

## Supporting Information

# Photoredox-catalyzed direct C(sp<sup>2</sup>)–H difluoromethylation of enamides or heterocycles with [bis(difluoroacetoxy)iodo]benzene

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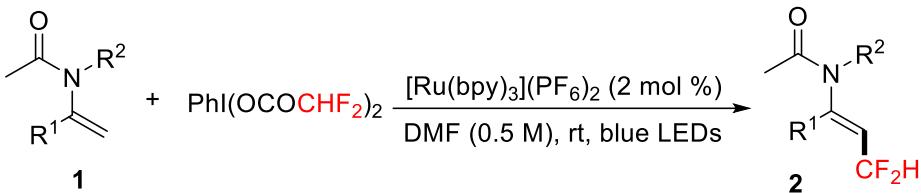
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### ***General Information***

All reactions were carried out in oven dried Schlenk tubes under nitrogen atmosphere. All of Enamides were prepared as reported in the reference.<sup>1</sup> [bis(difluoroacetoxy)iodo]benzene was prepared according to the reported method.<sup>2</sup> Dry *N,N*-dimethylformamide (DMF) was purchased from Energy Chemical, [Ru(bpy)<sub>3</sub>](PF<sub>6</sub>)<sub>2</sub> was purchased from Bidepharm.com. <sup>1</sup>H, <sup>19</sup>F, <sup>13</sup>C NMR spectra were recorded in CDCl<sub>3</sub> or DMSO-*d*<sub>6</sub> on Bruker Avance 400 MHz spectrometers. High resolution mass spectra (HRMS) were obtained using a commercial apparatus (ESI Source). Electrospray–ionisation HRMS data were acquired on a Q–Tof mass spectrometer (Waters SYNAPT G2-Si) LC-MS TOF. NMR spectra were taken using TMS (<sup>1</sup>H,  $\delta$  = 0), CDCl<sub>3</sub>(<sup>1</sup>H,  $\delta$  = 7.26), CDCl<sub>3</sub>(<sup>13</sup>C, CPD  $\delta$  = 77.0), DMSO-*d*<sub>6</sub>(<sup>1</sup>H,  $\delta$  = 2.50) and DMSO-*d*<sub>6</sub>(<sup>1</sup>H, CPD,  $\delta$  = 40.0) as the internal standards, respectively. Column chromatography was generally performed on silica gel (300-400 mesh) and reactions were monitored by thin layer chromatography (TLC) using UV light to visualize the course of the reactions.

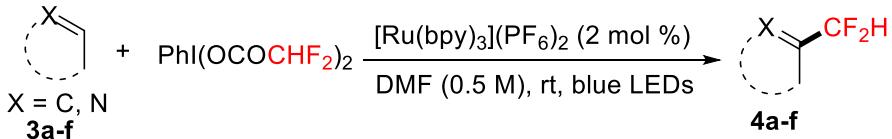
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**General procedure for the synthesis of (*E*)-*β*-difluoromethylated enamides 2**



Enamide **1** (0.3 mmol), [bis(difluoroacetoxy)iodo]benzene (0.45 mmol, 1.5 equiv) and  $[\text{Ru}(\text{bpy})_2](\text{PF}_6)_2$  (0.006 mmol, 2 mol %) were added sequentially into Schlenk tube under nitrogen. Then DMF (0.6 mL) was added rapidly by syringe. The resulting mixture was allowed to stir at room temperature under blue LEDs irradiation (30 W) for 12 hours. Upon completion, water (15 mL) was added, and the mixture was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 10$  mL). The organic phases were collected, washed with saturated brine solution and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . Then, the filtrate was concentrated under vacuum and the residue was purified by flash column chromatography using *n*-hexane /ethyl acetate as eluent to afford product **2**.

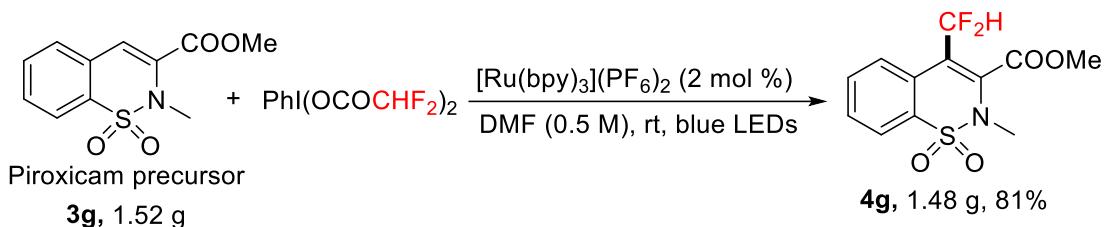
**General procedure for the synthesis of difluoromethylated heterocycles 4**



Heterocycle **3** (0.3 mmol), [bis(difluoroacetoxy)iodo]benzene (0.45 mmol, 1.5 equiv) and  $[\text{Ru}(\text{bpy})_2](\text{PF}_6)_2$  (0.006 mmol, 2 mol %) were added sequentially into Schlenk tube under nitrogen. Then DMF (0.6 mL) was added rapidly by syringe. The resulting mixture was allowed to stir at room temperature under blue LEDs irradiation (30 W) for 12 hours. Upon completion, water (15 mL) was added, and the mixture was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 10$  mL). The organic phases were collected, washed with saturated brine solution and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . Then, the filtrate was concentrated under vacuum and the residue was purified by flash column chromatography using *n*-hexane /ethyl acetate as eluent to afford product **4**.

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**Gram-scale and gram-scale synthesis of **4g****



Piroxicam precursor **3g** (6.0 mmol, 1.52 g), [bis(difluoroacetoxy)iodo]benzene (9.0 mmol, 1.5 equiv, 3.55 g) and  $[\text{Ru}(\text{bpy})_2](\text{PF}_6)_2$  (0.12 mmol, 2 mol %) were added sequentially into Schlenk tube under nitrogen. Then DMF (12 mL) was added rapidly by syringe. The resulting mixture was allowed to stir at room temperature under blue LEDs irradiation (30 W) for 12 hours. Upon completion, water (50 mL) was added, and the mixture was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 30$  mL). The organic phases were collected, washed with saturated brine solution and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . Then, the filtrate was concentrated under vacuum and the residue was purified by flash column chromatography using *n*-hexane /ethyl acetate as eluent to afford product **4g** (81%, 1.48 g).

**Table S1. Optimization of reaction conditions <sup>a</sup>**

Entry	Photocatalyst (%)	Solvent (M)	Yield <sup>b</sup> (%)
1	<i>fac</i> -Ir(ppy) <sub>3</sub> (5)	MeCN (0.2)	trace
2	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (5)	MeCN (0.2)	14
3	[Ir(ppy) <sub>2</sub> (dtbbpy)]PF <sub>6</sub> (5)	MeCN (0.2)	trace
4	Eosin Y (5)	MeCN (0.2)	trace
5	Mes-AcrClO <sub>4</sub> (5)	MeCN (0.2)	trace
6	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (5)	DCE (0.2)	21
7	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (5)	EA (0.2)	25
8	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (5)	Toluene (0.2)	trace
9	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (5)	Dioxane (0.2)	13
10	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (5)	DMF (0.2)	27
11	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (5)	NMP (0.2)	25
12	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (5)	DMSO (0.2)	trace
13	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (3)	DMF (0.2)	38
14	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (2)	DMF (0.2)	45
15	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (1)	DMF (0.2)	40
16 <sup>c</sup>	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (2)	DMF (0.2)	13
17 <sup>d</sup>	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (2)	DMF (0.2)	41
18	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (2)	DMF (0.1)	27
19	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (2)	DMF (0.4)	46
20	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (2)	DMF (0.5)	55
21	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O (2)	DMF (1)	50
22	[Ru(bpy) <sub>3</sub> ](PF <sub>6</sub> ) <sub>2</sub> (2)	DMF (0.5)	67
23	<i>fac</i> -Ir(ppy) <sub>3</sub> (2)	DMF (0.5)	42
24	[Ir(ppy) <sub>2</sub> (dtbbpy)]PF <sub>6</sub> (2)	DMF (0.5)	38
25	Eosin Y (2)	DMF (0.5)	18
26	Mes-AcrClO <sub>4</sub> (2)	DMF (0.5)	33

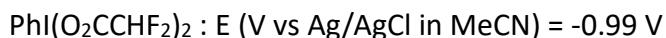
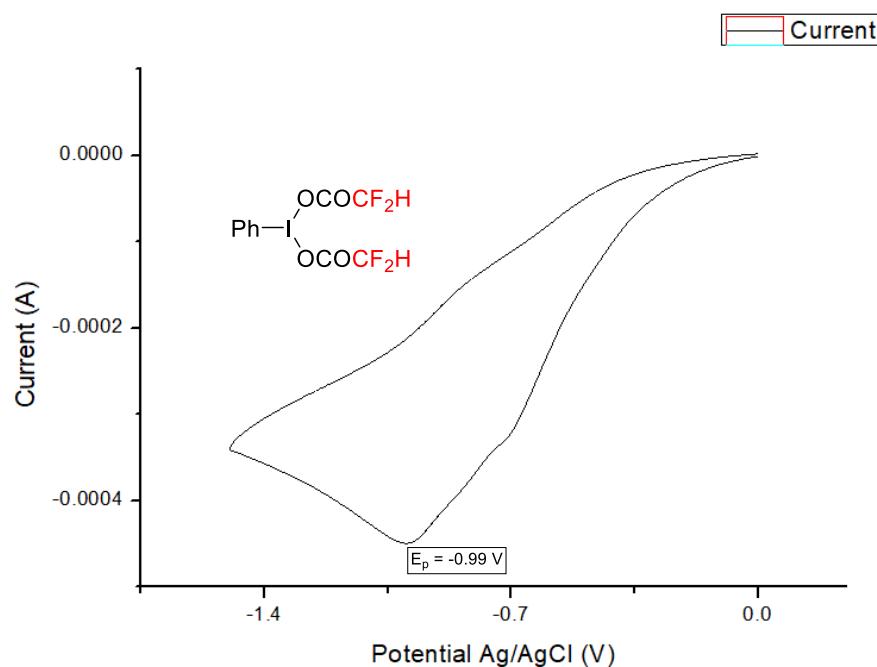
<sup>a</sup> Reaction conditions: *N*-benzyl-*N*-(1-phenylvinyl)acetamide **1a** (0.3 mmol), PhI(O<sub>2</sub>CCHF<sub>2</sub>)<sub>2</sub> (0.45 mmol, 1.5 equiv), Photocatalyst, solvent, room temperature, N<sub>2</sub>, under blue LEDs irradiation (30 W) for 12 h.

<sup>b</sup> <sup>1</sup>H NMR yield using mesitylene as internal standard. <sup>c</sup> 1.2 equiv. of PhI(O<sub>2</sub>CCHF<sub>2</sub>)<sub>2</sub> was used. <sup>d</sup> 2.0 equiv. of PhI(O<sub>2</sub>CCHF<sub>2</sub>)<sub>2</sub> was used.

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### Cyclic voltammetry study

Electrochemical measurements were performed using a CHI610E all-in-one potentiostat, using a standard three-electrode setup with a glassy carbon working electrode, platinum wire auxiliary electrode and a Ag/AgCl (satd. KCl) reference electrode. All solutions of the compounds under the study were 0.1 M in the supporting electrolyte  $n\text{Bu}_4\text{NPF}_6$  with the voltage scan rate of 100 mV/s. Anhydrous MeCN was used as solvent. Solutions were thoroughly bubbled with dry nitrogen for 2 min to remove oxygen before any experiment and kept under positive pressure of nitrogen.



**Figure S1.** Cyclic voltammetry of bis(difluoroacetoxy)iodo]benzene [0.02 M] in [0.1 M] TBAPF<sub>6</sub> in MeCN. Sweep Rate: 100 mV/s. Glassy carbon working electrode, Ag/AgCl (satd. KCl) reference electrode, Pt wire auxiliary electrode. Irreversible reduction.  $E_p = -0.99 \text{ V}$ .

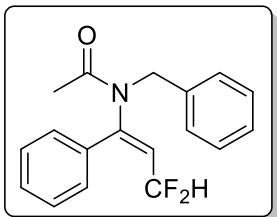
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## References

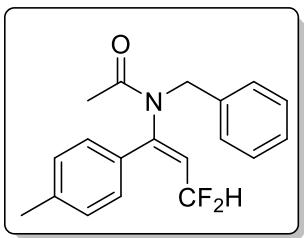
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5. Dai, P.; Yu, X.; Teng, P.; Zhang, W.-H.; Deng, C. *Org. Lett.*, **2018**, *20*, 6901.
6. Xu, H.-H.; Song, J.; Xu, H.-C. *ChemSusChem*, **2019**, *12*, 3060.

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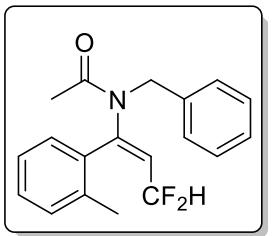
### Characterization data for products



(*E*)-*N*-benzyl-*N*-(3,3-difluoro-1-phenylprop-1-en-1-yl)acetamide (**2a**)<sup>3</sup>: 56.1 mg, 62% yield, colorless solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 7.52 – 7.41 (m, 3H), 7.33 – 7.22 (m, 5H), 7.19 – 7.14 (m, 2H), 6.06 (td, *J* = 54.8, 7.7 Hz, 1H), 5.55 (q, *J* = 7.9 Hz, 1H), 4.58 (s, 2H), 2.19 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 170.3, 148.23 (t, *J* = 14.0 Hz), 136.7, 133.2, 130.6, 129.1, 128.84 (t, *J* = 2.0 Hz), 128.6, 128.5, 127.6, 121.49 (t, *J* = 28.0 Hz), 112.91 (t, *J* = 228.5 Hz), 49.8, 22.6. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ ppm -106.91 (dd, *J* = 55.1, 8.0 Hz).

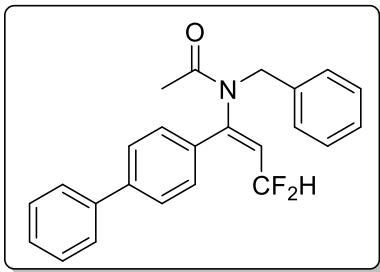


(*E*)-*N*-benzyl-*N*-(3,3-difluoro-1-(*p*-tolyl)prop-1-en-1-yl)acetamide (**2b**)<sup>3</sup>: 63.2 mg, 67% yield, colorless solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 7.33 – 7.22 (m, 5H), 7.20 – 7.11 (m, 4H), 6.07 (td, *J* = 54.9, 7.7 Hz, 1H), 5.49 (q, *J* = 7.9 Hz, 1H), 4.57 (s, 2H), 2.41 (s, 3H), 2.18 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 170.3, 148.24 (t, *J* = 14.0 Hz), 141.0, 136.7, 130.2, 129.8, 128.8, 128.6, 128.5, 127.5, 120.93 (t, *J* = 27.5 Hz), 113.04 (t, *J* = 228.5 Hz), 49.8, 22.6, 21.4. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ ppm -106.75 (dd, *J* = 55.3, 8.2 Hz).

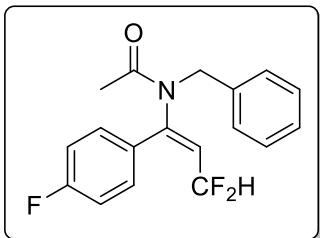


(*E*)-*N*-benzyl-*N*-(3,3-difluoro-1-(*o*-tolyl)prop-1-en-1-yl)acetamide (**2c**)<sup>3</sup>: 49.5 mg, 52% yield, colorless solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 7.38 – 7.32 (m, 1H), 7.30 – 7.20

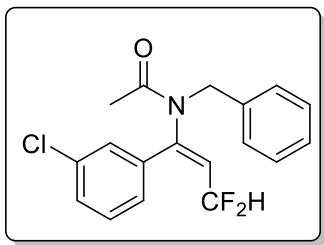
(m, 5H), 7.10 – 7.03 (m, 3H), 5.99 – 5.60 (m, 2H), 4.51 (s, 2H), 2.35 (s, 3H), 2.19 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.6, 148.18 (t,  $J$  = 14.0 Hz), 132.0, 131.2, 130.88 (t,  $J$  = 2.0 Hz), 130.2, 128.5, 127.6, 127.3, 126.2, 119.69 (t,  $J$  = 27.5 Hz), 113.37 (t,  $J$  = 229.0 Hz), 49.1, 23.0, 19.5.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -108.58 (d,  $J$  = 609.8 Hz).



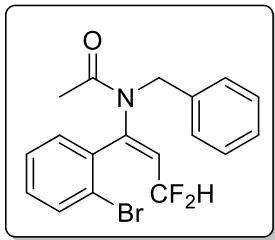
*(E)*-*N*-(1-([1,1'-biphenyl]-4-yl)-3,3-difluoroprop-1-en-1-yl)-*N*-benzylacetamide (**2d**)<sup>3</sup>: 49.8 mg, 44% yield, colorless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.67 (d,  $J$  = 8.3 Hz, 2H), 7.62 (d,  $J$  = 8.6 Hz, 2H), 7.49 (t,  $J$  = 7.5 Hz, 2H), 7.44 – 7.38 (m, 1H), 7.36 – 7.26 (m, 5H), 7.23 – 7.16 (m 2H), 6.14 (td,  $J$  = 54.8, 7.7 Hz, 1H), 5.57 (q,  $J$  = 7.9 Hz, 1H), 4.63 (s, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.3, 147.95 (t,  $J$  = 14.0 Hz), 143.5, 139.6, 136.67, 131.9, 129.3, 129.0, 128.7, 128.5, 128.1, 127.8, 127.6, 127.1, 121.50 (t,  $J$  = 27.5 Hz), 112.92 (t,  $J$  = 229.0 Hz), 49.9, 22.7.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -106.76 (dd,  $J$  = 55.3, 8.2 Hz).



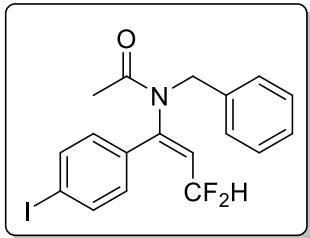
*(E)*-*N*-benzyl-*N*-(3,3-difluoro-1-(4-fluorophenyl)prop-1-en-1-yl)acetamide (**2e**)<sup>3</sup>: 59.2 mg, 62% yield, colorless solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.33 – 7.20 (m, 5H), 7.17 – 7.10 (m, 4H), 6.02 (td,  $J$  = 54.7, 7.6 Hz, 1H), 5.55 (q,  $J$  = 7.9 Hz, 1H), 4.58 (s, 2H), 2.18 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.2, 163.86 (d,  $J$  = 250.0 Hz), 147.22 (t,  $J$  = 14.0 Hz), 136.5, 130.85 (dt,  $J$  = 8.6, 1.6 Hz), 129.3, 128.6, 128.5, 127.7, 121.51 (t,  $J$  = 27.5 Hz), 116.37 (d,  $J$  = 22.0 Hz), 112.74 (t,  $J$  = 229.5 Hz), 49.9, 22.6.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -106.80 (dd,  $J$  = 54.9, 8.0 Hz), -108.73 (s).



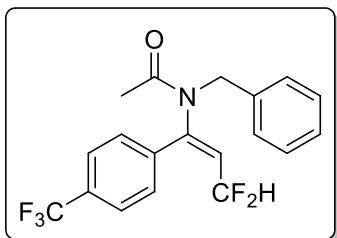
(*E*)-*N*-benzyl-*N*-(1-(3-chlorophenyl)-3,3-difluoroprop-1-en-1-yl)acetamide (**2f**)<sup>3</sup>: 65.3 mg, 65% yield, colorless solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 7.46 (ddd, *J* = 8.1, 2.1, 1.1 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.33 – 7.24 (m, 3H), 7.20 (t, *J* = 1.8 Hz, 1H), 7.18 – 7.11 (m, 3H), 6.03 (td, *J* = 54.6, 7.7 Hz, 1H), 5.59 (q, *J* = 7.9 Hz, 1H), 4.59 (s, 2H), 2.19 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 170.12, 146.85 (t, *J* = 13.5 Hz), 136.4, 135.4, 135.1, 130.7, 130.4, 128.58, 128.55, 127.7, 127.2, 122.36 (t, *J* = 28.0 Hz), 112.46 (t, *J* = 229.5 Hz), 50.0, 22.6. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ ppm -107.08 (dd, *J* = 54.5, 8.0 Hz).



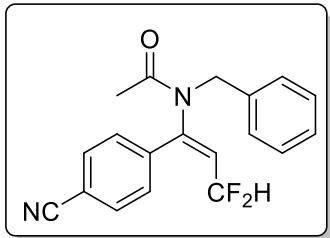
(*E*)-*N*-benzyl-*N*-(1-(2-bromophenyl)-3,3-difluoroprop-1-en-1-yl)acetamide (**2g**): 61.9 mg, 54% yield, light yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 7.64 (dd, *J* = 7.3, 1.9 Hz, 1H), 7.38 – 7.31 (m, 2H), 7.30 – 7.20 (m, 3H), 7.08 (d, *J* = 6.9 Hz, 3H), 6.00 – 5.64 (m, 2H), 4.50 (br, 2H), 2.39 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 171.0, 147.57 (t, *J* = 13.5 Hz), 136.8, 133.9, 133.3, 133.2, 131.6, 128.5, 127.5, 127.3, 122.4, 120.28 (t, *J* = 26.0 Hz), 112.94 (t, *J* = 229.5 Hz), 49.6, 23.2. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ ppm -108.32 (d, *J* = 1015.4 Hz). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> calcd for C<sub>18</sub>H<sub>16</sub>Br<sup>79</sup>F<sub>2</sub>NNaO<sup>+</sup> 402.0276, found 402.0283; calcd for C<sub>18</sub>H<sub>16</sub>Br<sup>81</sup>F<sub>2</sub>NNaO<sup>+</sup> 404.0255, found 404.0266.



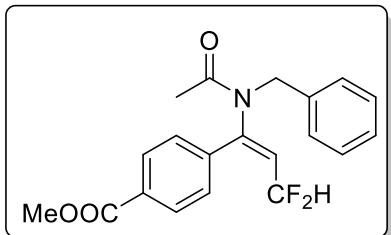
(*E*)-*N*-benzyl-*N*-(1-(2-bromophenyl)-3,3-difluoroprop-1-en-1-yl)acetamide (**2h**)<sup>3</sup>: 72.7 mg, 57% yield, light yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 7.79 (d, *J* = 8.4 Hz, 2H), 7.34 – 7.23 (m, 3H), 7.14 (dd, *J* = 7.6, 2.0 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.16 – 5.86 (m, 1H), 5.57 (q, *J* = 7.9 Hz, 1H), 4.58 (s, 2H), 2.17 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 170.2, 147.32 (t, *J* = 14.0 Hz), 138.4, 136.4, 132.7, 130.31 (t, *J* = 1.5 Hz), 128.6, 128.5, 127.7, 121.86 (t, *J* = 28.0 Hz), 112.58 (t, *J* = 229.5 Hz), 97.1, 50.0, 22.6. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ ppm -106.85 (dd, *J* = 54.5, 7.9 Hz).



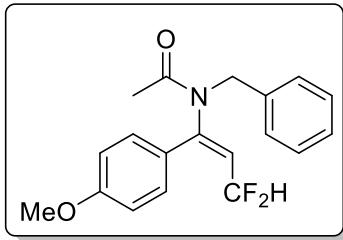
(*E*)-*N*-benzyl-*N*-(3,3-difluoro-1-(4-(trifluoromethyl)phenyl)prop-1-en-1-yl)acetamide (**2i**)<sup>3</sup>: 63.4 mg, 57% yield, colorless solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 7.70 (d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.33 – 7.27 (m, 3H), 7.18 – 7.12 (m, 2H), 6.00 (td, *J* = 54.5, 7.6 Hz, 1H), 5.67 (q, *J* = 7.9 Hz, 1H), 4.60 (s, 2H), 2.19 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 170.1, 146.89 (t, *J* = 13.5 Hz), 136.9, 136.3, 132.51 (q, *J* = 33.0 Hz), 129.2, 128.6, 128.5, 127.8, 126.12 (q, *J* = 3.7 Hz), 123.46 (q, *J* = 271.0 Hz), 122.82 (t, *J* = 27.5 Hz), 112.37 (t, *J* = 229.5 Hz), 50.2, 22.6. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ ppm -62.97 (s), -107.13 (dd, *J* = 54.4, 8.0 Hz).



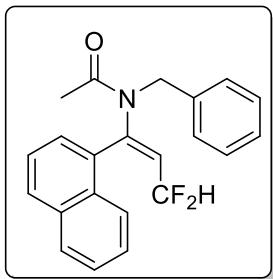
(*E*)-*N*-benzyl-*N*-(1-(4-cyanophenyl)-3,3-difluoroprop-1-en-1-yl)acetamide (**2j**): 52.8 mg, 54% yield, light yellow solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 7.73 (d, *J* = 8.3 Hz, 2H), 7.38 – 7.28 (m, 5H), 7.13 (dd, *J* = 7.2, 2.3 Hz, 2H), 5.98 (td, *J* = 54.4, 7.6 Hz, 1H), 5.70 (q, *J* = 8.0 Hz, 1H), 4.61 (s, 2H), 2.18 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 170.0, 146.51 (t, *J* = 13.5 Hz), 137.9, 136.0, 132.8, 129.4, 128.7, 128.4, 127.9, 123.1, 117.7, 114.3, 121.1 (t, *J* = 230.5 Hz), 50.3, 22.6. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ ppm -107.10 (dd, *J* = 54.2, 8.1 Hz). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> calcd for C<sub>19</sub>H<sub>16</sub>F<sub>2</sub>N<sub>2</sub>NaO<sup>+</sup> 349.1123, found 349.1118.



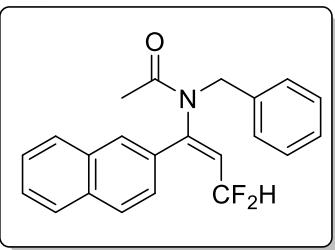
methyl (*E*)-4-(1-(*N*-benzylacetamido)-3,3-difluoroprop-1-en-1-yl)benzoate (**2k**): 48.3 mg, 45% yield, light yellow solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 8.11 (d, *J* = 8.4 Hz, 2H), 7.34 – 7.25 (m, 5H), 7.15 (dd, *J* = 7.4, 2.0 Hz, 2H), 6.03 (td, *J* = 54.6, 7.7 Hz, 1H), 5.64 (q, *J* = 7.9 Hz, 1H), 4.59 (s, 2H), 3.96 (s, 3H), 2.19 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 170.2, 166.0, 147.23 (t, *J* = 14.0 Hz), 137.5, 136.3, 132.0, 130.3, 128.8, 128.59, 128.56, 127.7, 122.58 (t, *J* = 28.0 Hz), 112.46 (t, *J* = 229.5 Hz), 52.5, 50.0, 22.6. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ ppm -107.13 (dd, *J* = 54.3, 8.3 Hz). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> calcd for C<sub>20</sub>H<sub>19</sub>F<sub>2</sub>NNaO<sub>3</sub><sup>+</sup> 382.1225, found 382.1230.



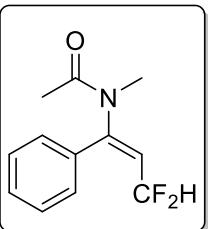
*(E)*-*N*-benzyl-*N*-(3,3-difluoro-1-(4-methoxyphenyl)prop-1-en-1-yl)acetamide (**2l**): 44.9 mg, 45% yield, light yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.33 – 7.22 (m, 3H), 7.21 – 7.14 (m, 4H), 6.99 – 6.93 (m, 2H), 6.07 (td,  $J$  = 54.9, 7.7 Hz, 1H), 5.46 (q,  $J$  = 7.9 Hz, 1H), 4.58 (s, 2H), 3.86 (s, 3H), 2.17 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.3, 161.3, 147.97 (t,  $J$  = 14.0 Hz), 136.7, 130.32 (t,  $J$  = 1.5 Hz), 128.6, 128.4, 127.5, 125.2, 120.19 (t,  $J$  = 27.5 Hz), 114.5, 113.14 (t,  $J$  = 228.5 Hz), 55.4, 49.8, 22.6.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -106.40 (dd,  $J$  = 54.4, 8.1 Hz). HRMS (ESI)  $m/z$ : [M+Na] $^+$  calcd for  $\text{C}_{19}\text{H}_{19}\text{F}_2\text{NNaO}_2^+$  354.1276, found 354.1278.



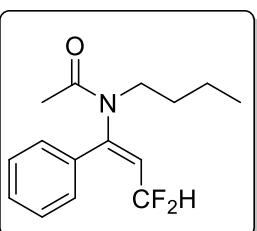
*(E)*-*N*-benzyl-*N*-(3,3-difluoro-1-(naphthalen-1-yl)prop-1-en-1-yl)acetamide (**2m**)<sup>3</sup>: 44.7 mg, 42% yield, light yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.98 – 7.89 (m, 2H), 7.75 (d,  $J$  = 8.3 Hz, 1H), 7.58 – 7.45 (m, 3H), 7.32 (dd,  $J$  = 7.1, 1.2 Hz, 1H), 7.29 – 7.20 (m, 3H), 7.08 – 7.00 (m, 2H), 5.95 – 5.56 (m, 2H), 4.47 (s, 2H), 2.45 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.6, 146.27 (t,  $J$  = 14.0 Hz), 136.9, 133.6, 131.38, 130.9, 129.9, 128.8, 128.7, 128.4, 127.7, 127.5, 127.4, 126.7, 125.0, 124.1, 121.31 (t,  $J$  = 27.5 Hz), 113.17 (t,  $J$  = 228.5 Hz), 49.4, 23.0.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -104.74 – -114.06 (m).



*(E)*-*N*-benzyl-*N*-(3,3-difluoro-1-(naphthalen-2-yl)prop-1-en-1-yl)acetamide (**2n**)<sup>3</sup>: 75.6 mg, 72% yield, yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.93 – 7.85 (m, 3H), 7.73 (d,  $J$  = 1.7 Hz, 1H), 7.62 – 7.56 (m, 2H), 7.34 – 7.26 (m, 4H), 7.19 (dd,  $J$  = 7.7, 1.8 Hz, 2H), 6.13 (td,  $J$  = 54.8, 7.7 Hz, 1H), 5.64 (q,  $J$  = 7.9 Hz, 1H), 4.63 (s, 2H), 2.24 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.4, 148.34 (t,  $J$  = 14.0 Hz), 136.7, 134.0, 132.8, 130.5, 129.41 (t,  $J$  = 2.0 Hz), 129.2, 128.7, 128.5, 127.8, 127.6, 127.2, 124.9, 121.70 (t,  $J$  = 28.0 Hz), 113.04 (t,  $J$  = 229.0 Hz), 50.0, 22.7.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -106.63 (dd,  $J$  = 54.7, 7.9 Hz).

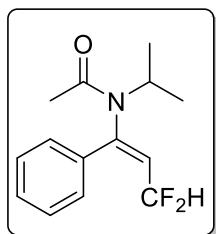


*(E)*-*N*-(3,3-difluoro-1-phenylprop-1-en-1-yl)-*N*-methylacetamide (**2o**): 34.3 mg, 51% yield, light yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.50 – 7.45 (m, 3H), 7.36 – 7.31 (m, 2H), 6.14 (td,  $J$  = 54.8, 7.7 Hz, 1H), 5.76 (q,  $J$  = 7.9 Hz, 1H), 3.02 (s, 3H), 2.12 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.6, 150.10 (t,  $J$  = 14.0 Hz), 133.4, 130.6, 129.1, 128.6, 119.31 (t,  $J$  = 28.0 Hz), 113.16 (t,  $J$  = 229.0 Hz), 35.4, 22.4.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -106.64 (dd,  $J$  = 54.4, 8.1 Hz). HRMS (ESI)  $m/z$ : [M+Na]<sup>+</sup> calcd for  $\text{C}_{12}\text{H}_{13}\text{F}_2\text{NNaO}^+$  248.0857, found 248.0866.

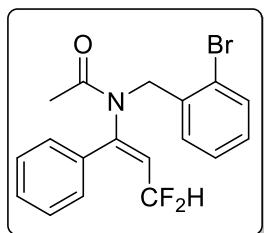


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(*E*)-*N*-butyl-*N*-(3,3-difluoro-1-phenylprop-1-en-1-yl)acetamide (**2p**): 40.4 mg, 50% yield, light yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.50 – 7.43 (m, 3H), 7.37 – 7.31 (m, 2H), 6.14 (td,  $J$  = 54.8, 7.7 Hz, 1H), 5.73 (q,  $J$  = 7.9 Hz, 1H), 3.37 – 3.29 (m, 2H), 2.18 (s, 3H), 1.52 – 1.42 (m, 2H), 1.24 (h,  $J$  = 7.4 Hz, 2H), 0.86 (t,  $J$  = 7.3 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.0, 148.69 (t,  $J$  = 13.5 Hz), 133.1, 130.6, 129.1, 128.70 (t,  $J$  = 1.5 Hz), 120.72 (t,  $J$  = 27.5 Hz), 113.07 (t,  $J$  = 228.5 Hz), 45.8, 29.8, 22.5, 19.9, 13.7.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -106.72 (dd,  $J$  = 54.9, 7.8 Hz). HRMS (ESI)  $m/z$ : [M+Na]<sup>+</sup> calcd for  $\text{C}_{15}\text{H}_{19}\text{F}_2\text{NNaO}^+$  290.1327, found 290.1336.



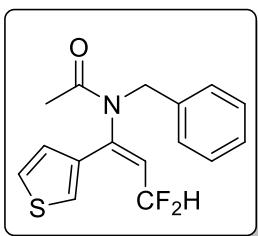
(*E*)-*N*-(3,3-difluoro-1-phenylprop-1-en-1-yl)-*N*-isopropylacetamide (**2q**): 32.9 mg, 43% yield, light yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.49 – 7.42 (m, 3H), 7.39 – 7.34 (m, 2H), 6.18 (td,  $J$  = 54.7, 7.7 Hz, 1H), 5.76 (q,  $J$  = 8.0 Hz, 1H), 4.53 (quint,  $J$  = 6.9 Hz, 1H), 2.15 (s, 3H), 1.04 (d,  $J$  = 6.9 Hz, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 169.7, 147.38 (t,  $J$  = 14.0 Hz), 134.9, 130.5, 128.92 (t,  $J$  = 2.0 Hz), 128.9, 123.30 (t,  $J$  = 27.5 Hz), 112.88 (t,  $J$  = 229.0 Hz), 48.3, 23.4, 20.7.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -106.91 (dd,  $J$  = 54.8, 9.0 Hz). HRMS (ESI)  $m/z$ : [M+Na]<sup>+</sup> calcd for  $\text{C}_{14}\text{H}_{17}\text{F}_2\text{NNaO}^+$  276.1170, found 276.1180.



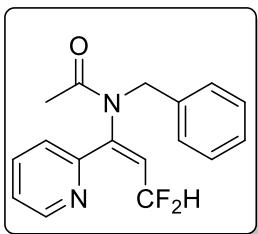
(*E*)-*N*-(2-bromobenzyl)-*N*-(3,3-difluoro-1-phenylprop-1-en-1-yl)acetamide (**2r**)<sup>3</sup>: 77.3 mg, 68% yield, colorless solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.53 – 7.41 (m, 4H), 7.29 – 7.21 (m, 3H), 7.19 – 7.09 (m, 2H), 6.06 (td,  $J$  = 54.8, 7.7 Hz, 1H), 5.70 (q,  $J$  = 7.9 Hz, 1H), 4.76 (s, 2H), 2.22 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.5, 148.30 (t,  $J$

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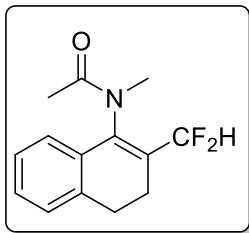
= 14.0 Hz), 135.5, 132.92, 132.86, 130.6, 130.2, 129.1, 128.8, 127.5, 123.5, 121.34 (t, *J* = 27.5 Hz), 112.86 (t, *J* = 229.0 Hz), 50.1, 22.6.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -106.95 (dd, *J* = 54.7, 8.0 Hz).



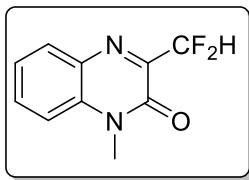
(*E*)-*N*-benzyl-*N*-(3,3-difluoro-1-(thiophen-3-yl)prop-1-en-1-yl)acetamide (**2s**)<sup>3</sup>: 45.9 mg, 50% yield, colorless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.41 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.35 (dd, *J* = 3.0, 1.3 Hz, 1H), 7.32 – 7.25 (m, 3H), 7.23 – 7.16 (m, 2H), 6.96 (dd, *J* = 5.0, 1.4 Hz, 1H), 6.21 (td, *J* = 54.9, 7.3 Hz, 1H), 5.52 (q, *J* = 7.9 Hz, 1H), 4.65 (s, 2H), 2.11 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.0, 143.26 (t, *J* = 14.0 Hz), 136.7, 135.1, 128.8, 128.5, 127.82 (t, *J* = 2.0 Hz), 127.7, 127.6, 126.9, 121.39 (t, *J* = 28.0 Hz), 112.67 (t, *J* = 229.0 Hz), 50.3, 22.5.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -106.95 (dd, *J* = 55.4, 8.4 Hz).



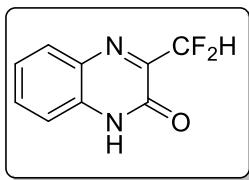
(*E*)-*N*-benzyl-*N*-(3,3-difluoro-1-(pyridin-2-yl)prop-1-en-1-yl)acetamide (**2t**): 34.5 mg, 38% yield, yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.71 (d, *J* = 4.7 Hz, 1H), 7.74 (td, *J* = 7.8, 1.8 Hz, 1H), 7.38 – 7.18 (m, 7H), 7.17 – 6.82 (m, 1H), 5.63 (q, *J* = 8.8 Hz, 1H), 4.69 (s, 2H), 2.08 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.4, 152.2, 150.1, 145.3, 137.2, 136.5, 129.1, 128.5, 127.8, 126.4, 124.3, 122.6, 111.84 (t, *J* = 229.5 Hz), 50.7, 22.4.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -110.46 (d, *J* = 55.6 Hz). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> calcd for  $\text{C}_{17}\text{H}_{16}\text{F}_2\text{N}_2\text{NaO}^+$  325.1123, found 325.1126.



*N*-(2-(difluoromethyl)-3,4-dihydronaphthalen-1-yl)-*N*-methylacetamide (**2u**)<sup>3</sup>: 48.5 mg, 64% yield, colorless solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 7.35 – 7.21 (m, 3H), 7.06 (dd, *J* = 7.4, 1.3 Hz, 1H), 6.44 (t, *J* = 55.4 Hz, 1H), 3.14 (s, 3H), 2.93 (t, *J* = 8.1 Hz, 2H), 2.69 – 2.50 (m, 2H), 1.94 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 171.0, 141.04 (t, *J* = 10.0 Hz), 137.3, 129.9, 129.00 (t, *J* = 24.5 Hz), 128.3, 127.3, 123.3, 112.05 (t, *J* = 231.0 Hz), 35.8, 26.7, 21.2, 19.39 (t, *J* = 2.5 Hz). <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ ppm -115.56 -- 120.87 (m).



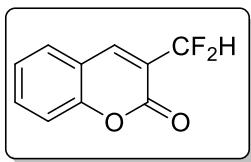
3-(difluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**4a**)<sup>4</sup>: 46.7 mg, 74% yield, light yellow solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 8.00 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.69 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 7.44 (ddd, *J* = 8.2, 7.3, 1.2 Hz, 1H), 7.39 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.96 (t, *J* = 53.7 Hz, 1H), 3.74 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 153.2, 148.61 (t, *J* = 22.0 Hz), 148.4, 134.0, 132.6, 131.9, 131.4, 124.4, 110.06 (t, *J* = 240.5 Hz), 29.0. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ ppm -124.37 (d, 54.6 Hz).



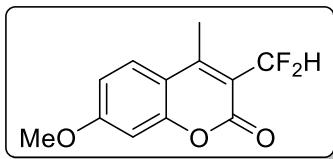
3-(difluoromethyl)quinoxalin-2(1*H*)-one (**4b**)<sup>4</sup>: 43.5 mg, 74% yield, light yellow solid. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ ppm 12.87 (s, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 2H), 7.07 (t, *J* = 53.3 Hz, 1H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ ppm 153.7, 150.26 (t, *J* = 21.5 Hz), 150.0, 133.4, 132.8, 131.2, 130.0, 124.4, 116.3,

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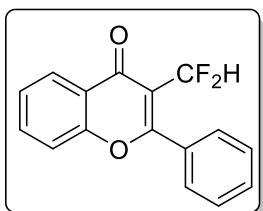
110.86 (t,  $J$  = 238.0 Hz).  $^{19}\text{F}$  NMR (376 MHz, DMSO- $d_6$ )  $\delta$  ppm -124.32 (d, 52.9 Hz).



3-(difluoromethyl)-2H-chromen-2-one (**4c**)<sup>5</sup>: 20.7 mg, 35% yield, colorless solid.  $^1\text{H}$  NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 8.08 (s, 1H), 7.69 – 7.58 (m, 2H), 7.43 – 7.32 (m, 2H), 6.76 (t,  $J$  = 54.7 Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 158.6, 154.1, 141.34 (t,  $J$  = 6.0 Hz), 133.5, 129.1, 125.1, 121.52 (t,  $J$  = 23.5 Hz), 117.7, 116.9, 110.10 (t,  $J$  = 237.5 Hz).  $^{19}\text{F}$  NMR (376 MHz, CDCl<sub>3</sub>)  $\delta$  ppm -119.41 (d,  $J$  = 55.0 Hz).

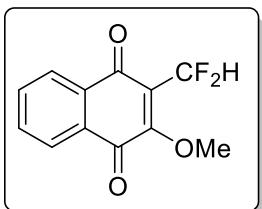


3-(difluoromethyl)-7-methoxy-4-methyl-2H-chromen-2-one (**4d**): 54.6 mg, 76% yield, colorless solid.  $^1\text{H}$  NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 7.66 (d,  $J$  = 9.0 Hz, 1H), 7.08 (t,  $J$  = 53.9 Hz, 1H), 6.92 (dd,  $J$  = 9.0, 2.5 Hz, 1H), 6.80 (d,  $J$  = 2.5 Hz, 1H), 3.90 (s, 3H), 2.64 (t,  $J$  = 1.9 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 163.9, 160.02 (t,  $J$  = 6.0 Hz), 155.0, 154.8, 126.6, 114.91 (t,  $J$  = 23.0 Hz), 113.3, 113.2, 112.31 (t,  $J$  = 235.5 Hz), 100.6, 55.8, 14.8.  $^{19}\text{F}$  NMR (376 MHz, CDCl<sub>3</sub>)  $\delta$  ppm -113.00 (d,  $J$  = 54.4 Hz). HRMS (ESI)  $m/z$ : [M+Na]<sup>+</sup> calcd for C<sub>12</sub>H<sub>10</sub>F<sub>2</sub>NaO<sub>3</sub><sup>+</sup> 263.0490, found 263.0500.

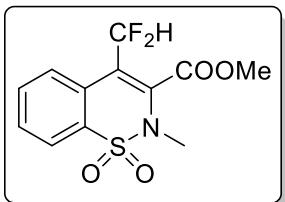


3-(difluoromethyl)-2-phenyl-4H-chromen-4-one (**4e**): 41.6 mg, 51% yield, colorless solid.  $^1\text{H}$  NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 8.27 (dd,  $J$  = 8.0, 1.7 Hz, 1H), 7.77 – 7.69 (m, 3H), 7.64 – 7.43 (m, 5H), 6.89 (t,  $J$  = 53.7 Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  ppm

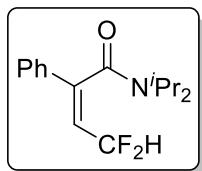
175.78 (t,  $J$  = 2.0 Hz), 166.64 (t,  $J$  = 3.5 Hz), 155.9, 134.5, 131.6, 131.4, 129.03 (t,  $J$  = 2.0 Hz), 128.5, 125.9, 125.8, 123.2, 118.1, 114.87 (t,  $J$  = 21.5 Hz), 111.86 (t,  $J$  = 236.5 Hz).  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -113.07 (d,  $J$  = 53.7 Hz). HRMS (ESI)  $m/z$ : [M+Na] $^+$  calcd for  $\text{C}_{16}\text{H}_{10}\text{F}_2\text{NaO}_2^+$  295.0541, found 295.0551.



**2-(difluoromethyl)-3-methoxynaphthalene-1,4-dione (4f):** 25.1 mg, 35% yield, brown solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.15 – 8.04 (m, 2H), 7.82 – 7.72 (m, 2H), 6.99 (t,  $J$  = 53.6 Hz, 1H), 4.34 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 182.21 (t,  $J$  = 2.5 Hz), 181.5, 159.73 (t,  $J$  = 2.5 Hz), 134.8, 133.7, 131.1, 126.5, 126.4, 121.43 (t,  $J$  = 20.5 Hz), 110.22 (t,  $J$  = 236.5 Hz), 62.4.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -119.57 (d,  $J$  = 54.0 Hz). HRMS (ESI)  $m/z$ : [M+Na] $^+$  calcd for  $\text{C}_{12}\text{H}_8\text{F}_2\text{NaO}_3^+$  261.0334, found 261.0338.



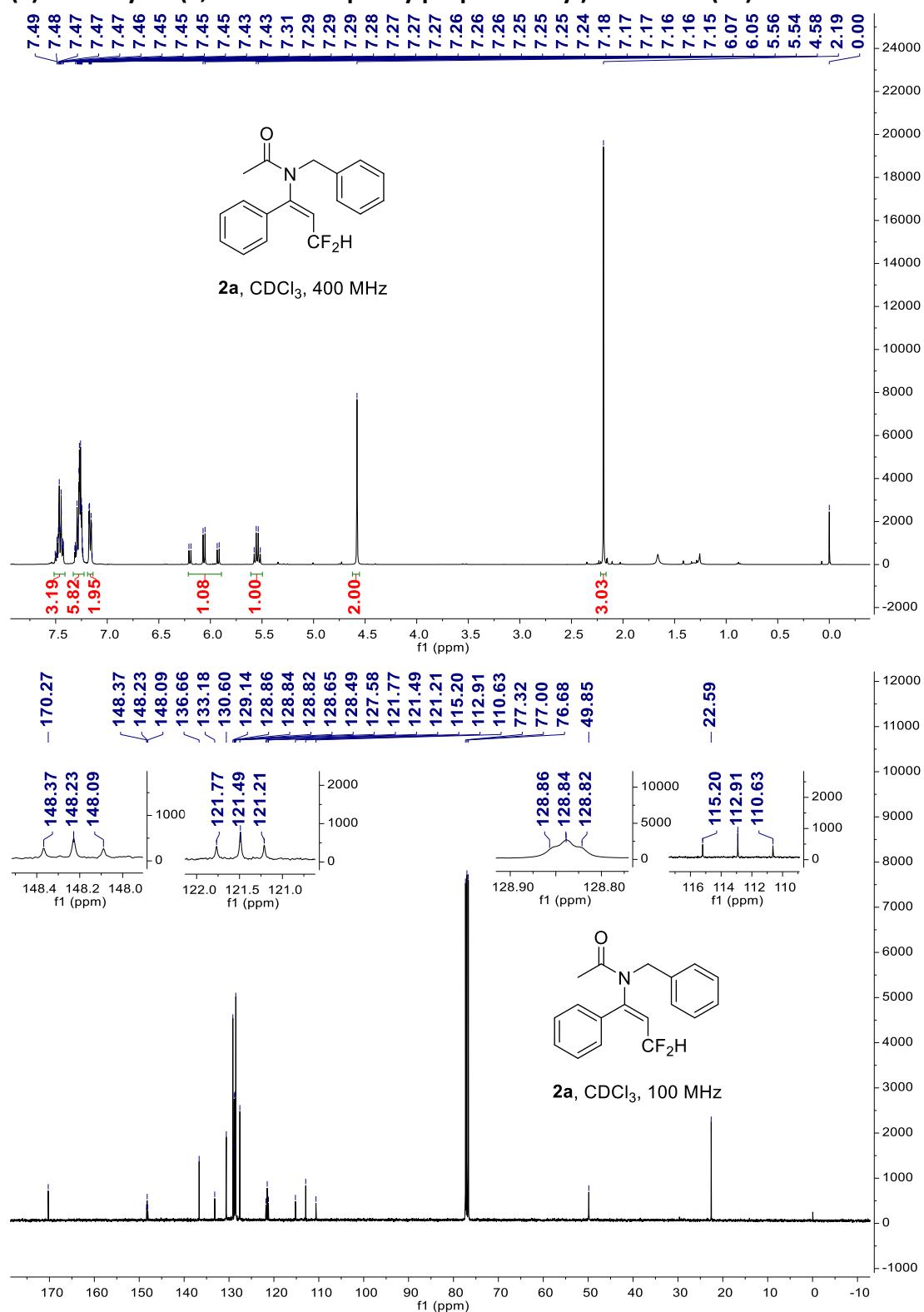
**methyl 4-(difluoromethyl)-2-methyl-2H-benzo[e][1,2]thiazine-3-carboxylate 1,1-dioxide (4g):** 1.48 g, 81% yield, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.07 (d,  $J$  = 7.6 Hz, 1H), 7.93 (dd,  $J$  = 7.6, 1.3 Hz, 1H), 7.75 – 7.61 (m, 2H), 6.93 (t,  $J$  = 52.9 Hz, 1H), 4.01 (s, 3H), 3.21 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 161.91, 135.75 (t,  $J$  = 8.5 Hz), 133.4, 132.0, 130.3, 128.1, 127.96 (t,  $J$  = 4.0 Hz), 122.22 (t,  $J$  = 25.0 Hz), 122.0, 112.56 (t,  $J$  = 236.5 Hz), 53.7, 35.2.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm -108.70 (d,  $J$  = 52.7 Hz). HRMS (ESI)  $m/z$ : [M+Na] $^+$  calcd for  $\text{C}_{12}\text{H}_{11}\text{F}_2\text{NNaO}_4\text{S}^+$  326.0269, found 326.0279.

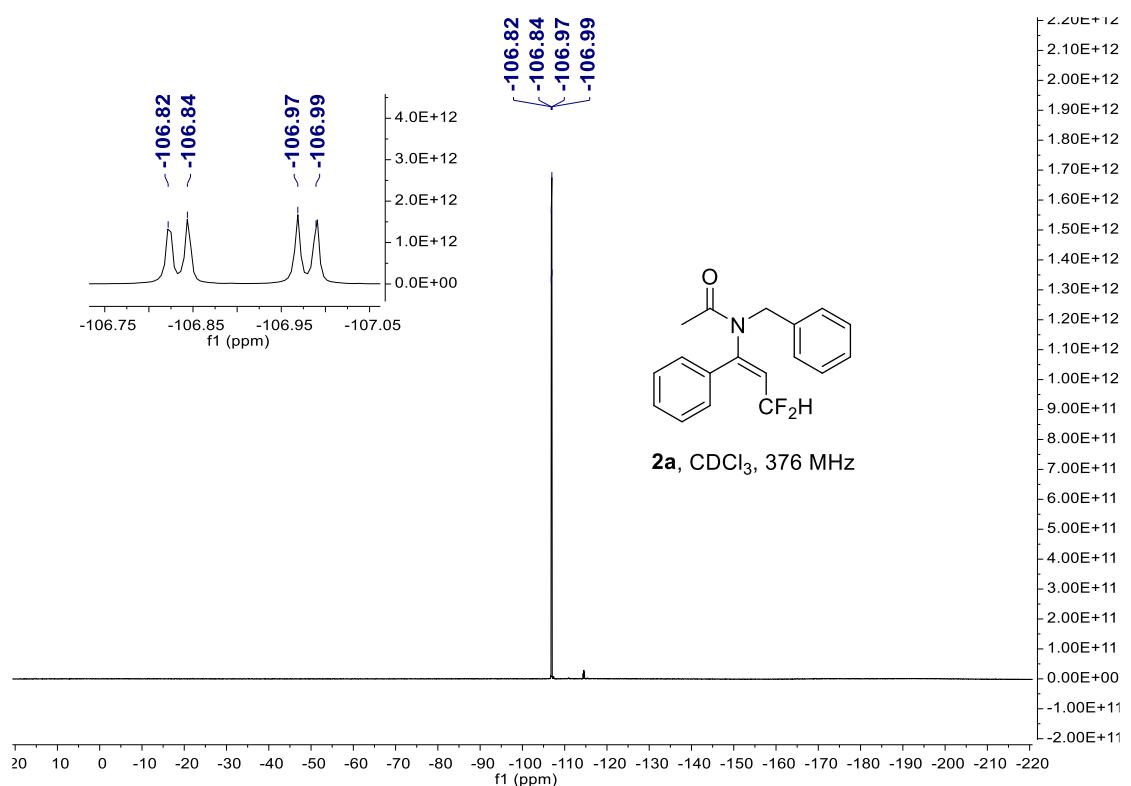


(*Z*)-4,4-difluoro-*N,N*-diisopropyl-2-phenylbut-2-enamide (**4h**)<sup>6</sup>: 68.3 mg, 81% yield, (*Z/E* = 87:13), light yellow oil. For major (*Z*)-isomer: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 7.50 – 7.43 (m, 2H), 7.43 – 7.36 (m, 3H), 6.41 (td, *J* = 55.5, 6.9 Hz, 1H), 6.06 – 5.97 (m, 1H), 3.79 (dt, *J* = 13.3, 6.7 Hz, 1H), 3.43 (hept, *J* = 6.8 Hz, 1H), 1.55 (d, *J* = 6.8 Hz, 6H), 0.92 (br, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 166.3, 146.98 (t, *J* = 12.5 Hz), 134.0, 129.7, 129.0, 126.1, 118.37 (t, *J* = 26.0 Hz), 113.12 (t, *J* = 231.0 Hz), 50.8, 46.0, 20.1, 19.9. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ ppm -106.96 (d, *J* = 318.4 Hz), -111.93 (d, *J* = 326.8 Hz).

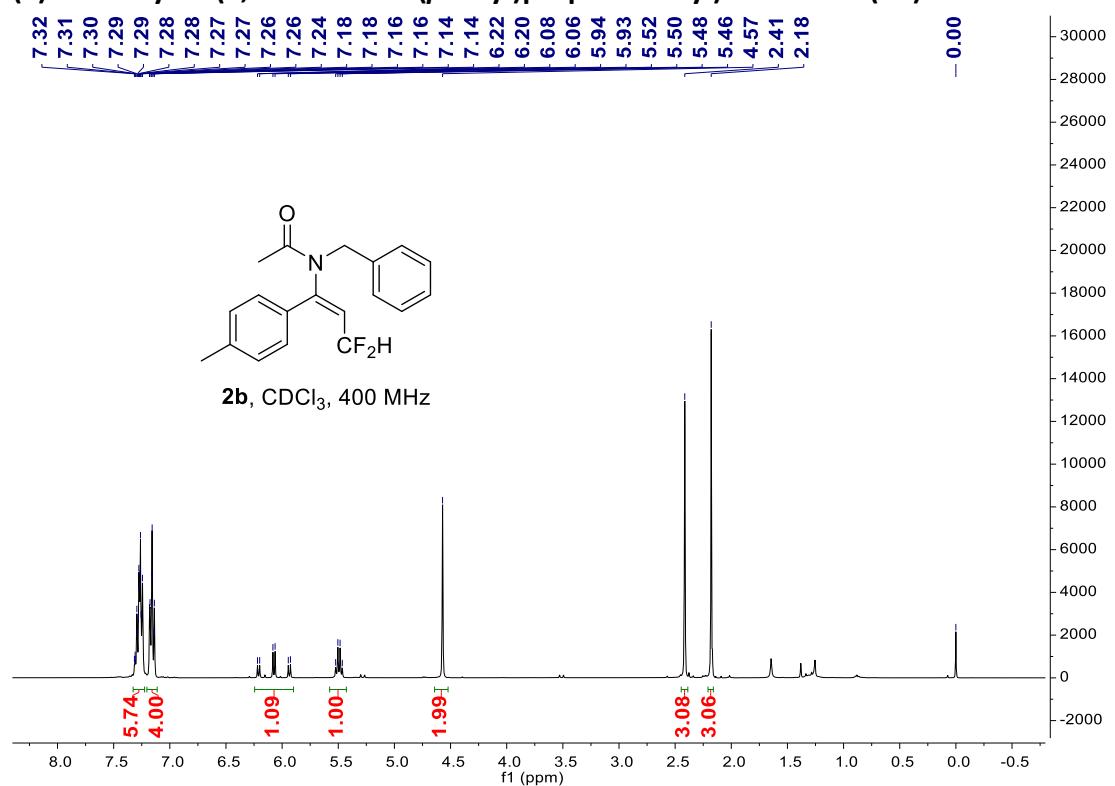
*<sup>1</sup>H, <sup>19</sup>F and <sup>13</sup>C NMR spectra of products:*

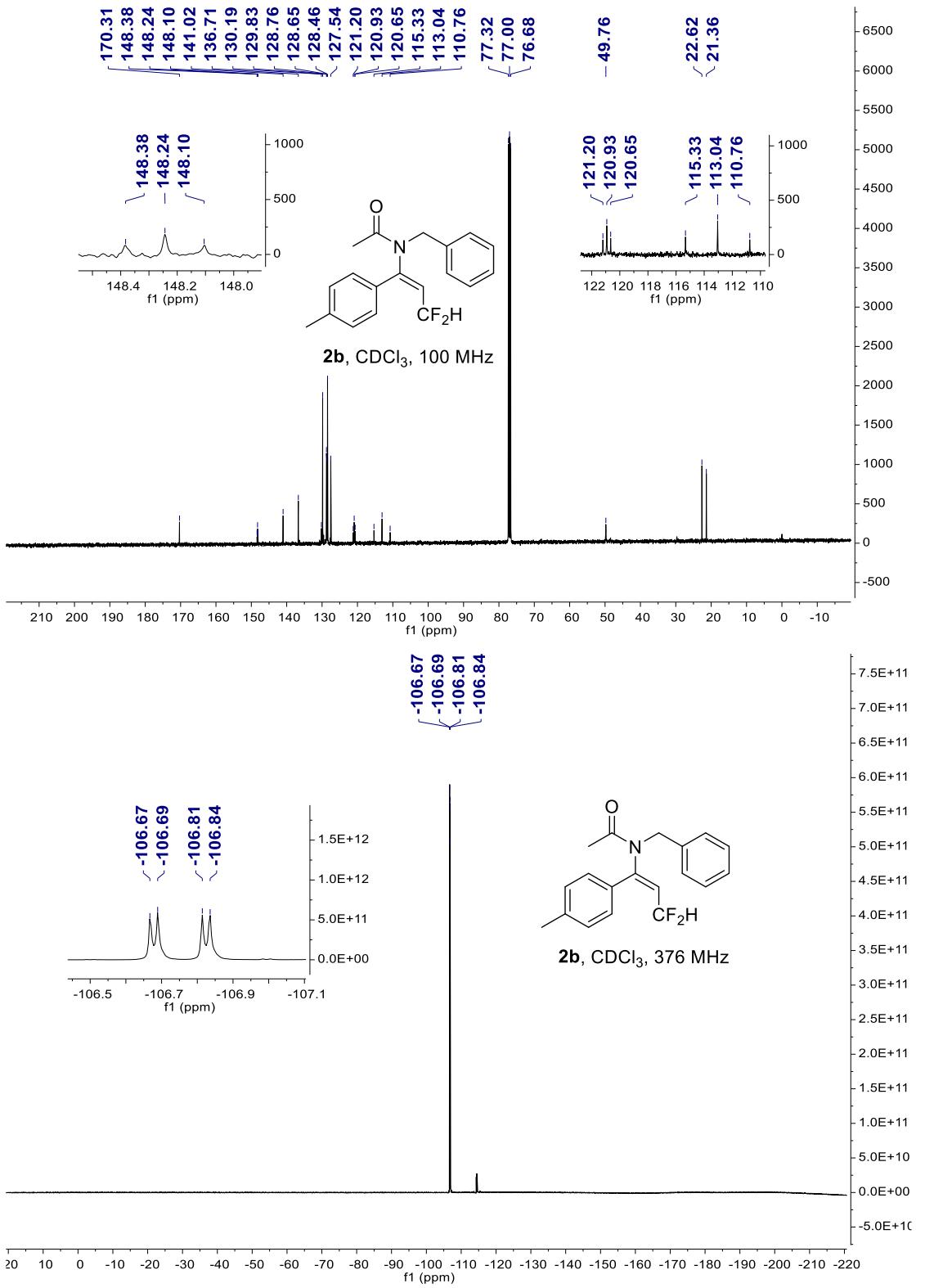
**(E)-N-benzyl-N-(3,3-difluoro-1-phenylprop-1-en-1-yl)acetamide (2a)**



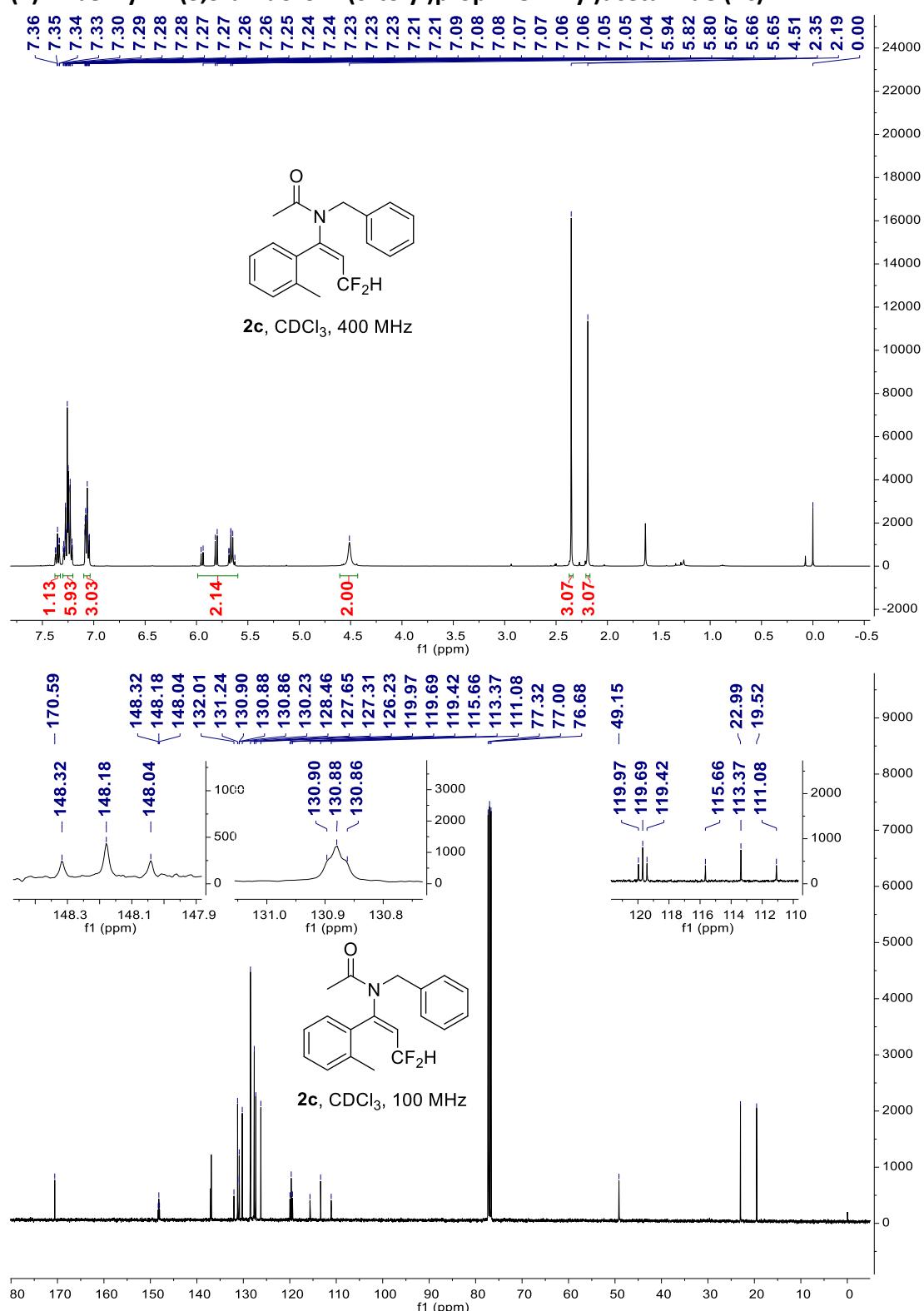


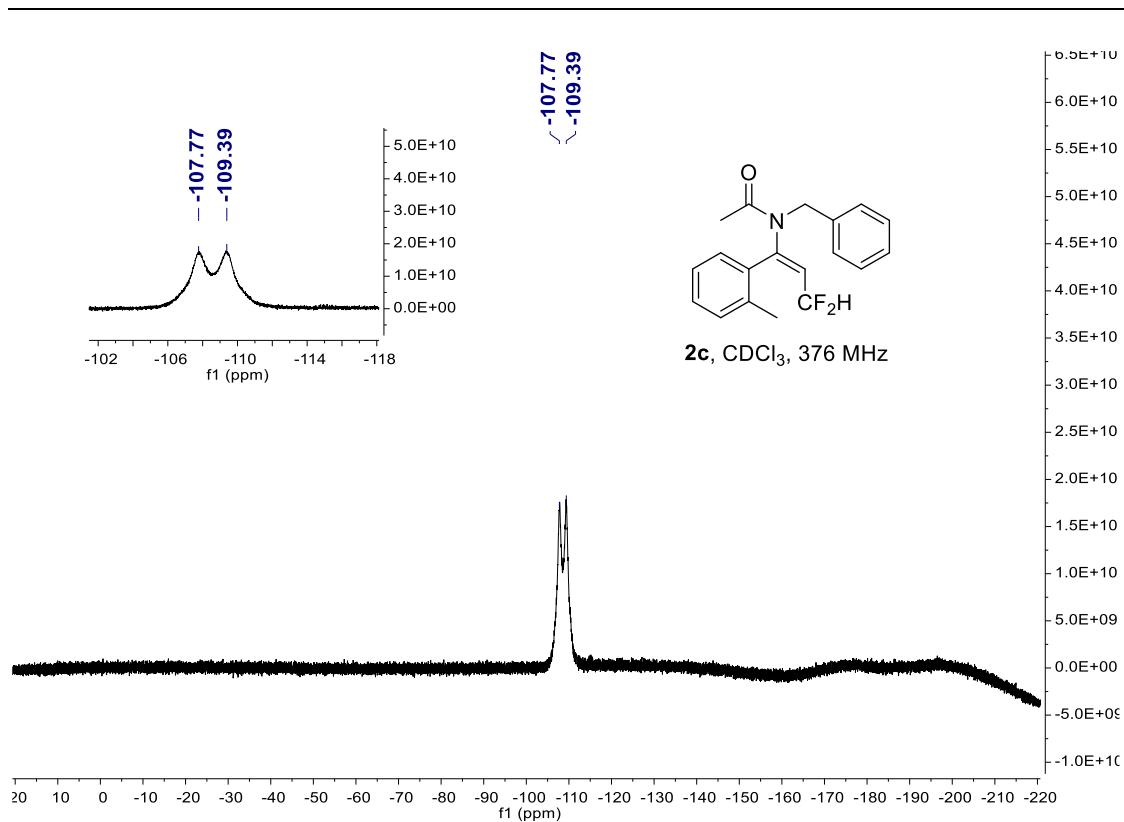
**(E)-N-benzyl-N-(3,3-difluoro-1-(p-tolyl)prop-1-en-1-yl)acetamide (2b)**



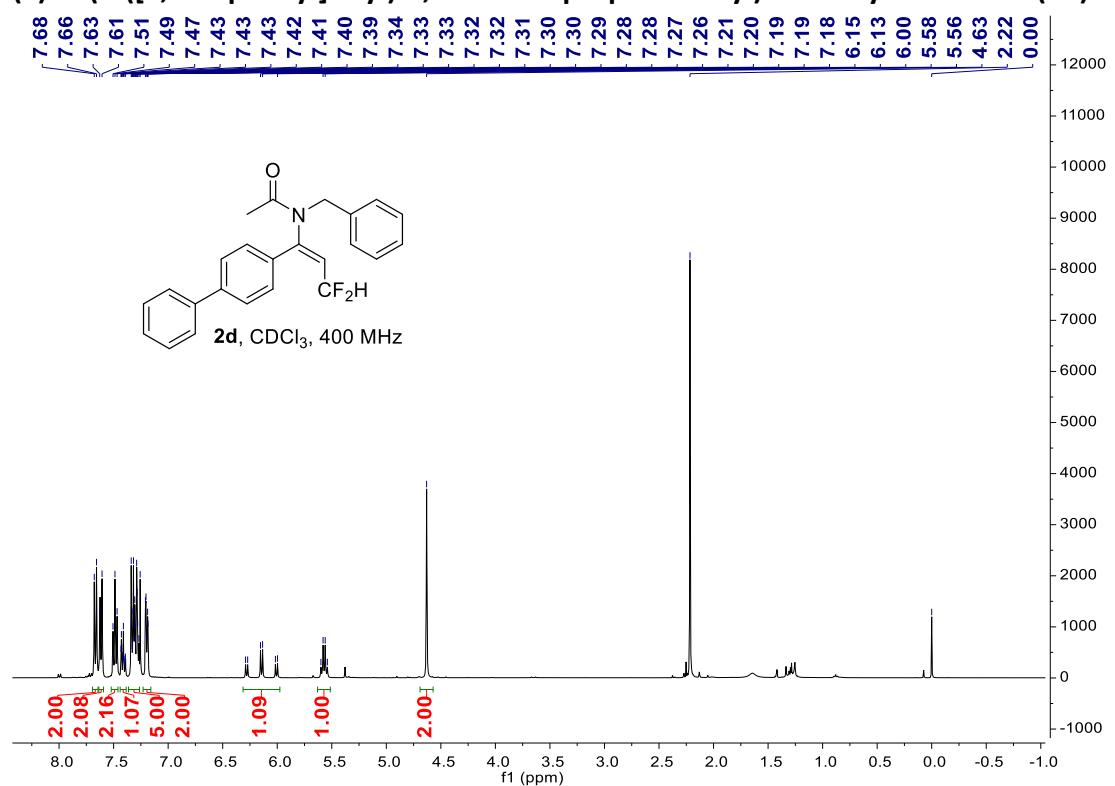


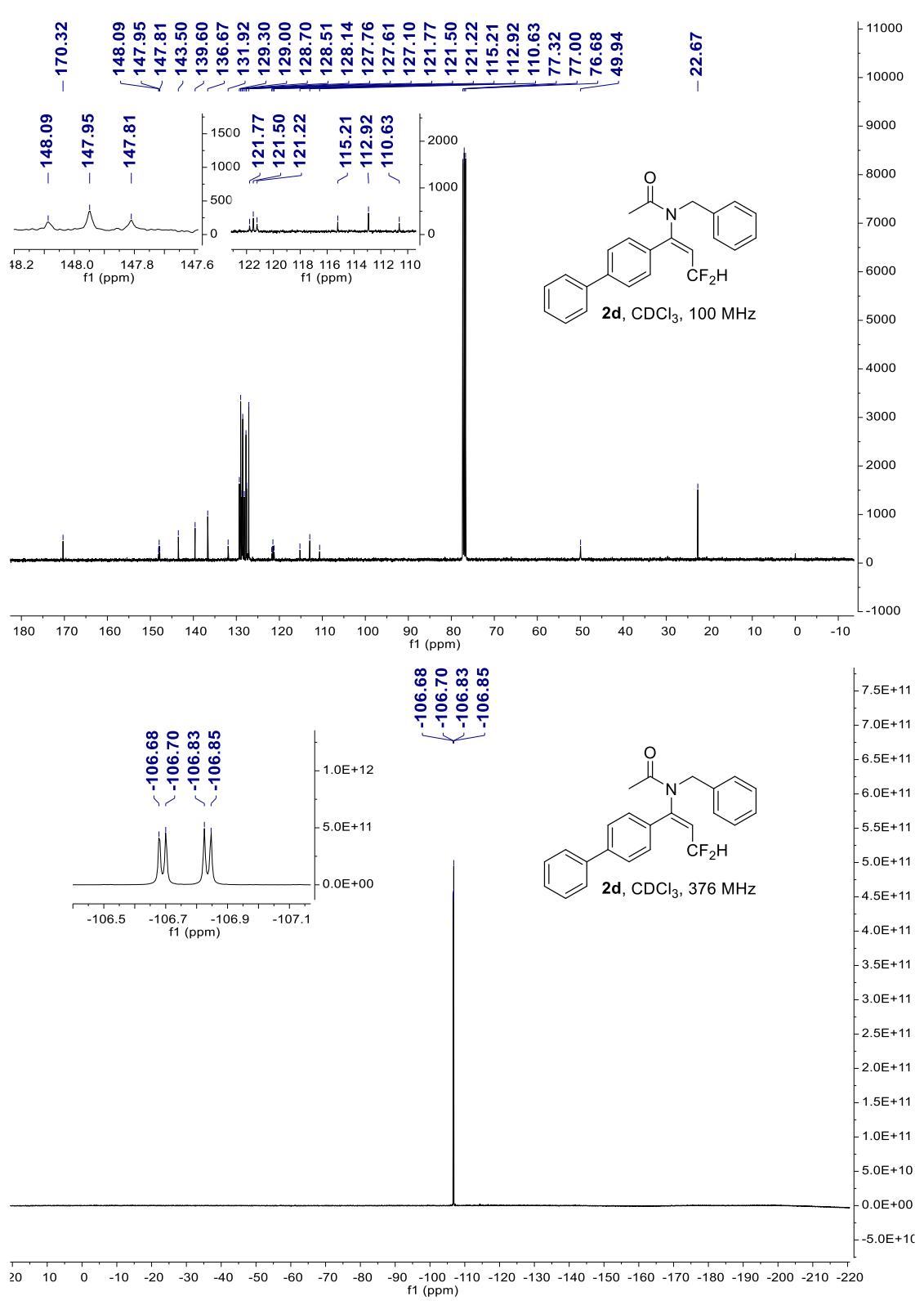
**(E)-N-benzyl-N-(3,3-difluoro-1-(*o*-tolyl)prop-1-en-1-yl)acetamide (2c)**



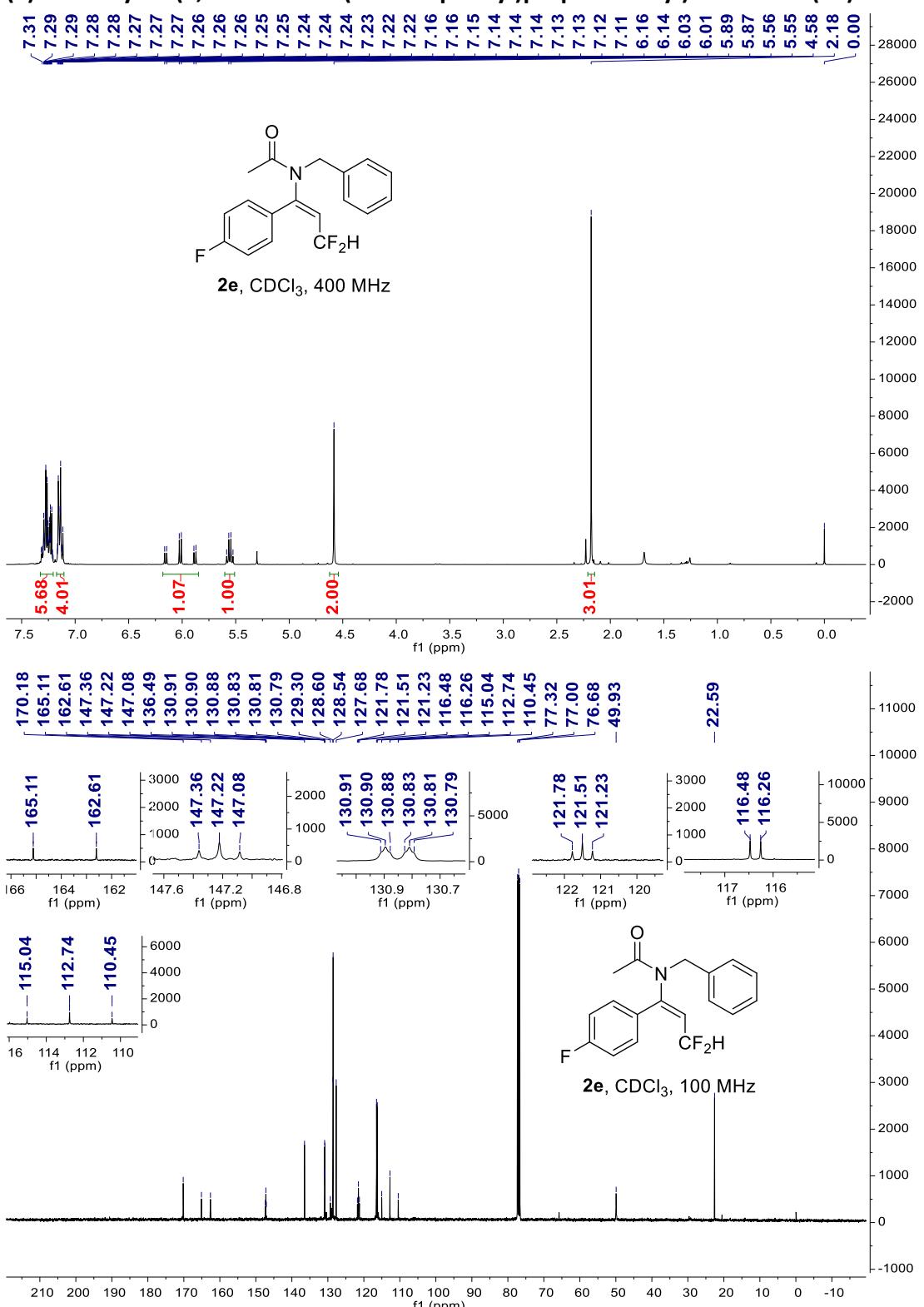


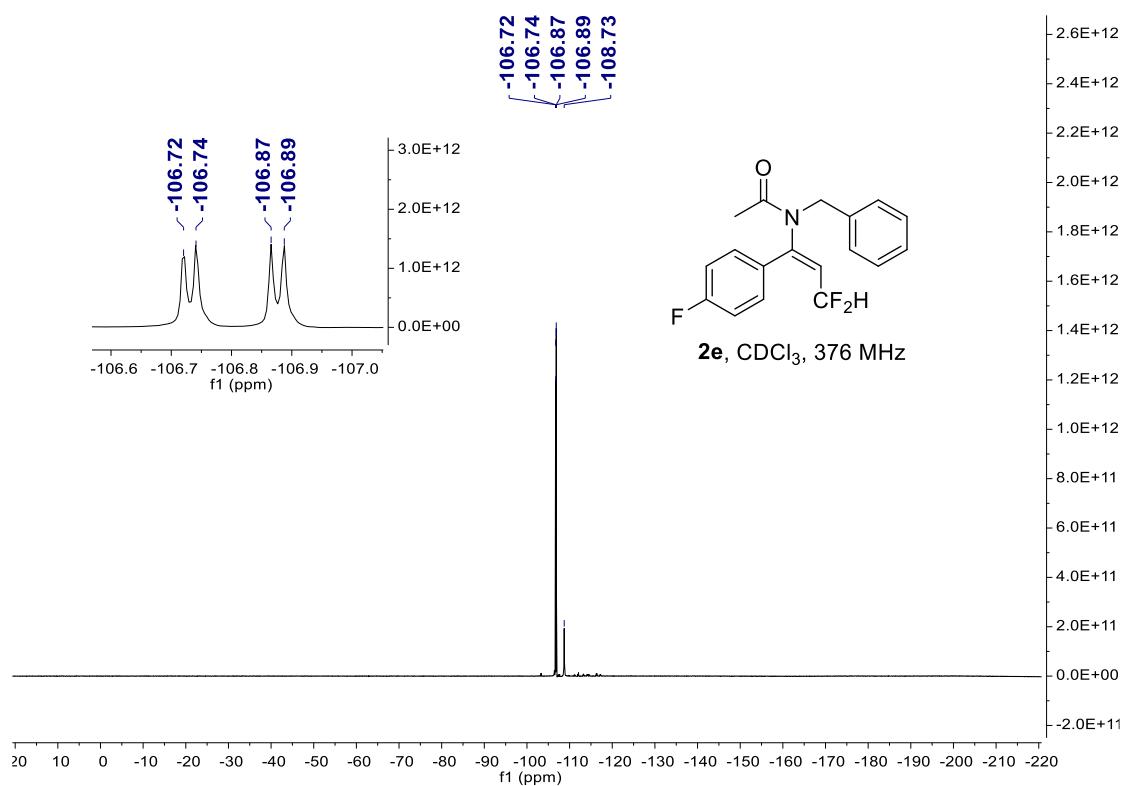
**(E)-N-(1-([1,1'-biphenyl]-4-yl)-3,3-difluoroprop-1-en-1-yl)-N-benzylacetamide (2d)**



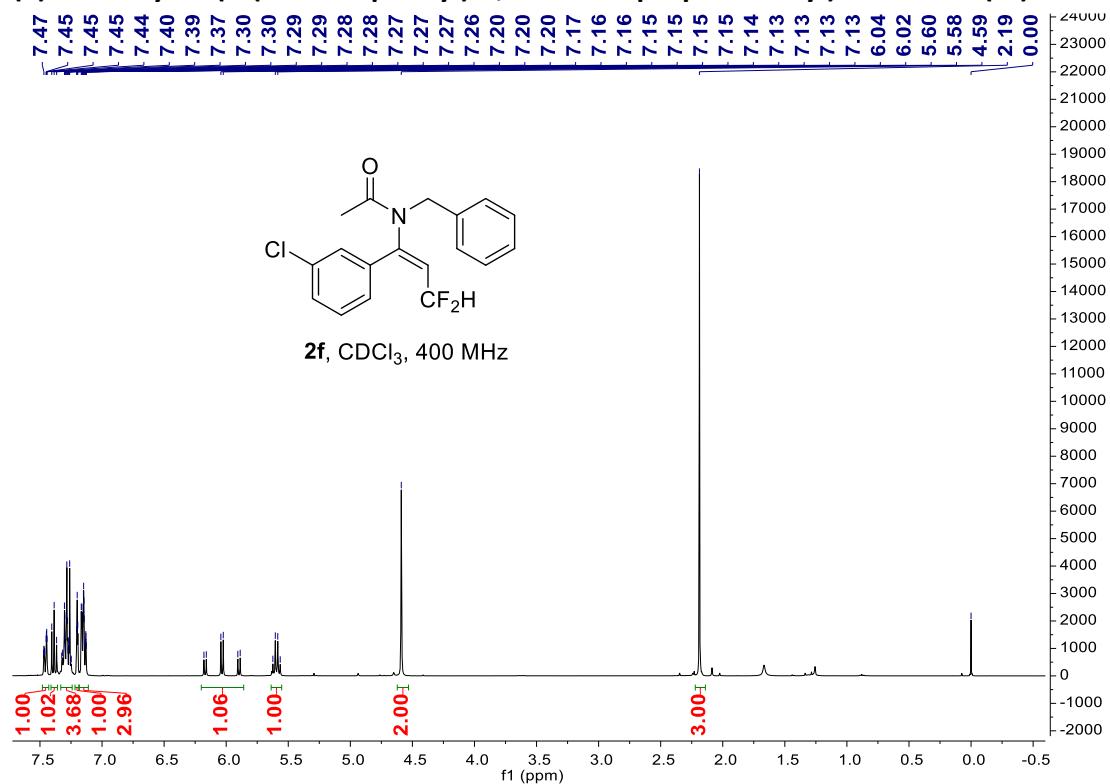


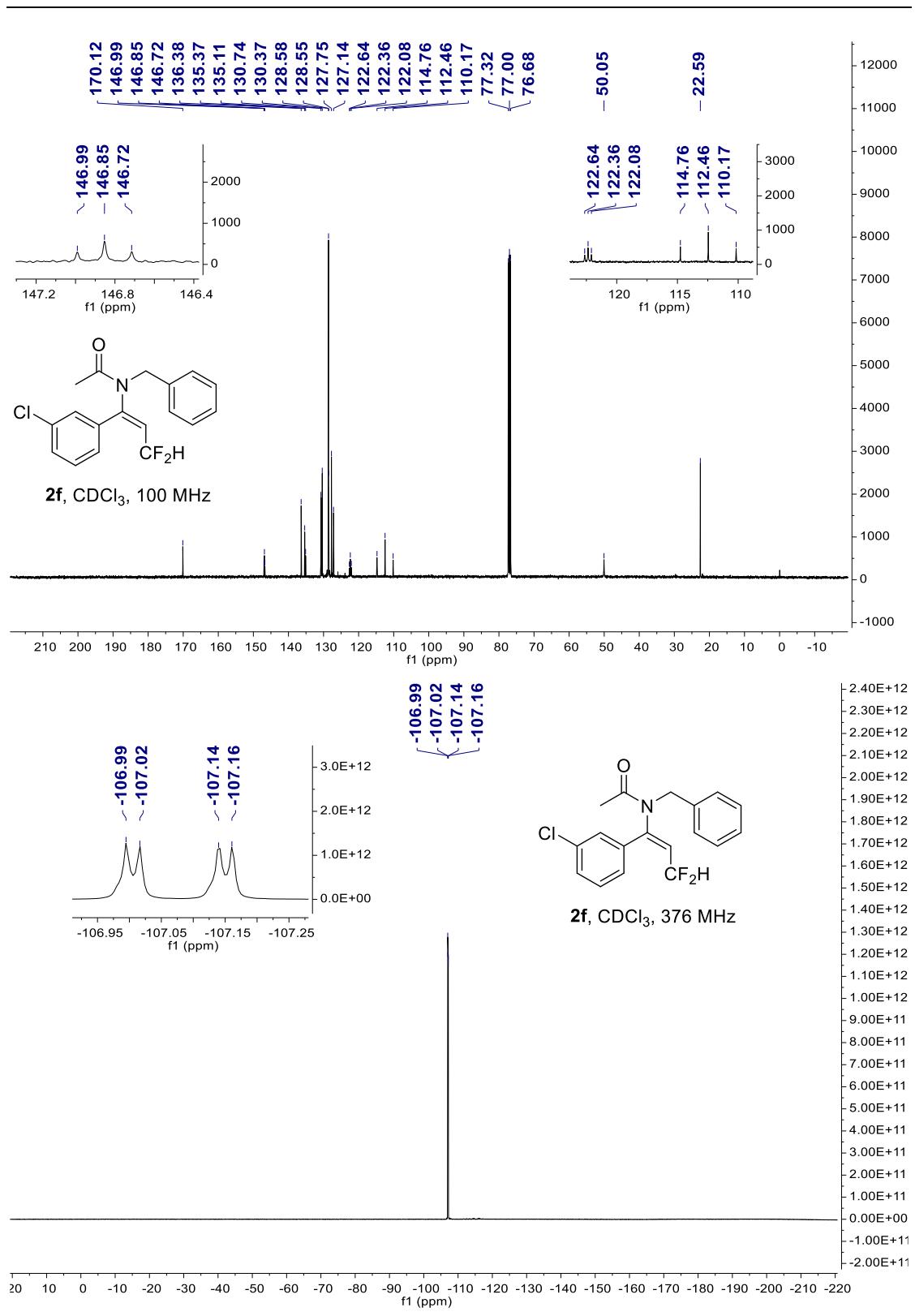
**(E)-N-benzyl-N-(3,3-difluoro-1-(4-fluorophenyl)prop-1-en-1-yl)acetamide (2e)**



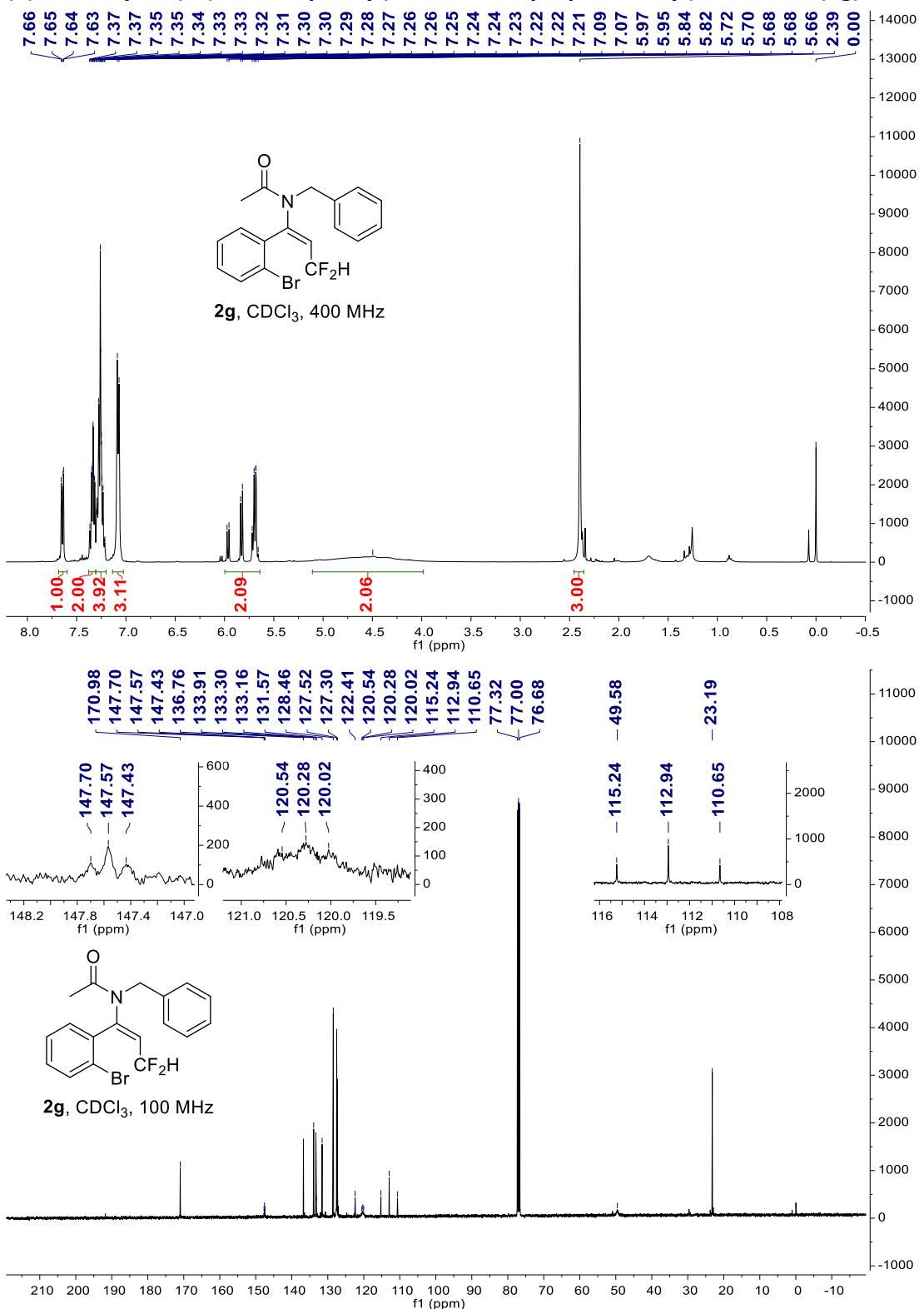


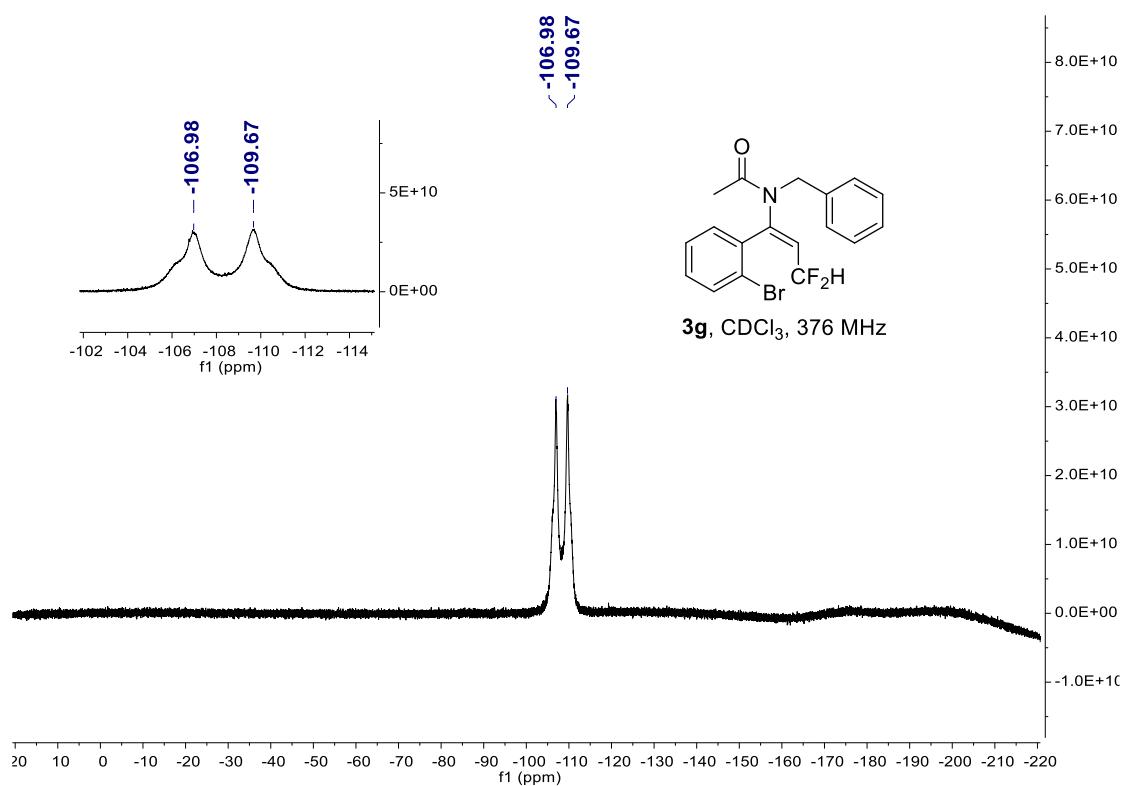
**(E)-N-benzyl-N-(1-(3-chlorophenyl)-3,3-difluoroprop-1-en-1-yl)acetamide (2f)**



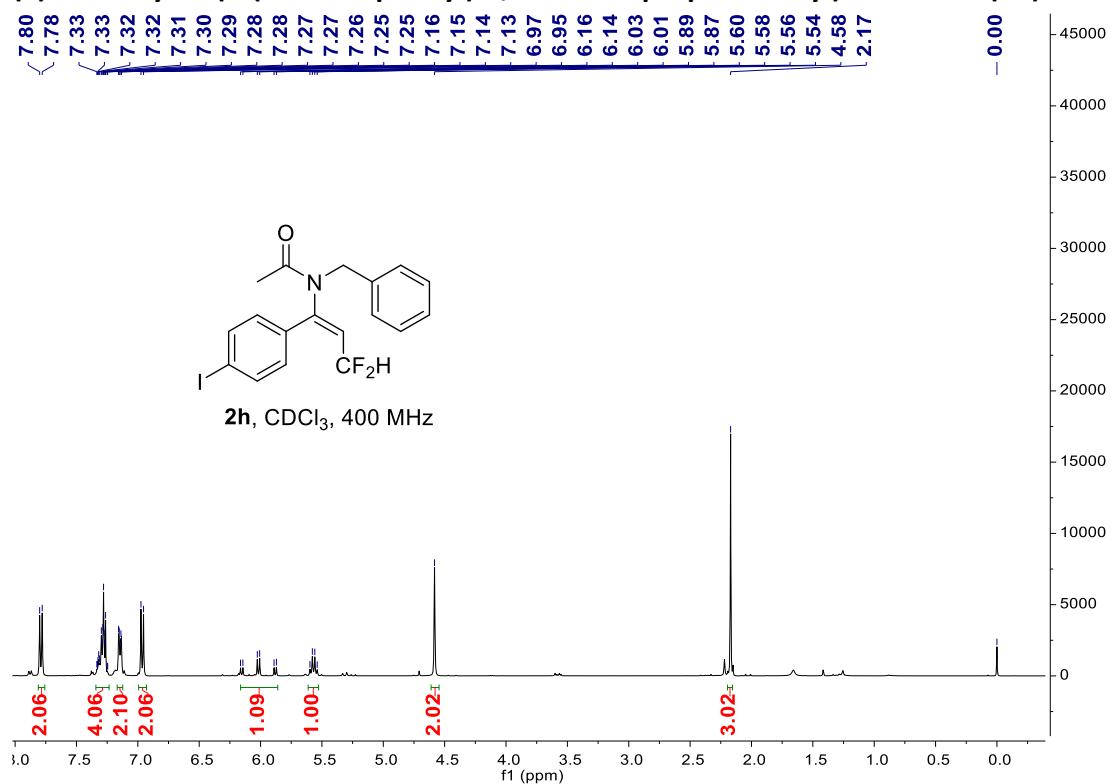


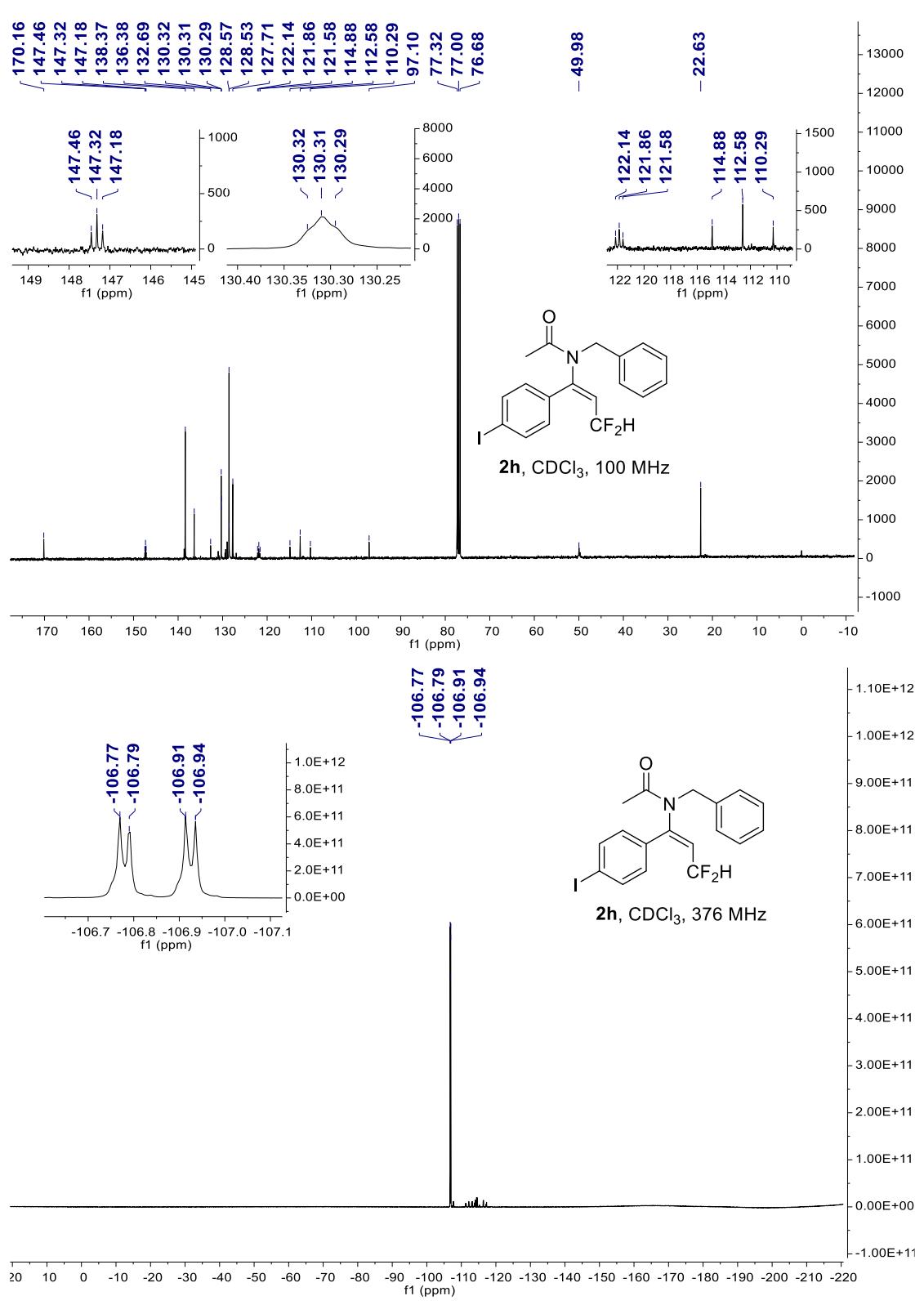
**(E)-N-benzyl-N-(1-(2-bromophenyl)-3,3-difluoroprop-1-en-1-yl)acetamide (2g)**





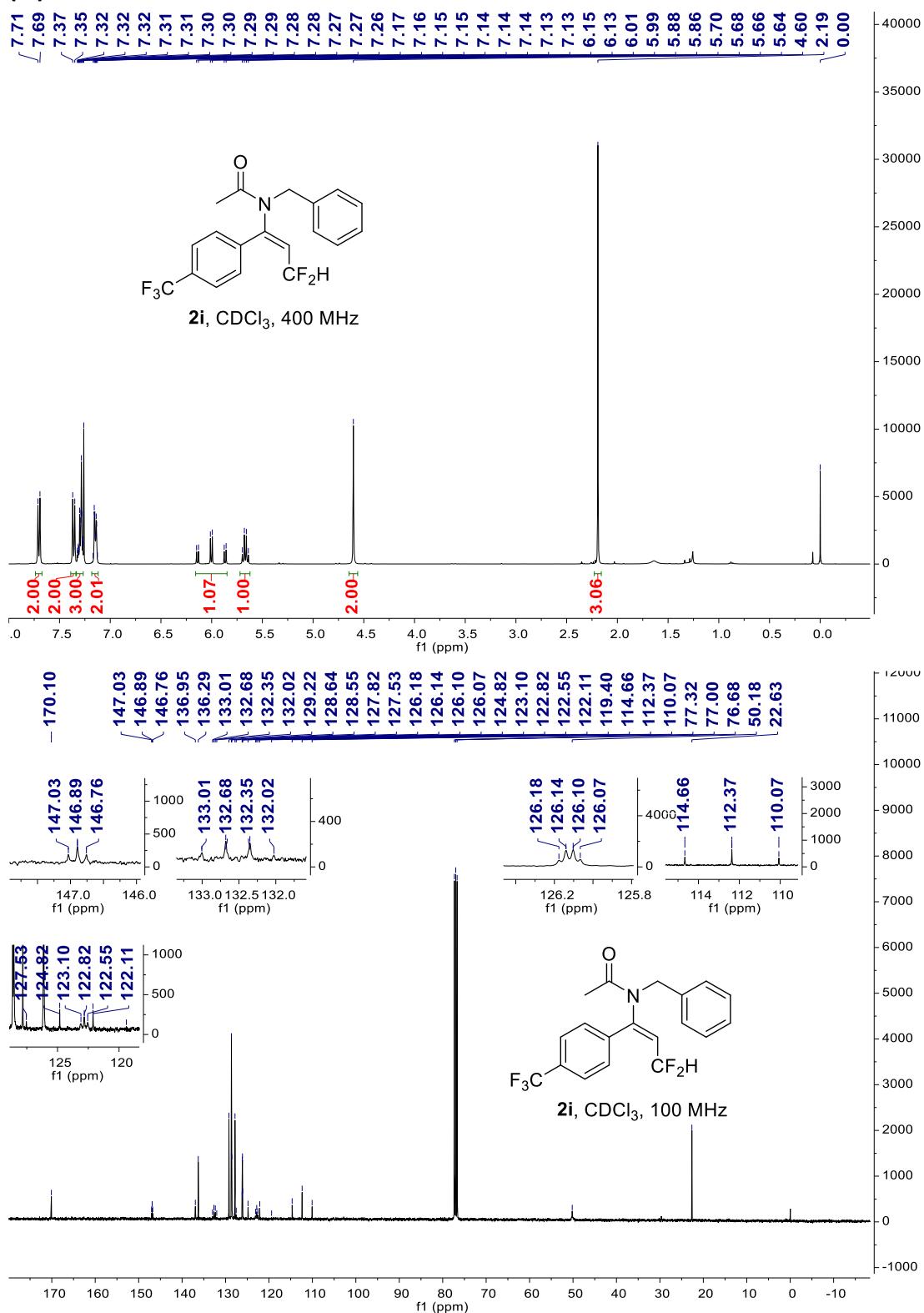
**(E)-N-benzyl-N-(1-(2-bromophenyl)-3,3-difluoroprop-1-en-1-yl)acetamide (3h)**

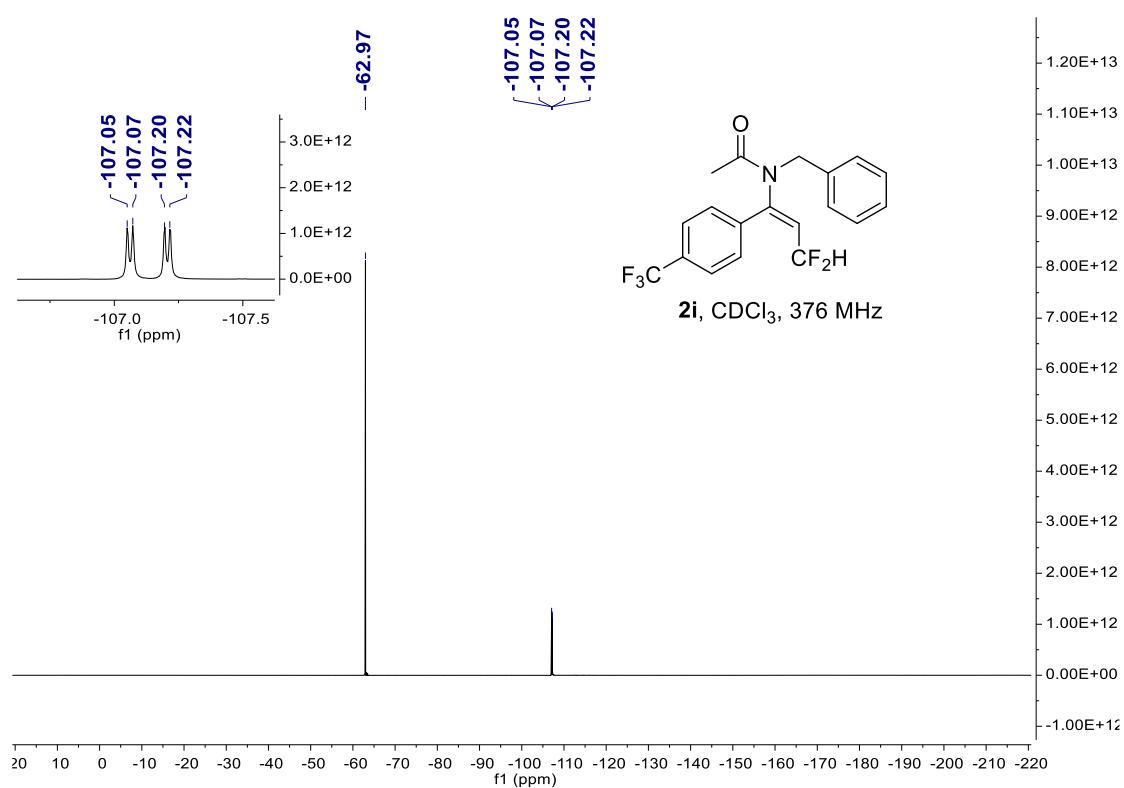




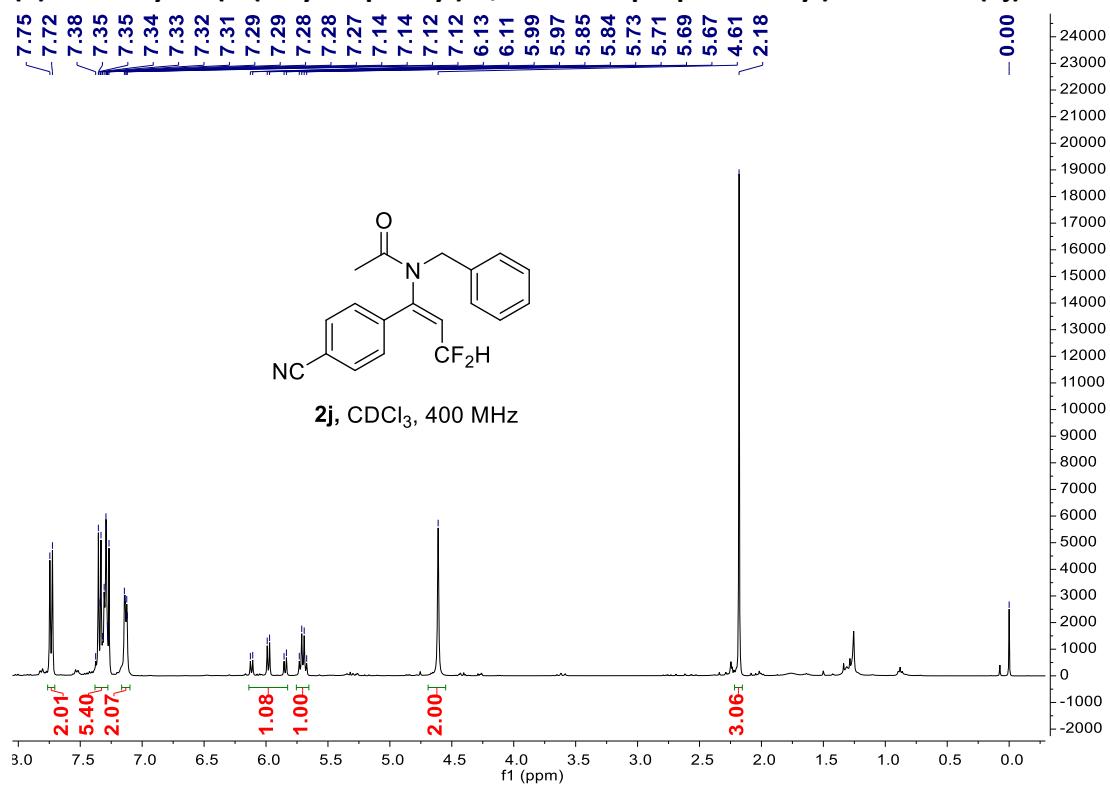
*(E)*-*N*-benzyl-*N*-(3,3-difluoro-1-(4-(trifluoromethyl)phenyl)prop-1-en-1-yl)acetamide

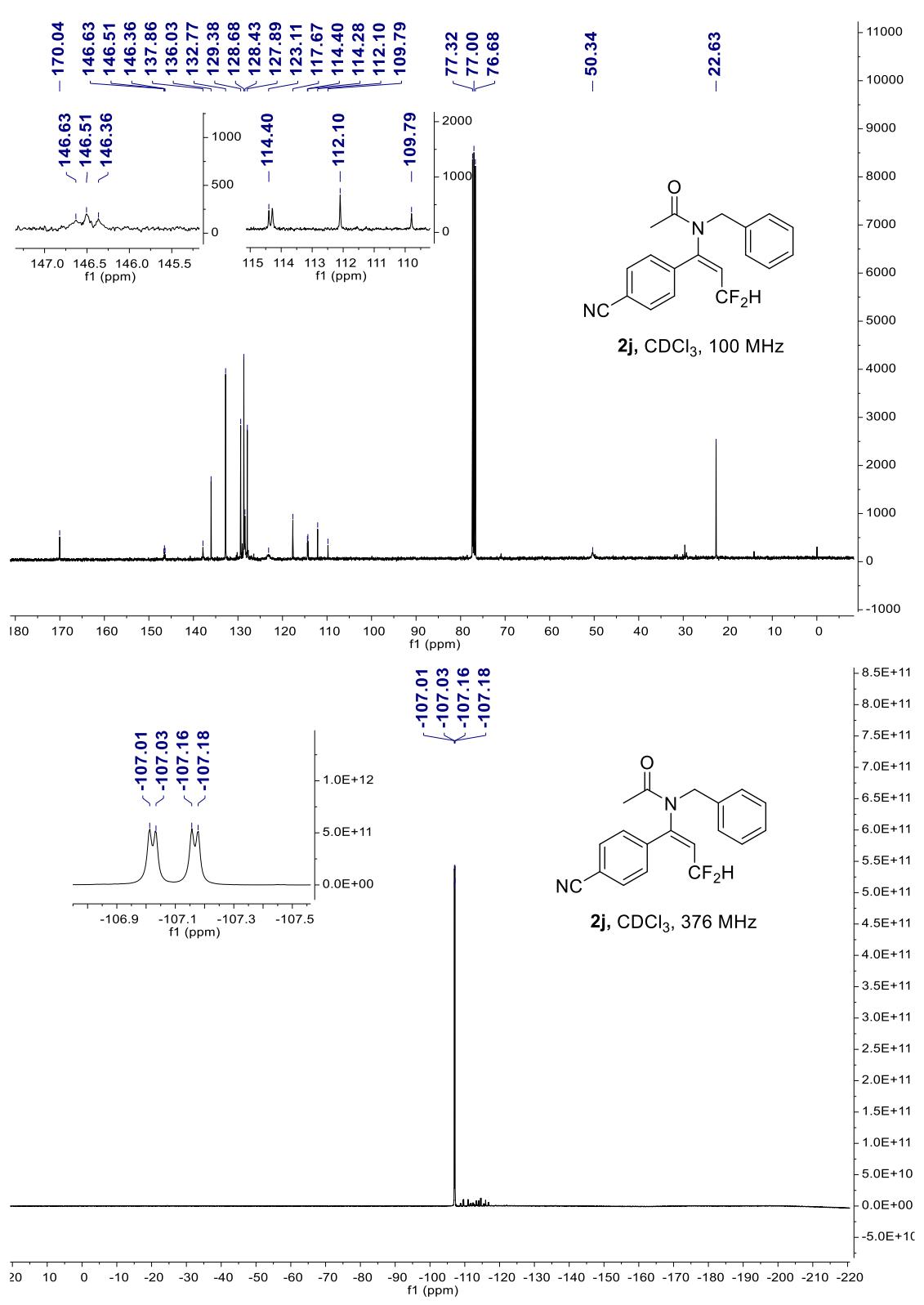
(2i)



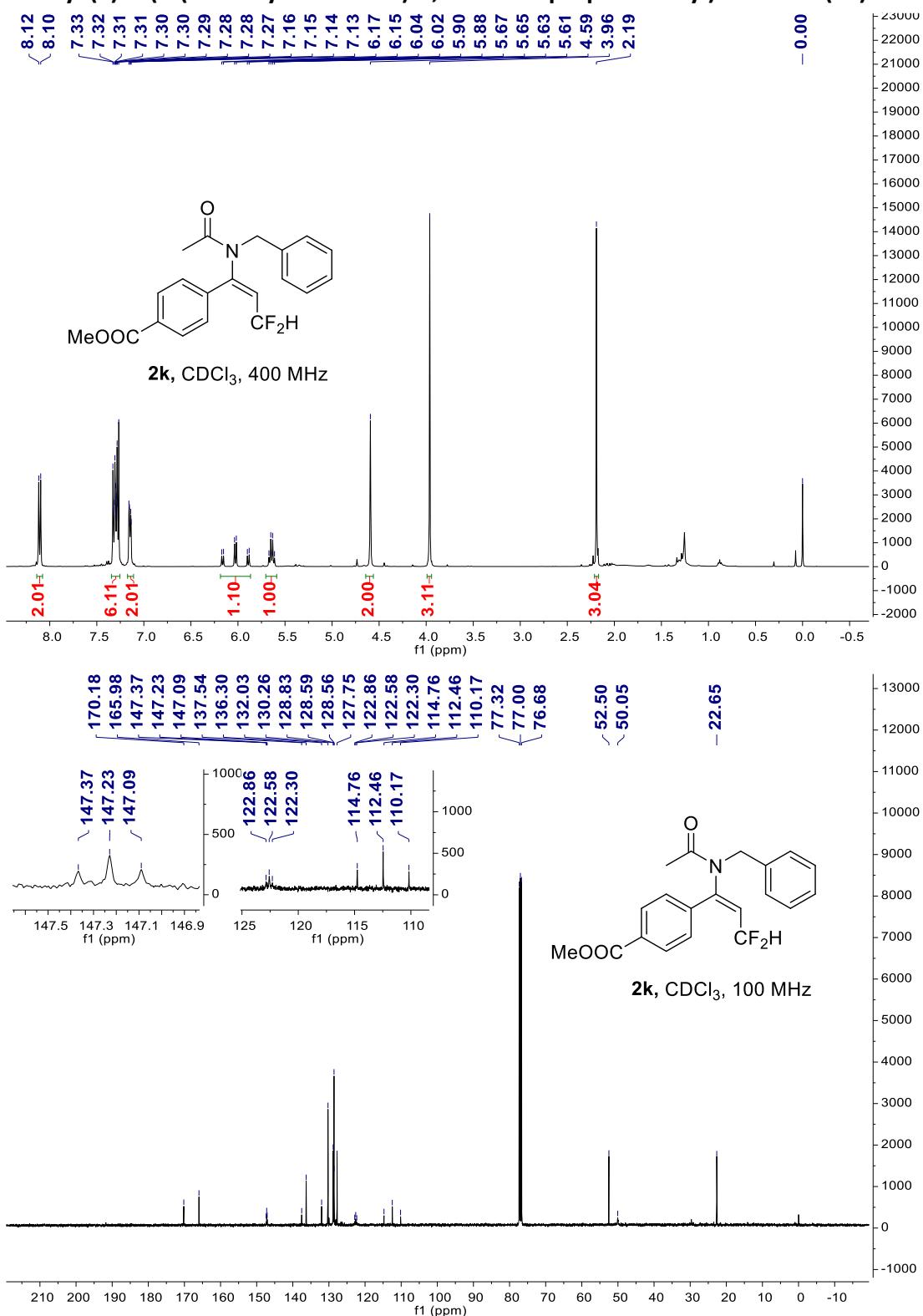


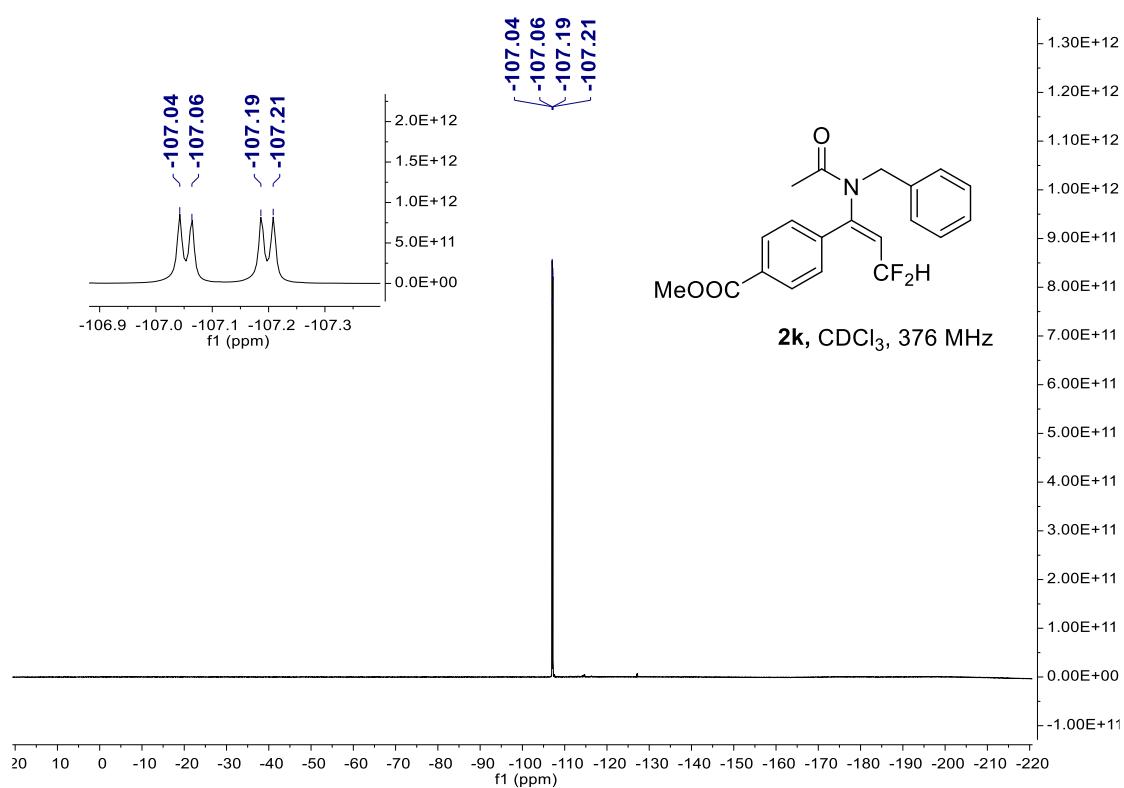
**(E)-N-benzyl-N-(1-(4-cyanophenyl)-3,3-difluoroprop-1-en-1-yl)acetamide (2j)**



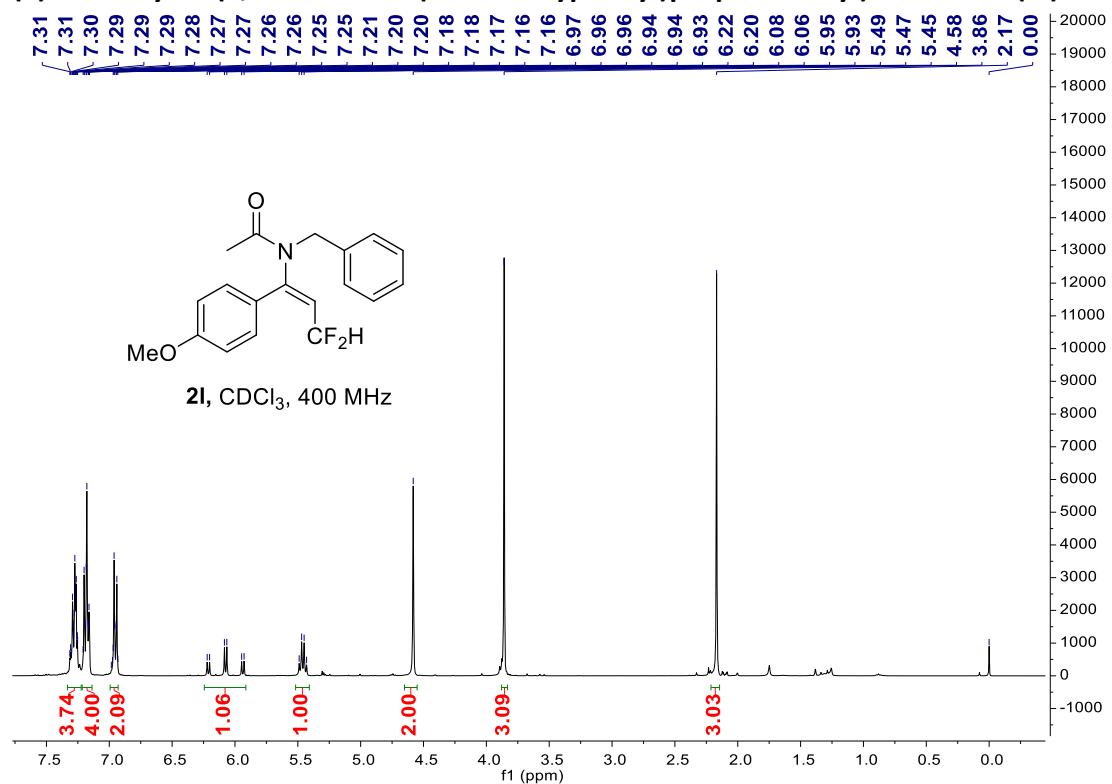


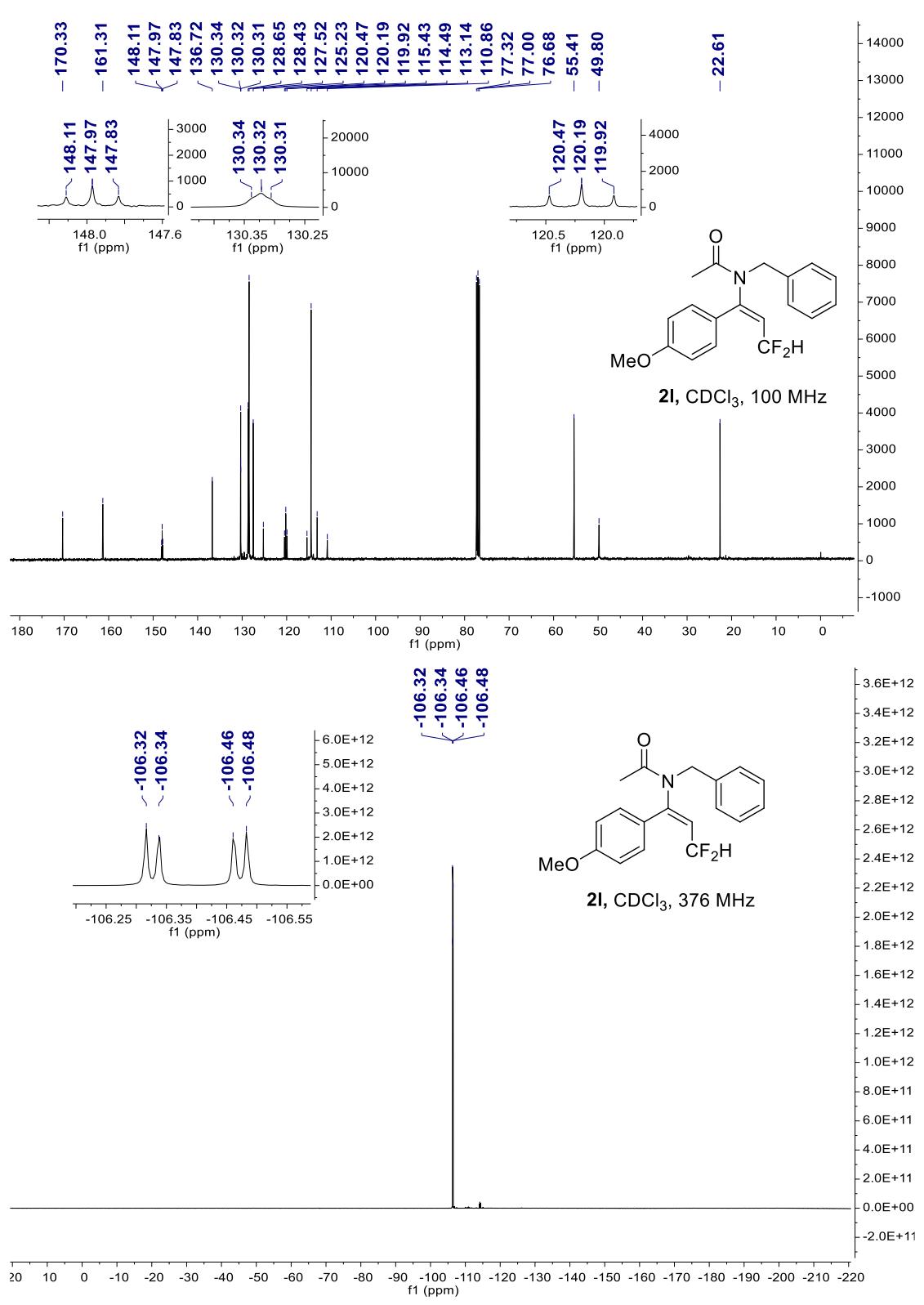
**methyl (E)-4-(1-(N-benzylacetamido)-3,3-difluoroprop-1-en-1-yl)benzoate (2k)**



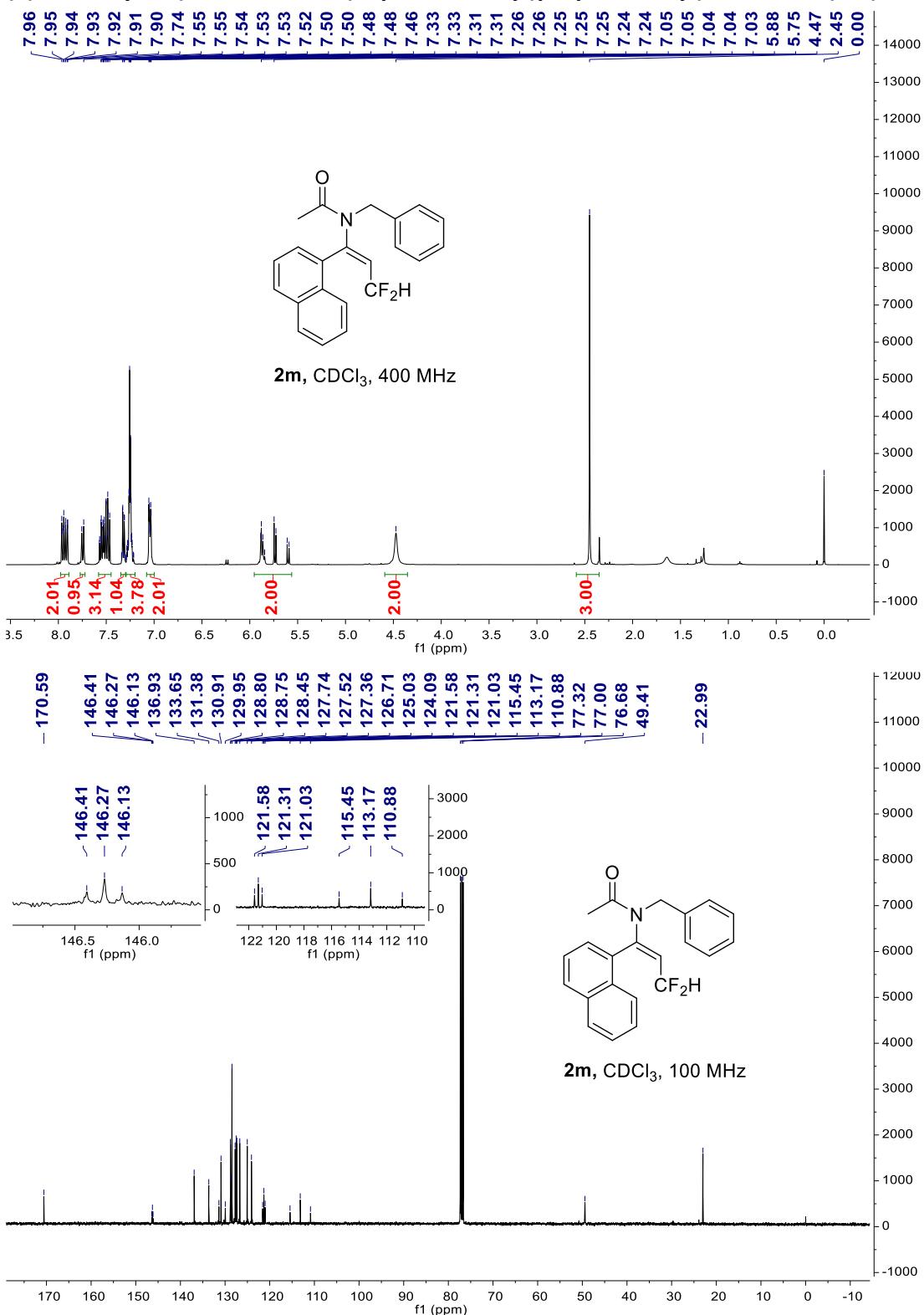


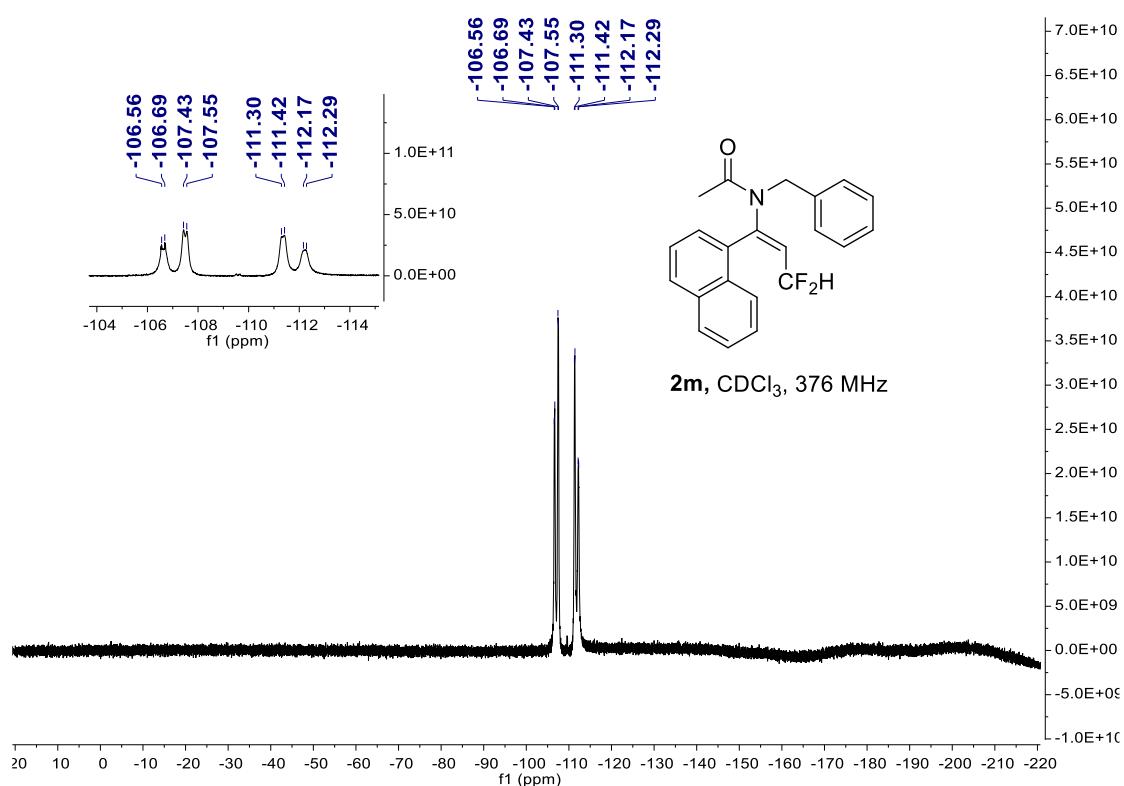
**(E)-N-benzyl-N-(3,3-difluoro-1-(4-methoxyphenyl)prop-1-en-1-yl)acetamide (2l)**



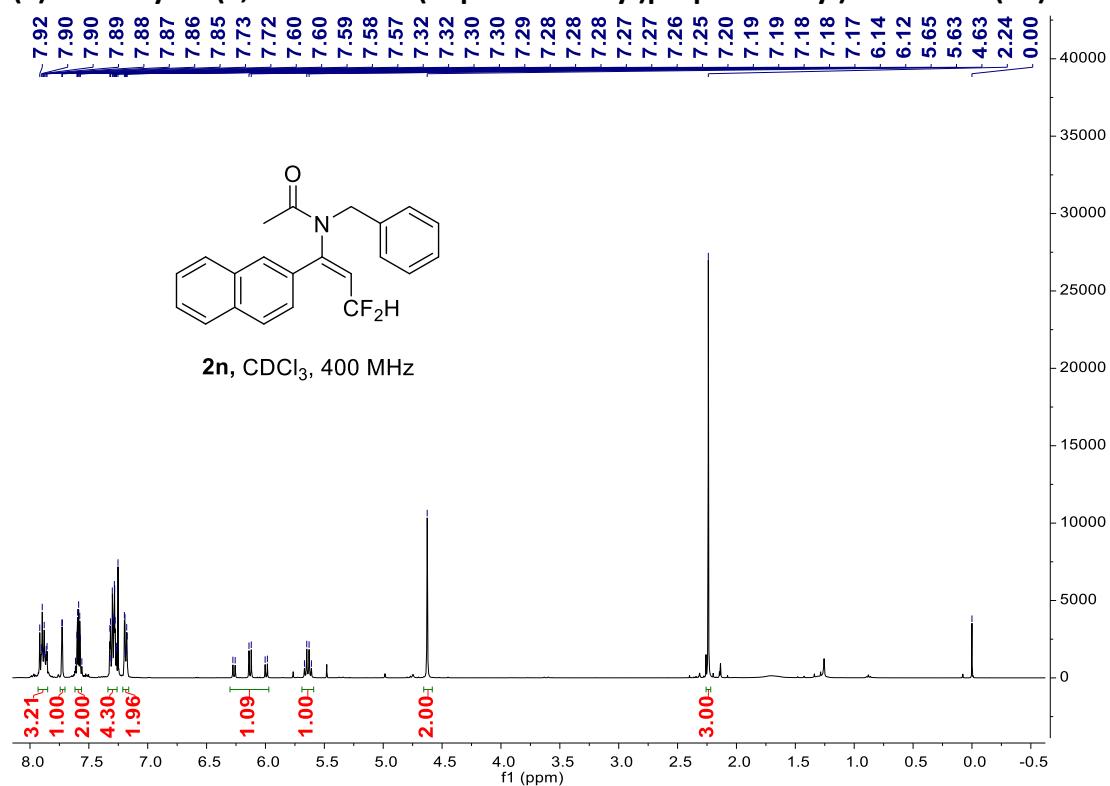


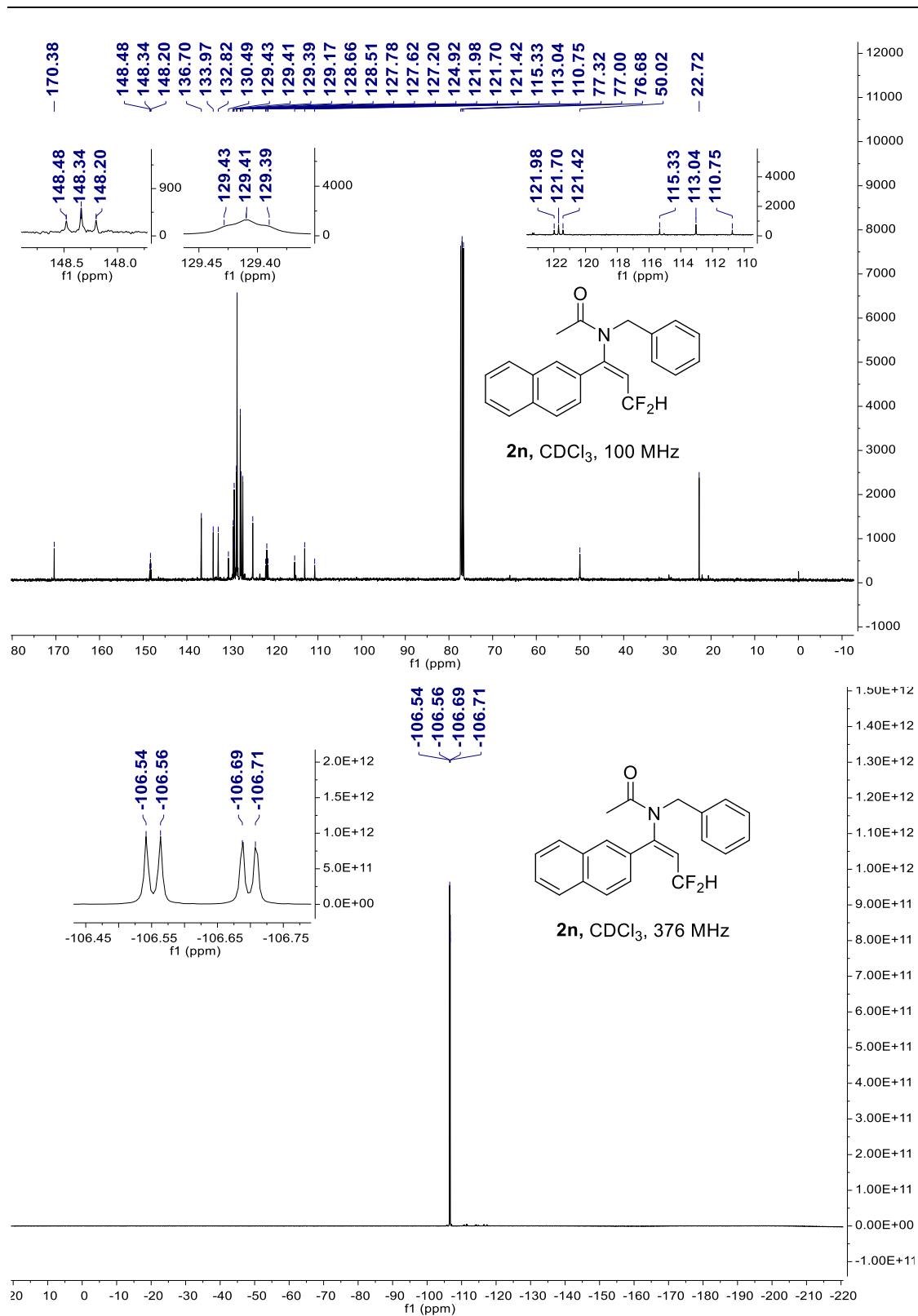
**(E)-N-benzyl-N-(3,3-difluoro-1-(naphthalen-1-yl)prop-1-en-1-yl)acetamide (2m)**



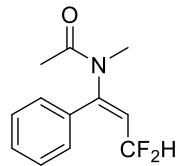


**(E)-N-benzyl-N-(3,3-difluoro-1-(naphthalen-2-yl)prop-1-en-1-yl)acetamide (2n)**

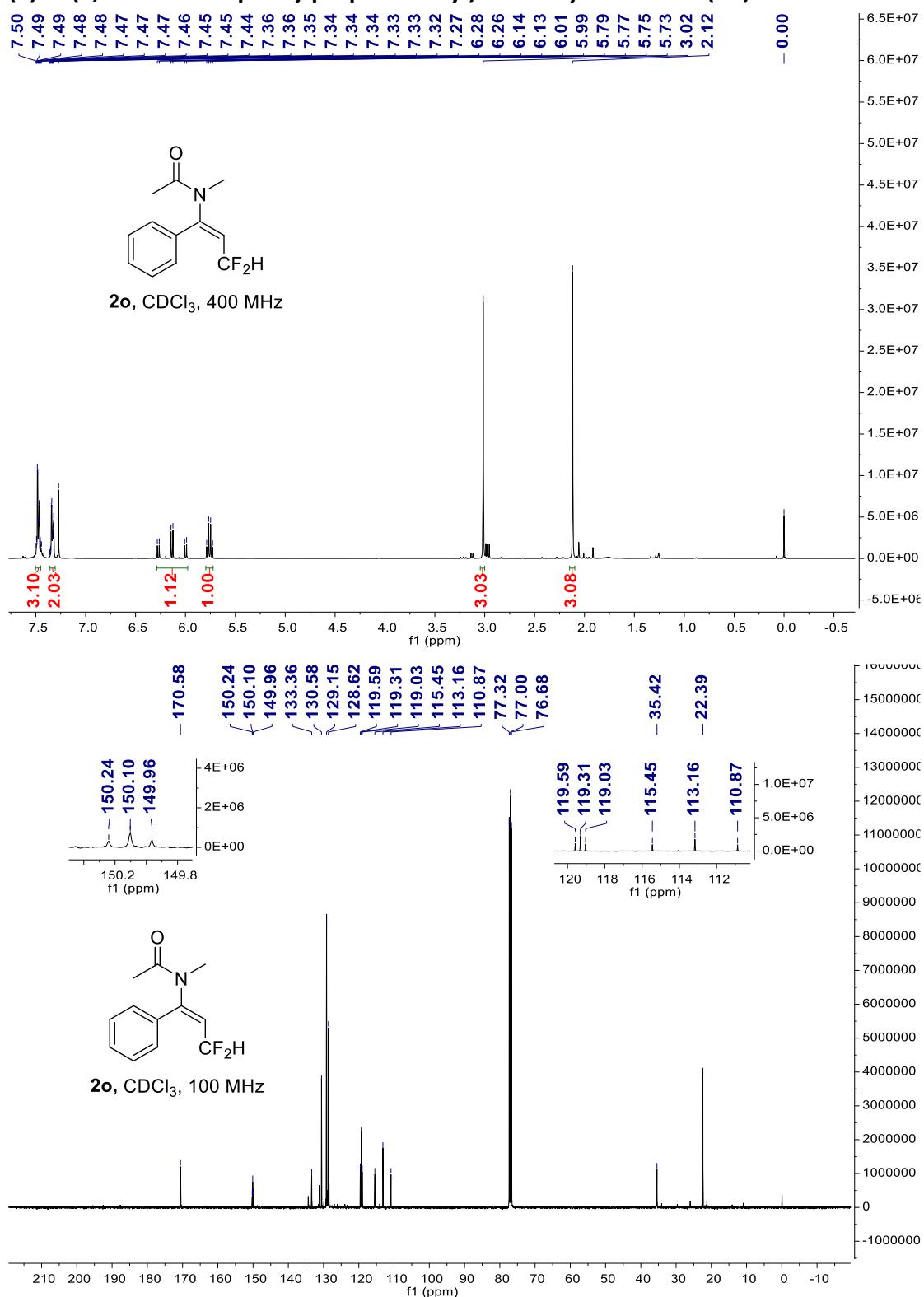


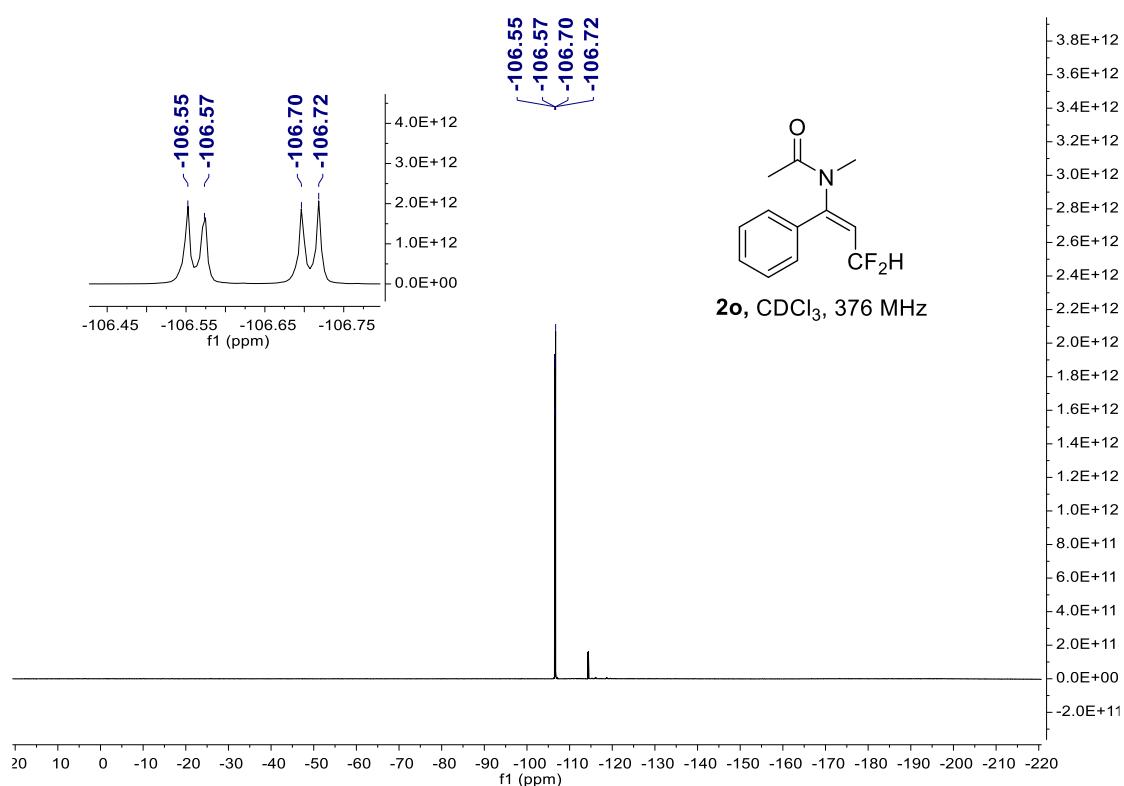


**(E)-N-(3,3-difluoro-1-phenylprop-1-en-1-yl)-N-methylacetamide (2o)**

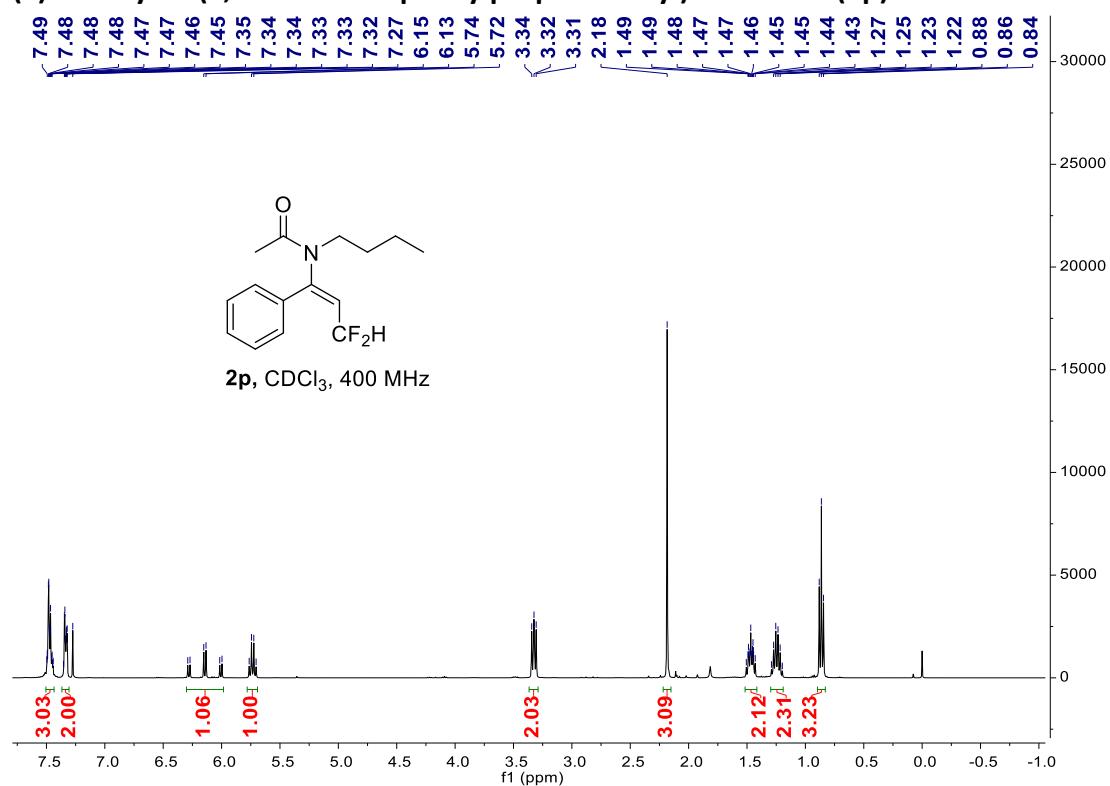


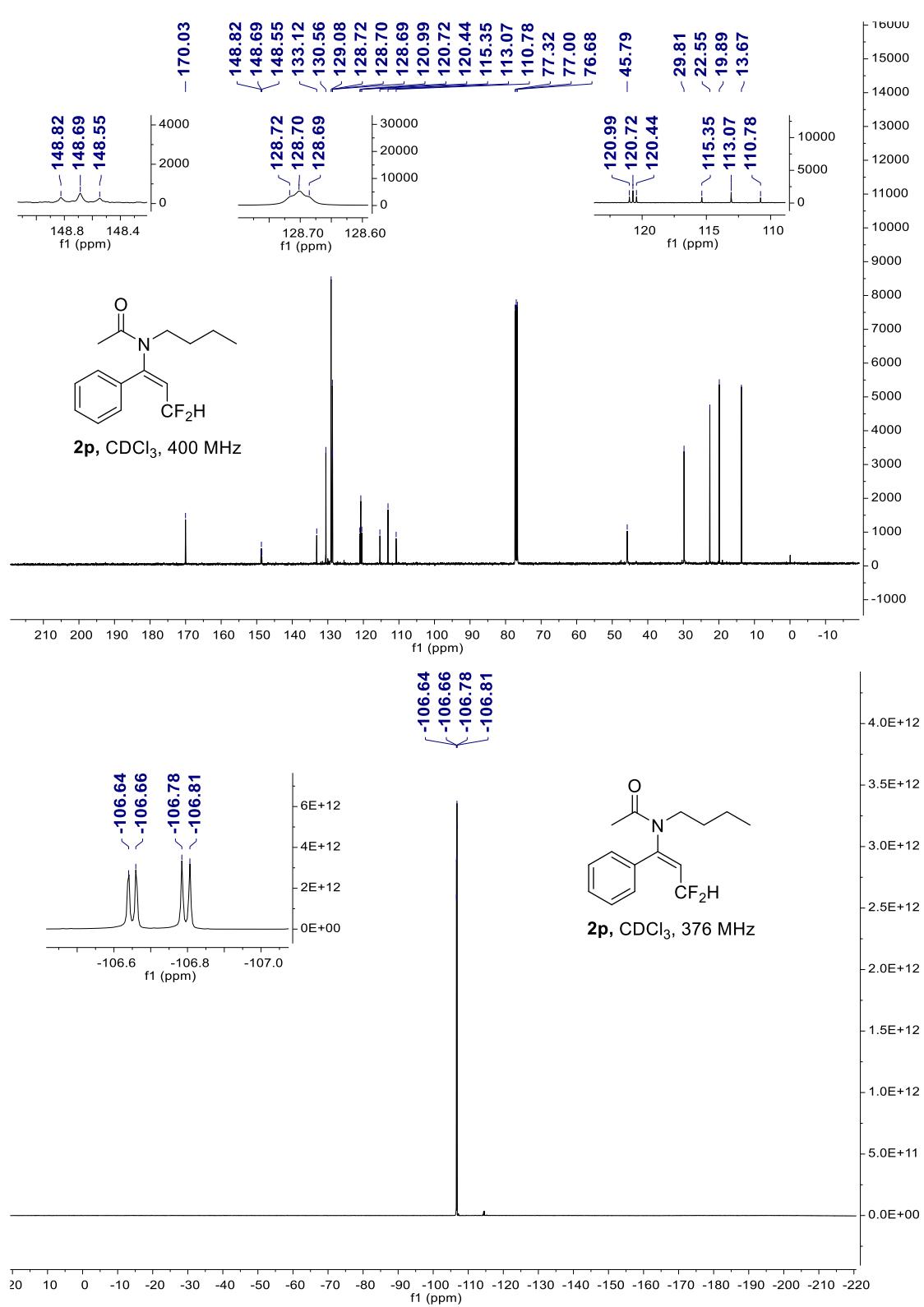
**2o**, CDCl<sub>3</sub>, 400 MHz



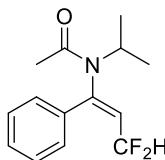


(*E*)-*N*-butyl-*N*-(3,3-difluoro-1-phenylprop-1-en-1-yl)acetamide (**2p**)

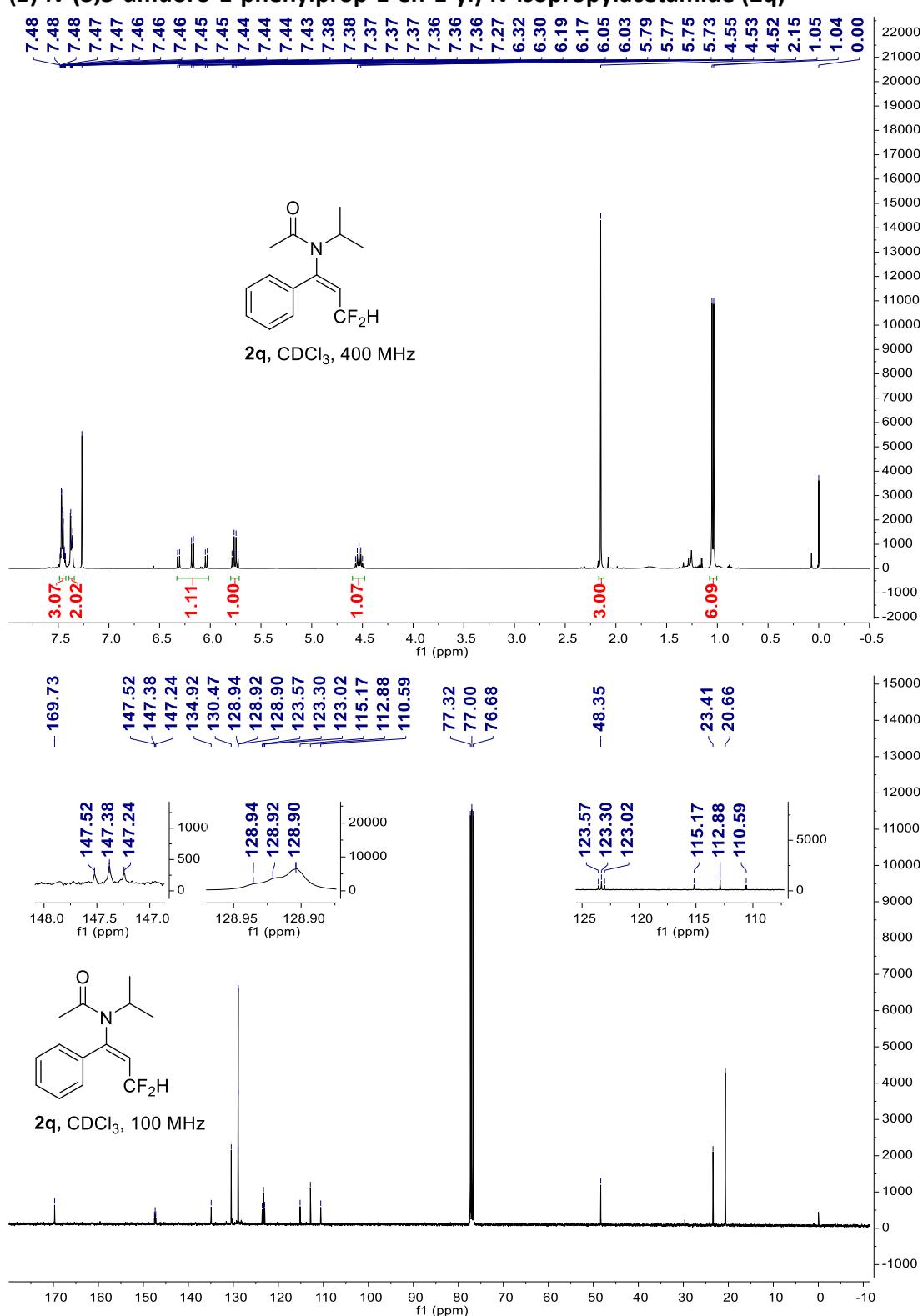


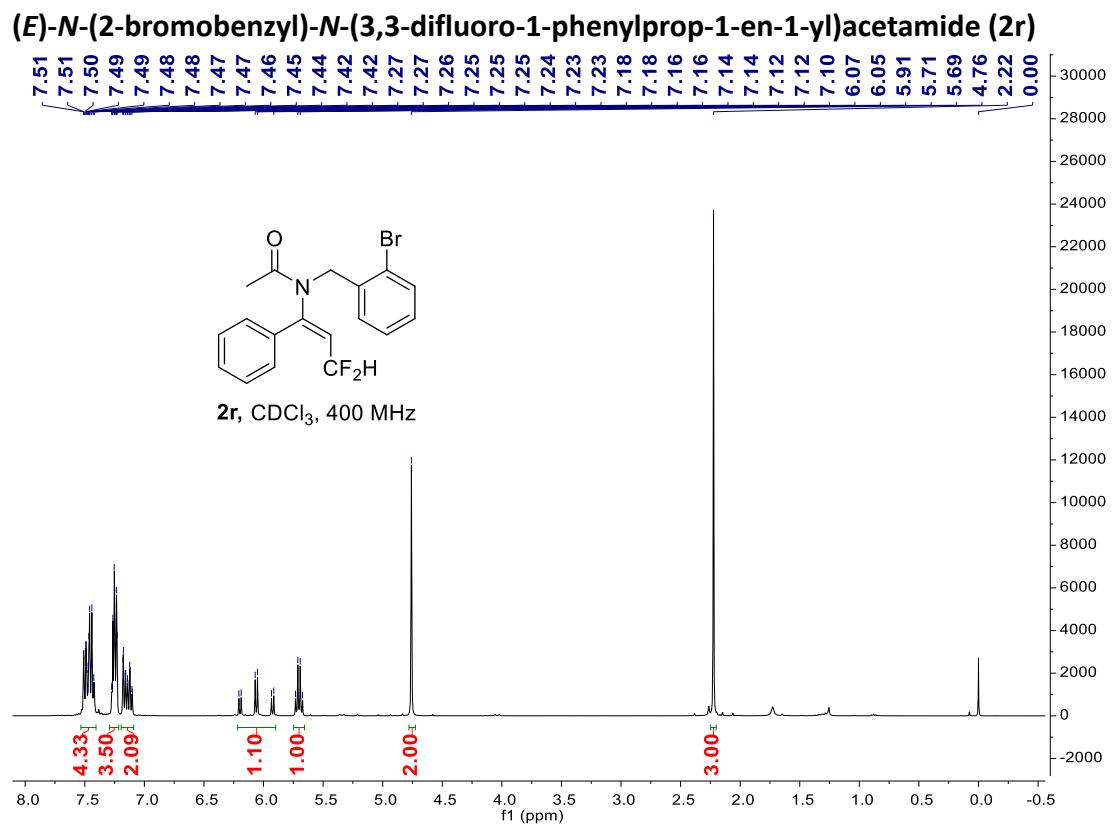
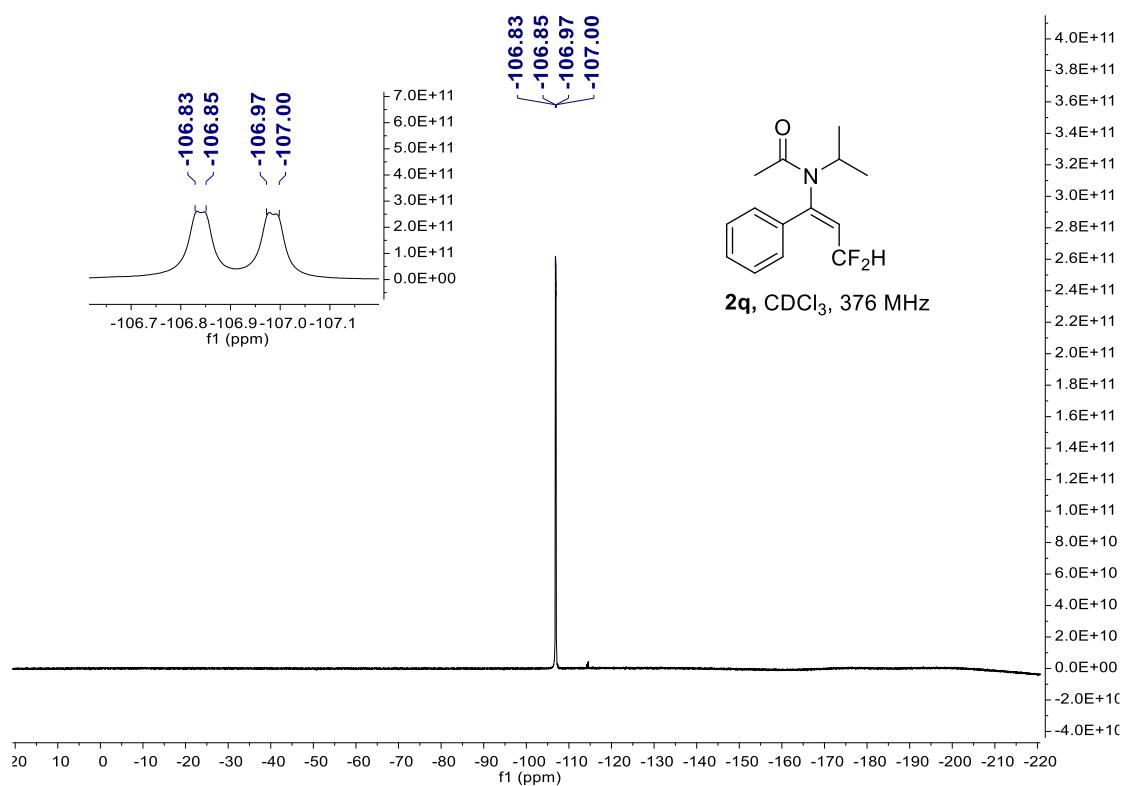


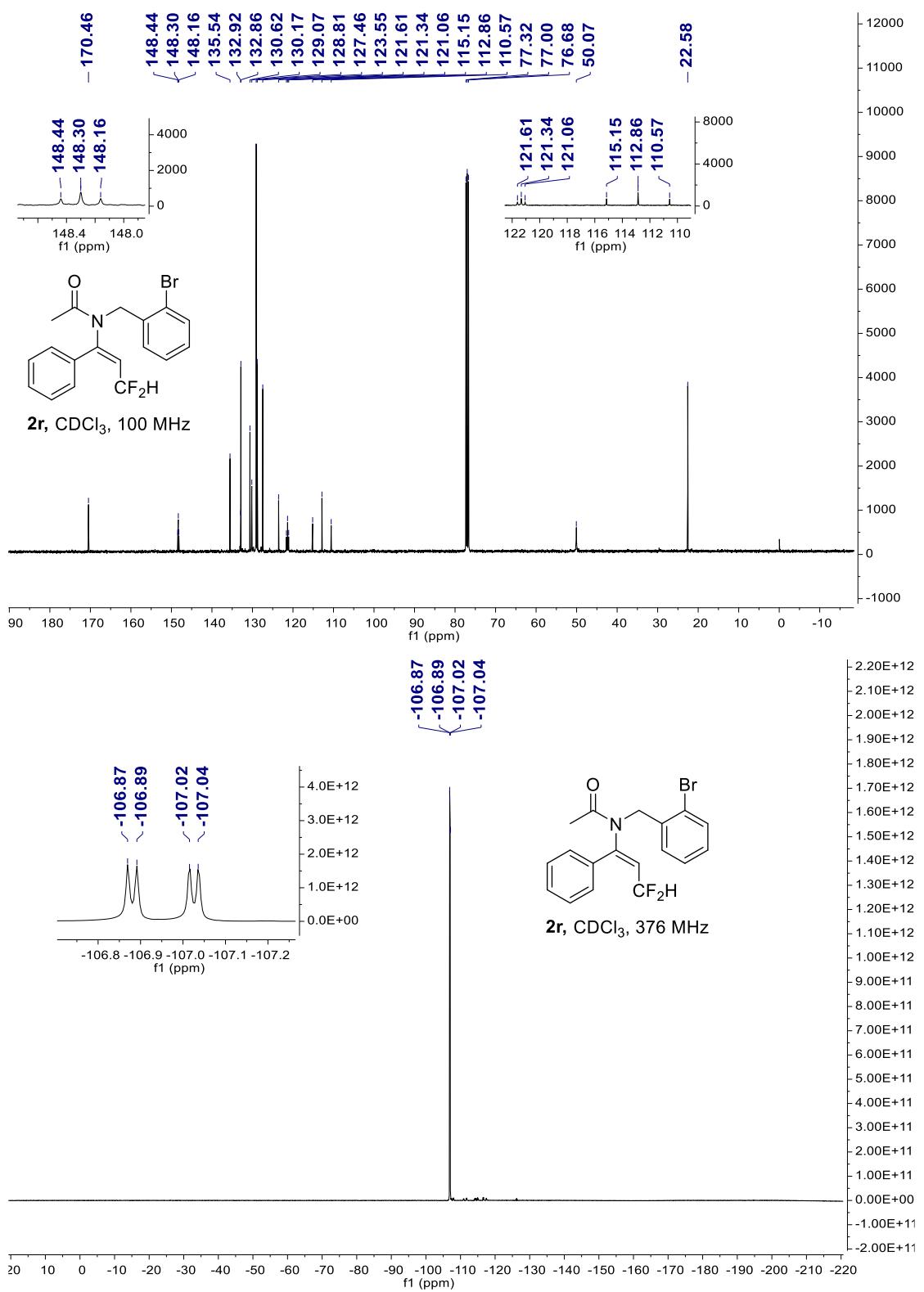
**(E)-N-(3,3-difluoro-1-phenylprop-1-en-1-yl)-N-isopropylacetamide (2q)**



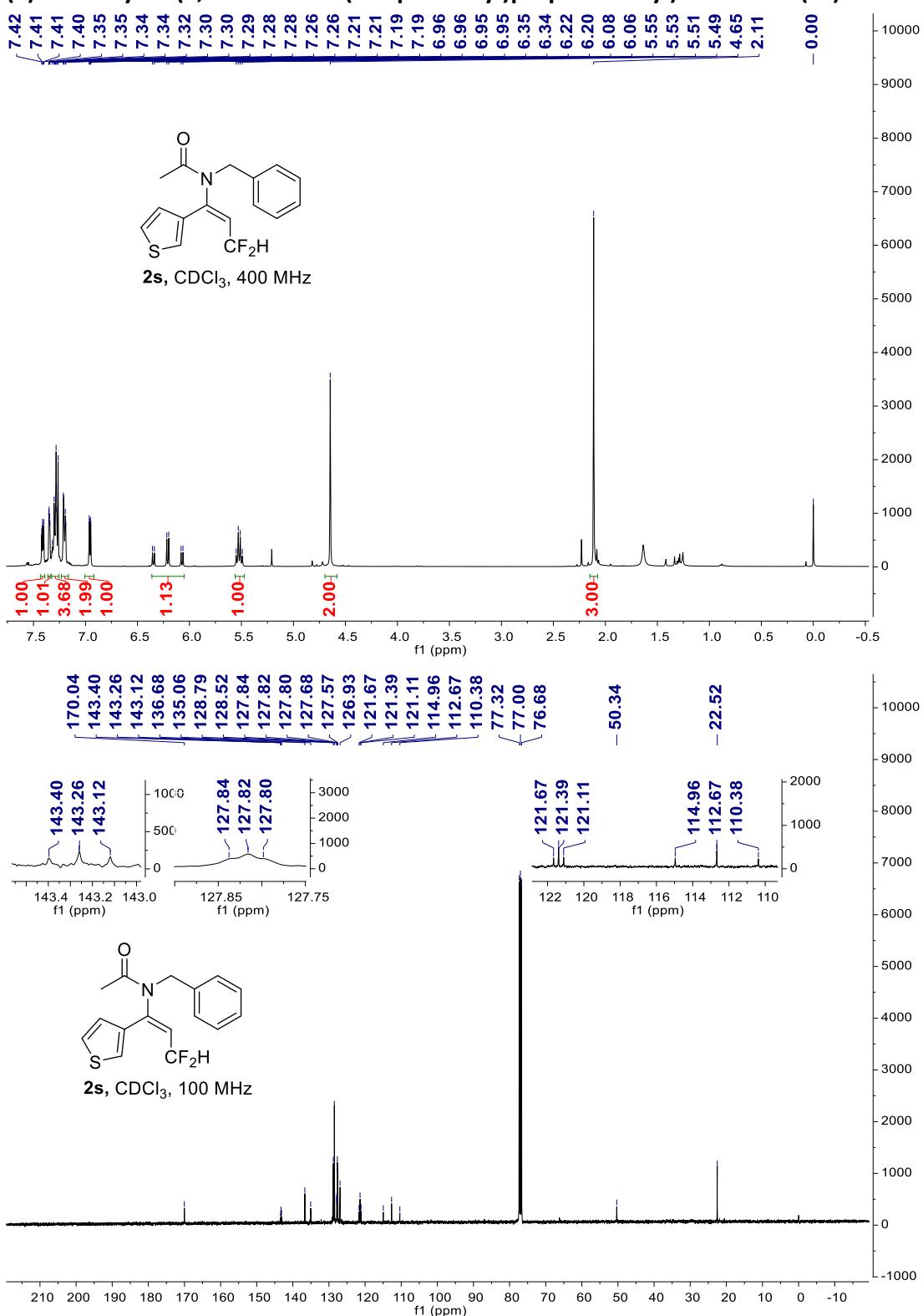
**2q**, CDCl<sub>3</sub>, 400 MHz

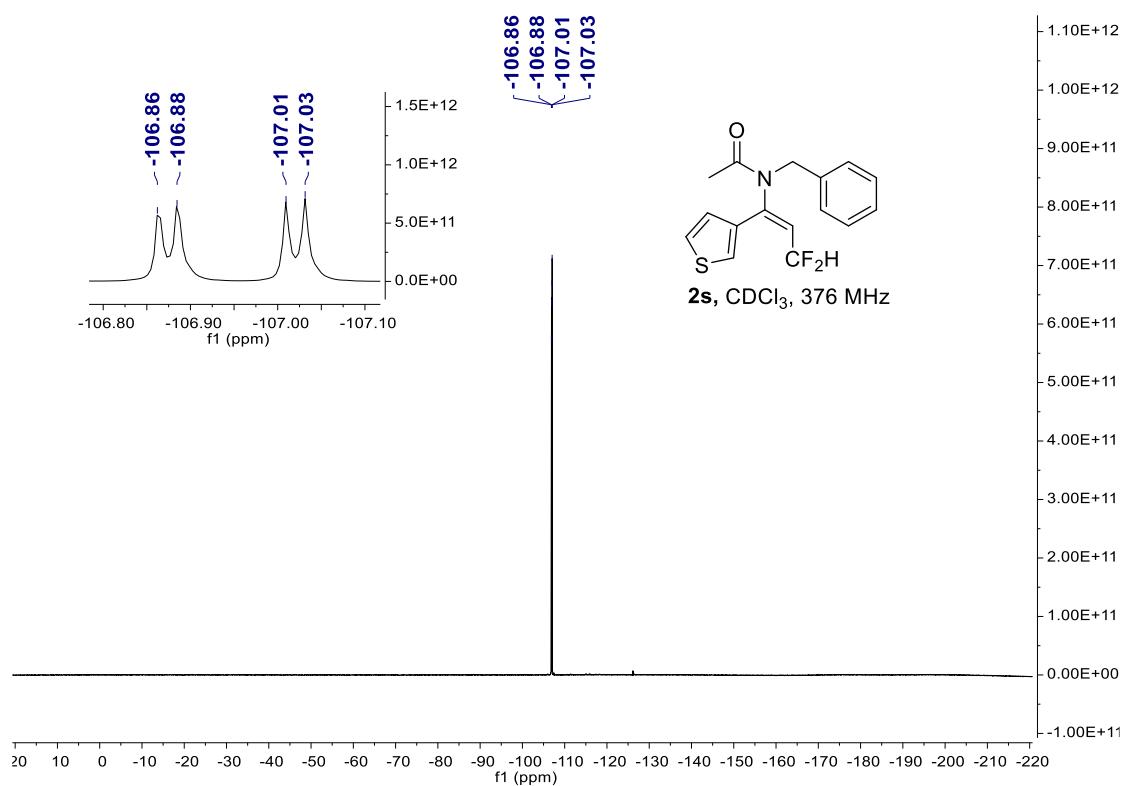




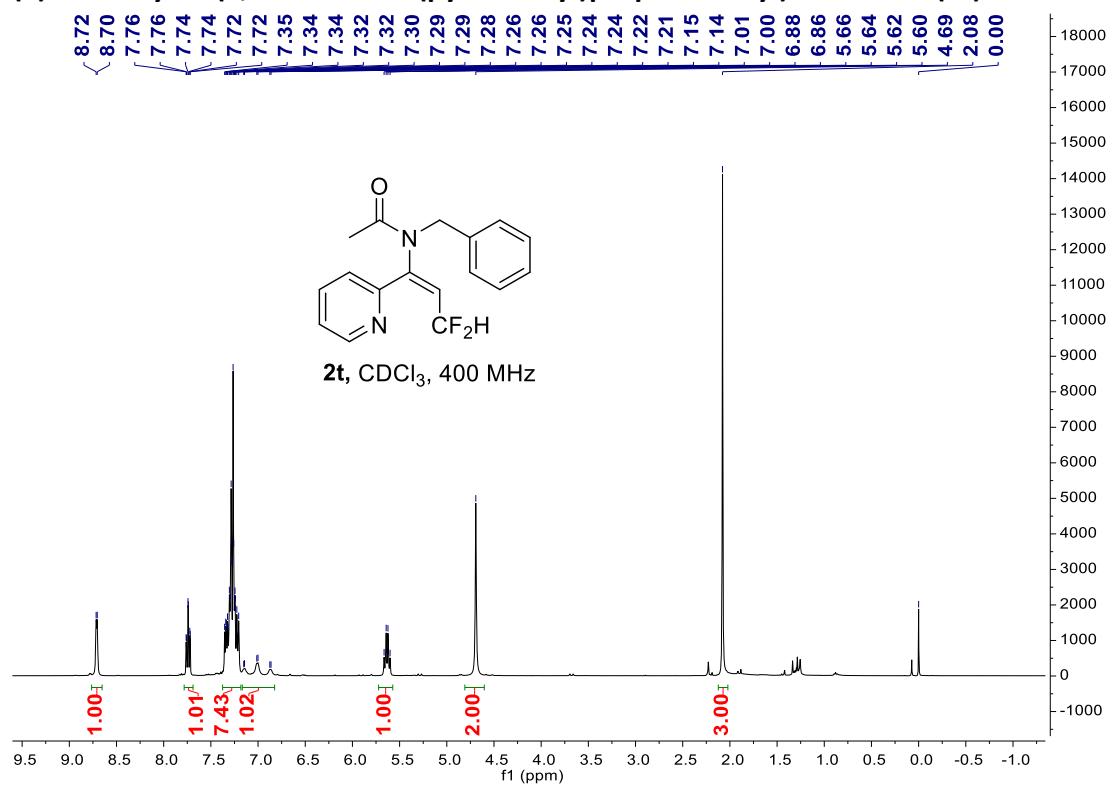


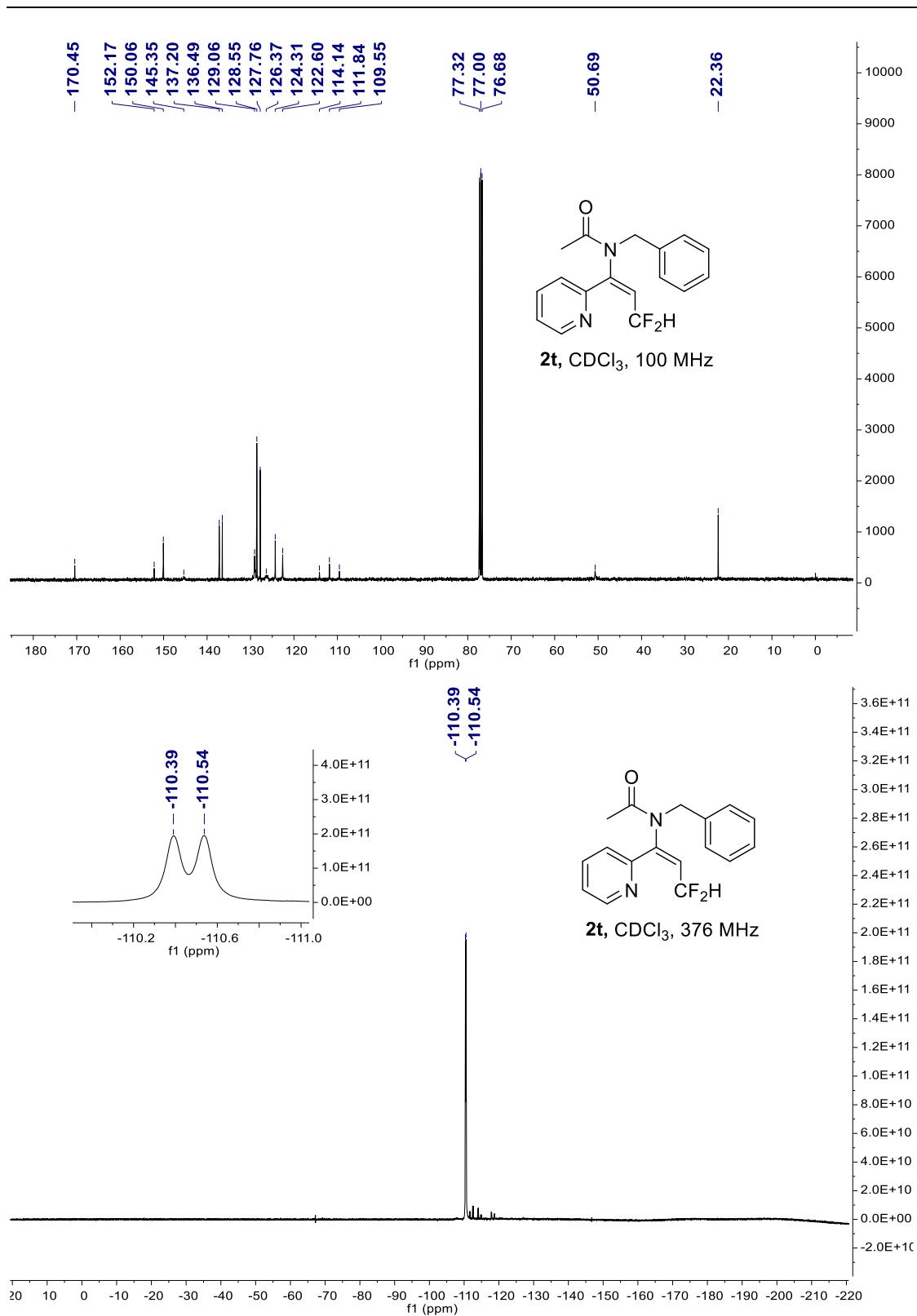
**(E)-N-benzyl-N-(3,3-difluoro-1-(thiophen-3-yl)prop-1-en-1-yl)acetamide (2s)**



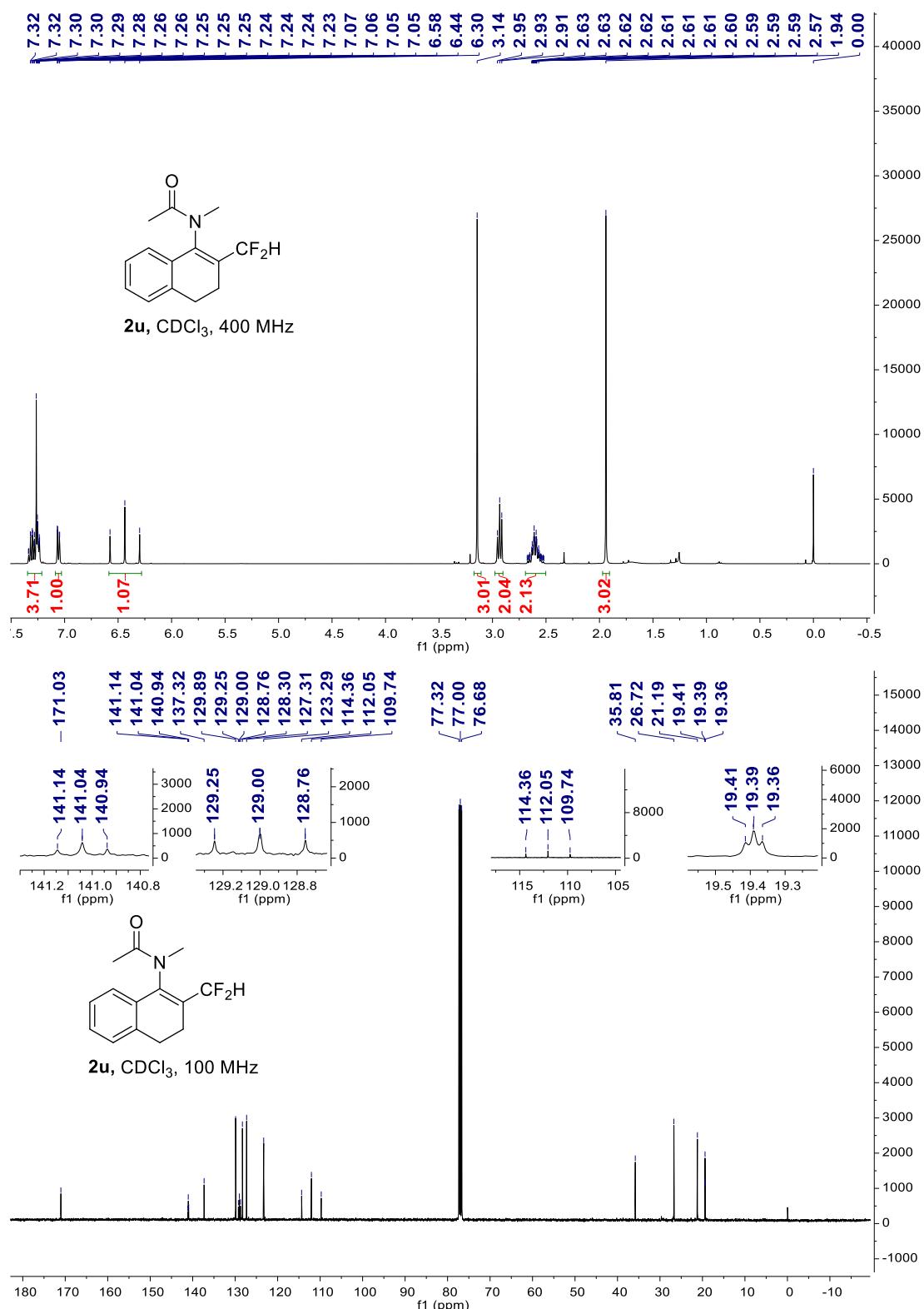


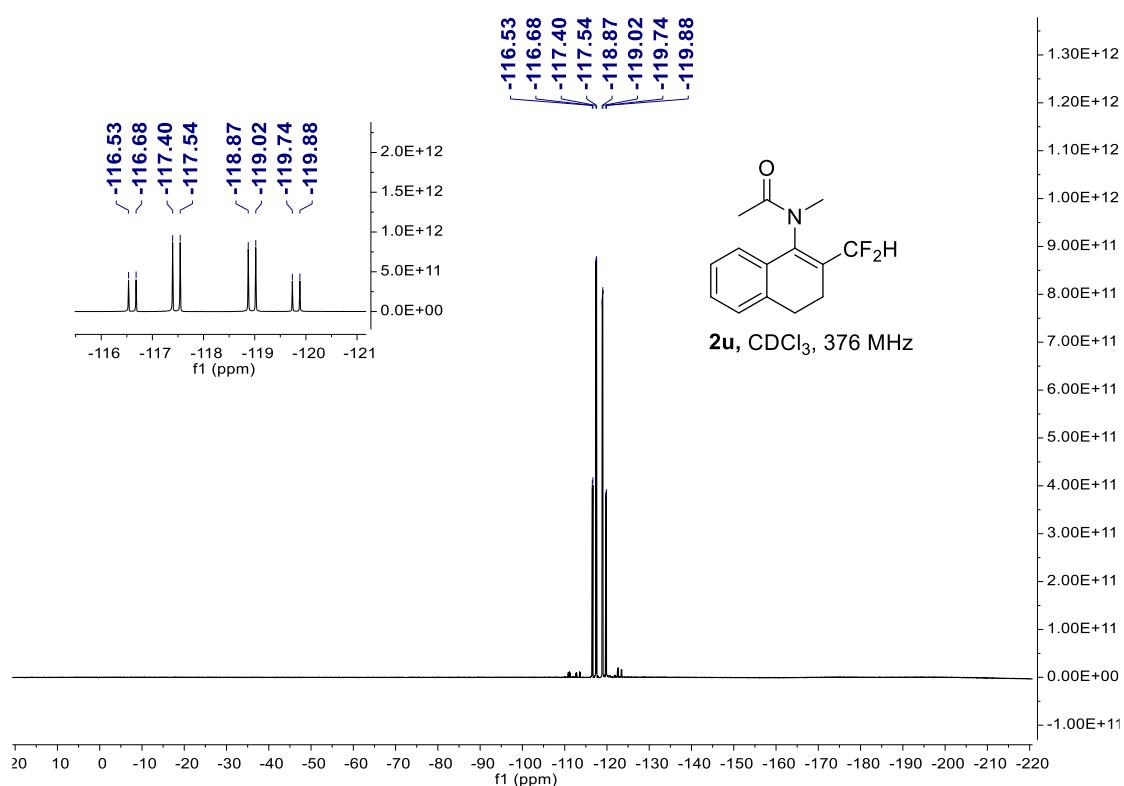
**(E)-N-benzyl-N-(3,3-difluoro-1-(pyridin-2-yl)prop-1-en-1-yl)acetamide (2t)**



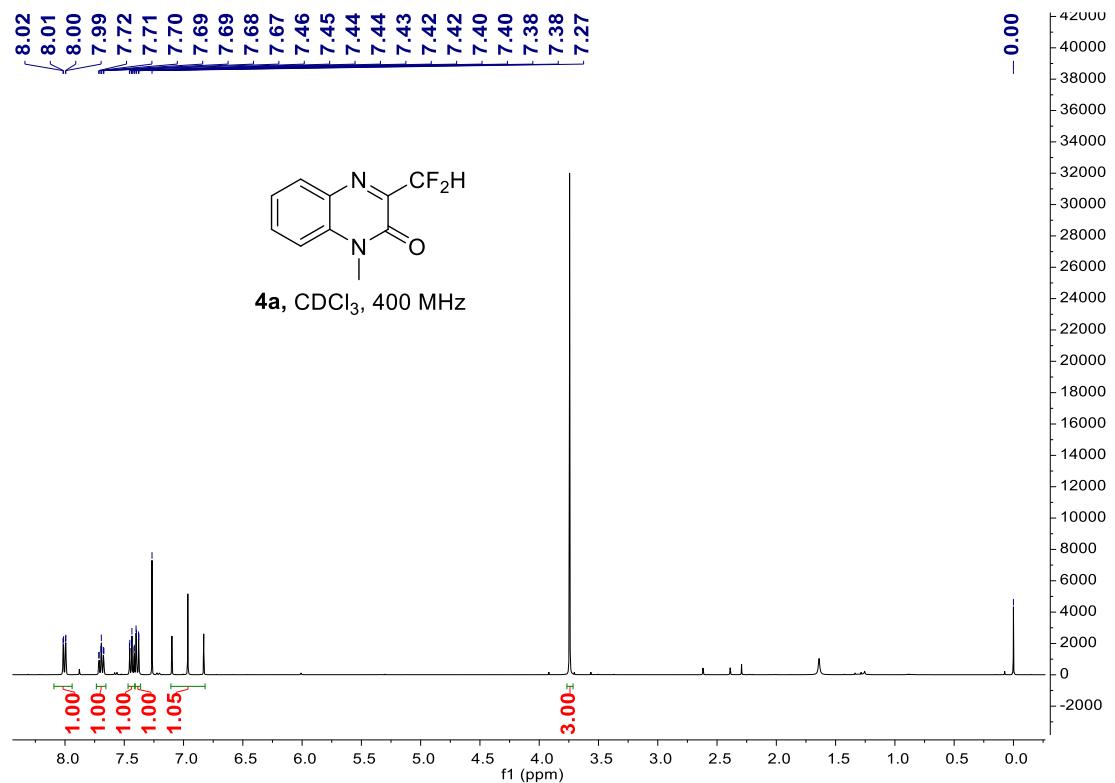


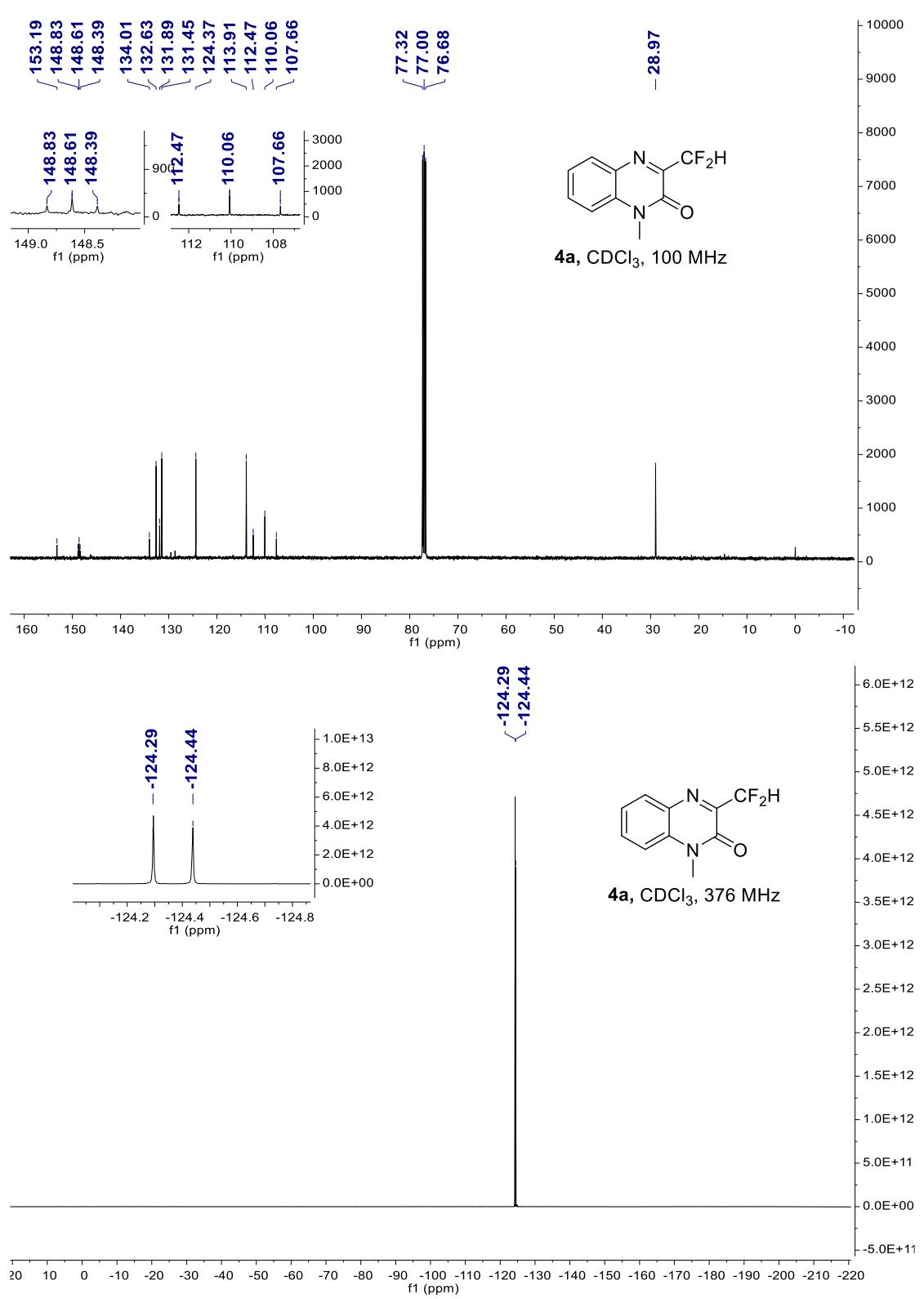
**N-(2-(difluoromethyl)-3,4-dihydronaphthalen-1-yl)-N-methylacetamide (2u)**



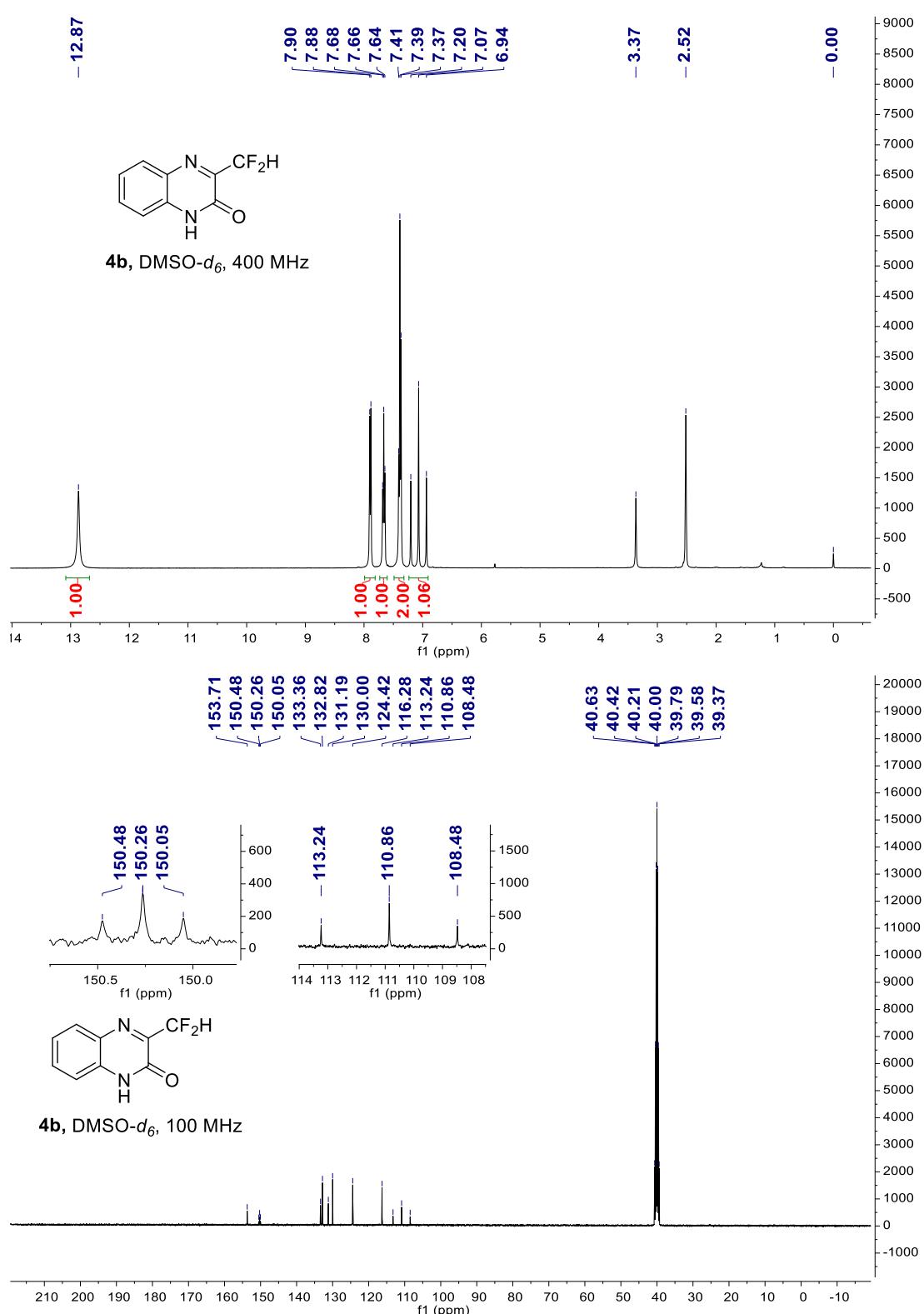


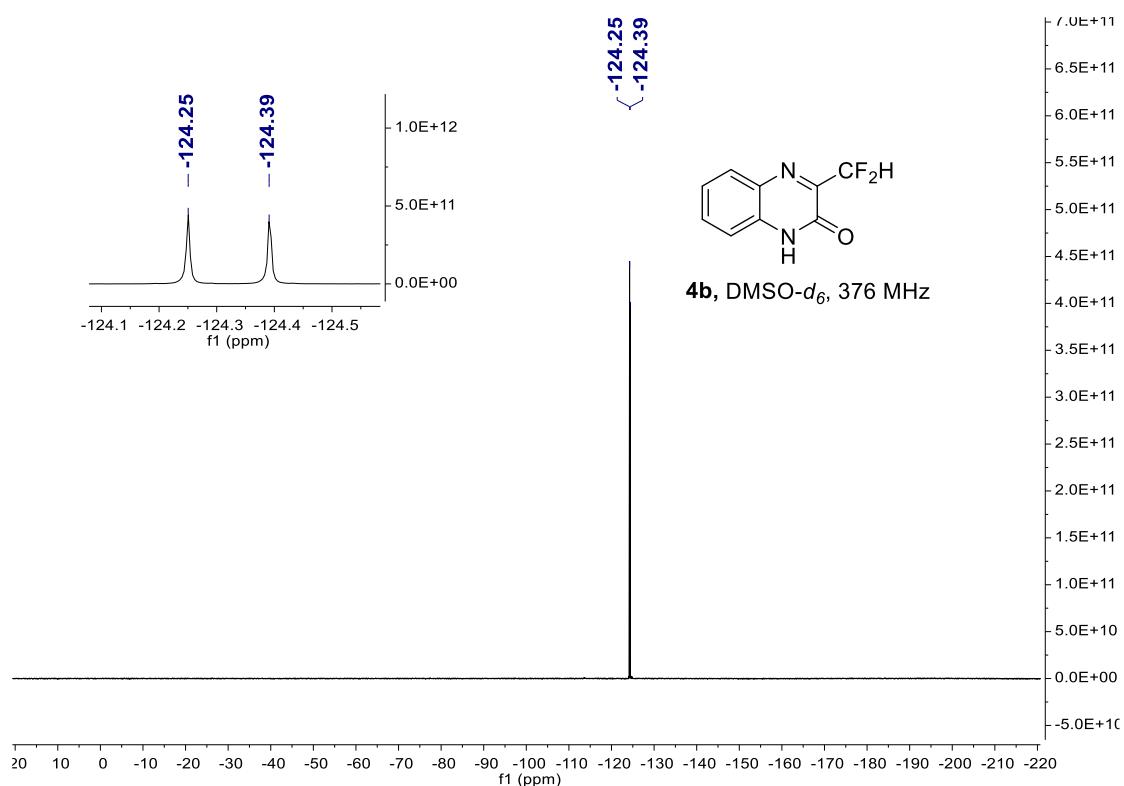
### 3-(difluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**4a**)



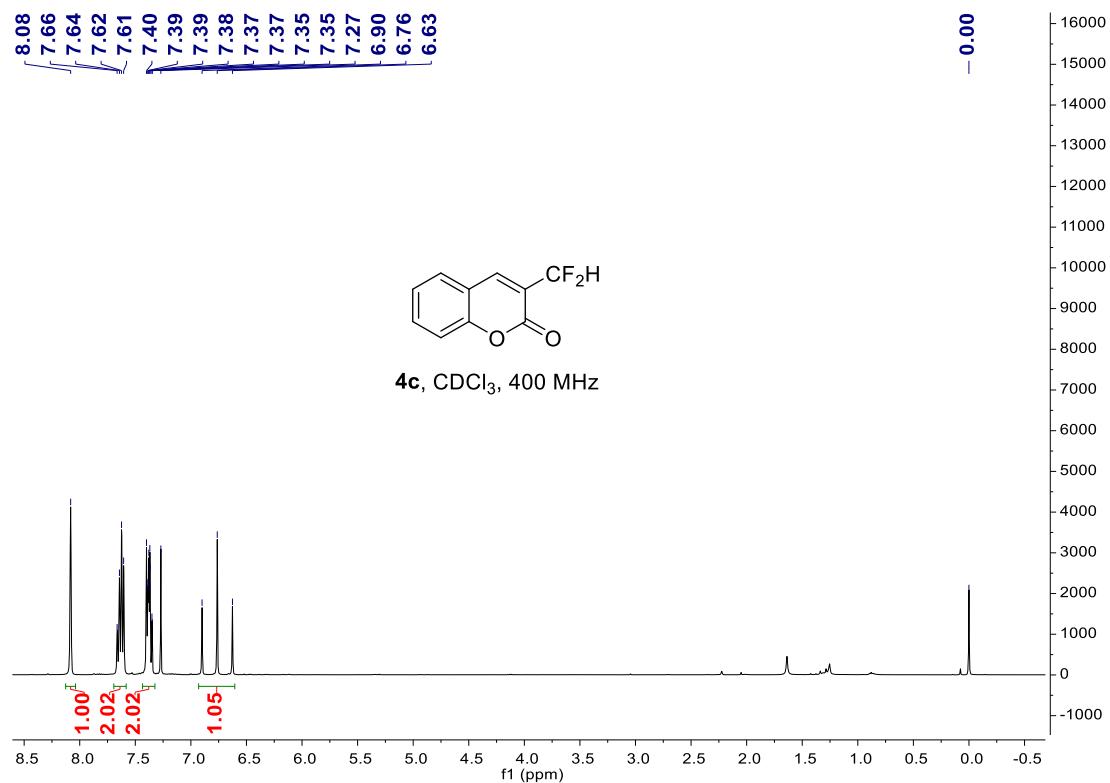


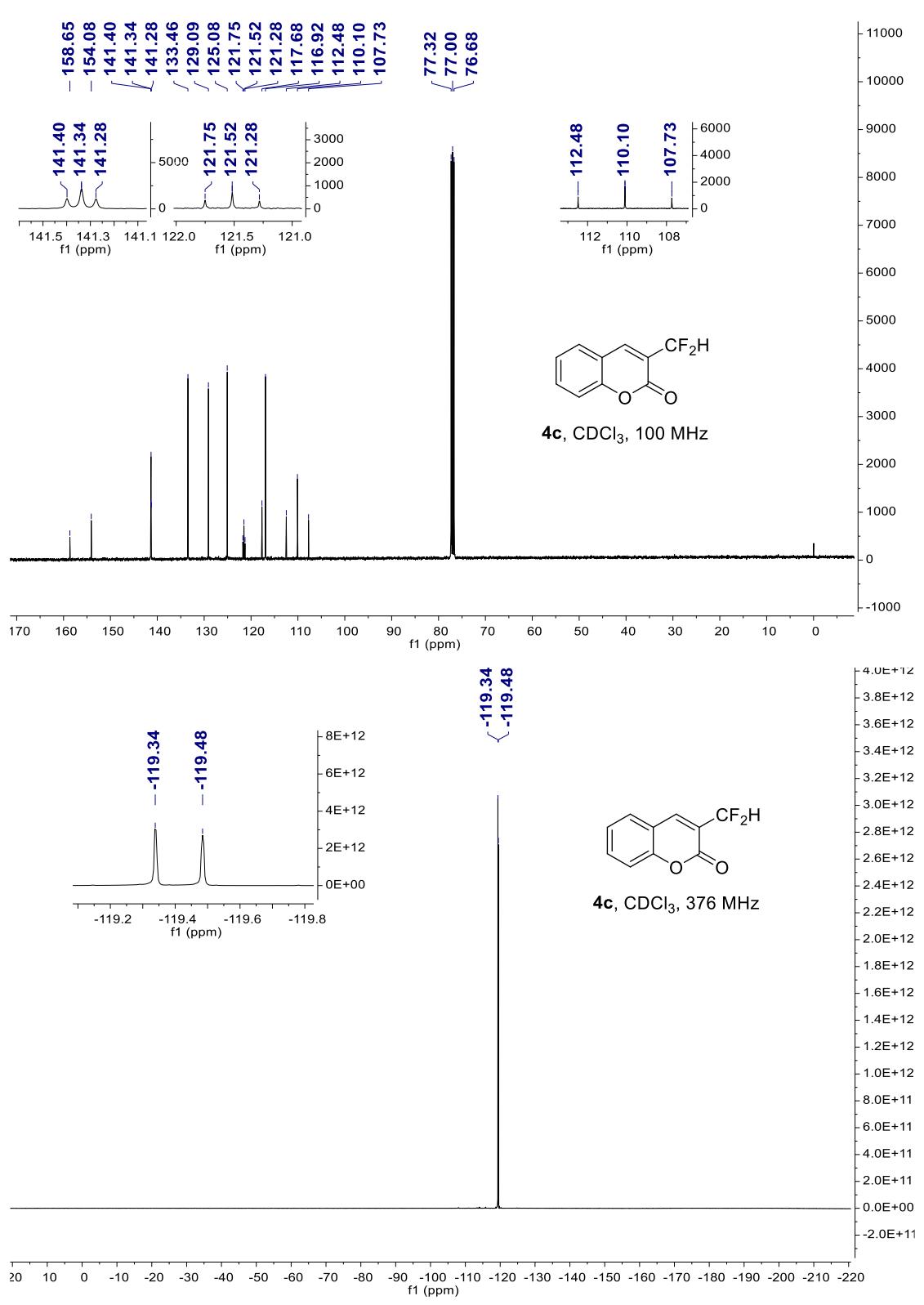
**3-(difluoromethyl)quinoxalin-2(1H)-one (4b)**



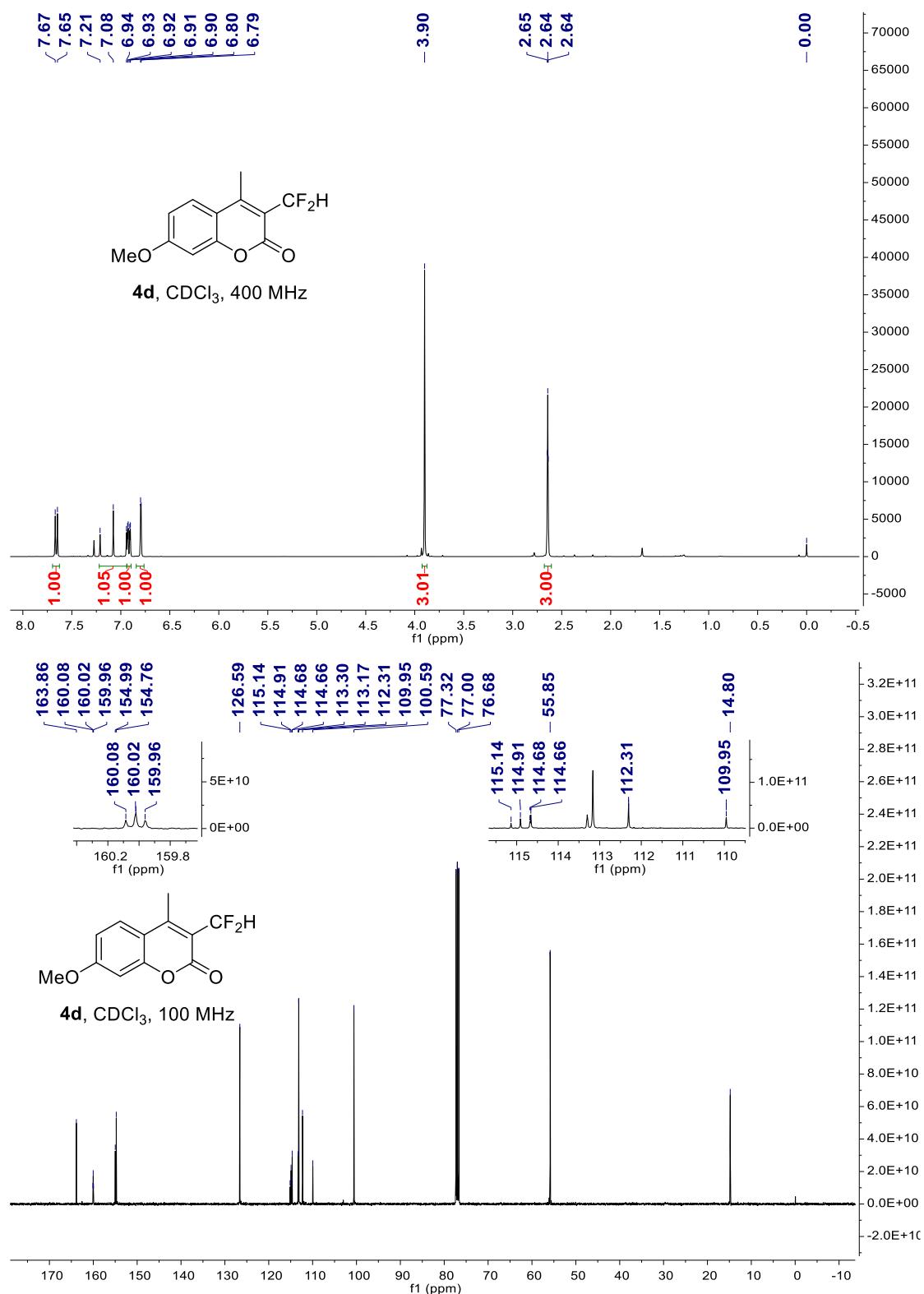


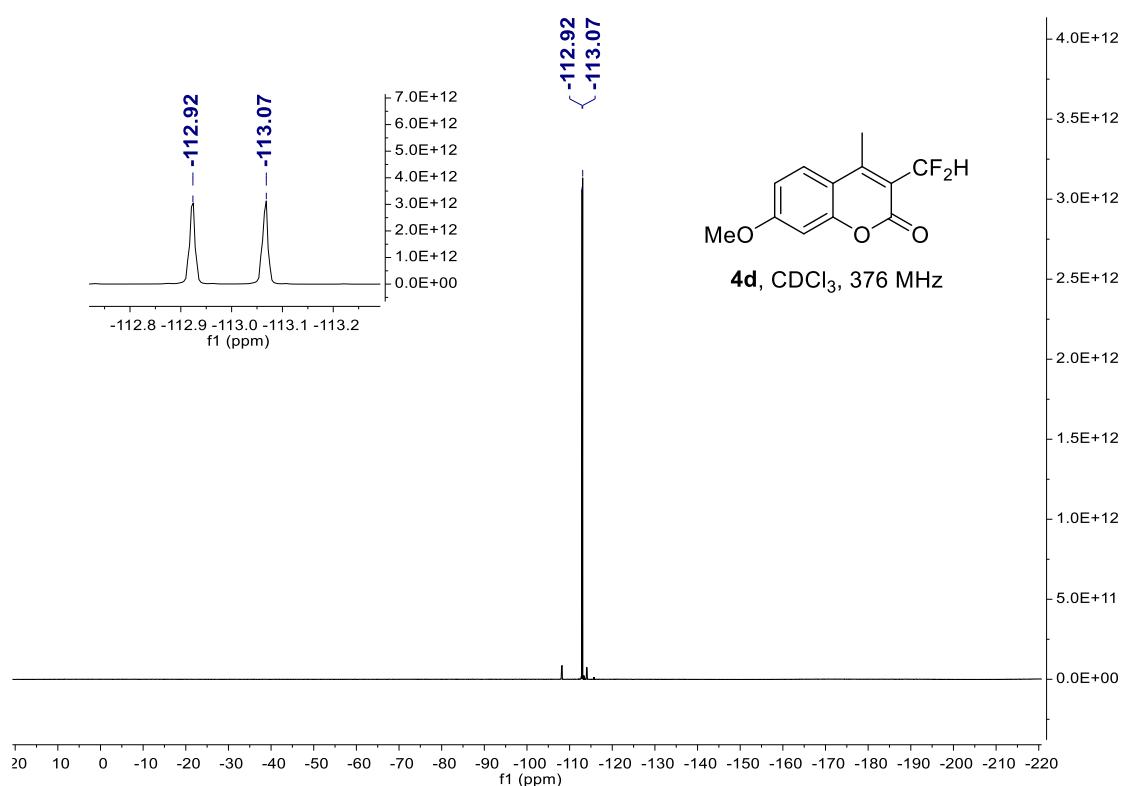
**3-(difluoromethyl)-2*H*-chromen-2-one (4c)**



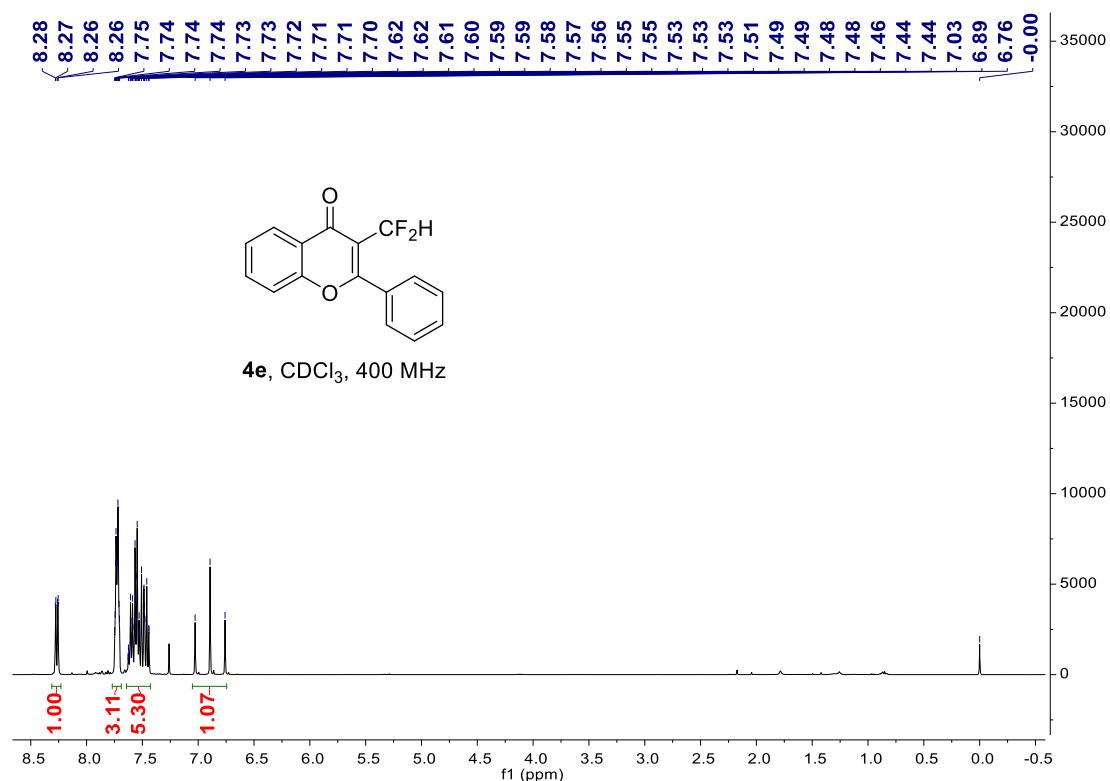


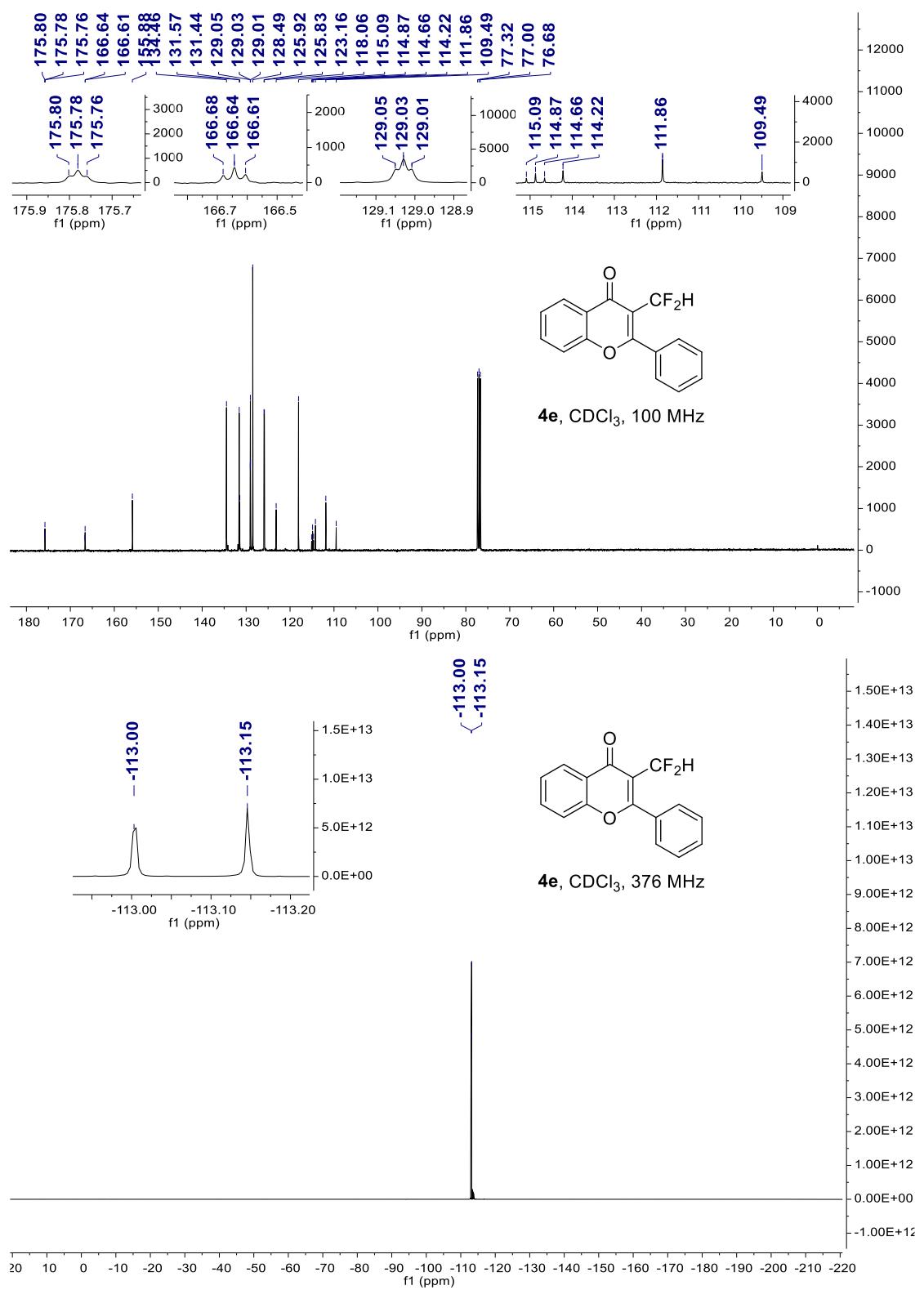
**3-(difluoromethyl)-7-methoxy-4-methyl-2*H*-chromen-2-one (**4d**)**



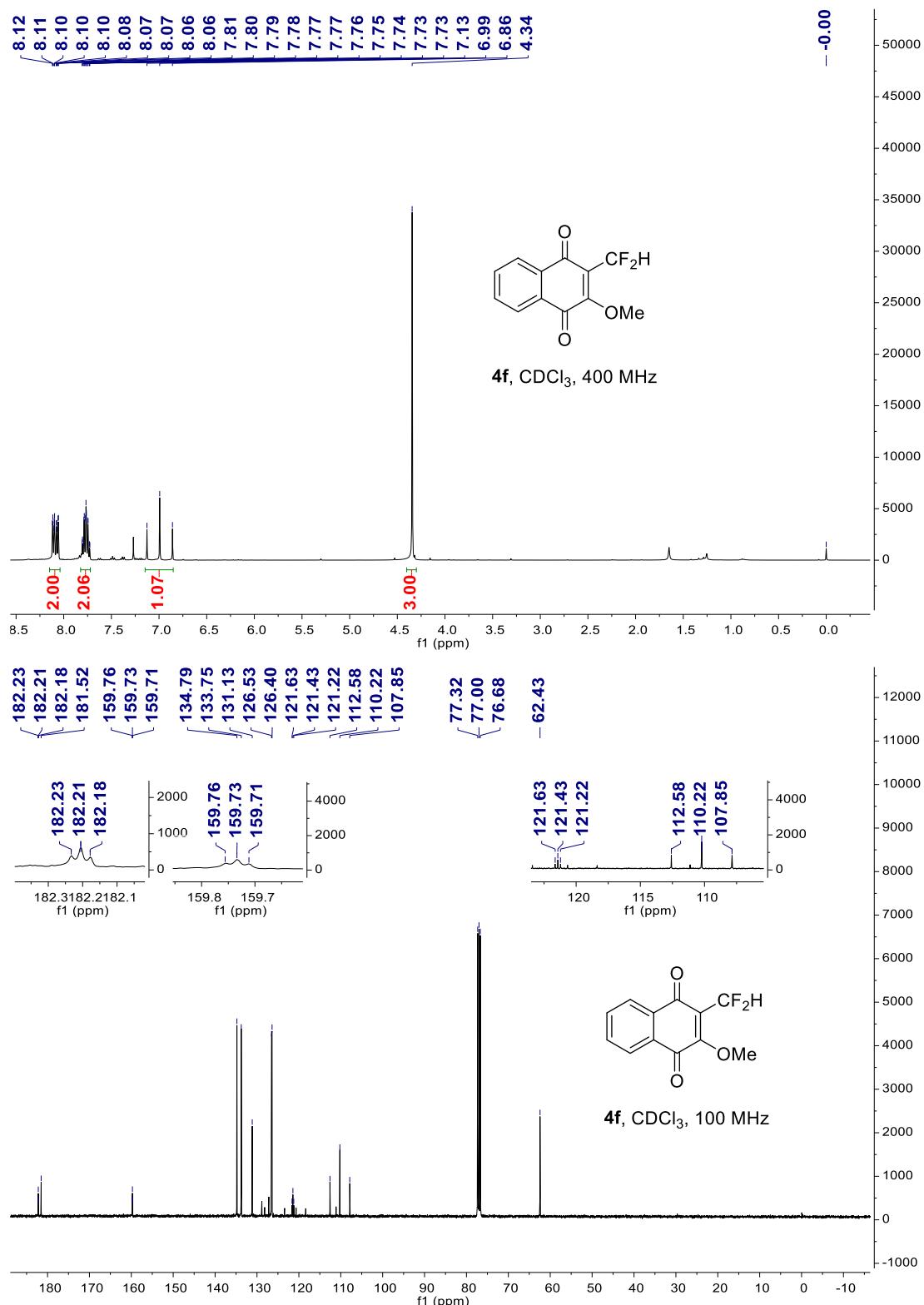


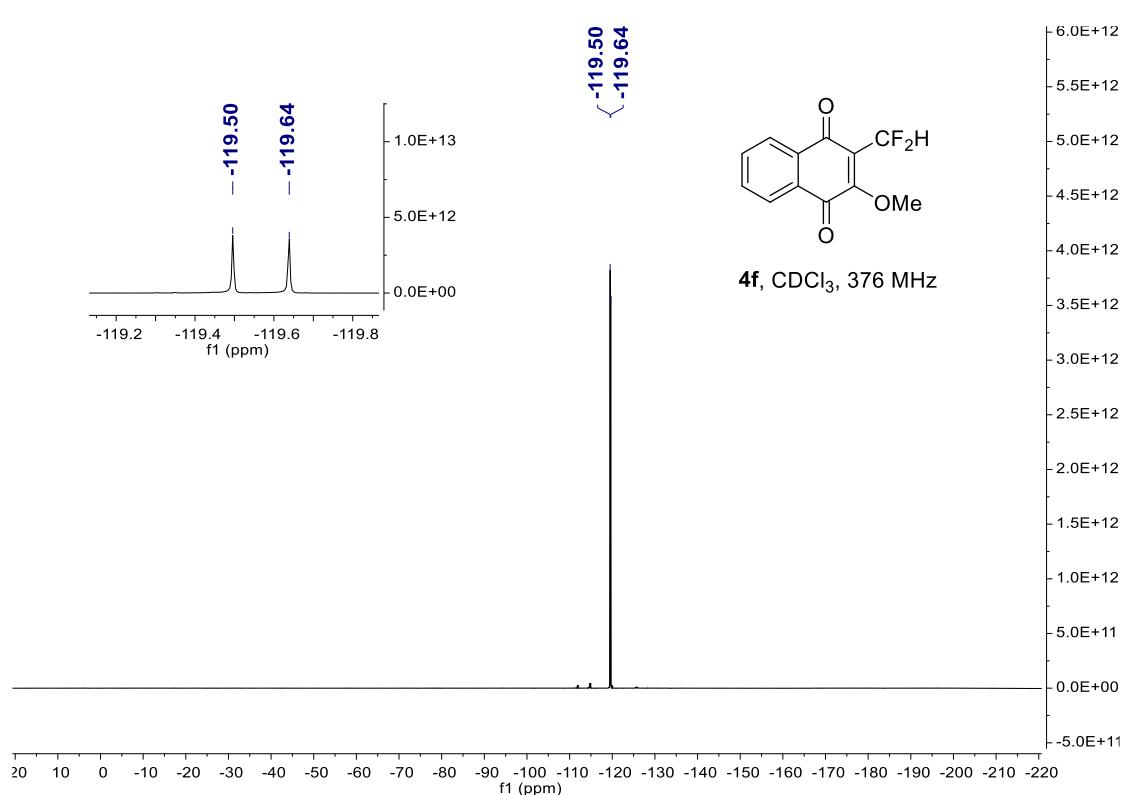
**3-(difluoromethyl)-2-phenyl-4*H*-chromen-4-one (4e)**



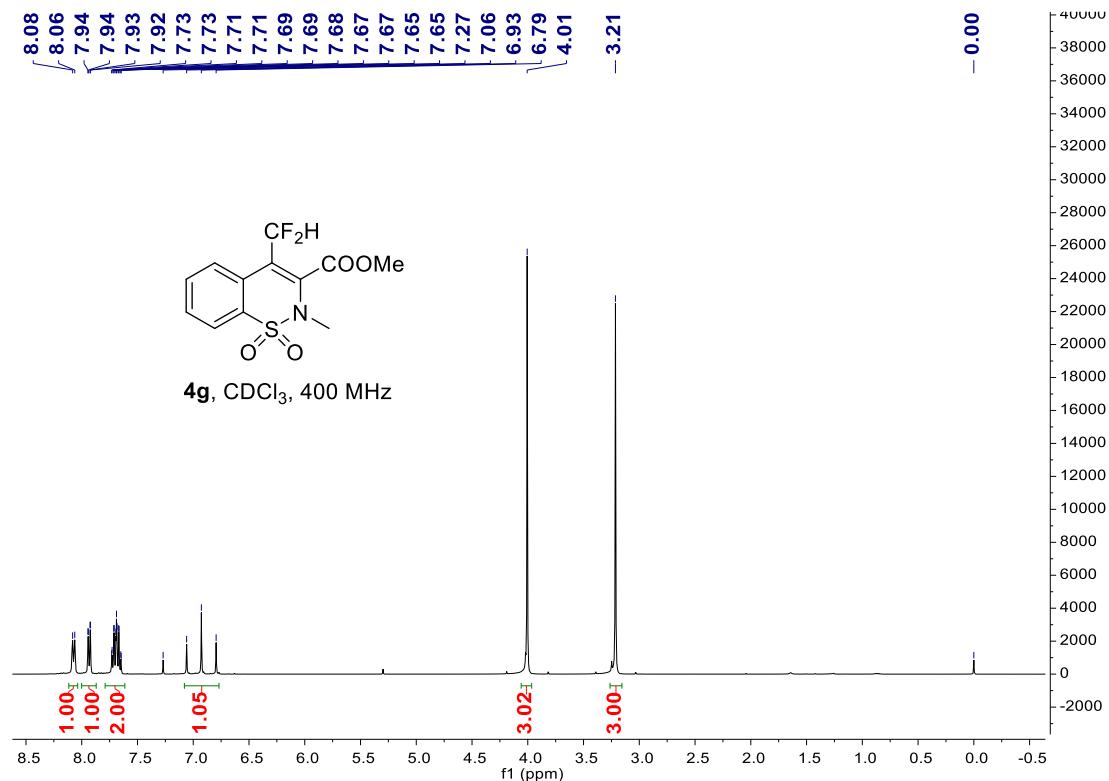


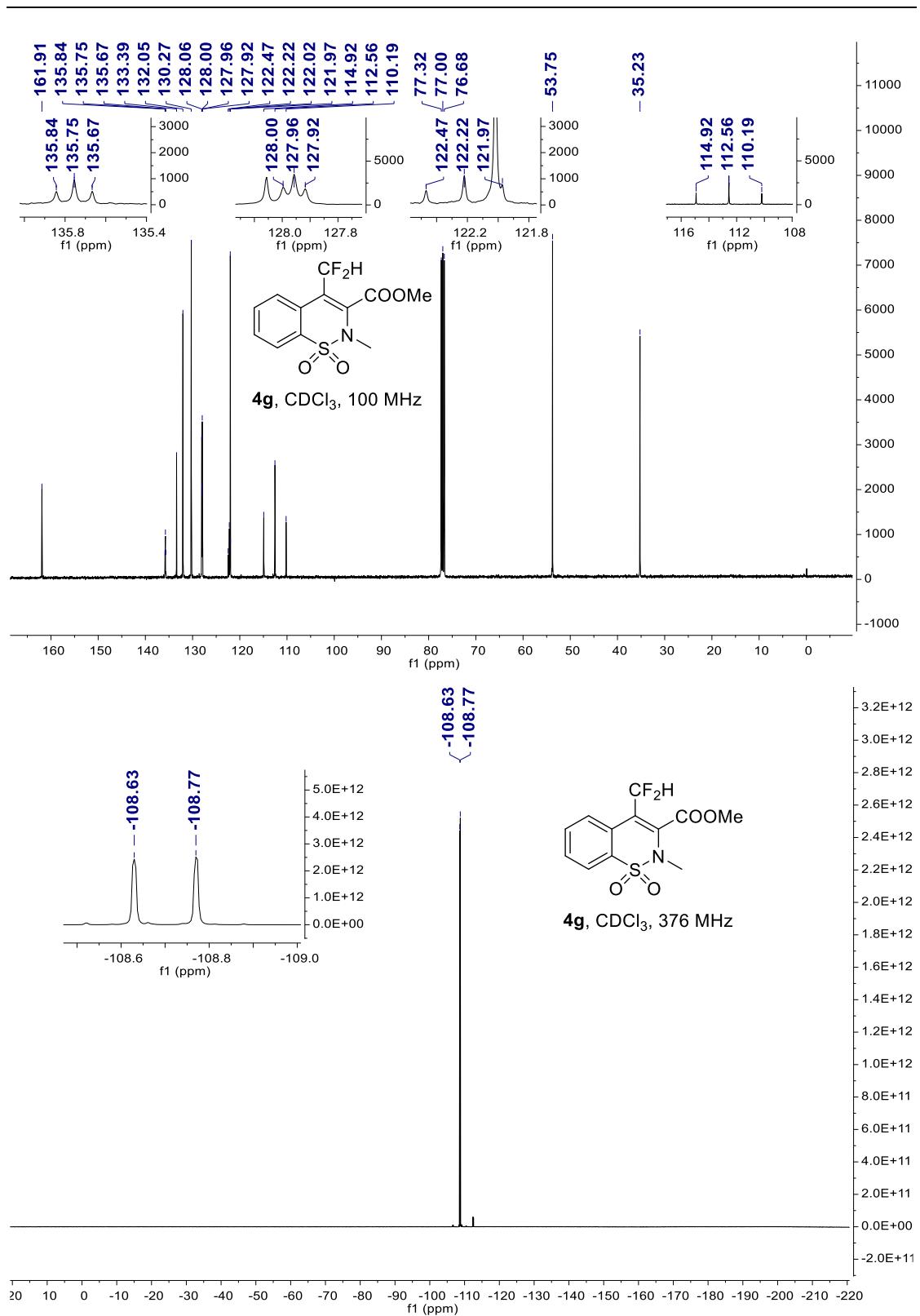
**2-(difluoromethyl)-3-methoxynaphthalene-1,4-dione (4f)**





**methyl 4-(difluoromethyl)-2-methyl-2H-benzo[e][1,2]thiazine-3-carboxylate 1,1-dioxide (4g)**





**(Z)-4,4-difluoro-N,N-diisopropyl-2-phenylbut-2-enamide (4h)**

