Supporting Information

Synthesis of 3-Trifluoromethylpyrazoles *via* Trifluoromethylation/Cyclization of α, β-Alkynic Hydrazones Using a Hypervalent Iodine Reagent

Guojing Ji,[a,b] Xi Wang,*[,a] Songnan Zhang,[a] Yan Xu,[a] Yuxuan Ye,[a] Ming Li,[b] Yan Zhang,[a] and Jianbo Wang*[,a]

Beijing National Laboratory of Molecular Sciences (BNLMS) and Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China

E-mail: wangjb@pku.edu.cn

[b]*College of Chemistry and Molecular Engineering, Qingdao University of Science and Technology, Qingdao 266042, China*

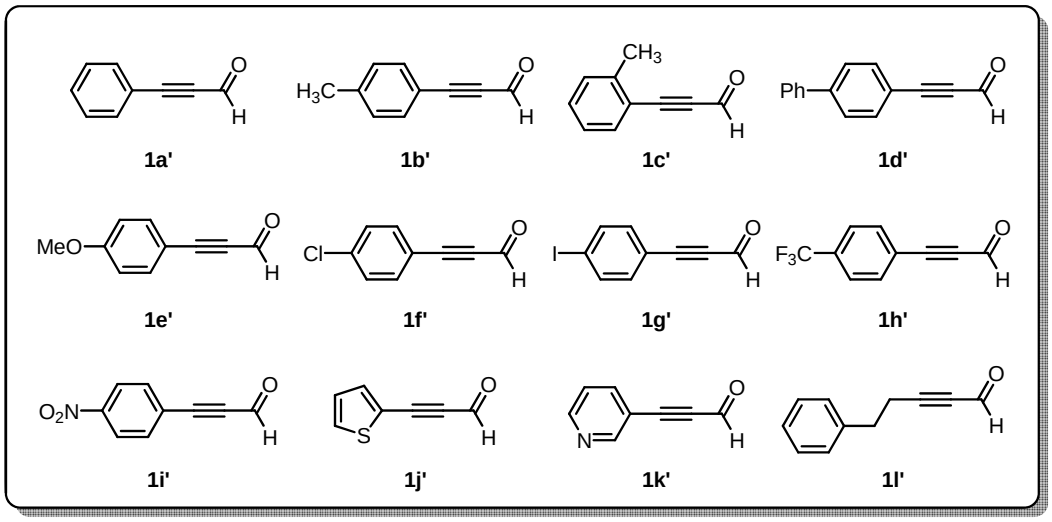
Content

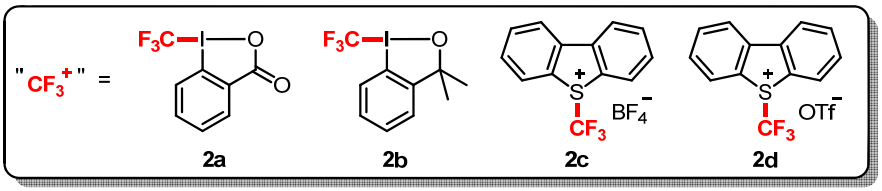
1. General

Unless noted otherwise, all reactions were performed under a nitrogen atmosphere in a reaction vessel. Room temperature (rt.) was approximately 23 °C. All solvents were freshly distilled and degassed according to the handbook *Purification of Laboratory Chemicals* (4^{th} Edition, Butterworth Heinemann, W. L. F. Armarego and Douglas Dalzell Perrin). The boiling point of petroleum ether (PE) was between 60 and 90 ^{o}C. Commercially available reagents were used as received. For chromatography, 200-300 mesh silica gel (Qingdao, China) was employed. ^{1}H NMR spectra were recorded on Bruker ARX 400 (400 MHz) and are referenced relative to tetramethylsilane (TMS) at δ 0.00 ppm; ^{13}C NMR spectra were recorded on Bruker ARX 400 (101 MHz) and are referenced relative to $CDCl_3$ at δ 77.0 ppm; ^{19}F NMR spectra were recorded on Bruker ARX 500 (470 MHz) and are referenced relative to $CFCl_3$ at δ 0.0 ppm. The data for NMR spectra are reported as follows: chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on Nicolet 5MX-S infrared spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Mass spectra were obtained on Agilent 7890A/5975C, HRMS were obtained on Bruker APEX IV FTMS.

2. Preparation of Starting Materials

The propargyl aldehydes **1a'**,[1] **1b'**,[1] **1c'**,[2] **1d'**,[3] **1e'**,[1] **1f'**,[1] **1h,**[1] **1l',**[3] **1g',**[4] **1i',**[5] **1j',**[6] **1k'**,[7] and Togni reagent **2a**,[8] Togni reagent **2b**[9] were prepared according to the previously reported literatures. Umemoto reagent **2c** was commercially available from J&K China and was used as received. Umemoto reagent **2d** was commercially available from Sigma-Aldrich China and was used as received.





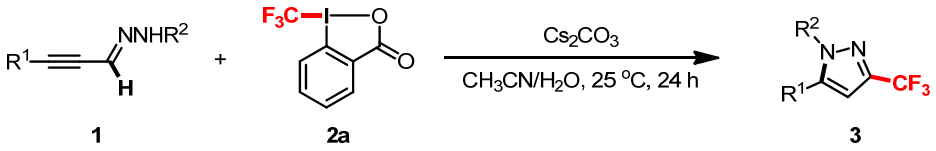
3. Typical Experimental Procedures for Preparation of *α, β*-Alkynic Hydrazones

A solution of corresponding propargyl aldehydes (5.0 mmol, 1.0 equiv) in methanol (2.0 mL) was stirred and heated to 60 ^{o}C until the propargyl aldehydes was dissolved. Pure hydrazine (5.0 mmol, 1.0 equiv) in methanol (3.0 mL) was stirred and heated to 60 ^{o}C until the hydrazine was dissolved. The resulting propargyl aldehydes solution was added to the solution of hydrazine in one portion. The mixture was stirred at 60 ^{o}C for 3~6 h. After the reaction was complete, the crude products were precipitated as a solid. The precipitates were washed by petroleum ether, were then kept in desiccator under vacuum to afford α, β-alkynic hydrazones. In the case when the crude products could not be obtained as solid precipitates after the reaction was completed (monitored by TLC), the solvent was removed by vacuum

and the crude residue was purified by silica gel column chromatography to afford α, β-alkynic hydrazones.

4. Synthesis of 3-Trifluoromethylpyrazoles *via* Trifluoromethylation/Cyclization of *α, β*-Alkynic Hydrazones

Typical Experimental Procedures

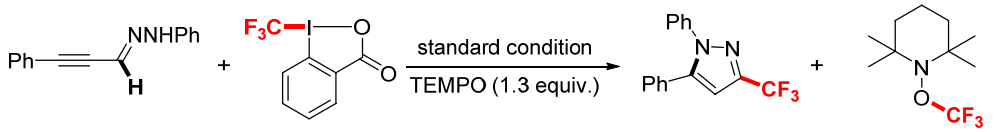


1 **2a** **3**

An oven-dried Schlenk tube equipped with a magnetic stir bar was charged with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1** (0.2 mmol, 1.0 equiv), sealed with a septum, and degassed by alternating vacuum evacuation and nitrogen backfill (three times) before a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) was added. The reaction was then stirred at 25 °C for 24 h. After the reaction was complete, the solvent was removed under reduced pressure with rotary evaporator. The crude residue was purified by silica gel column chromatography to afford pure product **3**.

5. Mechanistic Study Experiments

Radical Trapping Experiment



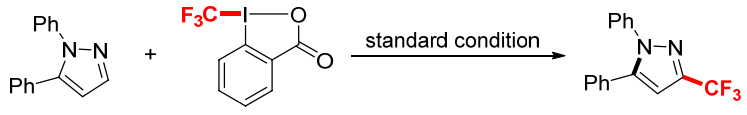
1a **2a** (1.3 equiv) **3a** 28% (^{19}F NMR yield) **4** 26% (^{19}F NMR yield)

Experimental Procedures

An oven-dried Schlenk tube equipped with a magnetic stir bar was charged with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1a** (44.0 mg, 0.20 mmol, 1.0 equiv), TEMPO (40.6 mg, 0.26

mmol, 1.3 equiv) sealed with a septum, and degassed by alternating vacuum evacuation and nitrogen backfill (three times) before a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) was added. The reaction was then stirred at 25 °C for 24 h. After the reaction was complete, the yield of the product **3a** (28%) and TEMPO-CF_3 adduct **4** (26%) based on was determined by ^{19}F NMR with 4-CF_3O-$C_6H_4OCH_3$ as internal standard.

Direct C-H Trifluoromethylation of diphenyl pyrazole

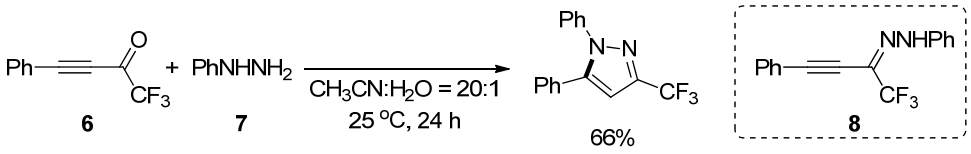


5 **2a** (1.3 equiv) **3a** trace

Experimental Procedures

An oven-dried Schlenk tube equipped with a magnetic stir bar was charged with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), 1,5-diphenyl-1*H*-pyrazole **5** (44.0 mg, 0.20 mmol, 1.0 equiv), sealed with a septum, and degassed by alternating vacuum evacuation and nitrogen backfill (three times) before a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) was added. The reaction was then stirred at 25 °C for 24 h. After the reaction was complete, the possible formation of **3a** was analyzed with GC-MS.

Condensation of alkynyl trifluoromethyl ketone 6 with phenylhydrazine 7



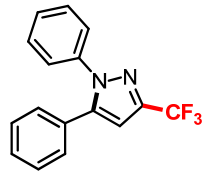
6 **7** **8**

Experimental Procedures

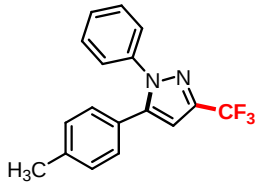
An oven-dried Schlenk tube equipped with a magnetic stir bar was charged with 1,1,1-trifluoro-4-phenylbut-3-yn-2-one **6** (39.6 mg, 0.20 mmol, 1.0 equiv), phenylhydrazine **7** (21.6 mg, 0.20 mmol, 1.0 equiv), sealed with a septum, and degassed by alternating vacuum evacuation and nitrogen backfill (three times) before a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) was added. The reaction was then stirred at 25 °C for 24 h. After the reaction was

complete, the solvent was removed under reduced pressure with rotary evaporator. The crude residue was purified by silica gel column chromatography to afford pure product **3a** as a yellow solid in 66% yield (38.1 mg).

6. Spectral Data of the Products

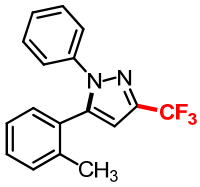


1,5-Diphenyl-3-(trifluoromethyl)-1*H*-pyrazole (3a):[10] The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1a** (44.0 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 ^oC for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 200:1) gave the desired product **3a** as a yellow solid in 70% yield (40.0 mg); **TLC R_f** = 0.65 (PE:EtOAc = 20:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36-7.29 (m, 8H), 7.23-7.21 (m, 2H), 6.75 (s, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 144.6, 143.2 (q, J^2 = 38.3 Hz), 139.2, 129.2, 129.1, 129.0, 128.8, 128.7, 128.4, 125.5, 121.3 (q, J^1 = 269.1 Hz), 105.5; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.6 (s, 3F); **EI-MS (*m/z*, relative intensity)** 288 (M^+, 100), 267 (52), 219 (9), 77 (24), 51 (15); **IR (film):** 1235, 1162, 1131, 977, 763, 695 cm^{-1}; **MP:** 79-81 ^oC.

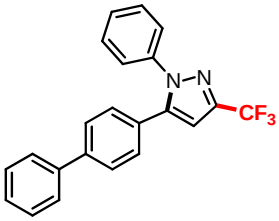


Phenyl-5-*p*-tolyl-3-(trifluoromethyl)-1*H*-pyrazole (3b):[11] The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1b** (46.8 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 ^oC for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 200:1) gave the desired product **3b** as a yellow oil in 59% yield (36.0 mg); **TLC R_f** = 0.65 (PE:EtOAc = 20:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36-7.30 (m, 5H), 7.13-7.08 (m, 4H), 6.71 (s, 1H), 2.34 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 144.8, 143.1 (q, J^2 = 38.3 Hz), 139.3, 139.0, 129.4, 129.0, 128.6, 128.3, 126.2, 125.5, 121.4 (q, J^1 = 269.1 Hz), 105.3, 21.2; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.2 (s, 3F); **EI-MS (*m/z*, relative intensity)** 302 (M^+, 100), 281 (28), 267 (9), 140 (9), 77 (15), 51 (9); **IR (film):** 1474, 1234, 1161, 1131, 977, 765, 692

cm^{-1}.

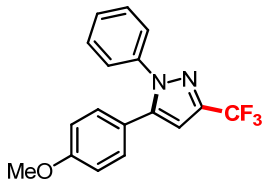


1-Phenyl-5-*o*-tolyl-3-(trifluoromethyl)-1*H*-pyrazole (3c):[11] The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1c** (46.8 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 °C for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 200:1) gave the desired product **3c** as a yellow oil in 62% yield (37.4 mg); **TLC R_f** = 0.70 (PE:EtOAc = 20:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32-7.20 (m, 9H), 6.65 (s, 1H), 2.00 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 143.9, 143.0 (q, J^2 = 38.1 Hz), 139.3, 137.1, 130.6, 129.6, 129.3, 128.9, 127.9, 126.0, 124.0, 123.8, 121.4 (q, J^1 = 270.1 Hz), 106.5, 19.8; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.1 (s, 3F); **EI-MS (*m/z*, relative intensity)** 302 (M^+, 100), 281 (16), 267 (16), 233 (17), 206 (47), 140 (16), 130 (17), 77 (30), 51 (12); **IR (film):** 1493, 1236, 1163, 1131, 976, 763, 690 cm^{-1}.

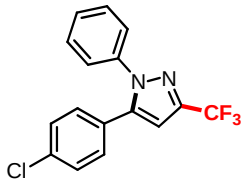


5-([1,1'-Biphenyl]-4-yl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3d): The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1d** (59.2 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 °C for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 100:1) gave the desired product **3d** as a yellow oil in 58% yield (42.3 mg); **TLC R_f**= 0.60 (PE:EtOAc = 20:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.59-7.54 (m, 4H), 7.44 (t, J = 7.5 Hz, 2H), 7.39-7.34 (m, 6H), 7.29-7.27 (m, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 144.3, 143.2 (q, J^2 = 38.4 Hz), 141.7, 139.8, 139.3, 129.1, 129.1, 128.9, 128.5, 127.9, 127.8, 127.2, 127.0, 125.5, 121.3 (q, J^1 = 268.9 Hz), 105.5; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.2 (s, 3F); **EI-MS (*m/z*, relative intensity)** 364 (M^+, 100), 343 (14), 267 (8), 152 (6), 77 (12), 51 (5); **IR (film):** 3031.1, 1471.2, 1233.2, 1131.2, 977.8, 765.4, 693.2

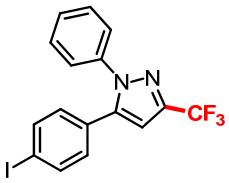
cm^{-1}; **HRMS (ESI)** calcd for: $C_{22}H_{16}F_3N_2$ $[M+H]^+$ 365.1260, found: 365.1256.



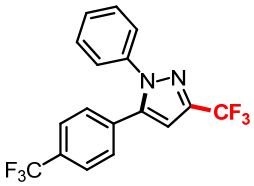
5-(4-Methoxyphenyl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3e):[11] The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1e** (50.0 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 °C for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 80:1) gave the desired product **3e** as a yellow oil in 63% yield (40.1 mg); **TLC R_f** = 0.40 (PE:EtOAc = 20:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35-7.30 (m, 5H), 7.14 (d, J = 8.3 Hz, 2H), 6.84 (d, J = 8.3 Hz, 2H), 6.69 (s, 1H), 3.80 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 160.1, 144.6, 143.1 (q, J^2 = 38.3 Hz), 139.4, 130.1, 129.1, 128.4, 125.5, 121.5, 121.4 (q, J^1 = 269.3 Hz), 114.1, 105.0, 55.3; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.2 (s, 3F); **EI-MS (*m/z*, relative intensity)** 318 (M^+, 100), 303 (21), 275 (8), 205 (6), 77 (14), 51 (6); **IR (film):** 1474, 1254, 1234, 1162, 1130, 977 cm^{-1}.



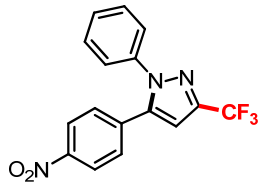
5-(4-Chlorophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3f):[12] The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv.), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1f** (50.8 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 °C for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 200:1) gave the desired product **3f** as a yellow oil in 65% yield (42.0 mg); **TLC R_f** = 0.65 (PE:EtOAc = 20:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39-7.38 (m, 3H), 7.31-7.29 (m, 4H), 7.15 (d, J = 8.6 Hz, 2H), 6.75 (s, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 143.4, 143.3 (q, J^2 = 38.6 Hz), 139.0, 135.2, 130.0, 129.2, 129.0, 128.7, 127.6, 125.5, 121.2 (q, J^1 = 269.0 Hz), 105.7; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.3 (s, 3F); **EI-MS (*m/z*, relative intensity)** 322 (M^+, 100), 301 (39), 267 (13), 190 (8), 133 (7), 77 (25), 51 (13); **IR (film):** 1469, 1233, 1133, 1094, 978, 732 cm^{-1}.



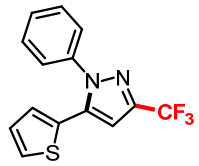
5-(4-Iodophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3g): The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1g** (69.2 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 °C for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 100:1) gave the desired product **3g** as a yellow solid in 64% yield (53.0 mg); **TLC R_f**= 0.60 (PE:EtOAc = 20:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (d, J = 8.2 Hz, 2H), 7.39-7.30 (m, 5H), 6.94 (d, J = 8.2 Hz, 2H), 6.75 (s, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 143.5, 143.3 (q, J^2 = 38.5 Hz), 138.9, 137.9, 130.3, 129.2, 128.7, 128.6, 125.5, 121.1 (q, J^1 = 268.9 Hz), 105.6, 95.2; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.2 (s, 3F); **EI-MS (*m/z*, relative intensity)** 414 (M^+, 100), 393 (11), 267 (16), 218 (11), 190 (11), 133 (12), 77 (14), 51 (9); **IR (film):** 1492, 1234, 1162, 1132, 977, 807, 692 cm^{-1}; **HRMS (ESI)** calcd for: $C_{16}H_{11}F_3IN_2$ $[M+H]^+$ 414.9914, found: 414.9905; **MP:** 89-91 °C.



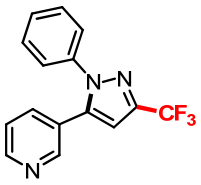
1-Phenyl-3-(trifluoromethyl)-5-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (3h): The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1h** (57.6 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 °C for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 200:1) gave the desired product **3h** as a yellow oil in 55% yield (39.4 mg); **TLC R_f** = 0.65 (PE:EtOAc = 20:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.59 (d, J = 8.3 Hz, 2H), 7.41-7.39 (m, 3H), 7.35 (d, J = 8.3 Hz, 2H), 7.31-7.29 (m, 2H), 6.82 (s, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 143.5 (q, J^2 = 38.6 Hz), 143.1, 138.8, 132.7, 131.0 (q, J^2 = 32.9 Hz), 129.4, 129.1, 128.9, 125.7 (q, J^3 = 3.7 Hz), 125.5, 123.7 (q, J^1 = 272.3 Hz), 121.1 (q, J^1 = 269.0 Hz), 106.2; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.3 (s, 3F), -62.9 (s, 3F); **EI-MS (*m/z*, relative intensity)** 356 (M^+, 100), 335 (56), 287 (14), 267 (14), 77 (30), 51 (14); **IR (film):** 1325, 1235, 1164, 1128, 1099, 979 cm^{-1}; **HRMS (ESI)** calcd for: $C_{17}H_{11}F_6N_2$ $[M+H]^+$ 357.0821, found: 357.0819.



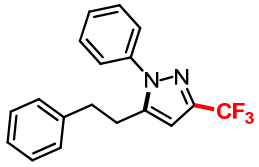
5-(4-Nitrophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3i):[11] The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1i** (53.0 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 °C for 24 h. Concentration and purification *via* silica gel chromatography (PE:EtOAc = 40:1) gave the desired product **3i** as a yellow oil in 72% yield (48.0 mg); **TLC R_f**= 0.30 (PE:EtOAc = 20:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.18 (d, J = 8.8 Hz, 2H), 7.43-7.40 (m, 5H), 7.32-7.29 (m, 2H), 6.89 (s, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 147.7, 143.5 (q, J^2 = 38.7 Hz), 142.2, 138.6, 135.2, 129.5, 129.1, 128.8, 125.5, 123.9, 120.9 (q, J^1 = 269.1 Hz), 106.6; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.3 (s, 3F); **EI-MS (*m/z*, relative intensity)** 333 (M^+, 100), 286 (33), 207 (18), 190 (15), 149 (13), 77 (20), 51 (15); **IR (film):** 1523, 1347, 1235, 1134, 979, 854, 721 cm^{-1}.



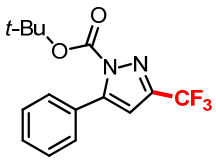
1-Phenyl-5-(thiophen-2-yl)-3-(trifluoromethyl)-1*H*-pyrazole (3j):[11] The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1j** (45.2 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 °C for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 20:1) gave the desired product **3j** as a yellow solid in 57% yield (33.5 mg); **TLC R_f** = 0.75 (PE:EtOAc = 4:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.45-7.38 (m, 5H), 7.32 (dd, J = 0.9 Hz, J = 5.1 Hz, 1H), 6.96 (dd, J = 3.7 Hz, J = 5.0 Hz, 1H), 6.86 (dd, J = 1.0 Hz, J = 3.6 Hz, 1H), 6.80 (s, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 143.1 (q, J^2 = 38.6 Hz), 138.9, 138.7, 129.7, 129.3, 129.2, 128.1, 127.5, 127.5, 126.4, 121.1 (q, J^1 = 269.1 Hz), 105.3; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.3 (s, 3F); **EI-MS (*m/z*, relative intensity)** 294 (M^+, 100), 273(31), 77 (19), 51 (14); **IR (film):** 1499, 1245, 1154, 1132, 1099, 974, 695 cm^{-1}; **MP:** 61-62 °C.



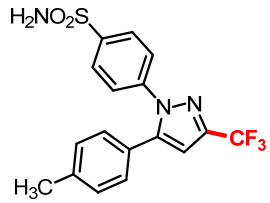
3-(1-Phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)pyridine (3k): The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1k** (44.3 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 ^oC for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 3:1) gave the desired product **3k** as a yellow solid in 57% yield (33.5 mg); **TLC R_f** = 0.5 (PE:EtOAc = 1:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.58 (d, J = 13.9 Hz, 2H), 7.48 (d, J = 7.9 Hz, 1H), 7.41-7.39 (m, 3H), 7.33-7.29 (m, 2H), 7.28-7.25 (m, 1H), 6.84 (s, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 149.9, 149.2, 143.5 (q, J^2 = 38.6 Hz), 141.3, 138.7, 135.8, 129.4, 128.9, 125.5, 123.3, 121.1 (q, J^1 = 269.0 Hz), 106.0; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.3 (s, 3F); **EI-MS (*m/z*, relative intensity)** 288 ($M-1^+$, 100), 268 (34), 220 (8), 192 (8), 77 (21), 51 (17); **IR (film):** 1491, 1243, 1163, 1131, 977, 768, 710 cm^{-1}; **HRMS (ESI)** calcd for: $C_{15}H_{11}F_3N_3$ $[M+H]^+$ 290.0900, found: 290.0894; **MP:** 76-78 ^oC.



5-Phenethyl-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3l): The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1l** (49.6 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 ^oC for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 100:1) gave the desired product **3l** as a yellow solid in 47% yield (30.2 mg); **TLC R_f** = 0.45 (PE:EtOAc = 20:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48-7.43 (m, 3H), 7.33-7.31 (m, 2H), 7.27-7.23 (m, 2H), 7.21-7.18 (m, 1H), 7.05 (d, J = 6.9 Hz, 2H), 6.49 (s, 1H), 2.97-2.85 (m, 4H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 144.8, 142.7 (q, J^2 = 38.1 Hz), 139.9, 138.8, 129.3, 129.0, 128.6, 128.2, 126.5, 125.8, 121.4 (q, J^1 = 268.6 Hz), 103.7, 34.9, 28.0; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.1 (s, 3F); **EI-MS (*m/z*, relative intensity)** 316 (M^+, 45), 297 (9), 225 (18), 205 (18), 91 (100), 77 (15); **IR (film):** 2912, 2849, 1483, 1246, 1128, 974, 697 cm^{-1}; **HRMS (ESI)** calcd for: $C_{18}H_{16}F_3N_2$ $[M+H]^+$ 317.1260, found: 317.1253; **MP:** 53-55 ^oC.



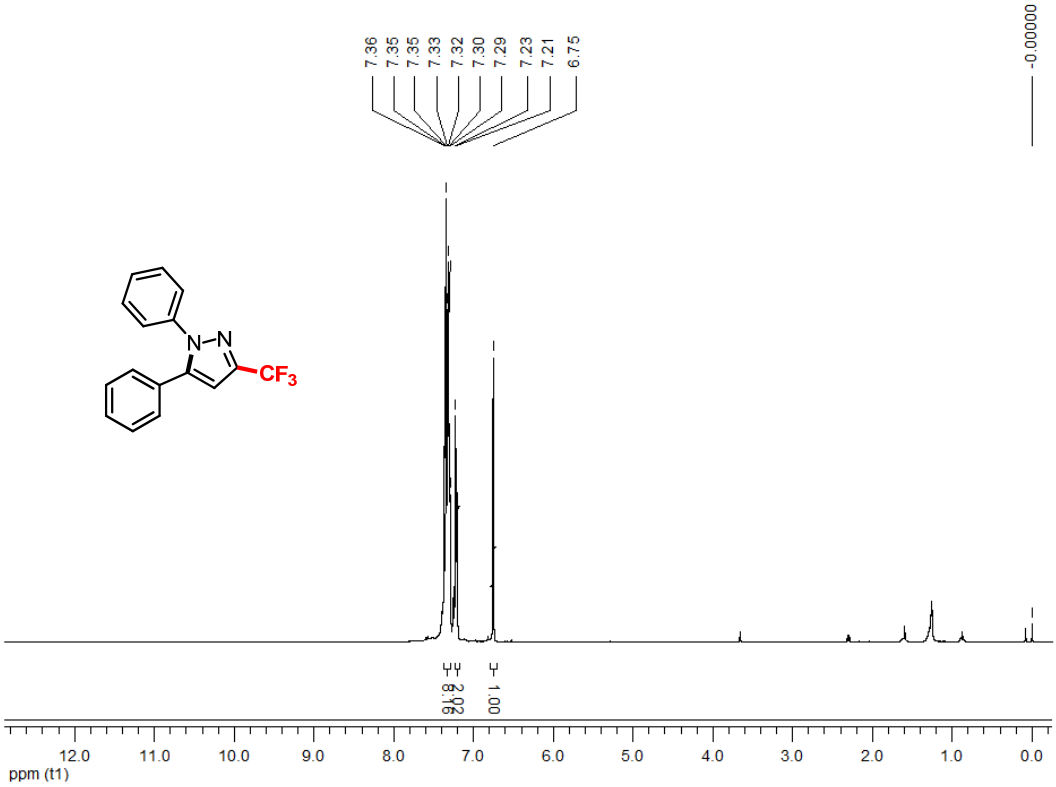
***tert*-Butyl 5-phenyl-3-(trifluoromethyl)-1*H*-pyrazole-1-carboxylate (3m):** The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1m** (48.8 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 °C for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 80:1) gave the desired product **3m** as a yellow solid in 30% yield (18.9 mg); **TLC R_f** = 0.40 (PE:EtOAc = 20:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.45-7.41 (m, 3H), 7.36-7.34 (m, 2H), 6.58 (s, 1H), 1.36 (s, 9H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 147.6, 147.0, 144.7 (q, J^2 = 38.8 Hz), 130.4, 129.2, 128.9, 128.1, 120.5 (q, J^1 = 270 Hz), 108.0, 86.6, 27.3; **^{19}F NMR (470 MHz $CDCl_3$)** δ -63.1 (s, 3F); **EI-MS (*m/z*, relative intensity)** 212 (100), 207 (30), 193 (12), 164 (21), 143 (18), 133 (18), 115 (9), 77 (10); **IR (film):** 1778, 1302, 1242, 1144, 1093, 967 cm^{-1}; **HRMS (ESI)** calcd for: $C_{15}H_{15}F_3N_2NaO_2$ $[M+Na]^+$ 335.0978, found: 335.0985; **MP:** 65-67 °C.



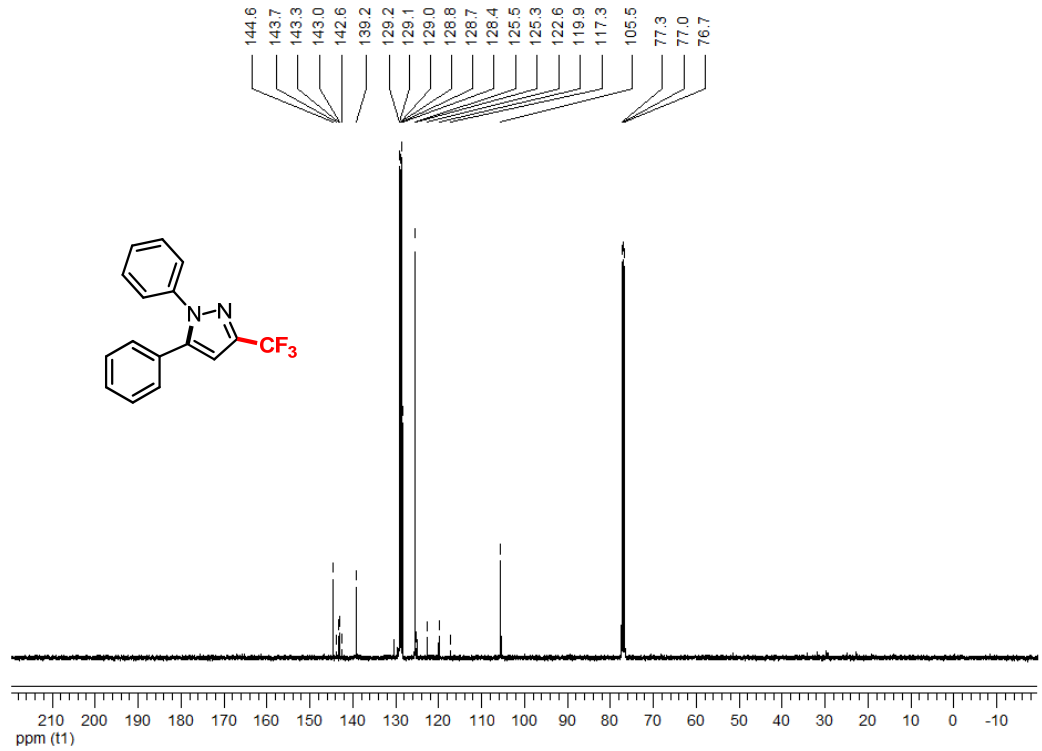
4-(5-(*p*-Tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (3n):[13] The title compound was prepared according to typical experimental procedures with cesium carbonate (130.3 mg, 0.40 mmol, 2.0 equiv), Togni reagent **2a** (82.2 mg, 0.26 mmol, 1.3 equiv), alkynic hydrazones **1n** (62.6 mg, 0.20 mmol, 1.0 equiv) in a solvent mixture of CH_3CN/H_2O (20:1, v/v) (1 mL) at 25 °C for 24 h. Concentration and purification via silica gel chromatography (PE:EtOAc = 4:1) gave the desired product **3n** as a yellow solid in 52% yield (40.0 mg); **R_f** = 0.65 (PE:EtOAc = 1:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.87 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.74 (s, 1H), 5.29 (s, 2H), 2.36 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 145.3, 144.0 (q, J^2 = 38.7 Hz), 142.4, 141.4, 139.8, 129.7, 128.7, 127.4, 125.6, 125.5, 121.0 (q, J^1 = 269.1 Hz), 106.3, 21.2; **^{19}F NMR (470 MHz $CDCl_3$)** δ -62.4 (s, 3F); **EI-MS (*m/z*, relative intensity)** 381 (M^+, 100), 362 (8), 281 (35), 207 (8), 140 (8), 115(9); **IR (film):** 1347, 1236, 1162, 1132, 734 cm^{-1}; **MP** = 152-153 °C.

7. NMR and MS Spectra

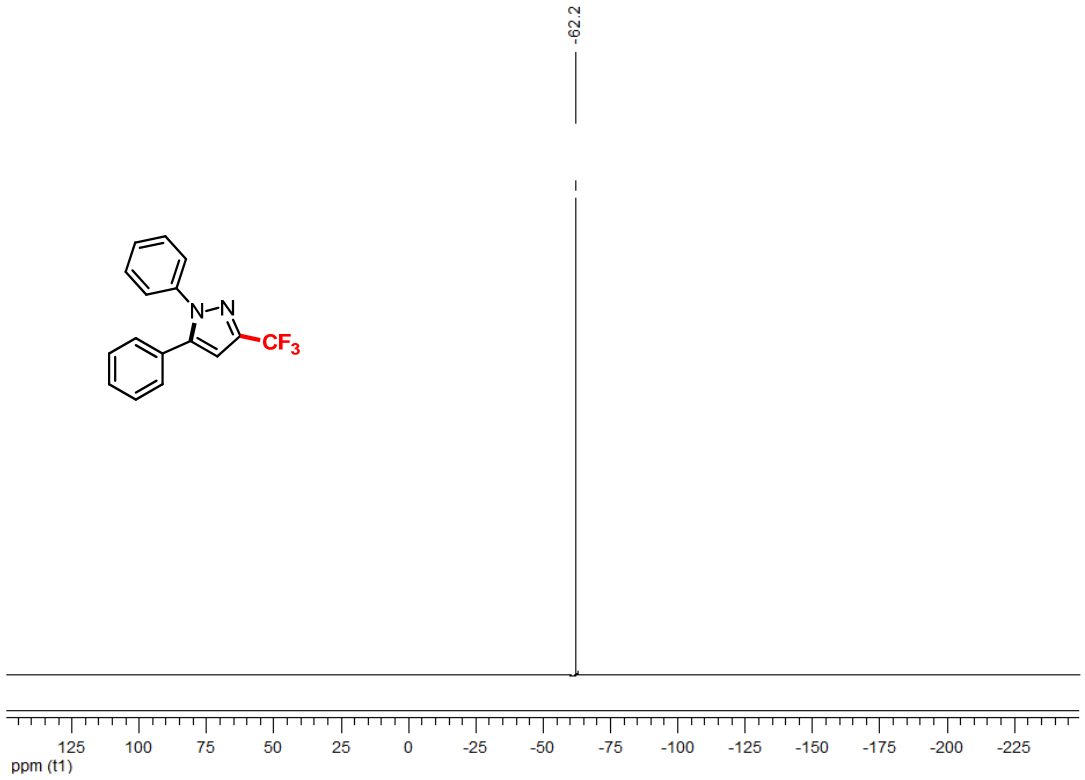
^{1}H NMR Spectrum of 1,5-diphenyl-3-(trifluoromethyl)-1*H*-pyrazole (3a)



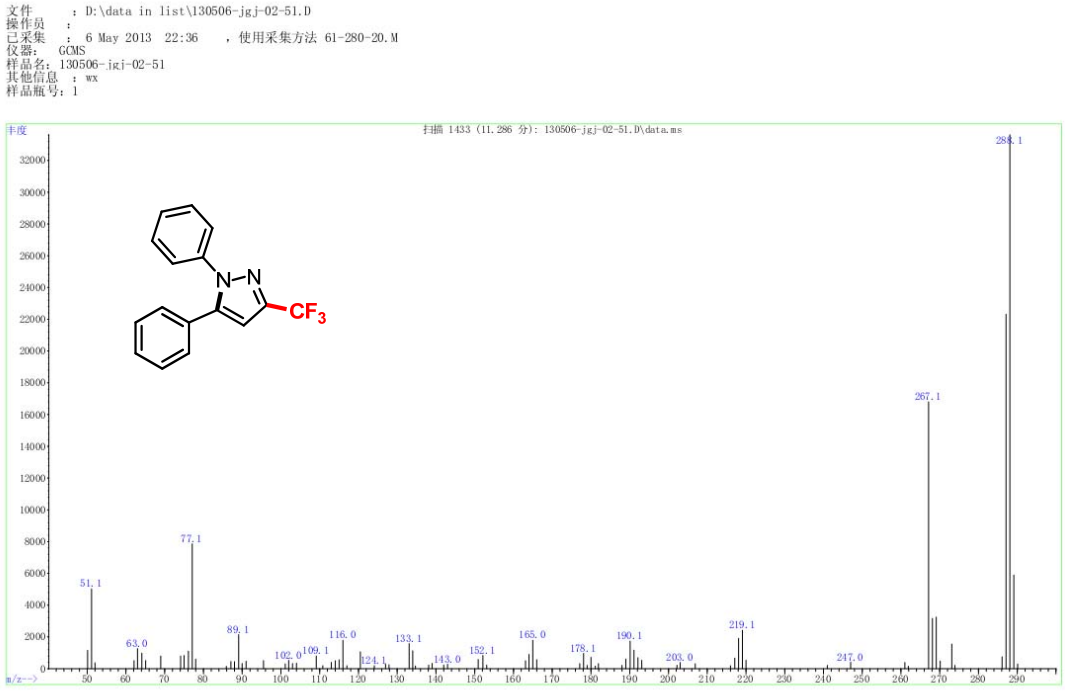
^{13}C NMR Spectrum of 1,5-diphenyl-3-(trifluoromethyl)-1*H*-pyrazole (3a)



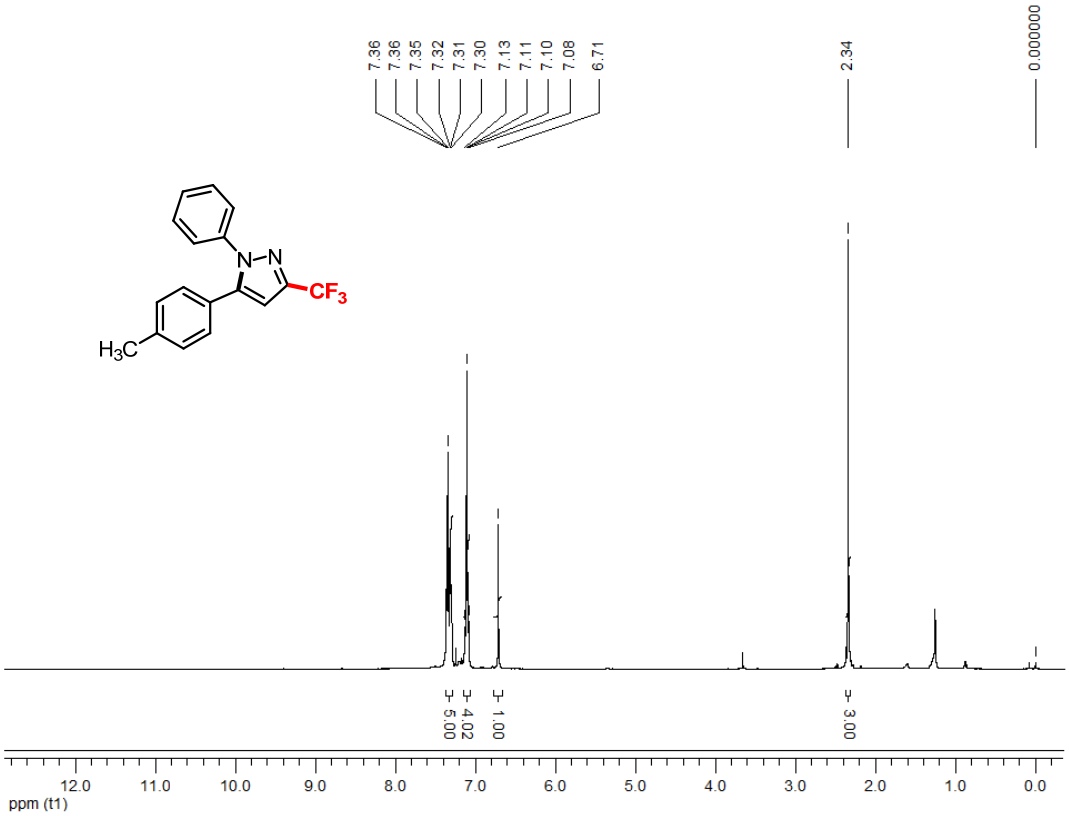
^{19}F NMR Spectrum of 1,5-diphenyl-3-(trifluoromethyl)-1*H*-pyrazole (3a)



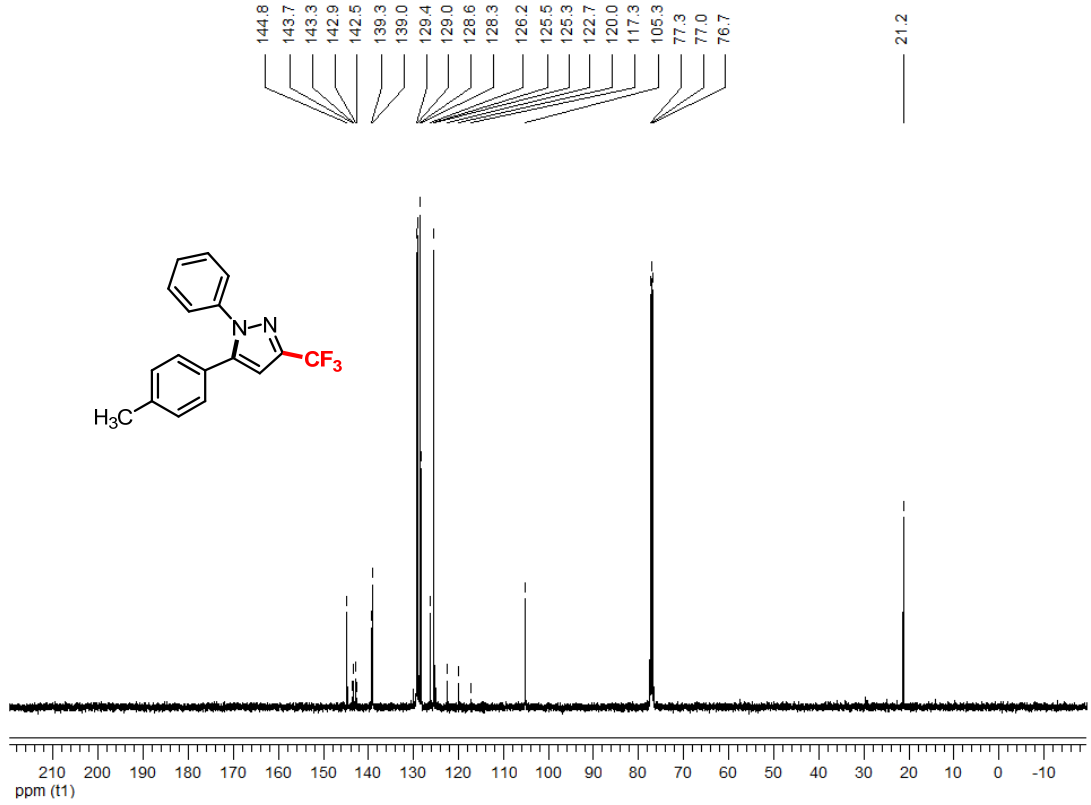
Mass Spectrum of 1,5-diphenyl-3-(trifluoromethyl)-1*H*-pyrazole (3a)



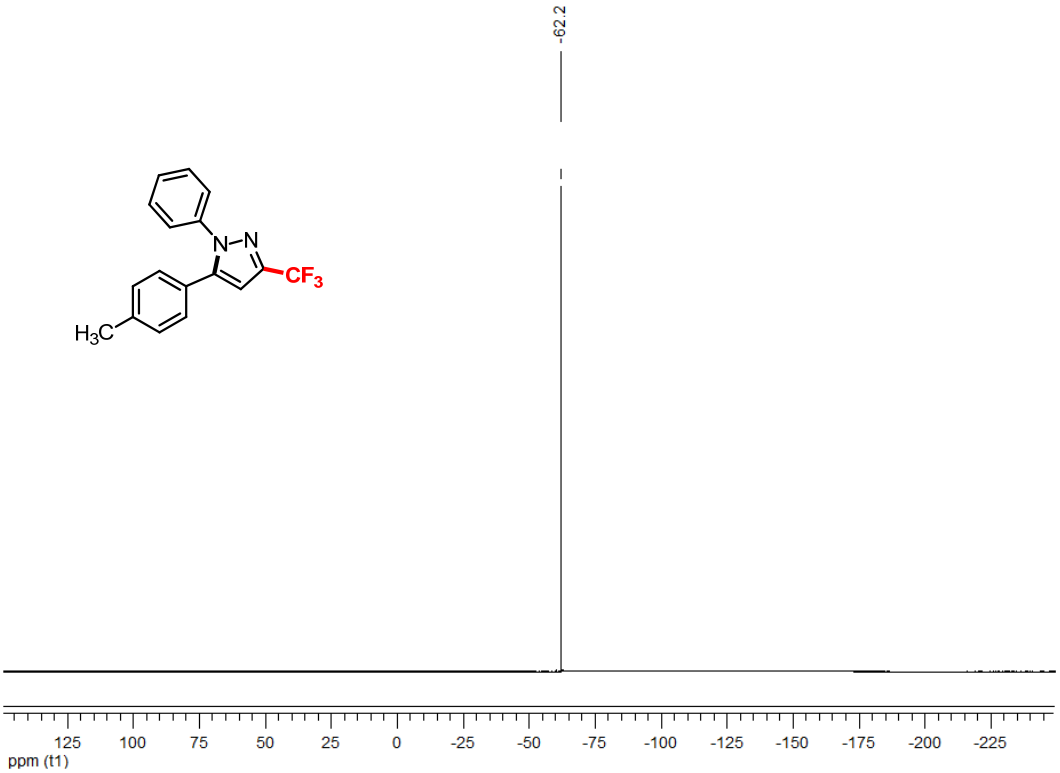
^{1}H NMR Spectrum of phenyl-5-*p*-tolyl-3-(trifluoromethyl)-1*H*-pyrazole (3b)



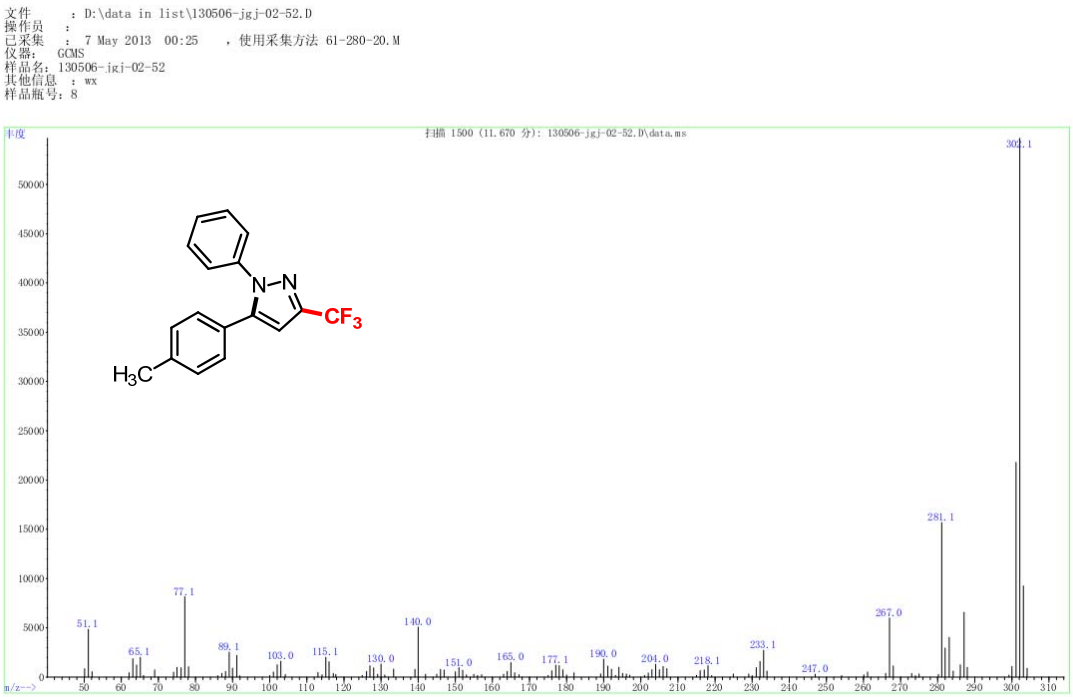
^{13}C NMR Spectrum of phenyl-5-*p*-tolyl-3-(trifluoromethyl)-1*H*-pyrazole (3b)



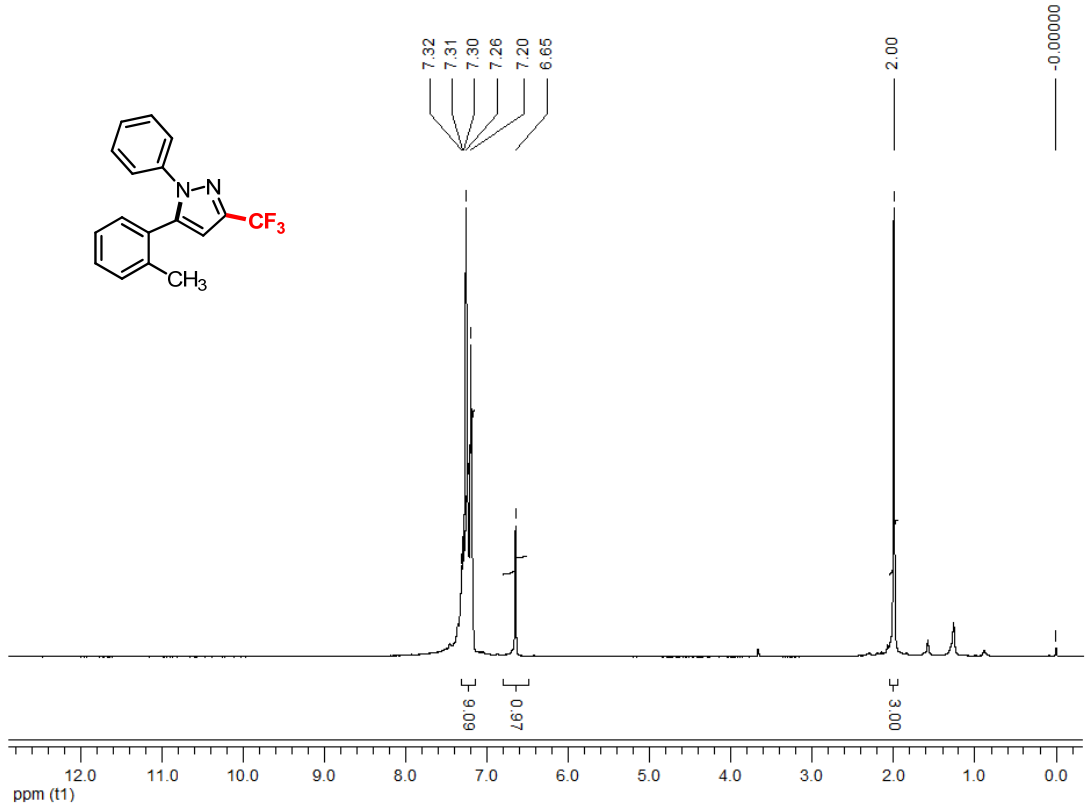
^{19}F NMR Spectrum of phenyl-5-*p*-tolyl-3-(trifluoromethyl)-1*H*-pyrazole (3b)



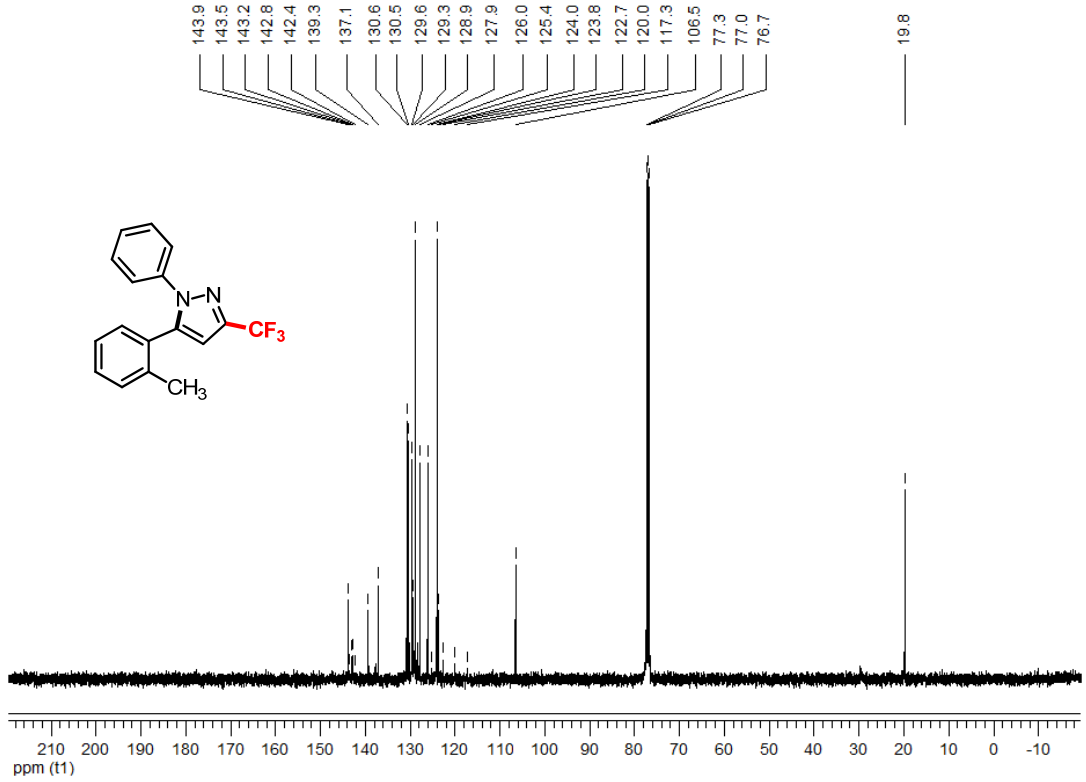
Mass Spectrum of phenyl-5-*p*-tolyl-3-(trifluoromethyl)-1*H*-pyrazole (3b)



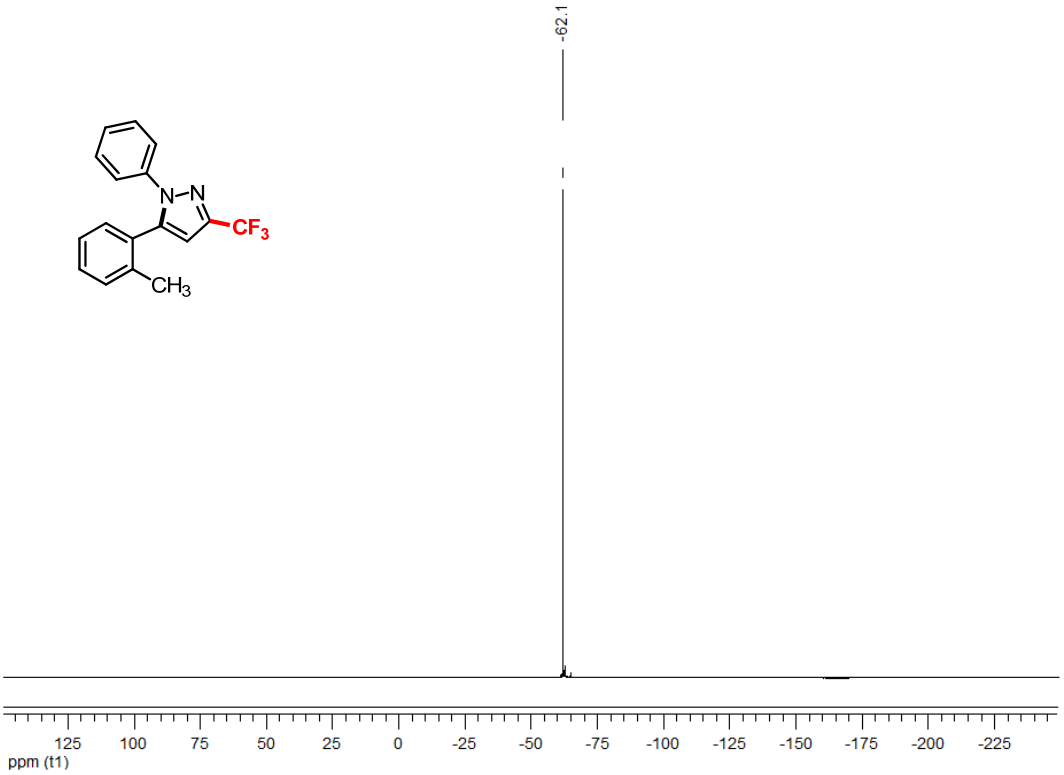
^{1}H NMR Spectrum of 1-phenyl-5-*o*-tolyl-3-(trifluoromethyl)-1*H*-pyrazole (3c):



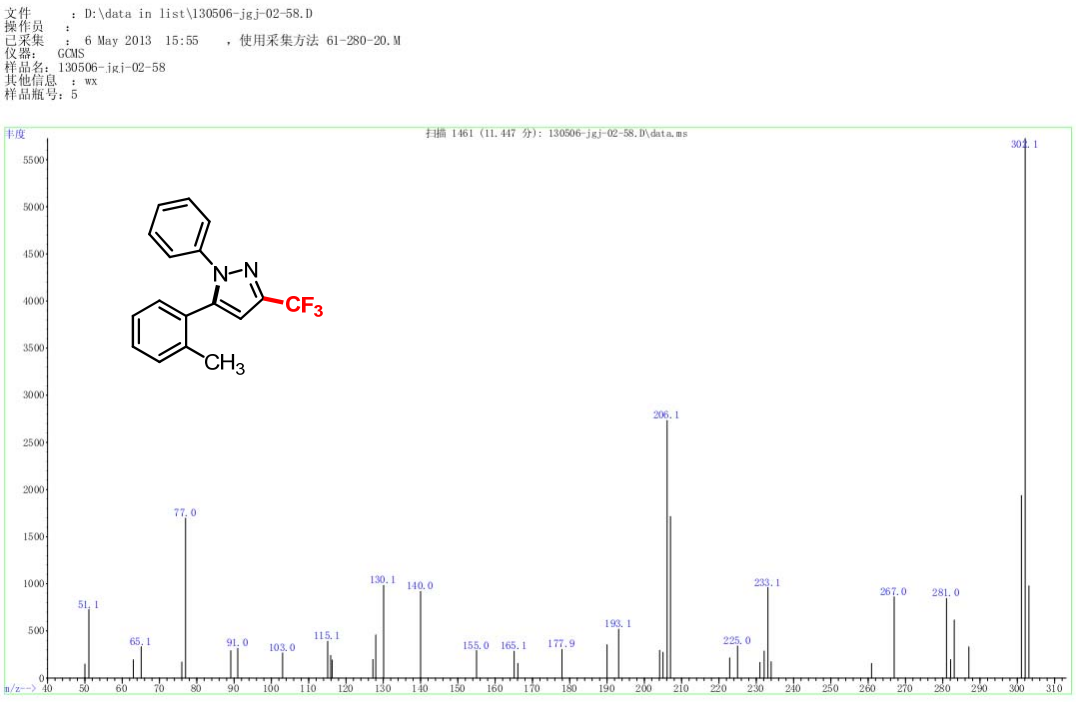
^{13}C NMR Spectrum of 1-phenyl-5-*o*-tolyl-3-(trifluoromethyl)-1*H*-pyrazole (3c):



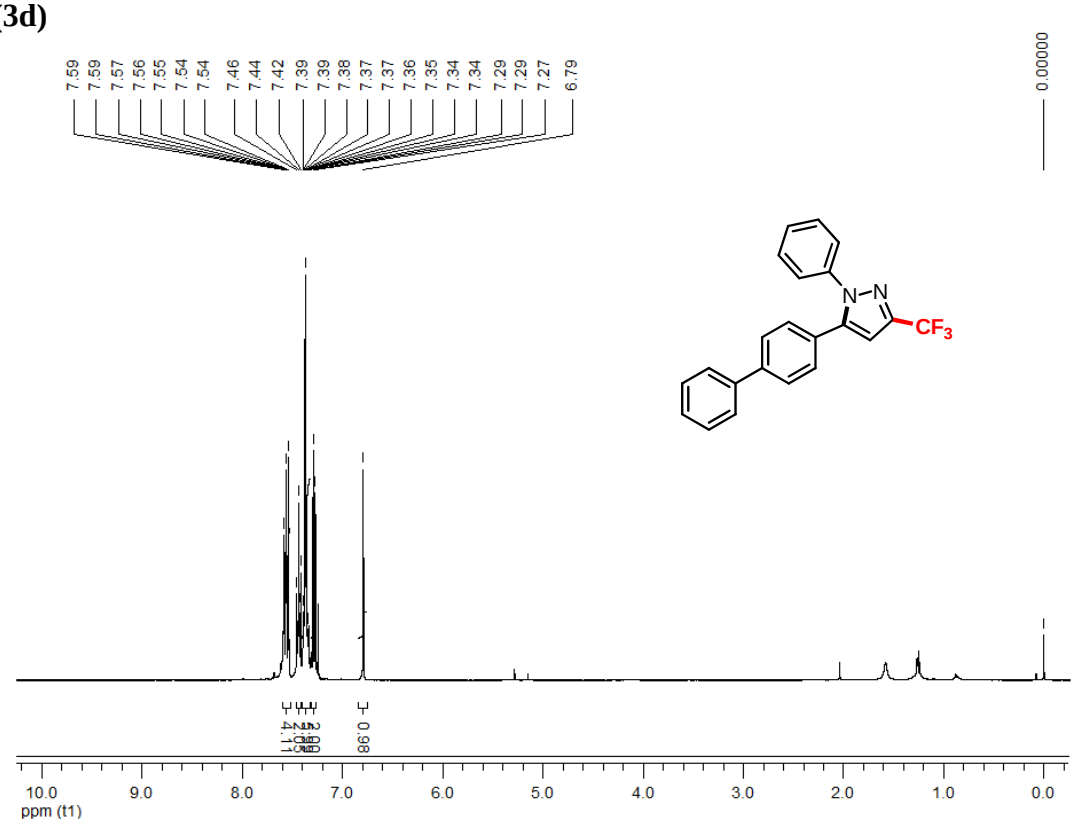
^{19}F NMR Spectrum of 1-phenyl-5-*o*-tolyl-3-(trifluoromethyl)-1*H*-pyrazole (3c):



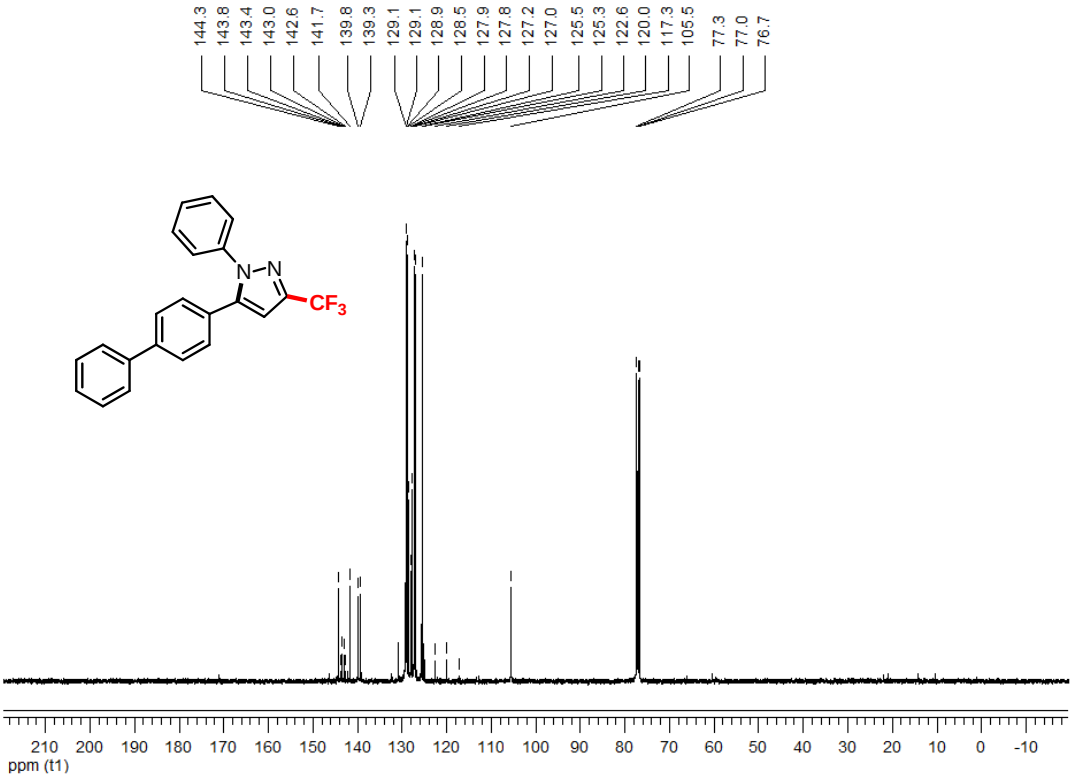
Mass Spectrum of 1-phenyl-5-*o*-tolyl-3-(trifluoromethyl)-1*H*-pyrazole (3c):



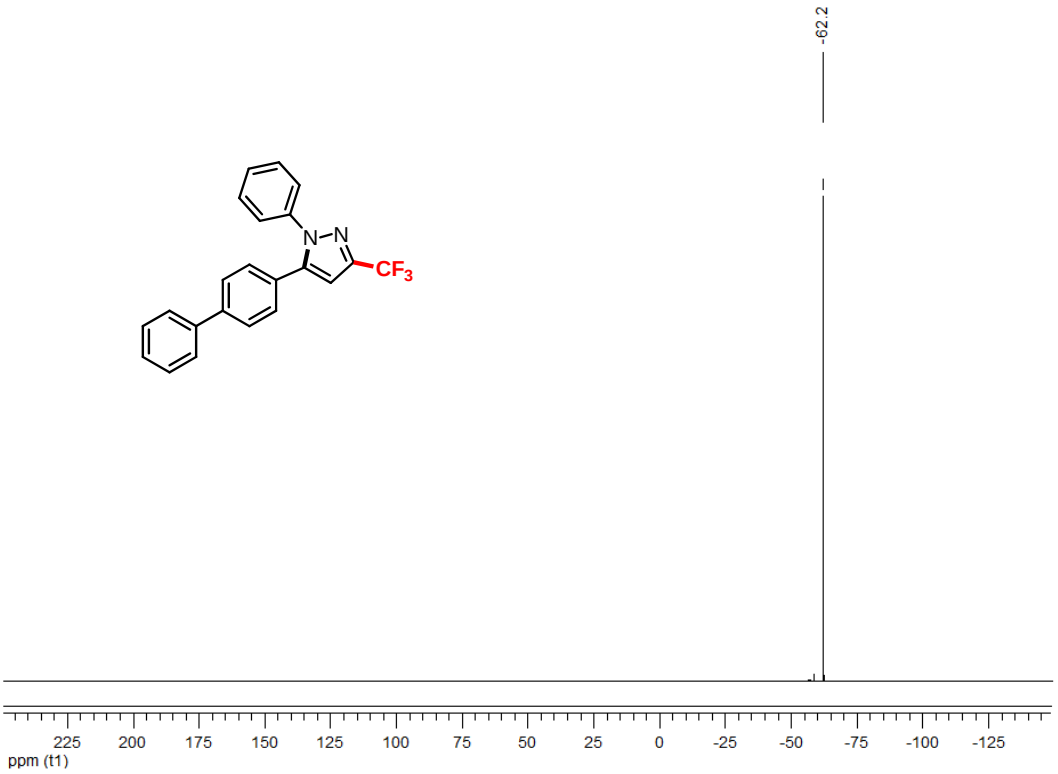
^{1}H NMR Spectrum of 5-([1,1'-biphenyl]-4-yl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3d)



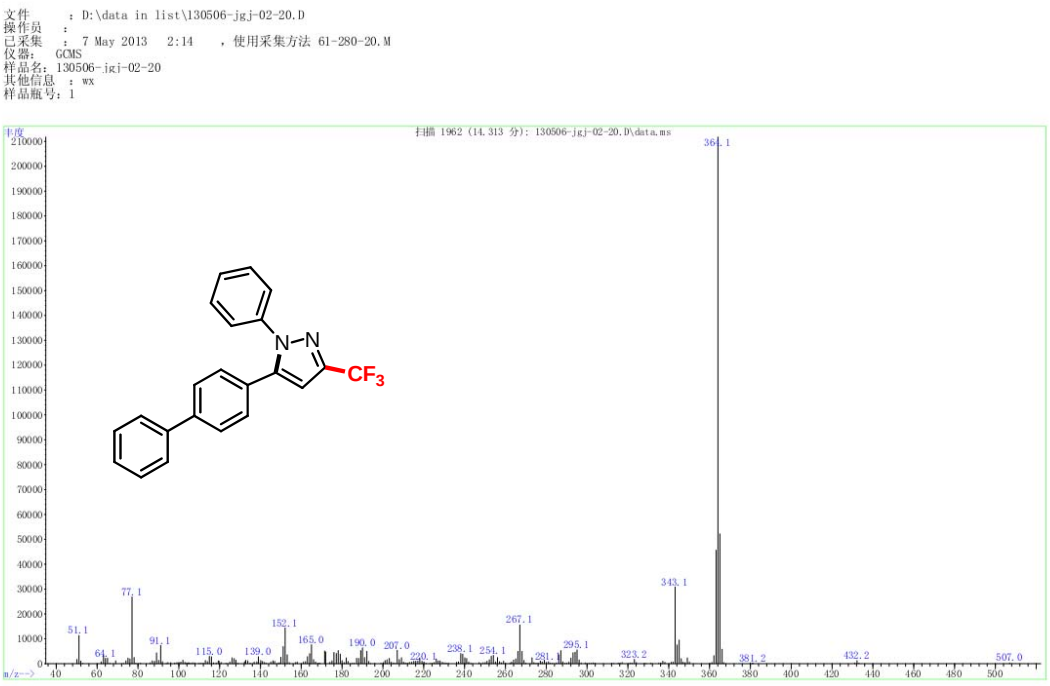
^{13}C NMR Spectrum of 5-([1,1'-biphenyl]-4-yl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3d)



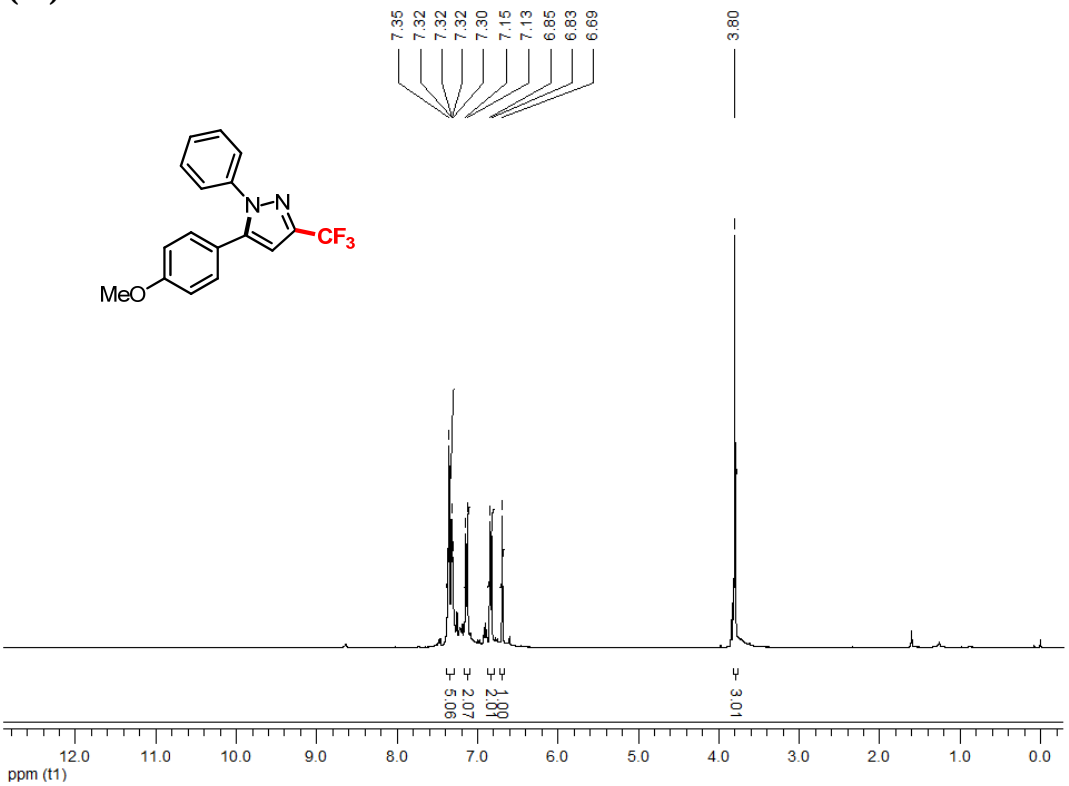
^{19}F NMR Spectrum of 5-([1,1'-biphenyl]-4-yl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3d)



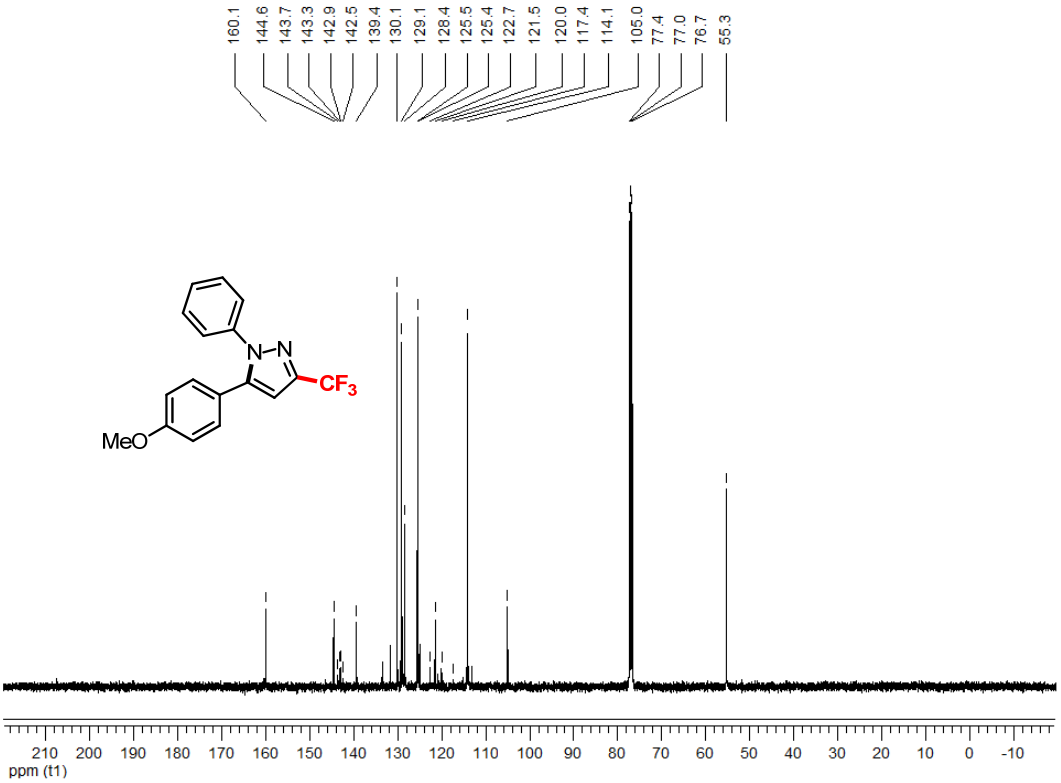
Mass Spectrum of 5-([1,1'-biphenyl]-4-yl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3d)



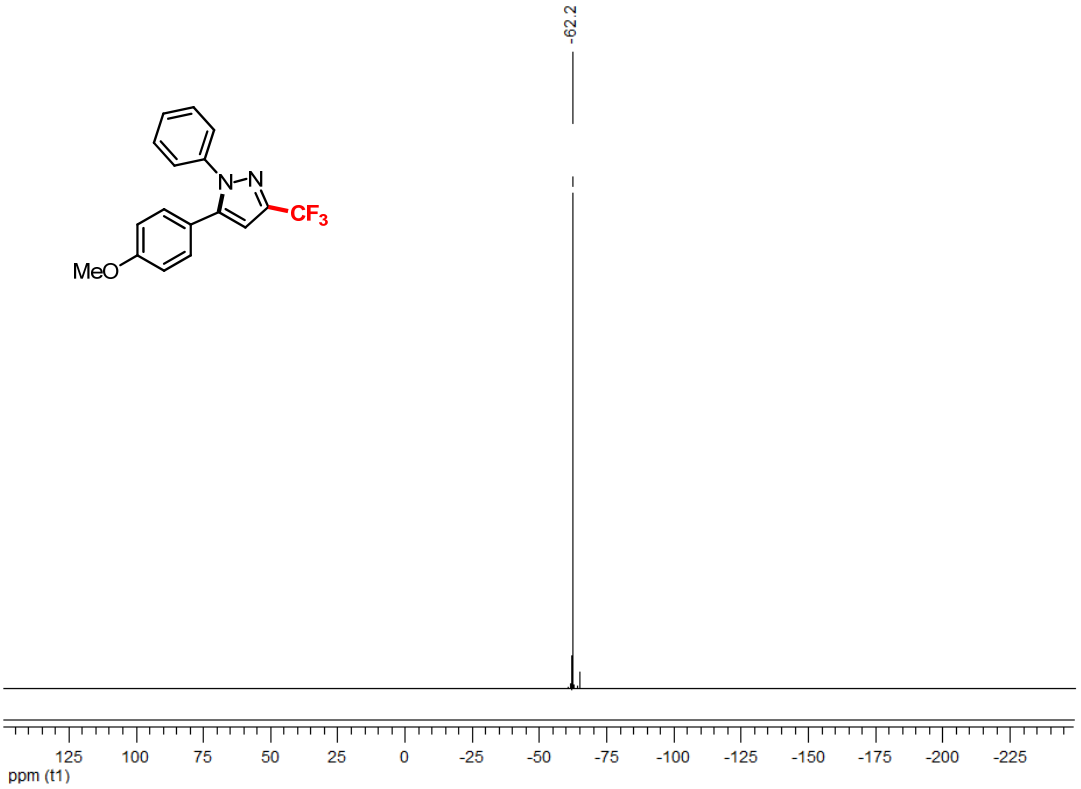
^{1}H NMR Spectrum of 5-(4-methoxyphenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3e)



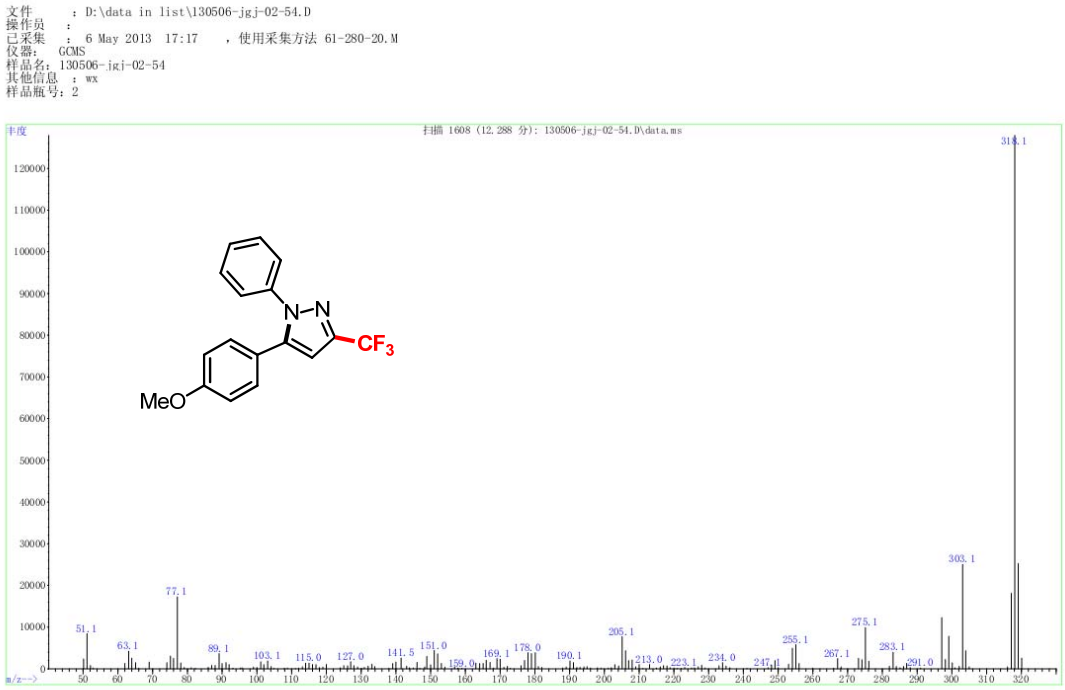
^{13}C NMR Spectrum of 5-(4-methoxyphenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3e)



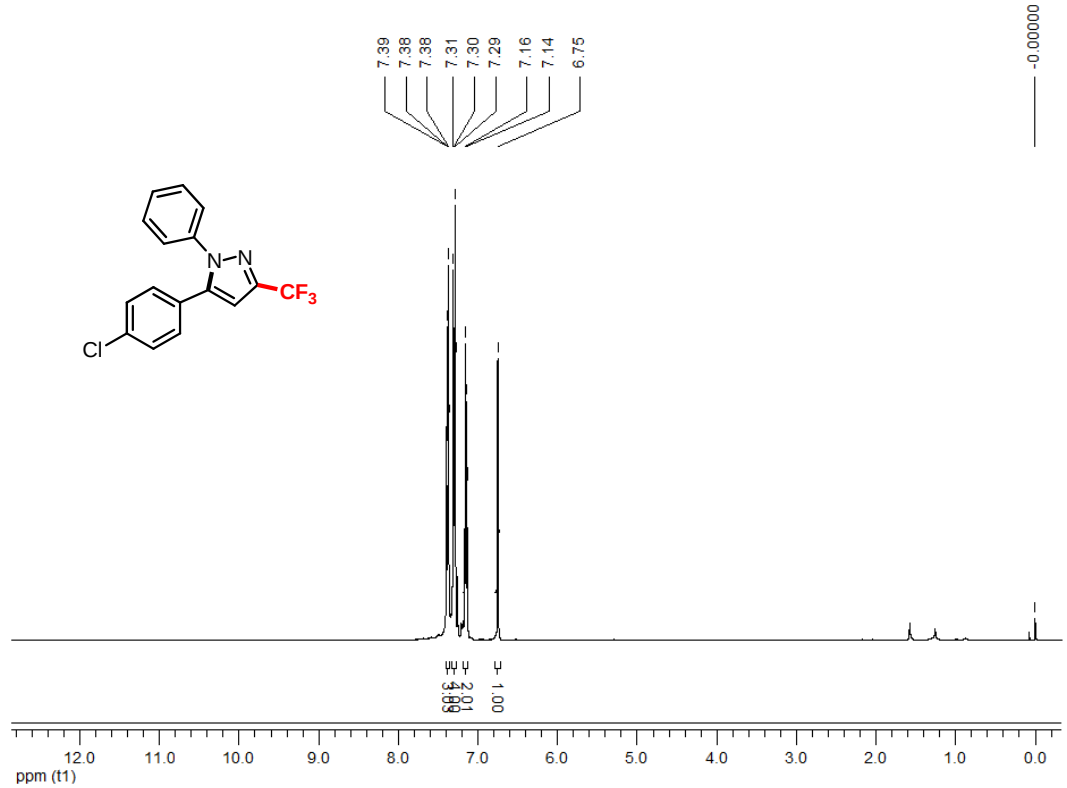
^{19}F NMR Spectrum of 5-(4-methoxyphenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3e)



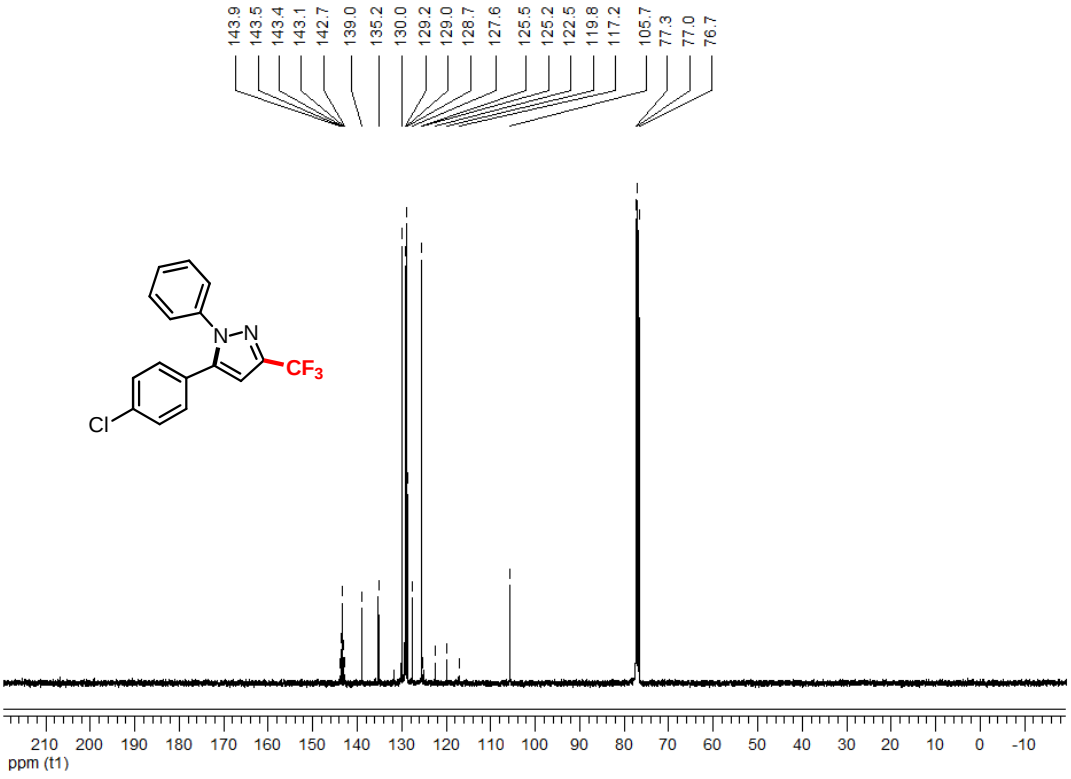
Mass Spectrum of 5-(4-methoxyphenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3e)



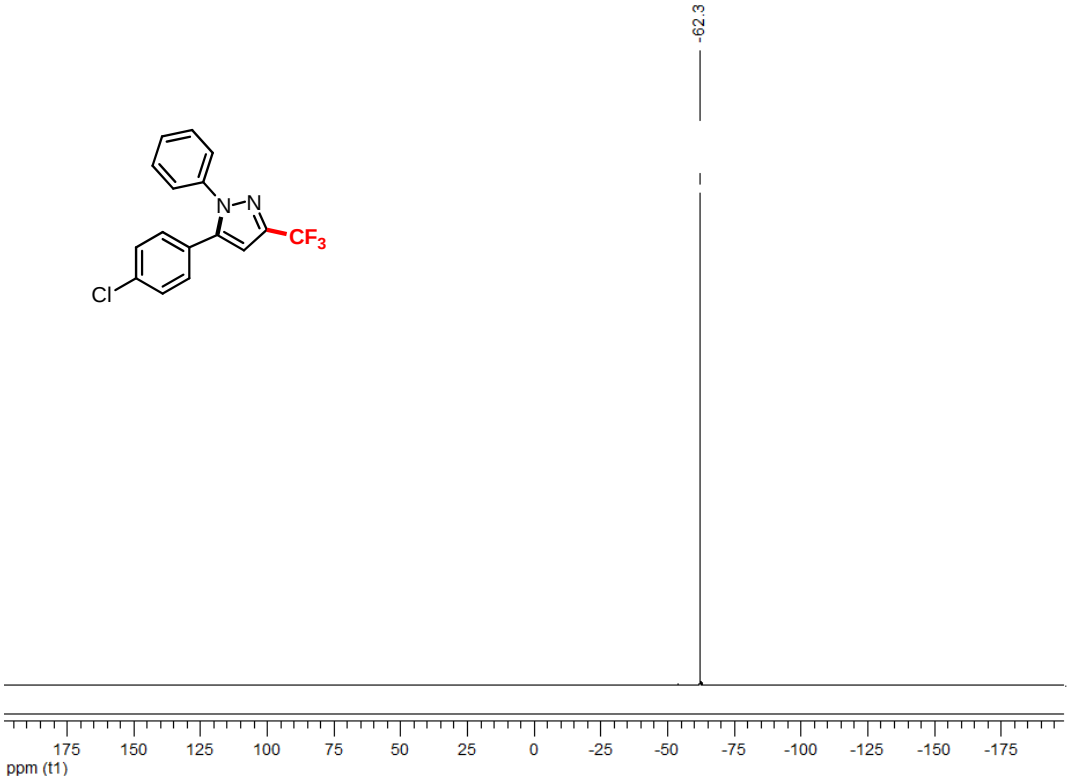
^{1}H NMR Spectrum of 5-(4-chlorophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3f)



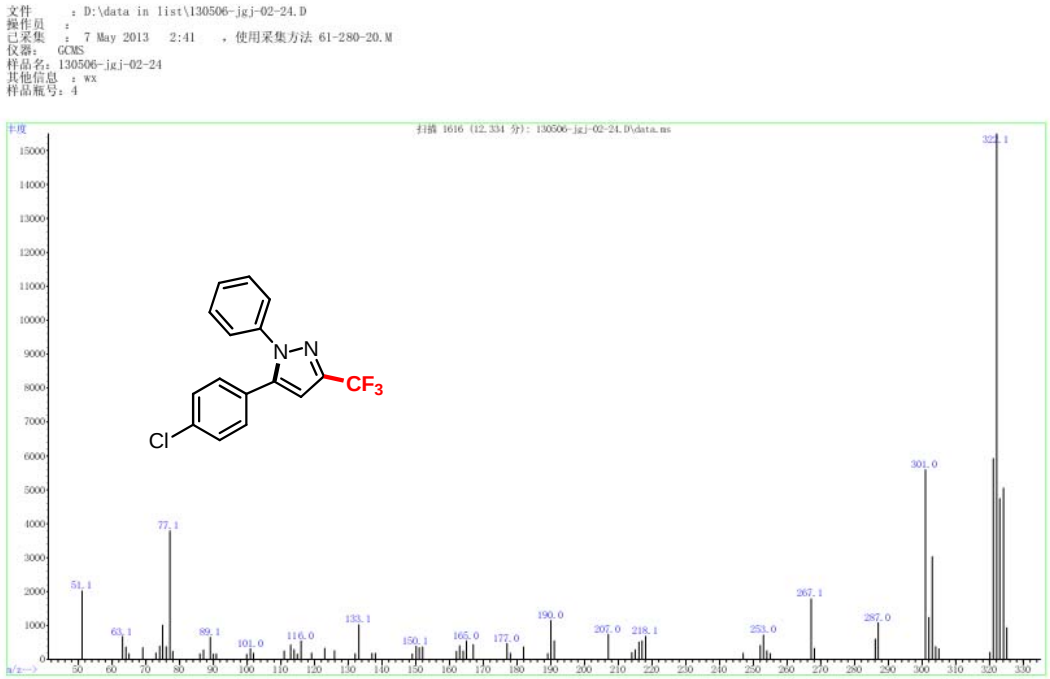
^{13}C NMR Spectrum of 5-(4-chlorophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3f)



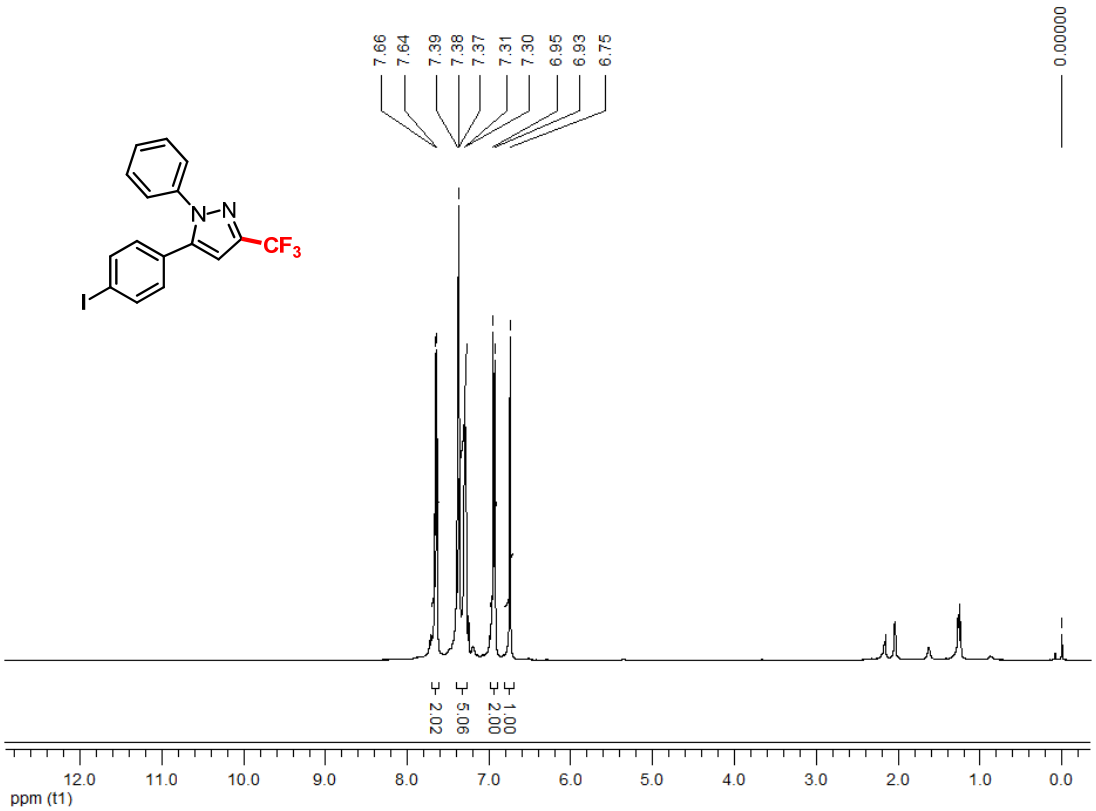
^{19}F NMR Spectrum of 5-(4-chlorophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3f)



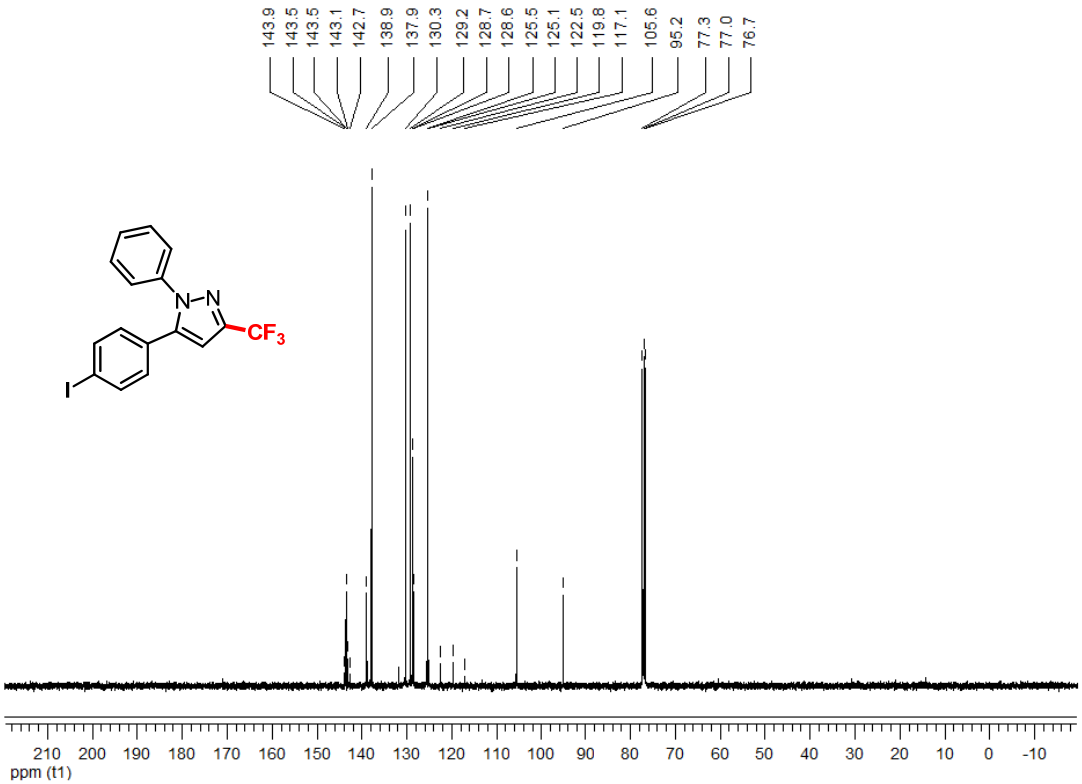
Mass Spectrum of 5-(4-chlorophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3f)



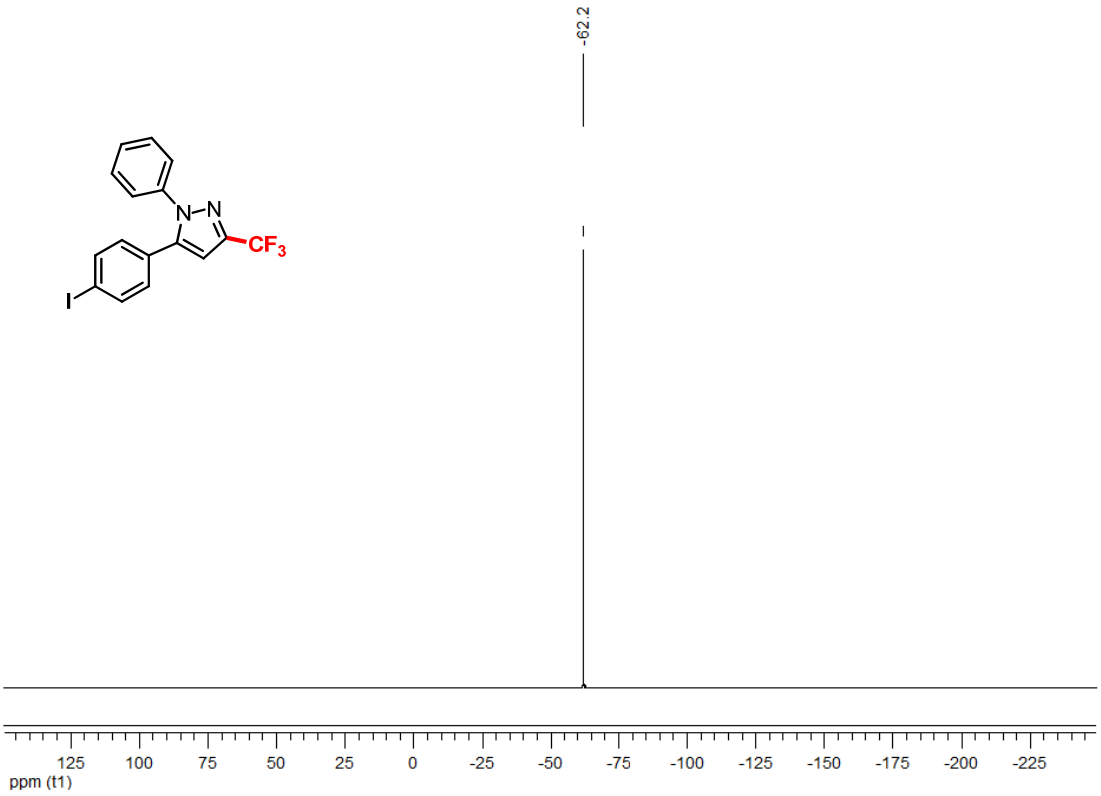
^{1}H NMR Spectrum of 5-(4-iodophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3g)



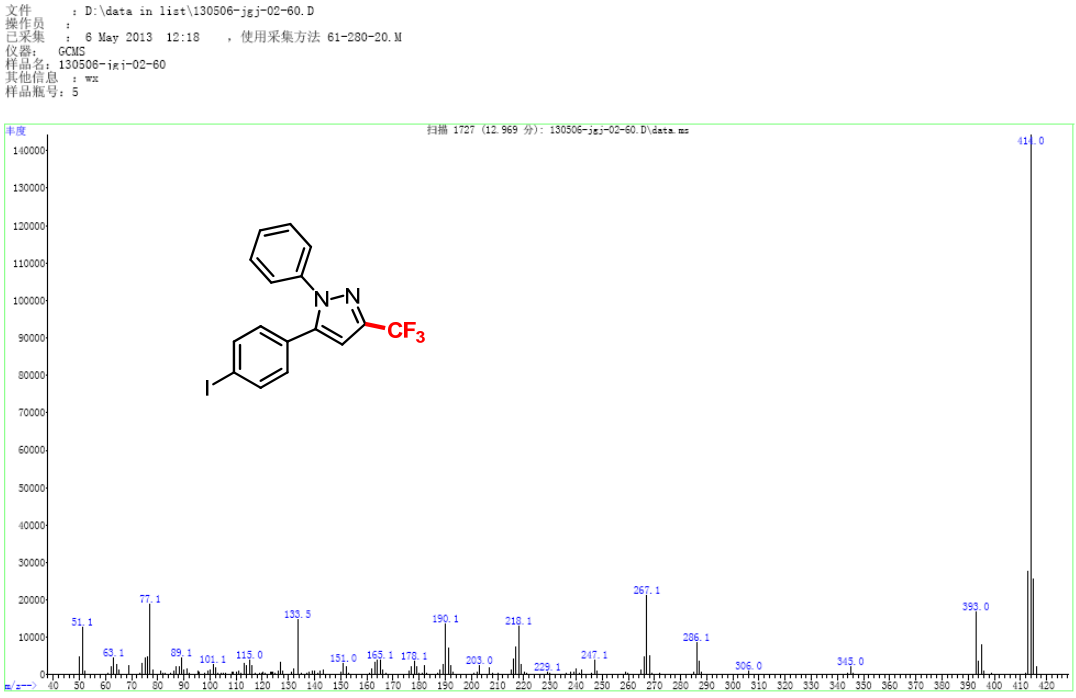
^{13}C NMR Spectrum of 5-(4-iodophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3g)



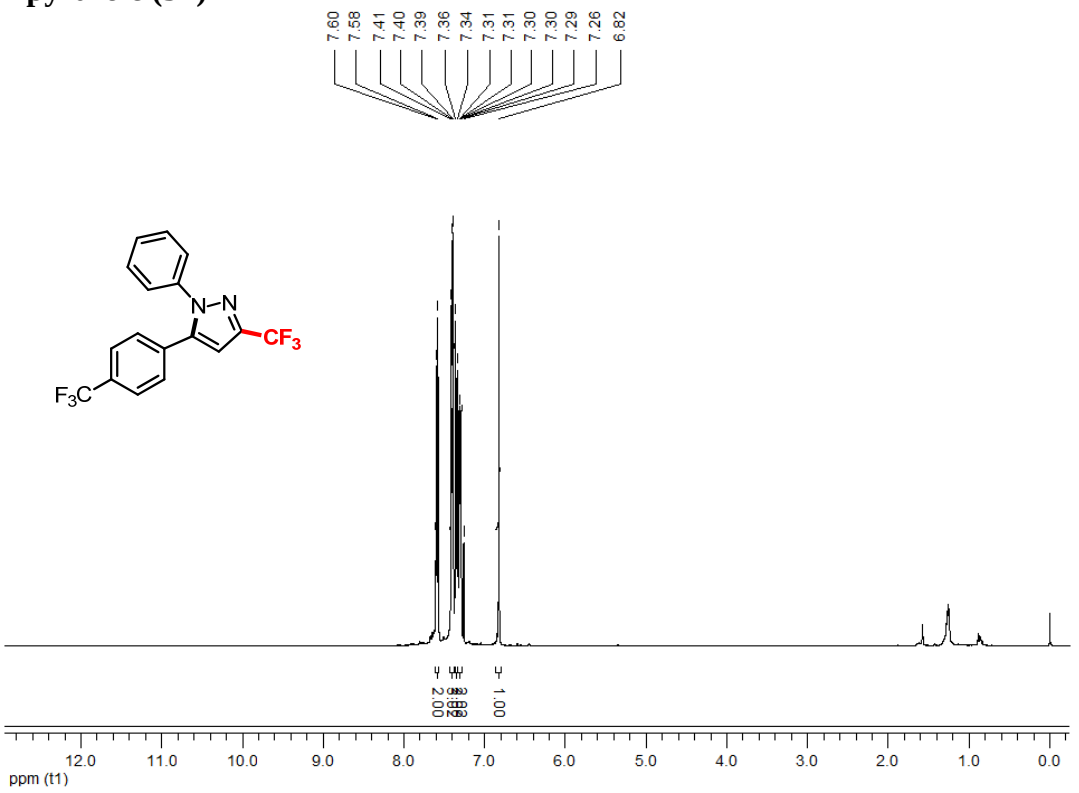
^{19}F NMR Spectrum of 5-(4-iodophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3g)



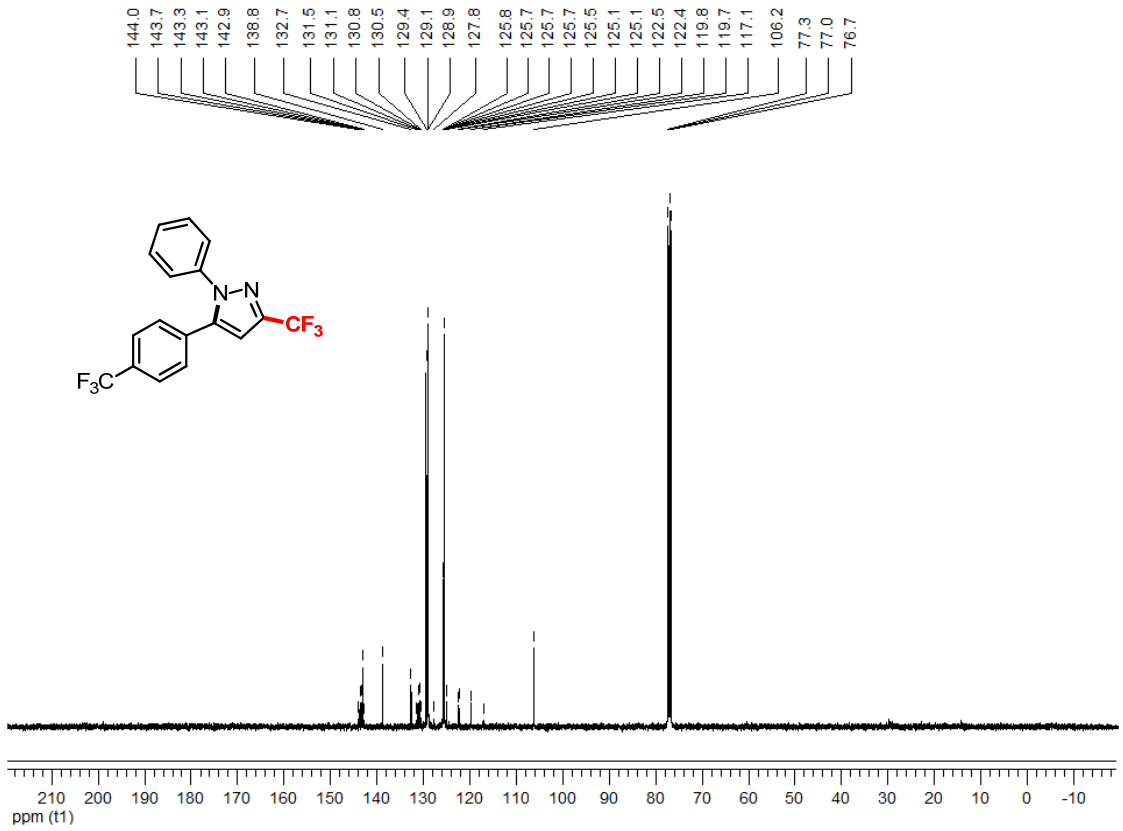
Mass Spectrum of 5-(4-iodophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3g)



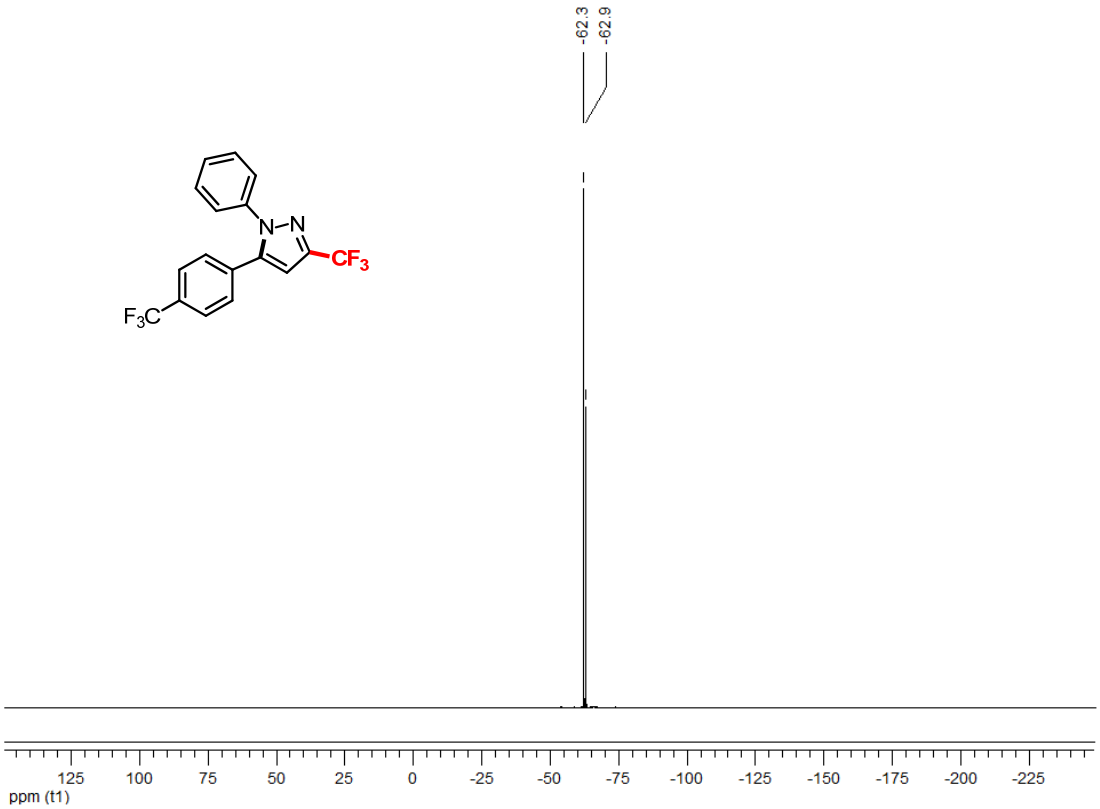
^{1}H NMR Spectrum of 1-phenyl-3-(trifluoromethyl)-5-(4-(trifluoromethyl)phenyl) -1*H*-pyrazole (3h)



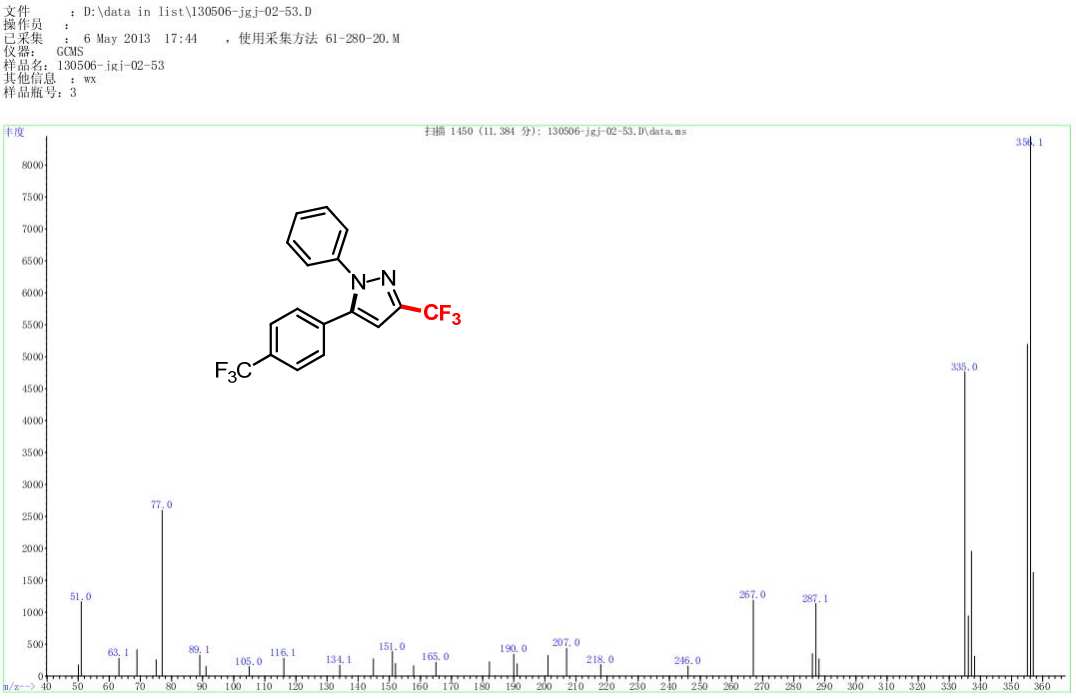
^{13}C NMR Spectrum of 1-phenyl-3-(trifluoromethyl)-5-(4-(trifluoromethyl)phenyl) -1*H*-pyrazole (3h)



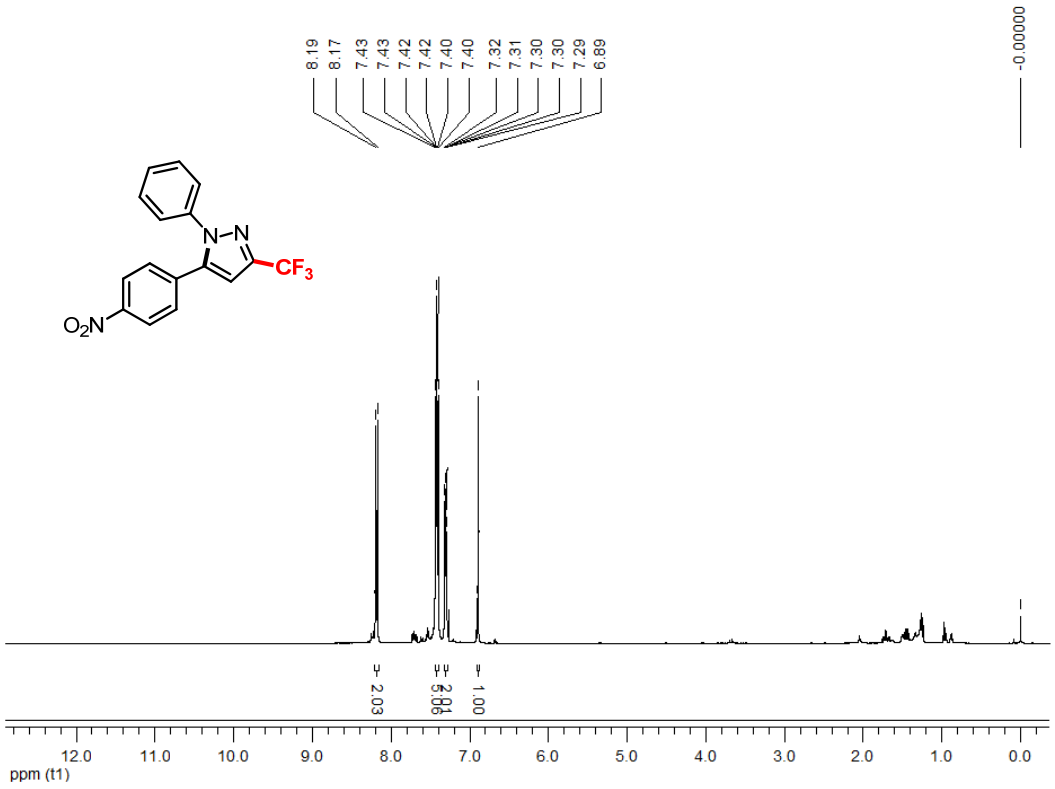
^{19}F NMR Spectrum of 1-phenyl-3-(trifluoromethyl)-5-(4-(trifluoromethyl)phenyl) -1*H*-pyrazole (3h)



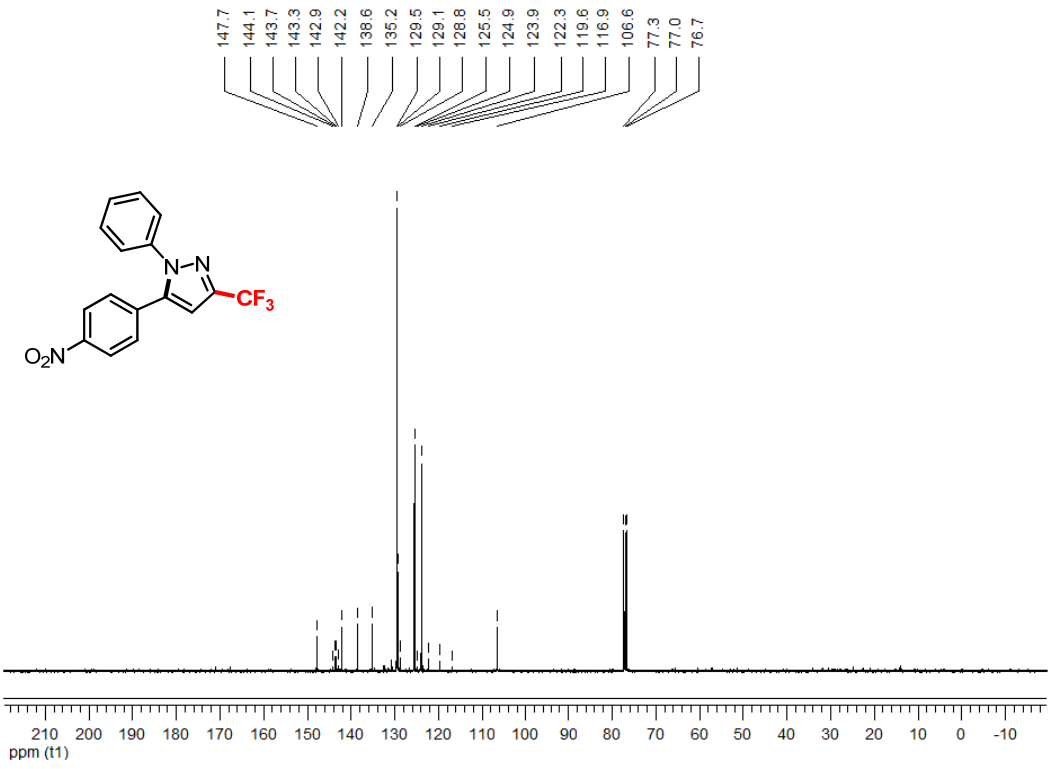
Mass Spectrum of 1-phenyl-3-(trifluoromethyl)-5-(4-(trifluoromethyl)phenyl) -1*H*-pyrazole (3h)



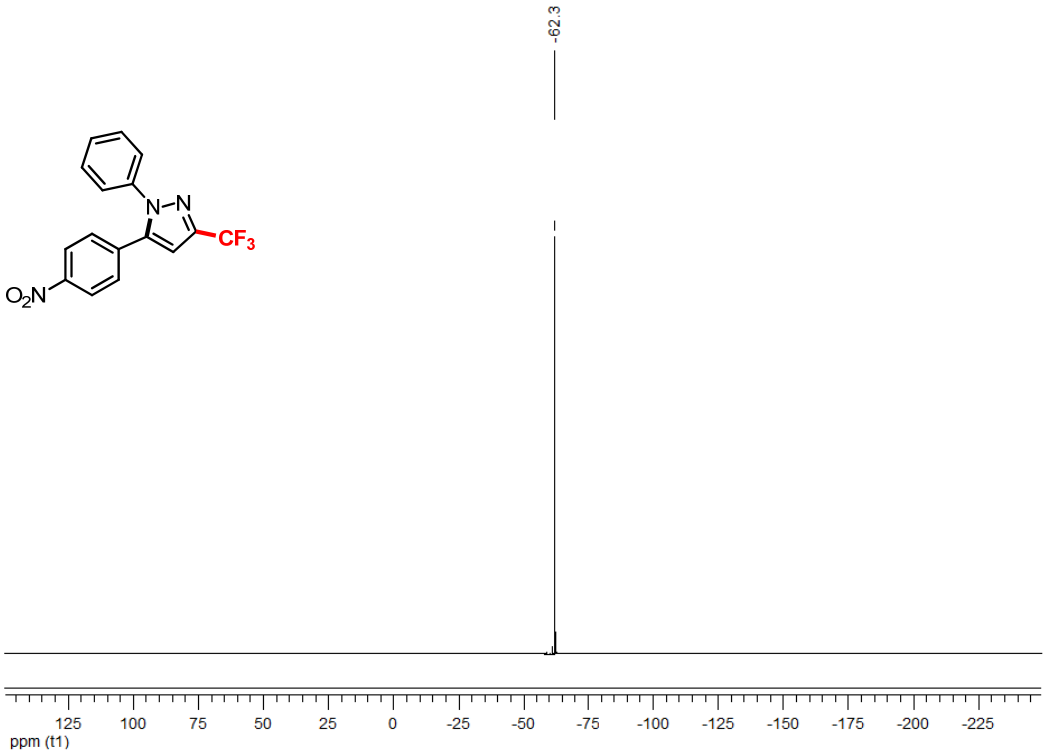
^{1}H NMR Spectrum of 5-(4-nitrophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3i)



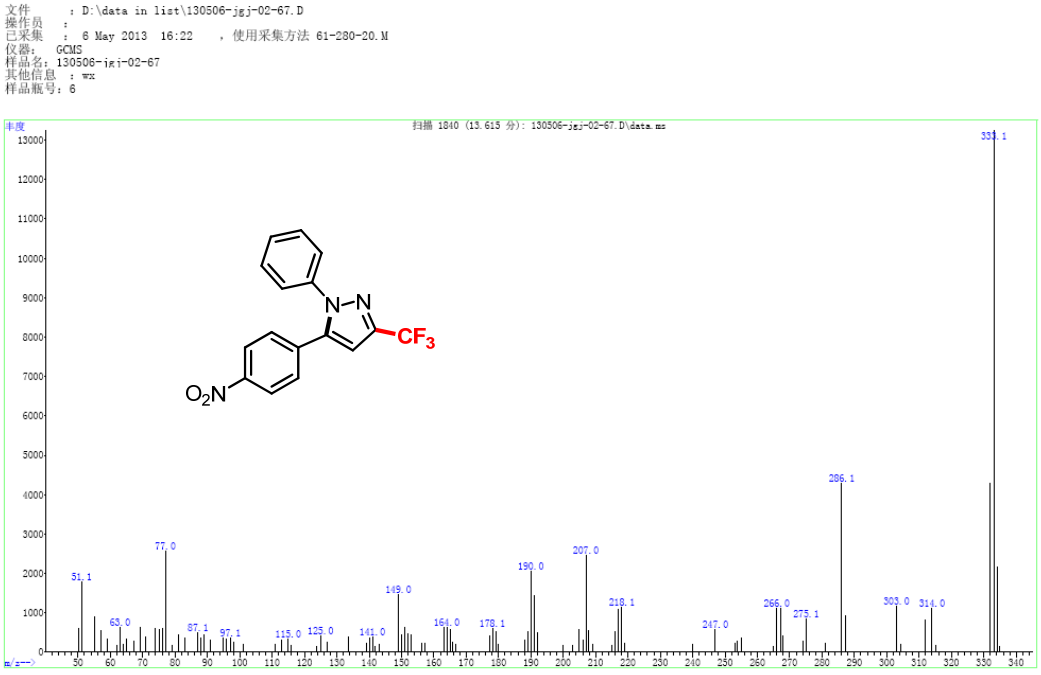
^{13}C NMR Spectrum of 5-(4-nitrophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3i)



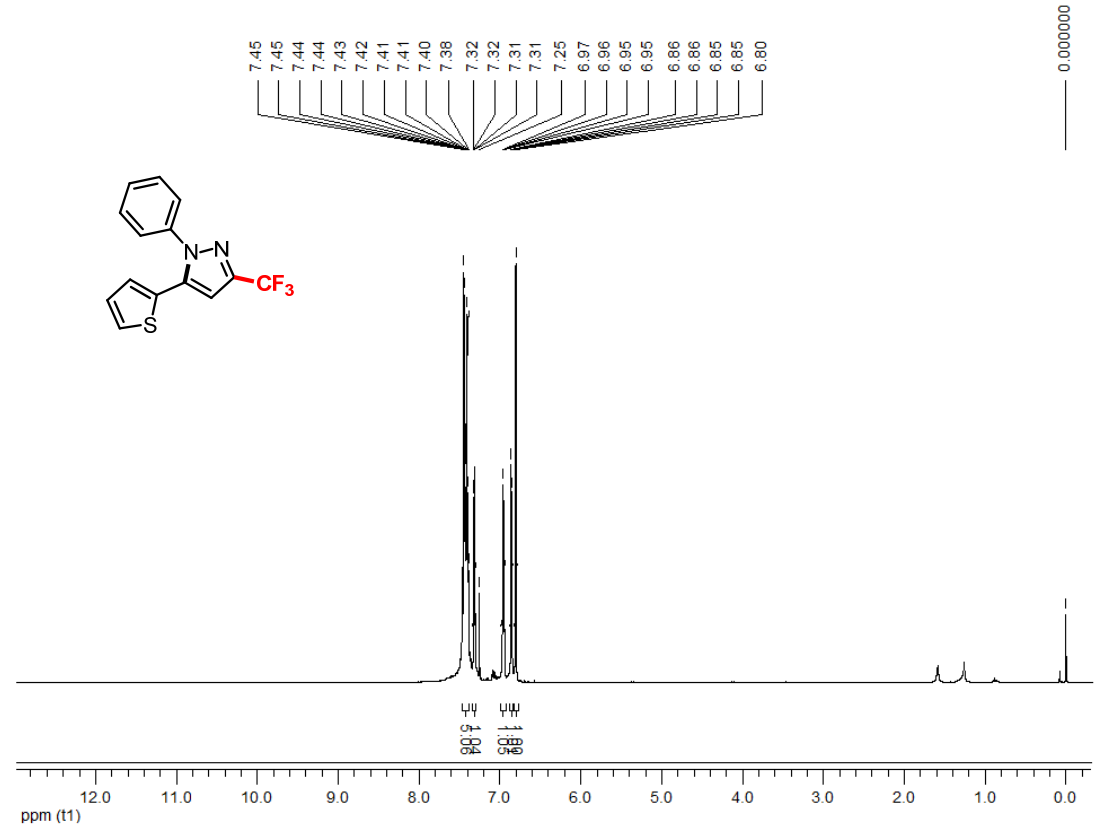
^{19}F NMR Spectrum of 5-(4-nitrophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*- pyrazole (3i)



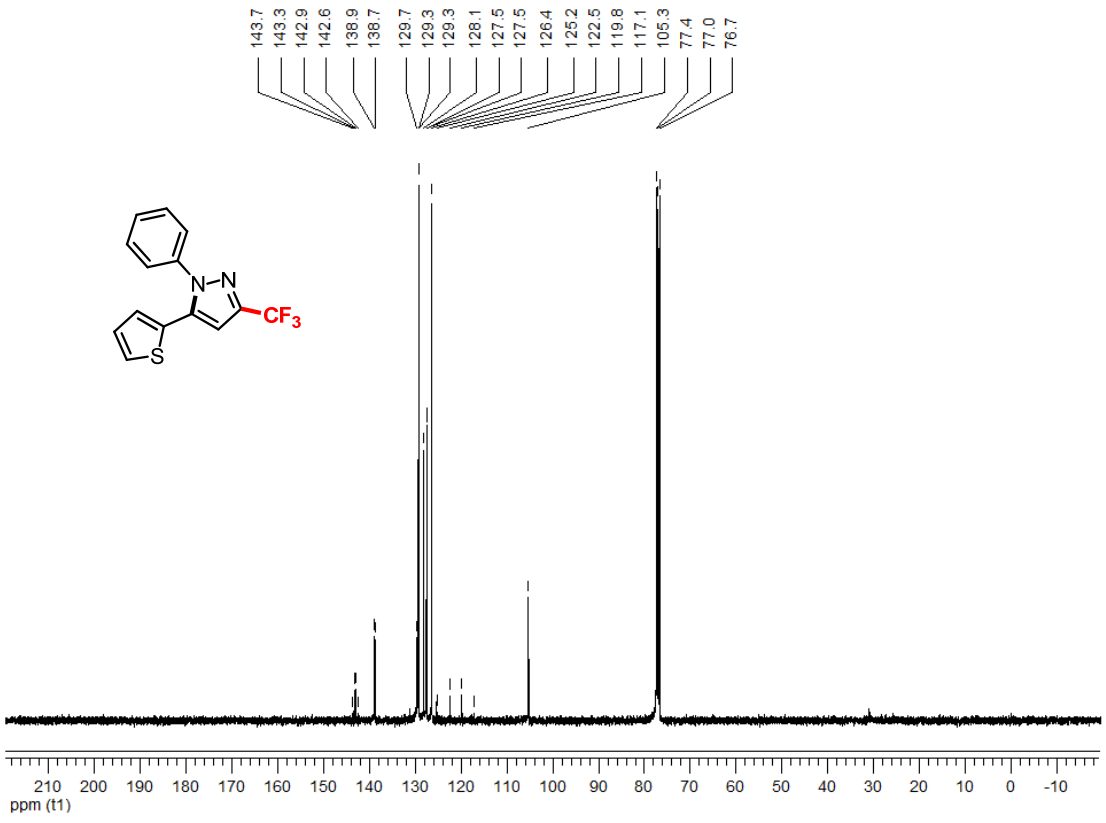
Mass Spectrum of 5-(4-nitrophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3i)



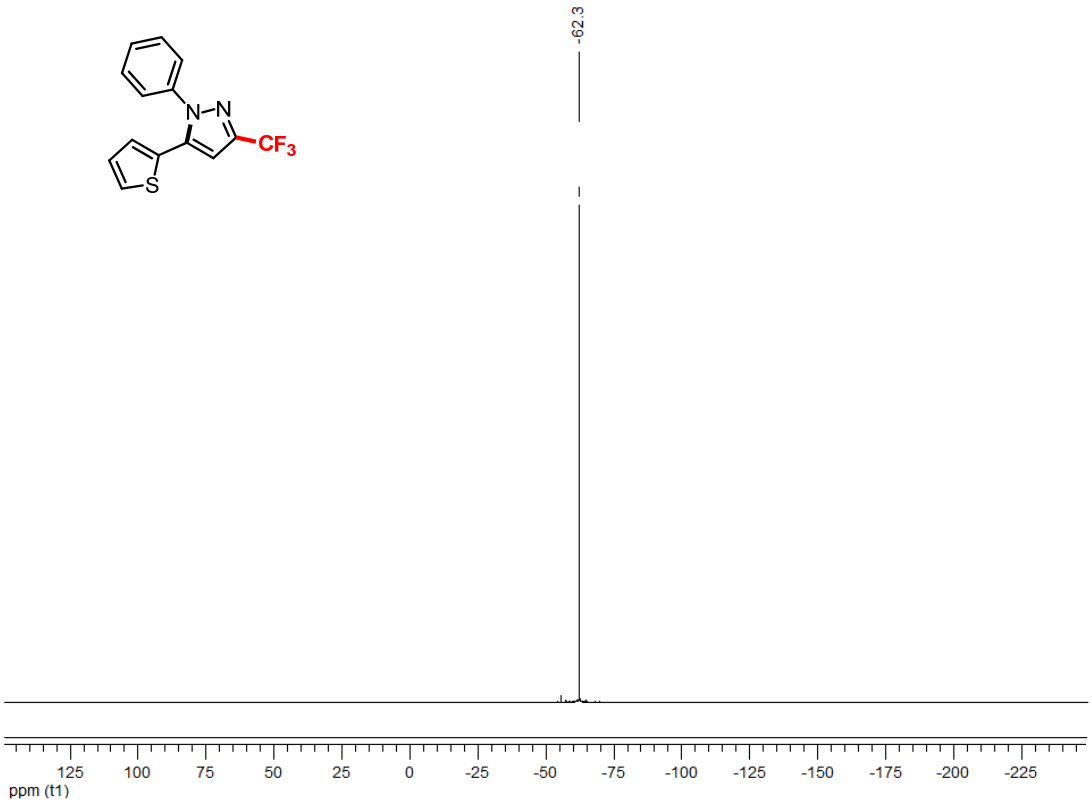
^{1}H NMR Spectrum of 1-phenyl-5-(thiophen-2-yl)-3-(trifluoromethyl)-1*H*- pyrazole (3j)



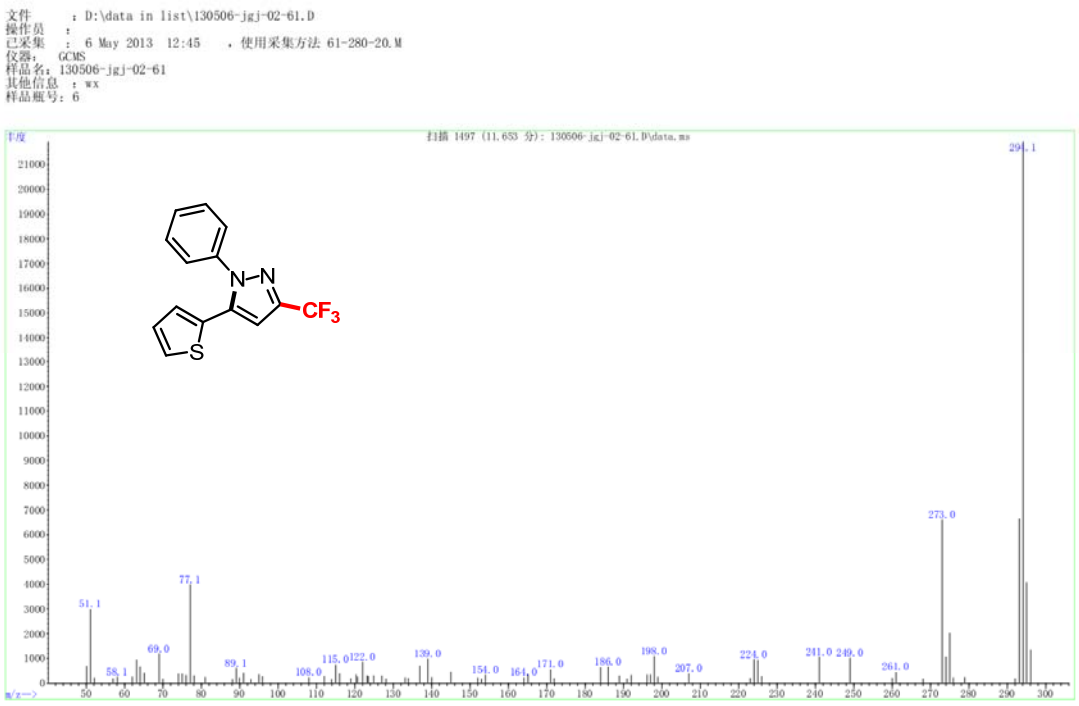
^{13}C NMR Spectrum of 1-phenyl-5-(thiophen-2-yl)-3-(trifluoromethyl)-1*H*- pyrazole (3j)



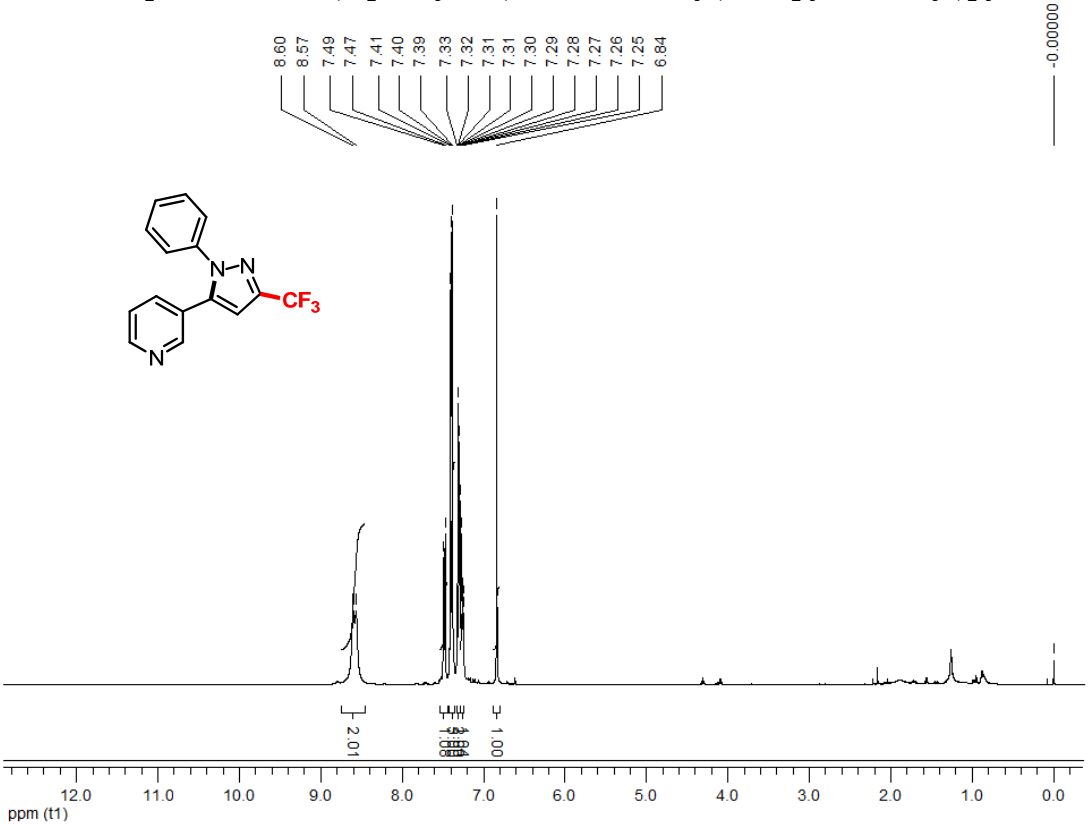
^{19}F NMR Spectrum of 1-phenyl-5-(thiophen-2-yl)-3-(trifluoromethyl)-1*H*- pyrazole (3j)



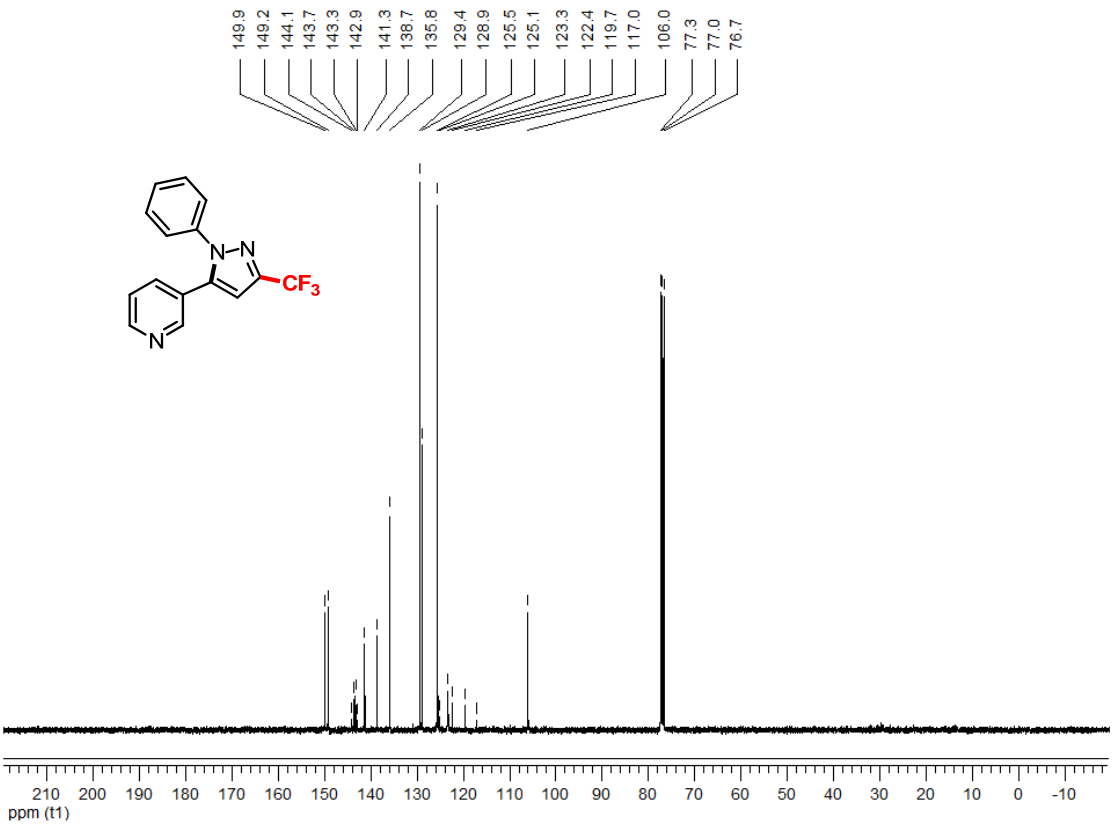
Mass Spectrum of 1-phenyl-5-(thiophen-2-yl)-3-(trifluoromethyl)-1*H*- pyrazole (3j)



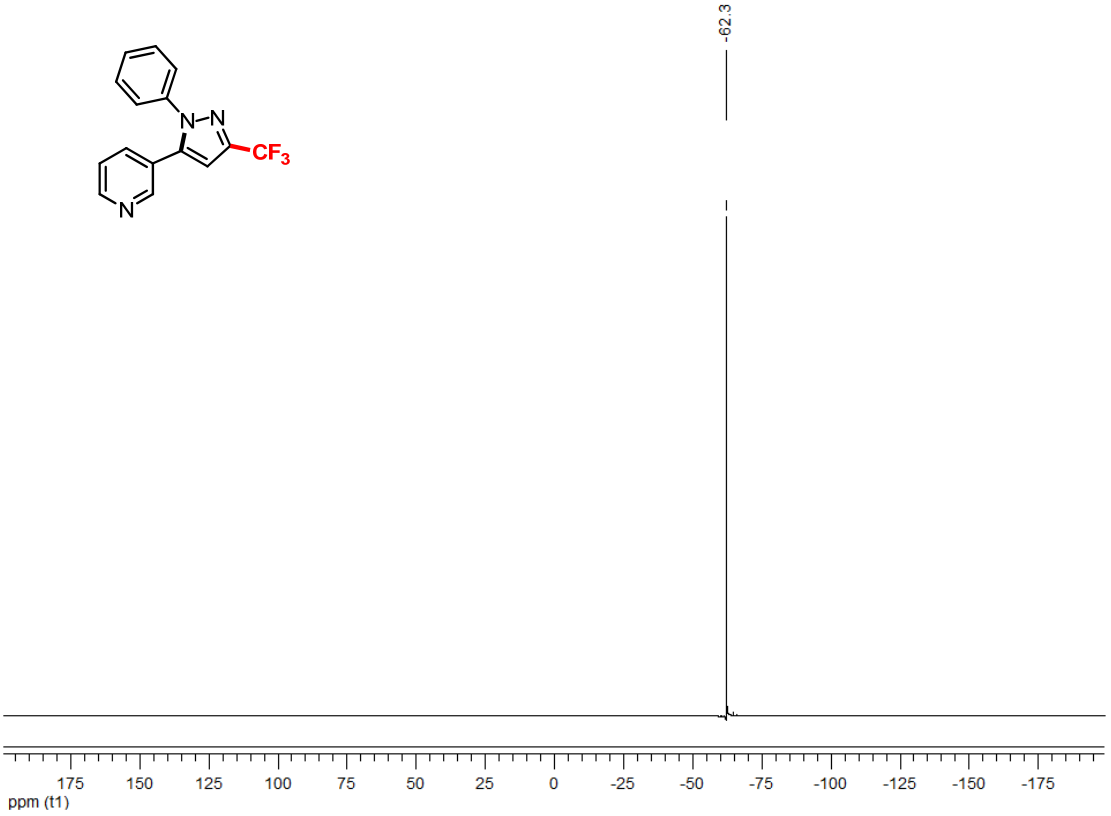
^{1}H NMR Spectrum of 3-(1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)pyridine (3k)



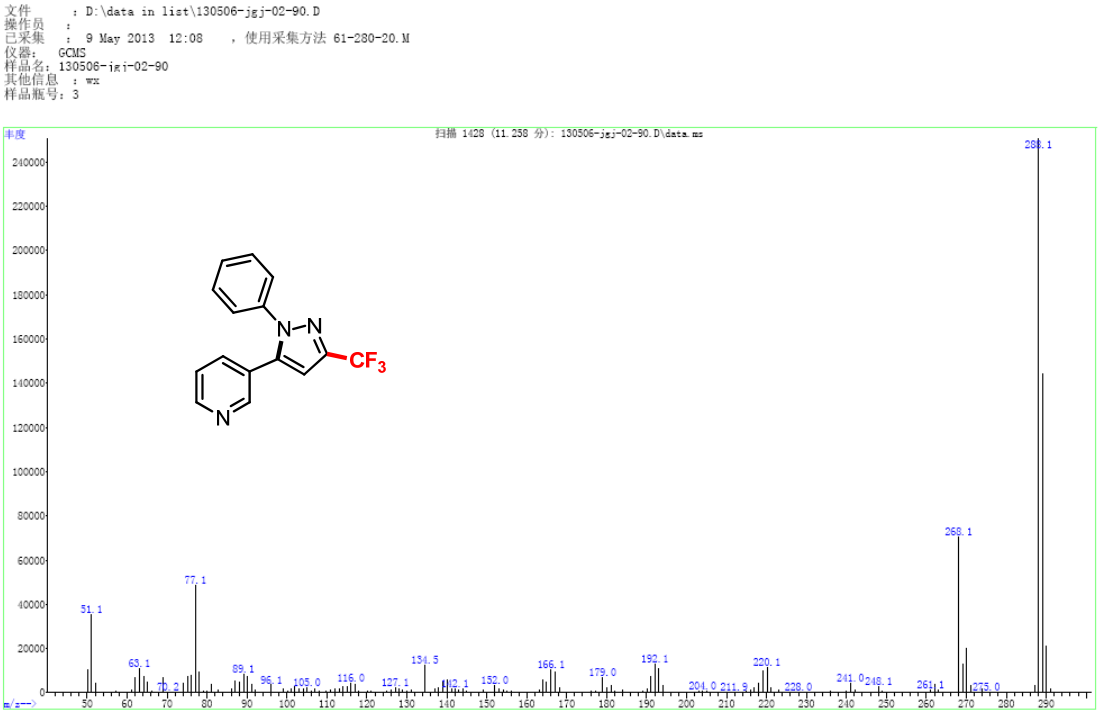
^{13}C NMR Spectrum of 3-(1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)pyridine (3k)



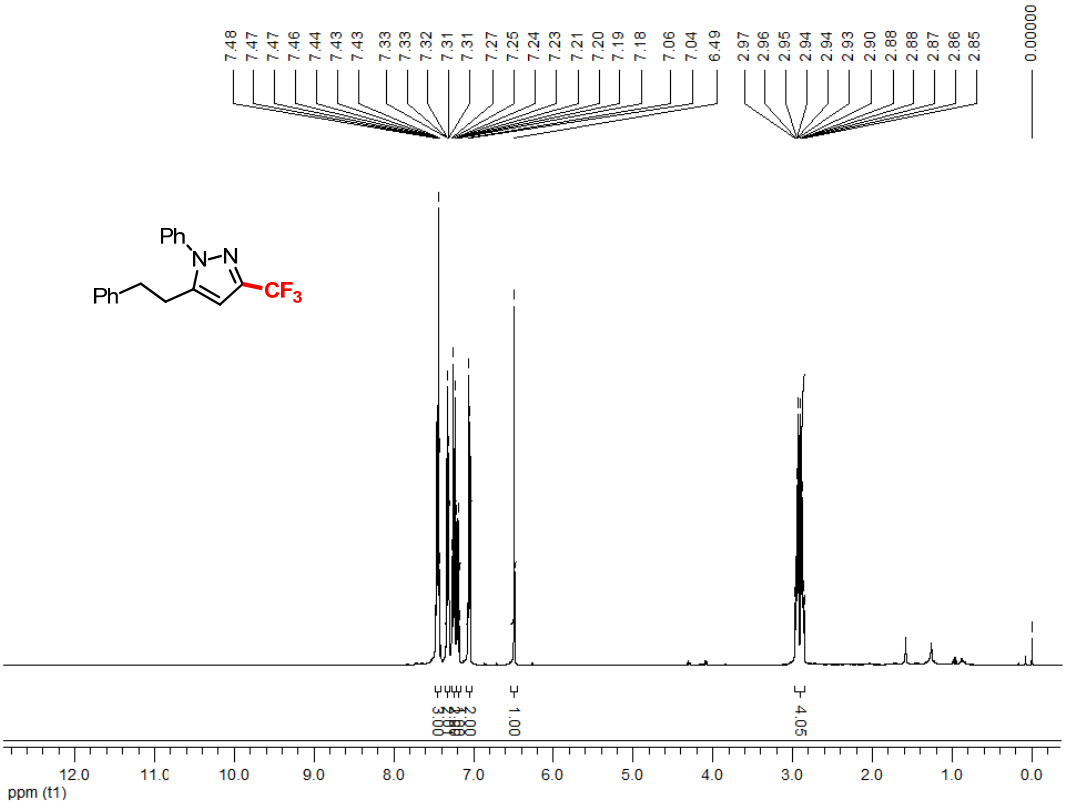
^{19}F NMR Spectrum of 3-(1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)pyridine (3k)



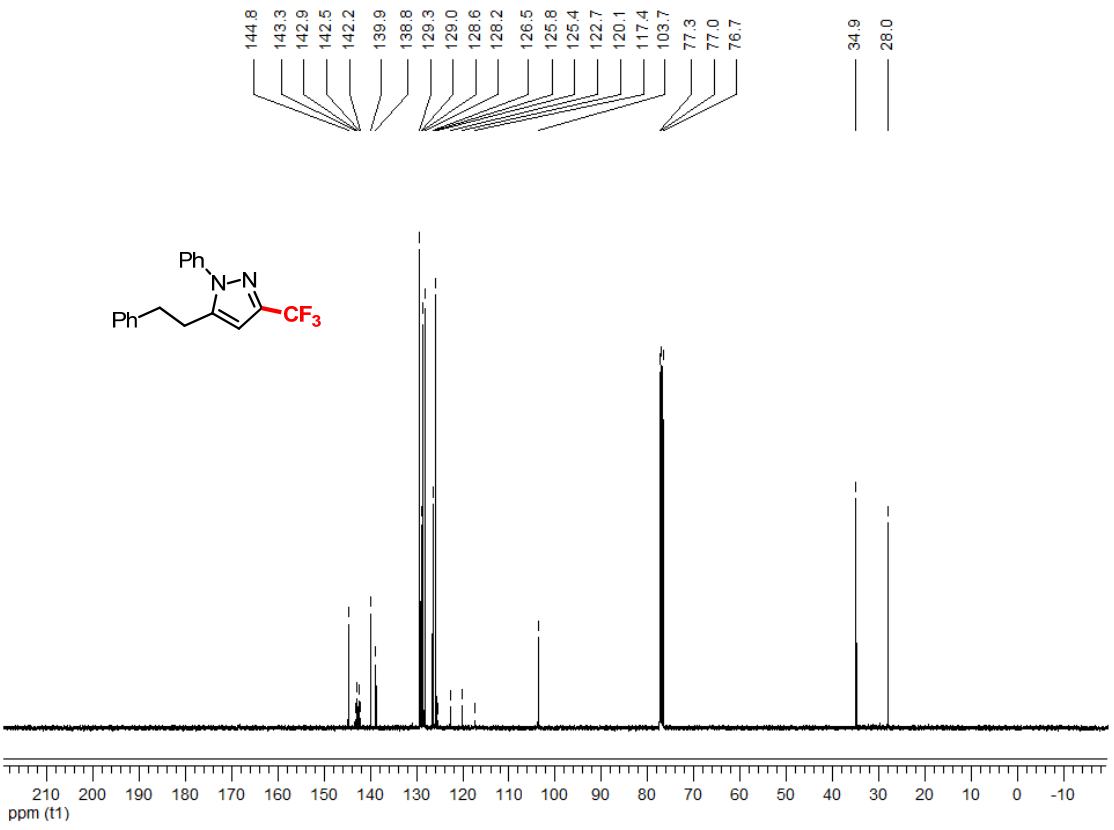
Mass Spectrum of 3-(1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)pyridine (3k)



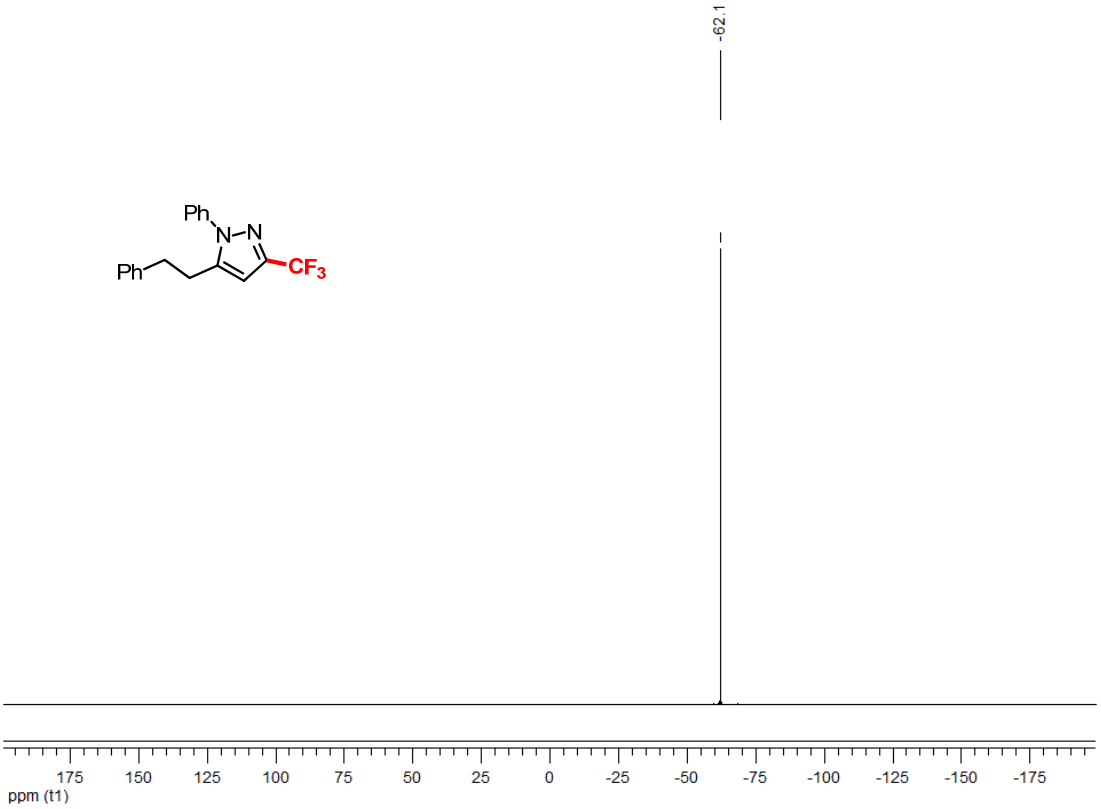
^{1}H NMR Spectrum of 5-phenethyl-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3l)



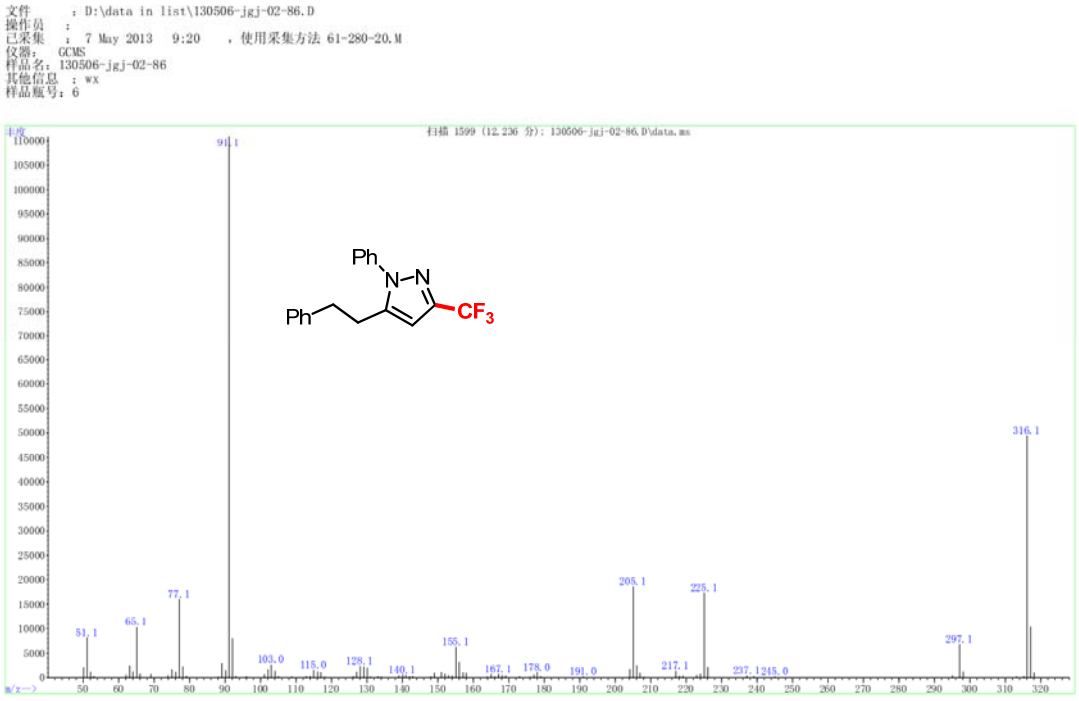
^{13}C NMR Spectrum of 5-phenethyl-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3l)



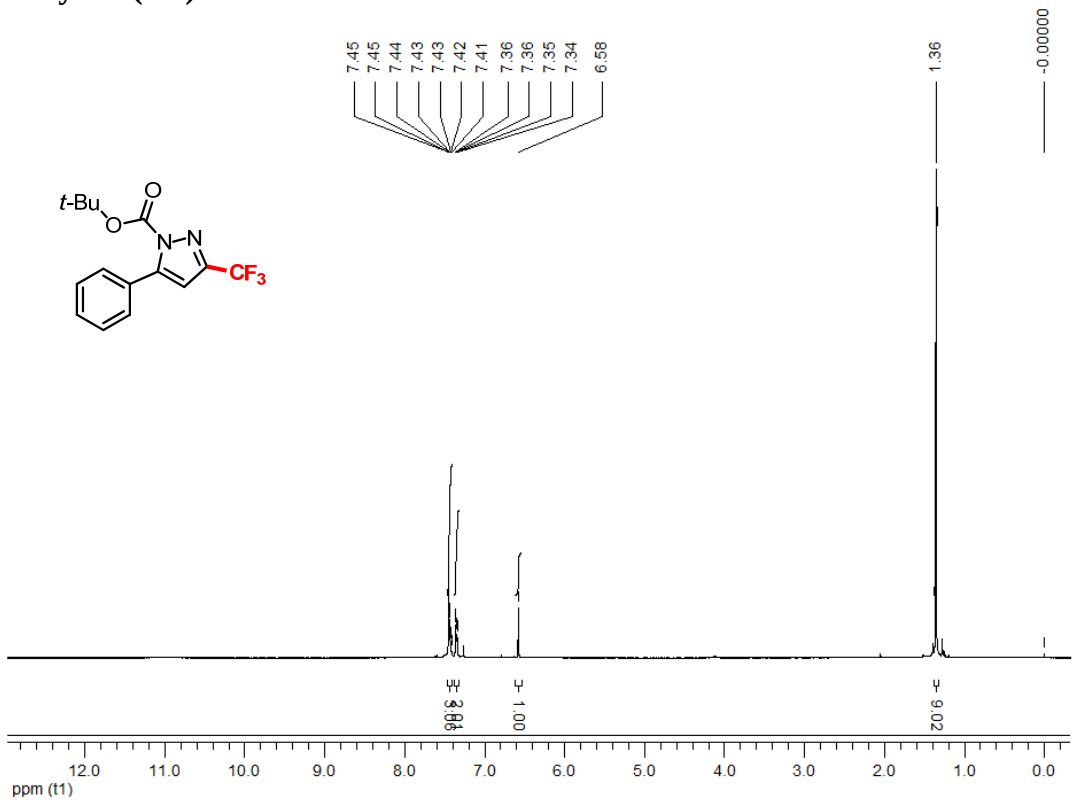
^{19}F NMR Spectrum of 5-phenethyl-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3l)



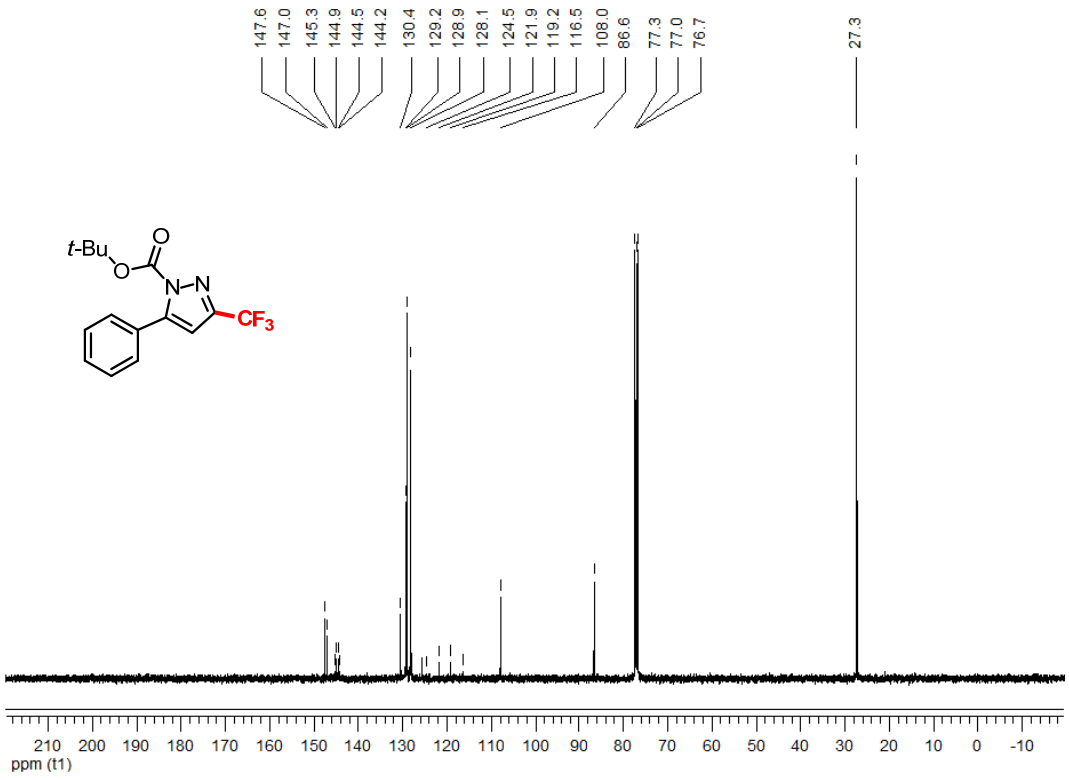
Mass Spectrum of 5-phenethyl-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (3l)



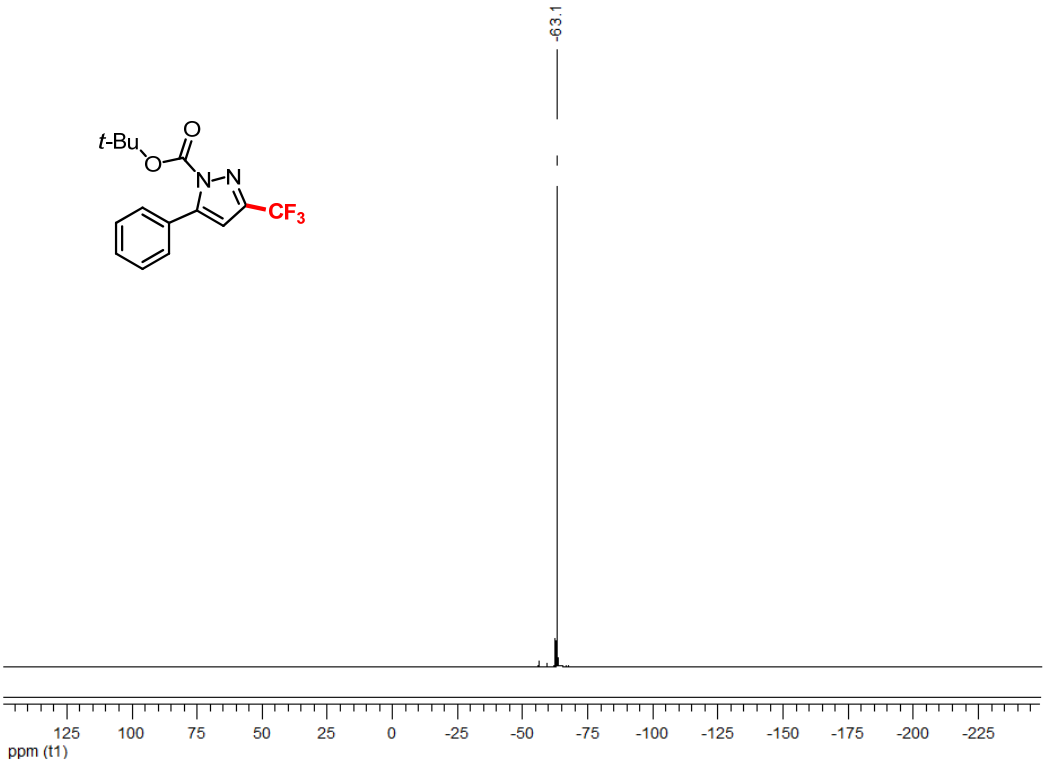
^{1}H NMR Spectrum of *tert*-butyl 5-phenyl-3-(trifluoromethyl)-1*H*-pyrazole-1-carboxylate (3m)



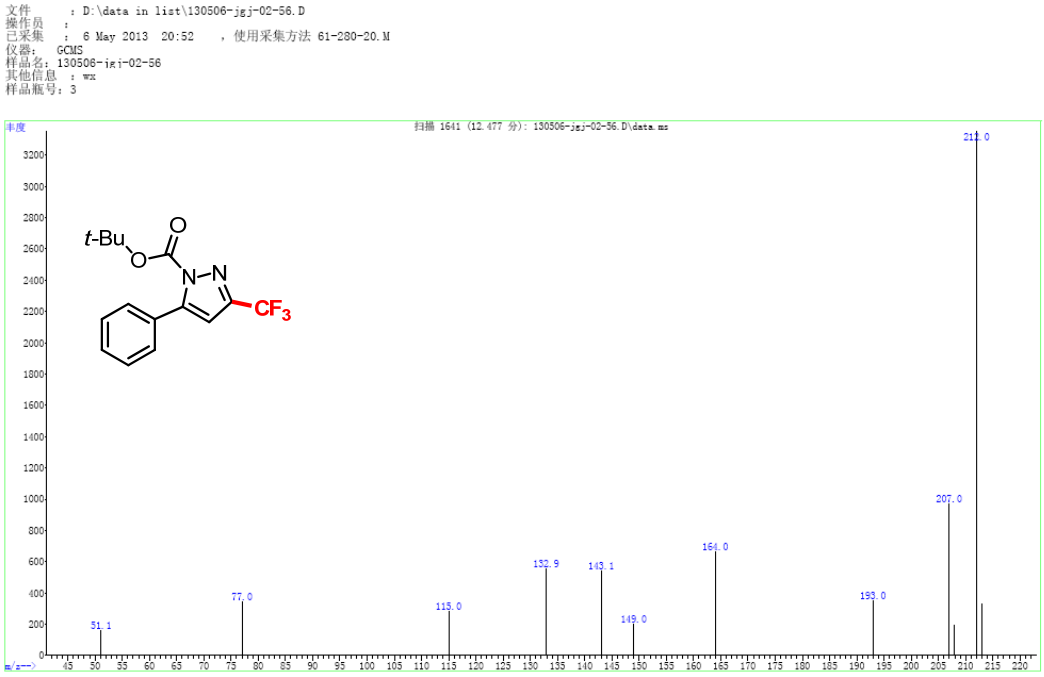
^{13}C NMR Spectrum of *tert*-butyl 5-phenyl-3-(trifluoromethyl)-1*H*-pyrazole-1-carboxylate (3m)



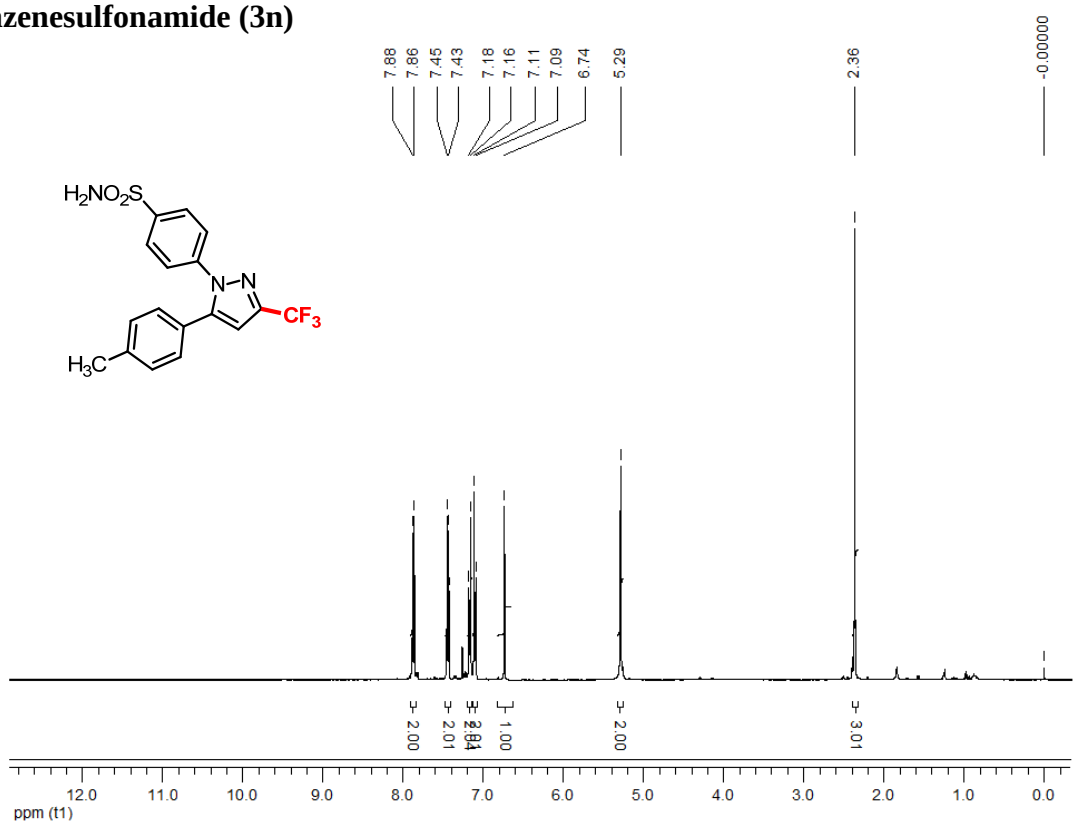
^{19}F NMR Spectrum of *tert*-butyl 5-phenyl-3-(trifluoromethyl)-1*H*-pyrazole-1-carboxylate (3m)



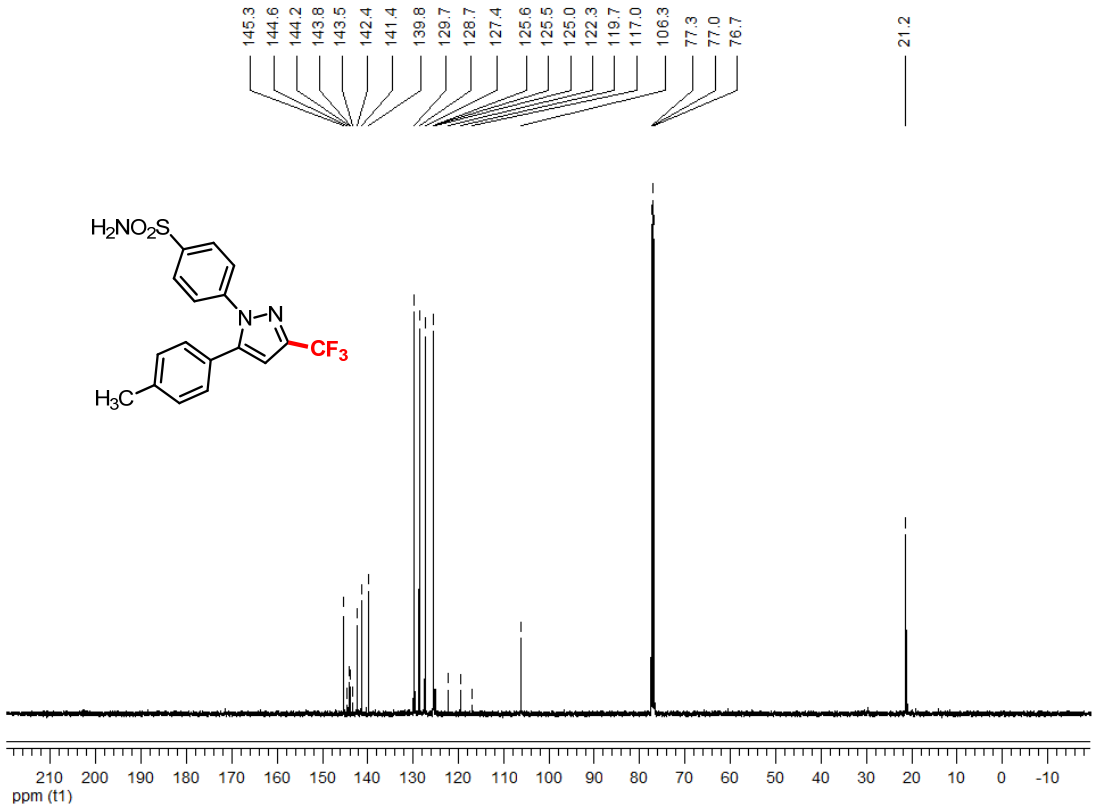
Mass Spectrum of *tert*-butyl 5-phenyl-3-(trifluoromethyl)-1*H*-pyrazole-1- carboxylate (3m)



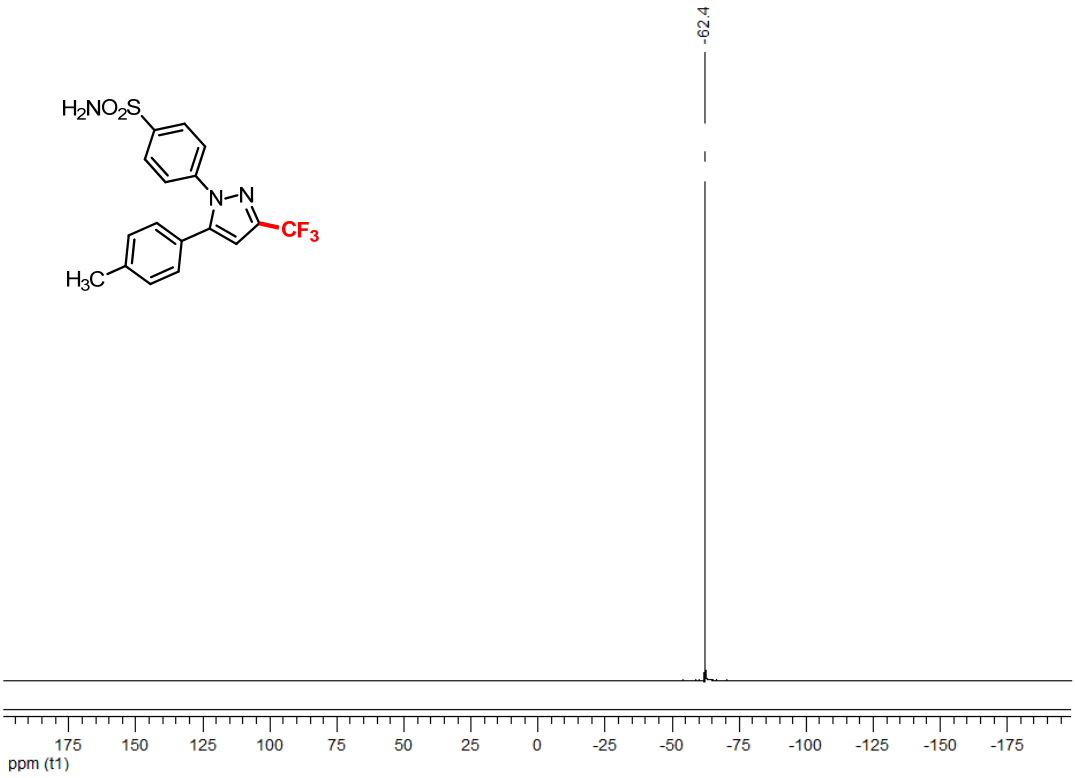
^{1}H NMR Spectrum of 4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl) benzenesulfonamide (3n)



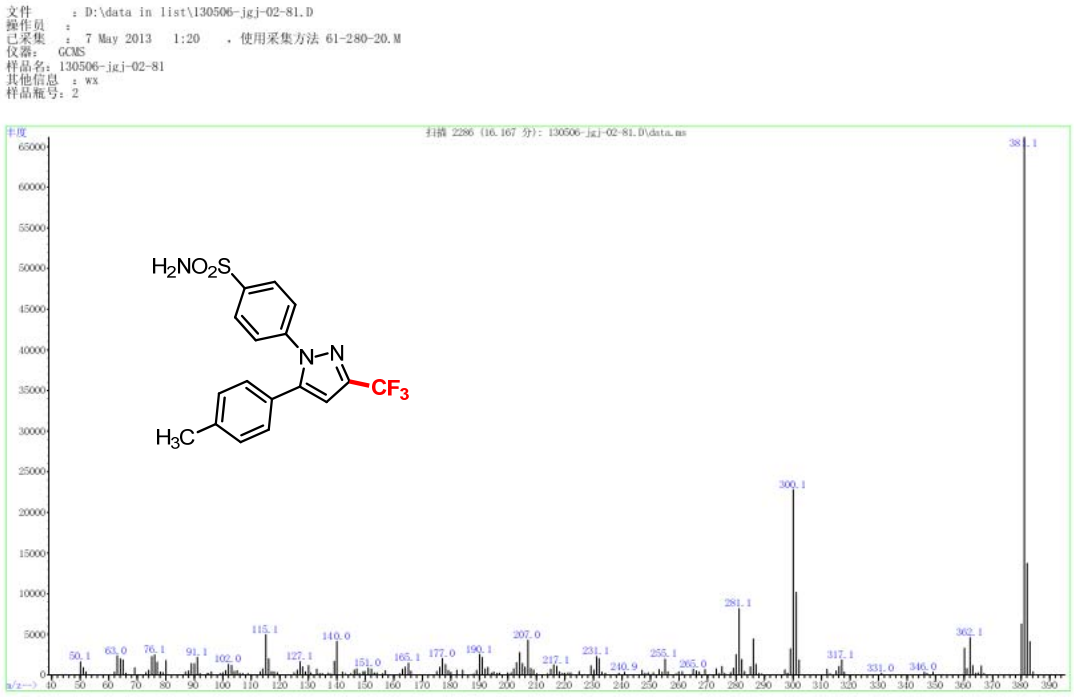
^{13}C NMR Spectrum of 4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl) benzenesulfonamide (3n)



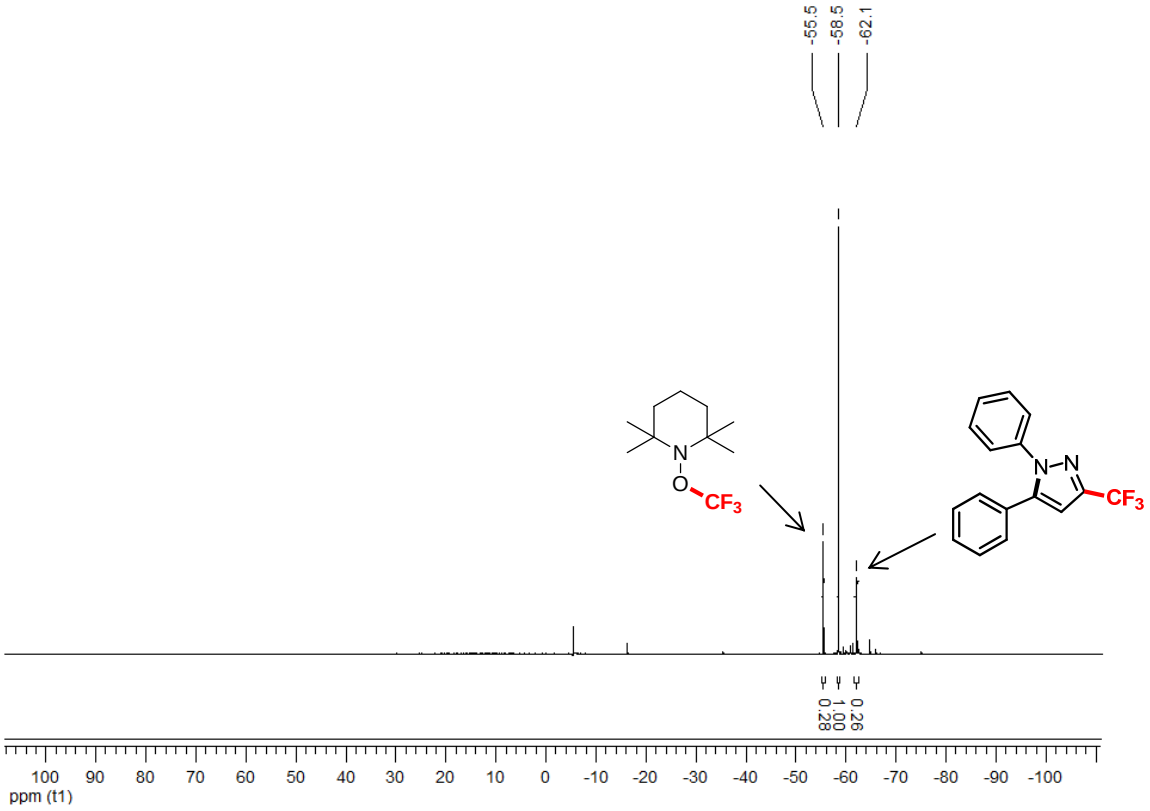
^{19}F NMR Spectrum of 4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl) benzenesulfonamide (3n)



Mass Spectrum of 4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl) benzenesulfonamide (3n)



^{19}F NMR Spectrum of crude product of TEMPO trapping experiments



8. References

1 F. Romanov-Michailidis, C. Besnard and A. Alexakis, *Org. Lett.* 2012, **14**, 4906.

2 Y. H. Zhang and Y. J. Xie, *Faming Zhuanli Shenqing*, 101898948, 01 Dec 2010.

3 E. V. Tretyakov, A. V. Tkachev, T. V. Rybalova, Y. V. Gatilov, D. W. Knight and S. F. Vasilevsky, *Tetrahedron*, 2000, **56**, 10075.

4 J. K. Fang, D. L. An, K. Wakamatsub, T. Ishikawab, T. Iwanagab, S. Toyotab, S. Akitac, D. Matsuoc, A. Oritac and J. Oterac, *Tetrahedron*, 2010, **66**, 5479.

5 A. Nowak-Król, B. Koszarna, S. Y. Yoo, J. Chromiński, M. K. Węcławski, C. H. Lee and D. T. Gryko, *J. Org. Chem.* 2011, **76**, 2627.

6 S. P. Park, S. H. Ahn and K. J. Lee, *Tetrahedron*, 2010, **66**, 3490.

7 K. Y. Lee, M. J. Lee, S. GowriSankar and J. N. Kim *Tetrahedron Lett.* 2004, **45**, 5043.

8 K. Stanek, R. Koller and A. Togni, *J. Org. Chem.* 2008, **73**, 7678.

9 I. Kieltsch, P. Eisenberger and A. Togni, *Angew. Chem. Int. Ed.* 2007, **46**, 754.

10 C. A. Dvorak, D. A. Rudolph, S. Ma and N. I. Carruthers, *J. Org. Chem.* 2005, **70**, 4188.

11 J. C. Sloop, C. L. Bumgardner and W. D. Loehle, *J. Fluorine Chem*. 2002, **118**, 135.

12 S. P. Singh, V. Kumar and R. Aggarwal, *J. Heterocyclic Chem*. 2006, **43**, 1003.

13 M. Gao, M. Wang, K. D. Miller, Q.-H. Zheng, *Eur. J. Med. Chem*. 2011, **46**, 4760.