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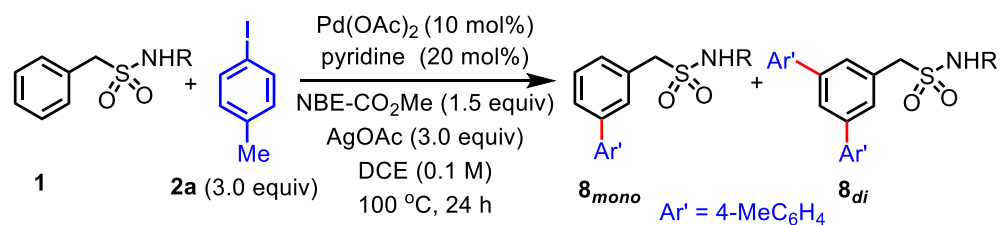
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## 1. General Information

Solvents and chemicals were obtained from Sigma-Aldrich, Acros and Alfa Aesar and used directly without further purification. 2-Carbomethoxynorbornene (NBE-CO<sub>2</sub>Me) was synthesized following the known procedure.<sup>1</sup> Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Vogel's permanganate. Preparative TLC was performed on 1.0 mm silica gel (Analtech). NMR spectra were recorded on a Varian Inova 400 instrument (400 MHz for <sup>1</sup>H; 100 MHz for <sup>13</sup>C), Bruker DRX-500 instrument (500 MHz for <sup>1</sup>H; 125 MHz for <sup>13</sup>C), Bruker DRX-600 instrument (600 MHz for <sup>1</sup>H; 150 MHz for <sup>13</sup>C). Chemical shifts were quoted in parts per million (ppm) referenced to 0.0 ppm for tetramethylsilane. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants, J, were reported in Hertz unit (Hz). Chemical shifts were reported in ppm referenced to the center line at 77.0 ppm of chloroform-d, 29.84 ppm of acetone-d<sub>6</sub>, 49.0 ppm of methanol-d<sub>4</sub> or 39.52 ppm of DMSO-d<sub>6</sub>. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight).

## 2. Experimental Section

### 2.1 Evaluation of Directing Groups for *meta*-Arylation of Benzylation of Benzylsulfonamides

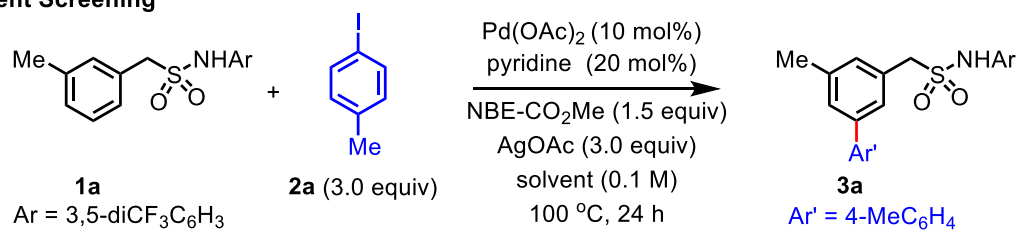


entry	R	yield (%) <sup>b</sup>		entry	R	yield (%) <sup>b</sup>	
		mono	di			mono	di
1	H	0	0	7	4-FC <sub>6</sub> H <sub>4</sub>	13	< 5
2	Me	0	0	8	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	9	< 5
3	<i>i</i> -Pr	0	0	9	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	15	< 5
4	<i>t</i> -Bu	0	0	10	C <sub>6</sub> F <sub>5</sub>	0	0
5	Ph	0	0	11	3,5-diNO <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	23	9
6	4-MeC <sub>6</sub> H <sub>4</sub>	0	0	12	3,5-diCF <sub>3</sub> C <sub>6</sub> H <sub>3</sub>	34	16

<sup>a</sup>Reaction conditions: substrates **1** (0.1 mmol), **2a** (3.0 equiv), Pd(OAc)<sub>2</sub> (10 mol %), pyridine (20 mol%), NBE-CO<sub>2</sub>Me (1.5 equiv), AgOAc (3.0 equiv), DCE (1.0 mL), 100 °C, 24 h. <sup>b</sup>The yields were determined by <sup>1</sup>H NMR analysis of the crude products using CH<sub>2</sub>Br<sub>2</sub> as the internal standard.

## 2.2 Optimization Reaction Conditions

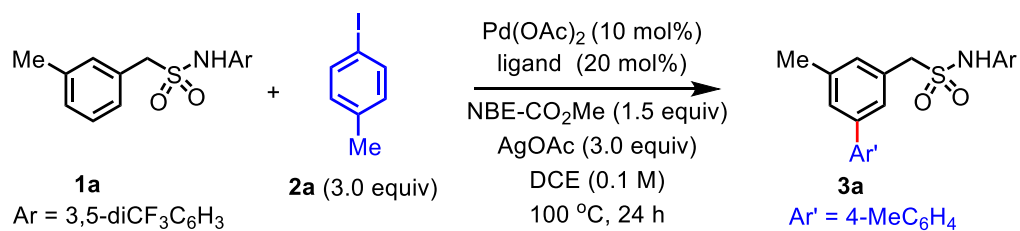
### Solvent Screening<sup>a</sup>



entry	solvent	yield of (%) <sup>b</sup>
1	TBME	24
2	1,4-dioxane	25
3	toluene	10
4	DMF	0
5	DMSO	0
6	CH <sub>3</sub> CN	0
7	CH <sub>2</sub> Cl <sub>2</sub>	21
8	CHCl <sub>3</sub>	37
9	ClCH <sub>2</sub> CH <sub>2</sub> Cl	42
10	HFIP	0
11	t-Amy-OH	0

<sup>a</sup>Reaction conditions: **1a** (0.1 mmol), **2a** (3.0 equiv), Pd(OAc)<sub>2</sub> (10 mol %), pyridine (20 mol%), NBE-CO<sub>2</sub>Me (1.5 equiv), AgOAc (3.0 equiv), solvent (1 mL), 100 °C, 24 h. <sup>b</sup>The yields were determined by <sup>1</sup>H NMR analysis of the crude products using CH<sub>2</sub>Br<sub>2</sub> as the internal standard.

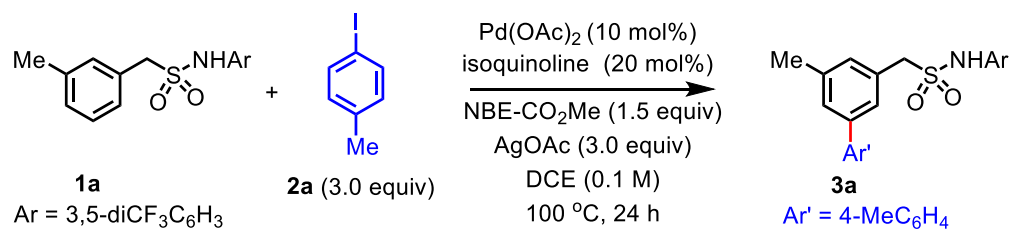
### Ligand Evaluation<sup>a</sup>



no ligand				
trace <sup>b</sup>	42%	69%	48%	23%
13%	20%	0%	45%	62%
53%	65%	32%	12%	trace
60%	65%	15%	38%	85%
54%	74%	71%	43%	
67%	37%	94%	75%	
48%	56%	65%	51%	

<sup>a</sup>Reaction conditions: **1a** (0.1 mmol), **2a** (3.0 equiv), Pd(OAc)<sub>2</sub> (10 mol %), ligand (20 mol%), NBE-CO<sub>2</sub>Me (1.5 equiv), AgOAc (3.0 equiv), DCE (1 mL), 100 °C, 24 h. <sup>b</sup>The yields were determined by <sup>1</sup>H NMR analysis of the crude products using CH<sub>2</sub>Br<sub>2</sub> as the internal standard.

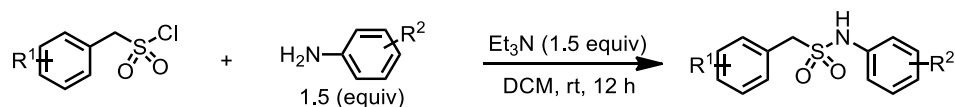
## Control experiments



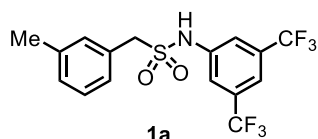
entry	deviation from standard conditions	yield of (%) <sup>b</sup>
1	none	94
2	2.0 equiv AgOAc	89
3	without AgOAc	<5
4	CsOAc instead of AgOAc	12
5	2.0 equiv <b>2a</b>	87
6	1.0 equiv NBE-CO <sub>2</sub> Me	90
7	norbornene instead of NBE-CO <sub>2</sub> Me	31
8	110 °C	93
9	90 °C	91
10	5 mol% Pd(OAc) <sub>2</sub> , 10 mol% isoquinoline	77

<sup>a</sup>Reaction conditions: **1a** (0.1 mmol), **2a** (3.0 equiv), Pd(OAc)<sub>2</sub> (10 mol %), isoquinoline (20 mol%), NBE-CO<sub>2</sub>Me (1.5 equiv), AgOAc (3.0 equiv), DCE (1 mL), 100 °C, 24 h. <sup>b</sup>The yields were determined by <sup>1</sup>H NMR analysis of the crude products using CH<sub>2</sub>Br<sub>2</sub> as the internal standard.

### 2.3 General Procedure for Synthesis of Benzylsulfonamide Substrates.

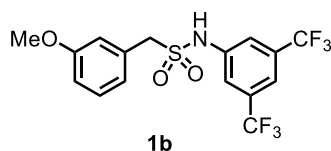


**General procedure for synthesis of benzylsulfonamide:**<sup>2</sup> benzylsulfonyl chloride (1.0 mmol) was added to a solution of aniline (1.5 mmol) and Et<sub>3</sub>N (151.5 mg, 1.5 mmol) in dry dichloromethane (5.0 mL) at room temperature. Then, the solution was stirred for 12 hours. After the reaction finished, the organic layer was washed with saturated aqueous sodium bicarbonate (10.0 mL), dried over sodium sulfate, filtered and concentrated. The residue was purified by column chromatography (ethyl acetate/hexane = 1/4) to yield the desired benzylsulfonamides.



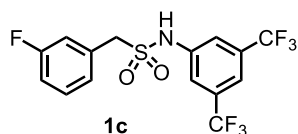
#### *N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(*m*-tolyl)methanesulfonamide (**1a**)

**1a** was obtained as white solid (361.3 mg, 91%); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.56 (s, 1H), 7.38 (s, 2H), 7.23 (s, 1H), 7.19–7.10 (m, 2H), 7.06–7.01 (m, 2H), 4.36 (s, 2H), 2.23 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 139.10, 139.03, 132.78 (q, *J* = 33.7 Hz), 131.40, 130.28, 128.99, 127.87, 127.12, 122.76 (q, *J* = 273.0 Hz), 118.87 (q, *J* = 3.2 Hz), 117.91–117.68 (m), 59.53, 20.95; HRMS (ESI-TOF) Calcd for C<sub>16</sub>H<sub>12</sub>F<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 396.0498; found: 396.0500.



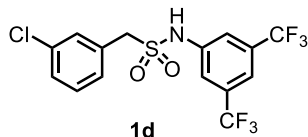
#### *N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-methoxyphenyl)methanesulfonamide (**1b**)

**1b** was obtained as white solid (392.6 mg, 95%); <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.57 (s, 1H), 7.38 (s, 2H), 7.24–7.20 (m, 1H), 6.89–6.86 (m, 1H), 6.82–6.79 (m, 2H), 6.74 (s, 1H), 4.39 (s, 2H), 3.74 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 160.03, 138.84, 132.84 (q, *J* = 33.9 Hz), 130.16, 128.71, 122.94, 122.73 (q, *J* = 272.9 Hz), 119.10 (q, *J* = 3.3 Hz, 2H), 118.10–117.84 (m), 116.42, 114.88, 59.53, 55.19; HRMS (ESI-TOF) Calcd for C<sub>16</sub>H<sub>12</sub>F<sub>6</sub>NO<sub>3</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 412.0448; found: 412.0448.



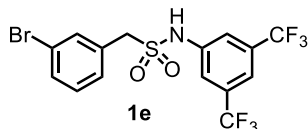
#### *N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-fluorophenyl)methanesulfonamide (**1c**)

**1c** was obtained as white solid (341.0 mg, 85%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.60 (s, 1H), 7.41 (s, 2H), 7.33–7.26 (m, 1H), 7.10–7.00 (m, 4H), 4.42 (s, 2H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 162.77 (d, *J* = 248.8 Hz), 138.63, 132.96 (q, *J* = 33.9 Hz), 130.71 (d, *J* = 8.4 Hz), 129.53 (d, *J* = 7.8 Hz), 126.53 (d, *J* = 3.1 Hz), 122.67 (q, *J* = 273.0 Hz), 119.05 (q, *J* = 3.1 Hz), 118.25–118.02 (m), 117.83 (d, *J* = 22.3 Hz), 116.67 (d, *J* = 20.9 Hz), 58.98; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -63.41, -111.57; HRMS (ESI-TOF) Calcd for C<sub>15</sub>H<sub>9</sub>F<sub>7</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 400.0248; found: 400.0249.



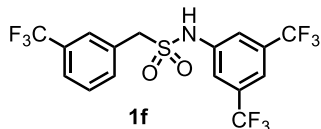
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-chlorophenyl)methanesulfonamide (1d)**

**1d** was obtained as white solid (380.1 mg, 91%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.52 (s, 1H), 7.80 (s, 2H), 7.67 (s, 1H), 7.41 (s, 1H), 7.37–7.28 (m, 3H), 4.72 (s, 2H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 139.13, 134.90, 132.79 (q, *J* = 33.6 Hz), 130.88, 130.22, 129.54, 129.38, 129.02, 122.75 (q, *J* = 273.1 Hz), 118.98 (q, *J* = 3.2 Hz), 117.99–117.77 (m), 58.97; HRMS (ESI-TOF) Calcd for C<sub>15</sub>H<sub>9</sub>ClF<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 415.9952; found: 415.9951.



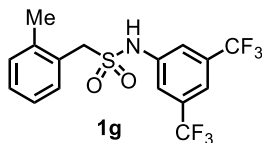
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-bromophenyl)methanesulfonamide (1e)**

**1e** was obtained as white solid (315.9 mg, 90%); <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.60 (s, 1H), 7.50–7.44 (m, 3H), 7.40 (s, 1H), 7.25–7.18 (m, 3H), 4.39 (s, 2H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 138.77, 133.70, 133.01 (q, *J* = 33.9 Hz), 132.62, 130.56, 129.60, 129.44, 122.97, 122.70 (q, *J* = 273.0 Hz), 119.03 (q, *J* = 3.1 Hz), 118.42–117.99 (m), 58.81; HRMS (ESI-TOF) Calcd for C<sub>15</sub>H<sub>9</sub>BrF<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 459.9447; found: 459.9450.



***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-(trifluoromethyl)phenyl)methanesulfonamide (1f)**

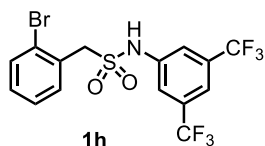
**1f** was obtained as white solid (392.6 mg, 87%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.66–7.57 (m, 2H), 7.56–7.44 (m, 3H), 7.41 (s, 2H), 7.07 (s, 1H), 4.49 (s, 2H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 138.55, 134.23, 133.09 (q, *J* = 33.9 Hz), 131.65 (q, *J* = 32.9 Hz), 129.73, 128.57, 127.45 (q, *J* = 3.5 Hz), 126.34 (q, *J* = 3.5 Hz), 123.33 (q, *J* = 272.6 Hz), 122.61 (q, *J* = 272.9 Hz), 118.79 (q, *J* = 3.3 Hz), 118.43–118.08 (m), 58.93; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -63.35, -63.49; HRMS (ESI-TOF) Calcd for C<sub>16</sub>H<sub>9</sub>F<sub>9</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 450.0216; found: 450.0218.



***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(*o*-tolyl)methanesulfonamide (1g)**

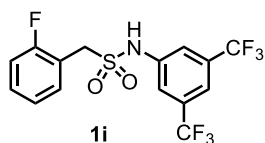
**1g** was obtained as white solid (349.3 mg, 88%); <sup>1</sup>H NMR (400 MHz, Acetone-*d*<sup>6</sup>) δ 9.42 (s, 1H), 7.74 (s, 2H), 7.64 (s, 1H), 7.27 (d, *J* = 7.5 Hz, 1H), 7.22–7.13 (m, 2H), 7.13–7.05 (m, 1H), 4.71 (s, 2H), 2.41 (s, 3H); <sup>13</sup>C NMR (125 MHz, Acetone-*d*<sup>6</sup>) δ 141.93, 139.39, 133.20, 132.88 (q, *J* = 33.3 Hz), 131.55, 129.89, 128.04, 124.19 (q, *J* = 272.2 Hz), 127.14–126.79 (m), 119.03 (q, *J* = 3.7 Hz), 117.30–116.97 (m), 57.56, 19.64; HRMS (ESI-TOF) Calcd for C<sub>16</sub>H<sub>12</sub>F<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 396.0498; found: 396.0501.





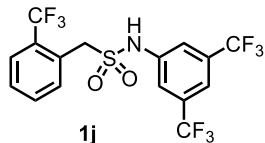
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(2-bromophenyl)methanesulfonamide (1h)**

**1h** was obtained as white solid (383.6 mg, 83%); <sup>1</sup>H NMR (400 MHz, Acetone-d<sup>6</sup>) δ 7.78 (s, 2H), 7.66–7.58 (m, 2H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.33–7.13 (m, 2H), 4.87 (s, 2H); <sup>13</sup>C NMR (100 MHz, Acetone-d<sup>6</sup>) δ 141.56, 134.37, 133.93, 132.73 (q, *J* = 33.3 Hz), 131.66, 129.51, 128.76, 126.23, 124.14 (q, *J* = 272.1 Hz), 118.84 (q, *J* = 3.3 Hz), 117.29–116.96 (m), 59.43; HRMS (ESI-TOF) Calcd for C<sub>15</sub>H<sub>9</sub>BrF<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 459.9447; found: 459.9447.



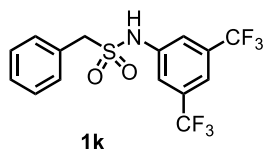
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(2-fluorophenyl)methanesulfonamide (1i)**

**1i** was obtained as white solid (333.0 mg, 83%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.55 (s, 1H), 7.46–7.37 (m, 3H), 7.34–7.26 (m, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.04 (s, 1H), 6.94 (t, *J* = 9.1 Hz, 1H), 4.52 (s, 2H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 160.99 (d, *J* = 249.3 Hz), 138.67, 132.69 (q, *J* = 33.8 Hz), 132.68 (d, *J* = 2.5 Hz), 131.75 (d, *J* = 8.4 Hz), 124.86 (d, *J* = 3.6 Hz), 122.73 (q, *J* = 273.0 Hz), 118.74 (q, *J* = 3.1 Hz), 118.02–117.80 (m), 115.76 (d, *J* = 21.3 Hz), 115.07 (d, *J* = 14.5 Hz), 52.67 (d, *J* = 2.8 Hz); <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -63.39, -116.95; HRMS (ESI-TOF) Calcd for C<sub>15</sub>H<sub>9</sub>F<sub>7</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 400.0248; found: 400.0251.



***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(2-(trifluoromethyl)phenyl)methanesulfonamide (1j)**

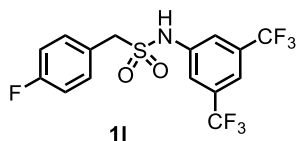
**1j** was obtained as white solid (383.6 mg, 85%); <sup>1</sup>H NMR (400 MHz, Acetone-d<sub>6</sub>) δ 9.64 (s, 1H), 7.83–7.76 (m, 3H), 7.76–7.61 (m, 3H), 7.57 (t, *J* = 7.6 Hz, 1H), 4.88 (s, 2H); <sup>13</sup>C NMR (100 MHz, Acetone-d<sup>6</sup>) δ 141.50, 134.84, 133.21 (d, *J* = 0.9 Hz), 132.97 (q, *J* = 33.3 Hz), 130.30, 130.25 (q, *J* = 30.0 Hz), 127.84–127.69 (m), 127.47 (q, *J* = 5.5 Hz), 125.10 (q, *J* = 273.6 Hz), 124.13 (q, *J* = 272.2 Hz), 119.39 (q, *J* = 3.5 Hz), 117.90–117.12 (m), 56.46; <sup>19</sup>F NMR (376 MHz, Acetone-d<sup>6</sup>) δ -58.73, -63.99; HRMS (ESI-TOF) Calcd for C<sub>16</sub>H<sub>9</sub>F<sub>9</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 450.0216; found: 450.0218.



***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-phenylmethanesulfonamide (1k)**

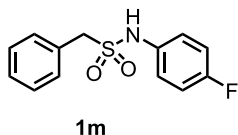
**1k** was obtained as white solid (367.1 mg, 96%); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.56 (s, 1H), 7.37 (s, 2H), 7.35–7.27 (m, 4H), 7.26–7.23 (m, 2H), 4.41 (s, 2H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 138.89, 132.80 (q, *J* = 33.7 Hz),

130.81, 129.56, 129.10, 127.28, 122.74 (q,  $J = 272.9$  Hz), 118.93 (q,  $J = 3.2$  Hz), 117.92–117.76 (m), 59.56; HRMS (ESI-TOF) Calcd for  $C_{15}H_{10}F_6NO_2S^-$ [M-H] $^-$ : 382.0342; found: 382.0341.



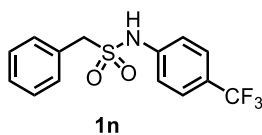
#### ***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(4-fluorophenyl)methanesulfonamide (1l)**

**1l** was obtained as white solid (361.0 mg, 90%);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.60 (s, 1H), 7.38 (s, 2H), 7.29–7.22 (m,  $J = 8.4, 5.4$  Hz, 2H), 7.02 (t,  $J = 8.5$  Hz, 2H), 6.89 (s, 1H), 4.41 (s, 2H);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  163.39 (d,  $J = 250.7$  Hz), 138.65, 132.97 (q,  $J = 33.9$  Hz), 132.66 (d,  $J = 8.5$  Hz), 123.30 (d,  $J = 3.3$  Hz), 122.67 (q,  $J = 272.9$  Hz), 119.00 (q,  $J = 3.4$  Hz), 118.22–117.91 (m), 116.27 (d,  $J = 21.9$  Hz), 58.69;  $^{19}F$  NMR (376 MHz,  $CDCl_3$ )  $\delta$  -63.44, -111.26; HRMS (ESI-TOF) Calcd for  $C_{15}H_9F_7NO_2S^-$ [M-H] $^-$ : 400.0248; found: 400.0248.



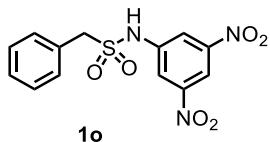
#### ***N*-(4-fluorophenyl)-1-phenylmethanesulfonamide (1m)**

**1m** was obtained as colorless crystal (238.5 mg, 90%);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.41–7.33 (m, 3H), 7.32–7.26 (m, 2H), 7.14–7.07 (m, 2H), 7.07–7.00 (m, 2H), 6.28 (s, 1H), 4.30 (s, 2H);  $^{13}C$  NMR (125 MHz,  $CDCl_3$ )  $\delta$  160.09 (d,  $J = 244.8$  Hz), 132.72 (d,  $J = 2.7$  Hz), 130.76, 128.97, 128.85, 128.28, 122.53 (d,  $J = 8.0$  Hz), 116.25 (d,  $J = 22.9$  Hz), 57.55; HRMS (ESI-TOF) Calcd for  $C_{13}H_{11}FNO_2S^-$ [M-H] $^-$ : 264.0500; found: 264.0503.



#### **1-Phenyl-*N*-(4-(trifluoromethyl)phenyl)methanesulfonamide (1n)**

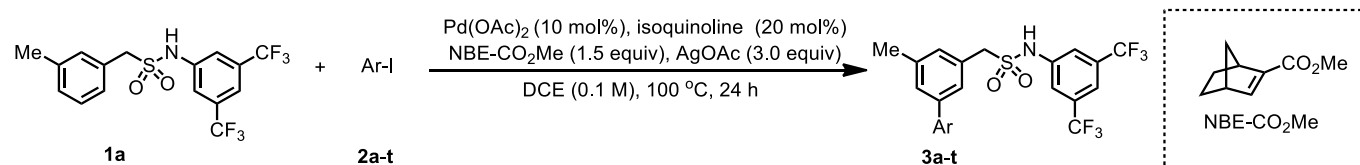
**1n** was obtained as colorless crystal (293.2 mg, 93%);  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  7.55 (d,  $J = 8.5$  Hz, 2H), 7.36–7.27 (m, 3H), 7.36–7.27 (m, 5H), 4.34 (s, 2H);  $^{13}C$  NMR (125 MHz,  $CDCl_3$ )  $\delta$  140.38, 130.78, 129.19, 128.94, 127.90, 126.79 (q,  $J = 3.7$  Hz), 126.35 (q,  $J = 32.9$  Hz), 123.92 (q,  $J = 271.6$  Hz), 118.56, 58.20; HRMS (ESI-TOF) Calcd for  $C_{14}H_{11}F_3NO_2S^-$ [M-H] $^-$ : 314.0468; found: 314.0469.



#### ***N*-(3,5-Dinitrophenyl)-1-phenylmethanesulfonamide (1o)**

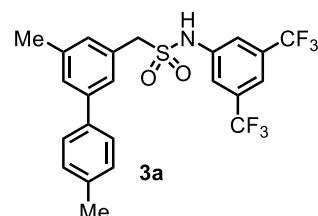
**1o** was obtained as yellow powder (300.0 mg, 89%);  $^1H$  NMR (500 MHz,  $DMSO-d_6$ )  $\delta$  10.94 (s, 1H), 8.41 (t,  $J = 2.0$  Hz, 1H), 8.16 (d,  $J = 2.0$  Hz, 2H), 7.35–7.22 (m, 5H), 4.74 (s, 2H);  $^{13}C$  NMR (125 MHz,  $DMSO-d_6$ )  $\delta$  148.39, 141.27, 131.17, 128.59, 128.49, 117.29, 111.79, 58.29; HRMS (ESI-TOF) Calcd for  $C_{13}H_{10}N_3O_6S^-$ [M-H] $^-$ : 336.0296; found: 336.0301.

## 2.4 General Procedure for the *meta*-C–H Arylation/Alkylation of Benzylsulfonamides.



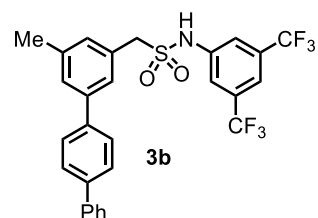
To a 10 mL sealed tube were added substrate **1a** (38.4 mg, 0.1 mmol), Pd(OAc)<sub>2</sub> (2.2 mg, 0.01 mmol), and AgOAc (50.0 mg, 0.3 mmol), isoquinoline (2.6 mg, 0.02 mmol, 2.4  $\mu$ L), NBE-CO<sub>2</sub>Me (22.8 mg, 0.15 mmol), aryl halide **2a-t** (0.3 mmol), and DCE (1.0 mL). The reaction mixture was heated to 100 °C for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of Celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by preparative TLC using an eluent of ethyl acetate/hexanes (1/4) to give the desired products **3a-t**.

All remaining products **4a-h**, **5a-l**, and **7a-h** were prepared using a procedure similar to that used to synthesize **3a-t**.



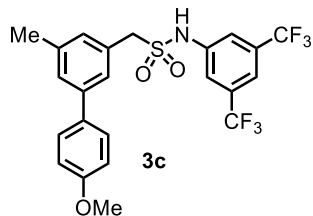
### *N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(4',5-dimethyl-[1,1'-biphenyl]-3-yl)methanesulfonamide (**3a**)

**3a** was obtained as white solid (43.8 mg, 90%); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.51 (s, 1H), 7.38 (s, 2H), 7.34 (s, 1H), 7.26 (d,  $J$  = 8.0 Hz, 2H), 7.22 (s, 1H), 7.19 (s, 1H), 7.15 (d,  $J$  = 7.9 Hz, 2H), 6.93 (s, 1H), 4.38 (s, 2H), 2.35 (s, 3H), 2.29 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  142.19, 139.48, 139.09, 137.56, 136.82, 132.80 (q,  $J$  = 33.7 Hz), 129.93, 129.48, 128.77, 127.66, 126.68, 126.43, 122.72 (q,  $J$  = 273.1 Hz), 118.54 (q,  $J$  = 3.2 Hz), 117.81–117.60 (m), 59.26, 21.06, 21.00; HRMS (ESI-TOF) Calcd for C<sub>23</sub>H<sub>18</sub>F<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 486.0968; found: 486.0972.



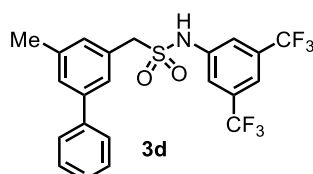
### *N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(5-methyl-[1,1':4',1''-terphenyl]-3-yl)methanesulfonamide (**3b**)

**3b** was obtained as white solid (48.3 mg, 88%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.62–7.55 (m, 4H), 7.51 (s, 1H), 7.47–7.42 (m, 4H), 7.42–7.33 (m, 4H), 7.27–7.23 (m, 2H), 6.98 (s, 1H), 4.41 (s, 2H), 2.31 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  141.74, 140.57, 140.44, 139.64, 139.04, 138.56, 132.83 (q,  $J$  = 33.7 Hz), 130.29, 128.87, 128.82, 127.77, 127.48, 127.46, 127.21, 127.00, 126.53, 122.70 (q,  $J$  = 273.1 Hz), 118.55 (q,  $J$  = 3.2 Hz), 117.85–117.74 (m), 59.29, 21.11; HRMS (ESI-TOF) Calcd for C<sub>28</sub>H<sub>20</sub>F<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 548.1124; found: 548.1125.



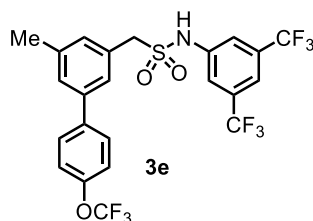
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(4'-methoxy-5-methyl-[1,1'-biphenyl]-3-yl)methanesulfonamide (3c)**

**3c** was obtained as white solid (35.7 mg, 71%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 (s, 1H), 7.38 (s, 2H), 7.34–7.28 (m, 3H), 7.17 (s, 2H), 6.91 (s, 1H), 6.88 (d,  $J = 8.6$  Hz, 2H), 4.38 (s, 2H), 3.82 (s, 3H), 2.29 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  159.45, 141.87, 139.48, 139.03, 132.83 (q,  $J = 33.6$  Hz), 132.23, 129.61, 128.56, 127.93, 127.69, 126.18, 122.71 (q,  $J = 273.1$  Hz), 118.66 (q,  $J = 3.0$  Hz), 117.92–117.75 (m), 114.22, 59.33, 55.30, 21.10; HRMS (ESI-TOF) Calcd for  $\text{C}_{23}\text{H}_{18}\text{F}_6\text{NO}_3\text{S}^-[\text{M-H}]^-$ : 502.0917; found: 502.0917.



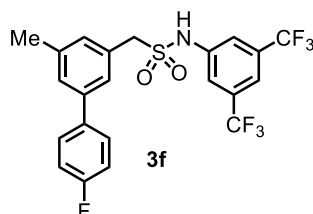
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(5-methyl-[1,1'-biphenyl]-3-yl)methanesulfonamide (3d)**

**3d** was obtained as white solid (43.0 mg, 91%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 (s, 1H), 7.41–7.28 (m, 8H), 7.22 (s, 1H), 7.10 (s, 1H), 6.98 (s, 1H), 4.41 (s, 2H), 2.31 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  142.30, 139.74, 139.56, 139.01, 132.85 (q,  $J = 33.8$  Hz), 130.22, 129.04, 128.78, 127.74), 127.72, 126.88, 126.64, 122.70 (q,  $J = 273.1$  Hz), 118.62 (q,  $J = 3.2$  Hz), 117.90–117.78 (m), 59.31, 21.09; HRMS (ESI-TOF) Calcd for  $\text{C}_{22}\text{H}_{16}\text{F}_6\text{NO}_2\text{S}^-[\text{M-H}]^-$ : 472.0811; found: 472.0814.



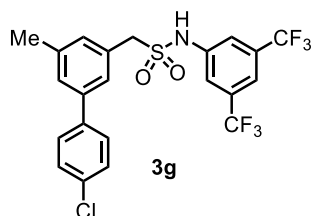
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(5-methyl-4'-(trifluoromethoxy)-[1,1'-biphenyl]-3-yl)methanesulfonamide (3e)**

**3e** was obtained as white solid (29.0 mg, 52%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 (s, 1H), 7.41–7.34 (m, 4H), 7.32 (s, 1H), 7.23–7.11 (m, 4H), 7.00 (s, 1H), 4.41 (s, 2H), 2.31 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  148.90, 140.86, 139.83, 139.01, 138.41, 132.87 (q,  $J = 33.7$  Hz), 130.60, 128.97, 128.20, 127.86, 126.60, 122.64 (q,  $J = 273.0$  Hz), 121.21, 120.61 (q,  $J = 204.1$  Hz), 118.42 (q,  $J = 3.3$  Hz), 117.88–117.69 (m), 59.18, 21.05;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -58.21, -63.44; HRMS (ESI-TOF) Calcd for  $\text{C}_{23}\text{H}_{15}\text{F}_9\text{NO}_3\text{S}^-[\text{M-H}]^-$ : 556.0634; found: 556.0638.



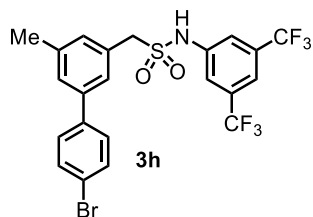
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(4'-fluoro-5-methyl-[1,1'-biphenyl]-3-yl)methanesulfonamide (3f)**

**3f** was obtained as white solid (40.3 mg, 82%); <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.54 (s, 1H), 7.40–7.35 (m, 4H), 7.33 (s, 1H), 7.20 (s, 1H), 7.10–7.05 (m, 2H), 7.01 (s, 1H), 6.86 (s, 1H), 4.43 (s, 2H), 2.34 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 162.69 (d, *J* = 247.4 Hz), 141.30, 139.65, 138.99, 135.94, 132.88 (q, *J* = 33.8 Hz), 130.26, 128.90, 128.54 (d, *J* = 8.1 Hz), 127.94, 126.53, 122.68 (q, *J* = 273.4 Hz), 118.80 (q, *J* = 3.2 Hz), 117.98–117.84 (m), 59.40, 21.11; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -63.36, -115.15; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -63.36, -115.15; HRMS (ESI-TOF) Calcd for C<sub>22</sub>H<sub>15</sub>F<sub>7</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>-</sup>: 490.0717; found: 490.0720.



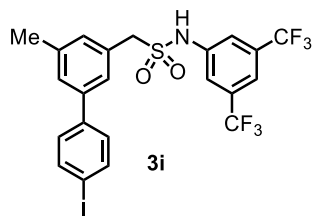
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(4'-chloro-5-methyl-[1,1'-biphenyl]-3-yl)methanesulfonamide (3g)**

**3g** was obtained as white solid (46.1 mg, 91%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.55 (s, 1H), 7.40–7.32 (m, 7H), 7.22 (s, 1H), 7.03 (s, 1H), 6.74 (s, 1H), 4.44 (s, 2H), 2.34 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 141.04, 139.77, 139.03, 138.15, 133.89, 132.87 (q, *J* = 33.7 Hz), 130.52, 128.93, 128.83, 128.09, 127.85, 126.46, 122.68 (q, *J* = 273.1 Hz), 118.48 (q, *J* = 3.3 Hz), 117.87–117.73 (m), 59.26, 21.04; HRMS (ESI-TOF) Calcd for C<sub>22</sub>H<sub>15</sub>ClF<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>-</sup>: 506.0422; found: 506.0422.



***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(4'-bromo-5-methyl-[1,1'-biphenyl]-3-yl)methanesulfonamide (3h)**

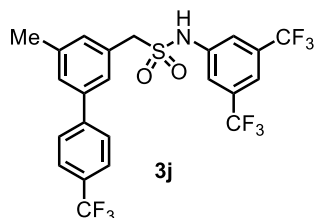
**3h** was obtained as white solid (50.2 mg, 91%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.55 (s, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.37 (s, 2H), 7.33 (s, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.21 (s, 1H), 7.01 (s, 1H), 6.85 (s, 1H), 4.43 (s, 2H), 2.33 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 141.05, 139.75, 139.07, 138.69, 132.86 (q, *J* = 33.8 Hz), 131.91, 130.61, 128.76, 128.46, 128.00, 126.44, 122.69 (q, *J* = 273.0 Hz), 122.07, 118.62 (q, *J* = 3.3 Hz), 117.92–117.71 (m), 59.31, 21.07; HRMS (ESI-TOF) Calcd for C<sub>22</sub>H<sub>15</sub>BrF<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>-</sup>: 549.9917; found: 549.9919.



***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(4'-iodo-5-methyl-[1,1'-biphenyl]-3-yl)methanesulfonamide (3i)**

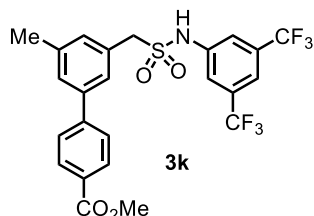
**3i** was obtained as white solid (43.1 mg, 72%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.69 (d, *J* = 8.2 Hz, 2H), 7.54 (s, 1H), 7.37 (s, 2H), 7.32 (s, 1H), 7.20 (s, 1H), 7.13 (d, *J* = 8.2 Hz, 2H), 7.02 (s, 1H), 7.00 (s, 1H), 4.41 (s, 2H), 2.32 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 141.15, 139.79, 139.26, 138.95, 137.90, 132.89 (q, *J* = 33.8 Hz), 130.63,

128.75, 128.68, 127.96, 126.38, 122.67 (q,  $J = 273.2$  Hz), 118.64 (q,  $J = 3.3$  Hz), 117.97–117.83 (m), 93.60, 59.30, 21.08; HRMS (ESI-TOF) Calcd for  $C_{22}H_{15}F_6INO_2S^- [M-H]^-$ : 597.9778; found: 597.9778.



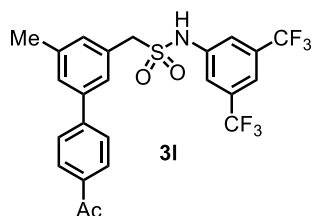
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(5-methyl-4'-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)methanesulfonamide (3j)**

**3j** was obtained as white solid (50.9 mg, 94%);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.58 (d,  $J = 8.2$  Hz, 2H), 7.51 (s, 1H), 7.46 (d,  $J = 8.2$  Hz, 2H), 7.37 (s, 2H), 7.36 (s, 1H), 7.28 (s, 1H), 7.22 (s, 1H), 7.01 (s, 1H), 4.42 (s, 2H), 2.31 (s, 3H);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  143.18, 140.81, 139.98, 138.97, 132.92 (q,  $J = 33.7$  Hz), 131.08, 129.78 (q,  $J = 32.5$  Hz), 129.14, 127.97, 127.15, 126.77, 125.70 (q,  $J = 3.5$  Hz), 124.08 (q,  $J = 272.0$  Hz), 122.64 (q,  $J = 273.0$  Hz), 118.38 (q,  $J = 3.1$  Hz), 117.91–117.76 (m), 59.17, 21.05;  $^{19}F$  NMR (376 MHz,  $CDCl_3$ )  $\delta$  -62.92, -63.41; HRMS (ESI-TOF) Calcd for  $C_{23}H_{15}F_9NO_2S^- [M-H]^-$ : 540.0685; found: 540.0686.



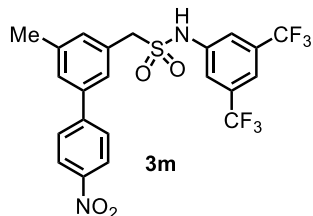
**Methyl 3'-((*N*-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-5'-methyl-[1,1'-biphenyl]-4-carboxylate (3k)**

**3k** was obtained as white solid (46.2 mg, 87%);  $^1H$  NMR (400 MHz, Acetone- $d_6$ )  $\delta$  9.39 (brs, 1H), 8.05 (d,  $J = 8.2$  Hz, 2H), 7.75 (s, 2H), 7.64 (d,  $J = 8.2$  Hz, 2H), 7.62 (s, 1H), 7.49 (s, 2H), 7.24 (s, 1H), 4.73 (s, 2H), 3.91 (s, 3H), 2.34 (s, 3H);  $^{13}C$  NMR (100 MHz, Acetone- $d_6$ )  $\delta$  167.00, 145.46, 142.10, 140.89, 139.95, 132.83 (q,  $J = 33.3$  Hz), 132.57, 130.71, 130.54, 130.15, 128.97, 128.09, 127.70, 124.12 (q,  $J = 272.2$  Hz), 119.07 (q,  $J = 3.3$  Hz), 117.38–117.16 (m), 59.65, 52.37, 21.14; HRMS (ESI-TOF) Calcd for  $C_{24}H_{20}F_6NO_4S [M+H]^+$ : 532.1012; found: 532.1016.



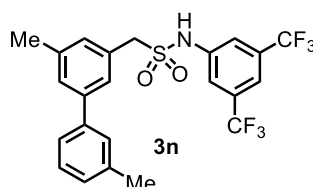
**1-(4'-Acetyl-5-methyl-[1,1'-biphenyl]-3-yl)-*N*-(3,5-bis(trifluoromethyl)phenyl)methanesulfonamide (3l)**

**3l** was obtained as white solid (41.7 mg, 81%);  $^1H$  NMR (400 MHz, Acetone- $d_6$ )  $\delta$  9.40 (s, 1H), 8.04 (d,  $J = 8.3$  Hz, 2H), 7.75 (s, 2H), 7.65 (d,  $J = 8.3$  Hz, 2H), 7.62 (s, 1H), 7.50 (s, 2H), 7.23 (s, 1H), 4.73 (s, 2H), 2.61 (s, 3H), 2.34 (s, 3H);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  197.49, 145.31, 142.11, 140.96, 139.94, 137.18, 132.83 (q,  $J = 33.3$  Hz), 132.55, 130.53, 129.71–129.58 (m), 128.96, 128.12, 127.74, 124.13 (q,  $J = 272.1$  Hz), 119.05, 117.25, 59.68, 26.72, 21.14; HRMS (ESI-TOF) Calcd for  $C_{24}H_{20}F_6NO_3S [M+H]^+$ : 516.1063; found: 516.1064.



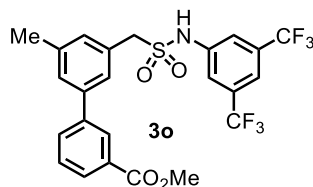
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(5-methyl-4'-nitro-[1,1'-biphenyl]-3-yl)methanesulfonamide (3m)**

**3m** was obtained as white solid (42.5 mg, 82%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.23 (d,  $J = 8.7$  Hz, 2H), 7.56 (d,  $J = 8.7$  Hz, 2H), 7.54 (s, 1H), 7.39 (s, 3H), 7.30 (s, 1H), 7.10 (s, 1H), 7.04 (s, 1H), 4.47 (s, 2H), 2.35 (s, 3H);  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  147.28, 146.15, 140.14, 139.78, 138.94, 132.90 (q,  $J = 33.7$  Hz), 131.83, 129.20, 128.31, 127.67, 126.88, 124.09, 122.62 (q,  $J = 273.0$  Hz), 118.64 (q,  $J = 3.2$  Hz), 118.00–117.86 (m), 59.30, 21.08; HRMS (ESI-TOF) Calcd for  $\text{C}_{22}\text{H}_{15}\text{F}_6\text{N}_2\text{O}_4\text{S}^-[\text{M-H}]^-$ : 517.0662; found: 517.0664.



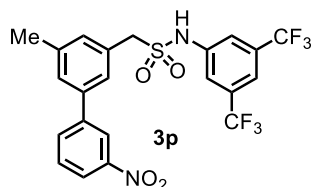
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3',5-dimethyl-[1,1'-biphenyl]-3-yl)methanesulfonamide (3n)**

**3n** was obtained as white solid (45.3 mg, 92%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.51 (s, 1H), 7.37 (s, 2H), 7.34 (s, 1H), 7.28–7.20 (m, 3H), 7.20–7.09 (m, 3H), 6.94 (s, 1H), 4.39 (s, 2H), 2.35 (s, 3H), 2.30 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  142.41, 139.71, 139.46, 139.06, 138.41, 132.77 (q,  $J = 33.7$  Hz), 130.10, 129.01, 128.64, 128.44, 127.61, 127.59, 126.65, 123.98, 122.70 (q,  $J = 273.1$  Hz), 118.54 (q,  $J = 3.0$  Hz), 117.82–117.59 (m), 59.33, 21.35, 21.06; HRMS (ESI-TOF) Calcd for  $\text{C}_{23}\text{H}_{18}\text{F}_6\text{NO}_2\text{S}^-[\text{M-H}]^-$ : 486.0968; found: 486.0971.



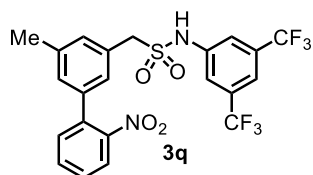
**Methyl 3'-((*N*-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-5'-methyl-[1,1'-biphenyl]-3-carboxylate (3o)**

**3o** was obtained as white solid (46.7 mg, 88%);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 (s, 1H), 7.95 (d,  $J = 7.4$  Hz, 1H), 7.55 (d,  $J = 7.6$  Hz, 1H), 7.50 (s, 2H), 7.45 (s, 2H), 7.41 (t,  $J = 7.7$  Hz, 1H), 7.35 (s, 1H), 7.32 (s, 1H), 7.01 (s, 1H), 4.46 (s, 2H), 3.91 (s, 3H), 2.31 (s, 3H);  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  167.13, 140.81, 139.95, 139.65, 139.29, 132.71 (q,  $J = 33.6$  Hz), 131.22, 130.76, 130.47, 128.88, 128.75, 128.71, 128.07, 127.89, 126.65, 122.72 (q,  $J = 273.0$  Hz), 118.59 (q,  $J = 3.3$  Hz), 117.71–117.57 (m), 59.27, 52.28, 21.03; HRMS (ESI-TOF) Calcd for  $\text{C}_{24}\text{H}_{19}\text{F}_6\text{NNaO}_4\text{S}^+[\text{M+Na}]^+$ : 554.0831; found: 554.0832.



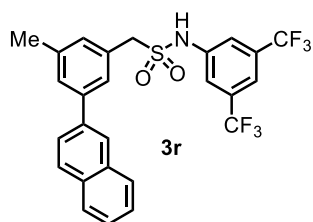
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(5-methyl-3'-nitro-[1,1'-biphenyl]-3-yl)methanesulfonamide (3p)**

**3p** was obtained as white solid (48.7 mg, 94%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.28 (s, 1H), 8.19 (d, *J* = 8.1 Hz, 1H), 7.73 (d, *J* = 7.7 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.53 (s, 1H), 7.40 (s, 1H), 7.37 (s, 2H), 7.30 (s, 1H), 7.10 (s, 1H), 7.00 (s, 1H), 4.48 (s, 2H), 2.36 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 148.60, 141.43, 140.19, 139.62, 139.05, 132.84 (q, *J* = 33.6 Hz), 132.78, 131.51, 129.79, 128.96, 128.27, 126.70, 122.64 (q, *J* = 273.3 Hz), 122.45, 121.70, 118.53 (q, *J* = 2.9 Hz), 117.89–117.75 (m), 59.39, 21.04; HRMS (ESI-TOF) Calcd for C<sub>22</sub>H<sub>15</sub>F<sub>6</sub>N<sub>2</sub>O<sub>4</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 517.0662; found: 517.0665.



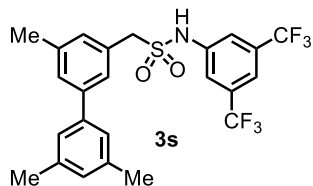
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(5-methyl-2'-nitro-[1,1'-biphenyl]-3-yl)methanesulfonamide (3q)**

**3q** was obtained as white solid (50.8 mg, 98%); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.86 (d, *J* = 8.1 Hz, 1H), 7.61–7.54 (m, 2H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.46 (s, 2H), 7.27–7.19 (m, 2H), 7.12 (s, 1H), 7.08 (s, 1H), 6.99 (s, 1H), 4.40 (s, 2H), 2.30 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 148.89, 139.66, 138.95, 138.49, 135.31, 132.83 (q, *J* = 33.7 Hz), 132.60, 131.60, 131.31, 129.59, 128.63, 128.01, 127.19, 124.27, 122.73 (q, *J* = 273.2 Hz), 118.97 (q, *J* = 3.4 Hz), 117.91–117.69 (m), 58.82, 20.99; HRMS (ESI-TOF) Calcd for C<sub>22</sub>H<sub>15</sub>F<sub>6</sub>N<sub>2</sub>O<sub>4</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 517.0662; found: 517.0663.



***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-methyl-5-(naphthalen-2-yl)phenyl)methanesulfonamide (3r)**

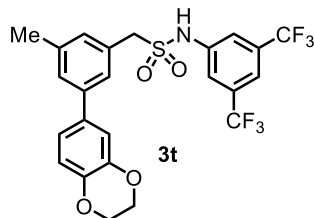
**3r** was obtained as white solid (47.1 mg, 90%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.88–7.73 (m, 4H), 7.56–7.41 (m, 5H), 7.37 (s, 3H), 7.18 (s, 1H), 6.95 (s, 1H), 4.42 (s, 2H), 2.32 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 142.14, 139.64, 138.99, 136.99, 133.42, 132.73 (q, *J* = 33.5 Hz), 132.66, 130.25, 129.22, 128.51, 128.10, 127.75, 127.57, 126.86, 126.38, 126.15, 125.71, 124.97, 122.65 (q, *J* = 273.0 Hz), 118.47 (q, *J* = 3.1 Hz), 117.78–117.58 (m), 59.26, 21.08; HRMS (ESI-TOF) Calcd for C<sub>26</sub>H<sub>18</sub>F<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 522.0968; found: 522.0967.



***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl)methanesulfonamide (3s)**

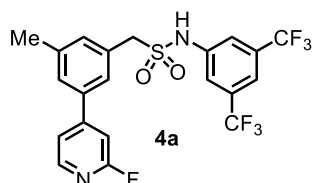
**3s** was obtained as white solid (45.1 mg, 90%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.52 (s, 1H), 7.37 (s, 2H), 7.34 (s, 1H), 7.23 (s, 1H), 7.07 (s, 1H), 6.99 (s, 2H), 6.95 (d, *J* = 3.6 Hz, 2H), 4.40 (s, 2H), 2.35–2.28 (m, 9H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 142.55, 139.77, 139.37, 139.02, 138.32, 132.76 (q, *J* = 33.6 Hz), 130.02, 129.34, 129.05, 127.57, 126.68, 124.79, 122.70 (q, *J* = 273.0 Hz), 118.66 (q, *J* = 2.9 Hz), 117.82–117.64 (m), 59.40, 21.23, 21.07; HRMS (ESI-TOF) Calcd for C<sub>24</sub>H<sub>20</sub>F<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 500.1124; found: 500.1128.





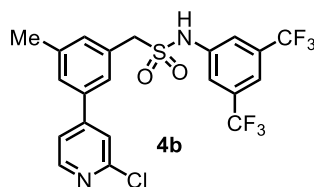
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-5-methylphenyl)methanesulfonamide (**3t**)**

**3t** was obtained as white solid (46.7 mg, 88%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 (s, 1H), 7.37 (s, 2H), 7.28 (s, 1H), 7.18 (s, 1H), 7.15 (s, 1H), 6.92 (s, 1H), 6.90 (s, 1H), 6.88–6.81 (m, 2H), 4.38 (s, 2H), 4.25 (s, 4H), 2.28 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  143.69, 143.47, 141.61, 139.46, 139.07, 133.24, 132.79 (q,  $J = 33.8$  Hz), 129.78, 128.56, 127.62, 126.28, 122.72 (q,  $J = 273.1$  Hz), 119.86, 118.57 (q,  $J = 3.1$  Hz), 117.85–117.69 (m), 117.54, 115.61, 64.41, 64.32, 59.36, 21.07; HRMS (ESI-TOF) Calcd for  $\text{C}_{24}\text{H}_{20}\text{F}_6\text{NO}_4\text{S}[\text{M}+\text{H}]^+$ : 532.1012; found: 532.1012.



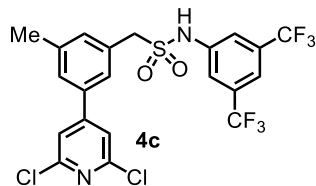
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-(2-fluoropyridin-4-yl)-5-methylphenyl)methanesulfonamide (**4a**)**

**4a** was obtained as white solid (31.0 mg, 63%);  $^1\text{H}$  NMR (400 MHz, Acetone- $d_6$ )  $\delta$  9.39 (brs, 1H), 8.26 (d,  $J = 5.2$  Hz, 1H), 7.73 (s, 2H), 7.63–7.55 (m, 3H), 7.47 (d,  $J = 5.2$  Hz, 1H), 7.34 (s, 1H), 7.19 (s, 1H), 4.75 (s, 2H), 2.35 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz, Acetone- $d_6$ )  $\delta$  165.48 (d,  $J = 235.2$  Hz), 153.98, 153.92, 149.08 (d,  $J = 16.0$  Hz), 142.11, 140.37, 137.97 (d,  $J = 3.4$  Hz), 134.04, 132.83 (q,  $J = 33.1$  Hz), 128.89, 128.08, 124.11 (q,  $J = 272.0$  Hz), 120.26 (d,  $J = 3.9$  Hz), 119.05 (q,  $J = 3.7$  Hz), 117.43–117.17 (m), 107.32 (d,  $J = 39.3$  Hz), 59.68, 21.08;  $^{19}\text{F}$  NMR (376 MHz, Acetone- $d_6$ )  $\delta$  -63.94, -70.26; HRMS (ESI-TOF) Calcd for  $\text{C}_{21}\text{H}_{16}\text{F}_7\text{N}_2\text{O}_2\text{S}[\text{M}+\text{H}]^+$ : 493.0815; found: 493.0816.



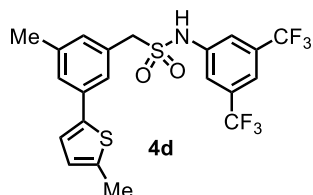
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-(2-chloropyridin-4-yl)-5-methylphenyl)methanesulfonamide (**4b**)**

**4b** was obtained as white solid (25.5 mg, 50%);  $^1\text{H}$  NMR (400 MHz, Acetone- $d_6$ )  $\delta$  9.40 (s, 1H), 8.42 (d,  $J = 5.2$  Hz, 1H), 7.71 (s, 2H), 7.61–7.54 (m, 4H), 7.52 (dd,  $J = 5.2, 1.5$  Hz, 1H), 7.33 (s, 1H), 4.75 (s, 2H), 2.35 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz, Acetone- $d_6$ )  $\delta$  152.80, 151.47, 151.13, 142.09, 140.41, 137.65, 134.03, 132.80 (q,  $J = 33.2$  Hz), 130.92, 128.89, 128.09, 124.10 (q,  $J = 272.3$  Hz), 122.28, 121.28, 119.03 (q,  $J = 3.3$  Hz), 117.41–117.11 (m), 59.70, 21.06; HRMS (ESI-TOF) Calcd for  $\text{C}_{21}\text{H}_{16}\text{ClF}_6\text{N}_2\text{O}_2\text{S}[\text{M}+\text{H}]^+$ : 509.0520; found: 509.0520.



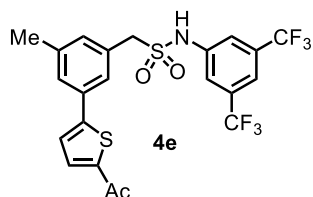
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-(2,6-dichloropyridin-4-yl)-5-methylphenyl)methanesulfonamide (4c)**

**4c** was obtained as white solid (45.1 mg, 83%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.56 (s, 1H), 7.39–7.34 (m, 3H), 7.28 (s, 3H), 7.17 (s, 1H), 7.15 (s, 1H), 4.47 (s, 2H), 2.34 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  152.60, 151.16, 140.56, 138.83, 136.85, 133.10, 132.99 (d,  $J = 32.7$  Hz), 128.87, 128.67, 126.61, 122.60 (q,  $J = 273.0$  Hz), 120.60, 118.67 (q,  $J = 3.1$  Hz), 118.14–117.98 (m), 59.32, 21.03; HRMS (ESI-TOF) Calcd for  $\text{C}_{21}\text{H}_{15}\text{Cl}_2\text{F}_6\text{N}_2\text{O}_2\text{S}[\text{M}+\text{H}]^+$ : 543.0130; found: 543.0133.



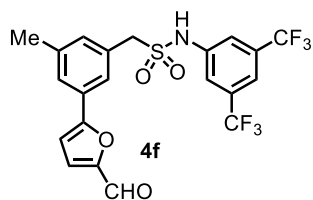
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-methyl-5-(5-methylthiophen-2-yl)phenyl)methanesulfonamide (4d)**

**4d** was obtained as white solid (35.0 mg, 71%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.54 (s, 1H), 7.43 (s, 2H), 7.31 (s, 1H), 7.14 (s, 1H), 7.08 (s, 1H), 6.95 (d,  $J = 3.4$  Hz, 1H), 6.86 (s, 1H), 6.66–6.63 (m, 1H), 4.34 (s, 2H), 2.45 (s, 3H), 2.28 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  140.22, 140.19, 139.68, 139.00, 135.63, 132.88 (q,  $J = 33.7$  Hz), 129.87, 127.95, 126.99, 126.24, 124.71, 123.39, 122.74 (q,  $J = 273.1$  Hz), 118.63 (q,  $J = 3.1$  Hz), 117.93–117.75 (m), 58.94, 21.03, 15.29; HRMS (ESI-TOF) Calcd for  $\text{C}_{21}\text{H}_{16}\text{F}_6\text{NO}_2\text{S}[\text{M}-\text{H}]^-$ : 492.0532; found: 492.0533.



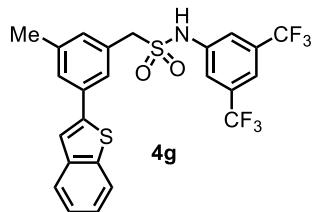
**1-(3-(5-Acetylthiophen-2-yl)-5-methylphenyl)-*N*-(3,5-bis(trifluoromethyl)phenyl)methanesulfonamide (4e)**

**4e** was obtained as white solid (31.8 mg, 61%);  $^1\text{H}$  NMR (400 MHz, Acetone- $\text{d}_6$ )  $\delta$  9.39 (s, 1H), 7.82 (d,  $J = 3.9$  Hz, 1H), 7.75 (s, 2H), 7.61 (s, 1H), 7.54 (s, 1H), 7.51 (s, 1H), 7.42 (d,  $J = 3.9$  Hz, 1H), 7.20 (s, 1H), 4.71 (s, 2H), 2.54 (s, 3H), 2.31 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz, Acetone- $\text{d}_6$ )  $\delta$  190.77, 151.81, 144.41, 142.10, 140.27, 134.78, 134.55, 133.26, 132.81 (q,  $J = 33.3$  Hz), 130.84, 127.75, 127.01, 125.43, 124.12 (q,  $J = 272.2$  Hz), 119.07 (q,  $J = 1.8$  Hz), 117.26, 59.56, 26.47, 20.99; HRMS (ESI-TOF) Calcd for  $\text{C}_{22}\text{H}_{18}\text{F}_6\text{NO}_3\text{S}_2[\text{M}+\text{H}]^+$ : 522.0627; found: 522.0628.



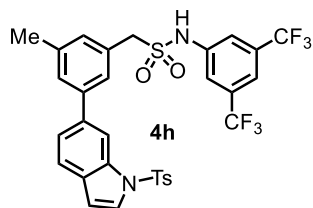
***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-(5-formylfuran-2-yl)-5-methylphenyl)methanesulfonamide (4f)**

**4f** was obtained as white solid (37.3 mg, 71%); <sup>1</sup>H NMR (400 MHz, Acetone-d<sup>6</sup>) δ 9.66 (s, 1H), 9.37 (s, 1H), 7.74 (s, 2H), 7.67 (s, 1H), 7.63 (s, 1H), 7.60 (s, 1H), 7.51 (d, *J* = 3.7 Hz, 1H), 7.23 (s, 1H), 7.05 (d, *J* = 3.7 Hz, 1H), 4.74 (s, 2H), 2.31 (s, 3H); <sup>13</sup>C NMR (150 MHz, Acetone-d<sup>6</sup>) δ 177.89, 158.83, 153.34, 142.09, 140.15, 133.78, 132.77 (q, *J* = 33.3 Hz), 130.79, 130.4, 126.69, 125.89, 124.71, 124.10 (q, *J* = 272.1 Hz), 119.17 (q, *J* = 3.6 Hz), 117.37–117.16 (m), 109.18, 59.64, 21.00; HRMS (ESI-TOF) Calcd for C<sub>21</sub>H<sub>16</sub>F<sub>6</sub>NO<sub>4</sub>S[M+H]<sup>+</sup>: 492.0699; found: 492.0702.



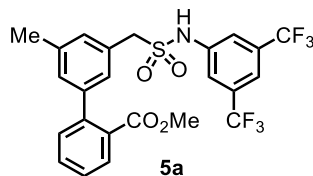
**1-(3-(Benzo[b]thiophen-2-yl)-5-methylphenyl)-N-(3,5-bis(trifluoromethyl)phenyl)methanesulfonamide (4g)**

**4g** was obtained as white solid (22.7 mg, 43%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.78 (d, *J* = 7.5 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.52 (s, 1H), 7.48 (s, 1H), 7.45 (s, 2H), 7.40 (s, 1H), 7.37–7.28 (m, 3H), 6.99 (s, 1H), 6.97 (s, 1H), 4.39 (s, 2H), 2.33 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 142.47, 140.38, 139.92, 139.40, 138.89, 135.29, 132.93 (q, *J* = 33.7 Hz), 131.15, 128.22, 128.10, 125.70, 124.67, 124.66, 123.69, 122.70 (q, *J* = 273.2 Hz), 122.22, 120.04, 118.71 (q, *J* = 3.1 Hz), 118.07–117.89 (m), 58.92, 21.06; HRMS (ESI-TOF) Calcd for C<sub>24</sub>H<sub>16</sub>F<sub>6</sub>NO<sub>2</sub>S<sub>2</sub>[M-H]<sup>-</sup>: 528.0532; found: 528.0534.



**N-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-methyl-5-(1-tosyl-1H-indol-6-yl)phenyl)methanesulfonamide (4h)**

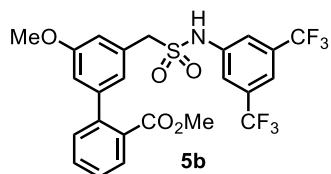
**4h** was obtained as white solid (34.0 mg, 51%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.10 (s, 1H), 7.77 (s, 1H), 7.75 (s, 1H), 7.57 (d, *J* = 3.6 Hz, 1H), 7.50 (s, 1H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.39 (s, 3H), 7.34 (s, 1H), 7.28–7.17 (m, 4H), 6.99 (s, 1H), 6.65 (d, *J* = 3.7 Hz, 1H), 4.47 (s, 2H), 2.33 (s, 3H), 2.31 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 145.12, 142.37, 139.53, 139.10, 136.73, 135.36, 135.18, 132.72 (q, *J* = 33.6 Hz), 130.23, 130.21, 129.94, 129.22, 127.88, 127.08, 126.99, 126.76, 122.69, 122.69 (q, *J* = 273.0 Hz), 121.59, 118.82 (q, *J* = 3.1 Hz), 117.92–117.67 (m), 111.87, 108.88, 59.53, 21.50, 21.12; HRMS (ESI-TOF) Calcd for C<sub>31</sub>H<sub>25</sub>F<sub>6</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>[M+H]<sup>+</sup>: 667.1154; found: 667.1151.



**Methyl 3'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-5'-methyl-[1,1'-biphenyl]-2-carboxylate (5a)**

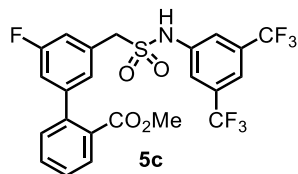
**5a** was obtained as white solid (52.0 mg, 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.93 (d, *J* = 7.8 Hz, 1H), 7.74 (s, 1H), 7.60–7.52 (m, 2H), 7.49–7.41 (m, 3H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.27 (s, 1H), 7.18 (s, 1H), 6.66 (s, 1H), 4.41 (s, 2H), 3.85 (s, 3H), 2.25 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 169.25, 142.40, 141.84, 139.26, 138.94, 132.58 (q, *J* = 33.6 Hz), 131.98, 130.52, 130.43, 130.20, 129.76, 129.65, 127.6, 127.49, 127.18, 122.82 (q, *J* = 272.9 Hz),

119.62 (q,  $J = 2.5$  Hz), 117.88–117.61 (m), 58.66, 52.61, 20.9; HRMS (ESI-TOF) Calcd for  $C_{24}H_{19}F_6NNaO_4S[M+Na]^+$ : 554.0831; found: 554.0832.



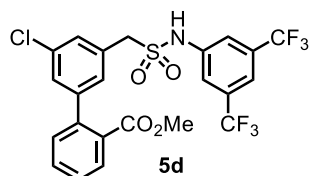
**Methyl 3'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-5'-methoxy-[1,1'-biphenyl]-2-carboxylate (5b)**

**5b** was obtained as white solid (46.5 mg, 85%);  $^1H$  NMR (400 MHz, Acetone- $d_6$ )  $\delta$  9.36 (s, 1H), 7.81–7.73 (m, 3H), 7.66 (s, 1H), 7.59–7.53 (m, 1H), 7.50–7.44 (m, 1H), 7.22 (d,  $J = 7.6$  Hz, 1H), 6.95 (s, 1H), 6.86 (s, 1H), 6.85–6.82 (m, 1H), 4.69 (s, 2H), 3.78 (s, 3H), 3.62 (s, 3H);  $^{13}C$  NMR (150 MHz, Acetone- $d_6$ )  $\delta$  169.25, 160.50, 143.78, 141.97, 141.90, 132.94 (q,  $J = 33.2$  Hz), 132.22, 132.02, 131.20, 130.92, 130.37, 128.45, 124.39, 124.17 (q,  $J = 272.1$  Hz), 119.28 (q,  $J = 3.4$  Hz), 117.65–117.05 (m), 116.48, 115.04, 59.38, 55.66, 52.30; HRMS (ESI-TOF) Calcd for  $C_{24}H_{19}F_6NNaO_5S[M+Na]^+$ : 570.0780; found: 570.0781.



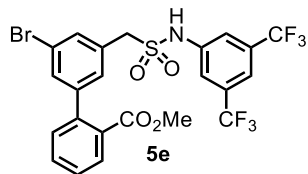
**Methyl 3'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-5'-fluoro-[1,1'-biphenyl]-2-carboxylate (5c)**

**5c** was obtained as white solid (43.9 mg, 82%);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.97 (d,  $J = 7.8$  Hz, 1H), 7.84 (s, 1H), 7.61–7.55 (m, 2H), 7.54–7.44 (m, 3H), 7.31 (d,  $J = 7.6$  Hz, 1H), 7.21 (s, 1H), 7.07 (d,  $J = 9.0$  Hz, 1H), 6.66 (d,  $J = 8.4$  Hz, 1H), 4.42 (s, 2H), 3.85 (s, 3H);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  168.80, 162.40 (d,  $J = 249.0$  Hz), 144.13 (d,  $J = 8.2$  Hz), 141.10, 138.97, 132.82 (q,  $J = 33.7$  Hz), 132.21, 130.71, 130.35, 129.57, 129.53, 128.25, 126.15 (d,  $J = 2.4$  Hz), 122.75 (q,  $J = 272.9$  Hz), 119.55 (q,  $J = 2.9$  Hz), 118.09–117.90 (m), 116.41 (d,  $J = 22.2$  Hz), 116.15 (d,  $J = 21.8$  Hz), 58.09, 52.69;  $^{19}F$  NMR (376 MHz,  $CDCl_3$ )  $\delta$  -63.46, -112.35; HRMS (ESI-TOF) Calcd for  $C_{23}H_{16}F_7NNaO_4S[M+Na]^+$ : 558.0580; found: 558.0584.



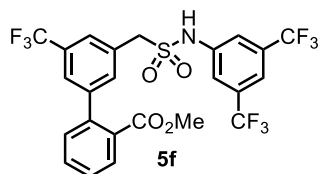
**Methyl 3'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-5'-chloro-[1,1'-biphenyl]-2-carboxylate (5d)**

**5d** was obtained as white solid (45.8 mg, 83%);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.98 (d,  $J = 7.4$  Hz, 1H), 7.84 (s, 1H), 7.62–7.56 (m, 2H), 7.54–7.46 (m, 3H), 7.35 (s, 1H), 7.34–7.30 (m, 2H), 6.90 (s, 1H), 4.40 (s, 2H), 3.86 (s, 3H);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  168.76, 143.59, 141.02, 138.97, 134.61, 132.90 (q,  $J = 33.7$  Hz), 132.27, 130.78, 130.40, 129.47, 129.30 (2C), 128.98, 128.54, 128.30, 122.76 (q,  $J = 273.0$  Hz), 119.41 (q,  $J = 3.2$  Hz), 118.16–117.97 (m), 57.93, 52.73; HRMS (ESI-TOF) Calcd for  $C_{23}H_{16}ClF_6NNaO_4S[M+Na]^+$ : 574.0285; found: 574.0286.



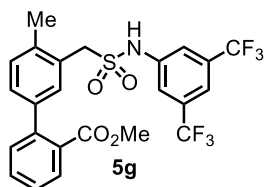
**Methyl 3'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-5'-bromo-[1,1'-biphenyl]-2-carboxylate (5e)**

**5e** was obtained as white solid (54.8 mg, 92%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (d,  $J = 7.8$  Hz, 1H), 7.81 (s, 1H), 7.63–7.55 (m, 2H), 7.52 (s, 2H), 7.51–7.46 (m, 2H), 7.37 (s, 1H), 7.31 (d,  $J = 7.8$  Hz, 1H), 7.06 (s, 1H), 4.40 (s, 2H), 3.85 (s, 3H);  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  168.75, 143.73, 140.86, 138.96, 132.91 (q,  $J = 33.8$  Hz), 132.25, 132.14, 131.85, 130.76, 130.42, 129.48, 129.04, 128.30, 122.76 (q,  $J = 273.0$  Hz), 122.45, 119.32 (q,  $J = 3.1$  Hz), 118.16–117.95 (m), 57.87, 52.72; HRMS (ESI-TOF) Calcd for  $\text{C}_{23}\text{H}_{16}\text{BrF}_6\text{NNaO}_4\text{S}[\text{M}+\text{Na}]^+$ : 617.9780; found: 617.9782.



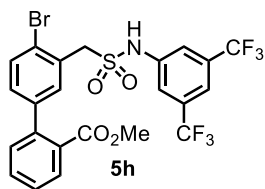
**Methyl 3'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-5'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxylate (5f)**

**5f** was obtained as white solid (50.3 mg, 86%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (d,  $J = 7.8$  Hz, 1H), 7.92 (s, 1H), 7.67 (s, 1H), 7.65–7.59 (m, 3H), 7.55–7.47 (m, 3H), 7.35 (d,  $J = 7.6$  Hz, 1H), 7.15 (s, 1H), 4.50 (s, 2H), 3.85 (s, 3H);  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  168.69, 142.90, 140.92, 138.89, 133.67, 133.01 (q,  $J = 33.7$  Hz), 132.44, 131.45 (q,  $J = 32.9$  Hz), 130.93, 130.55, 129.41, 128.75, 128.51, 126.00 (q,  $J = 3.3$  Hz), 125.70 (q,  $J = 3.1$  Hz), 123.30 (q,  $J = 272.6$  Hz), 122.71 (q,  $J = 272.9$  Hz), 118.97 (q,  $J = 3.1$  Hz), 118.13–117.92 (m), 57.89, 52.74;  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -63.20, -63.53; HRMS (ESI-TOF) Calcd for  $\text{C}_{24}\text{H}_{16}\text{F}_9\text{NNaO}_4\text{S}[\text{M}+\text{Na}]^+$ : 608.0549; found: 608.0545.



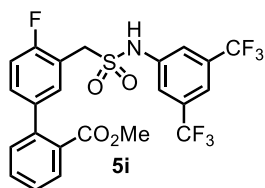
**Methyl 3'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-4'-methyl-[1,1'-biphenyl]-2-carboxylate (5g)**

**5g** was obtained as white solid (42.5 mg, 80%);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 (d,  $J = 7.7$  Hz, 1H), 7.85 (brs, 1H), 7.60–7.54 (m, 2H), 7.47–7.41 (m, 4H), 7.33 (d,  $J = 7.4$  Hz, 1H), 7.27 (dd,  $J = 7.8, 1.5$  Hz, 1H), 7.15 (d,  $J = 7.8$  Hz, 1H), 4.49 (s, 2H), 3.87 (s, 3H), 1.90 (s, 3H);  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  169.43, 142.32, 139.36, 139.03, 136.62, 132.58 (q,  $J = 33.7$  Hz), 132.11, 131.04, 130.63, 130.61, 130.58, 129.51, 128.85, 127.59, 126.29, 122.78 (q,  $J = 273.0$  Hz), 119.88 (q,  $J = 3.3$  Hz), 117.88–117.68 (m), 55.43, 52.70, 18.63; HRMS (ESI-TOF) Calcd for  $\text{C}_{24}\text{H}_{19}\text{F}_6\text{NNaO}_4\text{S}[\text{M}+\text{Na}]^+$ : 554.0831; found: 554.0833.



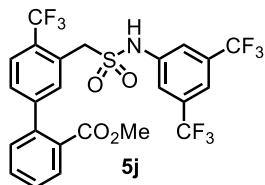
**Methyl 3'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-4'-bromo-[1,1'-biphenyl]-2-carboxylate (5h)**

**5h** was obtained as white solid (37.0 mg, 62%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (d,  $J = 8.0$  Hz, 1H), 7.90 (brs, 1H), 7.70 (s, 1H), 7.64–7.58 (m, 2H), 7.52–7.46 (m, 2H), 7.44–7.36 (m, 3H), 7.25 (d,  $J = 7.7$  Hz, 1H), 4.73 (s, 2H), 3.92 (s, 3H);  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  169.22, 141.47, 140.98, 138.52, 133.25, 132.67 (q,  $J = 33.6$  Hz), 132.48, 131.71, 131.09, 130.48, 130.19, 129.20, 128.16, 127.54, 124.93, 122.86 (q,  $J = 272.9$  Hz), 119.99 (q,  $J = 3.2$  Hz), 118.26–118.07 (m), 57.81, 52.90; HRMS (ESI-TOF) Calcd for  $\text{C}_{23}\text{H}_{16}\text{BrF}_6\text{NNaO}_4\text{S}[\text{M}+\text{Na}]^+$ : 617.9780; found: 617.9780.



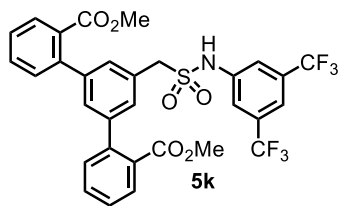
**Methyl 3'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-4'-fluoro-[1,1'-biphenyl]-2-carboxylate (5i)**

**5i** was obtained as white solid (41.2 mg, 77%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.98 (dd,  $J = 7.8, 1.0$  Hz, 1H), 7.74 (s, 1H), 7.63–7.52 (m, 3H), 7.51–7.44 (m, 3H), 7.39–7.31 (m, 2H), 6.98 (t,  $J = 9.0$  Hz, 1H), 4.51 (s, 2H), 3.88 (s, 3H);  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  169.14, 160.10 (d,  $J = 249.8$  Hz), 141.48, 138.62, 137.64 (d,  $J = 3.6$  Hz), 132.66 (q,  $J = 33.5$  Hz), 132.26, 131.86 (d,  $J = 1.5$  Hz), 130.84, 130.72 (d,  $J = 8.5$  Hz), 130.51, 129.53, 127.93, 122.80 (q,  $J = 272.9$  Hz), 119.62 (q,  $J = 3.1$  Hz), 118.18–117.97 (m), 115.64 (d,  $J = 22.5$  Hz), 115.16 (d,  $J = 15.1$  Hz), 52.74, 50.37 (d,  $J = 4.1$  Hz);  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -63.43, -120.78 HRMS (ESI-TOF) Calcd for  $\text{C}_{23}\text{H}_{16}\text{F}_7\text{NNaO}_4\text{S}[\text{M}+\text{Na}]^+$ : 558.0580; found: 558.0579.



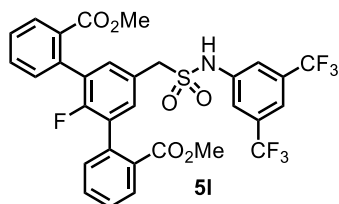
**Methyl 3'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxylate (5j)**

**5j** was obtained as white solid (43.3 mg, 74%);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07 (d,  $J = 7.9$  Hz, 1H), 7.95 (s, 1H), 7.70–7.63 (m, 2H), 7.58 (s, 1H), 7.56–7.51 (m, 2H), 7.41 (d,  $J = 7.6$  Hz, 1H), 7.36 (s, 2H), 4.66 (s, 2H), 3.93 (s, 3H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ )  $\delta$  169.27, 145.29, 141.25, 138.40, 132.71, 132.62 (q,  $J = 33.7$  Hz), 131.98, 131.22, 130.80, 128.95, 128.60, 128.52, 128.01 (q,  $J = 30.3$  Hz), 126.91 (q,  $J = 5.4$  Hz), 126.15, 123.36 (q,  $J = 274.2$  Hz), 122.79 (q,  $J = 272.9$  Hz), 120.41 (q,  $J = 3.1$  Hz), 118.46–118.23 (m), 54.86 (d,  $J = 2.6$  Hz), 53.02;  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -59.61, -63.52; HRMS (ESI-TOF) Calcd for  $\text{C}_{24}\text{H}_{16}\text{F}_9\text{NNaO}_4\text{S}[\text{M}+\text{Na}]^+$ : 608.0549; found: 608.0547.



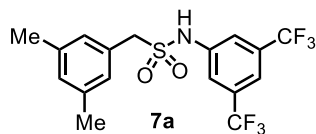
**Dimethyl 5'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-[1,1':3',1''-terphenyl]-2,2''-dicarboxylate (5k)**

**5k** was obtained as white solid (58.6 mg, 90%);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.90 (dd,  $J = 7.6, 0.7$  Hz, 2H), 7.62 (s, 2H), 7.55–7.50 (m, 3H), 7.46–7.41 (m, 2H), 7.29 (s, 1H), 7.26 (d,  $J = 7.3$  Hz, 2H), 7.19 (d,  $J = 1.2$  Hz, 2H), 4.46 (s, 2H), 3.79 (s, 6H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  168.73, 141.93, 141.64, 139.50, 132.73 (q,  $J = 33.6$  Hz), 131.75, 130.61, 130.31, 130.0, 129.31, 128.99, 127.77, 127.71, 122.79 (q,  $J = 273.0$  Hz), 119.33 (q,  $J = 3.4$  Hz), 117.66–117.44 (m), 58.12, 52.41; HRMS (ESI-TOF) Calcd for  $\text{C}_{31}\text{H}_{23}\text{F}_6\text{NNaO}_6\text{S}[\text{M}+\text{Na}]^+$ : 674.1042; found: 674.1043.



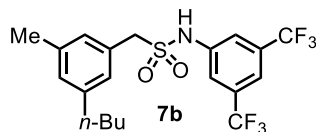
**Dimethyl 5'-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-2'-fluoro-[1,1':3',1''-terphenyl]-2,2''-dicarboxylate (5l)**

**5l** was obtained as white solid (62.9 mg, 94%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.67 (brs, 1H), 8.00 (d,  $J = 7.7$  Hz, 2H), 7.69 (s, 2H), 7.59–7.52 (m, 3H), 7.51–7.44 (m, 2H), 7.28 (s, 1H), 7.26 (s, 1H), 7.16 (d,  $J = 6.4$  Hz, 2H), 4.39 (s, 2H), 3.81 (s, 6H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  167.83, 156.32 (d,  $J = 248.3$  Hz), 139.46, 135.69, 132.84 (q,  $J = 33.5$  Hz), 132.12 (d,  $J = 1.6$  Hz), 132.03, 131.29, 130.43, 130.24, 129.60 (d,  $J = 17.8$  Hz), 128.38, 123.68, 122.76 (q,  $J = 266.8$  Hz), 119.41 (q,  $J = 2.2$  Hz), 117.71–117.59 (m), 57.26, 52.39;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -63.43, -119.23; HRMS (ESI-TOF) Calcd for  $\text{C}_{31}\text{H}_{22}\text{F}_7\text{NNaO}_6\text{S}[\text{M}+\text{Na}]^+$ : 692.0948; found: 692.0948.



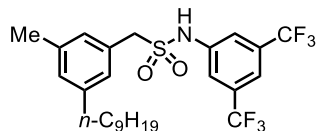
**N-(3,5-Bis(trifluoromethyl)phenyl)-1-(3,5-dimethylphenyl)methanesulfonamide (7a)**

**7a** was obtained as white solid (26.7 mg, 65%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57 (s, 1H), 7.39 (s, 2H), 6.96 (s, 1H), 6.83 (s, 3H), 4.34 (s, 2H), 2.21 (s, 6H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  139.08, 138.94, 132.76 (q,  $J = 33.7$  Hz), 131.10, 128.52, 127.05, 122.74 (q,  $J = 272.9$  Hz), 118.94 (q,  $J = 3.2$  Hz), 118.42–116.94 (m), 59.42, 20.86; HRMS (ESI-TOF) Calcd for  $\text{C}_{17}\text{H}_{14}\text{F}_6\text{NO}_2\text{S}[\text{M}-\text{H}]^-$ : 410.0655; found: 410.0656.



**N-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-butyl-5-methylphenyl)methanesulfonamide (7b)**

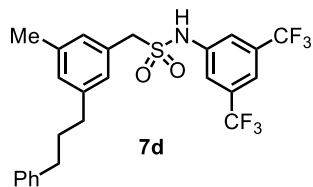
**7b** was obtained as white solid (27.2 mg, 60%);  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.56 (s, 1H), 7.37 (s, 2H), 7.08 (s, 1H), 6.96 (s, 1H), 6.86 (s, 1H), 6.81 (s, 1H), 4.34 (s, 2H), 2.46–2.42 (m, 2H), 2.22 (s, 3H), 1.47–1.40 (m, 2H), 1.32–1.24 (m, 2H), 0.87 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  144.08, 139.16, 138.93, 132.78 (q,  $J = 33.7$  Hz), 130.43, 128.77, 127.89, 127.04, 122.77 (q,  $J = 273.0$  Hz), 118.77 (q,  $J = 2.8$  Hz), 117.80–117.60 (m), 59.50, 35.17, 33.40, 22.33, 20.93, 13.75; HRMS (ESI-TOF) Calcd for  $\text{C}_{20}\text{H}_{20}\text{F}_6\text{NO}_2\text{S}^+[\text{M}-\text{H}]$ : 452.1124; found: 452.1123.



**7c**

### ***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-methyl-5-nonylphenyl)methanesulfonamide (7c)**

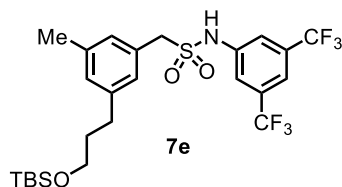
**7c** was obtained as white solid (31.4 mg, 60%);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57 (s, 1H), 7.37 (s, 2H), 6.97 (s, 1H), 6.87 (s, 1H), 6.83 (s, 2H), 4.34 (s, 2H), 2.51–2.41 (m, 2H), 2.24 (s, 2H), 1.51–1.38 (m, 3H), 1.36–1.22 (m, 12H), 0.88 (t,  $J = 6.9$  Hz, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  144.14, 139.06, 138.92, 132.78 (q,  $J = 33.6$  Hz), 130.41, 128.77, 127.88, 127.11, 122.75 (q,  $J = 272.9$  Hz), 118.92 (q,  $J = 3.1$  Hz), 117.99–117.52 (m), 59.43, 35.51, 31.85, 31.37, 29.49, 29.37, 29.34, 29.28, 22.65, 20.97, 14.09; HRMS (ESI-TOF) Calcd for  $\text{C}_{25}\text{H}_{30}\text{F}_6\text{NO}_2\text{S}^+[\text{M}-\text{H}]$ : 522.1907; found: 522.1908.



**7d**

### ***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-methyl-5-(3-phenylpropyl)phenyl)methanesulfonamide (7d)**

**7d** was obtained as white solid (24.2 mg, 47%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.55 (s, 1H), 7.36 (s, 2H), 7.31–7.23 (m, 2H), 7.20–7.08 (m, 3H), 6.96 (s, 2H), 6.84 (d,  $J = 8.6$  Hz, 2H), 4.33 (s, 2H), 2.59 (t,  $J = 7.6$  Hz, 2H), 2.53–2.45 (m, 2H), 2.22 (s, 3H), 1.88–1.75 (m, 2H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  143.47, 141.89, 139.07, 139.01, 132.78 (q,  $J = 33.8$  Hz), 130.42, 128.93, 128.35, 128.32, 127.92, 127.13, 125.82, 122.75 (q,  $J = 272.9$  Hz), 118.86 (q,  $J = 3.1$  Hz), 117.88–117.69 (m), 59.44, 35.40, 34.91, 32.68, 20.93; HRMS (ESI-TOF) Calcd for  $\text{C}_{25}\text{H}_{22}\text{F}_6\text{NO}_2\text{S}^+[\text{M}-\text{H}]$ : 514.1281; found: 514.1282.



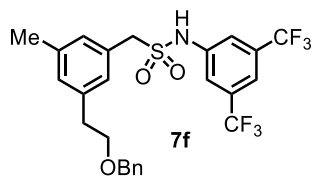
**7e**

### ***N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(3-(3-((*tert*-butyldimethylsilyloxy)propyl)-5-methylphenyl)methanesulfonamide (7e)**

**7e** was obtained as white solid (41.0 mg, 72%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.55 (s, 1H), 7.37 (s, 2H), 7.15 (s, 1H), 6.97 (s, 1H), 6.86 (s, 1H), 6.84 (s, 1H), 4.34 (s, 2H), 3.56 (t,  $J = 6.2$  Hz, 2H), 2.60–2.40 (m, 2H), 2.21 (s, 3H), 1.72–1.62 (m, 2H), 0.89 (s, 9H), 0.03 (s, 6H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  143.49, 139.18, 138.95, 132.76 (q,  $J = 33.5$  Hz), 130.52, 128.87, 127.96, 127.08, 122.76 (q,  $J = 273.0$  Hz), 118.74 (q,  $J = 3.2$  Hz), 117.78–117.57 (m),

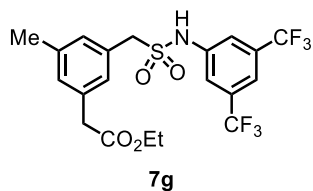


62.13, 59.50, 34.17, 31.65, 25.88, 20.90, 18.28, -5.39; HRMS (ESI-TOF) Calcd for C<sub>25</sub>H<sub>32</sub>F<sub>6</sub>NO<sub>3</sub>SSi<sup>-</sup>[M-H]<sup>-</sup>: 568.1782; found: 568.1784.



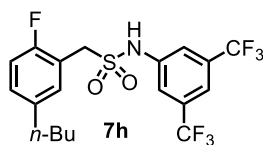
**1-(3-(2-(Benzyloxy)ethyl)-5-methylphenyl)-N-(3,5-bis(trifluoromethyl)phenyl)methanesulfonamide (7f)**

**7f** was obtained as white solid (23.9 mg, 45%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.55 (s, 1H), 7.33 (s, 2H), 7.32–7.20 (m, 5H), 7.02 (s, 1H), 6.94–6.80 (m, 3H), 4.46 (s, 2H), 4.30 (s, 2H), 3.62 (t, *J* = 6.7 Hz, 2H), 2.78 (t, *J* = 6.6 Hz, 2H), 2.24 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 140.23, 139.07, 139.02, 138.16, 132.71 (q, *J* = 33.5 Hz), 130.76, 129.47, 128.45, 128.35, 127.76, 127.70, 127.40, 122.78 (q, *J* = 273.0 Hz), 118.97 (q, *J* = 3.1 Hz), 117.76–117.62 (m), 72.88, 70.66, 59.05, 35.75, 20.95; HRMS (ESI-TOF) Calcd for C<sub>25</sub>H<sub>22</sub>F<sub>6</sub>NO<sub>3</sub>S<sup>-</sup>[M-H]<sup>-</sup>: 530.1230; found: 530.1229.



**Ethyl 2-(3-((N-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)methyl)-5-methylphenyl)acetate (7g)**

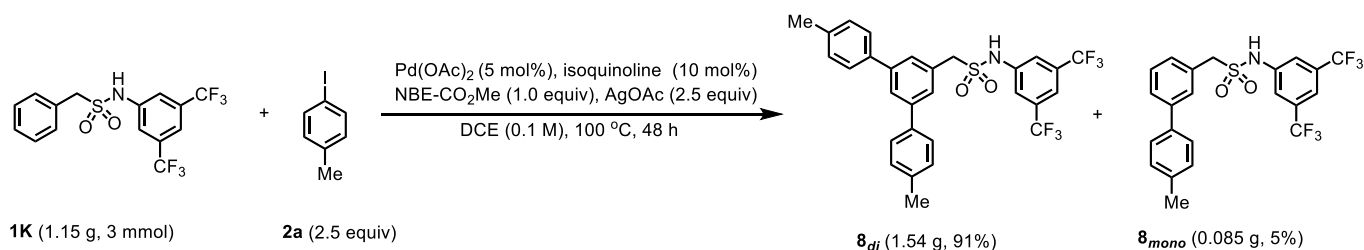
**7g** was obtained as white solid (21.7 mg, 45%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.57 (s, 1H), 7.49 (s, 2H), 7.41 (s, 1H), 7.04 (s, 1H), 6.95 (d, *J* = 4.5 Hz, 2H), 4.33 (s, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.50 (s, 2H), 2.24 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 171.83, 139.31, 139.24, 134.87, 132.71 (q, *J* = 33.6 Hz), 131.12, 130.44, 128.83, 127.91, 122.82 (q, *J* = 273.0 Hz), 119.14 (q, *J* = 3.4 Hz), 117.78–117.63 (m), 61.21, 58.87, 40.52, 20.90, 14.06; HRMS (ESI-TOF) Calcd for C<sub>20</sub>H<sub>20</sub>F<sub>6</sub>NO<sub>4</sub>S<sup>+</sup>[M+H]<sup>+</sup>: 484.1012; found: 484.1010.



**N-(3,5-bis(trifluoromethyl)phenyl)-1-(5-butyl-2-fluorophenyl)methanesulfonamide (7h)**

**7h** was obtained as white solid (25.1 mg, 55%); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.55 (s, 1H), 7.43 (s, 2H), 7.15 (dd, *J* = 7.0, 2.0 Hz, 1H), 7.11–7.05 (m, 1H), 6.95 (s, 1H), 6.88–6.79 (m, 1H), 4.48 (s, 2H), 2.59–2.41 (m, 2H), 1.54–1.44 (m, 2H), 1.35–1.25 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 159.26 (d, *J* = 246.7 Hz), 139.74 (d, *J* = 3.4 Hz), 138.76), 132.66 (q, *J* = 33.8 Hz), 132.19 (d, *J* = 1.9 Hz), 131.47 (d, *J* = 8.0 Hz), 122.74 (q, *J* = 273.0 Hz), 118.77 (q, *J* = 3.3 Hz), 118.03–117.66 (m), 115.40 (d, *J* = 21.5 Hz), 114.52 (d, *J* = 14.5 Hz), 52.81 (d, *J* = 2.6 Hz), 34.50, 33.42, 22.23, 13.77; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -63.37, -121.95; HRMS (ESI-TOF) Calcd for C<sub>19</sub>H<sub>17</sub>F<sub>7</sub>NO<sub>2</sub>S<sup>-</sup>[M-H]<sup>-</sup>: 456.0874; found: 456.0876.

## 2.5 Procedure for Gram-Scale Arylation of **1k**.



Substrate **1k** (1.15 g, 3.0 mmol), Pd(OAc)<sub>2</sub> (33.6 mg, 0.15 mmol), and AgOAc (7.5 mmol, 1.25 g) were weighed in air and placed in a sealed tube (100 mL) with a magnetic stir bar. To the reaction mixture, isoquinoline (38.7 mg, 0.3 mmol), NBE-CO<sub>2</sub>Me (456 mg, 3.0 mmol), aryl iodide **2a** (1.64 g, 7.5 mmol), and DCE (30 mL) were added. The reaction mixture was heated to 100 °C for 48 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated in vacuo, and the residue was purified by column chromatography (ethyl acetate/hexane = 1/4) to yield the **8<sub>di</sub>** (1.54 g, 91%) and **8<sub>mono</sub>** (85 mg, 5%).

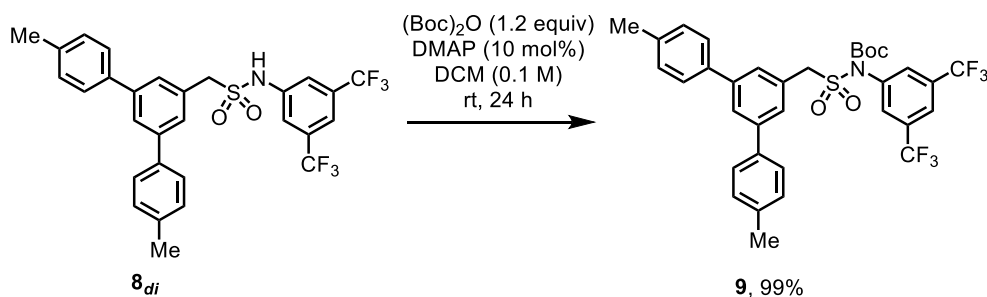
### *N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(4'-methyl-[1,1'-biphenyl]-3-yl)methanesulfonamide (**8<sub>di</sub>**)

**8<sub>di</sub>** was obtained as white solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.74 (s, 1H), 7.49 (s, 1H), 7.39 (s, 2H), 7.35 (d, *J* = 8.0 Hz, 4H), 7.32 (s, 2H), 7.19 (d, *J* = 8.0 Hz, 4H), 7.03 (s, 1H), 4.47 (s, 2H), 2.37 (s, 6H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 142.79, 138.95, 137.79, 136.84, 132.91 (q, *J* = 33.8 Hz), 129.58, 128.32, 127.78, 126.82, 126.65, 122.66 (q, *J* = 273.1 Hz), 118.31 (q, *J* = 3.0 Hz), 117.85–117.67 (m), 59.11, 21.05; HRMS (ESI-TOF) Calcd for C<sub>29</sub>H<sub>22</sub>F<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 562.1281; found: 562.1280.

### *N*-(3,5-Bis(trifluoromethyl)phenyl)-1-(4'-methyl-[1,1'-biphenyl]-3-yl)methanesulfonamide (**8<sub>mono</sub>**)

**8<sub>mono</sub>** was obtained as white solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.58–7.52 (m, 2H), 7.42 (s, 1H), 7.40–7.34 (m, 3H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.22–7.14 (m, 3H), 6.99 (brs, 1H), 4.45 (s, 2H), 2.37 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 142.29, 138.87, 137.74, 136.73, 132.87 (q, *J* = 33.8 Hz), 129.60, 129.50, 129.25, 129.22, 128.03, 127.88, 126.73, 122.69 (q, *J* = 273.1 Hz), 118.71 (q, *J* = 3.2 Hz), 117.96–117.73 (m), 59.35, 21.04; HRMS (ESI-TOF) Calcd for C<sub>22</sub>H<sub>16</sub>F<sub>6</sub>NO<sub>2</sub>S<sup>+</sup>[M-H]<sup>+</sup>: 472.0811; found: 472.0812.

## 2.6 Procedure for Synthesis of 9

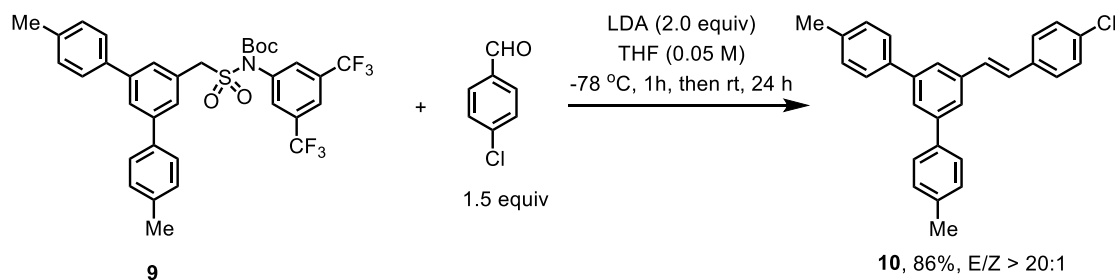


**8<sub>di</sub>** (563.6 mg, 1.0 mmol) was added to a solution of (Boc)<sub>2</sub>O (262.2 mg, 1.2 mmol) and DMAP (12.2 mg, 0.1 mmol) in dry dichloromethane (10 mL). The solution was stirred for 24 h at room temperature. After the reaction finished, the organic layer was washed with saturated aqueous sodium bicarbonate (10.0 mL), dried over sodium sulfate, filtered and concentrated. The residue was purified by column chromatography (ethyl acetate/hexane = 1/5) to yield the desired product **9** (663.5 mg, 99%) as white solid.

**tert-Butyl (3,5-bis(trifluoromethyl)phenyl)((4,4''-dimethyl-[1,1':3',1''-terphenyl]-5'-yl)methyl)sulfonyl)-carbamate (9)**

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.91 (t, *J* = 1.5 Hz, 1H), 7.66 (s, 1H), 7.57 (d, *J* = 1.6 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 4H), 7.24 (d, *J* = 7.8 Hz, 4H), 6.80 (s, 2H), 5.01 (s, 2H), 2.39 (s, 6H), 1.35 (s, 9H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 150.50, 142.99, 137.86, 137.23, 136.94, 132.04 (q, *J* = 34.1 Hz), 129.86 (q, *J* = 2.7 Hz), 129.59, 128.81, 127.95, 127.21, 126.97, 122.49–122.33 (m), 122.44 (q, *J* = 273.1 Hz), 86.08, 59.39, 27.72, 21.11; HRMS (ESI-TOF) Calcd for C<sub>34</sub>H<sub>30</sub>F<sub>6</sub>NO<sub>4</sub>S<sup>-</sup>[M-H]<sup>-</sup>: 662.1805; found: 662.1809.

## 2.7 Procedure for Synthesis of 10

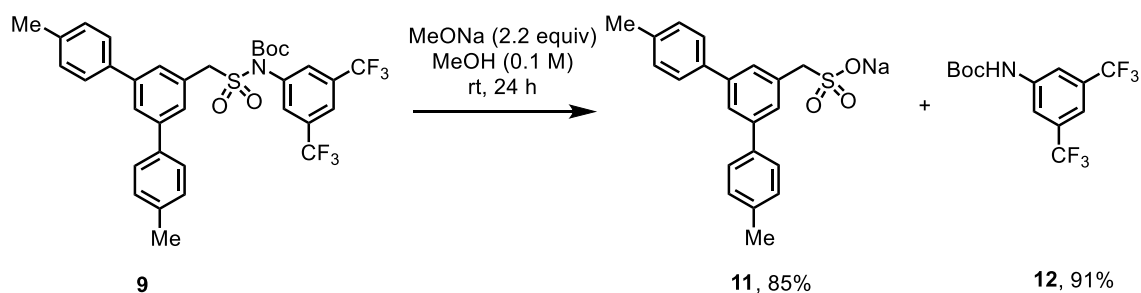


To a dried flask equipped with a magnetic stir bar was added LDA solution (0.3 mL, 2.0 M in THF), and dry THF (5.0 mL) under N<sub>2</sub>. A solution 4-chlorobenzaldehyde (56.2 mg, 0.4 mmol) and **9** (199.1 mg, 0.3 mmol) in THF (2.0 mL) was added slowly to the LDA/THF solution around 1 hour at -78 °C. The reaction mixture was stirred overnight while warming to room temperature. After the reaction mixture was quenched on saturated NH<sub>4</sub>Cl solution and extracted with ethylacetate (3 × 10 mL). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under vacuum. The resulting mixture was purified by column chromatography using ethyl acetate/hexane (1/20) as the eluent to yield the desired product **10** (101.9 mg, 86%) as white solid.

### (*E*)-5'-(4-chlorostyryl)-4,4''-dimethyl-1,1':3',1''-terphenyl (**10**)

White solid, <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.67 (s, 1H), 7.64 (s, 2H), 7.56 (d, *J* = 8.0 Hz, 4H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 7.9 Hz, 4H), 7.19 (d, *J* = 16.4 Hz, 1H), 7.14 (d, *J* = 16.4 Hz, 1H), 2.41 (s, 6H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 142.13, 138.11, 137.80, 137.35, 135.75, 133.24, 129.53, 129.25, 128.85, 127.84, 127.70, 127.09, 125.46, 123.92, 21.13.

## 2.8 Procedure for Synthesis of 11



**9** (199.1 mg, 0.3 mmol) was added to a solution of MeONa (35.6 mg, 0.66 mmol) in dry MeOH (3 mL). The solution was stirred for 24 h at room temperature. After the reaction finished, the reaction mixture was quenched with H<sub>2</sub>O (10 mL) and extracted with ethyl acetate (3×10 mL). The aqueous portion was concentrated under reduced pressure to afford a white solid. The resulting solid was washed with cold MeOH (0.2 mL) and ethyl acetate (5 mL). After washing, sodium sulfonate **11** was obtained (95.5 mg, 85%) as white solid. The combined organic portion was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The crude mixture was concentrated under reduced pressure and purified by column chromatography using ethyl acetate/hexane (1/10) as the eluent to yield the desired product **12** (89.8 mg, 91%) as white solid.

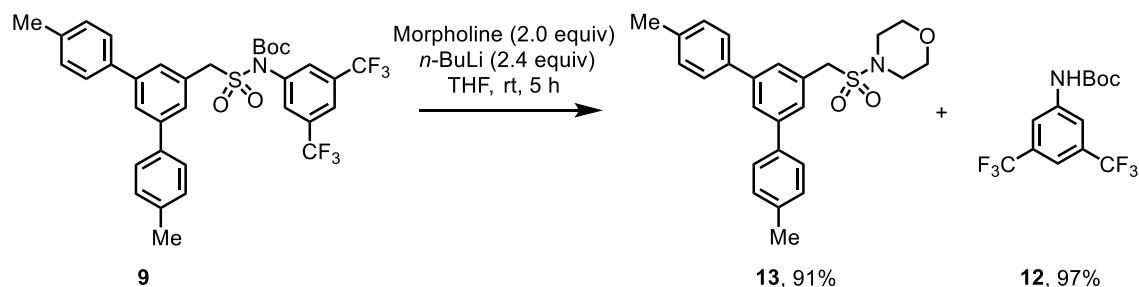
### Sodium (4,4''-dimethyl-[1,1':3',1''-terphenyl]-5'-yl)methanesulfonate (**11**)

<sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD) δ 7.69 (t, *J* = 1.6 Hz, 1H), 7.63 (d, *J* = 1.5 Hz, 2H), 7.58 (d, *J* = 8.1 Hz, 4H), 7.26 (d, *J* = 7.9 Hz, 4H), 4.18 (s, 2H), 2.38 (s, 6H); <sup>13</sup>C NMR (150 MHz, CD<sub>3</sub>OD) δ 142.84, 139.55, 138.24, 135.49, 130.4, 128.93, 128.06, 125.30, 58.56, 21.14; HRMS (ESI-TOF) Calcd for C<sub>21</sub>H<sub>20</sub>NaO<sub>3</sub>S[M+H]<sup>+</sup>: 375.1025; found: 375.1027.

### tert-Butyl (3,5-bis(trifluoromethyl)phenyl)carbamate (**12**)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.86 (s, 2H), 7.52 (s, 1H), 6.78 (s, 1H), 1.54 (s, 9H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 152.08, 139.88, 132.32 (q, *J* = 33.4 Hz), 123.13 (q, *J* = 272.8 Hz), 117.96, 117.09–114.66 (m), 81.94, 28.18.

## 2.9 Procedure for Synthesis of 13

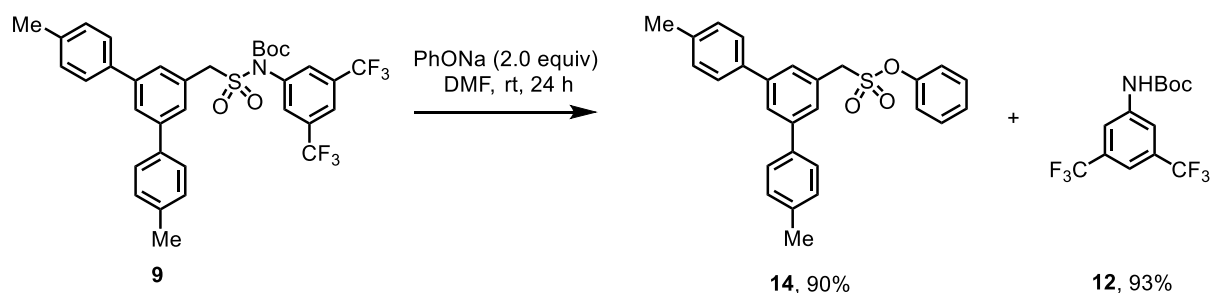


To a solution of morpholine (9.0  $\mu$ L, 0.1 mmol) in THF (0.3 mL) under  $N_2$  was added *n*-BuLi (0.45 mL, 2.7 M) at room temperature. After 10 mins, a solution of **9** (33.2 mg, 0.05 mmol) in THF (0.7 mL) was added, and then the mixture was stirred for 5 hours. Then the mixture was concentrated in vacuum, and the crude products were purified by the PTLC using EA/Hexane (1/2) as eluent to afford sulfonamide **13** as a light yellow solid (19.3 mg, 91%). The Boc-protected 3,5-bis(trifluoromethyl)aniline **12** was isolated as a white solid (16.0 mg, 97%).

### 4-(((4,4''-Dimethyl-[1,1':3',1''-terphenyl]-5'-yl)methyl)sulfonyl)morpholine (**13**)

white solid,  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  7.78 (t,  $J = 1.7$  Hz, 1H), 7.57 (d,  $J = 1.7$  Hz, 2H), 7.54 (d,  $J = 8.0$  Hz, 4H), 7.28 (d,  $J = 7.8$  Hz, 4H), 4.33 (s, 2H), 3.62 (t,  $J = 4.6$  Hz, 4H), 3.18 (t,  $J = 4.6$  Hz, 4H), 2.41 (s, 6H);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  142.26, 137.69, 137.34, 129.62, 129.37, 127.79, 127.03, 126.12, 66.70, 56.72, 46.26, 21.13; HRMS (ESI-TOF) Calcd for  $C_{25}H_{28}NO_3S[M+H]^+$ : 422.1784; found: 422.1786.

## 2.10 Procedure for Synthesis of **14**



A solution of **9** (33.2 mg, 0.05 mmol), and PhONa (11.6 mg, 0.1 mmol) in DMF (1.0 mL) was stirred at room temperature for 24 hours. The mixture was diluted by EA (2 mL) and pass through a pad of Celite to remove the insoluble salt. After concentration under vacuum, the crude products were purified by the PTLC using DCM/Hexane (1/1) as eluent to afford sulfonate ester **14** as a white solid (19.6 mg, 90%). The Boc-protected 3,5-bis(trifluoromethyl)aniline **12** was isolated as a white solid (15.6 mg, 93%).

### Phenyl (4,4'-dimethyl-[1,1':3,1''-terphenyl]-5'-yl)methanesulfonate (**14**)

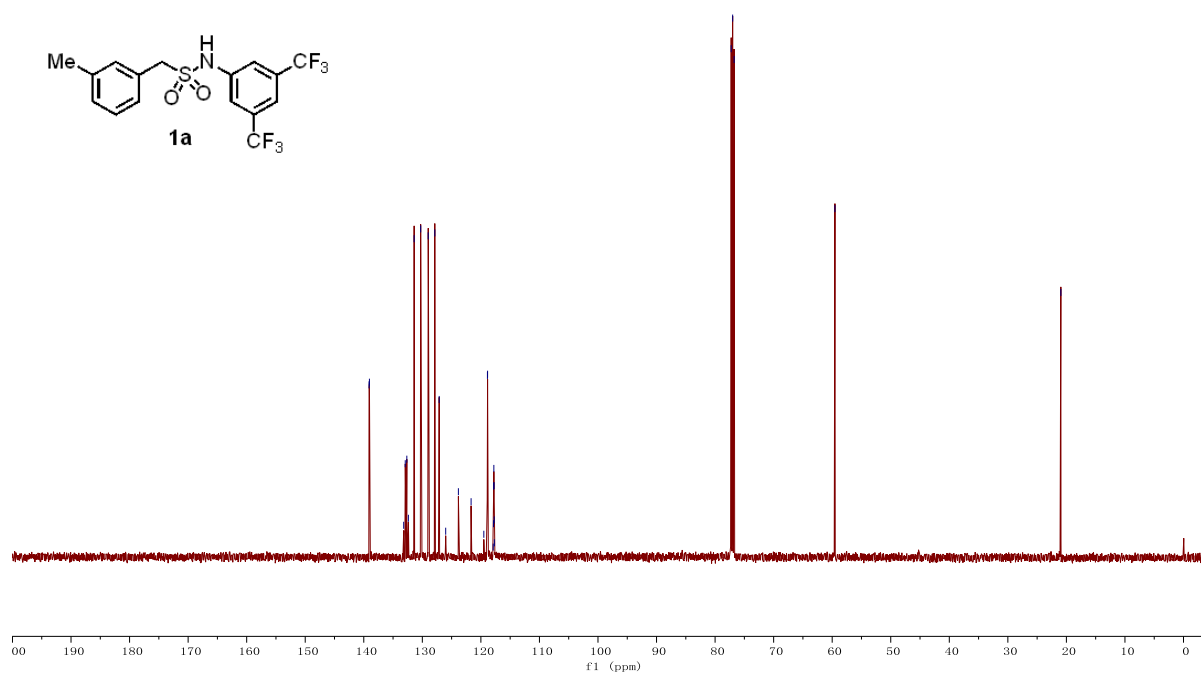
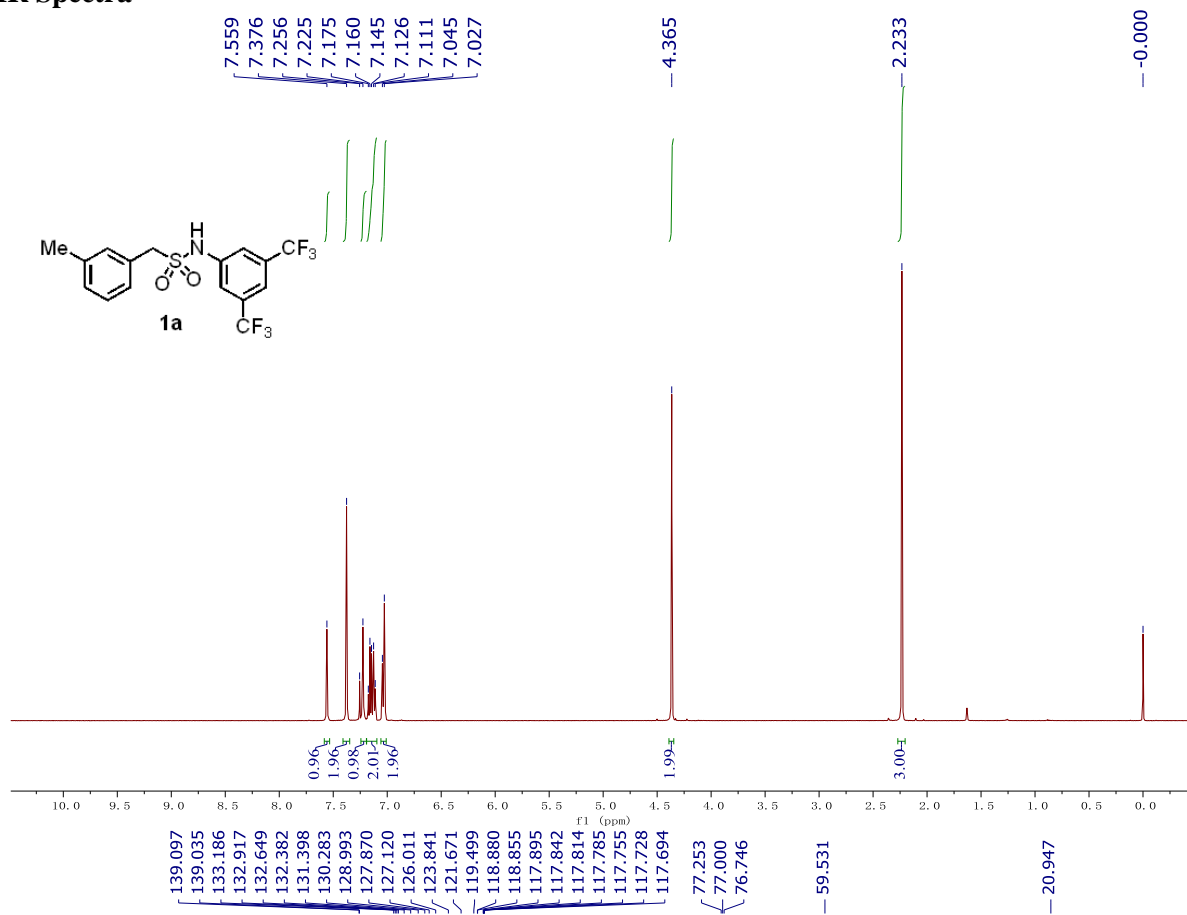
White solid,  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.80 (t,  $J = 1.7$  Hz, 1H), 7.60 (s, 2H), 7.52 (d,  $J = 7.8$  Hz, 4H), 7.36 (t,  $J = 7.8$  Hz, 2H), 7.30–7.25 (m, 5H), 7.18 (d,  $J = 7.9$  Hz, 2H), 4.62 (s, 2H), 2.40 (s, 6H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  149.31, 142.46, 137.65, 137.37, 129.90, 129.59, 128.02, 127.99, 127.15, 127.09, 126.59, 121.98, 56.88, 21.13; HRMS (ESI-TOF) Calcd for  $\text{C}_{27}\text{H}_{25}\text{O}_3\text{S}[\text{M}+\text{H}]^+$ : 429.1519; found: 429.1523.

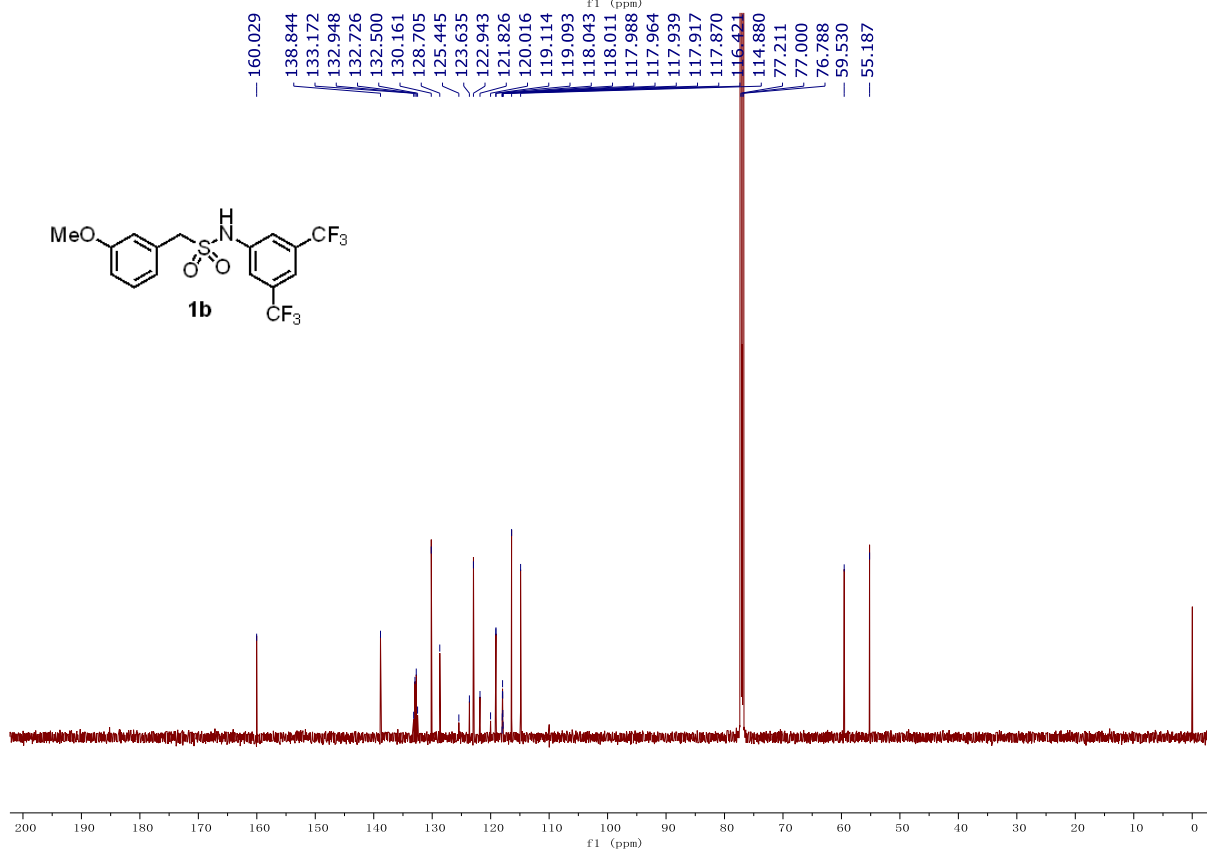
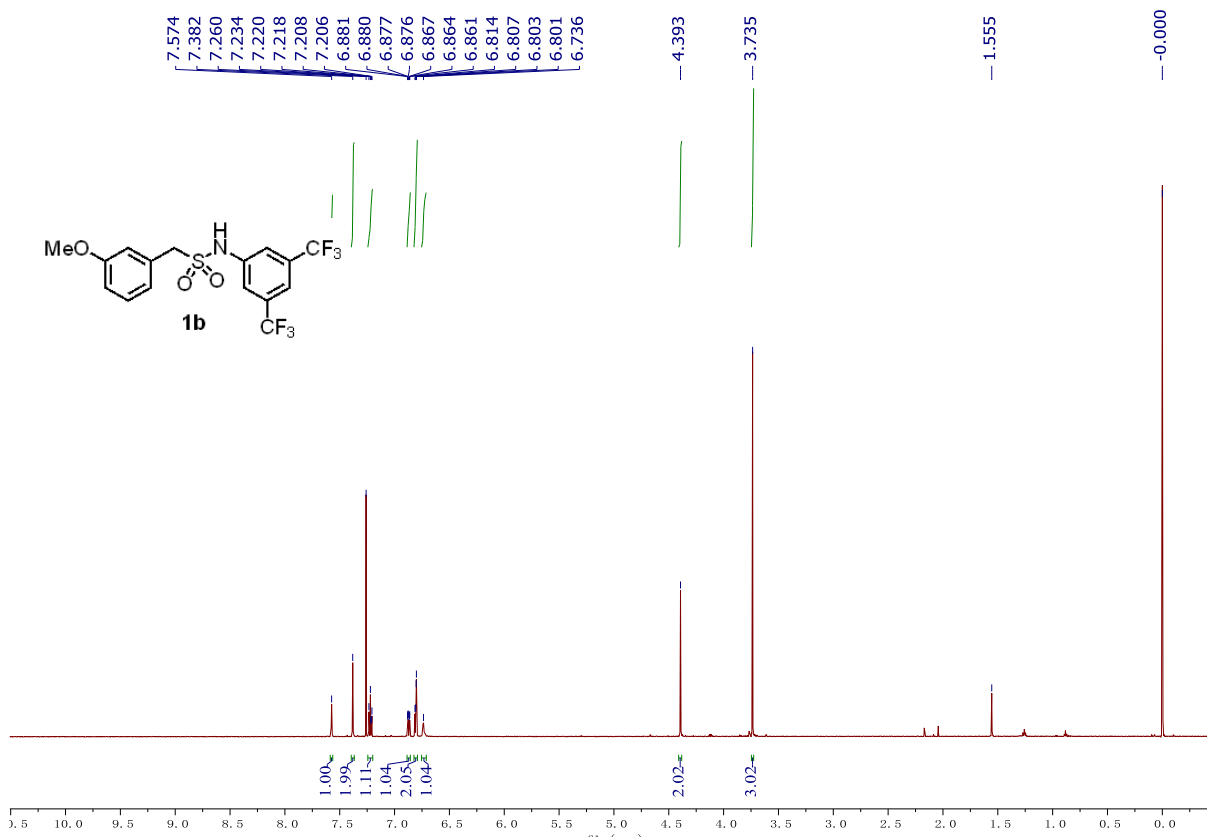
### 3. References

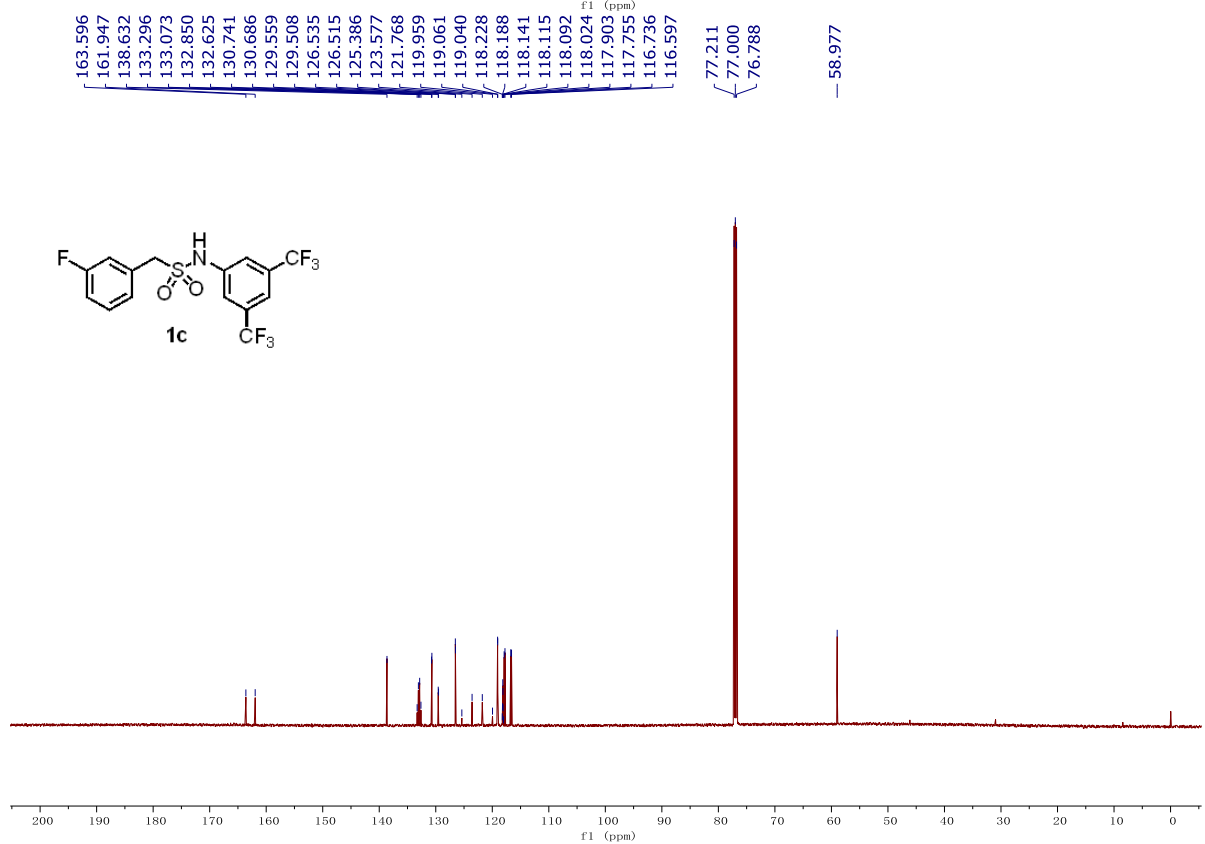
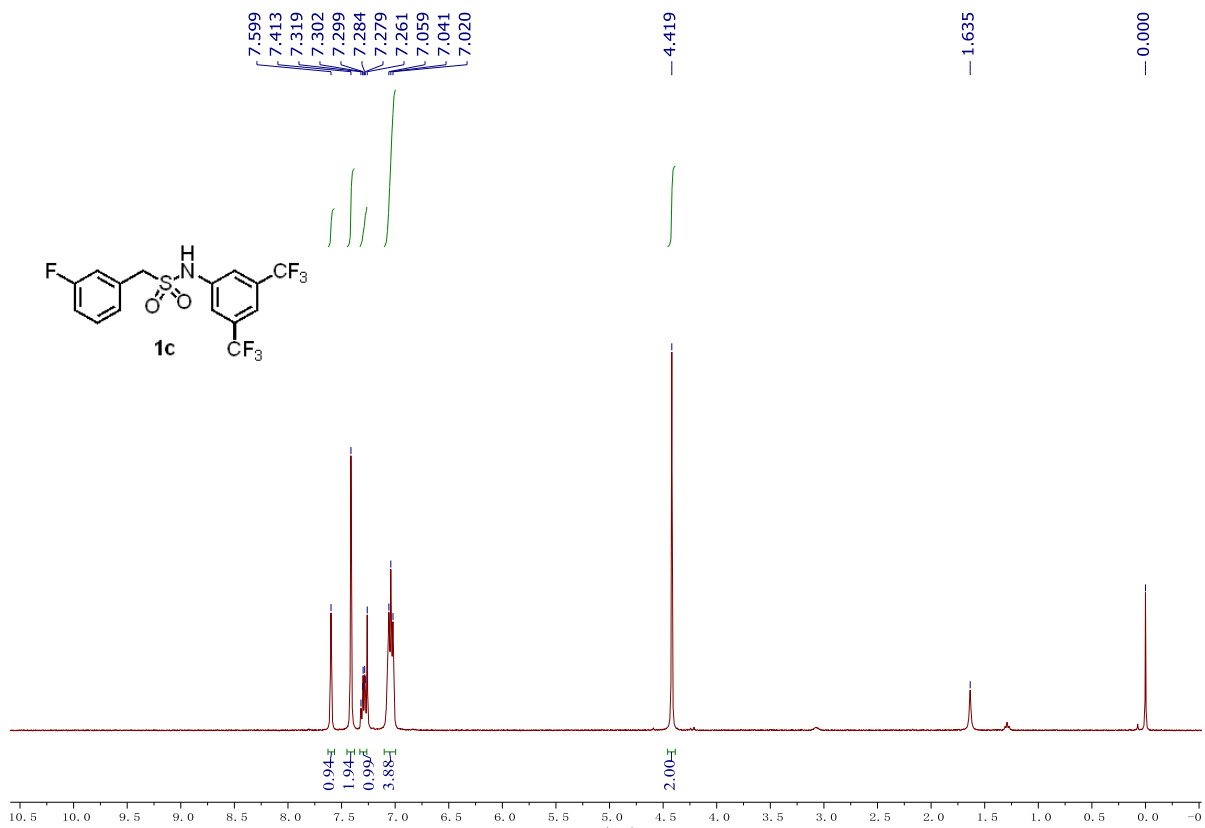
1. P. Wang, G.-C. Li, P. Jain, M. E. Farmer, J. He, P.-X. Shen, J.-Q. Yu, *J. Am. Chem. Soc.* **2016**, *138*, 14092.
2. H.-X. Dai, A. F. Stepan, M. S. Plummer, Y.-H. Zhang, J.-Q. Yu, *J. Am. Chem. Soc.* **2011**, *133*, 7222.

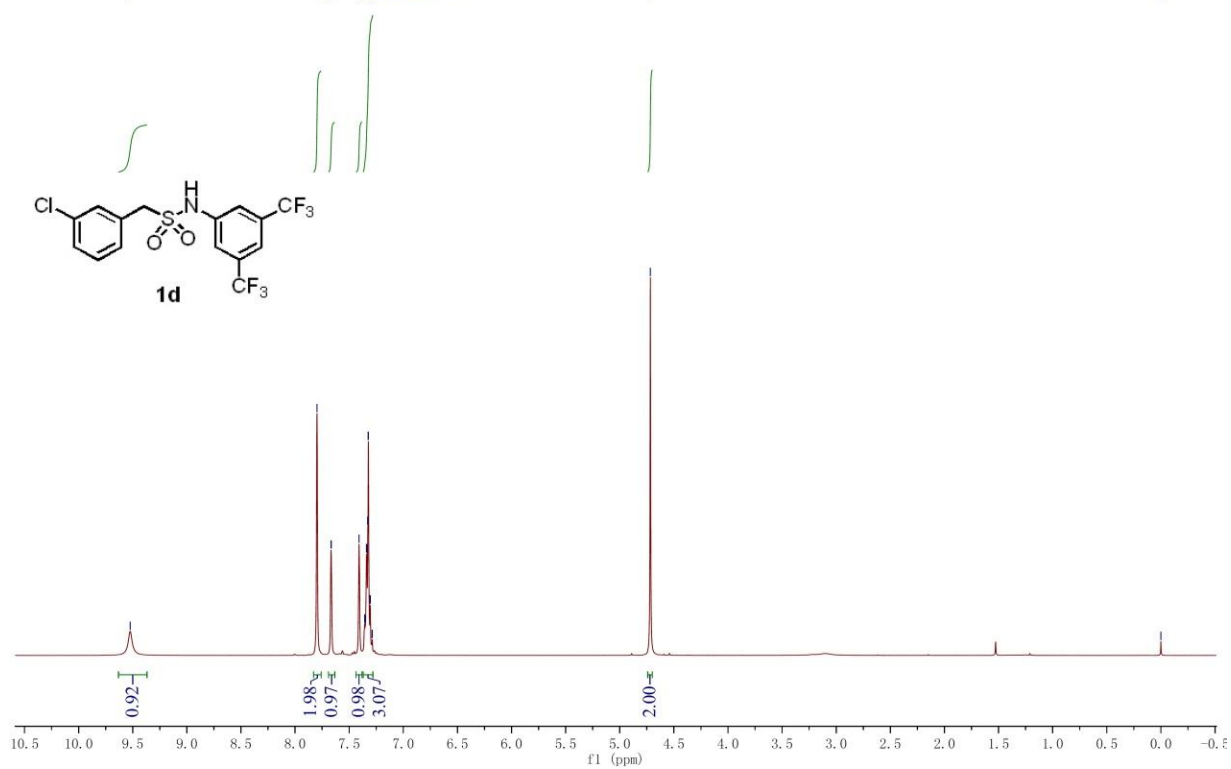
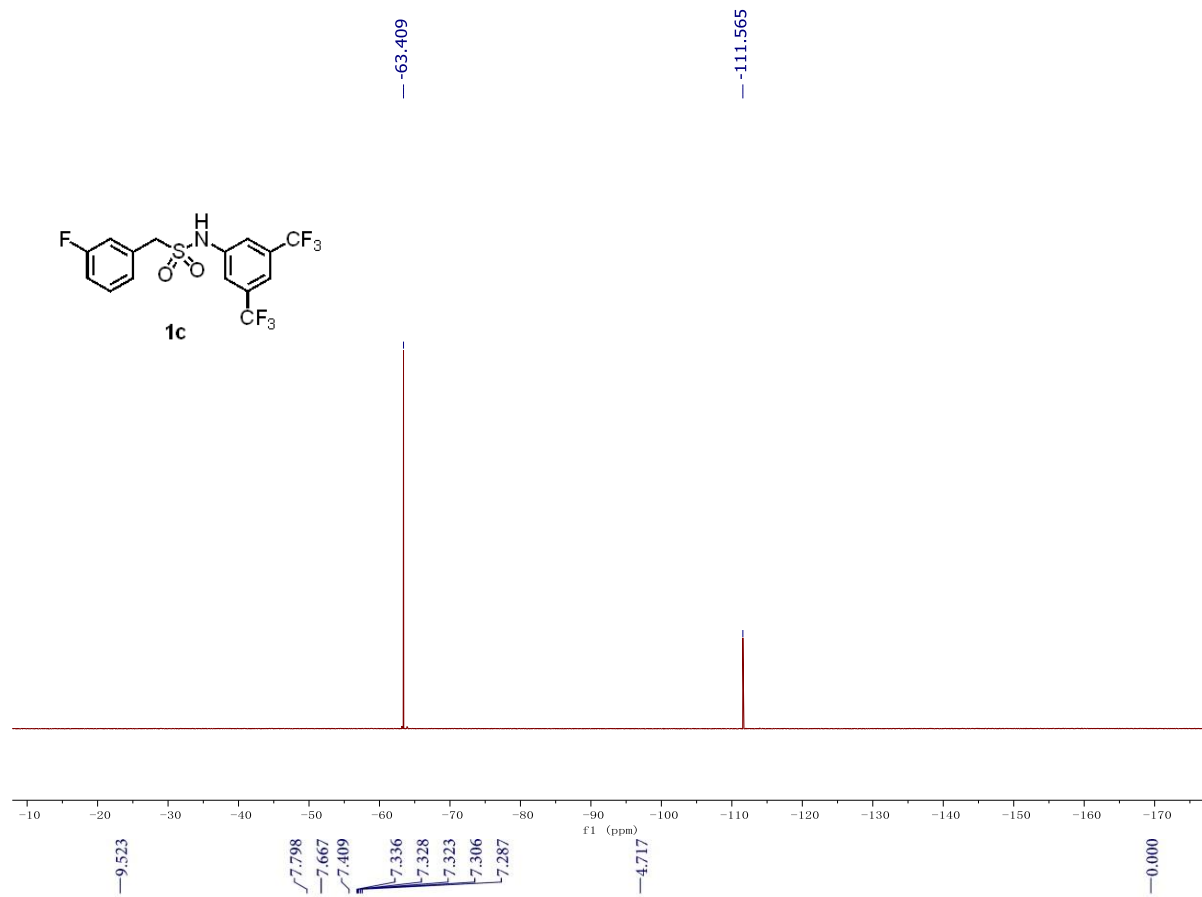


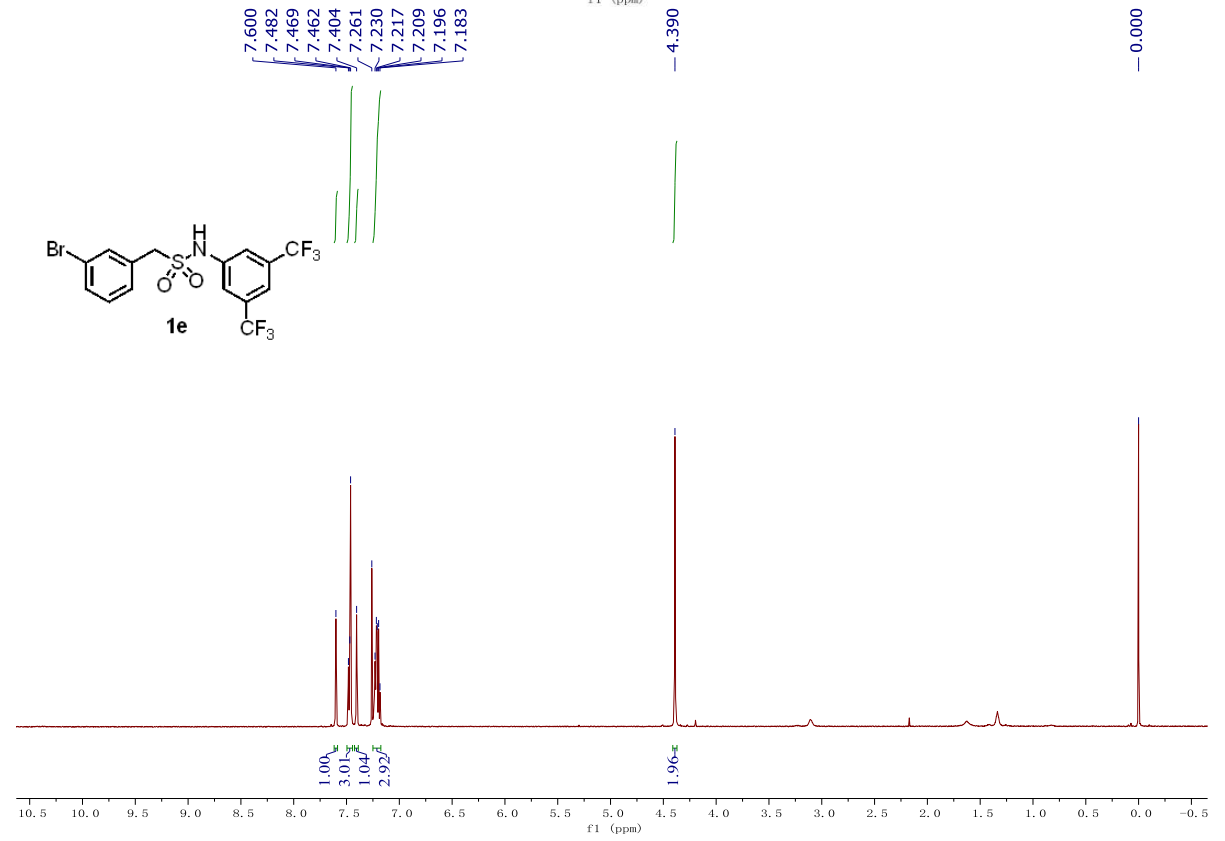
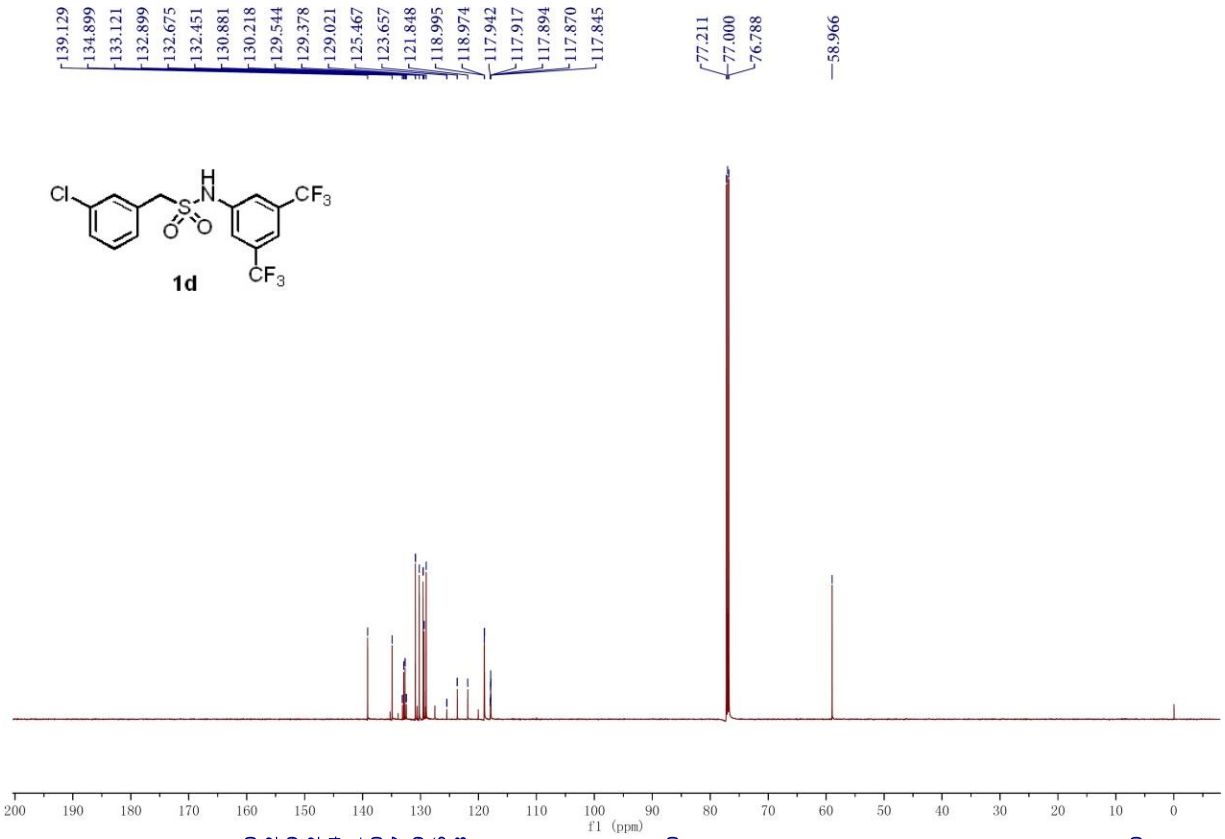
## 4. NMR Spectra

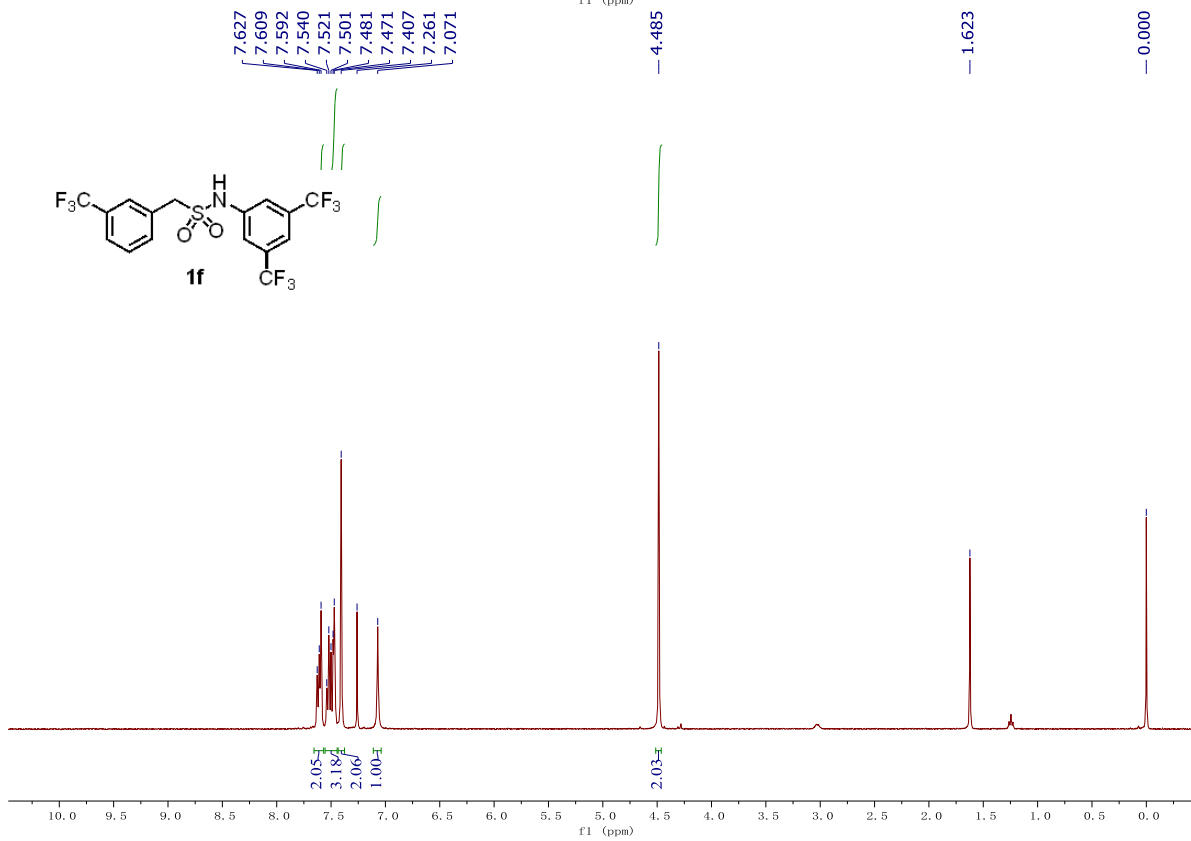
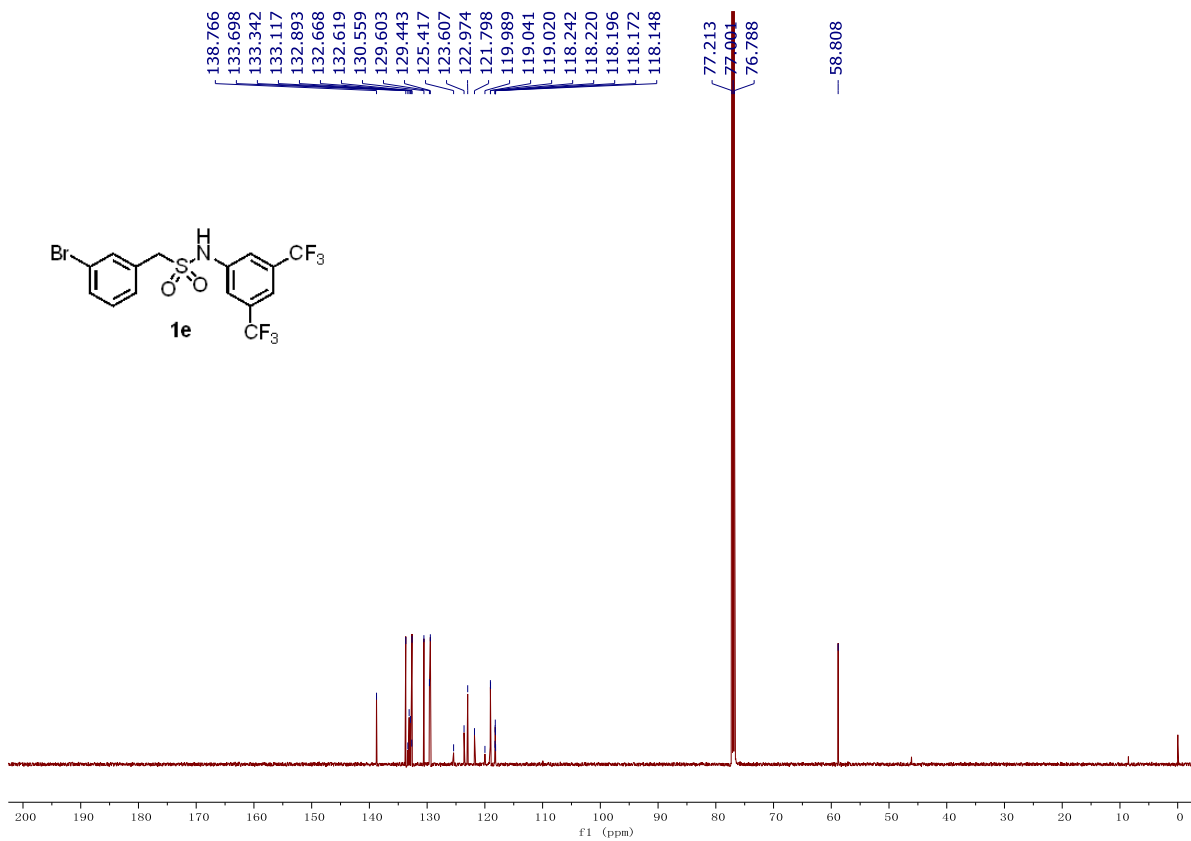


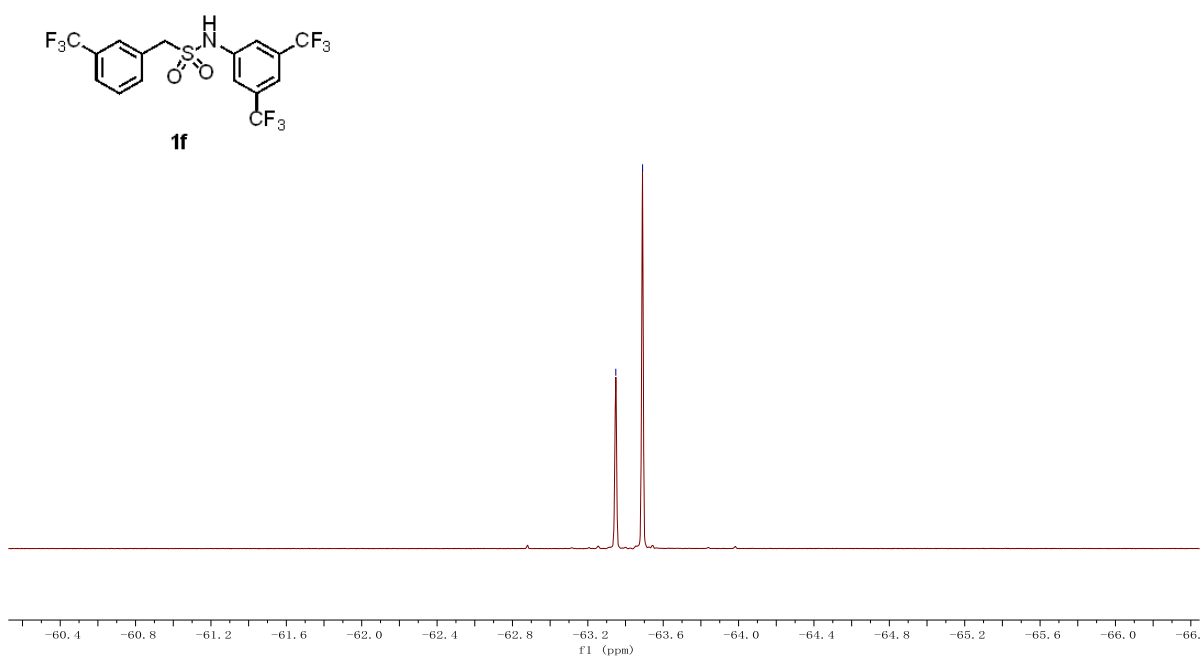
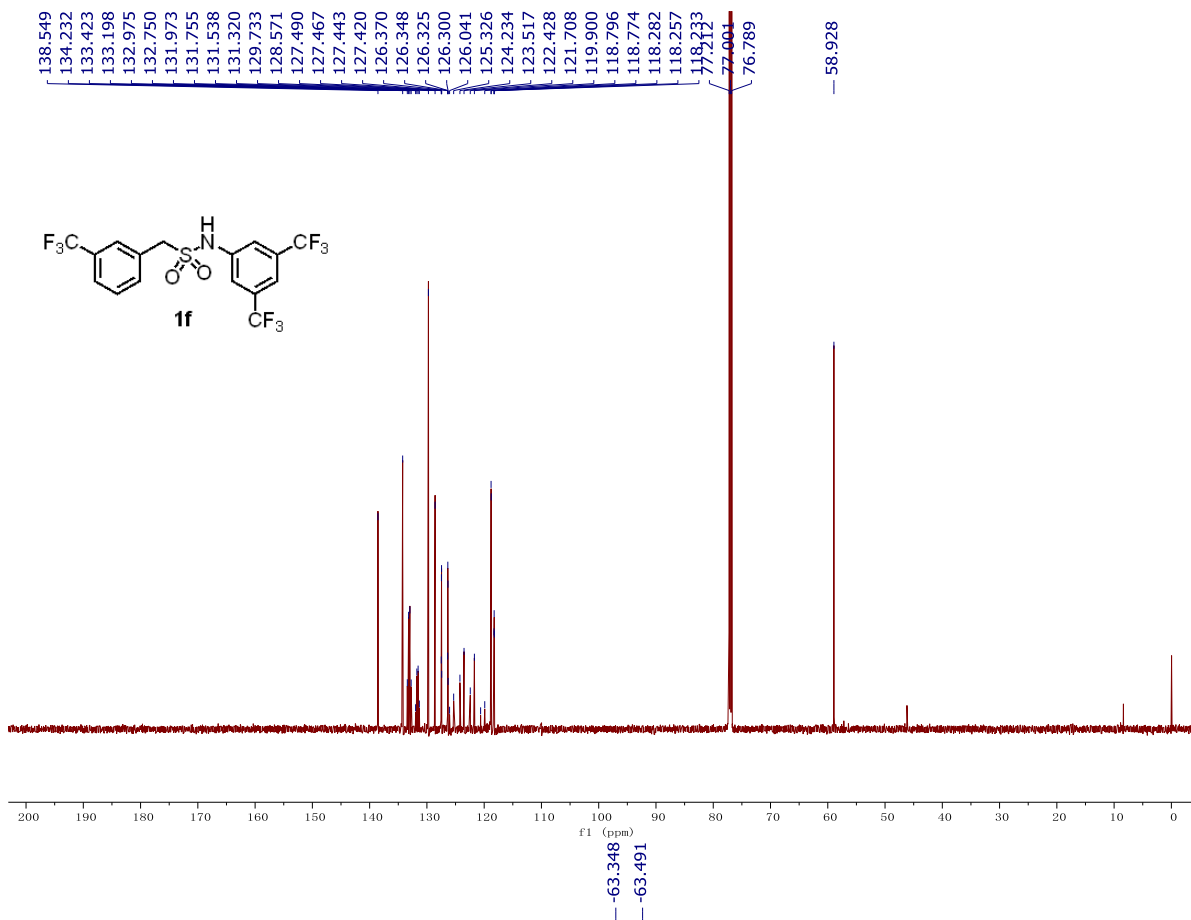


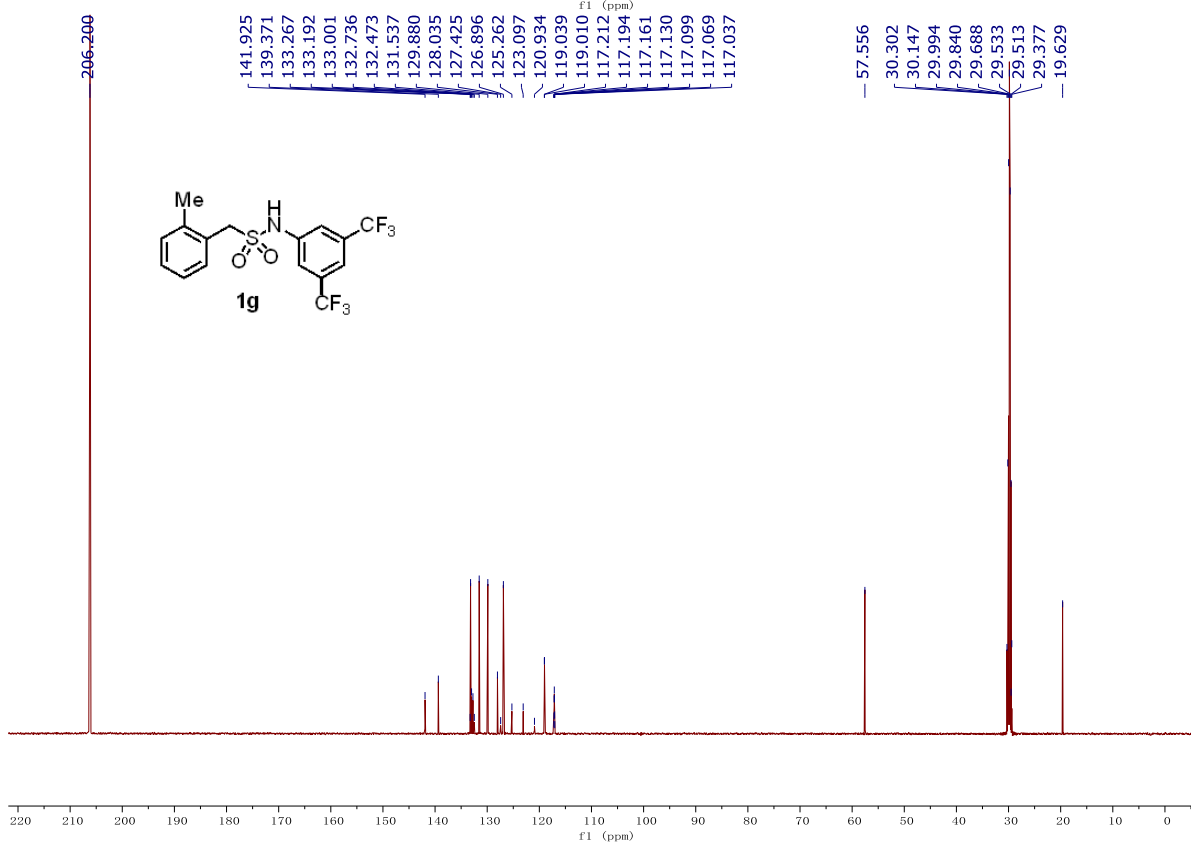
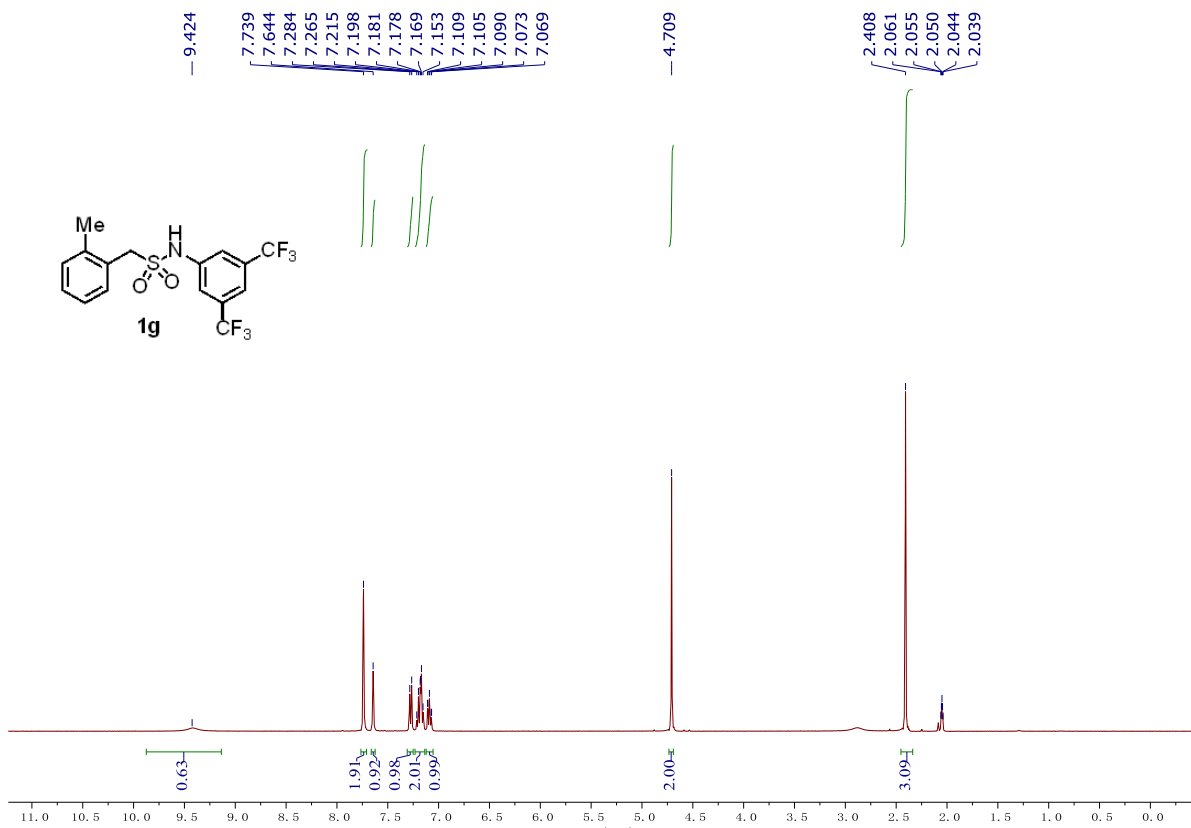




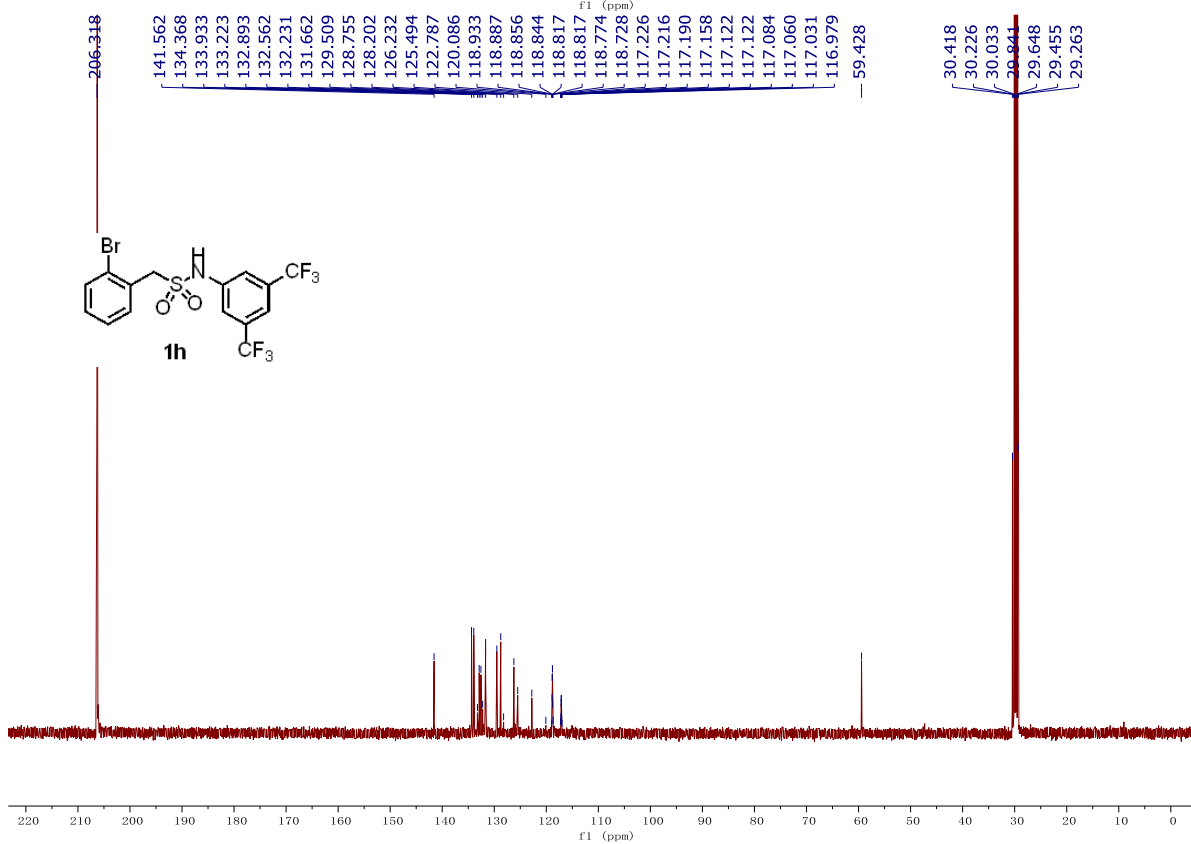
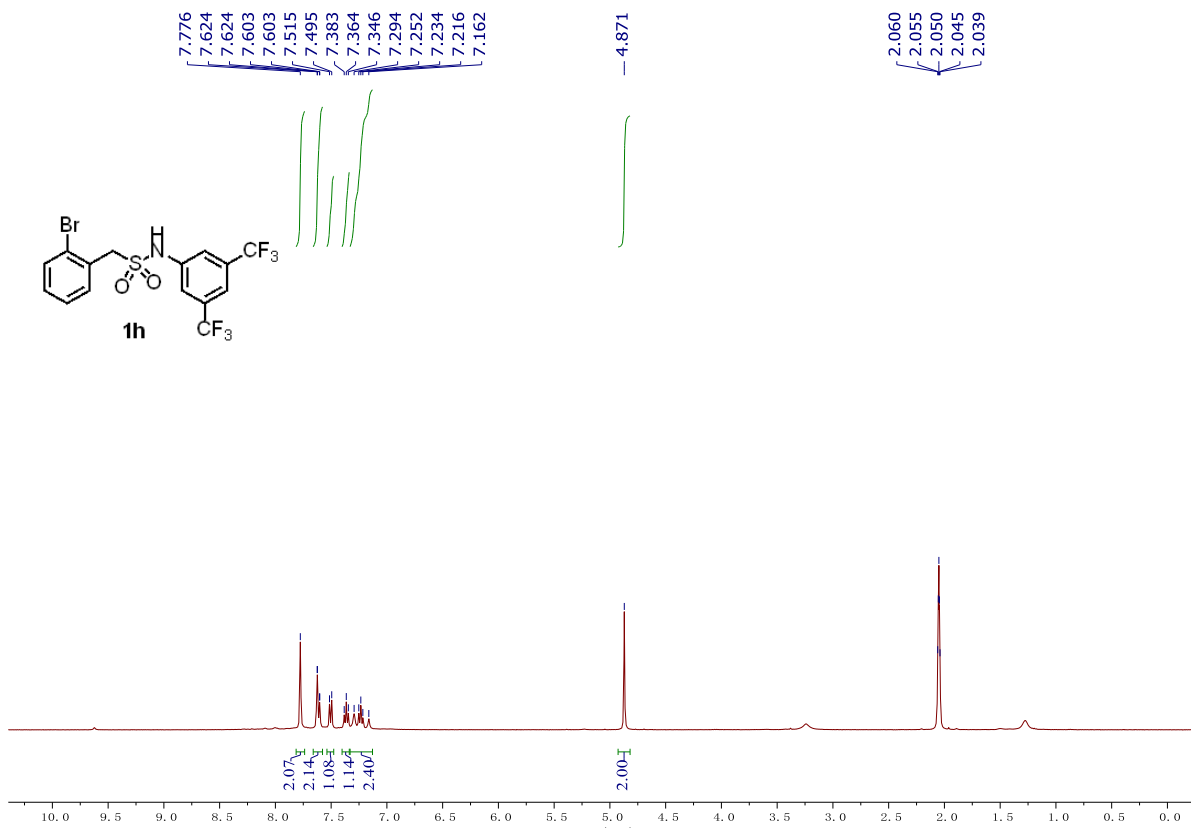


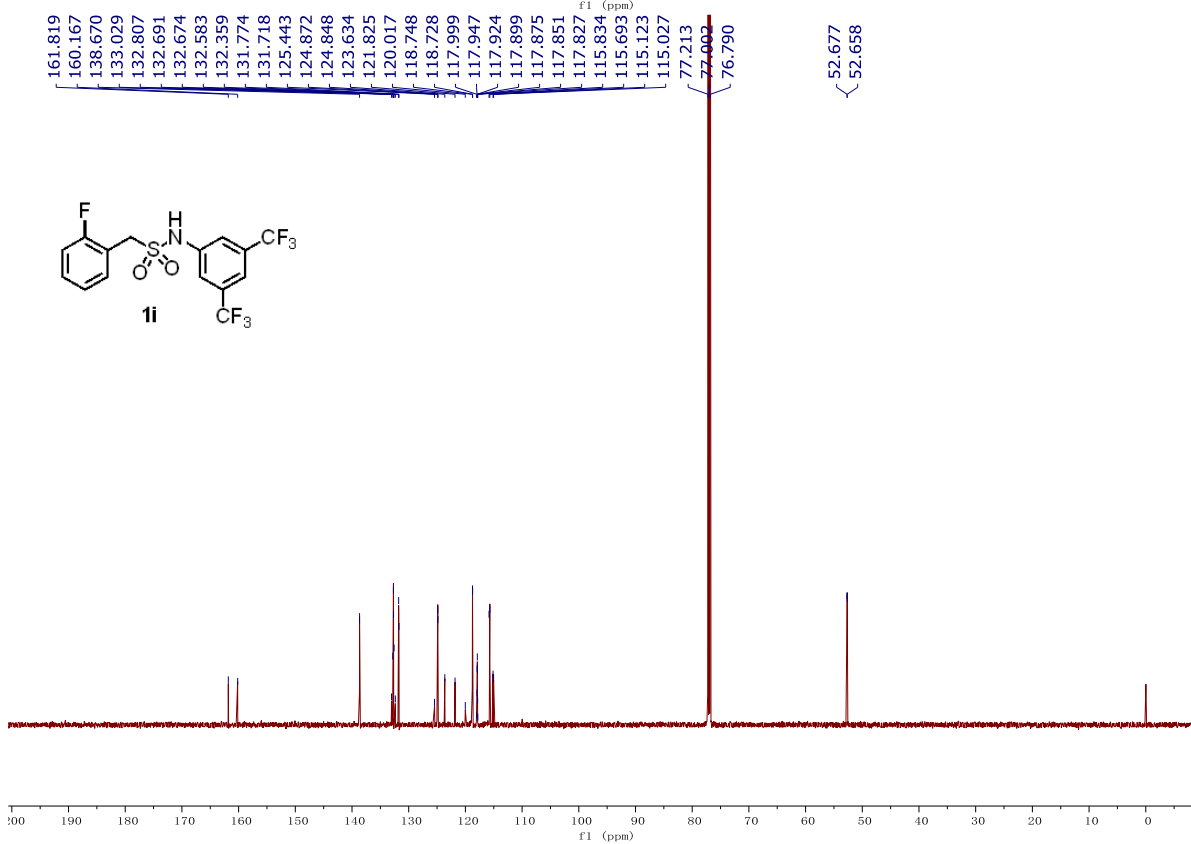
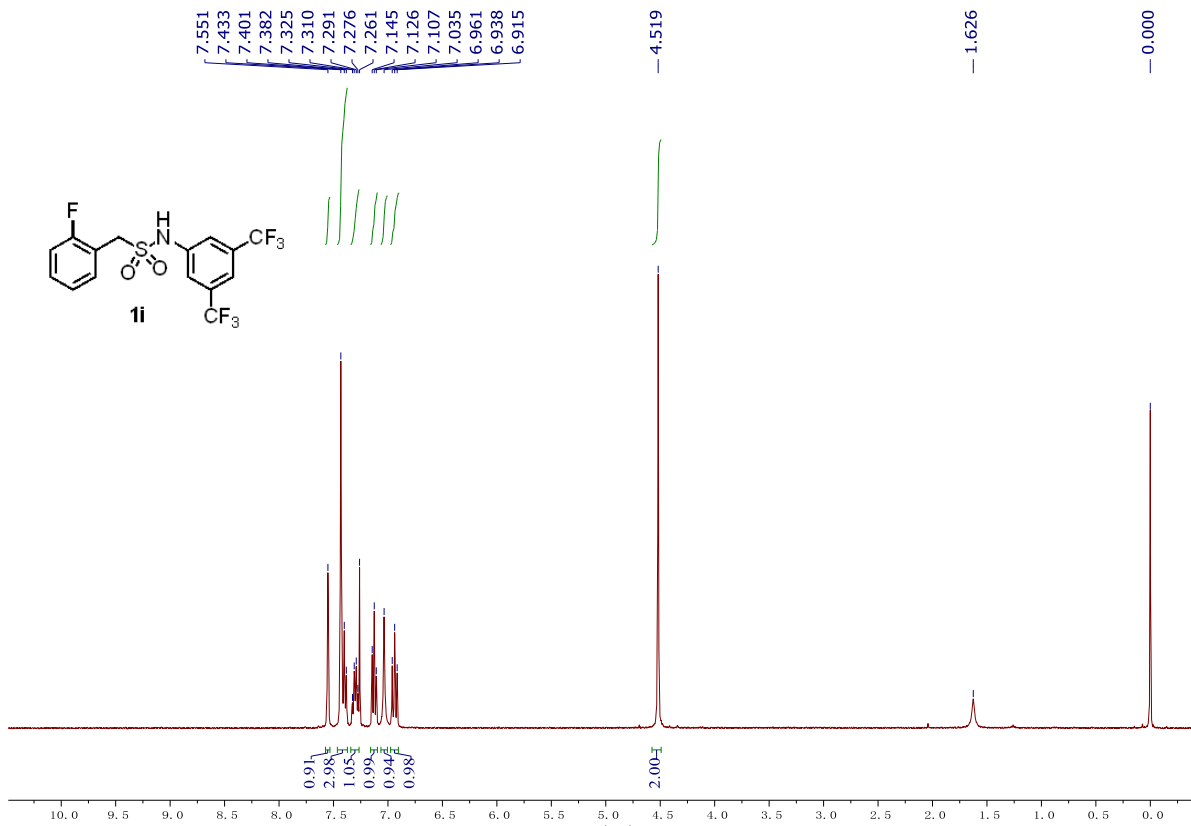


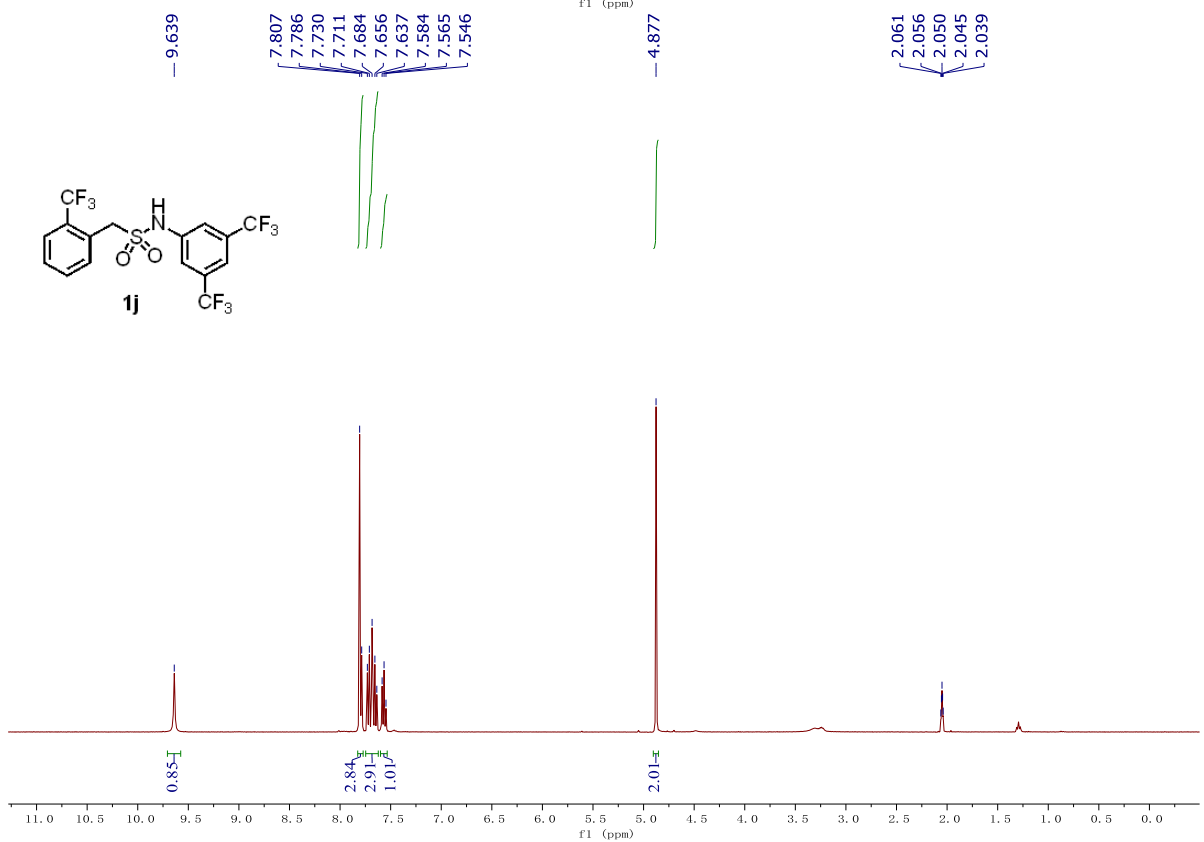
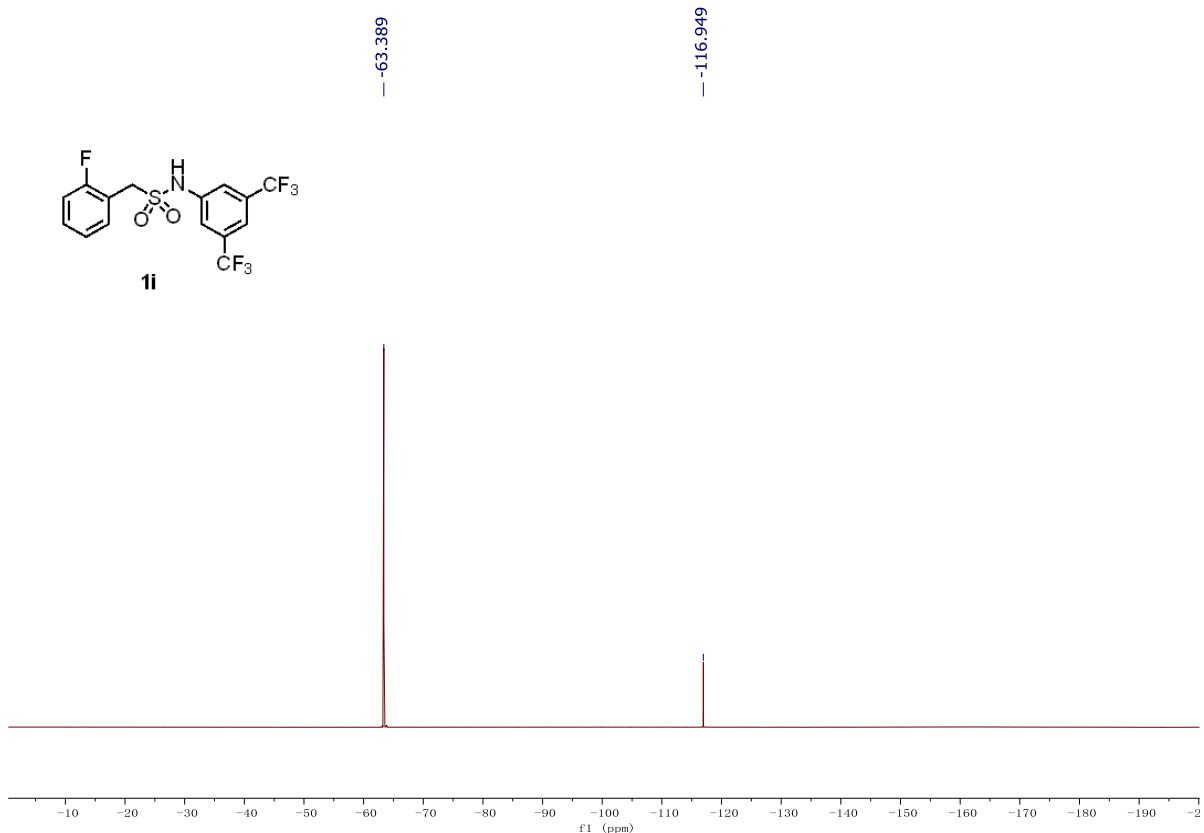


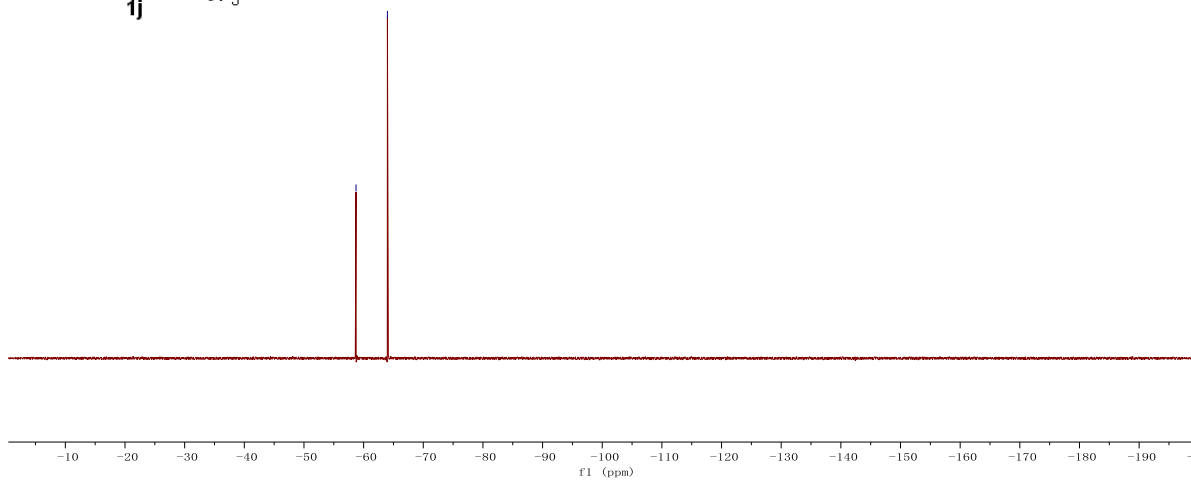
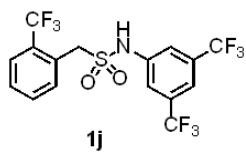
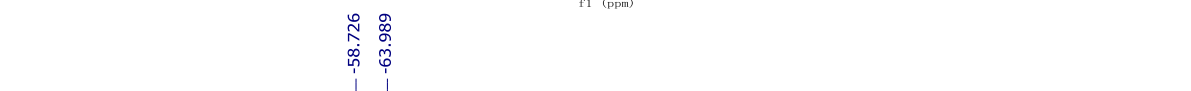
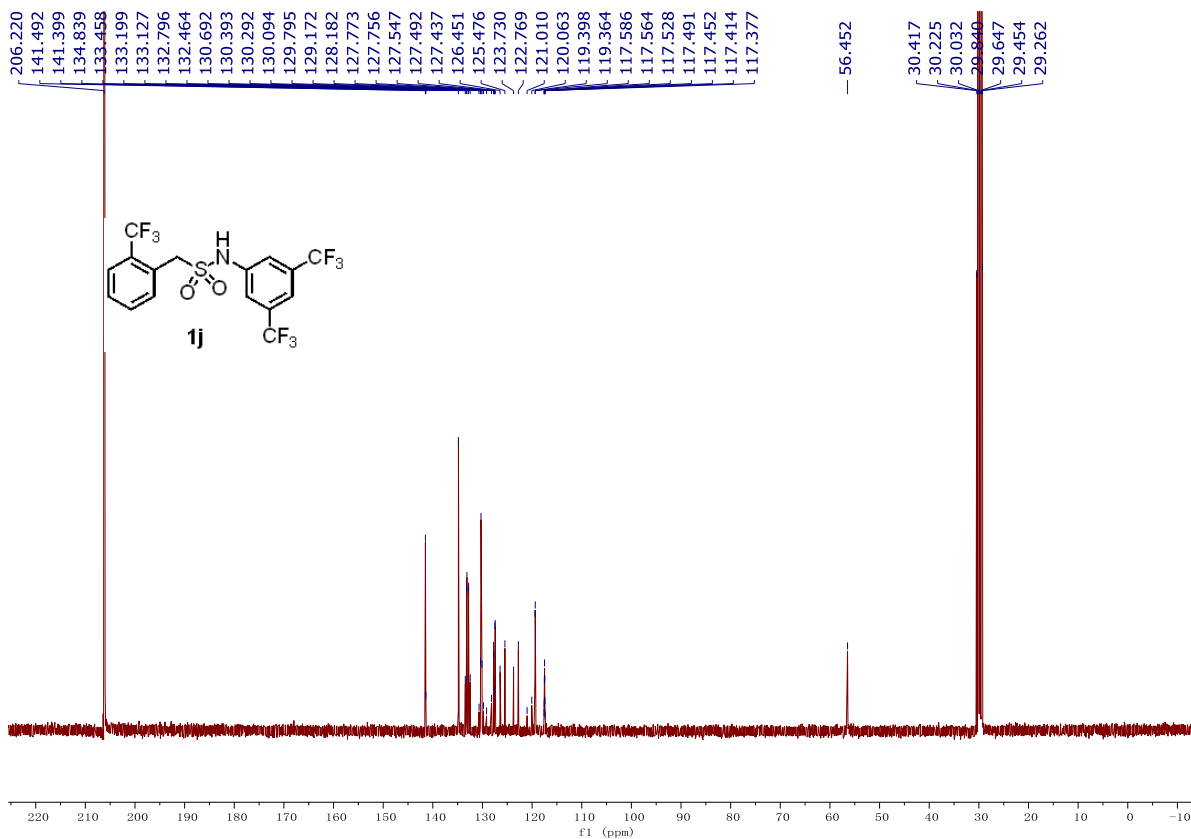


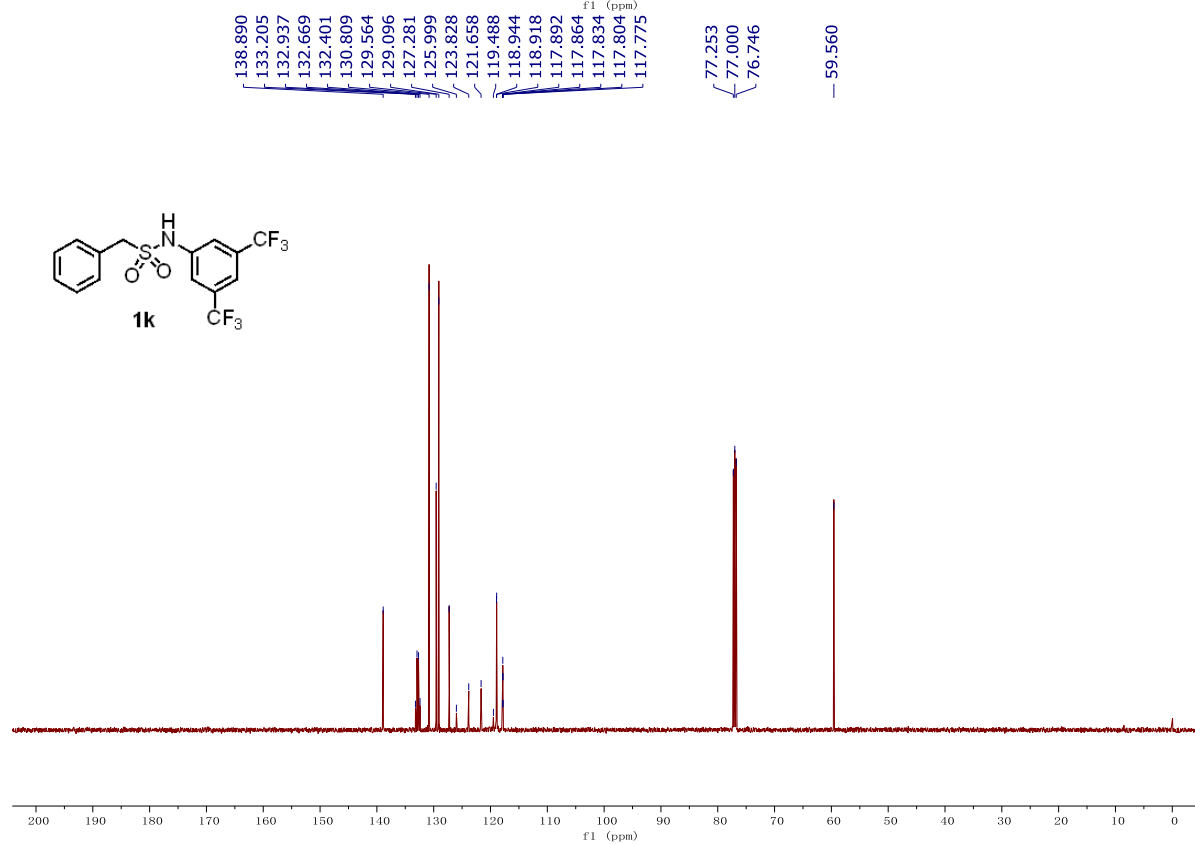
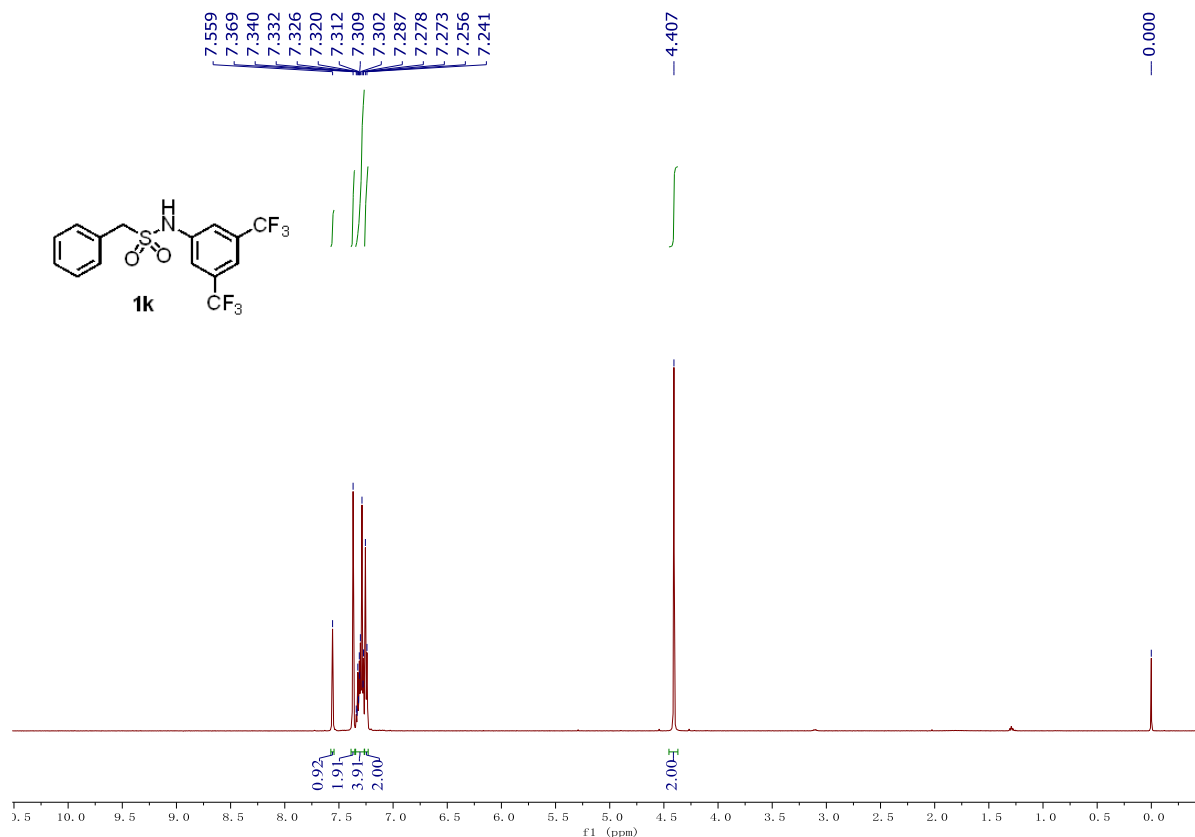


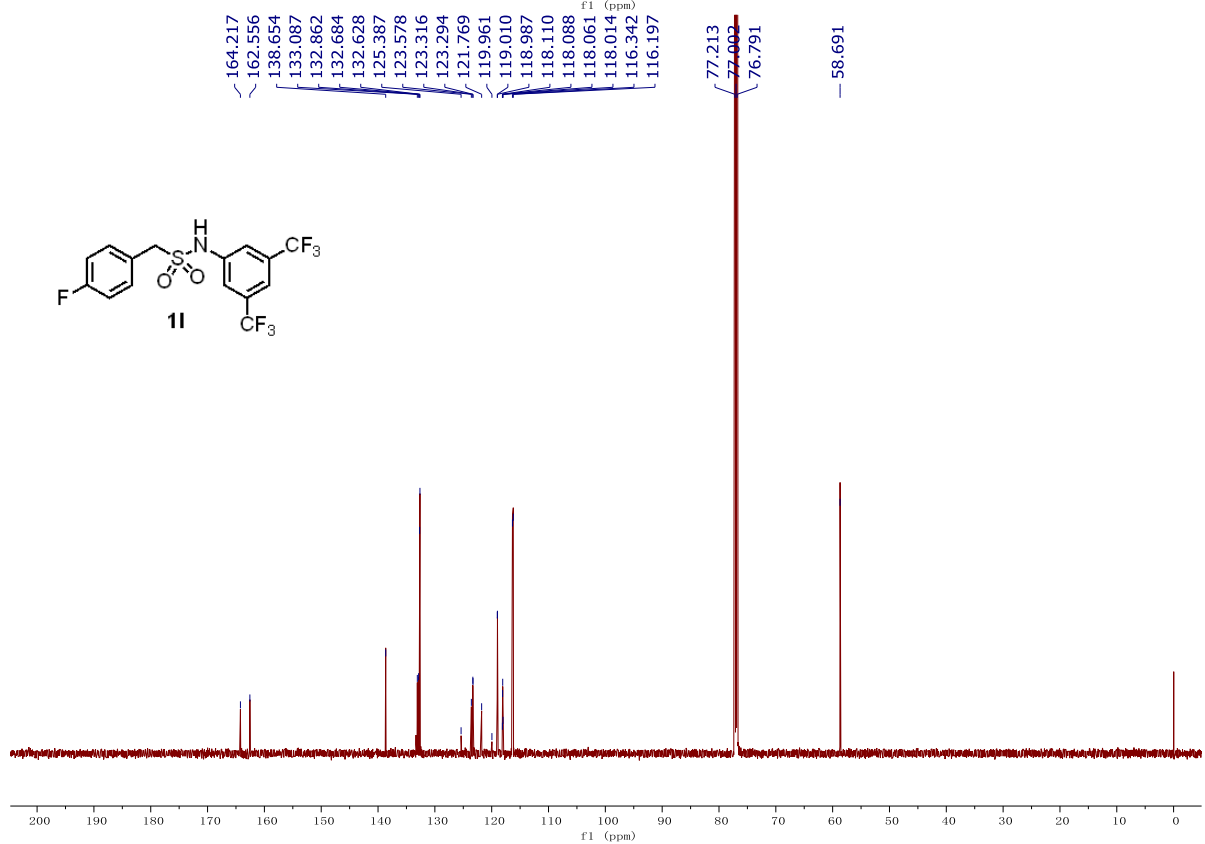
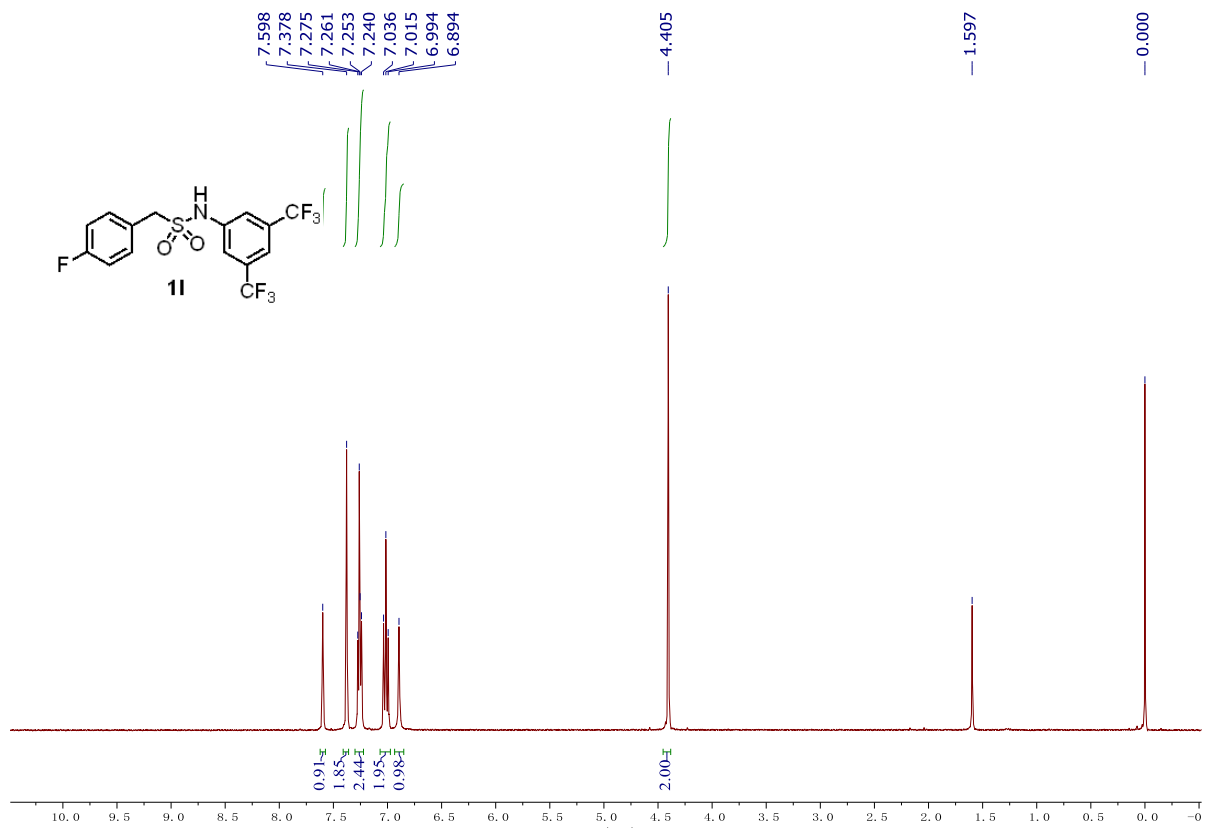


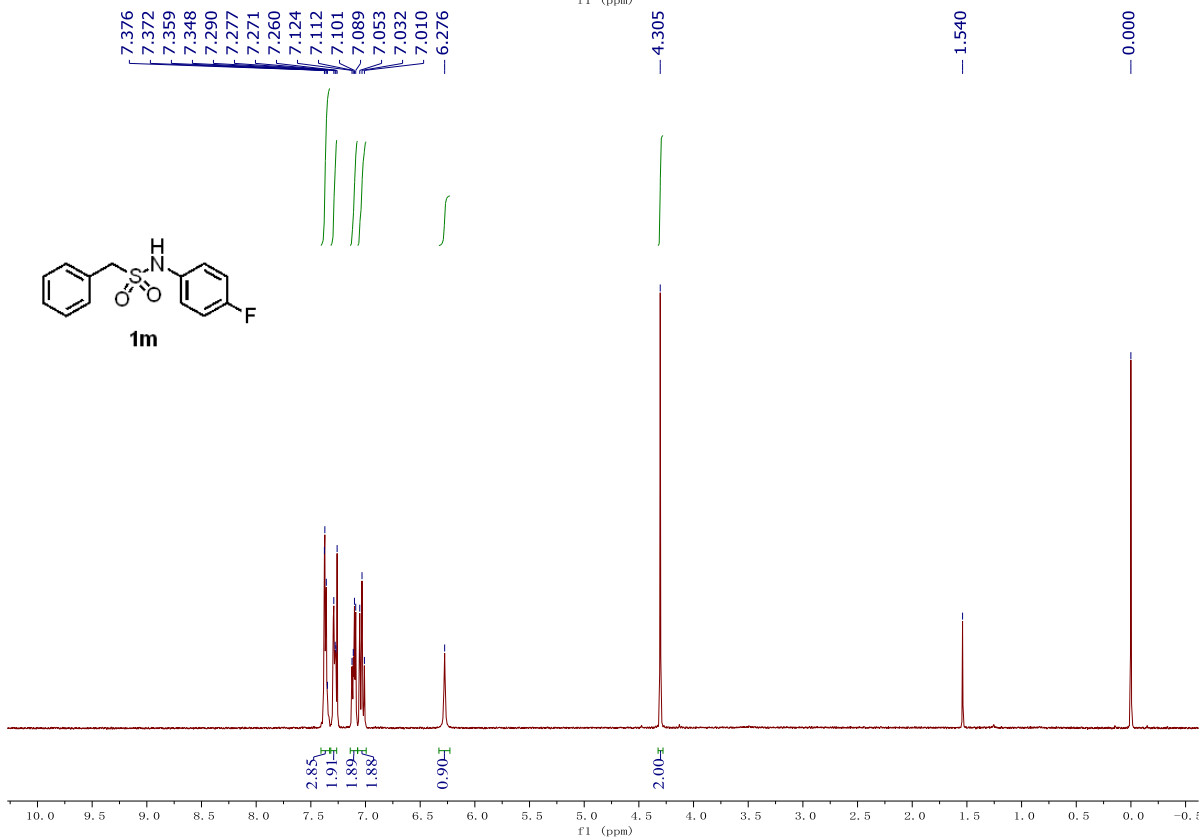
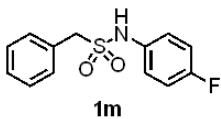
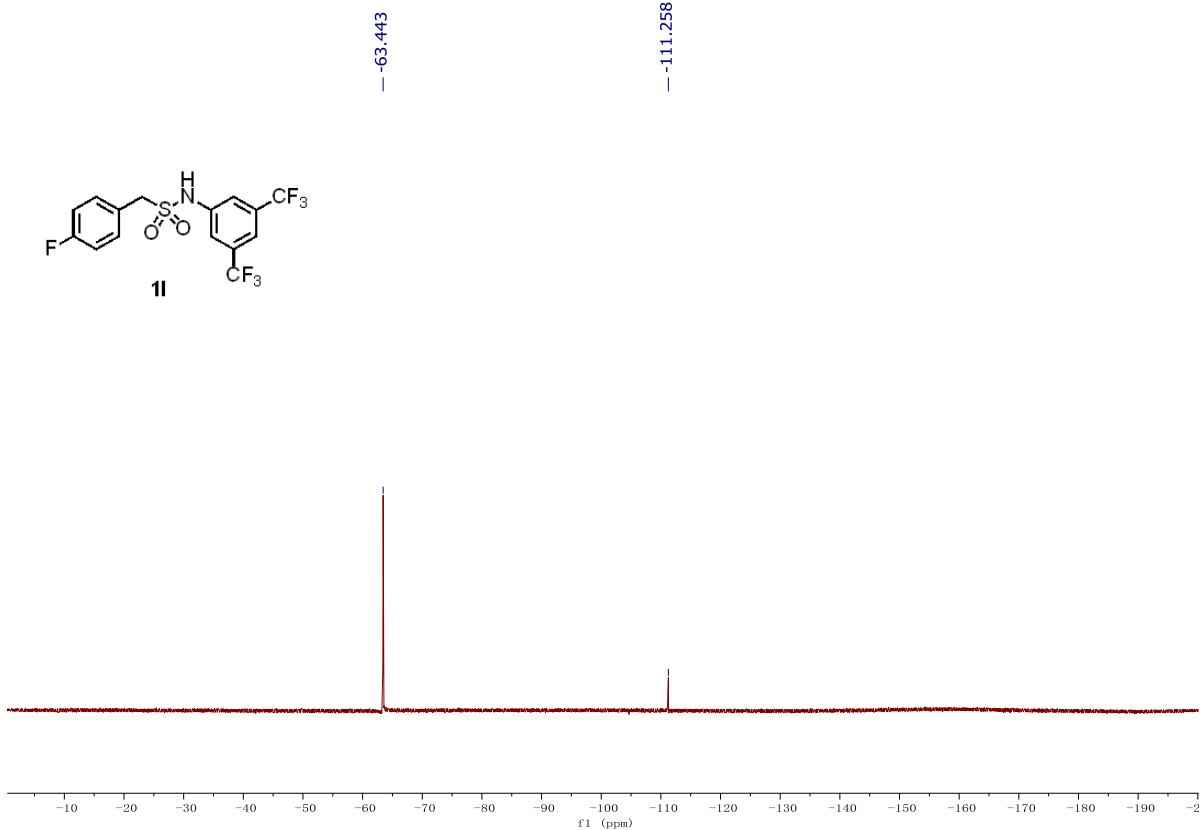
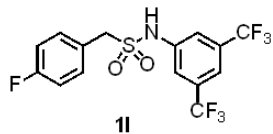


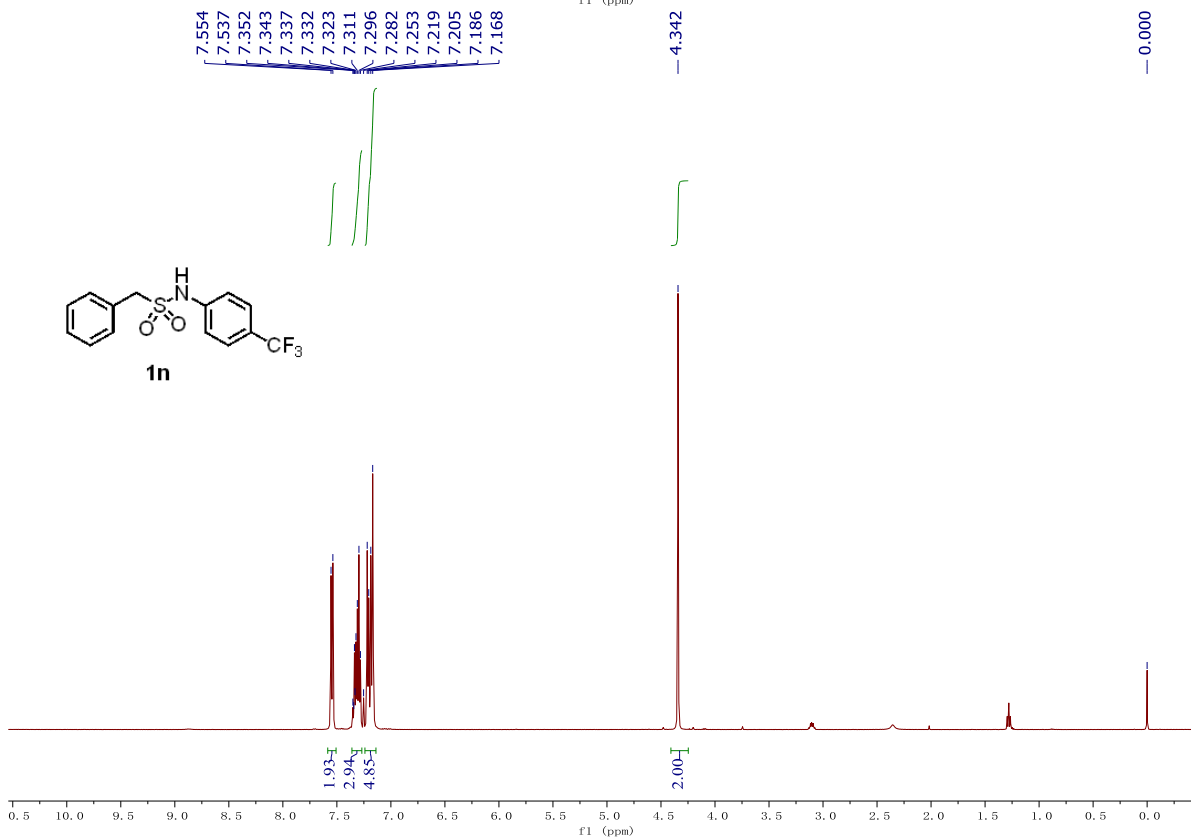
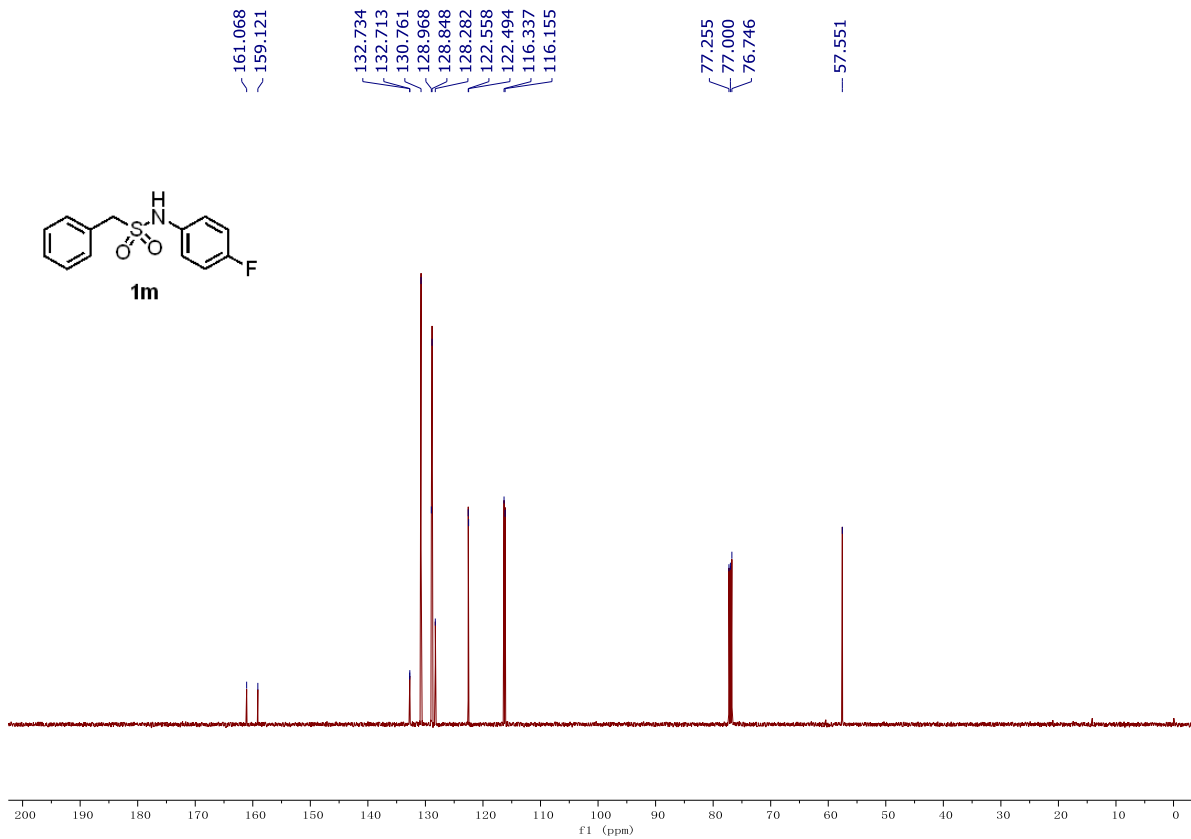




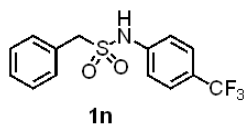




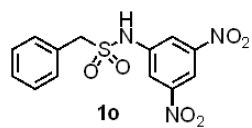
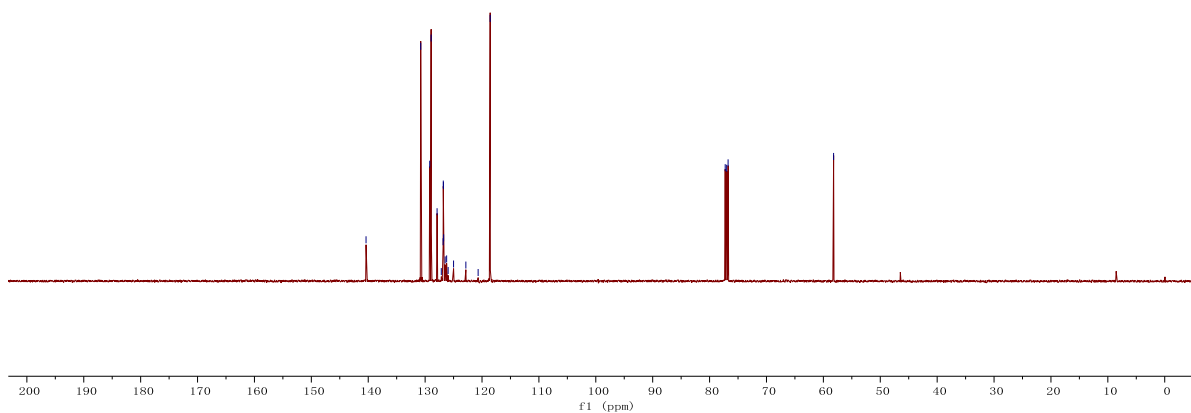




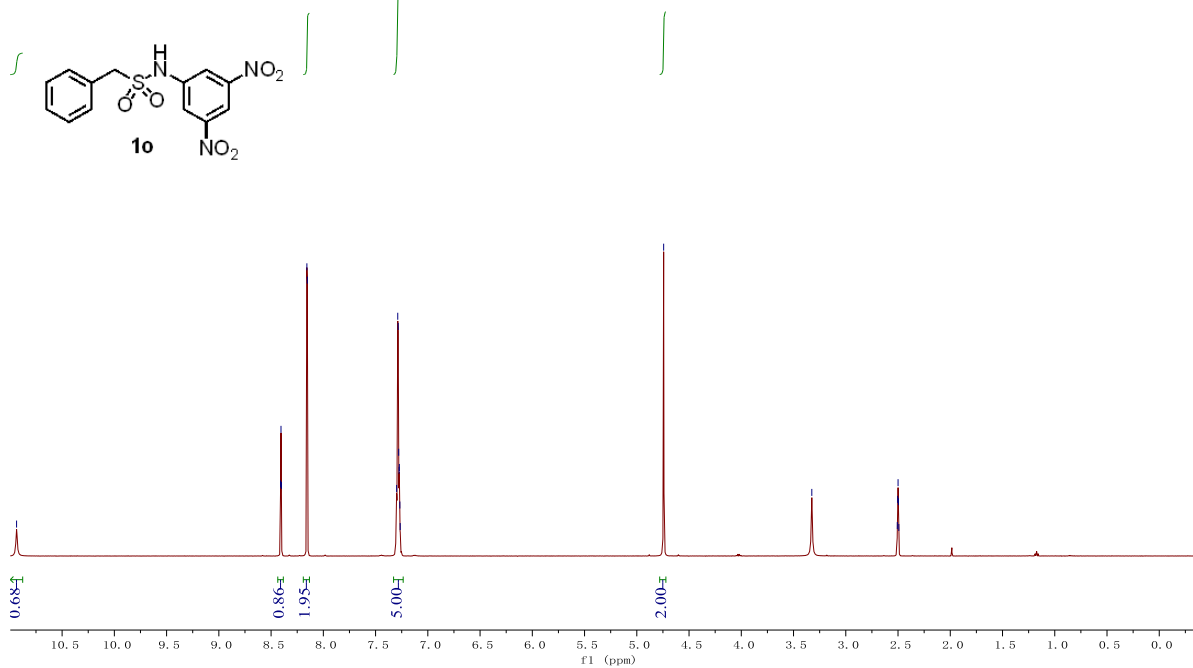


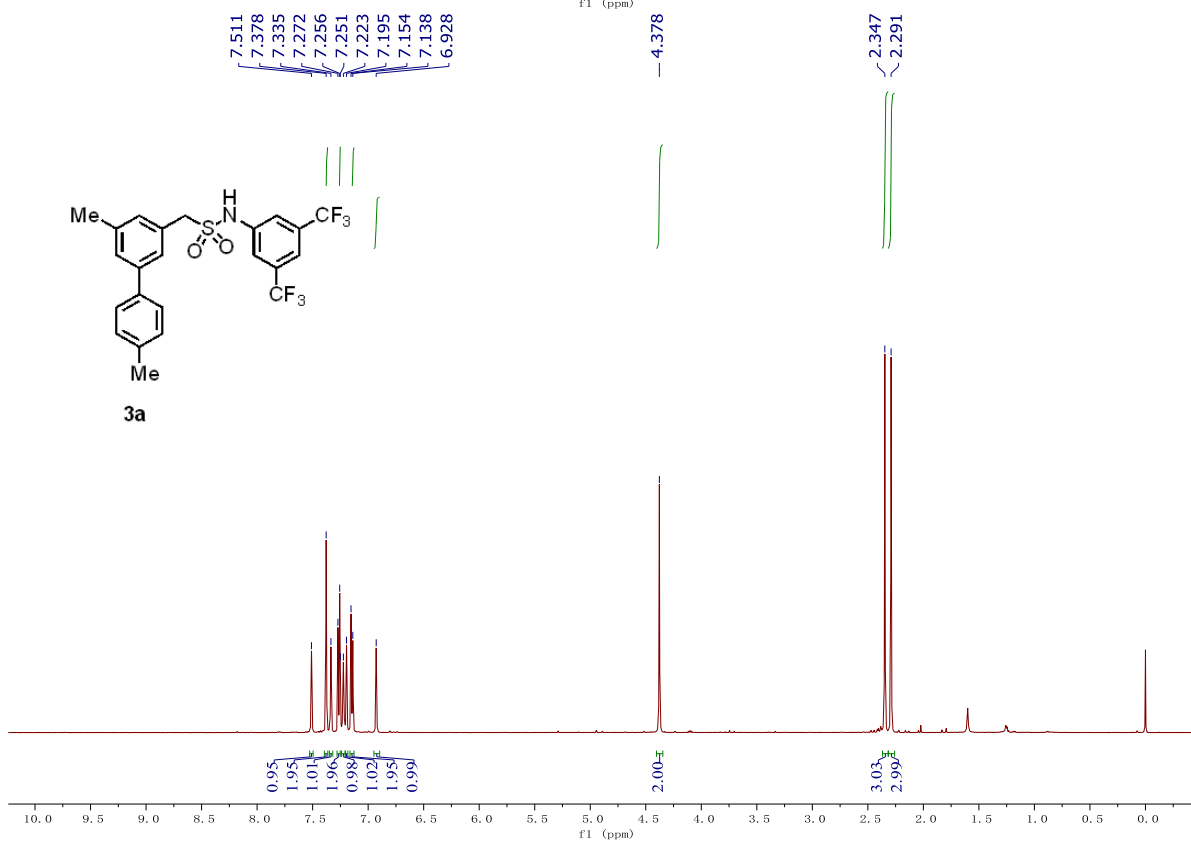
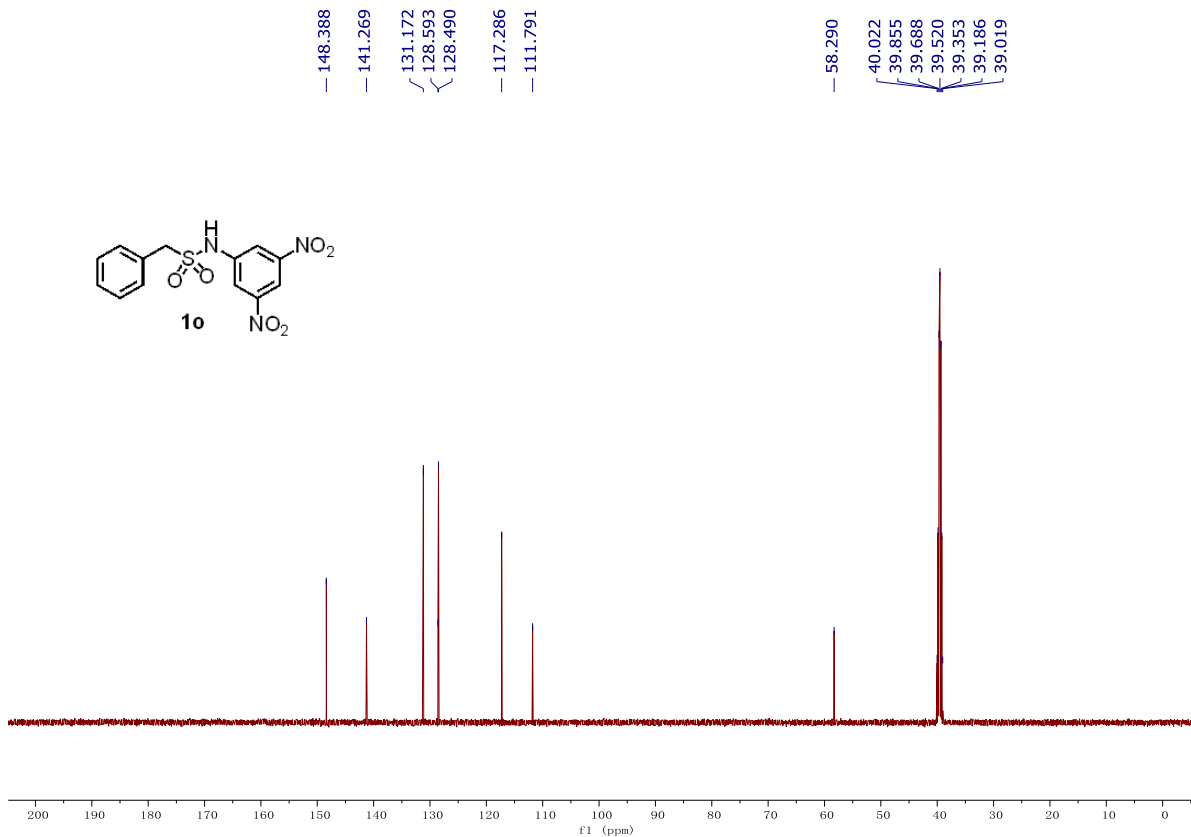


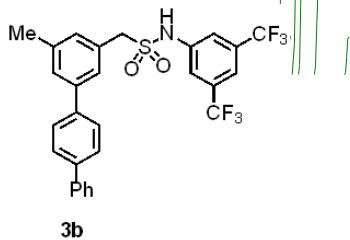
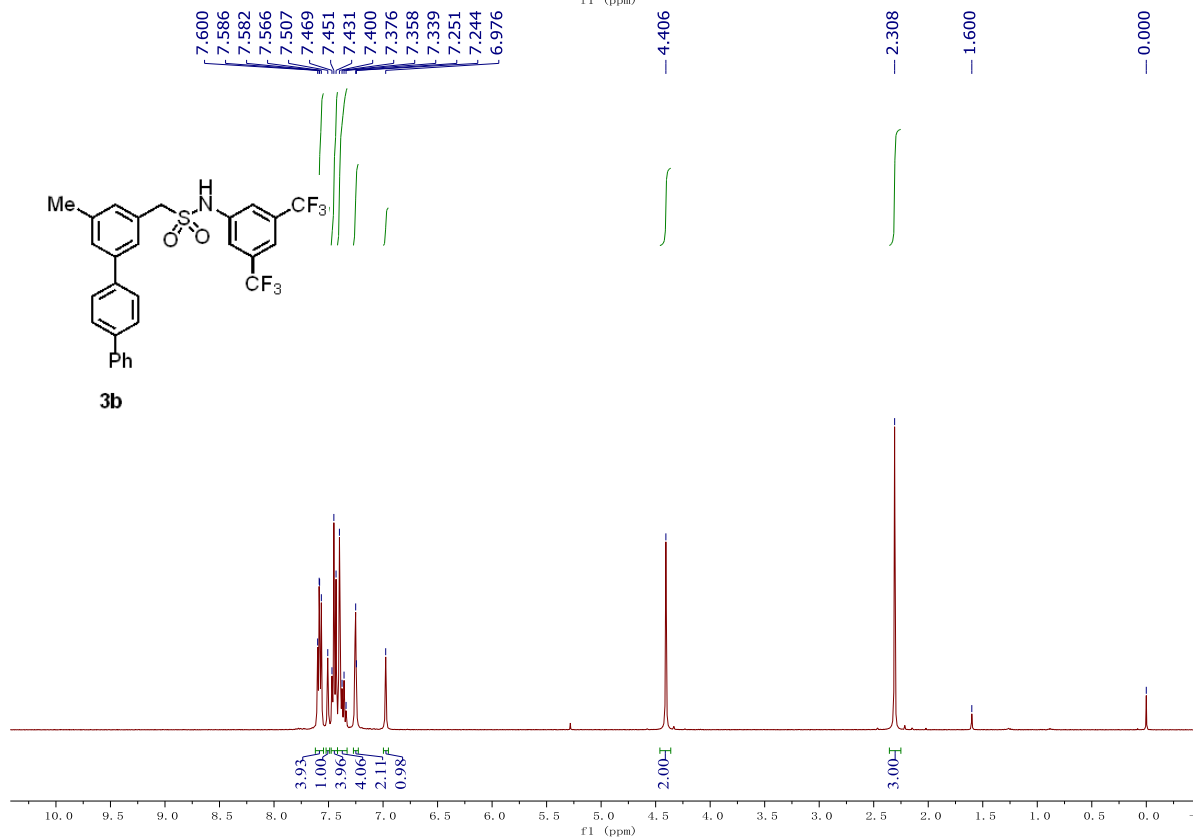
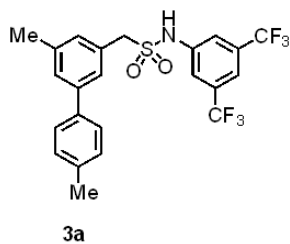
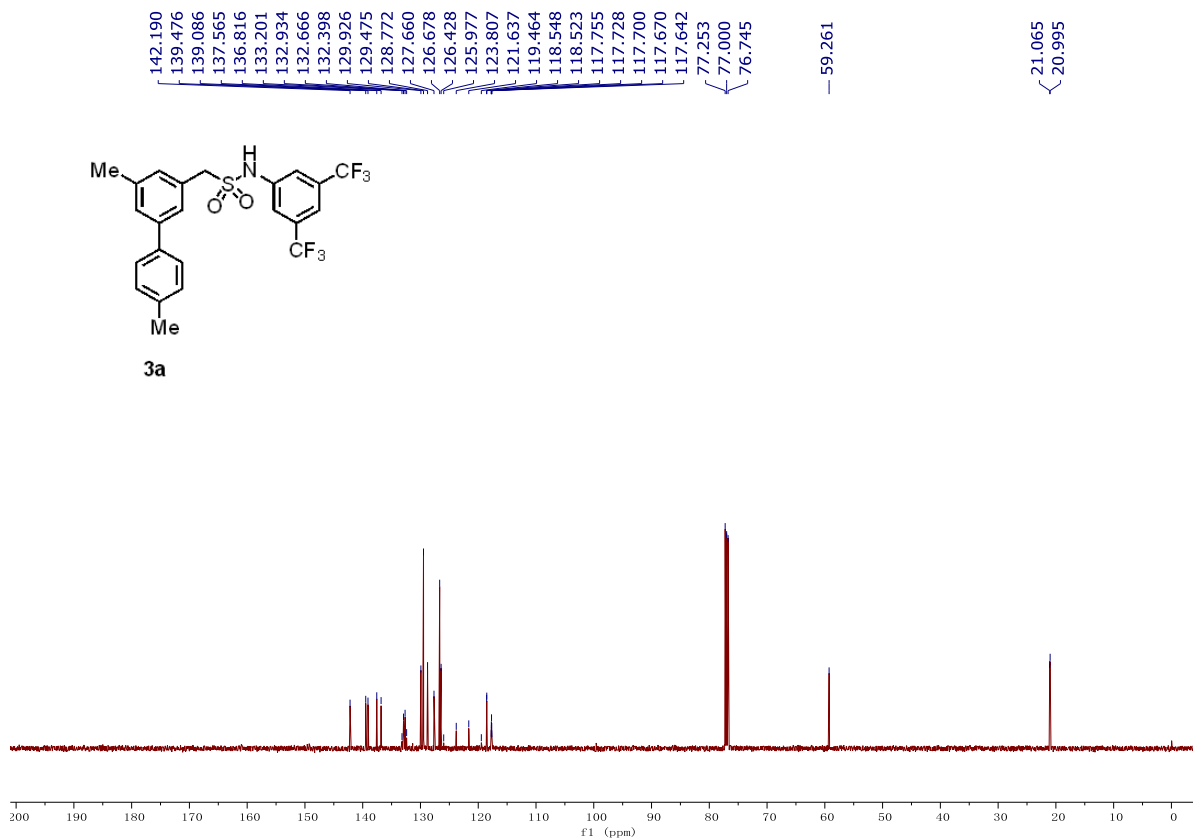
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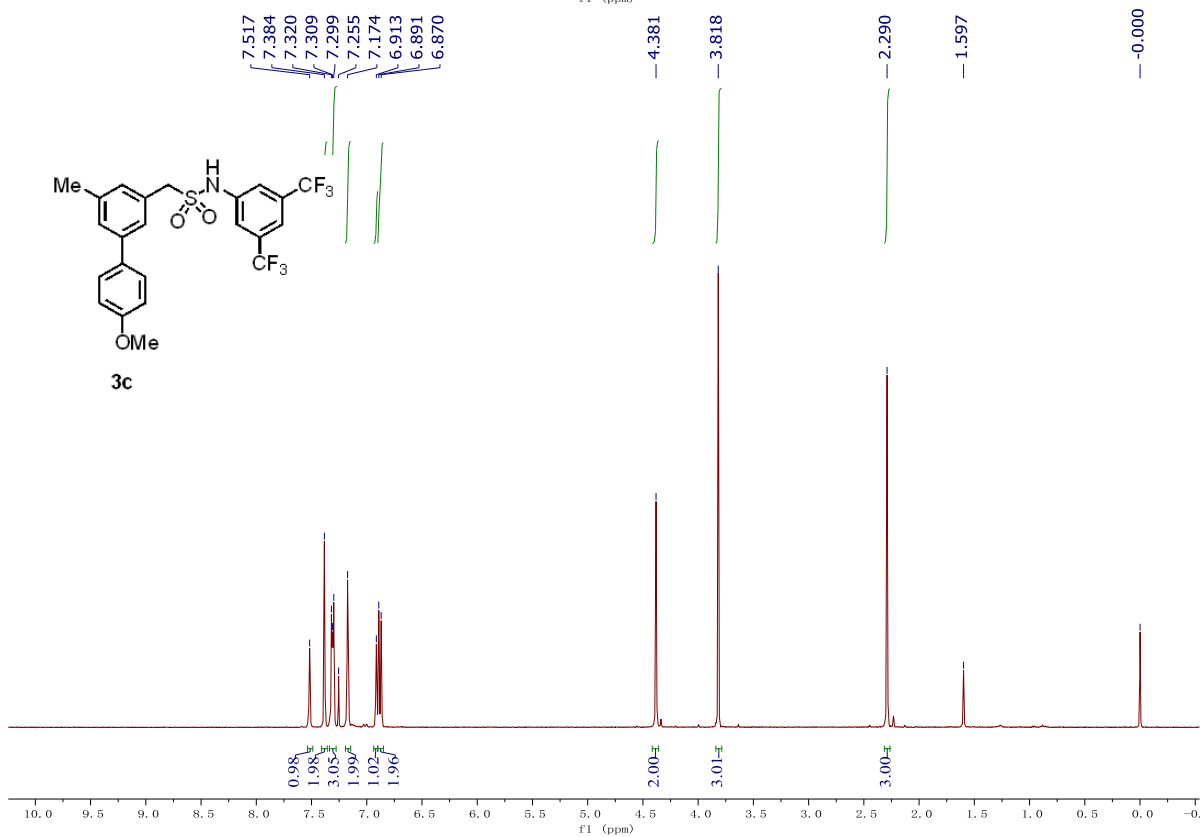
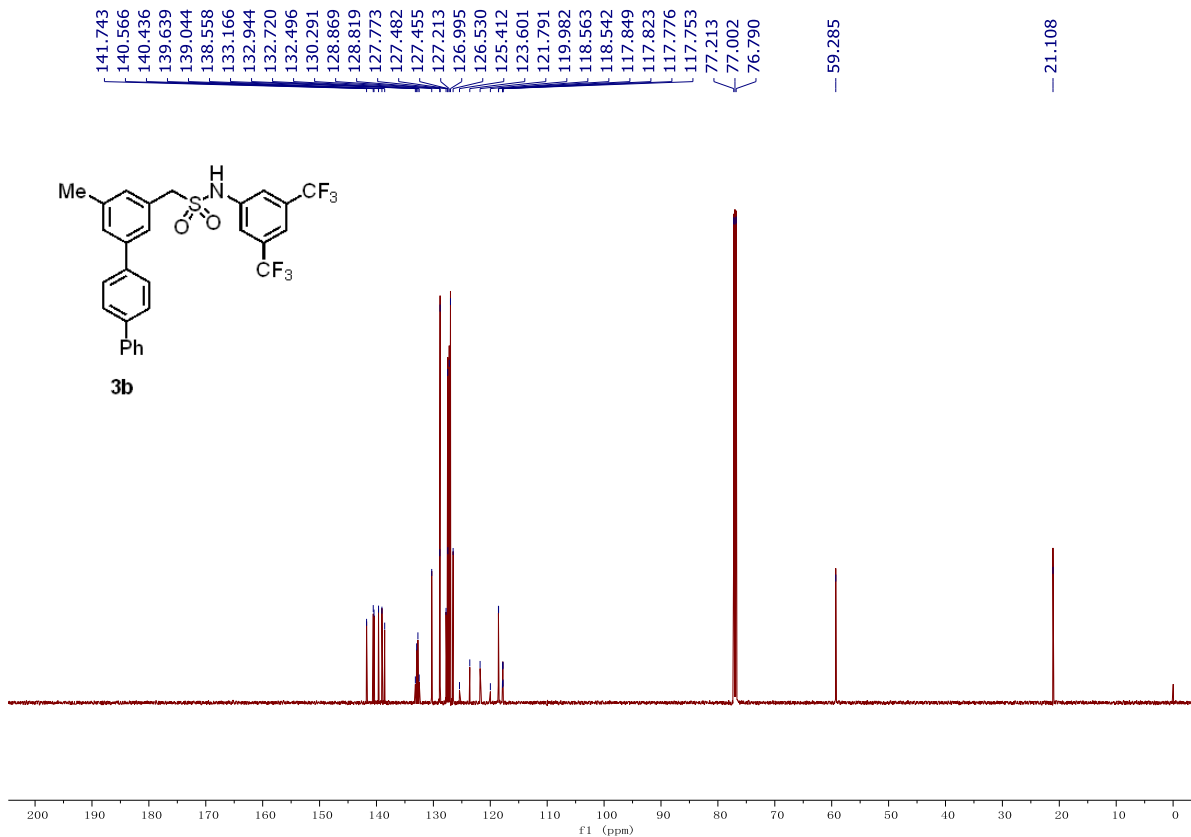


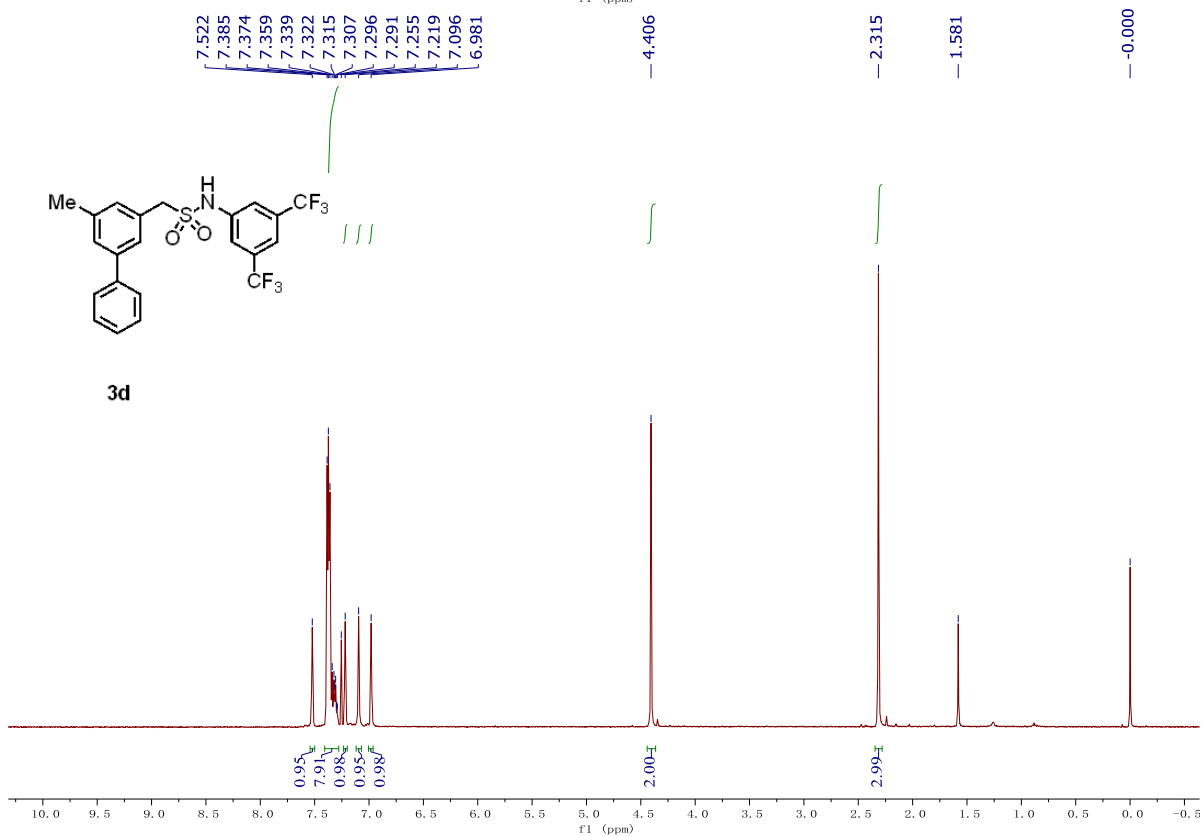
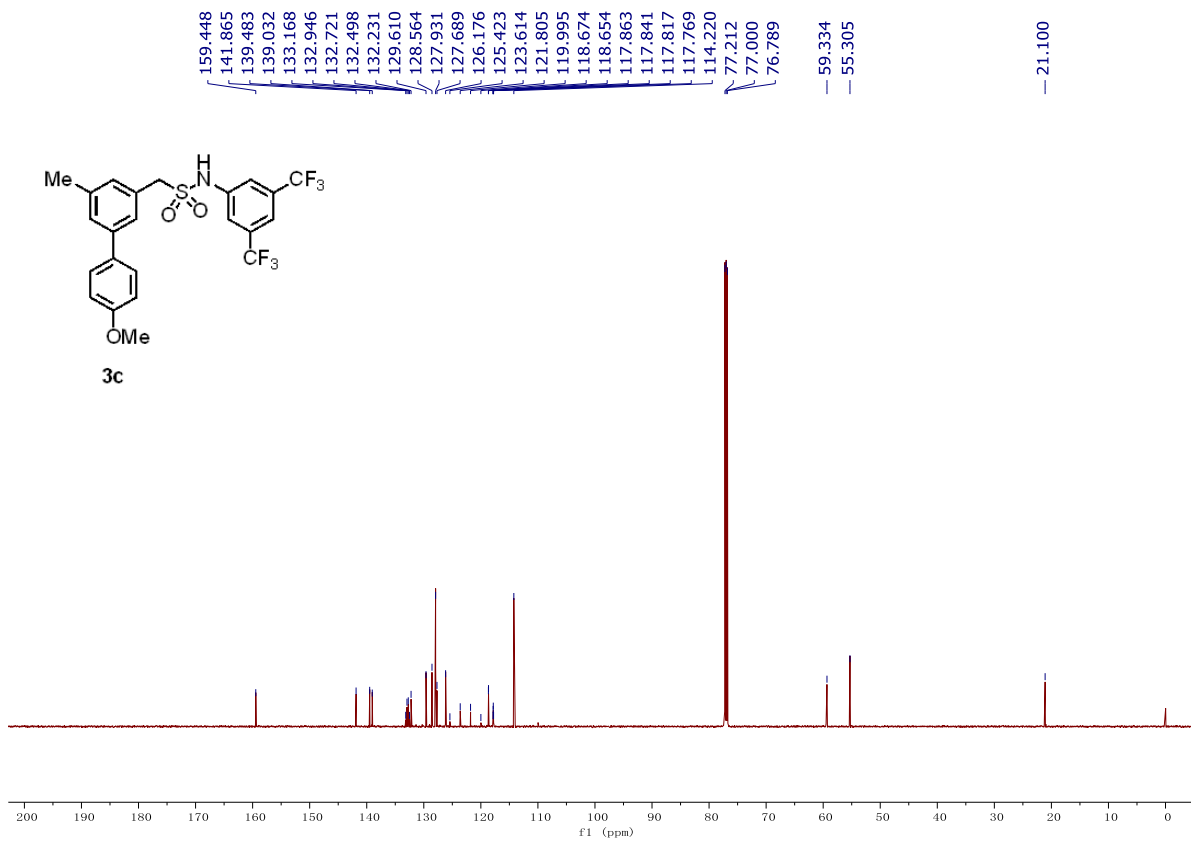
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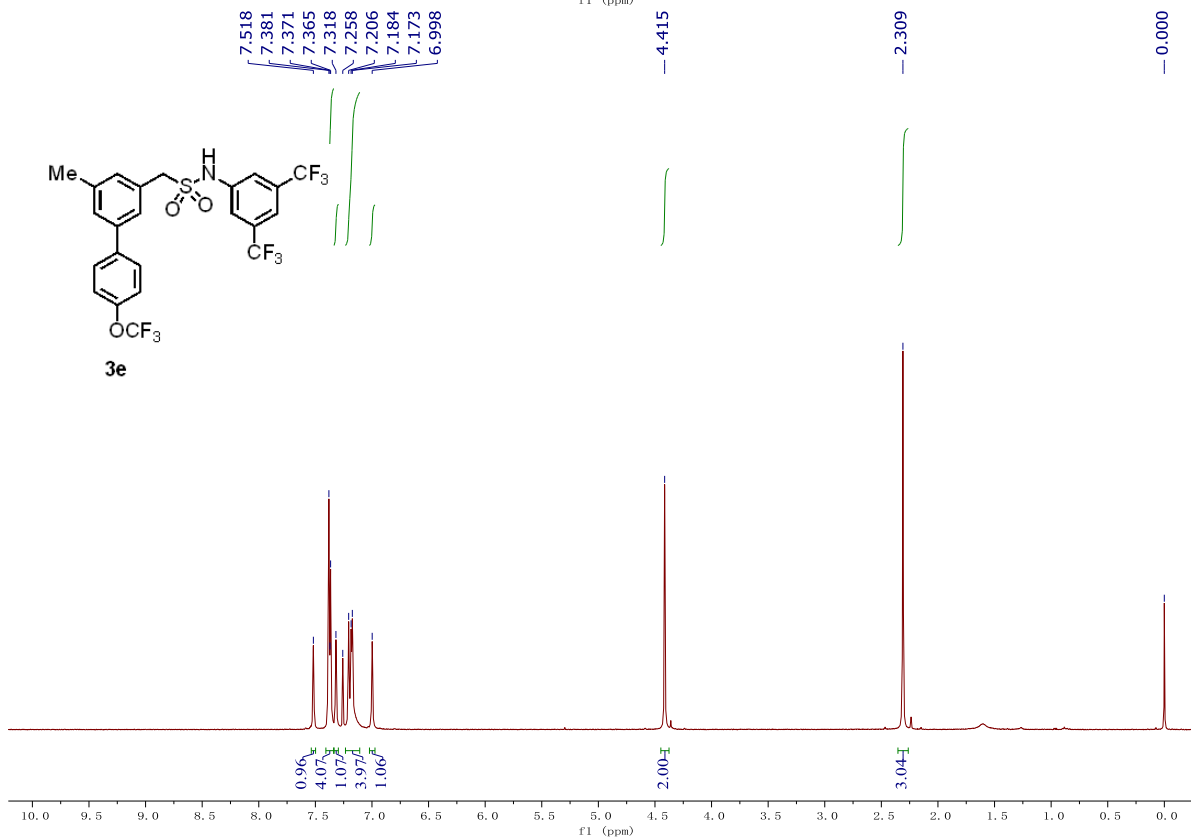
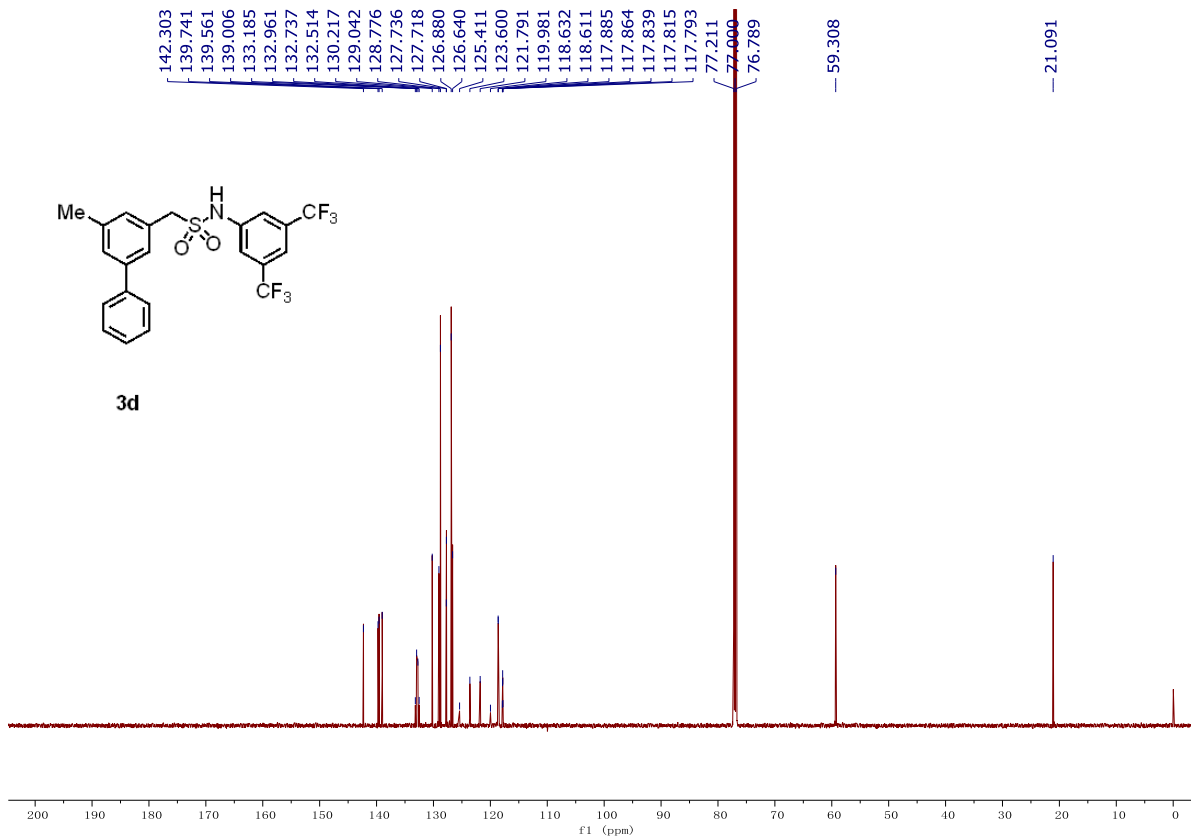


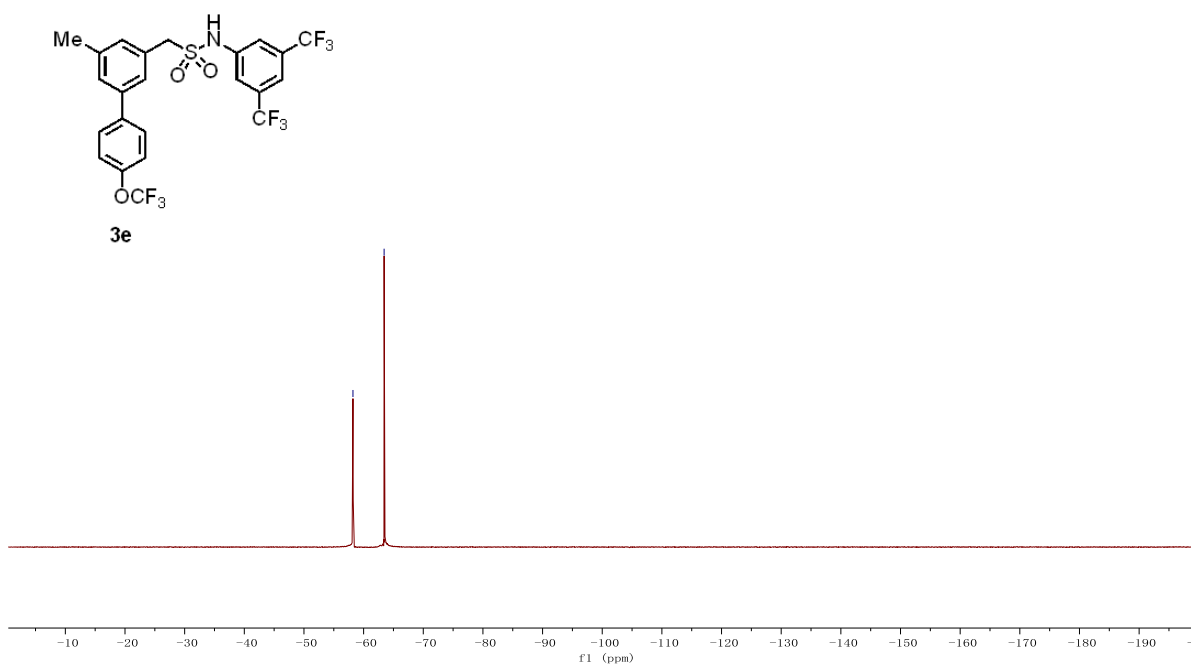
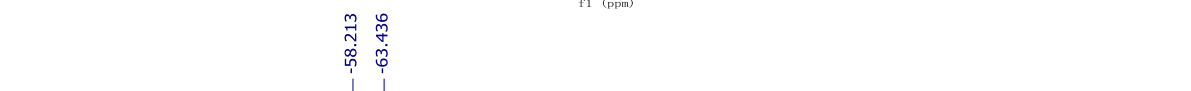
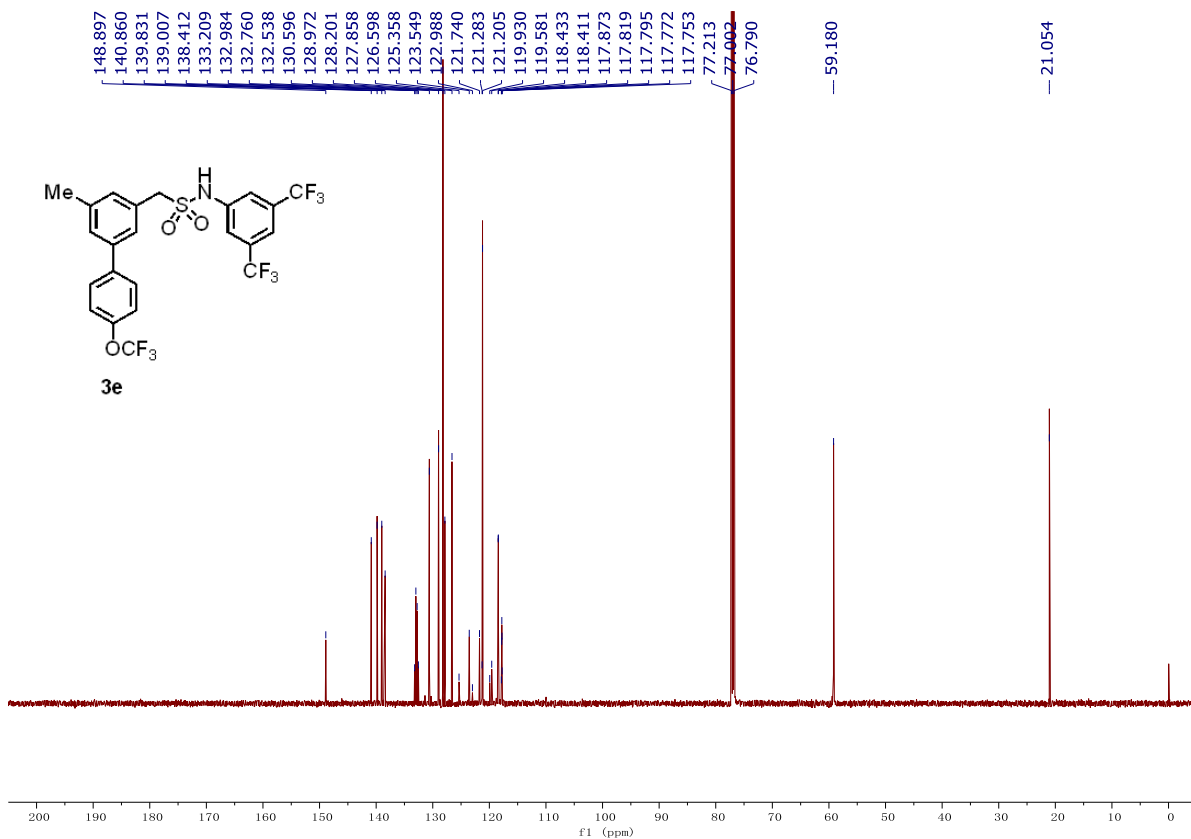


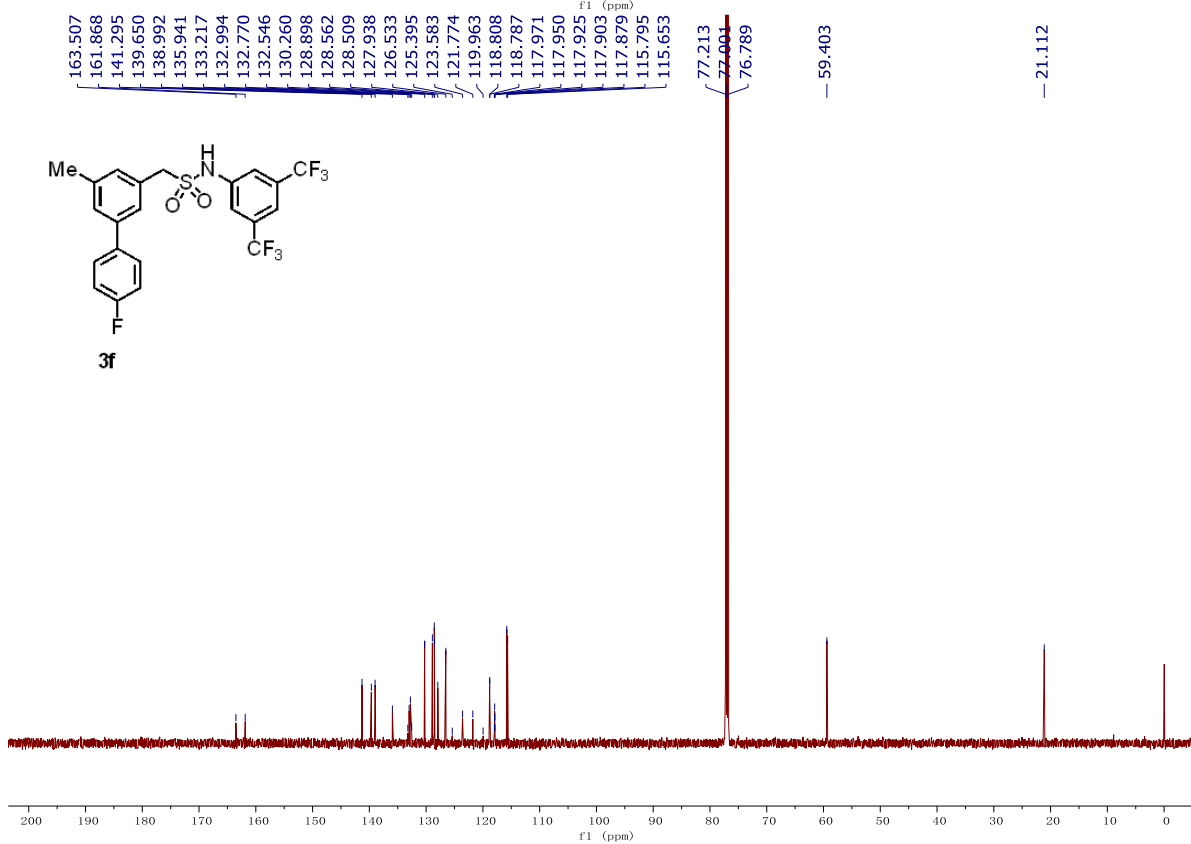
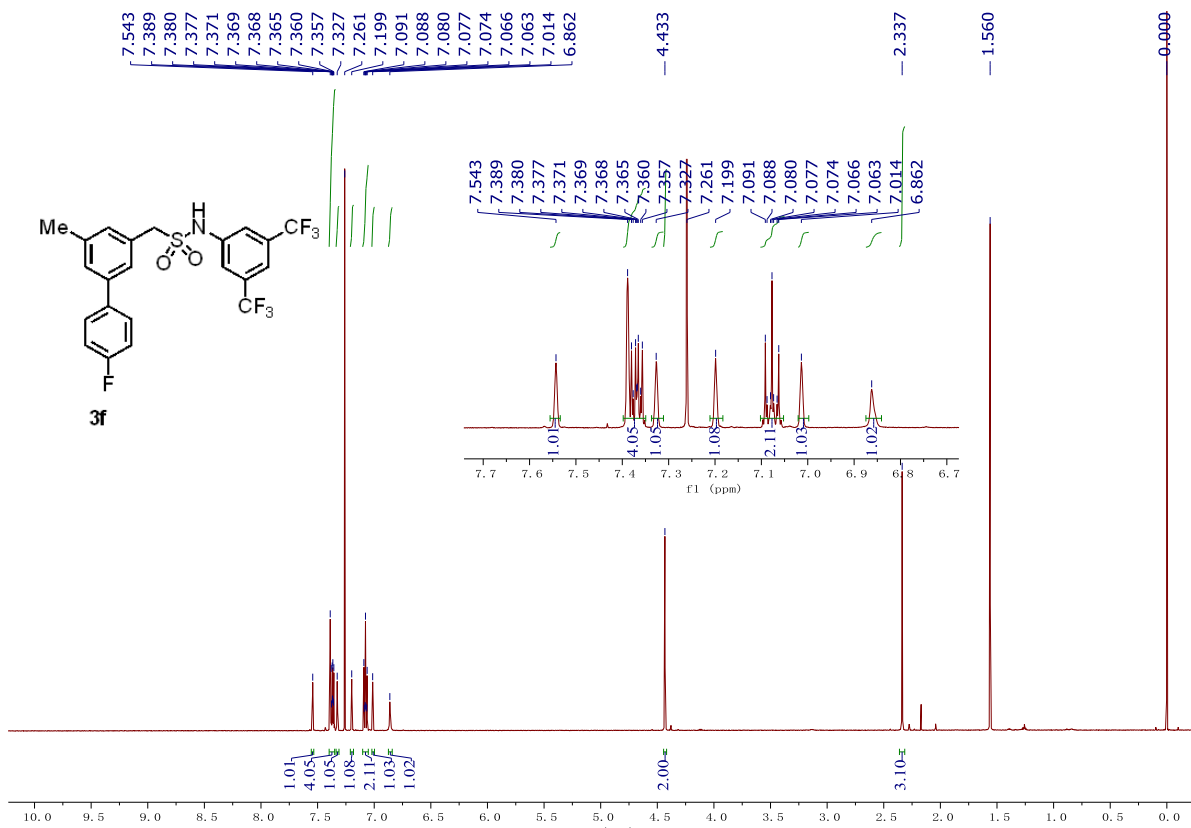




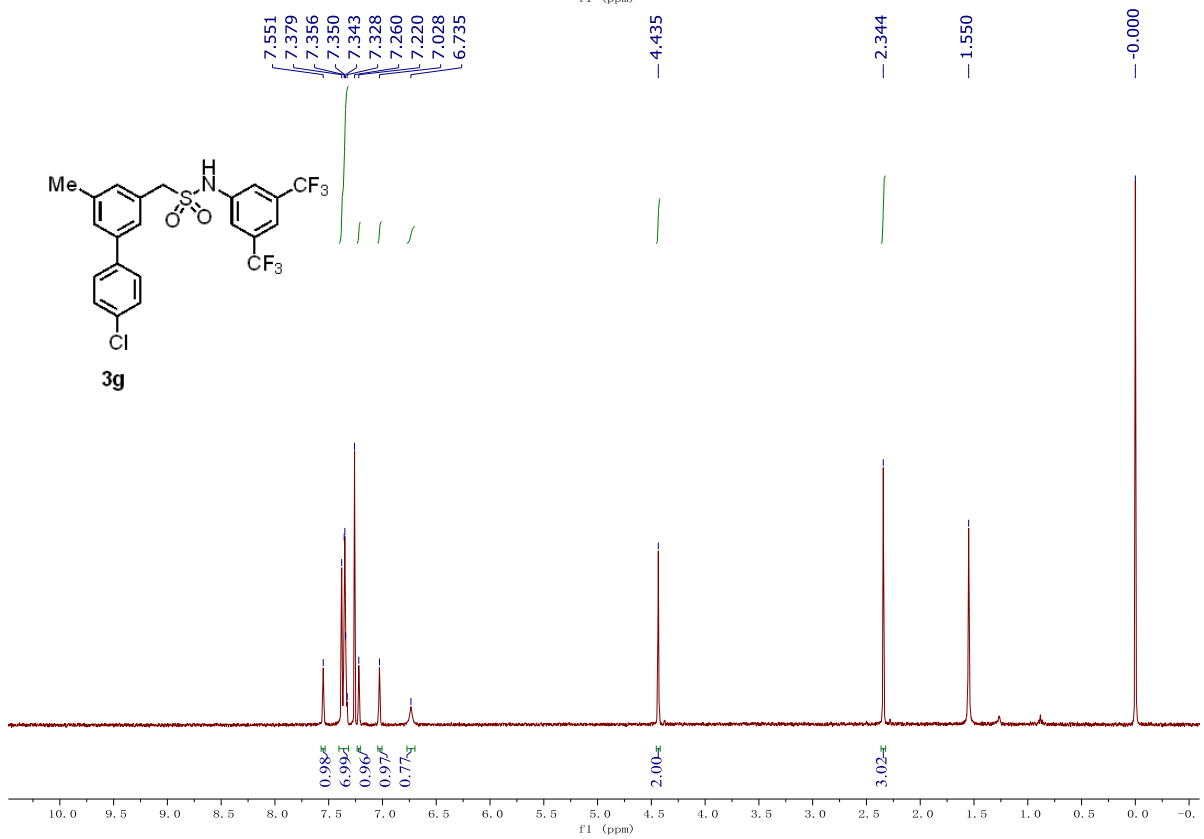
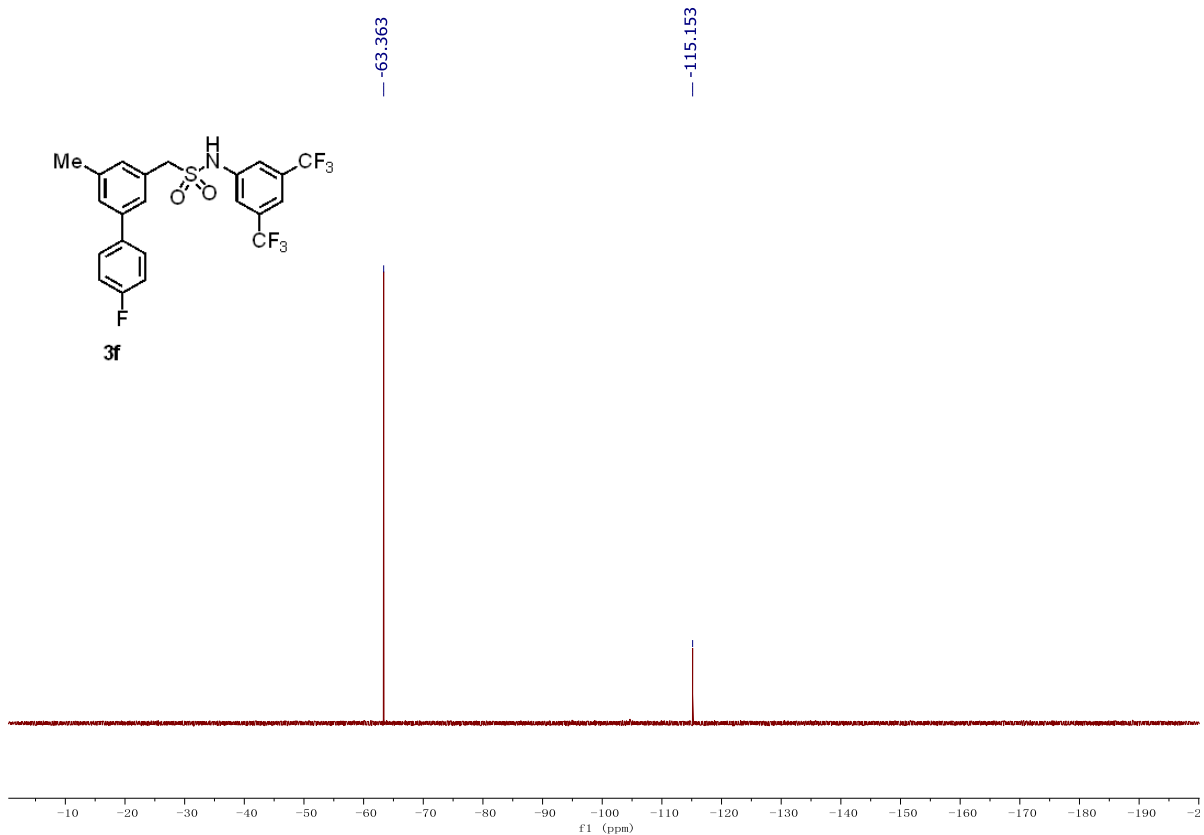


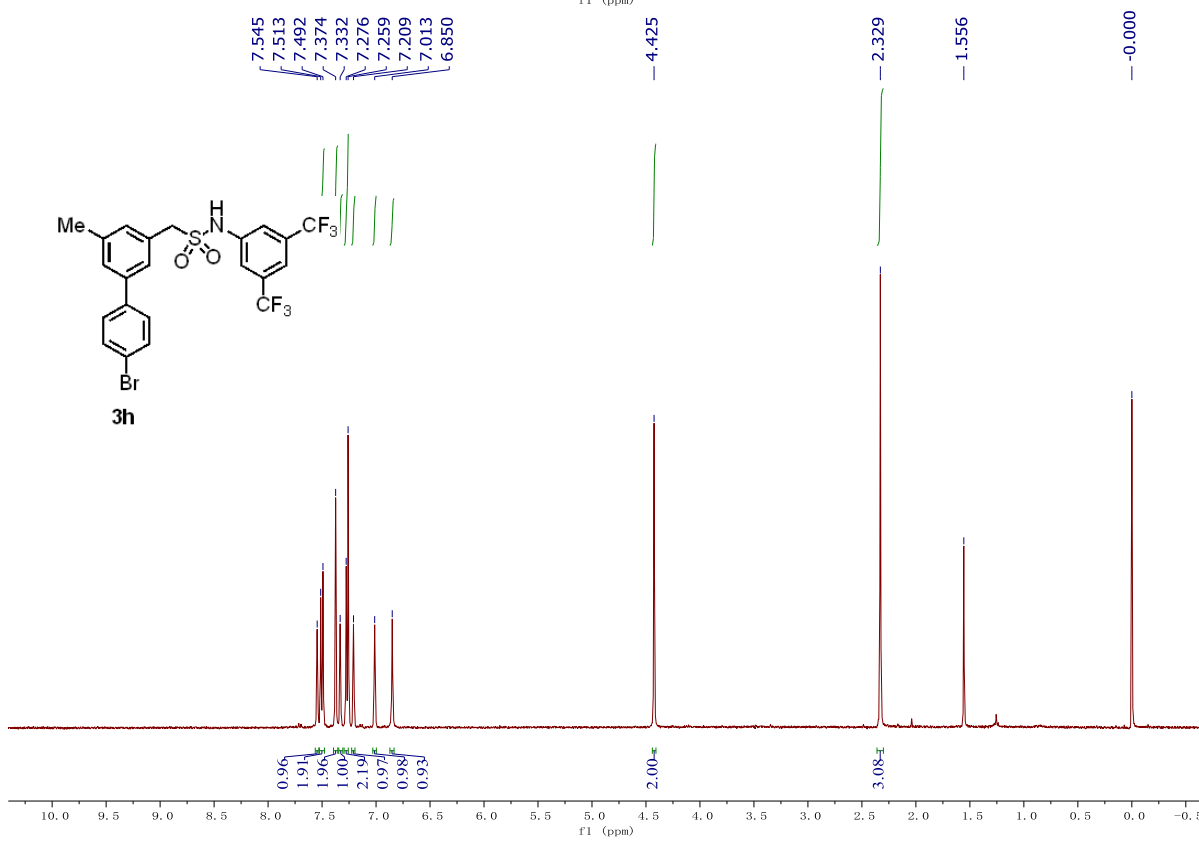
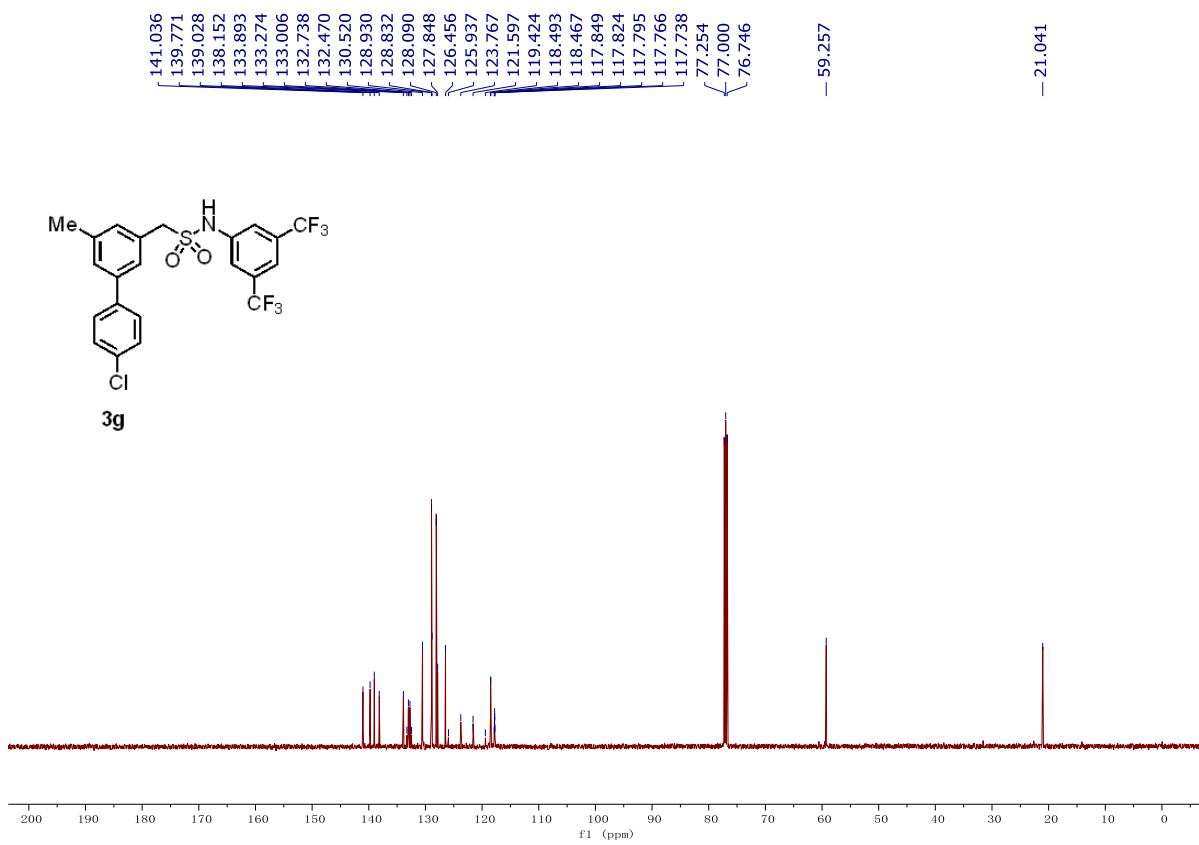


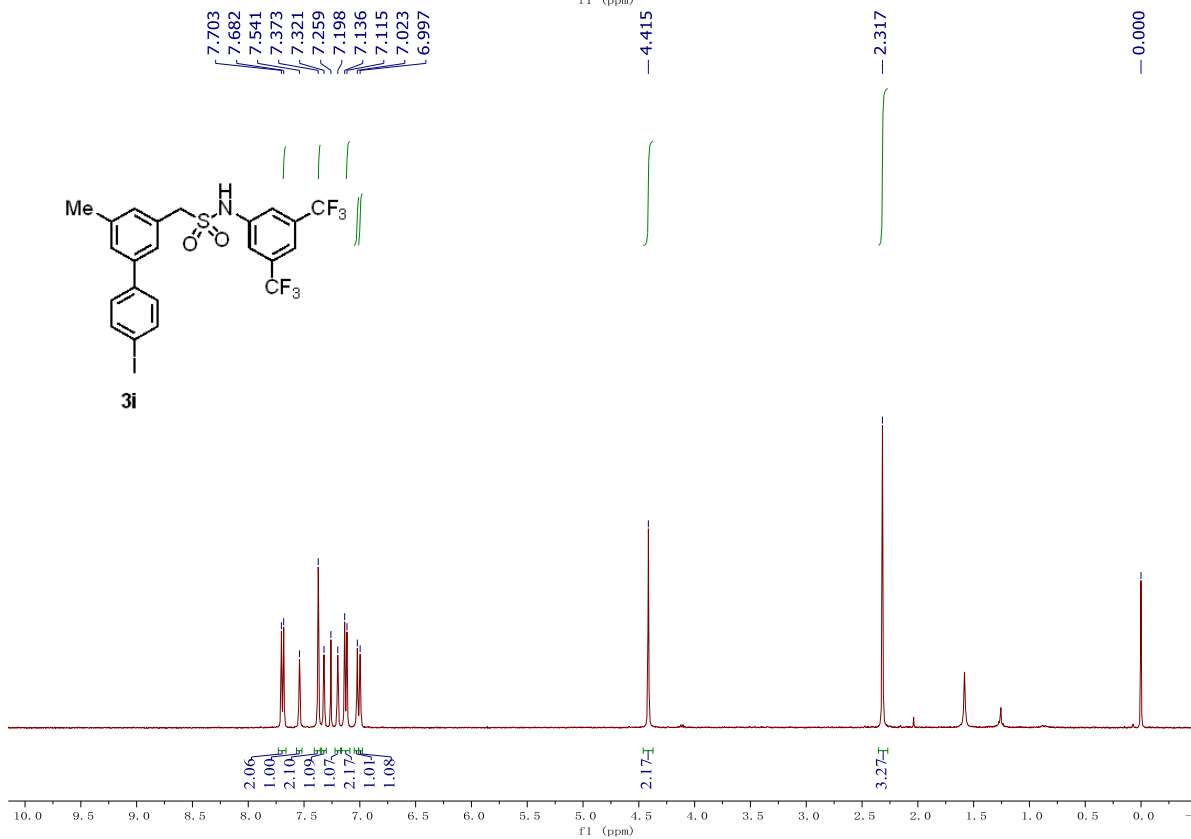
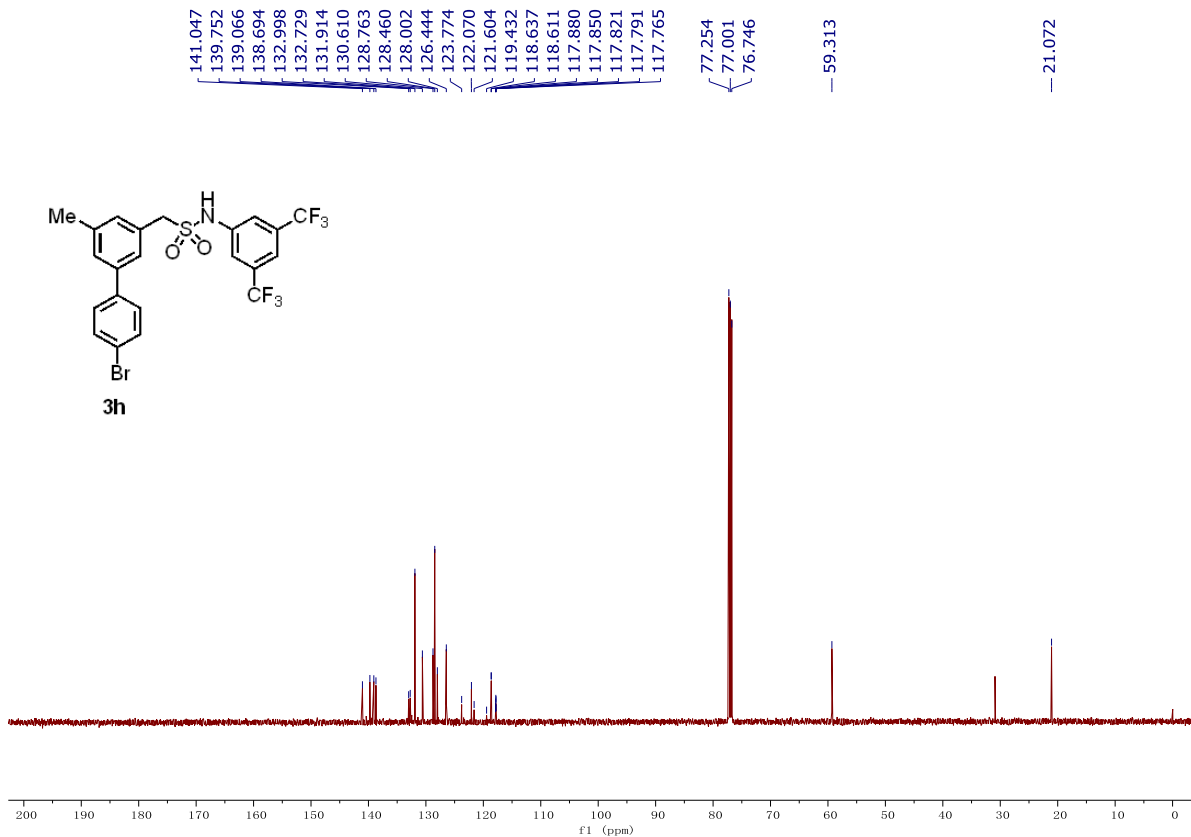


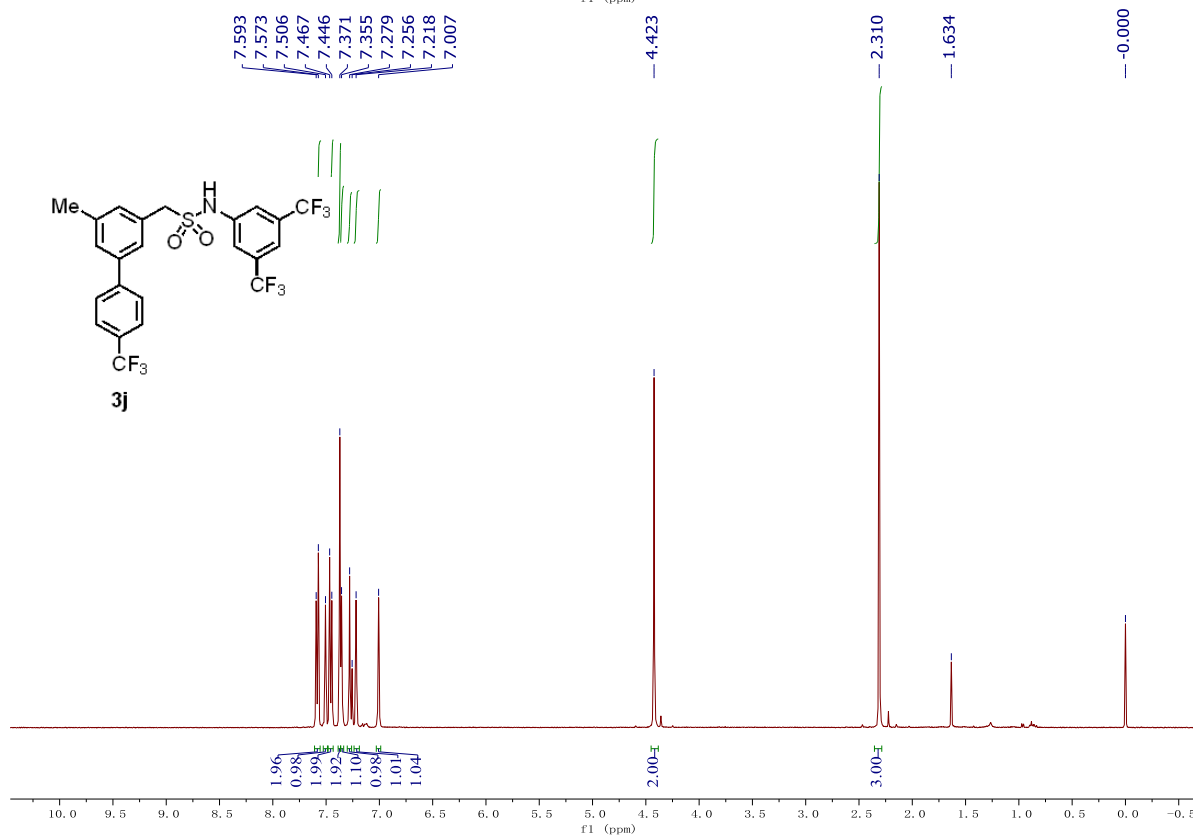
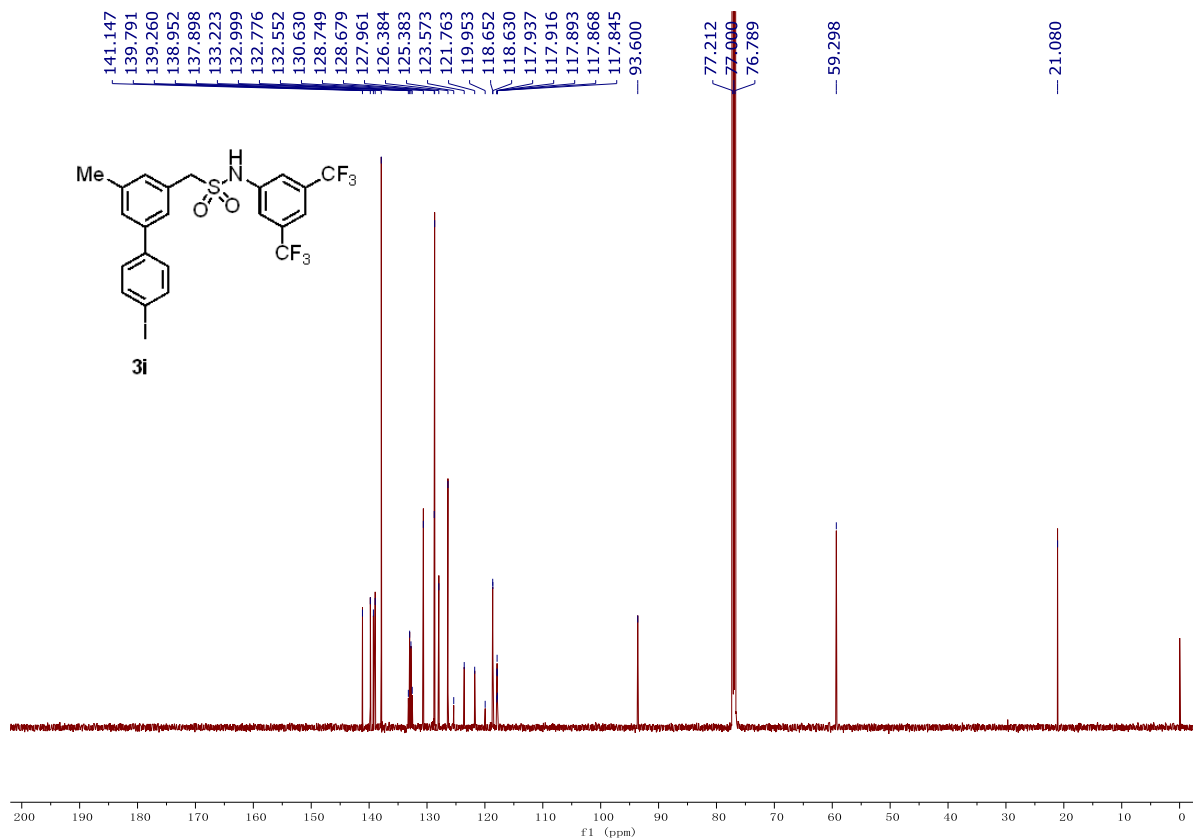


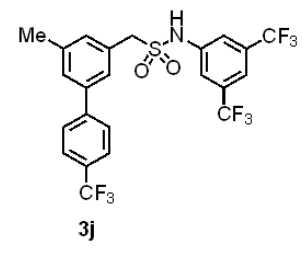
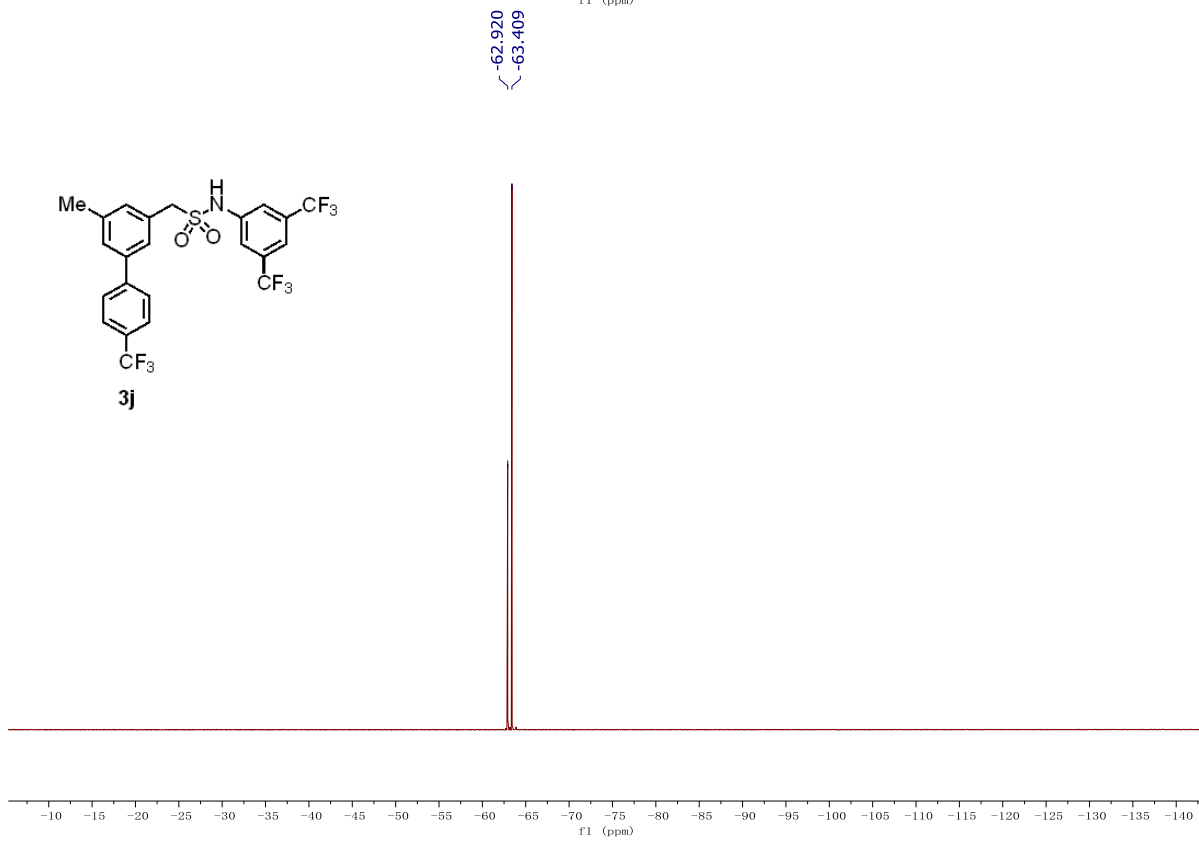
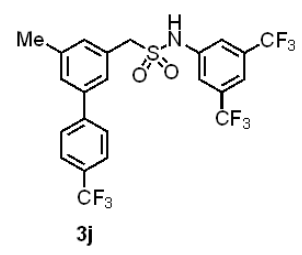
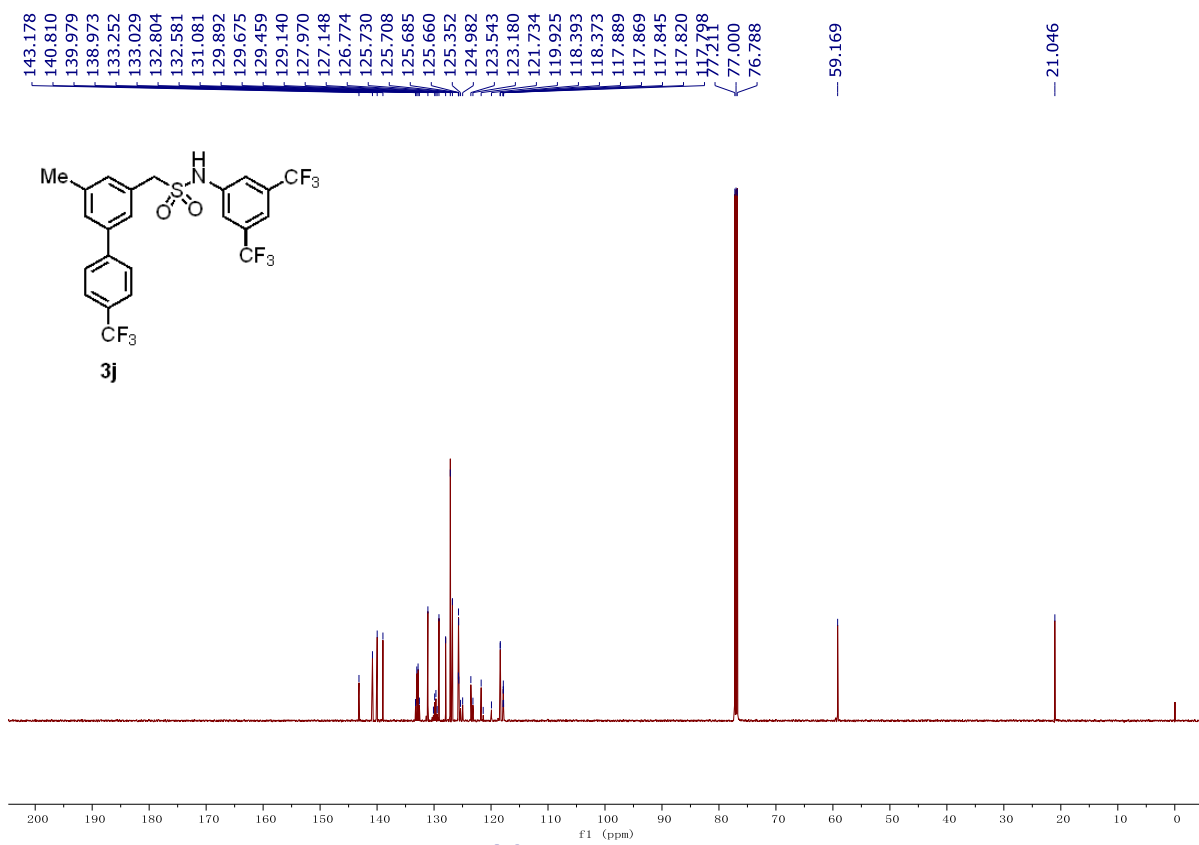


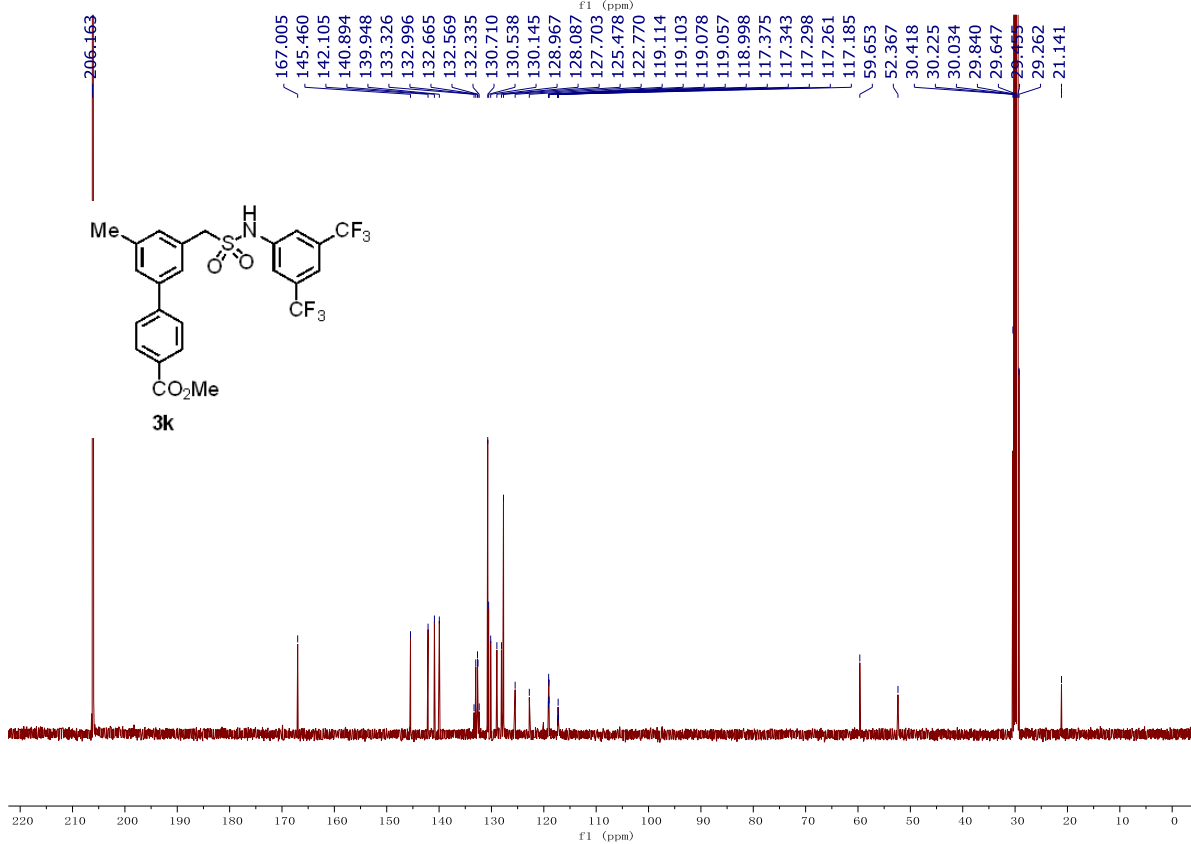
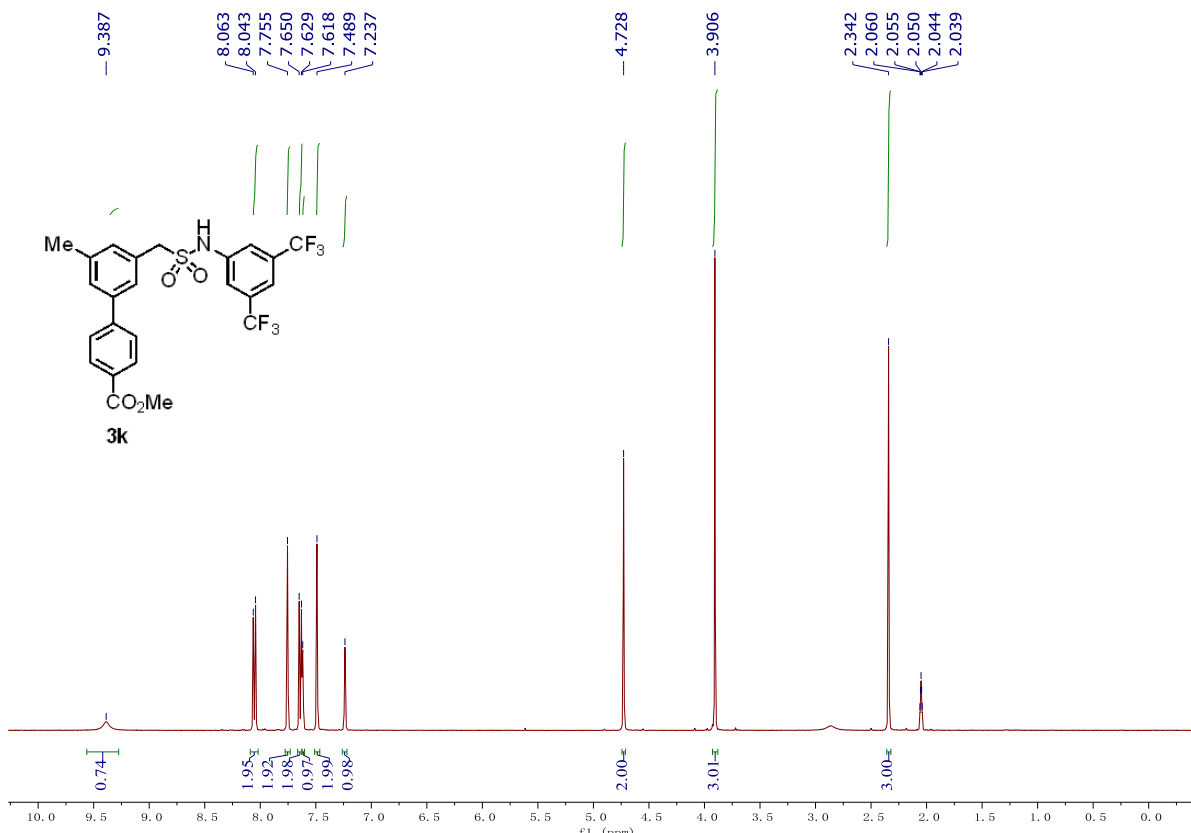


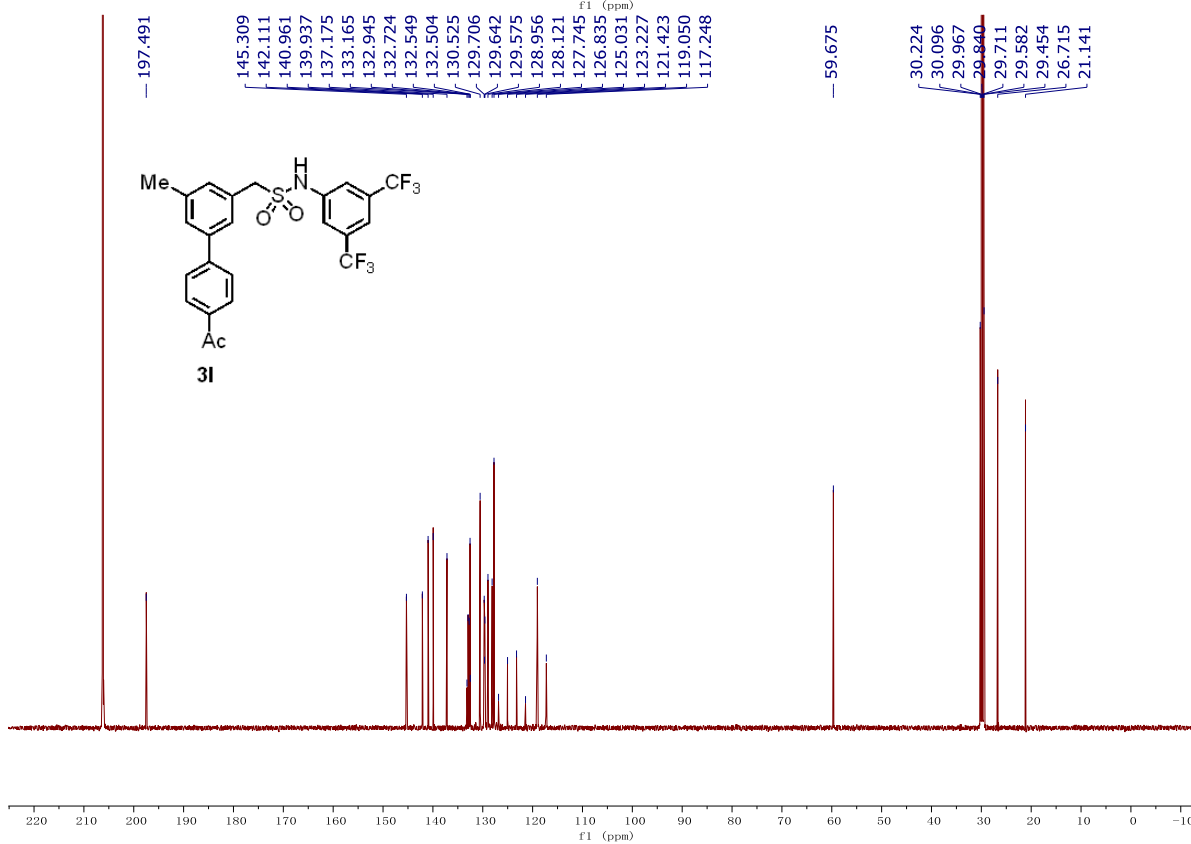
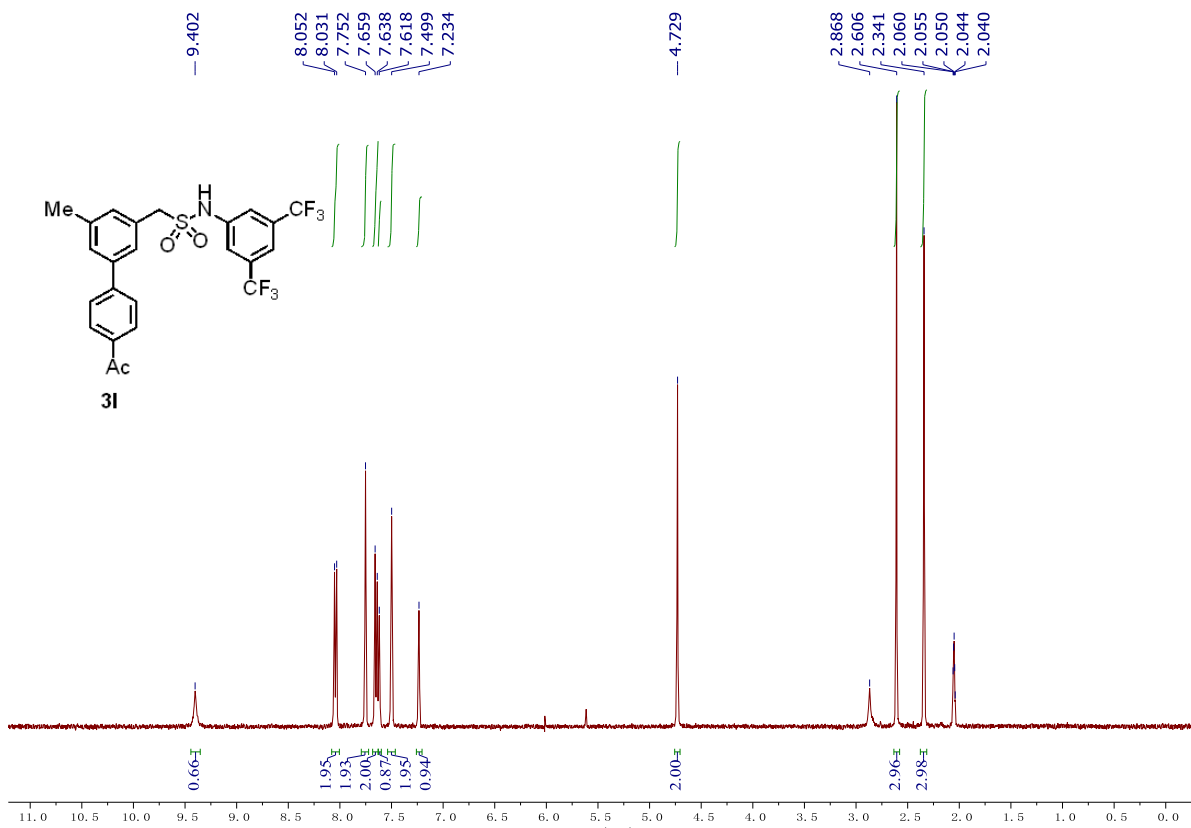


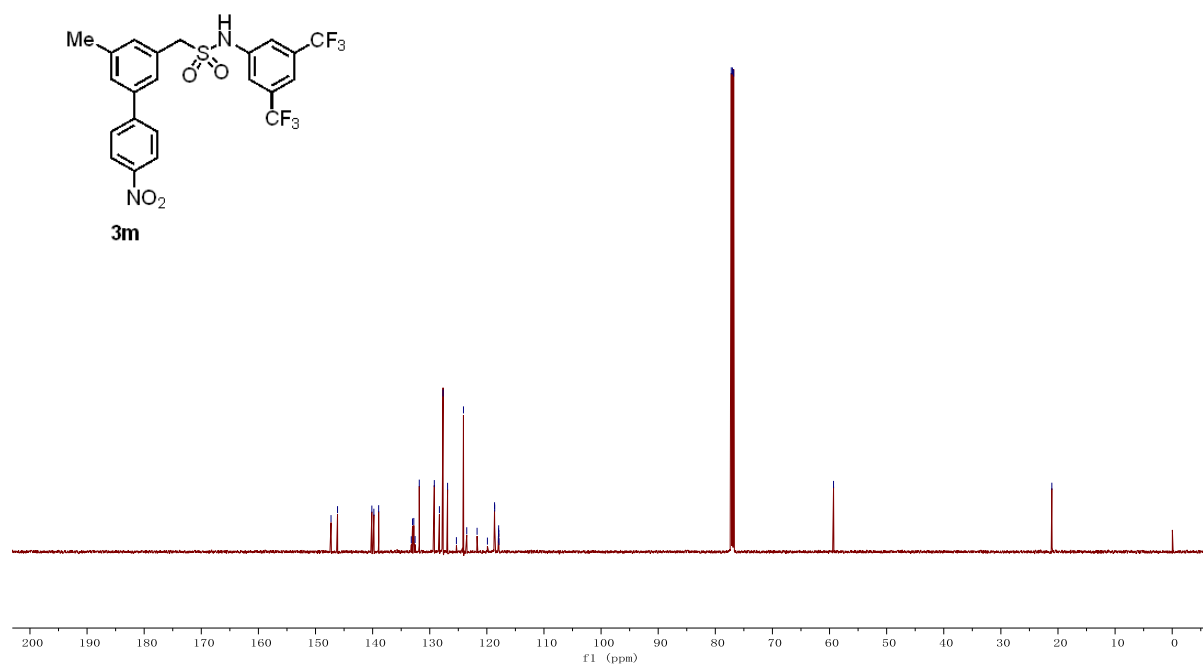
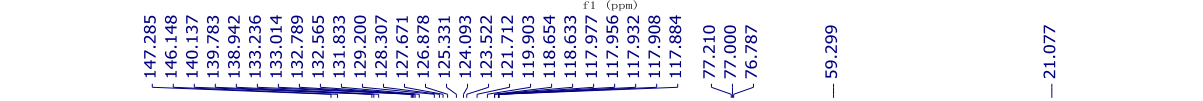
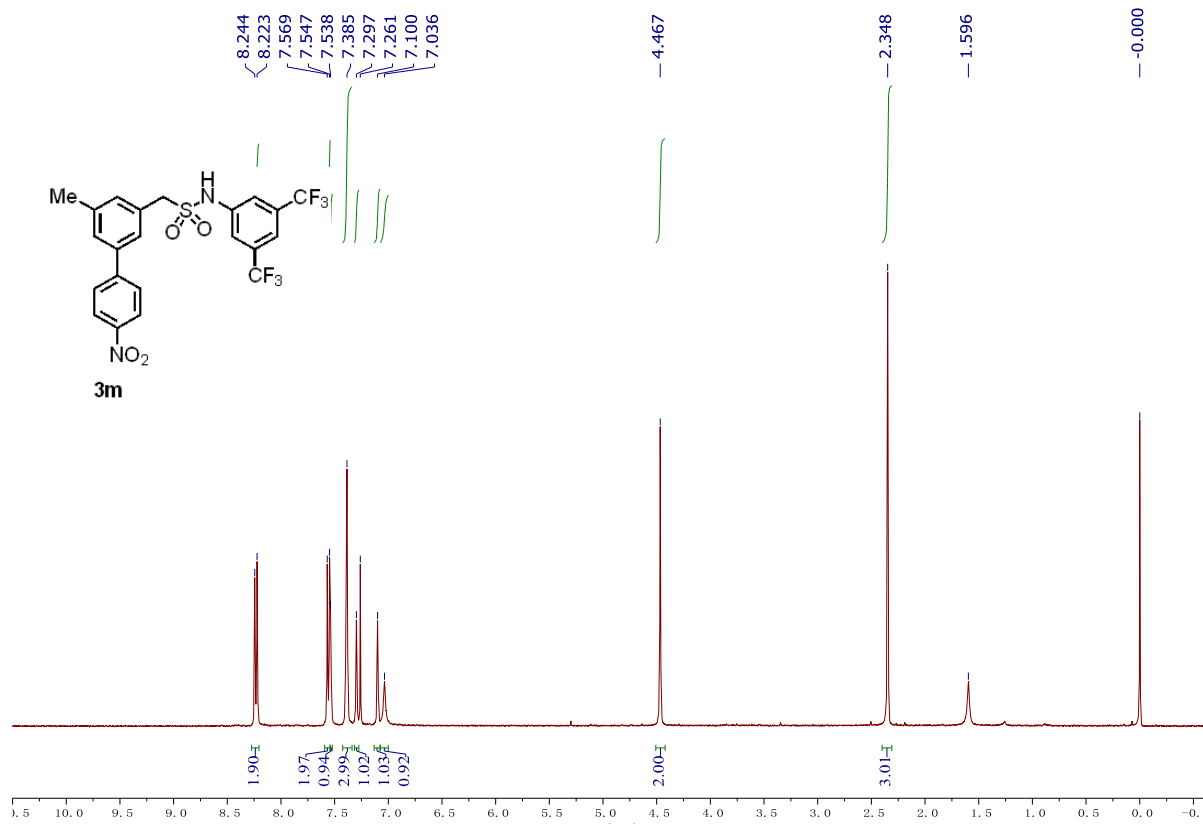




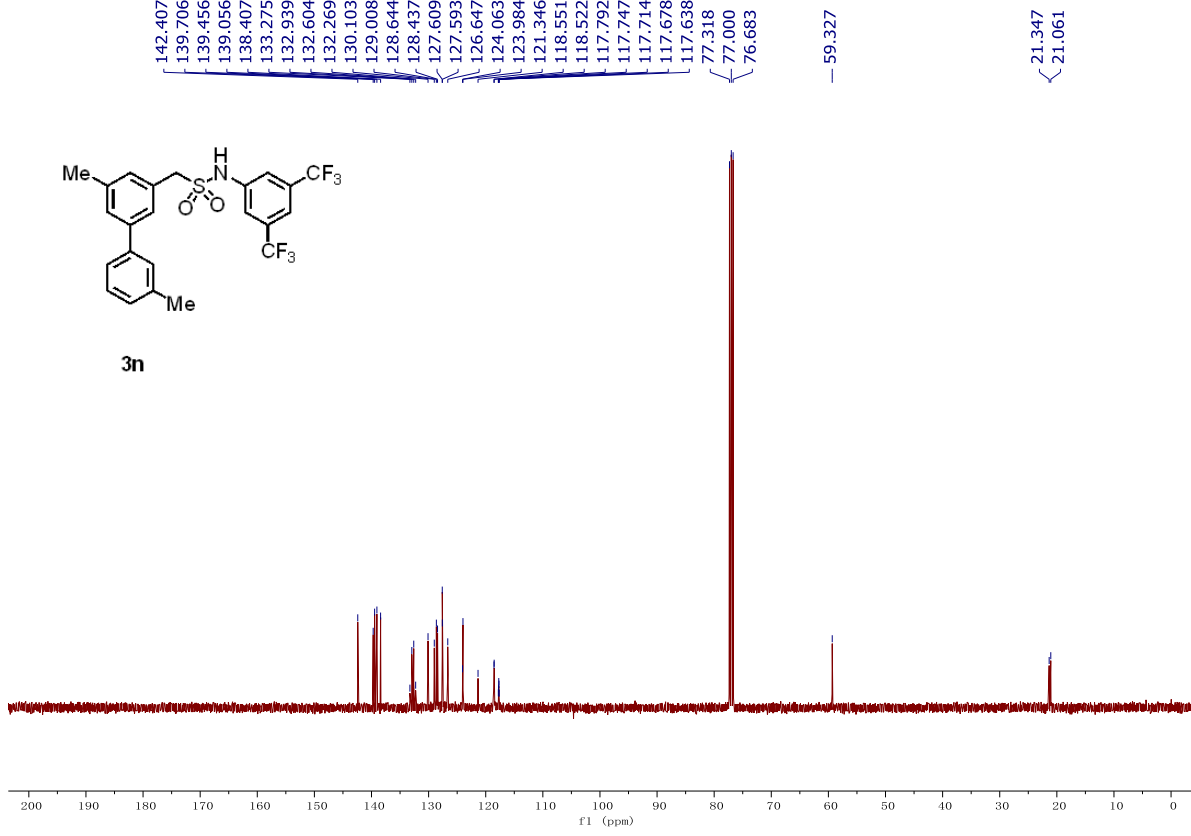
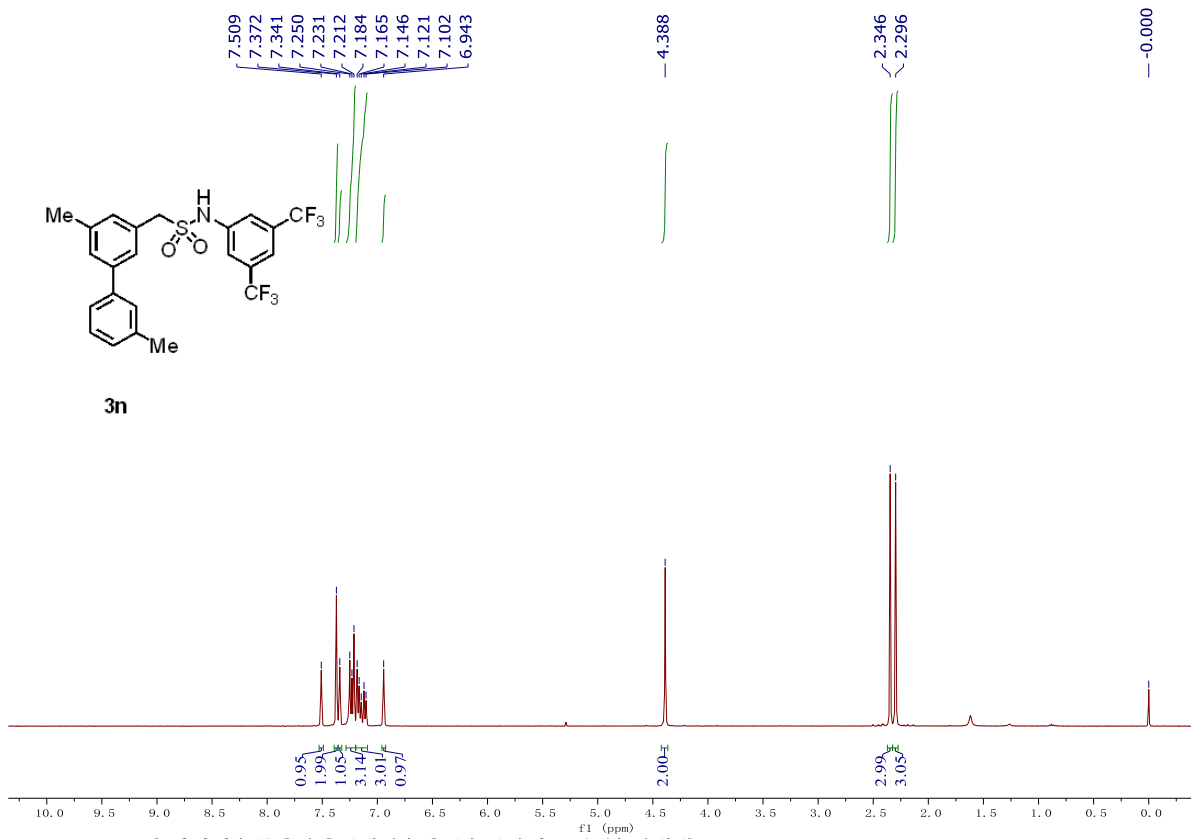


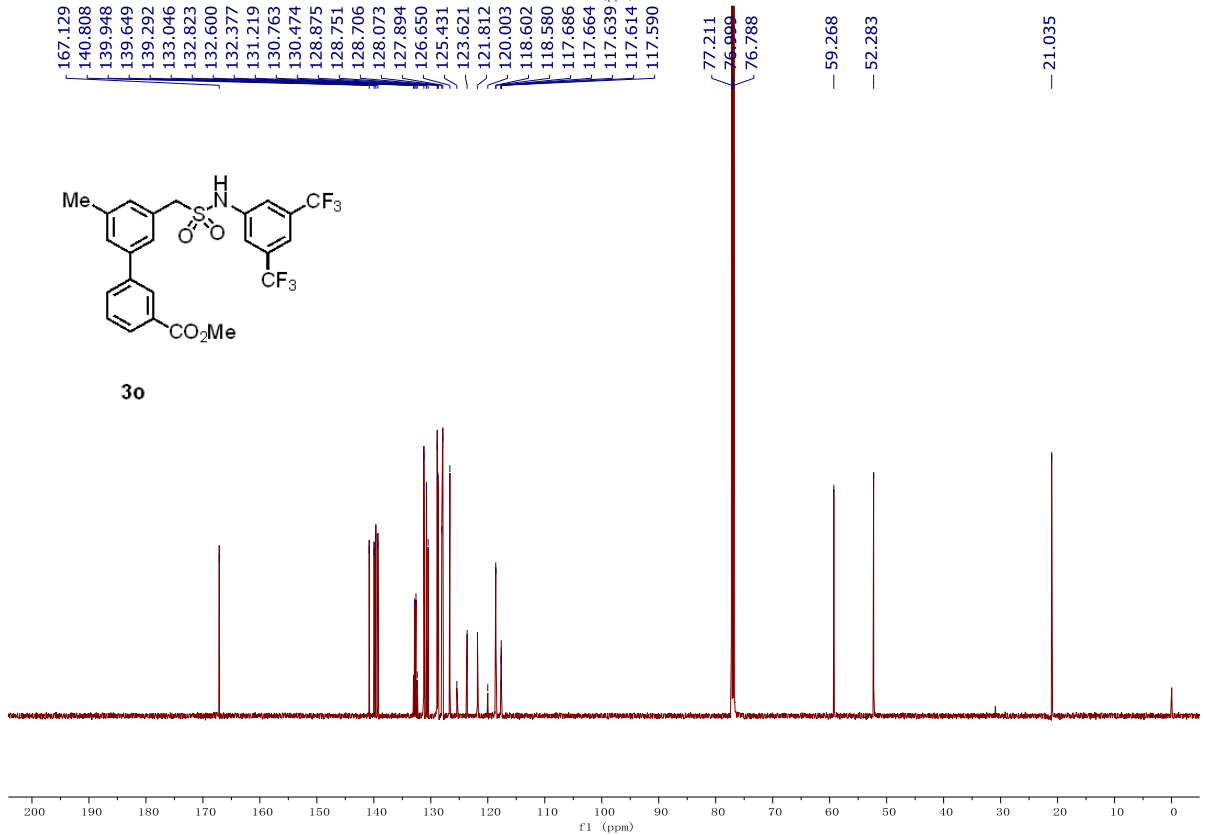
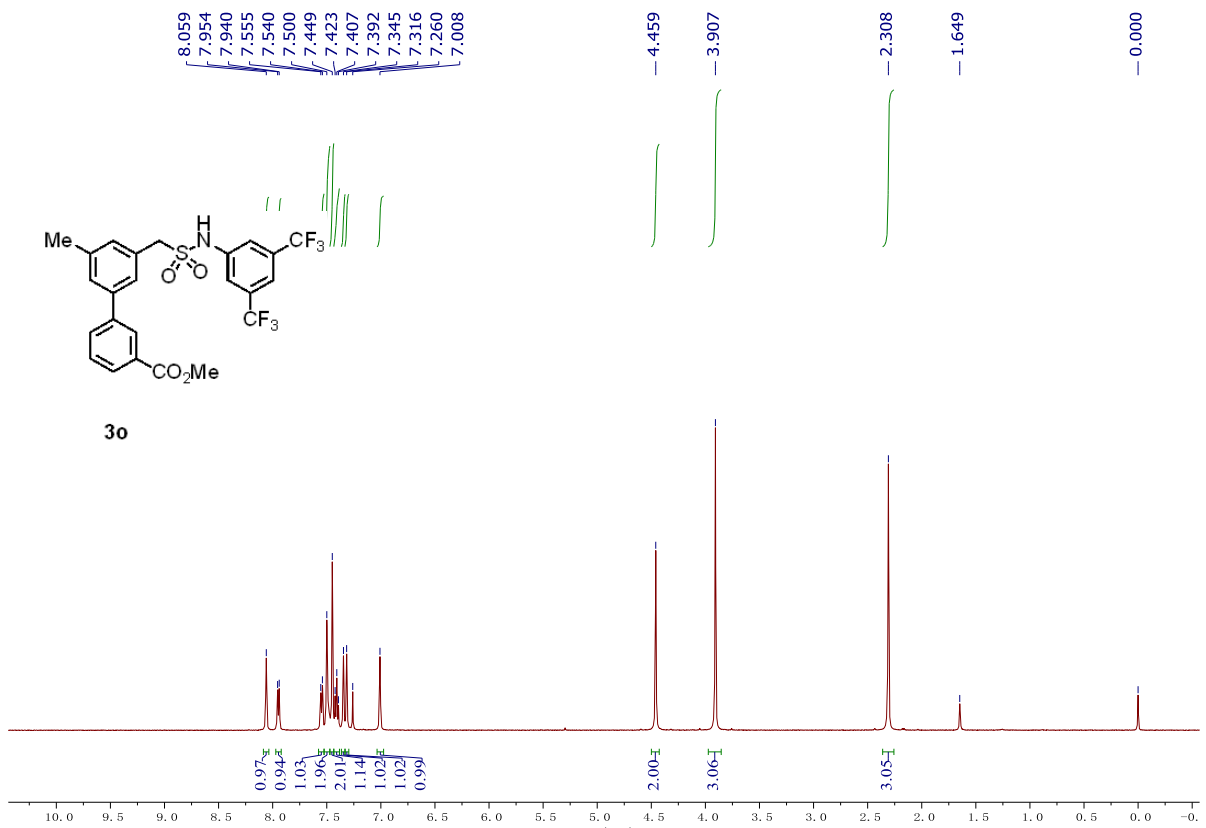


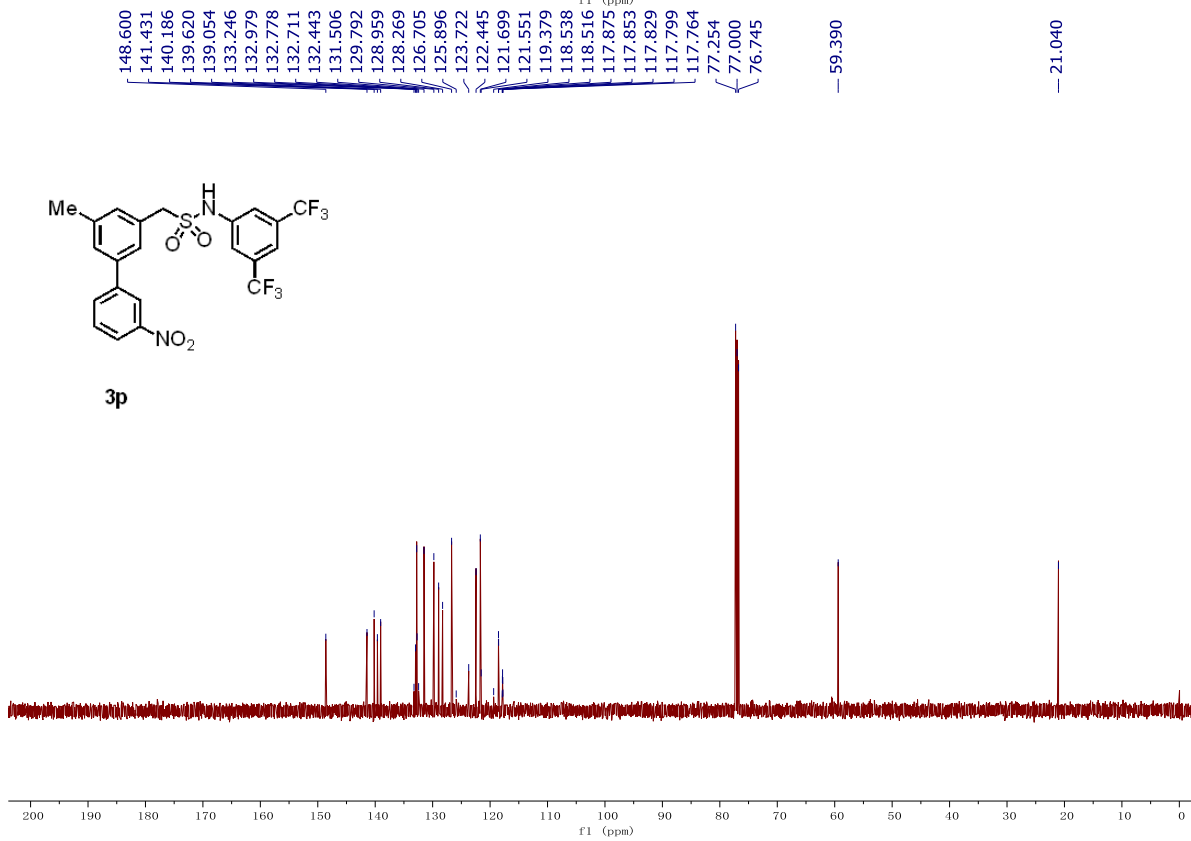
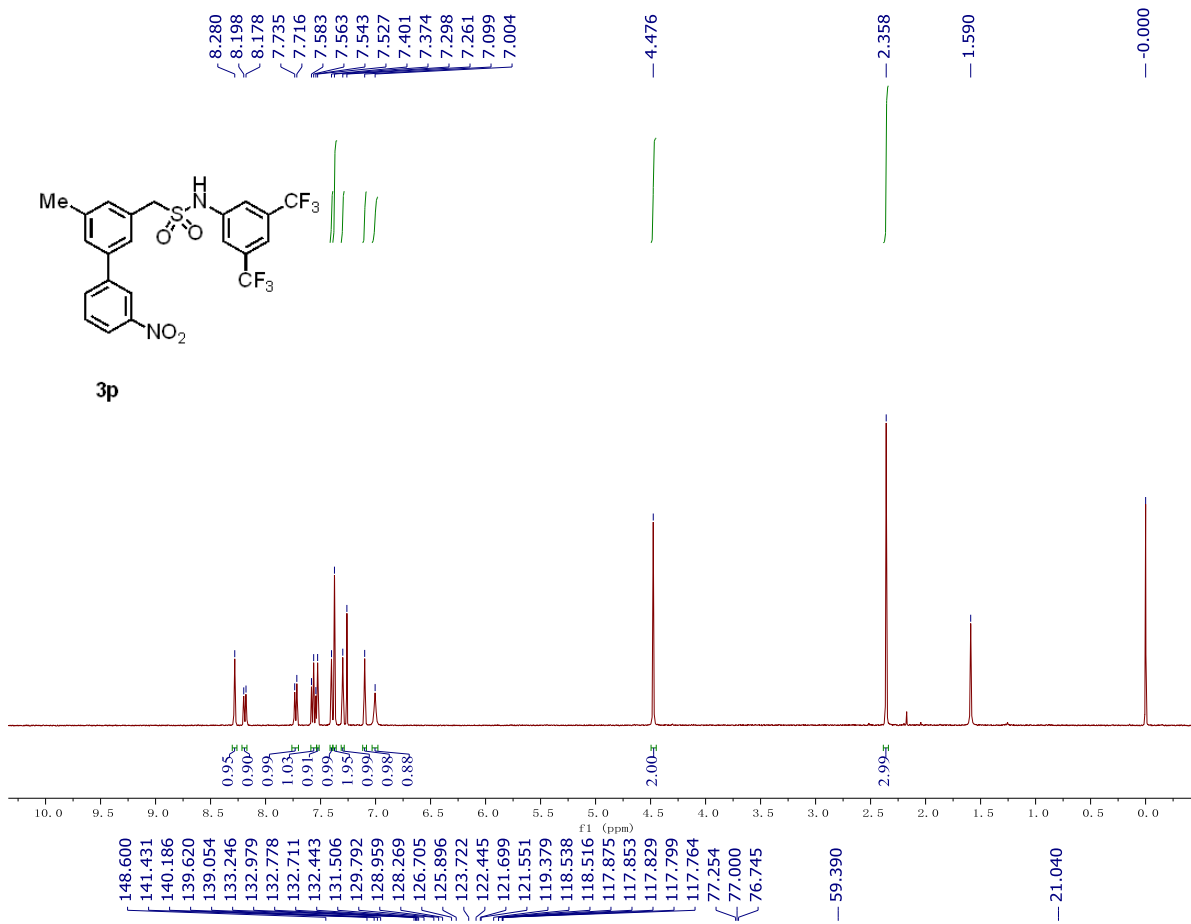


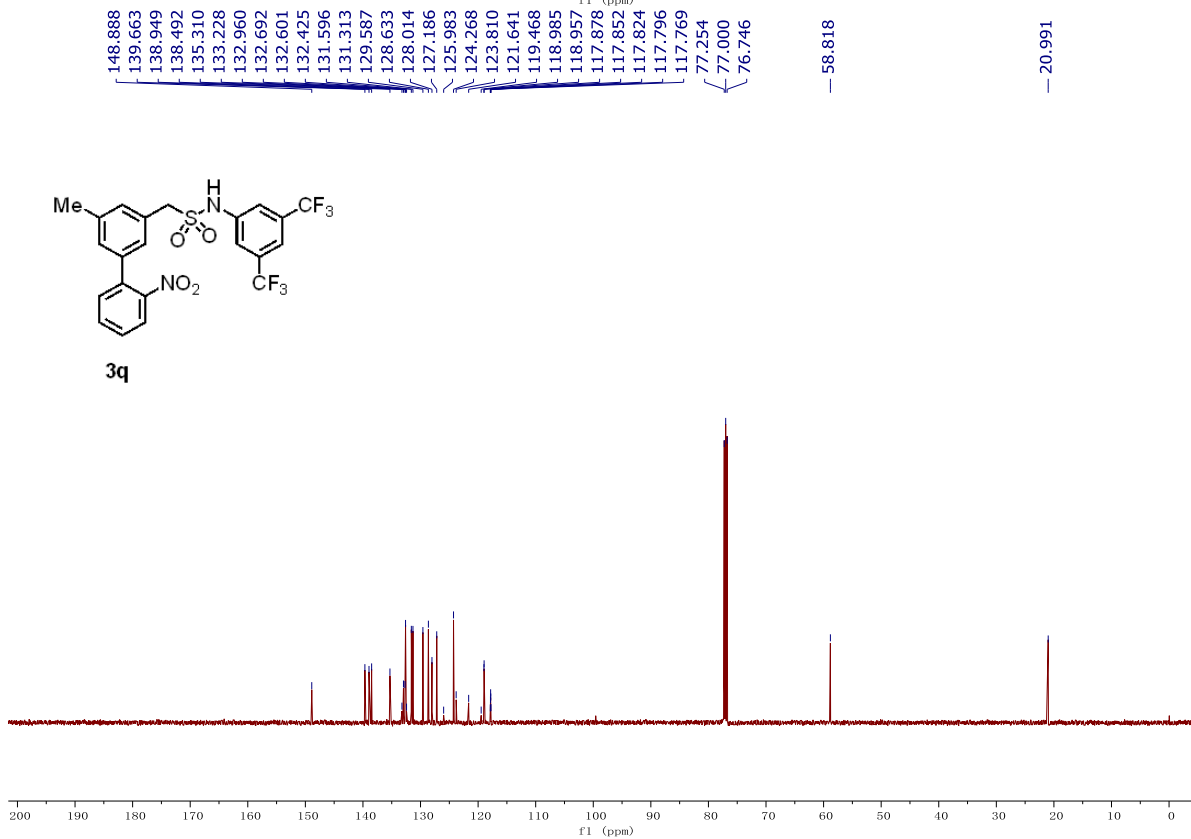
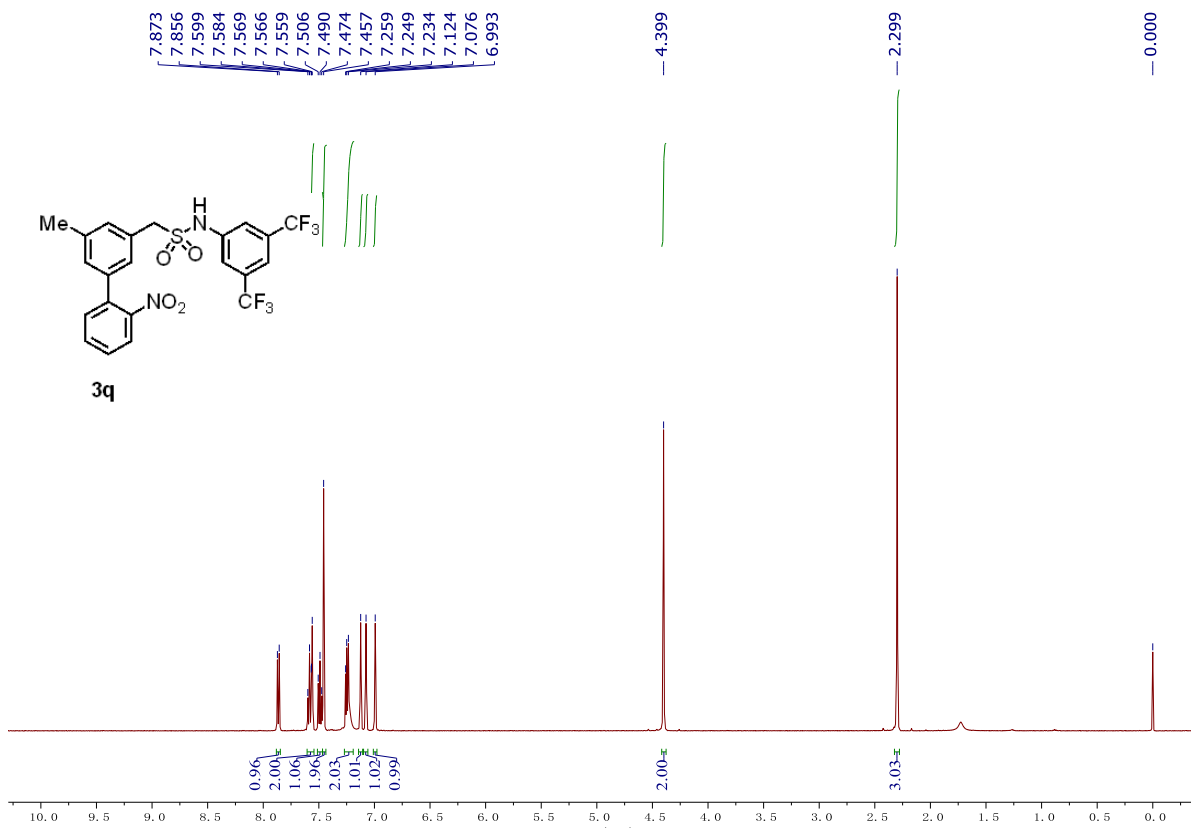


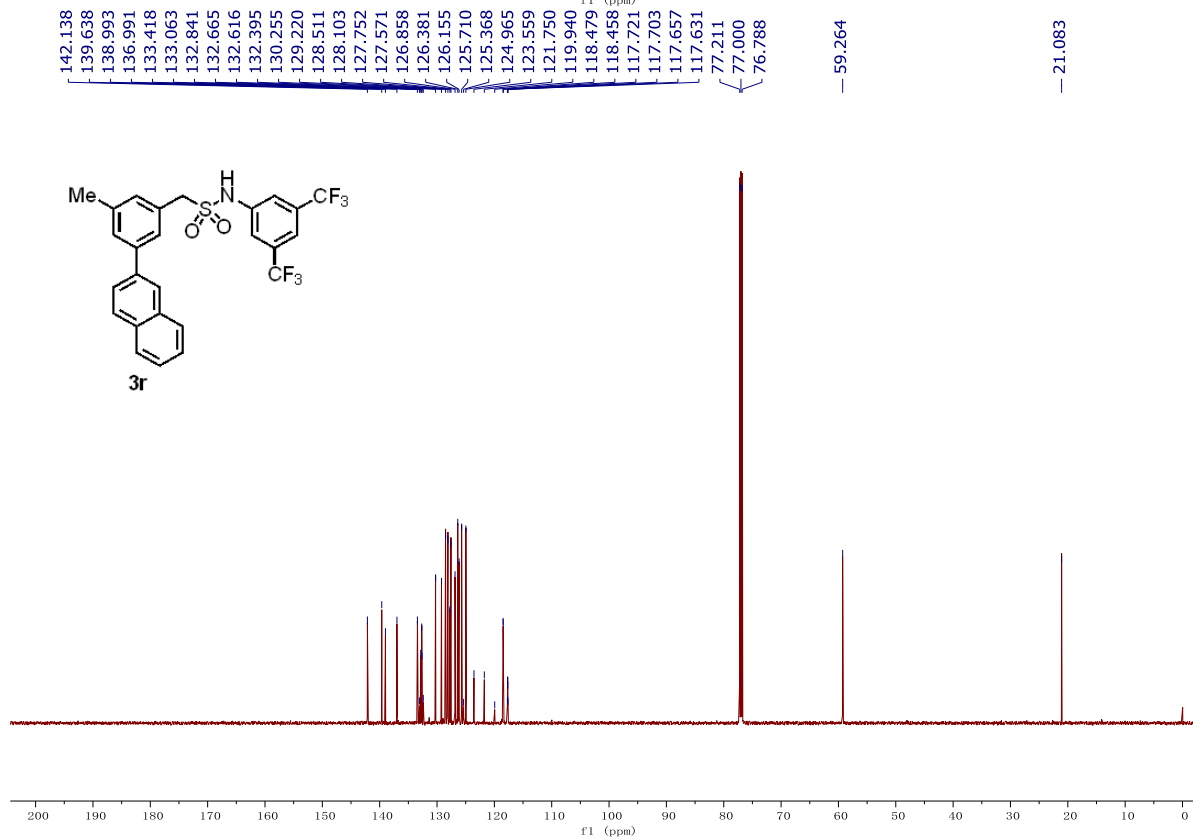
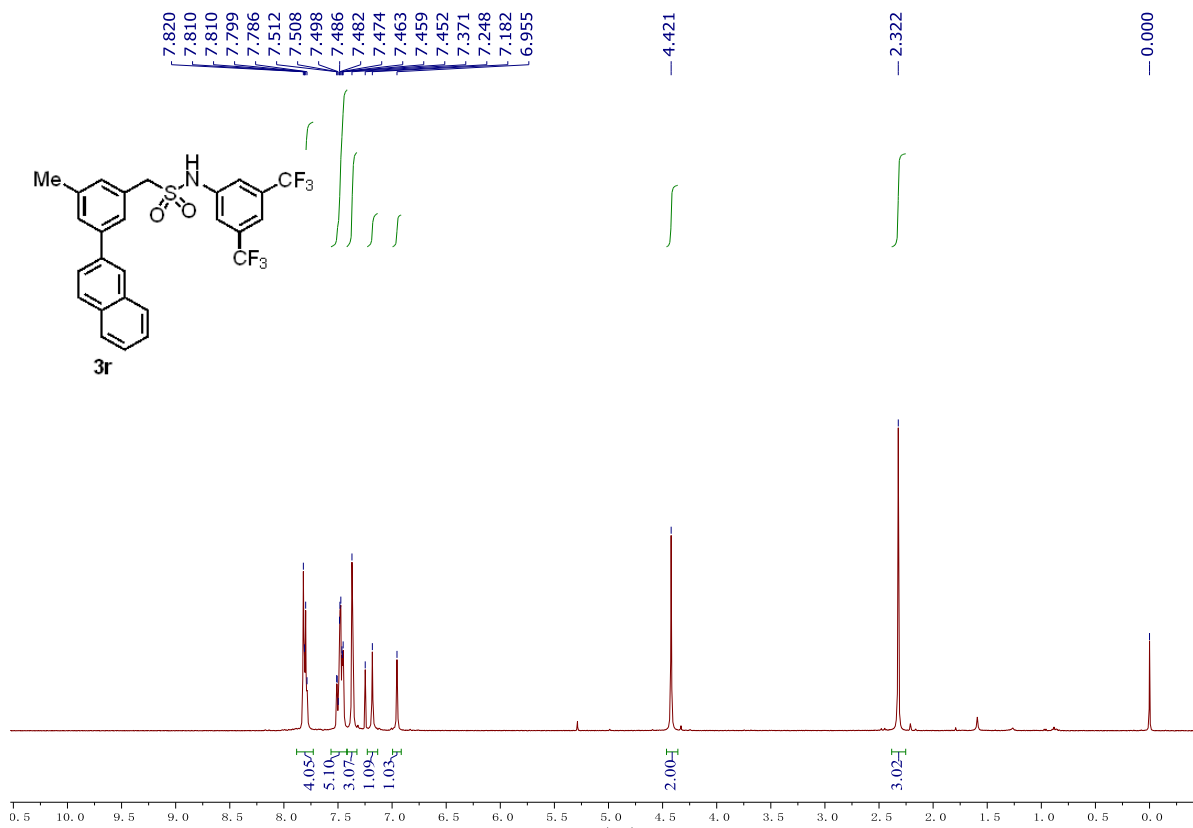


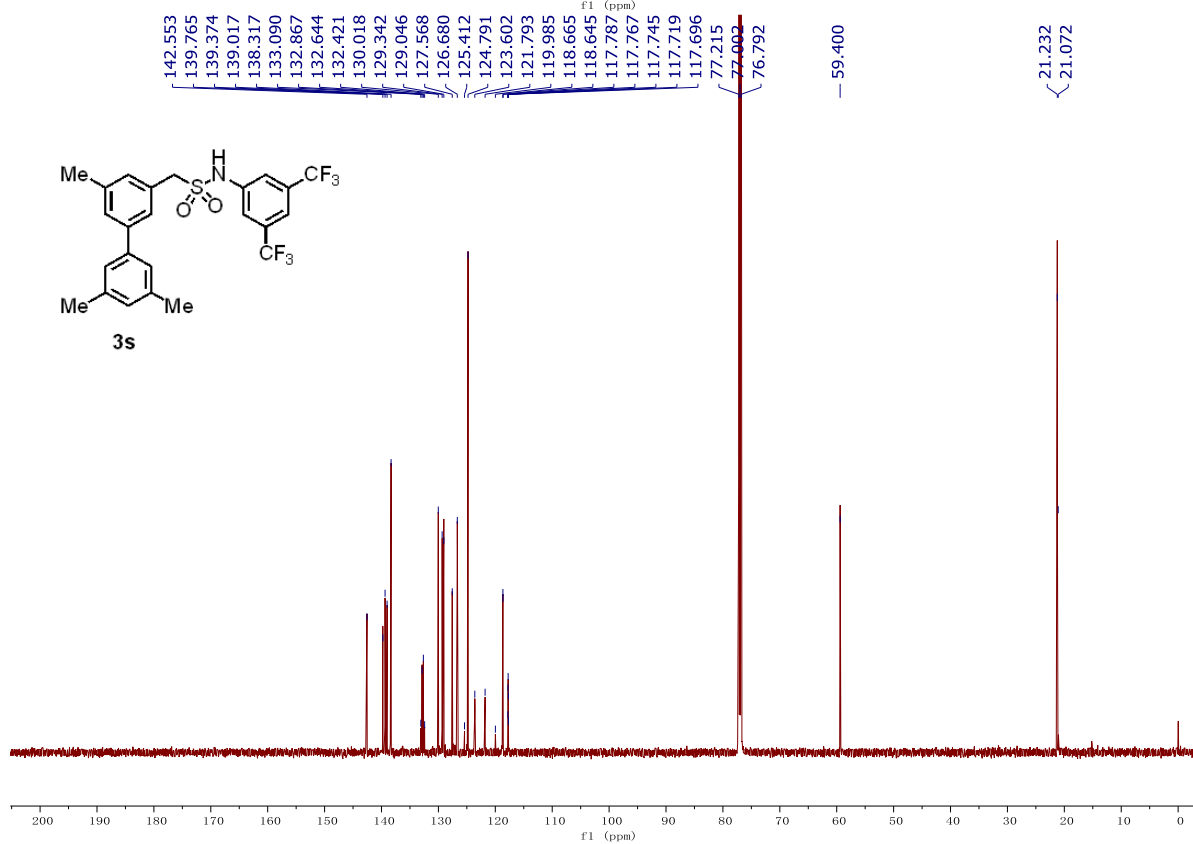
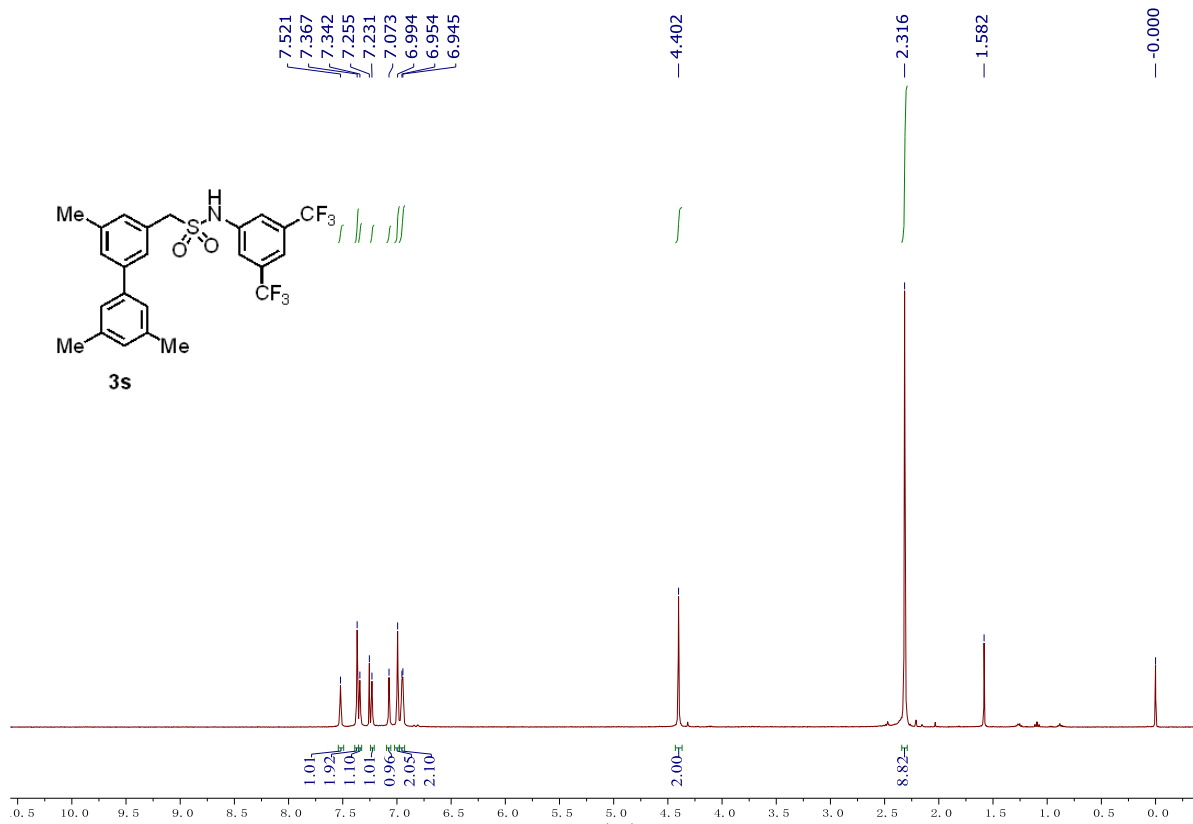


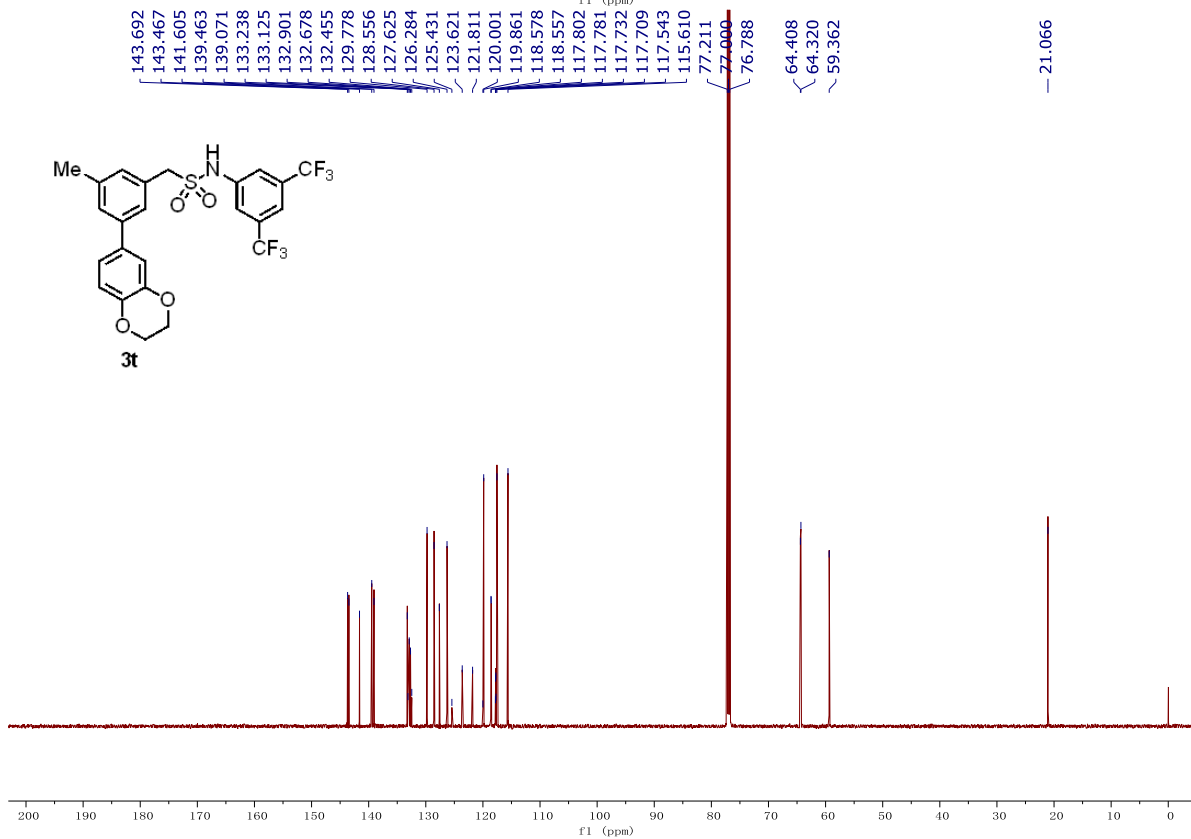
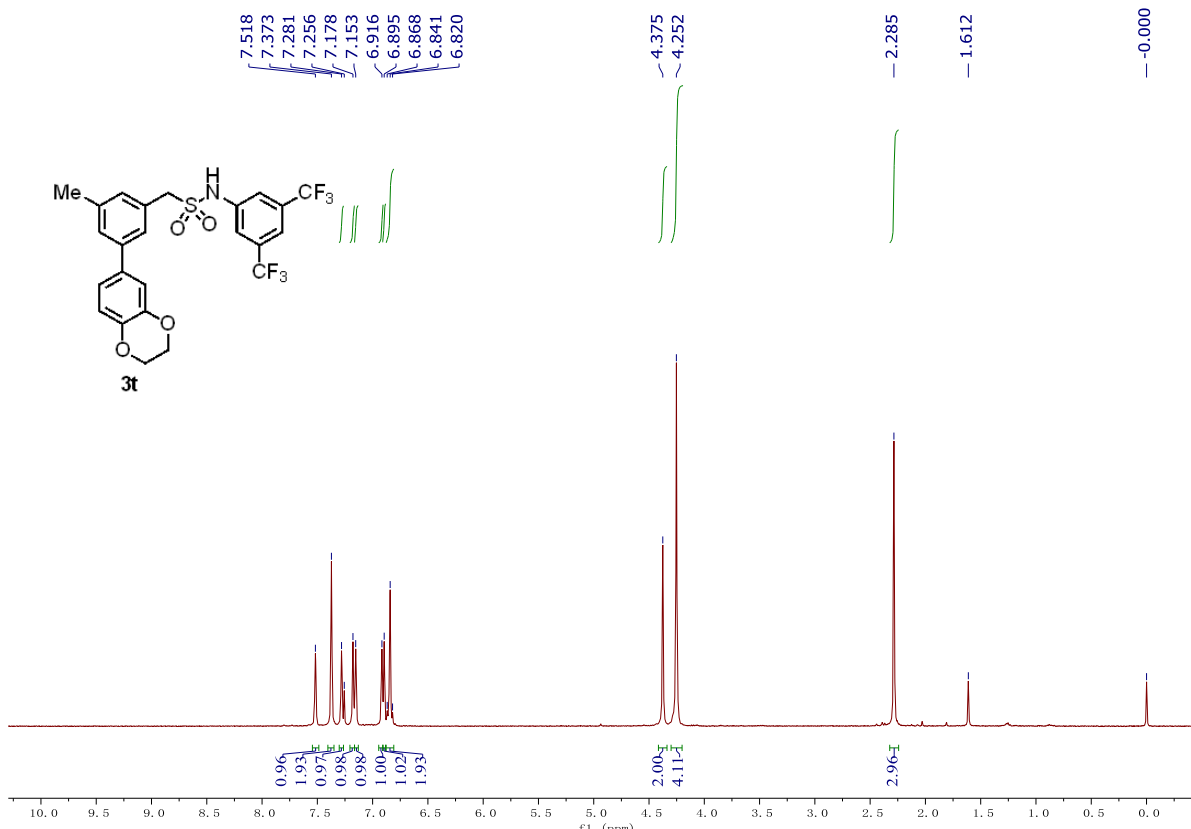


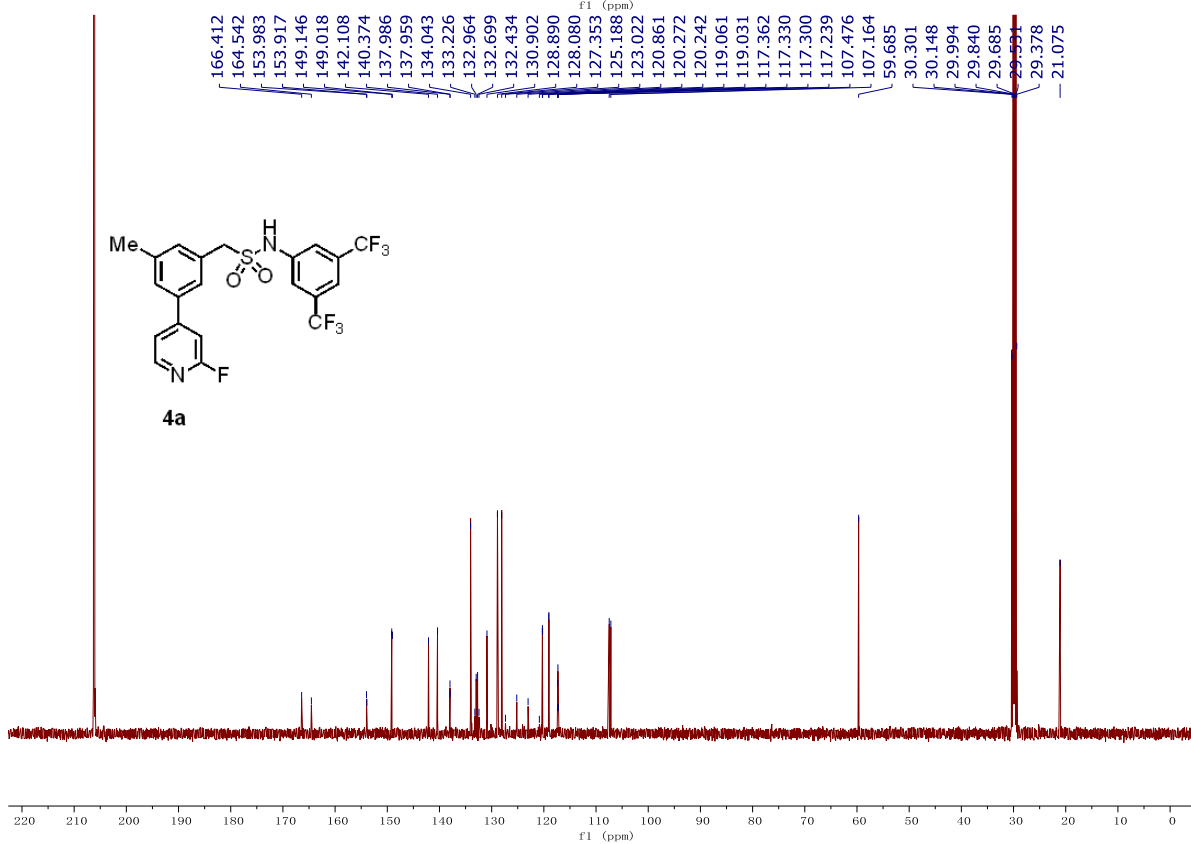
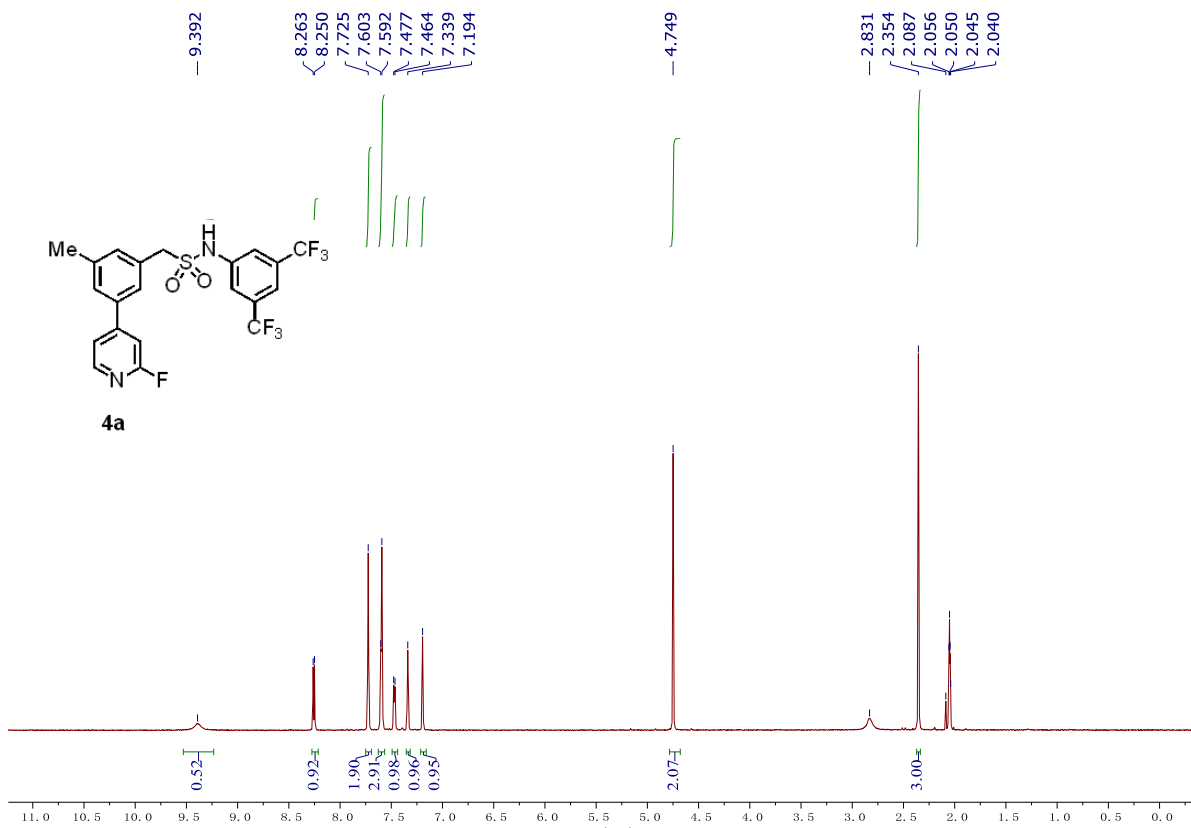




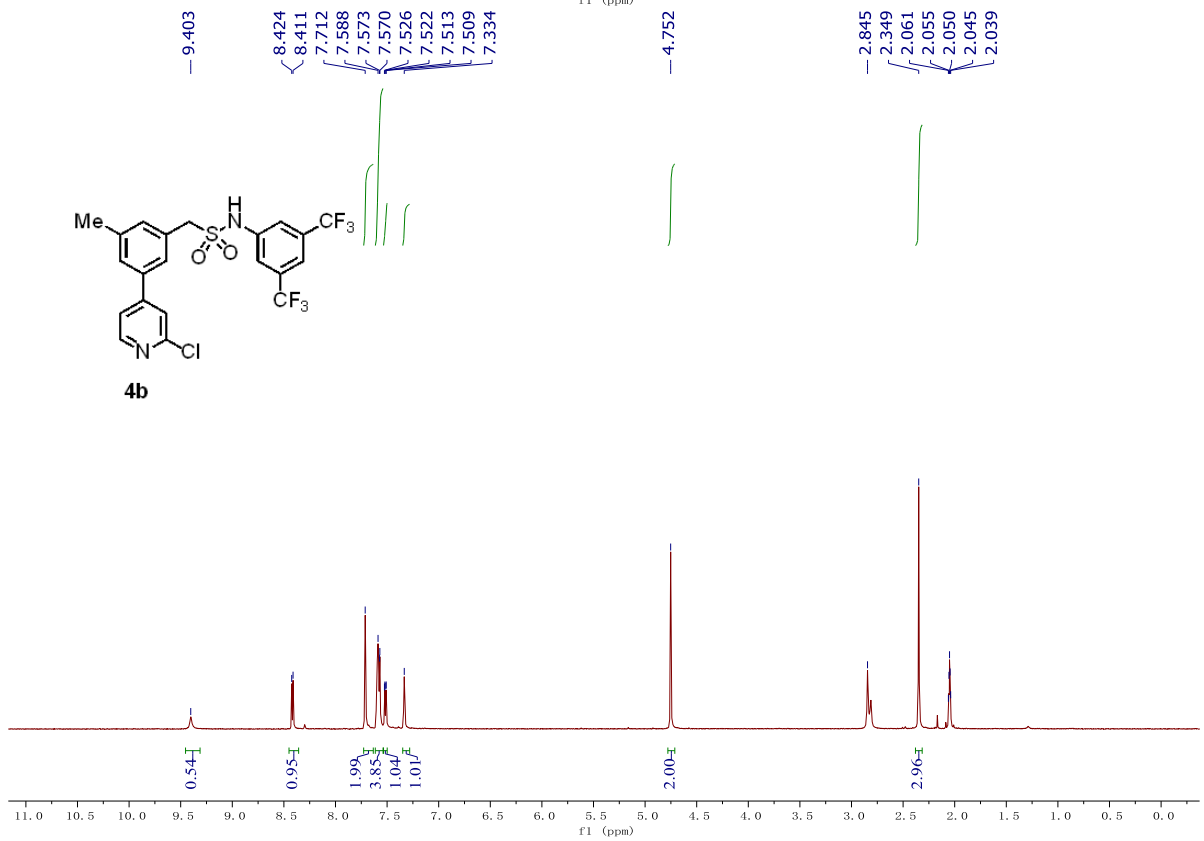
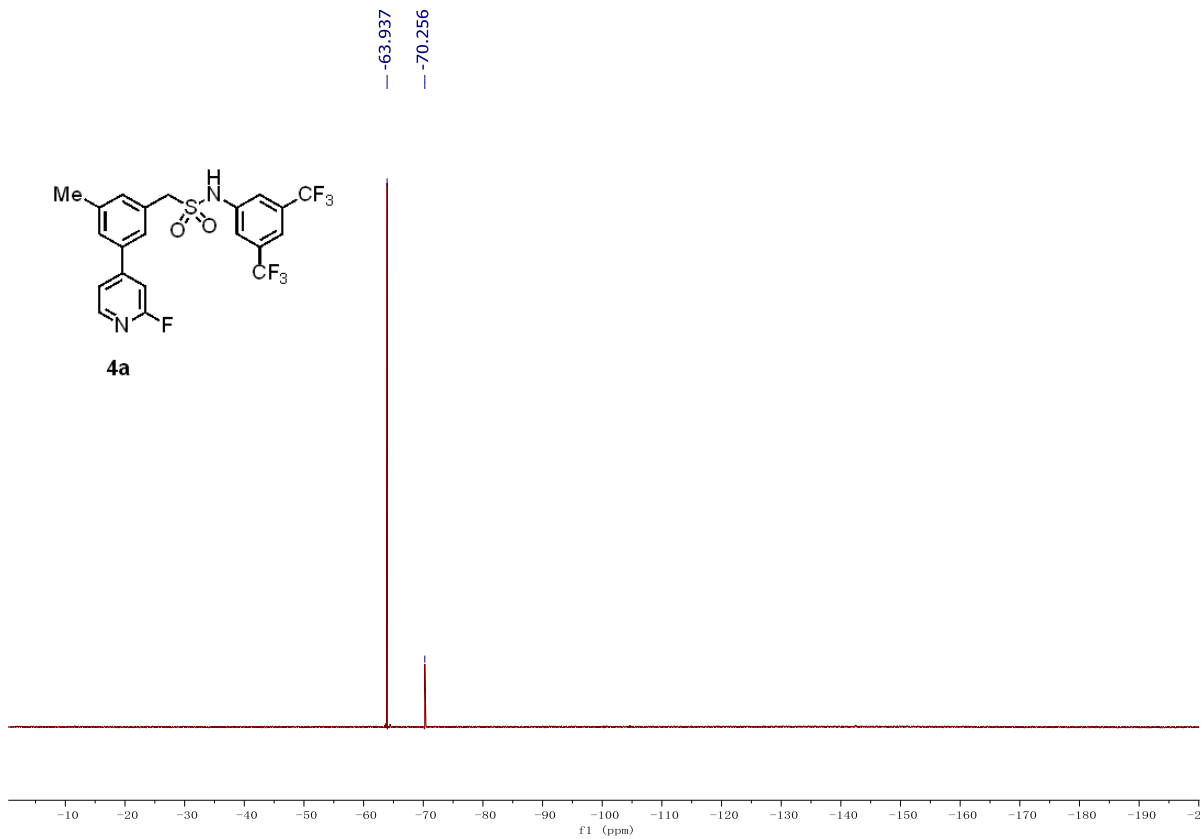


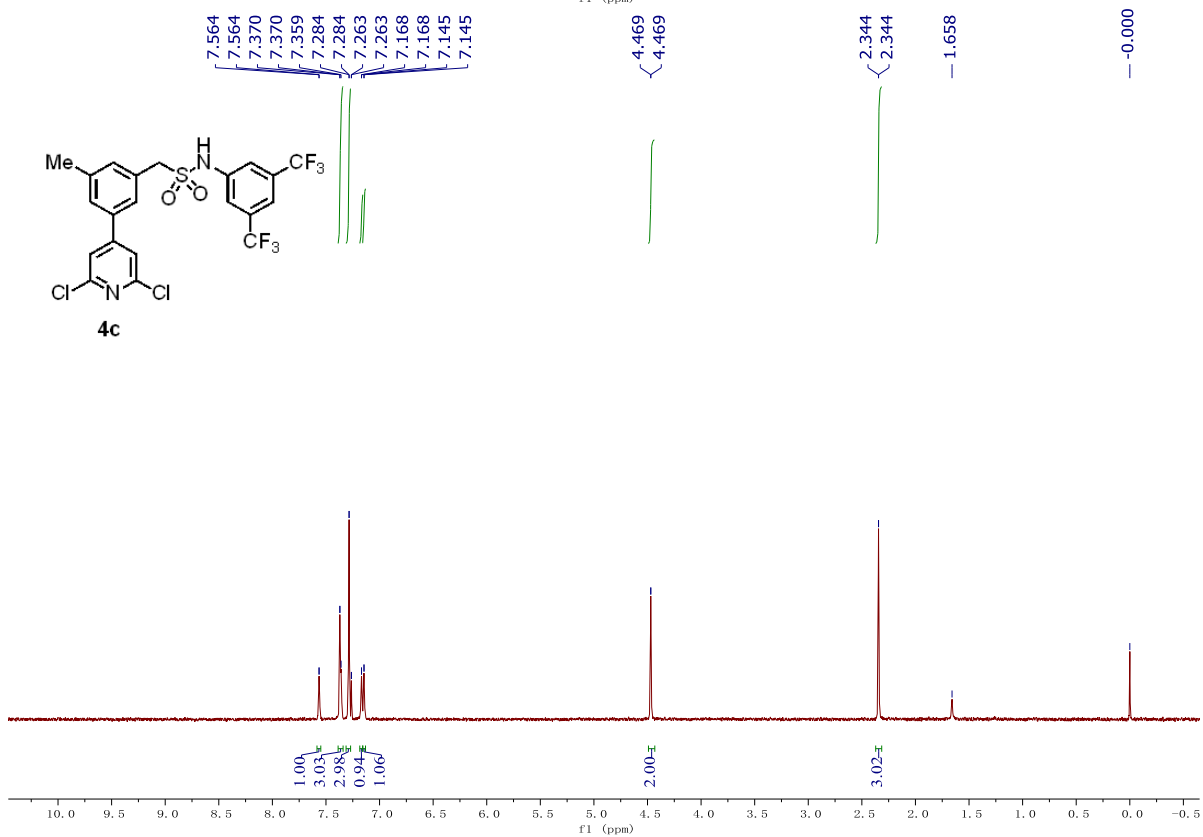
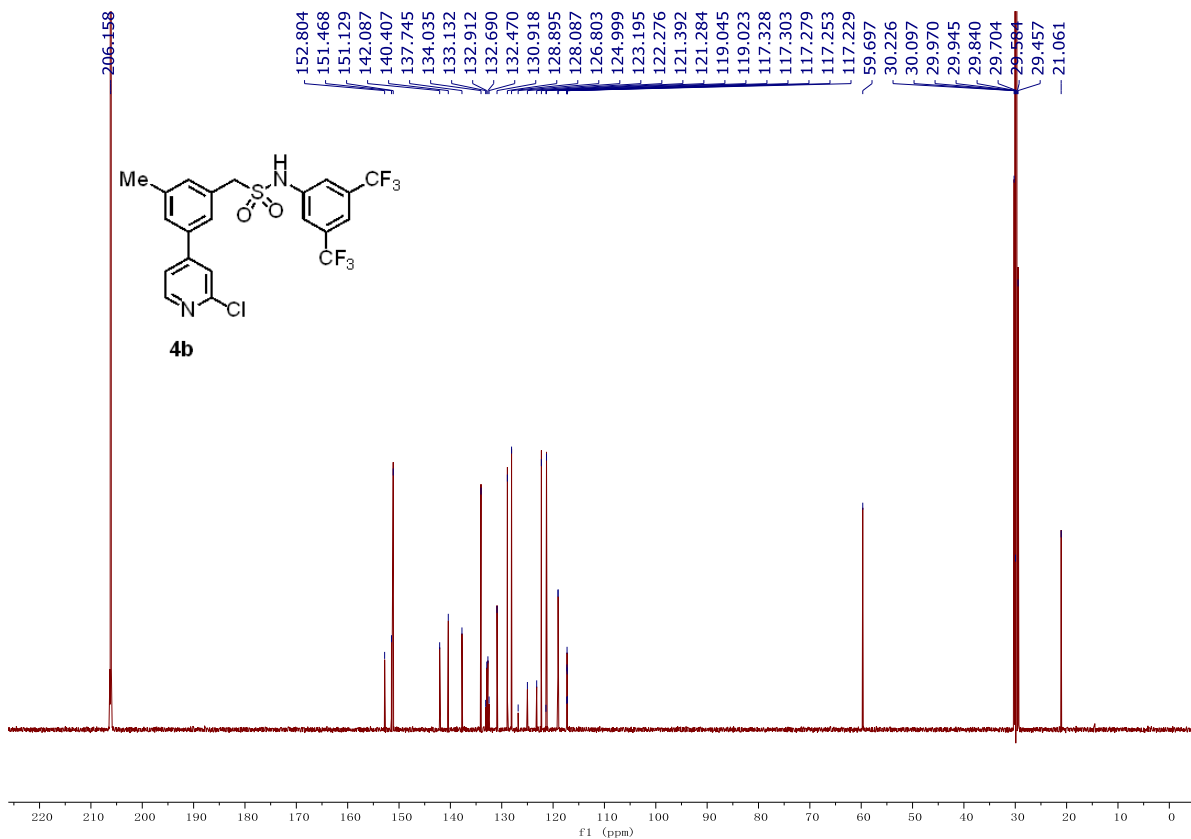


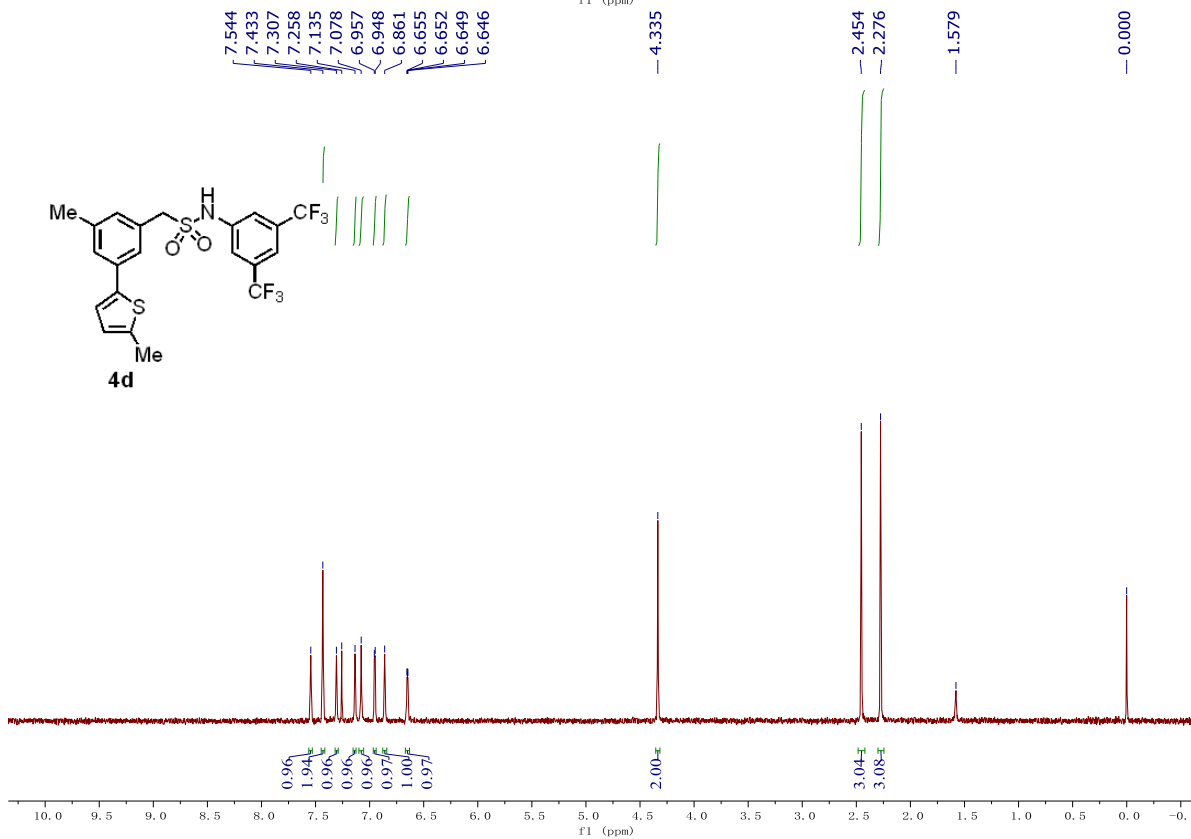
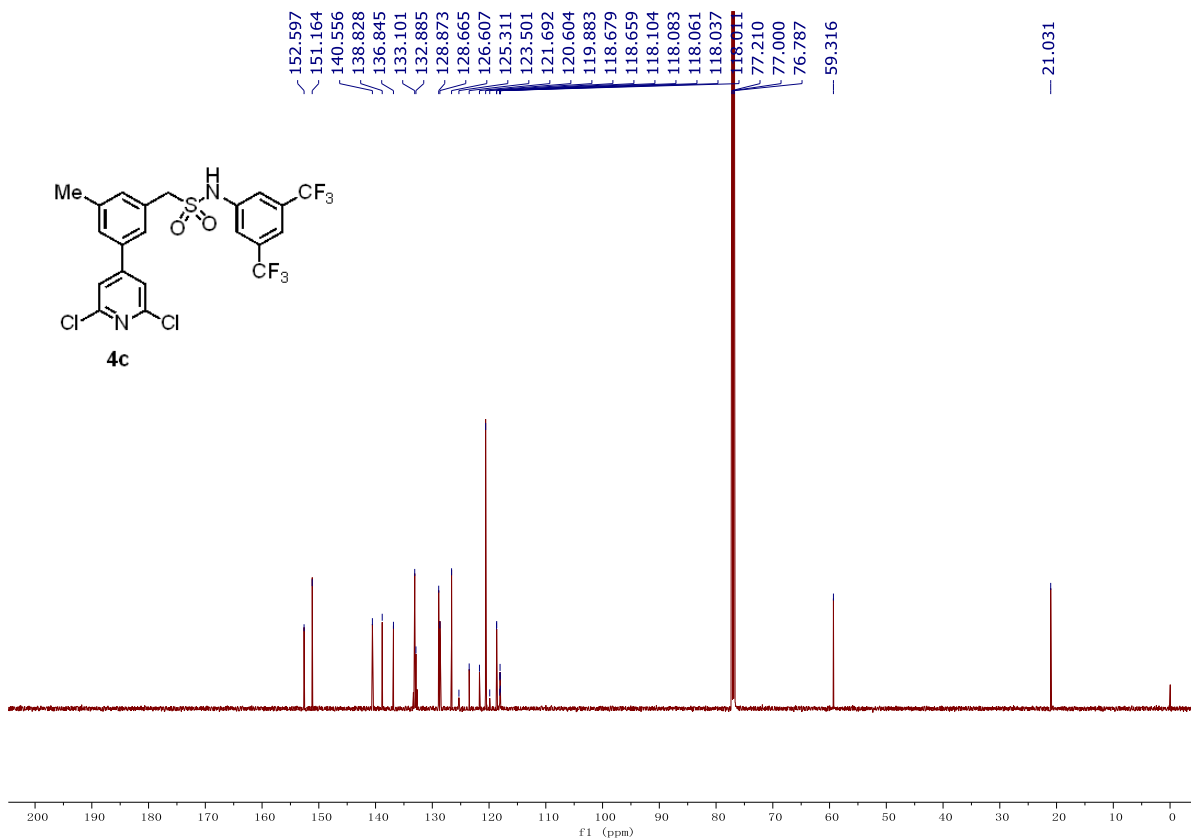


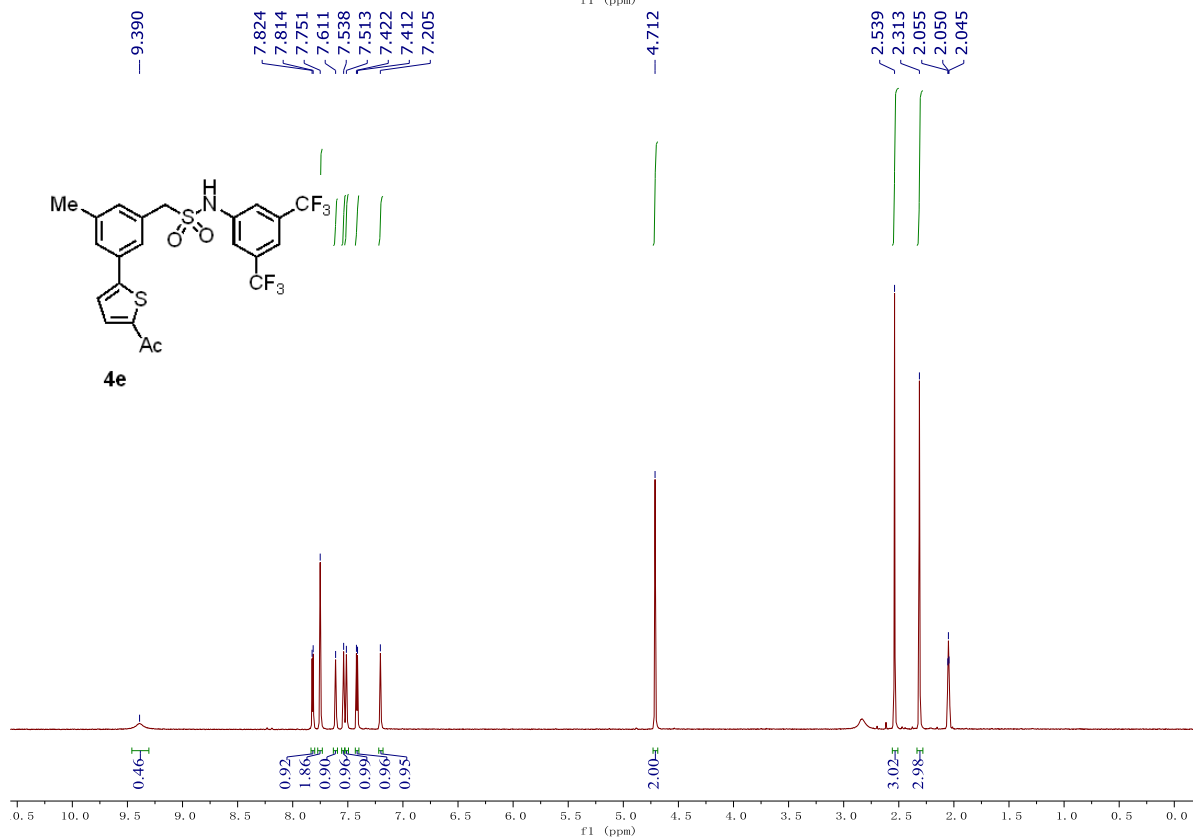
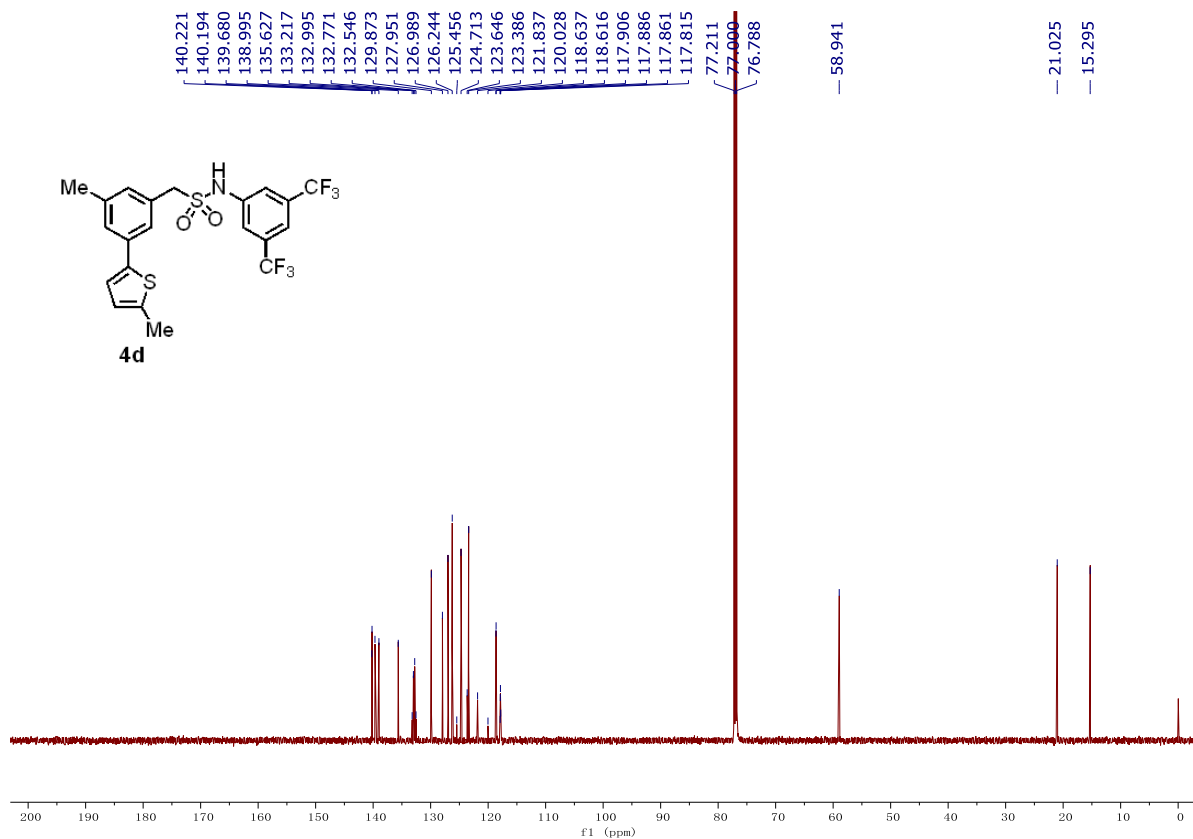


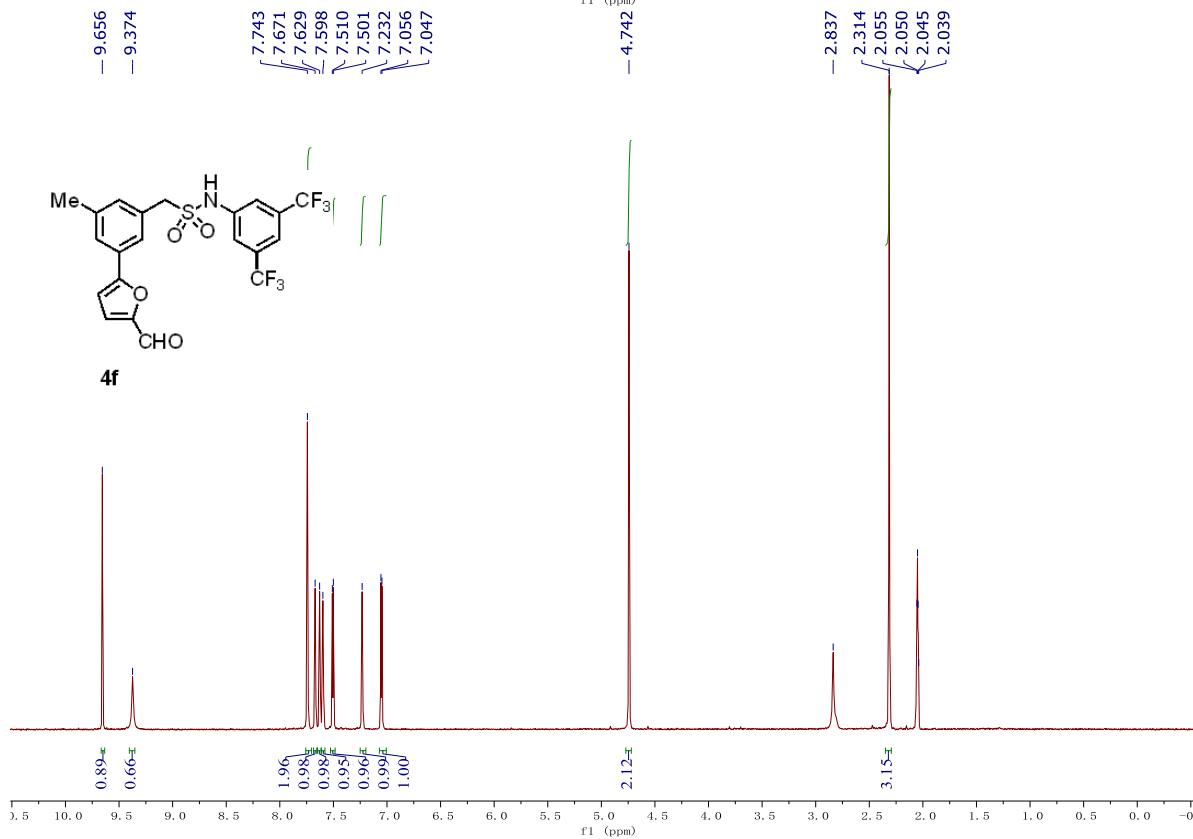
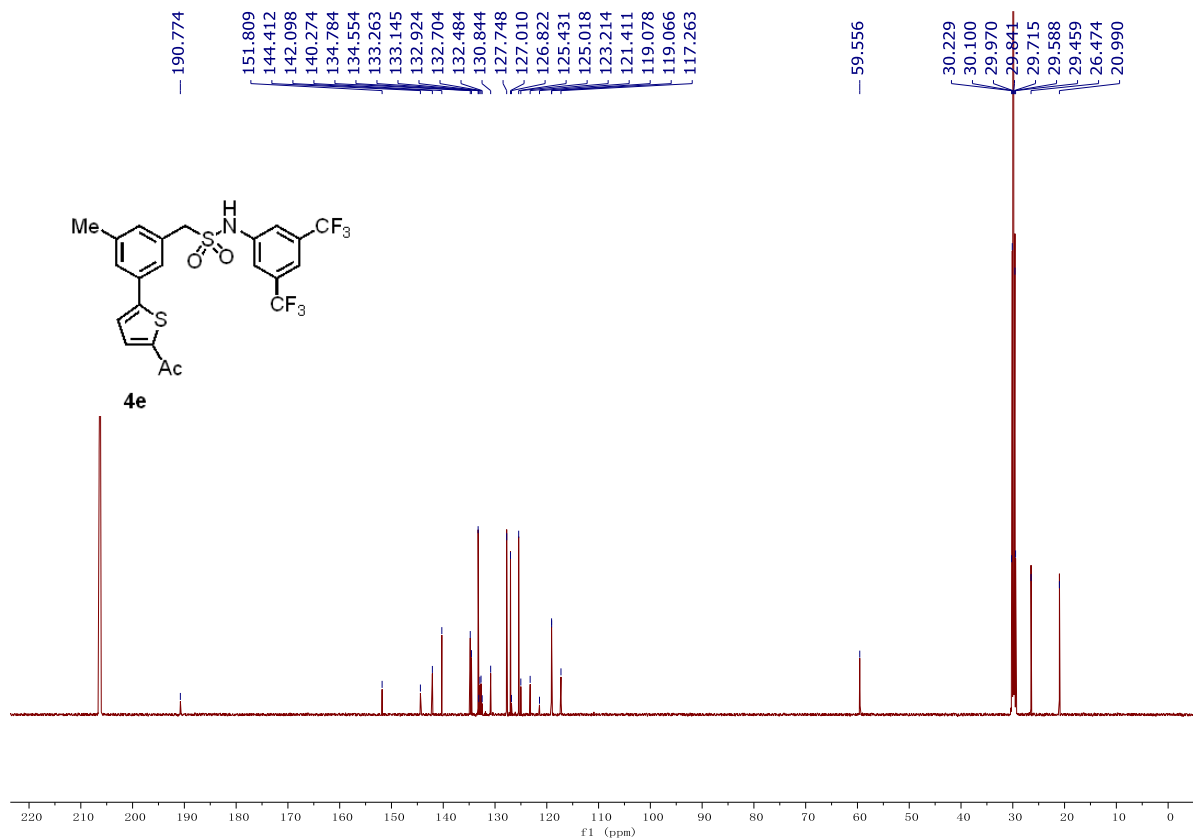


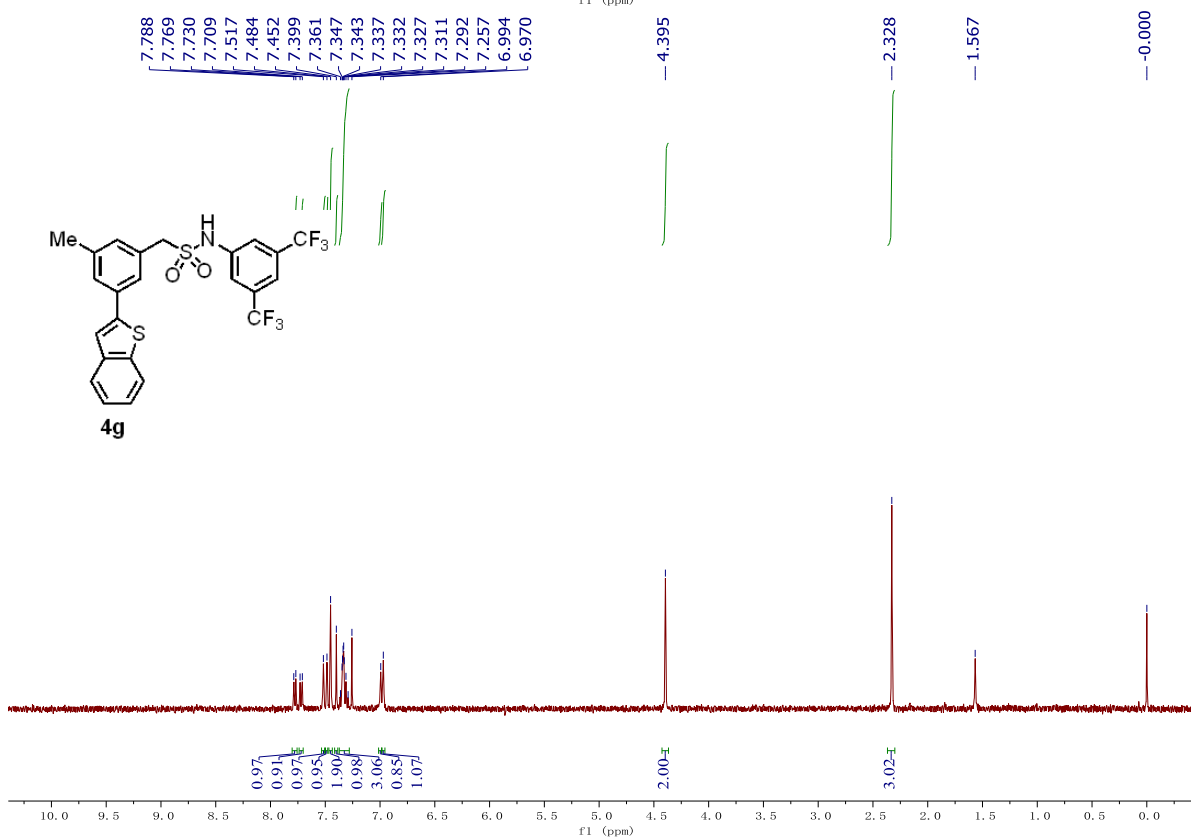
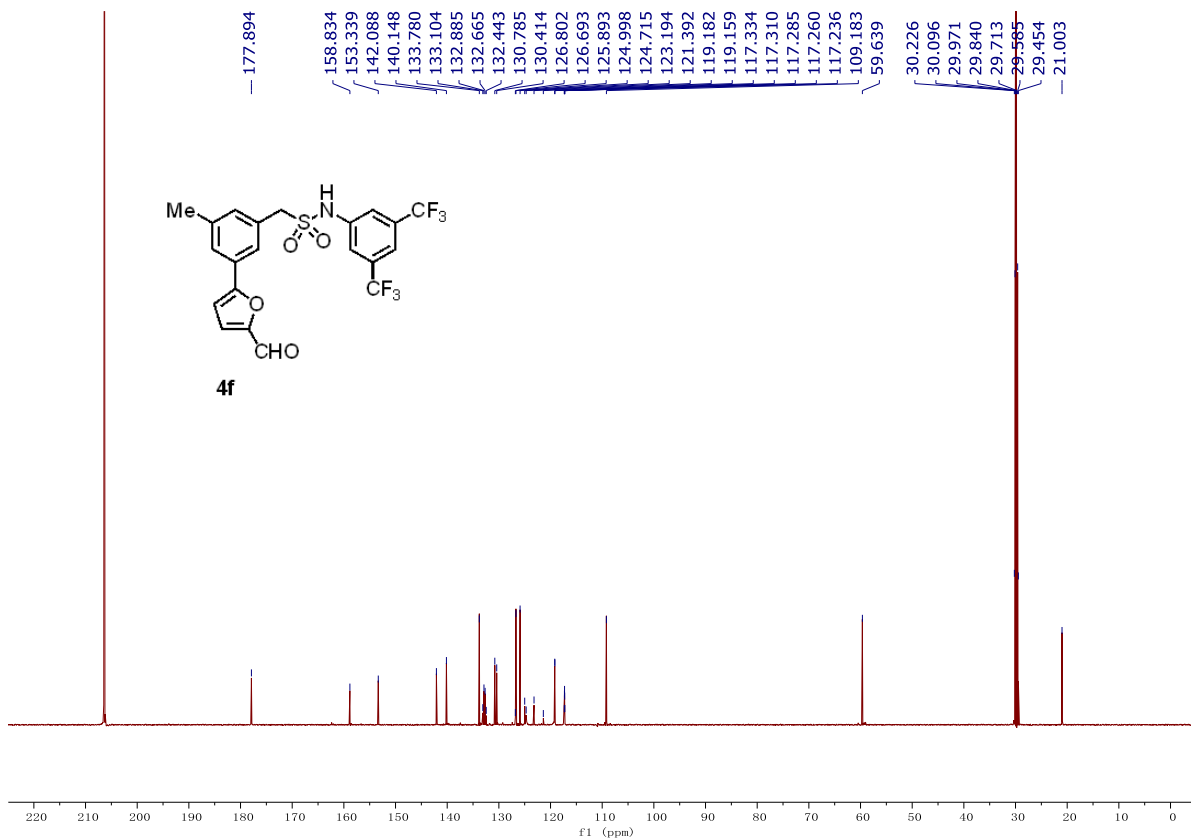


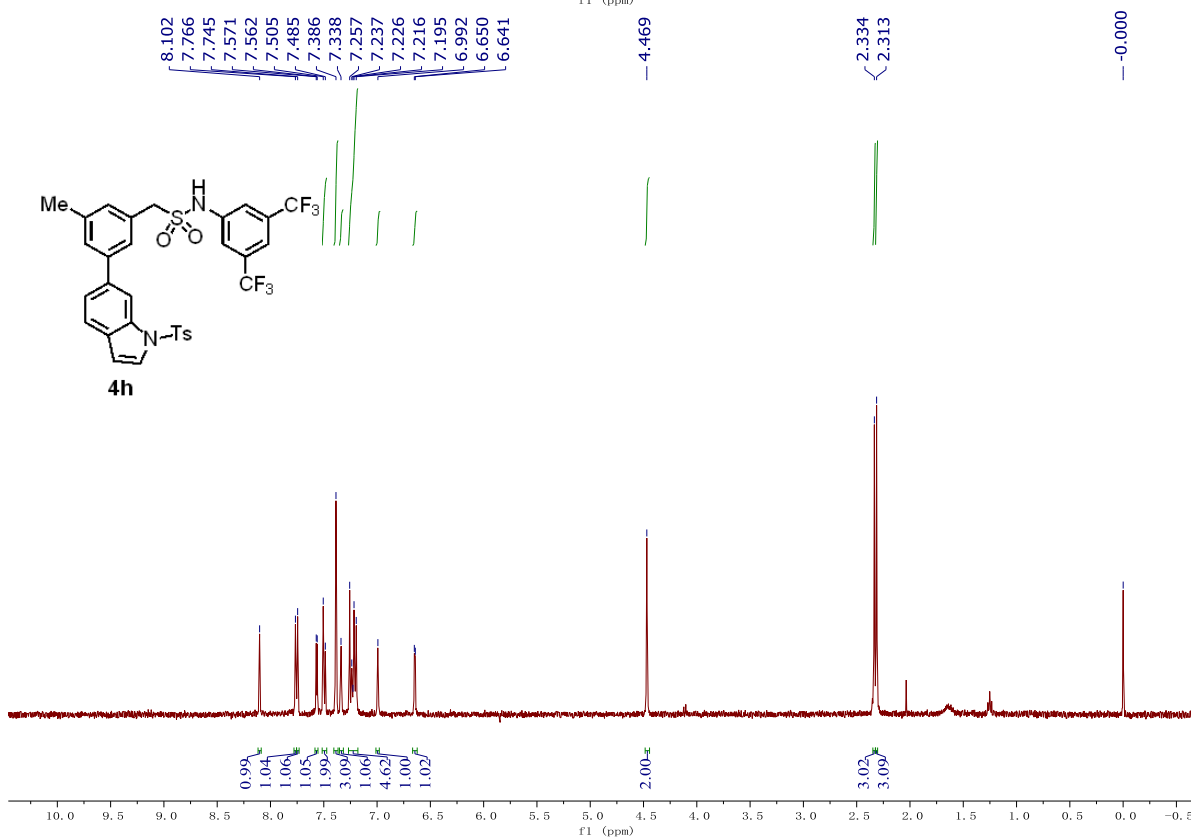
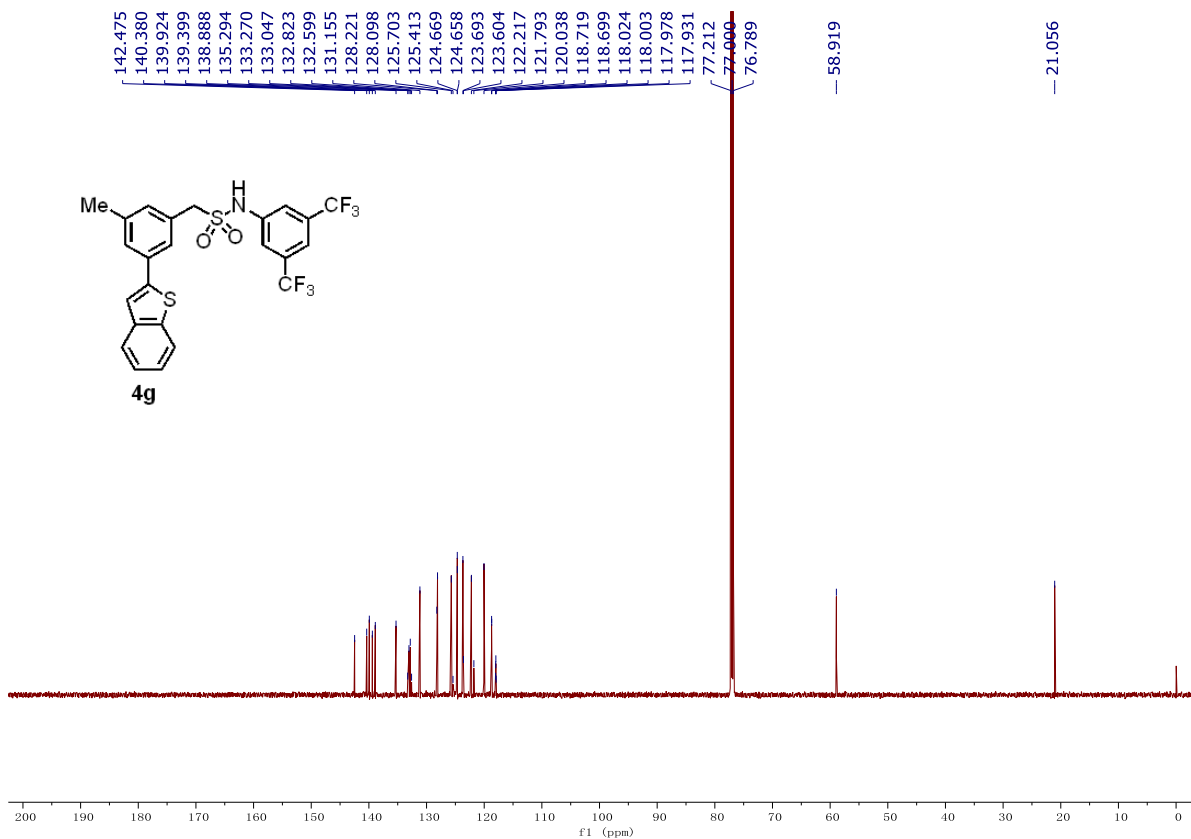


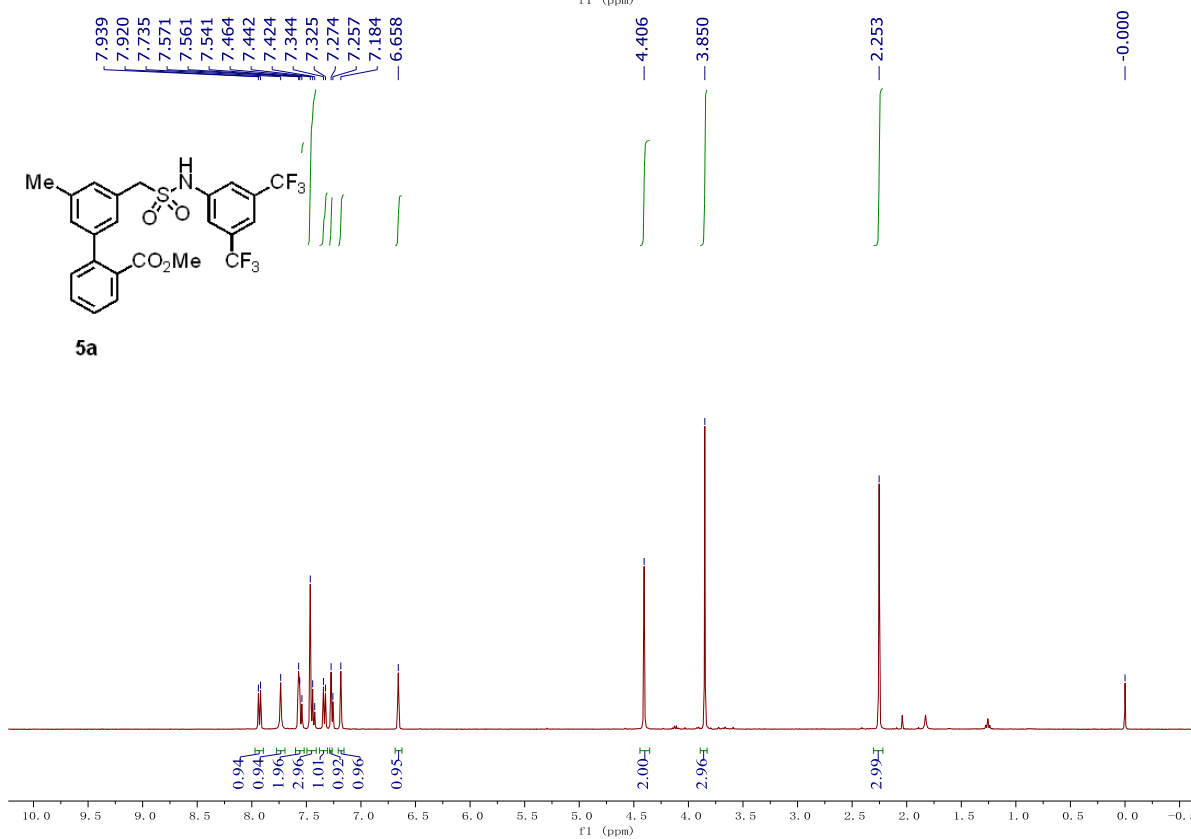
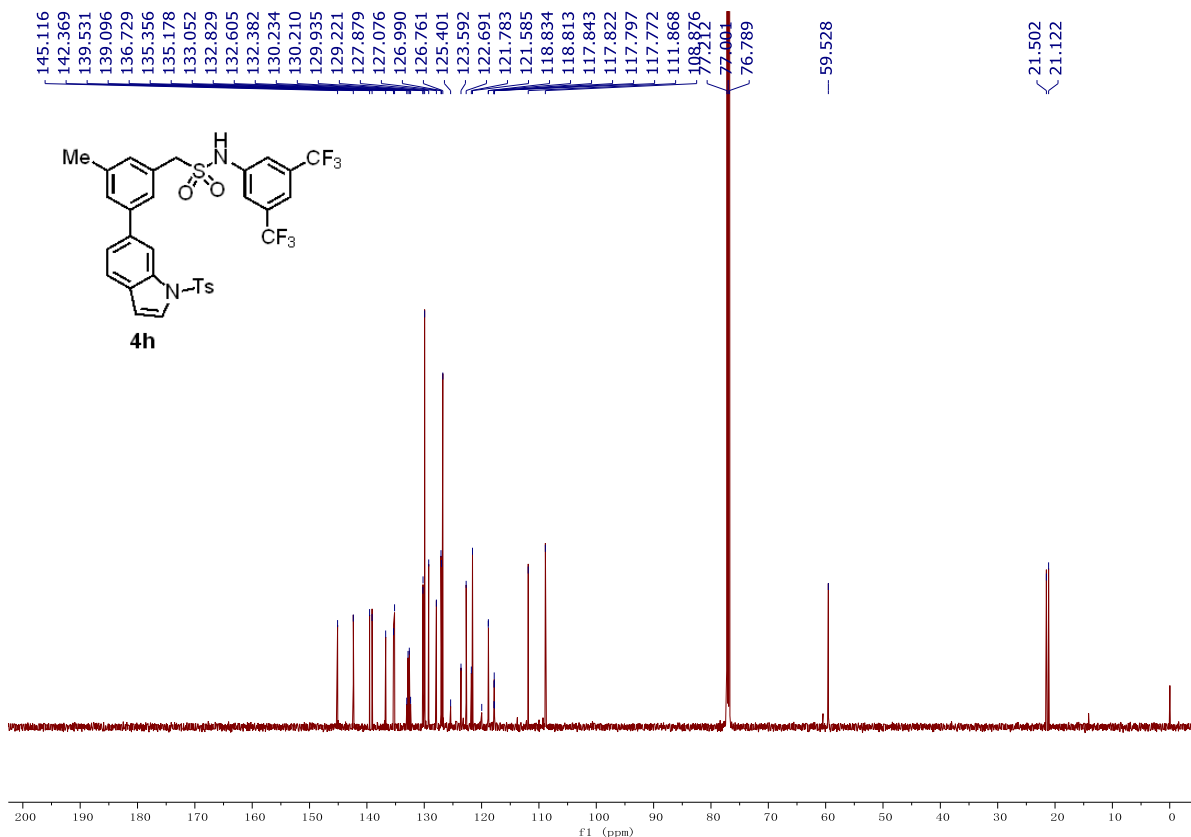




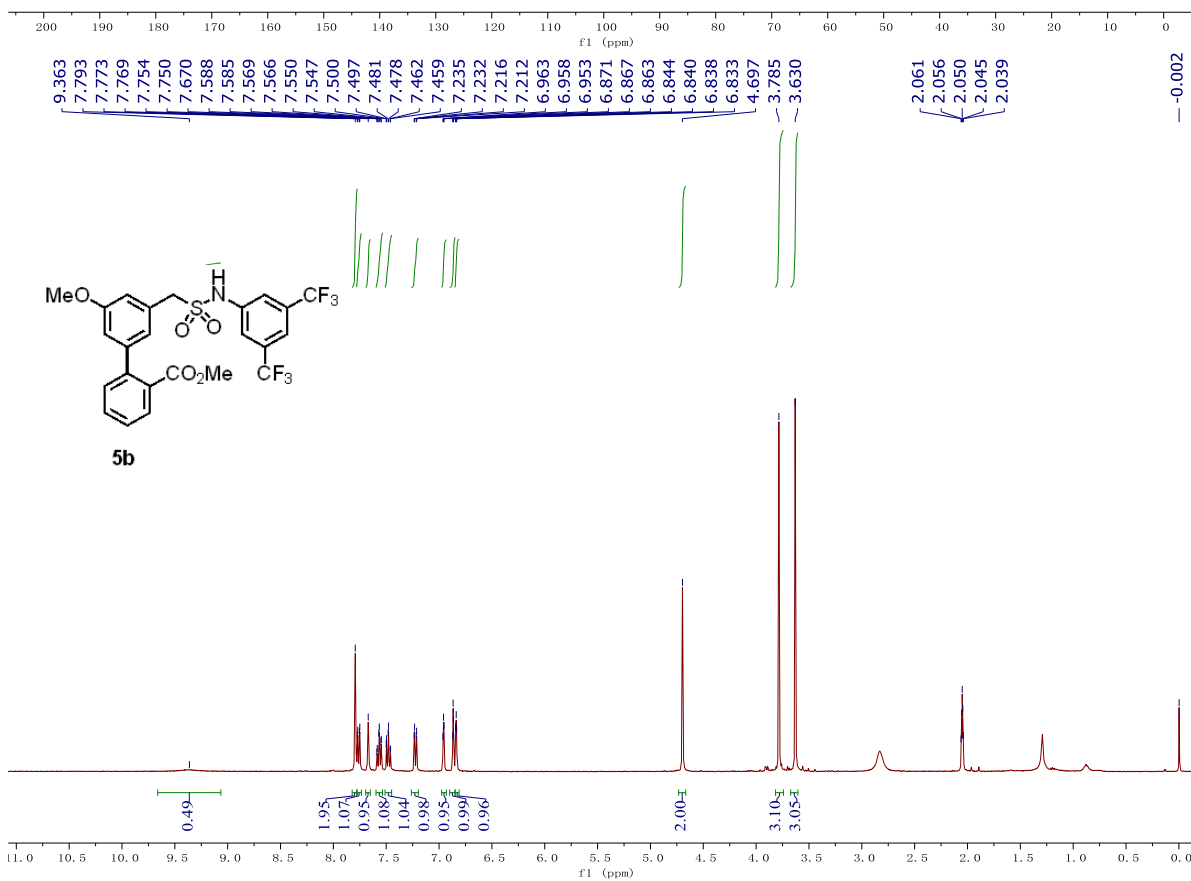
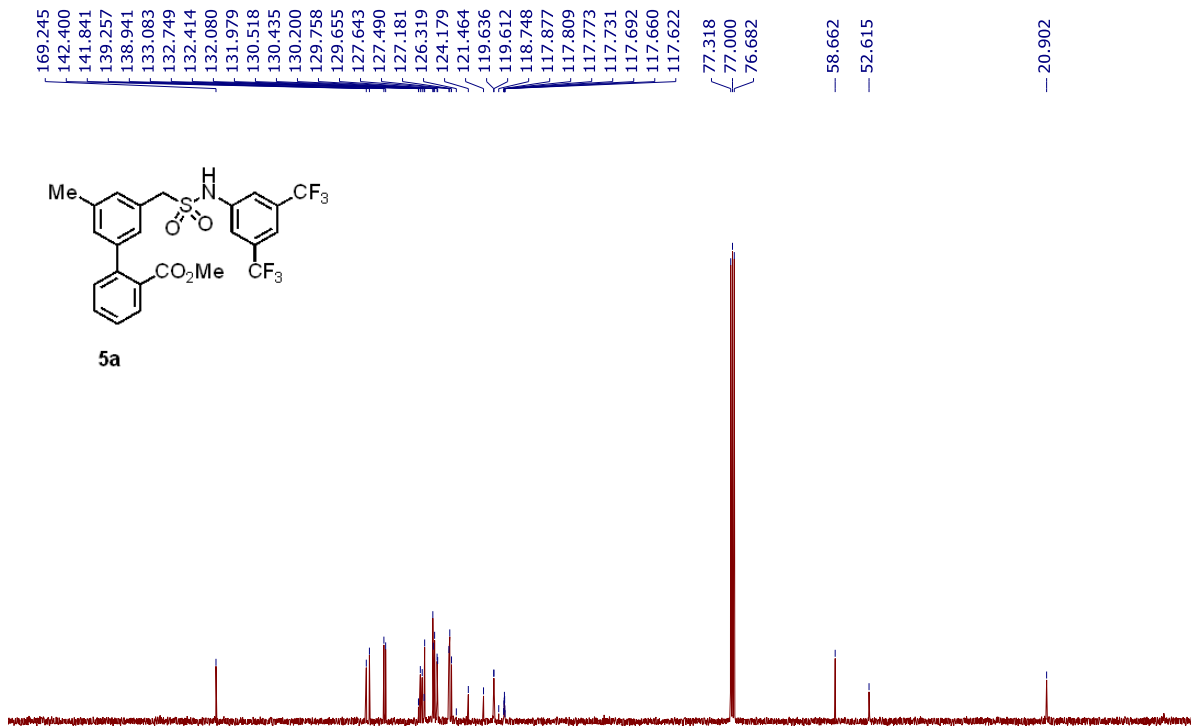


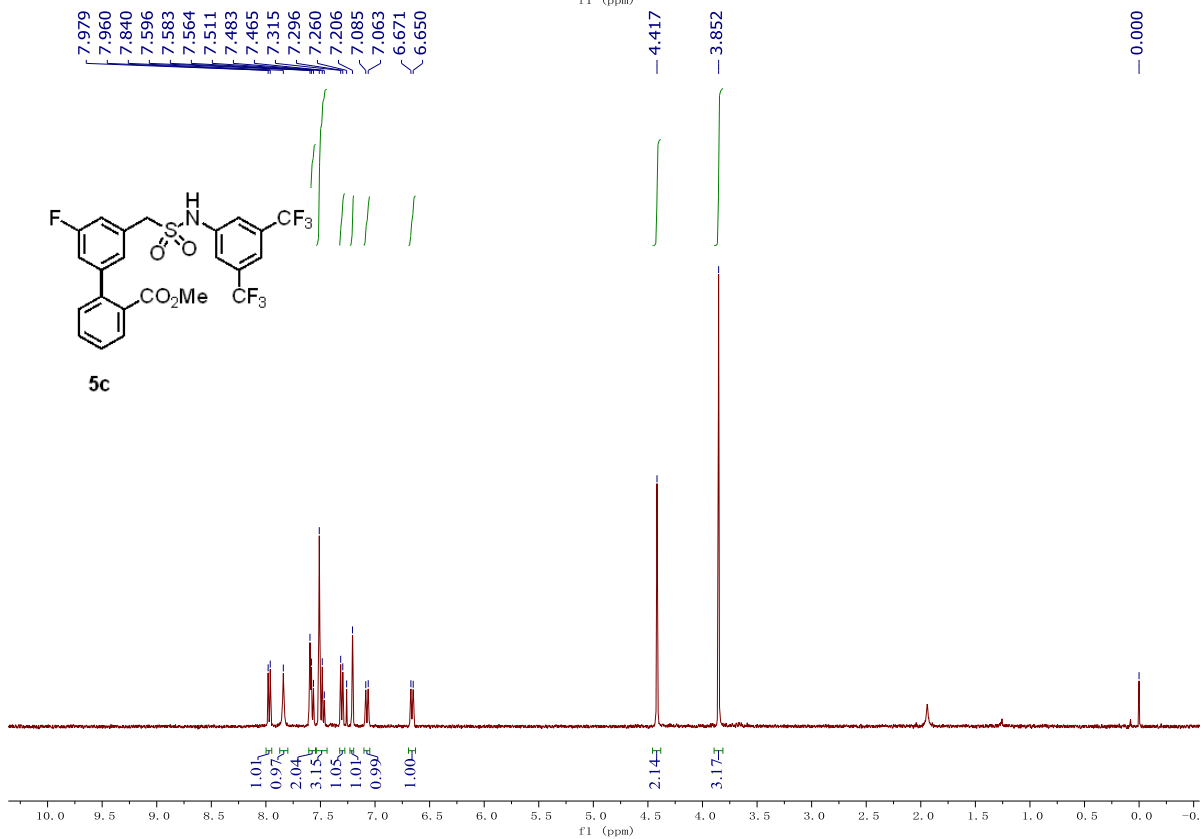
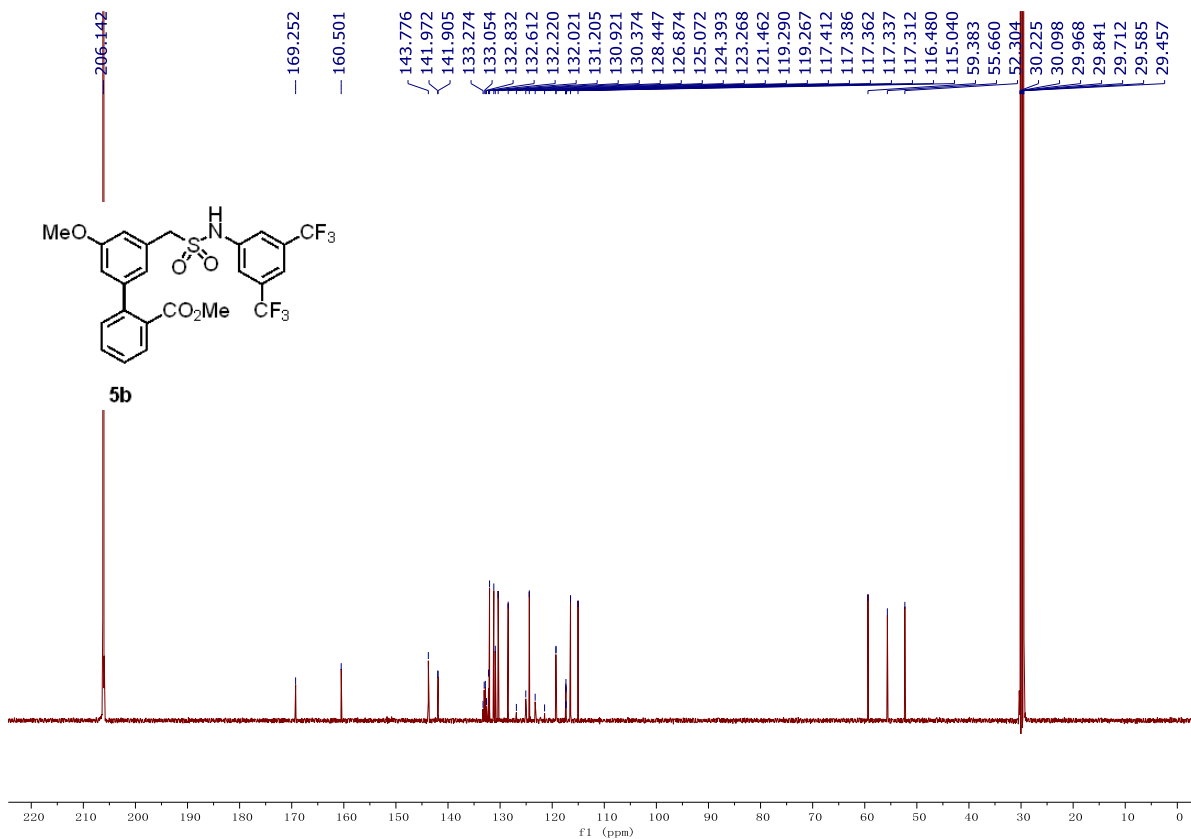


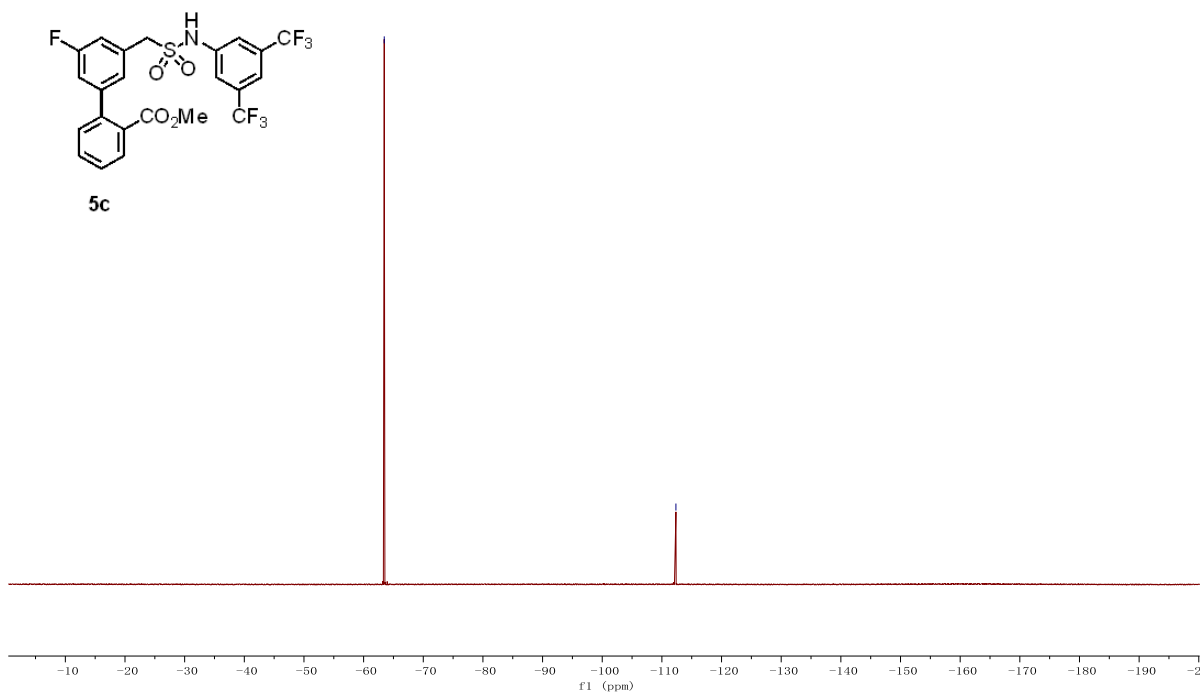
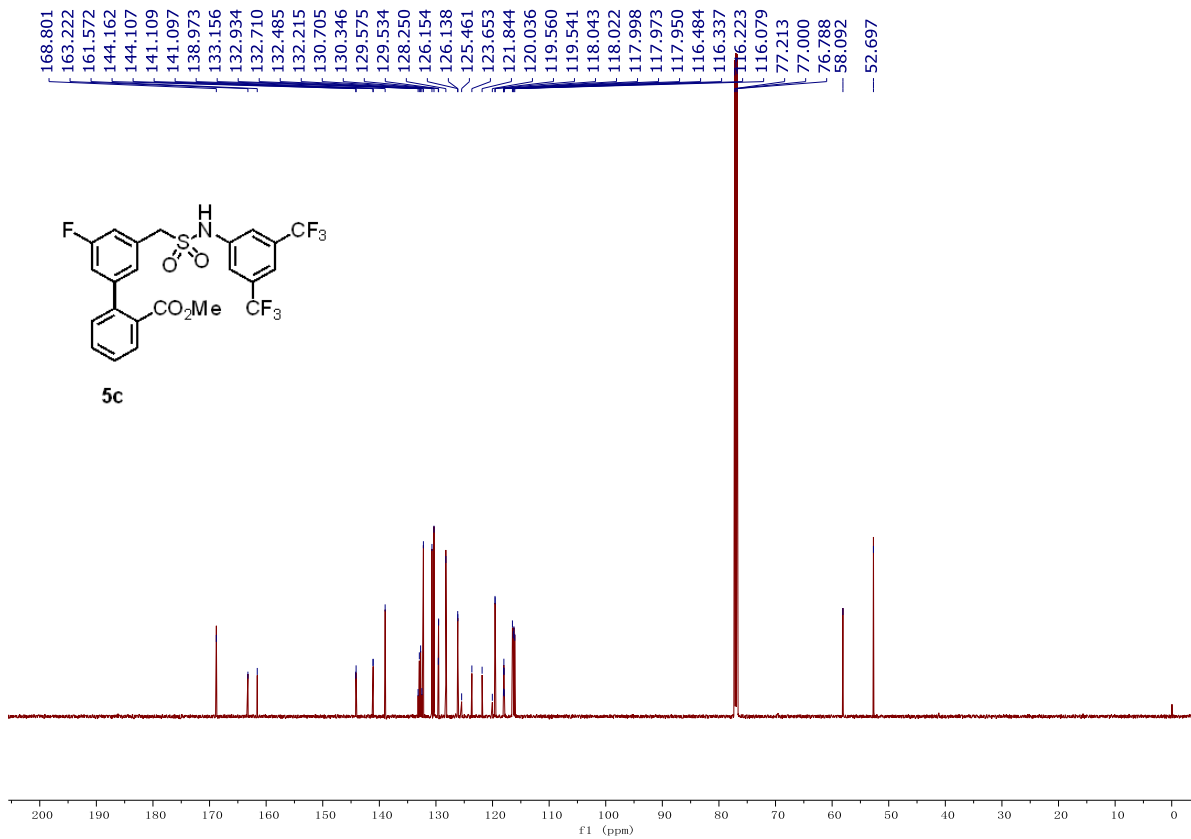


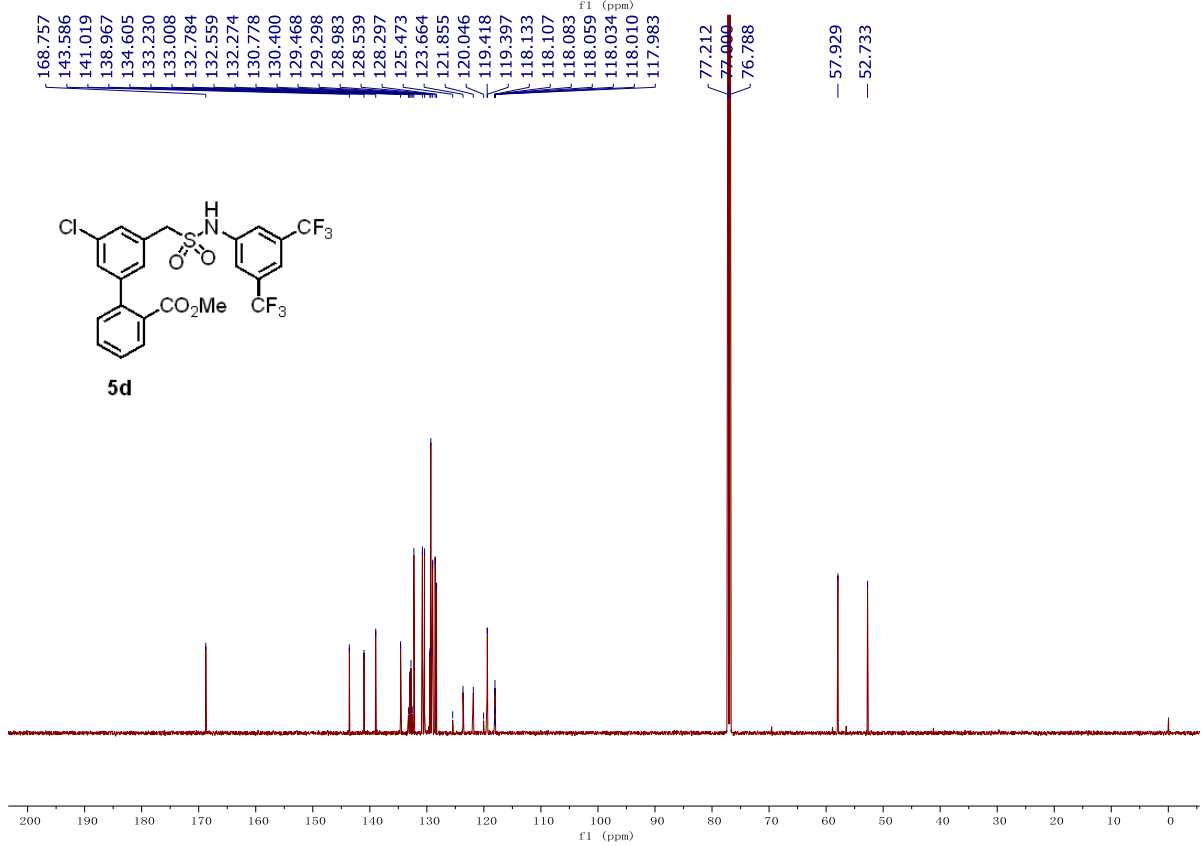
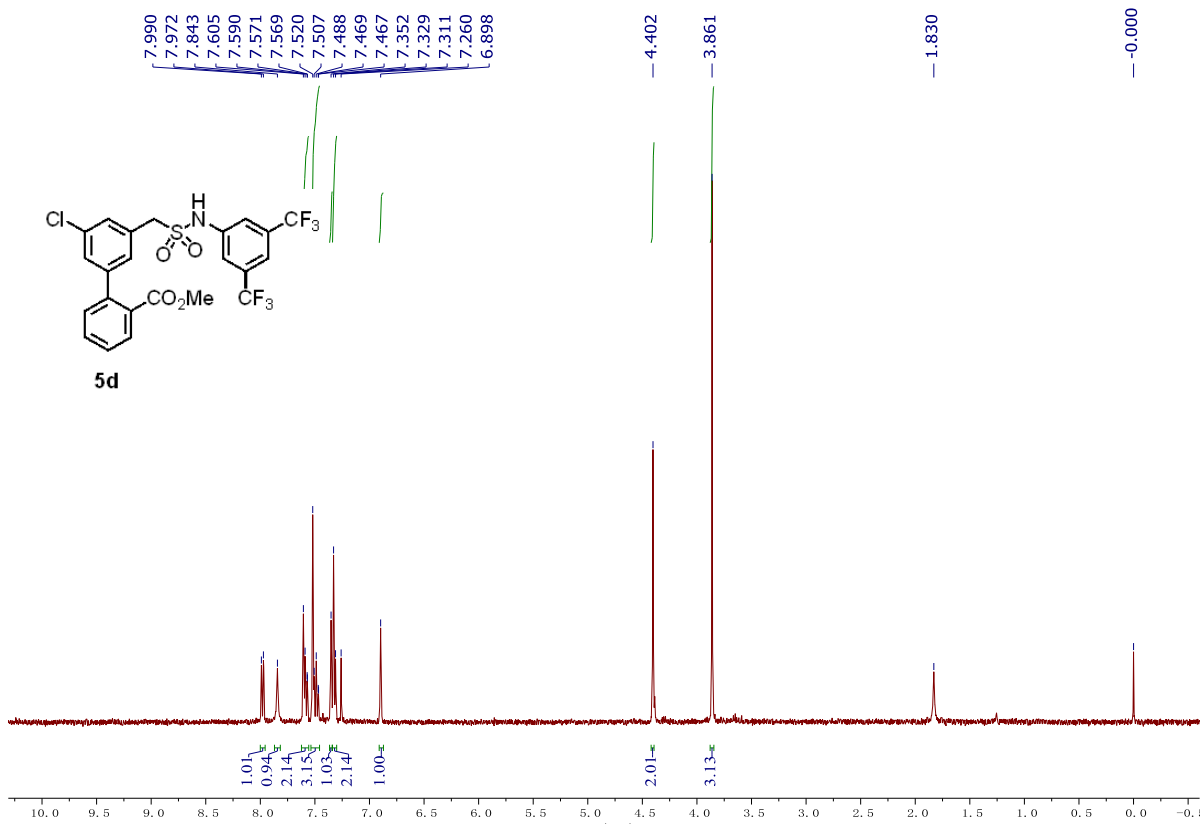


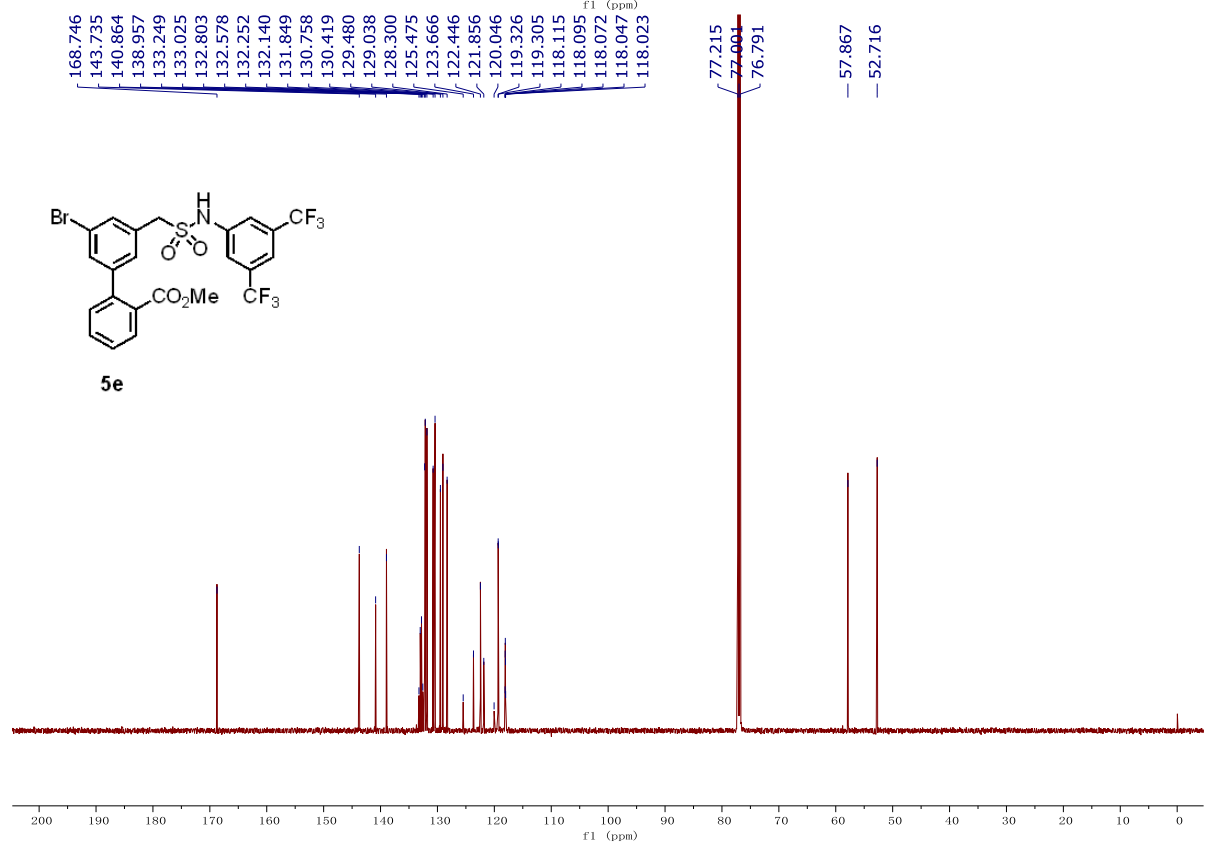
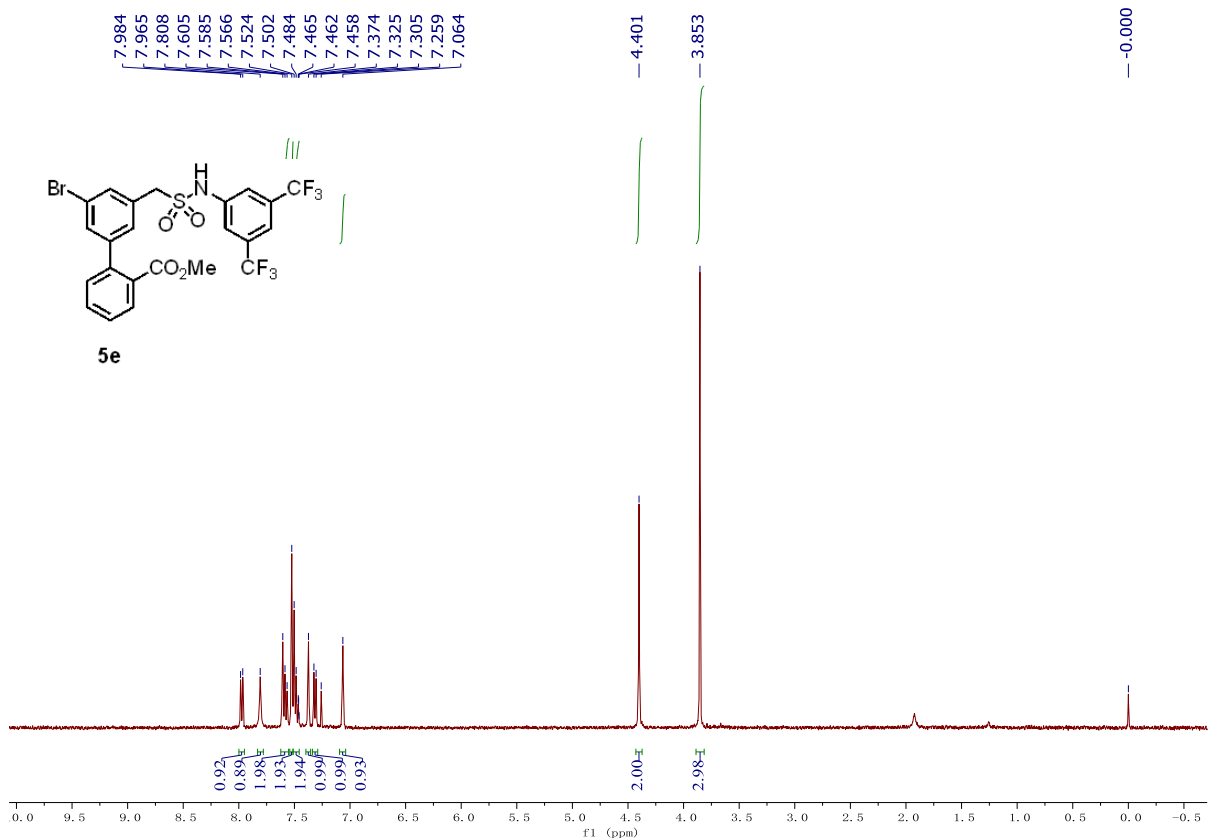


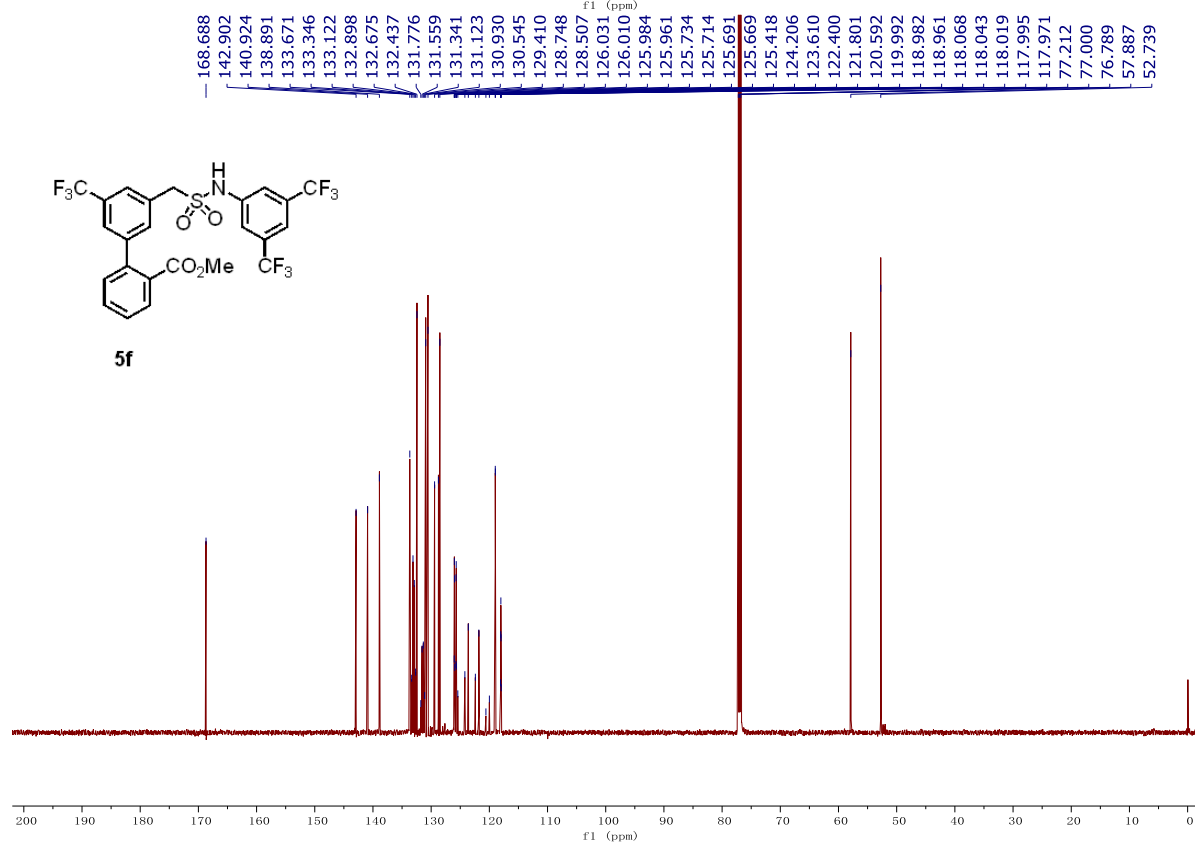
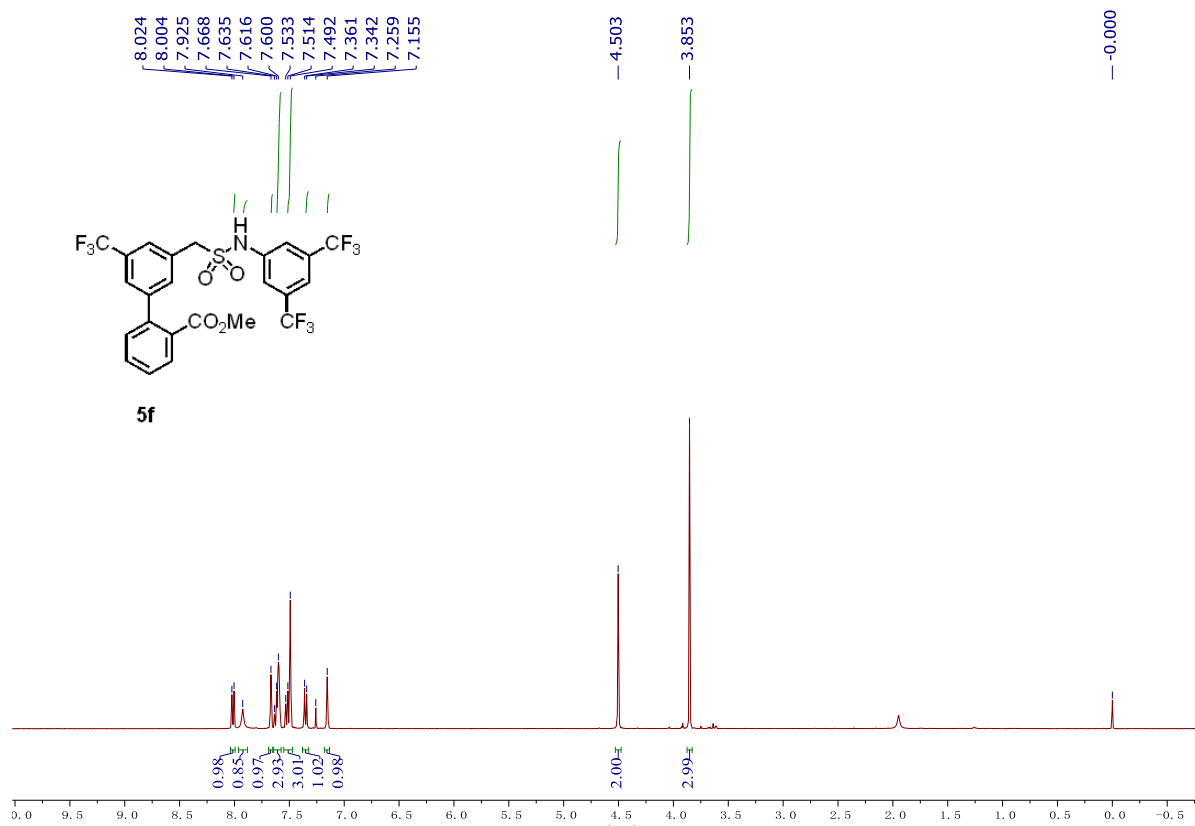


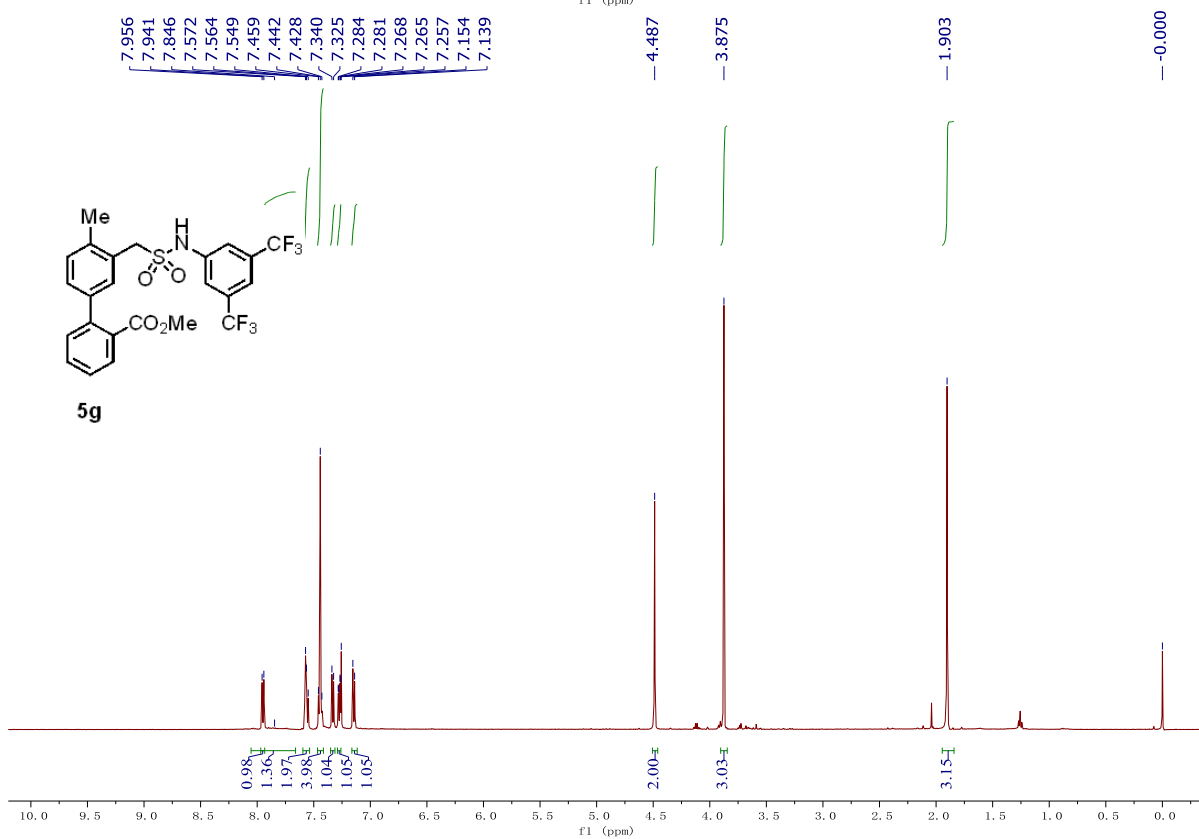
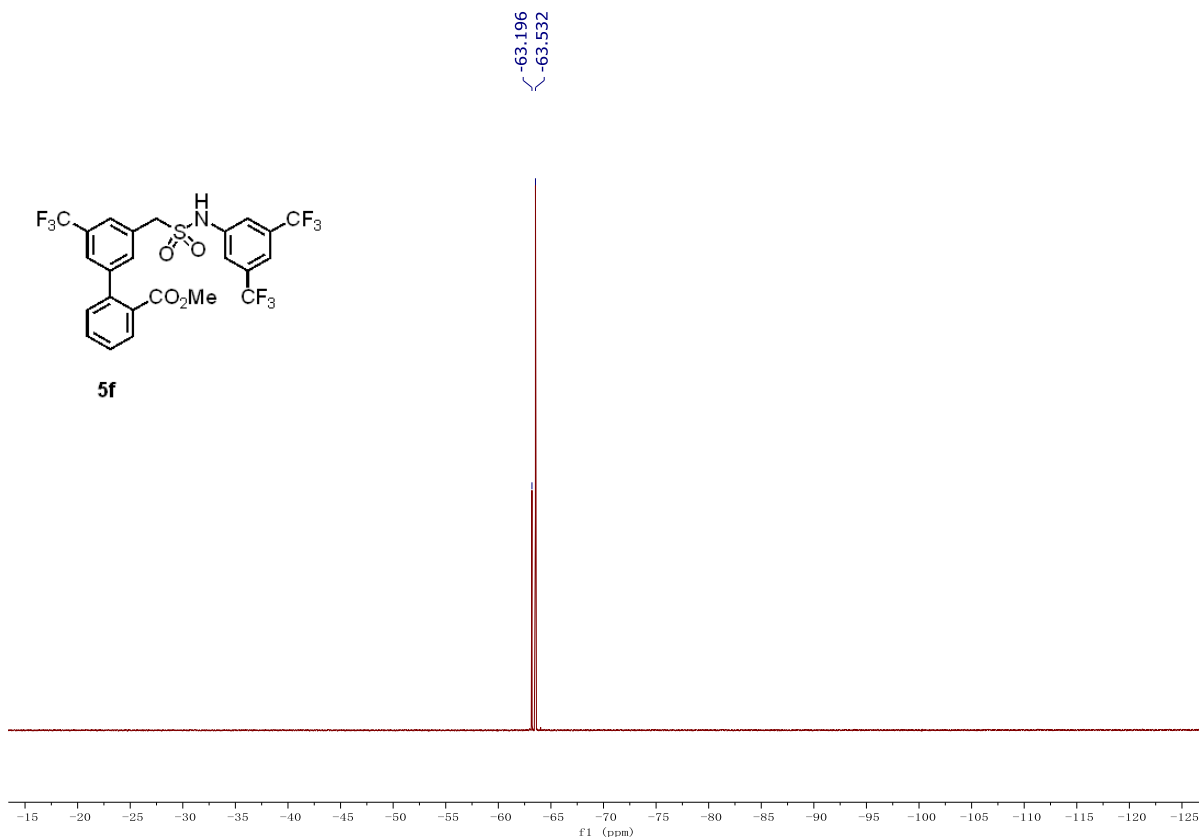


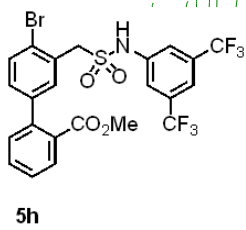
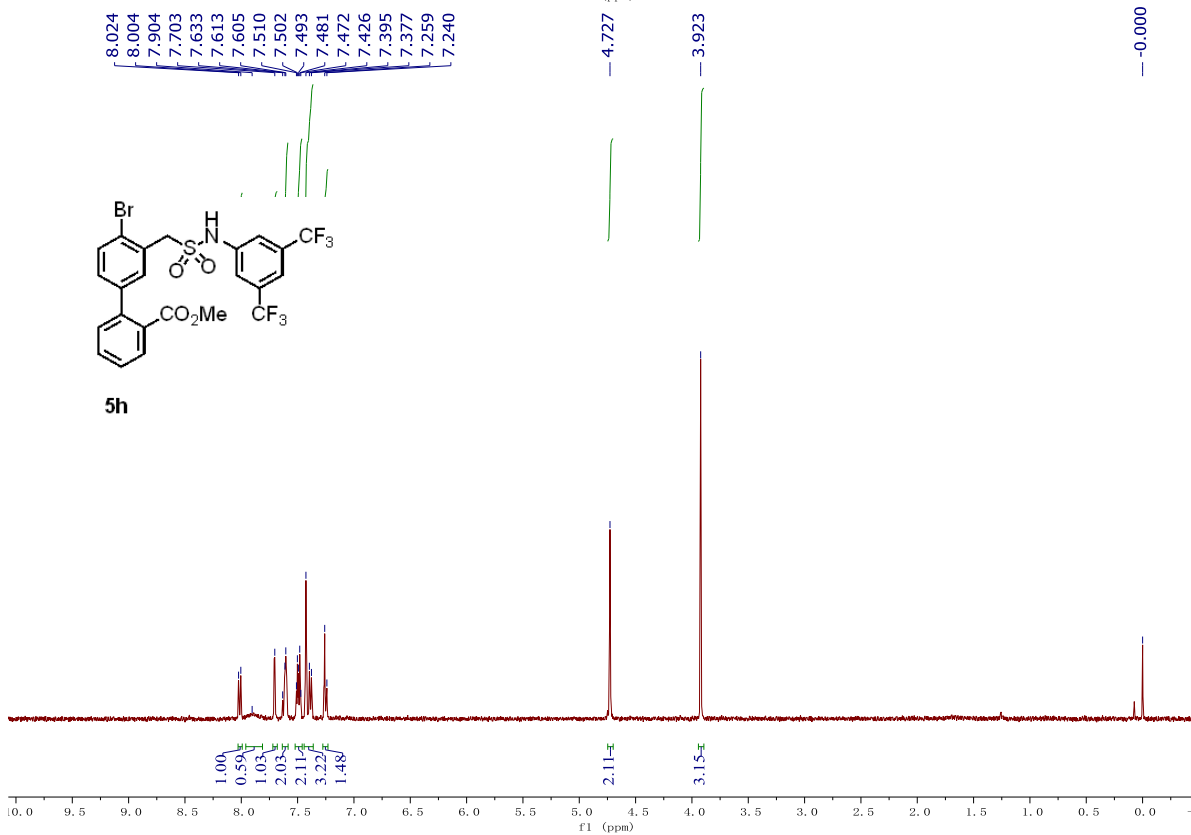
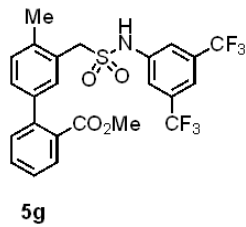
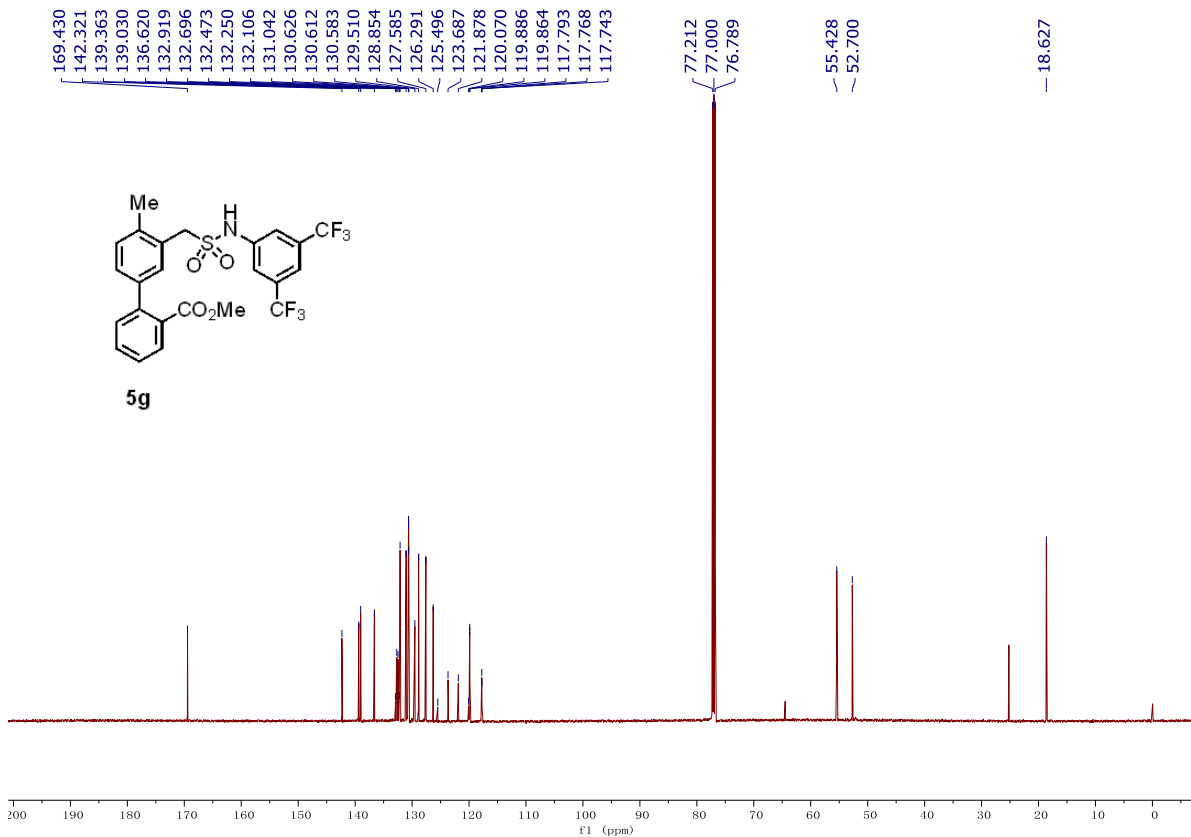




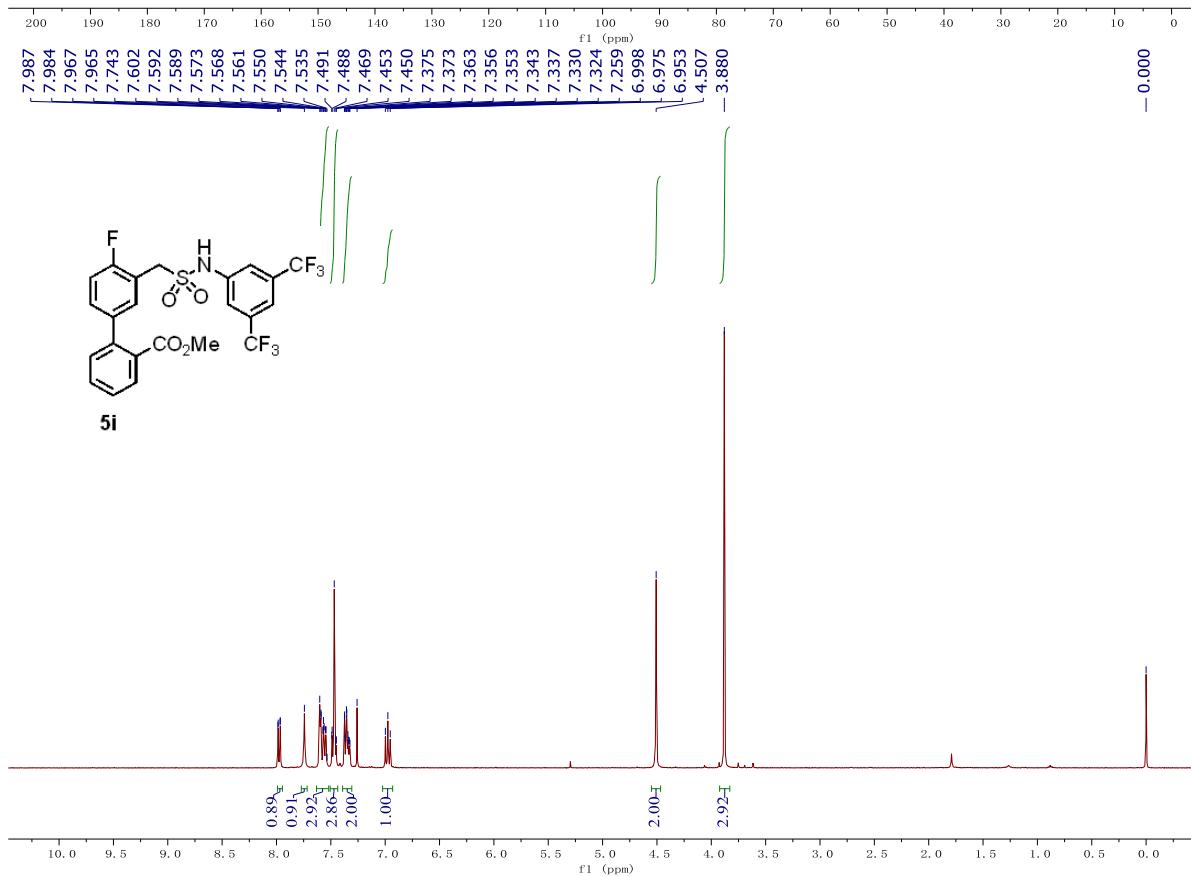
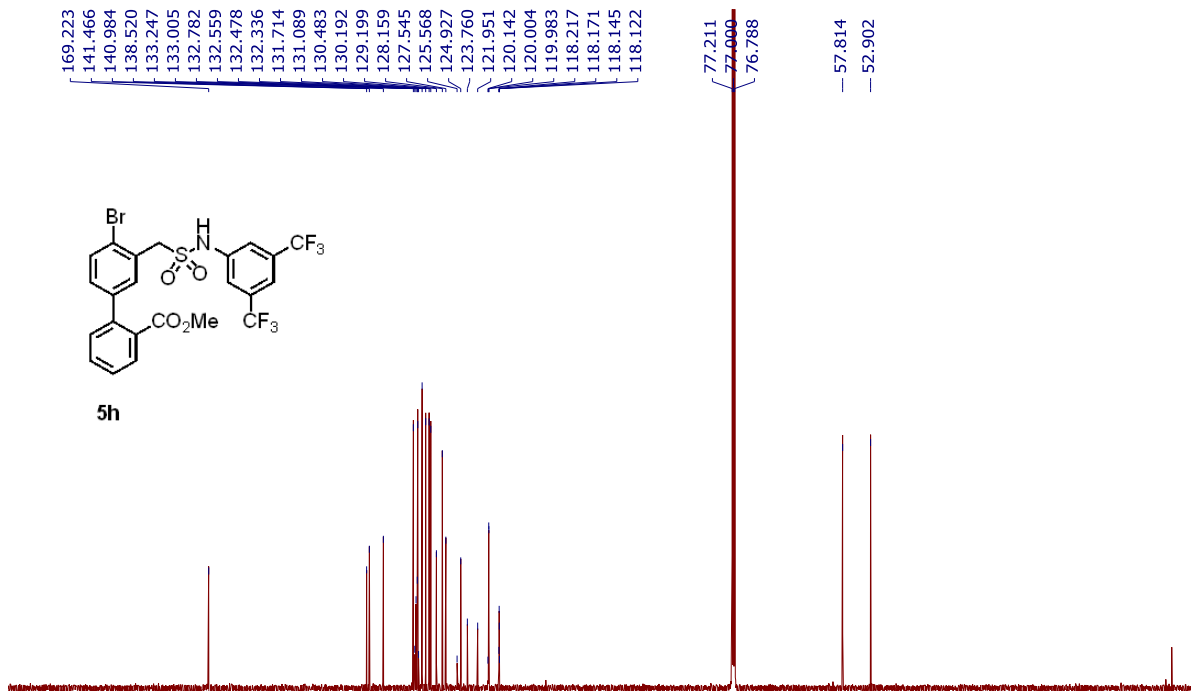


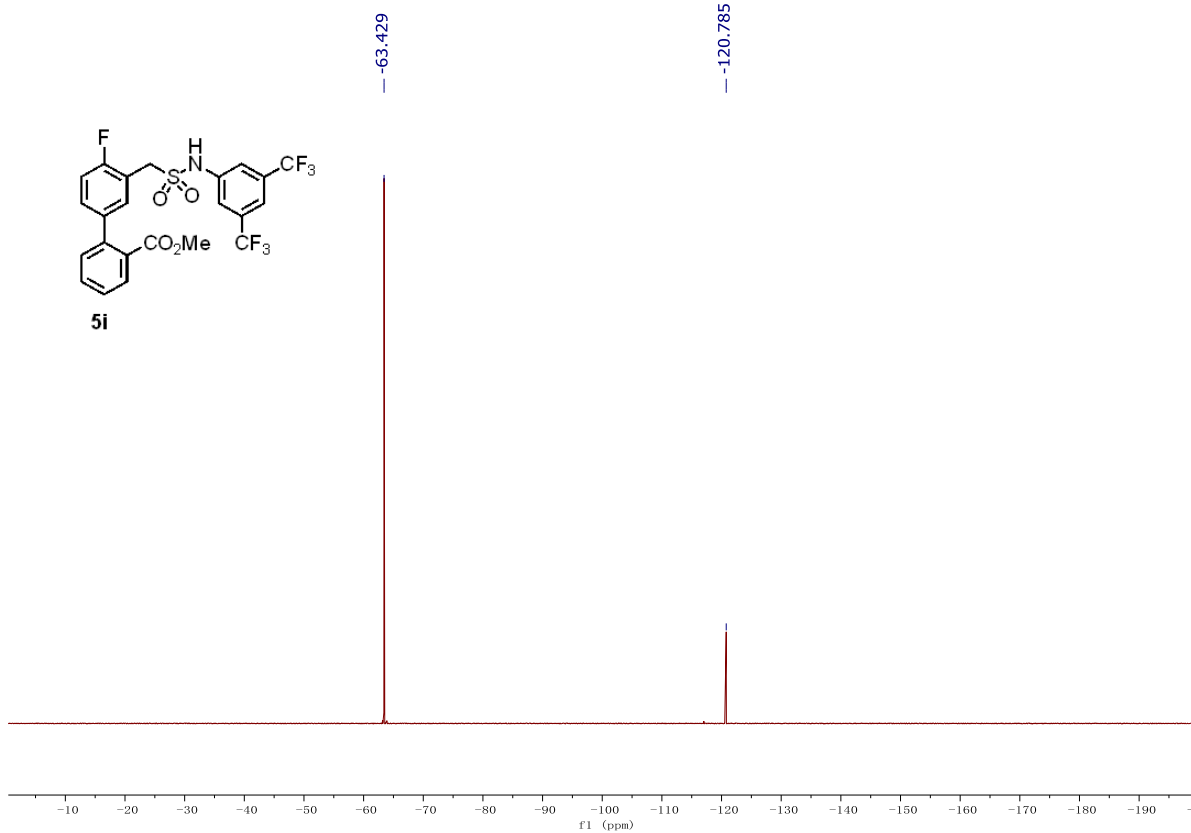
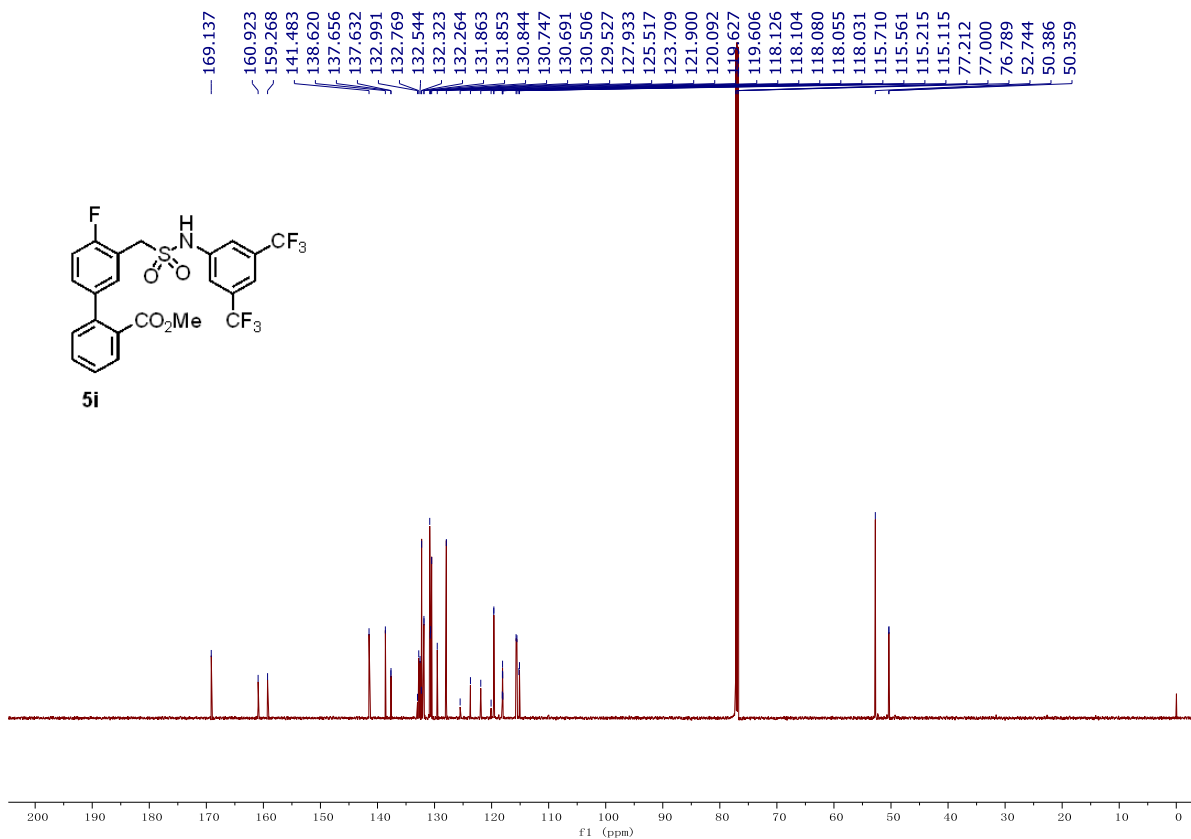


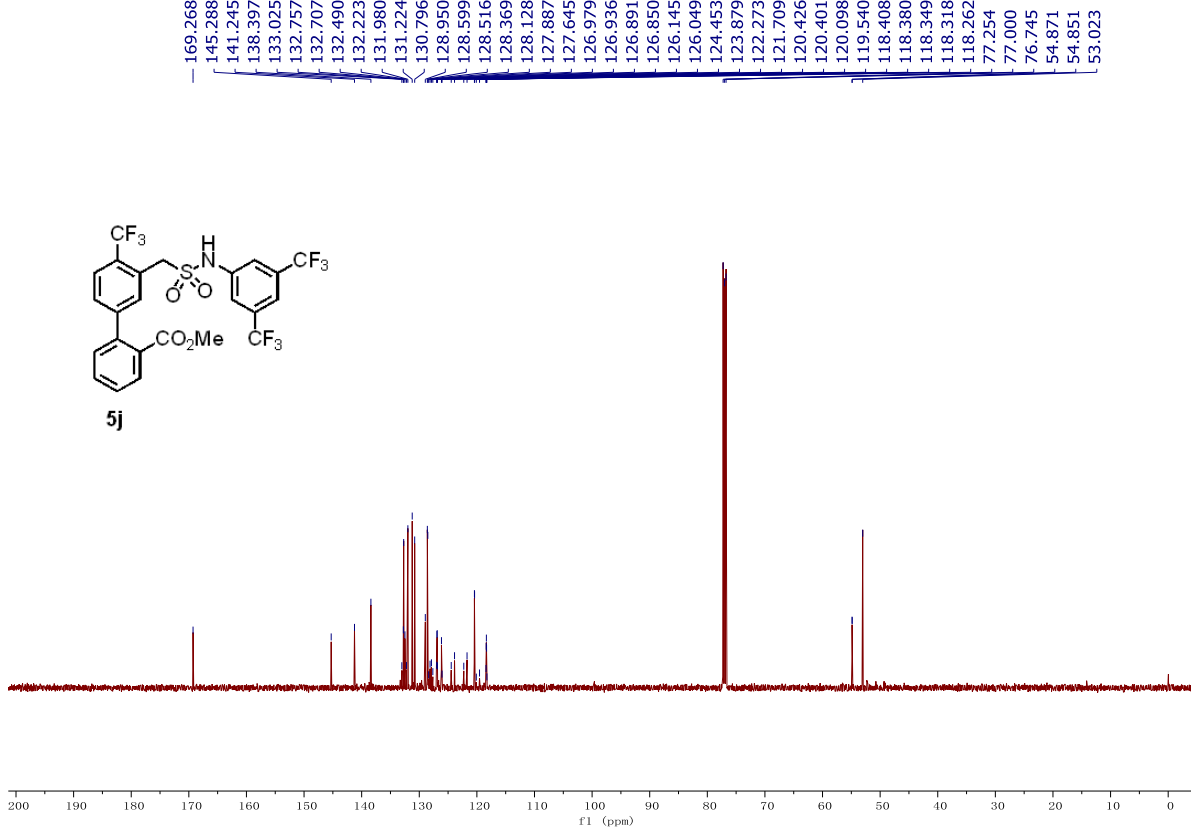
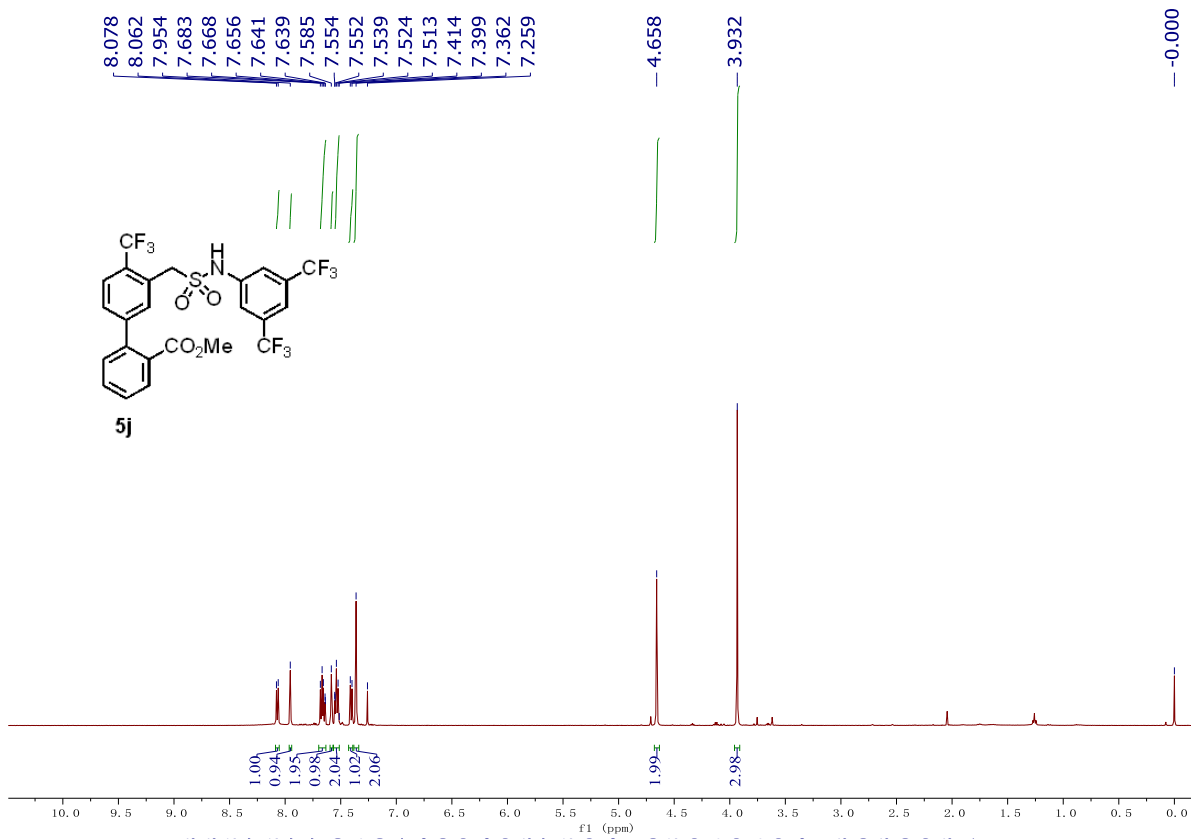










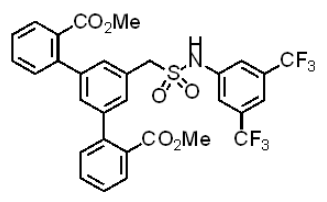




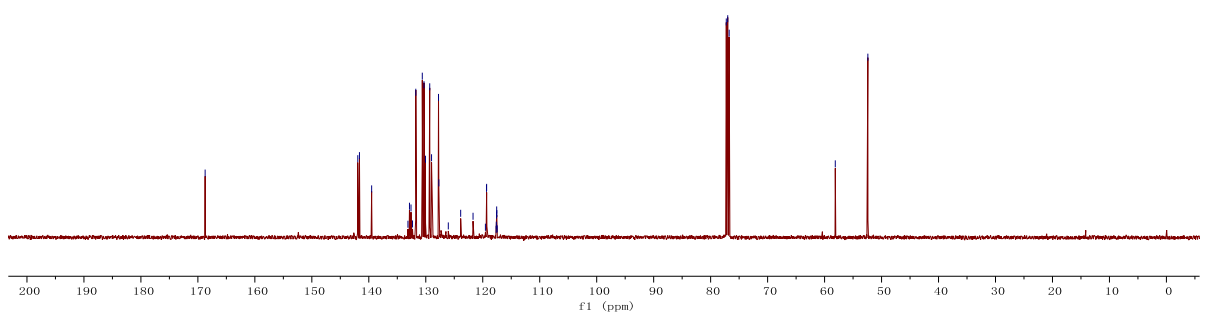
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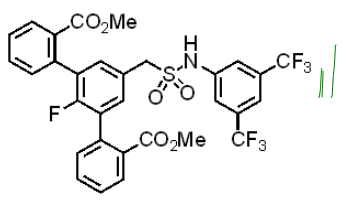


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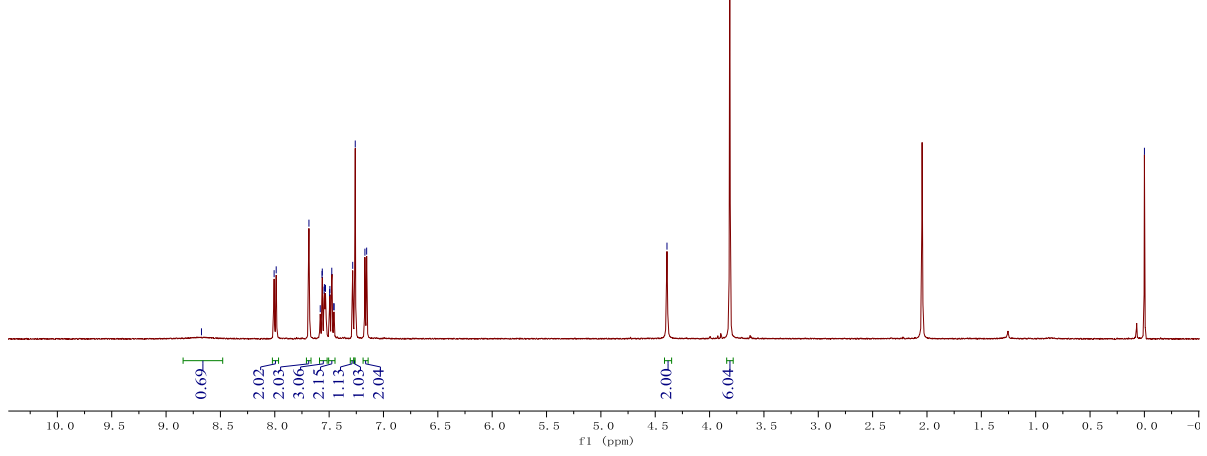
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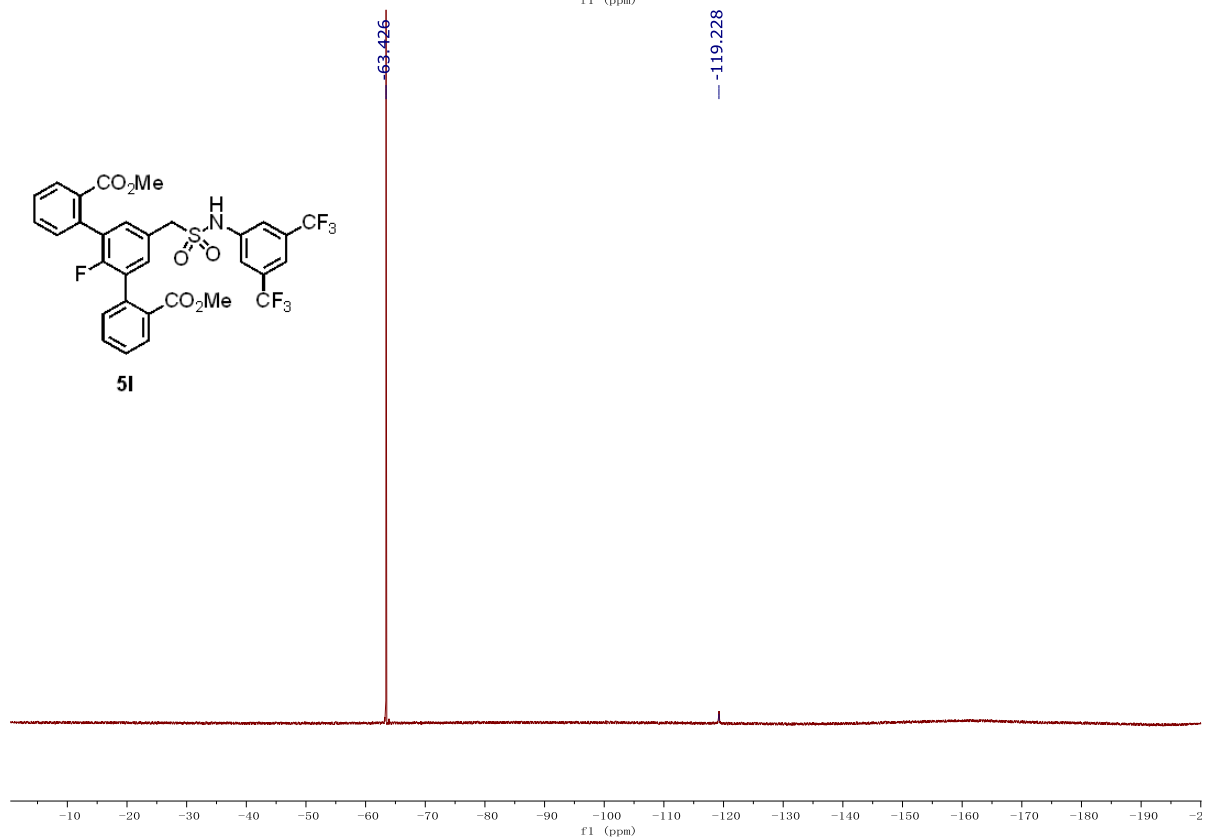
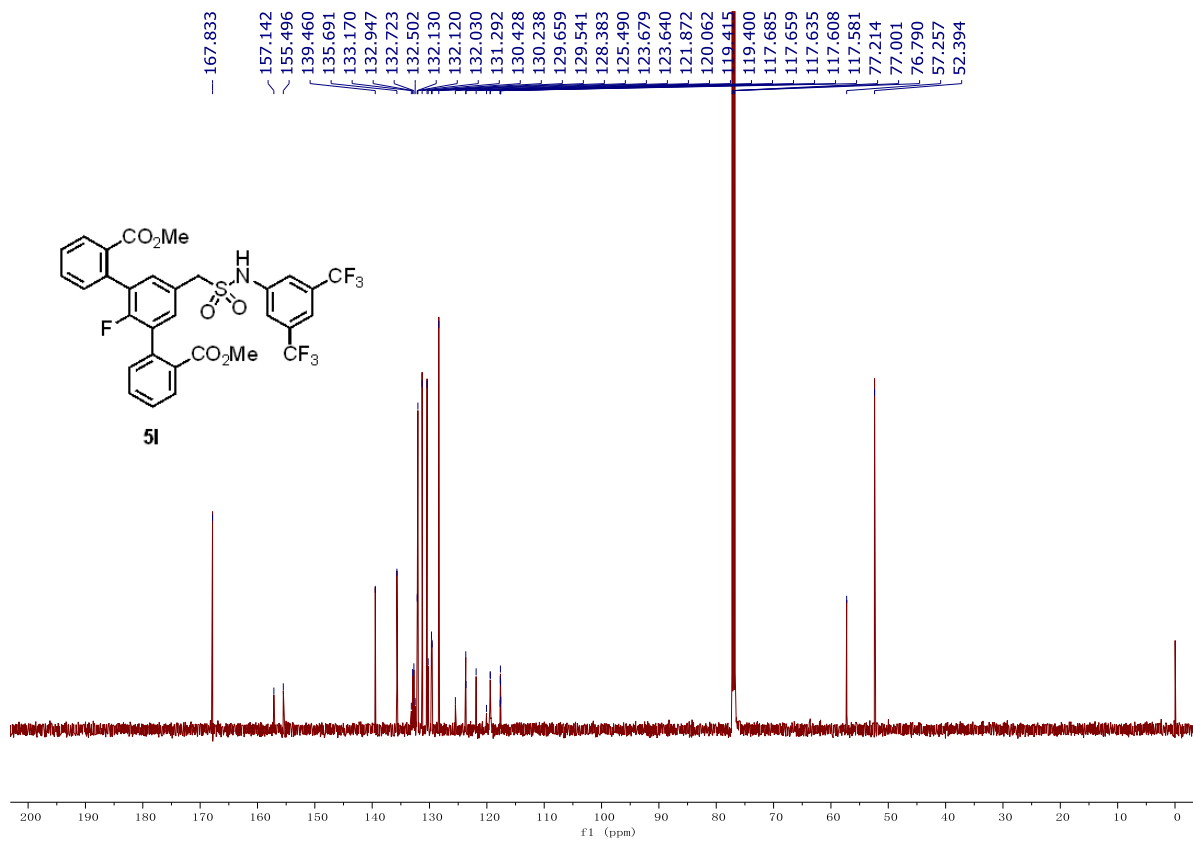
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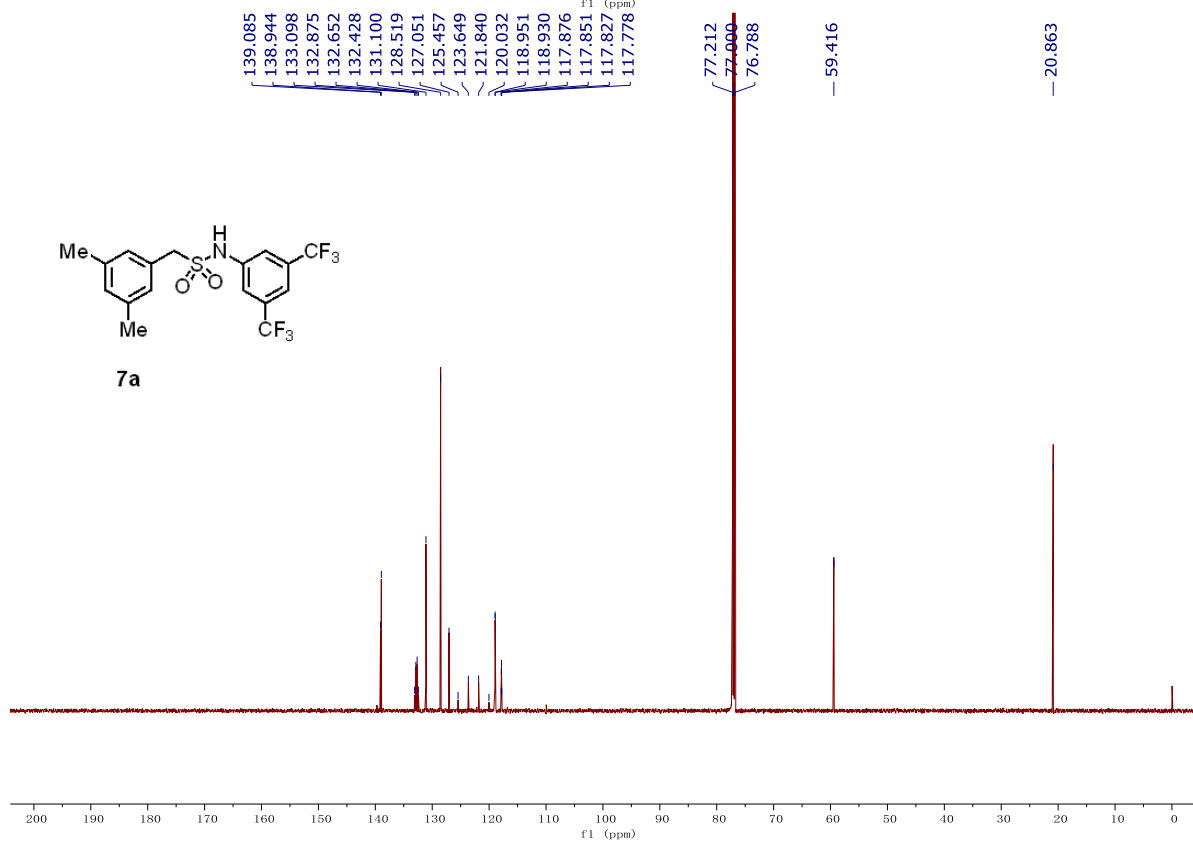
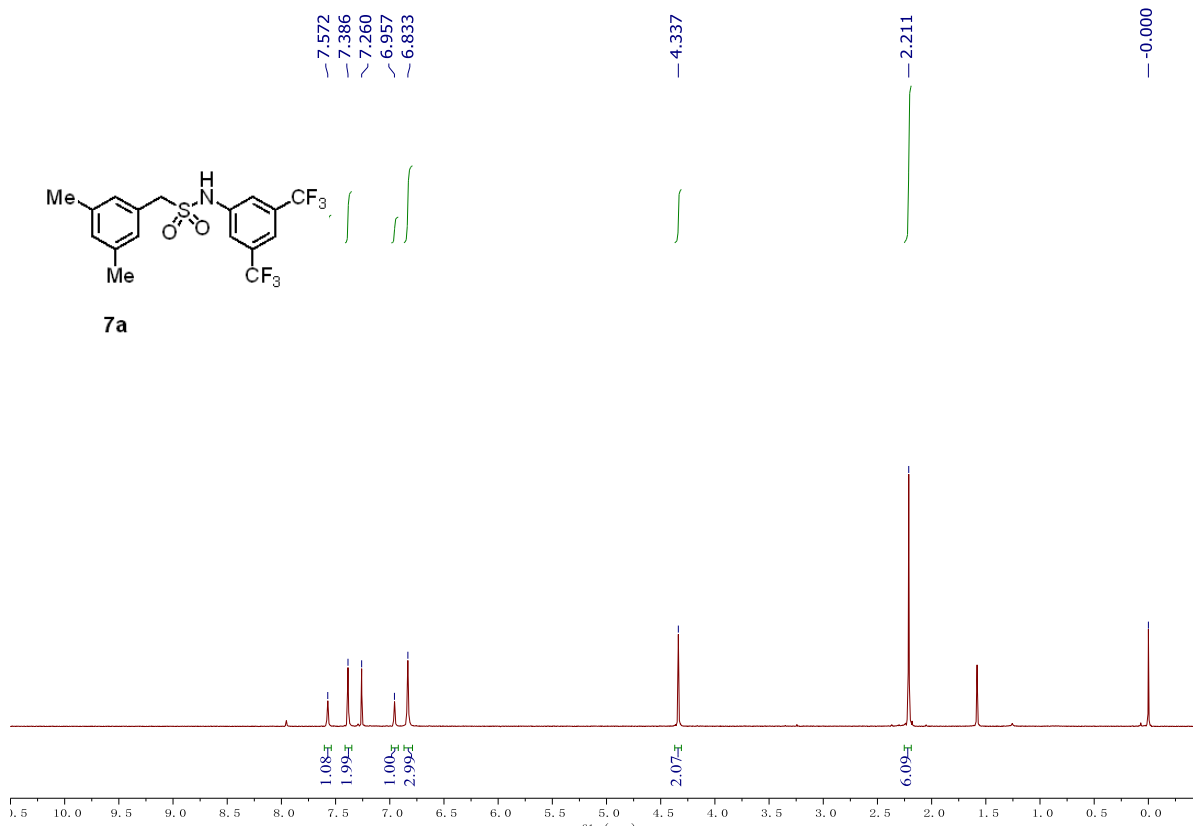
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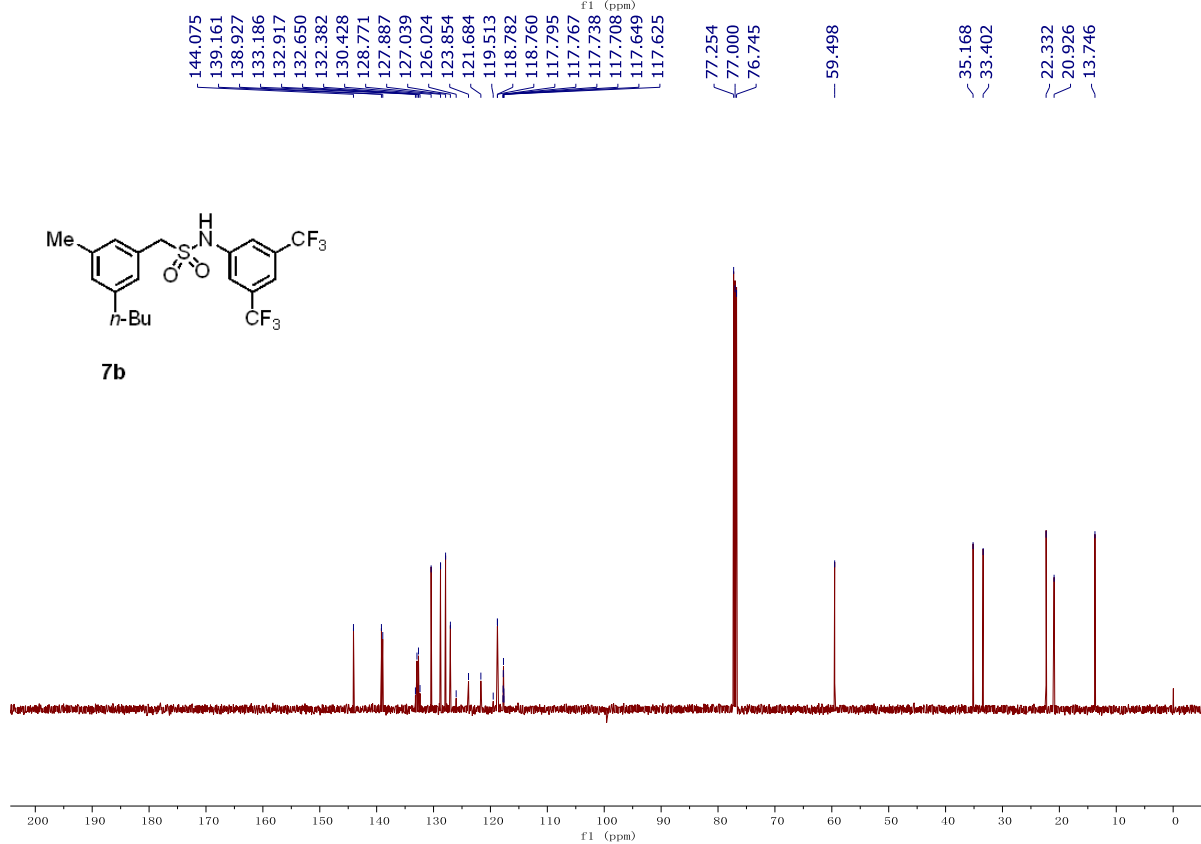
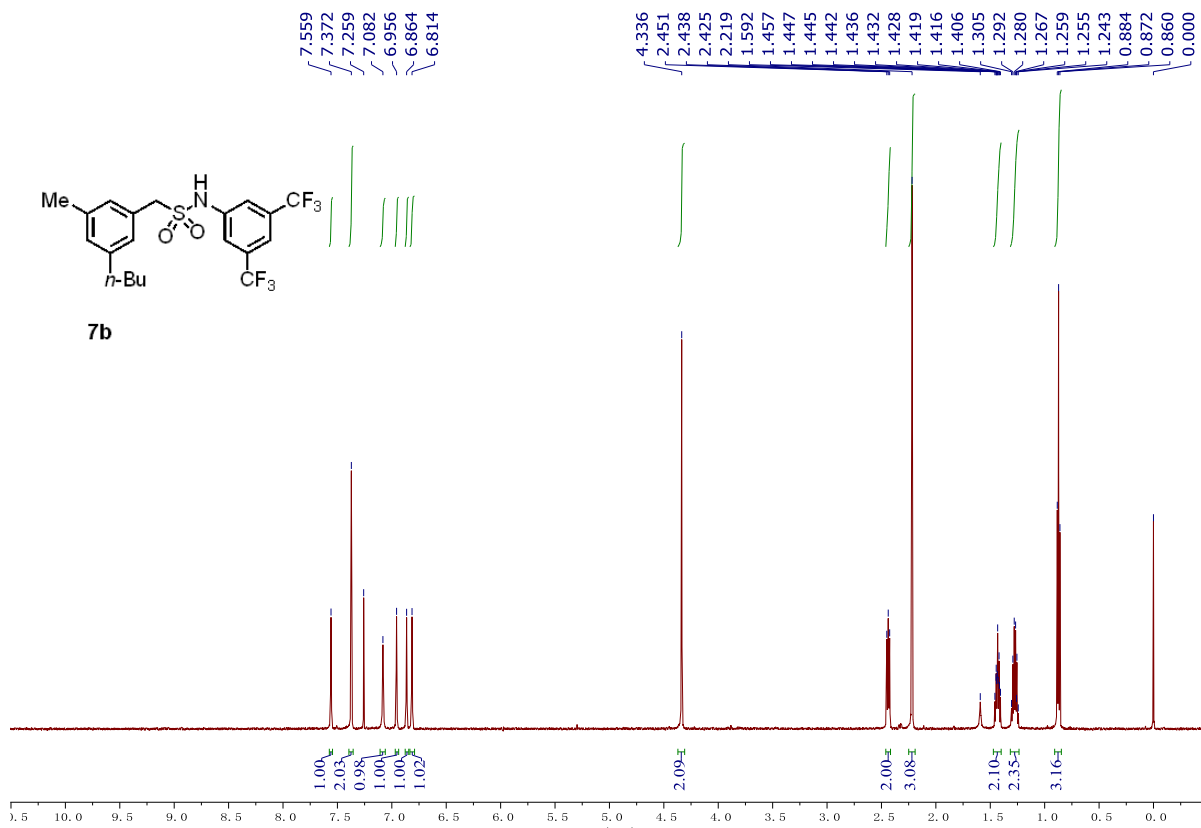
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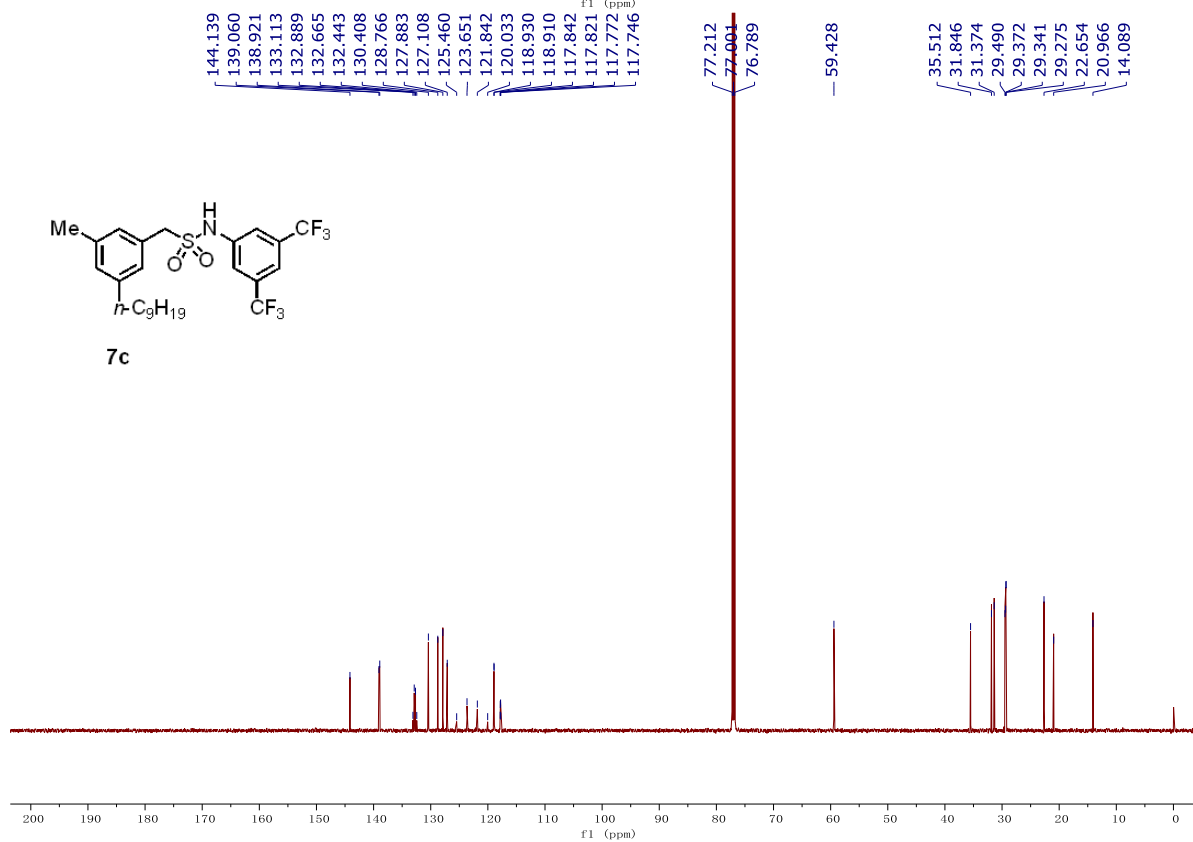
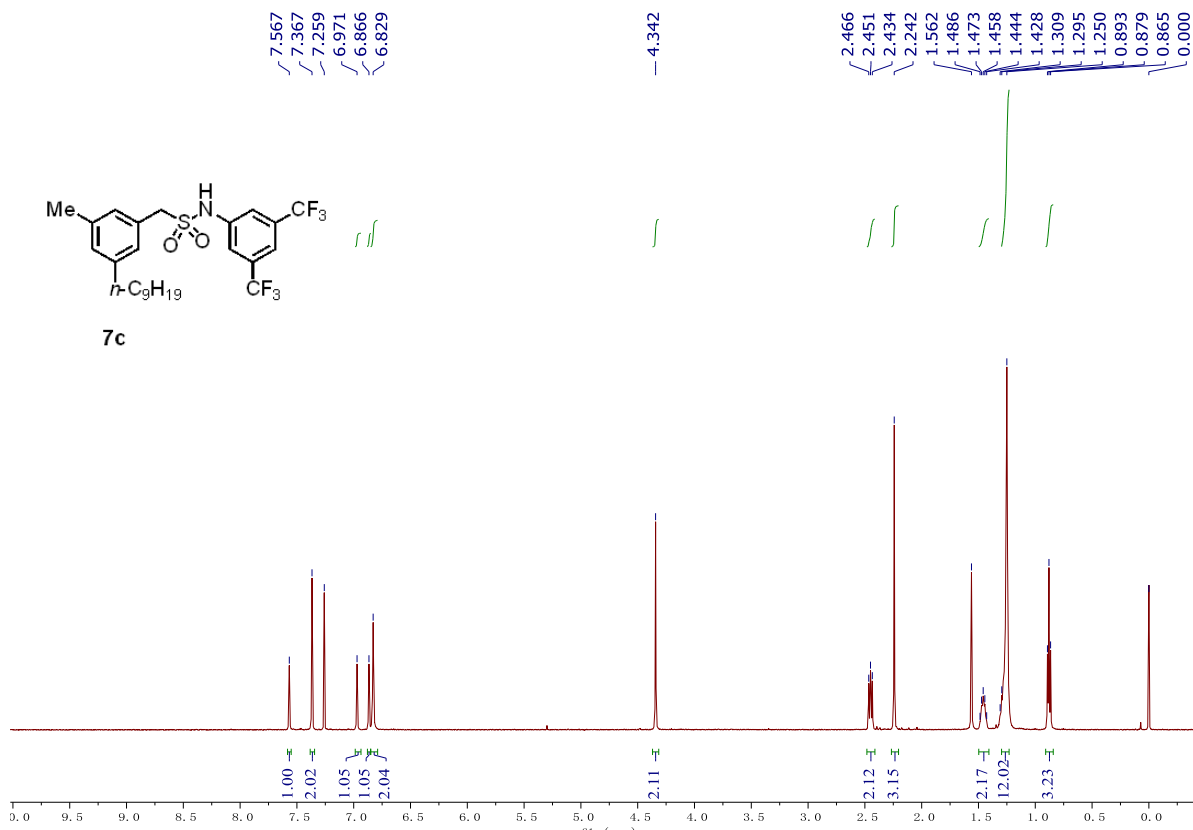
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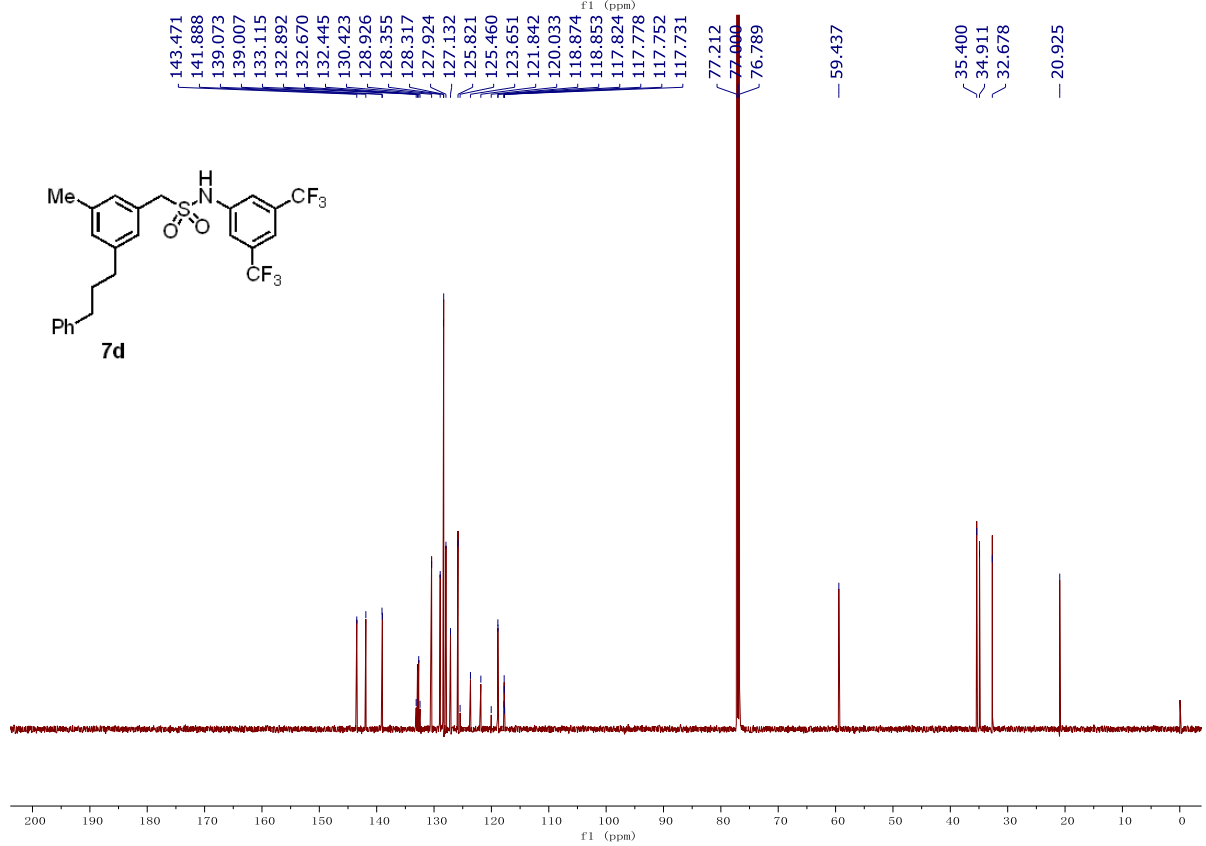
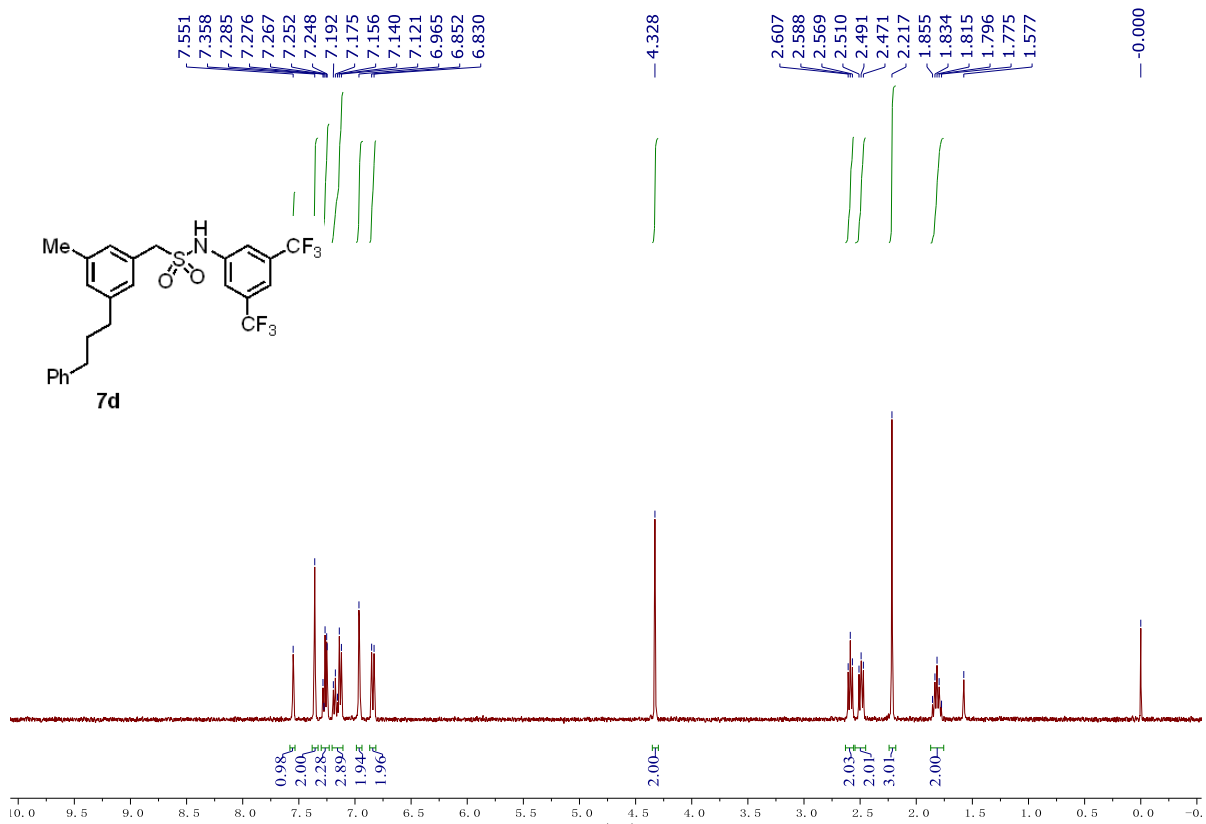




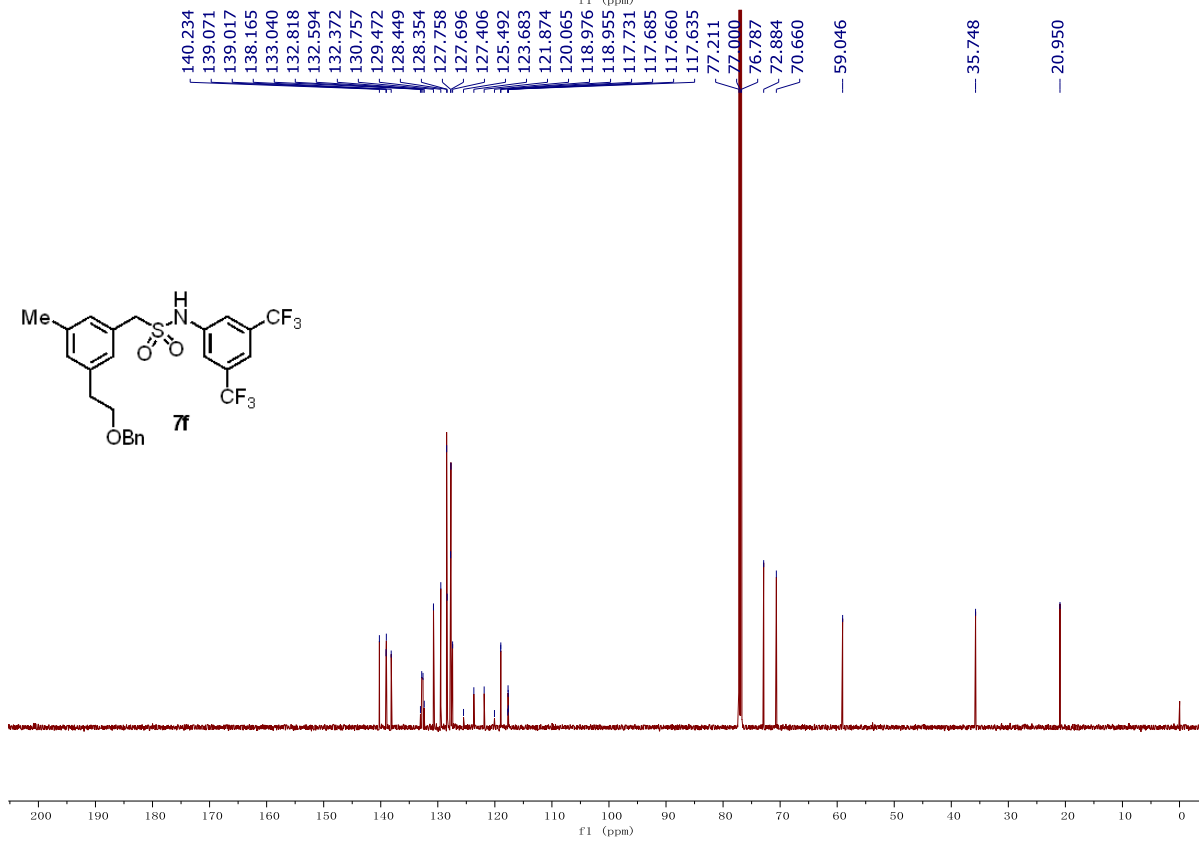
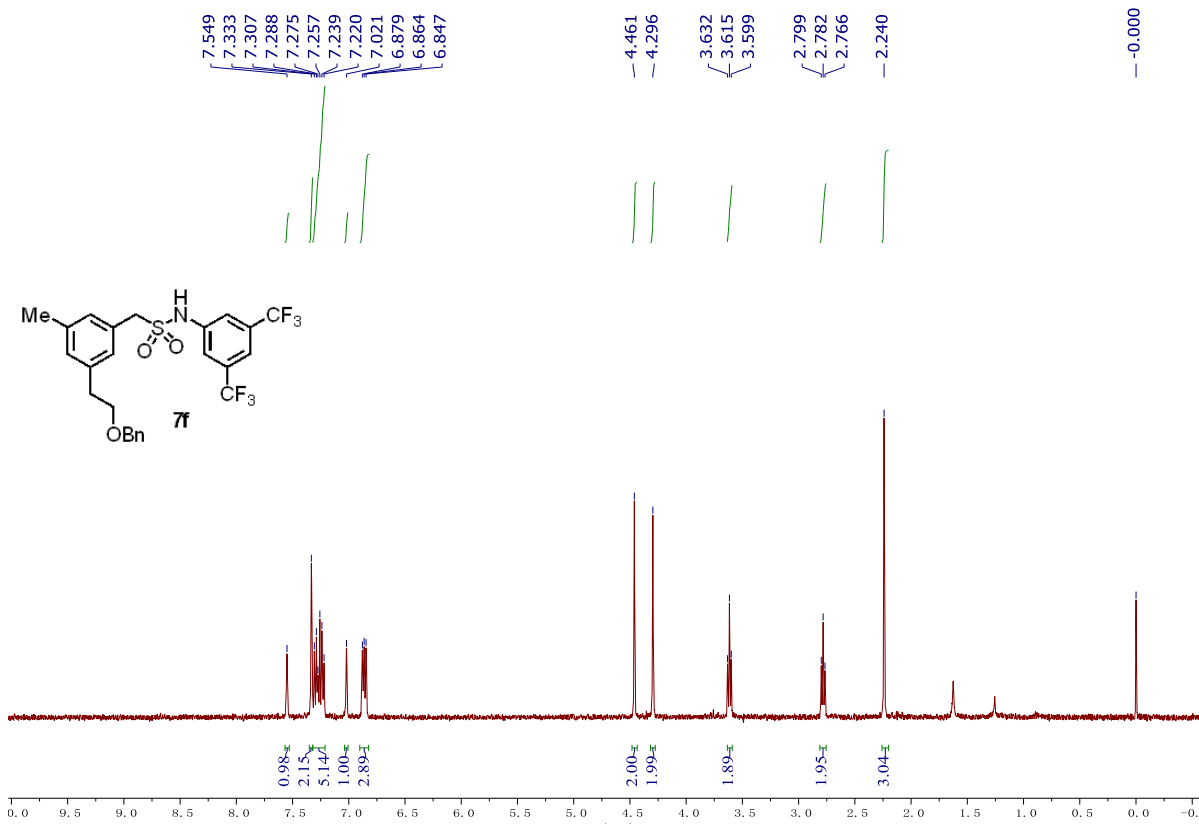


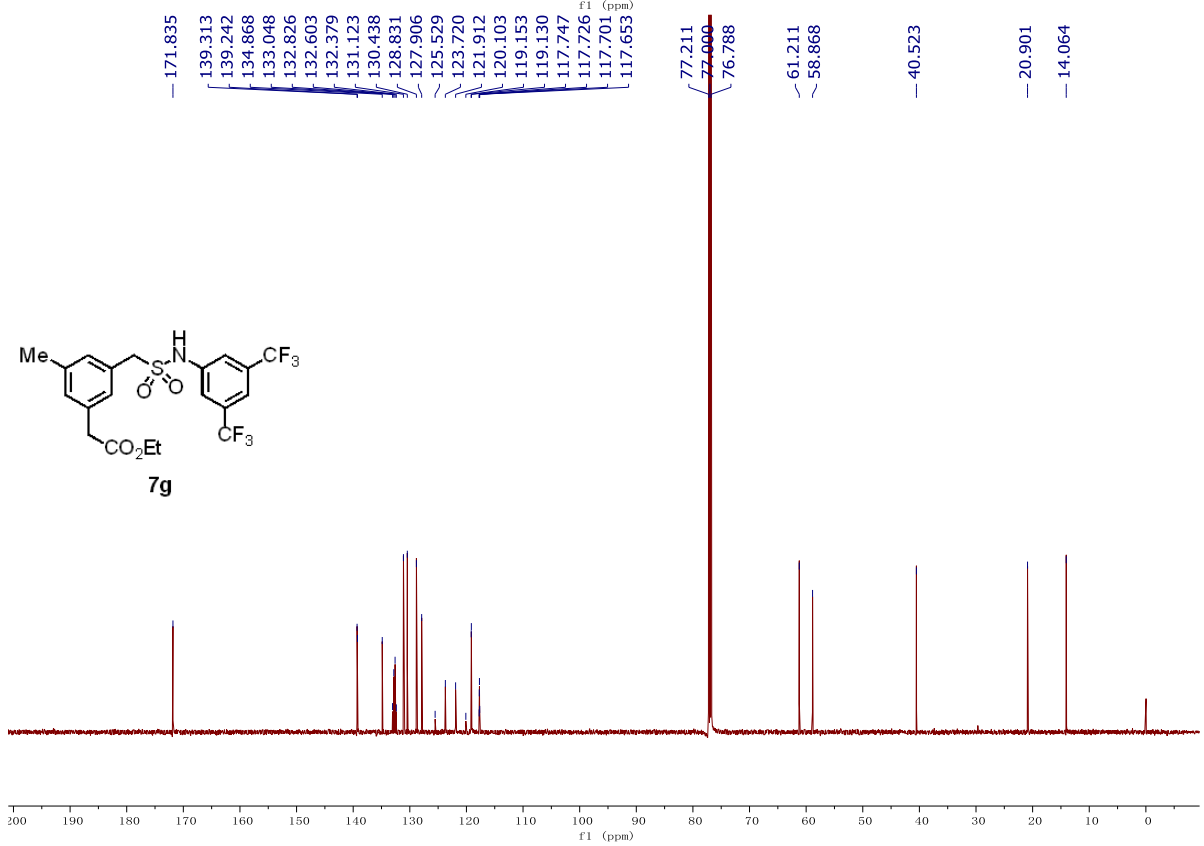
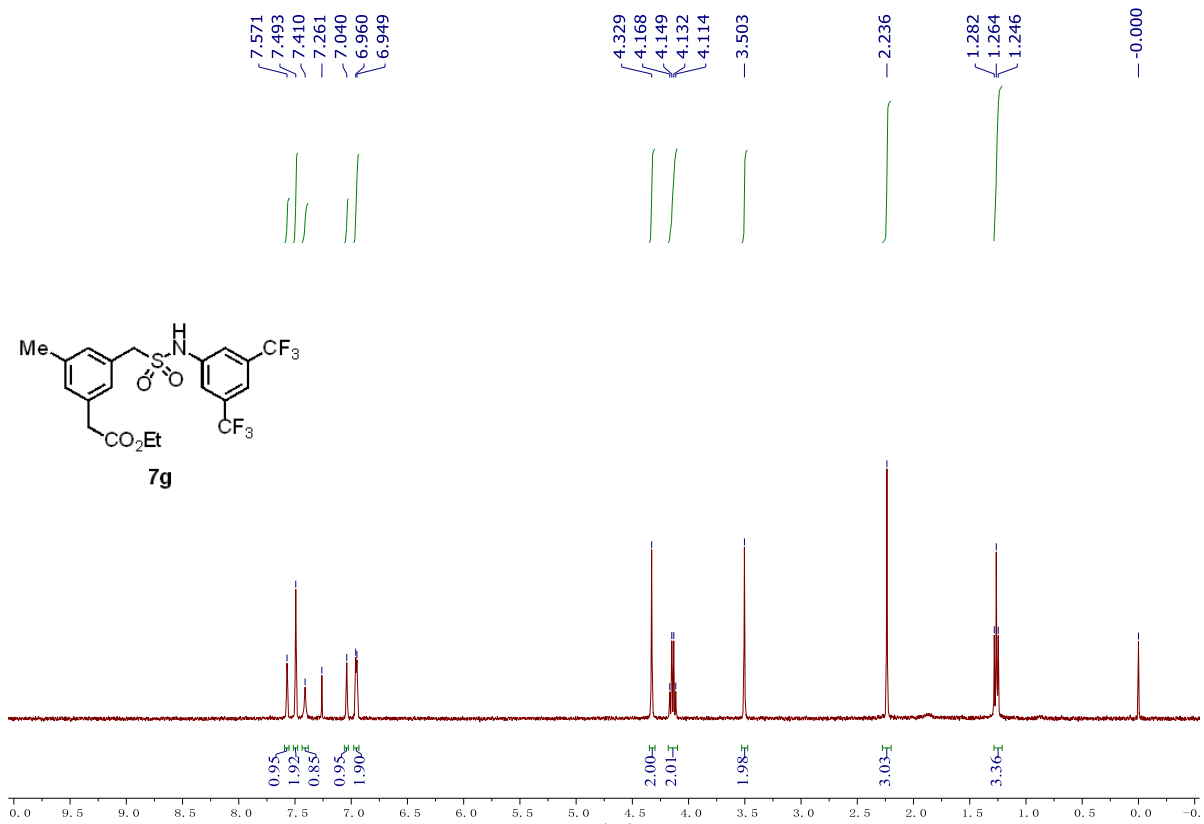


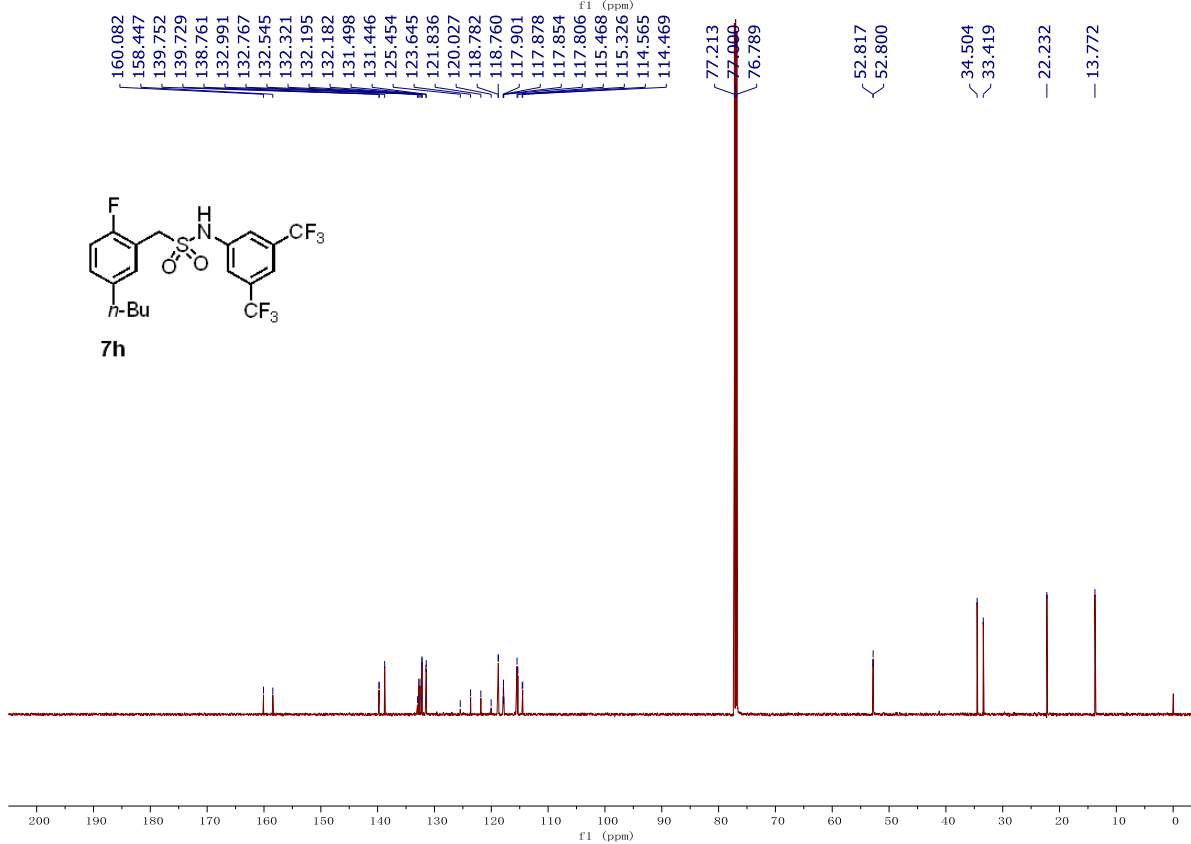
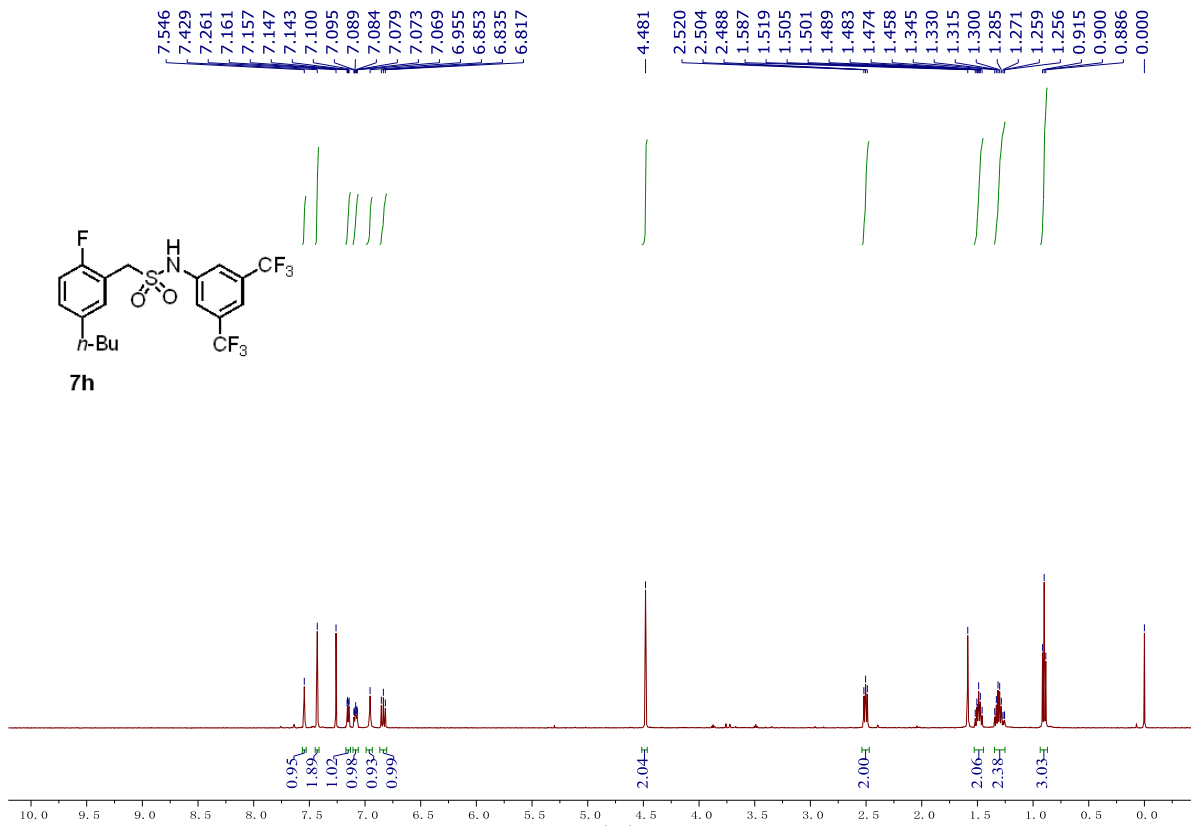


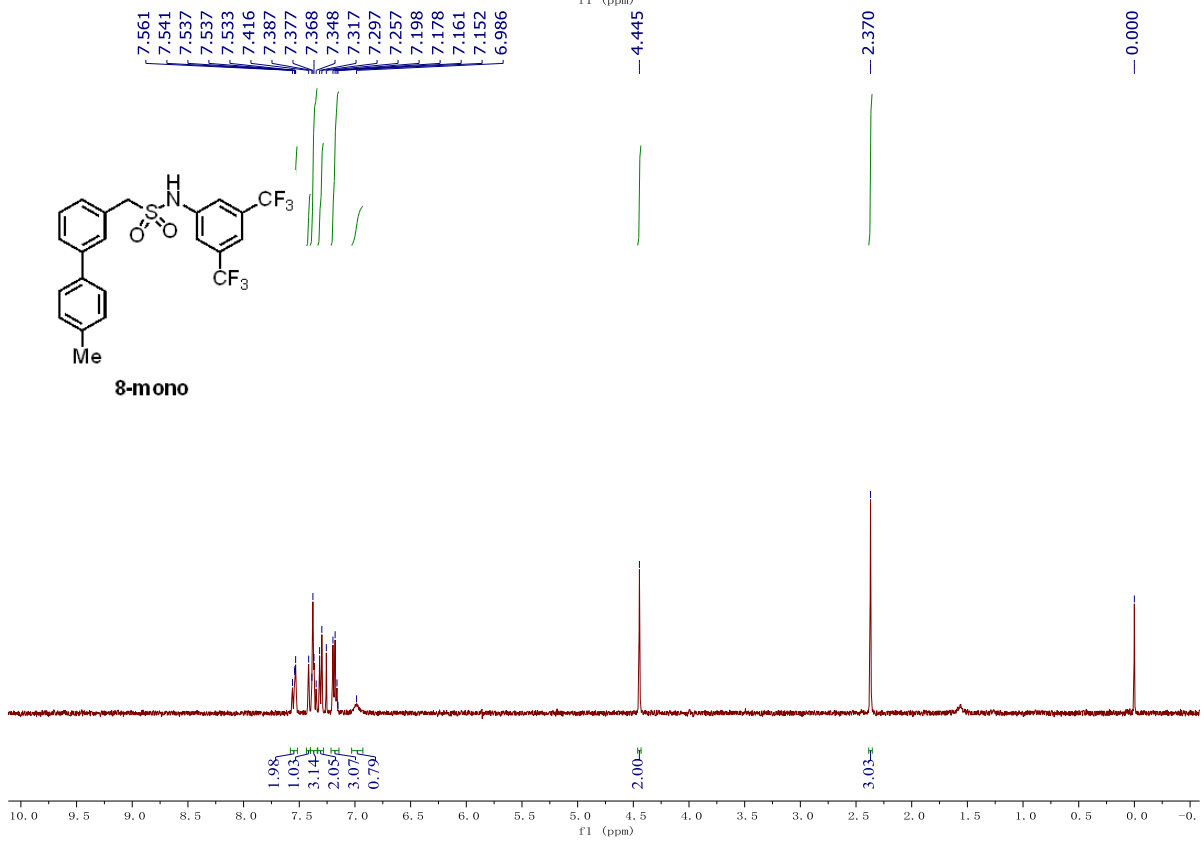
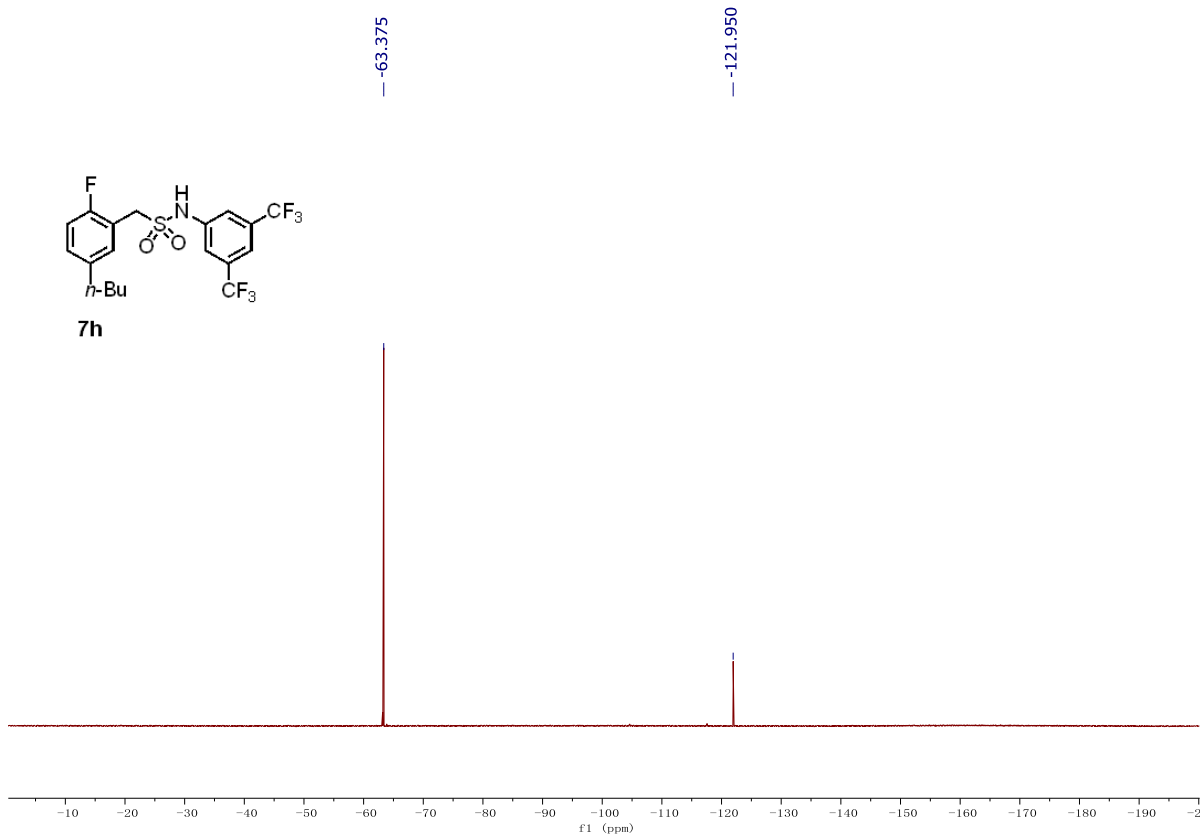


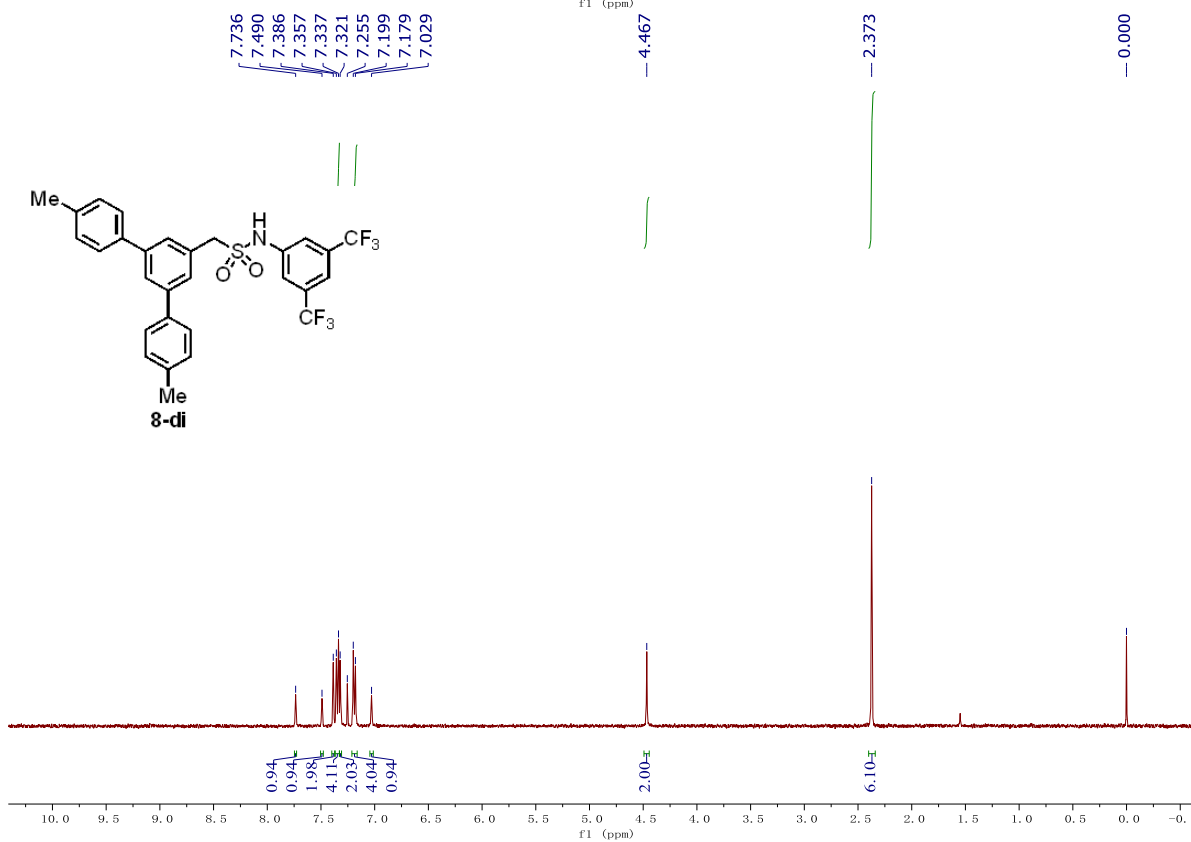
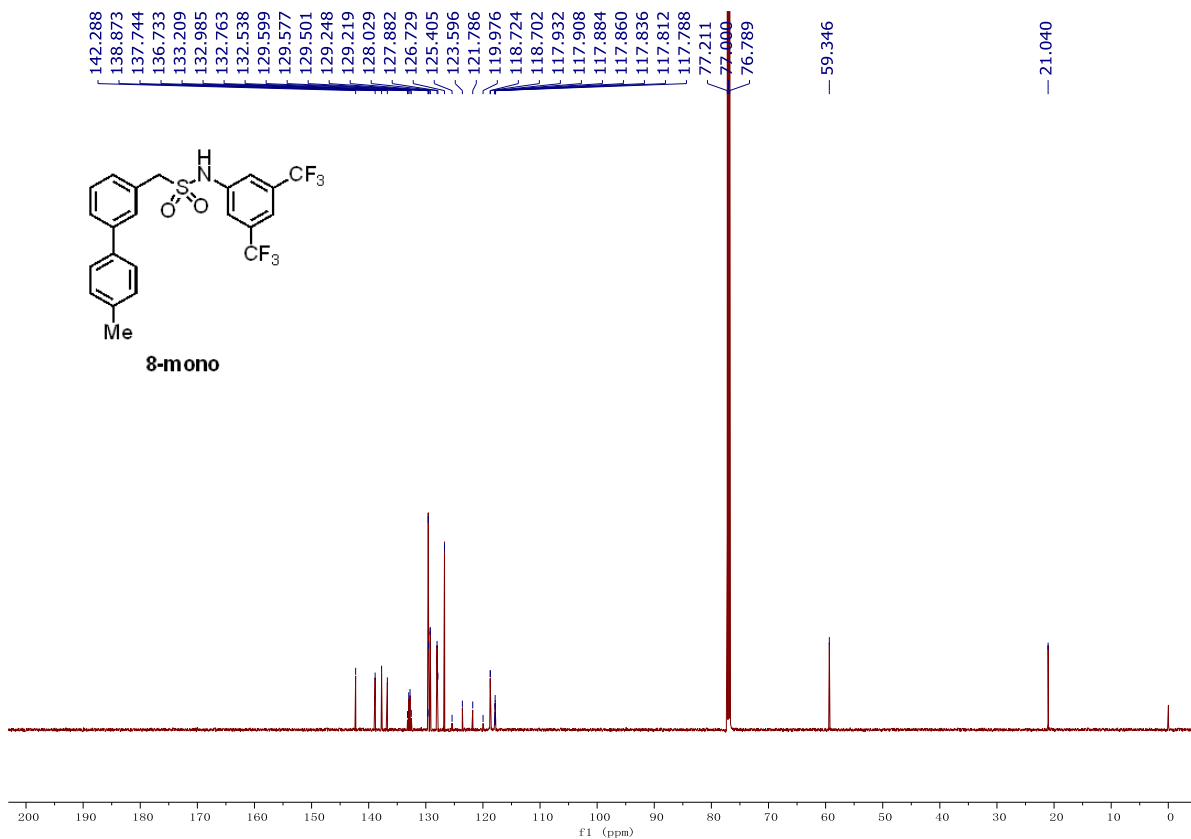




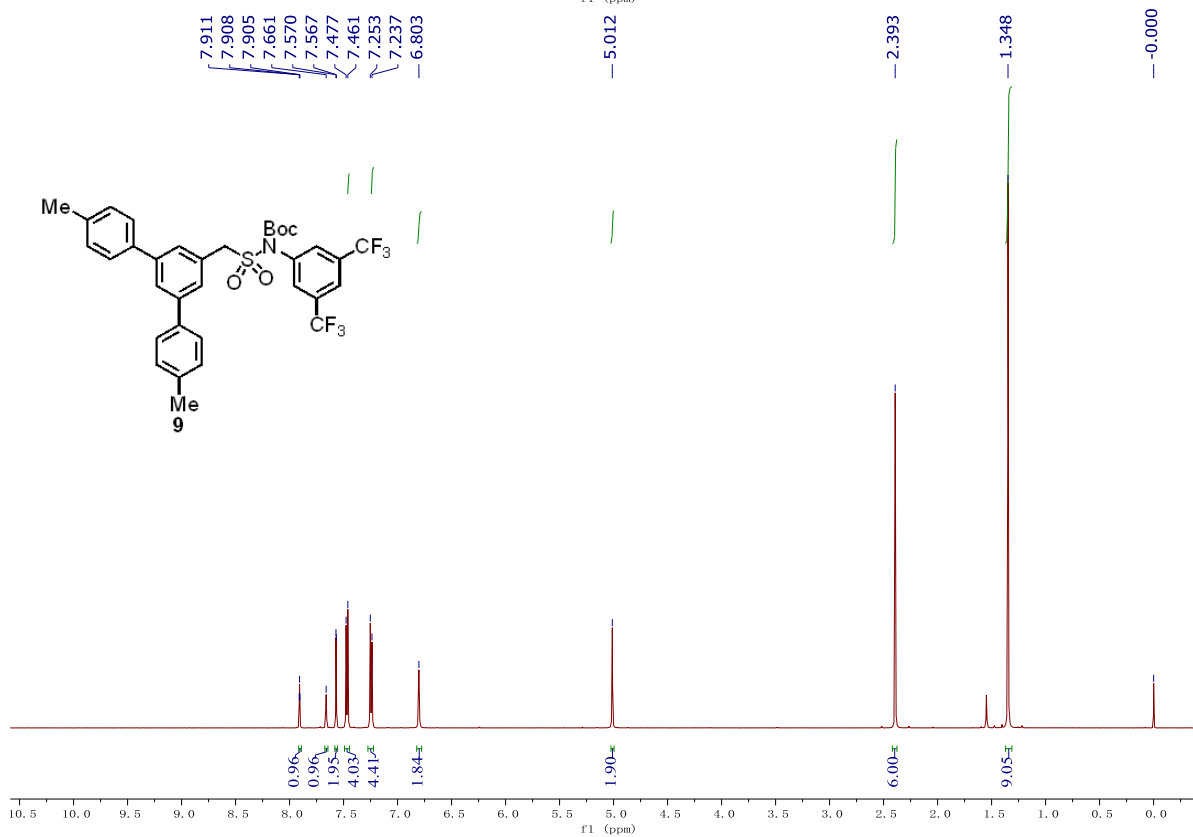
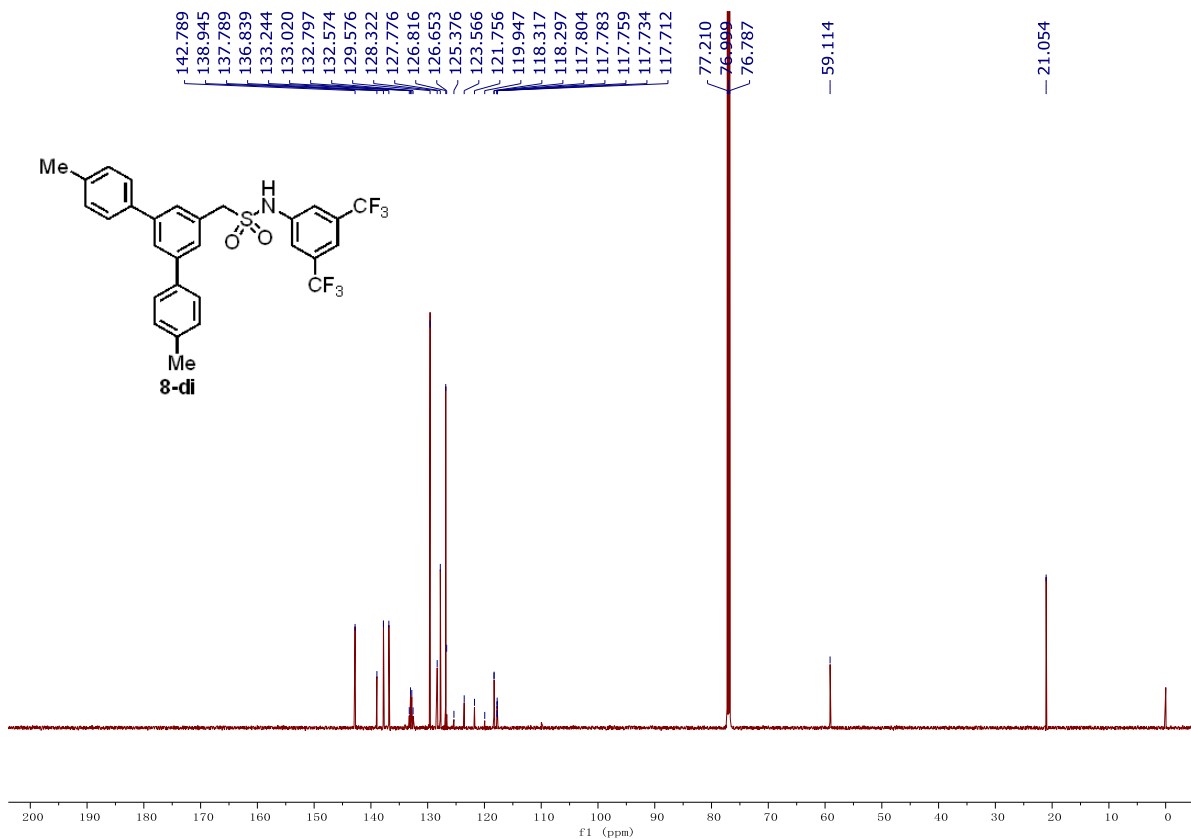


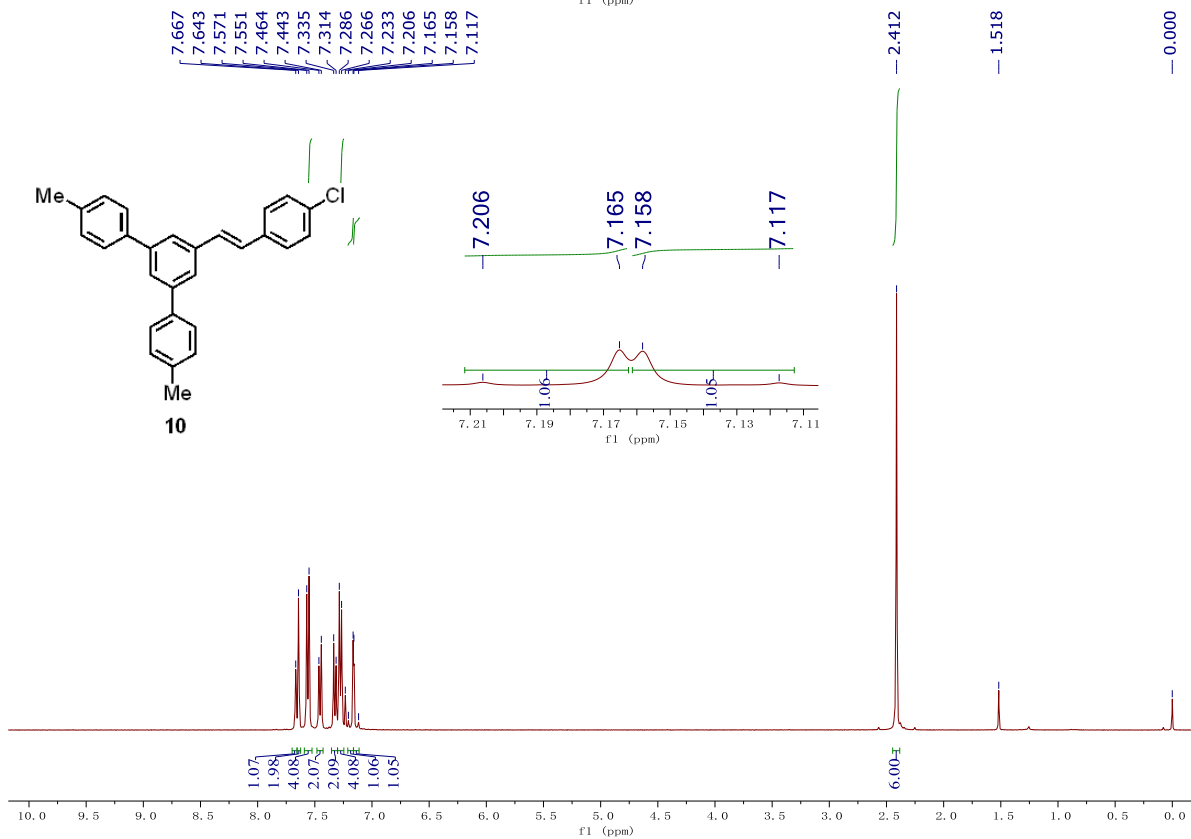
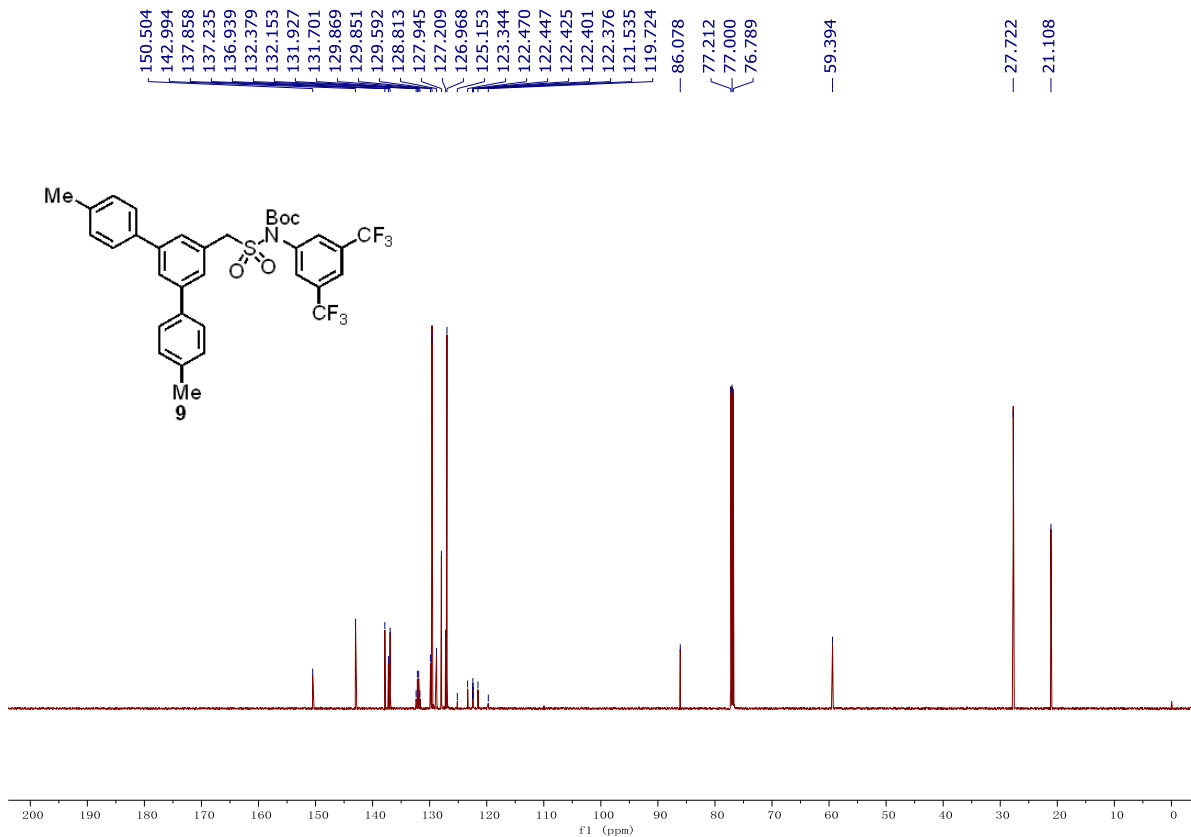


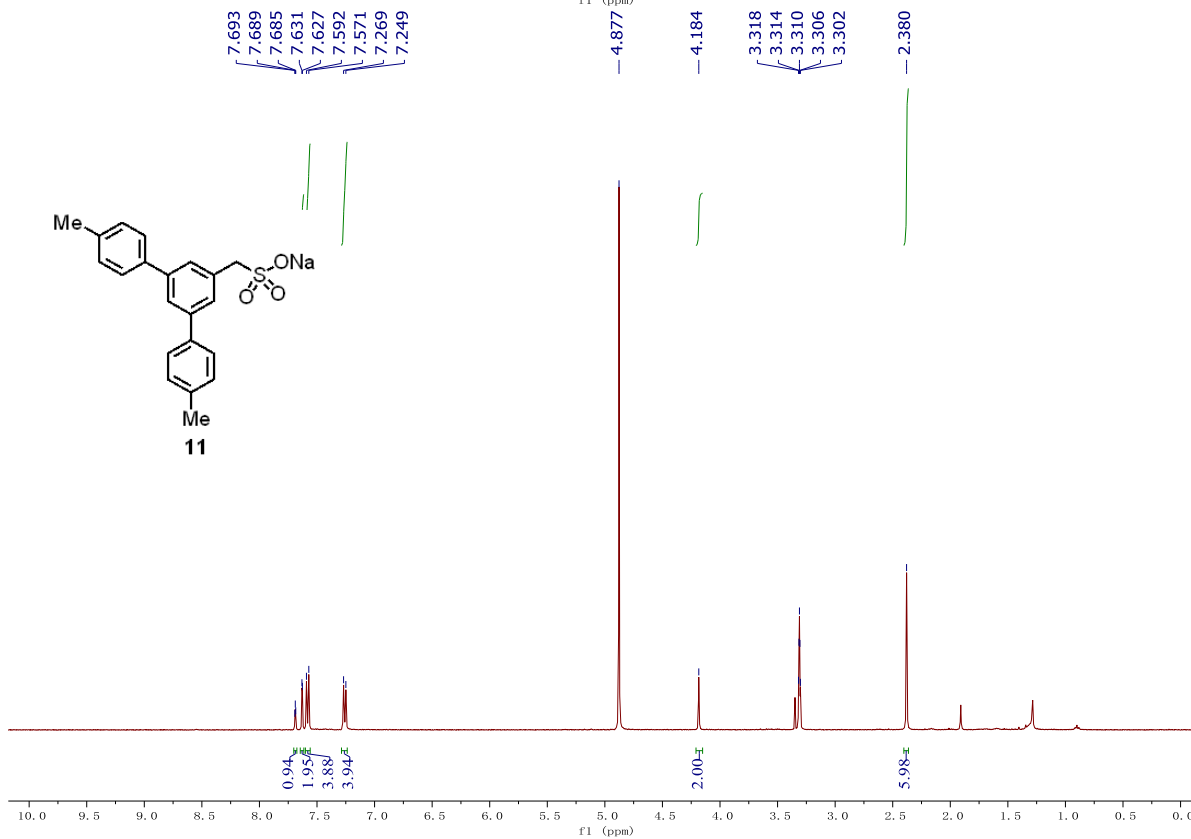
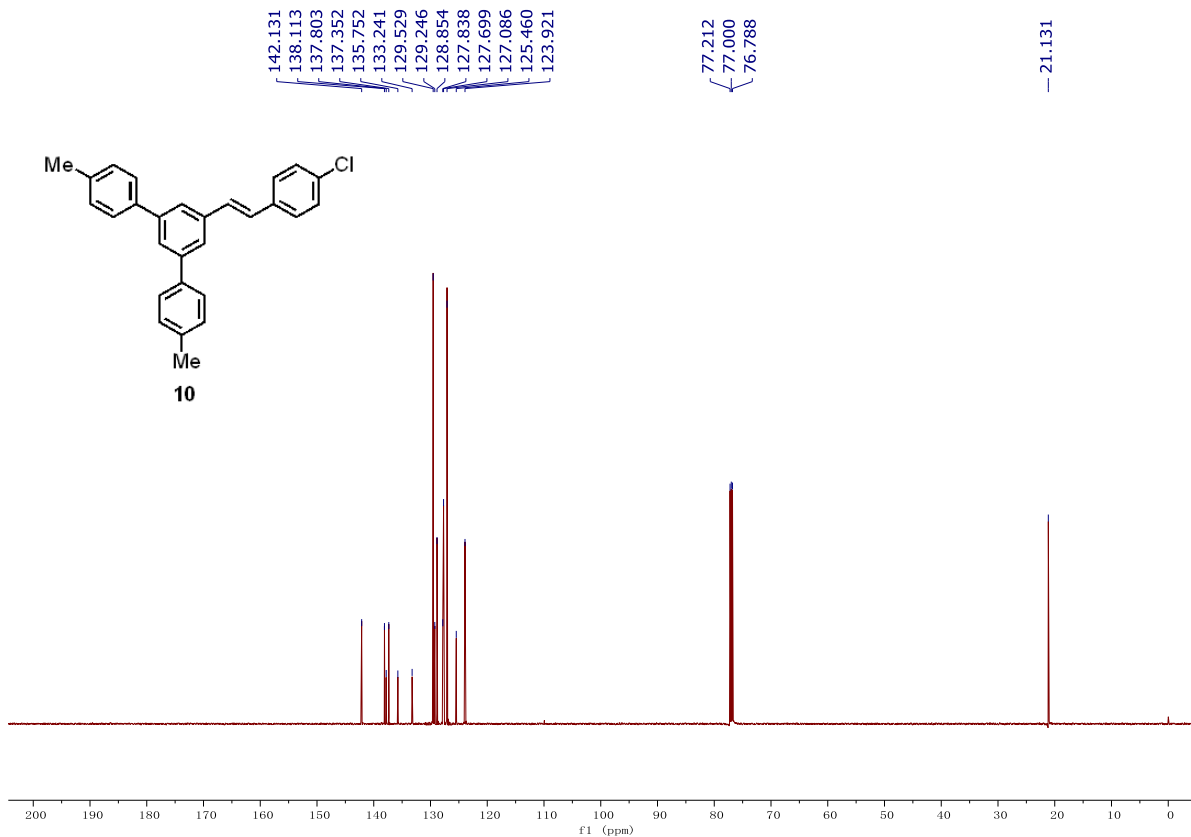


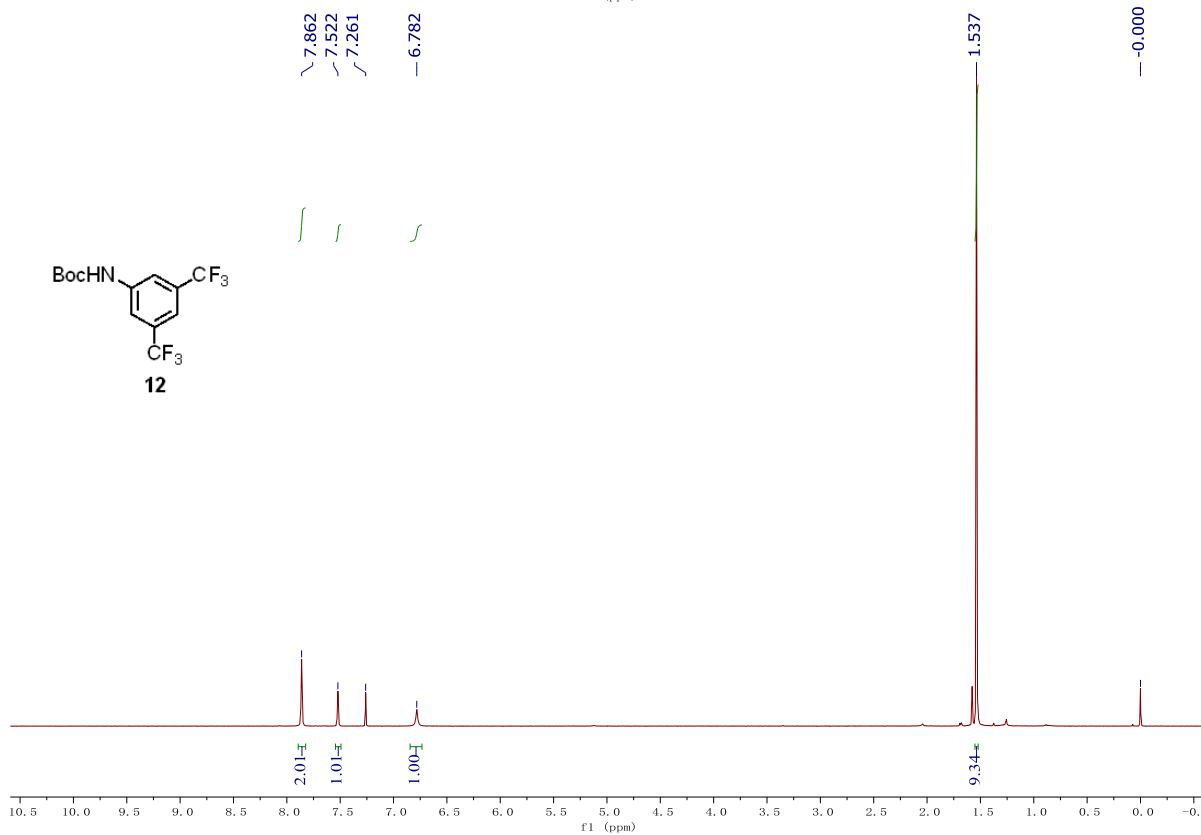
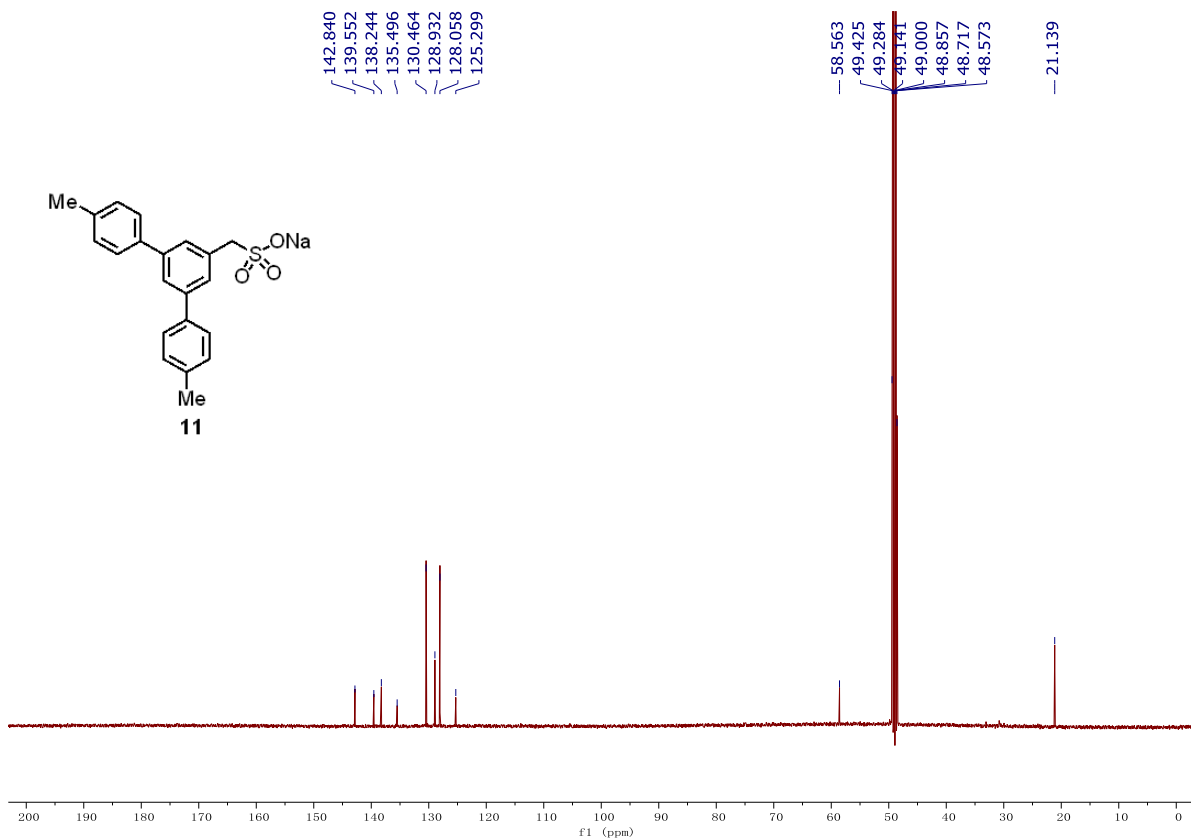


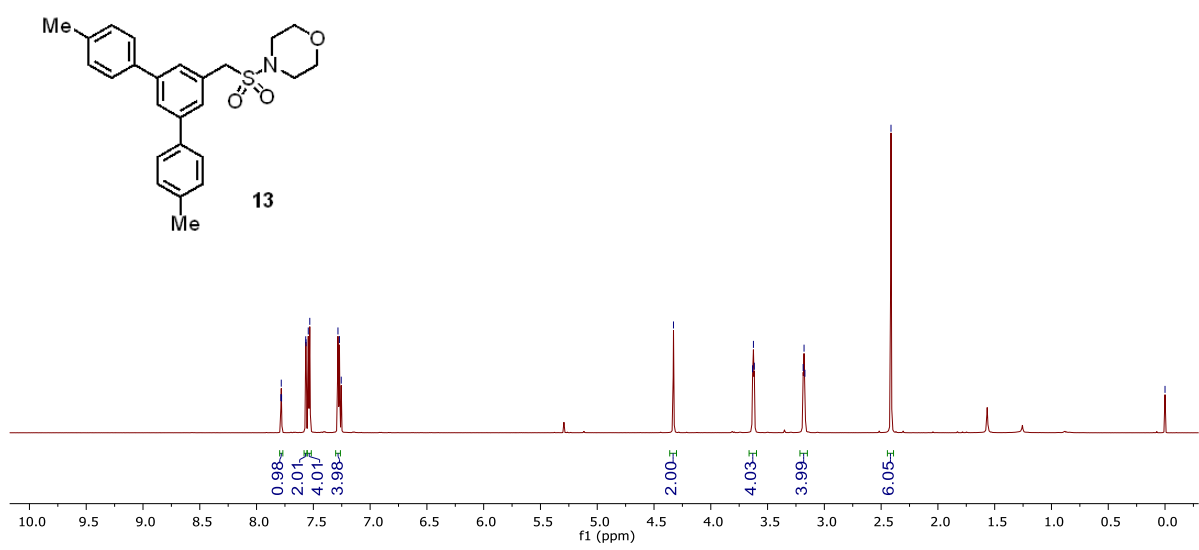
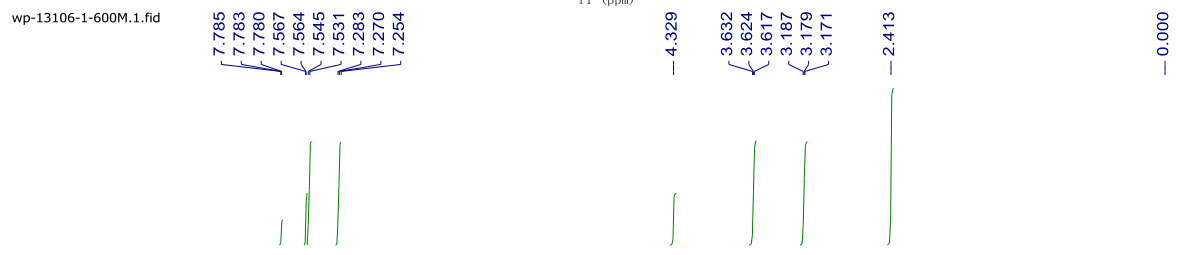
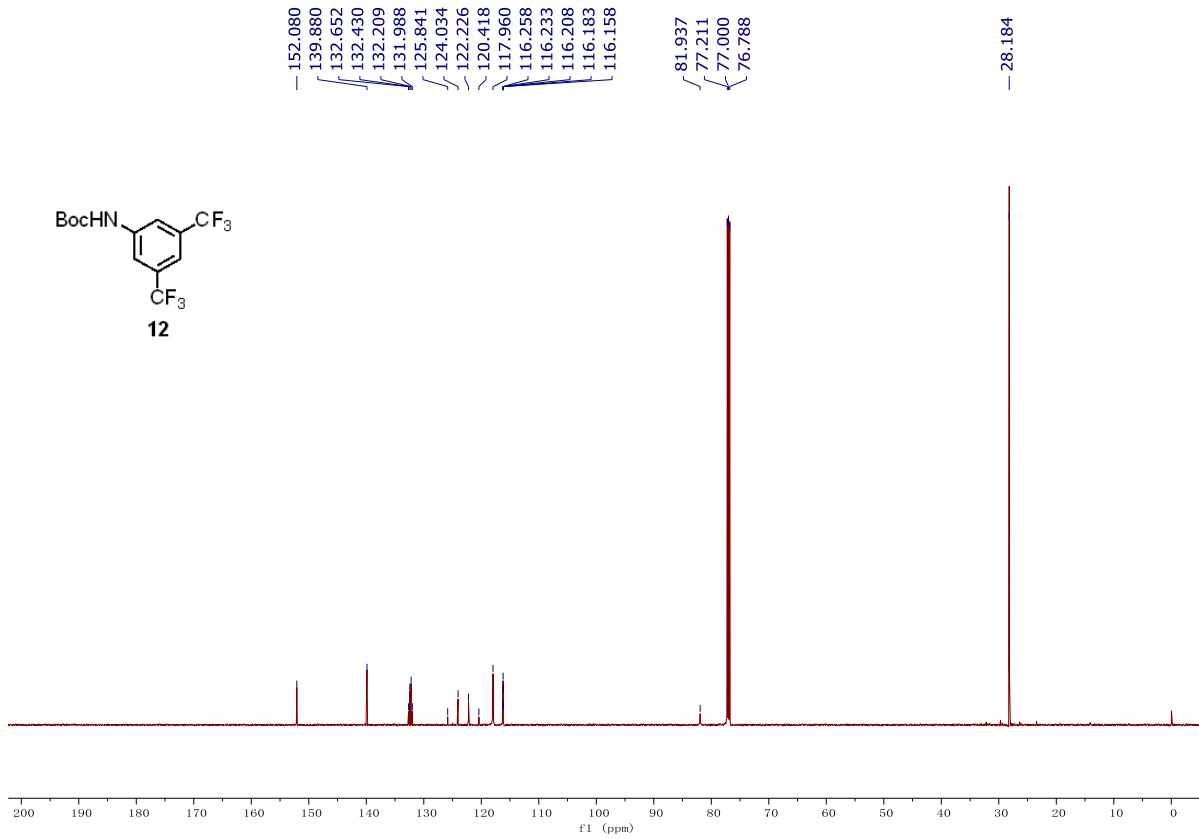












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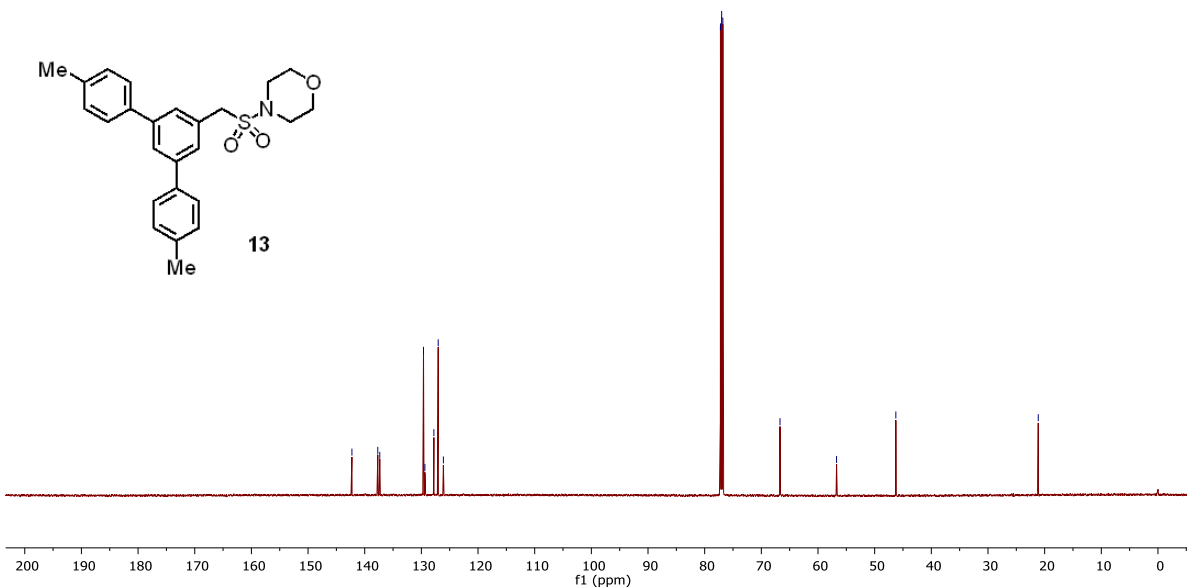
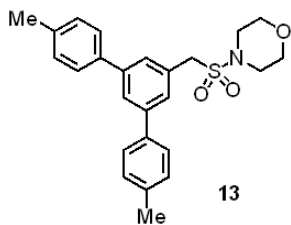
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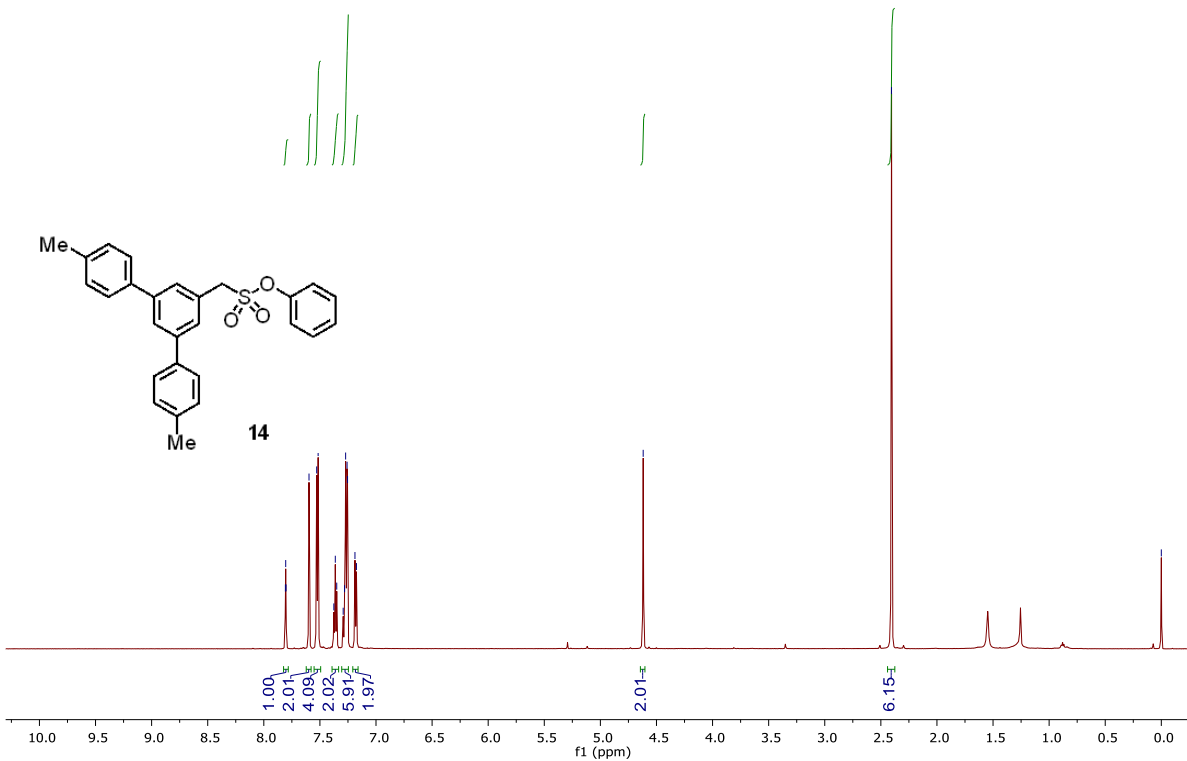
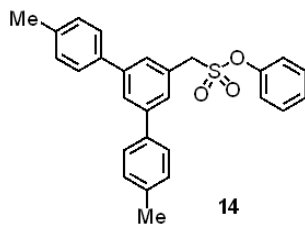
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