

Supporting Information  
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Supporting Information for

## **Electrochemical C(sp<sup>3</sup>)–H Fluorination**

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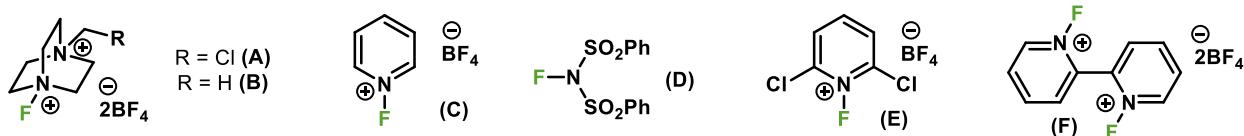
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## General methods

Reagents were purchased at the highest commercial quality and used without further purification unless otherwise stated. Isolated yields refer to chromatographically and spectroscopically (<sup>1</sup>H NMR) homogeneous material, unless otherwise stated. Acetonitrile (MeCN) was obtained by passing the previously degassed solvents through an activated alumina column.<sup>1</sup> For determination of <sup>19</sup>F NMR yields,  $\alpha,\alpha,\alpha$ -trifluorotoluene or 1,4-bis(trifluoromethyl)benzene was used as an internal standard (automatic baseline correction was applied). Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica plates (60 F<sub>254</sub>), using short-wave UV light (254 nm) for visualization, and phosphomolybdic acid, cerium sulfate, *p*-anisaldehyde, or potassium permanganate as developing agents. Flash column chromatography was performed using E. Merck silica gel (60, particle size 0.043–0.063 mm). NMR spectra were recorded on Bruker DRX-600, DRX-500, and AMX-400 instruments, and chemical shifts for <sup>1</sup>H and <sup>13</sup>C NMR are reported relative to the solvent peaks (7.26 ppm for <sup>1</sup>H NMR in CDCl<sub>3</sub>, 77.16 ppm for <sup>13</sup>C NMR in CDCl<sub>3</sub>).<sup>2</sup> <sup>19</sup>F{<sup>1</sup>H} NMR data were calibrated using trichlorofluoromethane as an external reference (0.0 ppm) unless otherwise specified. For compounds **S9**, **S11**, **24**, **25**, **26**, and **29**, NMR spectra were recorded on Bruker Avance 400MHz and Avance 600MHz instruments. Chemical shifts were reported relative to the solvent peaks (7.26 ppm for <sup>1</sup>H NMR in CDCl<sub>3</sub>; 77.0 ppm for <sup>13</sup>C NMR in CDCl<sub>3</sub>; 7.15 ppm for <sup>1</sup>H NMR in C<sub>6</sub>D<sub>6</sub>; 128.0 ppm for <sup>13</sup>C NMR in C<sub>6</sub>D<sub>6</sub>). The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer using ESI ion source, a Waters LC-TOF (I-Class and G2-XS) mass spectrometer using ESI or APCI ion sources, and a Thermo Fisher Scientific LTQ Orbitrap XL mass spectrometer using ESI ion source.

## Source of reagents:

Fluorinating agents **A**, **B**, **E**, and **F** were purchased from Combi-Blocks; **C** from Sigma-Aldrich; and **D** from Matrix-Scientific. NaNO<sub>3</sub> was purchased from Sigma-Aldrich.



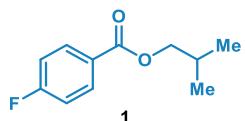
## Electrode materials/dimensions:

The reticulated vitreous carbon (RVC) electrodes were furnished from commercial RVC foam (pore size of 80 ppi, purchased from Ultramet and pore size of 100ppi, purchased from ERG Aerospace Corporation); Ni foam electrodes were furnished from commercial nickel foam (1.5 mm × 100 mm × 250 mm for battery, electric capacity etc., purchased from eBay). Other electrodes tested in this work were obtained from IKA. For experiments using an ElectraSyn vial, the dimensions of the electrodes were approximately W7 × D1.5 × H55 mm (with the submerged exterior surface of the electrode approximately W7 × D1.5 × H10 mm), unless otherwise noted. For assembly of a hand-made vial, see graphical guide in the Supporting Information of a previous paper from our group.<sup>3</sup> For experiments on larger scales, dimensions of electrodes have been specified in the relevant experimental section.

## Substrate synthesis

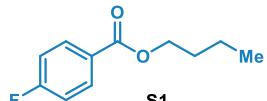
Commercial substrates were obtained from suppliers and used as received. All reactions described below were carried out without any precautions to exclude air and moisture, unless otherwise specified.

### isobutyl 4-fluorobenzoate, **1**



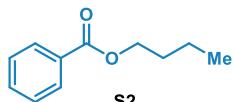
The title compound was prepared according to the reported procedure with slight modifications:<sup>4</sup> To a solution of isobutanol (1.48 g, 20.0 mmol), 4-dimethylaminopyridine (0.20 equiv, 0.49 g, 4.0 mmol), and Et<sub>3</sub>N (1.5 equiv, 4.2 mL, 30.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) was added 4-fluorobenzoyl chloride (1.2 equiv, 4.76 g, 3.54 mL, 24.0 mmol) dropwise at 0 °C, and the resulting mixture was warmed to room temperature and stirred for 6 h. The reaction was quenched by adding H<sub>2</sub>O (20 mL), and organic materials were extracted with CH<sub>2</sub>Cl<sub>2</sub> (40 mL) twice. The combined organics were dried over anhydrous MgSO<sub>4</sub> and concentrated *in vacuo*. Flash column chromatography (hexane/EtOAc = 50/1, v/v) gave **1** as a colorless liquid (3.74 g, 95%). The NMR data were consistent with those previously reported.<sup>5</sup>

### *n*-butyl 4-fluorobenzoate, **S1**



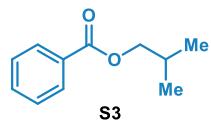
The title compound was prepared according to the reported procedure with slight modifications:<sup>4</sup> To a solution of *n*-butanol (1.48 g, 20.0 mmol), 4-dimethylaminopyridine (0.20 equiv, 0.49 g, 4.0 mmol), and Et<sub>3</sub>N (1.5 equiv, 4.2 mL, 30.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) was added 4-fluorobenzoyl chloride (1.2 equiv, 3.81 g, 24.0 mmol) dropwise at 0 °C, and the resulting mixture was warmed to room temperature and stirred for 6 h. The reaction was quenched by adding H<sub>2</sub>O (20 mL), and organic materials were extracted with CH<sub>2</sub>Cl<sub>2</sub> (40 mL) twice. The combined organics were dried over anhydrous MgSO<sub>4</sub> and concentrated *in vacuo*. Flash column chromatography (hexane/EtOAc = 50/1, v/v) gave **S1** as a colorless liquid (3.50 g, 89%). The NMR data were consistent with those previously reported.<sup>6</sup>

### *n*-butyl benzoate, **S2**



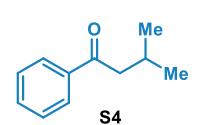
The title compound was prepared according to the reported procedure.<sup>7</sup> The NMR data were consistent with those previously reported.

### isobutyl benzoate, S3



The title compound was prepared according to the reported procedure.<sup>7</sup> The NMR data were consistent with those previously reported.

### 3-methyl-1-phenylbutan-1-one, S4

  
**S4**

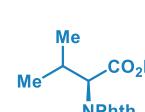
The title compound was prepared according to the reported procedure with slight modifications:<sup>8</sup> Under argon atmosphere, to a mixture of magnesium turnings (1.2 equiv, 12 mmol, 0.29 g), a crystal of iodine, and Et<sub>2</sub>O (20 mL) was added 1-bromo-2-methylpropane (2.0 equiv, 20 mmol, 2.7 g, 2.2 mL) dropwise, and the resulting mixture was heated at reflux and stirred for 1 h. After cooling down to rt, to the mixture was added benzonitrile (10 mmol, 1.03 g) and heated at reflux for 30 min. The reaction was quenched carefully by adding 1 M HCl (20 mL) at 0 °C, allowed to warm to room temperature, and stirred for 2 h. Organic materials were extracted with Et<sub>2</sub>O three times, and the combined organics were washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. Flash column chromatography (hexane/EtOAc = 90/10, v/v) gave **S4** as a pale yellow liquid (0.465 g, 2.87 mmol, 29%). The NMR data were consistent with those previously reported.

### N-(adamantan-1-yl)acetamide, S5

  
**S5**

Compound **S5** was obtained from a commercial supplier and purified by silica gel column chromatography (hexane/EtOAc = 1/2, v/v) prior to use.

### (*S*)-2-(1,3-dioxoisindolin-2-yl)-3-methylbutanoic acid (**L-N**-Phthaloylvaline, **27**) and methyl (*S*)-2-(1,3-dioxoisindolin-2-yl)-3-methylbutanoate (**L-N**-Phthaloylvaline methyl ester, **S6**)

  
 $R = H, \mathbf{27}$   
 $R = Me, \mathbf{S6}$

A mixture of L-leucine (1.17 g, 10.0 mmol) and phthalic anhydride (1.0 equiv, 1.48 g, 10.0 mmol) was stirred and heated at 170 °C for 1 h under reduced pressure. Cooling the reaction mixture to rt afforded spectroscopically pure **27** (2.41 g, 9.75 mmol, 97%). **27** was used for the next step without further purification as follows: to **27** (0.99 g, 4.00 mmol) in MeOH (40mL) was added thionyl chloride (4.0 equiv, 1.90 g, 16.0 mmol) at 0 °C dropwise. The resulting mixture was warmed to rt and stirred overnight. The reaction mixture was concentrated *in vacuo*, silica gel column chromatography (hexane/EtOAc = 5/1, v/v) gave **S6** (0.94 g, 90%) as a colorless liquid. The NMR data of **27** and **S6** were consistent with those previously reported.<sup>9</sup>

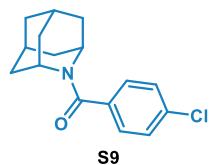
**(S)-2-(1,3-dioxoisooindolin-2-yl)-4-methylpentanoic acid (L-N-Phthaloylleucine, S7) and methyl (S)-2-(1,3-dioxoisooindolin-2-yl)-4-methylpentanoate (L-N-Phthaloylleucine methyl ester, S8)**



R = H, S7  
R = Me, S8

A mixture of L-leucine (1.31 g, 10.0 mmol) and phthalic anhydride (1.0 equiv, 1.48 g, 10.0 mmol) was stirred and heated at 170 °C for 1 h under reduced pressure. Cooling the reaction mixture to rt afforded spectroscopically pure **S7** (2.55 g, 9.76 mmol, 98%). **S7** was used for the next step without further purification as follows. To **S7** (1.04 g, 4.00 mmol) in MeOH (40 mL) was added thionyl chloride (4.0 equiv, 1.90 g, 16.0 mmol) at 0 °C dropwise. The resulting mixture was warmed to rt and stirred overnight. The reaction mixture was concentrated *in vacuo*, silica gel column chromatography (hexane/EtOAc = 5/1, v/v) gave **S8** (1.04 g, 95%) as a colorless liquid. The NMR data of **S7** and **S8** were consistent with those previously reported.<sup>9</sup>

**(*rel*-(1*r*,3*r*,5*r*,7*r*)-2-azaadamantan-2-yl)(4-chlorophenyl)methanone, S9**



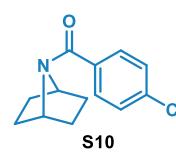
To a suspension of 2-azaadamantane hydrochloride (150 mg, 0.864 mmol) in CH<sub>2</sub>Cl<sub>2</sub> was added Et<sub>3</sub>N (0.301 mL, 2.16 mmol) and 4-chlorobenzoyl chloride (0.122 mL, 0.95 mmol) at rt, and the resulting mixture was stirred overnight. The reaction was quenched by adding water and the organic materials were extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organics were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. Flash column chromatography (Yamazen chromatography, HF silica SI40, M size, heptane/EtOAc = 60/40, v/v) gave **S9** (207 mg, 0.751 mmol, 87%) as a solid.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.37 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 4.89 (s, 1H), 3.86 (s, 1H), 2.13 (s, 2H), 2.02–1.79 (m, 8H), 1.73–1.66 (m, 2H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 168.1, 135.3, 135.1, 128.7, 128.0, 51.1, 44.9, 36.4, 35.6, 35.4, 26.8.

**HRMS (ESI, Orbitrap):** calcd for C<sub>16</sub>H<sub>19</sub>ClNO [M+H]<sup>+</sup> 276.1150, found 276.1129.

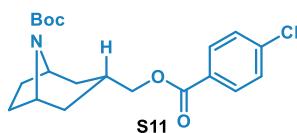
**(*rel*-(1*s*,4*s*)-7-azabicyclo[2.2.1]heptan-7-yl)(4-chlorophenyl)methanone, S10**



To a solution of 7-azabicyclo[2.2.1]heptane (100 mg, 1.03 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (4.0 mL) was added Et<sub>3</sub>N (0.287 mL, 2.06 mmol) and 4-chlorobenzoyl chloride (0.145 mL, 1.13 mmol) at rt, and the resulting mixture was stirred overnight. The reaction was quenched by adding water (excess) and the organic materials were extracted into CH<sub>2</sub>Cl<sub>2</sub>. The

combined organics were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. Flash column chromatography (Yamazen chromatography, HF silica SI40, M size, heptane/EtOAc = 50/50 to 30/70, v/v) gave **S10** (190 mg, 0.806 mmol, 78%) as a solid. The NMR data was consistent with those previously reported.<sup>10</sup>

**tert-butyl *rel*-(1*R*,3*r*,5*S*)-3-((4-chlorobenzoyl)oxy)methyl)-8-azabicyclo[3.2.1]octane-8-carboxylate, S11**



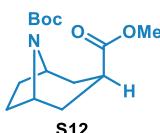
To a suspension of *tert*-butyl *rel*-(1*R*,3*r*,5*S*)-3-(hydroxymethyl)-8-azabicyclo[3.2.1]octane-8-carboxylate (400 mg, 1.66 mmol) in CH<sub>2</sub>Cl<sub>2</sub> was added Et<sub>3</sub>N (0.578 mL, 4.144 mmol) and 4-chlorobenzoyl chloride (0.234 mL, 1.823 mmol) at 0 °C, and the resulting mixture was warmed to rt and stirred overnight. The reaction was quenched by adding water and the organic materials were extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organics were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. Flash column chromatography (Yamazen chromatography, HF silica SI40, M size, heptane/EtOAc = 60/40, v/v) gave **S11** (291 mg, 0.766 mmol, 46%) as a solid.

**<sup>1</sup>H NMR (600 MHz, C<sub>6</sub>D<sub>6</sub>):** δ 7.83 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 8.5 Hz, 2H), 4.31 (br s, 1H), 4.14–3.99 (br m, 3H), 2.25–1.76 (br m, 3H), 1.64 (br s, 2H), 1.48 (s, 9H), 1.27–1.04 (br m, 4H).

**<sup>13</sup>C NMR (151 MHz, C<sub>6</sub>D<sub>6</sub>):** δ 165.2, 153.6, 139.4, 131.2, 129.3, 128.9, 78.6, 69.4, 52.9 (br), 52.1 (br), 32.0 (br), 31.2 (br), 29.5 (br), 28.8 (br), 28.7, 28.5.

**HRMS (ESI- Orbitrap):** calcd for C<sub>20</sub>H<sub>26</sub>ClNNaO<sub>4</sub> [M+Na]<sup>+</sup> 402.1443, found 402.1410.

**8-(*tert*-butyl) 3-methyl *rel*-(1*R*,3*s*,5*S*)-8-azabicyclo[3.2.1]octane-3,8-dicarboxylate, S12**



**S12** was obtained from a commercial supplier and used as received.

## Optimization table

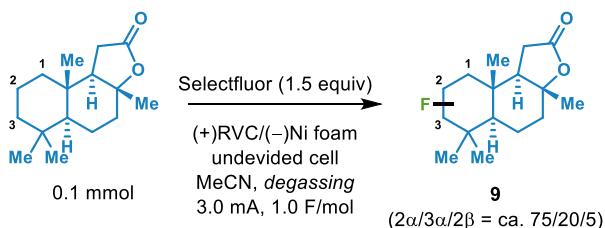
### Effect of degassing:

To a vial (for entries 1–6, 5 mL undivided ElectraSyn vial; for entries 7 and 8, hand-made vial) equipped with a stir bar was added (3a*R*)-(+)-sclareolide (25.0 mg, 0.10 mmol), Selectfluor (**A**, 1.5 equiv, 53.1 mg, 0.15 mmol), and MeCN (3.0 mL, 0.033 M). The vial cap was screwed on prior to electrolysis and a degassing operation was conducted as shown in Table S1.

The mixture was electrolyzed under Ar atmosphere as follows: anode, RVC; cathode, Ni foam; constant current, 3.0 mA; no reference electrode; total charge, 0.10 mmol substrate, 1.0 F/mol; no alternate polarity; stirring, 600 rpm.

The cap was removed after electrolysis, and to the reaction mixture was added an internal standard. The mixture was analyzed by  $^{19}\text{F}$  NMR without deuterium lock. Comparison of a total of three C(sp<sup>3</sup>)-F peaks of a mixture of fluorosclareolides (2 $\alpha$ -F, -178.5 ppm; 3 $\alpha$ -F, -186.8 ppm; 2 $\beta$ -F, -171.4 ppm, respectively). In every run, practically the same ratio of the isomers was observed. The ratio of isomers was determined to be ca. 75/20/5 of 2 $\alpha$ /3 $\alpha$ /2 $\beta$  and the sum total of these products was used to calculate the yield by way of relative integration to the internal standard in  $^{19}\text{F}$  NMR. The structures of 2 $\alpha$ -, 3 $\alpha$ -, and 2 $\beta$ -fluorosclareolides were assigned according to the reported data.<sup>11</sup>

Table S1.



entry	degassing before electrolysis	$^{19}\text{F}$ NMR yield/% <sup>a</sup>
1 <sup>b</sup>	Ar bubbling >5 min	0-35 (N = 5)
2 <sup>b</sup>	Ar bubbling >5 min with sonication	6-32 (N = 3)
3 <sup>b</sup>	high-vac/Ar-backfill >3 times	18-24 (N = 3)
4	under Ar (no bubbling)	38-53 (N = 3)
5	open to air (no bubbling)	0 (N = 2)
6	under O <sub>2</sub> (no bubbling)	0 (N = 1)
7 <sup>c</sup>	high-vac/Ar-backfill >3 times	36-47 (N = 3)
8 <sup>c</sup>	freeze-pump-thaw >3 times	38-49 (N = 4)

<sup>a</sup> N = number of iterations. <sup>b</sup> Continuous Ar bubbling during electrolysis.

<sup>c</sup> Reaction carried out in a hand-made vial.

### **Robustness of reaction:**

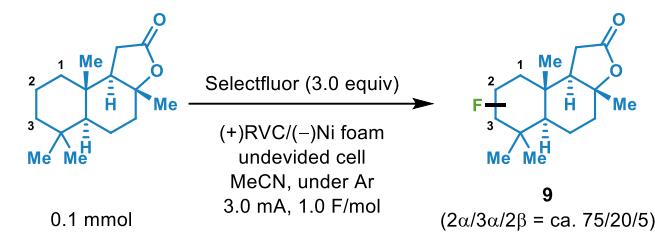
Unless otherwise specified in Table S2, the title experiments were carried out according to the following procedure.

To a 5 mL undivided ElectraSyn vial equipped with a stir bar was added (*3aR*)-(+)-sclareolide (25.0 mg, 0.10 mmol), Selectfluor (**A**, 3.0 equiv, 106 mg, 0.30 mmol), and MeCN (3.0 mL, 0.033 M). The vial cap was screwed on and the headspace of the vial was purged with Ar using a balloon, syringe and needle assembly at least for 5 min prior to electrolysis.

The mixture was electrolyzed under Ar atmosphere as follows: anode, RVC; cathode, Ni foam; constant current, 3.0 mA; no reference electrode; total charge, 0.10 mmol substrate, 1.0 F/mol; no alternate polarity; stirring, 600 rpm.

The cap was removed after electrolysis, and to the reaction mixture was added an internal standard. The reaction mixture was analyzed by <sup>19</sup>F NMR without deuterium lock. Relative integration of a total of three C(sp<sup>3</sup>)-F peaks of a mixture of fluorosclareolides (2 $\alpha$ -F, -178.5 ppm; 3 $\alpha$ -F, -186.8 ppm; 2 $\beta$ -F, -171.4 ppm, respectively. Ratio of the isomers are 2 $\alpha$ /3 $\alpha$ /2 $\beta$  = ca. 75/20/5) with that of the internal standard gave <sup>19</sup>F NMR yield. The peaks of fluorosclareolides were assigned according to a reported data.<sup>11</sup>

Table S2.



entry	deviation from above	<sup>19</sup> F NMR yield/%
1	none	55
2	different batch of Selectfluor <sup>a</sup>	30
3	identical to entry 2 <sup>b</sup>	47
4	bulk MeCN in 18 L steel drum	55
5	added 10 equiv of H <sub>2</sub> O	45
6	under N <sub>2</sub>	58
7	open to air	0
8	performed in 20 mL hand-made vial	52
9	longer anode (submerged ca. ×1.5 exterior area)	54
10	narrower anode (submerged ca. 1/2 exterior area)	38
11	electrolyzed immediately after install Ar balloon	51
12	stirred at 1,200 rpm	41
13	stirred at 100 rpm	59

<sup>a</sup> Used chunk crystal. Some crystals remained insoluble after electrolysis.

<sup>b</sup> Used ground powder of Selectfluor.

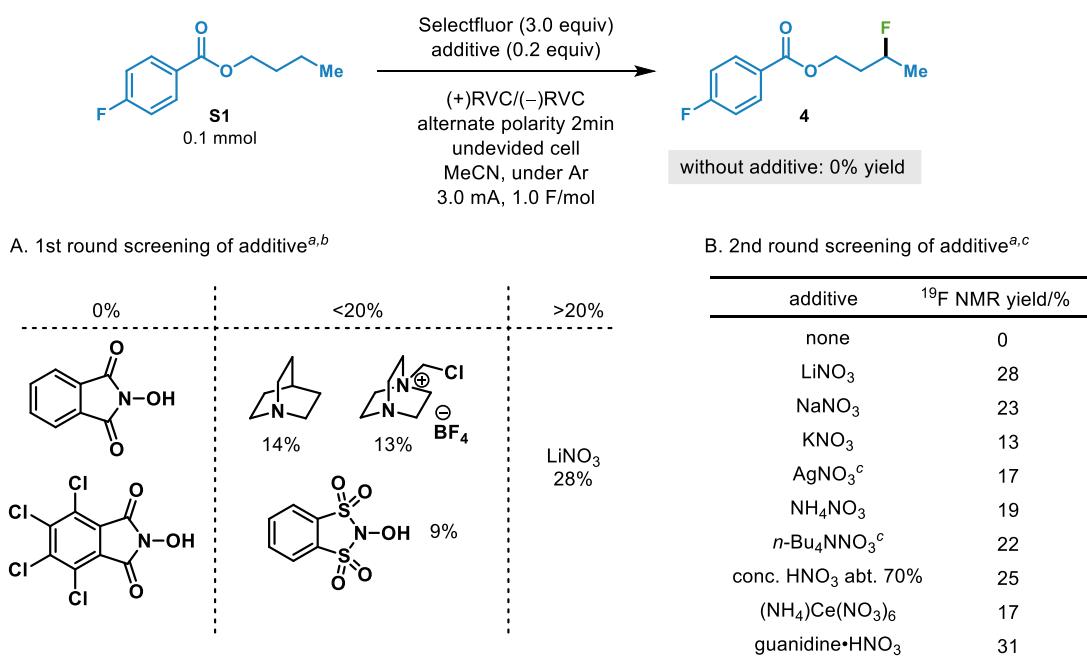
### Effect of additive:

To a 5 mL undivided ElectraSyn vial equipped with a stir bar was added *n*-butyl 4-fluorobenzoate (**S1**, 19.6 mg, 0.10 mmol), Selectfluor (**A**, 3.0 equiv, 106 mg, 0.30 mmol), additive (0.2 equiv, 0.02 mmol, unless otherwise specified in Table S3), and MeCN (3.0 mL, 0.033 M). The vial cap was screwed on and the headspace of the vial was purged with Ar using a balloon, syringe and needle assembly prior to electrolysis.

The mixture was electrolyzed under Ar atmosphere as follows: anode, RVC; cathode, RVC; constant current, 3.0 mA; no reference electrode; total charge, 0.10 mmol substrate, 1.0 F/mol; alternate polarity 2 min; stirring, 600 rpm.

The cap was removed after electrolysis, and to the reaction mixture was added an internal standard. The mixture was analyzed by <sup>19</sup>F NMR without deuterium lock. Relative integration of the C(sp<sup>3</sup>)-F peak of the desired product (~175.3 ppm) with that of the internal standard gave <sup>19</sup>F NMR yield.

Table S3.



<sup>a</sup> Yields determined by <sup>19</sup>F NMR. <sup>b</sup> Other 15 compounds were tested. <sup>c</sup> Formation of white precipitation before electrolysis.

### Reaction optimization:

Unless otherwise specified in Table S4, the title experiments were carried out according to the following general procedures.

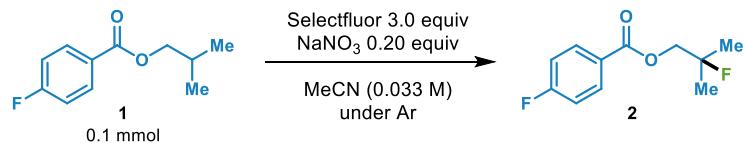
To a 5 mL undivided ElectraSyn vial equipped with a stir bar was added isobutyl 4-fluorobenzoate (**1**, 19.6 mg, 0.10 mmol), Selectfluor (**A**, 3.0 equiv, 106 mg, 0.30 mmol), NaNO<sub>3</sub> (0.2 equiv, 1.7 mg, 0.02 mmol), and MeCN (3.0 mL, 0.033 M). The vial cap was screwed on and a new septum cap installed on top of the cap. The headspace of the vial was purged with Ar using a balloon, syringe and needle assembly prior to electrolysis.

The mixture was electrolyzed under Ar atmosphere as follows: anode, RVC; cathode, RVC; constant current, 3.0 mA; no reference electrode; total charge, 0.10 mmol substrate, 2.0 F/mol; alternate polarity 2 min; stirring, 600 rpm.

The cap was removed after electrolysis, and to the reaction mixture was added an internal standard. The mixture was analyzed by <sup>19</sup>F NMR without deuterium lock. Relative integration of the C(sp<sup>3</sup>)-F peak of the desired product (-145.0 ppm) with that of the internal standard gave <sup>19</sup>F NMR yield.

For entries 1, 21, and 22; after determination of the  $^{19}\text{F}$  NMR yield, the reaction mixture was poured into saturated aqueous  $\text{NaHCO}_3$  and extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organics were washed with brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The crude material was purified by preparative thin-layer chromatography to furnish the desired product.

Table S4.

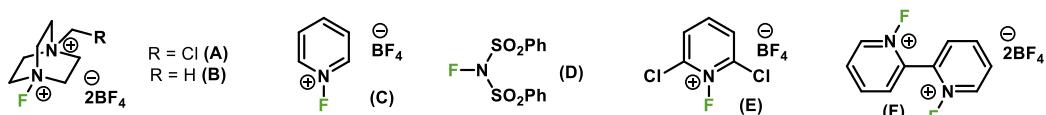


Conditions: (+)RVC/(-)RVC, undivided cell, 3.0 mA, alternate polarity 2 min, 2.0 F/mol

entry	deviation from above	yield/% <sup>a</sup>	entry	deviation from above	yield/% <sup>a</sup>
1	none	62 (54)	11	1.0 F/mol	38
2	no electricity	0	12	3.0 F/mol	53
3	no $\text{NaNO}_3$	0	13	6 mA	42
4	1.0 equiv $\text{NaNO}_3$	42	14 <sup>c</sup>	(+)RVC/(-)Ni foam	13
5	B instead of A	60	15 <sup>c</sup>	(+)RVC/(-)graphite	28
6	C instead of A	0	16 <sup>c</sup>	(+)RVC/(-)glassy carbon	0
7 <sup>b</sup>	D instead of A	0	17 <sup>c</sup>	(+)RVC/(-)Pt	0
8	E instead of A	0	18 <sup>c</sup>	(+)graphite/(-)RVC	21
9	F instead of A	0	19 <sup>c</sup>	(+)glassy carbon/(-)RVC	0
10	open to air	0	20 <sup>c</sup>	(+)Pt/(-)RVC	0
			21 <sup>d</sup>	0.067 M	69 (63)
			22 <sup>e</sup>	0.10 M	70 (66)

<sup>a</sup>  $^{19}\text{F}$  NMR yield. Isolated yields are shown in the parentheses. <sup>b</sup> 1.0 equiv of  $n\text{-Bu}_4\text{NBF}_4$  was added as electrolyte.

<sup>c</sup> No alternate polarity. <sup>d</sup> 0.2 mmol scale. <sup>e</sup> 0.3 mmol scale.



## Cyclic voltammogram

Cyclic voltammogram of  $n\text{-Bu}_4\text{NNO}_3$  (0.01 M in MeCN. 0.10 M  $n\text{-Bu}_4\text{NBF}_4$  was used as an electrolyte) was recorded using Pine WaveNow potentiostat at a scan rate of 100 mV/s, with a 3.0 mm PCTFE shroud glassy carbon disk working electrode, a platinum plate counter electrode, and an Ag/AgCl (3.0 M KCl<sub>aq</sub>) reference electrode. The oxidation peak potential  $E_p$  ( $\text{NO}_3^-/\text{NO}_3^\cdot$ ) was determined to be +2.2 V (Figure S1).

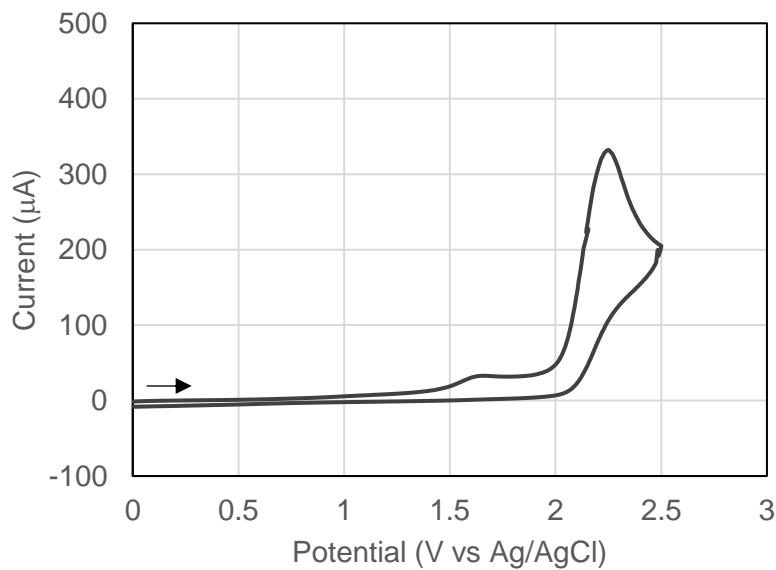
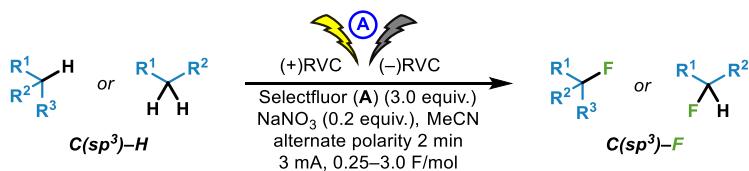


Figure S1. Cyclic voltammogram of  $n\text{-Bu}_4\text{NNO}_3$ .

## General procedure for electrochemical C(sp<sup>3</sup>)–H fluorination

### General procedure for small scale fluorination using IKA ElectraSyn 2.0:



Unless otherwise specified, the reaction was carried out on 0.3 mmol scale. To a 5 mL undivided ElectraSyn vial equipped with a stirrer bar was added substrate (0.30 mmol), Selectfluor (**A**, 3.0 equiv, 319 mg, 0.90 mmol), NaNO<sub>3</sub> (0.2 equiv, 5.1 mg, 0.06 mmol), and MeCN (3.0 mL). The vial cap equipped with a pair of RVC electrodes was screwed on, and headspace of the vial was purged with Ar using a balloon, syringe and needle assembly prior to electrolysis.

Reaction parameters of ElectraSyn device were set up as follows: constant current, 3.0 mA; no reference electrode; total charge, 0.30 mmol substrate, ranging from 0.25 to 3.0 F/mol; alternate polarity, 2 min; stirring, 600 rpm.

The mixture was electrolyzed under Ar atmosphere until complete or reasonable consumption of the starting material as judged by TLC. After electrolysis, the cap was removed, and the electrodes were taken out and rinsed with MeCN into the reaction mixture [<sup>19</sup>F NMR data of an aliquot in MeCN may be collected without deuterium lock]. The reaction mixture was poured into saturated aqueous NaHCO<sub>3</sub> (or H<sub>2</sub>O for **5**, **12**, **15**, **17**, and **19**) and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organics were washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo* [Crude <sup>1</sup>H and <sup>19</sup>F NMR data in CDCl<sub>3</sub> may be collected here]. The crude material was purified by silica gel column chromatography or preparative thin-layer chromatography to furnish the desired product. See Figure S2 for graphical guides.

**Graphical guide for the reaction using IKA ElectraSyn 2.0:**

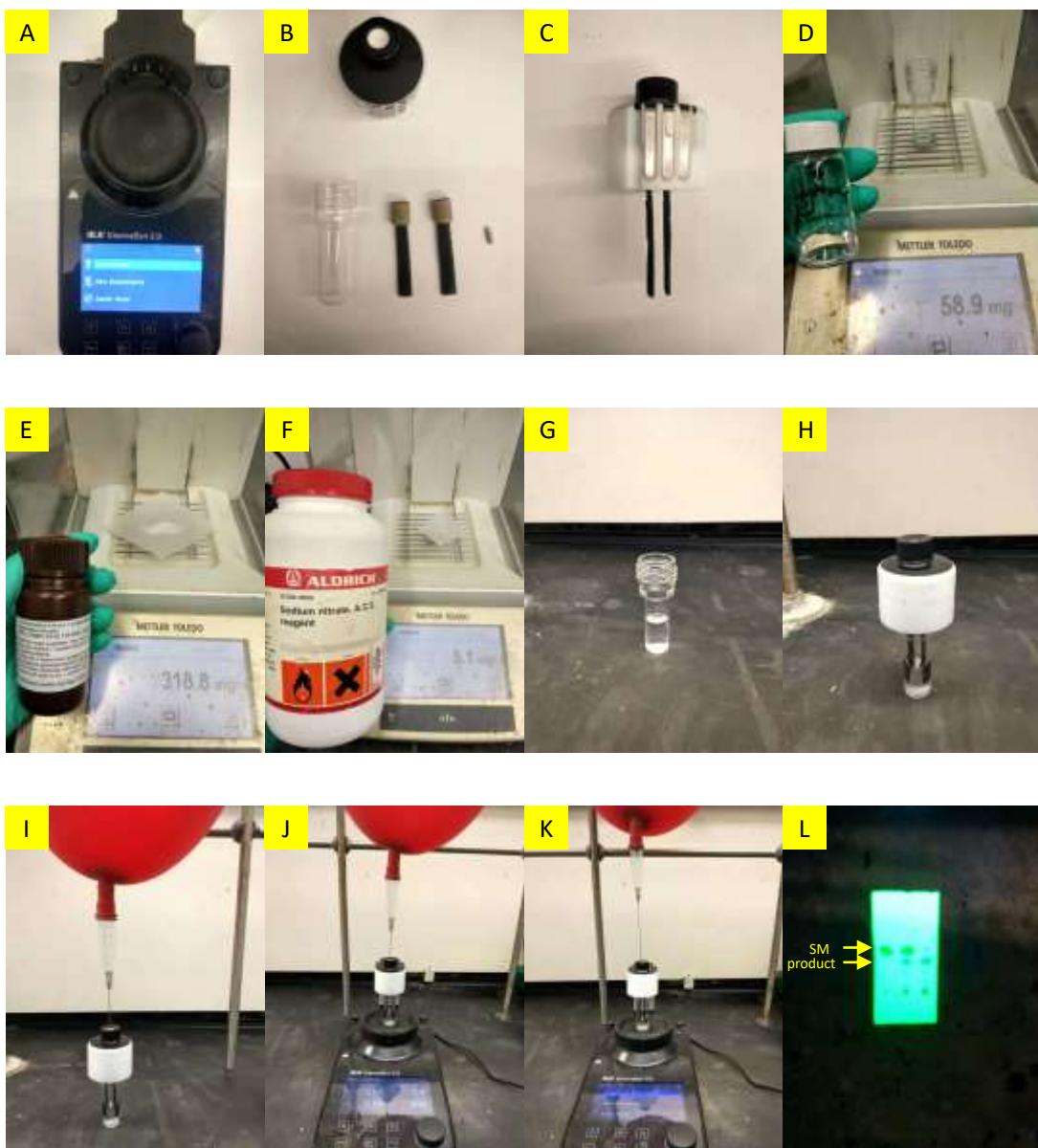
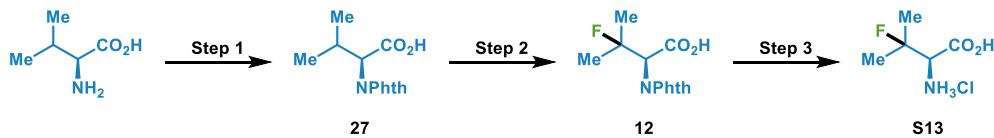


Figure S2. Graphical guide for the electrochemical fluorination of **1** using IKA ElectraSyn 2.0. **A**, ElectraSyn 2.0 stir plate; **B**, 5 mL vial, cap, stirrer bar, and RVC electrodes; **C**, an ElectraSyn 2.0 cap equipped with RVC electrodes; **D–F**, materials used in the reaction (**1** in the vial, Selectfluor, NaNO<sub>3</sub>); **G**, the vial equipped with stirrer bar after addition of MeCN. **H**, the cap was screwed on top of the vial; **I**, Ar balloon-syringe-needle assembly inserted through septum, no bubbling was applied; **J**, the vial on the ElectraSyn 2.0 stir plate; **K**, reaction system after electrolysis (added 2.0 F/mol); **L**, TLC visualized under short-wave UV light (left to right: starting material, co-spot, reaction mixture).

**Experimental procedures for 100 gram scale fluorination (Performed at Asymchem):**



**Step 1: Synthesis of (*S*)-2-(1,3-dioxoisindolin-2-yl)-3-methylbutanoic acid, **27****

To a dry and clean 5 L four-necked flask was added L-valine (395.27 g, 3.38 mol, 1.0 equiv), phthalic anhydride (500.00 g, 3.38 mol, 1.0 equiv) and glacial acetic acid (2.5 L). The resulting suspension was vigorously stirred, then warmed up to 120 °C over 30 min. The reaction mixture became clear after stirring for 8 hours at 120 °C. The reaction was then cooled to rt and the solvent was removed under reduced pressure. The crude material was diluted with CH<sub>2</sub>Cl<sub>2</sub> (1.2 L) and washed with water (3 × 1 L), then dried over with anhydrous MgSO<sub>4</sub>, filtered and evaporated to afford 710 g product **27** (85% isolated yield) as white powder.

**Step 2: Synthesis of (*R*)-2-(1,3-dioxoisindolin-2-yl)-3-fluoro-3-methylbutanoic acid, **12****

To a clean and dry homemade PVC electrolysis cell (37 cm × 34 cm × 7 cm), equipped with two RVC electrodes (30 cm × 30 cm, 100 ppi, each having a 30 cm × 16 cm immersion area) and connected to an EC-Workstation, was added (*S*)-2-(1,3-dioxoisindolin-2-yl)-3-methylbutanoic acid (**27**, 100.00 g, 0.4 mol, 1.0 equiv), Selectfluor (283.2 g, 0.8 mol, 2.0 equiv) and MeCN (4 L). The resulting solution was then degassed using nitrogen gas for 30 min, then electrolyzed with a constant current (2 mA/cm<sup>2</sup>) under nitrogen atmosphere for 21 h. After **27** was completely consumed (2.5 F/mol total current), the solvent was removed under reduced pressure. The residual solid was diluted with EtOAc (500 mL) and the insoluble salt was filtered off through a Buchner funnel. The filtrate was washed with water (3 × 1.2 L), dried over anhydrous MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (EtOAc:hexane = 1:8) to afford desired product **12** (81 g, 76% isolated yield) as a white solid. See Figure S3 for further information.

**Step 3: Synthesis of (*R*)-2-amino-3-fluoro-3-methylbutanoic acid hydrochloride, **S13****

In a dry and clean 2L four-necked round bottom, (*R*)-2-(1,3-dioxoisindolin-2-yl)-3-fluoro-3-methylbutanoic acid (**12**, 81 g, 0.3 mol, 1.0 equiv.) was dissolved in ethanol (1.5 L), followed by slowly adding hydrazine hydrate (26.25 g, 0.525 mol, 1.75 equiv.) at room temperature. A white solid was precipitated out after 30 min, and the suspension was agitated for another 20 h. The mixture was carefully acidified to pH = 4-5 with 2 M HCl (875 mL) and filtered. The filtrate was concentrated to afford a white crude solid which was triturated with 10 L EtOAc for 10 h. The filter cake was triturated again with 250

mL MeOH for 2 h. The combined filtrate was concentrated under vacuum to afford final product **S13** (48 g, 92% yield) as a white powder.

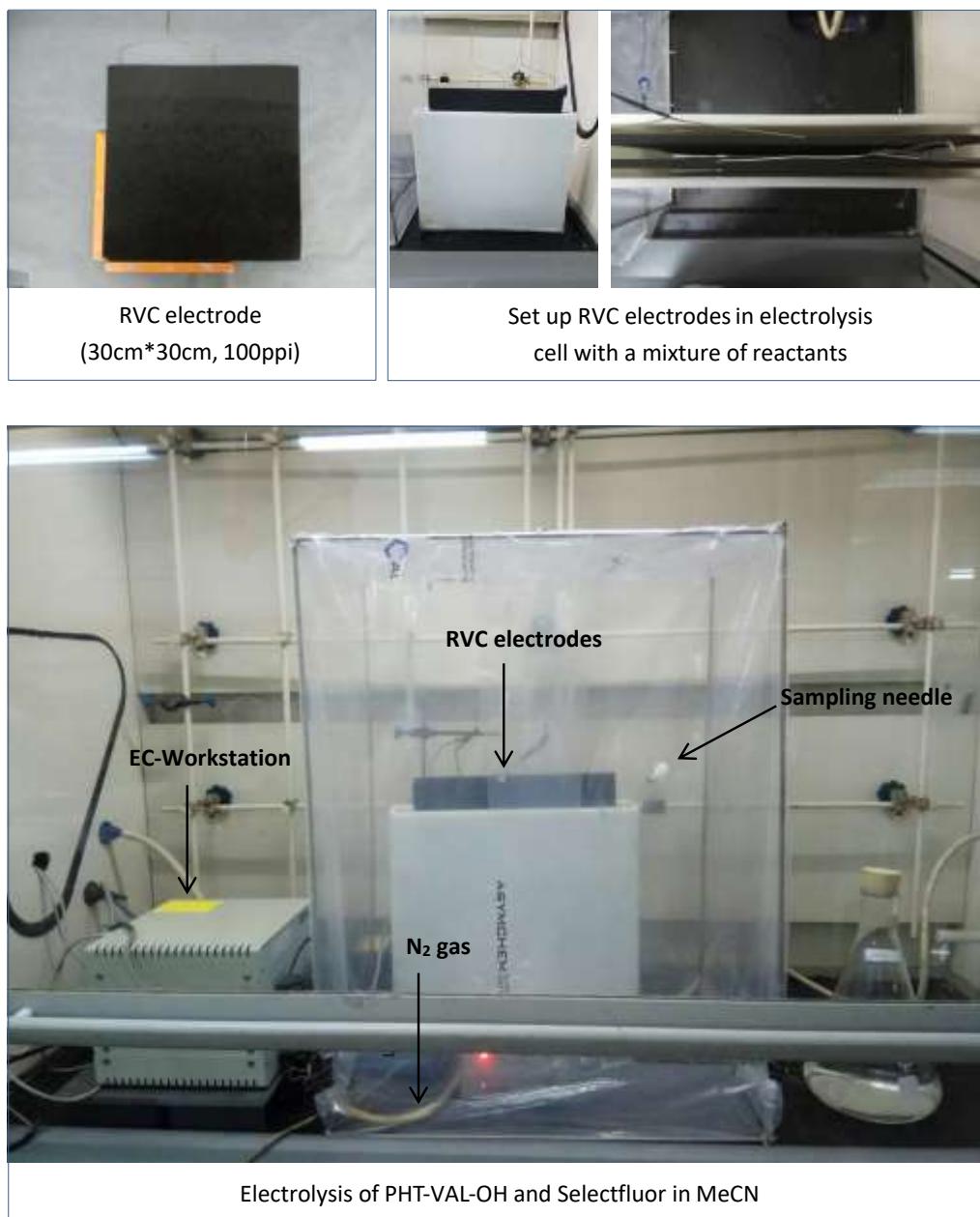
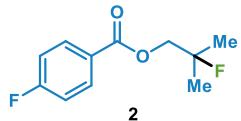


Figure S3. Reaction set up for 100 gram scale fluorination of protected L-valine **27**.

## Characterization data

### 2-fluoro-2-methylpropyl 4-fluorobenzoate, 2



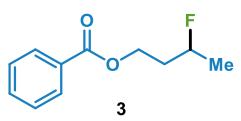
Following the general procedure with a total charge of 2.0 F/mol, the title compound was obtained in 66% yield (42.4 mg, 0.198 mmol) as a colorless liquid.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.14–8.06 (m, 2H), 7.13 (t, *J* = 8.6 Hz, 2H), 4.32 (d, *J* = 19.8 Hz, 2H), 1.47 (d, *J* = 21.1 Hz, 6H).

**<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>):** δ 166.1 (d, *J* = 254.2 Hz), 165.4, 132.4 (d, *J* = 9.3 Hz), 126.2 (d, *J* = 2.8 Hz), 115.8 (d, *J* = 21.6 Hz), 93.5 (d, *J* = 169.8 Hz), 69.8 (d, *J* = 24.8 Hz), 24.0 (d, *J* = 24.3 Hz).

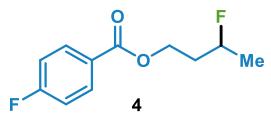
**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ -105.5, -146.0.

### 3-fluorobutyl benzoate, 3



Following the general procedure with a total charge of 2.0 F/mol, the title compound was obtained in 25% yield (16.1 mg, 0.075 mmol) as a pale yellow liquid. The NMR data were consistent with those previously reported.<sup>4</sup>

### 3-fluorobutyl 4-fluorobenzoate, 4



Following the general procedure with a total charge of 2.0 F/mol, the title compound was obtained in 30% yield (17.9 mg, 0.090 mmol) as a pale yellow liquid.

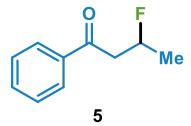
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.09–8.01 (m, 2H), 7.11 (dd, *J* = 9.0, 8.4 Hz, 2H), 4.98–4.76 (m, 1H), 4.52–4.33 (m, 2H), 2.15–2.01 (m, 2H), 1.41 (dd, *J* = 23.9, 6.2 Hz, 3H).

**<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>):** δ 165.9 (d, *J* = 253.7 Hz), 165.7, 132.3 (d, *J* = 9.4 Hz), 126.6 (d, *J* = 3.2 Hz), 115.7 (d, *J* = 22.0 Hz), 87.4, 61.4 (d, *J* = 5.0 Hz), 36.2 (d, *J* = 20.9 Hz), 21.3 (d, *J* = 22.5 Hz).

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ -105.9, -175.8.

**HRMS (APCI-TOF):** calcd for C<sub>11</sub>H<sub>13</sub>F<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> 215.0884, found 215.0882.

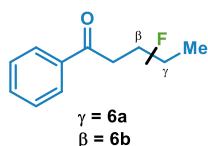
### **3-fluoro-1-phenylbutan-1-one, 5**



Following the general procedure with a total charge of 2.0 F/mol, the title compound was obtained in 40% yield (20.0 mg, 0.120 mmol) as a pale yellow liquid. The NMR data were consistent with those previously reported.<sup>12</sup> Note: <sup>1</sup>H NMR spectrum showed that it contains a small amount of inseparable (*E*)-1-phenylbut-2-en-1-one.<sup>13</sup> See the <sup>1</sup>H NMR spectrum.

**HRMS (ESI-TOF):** calcd for C<sub>10</sub>H<sub>12</sub>FO [M+H]<sup>+</sup> 167.0872, found 167.0871.

### **4-fluoro-1-phenylpentan-1-one, 6a and 3-fluoro-1-phenylpentan-1-one, 6b**



Following the general procedure with a total charge of 2.0 F/mol, a mixture of the title compounds was obtained in 45% yield (24.2 mg, 0.134 mmol, **6a/6b = ca. 2/1**) as a colorless liquid. The NMR data were consistent with those previously reported.<sup>14,15</sup> Note: <sup>19</sup>F NMR spectrum showed that it contains <10% of unidentifiable impurities appearing at -92.6 and -94.0 ppm. See the <sup>19</sup>F NMR spectrum.

For **6a**,

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.00–7.93 (m, 2H), 7.62–7.53 (m, 1H), 7.50–7.43 (m, 2H), 4.88–4.64 (m, 1H), 3.24–3.07 (m, 2H), 2.20–1.89 (m, 2H), 1.39 (dd, *J* = 23.9, 6.2 Hz, 3H).

**<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>):** δ 199.5, 137.0, 133.3, 128.8, 128.2, 90.4 (d, *J* = 164.7 Hz), 34.1 (d, *J* = 3.7 Hz), 31.2 (d, *J* = 20.8 Hz), 21.3 (d, *J* = 22.6 Hz).

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ -175.4 (s, 1F).

**HRMS (APCI-TOF):** calcd for C<sub>11</sub>H<sub>14</sub>FO [M+H]<sup>+</sup> 181.1029, found 181.1030.

For **6b**,

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.00–7.93 (m, 2H), 7.62–7.53 (m, 1H), 7.50–7.43 (m, 2H), 5.20–4.99 (m, 1H), 3.47 (ddd, *J* = 16.1, 16.0, 7.2 Hz, 1H), 3.11–2.99 (m, 1H), 1.86–1.63 (m, 2H), 1.04 (t, *J* = 7.4 Hz, 3H).

**<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>):** δ 197.2 (d, *J* = 5.5 Hz), 137.0, 133.5, 128.8, 128.3, 91.6 (d, *J* = 168.6 Hz), 43.5 (d, *J* = 23.3 Hz), 28.4 (d, *J* = 21.0 Hz), 9.4 (d, *J* = 5.4 Hz).

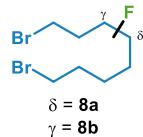
**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ –181.5 (s, 1F).

### fluorocyclododecane, 7



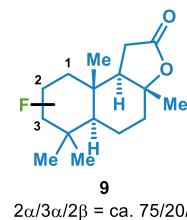
Following the general procedure with a total charge of 0.25 F/mol, the title compound was obtained in 31% yield (17.2 mg, 0.092 mmol) as a white solid. In the absence of NaNO<sub>3</sub>, the general procedure with a total charge of 1.0 F/mol afforded the title compounds in 35% yield (18.9 mg, 0.105 mmol). The NMR data were consistent with those previously reported.<sup>16</sup>

### 1,8-dibromo-4-fluoroctane, 8a and 1,8-dibromo-3-fluoroctane, 8b



Following the general procedure with a total charge of 2.0 F/mol, a mixture of the title compounds was obtained in 27% yield (23.3 mg, 0.081 mmol, **8a/8b = ca. 95/5**) as a colorless liquid. The NMR data was consistent with those previously reported.<sup>12</sup>

### fluorosclareolides, 9

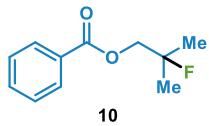


$2\alpha/3\alpha/2\beta = \text{ca. } 75/20/5$

Following the general procedure with a total charge of 1.0 F/mol, a mixture of the title compounds was obtained in 58% yield (46.3 mg, 0.174 mmol,  $2\alpha/3\alpha/2\beta = \text{ca. } 75/20/5$ ) as a white solid. In the absence of NaNO<sub>3</sub>, the general procedure with a total charge of 1.0 F/mol afforded the title compounds in 67% yield (54.0 mg, 0.201 mmol). The NMR data was consistent with those previously reported.<sup>11</sup>

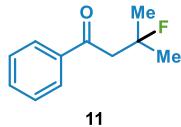
**HRMS (ESI-TOF):** calcd for C<sub>16</sub>H<sub>26</sub>FO<sub>2</sub> [M+H]<sup>+</sup> 269.1917, found 269.1912.

### 2-fluoro-2-methylpropyl benzoate, 10



Following the general procedure with a total charge of 2.0 F/mol, the title compound was obtained in 44% yield (25.9 mg, 0.132 mmol) as colorless liquid. The NMR data was consistent with those previously reported.<sup>4</sup>

### **3-fluoro-3-methyl-1-phenylbutan-1-one, 11**



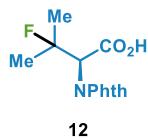
Following the general procedure with a total charge of 2.0 F/mol, the title compound was obtained in 55% yield (29.7 mg, 0.165 mmol) as colorless liquid.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.00–7.94 (m, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 3.33 (d, *J* = 15.3 Hz, 2H), 1.54 (d, *J* = 22.3 Hz, 6H).

**<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>):** δ 197.3 (d, *J* = 8.9 Hz), 137.6 (d, *J* = 2.3 Hz), 133.4, 128.7, 128.6, 94.7 (d, *J* = 166.8 Hz), 49.2 (d, *J* = 24.3 Hz), 27.2 (d, *J* = 23.8 Hz).

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ -129.3.

### **(R)-2-(1,3-dioxoisindolin-2-yl)-3-fluoro-3-methylbutanoic acid, 12**



Following the general procedure with a total charge of 2.0 F/mol, the title compound was obtained in 65% yield (50.3 mg, 0.195 mmol) as a white solid. SFC analysis revealed the enantiomeric excess of **12** to be 96% *ee*. See Figure S4.

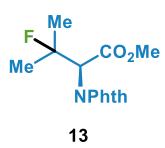
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.91 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.77 (dd, *J* = 5.5, 3.0 Hz, 2H), 5.06 (d, *J* = 12.7 Hz, 1H), 1.66 (d, *J* = 22.7 Hz, 3H), 1.58 (d, *J* = 22.1 Hz, 3H).

**<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>):** δ 170.4 (d, *J* = 8.6 Hz), 167.6, 134.6, 131.7, 124.0, 95.5 (d, *J* = 173.8 Hz), 58.1 (d, *J* = 26.4 Hz), 26.4 (d, *J* = 22.7 Hz), 24.3 (d, *J* = 23.5 Hz).

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ -137.0.

**HRMS (ESI-TOF):** calcd for C<sub>13</sub>H<sub>13</sub>FNO<sub>4</sub> ([M+H]<sup>+</sup>) 266.0829, found 266.0830.

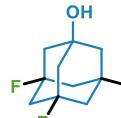
### **methyl (R)-2-(1,3-dioxoisindolin-2-yl)-3-fluoro-3-methylbutanoate, 13**



Following the general procedure with a total charge of 2.0 F/mol, the title compound was obtained in 66% yield (55.3 mg, 0.198 mmol) as a colorless liquid. The NMR data were consistent with those previously reported.<sup>9</sup>

### **3,5-difluoroadamantan-1-ol, 14a and 3,5,7-trifluoroadamantan-1-ol, 14b**

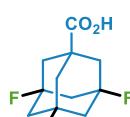
Following the general procedure with a total charge of 1.0 F/mol, a mixture of the title compounds was obtained in 64% yield (36.6 mg, **14a/14b** = ca. 9/1, determined by  $^{19}\text{F}$  NMR) as a white solid. The NMR data was consistent with those previously reported.<sup>17</sup>



R = H, 14a  
R = F, 14b

### **3,5-difluoroadamantane-1-carboxylic acid, 15a and 3,5,7-trifluoroadamantane-1-carboxylic acid, 15b**

Following the general procedure with a total charge of 1.0 F/mol, a mixture of the title compounds was obtained in 61% yield (40.3 mg, **15a/15b** = ca. 5/1, determined by  $^{19}\text{F}$  NMR) as a white solid. The NMR data were consistent with those previously reported.<sup>17</sup>



R = H, 15a  
R = F, 15b

### **N-(3,5-difluoroadamantan-1-yl)acetamide, 16a and N-(3,5,7-trifluoroadamantan-1-yl)acetamide, 16b**

Following the general procedure with a total charge of 1.0 F/mol, a mixture of the title compounds was obtained in 64% yield (44.5 mg, **16a/16b** = ca. 9/1, determined by  $^{19}\text{F}$  NMR) as a white solid. Note: In analogy to fluorinated 1-adamananols (**14a/14b**) described above, the authors have assigned the  $^{19}\text{F}$  NMR signal of the title compounds.  $^1\text{H}$  and  $^{13}\text{C}$  NMR of **16b** cannot be assigned properly due to overlapped signals of **16a**.

For **16a**,

**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  5.56 (s, 1H), 2.53–1.98 (m, 9H), 1.92 (s, 3H), 1.80 (p,  $J$  = 3.6, 3.2 Hz, 6H).

**$^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ ):**  $\delta$  169.8, 92.4 (dd,  $J$  = 188.1, 14.5 Hz), 55.2 (d,  $J$  = 26.0 Hz), 47.4 (t,  $J$  = 19.1 Hz), 45.8–45.0 (m), 40.7–40.1 (m), 39.0–38.5 (m), 29.2 (t,  $J$  = 11.3 Hz), 24.4.

**$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ):**  $\delta$  –138.5.

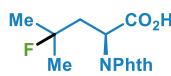
**HRMS (ESI-TOF):** calcd for  $\text{C}_{12}\text{H}_{18}\text{F}_2\text{NO} [\text{M}+\text{H}]^+$  230.1356, found 230.1362.

For **16b**,

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)**: δ -146.6.

**HRMS (ESI-TOF)**: calcd for C<sub>12</sub>H<sub>17</sub>F<sub>3</sub>NO [M+H]<sup>+</sup> 248.1262, found 248.1265.

**(S)-2-(1,3-dioxoisooindolin-2-yl)-4-fluoro-4-methylpentanoic acid, 17**



Following the general procedure with a total charge of 2.0 F/mol, the title compound was obtained in 63% yield (52.7 mg, 0.189 mmol) as a white solid.

17

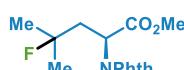
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**: δ 7.85 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.1 Hz, 2H), 5.17 (d, *J* = 9.9 Hz, 1H), 2.78 (ddd, *J* = 14.4, 14.3, 10.9 Hz, 1H), 2.45 (ddd, *J* = 28.6, 15.7, 2.0 Hz, 1H), 1.44 (d, *J* = 21.2 Hz, 3H), 1.35 (d, *J* = 21.4 Hz, 3H).

**<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)**: δ 174.4, 167.7, 134.3, 132.0, 123.7, 94.6 (d, *J* = 167.5 Hz), 48.3, 38.6 (d, *J* = 21.0 Hz), 28.0 (d, *J* = 24.3 Hz), 25.6 (d, *J* = 24.9 Hz).

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)**: δ -143.5.

**HRMS (ESI-TOF)**: calcd for C<sub>14</sub>H<sub>14</sub>FNNaO<sub>4</sub> [M+Na]<sup>+</sup> 302.0805, found 302.0806.

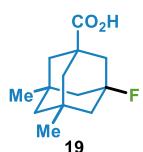
**methyl (S)-2-(1,3-dioxoisooindolin-2-yl)-4-fluoro-4-methylpentanoate, 18**



18

Following the general procedure with a total charge of 2.0 F/mol, the title compound was obtained in 60% yield (52.8 mg, 0.180 mmol) as a colorless liquid. The NMR data were consistent with those previously reported.<sup>9</sup>

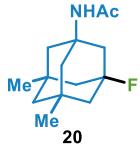
**3-fluoro-5,7-dimethyladamantane-1-carboxylic acid, 19**



Following the general procedure with a total charge of 0.5 F/mol on 0.2 mmol scale. The crude product was purified on preparative TLC plate with hexane/EtOAc = 3/1 as an eluent. R<sub>f</sub> = 0.40. The title compound was obtained in 83% yield (37.4 mg, 0.165 mmol) as a white solid. Physico-chemical characteristics and NMR data were consistent with those previously reported.<sup>18</sup>

**HRMS (ESI-TOF):** calcd for C<sub>13</sub>H<sub>19</sub>FO<sub>2</sub> [M-H]<sup>+</sup> 225.1291, found 269.1912.

**N-(3-fluoro-5,7-dimethyl-1-adamantyl)acetamide, 20**



Following the general procedure with a total charge of 0.25 F/mol on 0.2 mmol scale. The crude product was purified on preparative TLC plate with Et<sub>2</sub>O as an eluent. R<sub>f</sub> = 0.30. The title compound was obtained in 57% yield (27.1 mg, 0.113 mmol) as a white solid. M.p. = 109–110 °C.

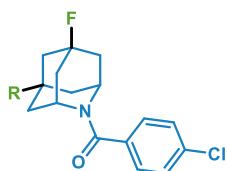
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 5.24 (br s, 1H), 2.04 (d, J = 5.7 Hz, 2H), 1.91 (s, 3H), 1.68–1.57 (m, 6H), 1.51 (dd, J = 11.0, 5.2 Hz, 2H), 1.18–1.09 (m, 2H), 0.95 (s, 6H).

**<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>):** δ 169.6, 93.5 (d, J = 183.6 Hz), 55.6 (d, J = 12.5 Hz), 49.5, 47.9 (d, J = 16.8 Hz), 46.5, 45.2 (d, J = 19.1 Hz), 34.8 (d, J = 10.2 Hz), 29.1, 24.7.

**<sup>13</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ –137.5.

**HRMS (ESI-TOF):** calcd for C<sub>14</sub>H<sub>22</sub>FNO [M+H]<sup>+</sup> 240.1764, found 240.1766.

**(4-chlorophenyl)(*rel*-(1*R*,3*S*,5*s*,7*s*)-5-fluoro-2-azaadamantan-2-yl)methanone, 24a and (4-chlorophenyl)(*rel*-(1*s*,3*s*,5*s*,7*s*)-5,7-difluoro-2-azaadamantan-2-yl)methanone, 24b**



Following the general procedure with a total charge of 1.1 F/mol, and column chromatography (Yamazen chromatography, HF silica SI40, M size, heptane/EtOAc = 60/40 to 50/50, v/v) gave **24a** (46.3 mg, 0.158 mmol) and **24b** (24.1 mg, 0.077 mmol) in 52% and 26% yields, respectively.

For **24a**,

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.42–7.37 (m, 2H), 7.36–7.32 (m, 2H), 5.16 (br s, 1H), 4.18 (br s, 1H), 2.49 (br s, 1H), 2.12–1.69 (br m, 10H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 168.3, 135.9, 134.3, 128.9, 128.1, 90.8 (d, J = 187.8 Hz), 53.5 (d, J = 10.8 Hz), 47.5 (d, J = 10.5 Hz), 41.7 (d, J = 18.4 Hz), 41.1 (d, J = 17.7 Hz), 40.8 (d, J = 18.1 Hz), 34.8, 33.9, 30.0 (d, J = 8.9 Hz).

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ –133.7. (CF<sub>3</sub>CO<sub>2</sub>H was used as an external standard, –76.55 ppm)

**HRMS (ESI, Orbitrap):** calcd for C<sub>16</sub>H<sub>18</sub>ClFNO [M+H]<sup>+</sup> 294.1055, found 294.1030.

For **24b**,

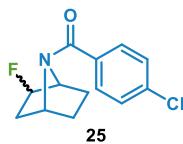
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.44–7.38 (m, 2H), 7.37–7.32 (m, 2H), 5.29 (br s, 1H), 4.34 (br s, 1H), 2.30–2.18 (br m, 2H), 2.12–1.76 (br m, 8H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 168.3, 136.4, 133.4, 129.1, 128.2, 91.9 (dd, *J* = 192.1, 13.1 Hz), 53.0–52.5 (br m), 47.2–47.0 (br m), 46.8 (t, *J* = 19.2 Hz), 40.7–40.1 (br m), 39.8–39.3 (br m).

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ –139.6.

**HRMS (ESI, Orbitrap):** calcd for C<sub>16</sub>H<sub>17</sub>ClF<sub>2</sub>NO [M+H]<sup>+</sup> 312.0961, found 312.0934.

#### (4-chlorophenyl)(*rel*-(1*S*,4*R*)-2-fluoro-7-azabicyclo[2.2.1]heptan-7-yl)methanone, **25**



Following the general procedure with a total charge of 3.0 F/mol, the title compound was obtained in 43% yield (32.1 mg, 0.127 mmol) as a solid with unassigned regio- and stereoisomers.

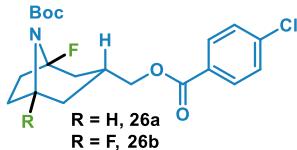
**<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):** δ 7.55 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 4.81 (br s, 1H), 4.78 (dd, *J* = 54.9, 6.4 Hz, 1H), 4.24 (br s, 1H), 2.13–1.72 (br m, 4H), 1.39–1.23 (m, 2H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 168.8, 136.7, 134.0, 129.5, 128.6, 94.0 (d, *J* = 186.7 Hz), 63.3, 52.8, 39.1, 27.1, 23.4.

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ –163.4. (CF<sub>3</sub>CO<sub>2</sub>H was used as an external standard, –76.55 ppm)

**HRMS (ESI, Orbitrap):** calcd for C<sub>13</sub>H<sub>14</sub>ClFNO [M+H]<sup>+</sup> 254.0742, found 254.0721.

**tert-butyl      *rel*-(1*S*,3*R*,5*S*)-3-(((4-chlorobenzoyl)oxy)methyl)-1-fluoro-8-azabicyclo[3.2.1]octane-8-carboxylate, **26a** and *tert*-butyl *rel*-(1*R*,3*s*,5*S*)-3-(((4-chlorobenzoyl)oxy)methyl)-1,5-difluoro-8-azabicyclo[3.2.1]octane-8-carboxylate, **26b****



Following the general procedure with a total charge of 1.0 F/mol, a mixture of the title compounds was obtained in 63% yield (72.7 mg, **26a/26b** = ca. 85/15, determined by  $^1\text{H}$  NMR in  $\text{C}_6\text{D}_6$ ) as a solid with unassigned regioisomers.  $^1\text{H}$  and  $^{13}\text{C}$  NMR of **26b** cannot be assigned properly due to overlapped signals of **26a**.

For **26a**,

**$^1\text{H}$  NMR (600 MHz,  $\text{C}_6\text{D}_6$ ):**  $\delta$  7.81 (d,  $J = 8.5$  Hz, 2H), 7.03 (d,  $J = 8.5$  Hz, 2H), 4.16 (br s, 1H), 4.00–3.90 (m, 2H), 2.63 (br s, 1H), 2.12–1.91 (br m, 3H), 1.73–1.64 (br m, 2H), 1.62–1.51 (m, 1H), 1.45 (s, 9H), 0.89–0.71 (m, 2H).

**$^{13}\text{C}$  NMR (151 MHz,  $\text{C}_6\text{D}_6$ ):**  $\delta$  165.1, 154.3, 139.6, 131.2, 129.0, 103.7 (d,  $J = 220.7$  Hz), 79.7, 68.6, 56.6, 35.6 (d,  $J = 20.8$  Hz), 34.3 (d,  $J = 28.2$  Hz), 30.4 (d,  $J = 9.9$  Hz), 29.1, 28.4, 22.8 (d,  $J = 9.6$  Hz). Only three aromatic carbon signals were observed probably due to overlapping  $\text{C}_6\text{D}_6$  signals.

**$^{19}\text{F}$  NMR (376 MHz,  $\text{C}_6\text{D}_6$ ):**  $\delta$  –127.5. ( $\text{CF}_3\text{CO}_2\text{H}$  was used as an external standard, –76.55 ppm)

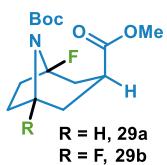
**HRMS (ESI, Orbitrap):** calcd for  $\text{C}_{20}\text{H}_{25}\text{ClFNNaO}_4$   $[\text{M}+\text{Na}]^+$  420.1348, found 420.1342.

For **26b**,

**$^{19}\text{F}$  NMR (376 MHz,  $\text{C}_6\text{D}_6$ ):**  $\delta$  –120.2. ( $\text{CF}_3\text{CO}_2\text{H}$  was used as an external standard, –76.55 ppm)

**HRMS (ESI, Orbitrap):** calcd for  $\text{C}_{20}\text{H}_{24}\text{ClF}_2\text{NNaO}_4$   $[\text{M}+\text{Na}]^+$  438.1254, found 438.1247.

### 8-(*tert*-butyl) 3-methyl *rel*-(1*S*,3*S*,5*S*)-1-fluoro-8-azabicyclo[3.2.1]octane-3,8-dicarboxylate, **29a** and 8-(*tert*-butyl) 3-methyl *rel*-(1*S*,3*S*,5*S*)-1,5-difluoro-8-azabicyclo[3.2.1]octane-3,8-dicarboxylate, **29b**



Following the general procedure with a total charge of 1.1 F/mol, **29a** was obtained in 57% yield (49.0 mg). Note: In analogy to **26a/26b** described above, the  $^{19}\text{F}$  NMR signals appearing at –123.1 ppm may be attributed to the corresponding difluorinated product **29b** (**29a/29b** = ca. 95/5).

For **29a**,

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 4.36–4.30 (m, 1H), 3.68 (s, 3H), 2.91–2.79 (m, 1H), 2.37 (t, *J* = 12.5 Hz, 1H), 2.16–2.02 (m, 4H), 1.90–1.81 (m, 1H), 1.70–1.60 (m, 1H), 1.48 (s, 9H), 1.41–1.32 (m, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 173.9 (d, *J* = 3.0 Hz), 154.0 (d, *J* = 4.0 Hz), 104.0 (d, *J* = 221.4 Hz), 80.6, 56.4 – 56.1 (m), 52.0, 36.6 (d, *J* = 10.4 Hz), 35.0 (d, *J* = 29.9 Hz), 34.7 (d, *J* = 20.0 Hz), 31.4, 28.3, 22.3 (d, *J* = 9.4 Hz).

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ –130.3. (CF<sub>3</sub>CO<sub>2</sub>H was used as an external standard, –76.55 ppm)

**HRMS (ESI, Orbitrap):** calcd for C<sub>14</sub>H<sub>22</sub>FKNO<sub>4</sub> [M+K]<sup>+</sup> 326.1170, found 326.1165.

## Determination of the enantiomeric excess of compound 12

The enantiomeric excesses were determined on a Waters SFC (UPC2) equipped with Daicel chiral columns (IA-3 through IH-3). The analyses revealed the enantiomeric excess of (*R*)-**12** to be 96% *ee*. (Figure S4)

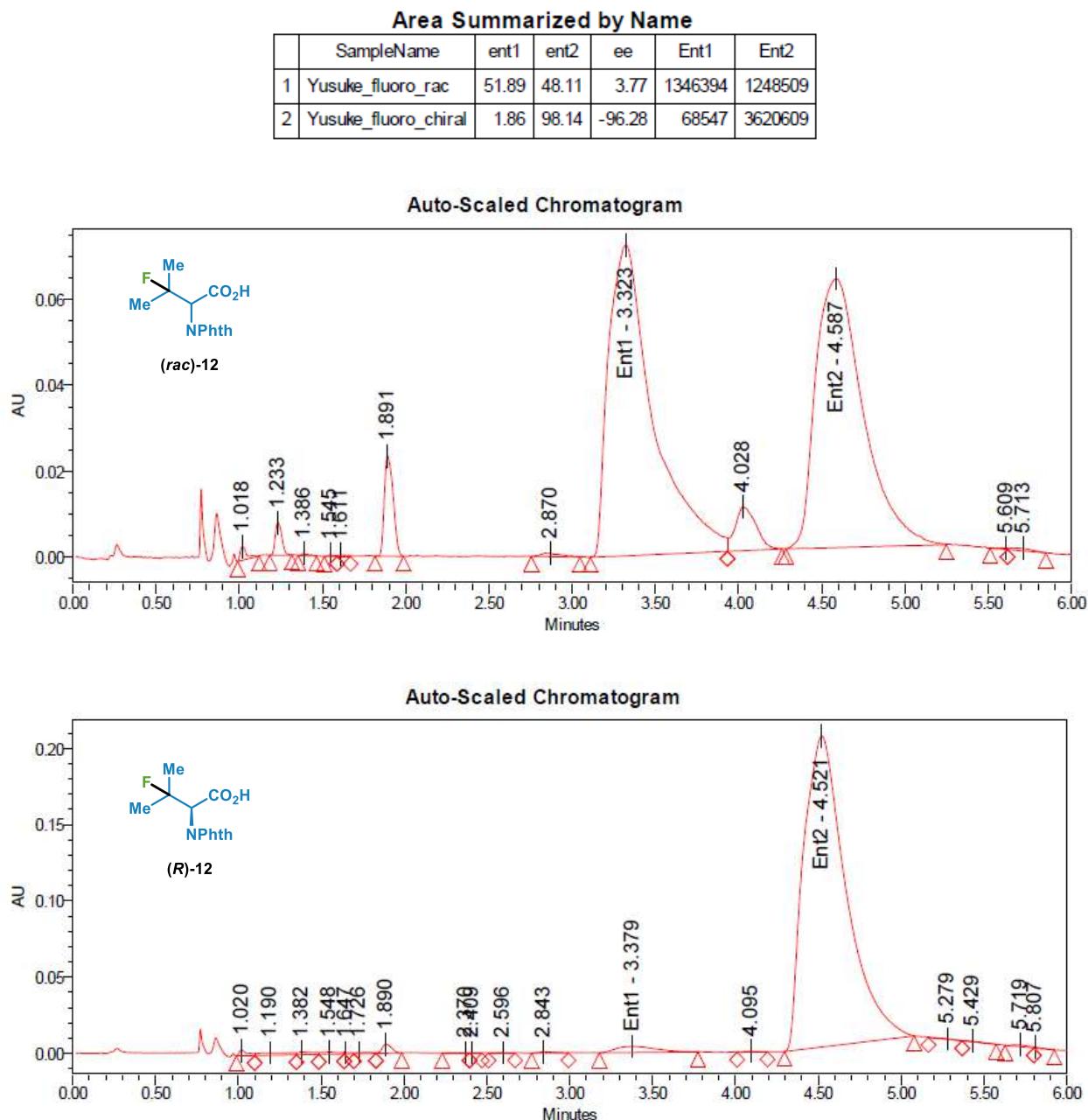


Figure S4. SFC traces of (*rac*)-**12** (top) and (*R*)-**12** (bottom).

## **Comparison with photochemical C(sp<sup>3</sup>)–H fluorination**

Compounds **S9**, **S10**, and **S12** were tested using previously reported conditions<sup>19</sup> for photochemical C(sp<sup>3</sup>)–H fluorination with some modifications as described below, and the results are summarized in Figure 1 in the manuscript.

### **Photochemical fluorination of **S9****

To a MeCN (2 mL) suspension of **S9** (20.0 mg, 0.073 mmol) were added Selectfluor (2.2 equiv, 56.5 mg, 0.160 mmol) and 1,2,4,5-tetracyanobenzene (0.1 equiv, 1.3 mg, 7.3 μmol) at rt. After bubbling with N<sub>2</sub> for 10 min, the reaction mixture was irradiated by a 26W UV-B bulb for 13 h. The crude material was directly purified by flash column chromatography (Yamazen chromatography, HF silica SI40, M size, heptane/EtOAc = 60/40, v/v), to give a mixture of **24a** and **24b** in 68% yield (14.4 mg, **24a/24b** = ca. 10/7, determined by <sup>1</sup>H NMR).

### **Photochemical fluorination of **S10****

To a MeCN (1.5 mL) solution of **S10** (13.0 mg, 0.055 mmol) were added Selectfluor (2.2 equiv, 43.0 mg, 0.121 mmol) and 1,2,4,5-tetracyanobenzene (0.1 equiv, 1.0 mg, 5.5 μmol) at rt. After bubbling with N<sub>2</sub> for 10 min, the reaction mixture was irradiated by a 26W UV-B bulb for 14 h. The reaction mixture was quenched by adding saturated aqueous NaHCO<sub>3</sub> and extracted with CH<sub>2</sub>Cl<sub>2</sub> twice. The combined organics were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. Anisole (5.3 mg, 0.049 mmol) was added to the crude material as an internal standard and the <sup>1</sup>H NMR yield of **25** was determined to be 26% along with recovery of **S10** in 28%.

### **Photochemical fluorination of **S12****

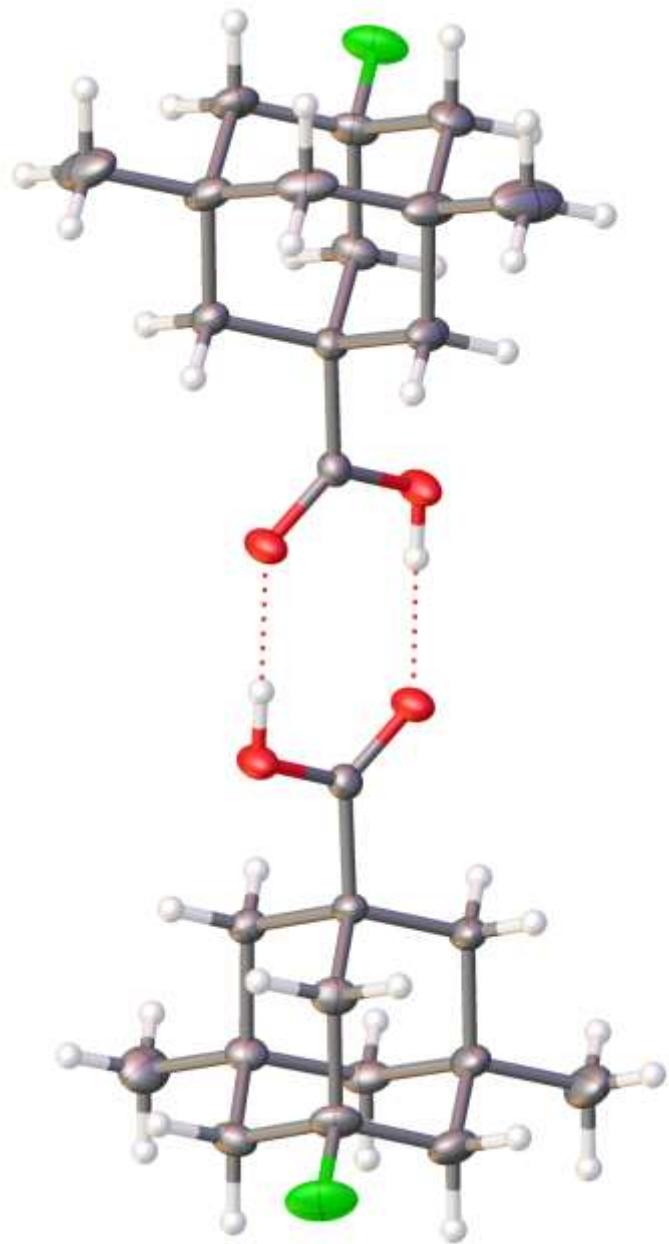
To a MeCN (3 ml) solution of **S12** (80.0 mg, 0.297 mmol) were added Selectfluor (2.2 equiv, 231 mg, 0.653 mmol) and 1,2,4,5-tetracyanobenzene (0.1 equiv, 5.3 mg, 0.030 mmol) at rt. After bubbling with N<sub>2</sub> for 10 min, the reaction mixture was irradiated by a 26W UV-B bulb for 15 h. The reaction mixture was quenched by adding saturated aqueous NaHCO<sub>3</sub> and extracted with CH<sub>2</sub>Cl<sub>2</sub> once. The combined organics were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. Anisole (10.2 mg, 0.0943 mmol) was added to the crude material as an internal standard and the <sup>1</sup>H NMR yield of **29** was determined to be 19% along with recovery of **S12** in 32%.

## X-ray crystal structure

Crystals of **19** and **20** were grown from hexane (slow evaporation) and hexane–diethyl ether, respectively. The single crystal X-ray diffraction studies were carried out on a Bruker D8 Venture Photon 2 MetalJet D2 C diffractometer equipped with Ga K<sub>α</sub> radiation ( $\lambda = 1.34139 \text{ \AA}$ ). The data were integrated using the Bruker SAINT Software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure. All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All carbon bonded hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Crystallographic data are summarized in Table S5–S8.

**Compound 19:**

CCDC 1886324



**Table S5.** Crystal data and structure refinement for **19**.

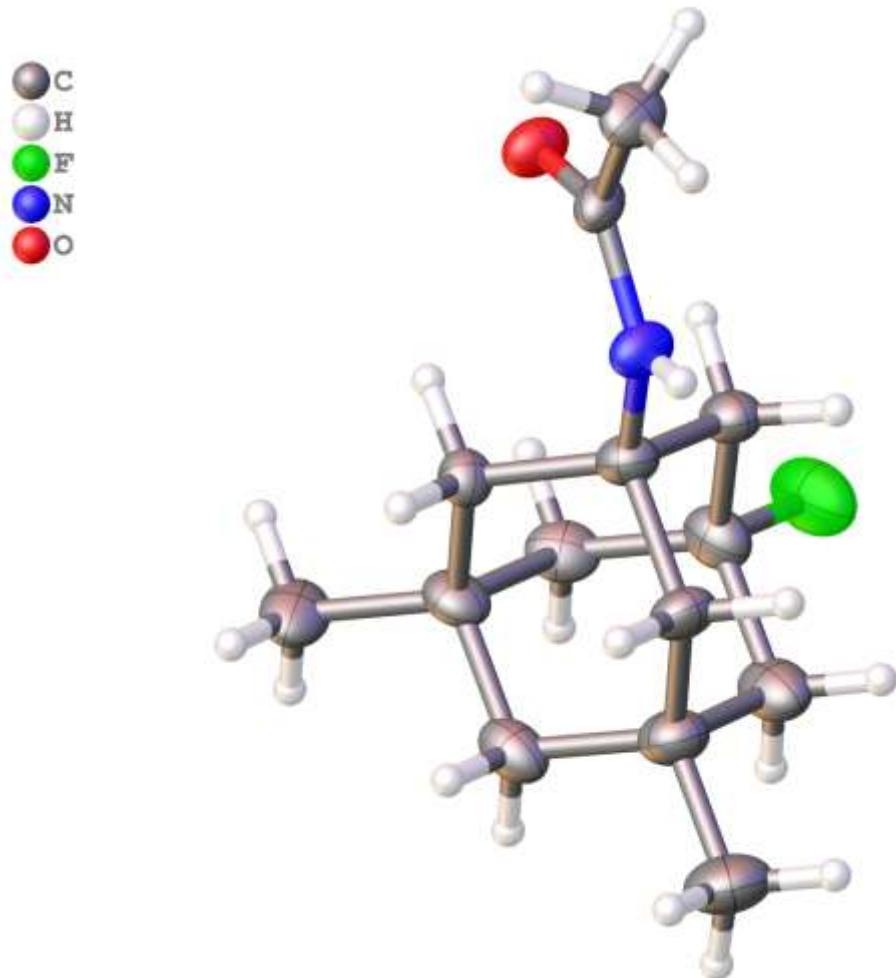
Empirical formula	C13 H19 F O2
Molecular formula	C13 H19 F O2
Formula weight	226.28
Temperature	100.15 K
Wavelength	1.34139 Å
Crystal system	Tetragonal
Space group	P4 <sub>3</sub> 2 <sub>1</sub> 2
Unit cell dimensions	a = 14.9454(5) Å b = 14.9454(5) Å c = 21.9502(8) Å
	α= 90°. β= 90°. γ = 90°.
Volume	4902.9(4) Å <sup>3</sup>
Z	16
Density (calculated)	1.226 Mg/m <sup>3</sup>
Absorption coefficient	0.479 mm <sup>-1</sup>
F(000)	1952
Crystal size	0.175 x 0.15 x 0.12 mm <sup>3</sup>
Crystal color, habit	colorless irregular
Theta range for data collection	3.112 to 56.967°.
Index ranges	-18<=h<=18, -17<=k<=16, -27<=l<=27
Reflections collected	42510
Independent reflections	5006 [R(int) = 0.0461]
Completeness to theta = 53.594°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.6581 and 0.5699
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	5006 / 0 / 295
Goodness-of-fit on F <sup>2</sup>	1.041
Final R indices [I>2sigma(I)]	R1 = 0.0303, wR2 = 0.0797
R indices (all data)	R1 = 0.0323, wR2 = 0.0814
Absolute structure parameter	0.00(4)
Largest diff. peak and hole	0.222 and -0.138 e.Å <sup>-3</sup>

**Table S6.** Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for **19**. U(eq) is defined as one third of the trace of the orthogonalized  $U^{ij}$  tensor.

	x	y	z	U(eq)
F(1)	1948(1)	4580(1)	2472(1)	42(1)
O(1)	3841(1)	2408(1)	3652(1)	25(1)
O(2)	4894(1)	3300(1)	4051(1)	23(1)
C(1)	4152(1)	3193(1)	3823(1)	19(1)
C(2)	3489(1)	3952(1)	3738(1)	18(1)
C(3)	2764(1)	3864(1)	4238(1)	19(1)
C(4)	2063(1)	4611(1)	4174(1)	22(1)
C(5)	2546(1)	5516(1)	4231(1)	25(1)
C(6)	3267(1)	5628(1)	3733(1)	26(1)
C(7)	3953(1)	4864(1)	3798(1)	24(1)
C(8)	3035(1)	3888(1)	3104(1)	24(1)
C(9)	2357(1)	4648(1)	3055(1)	25(1)
C(10)	2814(1)	5548(1)	3106(1)	30(1)
C(11)	1636(1)	4548(1)	3537(1)	25(1)
C(12)	1347(1)	4506(1)	4665(1)	34(1)
C(13)	3731(2)	6533(1)	3789(1)	41(1)
F(1')	8162(1)	-153(1)	5180(1)	36(1)
O(1')	6121(1)	2037(1)	4128(1)	28(1)
O(2')	5070(1)	1154(1)	3721(1)	24(1)
C(1')	5818(1)	1256(1)	3942(1)	18(1)
C(2')	6480(1)	497(1)	4003(1)	18(1)
C(3')	5997(1)	-410(1)	3973(1)	22(1)
C(4')	6677(1)	-1182(1)	4002(1)	26(1)
C(5')	7333(1)	-1089(1)	3468(1)	31(1)
C(6')	7836(1)	-192(1)	3490(1)	29(1)
C(7')	7140(1)	565(1)	3462(1)	25(1)
C(8')	7012(1)	561(1)	4605(1)	23(1)
C(9')	7682(1)	-208(1)	4621(1)	24(1)
C(10')	8345(1)	-127(1)	4099(1)	28(1)
C(11')	7211(1)	-1101(1)	4601(1)	27(1)
C(12')	6183(2)	-2079(1)	3981(1)	46(1)
C(13')	8490(2)	-96(2)	2959(1)	51(1)

**Compound 20:**

CCDC 1886323



**Table S7.** Crystal data and structure refinement for **20**.

Empirical formula	C14 H22 F N O	
Molecular formula	C14 H22 F N O	
Formula weight	239.32	
Temperature	100.0 K	
Wavelength	1.34139 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 14.098(8) Å	α= 90°.
	b = 9.432(4) Å	β= 96.06(4)°.
	c = 14.991(8) Å	γ = 90°.
Volume	1982.2(18) Å <sup>3</sup>	
Z	6	
Density (calculated)	1.203 Mg/m <sup>3</sup>	
Absorption coefficient	0.437 mm <sup>-1</sup>	
F(000)	780	
Crystal size	0.2 x 0.08 x 0.08 mm <sup>3</sup>	
Crystal color, habit	colorless block	
Theta range for data collection	2.579 to 54.480°.	
Index ranges	-17<=h<=17, -11<=k<=11, -18<=l<=18	
Reflections collected	25322	
Independent reflections	7355 [R(int) = 0.0644]	
Completeness to theta = 53.594°	99.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.1452 and 0.0600	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	7355 / 80 / 490	
Goodness-of-fit on F <sup>2</sup>	1.081	
Final R indices [I>2sigma(I)]	R1 = 0.0564, wR2 = 0.1641	
R indices (all data)	R1 = 0.0732, wR2 = 0.1778	
Absolute structure parameter	0.0(5)	
Largest diff. peak and hole	0.262 and -0.254 e.Å <sup>-3</sup>	

**Table S8.** Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for **20**. U(eq) is defined as one third of the trace of the orthogonalized  $U^{ij}$  tensor.

	x	y	z	U(eq)
F(1)	3363(2)	2804(4)	6965(2)	55(1)
O(1)	125(2)	4283(3)	5203(2)	34(1)
N(1)	650(2)	2161(4)	4720(2)	30(1)
C(1)	-1052(3)	2489(5)	4697(4)	36(1)
C(2)	-44(3)	3065(4)	4905(3)	27(1)
C(3)	1688(3)	2421(5)	4885(3)	30(1)
C(4)	2001(3)	2512(5)	5896(3)	32(1)
C(5)	3079(3)	2718(5)	6028(3)	36(1)
C(6)	3580(3)	1403(7)	5675(3)	44(1)
C(7)	3275(3)	1265(6)	4652(3)	39(1)
C(8)	2177(3)	1095(5)	4505(3)	34(1)
C(9)	3741(4)	-21(7)	4290(4)	54(1)
C(10)	3567(3)	2599(6)	4196(3)	37(1)
C(11)	3091(3)	3941(6)	4574(3)	34(1)
C(12)	3370(3)	4012(6)	5590(3)	36(1)
C(13)	3382(3)	5268(6)	4102(4)	44(1)
C(14)	1995(3)	3745(5)	4406(3)	28(1)
F(1A)	6719(2)	2771(4)	3610(2)	61(1)
C(1A)	2278(3)	2555(5)	1382(4)	36(1)
C(3A)	5004(3)	2775(5)	1542(3)	27(1)
C(4A)	5341(3)	2793(5)	2558(3)	31(1)
C(5A)	6421(3)	2778(6)	2670(3)	36(1)
C(6A)	6767(4)	1383(7)	2284(3)	52(1)
C(7A)	6450(3)	1329(5)	1268(3)	40(1)
C(8A)	5354(3)	1396(6)	1134(3)	39(1)
C(9A)	6804(5)	-54(7)	888(4)	68(2)
C(10A)	6873(4)	2599(6)	838(3)	39(1)
C(11A)	6519(3)	4001(6)	1222(3)	37(1)
C(12A)	6821(3)	3996(6)	2231(3)	43(1)
C(13A)	6902(4)	5275(7)	737(5)	62(2)

C(14A)	5419(3)	4000(5)	1076(3)	32(1)
O(1A)	3453(2)	877(4)	1904(2)	32(1)
N(1A)	3950(3)	3013(5)	1406(3)	29(1)
C(2A)	3280(3)	2070(6)	1596(3)	29(1)
O(1AB)	3498(10)	4419(15)	1796(11)	32(1)
N(1AB)	4022(14)	2340(20)	1359(15)	29(1)
C(2AB)	3287(9)	3191(19)	1530(14)	29(1)
F(1B)	10043(2)	2179(4)	10275(2)	49(1)
C(1B)	5631(3)	2589(5)	8029(4)	36(1)
C(3B)	8367(3)	2697(5)	8206(3)	29(1)
C(4B)	8684(3)	2485(5)	9222(3)	31(1)
C(5B)	9763(3)	2341(6)	9345(3)	38(1)
C(6B)	10055(3)	984(6)	8856(3)	40(1)
C(7B)	9753(3)	1179(5)	7837(3)	33(1)
C(8B)	8667(3)	1392(6)	7691(3)	35(1)
C(9B)	10056(4)	-135(6)	7354(4)	52(1)
C(10B)	10236(3)	2489(5)	7520(3)	34(1)
C(11B)	9948(3)	3849(6)	8013(3)	36(1)
C(12B)	10236(3)	3636(6)	9021(3)	39(1)
C(13B)	10436(4)	5159(7)	7665(4)	55(1)
C(14B)	8860(3)	3973(6)	7865(3)	35(1)
O(1B)	6802(2)	862(4)	8503(3)	32(1)
N(1B)	7354(3)	3010(5)	8060(3)	29(1)
C(2B)	6658(3)	2079(6)	8218(3)	29(1)
O(1BB)	6755(9)	4429(16)	8579(11)	32(1)
N(1BB)	7214(17)	2450(20)	8044(17)	29(1)
C(2BB)	6607(9)	3190(20)	8301(13)	29(1)

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## Troubleshooting and frequently asked questions

*Q. Is NaNO<sub>3</sub> essential for this fluorination?*

A. It strongly depends on substrate which you plan to use. For several substrates, you don't need to use NaNO<sub>3</sub>. As you can see Scheme 2 in this paper, for example, sclareolide can be fluorinated electrochemically even in the absence of NaNO<sub>3</sub>.

*Q. What can I do when the yield of the reaction is not reproducible?*

A. Check the voltage of the reaction. From our experiences, if the cell voltage is too high (above 4.0 V at 3.0 mA on 0.1–0.3 mmol scale without a reference electrode), this reaction does not proceed well. In that case, the reaction mixture turns yellow during electrolysis. Normal operational voltage range for this reaction is approximately 2.5–3.5 V and reaction mixture remains colorless or pale yellow.

When a high voltage is noted:

- Ensure there is sufficient contact between the electrode and ElectraSyn cap to avoid undesired increase of resistance in the circuit.
- Increasing the amount of electrolyte helps to reduce the resistance of the cell.
- Reducing the current value also helps to decrease the reaction potential. Please note that longer reaction time is required in this case to ensure the passage of the same amount of electricity.

*Q. What are the suitable current values for reactions on different scales?*

A. We typically use 3.0 mA on 0.1–0.3 mmol scales. The submerged exterior surface area of electrode is approximately W7 × D1.5 × H10 mm. The current values and exterior area of electrodes may be adjusted proportionally for other scales to maintain similar levels of current density (mA/cm<sup>2</sup>).

*Q. Where can I get the electrode materials?*

A. We purchased a block of RVC foam from Ultramet. Ni foam could be obtained from multiple suppliers since this material is very common as a battery cathode (we purchased it from eBay).

*Q. We notice that Selectfluor is poorly soluble in MeCN. Can we electrolyze this heterogeneous solution as is?*

A. Yes—Our preliminary experiments showed that solubility of Selectfluor in MeCN varies on its manufacturer, batch number, and crystal shape/size, etc. Qualitatively, 0.1 M Selectfluor in MeCN (for 0.1 mmol scale experiments) gives a homogeneous system whereas Selectfluor remained insoluble at higher concentrations. Even on the latter case, Selectfluor dissolves gradually during electrolysis so you can electrolyze it as is.

*Q. We notice that NaNO<sub>3</sub> looks insoluble in MeCN. Can we electrolyze this heterogeneous solution as is?*

A. Yes—NaNO<sub>3</sub> is practically insoluble in MeCN but it works efficiently. You can electrolyze it as is.

*Q. Is this reaction sensitive to water?*

A. A small amount of water does not significantly affect the outcome. This allows you to use commercial NaNO<sub>3</sub> without any precaution. However, large amount of water should be avoided since this could hinder the fluorination.

*Q. How air sensitive is the reaction?*

A. As you can see Table S1 and Table S2, this reaction is sensitive to air. We strongly recommend you to run this reaction under inert atmosphere.

*Q. Can I remove the balloon after replacing the headspace of vial with argon?*

A. No—Our preliminary experiments showed that removal of the Ar balloon before electrolysis resulted in diminished yields. The vial should be maintained under Ar atmosphere throughout the duration of the reaction, keeping it shielded from air.

*Q. What can I do if a significant amount of starting materials remains after electrolyzing for 3.0 F/mol?*

A. From our experiences, longer reaction time had only a minor impact on its outcome.

*Q. Can I reuse the electrodes, if yes, how should I wash them for the next reaction?*

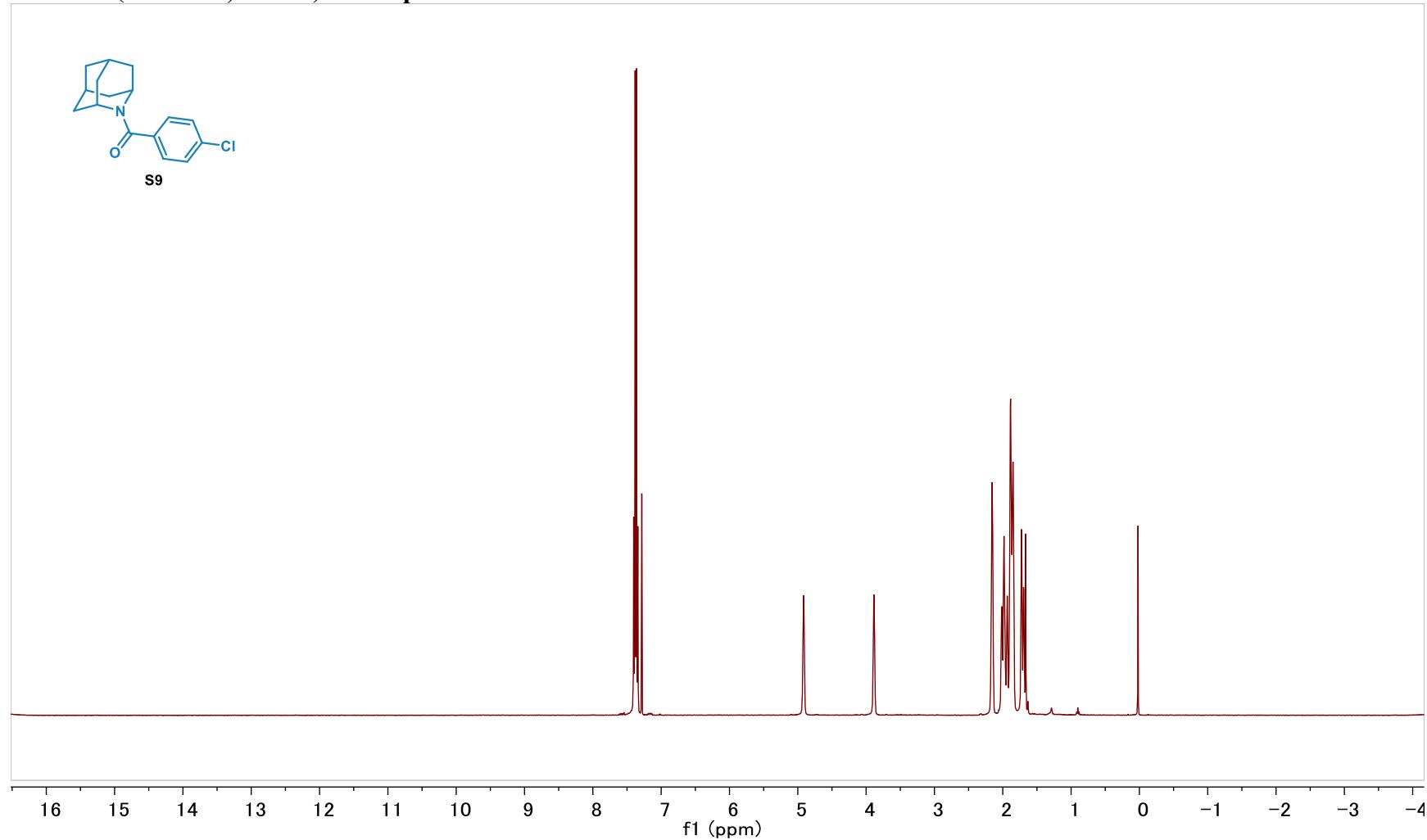
A. After the fluorination, RVC electrodes used are not dirty and their appearance remained unchanged so you can reuse them after a simple cleaning as follows: Wash with 1 N HCl, H<sub>2</sub>O several times, and acetone, sequentially, and allow to dry before setting up the next reaction. If the exterior of electrodes is shiny black with a metallic luster obviously, we recommend you do not reuse them again.

## References

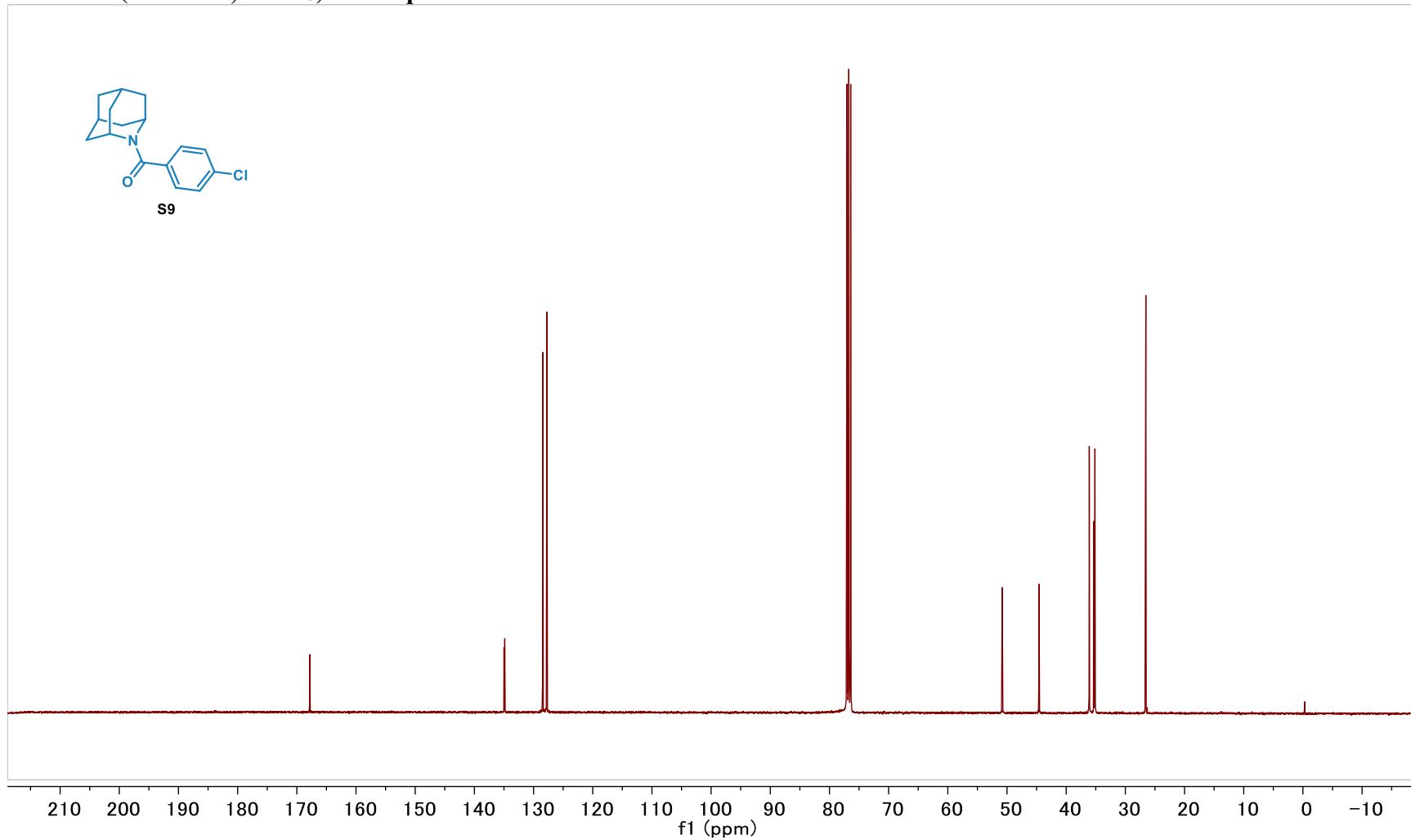
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## NMR spectra

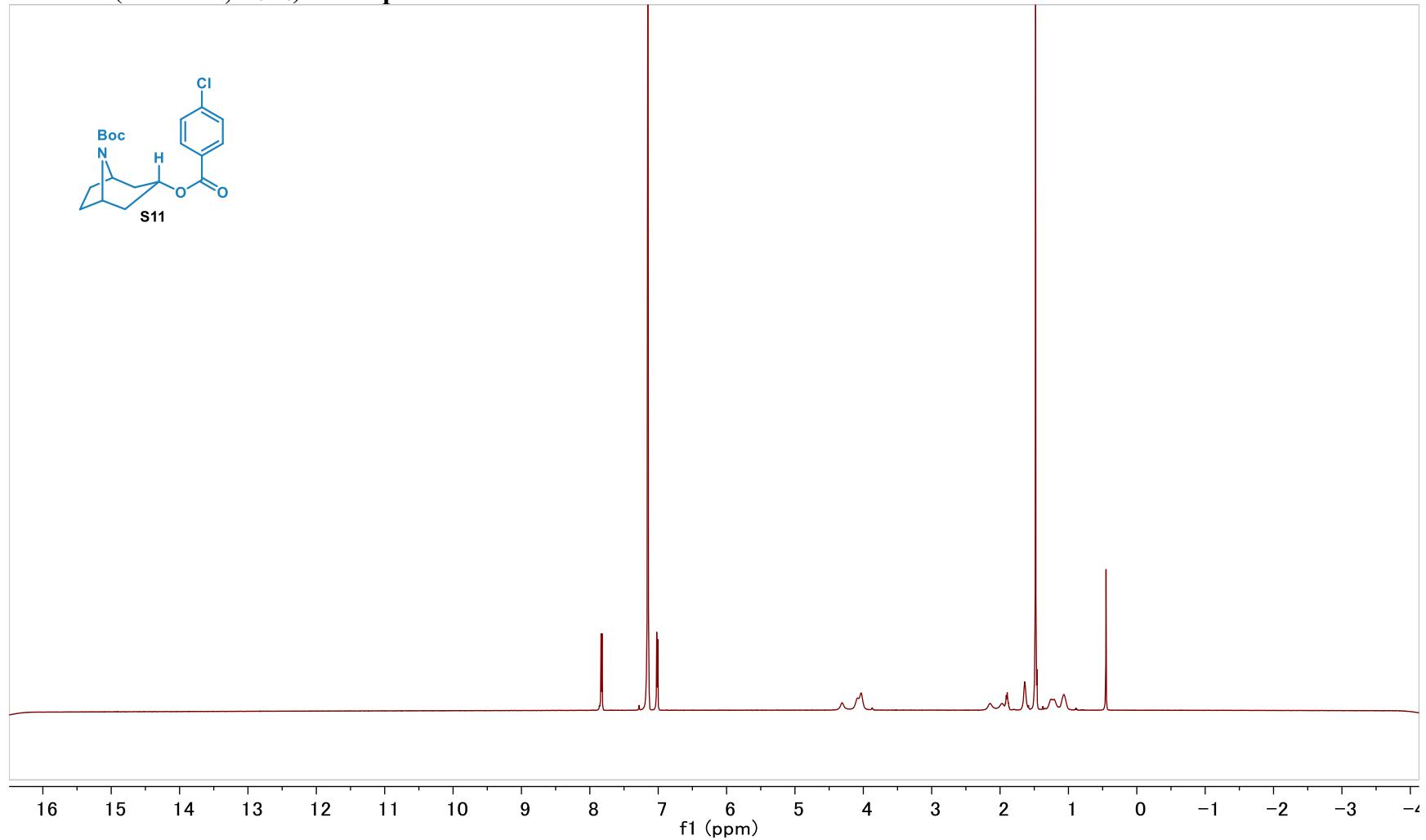
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound S9



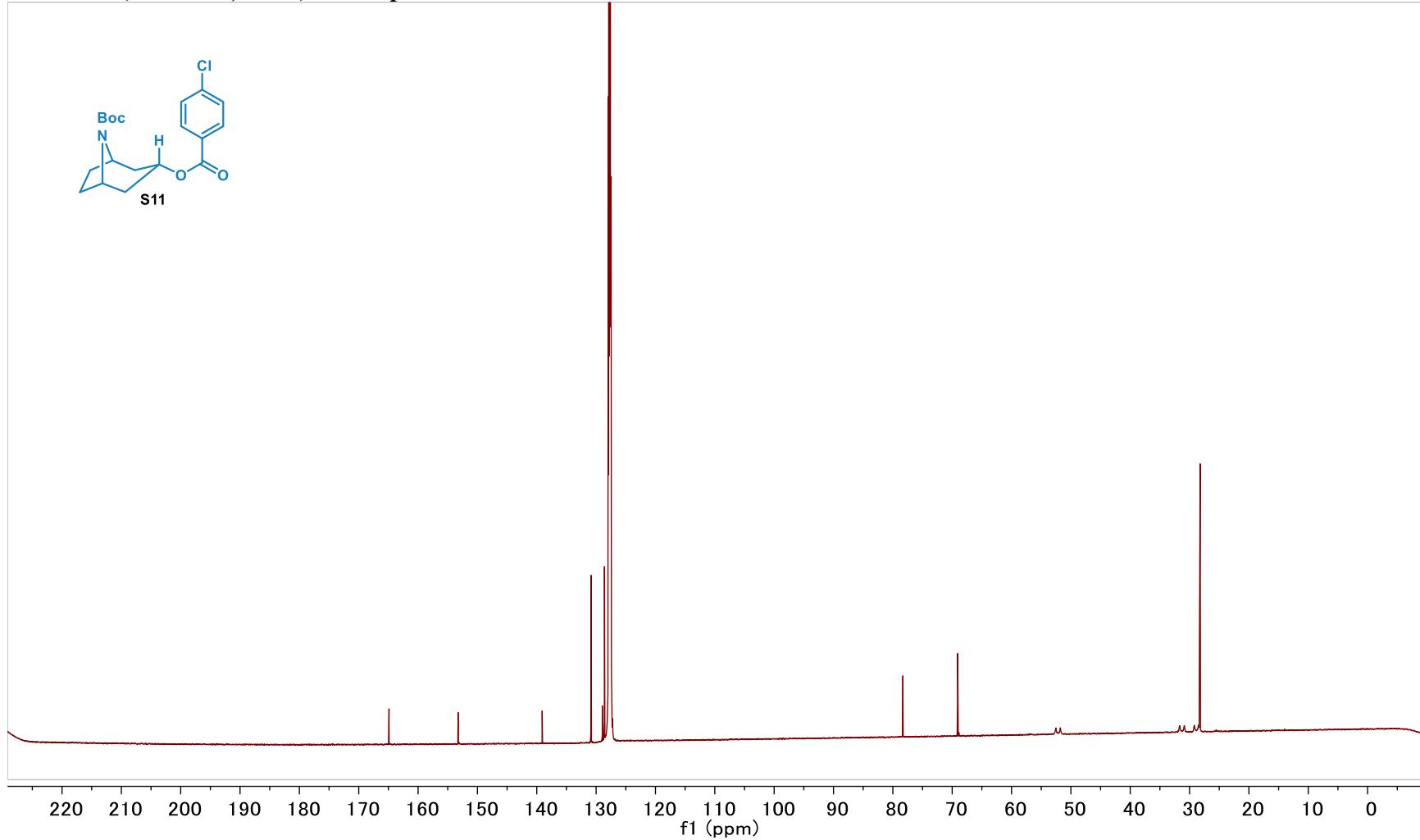
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) of compound S9



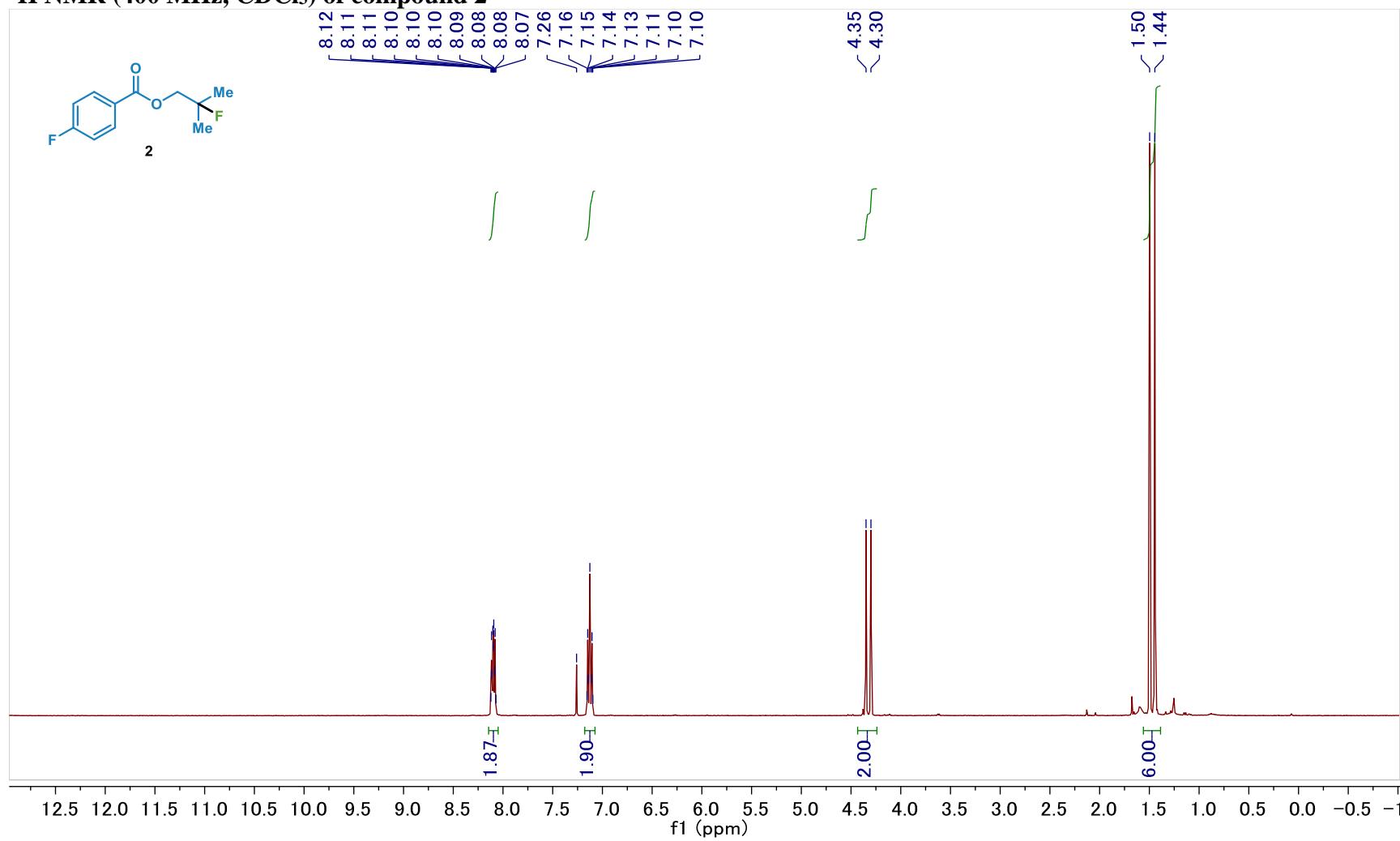
<sup>1</sup>H NMR (600 MHz, C<sub>6</sub>D<sub>6</sub>) of compound S11



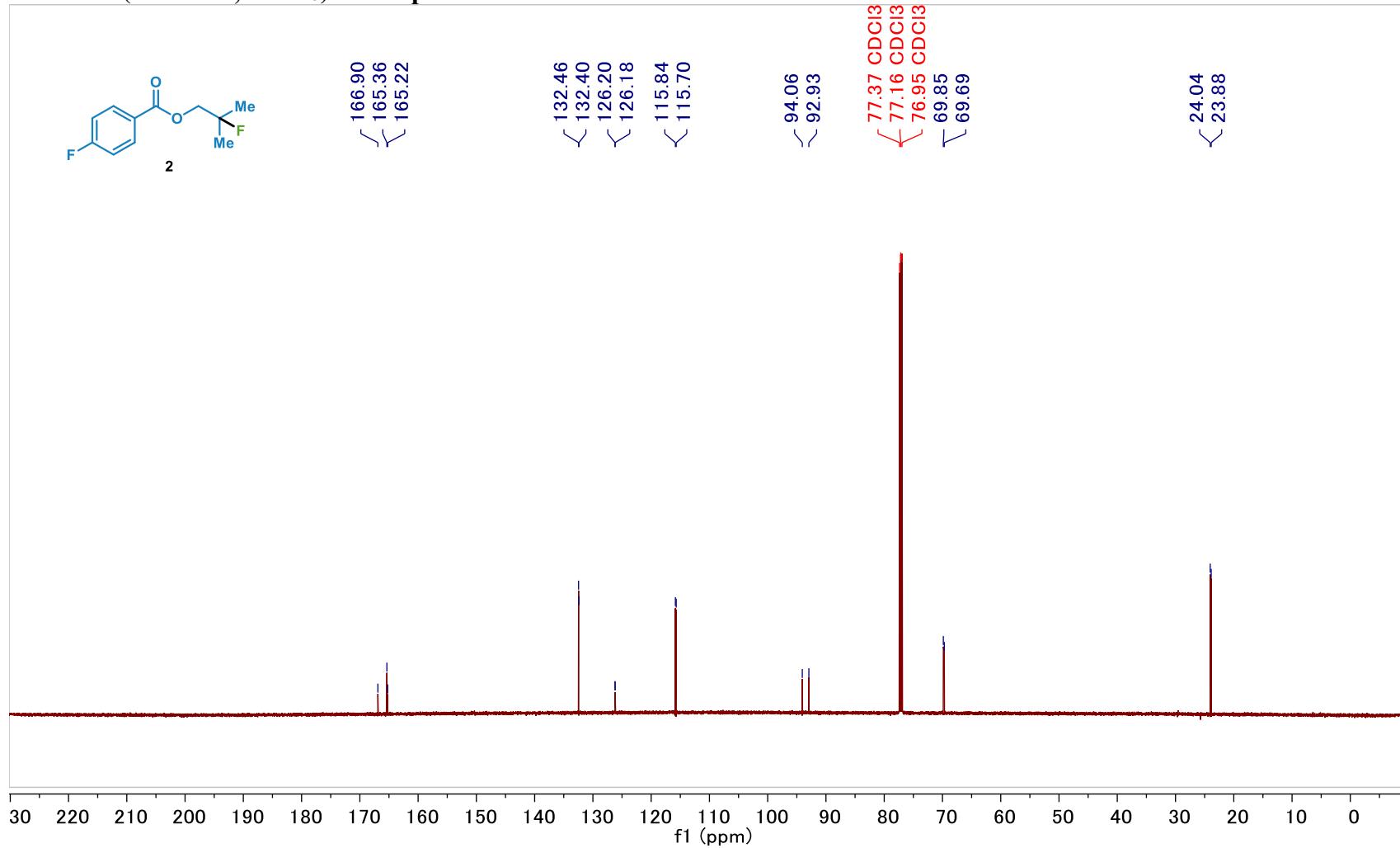
<sup>13</sup>C NMR (151 MHz, C<sub>6</sub>D<sub>6</sub>) of compound S11



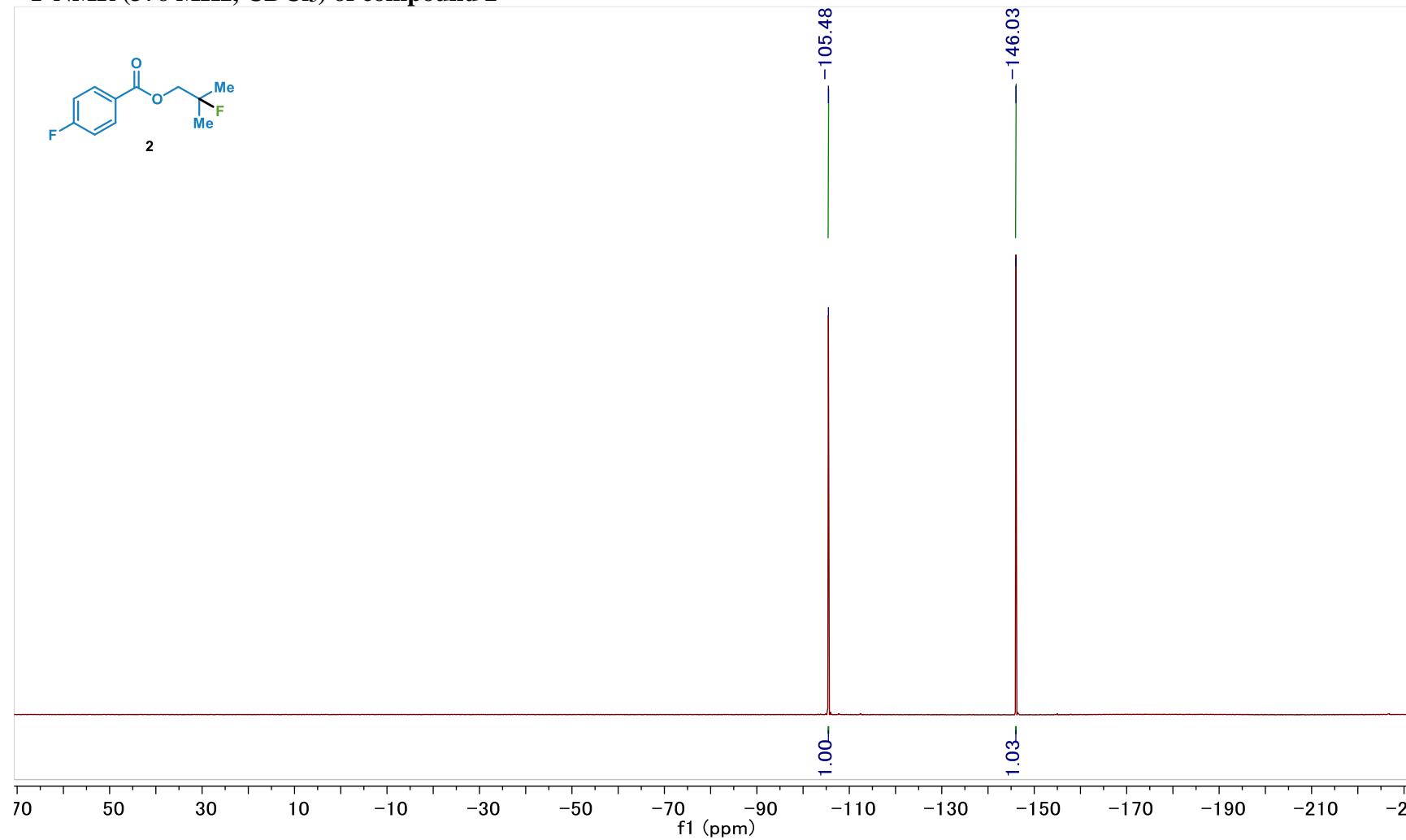
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 2



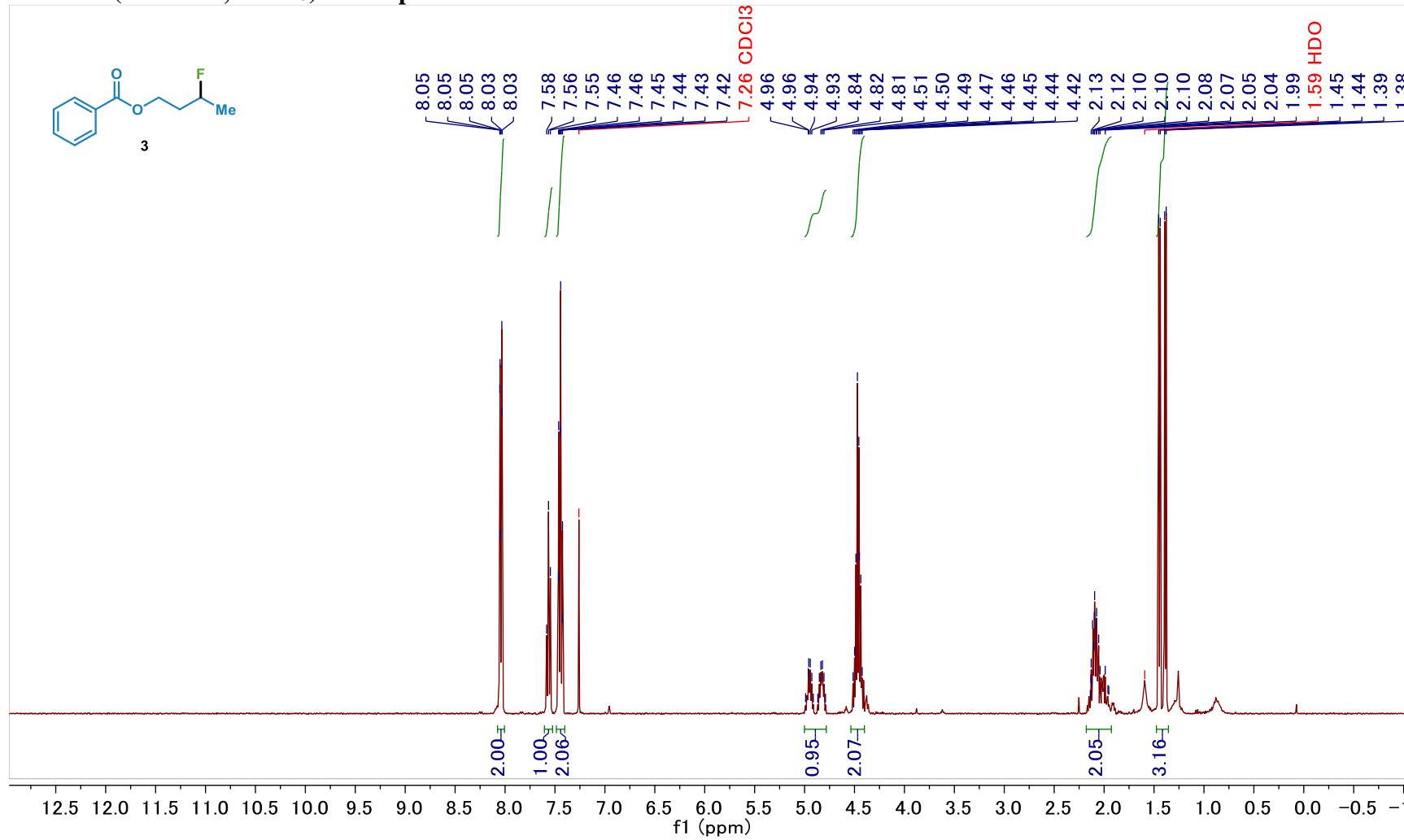
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 2



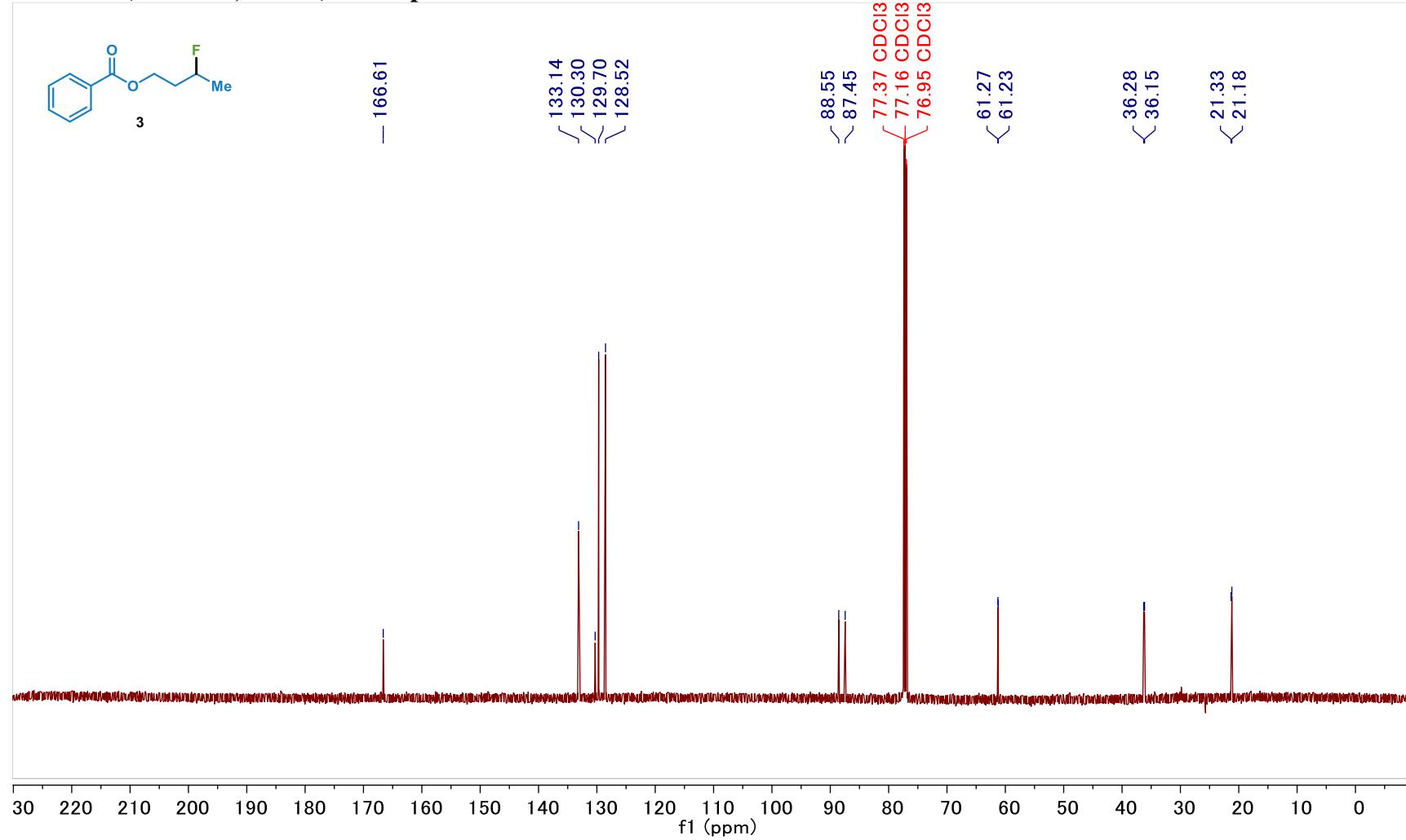
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 2



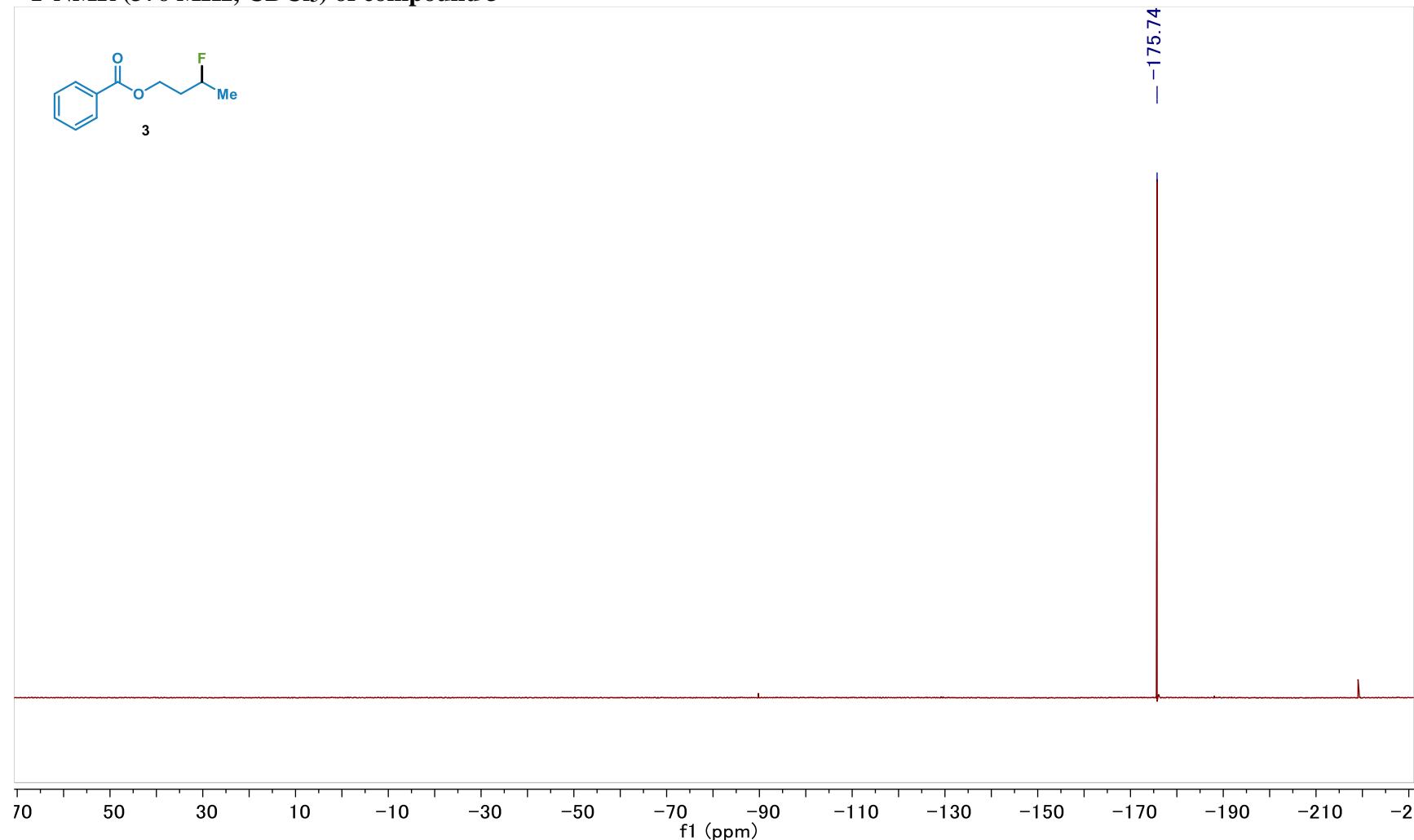
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 3



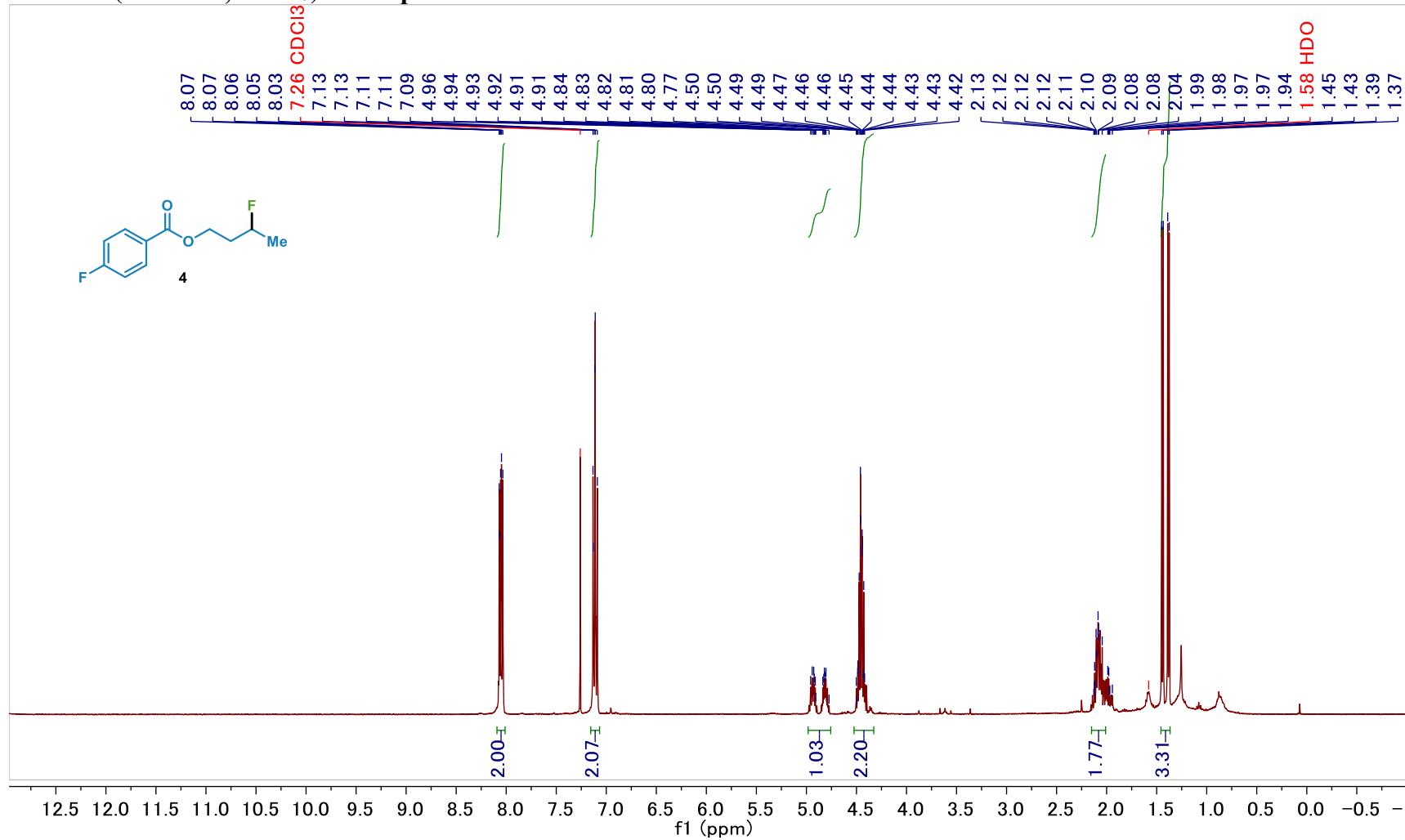
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 3



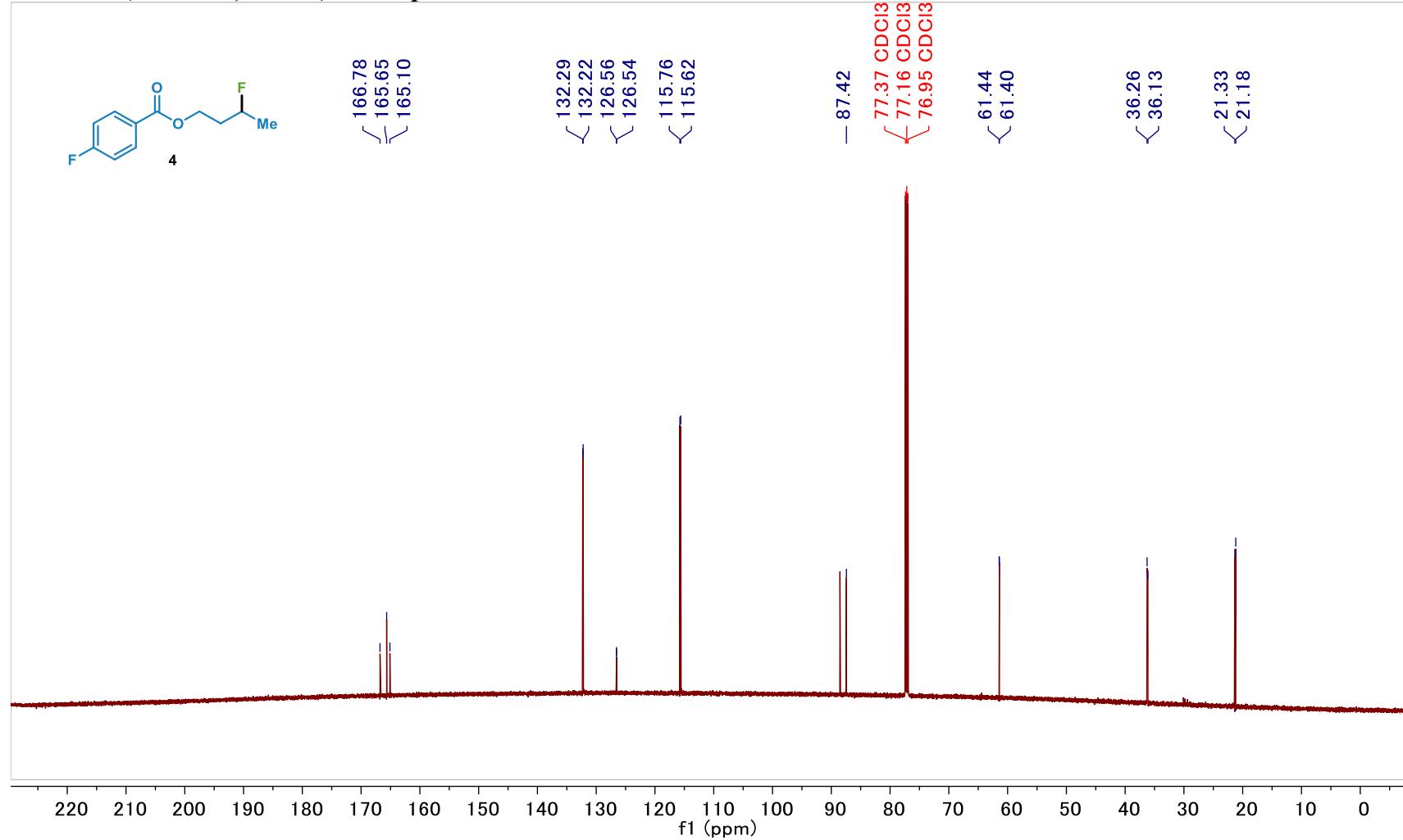
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 3



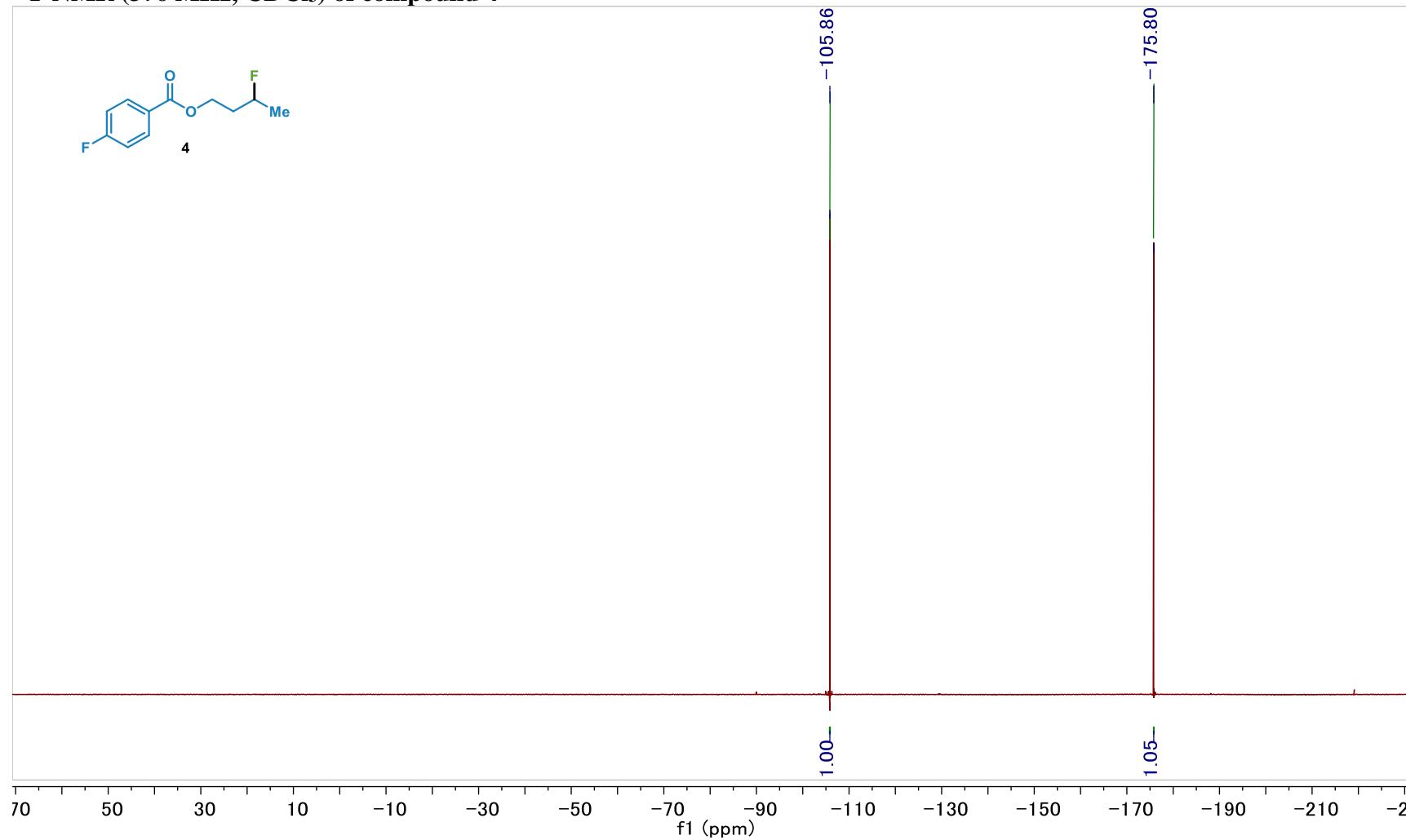
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 4



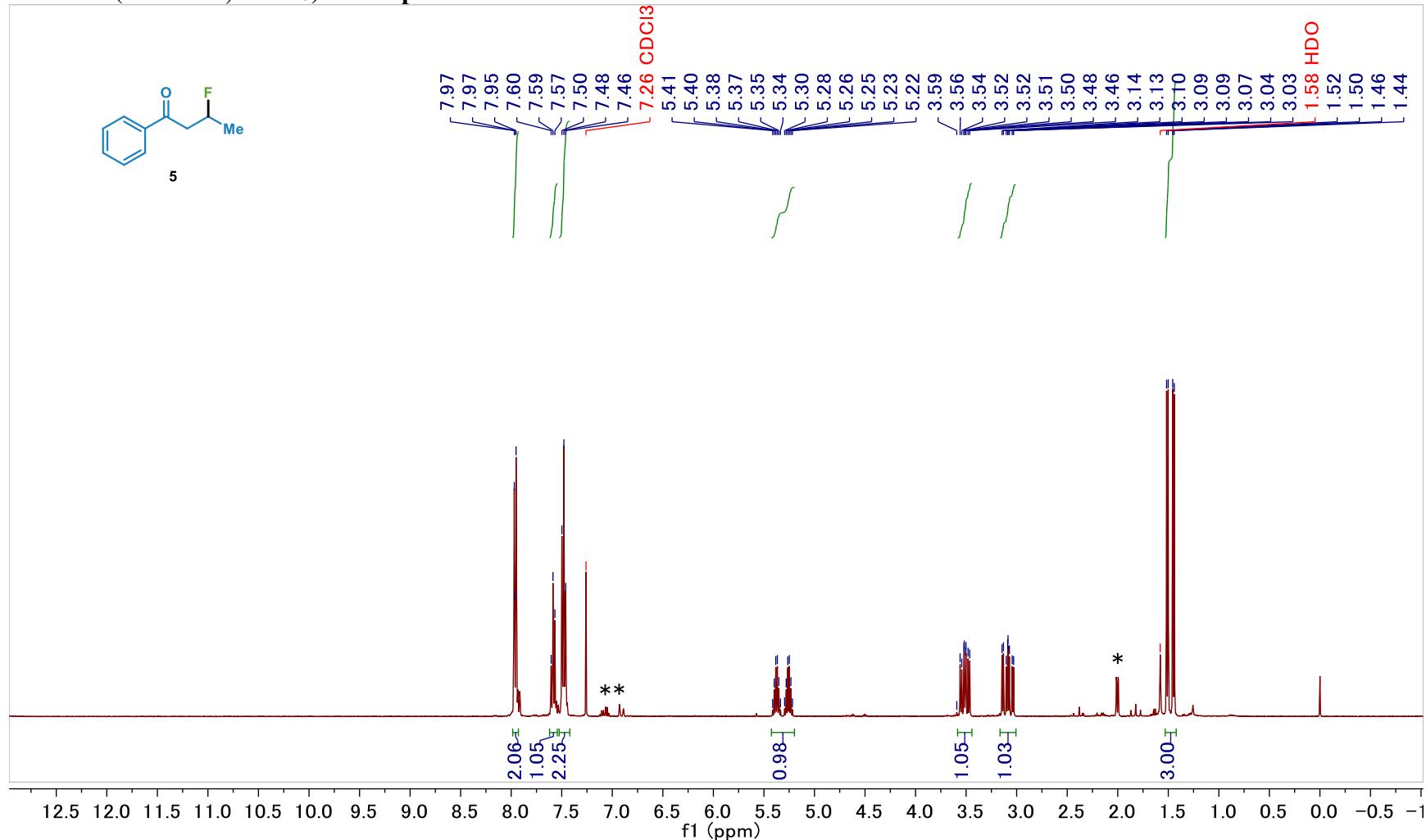
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 4



<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 4

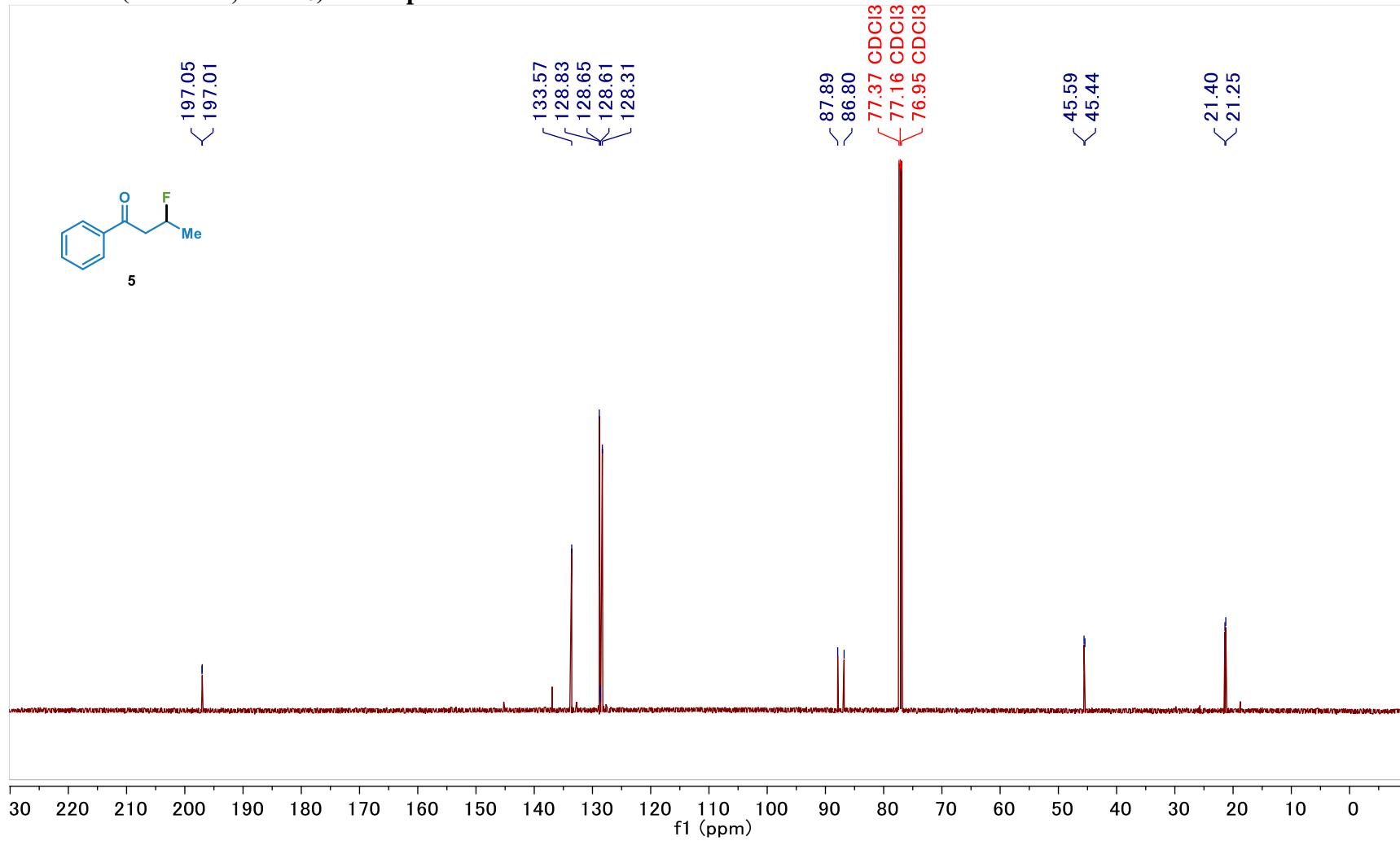


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 5

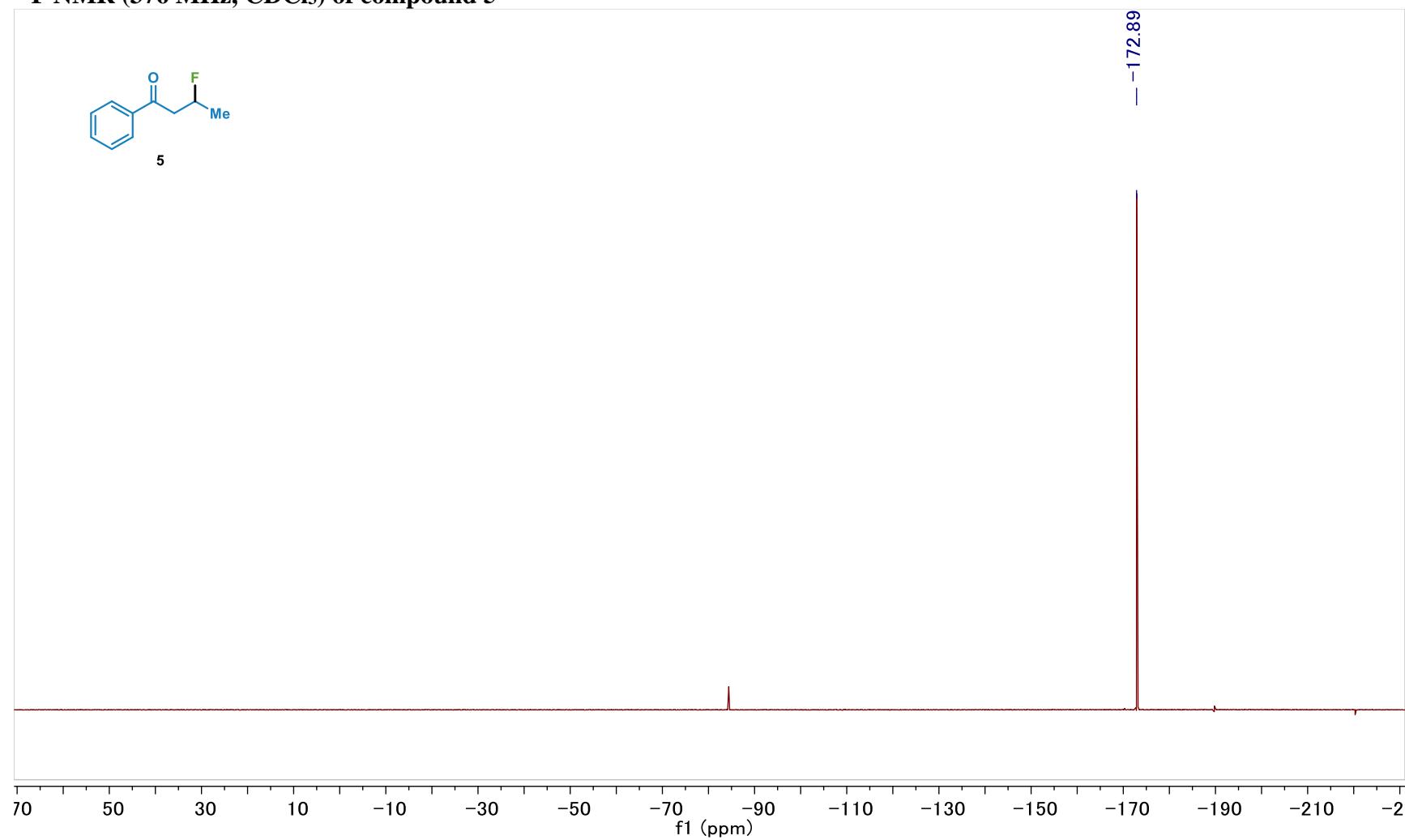


Peaks marked with asterisk (\*) indicate inseparable (E)-1-phenylbut-2-en-1-one.

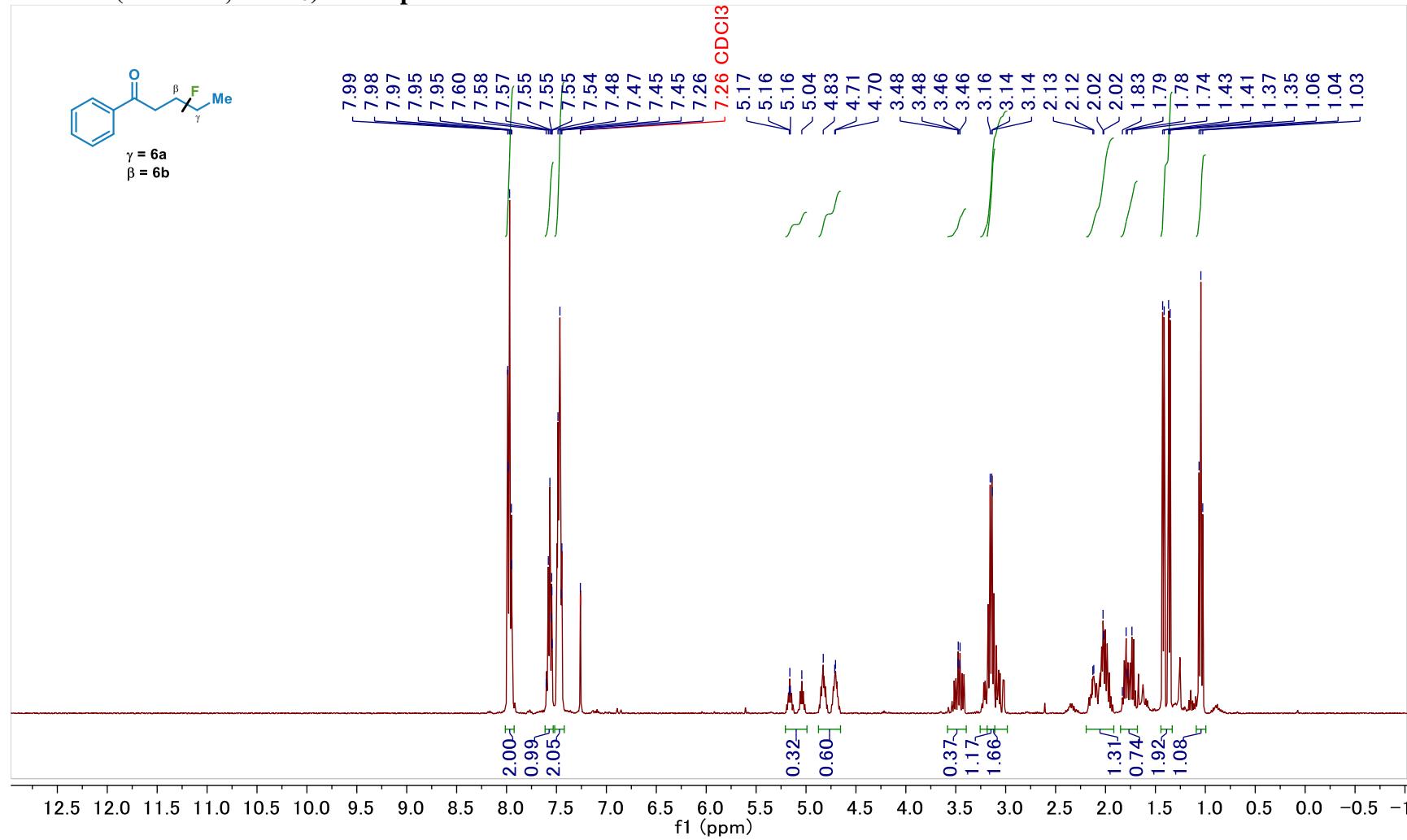
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 5



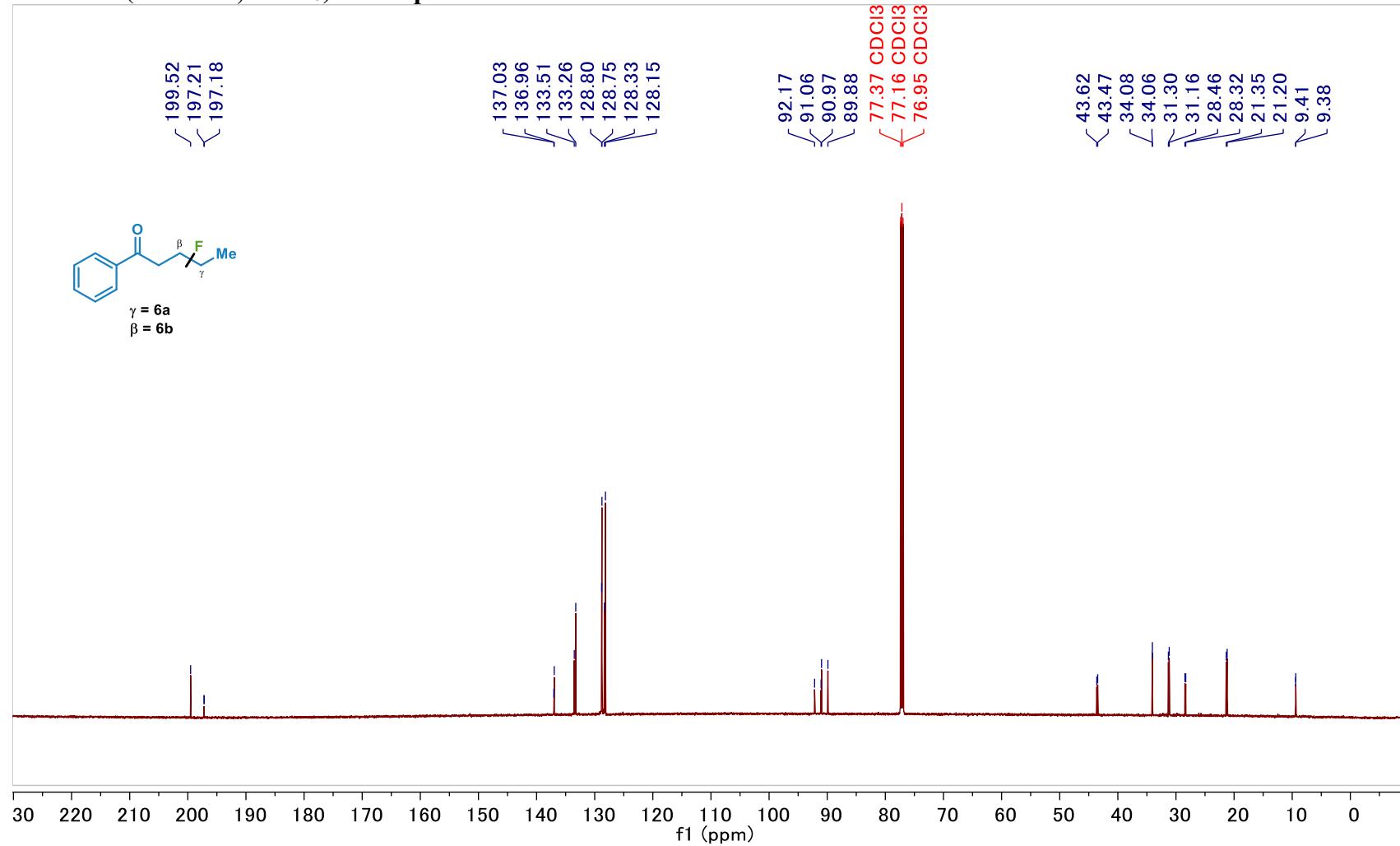
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 5



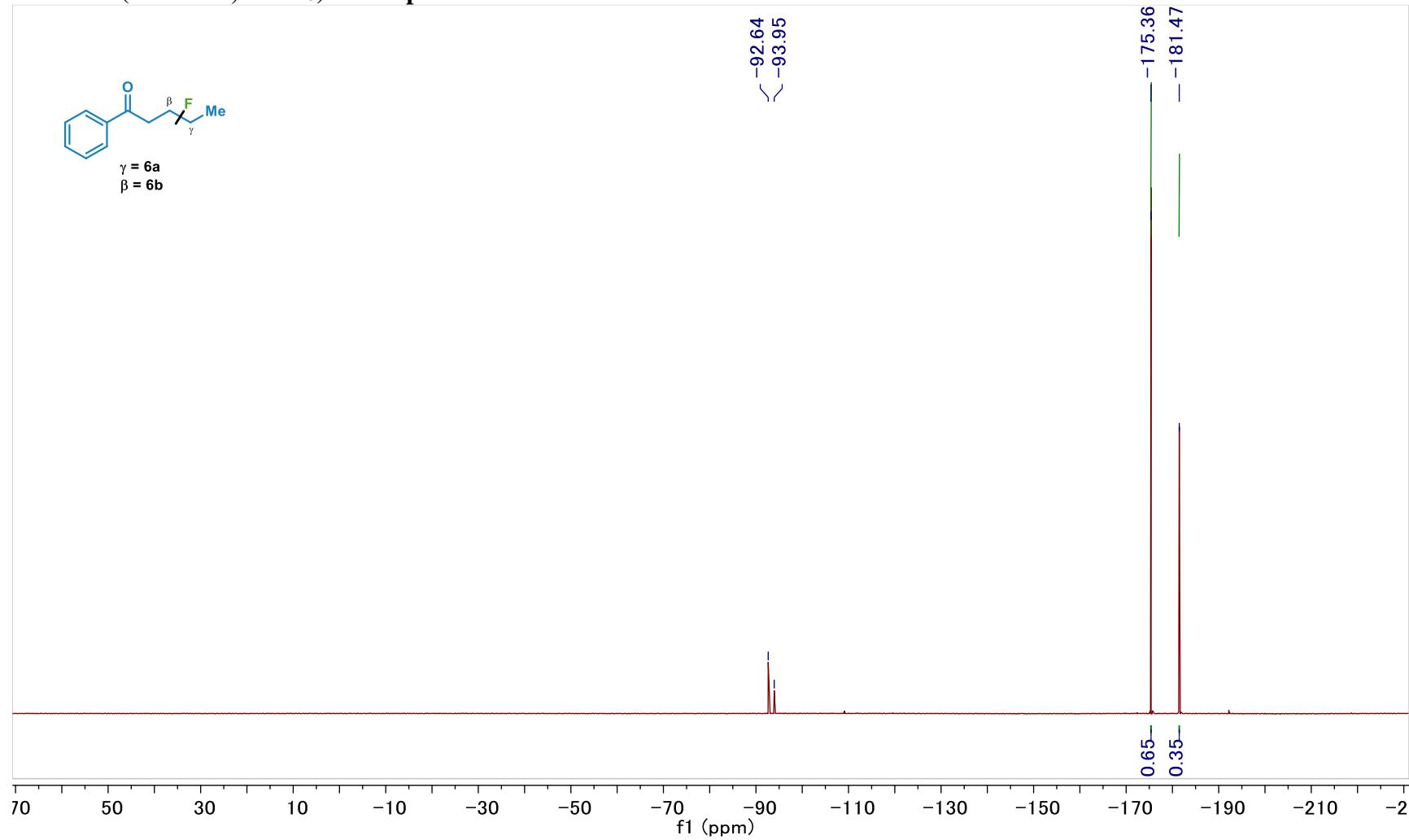
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 6



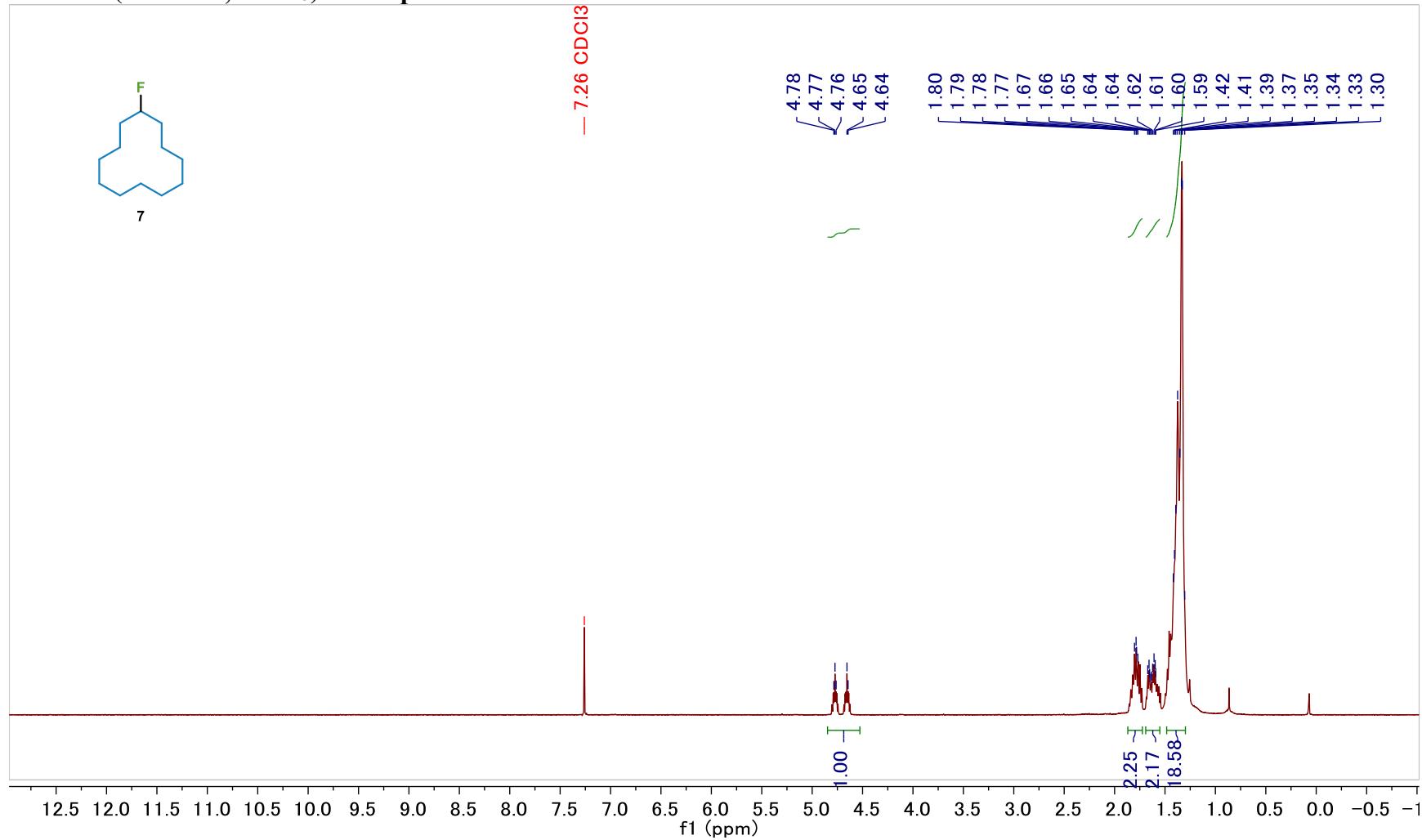
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 6



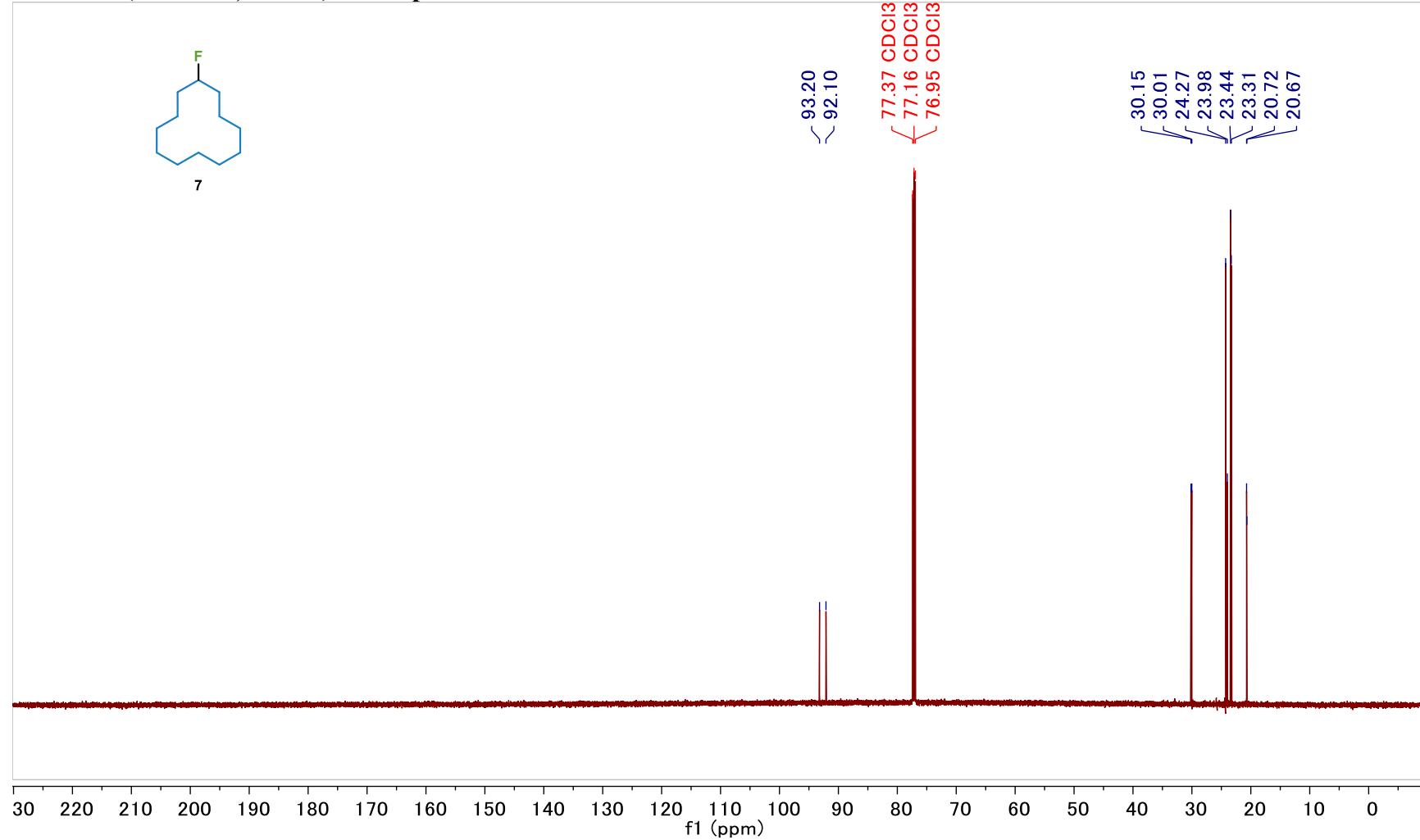
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 6



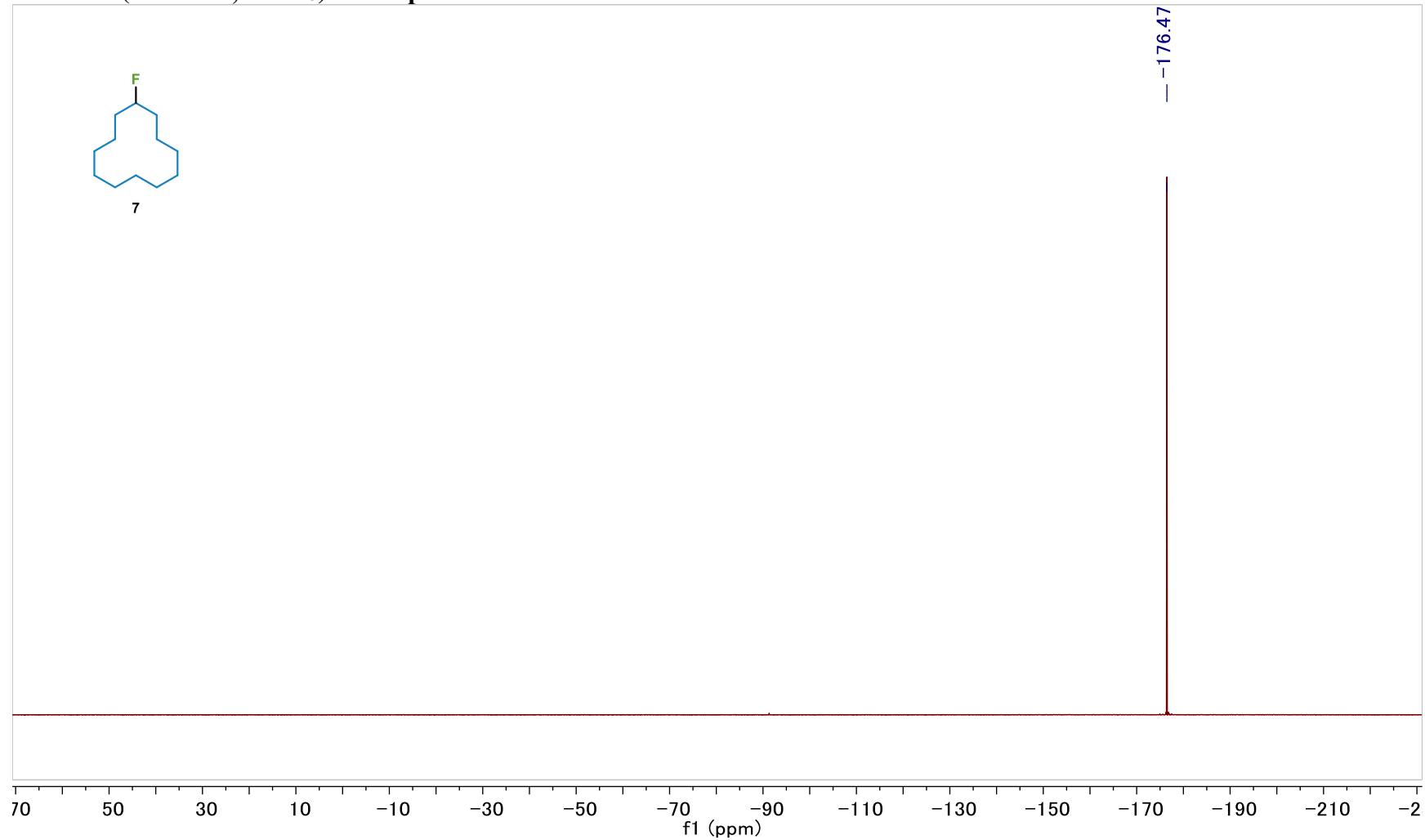
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 7



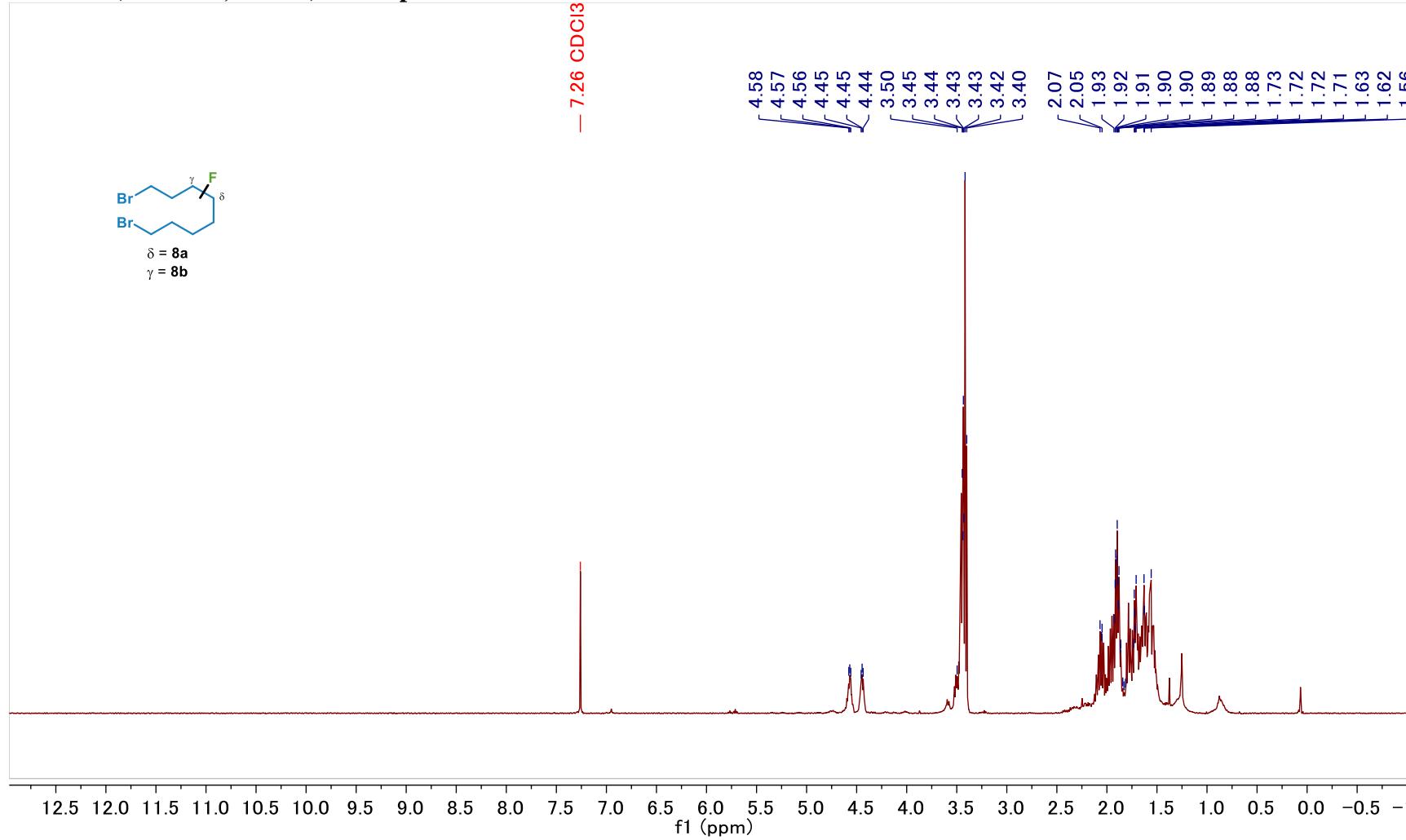
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 7



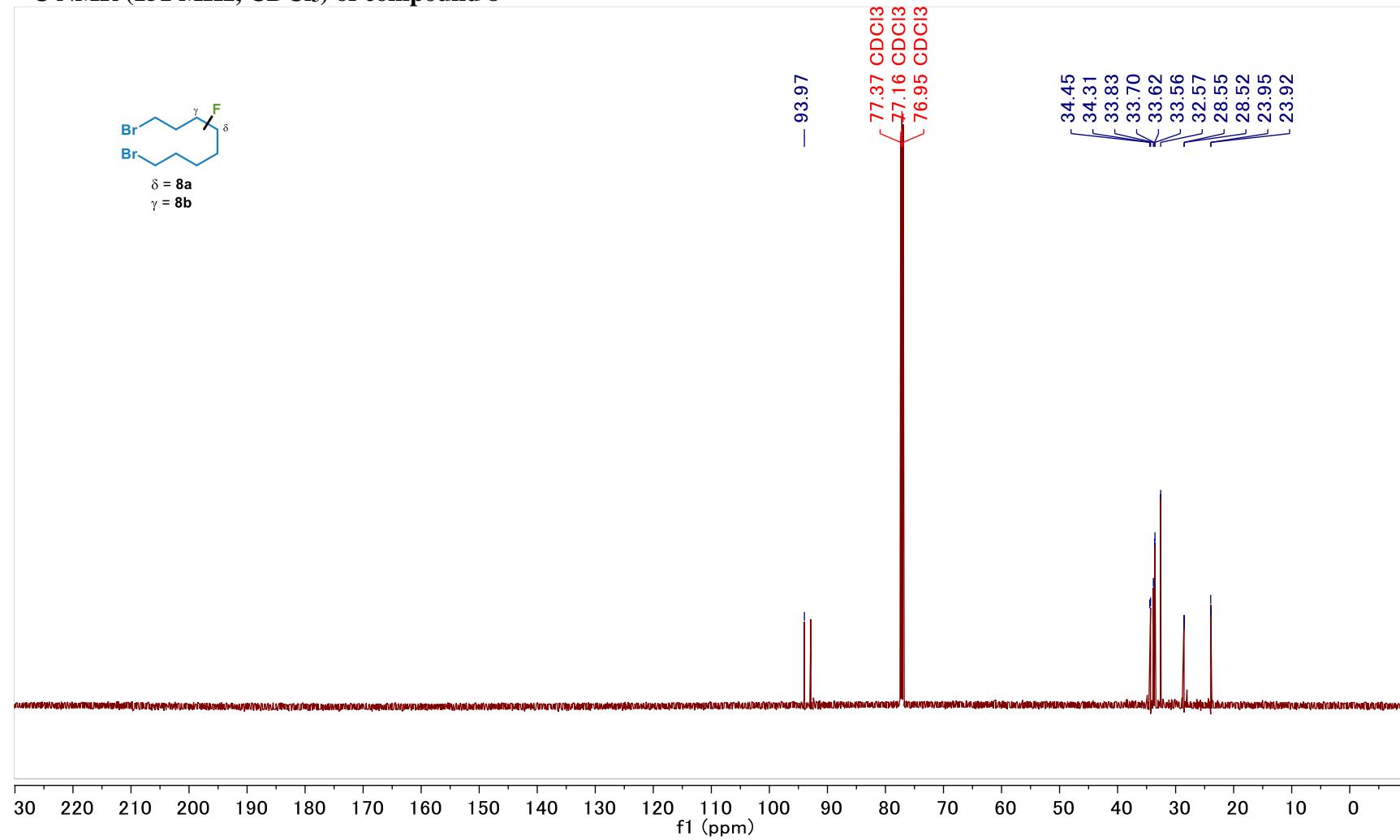
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 7



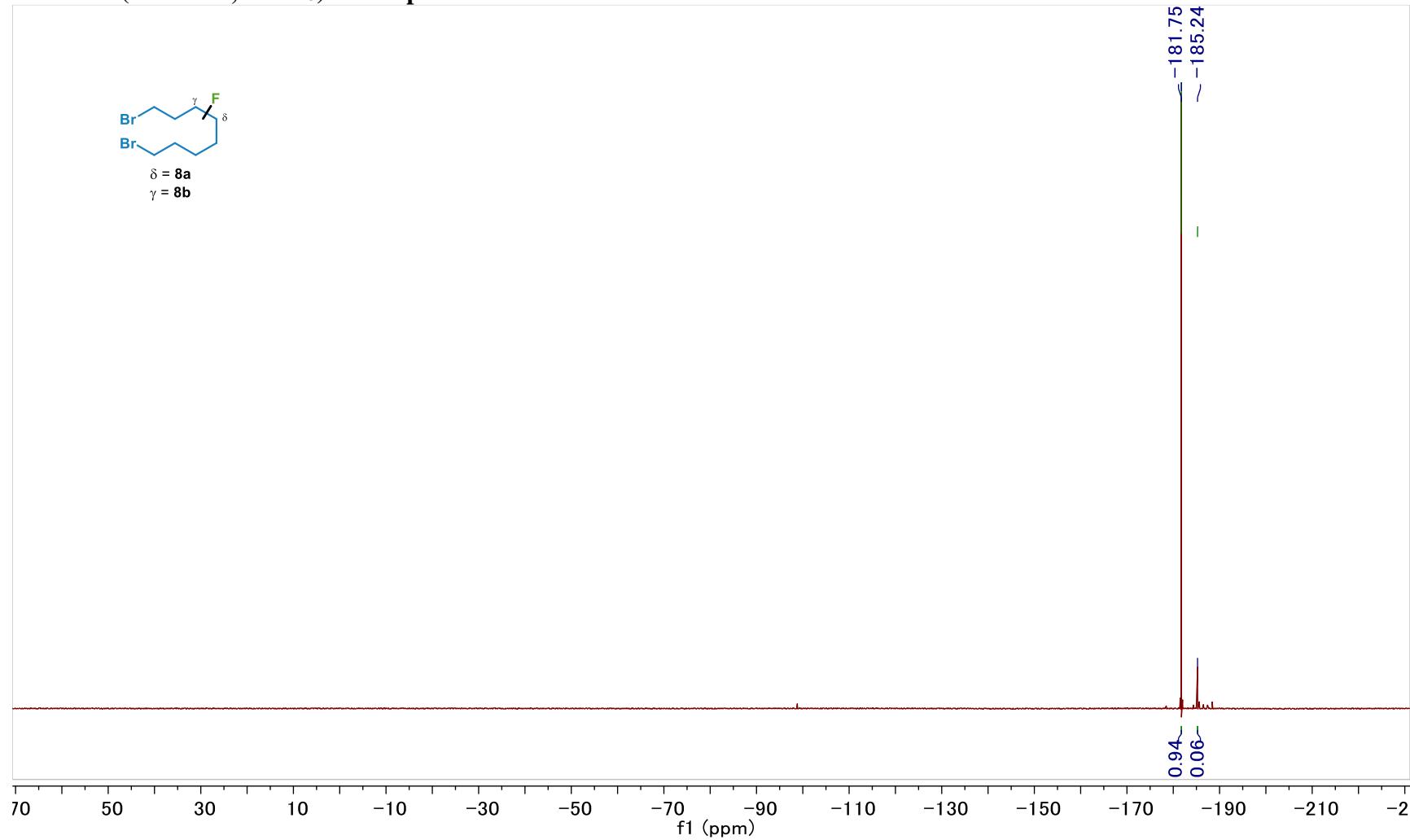
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 8



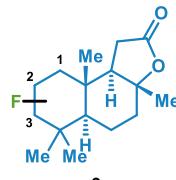
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 8



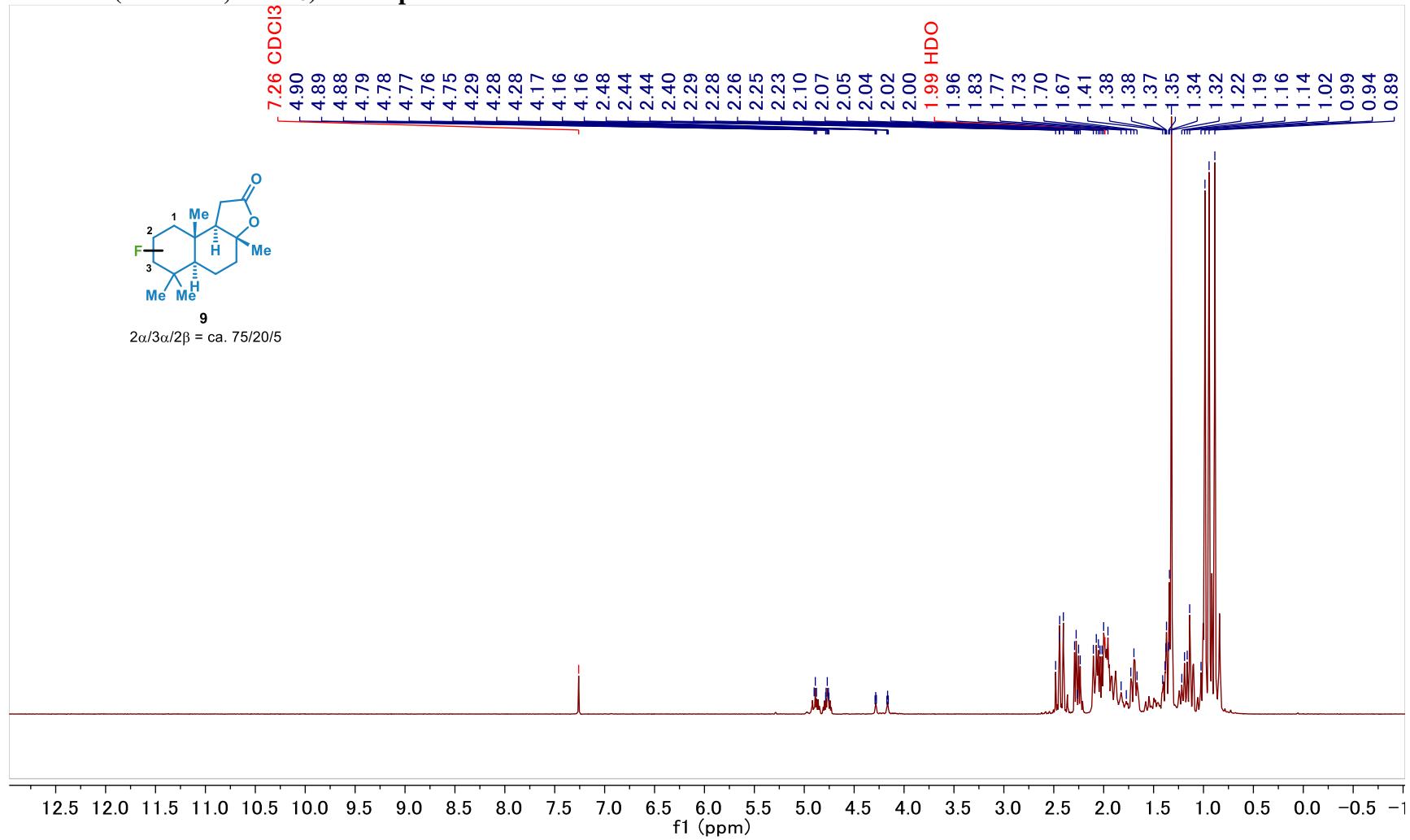
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 8



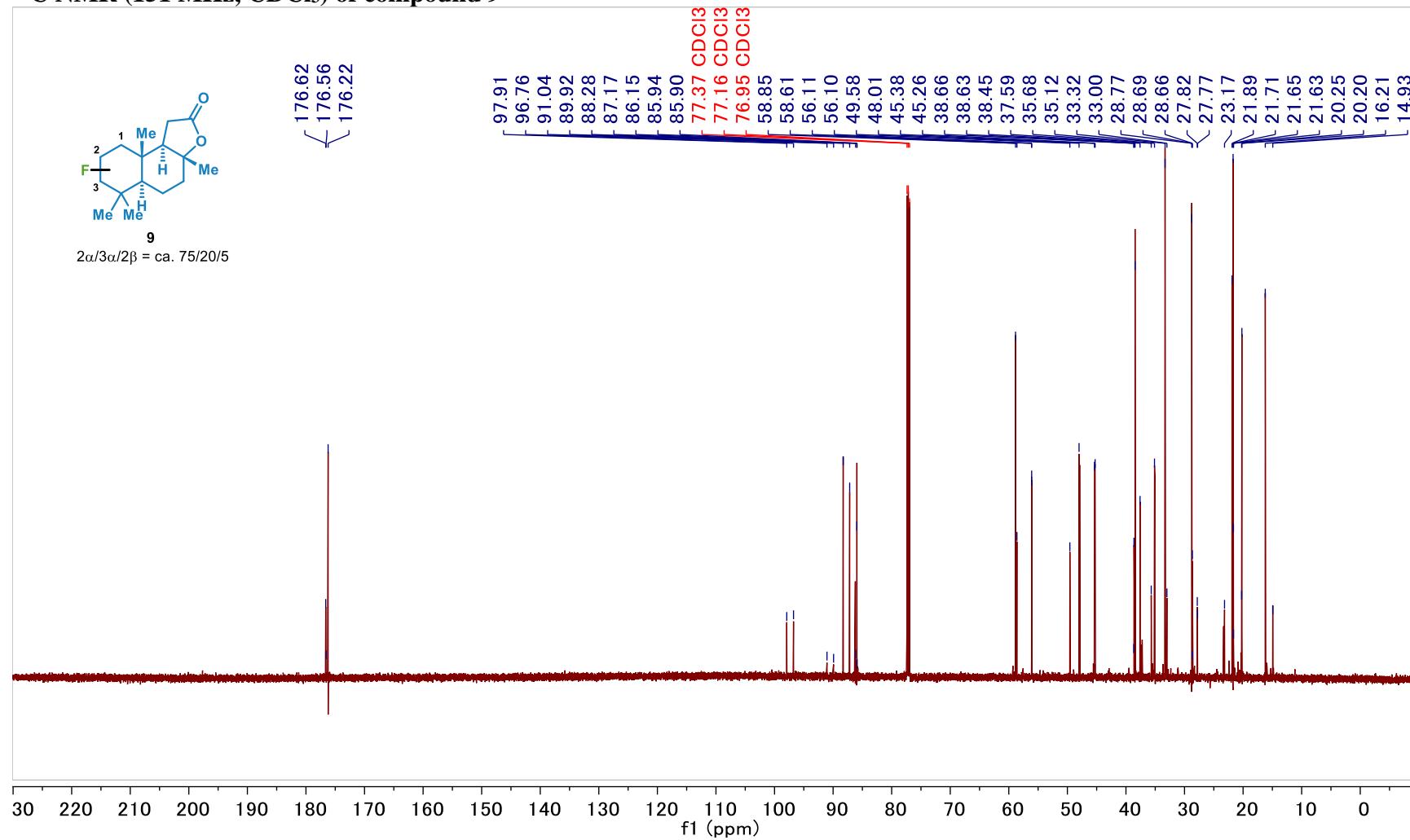
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 9**



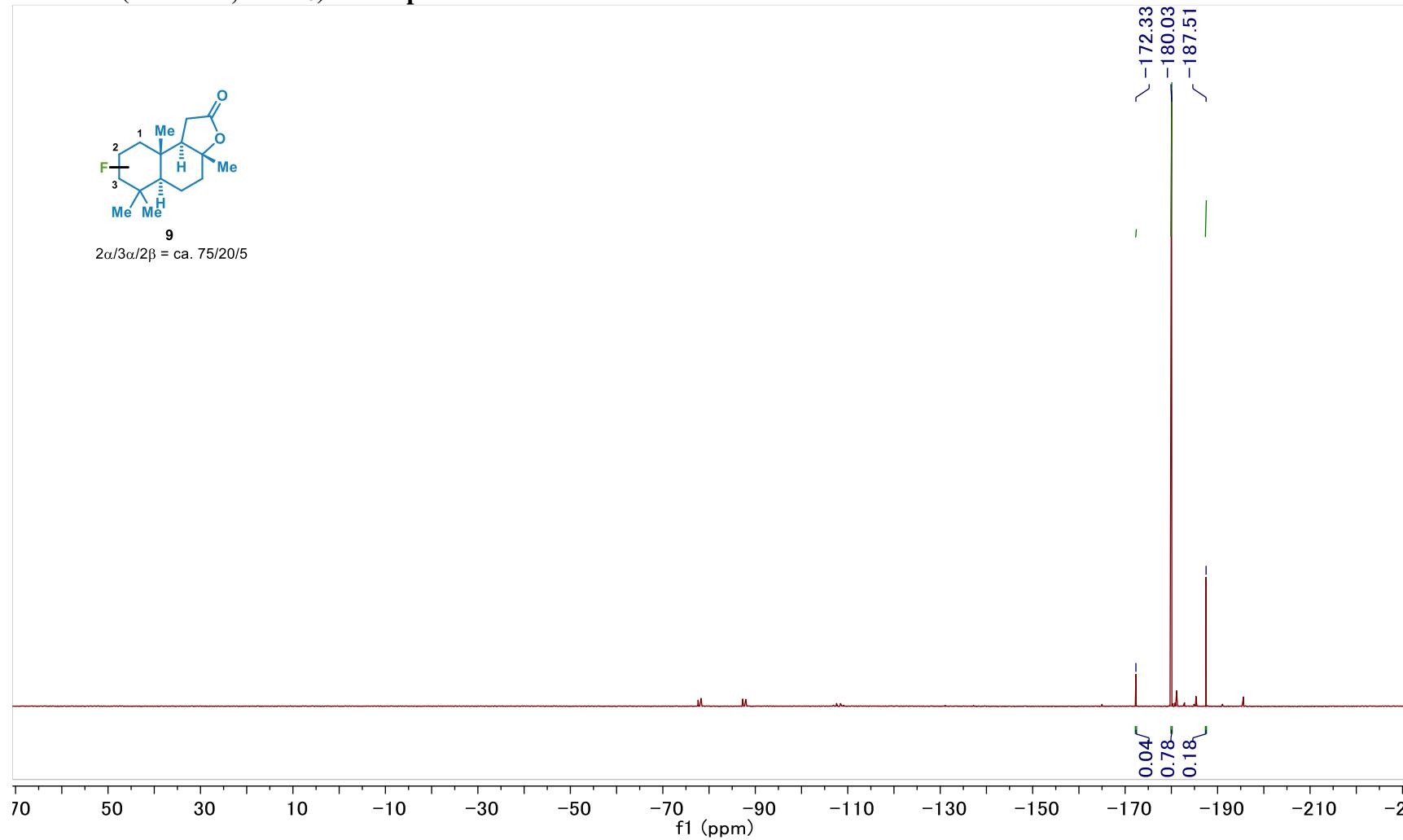
$$2\alpha/3\alpha/2\beta = \text{ca. } 75/20/5$$



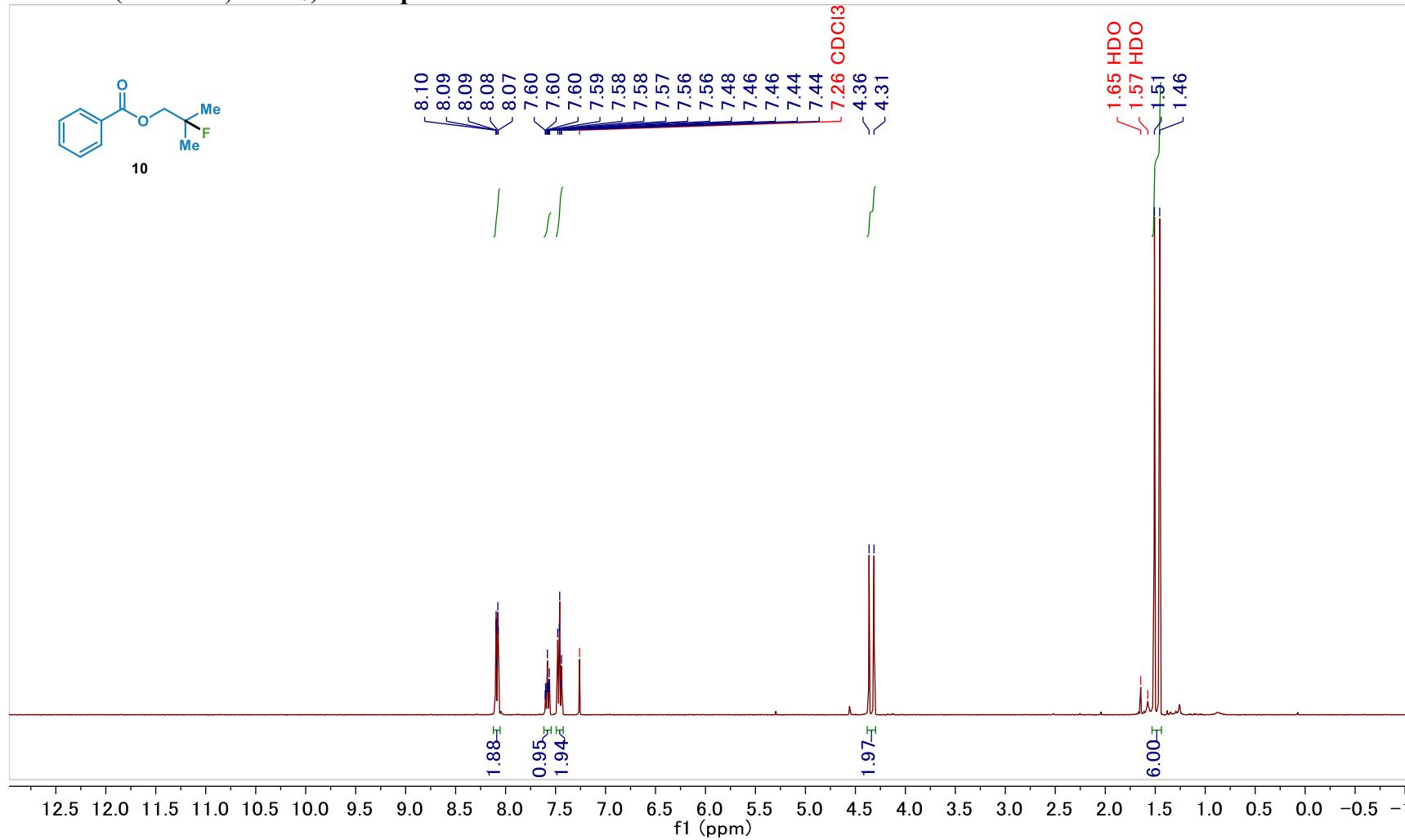
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 9



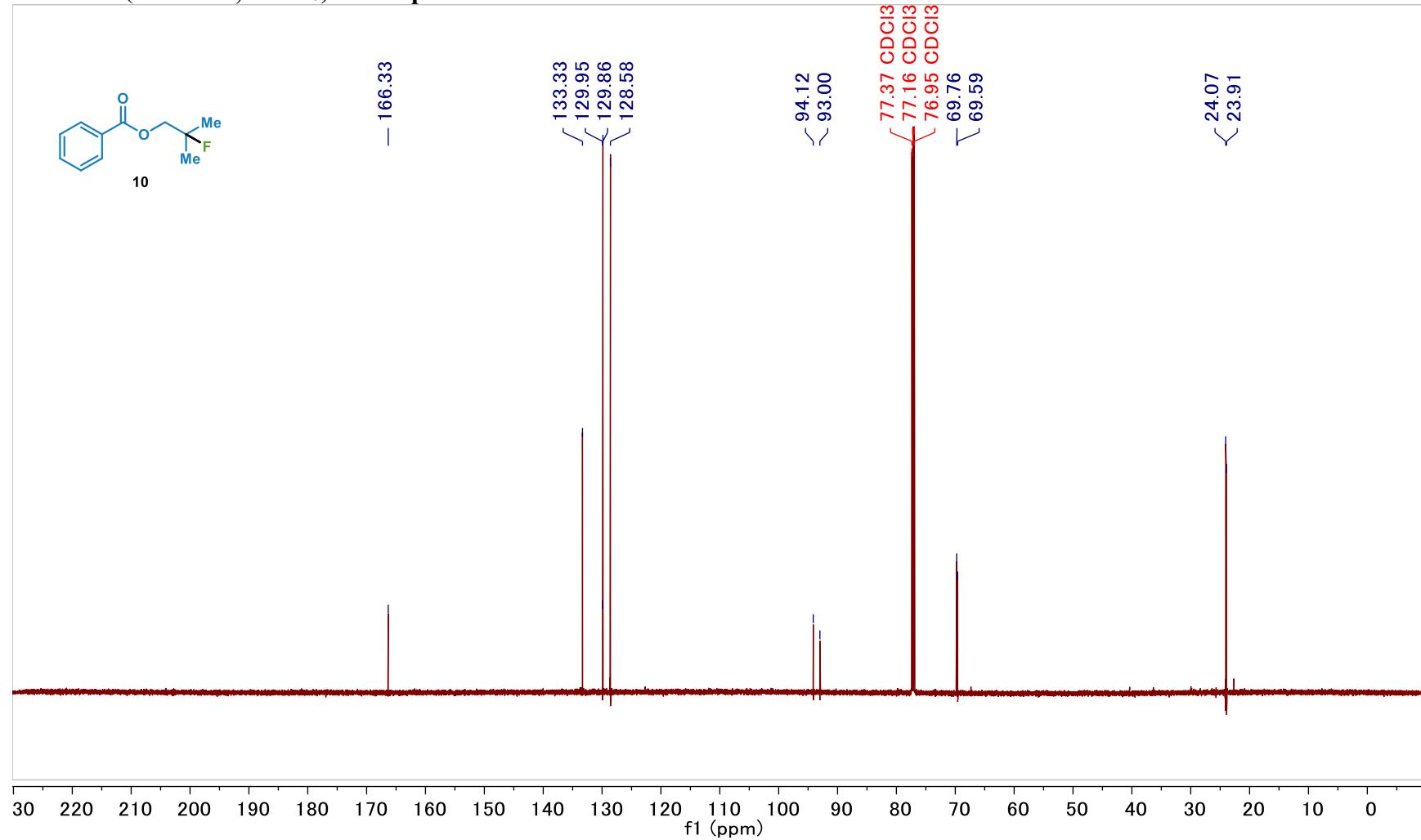
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 9



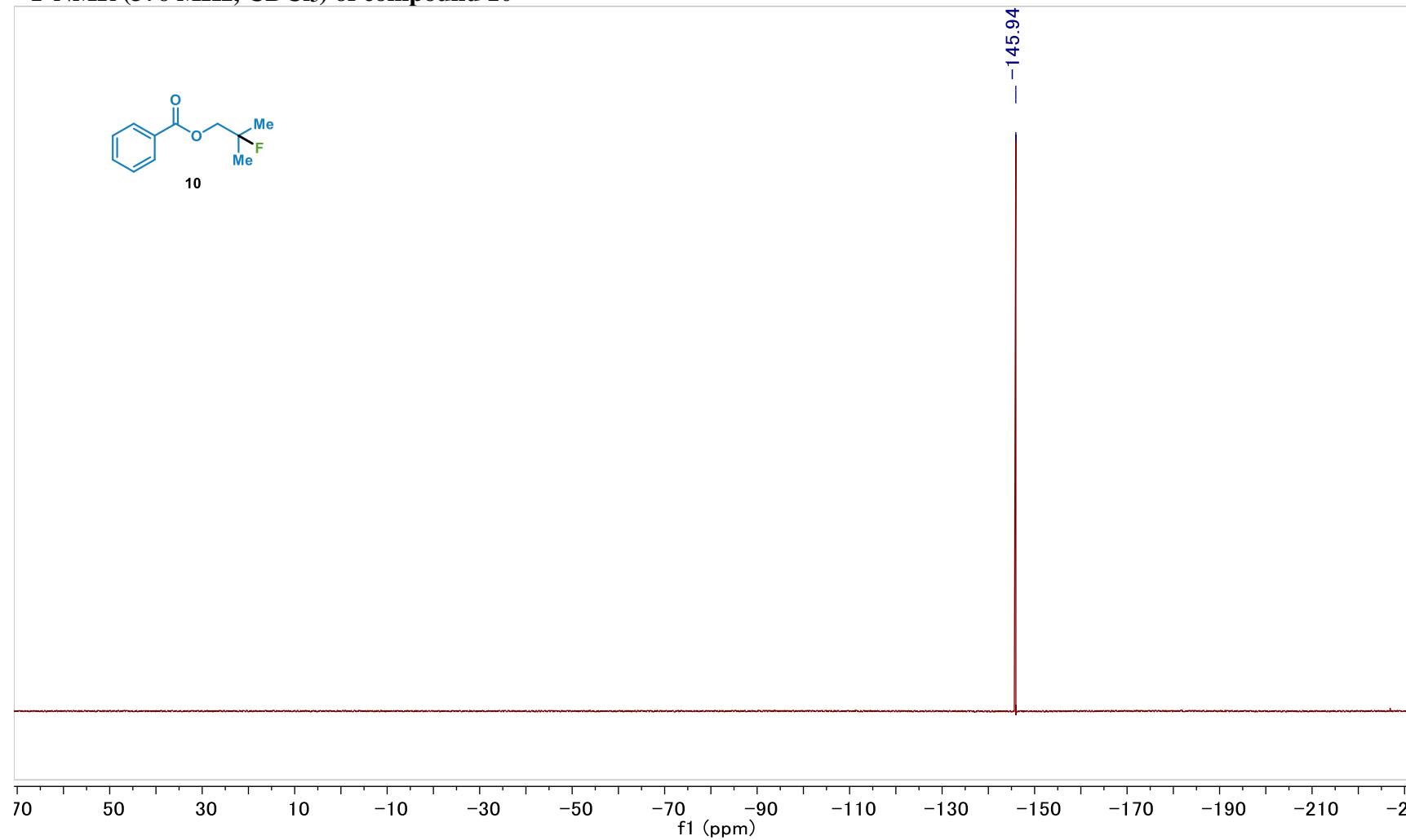
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 10



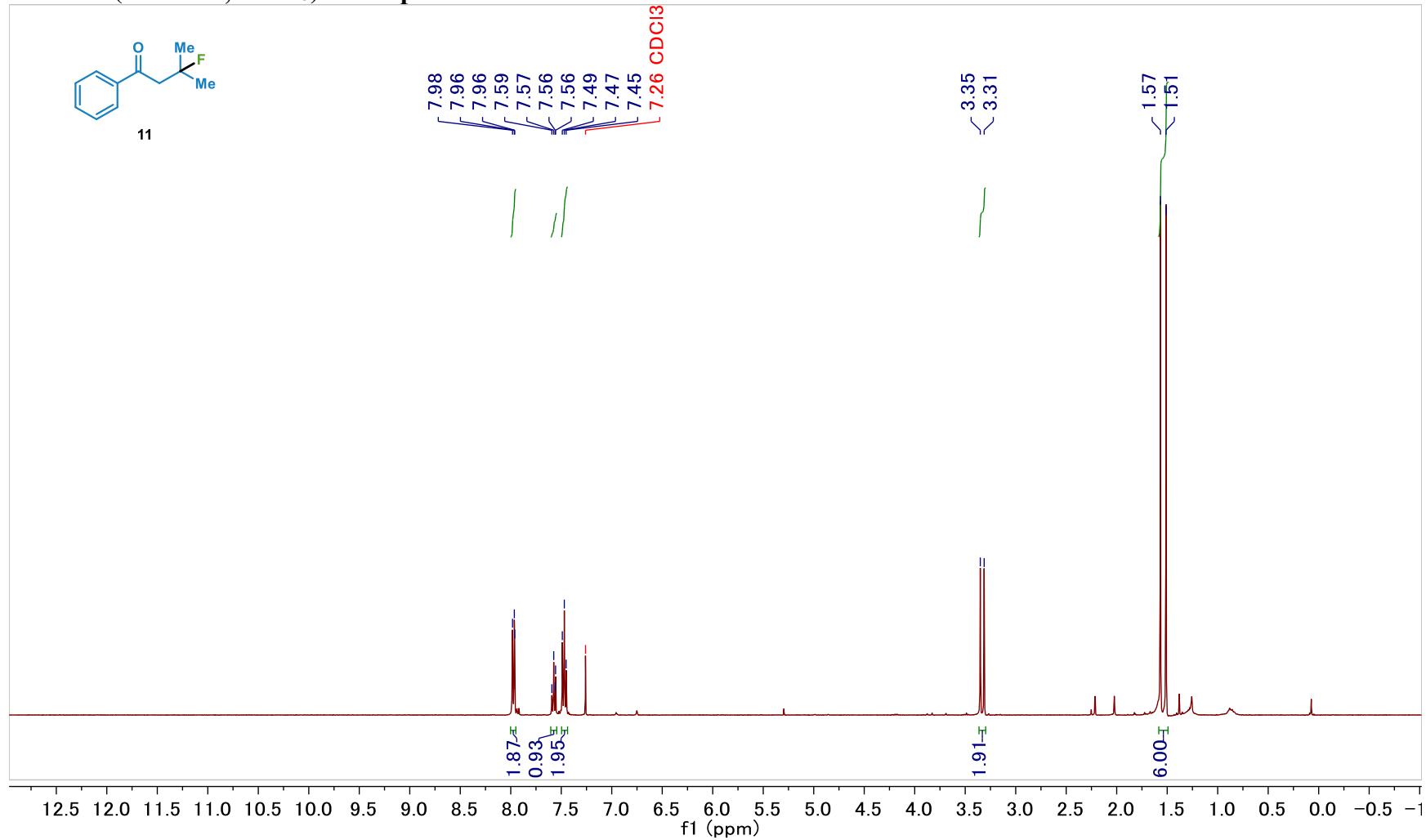
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 10



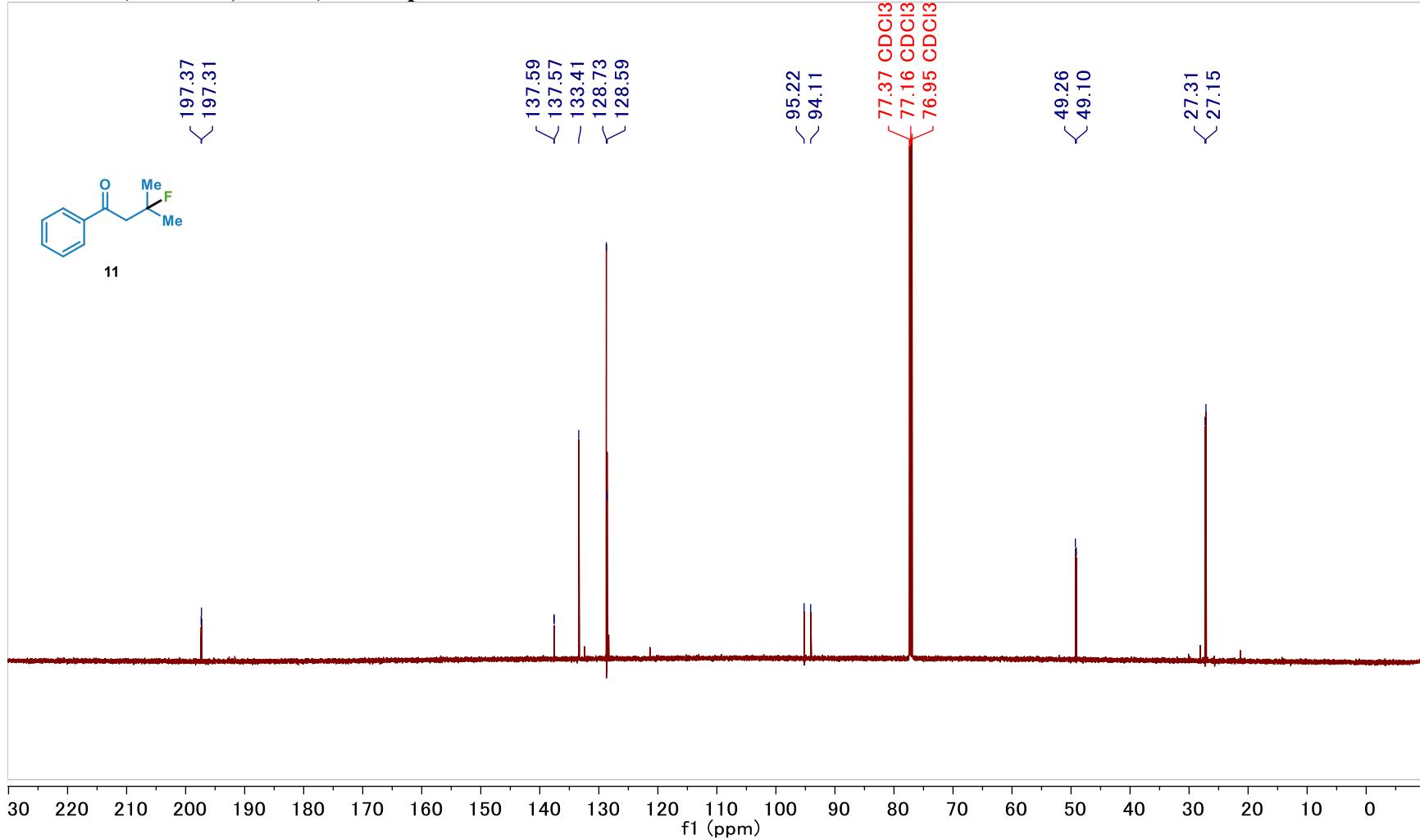
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 10



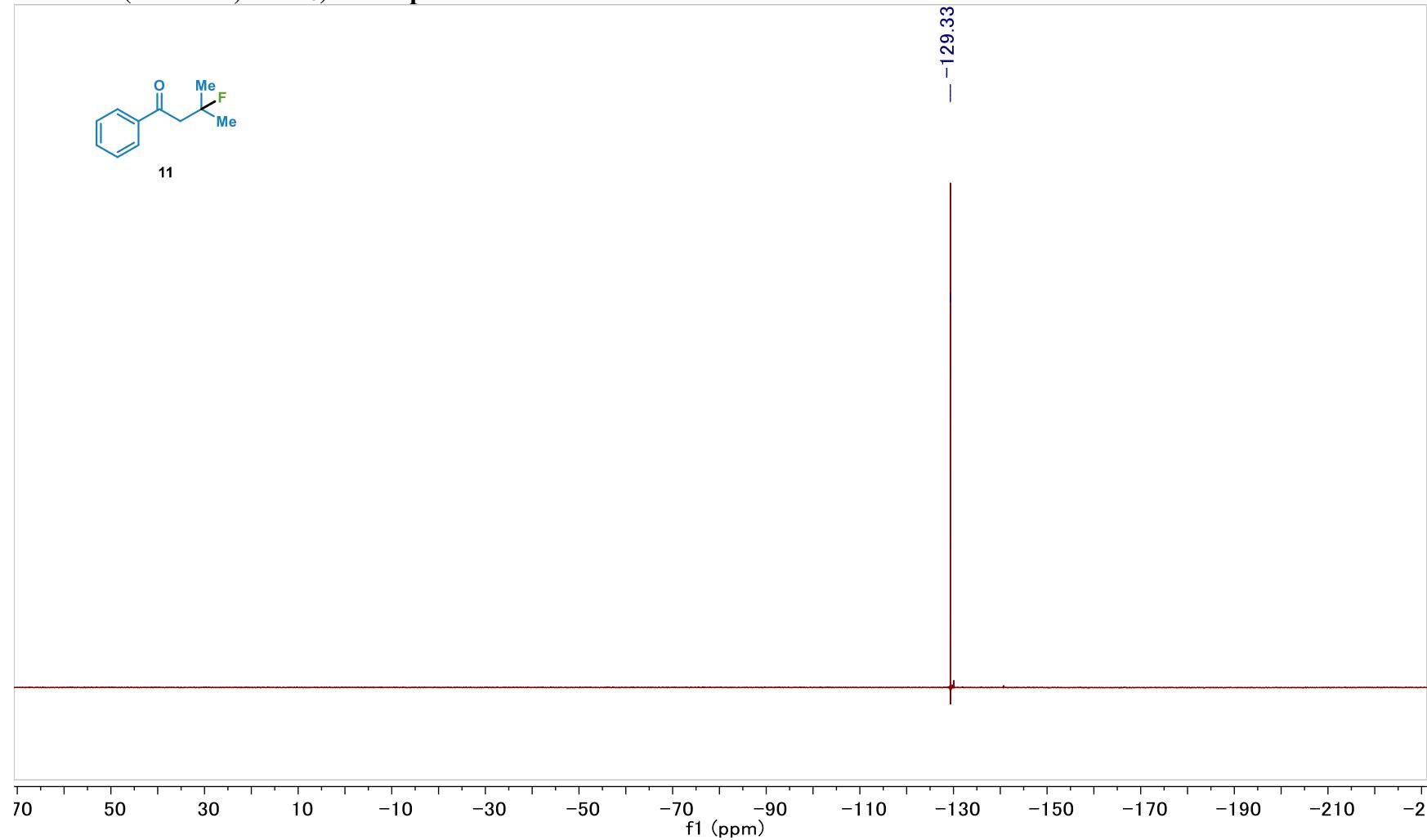
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 11



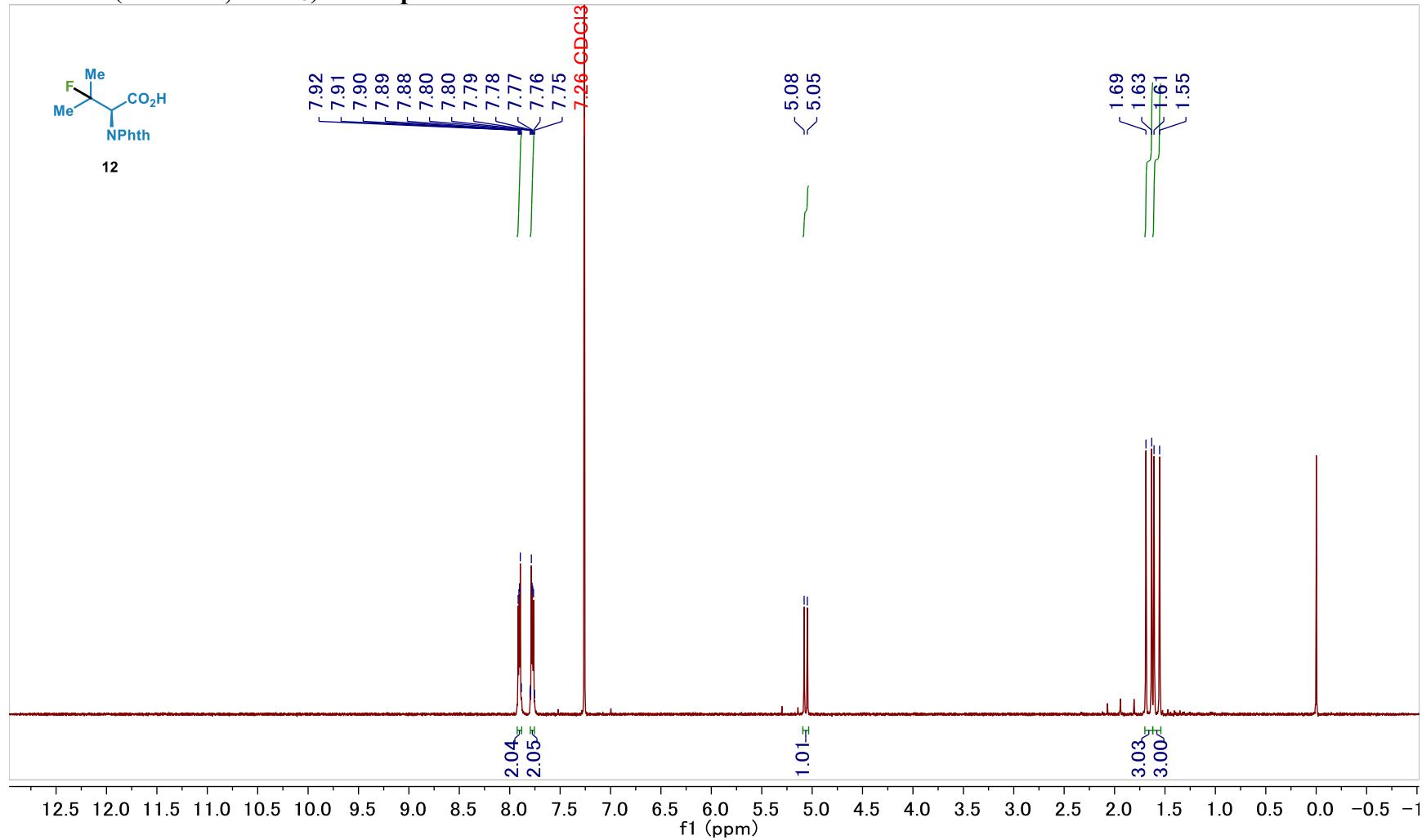
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 11



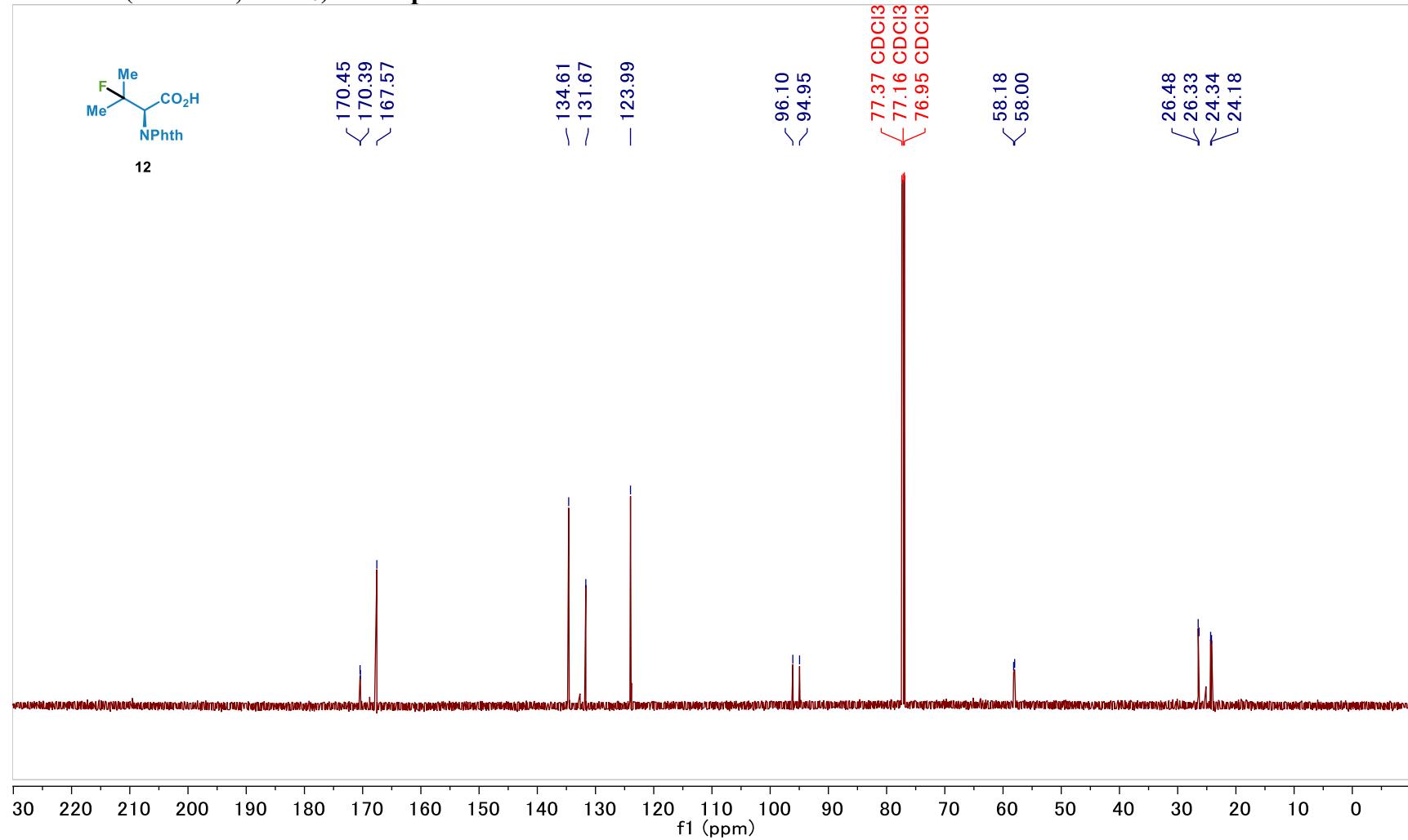
**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 11**



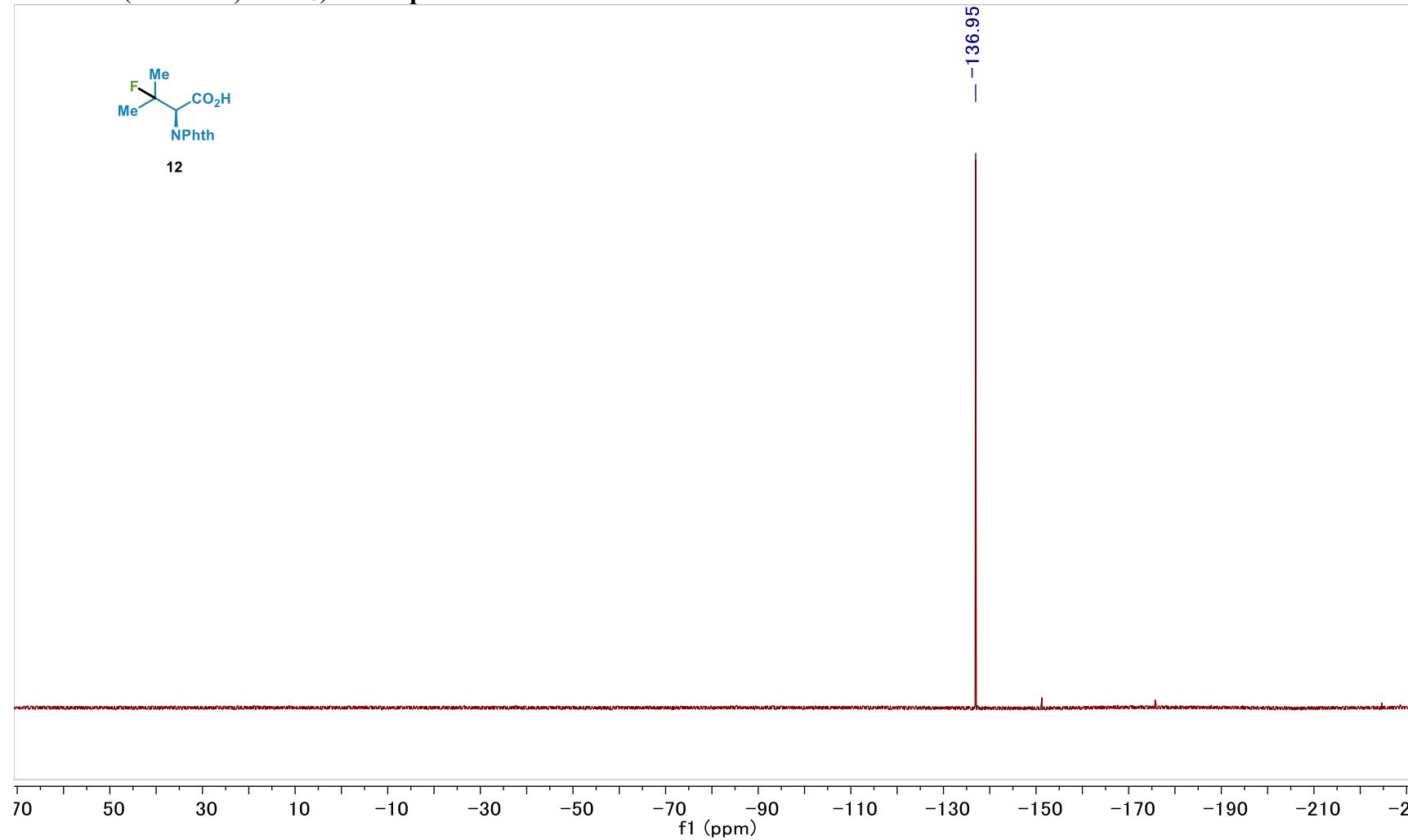
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 12



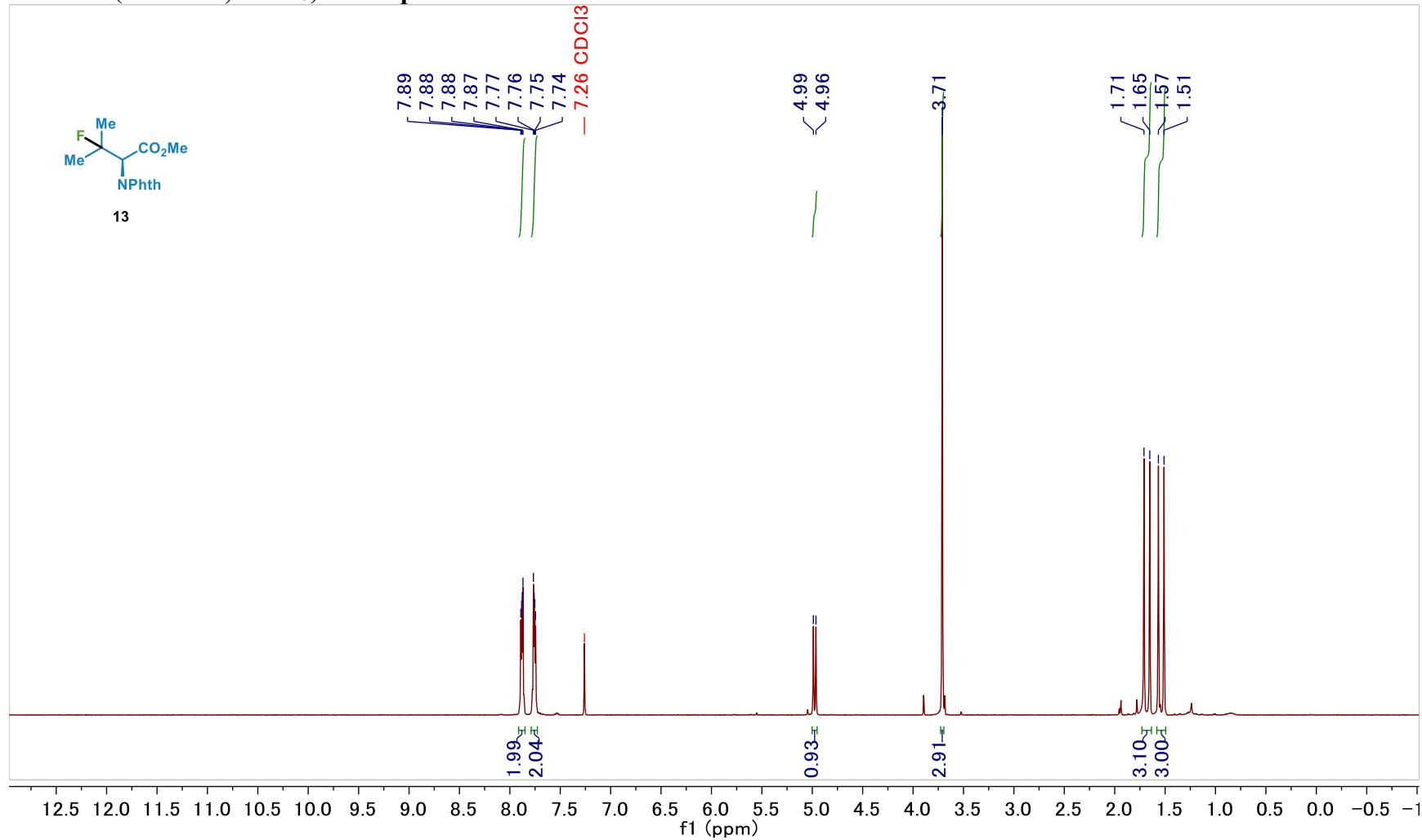
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 12



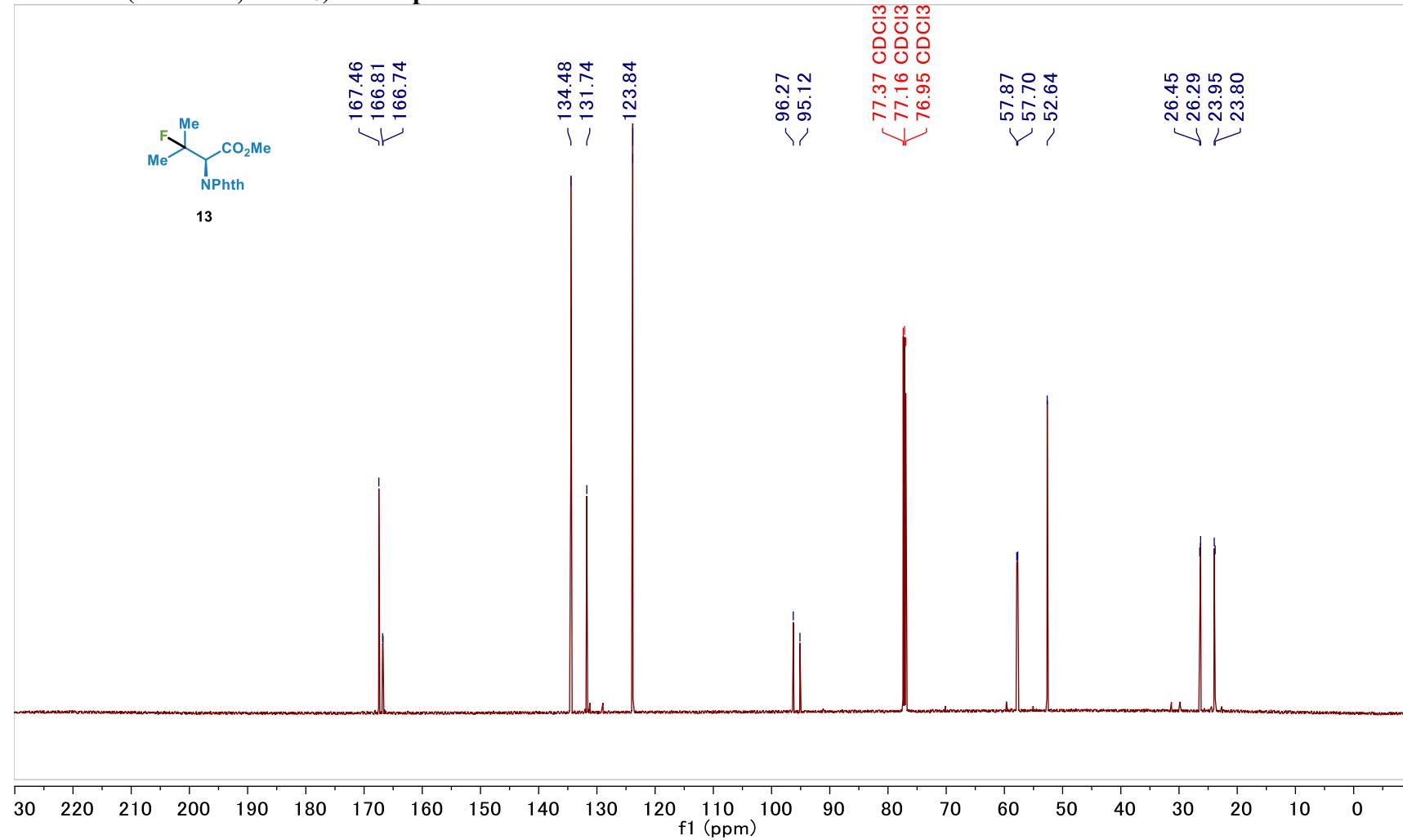
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 12



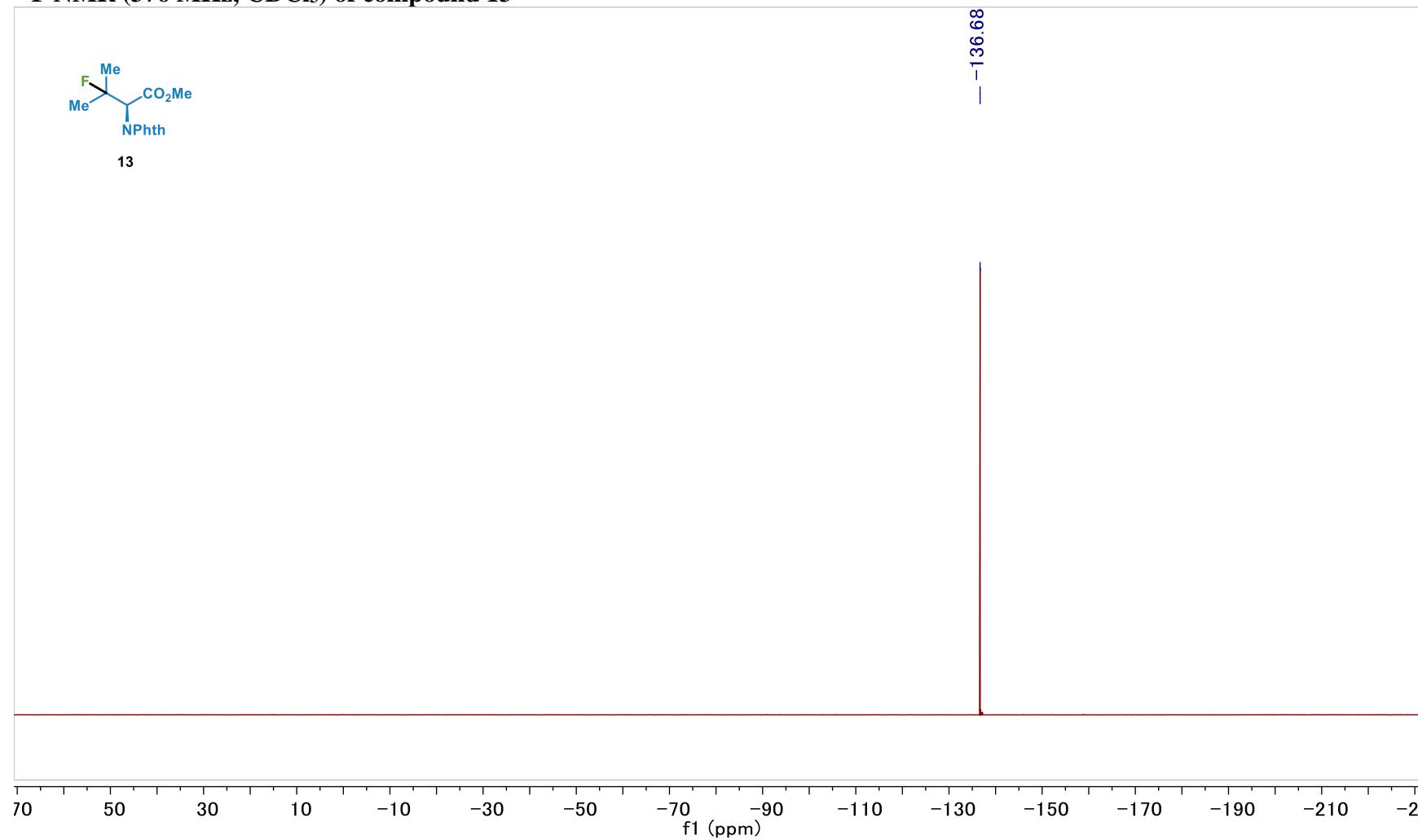
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 13



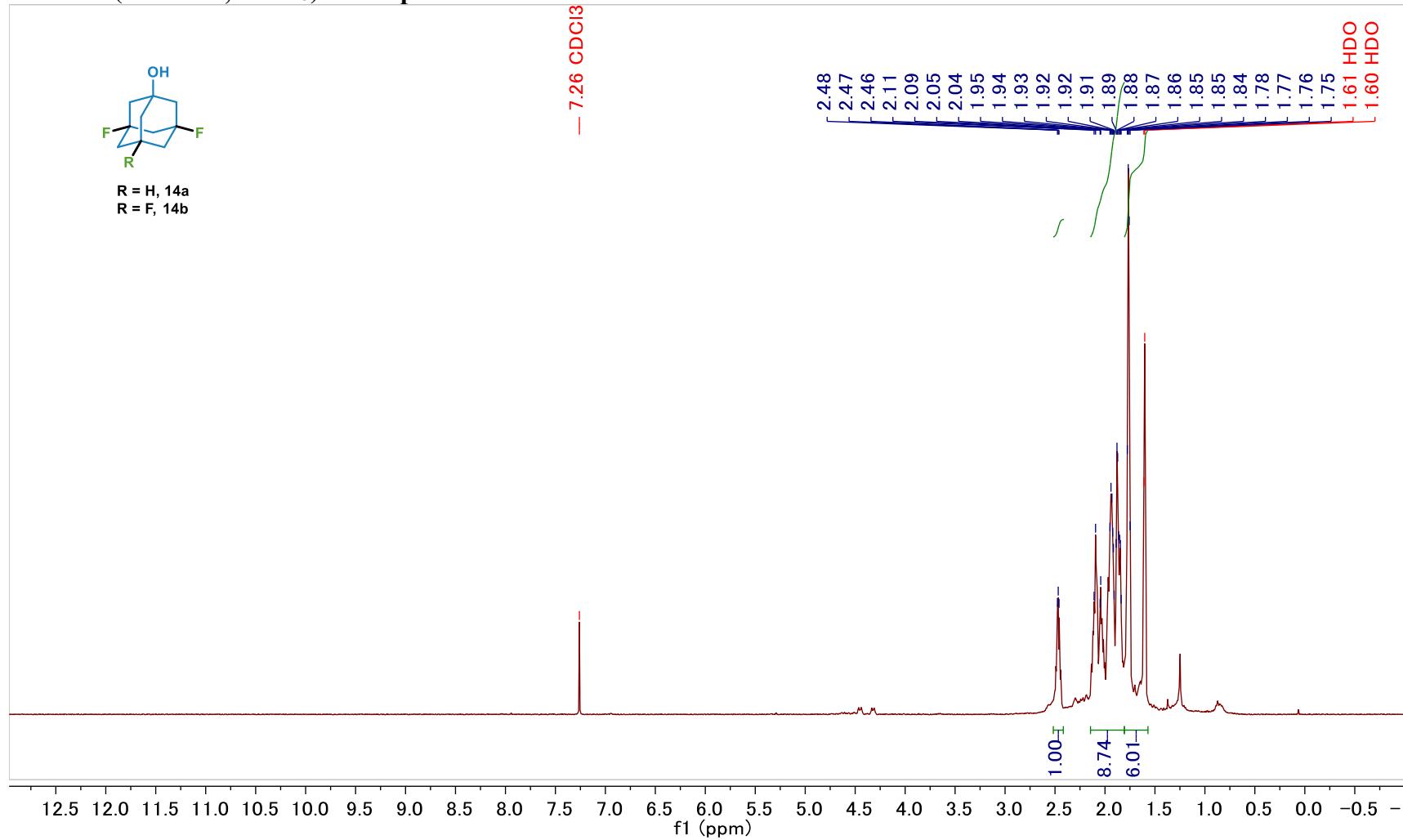
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 13



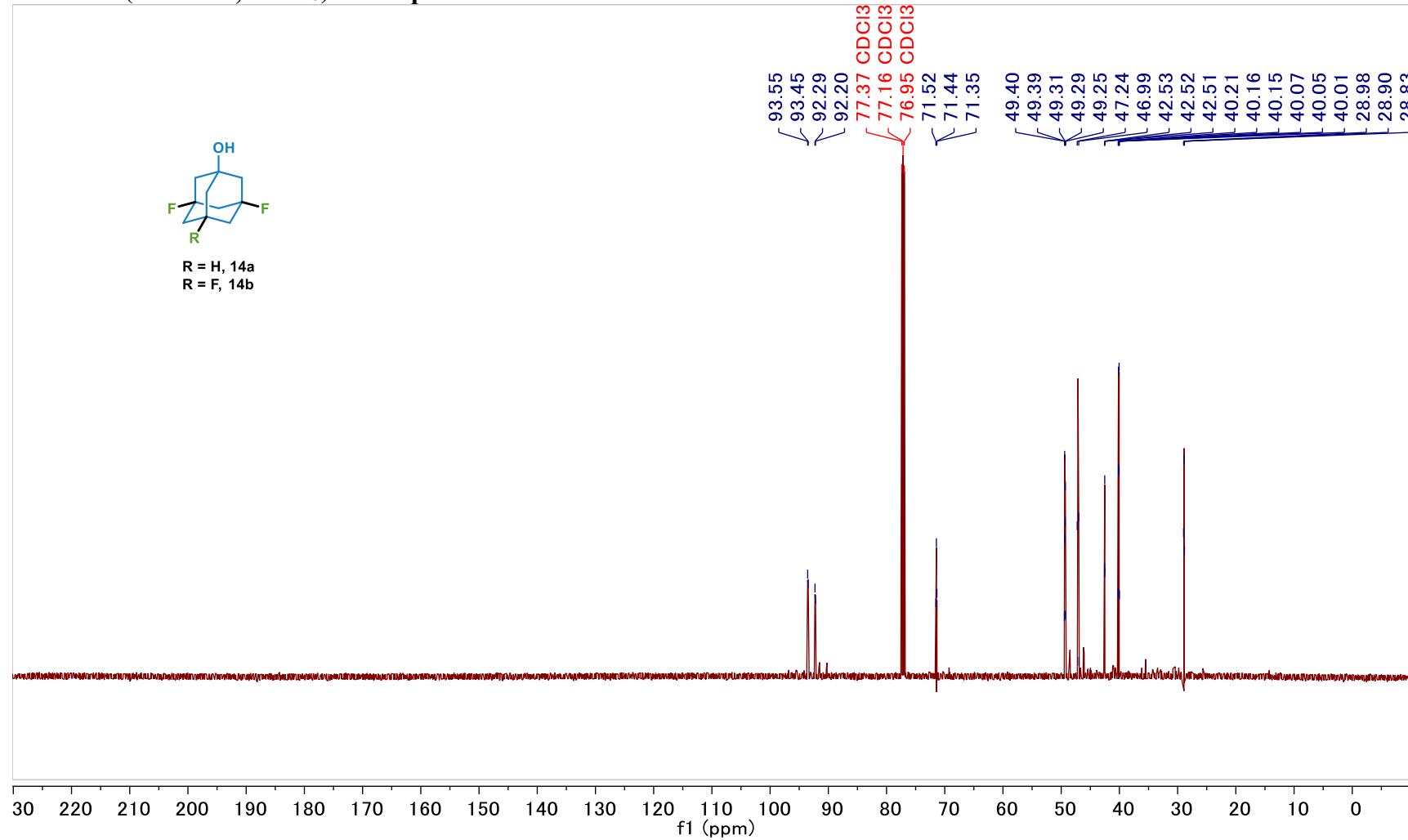
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 13



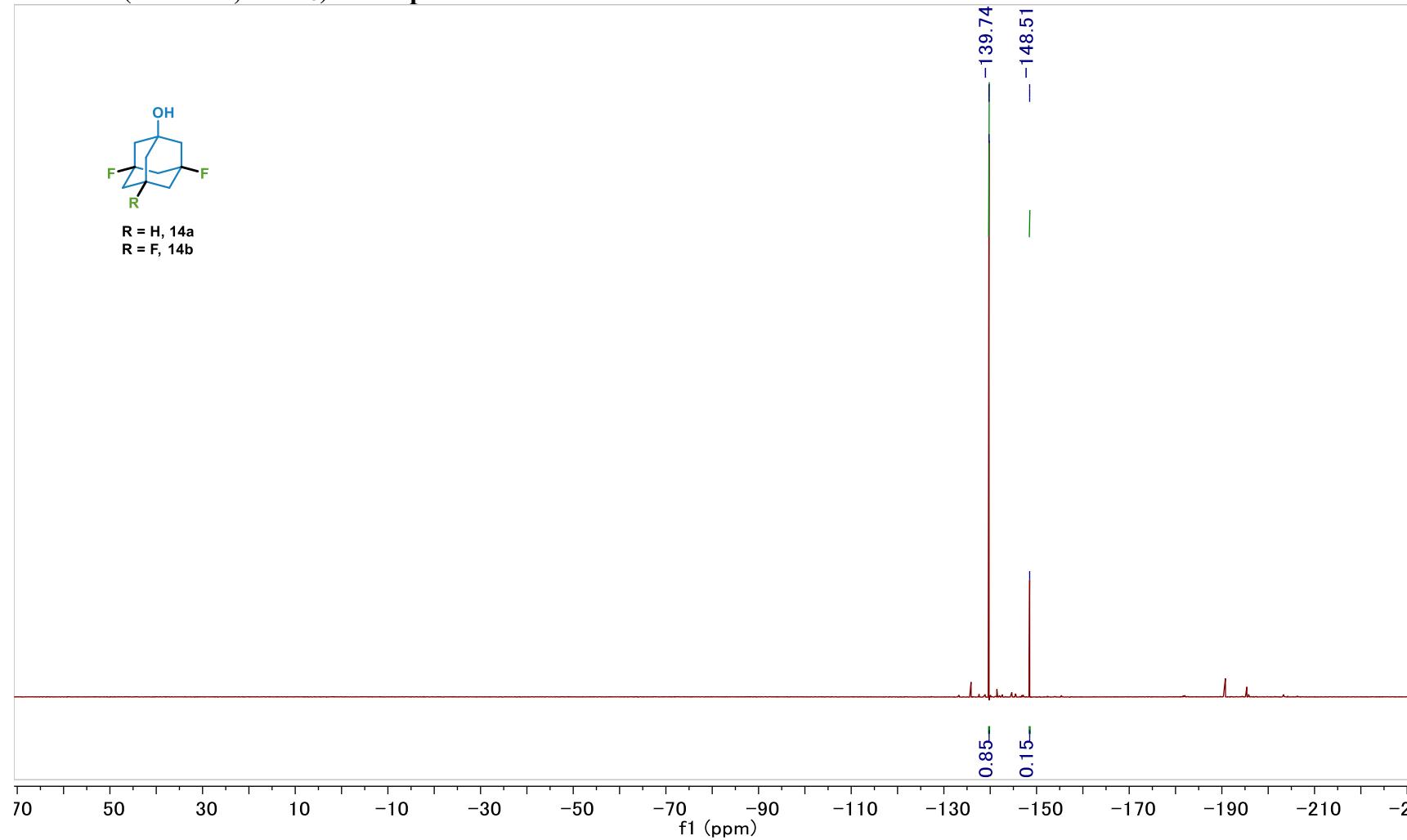
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 14



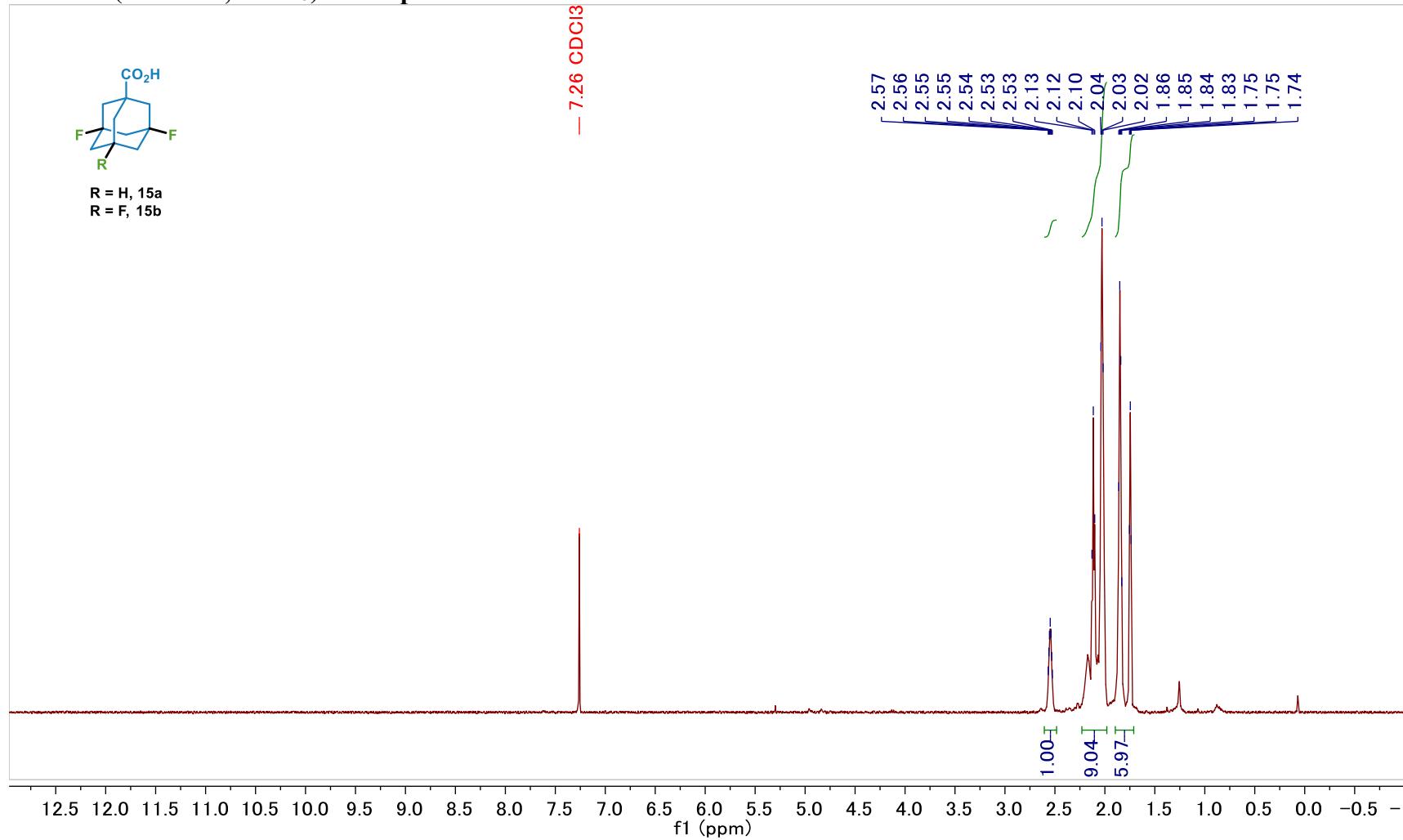
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 14



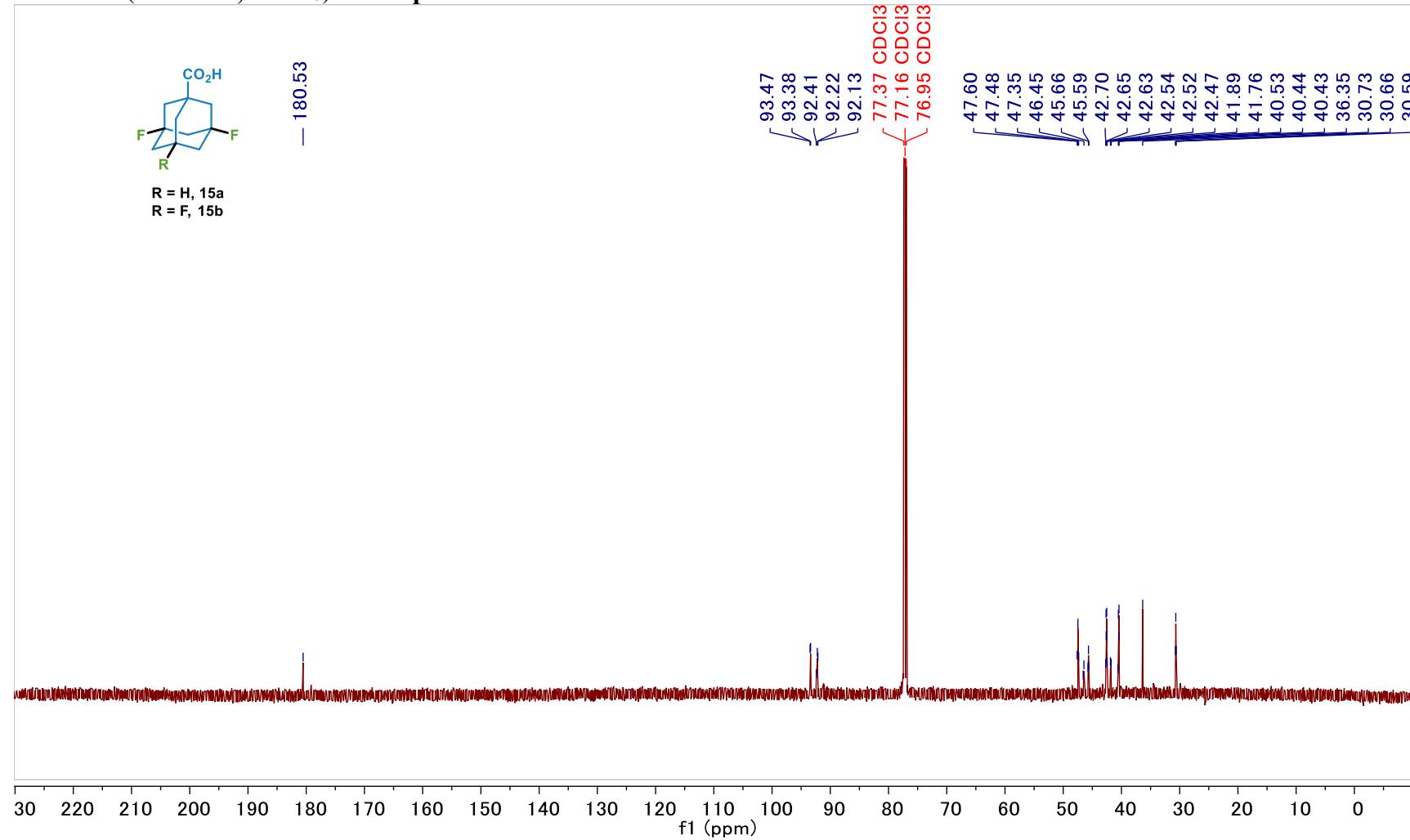
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 14



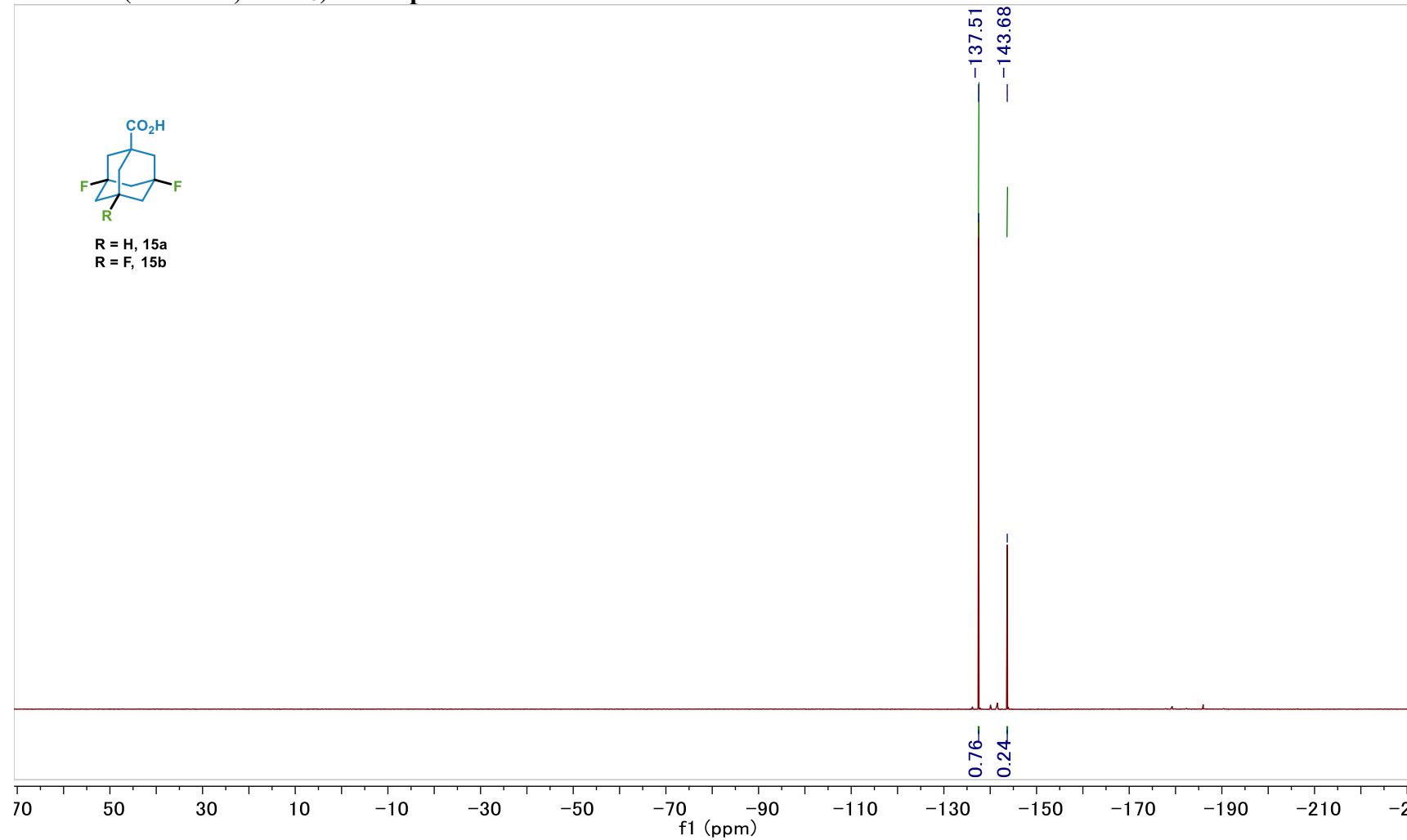
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 15



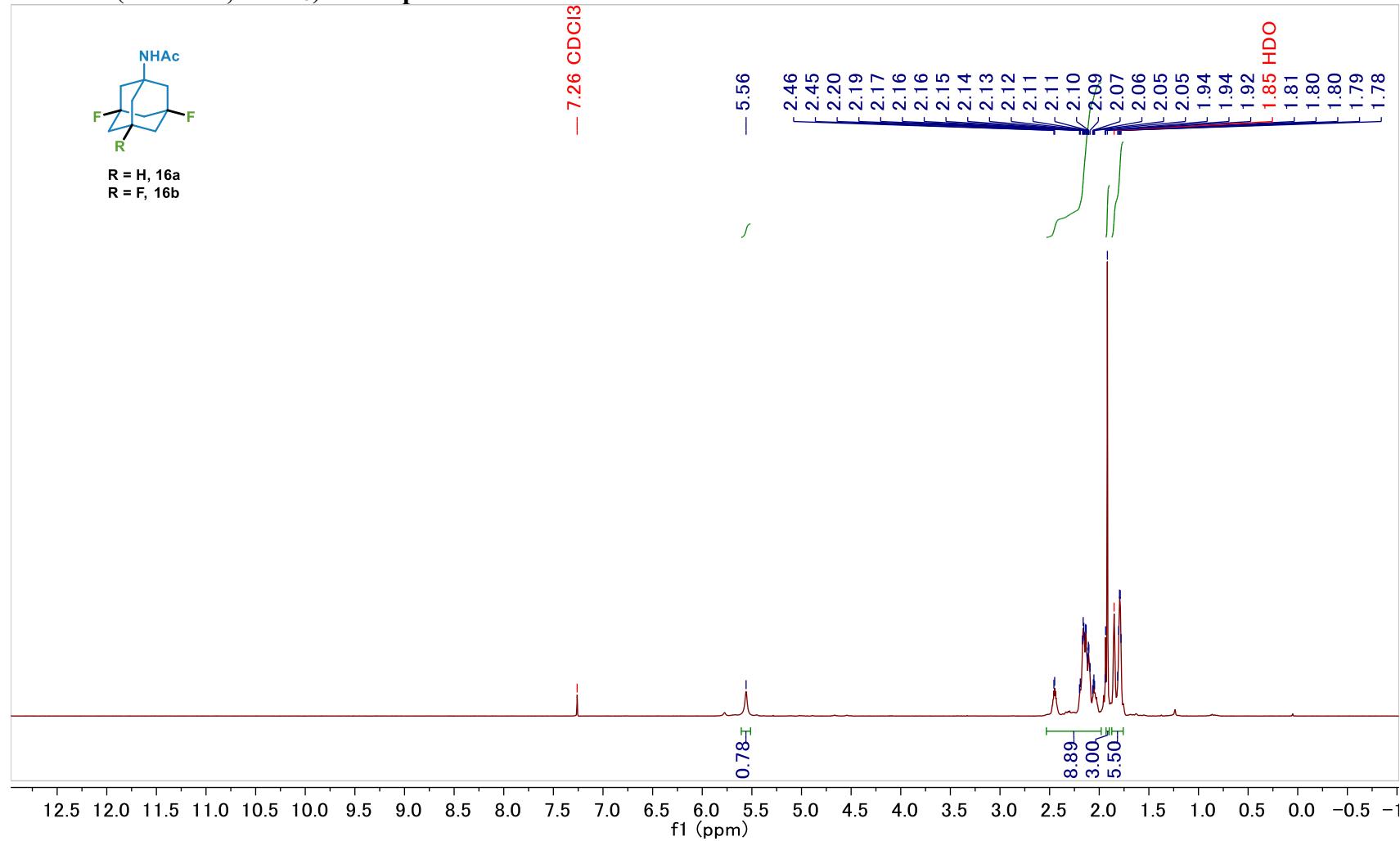
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 15



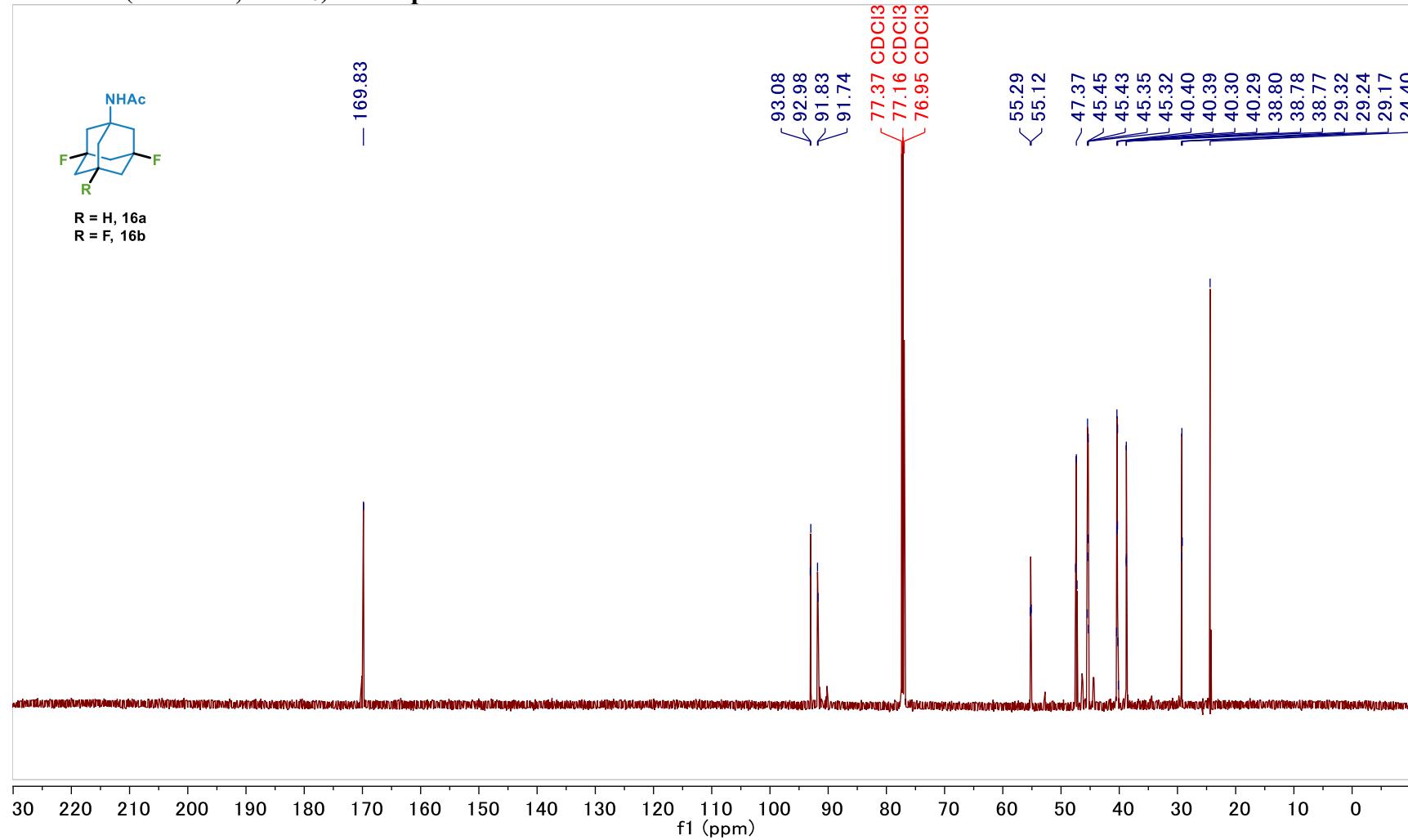
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 15



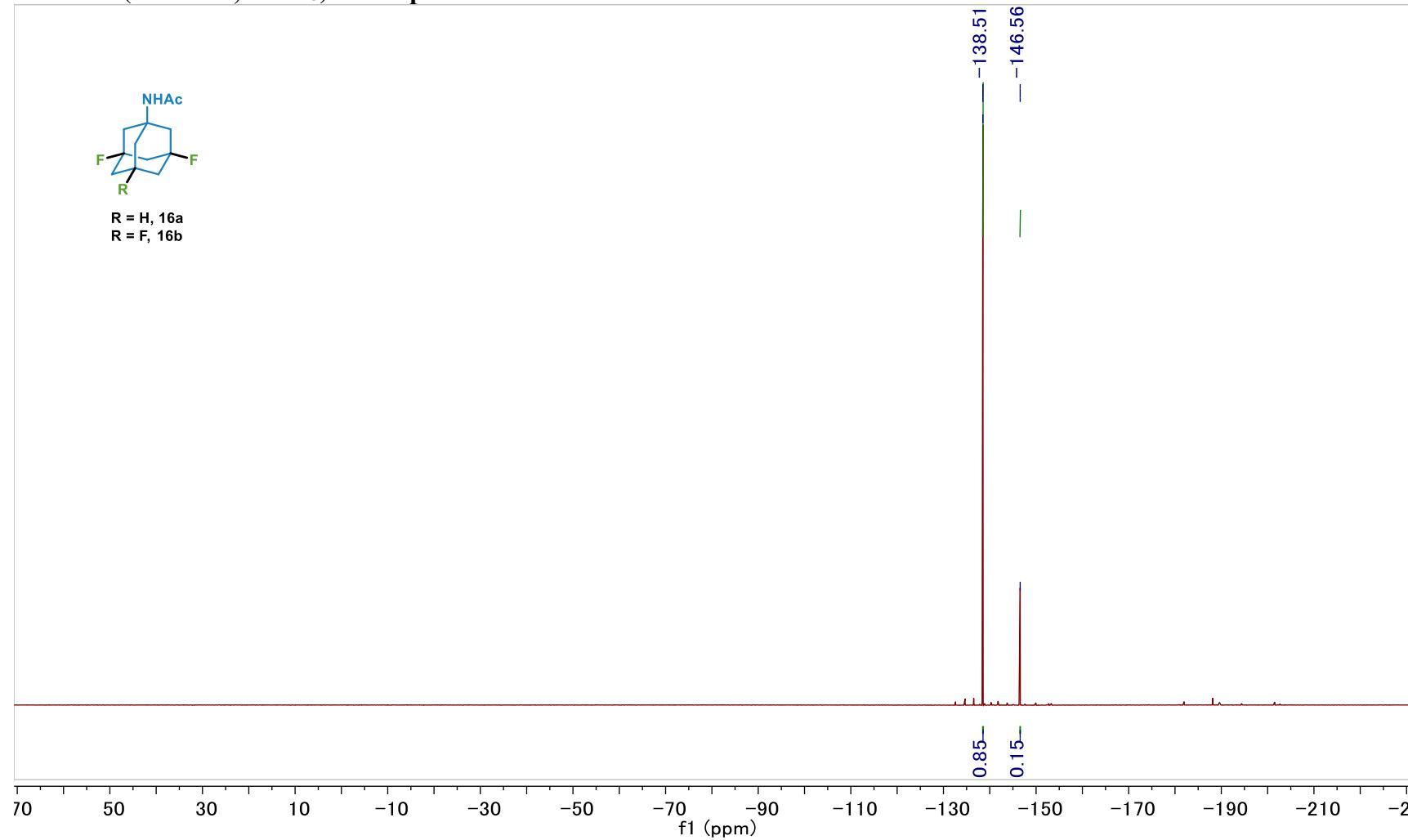
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 16



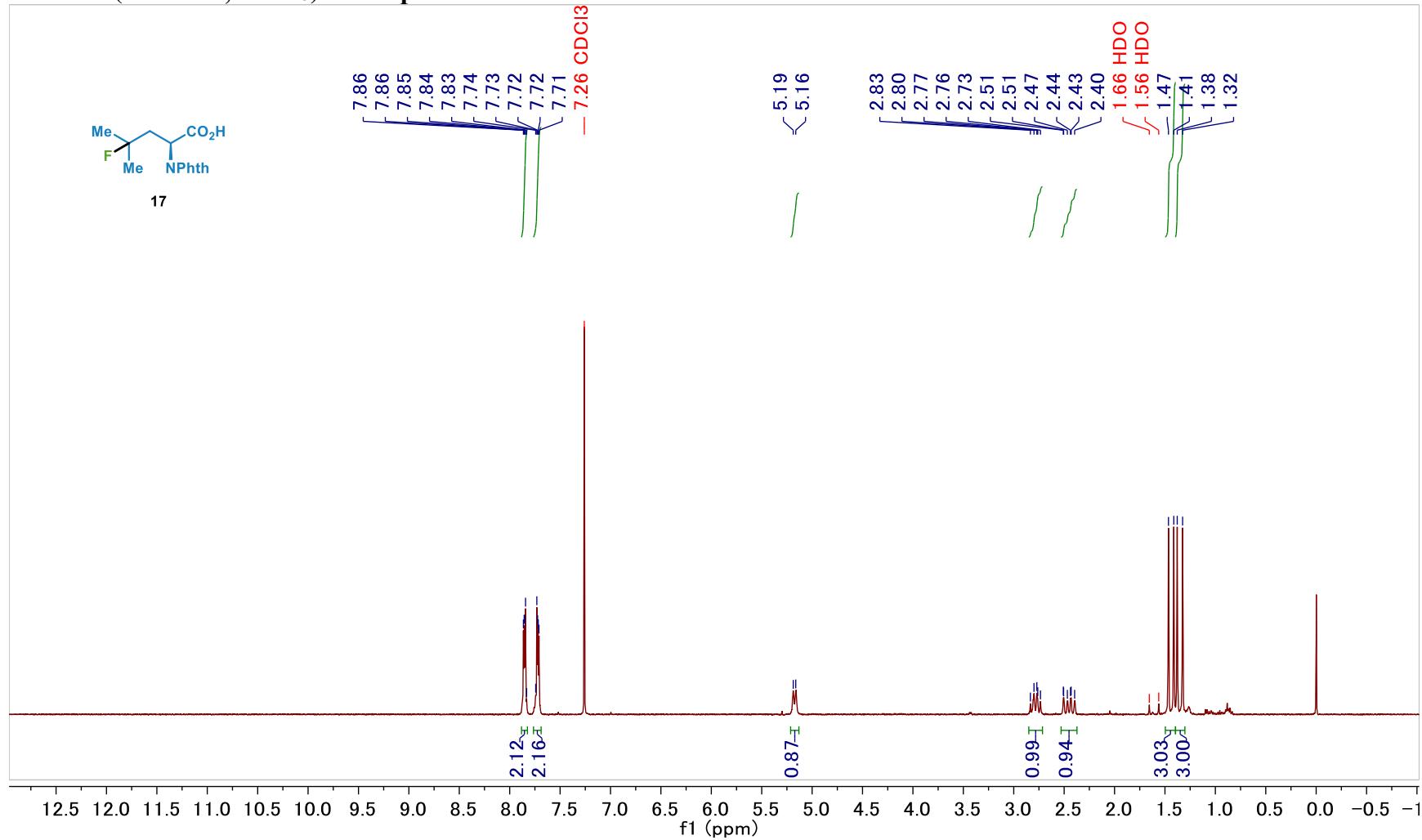
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 16



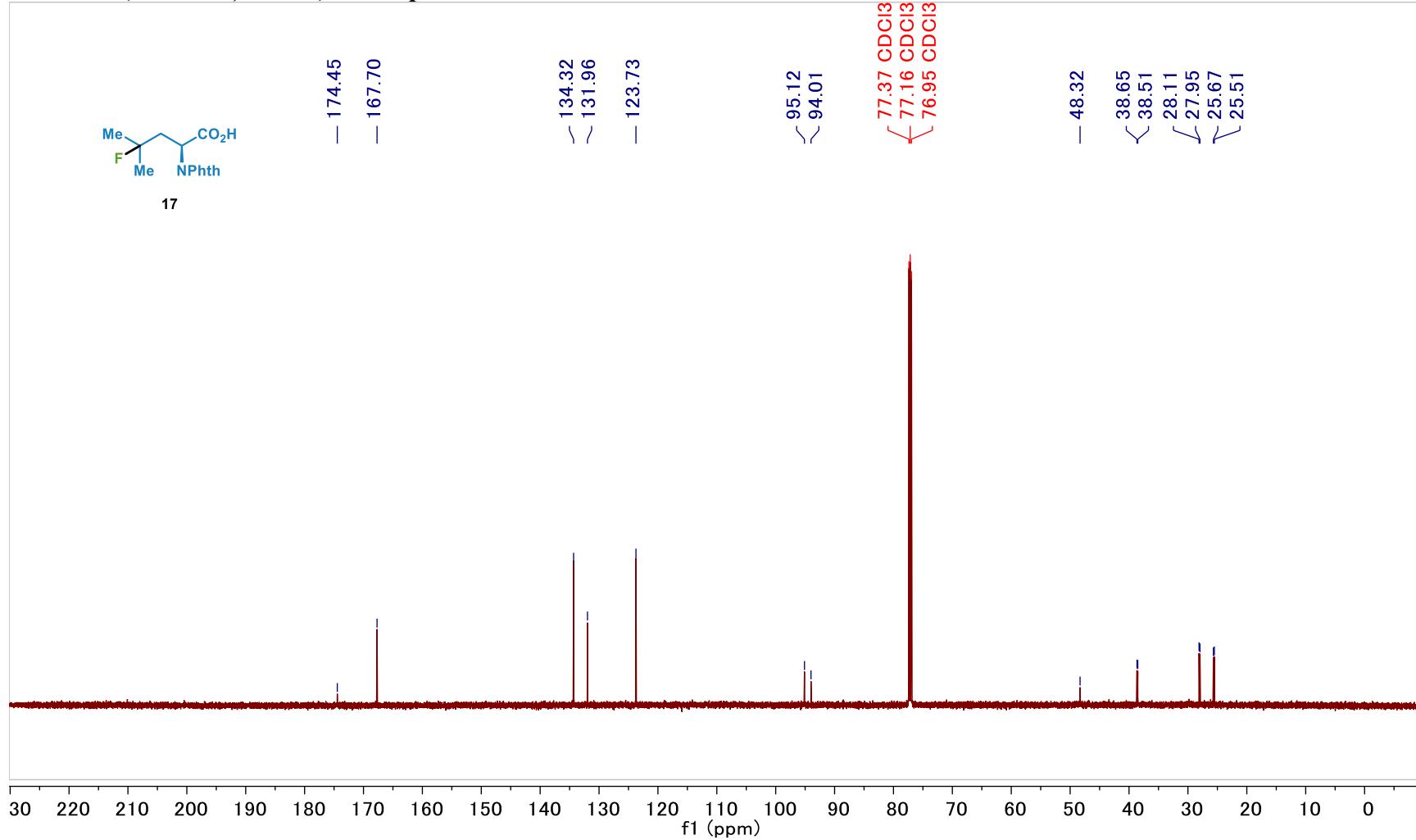
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 16



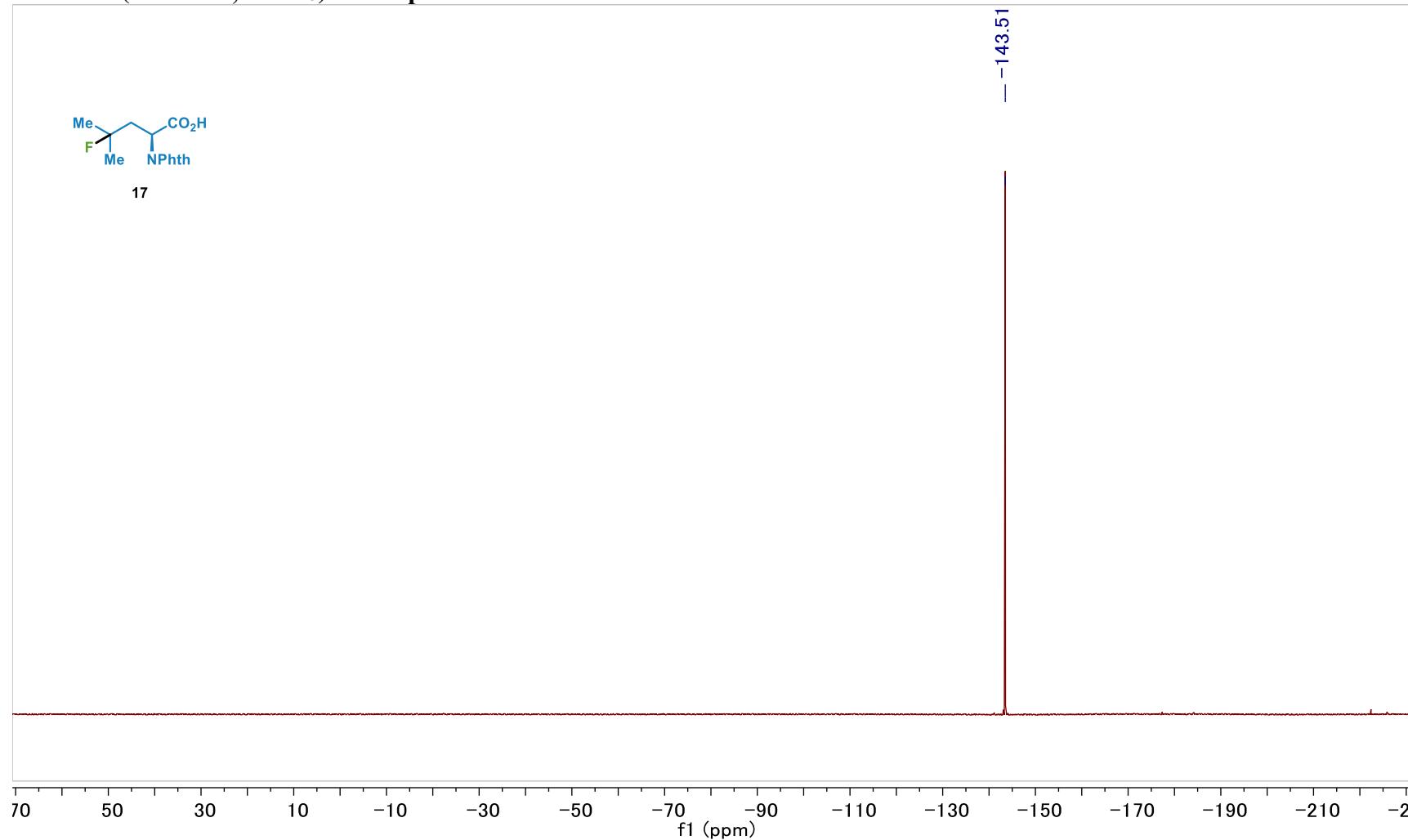
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 17



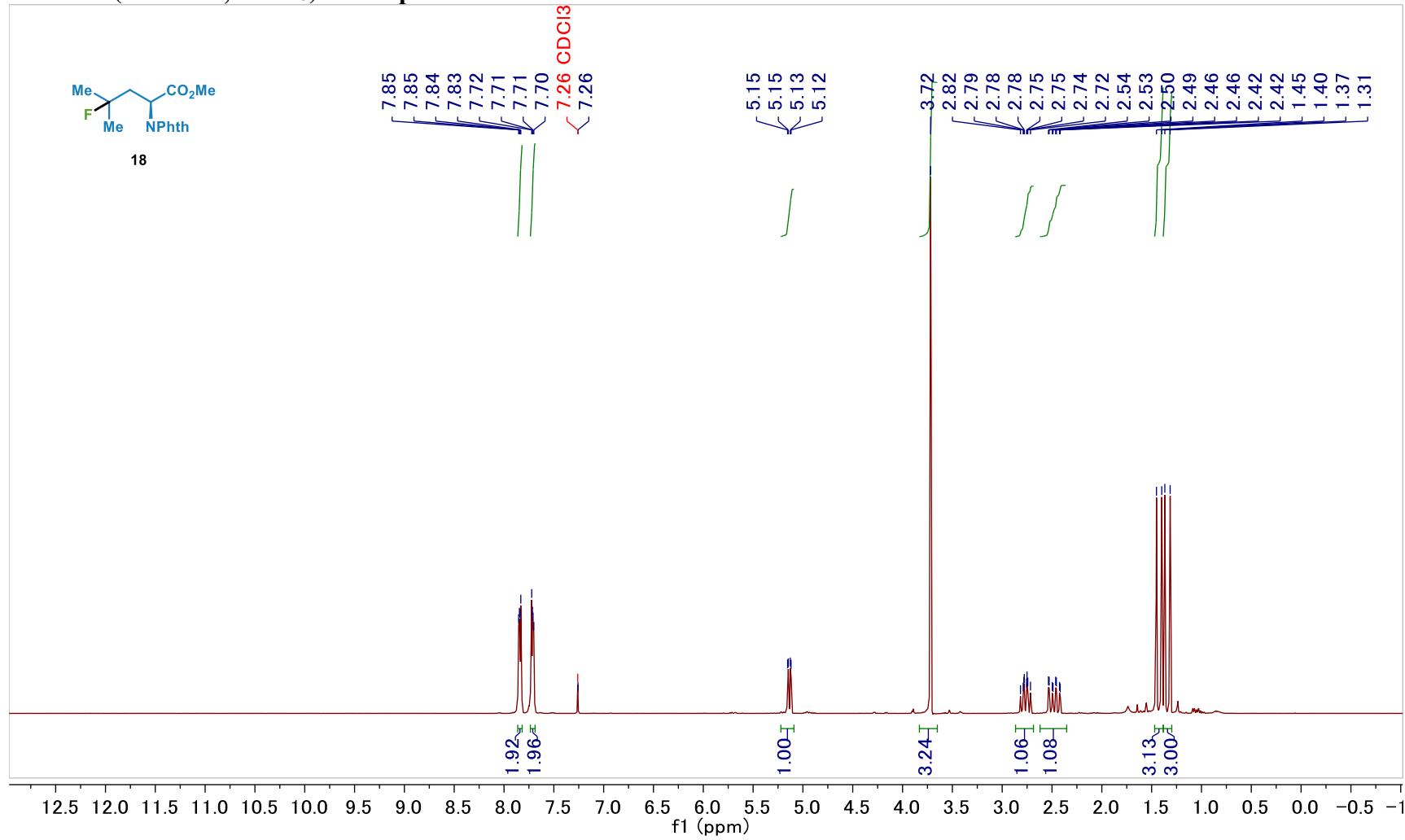
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 17



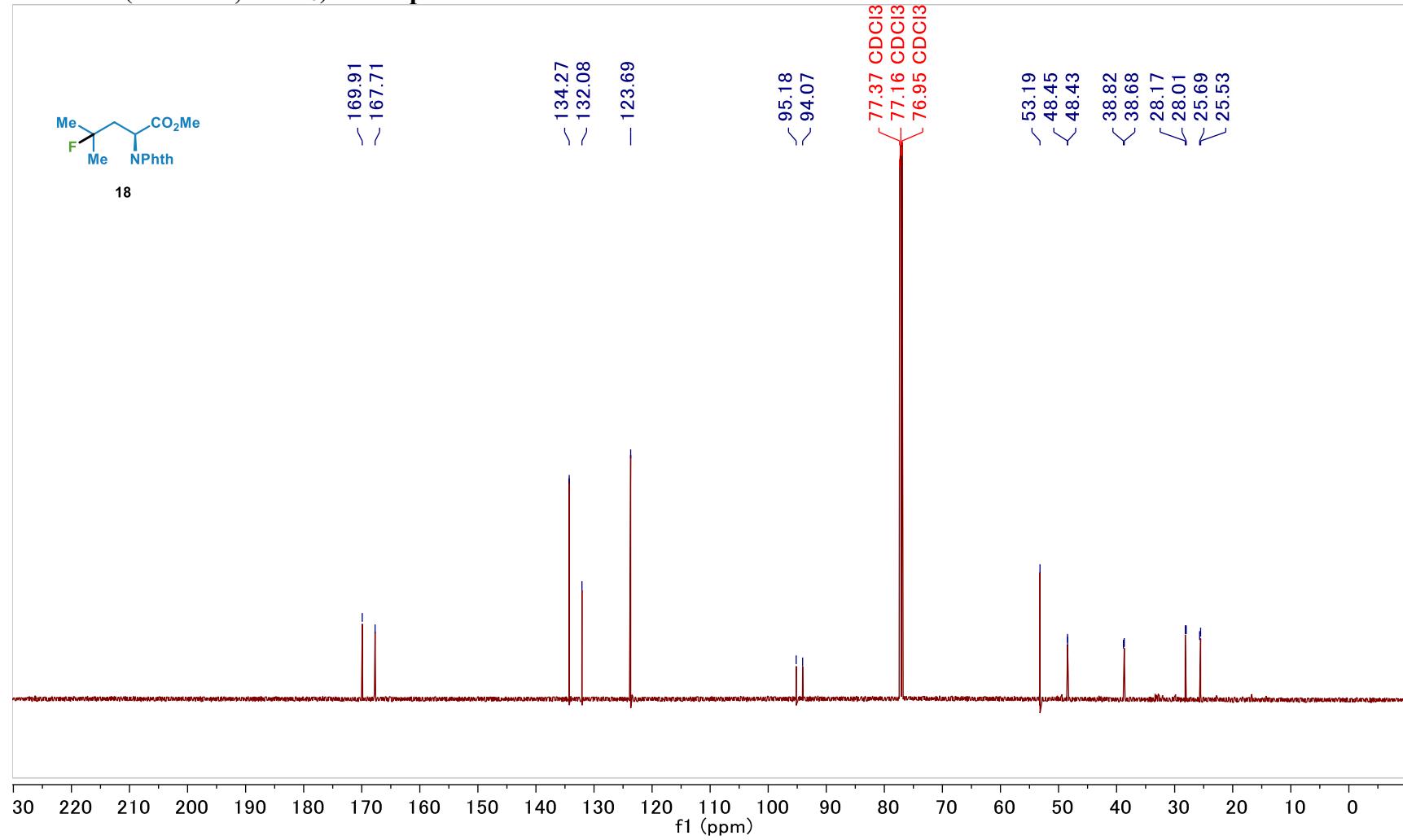
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 17



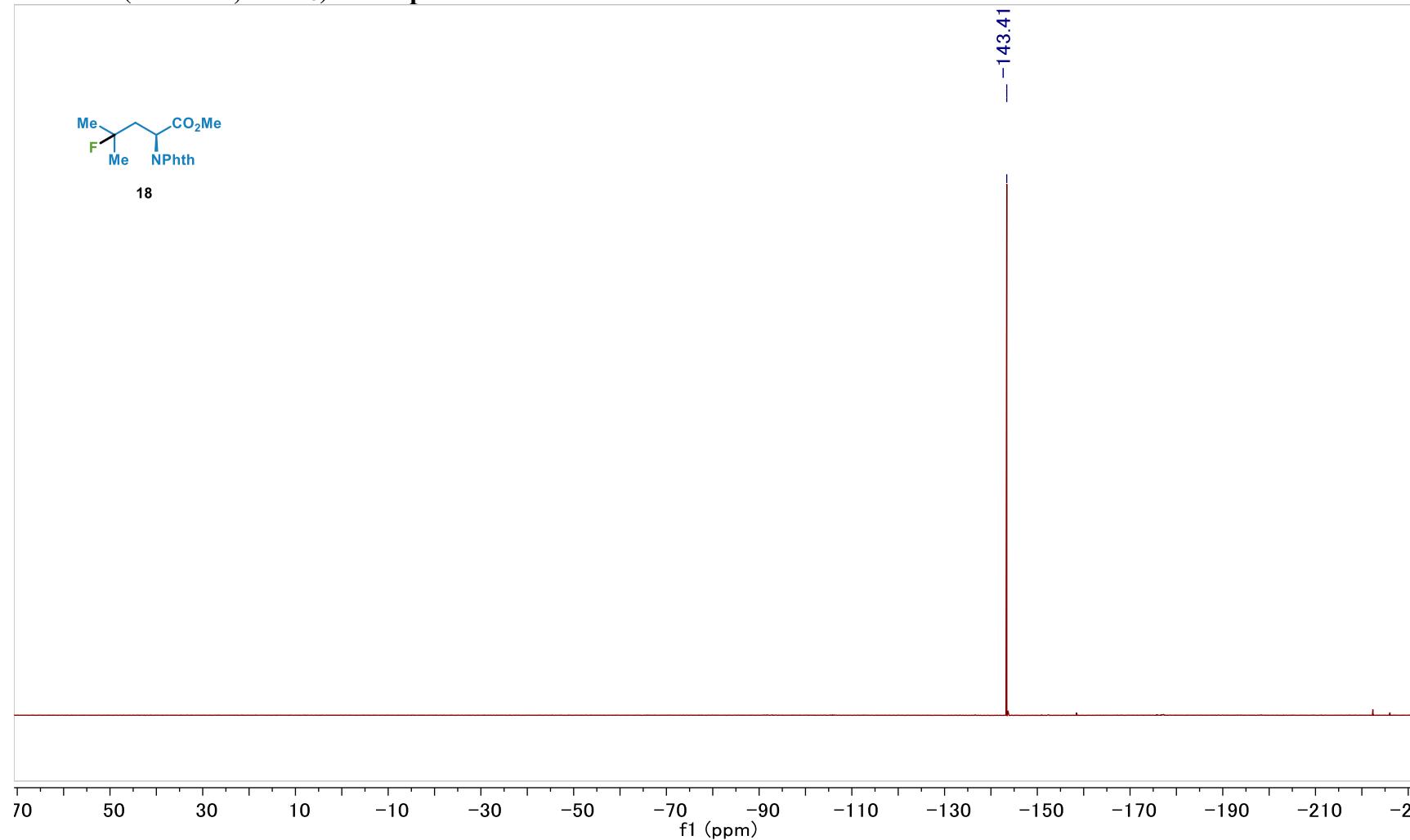
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 18



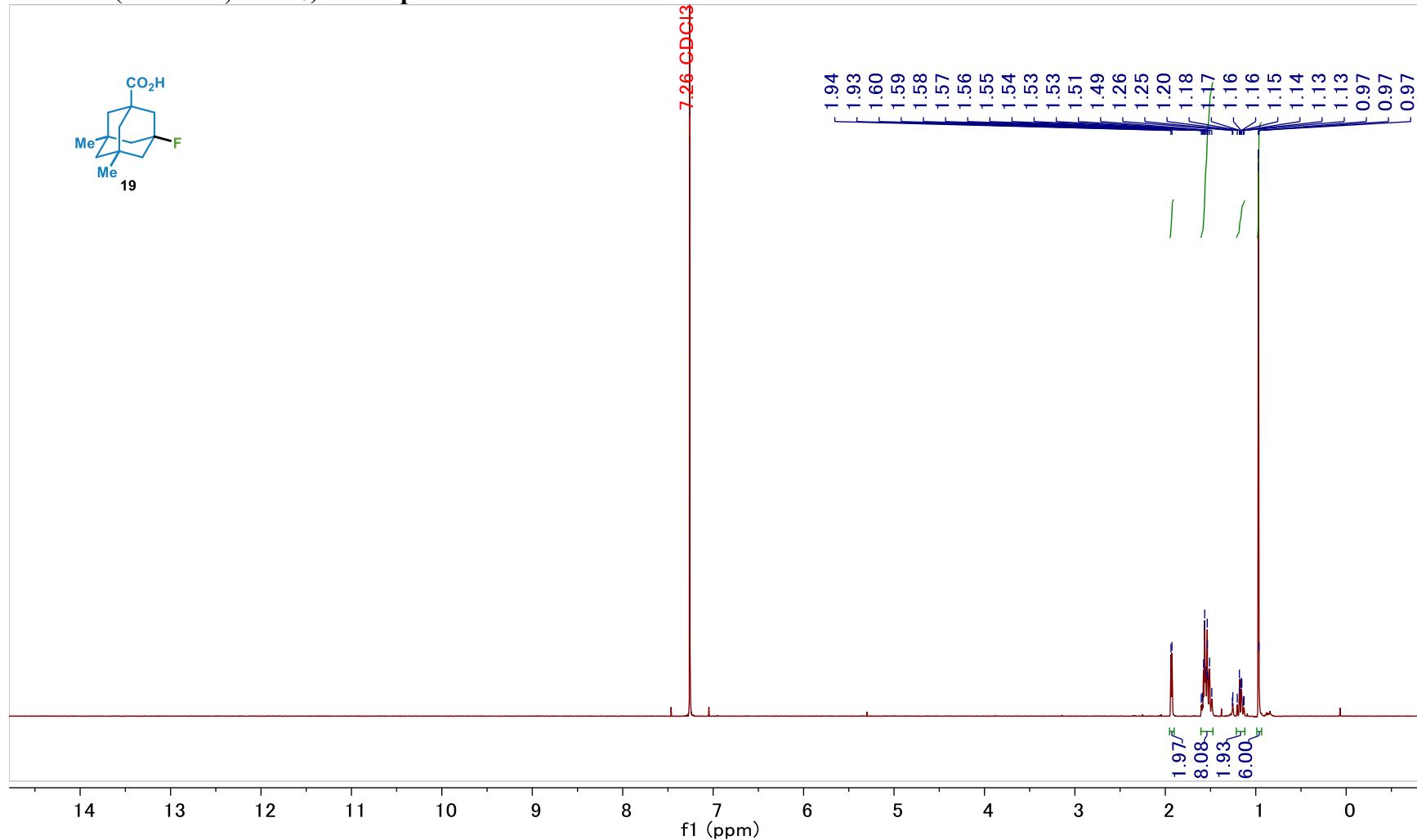
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 18



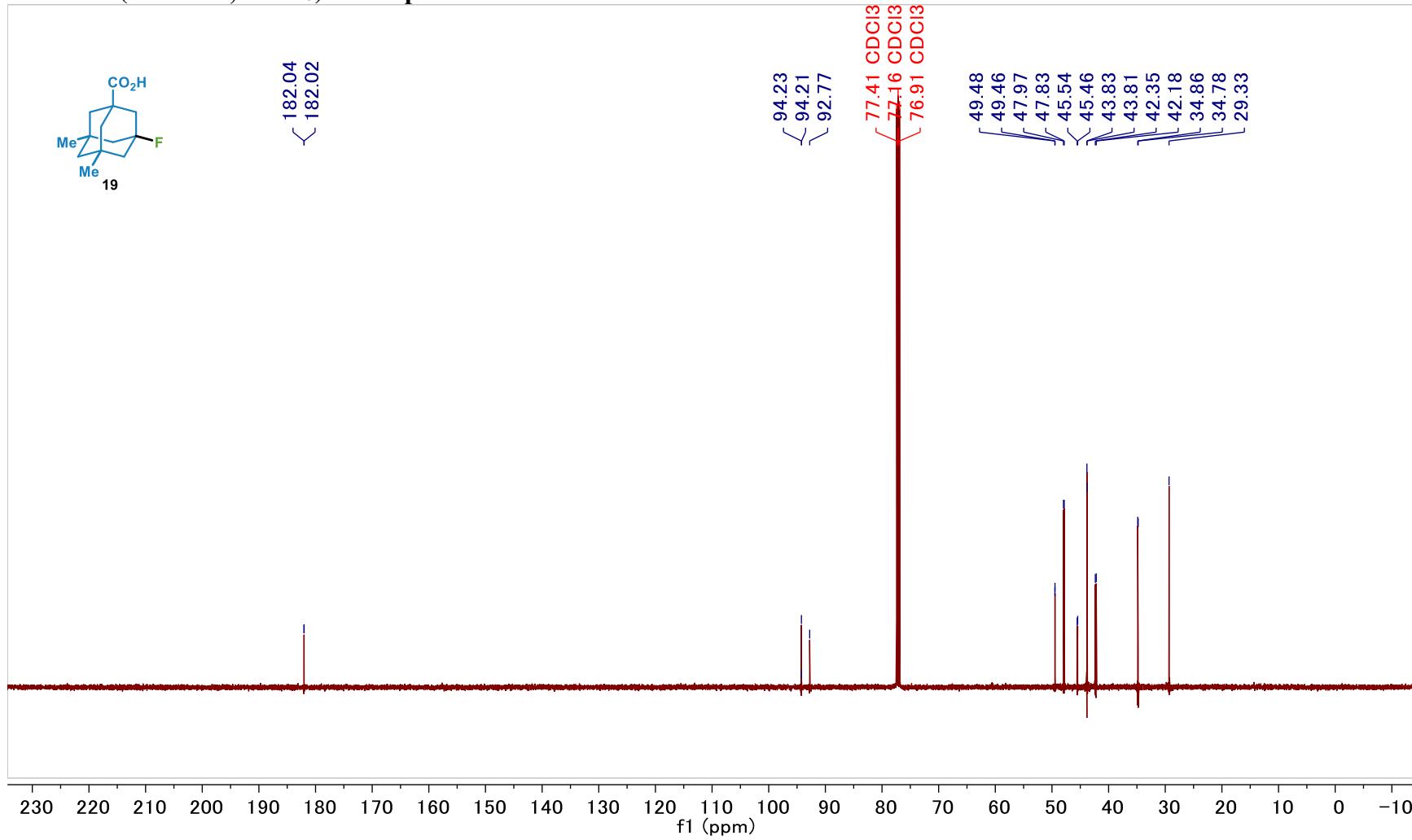
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 18



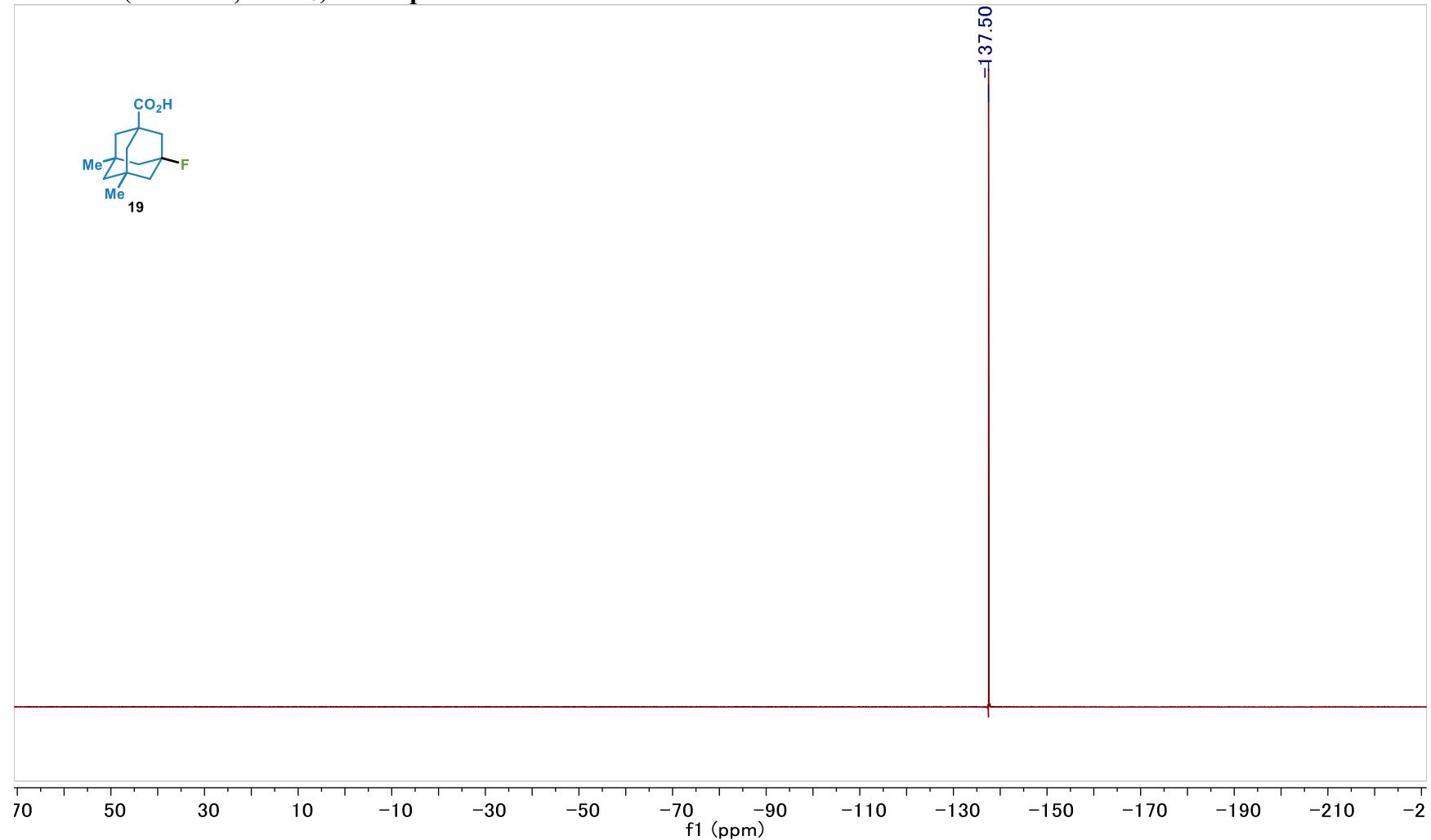
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) of compound 19



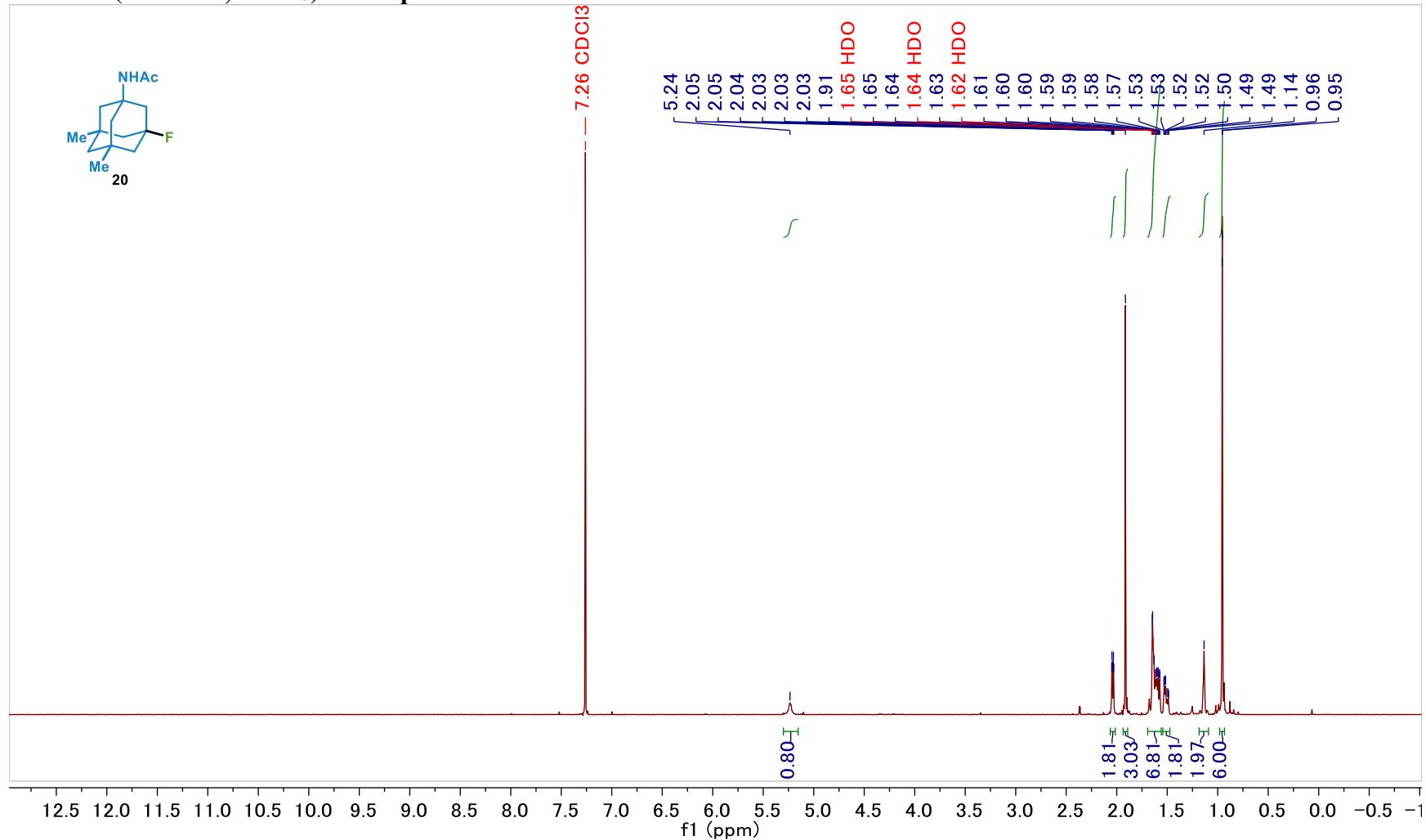
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) of compound 19



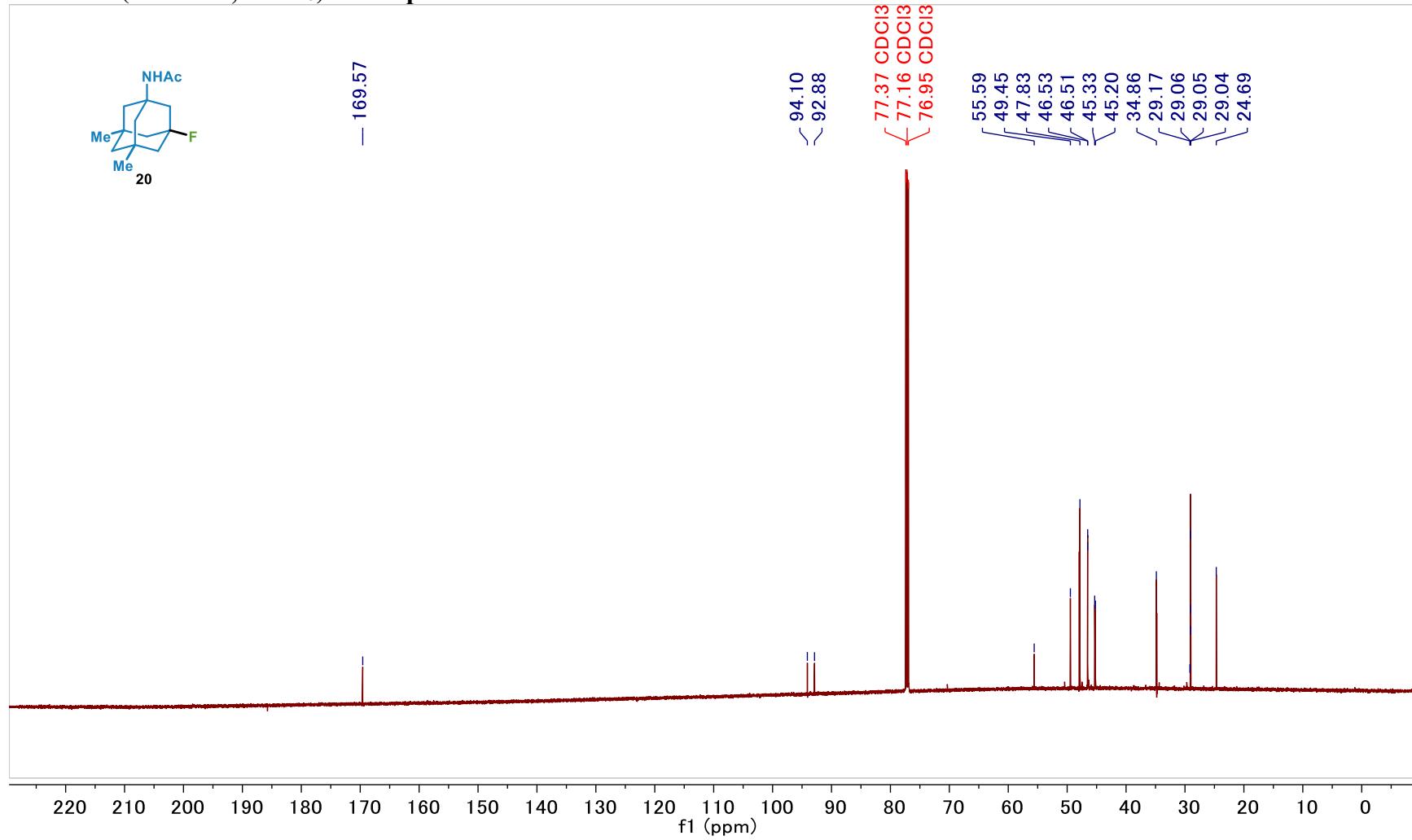
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 19



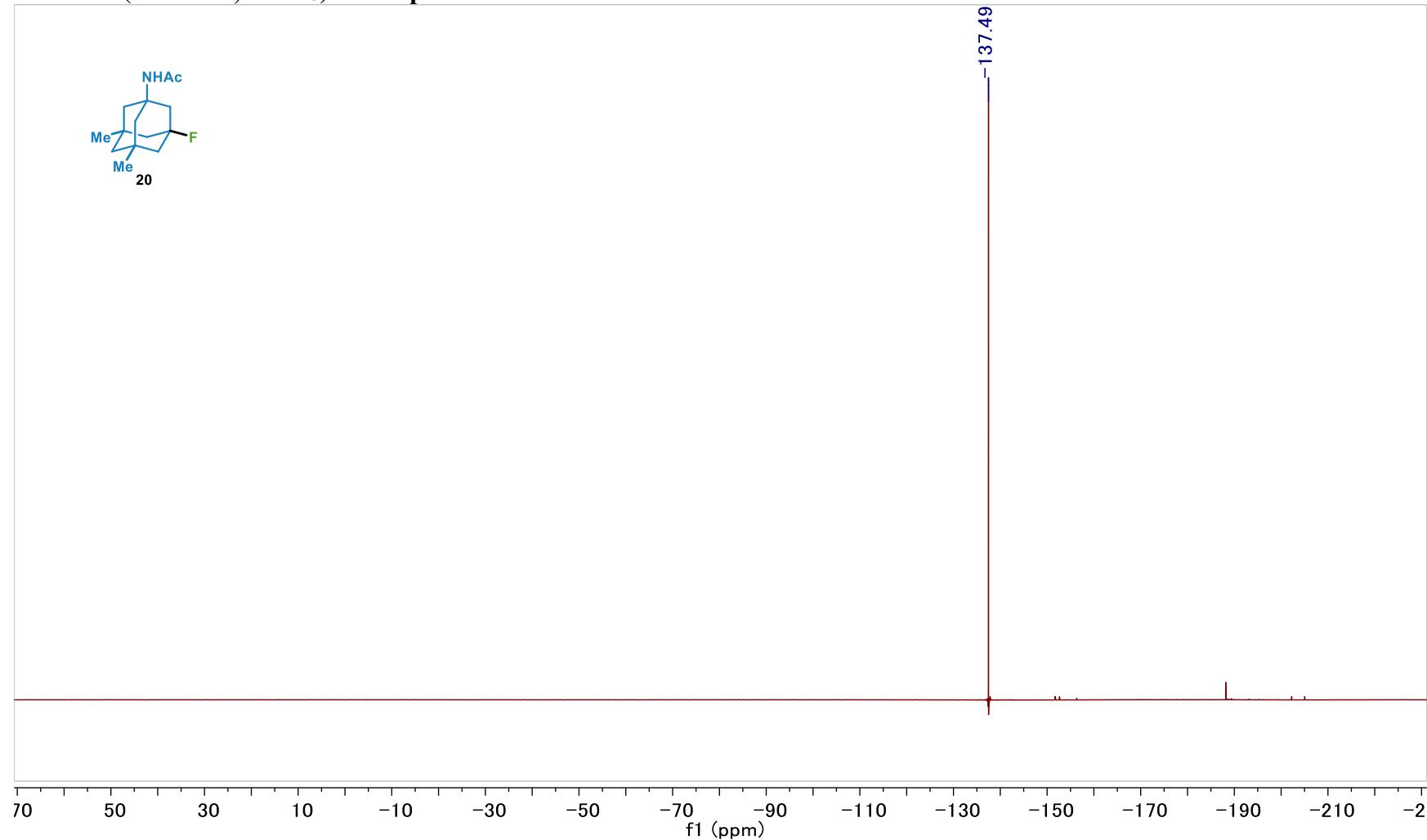
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 20



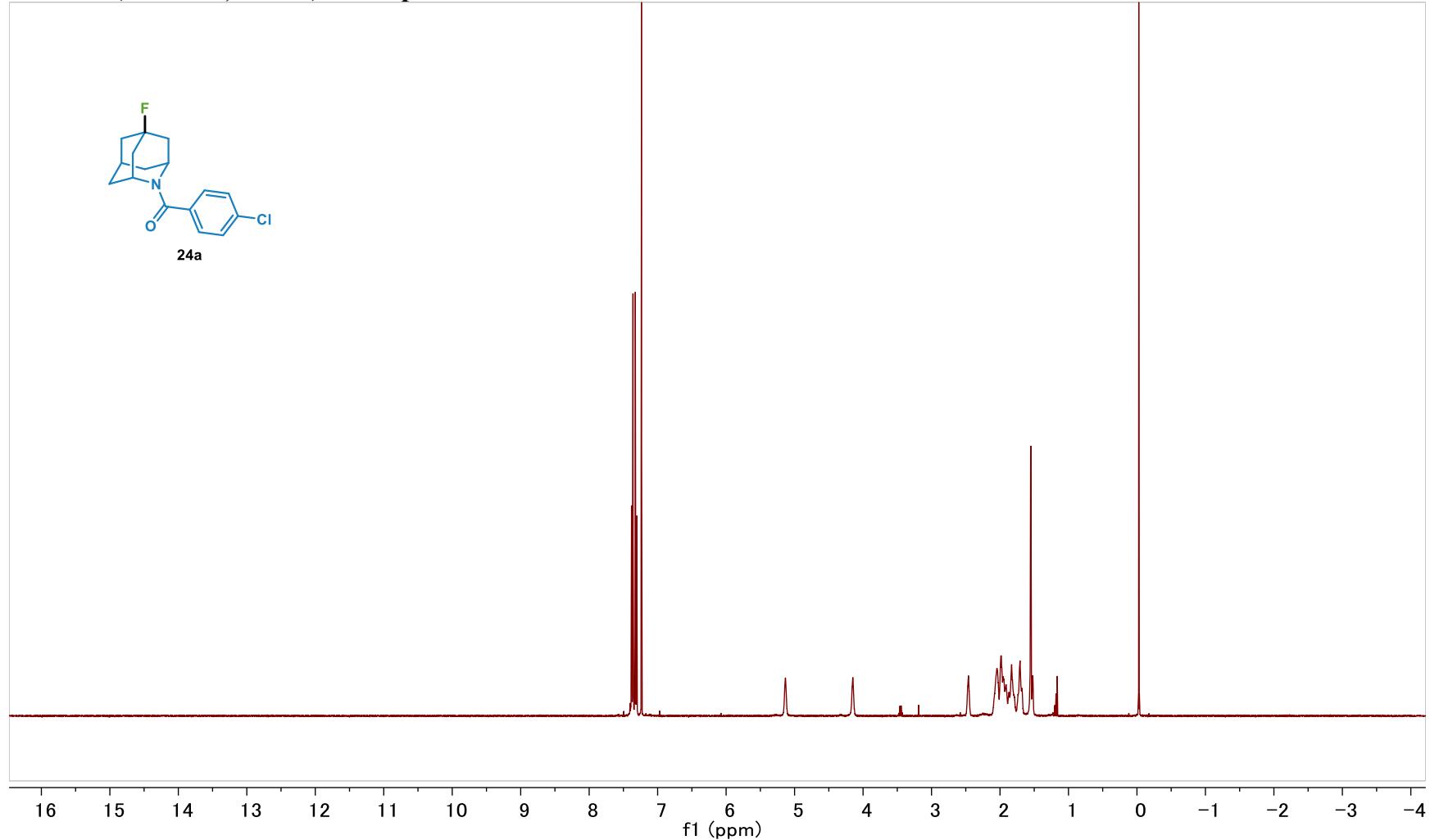
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) of compound 20



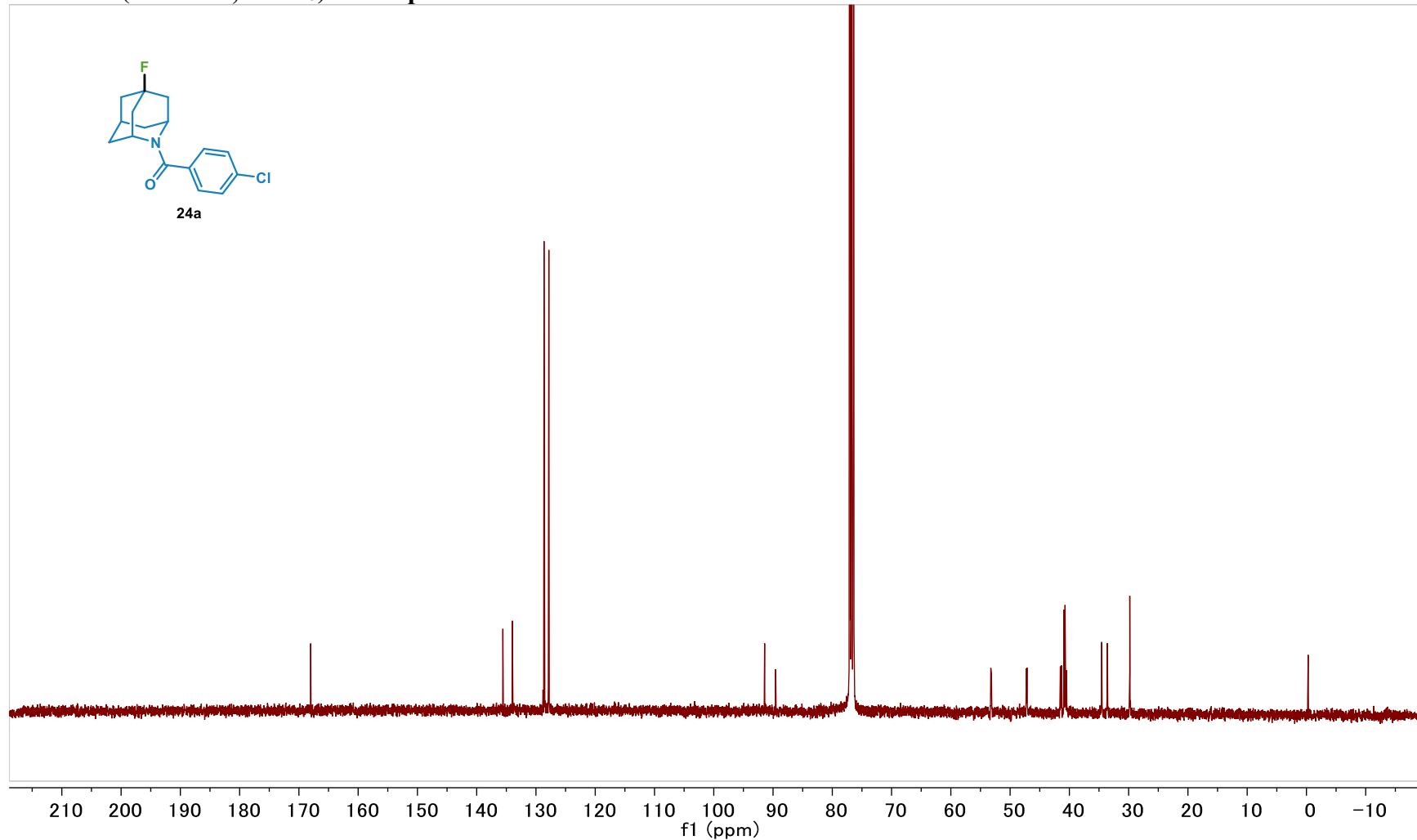
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 20



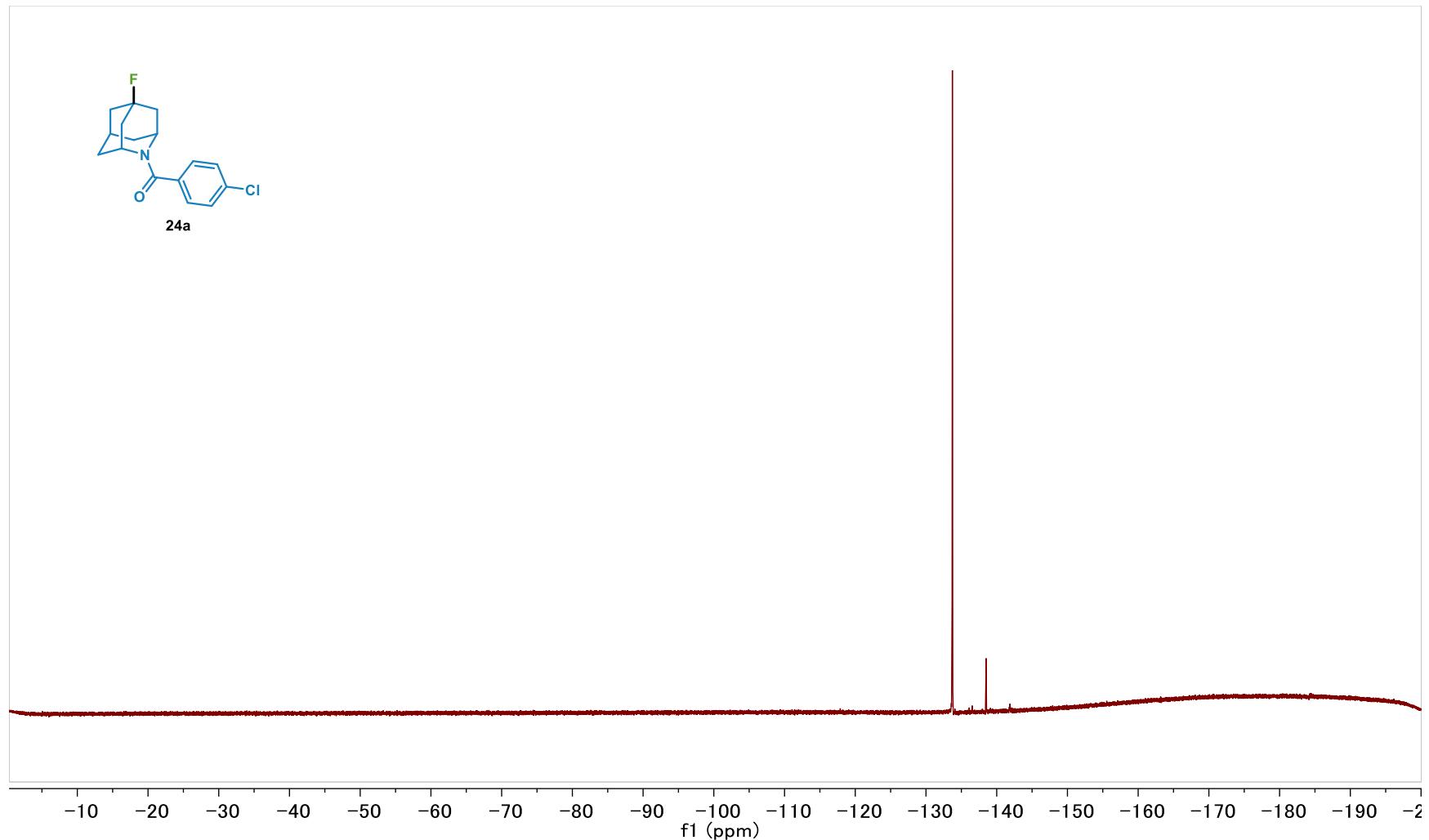
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 24a



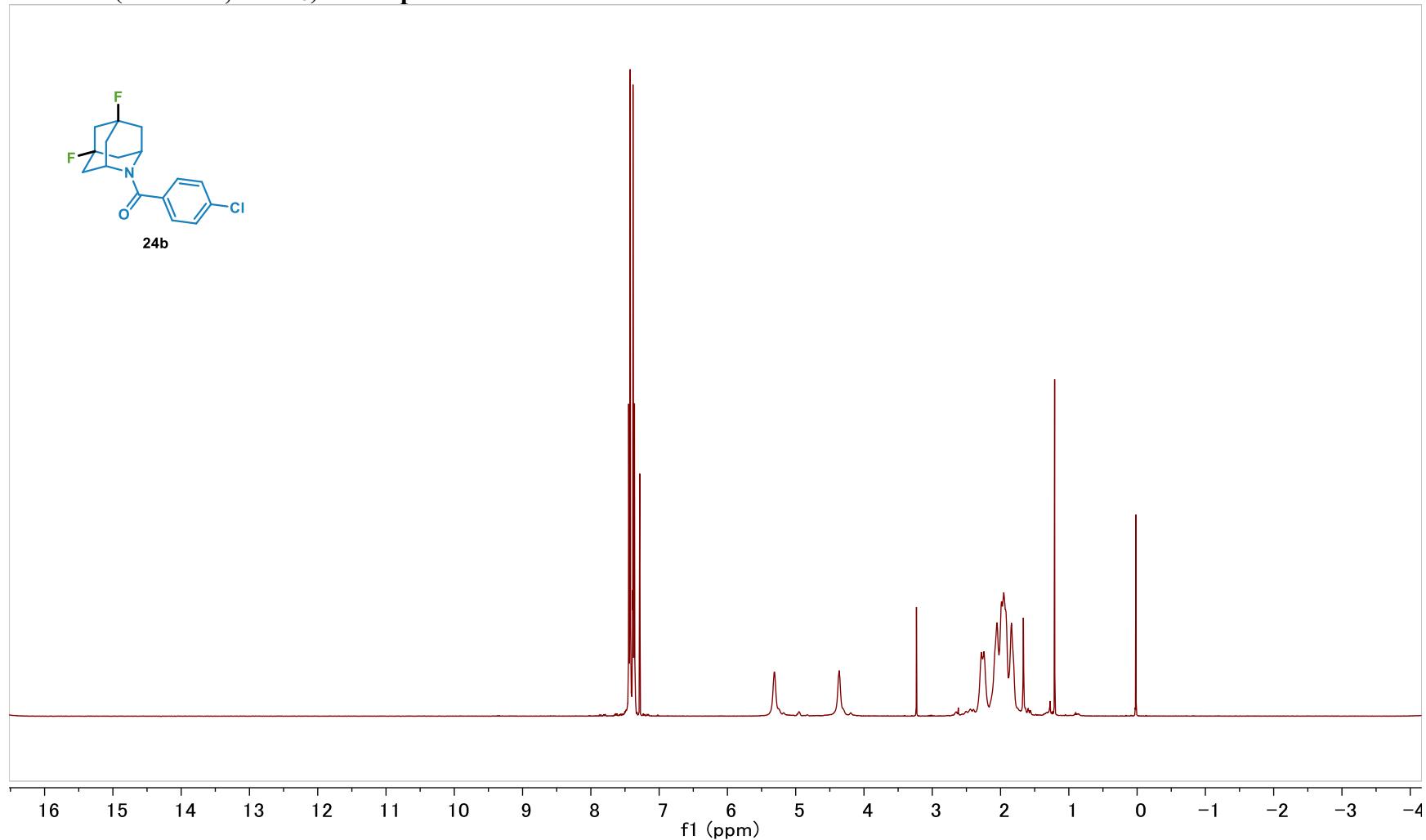
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) of compound 24a



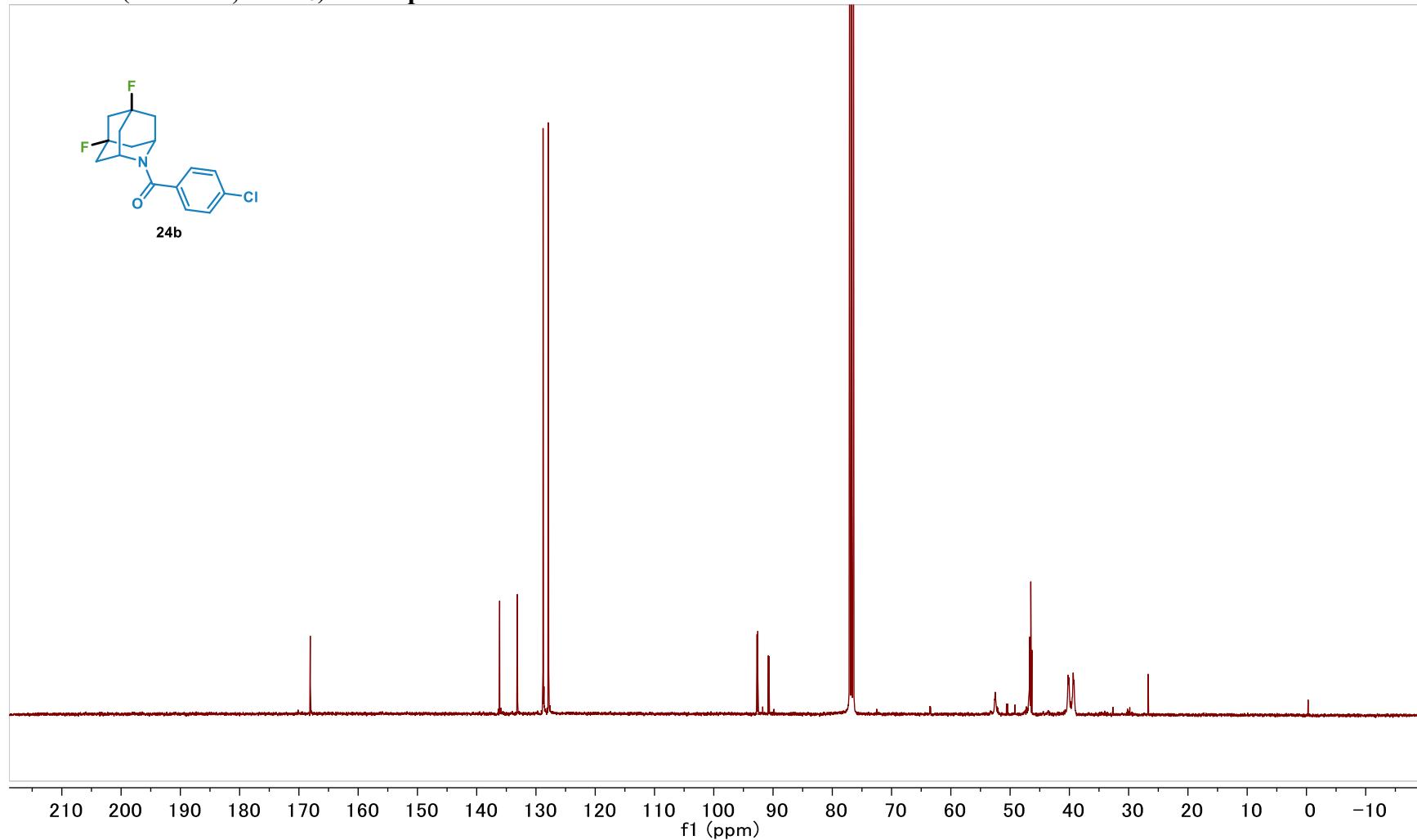
**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 24a**



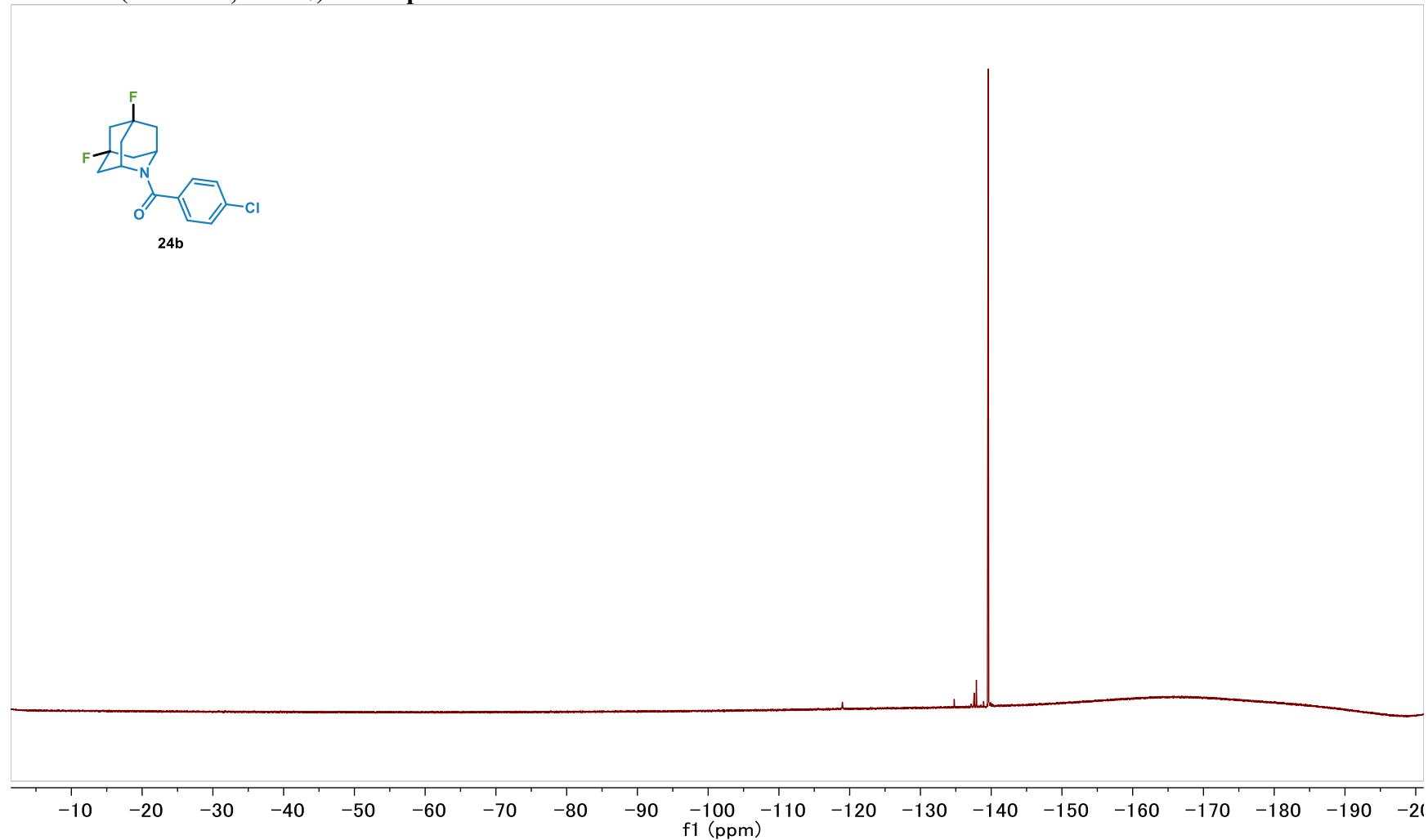
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 24b



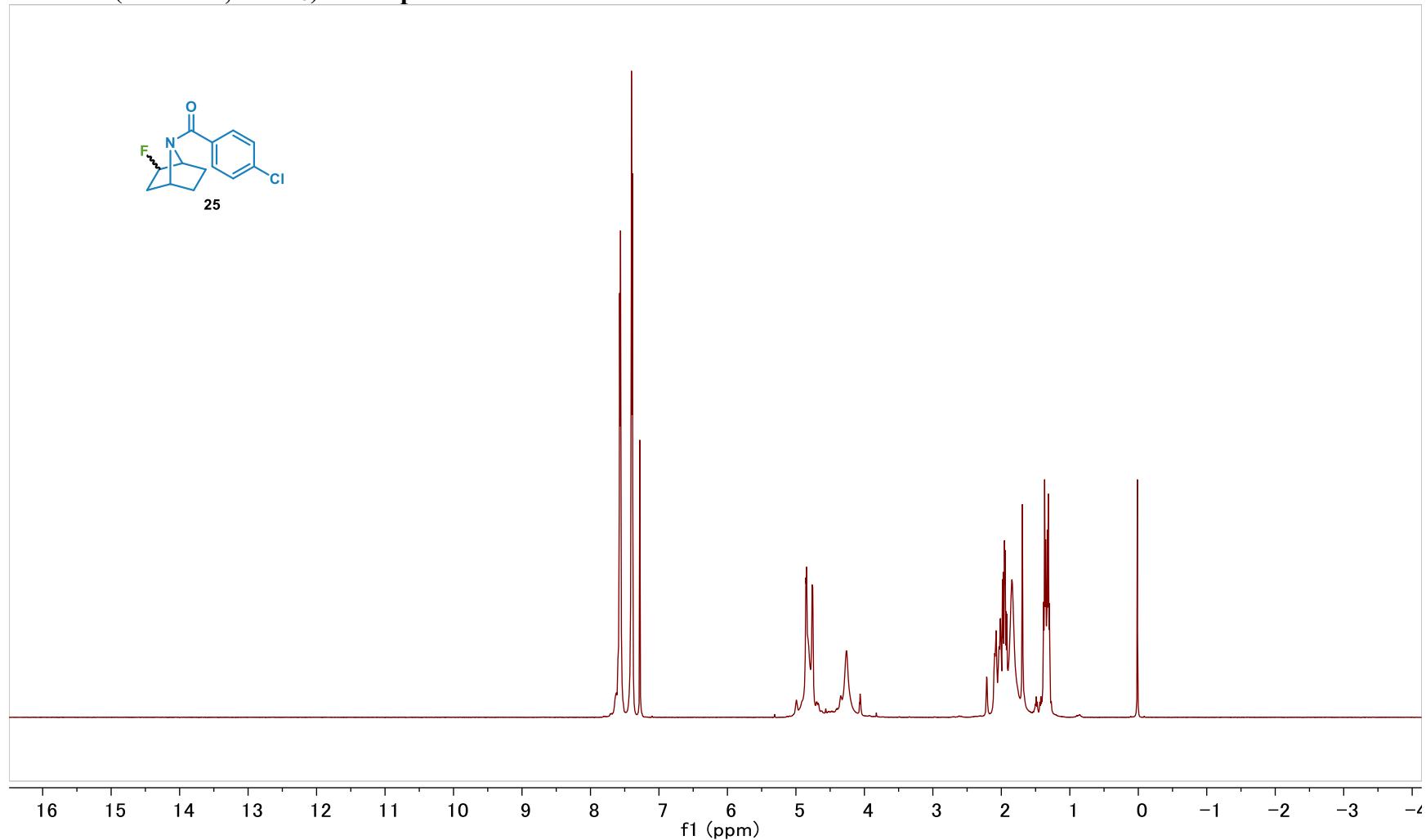
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) of compound 24b



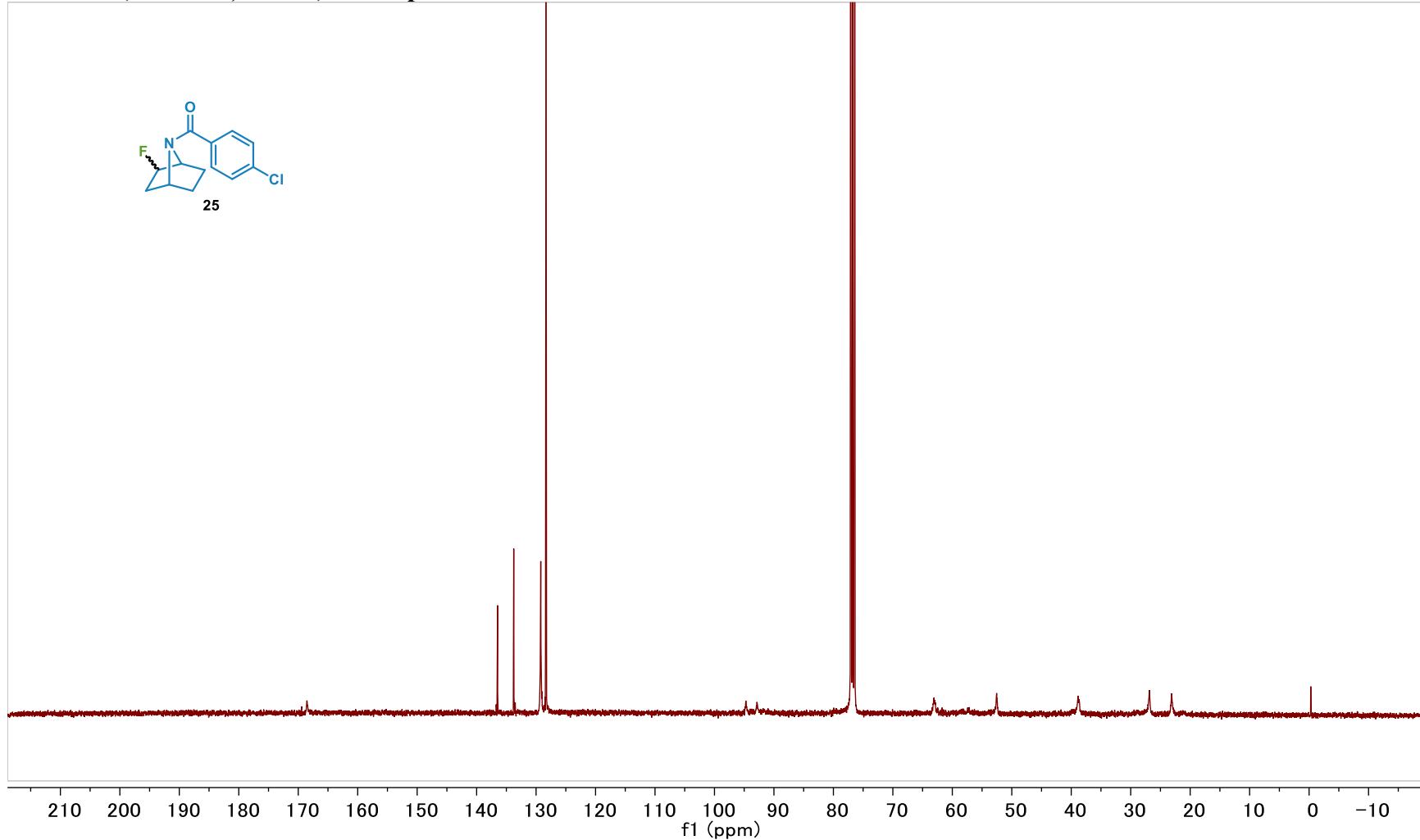
**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 24b**



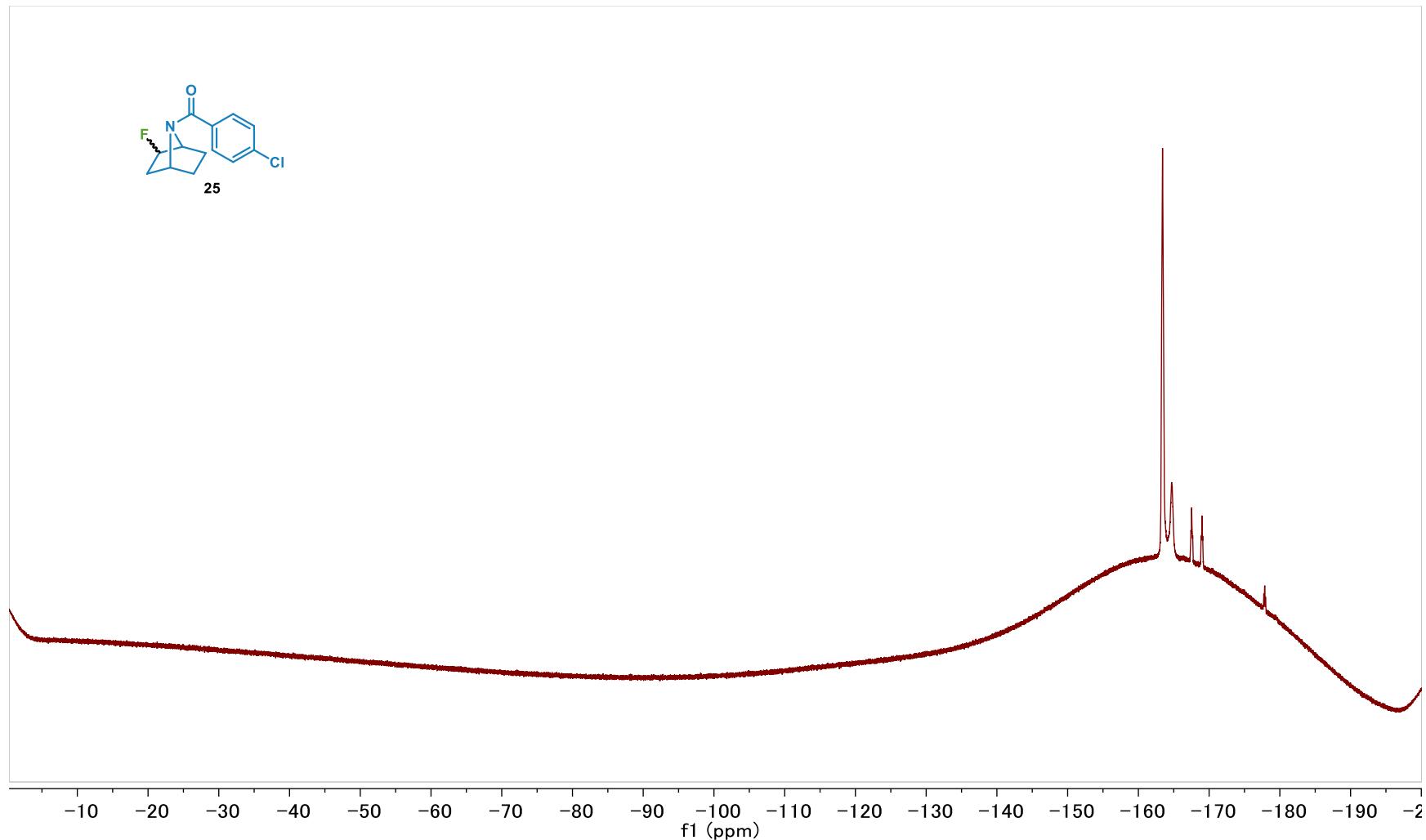
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) of compound 25



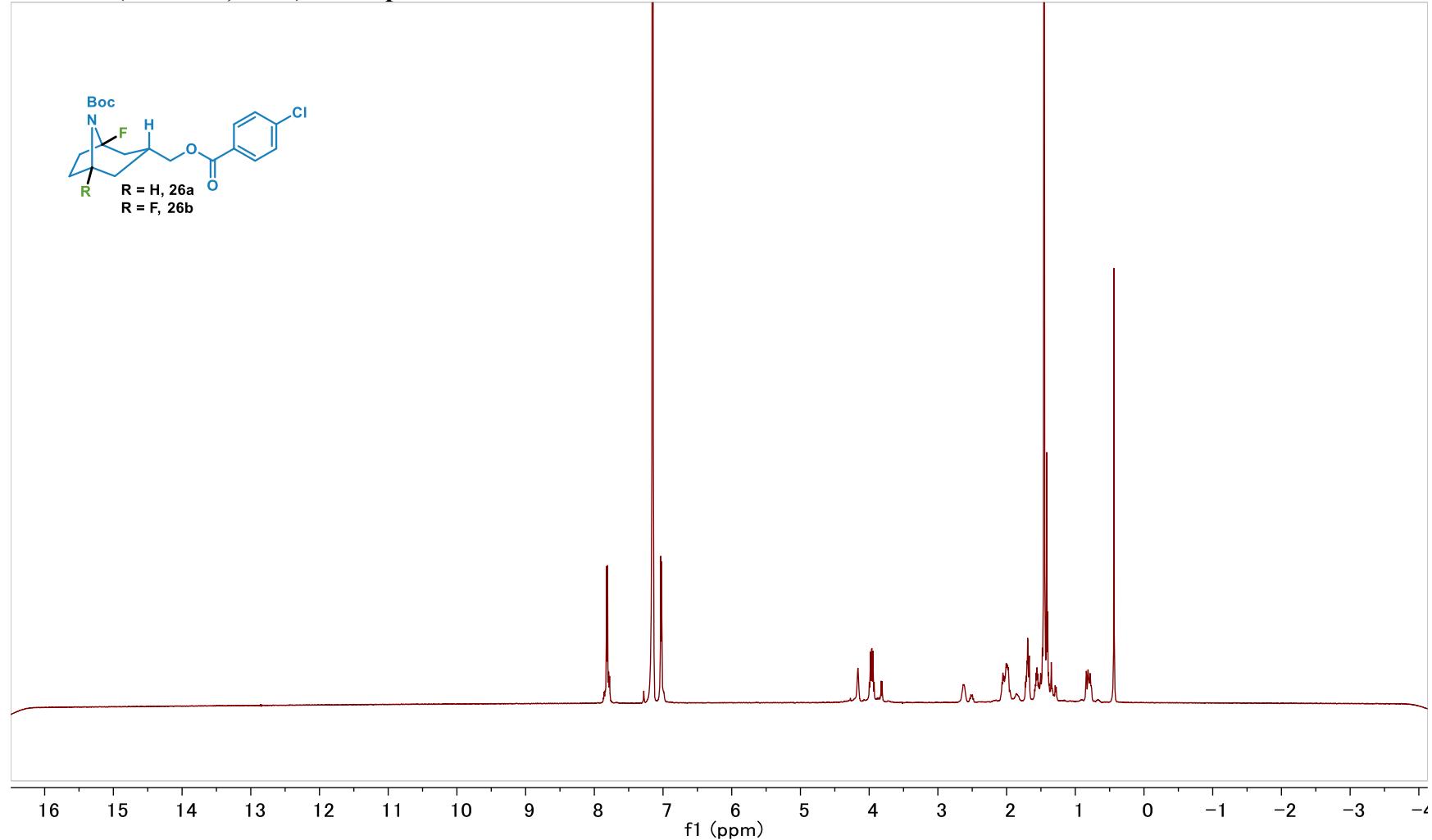
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) of compound 25



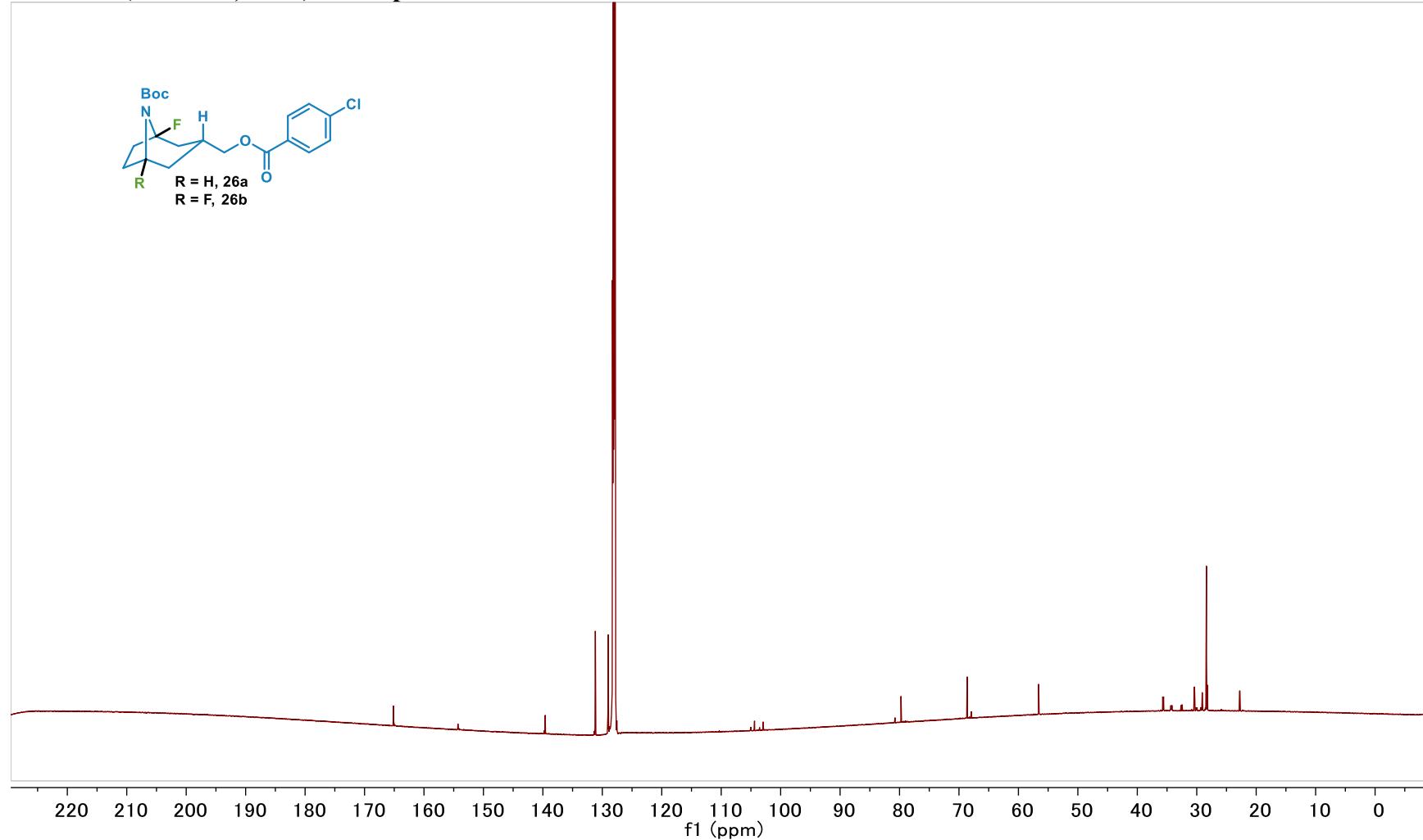
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 25



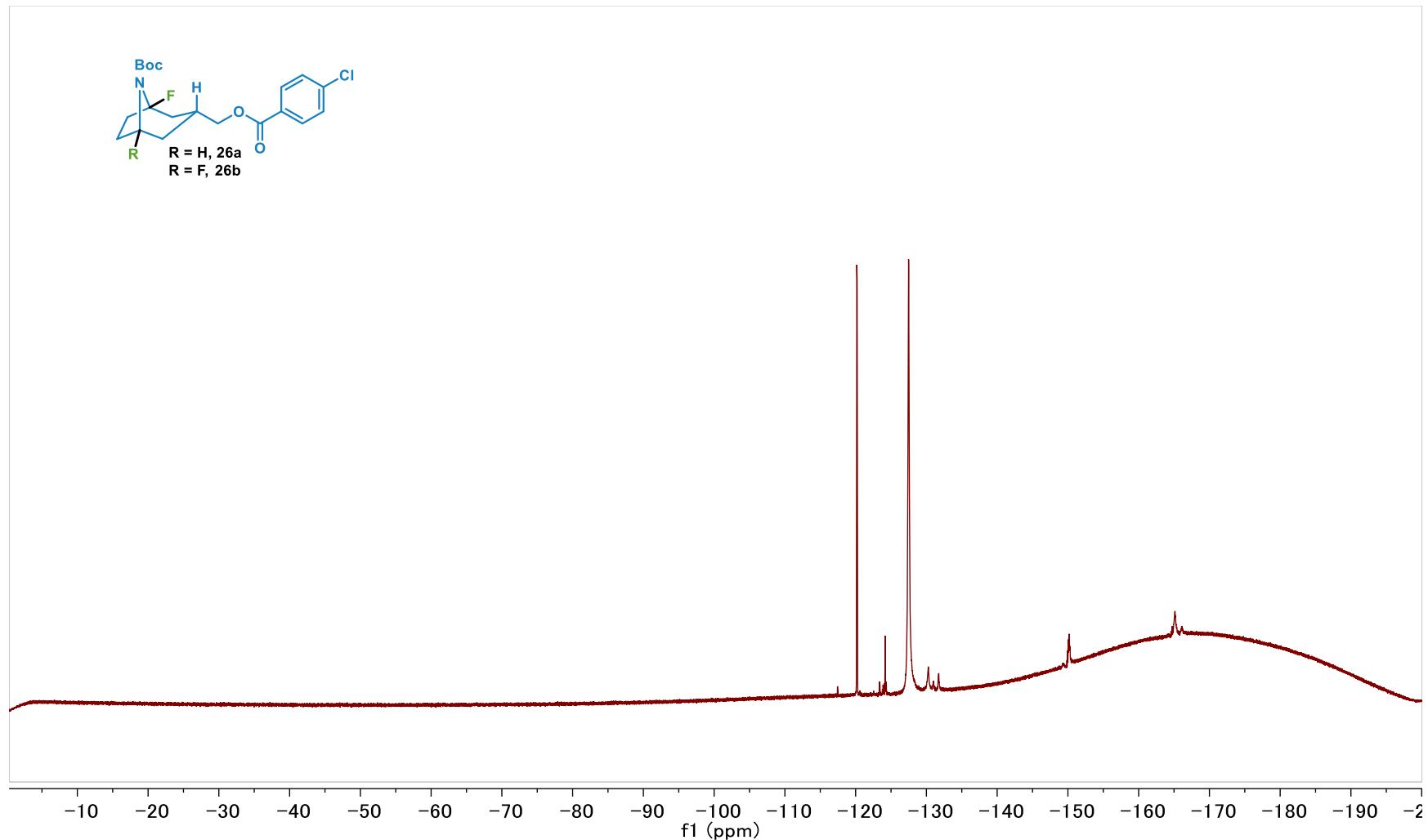
<sup>1</sup>H NMR (600 MHz, C<sub>6</sub>D<sub>6</sub>) of compound 26



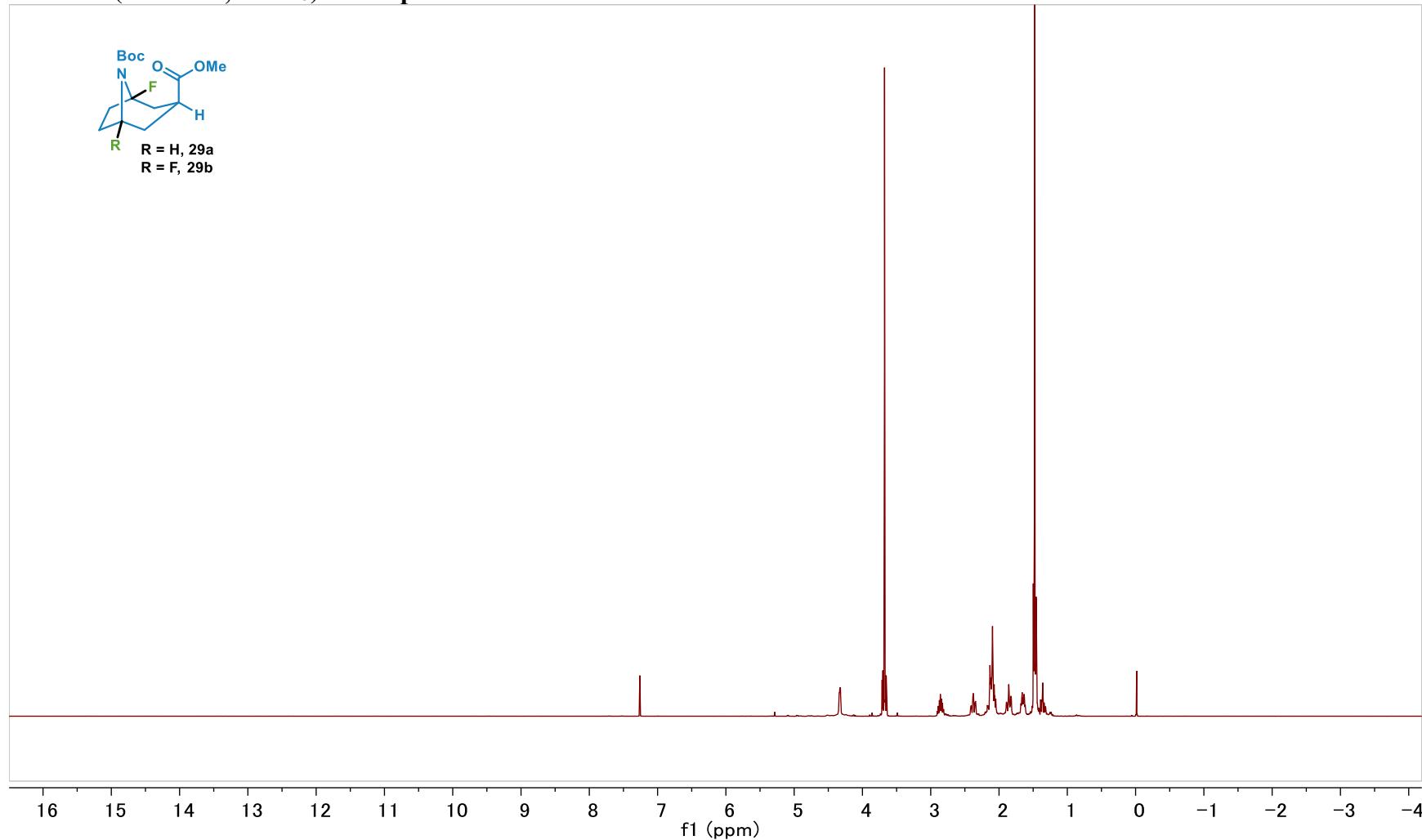
<sup>13</sup>C NMR (151 MHz, C<sub>6</sub>D<sub>6</sub>) of compound 26



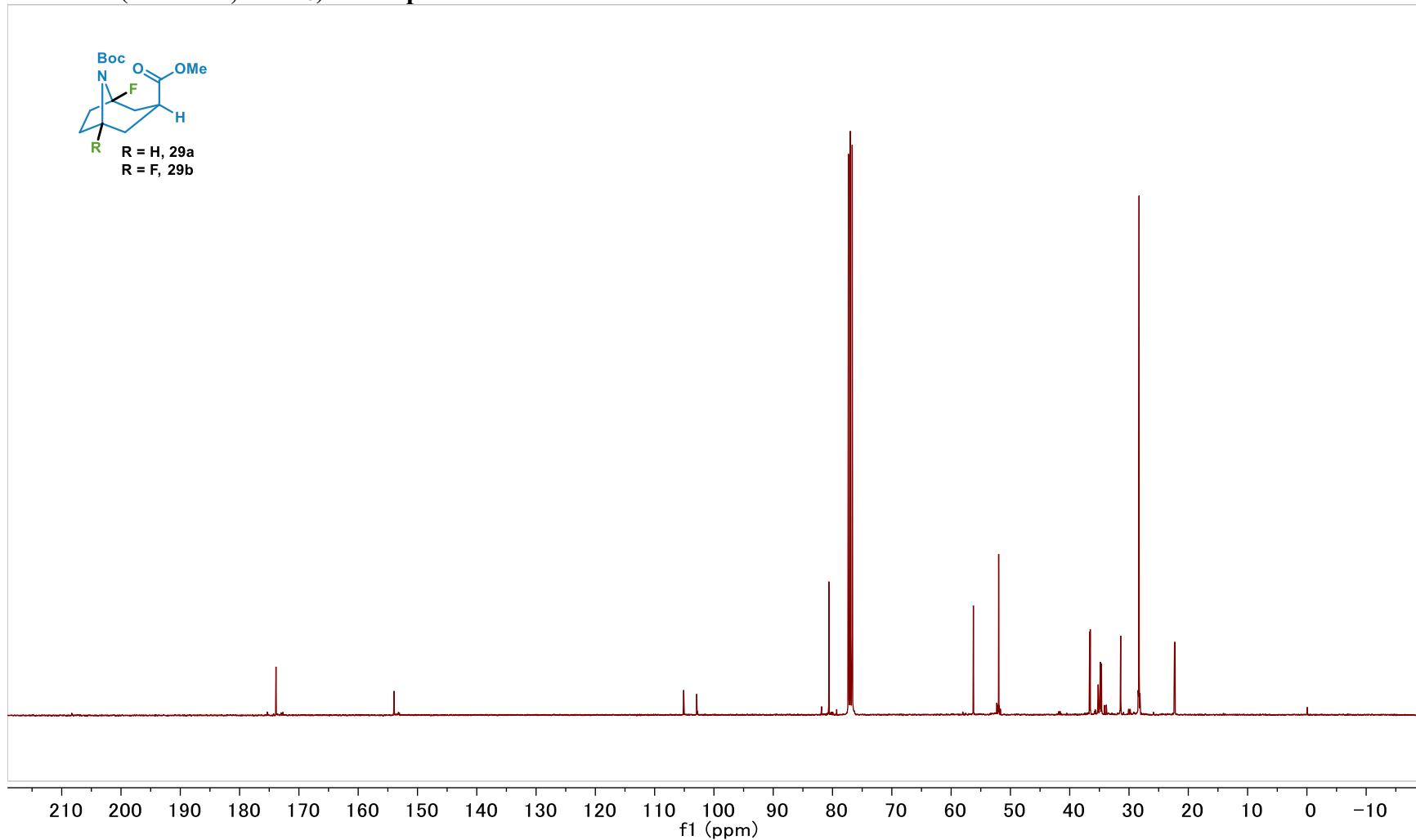
<sup>19</sup>F NMR (376 MHz, C<sub>6</sub>D<sub>6</sub>) of compound 26



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) of compound 29



<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) of compound 29



<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) of compound 29

