Palladium-Catalyzed Difluoromethylcarbonylation of Aryl Iodides

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Supporting Information

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1. General information

Unless otherwise noted, all cross-coupling reactions were run under an N_2 atmosphere and all glassware was oven dried before use. Chemicals were purchased from Shanghai Haohong Scientific Co., Ltd, Adamas-beta, Energy Chemical, bidepharm and were used without further purification. DMSO and DMF were purchased from Adamas-beta and dried with 4Å molecular sieves. $(DMPU)_2Zn(CF_2H)_2$,[1] was synthesized according to the published procedures. GCMS analysis was performed on a Thermo-Fischer Scientific ISQ QD single quadrupole mass spectrometer. Thin-layer chromatography (TLC) was performed on 0.20 mm silica gel F-254 plates, with resulting chromatograms visualized by fluorescence quenching or $KMnO_4$ stain. ^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded at 297K on a Bruker AVANCE AV 400 (400 MHz, 101MHz and 376 MHz) spectrometer. Data is reported in ppm using $CDCl_3$ as the solvent unless otherwise specified. Data is reported as: Chemical shifts (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (Hz), integrated intensity.

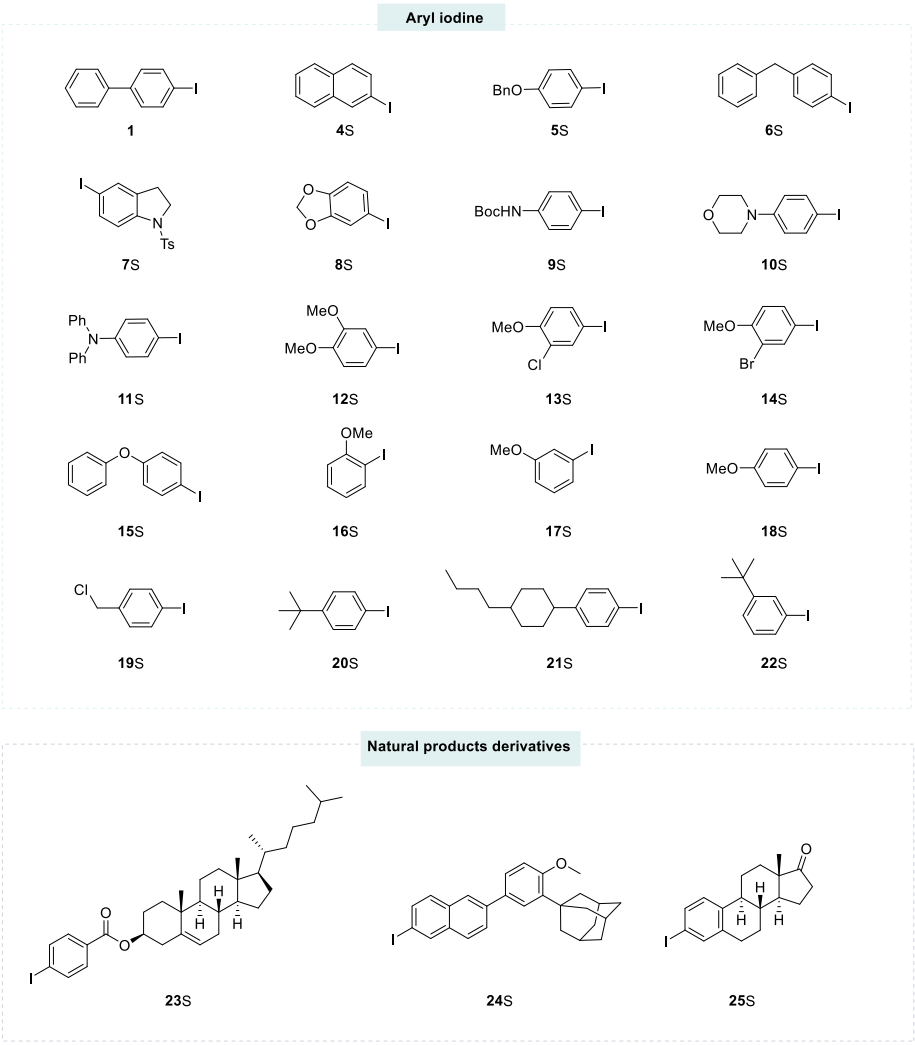
2.General Procedure: Preparation of $(DMPU)_2Zn(CF_2H)_2$

$(DMPU)_2Zn(CF_2H)_2$ **2** was synthesized according to Vicic's procedure[1].

7 mL (57.9 mmol) of DMPU was pre-cooled to -20 °C and then transferred to an oven-dried 300 mL round-bottom flask. To this solution, 10 g (55.2 mmol) HCF_2I was added, followed by the addition of 27.6 mL hexane solution of $Zn(Et)_2$ (1 M, 27.6 mmol) and 140 mL pentane. After the whole mixture was stirred at room temperature for 2 h, white solid was precipitated and collected by filtration. The solid was washed by pentane 3 times and dried under high-vac line, to give 10.4 g $(DMPU)_2Zn(CF_2H)_2$ (89% yield). The NMR data was consistent with previous report.

3. Synthesis of Aryl iodides

The aryl iodine **1, 4S, 5S, 6S, 8S, 10S, 11S, 12S, 13S, 14S, 15S, 16S, 17S, 18S, 19S, 20S, 21S, 22S** were purchase and used without further purification. **7S**[2]**, 9S**[3]**, 23S**[4]**, 24S**[5]**, 25S**[6], were prepared according to known literature procedures.

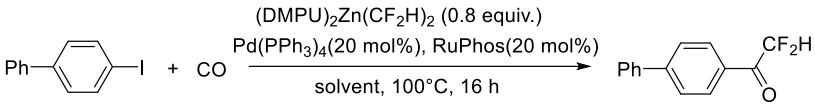


4.Optimization studies.

4.1 Screening of reaction conditions for difluoromethylation of Aryl iodides

General procedure: Catalyst (0.04 mmol, 0.2 equiv.), ligand (0.04 mmol, 0.2 equiv.), $(DMPU)_2Zn(CF_2H)_2$ (0.16 mmol, 0.8 equiv.), **3S** (55.8 mg, 0.2 mmol, 1.0 equiv.) were added in a dried 10 mL Schlenk tube and sealed it with a rubber plug. After it was evacuated and backfilled with a CO balloon three times, solvent was added via a syringe. The reaction mixture was allowed to stir at 100 ℃ for 16 h, After the reaction was completed, the mixture was diluted with EtOAc.

Table S1 The effects of solvent on the Difluoromethylcarbonylation of Aryl iodides [a-c].



1

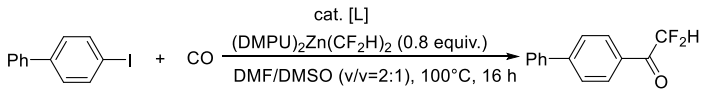
entry[a]	solvent	Yield (%)[b,c]
1	DMSO	32
2	DMSO/Toluene (v/v=1/1)	8
3	1,4-dioxane	N.D.
4	DMF	N.D.
5	DMF/DMSO (v/v=1/1)	54
6	**DMF/DMSO (v/v=2/1)**	**88**

[a] Reaction conditions: **1** (0.2 mmol), Catalyst (20 mol%), Ligand (20 mol%), CO (1 atm), $(DMPU)_2Zn(CF_2H)_2$ (0.16 mmol), solvent, at 100 °C for 16 h.

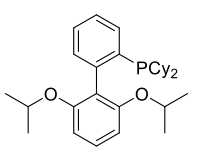
[b] Yields determined by ^{19}F NMR using $PhCF_3$ as internal standard.

[c] N.D.: Not Detected.

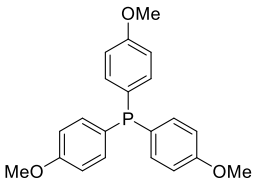
Table S2 The effects of catalysts and ligands on the Difluoromethylcarbonylation of Aryl iodides [a-c].



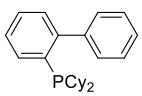
1



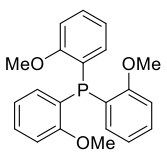
Ruphos
L1



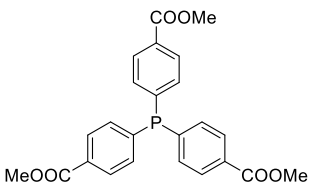
L2



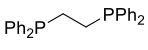
Johnphos
L3



L4



L5



L6

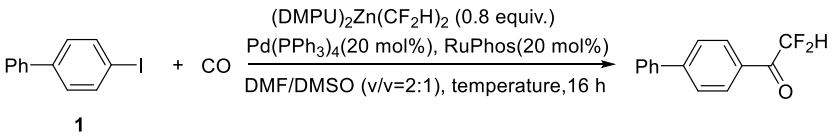
entry[a]	catalyst	ligand	Yield(%)[b,c]
1	$Ni(COD)_2$	dppf	N.D.
2	CuI	tpy	N.D.
3	**$Pd(PPh_3)_4$**	**L1**	**88**
4	$Pd(PPh_3)_4$	L2	71
5	$Pd(dmdba)_2$	L1	60
6	$Pd(PPh_3)_4$	L3	27
7	$Pd(PPh_3)_4$	L4	73
8	$Pd(PPh_3)_4$	L5	53
9	$Pd(PPh_3)_4$	L6	N.D.

[a] Reaction conditions: **1** (0.2 mmol), Catalyst (20 mol%), Ligand (20 mol%), CO (1 atm), $(DMPU)_2Zn(CF_2H)_2$ (0.16 mmol), solvent, at 100 °C for 16 h.

[b] Yields determined by ^{19}F NMR using $PhCF_3$ as internal standard.

[c] N.D.: Not Detected.

Table S3 The effects of temperature on the Difluoromethylcarbonylation of Aryl iodides [a-b].



1

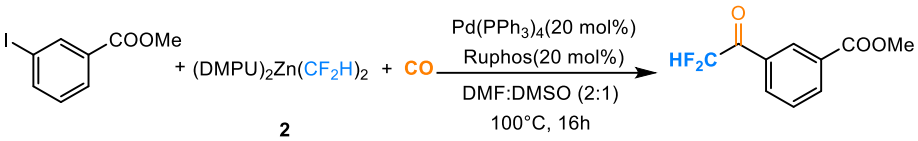
entry[a]	temperature (°C)	yield(%)[b]
1	60 °C	45
2	80 °C	60
3	**100 °C**	**88**

4	120 °C	62

[a] Reaction conditions: **1** (0.2 mmol), Catalyst (20 mol%), Ligand (20 mol%), CO (1 atm), $(DMPU)_2Zn(CF_2H)_2$ (0.16 mmol), solvent, at 100 °C for 16 h.

[b] Yields determined by ^{19}F NMR using $PhCF_3$ as internal standard.

Table S4 Screening of reaction conditions for difluoromethylation of electron-deficient Aryl iodides [a-c].



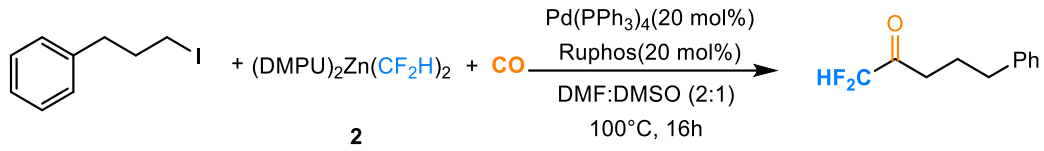
entry[a]	variation from standard conditions	yield(%)[b,c]
1	None	8%
2	$Pd(PPh_3)_4Cl_2$ instead of $Pd(PPh_3)_4$	trace
3	$Pd(OAc)_2$ instead of $Pd(PPh_3)_4$	N.D.
4	DMF as solvent	N.D.
5	DMSO as solvent	trace
6	DMF: DMSO (1:1) as solvent	trace
7	BINAP instead of Ruphos	N.D.
8	Johnphos instead of Ruphos	N.D.

[a] Reaction conditions: electron-deficient Aryl iodides (0.2 mmol), Catalyst (20 mol%), Ligand (20 mol%), CO (1 atm), $(DMPU)_2Zn(CF_2H)_2$ (0.16 mmol), solvent, at 100 °C for 16 h.

[b] Yields determined by ^{19}F NMR using $PhCF_3$ as internal standard.

[c] N.D.: Not Detected.

Table S5 Screening of reaction conditions for Difluoromethylation of alkyl iodide [a-c].



2

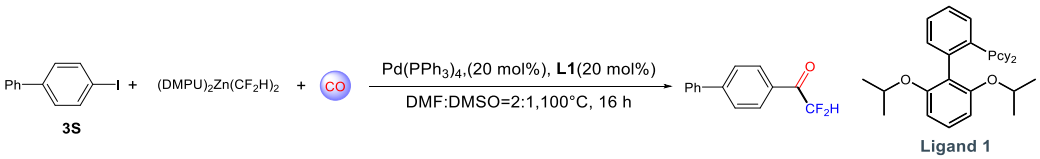
entry[a]	variation from standard conditions	yield(%)[b,c]
1	None	N.D.
2	$Pd(PPh_3)_4Cl_2$ instead of $Pd(PPh_3)_4$	N.D.
3	$Pd(OAc)_2$ instead of $Pd(PPh_3)_4$	N.D.
4	DMF as solvent	N.D.
5	DMSO as solvent	trace
6	DMF: DMSO (1:1) as solvent	N.D.
7	BINAP instead of Ruphos	N.D.
8	Johnphos instead of Ruphos	N.D.

[a] Reaction conditions: electron-deficient Aryl iodides (0.2 mmol), Catalyst (20 mol%), Ligand (20 mol%), CO (1 atm), $(DMPU)_2Zn(CF_2H)_2$ (0.16 mmol), solvent, at 100 ºC for 16 h.

[b] Yields determined by ^{19}F NMR using $PhCF_3$ as internal standard.

[c] N.D.: Not Detected.

5. General Procedure: Synthesis of Ketone Difluoromethyl Products

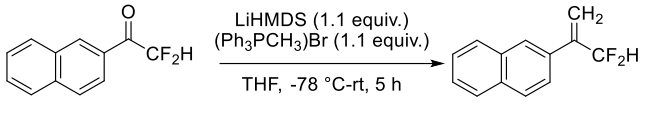


Take the reaction of **3** as an example: 4-iodo-1,1'-biphenyl **1** (0.2 mmol, 55.9 mg), $(DMPU)_2Zn(CF_2H)_2$ (0.16 mmol, 0.8 equiv. 67.5 mg), $Pd(PPh_3)_4$ (20 mol%, 46.2 mg), Ruphos (20 mol%, 18.7 mg) were added to the Schlenk tube in the mixed solvents, then stirring the reaction mixture at 100 °C under a balloon of CO overnight. Cool the

mixture to room temperature, extract with Saturated sodium bisulfite and EtOAc. Wash the organic phase with brine and dry over sodium sulfate. Filter and evaporate under reduced pressure. Purify the crude carboxylic acid by column chromatography on silica gel to obtain the product.

6. Further transformations:

6.1 Functional group conversion of compound 4



4 26

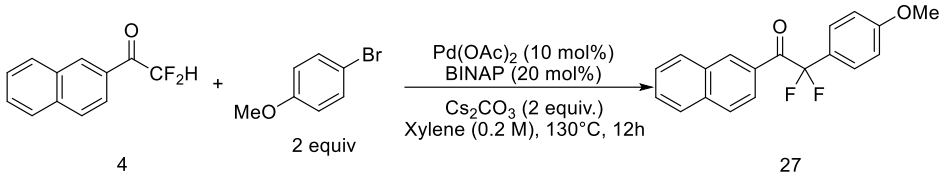
To a suspension of the phosphonium salt (78.1 mg, 0.22 mmol, 1.1 equiv.) in THF (0.16 M) was added 1M LiHMDS in THF (0.22 ml, 0.22 mmol, 1.1 equiv.) and the mixture was stirred at 0 ºC for 5 minutes. A solution of the **4** (41.2 mg, 0.2 mmol, 1 equiv.) in THF (0.6 M) was added at -78 °C. The resulting solution was allowed to warm to room temperature for 5 h. A small volume of water was added before near complete evaporation of THF. The reaction mixture was then mixed with $NaHCO_3$ and extracted with hexane (3x5ml). Optionally, the triphenylphosphine oxide precipitate could be dissolved in conc. acetic acid to extract additional product with hexane (water can be added if the phases do not separate). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated.

2 -(3 ,3 -difluoroprop-1-en- 2 -yl) naphthalene (26)[7], White solid, 29.0 mg, 71% yield, Rf =0.4 (petroleum ether).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.91 – 7.80 (m, 3H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.56 – 7.46 (m, 2H), 6.52 (t, *J* = 55.3 Hz, 1H), 5.88 (s, 1H), 5.78 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 141.9 (t, *J* = 20.0 Hz), 133.3, 132.0, 128.5, 128.4, 127.7, 126.7, 126.6, 126.3, 124.7, 119.4 (t, *J* = 9.5 Hz), 115.7 (t, *J* = 239.6 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -112.93.



4 27

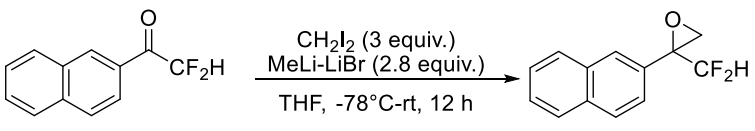
An oven-dried Schlenk tube containing a magnetic stirring bar was charged with $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), BINAP (24.9 mg, 0.04 mmol), and Cs_2CO_3 (130.3 mg, 0.4 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon three times. Xylene (0.5 mL) was added through the septum via syringe and the resulting mixture was stirred at room temperature for 15 min. Then **4** (41.2 mg, 0.2 mmol) and aryl bromide (74.4 mg, 0.4 mmol, 2 equiv.) were added. The Schlenk tube was sealed and the reaction mixture was heated at 130 ℃ with vigorous stirring for 12 h. The reaction mixture was cooled to room temperature and quenched with H_2O (20 mL). The solution was extracted with ether (3x10 mL), and the combined organic layers were washed with saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel using petroleum ether/ ethyl acetate (40/1) as eluent.

2,2-difluoro-2-(4-methoxyphenyl)-1-(naphthalen-2-yl) ethan-1-one (27)[8]**,** White solid, 35.0 mg, 56% yield, $\mathbf{R_f}$ =0.3 (petroleum ether: ethyl acetate, 50:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.04 (d, *J* = 10.5 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.87 (d, *J* = 6.3 Hz, 1H), 7.85 (d, *J* = 6.0 Hz, 1H), 7.70 – 7.48 (m, 4H), 6.98 (s, 1H), 6.96 (s, 1H), 3.82 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 189.2 (t, *J* = 31.5 Hz), 161.6, 136.0, 133.1 (t, *J* = 3.9 Hz), 132.3, 130.2, 129.5, 129.4, 128.6, 127.9, 127.4 (t, *J* = 5.9 Hz), 127.1, 125.4 (t, *J* = 28.2 Hz), 125.2, 117.4 (t, *J* = 262.6 Hz), 114.4, 55.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -95.59.



4 28

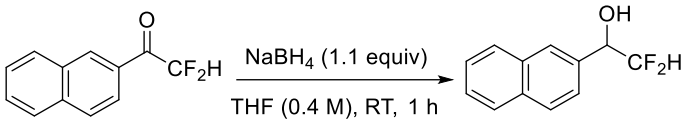
To a solution of **4** (41.2 mg, 0.2 mmol, 1 equiv.) in dry THF (3 mL) cooled to -78 °C was added diiodomethane (50 μL, 0.6 mmol, 3 equiv.) under an argon atmosphere. Then, MeLi-LiBr complex 1.5 M in diethyl ether (0.38 mL, 0.56 mmol, 2.8 equiv.) was added dropwise at -78 °C. The reaction mixture was stirred at that temperature for 1 h and then allowed to warm to room temperature overnight. The reaction mixture was quenched with water (3 mL) and extracted with Et_2O (3x5 mL). The organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated under vacuum (bath rt) to remove the solvent. The crude was purified via column chromatography (petroleum ether: ethyl acetate, 50:1, v/v) to afford the corresponding target compound in 66% yield (29.0 mg).

2-(difluoromethyl)-2-(naphthalen-2-yl) oxirane (28) [9]**,** White solid, 29.0 mg, 66% yield, $\mathbf{R}_f$ =0.3 (petroleum ether: ethyl acetate, 50:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.96 – 7.80 (m, 3H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.55 – 7.42 (m, 2H), 5.86 (t, *J* = 55.0 Hz, 1H), 3.34 (d, *J* = 5.0 Hz, 1H), 3.06 – 2.99 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 133.5, 133.0, 129.9, 128.5, 128.3, 127.9, 127.1, 126.9, 126.7, 124.4, 115.7 (t, *J* = 245.2 Hz), 58.5, 51.5 (t, *J* = 3.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -120.76 – -123.34 (m).



4 29

To an 8 mL vial equipped with a stir bar was added $NaBH_4$ (8.3 mg, 0.22 mmol, 1.1 equiv.) and **4** (41.2 mg, 0.2 mmol) in THF (0.4 M). The resulting suspension was stirred at room temperature for 1 hour. The reaction mixture was quenched with H_2O (3 mL) and extracted with CH_2Cl_2 (3x10 mL). The combined organic phases were washed with brine (10 mL), dried over Na_2SO_4, concentrated under reduced pressure, and purified by flash column chromatography using CH_2Cl_2 as eluent to afford the title product (33.7 mg, 81%) as a white solid.

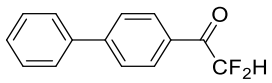
2,2-difluoro-1-(naphthalen-2-yl) ethan-1-ol (29)[10]**,** White solid, 33.7 mg, 81% yield, $\mathbf{R_f}$ =0.3 (petroleum ether: ethyl acetate, 6:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.4 Hz, 4H), 7.52 (dd, *J* = 16.6, 7.9 Hz, 3H), 5.86 (td, *J* = 56.4, 5.0 Hz, 1H), 4.95 (q, *J* = 8.8, 8.2 Hz, 1H), 3.02 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 133.6, 133.3 (t, *J* = 3.3 Hz), 133.1, 128.6, 128.2, 127.8, 126.7, 126.7, 126.6, 124.4, 115.9 (t, *J* = 245.6 Hz), 73.8 (t, *J* = 24.4 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -127.16 (d, *J* = 35.9 Hz).

7. Characterization of products



3

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

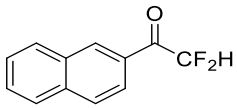
1-([1,1'-biphenyl]-4-yl)-2,2-difluoroethan-1-one (**3**)[11] (40.8 mg, 88%) White solid.

$\mathbf{R_f}$ =0.4 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.8 Hz, 2H), 7.75 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 6.9 Hz, 2H), 7.54 – 7.46 (m, 2H), 7.46 – 7.41 (m, 1H), 6.32 (t, *J* = 53.5 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.3 (t, *J* = 25.4 Hz), 147.7, 139.5, 130.4 (t, *J* = 2.2 Hz), 130.2, 129.2, 128.8, 127.7, 127.5, 111.5 (t, *J* = 253.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.72 (d, *J* = 54.1 Hz).



4

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

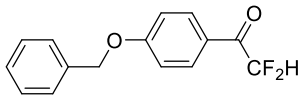
2,2-difluoro-1-(naphthalen-2-yl) ethan-1-one (**4**)[9] (33.4 mg, 81%) white solid.

$\mathbf{R_f}$ =0.4 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.06 (d, *J* = 8.7 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.92 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 6.42 (t, *J* = 1.5 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.6 (t, *J* = 25.1 Hz), 136.4, 132.6 (t, *J* = 3.3 Hz), 132.4, 130.1, 129.7, 129.1, 128.8, 128.0, 127.3, 124.1, 111.4 (t, *J* = 253.7 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -121.32 (d, *J* = 53.1 Hz).



5

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

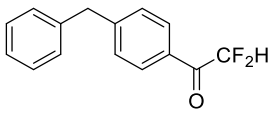
1-(4-(benzyloxy)phenyl)-2,2-difluoroethan-1-one (**5**)[7] (43.5 mg, 83%) colorless liquid.

R_f =0.3 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.58 (m, 2H), 7.49 – 7.32 (m, 6H), 7.30 – 7.27 (m, 1H), 6.28 (t, *J* = 53.5 Hz, 1H), 5.13 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 186.3 (t, *J* = 25.4 Hz), 163.8, 154.9, 132.3 (t, *J* = 2.3 Hz), 130.4, 125.9, 125.3, 120.7, 117.4, 111.6 (t, *J* = 253.6 Hz), 53.6.

^{19}F NMR (377 MHz, $CDCl_3$) δ -121.90 (d, *J* = 52.9 Hz).



6

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

1-(4-benzylphenyl)-2,2-difluoroethan-1-one (**6**) (37.4 mg, 76%) white soild.

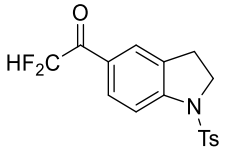
R_f =0.4 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.50 (td, *J* = 7.6, 1.4 Hz, 1H), 7.35 (td, *J* = 7.6, 1.3 Hz, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.27 – 7.20 (m, 2H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.10 (d, *J* = 6.8 Hz, 2H), 6.08 (t, *J* = 53.7 Hz, 1H), 4.27 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.3 (t, *J* = 24.5 Hz), 133.5, 132.5, 131.4, 130.2 (t, *J* = 4.0 Hz), 129.2, 128.6, 126.5, 126.3, 110.7 (t, *J* = 254.4 Hz), 39.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.80 (dd, *J* = 53.7, 1.7 Hz).

HRMS (ESI) m/z calcd for $C_{15}H_{13}F_2O$ [$(M+H)^+$]: 247.0929, found: 247.0923.



7

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

2,2-difluoro-1-(1-tosylindolin-5-yl) ethan-1-one (**7**) （52.0 mg, 74%) white solid.

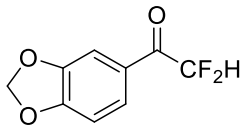
R_f =0.3 (petroleum ether: ethyl acetate, 10:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.6 Hz, 1H), 7.80 (s, 1H), 7.76 – 7.67 (m, 3H), 7.29 - 7.27 (d, *J* = 8.1 Hz, 2H), 6.22 (t, *J* = 53.6 Hz, 1H), 3.99 (t, *J* = 8.6 Hz, 2H), 3.06 (t, *J* = 8.6 Hz, 2H), 2.39 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 186.1 (t, *J* = 25.2 Hz), 148.0, 145.0, 133.8, 132.3, 131.2, 130.1, 127.3, 126.8, 126.7, 113.6, 111.5 (t, *J* = 253.9 Hz), 50.3, 27.2, 21.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.32 (d, *J* = 54.0 Hz).

HRMS (ESI) m/z calcd for $C_{17}H_{10}F_2NO_3S$ [$(M+H)^+$]: 352.0813, found: 352.0811.



8

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

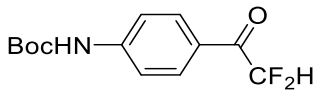
1-(benzo[d] [1,3] dioxol-5-yl)-2,2-difluoroethan-1-one (**8**)[8] (28.0 mg, 70%) white solid.

R_f =0.3 (petroleum ether: ethyl acetate, 50:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 9.9 Hz, 1H), 7.51 (s, 1H), 6.92 (d, *J* = 8.3 Hz, 1H), 6.24 (t, *J* = 53.7 Hz, 1H), 6.09 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 185.8 (t, *J* = 25.2 Hz), 153.5, 148.6, 127.0 (t, *J* = 3.3 Hz), 126.2, 111.5 (t, *J* = 253.8 Hz), 109.0 (t, *J* = 1.8 Hz), 108.5, 102.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.00 (d, *J* = 54.0 Hz).



9

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

tert-butyl (4-(2,2-difluoroacetyl) phenyl) carbamate (**9**) (40.1 mg, 74%) white solid.

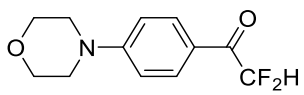
R_f =0.2 (petroleum ether: ethyl acetate, 5:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.8 Hz, 2H), 7.52 (d, *J* = 8.9 Hz, 2H), 6.78 (s, 1H), 6.26 (t, *J* = 53.6 Hz, 1H), 1.53 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 186.2 (t, *J* = 24.9 Hz), 152.0, 144.7, 131.5 (t, *J* = 2.9 Hz), 126.0, 117.7, 111.5 (t, *J* = 253.8 Hz), 81.9, 28.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.57 (d, *J* = 53.4 Hz).

HRMS (ESI) m/z calcd for $C_{13}H_{16}F_2NO_3$ $[(M+H)^+]$: 272.1093, found: 272.1090.



10

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

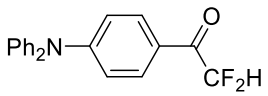
2,2-difluoro-1-(4-morpholinophenyl) ethan-1-one (**10**)[9] (32.3 mg, 67%) yellow solid.

R_f =0.3 (petroleum ether: ethyl acetate, 5:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 9.3, 1.0 Hz, 2H), 6.88 (d, *J* = 9.2 Hz, 2H), 6.25 (t, *J* = 53.8 Hz, 1H), 3.94 – 3.74 (m, 4H), 3.56 – 3.32 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 185.5 (t, *J* = 24.7 Hz), 155.2, 132.1 (d, *J* = 2.7 Hz), 121.8, 113.1, 111.8 (t, *J* = 253.3 Hz), 66.6, 47.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.22 (d, *J* = 54.0 Hz)



11

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

1-(4-(diphenyl amino) phenyl)-2,2-difluoroethan-1-one (**11**) (37.5mg, 58%) Yellow liquid.

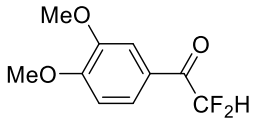
R_f =0.5 (petroleum ether: ethyl acetate, 3:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dt, *J* = 8.9, 1.0 Hz, 2H), 7.32 – 7.23 (m, 3H), 7.18 (s, 1H), 7.15 – 7.00 (m, 6H), 6.93 – 6.86 (m, 2H), 6.15 (t, *J* = 53.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 185.5 (t, *J* = 24.8 Hz), 153.7, 145.9, 131.6, 130.0, 126.7, 125.6, 123.3, 118.7, 111.8 (t, *J* = 255.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.23 (d, *J* = 54.2 Hz).

HRMS (ESI) m/z calcd for $C_{20}H_{10}F_2NO$ [$(M+H)^+$]: 324.1194, found: 324.1191.



12

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

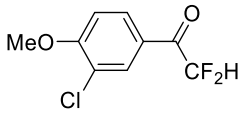
1-(3,4-dimethoxyphenyl)-2,2-difluoroethan-1-one (**12**)[10] (28.5 mg, 66%) Yellow liquid.

R_f =0.5 (petroleum ether: ethyl acetate, 3:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.57 (d, *J* = 2.0 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 6.28 (t, *J* = 53.7 Hz, 1H), 3.98 (s, 3H), 3.94 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 186.2 (t, *J* = 24.9 Hz), 155.0, 149.5, 125.2 (t, *J* = 3.6 Hz), 124.7 (t, *J* = 10.5 Hz), 111.5 (t, *J* = 253.7 Hz), 111.2, 110.4, 56.4, 56.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -108.04 (d, *J* = 56.7 Hz).



13

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

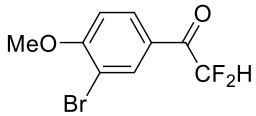
1-(3-chloro-4-methoxyphenyl)-2,2-difluoroethan-1-one (**13**)[8] (28.2 mg, 64%) yellow liquid.

R_f =0.5 (petroleum ether: ethyl acetate, 50:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 8.01 (d, *J* = 8.7 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 1H), 6.22 (t, *J* = 53.5 Hz, 1H), 4.00 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 185.5 (t, *J* = 25.5 Hz), 160.3, 131.9, 130.6, 124.9, 123.6, 111.7, 111.5 (t, *J* = 254.2 Hz), 56.7.

^{19}F NMR (377 MHz, $CDCl_3$) δ -121.17.



14

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

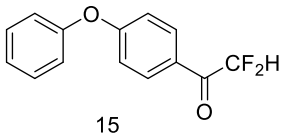
1-(3-bromo-4-methoxyphenyl)-2,2-difluoroethan-1-one (**14**)[7] (32.2 mg, 61%) Yellow liquid.

R_f =0.3 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.06 (d, *J* = 8.7 Hz, 1H), 6.99 (d, *J* = 9.3 Hz, 1H), 6.22 (t, *J* = 53.5 Hz, 1H), 4.00 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 185.4 (t, *J* = 25.7 Hz), 161.2, 135.2, 131.4 (t, *J* = 2.9 Hz), 125.4, 112.6, 111.6 (t, *J* = 254.0 Hz), 111.5, 56.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ -121.15.



15

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

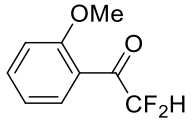
2,2-difluoro-1-(4-phenoxyphenyl) ethan-1-one (**15**)[10] (36.2 mg, 73%) white solid.

R_f =0.4 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 9.1 Hz, 2H), 7.43 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.25 – 7.20 (m, 1H), 7.10 (dt, *J* = 7.8, 1.1 Hz, 2H), 7.06 – 6.96 (m, 2H), 6.25 (t, *J* = 53.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 186.3 (t, *J* = 25.4 Hz), 163.8, 154.9, 132.3 (t, *J* = 2.3 Hz), 130.4, 125.9, 125.3, 120.7, 117.4, 111.6 (t, *J* = 255.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.33 (d, *J* = 52.8 Hz).



16

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

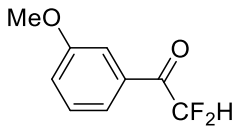
2,2-difluoro-1-(2-methoxyphenyl) ethan-1-one (**16**)[10] (29.0 mg, 78%) colorless liquid.

R_f =0.5 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.7 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.10 – 6.97 (m, 2H), 6.60 (t, *J* = 53.8 Hz, 1H), 3.94 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 189.3 (t, *J* = 24.5 Hz), 159.6, 136.0, 131.6, 123.4, 121.4, 112.0, 109.8 (t, *J* = 247.7 Hz), 56.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -128.63.



17

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

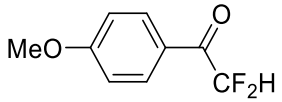
2,2-difluoro-1-(3-methoxyphenyl) ethan-1-one (**17**)[7] (26.8 mg, 72%) colorless liquid.

R_f =0.3 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 1H), 7.56 (s, 1H), 7.44 (t, *J* = 8.1 Hz, 1H), 7.22 (d, *J* = 8.7 Hz, 1H), 6.30 (t, *J* = 53.4 Hz, 1H), 3.87 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.51 (t, *J* = 25.4 Hz), 160.1, 132.8, 130.1, 122.5, 121.9,113.5, 111.1 (t, *J* = 253.6 Hz), 55.7.

^{19}F NMR (377 MHz, $CDCl_3$) δ -121.92.



18

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

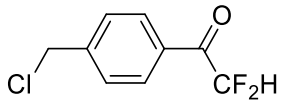
2,2-difluoro-1-(4-methoxyphenyl) ethan-1-one (**18**)[10] (28.3 mg, 76%) colorless liquid.

R_f =0.4 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 7.9 Hz, 2H), 6.25 (t, *J* = 53.7 Hz, 1H), 3.91 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 186.2 (t, *J* = 25.1 Hz), 165.0, 132.3 (d, *J* = 2.6 Hz), 124.6, 114.4, 111.7 (t, *J* = 253.7 Hz), 55.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ -121.32.



19

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

1-(4-(chloromethyl) phenyl)-2,2-difluoroethan-1-one (**19**) (31.4 mg, 77%) colorless liquid.

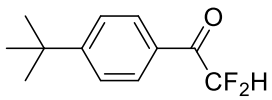
R_f =0.3 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.9 Hz, 2H), 7.56 (d, *J* = 7.9 Hz, 2H), 6.27 (t, *J* = 53.5 Hz, 1H), 4.63 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 186.9 (t, *J* = 25.8 Hz), 144.2, 131.0, 130.0 (t, *J* = 2.8 Hz), 128.8, 111.0 (t, *J* = 253.8 Hz), 44.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ -121.79.

HRMS (ESI) m/z calcd for $C_9H_8ClF_2O$ [$(M+H)^+$]: 205.0226, found: 205.0221.



20

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

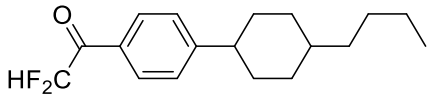
1-(4-(tert-butyl) phenyl)-2,2-difluoroethan-1-one (**20**)[8] (30.1 mg, 71%) white liquid.

R_f =0.4 (petroleum ether)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.9 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H), 6.28 (t, *J* = 53.6 Hz, 1H), 1.35 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.3 (t, *J* = 25.1 Hz), 159.2, 129.8 (t, *J* = 2.2 Hz), 129.0, 126.1, 111.4 (t, *J* = 253.6 Hz), 35.5, 31.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.90 (d, *J* = 53.8 Hz).



21

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

2,2-difluoro-1-(4-(4-propylcyclohexyl)phenyl)ethan-1-one (**21**) (46.5 mg, 79%) colorless liquid.

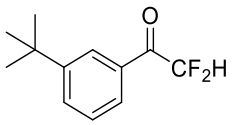
R_f =0.5 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 6.28 (t, *J* = 53.6 Hz, 1H), 2.56 (tt, *J* = 12.3, 3.1 Hz, 1H), 1.90 (d, *J* = 12.6 Hz, 4H), 1.55 – 1.40 (m, 2H), 1.36 – 1.28 (m, 5H), 1.25 (dd, *J* = 7.7, 4.5 Hz, 2H), 1.13 – 1.00 (m, 2H), 0.94 – 0.88 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.3 (t, *J* = 25.1 Hz), 156.0, 130.0 (t, *J* = 2.3 Hz), 129.4 (t, *J* = 1.8 Hz), 127.7, 111.4 (t, *J* = 253.5 Hz), 45.1, 37.3, 37.1, 34.0, 33.5, 29.3, 23.1, 14.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.89 (d, *J* = 53.5 Hz).

HRMS (ESI) m/z calcd for $C_{17}H_{23}F_2O$ $[(M+H)^+]$: 281.1711, found: 281.1708



22

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

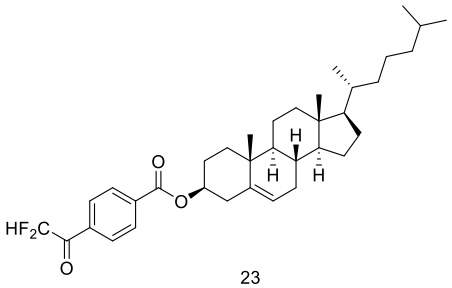
1-(3-(tert-butyl)phenyl)-2,2-difluoroethan-1-one (**22**)[10] (28.8 mg, 68%) colorless liquid.

R_f =0.5 (petroleum ether: ethyl acetate, 100:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (t, *J* = 1.9 Hz, 1H), 7.89 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.72 (m, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 6.32 (t, *J* = 53.5 Hz, 1H), 1.36 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.0 (t, *J* = 25.1 Hz), 152.4, 132.4, 131.5 (t, *J* = 0.1 Hz), 128.8, 127.1 (t, *J* = 2.8 Hz), 126.5 (t, *J* = 1.9 Hz), 111.3 (t, *J* = 253.6 Hz), 35.0, 31.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.87 (d, *J* = 53.6 Hz).



23

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-(2,2-difluoroacetyl)benzoate (**23**) (61.4 mg, 54%) white solid.

R_f =0.4 (petroleum ether: ethyl acetate, 20:1, v/v)

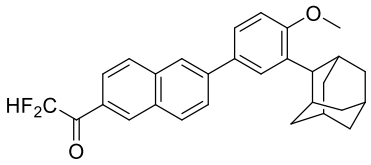
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.4 Hz, 2H), 8.13 (d, *J* = 8.3 Hz, 2H), 6.29 (t, *J* = 53.4 Hz, 1H), 5.43 (d, *J* = 5.1 Hz, 1H), 4.95 – 4.80 (m, 1H), 2.48 (d, *J* =

7.9 Hz, 2H), 2.05 – 1.97 (m, 3H), 1.96 – 1.90 (m, 1H), 1.87 – 1.79 (m, 1H), 1.78 – 1.70 (m, 1H), 1.54 – 1.45 (m, 6H), 1.42 – 1.29 (m, 6H), 1.23 – 1.10 (m, 6H), 1.07 (s, 4H), 1.05 – 0.95 (m, 4H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.87 (dd, *J* = 6.6, 1.9 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.5 (t, *J* = 25.0 Hz), 164.9, 139.5, 136.3, 134.5, 130.1, 129.7, 123.2, 111.3 (t, *J* = 254.1 Hz), 75.6, 56.8, 56.3, 50.2, 42.5, 39.8(d, *J* = 20.3 Hz), 38.3, 37.1, 36.8, 36.3, 35.9, 32.0 (d, *J* = 7.3 Hz), 29.9, 28.2 (t, *J* = 21.2 Hz), 24.4 , 24.0 , 23. , 22.7 , 21.6, 21.2, 19.5, 18.9, 12.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.91 (d, *J* = 54.0 Hz).

HRMS (ESI) m/z calcd for $C_{36}H_{51}F_2O_3$ $[(M+H)^+]$: 569.3801, found: 569.3795.



24

According to **general procedure II**, the crude product was purified by silica gel column chromatography to afford the desired product.

1-(6-(3-(adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)-2,2-difluoroethan-1-one (**24**) (50.9 mg, 57%) white solid.

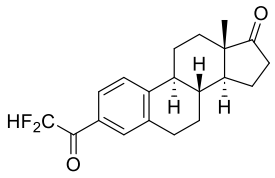
R_f =0.3 (petroleum ether: ethyl acetate, 50:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.12 – 7.95 (m, 4H), 7.85 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.62 (d, *J* = 2.4 Hz, 1H), 7.57 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 1H), 6.42 (t, *J* = 53.6 Hz, 1H), 3.91 (s, 3H), 2.22 – 2.08 (m, 9H), 1.80 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.5 (t, *J* = 25.0 Hz), 159.3, 142.9, 139.3, 136.9, 132.5 (d, *J* = 3.5 Hz), 132.2, 131.1, 130.6, 130.1, 128.4, 127.1, 126.1, 126.0, 124.9, 124.6, 112.3, 111.5 (t, *J* = 253.6 Hz), 55.3, 40.7, 37.2, 29.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.17 (d, *J* = 54.0 Hz).

HRMS (ESI) m/z calcd for $C_{29}H_{29}F_2O_2$ $[(M+H)^+]$: 447.2130, found: 447.2126.



25

According to **general procedure**, the crude product was purified by silica gel column chromatography to afford the desired product.

(8R,9S,13S,14S)-3-(2,2-difluoroacetyl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (**25**)[12] (28.6 mg, 43%) white solid.

R_f =0.3 (petroleum ether: ethyl acetate, 50:1, v/v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.3 Hz, 2H), 7.79 (s, 1H), 7.44 (d, *J* = 7.4 Hz, 1H), 2.98 (s, 2H), 2.61 – 2.41 (m, 2H), 2.36 (s, 1H), 2.17 (q, *J* = 9.2 Hz, 1H), 2.11 – 2.05 (m, 2H), 1.98 (dd, *J* = 8.8, 5.9 Hz, 1H), 1.68 (d, *J* = 8.9 Hz, 1H), 1.65 – 1.59 (m, 2H), 1.53 (t, *J* = 11.6 Hz, 3H), 0.92 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.5 (t, *J* = 25.0 Hz), 147.9, 137.7, 130.3, 129.3, 127.1, 126.1, 111.2 (t, *J* = 253.4 Hz), 50.6, 48.0, 44.9, 37.7, 35.9, 31.6, 29.3, 26.2, 25.6, 21.7, 13.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.88 (d, *J* = 54.0 Hz).

8. References

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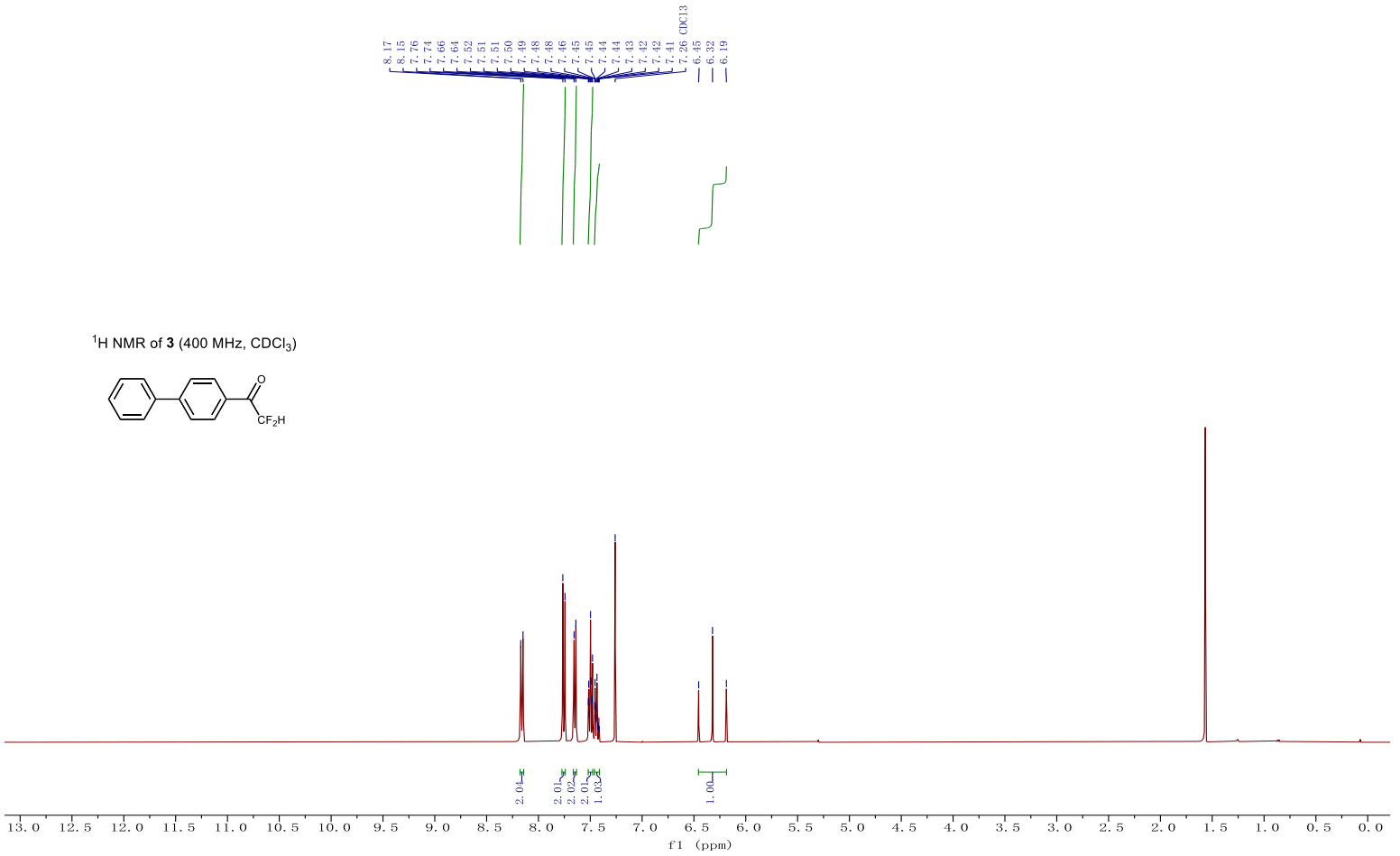
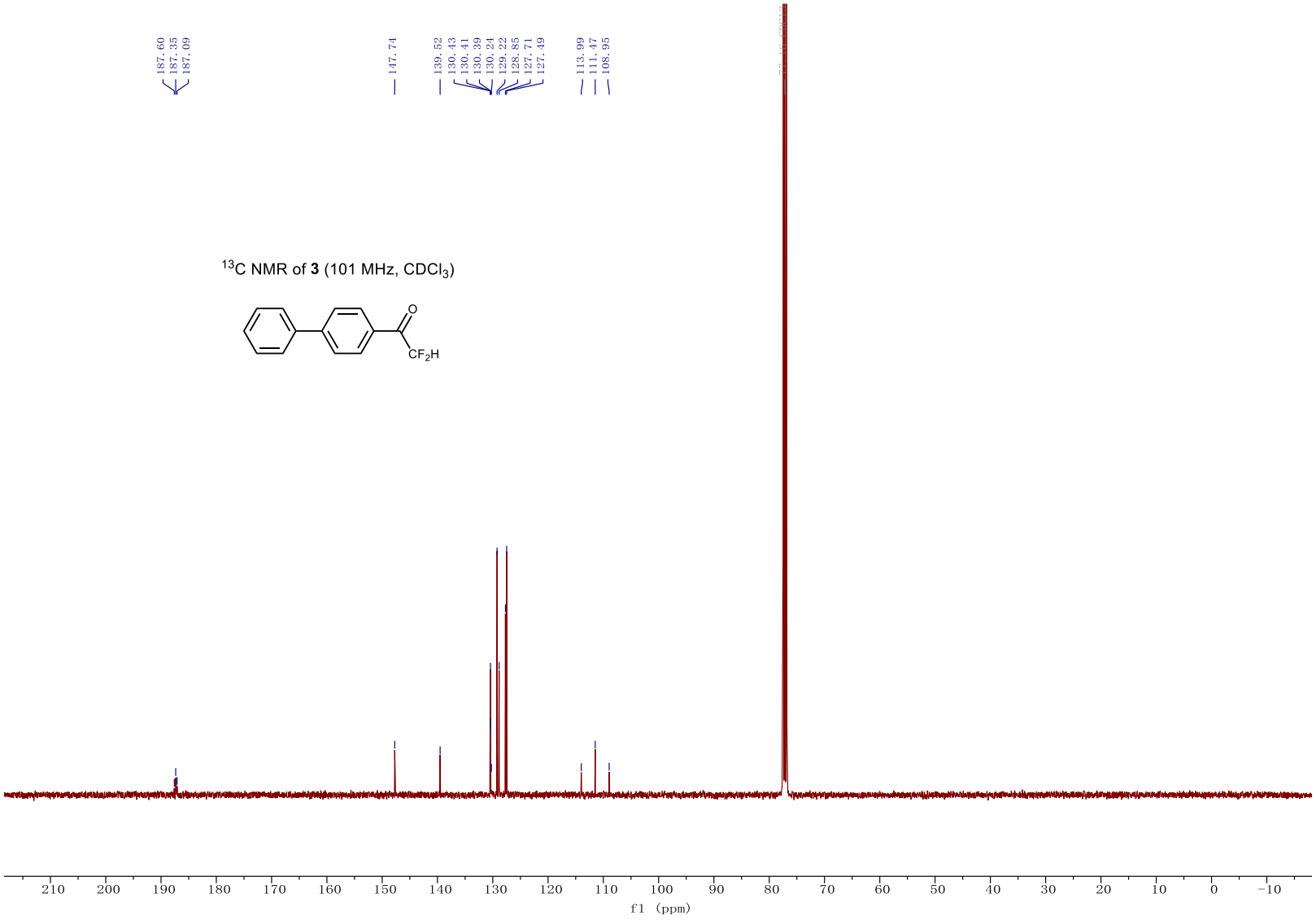
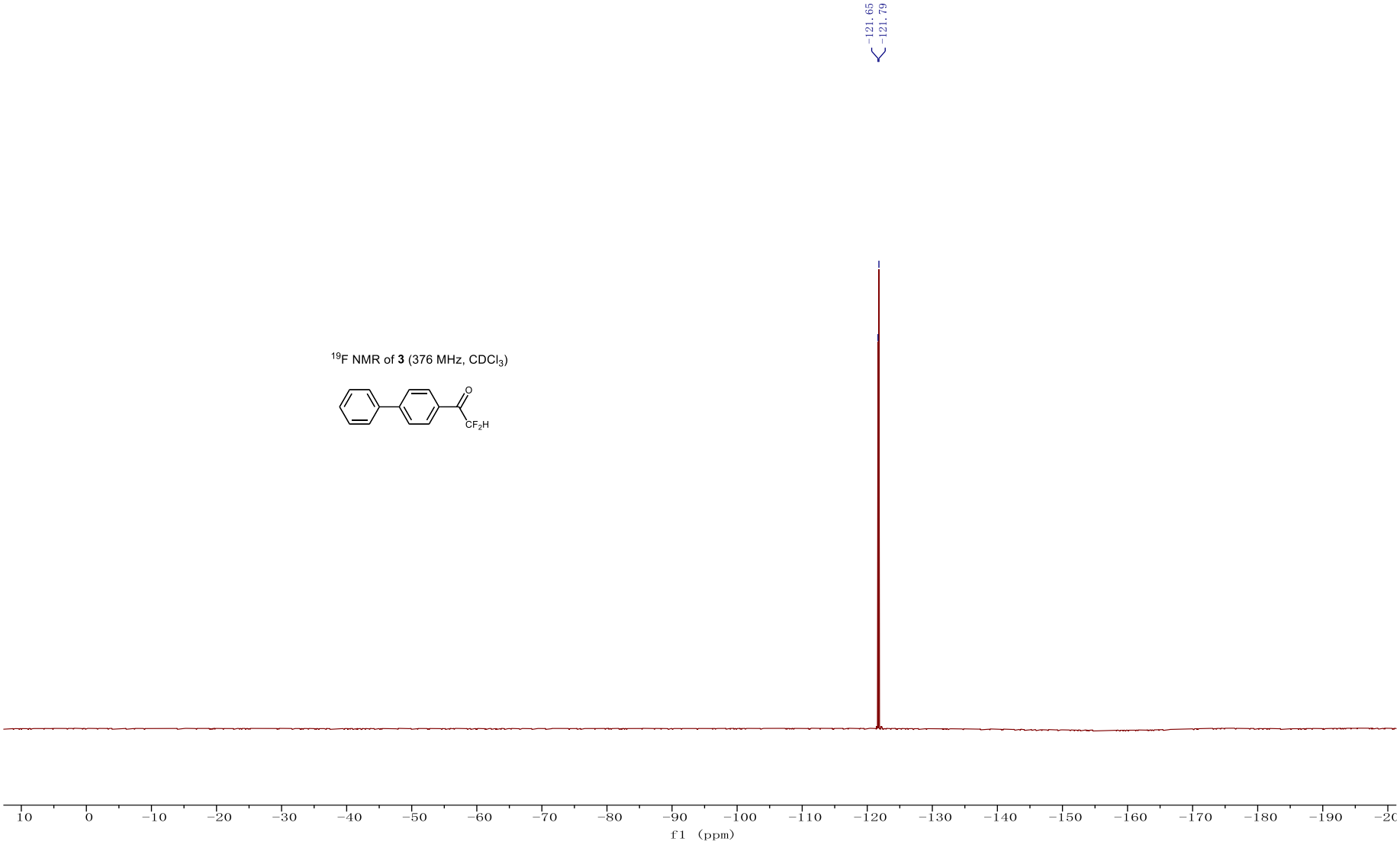
9. NMR Spectra

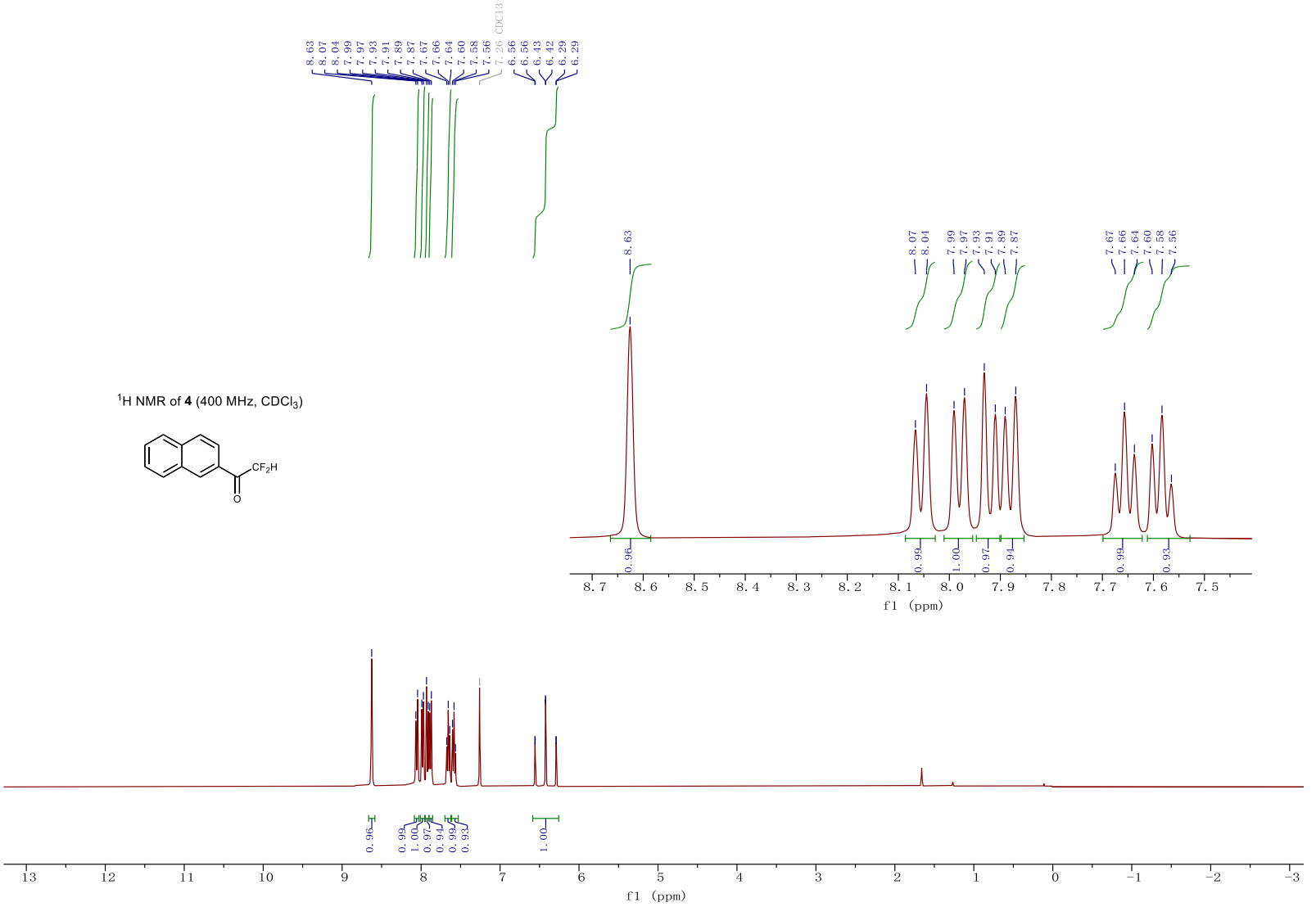


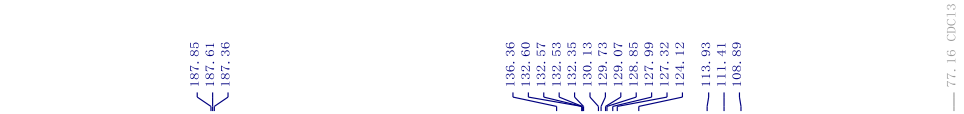


^{13}C NMR of **3** (101 MHz, $CDCl_3$)

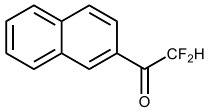
^{19}F NMR of **3** (376 MHz, $CDCl_3$)

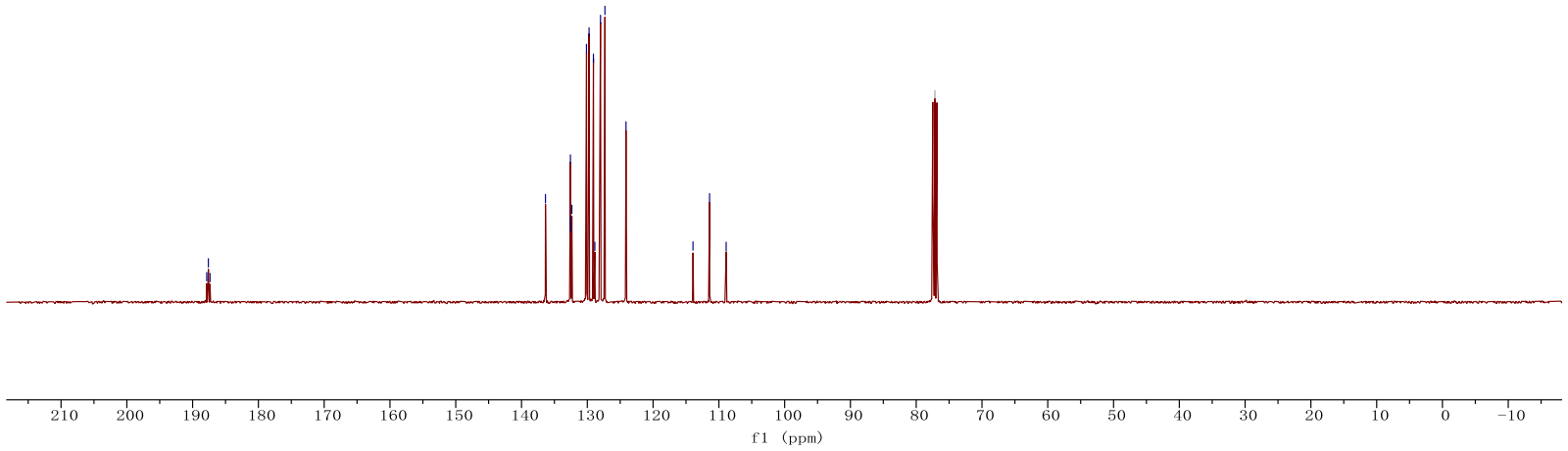



8.63
8.07
8.04
7.99
7.97
7.93
7.91
7.89
7.87
7.67
7.66
7.64
7.60
7.58
7.56
7.26 CDCl3
6.56
6.56
6.43
6.42
6.29
6.29
^{1}H NMR of **4** (400 MHz, $CDCl_3$)
CF_2H
O
0.96
0.99
1.00
0.97
0.94
0.99
0.93
1.00
f1 (ppm)

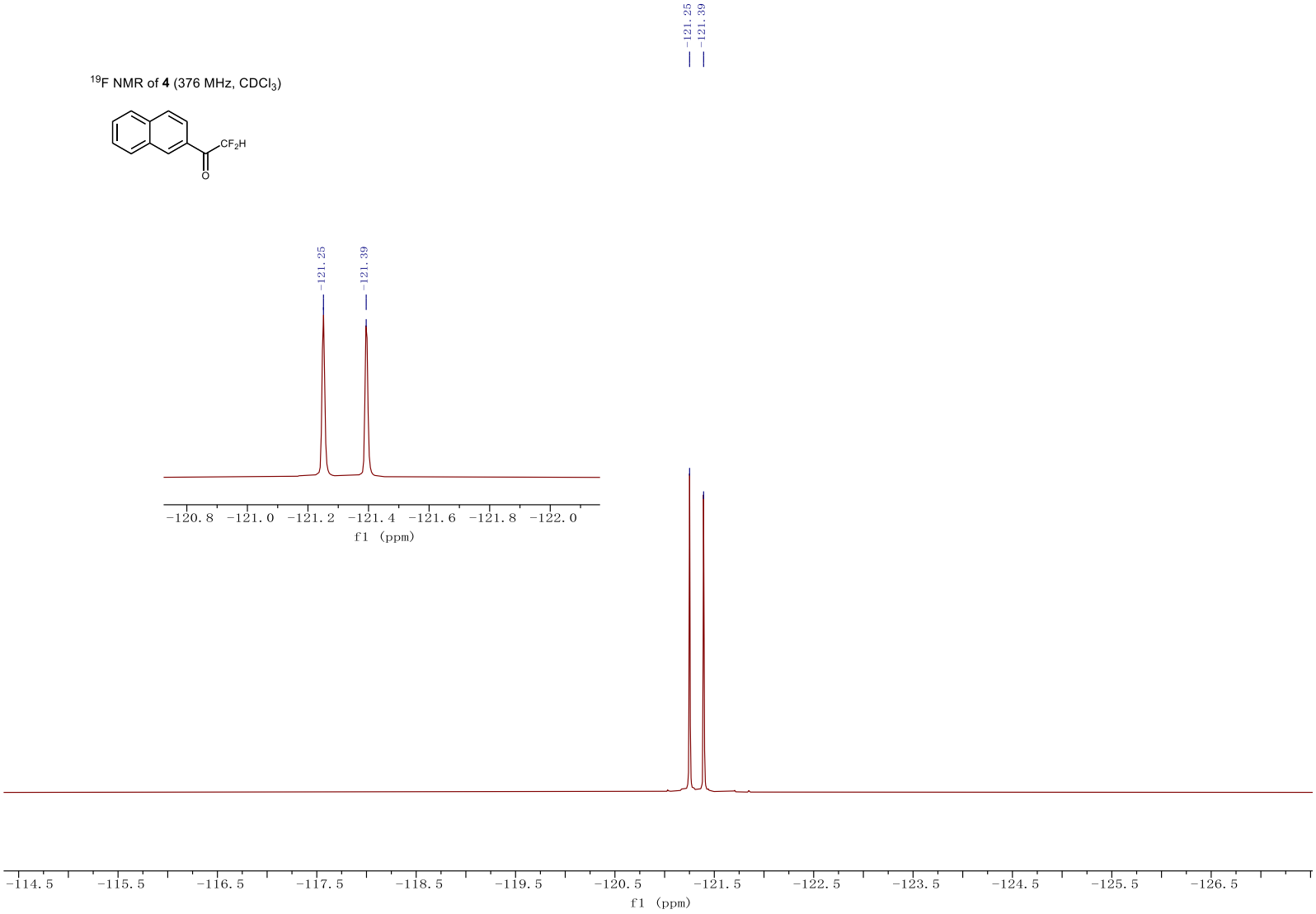


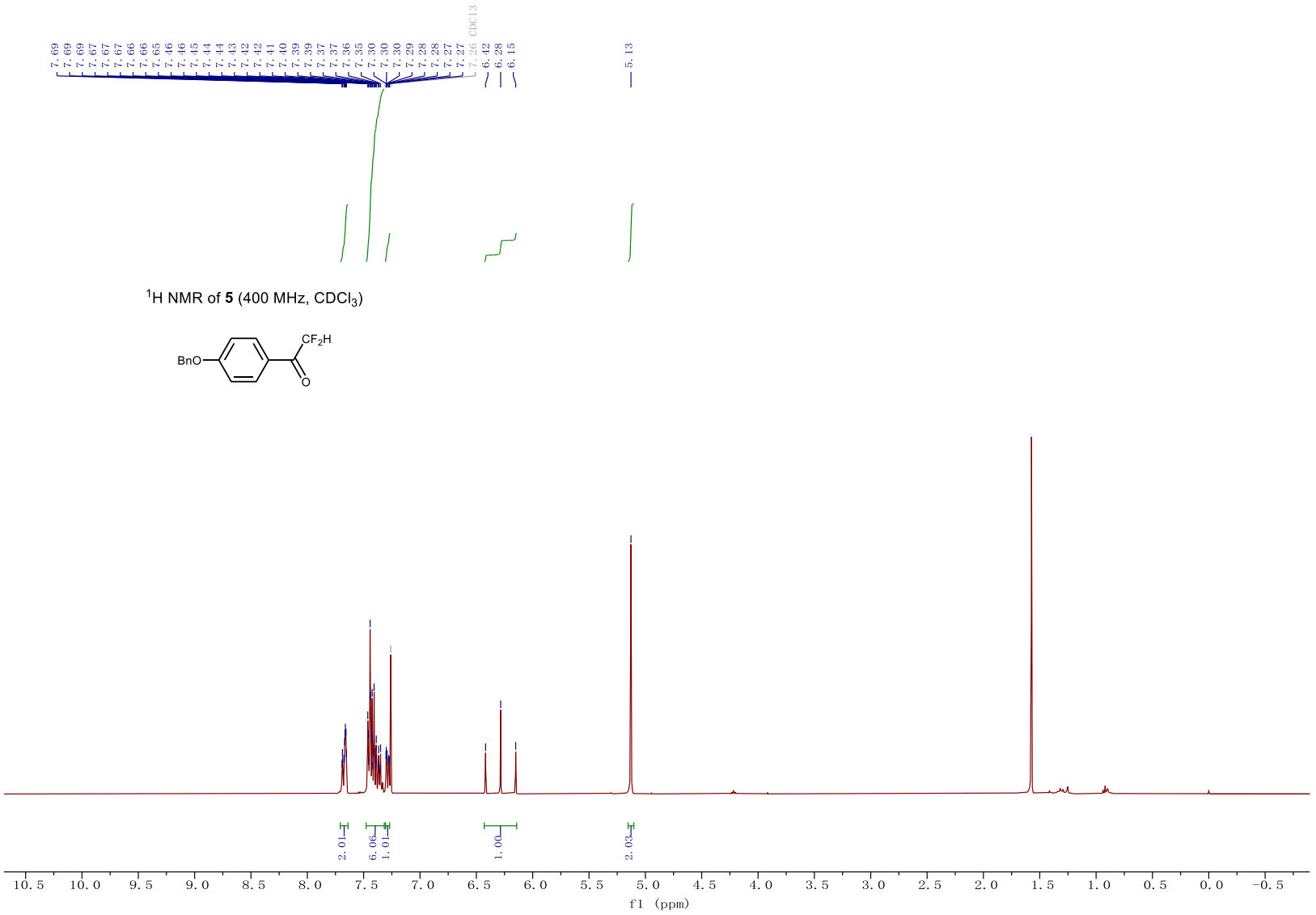
^{13}C NMR of **4** (101 MHz, $CDCl_3$)



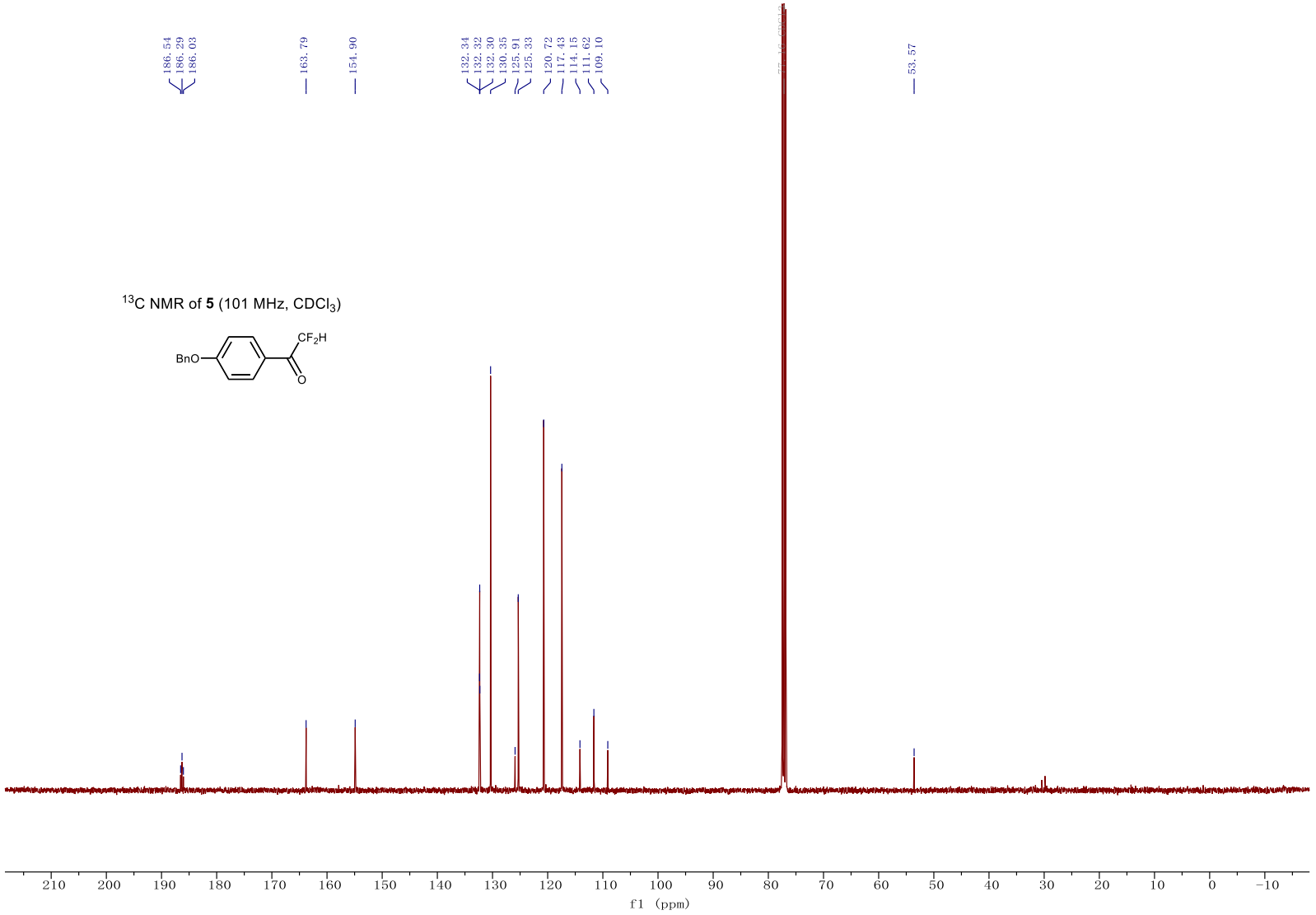


^{19}F NMR of **4** (376 MHz, $CDCl_3$)

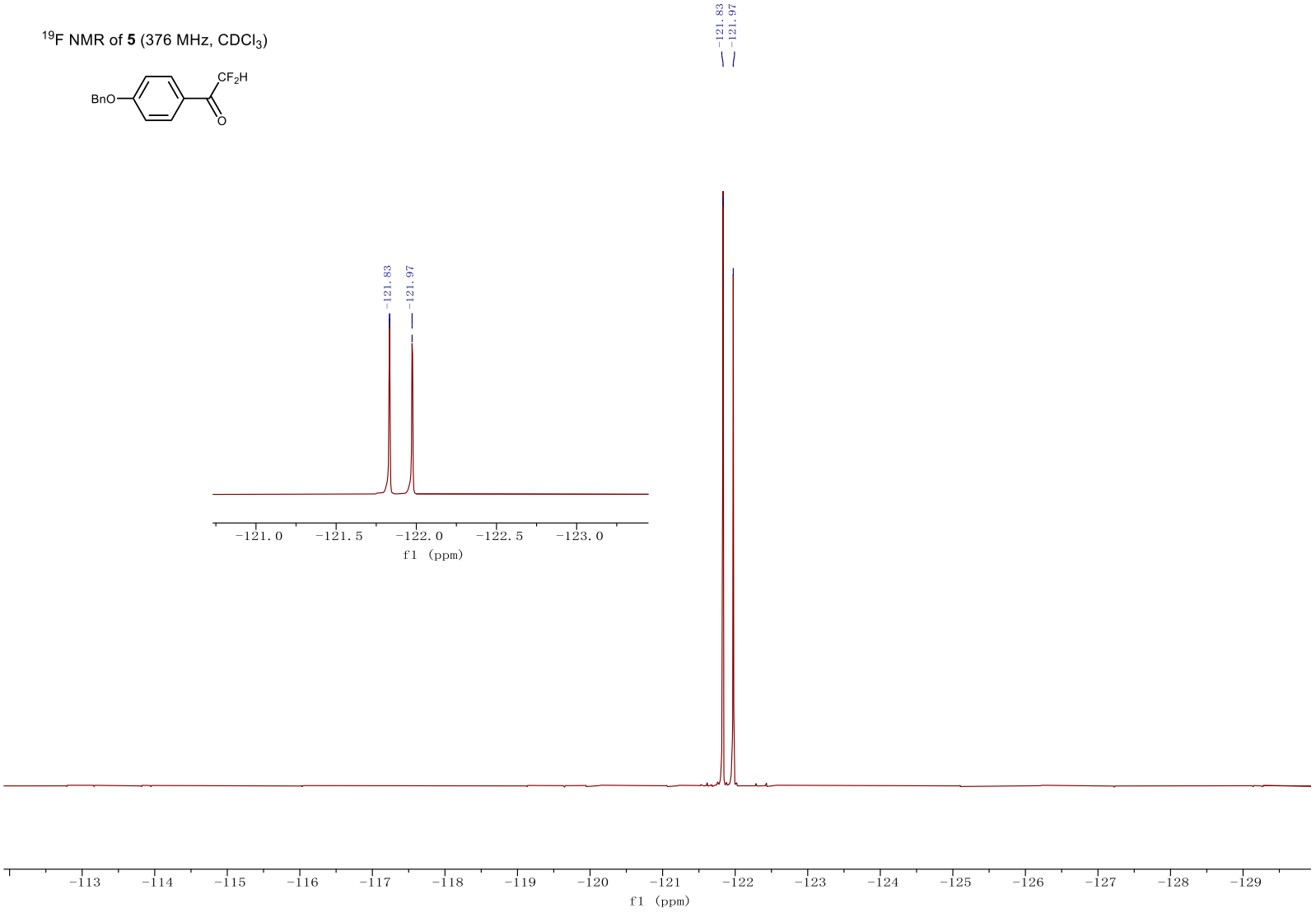


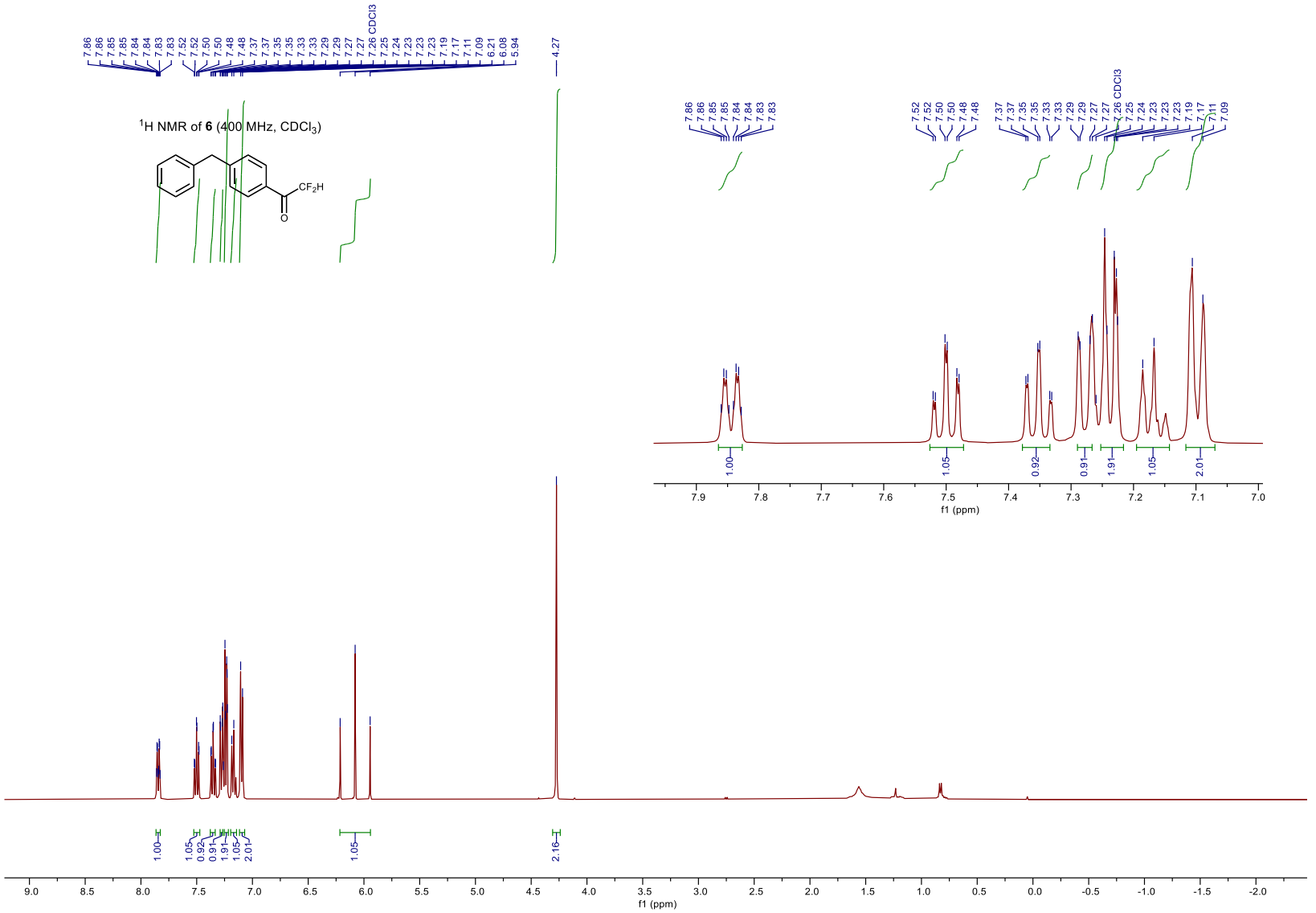


^{1}H NMR of **5** (400 MHz, $CDCl_3$)

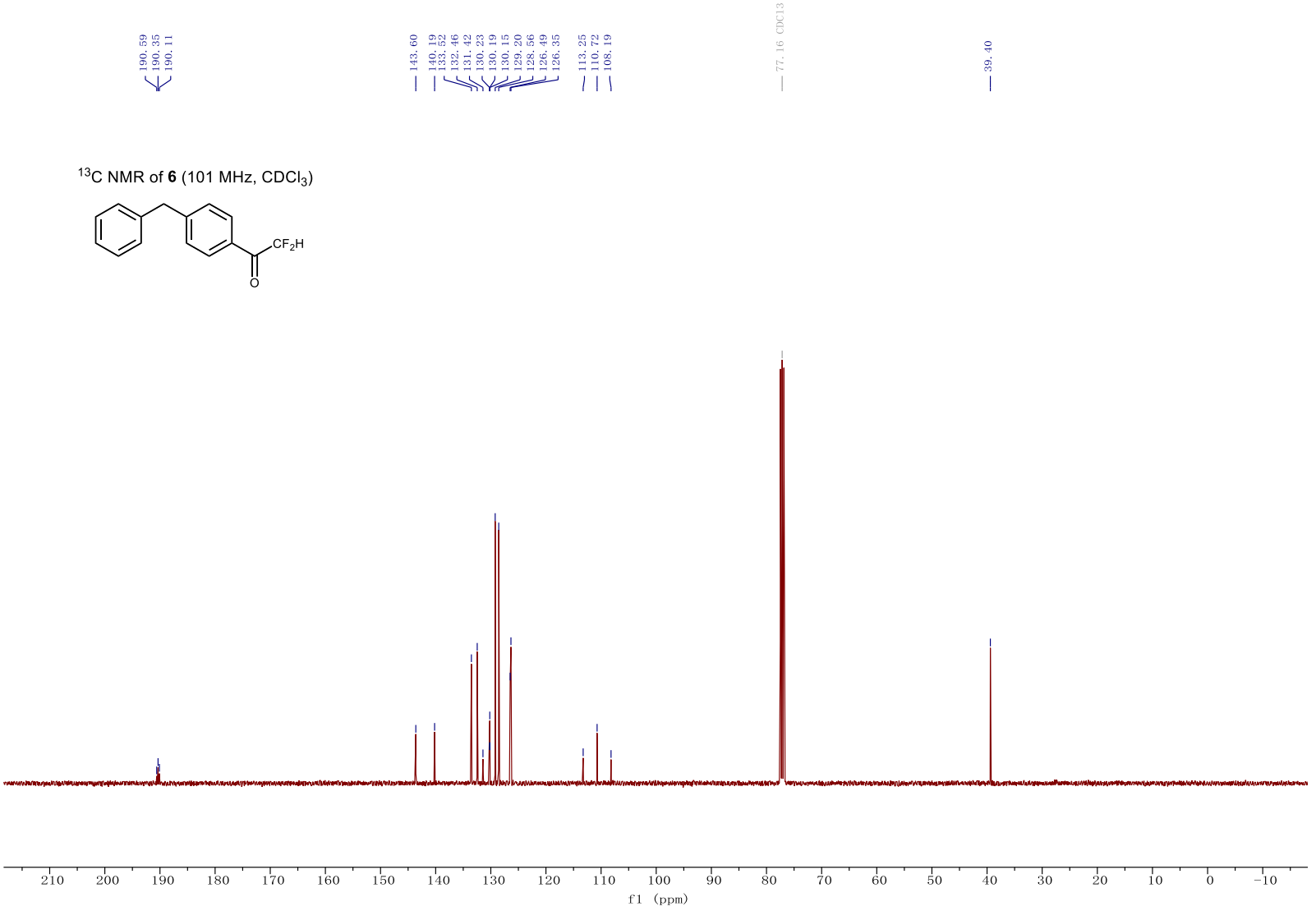

186.54
186.29
186.03
163.79
154.90
132.34
132.32
132.30
130.35
125.91
125.33
120.72
117.43
114.15
111.62
109.10
77.16 CDCl3
53.57
^{13}C NMR of **5** (101 MHz, $CDCl_3$)
BnO
CF_2H
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

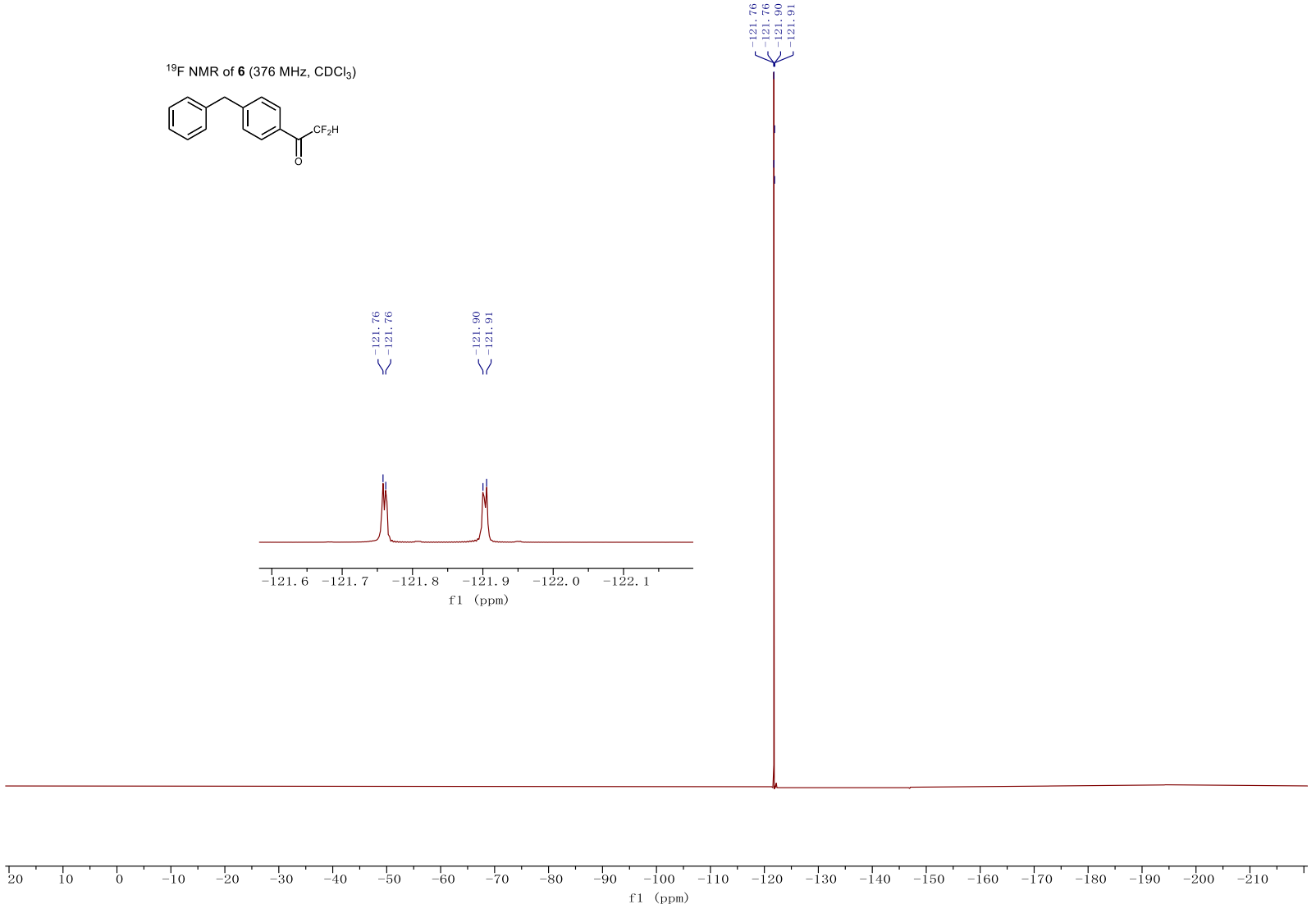
^{19}F NMR of **5** (376 MHz, $CDCl_3$)

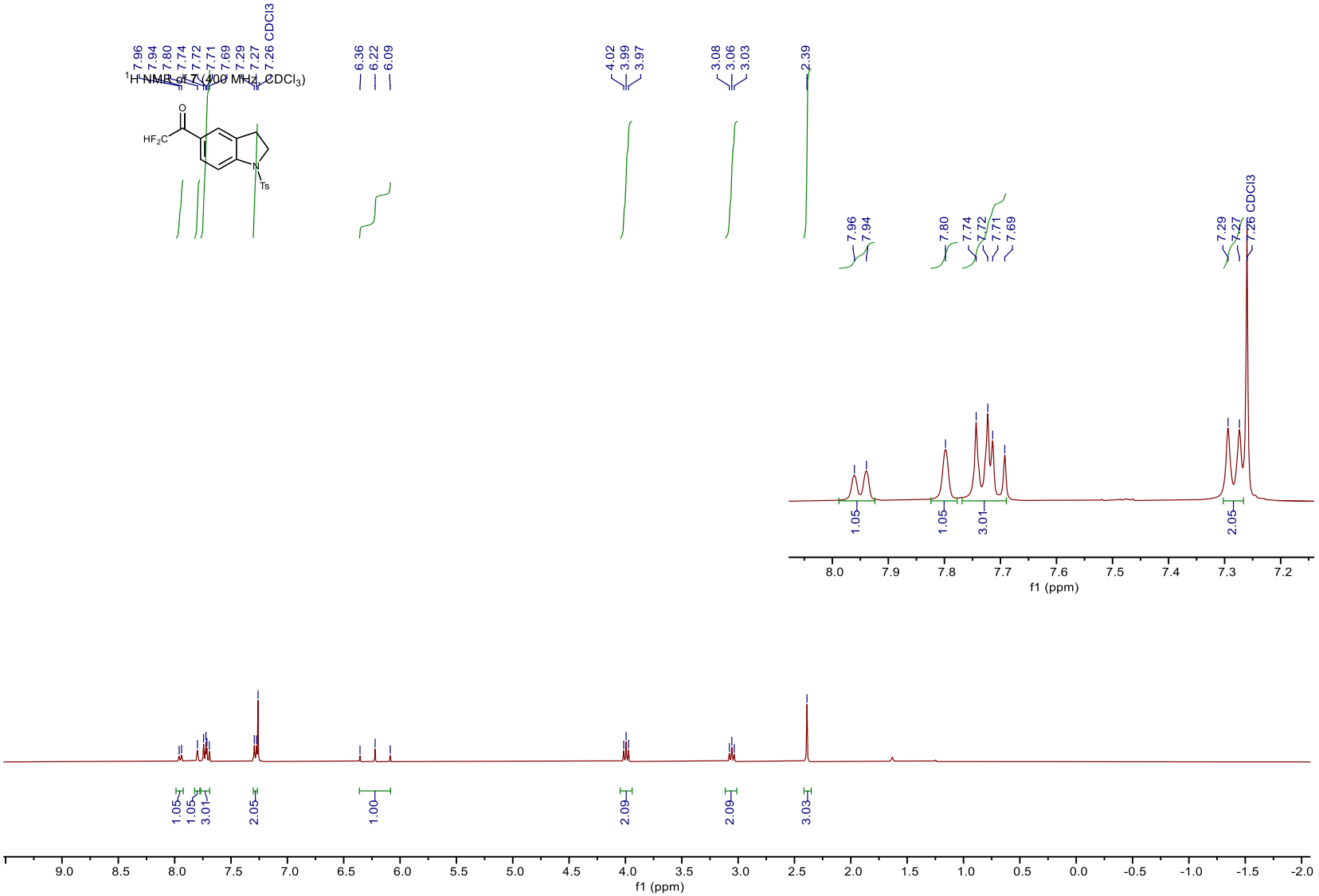


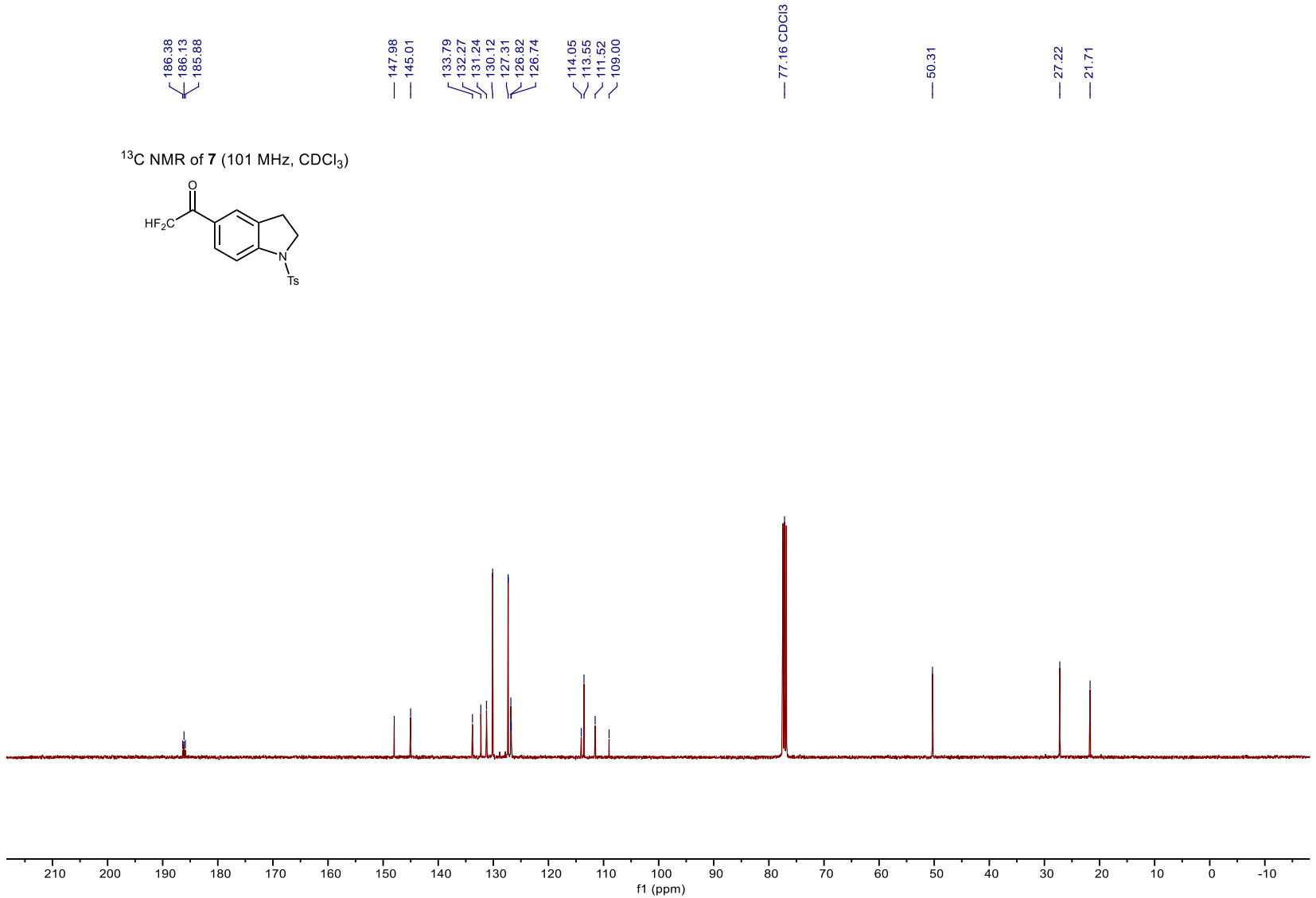

^{1}H NMR of **6** (400 MHz, $CDCl_3$)
CF_2H
O
CDCl3
f1 (ppm)

^{13}C NMR of **6** (101 MHz, $CDCl_3$)



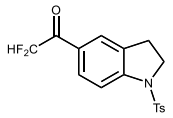

19F NMR of 6 (376 MHz, CDCl3)
CF2H
O
-121.76
-121.76
-121.90
-121.91
-121.76
-121.76
-121.90
-121.91
-121.6
-121.7
-121.8
-121.9
-122.0
-122.1
f1 (ppm)
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

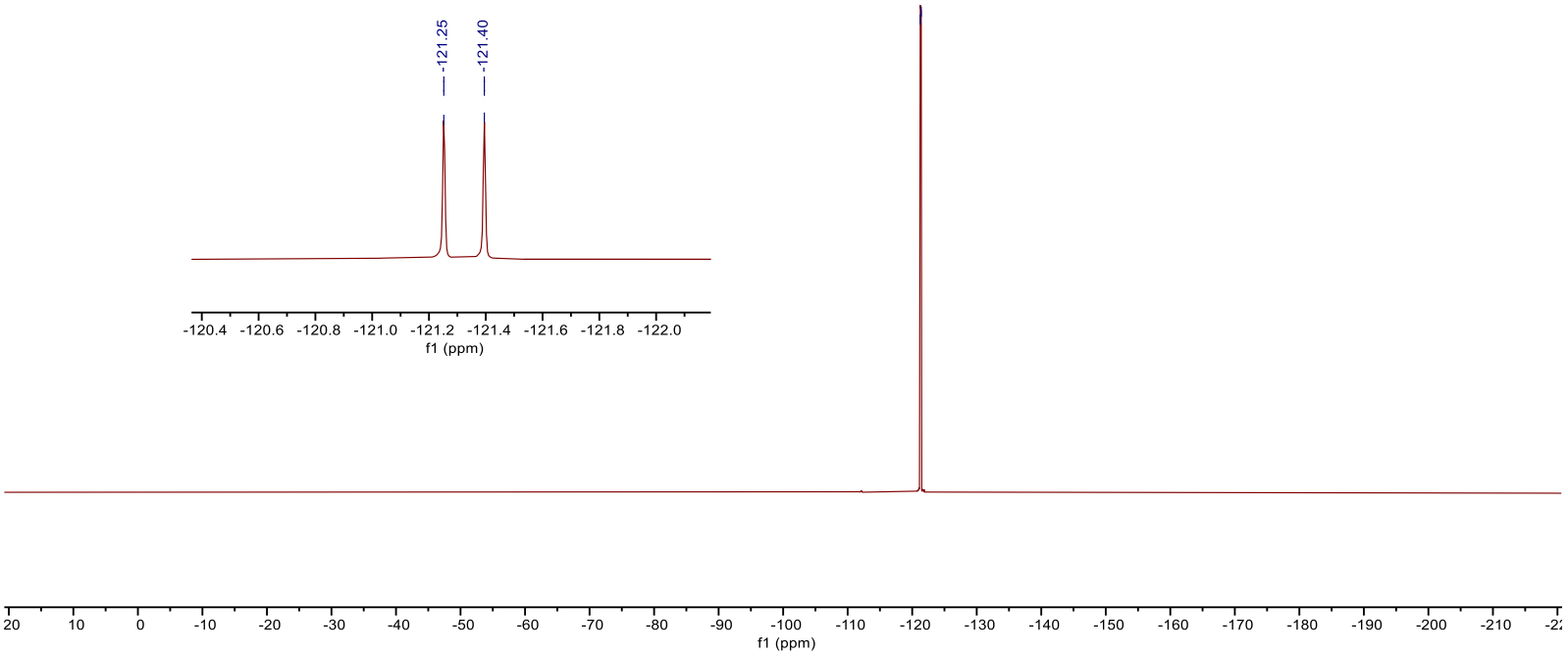

^{1}H NMR of 7 (400 MHz, $CDCl_3$)
7.96
7.94
7.80
7.74
7.72
7.71
7.69
7.29
7.27
7.26 CDCl3
6.36
6.22
6.09
4.02
3.99
3.97
3.08
3.06
3.03
2.39
O
HF_2C
N
Ts
1.05
1.05
3.01
2.05
1.00
2.09
2.09
3.03
f1 (ppm)



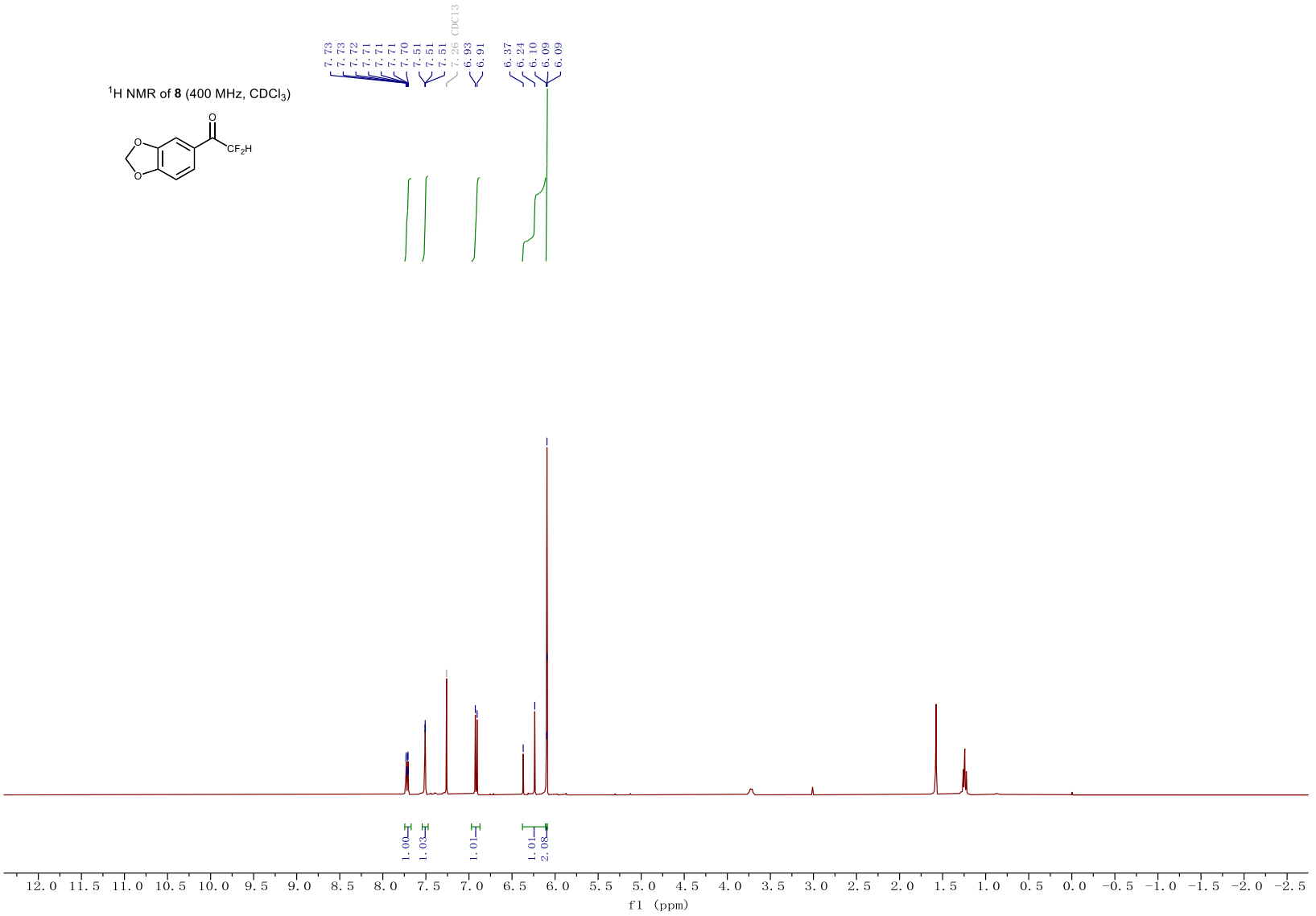
^{13}C NMR of **7** (101 MHz, $CDCl_3$)

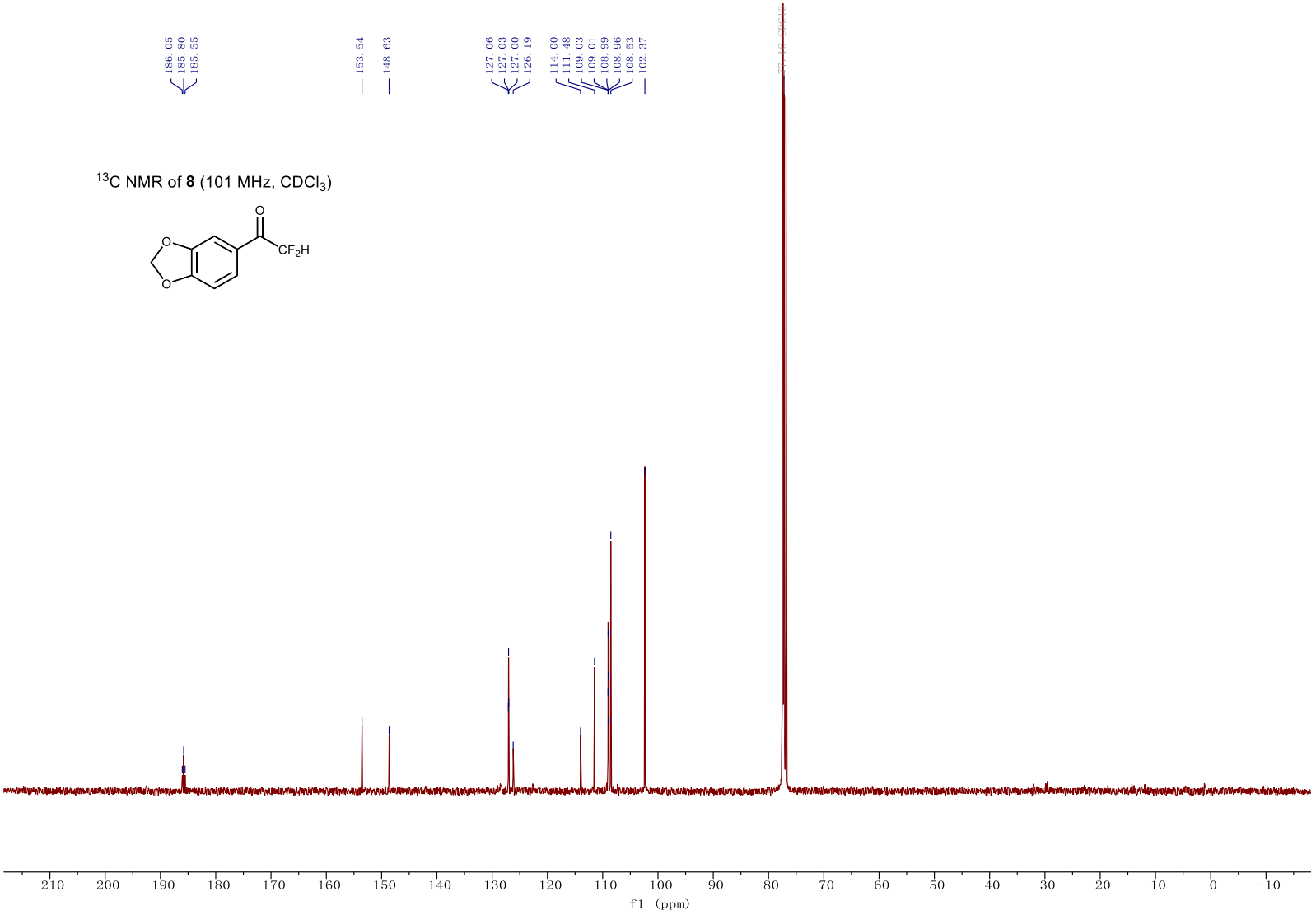
^{19}F NMR of **7** (376 MHz, $CDCl_3$)



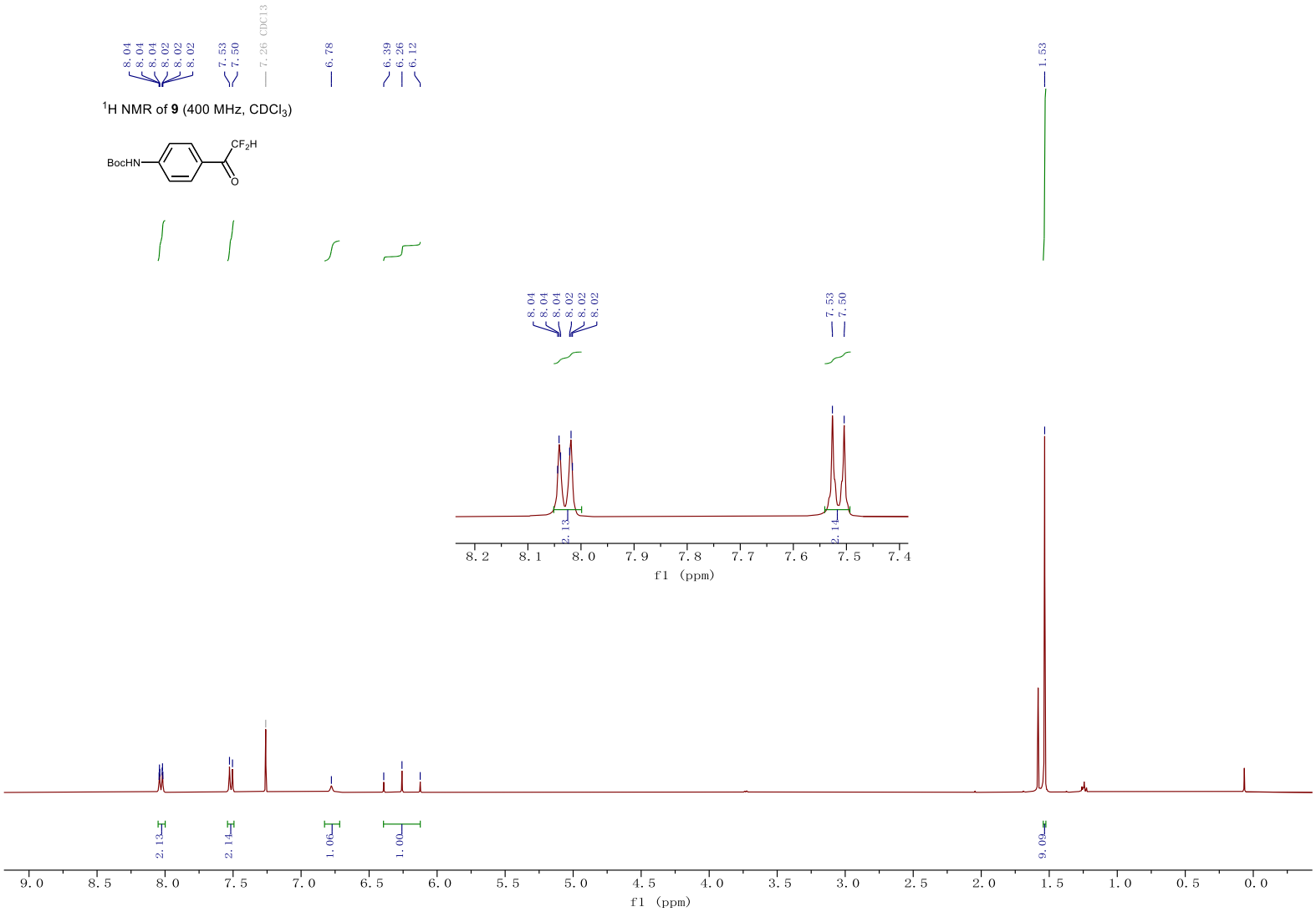


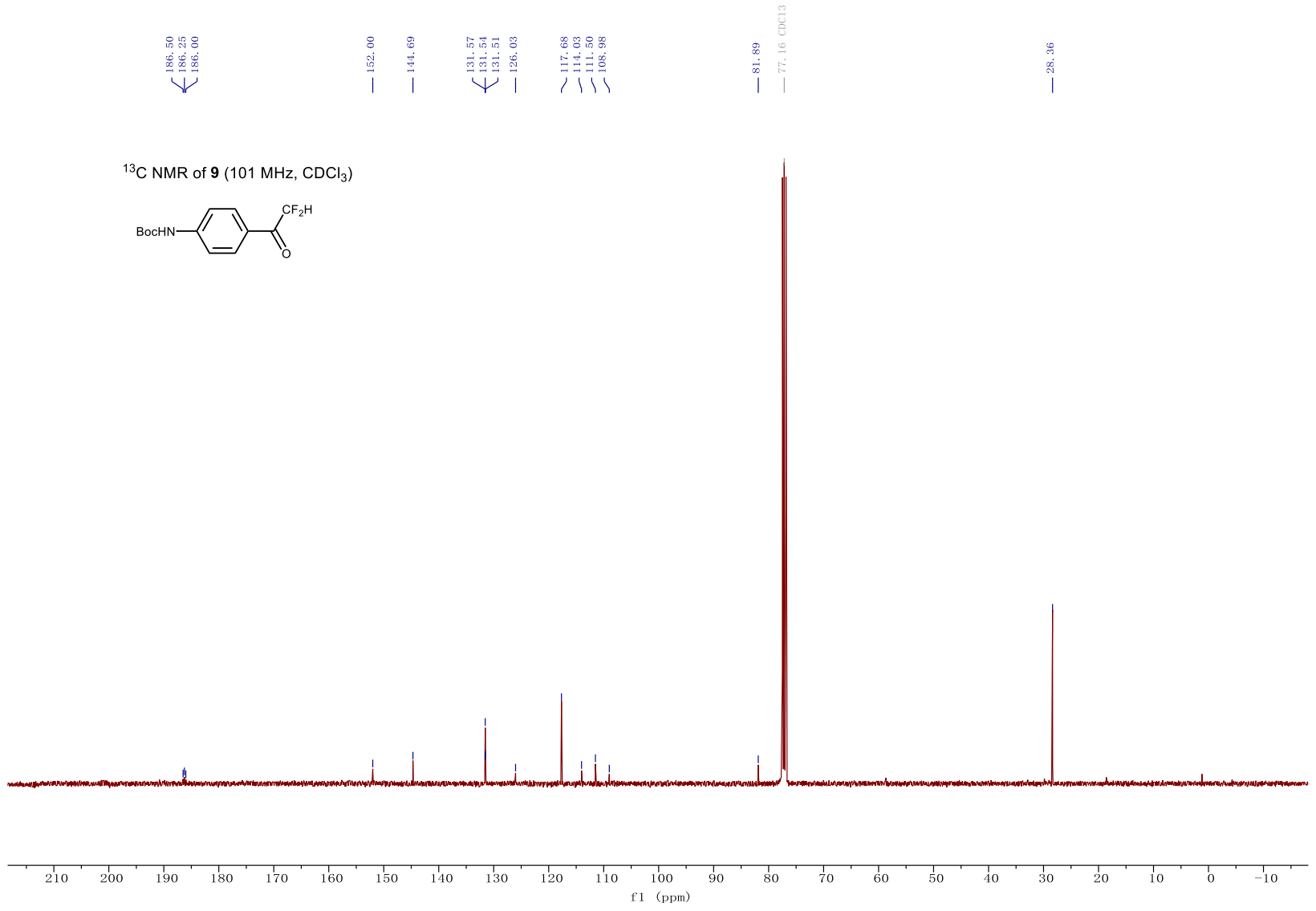
^{1}H NMR of **8** (400 MHz, $CDCl_3$)



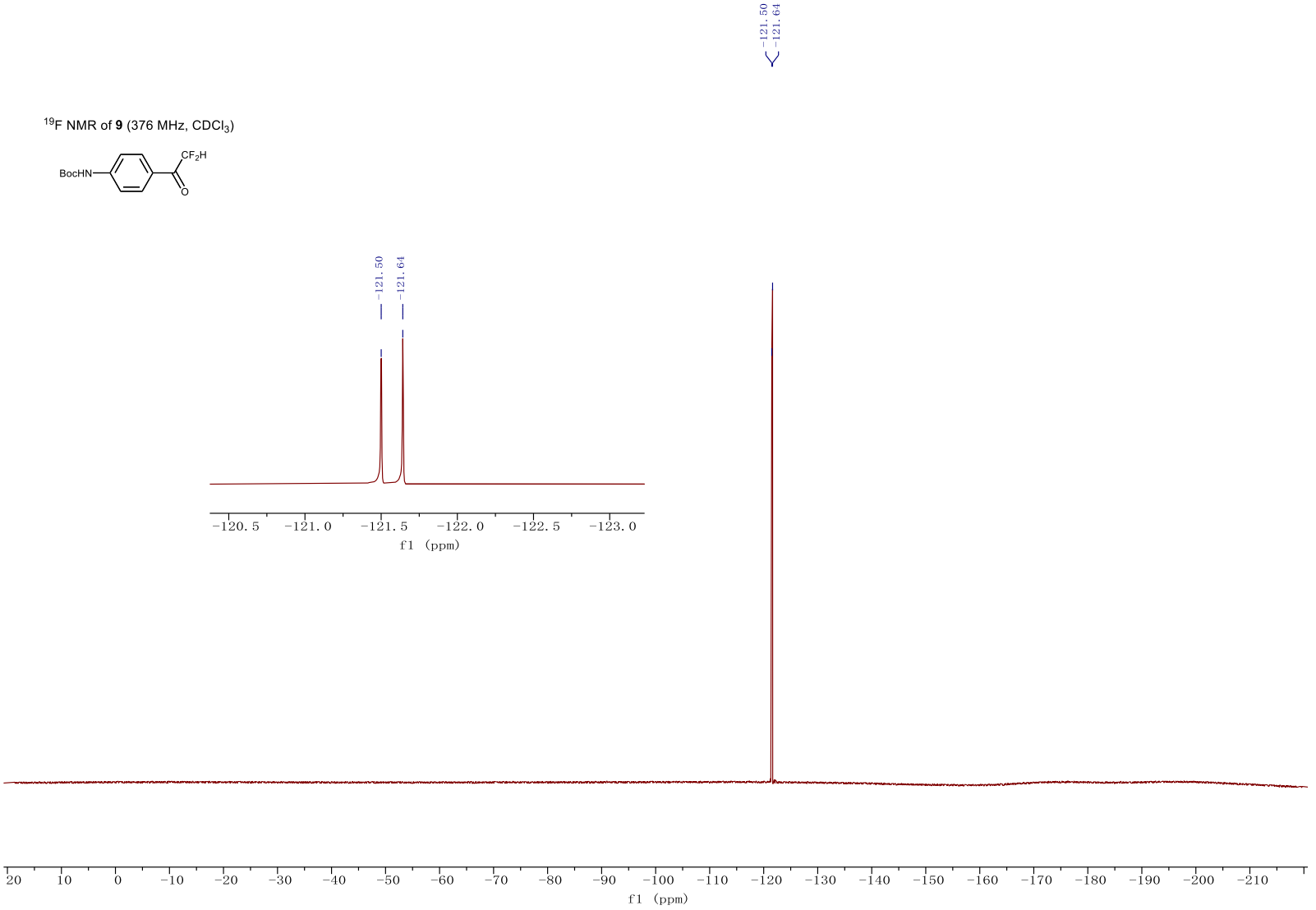

186.05
185.80
185.55
153.54
148.63
127.06
127.03
127.00
126.19
114.00
111.48
109.03
109.01
108.99
108.96
108.53
102.37
77.16 CDCl3
13C NMR of 8 (101 MHz, CDCl3)
O
O
O
CF2H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

^{19}F NMR of **8** (376 MHz, $CDCl_3$)

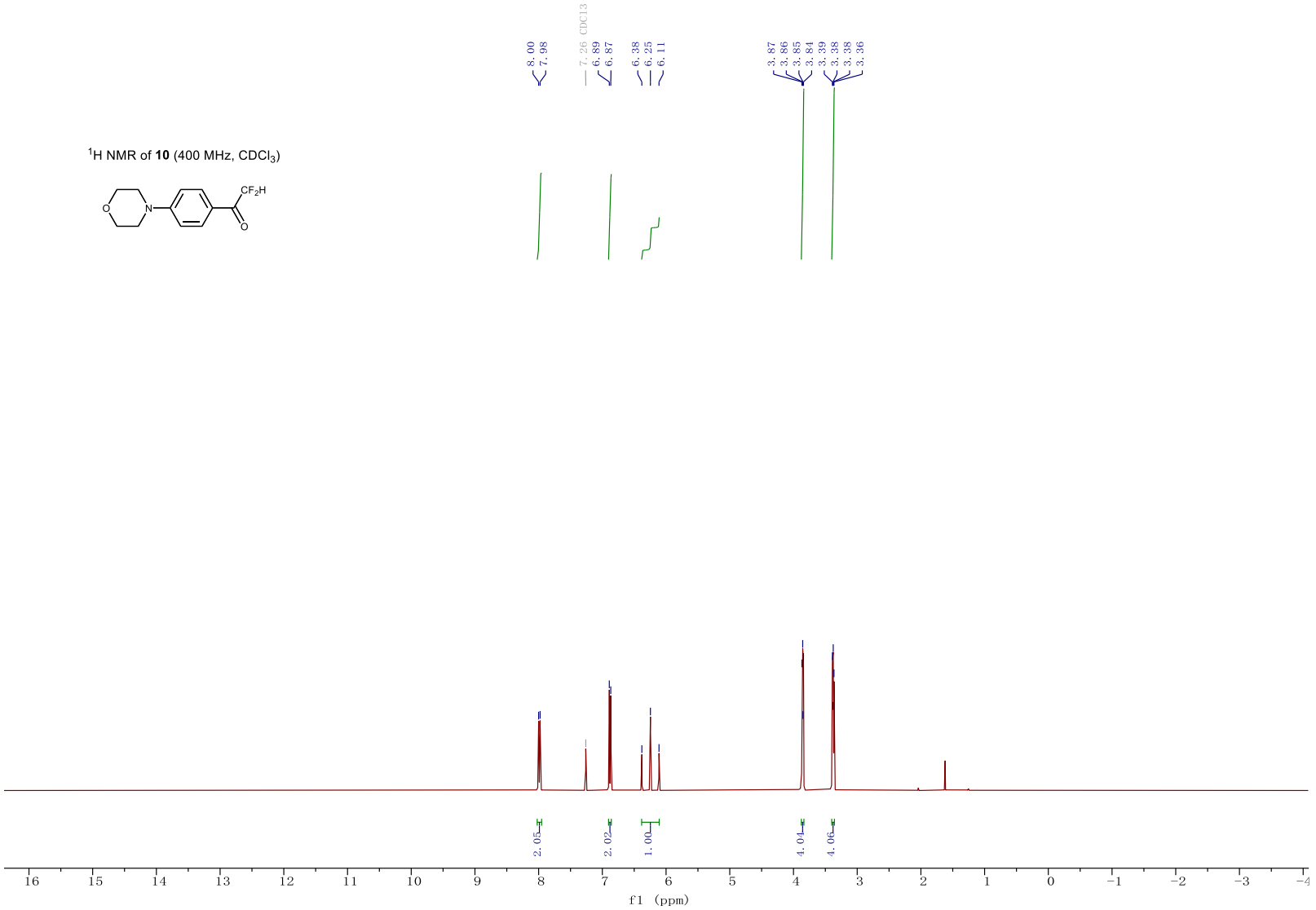

8.04
8.04
8.04
8.02
8.02
8.02
7.53
7.50
7.26 CDCl3
6.78
6.39
6.26
6.12
1.53
^{1}H NMR of **9** (400 MHz, $CDCl_3$)
BocHN
CF_2H
O
2.13
2.14
1.06
1.00
9.09
f1 (ppm)


186.50
186.25
186.00
152.00
144.69
131.57
131.54
131.51
126.03
117.68
114.03
111.50
108.98
81.89
77.16 CDCl3
28.36
^{13}C NMR of **9** (101 MHz, $CDCl_3$)
BocHN
CF_2H
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

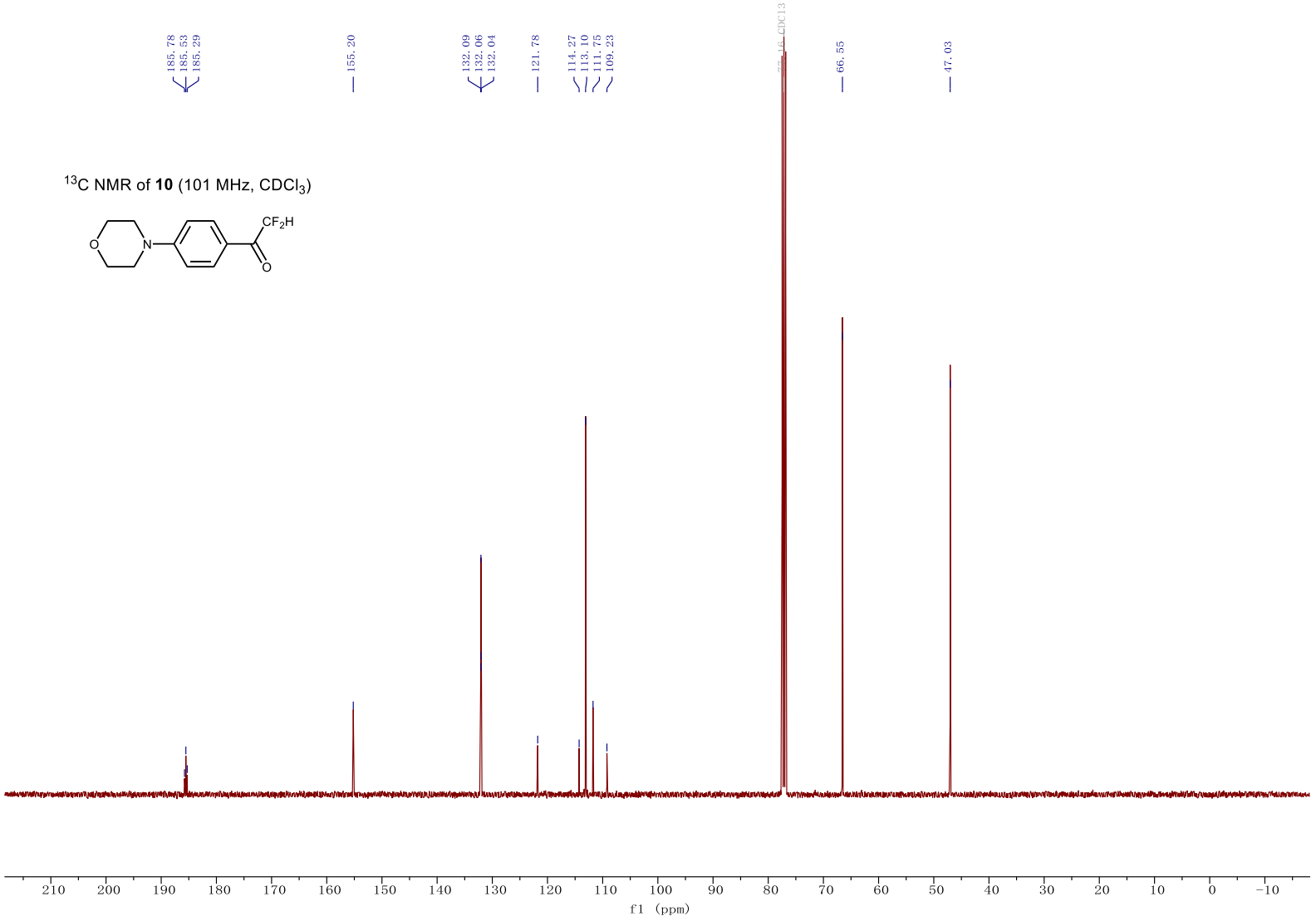
^{19}F NMR of **9** (376 MHz, $CDCl_3$)



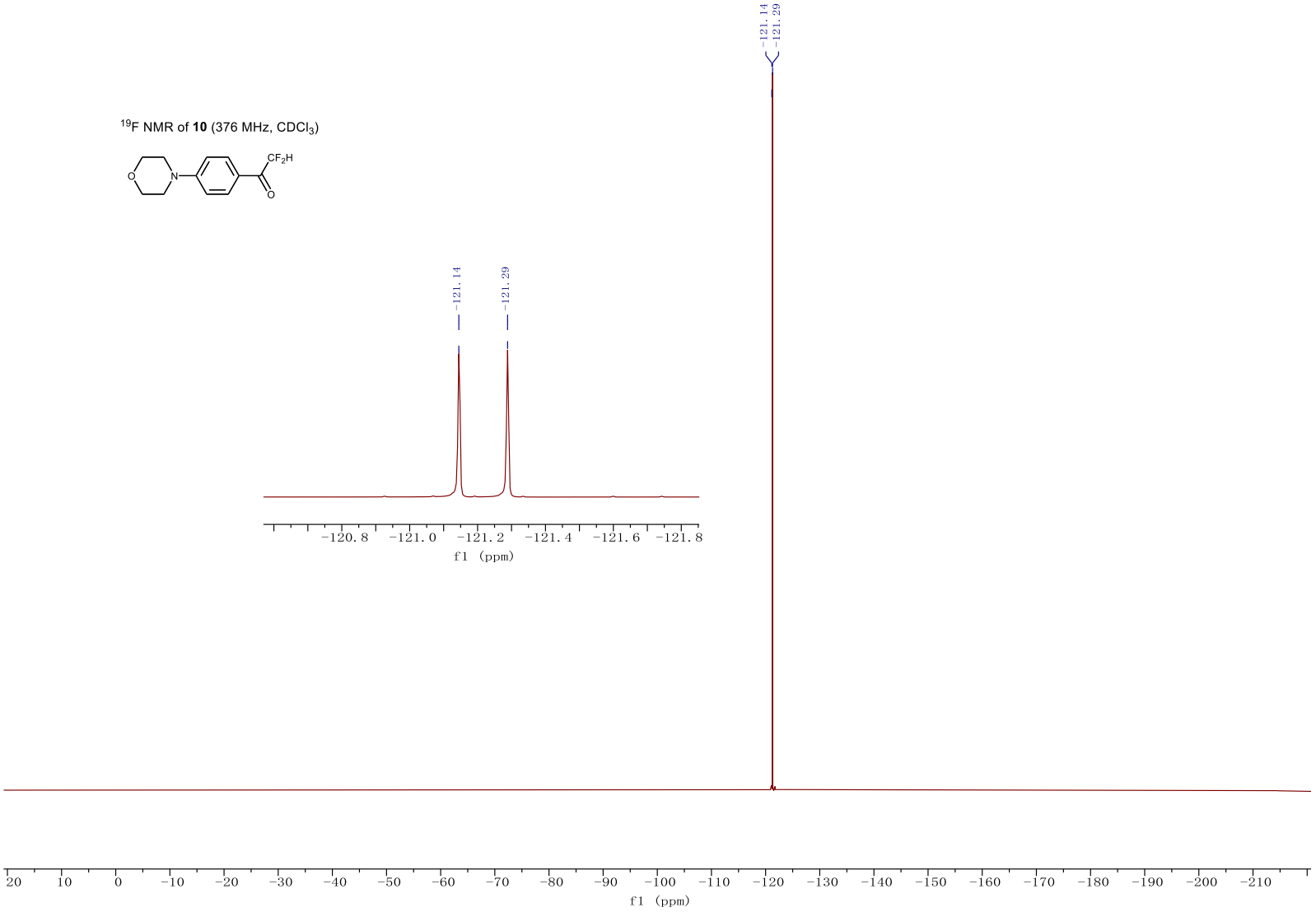
^{1}H NMR of **10** (400 MHz, $CDCl_3$)

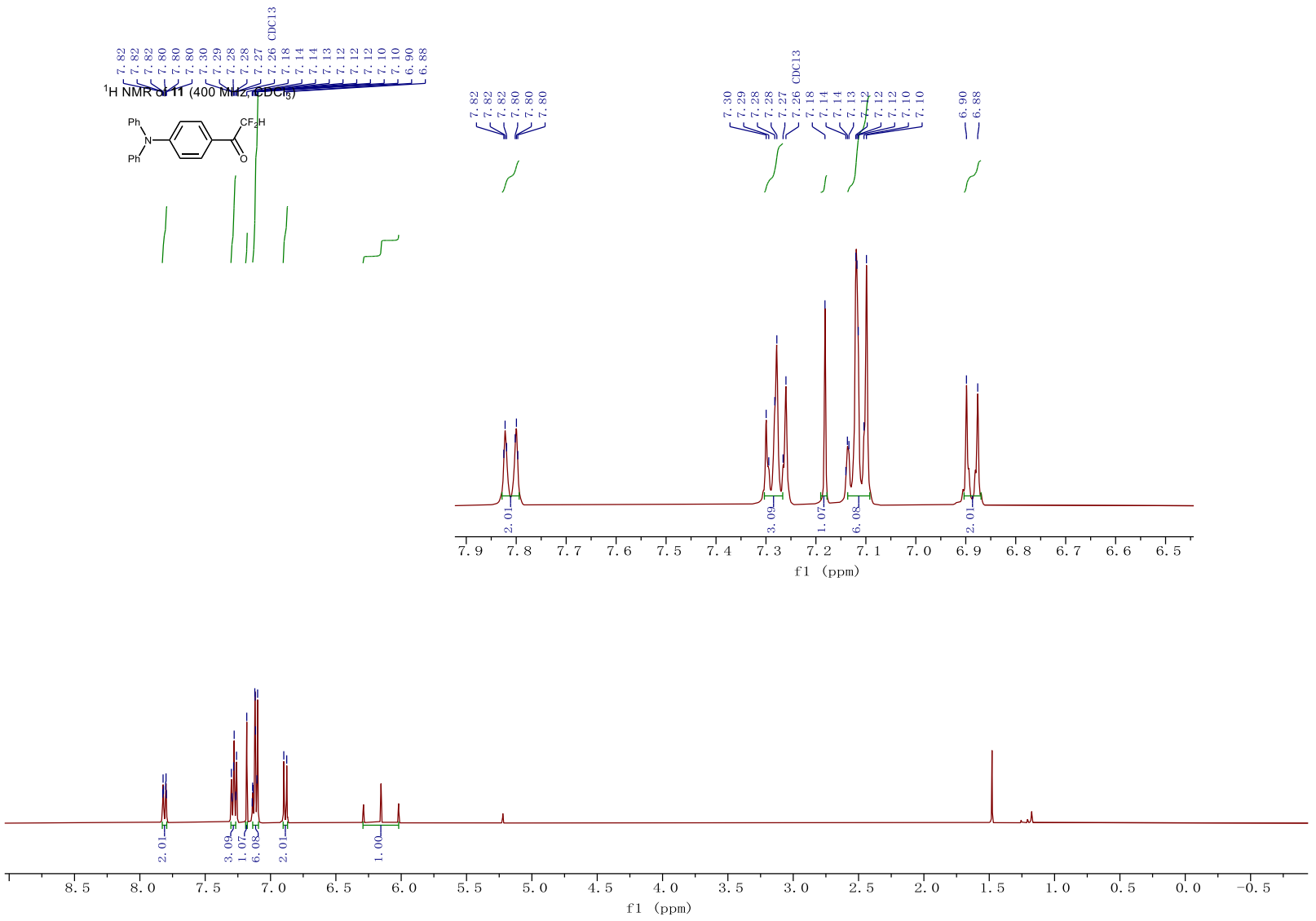


^{13}C NMR of **10** (101 MHz, $CDCl_3$)

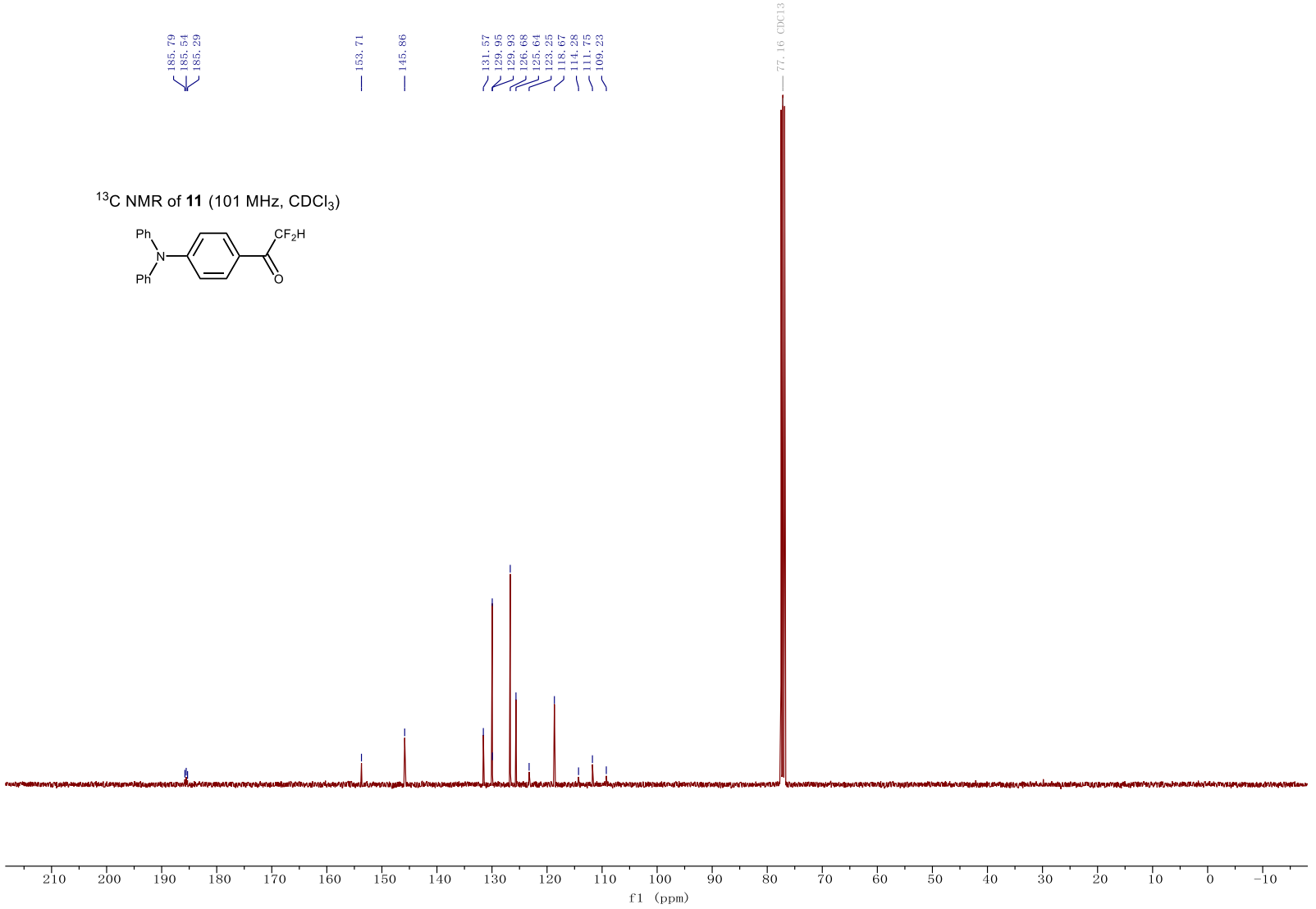


^{19}F NMR of **10** (376 MHz, $CDCl_3$)

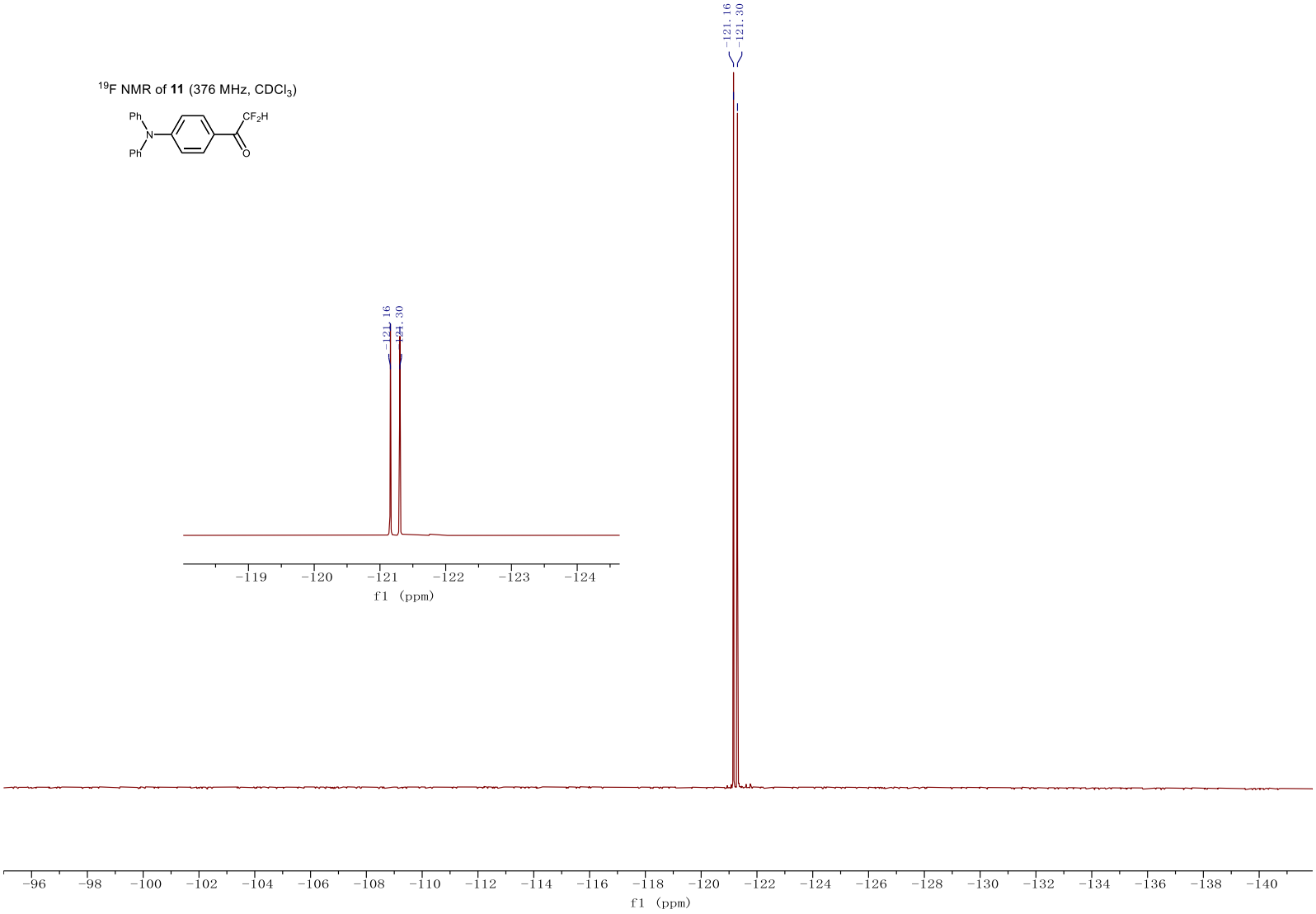


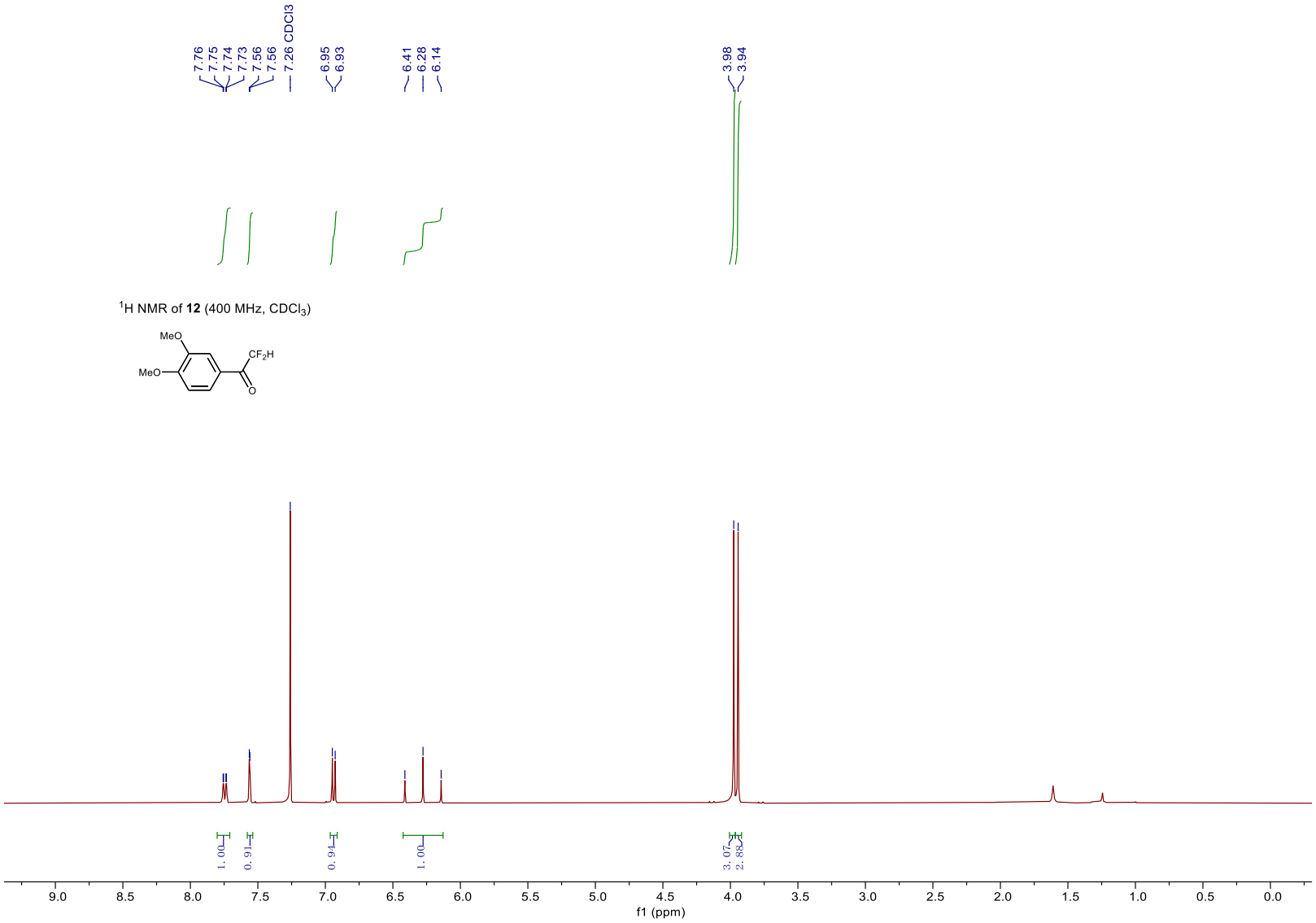

7.82
7.82
7.82
7.80
7.80
7.30
7.29
7.28
7.27
CDC13
7.26
7.18
7.14
7.14
7.13
7.12
7.12
7.12
7.10
7.10
6.90
6.88
Ph
N
Ph
CF2H
O
2.01
3.09
1.07
6.08
2.01
1.00
f1 (ppm)

^{13}C NMR of **11** (101 MHz, $CDCl_3$)

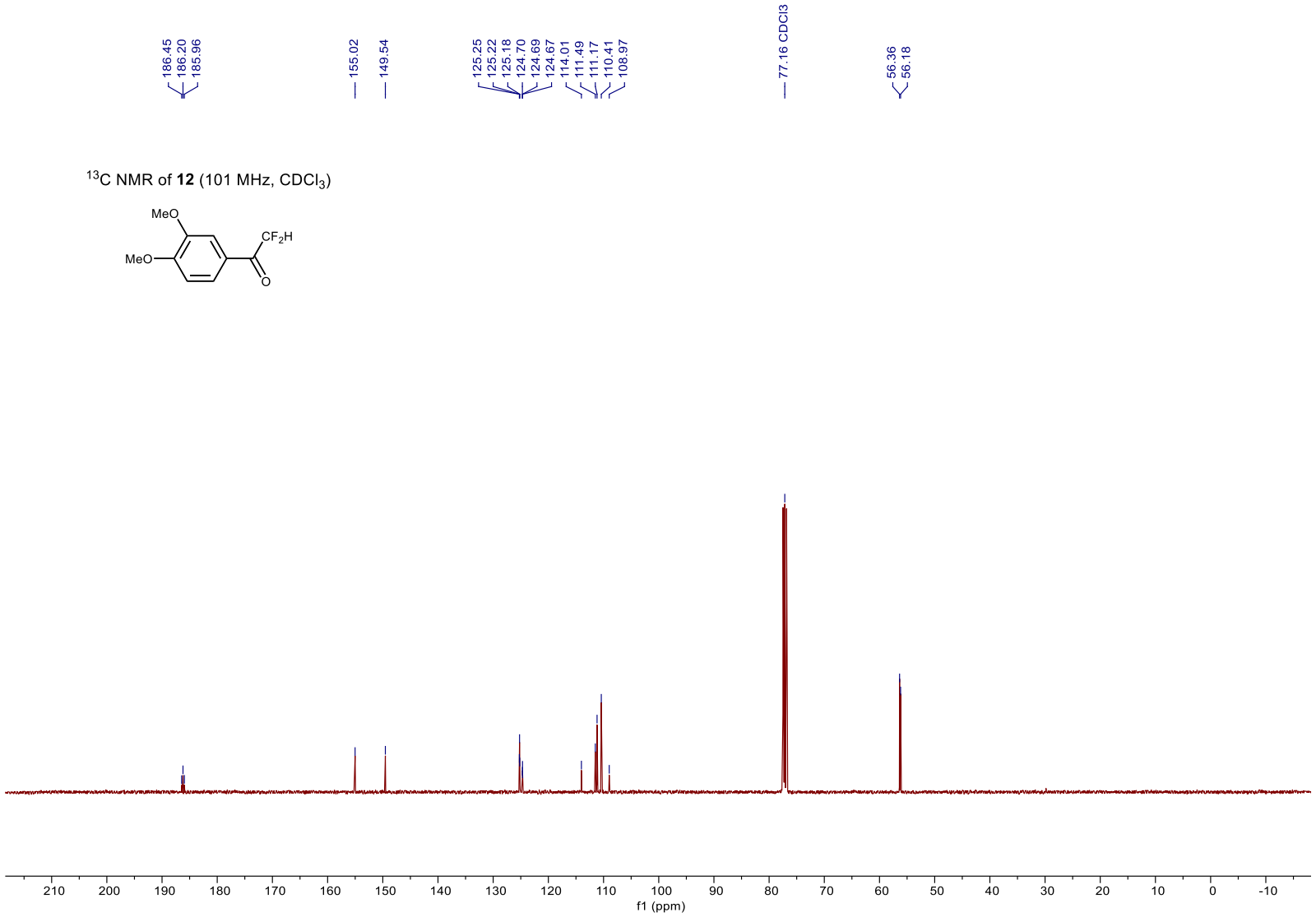


^{19}F NMR of **11** (376 MHz, $CDCl_3$)



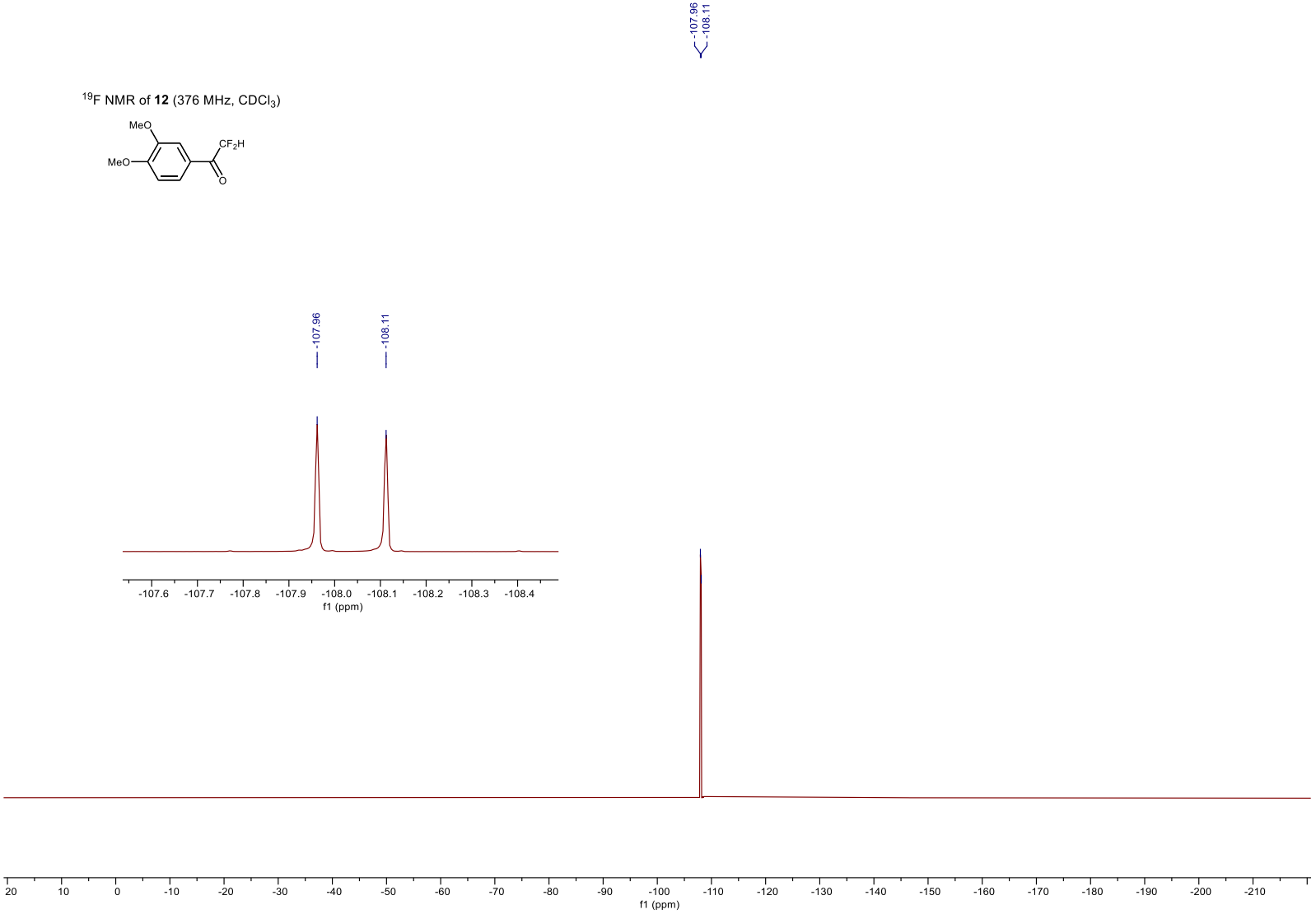


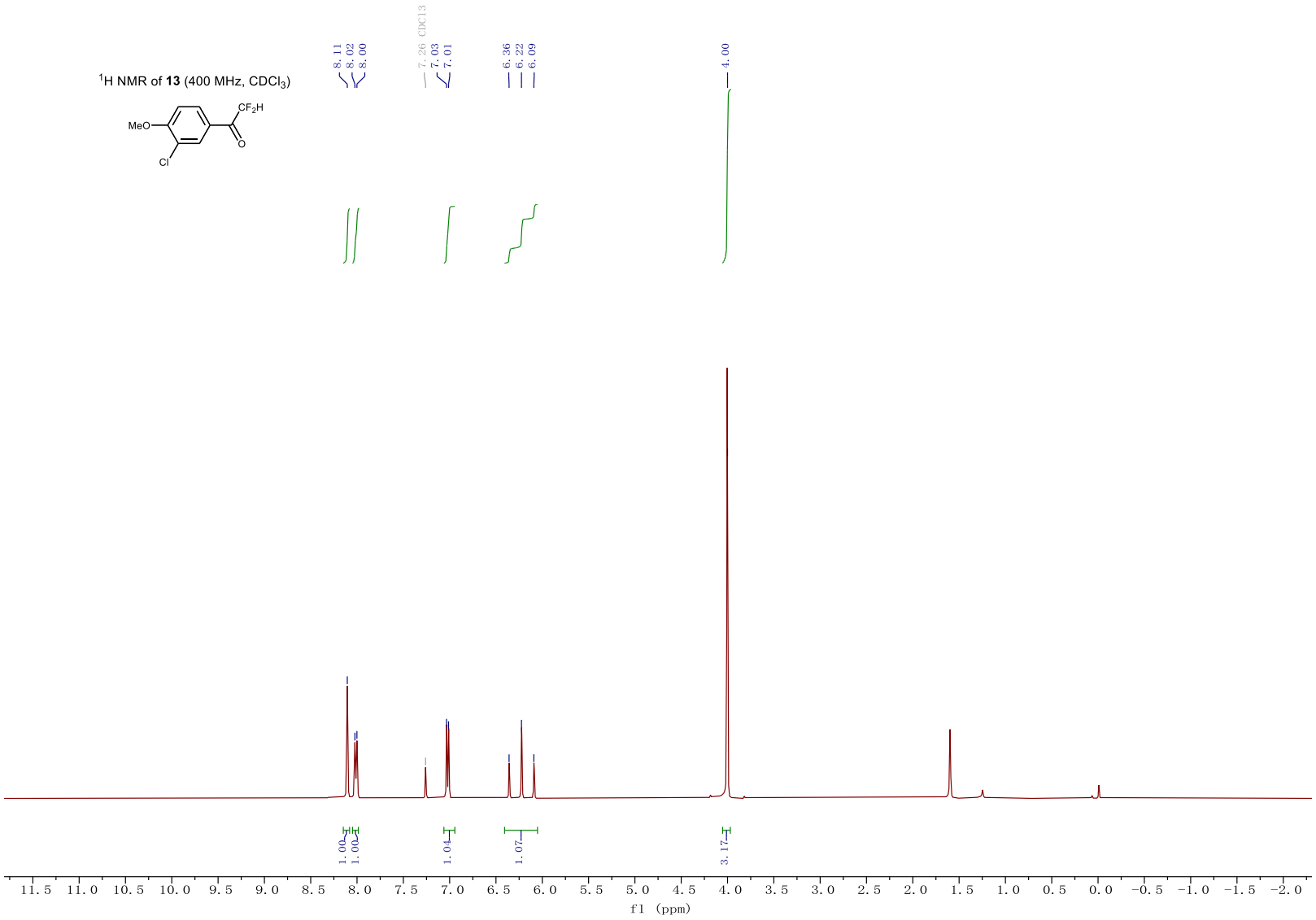
^{1}H NMR of **12** (400 MHz, $CDCl_3$)

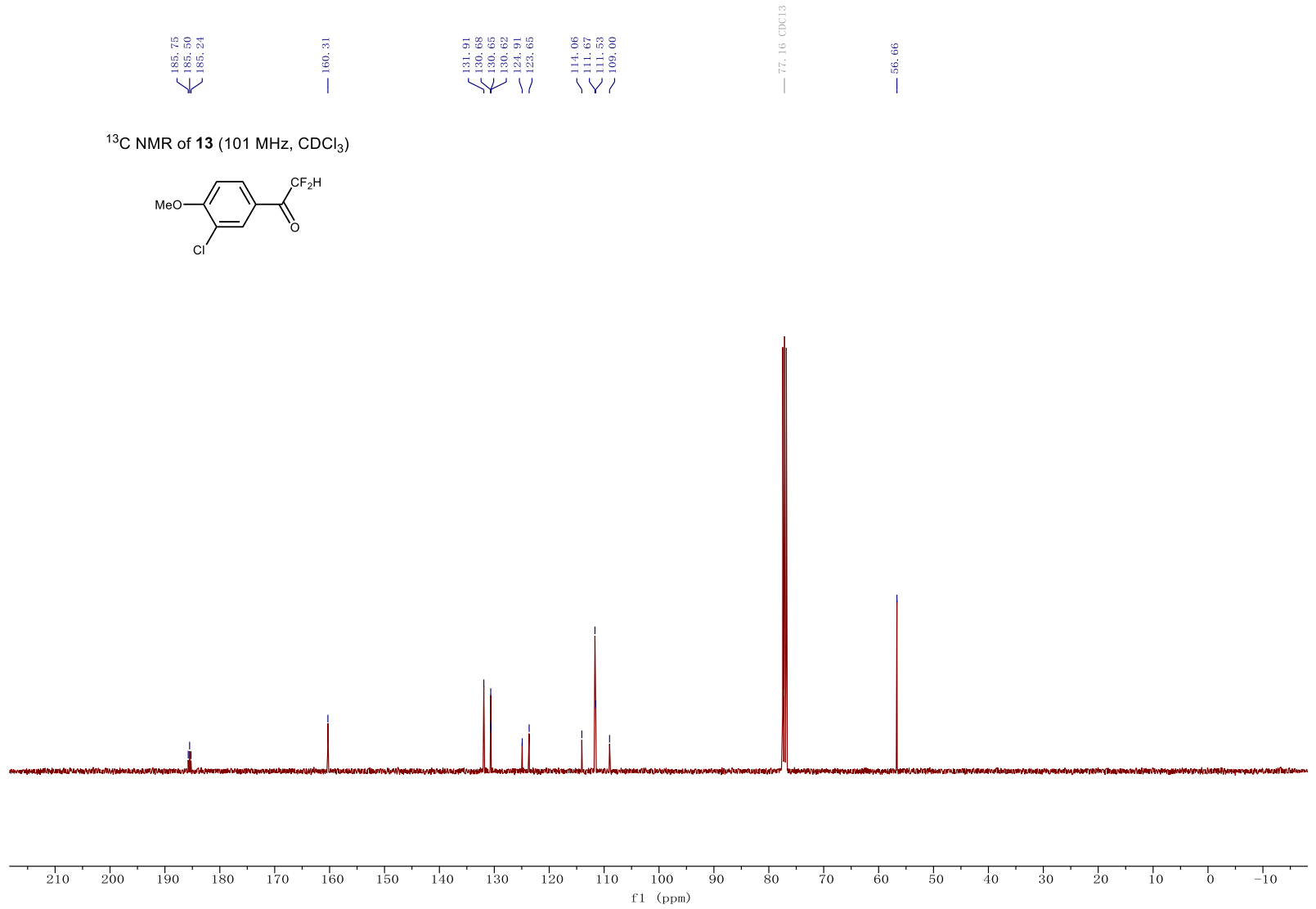


^{13}C NMR of **12** (101 MHz, $CDCl_3$)

^{19}F NMR of **12** (376 MHz, $CDCl_3$)

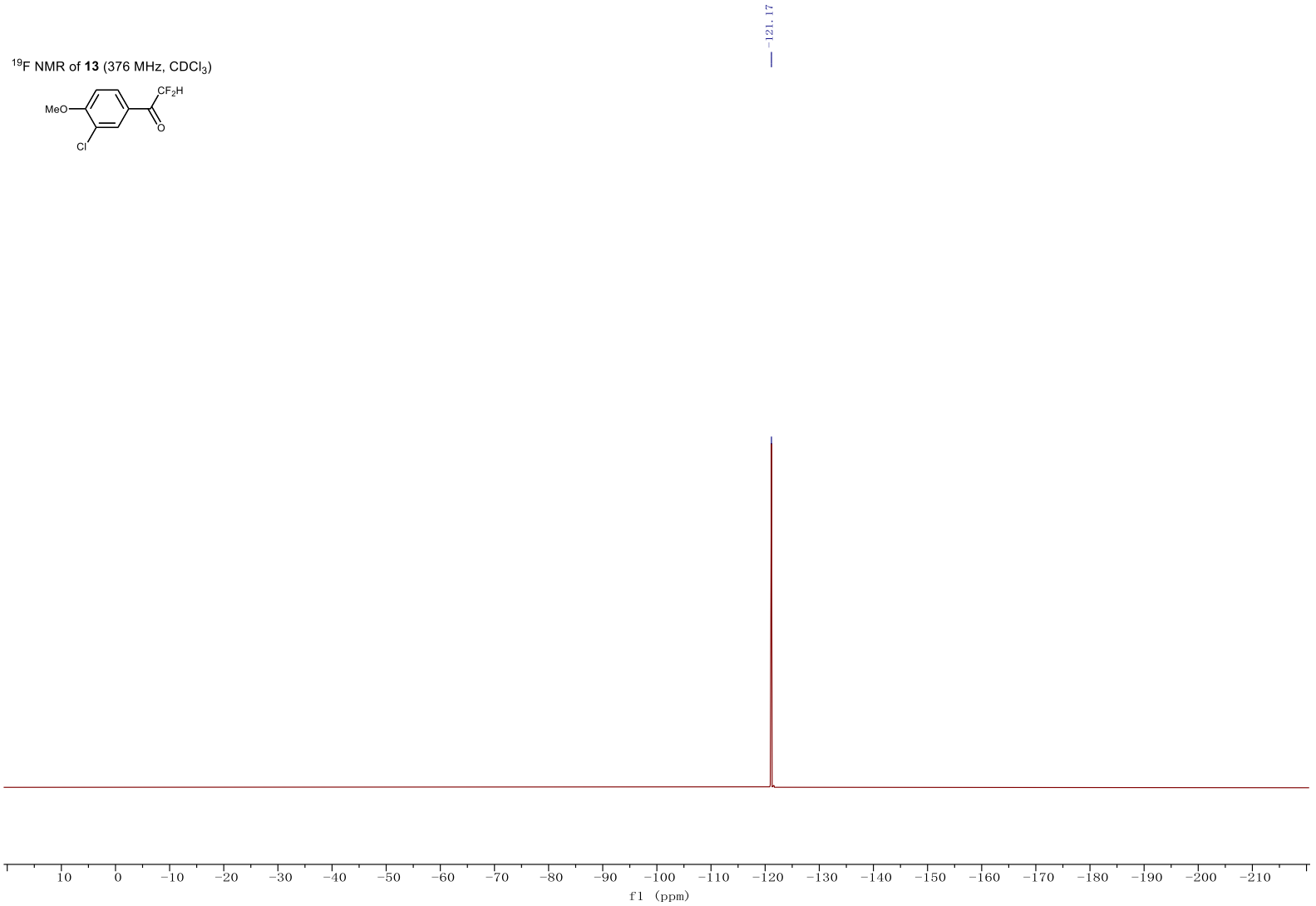


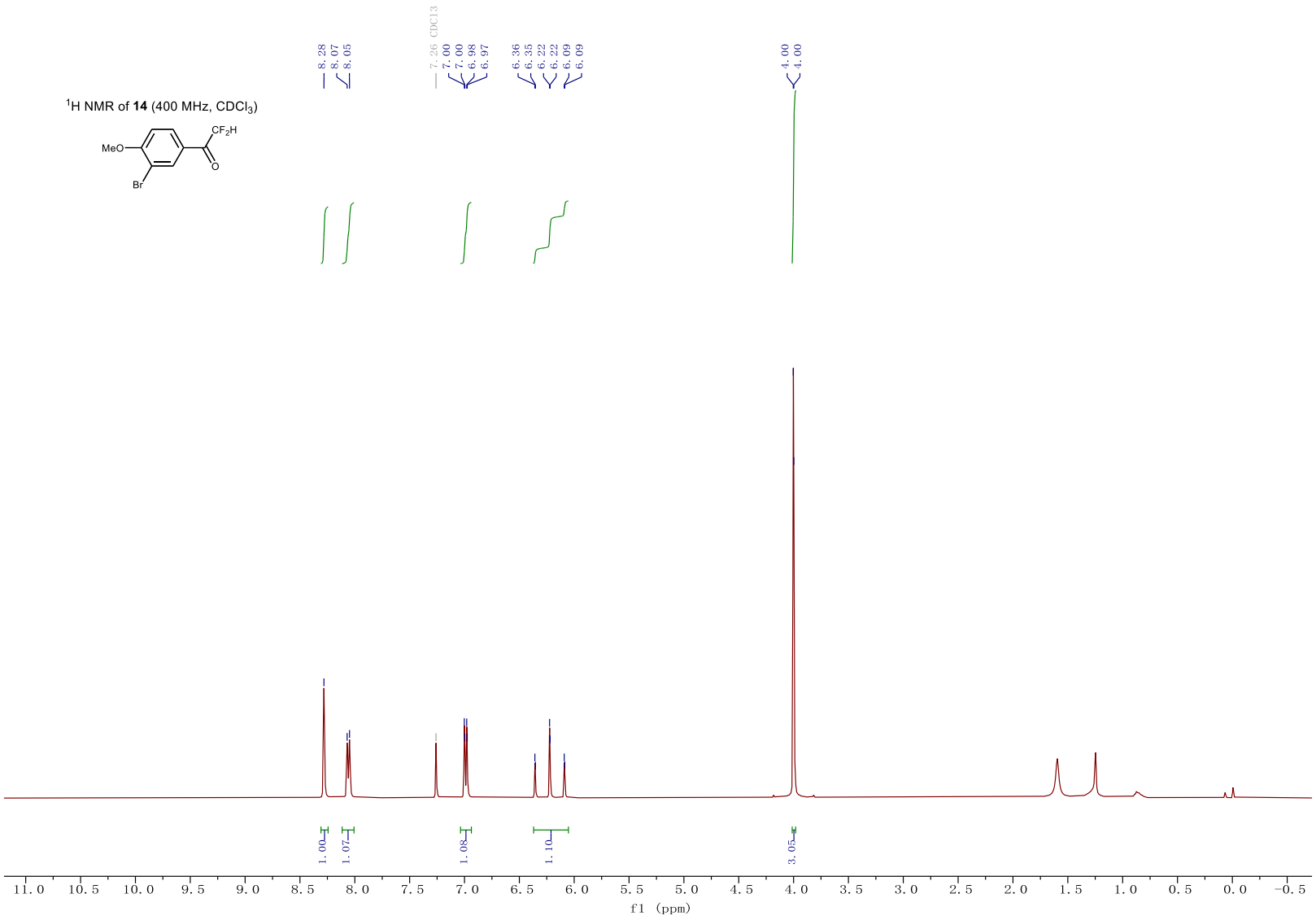

^{1}H NMR of **13** (400 MHz, $CDCl_3$)
MeO
CF_2H
O
Cl
8.11
8.02
8.00
7.26 CDCl3
7.03
7.01
6.36
6.22
6.09
4.00
1.00
1.00
1.04
1.07
3.17
f1 (ppm)

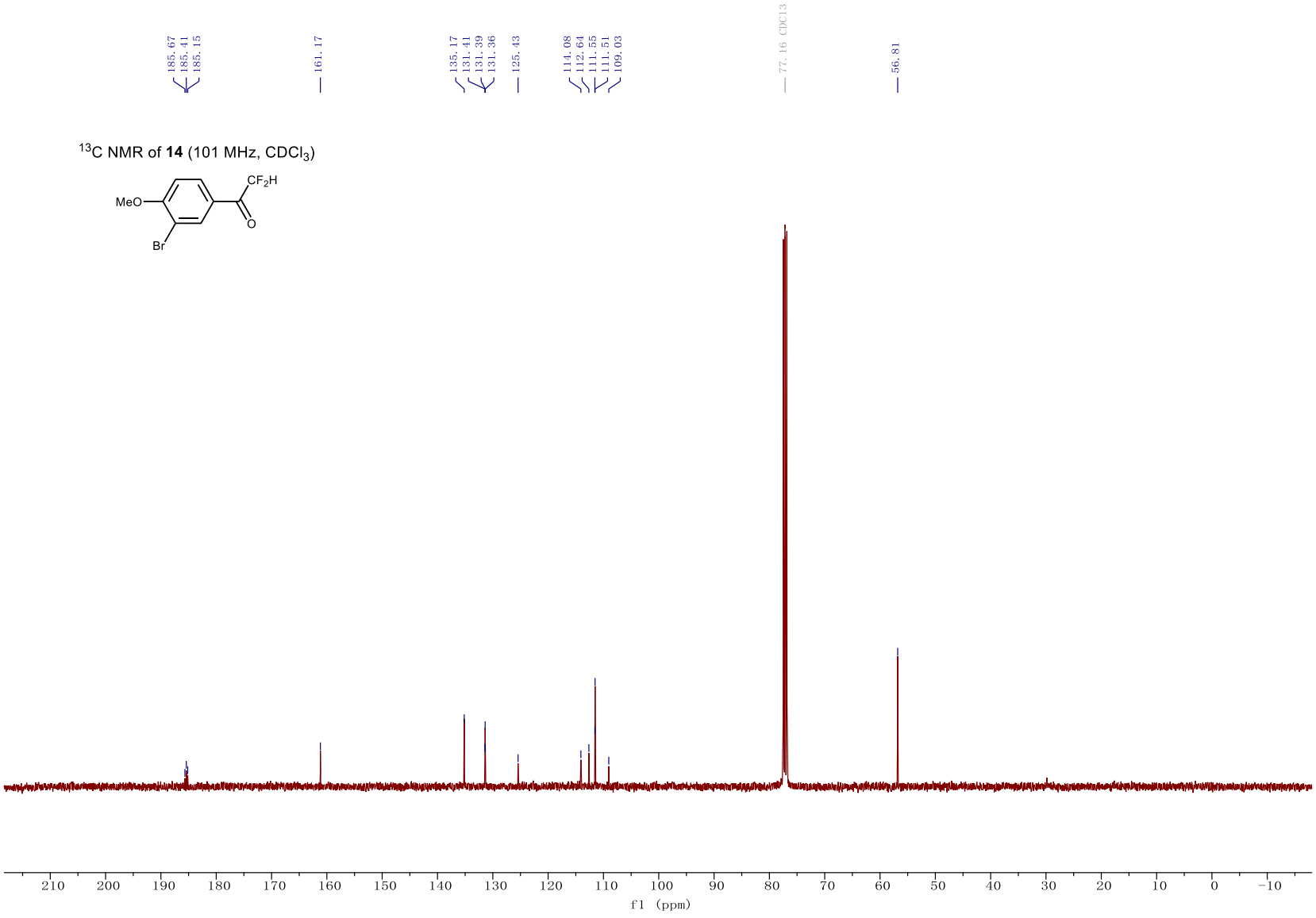


^{13}C NMR of **13** (101 MHz, $CDCl_3$)

^{19}F NMR of **13** (376 MHz, $CDCl_3$)

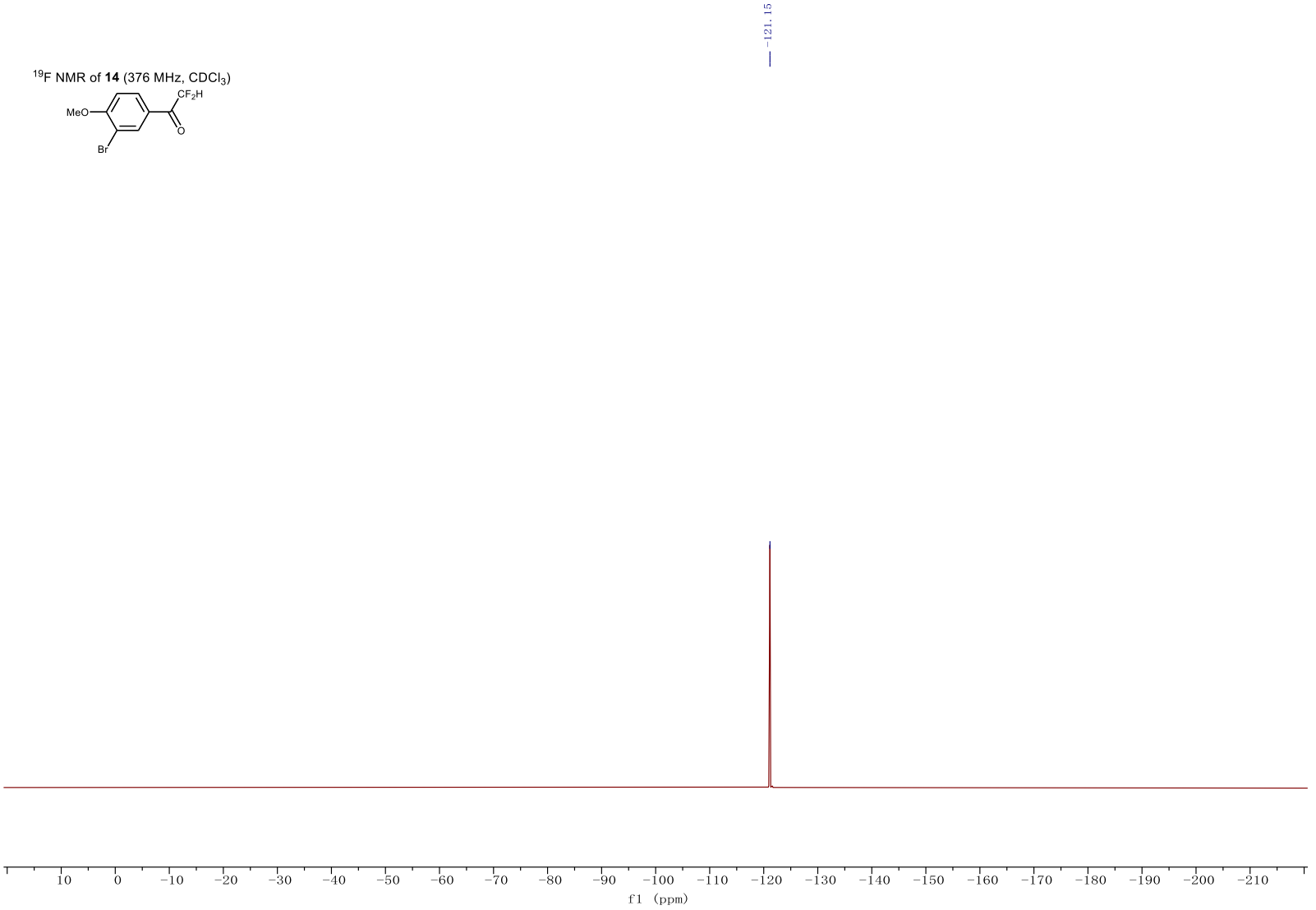


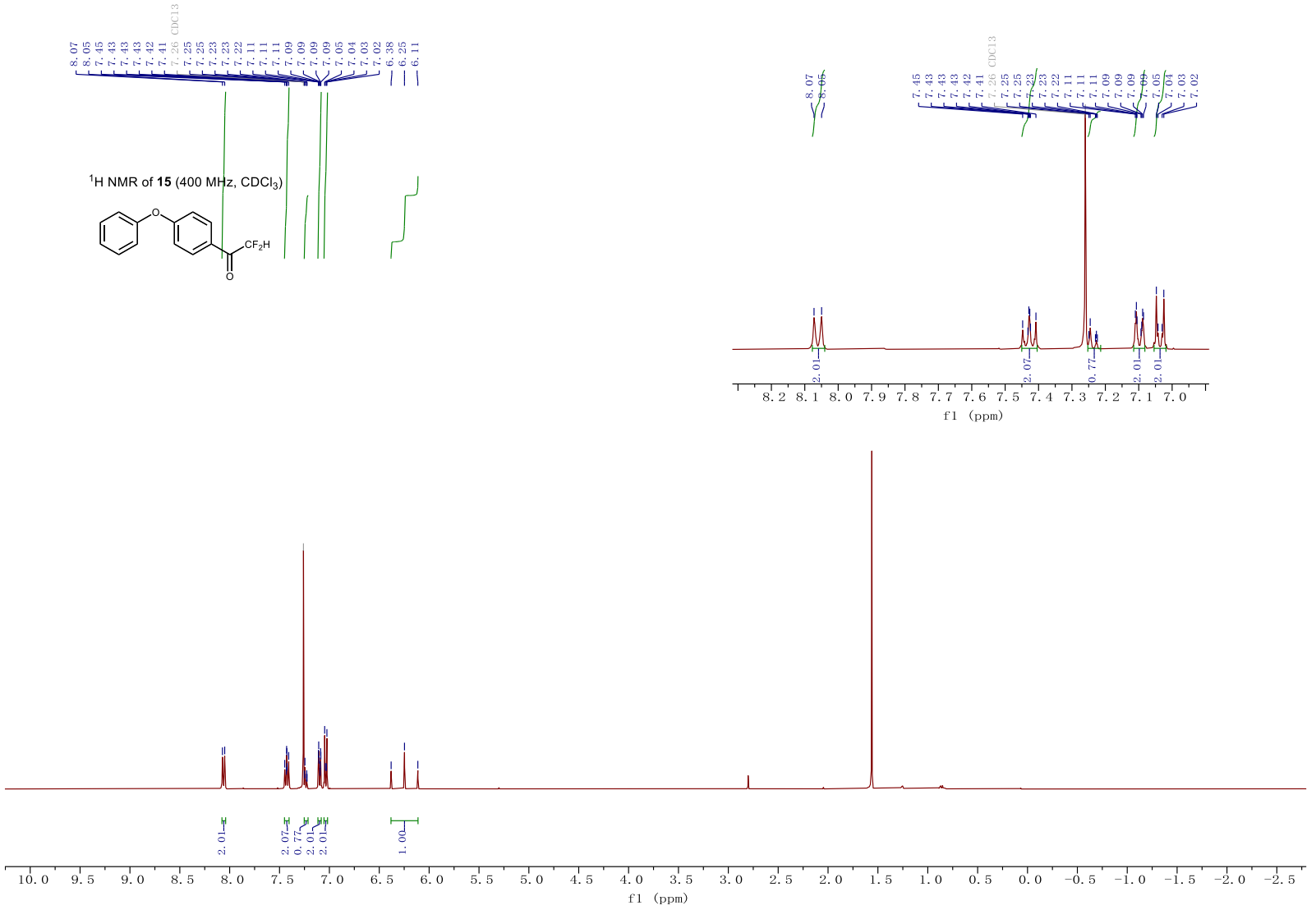

1H NMR of 14 (400 MHz, CDCl3)
MeO
CF2H
O
Br
8.28
8.07
8.05
7.26 CDCl3
7.00
7.00
6.98
6.97
6.36
6.35
6.22
6.22
6.09
6.09
4.00
4.00
1.00
1.07
1.08
1.10
3.05
f1 (ppm)



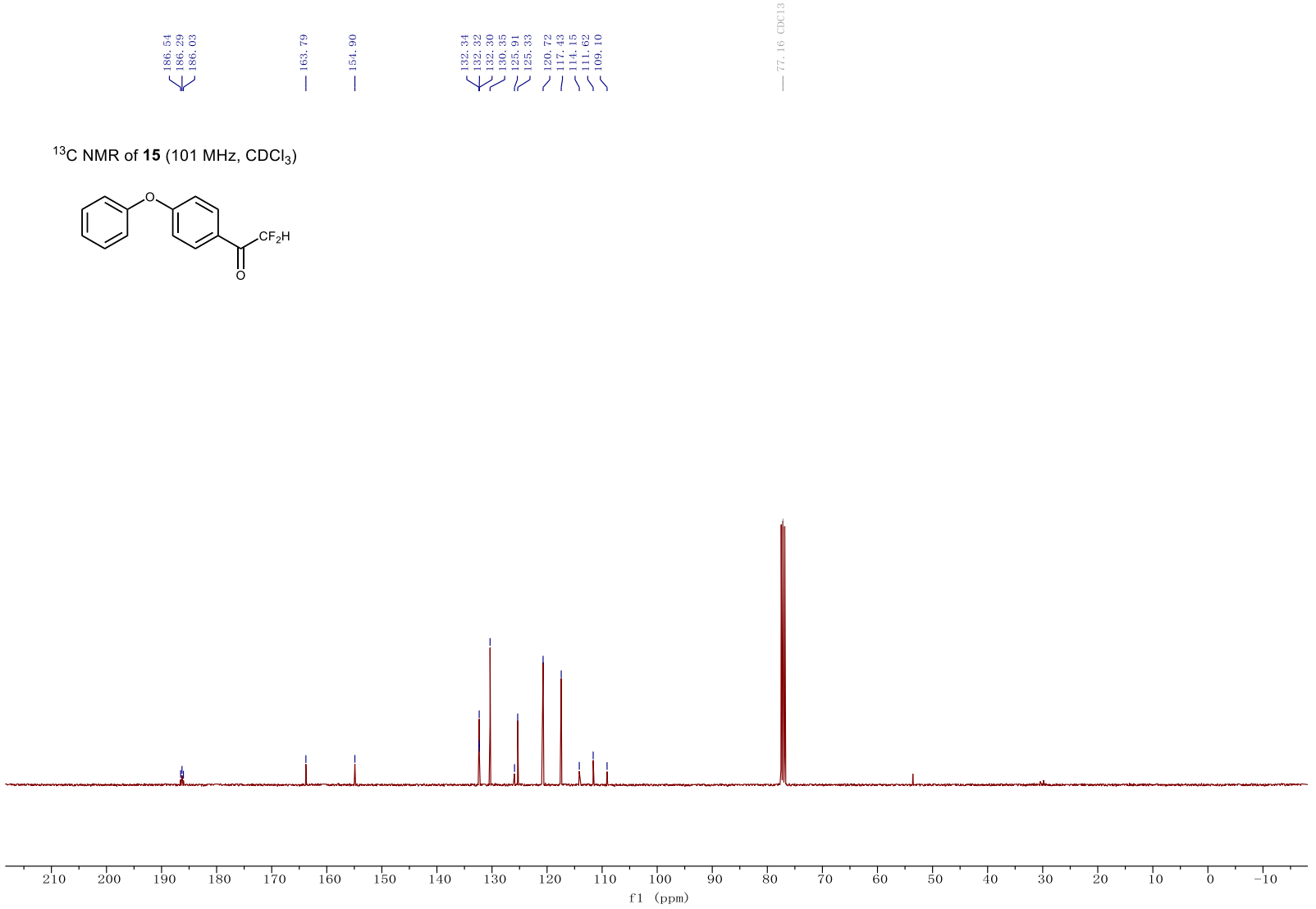
^{13}C NMR of **14** (101 MHz, $CDCl_3$)

^{19}F NMR of **14** (376 MHz, $CDCl_3$)

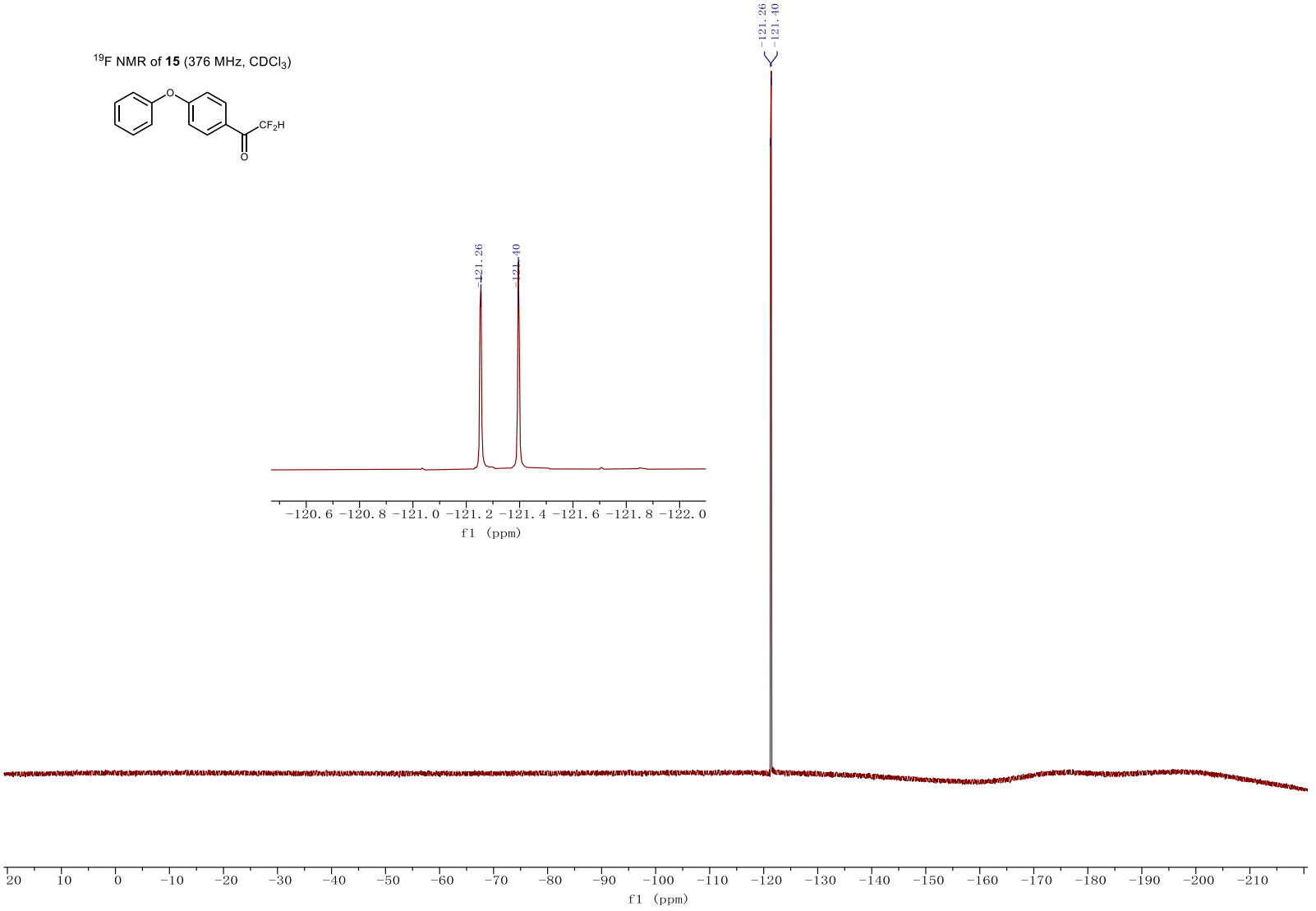


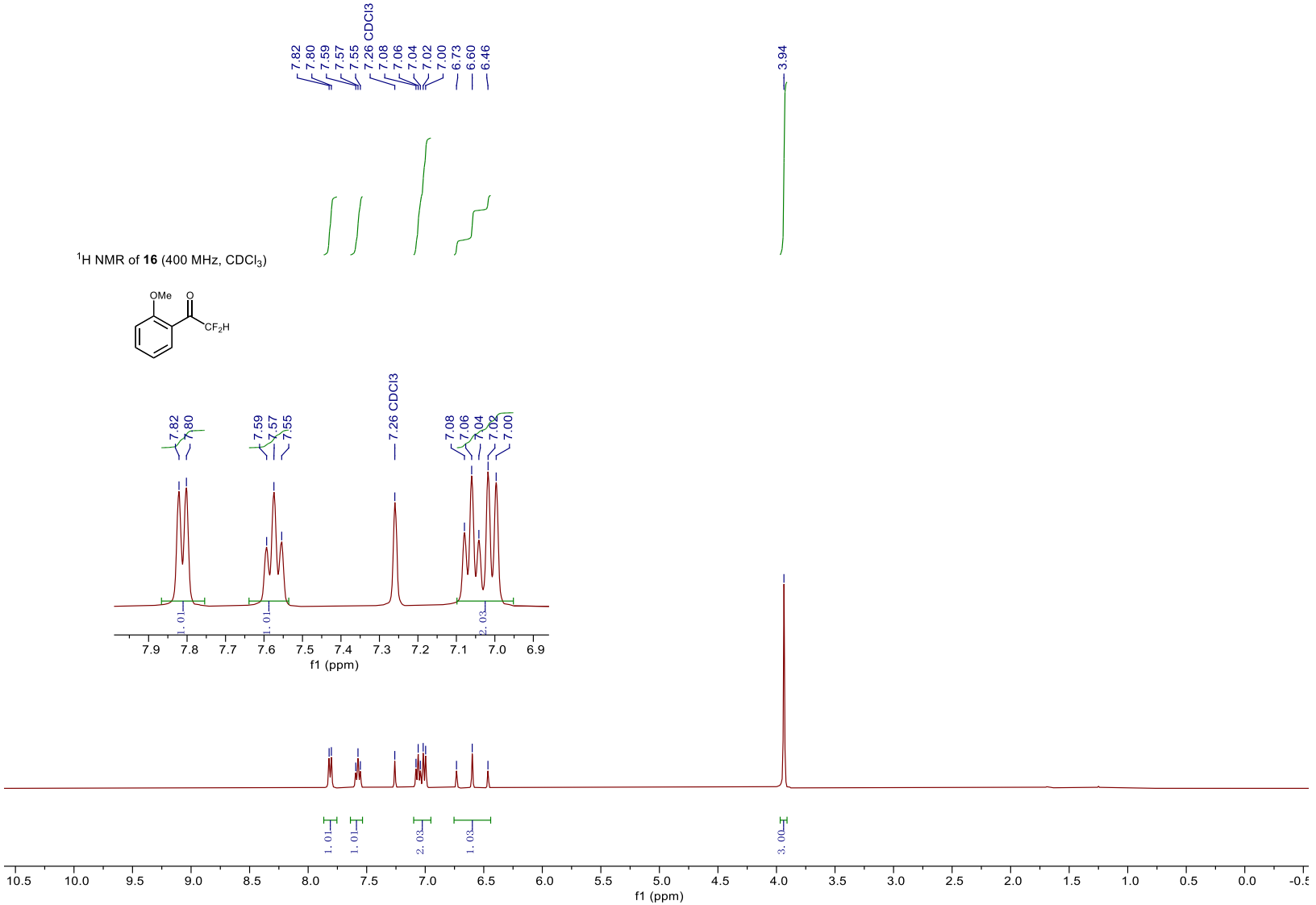

^{1}H NMR of **15** (400 MHz, $CDCl_3$)
CF_2H
O
f1 (ppm)

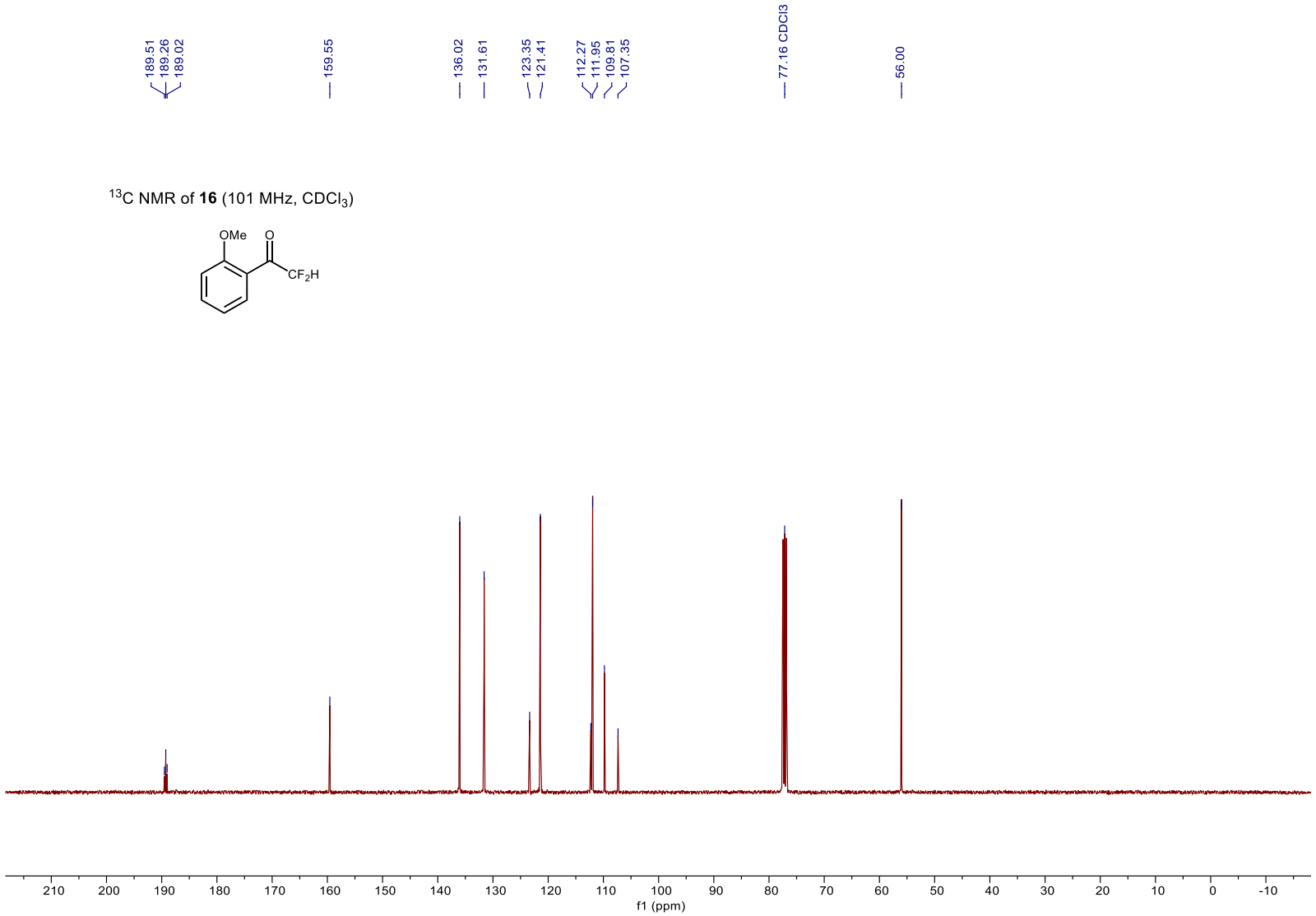
^{13}C NMR of **15** (101 MHz, $CDCl_3$)



^{19}F NMR of **15** (376 MHz, $CDCl_3$)

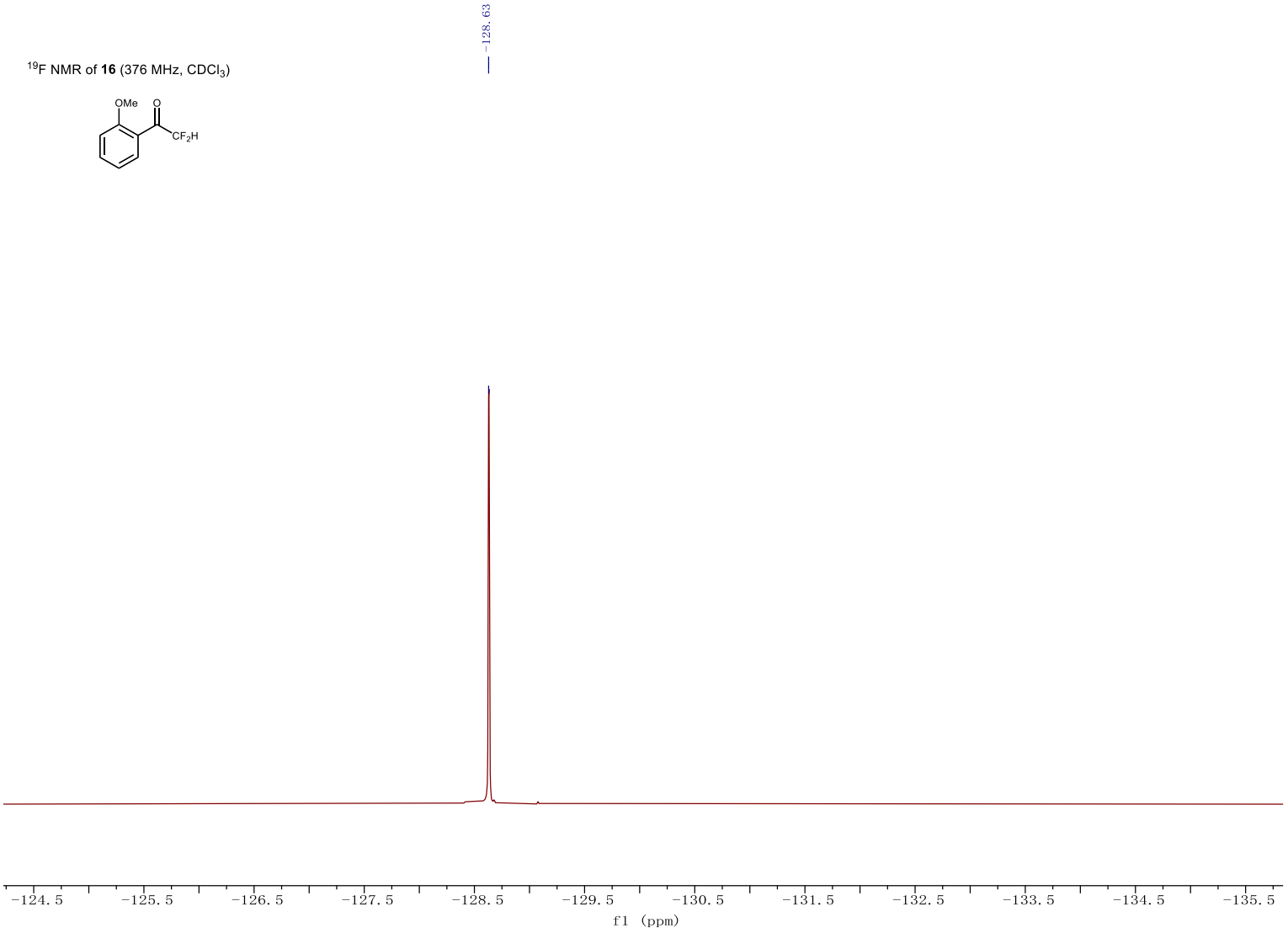



7.82
7.80
7.59
7.57
7.55
7.26 CDCl3
7.08
7.06
7.04
7.02
7.00
6.73
6.60
6.46
3.94
^{1}H NMR of **16** (400 MHz, $CDCl_3$)
OMe
O
CF_2H
1.01
1.01
2.03
1.03
3.00
f1 (ppm)

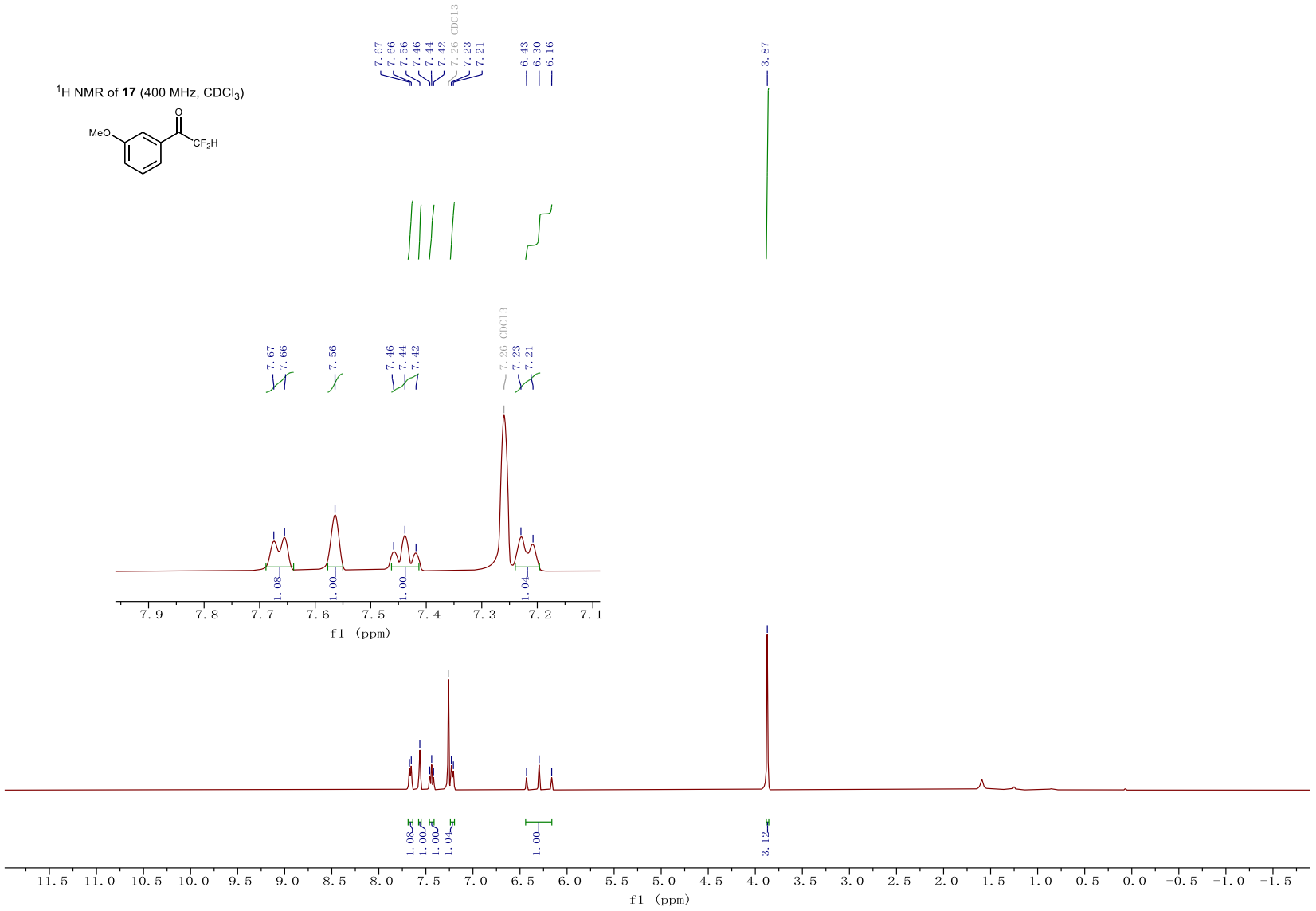


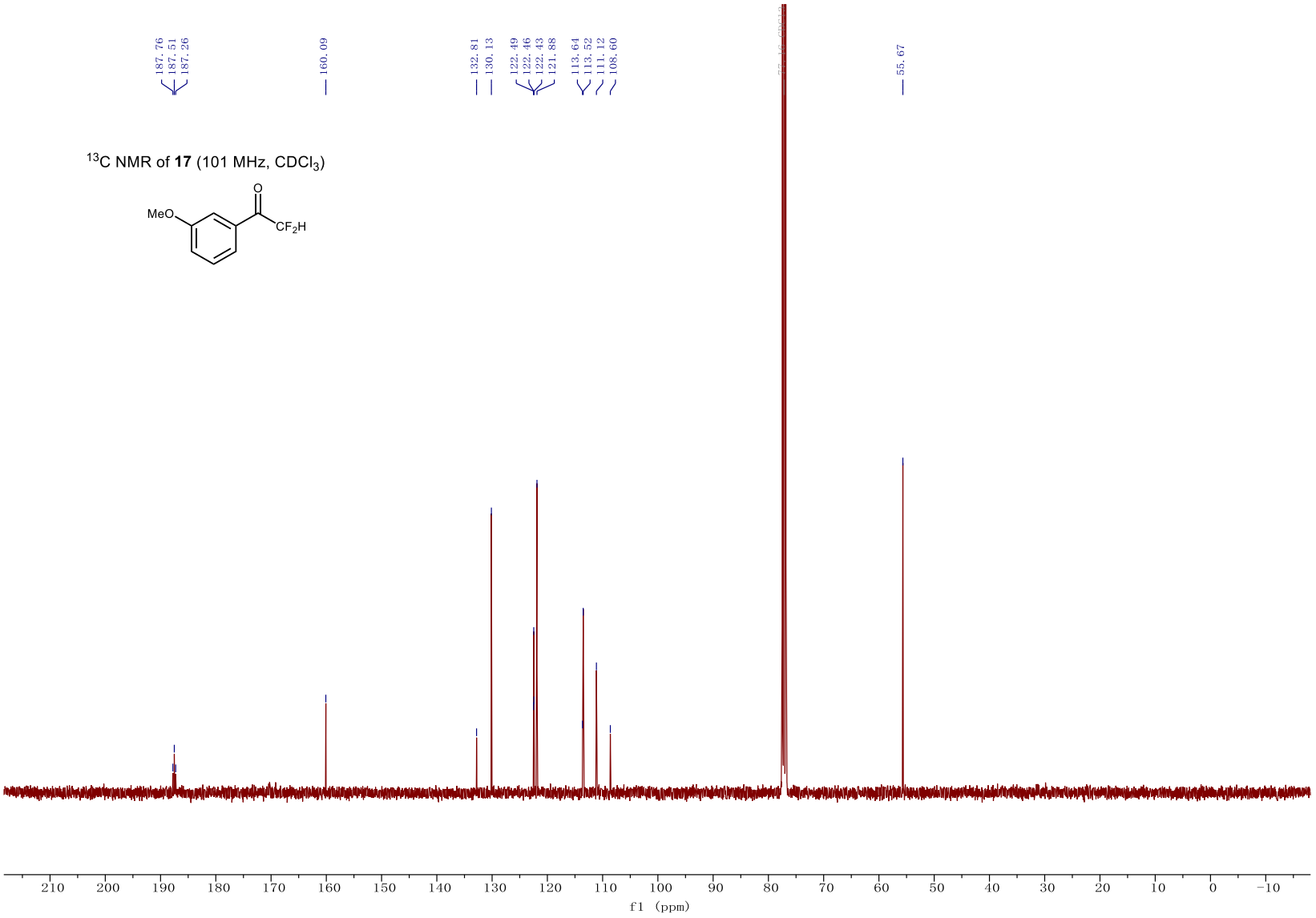
^{13}C NMR of **16** (101 MHz, $CDCl_3$)

^{19}F NMR of **16** (376 MHz, $CDCl_3$)

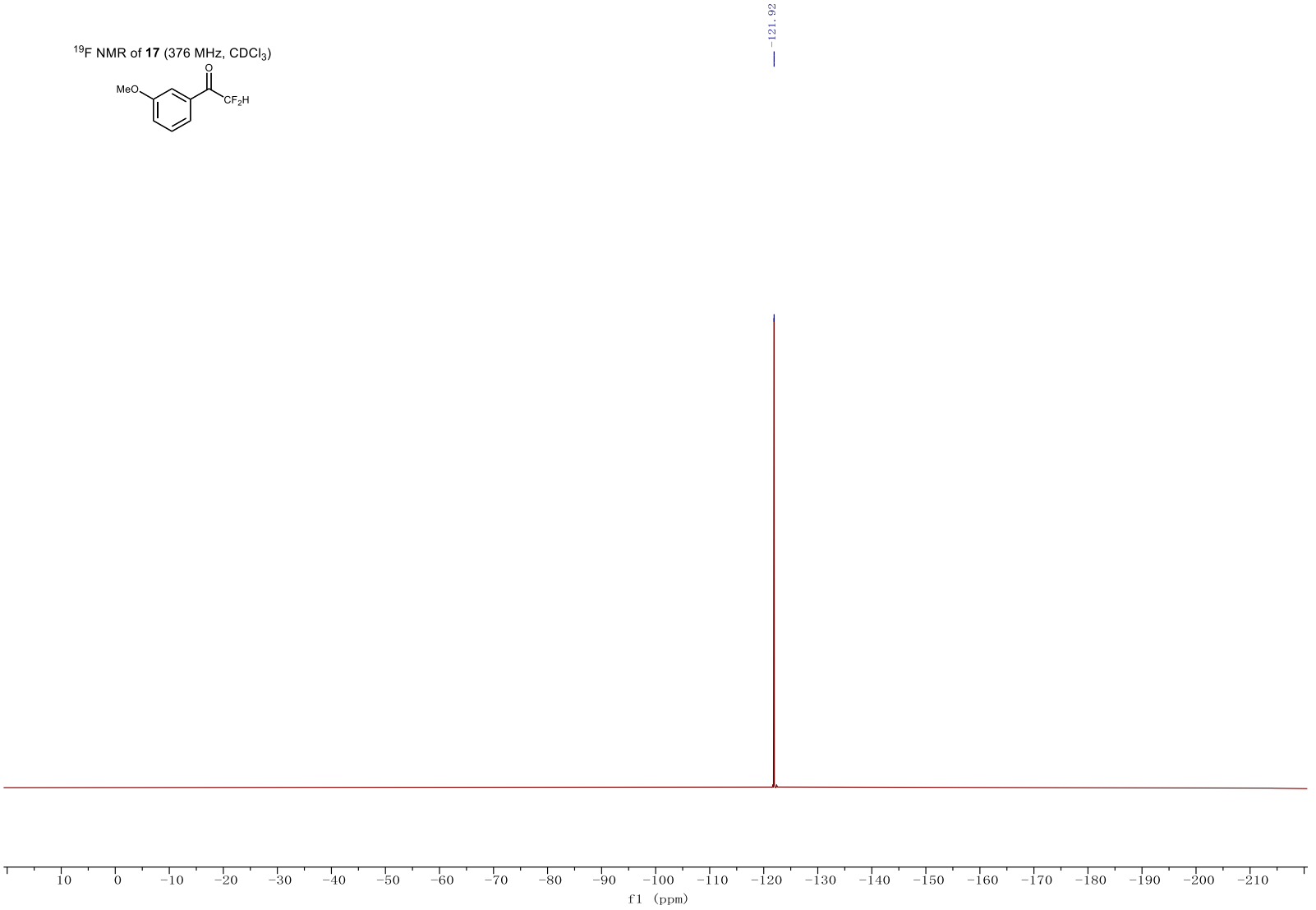


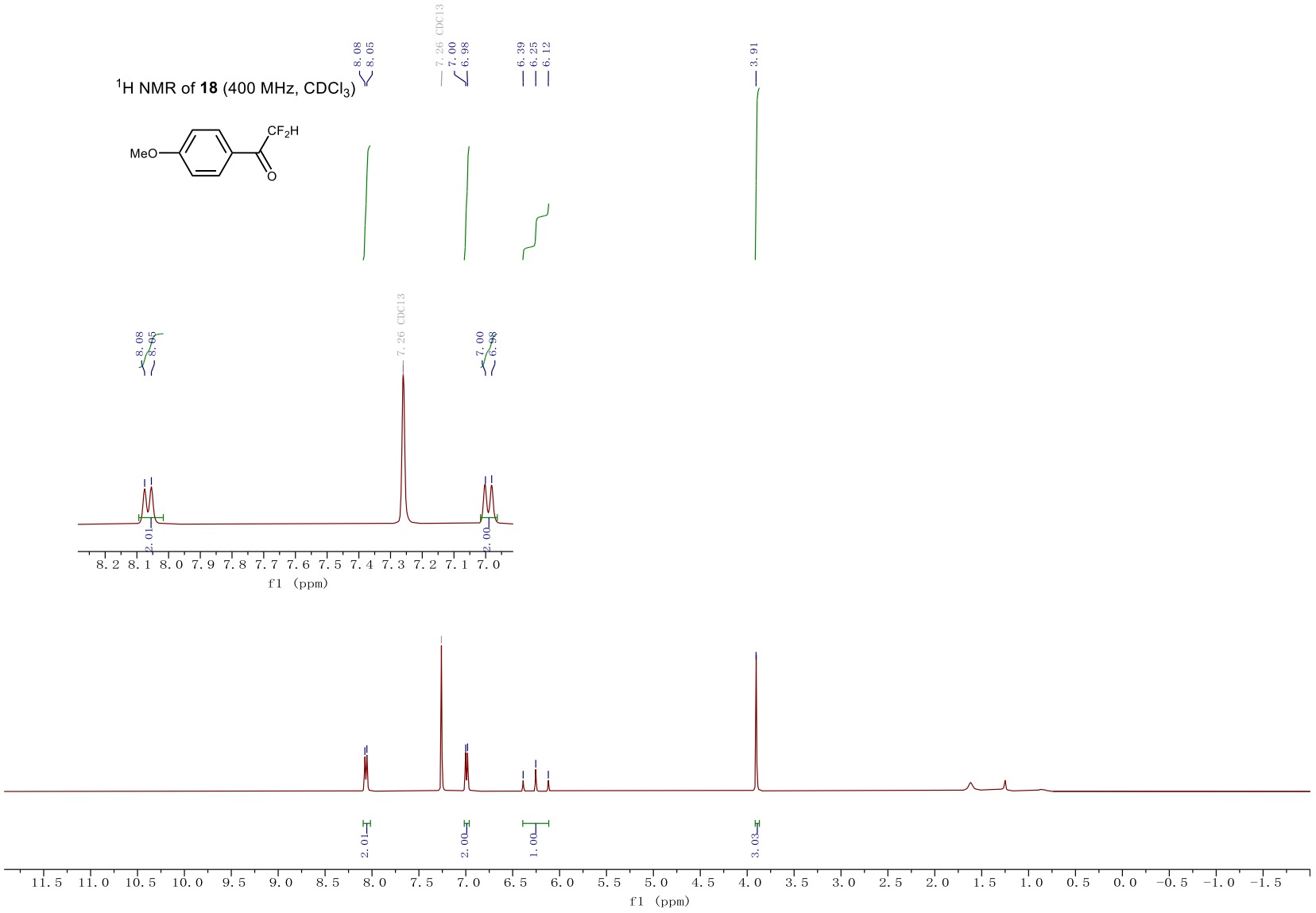
^{1}H NMR of **17** (400 MHz, $CDCl_3$)

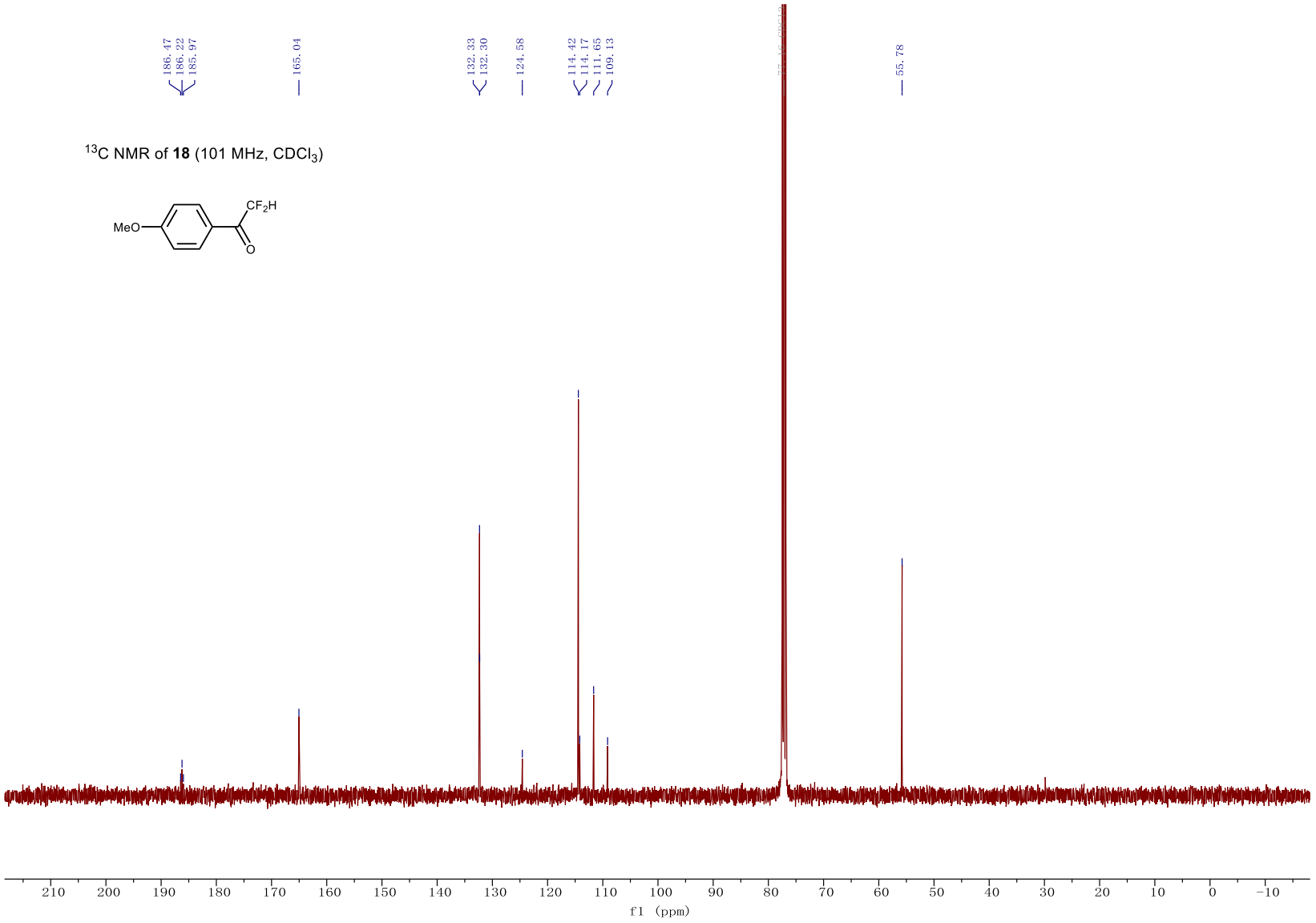



187.76
187.51
187.26
160.09
132.81
130.13
122.49
122.46
122.43
121.88
113.64
113.52
111.12
108.60
55.67
^{13}C NMR of **17** (101 MHz, $CDCl_3$)
MeO
O
CF_2H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

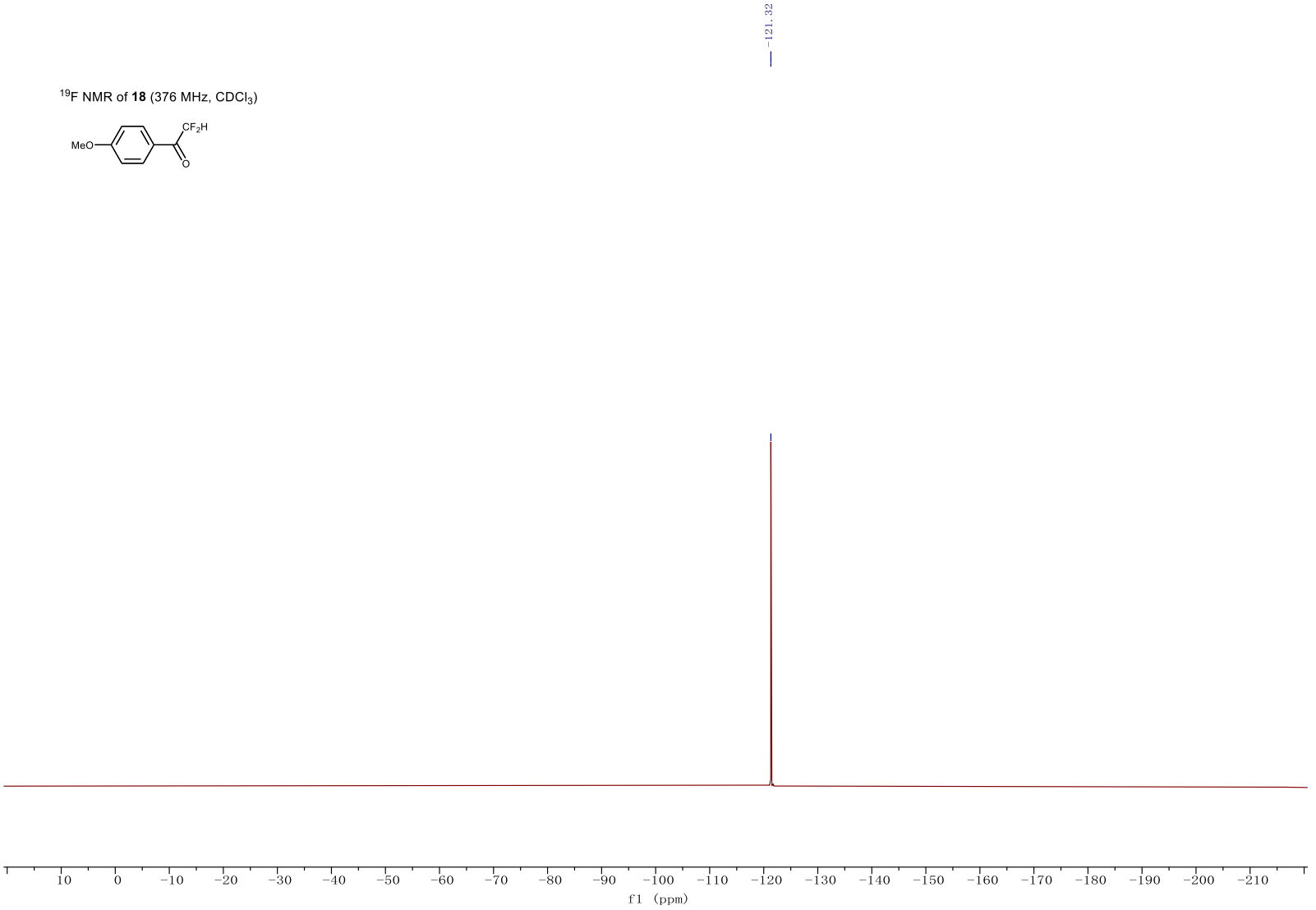
^{19}F NMR of **17** (376 MHz, $CDCl_3$)



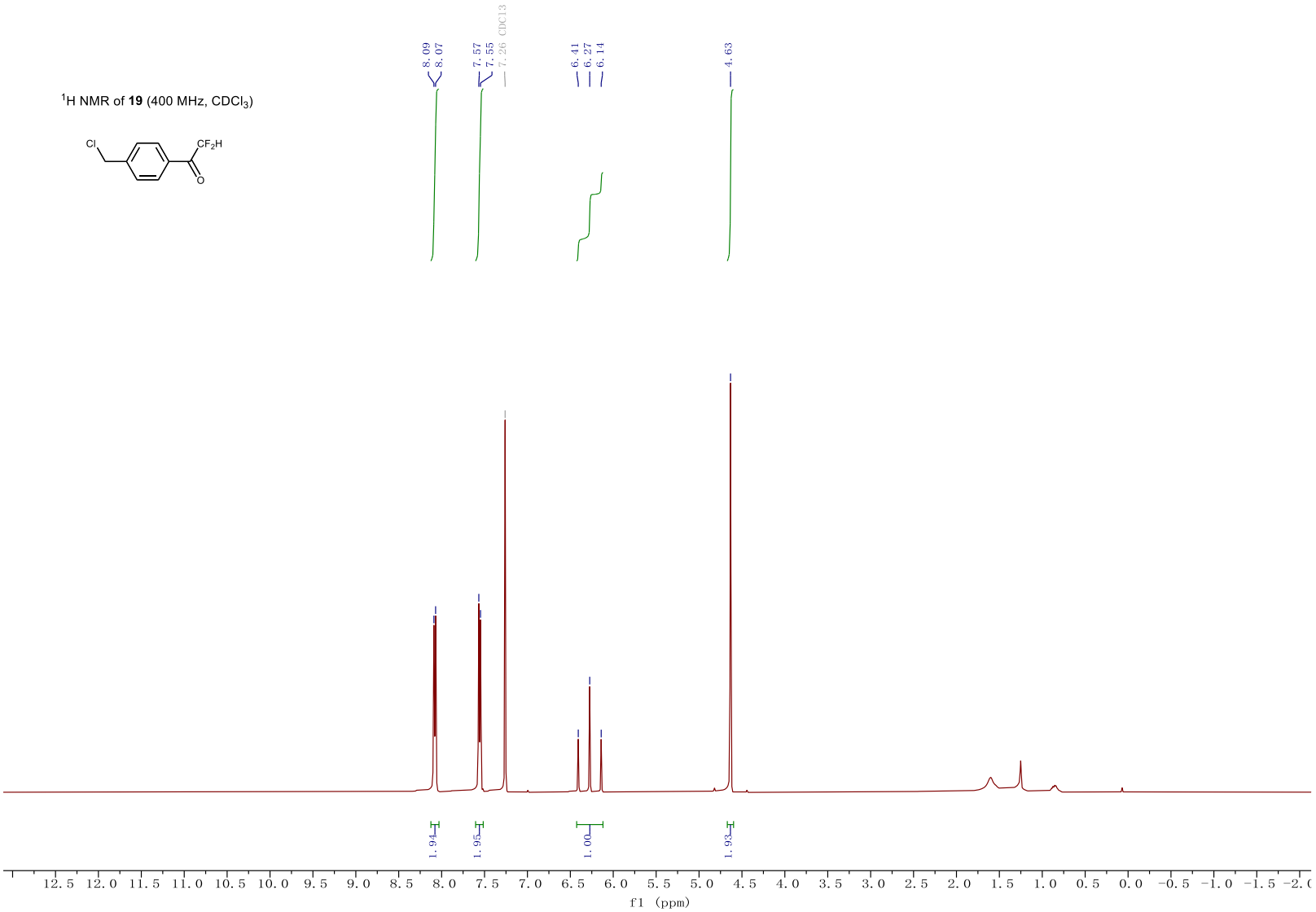

1H NMR of 18 (400 MHz, CDCl3)
MeO
CF2H
O
8.08
8.05
7.26 CDCl3
7.00
6.98
6.39
6.25
6.12
3.91
2.01
2.00
1.00
3.03
f1 (ppm)


186.47
186.22
185.97
165.04
132.33
132.30
124.58
114.42
114.17
111.65
109.13
55.78
^{13}C NMR of **18** (101 MHz, $CDCl_3$)
MeO
CF_2H
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

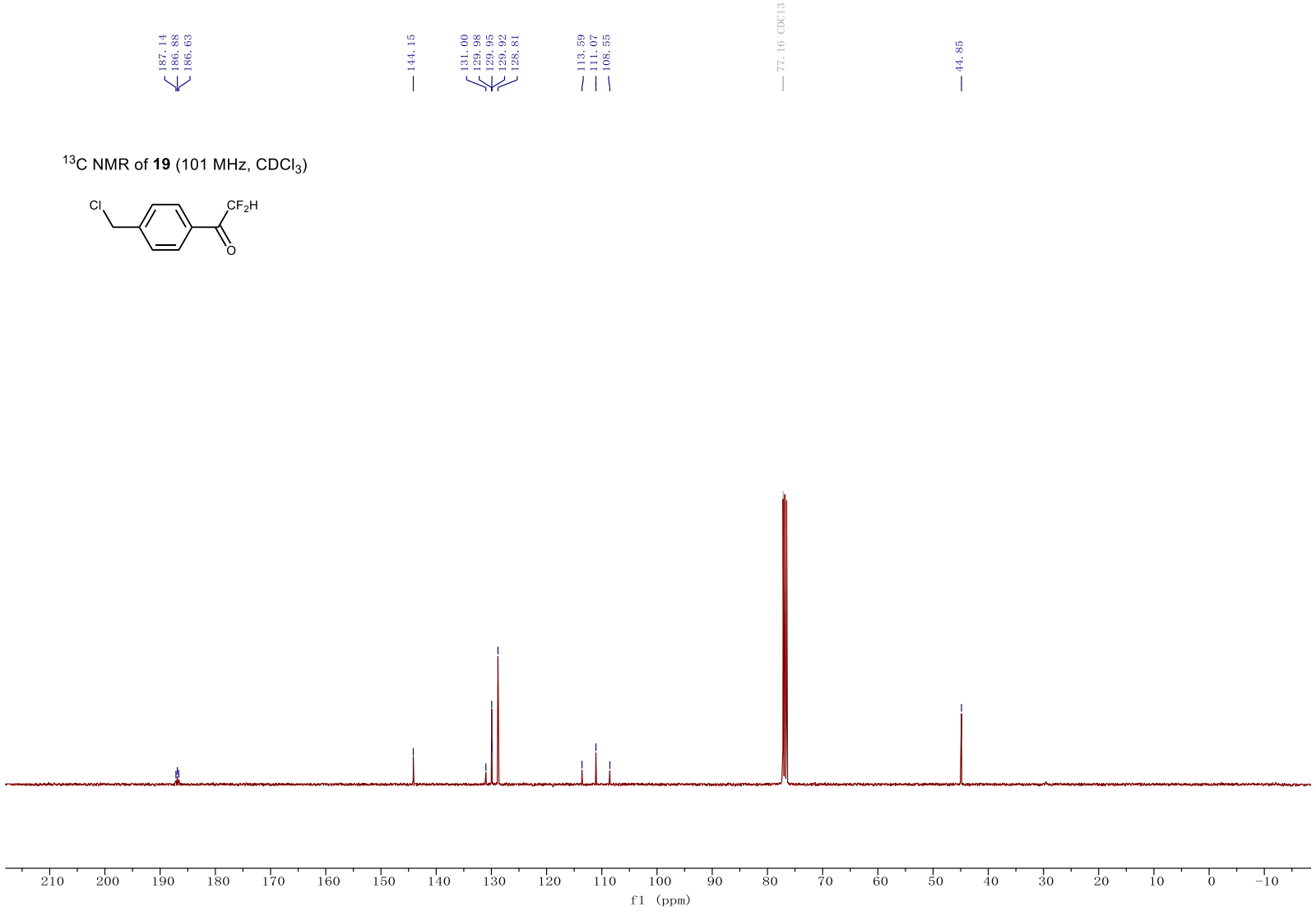
^{19}F NMR of **18** (376 MHz, $CDCl_3$)



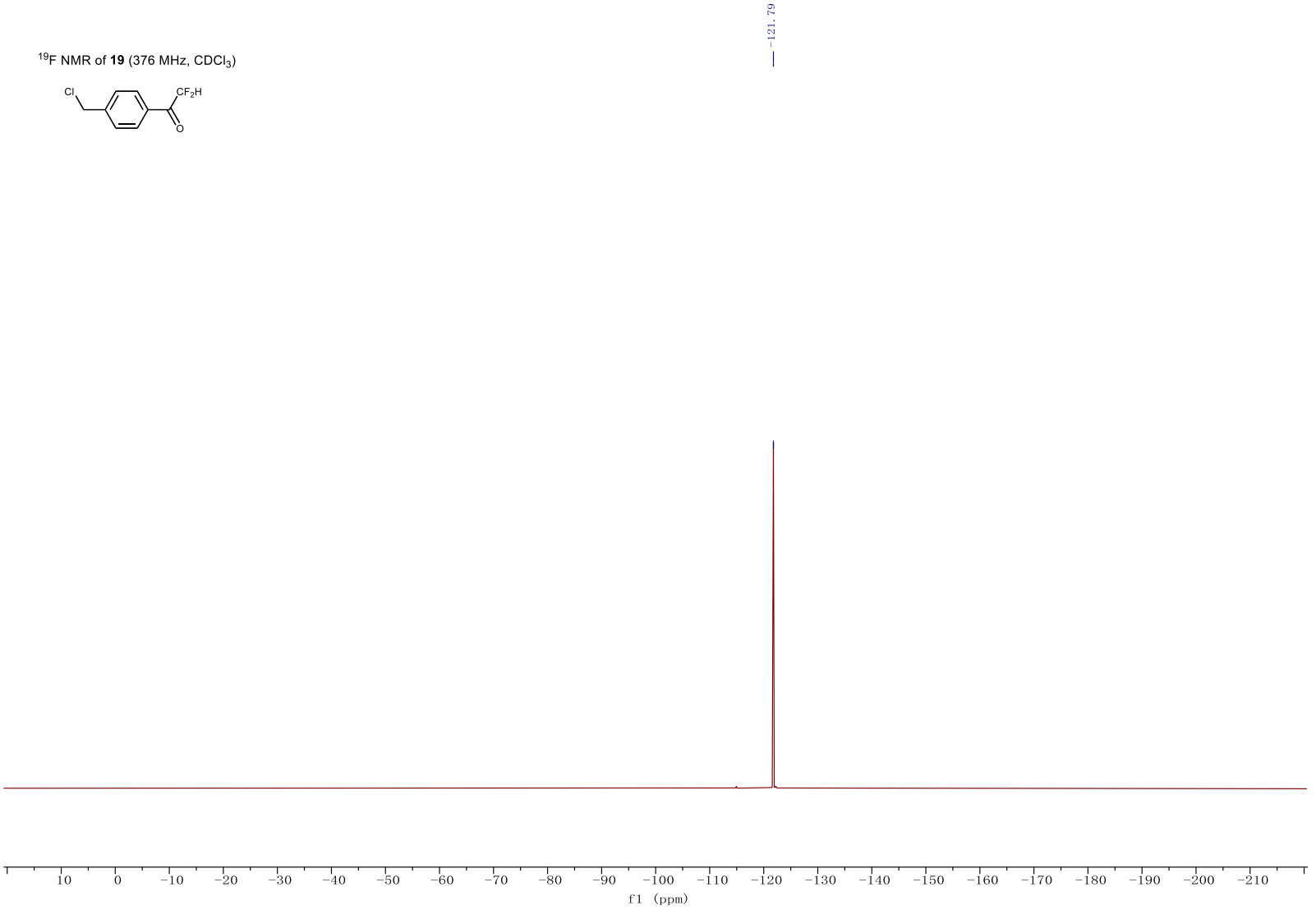
^{1}H NMR of **19** (400 MHz, $CDCl_3$)



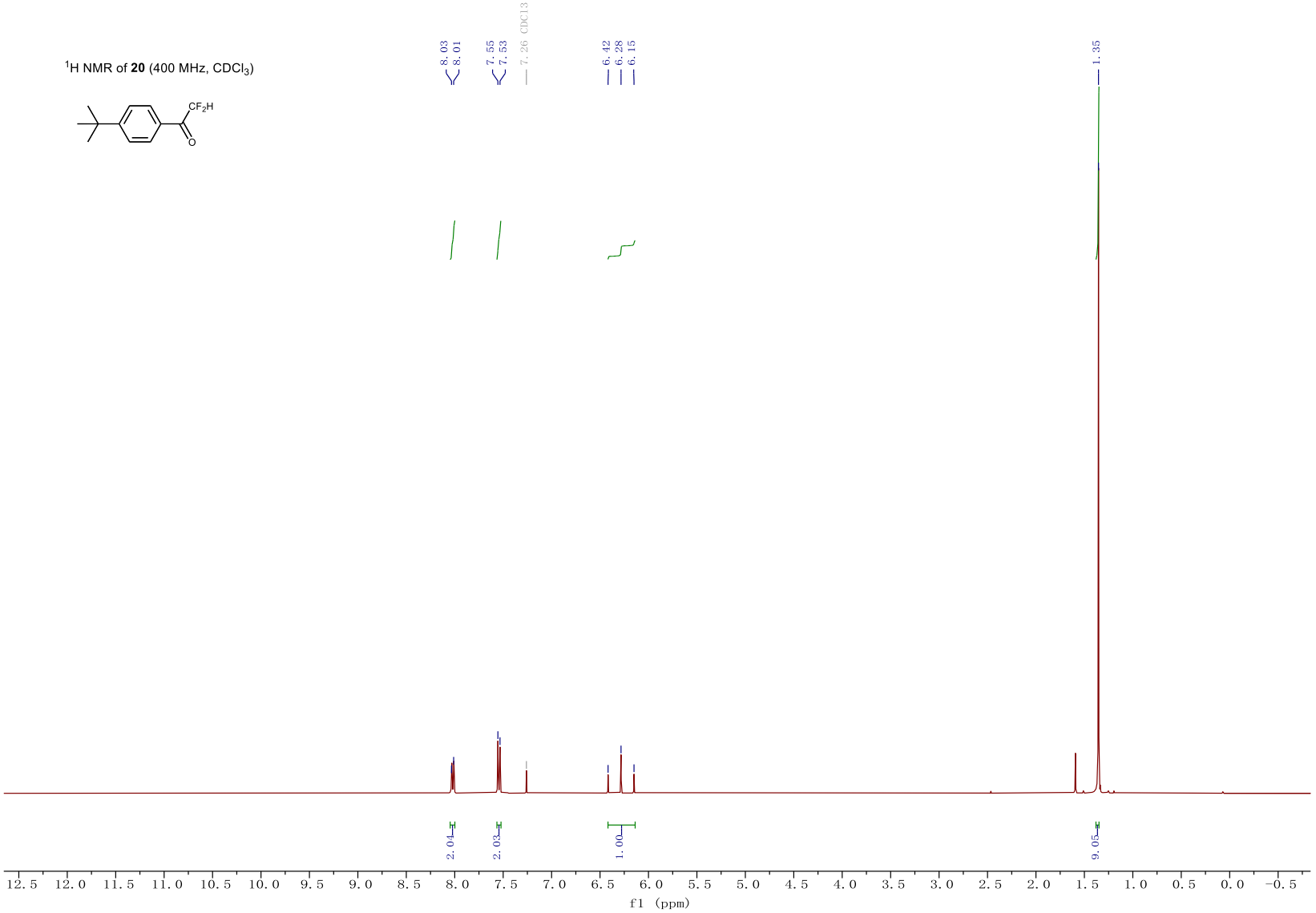
^{13}C NMR of **19** (101 MHz, $CDCl_3$)

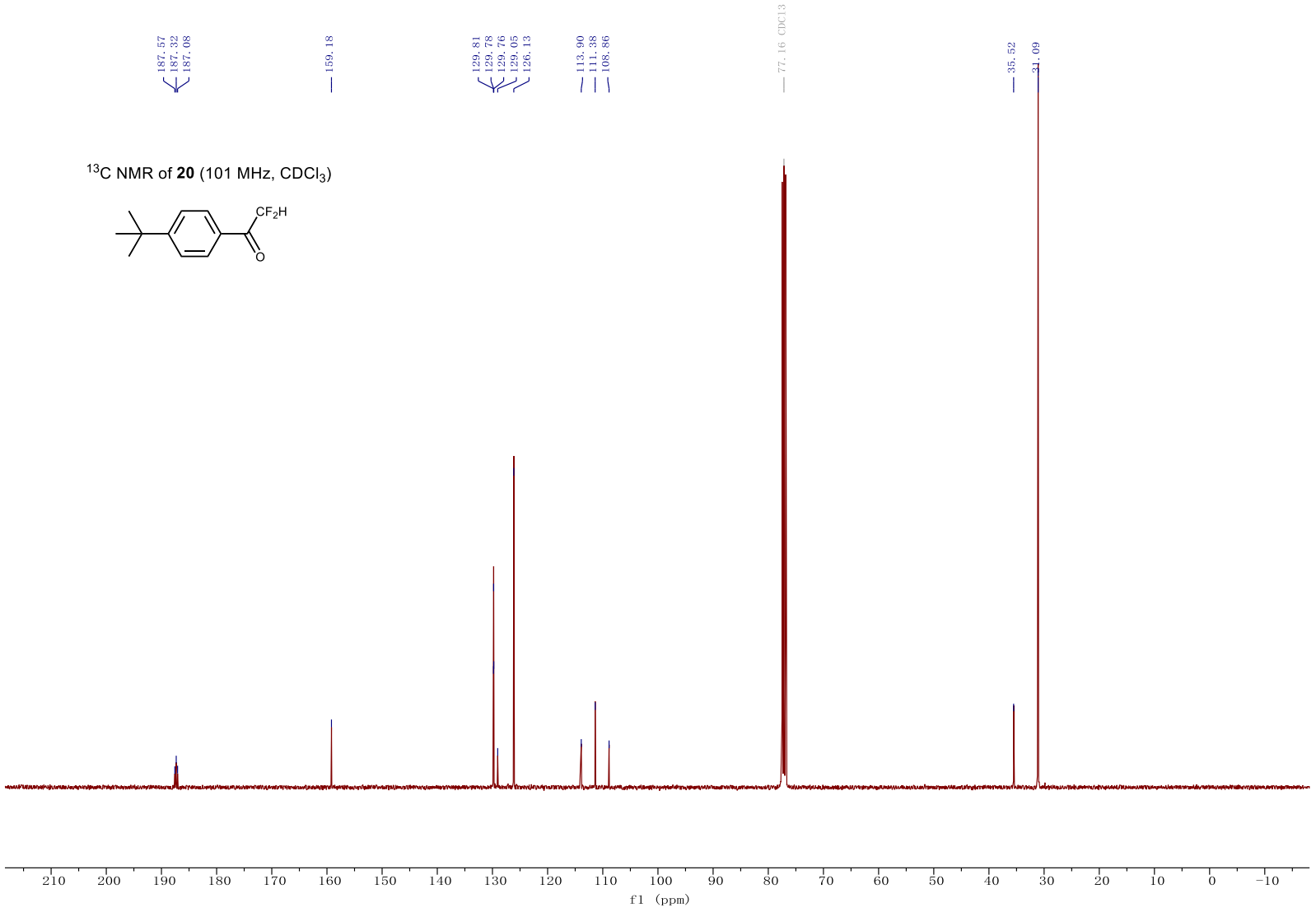


^{19}F NMR of **19** (376 MHz, $CDCl_3$)

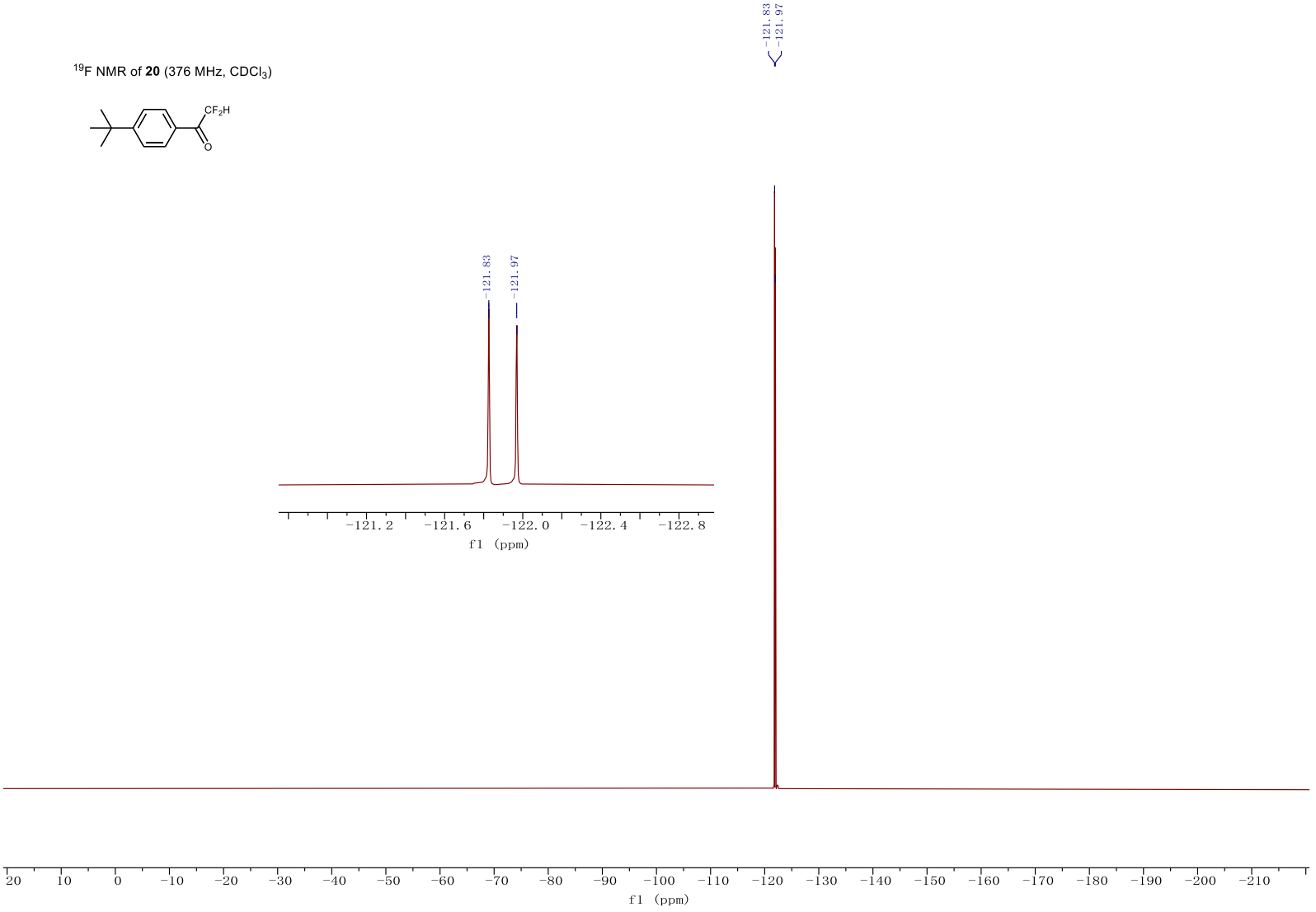


^{1}H NMR of **20** (400 MHz, $CDCl_3$)

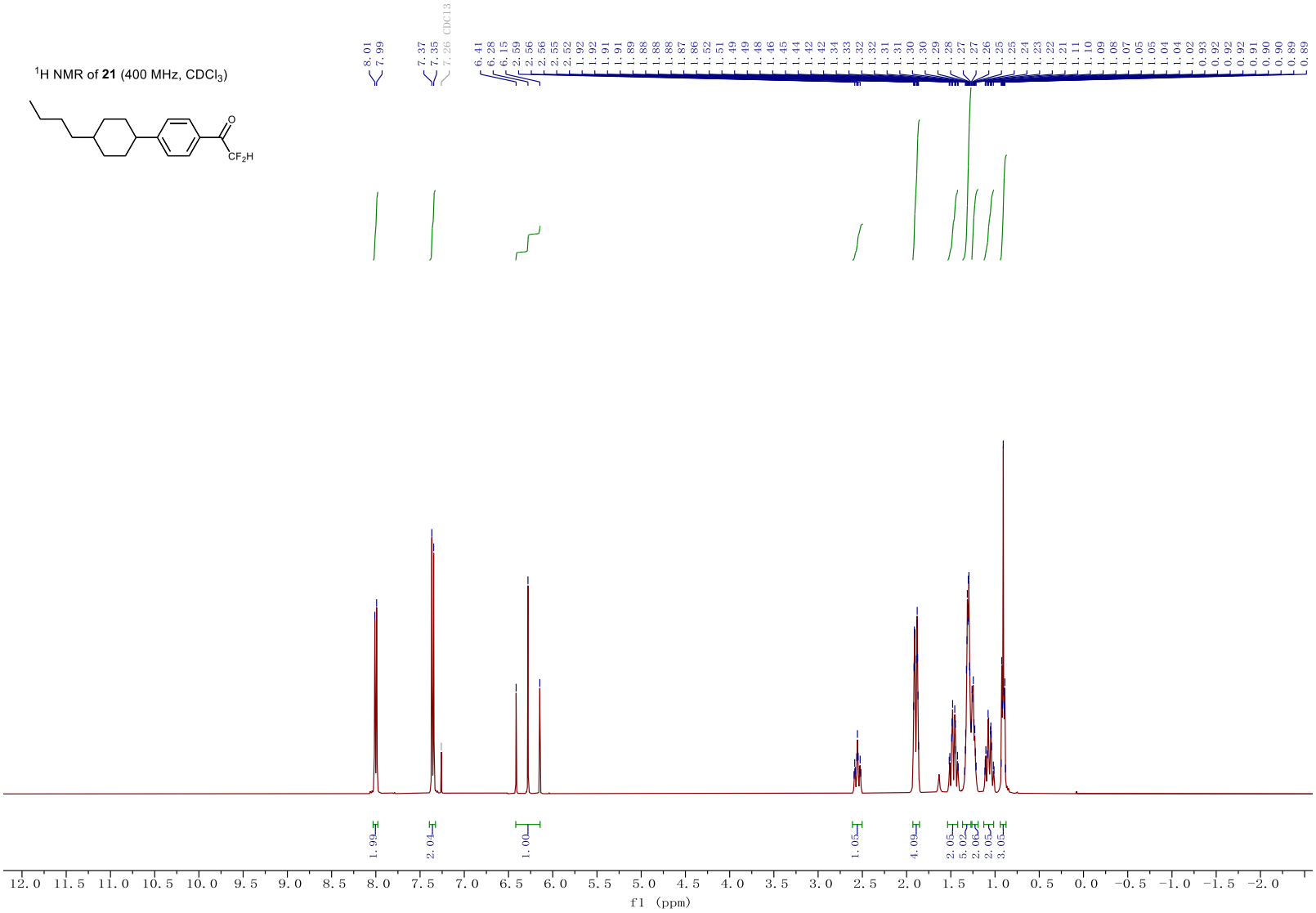



187.57
187.32
187.08
159.18
129.81
129.78
129.76
129.05
126.13
113.90
111.38
108.86
77.16 CDCl3
35.52
31.09
13C NMR of 20 (101 MHz, CDCl3)
CF2H
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

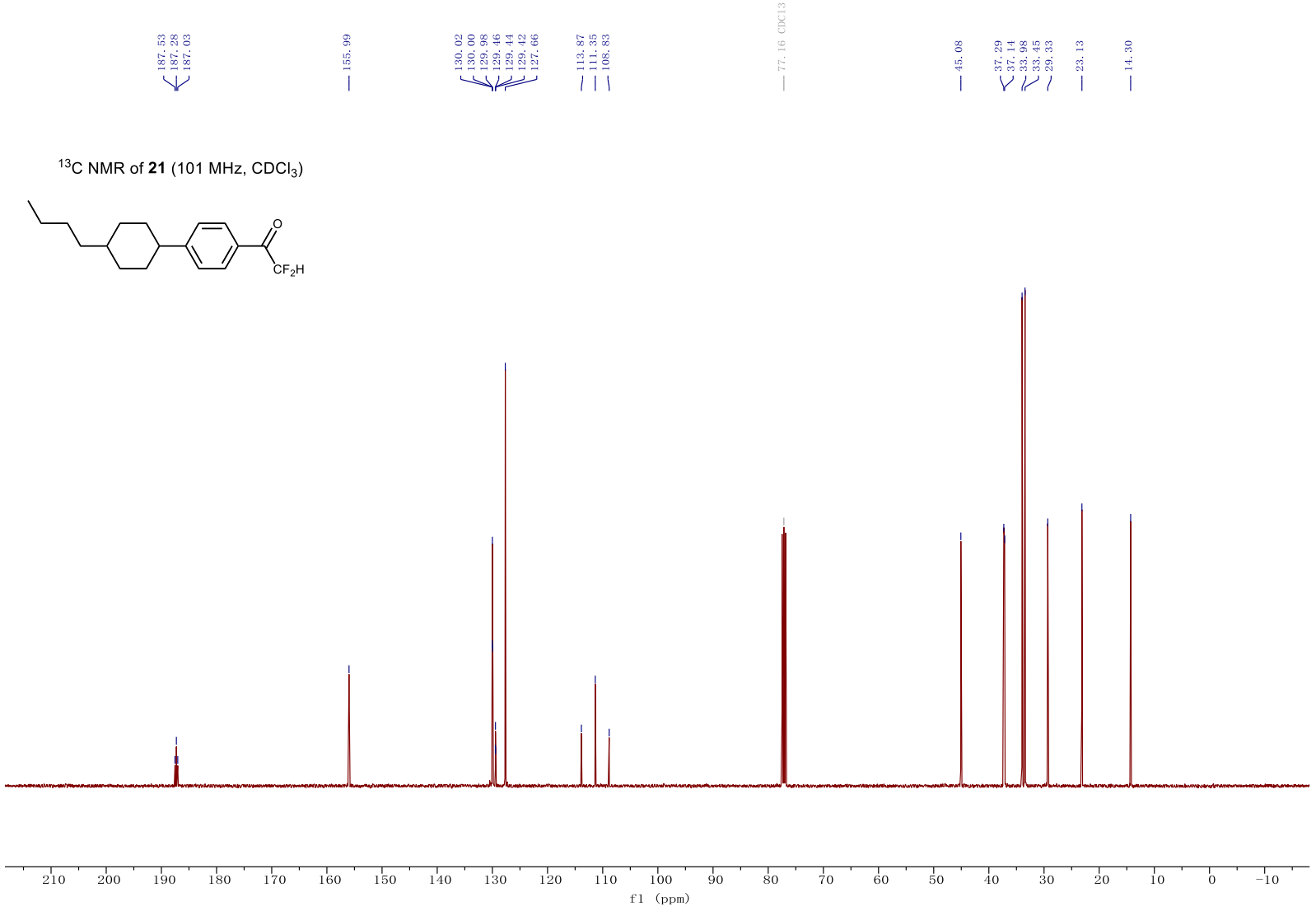
^{19}F NMR of **20** (376 MHz, $CDCl_3$)



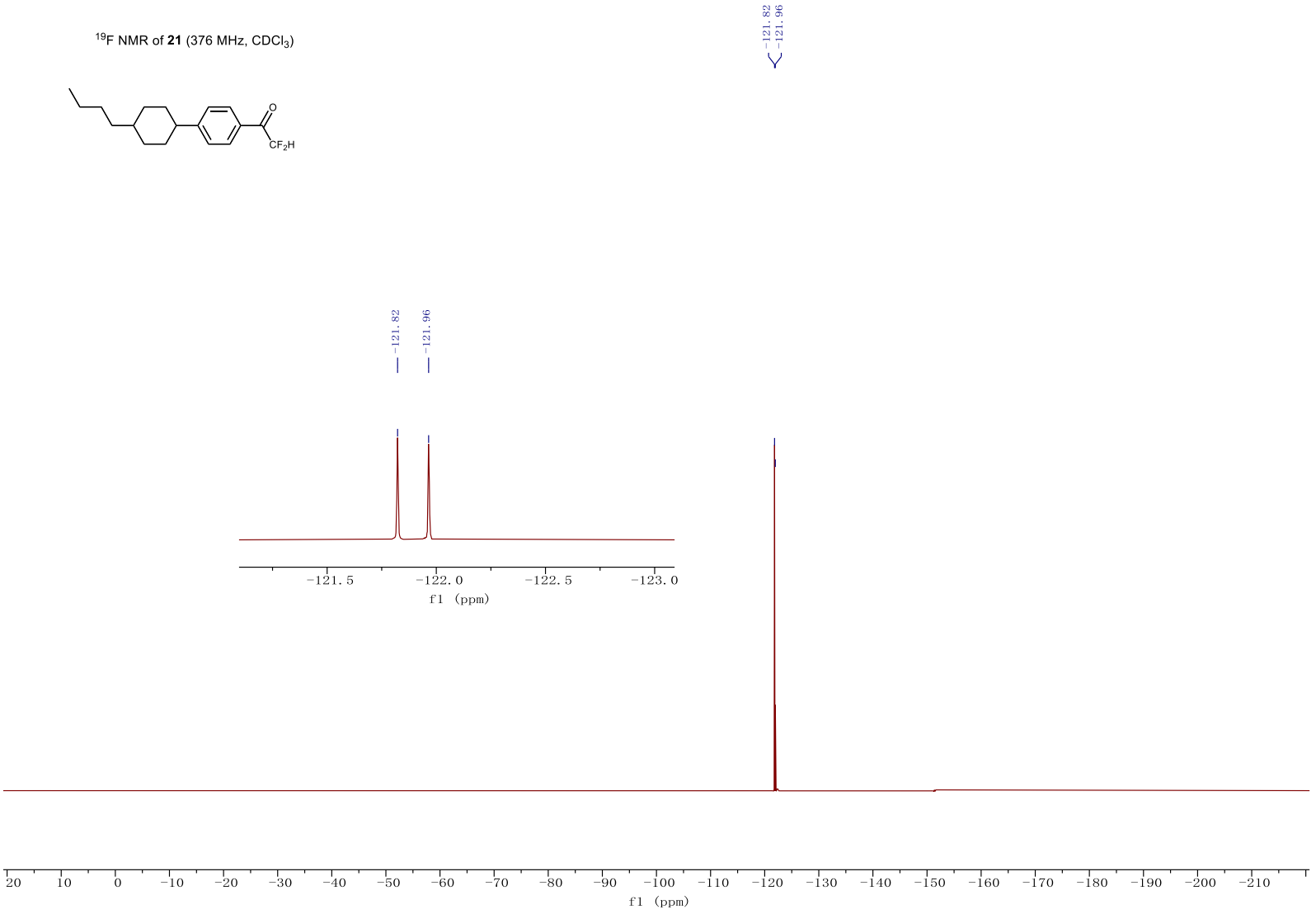
^{1}H NMR of **21** (400 MHz, $CDCl_3$)

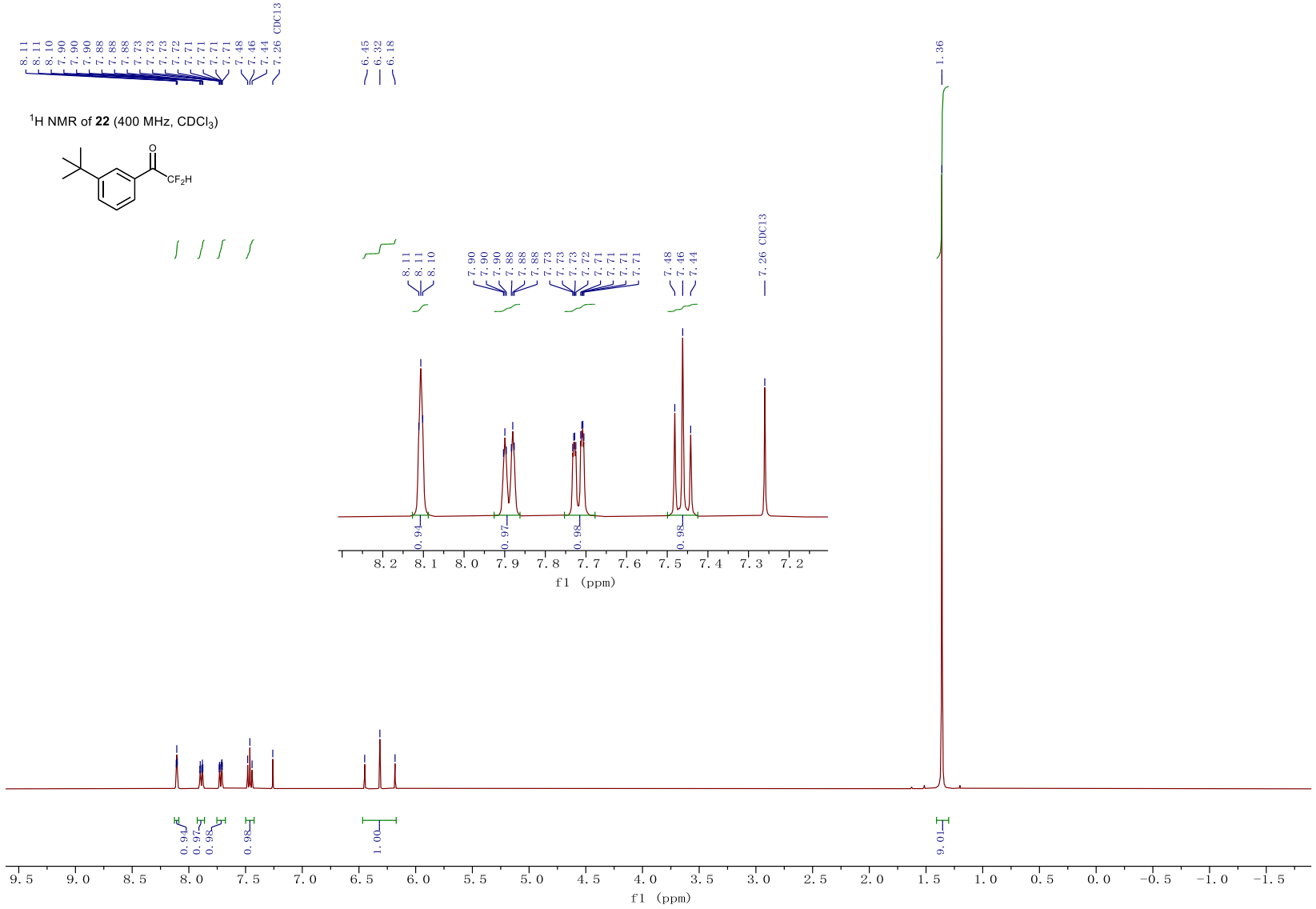


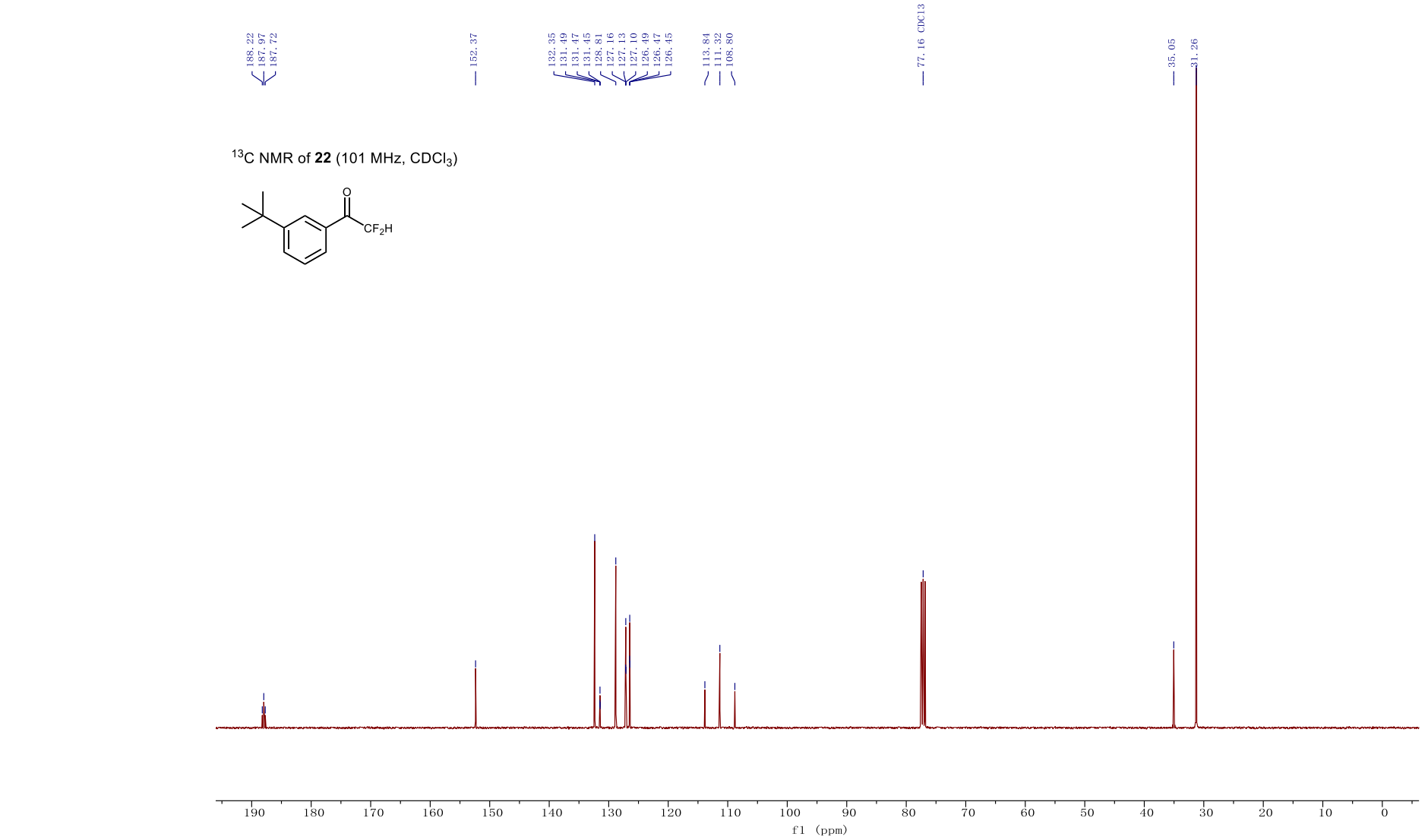
^{13}C NMR of **21** (101 MHz, $CDCl_3$)



^{19}F NMR of **21** (376 MHz, $CDCl_3$)

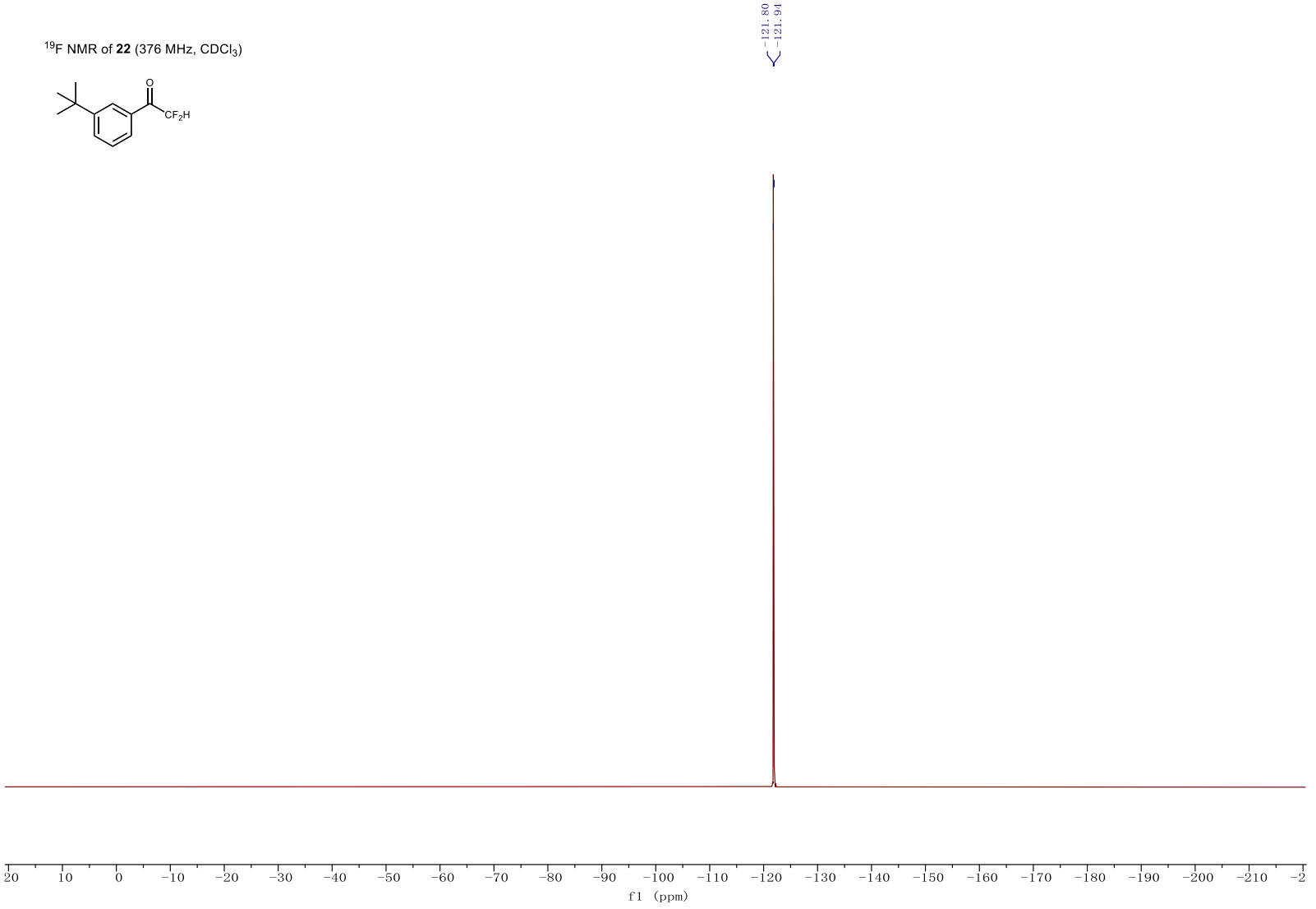


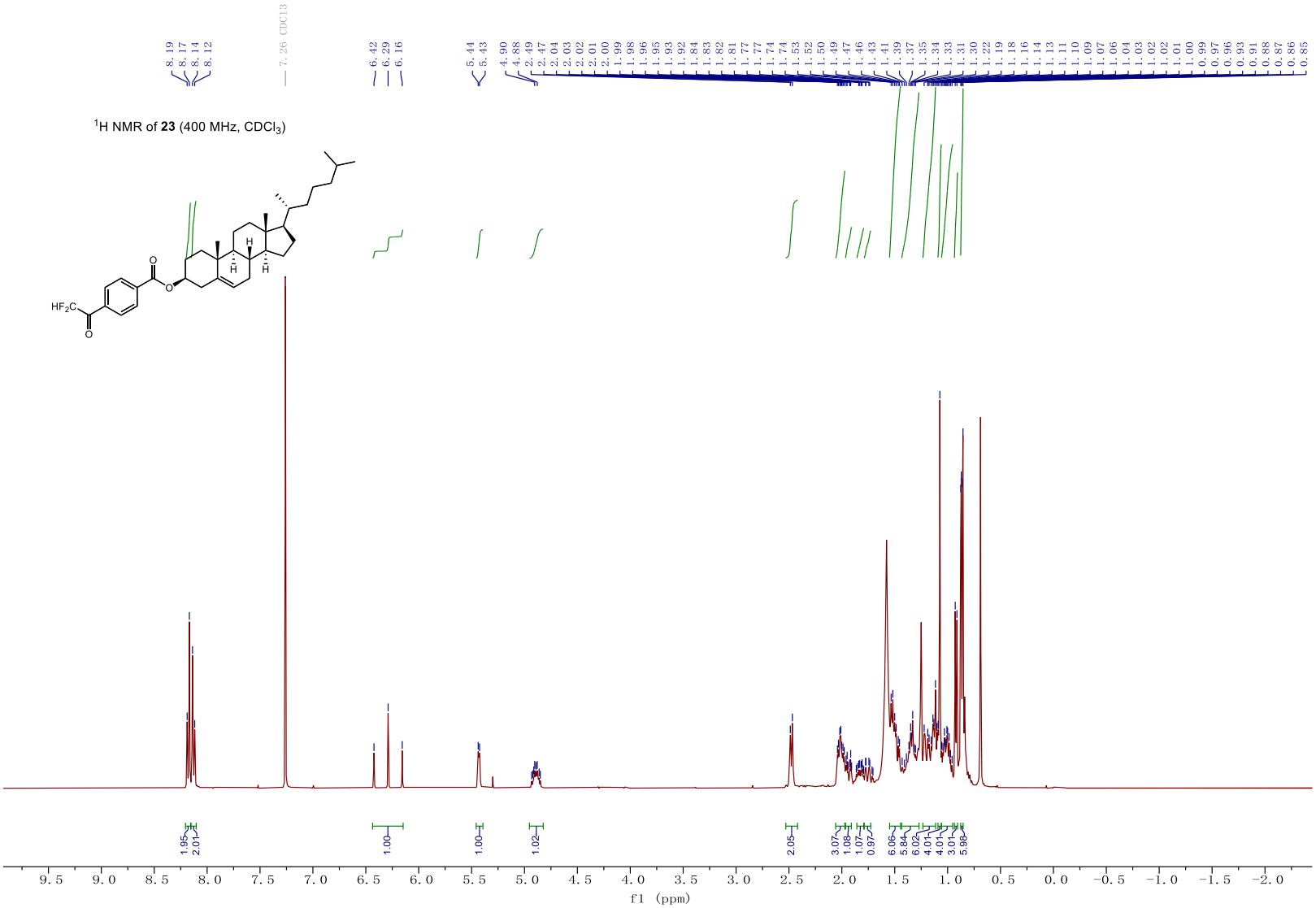

8.11
8.11
8.10
7.90
7.90
7.90
7.88
7.88
7.88
7.73
7.73
7.72
7.71
7.71
7.71
7.71
7.48
7.46
7.44
7.26 CDCl3
6.45
6.32
6.18
1.36
^{1}H NMR of **22** (400 MHz, $CDCl_3$)
CF_2H
0.94
0.97
0.98
0.98
1.00
9.01
f1 (ppm)

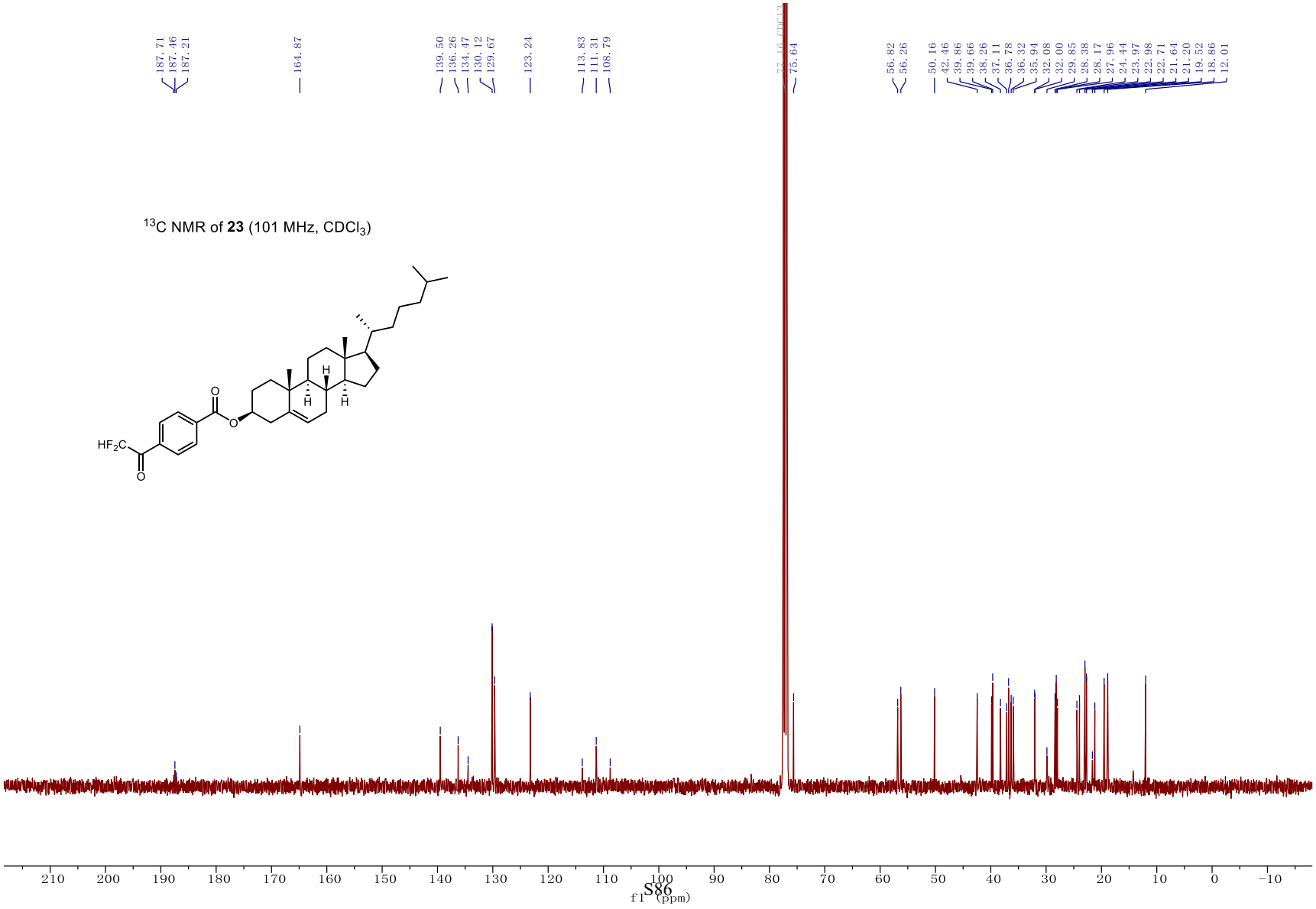


^{13}C NMR of **22** (101 MHz, $CDCl_3$)

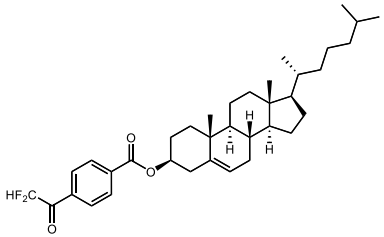
^{19}F NMR of **22** (376 MHz, $CDCl_3$)

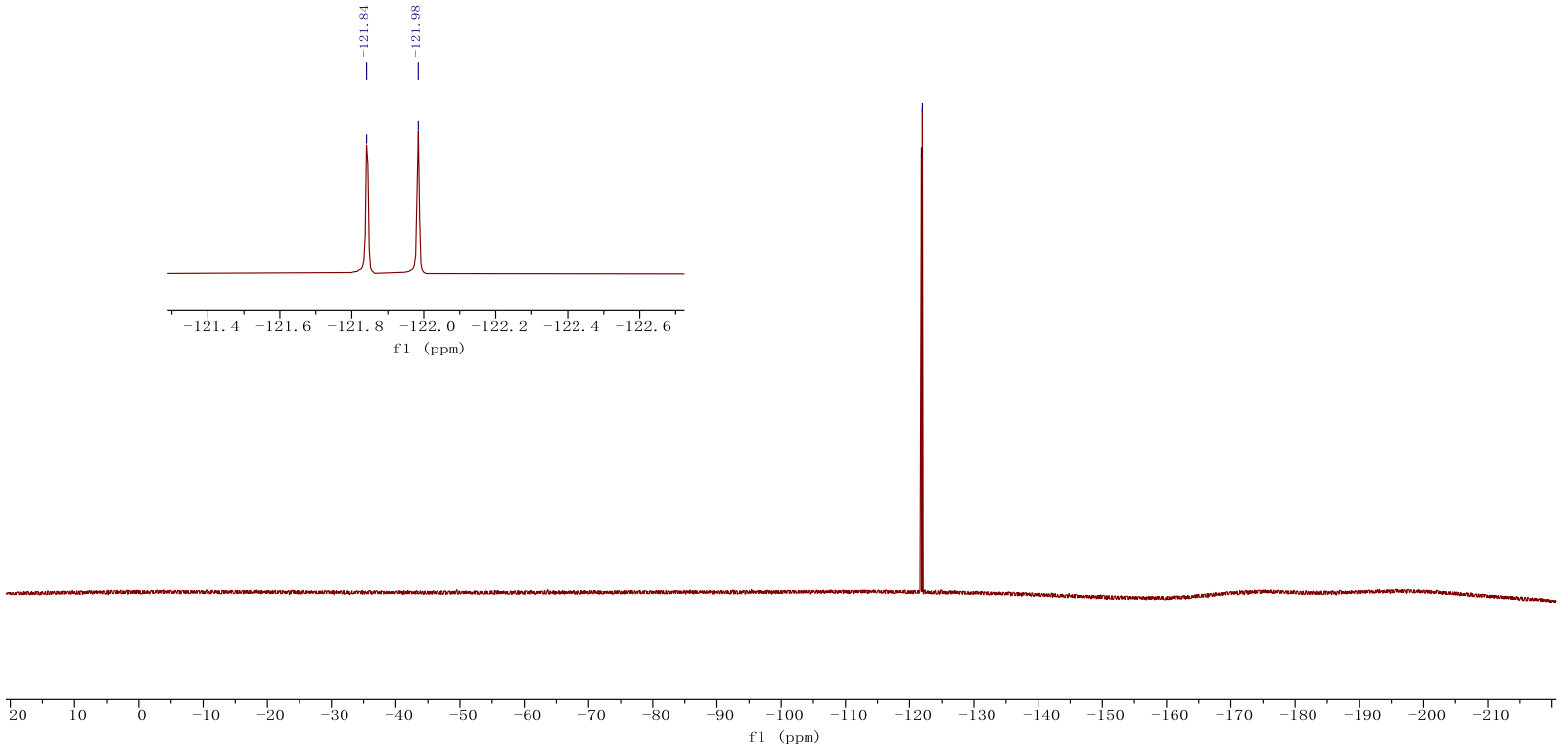


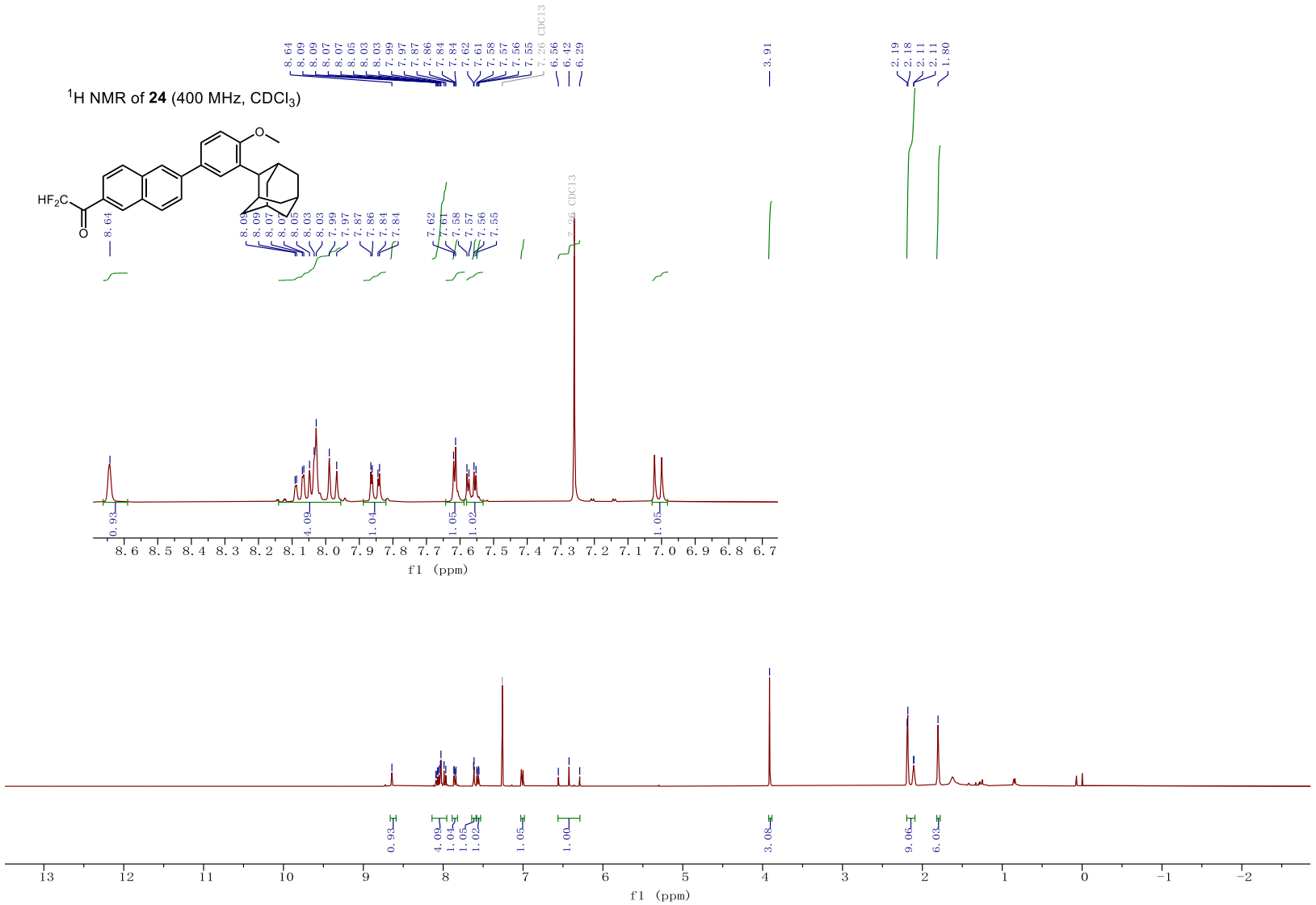

8.19
8.17
8.14
8.12
7.26 CDCl3
6.42
6.29
6.16
5.44
5.43
4.90
4.88
2.49
2.47
2.04
2.03
2.02
2.01
2.00
1.99
1.98
1.96
1.95
1.93
1.92
1.84
1.83
1.82
1.81
1.77
1.77
1.74
1.74
1.53
1.52
1.50
1.49
1.47
1.46
1.43
1.41
1.39
1.37
1.35
1.34
1.33
1.31
1.30
1.22
1.19
1.18
1.16
1.14
1.13
1.11
1.10
1.09
1.07
1.06
1.04
1.03
1.02
1.02
1.01
1.00
0.99
0.97
0.96
0.93
0.91
0.88
0.87
0.86
0.85
1H NMR of 23 (400 MHz, CDCl3)
HF2C
O
O
O
H
H
H
1.95
2.01
1.00
1.00
1.02
2.05
3.07
1.08
1.07
0.97
6.06
5.84
6.02
4.01
4.01
3.01
5.98
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
−1.5
−2.0
f1 (ppm)

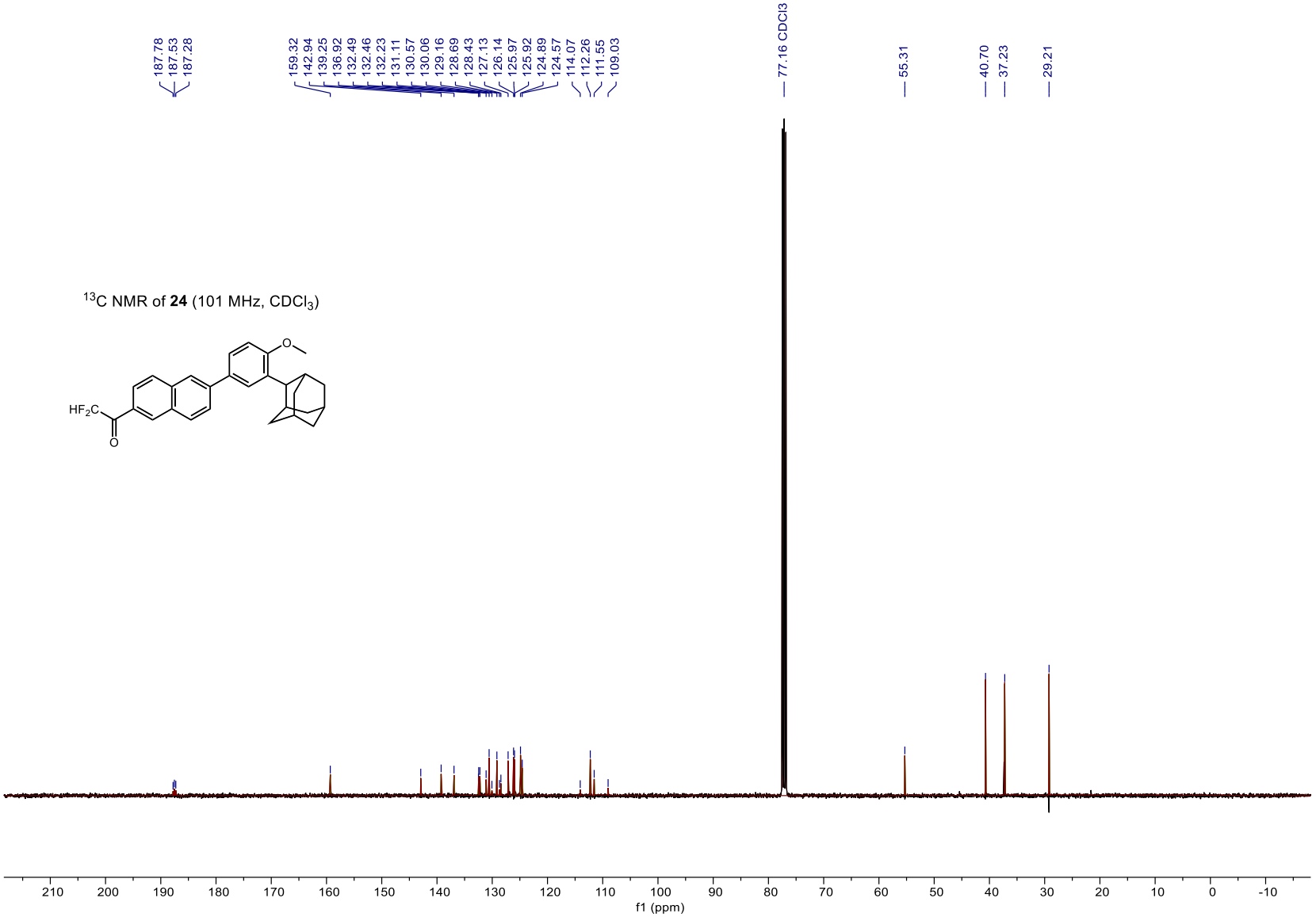

187.71
187.46
187.21
164.87
139.50
136.26
134.47
130.12
129.67
123.24
113.83
111.31
108.79
77.16 CDCl3
75.64
56.82
56.26
50.16
42.46
39.86
39.66
38.26
37.11
36.78
36.32
35.94
32.08
32.00
29.85
28.38
28.17
27.96
24.44
23.97
22.98
22.71
21.64
21.20
19.52
18.86
12.01
^{13}C NMR of **23** (101 MHz, $CDCl_3$)
HF_2C
O
O
O
H
H
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

^{19}F NMR of **23** (376 MHz, $CDCl_3$)

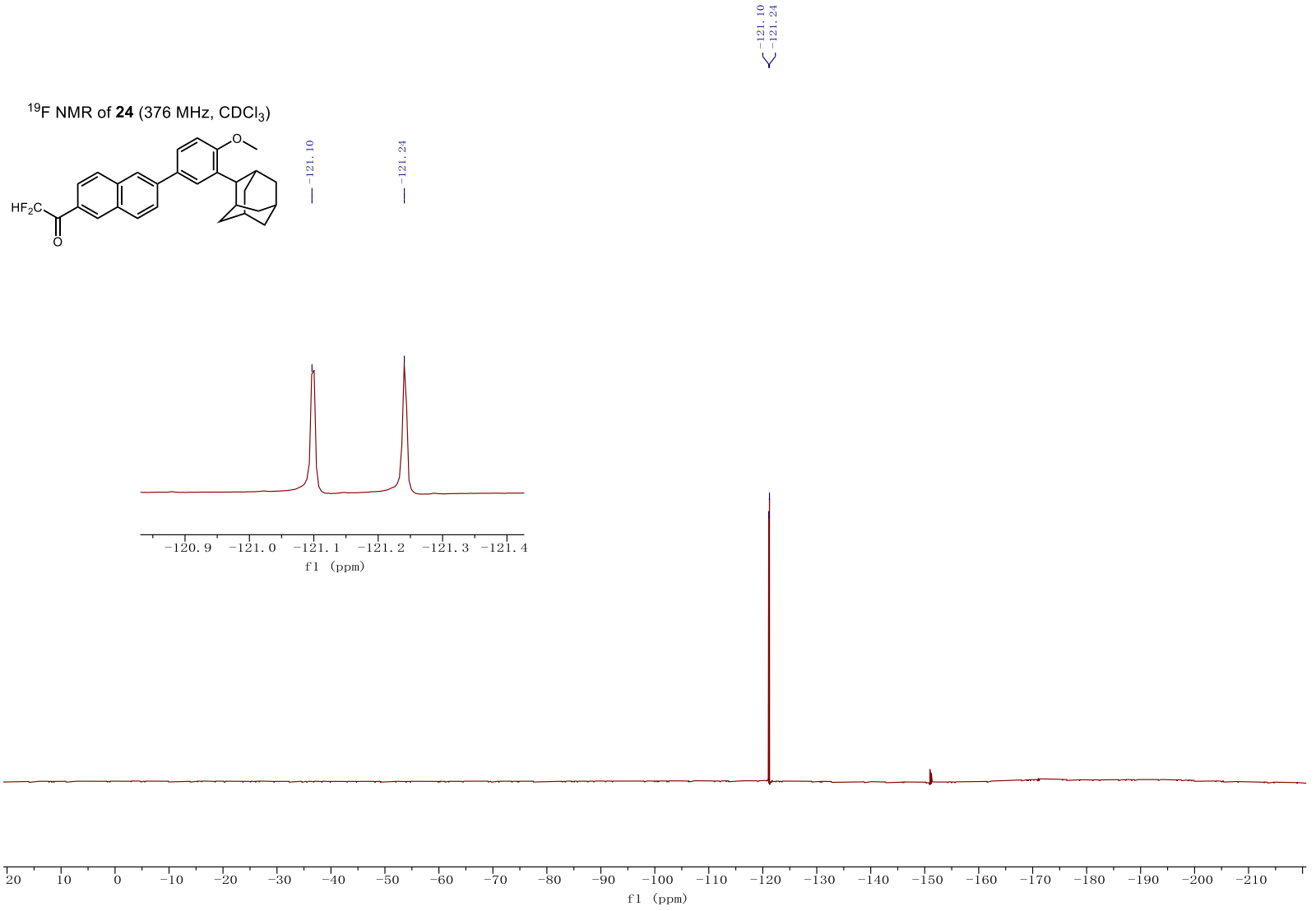


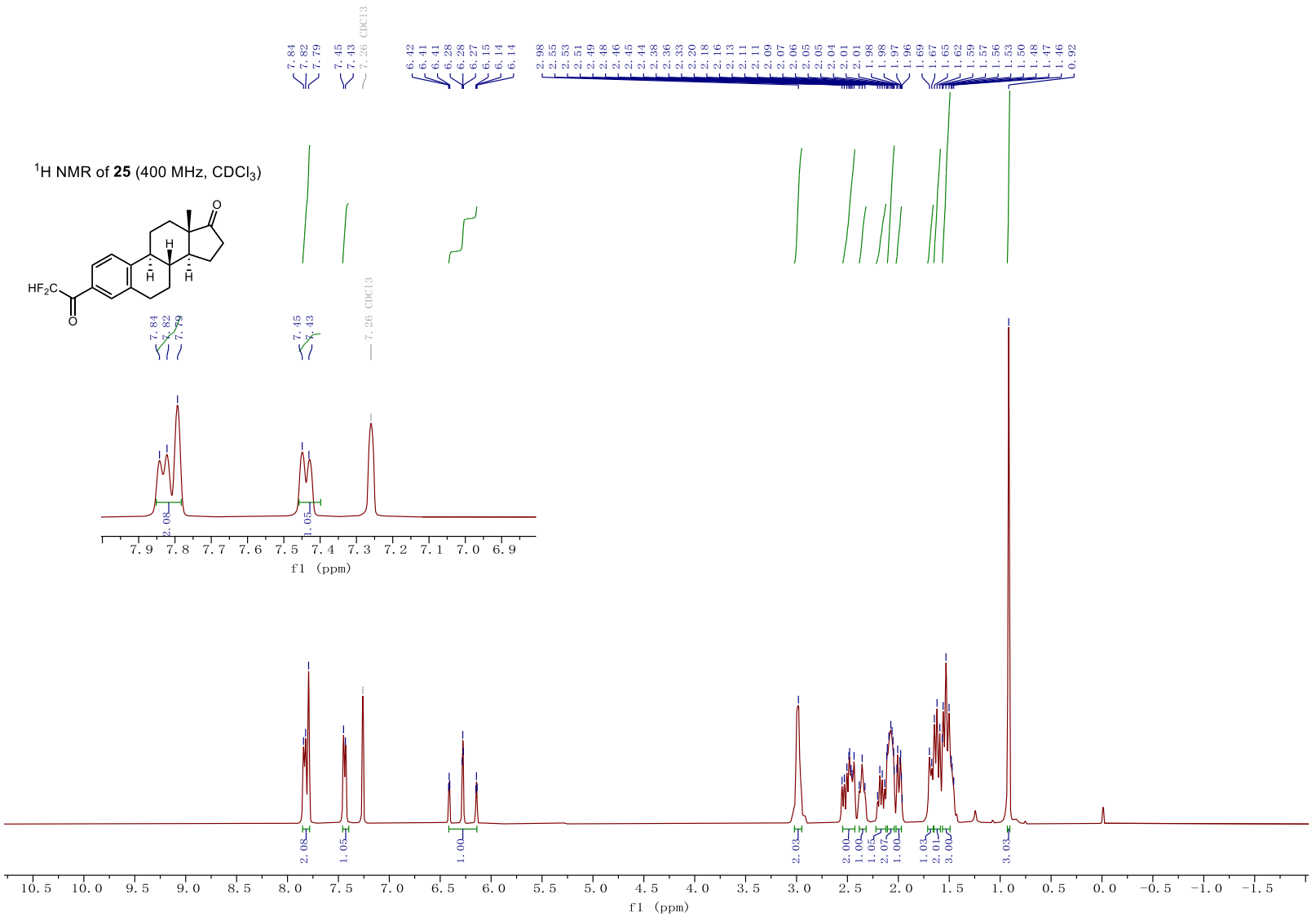


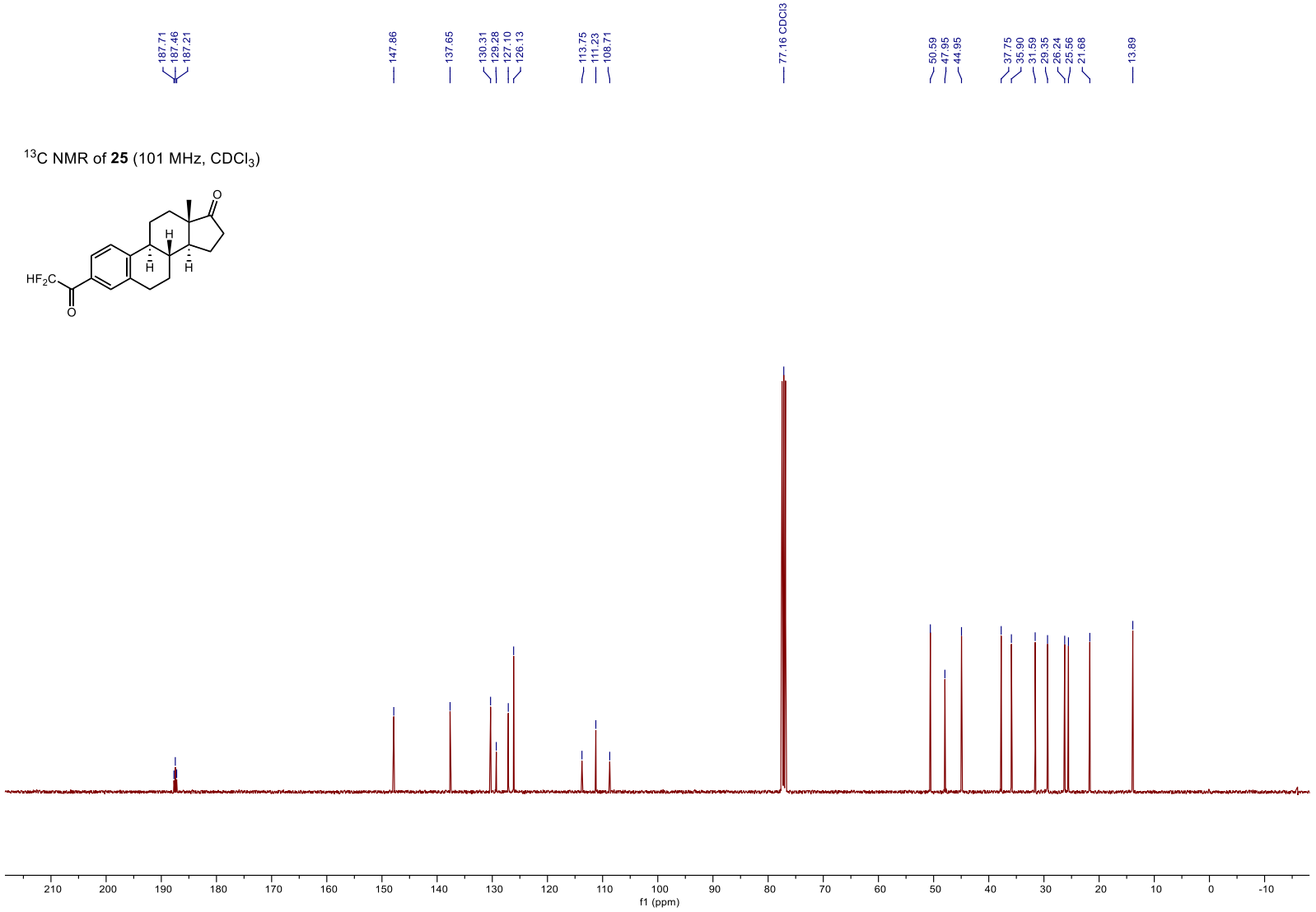

^{1}H NMR of **24** (400 MHz, $CDCl_3$)
HF_2C
O
f1 (ppm)
f1 (ppm)


187.78
187.53
187.28
159.32
142.94
139.25
136.92
132.49
132.46
132.23
131.11
130.57
130.06
129.16
128.69
128.43
127.13
126.14
125.97
125.92
124.89
124.57
114.07
112.26
111.55
109.03
77.16 CDCl3
55.31
40.70
37.23
29.21
^{13}C NMR of **24** (101 MHz, $CDCl_3$)
HF_2C
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

^{19}F NMR of **24** (376 MHz, $CDCl_3$)

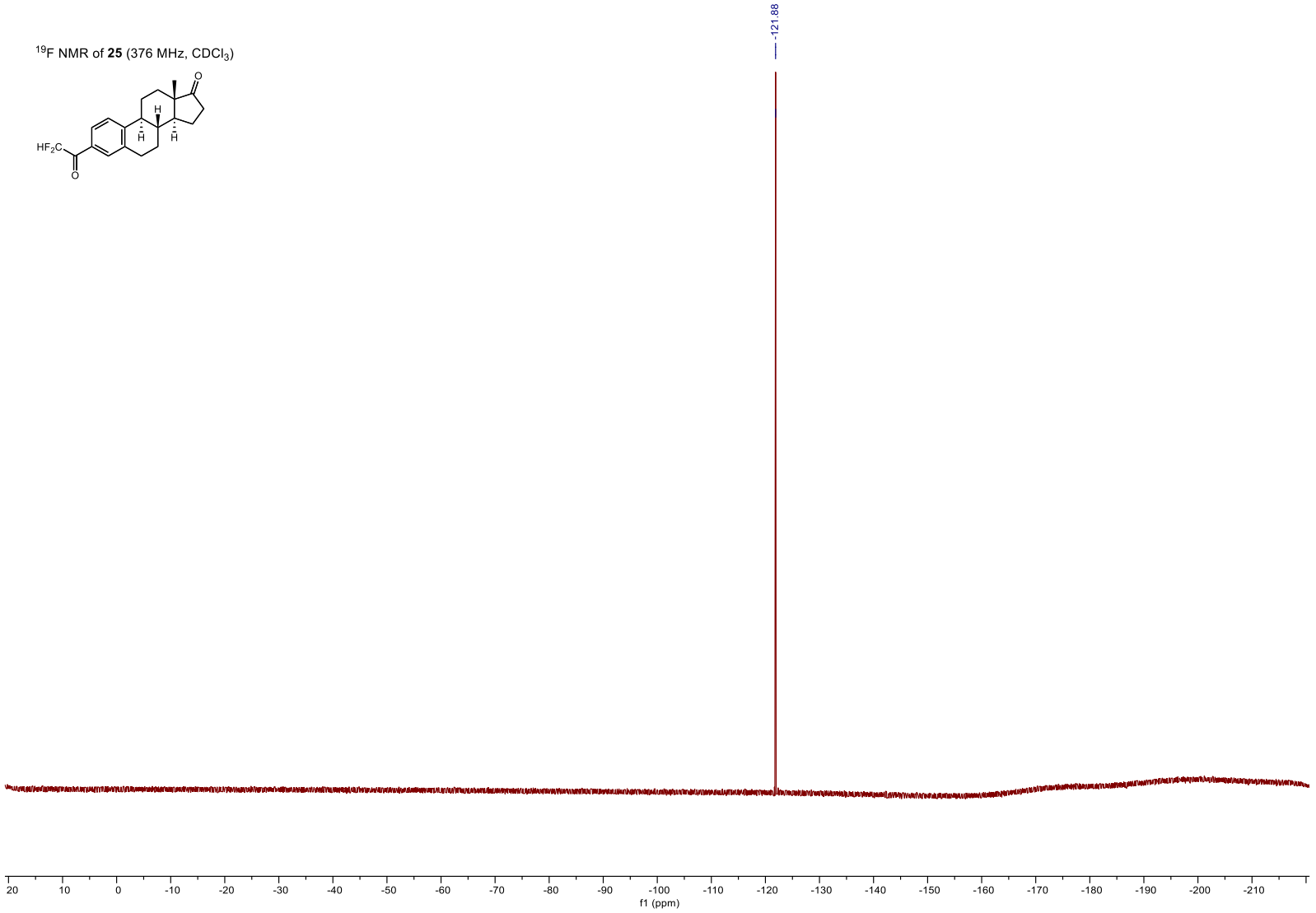



^{1}H NMR of **25** (400 MHz, $CDCl_3$)
HF_2C
O
H
H
H
O
7.84
7.82
7.79
7.45
7.43
7.26 CDCl3
6.42
6.41
6.41
6.28
6.28
6.27
6.15
6.14
6.14
2.98
2.55
2.53
2.51
2.49
2.48
2.46
2.45
2.44
2.38
2.36
2.33
2.20
2.18
2.16
2.13
2.11
2.11
2.09
2.07
2.06
2.05
2.05
2.04
2.01
2.01
1.98
1.98
1.97
1.96
1.69
1.67
1.65
1.62
1.59
1.57
1.56
1.53
1.50
1.48
1.47
1.46
0.92
2.08
1.05
1.00
2.03
2.00
1.00
1.05
2.07
1.00
1.03
2.01
3.00
3.03
f1 (ppm)

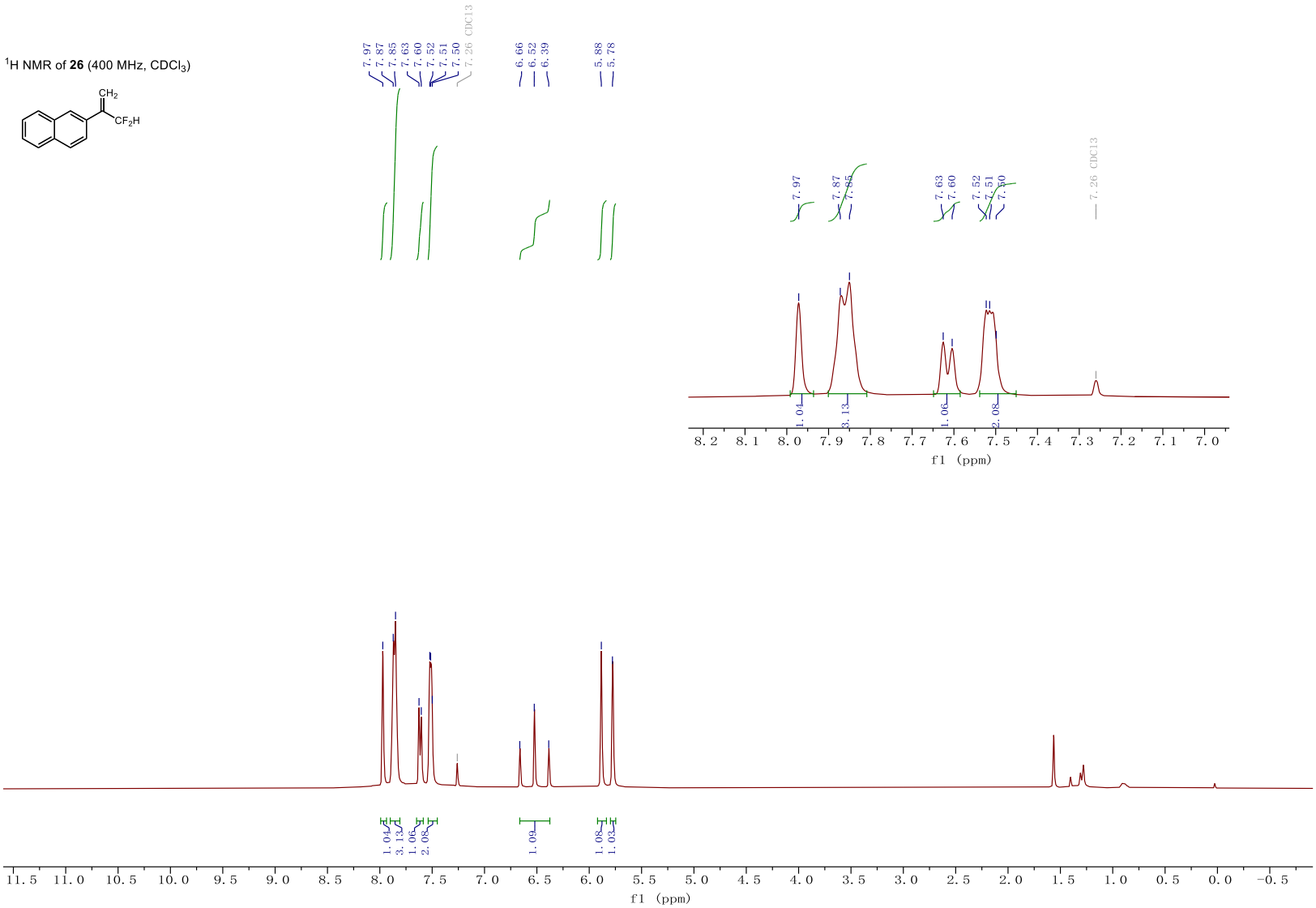


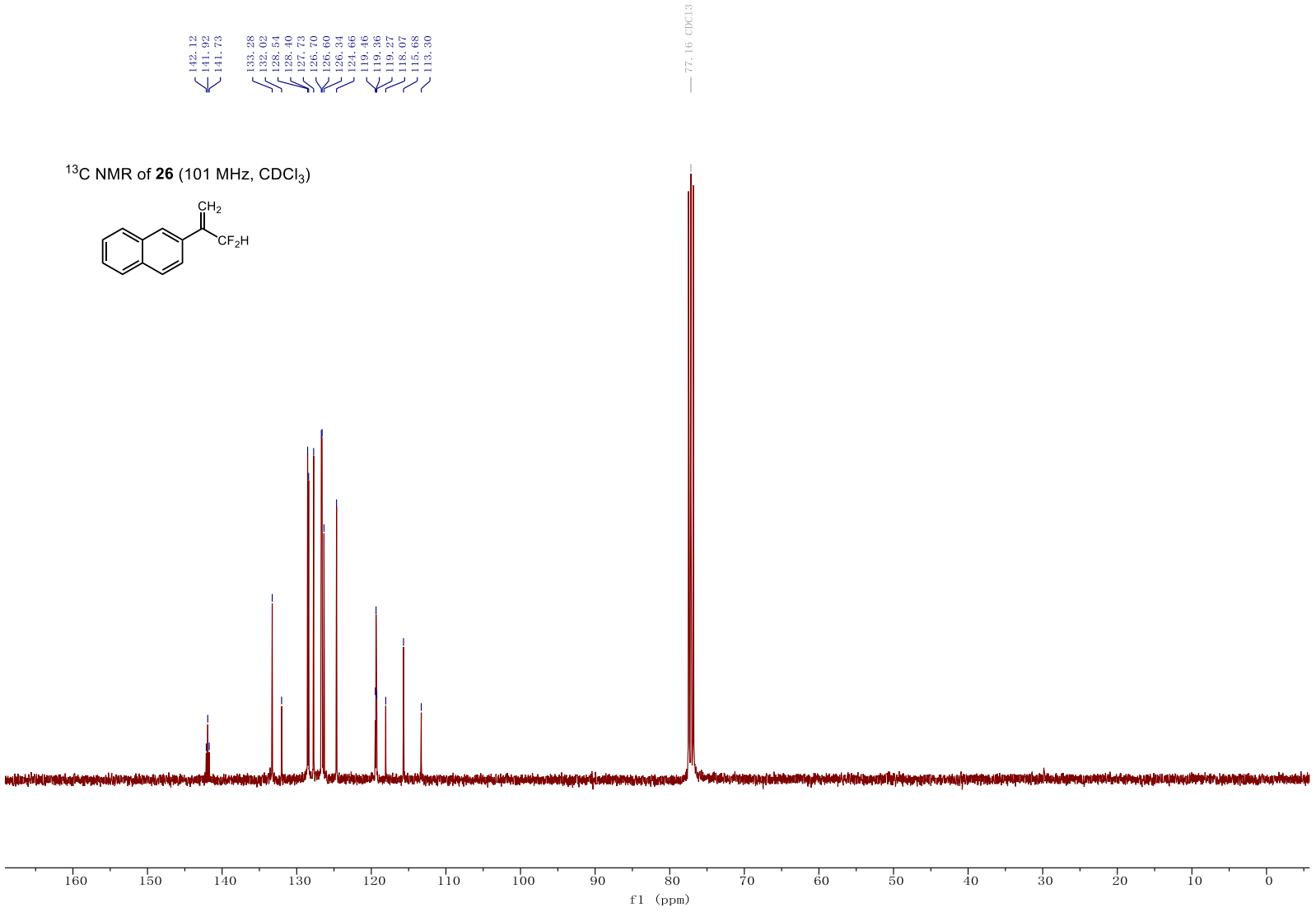
^{13}C NMR of **25** (101 MHz, $CDCl_3$)

^{19}F NMR of **25** (376 MHz, $CDCl_3$)

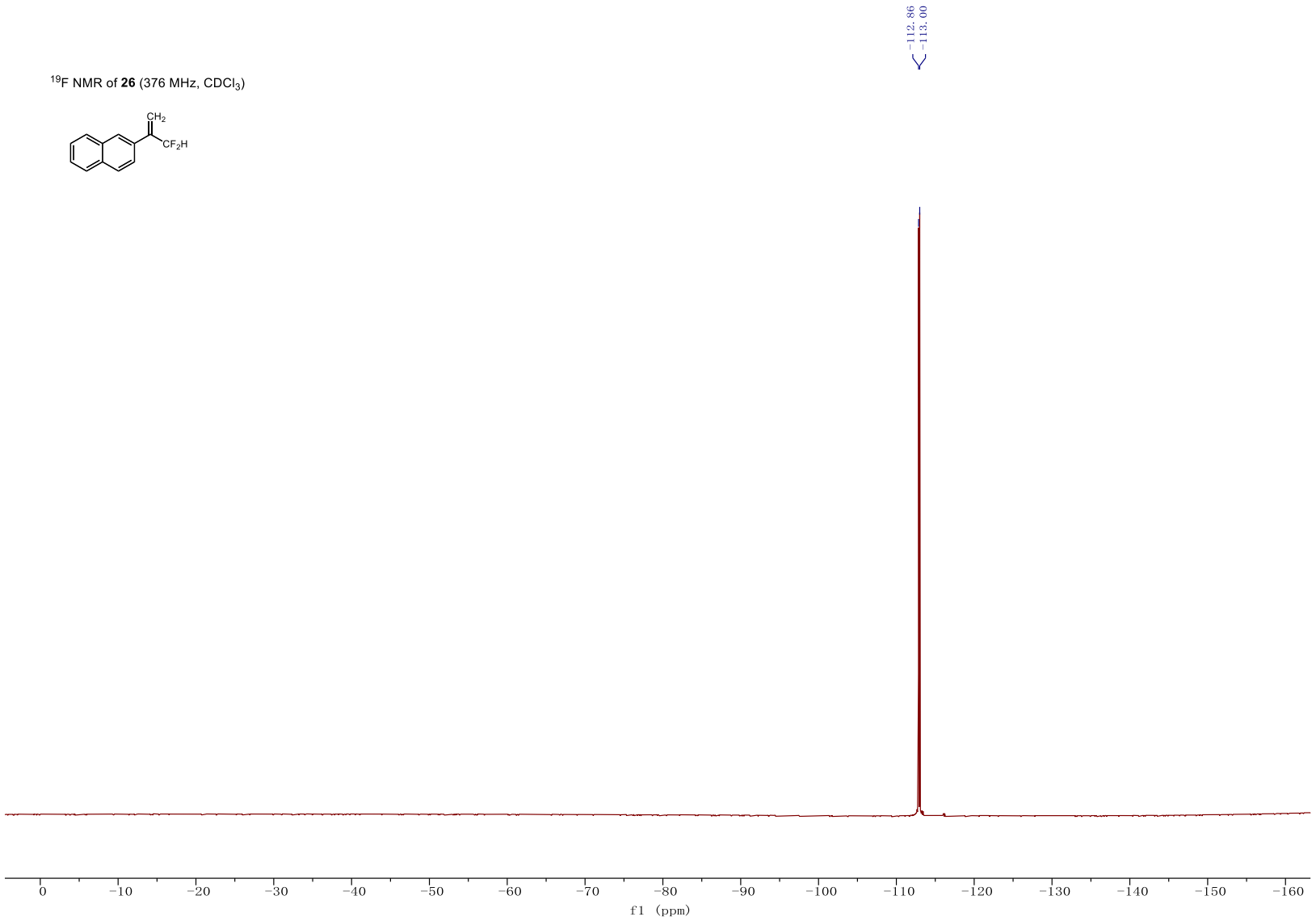


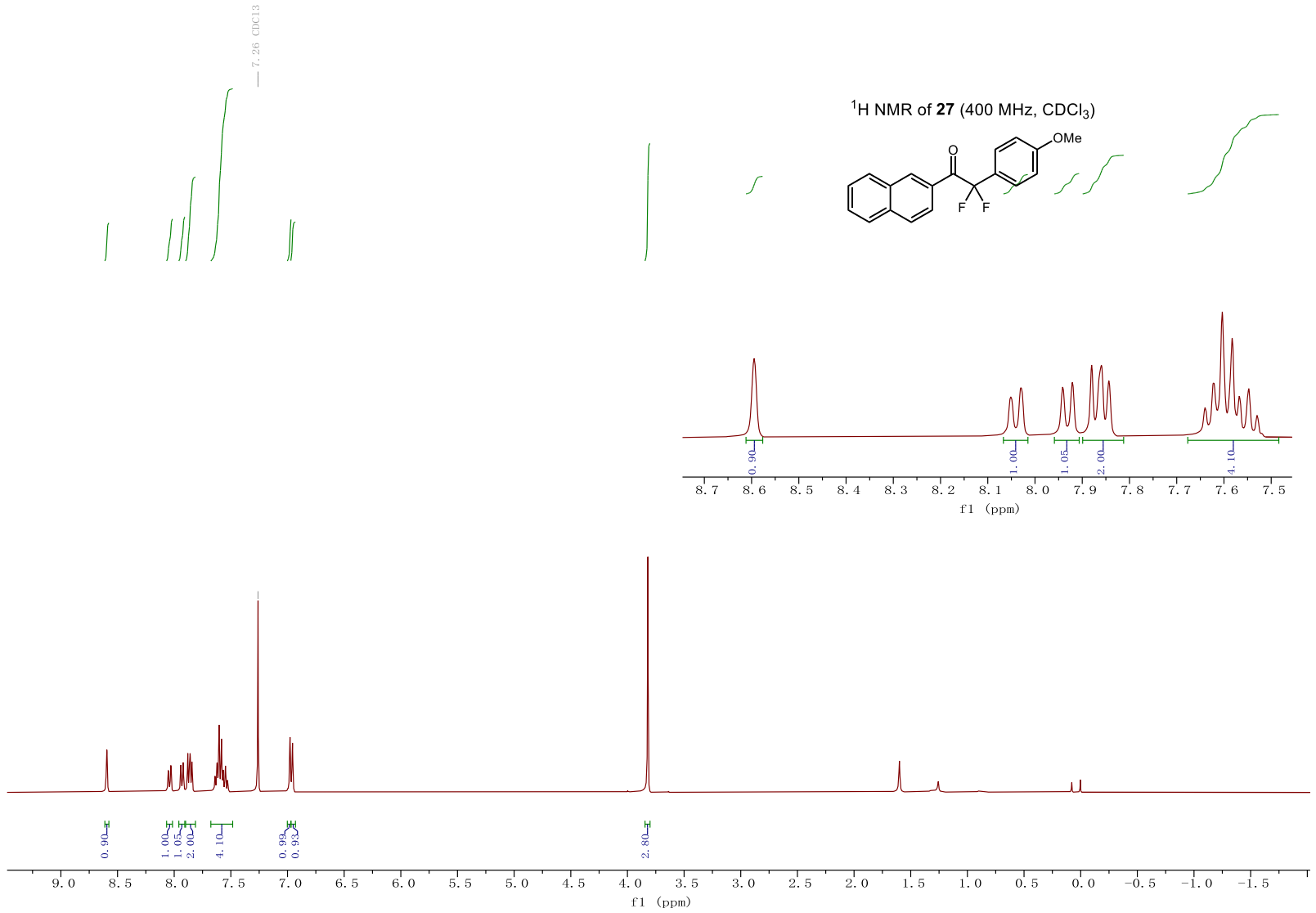
^{1}H NMR of **26** (400 MHz, $CDCl_3$)

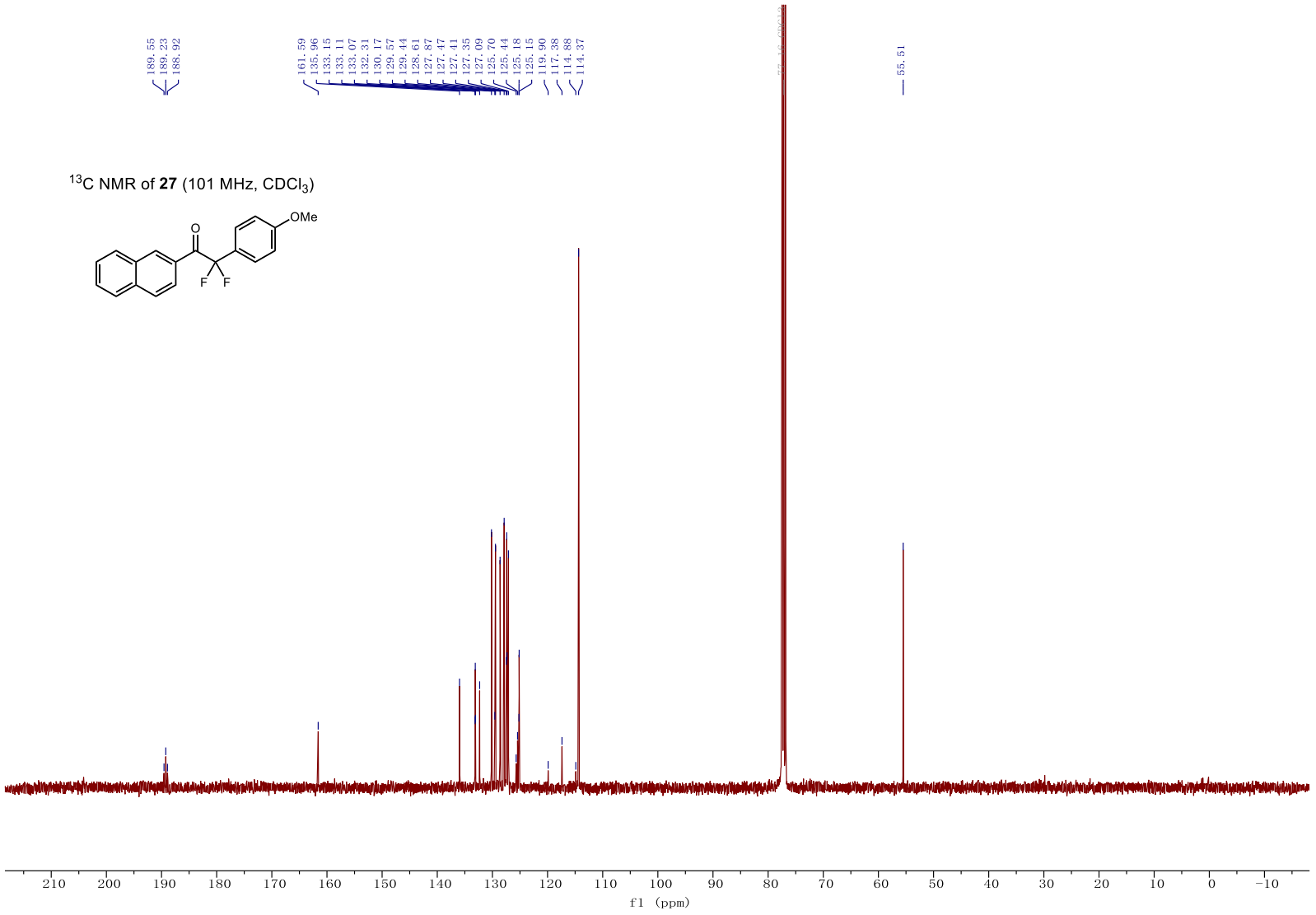



142.12
141.92
141.73
133.28
132.02
128.54
128.40
127.73
126.70
126.60
126.34
124.66
119.46
119.36
119.27
118.07
115.68
113.30
77.16 CDCl3
^{13}C NMR of **26** (101 MHz, $CDCl_3$)
CH_2
CF_2H
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

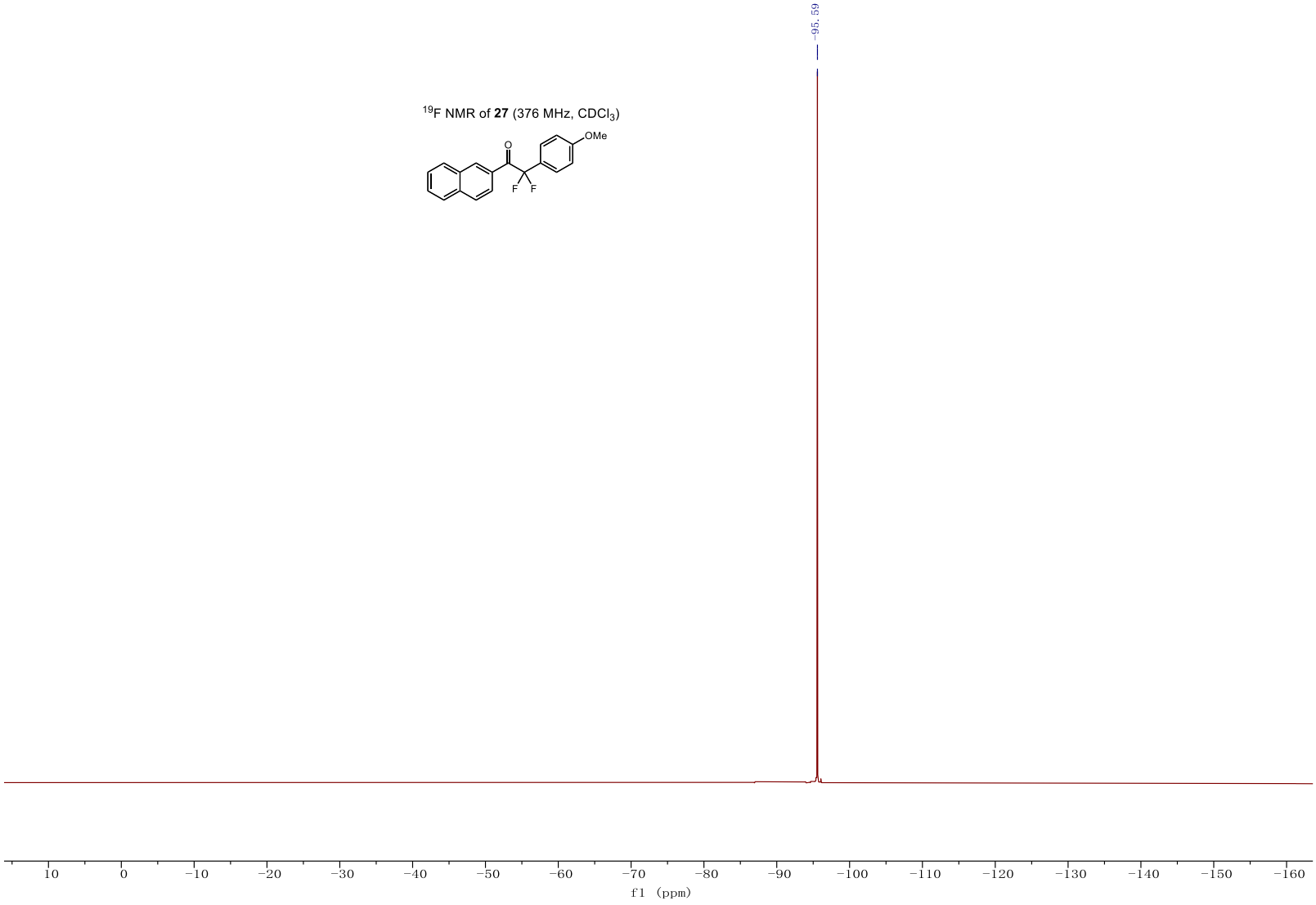
^{19}F NMR of **26** (376 MHz, $CDCl_3$)

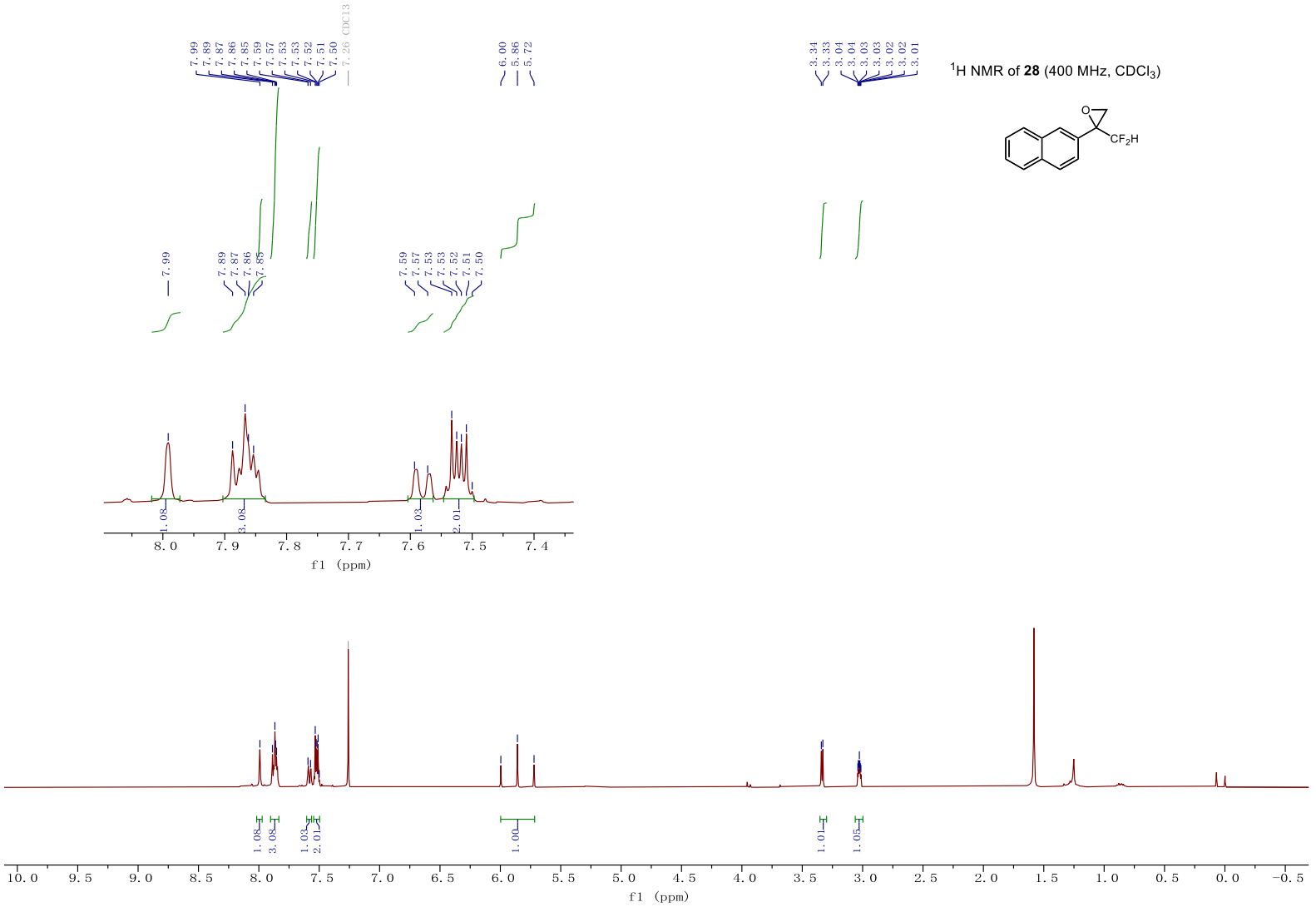


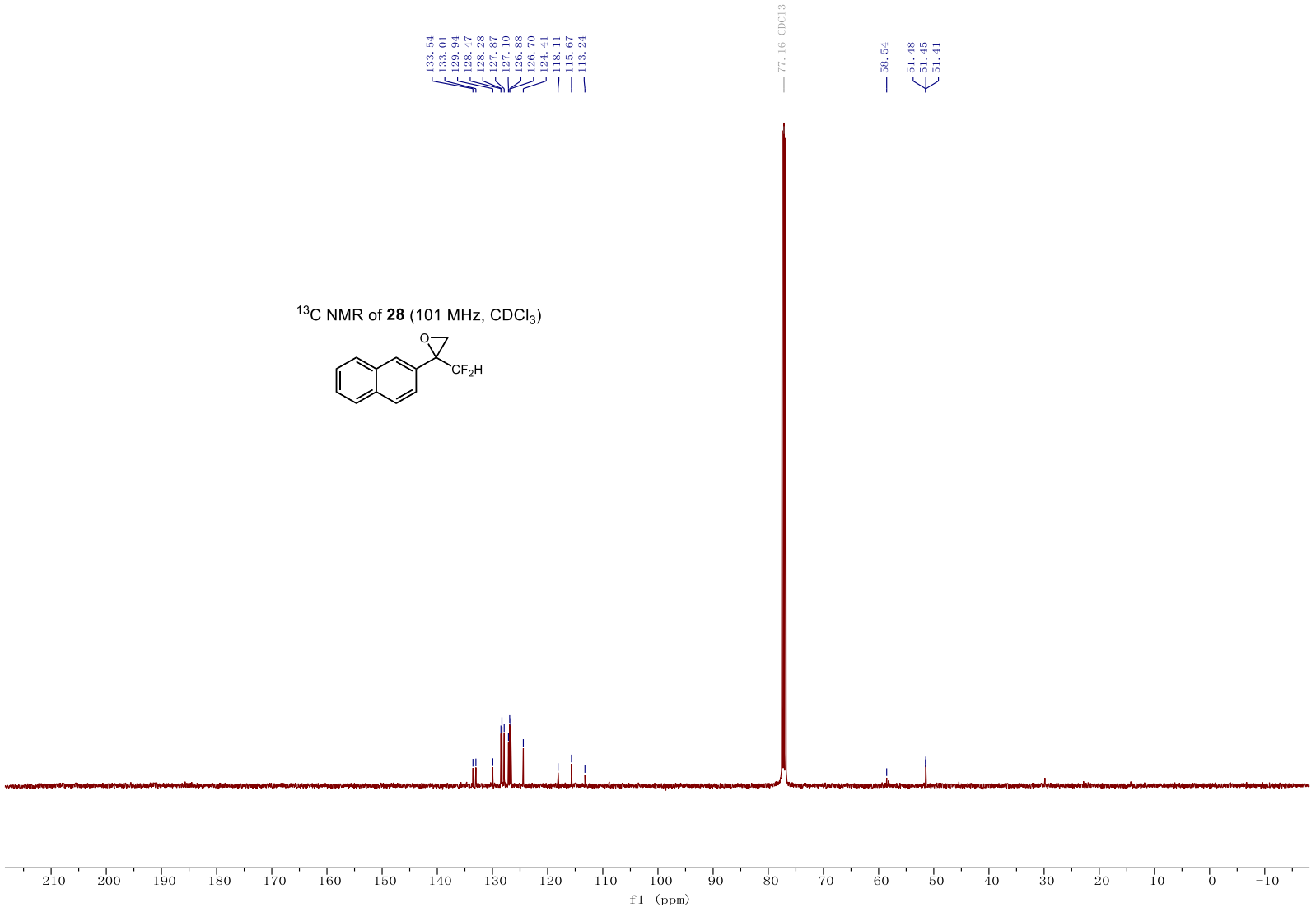

^{1}H NMR of **27** (400 MHz, $CDCl_3$)
OMe
O
F F
7.26 CDCl3
0.90
1.00
1.05
2.00
4.10
0.99
0.92
2.80
f1 (ppm)


189.55
189.23
188.92
161.59
135.96
133.15
133.11
133.07
132.31
130.17
129.57
129.44
128.61
127.87
127.47
127.41
127.35
127.09
125.70
125.44
125.18
125.15
119.90
117.38
114.88
114.37
77.16 CDCl3
55.51
13C NMR of 27 (101 MHz, CDCl3)
O
OMe
F
F
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

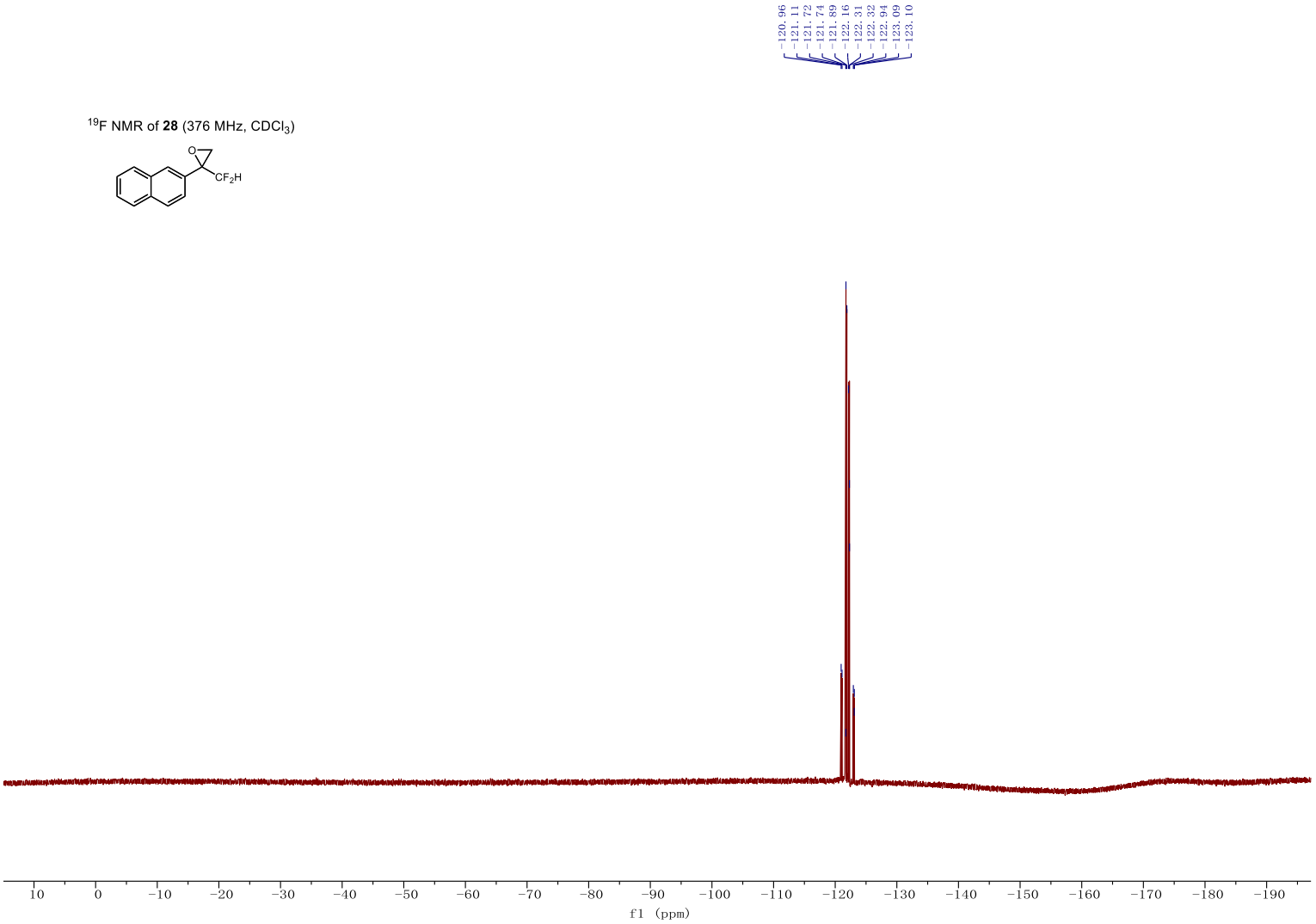
^{19}F NMR of **27** (376 MHz, $CDCl_3$)

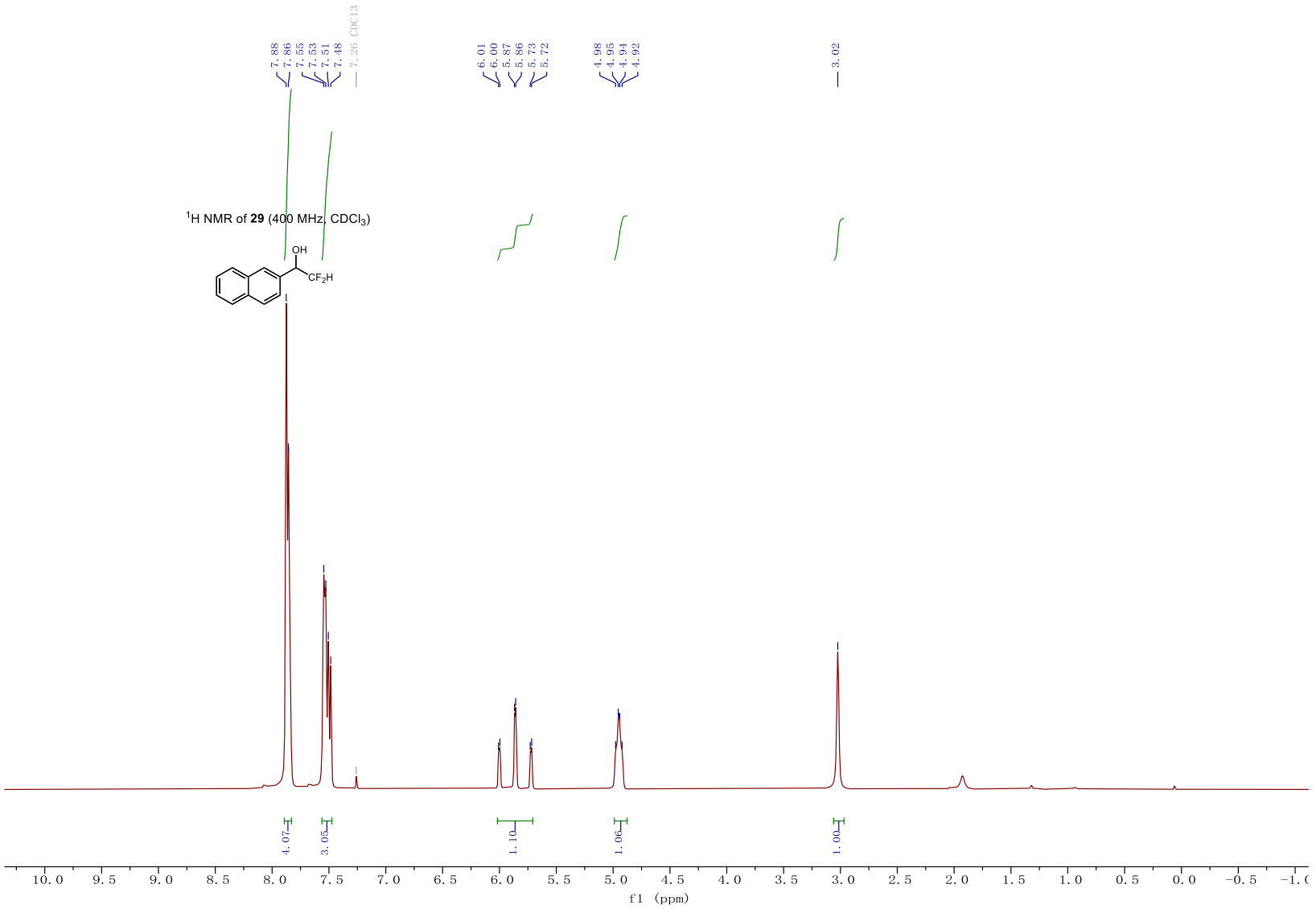


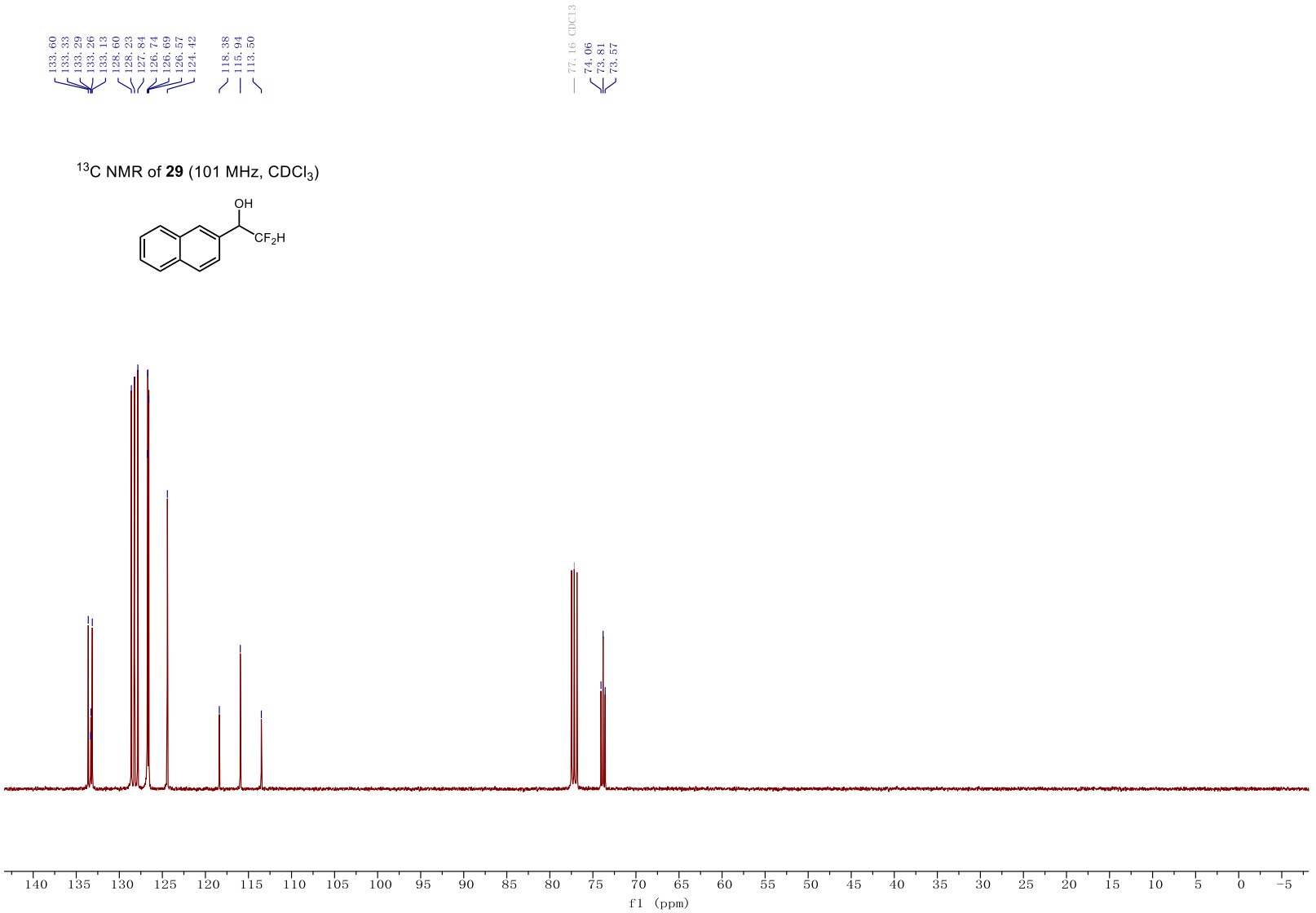

7.99
7.89
7.87
7.86
7.85
7.59
7.57
7.53
7.53
7.52
7.51
7.50
7.26 CDCl3
6.00
5.86
5.72
3.34
3.33
3.04
3.04
3.03
3.03
3.02
3.02
3.01
1H NMR of 28 (400 MHz, CDCl3)
CF2H
1.08
3.08
1.03
2.01
1.00
1.01
1.05
f1 (ppm)


133.54
133.01
129.94
128.47
128.28
127.87
127.10
126.88
126.70
124.41
118.11
115.67
113.24
77.16 CDCl3
58.54
51.48
51.45
51.41
^{13}C NMR of **28** (101 MHz, $CDCl_3$)
O
CF_2H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

^{19}F NMR of **28** (376 MHz, $CDCl_3$)




7.88
7.86
7.55
7.53
7.51
7.48
7.26 CDCl3
6.01
6.00
5.87
5.86
5.73
5.72
4.98
4.95
4.94
4.92
3.02
1H NMR of 29 (400 MHz, CDCl3)
OH
CF2H
4.07
3.05
1.10
1.06
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)


133.60
133.33
133.29
133.26
133.13
128.60
128.23
127.84
126.74
126.69
126.57
124.42
118.38
115.94
113.50
77.16 CDCl3
74.06
73.81
73.57
13C NMR of 29 (101 MHz, CDCl3)
OH
CF2H
140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 −5
f1 (ppm)

^{19}F NMR of **29** (376 MHz, $CDCl_3$)