

# Supporting information

## Palladium-Catalyzed Carbonylative Synthesis of 5-Trifluoromethyl-1,2,4-triazoles from Trifluoroacetimidohydrazides and Aryl Iodides

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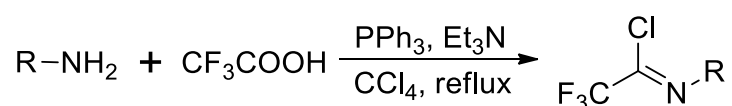
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## 1. General Information

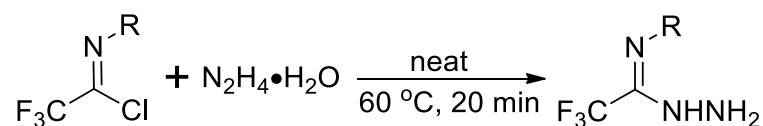
Unless otherwise noted, all reactions were carried out under N<sub>2</sub> atmosphere. All reagents were from commercial sources and used as received without further purification. All solvents were dried by standard techniques and distilled prior to use. Column chromatography was performed on silica gel (200-300 meshes) using petroleum ether (bp. 60~90 °C) and ethyl acetate as eluent. <sup>1</sup>H NMR spectra were recorded on a Bruker Avance operating at for <sup>1</sup>H NMR at 400 MHz, <sup>13</sup>C NMR at 100 MHz and <sup>19</sup>F NMR at 377 MHz and spectral data were reported in ppm relative to tetramethylsilane (TMS) as internal standard and CDCl<sub>3</sub> (<sup>1</sup>H NMR δ 7.26, <sup>13</sup>C NMR δ 77.16) as solvent. All coupling constants (*J*) are reported in Hz. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, dd = double doublet, ddd = double doublet of doublets, t = triplet, dt = double triplet, q = quatrimplet, m = multiplet, br = broad. Gas chromatography (GC) analyses were performed on a Shimadzu GC-2014C chromatograph equipped with a FID detector. Mass spectra (MS) were measured on spectrometer by direct inlet at 70 eV. Mass spectroscopy data of the products were collected on an HRMS-TOF instrument or Waters TOFMS GCT Premier using EI or ESI ionization. Melting points were measured with WRR digital point apparatus and not corrected.

### 1.1 Preparation of Fluorinated Imidoyl Chlorides<sup>1</sup>



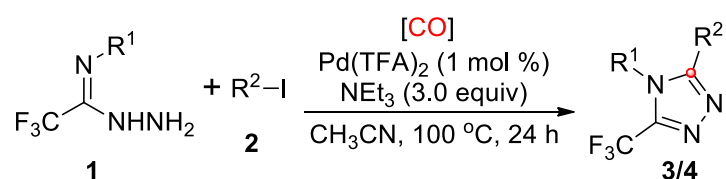
A 200 mL two-necked flask equipped with a septum cap, a condenser, and a Tefloncoated magnetic stir bar was charged with PPh<sub>3</sub> (34.5 g, 132 mmol), Et<sub>3</sub>N (7.3 mL, 53 mmol), CCl<sub>4</sub> (21.1 mL, 220 mmol), and TFA (3.4 mL, 44 mmol). After the solution was stirred for about 10 min (ice bath), amine (53 mmol) dissolved in CCl<sub>4</sub> (21.1 mL, 220 mmol) was added. The mixture was then refluxed under stirring for 3 h. After the reaction was completed, residual solid Ph<sub>3</sub>PO, PPh<sub>3</sub> and Et<sub>3</sub>N-HCl were washed with hexane several times. Then the hexane was filtered and concentrated under vacuum. The crude product was purified by column chromatography on silica gel or neutral alumina to afford the corresponding product.

## 1.2 Preparation of Trifluoroacetimidohydrazides



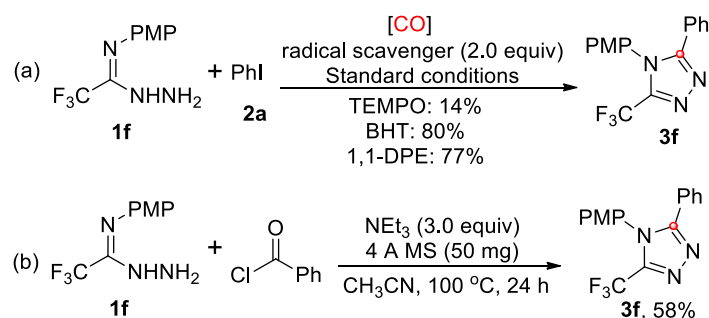
A 15 mL *In-Ex* tube equipped with a diaphragm cover, a condenser and a Teflon-coated magnetic stir bar was charged with trifluoroacetimidoyl chloride (3.0 mmol) and hydrazine hydrate 80% (0.375 g, 6.0 mmol). The solution was stirred at 60 °C for about 20 minutes. The crude product is then purified directly by column chromatography on silica gel or neutral alumina to obtain the corresponding trifluoroacetimidohydrazide product in almost quantitative yield.

## 2. General Procedure for the Synthesis of 5-Trifluoromethyl-1,2,4-triazoles



Under nitrogen atmosphere, **1** (0.3 mmol, 1.0 equiv.), **2** (0.45 mmol, 1.5 equiv.), 4 Å MS (50 mg), TFBen (1.5 mmol, 5 equiv, 315 mg), Pd(TFA)<sub>2</sub> (0.003 mmol, 1 mol %, 0.99 mg), NEt<sub>3</sub> (0.9 mmol, 3.0 equiv, 90.9 mg), CH<sub>3</sub>CN (2 mL) (extra dry) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 100 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3 × 10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc) to yield the 5-trifluoromethyl-1,2,4-triazole products **3** or **4**.

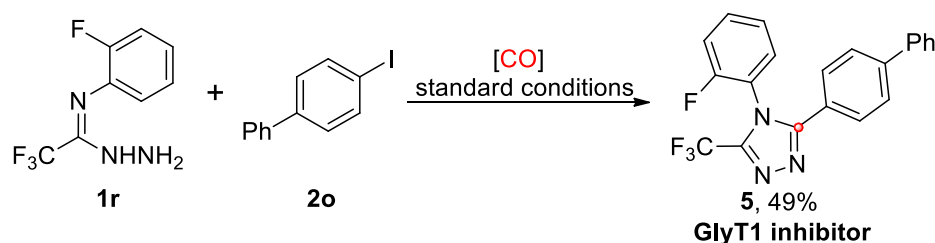
## 3. Control Experiments



**Eq a.** Under nitrogen atmosphere, **1f** (0.3 mmol, 1.0 equiv, 56.4 mg), **2a** (0.45 mmol, 1.5 equiv, 91.8 mg), 4 Å MS (50 mg), TFBen (1.5 mmol, 5 equiv, 315 mg), Pd(TFA)<sub>2</sub> (0.003 mmol, 1 mol %, 0.99 mg), NEt<sub>3</sub> (0.9 mmol, 3.0 equiv, 90.9 mg), CH<sub>3</sub>CN (2 mL) (extra dry) were added to an oven-dried 15 mL *In-Ex* tube. BHT (0.6 mmol, 2.0 equiv, 132.2 mg), TEMPO (0.6 mmol, 2.0 equiv, 93.6 mg) or 1,1-DPE (0.6 mmol, 2.0 equiv, 108 mg). Then the tube was sealed and the mixture was stirred at 100 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3 × 10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 3:1) to yield the 5-trifluoromethyl-1,2,4-triazole product **3f** in 14% yield (TEMPO), 80% yield (BHT), or 77% yield (1,1-DPE), respectively.

**Eq b.** Under nitrogen atmosphere, **1f** (0.3 mmol, 1.0 equiv, 56.4 mg), benzoyl chloride (0.45 mmol, 1.5 equiv, 63 mg), 4 Å MS (50 mg), NEt<sub>3</sub> (0.9 mmol, 3.0 equiv, 90.9 mg), CH<sub>3</sub>CN (2 mL) (extra dry) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 100 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3 × 10 mL). The extract was combined and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 3:1) to yield the 5-trifluoromethyl-1,2,4-triazole product **3f** in 58% yield.

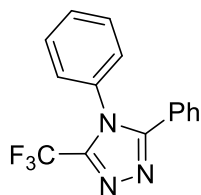
#### 4. Synthetic Application for the Synthesis of GlyT1 Inhibitor



Under nitrogen atmosphere, **1r** (0.3 mmol, 1.0 equiv, 66.3 mg), **2o** (0.45 mmol, 1.5 equiv, 126 mg), 4 Å MS (50 mg), TFBen (1.5 mmol, 5 equiv, 315 mg), Pd(TFA)<sub>2</sub> (0.003 mmol, 1 mol %, 0.99 mg), NEt<sub>3</sub> (0.9 mmol, 3.0 equiv, 90.9 mg), CH<sub>3</sub>CN (2 mL) (extra dry) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 100 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3 × 10 mL). The extract was combined and concentrated under vacuum. The

residue was purified by column chromatography on silica gel (petroleum ether/EtOAc) to yield the 5-trifluoromethyl-1,2,4-triazole product **5** as a white solid (56.3 mg, 49%).

## 5 Characterization Data of the Corresponding Products



3,4-diphenyl-5-(trifluoromethyl)-4H-1,2,4-triazole (**3a**)<sup>2</sup>

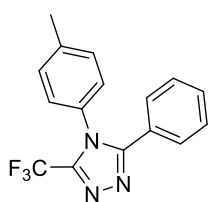
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, R<sub>f</sub> = 0.3) to give the titled product **3a** as a white solid (44.4 mg, 51%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.57 (t, *J* = 7.3 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 2H), 7.45 – 7.34 (m, 3H), 7.31 (d, *J* = 4.7 Hz, 2H), 7.29 (d, *J* = 4.5 Hz, 2H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.7, 145.8 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> 38.8 Hz), 133.1, 130.7, 130.6, 130.0, 128.7, 128.6, 127.4, 125.2, 118.1 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.2 Hz).

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -68.2.

M.p. 118.4-120.3°C



3-phenyl-4-(p-tolyl)-5-(trifluoromethyl)-4H-1,2,4-triazole (**3b**)<sup>2</sup>

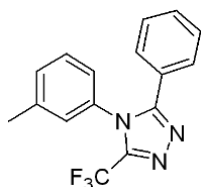
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, R<sub>f</sub> = 0.3) to give the titled product **3b** as a white solid (74.5 mg, 82%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.43 (d, *J* = 8.1 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.33 – 7.27 (m, 4H), 7.15 (d, *J* = 8.0 Hz, 2H), 2.43 (s, 3H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.7, 145.8 (C-F, q, <sup>2</sup>J<sub>(C-F)</sub> = 38.6 Hz), 141.0, 130.5, 130.3, 128.6, 128.6, 127.0, 125.3, 118.1 (C-F, q, <sup>1</sup>J<sub>(C-F)</sub> = 271.2 Hz), 21.3.

<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>) δ -61.0.

**M.p.** 160.8-161.5°C



3-Phenyl-4-(m-tolyl)-5-(trifluoromethyl)-4H-1,2,4-triazole (**3c**)<sup>2</sup>

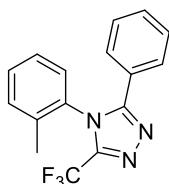
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R<sub>f</sub> = 0.4) to give the titled product **3c** as a white solid (62.7 mg, 69%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.44 (d, *J* = 7.2 Hz, 2H), 7.41 – 7.34 (m, 3H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.08 (d, *J* = 6.4 Hz, 2H), 2.39 (s, 3H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.6, 145.7 (C-F, q, <sup>2</sup>J<sub>(C-F)</sub> = 39.0 Hz), 140.3, 133.0, 131.5, 130.5, 129.6, 128.6, 127.7, 125.3, 124.4, 118.1 (C-F, q, <sup>1</sup>J<sub>(C-F)</sub> = 271.0 Hz), 21.2.

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -68.2.

**M.p.** 188.7-190.4 °C.



3-phenyl-4-(o-tolyl)-5-(trifluoromethyl)-4H-1,2,4-triazole (**3d**)<sup>2</sup>

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R<sub>f</sub> = 0.3) to give the titled product **3d** as a white solid (76.4 mg, 84%).

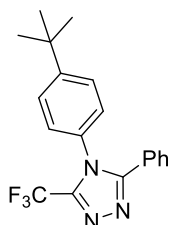
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.51 – 7.43 (m, 1H), 7.43 – 7.35 (m, 1H), 7.30 (dd, *J* = 15.2, 7.5 Hz, 1H), 1.88 (s, 1H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.3, 145.5 (C-F, q, <sup>2</sup>J<sub>(C-F)</sub> = 38.9 Hz), 135.6, 132.0, 131.6, 131.1, 130.7, 128.7, 128.0, 128.0, 127.4, 125.5, 118.1 (C-F, q, <sup>1</sup>J<sub>(C-F)</sub> = 271.3 Hz), 16.99.

<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>) δ -60.6.

M.p. 148.5-149.3 °C.

HRMS (ESI): [M+H]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>13</sub>F<sub>3</sub>N<sub>3</sub><sup>+</sup> 304.1056, found 304.1069.



4-(4-(tert-butyl)phenyl)-3-phenyl-5-(trifluoromethyl)-4H-1,2,4-triazole (**3e**)<sup>2</sup>

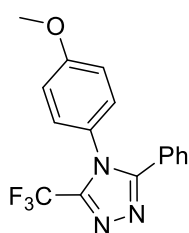
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, R<sub>f</sub> = 0.3) to give the titled product **3e** as a white solid (57.9 mg, 56%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.50 (d, *J* = 8.5 Hz, 2H), 7.45 – 7.40 (m, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 1.32 (d, *J* = 27.3 Hz, 9H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.7, 154.1, 145.7 (C-F, q, <sup>2</sup>J<sub>(C-F)</sub> = 38.7 Hz), 130.4, 130.1, 128.6, 128.5, 126.7, 125.3, 118.1 (C-F, q, <sup>1</sup>J<sub>(C-F)</sub> = 271.1 Hz), 34.9, 31.1.

<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>) δ -61.0.

M.p. 149.6-150.5 °C.



4-(4-methoxyphenyl)-3-phenyl-5-(trifluoromethyl)-4H-1,2,4-triazole (**3f**)<sup>2</sup>

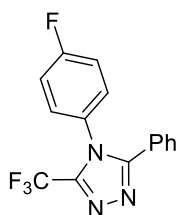
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, Rf = 0.3) to give the titled product **3f** as a white solid (76.6 mg, 80%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.44 (d, *J* = 8.2 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.29 (t, *J* = 7.8 Hz, 2H), 7.18 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 160.9, 156.8, 145.9 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 38.7 Hz), 130.5, 128.6, 128.5, 125.3, 125.2, 118.1 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.3 Hz), 115.0, 55.5.

**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -68.4.

**M.p.** 154.1-155.2 °C.



4-(4-fluorophenyl)-3-phenyl-5-(trifluoromethyl)-4H-1,2,4-triazole (**3g**)<sup>2</sup>

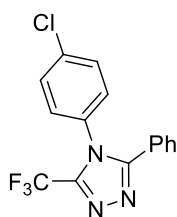
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, Rf = 0.3) to give the titled product **3g** as a white solid (86.6 mg, 94%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.44 – 7.38 (m, 3H), 7.35 – 7.27 (m, 3H), 7.24 – 7.17 (m, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 163.4 (C-F, d, <sup>1</sup>*J*<sub>(C-F)</sub> = 252.8 Hz), 156.8, 145.8 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 38.5 Hz), 130.8, 129.4 (C-F, d, <sup>3</sup>*J*<sub>(C-F)</sub> = 9.0 Hz), 129.0, 128.7 (C-F, d, <sup>4</sup>*J*<sub>(C-F)</sub> = 5.7 Hz), 125.0, 118.1 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.1 Hz), 117.2, 117.2 (C-F, d, <sup>2</sup>*J*<sub>(C-F)</sub> = 23.3 Hz).

**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -61.0, -108.2.

**M.p.** 171.7-172.6 °C





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4-(4-chlorophenyl)-3-phenyl-5-(trifluoromethyl)-4H-1,2,4-triazole (**3h**)<sup>2</sup>

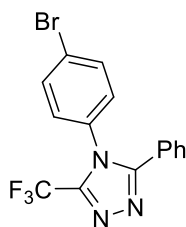
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, Rf = 0.3) to give the titled product **3h** as a white solid (75.6 mg, 78%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.50 (d, *J* = 8.7 Hz, 2H), 7.45 – 7.38 (m, 3H), 7.37 – 7.30 (m, 2H), 7.25 (d, *J* = 8.6 Hz, 2H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.6, 145.6 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 39.0 Hz), 137.0, 131.5, 130.8, 130.3, 128.8, 128.7, 128.7, 124.9, 118.0 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.3 Hz).

<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>) δ -68.1.

**M.p.** 182.2-184.0 °C



4-(4-bromophenyl)-3-phenyl-5-(trifluoromethyl)-4H-1,2,4-triazole (**3i**)<sup>2</sup>

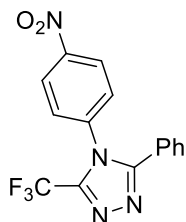
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, Rf = 0.3) to give the titled product **3i** as a white solid (91.4 mg, 83%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.64 (d, *J* = 8.7 Hz, 2H), 7.43 – 7.38 (m, 3H), 7.32 (dd, *J* = 7.9, 7.2 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.6, 145.5 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 39.7Hz), 133.3, 132.0, 130.8, 128.9, 128.8, 128.7, 125.1, 124.9, 118.0 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.3 Hz).

<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>) δ -60.6.

**M.p.** 176.5-178.1 °C;



4-(4-nitrophenyl)-3-phenyl-5-(trifluoromethyl)-4H-1,2,4-triazole (**3j**)<sup>2</sup>

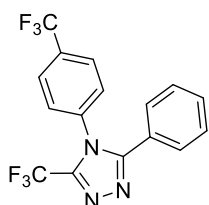
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, R<sub>f</sub> = 0.6) to give the titled product **3j** as a yellow solid (81.2 mg, 81%).

<sup>1</sup>H NMR (400 MHz, DMSO) δ 8.38 (d, *J* = 9.1 Hz, 2H), 7.80 (d, *J* = 9.1 Hz, 2H), 7.56 – 7.50 (m, 3H), 7.47 (dd, *J* = 10.1, 4.8 Hz, 2H).

<sup>13</sup>C NMR (101 MHz, DMSO) δ 156.34, 152.5 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 39.0 Hz), 147.7, 141.6, 131.2, 129.2, 128.9, 127.1, 125.9, 125.0, 119.2 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 269.9 Hz), 39.5.

<sup>19</sup>F NMR (377 MHz, DMSO) δ -59.5.

**M.p.** 155.2-157.3°C



3-phenyl-5-(trifluoromethyl)-4-(4-(trifluoromethyl)phenyl)-4H-1,2,4-triazole (**3k**)<sup>2</sup>

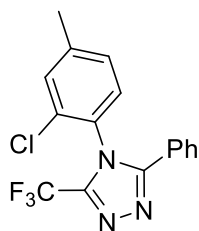
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, R<sub>f</sub> = 0.3) to give the titled product **3k** as a white solid (84.6 mg, 79%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.52 – 7.41 (m, 5H), 7.40 – 7.34 (m, 2H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.6, 145.5 (C-F, q, <sup>4</sup>*J*<sub>(C-F)</sub> = 39.3 Hz), 136.1, 132.9 (C-F, q, <sup>3</sup>*J*<sub>(C-F)</sub> = 33.5 Hz), 131.0, 128.9, 128.8, 128.1, 127.3, 124.7, 123.1 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 272.9 Hz), 118.0 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.2 Hz).

<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>) δ -60.5.

**M.p.** 139.2-141.3 °C.



4-(2-chloro-4-methylphenyl)-3-phenyl-5-(trifluoromethyl)-4H-1,2,4-triazole (**3l**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, Rf = 0.4) to give the titled product **3l** as a white solid (78.5 mg, 81%).

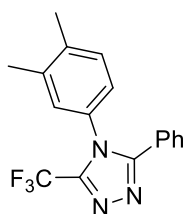
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.50 – 7.46 (m, 2H), 7.44 – 7.38 (m, 2H), 7.32 (t, *J* = 7.5 Hz, 3H), 7.27 – 7.24 (m, 1H), 2.41 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 156.5, 145.4 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 39.2 Hz), 138.8, 133.1, 130.8, 130.5, 130.4, 129.8, 129.5, 128.7, 128.2, 125.3, 118.0 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.4 Hz), 20.8.

**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -62.0.

**M.p.** 165.8-167.8 °C

**HRMS (ESI):** [M+H]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>12</sub>ClF<sub>3</sub>N<sub>3</sub><sup>+</sup> 338.0666, found 338.0672.



4-(3,4-dimethylphenyl)-3-phenyl-5-(trifluoromethyl)-4H-1,2,4-triazole (**3m**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, Rf = 0.3) to give the titled product **3m** as a white solid (85.6 mg, 90%).

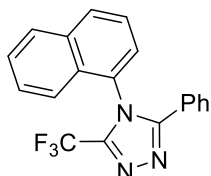
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.49 – 7.44 (m, 2H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.07 – 6.97 (m, 2H), 2.34 (s, 3H), 2.28 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 156.6, 145.9 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 38.4 Hz), 139.7, 138.7, 130.8, 130.5, 130.5, 128.6, 128.6, 127.9, 125.5, 124.6, 118.2 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.0 Hz), 19.8, 19.7.

<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>) δ -60.9.

M.p. 115.5-117.4 °C;

HRMS (ESI): [M+H]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>15</sub>F<sub>3</sub>N<sub>3</sub><sup>+</sup> 318.1213, found 318.1220.



4-(naphthalen-1-yl)-3-phenyl-5-(trifluoromethyl)-4H-1,2,4-triazole (**3n**)<sup>2</sup>

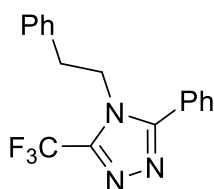
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, R<sub>f</sub> = 0.2) to give the titled product **3n** as a white solid (87.5 mg, 86%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.08 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.54 (ddt, *J* = 16.6, 8.1, 4.2 Hz, 5H), 7.42 – 7.36 (m, 2H), 7.31 – 7.27 (m, 1H), 7.20 (d, *J* = 8.4 Hz, 1H), 7.15 (t, *J* = 7.7 Hz, 2H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 157.3, 146.5 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 38.9 Hz), 131.5, 130.6, 129.7, 129.3, 128.6, 128.6, 128.5, 128.0, 127.4, 126.3, 125.3, 125.0, 121.4, 118.1 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.5 Hz).

<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>) δ -61.7.

M.p. 170.2-171.8 °C;



4-phenethyl-3-phenyl-5-(trifluoromethyl)-4H-1,2,4-triazole (**3o**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, R<sub>f</sub> = 0.3) to give the titled product **3o** as a white solid (61.8 mg, 65%).

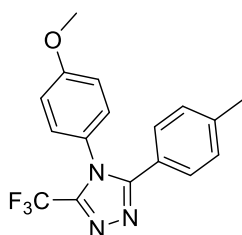
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.55 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.44 – 7.38 (m, 2H), 7.19 (dd, *J* = 4.9, 1.8 Hz, 3H), 6.84 (dd, *J* = 6.4, 3.0 Hz, 2H), 4.46 – 4.23 (m, 2H), 2.98 – 2.83 (m, 2H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 157.3, 144.7 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 39.2 Hz), 135.4, 130.7, 129.0, 128.8, 128.4, 127.3, 125.6, 118.6 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 270.9 Hz), 46.6, 36.5.

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)** δ -69.1.

**M.p.** 64.5-66.4 °C

**HRMS (ESI):** [M+H]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>15</sub>F<sub>3</sub>N<sub>3</sub><sup>+</sup> 318.1213, found 318.1218.



4-(4-methoxyphenyl)-3-(p-tolyl)-5-(trifluoromethyl)-4H-1,2,4-triazole (**4a**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, R<sub>f</sub> = 0.3) to give the titled product **4a** as a white solid (80.7 mg, 81%).

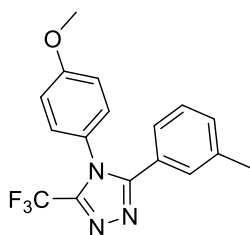
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.32 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 3.86 (s, 3H), 2.31 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 160.8, 156.9, 145.8 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 38.6 Hz) 140.8, 129.3, 128.5, 128.5, 125.4, 122.4, 118.2 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.1 Hz), 114.9, 55.5, 21.4.

**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -61.1.

**M.p.** 133.6 - 135.6 °C

**HRMS (ESI):** [M+H]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>15</sub>F<sub>3</sub>N<sub>3</sub>O<sup>+</sup> 334.1162, found 334.1170.



4-(4-methoxyphenyl)-3-(m-tolyl)-5-(trifluoromethyl)-4H-1,2,4-triazole (**4b**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate =3:1, Rf = 0.3) to give the titled product **4b** as a white solid (83.7 mg, 84%).

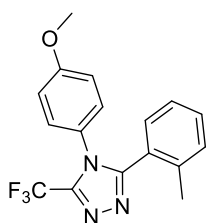
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.43 (s, 1H), 7.19 (d, *J* = 8.8 Hz, 3H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 8.9 Hz, 2H), 3.86 (s, 3H), 2.29 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 160.9, 157.0, 145.9 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 38.6 Hz), 138.6, 131.3, 129.6, 128.6, 128.4, 125.4, 125.2, 118.2 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.1 Hz), 114.9, 55.6, 21.2.

**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -61.1.

**M.p.** 113.7 - 115.6 °C

**HRMS (ESI):** [M+H]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>15</sub>F<sub>3</sub>N<sub>3</sub>O<sup>+</sup> 334.1162, found 334.1167.



4-(4-methoxyphenyl)-3-(o-tolyl)-5-(trifluoromethyl)-4H-1,2,4-triazole (**4c**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, Rf = 0.3) to give the titled product **4c** as a white solid (50.2 mg, 50%).

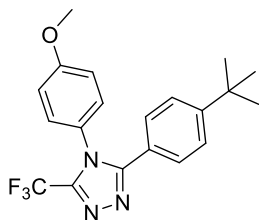
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.32 – 7.25 (m, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.13 – 7.10 (m, 2H), 7.07 (d, *J* = 8.9 Hz, 2H), 6.86 (d, *J* = 9.0 Hz, 2H), 3.79 (s, 3H), 2.24 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 160.5, 157.3, 145.3 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 39.2 Hz), 138.4, 130.6, 130.6, 130.55, 128.1, 125.6, 124.9, 124.9, 118.3 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.2 Hz), 114.6, 55.5, 20.0.

**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -61.1.

**M.p.** 105.1 - 107.0 °C

**HRMS (ESI):** [M+H]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>15</sub>F<sub>3</sub>N<sub>3</sub>O<sup>+</sup> 334.1162, found 334.1171.



3-(4-(tert-butyl)phenyl)-4-(4-methoxyphenyl)-5-(trifluoromethyl)-4H-1,2,4-triazole (**4d**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1,  $R_f$  = 0.3) to give the titled product **4d** as a white solid (110.0 mg, 98%).

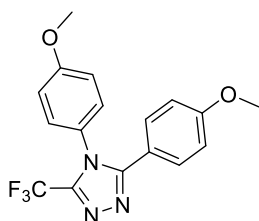
**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.39 (d,  $J$  = 8.7 Hz, 2H), 7.31 (d,  $J$  = 8.7 Hz, 2H), 7.21 (d,  $J$  = 8.9 Hz, 2H), 6.99 (d,  $J$  = 9.0 Hz, 2H), 3.87 (s, 3H), 1.26 (s, 9H).

**$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  160.9, 156.7, 153.9, 145.8 (C-F, q,  $^2J_{(\text{C-F})}$  = 38.5 Hz), 128.6, 128.2, 125.6, 125.5, 122.4, 118.6 (C-F, q,  $^1J_{(\text{C-F})}$  = 271.1 Hz), 115.0, 55.6, 34.8, 31.0.

**$^{19}\text{F}$  NMR (377 MHz,  $\text{CDCl}_3$ )**  $\delta$  -61.1.

**M.p.** 77.8 - 79.6 °C

**HRMS (ESI):**  $[\text{M}+\text{H}]^+$  calcd. for  $\text{C}_{20}\text{H}_{21}\text{F}_3\text{N}_3\text{O}^+$  376.1631, found 376.1637.



4-phenethyl-3-(trifluoromethyl)-4H-1,2,4-triazole (**4e**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1,  $R_f$  = 0.3) to give the titled product **4e** as a white solid (90.6 mg, 86%).

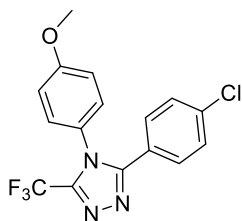
**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.97 (d,  $J$  = 8.6 Hz, 2H), 7.54 (d,  $J$  = 8.6 Hz, 2H), 7.20 (d,  $J$  = 8.9 Hz, 2H), 6.99 (d,  $J$  = 9.0 Hz, 2H), 3.90 (s, 1H), 3.87 (s, 2H).

**$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  161.2, 160.9, 156.7, 145.7 (C-F, q,  $^2J_{(\text{C-F})}$  = 38.3 Hz), 130.1, 128.6, 125.5, 117.6, 115.0, 118.2 (C-F, q,  $^1J_{(\text{C-F})}$  = 271.1 Hz), 114.1, 55.6, 55.3.

**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -61.1.

**M.p.** 160.5 - 162.3 °C

**HRMS (ESI):** [M+H]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>15</sub>F<sub>3</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> 350.1111, found 350.1107.



3-(chlorodifluoromethyl)-4-phenyl-4H-1,2,4-triazole (**4f**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, R<sub>f</sub> = 0.3) to give the titled product **4f** as a white solid (102.5 mg, 97%).

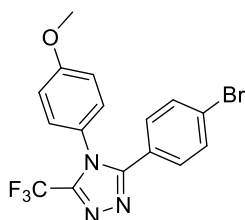
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.38 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.19 (d, *J* = 8.9 Hz, 2H), 6.99 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 161.1, 155.9, 146.1 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 38.9 Hz), 136.9, 129.8, 129.0, 128.5, 125.0, 123.8, 108.1 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.3 Hz), 115.2, 55.6.

**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -61.2.

**M.p.** 145.2 - 147.0 °C

**HRMS (ESI):** [M+H]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>12</sub>ClF<sub>3</sub>N<sub>3</sub>O<sup>+</sup> 354.0616, found 354.0621.



3-(4-bromophenyl)-4-(4-methoxyphenyl)-5-(trifluoromethyl)-4H-1,2,4-triazole (**4g**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, R<sub>f</sub> = 0.3) to give the titled product **4g** as a white solid (110.5 mg, 93%).

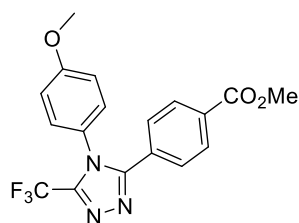


**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.44 (d, *J* = 8.6 Hz, 2H), 7.31 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 8.9 Hz, 2H), 6.99 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 161.0, 155.9, 146.1 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 38.8 Hz), 131.9, 130.0, 128.5, 125.3, 125.0, 124.3, 118.1 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 271.3 Hz), 115.2, 55.6.

**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -61.6.

**HRMS (ESI):** [M+H]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>12</sub>BrF<sub>3</sub>N<sub>3</sub>O<sup>+</sup> 398.0110, found 398.0112.



methyl 4-(4-(4-methoxyphenyl)-5-(trifluoromethyl)-4H-1,2,4-triazol-3-yl)benzoate (**4h**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, *R*<sub>f</sub> = 0.4) to give the titled product **4h** as a white solid (79.2 mg, 70%).

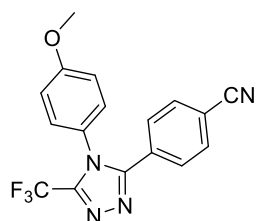
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.39 (d, *J* = 8.9 Hz, 2H), 7.19 (d, *J* = 8.9 Hz, 2H), 6.99 (d, *J* = 8.9 Hz, 2H), 6.81 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H), 3.78 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 166.1, 161.1, 155.9, 146.3 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 39.0 Hz), 131.8, 129.8, 129.5, 128.6, 128.5, 125.0, 118.1 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.4 Hz), 115.2, 55.6, 52.4.

**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -61.1.

**M.p.** 127.3 - 129.1 °C

**HRMS (ESI):** [M+H]<sup>+</sup> calcd. for C<sub>18</sub>H<sub>15</sub>F<sub>3</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> 378.1060, found 378.1075.



4-(4-(4-methoxyphenyl)-5-(trifluoromethyl)-4H-1,2,4-triazol-3-yl)benzotrile (**4i**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1, Rf = 0.5) to give the titled product **4i** as a white solid (76.4 mg, 74%).

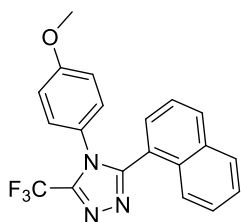
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.65 – 7.54 (m, 4H), 7.21 (d, *J* = 8.8 Hz, 2H), 7.02 (d, *J* = 8.9 Hz, 2H), 3.89 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 161.3, 155.0, 146.6 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 39.1 Hz), 132.4, 129.6, 129.0, 128.4, 124.6, 118.0 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 271.7 Hz), 117.8, 115.4, 114.3, 55.7.

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)** δ -68.4.

**M.p.** 210.3 - 212.1 °C

**HRMS (ESI):** [M+H]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>12</sub>F<sub>3</sub>N<sub>4</sub>O<sup>+</sup> 345.0958, found 345.0966.



4-(4-methoxyphenyl)-3-(naphthalen-1-yl)-5-(trifluoromethyl)-4H-1,2,4-triazole (**4j**)

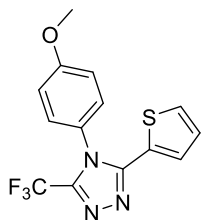
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, Rf = 0.3) to give the titled product **4j** as a yellow oil (59.8 mg, 54%).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.92 – 7.79 (m, 3H), 7.53 – 7.45 (m, 2H), 7.37 – 7.29 (m, 2H), 7.05 (d, *J* = 8.9 Hz, 2H), 6.73 (d, *J* = 8.9 Hz, 2H), 3.67 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 160.4, 156.5, 145.6 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 38.9 Hz), 133.3, 131.9, 131.0, 129.3, 128.3, 128.0, 127.3, 126.5, 124.9, 124.7, 124.4, 122.4, 118.2 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.3 Hz), 114.4, 55.3.

**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -61.0.

**HRMS (ESI):** [M+ H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>15</sub>F<sub>3</sub>N<sub>3</sub>O<sup>+</sup> 370.1162, found 370.1167.



4-(4-methoxyphenyl)-3-(thiophen-2-yl)-5-(trifluoromethyl)-4H-1,2,4-triazole (**4k**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 3:1,  $R_f = 0.3$ ) to give the titled product **4k** as a white solid (45.8 mg, 47%)

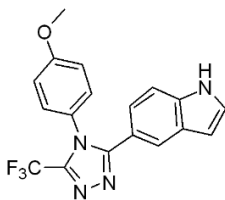
**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.38 (dd,  $J = 5.0, 1.1$  Hz, 1H), 7.28 (d,  $J = 8.9$  Hz, 2H), 7.08 – 7.03 (m, 3H), 6.96 (dd,  $J = 5.0, 3.8$  Hz, 1H), 3.92 (s, 3H).

**$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  161.5, 152.9, 145.6 (C-F, q,  $^2J_{\text{(C-F)}} = 39.1$  Hz), 129.4, 129.2, 129.1, 127.6, 126.5, 124.6, 118.1 (C-F, q,  $^1J_{\text{(C-F)}} = 271.0$  Hz), 115.2, 55.7.

**$^{19}\text{F}$  NMR (377 MHz,  $\text{CDCl}_3$ )**  $\delta$  -70.6.

**M.p.** 131.3 - 133.3 °C

**HRMS (ESI):**  $[\text{M} + \text{H}]^+$  calcd. for  $\text{C}_{14}\text{H}_{11}\text{F}_3\text{N}_3\text{OS}^+$  326.0569, found 326.0580.



4-(4-(4-methoxyphenyl)-5-(trifluoromethyl)-1,2,4-triazol-3-yl)-1H-indole (**4l**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 1:1,  $R_f = 0.2$ ) to give the titled product **4l** as a white solid (94.5 mg, 88%).

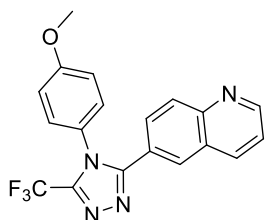
**$^1\text{H}$  NMR (400 MHz, DMSO)**  $\delta$  11.35 (s, 1H), 7.66 (s, 1H), 7.52 (d,  $J = 8.9$  Hz, 2H), 7.41 – 7.36 (m, 2H), 7.18 (dd,  $J = 8.5, 1.6$  Hz, 1H), 7.05 (d,  $J = 9.0$  Hz, 2H), 6.47 – 6.38 (m, 1H), 3.79 (s, 3H).

**$^{13}\text{C}$  NMR (101 MHz, DMSO)**  $\delta$  160.2, 158.2, 144.5 (C-F, q,  $^2J_{\text{(C-F)}} = 37.6$  Hz), 136.5, 129.3, 127.2, 126.9, 125.4, 121.5, 121.4, 118.4 (C-F, q,  $^1J_{\text{(C-F)}} = 270.6$  Hz), 115.9, 114.7, 111.5, 101.8, 55.5, 39.5.

**$^{19}\text{F}$  NMR (377 MHz, DMSO)**  $\delta$  -60.3.

**M.p.** 119.1 - 120.9 °C

**HRMS (ESI):**  $[M+H]^+$  calcd. for  $C_{18}H_{14}F_3N_4O^+$  359.1114, found 359.1123.



5-6-(4-(4-methoxyphenyl)-5-(trifluoromethyl)-4H-1,2,4-triazol-3-yl)quinoline (**4m**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 1:1,  $R_f = 0.2$ ) to give the titled product **4m** as a white solid (88.2 mg, 79%).

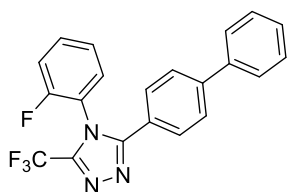
**$^1H$  NMR (400 MHz,  $CDCl_3$ )**  $\delta$  8.94 (dd,  $J = 4.2, 1.7$  Hz, 1H), 8.09 – 8.03 (m, 2H), 8.00 (d,  $J = 8.9$  Hz, 1H), 7.68 (dd,  $J = 8.9, 2.0$  Hz, 1H), 7.42 (dd,  $J = 8.3, 4.2$  Hz, 1H), 7.24 (s, 1H), 7.00 (d,  $J = 8.9$  Hz, 2H), 3.87 (s, 3H).

**$^{13}C$  NMR (101 MHz,  $CDCl_3$ )**  $\delta$  161.1, 156.2, 152.0, 148.4, 146.2 (C-F, q,  $^2J_{(C-F)} = 38.7$  Hz), 136.7, 130.0, 129.3, 128.6, 128.3, 127.7, 125.2, 123.5, 122.0 (C-F, q,  $^1J_{(C-F)} = 271.3$  Hz), 115.2, 55.6.

**$^{19}F$  NMR (377 MHz,  $CDCl_3$ )**  $\delta$  -61.1.

**M.p.** 134.3 - 136.3 °C

**HRMS (ESI):**  $[M+H]^+$  calcd. for  $C_{19}H_{14}F_3N_4O^+$  371.1114, found 371.1121.



3-([1,1'-biphenyl]-4-yl)-4-(2-fluorophenyl)-5-(trifluoromethyl)-4H-1,2,4-triazole (**5**)<sup>3</sup>

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 1:1,  $R_f = 0.2$ ) to give the titled product as a white solid (56.3 mg, 49%).

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**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.63 – 7.58 (m, 1H), 7.57 – 7.52 (m, 6H), 7.43 (t, *J* = 7.4 Hz, 3H), 7.39 – 7.32 (m, 2H), 7.32 – 7.26 (m, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 157.2 (C-F, d, <sup>1</sup>*J*<sub>(C-F)</sub> = 255.0 Hz), 156.8, 145.8 (C-F, q, <sup>2</sup>*J*<sub>(C-F)</sub> = 39.0 Hz), 143.6, 139.5, 133.1 (C-F, d, <sup>5</sup>*J*<sub>(C-F)</sub> = 7.7 Hz), 130.6, 129.4, 128.8 (C-F, d, <sup>2</sup>*J*<sub>(C-F)</sub> = 25.2 Hz), 128.1, 127.4, 127.0, 125.3 (C-F, d, <sup>6</sup>*J*<sub>(C-F)</sub> = 4.0 Hz), 123.7, 121.0 (C-F, d, <sup>4</sup>*J*<sub>(C-F)</sub> = 13.3 Hz), 118.0 (C-F, q, <sup>1</sup>*J*<sub>(C-F)</sub> = 271.3 Hz), 117.3 (C-F, d, <sup>3</sup>*J*<sub>(C-F)</sub> = 19.1 Hz).

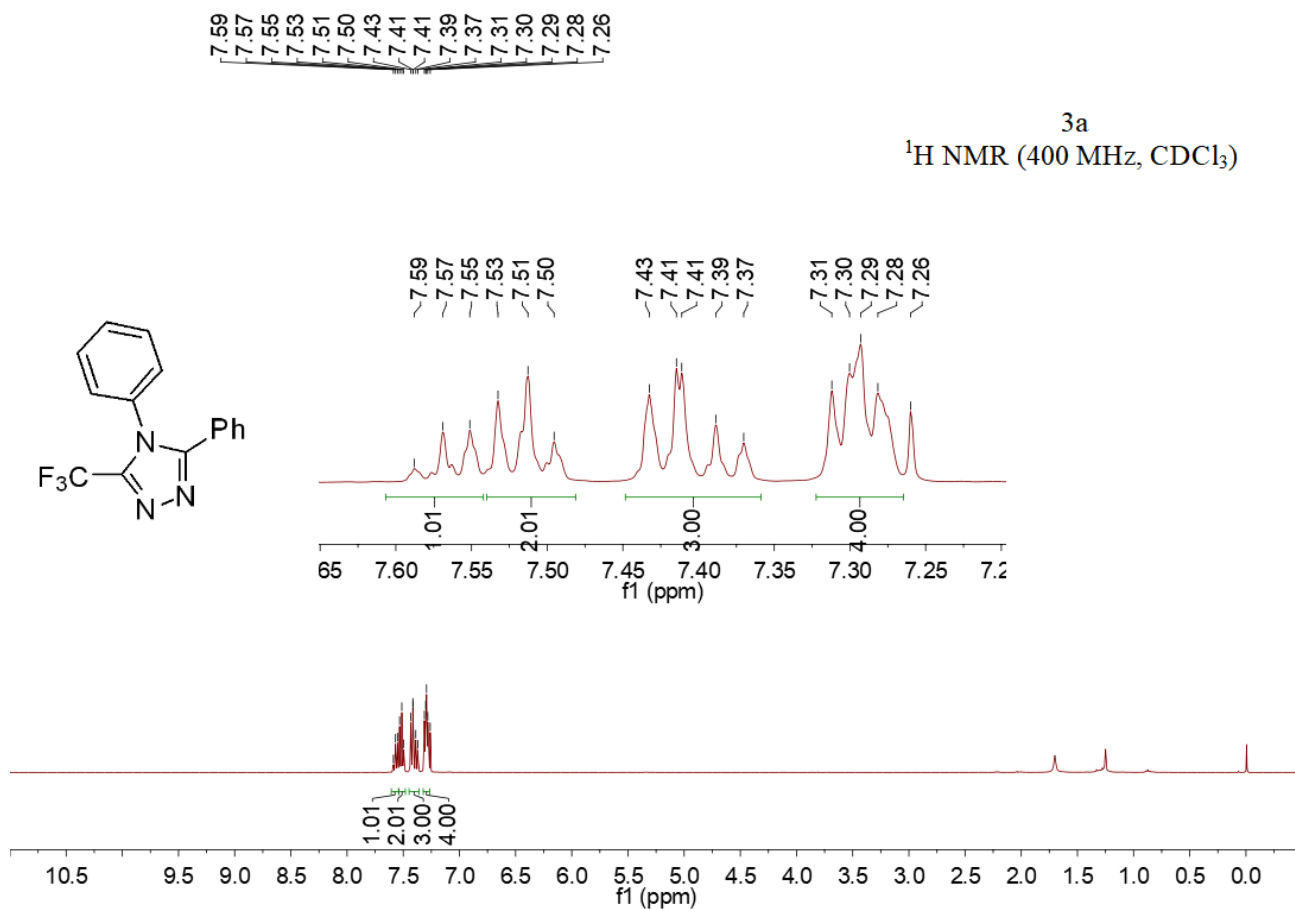
**<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -62.1, -119.5.

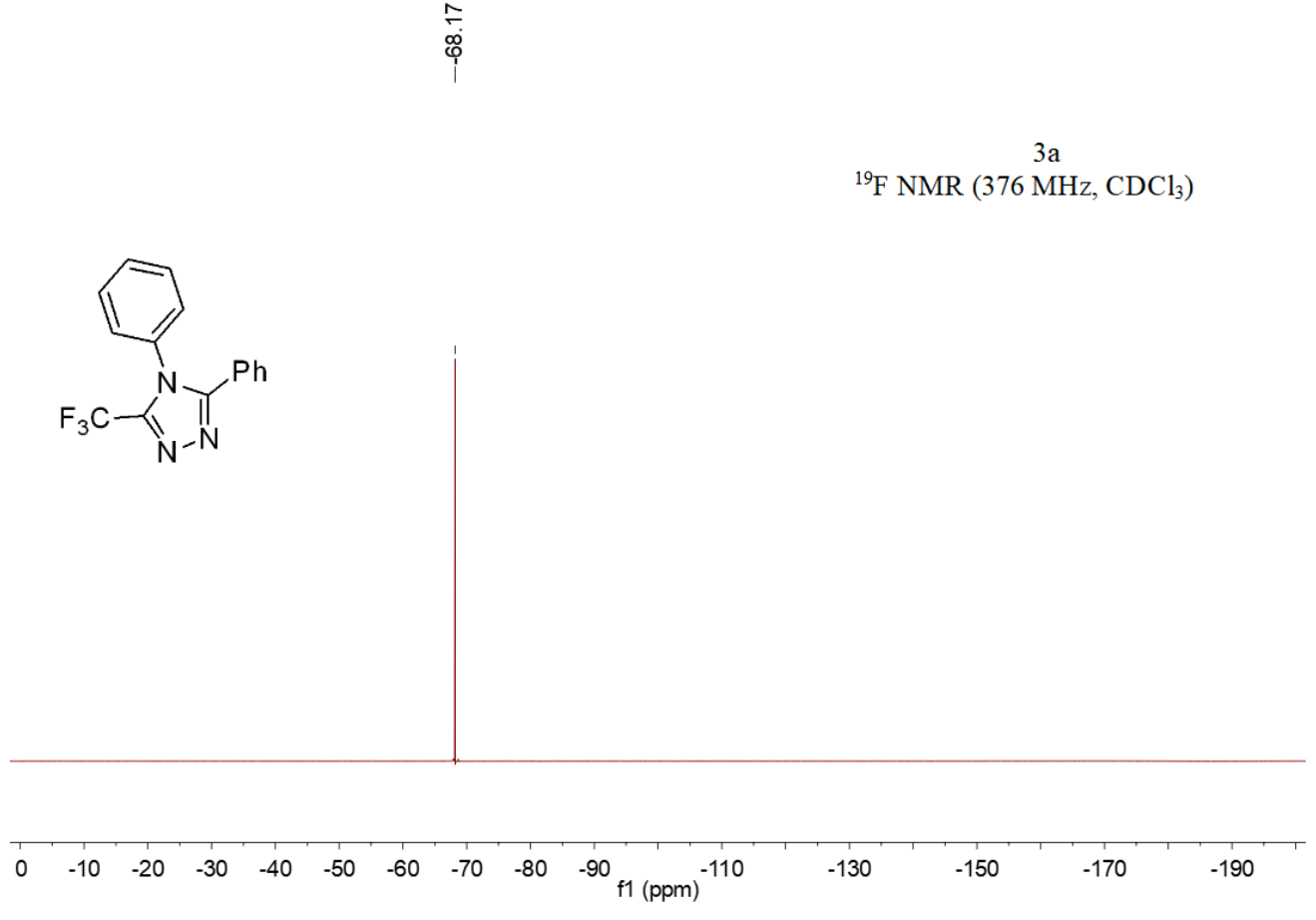
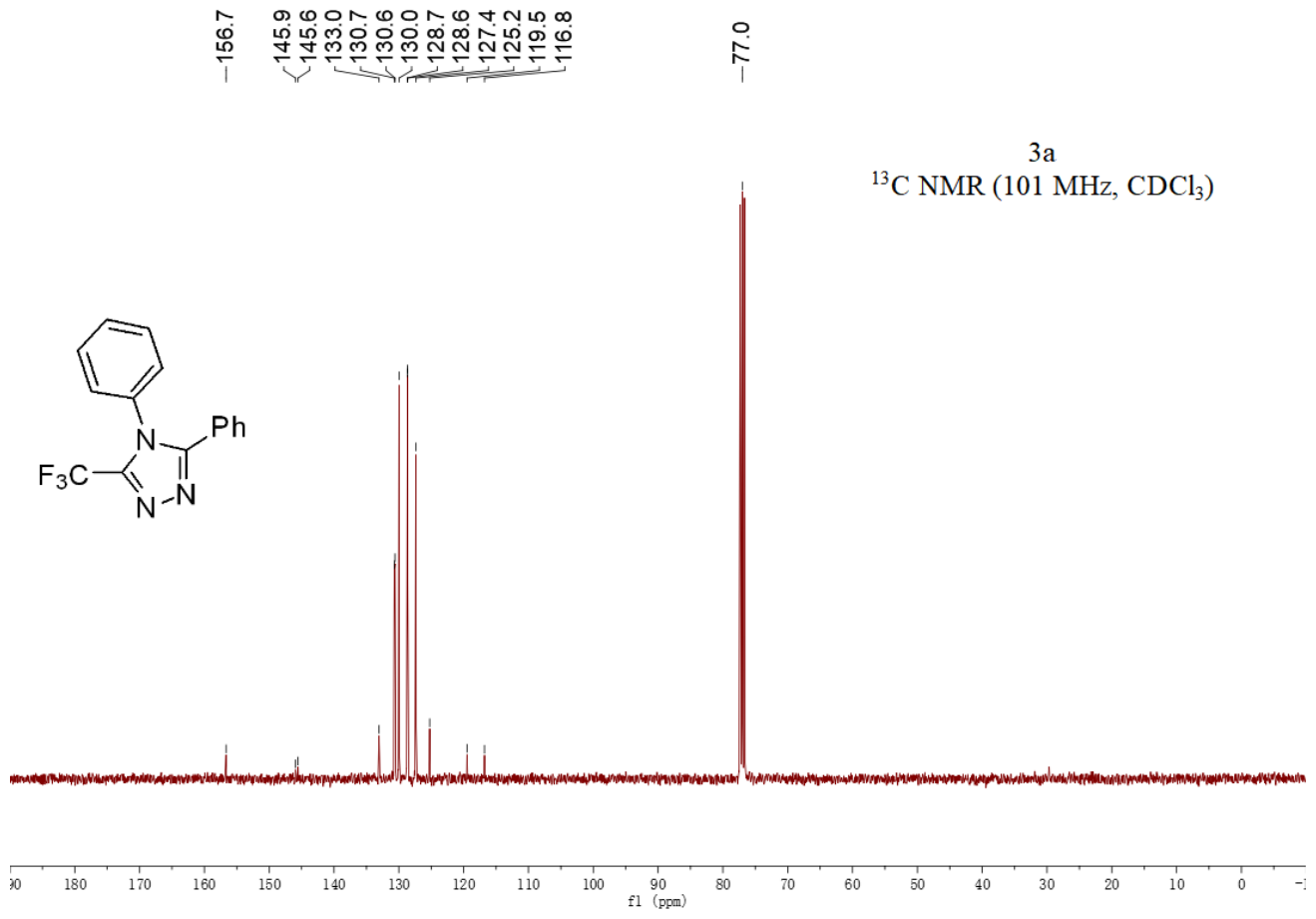
**M.p.** 151.4 -153.4 °C

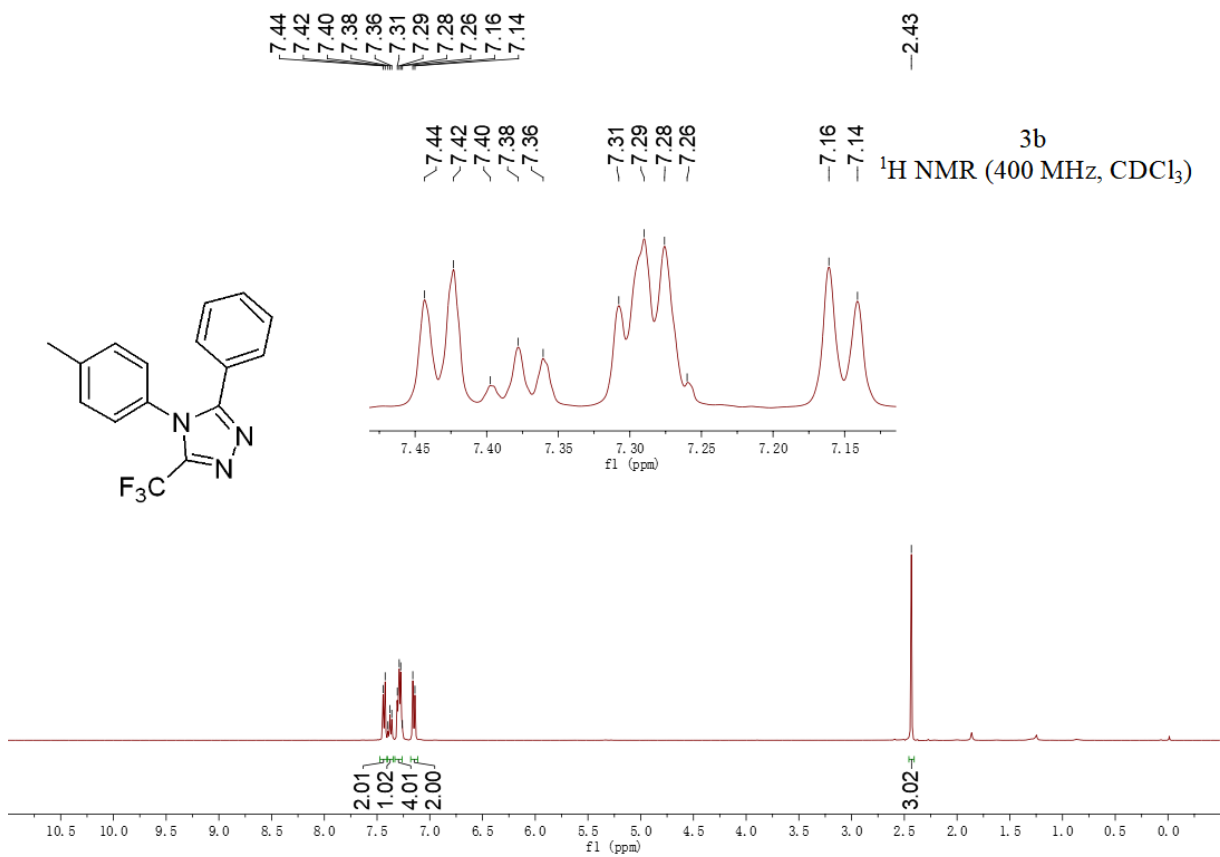
## 6 References

- (1) Tamura, K.; Mizukami, H.; Maeda, K.; Watanabe, H.; Uneyama, K., One-pot synthesis of trifluoroacetimidoyl halides. *J. Org. Chem.* **1993**, *58*, 32-35.
- (2) Hu, S.; Yang, Z.; Chen, Z.; Wu, X.-F., Metal-Free Synthesis of 5-Trifluoromethyl-1,2,4-Triazoles from Iodine-Mediated Annulation of Trifluoroacetimidoyl Chlorides and Hydrazones. *Adv. Synth. Catal.* **2019**, *361*, 4949-4954.
- (3) Shivarama Holla, B.; Narayana Poojary, K.; Sooryanarayana Rao, B.; Shivananda, M. K., New bis-aminomercaptotriazoles and bis-triazolothiadiazoles as possible anticancer agents. *Eur. J. Med. Chem.* **2002**, *37*, 511-517.

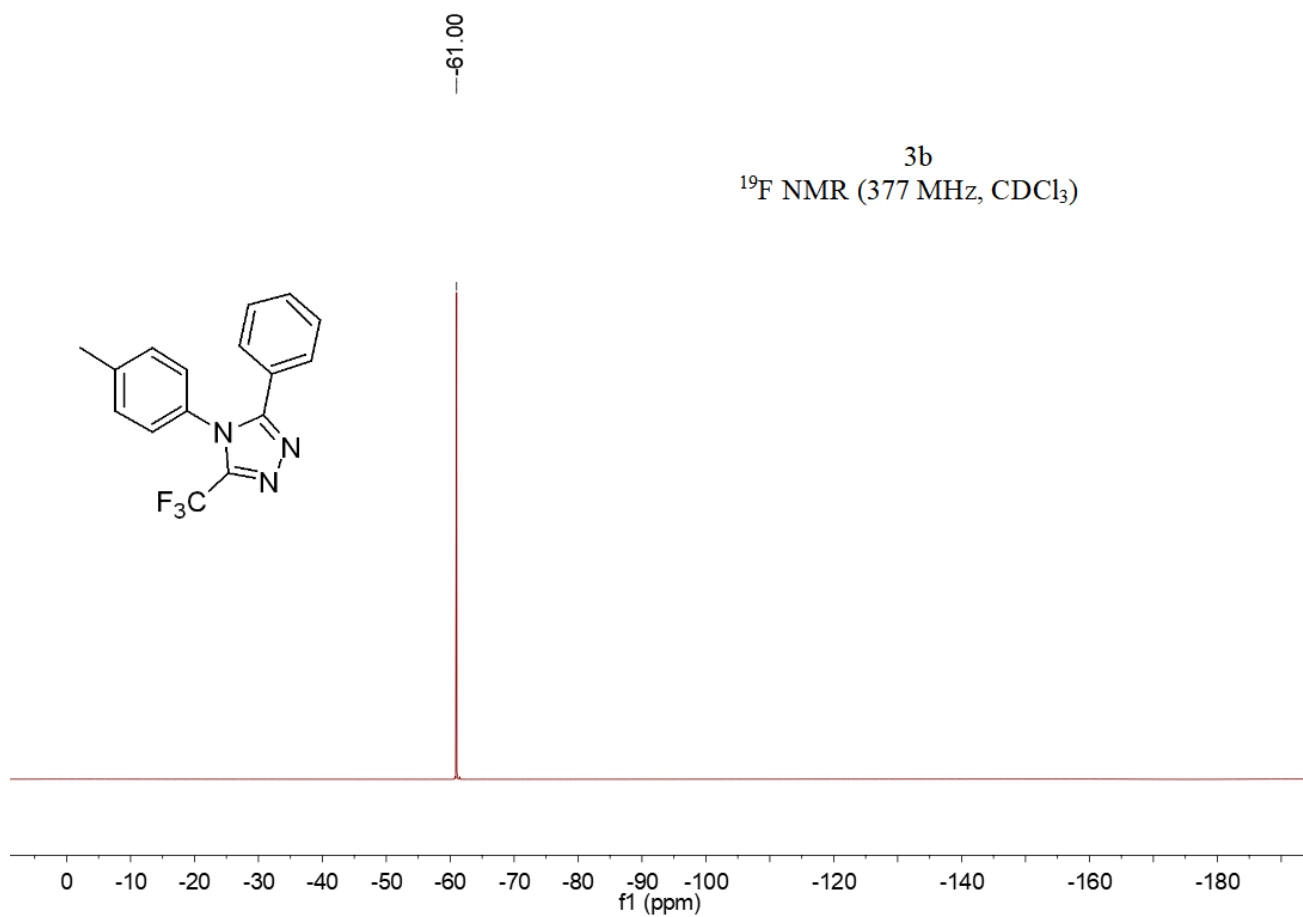
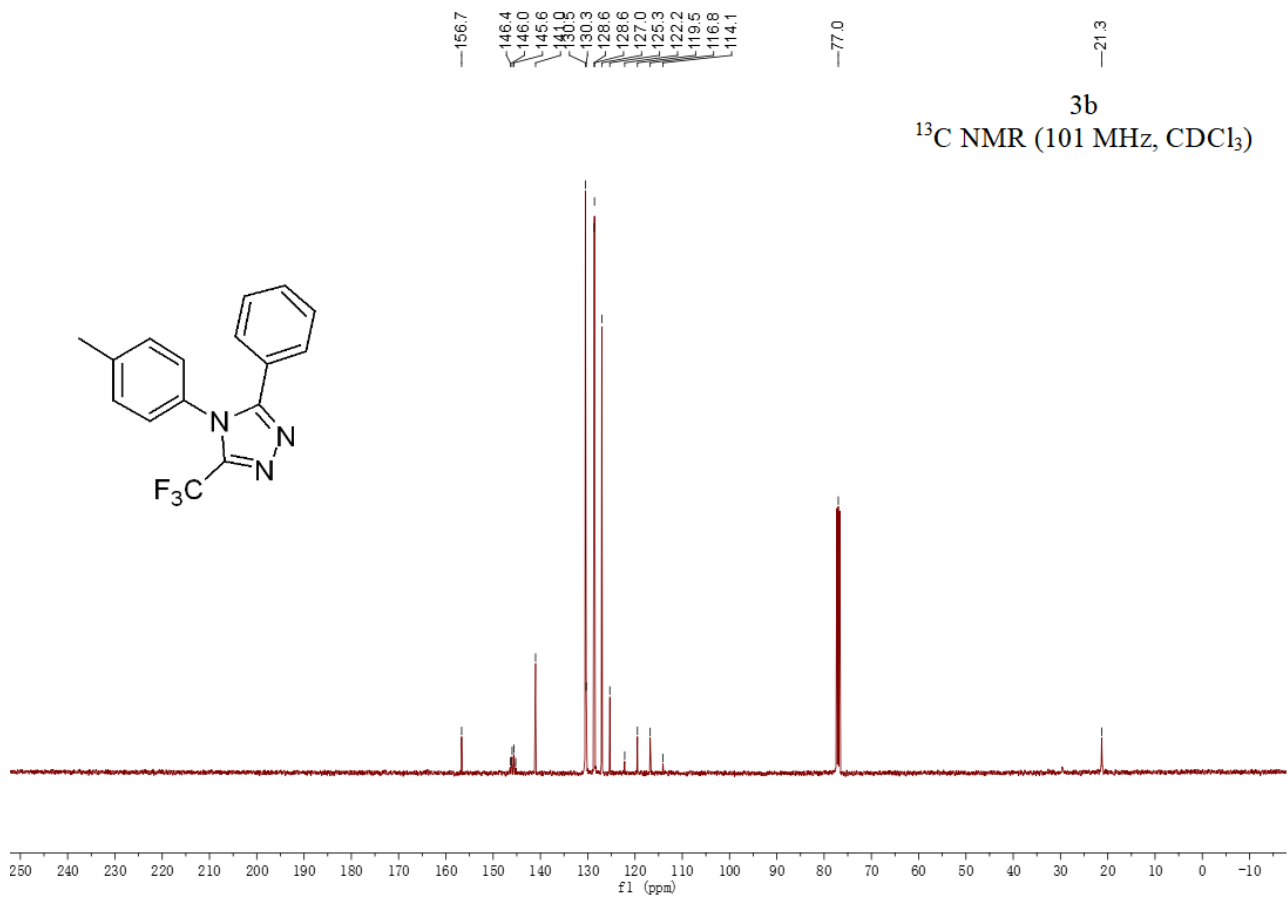
# 7 Copy of $^1\text{H}$ , $^{13}\text{C}$ and $^{19}\text{F}$ NMR Spectra of Products

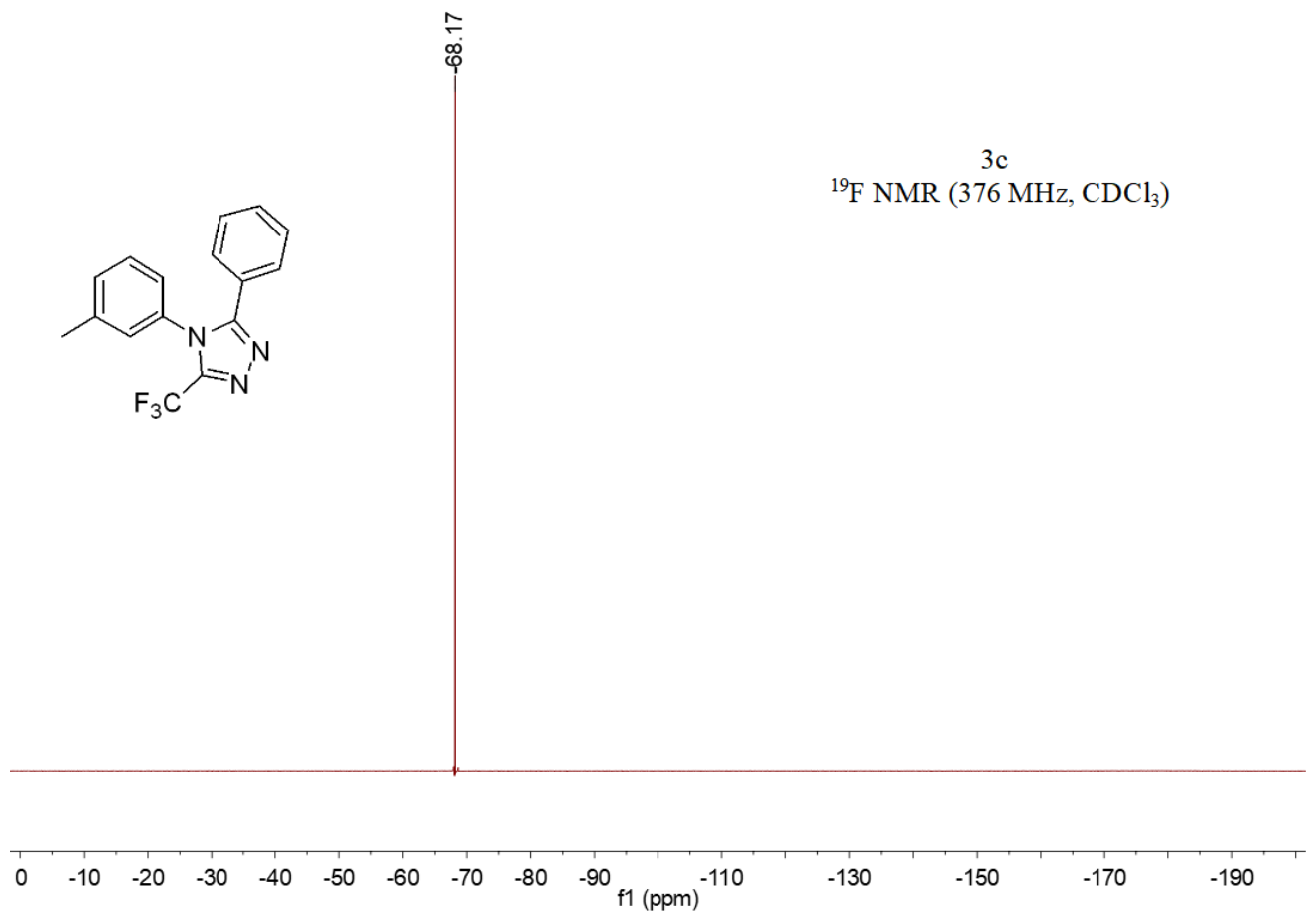
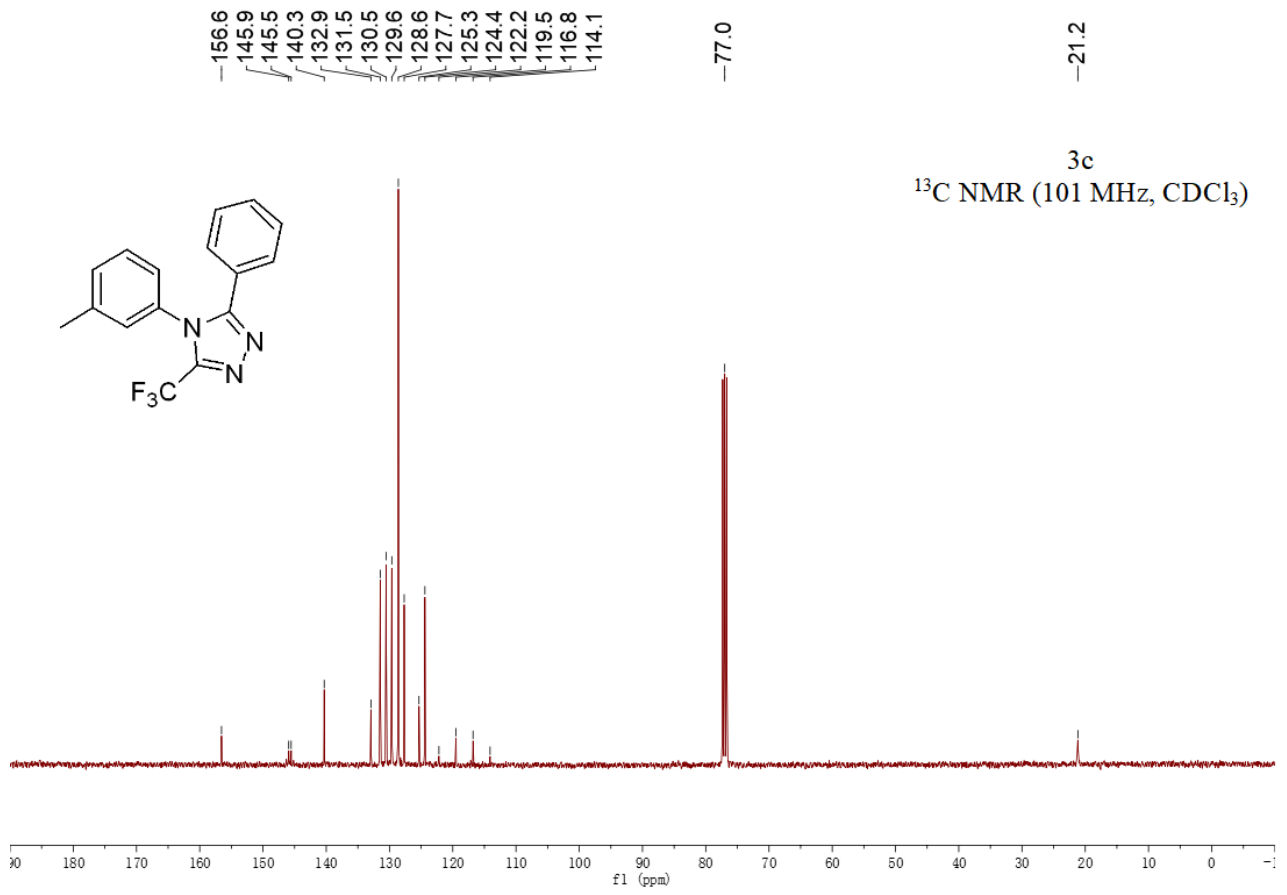


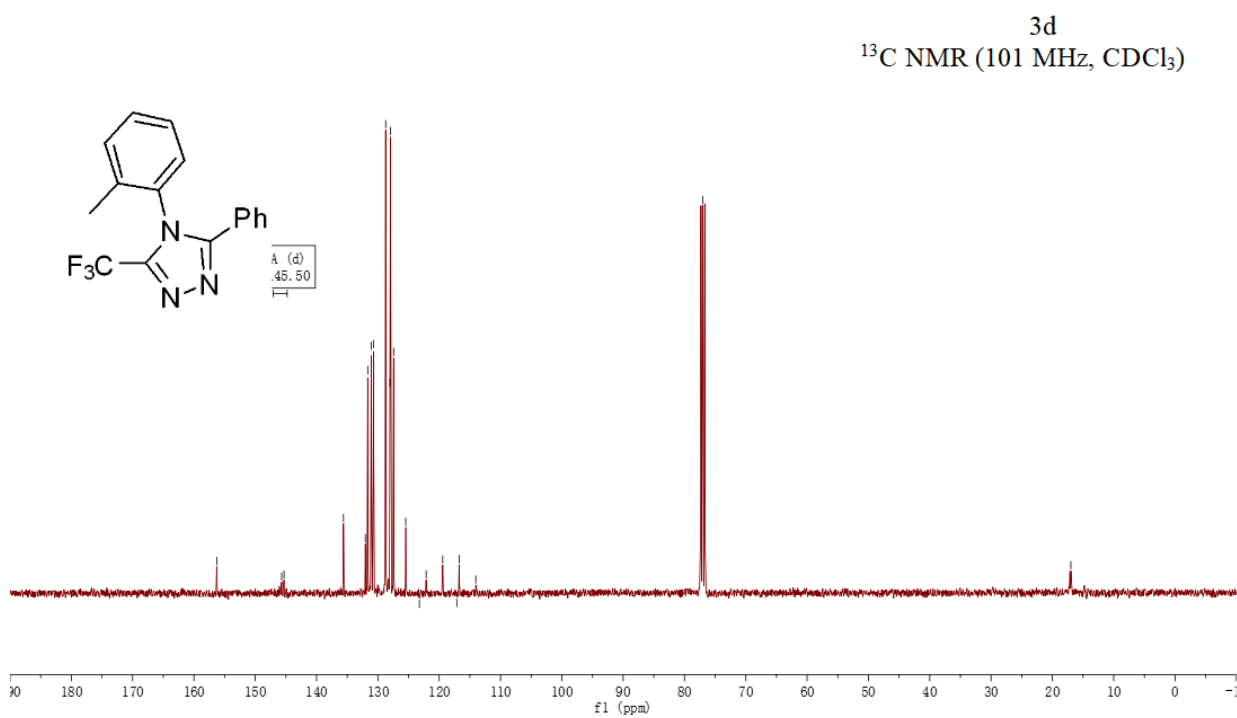
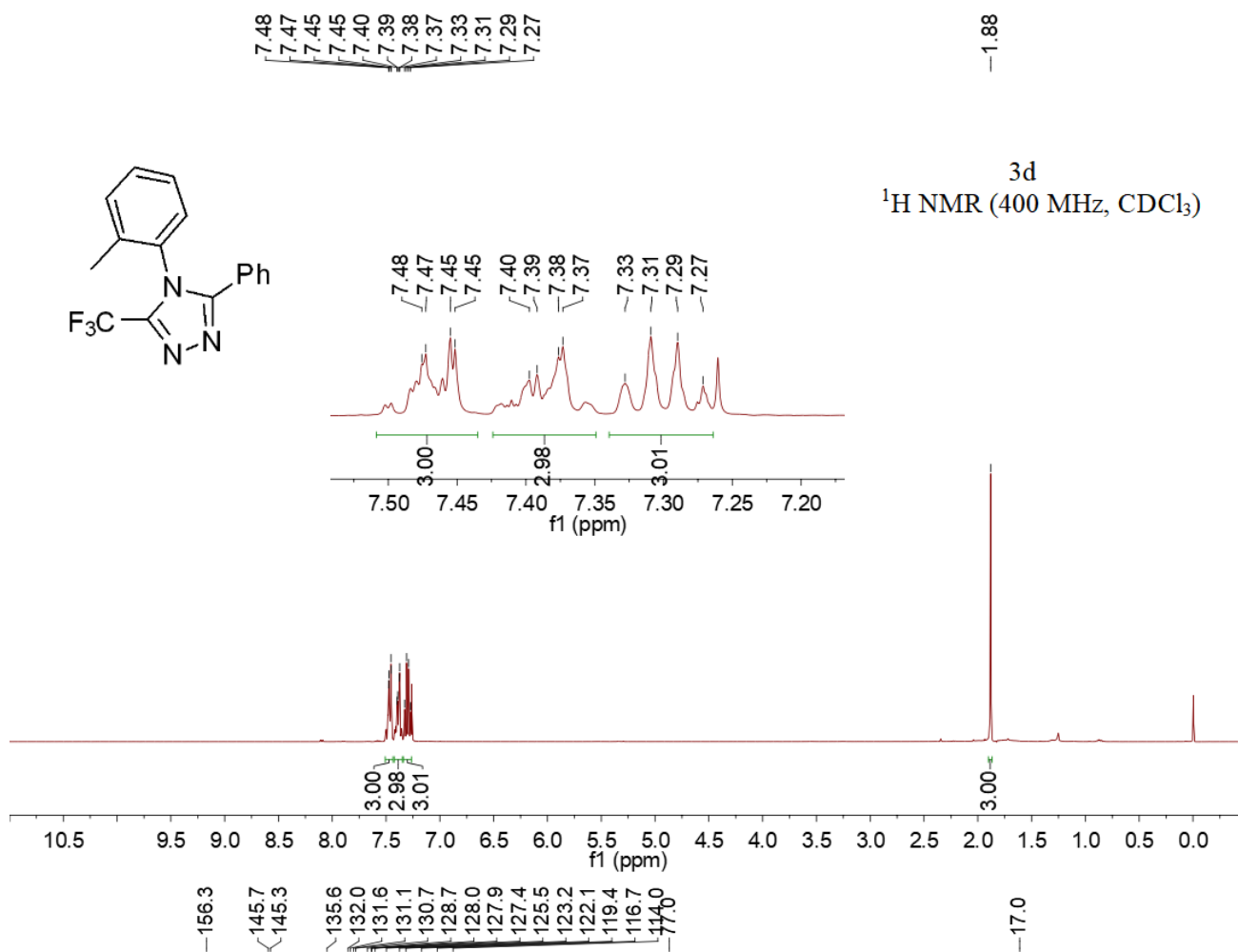


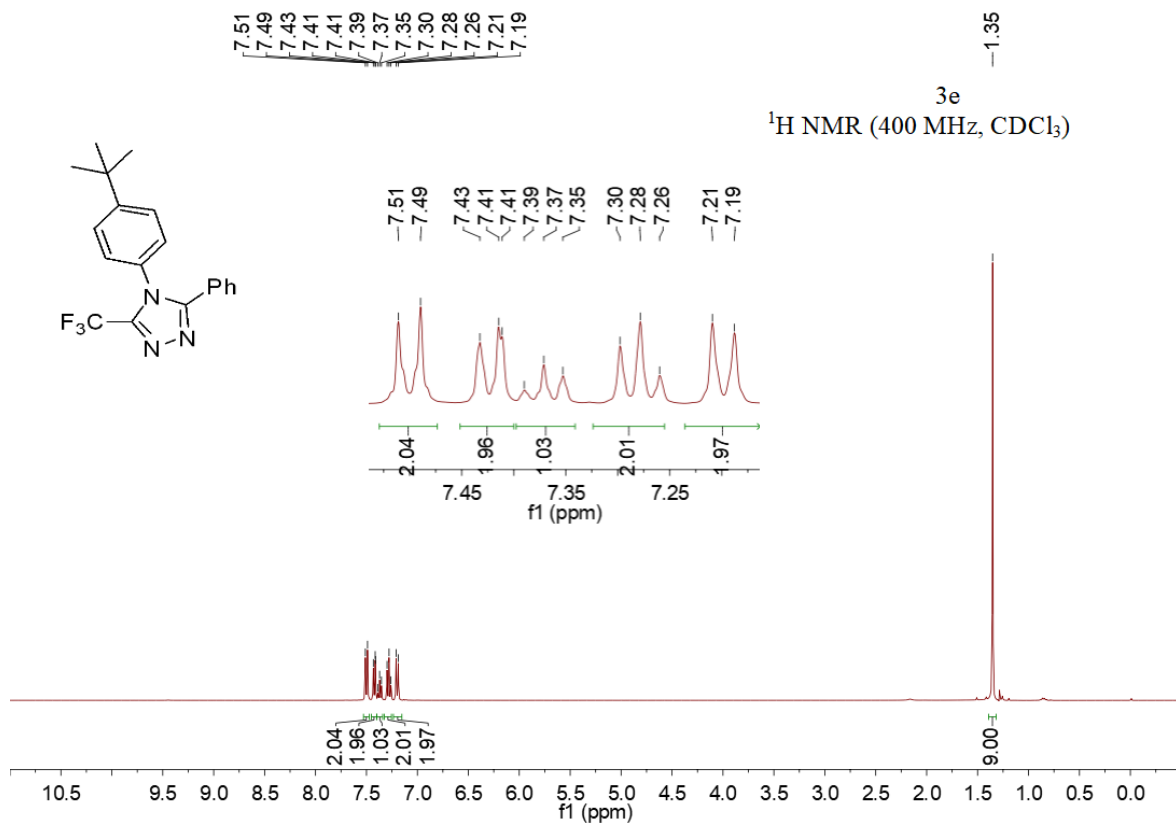
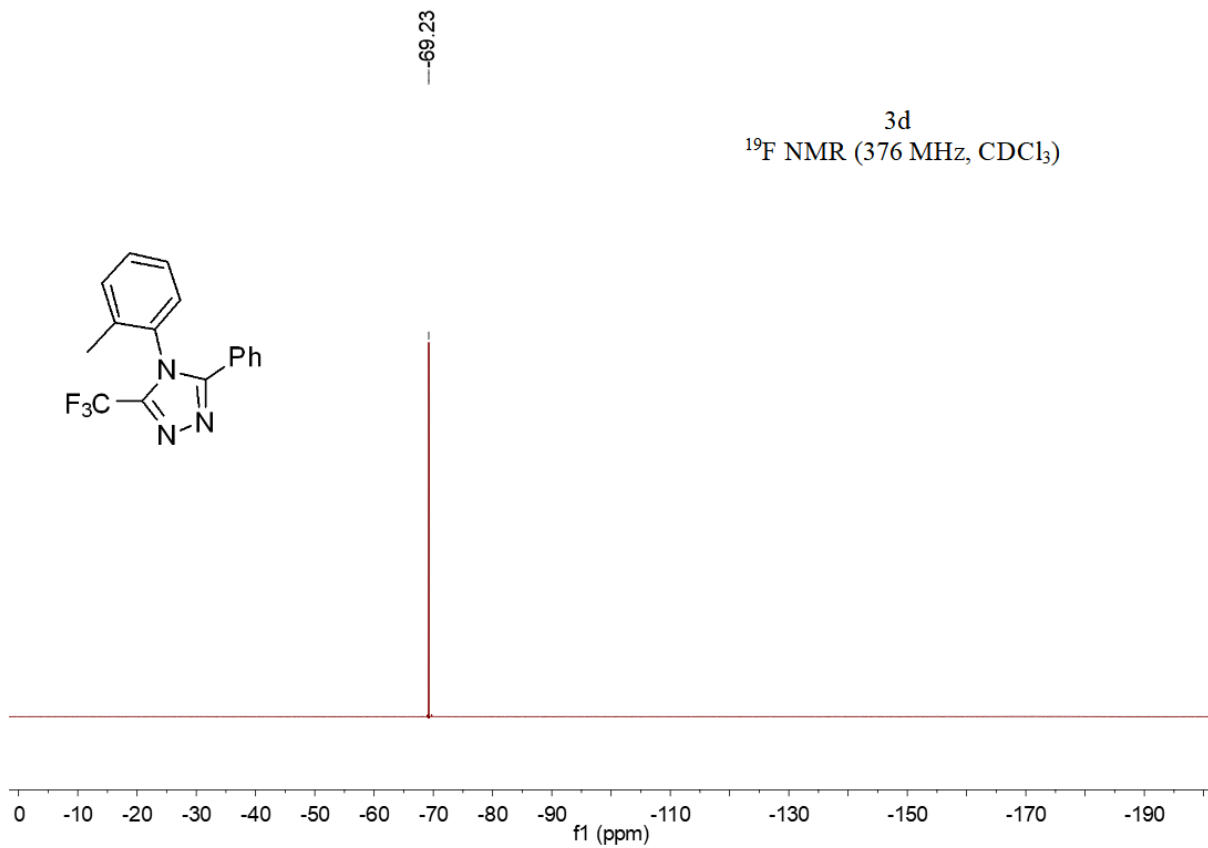


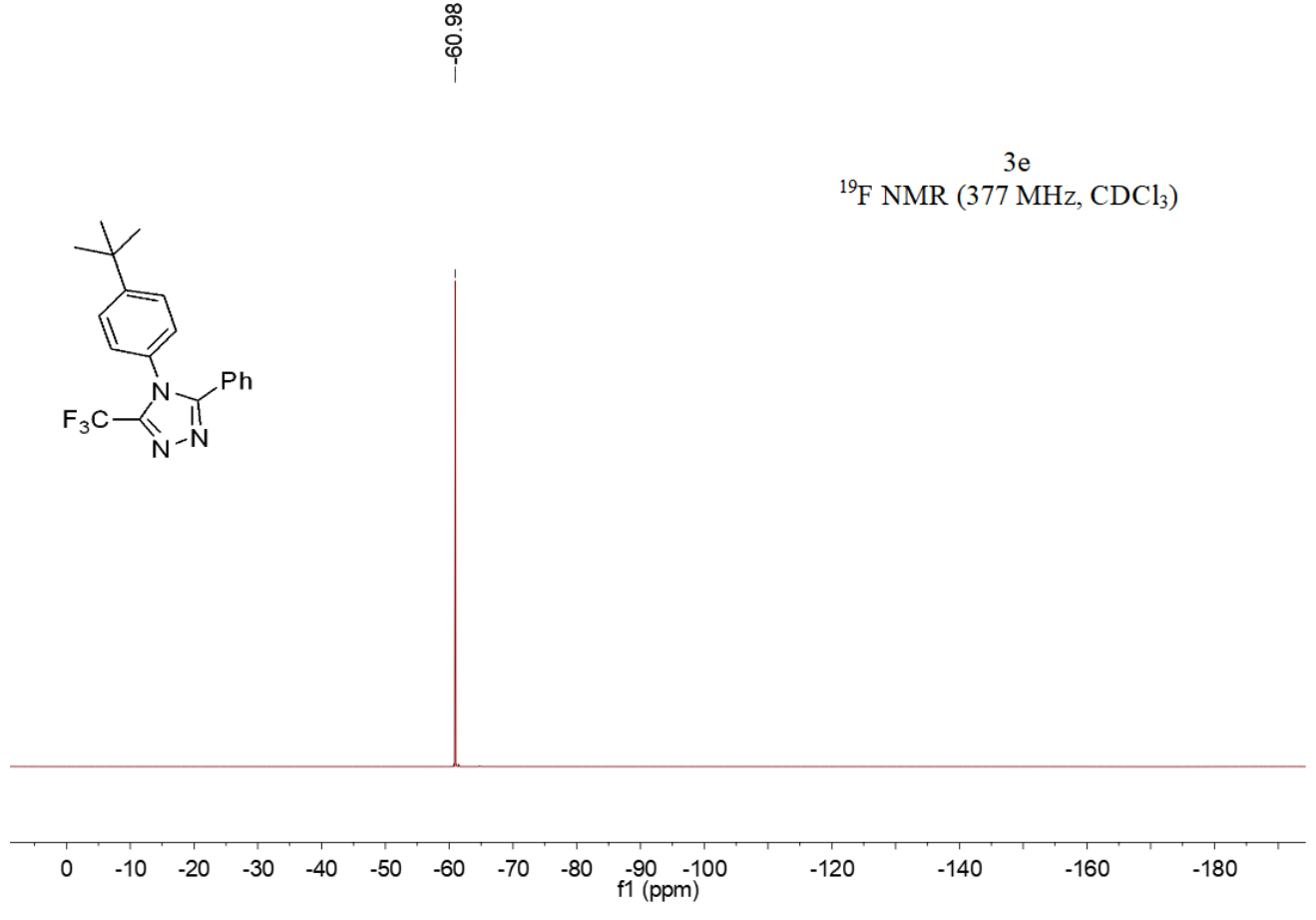
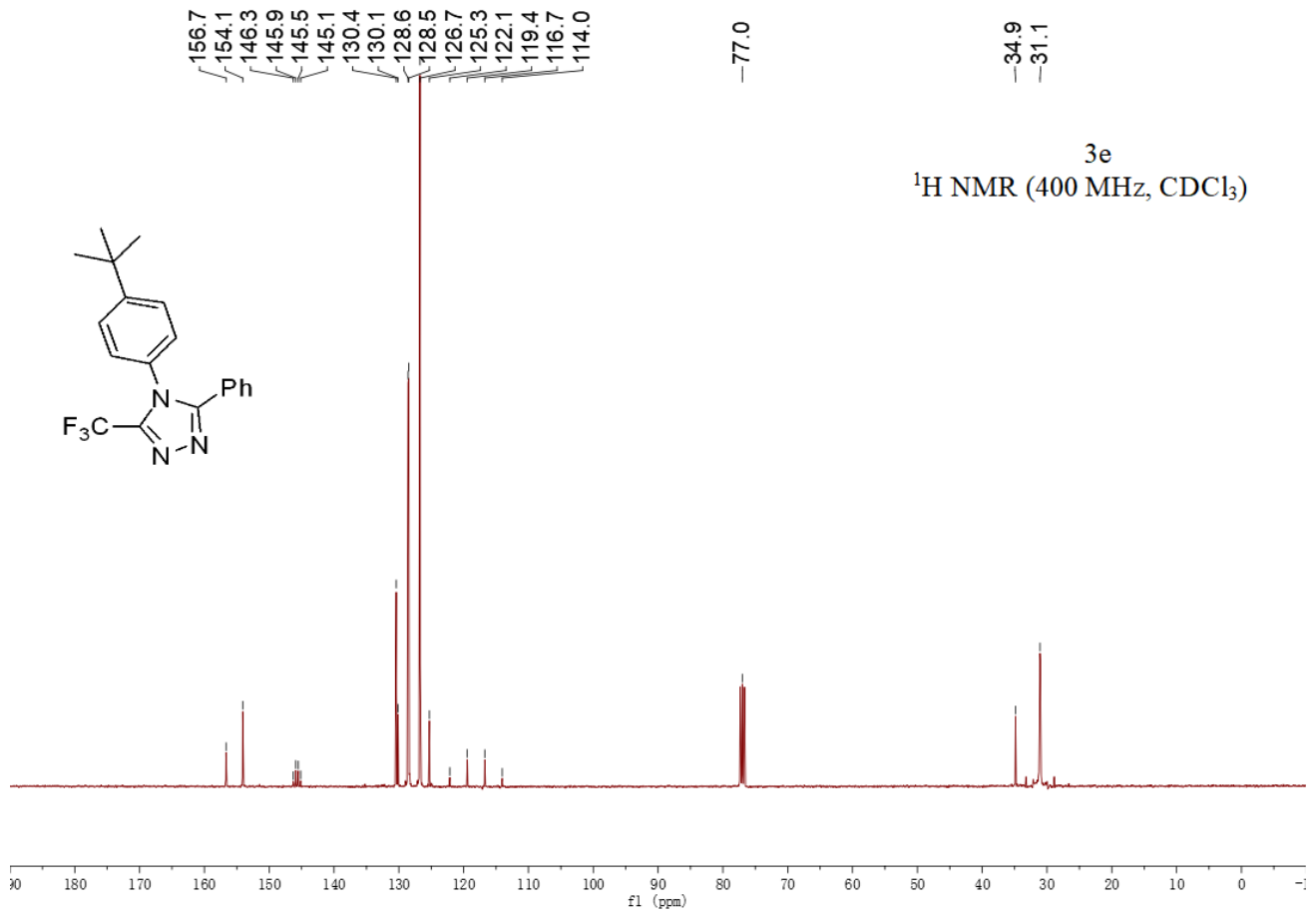


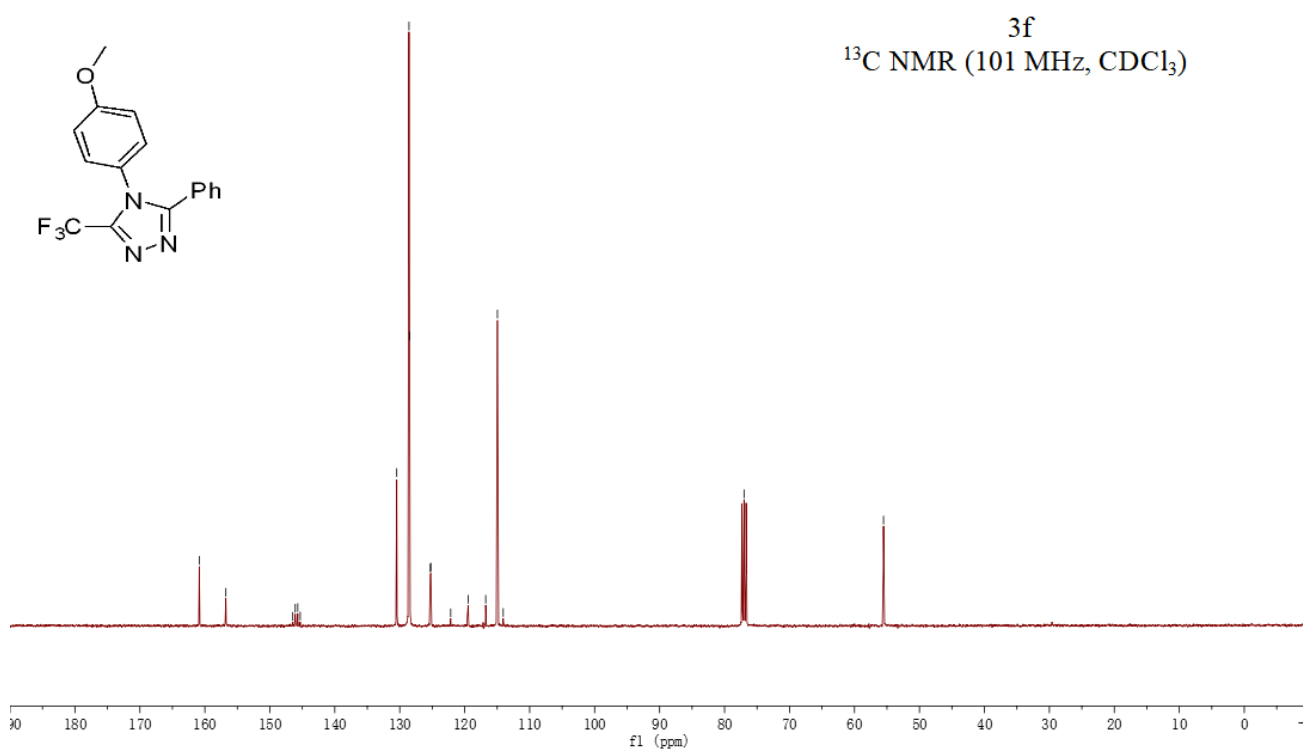
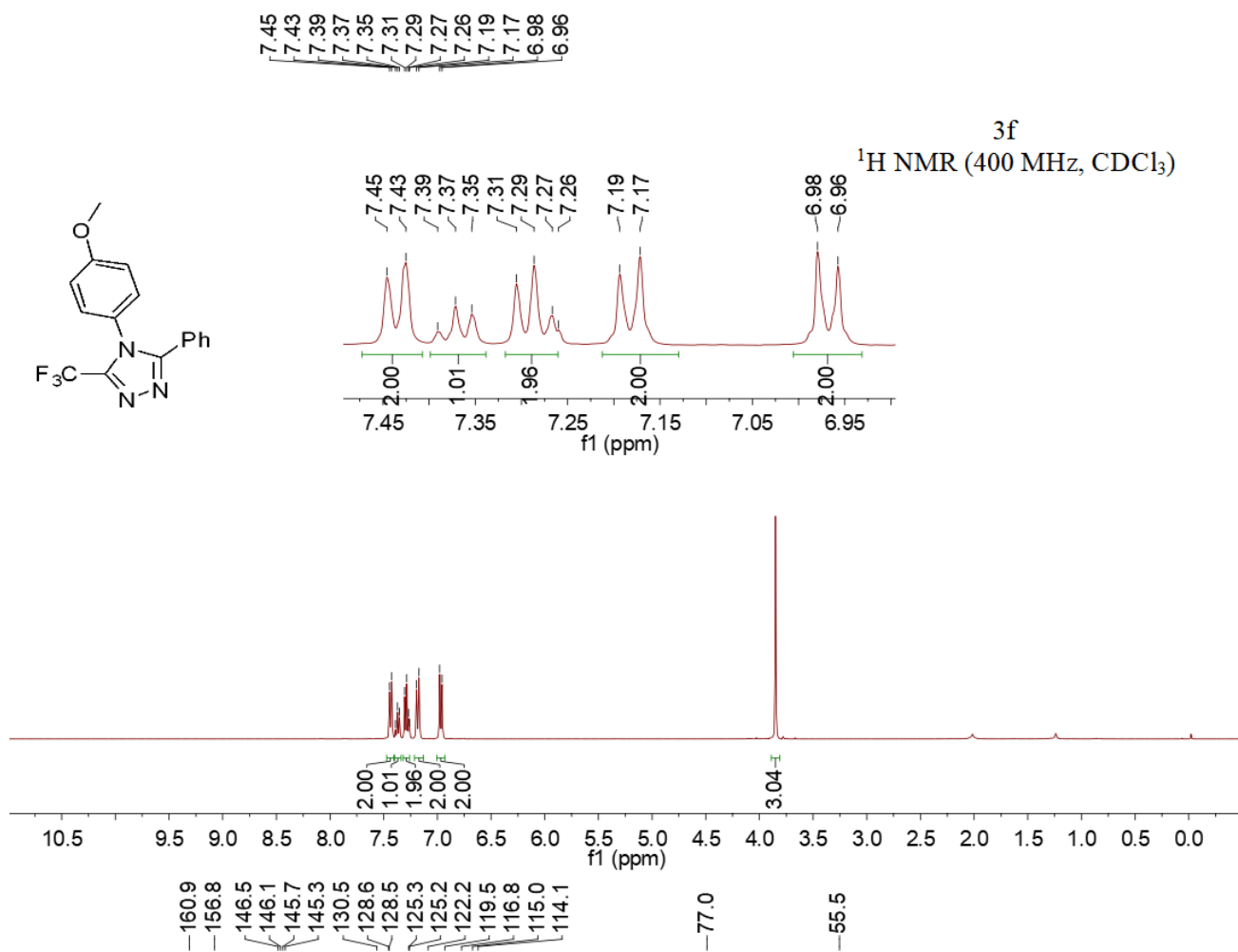


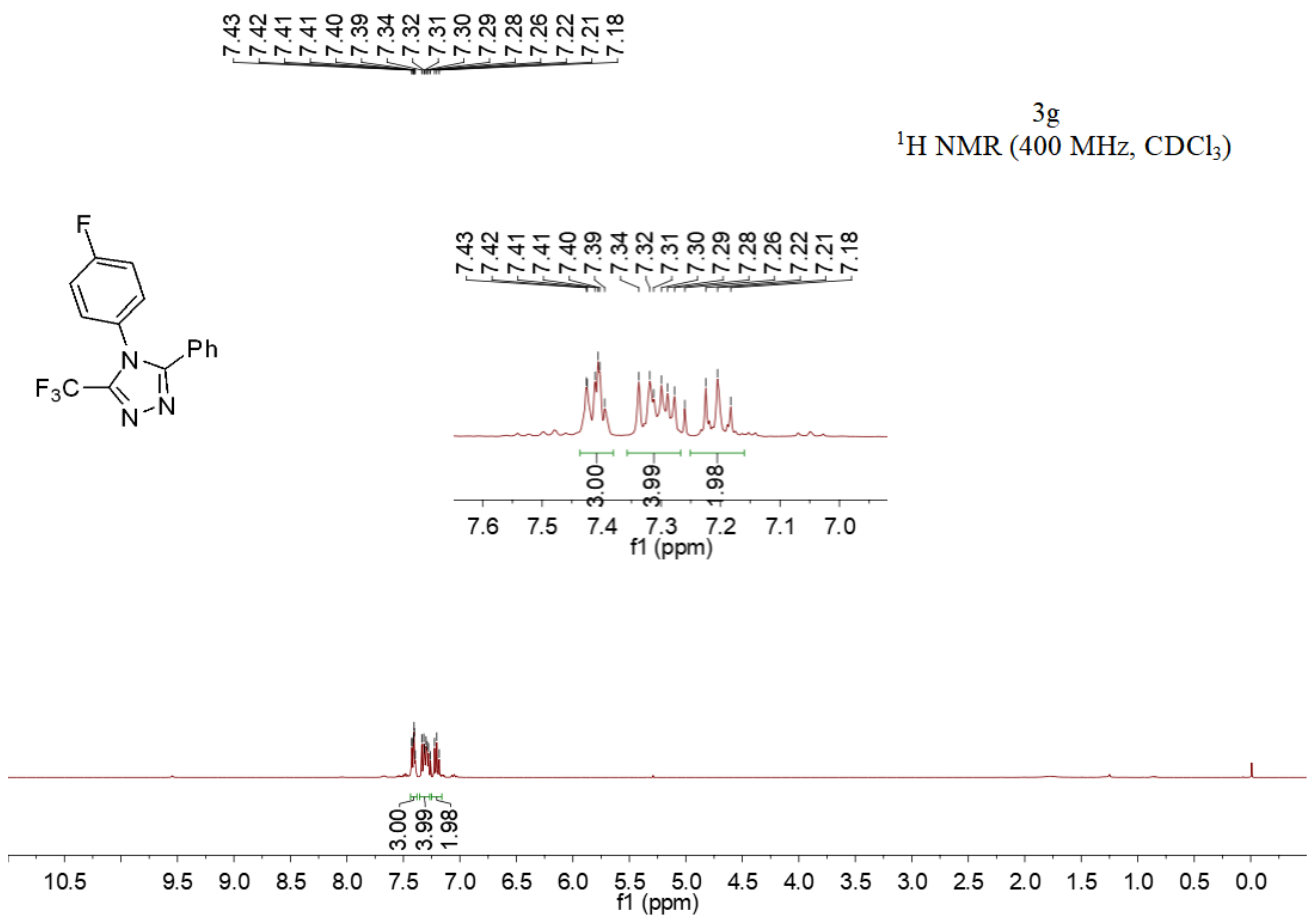
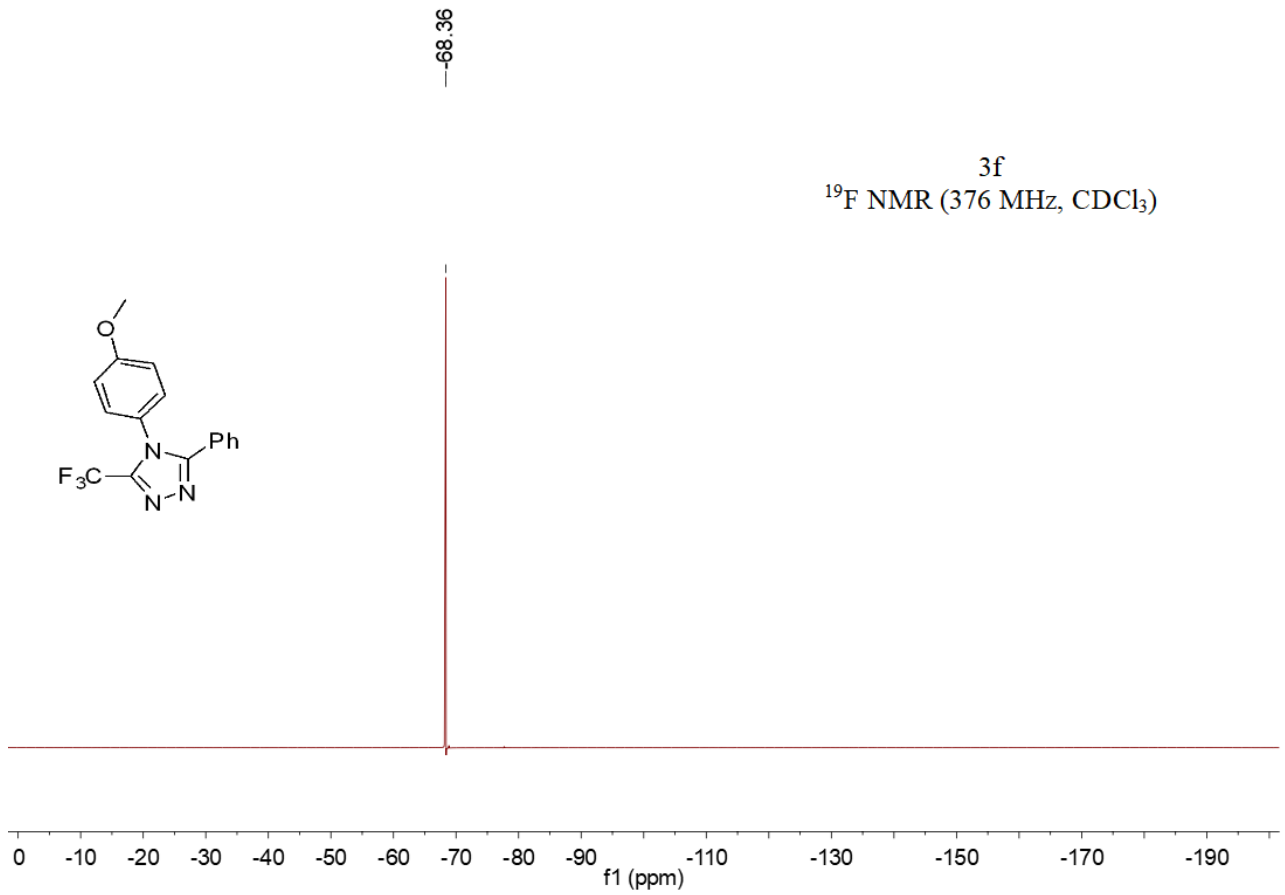


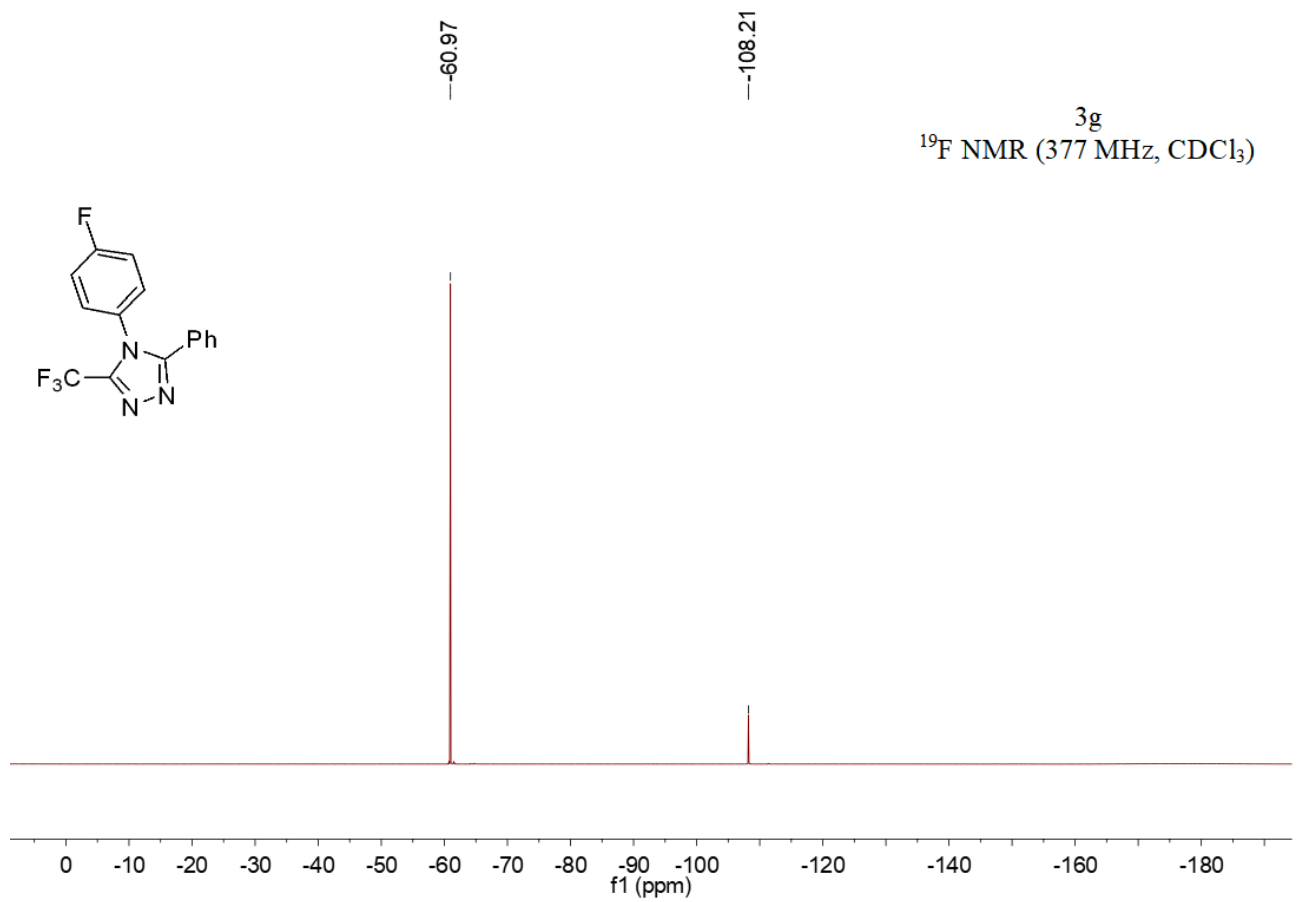
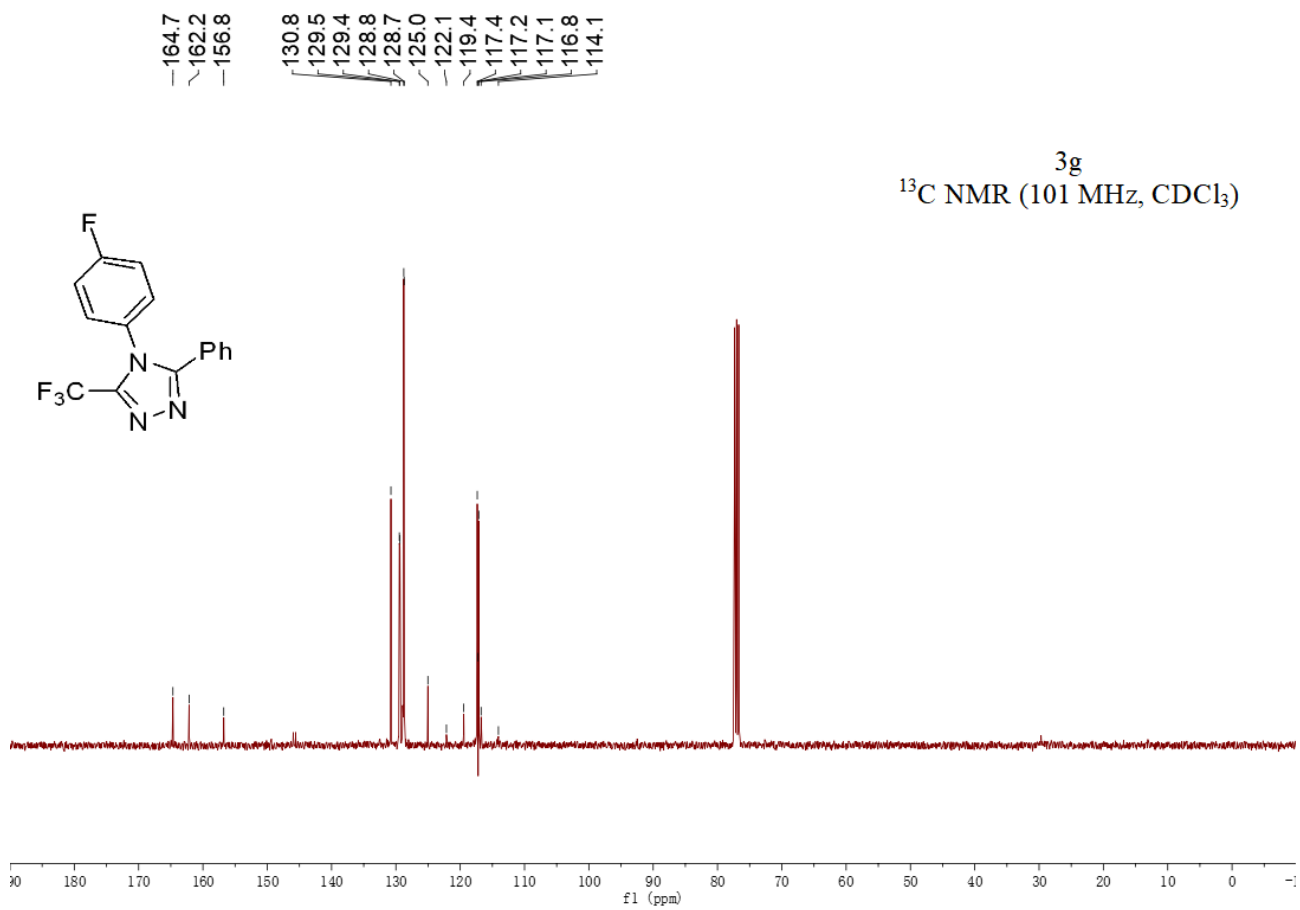










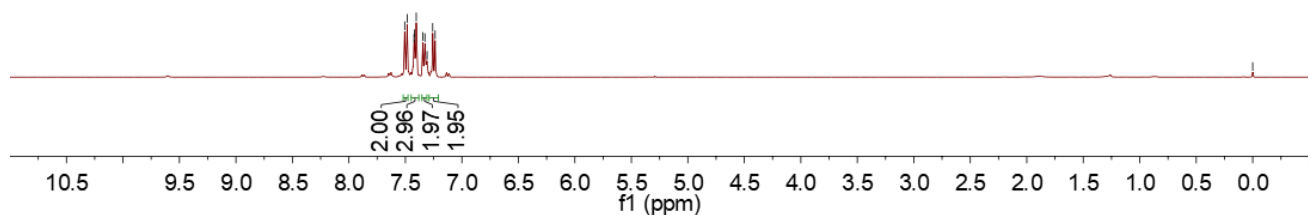
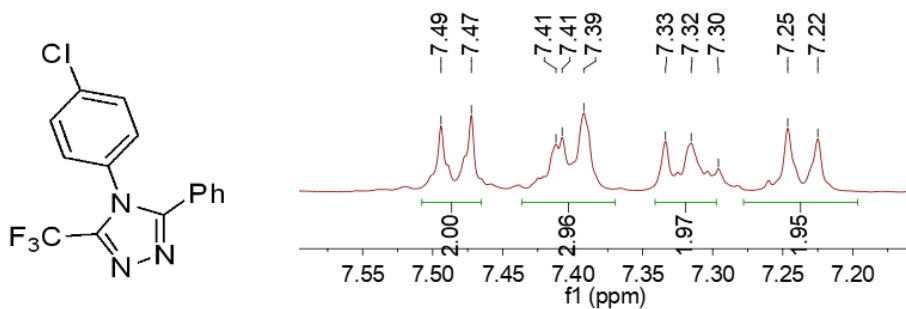




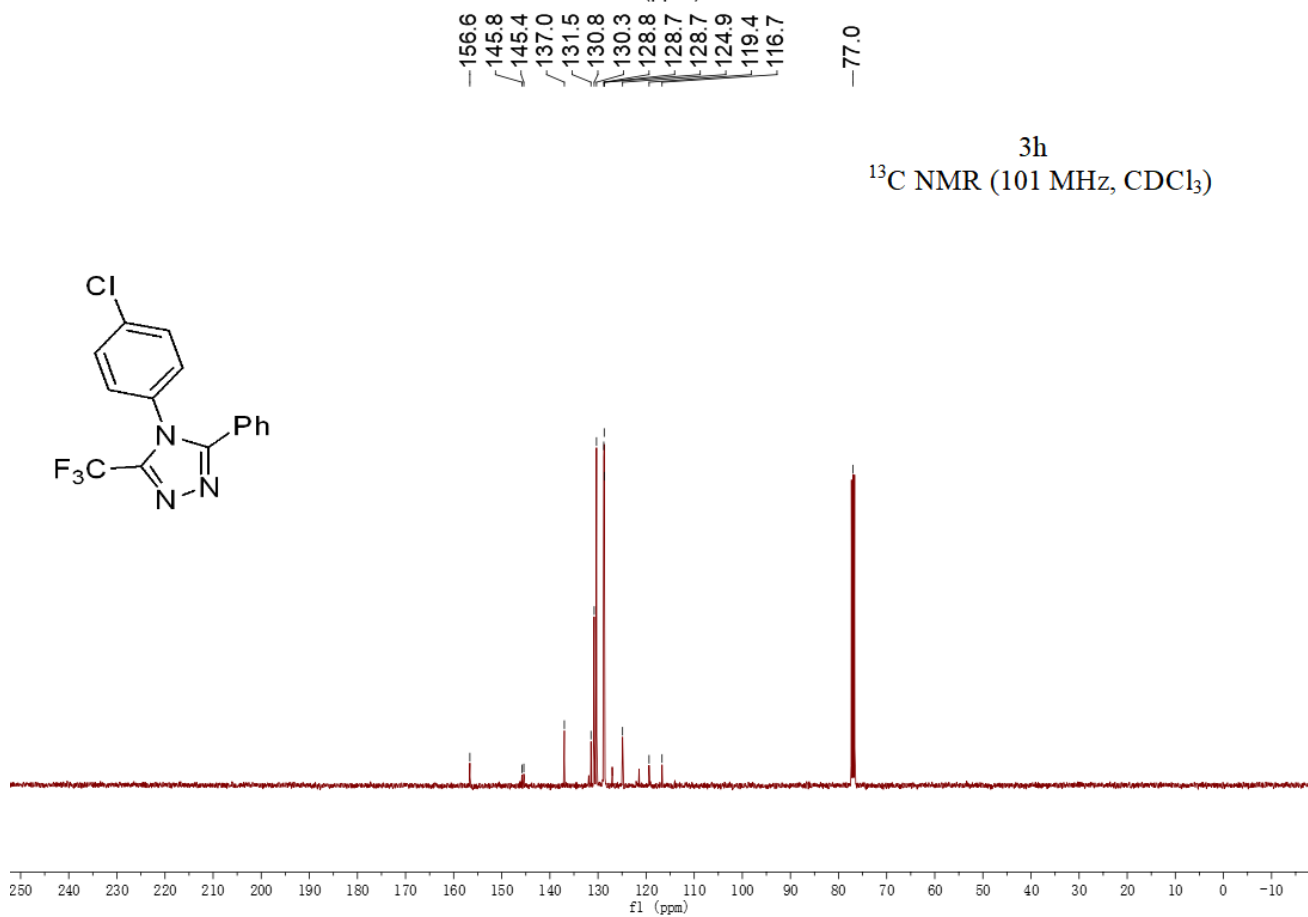
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7.40  
7.35  
7.33  
7.31  
7.26  
7.24

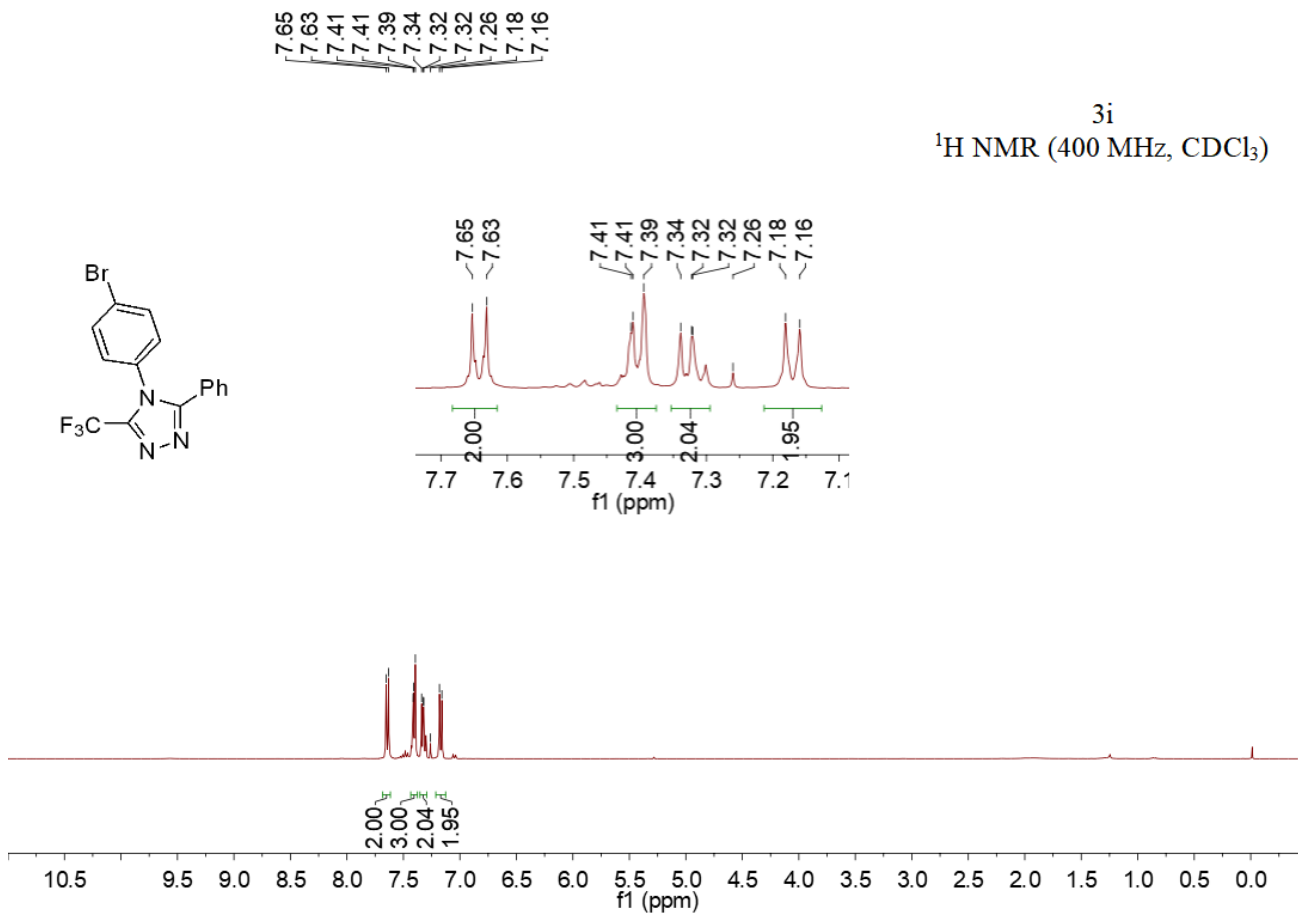
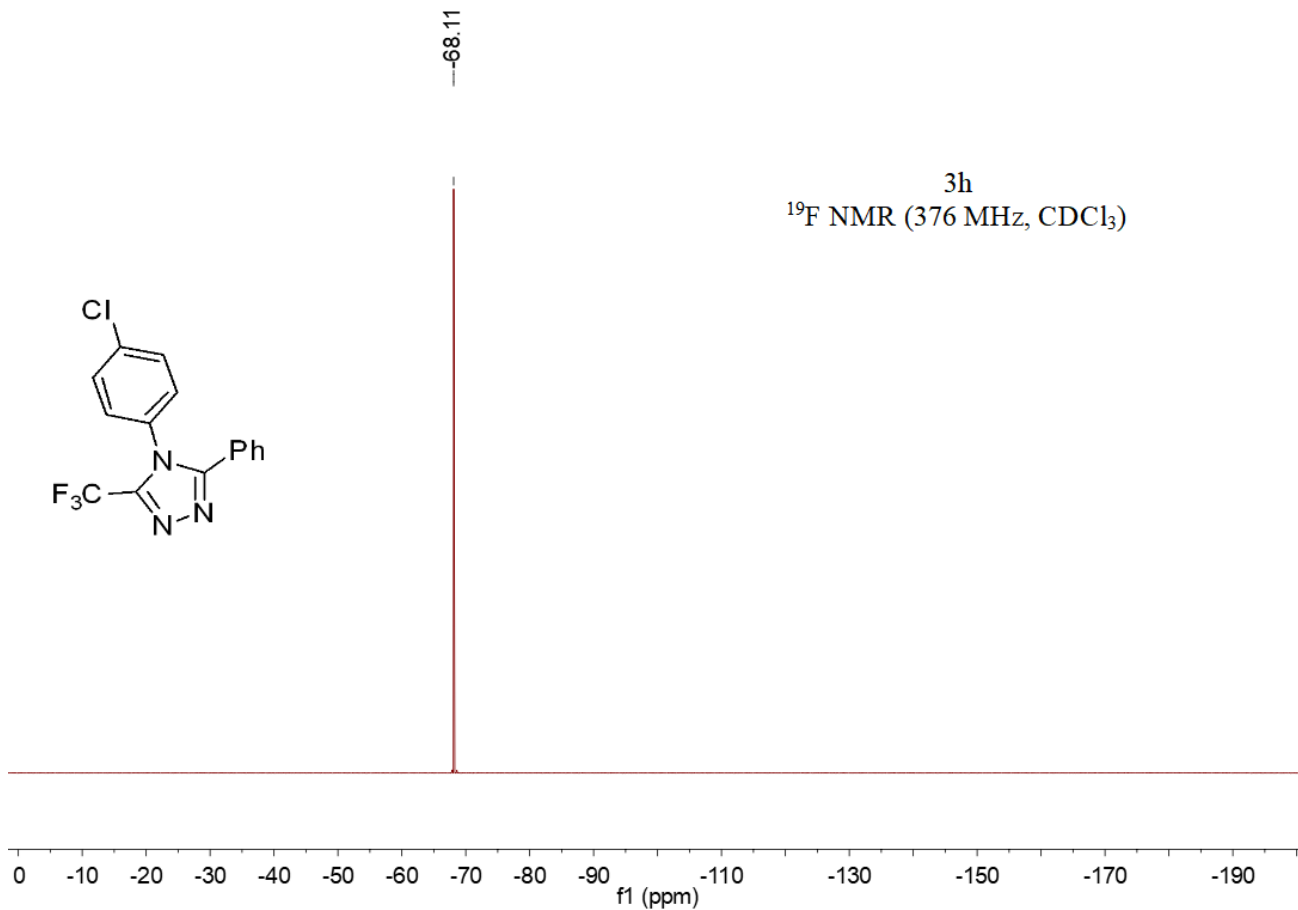
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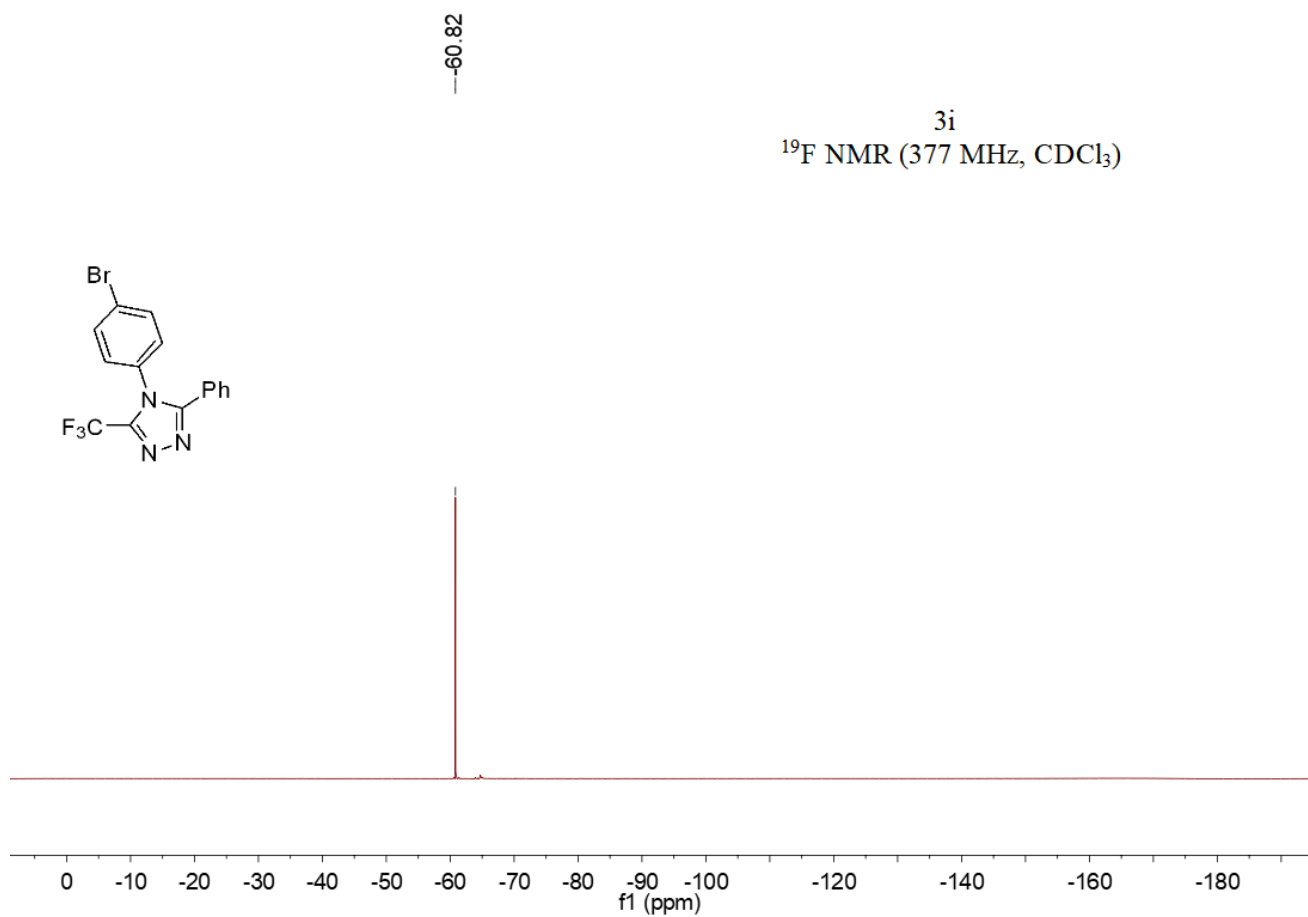
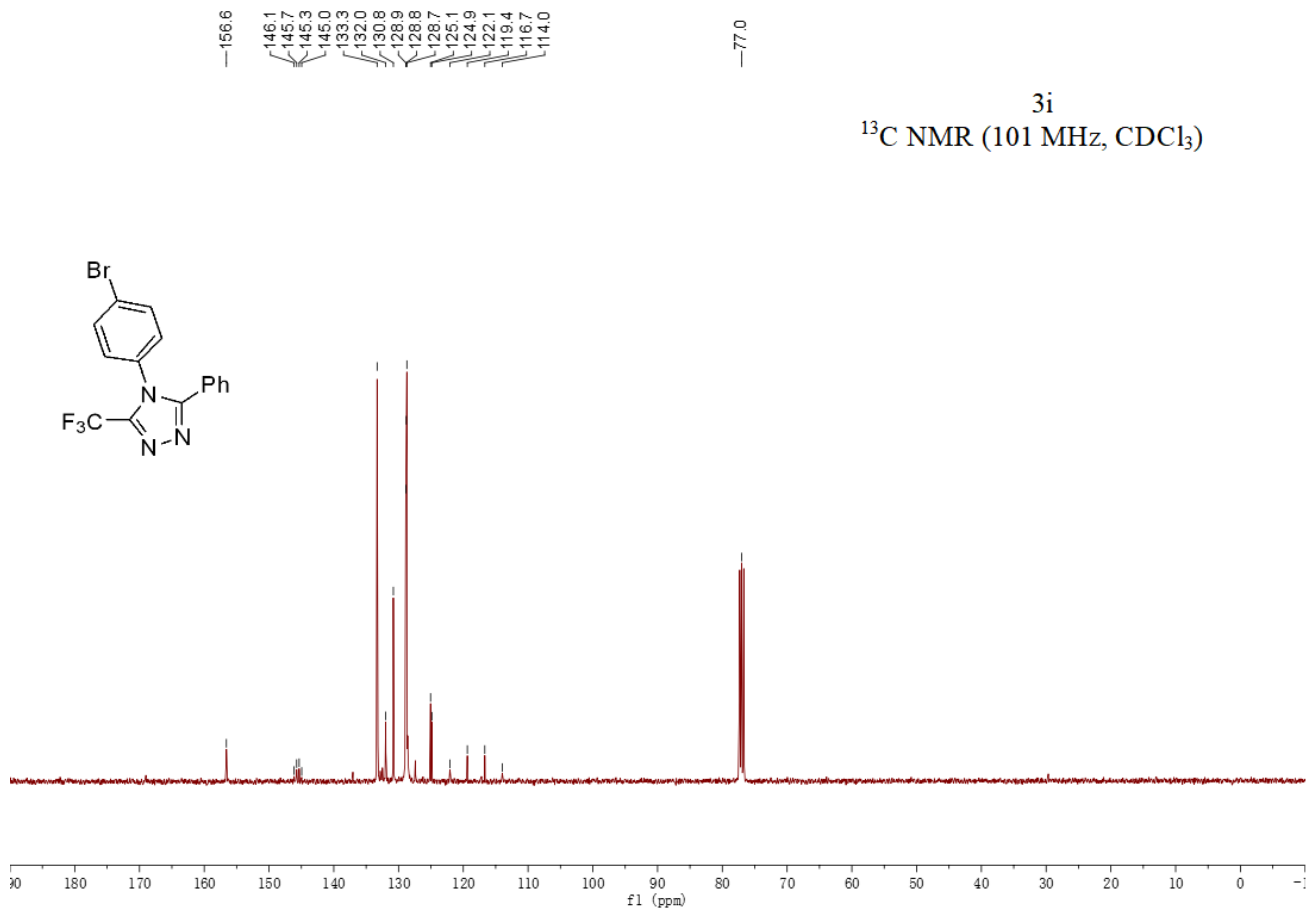
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<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

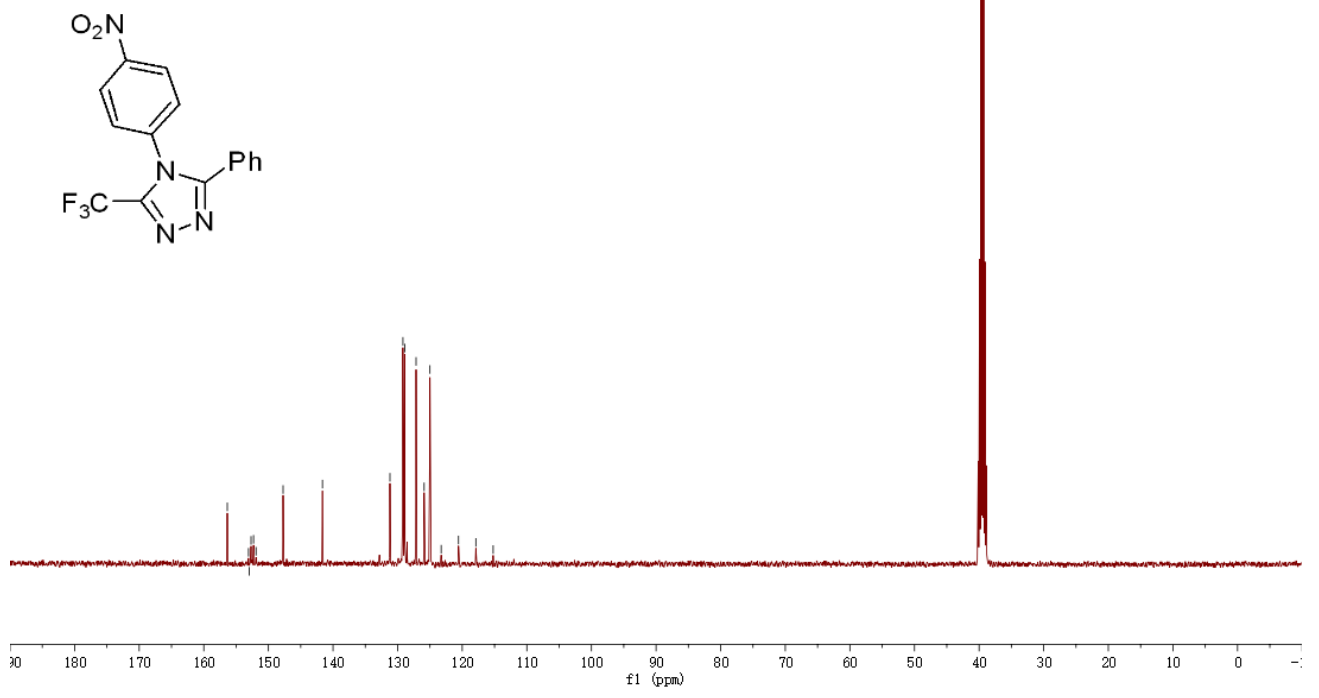
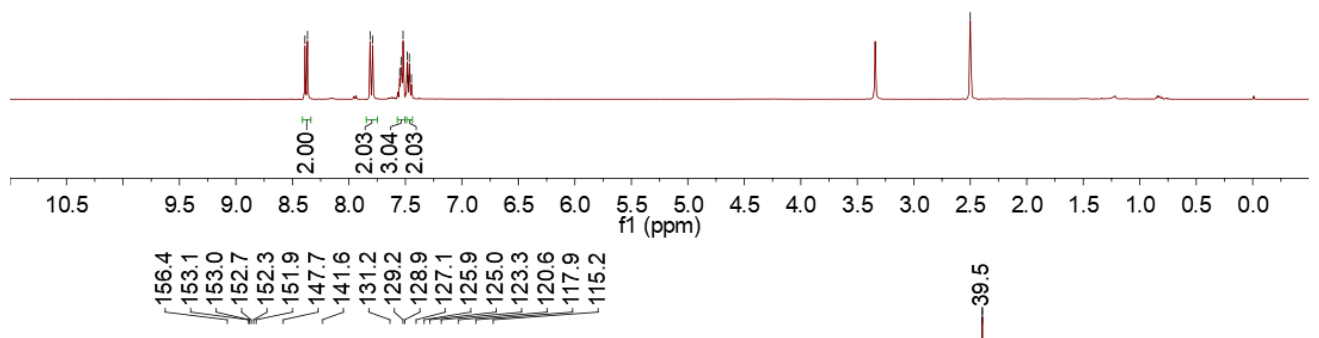
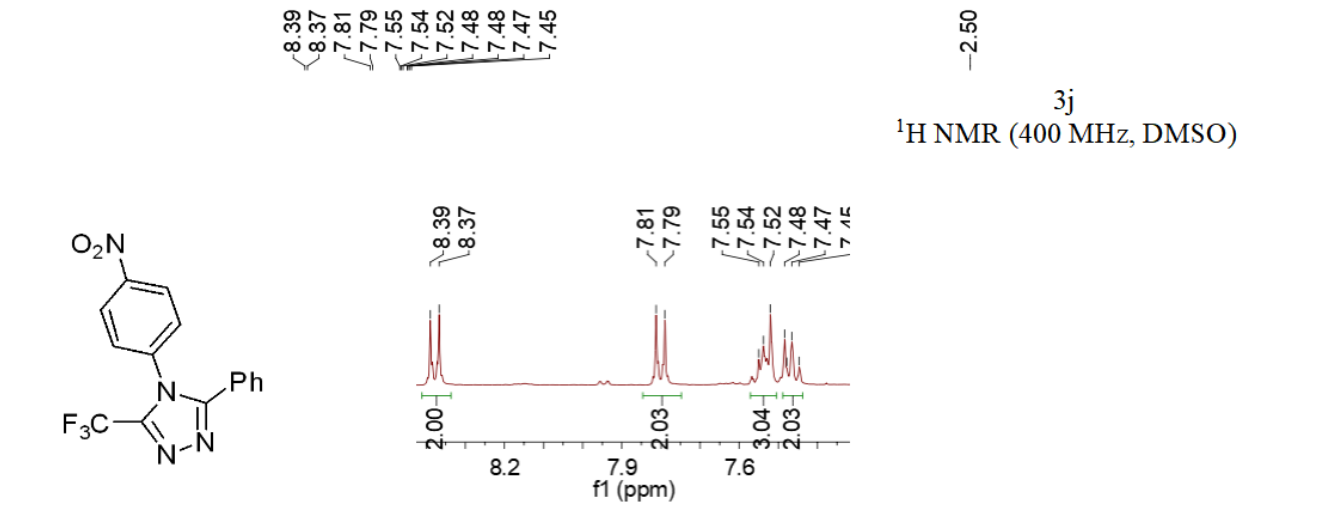


3h  
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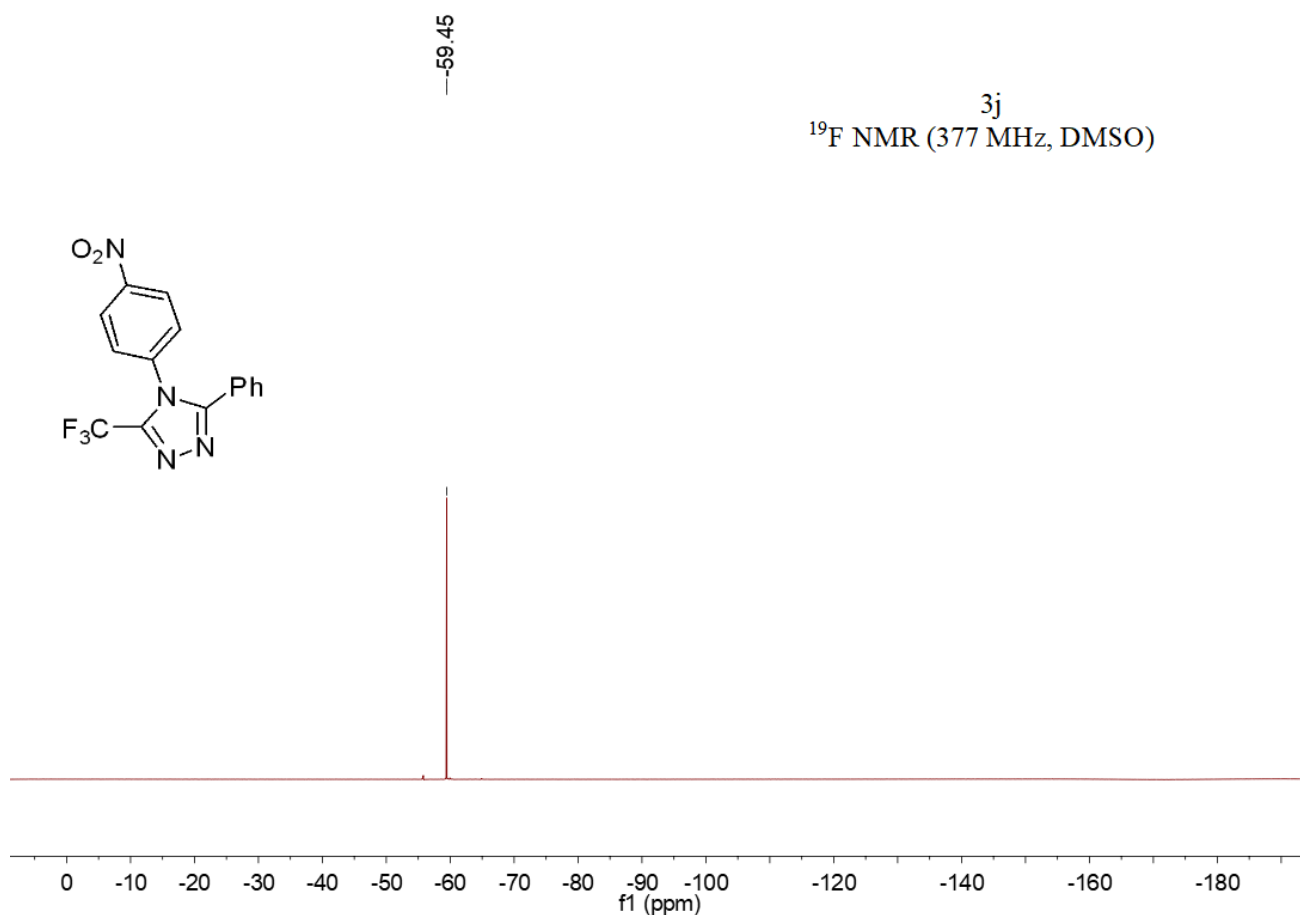
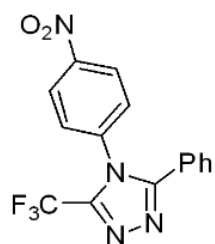




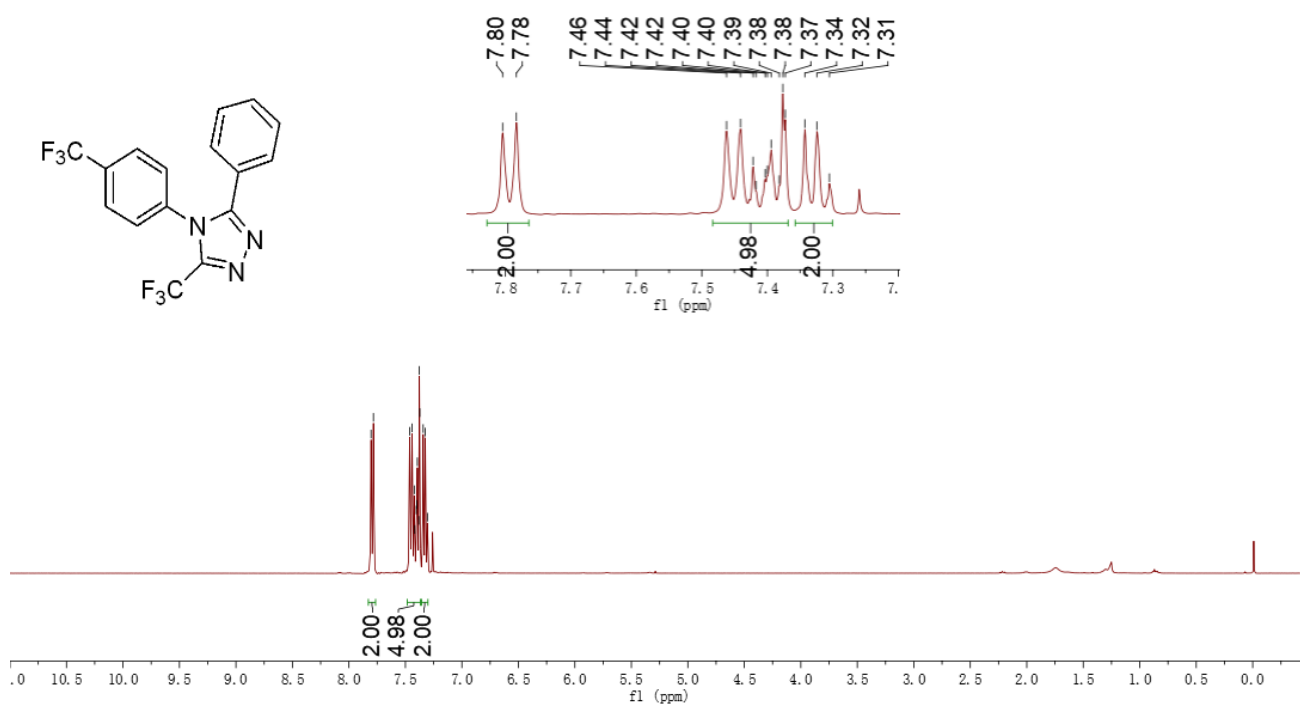
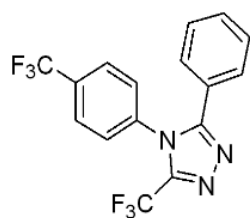


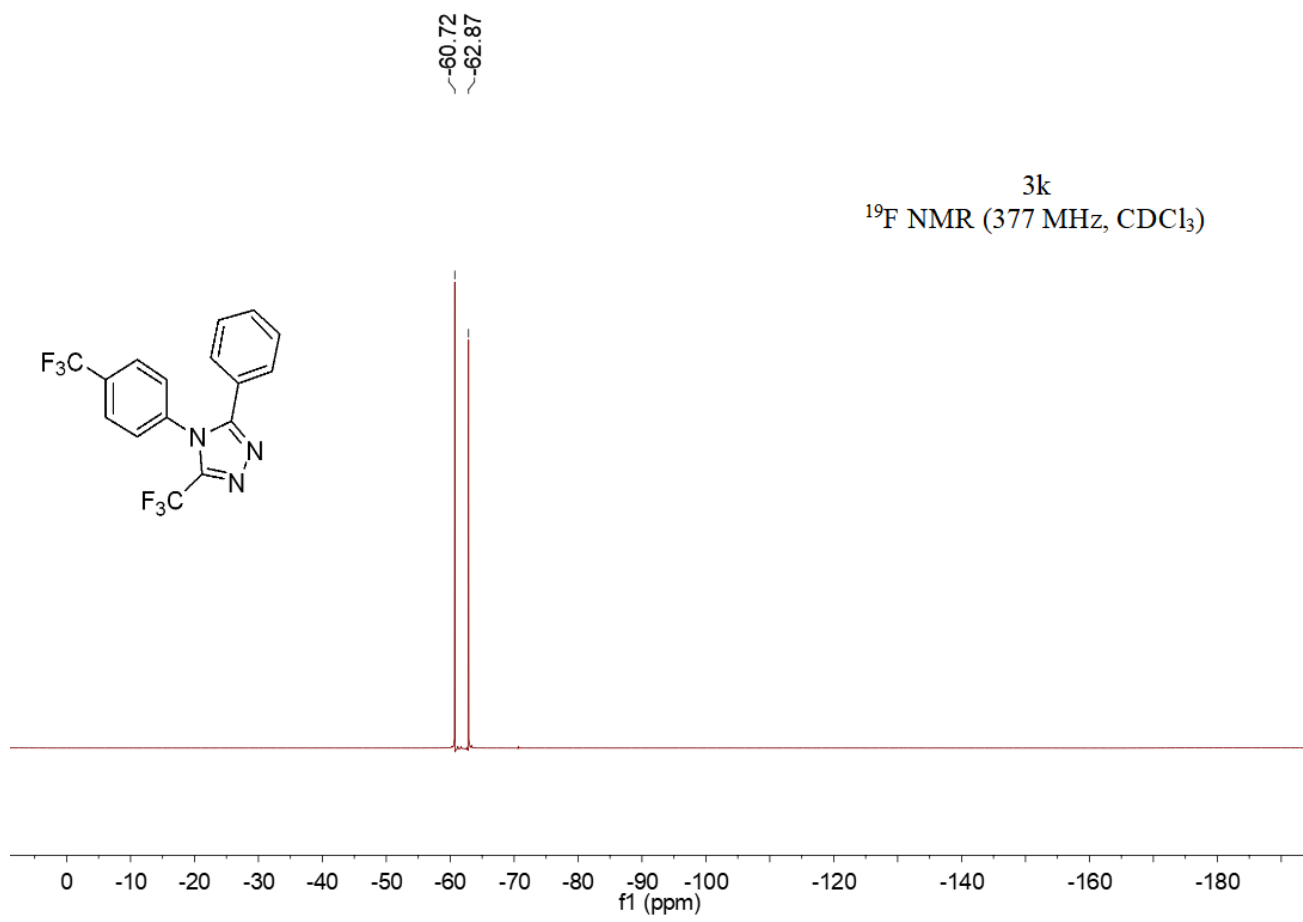
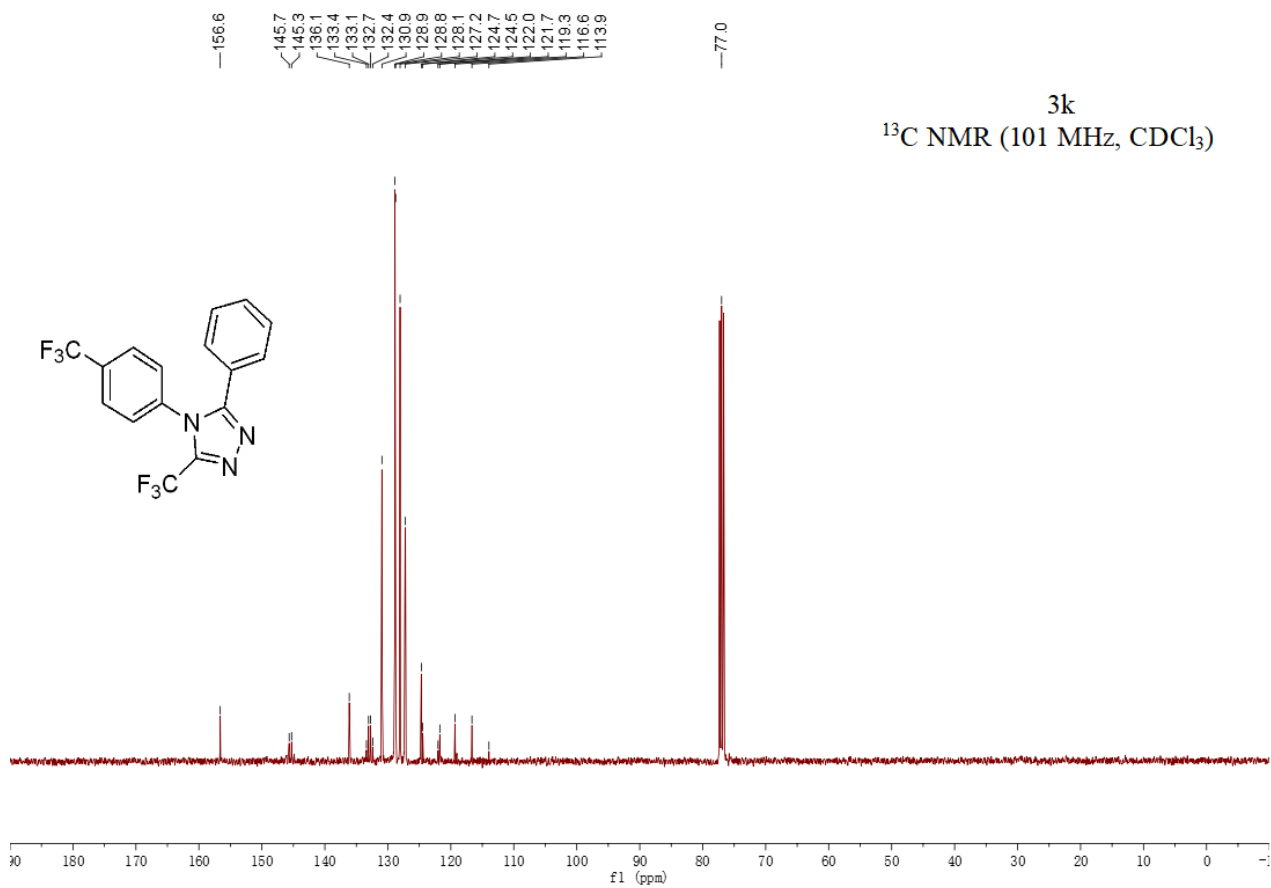


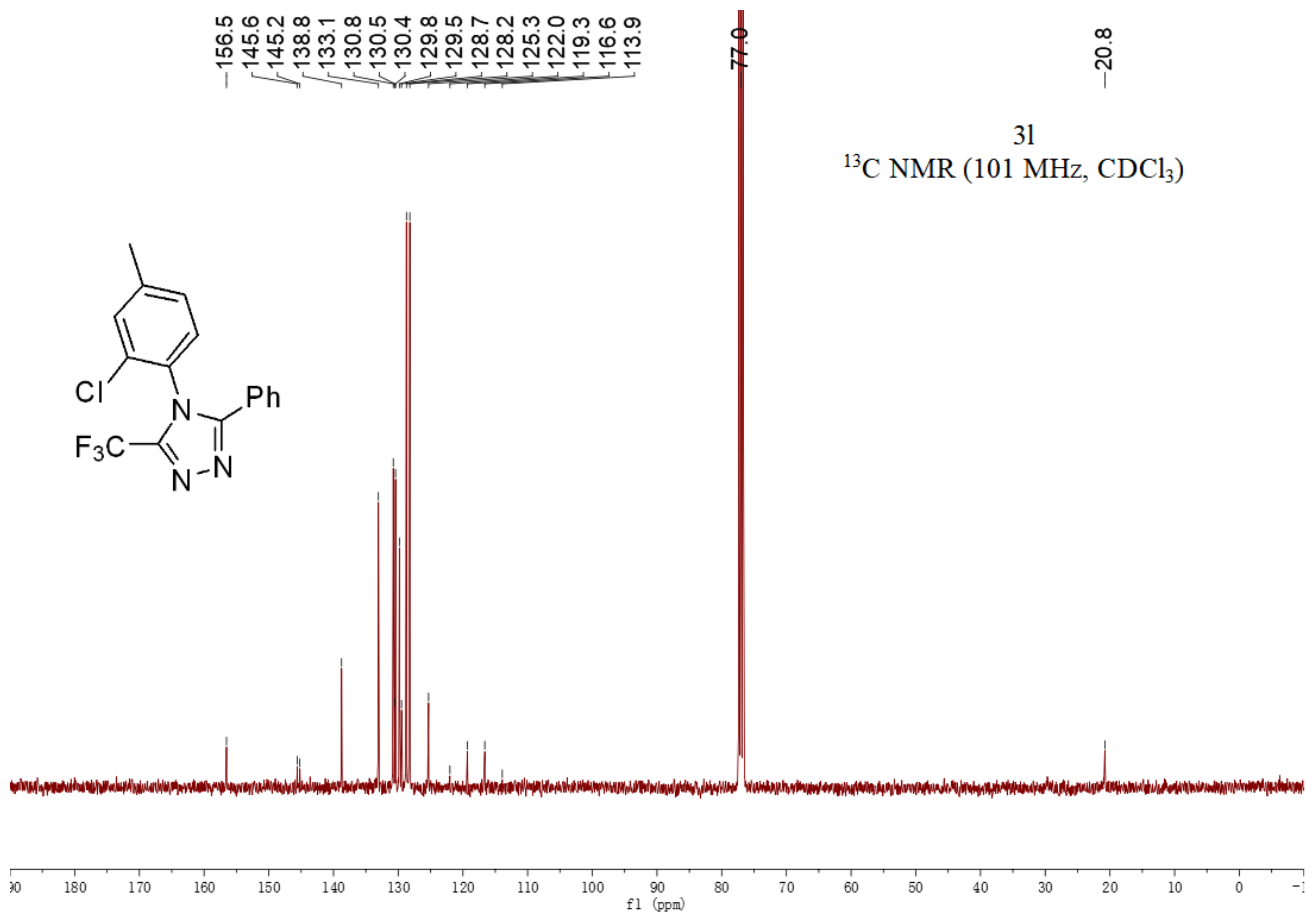
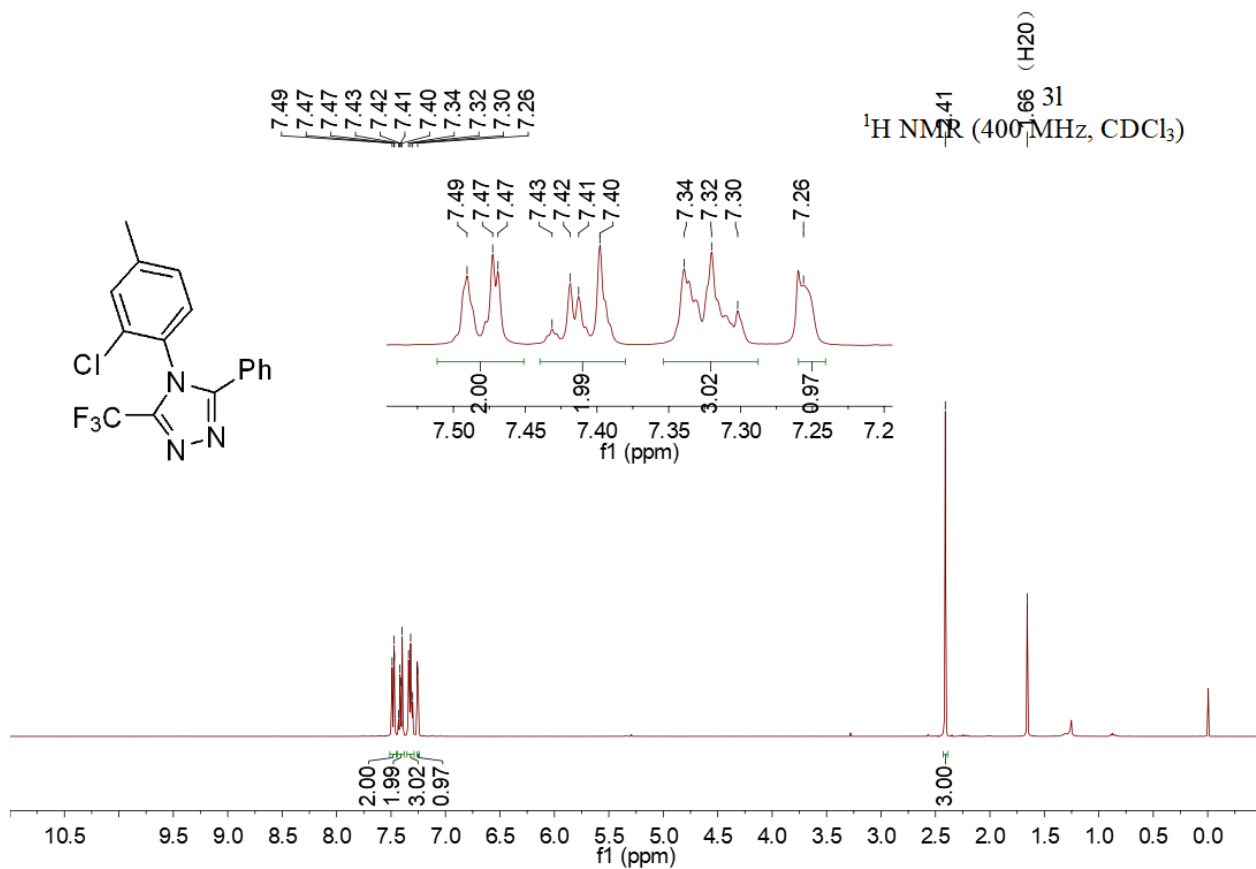
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<sup>19</sup>F NMR (377 MHz, DMSO)

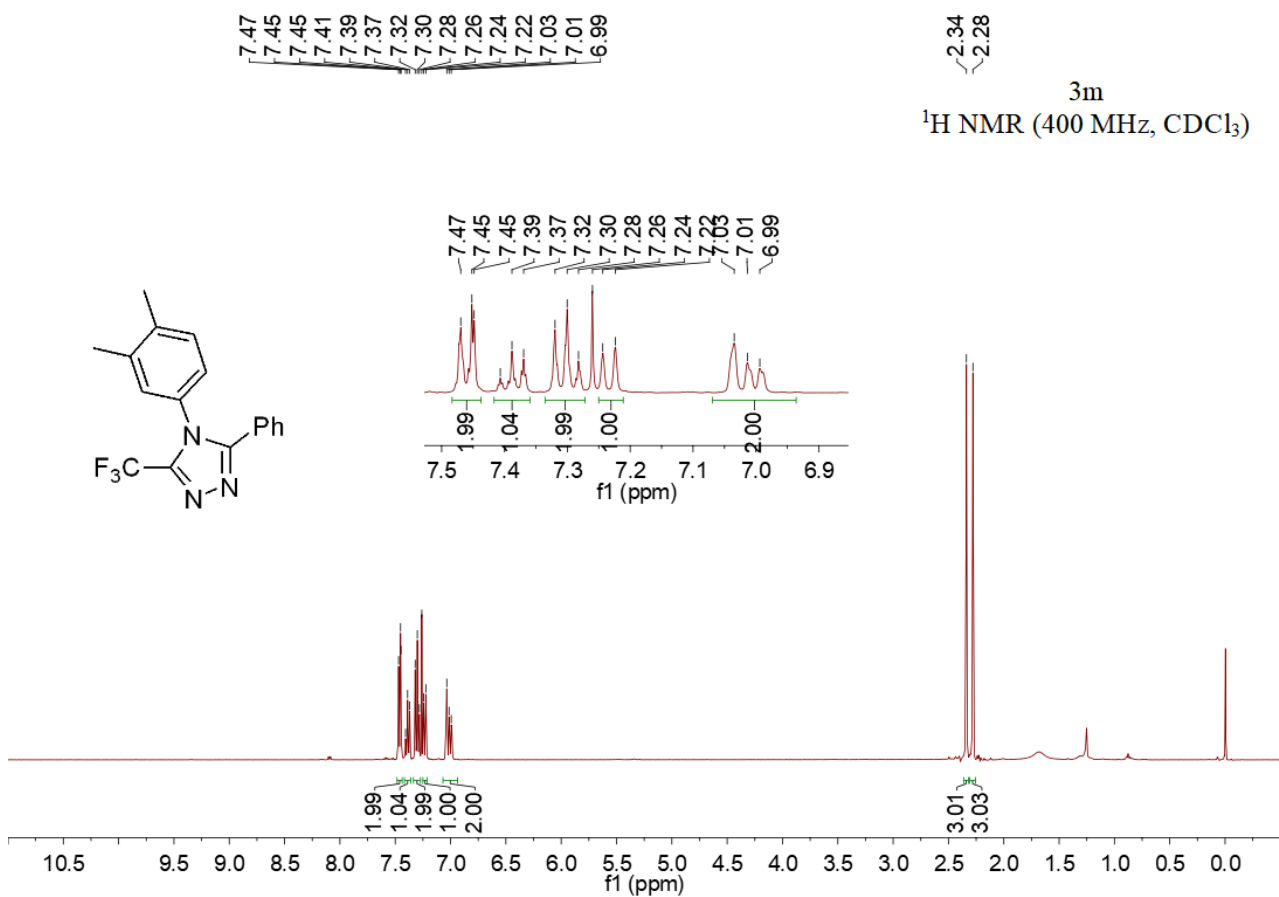
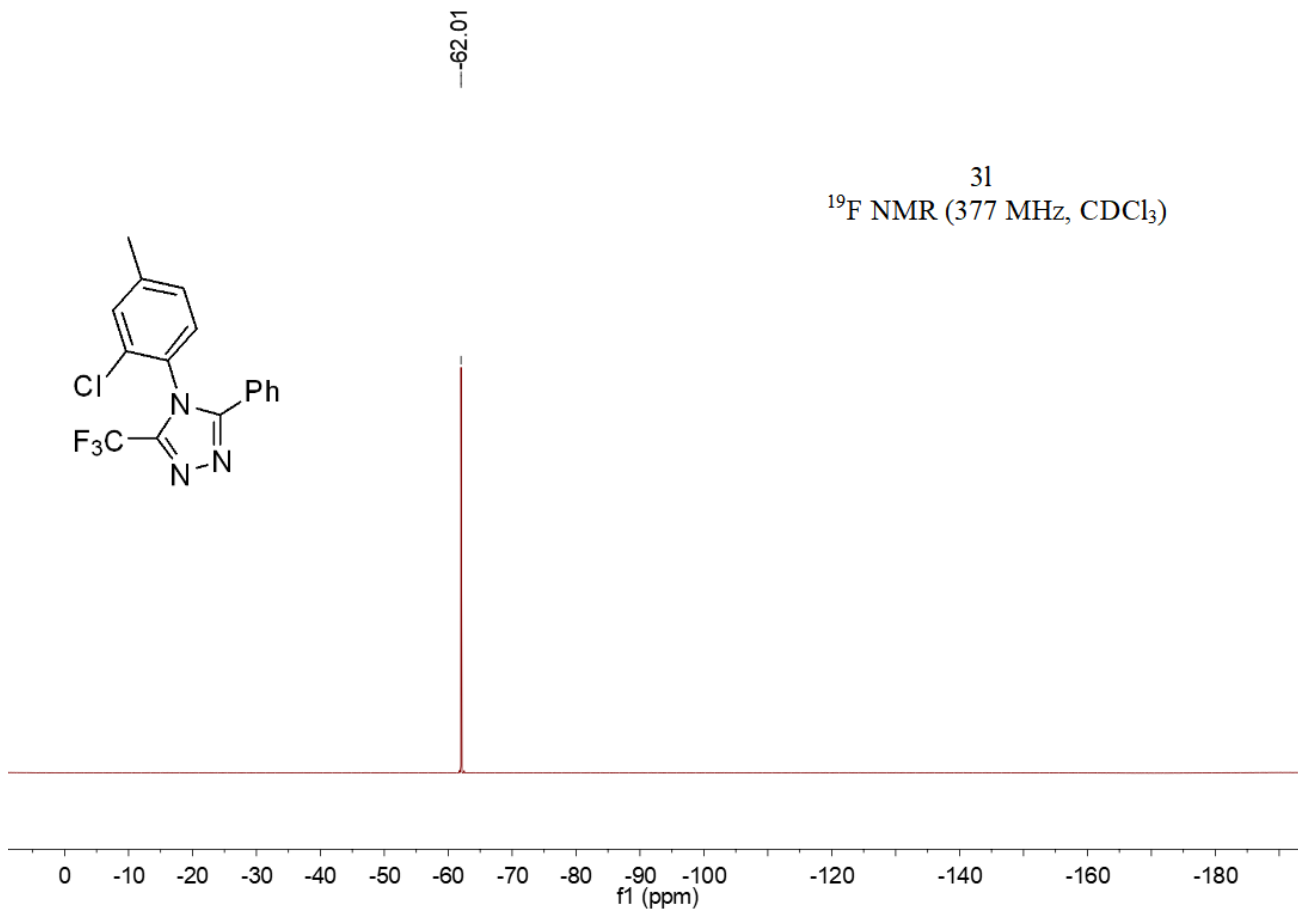


3k  
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

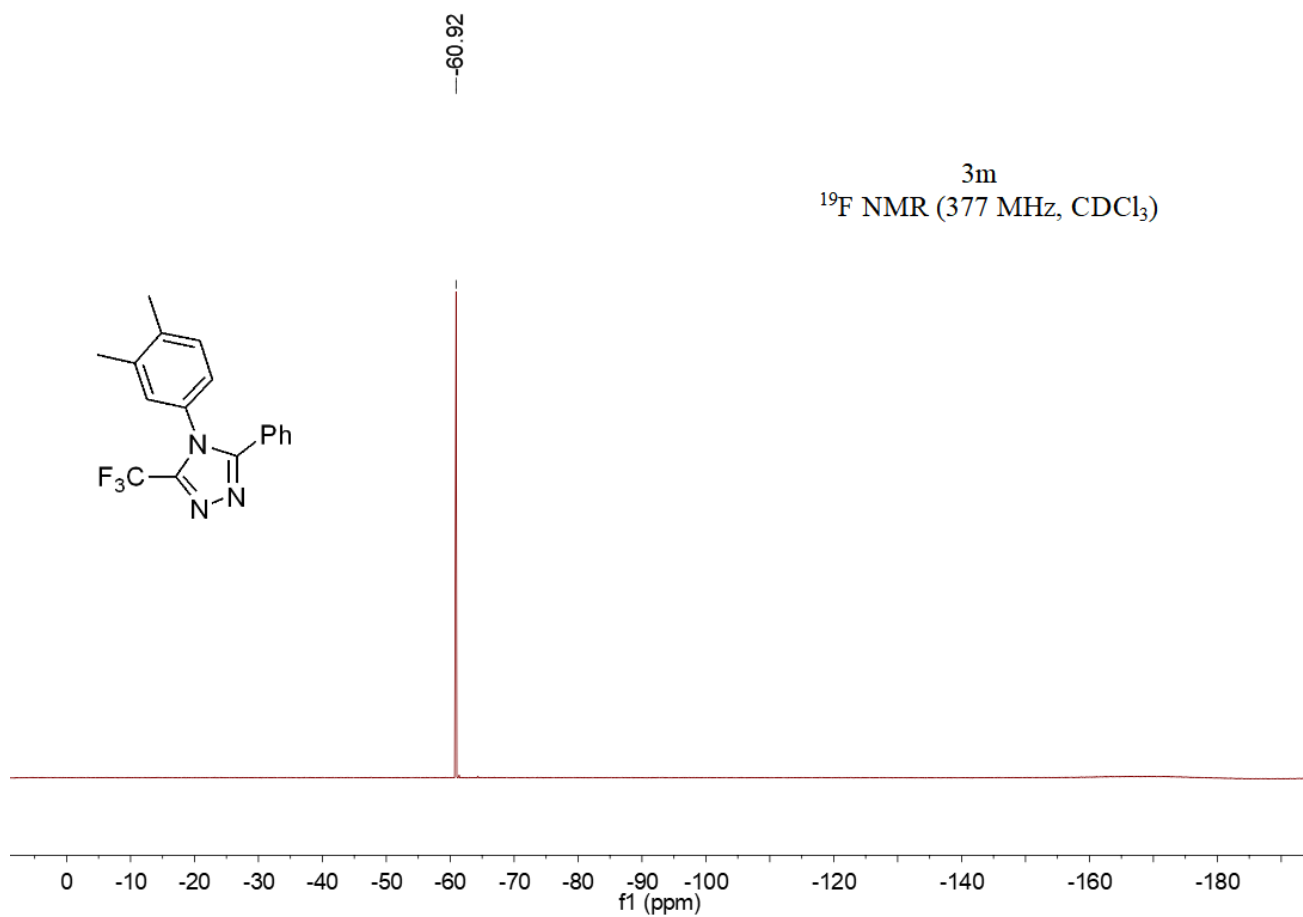
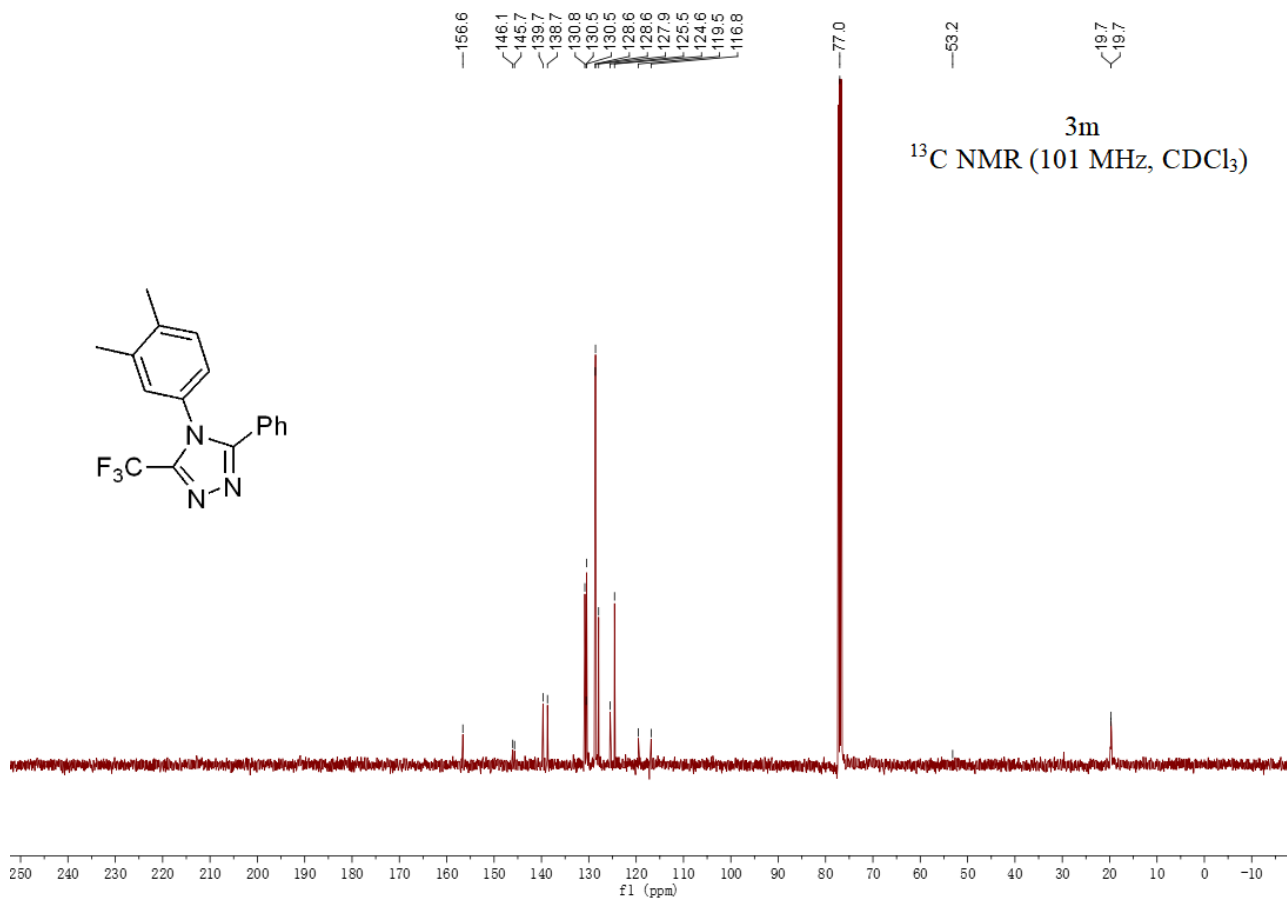








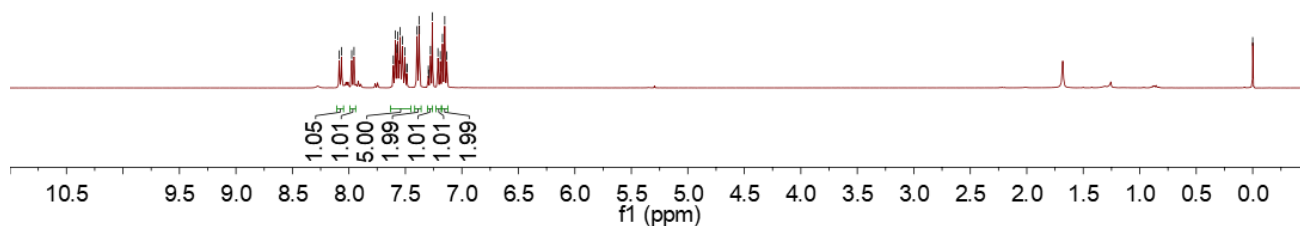
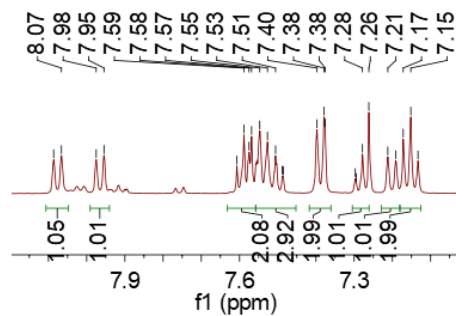
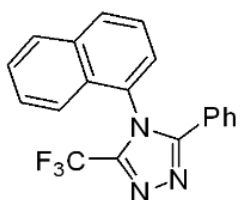




8.09  
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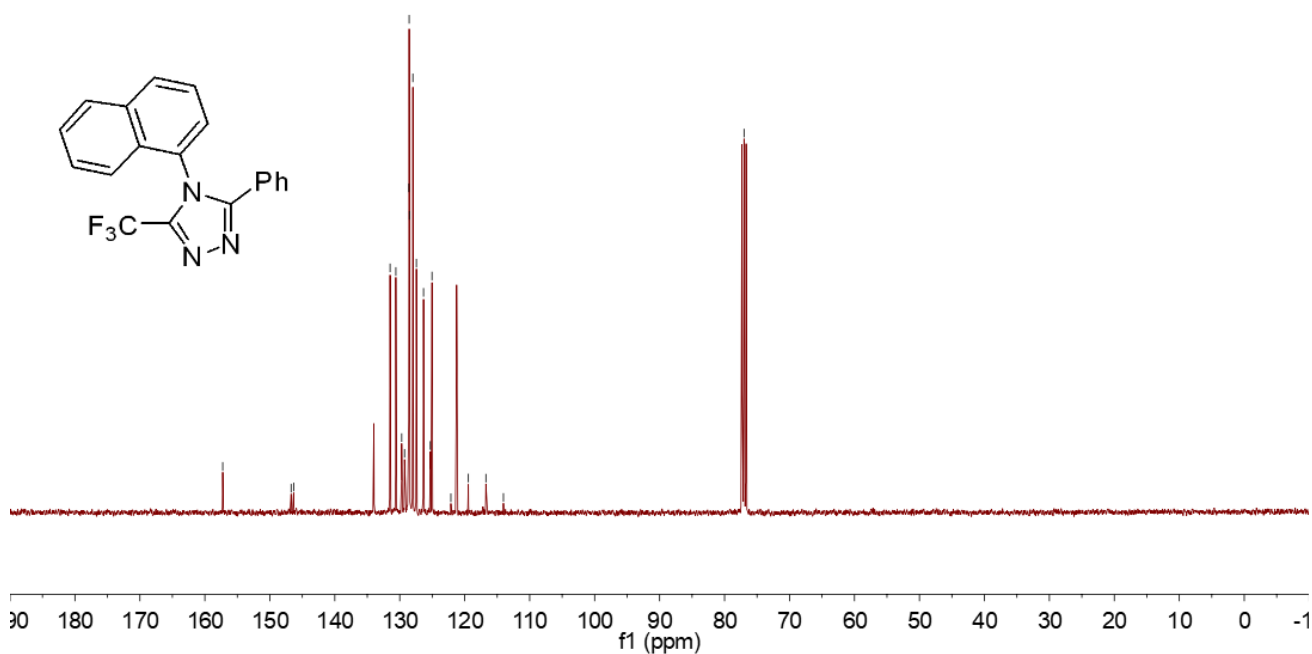
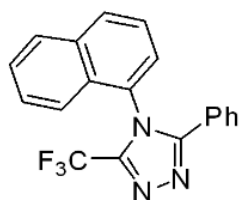
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3n  
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

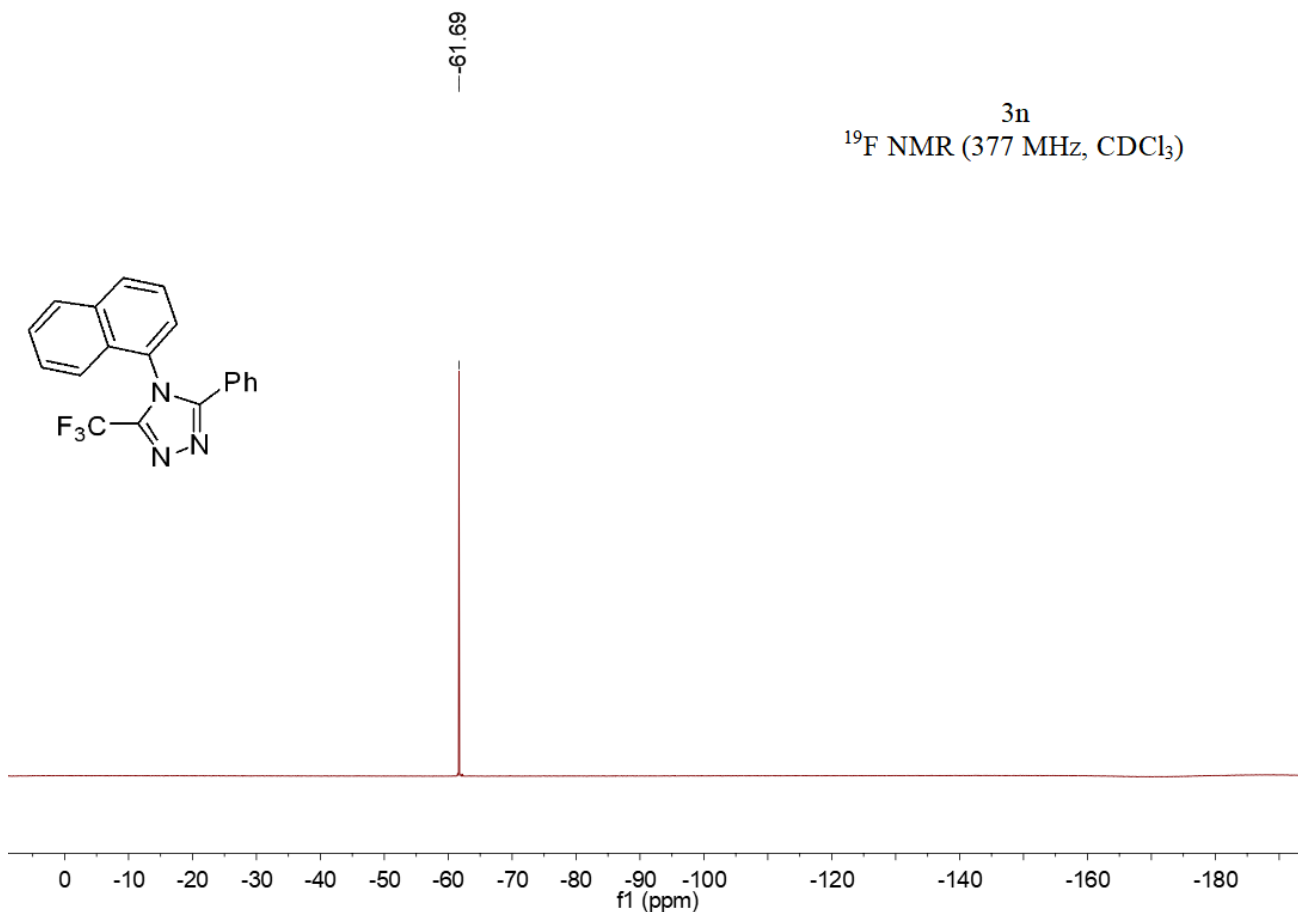


157.25  
146.72  
146.33  
131.49  
130.60  
129.70  
129.26  
128.59  
128.55  
128.51  
127.98  
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77.00

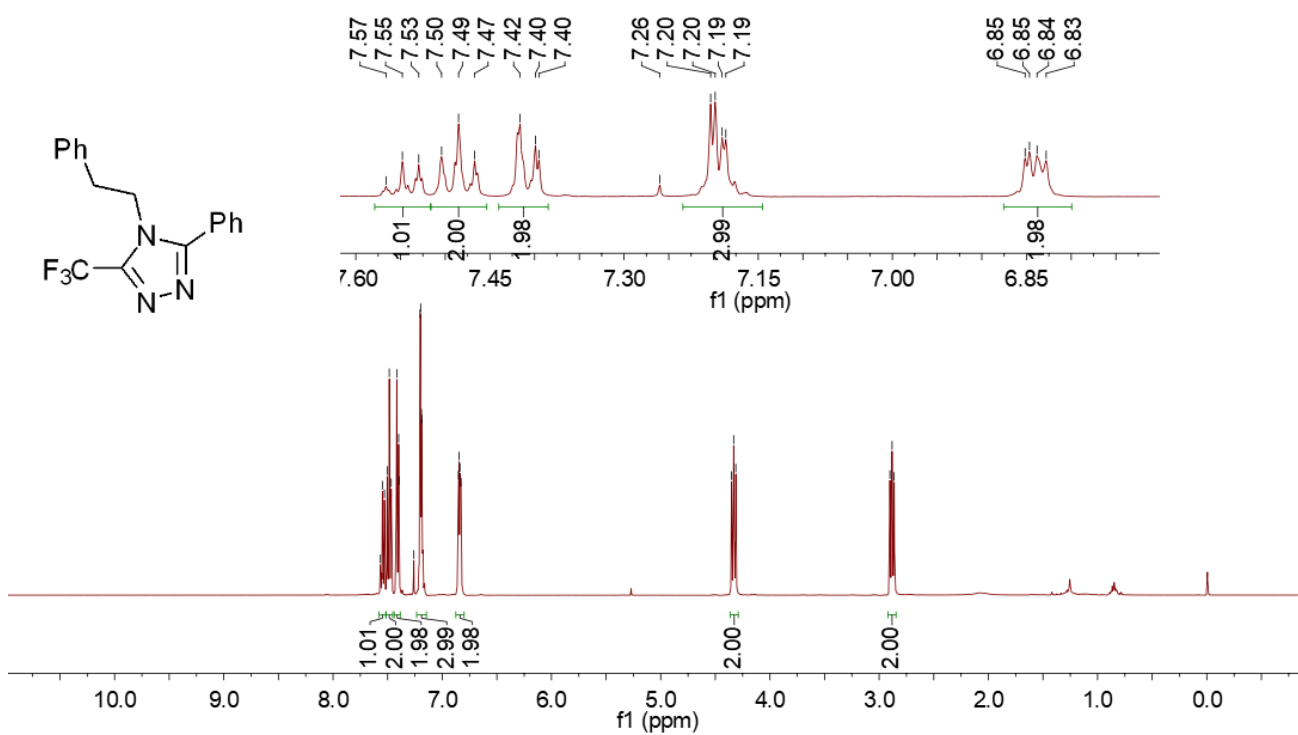
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<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

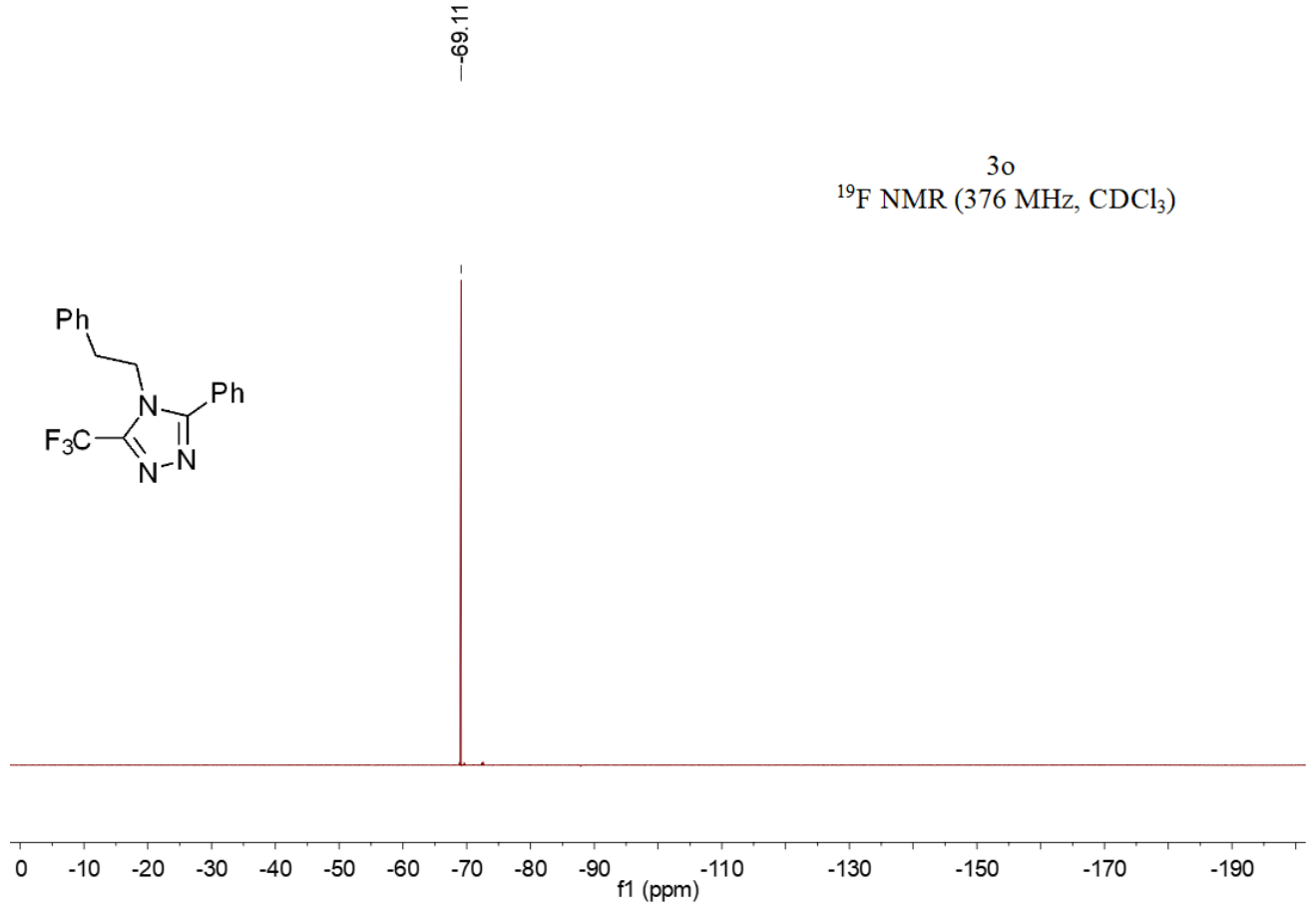
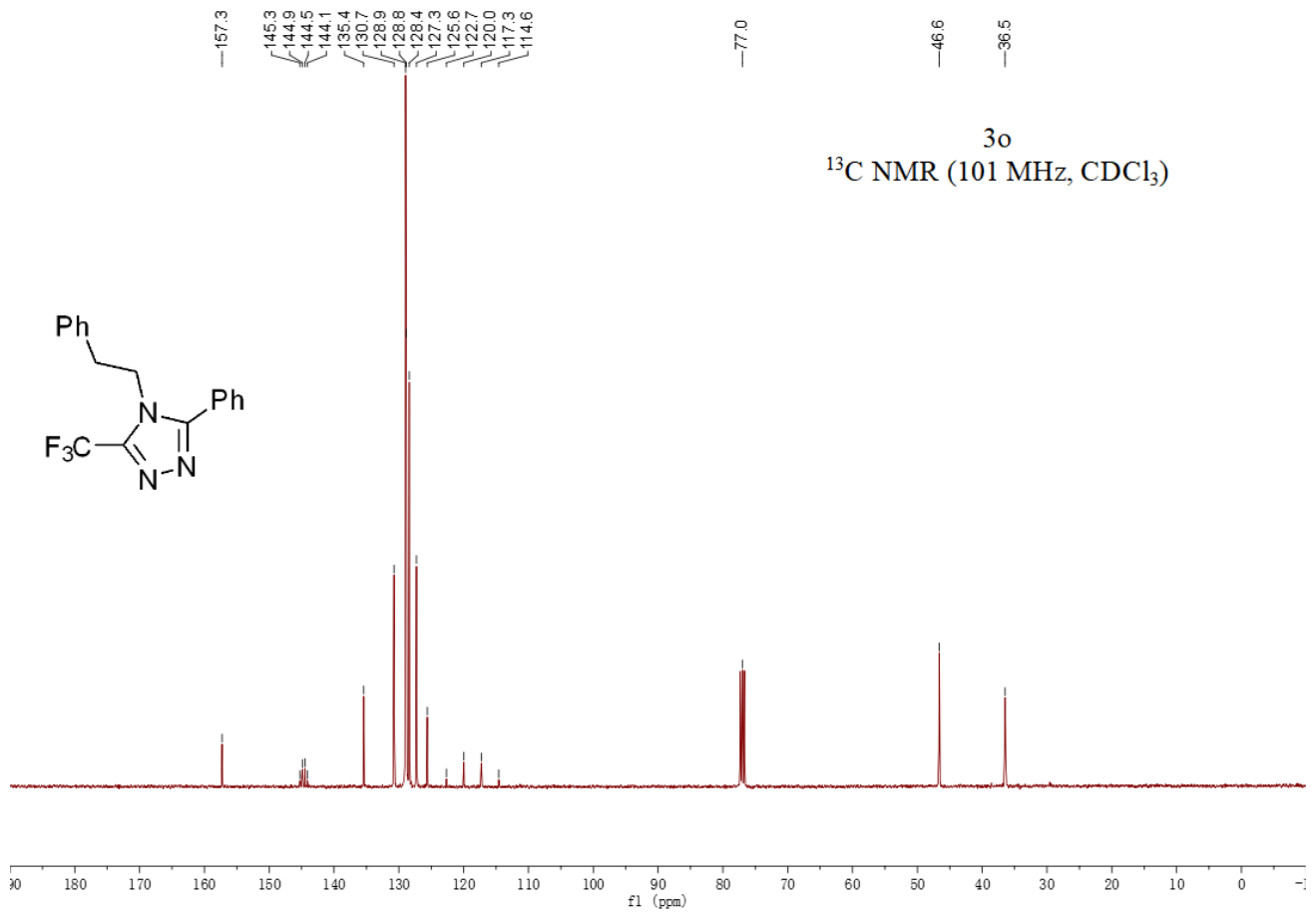


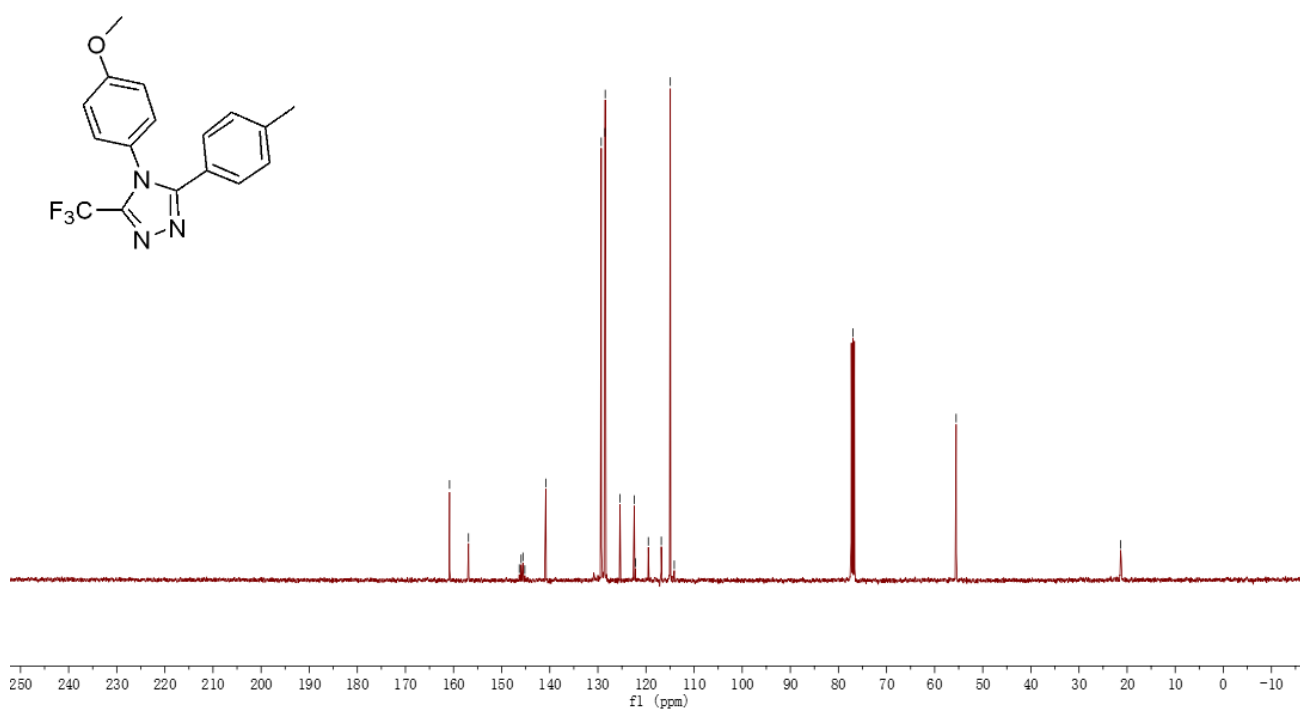
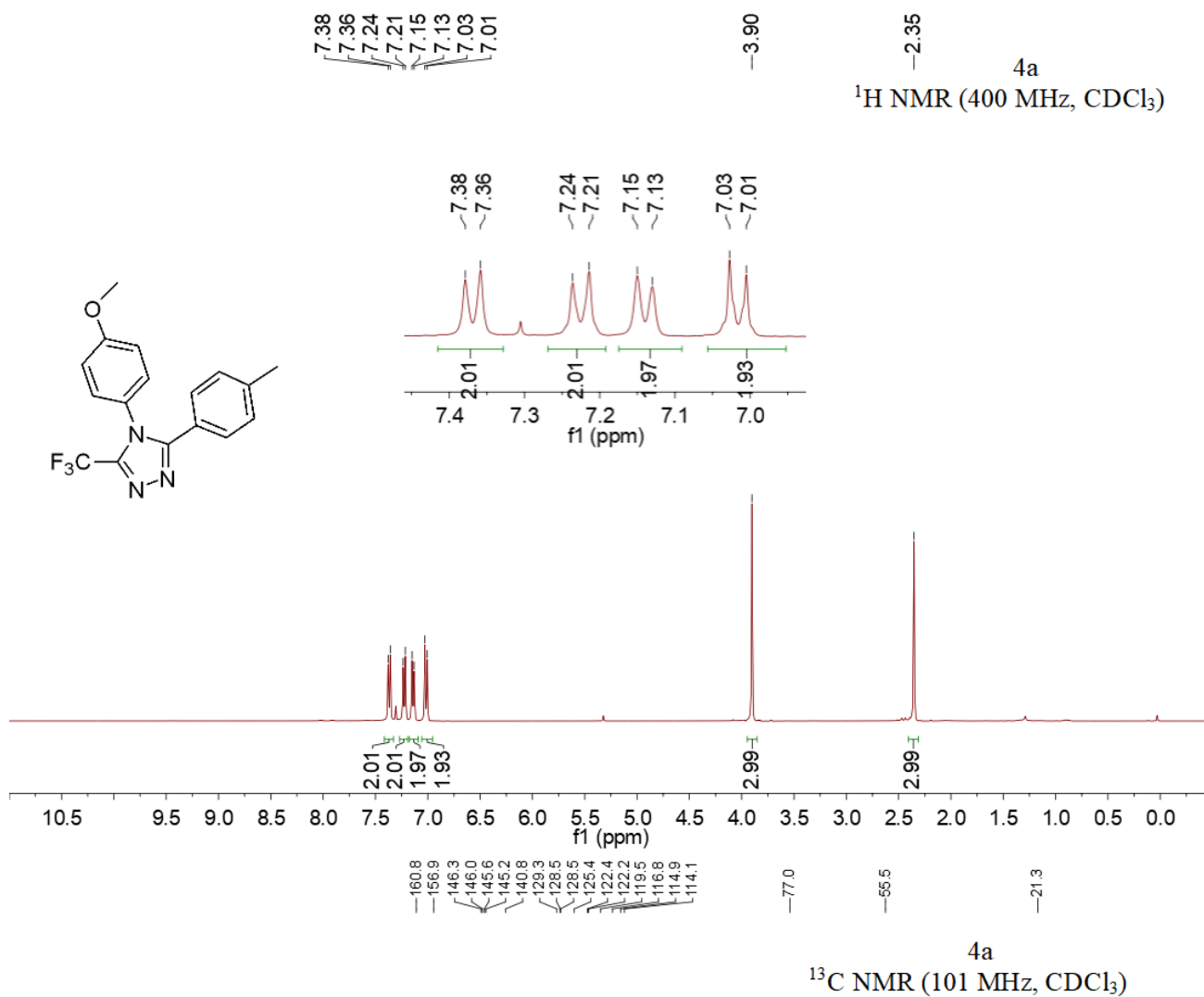
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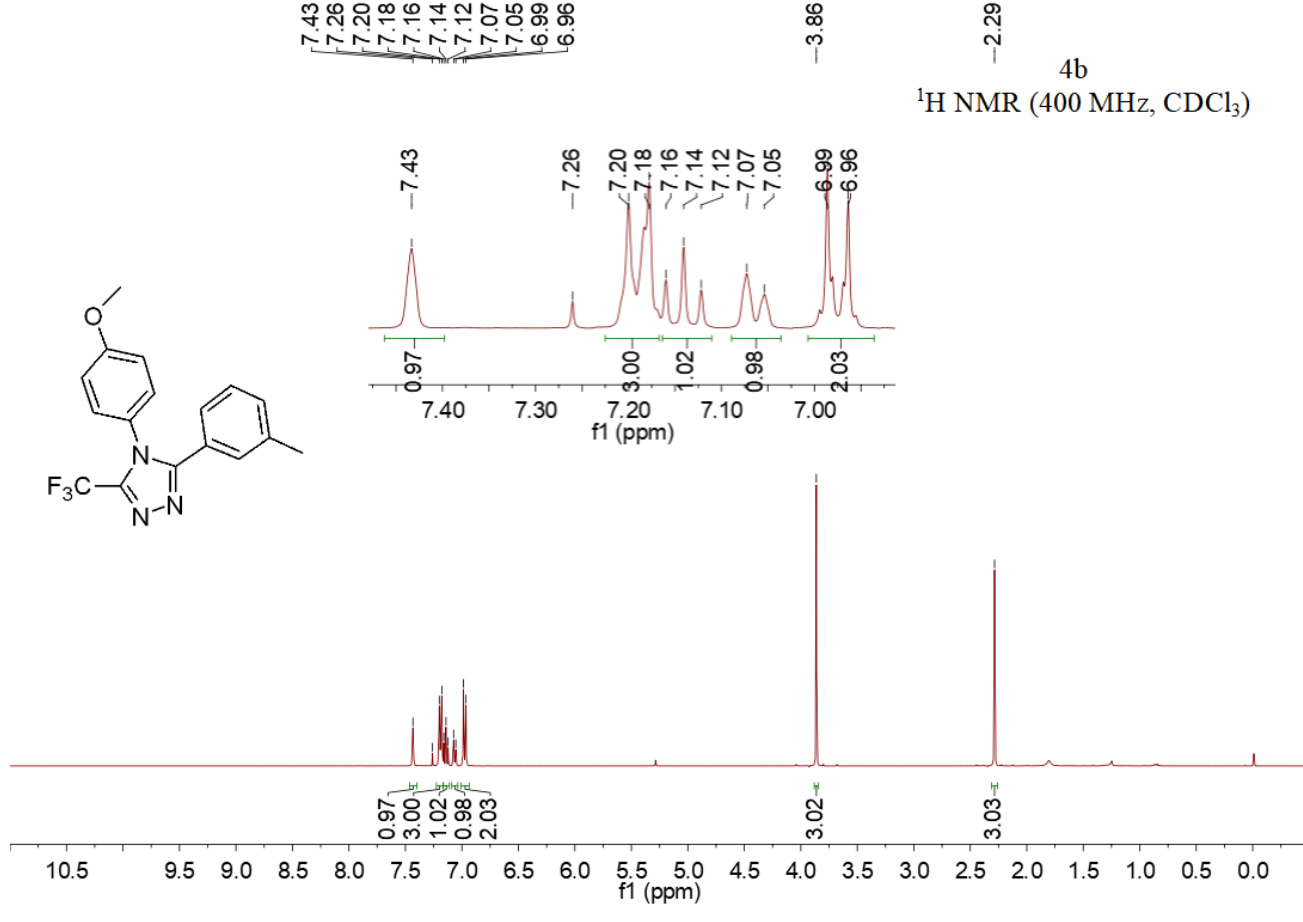
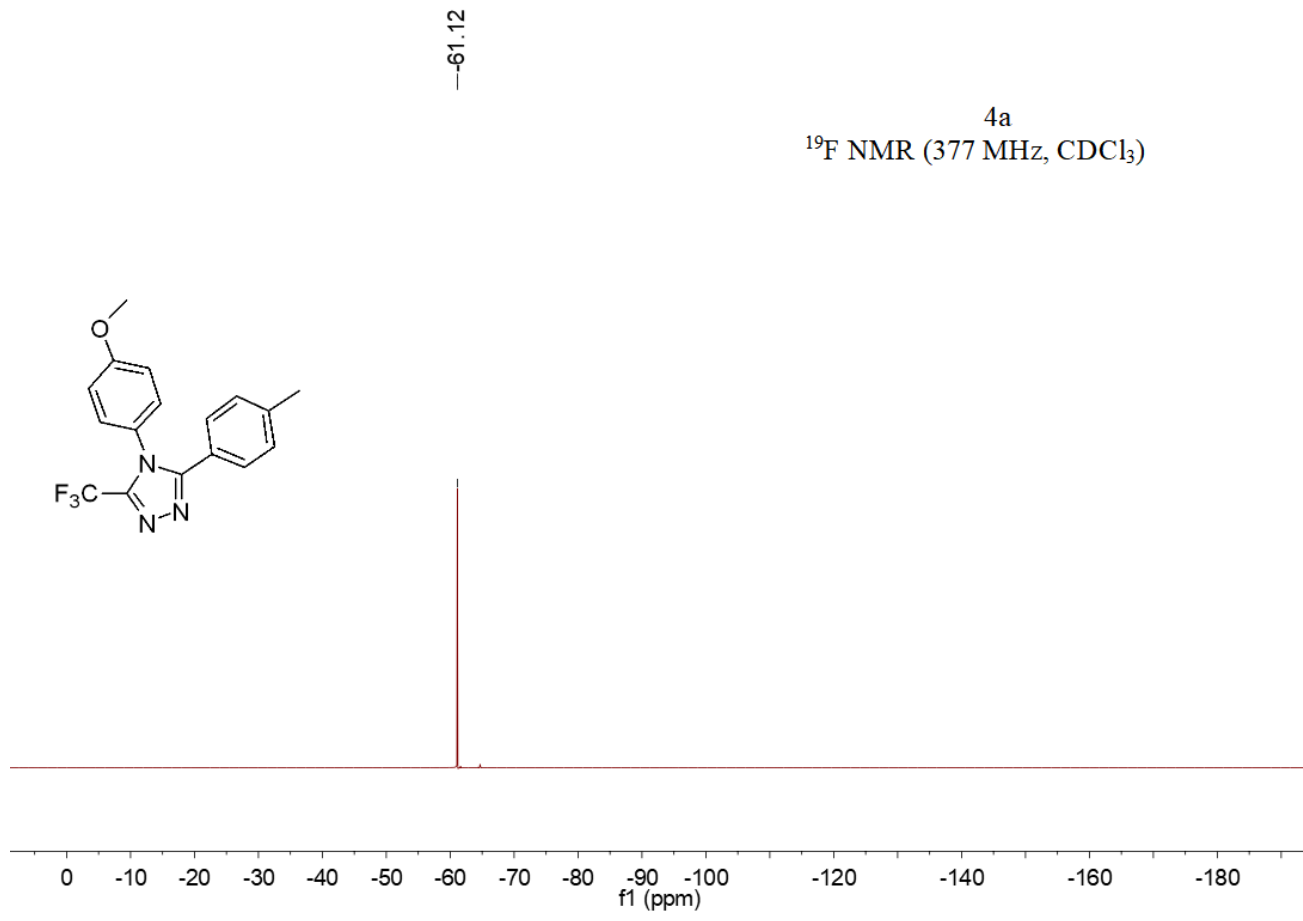


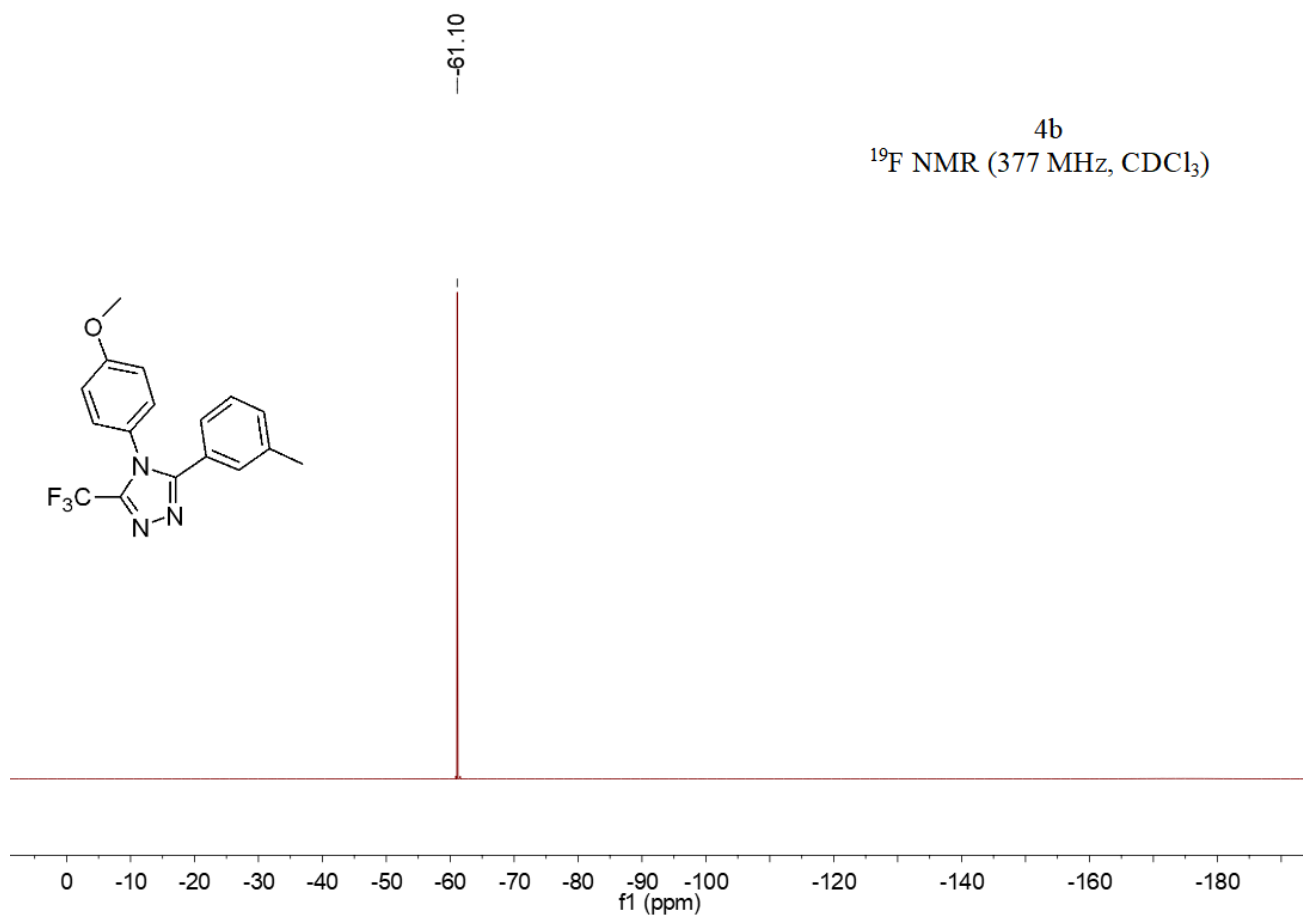
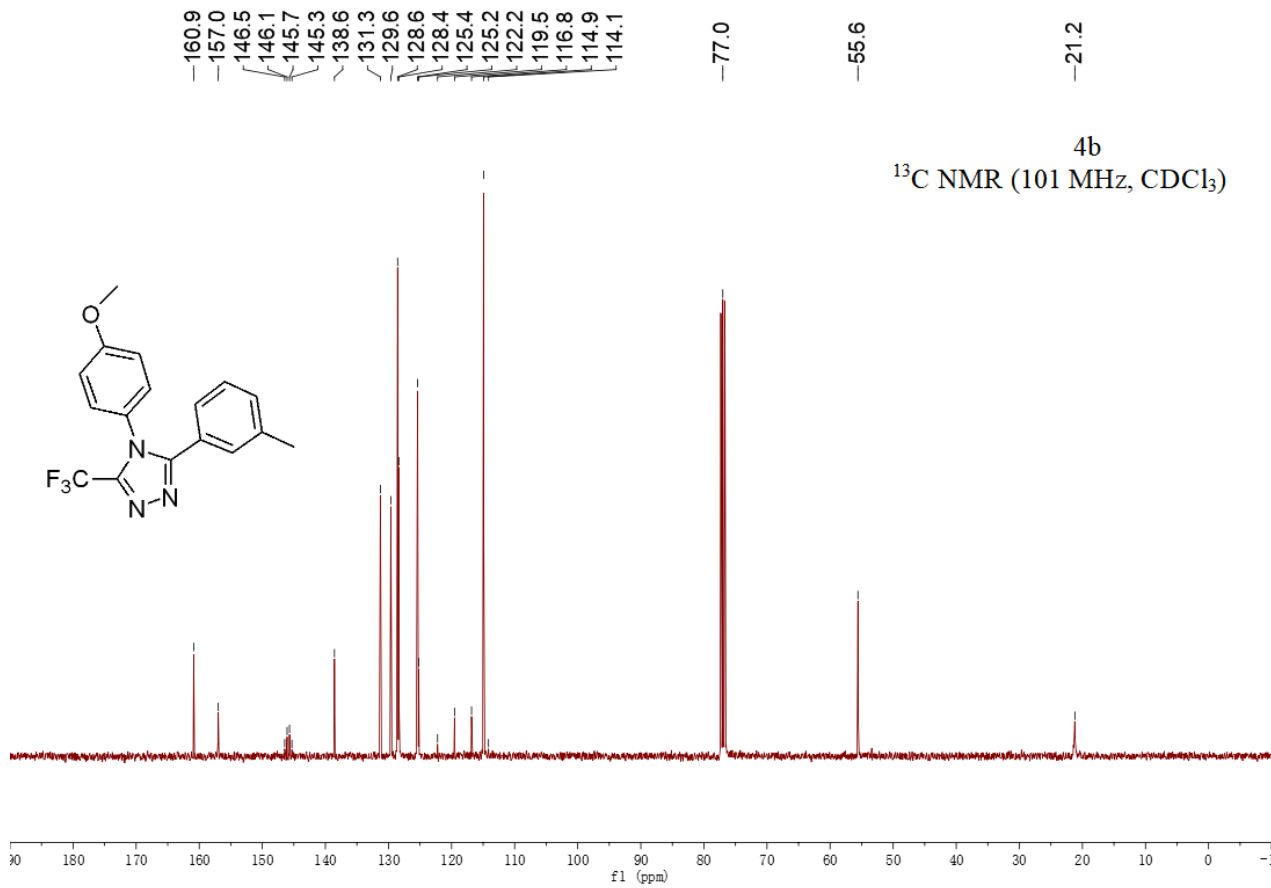
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<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

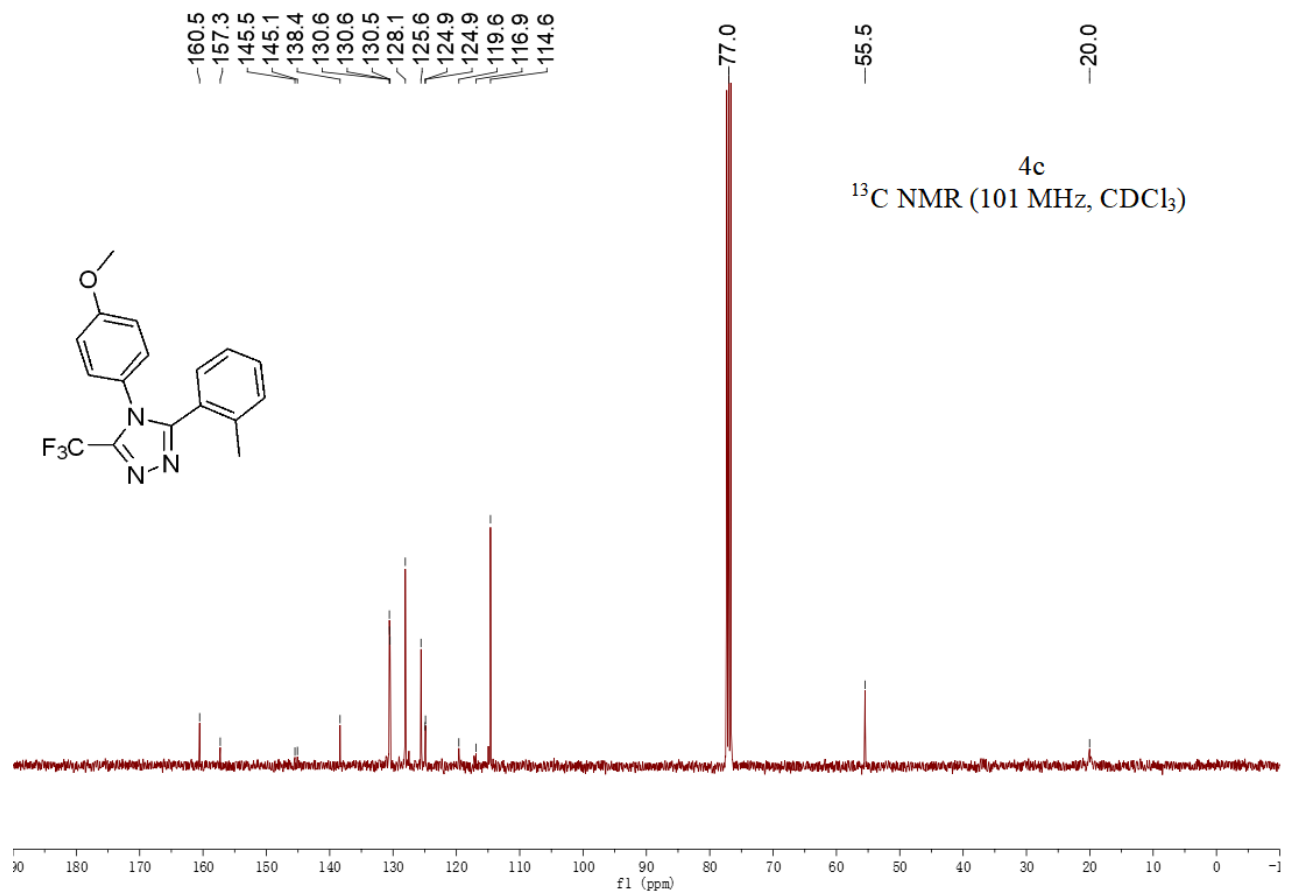
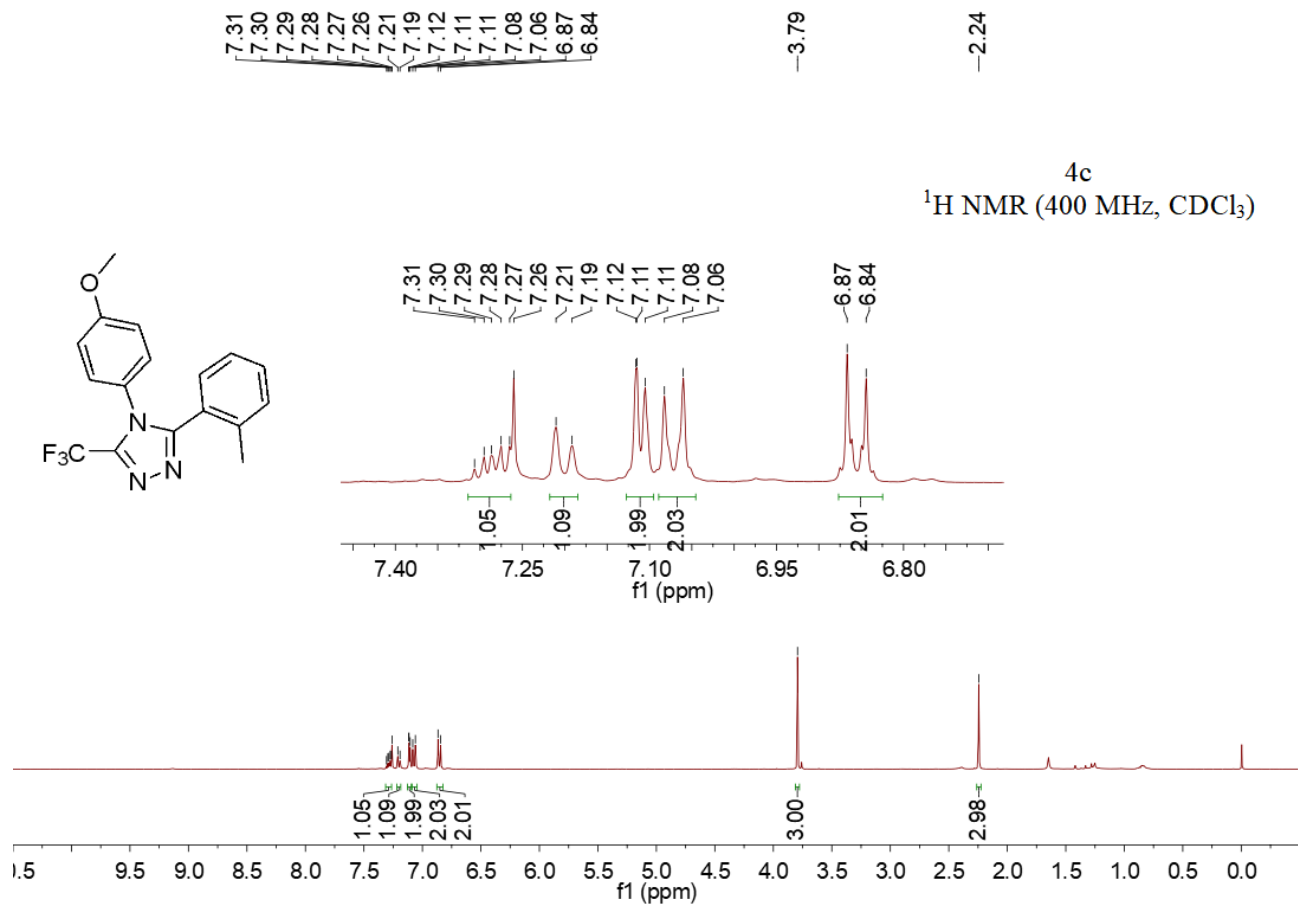




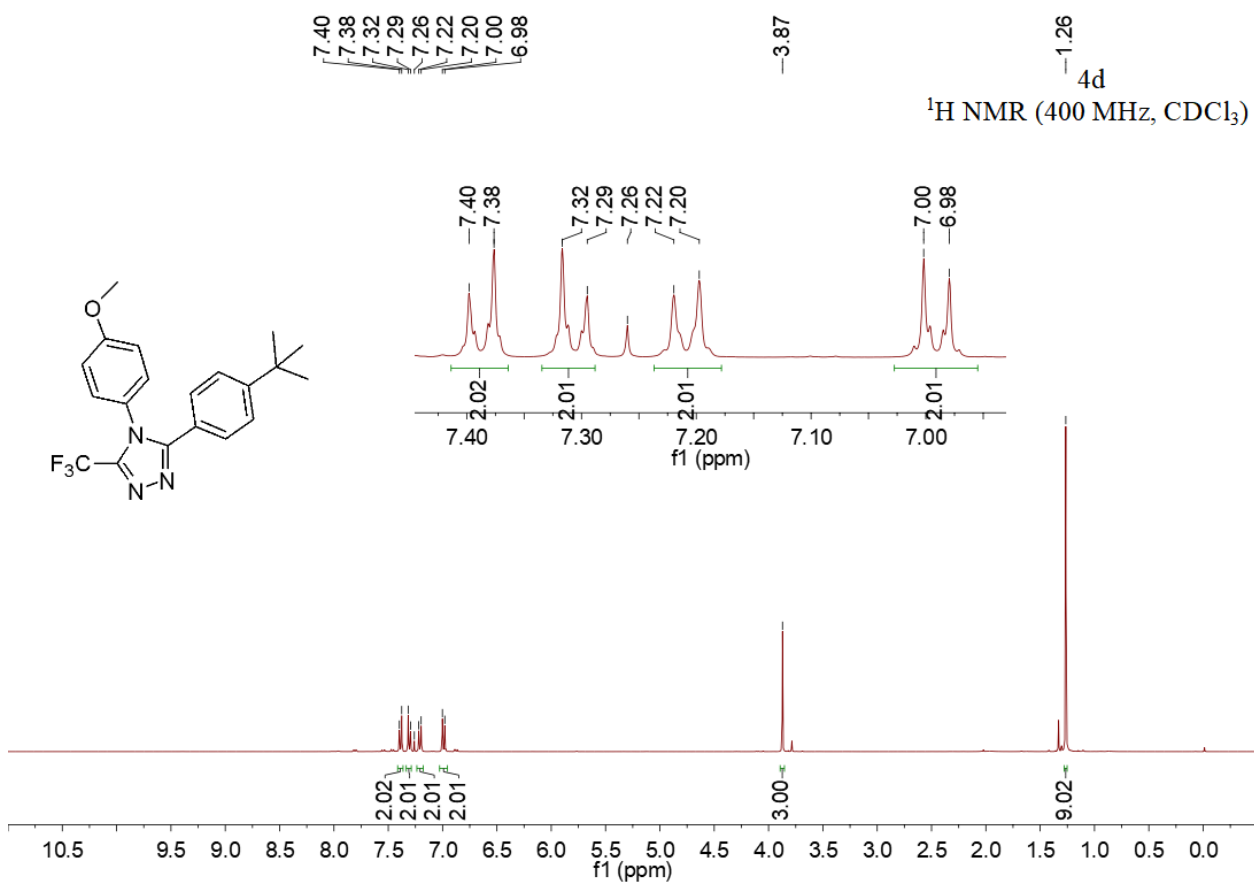
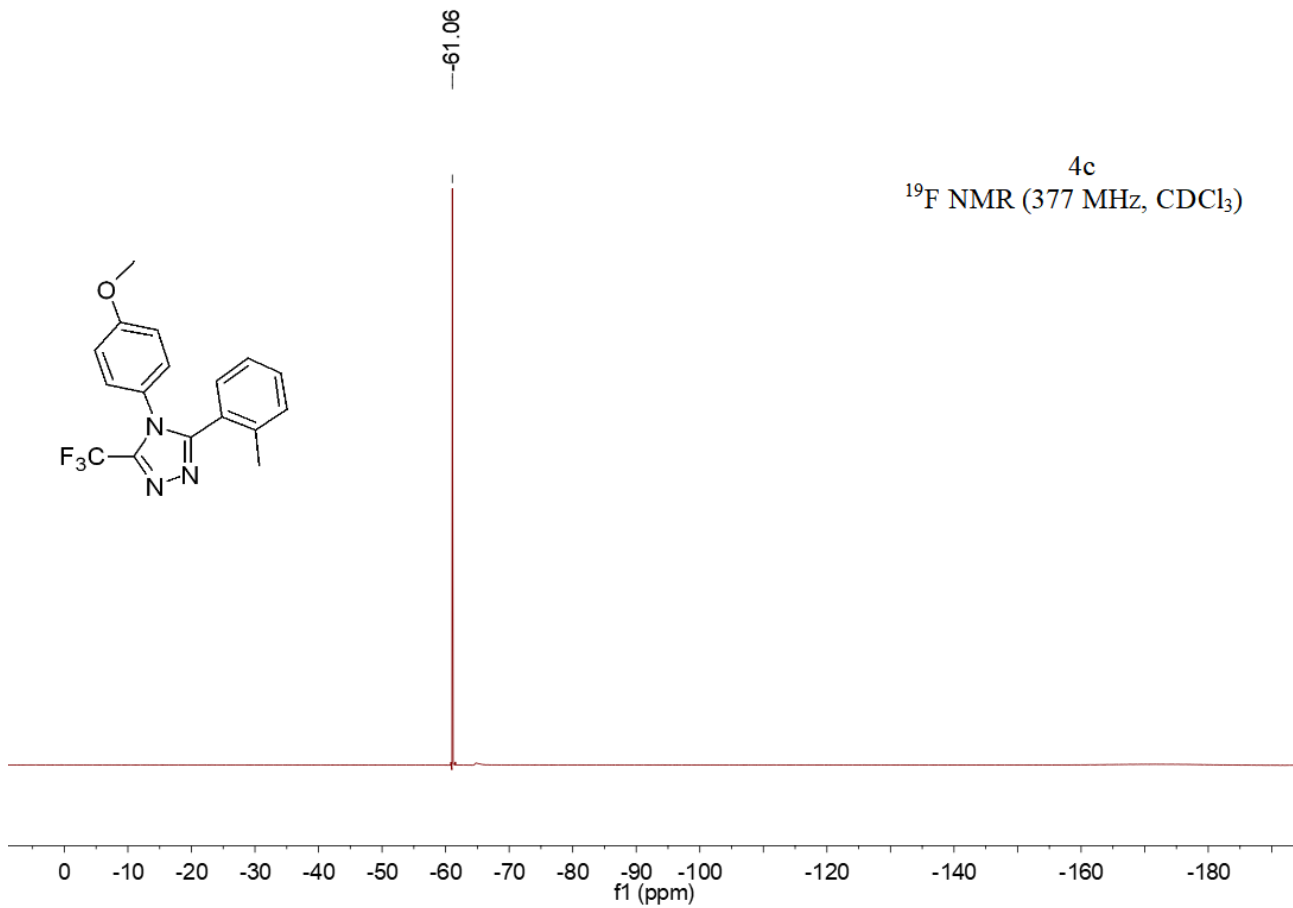


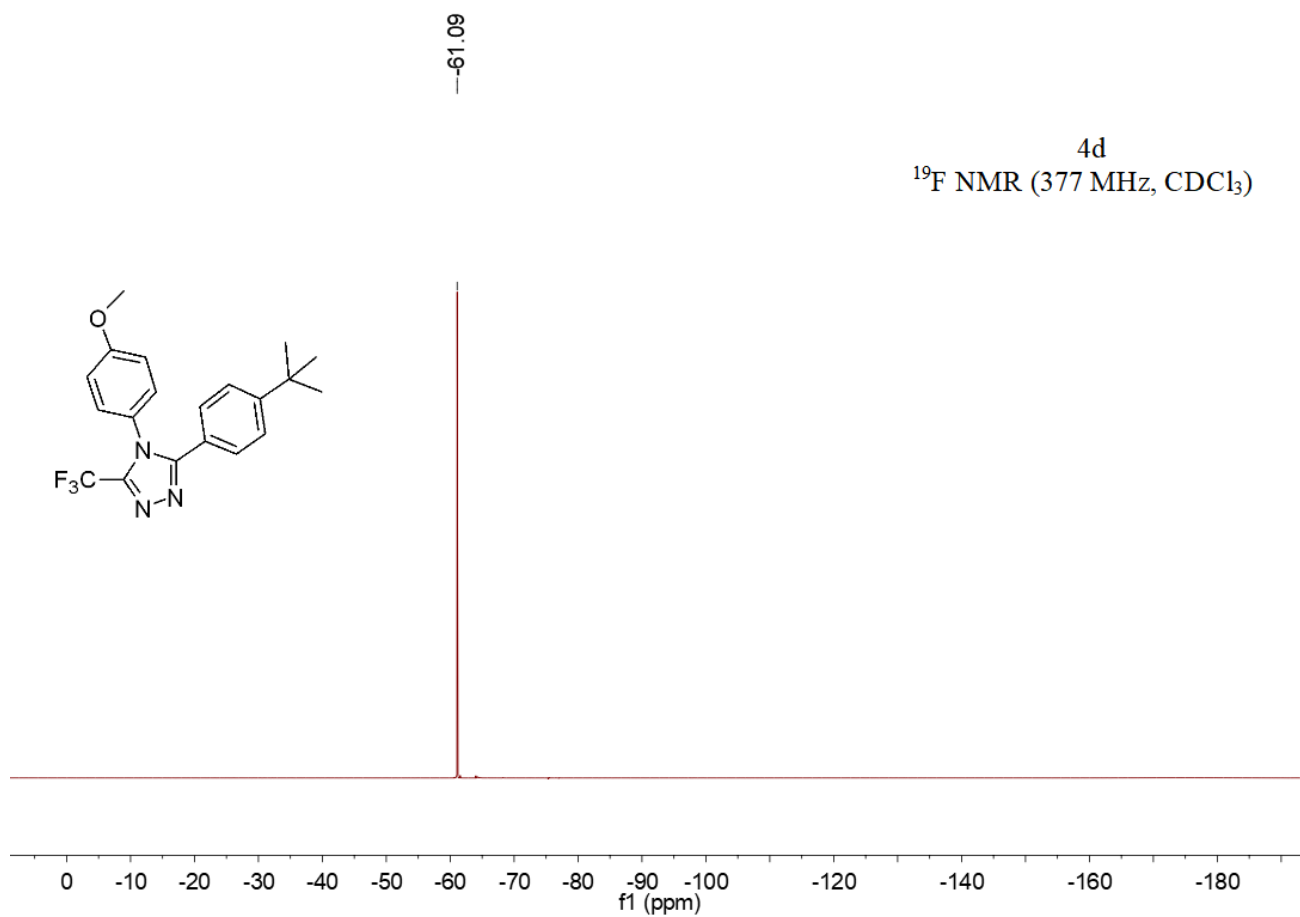
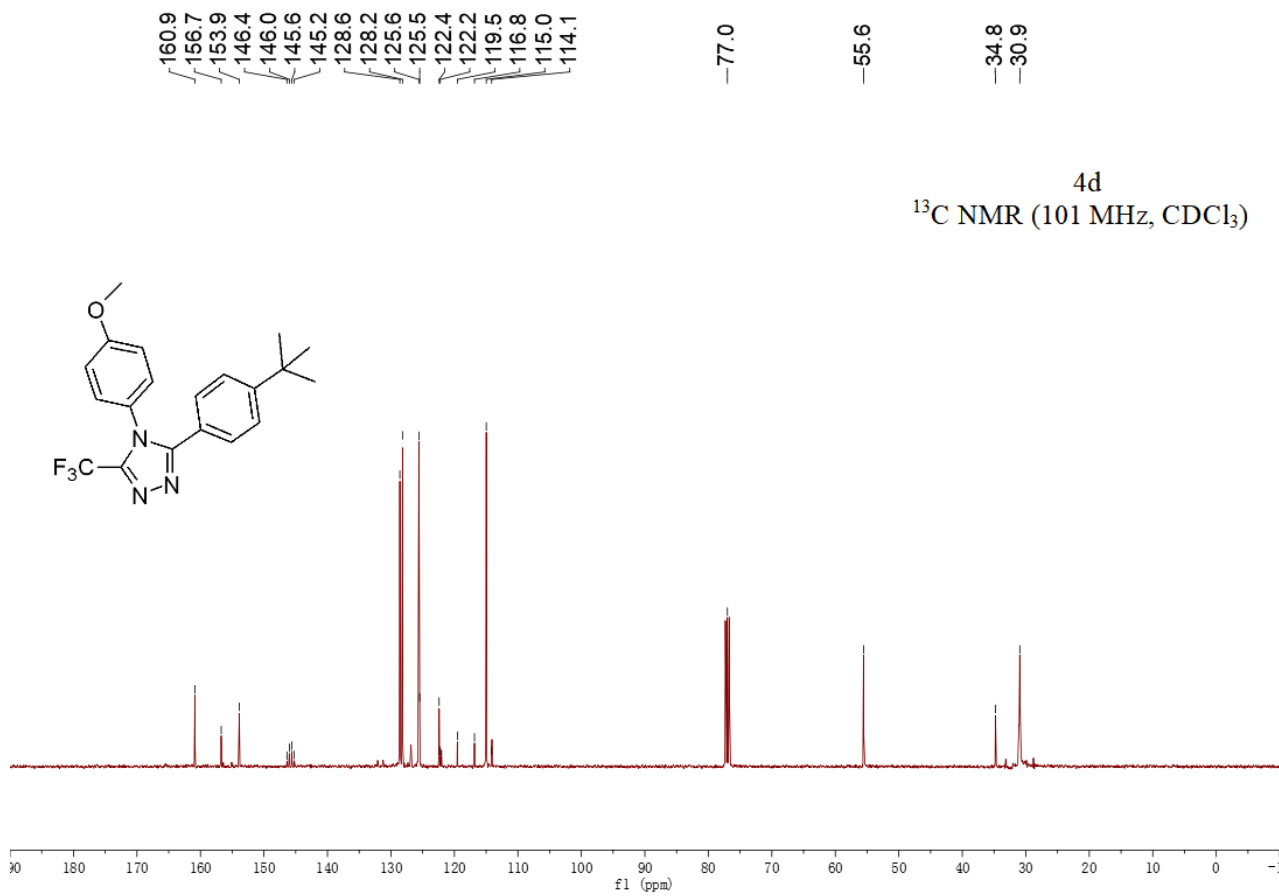


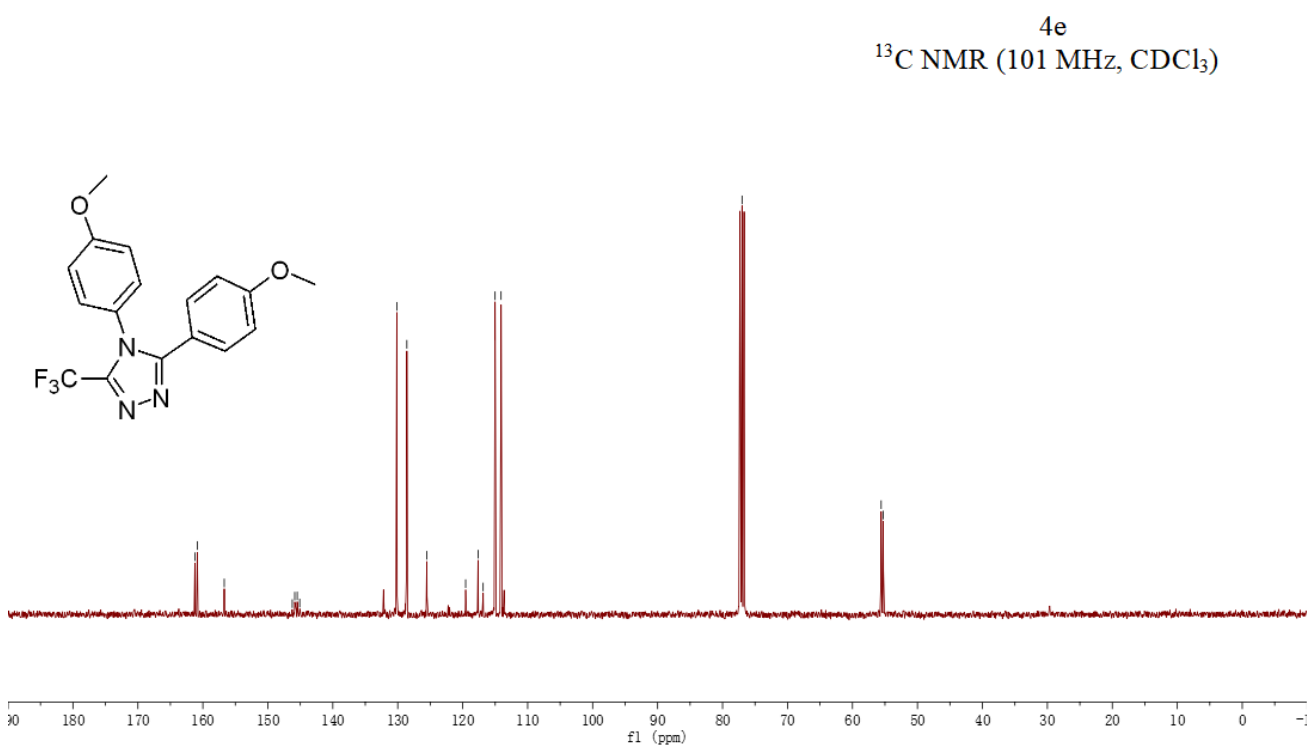
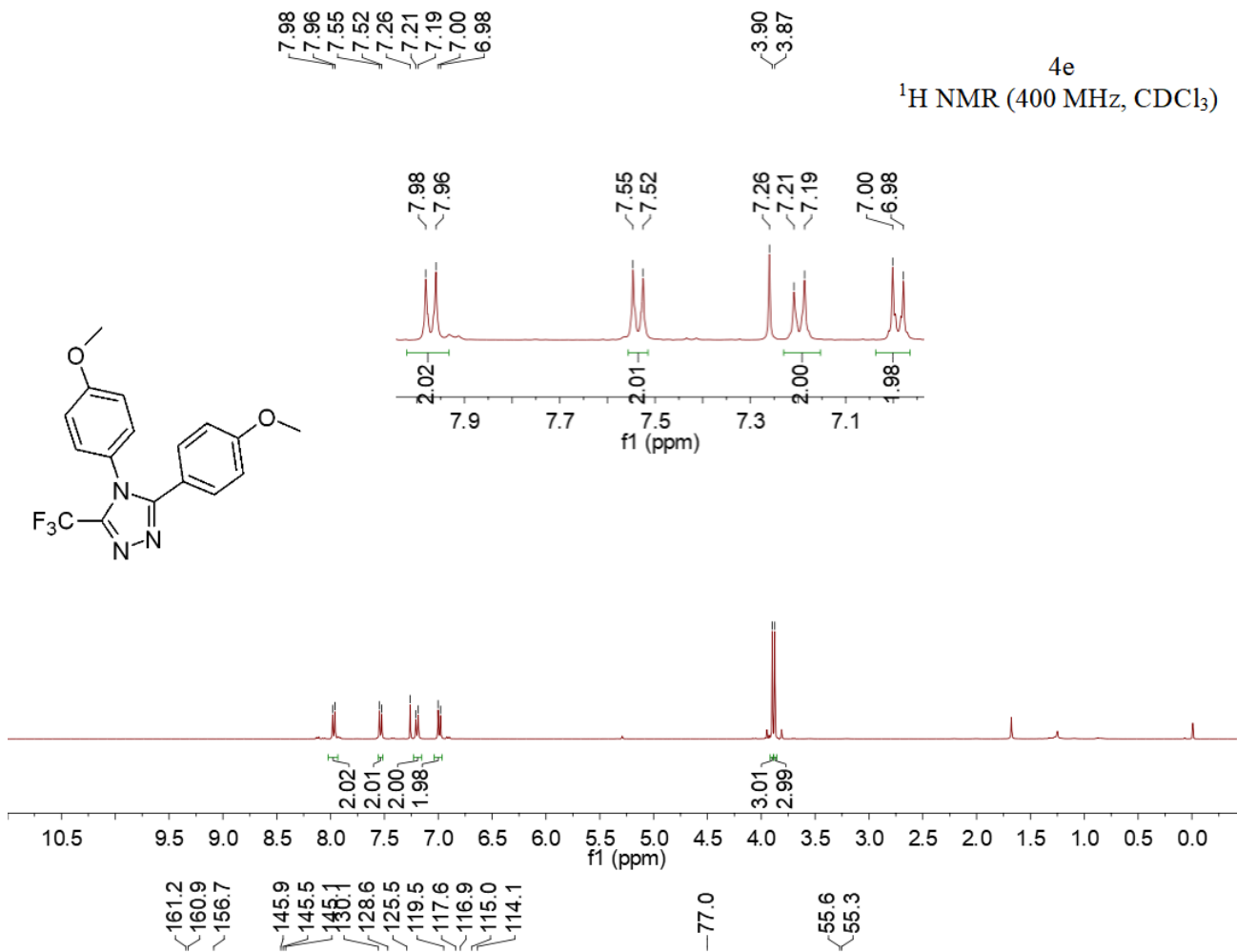


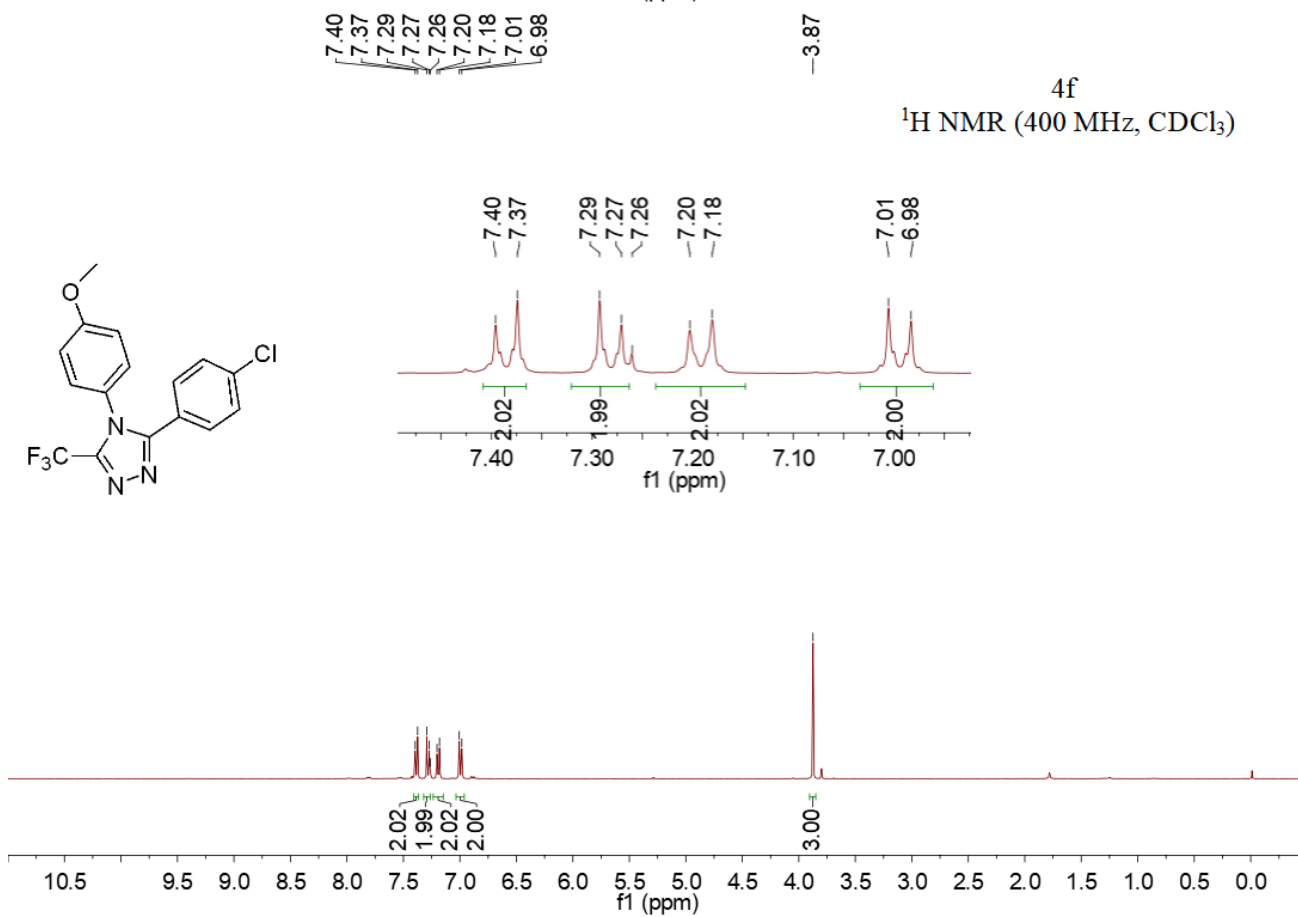
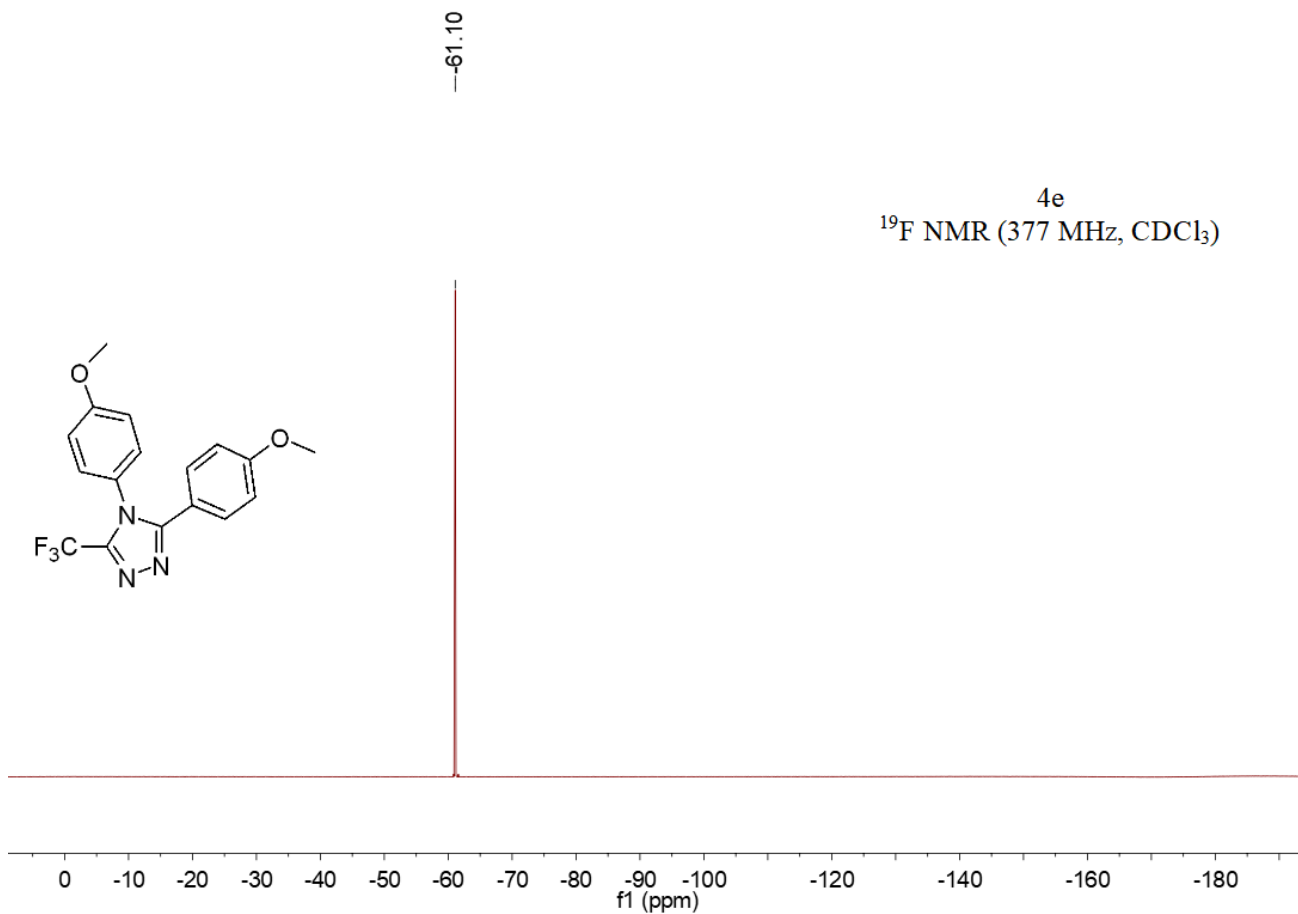


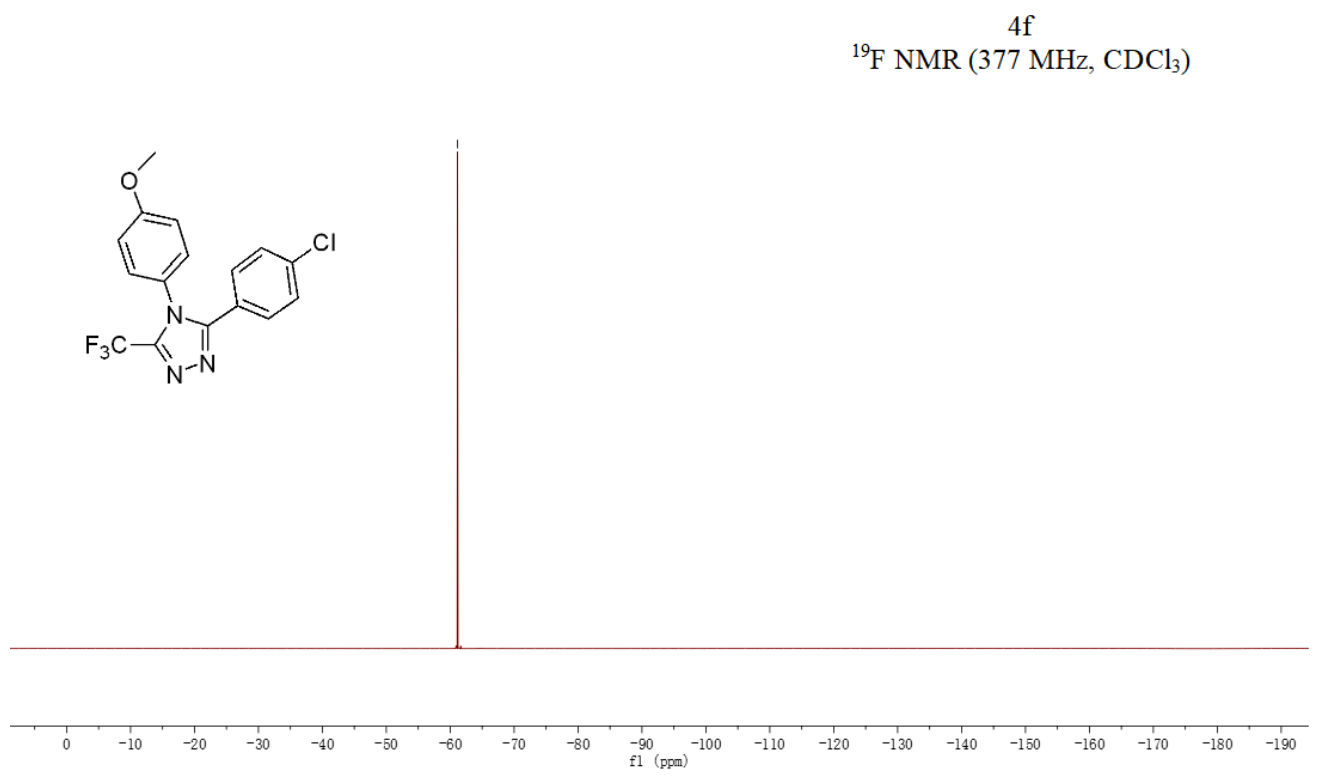
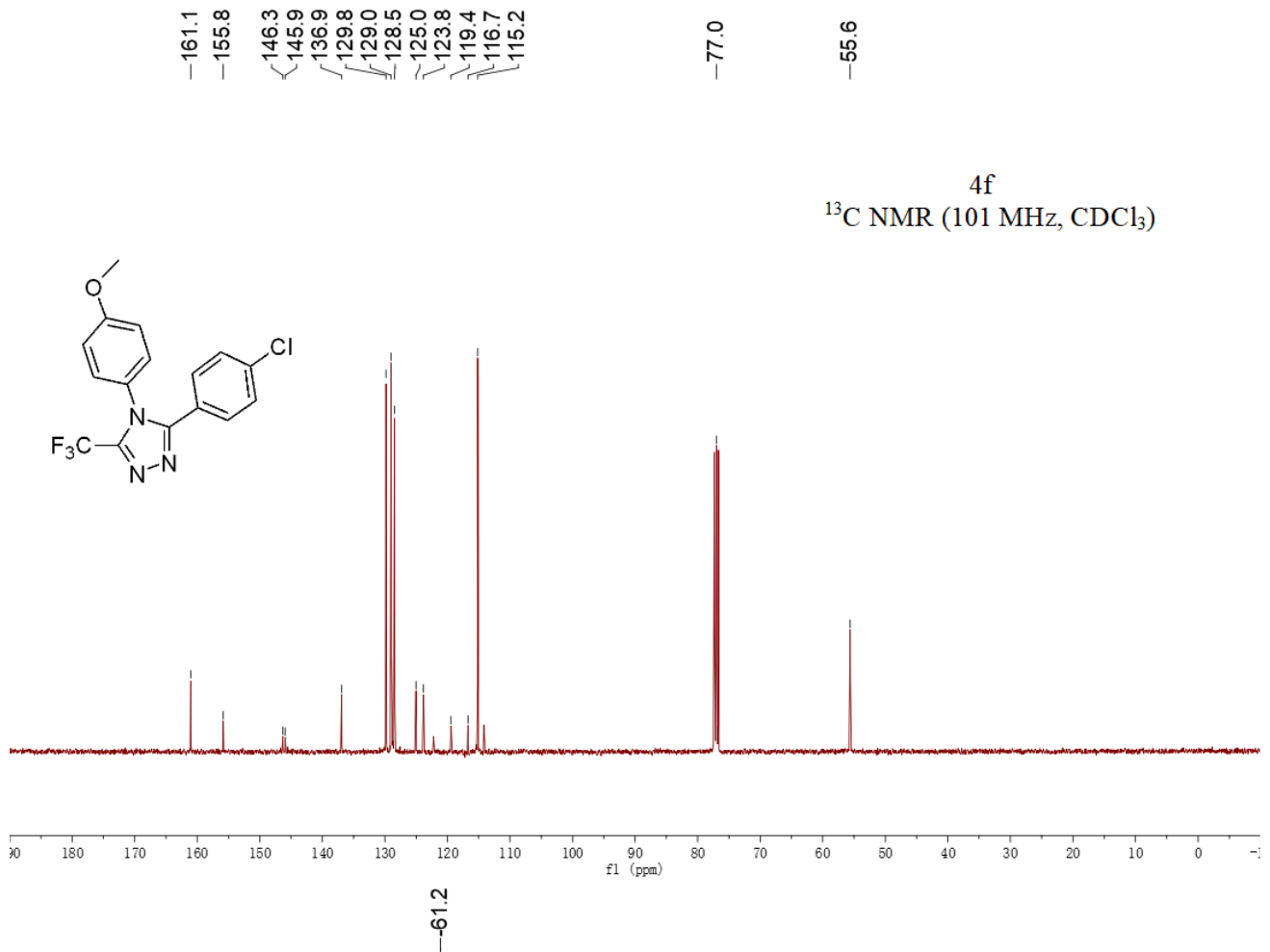


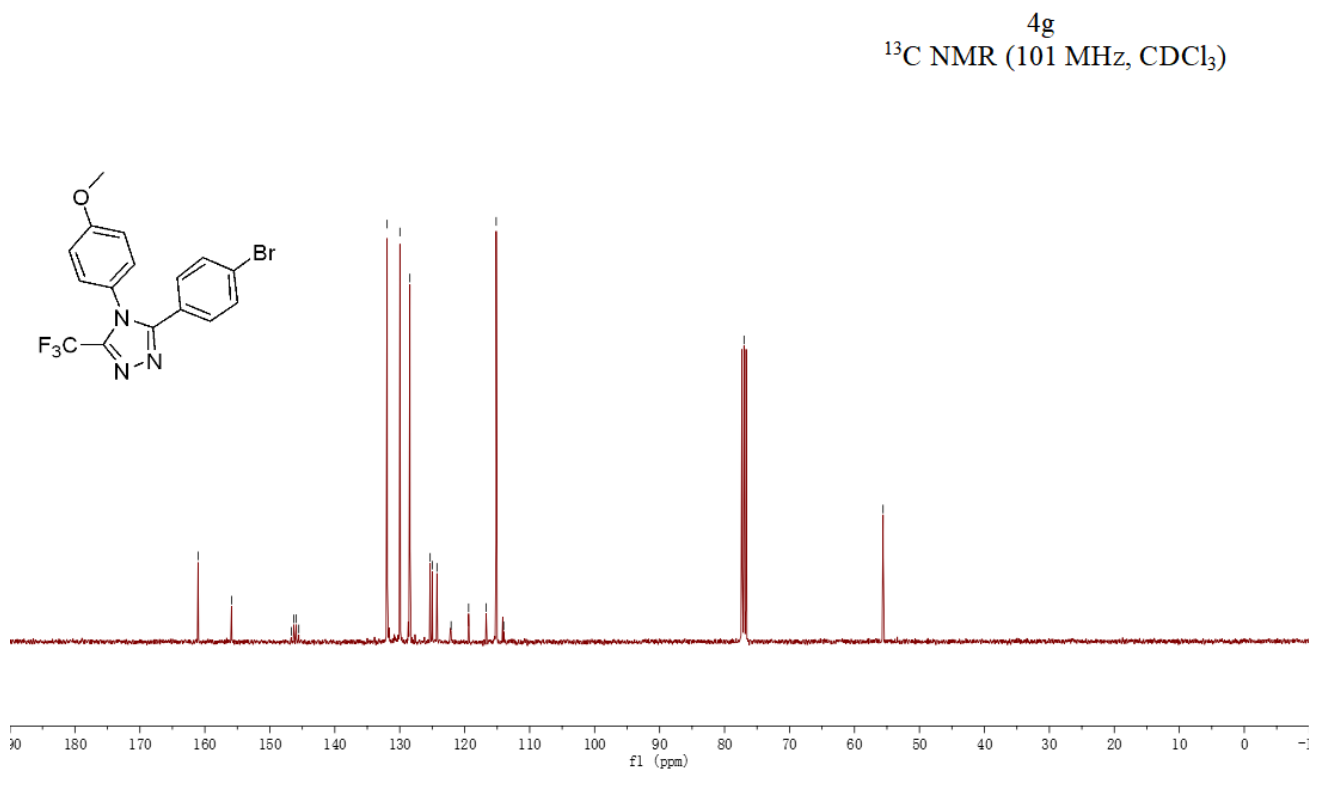
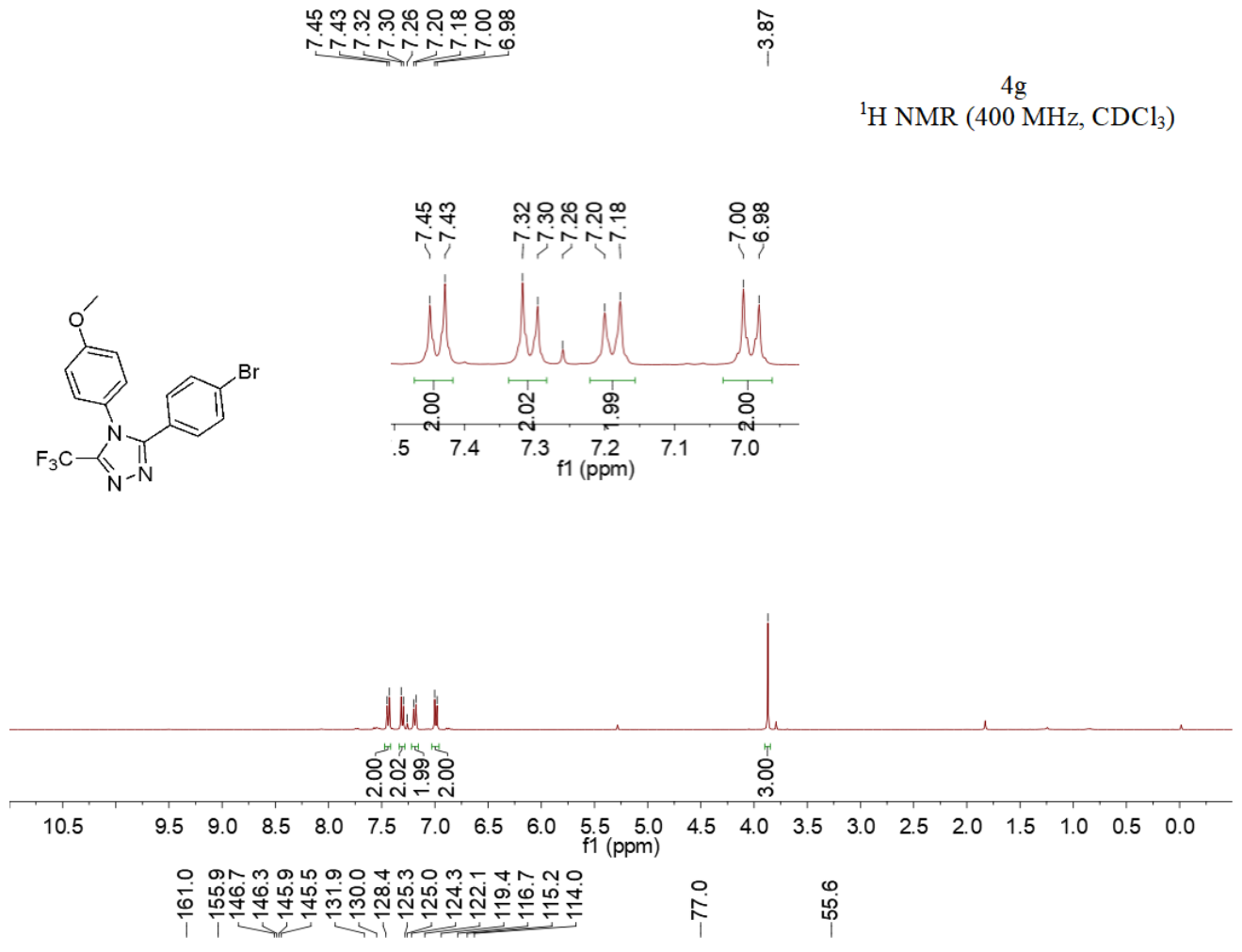


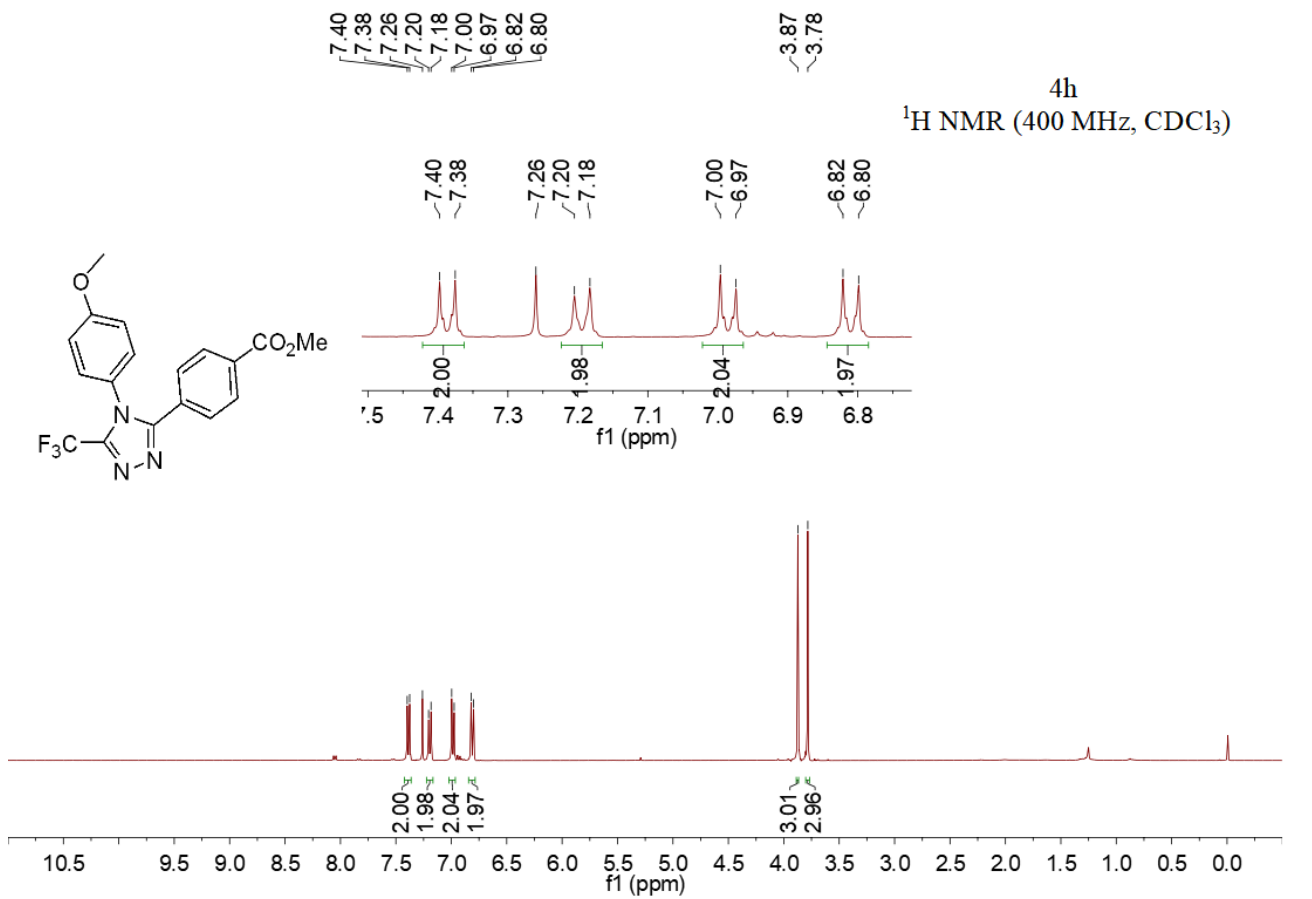
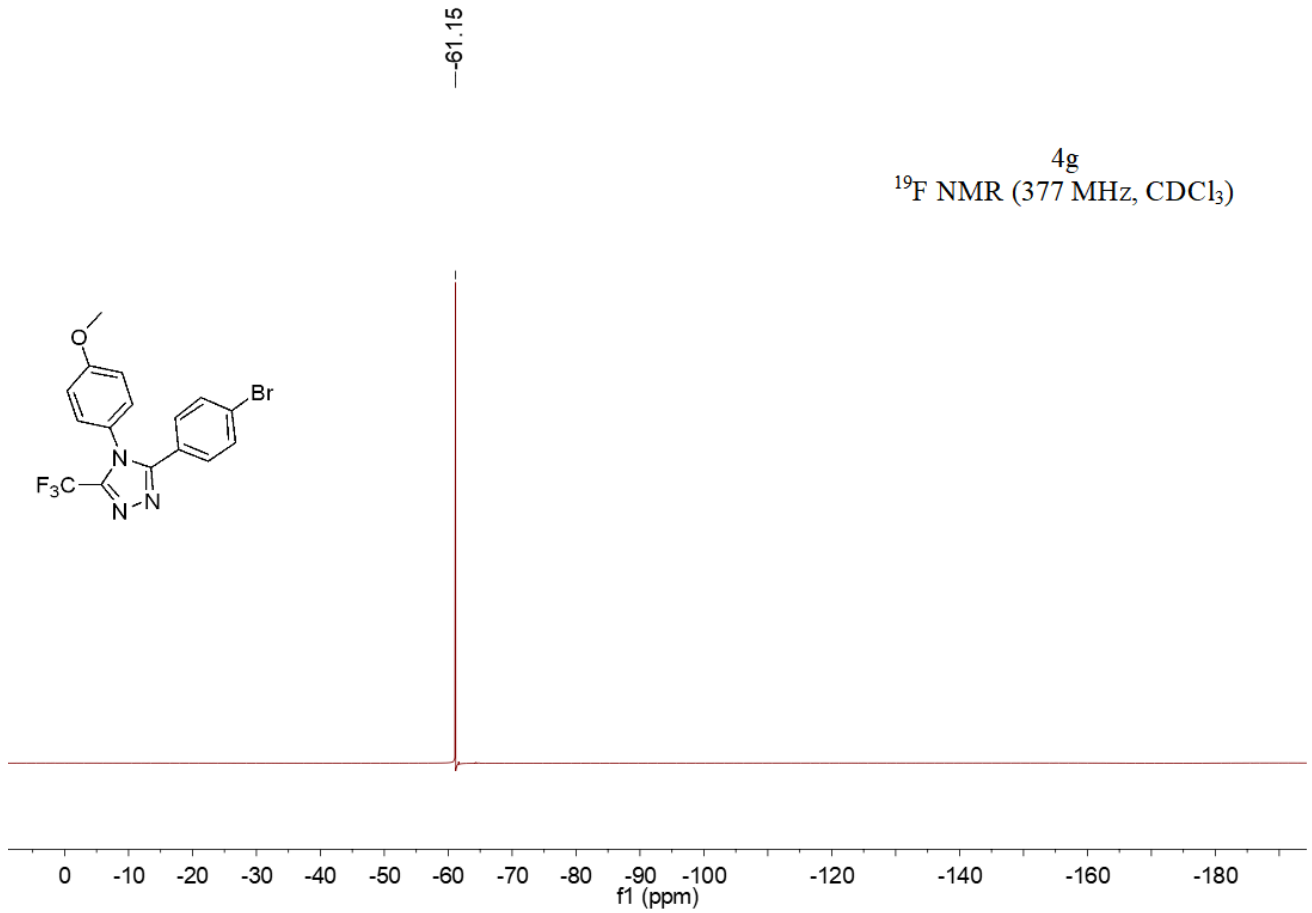


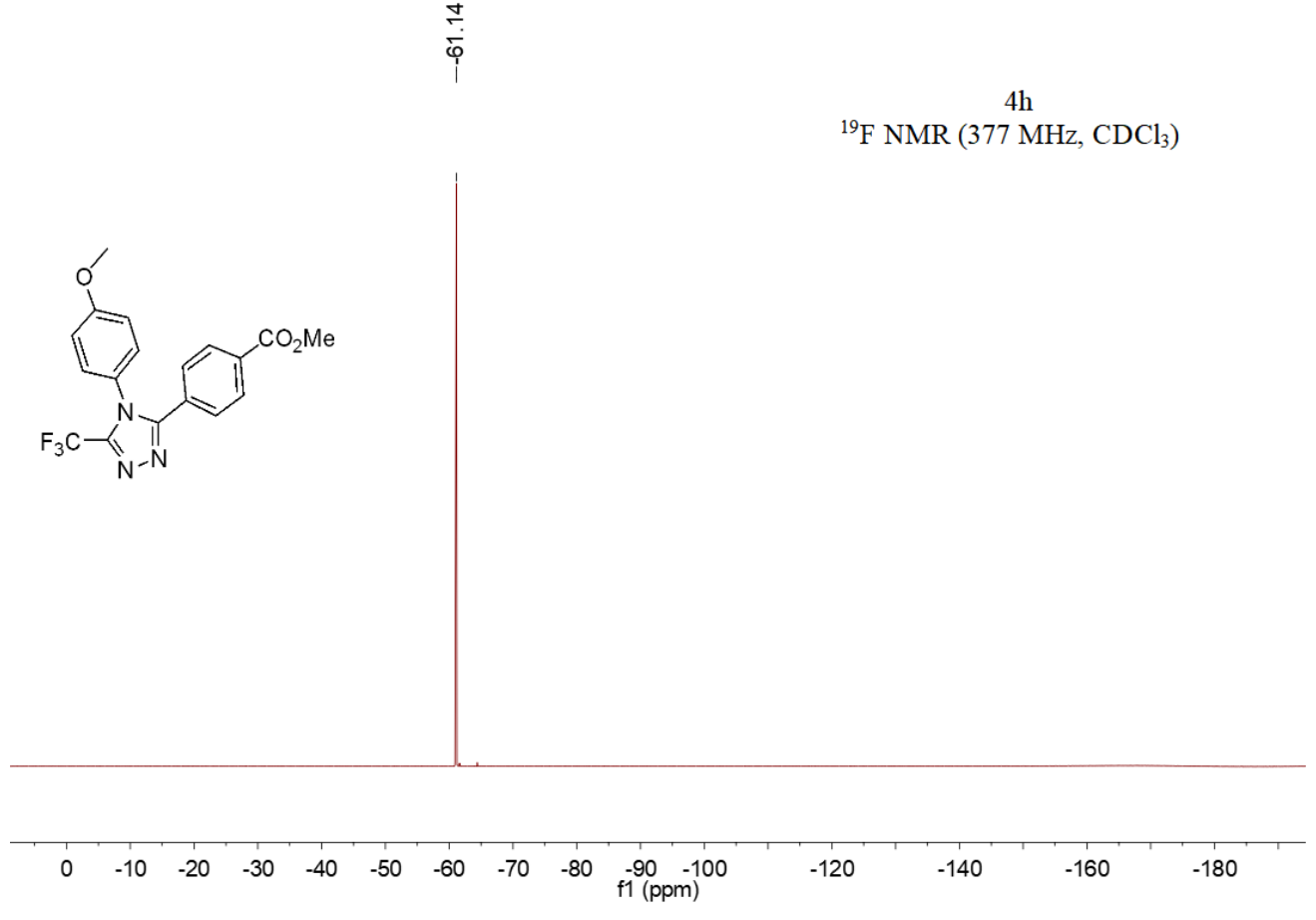
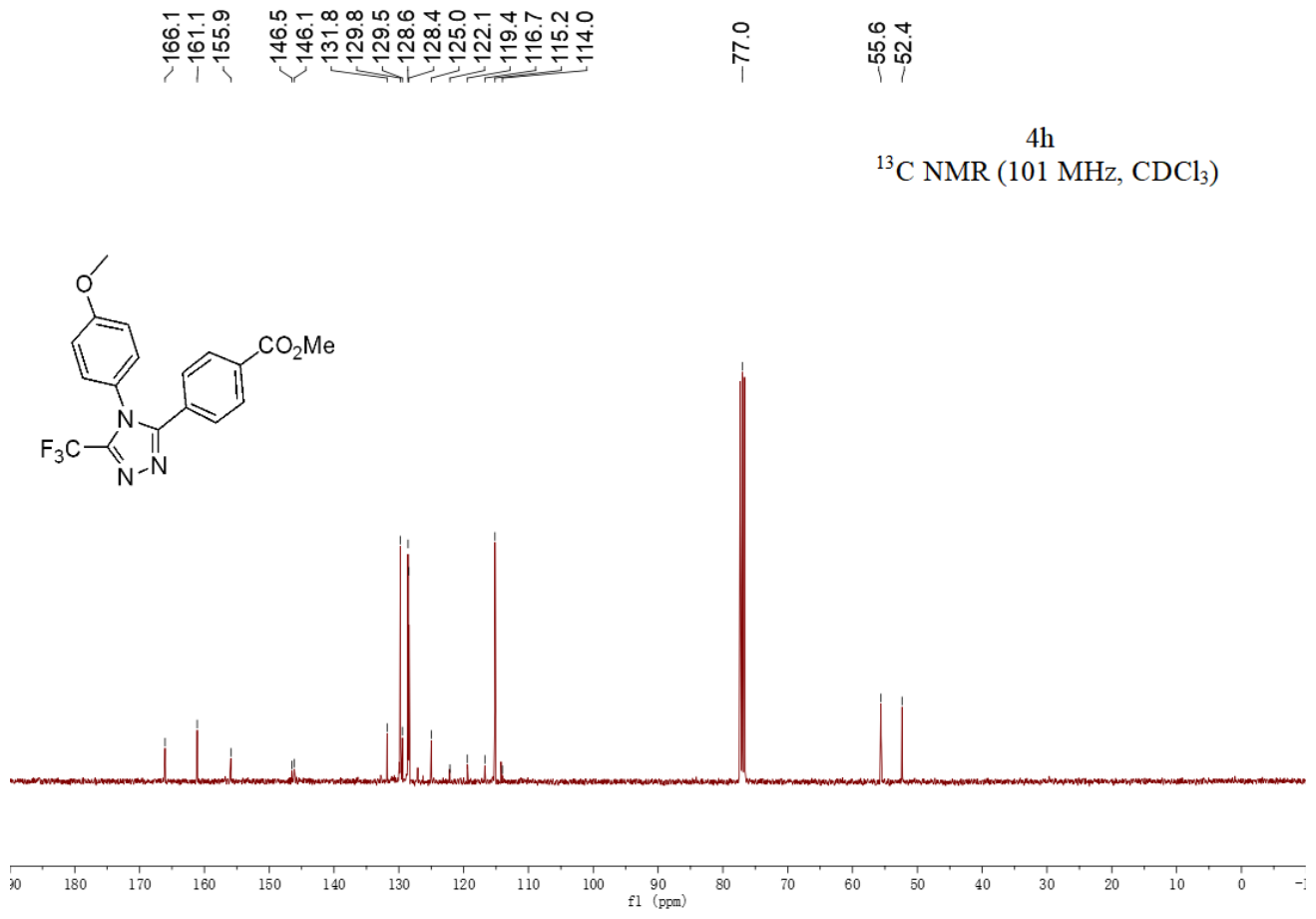




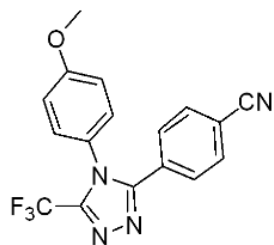






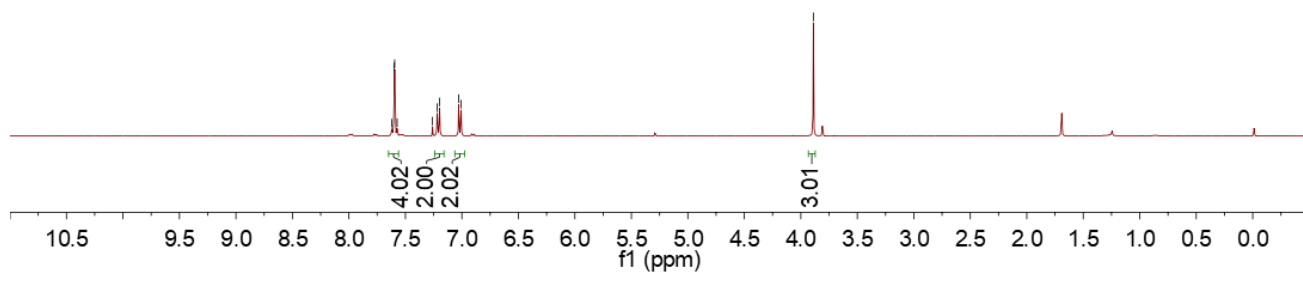
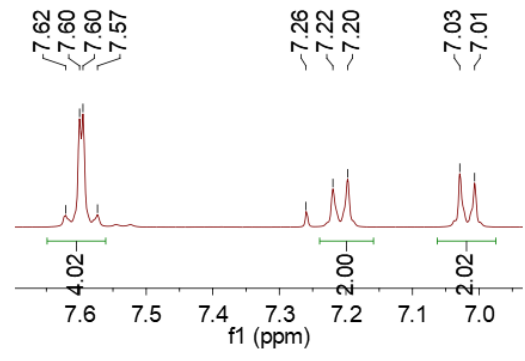






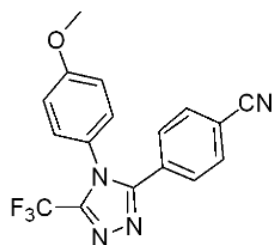
7.62  
7.60  
7.60  
7.57  
7.26  
7.22  
7.20  
7.03  
7.01

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

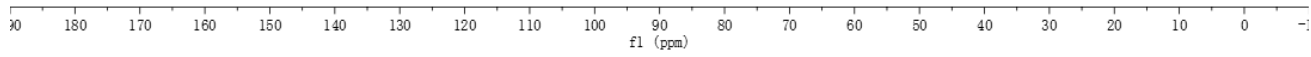


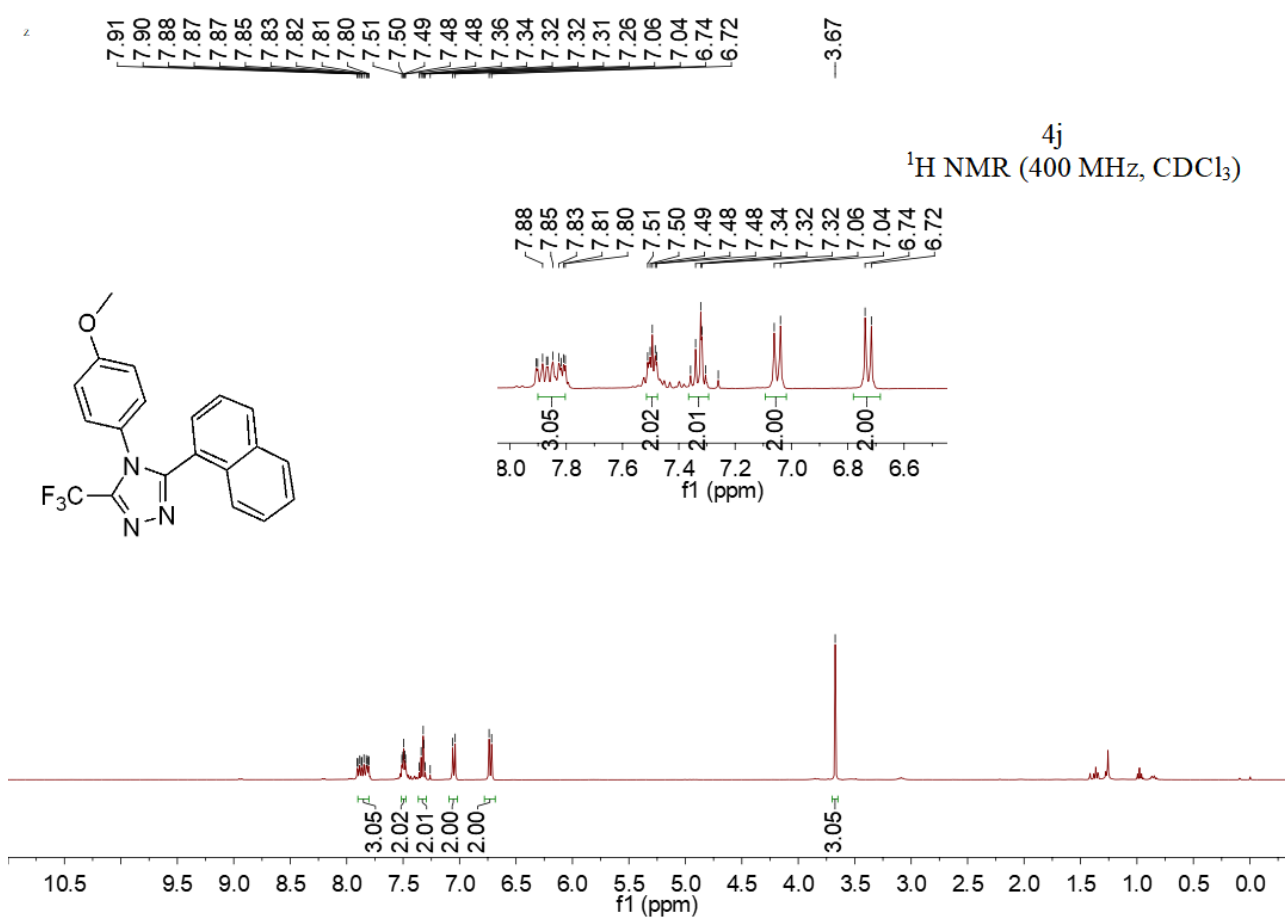
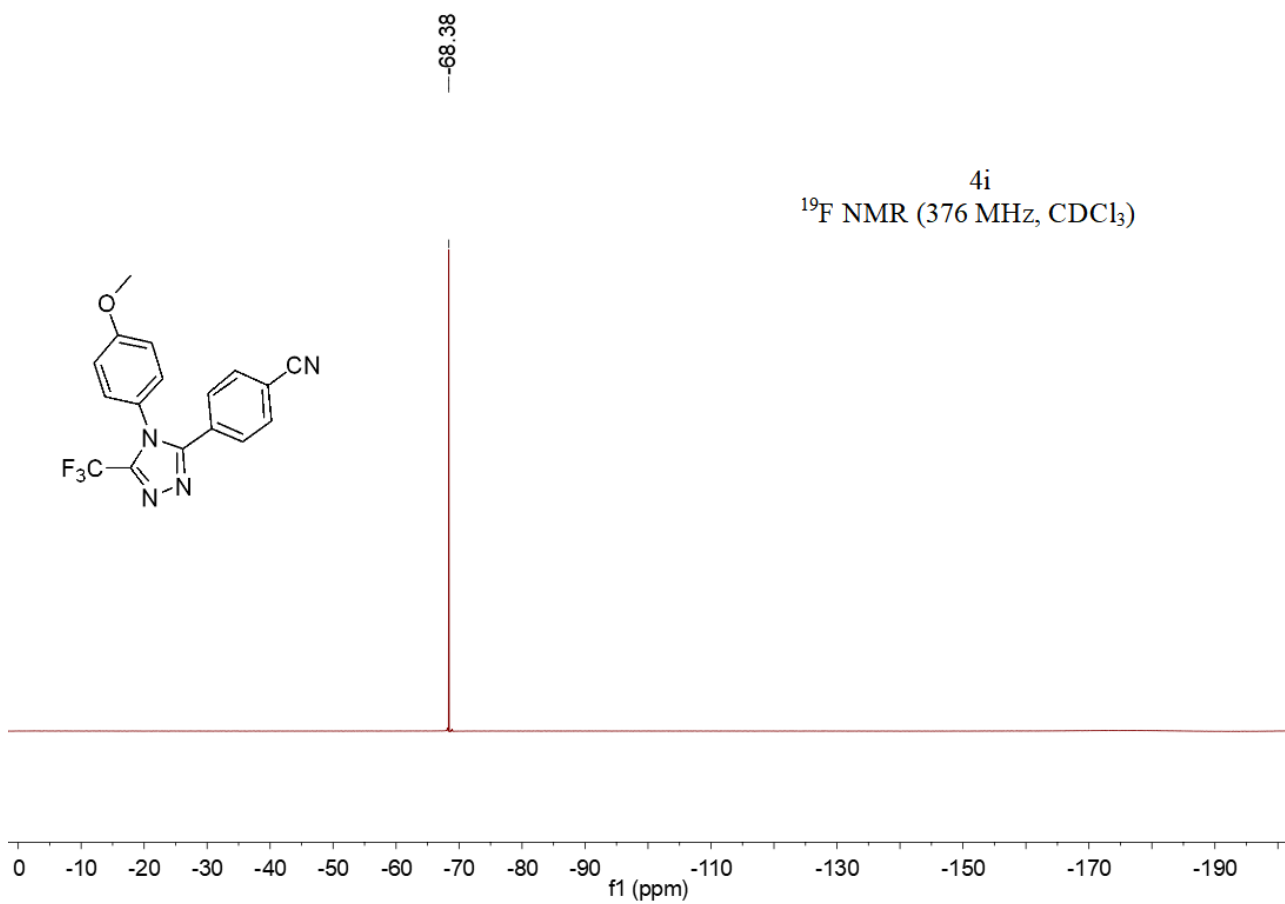
161.3  
155.0  
146.8  
146.4  
132.4  
129.6  
129.0  
128.4  
124.6  
122.3  
119.3  
117.8  
116.6  
115.4  
114.3  
113.9

4i  
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)



A (d)  
117.96

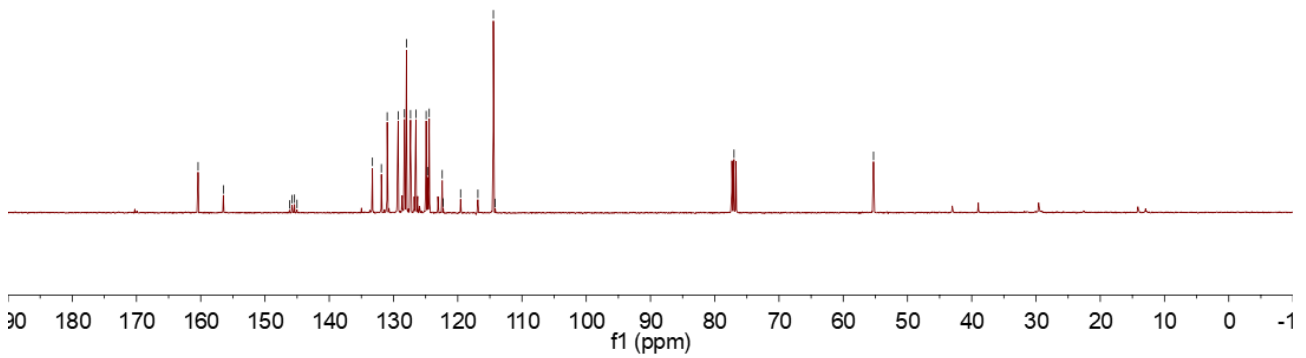
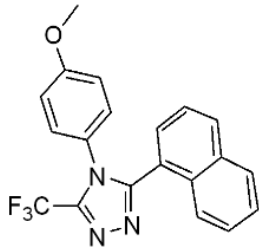




160.41  
156.48  
145.79  
145.40  
145.02  
133.27  
131.89  
130.98  
129.28  
128.29  
127.98  
127.34  
126.51  
124.92  
124.71  
124.44  
122.41  
119.56  
116.86  
114.45  
114.00

55.28

4j  
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)



61.0

4j  
<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)

