Supporting information

Synthesis of 5-trifluoromethyl-1,2,3-triazoles via base-mediated cascade annulation of diazo compounds with trifluoroacetimidoyl chlorides

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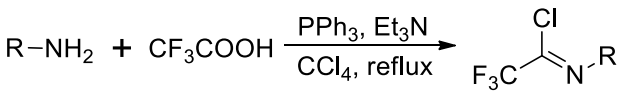
Contents

1. General Information

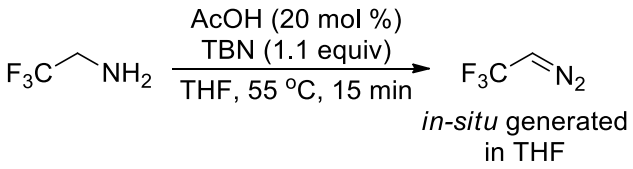
Unless otherwise noted, all reactions were carried out under N_2 atmosphere. All reagents were from commercial sources and used as received without further purification. All solvents were dried by standard techniques and distilled prior to use. Column chromatography was performed on silica gel (200-300 meshes) using petroleum ether (bp. 60~90 °C) and ethyl acetate as eluent. ^{1}NMR spectra were recorded on a Bruker Avance operating at for ^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz and ^{19}F NMR at 377 MHz and spectral data were reported in ppm relative to tetramethylsilane (TMS) as internal standard and $CDCl_3$ (^{1}H NMR δ 7.26, ^{13}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 = quatriplet, 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**[1]

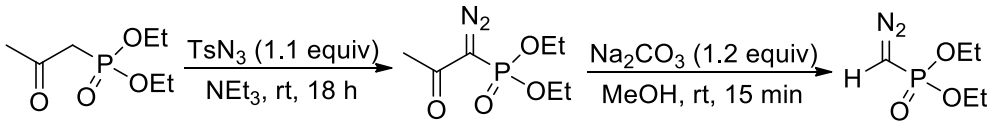


A 200 mL two-necked flask equipped with a septum cap, a condenser, and a Tefloncoated magnetic stir bar was charged with PPh_3 (34.5 g, 132 mmol), Et_3N (7.3 mL, 53 mmol), CCl_4 (21.1 mL, 220 mmol), and TFA (3.4 mL, 44 mmol) (or other corresponding fluorinated acids). After the solution was stirred for about 10 min (ice bath), amine (53 mmol) dissolved in CCl_4 (21.1 mL, 220 mmol) was added. The mixture was then refluxed under stirring (3 h). After the reaction was completed, residual solid Ph_3PO, PPh_3 and Et_3N-HC1 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 Diazo Compounds[2-4]

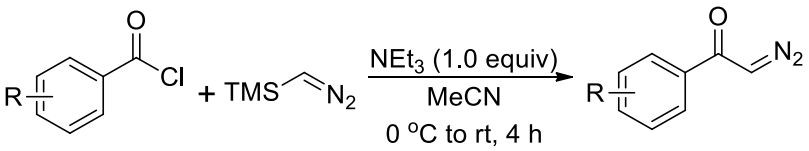


To a stirred solution of $CF_3CH_2NH_2$ (1.0 mmol, 1.0 equiv) in THF (5 mL), tBuONO (126.1 mg, 1.1 mmol, 90% tech., 1.2 equiv) and HOAc (12.0 mg, 0.2 mmol, 0.2 equiv) were added. The solution was heated at 55 °C for 15 minutes, whereas the mixture became deeply yellow. Then, the heating was stopped and the reaction mixture was cooled down to room temperature. The 2,2,2-trifluorodiazoethane was *in-situ* generated as a THF solutions.



A mixture of diethyl (2-oxopropyl)phosphonate (1.15 mL, 6.00 mmol, 1.0 equiv), tosyl azide (1.3 g, 6.6 mmol, 1.1 equiv) and triethylamine (6 mL) was stirred at room temperature for 18 h. After evaporation of the triethylamine under reduced pressure, the residue was dissolved in diethyl ether (50 mL). The precipitate was filtered off, the filtrate was evaporated and the residue was purified by column chromatography using EtOAc/pentane 50:50 as mobile phase affording the corresponding diethyl (1-diazo-2-oxopropyl)phosphonate as a yellow oil (0.810 g, 3.68 mmol, 61%).

To a solution of diethyl (1-diazo-2-oxopropyl)phosphonate (694 mg, 3.15 mmol, 1.0 equiv) in MeOH (9.0 mL) was added Na_2CO_3 (401 mg, 3.78 mmol, 1.20 equiv). The mixture was stirred at room temperature for 15 min and the precipitate was filtered off. Then, the filtrate was evaporated and the residue was purified by column chromatography using EtOAc/PE 50:50 as mobile phase affording the corresponding diethyl (diazomethyl)phosphonate as a yellow oil (533 mg, 2.99 mmol, 95%).



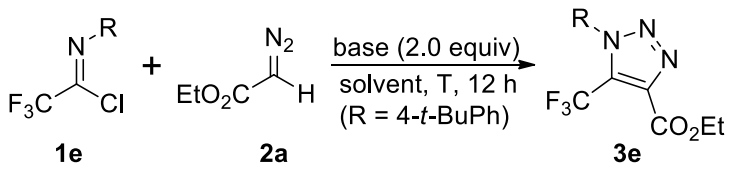
To (trimethylsilyl)diazomethane (1.2 equiv) and triethylamine (1.0 equiv) was dissolved in MeCN at 0 °C. To this mixture the corresponding benzoyl chloride (1.0 equiv) was added dropwise

under N_2 atmosphere. The reaction mixture was allowed to warm to room temperature and stirred for 4 hours or until the full consumption of the benzoyl chloride. The solvent was evaporated and Na_2CO_3 (sat. aq.) was added before extracting with Et_2O. The combined organic phase was dried and the solvent was evaporated. The residue was purified by flash chromatography using PE/EtOAc (10:1).

CAUTION: Diazo compounds are potentially explosive! Although no accident occurred during the course of this study, stringent safety precautions are necessary for all reactions of diazo compounds.

2. Experimental Procedures

2.1 Optimization of the Reaction Conditions



1e **2a** **3e**

2.1.1 Screening of Base[a]

Entry	Base	Yield (%)[b]
1	NaH	82
2	**Cs_2CO_3**	**94 (86)**[c]
3	*t*-BuOK	66
4	HMPA	trace
5	Et_3N	69
6	DABC	60
7	K_3PO_4	trace
8	K_3CO_3	73
9	DBU	20[c]

[a]Reaction conditions: **1e** (0.2 mmol), **2a** (0.3 mmol), base (2 equiv), 4 Å MS (40 mg), MeCN (2.0 mL) at 60 °C under N_2 atmosphere for 12 h. [b]Yields determined by GC analysis using dodecane as an internal standard. [c]Isolated Yield.

2.1.2 Screening of Solvent[a]

Entry	Solvent	Yield (%)[b]
1	Dioxane	81
2	**MeCN**	**94 (86)**[c]
3	DMF	83
4	DMSO	68[c]
5	Toluene	63
6	DCE	68

[a]Reaction conditions: **1e** (0.2 mmol), **2a** (0.3 mmol), Cs_2CO_3 (2 equiv), 4 Å MS (40 mg) solvent (2 mL) at 60 °C under N_2 atmosphere for 12 h. [b]Yields determined by GC analysis using dodecane as an internal standard. [c]Isolated Yield.

2.1.3 Screening of Temperature[a]

Entry	Temperature	Yield (%)[b]
1	30	86
2	80	83

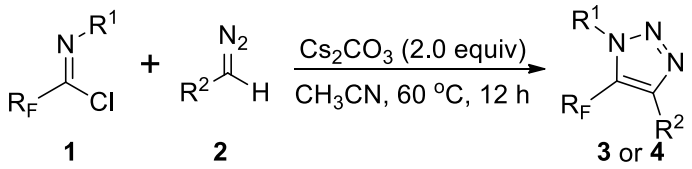
[a]Reaction conditions: **1e** (0.2 mmol), **2a** (0.3 mmol), Cs_2CO_3 (2 equiv), 4 Å MS (40 mg) MeCN (2.0 mL) at the specified temperature under N_2 atmosphere for 12 h. [b]Yields determined by GC analysis using dodecane as an internal standard.

2.1.4 Screening of Time[a]

Entry	Time (h)	Yield (%)[b]
1	6	84
2	**12**	**94 (86)**[c]

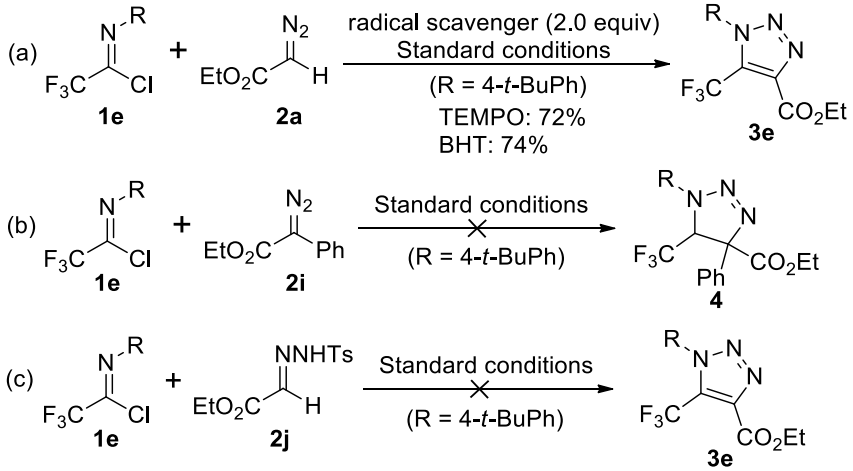
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), Cs_2CO_3 (2 equiv), 4 Å MS (40 mg) MeCN (2.0 mL) at specified temperature under N_2 atmosphere for the specified time. [b]Yields determined by GC analysis using dodecane as an internal standard. [c]Isolated yield.

2.2 General Procedure for the Synthesis of 3/4



Under nitrogen atmosphere, trifluoroacetimidoyl chloride **1** (0.2 mmol, 1.0 equiv), diazo compound **2** (0.3 mmol, 1.5 equiv), Cs_2CO_3 (0.1304 g, 0.4 mmol, 2.0 equiv), 4 Å MS (40 mg), MeCN (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 60 °C (oil bath) for 12 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 product **3/4**.

3 The Control Experiments



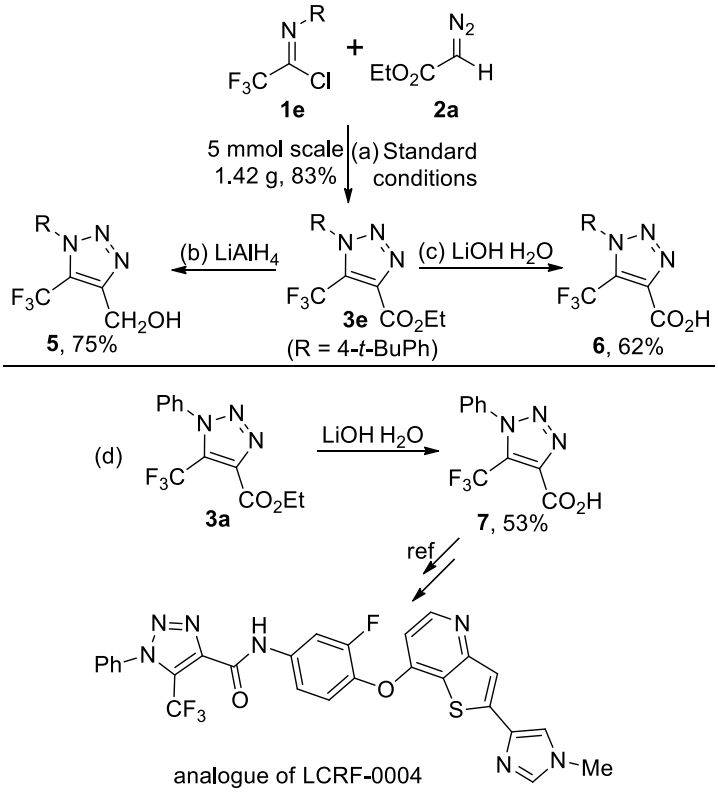
Eq a: Under nitrogen atmosphere, trifluoroacetimidoyl chloride **1e** (0.2 mmol, 1.0 equiv), ethyl 2-diazoacetate **2a** (0.3 mmol, 1.5 equiv), Cs_2CO_3 (0.1304 g, 0.4 mmol, 2.0 equiv), 4 Å MS (40 mg),

TEMPO (62.5 mg, 0.4 mmol, 2.0 equiv) or BHT (88.1mg, 0.4 mmol, 2.0 equiv), MeCN (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 60 °C (oil bath) for 12 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 product **3e** as a yellow oily liquid in 72% (TEMPO) or 74% (BHT) yield.

Eq b: Under nitrogen atmosphere, trifluoroacetimidoyl chloride **1e** (0.2 mmol, 1.0 equiv), ethyl 2-diazo-2-phenylacetate **2i** (0.3 mmol, 1.5 equiv), Cs_2CO_3 (0.1304 g, 0.4 mmol, 2.0 equiv), 4 Å MS (40 mg), MeCN (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 60 °C (oil bath) for 12 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 desired product **4** was not detected.

Eq c: Under nitrogen atmosphere, trifluoroacetimidoyl chloride **1e** (0.2 mmol, 1.0 equiv), ethyl 2-(2-tosylhydrazono)acetate **2j** (0.3 mmol, 1.5 equiv), Cs_2CO_3 (0.1304 g, 0.4 mmol, 2.0 equiv), 4 Å MS (40 mg), MeCN (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 60 °C (oil bath) for 12 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 desired product **3e** was not detected.

4 Gram-Scale Reaction and Synthetic Transformations



Eq a: Gram-Scale Reaction: Under nitrogen atmosphere, trifluoroacetimidoyl chloride **1e** (1.315 g, 5 mmol, 1.0 equiv), ethyl 2-diazoacetate **2a** (0.855 g, 7.5 mmol, 1.5 equiv), Cs_2CO_3 (3.26 g, 10 mmol, 2.0 equiv), 4 Å MS (1 g), MeCN (30 mL) (extra dry) were added to an oven-dried 100 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 60 °C (oil bath) for 12 h. After the reaction was completed, the mixture was slowly cooled to room temperature, and extracted with EtOAc for three times (3×50 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 product **3e** as a yellow oily liquid in 83% yield (1.42 g).

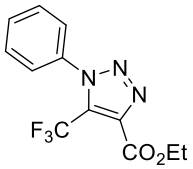
Eq b:[5] Under nitrogen atmosphere, $LiAlH_4$ (0.8 mmol) was added in dry THF (2 mL). Compound **3e** (0.2 mmol) was solved in dry THF (1 mL) and added slowly to the above mixture at room temperature. After stirring 30 min at room temperature, the mixture was refluxed for 8 hours. After cooling, excess $LiAlH_4$ was destroyed by the addition of ice-cold water. Then, 5% H_2SO_4 (3 mL) was added and the mixture was extracted with EtOAc for three times (3×10 mL). The organic phase was washed with water and dried over sodium sulphate. The solvent was removed under reduced

pressure and the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5:1, Rf = 0.4) to give the product **5** as a yellow oily liquid (44.9 mg, 75%).

Eq c:[6] Under air atmosphere, $LiOH·H_2O$ (0.3 mmol) was added in one portion to a solution of compound **3e** (0.2 mmol) in THF/water (1:1, 4 mL). The reaction mixture was stirred until the solid had dissolved and was then left overnight at room temperature. The solvents were removed in vacuo, and the residue was dissolved in water (3 mL). The resulting solution was washed with diethyl ether (2 mL). The aqueous layer was concentrated to half of its volume and then acidified with 30% hydrochloric acid (3 mL). The mixture was extracted with EtOAc for three times (3× 10 mL). The organic phase was washed with water and dried over sodium sulphate. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (ethyl acetate = 1, Rf = 0.2) to give the product **6** as a white solid (38.8 mg, 62%).

Eq d:[6] Under air atmosphere, $LiOH·H_2O$ (0.3 mmol) was added in one portion to a solution of compound **3a** (0.2 mmol) in THF/water (1:1, 4 mL). The reaction mixture was stirred until the solid had dissolved and was then left overnight at room temperature. The solvents were removed in vacuo, and the residue was dissolved in water (3 mL). The resulting solution was washed with diethyl ether (2 mL). The aqueous layer was concentrated to half of its volume and then acidified with 30% hydrochloric acid (3 mL). The mixture was extracted with EtOAc for three times (3× 10 mL). The organic phase was washed with water and dried over sodium sulphate. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (ethyl acetate = 1, Rf = 0.2) to give the product **7** as a yellow oily liquid (27.3 mg, 53%).

5 Characterization Data of the Corresponding Products



Ethyl 1-phenyl-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3a**)

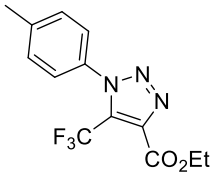
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3a** as a yellow oily liquid (45.7 mg, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.53 (m, 3H), 7.46 (d, *J* = 7.2 Hz, 2H), 4.49 (q, *J* = 7.1 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 139.4, 135.4, 131.2, 129.6, 129.5 (q, $J_{(C-F)}$ = 42.3 Hz), 125.7, 118.8 (q, $J_{(C-F)}$ = 271.2 Hz), 62.4, 14.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.5.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{12}H_{11}F_3N_3O_2$ 286.0798, found 286.0801.



Ethyl 1-(p-tolyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3b**)

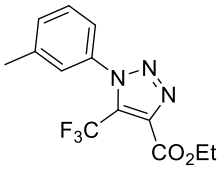
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3b** as a yellow oily liquid (47.9 mg, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 4H), 4.48 (q, *J* = 7.1 Hz, 2H), 2.45 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 141.7, 139.3, 133.0, 130.1, 129.5 (q, $J_{(C-F)}$ = 42.2 Hz), 125.5, 118.9 (q, $J_{(C-F)}$ = 271.2 Hz), 62.4, 21.3, 14.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.6.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{13}H_{13}F_3N_3O_2$ 300.0954, found 300.0963.



Ethyl 1-(m-tolyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3c**)

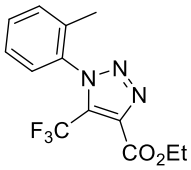
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3c** as a yellow oily liquid (54.4 mg, 91%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.39 (m, 2H), 7.29 – 7.24 (m, 2H), 4.51 (q, *J* = 7.1 Hz, 2H), 2.47 (s, 3H), 1.46 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 140.0, 139.3, 135.4, 131.9, 129.9 (q, $J_{(C-F)}$ = 42.1 Hz), 129.3, 126.2, 122.8, 118.8 (q, $J_{(C-F)}$ = 271.2 Hz), 62.4, 21.2, 14.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.6.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{13}H_{13}F_3N_3O_2$ 300.0954, found 300.0960.



Ethyl 1-(o-tolyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3d**)

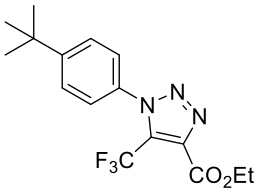
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.4) to give the titled product **3d** as a yellow oily liquid (49.1 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (t, *J* = 7.5 Hz, 1H), 7.43 – 7.32 (m, 2H), 7.26 (d, *J* = 7.7 Hz, 1H), 4.50 (q, *J* = 7.1 Hz, 2H), 2.04 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 138.9, 135.1, 134.7, 131.5, 131.3, 130.3 (q, $J_{(C-F)}$ = 42.0 Hz), 126.9, 126.9, 118.8 (q, $J_{(C-F)}$ = 271.2 Hz), 62.4, 16.9, 14.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -56.8.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{13}H_{13}F_3N_3O_2$ 300.0954, found 300.0962.



Ethyl 1-(4-(tert-butyl)phenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3e**)

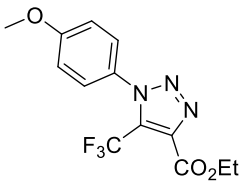
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3e** as a yellow oily liquid (58.7 mg, 86%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.7 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 4.49 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H), 1.36 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 154.7, 139.3, 132.8, 129.5 (q, $J_{(C-F)}$ = 42.1 Hz), 126.5, 125.2, 118.9 (q, $J_{(C-F)}$ = 271.2 Hz), 62.4, 35.0, 31.2, 14.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.6.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{16}H_{19}F_3N_3O_2$ 342.1424, found 342.1433.



Ethyl 1-(4-methoxyphenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3f**)

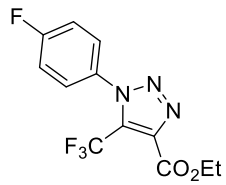
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3f** as a yellow oily liquid (54.9 mg, 87%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.9 Hz, 2H), 7.03 (d, *J* = 9.0 Hz, 2H), 4.48 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 159.1, 139.2, 129.5 (q, $J_{(C-F)}$ = 42.1 Hz), 128.1, 127.1, 118.9 (q, $J_{(C-F)}$ = 271.1 Hz), 114.6, 62.4, 55.7, 14.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.7.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{13}H_{13}F_3N_3O_3$ 316.0904, found 316.0910.



Ethyl 1-(4-fluorophenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3g**)

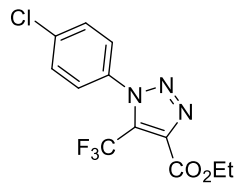
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3g** as a yellow oily liquid (43.7 mg, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.46 (m, 2H), 7.31 – 7.26 (m, 2H), 4.51 (q, *J* = 7.1 Hz, 2H), 1.46 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.9 (d, $J_{(C-F)}$ = 252.9 Hz), 158.9, 139.5, 131.4 (d, $J_{(C-F)}$ = 2.5 Hz), 129.7 (q, $J_{(C-F)}$ = 42.2 Hz), 127.9 (d, $J_{(C-F)}$ = 9.2 Hz), 118.8(q, $J_{(C-F)}$ = 271.3 Hz), 116.8 (d, $J_{(C-F)}$ = 23.5 Hz), 62.5, 14.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.5, -107.8.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{12}H_{10}F_4N_3O_2$ 304.0704, found 304.0712.



Ethyl 1-(4-chlorophenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3h**)

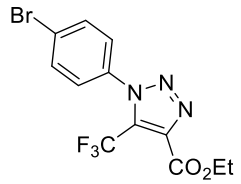
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3h** as a yellow oily liquid (51.8 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.7 Hz, 2H), 7.42 (d, *J* = 8.7 Hz, 2H), 4.50 (q, *J* = 7.1 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 139.6, 137.6, 133.8, 129.9, 129.5 (q, $J_{(C-F)}$ = 42.3 Hz), 127.0, 118.7 (q, $J_{(C-F)}$ = 271.1 Hz), 62.5, 14.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.4.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{12}H_{10}ClF_3N_3O_2$ 320.0408, found 320.0414.



Ethyl 1-(4-bromophenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3i**)

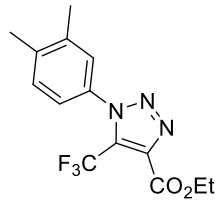
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3i** as a yellow oily liquid (38.6 mg, 53%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.6 Hz, 2H), 7.35 (d, *J* = 8.6 Hz, 2H), 4.50 (q, *J* = 7.1 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 139.6, 134.3, 132.9, 129.5 (q, $J_{(C-F)}$ = 42.1 Hz), 127.2, 125.7, 118.7 (q, $J_{(C-F)}$ = 271.4 Hz), 62.5, 14.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.4.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{12}H_{10}BrF_3N_3O_2$ 363.9903, found 363.9909.



Ethyl 1-(3,4-dimethylphenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3k**)

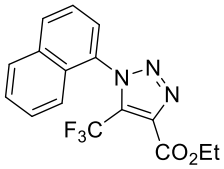
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3k** as a yellow oily liquid (48.9 mg, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.0 Hz, 1H), 7.21 (s, 1H), 7.16 (d, *J* = 9.8 Hz, 1H), 4.48 (q, *J* = 7.1 Hz, 2H), 2.34 (d, *J* = 6.6 Hz, 6H), 1.43 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 140.3, 139.2, 138.3, 133.1, 130.4, 129.4 (q, $J_{(C-F)}$ = 42.1 Hz), 126.5, 122.9, 118.9 (q, $J_{(C-F)}$ = 271.4 Hz), 62.3, 19.8, 19.7, 14.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.7.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{14}H_{15}F_3N_3O_2$ 314.1111, found 314.1118.



Ethyl 1-(naphthalen-1-yl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3l**)

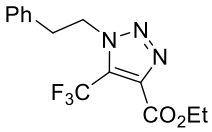
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product **3l** as a yellow oily liquid (36.9 mg, 55%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.1 Hz, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.65 – 7.49 (m, 4H), 7.10 (d, *J* = 8.4 Hz, 1H), 4.54 (q, *J* = 7.1 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 139.0, 133.9, 132.0, 131.7, 131.4 (q, $J_{(C-F)}$ = 42.2 Hz), 129.3, 128.5, 128.4, 127.5, 125.1, 124.7, 121.2, 118.7 (q, $J_{(C-F)}$ = 271.5 Hz), 62.5, 14.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -56.6.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{16}H_{13}F_3N_3O_2$ 336.0954, found 336.0953.



Ethyl 1-phenethyl-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3m**)

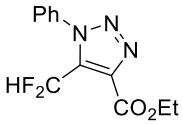
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3m** as a yellow oily liquid (36.3 mg, 58%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 3H), 7.15 (d, *J* = 6.7 Hz, 2H), 4.78 (t, 2H), 4.46 (q, *J* = 7.1 Hz, 2H), 3.24 (t, 2H), 1.43 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 139.3, 135.6, 129.0, 128.7, 128.6 (q, $J_{(C-F)}$ = 42.1 Hz), 127.5, 119.3 (q, $J_{(C-F)}$ = 270.7 Hz), 62.3, 52.8, 36.8, 14.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -56.8.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{14}H_{15}F_3N_3O_2$ 314.1111, found 314.1124.



Ethyl 5-(difluoromethyl)-1-phenyl-1H-1,2,3-triazole-4-carboxylate (**3n**)

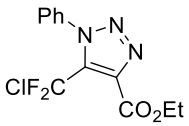
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3n** as a yellow oily liquid (42.2 mg, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.56 (m, 5H), 4.52 (q, *J* = 7.1 Hz, 2H), 1.48 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 135.9, 133.5 (t, $J_{(C-F)}$ = 25.3 Hz), 130.8, 129.4, 125.6, 120.3, 106.7 (t, $J_{(C-F)}$ = 238.8 Hz), 62.3, 14.2.

^{19}F NMR (377 MHz, $CDCl_3$) δ -113.2.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{12}H_{12}F_2N_3O_2$ 268.0892, found 268.0899.



Ethyl 5-(chlorodifluoromethyl)-1-phenyl-1H-1,2,3-triazole-4-carboxylate (**3o**)

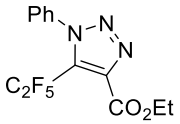
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3o** as a yellow oily liquid (59.1 mg, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.52 (m, 3H), 7.47 (d, *J* = 7.2 Hz, 2H), 4.49 (q, *J* = 7.1 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 137.7, 135.6, 134.3 (t, $J_{(C-F)}$ = 34.8 Hz), 131.1, 129.5, 126.1, 119.5 (t, $J_{(C-F)}$ = 289.6 Hz), 62.4, 14.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -45.7.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{12}H_{11}ClF_2N_3O_2$ 302.0502, found 302.0511.



Ethyl 5-(perfluoroethyl)-1-phenyl-1H-1,2,3-triazole-4-carboxylate (**3p**)

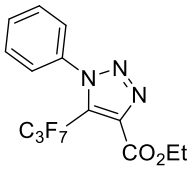
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3p** as a yellow oily liquid (64.4 mg, 96%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 7.7 Hz, 2H), 4.48 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 140.7, 135.6, 131.3, 129.2, 128.1 (t, $J_{(C-F)}$ = 30.9 Hz), 126.8, 118.1 (tq, $J_{(C-F)}$ = 287.4 Hz, 37.1 Hz), 109.8 (qt, $J_{(C-F)}$ = 260.1 Hz, 41.9 Hz), 62.4, 14.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -83.1, -107.0.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{13}H_{11}F_5N_3O_2$ 336.0766, found 336.0775.



Ethyl 5-(perfluoropropyl)-1-phenyl-1H-1,2,3-triazole-4-carboxylate (**3q**)

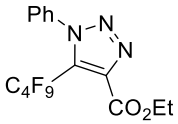
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3q** as a yellow oily liquid (75.5 mg, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 4.47 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 140.9, 135.6, 131.3, 129.1, 127.9 (t, $J_{(C-F)}$ = 31.4 Hz), 126.9, 117.4 (qt, $J_{(C-F)}$ = 288.0 Hz, 33.8 Hz), 112.1 (tt, $J_{(C-F)}$ = 259.8 Hz, 34.3 Hz),108.2 (tm, $J_{(C-F)}$ = 267.7 Hz), 62.4, 13.9.

^{19}F NMR (377 MHz, $CDCl_3$) δ -80.1, -103.9, -123.6.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{14}H_{11}F_7N_3O_2$ 386.0734, found 386.0741.



Ethyl 5-(perfluorobutyl)-1-phenyl-1H-1,2,3-triazole-4-carboxylate (**3r**)

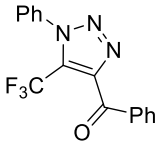
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.4) to give the titled product **3r** as a yellow oily liquid (77.5 mg, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 4.47 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 140.9, 135.6, 131.3, 129.1, 128.0 (t, $J_{(C-F)}$ = 31.3 Hz), 126.9, 118.5 (tt, $J_{(C-F)}$ = 287.9 Hz, 33.1 Hz), 111.4 (qt, $J_{(C-F)}$ = 261.7 Hz, 35.5 Hz), 62.4, 13.9.

^{19}F NMR (377 MHz, $CDCl_3$) δ -81.0, -103.2, -120.0, -126.1.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{15}H_{11}F_9N_3O_2$ 436.0702, found 436.0709.



Phenyl(1-phenyl-5-(trifluoromethyl)-1H-1,2,3-triazol-4-yl)methanone (**4a**)

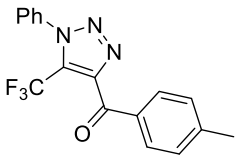
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.4) to give the titled product **4a** as a yellow oily liquid (35.5 mg, 56%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.5 Hz, 2H), 7.70 – 7.53 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 185.2, 145.9, 135.8, 135.4, 134.3, 131.2, 130.7, 129.6, 129.1 (q, $J_{(C-F)}$ = 41.9 Hz), 128.7, 125.6, 119.1 (q, $J_{(C-F)}$ = 270.9 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -56.0.

HRMS (EI) m/z: [M] calcd. for $C_{16}H_{10}F_3N_3O$ 317.0776, found 317.0777.



(1-phenyl-5-(trifluoromethyl)-1H-1,2,3-triazol-4-yl)(p-tolyl)methanone (**4b**)

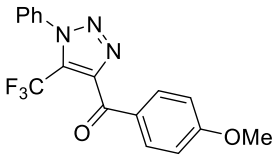
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **4b** as a yellow oily liquid (45.1 mg, 68%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 6.8 Hz), 7.66 – 7.54 (m), 7.49 (d, *J* = 7.4 Hz), 7.46 – 7.41 (m), 2.46 (s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 185.5, 146.0, 138.6, 135.7 (q, $J_{(C-F)}$ = 40.0 Hz), 135.2, 131.2, 131.1, 129.7, 128.6, 128.1, 125.7, 119.1 (q, $J_{(C-F)}$ = 270.9 Hz), 21.4.

^{19}F NMR (377 MHz, $CDCl_3$) δ -56.0.

HRMS (EI) m/z: [M] calcd. for $C_{17}H_{12}F_3N_3O$ 331.0932, found 331.0934.



(4-methoxyphenyl)(1-phenyl-5-(trifluoromethyl)-1H-1,2,3-triazol-4-yl)methanone (**4c**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **4c** as a white solid (20.8 mg, 30%).

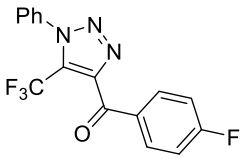
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.9 Hz), 7.66 – 7.58 (m), 7.56 (d, *J* = 7.3 Hz), 7.02 (d, *J* = 8.9 Hz), 3.91 (s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 183.6, 164.6, 146.2, 135.5, 133.2, 131.1, 129.6, 129.2 (q, $J_{(C-F)}$ = 42.3 Hz), 128.9, 125.6, 119.1 (q, $J_{(C-F)}$ = 270.7 Hz), 114.0, 55.6.

^{19}F NMR (377 MHz, $CDCl_3$) δ -56.0.

M.p. 90.6 - 92.8 °C

HRMS (EI) m/z: [M] calcd. for $C_{17}H_{12}F_3N_3O_2$ 347.0882, found 347.0881.



(4-fluorophenyl)(1-phenyl-5-(trifluoromethyl)-1H-1,2,3-triazol-4-yl)methanone (**4d**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **4d** as a white solid (55.7 mg, 83%).

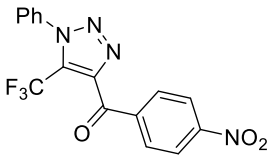
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 – 8.24 (m, 2H), 7.69 – 7.58 (m, 3H), 7.56 (d, *J* = 7.4 Hz, 2H), 7.23 (t, *J* = 8.6 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 183.4, 166.5 (d, $J_{(C-F)}$ = 257.1 Hz), 145.7, 135.4, 133.6 (d, $J_{(C-F)}$ = 9.6 Hz), 132.2, 132.2, 131.3, 129.7 (q, $J_{(C-F)}$ = 42.2 Hz), 129.7, 125.6, 119.0 (q, $J_{(C-F)}$ = 270.9 Hz), 115.9 (d, $J_{(C-F)}$ = 22.0 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -56.1, -102.8.

M.p. 68.3 - 70.2 °C

HRMS (EI) m/z: [M] calcd. for $C_{16}H_9F_4N_3O$ 335.0682, found 335.0684.



(4-nitrophenyl)(1-phenyl-5-(trifluoromethyl)-1H-1,2,3-triazol-4-yl)methanone (**4e**)

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **4e** as a white solid (34.8 mg, 48%).

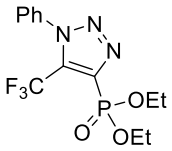
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 – 8.36 (m), 7.70 – 7.59 (m), 7.55 (d, *J* = 7.5 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) δ 183.3, 150.7, 144.9, 140.3, 135.2, 131.8, 131.5, 130.5 (q, $J_{(C-F)}$ = 42.5 Hz), 129.7, 125.6, 123.7, 118.9 (q, $J_{(C-F)}$ = 271.4 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -56.2.

M.p. 183.4 - 185.7 °C

HRMS (EI) m/z: [M] calcd. for $C_{16}H_9F_3N_4O_3$ 362.0627, found 362.0625.



Diethyl (1-phenyl-5-(trifluoromethyl)-1H-1,2,3-triazol-4-yl)phosphonate (**4f**)

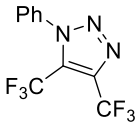
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.4) to give the titled product **4f** as a yellow oily liquid (44.0 mg, 63%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.51 (m, 3H), 7.44 (d, *J* = 7.5 Hz, 2H), 4.38 – 4.29 (m, 4H), 1.41 (t, *J* = 7.1 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8 (d, $J_{(C-P)}$ = 236.2 Hz), 135.0, 132.4 (q, $J_{(C-F)}$ = 42.0 Hz), 131.2, 129.6, 125.7, 118.9 (q, $J_{(C-F)}$ = 271.0 Hz), 63.9, 63.8, 16.3, 16.2.

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.2.

HRMS (EI) m/z: [M] calcd. for $C_{13}H_{15}F_3N_3O_3P$ 349.0803, found 349.0802.



1-phenyl-4,5-bis(trifluoromethyl)-1H-1,2,3-triazole (**4g**)

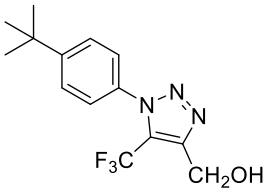
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **4g** as a yellow oily liquid (22.5 mg, 40%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.56 (m, 3H), 7.50 (d, *J* = 7.6 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.1 (q, $J_{(C-F)}$ = 41.0 Hz), 134.8, 131.6, 129.7, 127.5 (q, $J_{(C-F)}$ = 43.9 Hz), 125.7, 119.4 (q, $J_{(C-F)}$ = 269.7 Hz), 118.4 (q, $J_{(C-F)}$ = 271.0 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -56.1, -60.4.

HRMS (ESI): $[M+Na]^+$ calcd. for $C_{10}H_5F_6N_3Na$ 304.0280, found 304.0281.



(1-(4-(tert-butyl)phenyl)-5-(trifluoromethyl)-1H-1,2,3-triazol-4-yl)methanol (**5**)

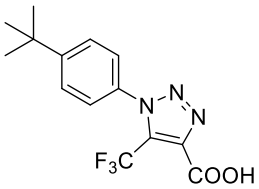
Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, Rf = 0.4) to give the titled product **5** as a yellow oily liquid (44.9 mg, 75%).

^{1}H NMR (400 MHz, DMSO) δ 7.69 (d, *J* = 8.6 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 2H), 5.62 (t, *J* = 5.6 Hz, 1H), 4.72 (d, *J* = 5.2 Hz, 2H), 1.37 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.3, 147.3, 132.9, 126.4, 125.2 (q, $J_{(C-F)}$ = 40.2 Hz), 125.2, 119.9 (q, $J_{(C-F)}$ = 269.2 Hz), 55.7, 35.0, 31.2.

^{19}F NMR (377 MHz, $CDCl_3$) δ -56.2.

HRMS (EI) m/z: [M] calcd. for $C_{14}H_{16}F_3N_3O$ 299.1245, found 299.1245.



1-(4-(tert-butyl)phenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylic acid (**6**)

Upon completion the mixture was concentrated and purified via flash column chromatography (ethyl acetate = 1, Rf = 0.2) to give the titled product **6** as a white solid (38.8 mg, 62%).

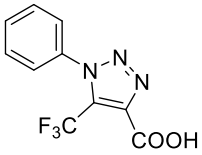
^{1}H NMR (400 MHz, DMSO) δ 7.66 (d, *J* = 8.5 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 1.36 (s, 9H).

^{13}C NMR (101 MHz, DMSO) δ 167.4, 158.7, 152.4, 138.5, 131.5, 130.8, 129.7 (q, $J_{(C-F)}$ = 41.2 Hz), 124.8 (q, $J_{(C-F)}$ = 269.2 Hz), 39.9, 36.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.3.

M.p. 157.2 - 160.1 °C

HRMS (ESI): $[M+Na]^+$ calcd. for $C_{14}H_{14}F_3N_3NaO_2$ 336.0930, found 336.0930.



1-phenyl-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylic acid (**7**)[7]

Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 2:1, Rf = 0.3) to give the titled product **7** as a yellow oily liquid (27.3 mg, 53%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.75 (s, 1H), 7.67 – 7.55 (m, 3H), 7.49 (d, *J* = 7.5 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 138.3, 135.3, 131.4, 130.5 (q, $J_{(C-F)}$ = 42.7 Hz), 129.6, 125.8, 118.6 (q, $J_{(C-F)}$ = 271.7 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -55.5.

6 References

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(2) Z. Chen, Y. Zheng, J.-A. Ma, *Angew. Chem. Int. Ed.* **2017**, *56*, 4569-4574.

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(5) K. Dabak, A. Akar, *Heterocyclic Communications* **2002**, *8*, 385-390.

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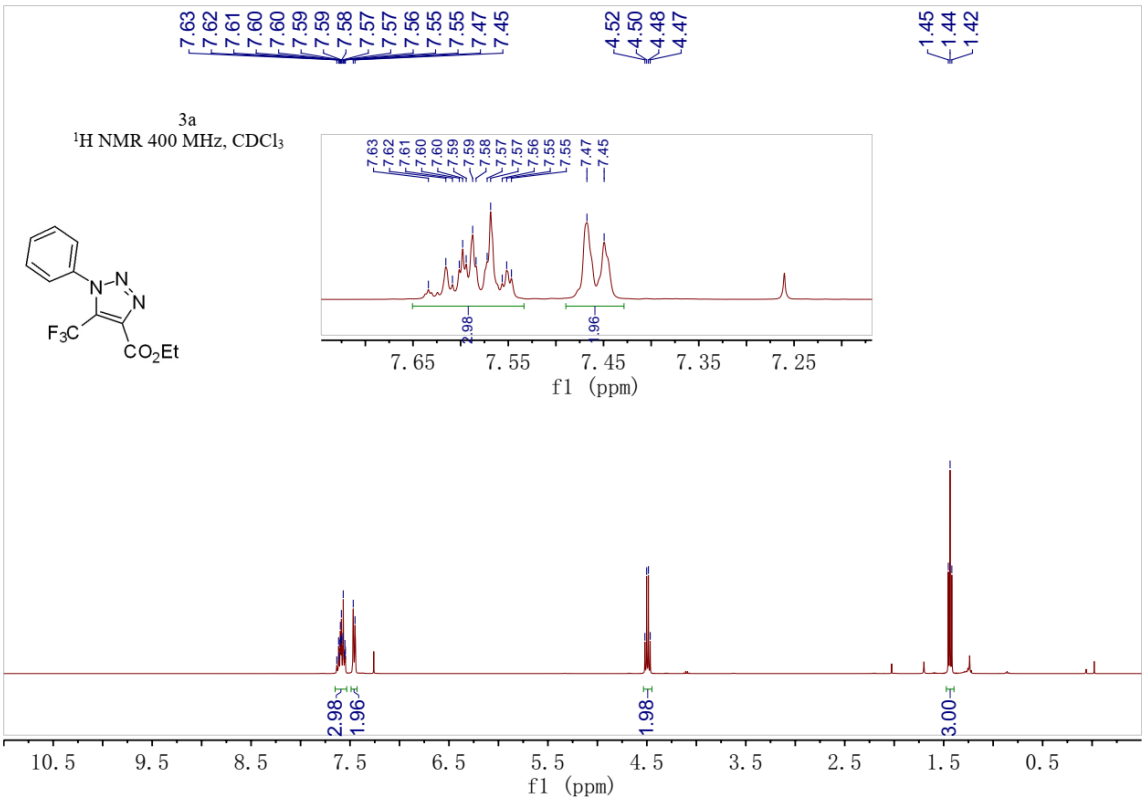
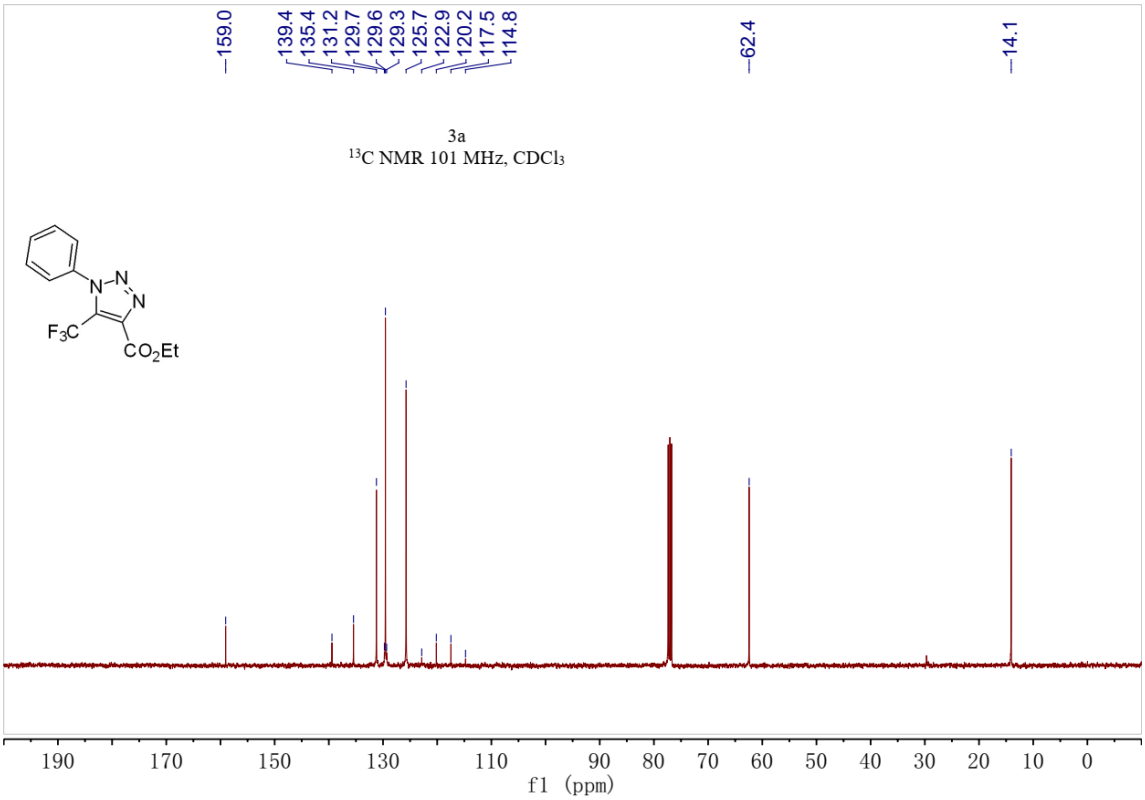
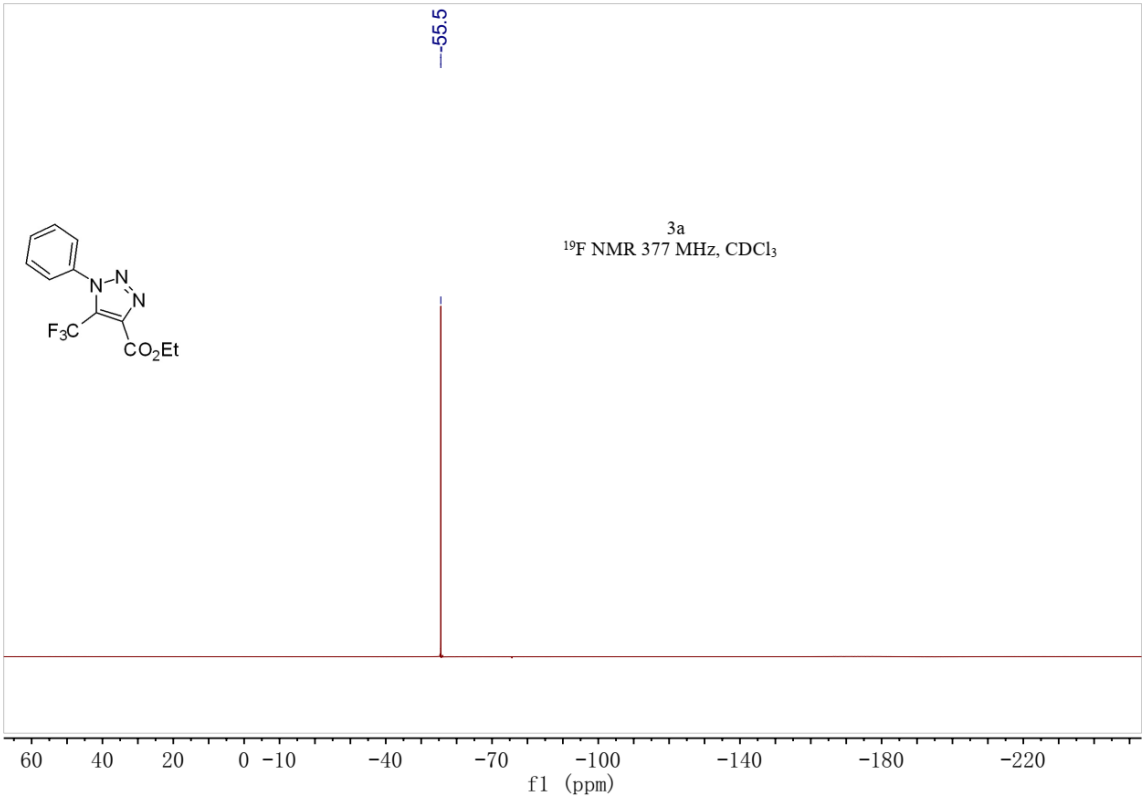
7 Copy of ^{1}H, ^{13}C and ^{19}F NMR Spectra of Products



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F3C
CO2Et
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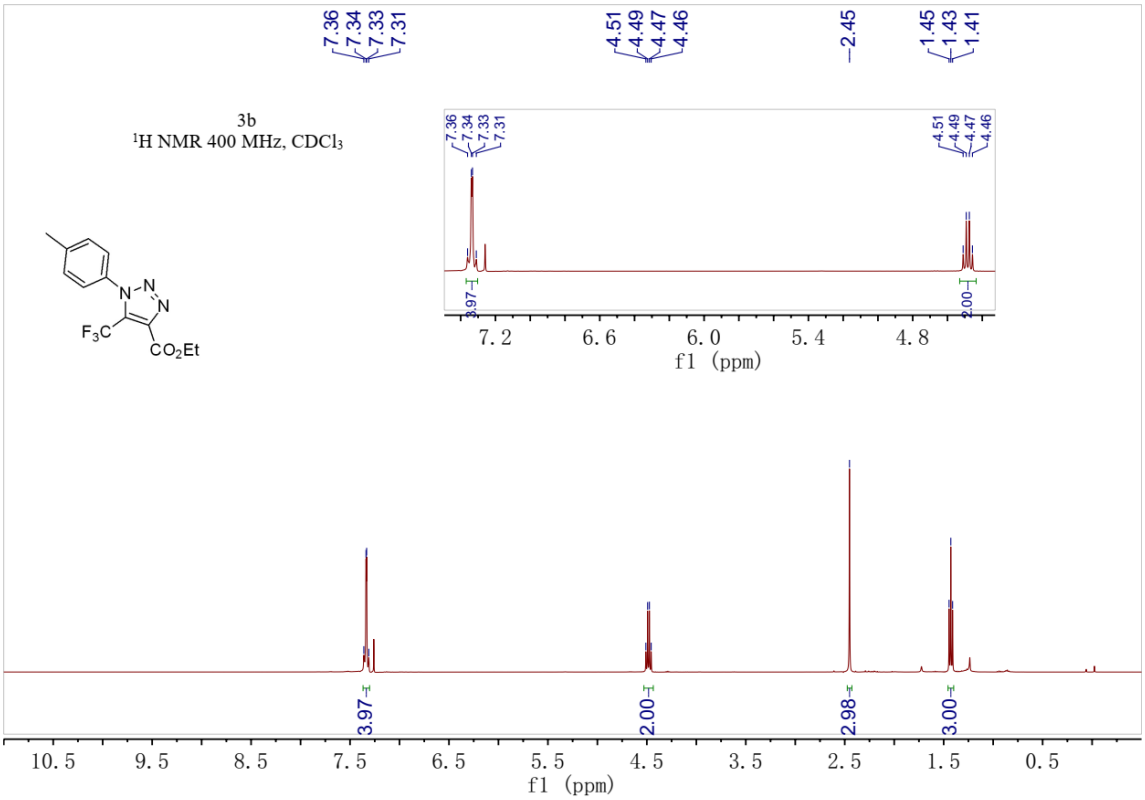
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1.43
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3b
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F3C
CO2Et
3.97
2.00
7.2 6.6 6.0 5.4 4.8
f1 (ppm)
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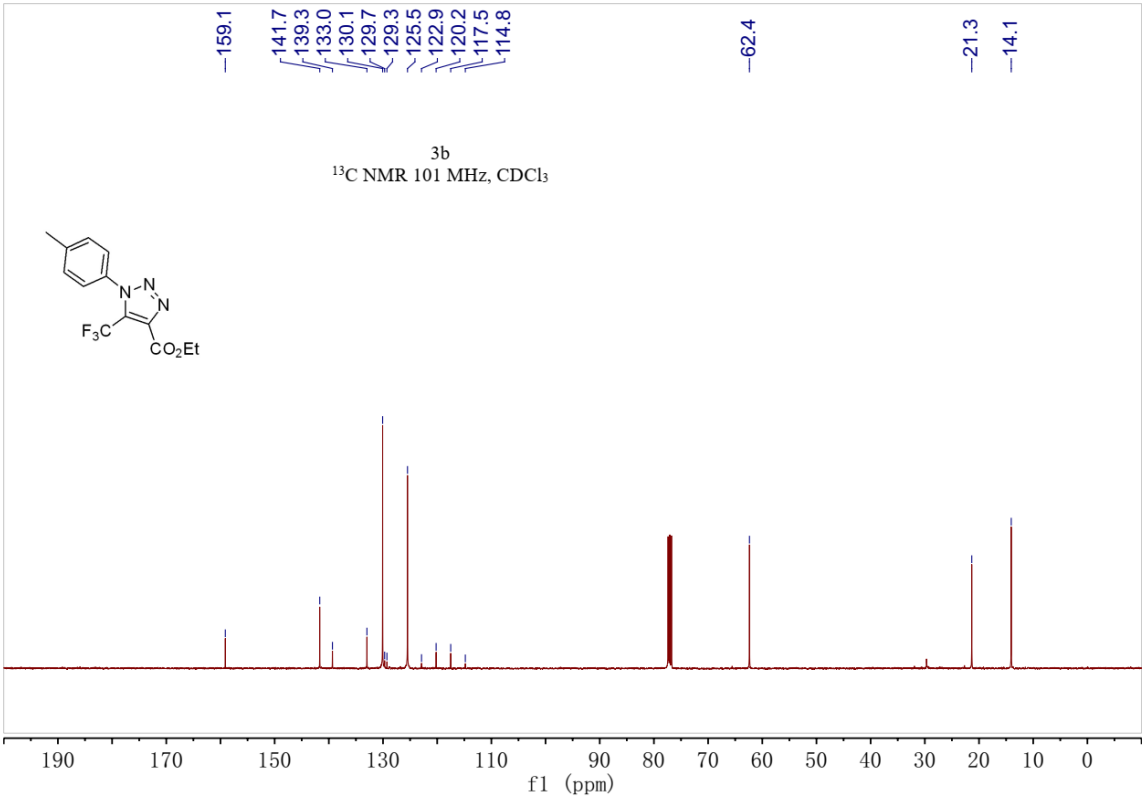
f1 (ppm)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125.5
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120.2
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114.8
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21.3
14.1
3b
13C NMR 101 MHz, CDCl3
F3C
CO2Et
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170
150
130
110
90
80
70
60
50
40
30
20
10
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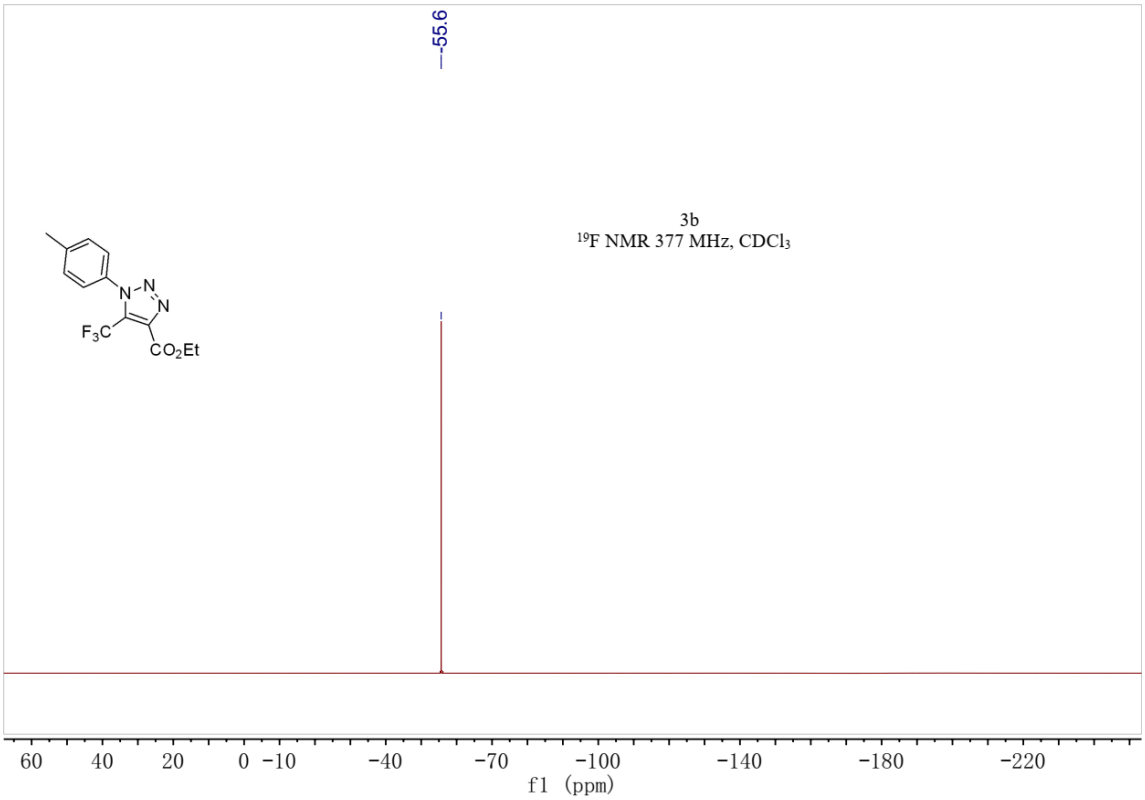
f1 (ppm)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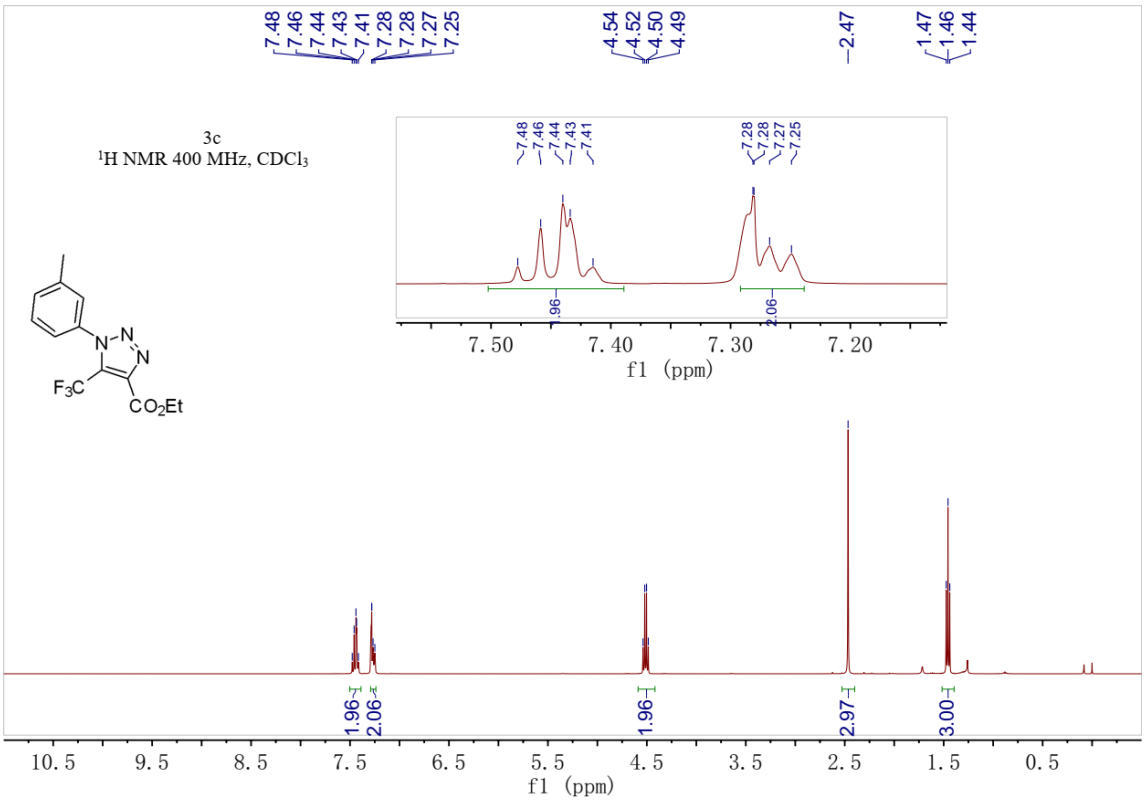
f1 (ppm)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2.47
1.47
1.46
1.44
3c
1H NMR 400 MHz, CDCl3
F3C
CO2Et
1.96
2.06
7.50
7.40
7.30
7.20
f1 (ppm)
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2.06
1.96
2.97
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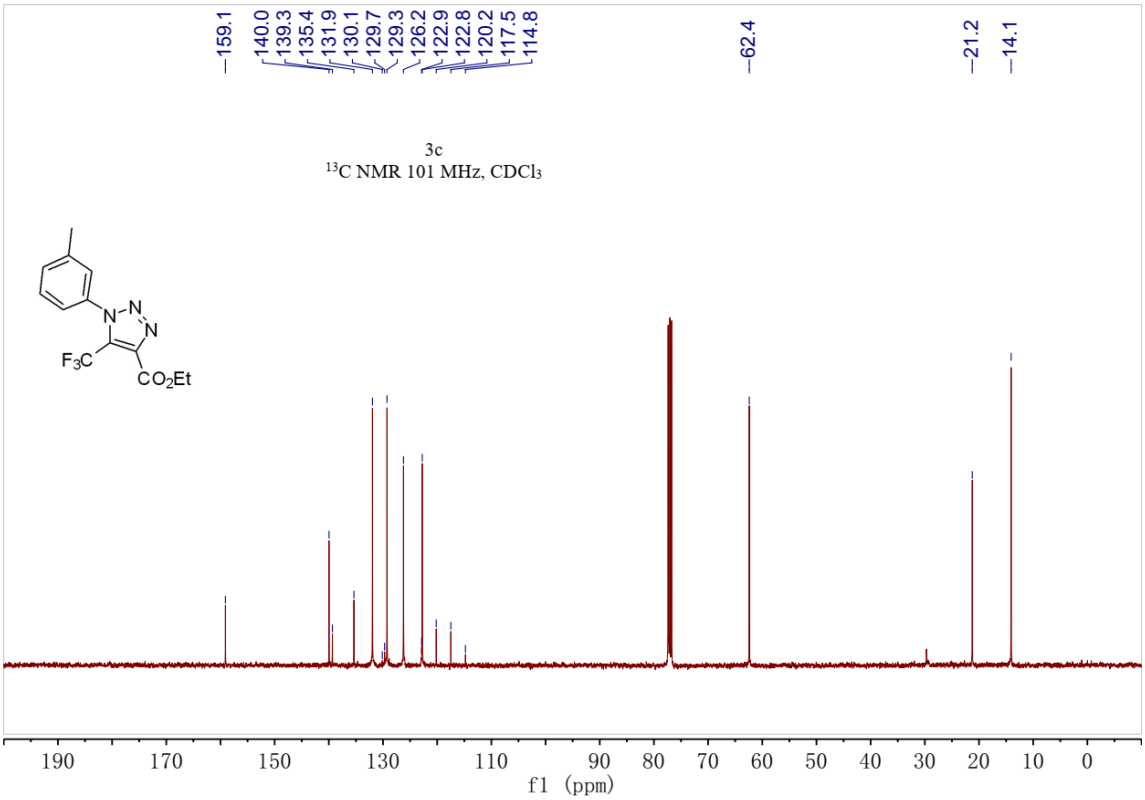
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62.4
21.2
14.1
3c
13C NMR 101 MHz, CDCl3
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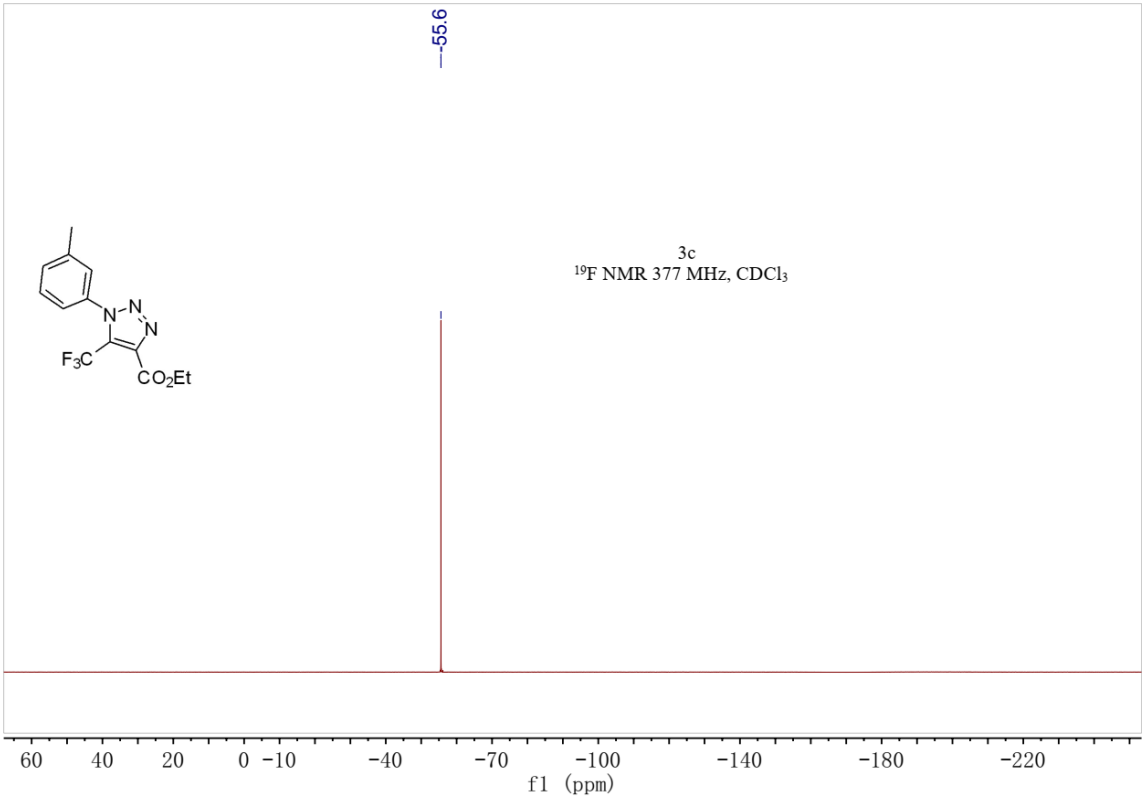
f1 (ppm)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F3C
CO2Et
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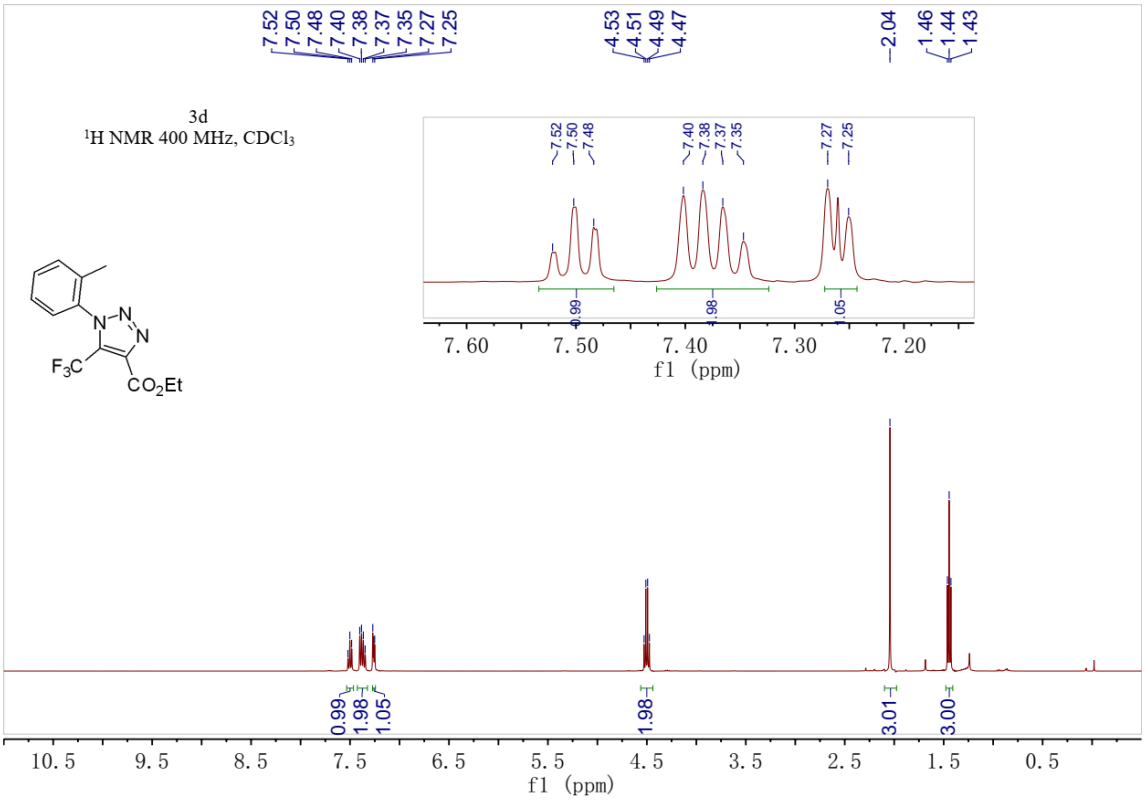
f1 (ppm)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2.04
1.46 1.44 1.43
3d
1H NMR 400 MHz, CDCl3
F3C
CO2Et
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3.00
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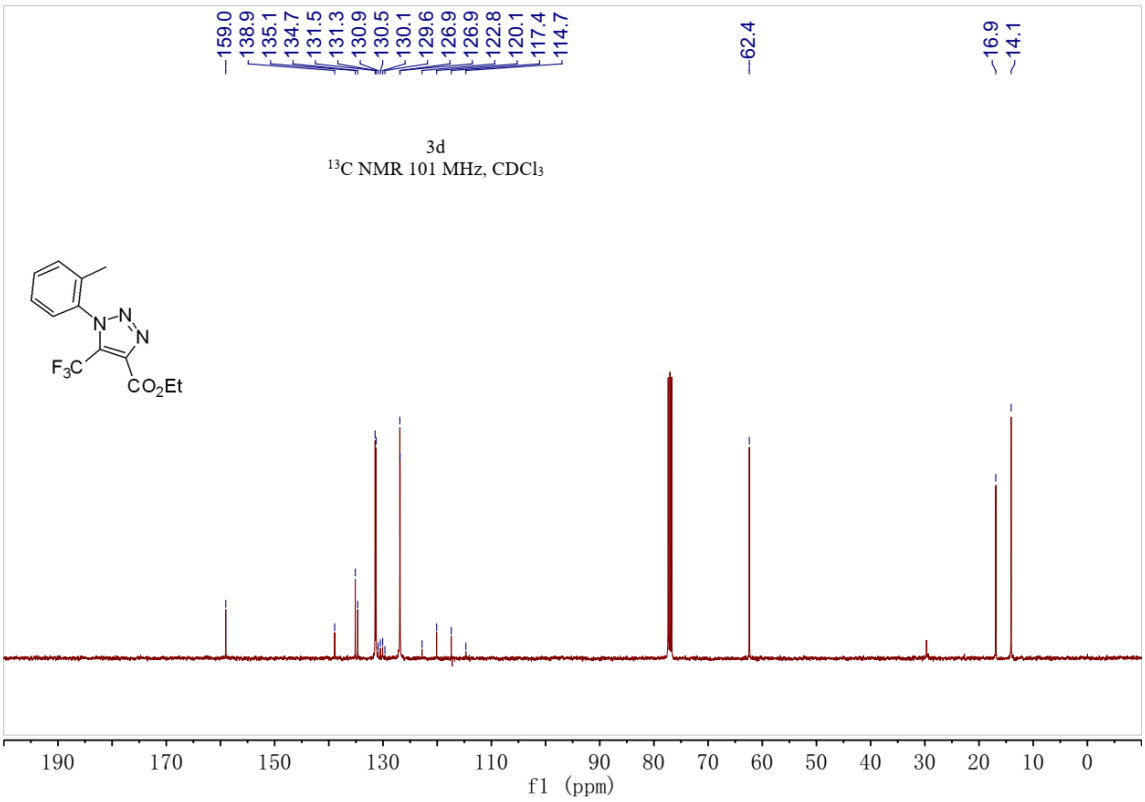
f1 (ppm)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120.1
117.4
114.7
62.4
16.9
14.1
3d
13C NMR 101 MHz, CDCl3
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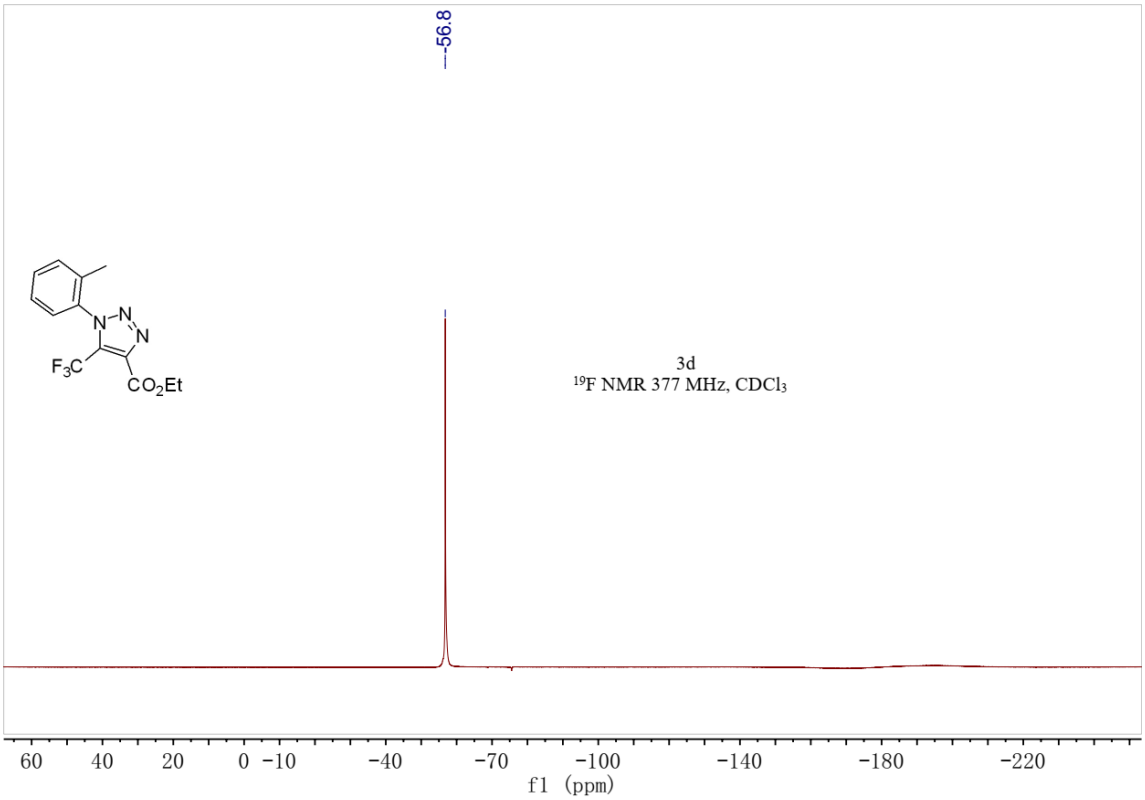
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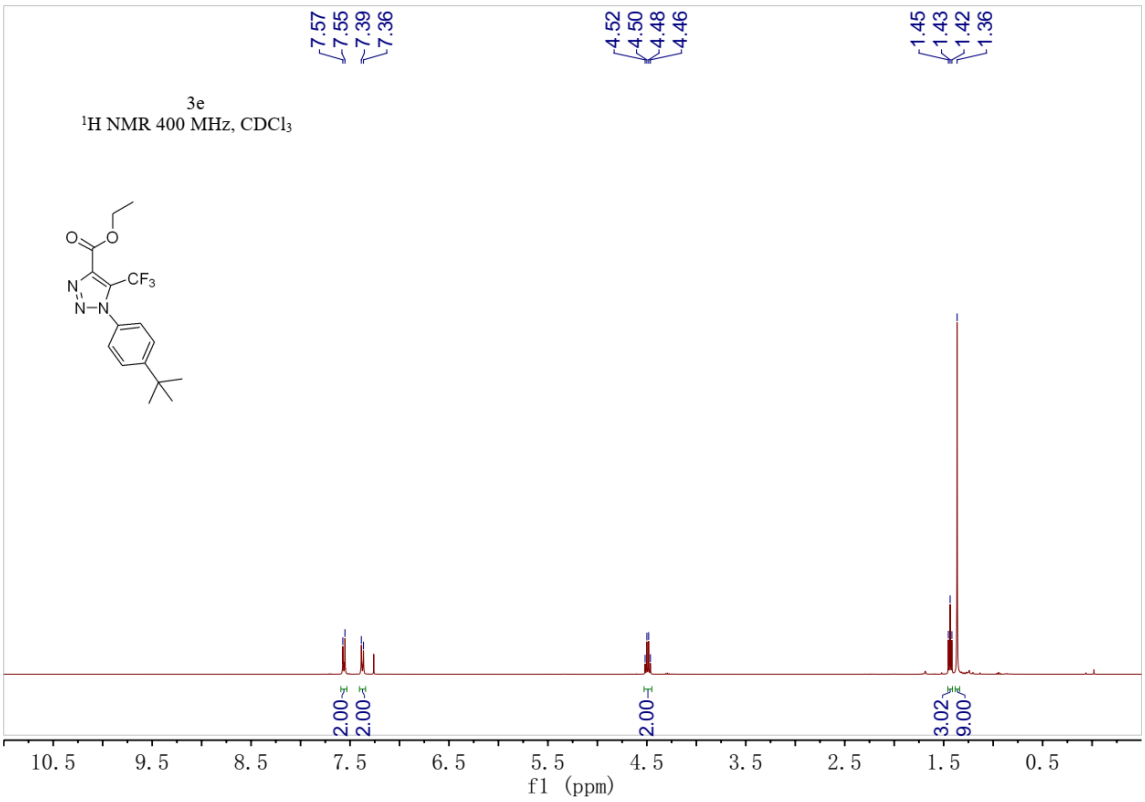
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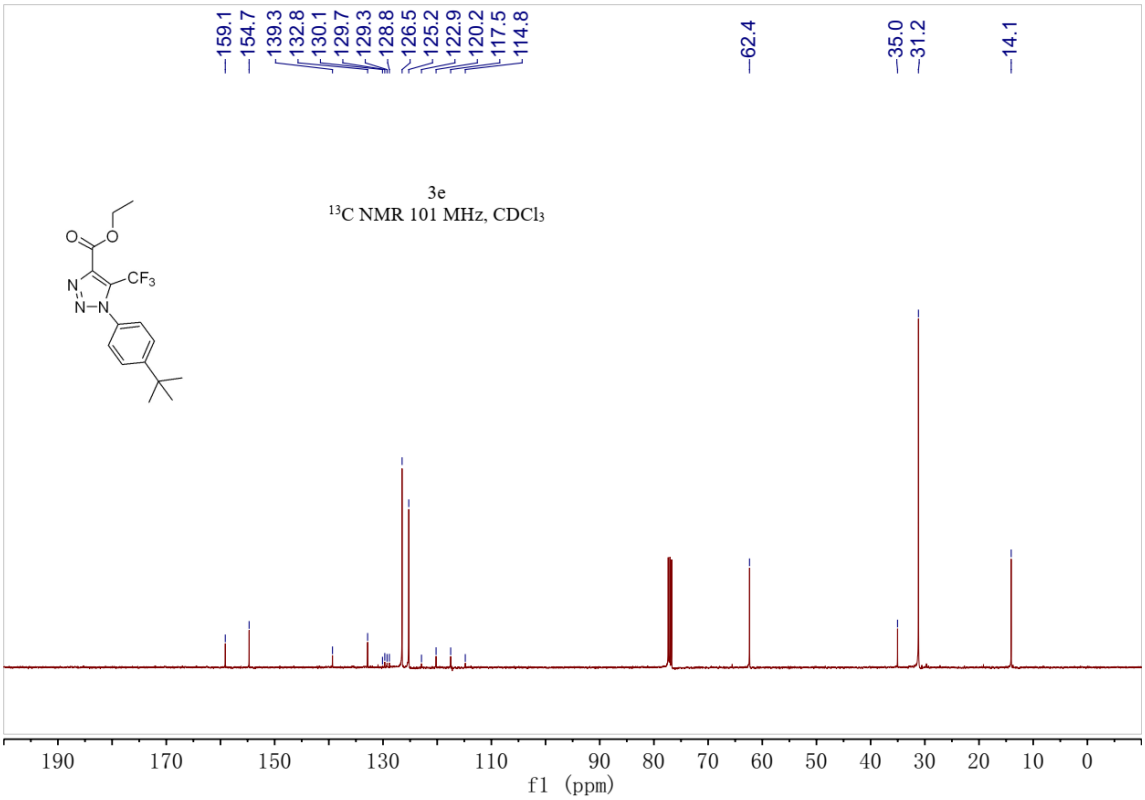
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62.4
35.0
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3e
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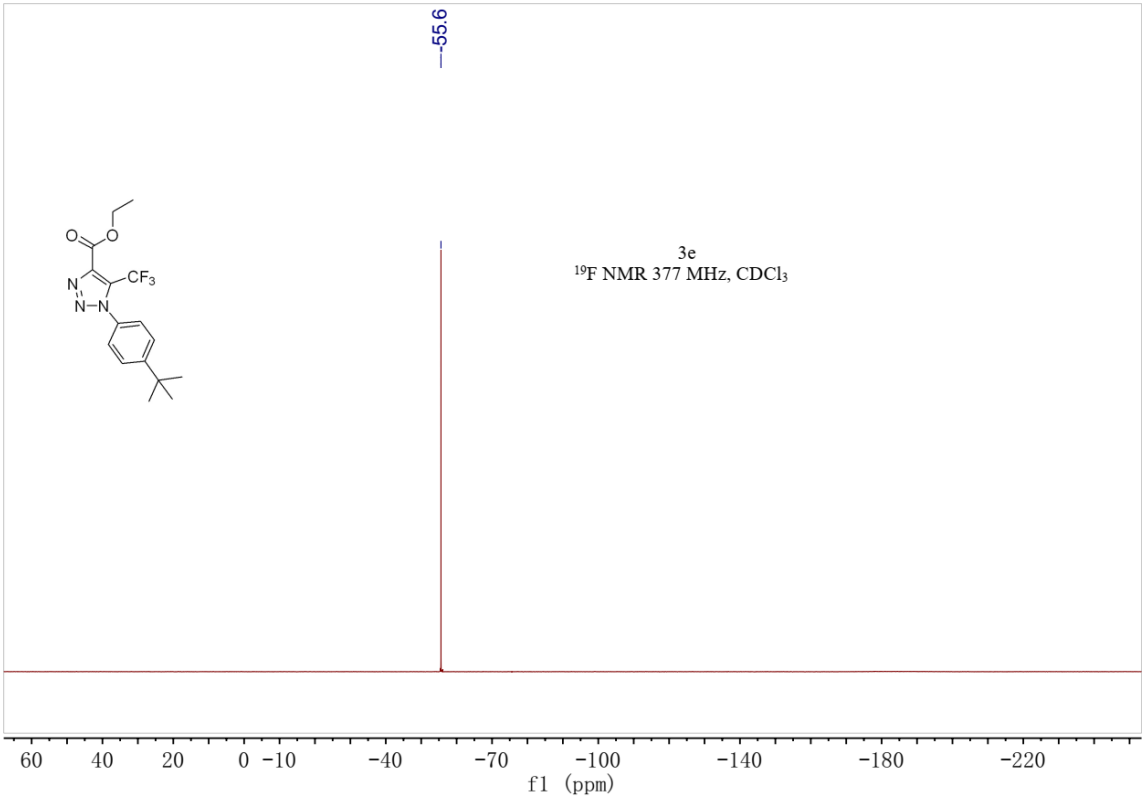
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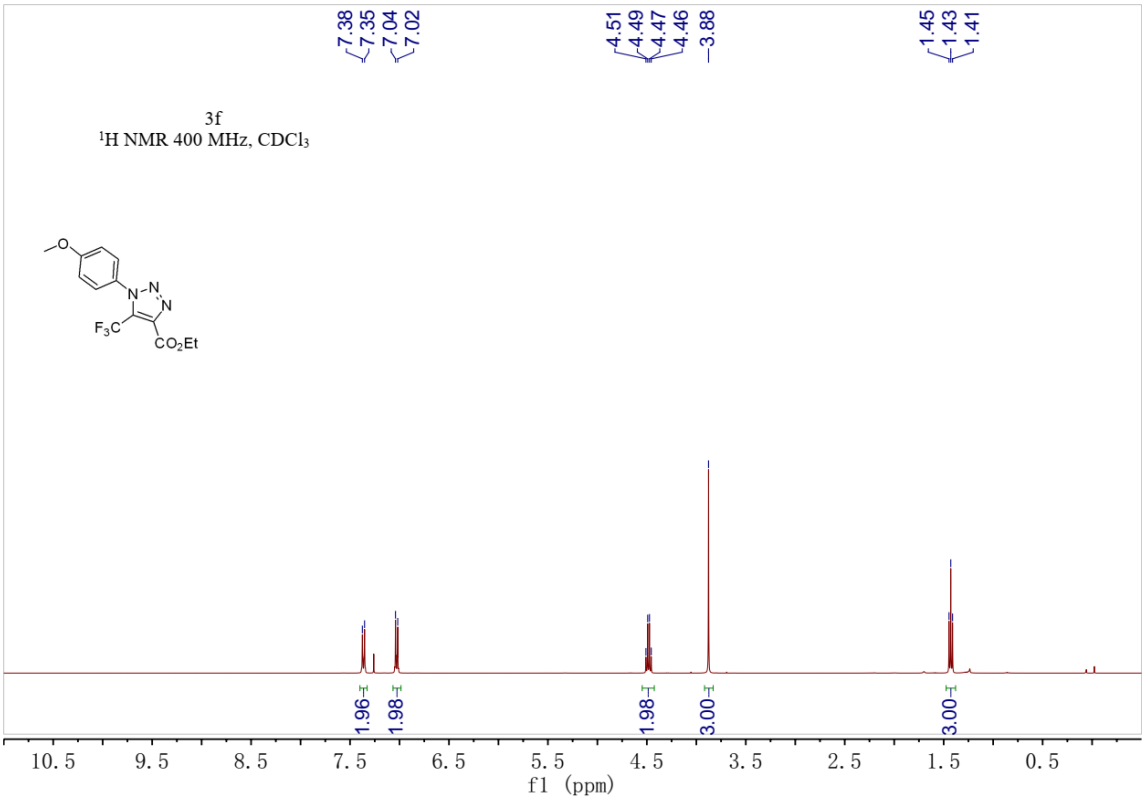
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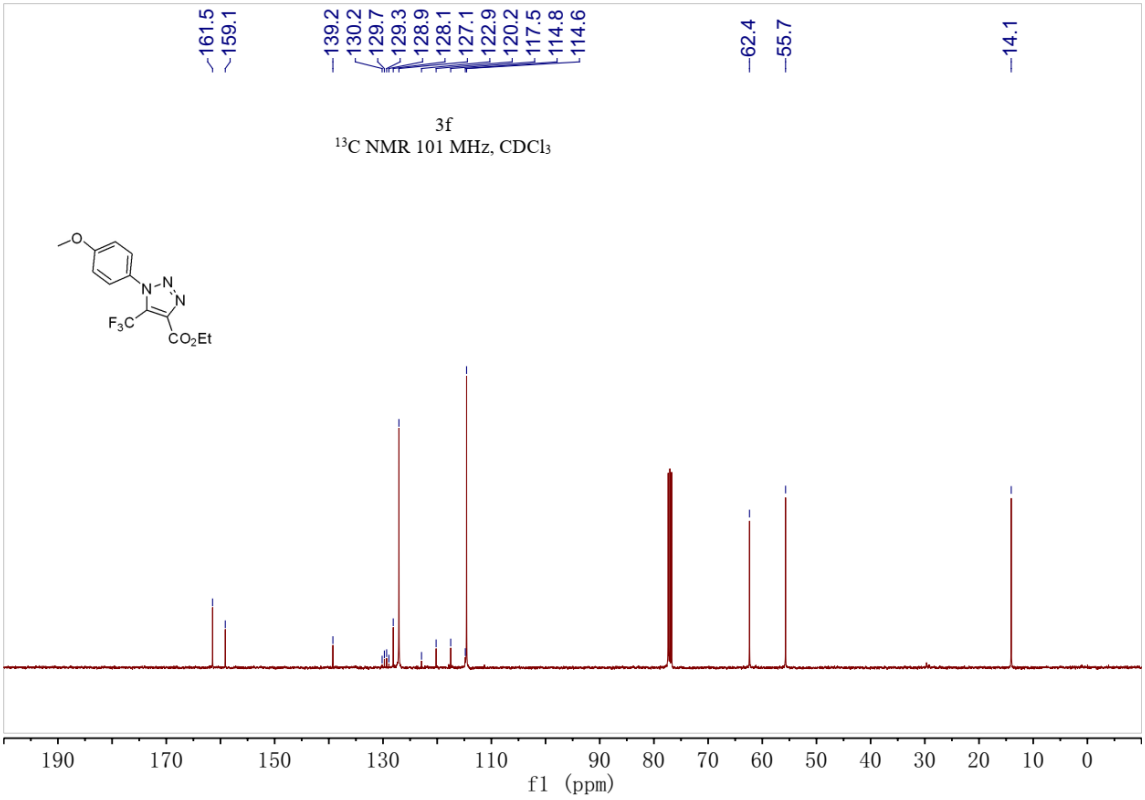
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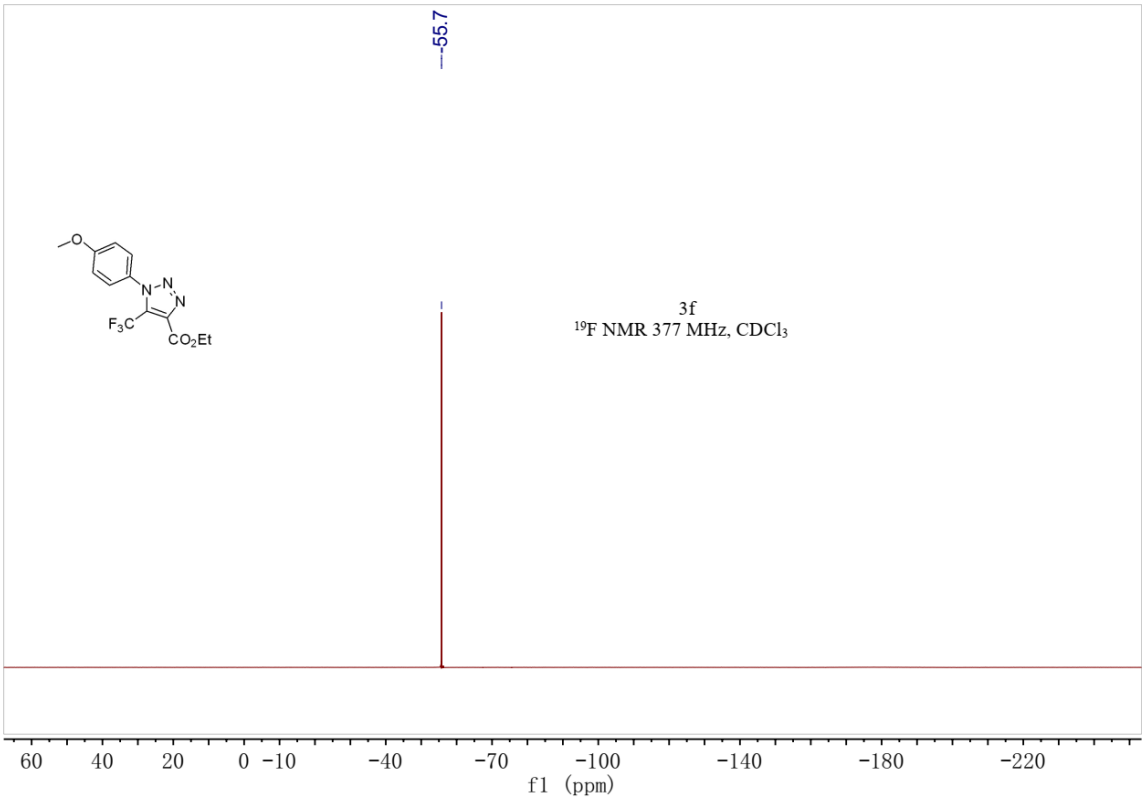
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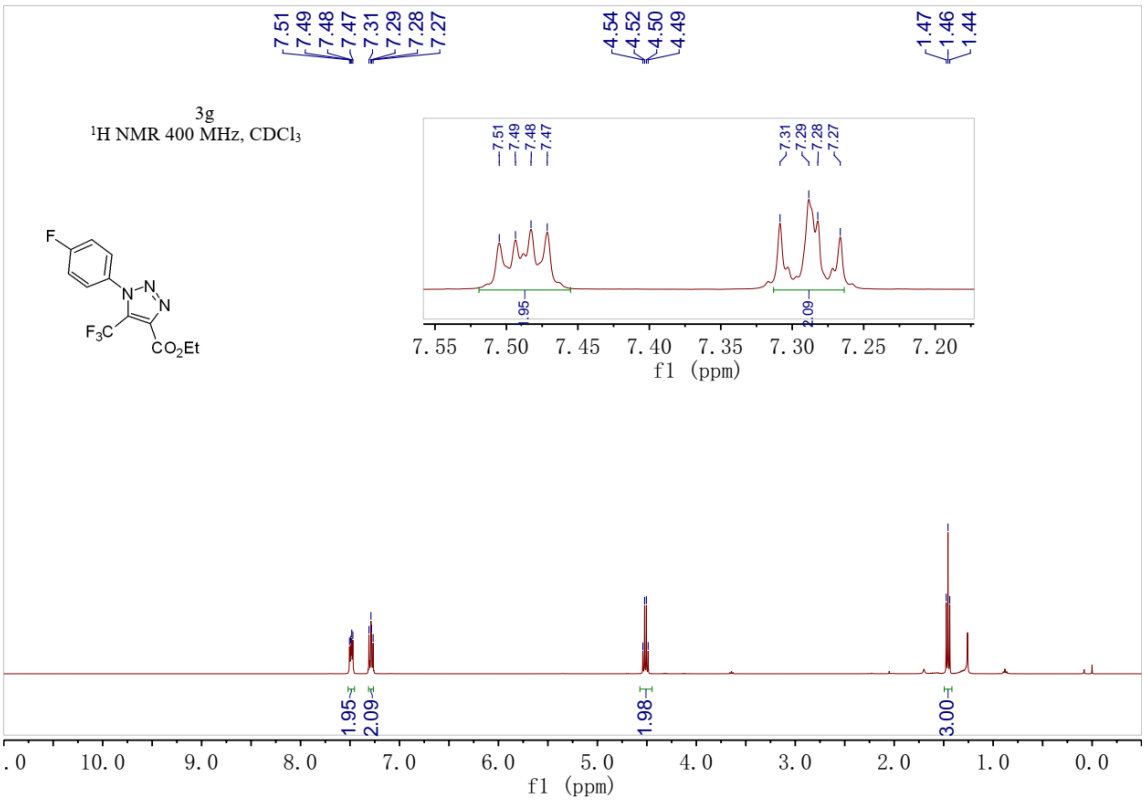
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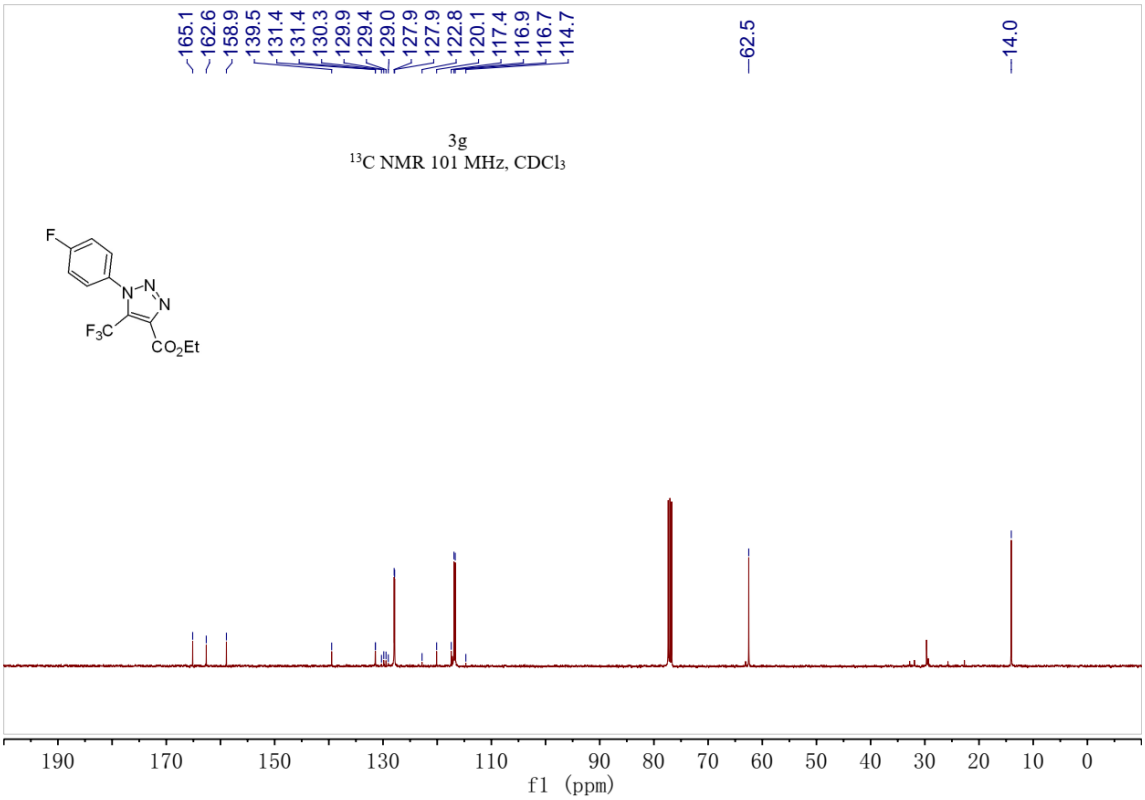
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116.9
116.7
114.7
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13C NMR 101 MHz, CDCl3
F
F3C
CO2Et
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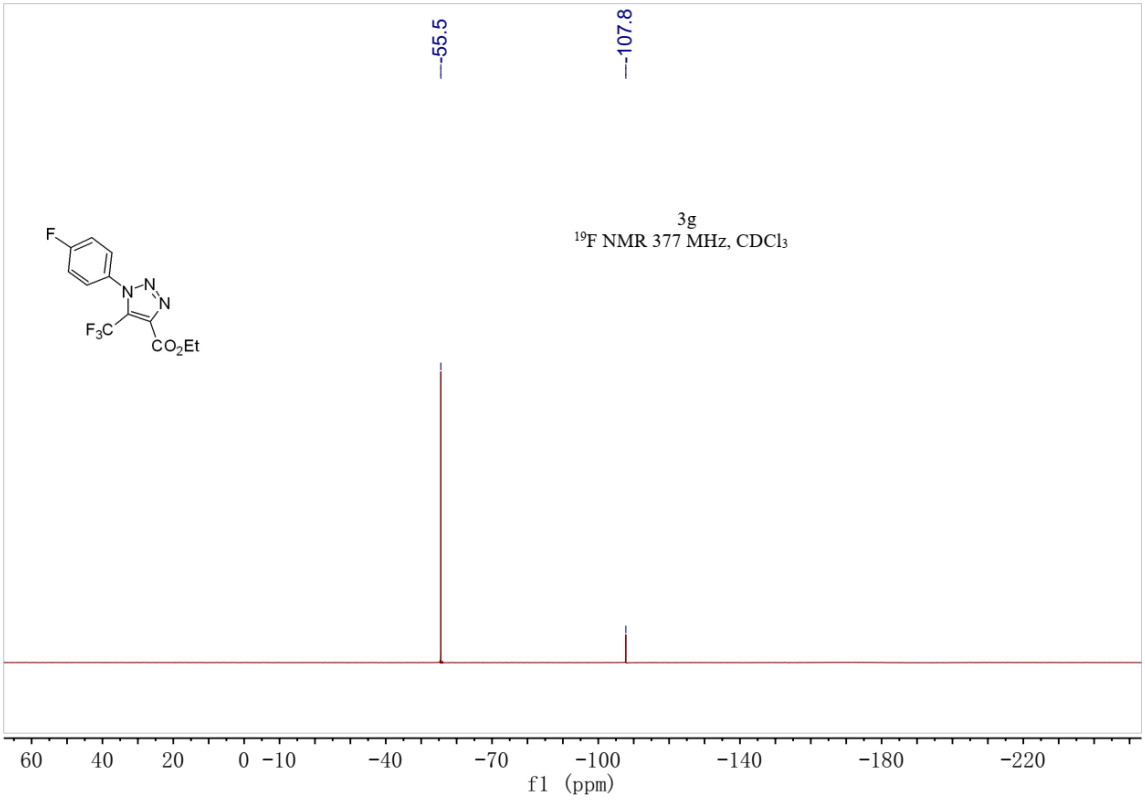
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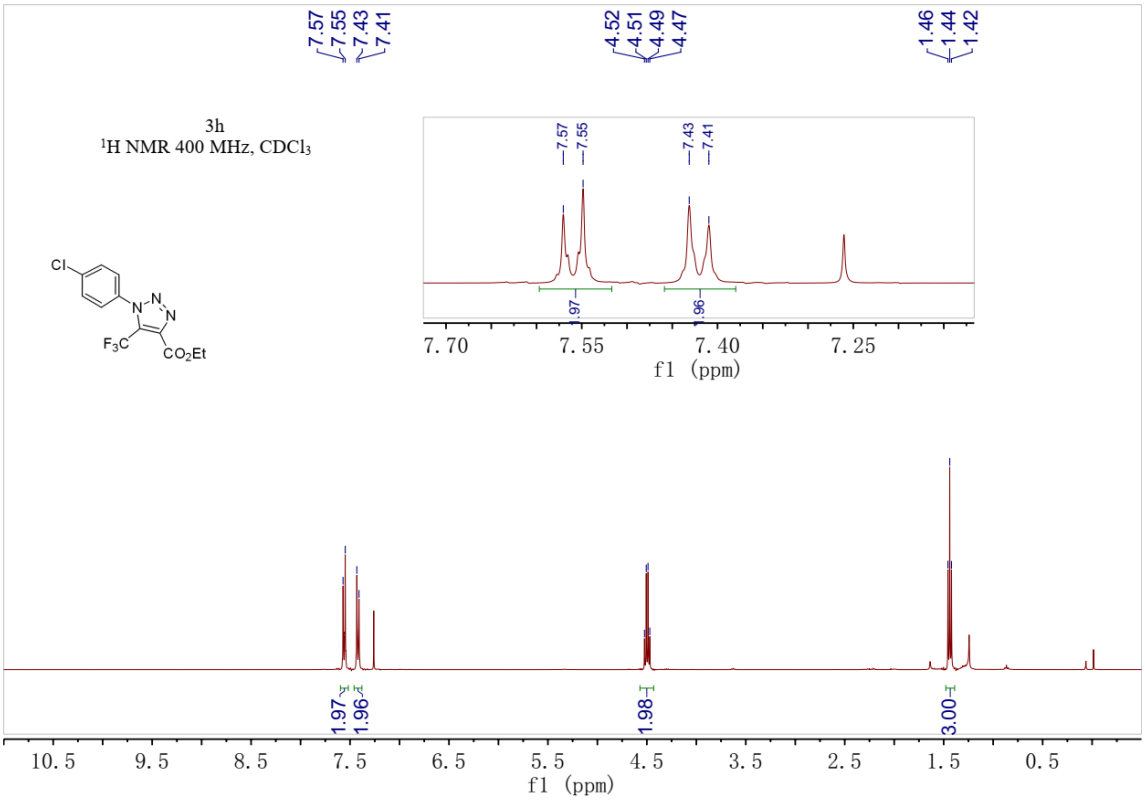
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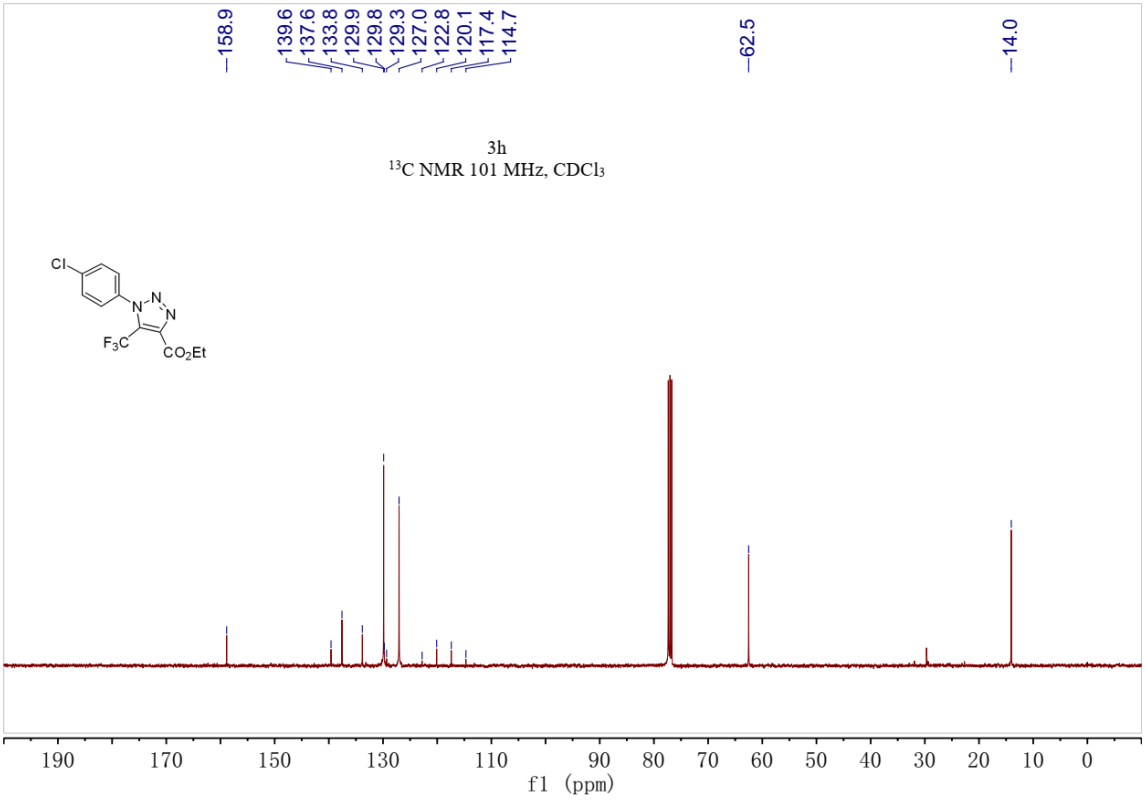
f1 (ppm)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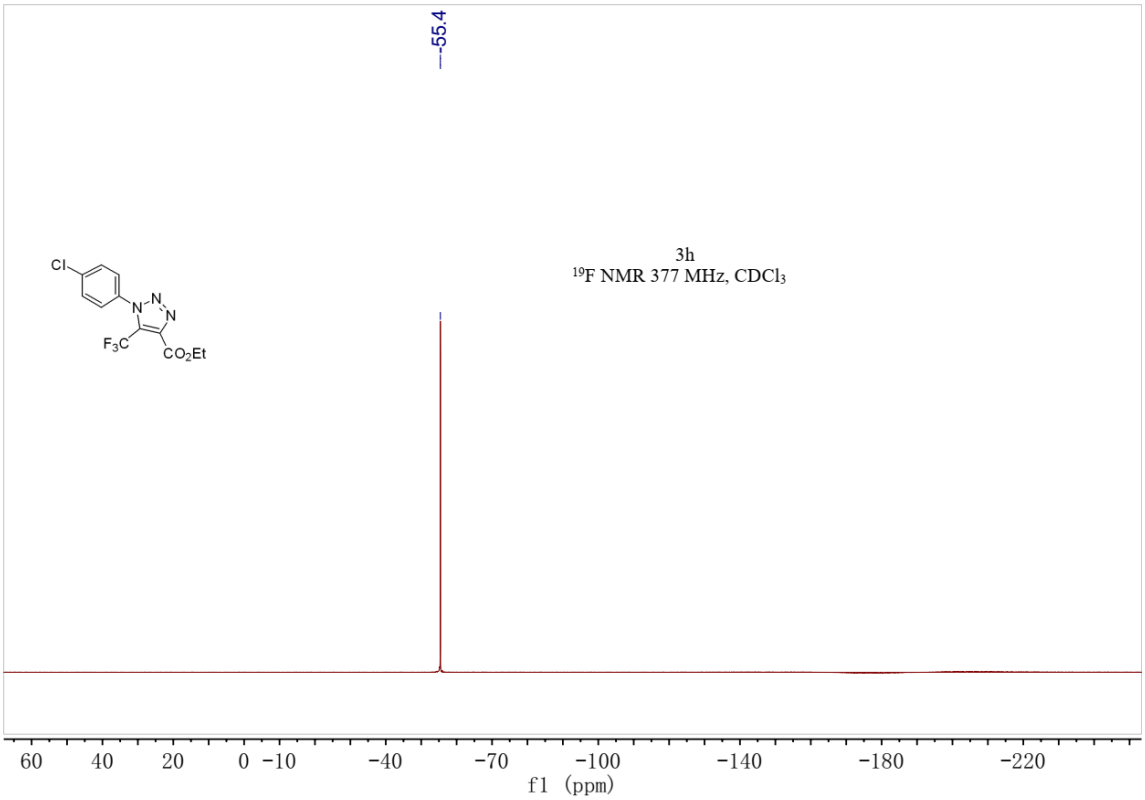
139.6
137.6
133.8
129.9
129.8
129.3
127.0
122.8
120.1
117.4
114.7
62.5
14.0
3h
13C NMR 101 MHz, CDCl3
Cl
N
N
N
F3C
CO2Et
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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F3C
CO2Et
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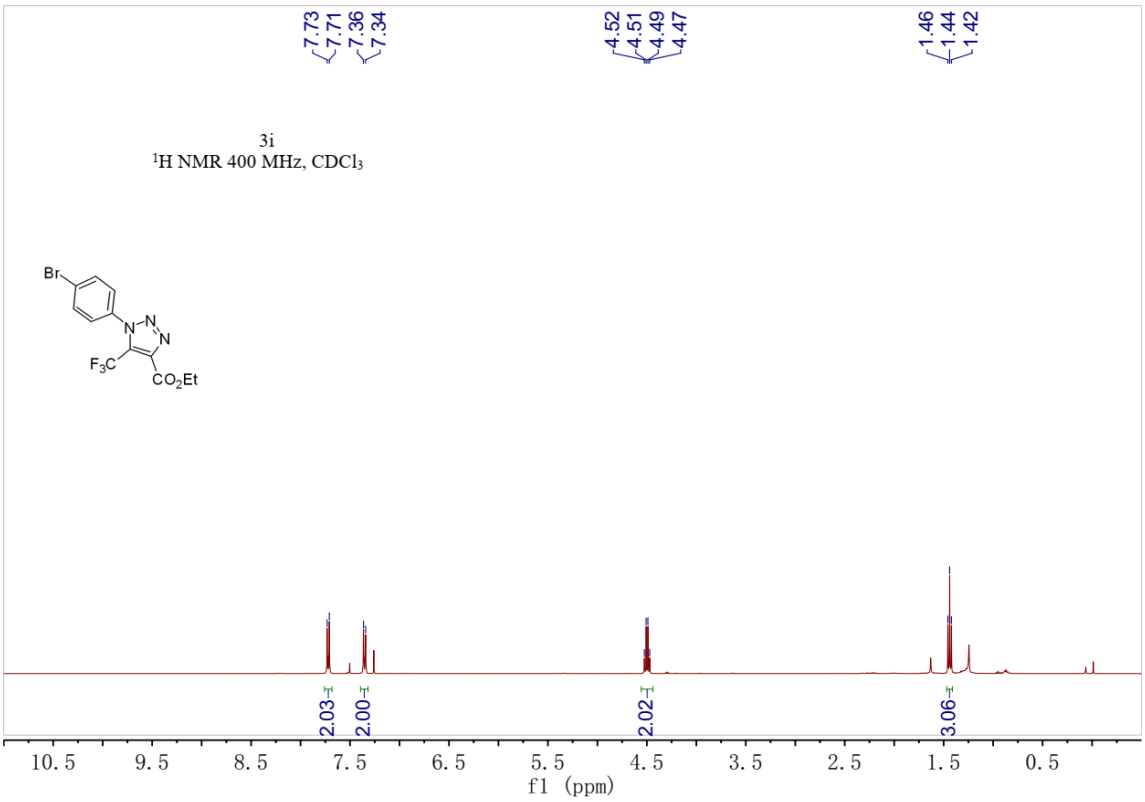
-40
-70
-100
-140
-180
-220
f1 (ppm)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4.49
4.47
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1.44
1.42
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1H NMR 400 MHz, CDCl3
Br
N
N
N
F3C
CO2Et
2.03
2.00
2.02
3.06
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
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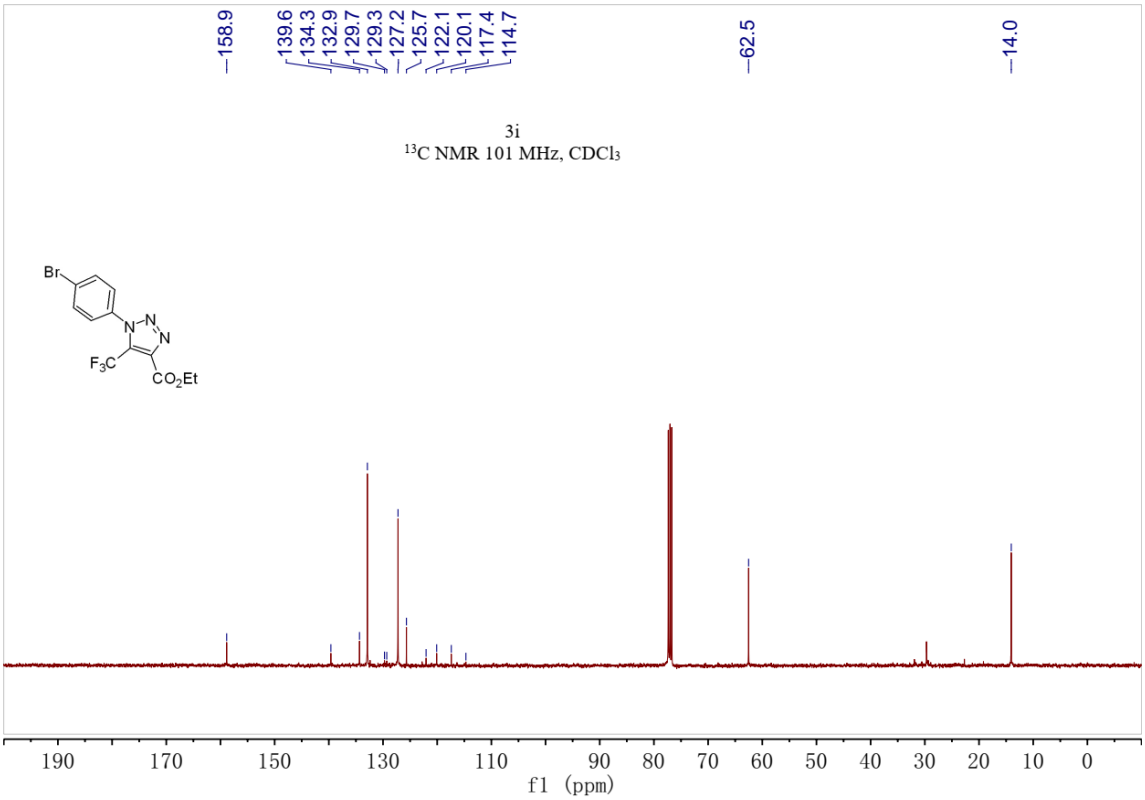
f1 (ppm)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134.3
132.9
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125.7
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120.1
117.4
114.7
62.5
14.0
3i
13C NMR 101 MHz, CDCl3
Br
N
N
N
F3C
CO2Et
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170
150
130
110
90
80
70
60
50
40
30
20
10
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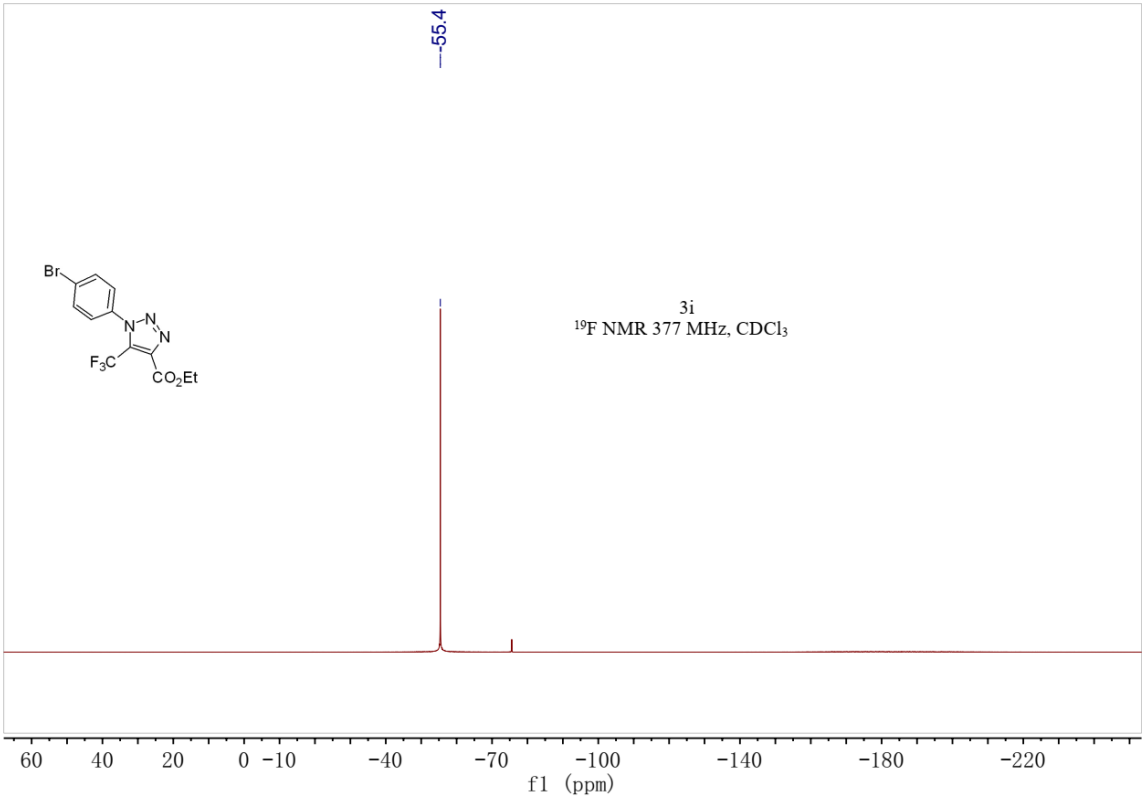
f1 (ppm)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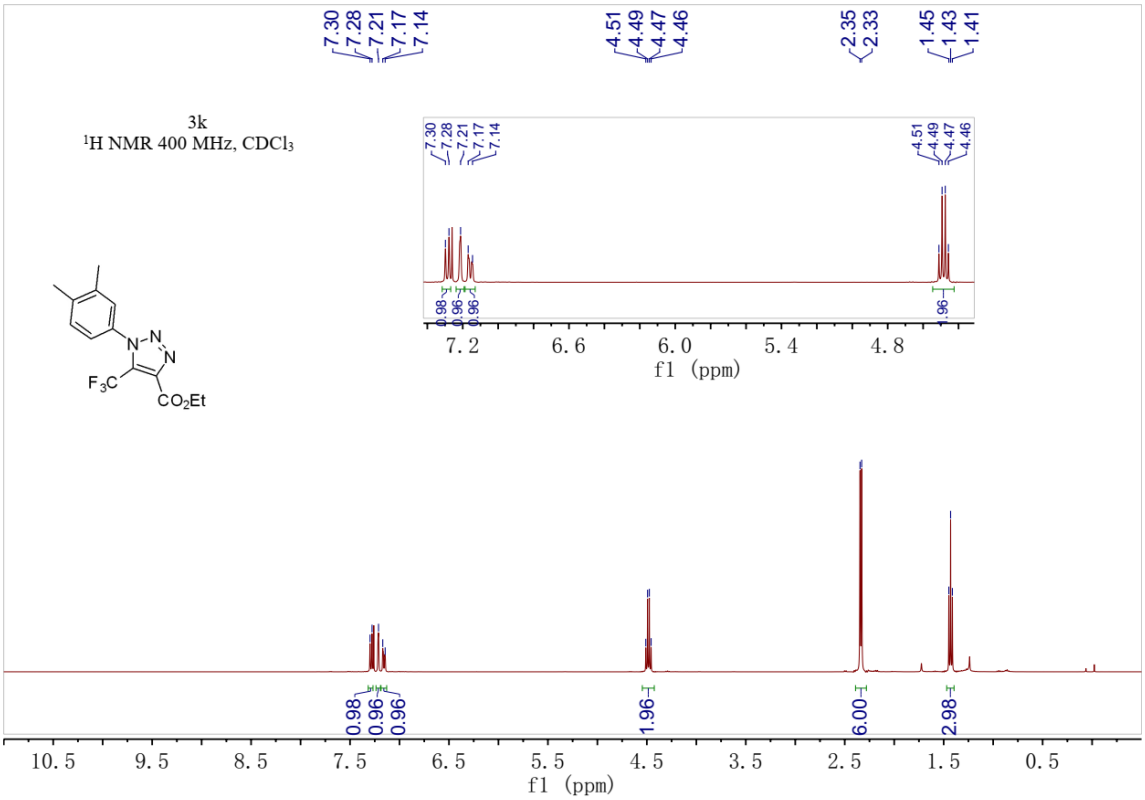
Br
N
N
N
F3C
CO2Et
3i
19F NMR 377 MHz, CDCl3
60
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)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7.28
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7.17
7.14
4.51
4.49
4.47
4.46
2.35
2.33
1.45
1.43
1.41
3k
1H NMR 400 MHz, CDCl3
N
N
N
F3C
CO2Et
0.98
0.96
0.96
1.96
6.00
2.98
10.5
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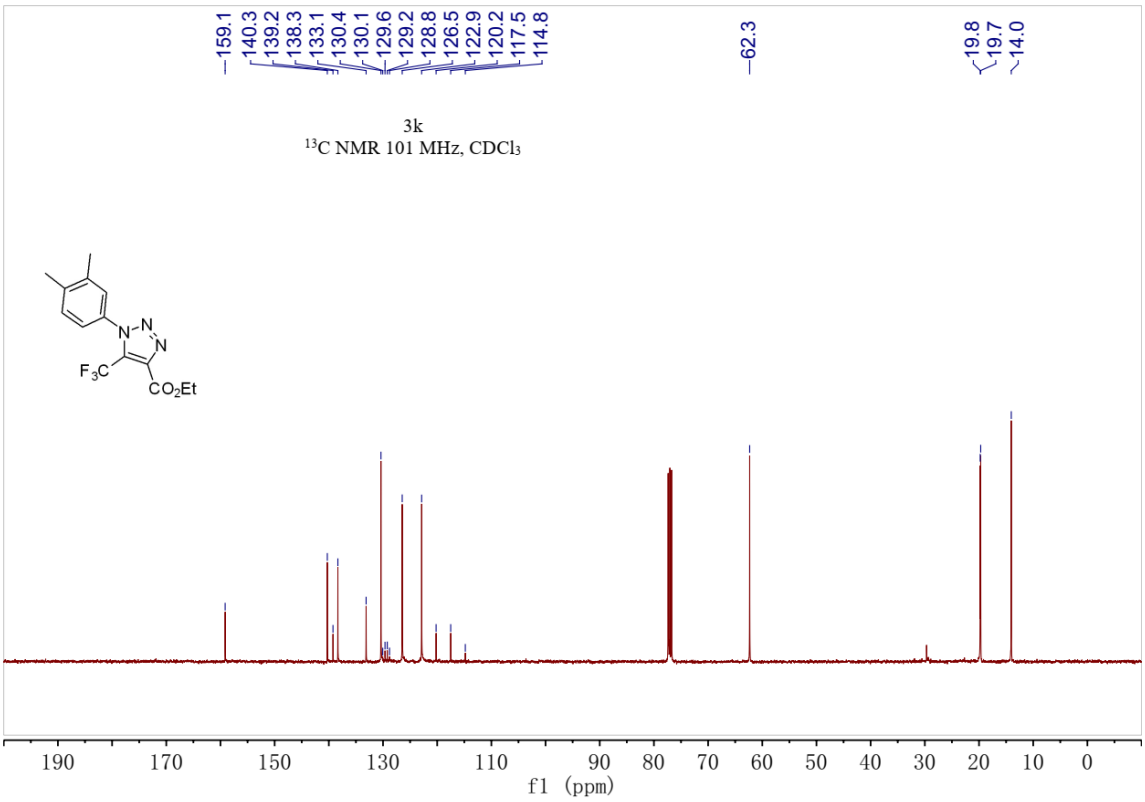
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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140.3
139.2
138.3
133.1
130.4
130.1
129.6
129.2
128.8
126.5
122.9
120.2
117.5
114.8
62.3
19.8
19.7
14.0
3k
13C NMR 101 MHz, CDCl3
F3C
CO2Et
190
170
150
130
110
90
80
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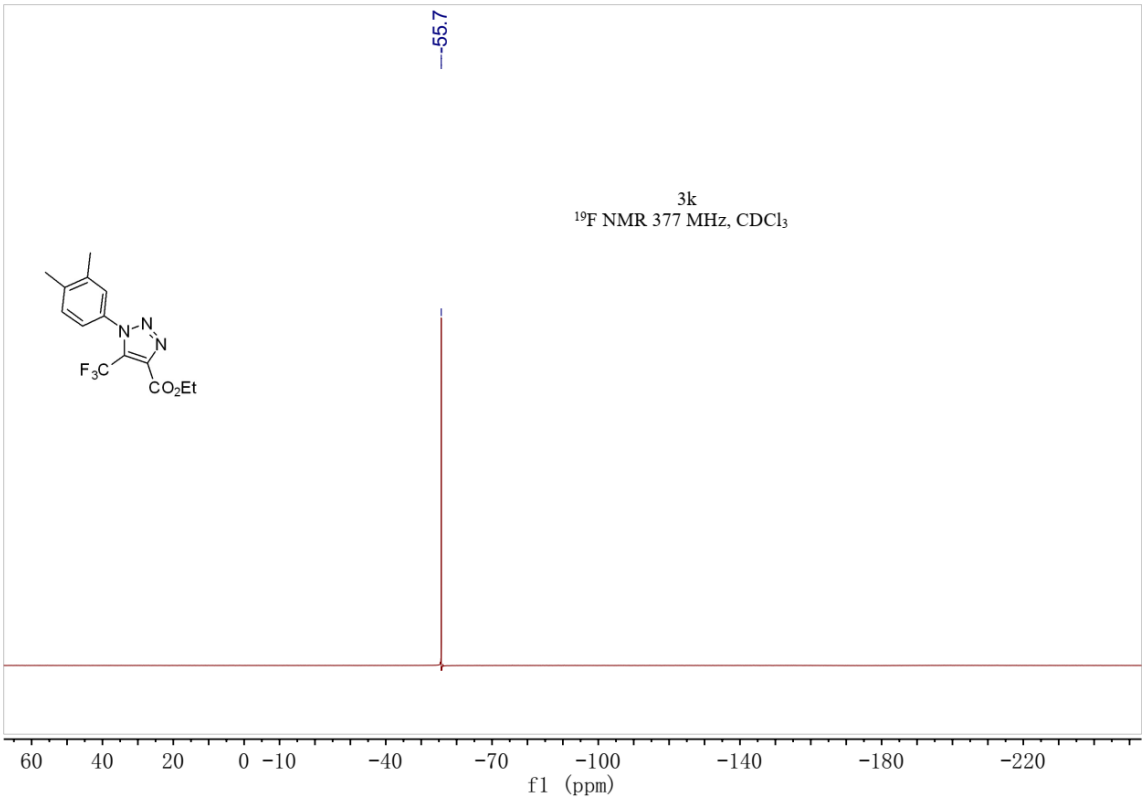
60
50
40
30
20
10
0
f1 (ppm)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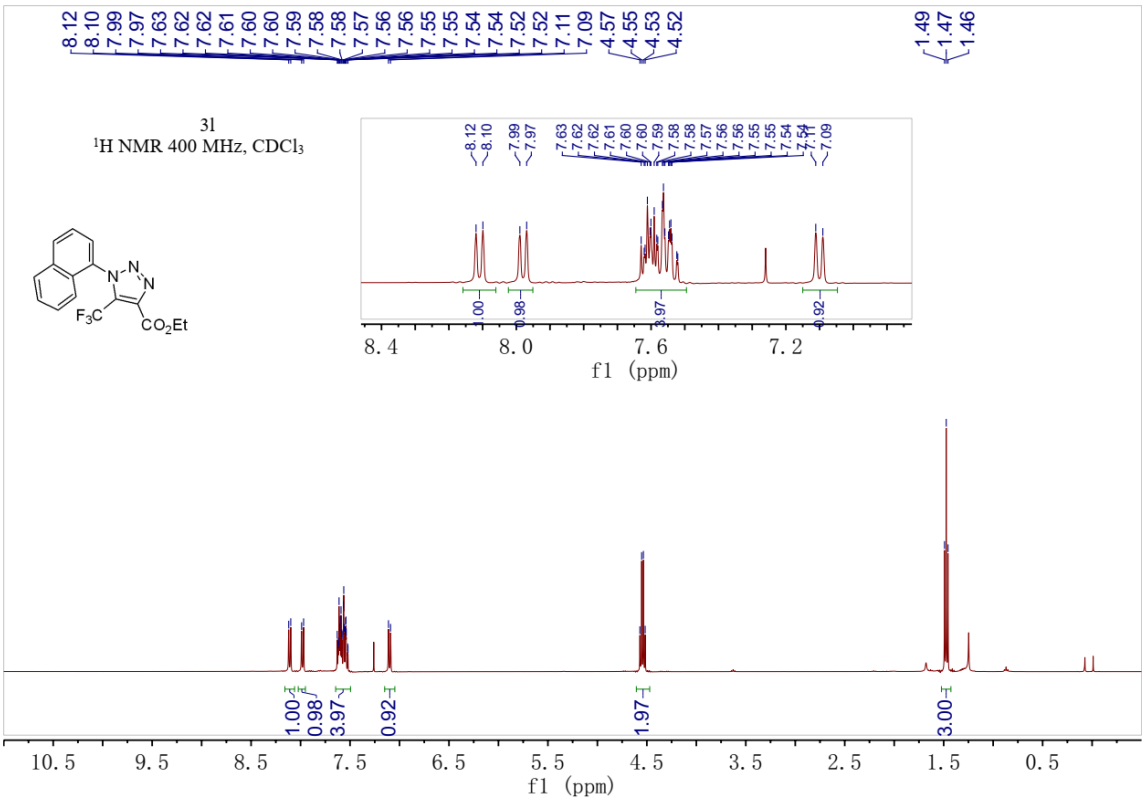
3k
19F NMR 377 MHz, CDCl3
F3C
CO2Et
60
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)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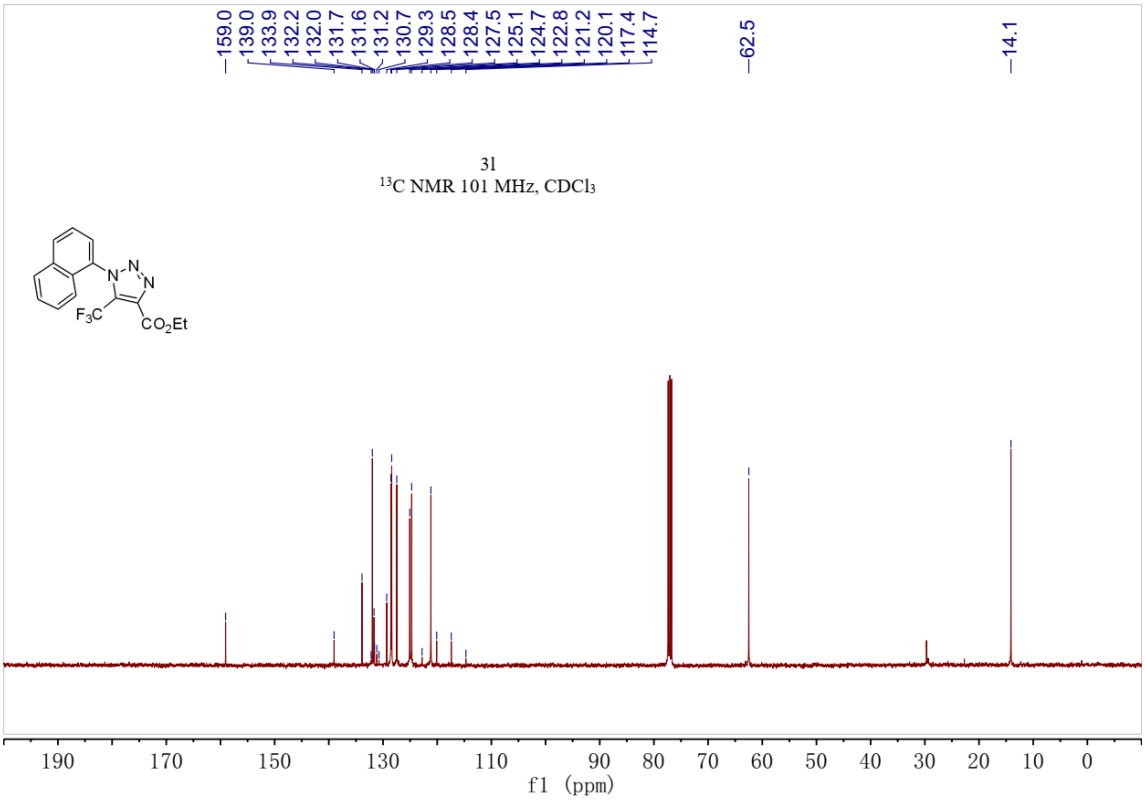
8.10
7.99
7.97
7.63
7.62
7.62
7.61
7.60
7.60
7.59
7.58
7.58
7.57
7.56
7.55
7.55
7.54
7.54
7.52
7.52
7.11
7.09
4.57
4.55
4.53
4.52
1.49
1.47
1.46
3l
1H NMR 400 MHz, CDCl3
F3C
CO2Et
1.00
0.98
3.97
0.92
1.97
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)
8.4
8.0
7.6
7.2
f1 (ppm)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133.9
132.2
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131.7
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131.2
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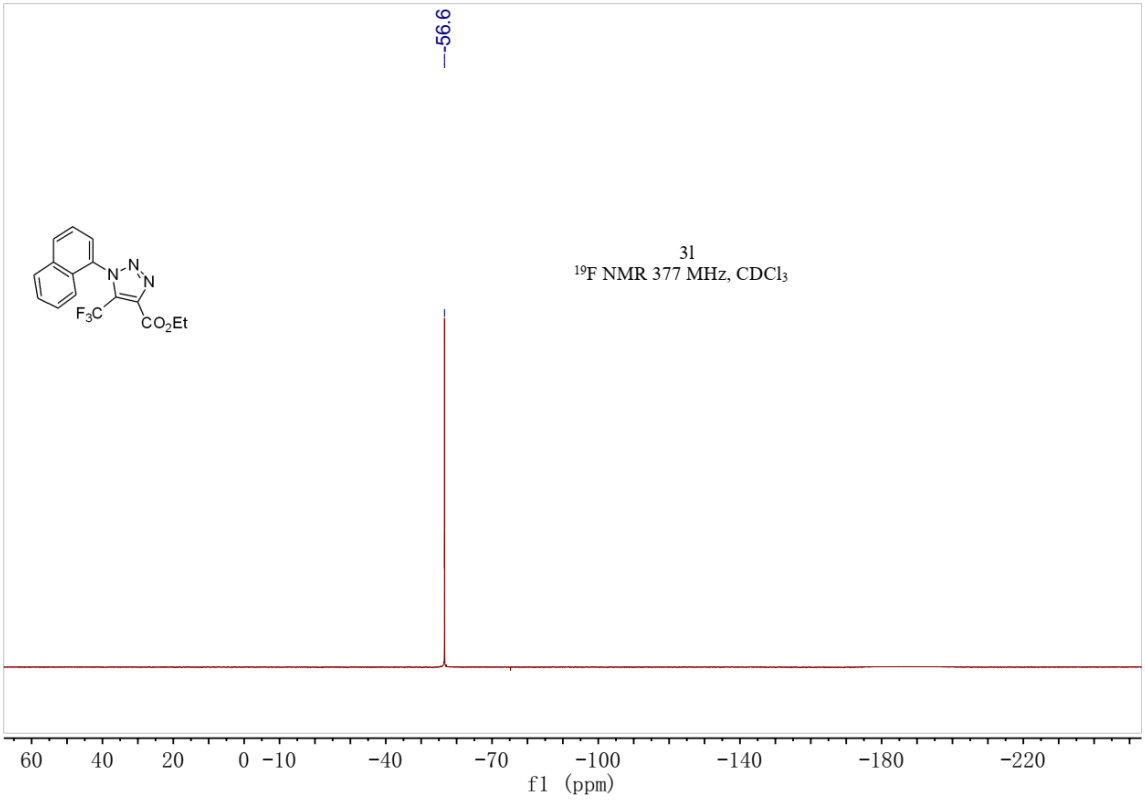
129.3
128.5
128.4
127.5
125.1
124.7
122.8
121.2
120.1
117.4
114.7
62.5
14.1
3l
13C NMR 101 MHz, CDCl3
F3C
CO2Et
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-56.6
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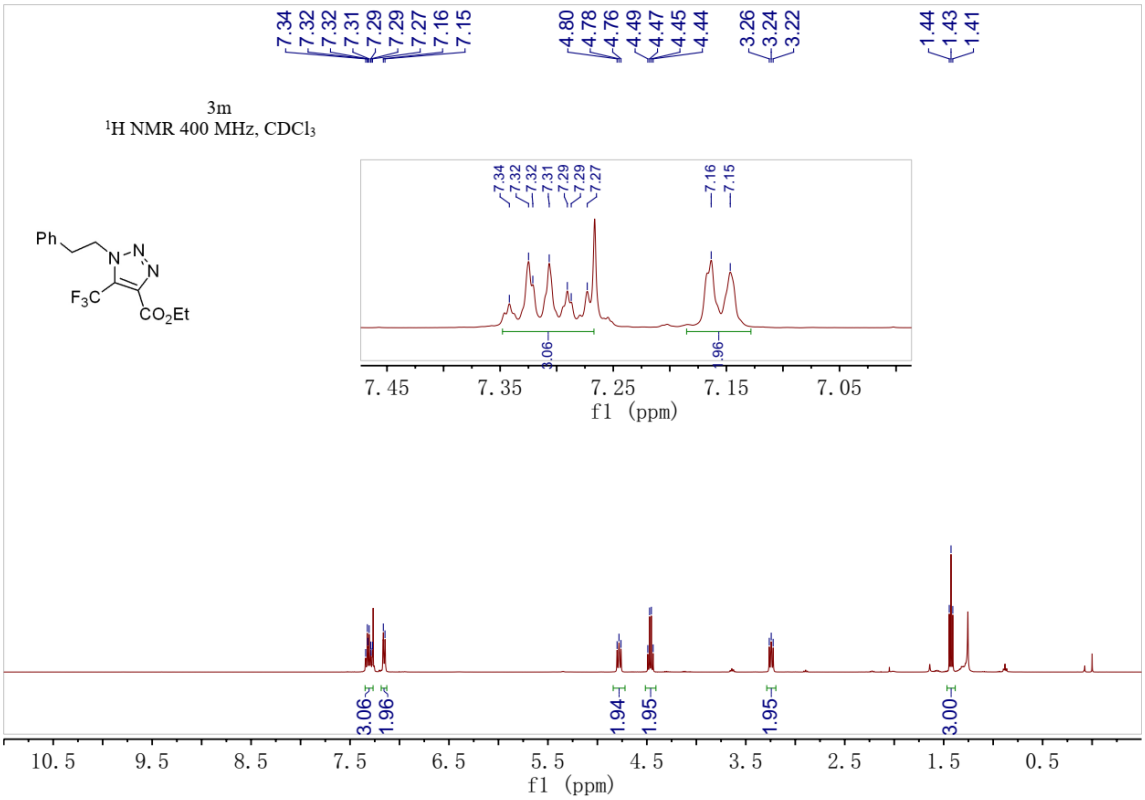
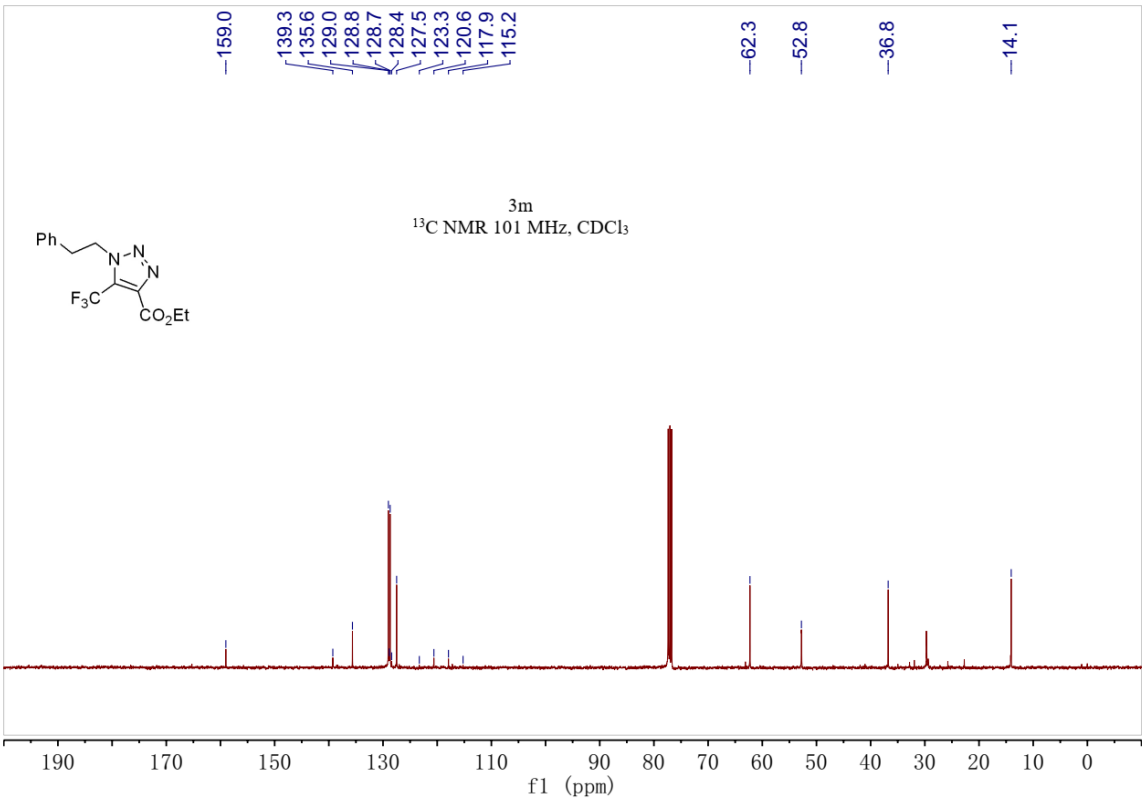
19F NMR 377 MHz, CDCl3
F3C
CO2Et
60 40 20 0 -10 -40 -70 -100 -140 -180 -220
f1 (ppm)


7.34 7.32 7.32 7.31 7.29 7.29 7.27 7.16 7.15
4.80 4.78 4.76 4.49 4.47 4.45 4.44
3.26 3.24 3.22
1.44 1.43 1.41
3m
1H NMR 400 MHz, CDCl3
Ph
F3C
CO2Et
3.06
1.96
7.45 7.35 7.25 7.15 7.05
f1 (ppm)
3.06 1.96 1.94 1.95 1.95 3.00
10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5
f1 (ppm)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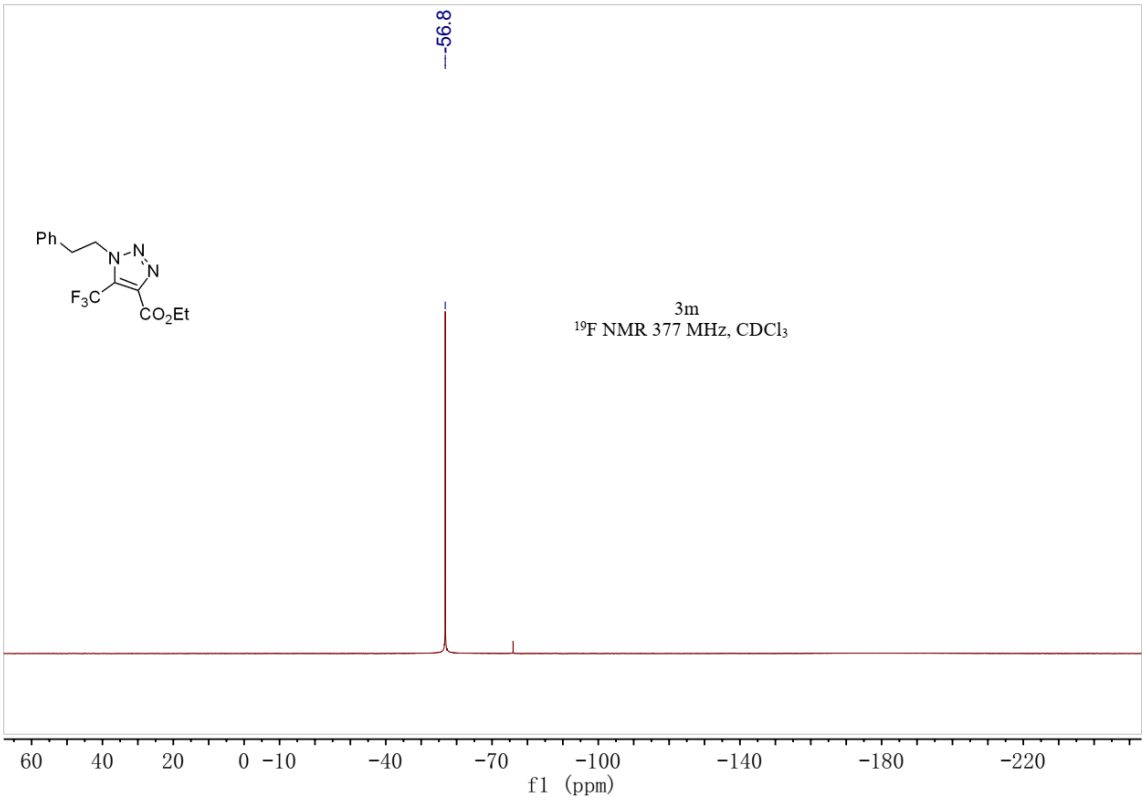
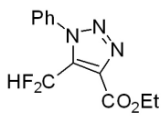
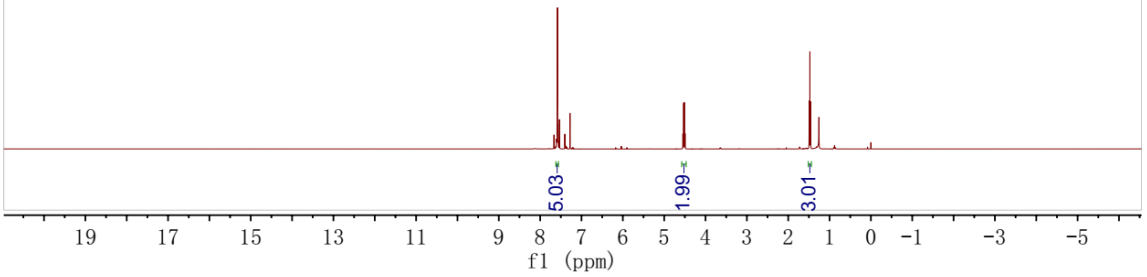
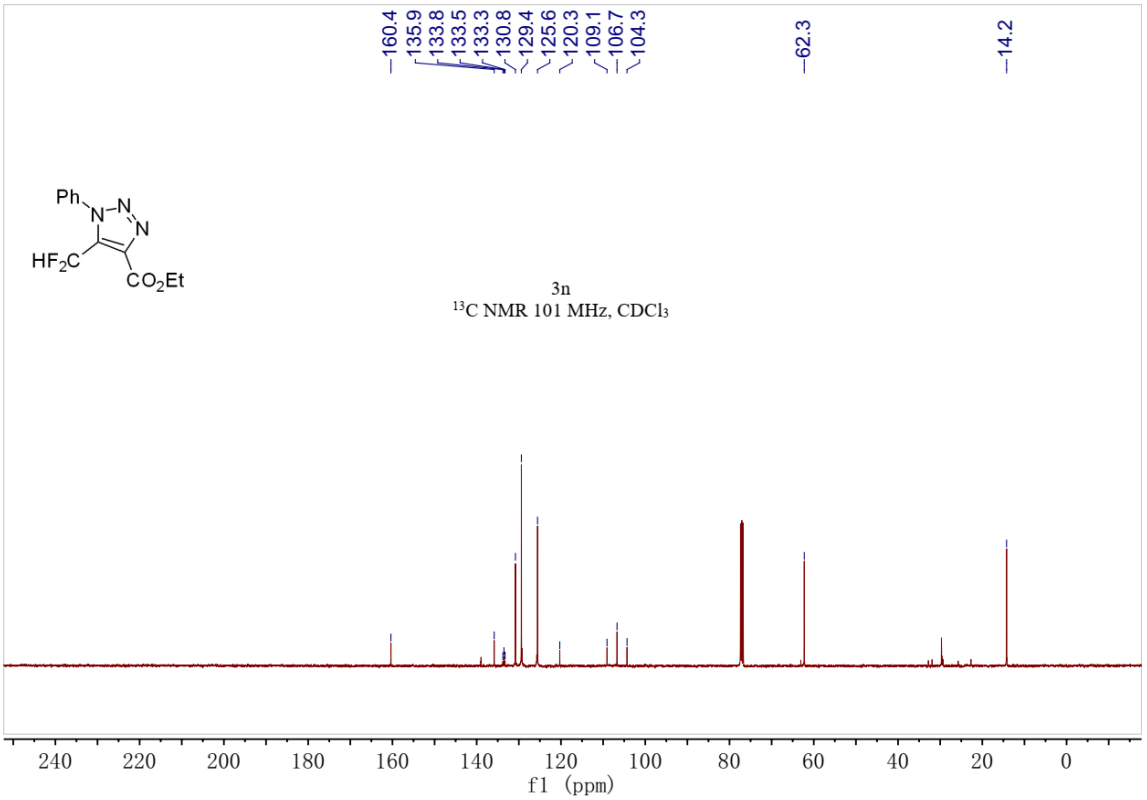
139.3
135.6
129.0
128.8
128.7
128.4
127.5
123.3
120.6
117.9
115.2
62.3
52.8
36.8
14.1
3m
13C NMR 101 MHz, CDCl3
Ph
F3C
CO2Et
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-56.8
Ph
F3C
CO2Et
3m
19F NMR 377 MHz, CDCl3
60
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)

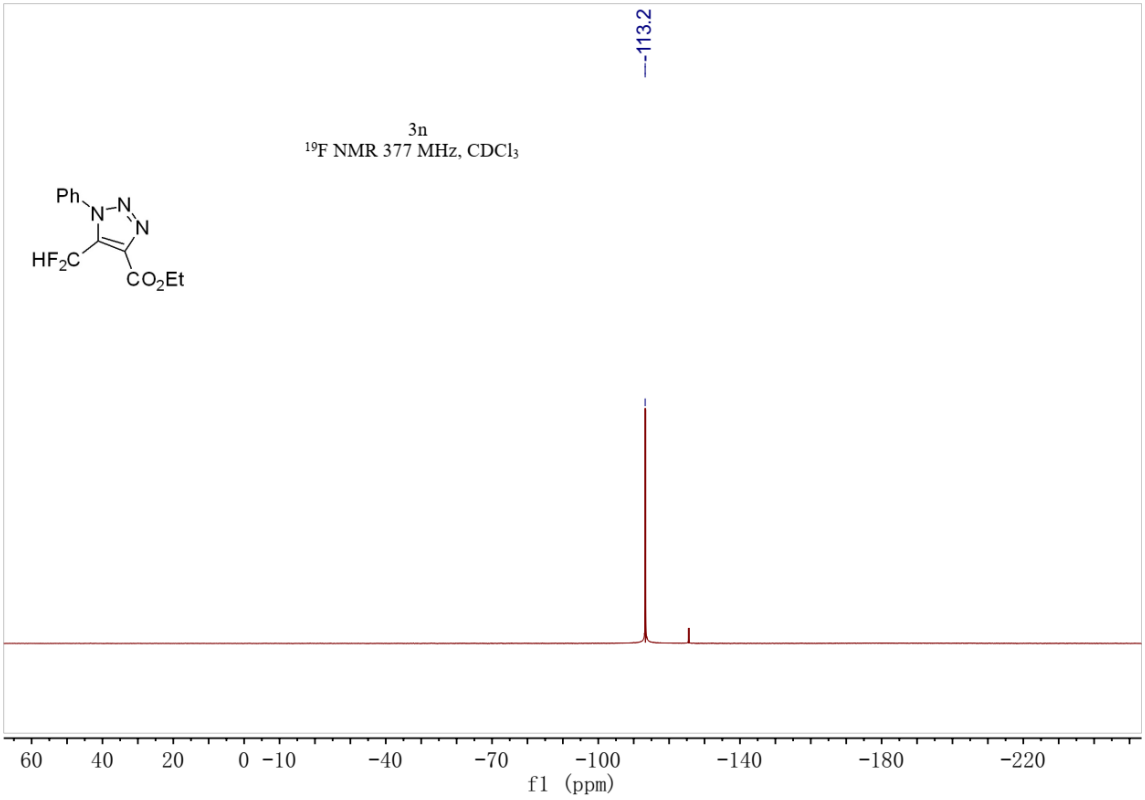
3n
^{1}H NMR 400 MHz, $CDCl_3$

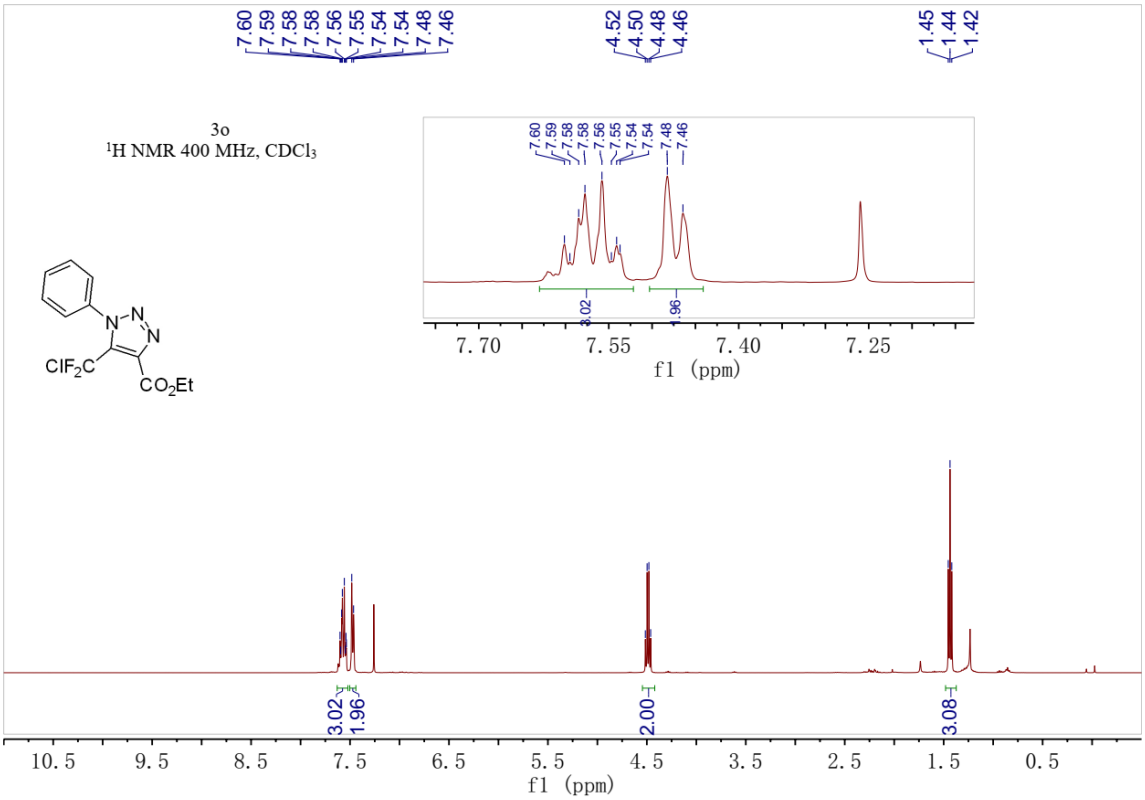






3n
^{13}C NMR 101 MHz, $CDCl_3$


-113.2
3n
19F NMR 377 MHz, CDCl3
Ph
HF2C
CO2Et
60
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)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7.59
7.58
7.58
7.56
7.55
7.54
7.54
7.48
7.46
4.52
4.50
4.48
4.46
1.45
1.44
1.42
3o
1H NMR 400 MHz, CDCl3
ClF2C
CO2Et
3.02
1.96
7.70
7.55
7.40
7.25
f1 (ppm)
3.02
1.96
2.00
3.08
10.5
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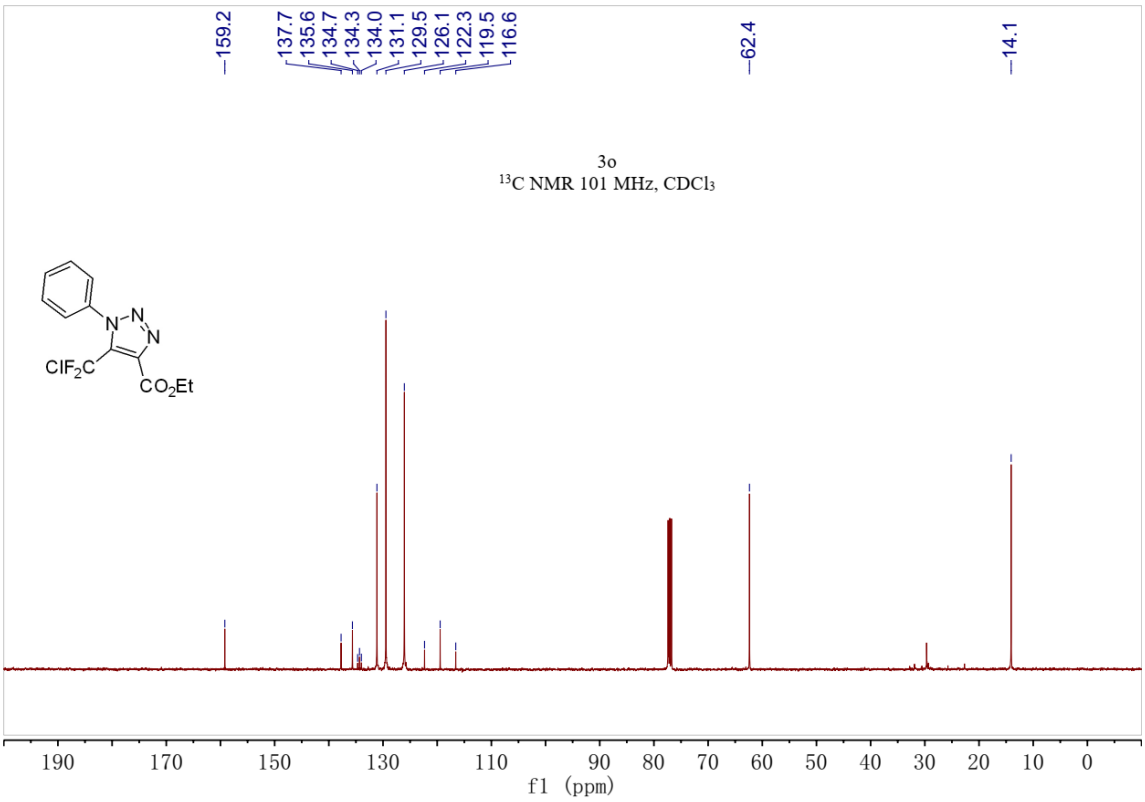
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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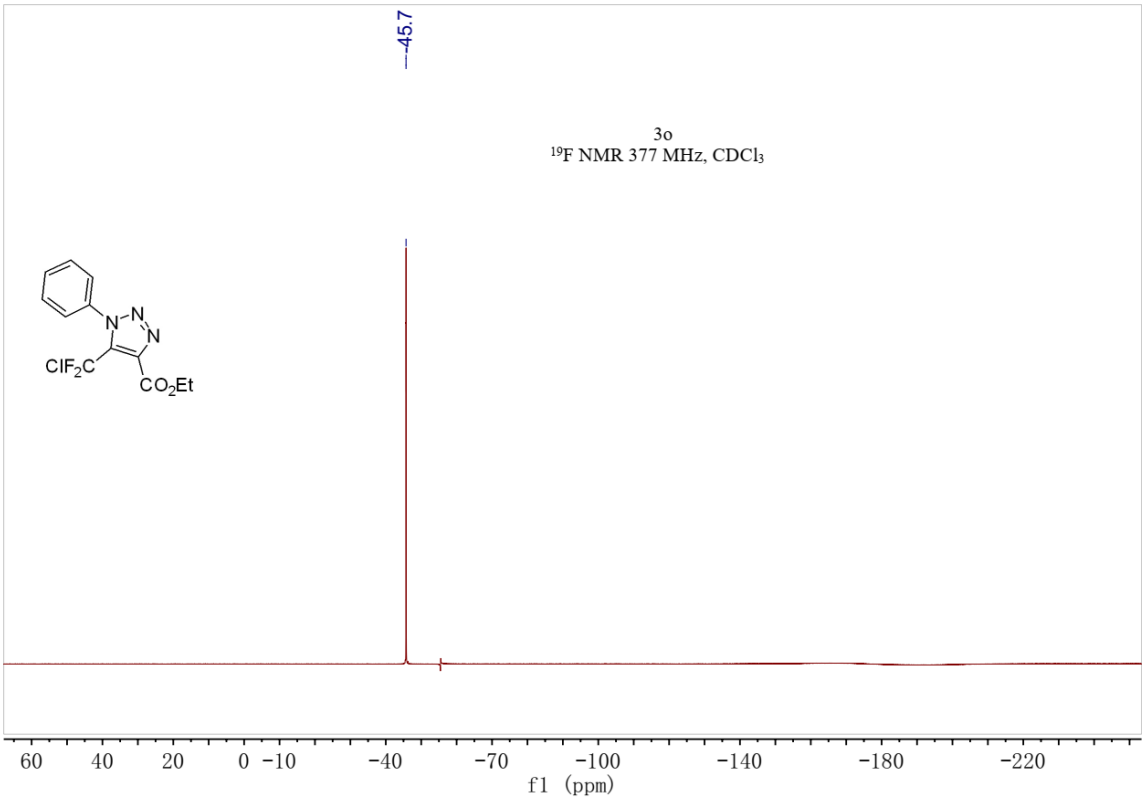
135.6
134.7
134.3
134.0
131.1
129.5
126.1
122.3
119.5
116.6
62.4
14.1
3o
13C NMR 101 MHz, CDCl3
ClF2C
CO2Et
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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ClF2C
CO2Et
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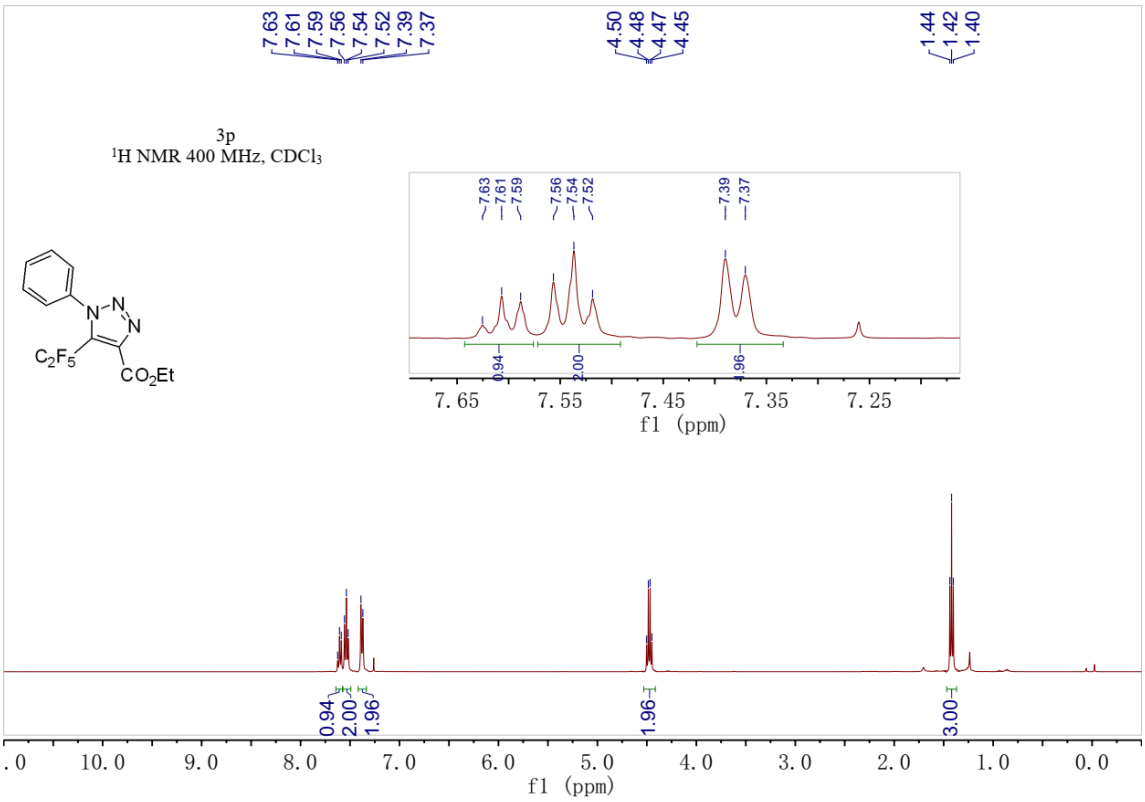
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)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7.39
7.37
4.50
4.48
4.47
4.45
1.44
1.42
1.40
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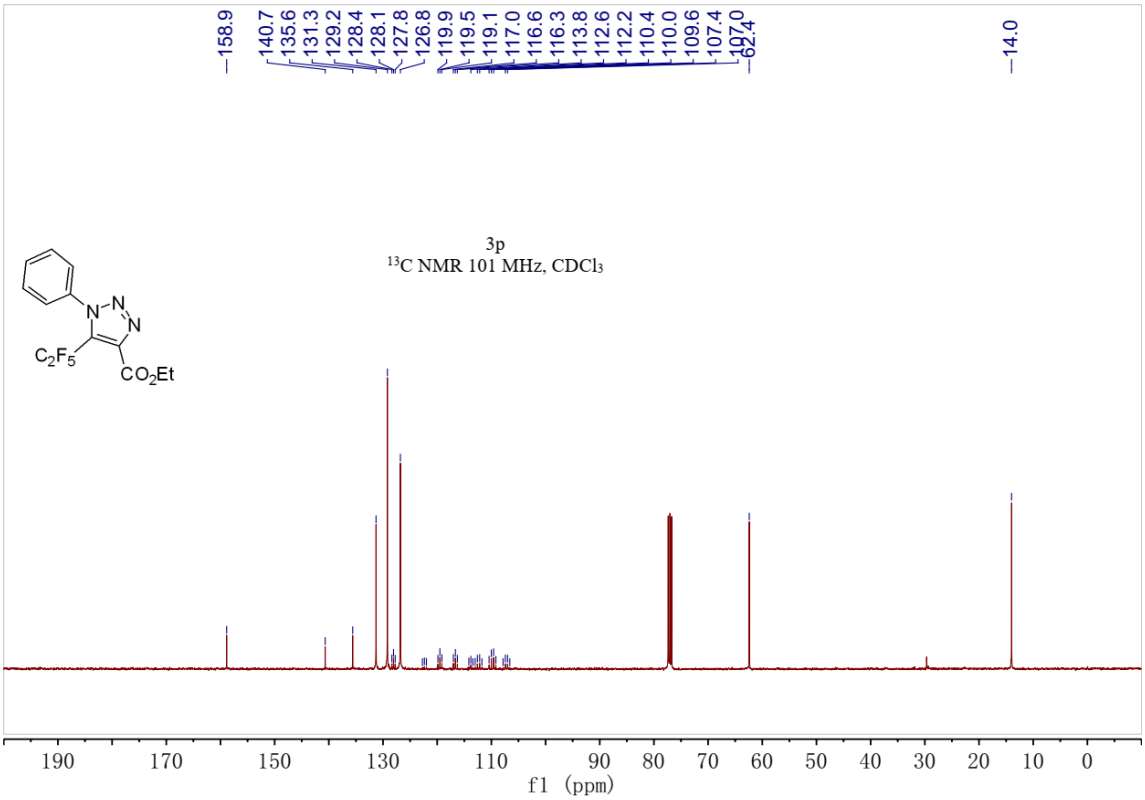
C2F5
CO2Et
0.94
2.00
1.96
1.96
3.00
f1 (ppm)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131.3
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128.1
127.8
126.8
119.9
119.5
119.1
117.0
116.6
116.3
113.8
112.6
112.2
110.4
110.0
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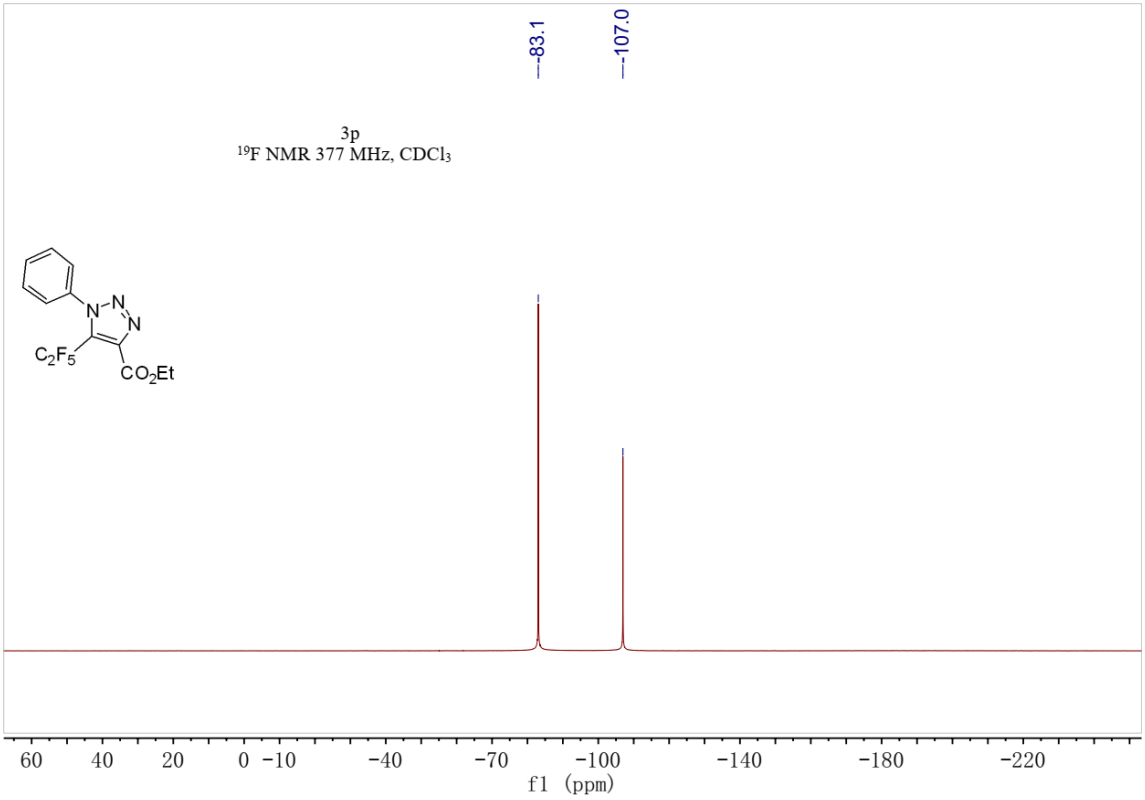
107.4
107.0
62.4
14.0
3p
13C NMR 101 MHz, CDCl3
C2F5
CO2Et
f1 (ppm)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-107.0
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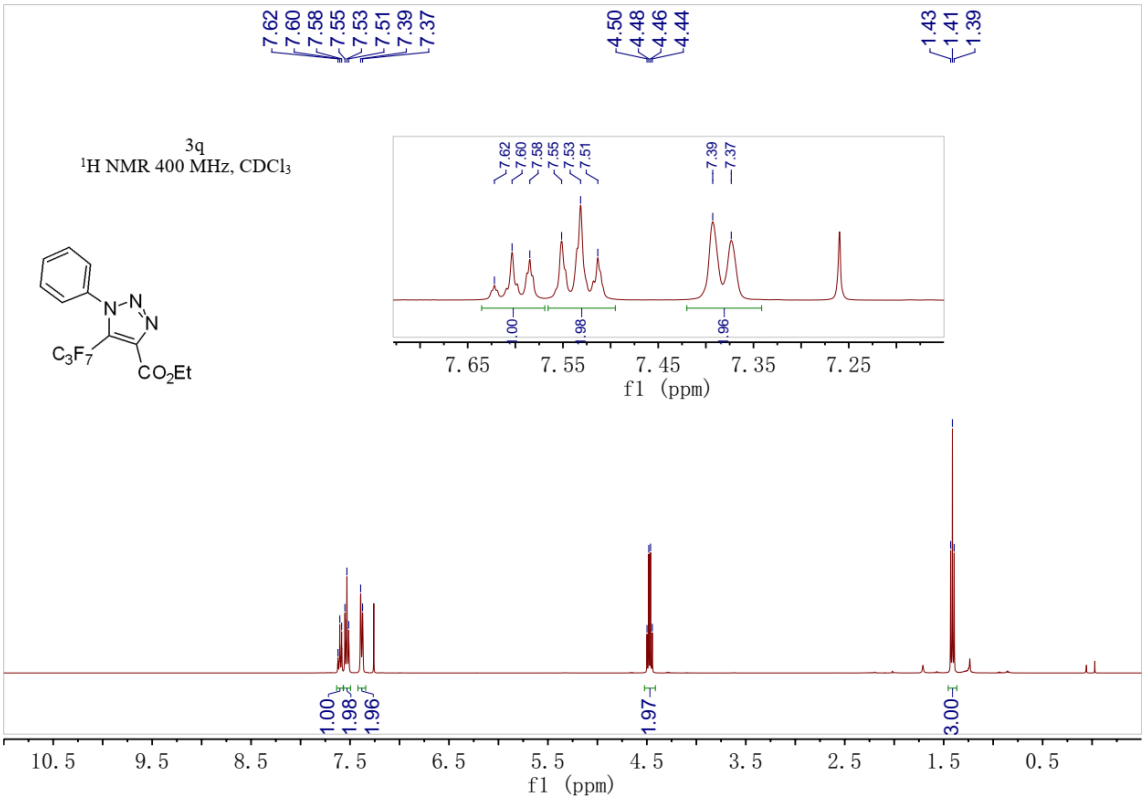
C2F5
CO2Et
60 40 20 0 -10 -40 -70 -100 -140 -180 -220
f1 (ppm)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7.39
7.37
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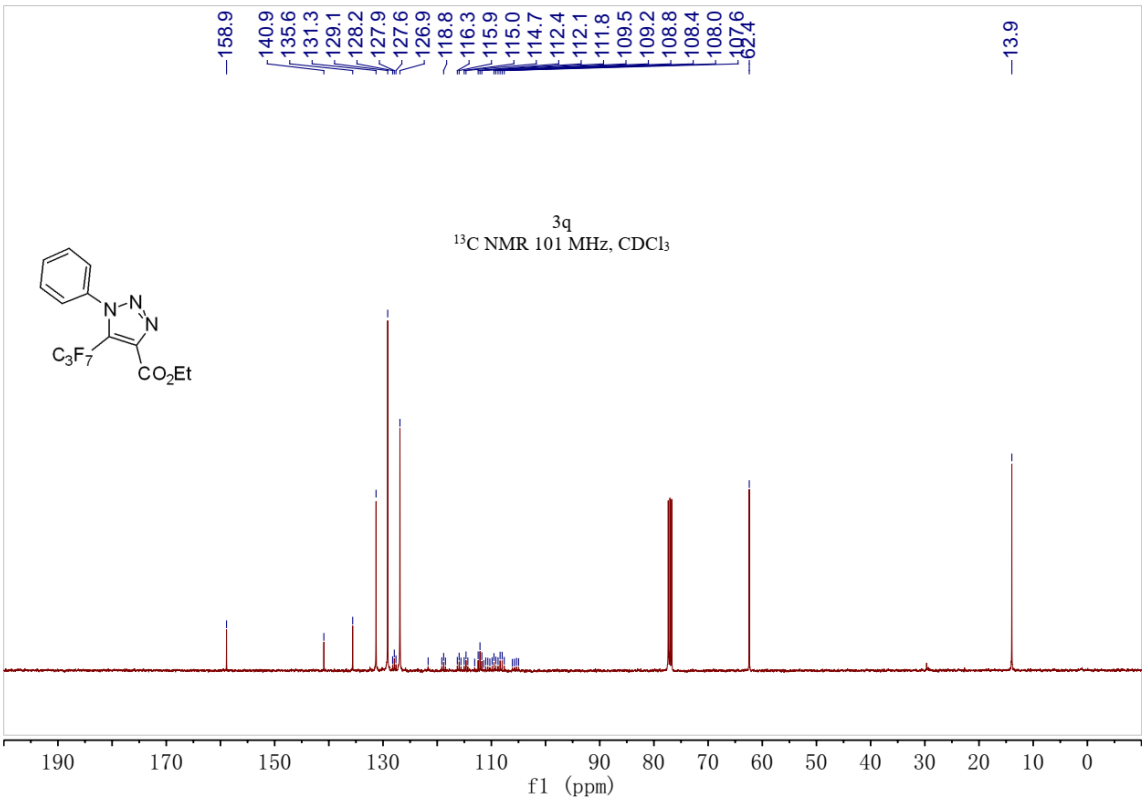
4.48
4.46
4.44
1.43
1.41
1.39
3q
1H NMR 400 MHz, CDCl3
C3F7
CO2Et
1.00
1.98
1.96
1.97
3.00
10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5
f1 (ppm)
7.65 7.55 7.45 7.35 7.25
f1 (ppm)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115.9
115.0
114.7
112.4
112.1
111.8
109.5
109.2
108.8
108.4
108.0
107.6
62.4
13.9
3q
13C NMR 101 MHz, CDCl3
C3F7
CO2Et
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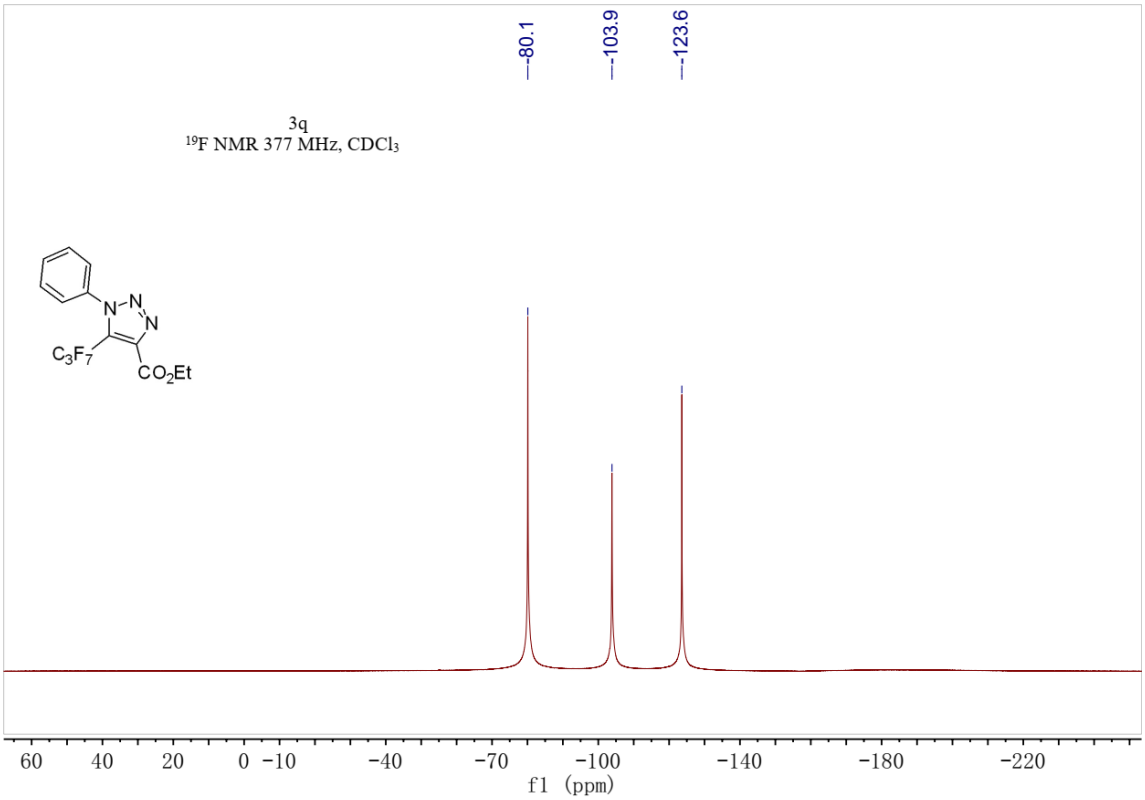
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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C3F7
CO2Et
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40
20
0
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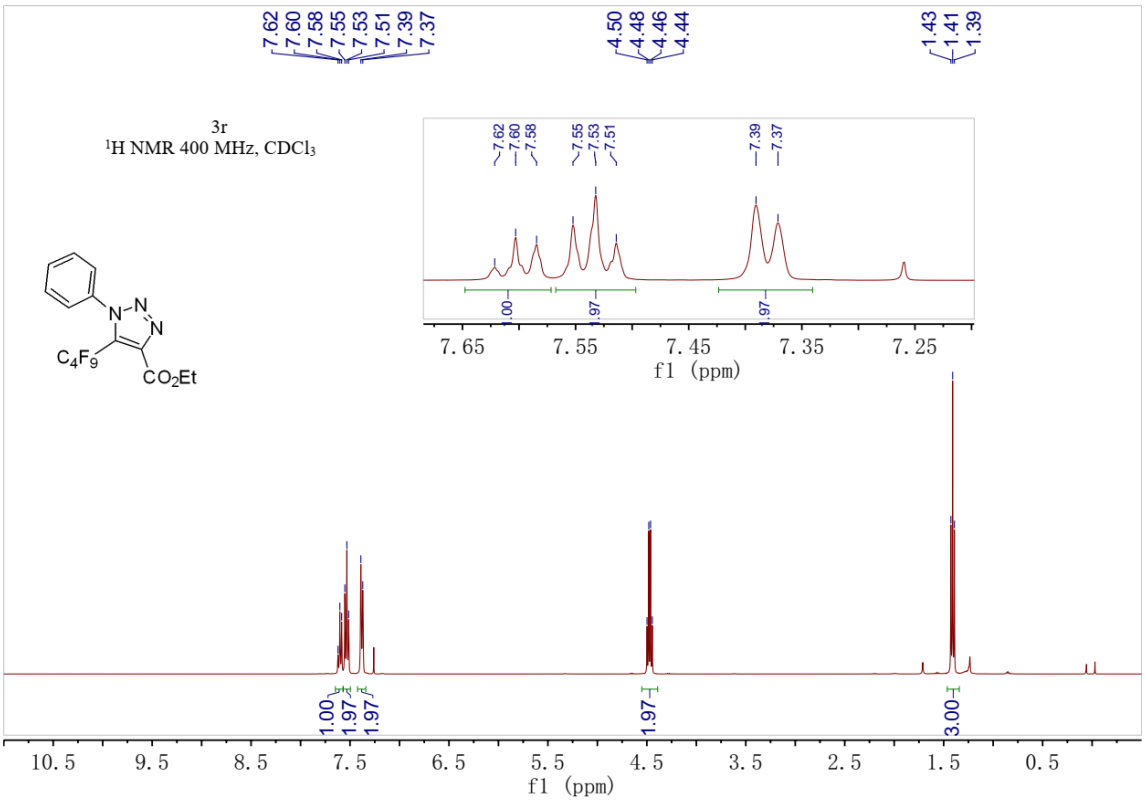
-40
-70
-100
-140
-180
-220
f1 (ppm)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7.51
7.39
7.37
4.50
4.48
4.46
4.44
1.43
1.41
1.39
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C4F9
CO2Et
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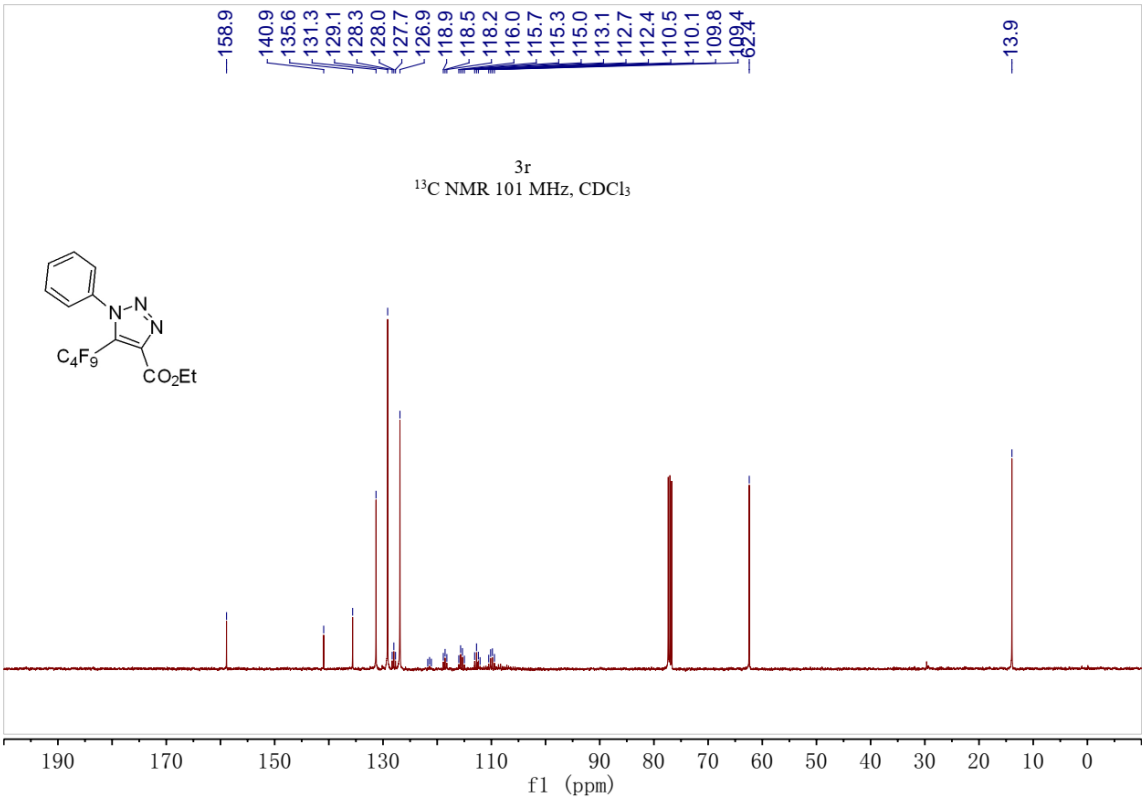
1.97
1.97
3.00
f1 (ppm)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128.3
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118.9
118.5
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116.0
115.7
115.3
115.0
113.1
112.7
112.4
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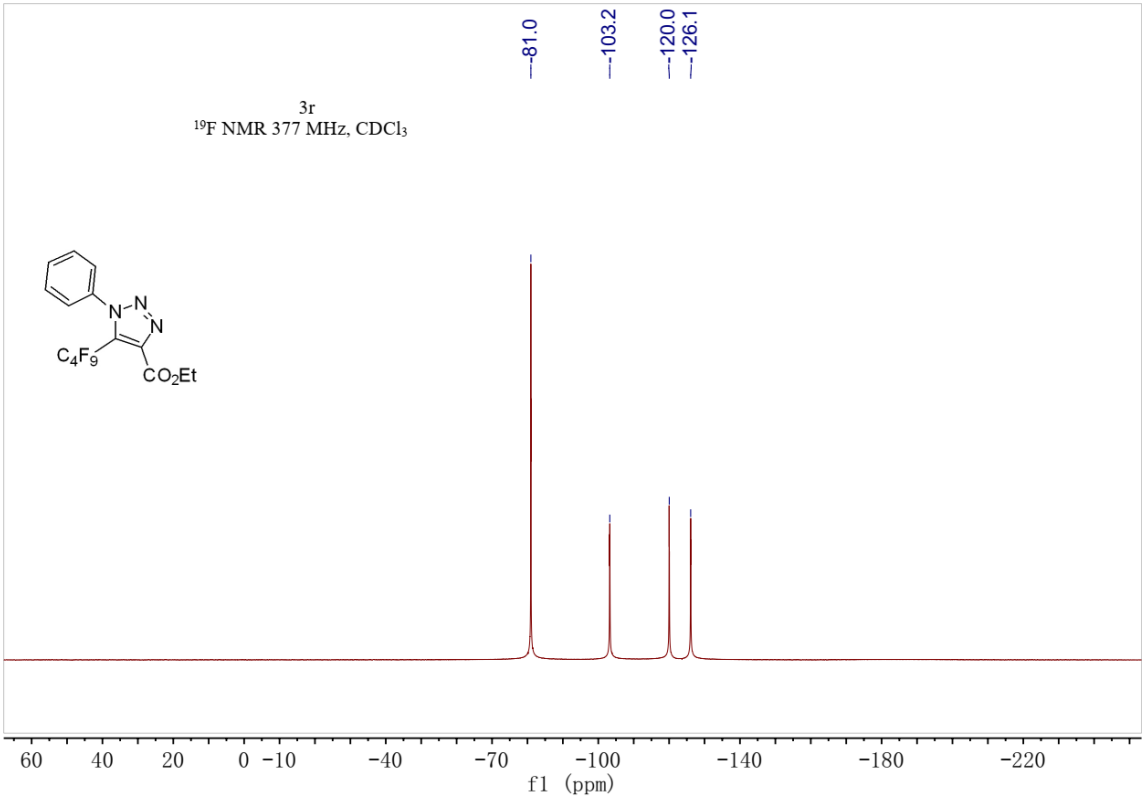
109.8
62.4
13.9
3r
13C NMR 101 MHz, CDCl3
C4F9
CO2Et
f1 (ppm)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-120.0
-126.1
3r
19F NMR 377 MHz, CDCl3
C4F9
CO2Et
60
40
20
0
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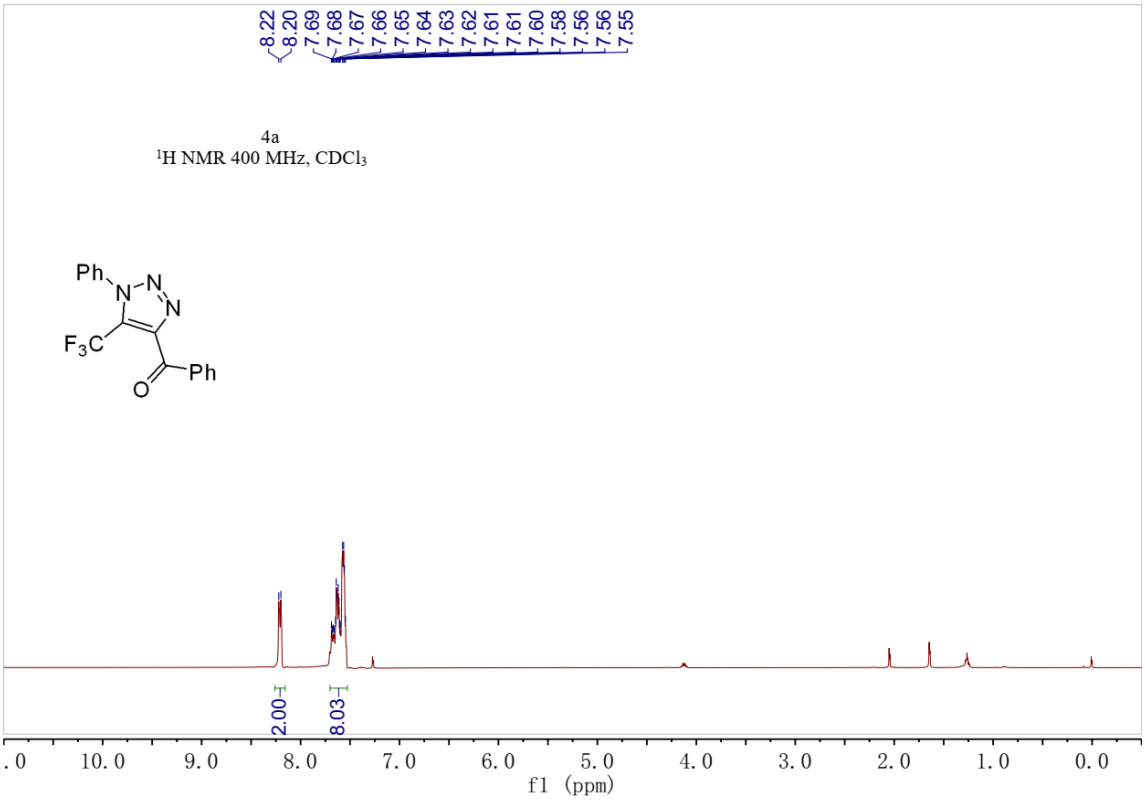
-40
-70
-100
-140
-180
-220
f1 (ppm)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7.60
7.58
7.56
7.56
7.55
4a
1H NMR 400 MHz, CDCl3
Ph
F3C
Ph
O
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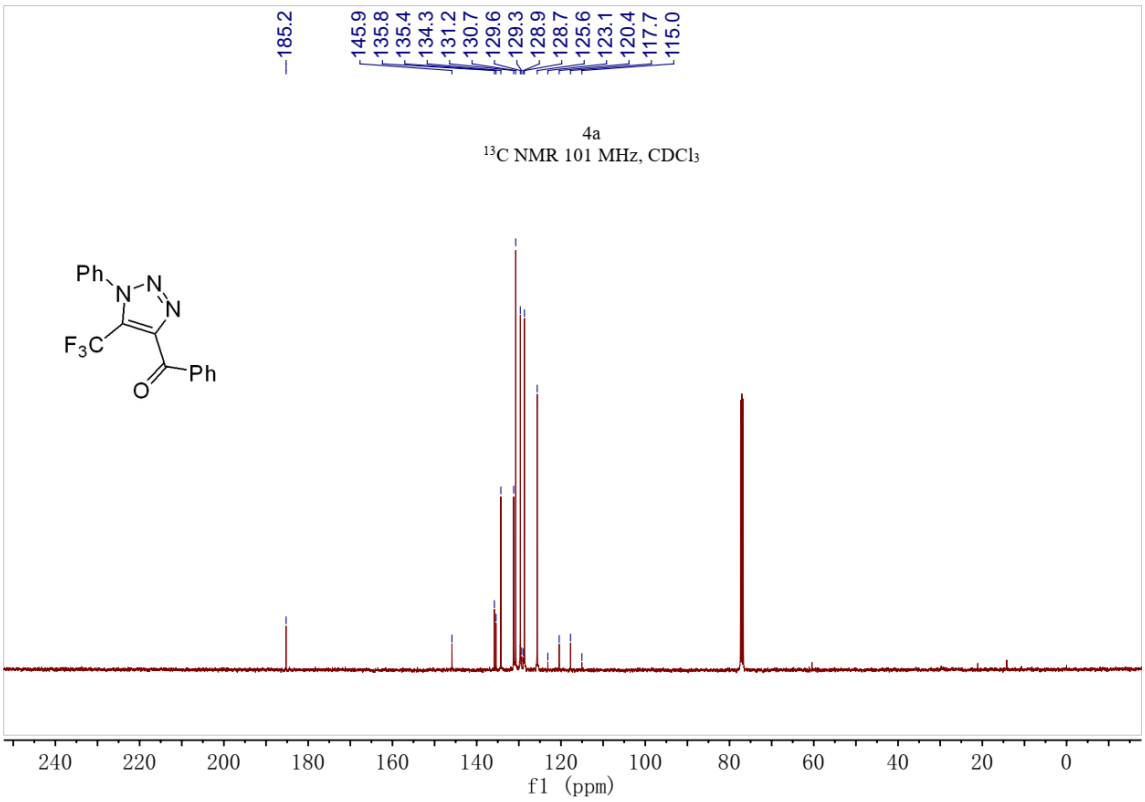
8.03
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)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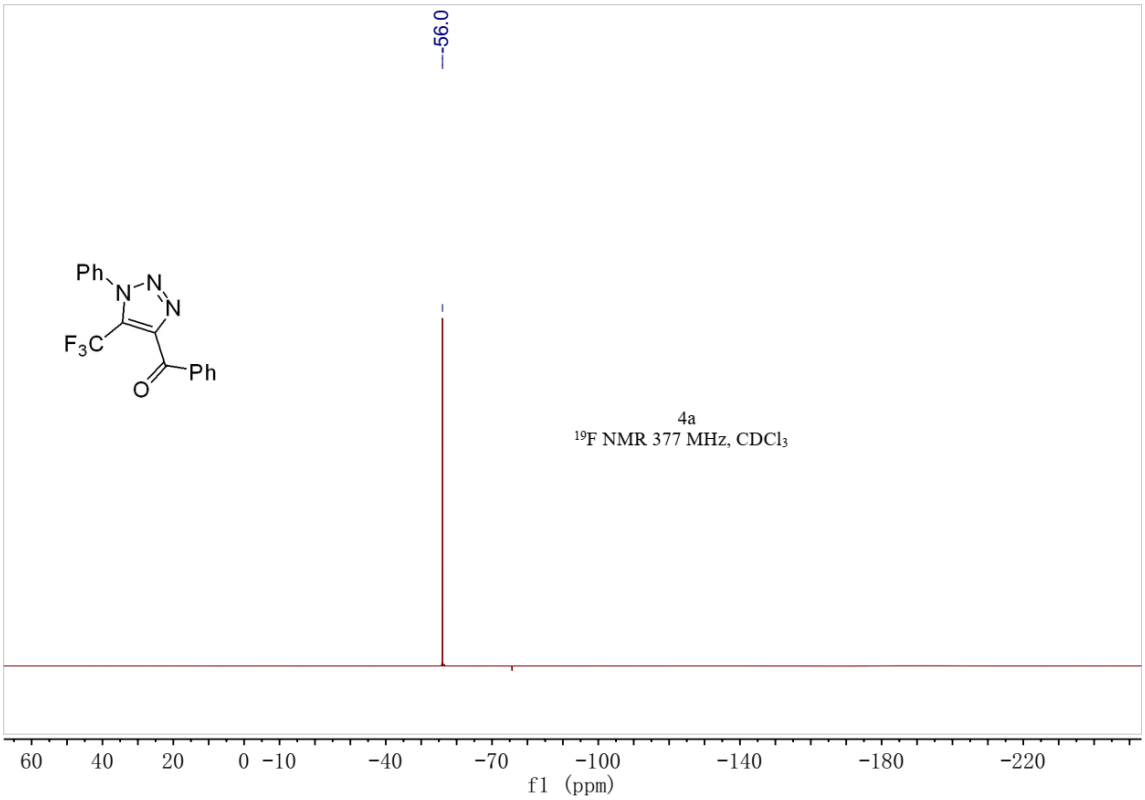
145.9
135.8
135.4
134.3
131.2
130.7
129.6
129.3
128.9
128.7
125.6
123.1
120.4
117.7
115.0
4a
13C NMR 101 MHz, CDCl3
Ph
N
N
N
F3C
O
Ph
240
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)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Ph
N
N
N
F3C
O
Ph
4a
19F NMR 377 MHz, CDCl3
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40
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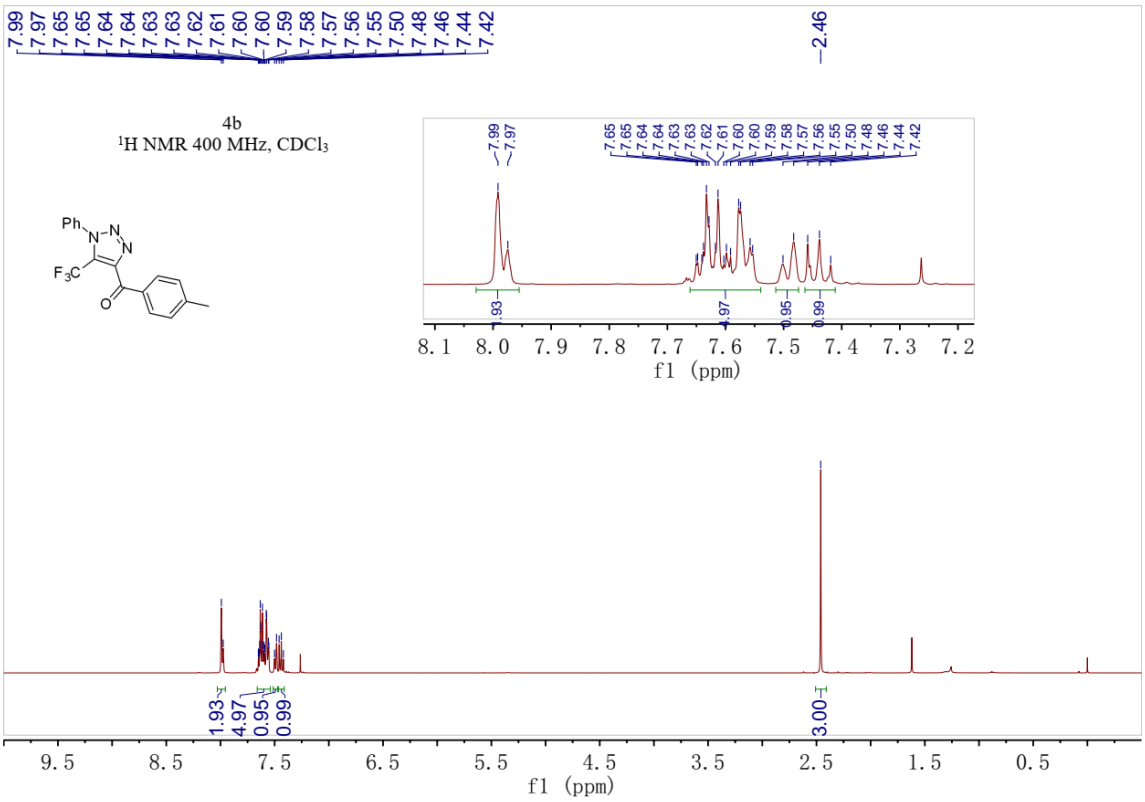
-40
-70
-100
-140
-180
-220
f1 (ppm)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7.65
7.65
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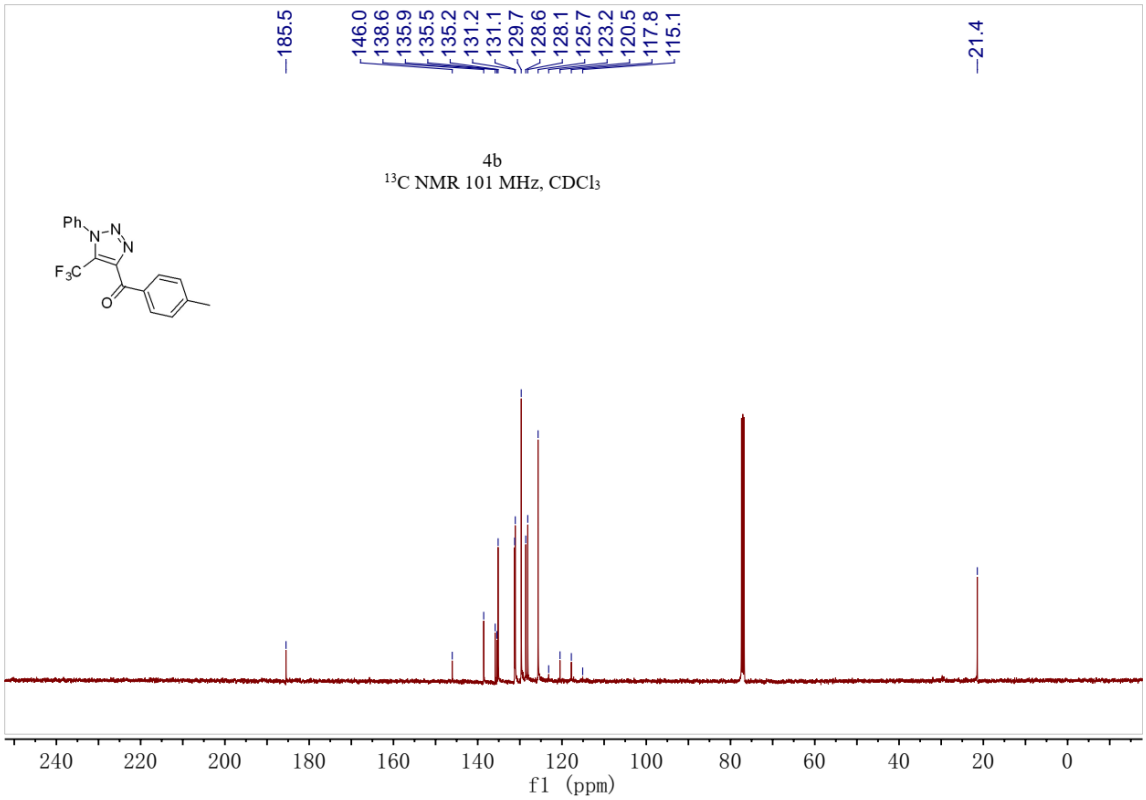
7.64
7.63
7.63
7.62
7.61
7.60
7.60
7.59
7.58
7.57
7.56
7.55
7.50
7.48
7.46
7.44
7.42
2.46
4b
1H NMR 400 MHz, CDCl3
Ph
N
N
N
F3C
O
1.93
4.97
0.95
0.99
3.00
f1 (ppm)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138.6
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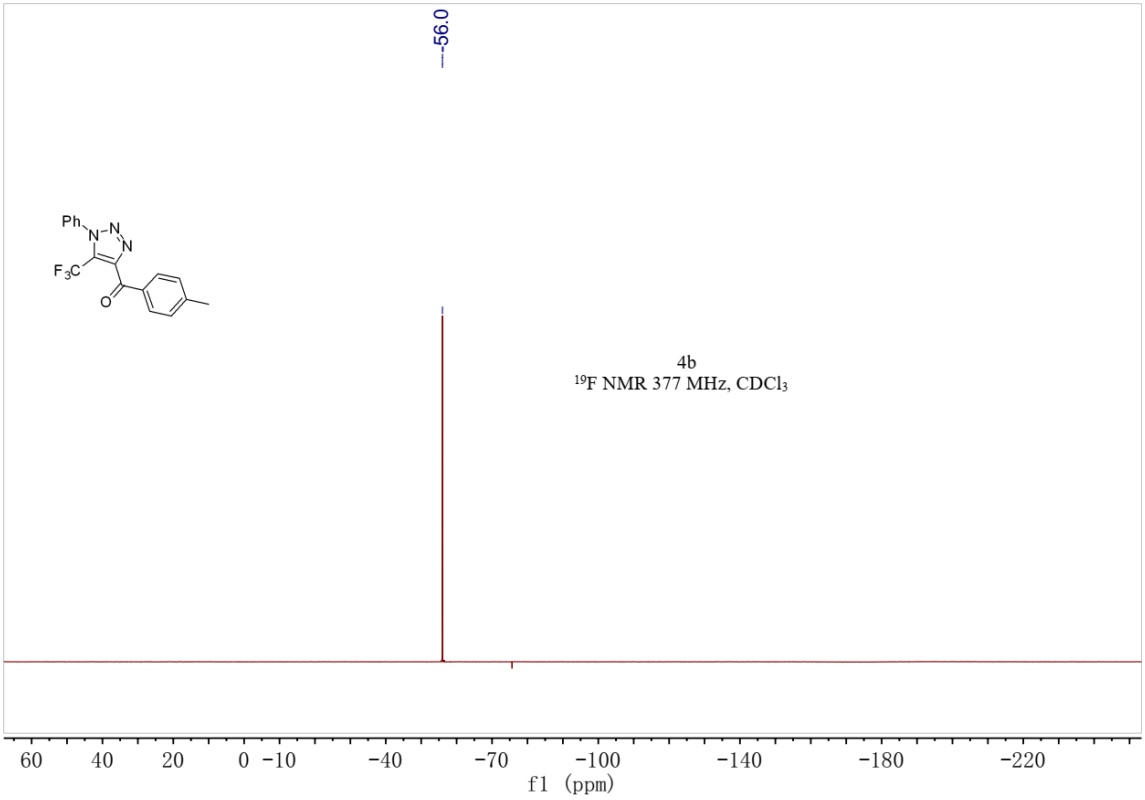
135.2
131.2
131.1
129.7
128.6
128.1
125.7
123.2
120.5
117.8
115.1
21.4
4b
13C NMR 101 MHz, CDCl3
Ph
N
N
N
F3C
O
f1 (ppm)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Ph
N
N
N
F3C
O
4b
19F NMR 377 MHz, CDCl3
60
40
20
0
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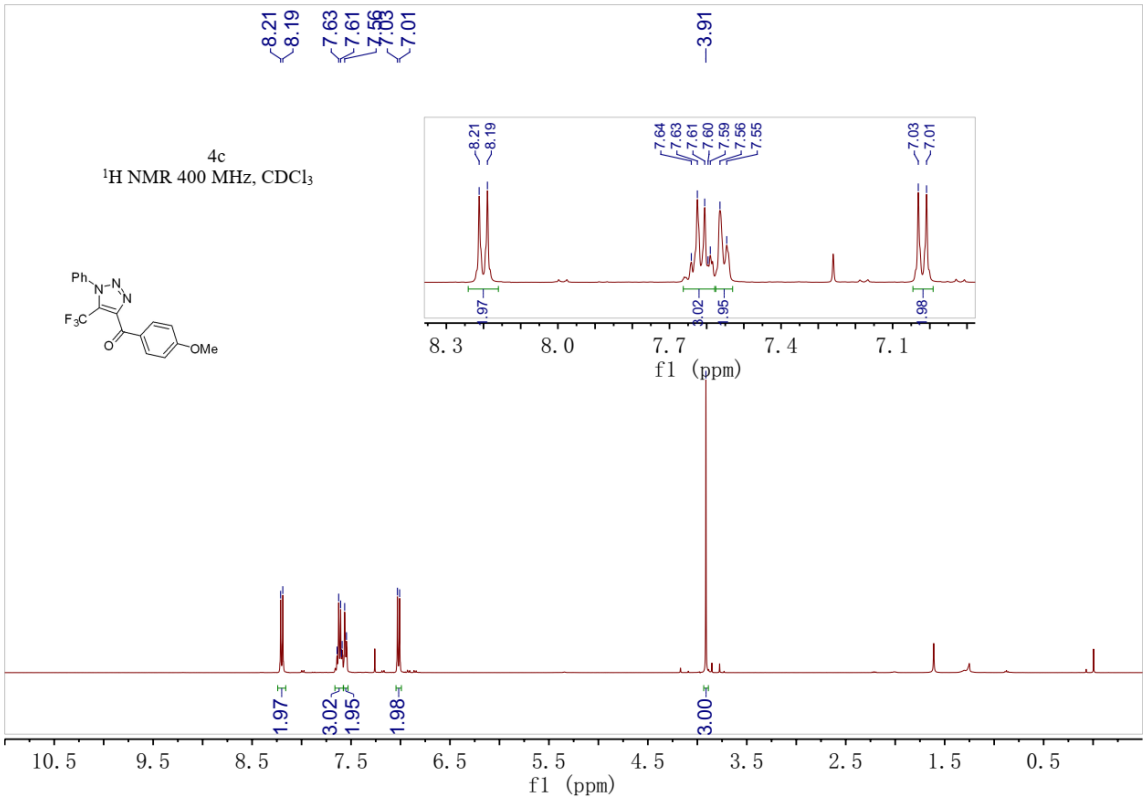
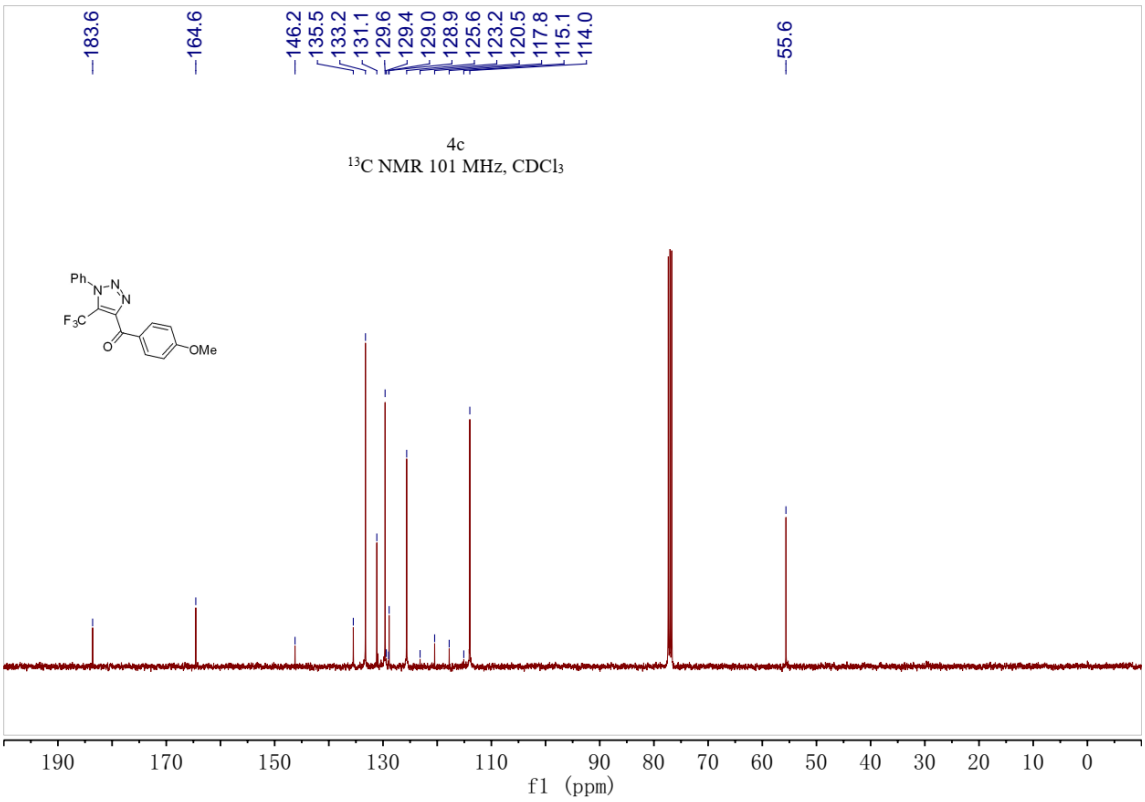
-40
-70
-100
-140
-180
-220
f1 (ppm)


8.21
8.19
7.63
7.61
7.56
7.03
7.01
3.91
4c
1H NMR 400 MHz, CDCl3
Ph
N
N
N
F3C
O
OMe
1.97
3.02
1.95
1.98
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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164.6
146.2
135.5
133.2
131.1
129.6
129.4
129.0
128.9
125.6
123.2
120.5
117.8
115.1
114.0
55.6
4c
13C NMR 101 MHz, CDCl3
Ph
F3C
OMe
190
170
150
130
110
90
80
70
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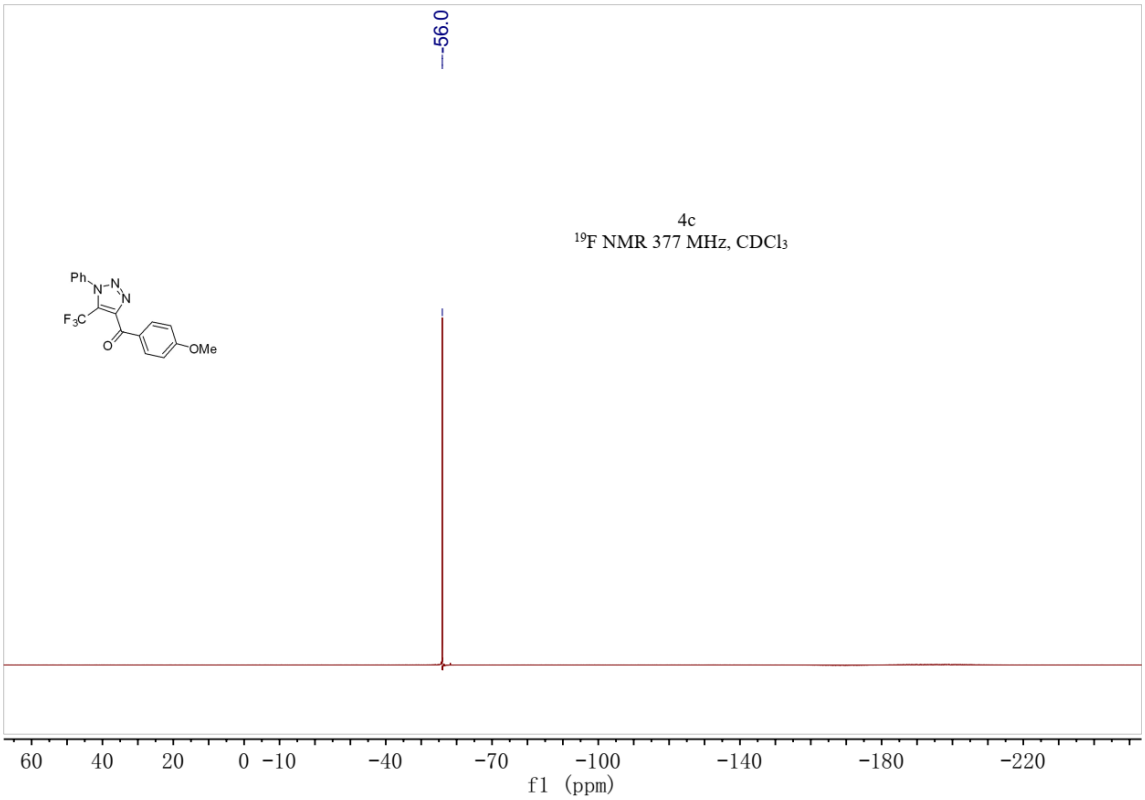
50
40
30
20
10
0
f1 (ppm)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4c
19F NMR 377 MHz, CDCl3
Ph
F3C
OMe
60
40
20
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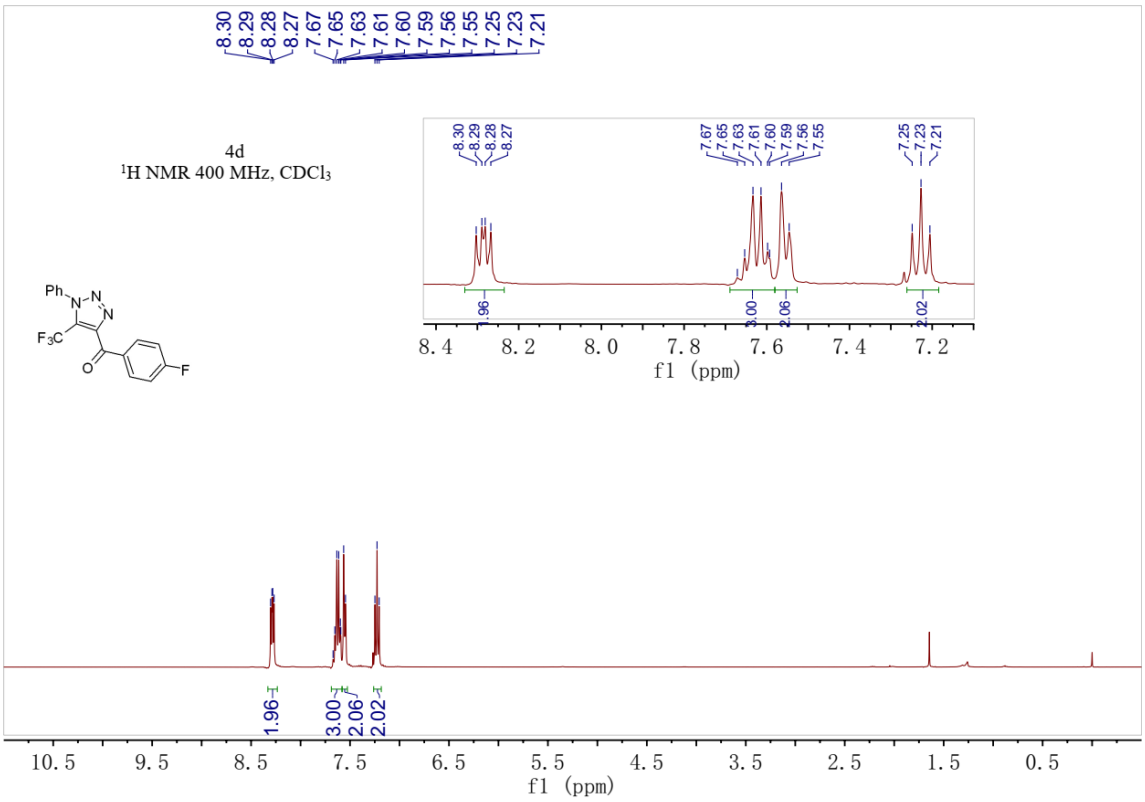
-70
-100
-140
-180
-220
f1 (ppm)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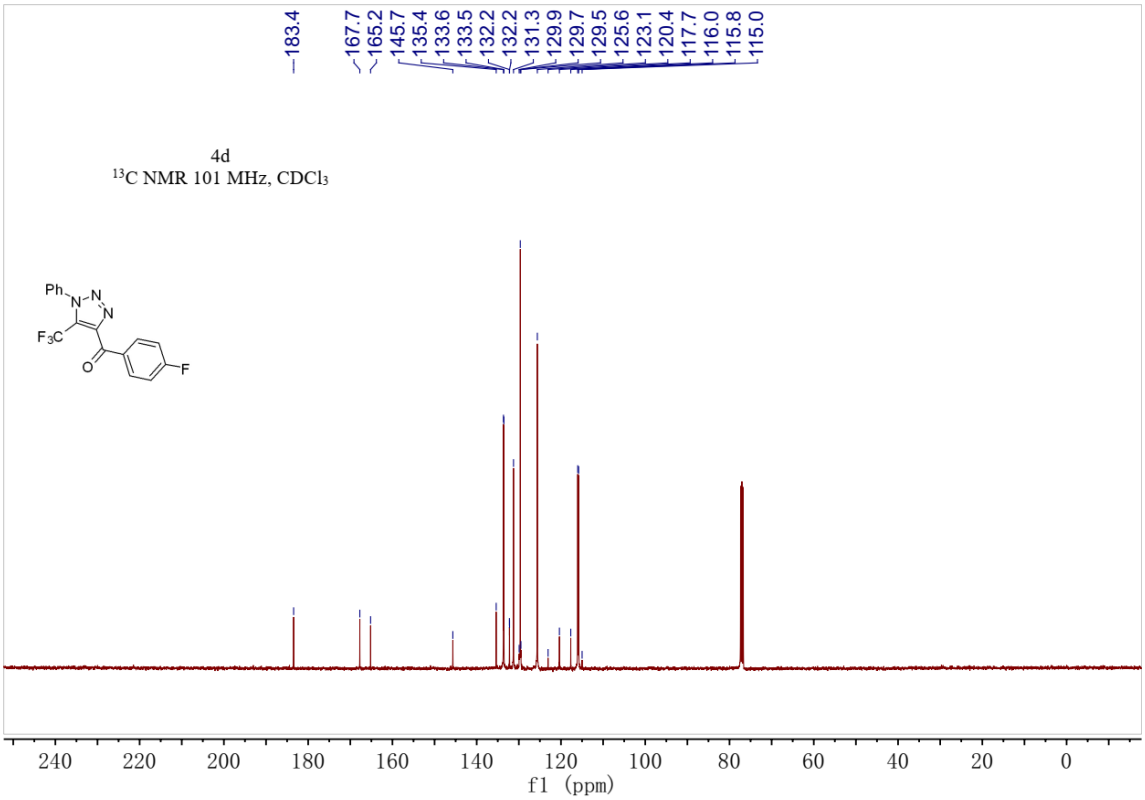
8.29
8.28
8.27
7.67
7.65
7.63
7.61
7.60
7.59
7.56
7.55
7.25
7.23
7.21
4d
1H NMR 400 MHz, CDCl3
Ph
N
N
N
F3C
O
F
1.96
3.00
2.06
2.02
8.4
8.2
8.0
7.8
7.6
7.4
7.2
f1 (ppm)
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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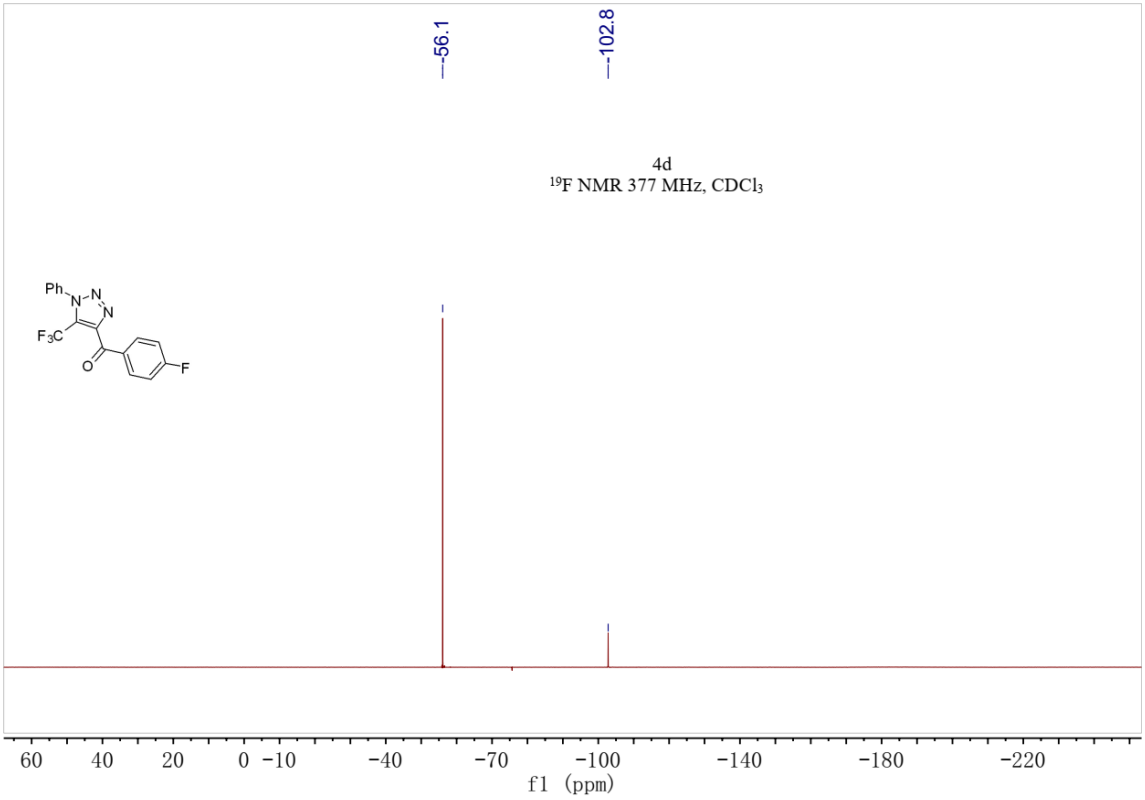
167.7
165.2
145.7
135.4
133.6
133.5
132.2
132.2
131.3
129.9
129.7
129.5
125.6
123.1
120.4
117.7
116.0
115.8
115.0
4d
13C NMR 101 MHz, CDCl3
Ph
N
N
N
F3C
O
F
240
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)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-102.8
4d
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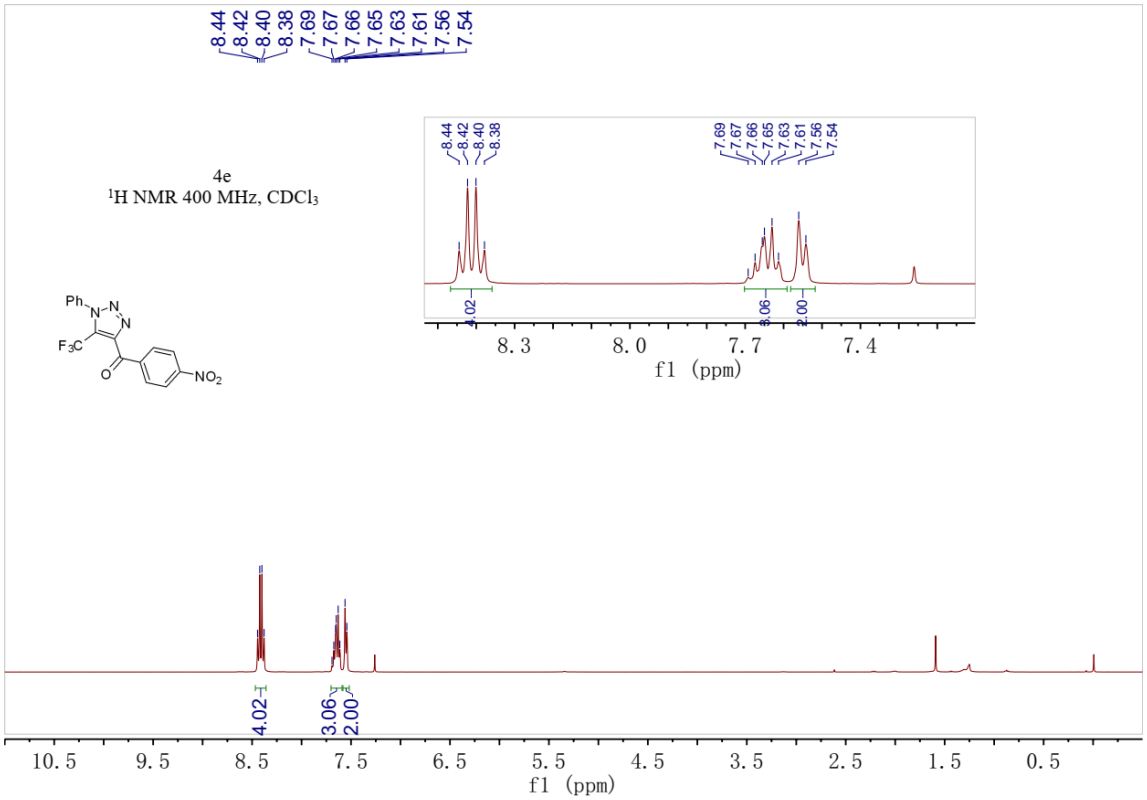
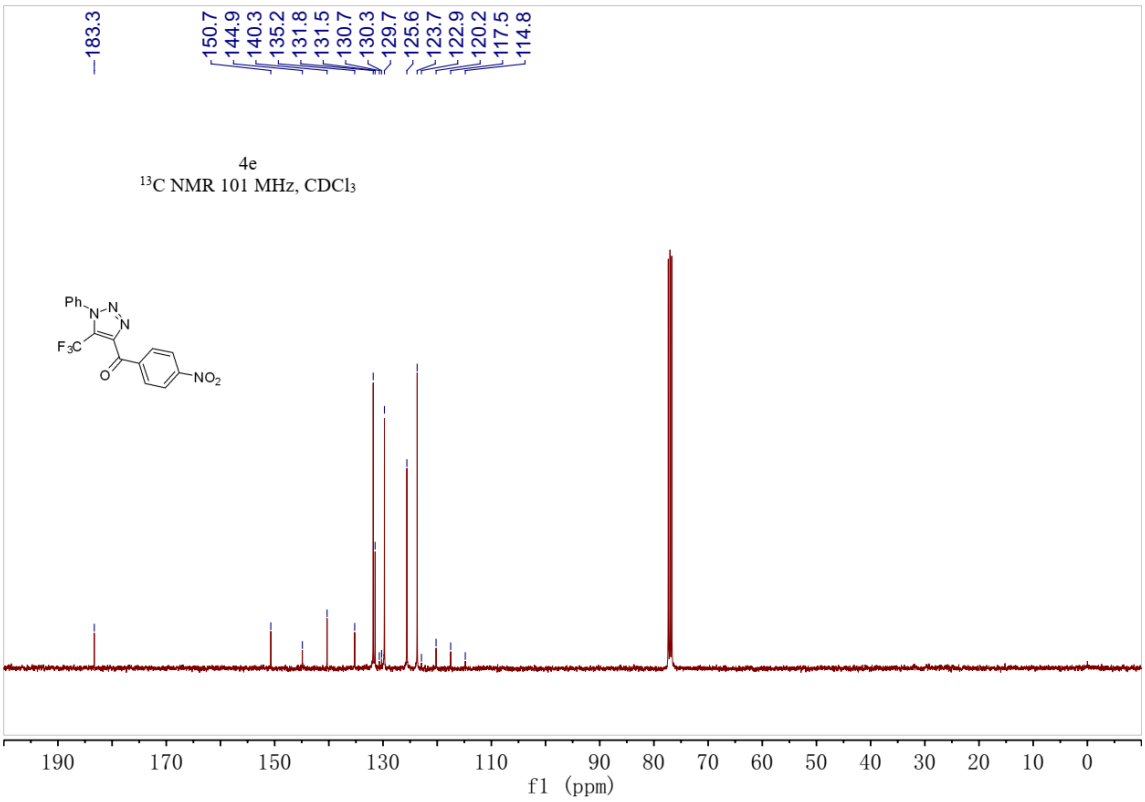
Ph
N
N
N
F3C
O
F
60
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)


8.44
8.42
8.40
8.38
7.69
7.67
7.66
7.65
7.63
7.61
7.56
7.54
4e
1H NMR 400 MHz, CDCl3
Ph
N
N
N
F3C
O
NO2
4.02
3.06
2.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)
8.3
8.0
7.7
7.4
f1 (ppm)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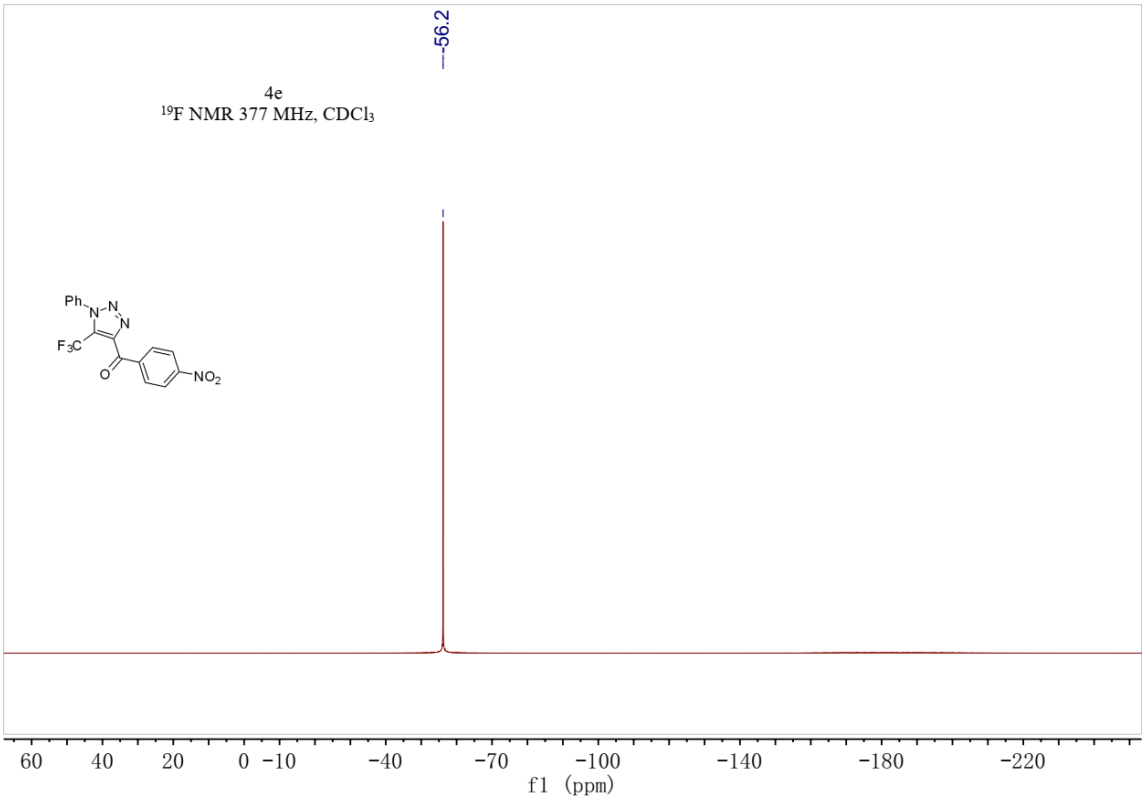
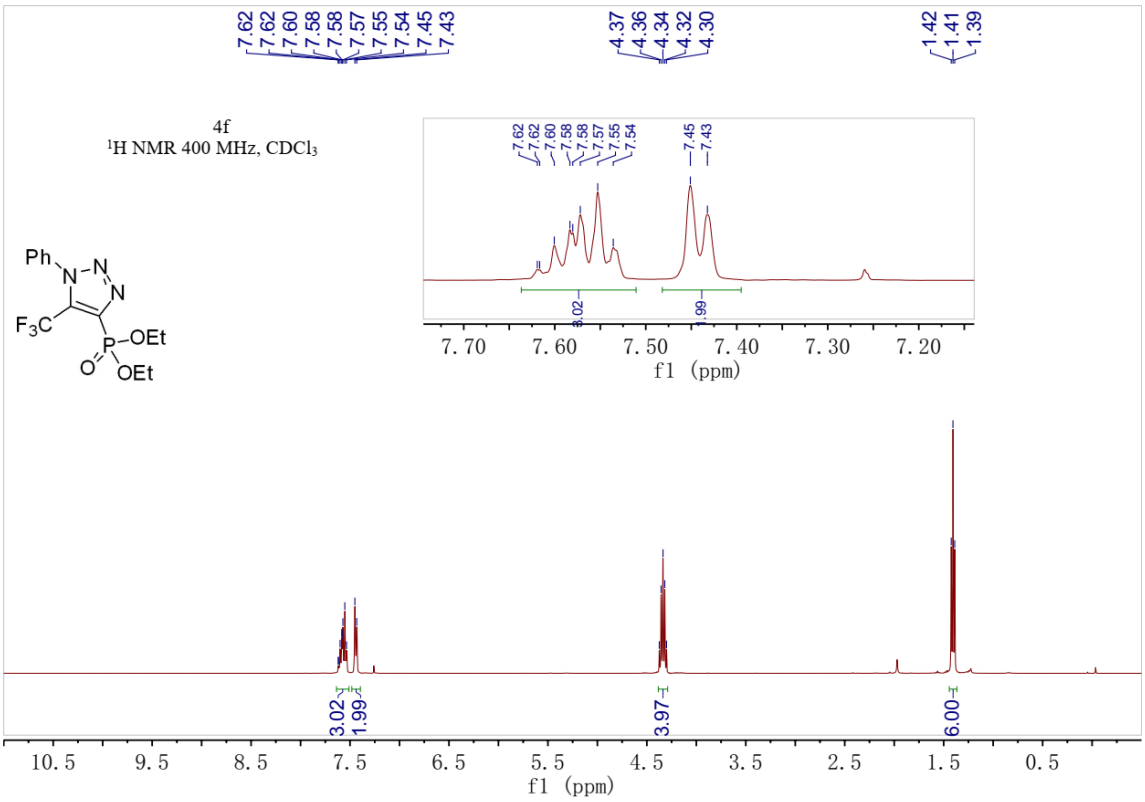
150.7
144.9
140.3
135.2
131.8
131.5
130.7
130.3
129.7
125.6
123.7
122.9
120.2
117.5
114.8
4e
13C NMR 101 MHz, CDCl3
Ph
N
N
N
F3C
O
NO2
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-56.2
4e
19F NMR 377 MHz, CDCl3
Ph
N
N
N
F3C
O
NO2
60
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)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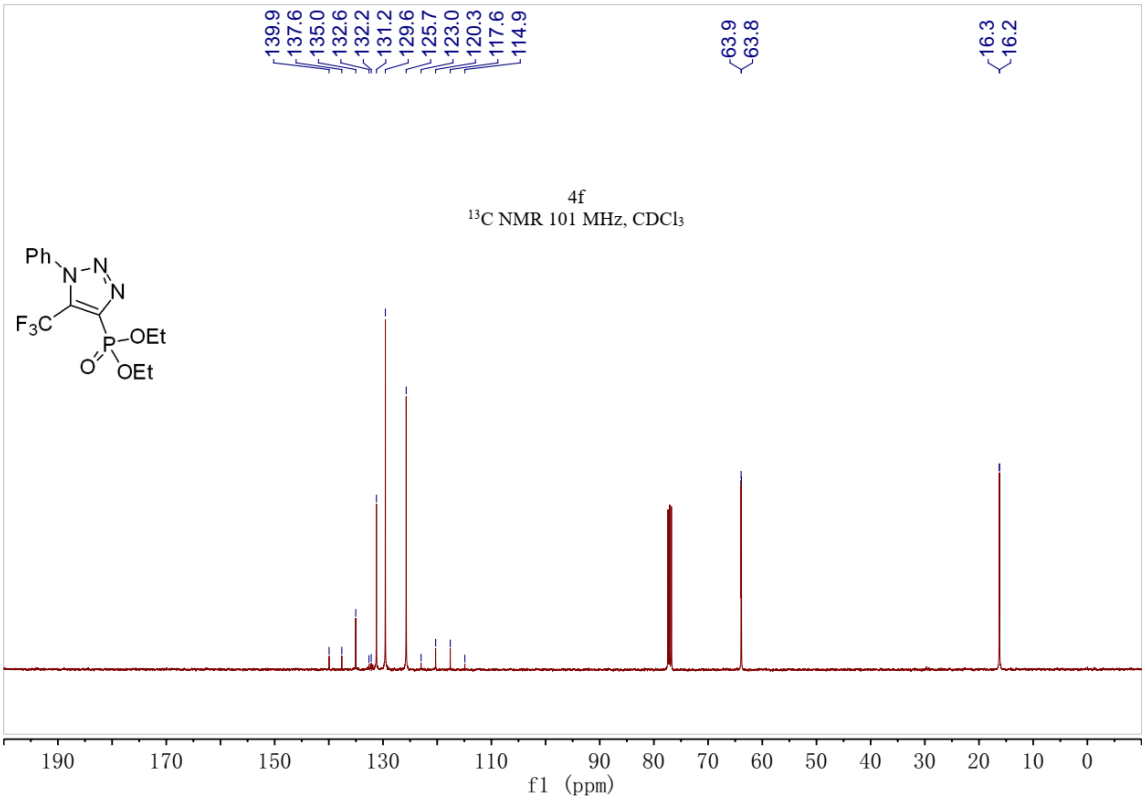
7.62
7.60
7.58
7.58
7.57
7.55
7.54
7.45
7.43
4.37
4.36
4.34
4.32
4.30
1.42
1.41
1.39
4f
1H NMR 400 MHz, CDCl3
Ph
N-N
N
F3C
P-OEt
O
OEt
8.02
1.99
7.70
7.60
7.50
7.40
7.30
7.20
f1 (ppm)
3.02
1.99
3.97
6.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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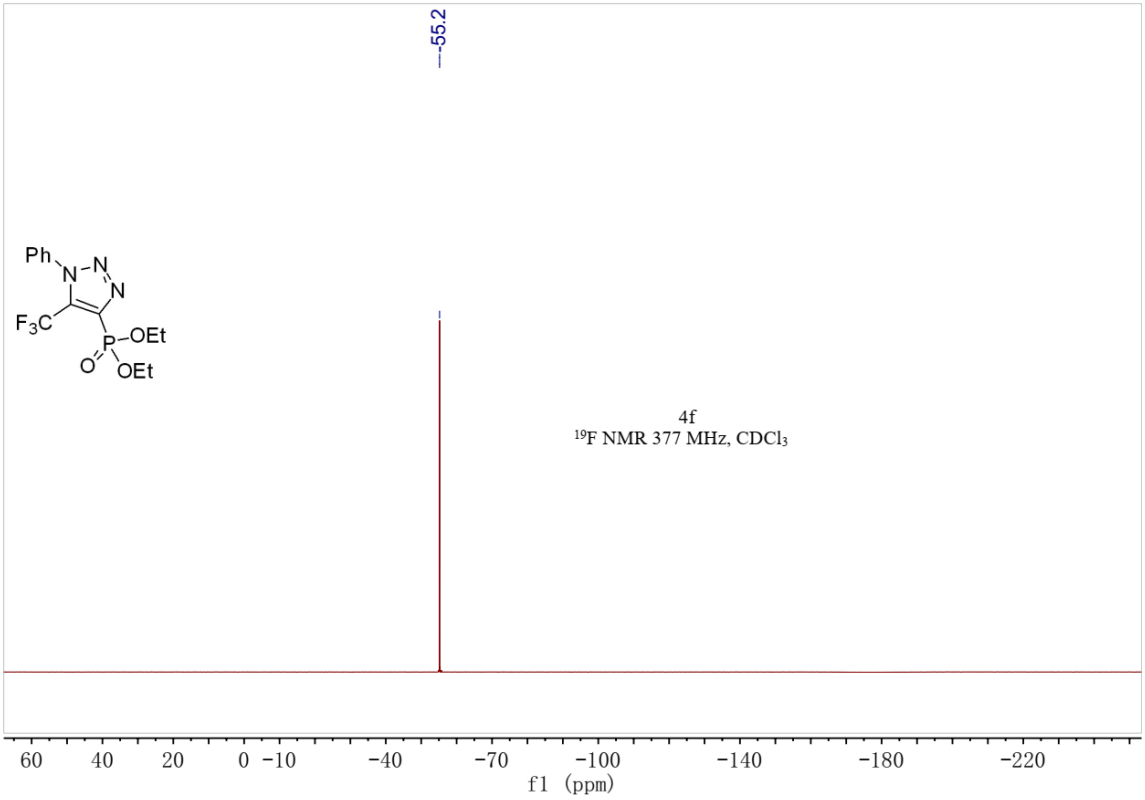
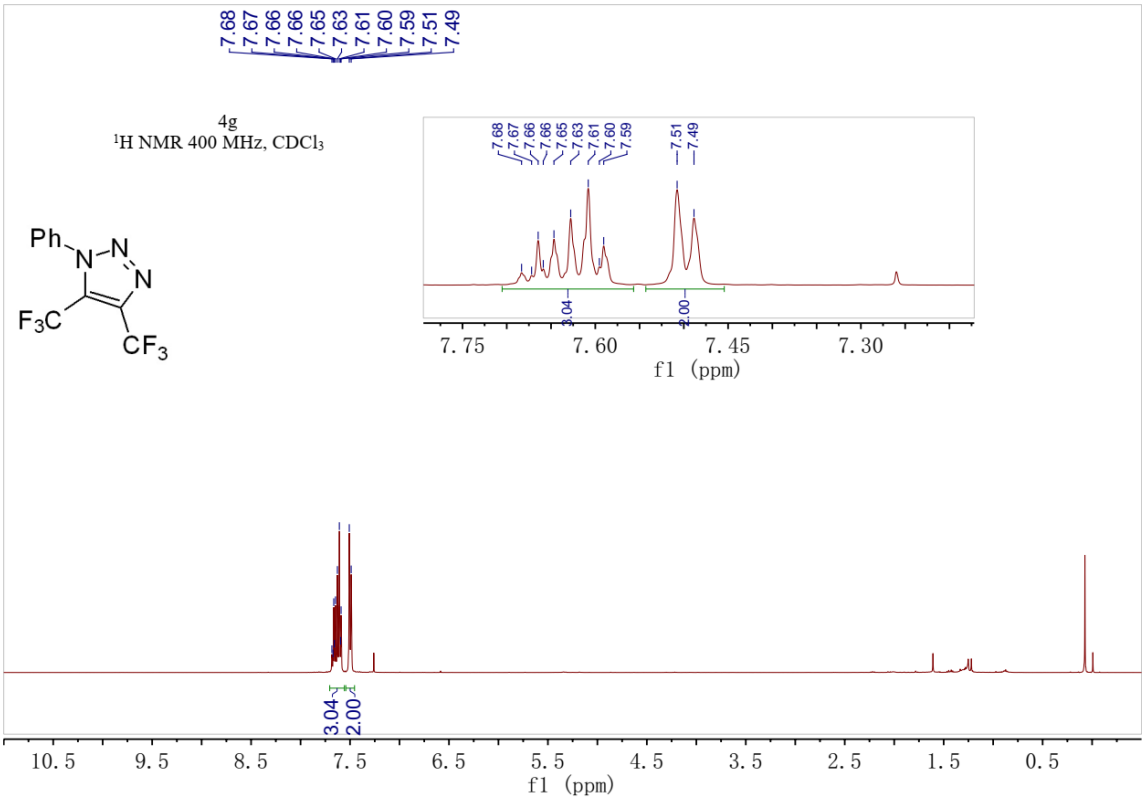
137.6
135.0
132.6
132.2
131.2
129.6
125.7
123.0
120.3
117.6
114.9
63.9
63.8
16.3
16.2
4f
13C NMR 101 MHz, CDCl3
Ph
N-N
N
F3C
P-OEt
O
OEt
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-55.2
Ph
N
N
N
F3C
P
OEt
O
OEt
4f
19F NMR 377 MHz, CDCl3
60
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)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7.67
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7.63
7.61
7.60
7.59
7.51
7.49
4g
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Ph
N
N
N
F3C
CF3
3.04
2.00
7.75
7.60
7.45
7.30
f1 (ppm)
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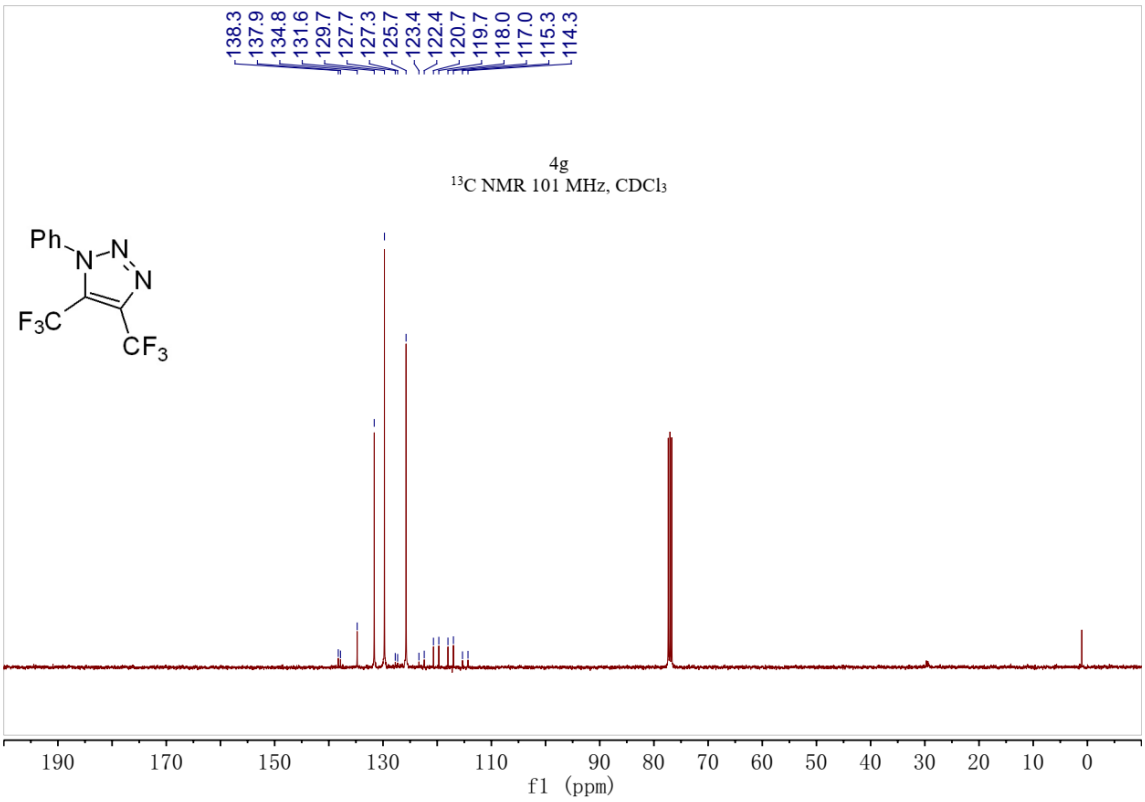
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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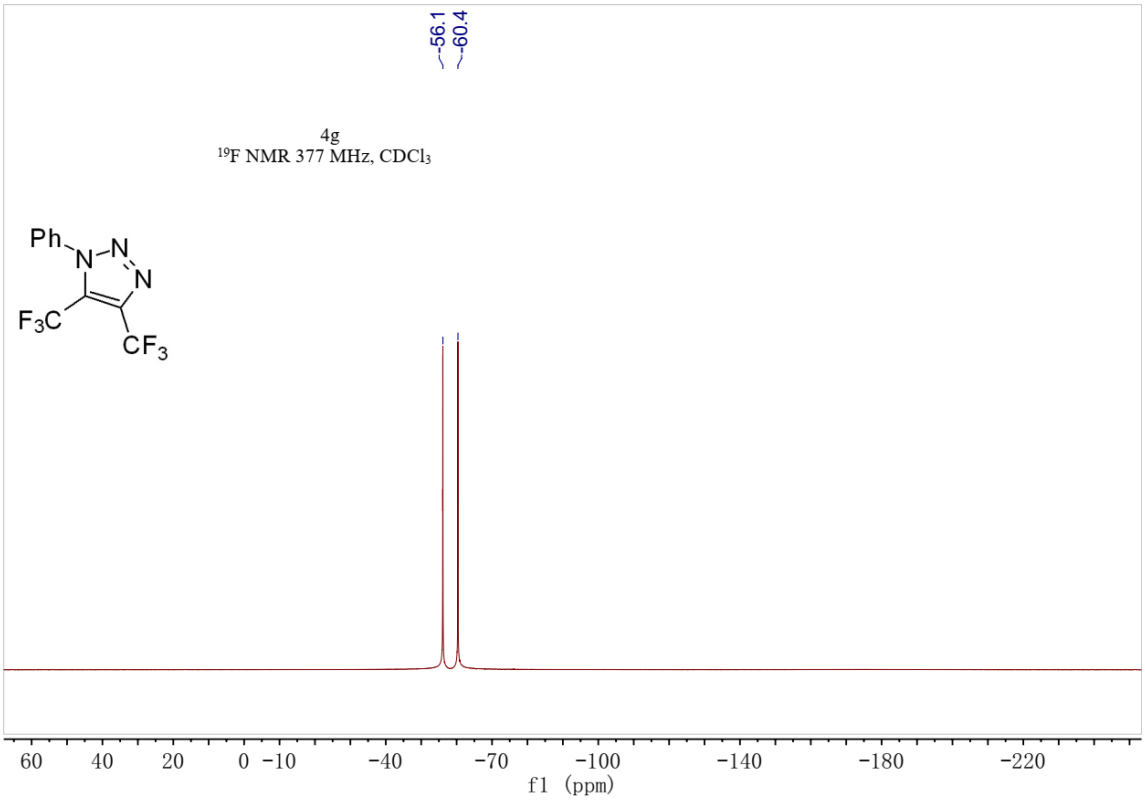
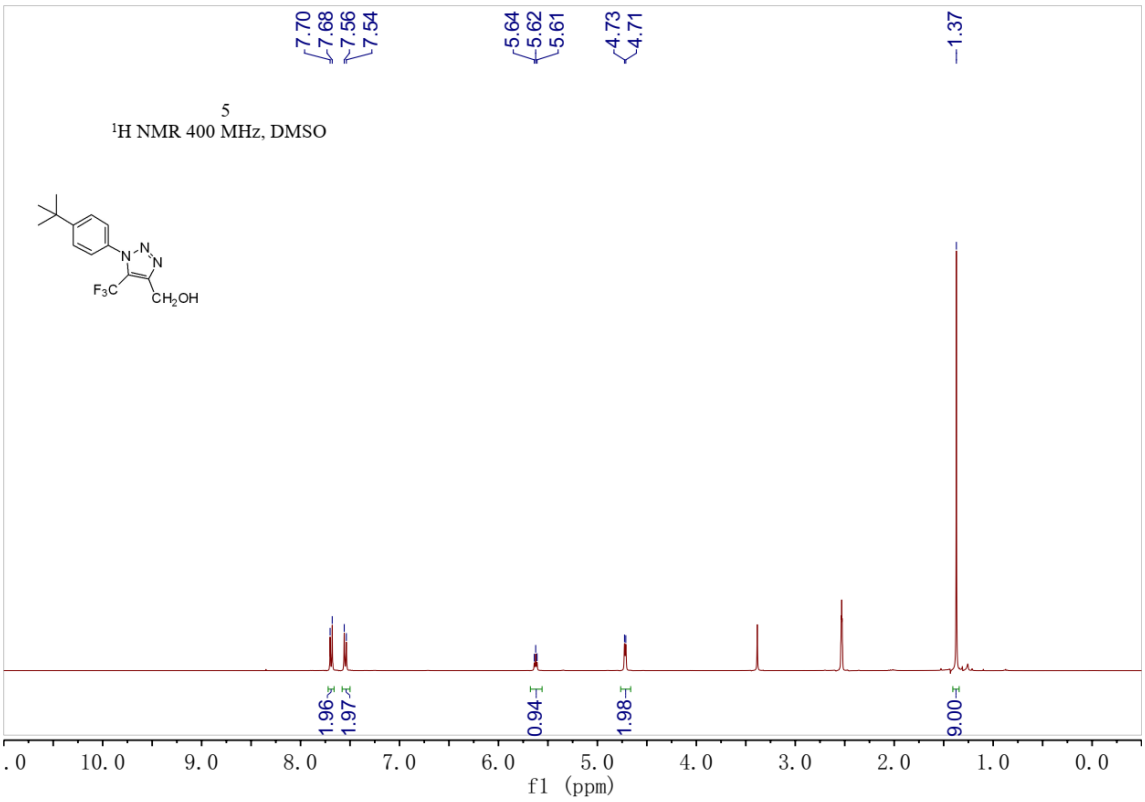
137.9
134.8
131.6
129.7
127.7
127.3
125.7
123.4
122.4
120.7
119.7
118.0
117.0
115.3
114.3
4g
13C NMR 101 MHz, CDCl3
Ph
N
N
N
F3C
CF3
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-56.1
-60.4
4g
19F NMR 377 MHz, CDCl3
Ph
N
N
N
F3C
CF3
60
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)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7.68
7.56
7.54
5.64
5.62
5.61
4.73
4.71
1.37
5
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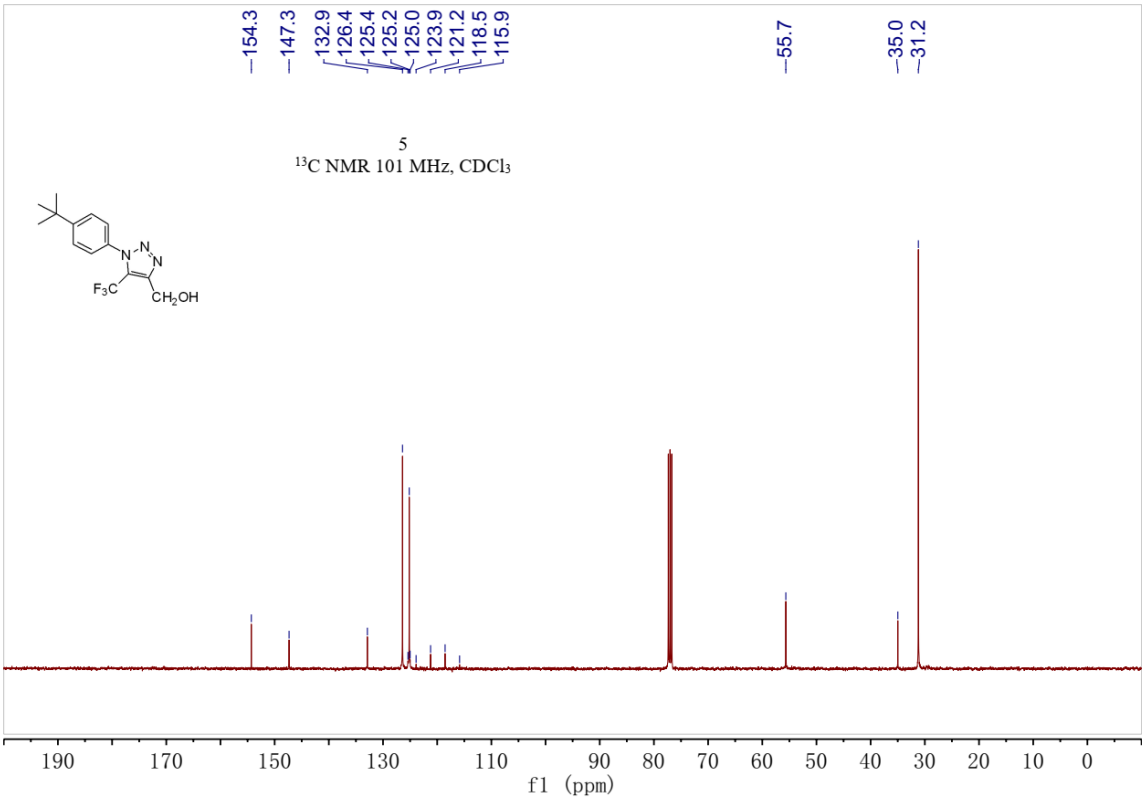
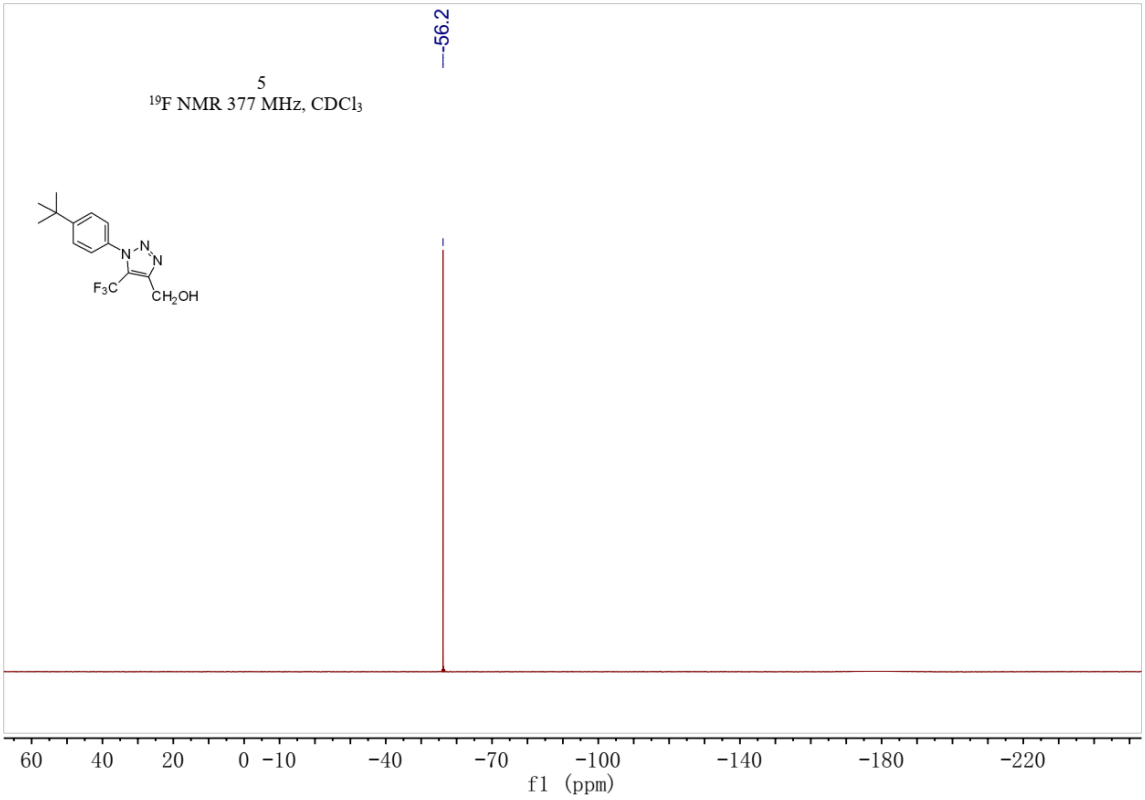
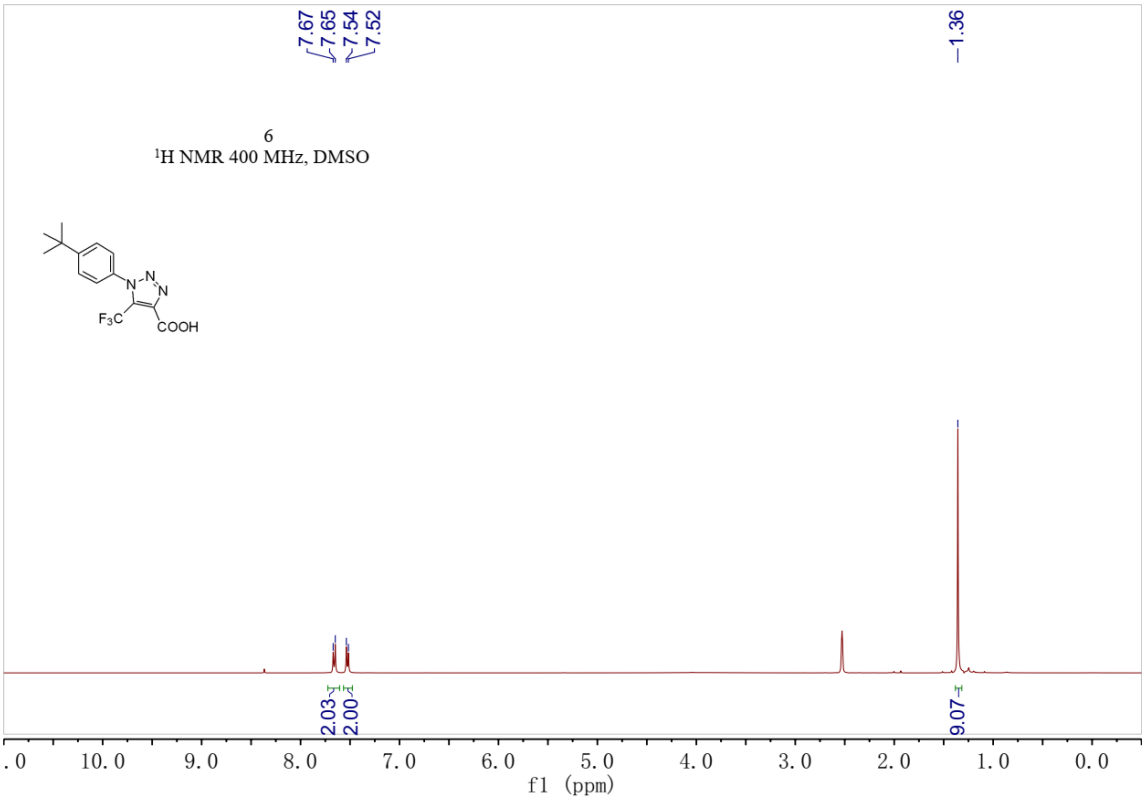
F3C
CH2OH
1.96
1.97
0.94
1.98
9.00
f1 (ppm)


154.3
147.3
132.9
126.4
125.4
125.2
125.0
123.9
121.2
118.5
115.9
55.7
35.0
31.2
5
13C NMR 101 MHz, CDCl3
F3C
CH2OH
f1 (ppm)


-56.2
5
19F NMR 377 MHz, CDCl3
F3C
CH2OH
60
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)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7.52
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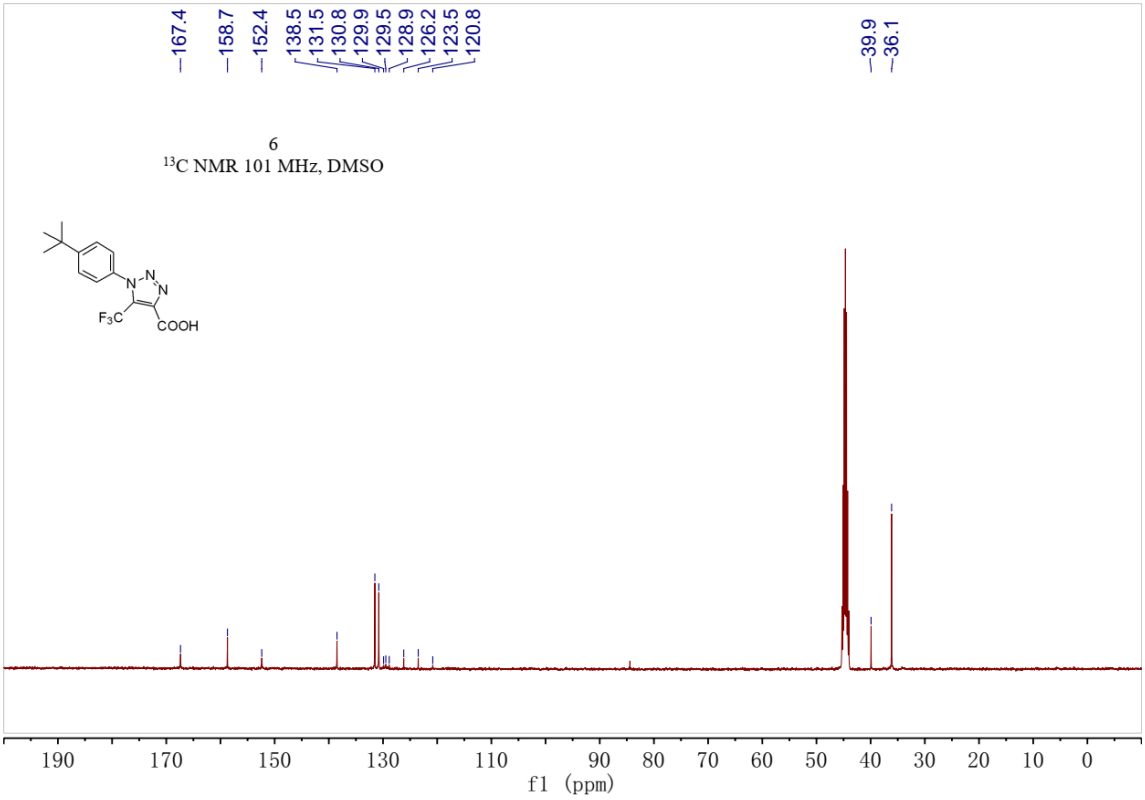
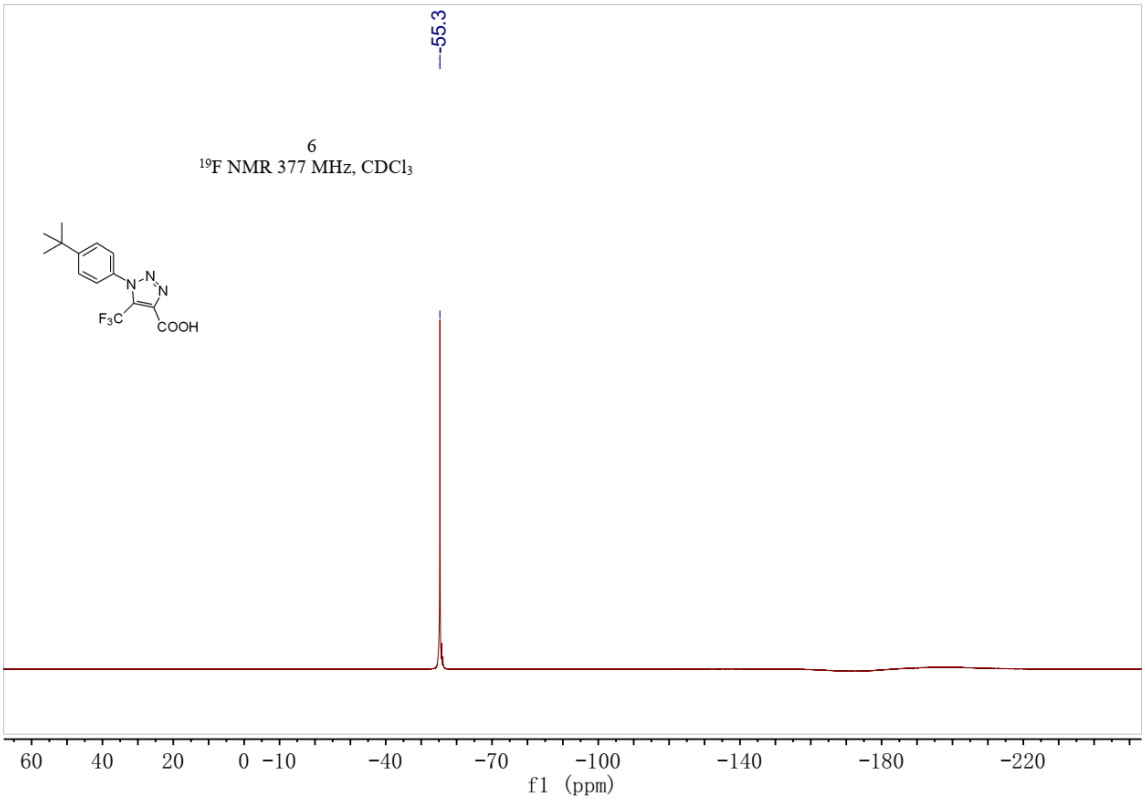
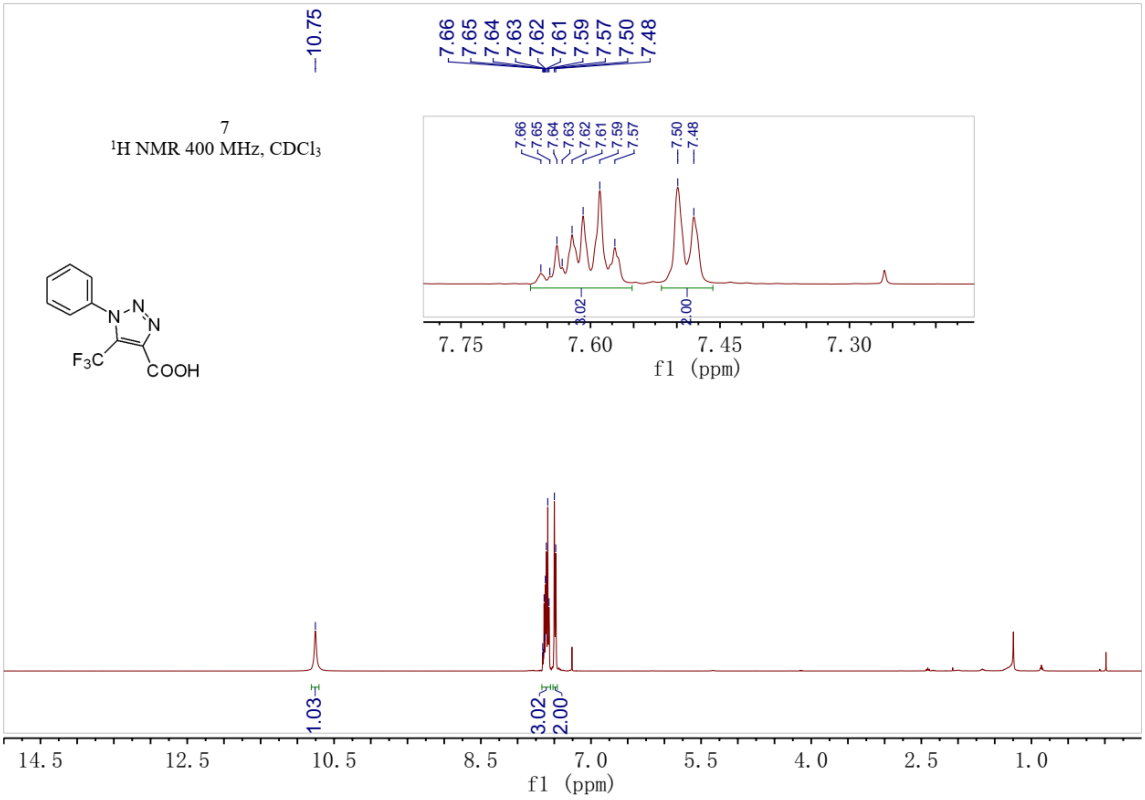
6
1H NMR 400 MHz, DMSO
F3C
COOH
2.03
2.00
9.07
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


167.4
158.7
152.4
138.5
131.5
130.8
129.9
129.5
128.9
126.2
123.5
120.8
39.9
36.1
6
13C NMR 101 MHz, DMSO
F3C
COOH
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-55.3
6
19F NMR 377 MHz, CDCl3
F3C
COOH
60
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)


7
1H NMR 400 MHz, CDCl3
10.75
7.66
7.65
7.64
7.63
7.62
7.61
7.59
7.57
7.50
7.48
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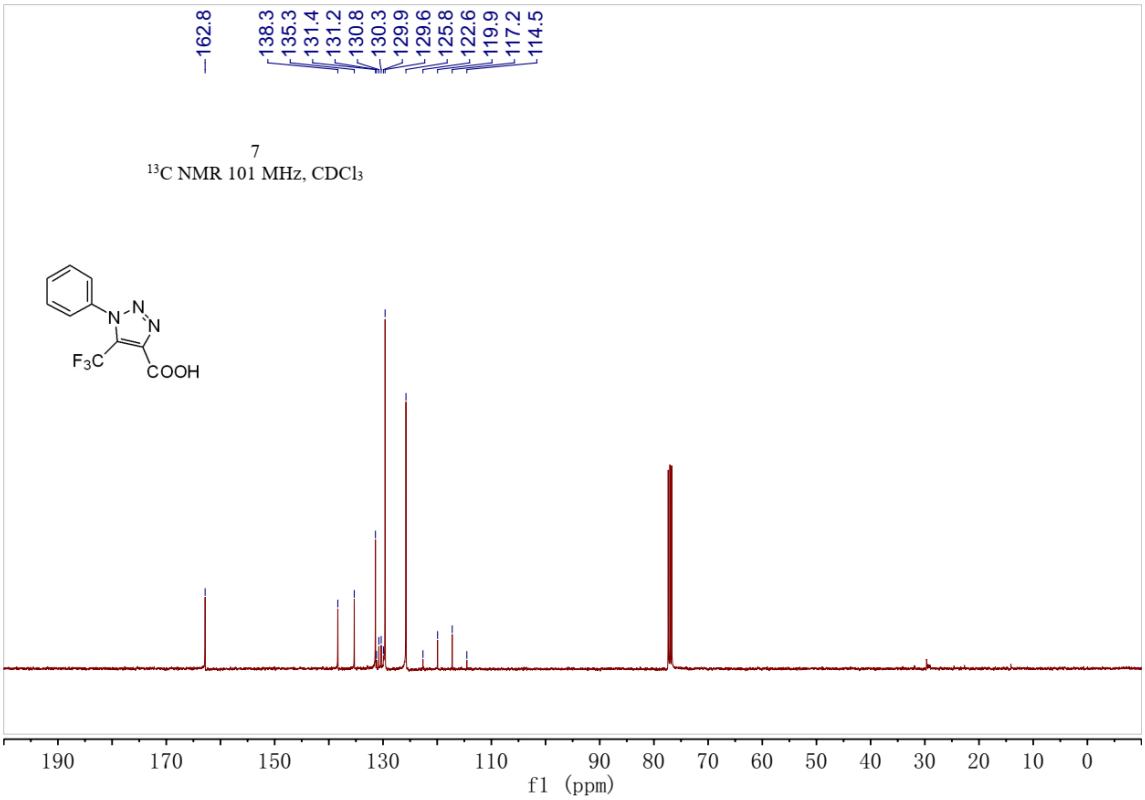
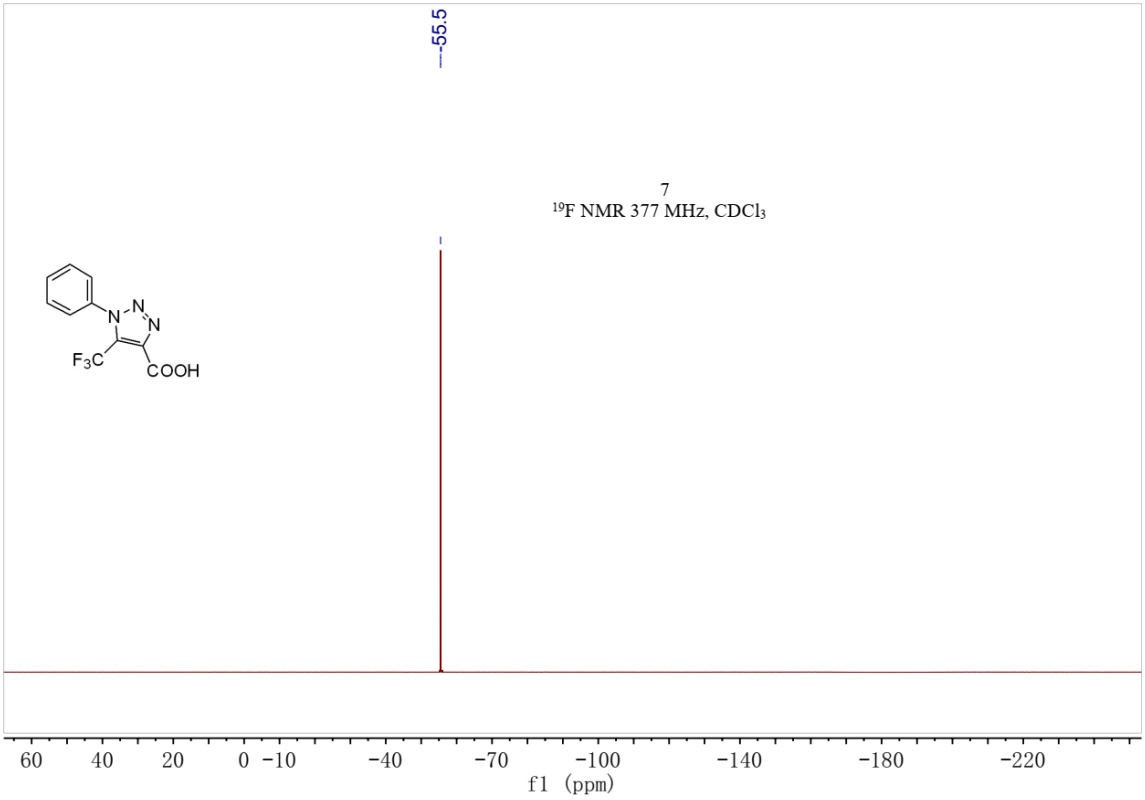
2.00
1.03
3.02
2.00
F3C
COOH
f1 (ppm)


7
13C NMR 101 MHz, CDCl3
162.8
138.3
135.3
131.4
131.2
130.8
130.3
129.9
129.6
125.8
122.6
119.9
117.2
114.5
F3C
COOH
f1 (ppm)


-55.5
7
19F NMR 377 MHz, CDCl3
F3C
COOH
60
40
20
0
-10
-40
-70
-100
-140
-180
-220
f1 (ppm)