Supporting Information

Regioselective [3+2] Cycloaddition of Di/trifluoromethylated Hydrazonoyl Chlorides with Fluorinated Nitroalkenes: A Facile Access to 3-Di/trifluoroalkyl-5-fluoropyrazoles

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1. General Considerations

General Analytical Information. ^{1}H, ^{13}C, and ^{19}F nuclear magnetic resonance (NMR) spectroscopy were performed on a Bruker AV 400 MHz instrument at 400 MHz (^{1}H NMR), 100 MHz (^{13}C NMR), and 376 MHz (^{19}F NMR), or on a Bruker AV 600 MHz instrument at 600 MHz (^{1}H NMR) and 565 MHz (^{19}F NMR). All ^{1}H NMR spectra were referenced to tetramethylsilane (TMS, 0 ppm), or the residual proton signals of d_1-chloroform ($CDCl_3$, 7.26 ppm) or dimethyl sulfoxide-d_6 (DMSO-d_6, 2.50 ppm) and were reported in parts per million (ppm). All ^{13}C NMR spectra were referenced to the residual carbon signals of $CHCl_3$ (77.16 ppm) or DMSO-d_6 (39.52 ppm) and were obtained with ^{1}H decoupling. Coupling constants (*J*) were reported in hertz (Hz) and the multiplicity of signals was denoted as s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), and m (multiplet). High-resolution mass spectrometry (HRMS) spectra were recorded on a Bruker microOTOF-QII instrument. Single-crystal X-ray diffraction (SCXRD) experiments were carried out at 100(2) K using a Bruker D8 VENTURE diffractometer equipped with Mo-Kα radiation (λ = 0.71073 Å). The melting points of compounds were determined using a SGW X-4A digital melting point apparatus and were reported without correction. Thin-layer chromatography (TLC) was performed on precoated GF254 silica gel plates (Qingdao Marine Chemical Inc.), and compounds were visualized using UV light at 254 nm. Flash chromatography was employed to purify compounds using silica gel (200–300 mesh, Qingdao Marine Chemical Inc.).

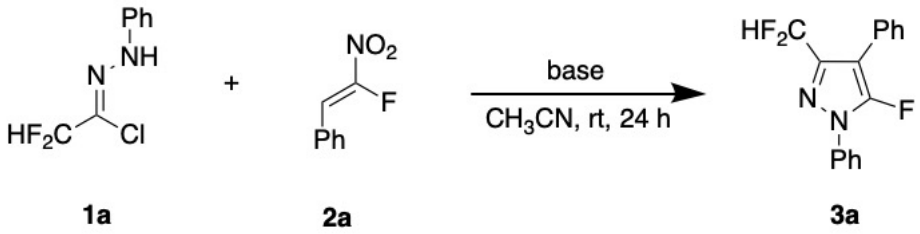
General Reagents Information. Tetrahydrofuran (THF), acetonitrile, and toluene were subjected to a distillation process involving sodium/benzophenone, while CH_2Cl_2 underwent a similar distillation procedure utilizing CaH_2. All purchased reagents were used without further purification. Analytical thin layer chromatography was performed on 0.20 mm Qingdao Haiyang silica gel plates. Silica gel (200–300mesh) (from Qingdao Haiyang Chem. Company, Ltd.) was used for flash chromatography.

General Manipulation Considerations. The eluents employed for column

chromatography are presented in volumetric ratios of solvents. The reported yields in the publication represent isolated yields, unless otherwise specified. The newly synthesized starting materials and resulting products underwent characterization using ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectroscopies, as well as high-resolution mass spectrometry (HRMS).

2. Experimental Procedures

2.1 Screening reaction conditions for the formation of 3a



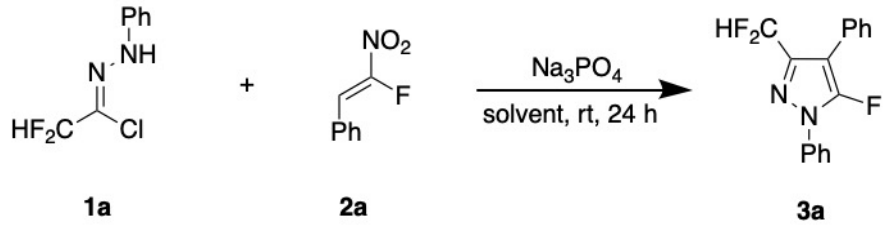
1a **2a** **3a**

Table S1. Screening of bases

Entry[a]	Base	Yield (%)[b]
1	2,6-lutidine	NR
2	DMAP	trace
3	NaH	5
4	NaOH	ND
5	^{t}BuONa	ND
6	Na_2CO_3	24
7	$NaHCO_3$	6
8	NaH_2PO_4	NR
9	Na_2HPO_4	NR
10	KOAc	trace
11	K_3PO_4	11
12	KF	18
13	K_2CO_3	20

14	$KHCO_3$	20
15	Na_3PO_4	42
16	CsF	40
17	Cs_2CO_3	ND

[a] 2,2-difluoro-*N*-phenylacetohydrazonoyl chloride **1a** (20.5 mg, 0.1 mmol), fluoronitroalkene **2a** (16.7 mg, 0.1 mmol) and base (0.2 mmol) in CH_3CN (1.0 mL) at room temperature for 24 hours unless otherwise indicated. [b] Yield of isolated pyrazole **3a**.



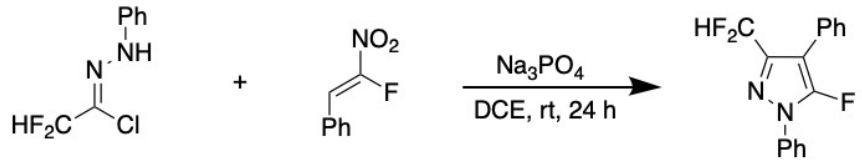
1a **2a** **3a**

Table S2. Screening of solvents

Entry[a]	Solvent	Yield (%)[b]
1	toluene	10
2	THF	11
3	AcOEt	11
4	Acetone	12
5	dioxane	23
6	CH_3CN	42
7	DCE	50
8	DMSO	trace
9	DMF	trace
10	NMP	trace
11	DCM	trace
12	Methanol	trace
13	DMI	trace
14	CH_3Cl	trace
15	EtOH	trace

[a] 2,2-difluoro-*N*-phenylacetohydrazonoyl chloride **1a** (20.5 mg, 0.1 mmol), fluoronitroalkene **2a** (16.7 mg, 0.1

mmol) and Na_3PO_4 (32.8 mg, 0.2 mmol) in solvent (1.0 mL) at room temperature for 24 hours unless otherwise indicated. [b] Yield of isolated pyrazole **3a**.

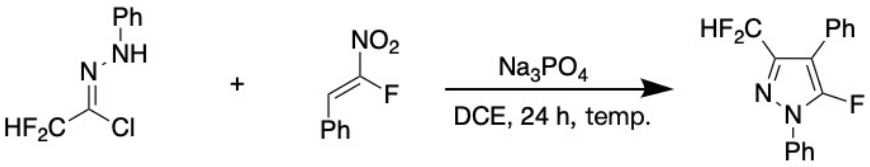


1a **2a** **3a**

Table S3. Screening of the molar ratio of 1a and 2a

Entry[a]	**1a** (equivalent)	Yield (%)[b]
1	0.5	42
2	1.0	50
3	1.5	66
4	2.0	31

[a] 2,2-difluoro-*N*-phenylacetohydrazonoyl chloride **1a**, fluoronitroalkene **2a** (16.7 mg, 0.1 mmol) and Na_3PO_4 (32.8 mg, 0.2 mmol) in DCE (1.0 mL) at room temperature for 24 hours unless otherwise indicated. [b] Yield of isolated pyrazole **3a**.



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

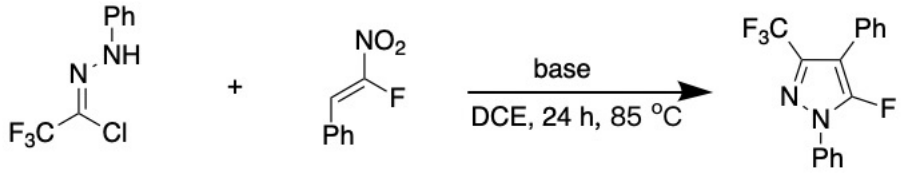
Table S4. Survey on the reaction temperatures

Entry[a]	Temp.(°C)	Yield (%)[b]
1	25	66
2	35	81
3	45	80
4	65	75
5	85	85
6	105	70

[a] 2,2-difluoro-*N*-phenylacetohydrazonoyl chloride **1a** (30.7 mg, 0.15 mmol), fluoronitroalkene **2a** (16.7 mg, 0.1 mmol) and Na_3PO_4 (32.8 mg, 0.2 mmol) in DCE (1.0 mL) at room temperature for 24 hours unless otherwise

indicated. [b] Yield of isolated pyrazole **3a**.

2.2 Screening reaction conditions for the formation of 5a



4a **2a** **5a**

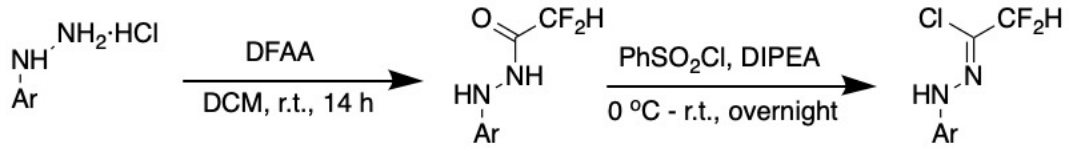
Table S5. Screening of bases

Entry[a]	Base	Yield (%)[b]
1	Na_3PO_4	70
2	Na_2CO_3	trace
3	K_3PO_4	80
4	K_2CO_3	83
5[c]	K_2CO_3	80
6[d]	K_2CO_3	82
7[e]	K_2CO_3	86
8[f]	K_2CO_3	67
9[g]	K_2CO_3	86
10[h]	K_2CO_3	87

[a] 2,2,2-trifluoro-*N*-phenylacetohydrazonoyl chloride **4a** (33.4 mg, 0.15 mmol), fluoronitroalkene **2a** (16.7 mg, 0.1 mmol) and base (0.2 mmol) in DCE (1.0 mL) at 85 ºC for 24 hours unless otherwise indicated. [b] Yield of isolated pyrazole **5a**. [c] 0.20 mmol (2.0 equiv.) of 2,2,2-trifluoro-*N*-phenylacetohydrazonoyl chloride **4a** was employed. [d] 0.25 mmol (2.5 equiv.) of 2,2,2-trifluoro-*N*-phenylacetohydrazonoyl chloride **4a** was employed. [e] 0.30 mmol (3.0 equiv.) of 2,2,2-trifluoro-*N*-phenylacetohydrazonoyl chloride **4a** was employed. [f] **4a** (0.3 mmol), **2a** (0.1 mmol), and K_2CO_3 (0.1 mmol) in in DCE (1.0 mL) at 85 °C for 24 hours. [g] **4a** (0.3 mmol), **2a** (0.1 mmol), and K_2CO_3 (0.3 mmol) in in DCE (1.0 mL) at 85 °C for 24 hours. [h] **4a** (0.3 mmol), **2a** (0.1 mmol), and K_2CO_3 (0.4 mmol) in DCE (1.0 mL) at 85 °C for 24 hours.

2.3 Preparation of starting materials

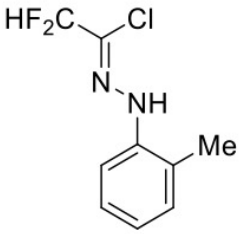
General procedure A[1,2,3,4]



Step 1: Phenylhydrazine hydrochloride (2.0 g, 12.4 mmol), dichloromethane (20 mL), triethylamine (3.5 mL, 2.0 equiv.), and a solution of difluoroacetic anhydride (1.6 mL, 1.0 equiv.) in dichloromethane (20 mL) was added to a 100 mL round-bottom flask. The mixture was stirred for 14 hours at room temperture. The resulting mixture was subsequently washed with saturated aqueous $NaHCO_3$ solution, concentrated and subjected to silica gel column chromatography purification to give 2,2-difluoro-*N*'-phenylacetohydrazide as a light yellow solid.

Step 2: A solution of 2,2-difluoro-*N*'-phenylacetohydrazide (1.9 g, 10 mmol) in EtOAc (30 mL) was added with dropwise addition of benzensulfonyl chloride (1.4 mL, 10.5 mmol) at room temperature. The resulting mixture was then cooled to 0 ℃, and *N*,*N*-diisopropylethylamine (DIPEA, 1.8 mL, 10.5 mmol) was added dropwise. The resultant mixture was stirred at room temperature overnight. The mixture was then diluted with EtOAc, and the organic layer was subsequently washed with water (3 × 20 mL). The combined organic extracts were dried over sodium sulfate, filtered, concentrated, and purified by silica gel column chromatography to yield 2,2-difluoro-*N*'-phenylethanehydrazonoyl chloride as a yellow liquid (1.3 g, 64%). Other difluoromethyl hydrazonyl chlorides 1b–1h were prepared through general procedure A, with yields ranging from 10% to 77%.

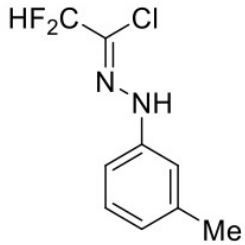
(*Z*)-2,2-difluoro-*N*-(*o*-tolyl)acetohydrazonoyl chloride (1b)



1b

Obtained as a yellow liquid after column chromatography (petroleum ether/ethyl acetate = 100:1, R_f = 0.7), 721.5 mg, 33% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.35 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.19 (td, *J* = 7.8, 1.7 Hz, 1H), 7.14–7.03 (m, 1H), 6.91 (td, *J* = 7.4, 1.3 Hz, 1H), 6.31 (t, $^2J_{H-F}$ = 53.9 Hz, 1H), 2.23 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.30 (d, $^2J_{F-H}$ = 54.0 Hz, CF_2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.8, 130.8, 127.4, 122.2, 121.7, 118.8 (t, $^2J_{C-F}$ = 33.3 Hz), 113.6, 111.3 (t, $^1J_{C-F}$ = 238.3 Hz), 16.7. **HRMS** (ESI) m/z $[M+Na]^+$ calcd. for $C_9H_9N_2F_2NaCl^+$ 241.0320; found 241.0318.

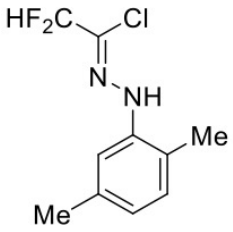
(Z)-2,2-difluoro-*N*-(*m*-tolyl)acetohydrazonoyl chloride (1c)



1c

Obtained as a yellow liquid after column chromatography (petroleum ether/ethyl acetate = 100:1, R_f = 0.5), 524.7 mg, 24% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.06 (t, *J* = 7.8 Hz, 1H), 6.85–6.64 (m, 3H), 6.18 (t, $^2J_{H-F}$ = 54.0 Hz, 1H), 2.21 (s, 3H). **^{19}F NMR** (565 MHz, $CDCl_3$) δ -115.07 (d, $^2J_{F-H}$ = 54.1 Hz, CF_2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.0, 139.6, 129.3, 123.4, 117.6 (t, $^2J_{C-F}$ = 33.3 Hz), 114.5, 111.4 (t, $^1J_{C-F}$ = 238.1 Hz), 111.0, 21.5. **HRMS** (ESI) m/z $[M+Na]^+$ calcd. for $C_9H_9N_2F_2NaCl^+$ 241.0320; found 241.0319.

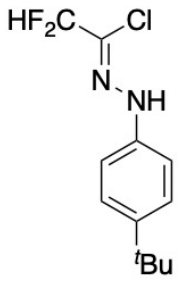
(*Z*)-*N*-(2,5-dimethylphenyl)-2,2-difluoroacetohydrazonoyl chloride (1d)



1d

Obtained as a yellow liquid after column chromatography (petroleum ether/ethyl acetate = 100:1, R_f = 0.7), 767.8 mg, 33% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.13 (d, *J* = 1.8 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.67 (dd, *J* = 7.7, 1.8 Hz, 1H), 6.26 (t, $^2J_{H–F}$ = 54.0 Hz, 1H), 2.27 (s, 3H), 2.08 (s, 3H). **^{19}F NMR** (565 MHz, $CDCl_3$) δ -114.83 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.6, 137.2, 130.7, 123.1, 118.9, 118.5 (t, $^2J_{C–F}$ = 33.3 Hz), 114.3, 111.5 (t, $^1J_{C–F}$ = 238.2 Hz), 21.3, 16.1. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{10}H_{12}N_2F_2Cl^+$ 233.0657; found 233.0663.

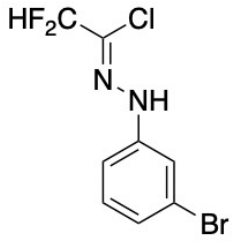
(*Z*)-*N*-(4-(*tert*-butyl)phenyl)-2,2-difluoroacetohydrazonoyl chloride (1e)



1e

Obtained as a pink solid after column chromatography (petroleum ether, R_f = 0.5), 521.4 mg, 20% yield, m.p. 76–78 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.43–7.31 (m, 2H), 7.18–6.90 (m, 2H), 6.32 (t, $^2J_{H–F}$ = 54.0 Hz, 1H), 1.31 (s, 9H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.33 (d, $^2J_{F–H}$ = 54.1 Hz, CF_2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.5, 139.5, 126.3, 117.4 (t, $^2J_{C–F}$ = 33.2 Hz), 113.5, 111.3(t, $^1J_{C–F}$ = 238.0 Hz), 31.4. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{12}H_{16}N_2F_2Cl^+$ 261.0970; found 261.0977.

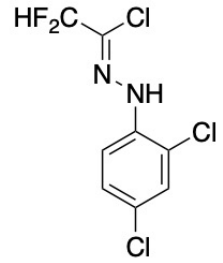
(*Z*)-*N*-(3-bromophenyl)-2,2-difluoroacetohydrazonoyl chloride (1f)



1f

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.3), 992.2 mg, 35% yield, m.p. 70–72 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.31 (t, *J* = 2.0 Hz, 1H), 7.20–7.03 (m, 2H), 7.02–6.86 (m, 1H), 6.31 (t, $^2J_{H–F}$ = 53.9 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.67 (d, $^2J_{F–H}$ = 53.9 Hz, CF_2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.1, 130.8, 125.3, 123.4, 119.2 (t, $^2J_{C–F}$ = 33.5 Hz), 116.8, 112.4, 111.0 (t, $^1J_{C–F}$ = 238.9 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_8H_7N_2F_2BrCl^+$ 282.9449; found 282.9456.

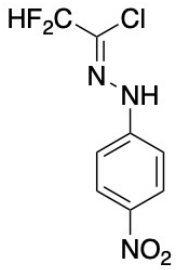
(*Z*)-*N*-(2,4-dichlorophenyl)-2,2-difluoroacetohydrazonoyl chloride (1g)



1g

Obtained as an orange liquid after column chromatography (petroleum ether/ethyl acetate = 10:1, R_f = 0.3), 2.1 g, 77% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.00–6.91 (m, 2H), 6.88 (dd, *J* = 8.8, 2.2 Hz, 1H), 6.11 (t, $^2J_{H–F}$ = 53.8 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.49 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.6, 128.8, 128.1, 126.9, 121.24 (t, $^2J_{C–F}$ = 33.4 Hz), 118.6, 115.3, 111.0 (t, $^1J_{C–F}$ = 239.4 Hz). **HRMS** (ESI) m/z $[M+Na]^+$ calcd. for $C_8H_5N_2F_2Cl_3Na^+$ 294.9384; found 293.9486.

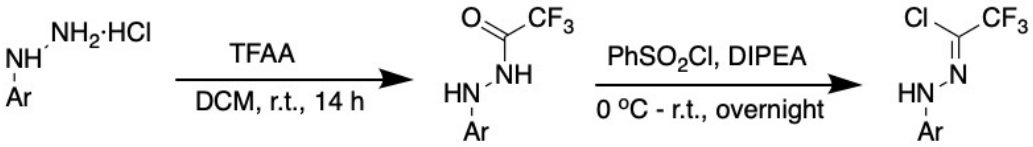
(*Z*)-2,2-difluoro-*N*-(4-nitrophenyl)acetohydrazonoyl chloride (1h)



1h

Obtained as an orange solid after column chromatography (petroleum ether/ethyl acetate = 20:1, R_f = 0.3), 502.9 mg, 23% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.23 (d, *J* = 9.1 Hz, 2H), 7.20 (d, *J* = 9.1 Hz, 2H), 6.34 (t, $^2J_{H-F}$ = 53.8 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -116.16 (d, $^2J_{F-H}$ = 53.8 Hz, CF_2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 146.9, 142.6, 126.0, 122.2 (t, $^2J_{C-F}$ = 33.6 Hz), 113.4, 110.6 (t, $^1J_{C-F}$ = 240.3 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_8H_7N_3O_2F_2Cl^+$ 250.0195; found 250.0200.

General procedure B[1,2,3]

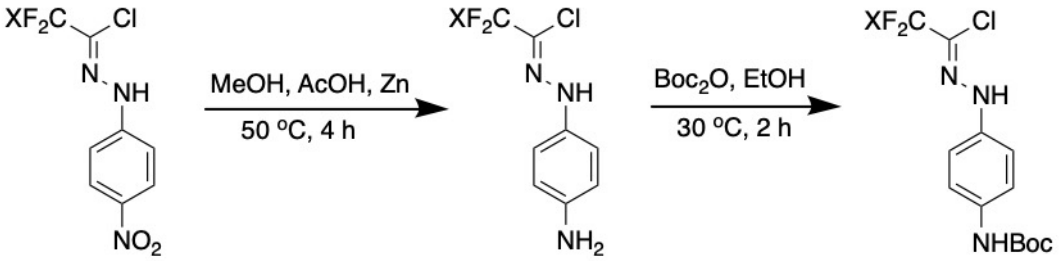


Step 1: Phenylhydrazine hydrochloride (2.0 g, 12.4 mmol), dichloromethane (20 mL), triethylamine (3.5 mL, 2.0 equiv.), and a solution of trifluoroacetic anhydride (1.8 mL, 1.0 equiv.) in dichloromethane (20 mL) was added to a 100 mL round-bottom flask. The mixture was stirred for 14 hours at room temperature, The resulting mixture was subsequently washed with saturated aqueous $NaHCO_3$ solution, concentrated and subjected to silica gel column chromatography purification to give 2,2,2-trifluoro-*N*'-phenylacetohydrazide as a dark red solid.

Step 2: A solution of 2,2,2-trifluoro-*N*'-phenylacetohydrazide (2.0 g, 10 mmol) in EtOAc (30 mL) was subjected to dropwise addition of benzensulfonyl chloride (1.4 mL, 10.5 mmol) at room temperature. The resulting mixture was cooled to 0 °C, and *N*,*N*-diisopropylethylamine (DIPEA, 1.8 mL, 10.5 mmol) was added dropwise. The mixture was stirred at room temperature overnight. The reaction mixture was then

diluted with EtOAc, and the organic layer was subsequently washed with water (3 × 20 mL). The combined organic extracts were dried over sodium sulfate, filtered, concentrated, and purified by silica gel column chromatography, affording 2,2,2-trifluoro-*N*'-phenylethanehydrazonoyl chloride as a yellow liquid (1.9 g, 86%). Other trifluoromethyl hydrazonyl chlorides were also synthesized with yields ranging from 61% to 83%.

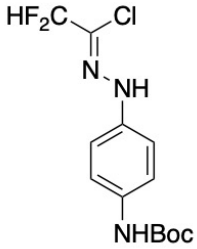
General procedure C[5]



Step 1: *N*-(4-nitrocyclohexa-1,5-dien-1-yl)acetohydrazonoyl chloride (10 mmol) were dissolved in MeOH:AcOH (V:V = 2:1). Reduced zinc powder (100 mmol) was then added to the solution, and the mixture was heated to 50 °C for 4 hours. The reaction mixture was diluted with EtOAc, and the aqueous layer was extracted twice with EtOAc. The organic layers were combined, washed with brine, and dried over anhydrous $MgSO_4$. The dried mixture was filtered and evaporated under vacuum. The resulting residue was purified using column chromatography (PE/EA = 3:1) to afford 4-(amino)-phenyl derived hydrazonoyl chlorides.

Step 2: 4-(amino)-phenyl derived hydrazonoyl chlorides (10 mmol) in ethanol (20 mL) was reacted with Boc_2O (11 mmol). The reaction mixture was stirred at 30 °C until complete conversion of starting materials was achieved, as confirmed by TLC analysis. The resulting organic phase was extracted with EtOAc, concentrated under vacuum, and the residue was purified by flash chromatography on silica gel, eluting with a mixture of petroleum ether and ethyl acetate to afford the desired products **1z** and **4z**.

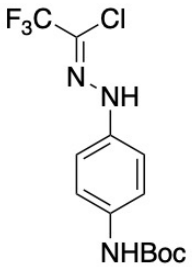
***tert*-Butyl(*Z*)-(4-(2-(1-chloro-2,2-ifluoroethylidene)hydrazineyl)phenyl)-carbamate (1z)**



1z

Obtained as a white solid after column chromatography (petroleum ether/ethyl acetate = 3:1, R_f = 0.6), 84.7 mg, 53% yield, m.p. 95–97 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.06–6.98 (m, 2H), 6.48 (s, 1H), 6.30 (t, $^2J_{H–F}$ = 54.0 Hz, 1H), 1.51 (s, 9H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.29 (d, $^2J_{F–H}$ = 53.9 Hz, CF_2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.1, 137.7, 133.2, 120.2, 117.4 (t, $^2J_{C–F}$ = 33.2 Hz), 114.3, 111.3 (t, $^1J_{C–F}$ = 238.1 Hz), 80.5, 28.4. **HRMS** (ESI) m/z $[M+Na]^+$ calcd. for $C_{13}H_{16}N_3O_2F_2ClNa^+$ 342.0797; found 342.0794.

***tert*-Butyl(*Z*)-(4-(2-(1-chloro-2,2,2-trifluoroethylidene)hydrazineyl)phenyl) carbamate (4z)**

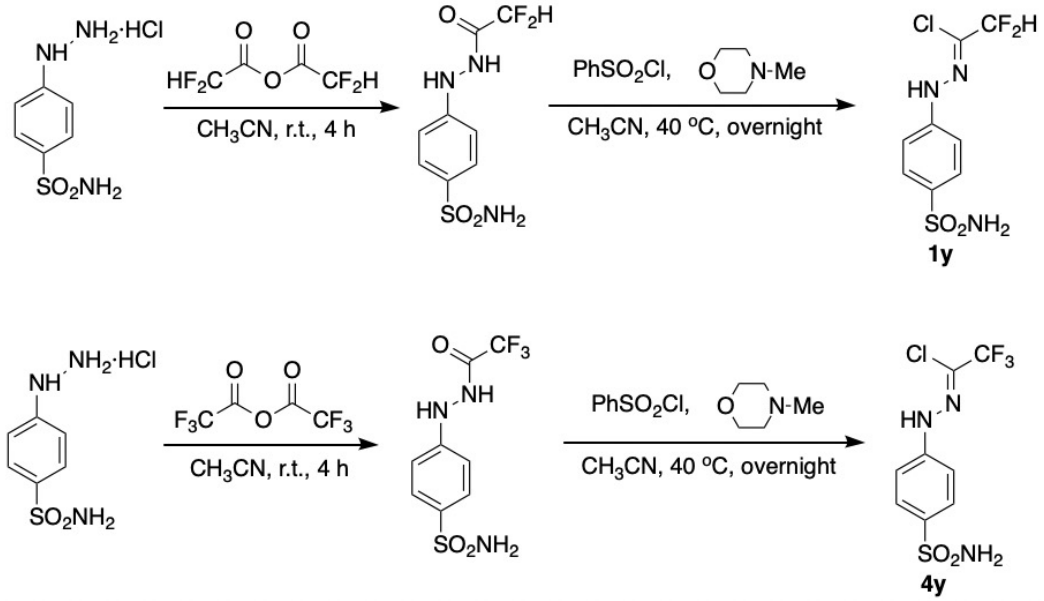


4z

Obtained as a yellow solid after column chromatography (petroleum ether/ethyl acetate = 10:1, R_f = 0.2), 1.5 g, 45% yield, m.p. 95–97 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.06 (d, *J* = 8.5 Hz, 2H), 6.50 (s, 1H), 1.51 (s, 9H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -67.66 (s, CF_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.0, 137.4, 133.6, 120.2, 118.4 (q, $^1J_{C–F}$ = 272.0 Hz), 114.6, 110.9 (q, $^2J_{C–F}$ = 43.6 Hz), 80.5,

28.4. **HRMS** (ESI) m/z $[M+Na]^+$ calcd. for $C_{13}H_{15}N_3O_2F_3ClNa^+$ 360.0703; found 360.0697.

General procedure D[3]

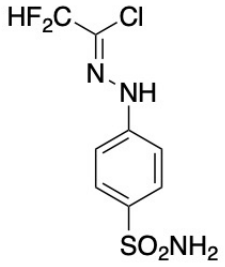


Step 1: 4-Sulfonamide-phenylhydrazinehydrochloride (10 mmol) was slurried in acetonitrile (15 mL) and cooled to 5–10 °C. Difluoroacetic acid anhydride or trifluoroacetic acid anhydride (15 mmol) was added dropwise, and the reaction mixture was heated to room temperature for 4 hours. The slurry was concentrated in vacuo to approximately 1/3 of the original volume and hexane was added to precipitate the product out. The slurry was cooled to 0–5 °C for 1 h, filtered and washed with hexane. The filter cake was collected and dried in vacuo at 50 °C.

Step 2: 4-(2-(2,2-difluoroacetyl)hydrazineyl)benzenesulfonamide (2.7 g, 10 mmol) or 4-(2-(2,2,2-trifluoroacetyl)hydrazineyl)benzenesulfonamide (2.8 g, 10 mmol) was slurried in acetonitrile (20 mL) and cooled to 0 °C in an ice bath. Benzenesulfonyl chloride (1.5 mL, 12 mmol) was added, and followed by dropwise addition of *N*-Methylmorpholine (1.2 mL, 10.5 mmol). The reaction mixture was heated overnight at 40 °C. The organic layer was separated from the aqueous layer and washed with brine (10 mL). The combined organic extracts were dried over $MgSO_4$, filtered, concentrated and purified by silica gel column chromatography to obtain the desired product **1y** and

4y.

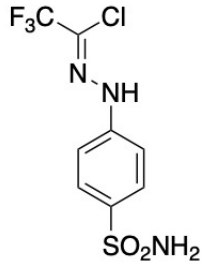
(*Z*)-2,2-difluoro-*N*-(4-sulfamoylphenyl)acetohydrazonoyl chloride (1y)



1y

Obtained as a white solid after column chromatography (petroleum ether/ethyl acetate = 3:1, R_f = 0.3), 1.3 g, 45% yield, m.p. 154–156 ℃. **^{1}H NMR** (400 MHz, DMSO) δ 10.73 (s, 1H), 7.77 (d, *J* = 8.8 Hz, 2H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.23 (s, 2H), 6.85 (t, $^2J_{H–F}$ = 53.4 Hz, 1H). **^{19}F NMR** (376 MHz, DMSO) δ -115.32 (d, $^2J_{F–H}$ = 53.5 Hz, CF_2H). **^{13}C NMR** (100 MHz, DMSO) δ 146.2, 137.2, 127.8, 117.9 (t, $^2J_{C–F}$ = 33.0 Hz), 113.93, 111.81 (t, $^1J_{C–F}$ = 236.7 Hz). **HRMS** (ESI) m/z $[M+Na]^+$ calcd. for $C_8H_8N_3O_2F_2SClNa^+$ 305.9892; found 305.9881.

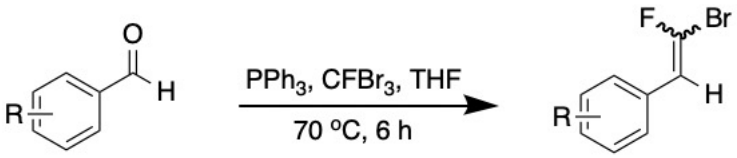
(*Z*)-2,2,2-trifluoro-*N*-(4-sulfamoylphenyl)acetohydrazonoyl chloride (4y)



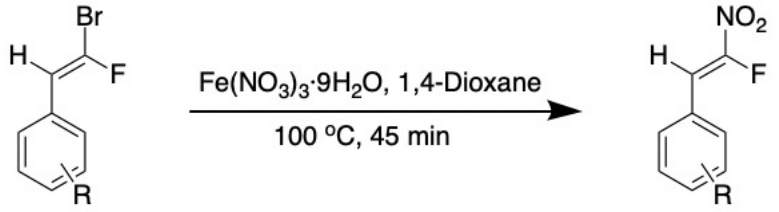
4y

Obtained as a white solid after column chromatography (petroleum ether/ethyl acetate = 3:1, R_f = 0.3), 1.5 g, 49% yield, m.p. 150–152 ℃. **^{1}H NMR** (400 MHz, DMSO) δ 11.00 (s, 1H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.26 (s, 2H). **^{19}F NMR** (376 MHz, DMSO) δ -66.75 (s, CF_3). **^{13}C NMR** (100 MHz, DMSO) δ 145.7, 137.9, 127.9, 119.0 (q, $^1J_{C–F}$ = 270.9 Hz), 114.3, 110.6 (q, $^2J_{C–F}$ = 42.2 Hz). **HRMS** (ESI) m/z $[M+Na]^+$ calcd. for $C_8H_7N_3O_2F_3SClNa^+$ 323.9797; found 323.9789.

General procedure E[6]

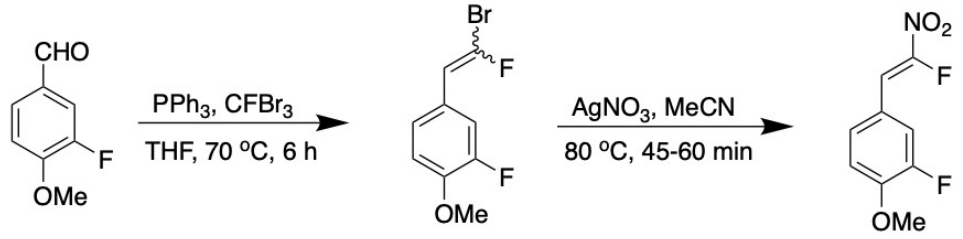


An oven-dried screw-capped reaction tube was charged with PPh_3 (7.0 mmol) and $CFBr_3$ (6.1 mmol). The mixture was dissolved in THF (5.0 mL) and heated at 70 °C for 15 min. After that, the reaction mixture was cooled to room temperature and appropriate aldehyde (4.7 mmol) and remaining PPh_3 (7.0 mmol) were added to the reaction mixture. The reaction mixture was then heated at 70 °C for 6 h. After completion of the reaction, the crude reaction mixture was poured into cold water and extracted with petroleum ether (4 × 20 mL). All organic fractions were then dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude reaction mixture was then purified by flash column chromatography using petroleum ether as eluent. The product was obtained as a mixture of E and Z isomer (consistent with the literature report; the ratio was determined by ^1H NMR). α-Fluorobromoalkenes are volatile compounds extra precaution should be taken while concentrating in vacuo to avoid losing the compounds.



An oven-dried screw-capped pressure tube was charged with appropriate α-fluorobromoalkene (1.0 equiv.) and $Fe(NO_3)_3 \cdot 9H_2O$ (3.0 equiv.). The mixture was dissolved in 1,4-dioxane (0.5 M) and heated at 100 °C for 45 min. After completion of the reaction, the crude reaction mixture was poured into water and extracted with petroleum ether (5 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The product was obtained after purification by column chromatography (EtOAc/Petroleum Ether = 9:1) on silica gel.

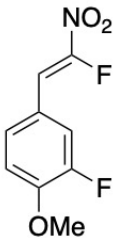
General procedure E[7]



Step 1: PPh_3 (7.0 mmol) and $CFBr_3$ (6.1 mmol) were charged into a 50 mL round bottom flask. The mixture was dissolved in THF (5.0 mL) and heated at reflux for 15 min at 70 °C. After that, the reaction mixture was cooled to room temperature, and appropriate 3-fluoro-4-methoxybenzaldehyde (4.7 mmol) and the remaining PPh_3 (7.0 mmol) were added to the reaction mixture. The reaction mixture was then heated at 70 °C. After completion of the reaction, the crude reaction mixture was poured into cold water and extracted with petroleum ether (4 × 20mL). All organic fractions were then dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude reaction mixture was then purified by flash column chromatography using petroleum ether as eluent.

Step 2: 4-(2-bromo-2-fluorovinyl)-2-fluoro-1-methoxybenzene was placed into 10 mL vial and dissolved in MeCN (5.0 mL/1.0 mmol), then $AgNO_3$ (1.3 equiv.) was added. Vial was closed and the reaction mixture was heated at 80 °C (oil bath) with stirring for 45−60 min (TLC monitoring). Mixture was cooled to r.t. and filtered through Celite. After that Celite was washed with EtOAc. Filtrate was evaporated and crude product was purified by column chromatography (PE) to give target nitroalkenes **2y**.

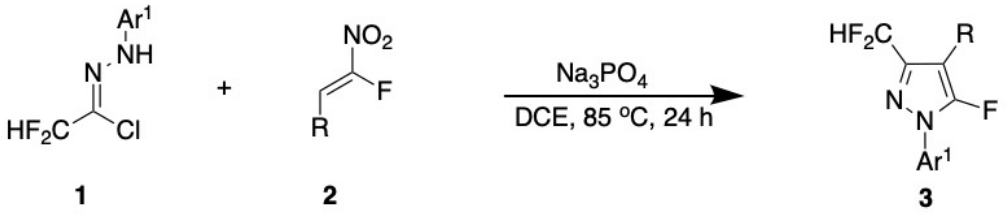
(*Z*)-2-fluoro-4-(2-fluoro-2-nitrovinyl)-1-(Methoxy)benzene (2y)



2y

Obtained as a yellow solid after column chromatography (petroleum ether, R_f = 0.4), 1.2 g, 53% yield, m.p. 94–96 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 (dd, $^3J_{H–F}$ = 11.9 Hz, $^4J_{H–F}$ = 2.2 Hz, 1H), 7.42–7.31 (m, 2H), 7.04 (t, $^3J_{H–F}$ = 8.5 Hz, 1H), 3.97 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -112.97 (d, $^3J_{F–H}$ = 26.2 Hz, F), -132.82 (t, $^3J_{F–H}$ = 10.1 Hz, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.6, 128.5 (dd, $^2J_{C–F}$ = 7.0 Hz, $^3J_{C–F}$ = 3.5 Hz), 118.0, 117.9, 117.8, 117.7, 113.5 (d, $^3J_{C–F}$ = 2.3 Hz), 109.3 (dd, $^2J_{C–F}$ = 6.4, $^3J_{C–F}$ 2.6 Hz), 56.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_9H_8NO_3F_2^+$ 216.0472; found 216.0479.

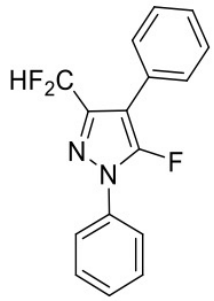
2.4 General procedure F for the reaction of hydrazonyl chlorides 1 with α-fluoronitroalkene 2



1 **2** **3**

To a 10 mL sealed screw–capped pressure tube equipped with a stirring bar and dried in an oven, hydrazone acyl chloride (**1**, 0.15 mmol), α-fluoronitroalkene (**2**, 0.1 mmol) and Na_3PO_4 (32.8 mg, 0.2mmol). 1,2-Dichloroethane (1.0 mL) was transferred into the tube through a syringe. The resulting mixture was stirred at 85 °C for 24 hours. The reaction mixture was extracted with EtOAc. The combined organic phases were concentrated in vacuo, and the residue was purified by flash chromatography on silica gel (eluted with petroleum ether/ethyl acetate) to obtain the desired product **3**.

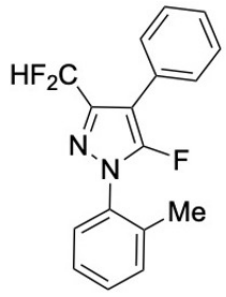
3-(Difluoromethyl)-5-fluoro-1,4-diphenyl-1*H*-pyrazole (3a)



3a

Obtained as a white solid after column chromatography (petroleum ether, R_f = 0.2), 24.0 mg, 85% yield, m.p. 59–61 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63–7.56 (m, 2H), 7.53–7.46 (m, 2H), 7.45–7.38 (m, 2H), 7.39–7.31 (m, 2H), 7.32–7.23 (m, 2H), 6.62 (t, $^2J_{H–F}$ = 53.7 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.24 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H), -131.17 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.8 (d, $^1J_{C–F}$ = 285.5 Hz), 142.9 (td, $^2J_{C–F}$ = 28.6 Hz, $^3J_{C–F}$ = 8.7 Hz), 136.5 (d, $^3J_{C–F}$ = 2.9 Hz), 129.5, 128.8 (d, $^4J_{C–F}$ = 2.8 Hz), 128.3, 127.9, 127.8 (d, $^3J_{C–F}$ = 4.2 Hz), 121.9 (d, $^3J_{C–F}$ = 3.9 Hz), 112.2 (t, $^1J_{C–F}$ = 235.0 Hz), 103.2 (d, $^2J_{C–F}$ = 11.1 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{12}N_2F_3^+$ 289.0953; found 289.0955.

3-(Difluoromethyl)-5-fluoro-4-phenyl-1-(*o*-tolyl)-1*H*-pyrazole (3b)

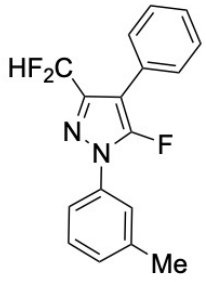


3b

Obtained as an orange liquid after column chromatography (ether/petroleum ether = 1:50, R_f = 0.4), 21.8 mg, 72% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54–7.47 (m, 2H), 7.44 (s, 1H), 7.40–7.37 (m, 3H), 7.35–7.28 (m, 2H), 7.16 (d, *J* = 7.6 Hz, 1H), 6.64 (t, $^2J_{H–F}$ = 54.3 Hz, 1H), 2.38 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.23 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H), -131.17 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.3 (d, $^1J_{C–F}$ = 282.6 Hz), 141.8 (td, $^2J_{C–F}$ = 28.3 Hz, $^3J_{C–F}$ = 8.1 Hz), 134.2, 133.7 (d, $^4J_{C–F}$ = 2.1 Hz), 130.3, 129.1, 127.7, 127.6 (q, $^4J_{C–F}$ = 2.0 Hz), 126.7, 126.1, 125.9, 111.2 (t, $^1J_{C–F}$ = 235.2 Hz),

100.7 (d, $^{2}J_{C–F}$ = 10.7 Hz), 16.5 (d, $^{5}J_{C–F}$ = 2.1 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{14}N_2F_3^+$ 303.1109; found 303.1110.

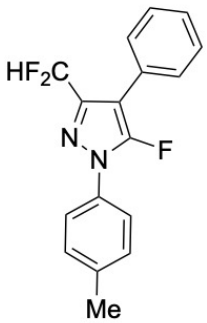
3-(Difluoromethyl)-5-fluoro-4-phenyl-1-(*m*-tolyl)-1*H*-pyrazole (3c)



3c

Obtained as an orange liquid after column chromatography (ether/petroleum ether = 1:50, R_f = 0.2), 23.6 mg, 78% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56–7.51 (m, 2H), 7.42–7.34 (m, 3H), 7.32–7.25 (m, 4H), 6.63 (t, $^{2}J_{H–F}$ = 53.7 Hz, 1H), 2.19 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.03 (d, $^{2}J_{F–H}$ = 53.8 Hz, CF_2H), -131.66 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.7 (d, $^{1}J_{C–F}$ = 285.1 Hz), 141.7 (td, $^{2}J_{C–F}$ = 28.4 Hz, $^{3}J_{C–F}$ = 8.5 Hz), 138.7, 135.3 (d, $^{4}J_{C–F}$ = 3.0 Hz), 128.2, 128.0, 127.7 (d, $^{4}J_{C–F}$ = 2.7 Hz), 126.8, 121.6 (d, $^{3}J_{C–F}$ = 3.3 Hz), 117.9 (d, $^{3}J_{C–F}$ = 4.3 Hz), 111.1 (t, $^{1}J_{C–F}$ = 235.6 Hz), 102.0 (d, $^{2}J_{C–F}$ = 11.4 Hz), 20.4. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{14}N_2F_3^+$ 303.1109; found 303.1115.

3-(difluoromethyl)-5-fluoro-4-phenyl-1-(*p*-tolyl)-1*H*-pyrazole (3d)

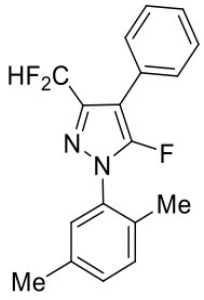


3d

Obtained as a yellow solid after column chromatography (ether/petroleum ether = 1:50, R_f = 0.4), 19.4 mg, 64% yield, m.p. 58–60 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54–

7.45 (m, 4H), 7.43–7.34 (m, 2H), 7.34–7.25 (m, 1H), 7.25 (d, J = 8.3 Hz, 2H), 6.63 (t, $^{2}J_{H-F}$ = 53.7 Hz, 1H), 2.35 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.18 (d, $^{2}J_{F-H}$ = 53.8 Hz, CF_2H), -131.52 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.7 (d, $^{1}J_{C-F}$ = 284.6 Hz), 141.6 (td, $^{2}J_{C-F}$ = 28.3 Hz, $^{3}J_{C-F}$ = 8.1 Hz), 137.3, 133.0 (d, $^{4}J_{C-F}$ = 2.8 Hz), 129.0, 127.7 (d, $^{4}J_{C-F}$ = 2.3 Hz), 126.8 (d, $^{3}J_{C-F}$ = 4.3 Hz), 126.7, 120.9 (d, $^{3}J_{C-F}$ = 3.6 Hz), 111.2 (t, $^{1}J_{C-F}$ = 235.0 Hz), 101.9 (d, $^{2}J_{C-F}$ = 11.2 Hz), 20.1. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{14}N_2F_3^+$ 303.1109; found 303.1106.

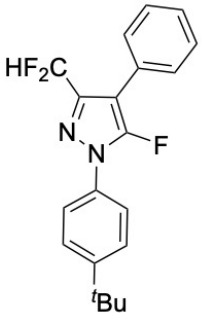
3-(Difluoromethyl)-1-(2,5-dimethylphenyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3e)



3e

Obtained as an orange liquid after column chromatography (ether/petroleum ether = 1:50, R_f = 0.3), 22.8 mg, 72% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55–7.50 (m, 2H), 7.40–7.36 (m, 2H), 7.32–7.26 (m, 1H), 7.18–7.10 (m, 3H), 6.62 (t, $^{2}J_{H-F}$ = 53.7 Hz, 1H), 2.31 (s, 3H), 2.13 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -110.96 (d, $^{2}J_{F-H}$ = 52.8 Hz, CF_2H), -131.62 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.3 (d, $^{1}J_{C-F}$ = 282.3 Hz), 141.7 (td, $^{2}J_{C-F}$ = 28.4 Hz, $^{3}J_{C-F}$ = 8.3 Hz), 135.9, 133.4 (d, $^{4}J_{C-F}$ = 2.1 Hz), 130.8, 129.9 (d, $^{3}J_{C-F}$ = 16.0 Hz), 127.7, 127.6 (q, $^{4}J_{C-F}$ = 2.0 Hz), 126.9 (d, $^{3}J_{C-F}$ = 4.3 Hz), 126.6 (d, J = 8.4 Hz), 111.3 (t, $^{1}J_{C-F}$ = 235.3 Hz), 100.6 (d, $^{2}J_{C-F}$ = 10.9 Hz), 19.7, 15.9 (d, $^{5}J_{C-F}$ = 2.1 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{18}H_{16}N_2F_3^+$ 317.1266; found 317.1265.

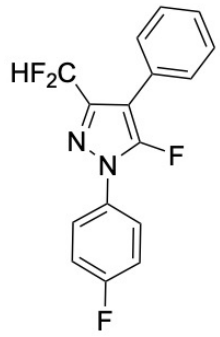
1-(4-(*tert*-Butyl)phenyl)-3-(difluoromethyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3f)



3f

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.2), 28.9 mg, 84% yield, m.p. 64–66 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 4.2, 2.4 Hz, 4H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.31–7.26 (m, 1H), 6.63 (t, $^2J_{H–F}$ = 53.7 Hz, 1H), 1.29 (s, 9H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.11 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H), -131.56 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.6, 149.7 (d, $^1J_{C–F}$ = 284.5 Hz), 142.7 (td, $^2J_{C–F}$ = 27.9 Hz, $^3J_{C–F}$ = 8.6 Hz), 133.9 (d, $^4J_{C–F}$ = 2.9 Hz), 128.8, 127.9 (d, $^3J_{C–F}$ = 4.2 Hz), 127.8, 126.4, 121.7 (d, $^4J_{C–F}$ = 3.6 Hz), 112.3 (t, $^1J_{C–F}$ = 235.2 Hz), 102.9 (d, $^2J_{C–F}$ = 11.2 Hz), 34.8, 31.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{20}H_{20}N_2F_3^+$ 345.1579; found 345.1582.

3-(Difluoromethyl)-5-fluoro-1-(4-fluorophenyl)-4-phenyl-1*H*-pyrazole (3g)

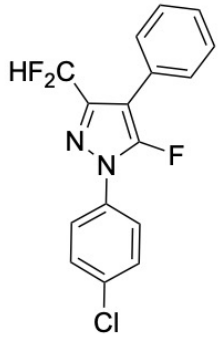


3g

Obtained as a yellow solid after column chromatography (petroleum ether, R_f = 0.2), 15.3 mg, 50% yield, m.p. 52–54 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62–7.56 (m, 2H), 7.49 (d, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.18–7.12 (m, 2H), 6.62 (t, $^2J_{H–F}$ = 53.7 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.42 (d, $^2J_{F–H}$ = 53.6 Hz, CF_2H), -112.58–-112.61 (m, F), -131.56 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.1 (d, $^1J_{C–F}$ = 248.9 Hz), 149.7 (d, $^1J_{C–F}$ = 285.0 Hz), 142.9 (td, $^2J_{C–F}$ = 28.5 Hz, $^3J_{C–F}$

= 9.5 Hz), 133.9–131.0 (m), 128.80, 128.75 (d, $^{4}J_{C–F}$ = 2.6 Hz), 127.9, 123.9 (dd, $^{3}J_{C–F}$ = 8.6 Hz, $^{4}J_{C–F}$ = 3.8 Hz), 116.6, 116.4, 112.0 (t, $^{1}J_{C–F}$ = 235.5 Hz), 103.2 (d, $^{2}J_{C–F}$ = 11.0 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{11}N_2F_4^+$ 307.0858; found 307.0866.

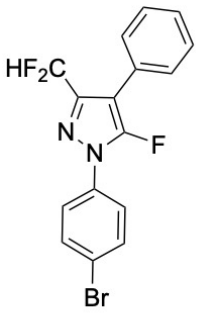
1-(4-Chlorophenyl)-3-(difluoromethyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3h)



3h

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.2), 20.3 mg, 63% yield, m.p. 53–55 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 7.6 Hz, 2H), 7.39 (dd, *J* = 17.0, 8.3 Hz, 4H), 7.30 (t, *J* = 7.2 Hz, 1H), 6.61 (t, $^{2}J_{H–F}$ = 53.6 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.52 (d, $^{2}J_{F–H}$ = 53.5 Hz, CF_2H), -130.87 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.7 (d, $^{1}J_{C–F}$ = 286.0 Hz), 143.2 (td, $^{2}J_{C–F}$ = 28.5 Hz, $^{3}J_{C–F}$ = 9.5 Hz), 135.1 (d, $^{3}J_{C–F}$ = 2.9 Hz), 133.9, 129.7, 128.8, 128.7 (d, $^{4}J_{C–F}$ = 1.9 Hz), 127.9, 122.9 (d, $^{3}J_{C–F}$ = 4.2 Hz), 111.9 (t, $^{1}J_{C–F}$ = 236.1 Hz), 103.5 (d, $^{2}J_{C–F}$ = 11.2 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{11}N_2F_3Cl^+$ 323.0563; found 323.0562.

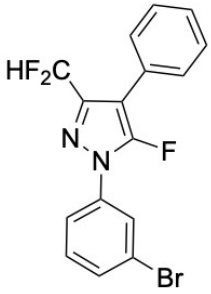
1-(4-Bromophenyl)-3-(difluoromethyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3i)



3i

Obtained as a red liquid after column chromatography (petroleum ether, R_f = 0.2), 22.1 mg, 60% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60–7.55 (m, 2H), 7.52 (dd, *J* = 9.0, 1.8 Hz, 2H), 7.50–7.46 (m, 2H), 7.37 (m, 2H), 7.33–7.27 (m, 1H), 6.62 (t, $^2J_{H-F}$ = 53.7 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.56 (d, $^2J_{F-H}$ = 53.6 Hz, CF_2H), -130.78 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.7 (d, $^1J_{C-F}$ = 285.8 Hz), 142.2 (td, $^2J_{C-F}$ = 28.3 Hz, $^3J_{C-F}$ = 8.6 Hz), 134.6 (d, $^4J_{C-F}$ = 2.9 Hz), 131.7, 127.8, 127.7 (d, $^4J_{C-F}$ = 1.9 Hz), 126.9, 126.4 (d, $^3J_{C-F}$ = 4.3 Hz), 122.1 (d, $^3J_{C-F}$ = 4.4 Hz), 110.9 (t, $^1J_{C-F}$ = 235.5 Hz), 102.5 (d, $^2J_{C-F}$ = 11.4 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{11}N_2F_3Br^+$ 367.0058; found 367.0067.

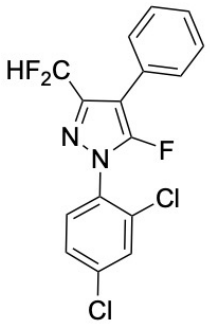
1-(3-Bromophenyl)-3-(difluoromethyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3j)



3j

Obtained as an orange liquid after column chromatography (petroleum ether, R_f = 0.1), 27.5 mg, 75% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (q, *J* = 1.8 Hz, 1H), 7.66 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.60–7.50 (m, 3H), 7.51–7.43 (m, 2H), 7.42–7.34 (m, 2H), 6.70 (t, $^2J_{H-F}$ = 53.6 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.60 (d, $^2J_{F-H}$ = 53.7 Hz, CF_2H), -130.45 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.8 (d, $^1J_{C-F}$ = 286.5 Hz), 143.4 (td, $^2J_{C-F}$ = 28.5 Hz, $^3J_{C-F}$ = 8.5 Hz), 137.5 (d, $^4J_{C-F}$ = 3.0 Hz), 131.2, 130.8, 128.82, 128.77 (d, $^4J_{C-F}$ = 2.1 Hz), 128.0, 127.4 (d, $^3J_{C-F}$ = 4.3 Hz), 124.75 (d, $^3J_{C-F}$ = 4.0 Hz), 123.1, 119.9 (d, $^3J_{C-F}$ = 5.0 Hz), 111.9 (t, $^1J_{C-F}$ = 235.8 Hz), 103.6 (d, $^2J_{C-F}$ = 11.3 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{11}N_2F_3Br^+$ 367.0058; found 367.0062.

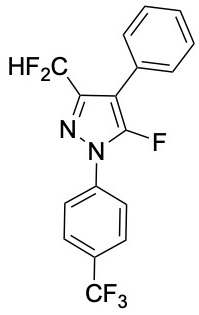
1-(2,4-Dichlorophenyl)-3-(difluoromethyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3k)



3k

Obtained as an orange solid after column chromatography (petroleum ether/ethyl acetate = 20:1, R_f = 0.7), 20.0 mg, 56% yield, m.p. 66–68 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57–7.47 (m, 3H), 7.44–7.40 (m, 1H), 7.40–7.34 (m, 3H), 7.33–7.28 (m, 1H), 6.61 (t, $^2J_{H–F}$ = 53.6 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.61 (d, $^2J_{F–H}$ = 53.7 Hz, CF_2H), -129.26 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.5 (d, $^1J_{C–F}$ = 285.2 Hz), 143.1 (td, $^2J_{C–F}$ = 28.5 Hz, $^3J_{C–F}$ = 7.2 Hz), 135.9, 131.4, 129.4, 128.8, 127.8, 127.7 (d, $^4J_{C–F}$ = 2.0 Hz), 127.2, 126.9, 110.9 (t, $^1J_{C–F}$ = 235.8 Hz), 101.3 (d, $^2J_{C–F}$ = 9.8 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{10}N_2F_3Cl_2^+$ 357.0173; found 357.0176.

3-(Difluoromethyl)-5-fluoro-4-phenyl-1-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (3l)

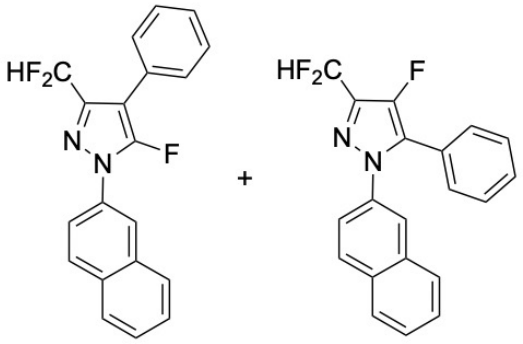


3l

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.2), 22.1 mg, 62% yield, m.p. 38–40 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.79 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.44 – 7.37 (m, 1H), 6.71 (t, $^2J_{H–F}$ = 53.6 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.57 (s, CF_3), -111.78 (d, $^2J_{F–H}$ = 53.6 Hz, CF_2H), -130.12 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.9 (d, $^1J_{C–F}$ = 287.1 Hz), 143.8 (td, $^2J_{C–F}$ = 28.5 Hz, $^3J_{C–F}$ = 8.6 Hz), 139.3, 130.2,

129.8, 128.9, 128.8 (d, $^4J_{C–F}$ = 2.3 Hz), 128.1, 127.2 (d, $^3J_{C–F}$ = 4.3 Hz), 126.8 (q, $^4J_{C–F}$ = 3.8 Hz), 121.4 (d, $^3J_{C–F}$ = 5.1 Hz), 111.9 (t, $^1J_{C–F}$ = 235.9 Hz), 103.9 (d, $^2J_{C–F}$ = 11.7 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{11}N_2F_6^+$ 357.0826; found 357.0823.

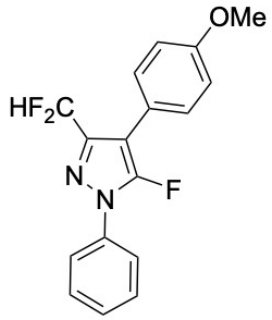
3-(Difluoromethyl)-5-fluoro-1-(naphthalen-2-yl)-4-phenyl-1*H*-pyrazole (3m)



3m **3m'**

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.1), 27.1 mg, 80% yield, m.p. 90–92 °C. Regioisomer ratio: 3m:3m' = 6:1. Major isomer: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 2.2 Hz, 1H), 7.91 (d, *J* = 8.9 Hz, 1H), 7.86–7.81 (m, 2H), 7.76 (dt, *J* = 8.9, 2.0 Hz, 1H), 7.55–7.45 (m, 3H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.33–7.05 (m, 2H), 6.70 (td, $^2J_{H–F}$ = 53.8 Hz, $^3J_{H–F}$ = 18.9 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.27 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H), -113.78 (dd, $^2J_{F–H}$ = 53.8 Hz, $^4J_{F–F}$ = 4.9 Hz, CF_2H), -130.77 (s, F), -172.80 (t, $^4J_{F–F}$ = 5.1 Hz, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.9 (d, $^1J_{C–F}$ = 285.5 Hz), 141.9 (td, $^2J_{C–F}$ = 28.4 Hz, $^3J_{C–F}$ = 8.5 Hz), 132.8 (d, $^4J_{C–F}$ = 2.9 Hz), 132.1, 131.4, 128.6, 128.1–127.9 (m), 127.7 (d, $^4J_{C–F}$ = 2.9 Hz), 127.2, 126.8, 126.7 (d, $^3J_{C–F}$ = 4.3 Hz), 126.2, 125.9, 125.1, 123.4, 118.9 (d, $^3J_{C–F}$ = 4.0 Hz), 111.1 (t, $^1J_{C–F}$ = 235.4 Hz), 102.3 (d, $^2J_{C–F}$ = 11.4 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{20}H_{14}N_2F_3^+$ 339.1109; found 339.1107.

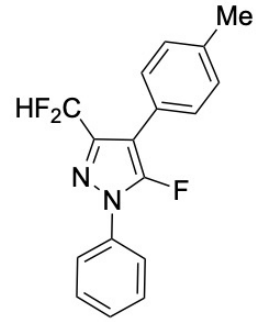
3-(Difluoromethyl)-5-fluoro-4-(4-methoxyphenyl)-1-phenyl-1*H*-pyrazole (3n)



3n

Obtained as an orange liquid after column chromatography (petroleum ether, R_f = 0.1), 21.6 mg, 68% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.8 Hz, 2H), 7.54–7.43 (m, 4H), 7.42 (d, *J* = 7.4 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 6.69 (t, $^2J_{H–F}$ = 53.7 Hz, 1H), 3.85 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.31 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H), -131.84 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.3, 149.6 (d, $^1J_{C–F}$ = 284.1 Hz), 142.8 (td, $^2J_{C–F}$ = 28.0 Hz, $^3J_{C–F}$ = 9.5 Hz), 136.6 (d, $^4J_{C–F}$ = 2.6 Hz), 132.9, 130.0 (d, $^4J_{C–F}$ = 2.4 Hz), 129.5, 128.2, 124.5, 123.9, 121.8 (d, $^3J_{C–F}$ = 4.0 Hz), 112.3 (t, $^1J_{C–F}$ = 236.8 Hz), 109.9 (d, $^2J_{C–F}$ = 11.2 Hz), 55.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{13}N_2F_3O^+$ 319.1047; found 319.1053.

3-(Difluoromethyl)-5-fluoro-1-phenyl-4-(*p*-tolyl)-1*H*-pyrazole (3o)

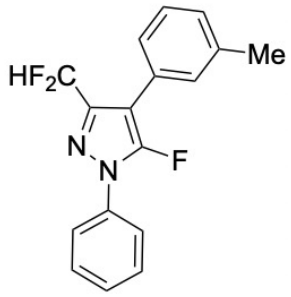


3o

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.1), 17.2 mg, 57% yield, m.p. 58–60 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.9 Hz, 2H), 7.47–7.36 (m, 4H), 7.35–7.29 (m, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.62 (t, $^2J_{H–F}$ = 53.7 Hz, 1H), 2.32 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.33 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H), -131.45 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.7 (d, $^1J_{C–F}$ = 285.0 Hz), 141.8

(td, $^{2}J_{C–F}$ = 28.2 Hz, $^{3}J_{C–F}$ = 8.5 Hz), 136.7, 135.5 (d, $^{4}J_{C–F}$ = 2.9 Hz), 128.4, 127.6 (q, $^{4}J_{C–F}$ = 2.0 Hz), 127.1, 123.7 (d, $^{3}J_{C–F}$ = 4.3 Hz), 120.8 (d, $^{3}J_{C–F}$ = 4.0 Hz), 111.1 (t, $^{1}J_{C–F}$ = 235.3 Hz), 102.1 (d, $^{2}J_{C–F}$ = 11.5 Hz), 20.2. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{14}N_2F_3^+$ 303.1109; found 303.1106.

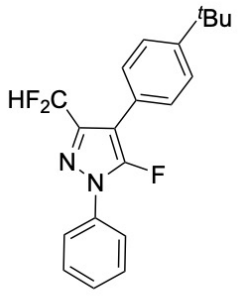
3-(Difluoromethyl)-5-fluoro-1-phenyl-4-(*m*-tolyl)-1*H*-pyrazole (3p)



3p

Obtained as an orange liquid after column chromatography (petroleum ether, R_f = 0.1), 21.8 mg, 72% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64–7.56 (m, 2H), 7.44 (t, *J* = 7.9 Hz, 2H), 7.37–7.22 (m, 4H), 7.11 (d, *J* = 7.0 Hz, 1H), 6.63 (t, $^{2}J_{H–F}$ = 53.9 Hz, 1H), 2.34 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.38 (d, $^{2}J_{F–H}$ = 53.8 Hz, CF_2H), -131.21 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.8 (d, $^{1}J_{C–F}$ = 285.1 Hz), 142.9 (td, $^{2}J_{C–F}$ = 28.0 Hz, $^{3}J_{C–F}$ = 8.3 Hz), 138.4, 136.6 (d, $^{3}J_{C–F}$ = 2.8 Hz), 129.5, 129.4 (q, $^{4}J_{C–F}$ = 2.1 Hz), 128.7, 128.2, 127.6 (d, $^{3}J_{C–F}$ = 4.4 Hz), 125.9 (q, $^{4}J_{C–F}$ = 1.9 Hz), 121.9 (d, $^{3}J_{C–F}$ = 4.0 Hz), 112.1 (t, $^{1}J_{C–F}$ = 235.4 Hz), 103.3 (d, $^{2}J_{C–F}$ = 11.3 Hz), 21.5. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{14}N_2F_3^+$ 303.1109; found 303.1099.

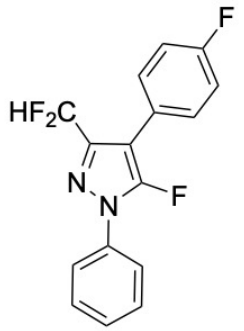
4-(4-(*tert*-Butyl)phenyl)-3-(difluoromethyl)-5-fluoro-1-phenyl-1*H*-pyrazole (3q)



3q

Obtained as a white liquid after column chromatography (petroleum ether, R_f = 0.1), 21.4 mg, 62% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.8 Hz, 2H), 7.47–7.39 (m, 6H), 7.34 (t, *J* = 7.5 Hz, 1H), 6.64 (t, $^2J_{H–F}$ = 53.7 Hz, 1H), 1.29 (s, 9H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.44 (d, $^2J_{F–H}$ = 53.7 Hz, CF_2H), -131.27 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.7 (d, $^1J_{C–F}$ = 284.1 Hz), 149.8, 141.8 (td, $^2J_{C–F}$ = 28.6 Hz, $^3J_{C–F}$ = 8.6 Hz), 135.5 (d, $^4J_{C–F}$ = 2.4 Hz), 129.9 (d, $^4J_{C–F}$ = 2.8 Hz), 128.5, 127.3 (d, $^4J_{C–F}$ = 2.2 Hz), 127.1, 124.7, 123.7 (d, $^3J_{C–F}$ = 4.4 Hz), 120.8 (d, $^3J_{C–F}$ = 4.1 Hz), 111.1 (t, $^1J_{C–F}$ = 235.6 Hz), 102.0 (d, $^2J_{C–F}$ = 11.3 Hz), 33.6, 30.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{20}H_{20}N_2F_3^+$ 345.1579; found 345.1587.

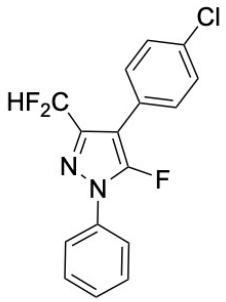
3-(Difluoromethyl)-5-fluoro-4-(4-fluorophenyl)-1-phenyl-1*H*-pyrazole (3r)



3r

Obtained as a yellow solid after column chromatography (petroleum ether, R_f = 0.1), 23.9 mg, 78% yield, m.p. 59–61 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.9 Hz, 2H), 7.54 (q, *J* = 8.3 Hz, 4H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.15 (t, *J* = 8.7 Hz, 2H), 6.69 (t, $^2J_{H–F}$ = 53.7 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.01 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H), -113.75–-113.83 (m, F), -131.43 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.3 (d, $^1J_{C–F}$ = 247.6 Hz), 148.7 (d, $^1J_{C–F}$ = 285.0 Hz), 141.8 (td, $^2J_{C–F}$ = 28.9 Hz, $^3J_{C–F}$ = 8.6 Hz), 135.4 (d, $^4J_{C–F}$ = 2.6 Hz), 132.0 (t, $^3J_{C–F}$ = 8.4 Hz), 129.5 (dd, $^3J_{C–F}$ = 8.2 Hz, $^4J_{C–F}$ = 2.2 Hz), 128.5, 127.3, 120.8 (d, $^3J_{C–F}$ = 3.9 Hz), 115.9, 115.6, 114.9, 114.6, 111.3 (t, $^1J_{C–F}$ = 235.2 Hz), 107.8 (d, $^2J_{C–F}$ = 6.3 Hz), 101.1 (d, $^2J_{C–F}$ = 11.4 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{11}N_2F_4^+$ 307.0858; found 307.0860.

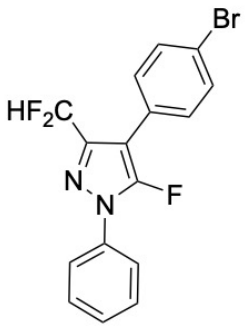
4-(4-Chlorophenyl)-3-(difluoromethyl)-5-fluoro-1-phenyl-1*H*-pyrazole (3s)



3s

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.2), 17.4 mg, 54% yield, m.p. 90–92 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.7 Hz, 2H), 7.53 (dd, *J* = 8.2, 6.2 Hz, 4H), 7.46–7.39 (m, 3H), 6.70 (t, $^2J_{H–F}$ = 53.7 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -110.94 (d, $^2J_{F–H}$ = 53.5 Hz, CF_2H), -130.77 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.8 (d, $^1J_{C–F}$ = 285.8 Hz), 142.9 (td, $^2J_{C–F}$ = 28.9 Hz, $^3J_{C–F}$ = 8.0 Hz), 136.4 (d, $^4J_{C–F}$ = 2.9 Hz), 133.9, 130.0 (q, $^4J_{C–F}$ = 2.2 Hz), 129.6, 129.0, 128.4, 126.3 (d, $^3J_{C–F}$ = 4.4 Hz), 121.9 (d, $^3J_{C–F}$ = 3.9 Hz), 112.4 (t, $^1J_{C–F}$ = 235.2 Hz), 102.0 (d, $^2J_{C–F}$ = 11.3 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{11}N_2F_3Cl^+$ 323.0563; found 323.0571.

4-(4-Bromophenyl)-3-(difluoromethyl)-5-fluoro-1-phenyl-1*H*-pyrazole (3t)

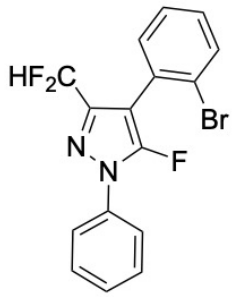


3t

Obtained as a white solid after column chromatography (petroleum ether, R_f = 0.2), 27.5 mg, 75% yield, m.p. 79–81 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64–7.57 (m, 2H), 7.55–7.47 (m, 2H), 7.46 (dd, *J* = 8.7, 7.1 Hz, 2H), 7.37 (dd, *J* = 15.7, 7.9 Hz, 3H), 6.62 (t, $^2J_{H–F}$ = 53.9 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -110.91 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H), -130.67 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.7 (d, $^1J_{C–F}$ = 286.5 Hz), 141.7

(td, $^{2}J_{C–F}$ = 29.6 Hz, $^{3}J_{C–F}$ = 8.6 Hz), 135.3 (d, $^{4}J_{C–F}$ = 2.9 Hz), 130.9, 129.2 (d, $^{4}J_{C–F}$ = 2.2 Hz), 128.5, 127.4, 125.7 (d, $^{3}J_{C–F}$ = 4.3 Hz), 120.9, 120.8 (d, $^{3}J_{C–F}$ = 3.9 Hz), 111.3 (t, $^{1}J_{C–F}$ = 235.2 Hz), 101.0 (d, $^{2}J_{C–F}$ = 11.2 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{11}N_2F_3Br^+$ 367.0058; found 367.0066.

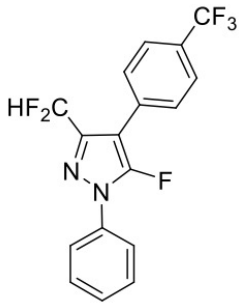
4-(2-Bromophenyl)-3-(difluoromethyl)-5-fluoro-1-phenyl-1*H*-pyrazole (3u)



3u

Obtained as a white liquid after column chromatography (petroleum ether, R_f = 0.1), 25.7 mg, 70% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79–7.65 (m, 3H), 7.53 (t, *J* = 7.9 Hz, 2H), 7.48–7.37 (m, 3H), 7.32–7.24 (m, 1H), 6.64 (t, $^{2}J_{H–F}$ = 53.8 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.42 (d, $^{2}J_{F–H}$ = 52.5 Hz, CF_2H), -126.02 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.6 (d, $^{1}J_{C–F}$ = 285.8 Hz), 143.6 (td, $^{2}J_{C–F}$ = 27.6 Hz, $^{3}J_{C–F}$ = 8.7 Hz), 136.5 (d, $^{4}J_{C–F}$ = 3.0 Hz), 132.9 (d, $^{4}J_{C–F}$ = 3.4 Hz), 130.2, 129.5, 129.1, 128.8 (d, $^{3}J_{C–F}$ = 3.9 Hz), 128.3, 127.4, 124.8, 123.8, 121.9 (d, $^{3}J_{C–F}$ = 4.0 Hz), 111.5 (t, $^{1}J_{C–F}$ = 235.9 Hz), 102.3 (d, $^{2}J_{C–F}$ = 13.7 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{11}N_2F_3Br^+$ 367.0058; found 367.0065.

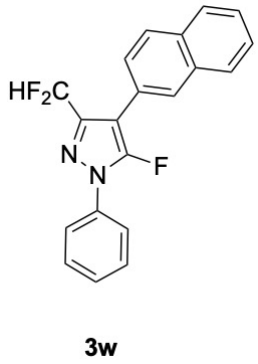
3-(Difluoromethyl)-5-fluoro-1-phenyl-4-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (3v)



3v

Obtained as a yellow solid after column chromatography (petroleum ether, R_f = 0.1), 26.7 mg, 75% yield, m.p. 60–62 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74–7.66 (m, 6H), 7.57–7.51 (m, 2H), 7.47–7.42 (m, 1H), 6.72 (t, $^2J_{H–F}$ = 53.7 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.67 (s, CF_3), -110.76 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H), -130.07 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.0 (d, $^1J_{C–F}$ = 286.5 Hz), 142.9 (td, $^2J_{C–F}$ = 29.5 Hz, $^3J_{C–F}$ = 7.6 Hz), 136.2 (d, $^4J_{C–F}$ = 2.9 Hz), 131.6 (d, $^3J_{C–F}$ = 5.2 Hz), 129.6, 128.9 (d, $^4J_{C–F}$ = 2.3 Hz), 128.5, 125.7 (q, $^3J_{C–F}$ = 3.9 Hz), 121.9 (d, $^3J_{C–F}$ = 3.9 Hz), 112.4 (t, $^1J_{C–F}$ = 235.0 Hz), 101.8 (d, $^2J_{C–F}$ = 10.8 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{11}N_2F_6^+$ 357.0826; found 357.0826.

3-(Difluoromethyl)-5-fluoro-4-(naphthalen-1-yl)-1-phenyl-1*H*-pyrazole (3w)

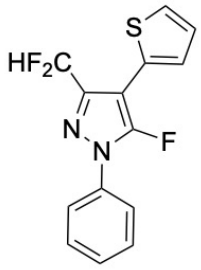


3w

Obtained as a yellow liquid after column chromatography (petroleum ether, R_f = 0.1), 23.7 mg, 70% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01–7.89 (m, 2H), 7.82–7.70 (m, 3H), 7.61–7.48 (m, 6H), 7.43 (t, *J* = 7.4 Hz, 1H), 6.60 (t, $^2J_{H–F}$ = 53.7 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -112.61 (dd, $^2J_{F–H}$ = 275.2 Hz, $^6J_{F–H}$ = 54.0 Hz, CF_2H), -128.67 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.2 (d, $^1J_{C–F}$ = 285.1 Hz), 144.3 (td, $^2J_{C–F}$ = 27.4 Hz, $^3J_{C–F}$ = 8.6 Hz), 136.7 (d, $^3J_{C–F}$ = 3.0 Hz), 135.3, 133.7, 132.2, 129.6, 129.3, 129.2,

128.5, 128.2, 126.6, 126.2, 125.3, 125.2, 124.7 (d, $^{3}J_{C-F}$ = 3.3 Hz), 121.8 (d, $^{3}J_{C-F}$ = 4.1 Hz), 111.3 (t, $^{1}J_{C-F}$ = 236.2 Hz), 101.1 (d, $^{2}J_{C-F}$ = 14.2 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{20}H_{14}N_2F_3^+$ 339.1109; found 339.1102.

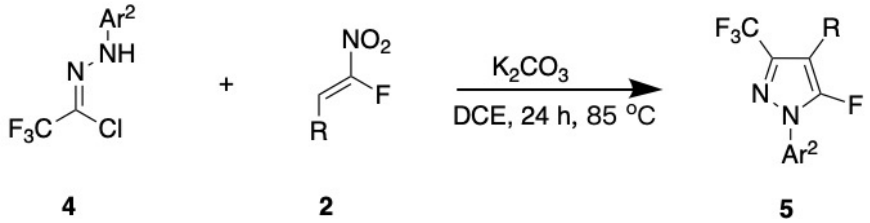
3-(Difluoromethyl)-5-fluoro-1-phenyl-4-(thiophen-2-yl)-1*H*-pyrazole (3x)



3x

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.1), 7.9 mg, 27% yield, m.p. 83–85 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74–7.64 (m, 2H), 7.54 (d, *J* = 7.5 Hz, 2H), 7.47–7.40 (m, 1H), 7.40–7.33 (m, 2H), 7.12 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.73 (t, $^{2}J_{H-F}$ = 53.6 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -112.64 (d, $^{2}J_{F-H}$ = 53.4 Hz, CF_2H), -127.91 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.9 (d, $^{1}J_{C-F}$ = 288.2 Hz), 141.4 (d, $^{3}J_{C-F}$ = 5.7 Hz), 141.2, 140.4 (td, $^{2}J_{C-F}$ = 28.0 Hz, $^{3}J_{C-F}$ = 8.0 Hz), 135.2, 128.46, 128.51 (d, $^{4}J_{C-F}$ = 2.3 Hz), 127.4, 120.9 (d, $^{3}J_{C-F}$ = 3.8 Hz), 110.4 (t, $^{1}J_{C-F}$ = 235.8 Hz), 110.3, 107.1 (q, $^{4}J_{C-F}$ = 2.5 Hz), 94.1 (d, $^{2}J_{C-F}$ = 12.6 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{14}H_{10}N_2F_3S^+$ 295.0517; found 295.0524.

2.5 General procedure G for the reaction of hydrazonyl chlorides 4 with α-fluoronitroalkene 2

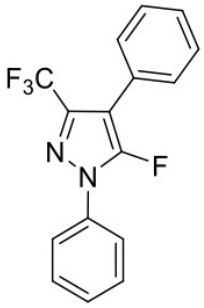


4 **2** **5**

To a 10 ml sealed screw-capped pressure tube equipped with a stirring bar and dried in an oven, hydrazone acyl chloride (**4**, 0.3 mmol), α-fluoronitroalkenes (**2**, 0.1 mmol) and

K_2CO_3 (55.3 mg, 0.4 mmol). 1,2-Dichloroethane (1.0 mL) was transferred into the tube through a syringe. The resulting mixture was stirred at 85 °C for 24 hours. The reaction mixture was extracted with EtOAc. The combined organic phases were concentrated in vacuo, and the residue was purified by flash chromatography on silica gel (eluted with petroleum ether/ethyl acetate) to obtain the desired product **5**.

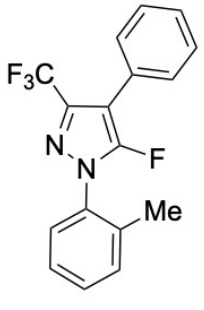
5-Fluoro-1,4-diphenyl-3-(trifluoromethyl)-1*H*-pyrazole (5a)



5a

Obtained as a yellow liquid after column chromatography (petroleum ether, R_f = 0.1), 25.7 mg, 87% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.9 Hz, 2H), 7.45 (d, *J* = 7.6 Hz, 2H), 7.39 (td, *J* = 10.0, 3.2 Hz, 4H), 7.33 (dd, *J* = 12.2, 4.8 Hz, 2H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.04 (s, CF_3), -130.83 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.6 (d, $^1J_{C–F}$ = 285.5 Hz), 137.9 (qd, $^2J_{C–F}$ = 37.4 Hz, $^3J_{C–F}$ = 8.6 Hz), 135.2 (d, $^4J_{C–F}$ = 2.9 Hz), 128.5, 128.0 (t, $^4J_{C–F}$ = 1.5 Hz), 127.7, 127.5, 127.2, 125.9 (d, $^3J_{C–F}$ = 3.9 Hz), 121.0 (d, $^3J_{C–F}$ = 3.7 Hz), 119.7 (qd, $^1J_{C–F}$ = 271.1 Hz, $^4J_{C–F}$ = 1.2 Hz), 104.3–100.7 (m). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{11}N_2F_4^+$ 307.0858; found 307.0854.

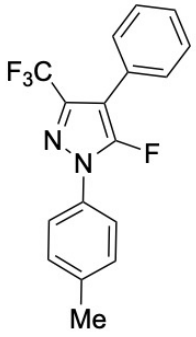
5-Fluoro-1-phenyl-4-(*o*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazole (5b)



5b

Obtained as a yellow solid after column chromatography (petroleum ether, R_f = 0.1), 22.4 mg, 70% yield, m.p. 54–56 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (s, 2H), 7.47 (d, *J* = 6.0 Hz, 5H), 7.43–7.37 (m, 2H), 2.45 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.02 (s, CF_3), -130.80 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.3 (d, $^1J_{C–F}$ = 282.6 Hz), 139.0 (qd, $^2J_{C–F}$ = 37.1 Hz, $^3J_{C–F}$ = 8.1 Hz), 135.4, 135.3, 134.5 (d, $^4J_{C–F}$ = 2.1 Hz), 131.4, 131.3, 130.4, 129.9, 129.2, 129.0, 128.8, 128.7, 128.1, 127.9, 127.2, 126.9, 120.8 (qd, $^1J_{C–F}$ = 271.6 Hz, $^4J_{C–F}$ = 1.2 Hz), 105.6–96.3 (m), 21.8–13.4 (m). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{13}N_2F_4^+$ 321.1015; found 321.1007.

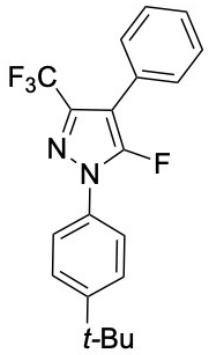
5-Fluoro-4-phenyl-1-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazole (5c)



5c

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.1), 25.0 mg, 78% yield, m.p. 56–58 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62–7.54 (m, 2H), 7.46 (d, *J* = 6.7 Hz, 4H), 7.41 (dd, *J* = 5.6, 2.8 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.43 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -60.99 (s, CF_3), -131.14 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.6 (d, $^1J_{C–F}$ = 284.9 Hz), 138.76, 138.75 (qd, $^2J_{C–F}$ = 38.1 Hz, $^3J_{C–F}$ = 8.3 Hz), 133.9 (d, $^4J_{C–F}$ = 3.0 Hz), 130.9 (d, $^3J_{C–F}$ = 7.9 Hz), 130.1, 129.1, 128.7, 128.2, 127.2 (d, $^3J_{C–F}$ = 4.1 Hz), 122.1 (d, $^4J_{C–F}$ = 3.5 Hz), 120.9 (qd, $^1J_{C–F}$ = 269.5 Hz, $^4J_{C–F}$ = 1.7 Hz), 103.6–102.3 (m), 21.1. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{13}N_2F_4^+$ 321.1015; found 321.1022.

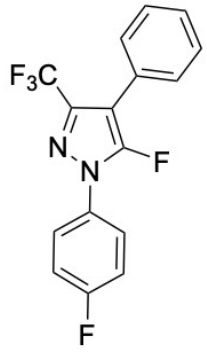
1-(4-(*tert*-Butyl)phenyl)-5-fluoro-4-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5d)



5d

Obtained as a yellow solid after column chromatography (petroleum ether, R_f = 0.1), 29.4 mg, 81% yield, m.p. 60–62 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.53 (dd, *J* = 8.7, 2.0 Hz, 2H), 7.46 (dt, *J* = 13.1, 4.2 Hz, 4H), 7.41–7.36 (m, 1H), 1.36 (d, *J* = 2.0 Hz, 9H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.00 (s, CF_3), -131.25 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.9, 149.6 (d, $^1J_{C–F}$ = 285.1 Hz), 138.8 (qd, $^2J_{C–F}$ = 38.0 Hz, $^3J_{C–F}$ = 9.4 Hz), 133.7 (d, $^4J_{C–F}$ = 2.9 Hz), 129.1, 128.7, 128.2, 127.2 (d, $^3J_{C–F}$ = 4.0 Hz), 126.5, 121.9 (d, $^4J_{C–F}$ = 3.6 Hz), 120.8 (qd, $^1J_{C–F}$ = 271.0 Hz, $^4J_{C–F}$ = 1.5 Hz), 103.3(d, $^2J_{C–F}$ = 14.6 Hz), 34.8, 31.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{20}H_{19}N_2F_4^+$ 363.1484; found 363.1492.

5-Fluoro-1-(4-fluorophenyl)-4-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5e)

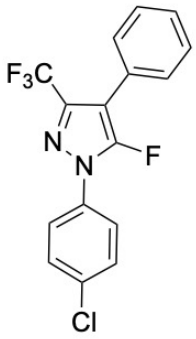


5e

Obtained as an orange liquid after column chromatography (petroleum ether, R_f = 0.1), 13.0 mg, 40% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71–7.68 (m, 2H), 7.51–7.43 (m, 4H), 7.40 (dq, *J* = 5.3, 2.7 Hz, 1H), 7.38–7.20 (m, 2H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.13 (s, CF_3), -112.04 –-112.01 (m, F), -131.13 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.3 (d, $^1J_{C–F}$ = 249.3 Hz), 149.6 (d, $^1J_{C–F}$ = 285.1 Hz), 139.2 (qd, $^2J_{C–F}$ = 37.4 Hz, $^3J_{C–F}$

= 9.0 Hz), 135.8, 132.4, 129.1, 128.8, 128.4, 126.9, 124.1 (dd, $^{3}J_{C–F}$ = 8.6 Hz, $^{4}J_{C–F}$ = 3.8 Hz), 120.8 (qd, $^{1}J_{C–F}$ = 271.1, $^{4}J_{C–F}$ = 1.4 Hz), 116.6 (d, $^{2}J_{C–F}$ = 23.3 Hz), 103.6 (d, $^{2}J_{C–F}$ = 13.2 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{10}N_2F_5^+$ 325.0764; found 325.0771.

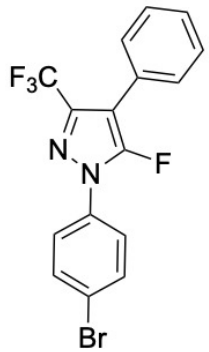
1-(4-Chlorophenyl)-5-fluoro-4-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5f)



5f

Obtained as a white liquid after column chromatography (petroleum ether, R_f = 0.1), 31.3 mg, 92% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 2H), 7.48–7.30 (m, 6H), 7.28–7.14 (m, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.18 (s, CF_3), -130.45 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.6 (d, $^{1}J_{C–F}$ = 285.6 Hz), 139.4 (qd, $^{2}J_{C–F}$ = 37.4 Hz, $^{3}J_{C–F}$ = 9.0 Hz), 134.8 (d, $^{3}J_{C–F}$ = 3.0 Hz), 134.4, 129.8, 129.1, 128.8, 128.4, 123.1 (d, $^{3}J_{C–F}$ = 4.1 Hz), 120.8 (qd, $^{1}J_{C–F}$ = 270.2 Hz, $^{4}J_{C–F}$ = 2.0 Hz), 109.9. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{10}N_2F_4Cl^+$ 341.0469; found 341.0475.

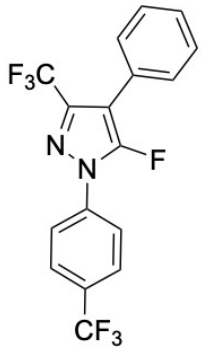
1-(4-Bromophenyl)-5-fluoro-4-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5g)



5g

Obtained as a brown liquid after column chromatography (petroleum ether, R_f = 0.1), 23.5 mg, 61% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69–7.64 (m, 2H), 7.61 (dd, *J* = 8.9, 1.8 Hz, 2H), 7.46 (d, *J* = 4.4 Hz, 4H), 7.42 (dd, *J* = 8.2, 4.3 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.20 (s, CF_3), -130.34 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.6 (d, $^1J_{C–F}$ = 286.1 Hz), 139.8–139.4 (qd, $^2J_{C–F}$ = 37.8 Hz, $^3J_{C–F}$ = 9.3 Hz), 135.3 (d, $^3J_{C–F}$ = 3.0 Hz), 132.8, 129.4, 129.1, 128.8, 128.4, 123.3 (d, $^3J_{C–F}$ = 4.3 Hz), 122.3, 120.8 (qd, $^1J_{C–F}$ = 270.5 Hz, $^4J_{C–F}$ = 1.5 Hz), 103.9 (d, $^2J_{C–F}$ = 13.1 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{10}N_2F_4Br^+$ 384.9963; found 384.9957.

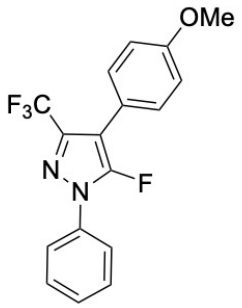
5-Fluoro-4-phenyl-3-(trifluoromethyl)-1-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (5h)



5h

Obtained as a white solid after column chromatography (petroleum ether, R_f = 0.1), 17.6 mg, 47% yield, m.p. 53–55 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70–7.67 (m, 2H), 7.47 (d, *J* = 4.5 Hz, 4H), 7.43–7.38 (m, 1H), 7.23 (t, *J* = 8.1 Hz, 2H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.2 (s, CF_3), -67.8 (s, CF_3), -130.5 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.88 (d, $^1J_{C–F}$ = 286.7 Hz), 139.9 (qd, $^2J_{C–F}$ = 37.7 Hz, $^3J_{C–F}$ = 8.7 Hz), 139.0, 129.2, 129.1, 128.8, 128.5, 126.9 (q, $^3J_{C–F}$ = 3.8 Hz), 126.5 (dd, $^3J_{C–F}$ = 7.8 Hz, $^4J_{C–F}$ = 4.0 Hz), 124.9 (d, $^4J_{C–F}$ = 2.2 Hz), 121.7 (d, $^3J_{C–F}$ = 4.7 Hz), 120.7 (qd, $^1J_{C–F}$ = 271.4 Hz, $^4J_{C–F}$ = 1.2 Hz), 119.4 (q, $^1J_{C–F}$ = 277.6 Hz), 106.8–102.5 (m). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{10}N_2F_7^+$ 375.0732; found 375.0725.

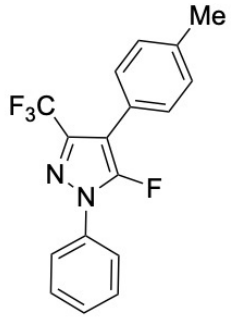
5-Fluoro-4-(4-methoxyphenyl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5i)



5i

Obtained as a brown liquid after column chromatography (petroleum ether/ethyl acetate = 100:1, R_f = 0.4), 13.5 mg, 40% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68– 7.59 (m, 2H), 7.48–7.44 (m, 2H), 7.35 (dd, *J* = 15.9, 8.0 Hz, 3H), 7.00–6.88 (m, 2H), 3.79 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.19 (s, CF_3), -131.32 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.6, 149.6 (d, $^1J_{C–F}$ = 283.9 Hz), 139.0 (qd, $^2J_{C–F}$ = 37.9 Hz, $^3J_{C–F}$ = 9.5 Hz), 136.4 (d, $^4J_{C–F}$ = 2.6 Hz), 130.3, 129.6, 128.5, 122.1 (d, $^3J_{C–F}$ = 3.9 Hz), 121.0 (qd, $^1J_{C–F}$ = 274.7 Hz, $^4J_{C–F}$ = 1.7 Hz), 119.2 (d, $^3J_{C–F}$ = 4.0 Hz), 114.2, 103.3 (d, $^2J_{C–F}$ = 14.2 Hz), 55.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{19}N_2OF_4^+$ 337.0964; found 337.0972.

5-Fluoro-1-phenyl-4-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazole (5j)

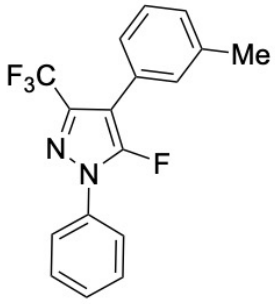


5j

Obtained as an orange liquid after column chromatography (petroleum ether, R_f = 0.2), 25.6 mg, 80% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67–7.60 (m, 2H), 7.45 (td, *J* = 8.0, 3.8 Hz, 2H), 7.38–7.32 (m, 1H), 7.29 (d, *J* = 7.8 Hz, 2H), 7.23–7.15 (m, 2H), 2.33 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.12 (s, CF_3), -131.03 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.7 (d, $^1J_{C–F}$ = 284.6 Hz), 139.1 (qd, $^2J_{C–F}$ = 37.5 Hz, $^3J_{C–F}$ = 9.0 Hz), 138.2, 136.3 (d, $^4J_{C–F}$ = 2.9 Hz), 130.9 (d, $^3J_{C–F}$ = 7.7 Hz), 130.2, 129.6, 129.5, 129.1–

128.8 (m), 128.5, 124.0 (d, $^{3}J_{C–F}$ = 4.0 Hz), 122.1 (d, $^{4}J_{C–F}$ = 3.8 Hz), 120.9 (qd, $^{1}J_{C–F}$ = 271.1 Hz, $^{4}J_{C–F}$ = 1.7 Hz), 103.5 (d, $^{2}J_{C–F}$ = 12.5 Hz), 21.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{13}N_2F_4^+$ 321.1015; found 321.1021.

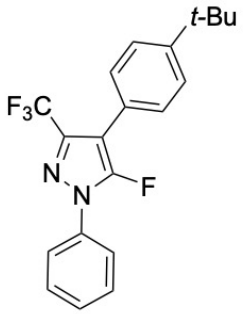
5-Fluoro-1-phenyl-4-(*m*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazole (5k)



5k

Obtained as an orange liquid after column chromatography (petroleum ether, R_f = 0.1), 22.4 mg, 70% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69–7.60 (m, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.30–7.12 (m, 4H), 2.34 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.06 (s, CF_3), -130.81 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.7 (d, $^{1}J_{C–F}$ = 285.2 Hz), 139.1 (qd, $^{2}J_{C–F}$ = 37.3 Hz, $^{3}J_{C–F}$ = 8.8 Hz), 138.4, 136.3 (d, $^{4}J_{C–F}$ = 2.9 Hz), 129.8, 129.6, 129.1, 128.6 (d, $^{3}J_{C–F}$ = 7.3 Hz), 126.9 (d, $^{3}J_{C–F}$ = 4.0 Hz), 126.2, 123.6 (qd, $^{1}J_{C–F}$ = 272.5 Hz, $^{4}J_{C–F}$ = 1.6 Hz), 122.1 (d, $^{4}J_{C–F}$ = 3.9 Hz), 103.7 (d, $^{2}J_{C–F}$ = 13.0 Hz), 21.5. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{13}N_2F_4^+$ 321.1015; found 321.1015.

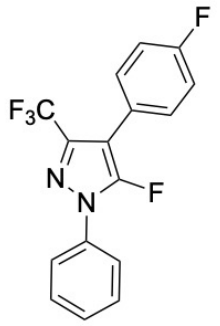
4-(4-(*tert*-Butyl)phenyl)-5-fluoro-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5l)



5l

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.1), 31.9 mg, 88% yield, m.p. 87–89 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.9 Hz, 2H), 7.42 (dd, *J* = 20.8, 7.9 Hz, 4H), 7.33 (d, *J* = 7.9 Hz, 3H), 1.28 (s, 9H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.05 (s, CF_3), -130.81 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.3, 149.7 (d, $^1J_{C–F}$ = 285.0 Hz), 139.0 (qd, $^2J_{C–F}$ = 37.3 Hz, $^3J_{C–F}$ = 9.0 Hz), 136.4 (d, $^4J_{C–F}$ = 2.9 Hz), 129.6, 128.7, 128.5, 125.7, 124.0 (d, $^3J_{C–F}$ = 4.0 Hz), 122.1 (d, $^3J_{C–F}$ = 4.0 Hz), 121.0 (qd, $^1J_{C–F}$ = 270.1 Hz, $^4J_{C–F}$ = 1.2 Hz), 103.5 (d, $^2J_{C–F}$ = 13.2 Hz), 34.7, 31.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{20}H_{19}N_2F_4^+$ 363.1484; found 364.1475.

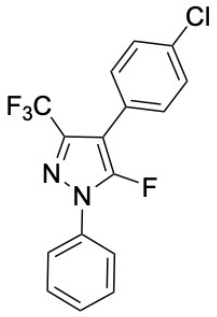
5-Fluoro-4-(4-fluorophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5m)



5m

Obtained as a brown solid after column chromatography (petroleum ether, R_f = 0.1), 16.5 mg, 51% yield, m.p. 50–53 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 8.1, 1.9 Hz, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.37 (dd, *J* = 8.3, 5.4 Hz, 3H), 7.08 (t, *J* = 8.7 Hz, 2H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.16 (s, CF_3), -113.09–-113.13 (m, F), -130.99 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.7 (d, $^1J_{C–F}$ = 248.2 Hz), 149.7 (d, *J* = 285.1 Hz), 139.0 (qd, $^2J_{C–F}$ = 37.6 Hz, $^3J_{C–F}$ = 9.0 Hz), 136.2 (d, *J* = 2.8 Hz), 130.9 (dt, $^3J_{C–F}$ = 8.3 Hz, $^4J_{C–F}$ = 1.5 Hz), 129.9, 129.7, 129.6, 129.2 (d, $^2J_{C–F}$ = 35.0 Hz), 128.7, 122.1 (d, $^4J_{C–F}$ = 3.8 Hz), 120.9 (qd, $^1J_{C–F}$ = 270.1 Hz, $^4J_{C–F}$ = 2.0 Hz), 115.9 (d, $^2J_{C–F}$ = 21.7 Hz), 113.6, 105.9–97.3 (m). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{10}N_2F_5^+$ 325.0764; found 325.0771.

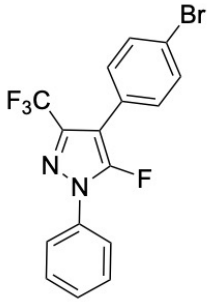
4-(4-Chlorophenyl)-5-fluoro-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5n)



5n

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.1), 22.1 mg, 65% yield, m.p. 55–57 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.8 Hz, 2H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.42–7.32 (m, 5H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.12 (s, CF_3), -130.50 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.7 (d, $^1J_{C–F}$ = 285.7 Hz), 142.9, 138.9 (qd, $^2J_{C–F}$ = 37.9 Hz, $^3J_{C–F}$ = 8.9 Hz), 136.2 (d, $^4J_{C–F}$ = 2.9 Hz), 134.4, 130.3, 129.6, 129.1, 128.7, 125.5 (d, $^3J_{C–F}$ = 4.1 Hz), 122.1 (d, $^3J_{C–F}$ = 3.8 Hz), 120.4 (qd, $^1J_{C–F}$ = 270.0 Hz, $^4J_{C–F}$ = 1.8 Hz), 113.6, 102.5 (d, $^2J_{C–F}$ = 12.6 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{10}N_2F_4Cl^+$ 341.0469; found 341.0476.

4-(4-Bromophenyl)-5-fluoro-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5o)

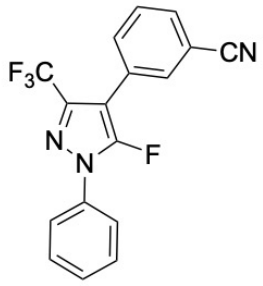


5o

Obtained as a red solid after column chromatography (petroleum ether, R_f = 0.2), 33.9 mg, 88% yield, m.p. 85–87 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.9 Hz, 2H), 7.61 (dd, *J* = 11.6, 8.3 Hz, 2H), 7.57–7.49 (m, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 9.1 Hz, 2H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.09 (s, CF_3), -130.41 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.6 (d, $^1J_{C–F}$ = 285.4 Hz), 138.9 (qd, $^2J_{C–F}$ = 37.3 Hz, $^3J_{C–F}$ = 8.9 Hz), 136.1 (d, $^4J_{C–F}$ = 2.9 Hz), 132.8, 132.0, 130.6, 129.6, 128.7, 124.2 (qd, $^1J_{C–F}$ = 288.9

Hz, $^{4}J_{C–F}$ = 1.0 Hz), 126.0 (d, $^{3}J_{C–F}$ = 4.1 Hz), 122.6, 122.1 (d, $^{3}J_{C–F}$ = 3.8 Hz), 108.9 (d, $^{2}J_{C–F}$ = 6.2 Hz), 102.5 (d, $^{2}J_{C–F}$ = 12.7 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{10}N_2F_4Br^+$ 384.9963; found 384.9956.

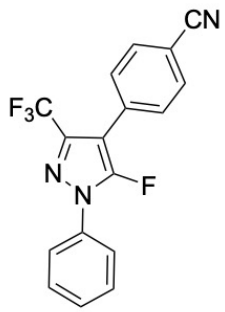
3-(5-Fluoro-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-4-yl)benzonitrile (5p)



5p

Obtained as an orange liquid after column chromatography (petroleum ether/ethyl acetate = 5:1, R_f = 0.2), 19.9 mg, 60% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.75–7.66 (m, 4H), 7.63–7.52 (m, 3H), 7.47 (dd, *J* = 8.4, 6.4 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.03 (s, CF_3), -129.89 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.8 (d, $^{1}J_{C–F}$ = 286.4 Hz), 141.6, 138.8 (qd, $^{2}J_{C–F}$ = 37.9 Hz, $^{3}J_{C–F}$ = 8.8 Hz), 135.9 (d, $^{4}J_{C–F}$ = 3.0 Hz), 133.4, 132.4, 131.8, 129.8, 129.7, 129.5, 128.9, 128.6 (d, $^{3}J_{C–F}$ = 4.3 Hz), 122.2 (d, $^{3}J_{C–F}$ = 3.7 Hz), 120.7 (qd, $^{1}J_{C–F}$ = 271.4 Hz, $^{4}J_{C–F}$ = 2.0 Hz), 118.3, 113.9, 113.2, 101.5 (d, $^{2}J_{C–F}$ = 12.3 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{10}N_3F_4^+$ 332.0811; found 332.0819.

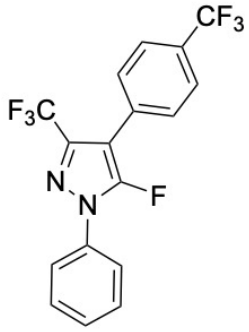
4-(5-Fluoro-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-4-yl)benzonitrile (5q)



5q

Obtained as a white solid after column chromatography (petroleum ether/ethyl acetate = 5:1, R_f = 0.2), 20.2 mg, 61% yield, m.p. 104–106 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.62 (dd, *J* = 8.0, 1.9 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.03 (s, CF_3), -129.28 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.8 (d, $^1J_{C–F}$ = 287.3 Hz), 138.9 (qd, $^2J_{C–F}$ = 38.8 Hz, $^3J_{C–F}$ = 9.5 Hz), 135.9 (d, $^4J_{C–F}$ = 2.8 Hz), 132.6, 131.9 (d, $^3J_{C–F}$ = 4.3 Hz), 129.7, 129.5, 129.0, 122.2 (d, $^3J_{C–F}$ = 3.7 Hz), 120.7 (qd, $^1J_{C–F}$ = 270.2 Hz, $^4J_{C–F}$ = 1.8 Hz), 118.4, 112.1, 101.9 (d, $^2J_{C–F}$ = 11.4 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{10}N_3F_4^+$ 332.0811; found 332.0802.

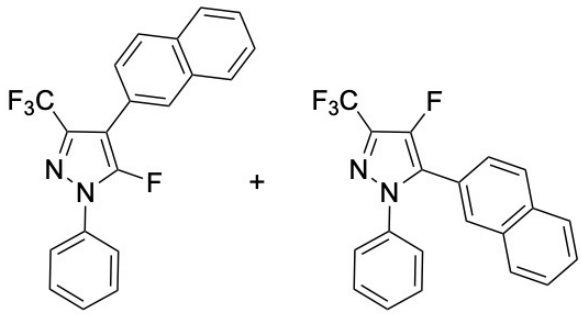
5-Fluoro-1-phenyl-3-(trifluoromethyl)-4-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (5r)



5r

Obtained as an orange solid after column chromatography (petroleum ether, R_f = 0.1), 26.6 mg, 71% yield, m.p. 90–92 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (t, *J* = 7.7 Hz, 4H), 7.54 (d, *J* = 7.9 Hz, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.06 (s, CF_3), -62.74 (s, CF_3), -130.00 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.9 (d, $^1J_{C–F}$ = 286.5 Hz), 142.9, 138.9 (qd, $^2J_{C–F}$ = 38.0 Hz, $^3J_{C–F}$ = 8.8 Hz), 136.1 (d, $^4J_{C–F}$ = 2.9 Hz), 130.8, 130.5 (d, $^3J_{C–F}$ = 6.4 Hz), 130.2, 129.5 (d, $^2J_{C–F}$ = 33.0 Hz), 128.9, 125.7 (q, $^3J_{C–F}$ = 3.8 Hz), 124.0 (q, $^1J_{C–F}$ = 272.2 Hz), 122.1 (d, $^4J_{C–F}$ = 3.7 Hz), 121.0 (qd, $^1J_{C–F}$ = 270.3 Hz, $^4J_{C–F}$ = 2.1 Hz), 113.6, 102.3 (d, $^2J_{C–F}$ = 12.8 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{10}N_2F_7^+$ 375.0732; found 375.0730.

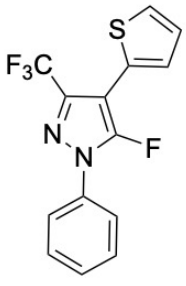
5-Fluoro-4-(naphthalen-2-yl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5s)



5s **5s'**

Obtained as a yellow solid after column chromatography (petroleum ether, R_f = 0.1), 28.5 mg, 80% yield, m.p. 53–55 °C. Regioisomer ratio: 5s:5s' = 2.5:1. Major isomer: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95–7.89 (m, 2H), 7.81–7.72 (m, 2H), 7.57–7.48 (m, 6H), 7.46–7.41 (m, 1H), 7.18 (d, *J* = 1.7 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.35 (d, $^4J_{F–F}$ = 6.9 Hz, CF_3), -61.59 (s, CF_3), -127.95 (s, F), -168.12 (q, $^4J_{F–F}$ = 7.2 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.2 (d, $^1J_{C–F}$ = 285.4 Hz), 144.8 (d, $^1J_{C–F}$ = 257.2 Hz), 140.7 (qd, $^2J_{C–F}$ = 37.4 Hz, $^3J_{C–F}$ = 9.6 Hz), 139.1, 136.4 (d, $^3J_{C–F}$ = 2.9 Hz), 133.7, 132.3, 131.4, 130.7, 129.8, 129.6, 129.5, 129.3, 129.1, 128.7, 128.6 (d, $^3J_{C–F}$ = 5.2 Hz), 128.3, 127.5, 126.72, 126.69, 126.2, 125.3, 125.2, 125.1, 124.7, 124.2 (d, $^4J_{C–F}$ = 3.3 Hz), 123.9, 120.6 (qd, $^1J_{C–F}$ = 257.3 Hz, $^4J_{C–F}$ = 2.2 Hz), 122.0 (d, $^3J_{C–F}$ = 4.0 Hz), 101.4 (d, $^2J_{C–F}$ = 15.2 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{20}H_{13}N_2F_4^+$ 357.1015; found 357.1006.

5-Fluoro-1-phenyl-4-(thiophen-2-yl)-3-(trifluoromethyl)-1*H*-pyrazole (5t)

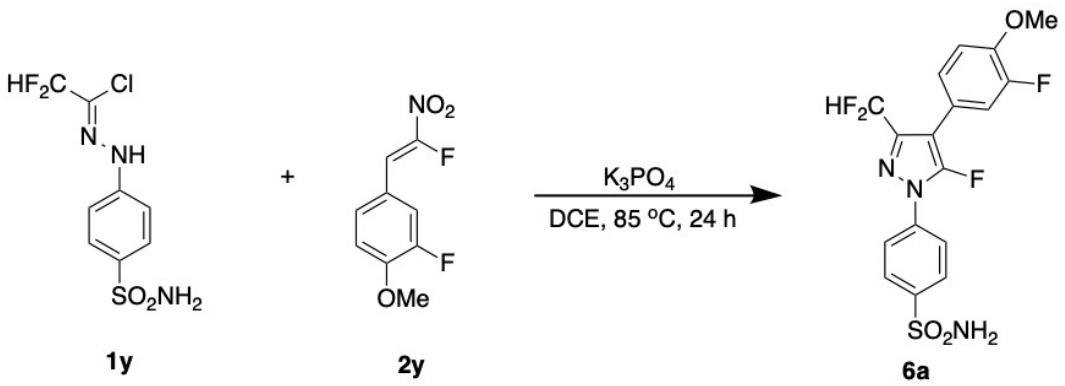


5t

Obtained as an orange liquid after column chromatography (petroleum ether, R_f = 0.1), 10.3 mg, 33% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74–7.63 (m, 2H), 7.60–7.48 (m, 2H), 7.48–7.37 (m, 2H), 7.26 (s, 1H), 7.13 (dd, *J* = 5.2, 3.6 Hz, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.14 (s, CF_3), -127.39 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.3

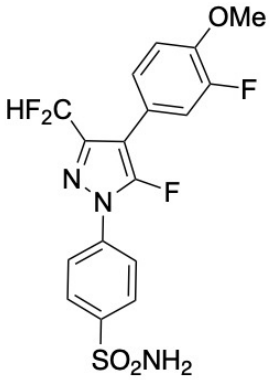
(d, $^{1}J_{C-F}$ = 536.9 Hz), 138.6 (qd, $^{2}J_{C-F}$ = 43.7 Hz, $^{3}J_{C-F}$ = 10.5 Hz), 136.1 (d, $^{4}J_{C-F}$ = 2.7 Hz), 129.9, 129.6, 128.7, 127.8–127.6 (m), 127.5, 126.8 (d, $^{3}J_{C-F}$ = 5.5 Hz), 126.4 (d, $^{4}J_{C-F}$ = 1.4 Hz), 122.1 (d, $^{3}J_{C-F}$ = 3.8 Hz), 121.2 (qd, $^{1}J_{C-F}$ = 301.8 Hz, $^{4}J_{C-F}$ = 3.0 Hz), 97.4 (d, $^{3}J_{C-F}$ = 3.6 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{14}H_9N_2F_4S^+$ 313.0423; found 313.0432.

2.6 General procedure H for synthetic transformations



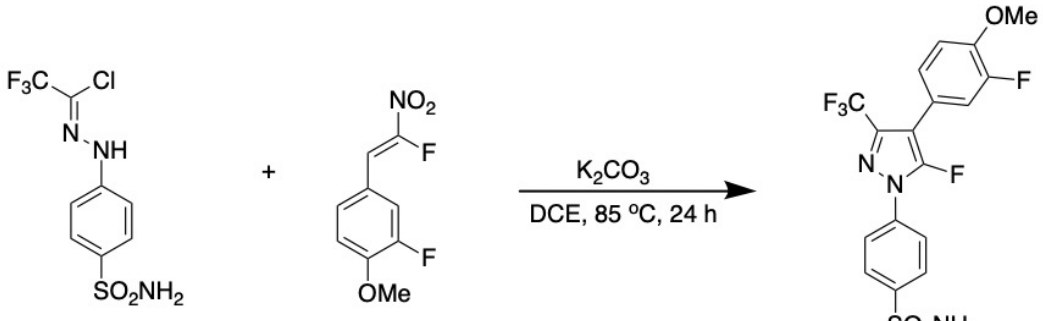
To a 10 mL sealed tube equipped with a stirring bar and dried in an oven, 4-sulfamoyl-phenyl derived hydrazonoyl chlorides (**1y**, 0.15 mmol), (*Z*)-2-fluoro-4-(2-fluoro-2-nitrovinyl)-1-methoxybenzene (**2y**, 0.1 mmol) and K_3PO_4 (42.5 mg, 0.2 mmol). DCE (1.0 mL) was transferred into the tube via a syringe. The resulting mixture was stirred at 85 ℃ for 24 h. The combined organic phases were concentrated in vacuo, and the residue was purified by flash chromatography on silica gel (eluted with petroleum ether/ethyl acetate) to obtain the desired product **6a**.

4-(3-(Difluoromethyl)-5-fluoro-4-(3-fluoro-4-methoxyphenyl)-1*H*-pyrazol-1-yl)be-nzenesulfonamide (6a)



6a

Obtained as a white solid after column chromatography (petroleum ether/ethyl acetate = 3:1, R_f = 0.2), 8.3 mg, 20% yield, m.p. 100–102 °C. **^{1}H NMR** (600 MHz, DMSO) δ 8.02–7.97 (m, 2H), 7.90 (dd, *J* = 8.7, 1.4 Hz, 2H), 7.71–7.61 (m, 1H), 7.49 (s, 2H), 7.35 (dd, *J* = 12.2, 2.0 Hz, 1H), 7.29 (d, *J* = 2.1 Hz, 1H), 7.14 (t, $^2J_{H–F}$ = 52.9 Hz, 1H), 3.85 (s, 3H). **^{19}F NMR** (376 MHz, DMSO) δ -112.70 (d, $^2J_{F–H}$ = 53.1 Hz, CF_2H), -129.08 (s, F), -132.90–-137.01 (m, F). **^{13}C NMR** (100 MHz, DMSO) δ 151.7 (d, $^1J_{C–F}$ = 244.3 Hz), 150.0 (d, $^1J_{C–F}$ = 286.6 Hz), 147.5 (td, $^2J_{C–F}$ = 26.9 Hz, $^3J_{C–F}$ = 10.1 Hz), 146.2, 137.2, 127.8 (d, $^3J_{C–F}$ = 8.9 Hz), 122.6 (d, $^4J_{C–F}$ = 4.1 Hz), 117.9 (t, $^2J_{C–F}$ = 33.0 Hz), 113.9, 111.8 (t, $^1J_{C–F}$ = 236.7 Hz), 102.1 (d, $^2J_{C–F}$ = 11.5 Hz), 56.6. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{14}N_3F_4O_3S^+$ 416.0692; found 416.0693.

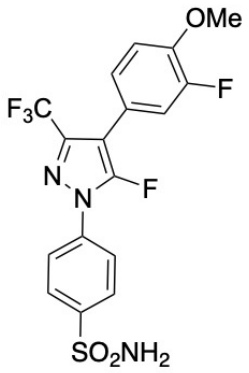


4y **2y** **6b**

To a 10 mL sealed tube equipped with a stirring bar and dried in an oven, the 4-sulfamoyl-phenyl derived hydrazonoyl chlorides (**4y**, 0.3 mmol), (*Z*)-2-fluoro-4-(2-fluoro-2-nitrovinyl)-1-methoxybenzene (**2y**, 0.1 mmol) and K_2CO_3 (55.3 mg, 0.2 mmol). DCE (1.0 mL) was transferred into the tube via a syringe. The resulting mixture was stirred at 85 °C for 24 h. The combined organic phases were concentrated in vacuo,

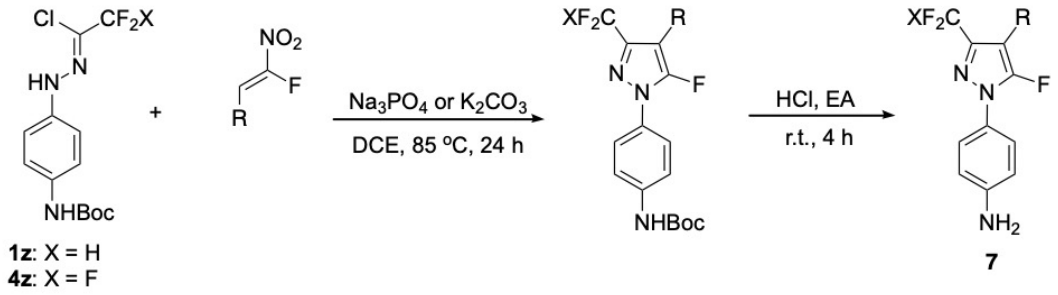
and the residue was purified by flash chromatography on silica gel (eluted with petroleum ether/ethyl acetate) to obtain the desired product **6b**.

4-(5-Fluoro-4-(3-fluoro-4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide (6b)



6b

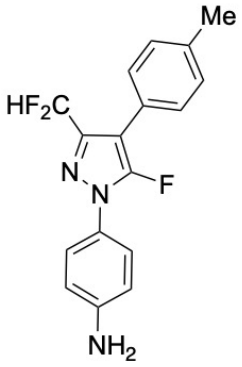
Obtained as a yellow solid after column chromatography (petroleum ether/ethyl acetate = 3:1, R_f = 0.2), 17.3 mg, 40% yield, m.p. 55–57 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.7 Hz, 1H), 8.00–7.87 (m, 2H), 7.47 (d, *J* = 8.6 Hz, 1H), 7.24–7.13 (m, 1H), 7.11–6.88 (m, 2H), 4.93 (d, *J* = 12.3 Hz, 2H), 3.95 (s, 3H). **^{19}F NMR** (376 MHz, CDCl3) δ -61.53 (s, CF3), -128.99 (s, F), -134.21–-134.27 (m, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.4 (d, $^1J_{C–F}$ = 222.7 Hz), 151.1 (d, $^1J_{C–F}$ = 246.8 Hz), 140.9 (d, $^2J_{C–F}$ = 11.4 Hz), 140.6, 139.0 (qd, $^2J_{C–F}$ = 37.7 Hz, $^3J_{C–F}$ = 8.8 Hz), 138.4 (d, $^3J_{C–F}$ = 3.3 Hz), 127.1, 126.8, 124.1, 120.7 (d, $^3J_{C–F}$ = 5.1 Hz), 119,5 (qd, $^1J_{C–F}$ = 271.8 Hz, $^4J_{C–F}$ = 1.7 Hz), 117.9–117.7 (m), 116.8–116.3 (m), 115.8 (d, $^2J_{C–F}$ = 19.8 Hz), 112.8 (d, $^4J_{C–F}$ = 2.5 Hz), 112.5 (d, $^4J_{C–F}$ = 2.4 Hz), 102.2 (d, $^2J_{C–F}$ = 15.4 Hz), 55.2. **HRMS** (ESI) m/z $[M+Na]^+$ calcd. for $C_{17}H_{12}N_3O_3F_5SNa^+$ 456.0417; found 456.0411.



Step 1: To a 10 mL sealed tube equipped with a stirring bar and dried in an oven, 4-(N-Boc-amino)-phenyl derived hydrazonoyl chlorides (1z, 0.15 mmol; **4z**, 0.3 mmol), α-fluoronitroalkene (2, 0.1 mmol) and Na_3PO_4 (32.8 mg, 0.2 mmol for 1z), K_2CO_3 (55.3 mg, 0.4 mmol for **4z**). 1,2-Dichloroethane (1.0 mL) was transferred into the tube through a syringe. The resulting mixture was stirred at 85 °C for 24 hours. The reaction mixture was extracted with EtOAc. The combined organic phases were concentrated in vacuo, and the residue was purified by flash chromatography on silica gel (eluted with petroleum ether/ethyl acetate) to obtain *N*^{1}-4-(N-Boc-amino)-phenyl pyrazoles.

Step 2: *N*^{1}-4-(N-Boc-amino)-phenyl pyrazoles (10.0 mmol) was solubilized in a mixture of hydrochloric acid and ethyl acetate (V : V = 1 : 2) and stirred at room temperature for 4 hours. Saturated sodium bicarbonate solution (5.0 mL) was added, and the resulting solution was diluted with ethyl acetate. The aqueous layer was then extracted three times with ethyl acetate. The organic layers were combined, and the resulting mixture was dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was purified by means of column chromatography, affording product **7**.

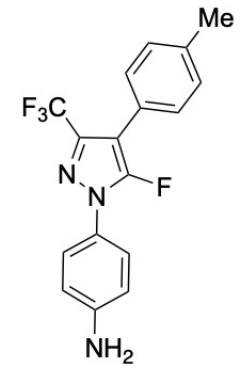
4-(3-(Difluoromethyl)-5-fluoro-4-(*p*-tolyl)-1*H*-pyrazol-1-yl)aniline (7a)



7a

Obtained as a white solid after column chromatography (petroleum ether/ethyl acetate = 3:1, R_f = 0.6), 10.8 mg, 34% yield, m.p. 74–76 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50–7.36 (m, 4H), 7.29–7.22 (m, 2H), 6.83–6.54 (m, 3H), 3.86 (s, 2H), 2.39 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.00 (d, $^2J_{F–H}$ = 53.7 Hz, CF_2H), -132.45 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.5 (d, $^1J_{C–F}$ = 282.7 Hz), 146.7, 142.2 (td, $^2J_{C–F}$ = 28.2 Hz, $^3J_{C–F}$ = 8.6 Hz), 137.5, 129.5, 128.6 (d, $^4J_{C–F}$ = 1.9 Hz), 127.6 (d, $^4J_{C–F}$ = 2.5 Hz), 125.1 (d, $^3J_{C–F}$ = 4.2 Hz), 123.9 (d, $^3J_{C–F}$ = 2.9 Hz), 115.2, 112.3 (t, J = 235.2 Hz), 102.5 (d, $^2J_{C–F}$ = 11.5 Hz), 21.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{15}N_3F_3^+$ 318.1218; found 318.1224.

4-(5-Fluoro-4-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)aniline (7b)

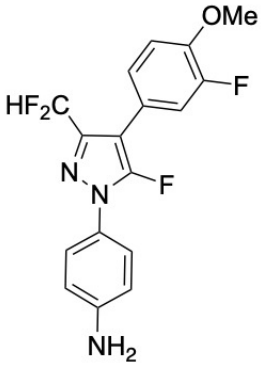


7b

Obtained as a white solid after column chromatography (petroleum ether/ethyl acetate = 3:1, R_f = 0.3), 15.1 mg, 45% yield, m.p. 70–72 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45–7.39 (m, 2H), 7.36 (d, J = 7.8 Hz, 2H), 7.29–7.22 (m, 2H), 6.78–6.74 (m, 2H),

3.89 (s, 2H), 2.40 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -60.89 (s, CF_3), -132.02 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.4 (d, $^1J_{C–F}$ = 282.4 Hz), 146.9, 138.2 (qd, $^2J_{C–F}$ = 37.3 Hz, $^3J_{C–F}$ = 9.4 Hz), 137.9, 130.9, 129.4, 128.9, 127.3 (d, $^4J_{C–F}$ = 2.7 Hz), 124.4 (d, $^3J_{C–F}$ = 4.0 Hz), 124.1 (d, $^4J_{C–F}$ = 2.9 Hz), 124.3 (qd, $^1J_{C–F}$ =270.9 Hz, $^4J_{C–F}$ =1.7 Hz), 115.2, 102.9 (d, $^2J_{C–F}$ = 12.8 Hz), 21.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{14}N_3F_4^+$ 336.1124; found 336.1132.

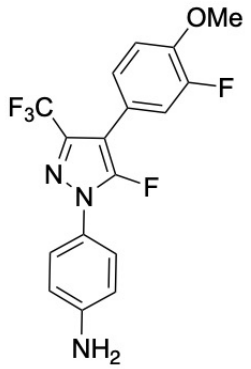
1-(4-Aminophenyl)-3-(difluoromethyl)-5-fluoro-4-(3-fluoro-4-Methoxyphenyl)phen-yl)-1*H*-pyrazole (7c)



7c

Obtained as a white solid after column chromatography (petroleum ether/ethyl acetate = 3:1, R_f = 0.4), 13.0 mg, 37% yield, m.p. 72–74 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.1 Hz, 2H), 7.36–7.28 (m, 2H), 7.03 (t, *J* = 8.9 Hz, 1H), 6.82–6.52 (m, 3H), 3.93 (s, 3H), 3.75 (s, 2H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -110.75 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H), -132.05 9 (s, F), -134.76–-134.81 (m, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 152.2 (d, *J* = 245.7 Hz), 149.5 (d, *J* = 283.4 Hz), 147.2, 147.1, 146.8, 141.8 (td, $^2J_{C–F}$ = 28.5 Hz, $^3J_{C–F}$ = 8.3 Hz), 127.4, 124.7, 123.9 (d, $^3J_{C–F}$ = 2.9 Hz), 121.3–120.5 (m), 116.6, 116.4, 115.2, 113.5 (d, $^4J_{C–F}$ = 2.4 Hz), 112.5 (t, $^1J_{C–F}$ = 234.7 Hz), 101.2 (d, $^2J_{C–F}$ = 10.7 Hz), 56.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{14}N_3F_4O^+$ 352.1073; found 352.1064.

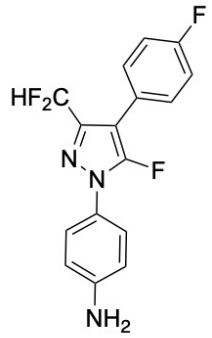
4-(5-Fluoro-4-(3-fluoro-4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide (7d)



7d

Obtained as a white solid after column chromatography (petroleum ether/ethyl acetate = 3:1, R_f = 0.4), 19.9 mg, 54% yield, m.p. 71–73°C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.2 Hz, 2H), 7.14 (q, *J* = 11.0, 8.2 Hz, 2H), 6.95 (t, *J* = 8.7 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 2H), 4.04 (s, 2H), 3.85 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -60.99 (s, CF_3), -131.67 (s, F), -133.61–-136.31 (m, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 152.2 (d, $^1J_{C–F}$ = 246.1 Hz), 149.4 (d, $^1J_{C–F}$ = 283.2 Hz), 147.6 (d, $^3J_{C–F}$ = 10.5 Hz), 147.1, 139.0, 138.0 (qd, $^2J_{C–F}$ = 37.2 Hz, $^3J_{C–F}$ = 9.1 Hz), 127.1 (d, $^4J_{C–F}$ = 2.9 Hz), 125.1, 124.1 (d, $^4J_{C–F}$ = 2.8 Hz), 121.0 (qd, $^1J_{C–F}$ = 271.0 Hz, $^4J_{C–F}$ = 1.6 Hz), 120.1 (dd, $^3J_{C–F}$ = 7.6 Hz, $^4J_{C–F}$ = 4.2 Hz), 116.9 (d, $^3J_{C–F}$ = 19.7 Hz), 115.1, 113.5 (d, $^4J_{C–F}$ = 2.4 Hz), 101.7 (d, $^2J_{C–F}$ = 12.6 Hz), 56.3. **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{17}H_{13}N_3F_5O^+$ 370.0979; found 370.0978.

4-(3-(Difluoromethyl)-5-fluoro-4-(4-fluorophenyl)-1*H*-pyrazol-1-yl)aniline (7e)

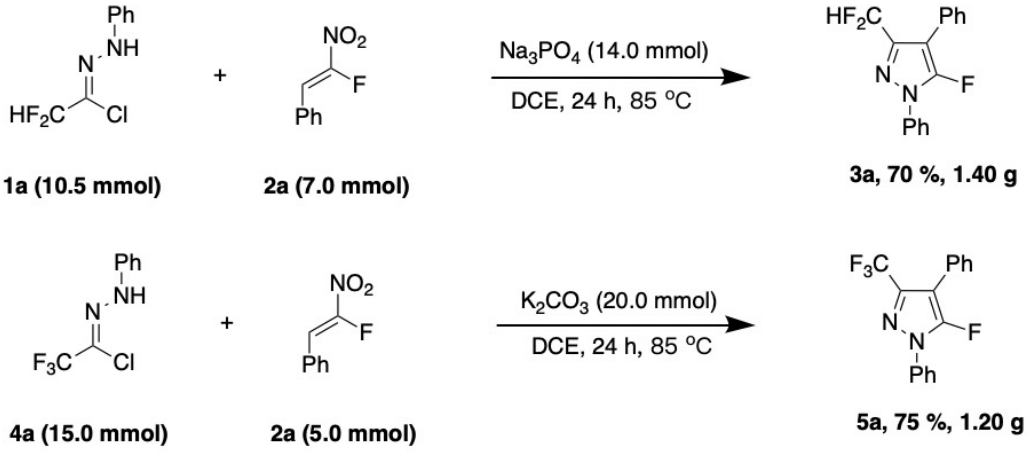


7e

Obtained as a red solid after column chromatography (petroleum ether/ethyl acetate = 3:1, R_f = 0.3), 11.2 mg, 35% yield, m.p. 70–72 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.13 (t, *J* = 8.4 Hz, 2H), 6.85–6.50

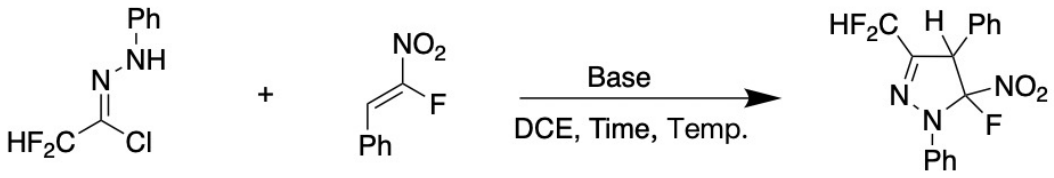
(m, 3H), 3.88 (s, 2H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -110.69 (d, $^2J_{F–H}$ = 53.8 Hz, CF_2H), -114.12–-114.19 (m, F), -132.42 (s, F). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.3 (d, $^1J_{C–F}$ = 247.3 Hz), 149.5 (d, $^1J_{C–F}$ = 283.0 Hz), 146.8, 141.9 (td, $^2J_{C–F}$ = 28.3 Hz, $^3J_{C–F}$ = 8.1 Hz), 130.5 (dd, $^3J_{C–F}$ = 8.1 Hz, $^4J_{C–F}$ = 2.3 Hz), 128.7, 127.6, 127.4 (d, $^4J_{C–F}$ = 2.6 Hz), 123.9 (d, $^4J_{C–F}$ = 3.0 Hz), 115.8, 115.6, 115.2, 112.5 (t, $^1J_{C–F}$ = 234.7 Hz), 101.5 (d, $^2J_{C–F}$ = 11.5 Hz). **HRMS** (ESI) m/z $[M+H]^+$ calcd. for $C_{16}H_{12}N_3F_4^+$ 322.0967; found 322.0967.

2.7 General procedure I for gram-scale experiments



To a 10 mL sealed screw-capped pressure tube equipped with a stirring bar and dried in an oven, hydrazone acyl chloride **1a** (2.2 g, 10.5 mmol) or **4a** (3.3 g, 15.0 mmol), fluoronitroalkenes **2a** (1.2 g, 7.0 mmol for **3a**; 836.0 mg, 5.0 mmol for **5a**) and Na_3PO_4 (2.3 g, 14.0 mmol for **3a**), K_2CO_3 (2.8 g, 20.0 mmol for **5a**). 1,2-Dichloroethane (70.0 mL for **3a**; 50.0 mL for **5a**) was transferred into the tube through a syringe. The resulting mixture was stirred at 85 °C for 24 hours. The reaction mixture was extracted with EtOAc. The combined organic phases were concentrated in vacuo, and the residue was purified by flash chromatography on silica gel (eluted with petroleum ether/ethyl acetate) to obtain the desired product. Compound **3a** was obtained with 1.4 g in 70% yield, and compound **5a** was obtained with 1.2 g in 75% yield.

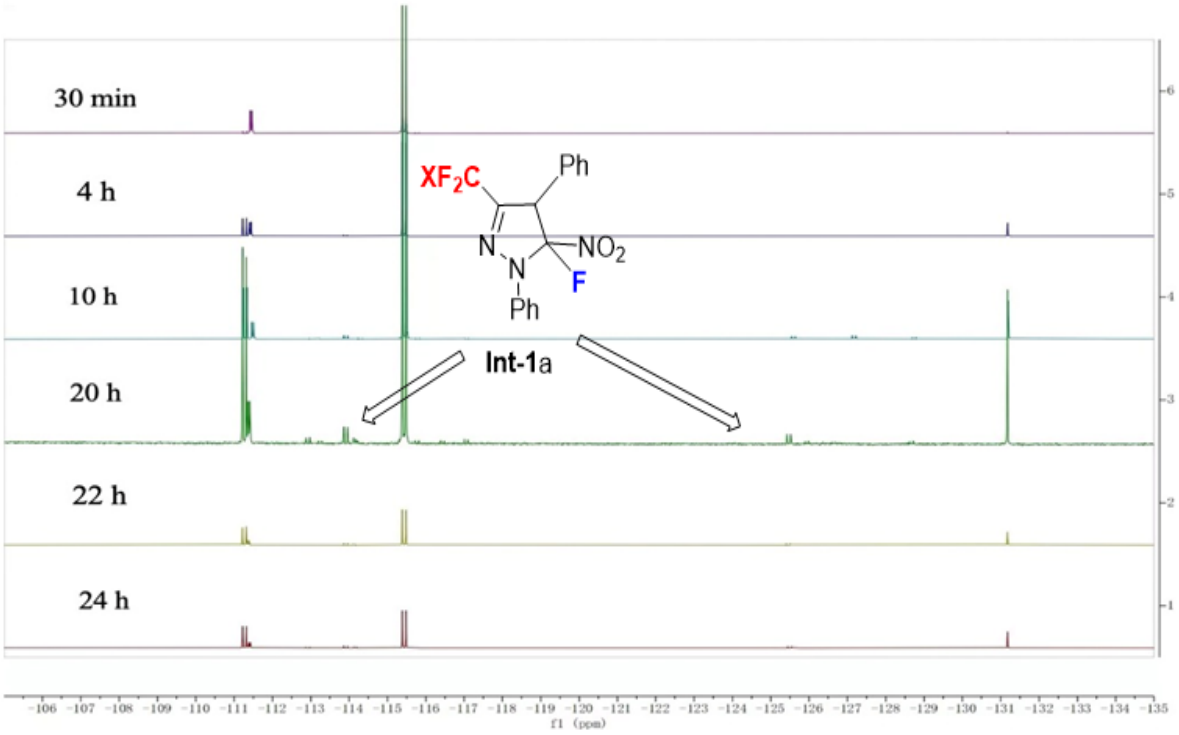
3. Mechanistic studies



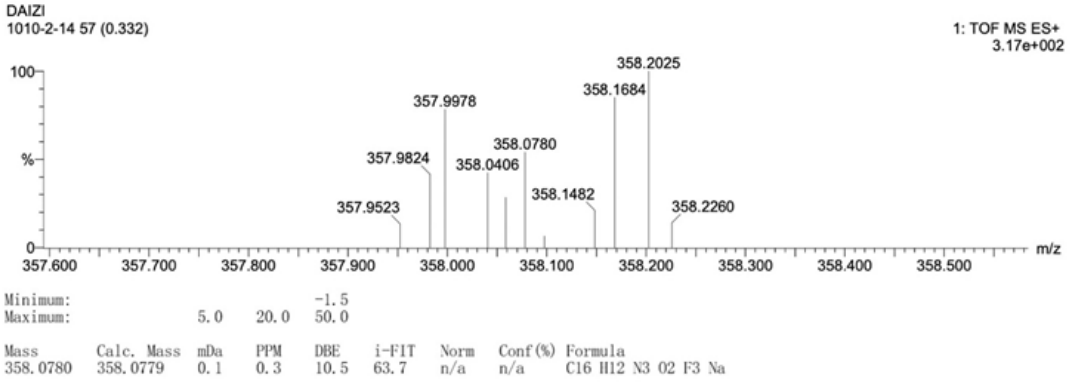
1a **2a** **Int-1a**

The mechanism was confirmed by the template reaction of 2,2-difluoro-*N*-phenylacetohydrazonoyl chloride **1a** and (2-fluoro-2-nitrovinyl)benzene **2a**. Although attempts were made to isolate the intermediate pyrazoline by reaction monitoring, it was not detected. Subsequently, the reaction conditions were altered by adjusting the alkalinity and temperature; however, no product was obtained. Finally, the presence of the pyrazoline **Int-1a** was confirmed through monitoring **^{19}F-NMR** and **ESI/MS**.

a) **^{19}F- NMR** analysis of reaction progress



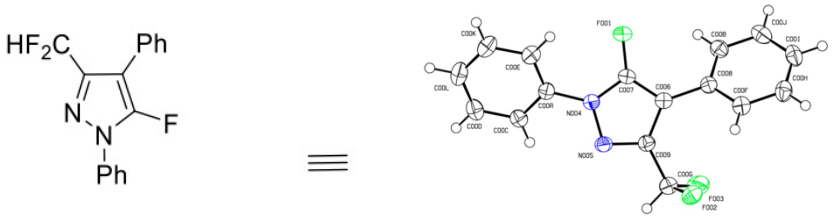
b) **ESI/MS** analysis of reaction progress



4. X-Ray crystallographic data

The following single crystals were grown by solvent diffusion method in 10 mL test tube. About 20 mg of the corresponding sample was dissolved in 1 mL dichloromethane at the bottom of the tube, and then 5 mL of n-hexane was added to the upper part of the liquid surface. The test tube was sealed with plastic film. We pricked several holes on the plastic film to let the solvent slowly evaporated at room temperature. The single crystal of the target compound was obtained after several days and subjected to X-ray analysis.

The X-ray crystallographic structure for **3a**. Crystal data has been deposited to CCDC, number: 2247785.

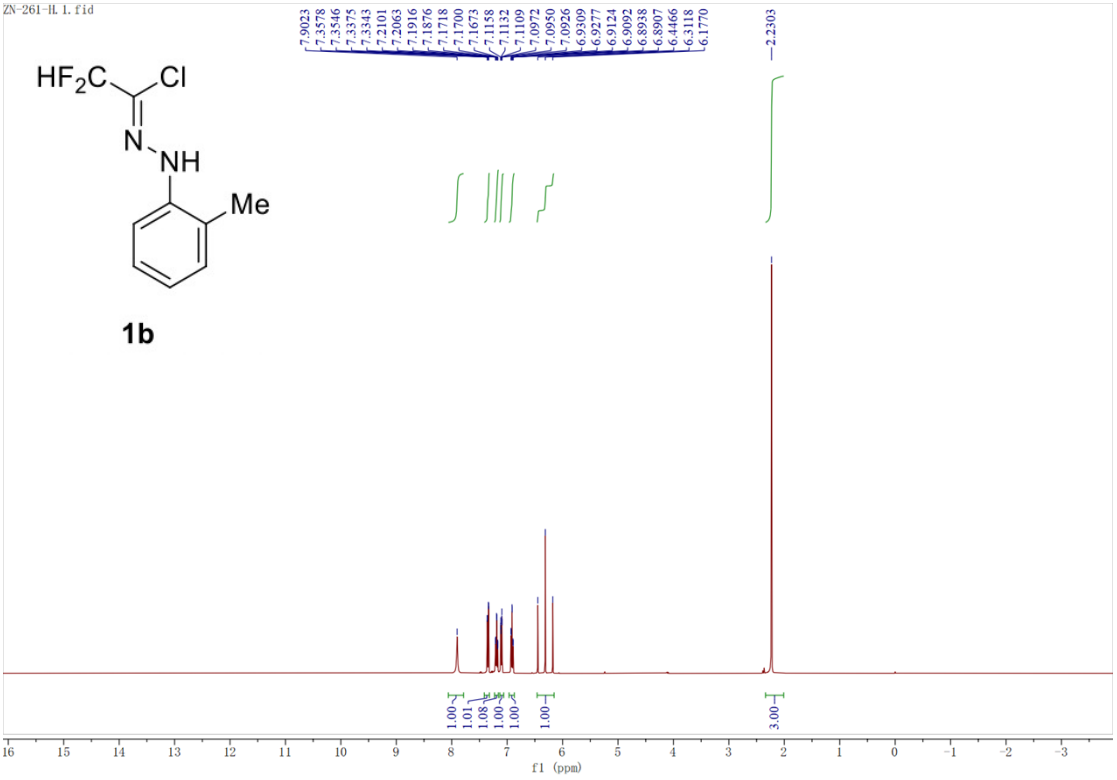


Identification code	LMH01_0m
Empirical formula	$C_{16}H_{11}F_3N_2$
Formula weight	288.27
Temperature/K	296.15

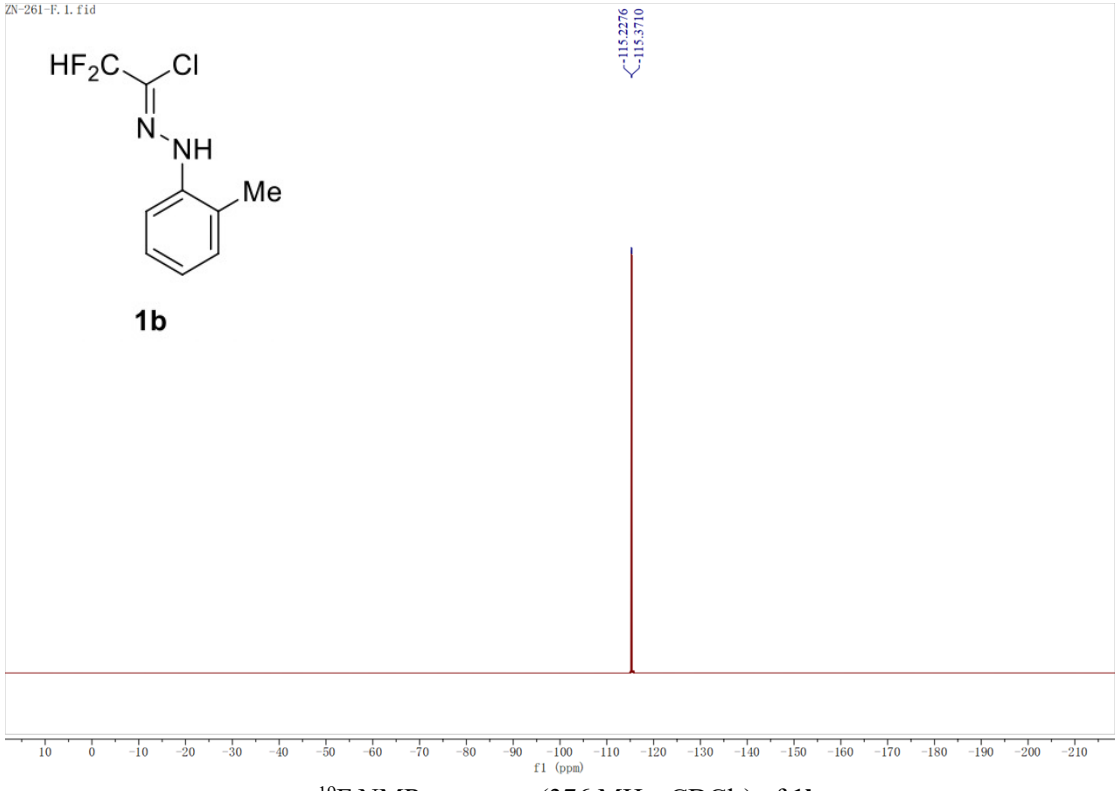
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	5.6195(6)
b/Å	18.5139(15)
c/Å	12.9119(10)
α/°	90
β/°	99.887(3)
γ/°	90
Volume/Å3	1323.39(19)
Z	4
ρcalcg/cm3	1.447
μ/mm-1	0.116
F(000)	592.0
Crystal size/mm3	0.32 × 0.26 × 0.16
Radiation	MoKα (λ = 0.71073)
2Θrange for data collection/°	4.4 to 59.282
Index ranges	$-7 \leq h \leq 7$, $-25 \leq k \leq 25$, $-17 \leq l \leq 17$
Reflections collected	23856
Independent reflections	3722 [R_{int} = 0.0580, R_{sigma} = 0.0484]
Data/restraints/parameters	3722/0/190
Goodness-of-fit on F2	1.027
Final R indexes [I>=2σ (I)]	R_1 = 0.0465, wR_2 = 0.0961
Final R indexes [all data]	R_1 = 0.0819, wR_2 = 0.1091
Largest diff. peak/hole / e Å-3	0.23/-0.25

5. NMR spectra of the related compounds

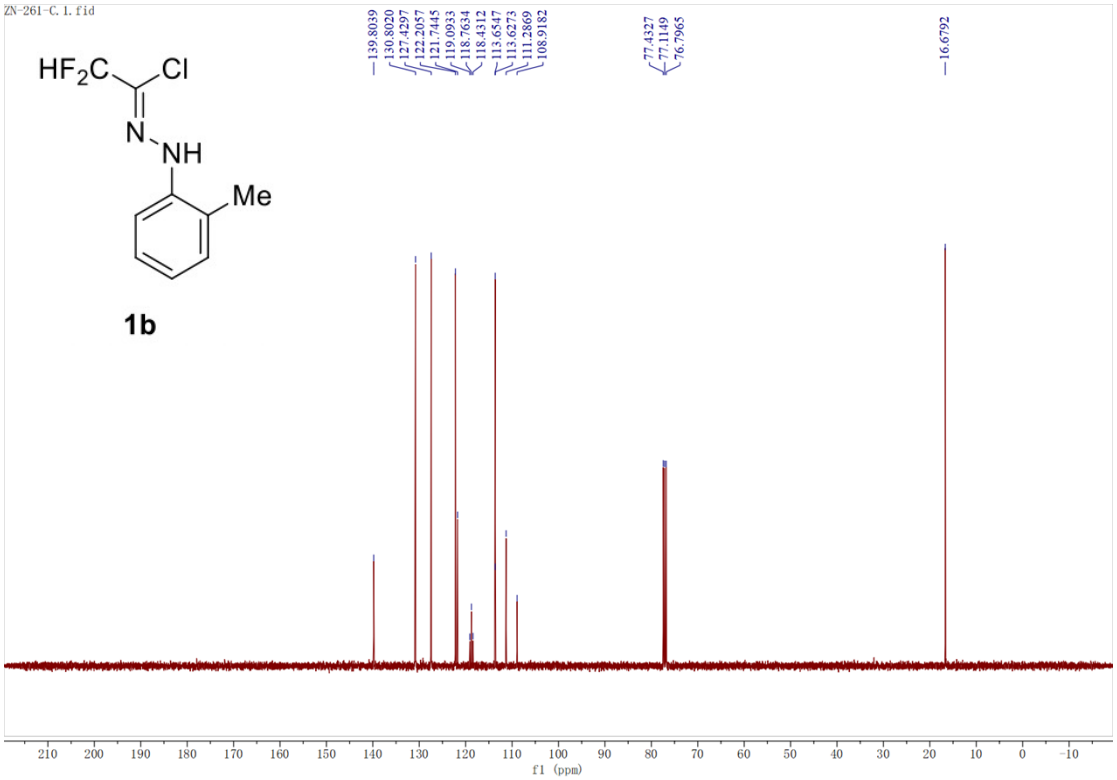
(*Z*)-2,2-difluoro-*N*-(*o*-tolyl)acetohydrazonoyl chloride (1b)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **1b**

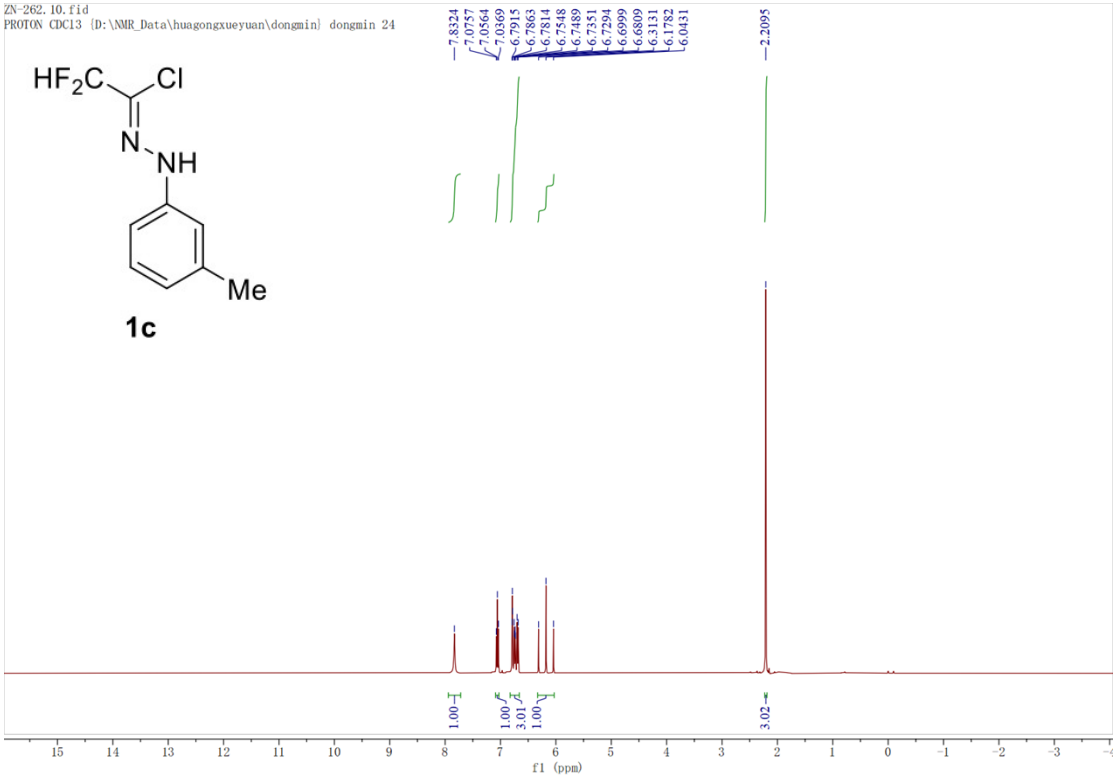


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **1b**

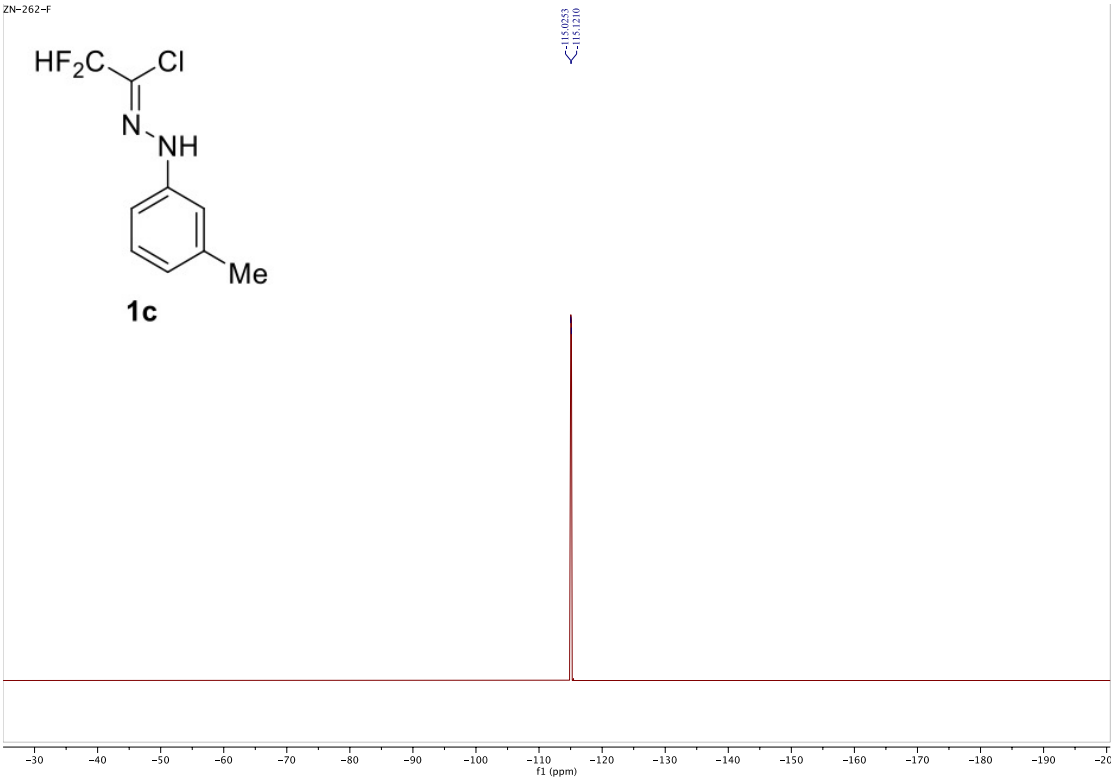


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **1b**

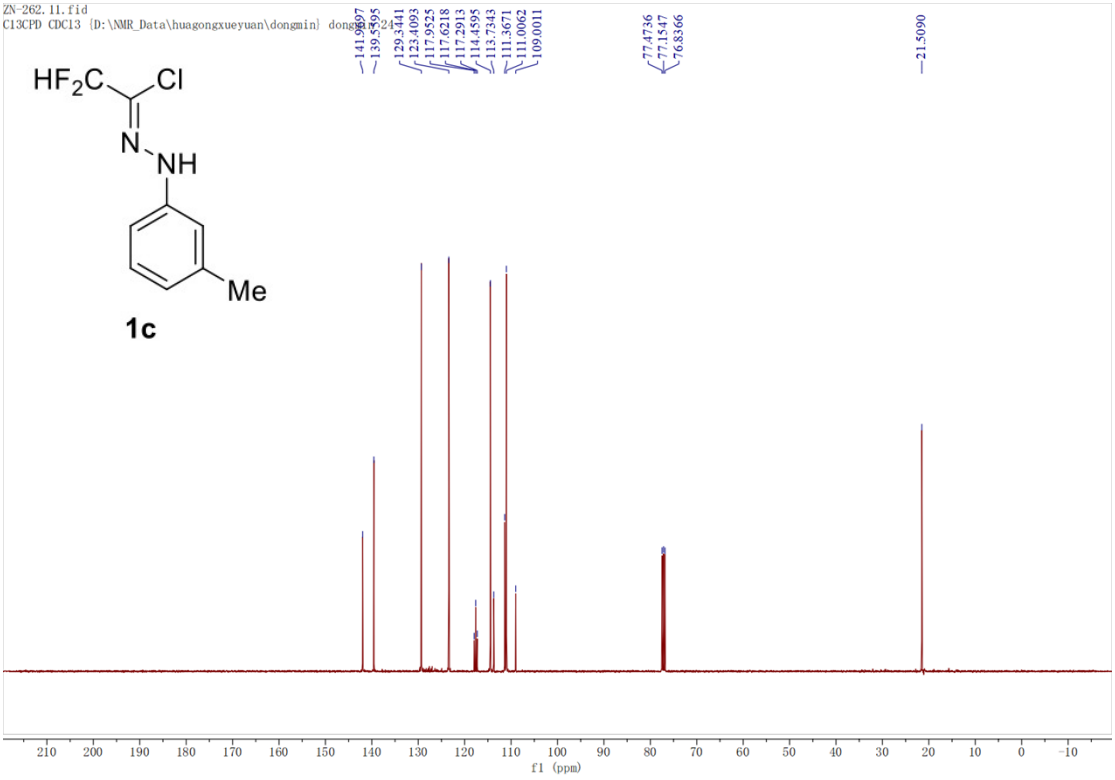
(Z)-2,2-difluoro-*N*-(*m*-tolyl)acetohydrazonoyl chloride (1c)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **1c**

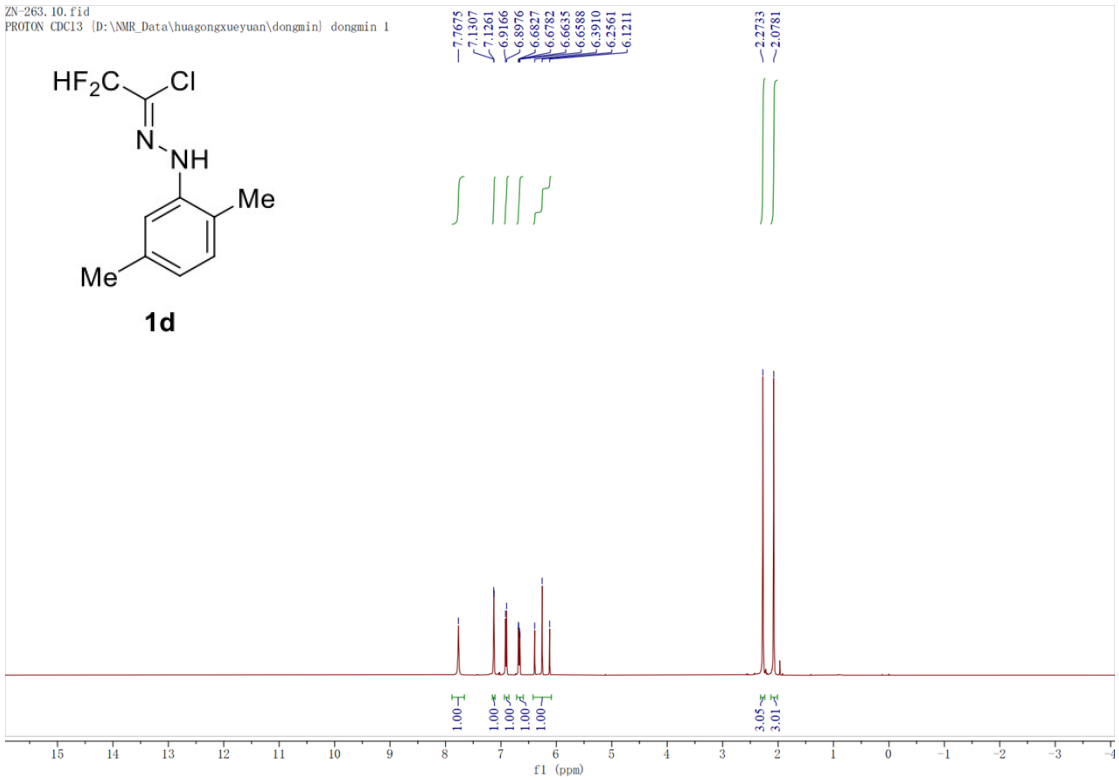


^{19}F NMR spectrum (565 MHz, $CDCl_3$) of **1c**

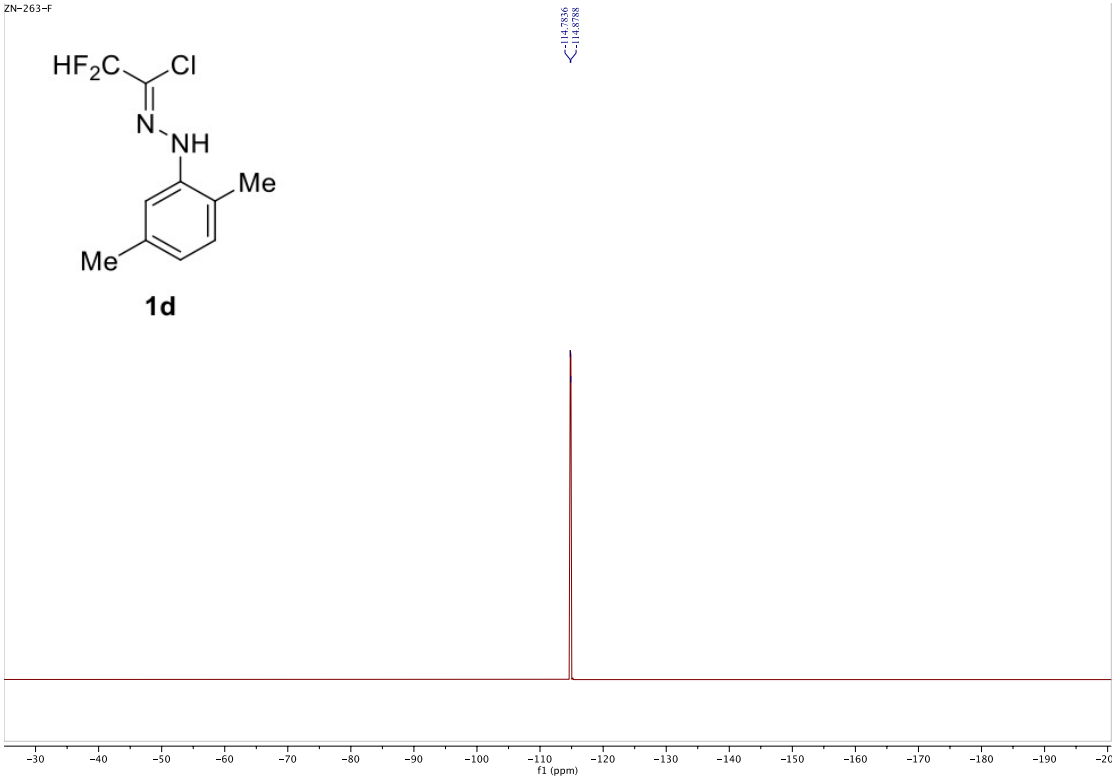


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **1c**

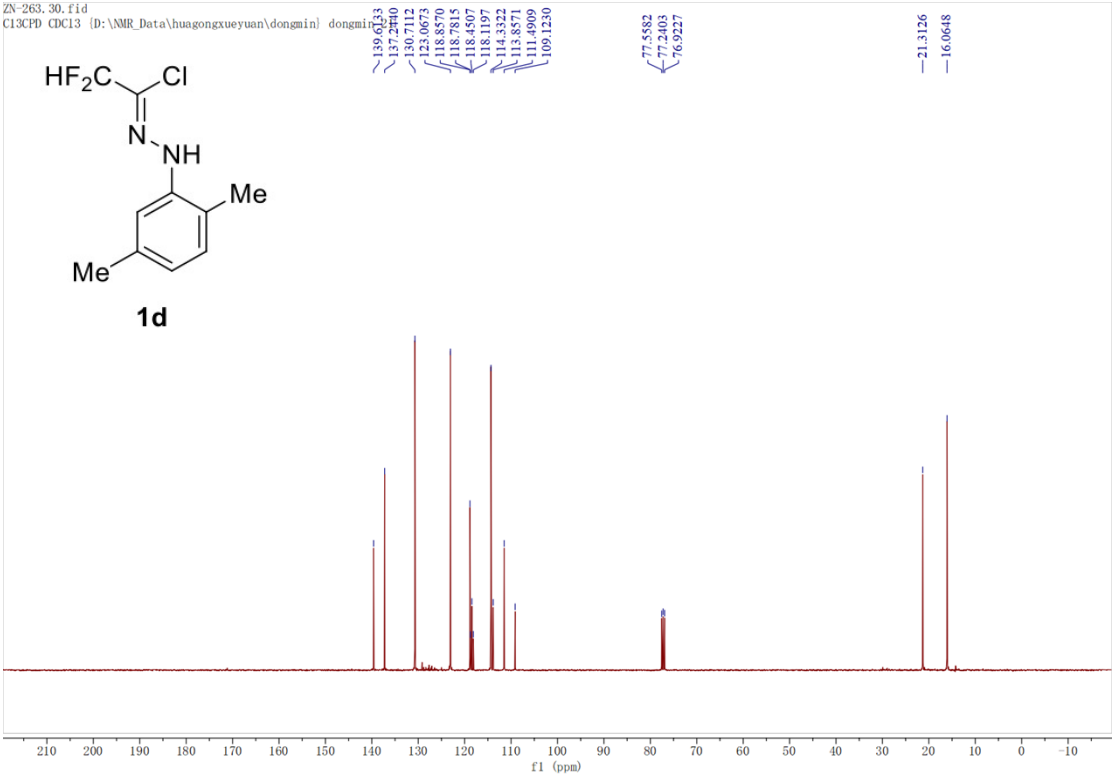
(*Z*)-*N*-(2,5-dimethylphenyl)-2,2-difluoroacetohydrazonoyl chloride (1d)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **1d**

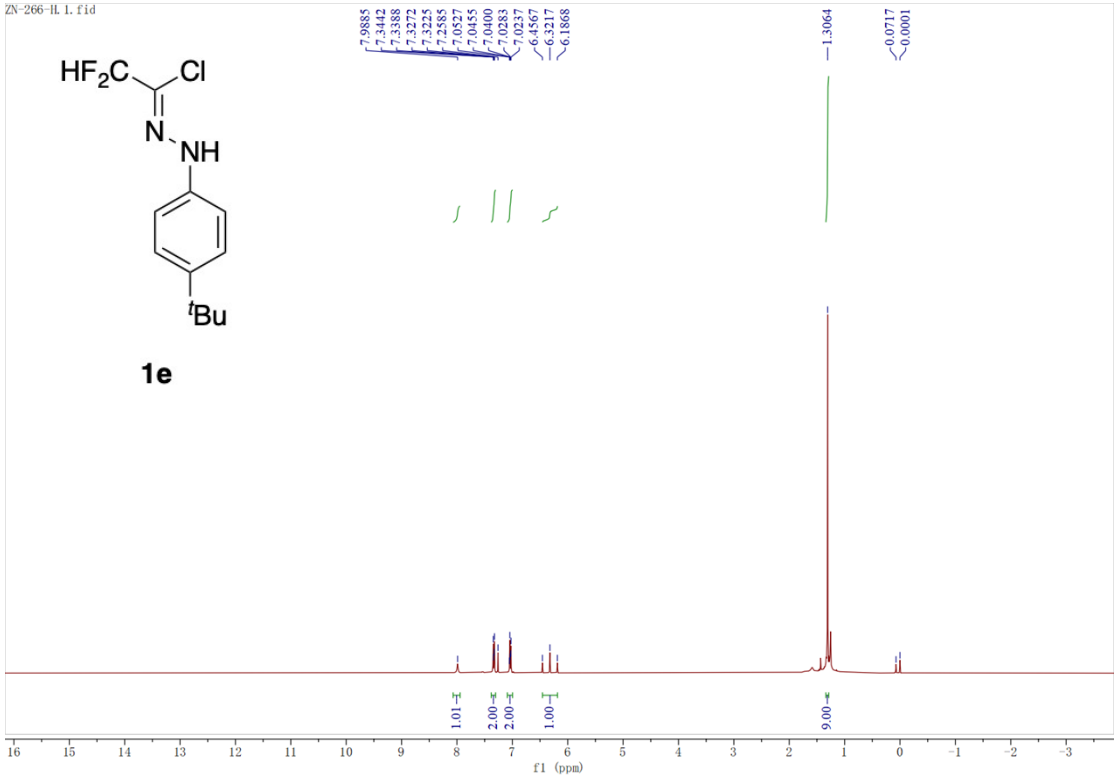


^{19}F NMR spectrum (565MHz, $CDCl_3$) of **1d**

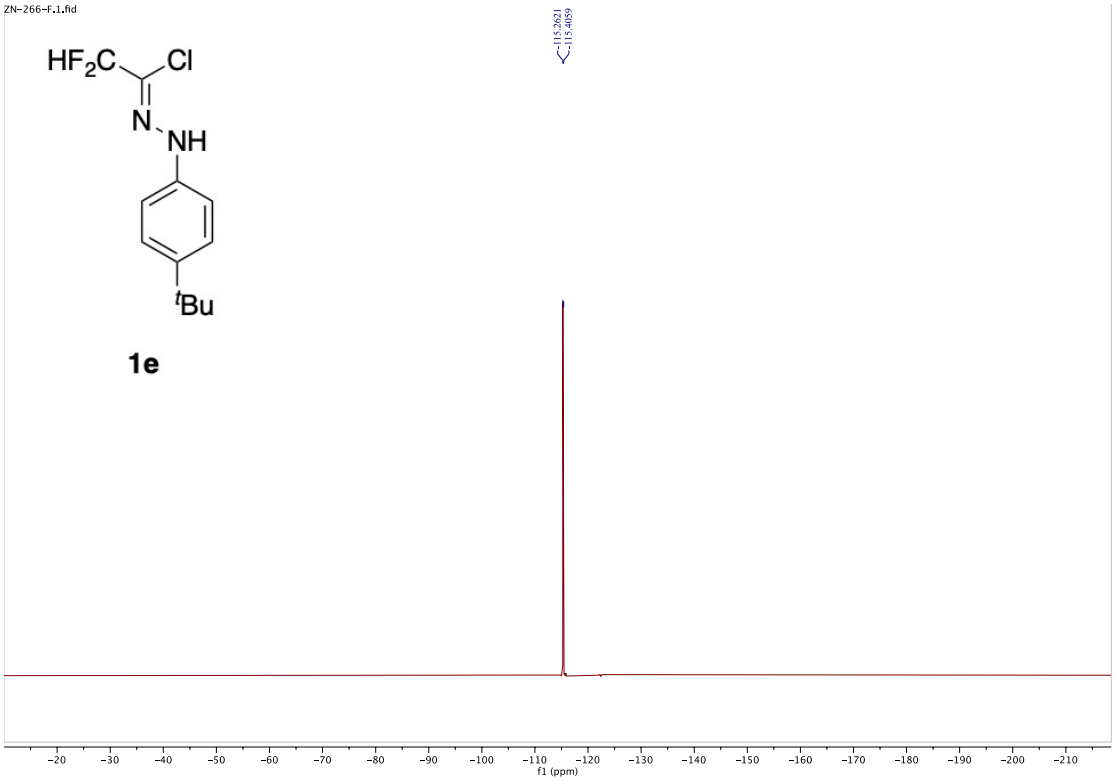


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **1d**

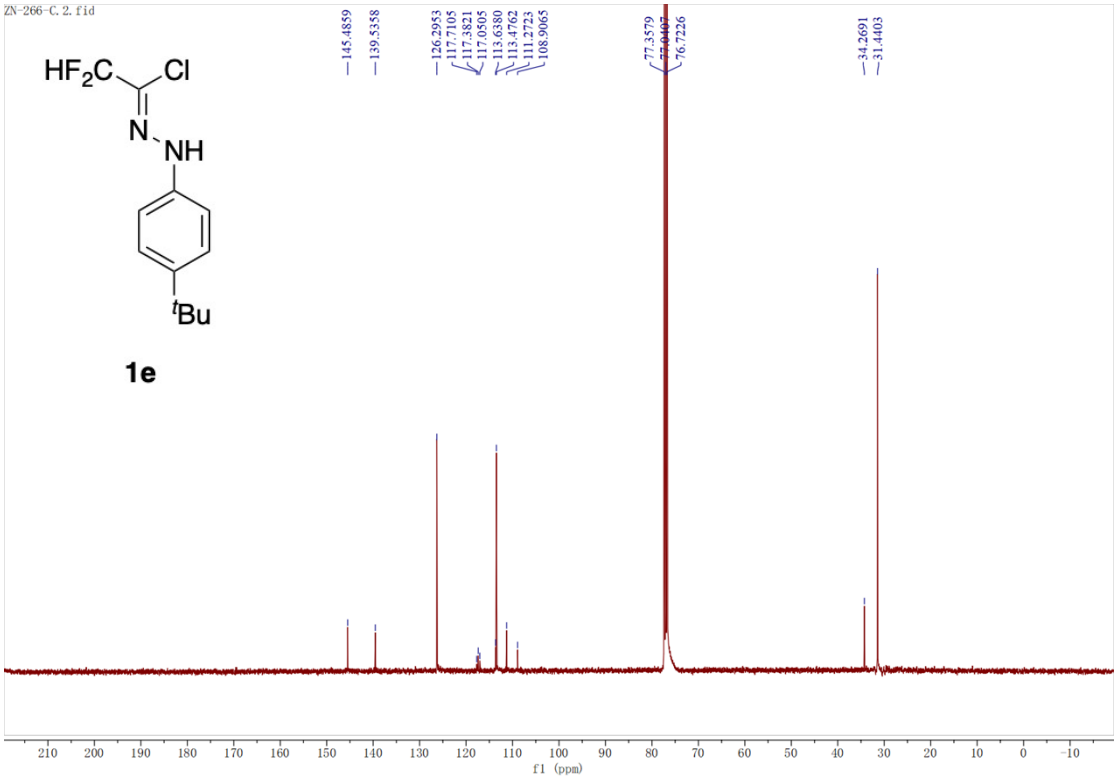
(*Z*)-*N*-(4-(*tert*-butyl)phenyl)-2,2-difluoroacetohydrazonoyl chloride (1e)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **1e**

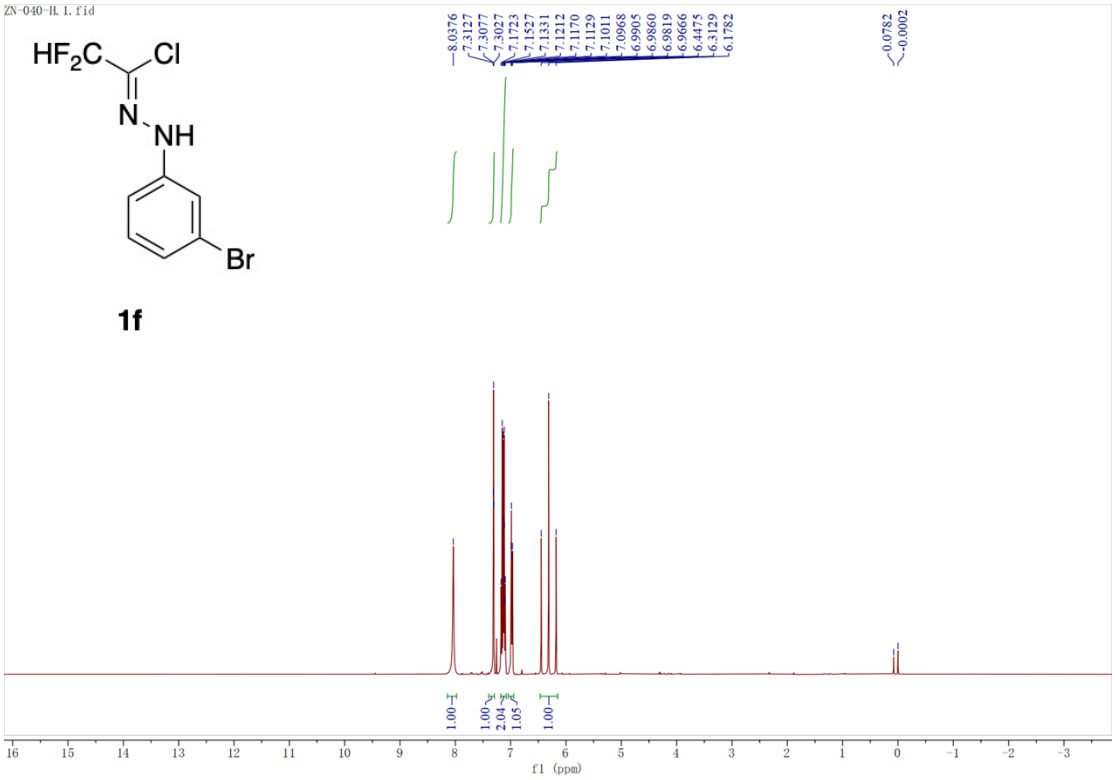


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **1e**

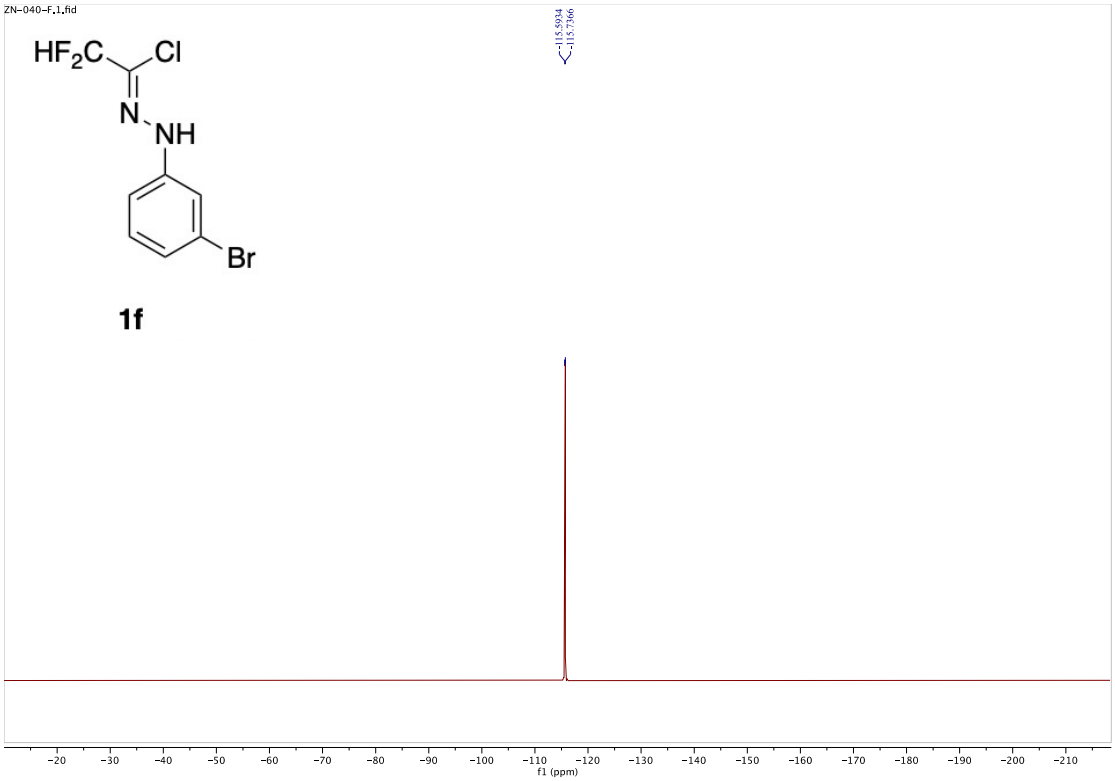


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **1e**

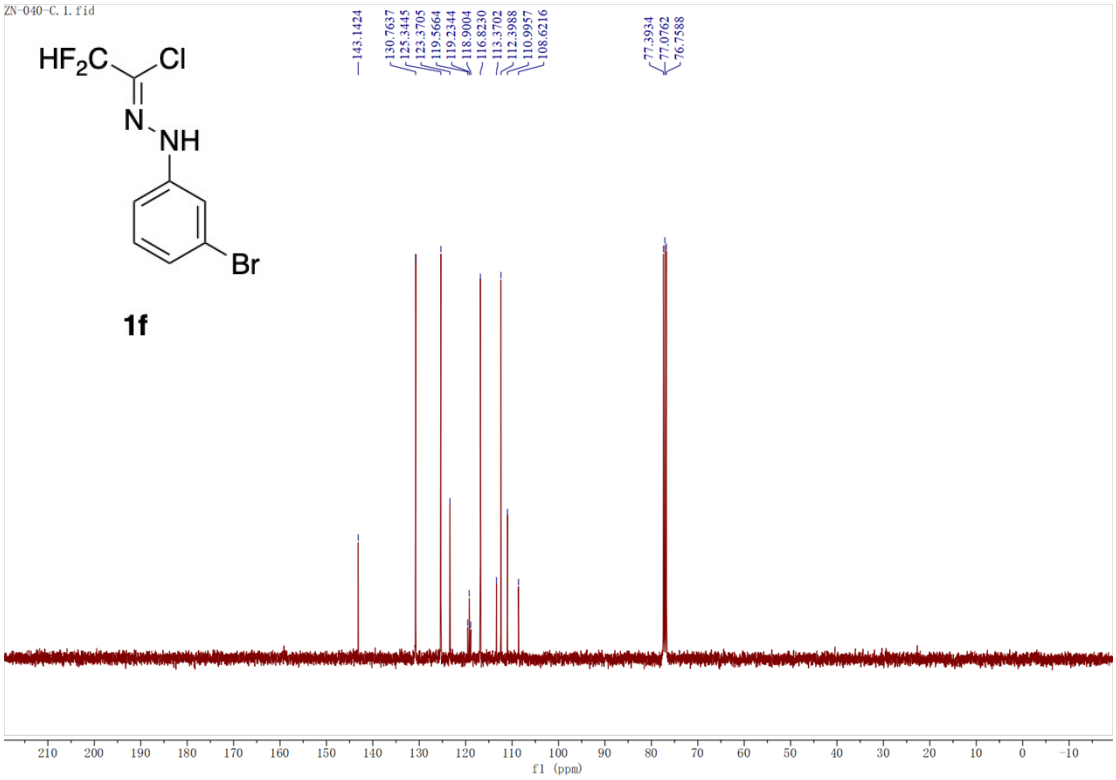
(*Z*)-*N*-(3-bromophenyl)-2,2-difluoroacetohydrazonoyl chloride (1f)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **1f**

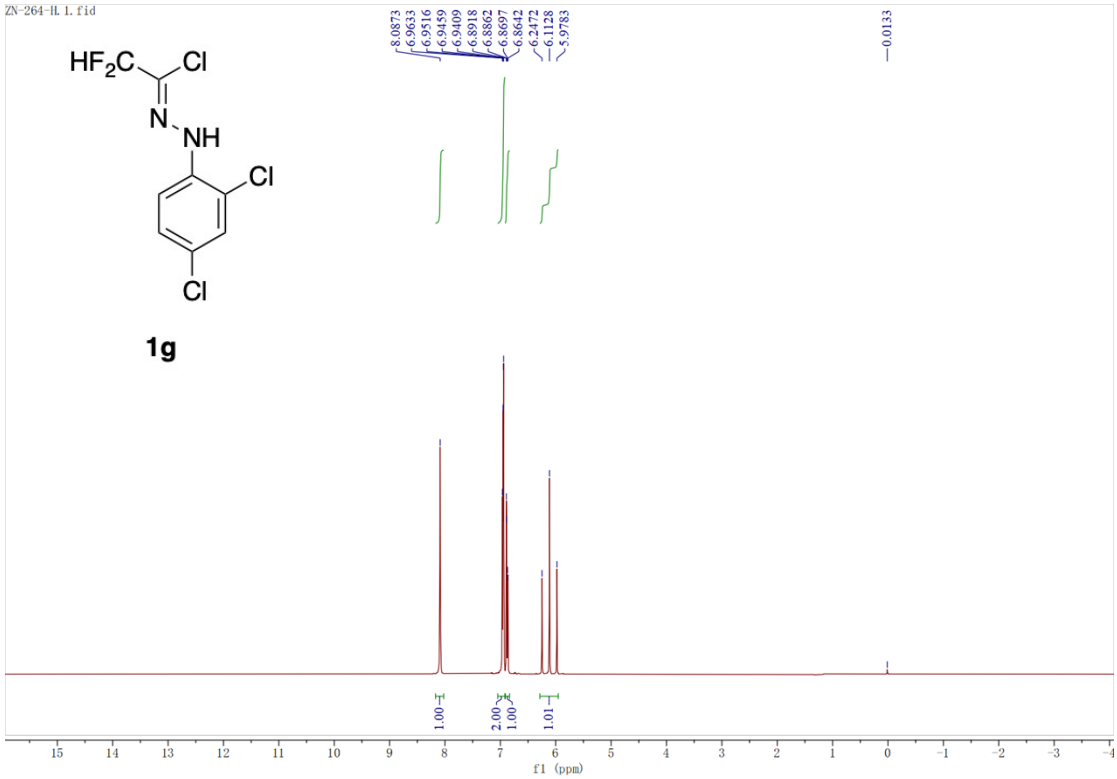


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **1f**



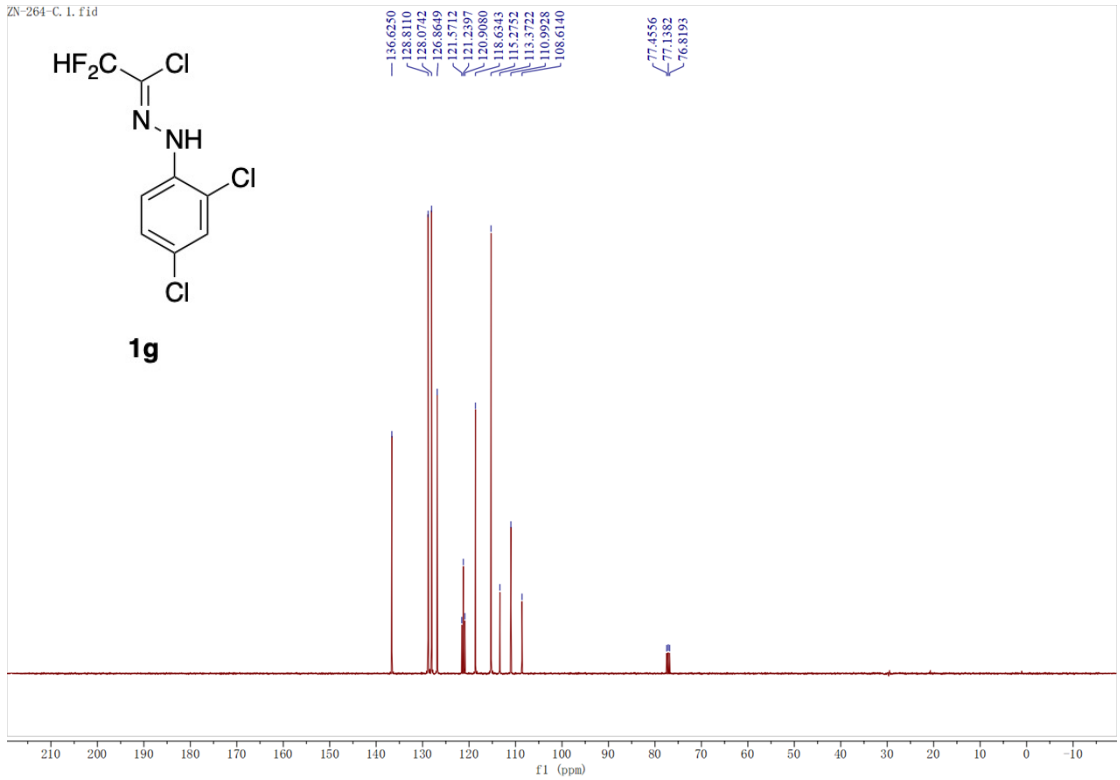
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **1f**

(*Z*)-*N*-(2,4-dichlorophenyl)-2,2-difluoroacetohydrazonoyl chloride (1g)



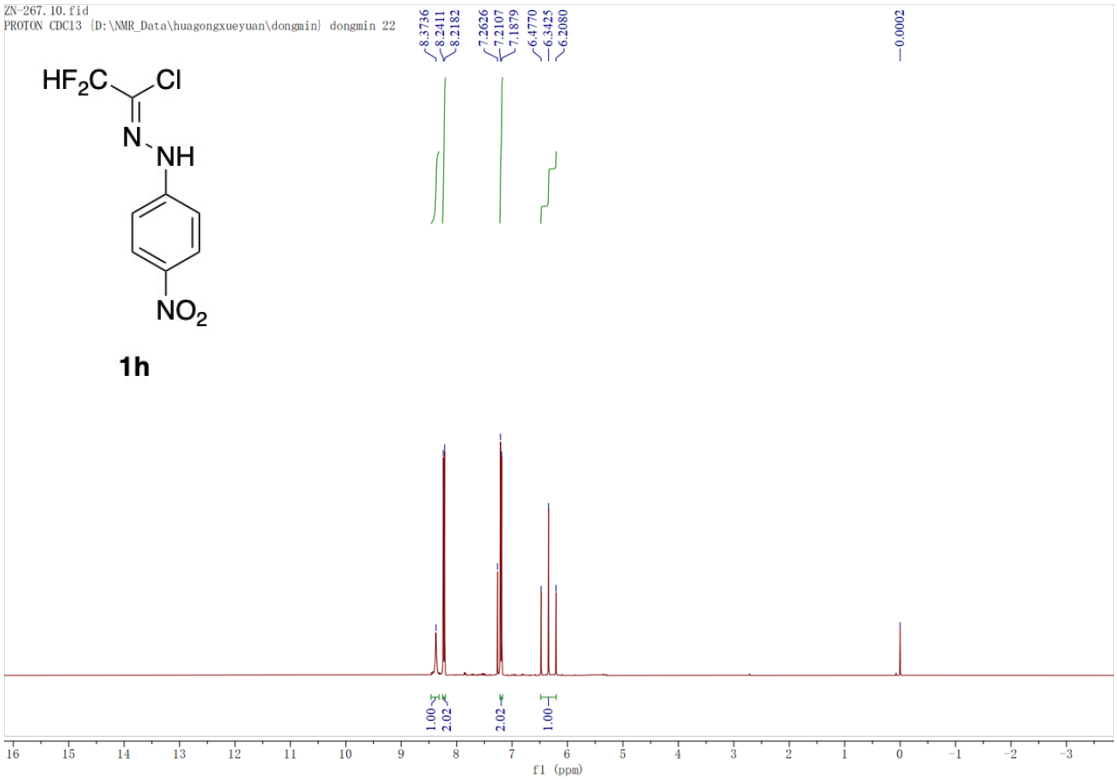
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **1g**

^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **1g**

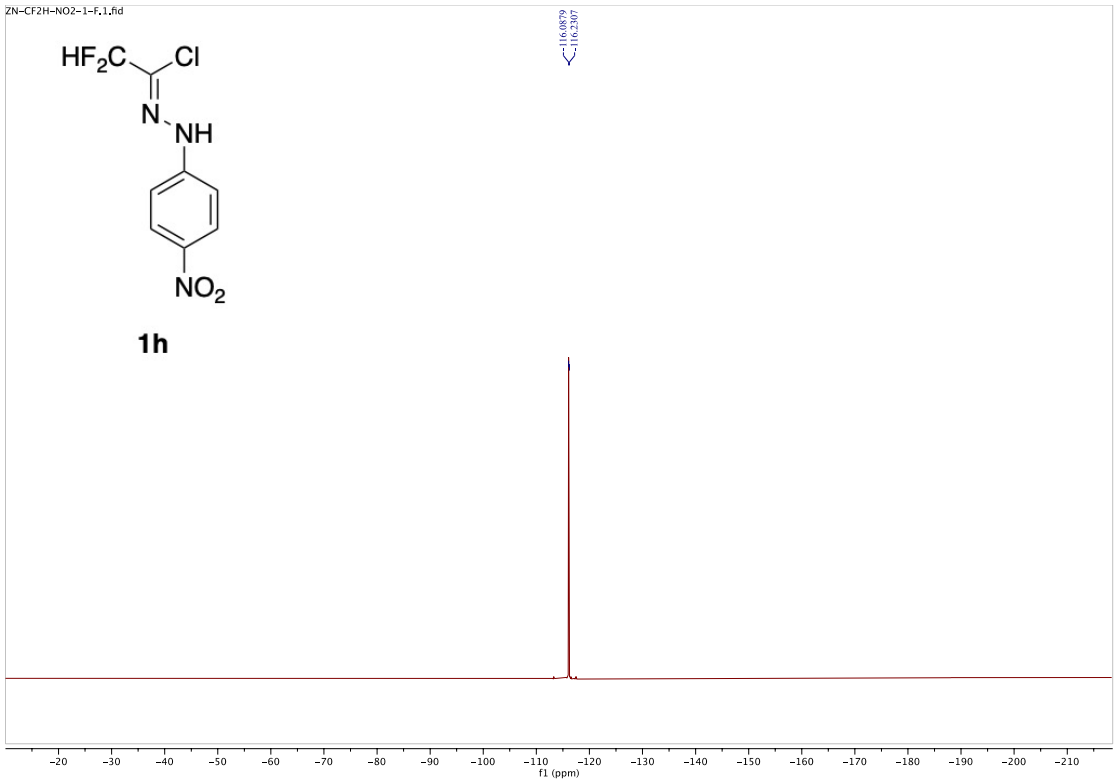


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **1g**

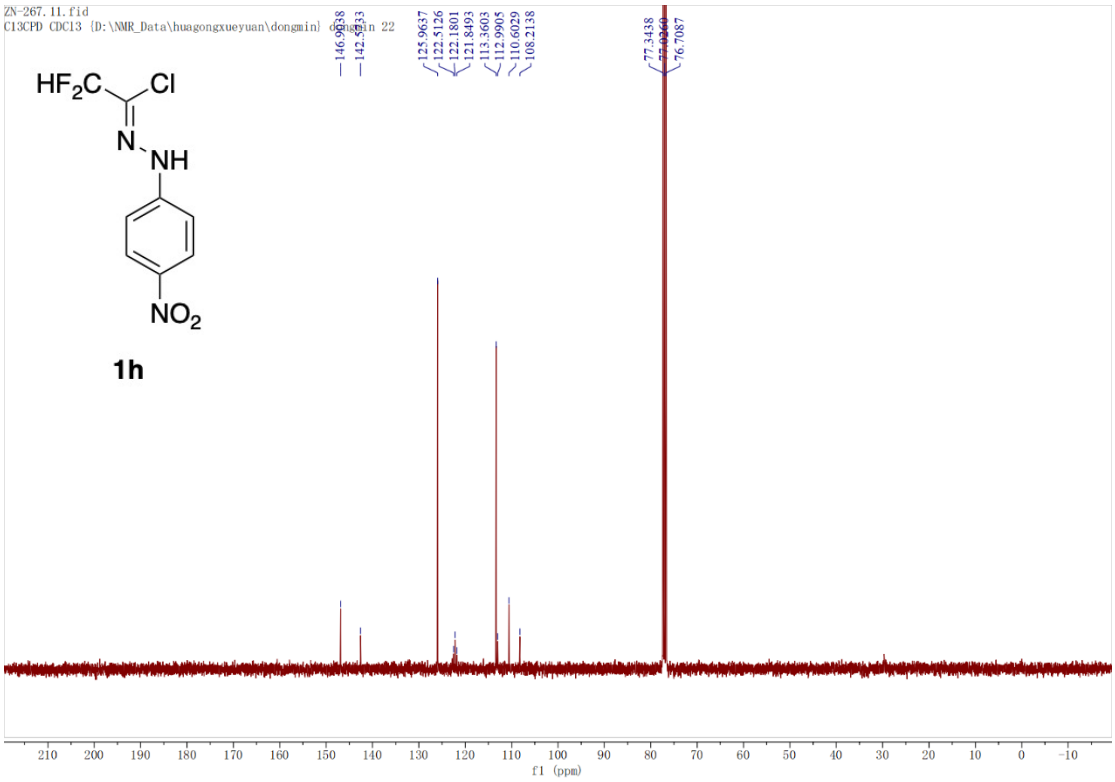
(*Z*)-2,2-difluoro-*N*-(4-nitrophenyl)acetohydrazonoyl chloride (1h)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **1h**

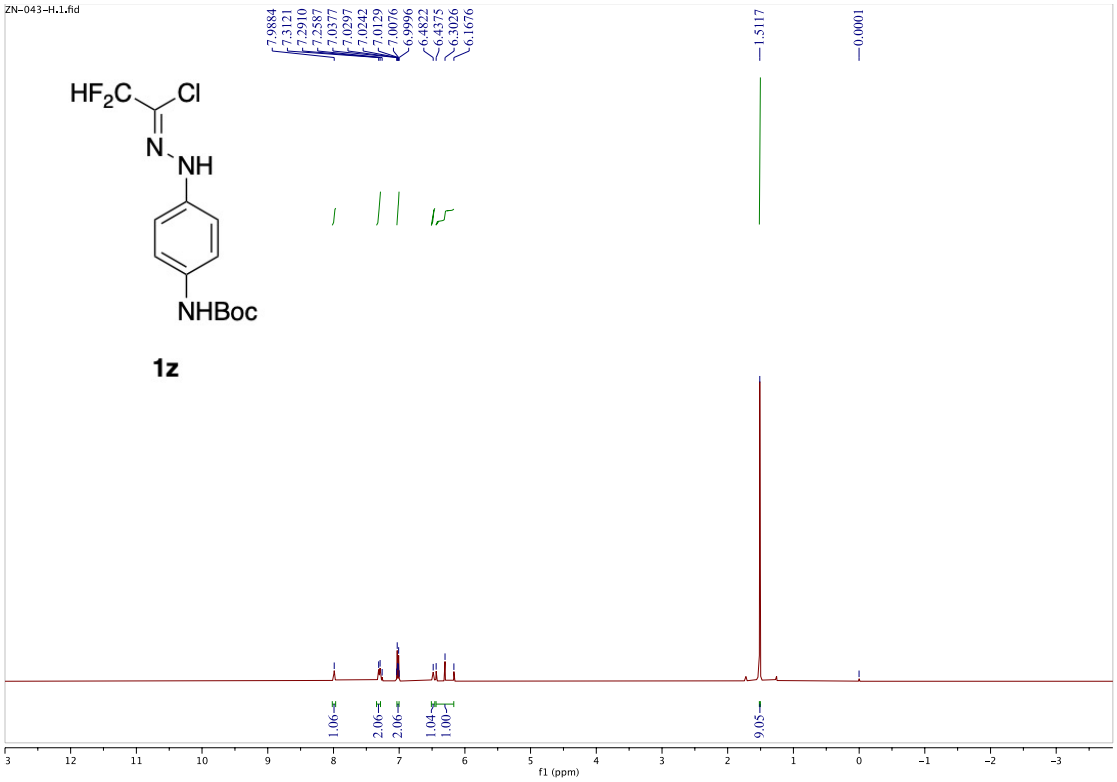


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **1h**

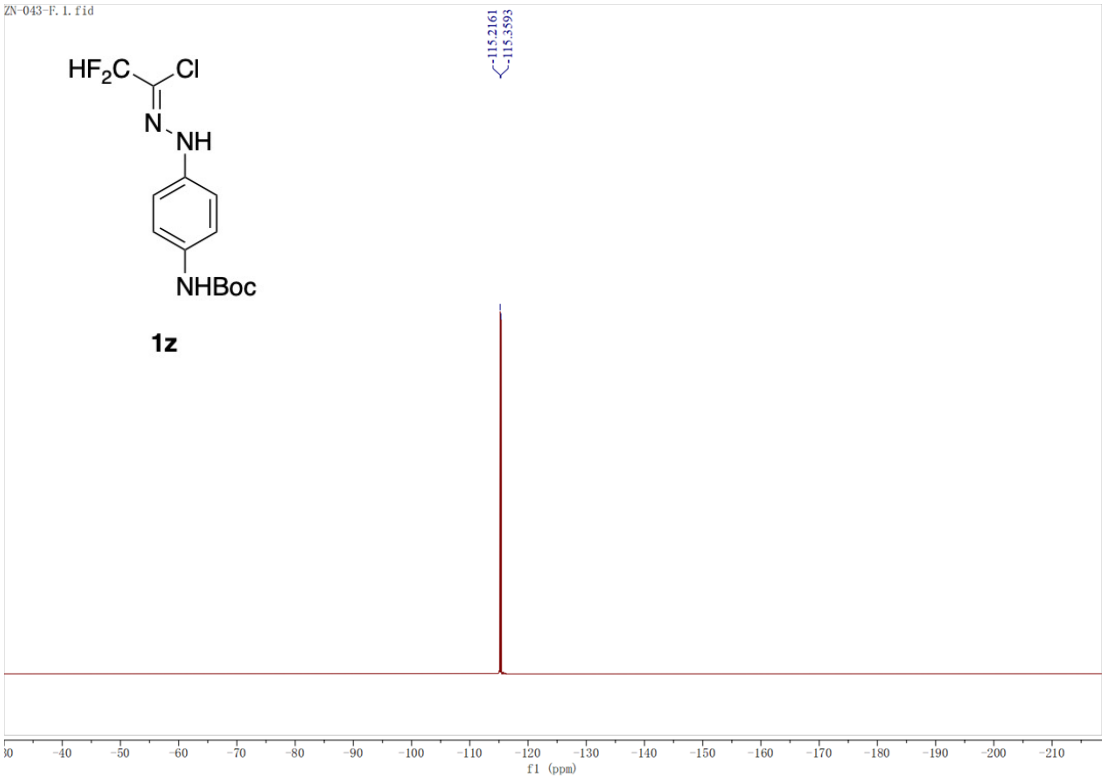


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **1h**

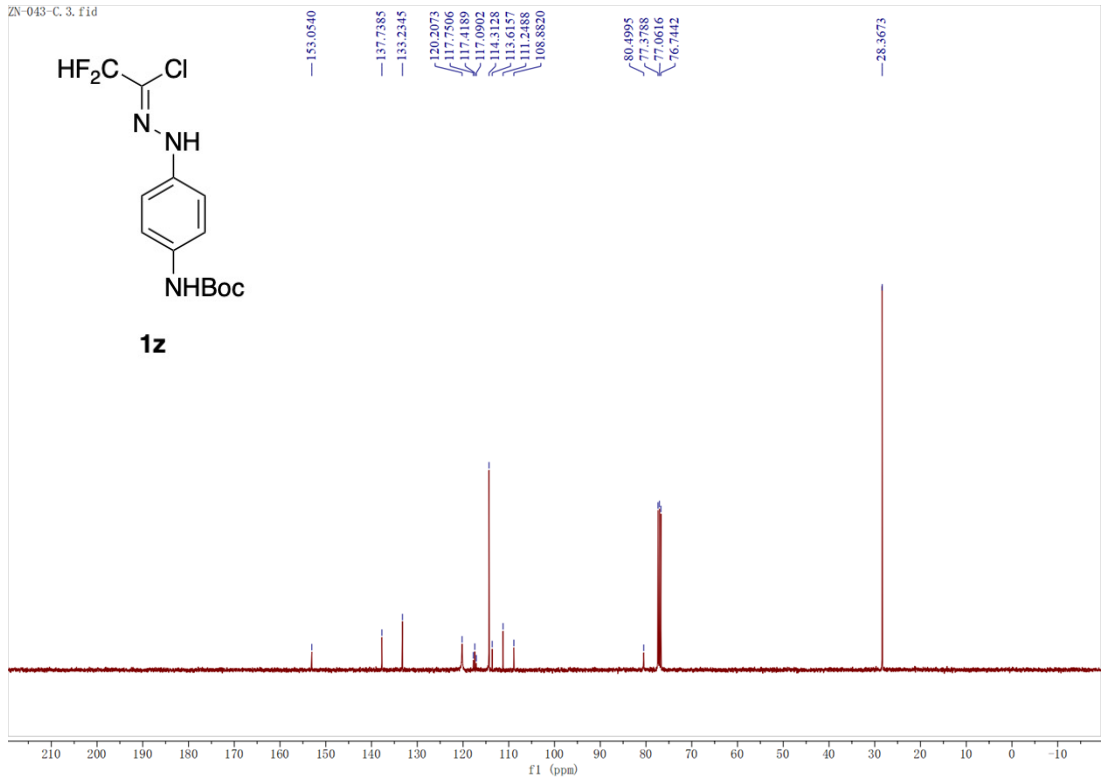
tert-Butyl(*Z*)-(4-(2-(1-chloro-2,2-difluoroethylidene)hydrazineyl)phenyl)carbama-te (1z)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **1z**

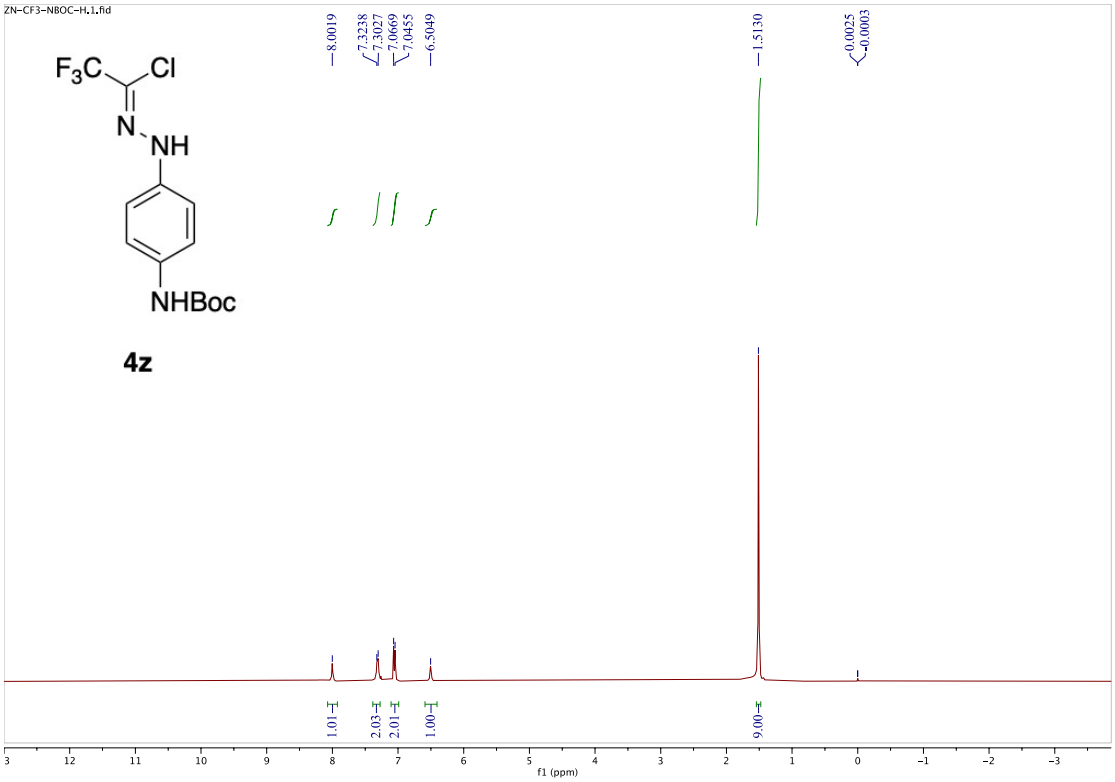


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **1z**

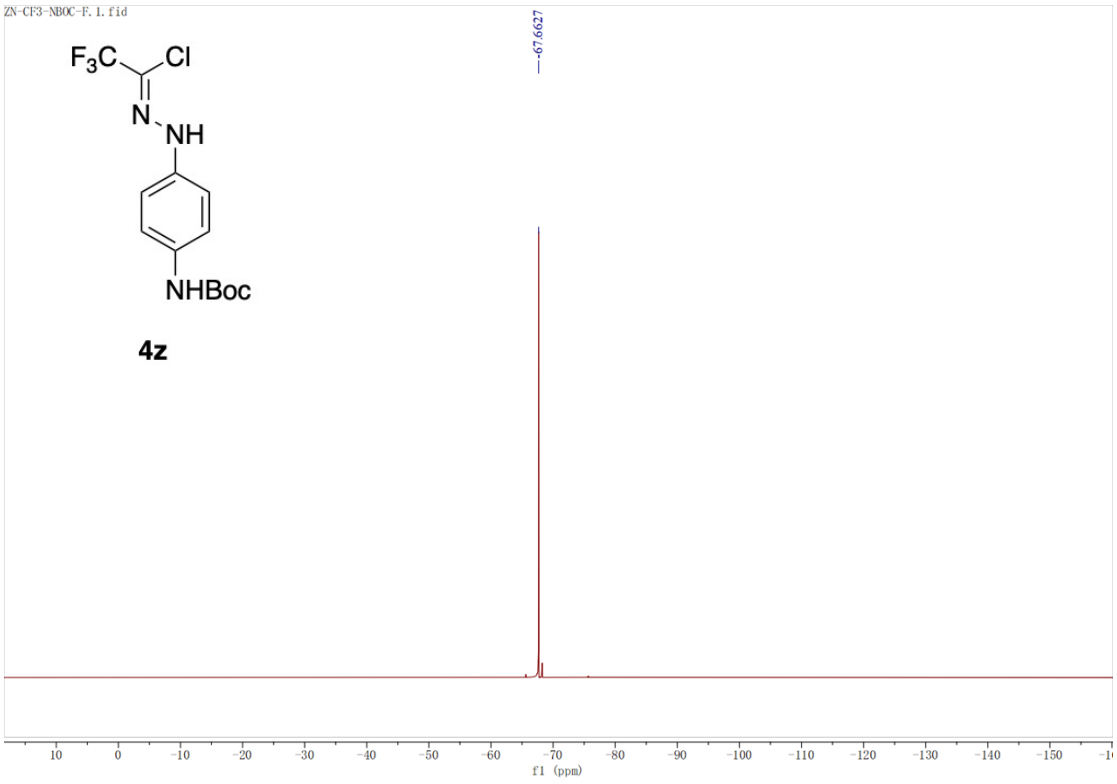


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **1z**

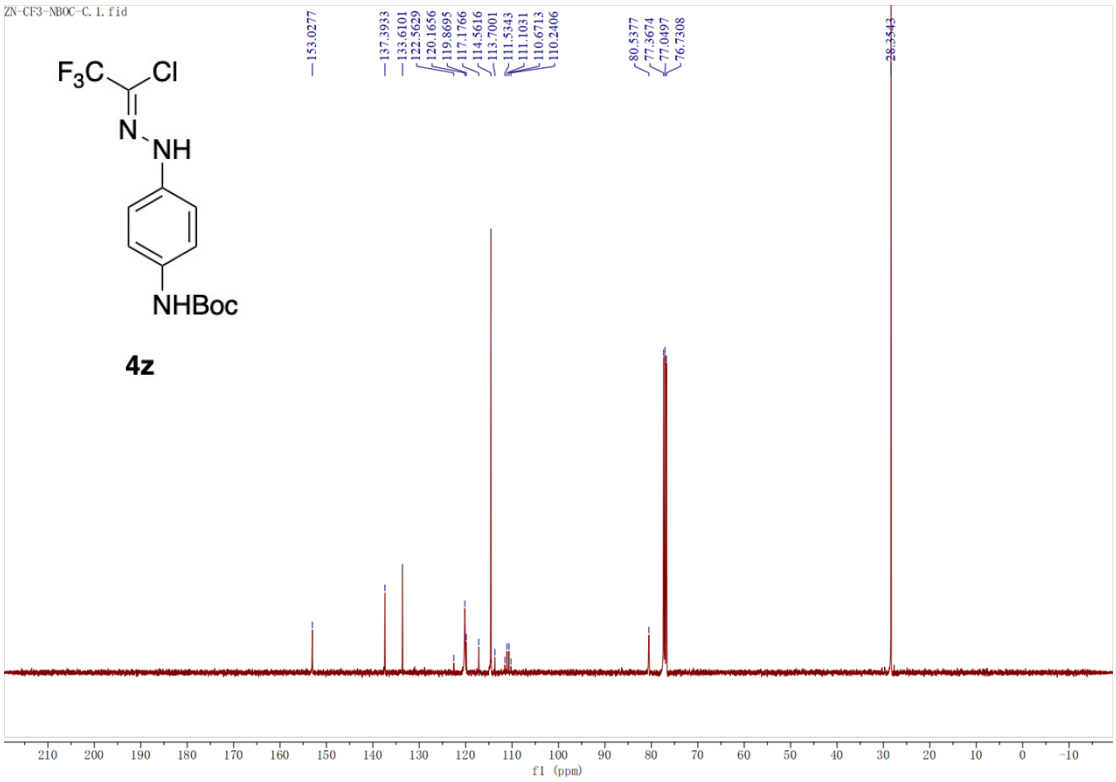
***tert*-Butyl(*Z*)-(4-(2-(1-chloro-2,2,2-trifluoroethylidene)hydrazineyl)phenyl)carbamate (4z)**



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **4z**

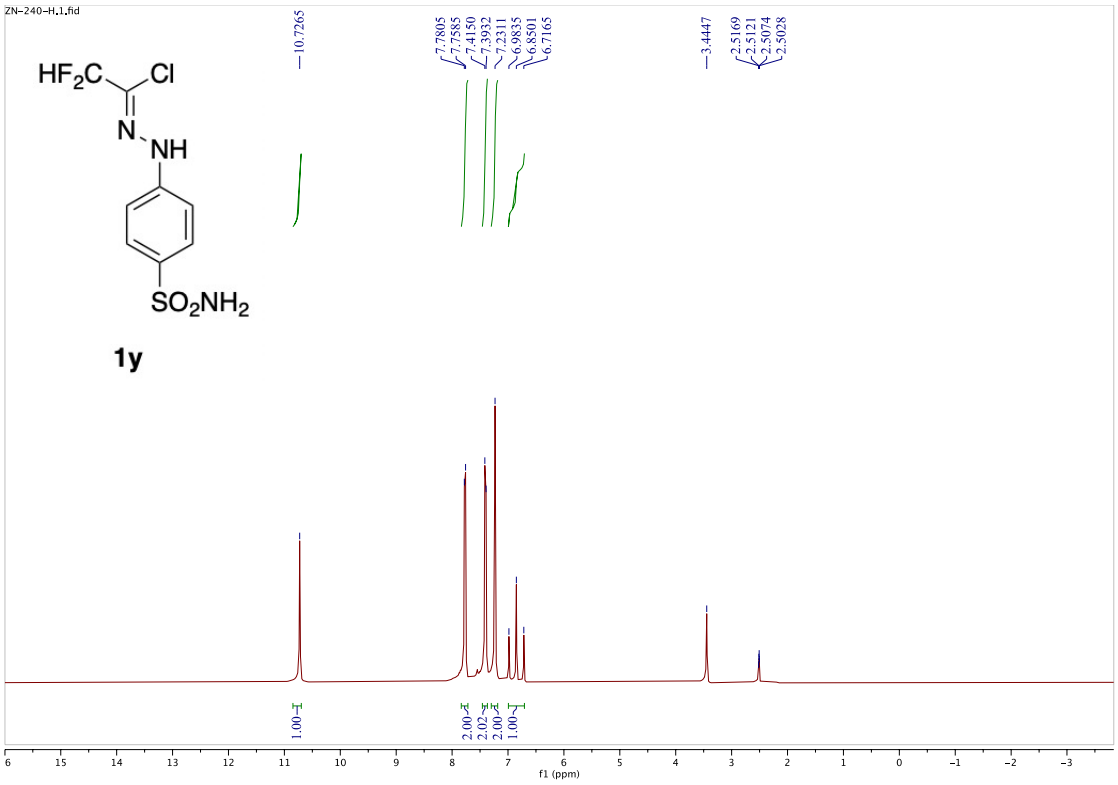


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **4z**

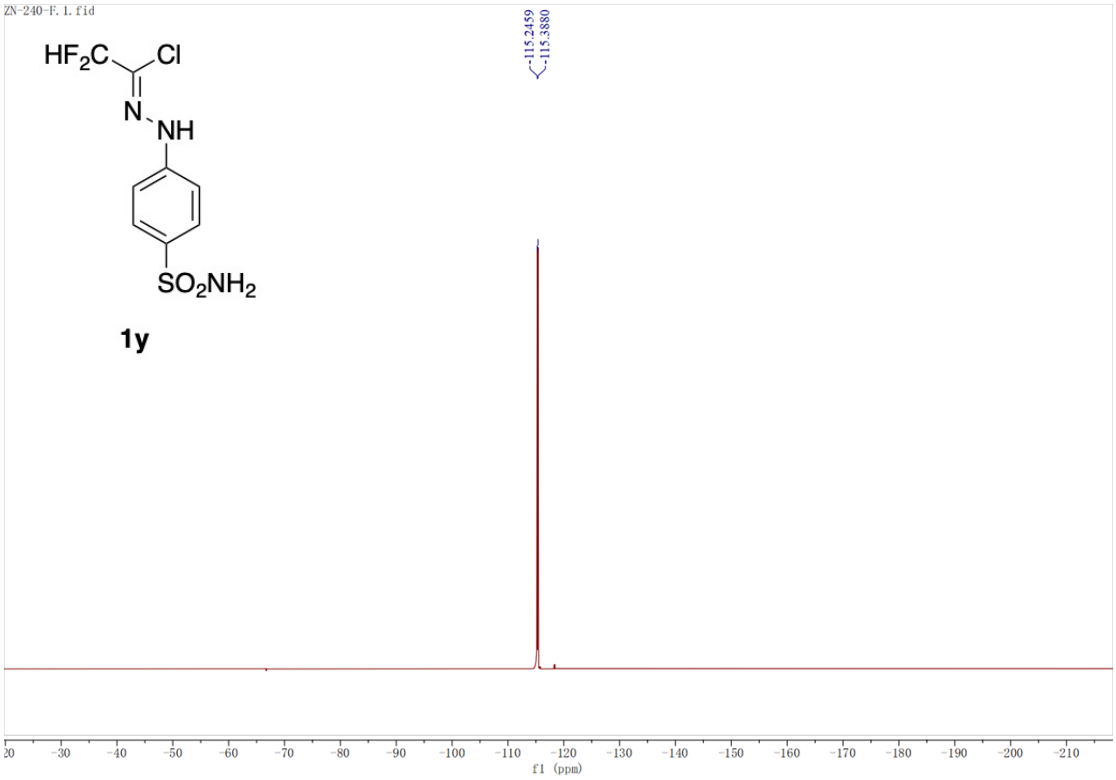


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **4z**

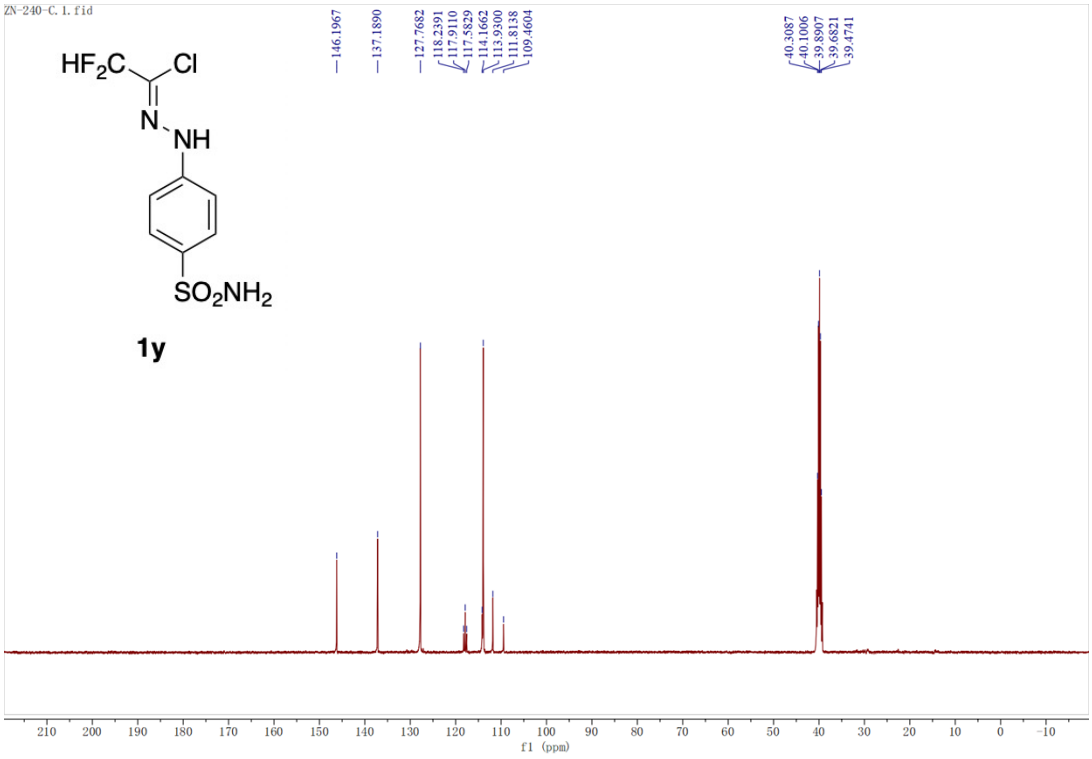
(*Z*)-2,2-difluoro-*N*-(4-sulfamoylphenyl)acetohydrazonoyl chloride (1y)



^{1}H NMR spectrum (400 MHz, d_6-DMSO) of **1y**

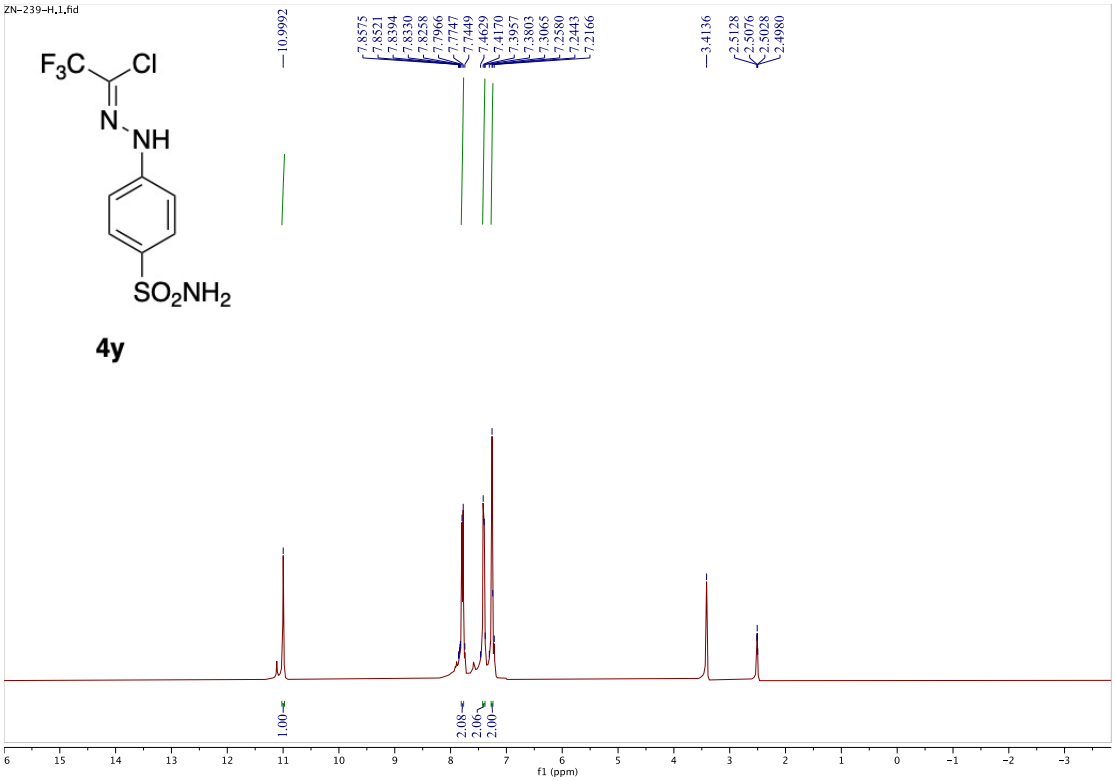


^{19}F NMR spectrum (376 MHz, d_6-DMSO) of **1y**

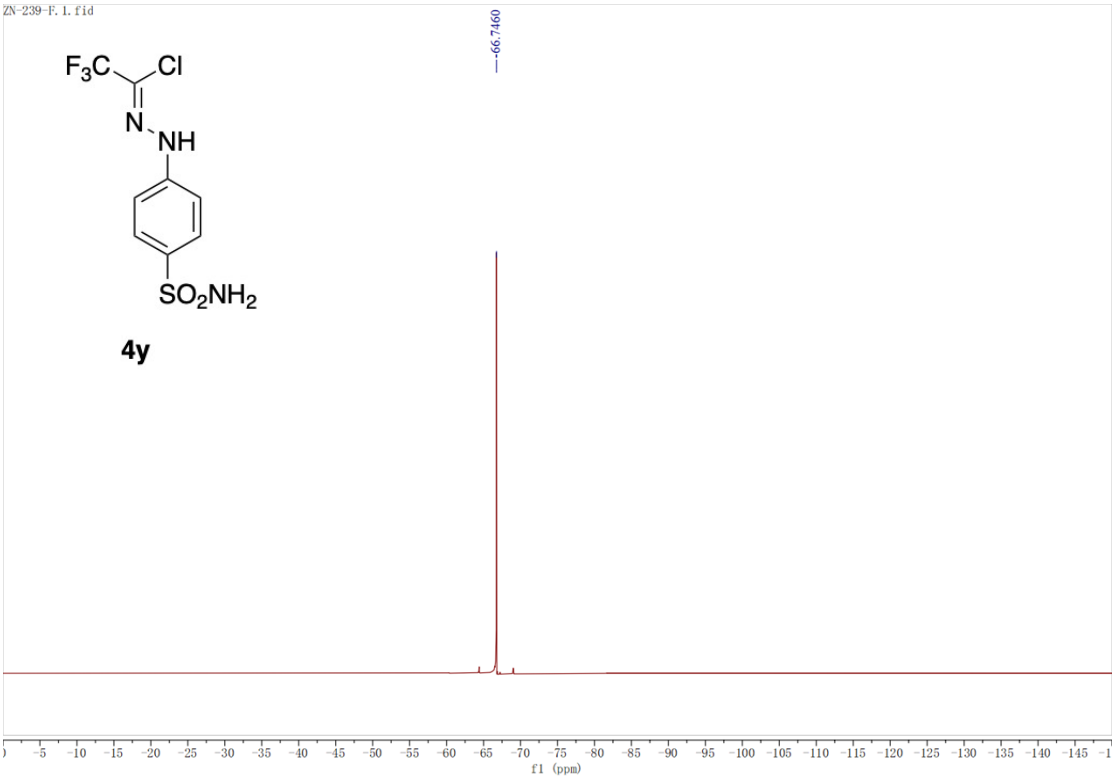


^{13}C NMR spectrum (100 MHz, d_6-DMSO) of **1y**

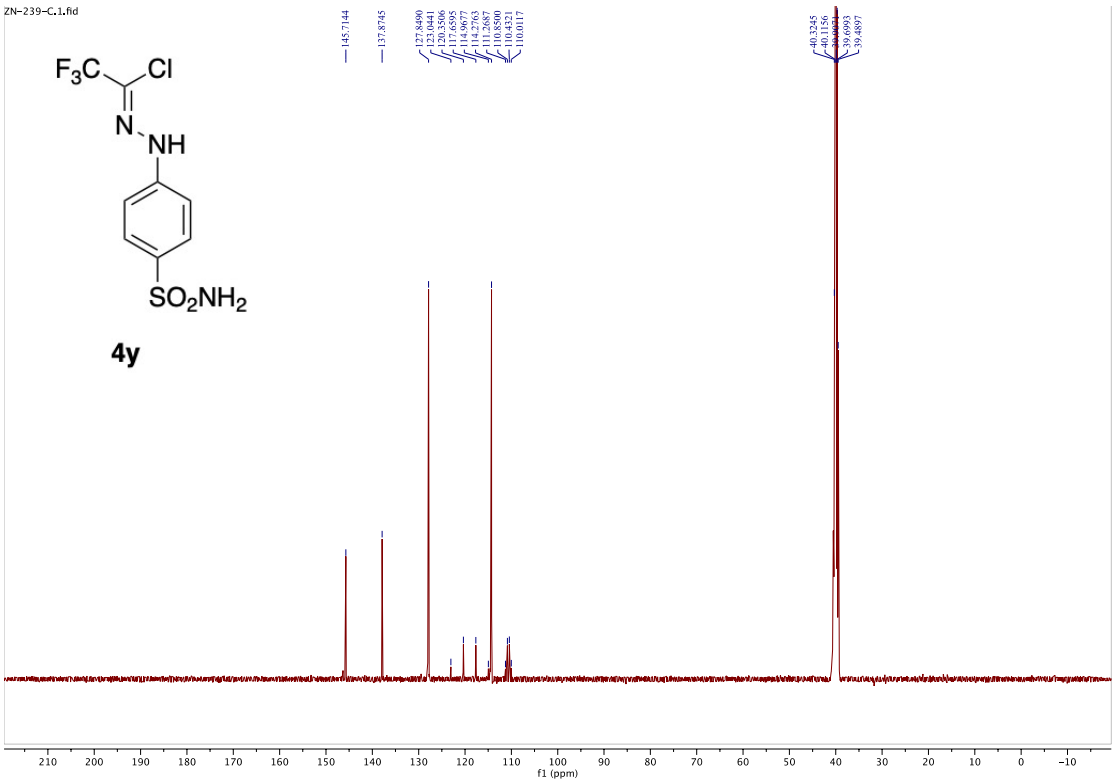
(*Z*)-2,2,2-trifluoro-*N*-(4-sulfamoylphenyl)acetohydrazonoyl chloride (4y)



^{1}H NMR spectrum (400 MHz, d_6-DMSO) of **4y**

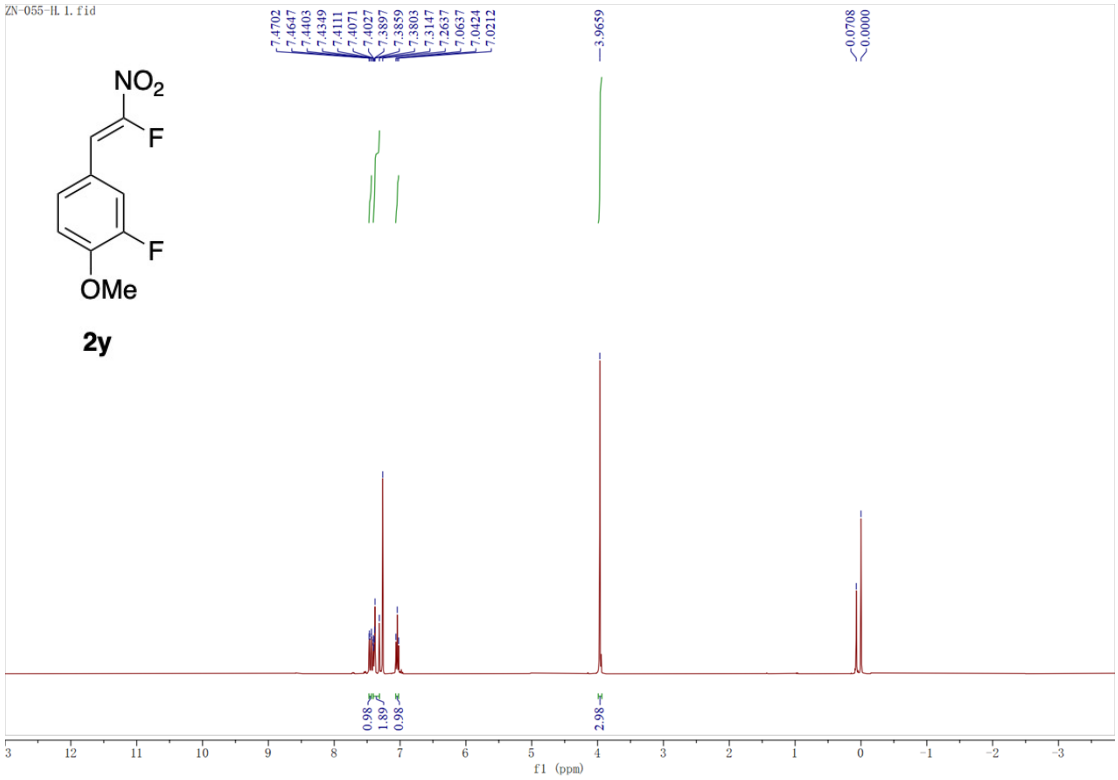


^{19}F NMR spectrum (376 MHz, d_6-DMSO) of **4y**

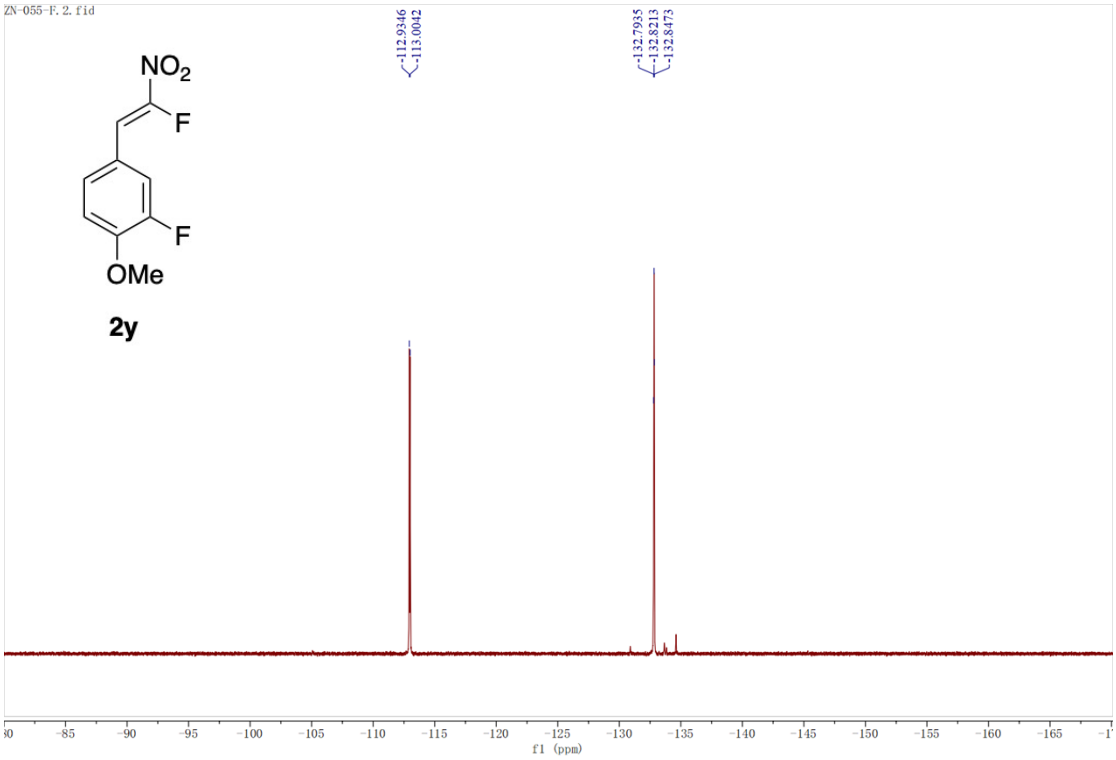


^{13}C NMR spectrum (100 MHz, d_6-DMSO) of **4y**

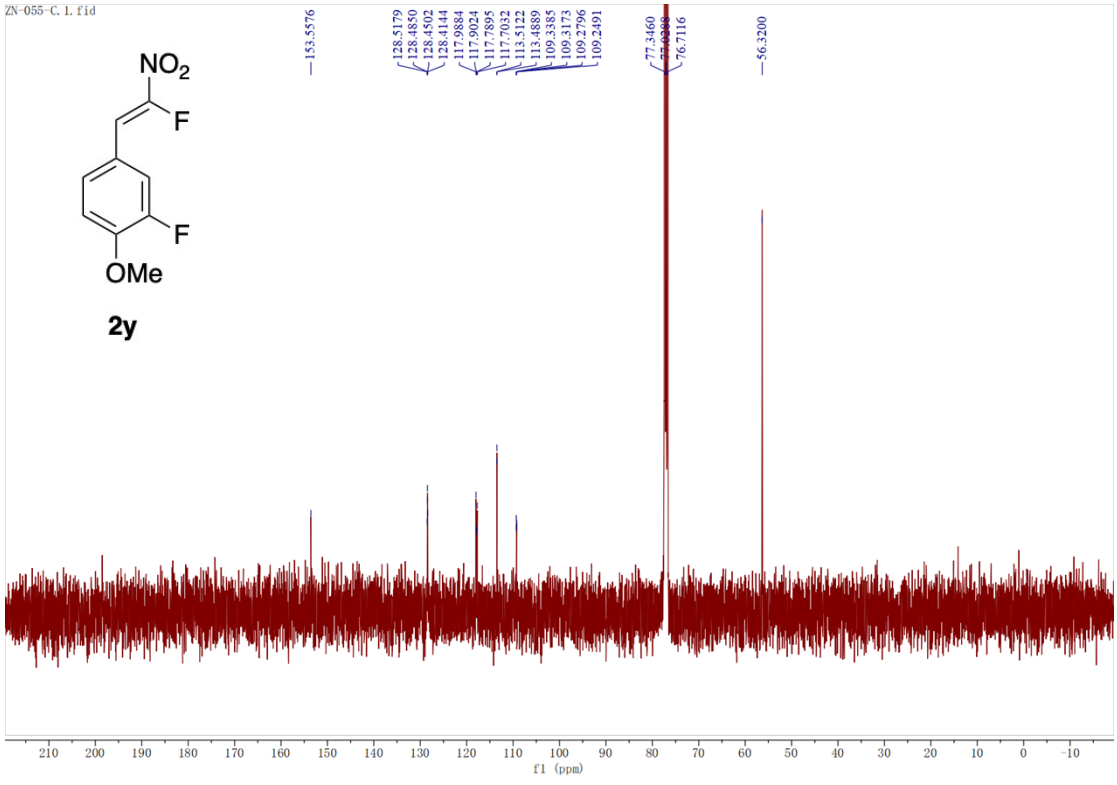
(*Z*)-2-fluoro-4-(2-fluoro-2-nitrovinyl)-1-(methoxyphenyl) benzene (2y)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **2y**

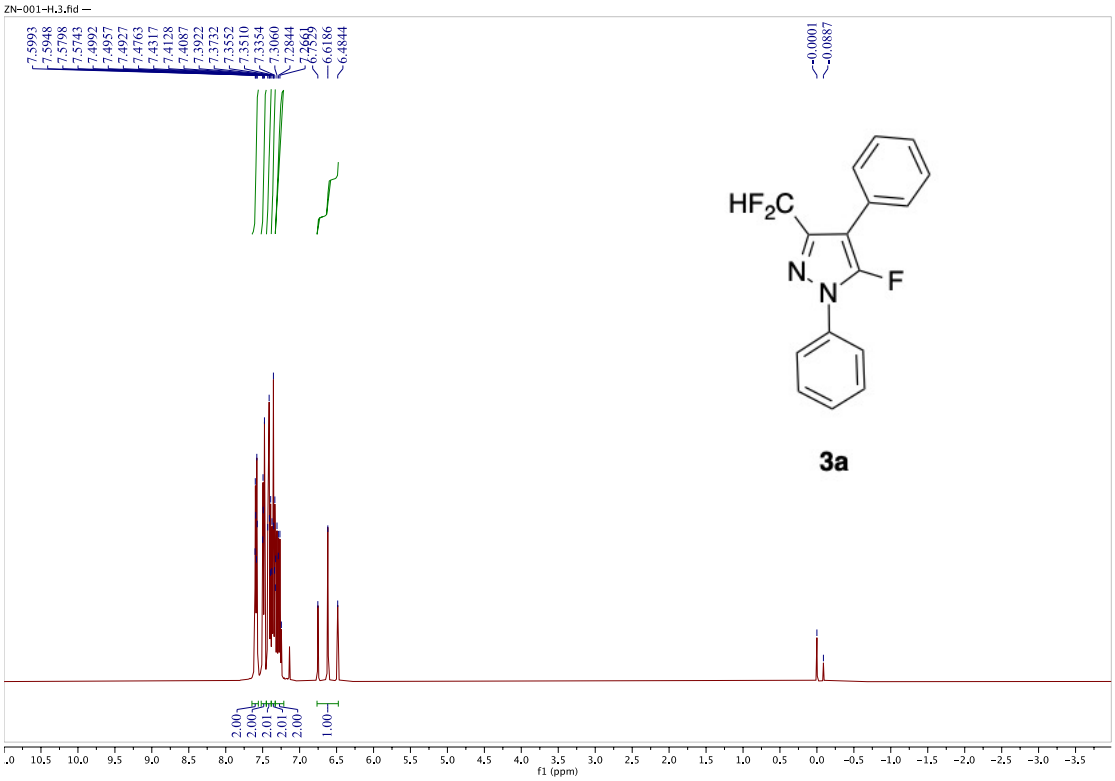


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **2y**

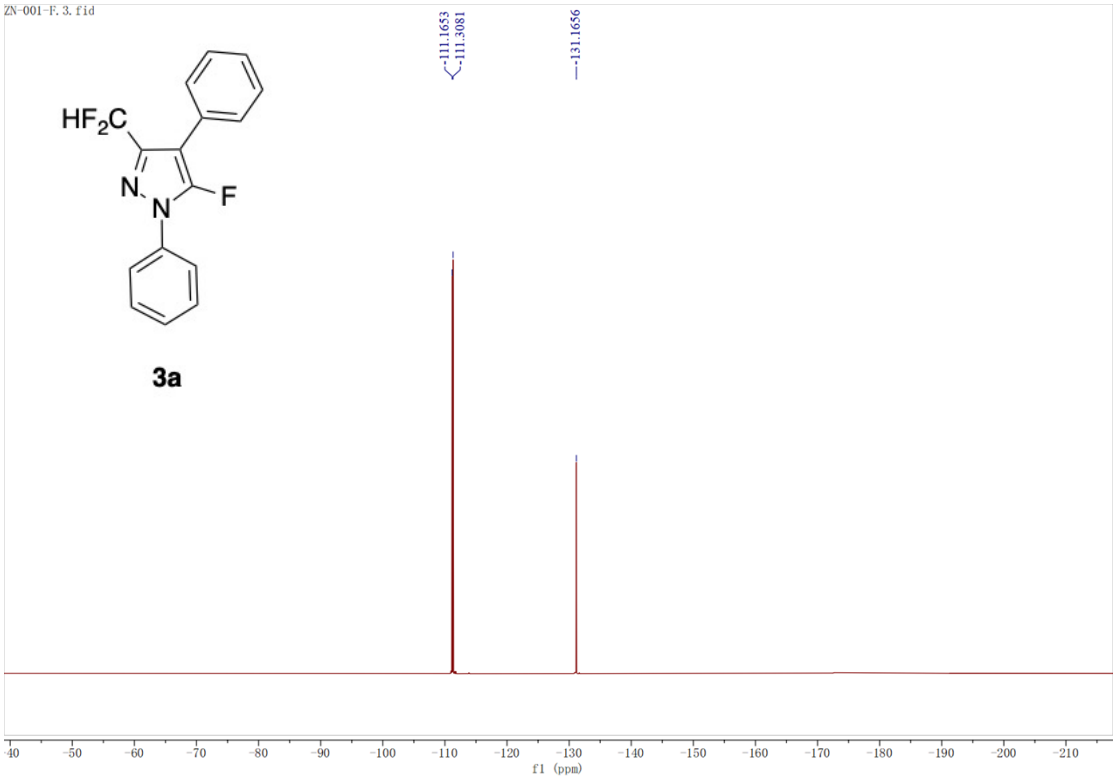


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **2y**

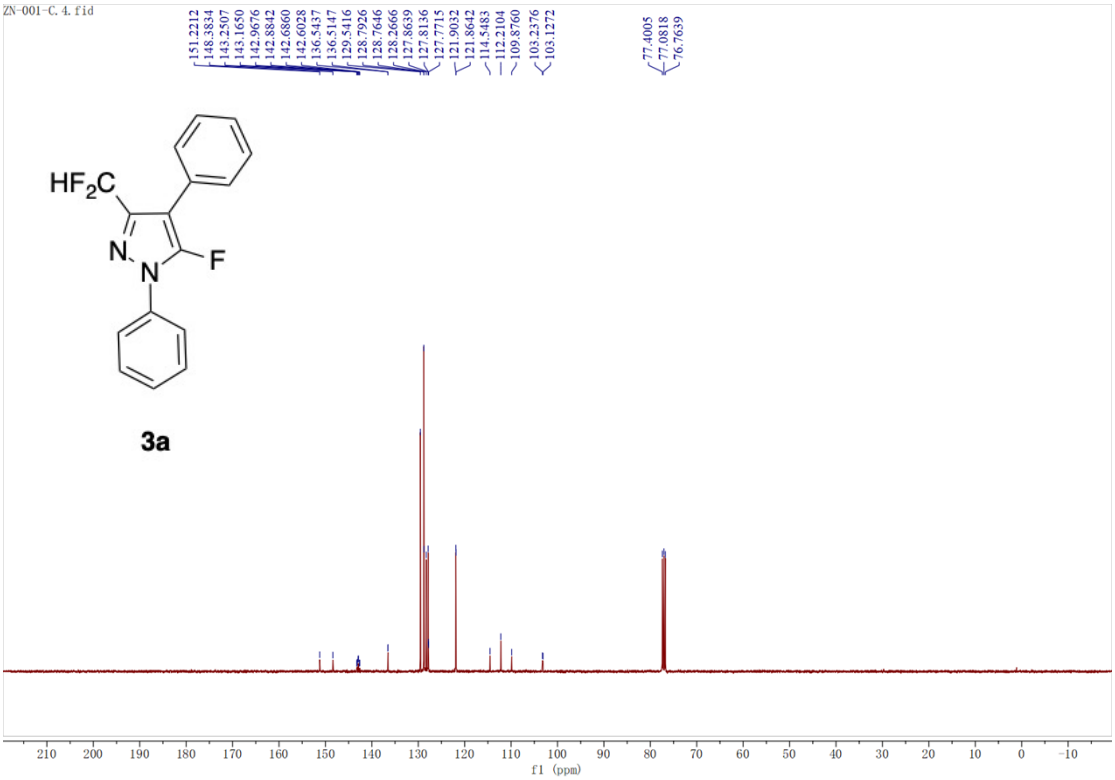
3-(Difluoromethyl)-5-fluoro-1,4-diphenyl-1*H*-pyrazole (3a)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3a**

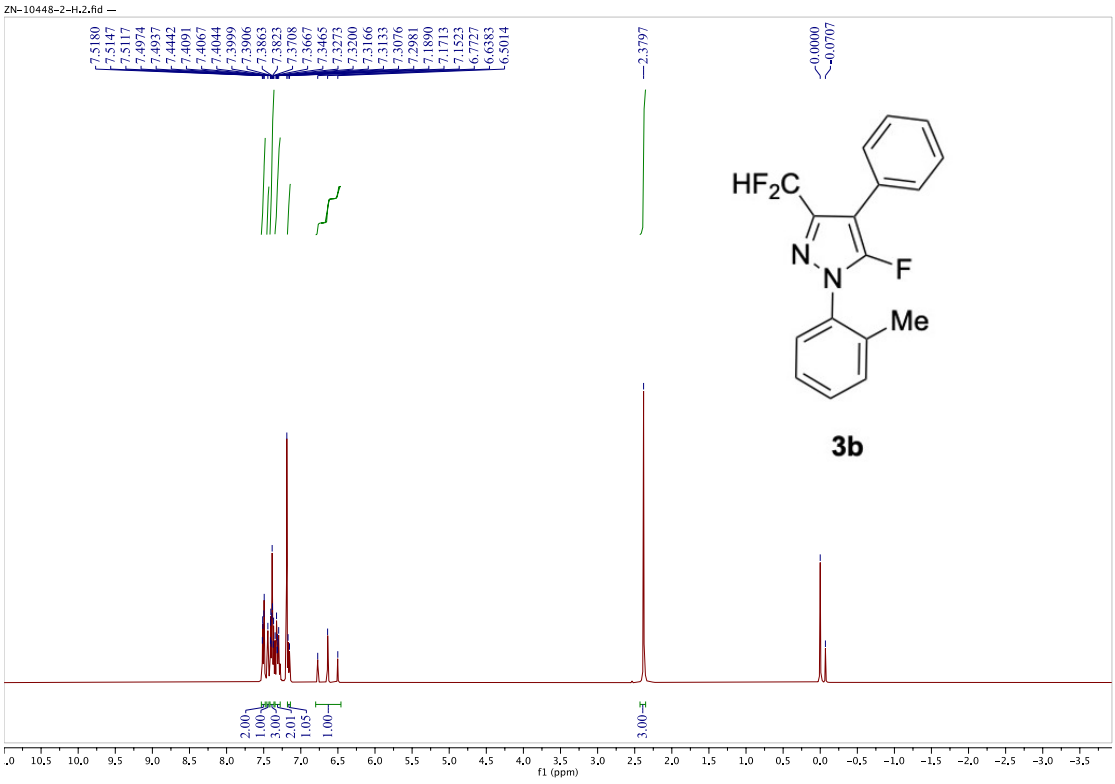


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3a**

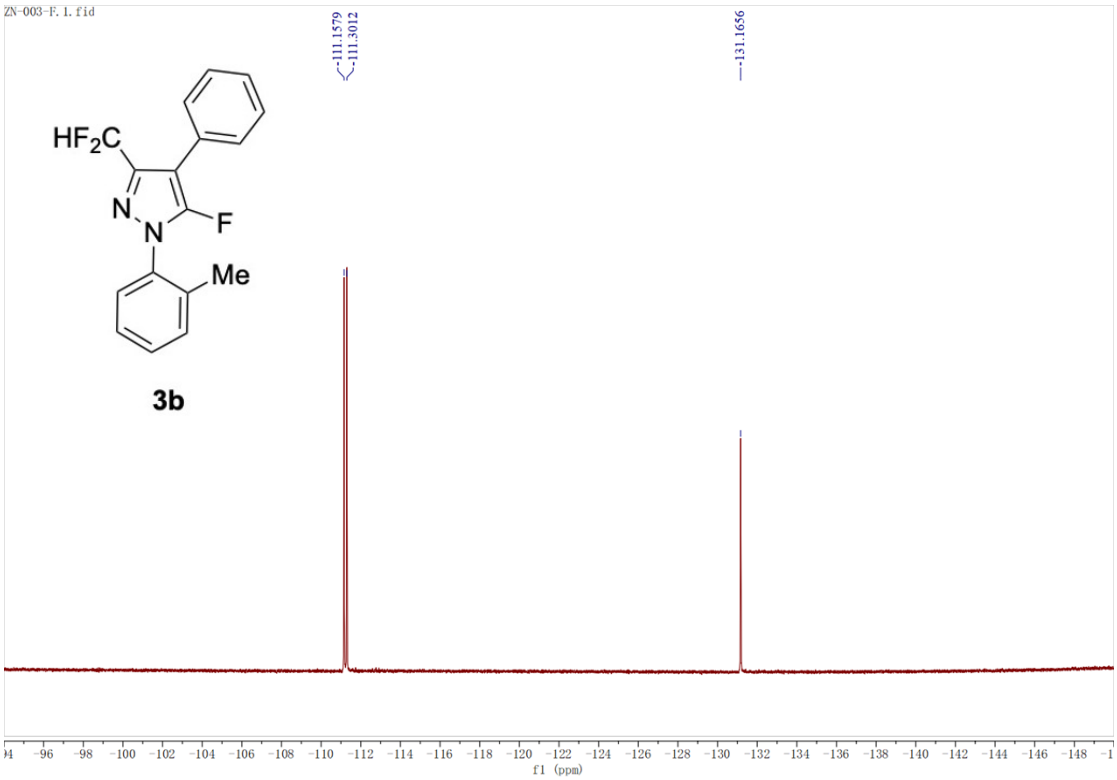


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3a**

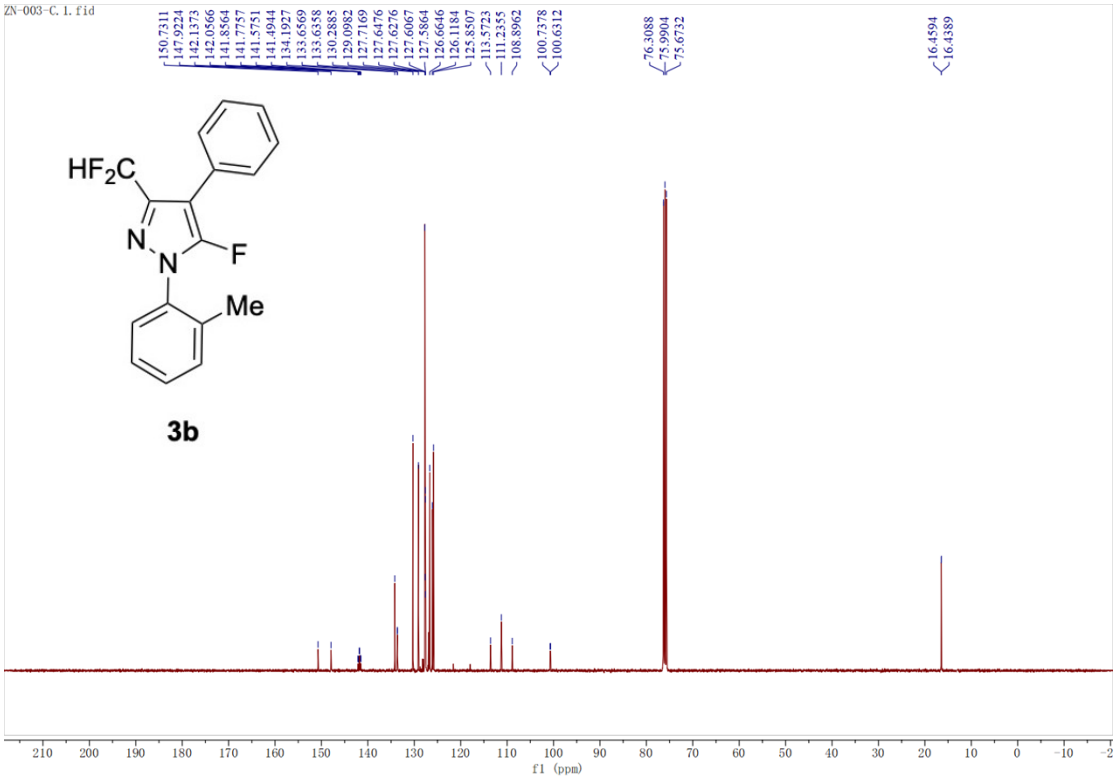
3-(Difluoromethyl)-5-fluoro-4-phenyl-1-(*o*-tolyl)-1*H*-pyrazole (3b)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3b**

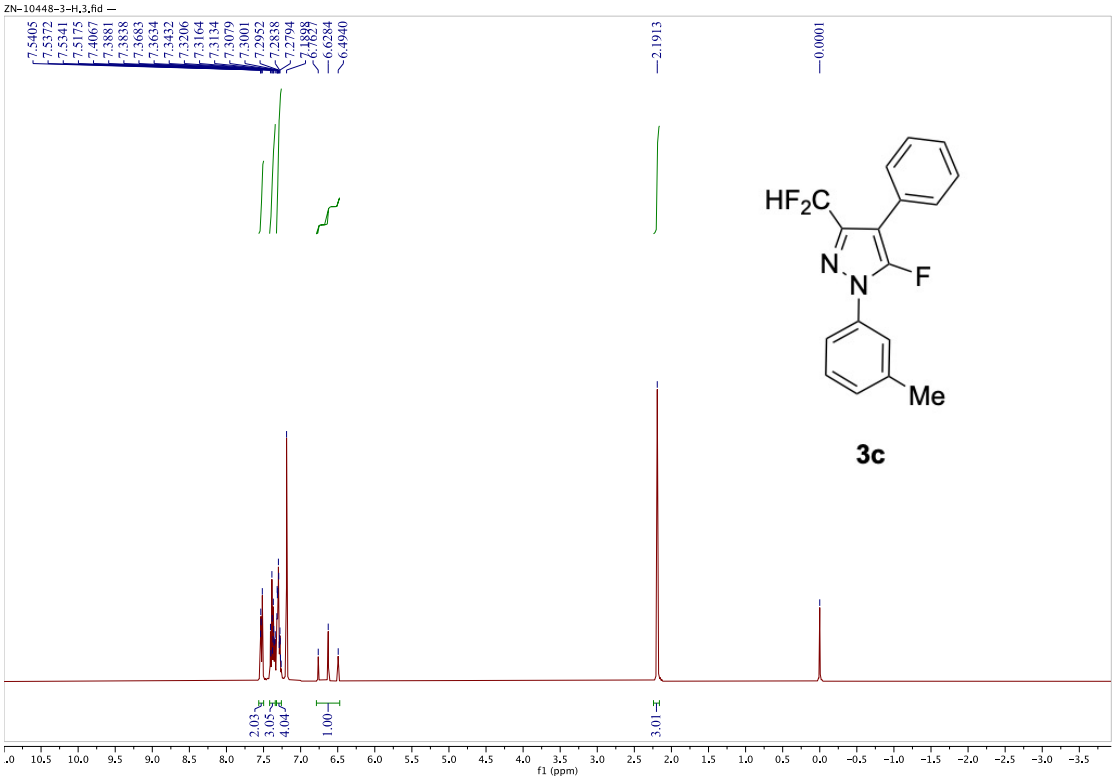


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3b**

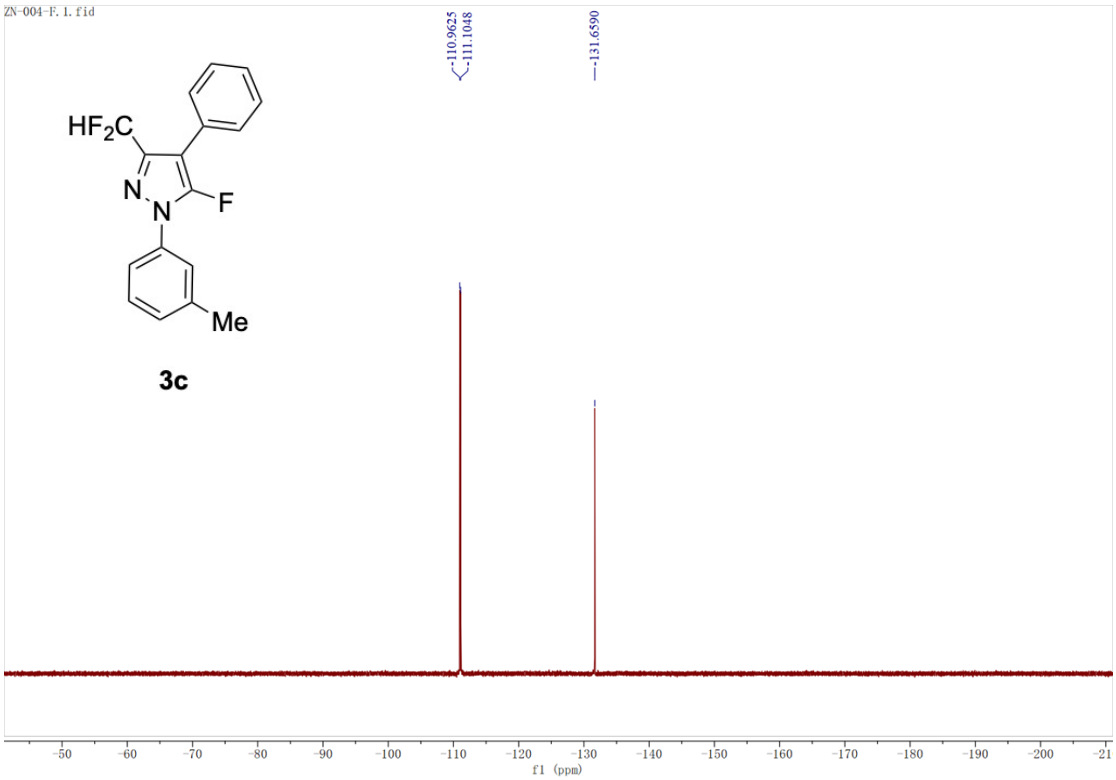


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3b**

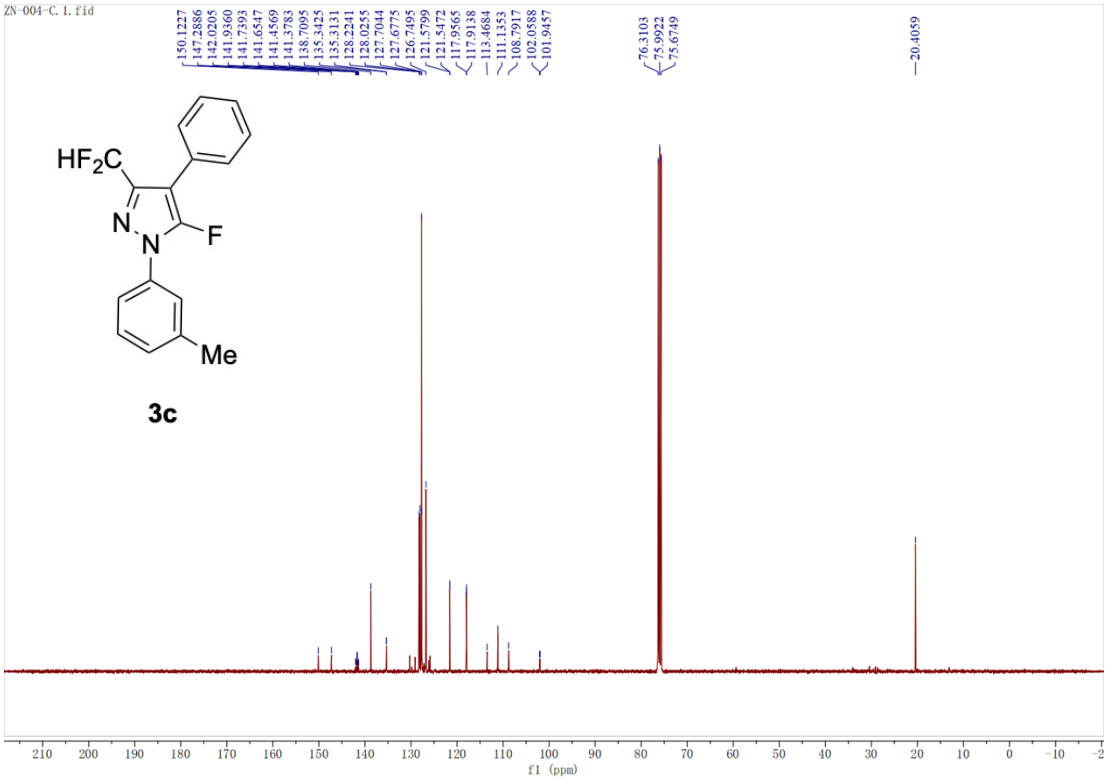
3-(Difluoromethyl)-5-fluoro-4-phenyl-1-(*m*-tolyl)-1*H*-pyrazole (3c)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3c**

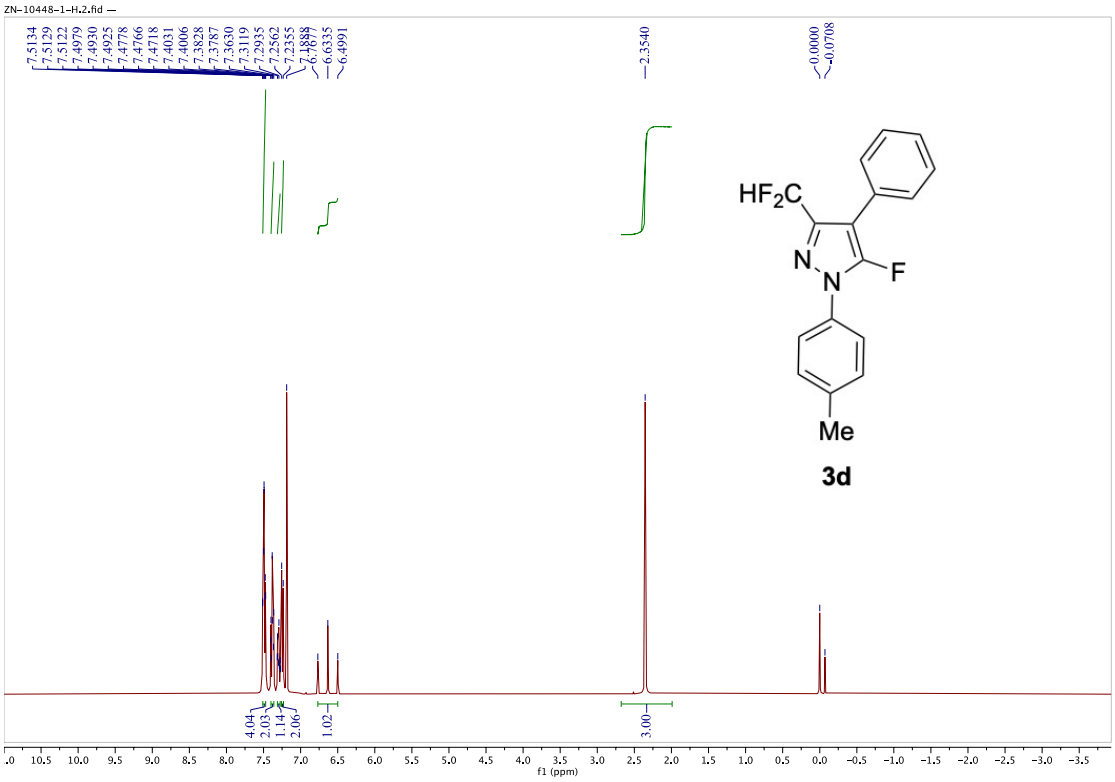


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3c**

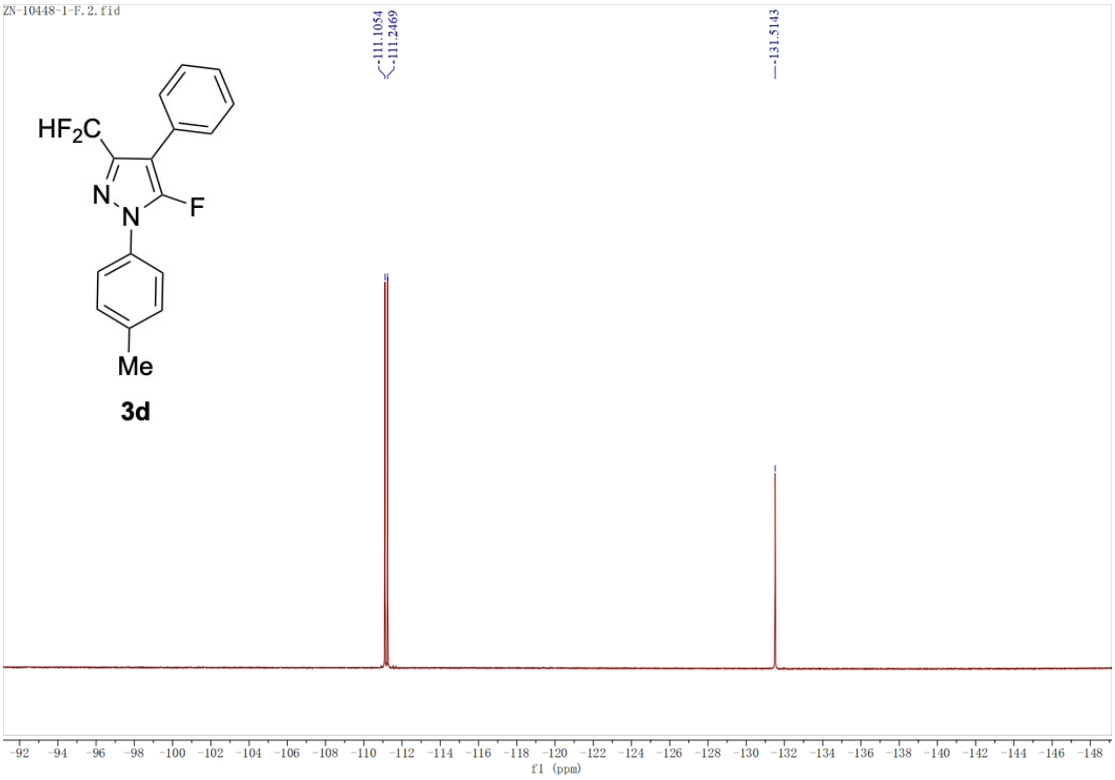


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3c**

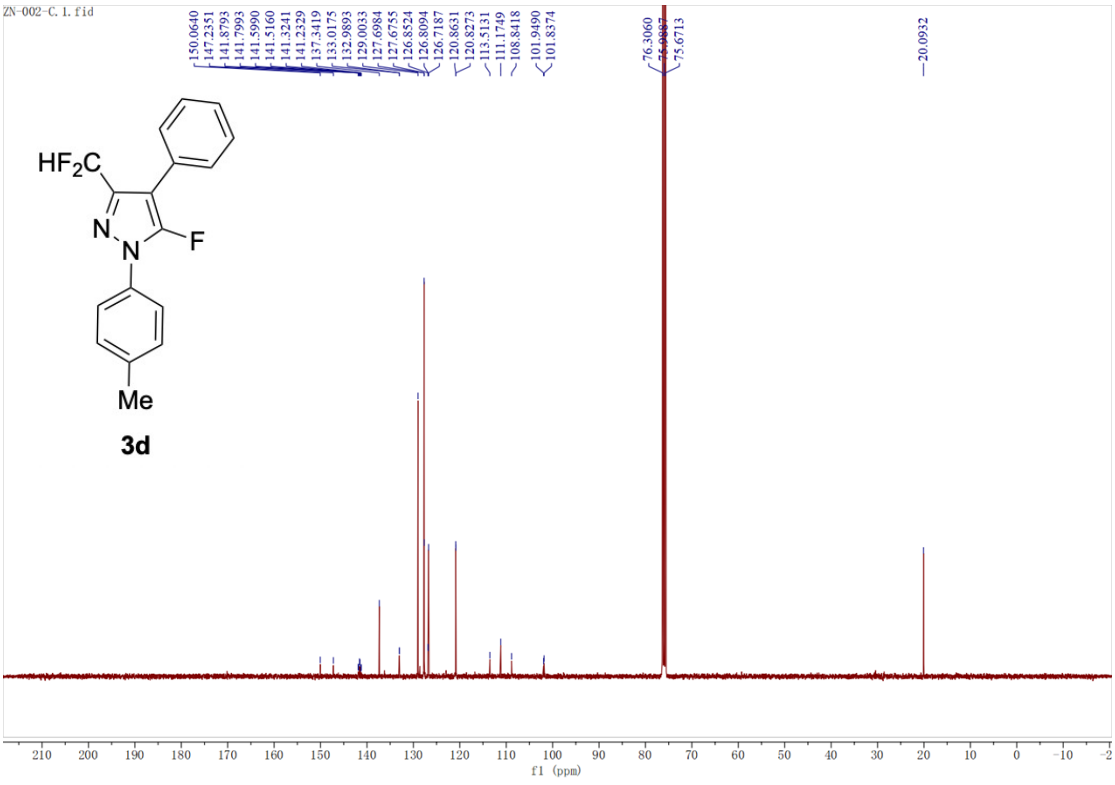
3-(Difluoromethyl)-5-fluoro-4-phenyl-1-(*p*-tolyl)-1*H*-pyrazole (3d)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3d**

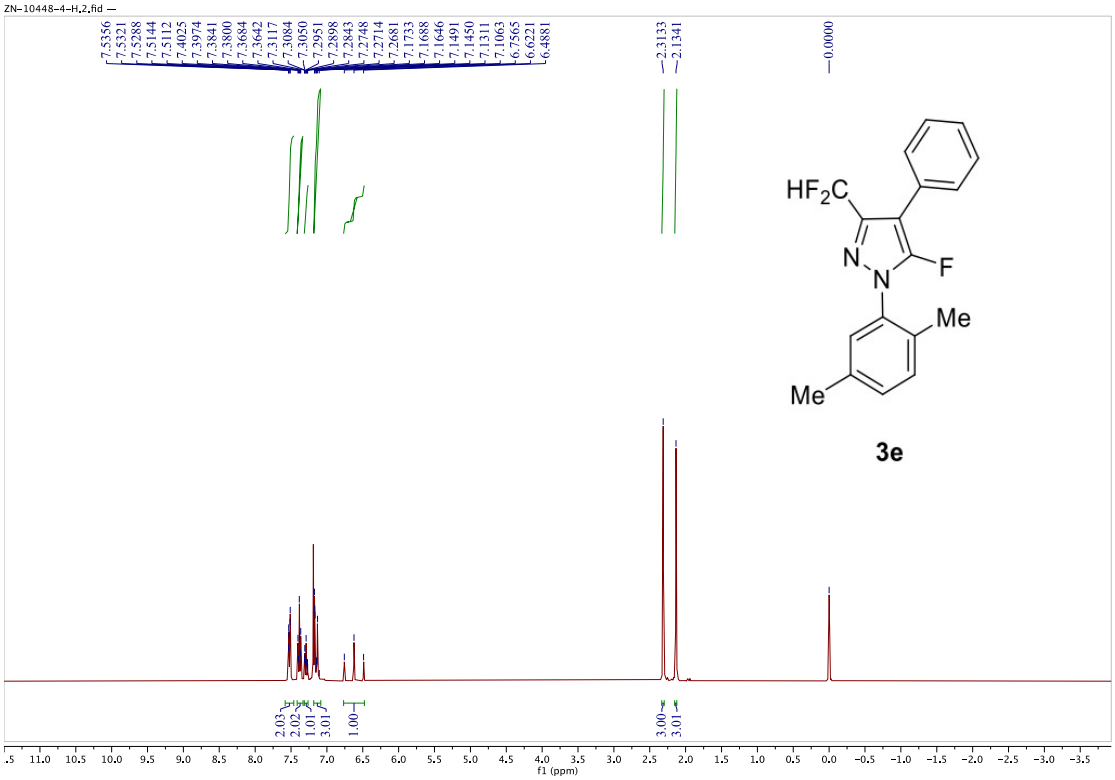


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3d**

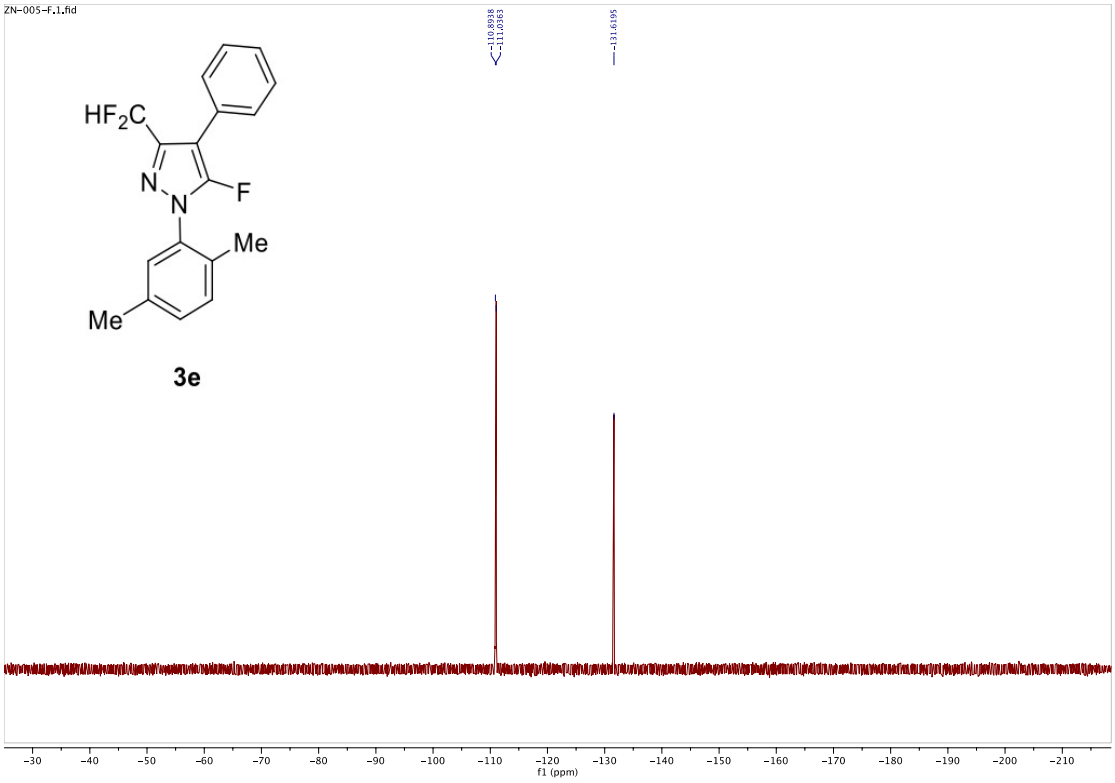


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3d**

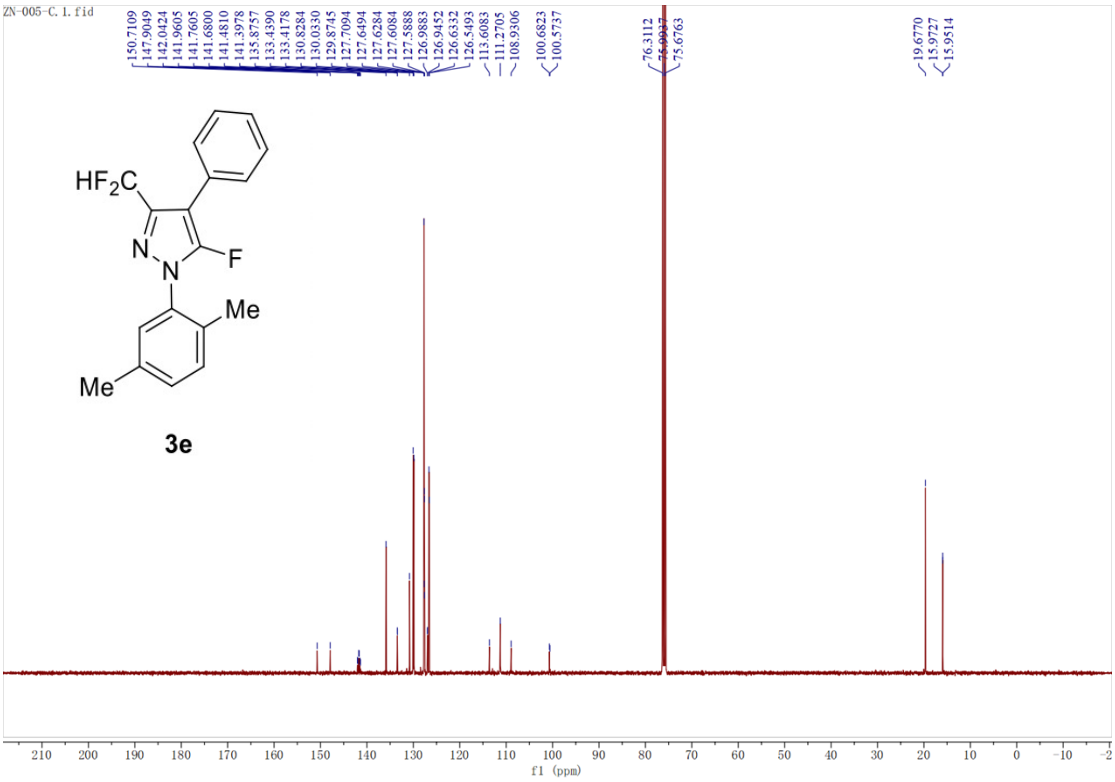
3-(Difluoromethyl)-1-(2,5-dimethylphenyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3e)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3e**

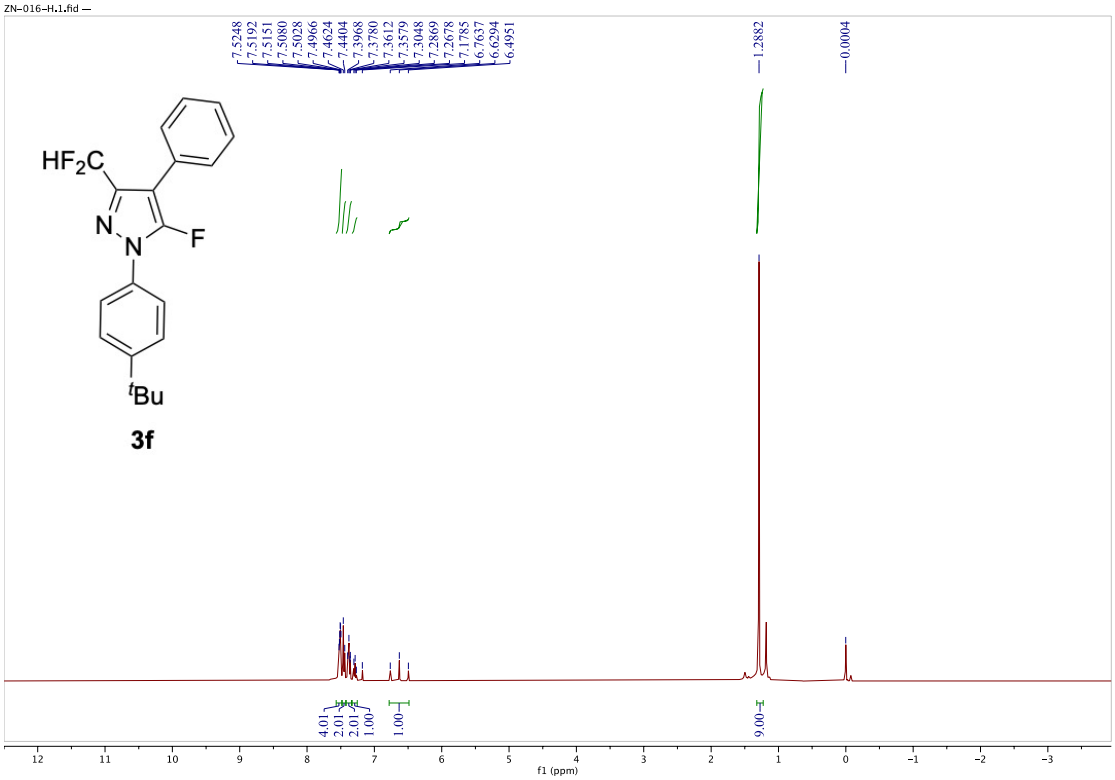


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3e**

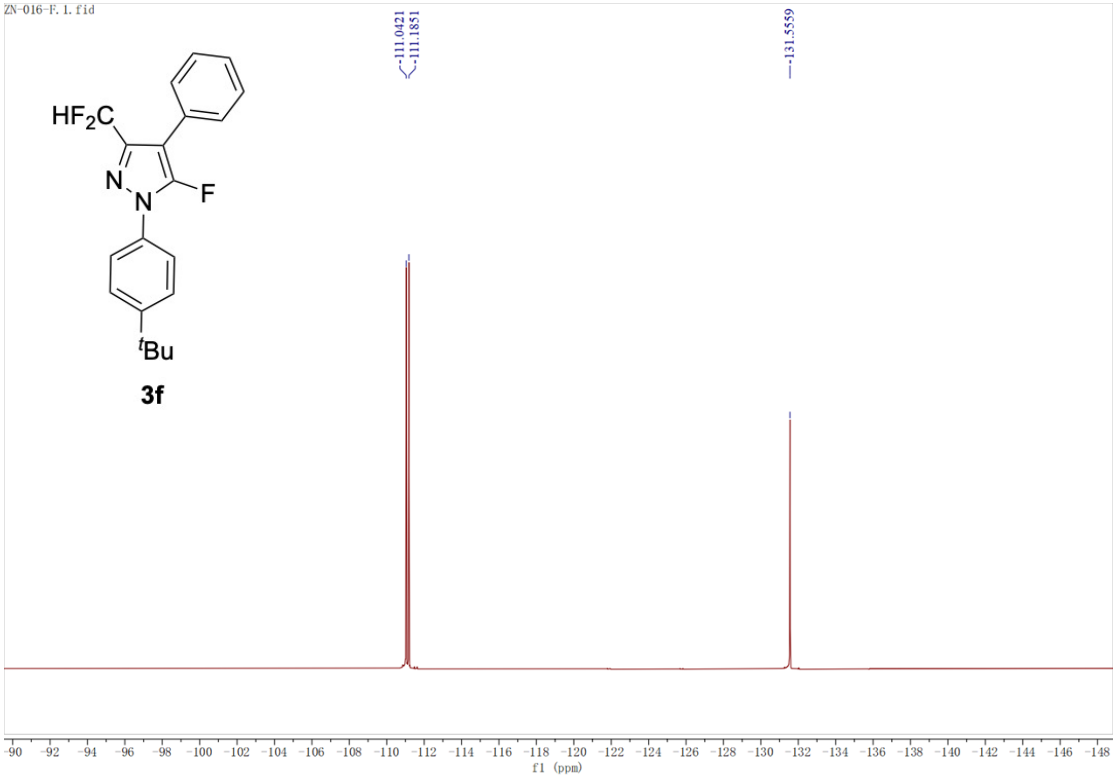


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3e**

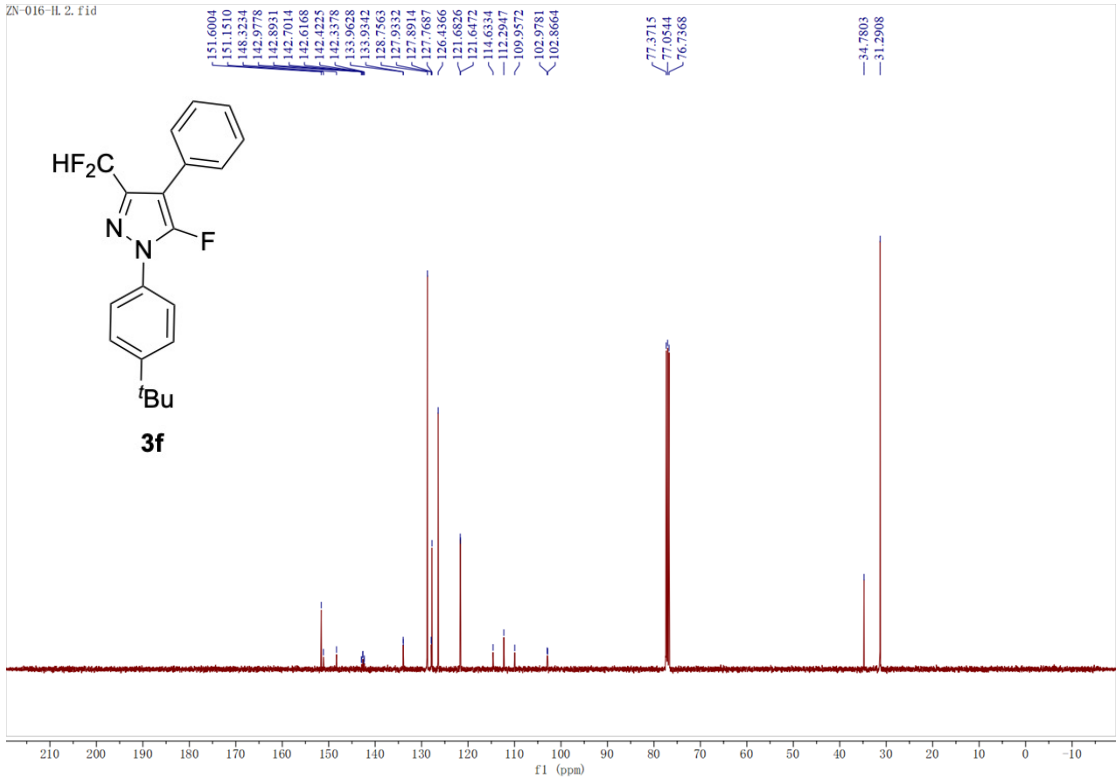
1-(4-(*tert*-Butyl)phenyl)-3-(difluoromethyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3f)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3f**

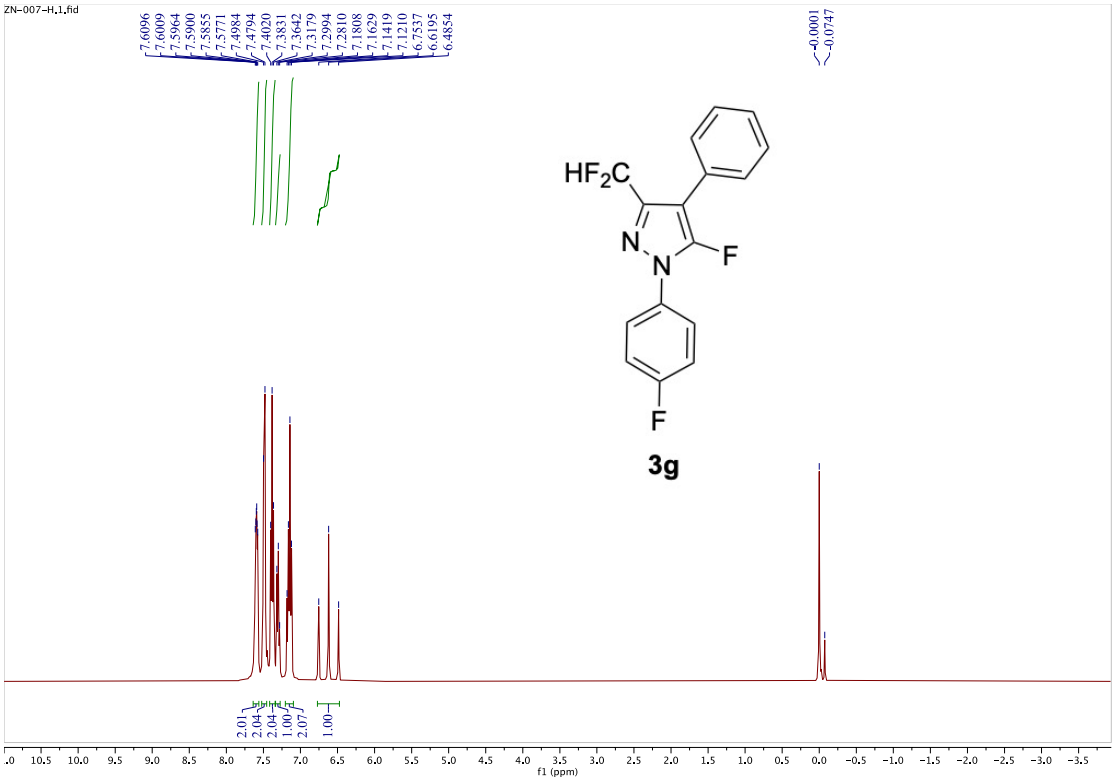


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3f**

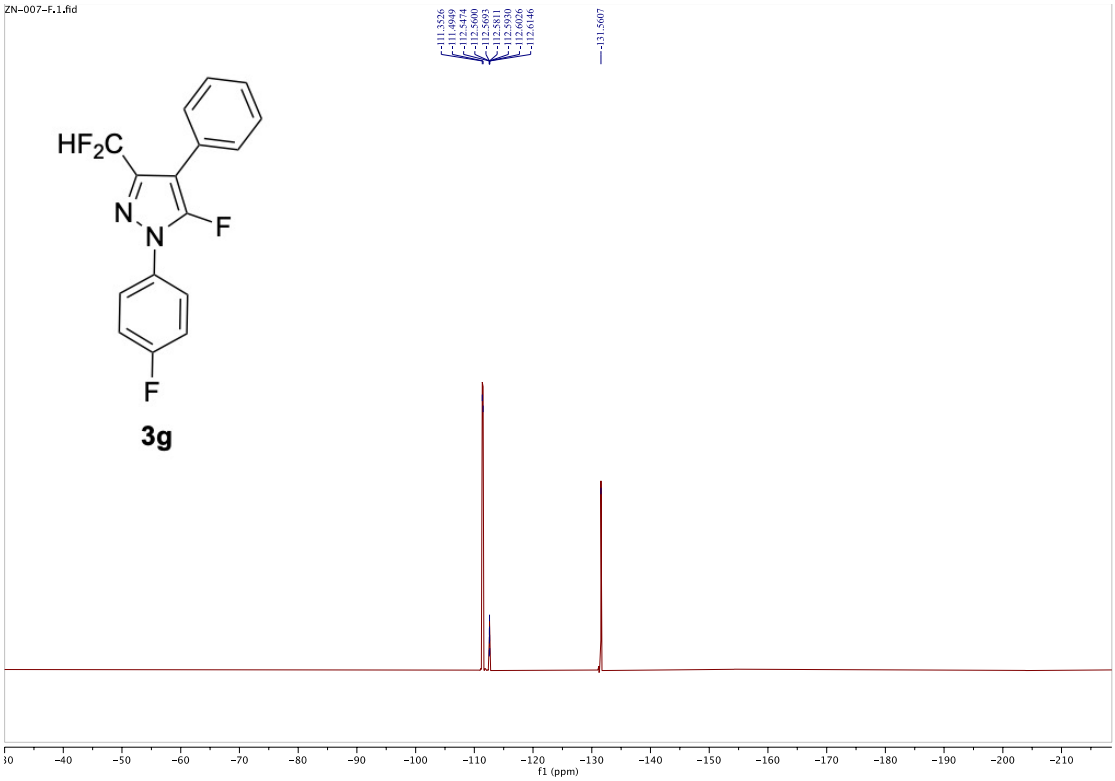


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3f**

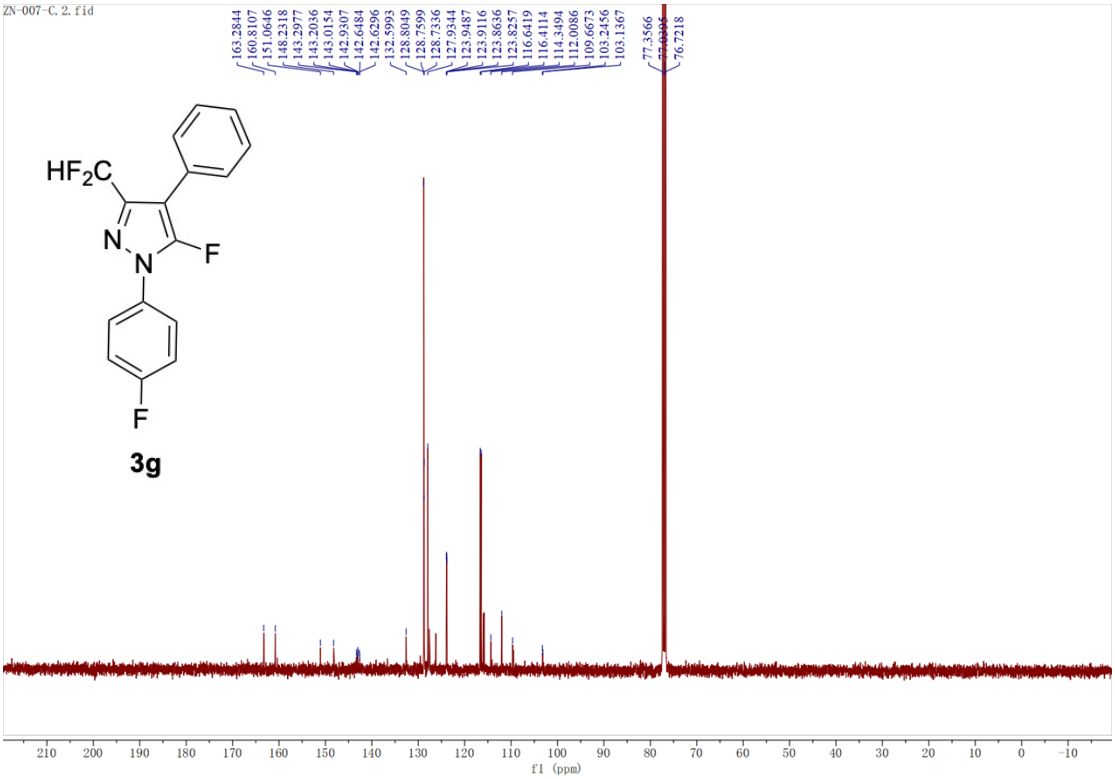
3-(Difluoromethyl)-5-fluoro-1-(4-fluorophenyl)-4-phenyl-1*H*-pyrazole (3g)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3g**

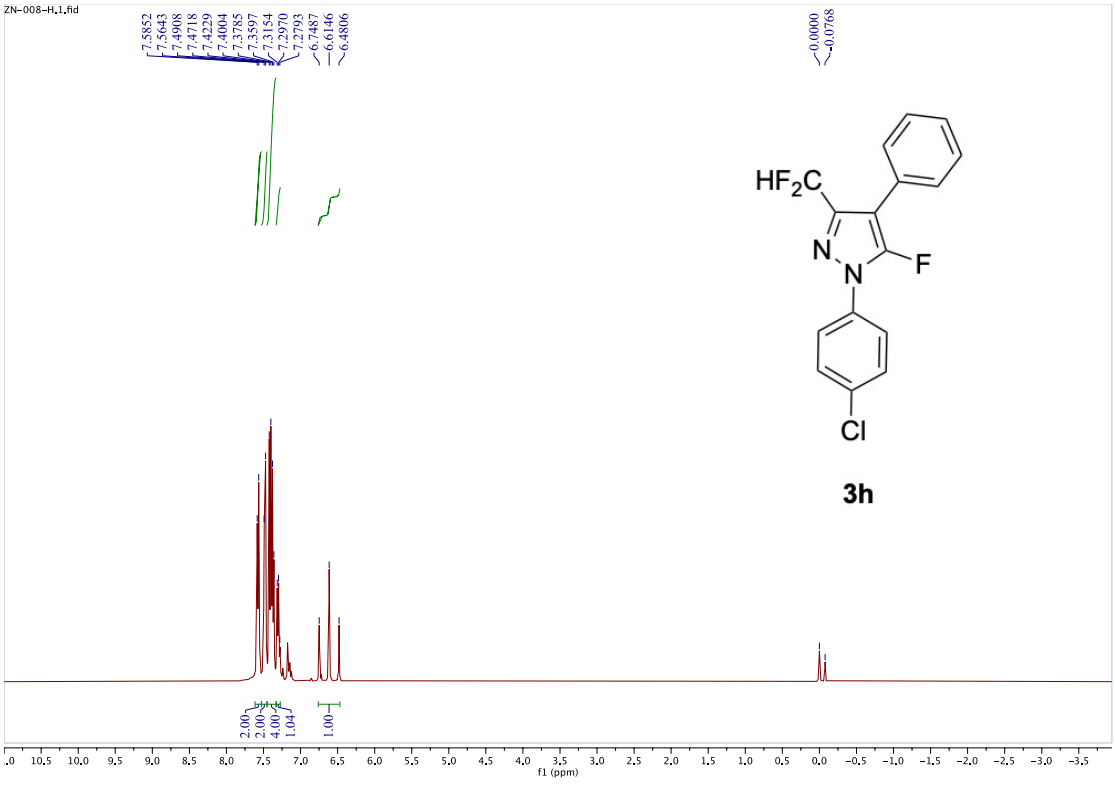


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3g**

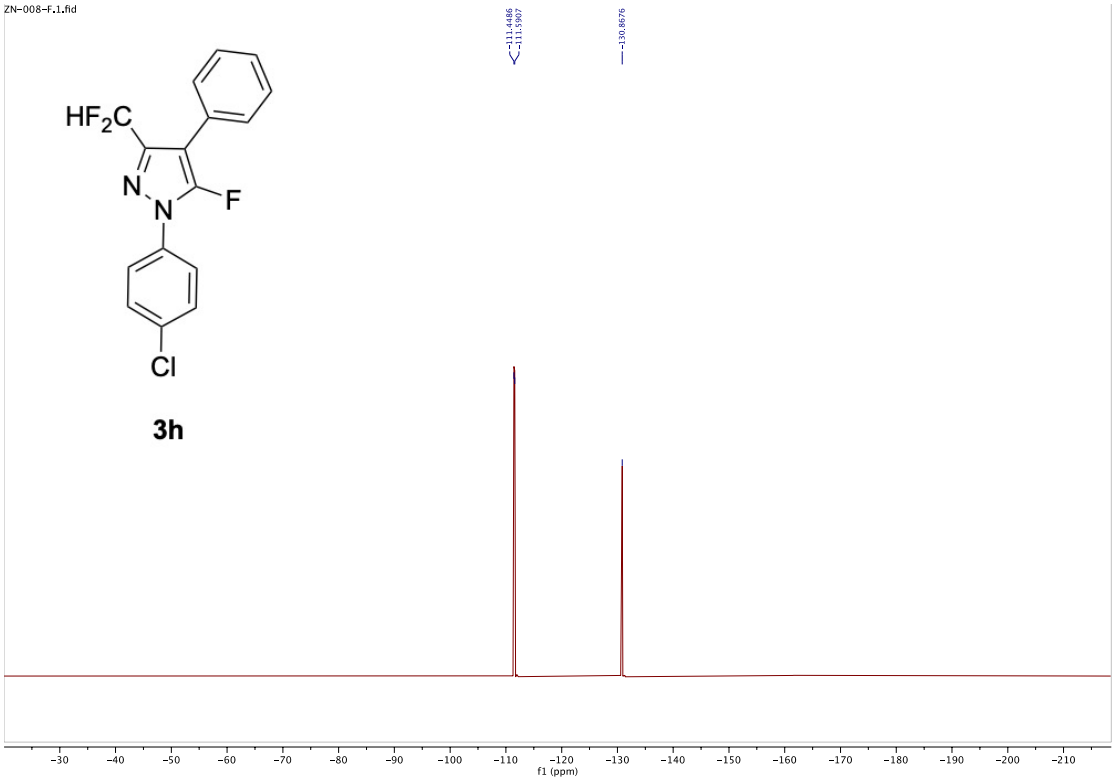


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3g**

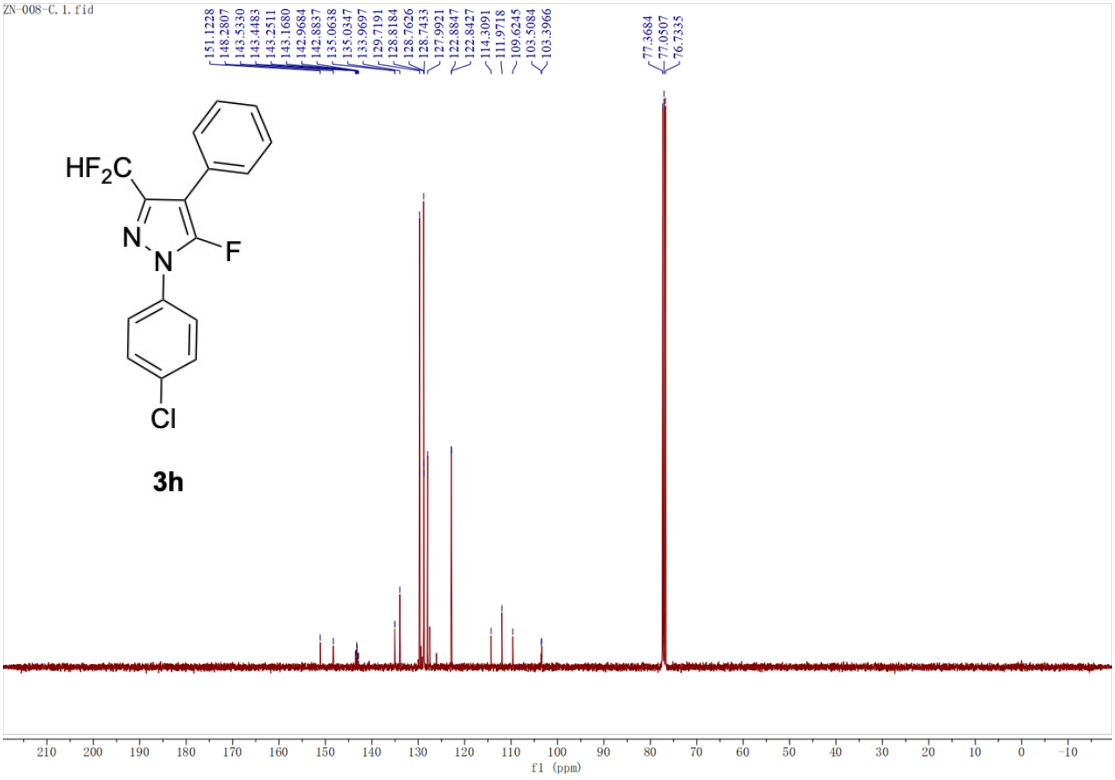
1-(4-Chlorophenyl)-3-(difluoromethyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3h)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3h**

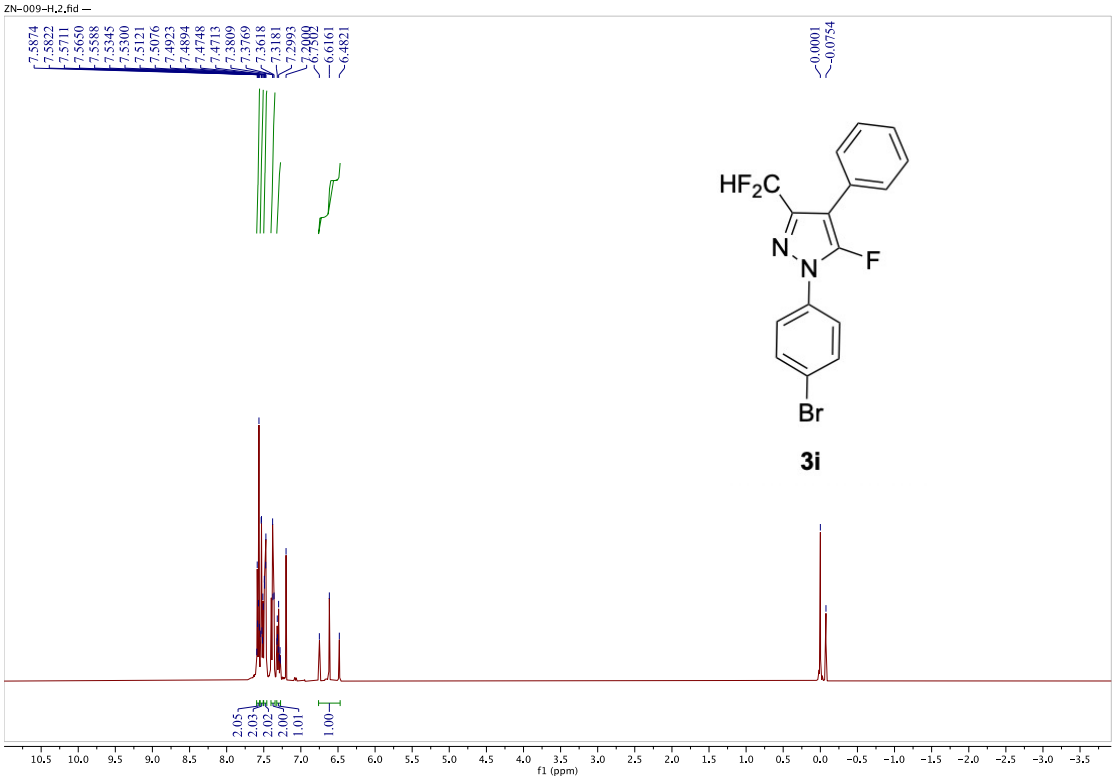


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3h**

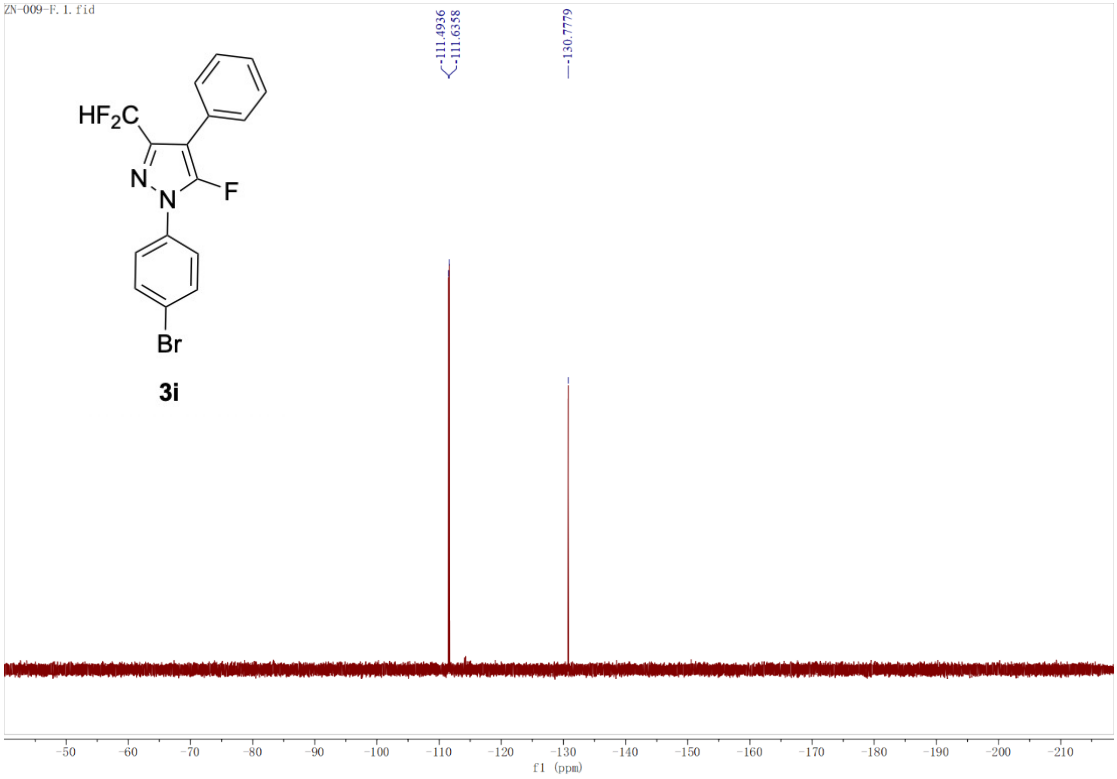


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3h**

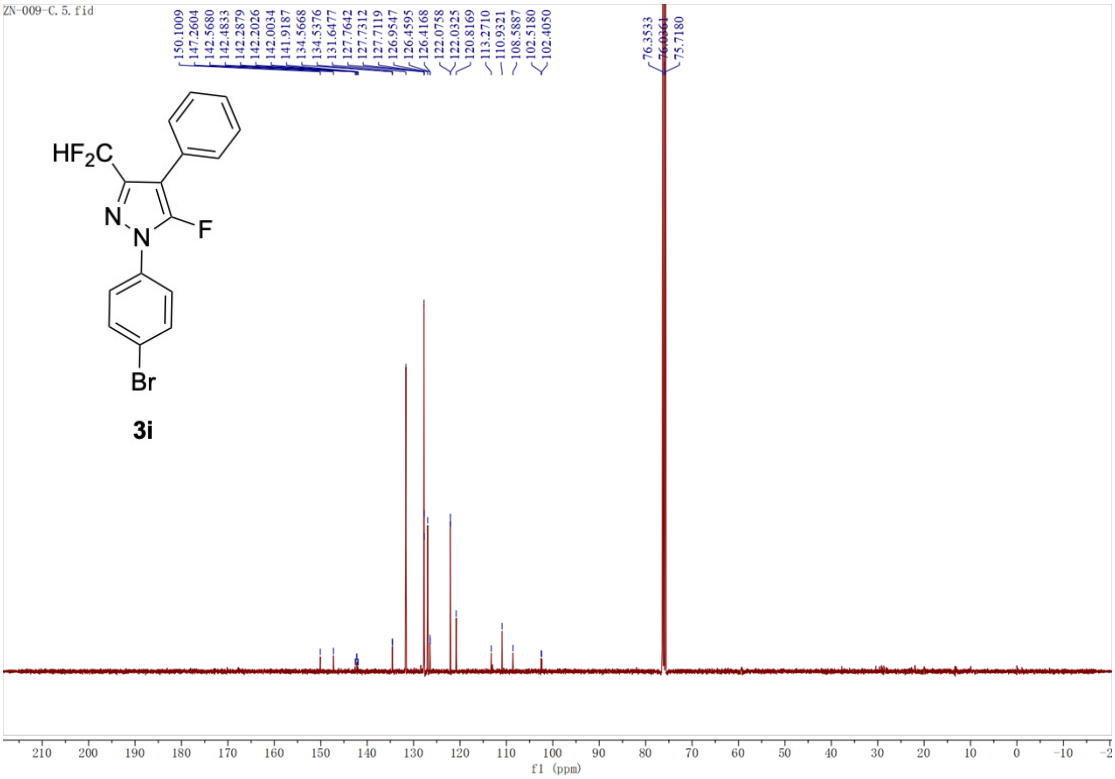
1-(4-Bromophenyl)-3-(difluoromethyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3i)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3i**

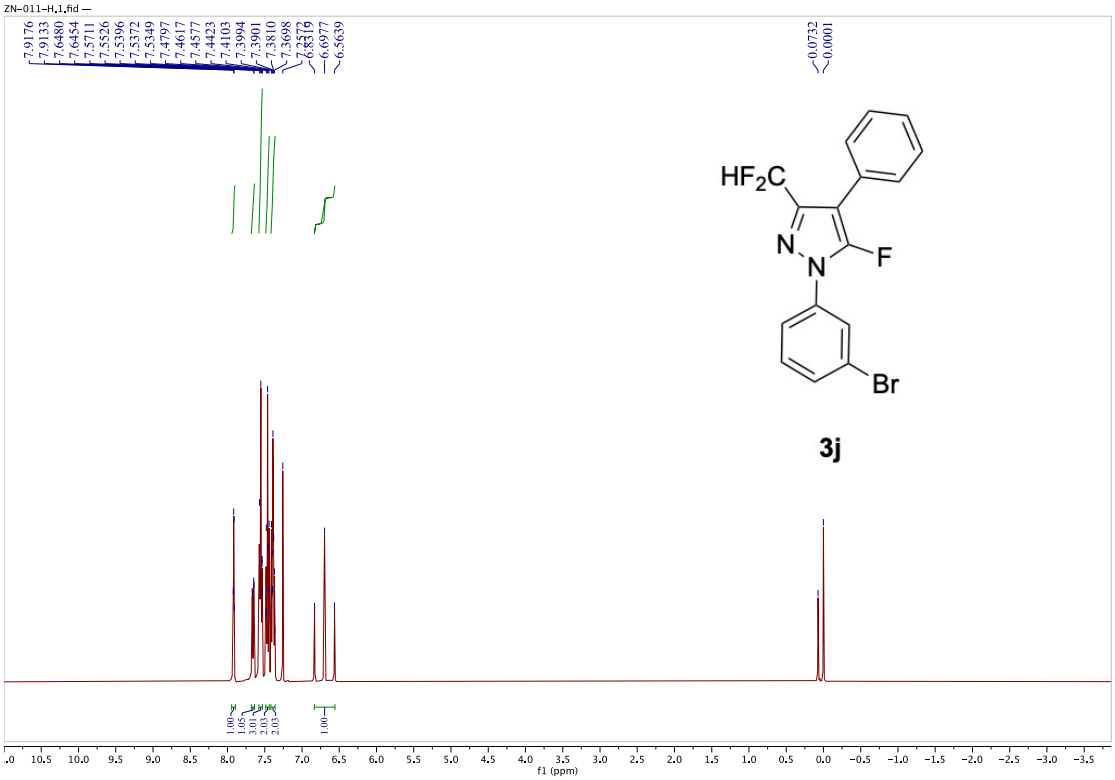


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3i**

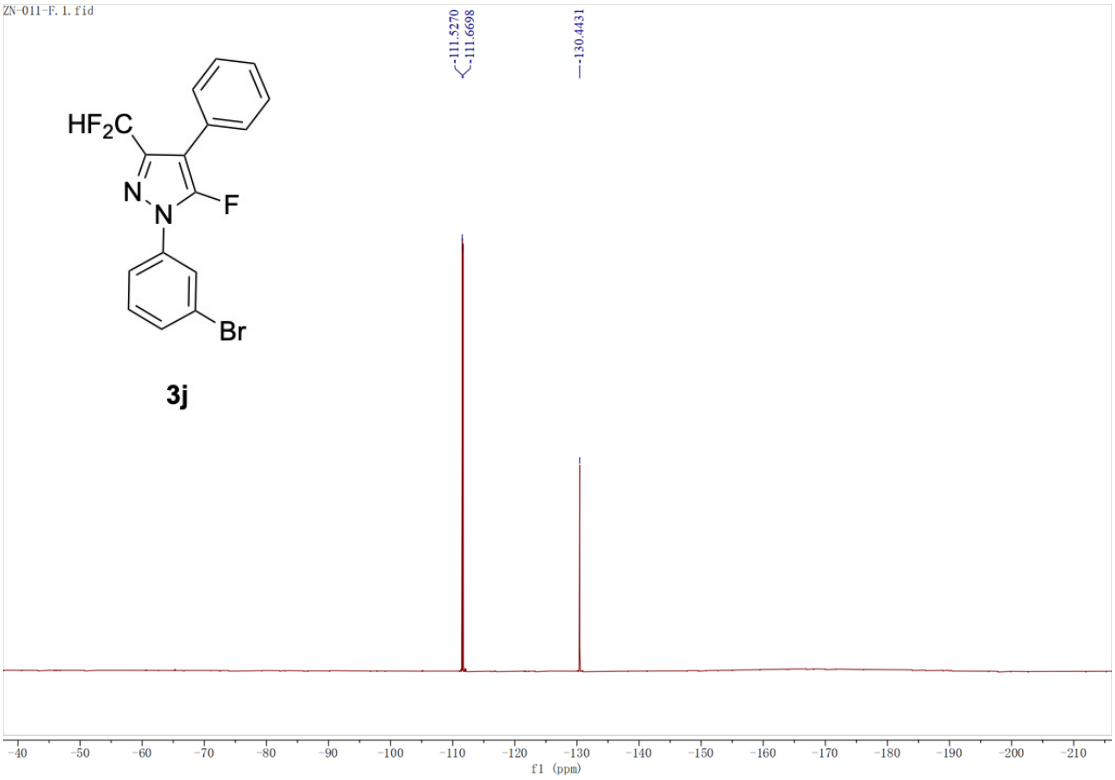


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3i**

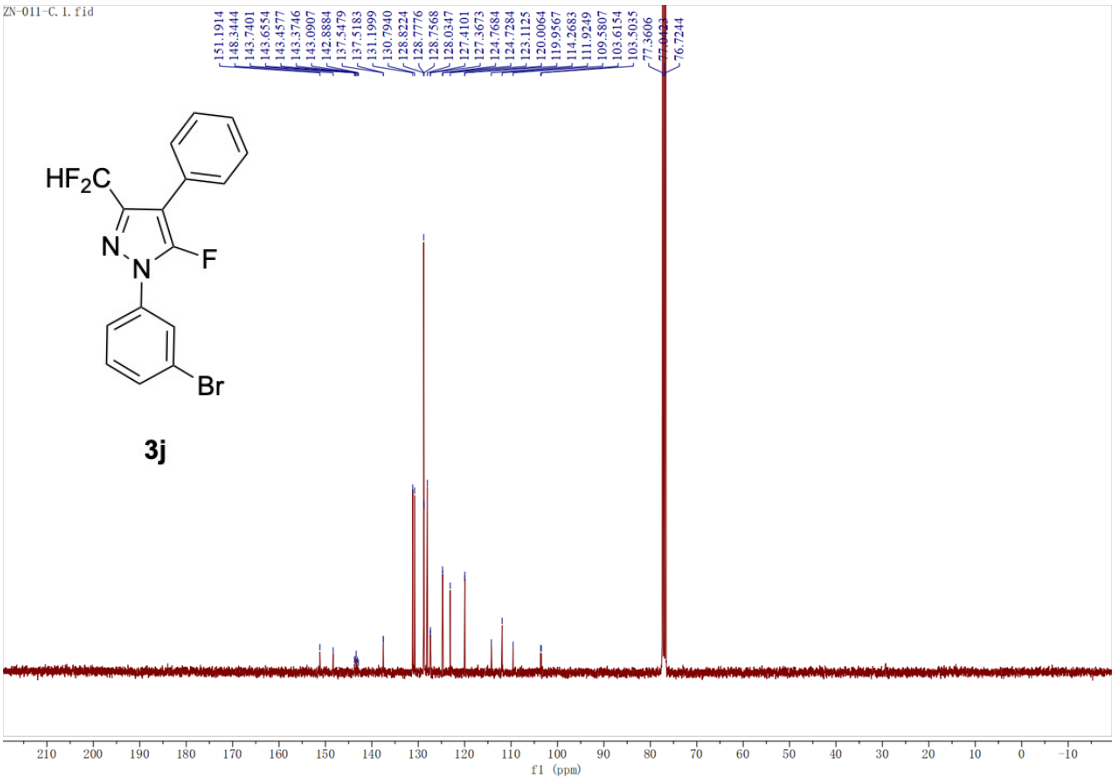
1-(3-Bromophenyl)-3-(difluoromethyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3j)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3j**

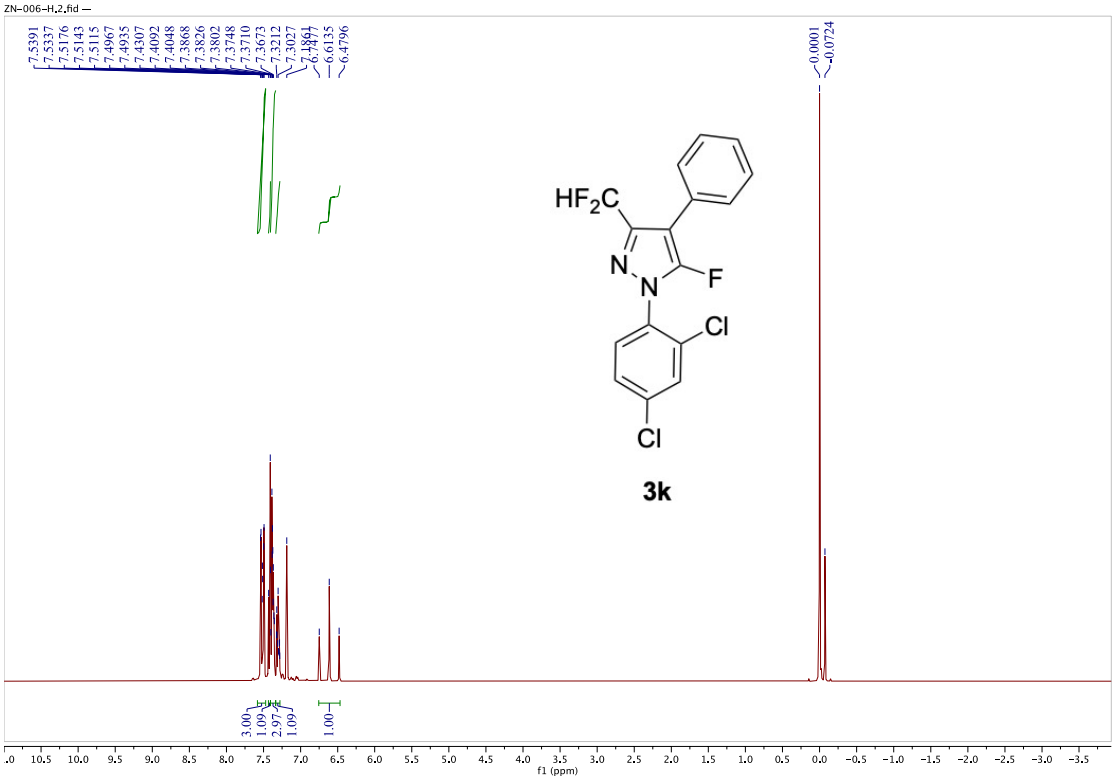


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3j**

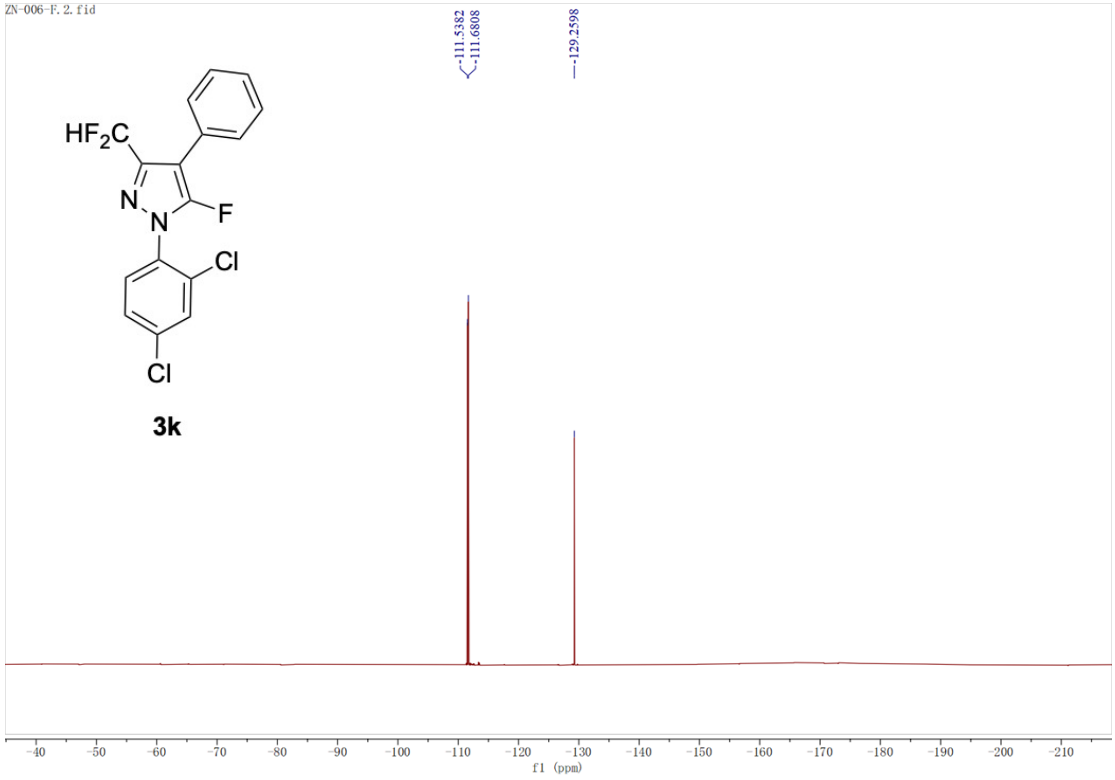


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3j**

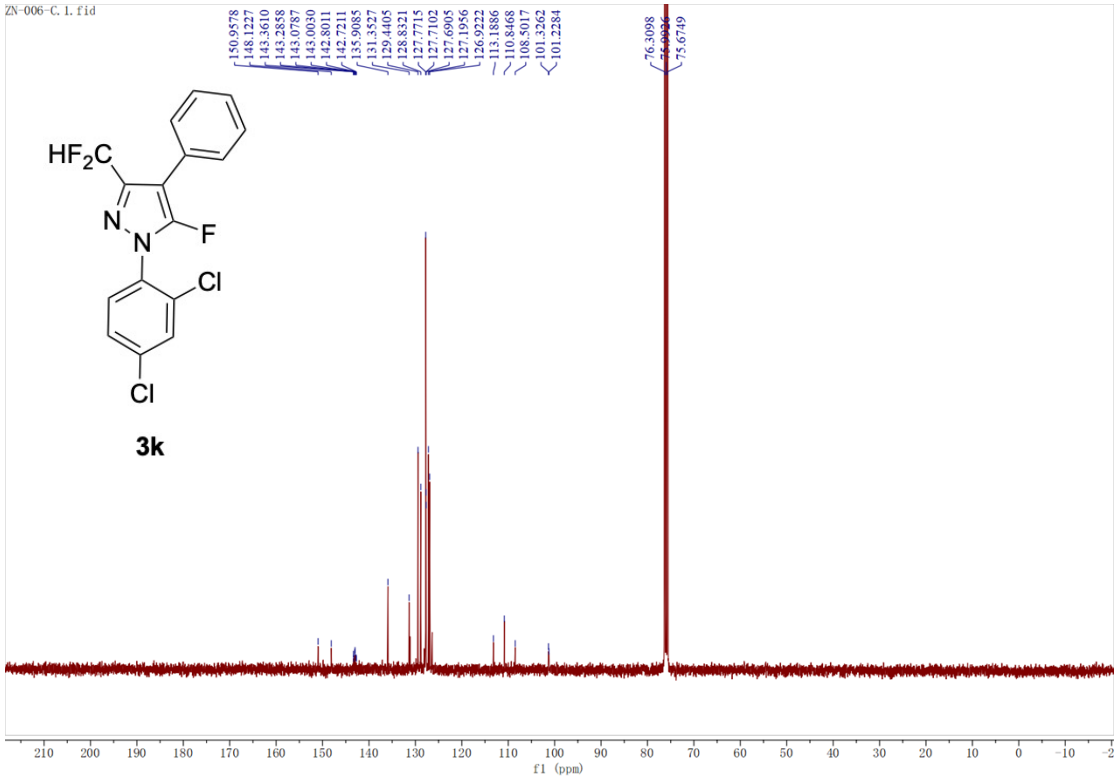
1-(2,4-Dichlorophenyl)-3-(difluoromethyl)-5-fluoro-4-phenyl-1*H*-pyrazole (3k)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3k**

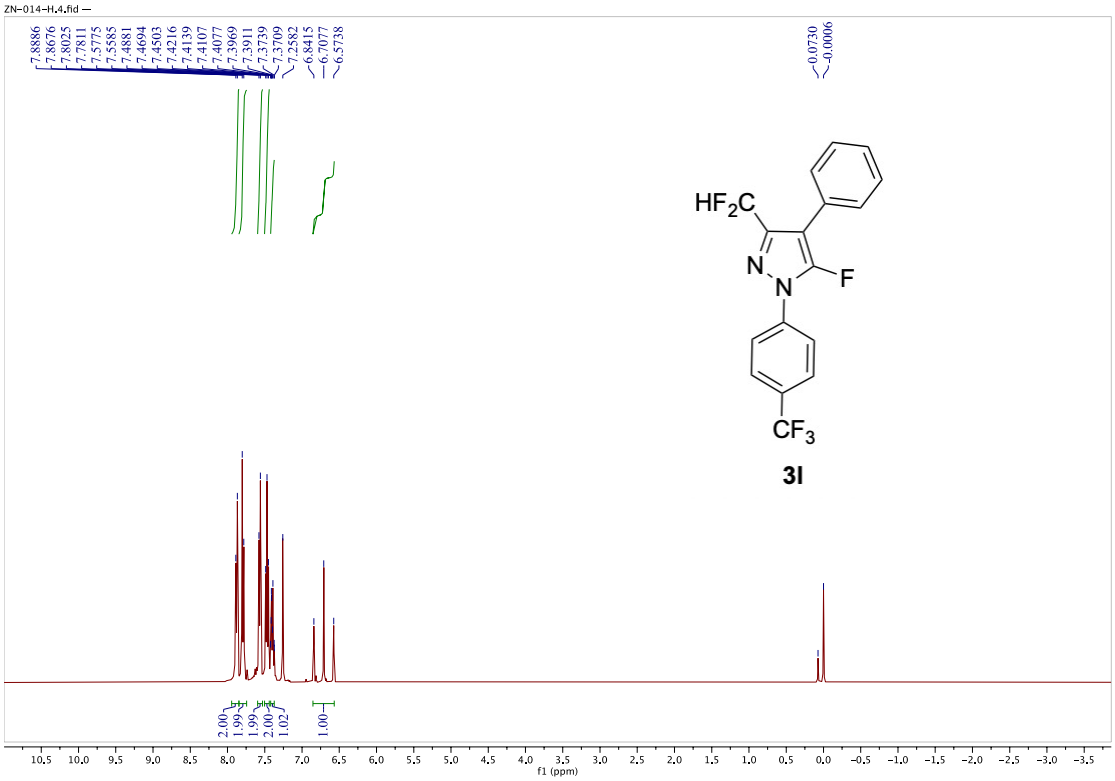


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3k**

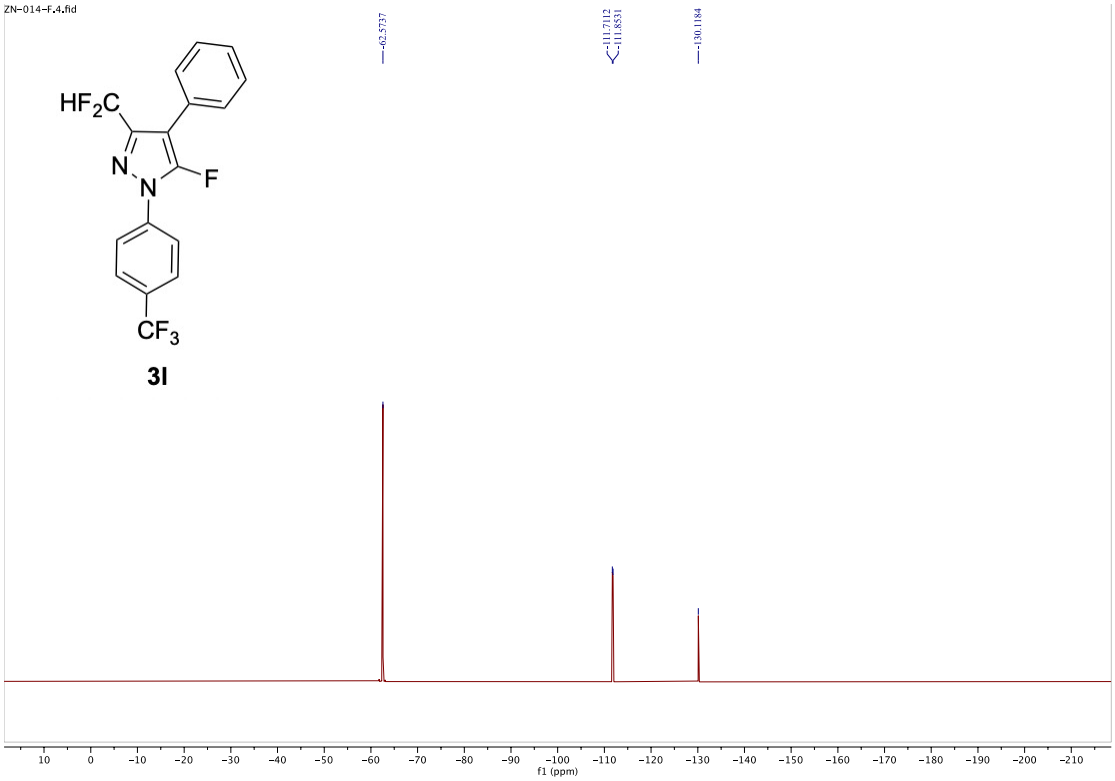


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3k**

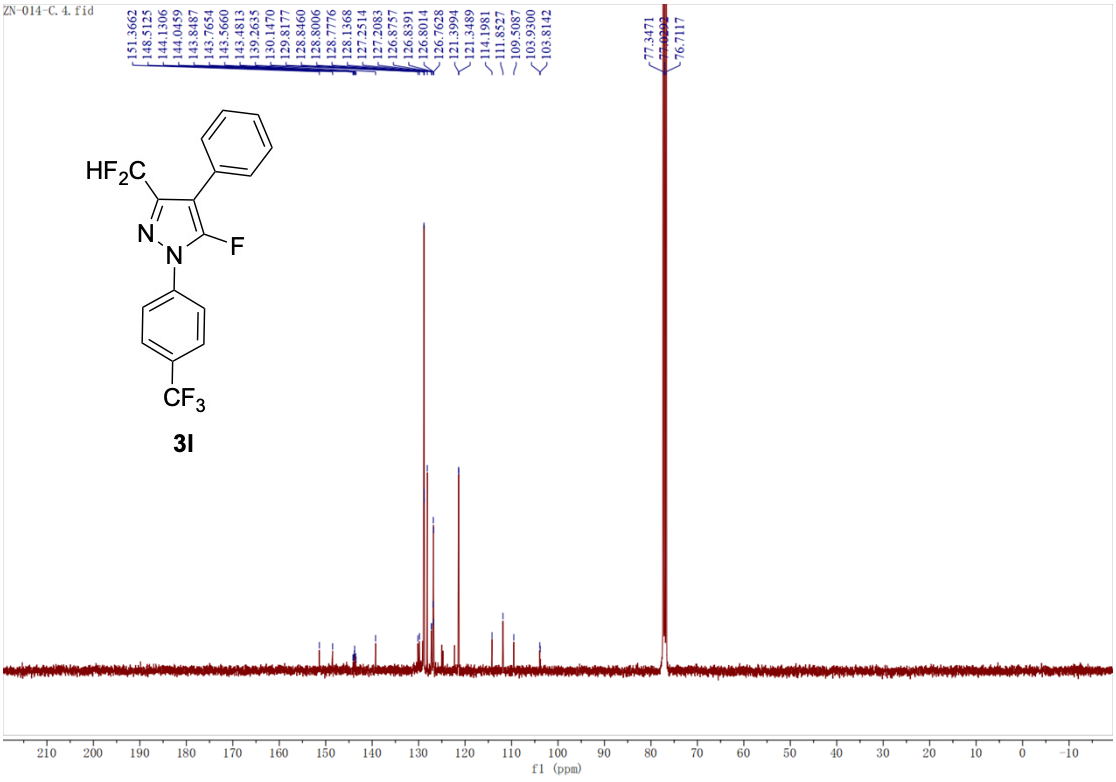
3-(Difluoromethyl)-5-fluoro-4-phenyl-1-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (3l)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3l**

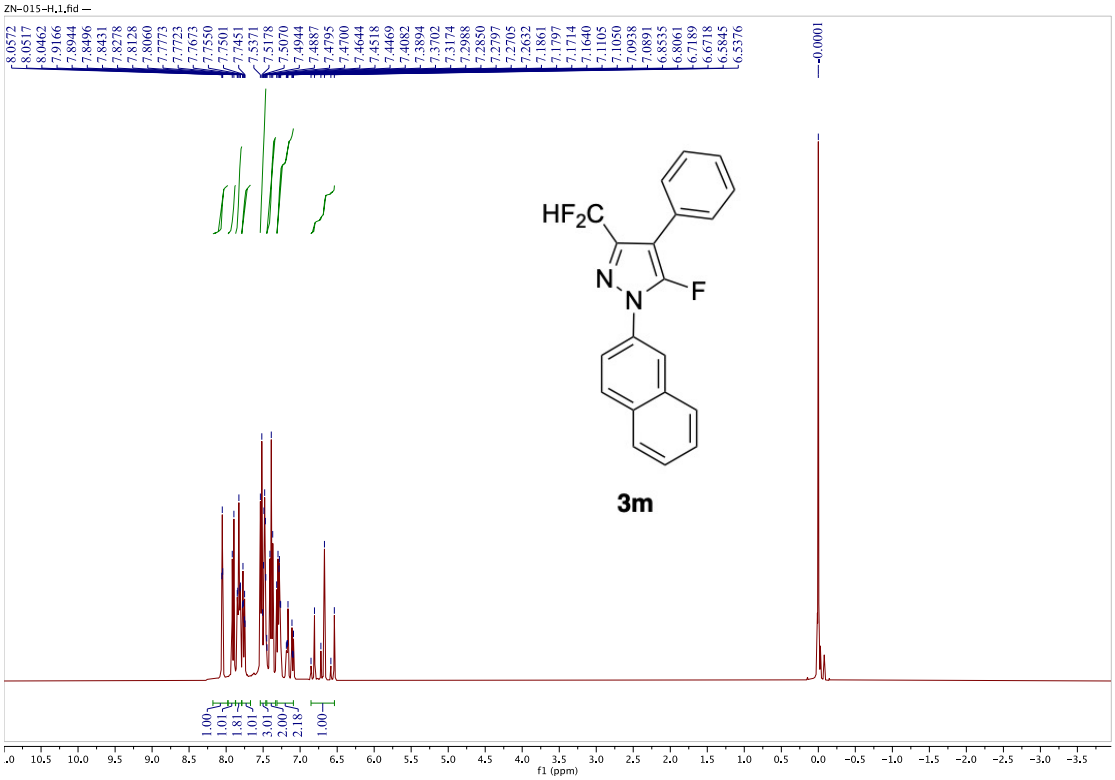


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3l**

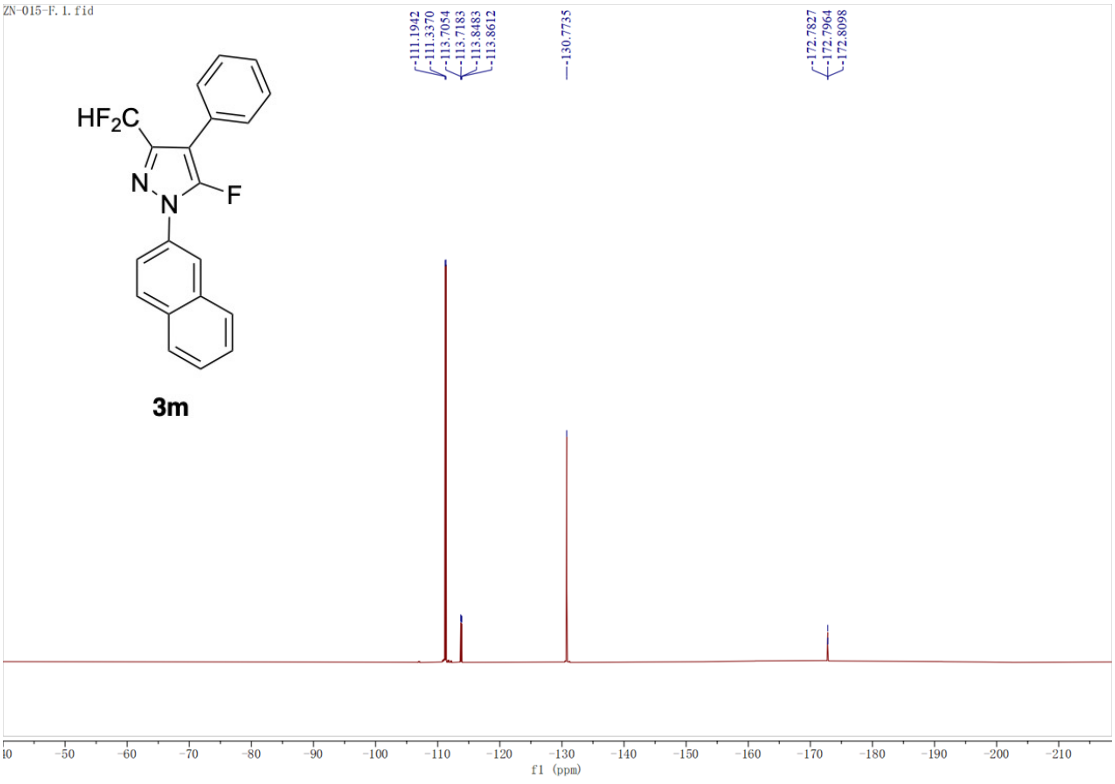


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3l**

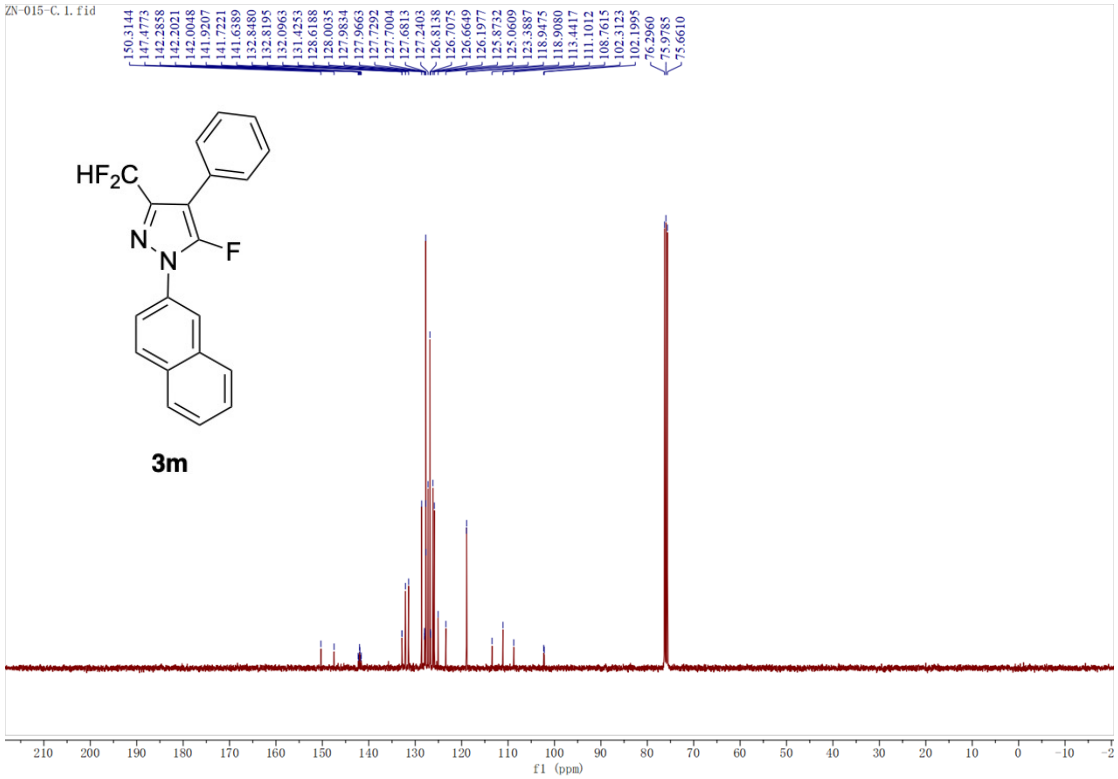
3-(Difluoromethyl)-5-fluoro-1-(naphthalen-2-yl)-4-phenyl-1*H*-pyrazole (3m)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3m**

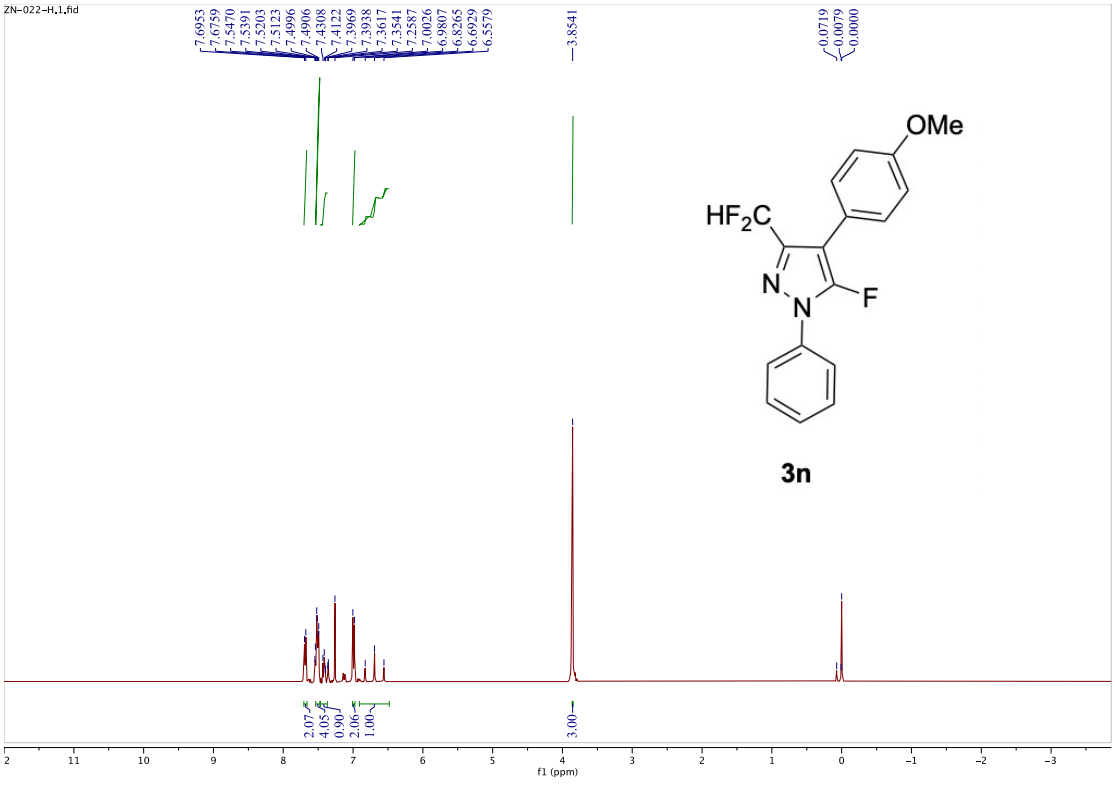


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3m**

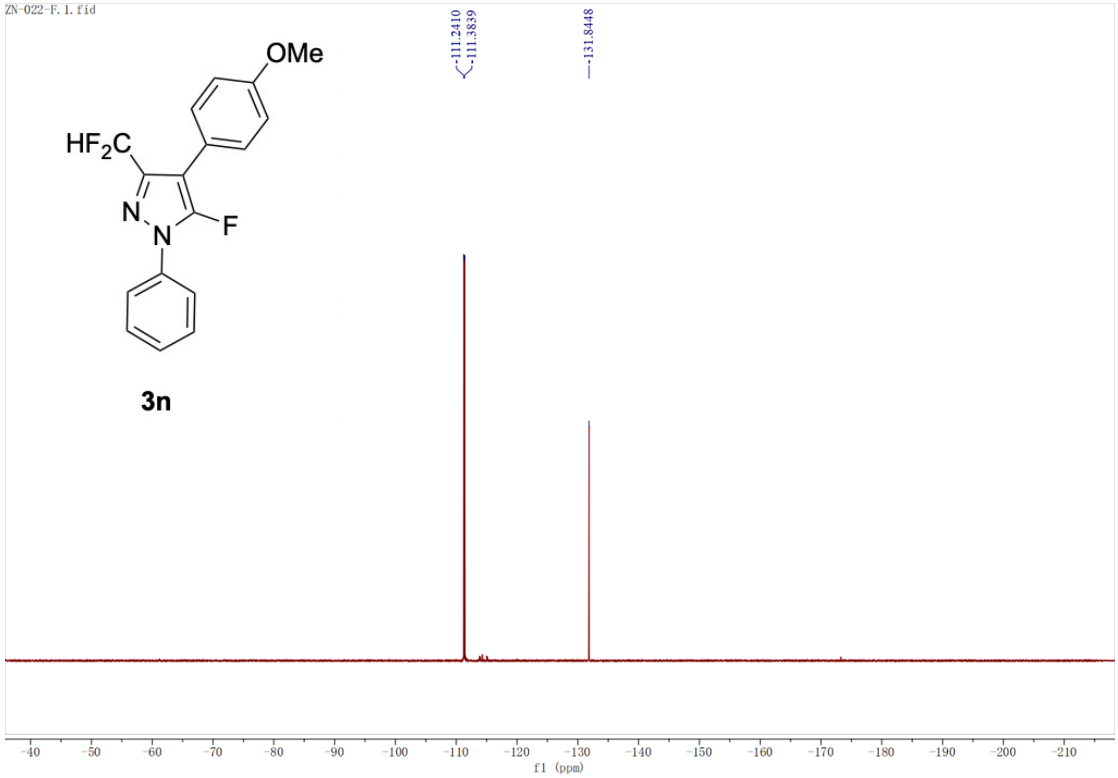


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3m**

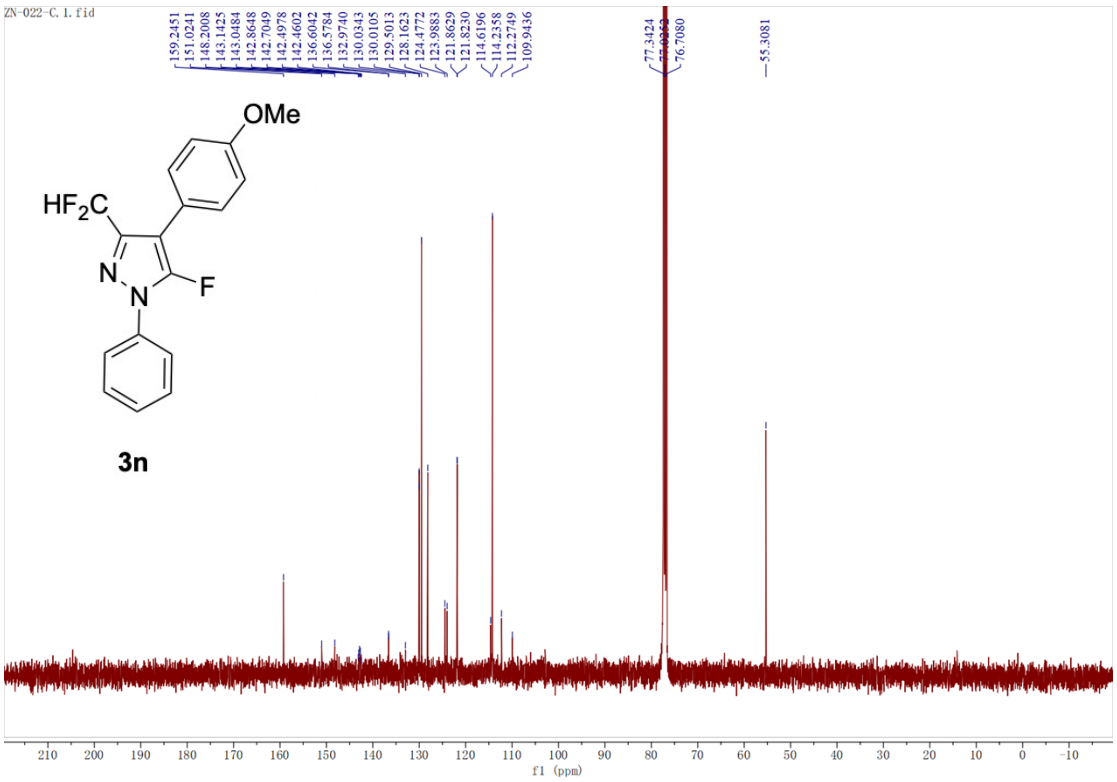
3-(Difluoromethyl)-5-fluoro-4-(4-methoxyphenyl)-1-phenyl-1*H*-pyrazole (3n)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3n**

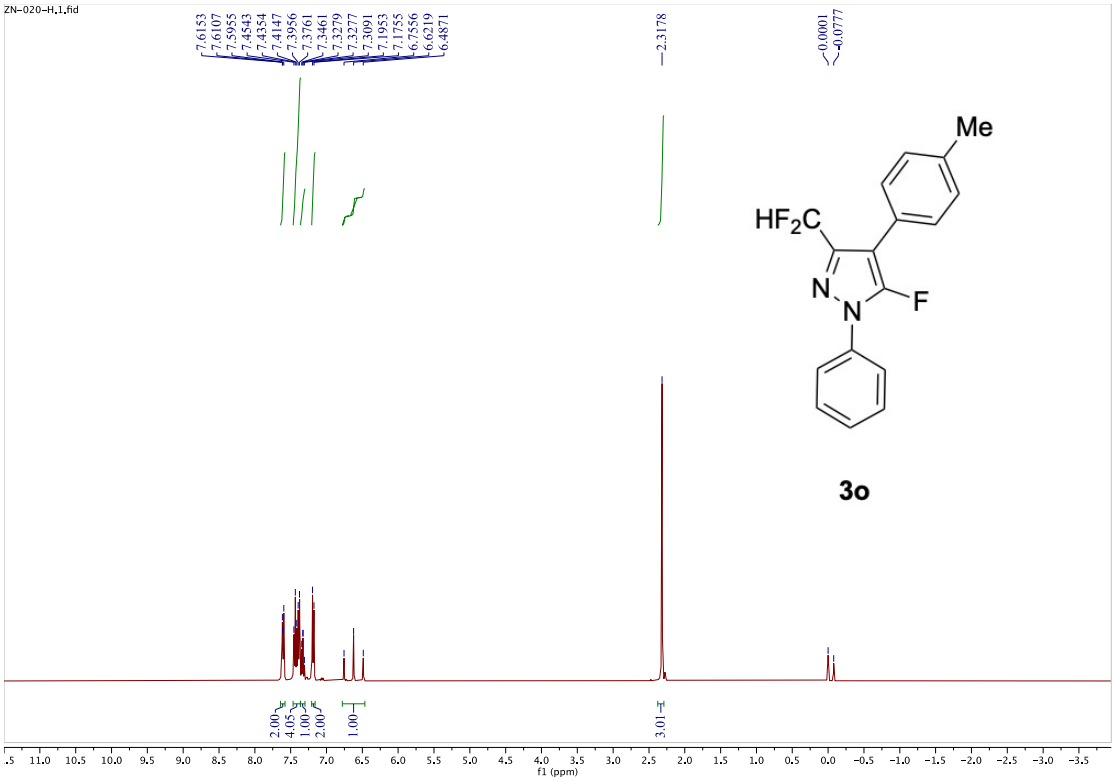


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3n**

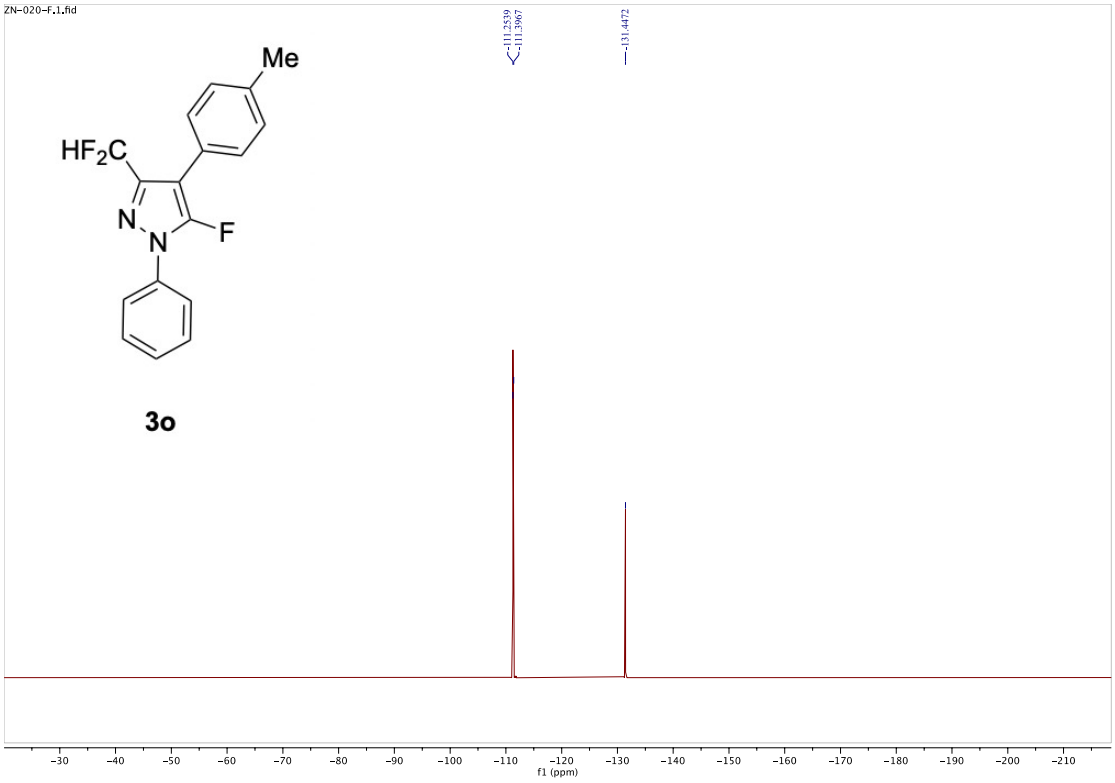


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3n**

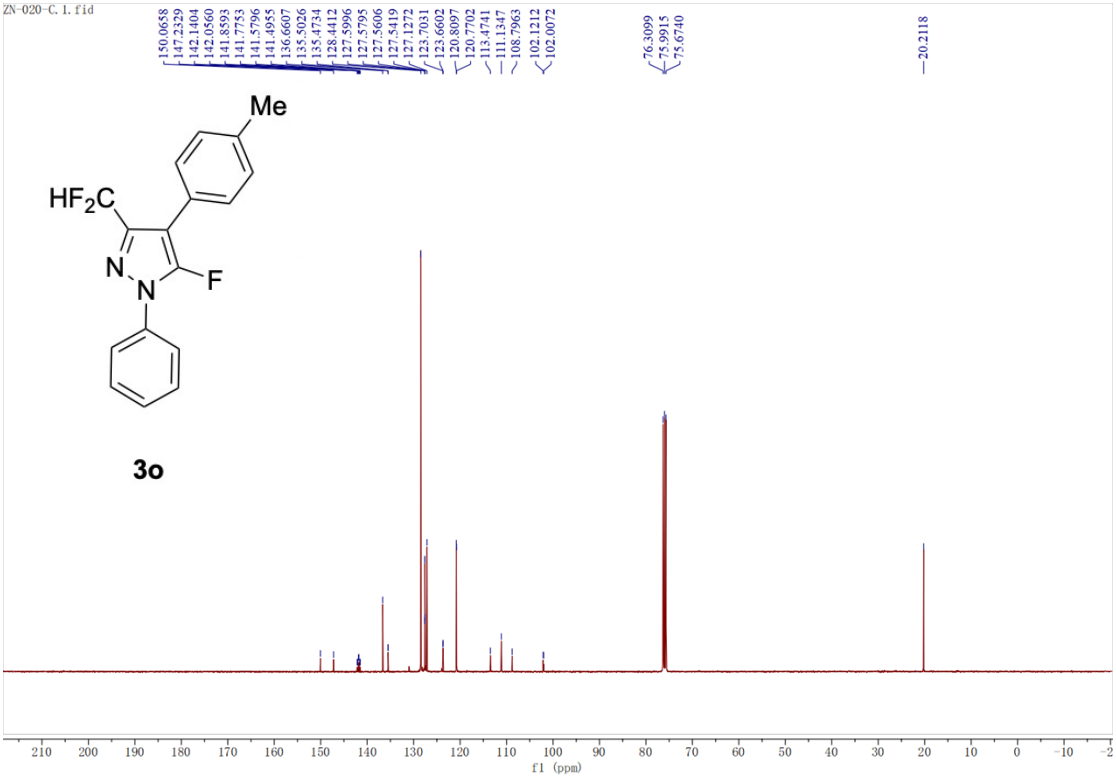
3-(Difluoromethyl)-5-fluoro-1-phenyl-4-(*p*-tolyl)-1*H*-pyrazole (3o)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3o**

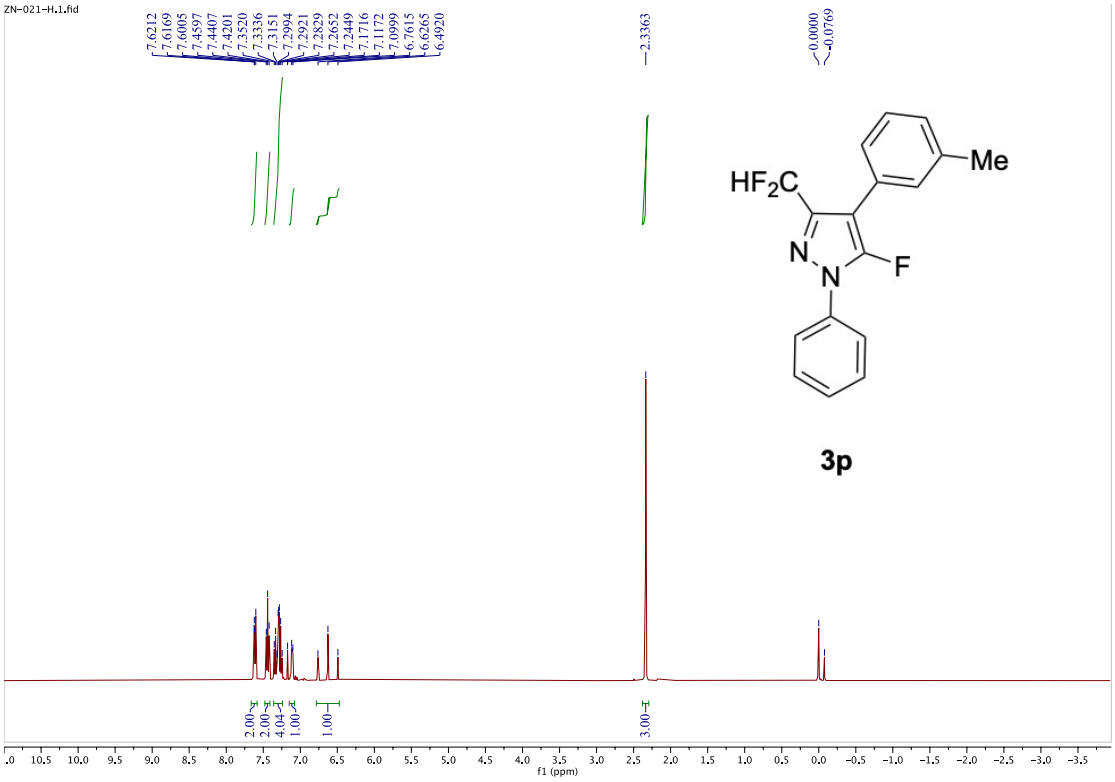


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3o**

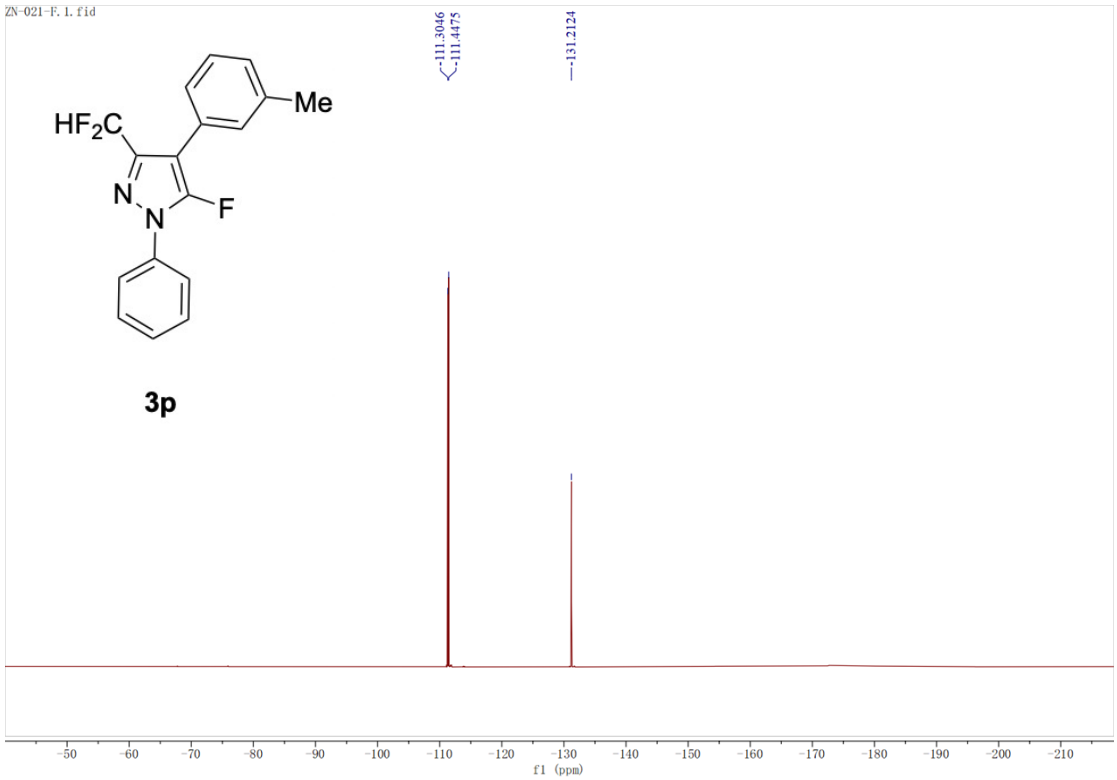


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3o**

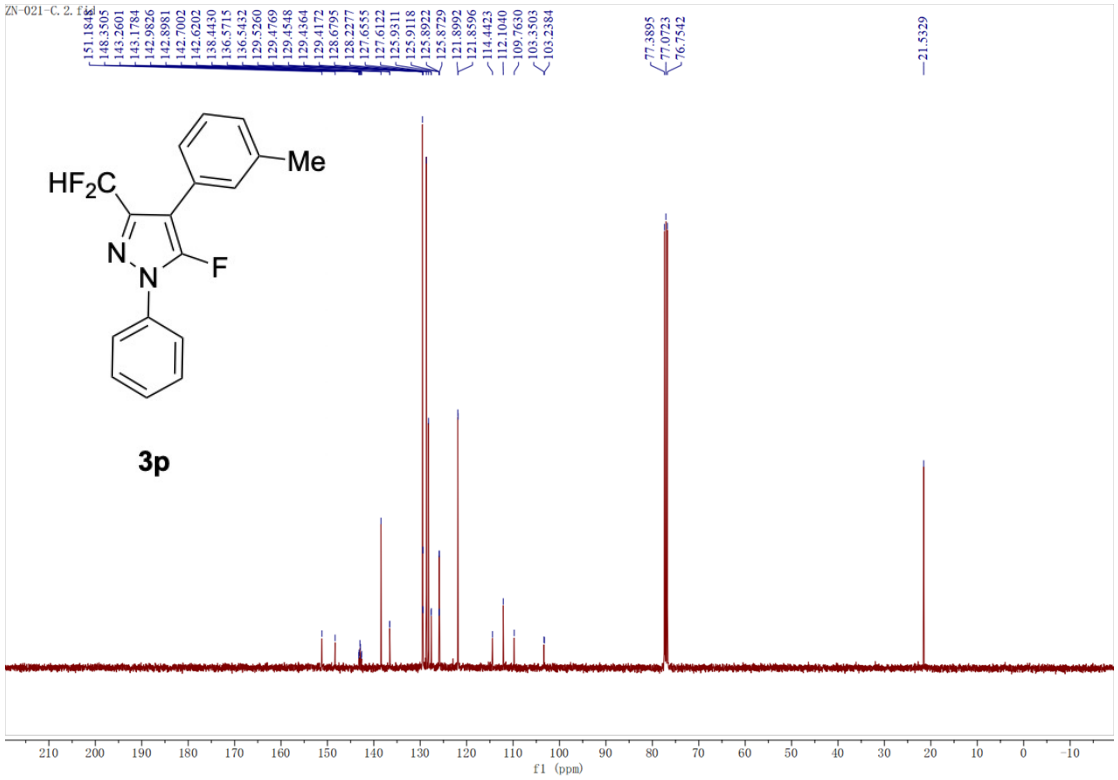
3-(Difluoromethyl)-5-fluoro-1-phenyl-4-(*m*-tolyl)-1*H*-pyrazole (3p)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3p**

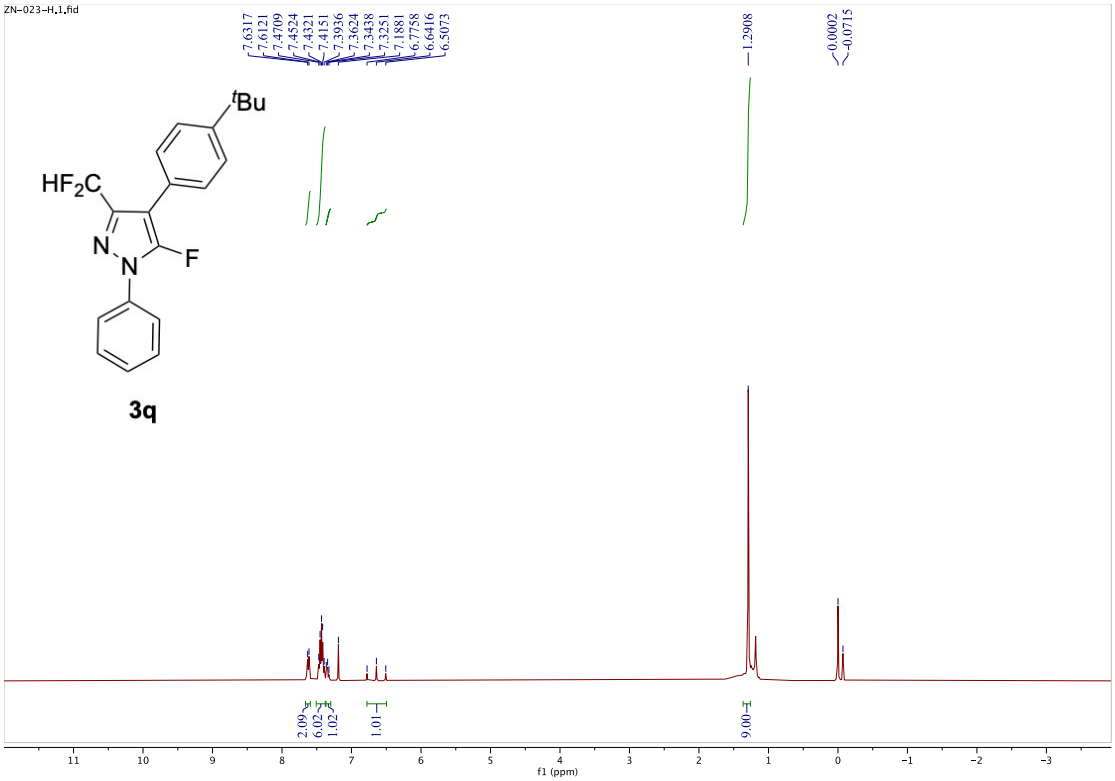


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3p**

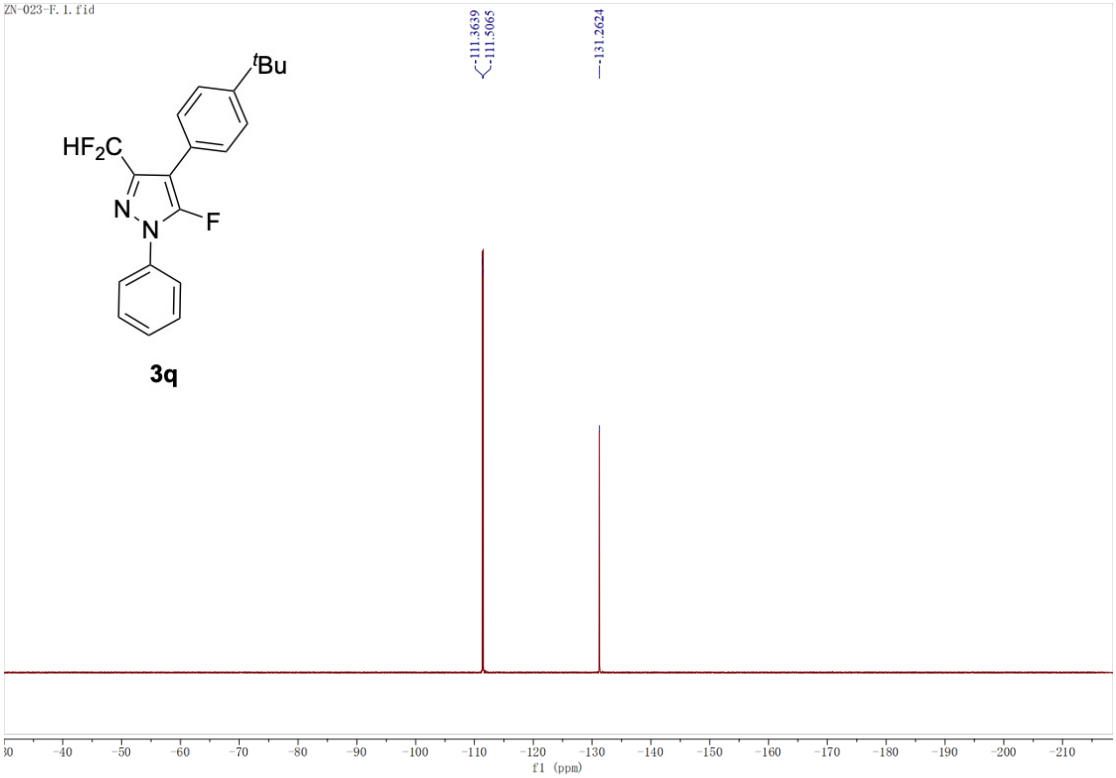


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3p**

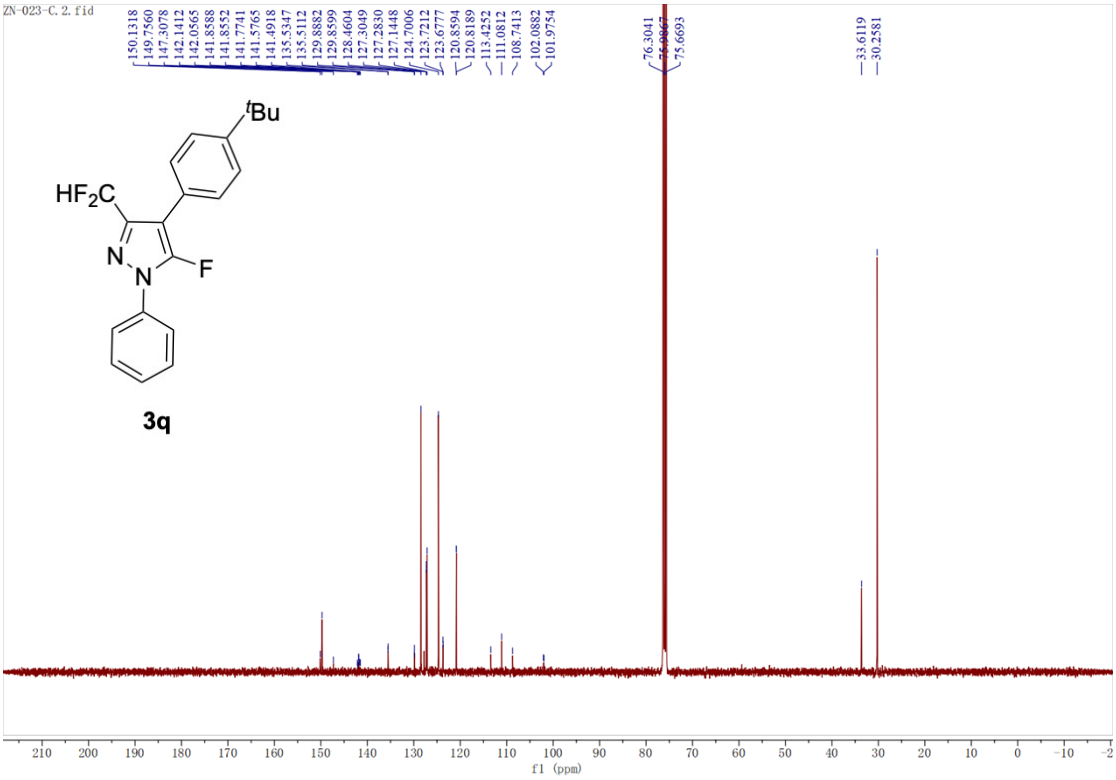
4-(4-(*tert*-Butyl)phenyl)-3-(difluoromethyl)-5-fluoro-1-phenyl-1*H*-pyrazole (3q)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3q**

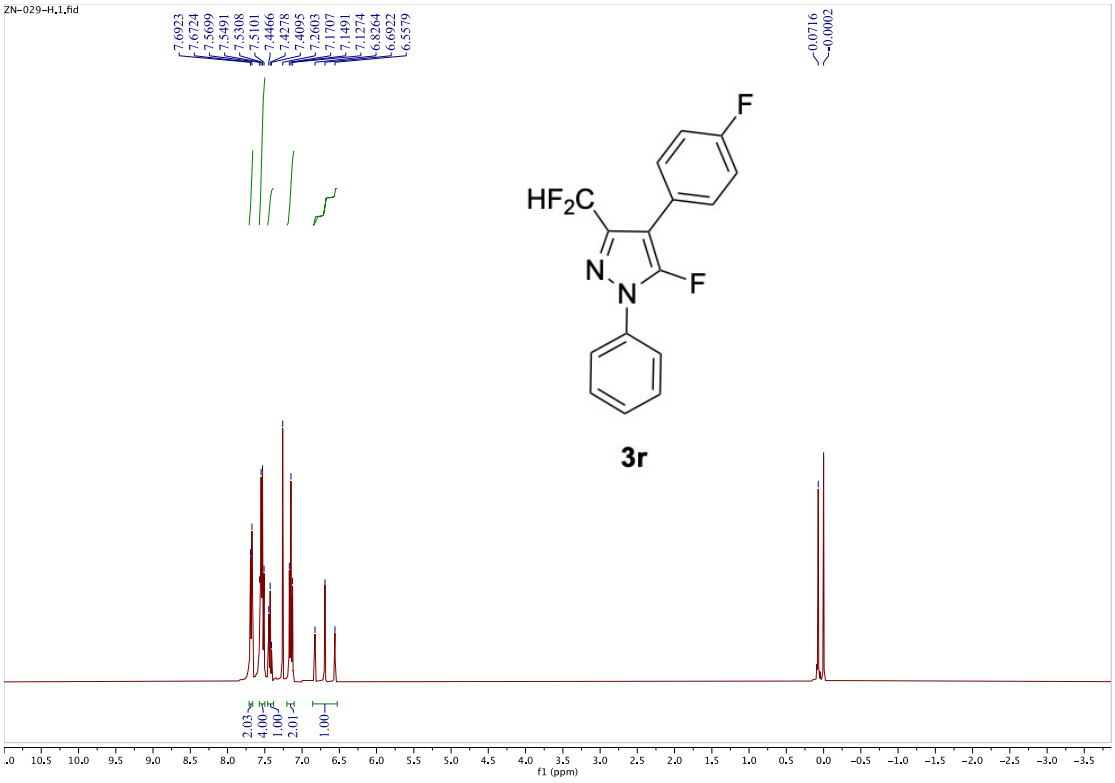


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3q**

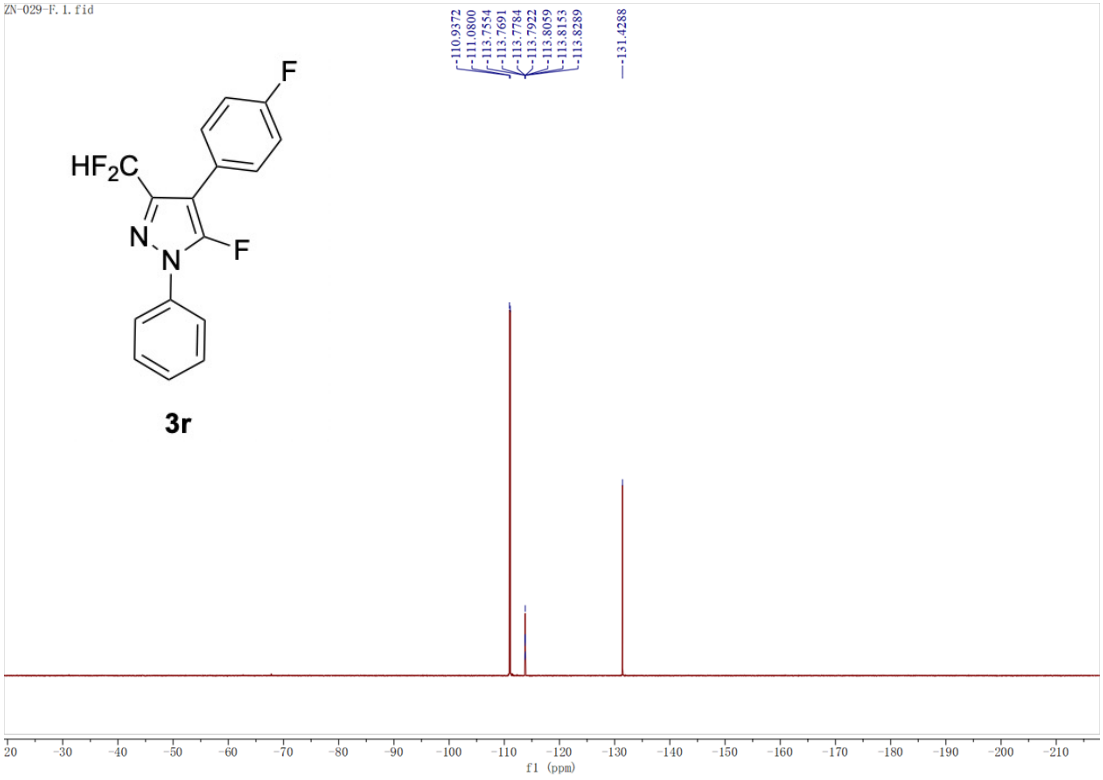


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3q**

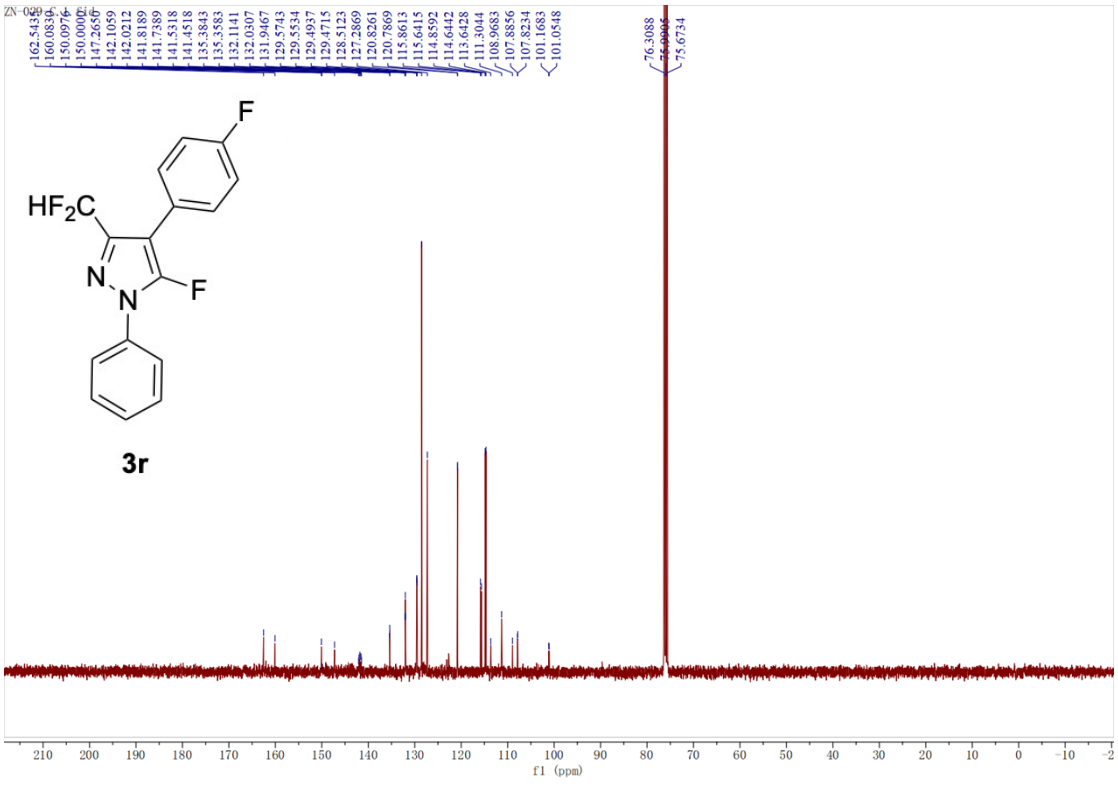
3-(Difluoromethyl)-5-fluoro-4-(4-fluorophenyl)-1-phenyl-1*H*-pyrazole (3r)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3r**

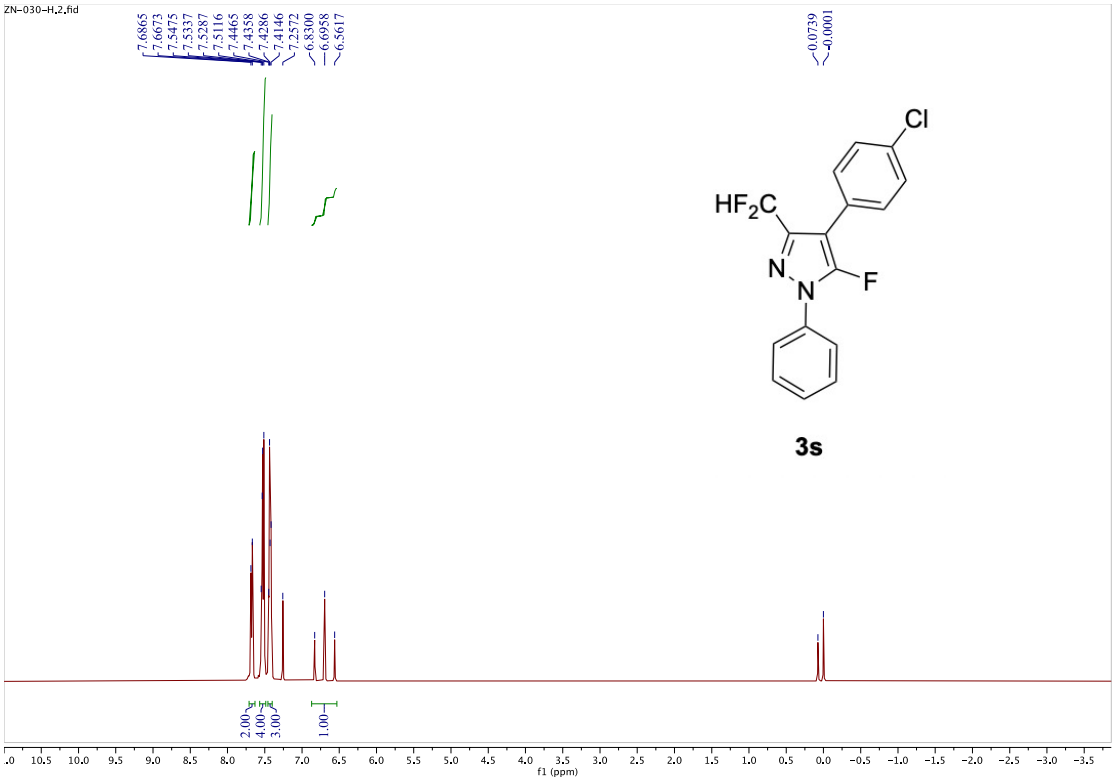


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3r**

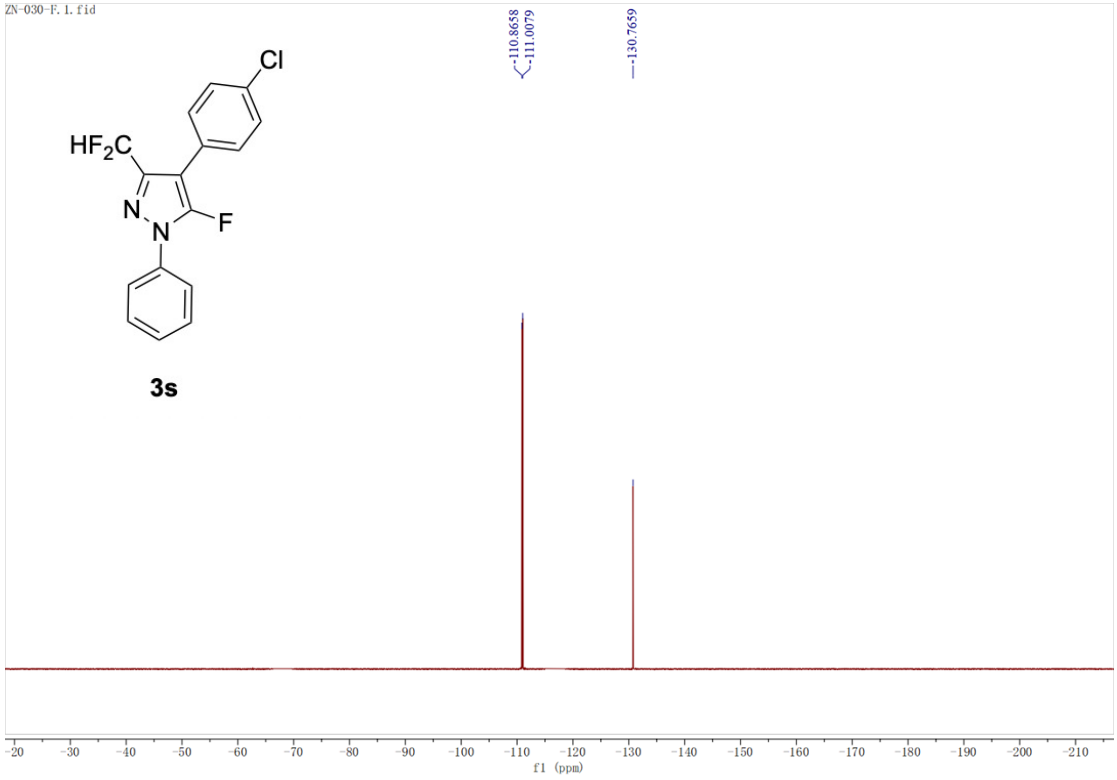


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3r**

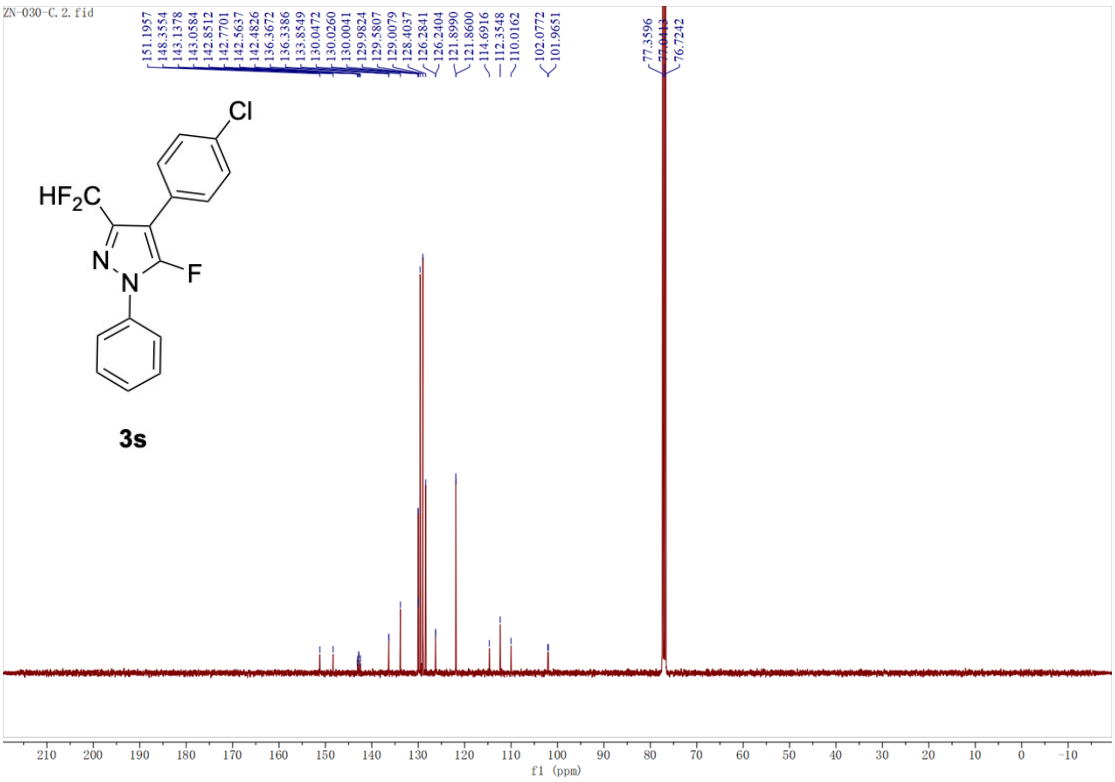
4-(4-Chlorophenyl)-3-(difluoromethyl)-5-fluoro-1-phenyl-1*H*-pyrazole (3s)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3s**

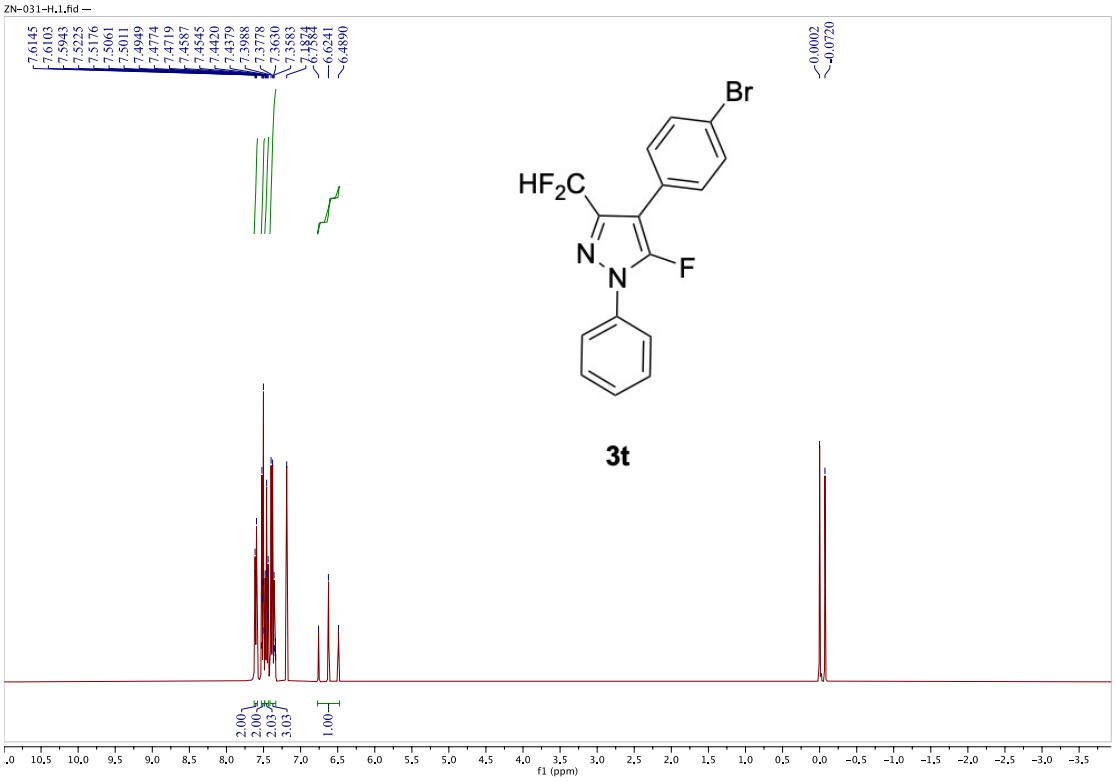


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3s**

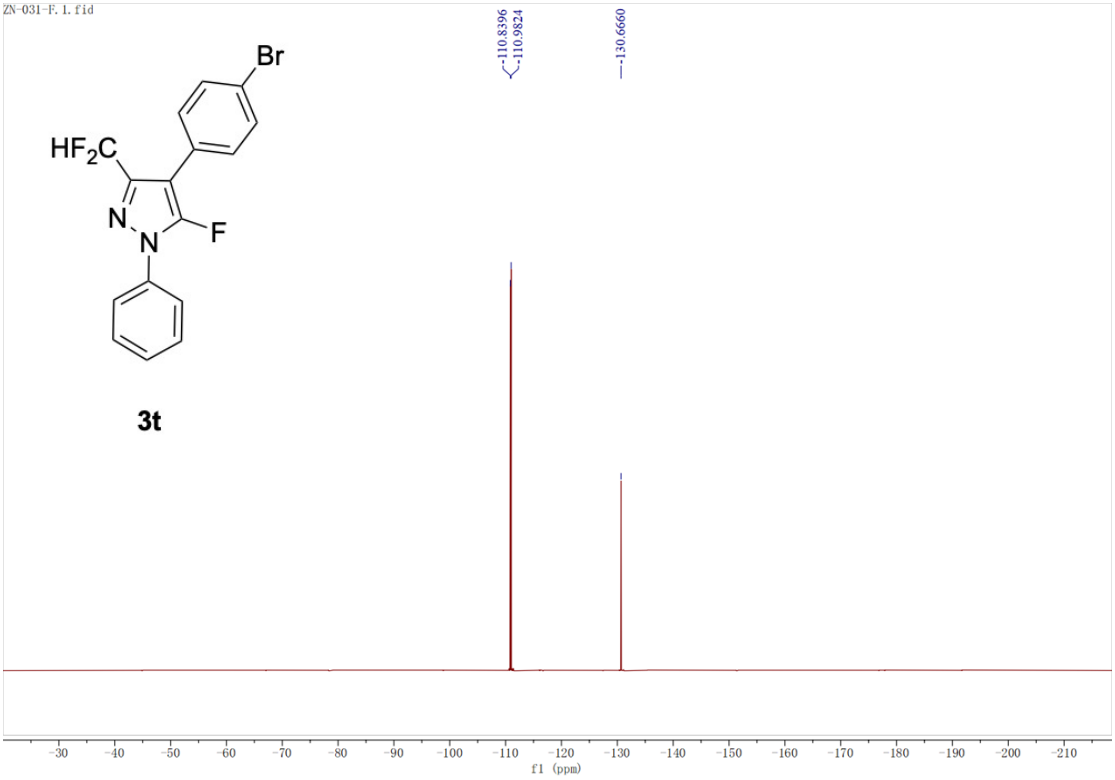


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3s**

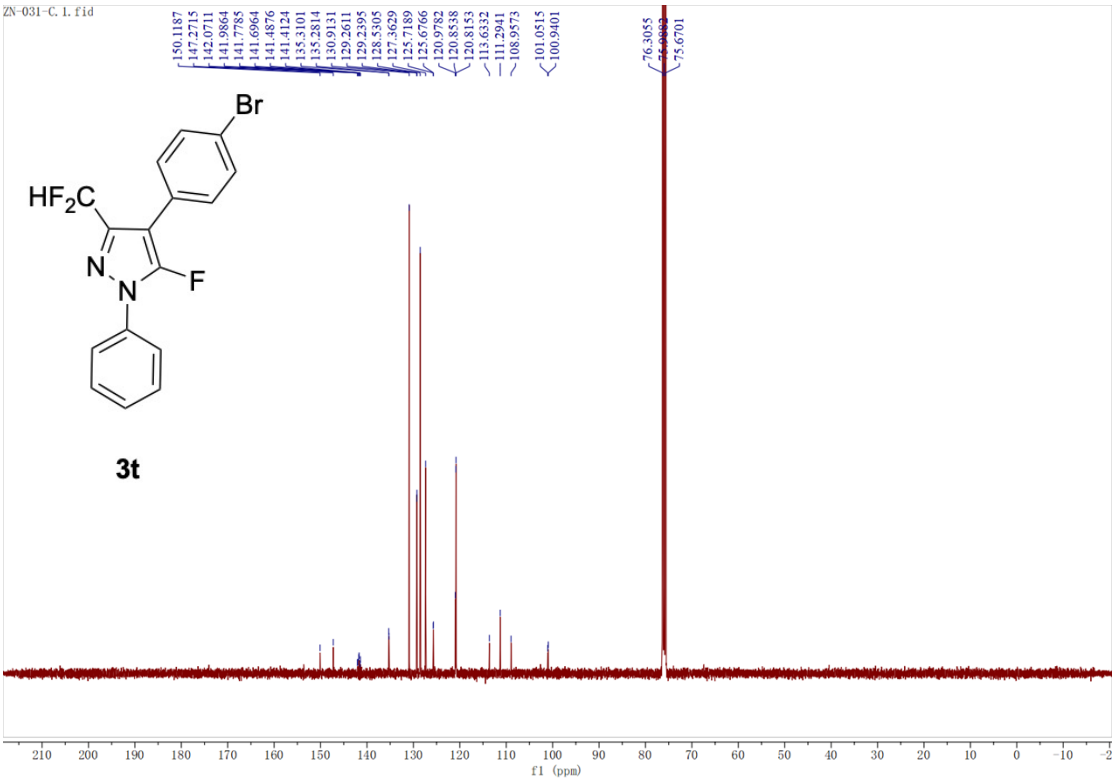
4-(4-Bromophenyl)-3-(difluoromethyl)-5-fluoro-1-phenyl-1*H*-pyrazole (3t)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3t**

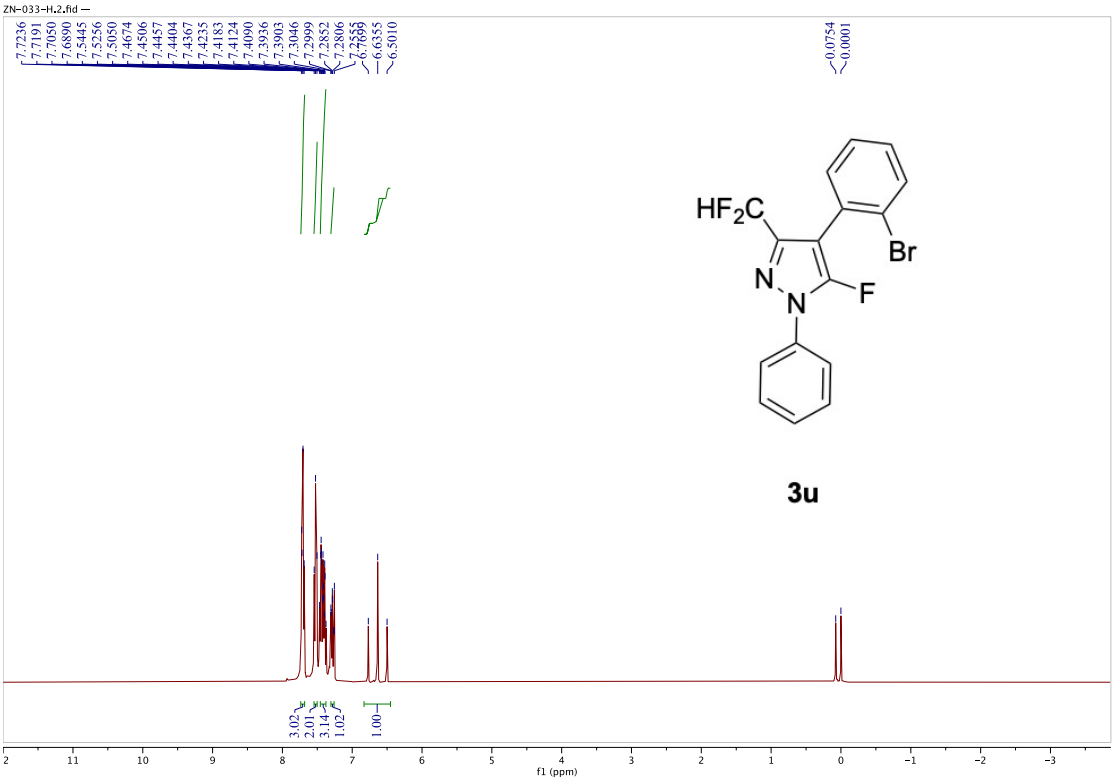


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3t**

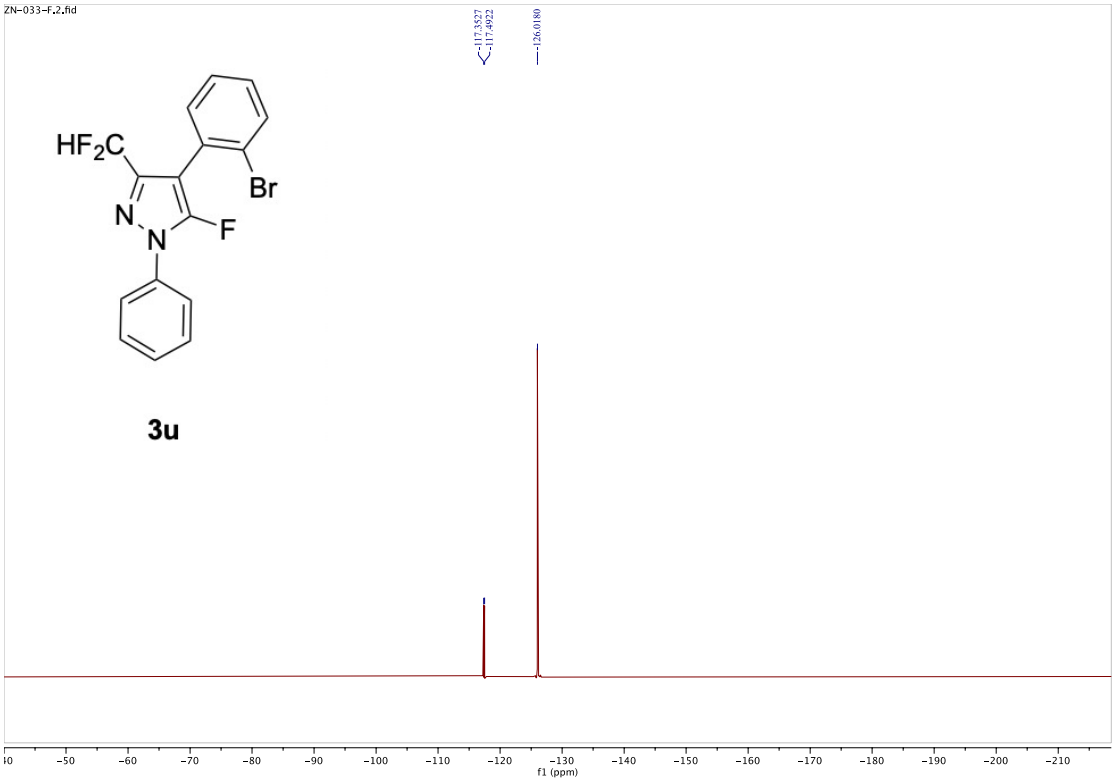


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3t**

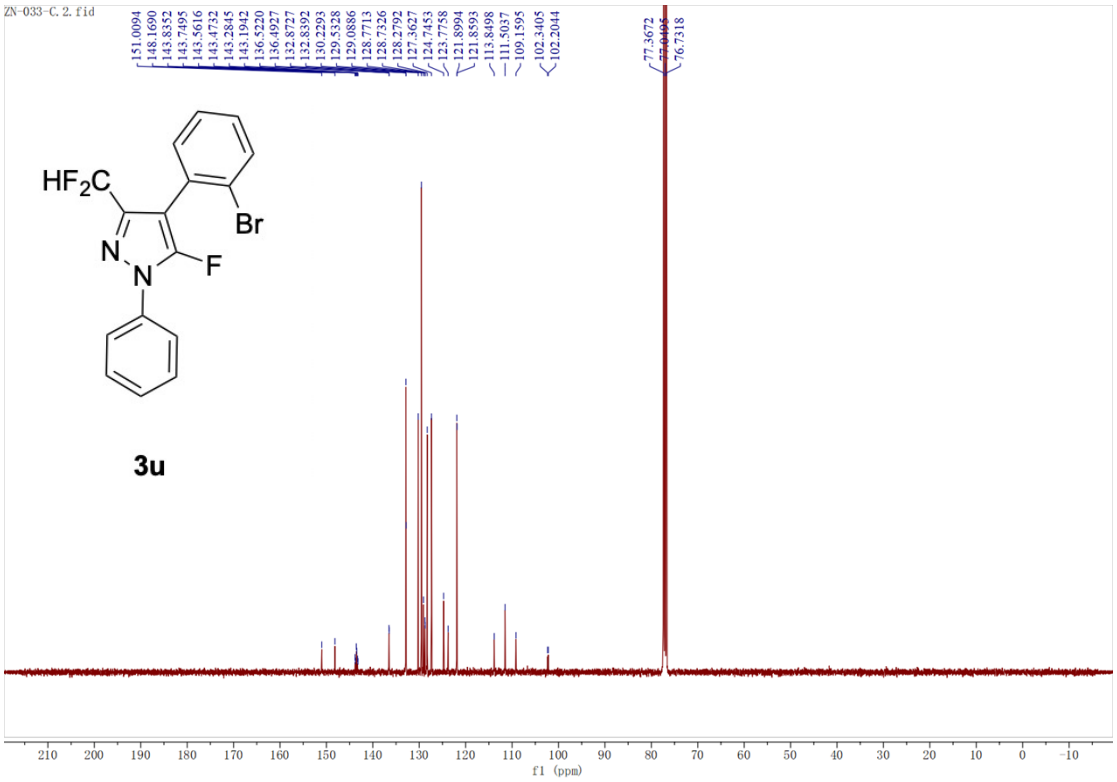
4-(2-Bromophenyl)-3-(difluoromethyl)-5-fluoro-1-phenyl-1*H*-pyrazole (3u)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3u**

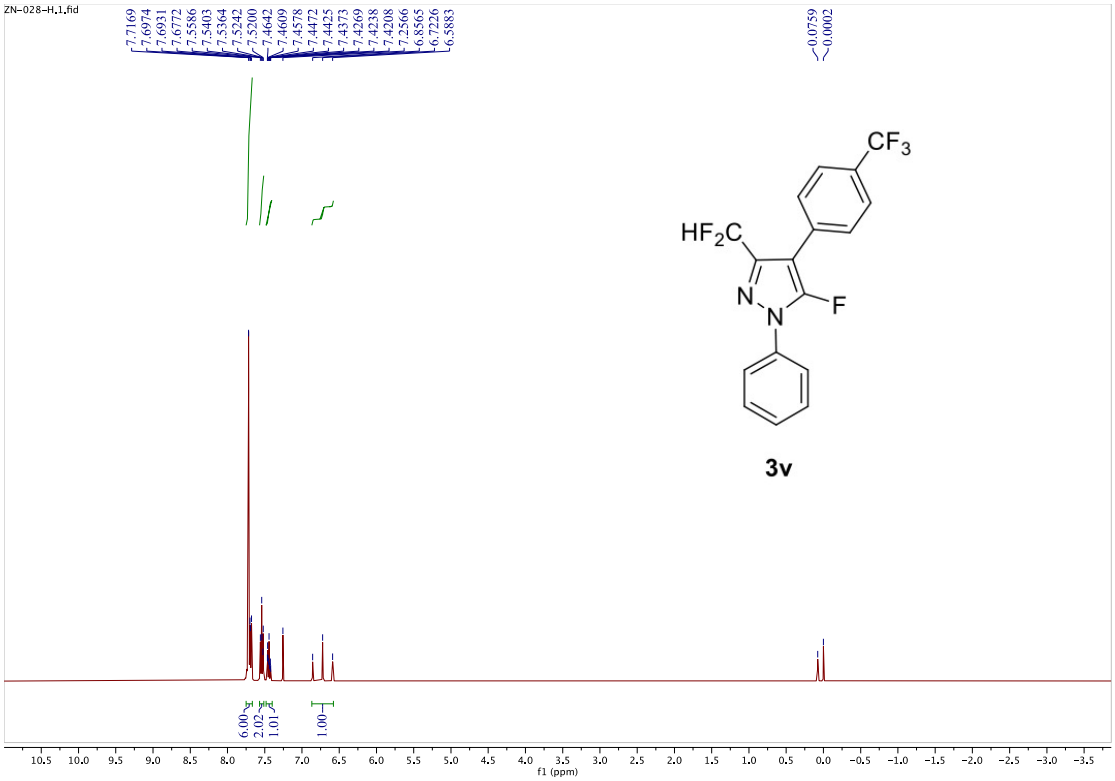


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3u**

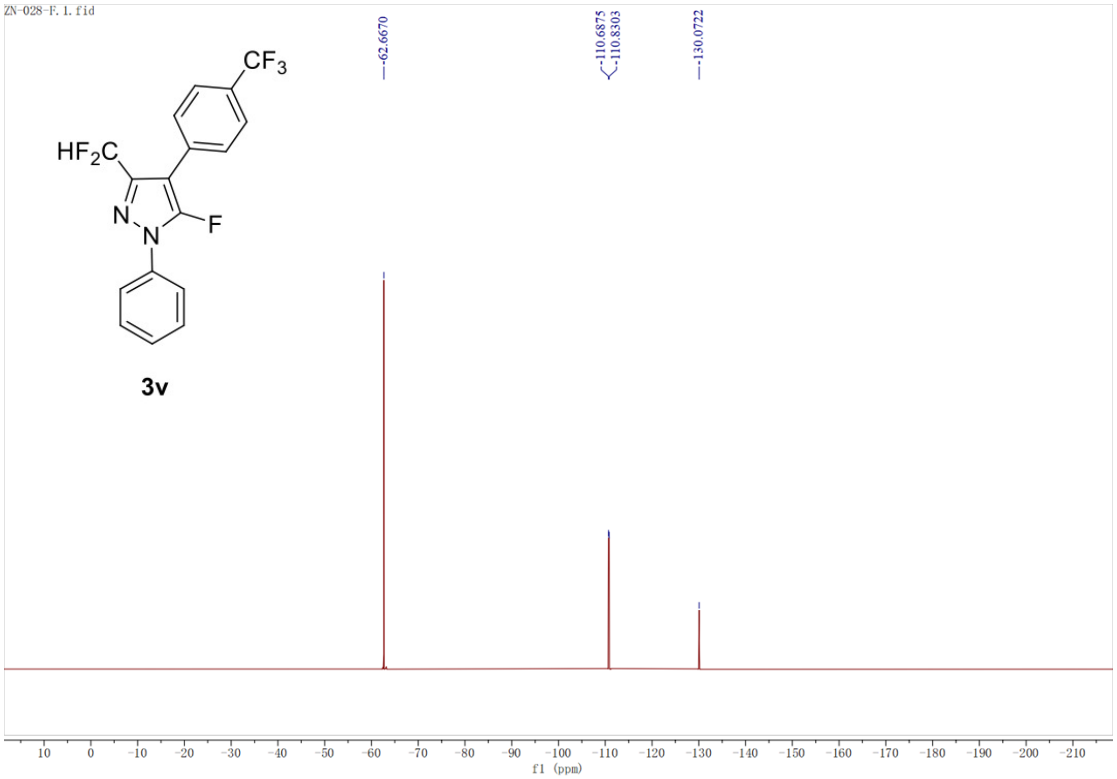


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3u**

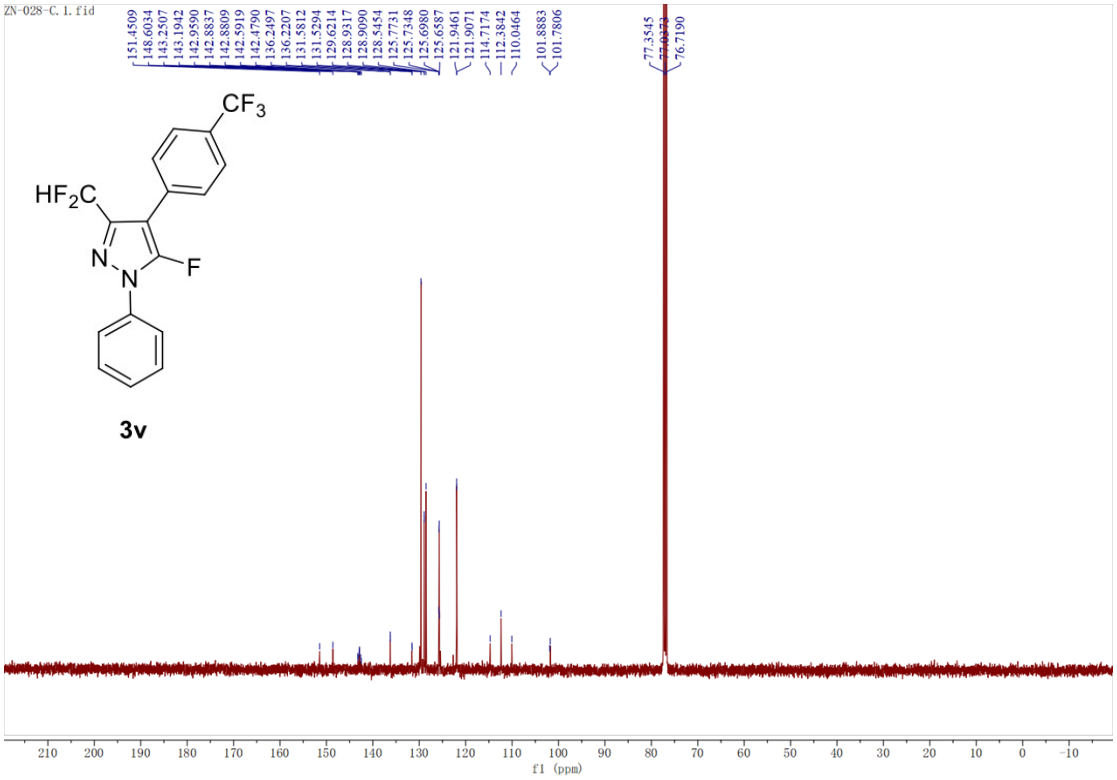
3-(Difluoromethyl)-5-fluoro-1-phenyl-4-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (3v)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3v**

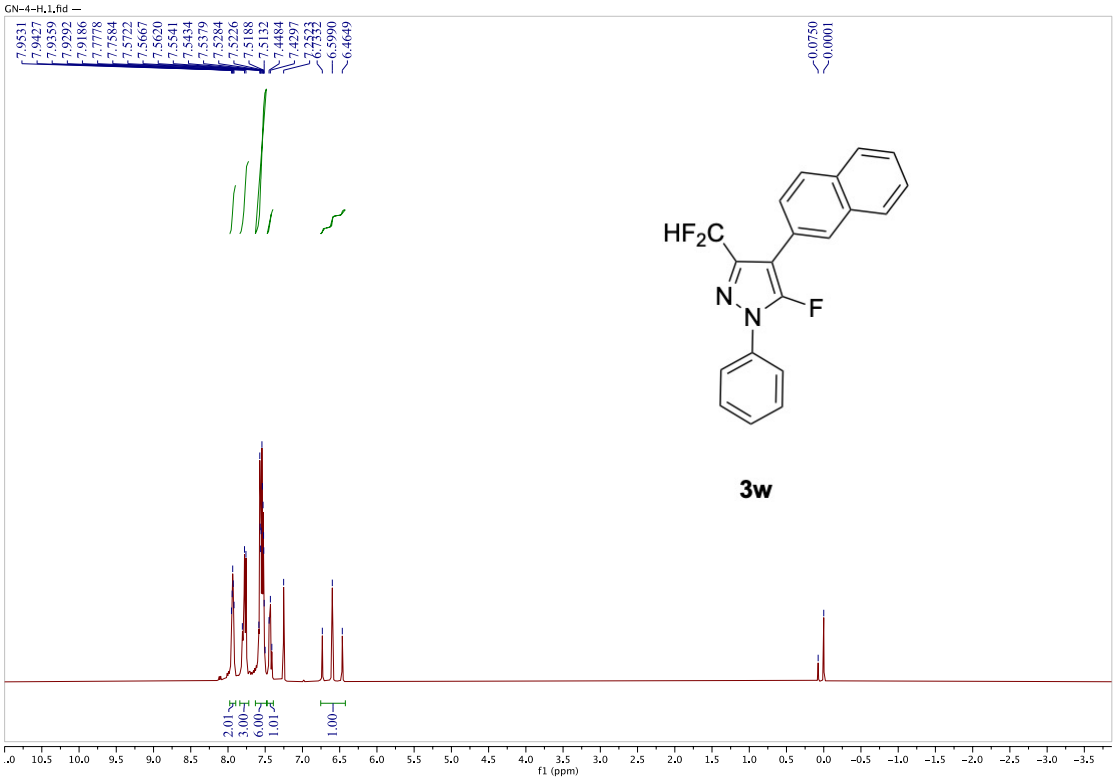


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3v**

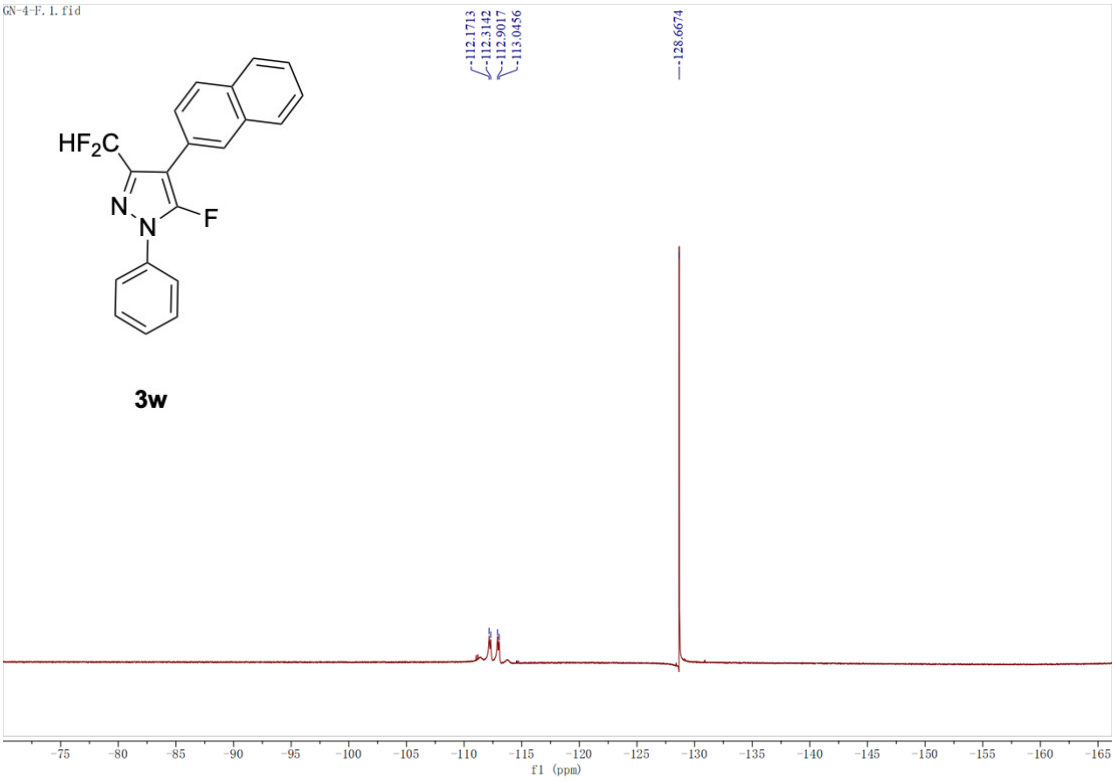


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3v**

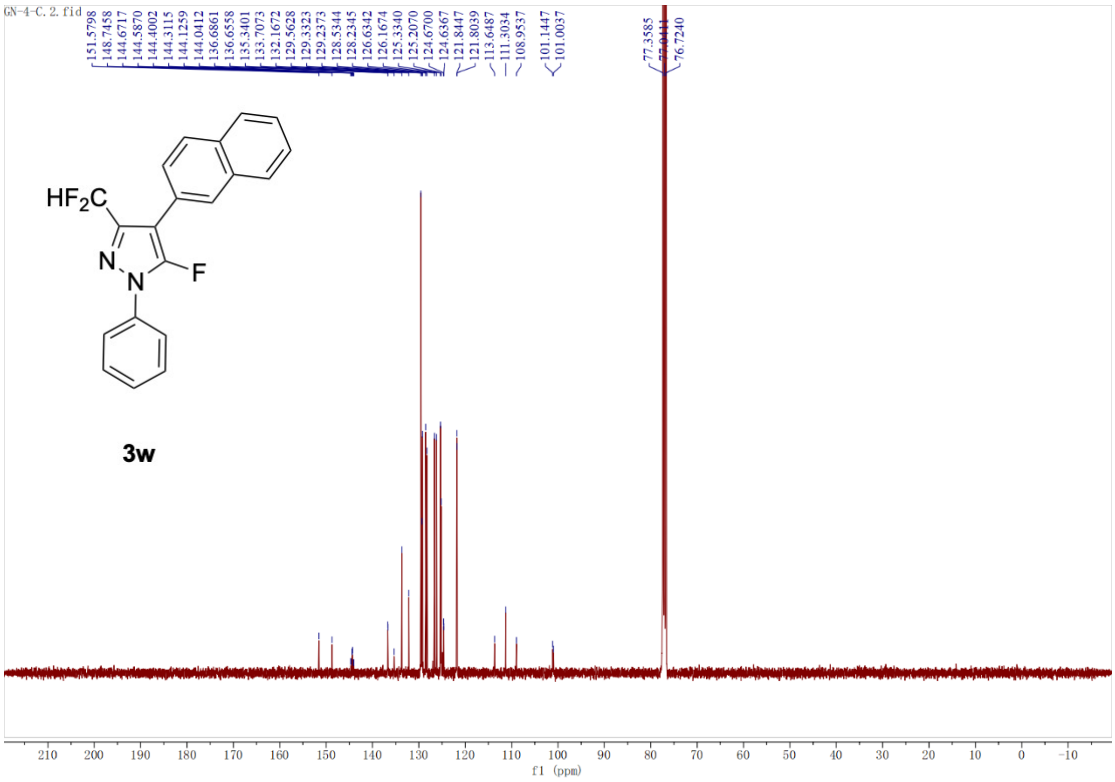
3-(Difluoromethyl)-5-fluoro-4-(naphthalen-1-yl)-1-phenyl-1*H*-pyrazole (3w)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3w**

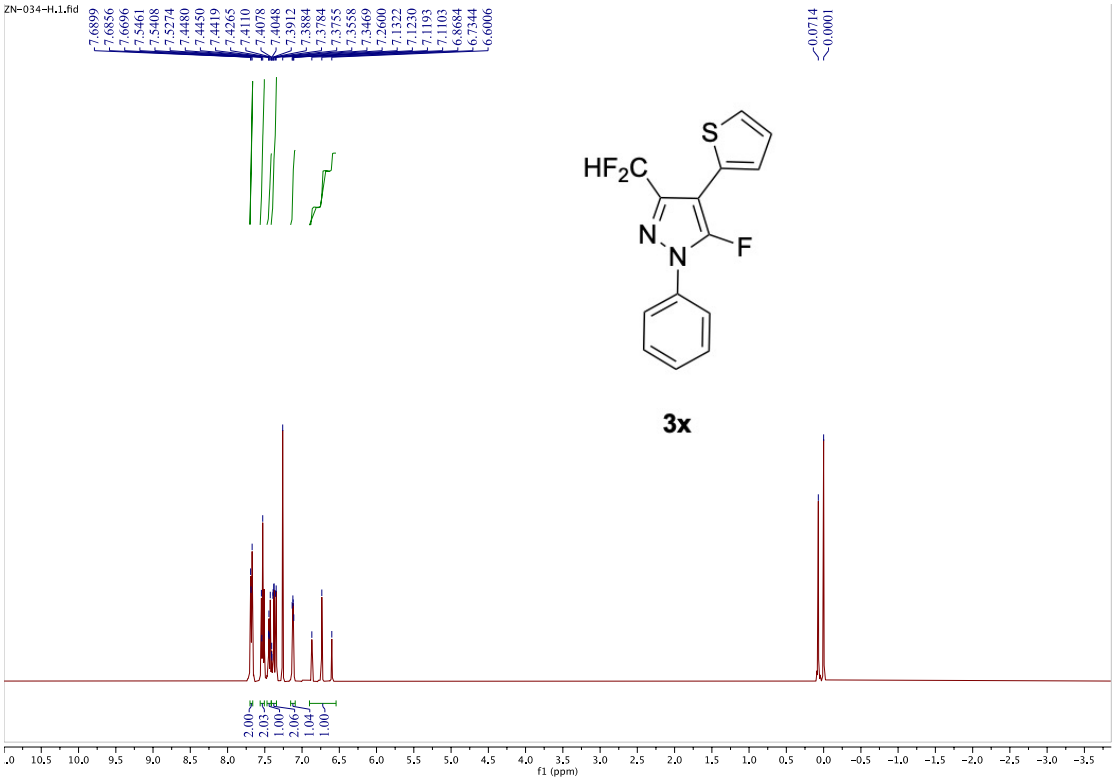


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3w**

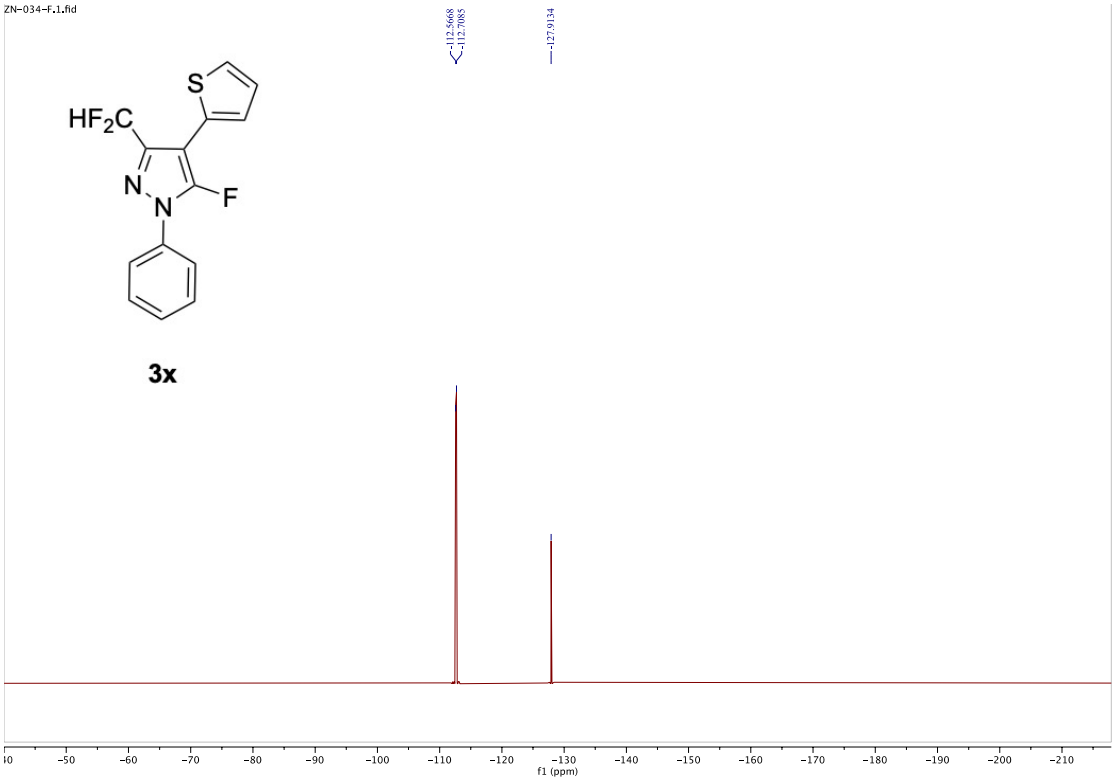


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3w**

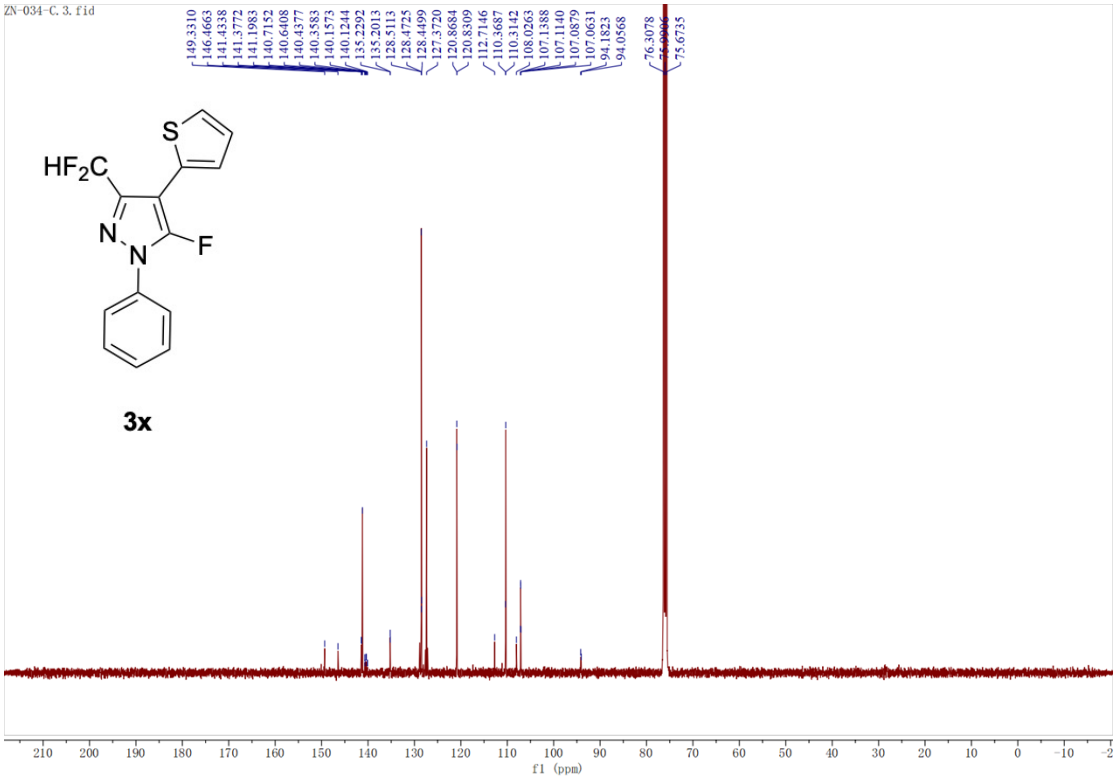
3-(Difluoromethyl)-5-fluoro-1-phenyl-4-(thiophen-2-yl)-1*H*-pyrazole (3x)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3x**

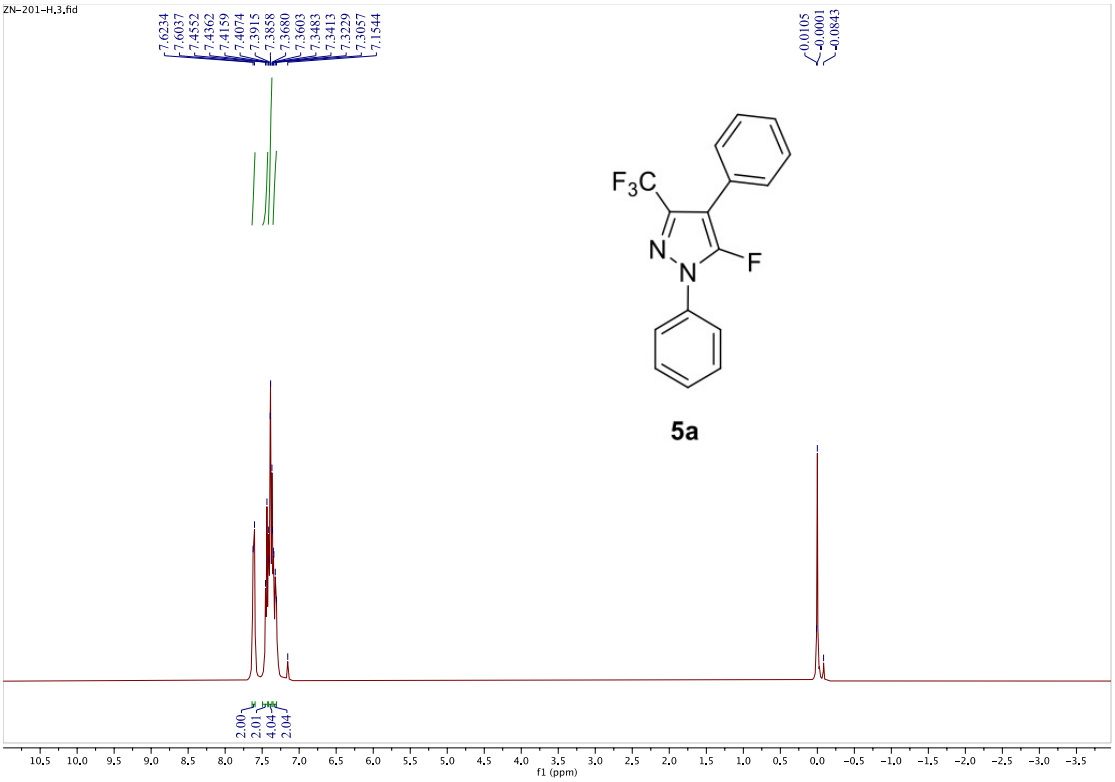


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3x**

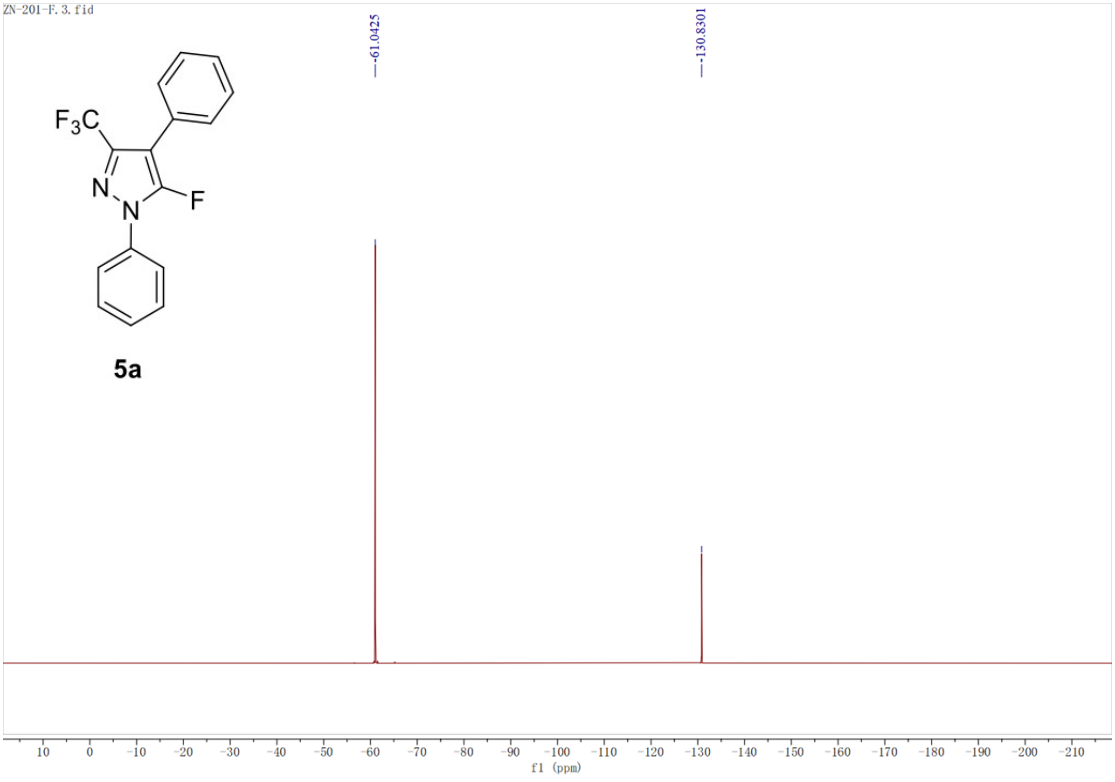


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **3x**

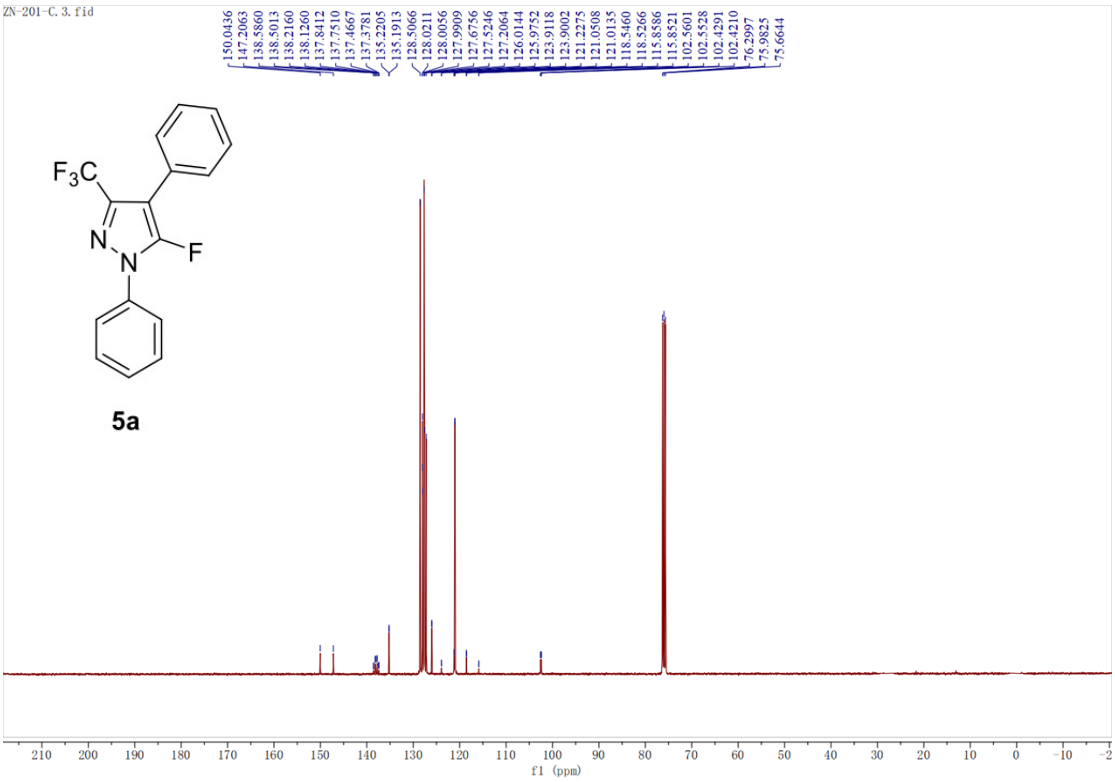
5-Fluoro-1,4-diphenyl-3-(trifluoromethyl)-1*H*-pyrazole (5a)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5a**

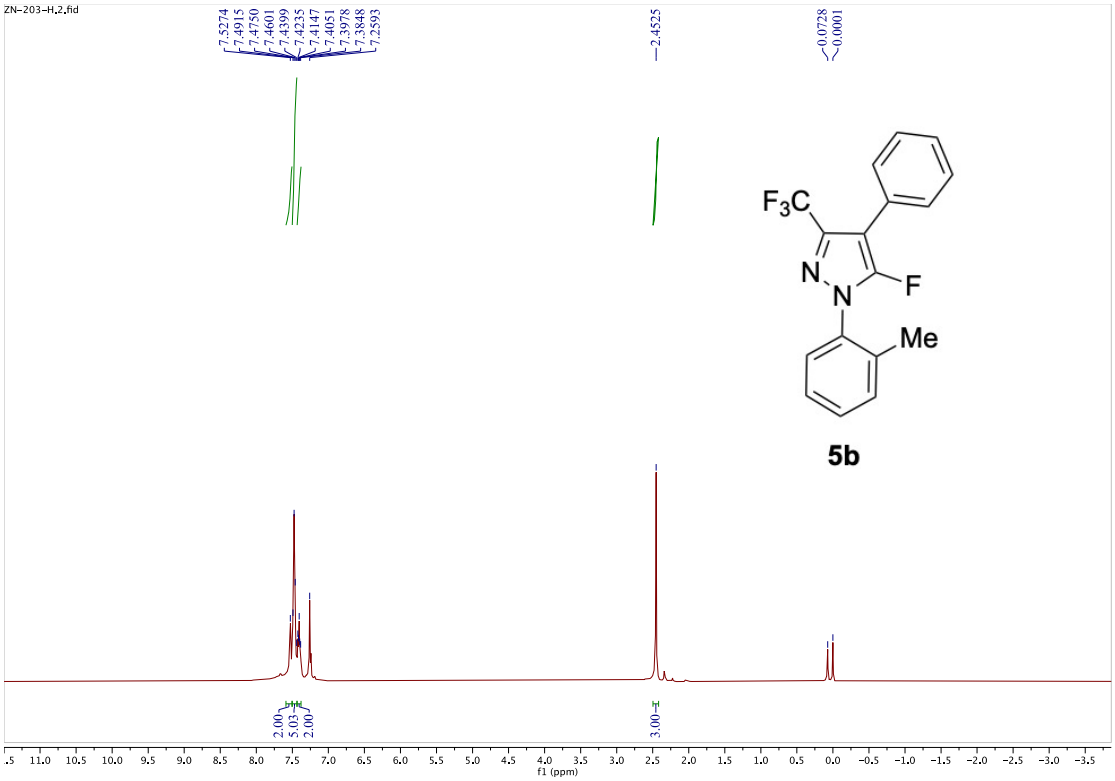


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5a**

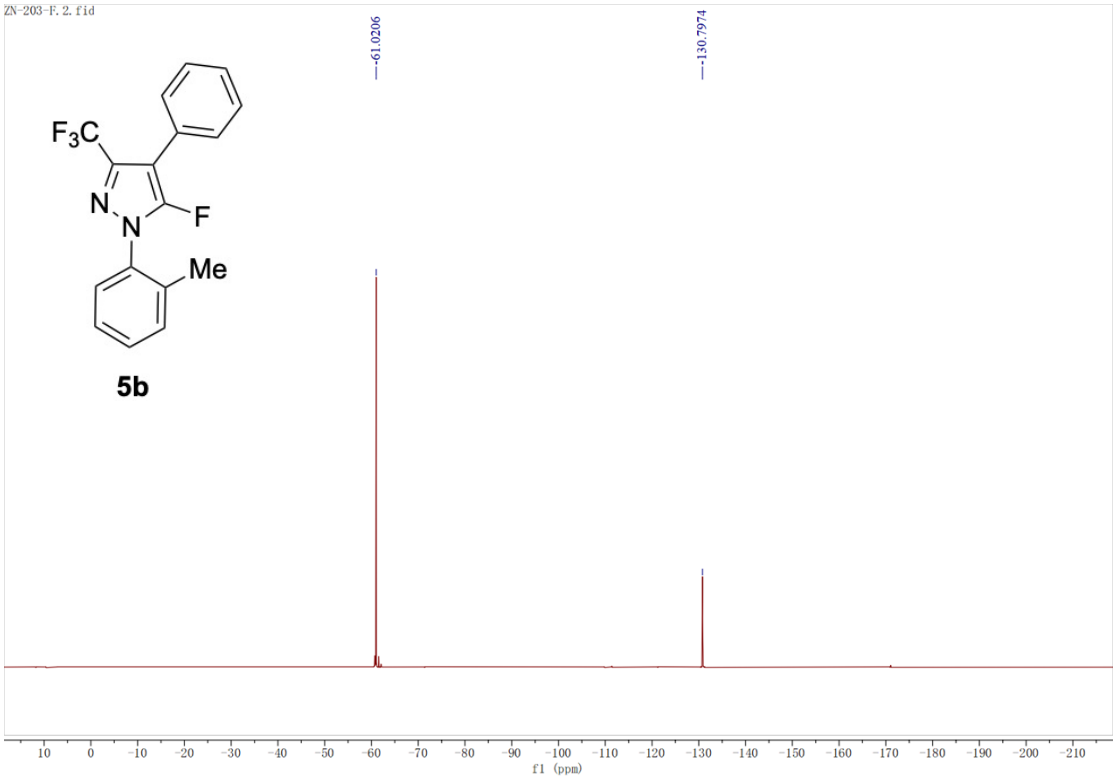


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5a**

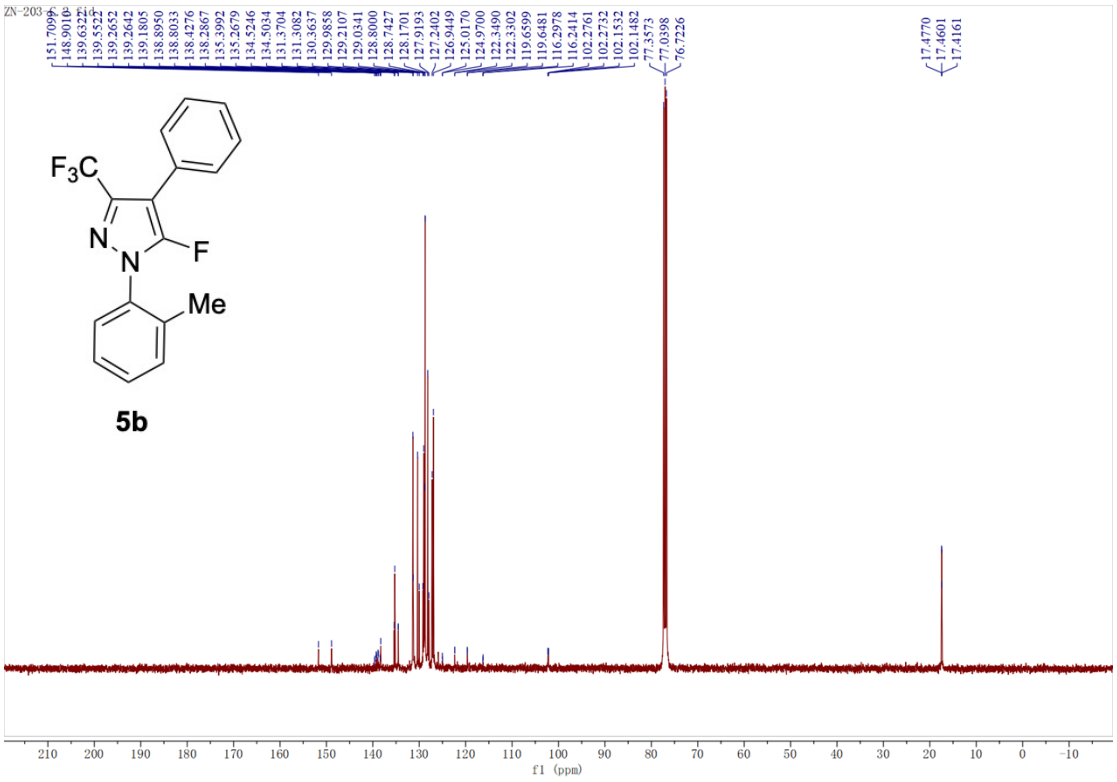
5-Fluoro-1-phenyl-4-(*o*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazole (5b)



^{19}H NMR spectrum (400 MHz, $CDCl_3$) of **5b**

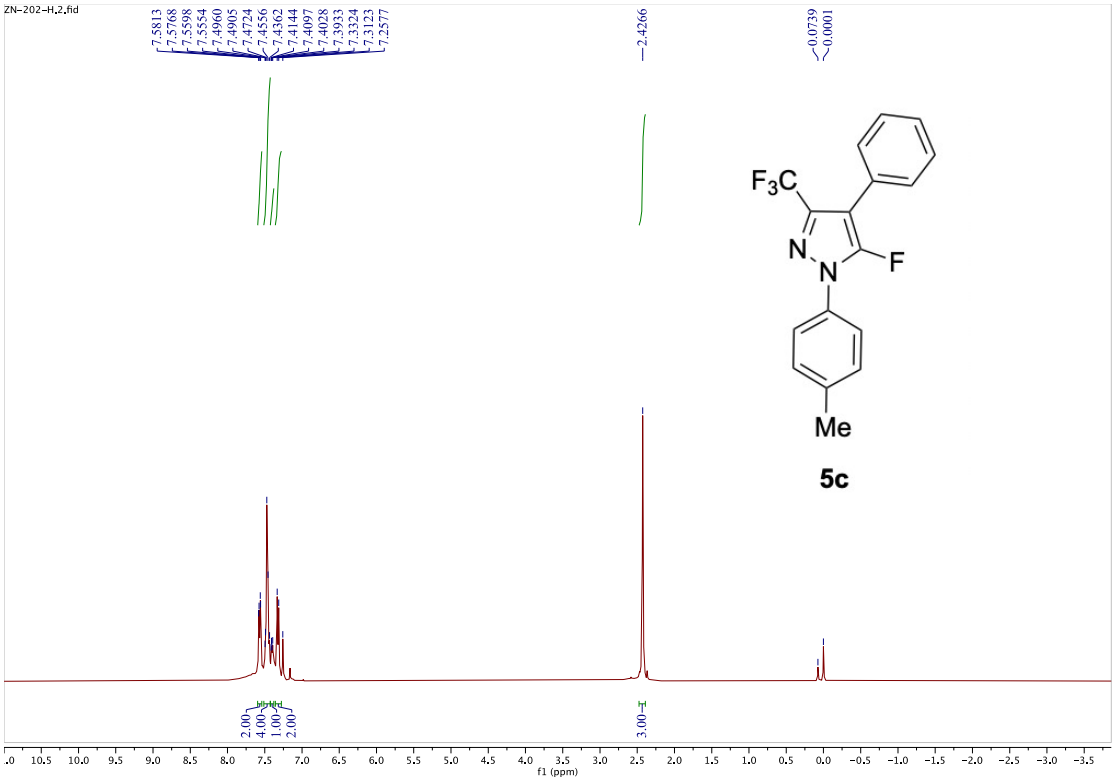


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5b**

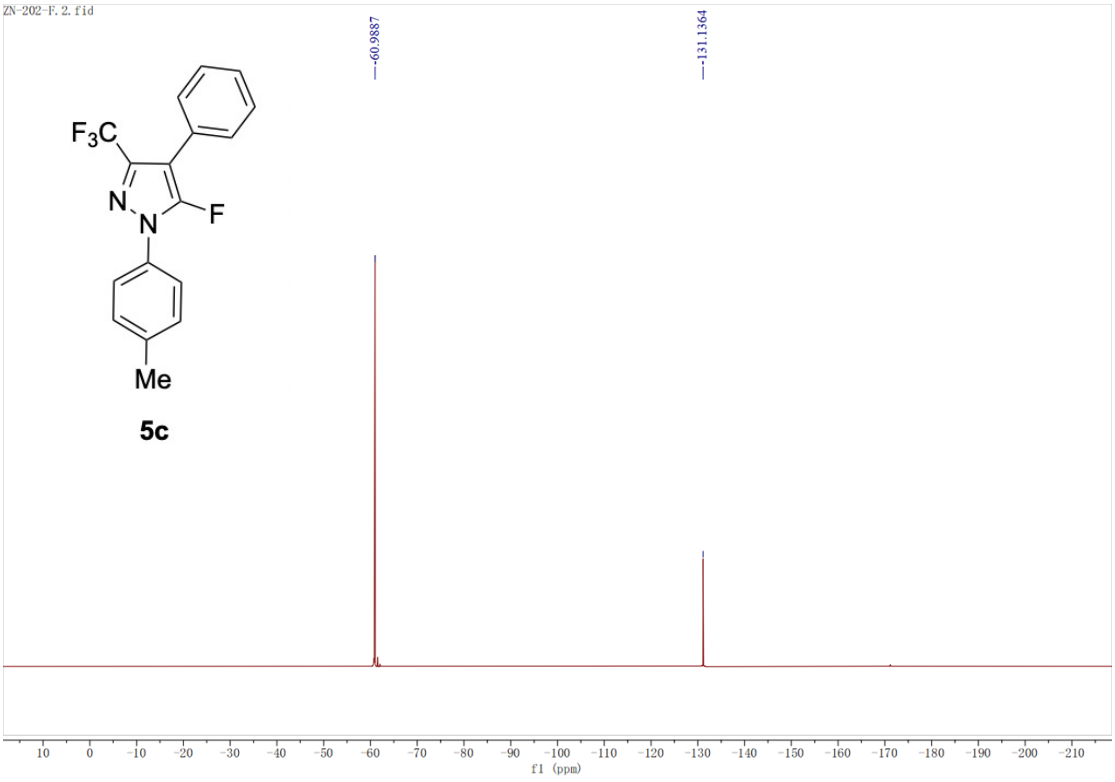


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5b**

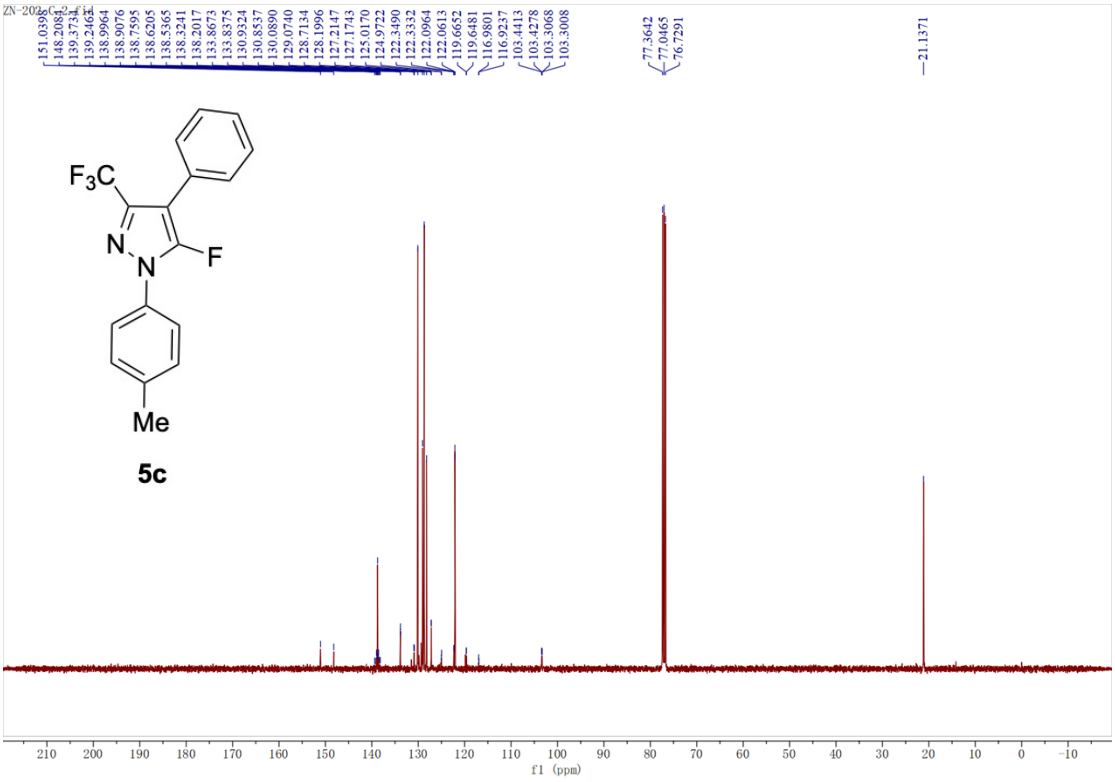
5-Fluoro-4-phenyl-1-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazole (5c)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5c**

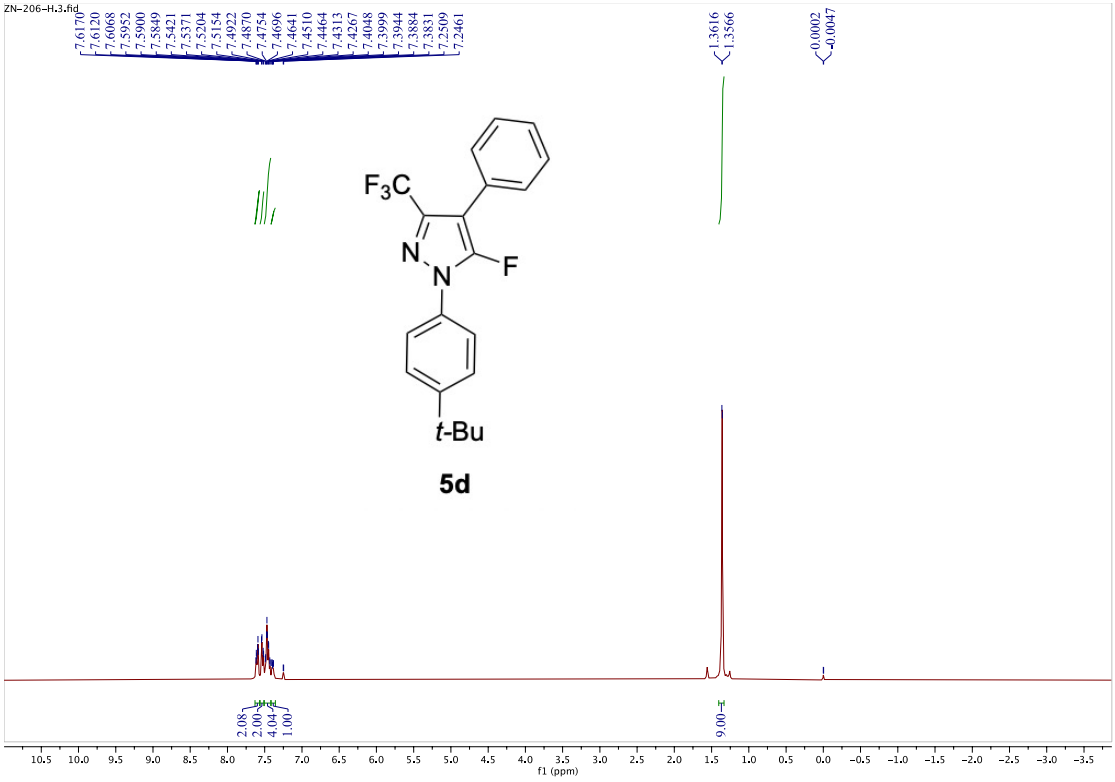


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5c**

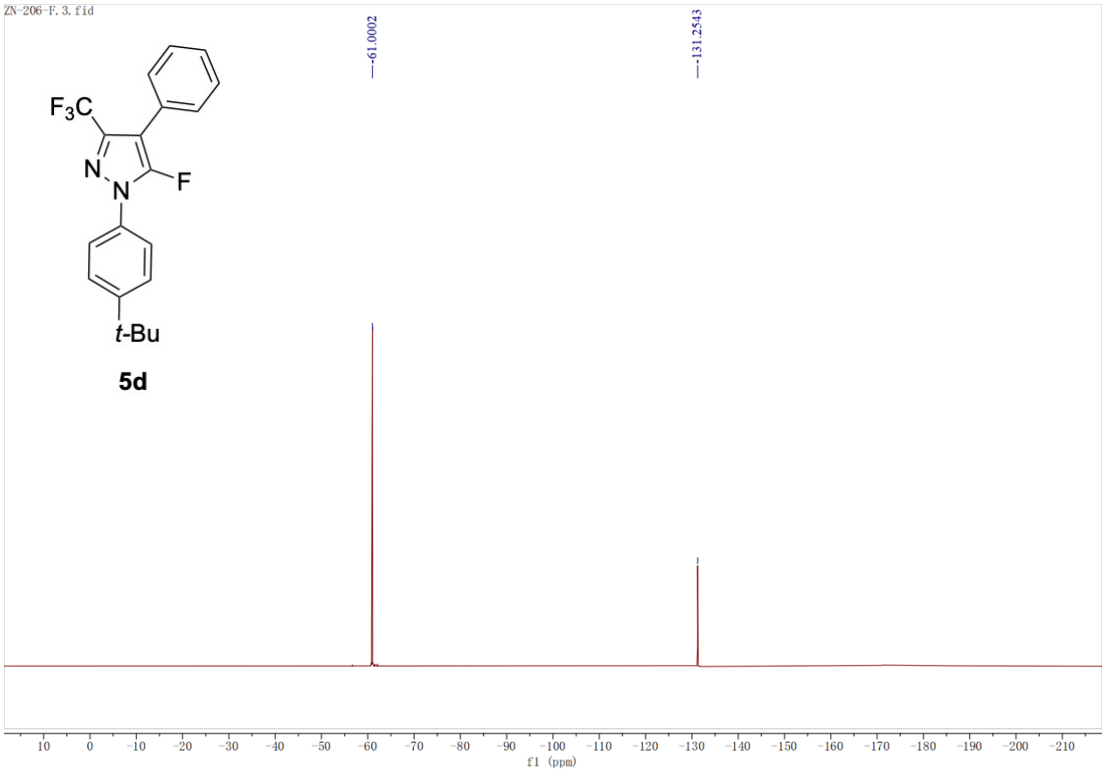


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5c**

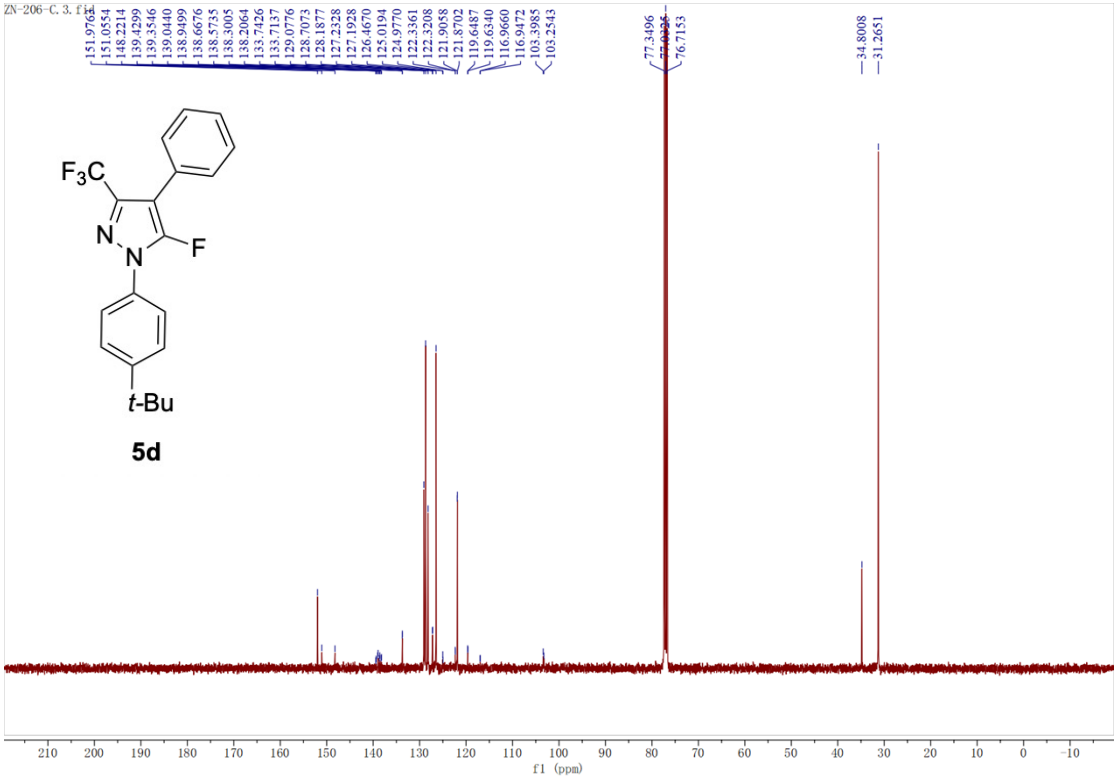
1-(4-(*tert*-Butyl)phenyl)-5-fluoro-4-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5d)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5d**

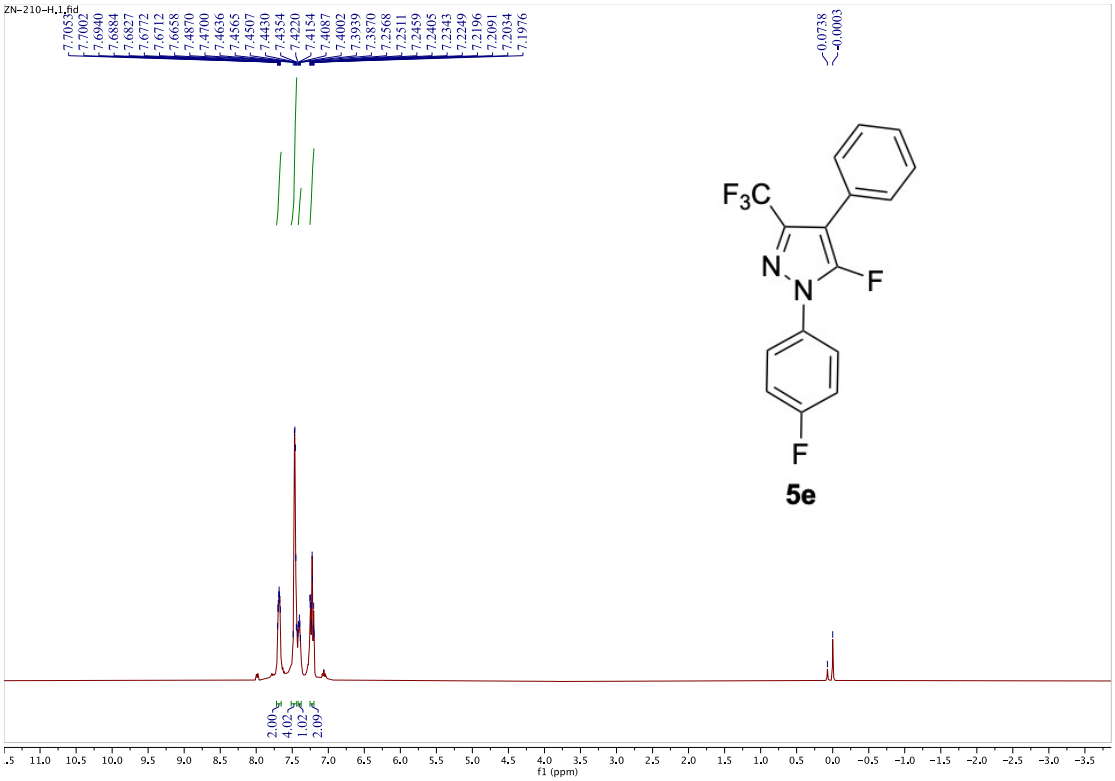


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5d**

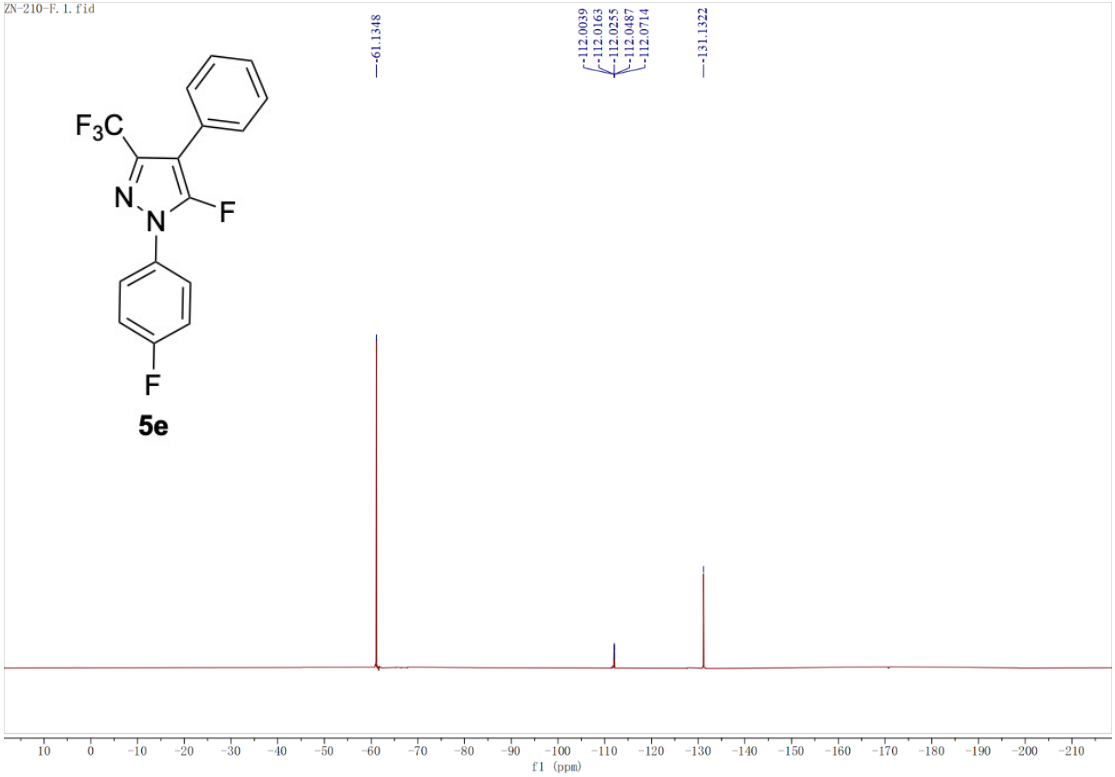


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5d**

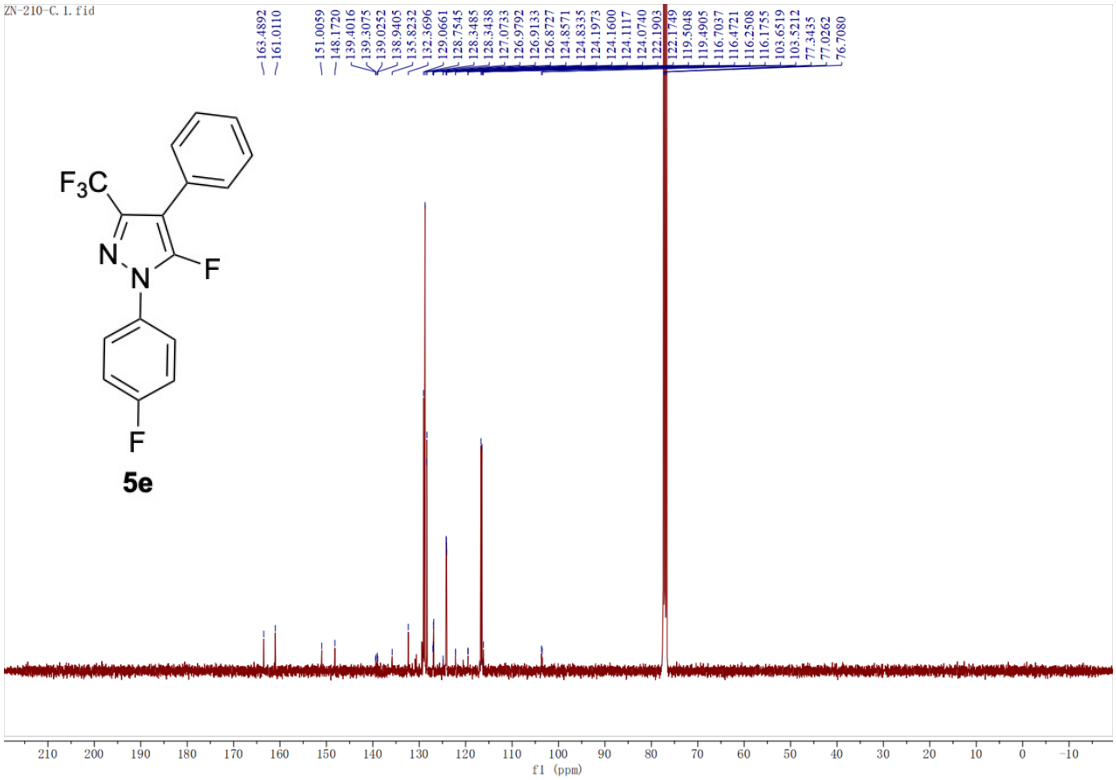
5-Fluoro-1-(4-fluorophenyl)-4-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5e)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5e**

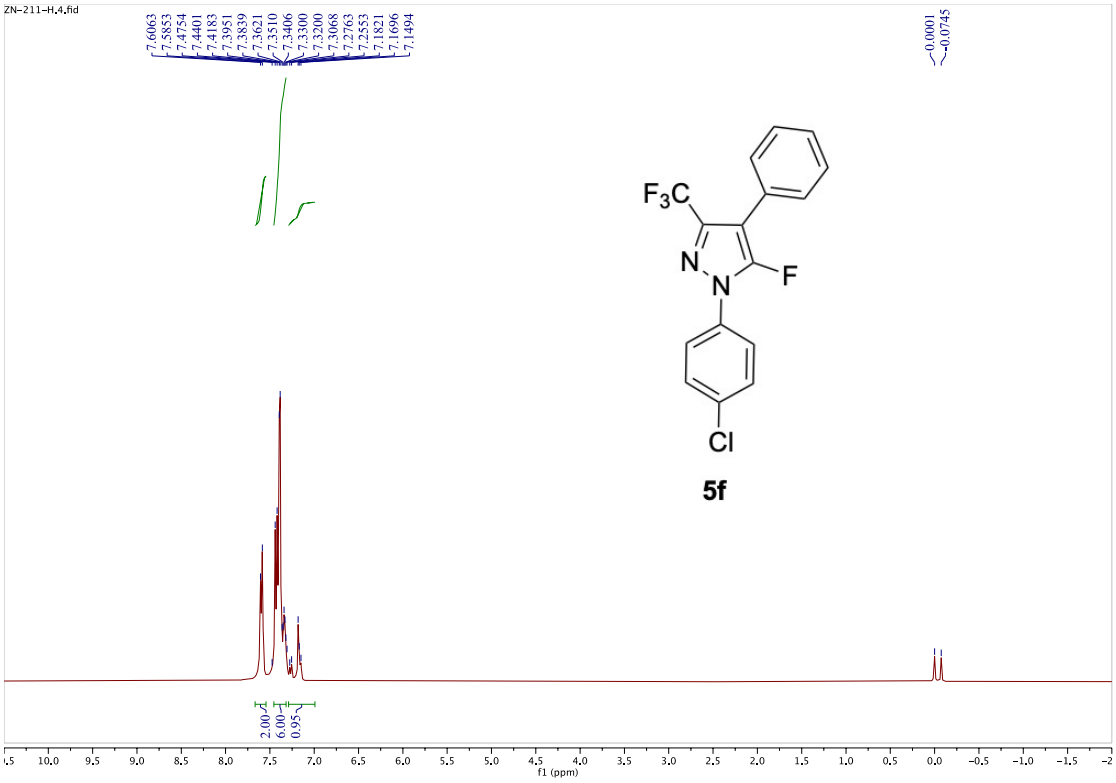


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5e**

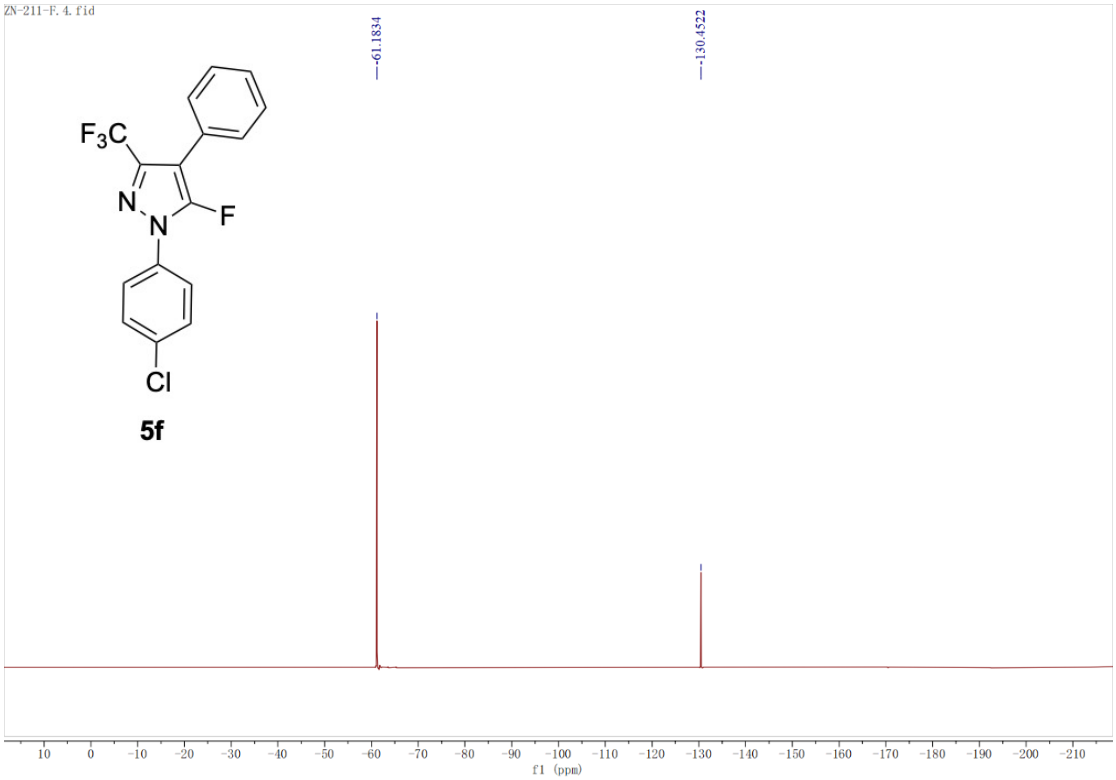


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5e**

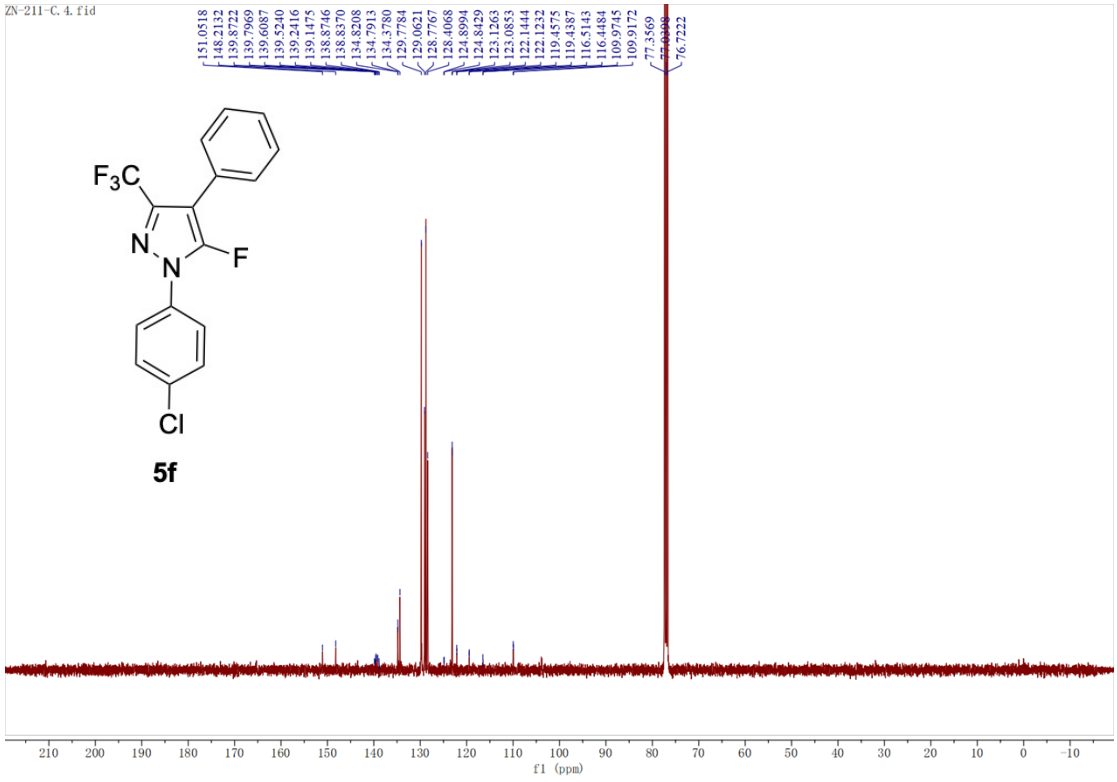
1-(4-Chlorophenyl)-5-fluoro-4-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5f)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5f**

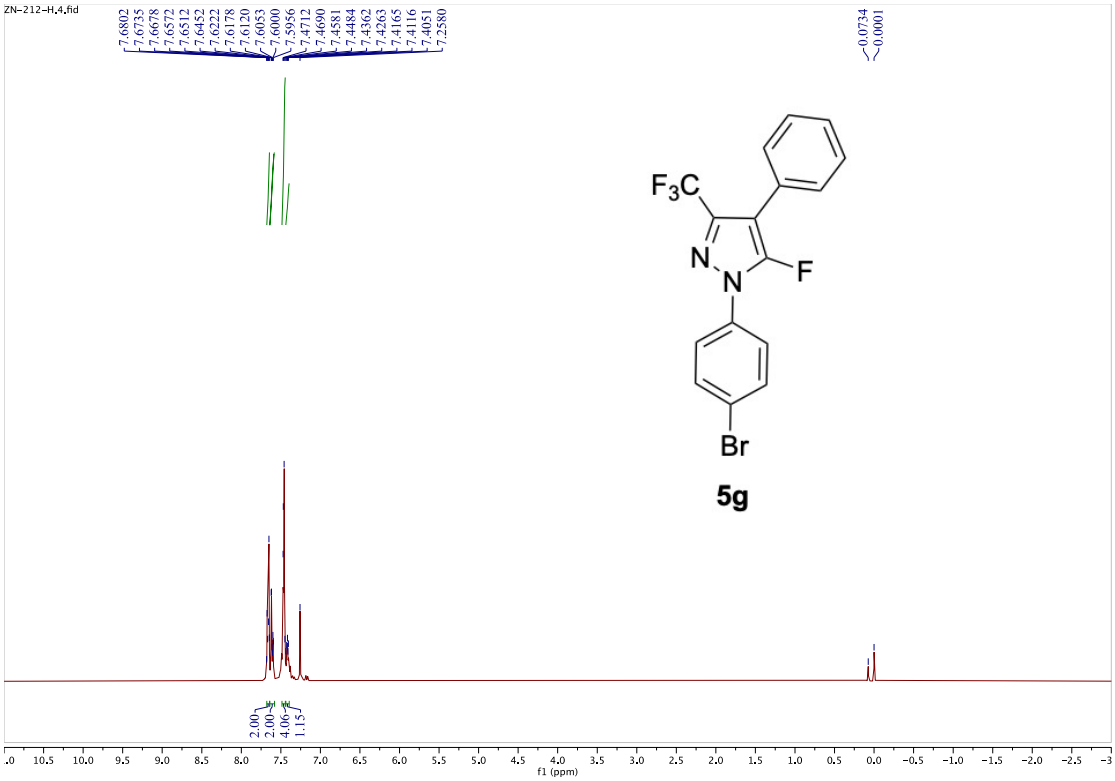


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5f**

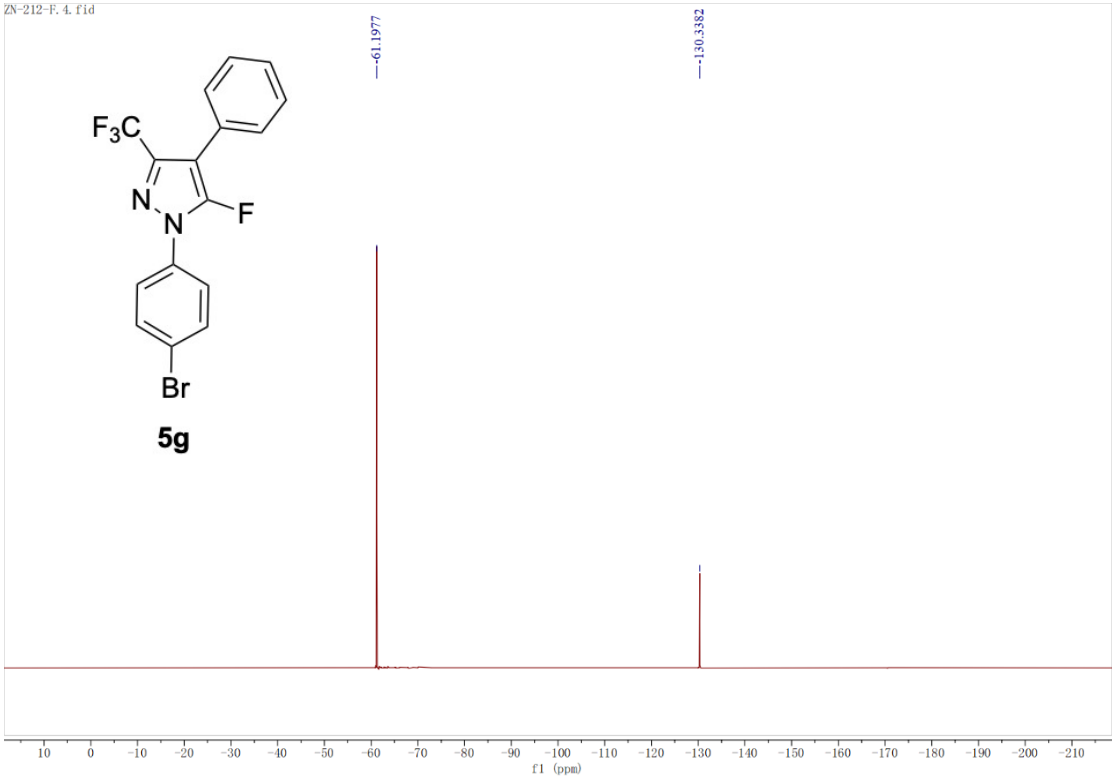


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5f**

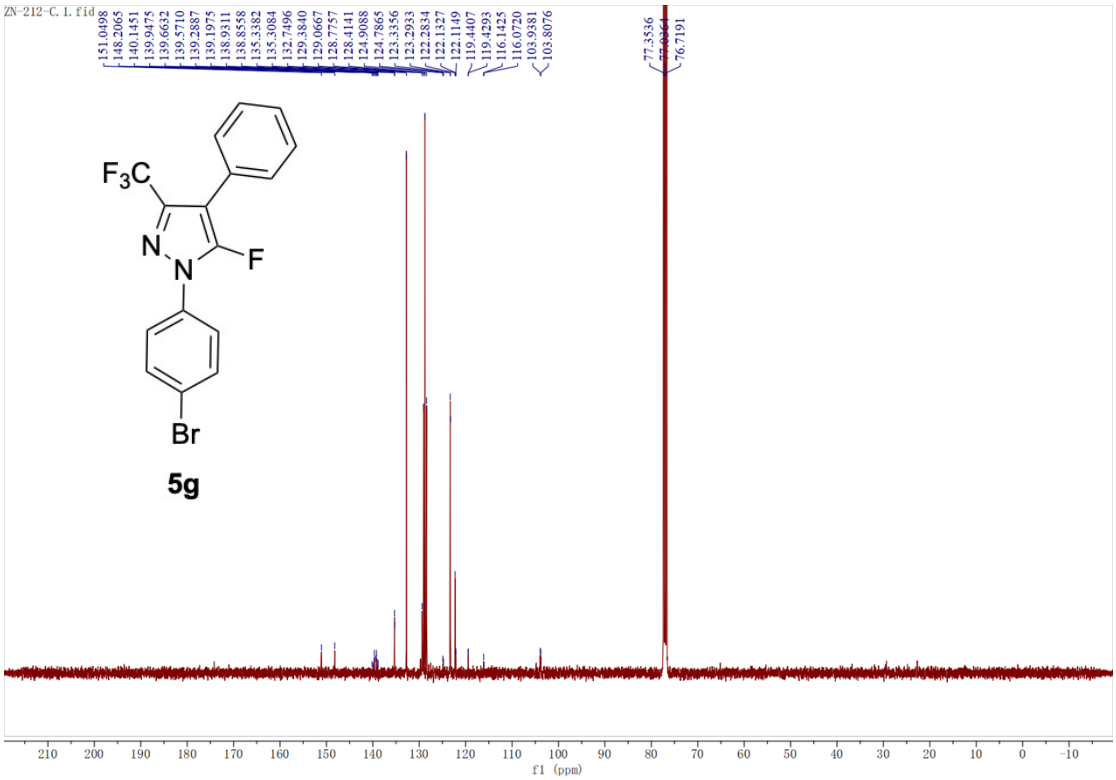
1-(4-Bromophenyl)-5-fluoro-4-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5g)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5g**

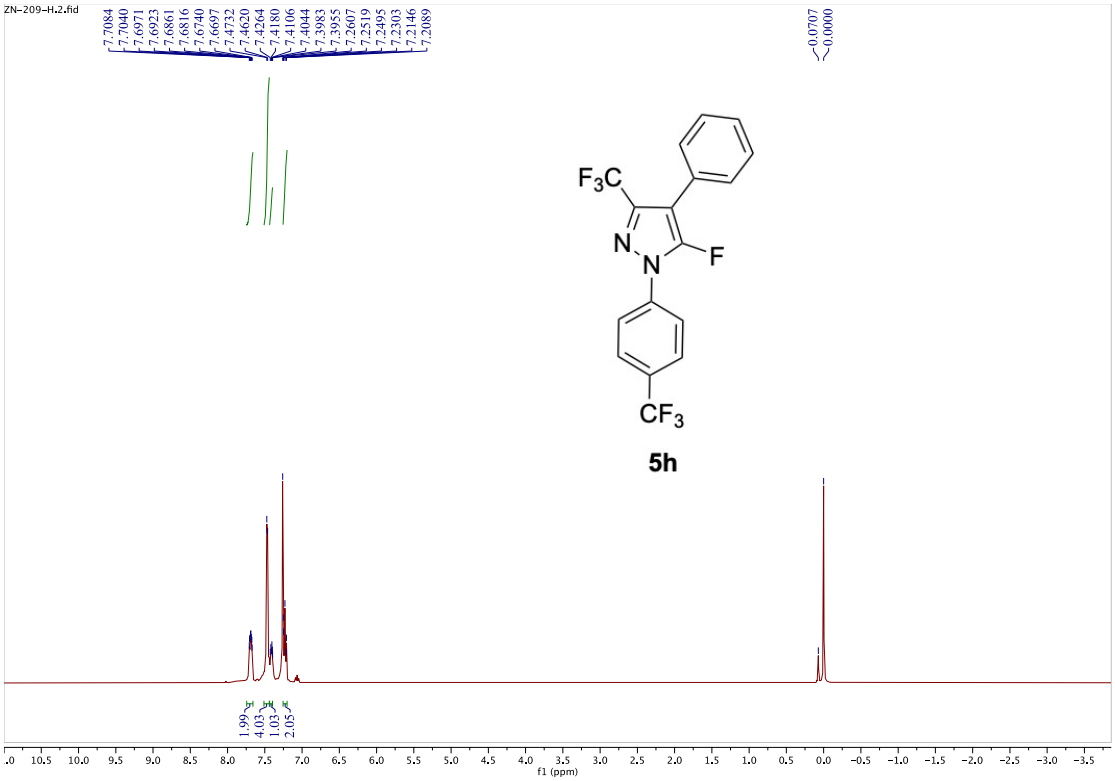


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5g**

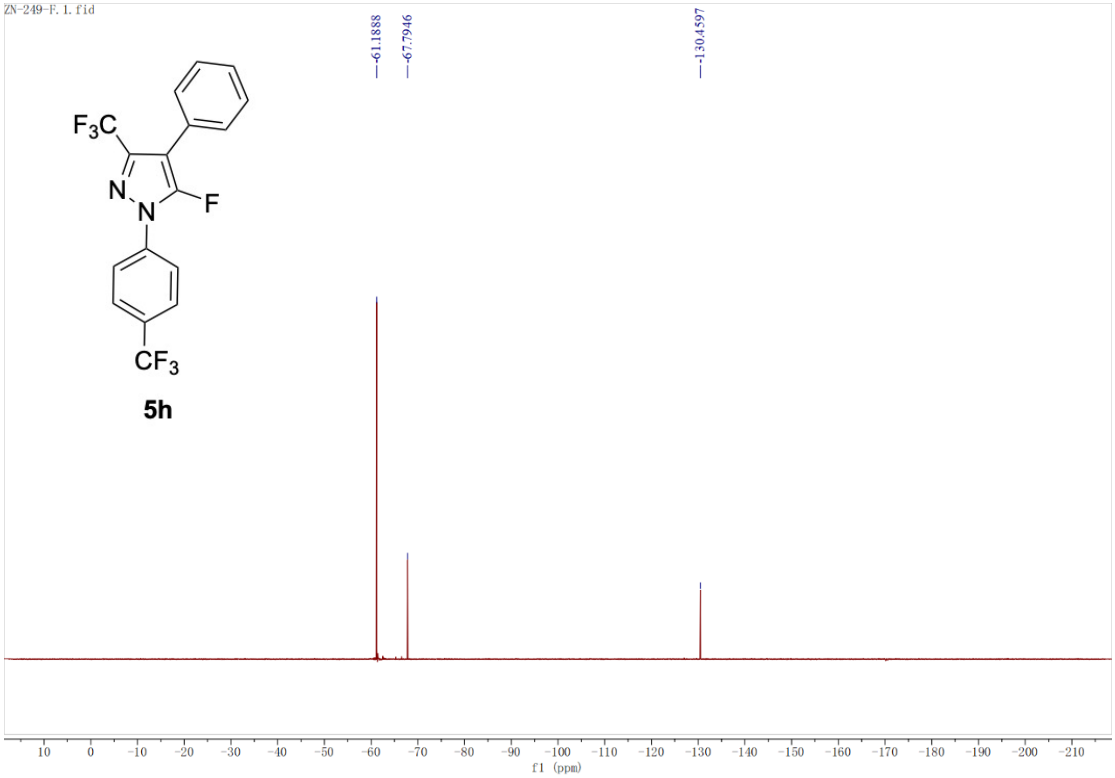


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5g**

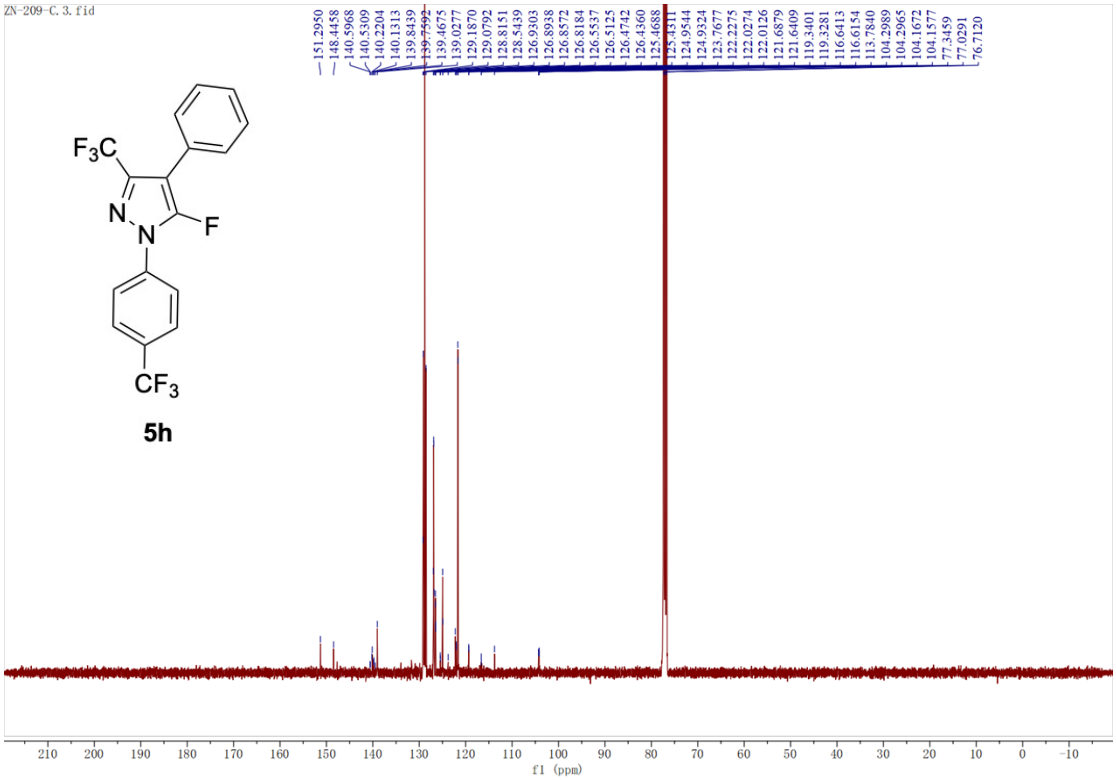
5-Fluoro-4-phenyl-3-(trifluoromethyl)-1-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (5h)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5h**

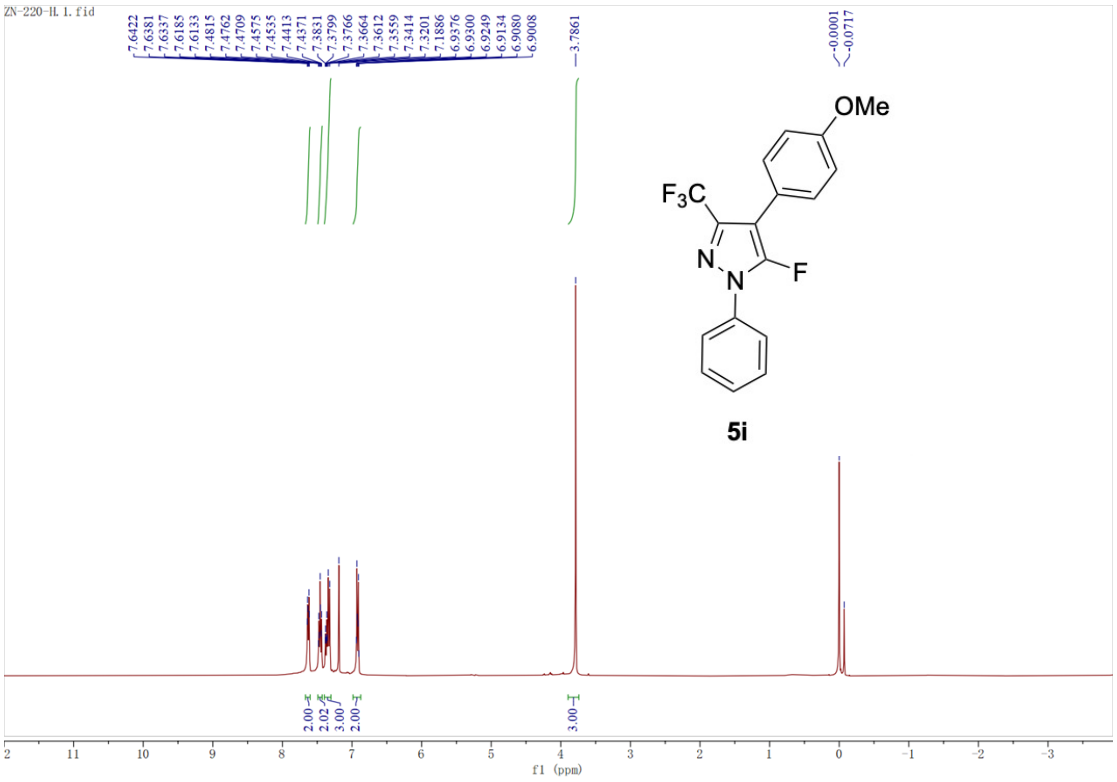


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5h**

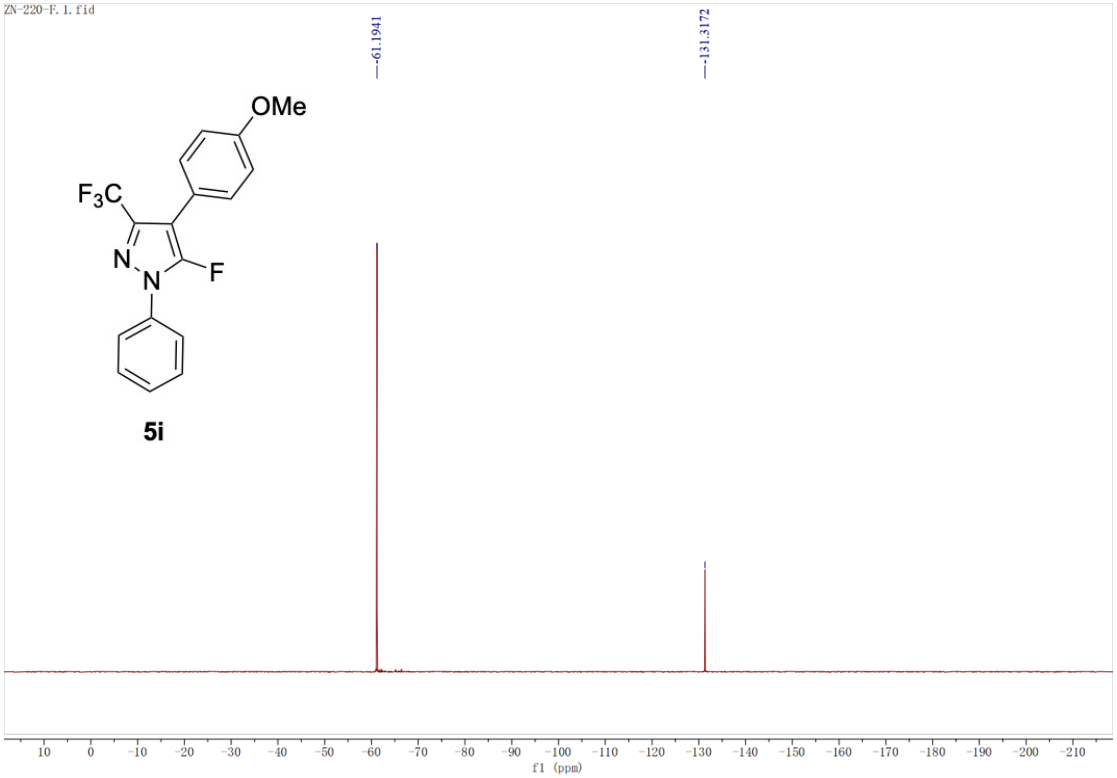


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5h**

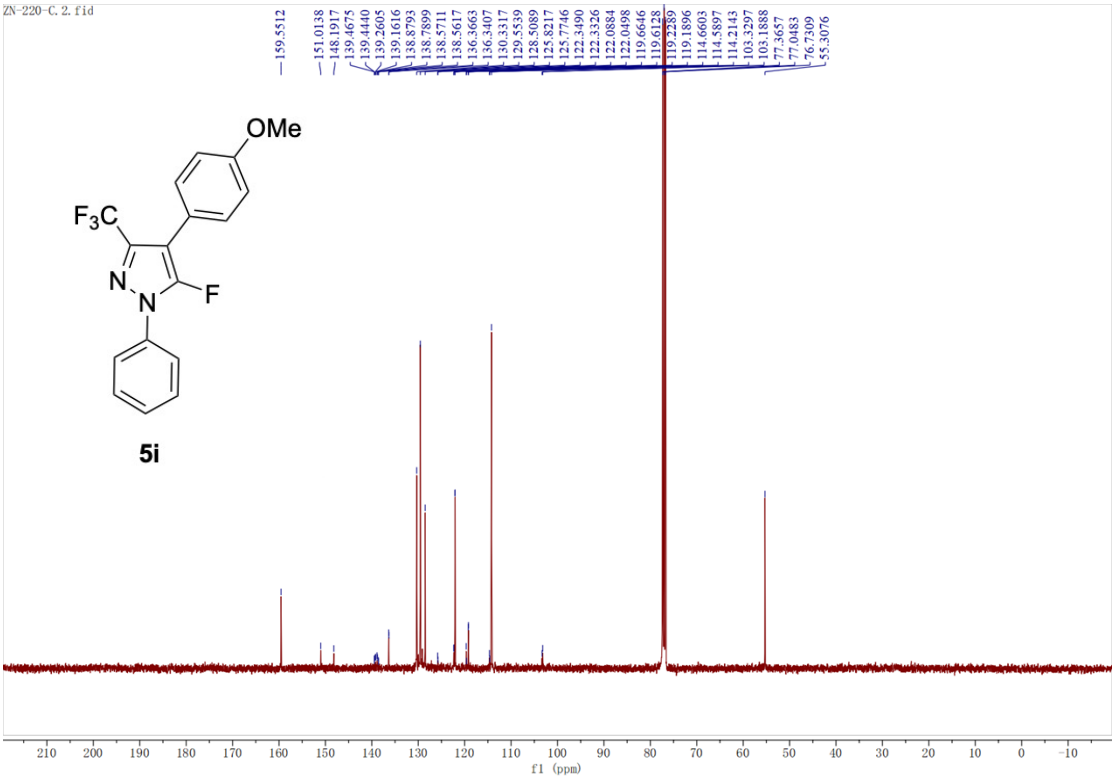
5-Fluoro-4-(4-methoxyphenyl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5i)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5i**

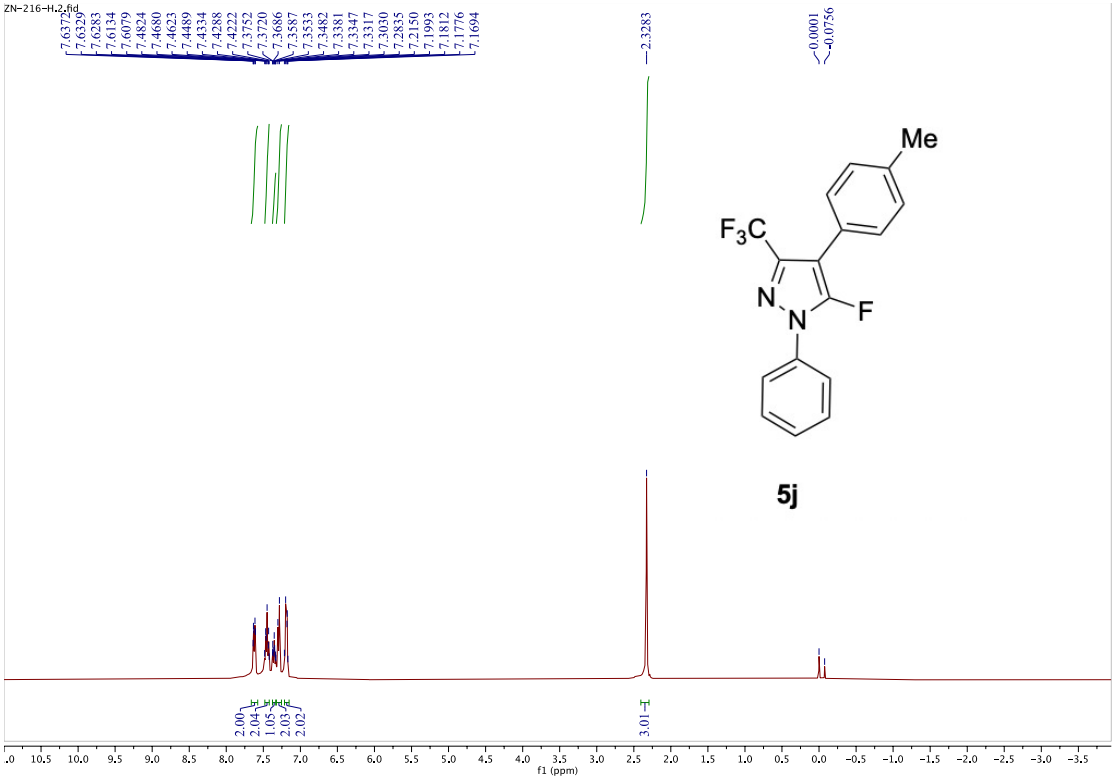


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5i**

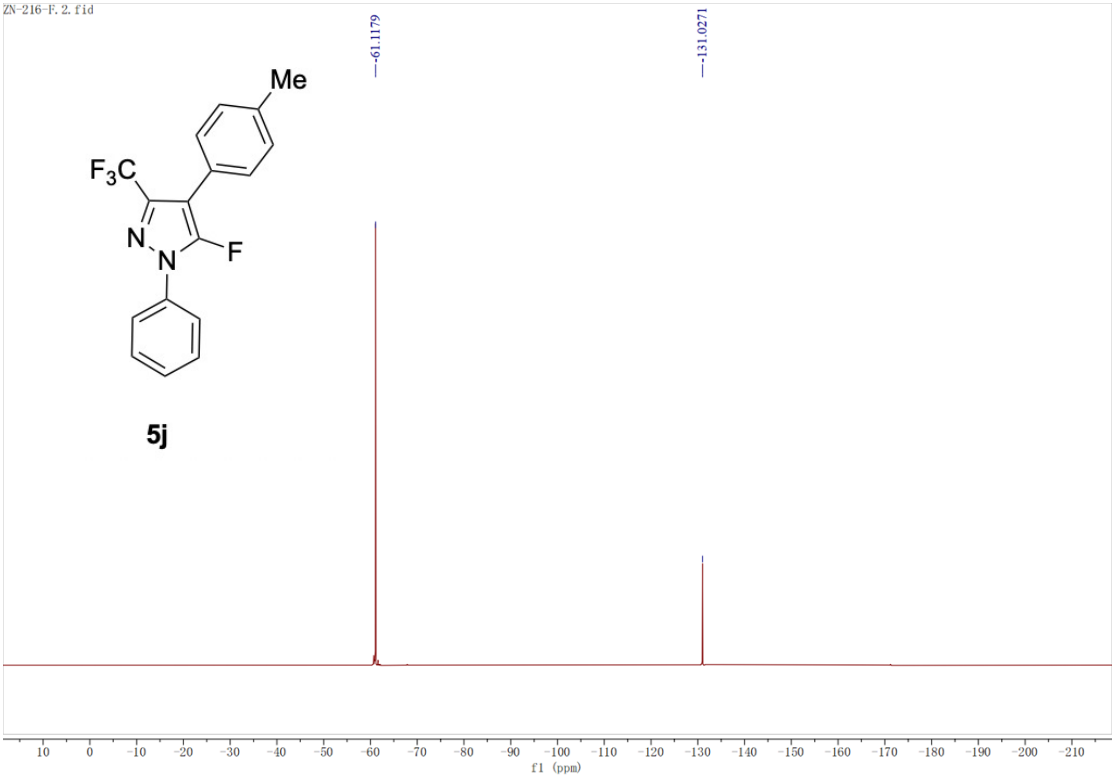


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5i**

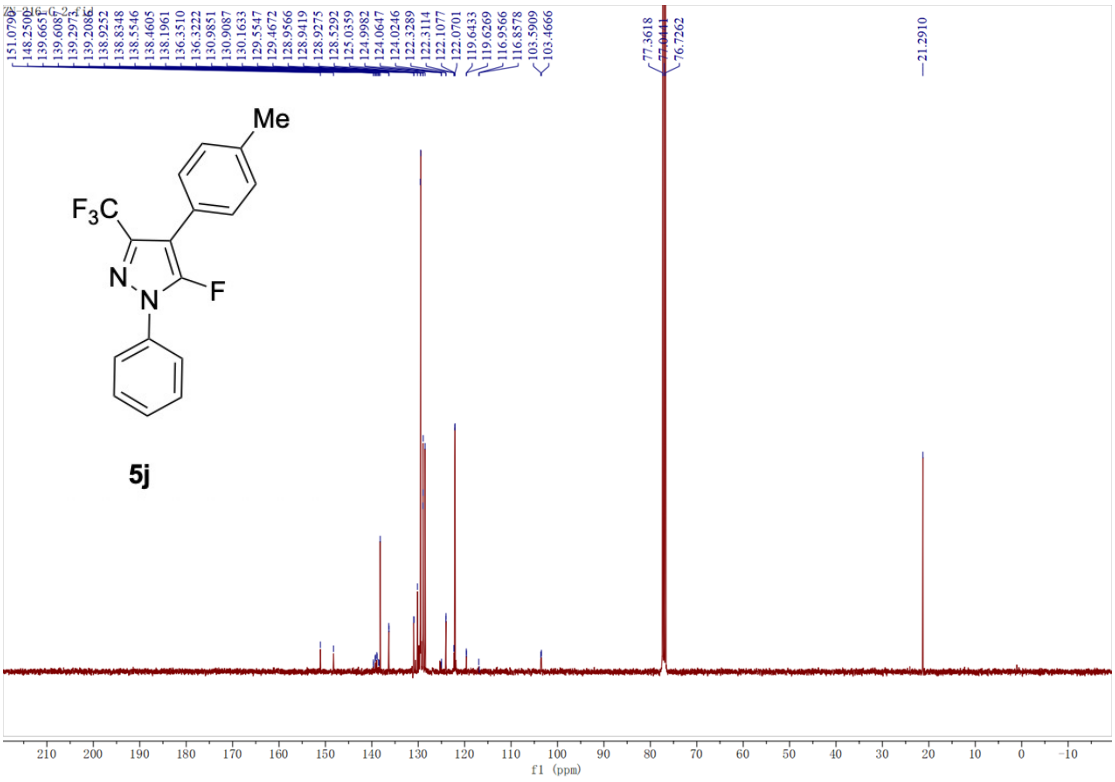
5-Fluoro-1-phenyl-4-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazole (5j)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5j**

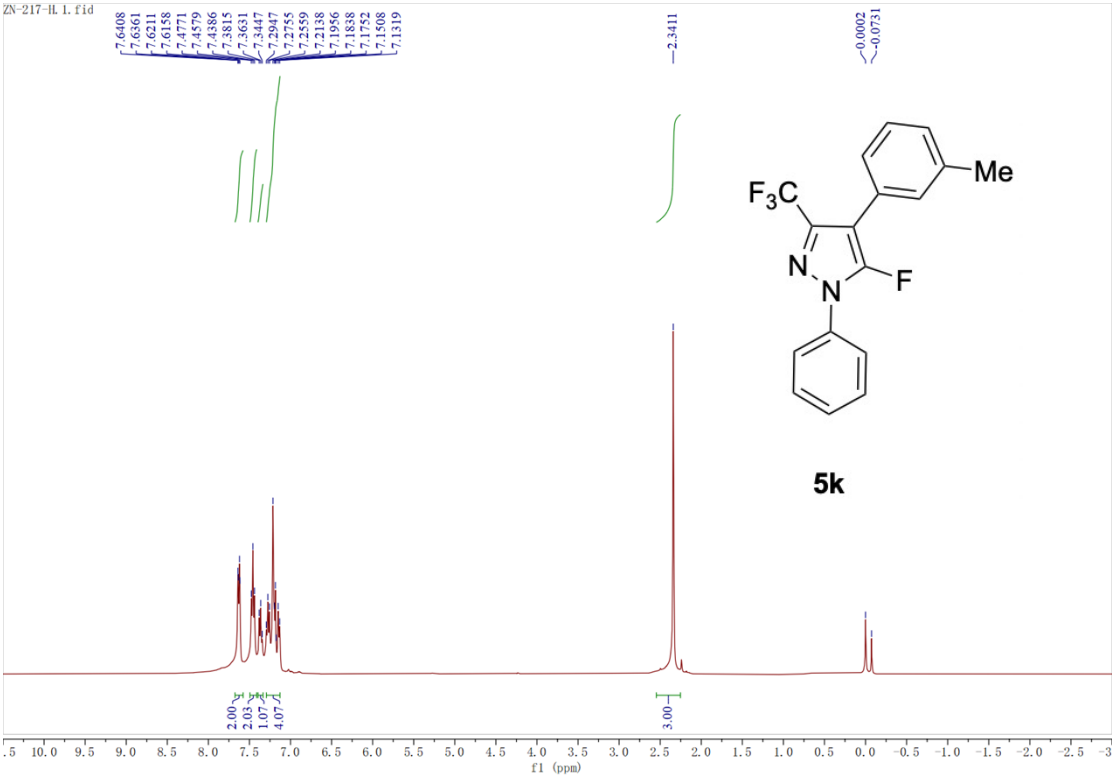


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5j**

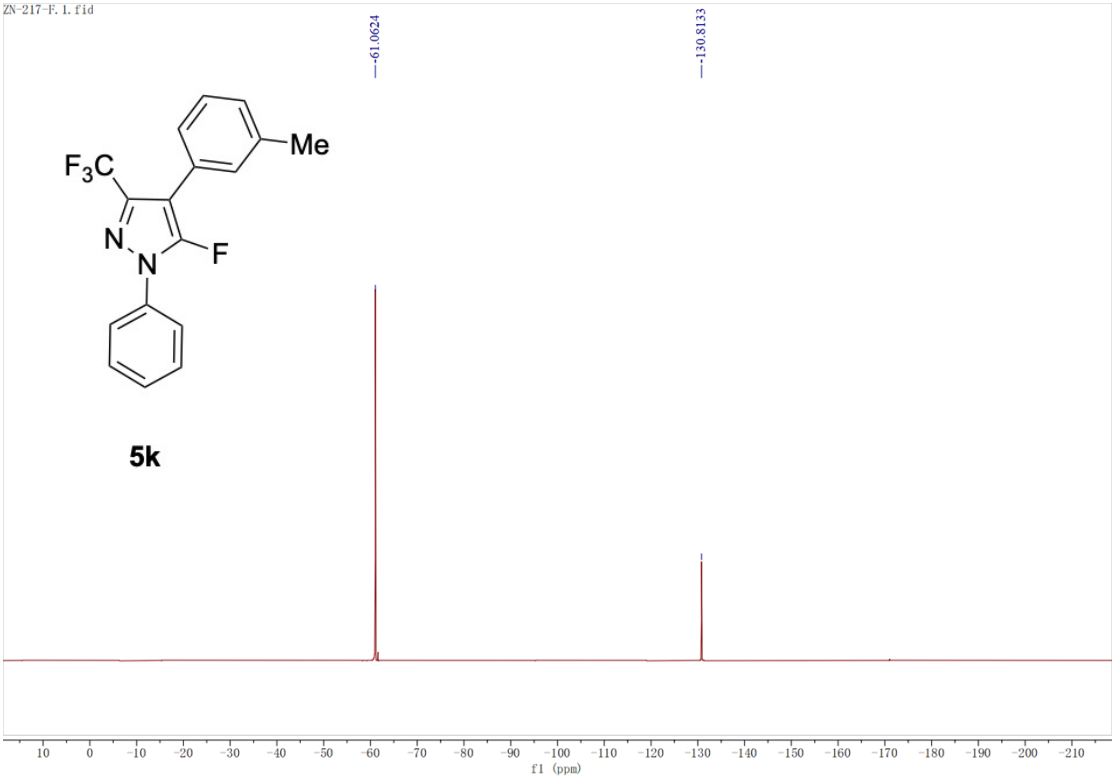


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5j**

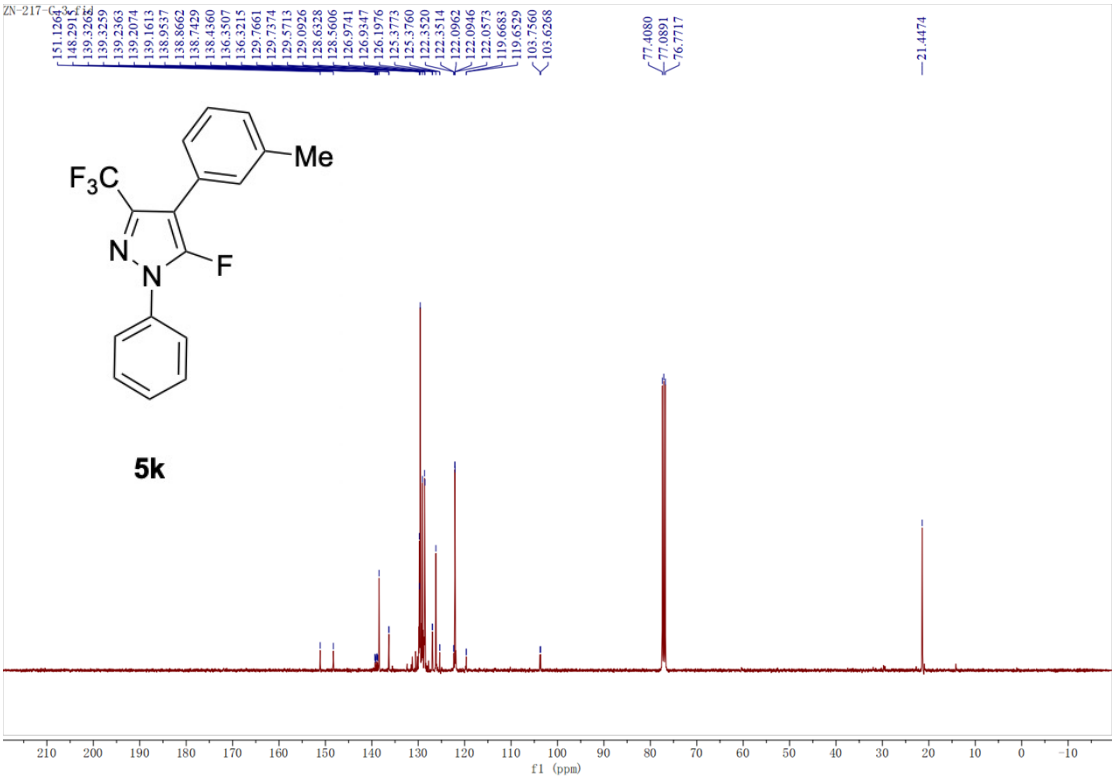
5-Fluoro-1-phenyl-4-(*m*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazole (5k)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5k**

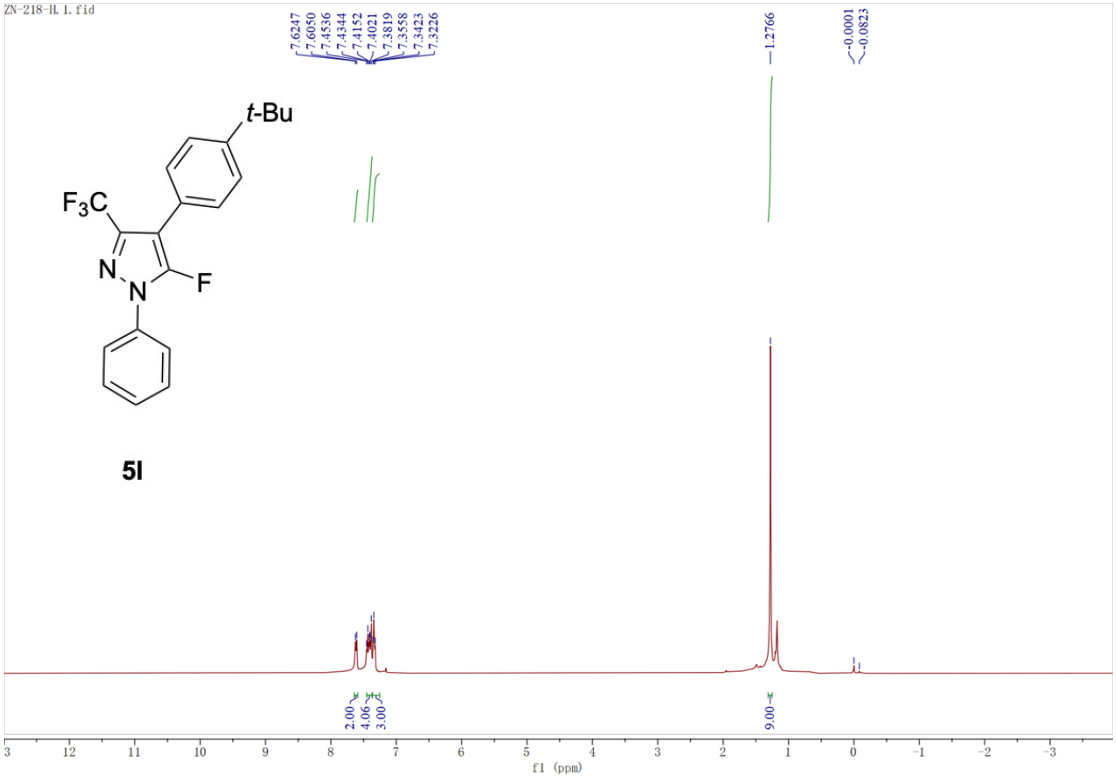


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5k**

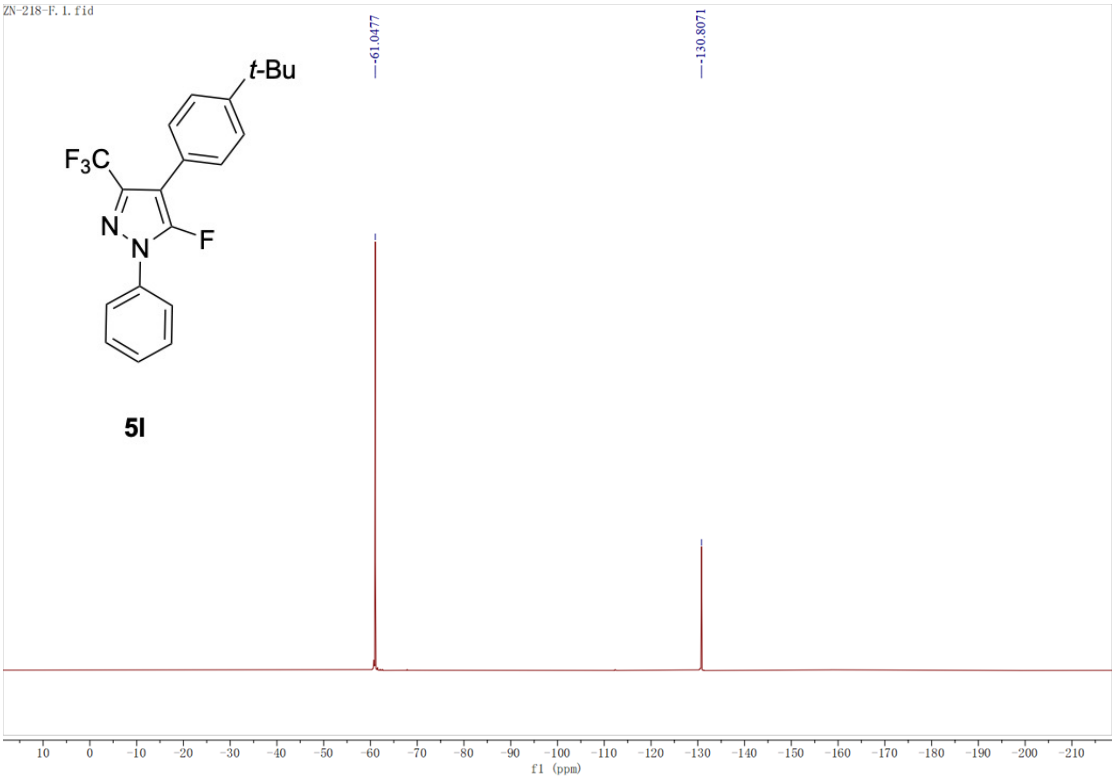


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5k**

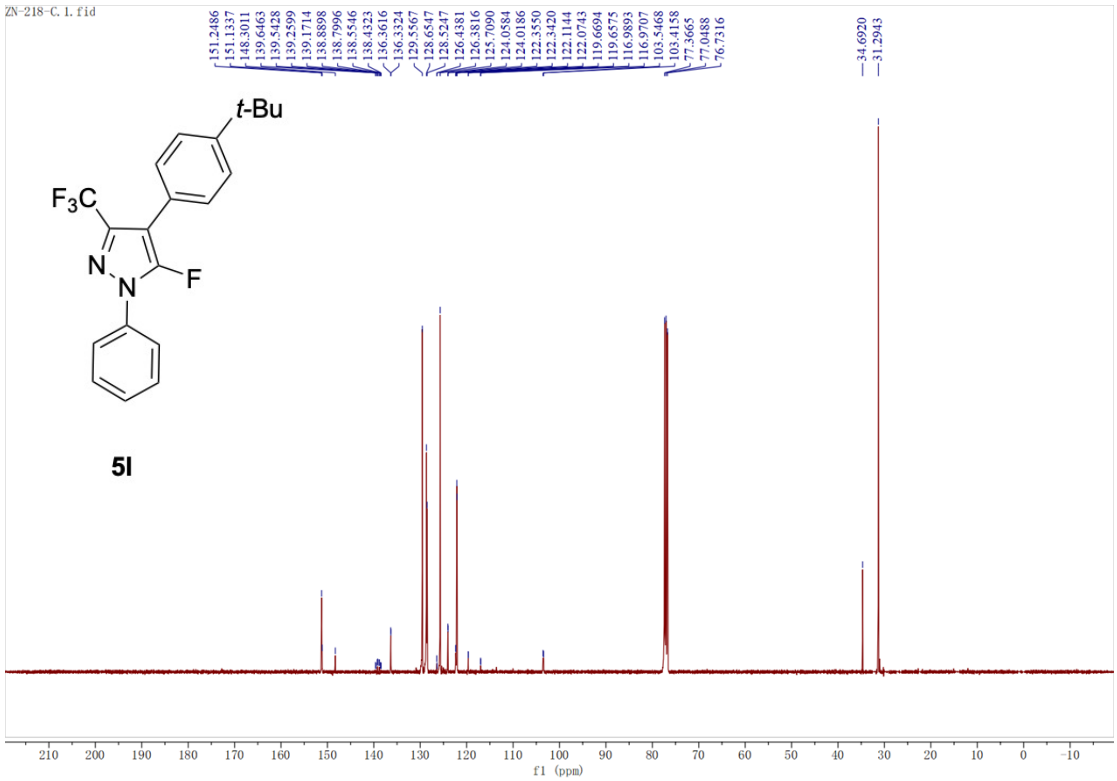
4-(4-(*tert*-Butyl)phenyl)-5-fluoro-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5l)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5l**

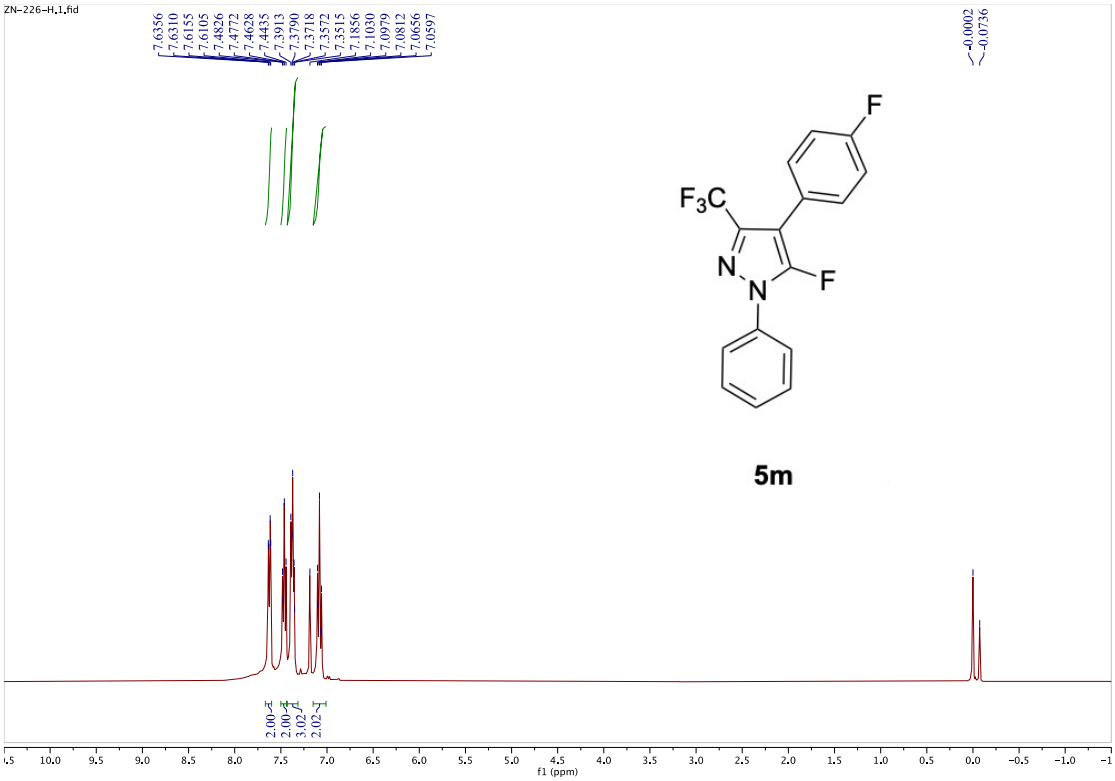


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5l**

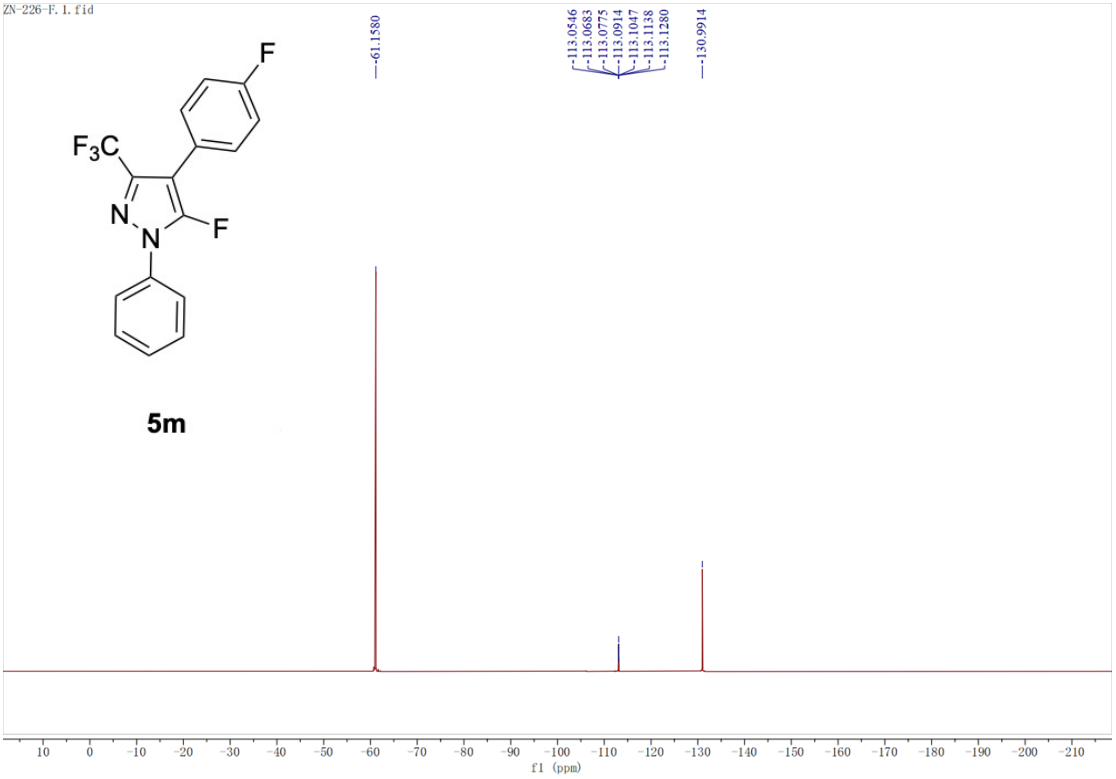


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5l**

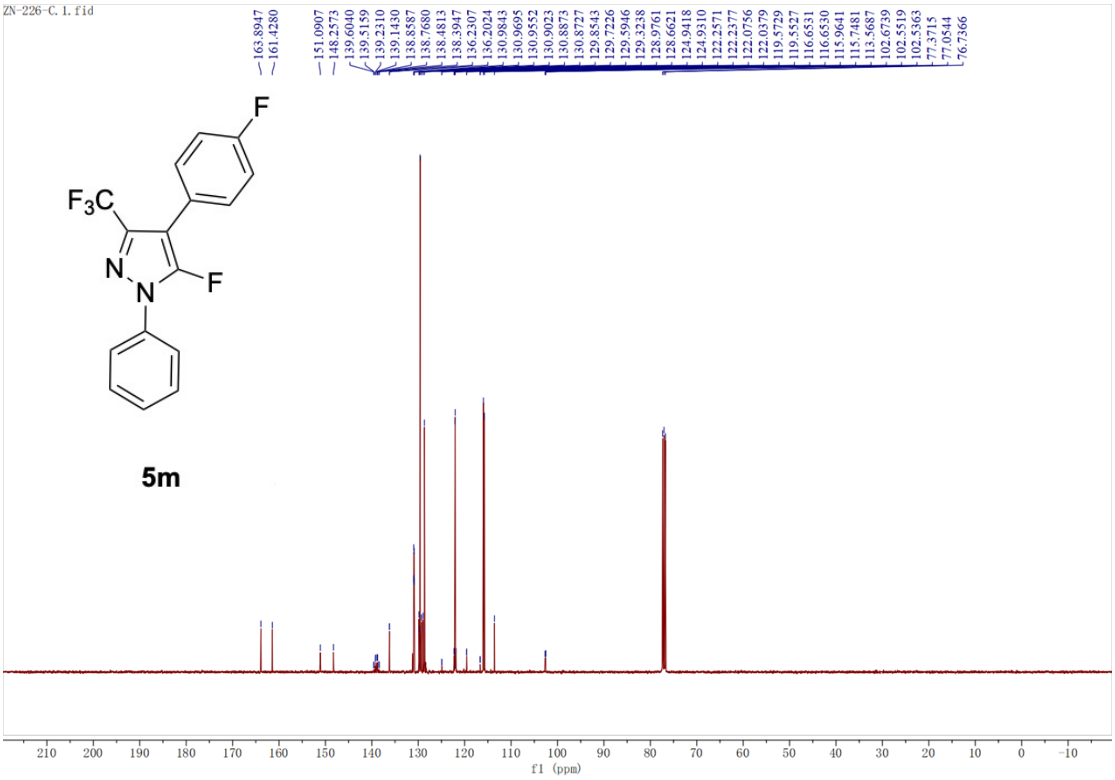
5-Fluoro-4-(4-fluorophenyl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5m)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5m**

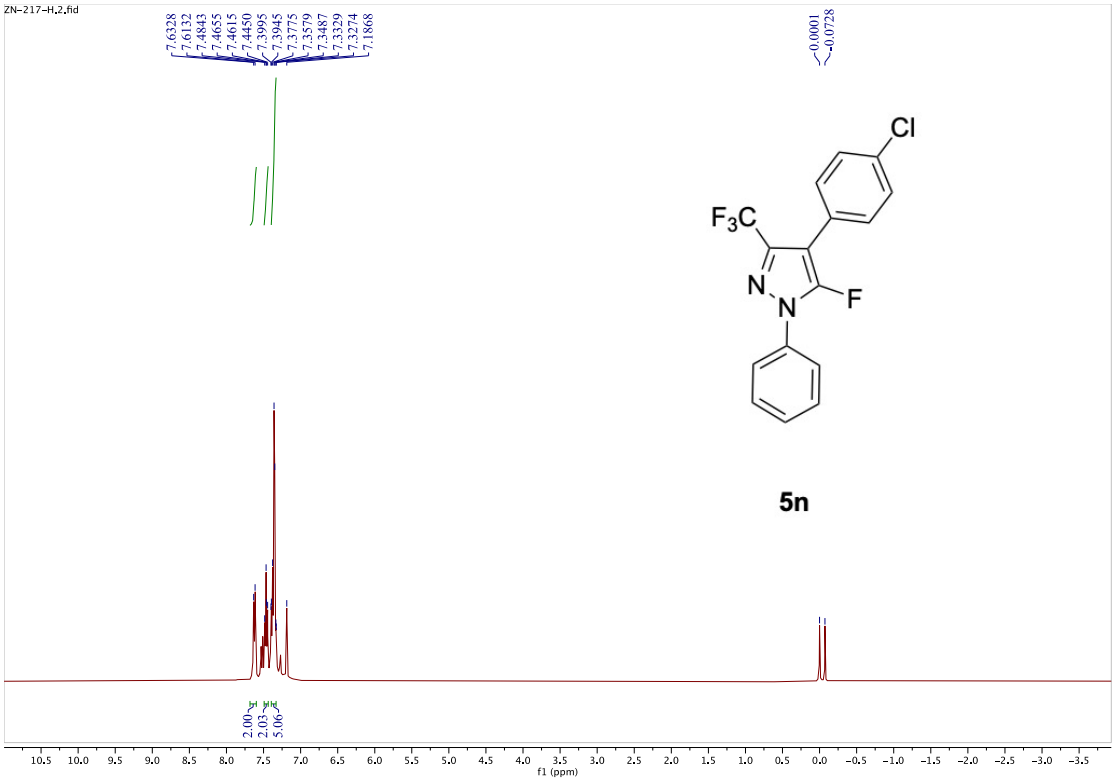


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5m**

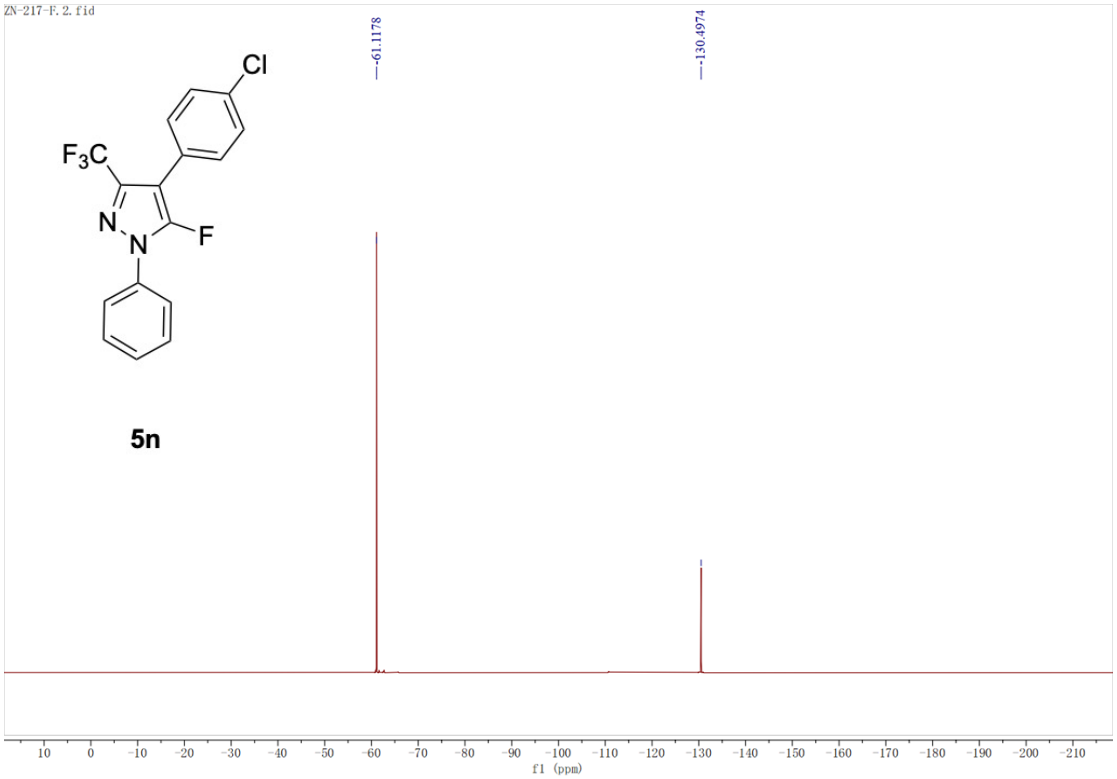


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5m**

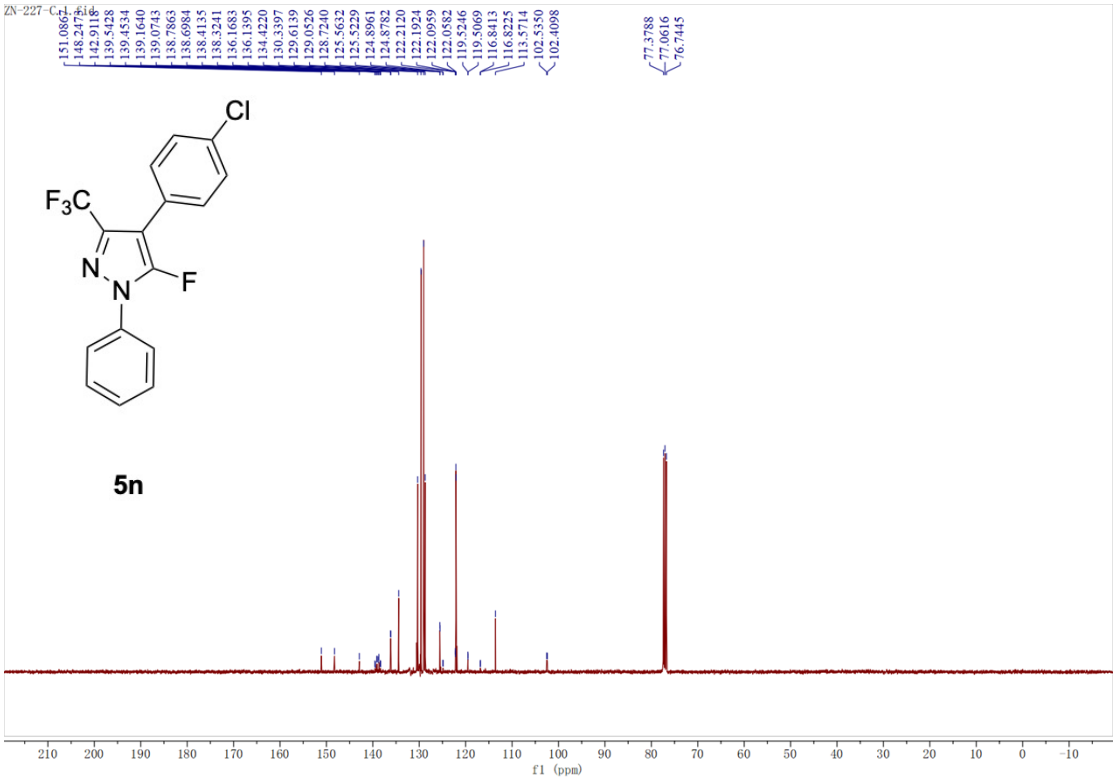
4-(4-Chlorophenyl)-5-fluoro-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5n)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5n**

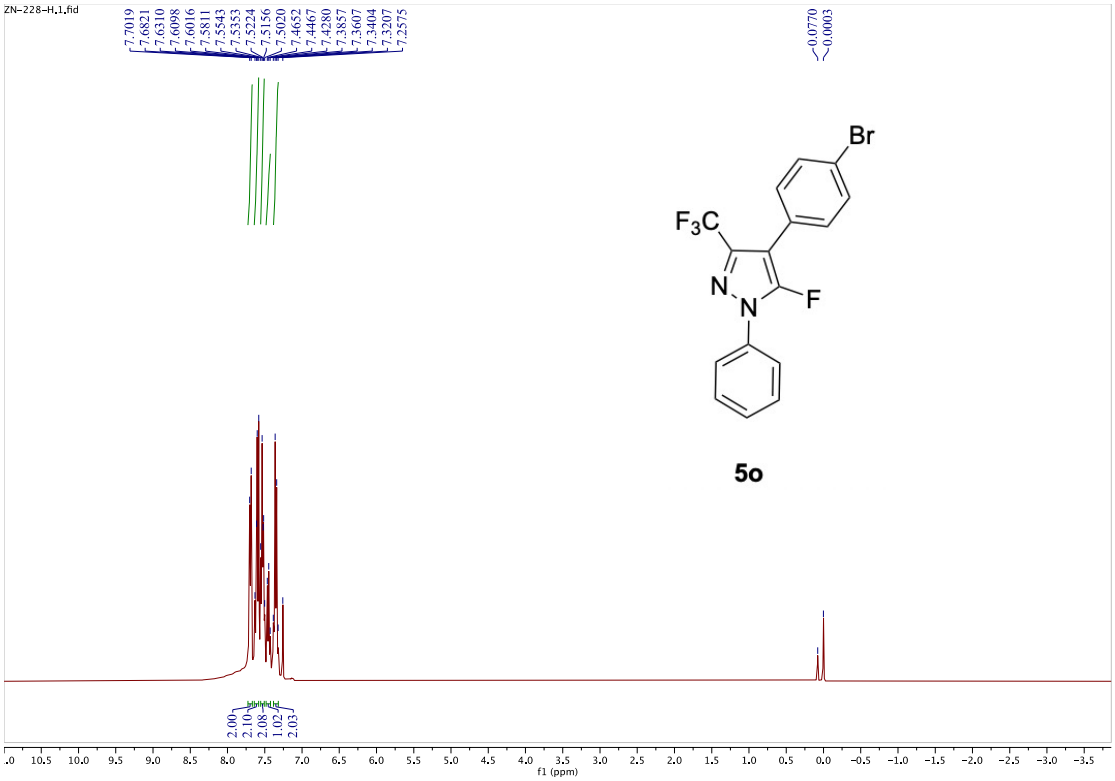


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5n**

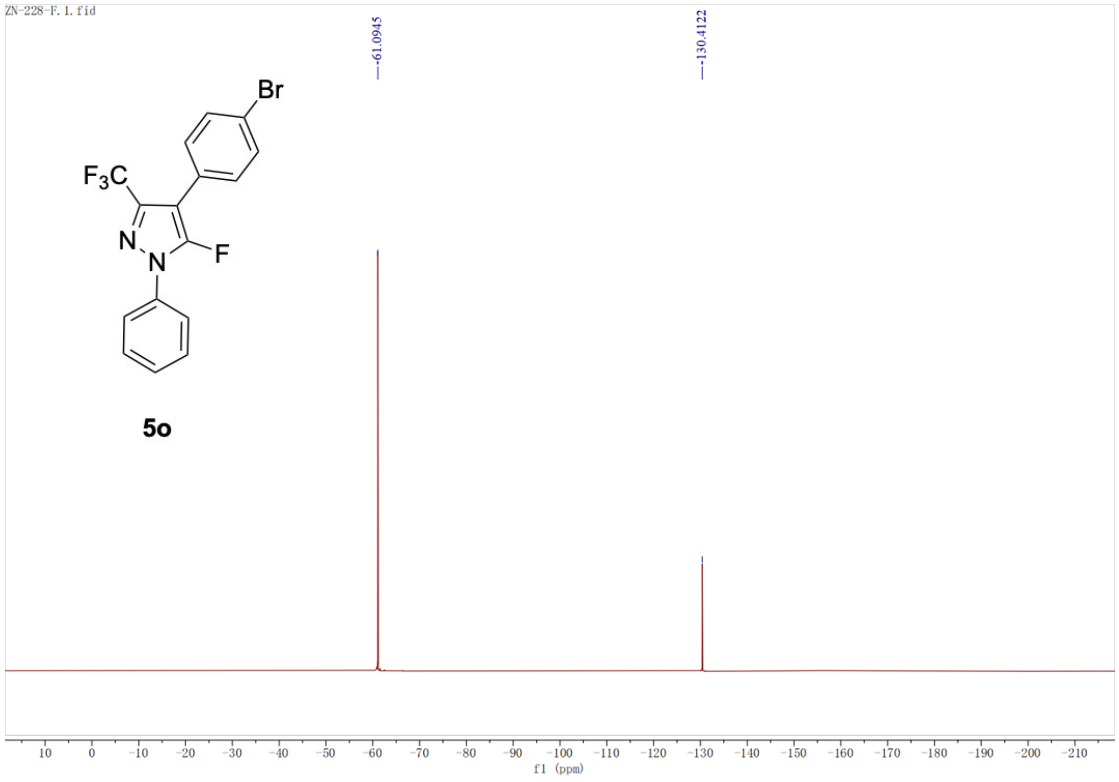


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5n**

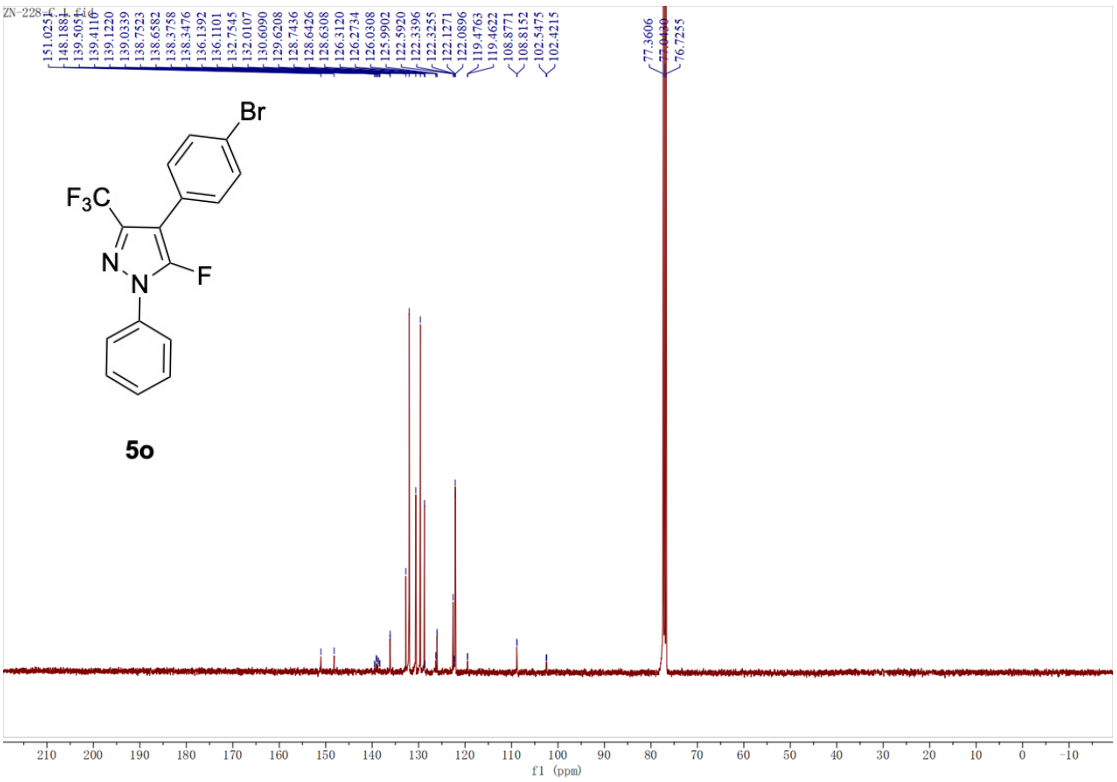
4-(4-Bromophenyl)-5-fluoro-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5o)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5o**

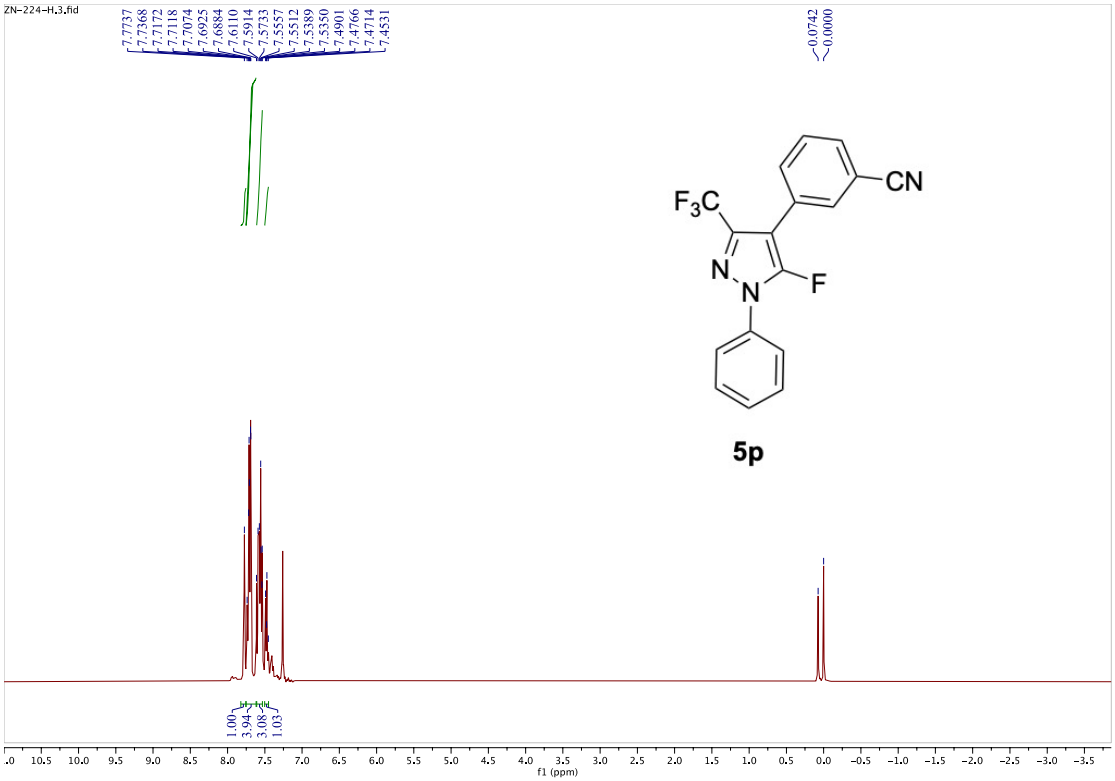


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5o**

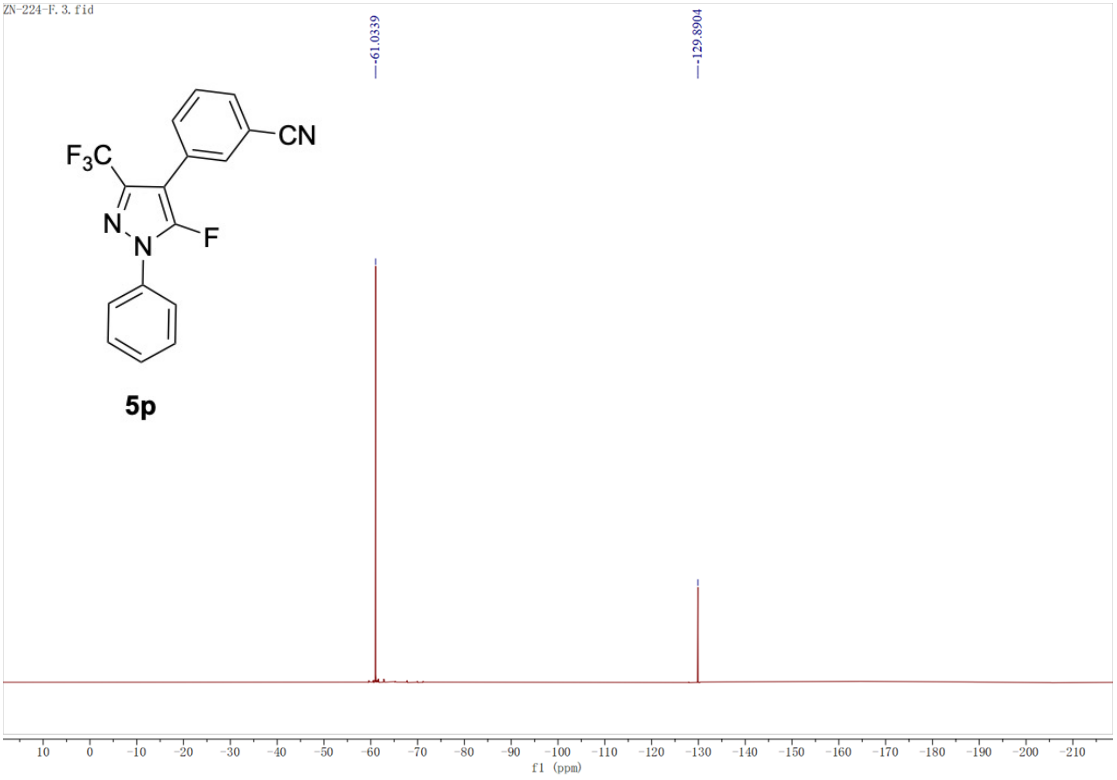


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5o**

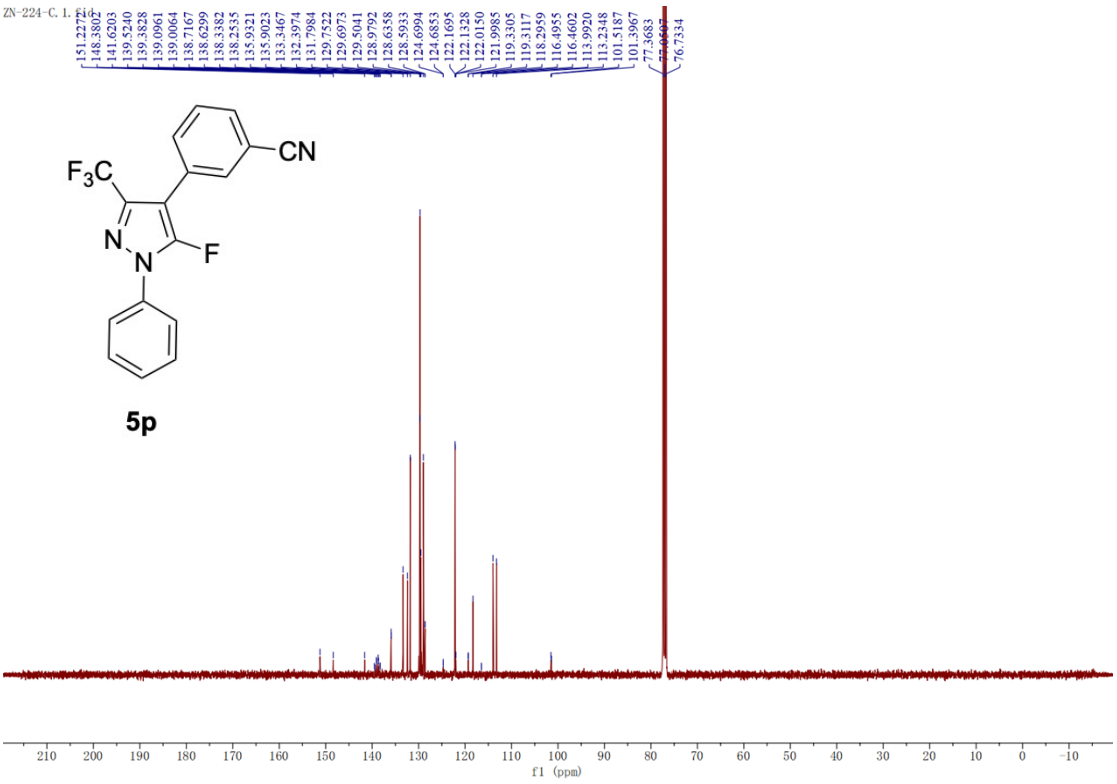
3-(5-Fluoro-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-4-yl)benzonitrile (5p)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5p**

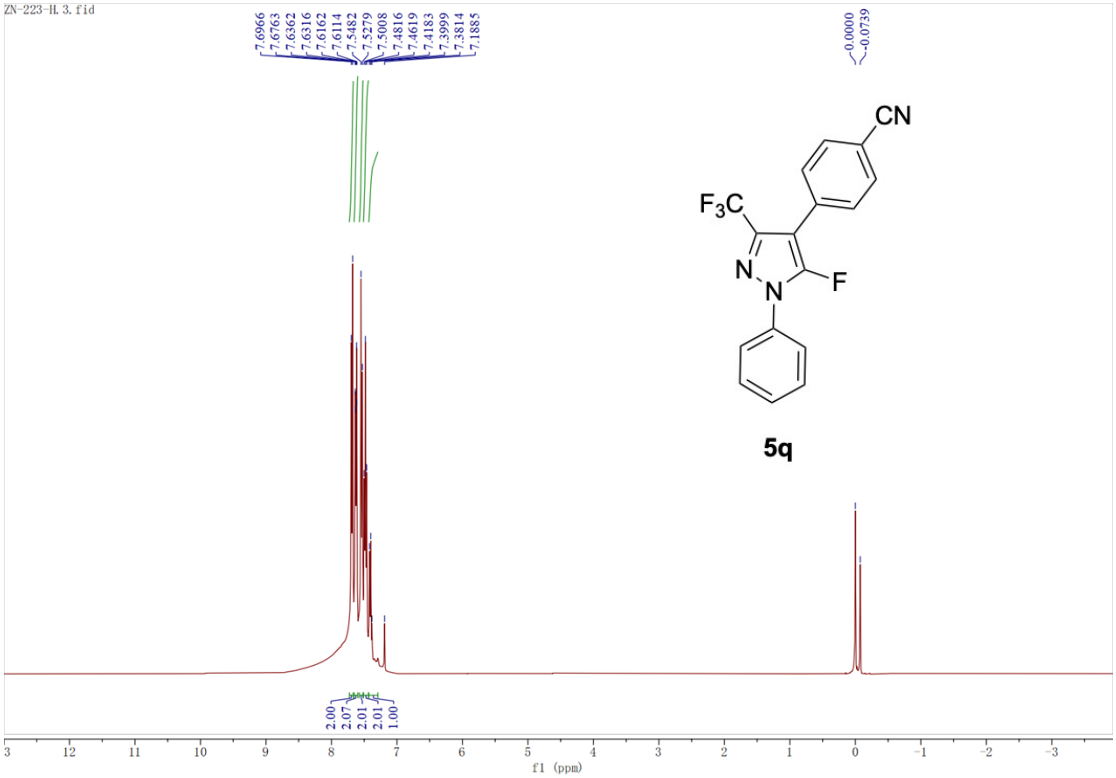


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5p**

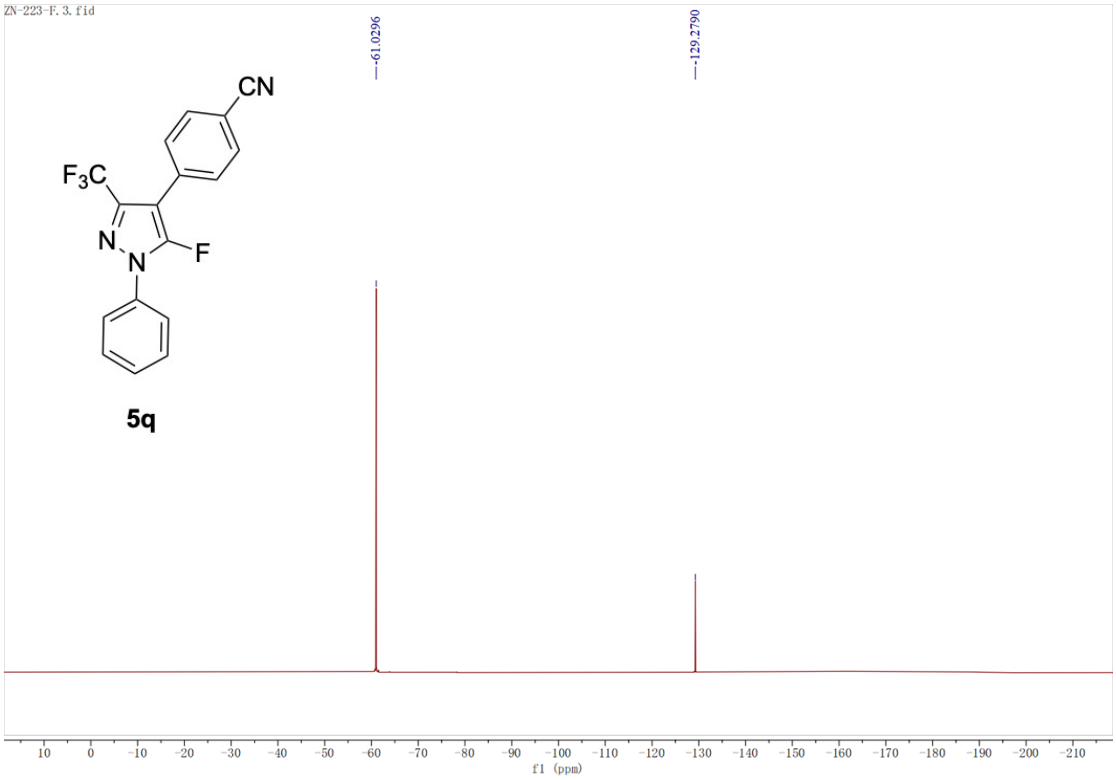


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5p**

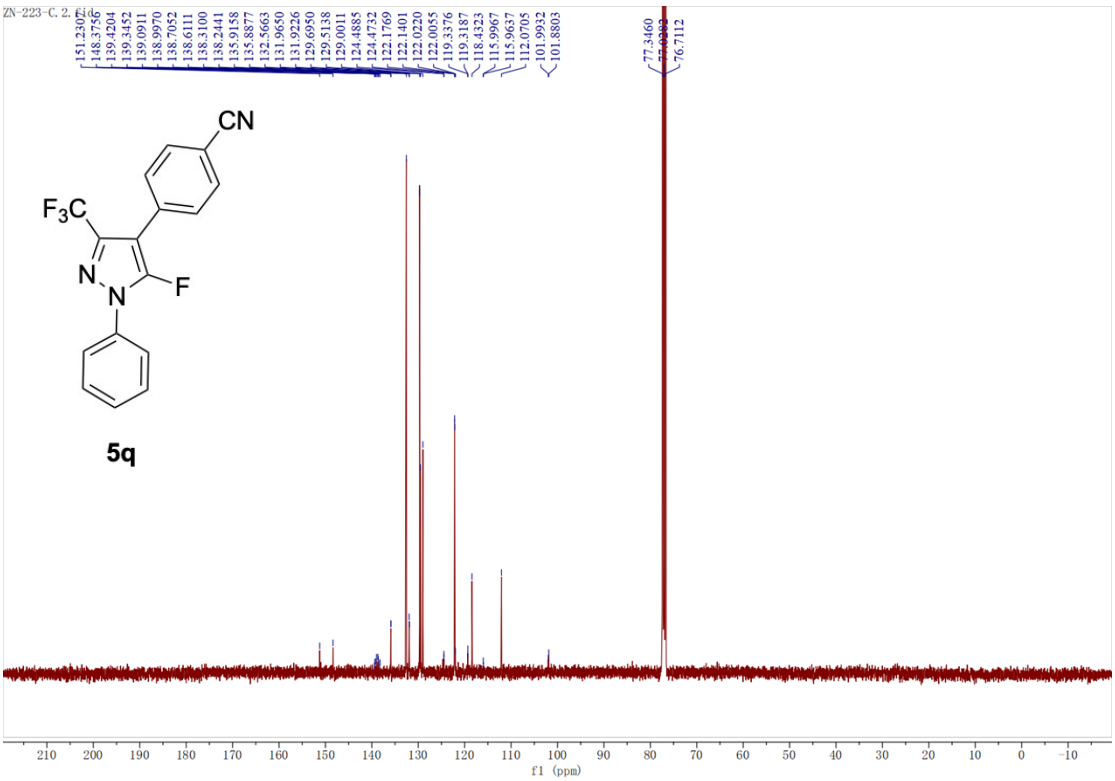
4-(5-Fluoro-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-4-yl)benzonitrile (5q)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5q**

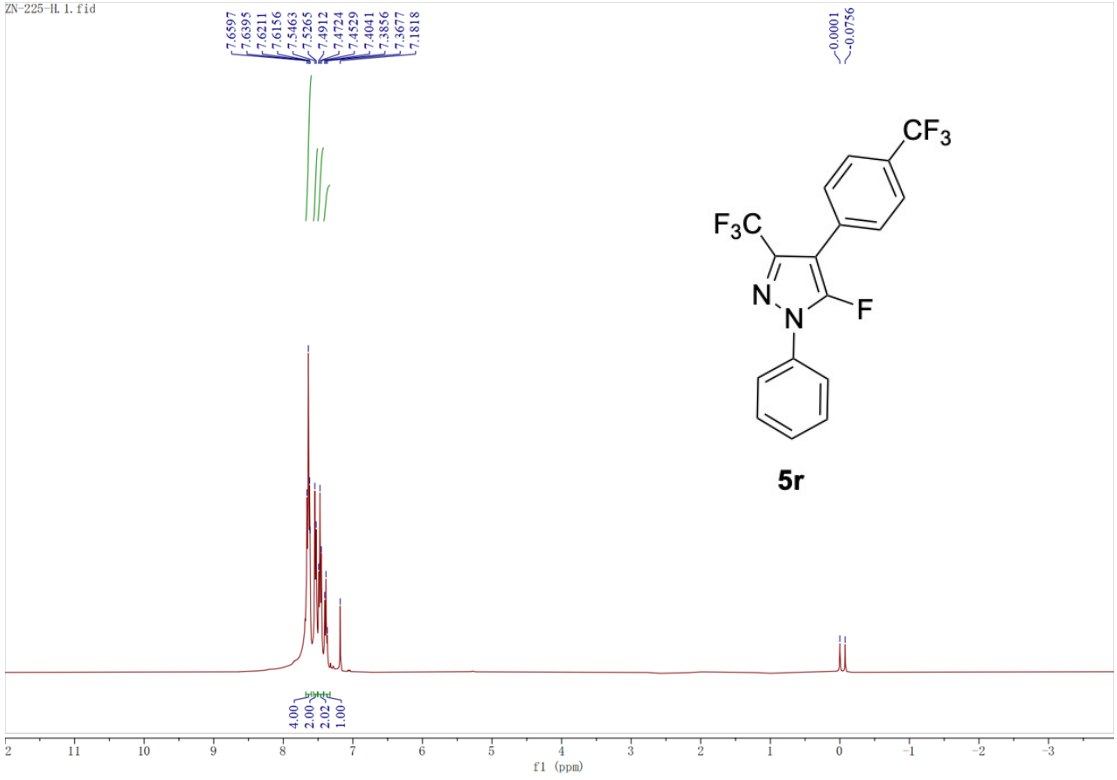


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5q**

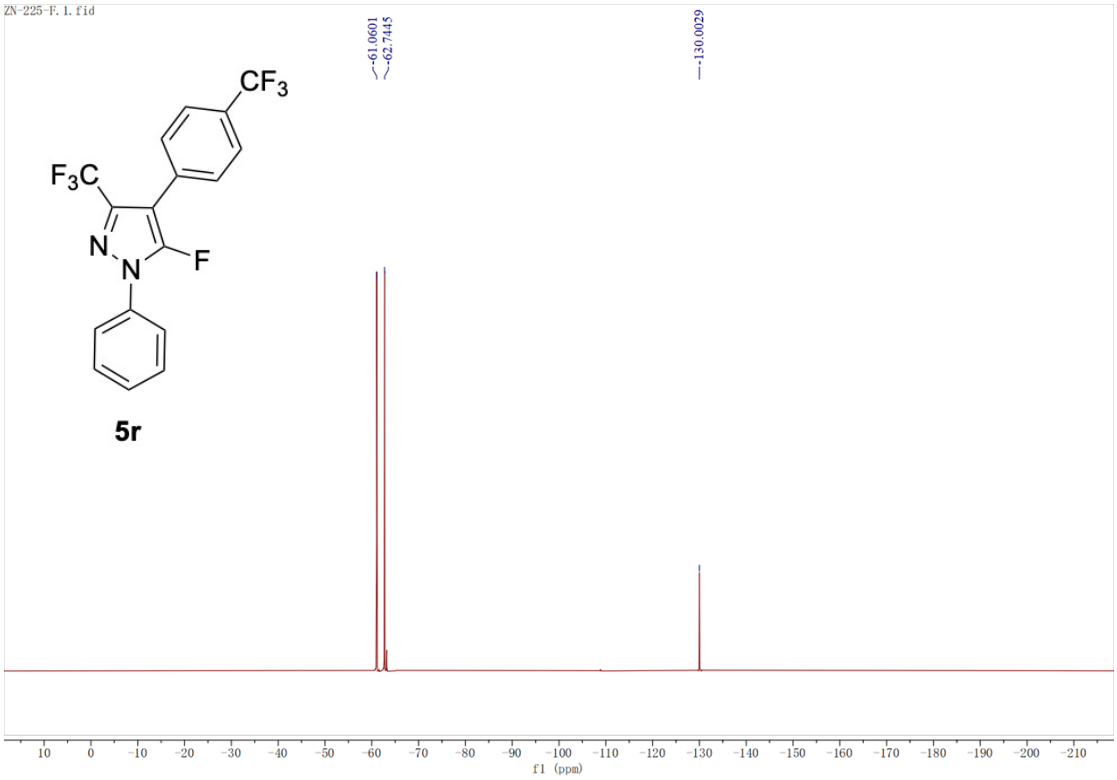


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5q**

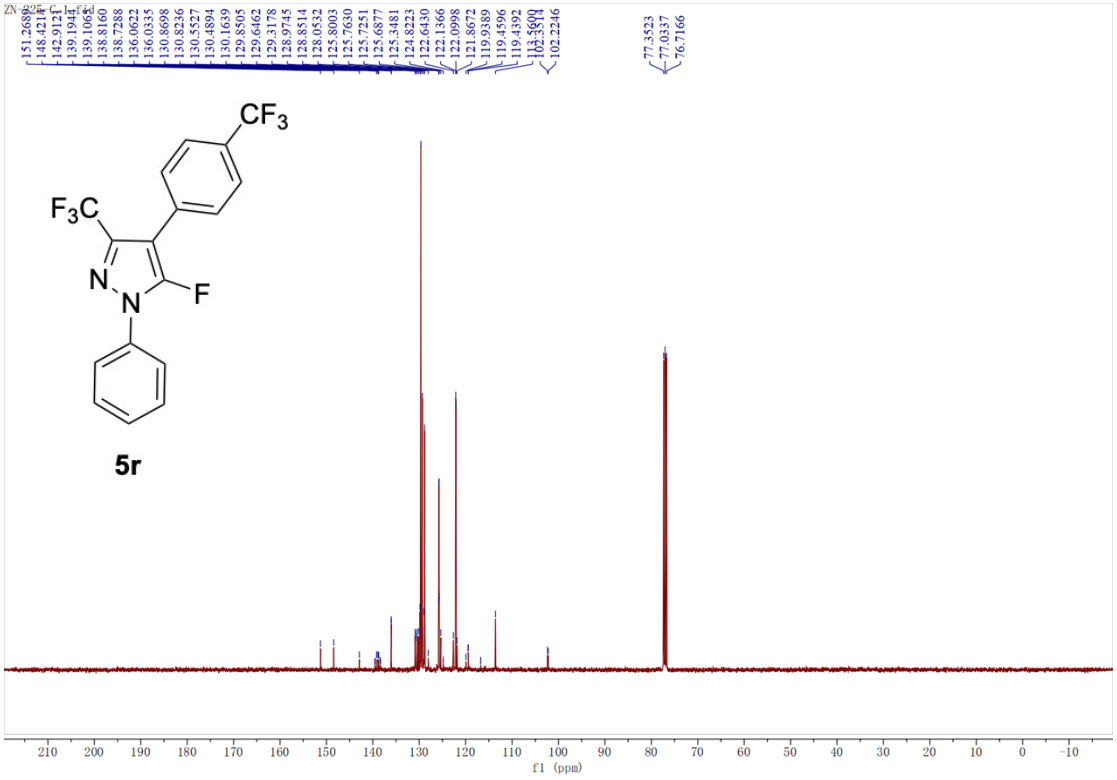
5-Fluoro-1-phenyl-3-(trifluoromethyl)-4-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (5r)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5r**

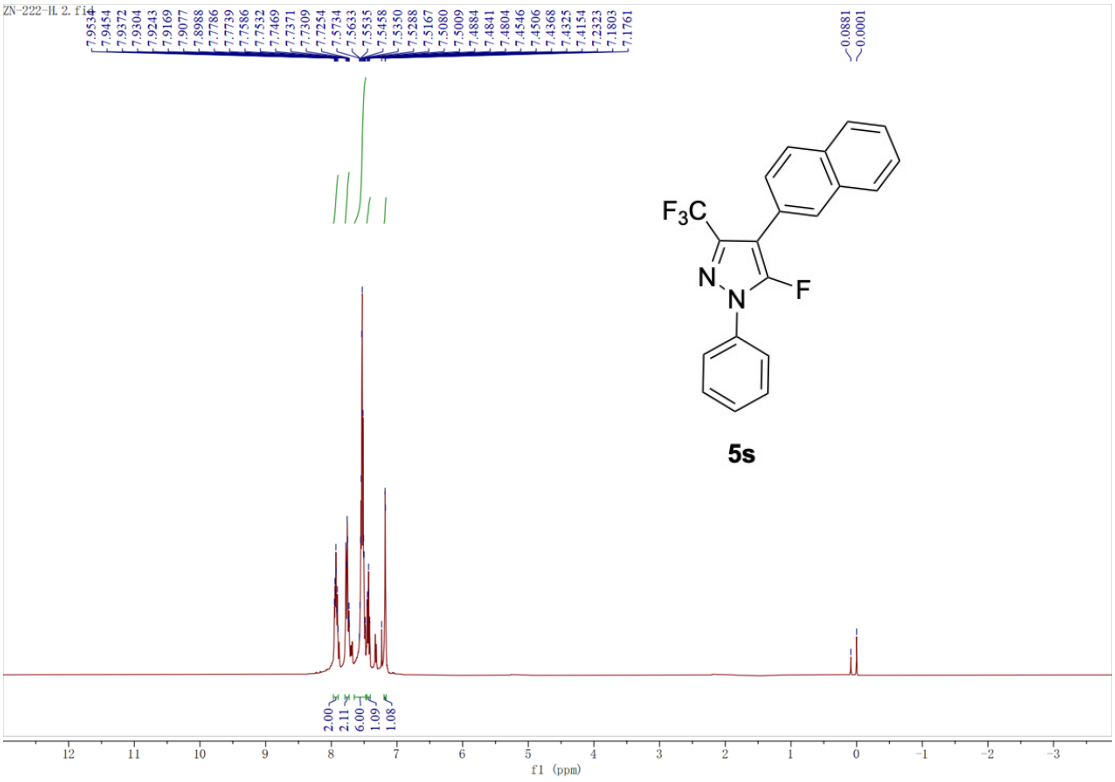


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5r**

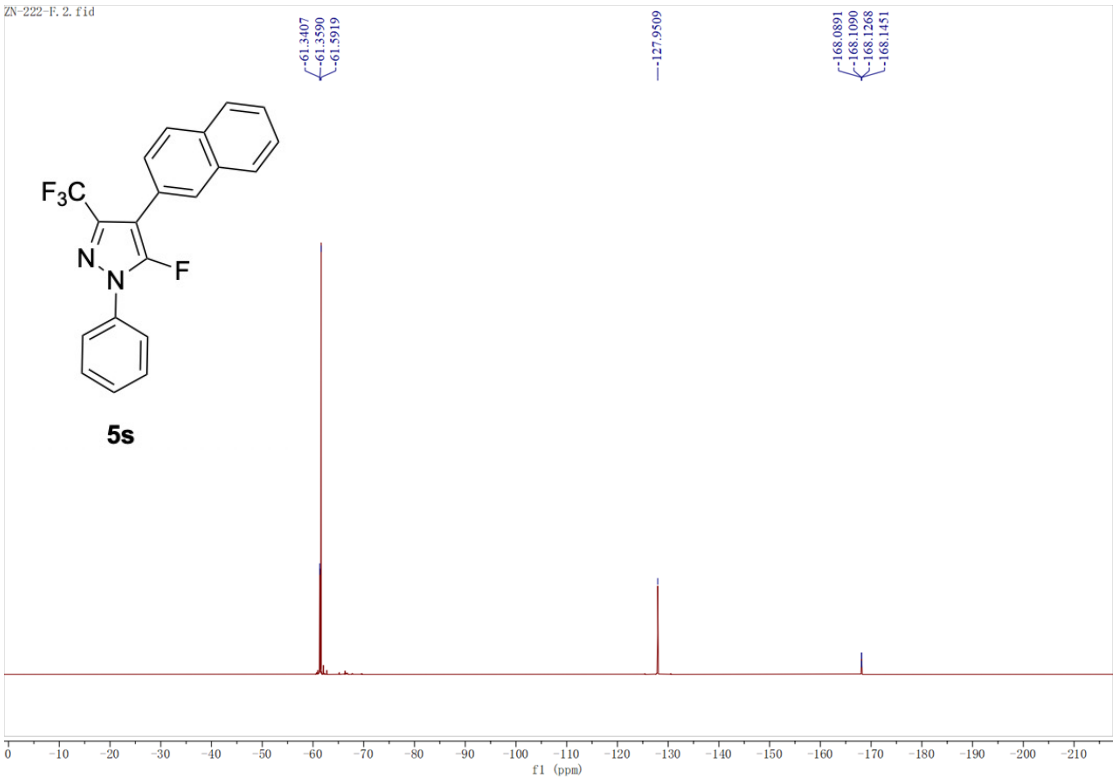


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5r**

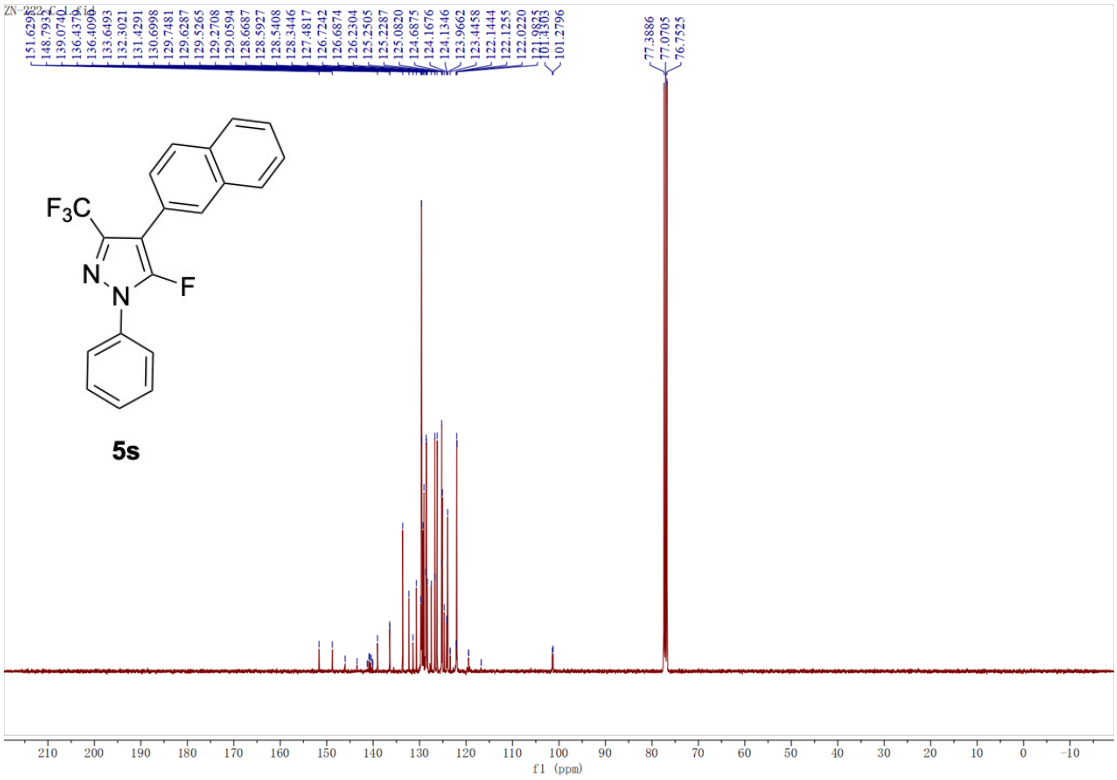
5-Fluoro-4-(naphthalen-2-yl)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole (5s)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5s**

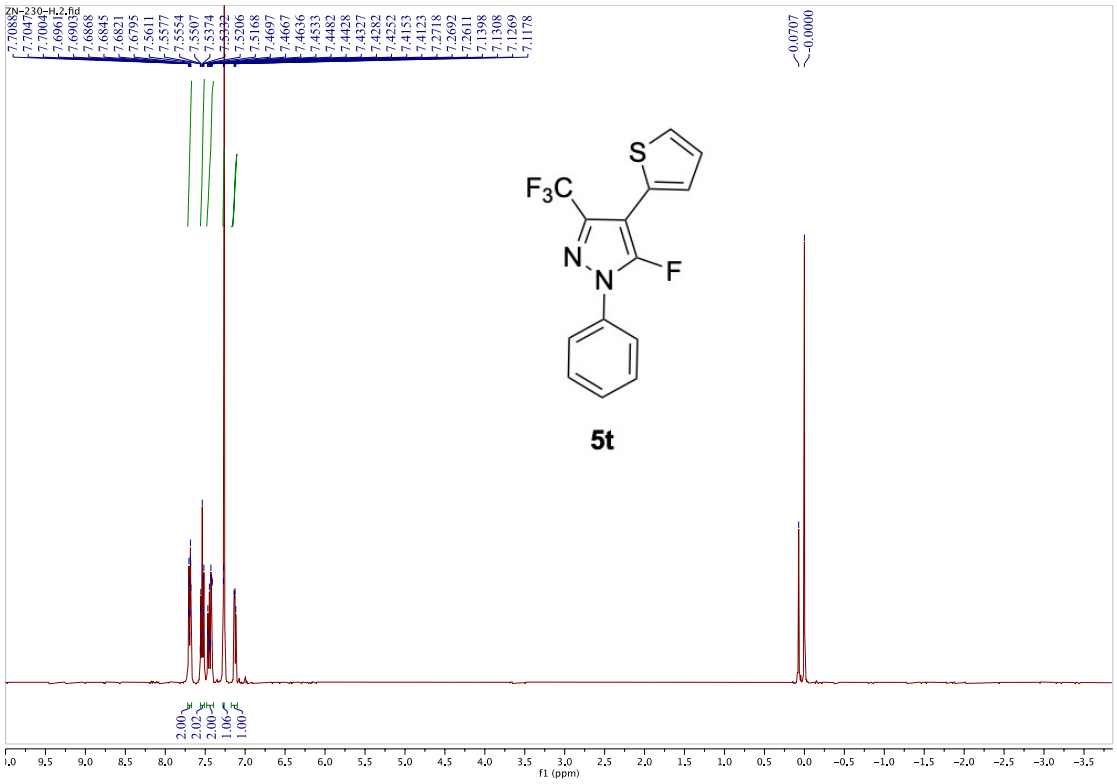


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5s**

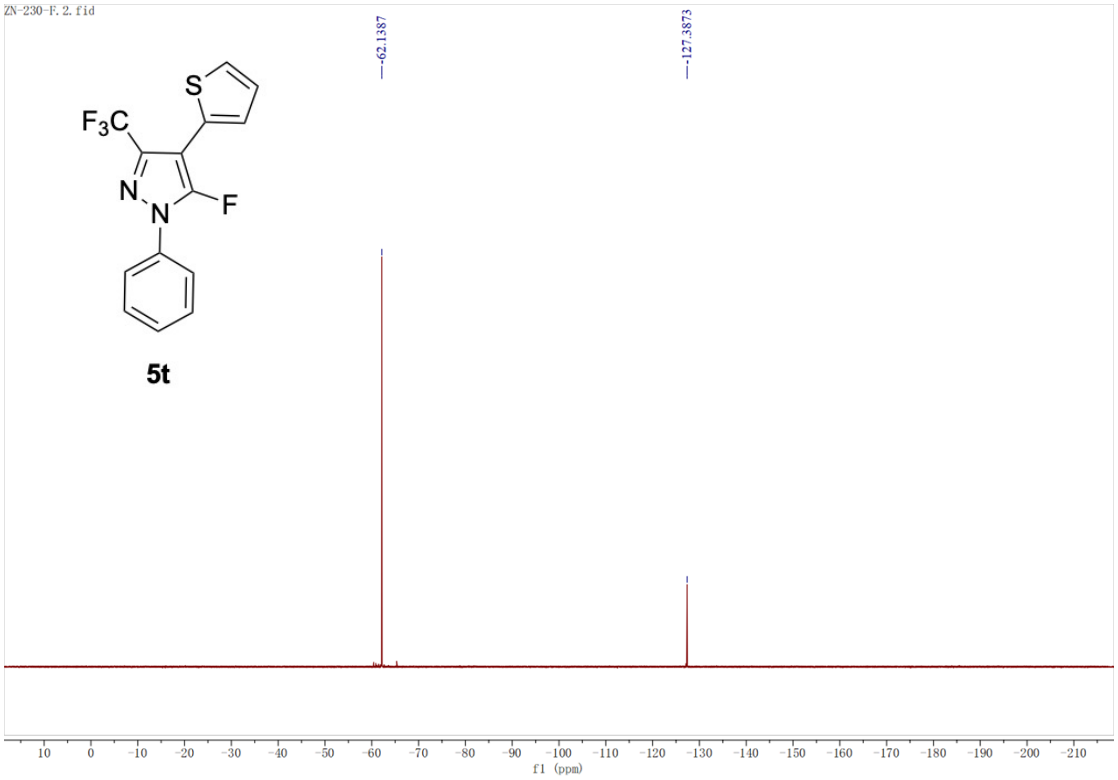


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5s**

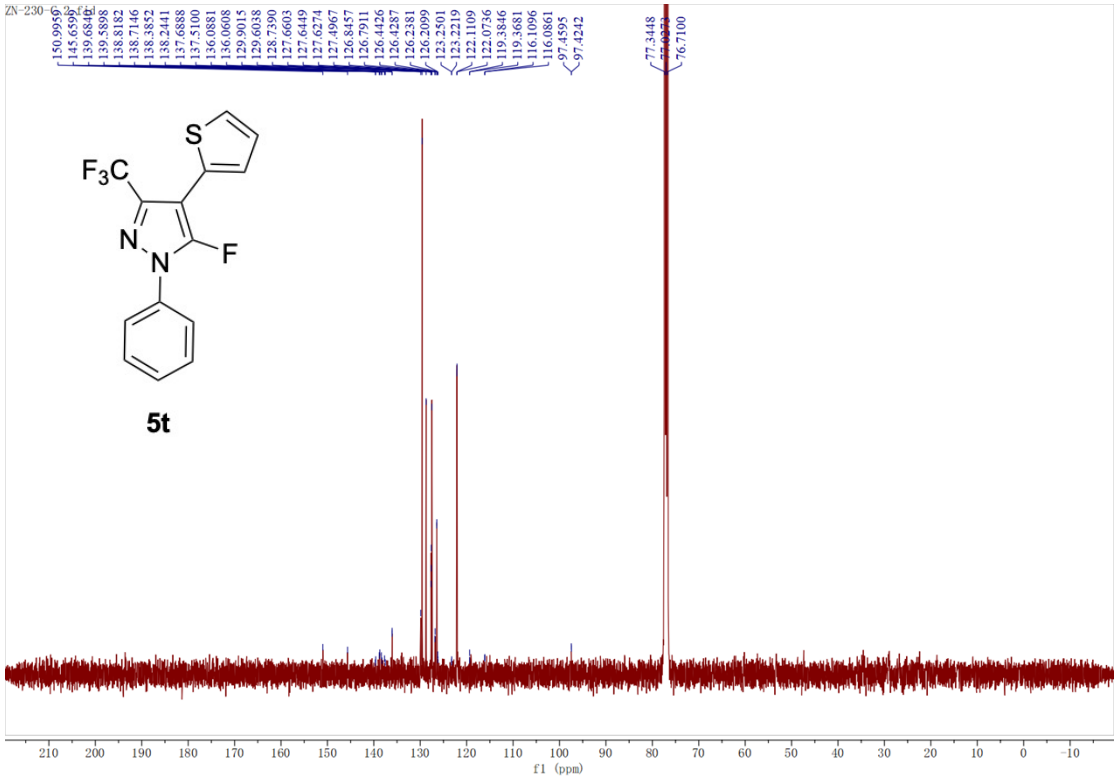
5-Fluoro-1-phenyl-4-(thiophen-2-yl)-3-(trifluoromethyl)-1*H*-pyrazole (5t)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **5t**

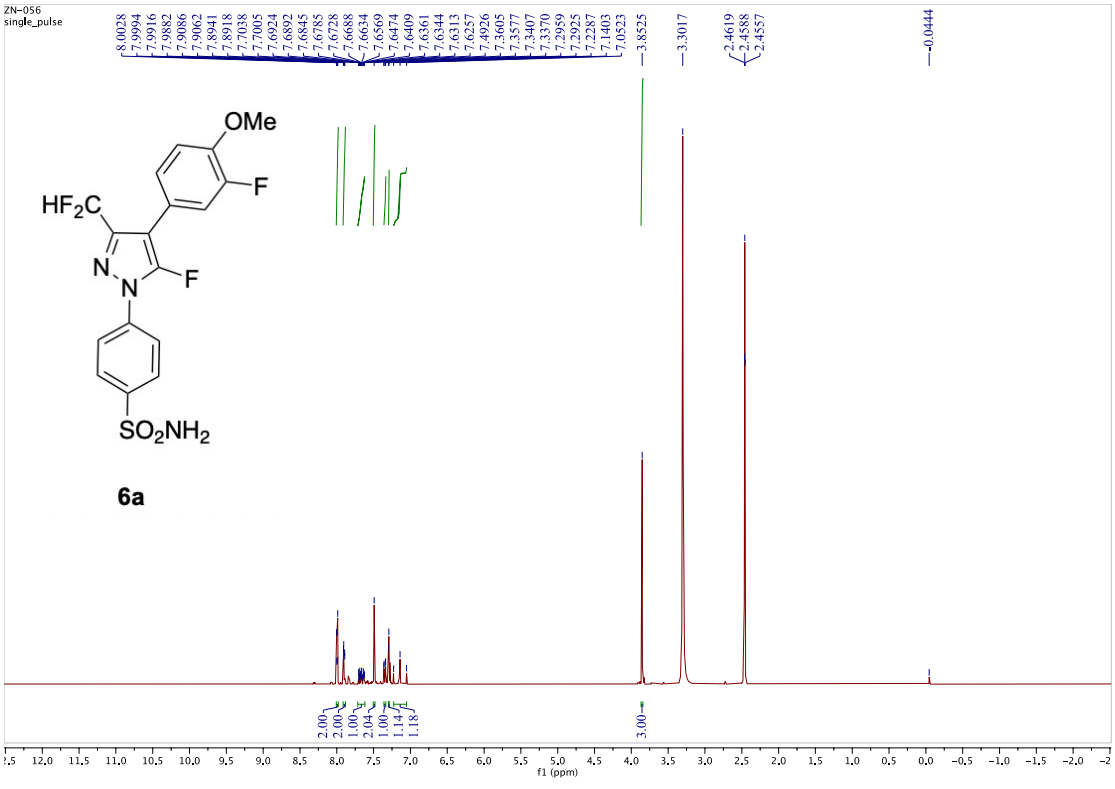


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **5t**

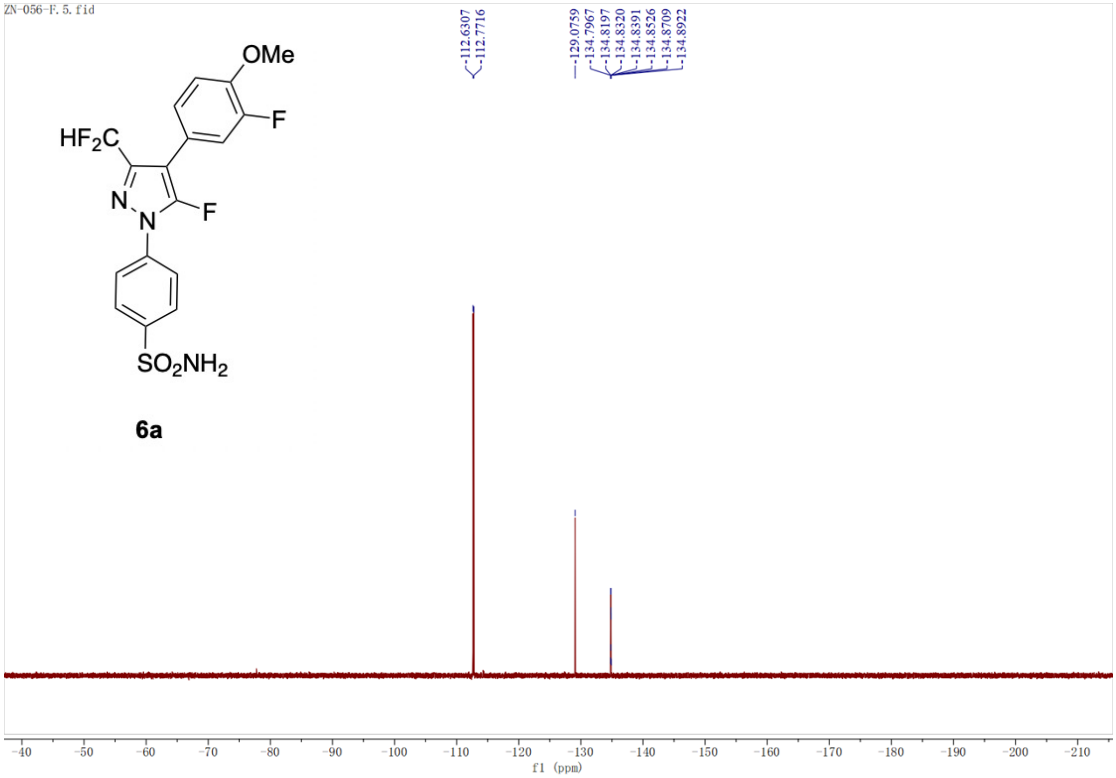


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **5t**

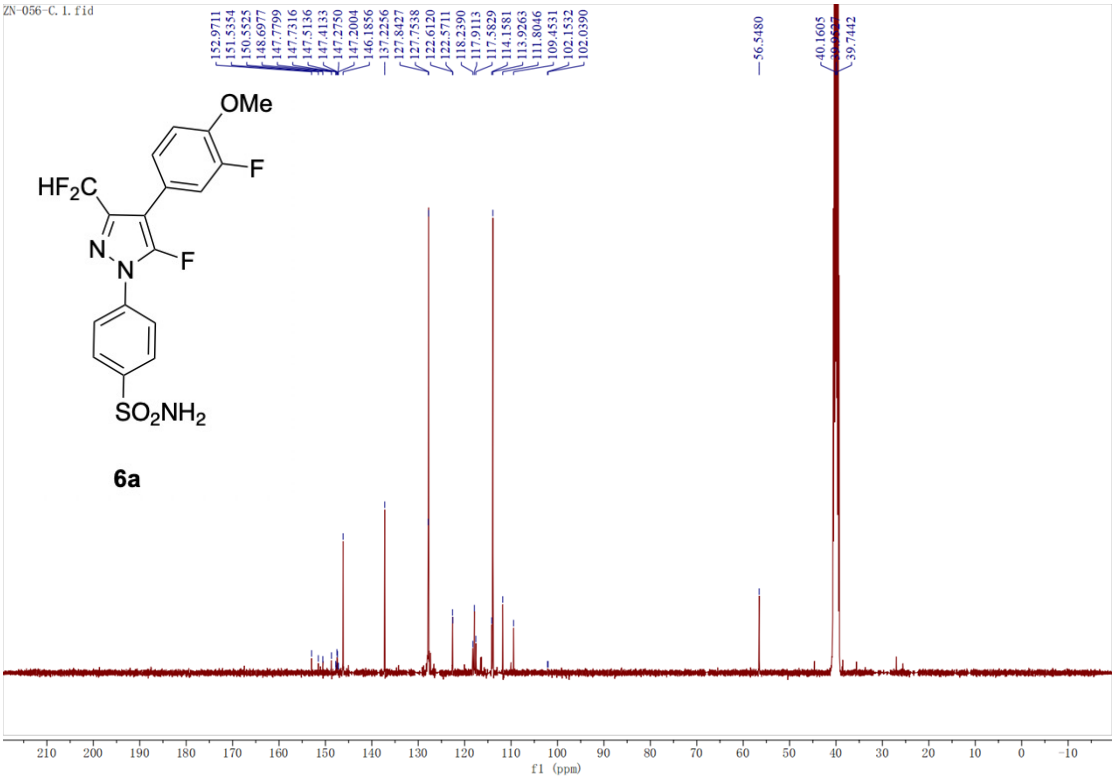
4-(3-(Difluoromethyl)-5-fluoro-4-(3-fluoro-4-methoxyphenyl)-1*H*-pyrazol-1-yl)be-nzenesulfonamide (6a)



^{1}H NMR spectrum (600 MHz, d_6-DMSO) of **6a**

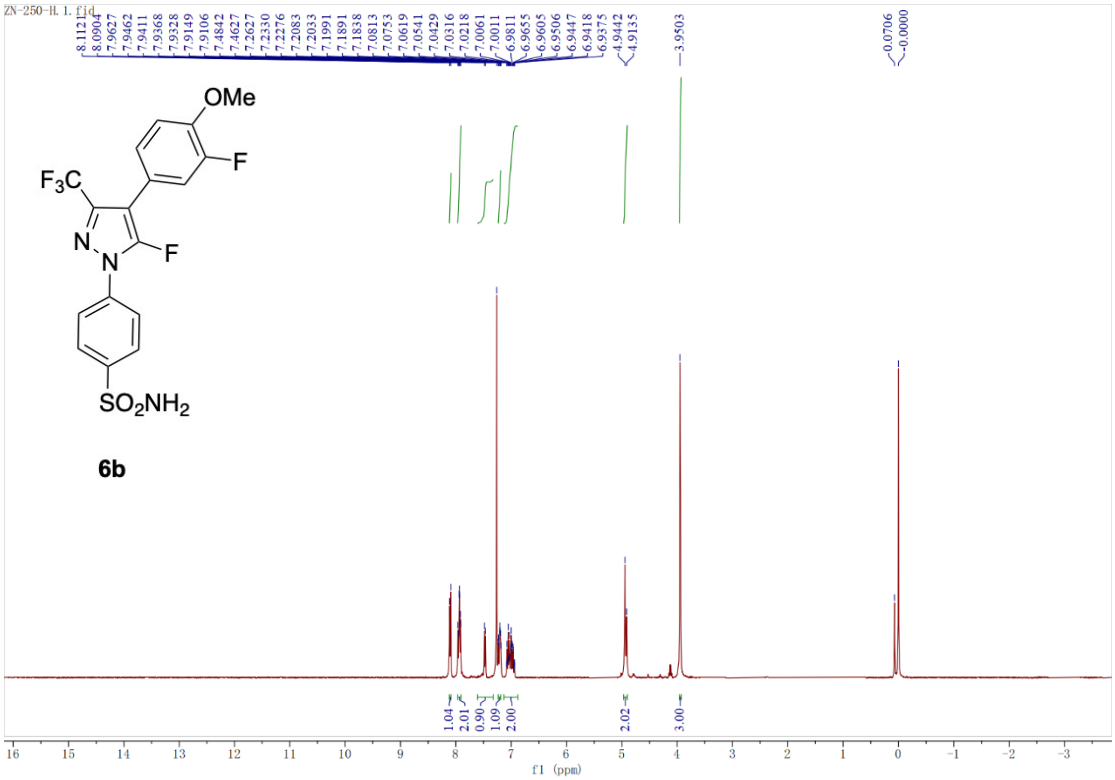


^{19}F NMR spectrum (376 MHz, d_6-DMSO) of **6a**

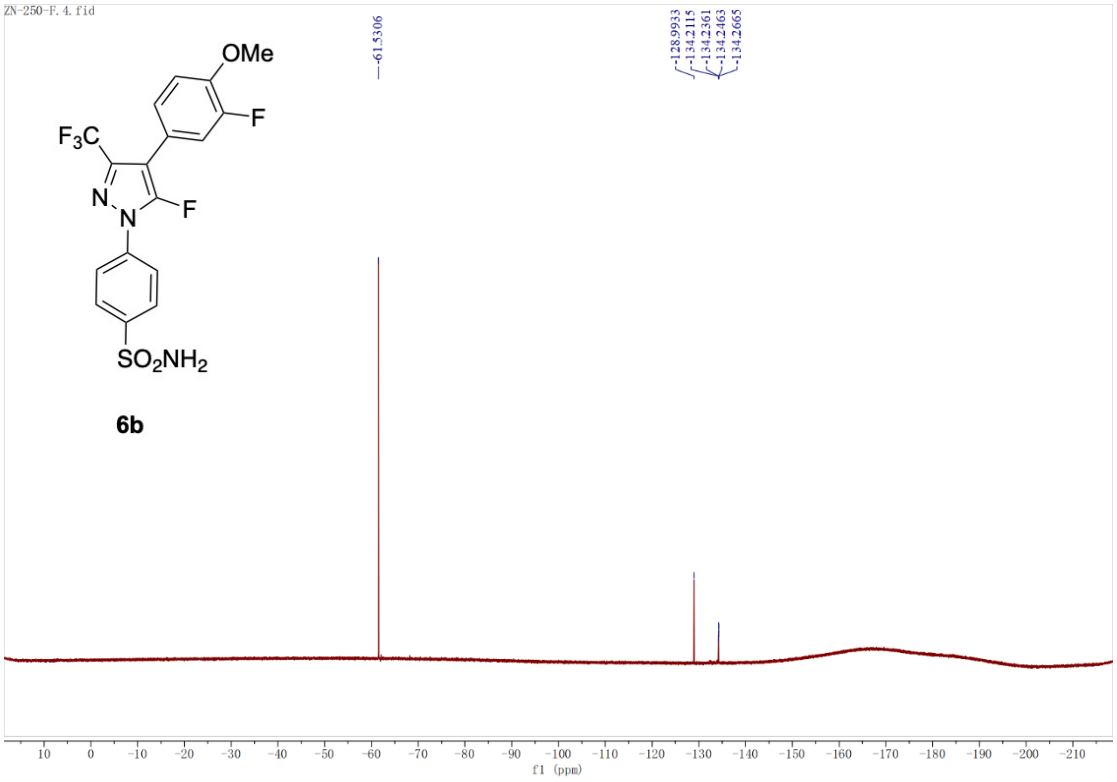


^{13}C NMR spectrum (100 MHz, d_6-DMSO) of **6a**

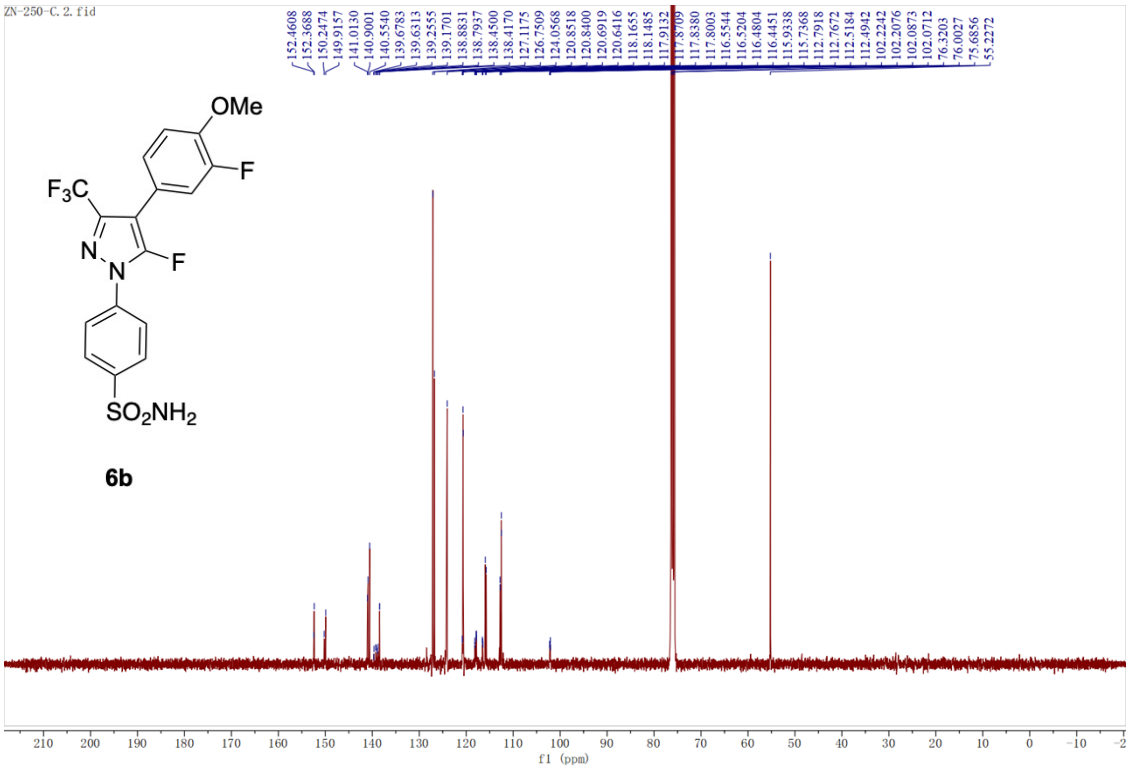
4-(5-Fluoro-4-(3-fluoro-4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide (6b)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **6b**

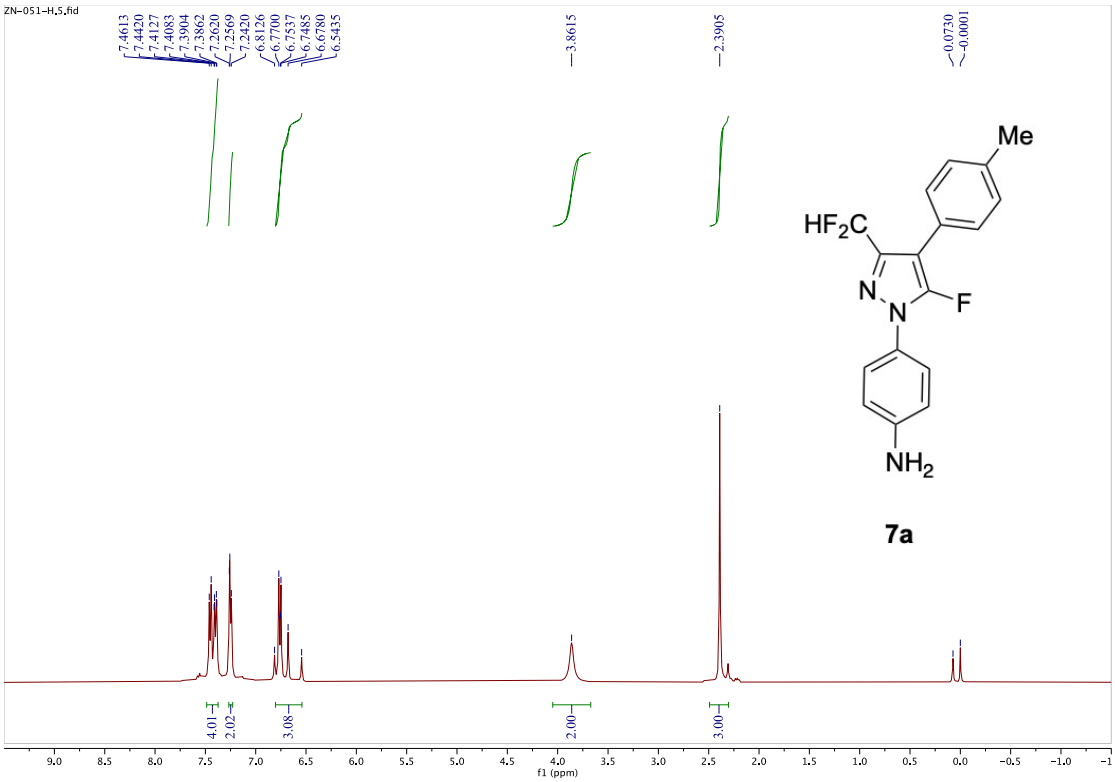


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **6b**

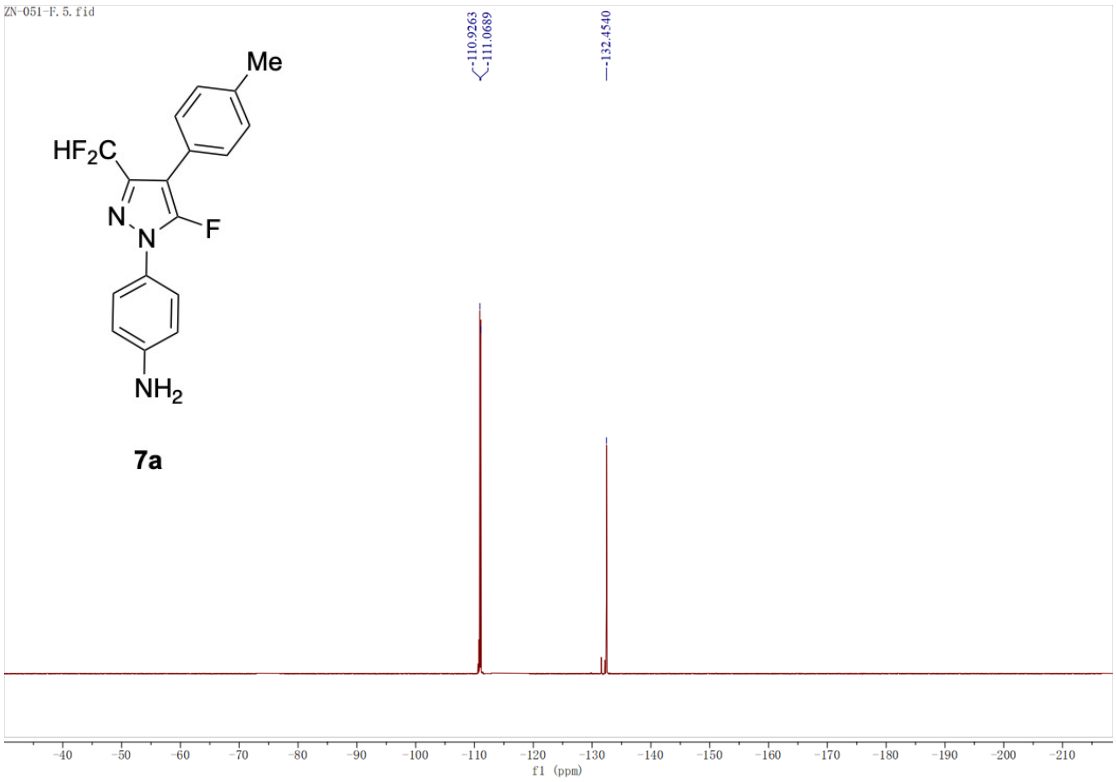


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **6b**

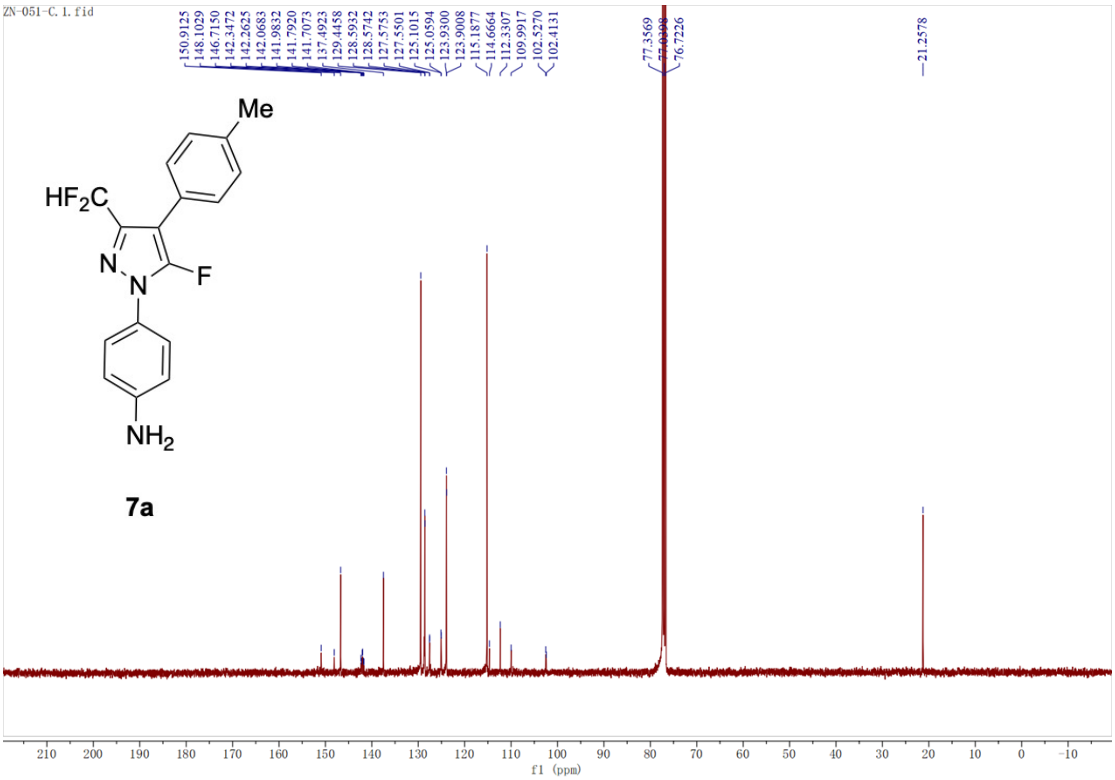
4-(3-(Difluoromethyl)-5-fluoro-4-(*p*-tolyl)-1*H*-pyrazol-1-yl)aniline (7a)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **7a**

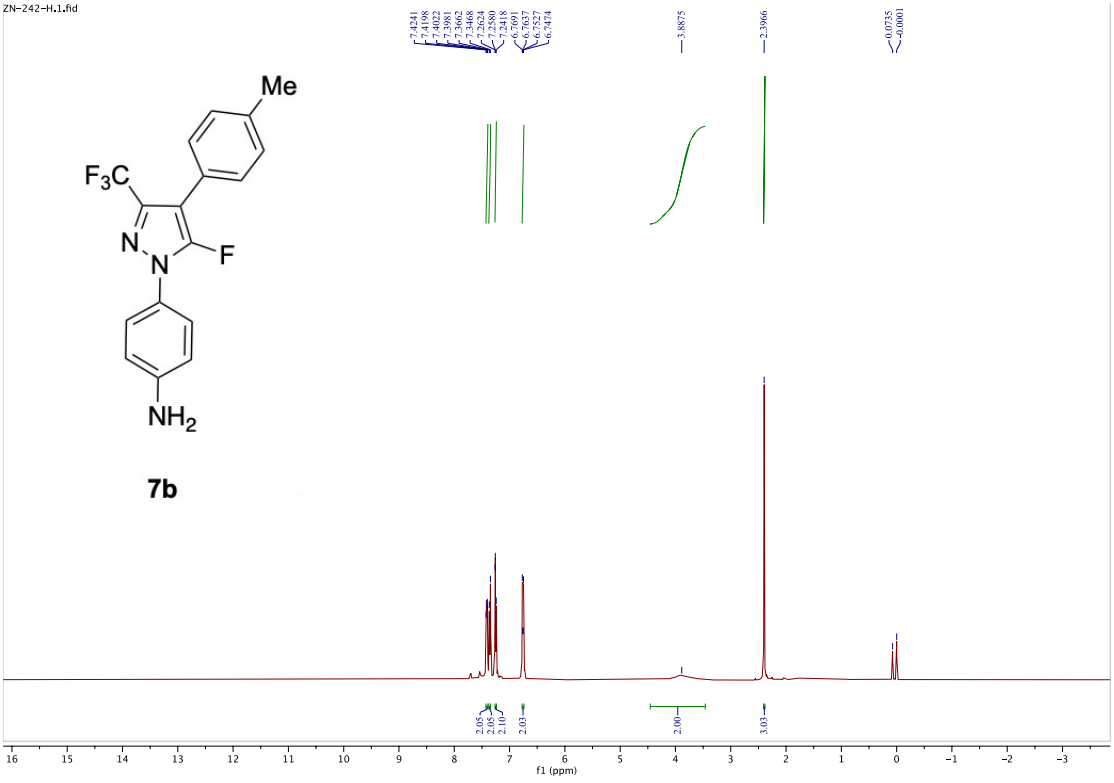


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **7a**

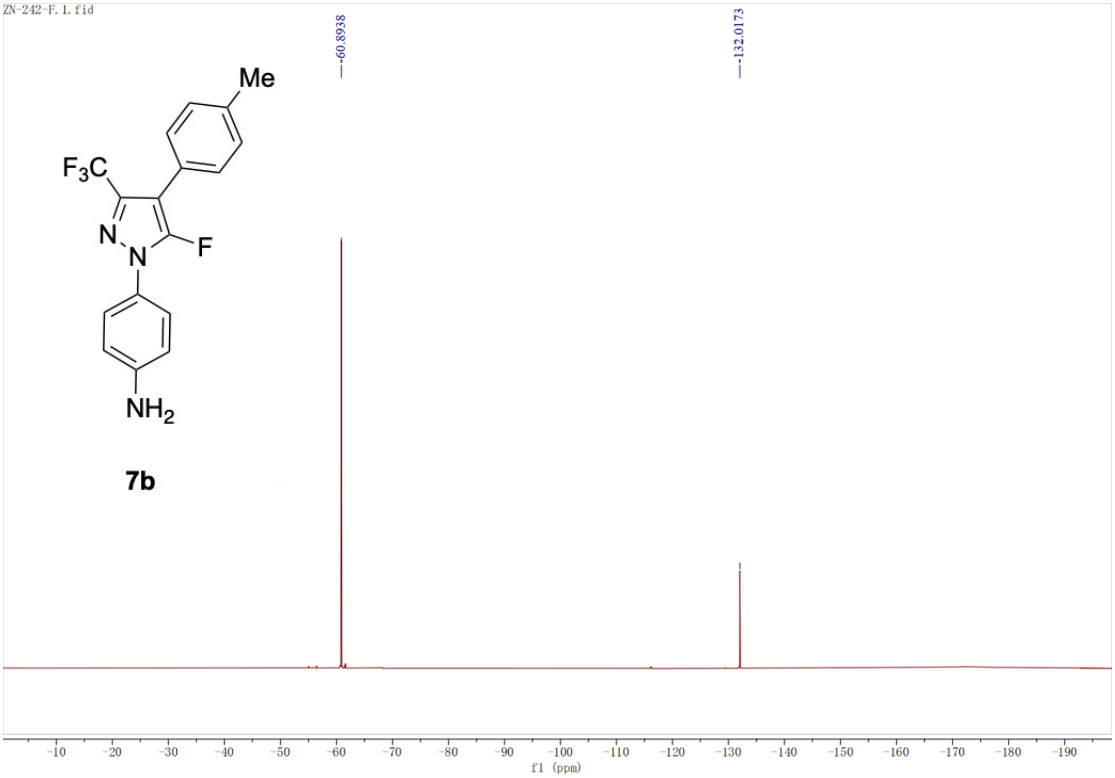


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **7a**

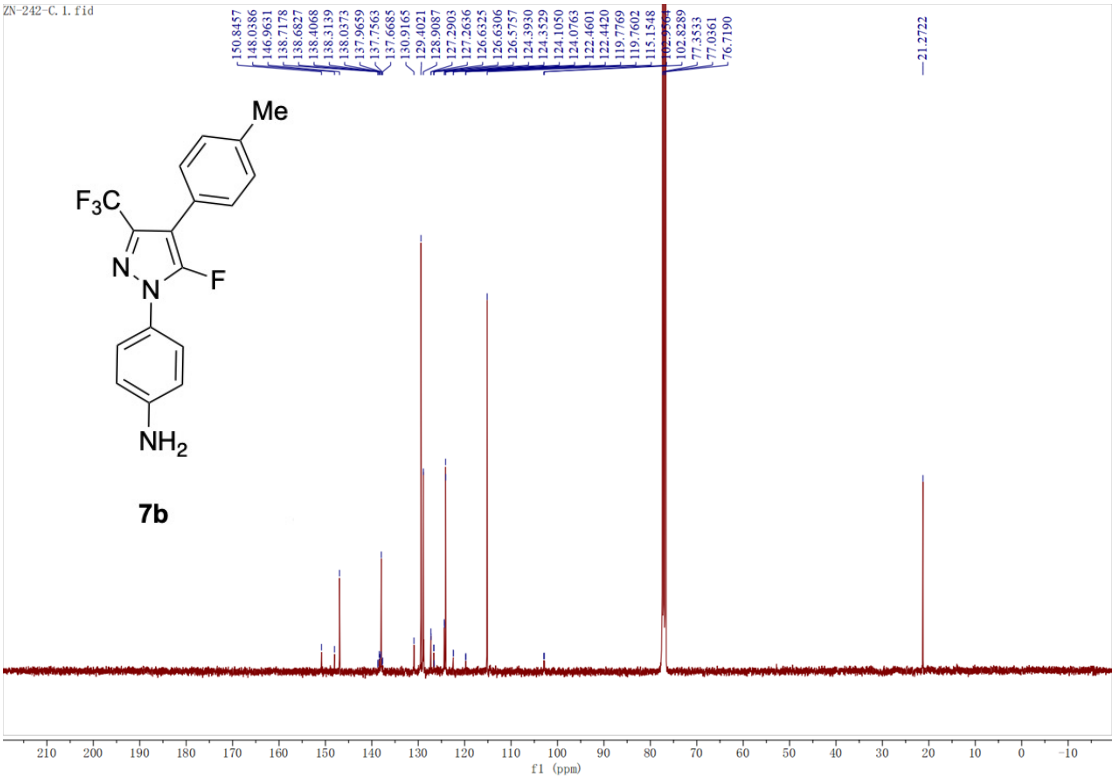
4-(5-Fluoro-4-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)aniline (7b)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **7b**

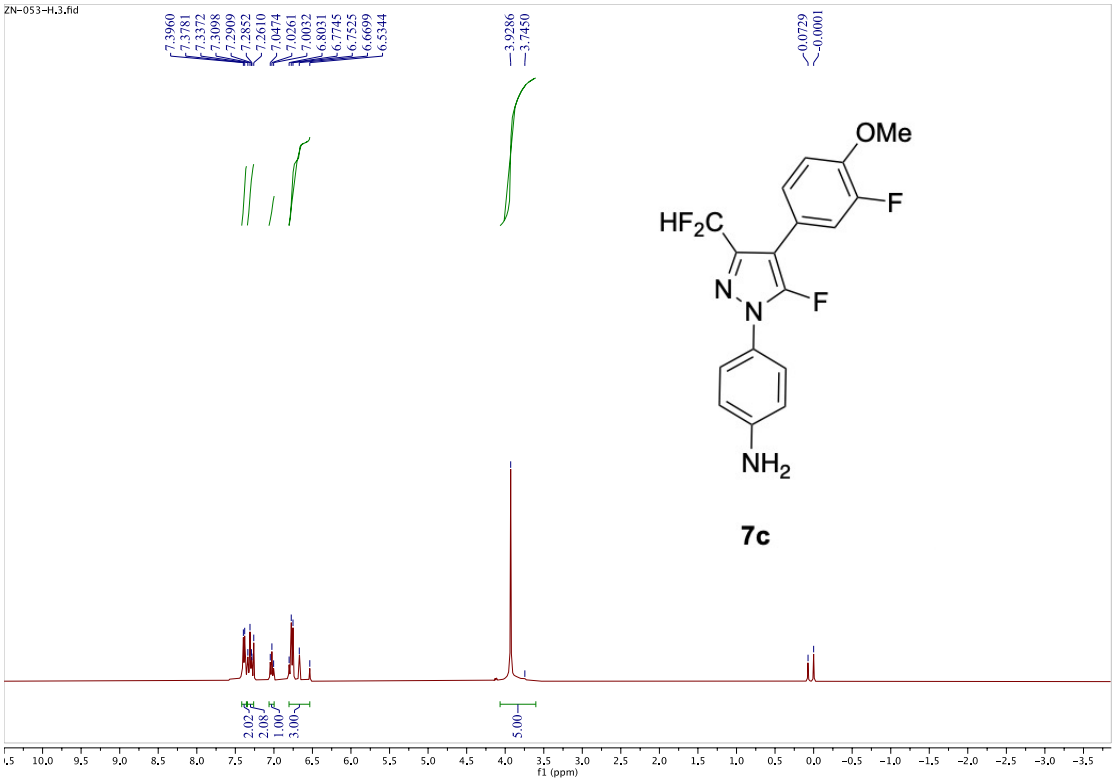


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **7b**

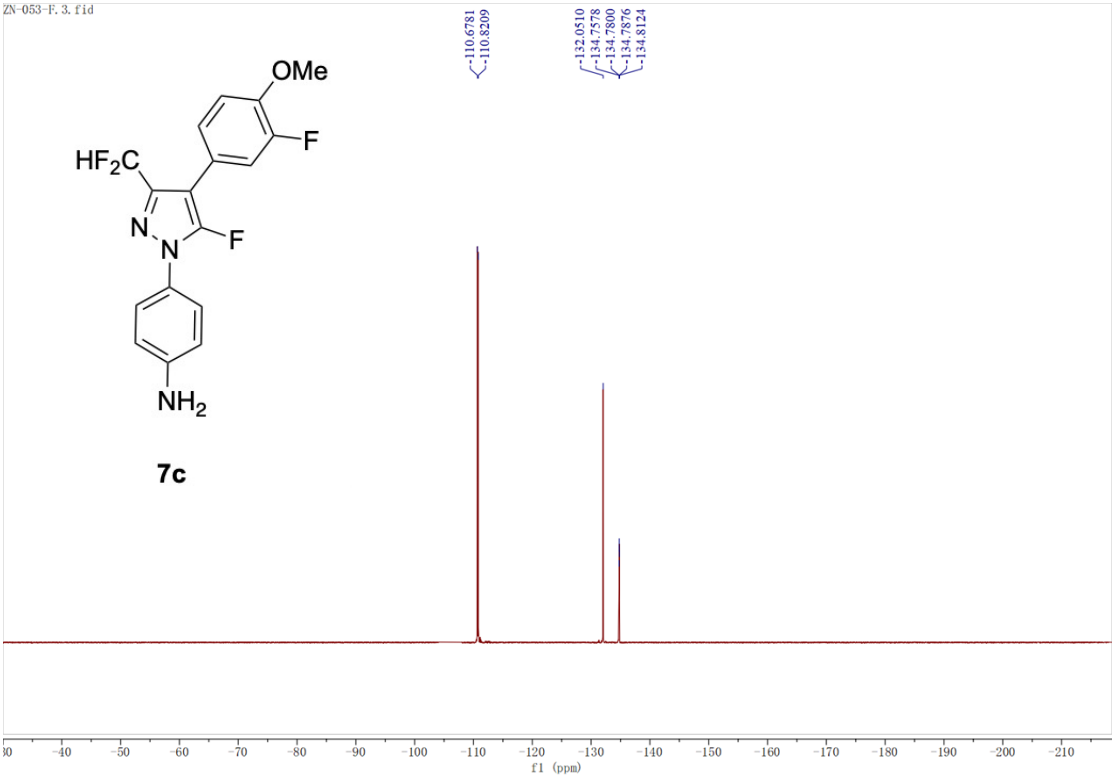


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **7b**

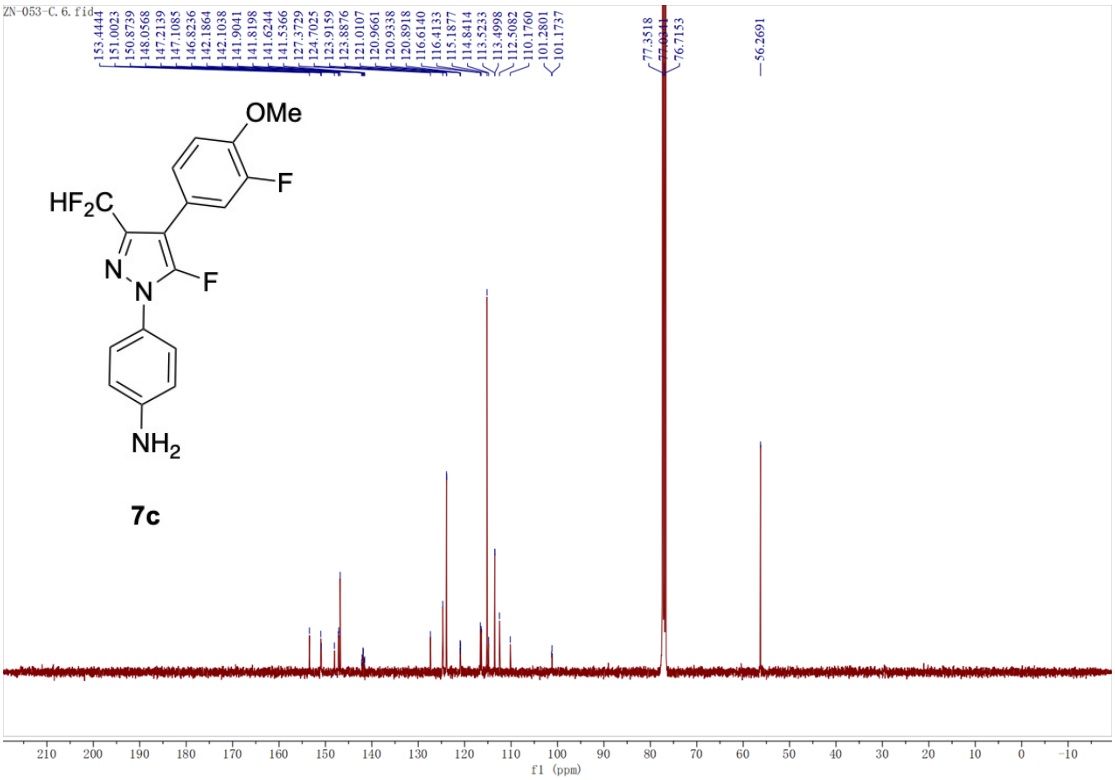
1-(4-Aminophenyl)-3-(difluoromethyl)-5-fluoro-4-(3-fluoro-4-Methoxyphenyl)phen-yl)-1*H*-pyrazole (7c)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **7c**

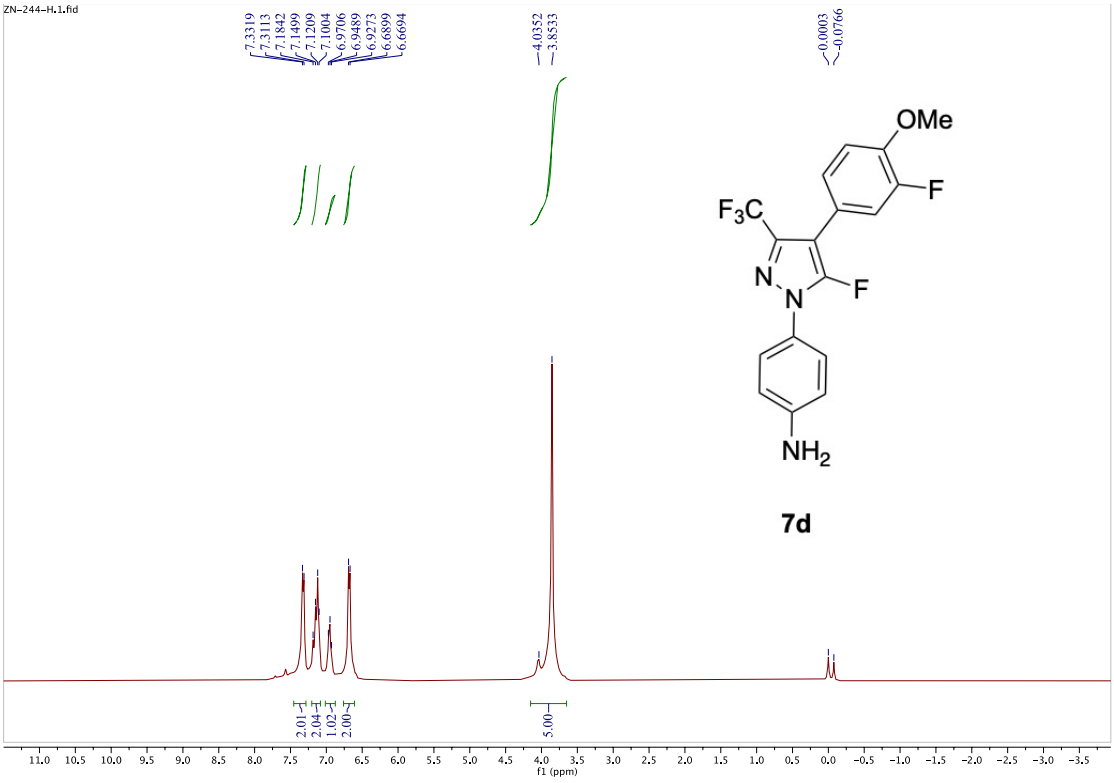


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **7c**

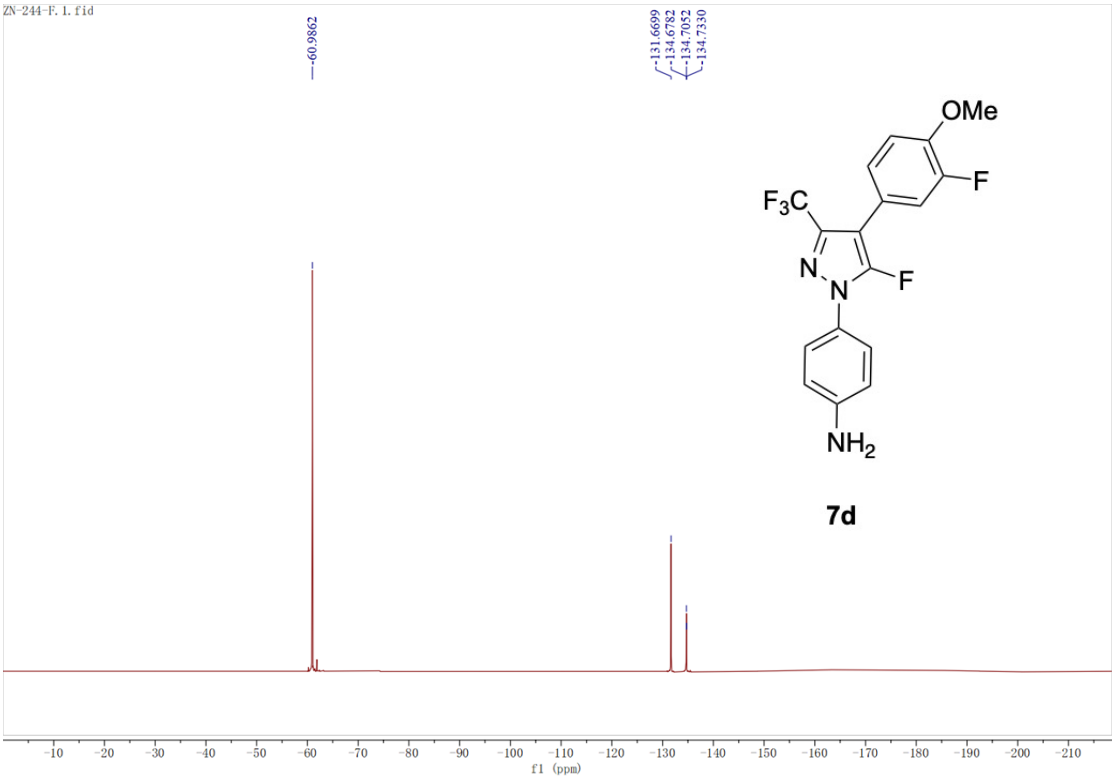


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **7c**

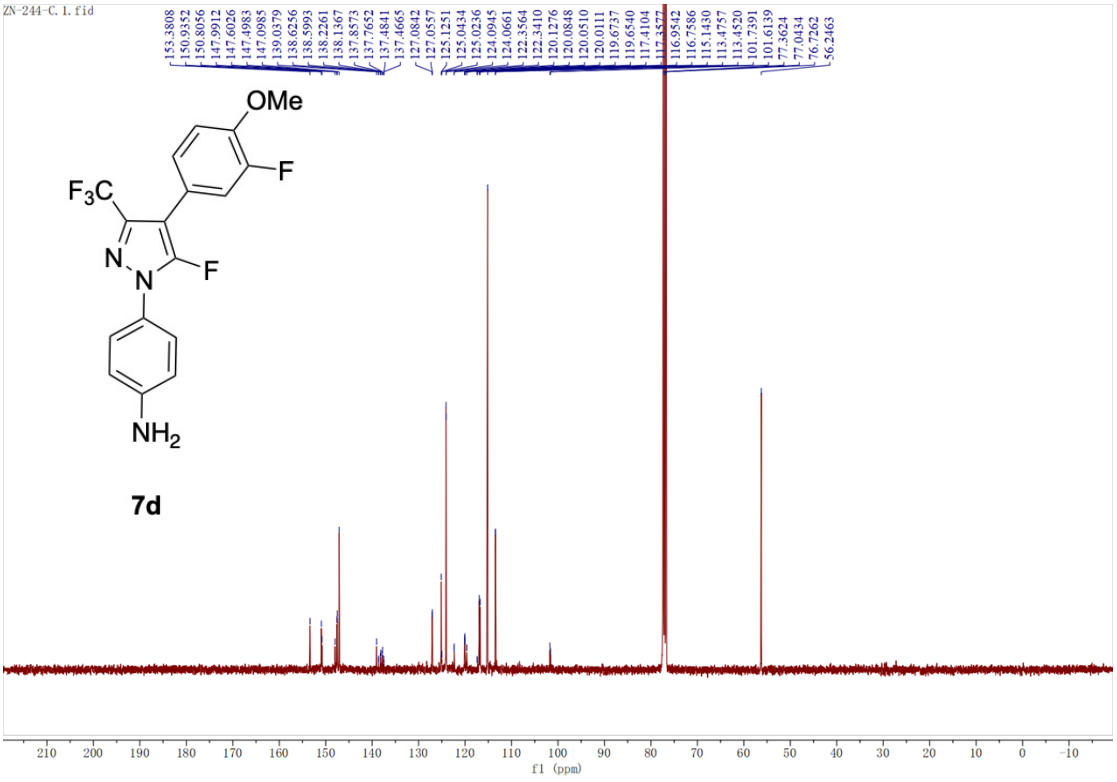
4-(5-Fluoro-4-(3-fluoro-4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide (7d)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **7d**

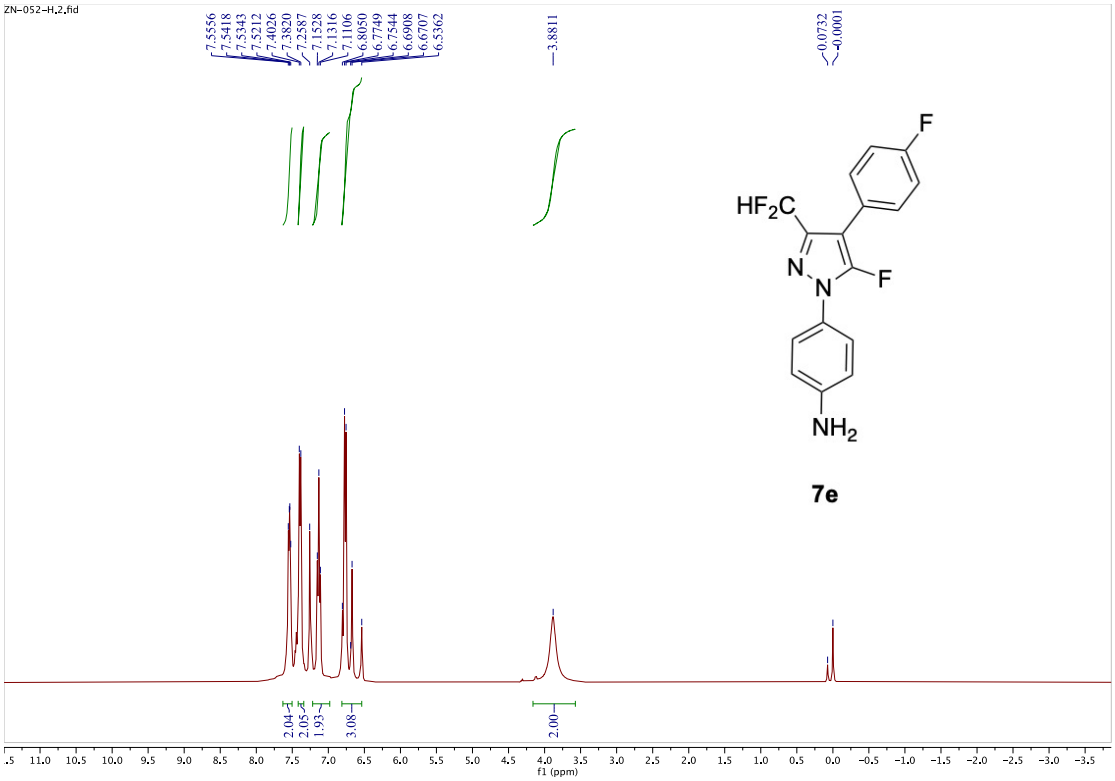


^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **7d**

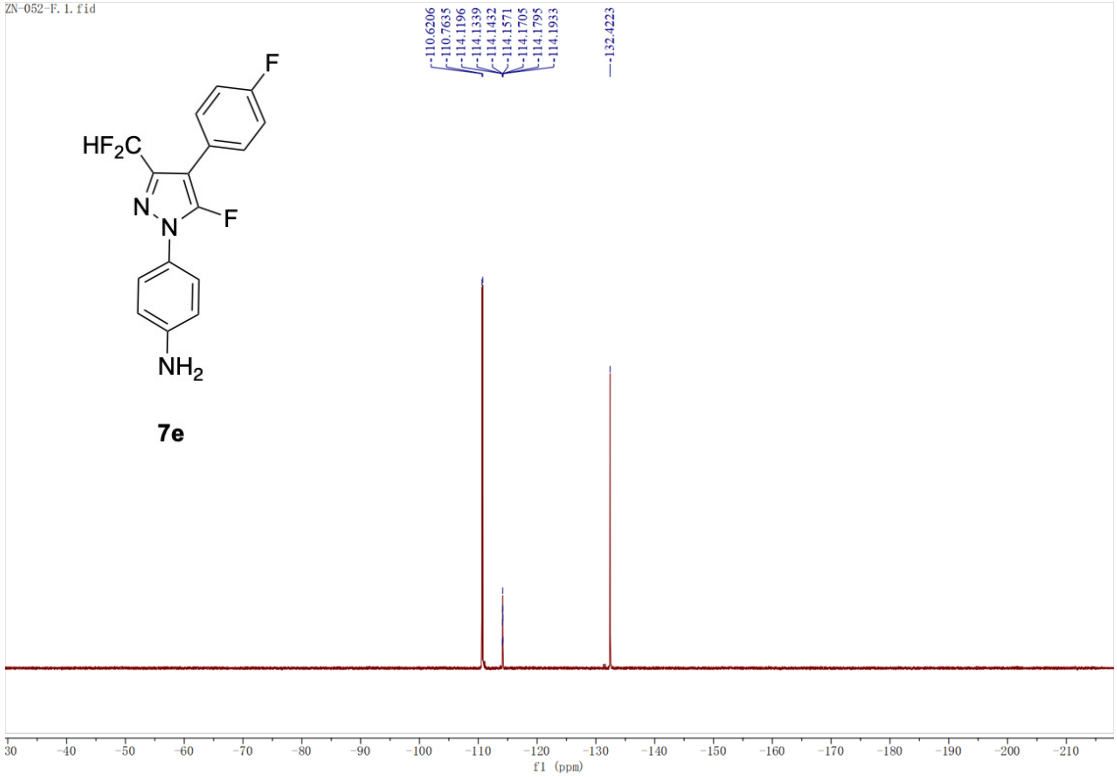


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **7d**

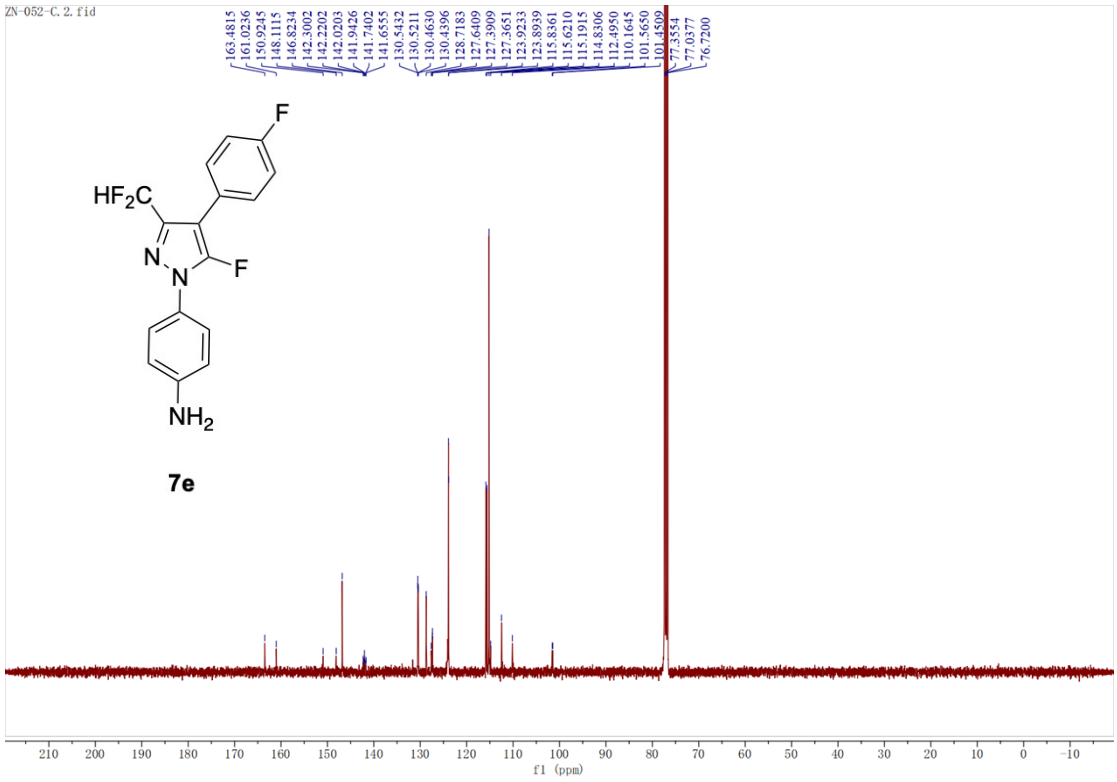
4-(3-(Difluoromethyl)-5-fluoro-4-(4-fluorophenyl)-1*H*-pyrazol-1-yl)aniline (7e)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **7e**



^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **7e**



^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **7e**

6. Inhibitory activity evaluation towards cyclooxygenase-2

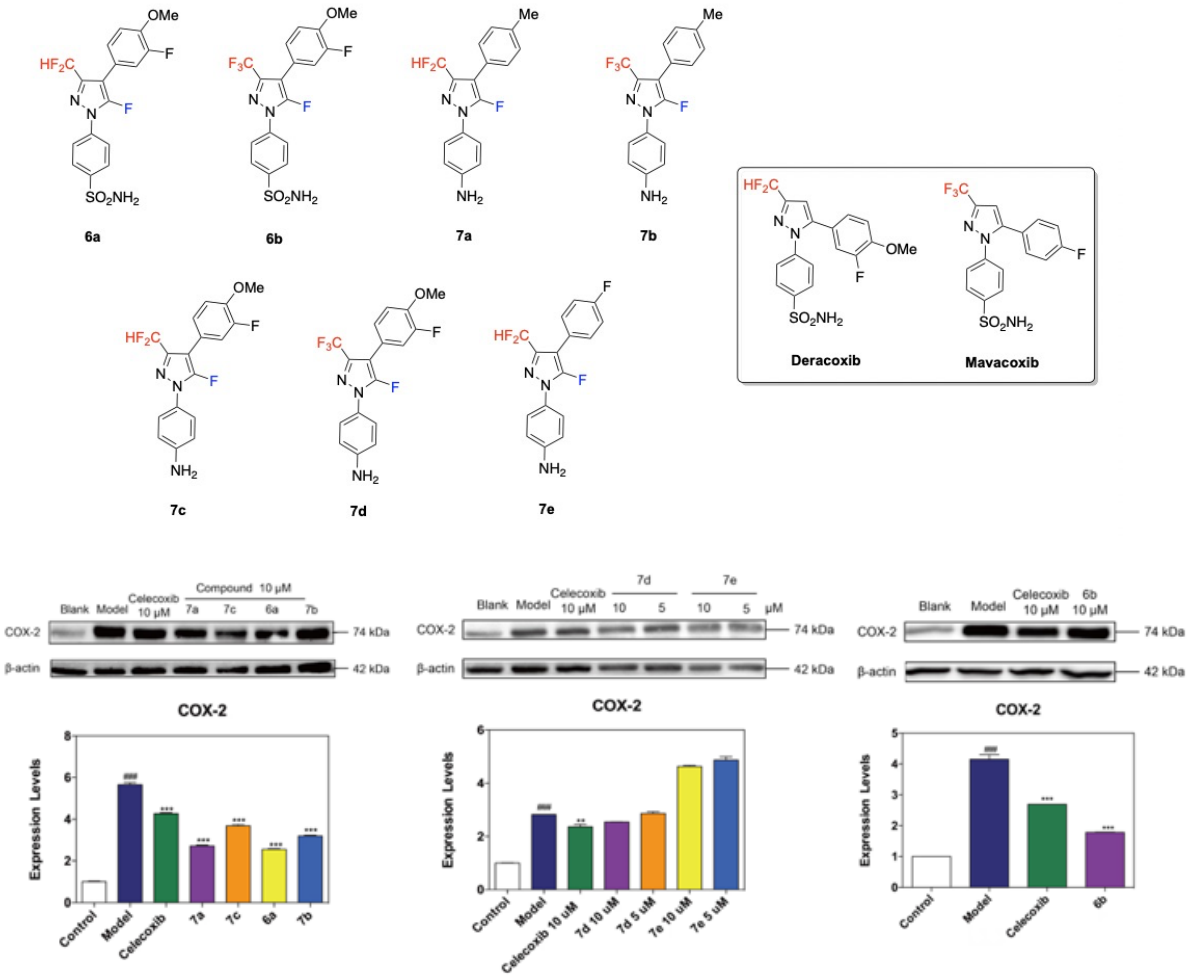


Figure Inhibitory activity evaluation towards cyclooxygenase-2. RAW264.7 cells were treated with compound **6a**, **6b**, **7a**, **7b**, **7c**, **7d**, **7e** and Celecoxib at indicated concentrations for 48 h. The data were analyzed using one-analysis of variance (ANOVA) followed by Tukey's test. ** $p < 0.01$, *** $p < 0.001$ versus LPS-induced cells without pyrazole treatment. $^{###}$ $p < 0.001$ versus normal cells with LPS-induced cells.

Method

1.1. Cell Culture

RAW264.7 cells were maintained in HyClone Dulbecco's Modified Eagle Medium (DMEM) with high glucose containing 10% Fetal Bovine Serum (FBS) and 1% antibiotics (penicillin and streptomycin). The cells were incubated at 37 °C in a 5%

CO_2 humidifified incubator.

1.2. Western Blot Analysis

Cell pellets were resuspended in 150 μL radioimmunoprecipitation (RIPA) lysis buffer with phenylmethanesulfonyl fluoride (PMSF, Solarbio, China). Total protein concentration was determined using the Bradford 1x dye reagent (Solarbio, China) at 562 nm. Equal amounts of protein (15 μg) were electrophoresed using sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), and the separated protein bands were transferred onto a polyvinylidene fluoride (PVDF) membrane (Merck Millipore, USA). Then, the membranes were blocked with 5% milk in TBST (a mixture of tris-buffered saline (TBS) (a buffer solution) and Polysorbate 20) for 1 h and incubated with 1:1000 diluted primary antibodies COX-2 (CST, USA) and β-actin (Proteintech, USA) at 4 °C for 16 h.

7. References

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