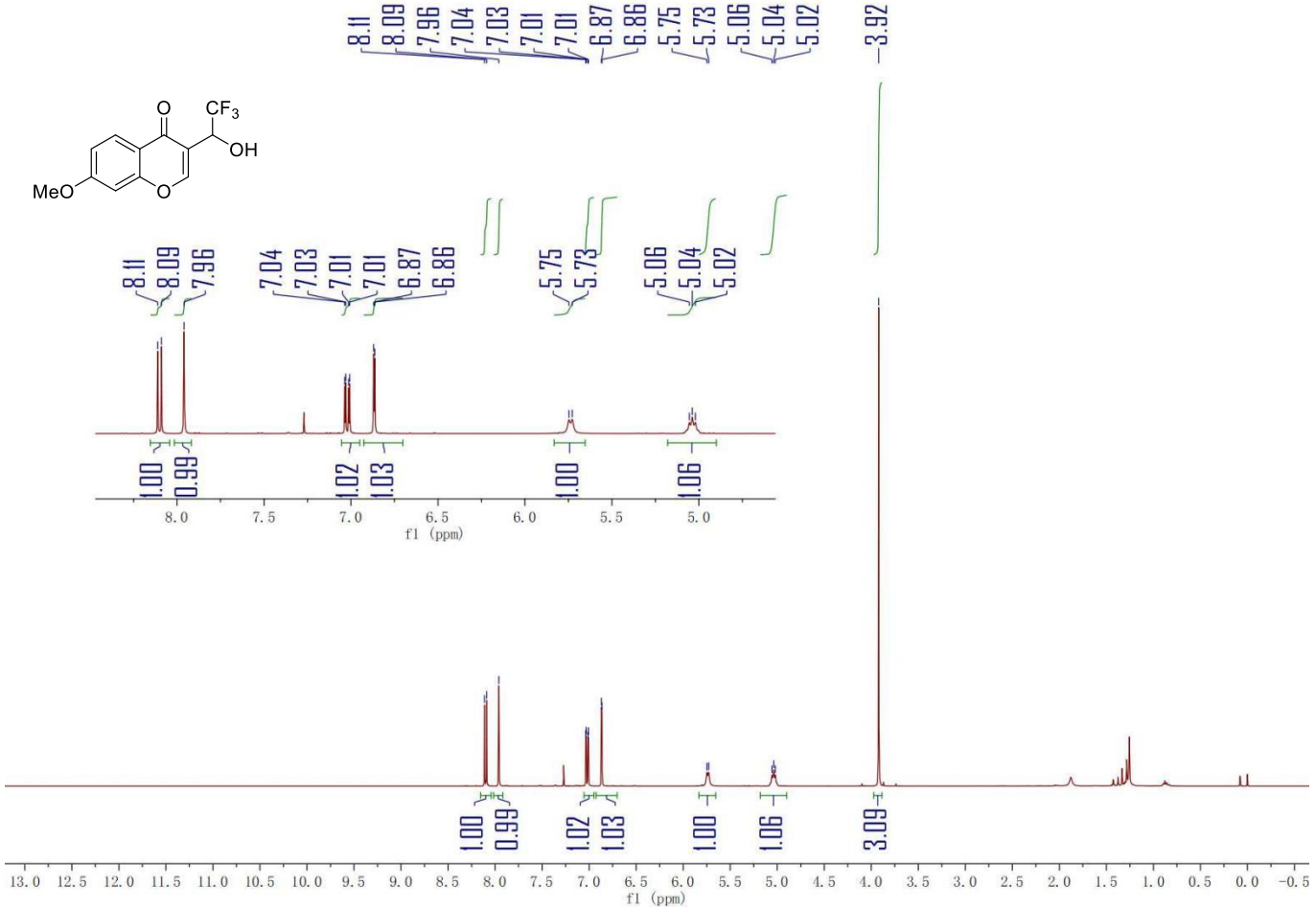


Fig. S47. ^{1}H NMR spectrum of compound **4e**

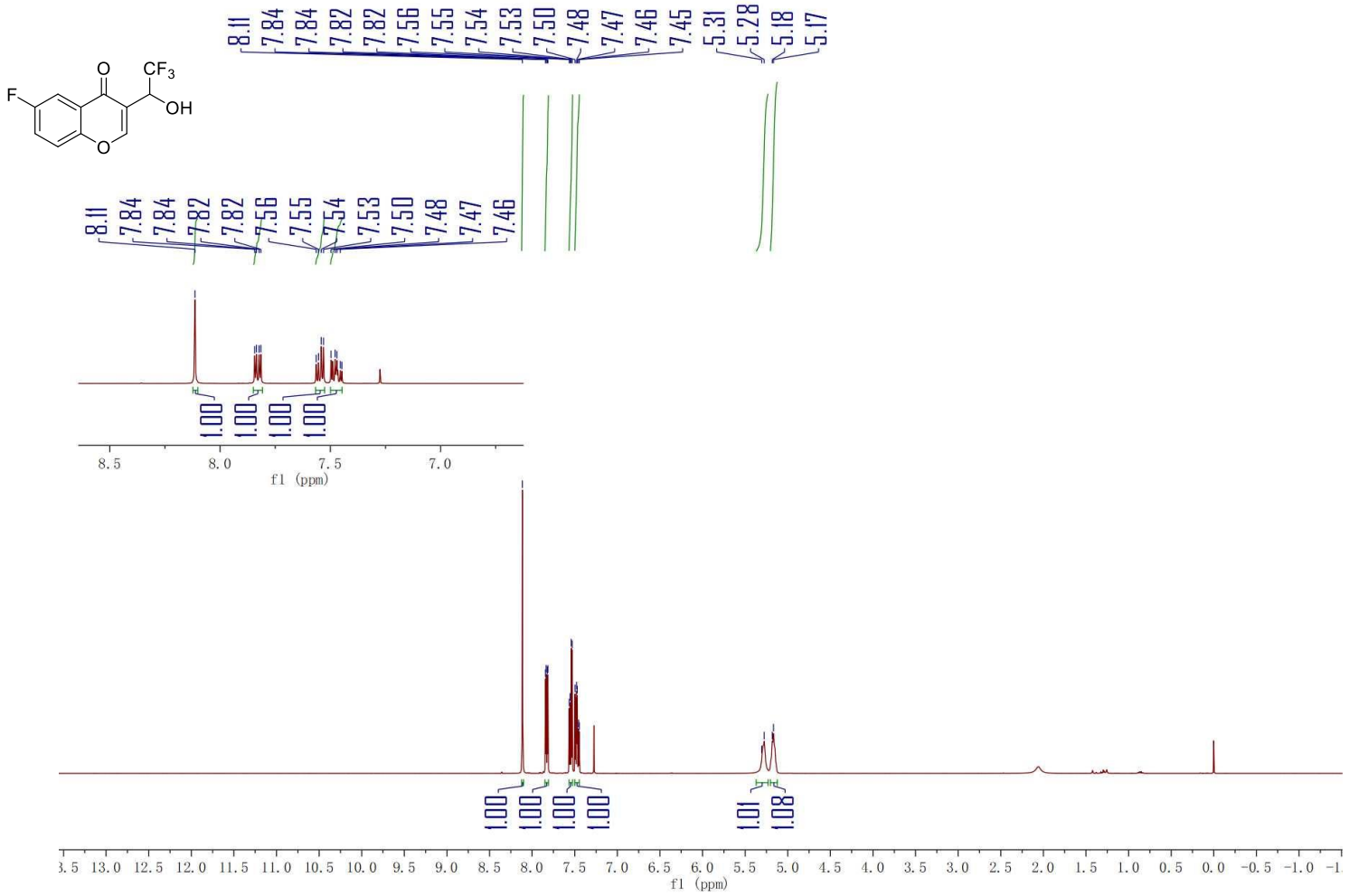


Fig. S48. ^{1}H NMR spectrum of compound **4f**

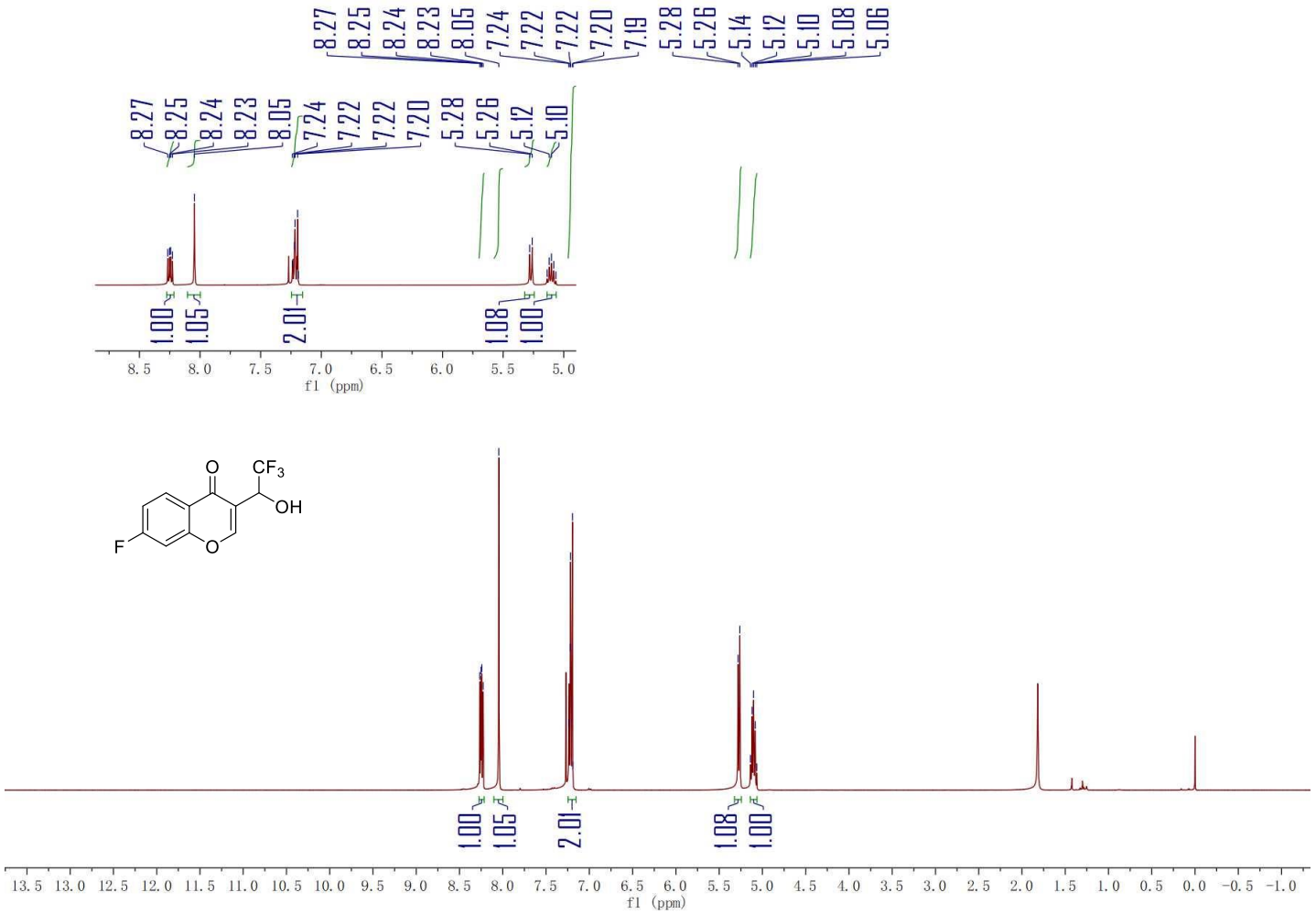


Fig. S49. ^{1}H NMR spectrum of compound **4g**

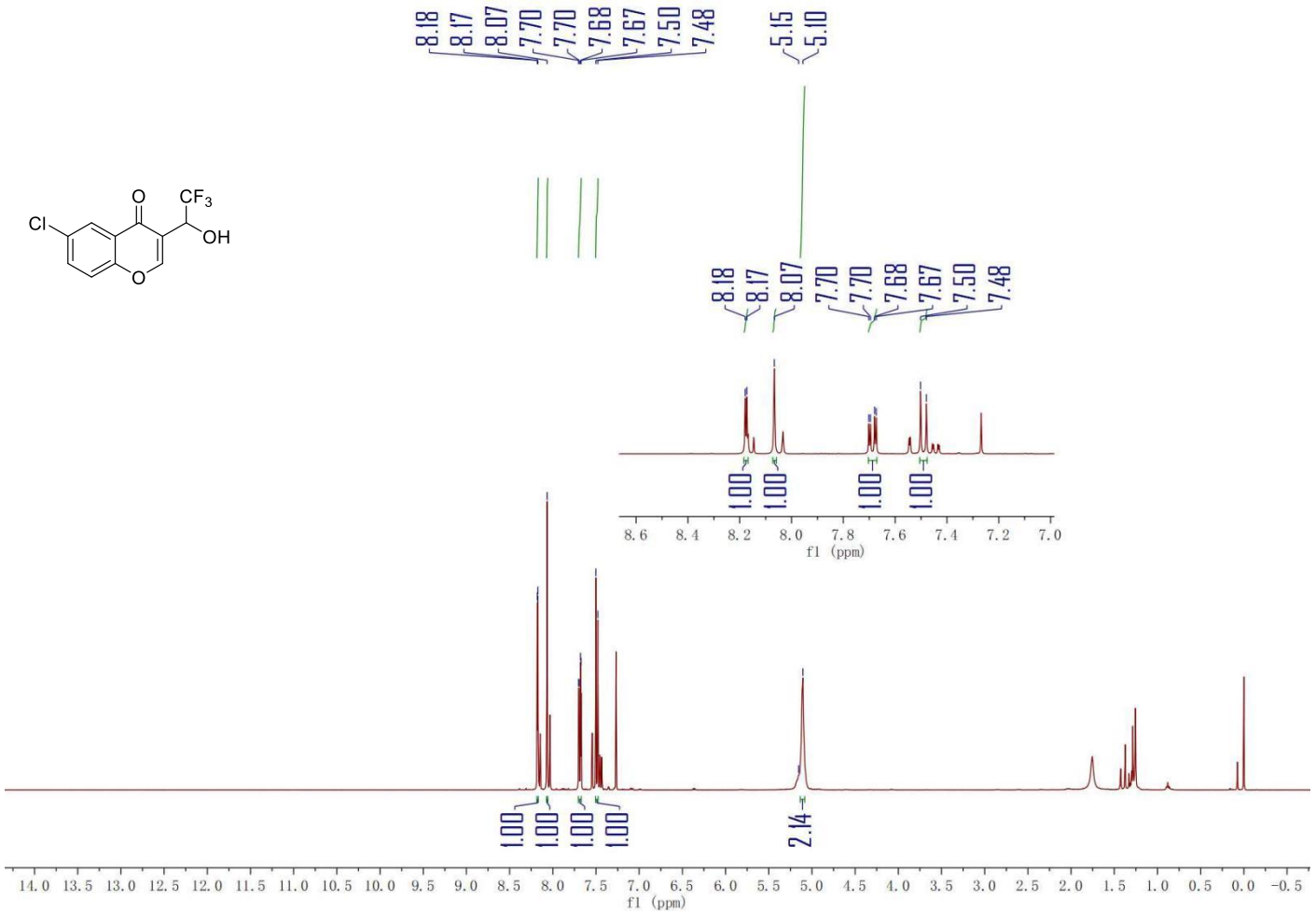


Fig. S50. ^{1}H NMR spectrum of compound **4h**

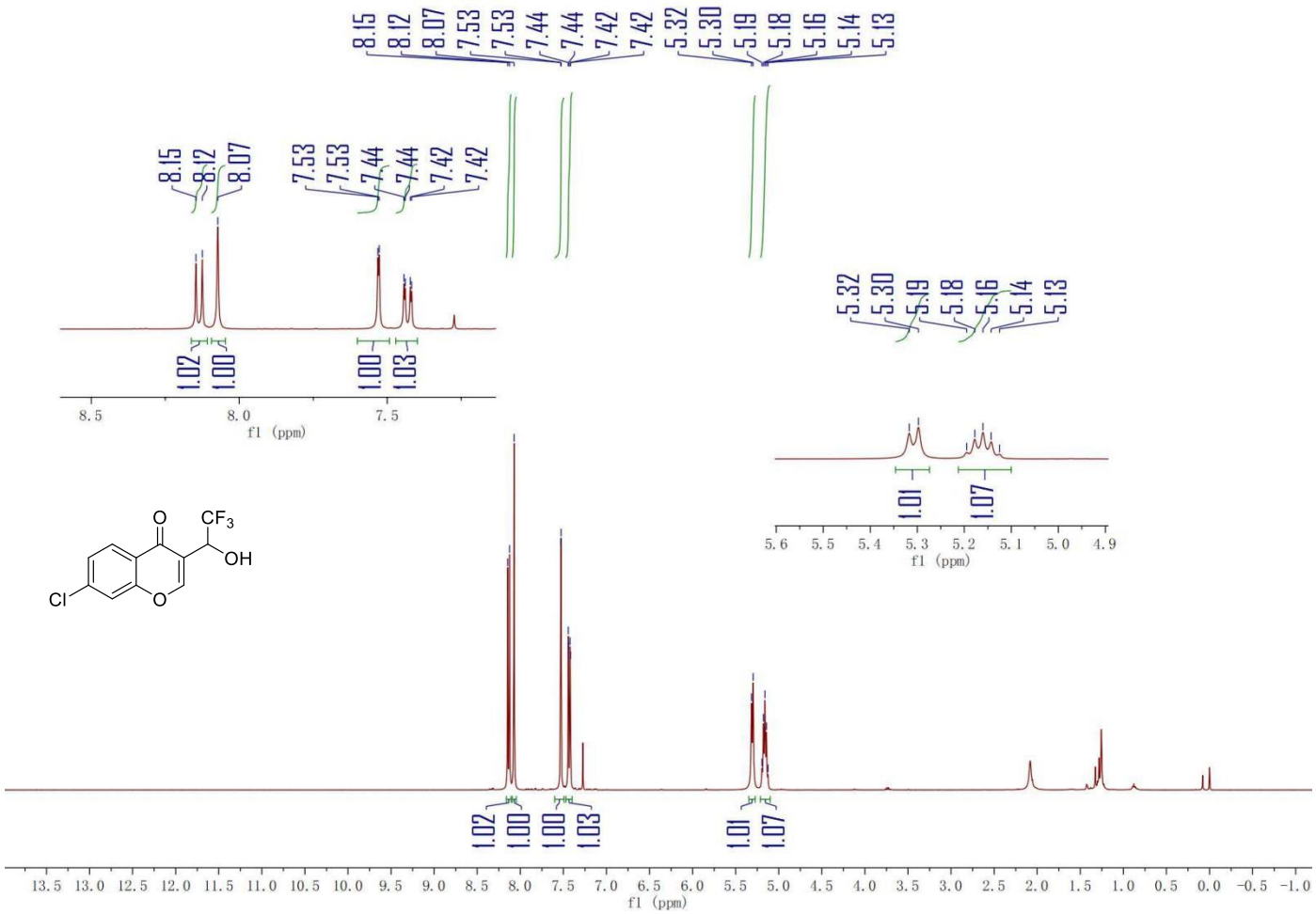


Fig. S51. ^{1}H NMR spectrum of compound **4i**

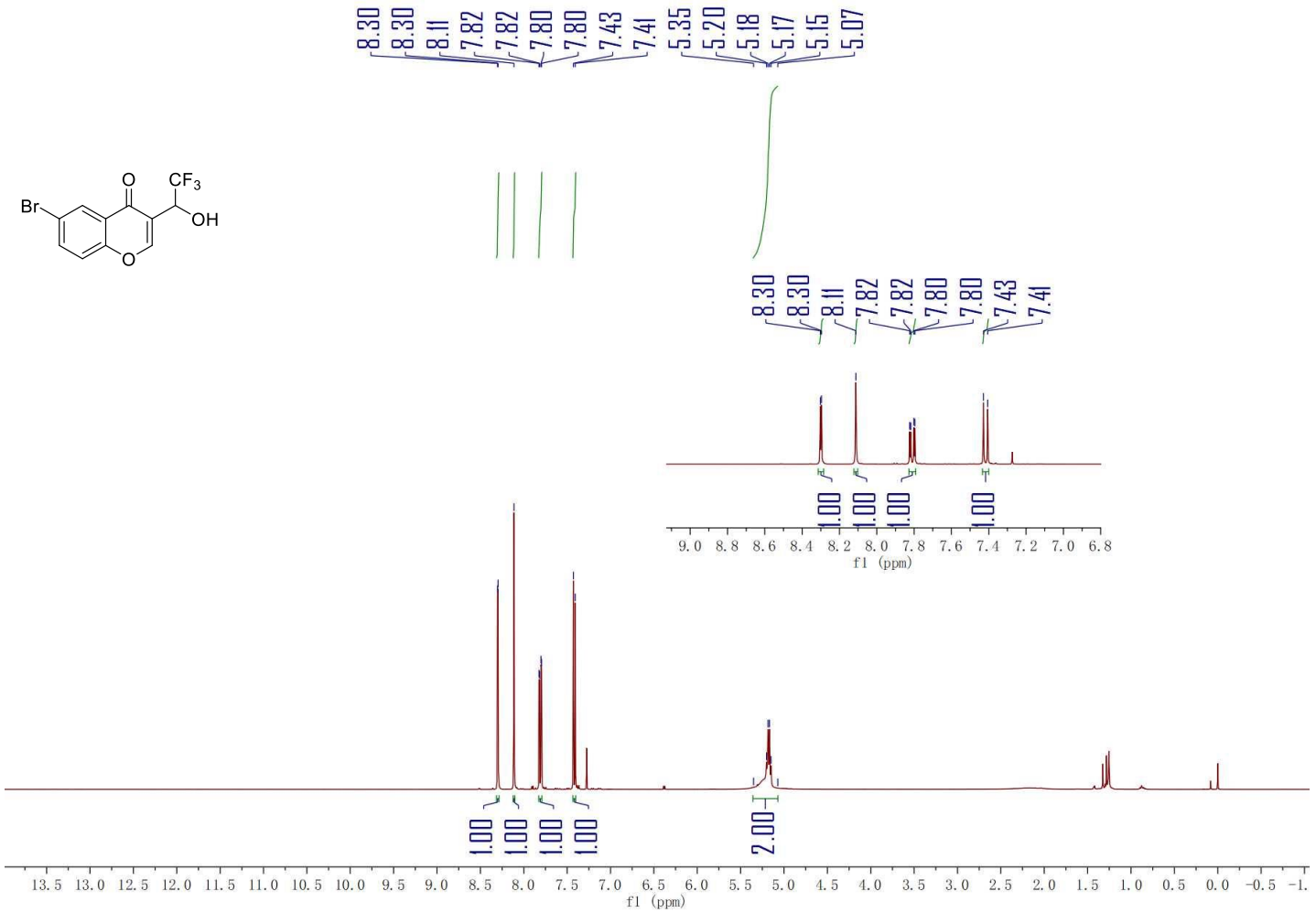


Fig. S52. ^{1}H NMR spectrum of compound **4j**

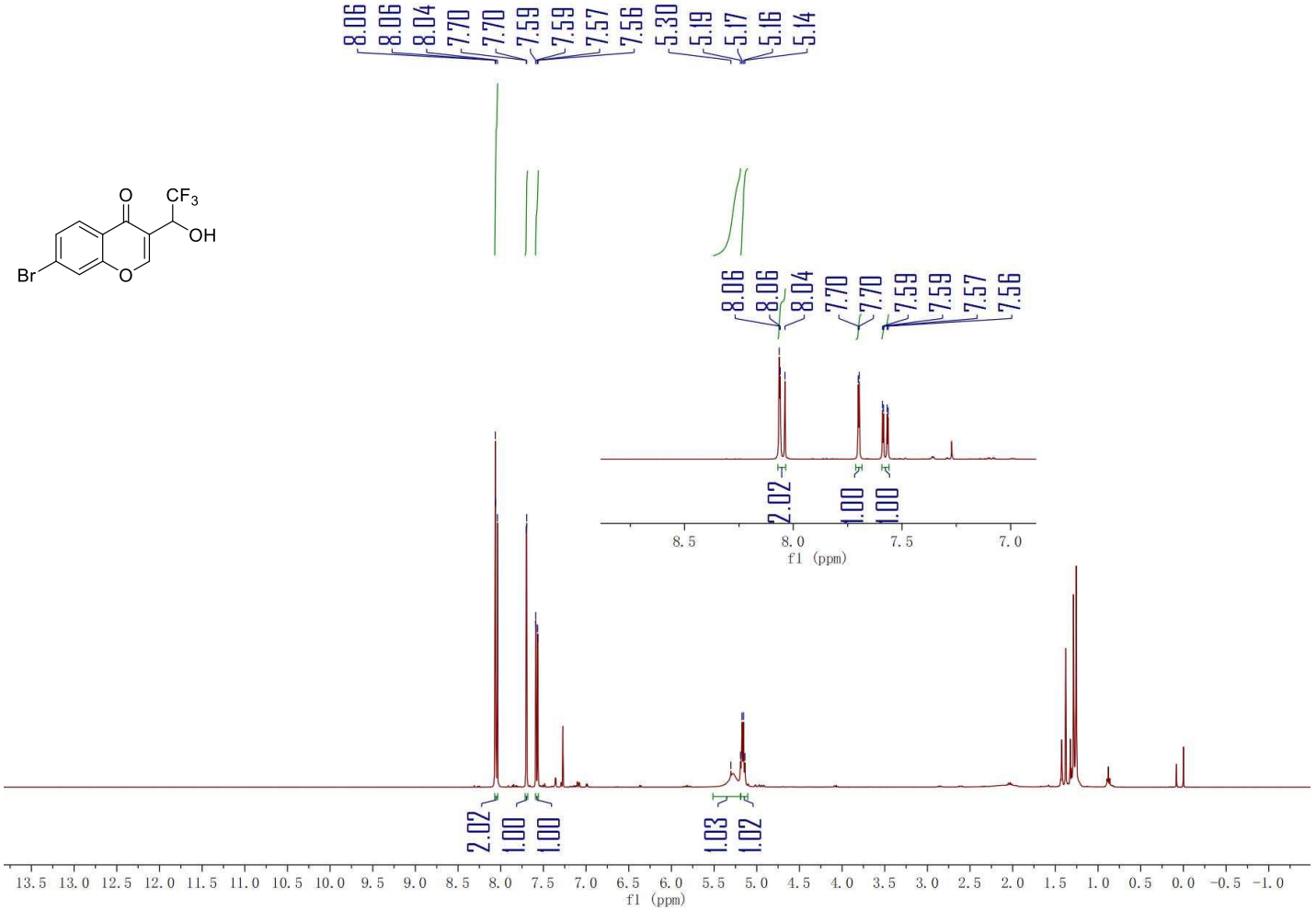


Fig. S53. ^{1}H NMR spectrum of compound **4k**

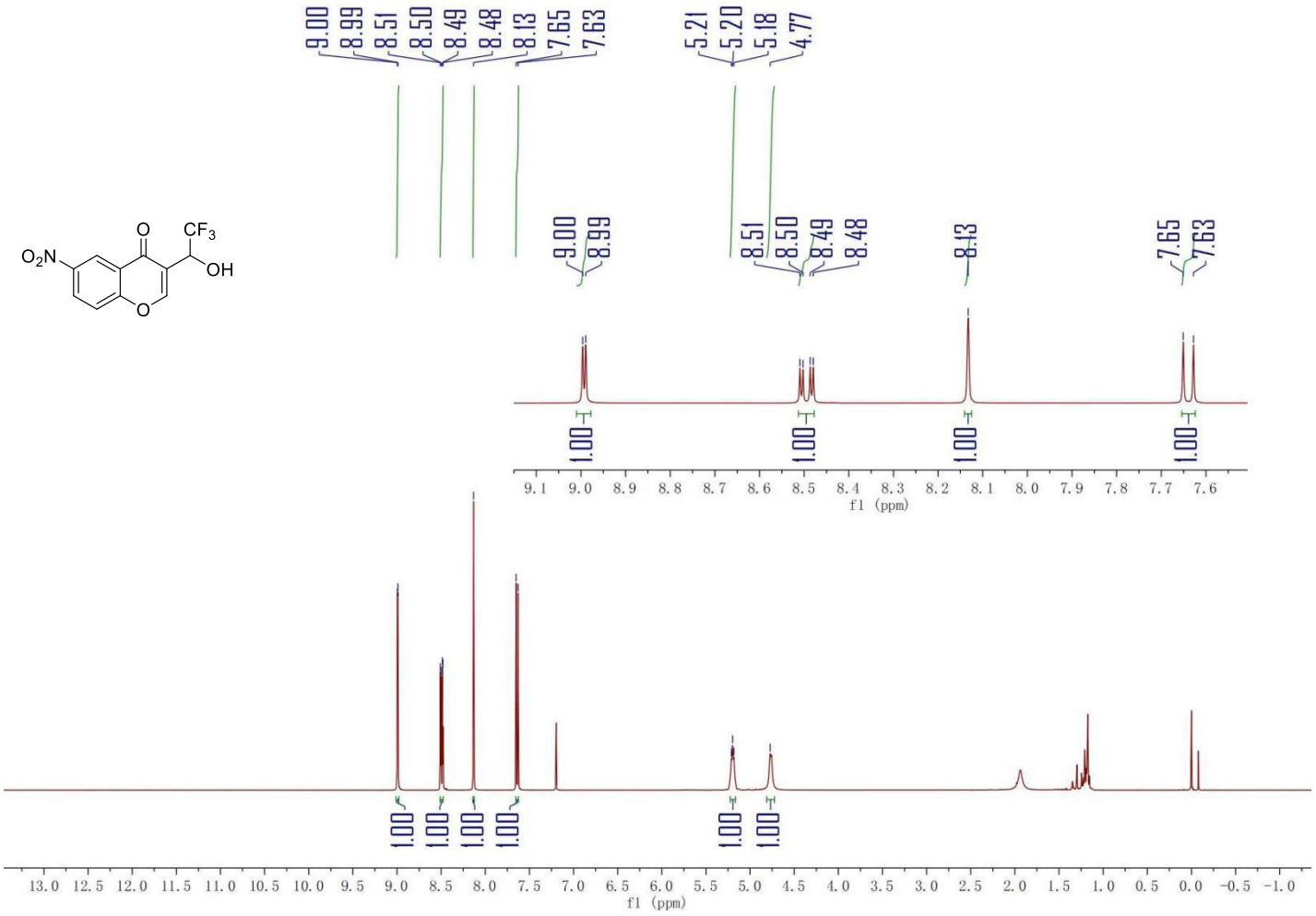


Fig. S54. ^{1}H NMR spectrum of compound **4l**

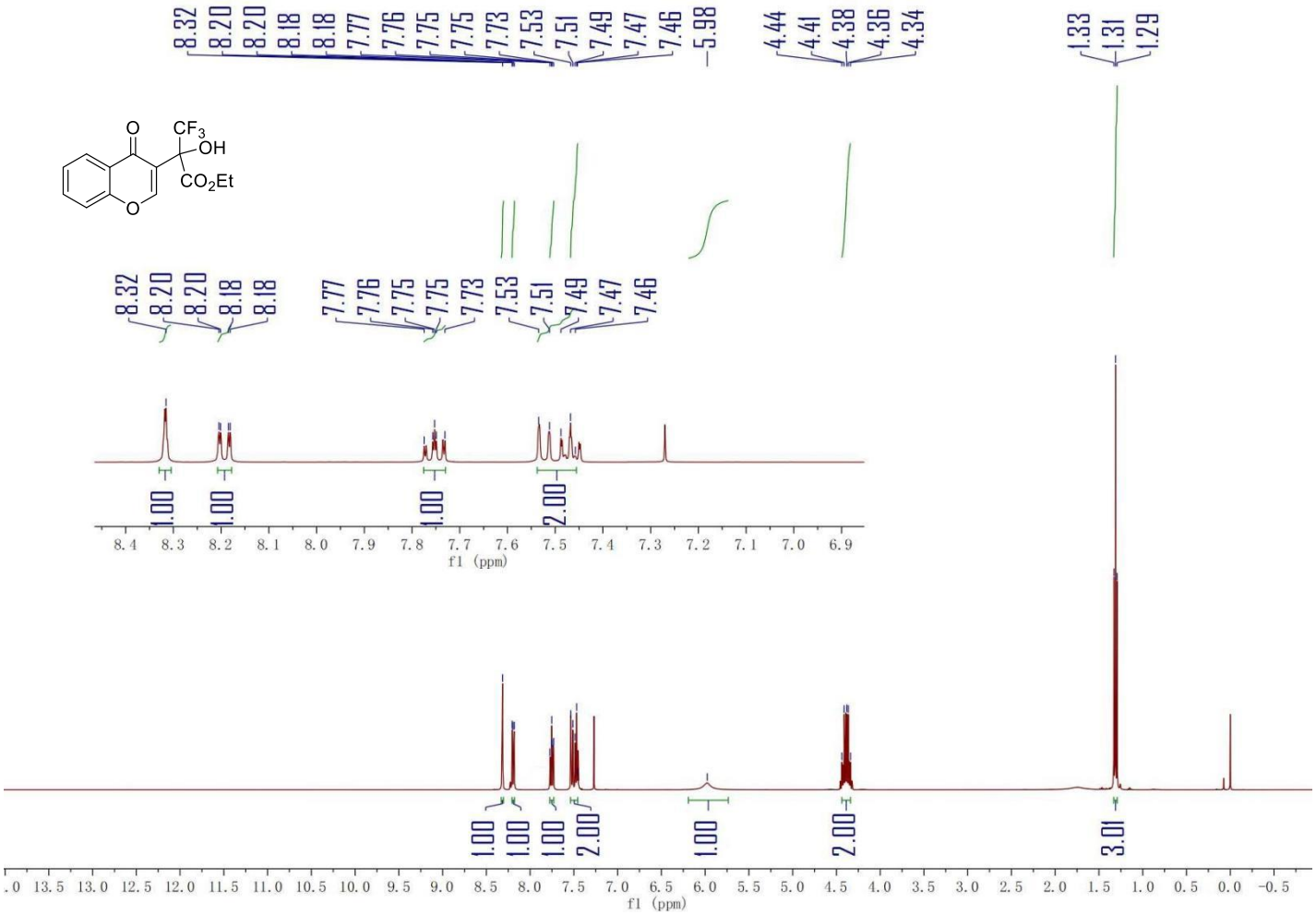


Fig. S55. ^{1}H NMR spectrum of compound **5a**

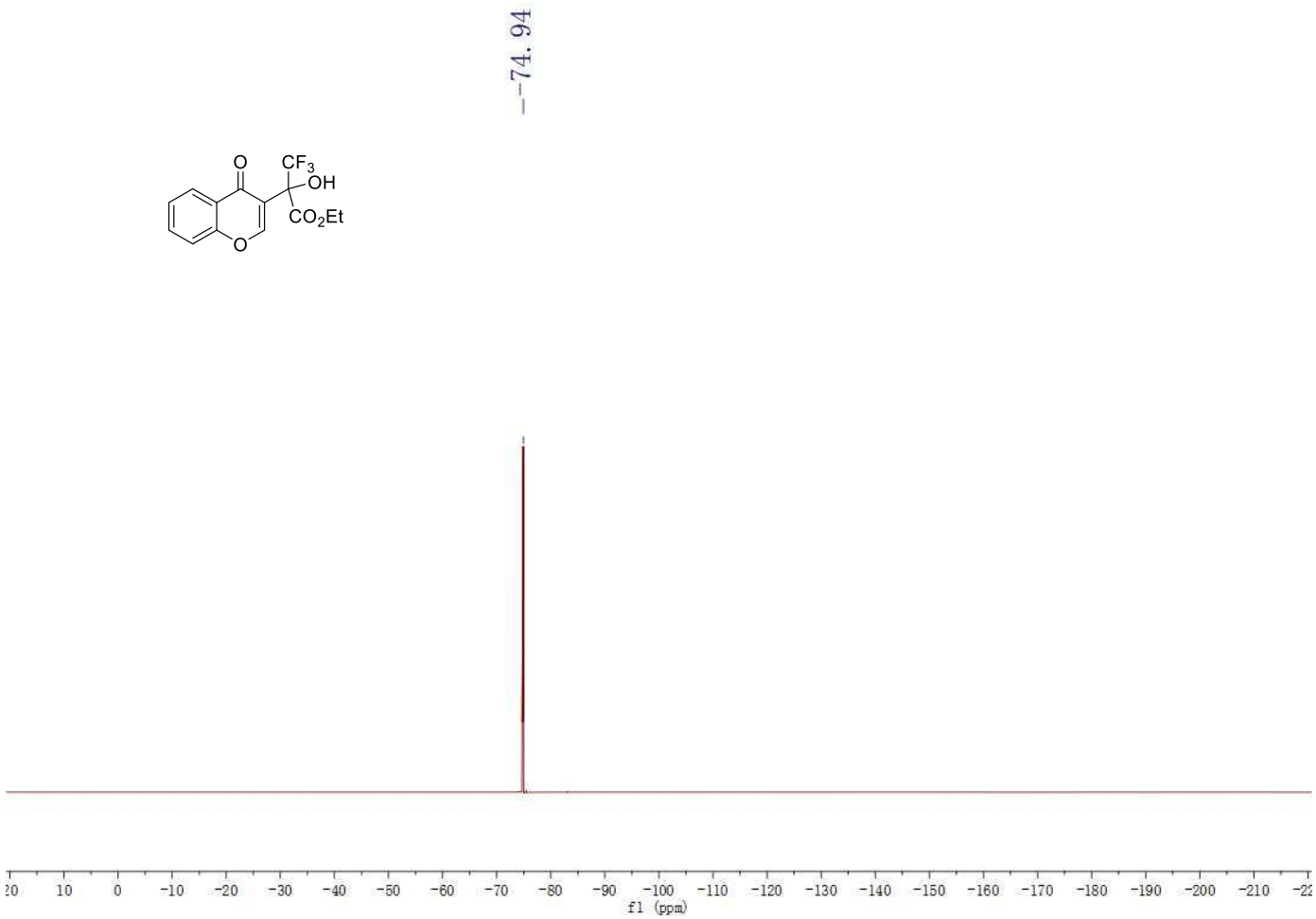


Fig. S56. ^{1}H NMR spectrum of compound **5a**

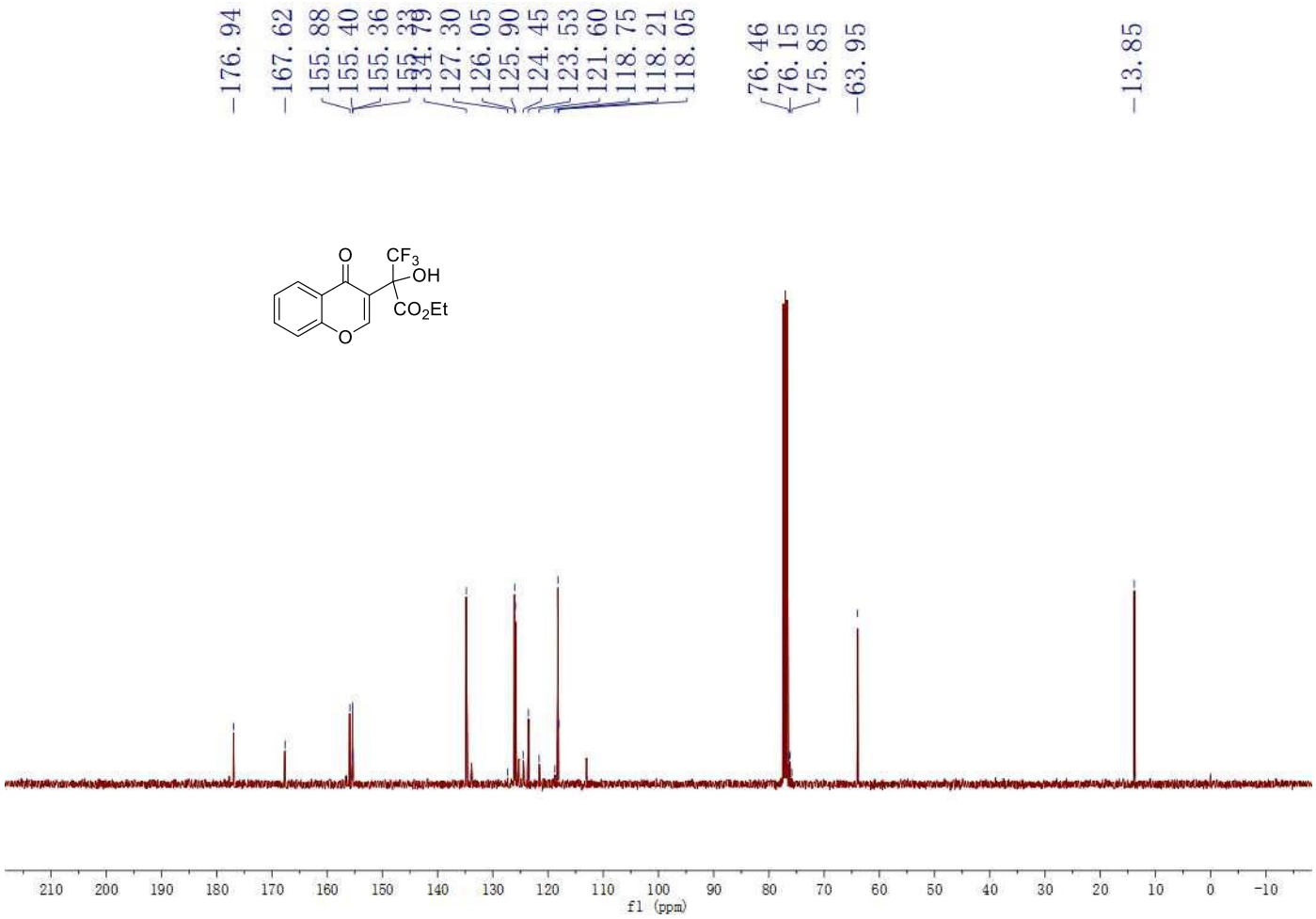


Fig. S57. ^{1}H NMR spectrum of compound **5a**

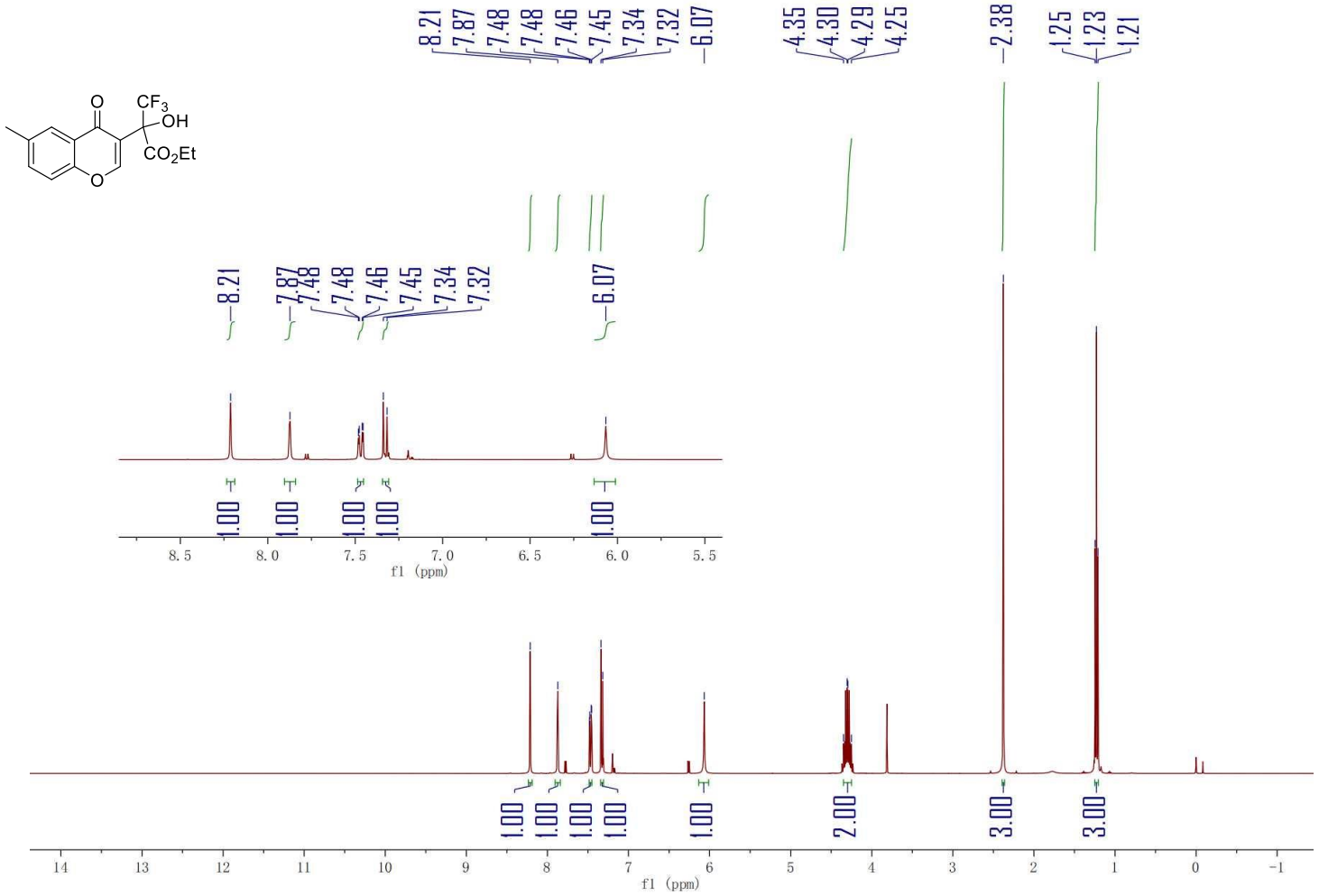


Fig. S58. ^{1}H NMR spectrum of compound **5b**

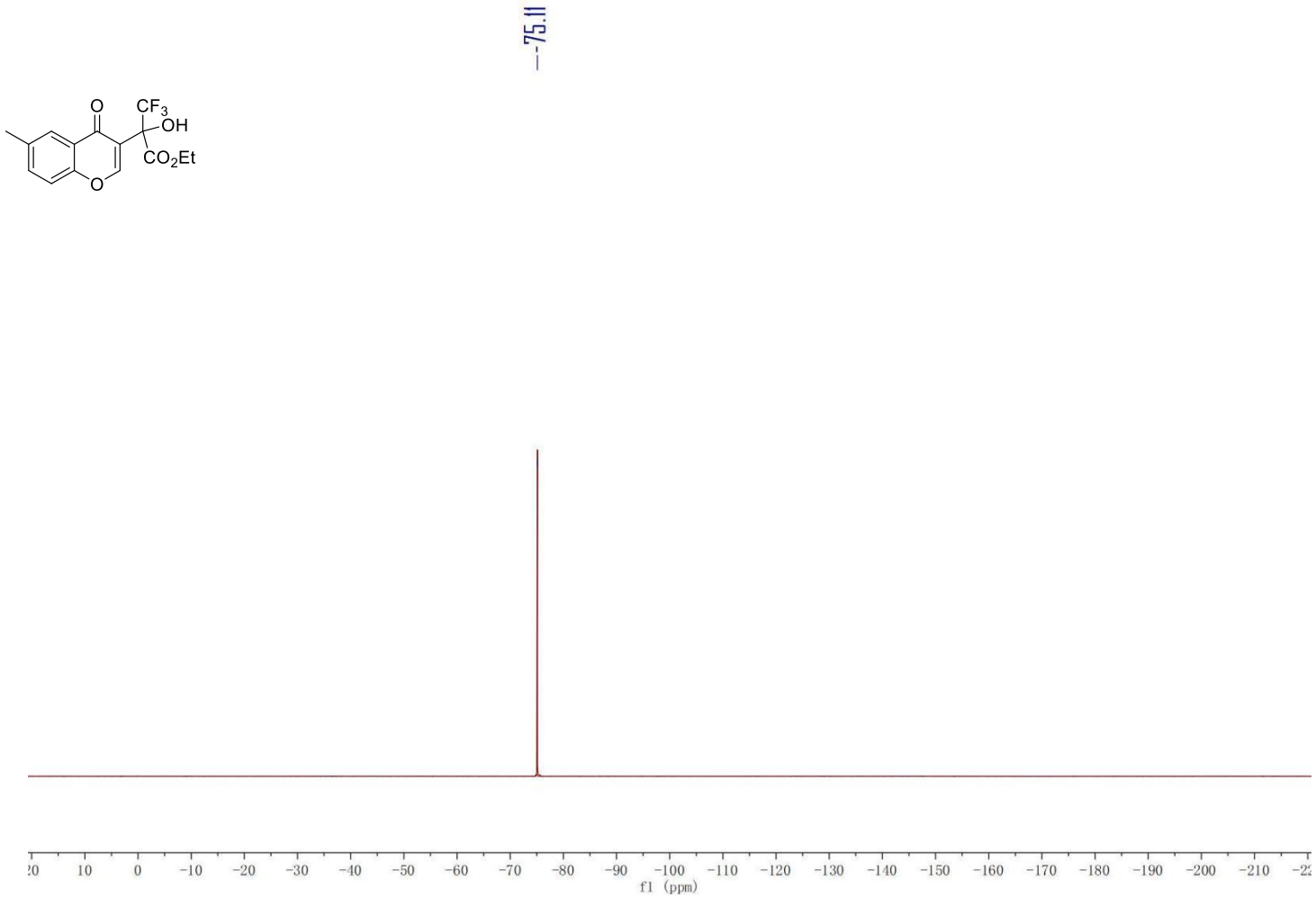


Fig. S59. ^{19}F NMR spectrum of compound **5b**

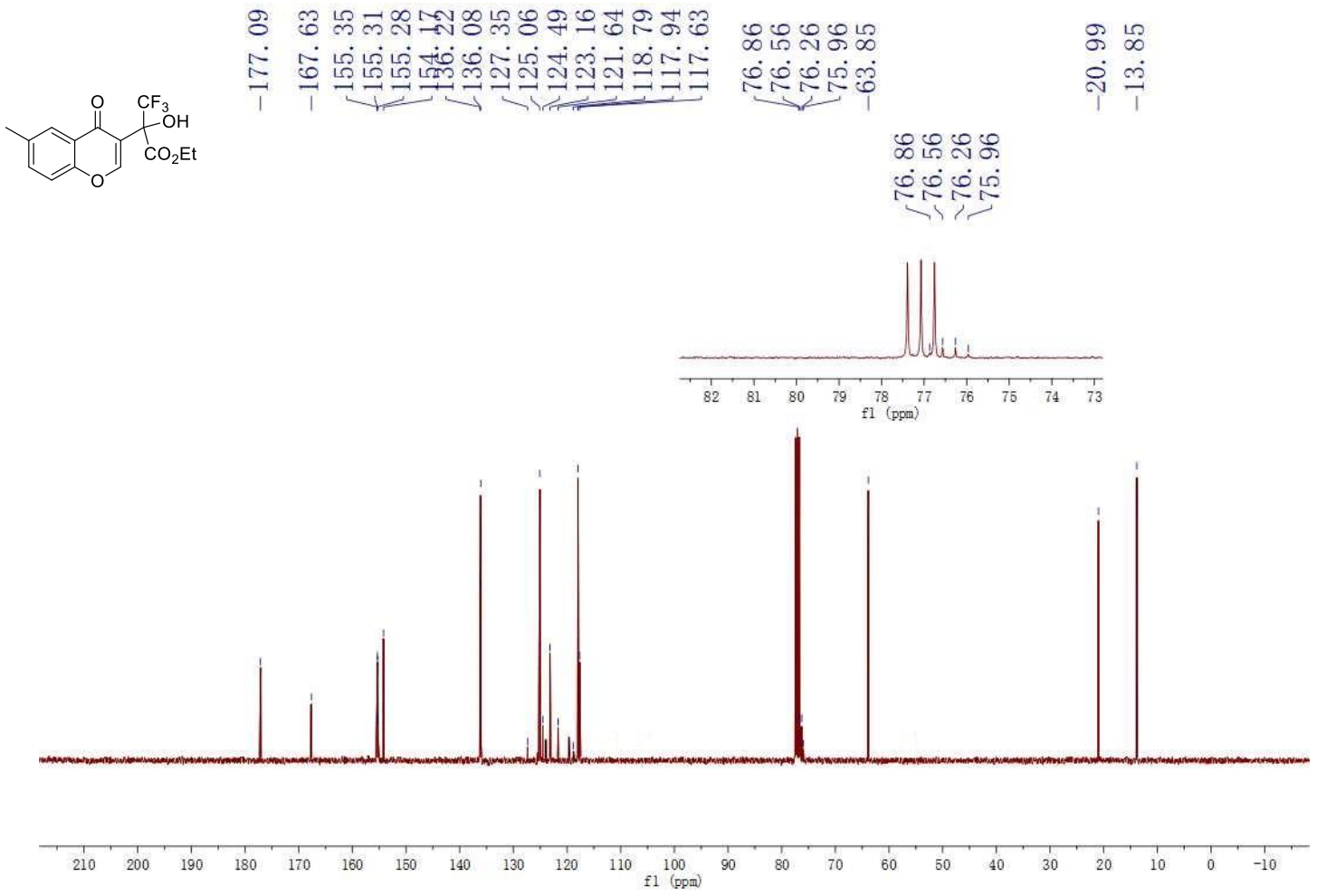


Fig. S60. ^{19}F NMR spectrum of compound **5b**

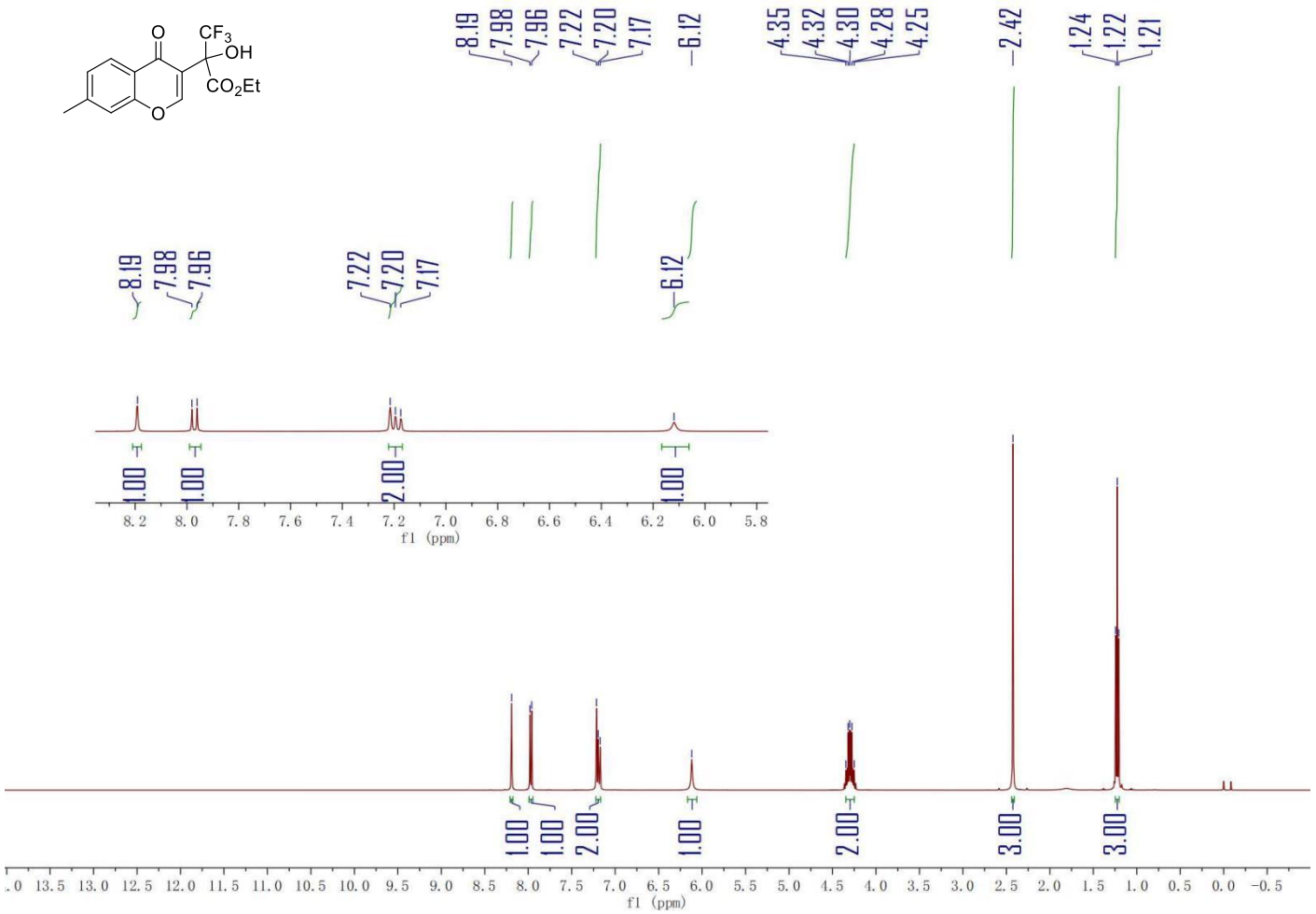


Fig. S61. ^{1}H NMR spectrum of compound **5c**

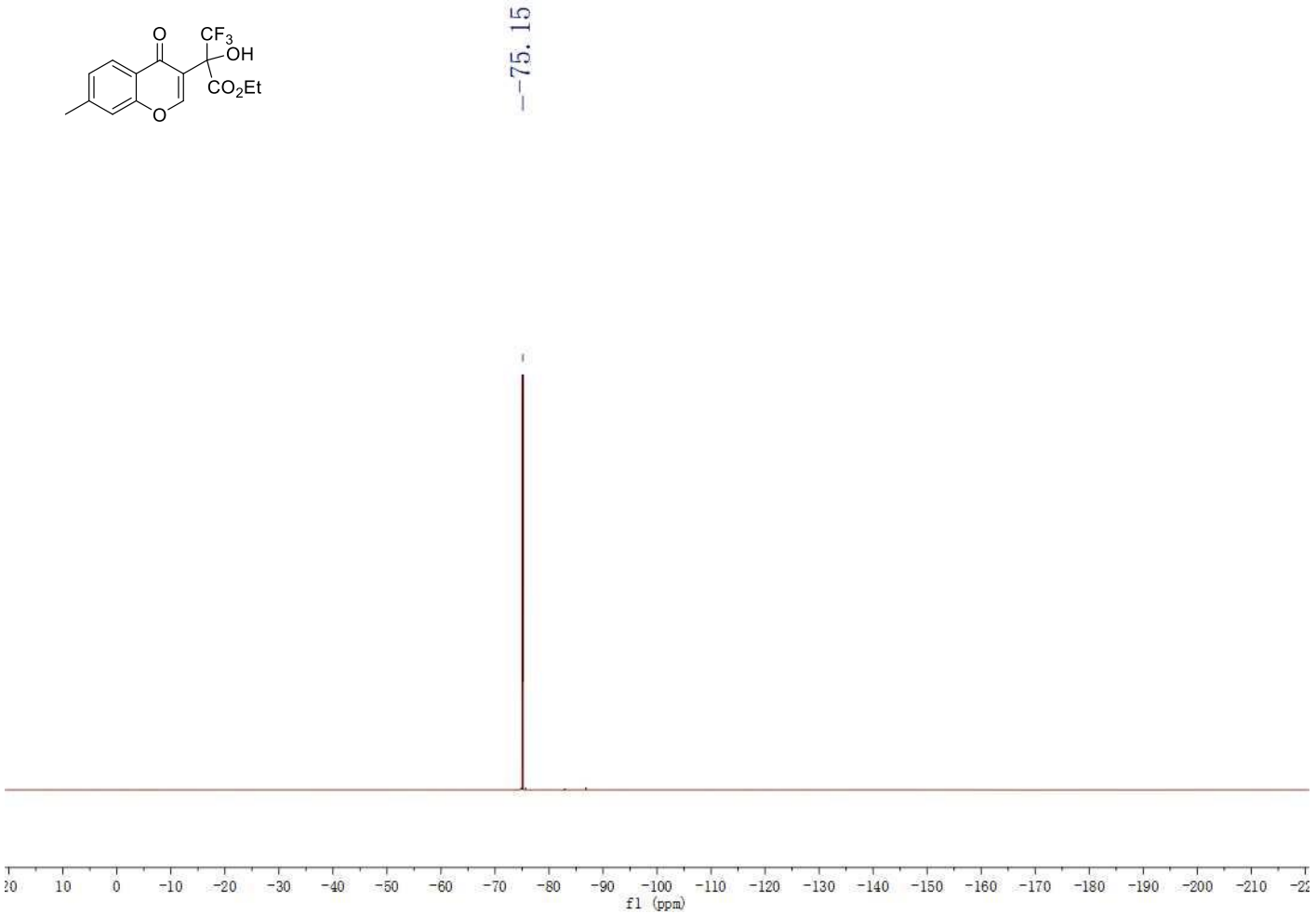


Fig. S62. ^{19}F NMR spectrum of compound **5c**

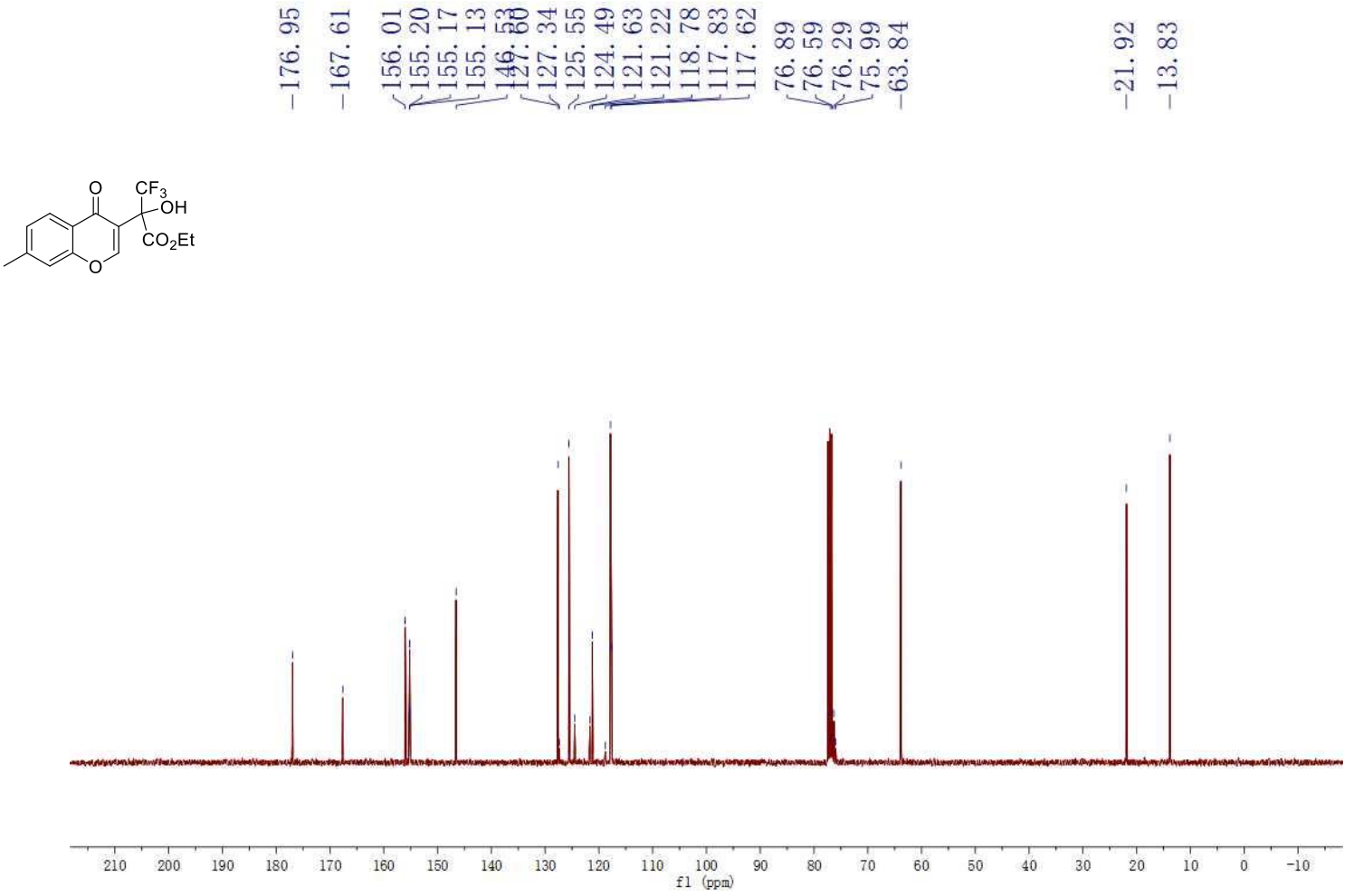


Fig. S63. ^{13}C NMR spectrum of compound **5c**

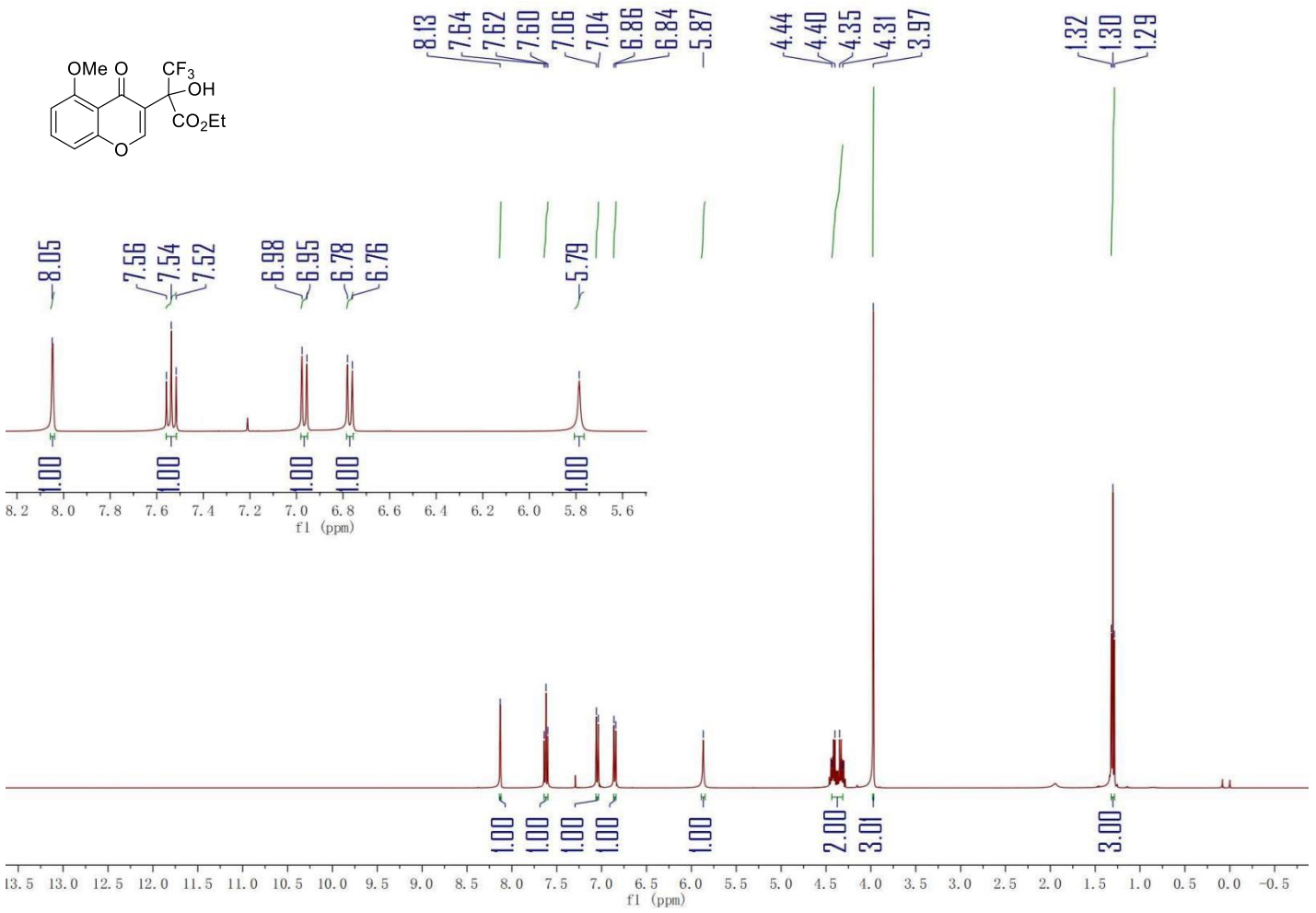


Fig. S64. ^{1}H NMR spectrum of compound **5d**

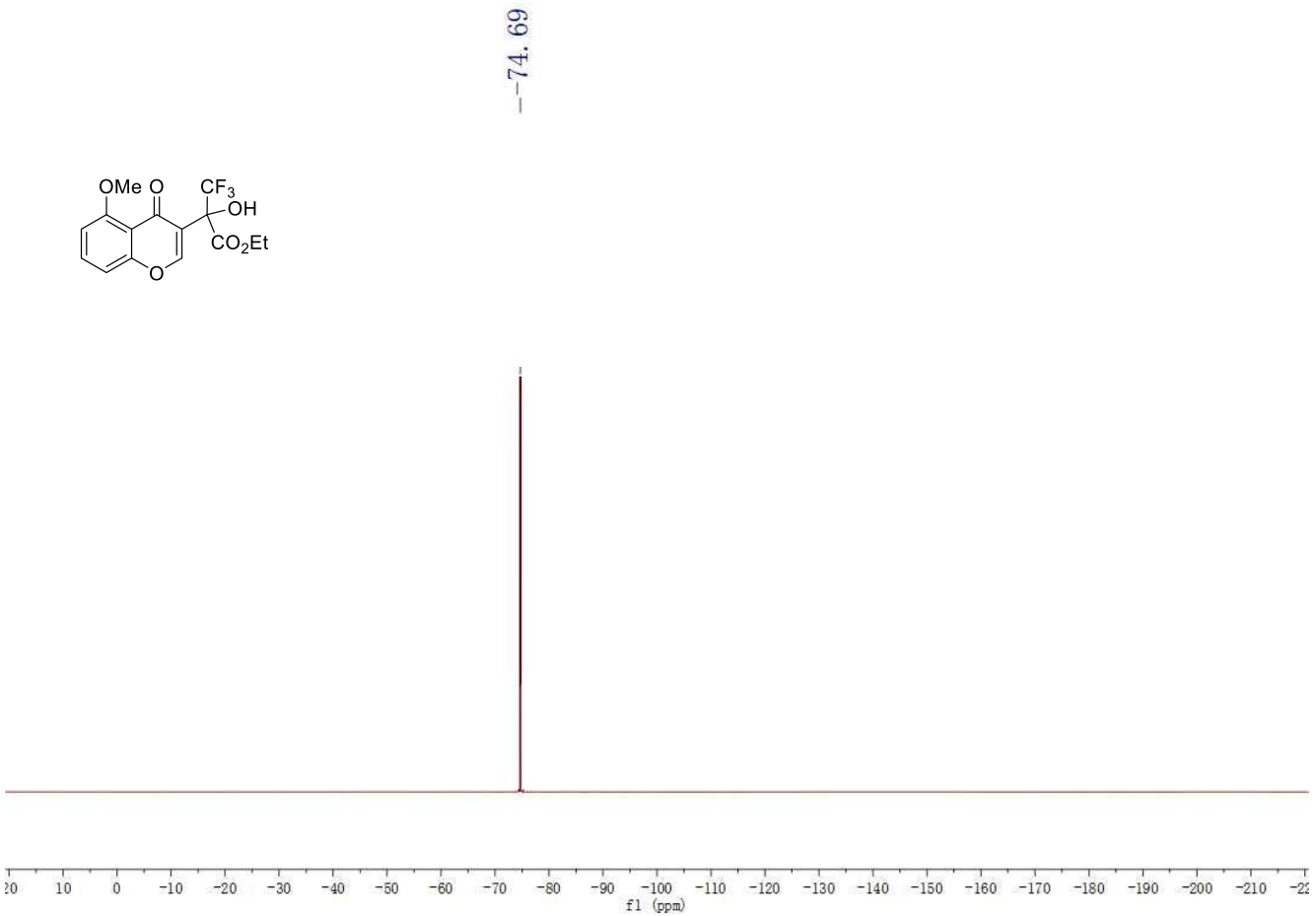


Fig. S65. ^{19}F NMR spectrum of compound **5d**

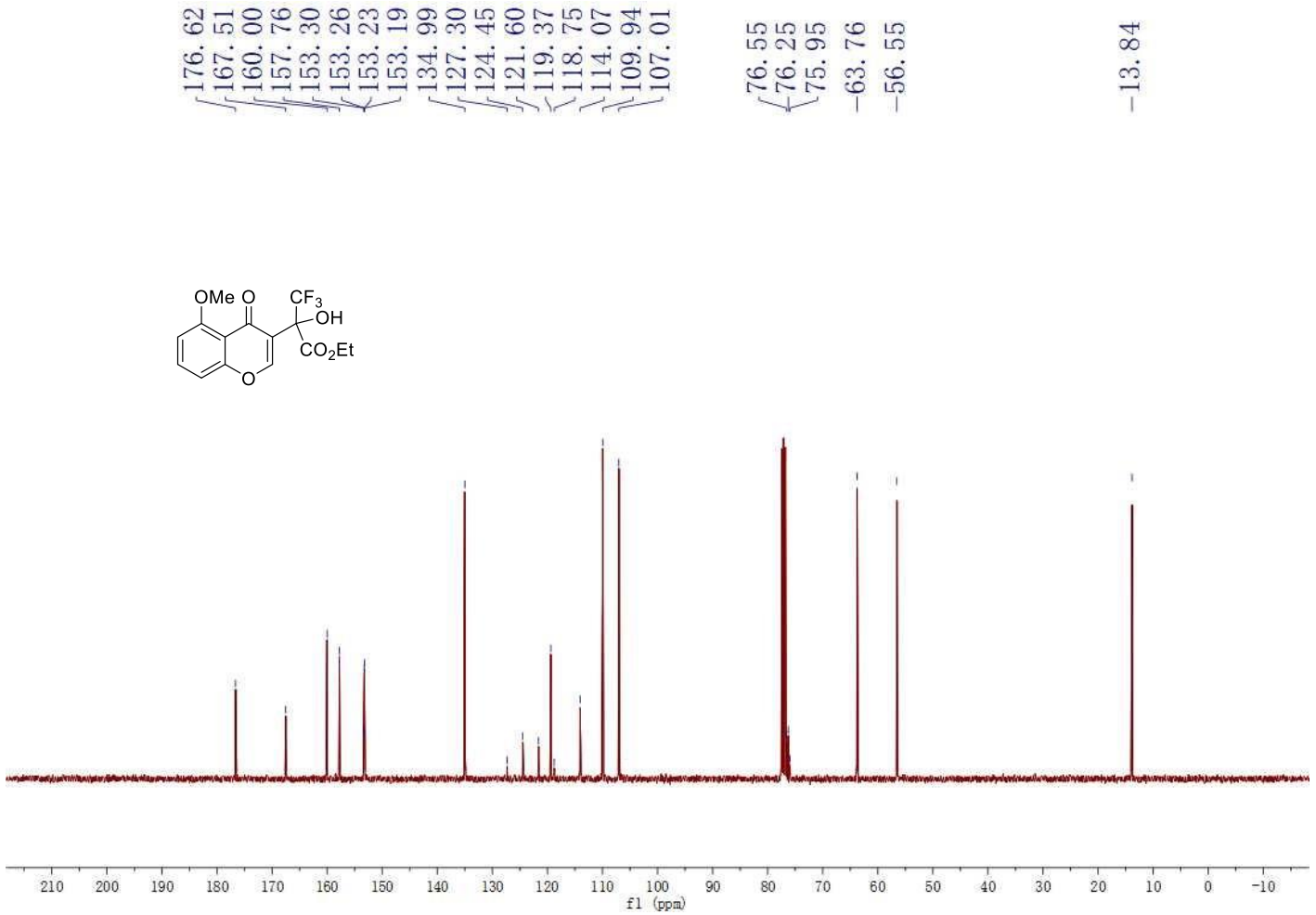


Fig. S66. ^{13}C NMR spectrum of compound **5d**

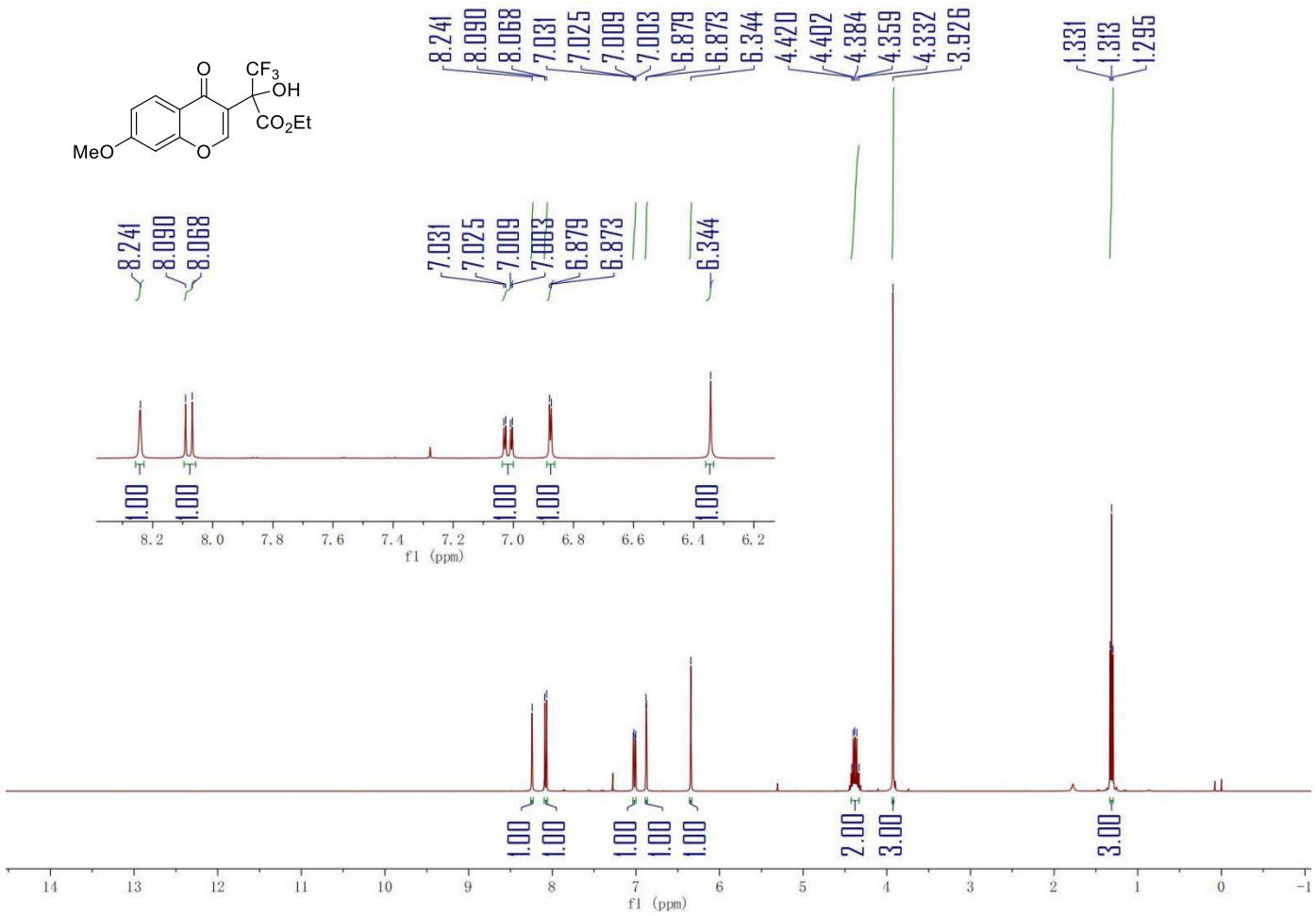


Fig. S67. ^{1}H NMR spectrum of compound **5e**

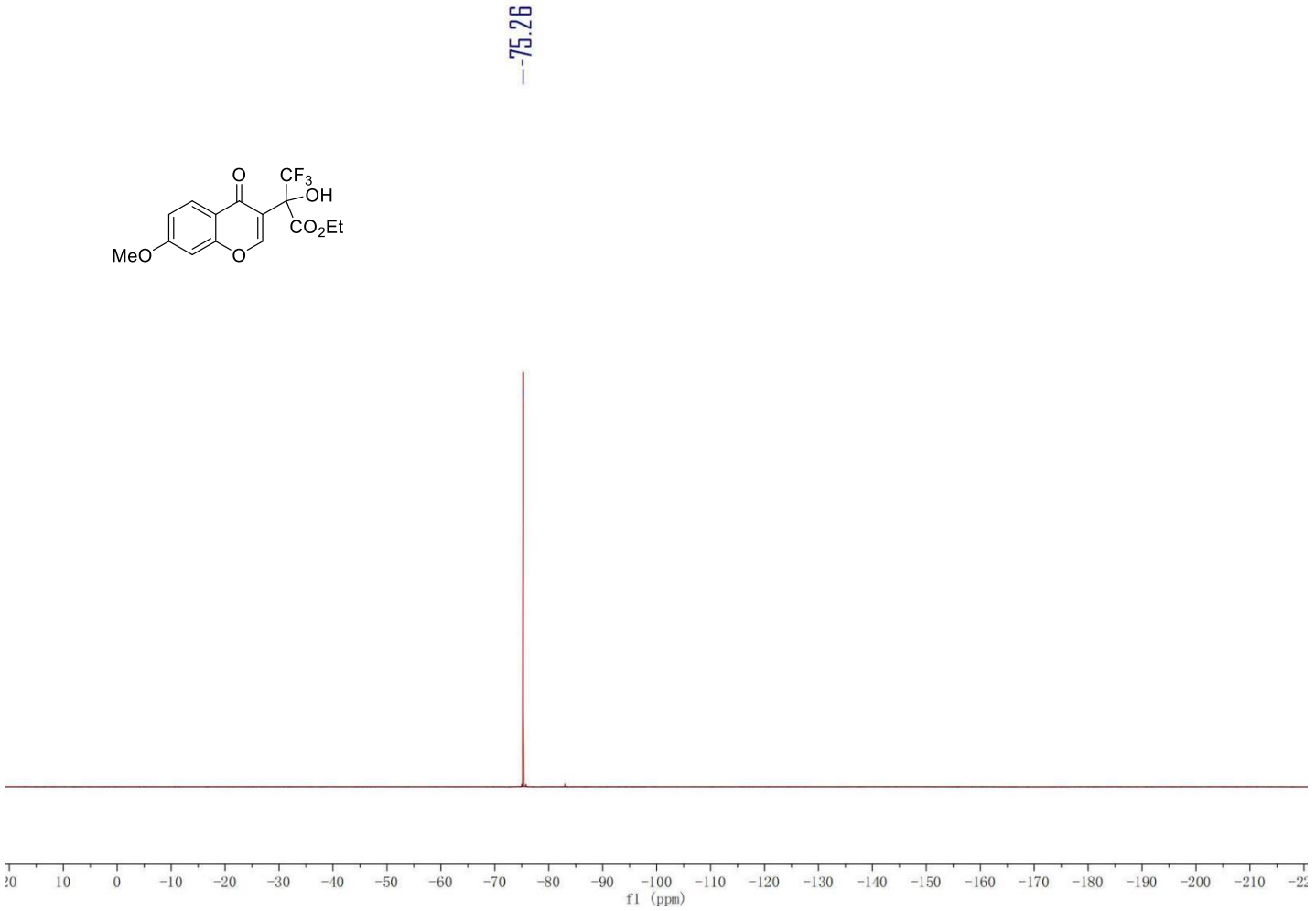


Fig. S68. ^{19}F NMR spectrum of compound **5e**

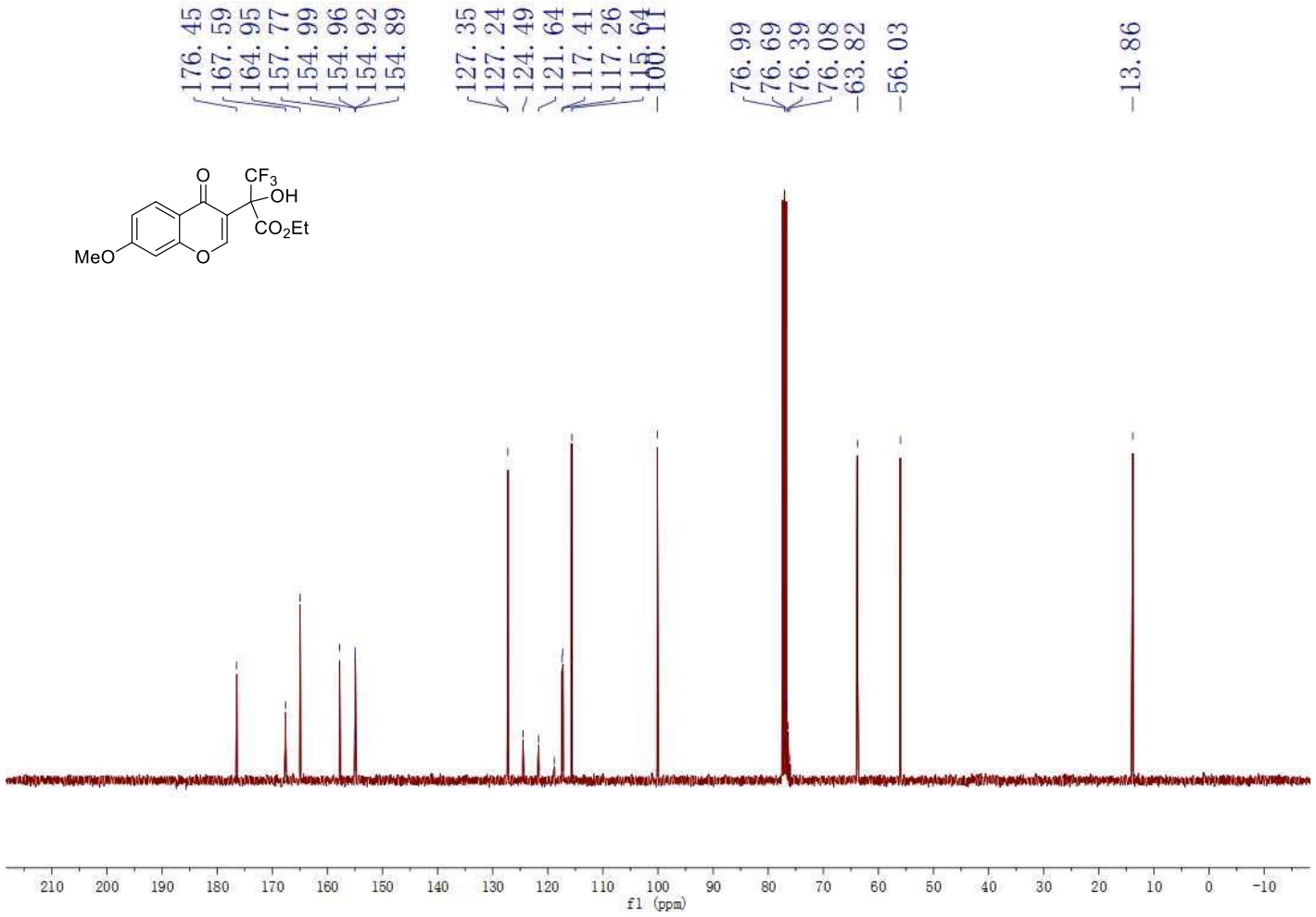


Fig. S69. ^{19}F NMR spectrum of compound **5e**

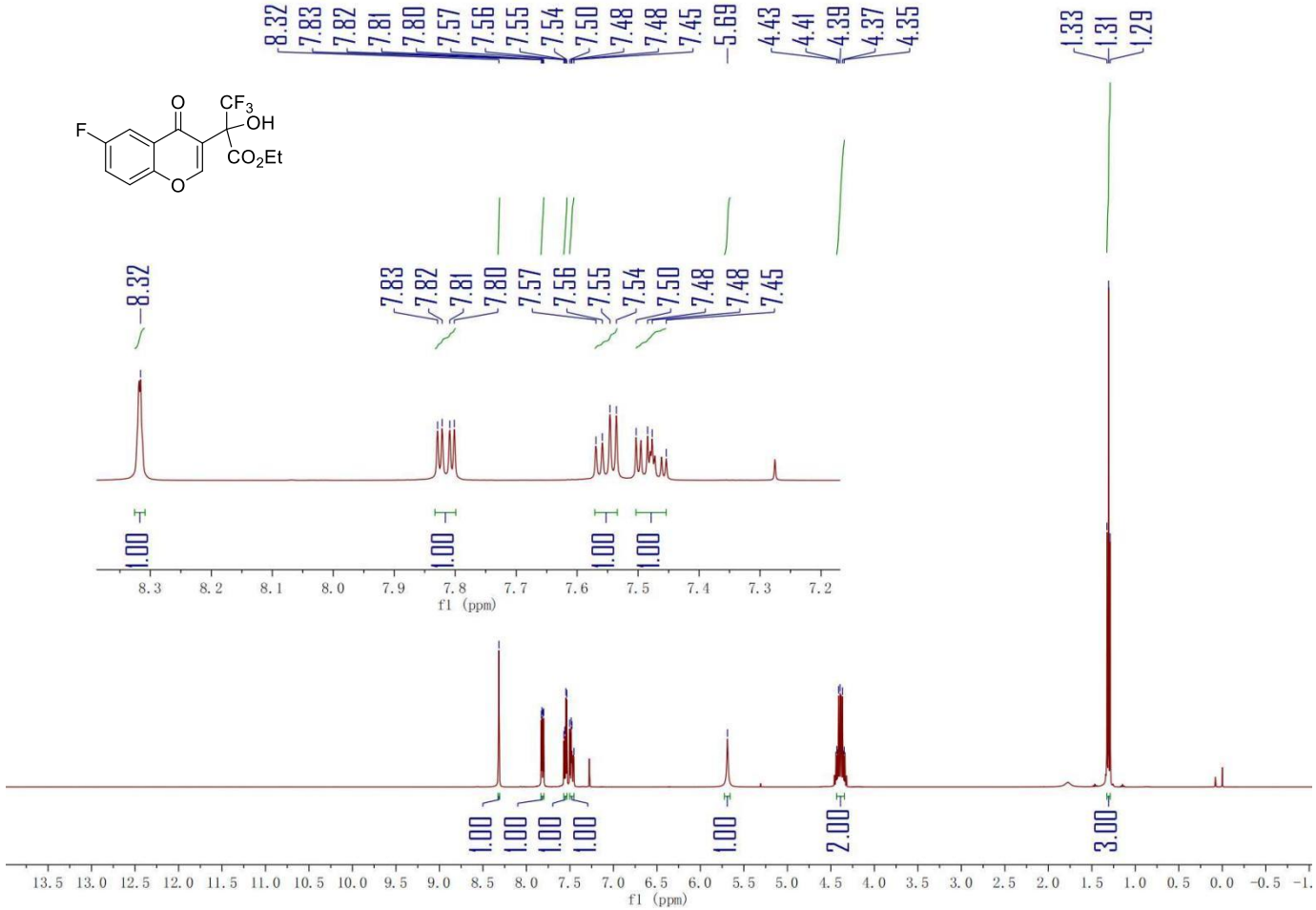


Fig. S70. ^{1}H NMR spectrum of compound **3f**

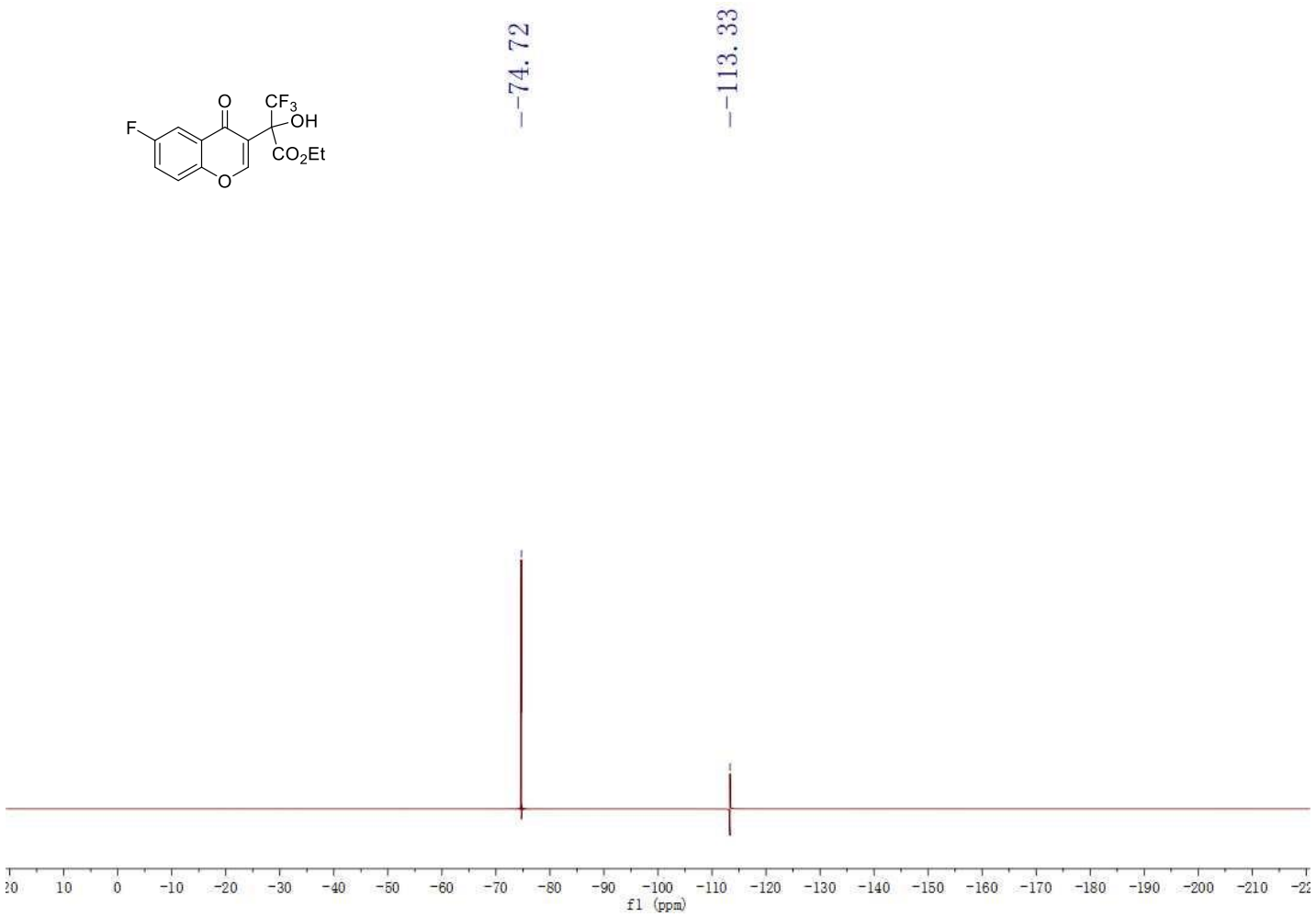


Fig. S71. ^{19}F NMR spectrum of compound **3f**

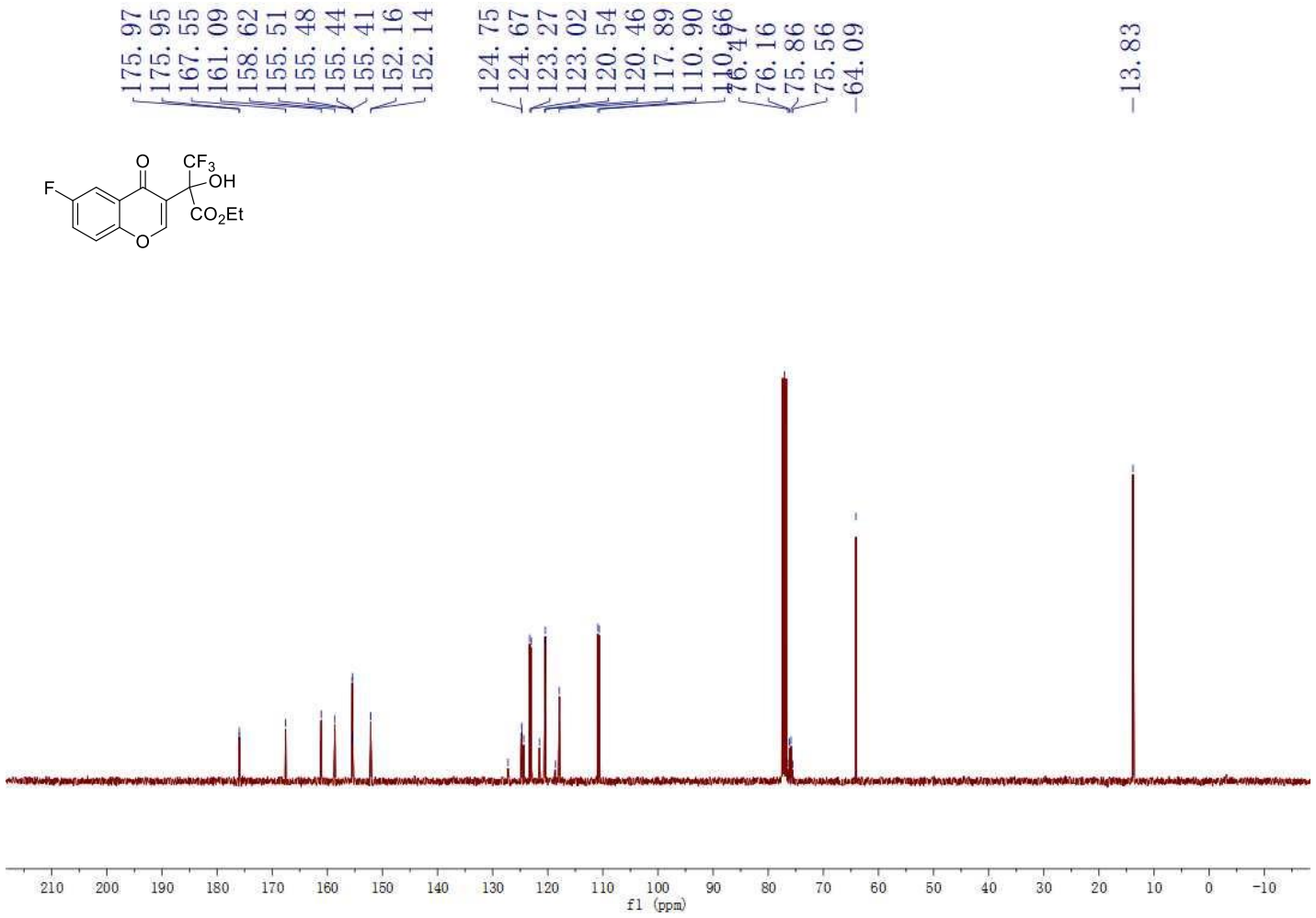


Fig. S72. ^{13}C NMR spectrum of compound **3f**

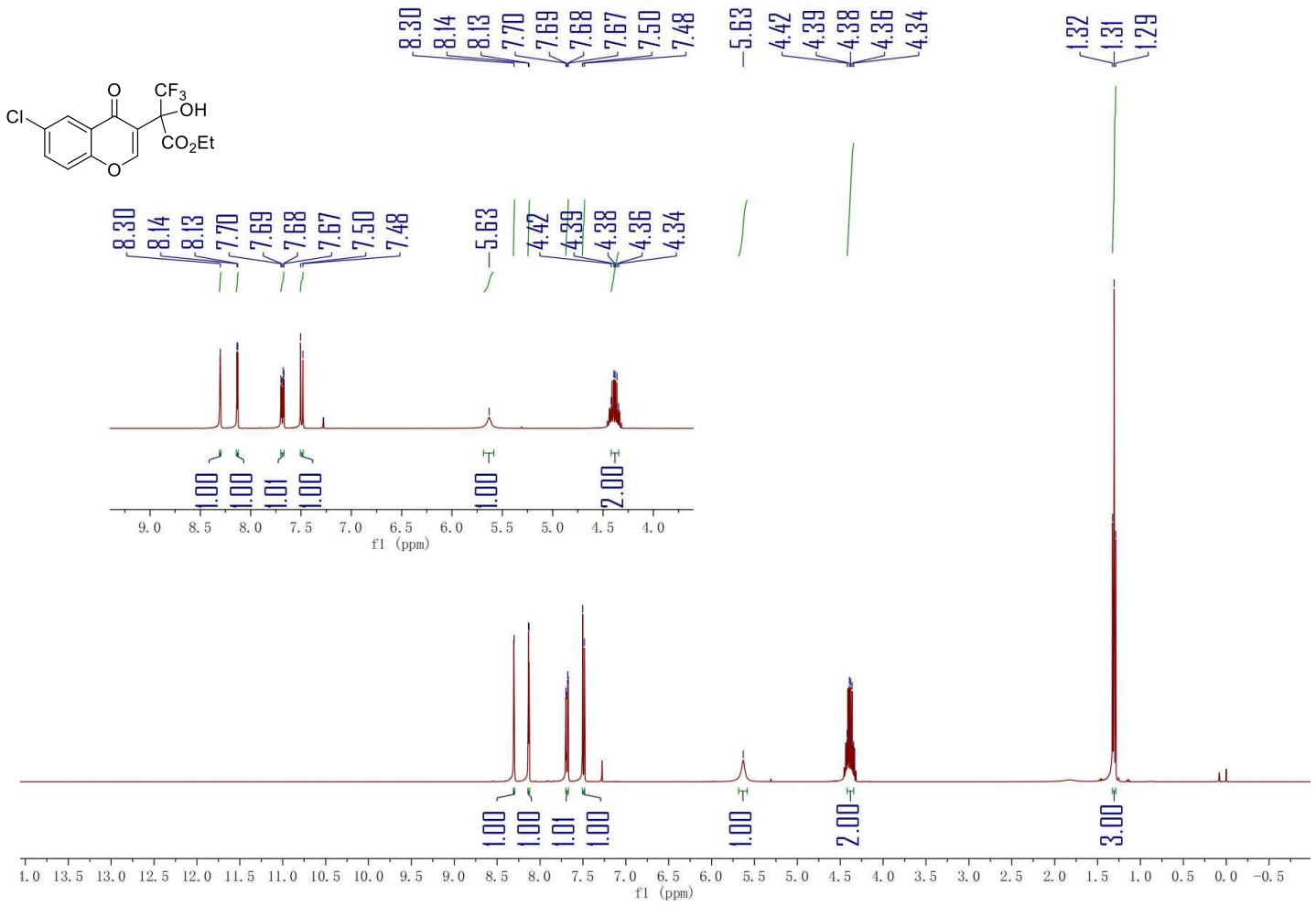


Fig. S73. ^{1}H NMR spectrum of compound **5g**

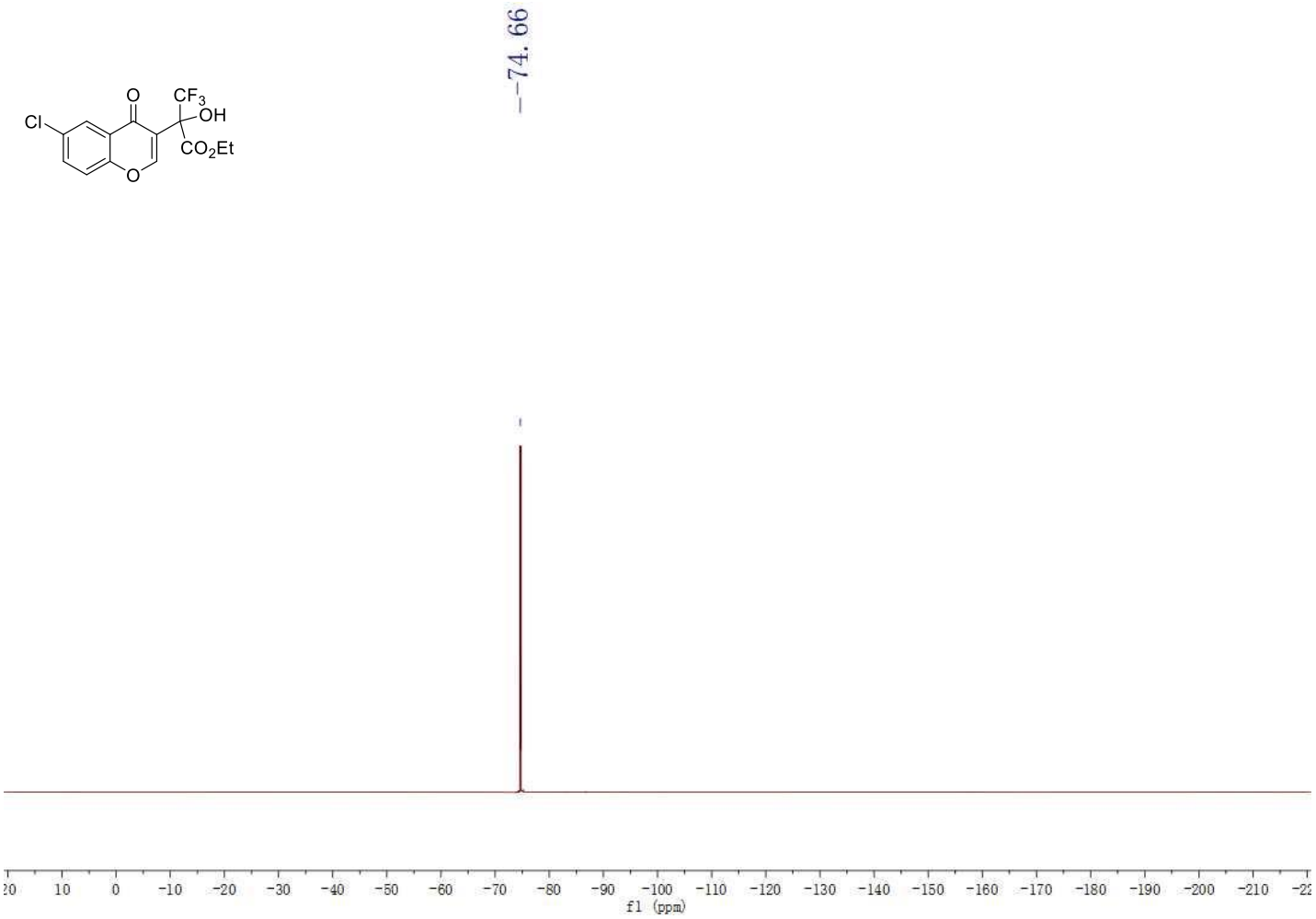


Fig. S74. ^{19}F NMR spectrum of compound **5g**

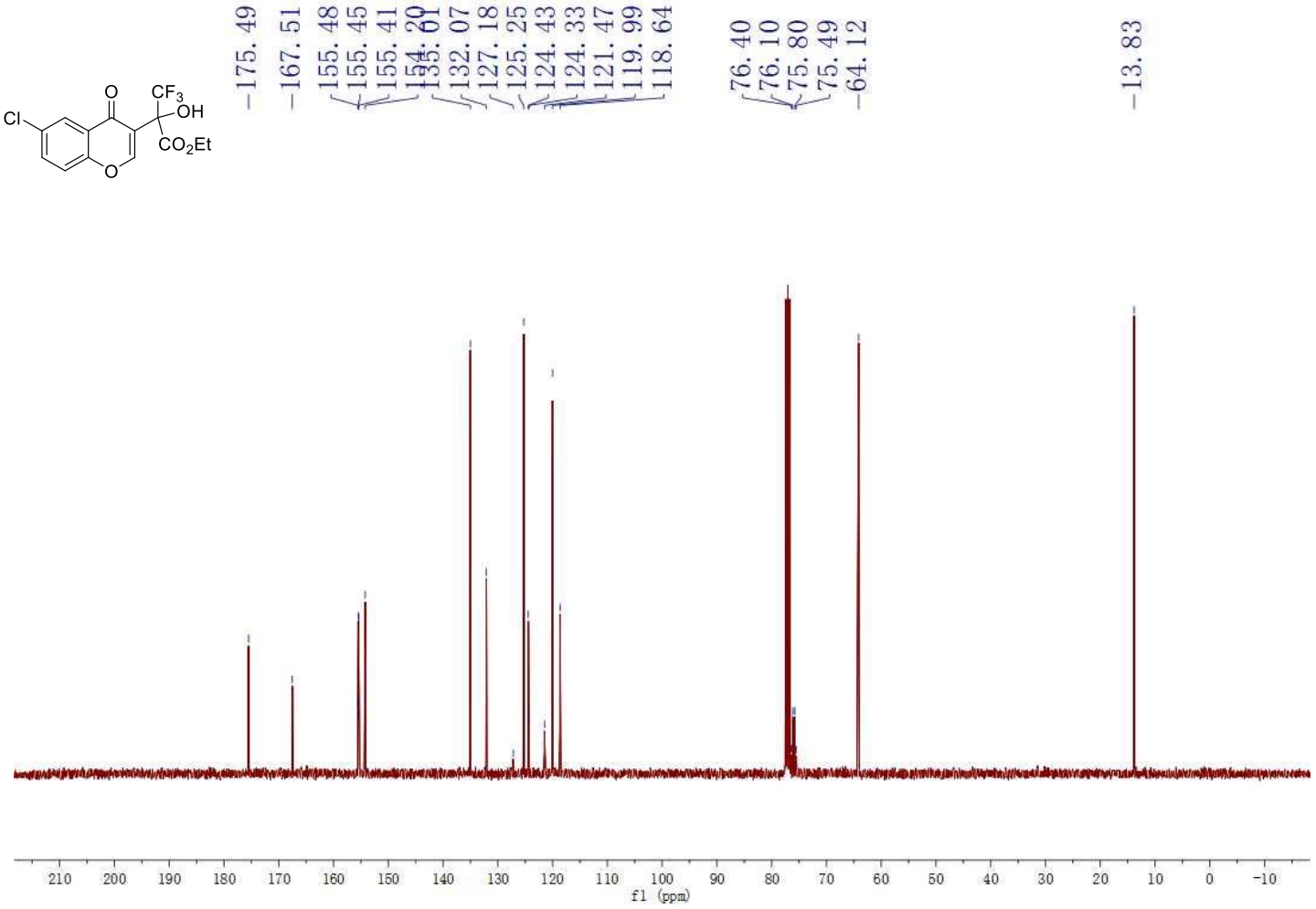


Fig. S75. ^{13}C NMR spectrum of compound **5g**

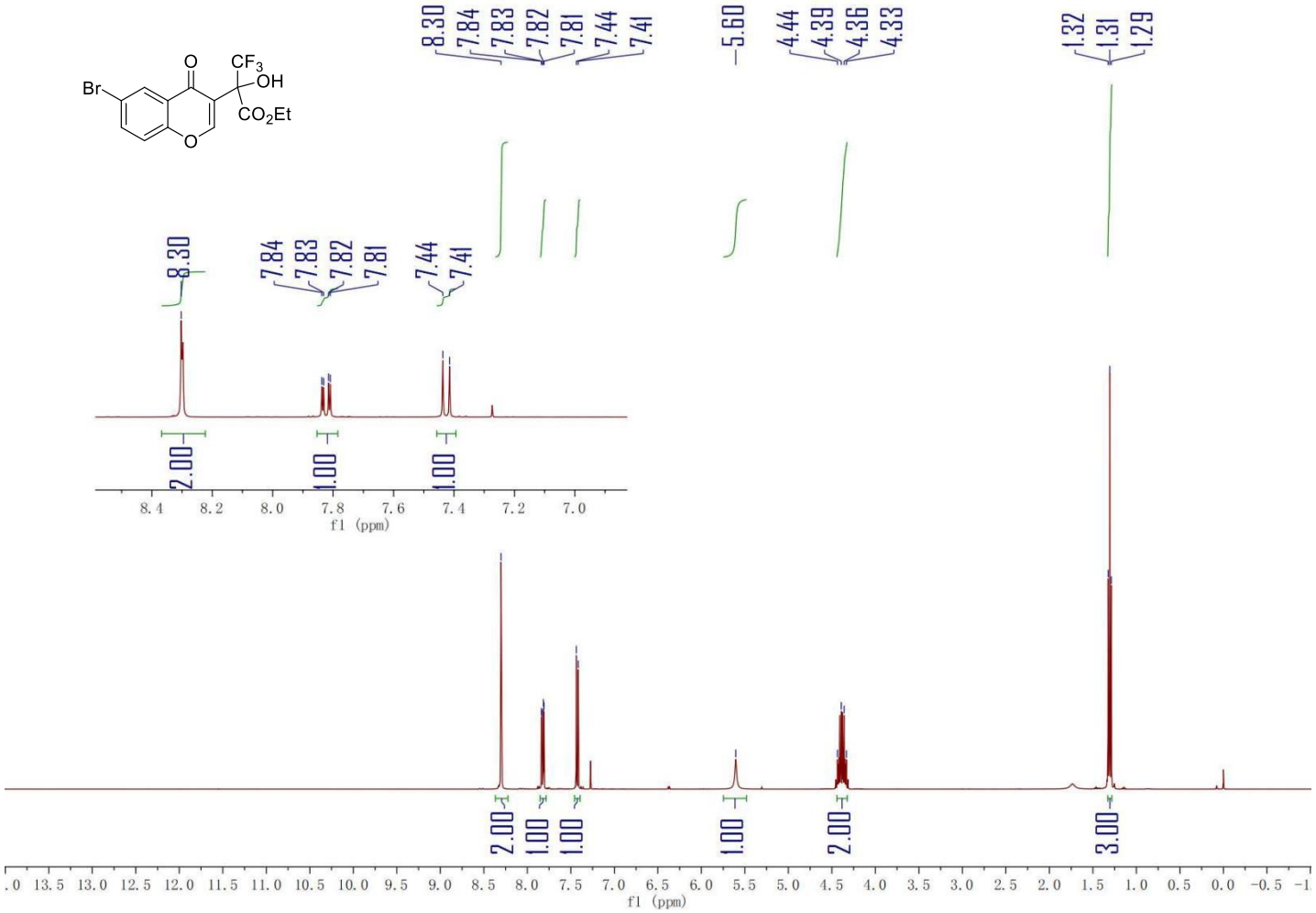


Fig. S76. ^{1}H NMR spectrum of compound **5h**

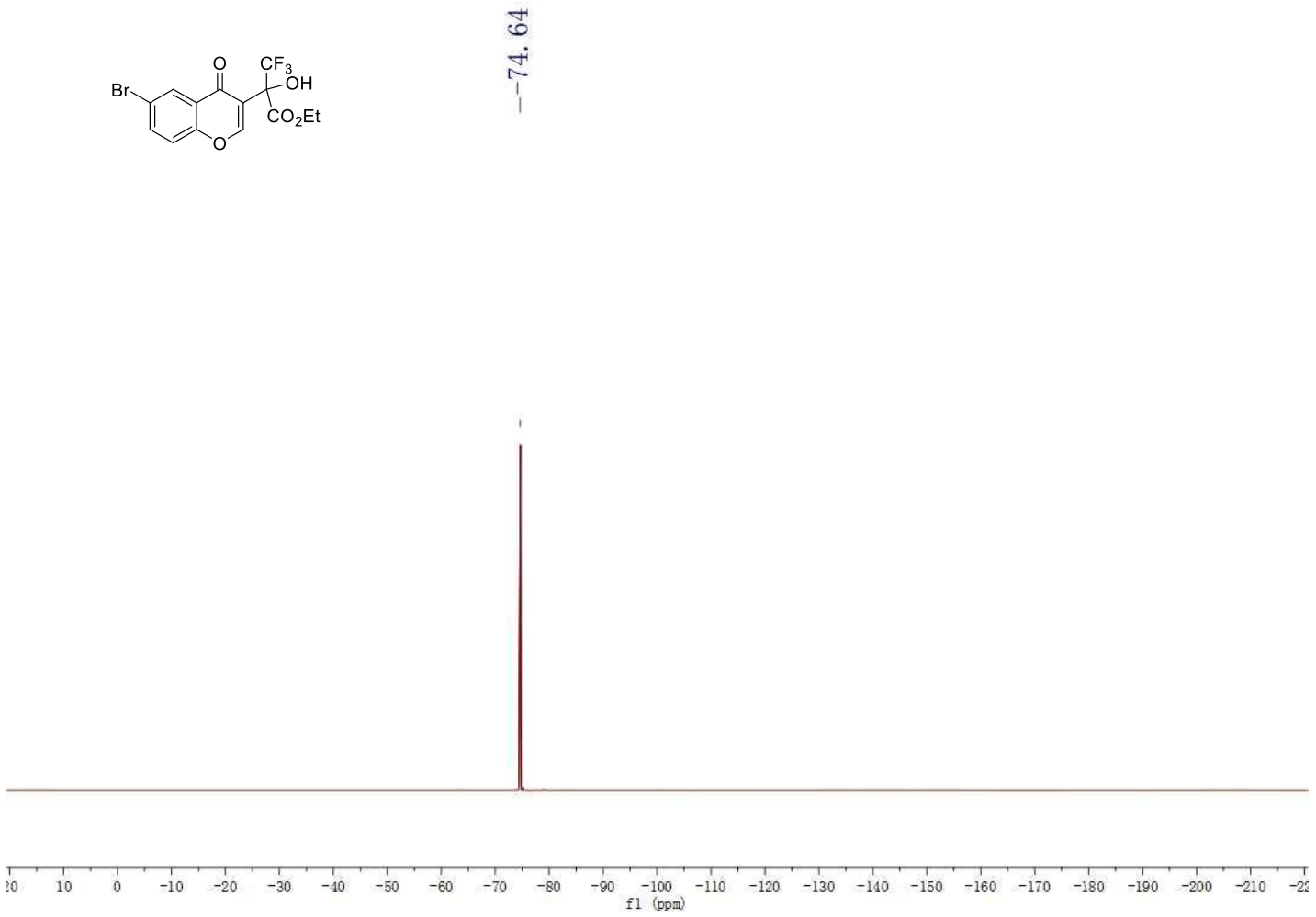


Fig. S77. ^{19}F NMR spectrum of compound **5i**

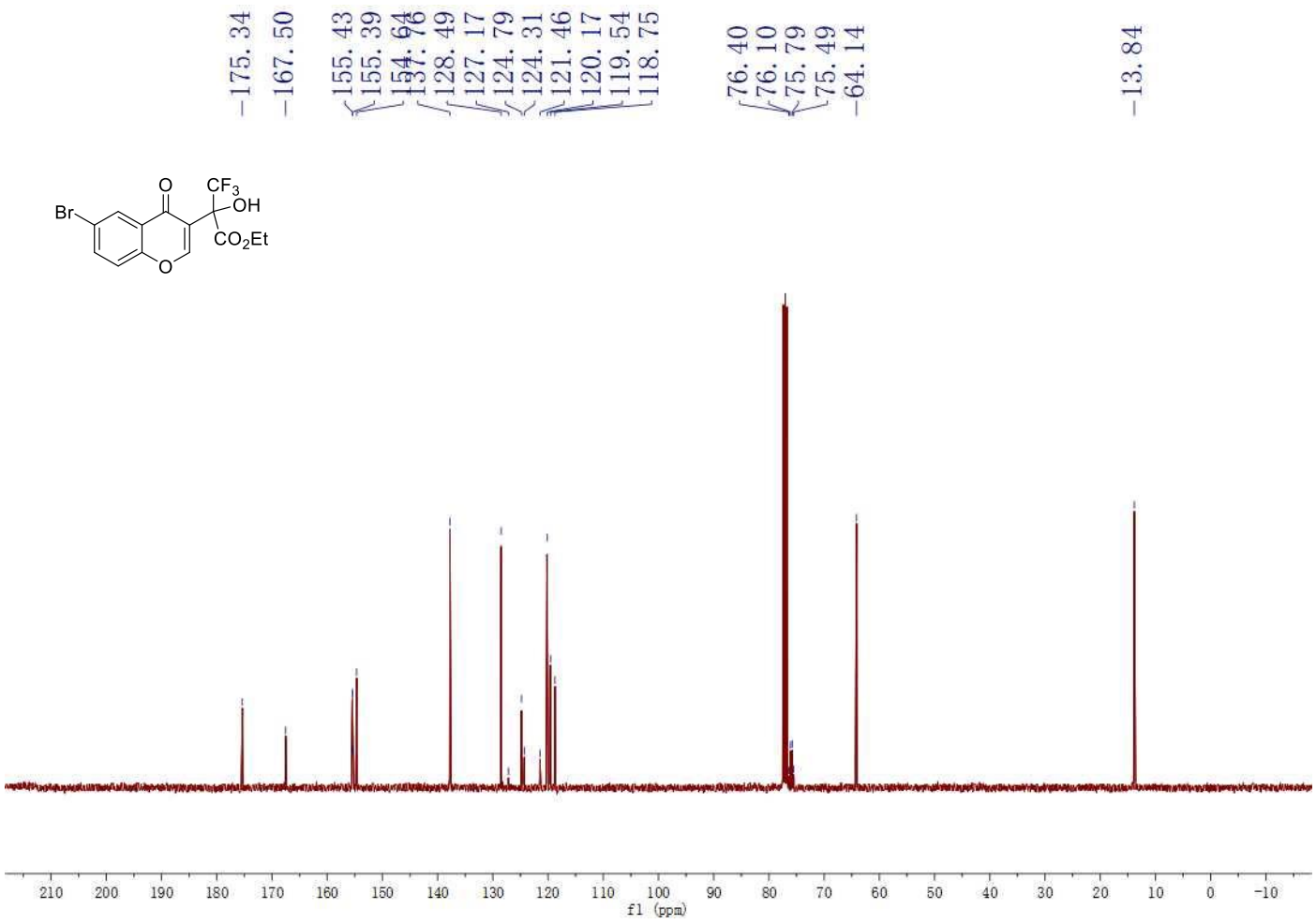


Fig. S78. ^{13}C NMR spectrum of compound **5h**

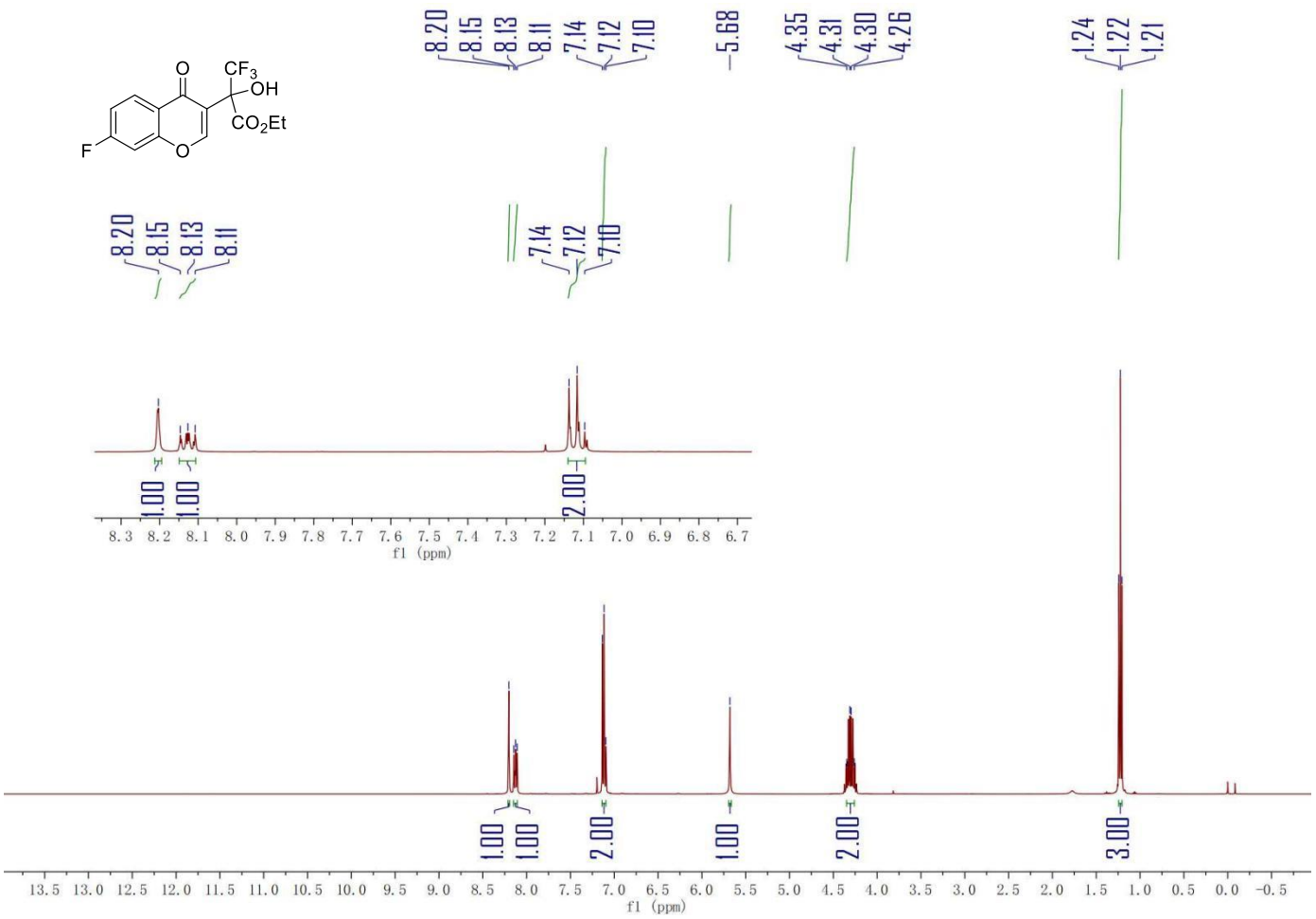


Fig. S79. ^{1}H NMR spectrum of compound **5i**

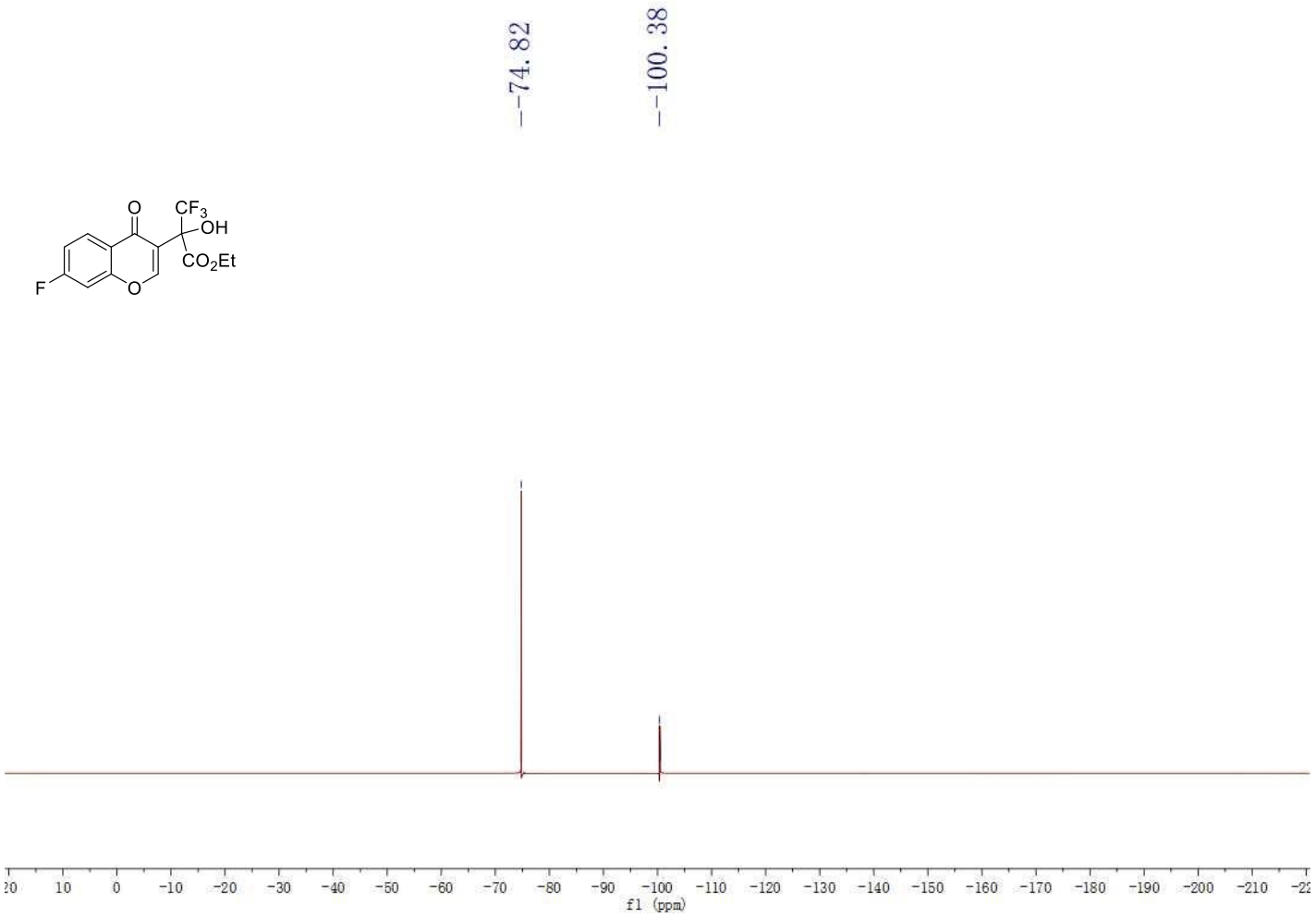


Fig. S80. ^{19}F NMR spectrum of compound **5i**

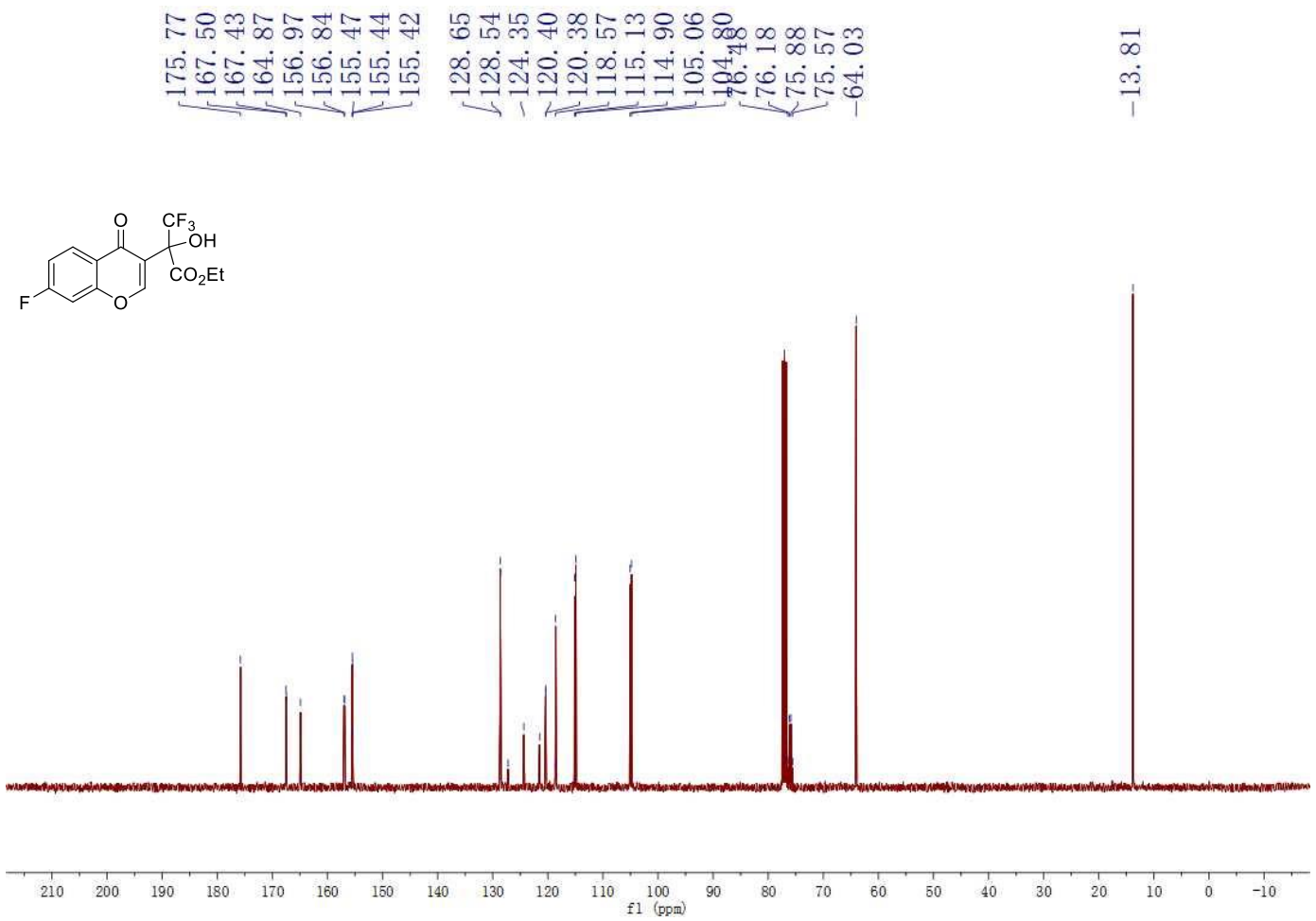


Fig. S81. ^{13}C NMR spectrum of compound **5i**

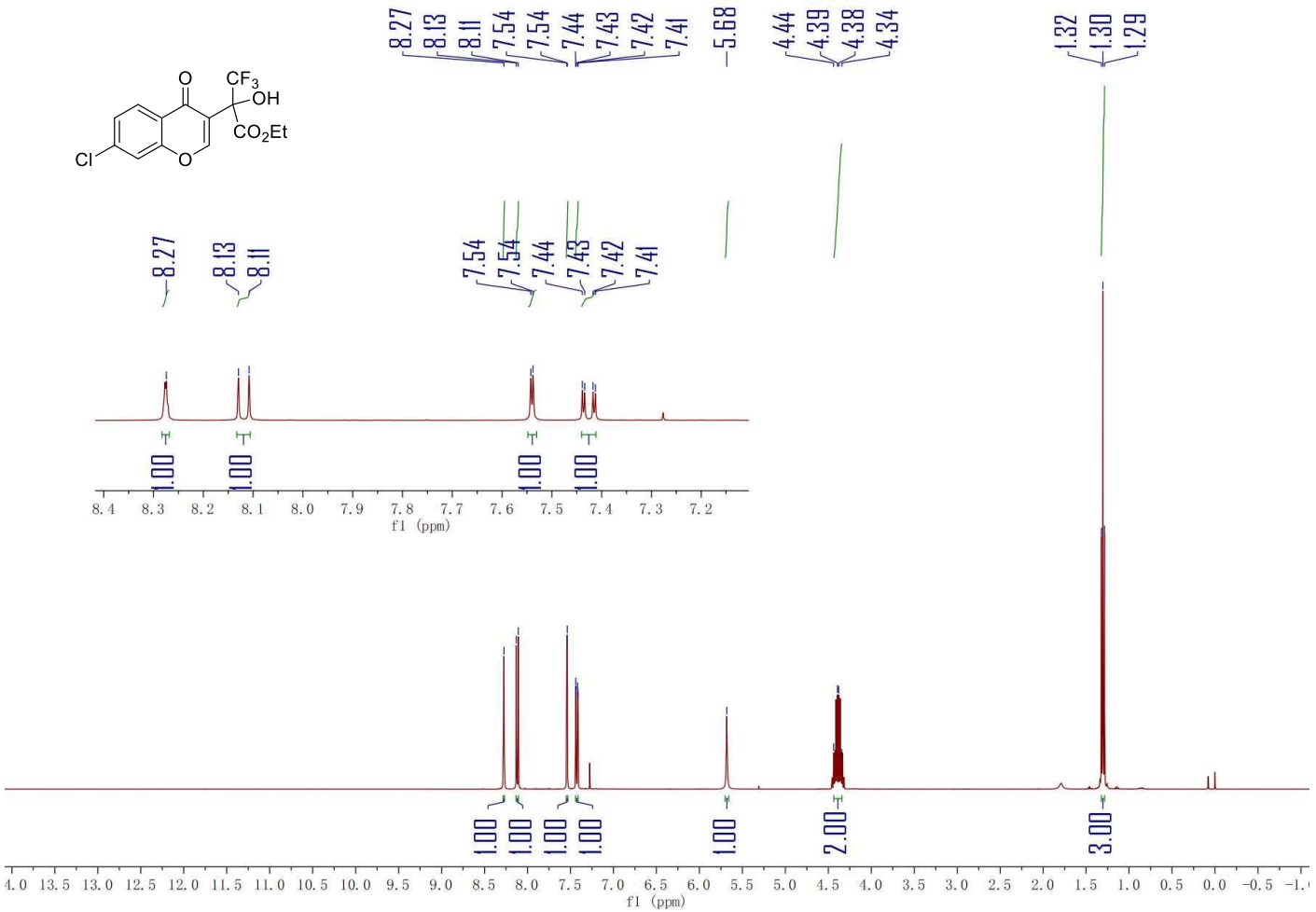


Fig. S82. ^{13}C NMR spectrum of compound **5j**

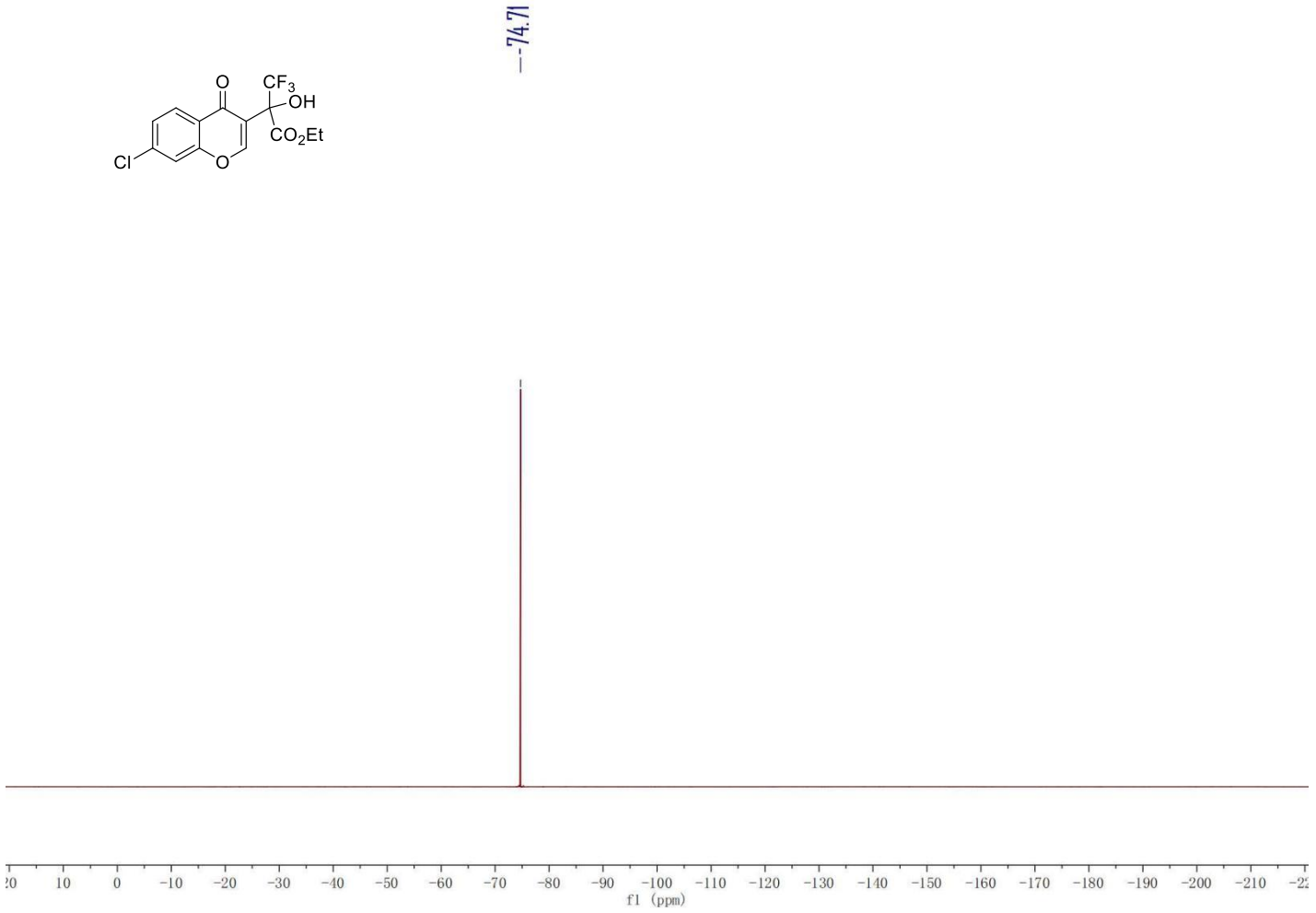


Fig. S83. ^{1}H NMR spectrum of compound **5j**

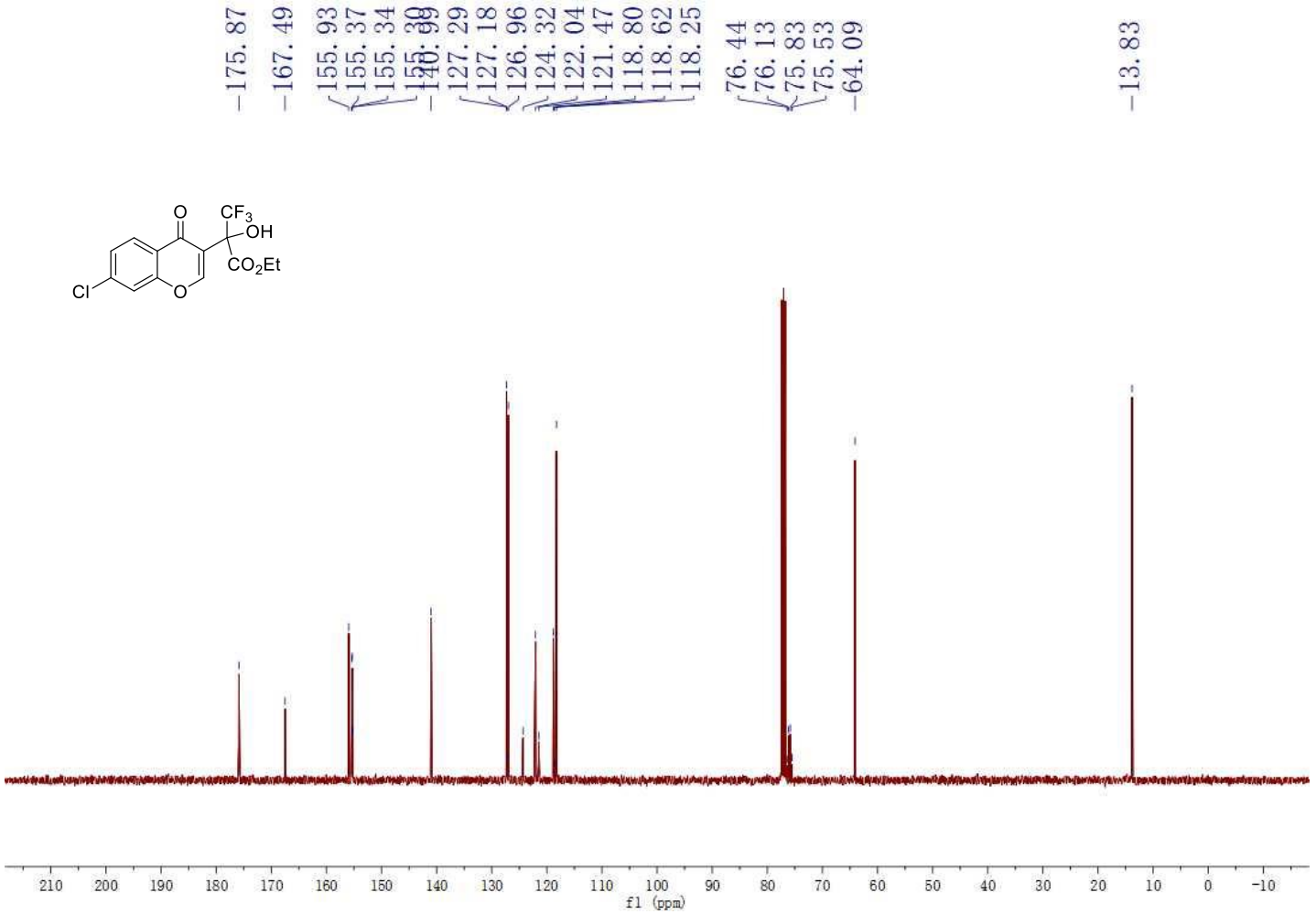


Fig. S84. ^{19}F NMR spectrum of compound **5j**

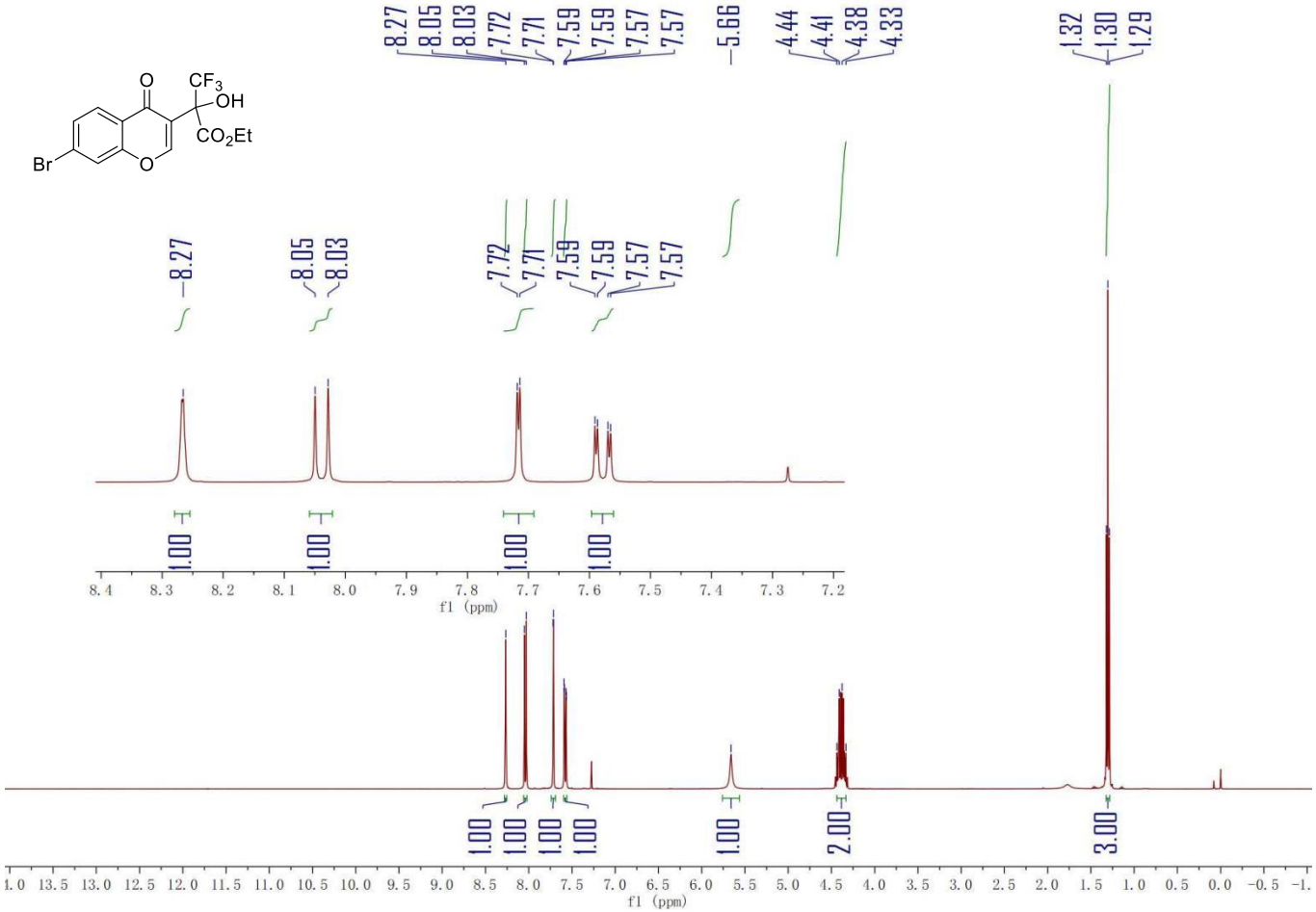


Fig. S85. ^{1}H NMR spectrum of compound **5k**

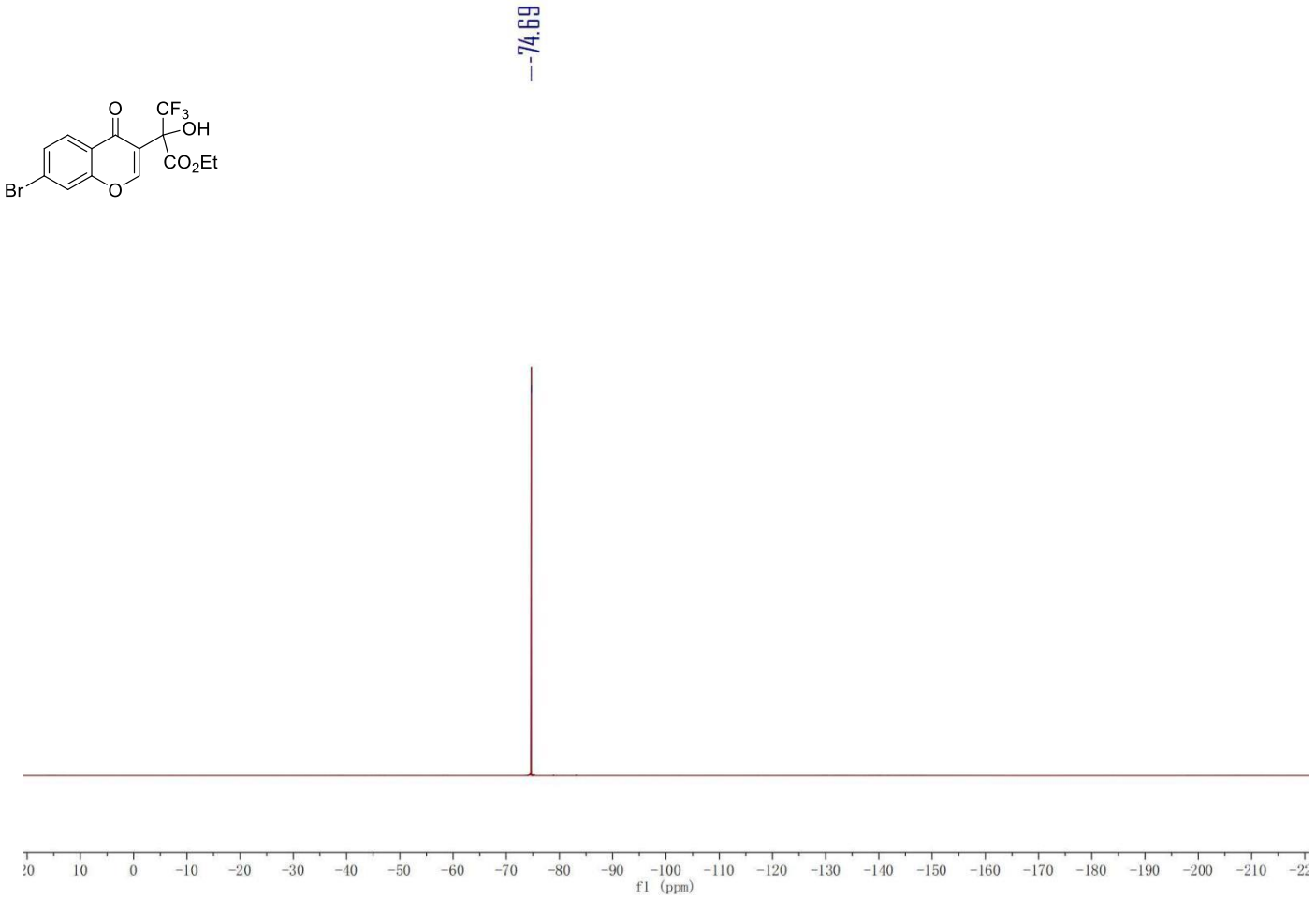


Fig. S86. ^{19F} NMR spectrum of compound **5k**

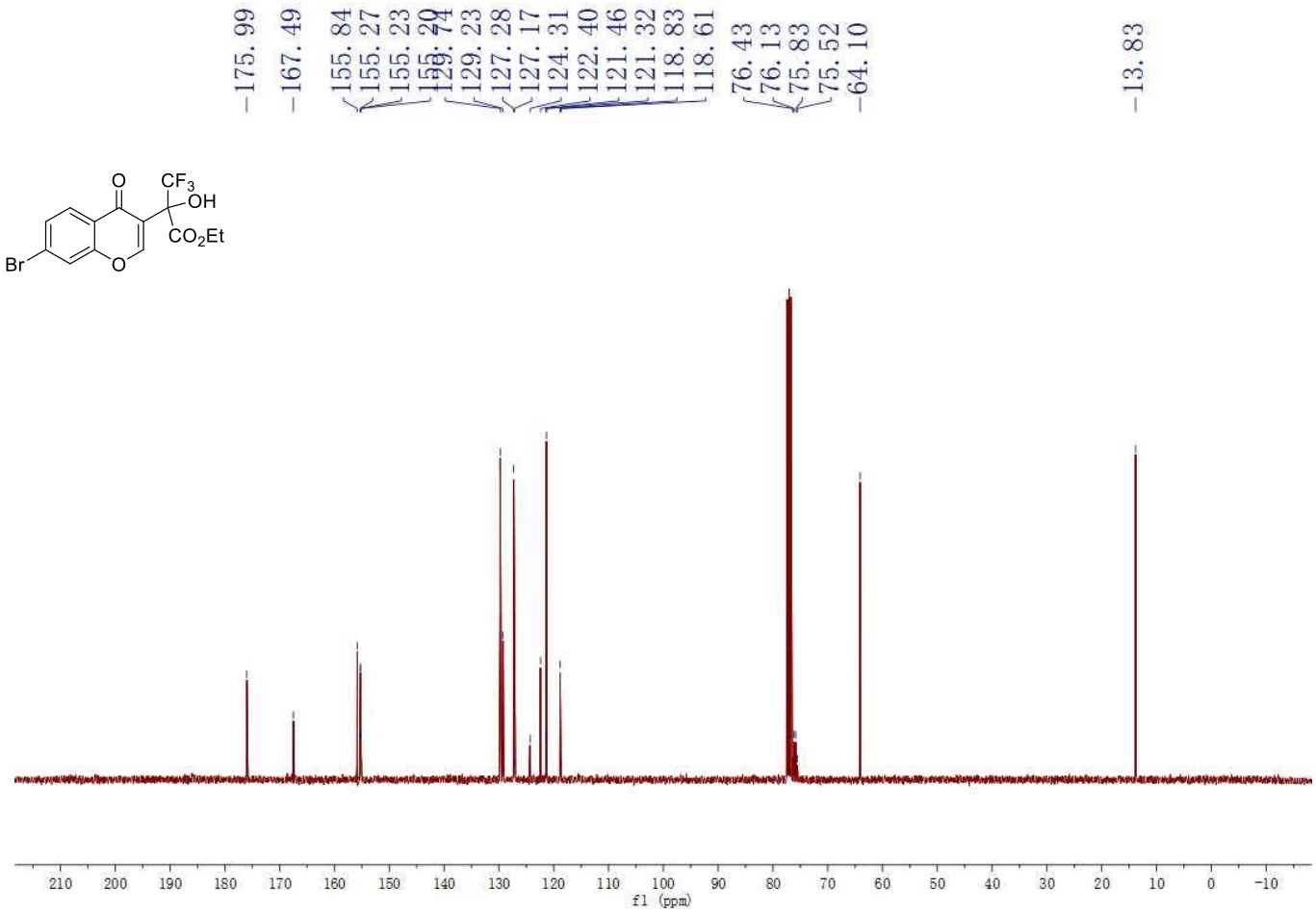


Fig. S87. ^{13}C NMR spectrum of compound **5k**

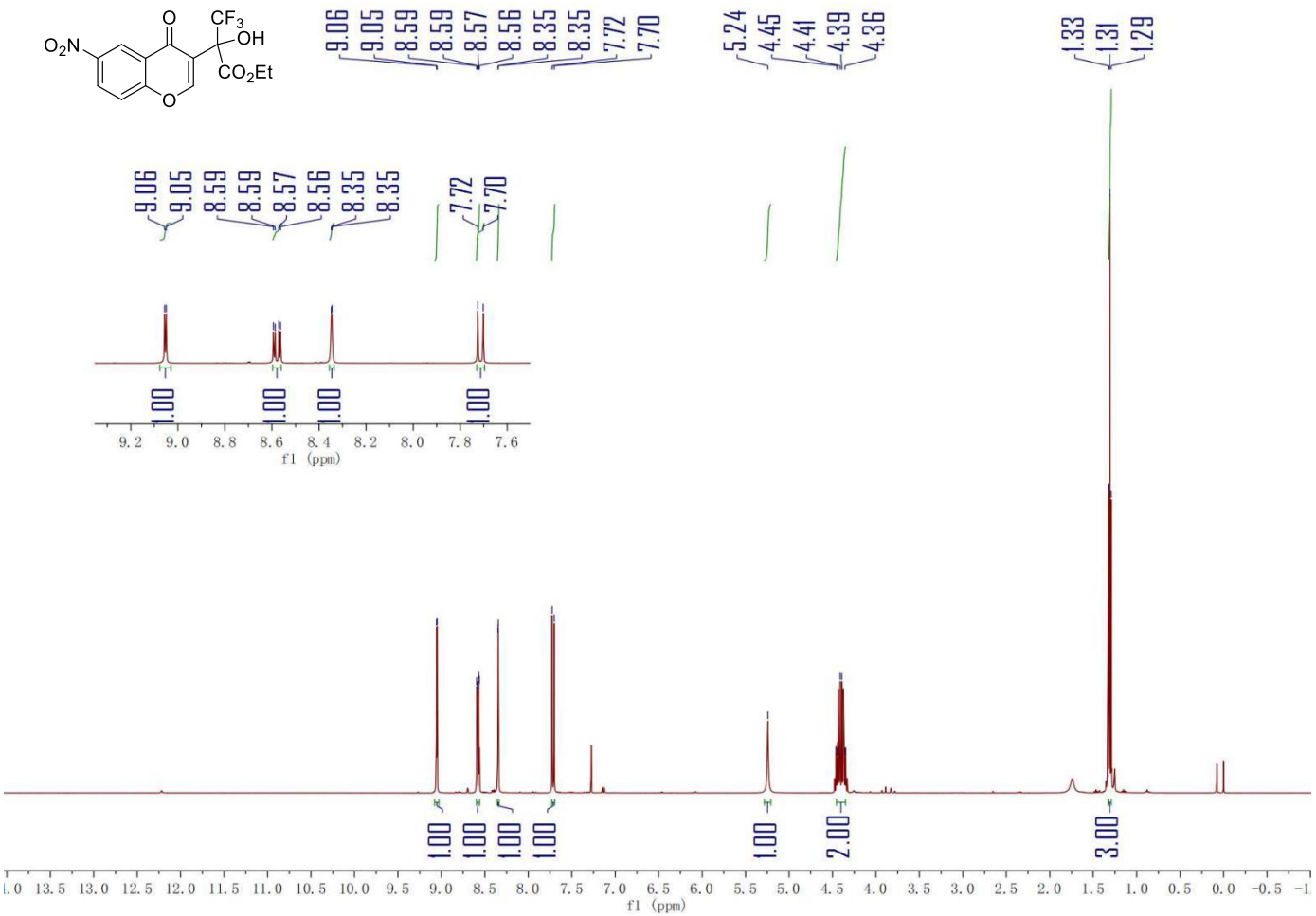


Fig. S88. ^{1}H NMR spectrum of compound **5l**

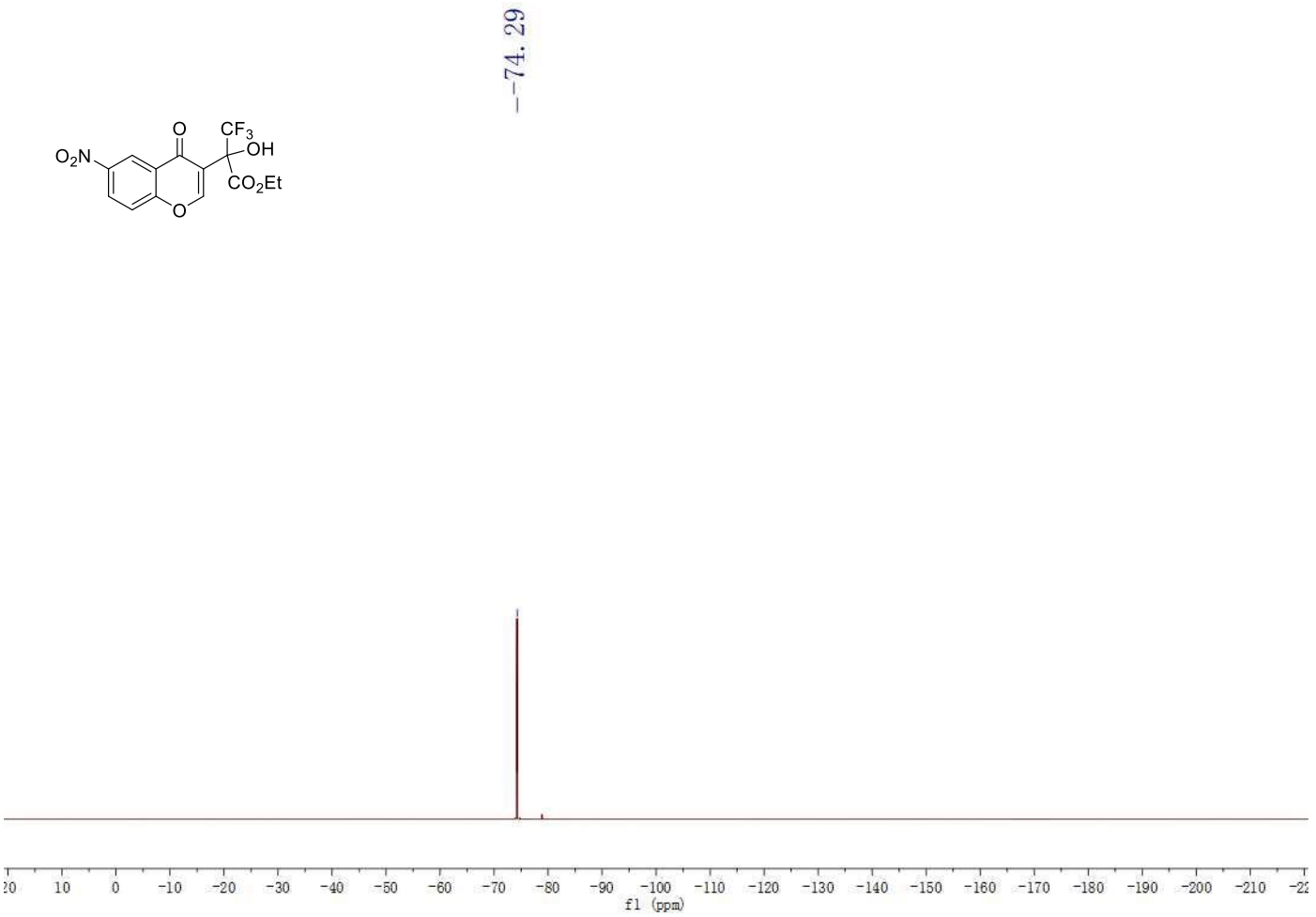


Fig. S89. ^{19F} NMR spectrum of compound **5l**

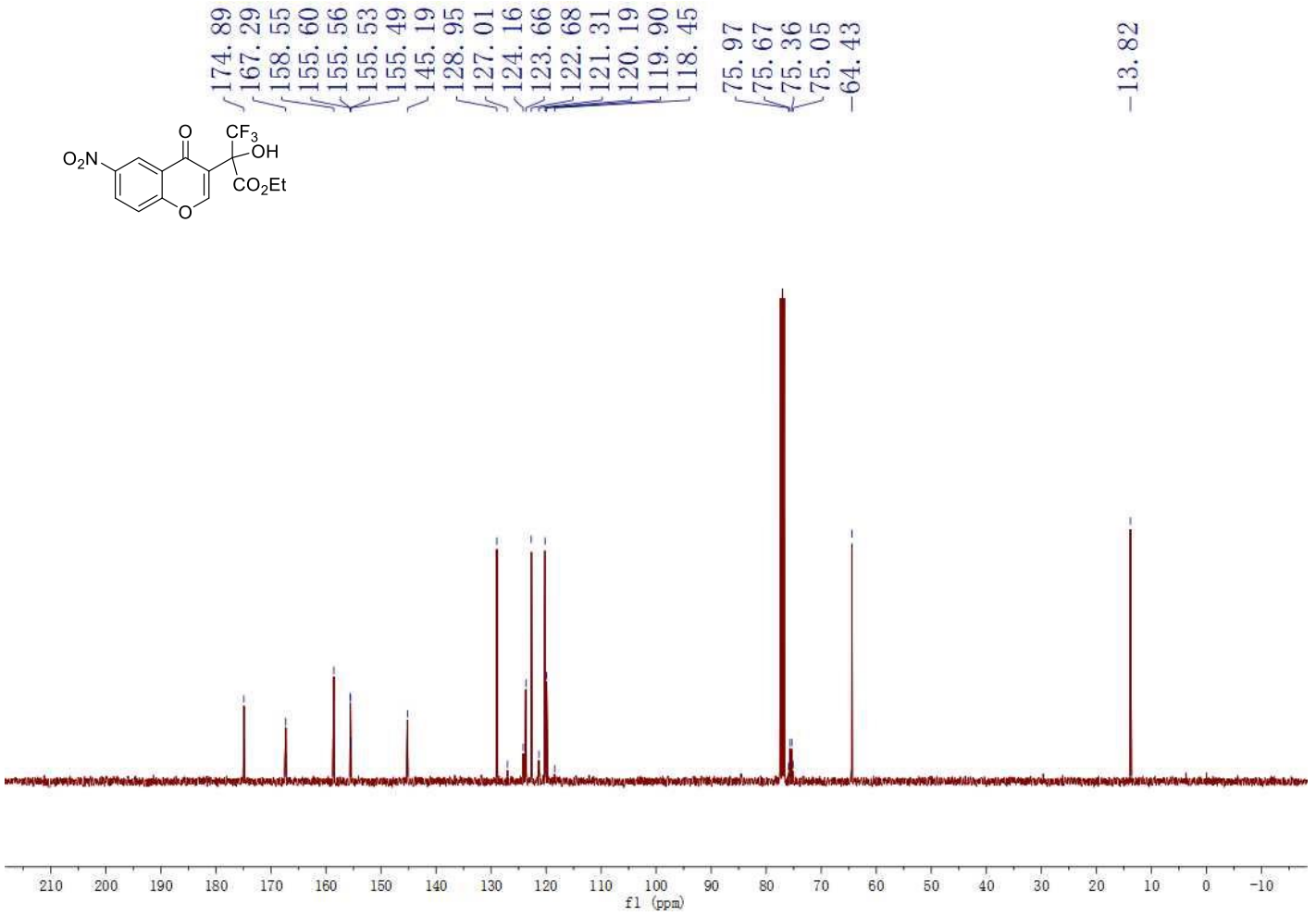


Fig. S90. ^{13}C NMR spectrum of compound **5l**

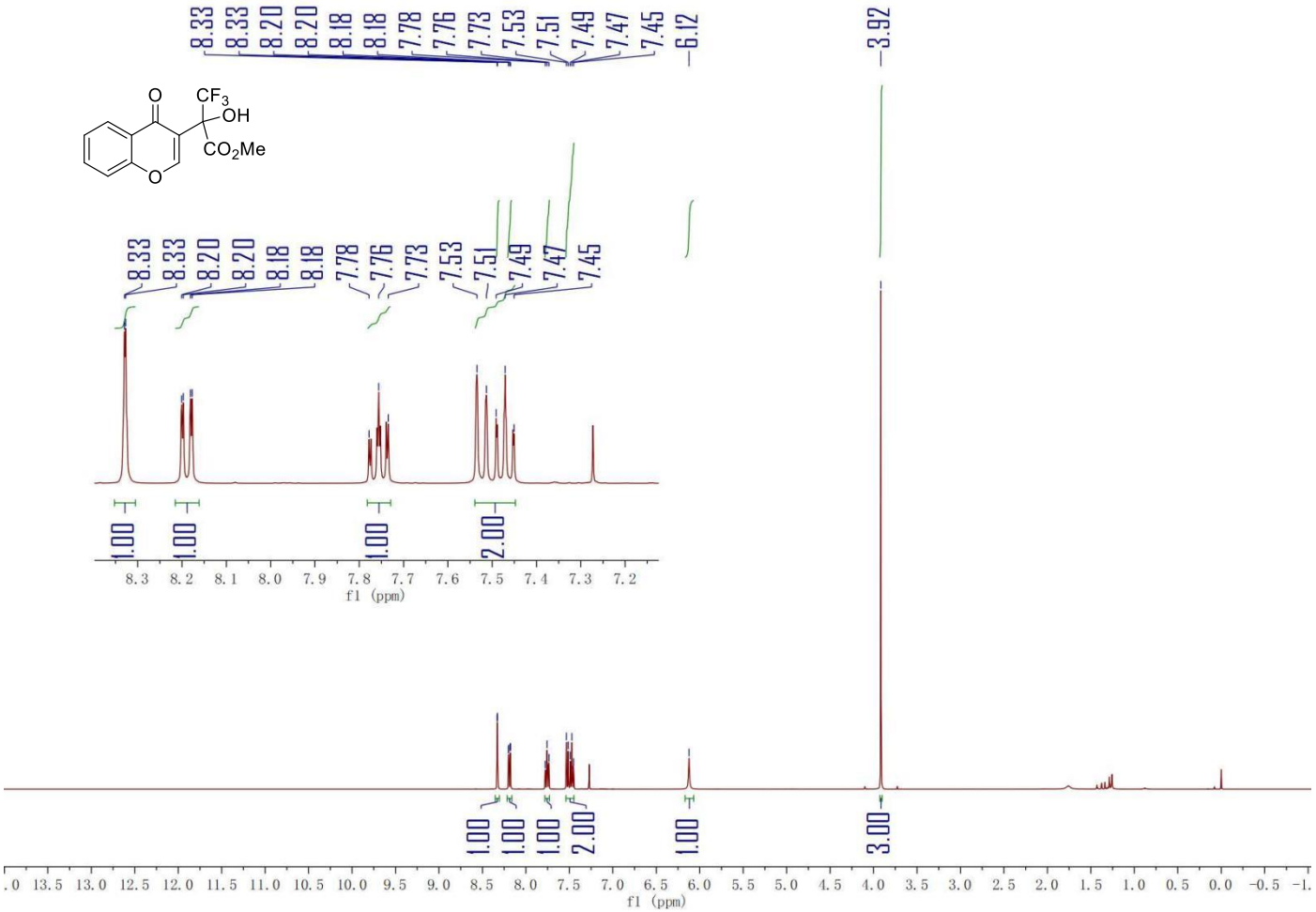


Fig. S91. ^{1}H NMR spectrum of compound **5m**

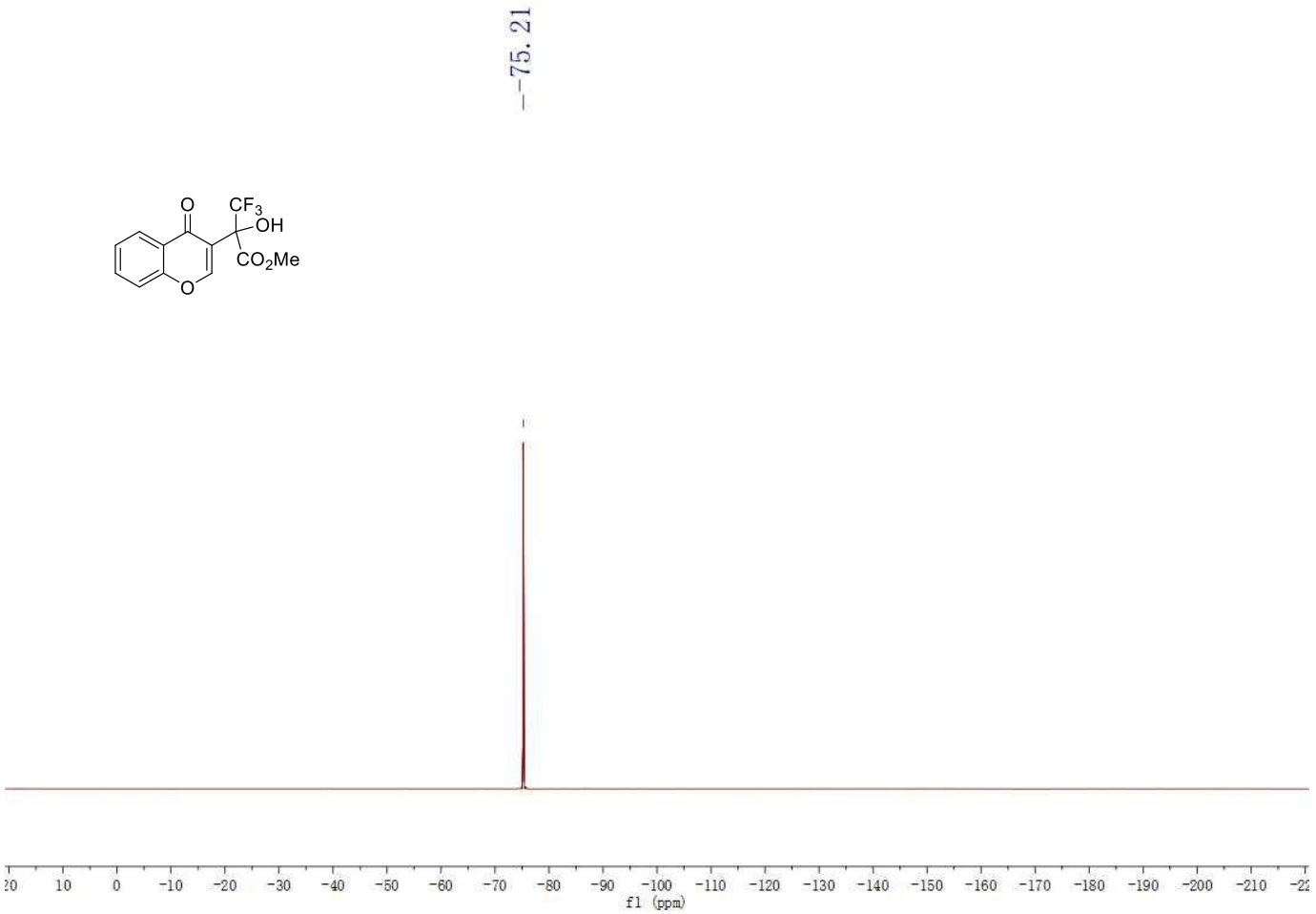


Fig. S92. ^{19F} NMR spectrum of compound **5m**

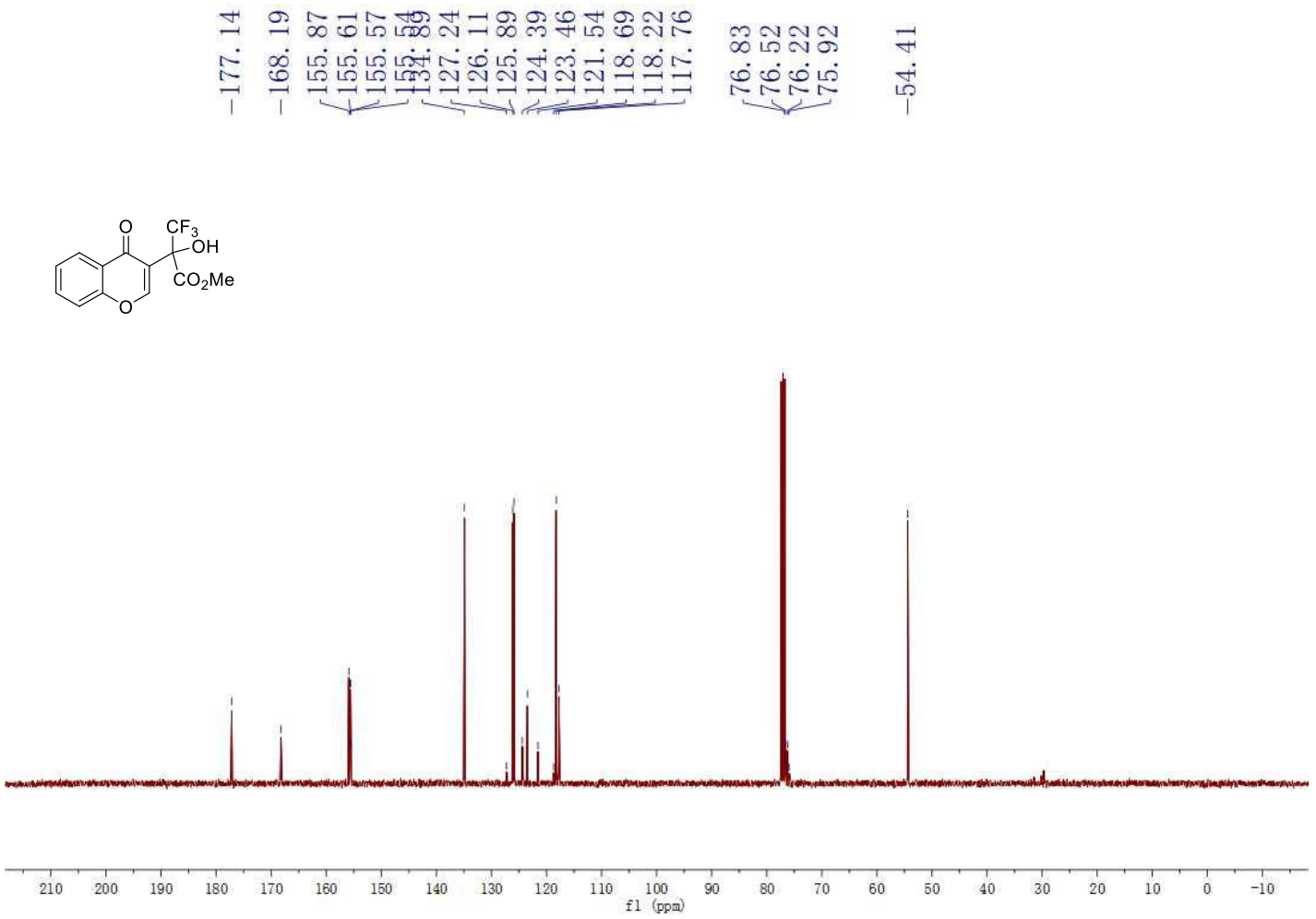


Fig. S93. ^{13}C NMR spectrum of compound **5m**

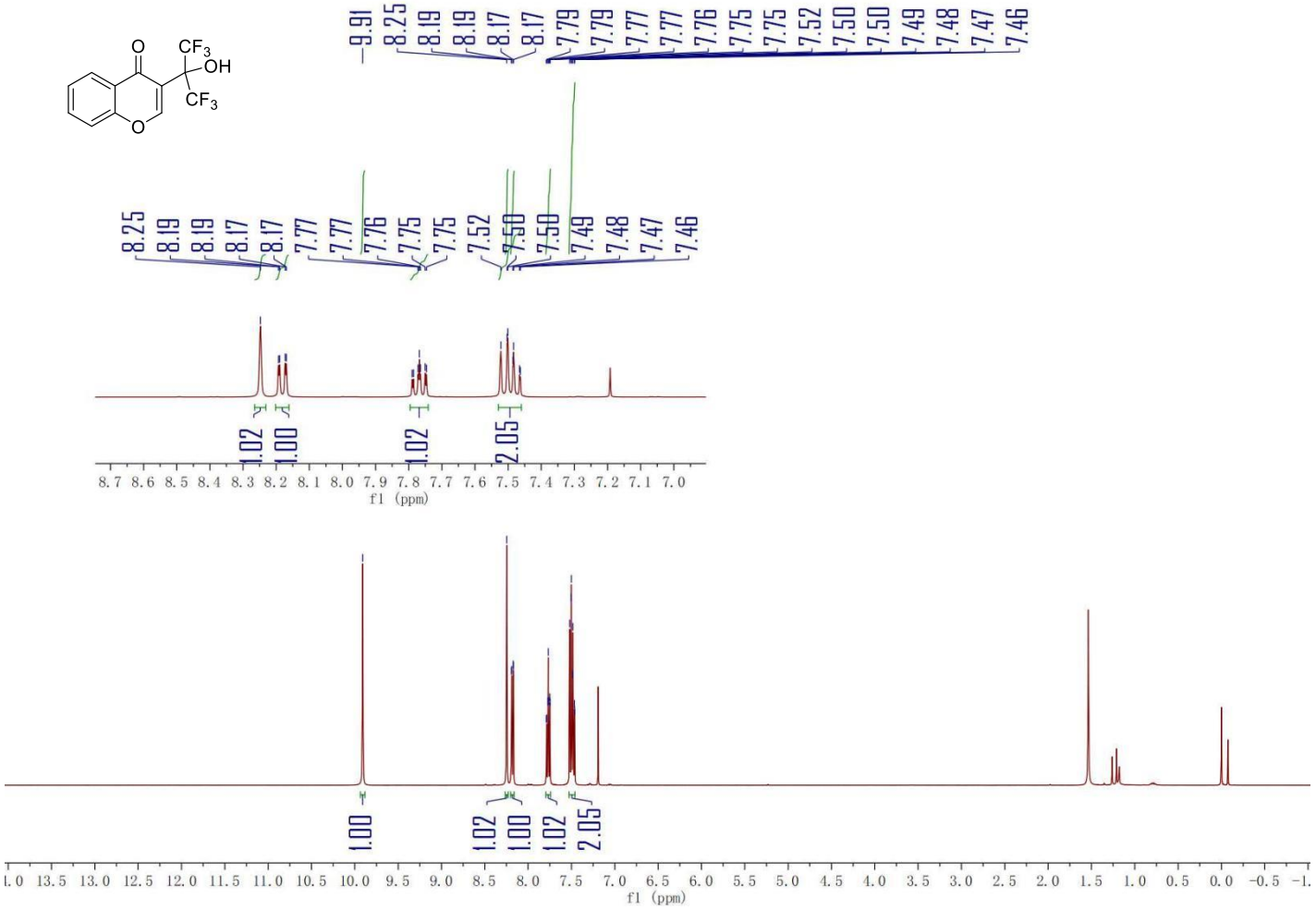


Fig. S94. ^{1}H NMR spectrum of compound **5n**

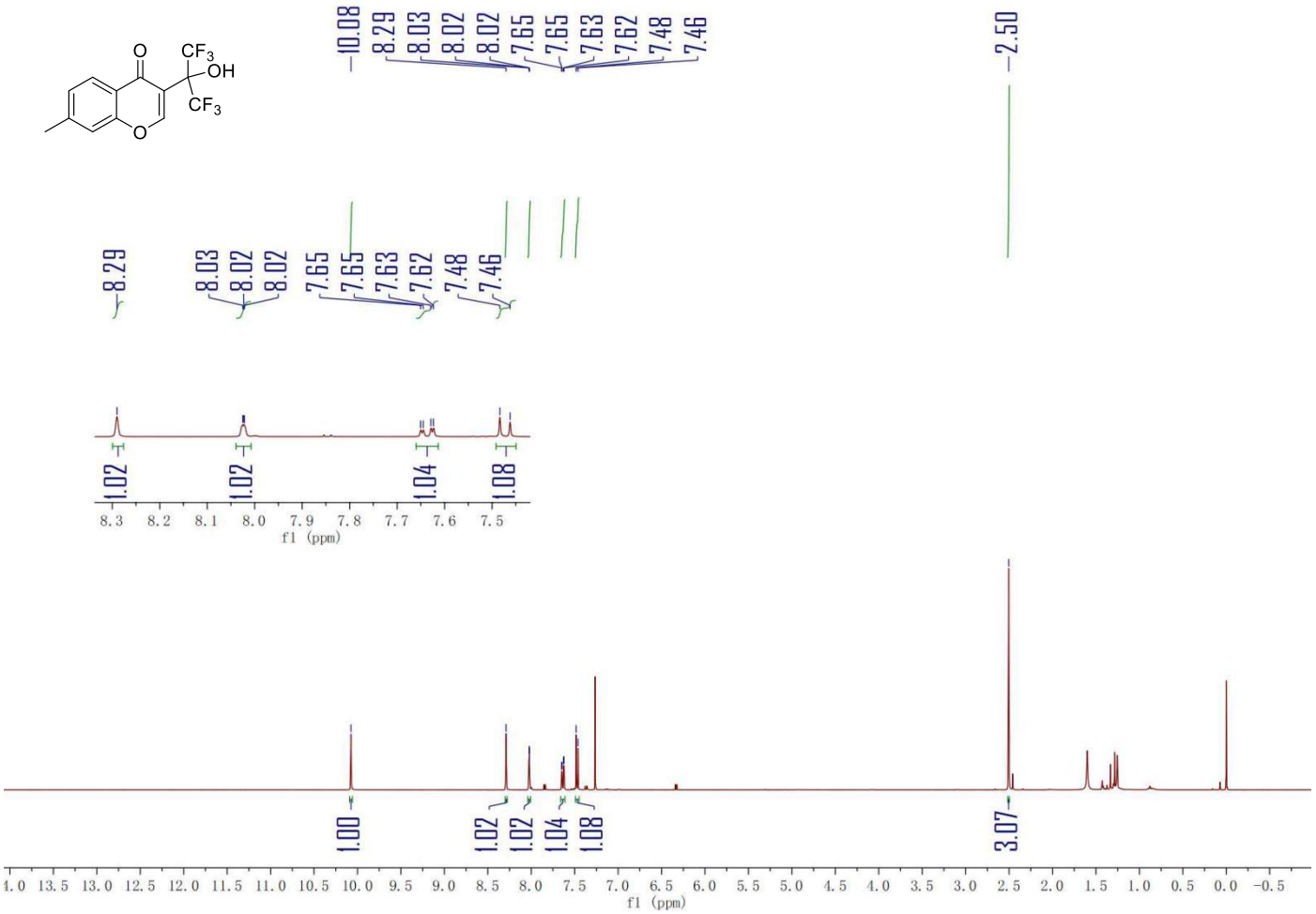


Fig. S95. ^{1}H NMR spectrum of compound **5o**

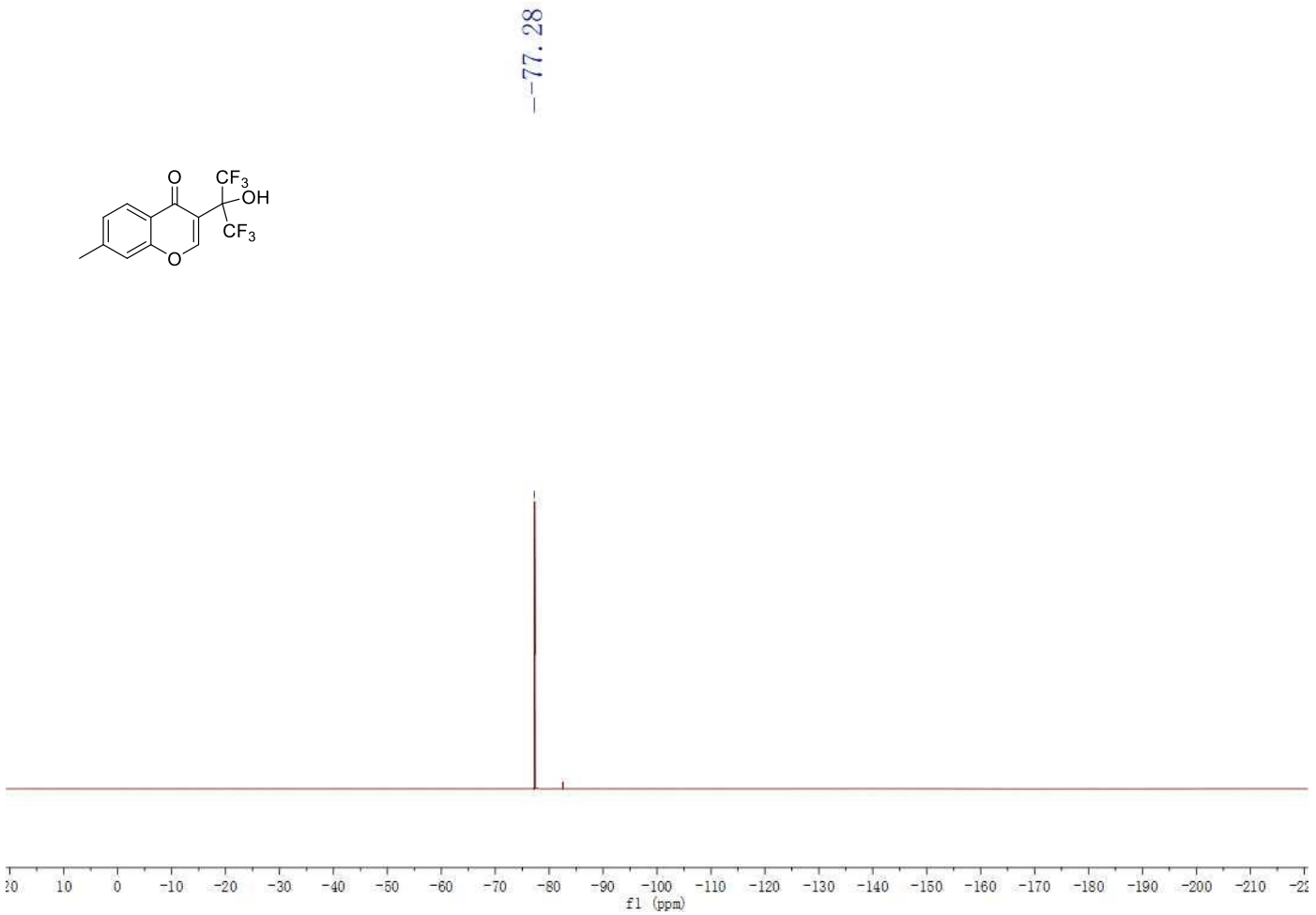


Fig. S96. ^{19}F NMR spectrum of compound **5o**

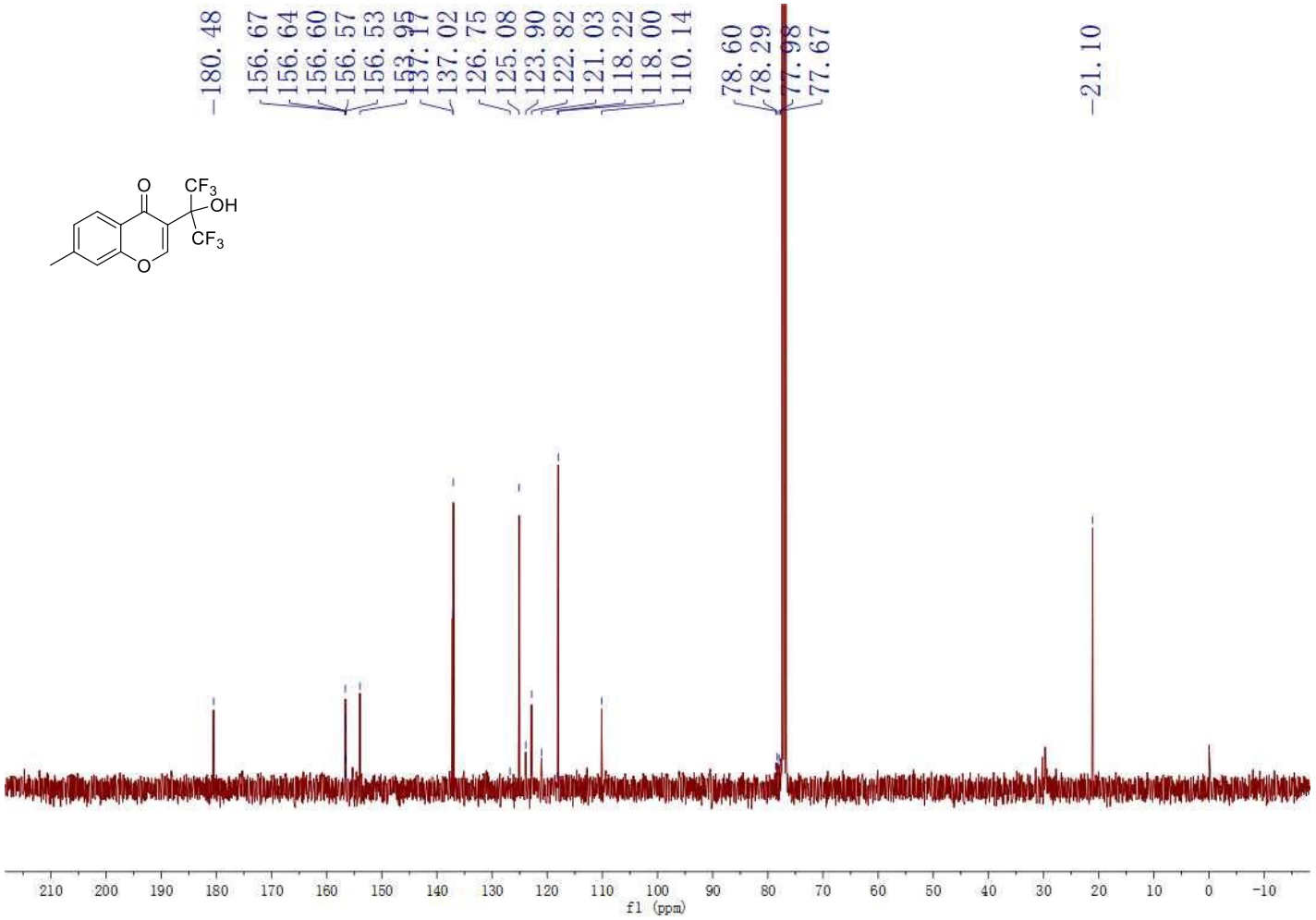


Fig. S97. ^{13}C NMR spectrum of compound **5o**

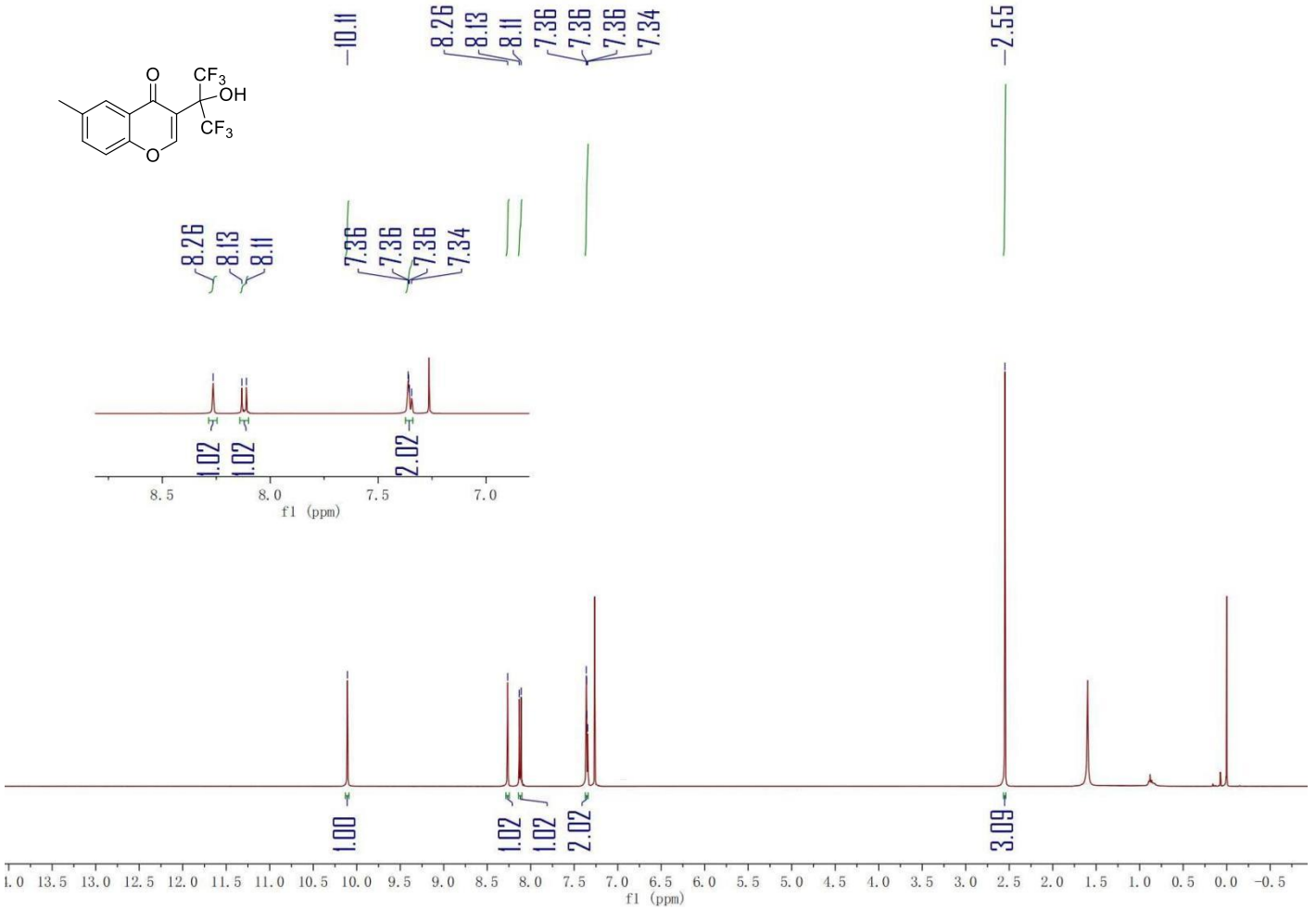


Fig. S98. ^{1}H NMR spectrum of compound **5p**

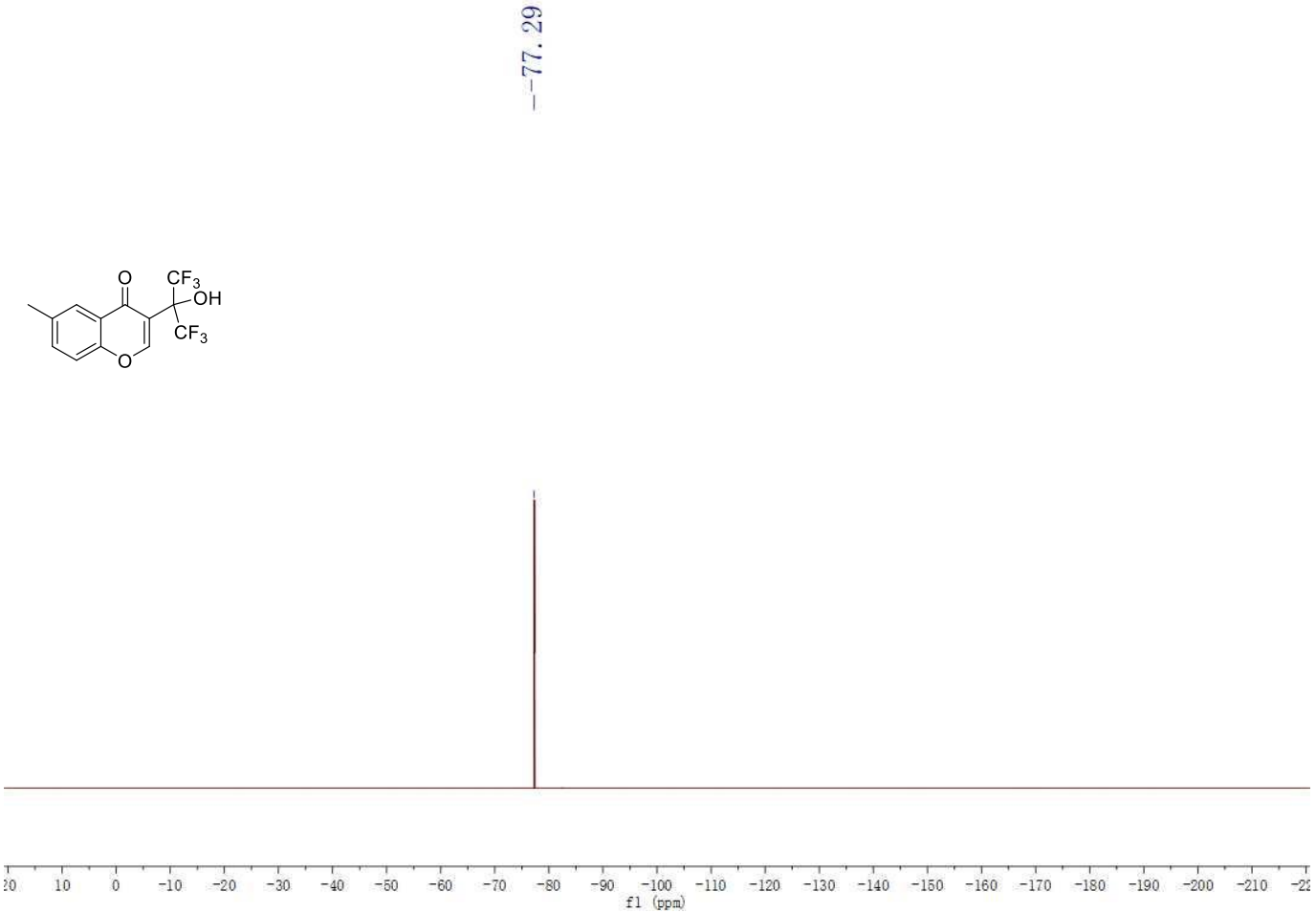


Fig. S99. ^{19F} NMR spectrum of compound **5p**

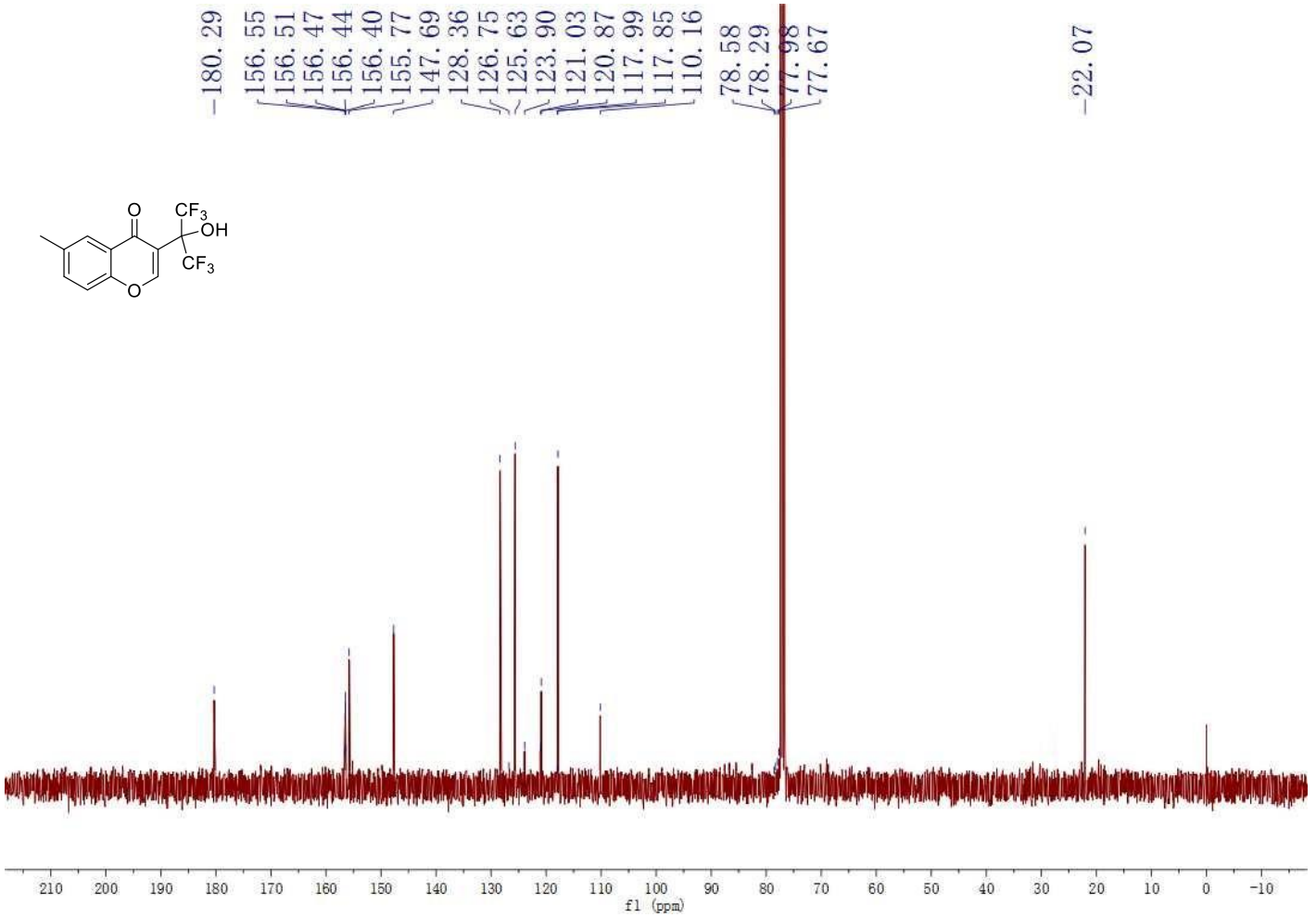


Fig. S100. ^{13}C NMR spectrum of compound **5p**

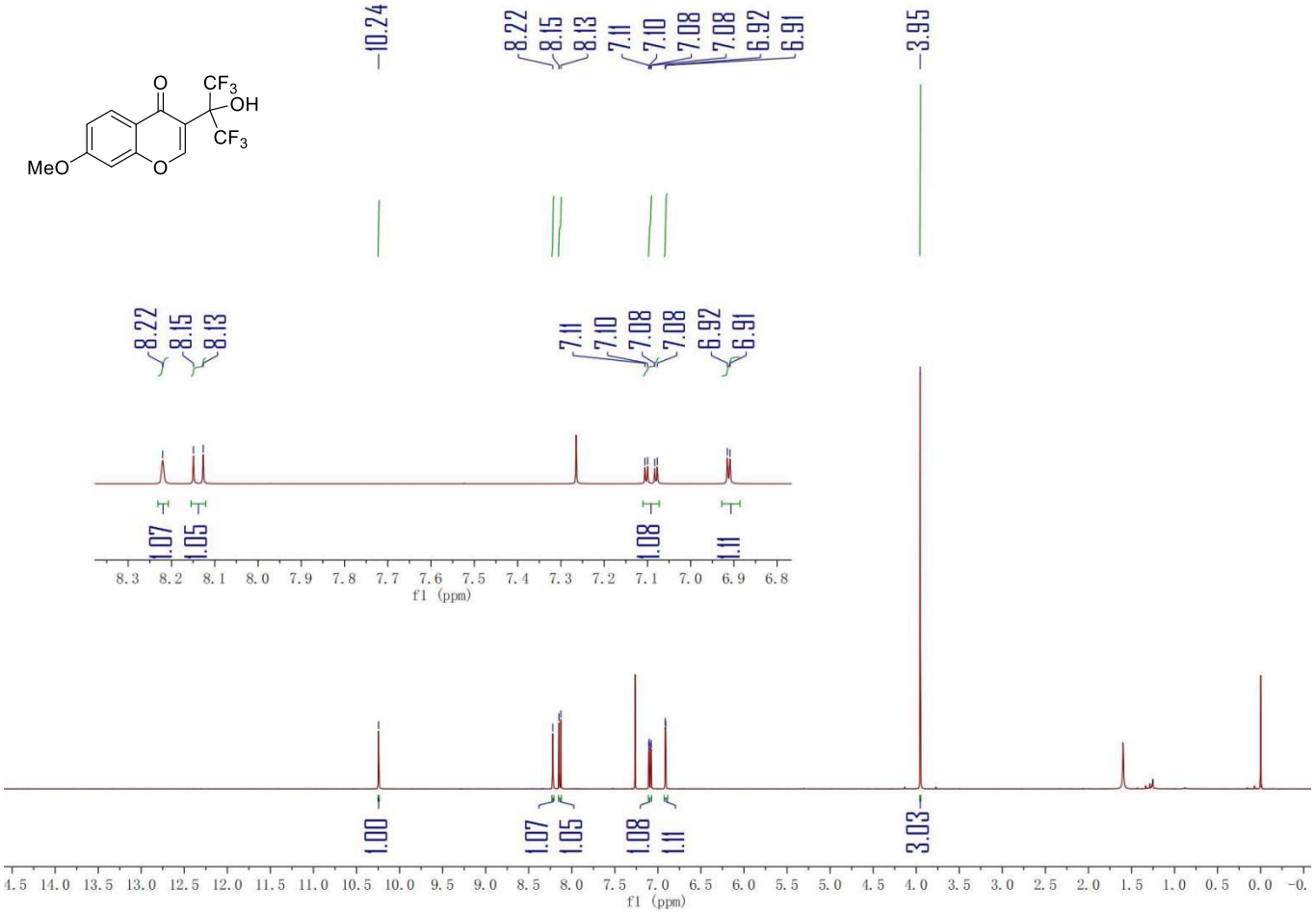


Fig. S101. ^{1}H NMR spectrum of compound **5q**

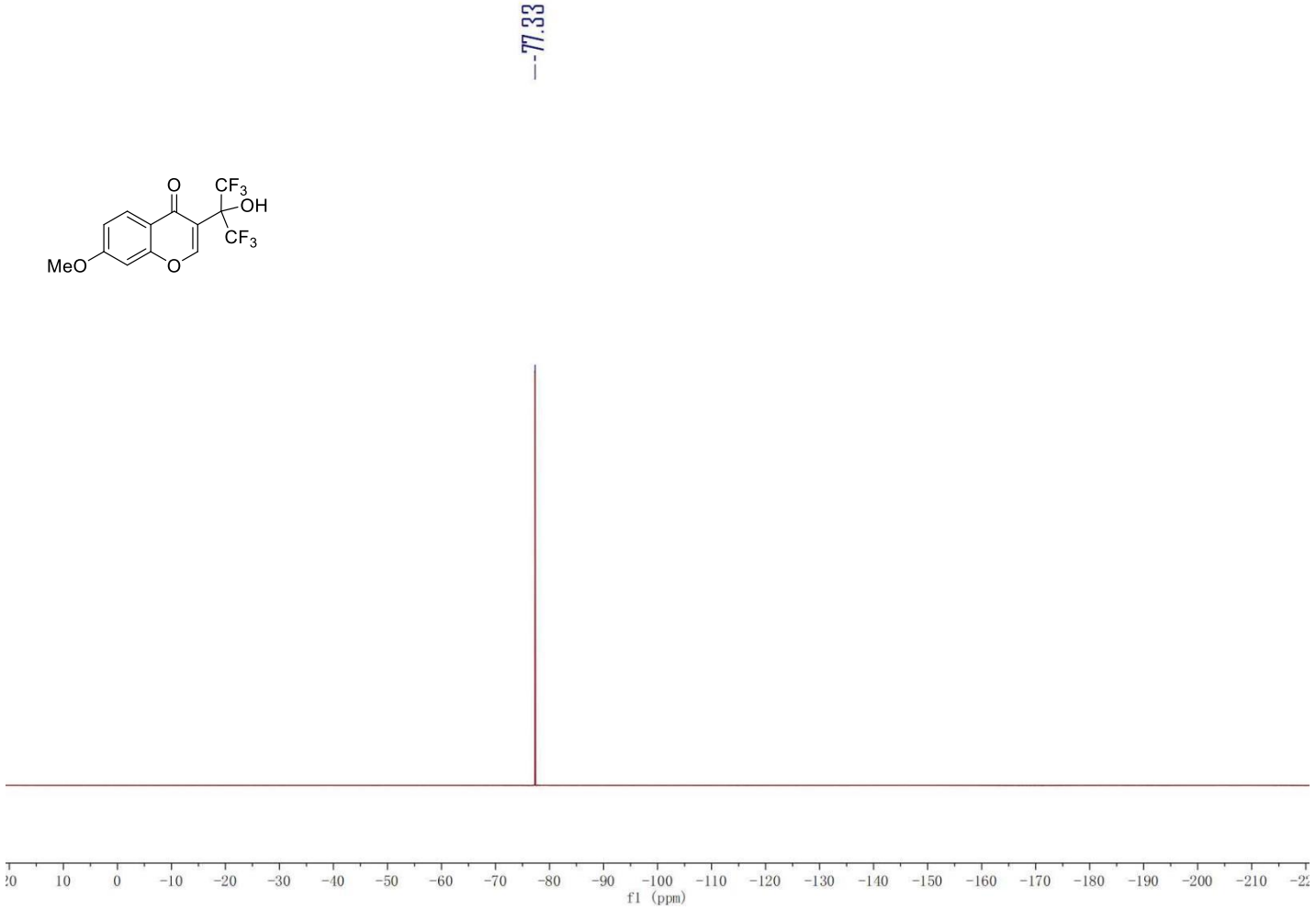


Fig. S102. ^{19F} NMR spectrum of compound **5q**

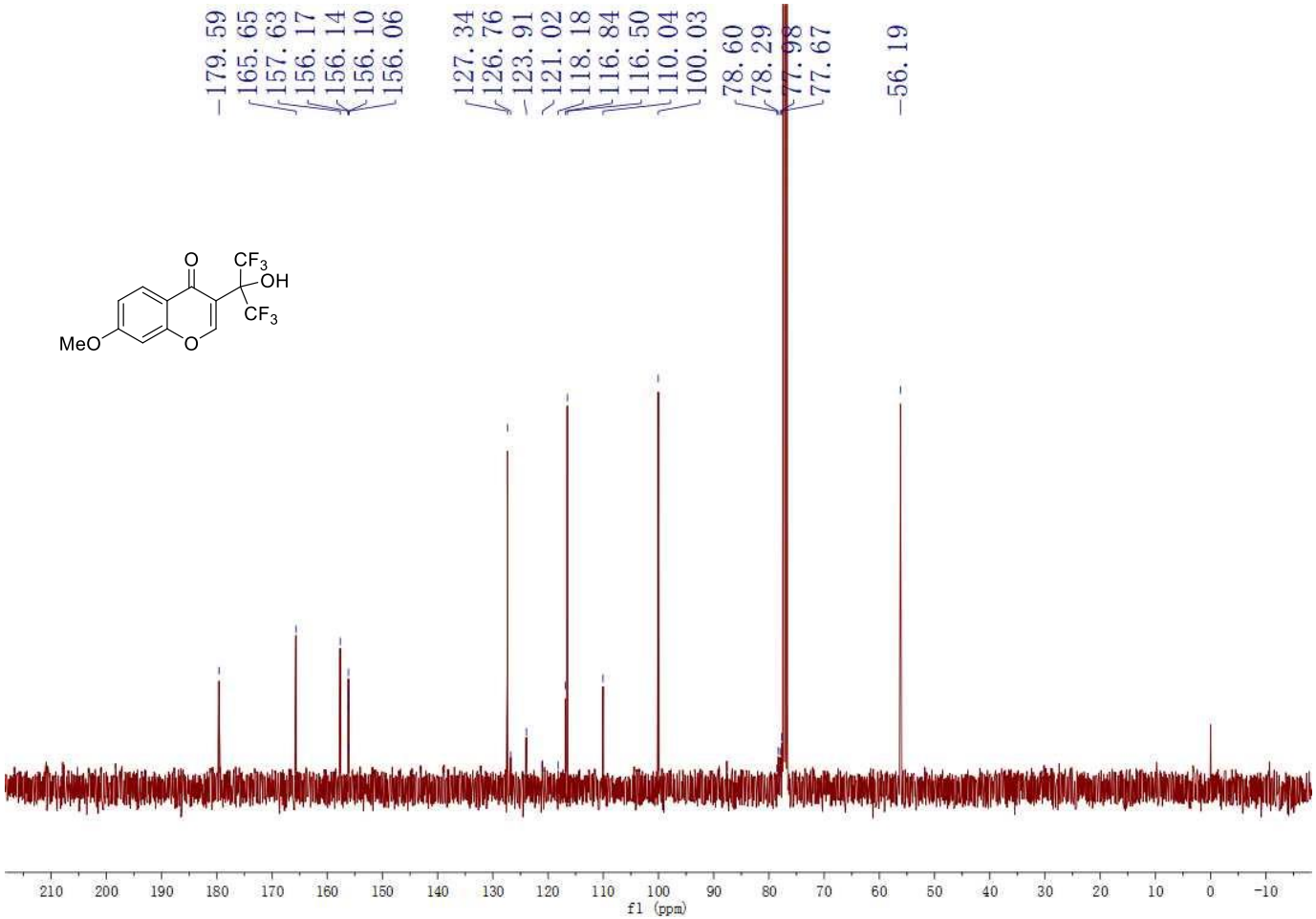


Fig. S103. ^{13}C NMR spectrum of compound **5q**

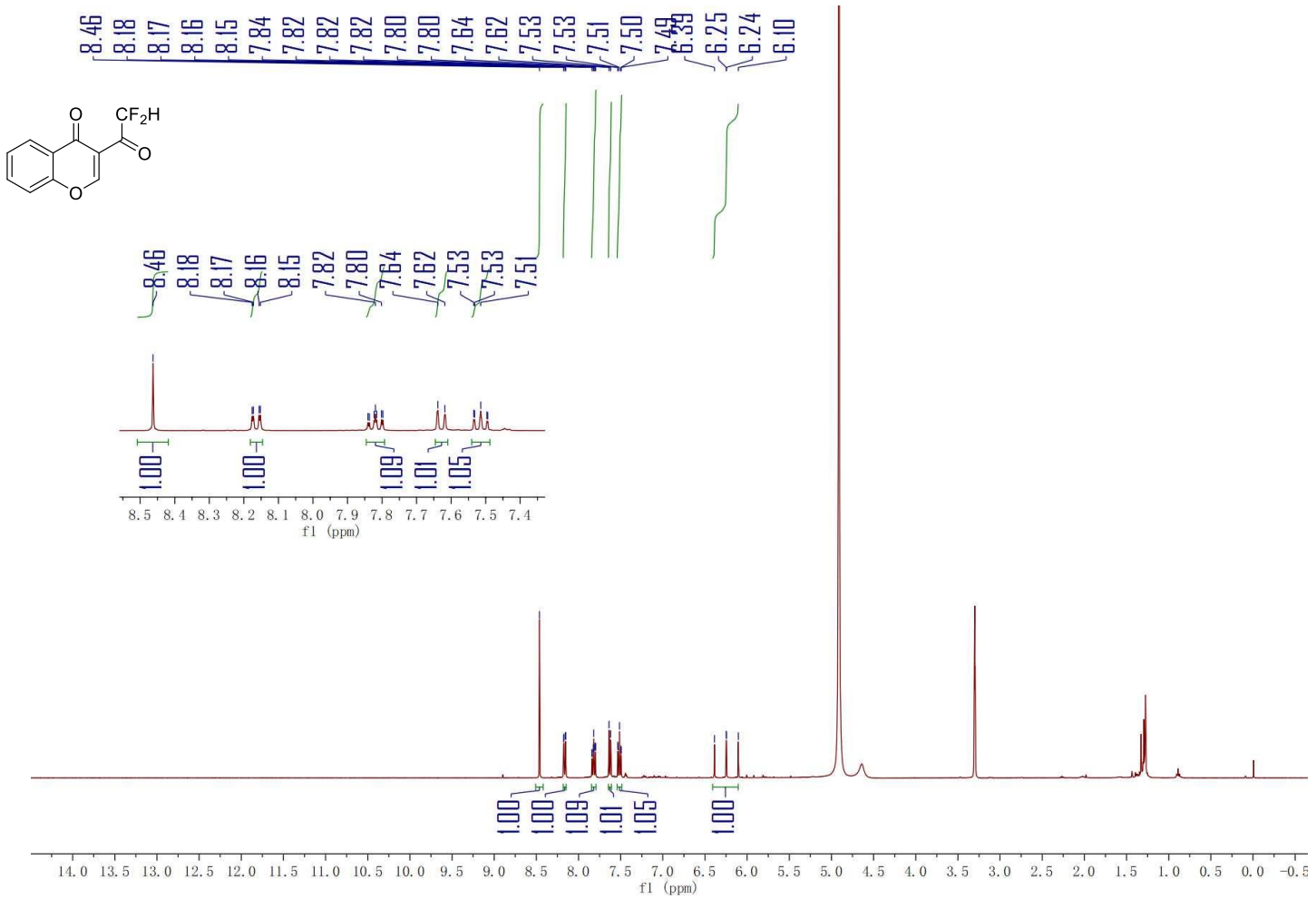


Fig. S104. ^{1}H NMR spectrum of compound **6a**

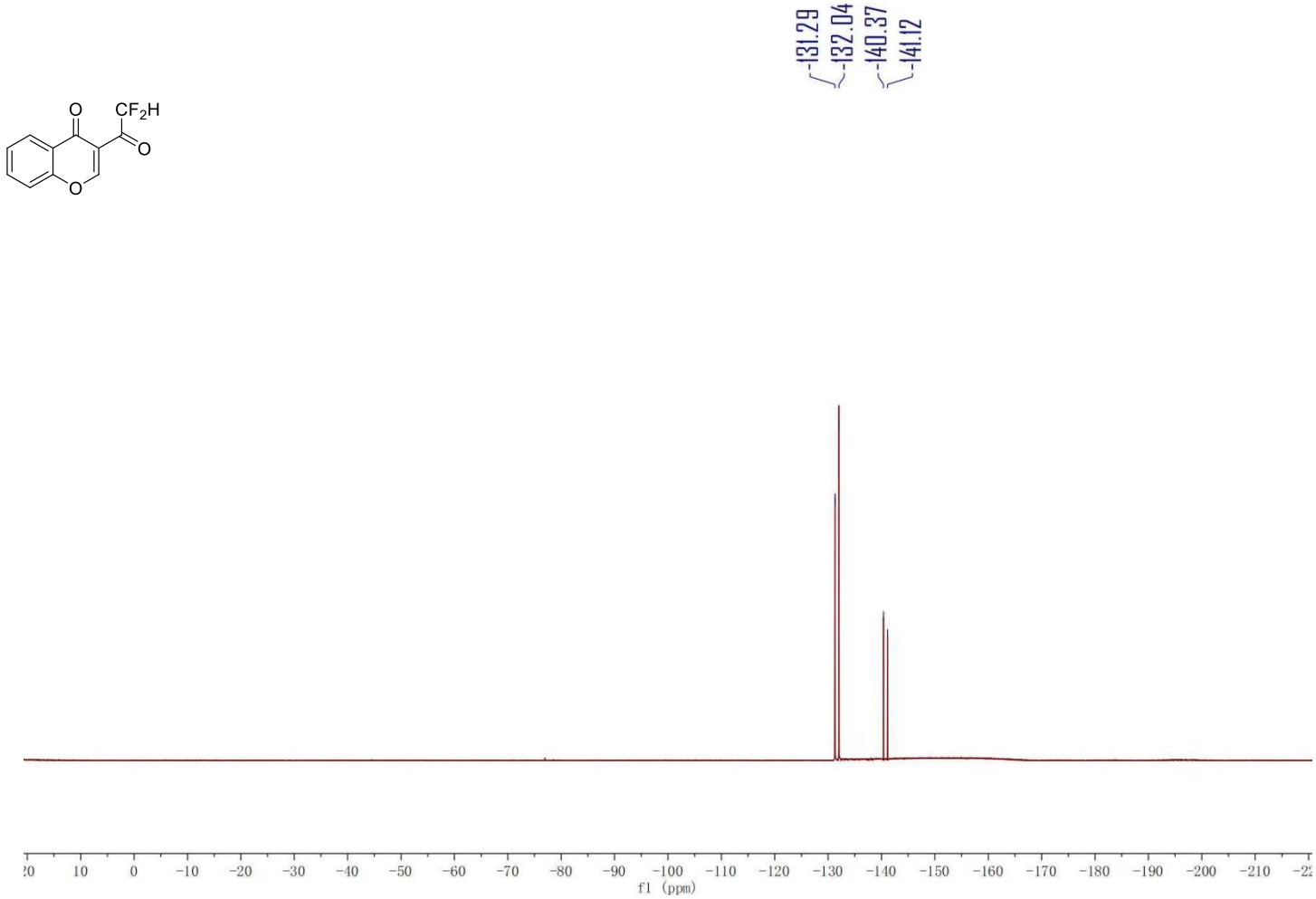


Fig. S105. ^{19}F NMR spectrum of compound **6a**

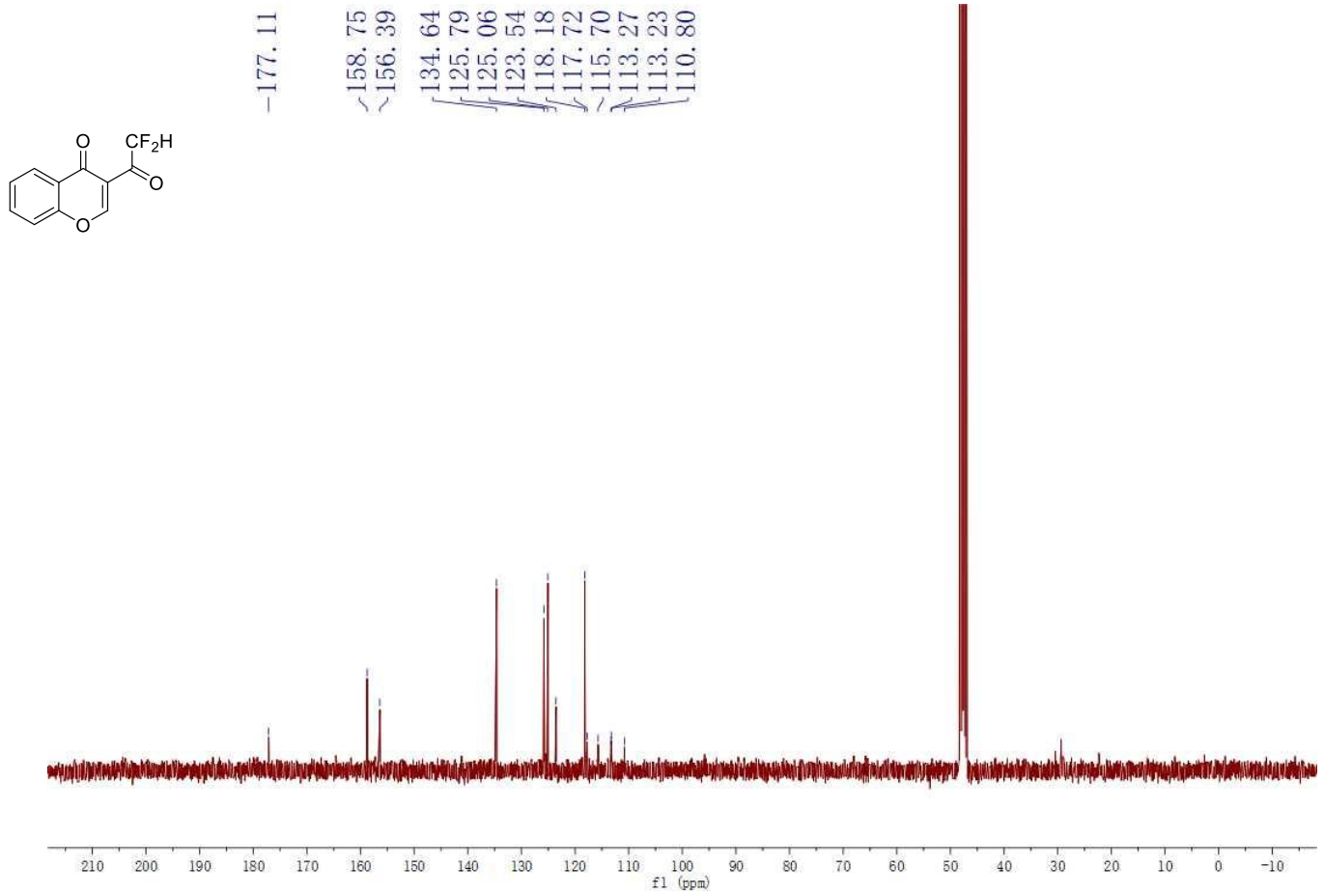


Fig. S106. ^{13}C NMR spectrum of compound **6a**

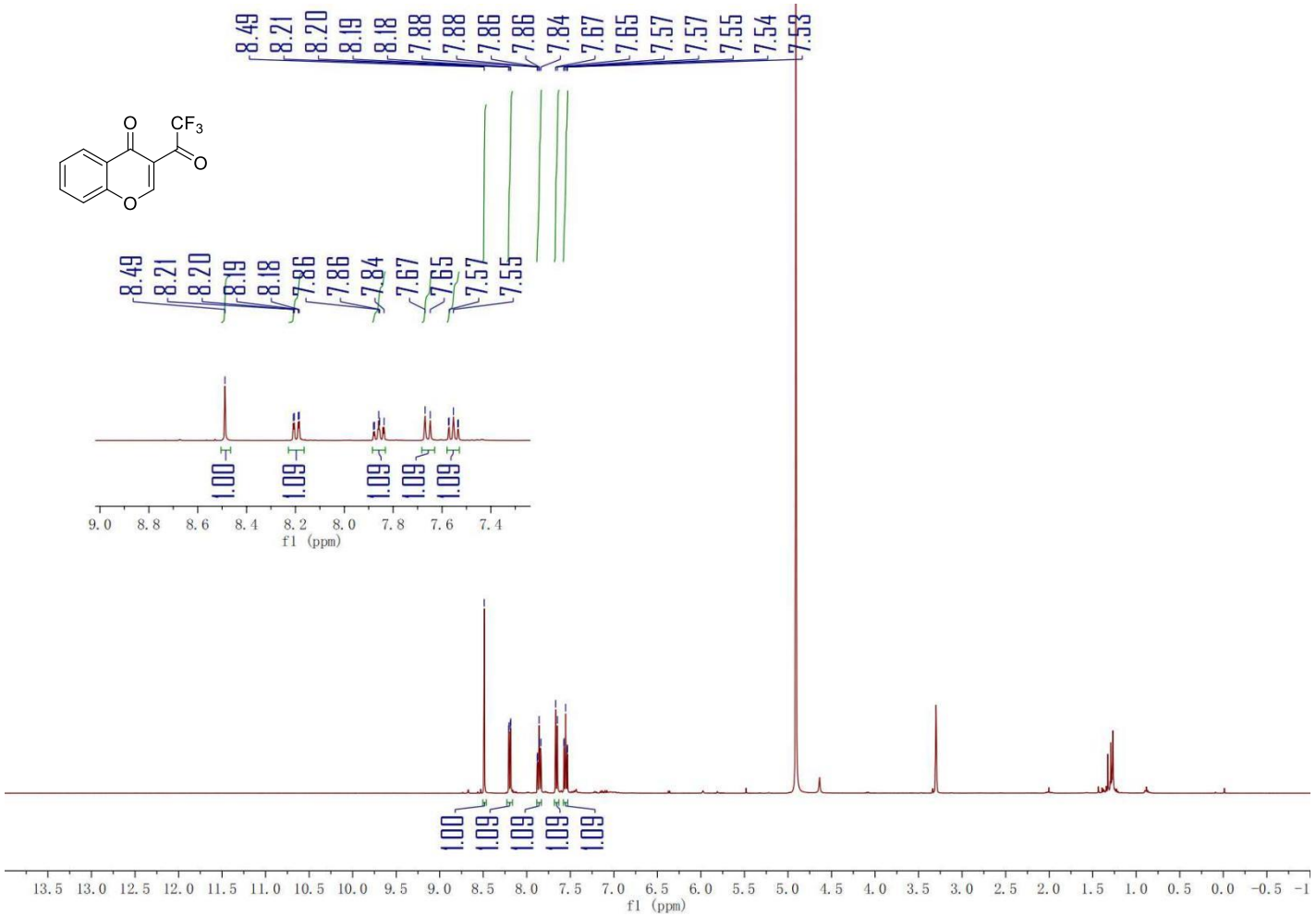


Fig. S107. ^{13}C NMR spectrum of compound **6b**

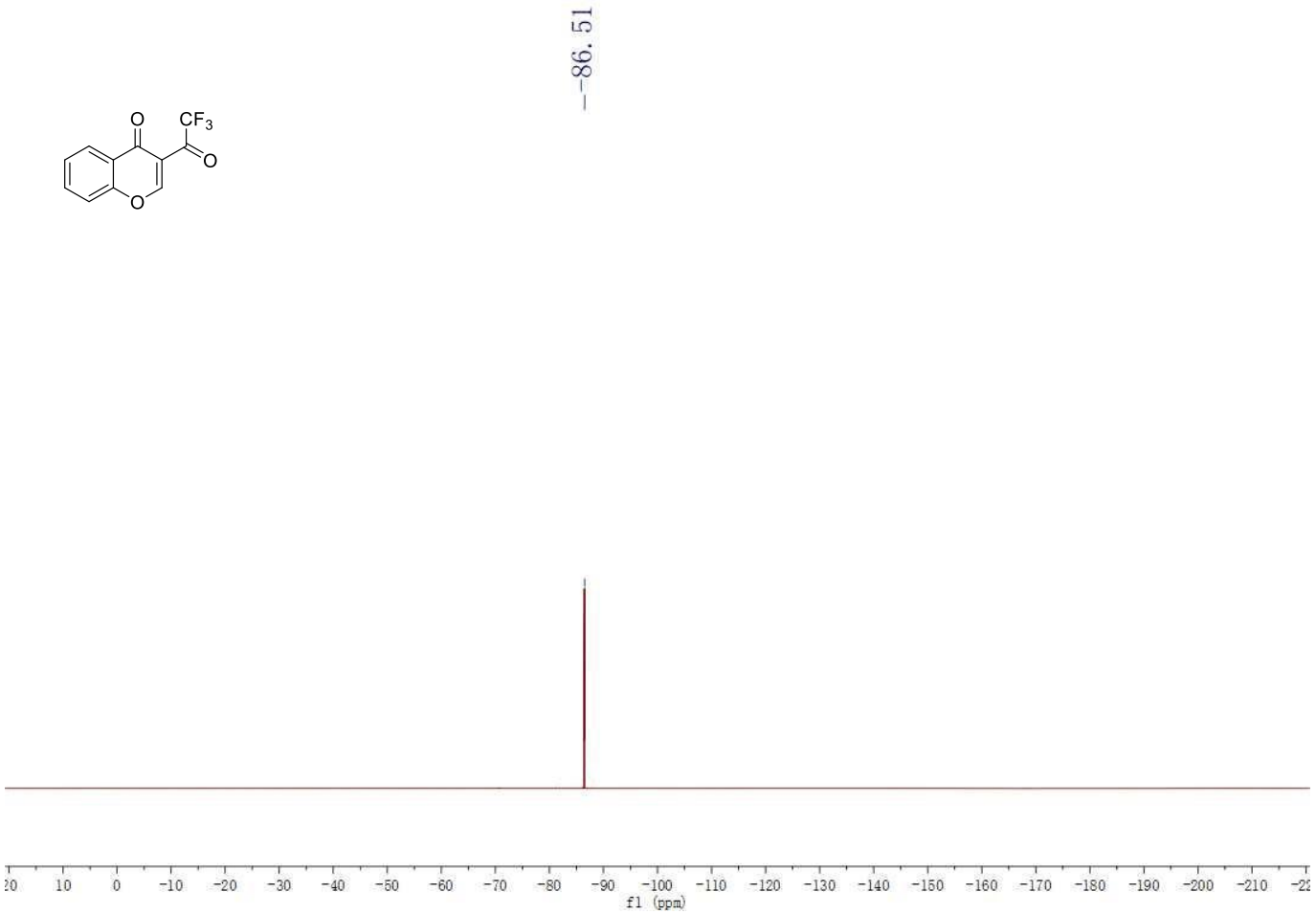


Fig. S108. ^{19}F NMR spectrum of compound **6b**

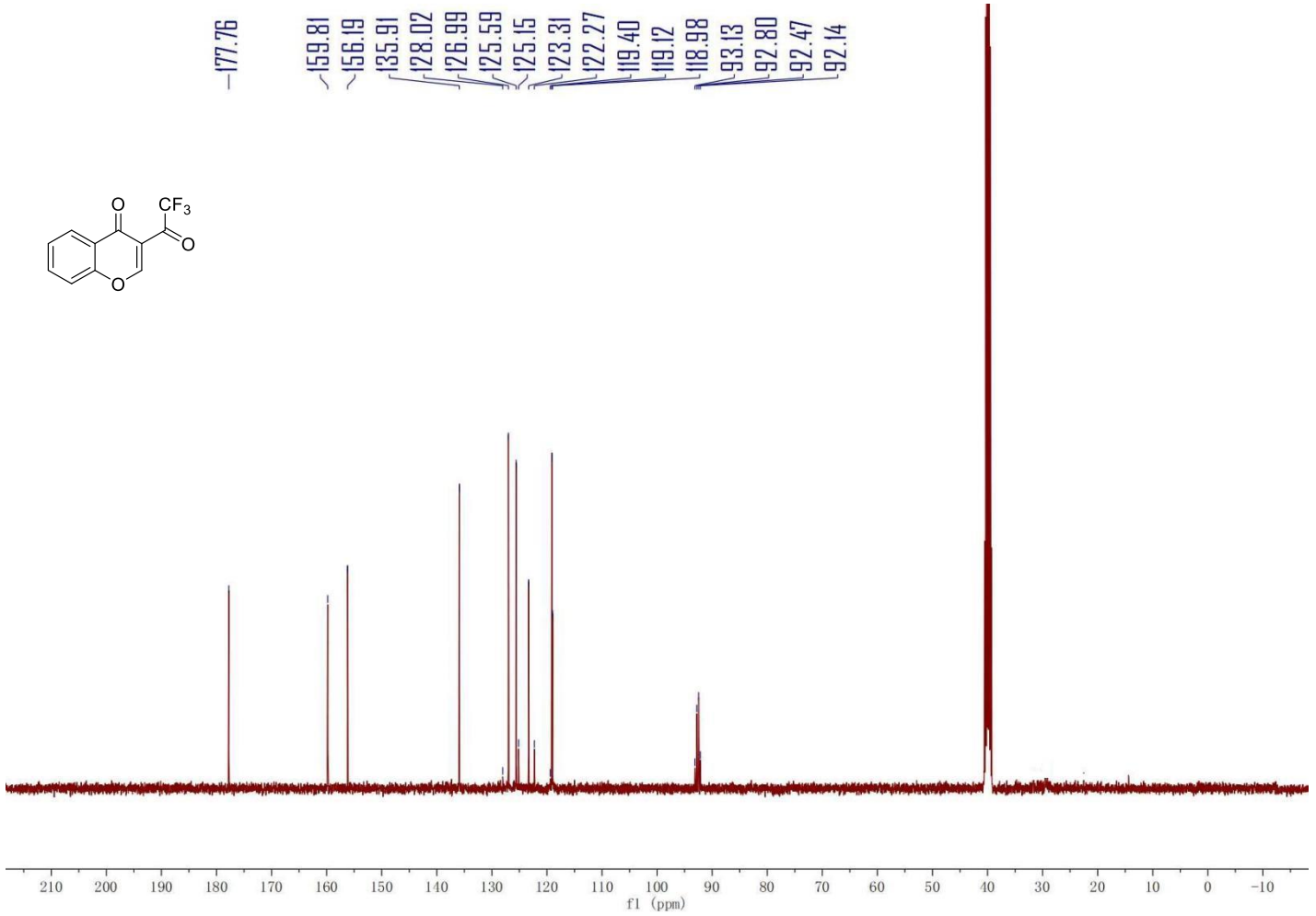


Fig. S109. ^{13}C NMR spectrum of compound **6b**

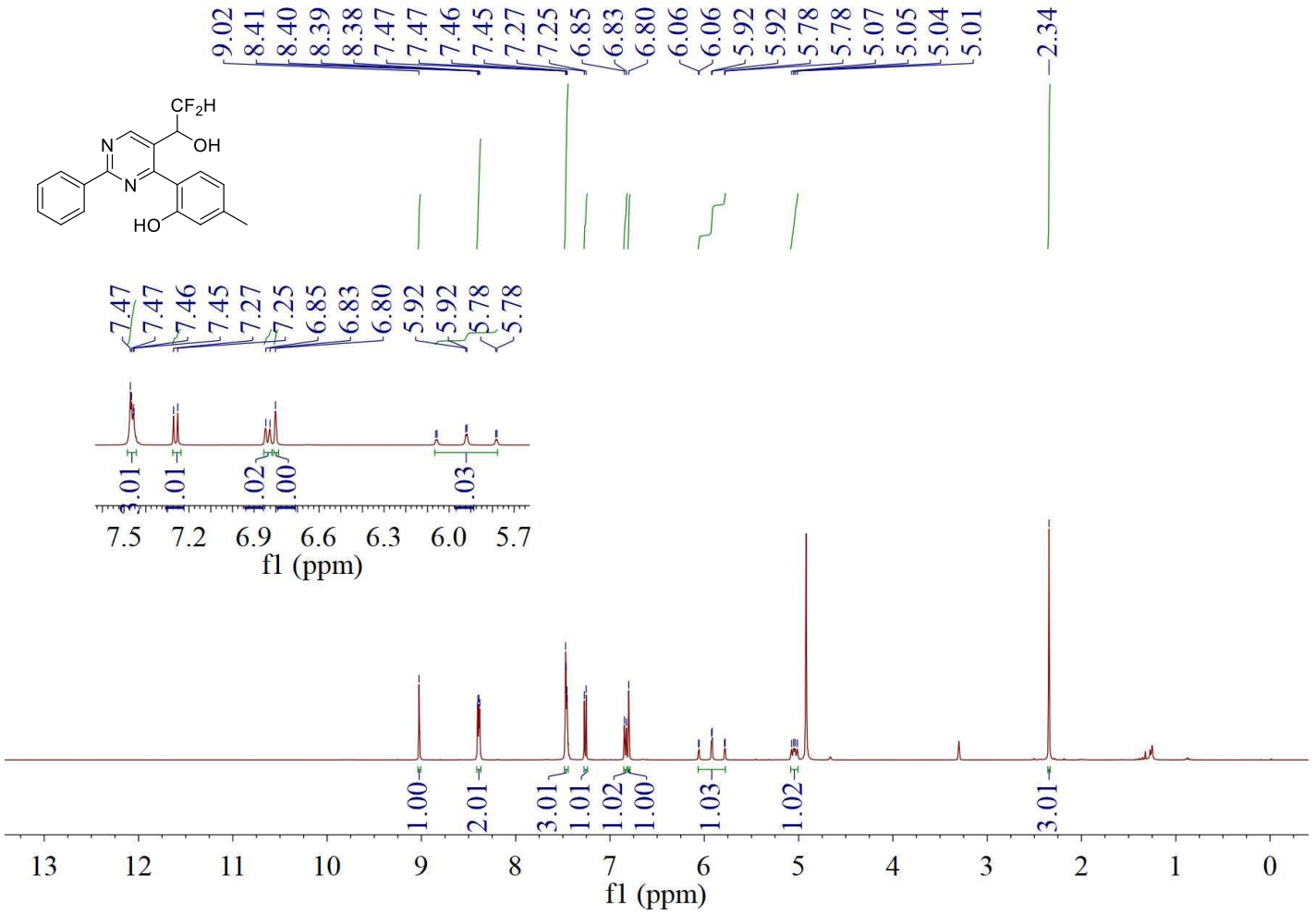


Fig. S110. ^{1}H NMR spectrum of compound **6c**

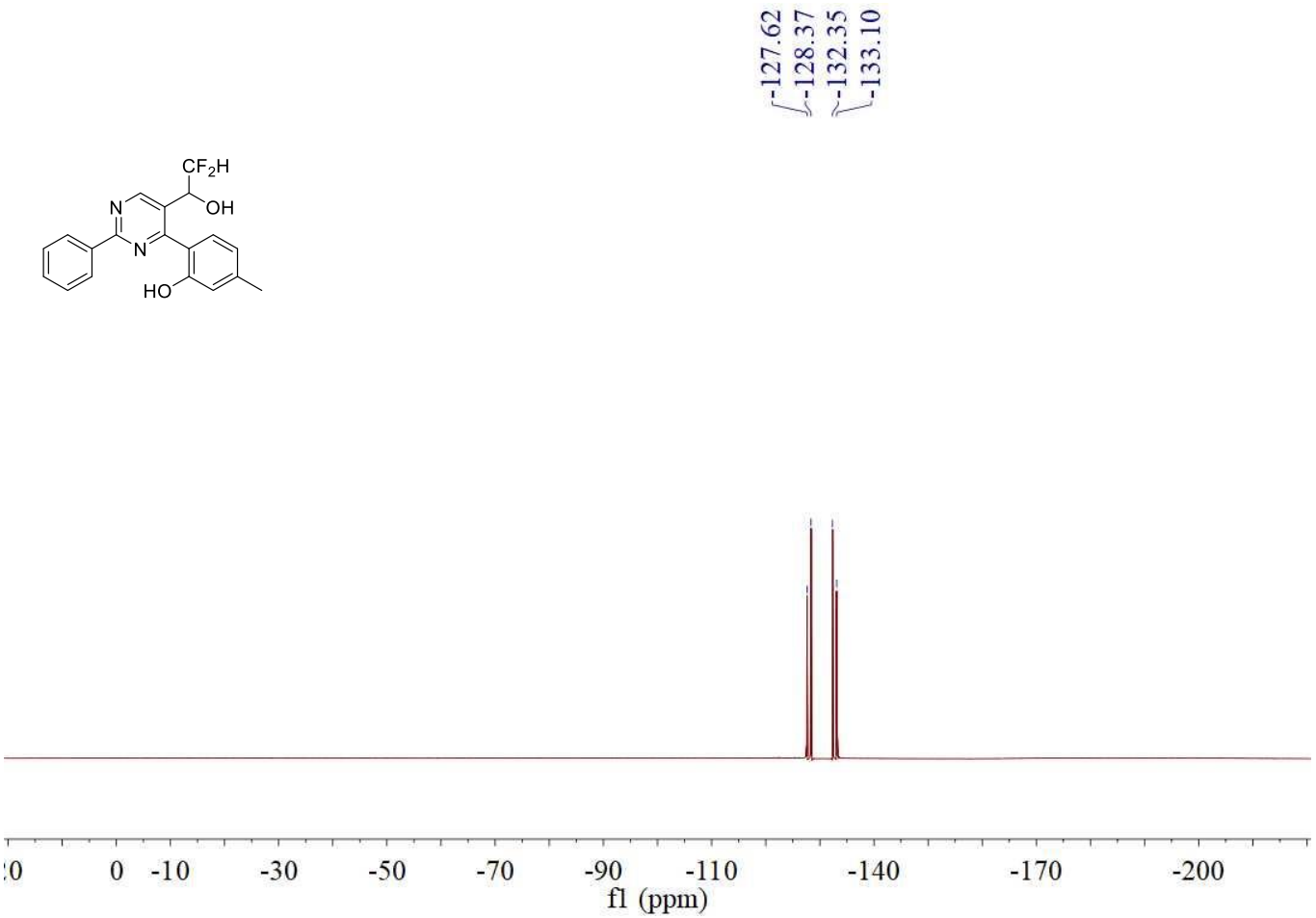


Fig. S111. ^{19}F NMR spectrum of compound **6c**

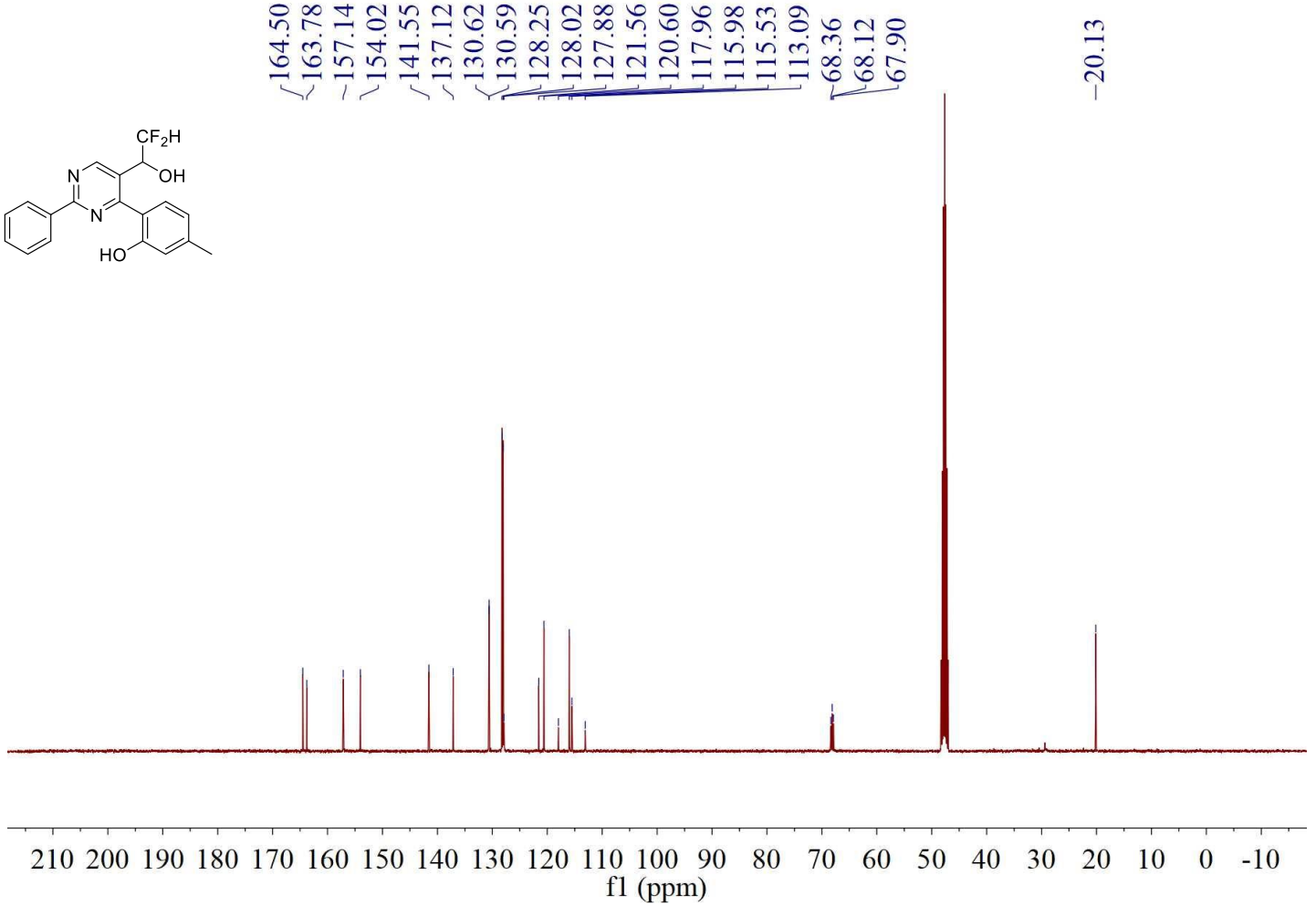


Fig. S112. ^{13}C NMR spectrum of compound **6c**

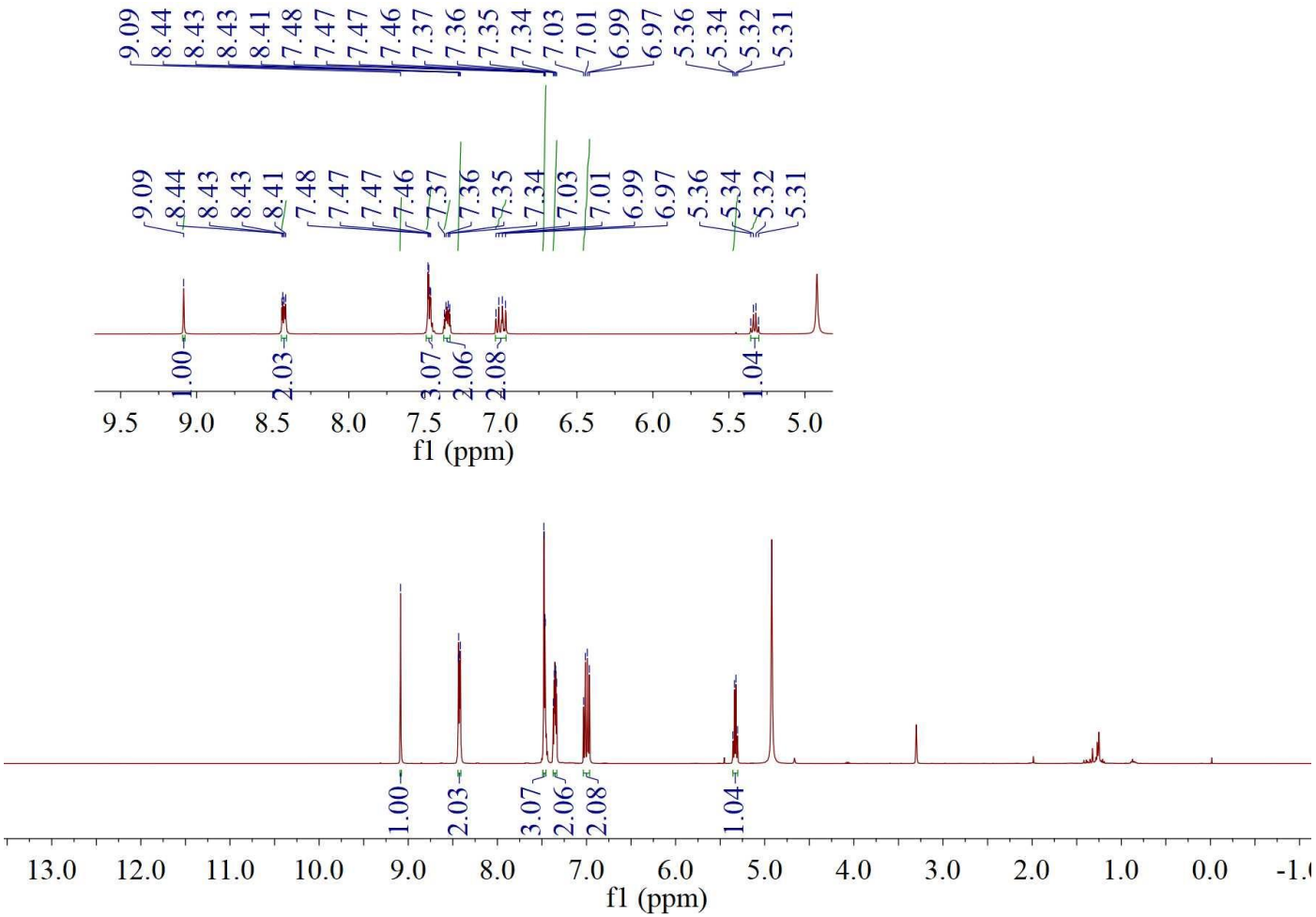


Fig. S113. ^{1}H NMR spectrum of compound **6d**

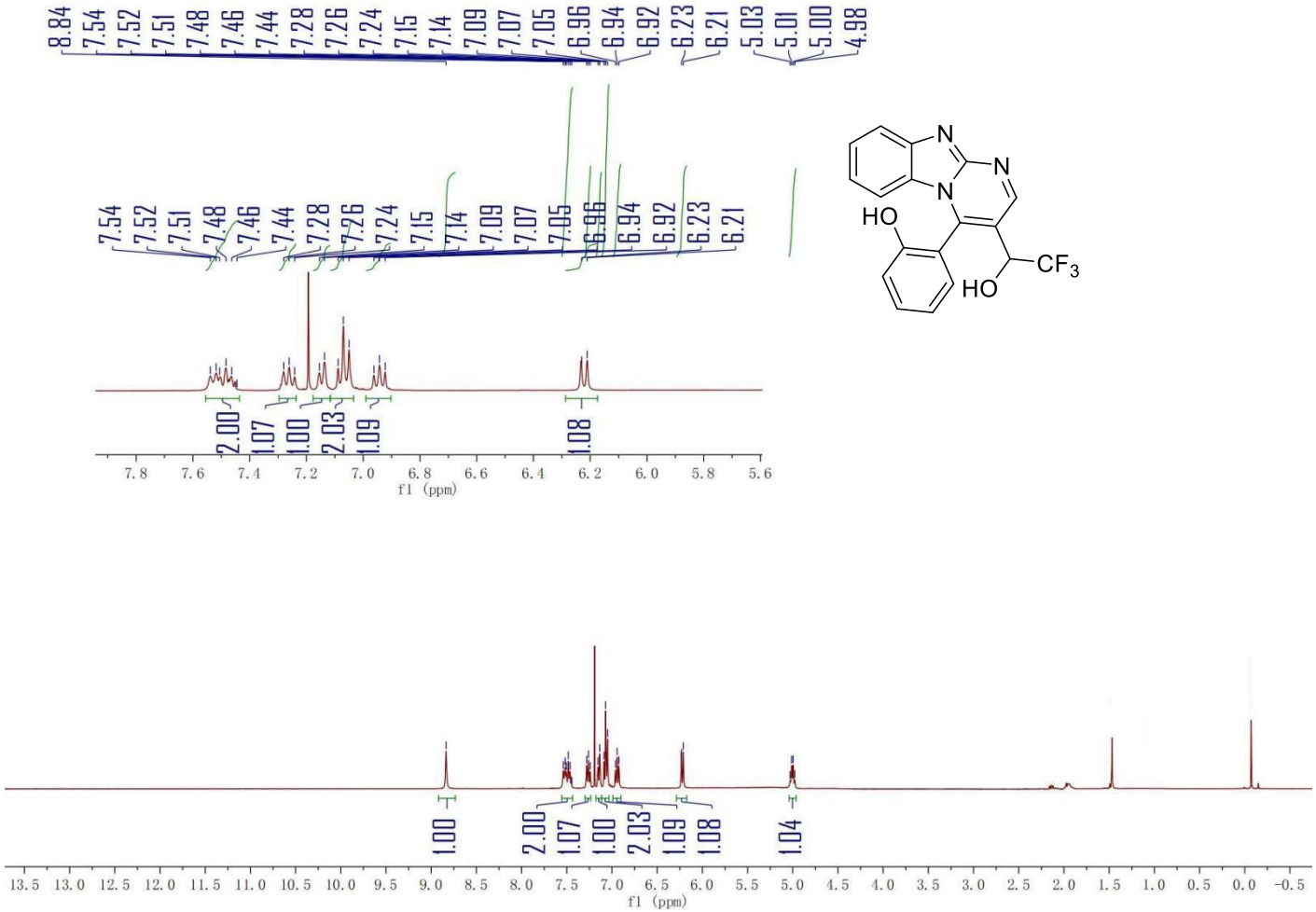


Fig. S114. ^{1}H NMR spectrum of compound **6e**

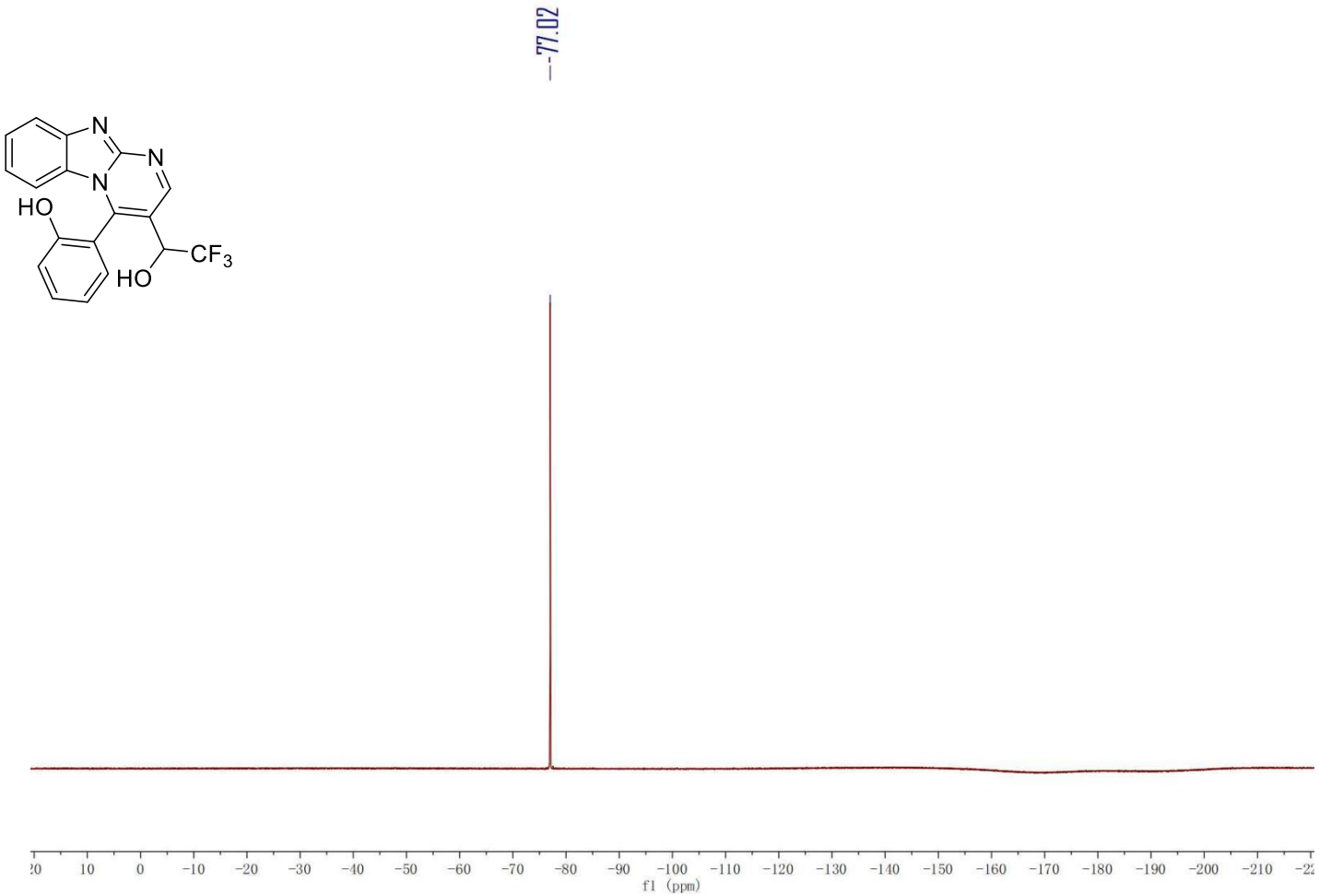


Fig. S115. ^{19}F NMR spectrum of compound **6e**

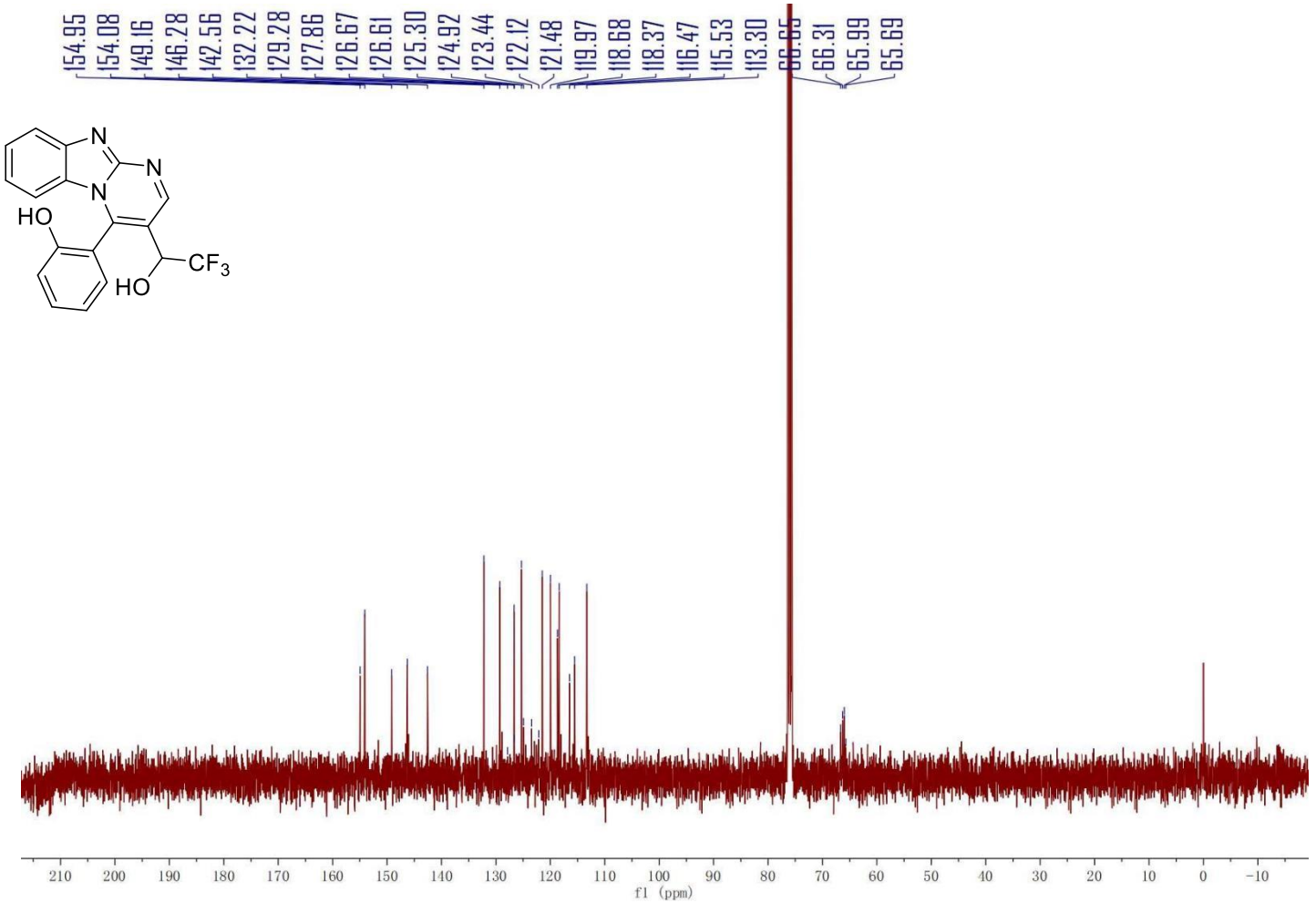


Fig. S116. ^{13}C NMR spectrum of compound **6e**

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