Supporting Information

Electrochemical oxidative selective halogenation of pyrazolones for the synthesis of 4-halopyrazolones

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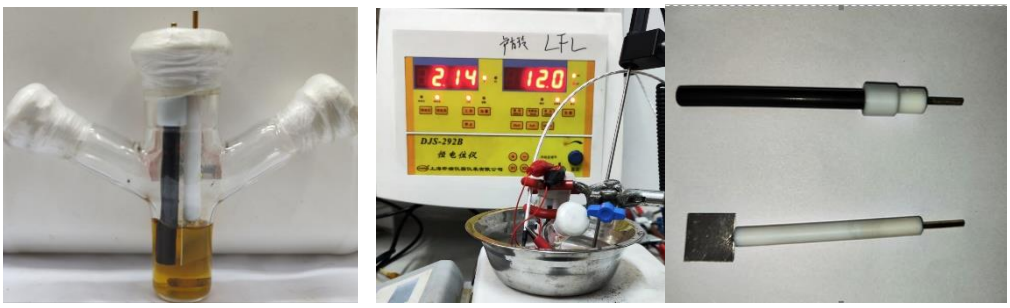
General information

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. The instrument for electrolysis was dual display potentiostat (DJS-292B) (made in China). The anodic electrode was graphite rod (ϕ 6 mm) and cathodic electrode was platinum plate (15 mm×15 mm×0.3 mm). Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (boiling point was between 60-90 ^{o}C). Gradient flash chromatography was conducted eluting with a continuous gradient from petroleum to the indicated solvent, and they were listed as volume/volume ratios. NMR spectra were recorded on a Bruker spectrometer at 600 MHz (^{1}H NMR), 151 MHz (^{13}C NMR), 565 MHz (^{19}F NMR). Chemical shifts were reported relative to tetramethylsilane, dimethyl sulfoxide (2.50 ppm for ^{1}H, 39.6 ppm for ^{13}C), respectively. And all ^{1}H, ^{13}C and ^{19}F NMR data spectra were reported in delta (δ) units, parts per million (ppm) downfield from the internal standard. Coupling constants were reported in Hertz (Hz). LC-MS spectra were recorded on a AB SCIEX TripleTOF 5600$^{+\cdot}$

Experimental procedure

General procedure for the preparation of 3:

In an oven-dried undivided three-necked bottle (20 mL) equipped with a stir bar, pyrazolones **1** (0.3 mmol), $^{n}Bu_4NBr$ (0.90 mmol, 290.1 mg), 95%EtOH (7.0 mL) was added. The bottle was equipped with graphite rod (ϕ 6 mm, about 15 mm immersion depth in solution) as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current of 12 mA under Ar atmosphere at room temperature for 3.5 h. After completion of the reaction, as indicated by TLC and LC-MS, the crude mixture product was obtained by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 7: 1).



A **B** **C**

Figure **S1**. The experimental setup for electrolysis. (**A:** The electrochemical reaction apparatus used. **B** and **C:** The electrodes used in the reaction.)

Procedure for gram scale synthesis of 3a:

The reactor for the 5 mmol gram-scale synthesis: 1a (0.94 g, 5 mmol), **2a** (4.84 g, 15 mmol), The bottle was equipped with graphite rod (ϕ 6 mm, about 15 mm immersion depth in solution) as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current of 12 mA under Ar atmosphere in 100 mL 95% EtOH at room temperature for 81 h (Figure **S2D**). The reaction was monitored by TLC. After completion of the reaction, as indicated by TLC and LC-MS, the crude mixture product was obtained by flash column chromatography on silica gel using petroleum ether/ethyl acetate as eluent (petroleum ether: ethyl acetate = 7: 1) to afford an isolated yield of **3a** (1.1 g, 80% yield).

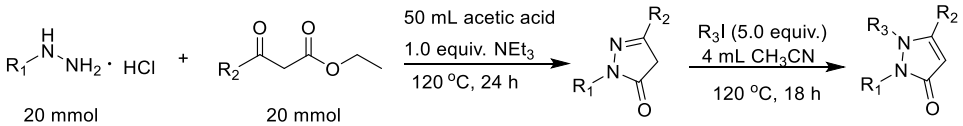
The reactor for the 500 mmol gram-scale synthesis: In an oven-dried undivided beaker (5 L) equipped with a stir bar, antipyrine **1a** (0.5 mol, 94 g), $^{n}Bu_4NBr$ (1.5 mol, 483 g), 95% EtOH (3 L) were added. The electrolysis was conducted using a flow electrolytic cell equipped with a C (+)

anode and a Ni (-) cathode with exposed surface area of 91 cm^2 and interelectrode distance of 1 cm (Figure **S2 E and F**). The solution containing antipyrine (0.5 mol, 94g), $^{n}Bu_4NBr$ (1.5 mol, 483 g, 3 equiv.) in 95% EtOH (3 L) was pushed using a syringe pump to pass through the flow electrolytic cell operated with a flow rate of 0.35 mL min^{-1} and a constant current (340 mA). The workup procedure was the same as described above.

D **E** **F**

Figure **S2**. The experimental setup for electrolysis. (**D:** 5 mmol scale-up reaction apparatus diagram. **E** and **F:** Exploded view of the flow reactor with a C anode and a Ni cathode.)

General procedure for the preparation of 1



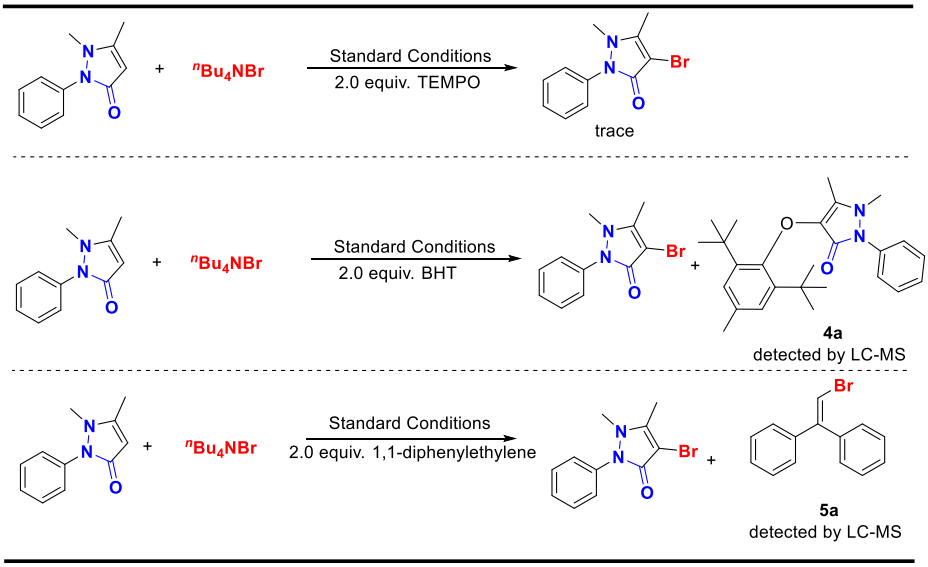
Step1: In a 100 mL flask was charged with *β*-ketoester (20 mmol) and substituted phenylhydrazine (20 mmol, for HCl salt 20 mmol of triethylamine was added), then 50 mL of acetic acid was added. The content was refluxed for 24h, the contents cooled, and solvent was removed in vacuo. To the precipitate in flask was added ethylacetate to suspend the product and was then filtered to obtain pure compound. The obtained product was dried to yield substituted pyrazolone.

Step2: To a stirred solution of substituted pyrazolone (1.0 equiv.) in acetonitrile (4.0 mL), methyl iodide/alkyl iodide (5.0 equiv.) was added. The reaction mixture was heated in a sealed tube for 18 h. After completion of the reaction, as indicated by TLC, followed by addition of 20 mL saturated $NaHSO_3$, the resulting mixture was extracted with DCM. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography to give the products **1** (petroleum ether: ethyl acetate = 1:2).

Mechanism research

In an effort to glean insights into the mechanism, related control experiments and cyclic

voltammetry (CV) experiments were conducted (Scheme 1). Upon the addition of stoichiometric amounts of radical scavengers 2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) into the reaction system, this conversion was obviously suppressed. The adducts **4a** and **5a** indicated thar this reaction probably underwent a radical pathway, bromide radical and antipyrine radical might be involved in the transformation (**Figure S3** and **Figure S4**).



Scheme 1. Control experiments.

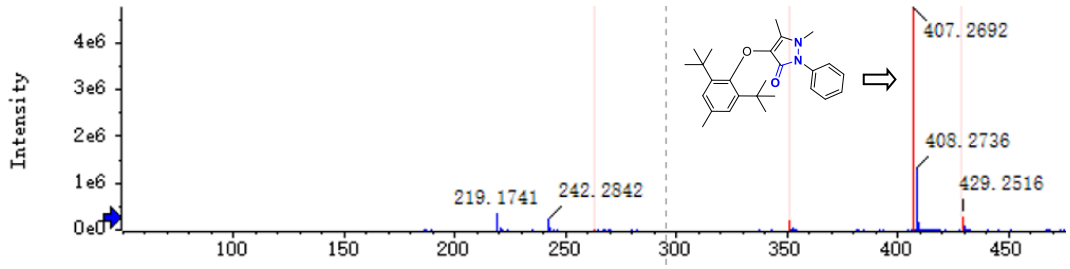


Figure **S3.** Free radical capture experiment (antipyrine-BHT)

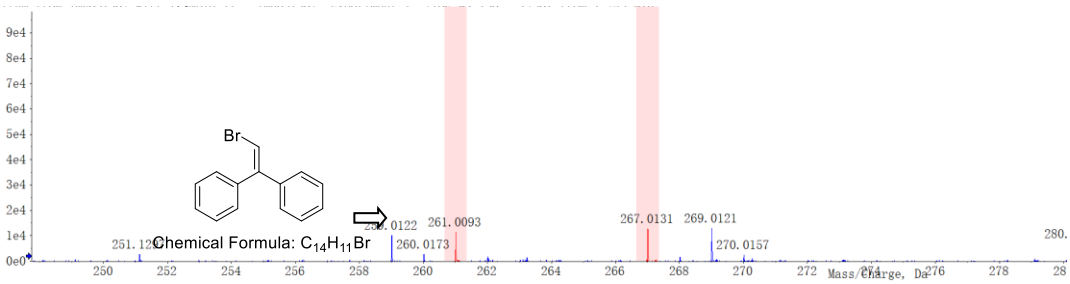


Figure **S4.** Free radical capture experiment (DPE−Br)

General procedure for cyclic voltammetry (CV):

Cyclic voltammetry was performed in a three-electrode cell connected to a schlenk line under air at room temperature. The working electrode was a glassy carbon electrode, the counter electrode

a platinum wire. The reference was an Ag/AgCl electrode submerged in saturated aqueous KCl solution. 10 mL of CH_3CN containing 0.01 M $^nBu_4NBF_4$ were poured into the electrochemical cell in all experiments. The scan rate is 0.1 V/s, ranging from 0 V to 3.5 V. The peak potentials *vs*. Ag/AgCl for used. Cyclic voltammetry (CV) experiments of antipyrine **1a** and $^nBu_4NBr$ **2a** were performed. An obvious oxidation potential peak of substrate **1a** could be observed at 1.55 V, and the CV of tetrabutylammonium bromide **2a** in acetonitrile exhibits two oxidation peaks, one at 1.54 V and the other at 2.01 V. This result indicated that **2a** and **1a** were probably oxidized to produce radicals at the same time in this system.

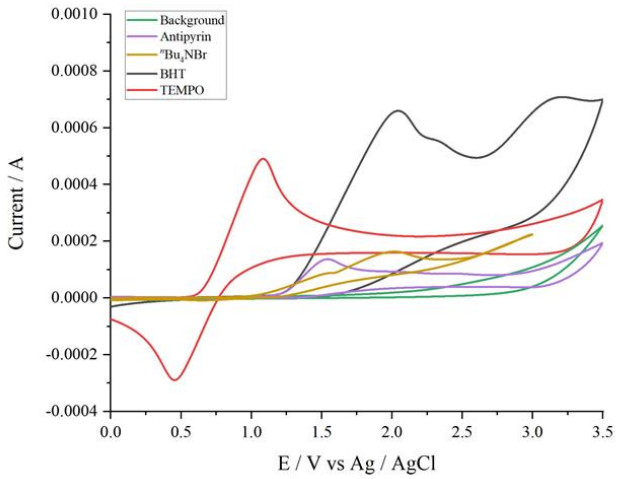
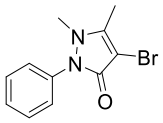
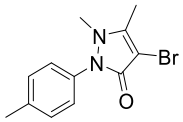


Figure **S5** Cyclic voltammetry

Detail descriptions for products

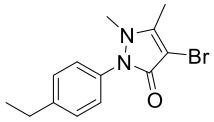


4-bromo-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3a).[1] (White solid was obtained in 94% isolated yield, 75.3 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.51 (m, 2H), 7.35 (m, 3H), 3.12 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.84, 155.02, 135.21, 129.66, 127.47, 124.78, 87.82, 36.49, 12.59.



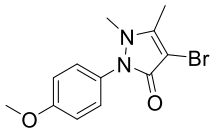
4-bromo-1,5-dimethyl-2-(p-tolyl)-1,2-dihydro-3H-pyrazol-3-one (3b). (White solid was obtained in 65% isolated yield, 53.9 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.31 (d, 2H, J = 8.0 Hz), 7.22 (d, 2H, J = 8.0 Hz), 3.10 (s, 3H), 2.35 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (151 MHz, DMSO - d_6) δ 161.77, 154.33, 137.18, 132.67, 130.13, 125.09, 87.57, 36.26, 21.09, 12.53.

HRMS (ESI) calcd for $C_{12}H_{13}BrN_2O$: 281.0284 ($M+H^+$), found: 281.0290.



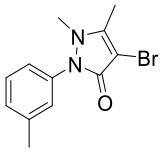
4-bromo-2-(4-ethylphenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one (3c). (White solid was obtained in 80% isolated yield, 70.5mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.34 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 3.10 (s, 3H), 2.65 (q, J = 7.6 Hz, 2H), 2.29 (s, 3H), 1.20 (t, J = 7.6 Hz, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.78, 154.35, 143.35, 132.85, 128.95, 125.09, 87.62, 36.29, 28.21, 15.96, 12.53.

HRMS (ESI) calcd for $C_{13}H_{15}BrN_2O$: 295.0441 ($M+H^+$), found:295.0443.



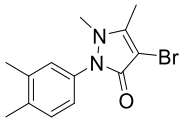
4-bromo-2-(4-methoxyphenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one(3d). (White solid was obtained in 30% isolated yield, 26.6 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.25 (d, J = 8.9 Hz, 2H), 7.07 (d, J = 8.9 Hz, 2H), 3.80 (s, 3H), 3.09 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.80, 158.99, 153.31, 127.80, 127.53, 114.93, 87.04, 55.91, 35.87, 12.46.

HRMS (ESI) calcd for $C_{12}H_{13}BrN_2O_2$: 297.0233 ($M+H^+$), found:297.0238.



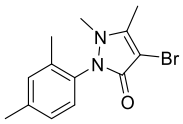
4-bromo-1,5-dimethyl-2-(m-tolyl)-1,2-dihydro-3H-pyrazol-3-one(3e). (White solid was obtained in 49% isolated yield, 41.1 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.39 (t, J = 7.8 Hz, 1H), 7.20-7.14 (m, 2H), 7.12 (dd, J = 7.8, 2.3 Hz, 1H), 3.11 (s, 3H), 2.36 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.86, 154.84, 139.22, 135.18, 129.45, 128.20, 125.35, 122.00, 87.78, 36.46, 21.37, 12.57.

HRMS (ESI) calcd for $C_{12}H_{13}BrN_2O$: 281.0284 ($M+H^+$), found: 281.0286.



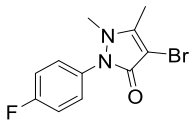
4-bromo-2-(3,4-dimethylphenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one (3f). (White solid was obtained in 84% isolated yield, 74.1 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.25 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 2.3 Hz, 1H), 7.03 (dd, J = 8.0, 2.3 Hz, 1H), 3.09 (s, 3H), 2.28 (s, 3H), 2.26 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.80, 154.09, 137.75, 136.07, 132.89, 130.49, 126.28, 122.71, 87.53, 36.21, 19.84, 19.44, 12.50.

HRMS (ESI) calcd for $C_{13}H_{15}BrN_2O$: 295.0441 ($M+H^+$), found: 295.0441.



4-bromo-2-(2,4-dimethylphenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one (3g). (White solid was obtained in 59% isolated yield, 52.0 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.21 (s, 1H), 7.14 (d, J = 8.2 Hz, 1H), 7.06 (d, J = 7.9 Hz, 1H), 3.04 (s, 3H), 2.34 (s, 3H), 2.28 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.39, 151.96, 139.35, 137.29, 131.98, 131.46, 128.63, 127.86, 85.75, 35.00, 21.14, 17.65, 12.32.

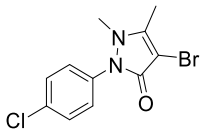
HRMS (ESI) calcd for $C_{13}H_{15}BrN_2O$: 295.0441 ($M+H^+$), found:295.0445.



4-bromo-2-(4-fluorophenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one (3h). (White solid was obtained in 71% isolated yield, 60.5 mg). ^{1}H NMR (600 MHz, DMSO-

d_6) δ 7.45 – 7.30 (m, 4H), 3.12 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.98, 160.36, 154.87, 131.51 (d, J = 2.9 Hz), 127.31 (d, J = 8.8 Hz), 116.56 (d, J = 22.9 Hz), 87.49, 36.31, 12.55. ^{19}F NMR (565 MHz, DMSO- d_6) δ -114.52.

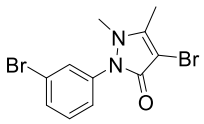
HRMS (ESI) calcd for $C_{11}H_{10}BrFN_2O$: 285.0033 ($M+H^+$), found: 285.0035.



4-bromo-2-(4-chlorophenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one(3i).

(White solid was obtained in 89% isolated yield, 79.8 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.58 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 8.8 Hz, 2H), 3.13 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.90, 155.86, 134.14, 131.63, 129.65, 126.13, 87.95, 36.66, 12.65.

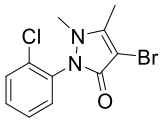
HRMS (ESI) calcd for $C_{11}H_{10}BrClN_2O$: 300.9738 ($M+H^+$), found: 300.9743.



4-bromo-2-(3-bromophenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one (3j).

(White solid was obtained in 84% isolated yield, 82.3 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.60 - 7.53 (m, 2H), 7.48 (t, J = 8.0 Hz, 1H), 7.37-7.35 (m, 1H), 3.14 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 162.02, 156.41, 136.72, 131.56, 130.01, 126.79, 123.14, 122.15, 87.98, 36.83, 12.69.

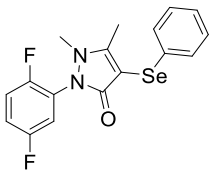
HRMS (ESI) calcd for $C_{11}H_{10}Br_2N_2O$: 344.9233 ($M+H^+$), found: 344.9240.



4-bromo-2-(2-chlorophenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one (3k).

(White solid was obtained in 93% isolated yield, 83.7 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.68 (dd, J = 7.9, 1.6 Hz, 1H), 7.57-7.49 (m, 2H), 7.47 (dd, J = 7.7, 1.9 Hz, 1H), 3.07 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.64, 152.94, 133.50, 132.66, 131.86, 131.84, 130.91, 128.81, 85.59, 35.21, 12.38.

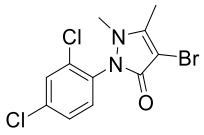
HRMS (ESI) calcd for $C_{11}H_{10}BrClN_2O$: 300.9738 ($M+H^+$), found: 300.9745.



4-bromo-2-(2,5-difluorophenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one (3l). (White solid was obtained in 58% isolated yield, 52.5 mg). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.52 (m, 1H), 7.42 (m, 2H), 3.14 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.85, 159.06-157.46 (dd), 154.84, 155.30-153.64 (dd, *J* = 247.7, 2.9 Hz), 123.78-123.61 (dd, *J* = 14.7, 10.7 Hz), 118.65-118.44 (dd, *J* = 22.6, 9.4 Hz), 118.12 (dd, *J* = 23.8, 8.2 Hz), 116.98 (d, *J* = 25.5 Hz), 85.90, 35.71, 12.54.

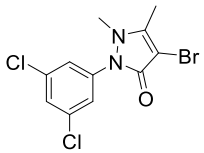
^{19}F NMR (565 MHz, DMSO- d_6) δ -116.78 (dq, *J* = 15.7, 8.0 Hz), -125.23 (ddt, *J* = 15.5, 9.8, 4.7 Hz).

HRMS (ESI) calcd for $C_{11}H_9BrF_2N_2O$: 302.9939 ($M+H^+$), found:302.9931.



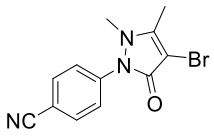
4-bromo-2-(2,4-dichlorophenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one (3m). (White solid was obtained in 63% isolated yield, 62.9 mg). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.89 (d, *J* = 2.3 Hz, 1H), 7.61 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.50 (d, *J* = 8.5 Hz, 1H), 3.09 (s, 3H), 2.28 (s, 3H).^{13}C NMR (151 MHz, DMSO- d_6) δ 161.67, 153.62, 135.55, 134.62, 132.94, 131.85, 130.54, 129.02, 85.60, 35.33, 12.42.

HRMS (ESI) calcd for $C_{11}H_9BrCl_2N_2O$: 334.9348 ($M+H^+$), found: 334.9349.



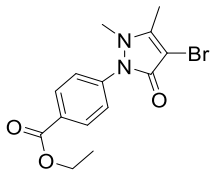
4-bromo-2-(2,4-dichlorophenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one (3n). (White solid was obtained in 77% isolated yield, 77.3 mg). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.61 (t, *J* = 1.9 Hz, 1H), 7.44 (d, *J* = 1.9 Hz, 2H), 3.16 (s, 3H), 2.31 (s, 3H).^{13}C NMR (151 MHz, DMSO- d_6) δ 162.19, 157.63, 137.53, 134.91, 126.57, 122.38, 87.98, 37.13, 12.76

HRMS (ESI) calcd for $C_{11}H_9BrCl_2N_2O$: 334.9348 ($M+H^+$), found: 334.9350.



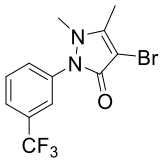
4-bromo-2-(3,5-dichlorophenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one (3o). (White solid was obtained in 50% isolated yield, 43.6 mg). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.99 (d, J = 8.7 Hz, 2H), 7.57 (d, J = 8.6 Hz, 2H), 3.16 (s, 3H), 2.33 (s, 3H).^{13}C NMR (151 MHz, DMSO- d_6) δ 161.92, 157.94, 139.18, 133.86, 123.67, 118.95, 108.92, 88.70, 37.37, 12.85.

HRMS (ESI) calcd for $C_{12}H_{10}BrN_3O$: 292.0080 ($M+H^+$), found: 292.0082.



ethyl 4-(4-bromo-2,3-dimethyl-5-oxo-2,5-dihydro-1H-pyrazol-1-yl)benzoate (3p). (White solid was obtained in 58% isolated yield, 58.8 mg). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.9 (d, 2H), 7.51 (d, 2H), 4.34 (q, J = 7.1 Hz, 2H), 3.16 (s, 3H), 2.33 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 165.57, 161.88, 157.26, 139.26, 130.64, 127.84, 123.30, 88.67, 61.32, 37.21, 14.64, 12.78.

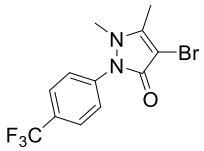
HRMS (ESI) calcd for $C_{14}H_{15}BrN_2O_3$: 339.0339 ($M+H^+$), found: 339.0336.



4-bromo-2-(3,4-difluorophenyl)-1,5-dimethyl-1,2-dihydro-3H-pyrazol-3-one (3q). (Yellow solid was obtained in 63% isolated yield, 62.5 mg). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.80-7.70 (m, 3H), 7.66 (d, J = 8.0, 1H), 3.16 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 162.14, 156.88, 136.05, 131.01, 130.35 (q, J = 32.3 Hz), 127.81, 124.23 (q, J = 272.5 Hz), 123.67 (q, J = 3.6 Hz), 120.46 (q, J = 3.9 Hz), 88.10, 36.93, 12.71.

^{19}F NMR (565 MHz, DMSO- d_6) δ -61.22.

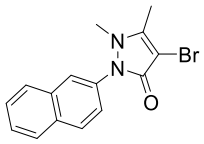
HRMS (ESI) calcd for $C_{12}H_{10}BrF_3N_2O$: 335.0001 ($M+H^+$), found: 335.0001.



4-bromo-1,5-dimethyl-2-(4-(trifluoromethyl)phenyl)-1,2-dihydro-3H-pyrazol-3-one (3r). (Yellow solid was obtained in 85% isolated yield, 89.5 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.89 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.4 Hz, 2H), 3.17 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.99, 157.39, 138.73, 126.85 (dd, J = 25.7, 57.4 Hz), 126.81, 124.53 (dd, J = 135.9, 273.31 Hz), 123.83, 88.55, 37.16, 12.77.

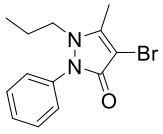
^{19}F NMR (565 MHz, DMSO- d_6) δ -60.82.

HRMS (ESI) calcd for $C_{12}H_{10}BrF_3N_2O$: 335.0001 ($M+H^+$), found: 334.9999.



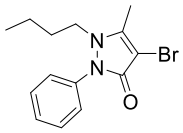
4-bromo-1,5-dimethyl-2-(naphthalen-2-yl)-1,2-dihydro-3H-pyrazol-3-one (3s). (Colorless oil was obtained in 67% isolated yield, 63.5 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 8.05 (d, J = 8.8 Hz, 1H), 8.03-7.96 (m, 2H), 7.89 (d, J = 2.1 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.52 (dd, J = 8.7, 2.2 Hz, 1H), 3.18 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 162.11, 155.29, 133.35, 132.81, 131.98, 129.44, 128.36, 128.15, 127.36, 126.93, 123.31, 122.86, 87.90, 36.67, 12.66.

HRMS (ESI) calcd for $C_{15}H_{13}BrN_2O$: 317.0284 ($M+H^+$), found: 317.0290.



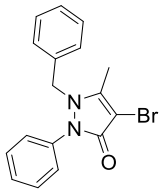
4-bromo-5-methyl-2-phenyl-1-propyl-1,2-dihydro-3H-pyrazol-3-one (3t). (White solid was obtained in 82% isolated yield, 72.3 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.55 -7.48 (m, 2H), 7.41-7.32 (m, 3H), 3.61-3.57 (m, 2H), 2.33 (s, 3H), 1.30-1.22 (m, 2H), 0.66 (t, J = 7.4 Hz, 3H).^{13}C NMR (151 MHz, DMSO- d_6) δ 162.25, 153.73, 135.12, 129.70, 127.68, 125.17, 87.83, 49.34, 20.13, 12.56, 11.15.

HRMS (ESI) calcd for $C_{13}H_{15}BrN_2O$: 295.0441 ($M+H^+$), found: 295.0435.



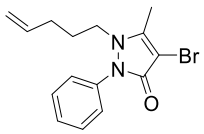
4-bromo-1-butyl-5-methyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3u). (White solid was obtained in 62% isolated yield, 57.3 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.53-7.51 (m, 2H), 7.41-7.29 (m, 3H), 3.64 - 3.58 (m, 2H), 2.32 (s, 3H), 1.23-1.19 (m, 2H), 1.09-1.03 (m, 2H), 0.71 (t, J = 7.3 Hz, 3H).^{13}C NMR (151 MHz, DMSO- d_6) δ 162.22, 153.72, 135.08, 129.70, 127.67, 125.14, 88.13, 47.65, 28.49, 19.53, 13.91, 12.52**.**

HRMS (ESI) calcd for $C_{14}H_{17}BrN_2O$: 309.0597 ($M+H^+$), found: 309.0600.



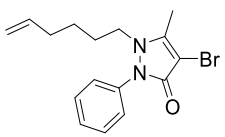
1-benzyl-4-bromo-5-methyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3v). (White solid was obtained in 77% isolated yield, 79.0 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.54-7.51 (m, 2H), 7.40-7.37 (m, 1H), 7.34-7.30 (m, 2H), 7.30 -7.25 (m, 3H), 6.95-6.90 (m, 2H), 4.84 (s, 2H), 2.39 (s, 3H).^{13}C NMR (151 MHz, DMSO- d_6) δ 162.18, 153.89, 135.03, 134.49, 129.75, 129.06, 128.62, 128.03, 127.64, 124.98, 89.42, 51.22, 12.97.

HRMS (ESI) calcd for $C_{17}H_{15}BrN_2O$: 343.0441 ($M+H^+$), found: 343.0433.



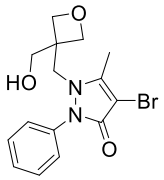
4-bromo-5-methyl-1-(pent-4-en-1-yl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3w). (Yellow oil was obtained in 60% isolated yield, 57.7 mg). ^{1}H NMR (600 MHz, DMSO-d6) ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.55-7.49 (m, 2H), 7.41-7.33 (m, 3H), 5.65-5.55 (m, 1H), 4.89-4.83 (m, 2H), 3.62 (d, J = 6.8 Hz, 2H), 2.32 (s, 3H), 1.83 (q, J = 7.3 Hz, 2H), 1.38-1.28 (m, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 162.26, 153.74, 137.61, 135.06, 129.70, 127.67, 125.08, 115.85, 88.34, 47.33, 30.18, 25.29, 12.52.

HRMS (ESI) calcd for $C_{15}H_{17}BrN_2O$: 321.0597 ($M+H^+$), found: 321.0592.



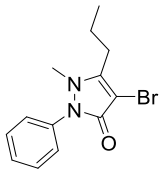
4-bromo-1-(hex-5-en-1-yl)-5-methyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3x). (Yellow oil was obtained in 77% isolated yield, 77.3 mg). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.55-7.50 (m, 2H), 7.40-7.33 (m, 3H), 5.65 (m, 1H), 4.88 (d, *J* = 12.6 Hz, 2H), 3.62 (t, *J* = 7.5 Hz, 2H), 2.32 (s, 3H), 1.89-1.82 (m, 2H), 1.24-1.22 (m, 2H), 1.17-1.09 (m, 2H). ^{13}C NMR (151 MHz, DMSO) δ 162.24, 153.70, 138.48, 135.03, 129.70, 127.67, 125.09, 115.51, 88.15, 47.70, 32.90, 25.75, 25.27, 12.51.

HRMS (ESI) calcd for $C_{16}H_{19}BrN_2O$: 335.0754 ($M+H^+$), found: 335.0746.



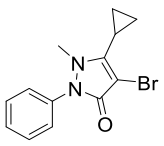
4-bromo-1-((3-(hydroxymethyl)oxetan-3-yl)methyl)-5-methyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3y). (Yellow oil was obtained in 70% isolated yield, 73.5 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.62-7.57 (m, 2H), 7.53-7.47 (m, 2H), 7.40-7.35 (m, 1H), 5.06 - 5.01 (m, 1H), 4.37 (s, 2H), 4.37-4.30 (m, 4H), 3.62 (d, 2H), 2.19 (s, 3H).^{13}C NMR (151 MHz, DMSO- d_6) δ 150.33, 147.13, 138.21, 129.62, 127.64, 122.73, 81.40, 75.50, 74.50, 62.37, 44.72, 13.29.

HRMS (ESI) calcd for $C_{15}H_{17}BrN_2O_3$: 353.0495 ($M+H^+$), found: 353.0486.



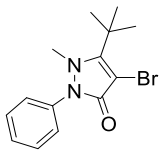
4-bromo-1-methyl-2-phenyl-5-propyl-1,2-dihydro-3H-pyrazol-3-one (3z). (White solid was obtained in 83% isolated yield, 73.2 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.54 -7.48 (m, 2H), 7.40-7.32 (m, 3H), 3.13 (s, 3H), 2.67 (t, *J* = 7.6 Hz, 2H), 1.70-1.62 (m , 2H), 1.00 (t, *J* = 7.3 Hz, 3H).^{13}C NMR (151 MHz, DMSO- d_6) δ 161.85, 157.94, 135.16, 129.66, 127.49, 124.86, 88.05, 36.49, 27.85, 21.06, 13.95.

HRMS (ESI) calcd for $C_{13}H_{15}BrN_2O$: 295.0441 ($M+H^+$), found: 295.0443.



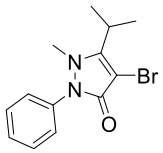
4-bromo-5-cyclopropyl-1-methyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3za). (White solid was obtained in 25% isolated yield, 21.9 mg). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.54-7.48 (m, 2H), 7.39-7.33 (m, 3H), 3.19 (s, 3H), 1.88-1.84 (m, 1H), 1.13-1.06 (m, 4H).^{13}C NMR (151 MHz, DMSO- d_6) δ 161.90, 157.27, 135.10, 129.63, 127.39, 124.63, 87.65, 36.92, 7.93, 6.38.

HRMS (ESI) calcd for $C_{13}H_{13}BrN_2O$: 293.0284 ($M+H^+$), found: 293.0290.



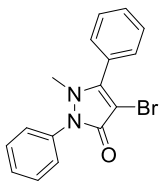
4-bromo-5-(tert-butyl)-1-methyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3zb). (White solid was obtained in 91% isolated yield, 84.1 mg). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.54-7.48 (m, 2H), 7.47-7.42 (m, 2H), 7.36-7.31 (m, 1H), 3.12 (s, 3H), 1.51 (s, 9H).^{13}C NMR (151 MHz, DMSO- d_6) δ 165.04, 161.52, 134.82, 129.64, 127.01, 123.67, 92.46, 41.40, 34.77, 29.43.

HRMS (ESI) calcd for $C_{14}H_{17}BrN_2O$: 309.0597 ($M+H^+$), found: 309.0601.



4-bromo-1-isopropyl-5-methyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3zc). (White solid was obtained in 76% isolated yield, 67.0 mg). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.51 (t, J = 7.8 Hz, 2H), 7.39-7.33 (m, 3H), 3.23-3.19 (m, 1H), 3.13 (s, 3H), 1.37 (d, J = 7.2 Hz, 6H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 161.96, 161.72, 134.94, 129.64, 127.41, 124.68, 87.12, 36.84, 26.96, 19.51.

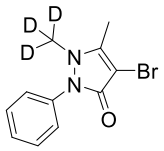
HRMS (ESI) calcd for $C_{13}H_{15}BrN_2O$: 295.0441 ($M+H^+$), found: 295.0444.



4-bromo-1-methyl-2,5-diphenyl-1,2-dihydro-3H-pyrazol-3-one (3zd). (White solid was obtained in 71% isolated yield, 70.1 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.78-7.72 (m, 2H), 7.67-7.59 (m, 3H), 7.62-7.53 (m, 4H), 7.42-7.36 (m, 1H), 2.93 (s, 3H). ^{13}C NMR (151

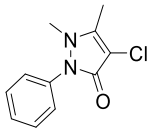
MHz, DMSO- d_6) δ 161.52, 156.85, 135.05, 131.42, 129.80, 129.69, 129.56, 128.00, 127.44, 124.32, 90.02, 39.47.

HRMS (ESI) calcd for $C_{16}H_{13}BrN_2O$: 329.0284 ($M+H^+$), found: 329.0276.



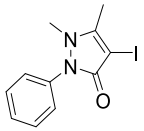
4-bromo-5-methyl-1-(methyl-d3)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3ze). (White solid was obtained in 91% isolated yield, 73.5 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.54-7.49 (m, 2H), 7.40-7.32 (m, 3H), 2.30 (s, 3H).^{13}C NMR (151 MHz, DMSO- d_6) δ 163.98, 158.42, 135.51, 129.61, 127.28, 124.63, 87.71, 59.75, 14.74.

HRMS (ESI) calcd for $C_{11}H_8D_3BrN_2O$: 270.0316 ($M+H^+$), found: 270.0312.



4-chloro-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3zf). (White solid was obtained in 91% isolated yield, 60.6 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.55-7.49 (m, 2H), 7.40-7.33 (m, 3H), 3.10 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ161.06, 153.17, 135.06, 129.68, 127.49, 124.75, 99.99, 36.41, 11.34.

HRMS (ESI) calcd for $C_{11}H_{11}ClN_2O$: 223.0633 ($M+H^+$), found: 223.0629.



4-iodo-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3zg). (White solid was obtained in 40% isolated yield, 37.7 mg). ^{1}H NMR (600 MHz, DMSO- d_6) δ 7.50 (t, J = 7.5 Hz, 2H), 7.38-7.31 (m, 3H), 3.14 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 163.98, 158.46, 135.52, 129.61, 127.28, 124.64, 59.86, 36.70, 14.77.

HRMS (ESI) calcd for $C_{11}H_{11}IN_2O$: 314.9989 ($M+H^+$), found: 314.9993.

References

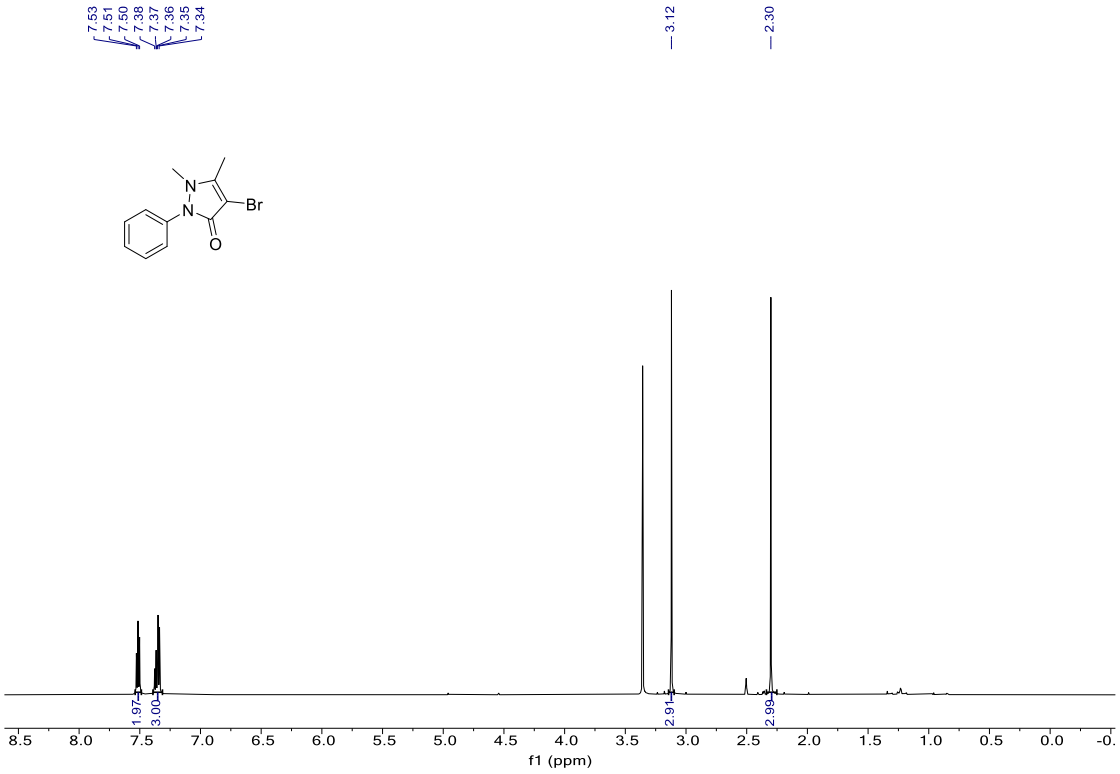
(1) Thupyai, A.; Pimpasri, C.; Yotphan, S., DABCO-catalyzed silver-promoted direct thiolation of pyrazolones with diaryl disulfides. *Org. Biomol. Chem.*, **2018**, *16*, 424-432;

(2) Kumar, V.; Chang, C.-K.; Tan, K.-P.; Jung, Y.-S.; Chen, S.-H.; Cheng, Y.-S. E.; Liang, P.-H.,Identification, Synthesis, and Evaluation of New Neuraminidase Inhibitors. *Org. Lett.* **2014**, *16*, 5060-5063.

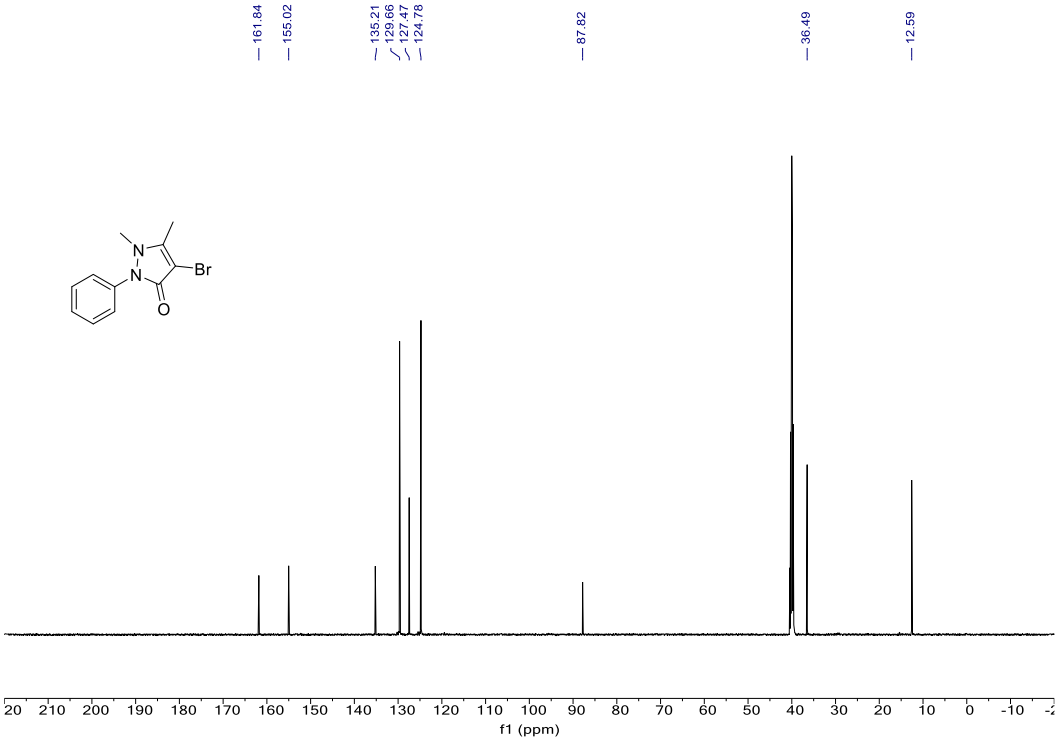
(3) Changmai, S.; Sultana, S.; Sarma, B.; Gogoi, S., Pd(ii)-Catalyzed alkyne annulation through allylic isomerization: synthesis of spiro-cyclopentadiene pyrazolones. *Chem. Commun.*, **2021**, *57*, 6027-6030.

Copies of ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra

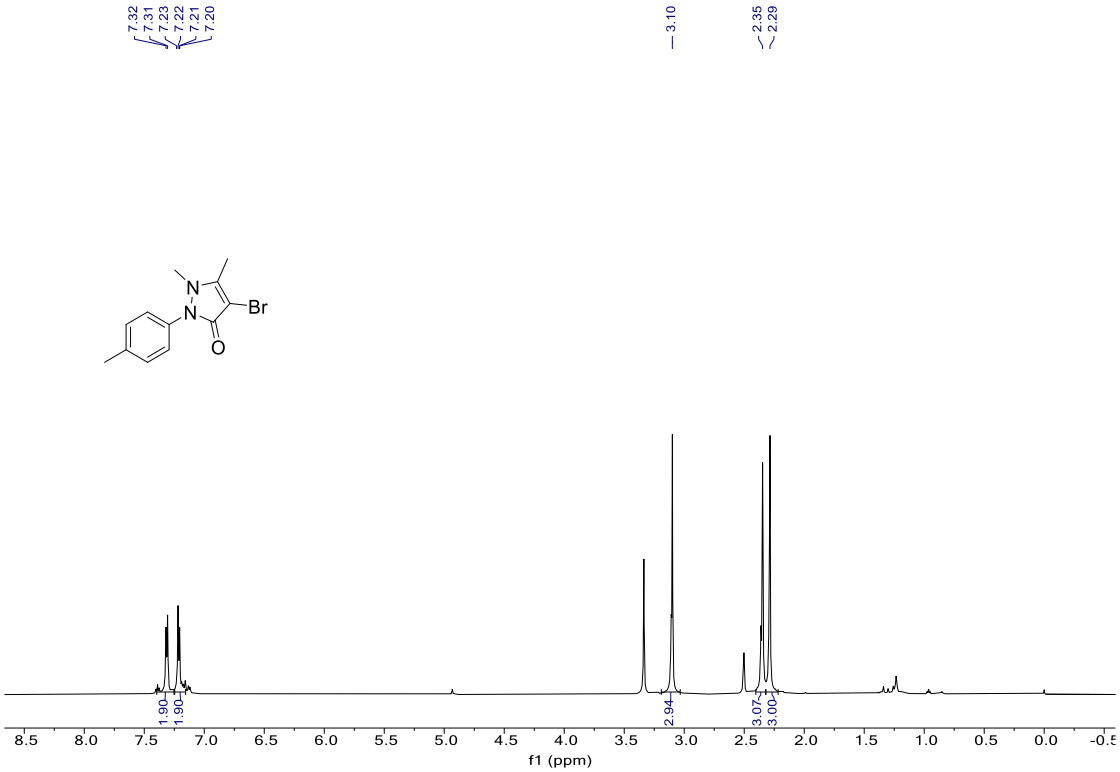
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3a**



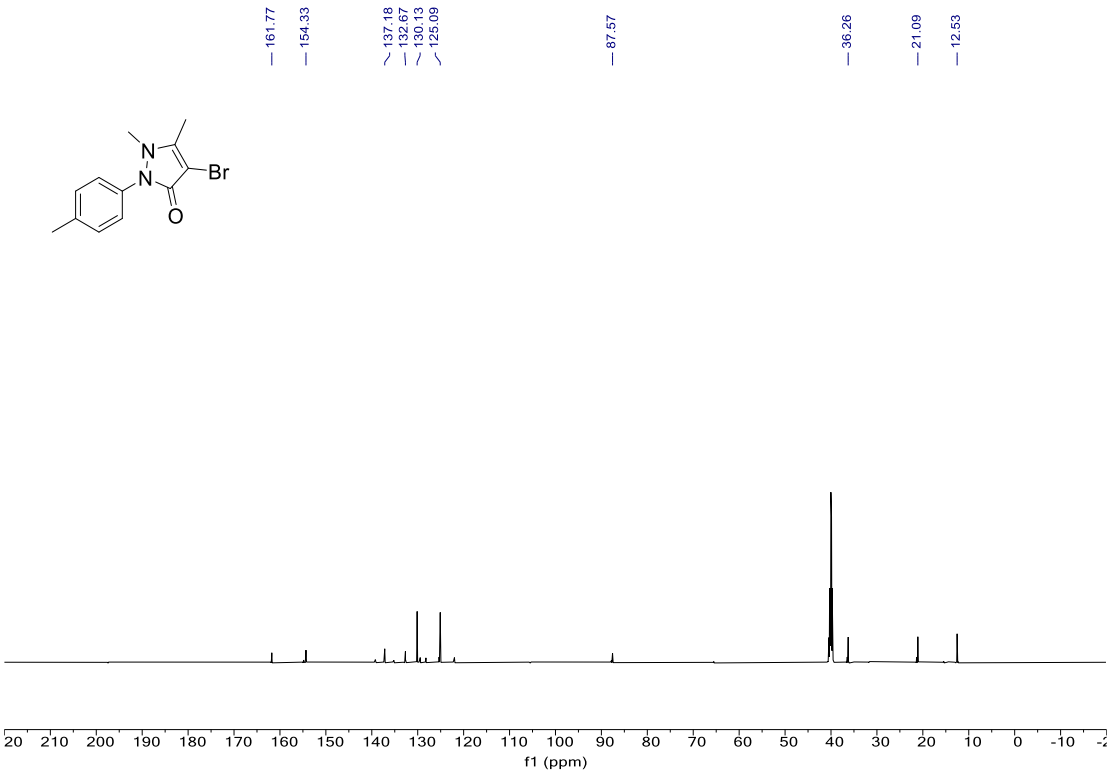
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3a**



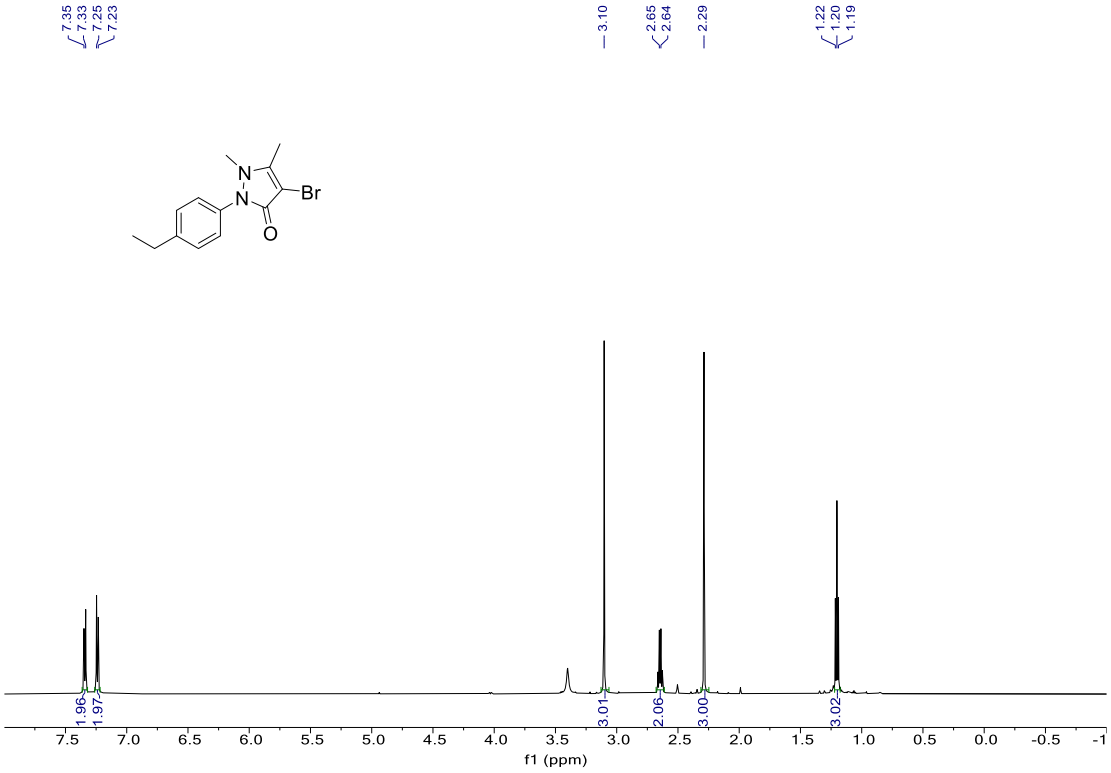
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3b**



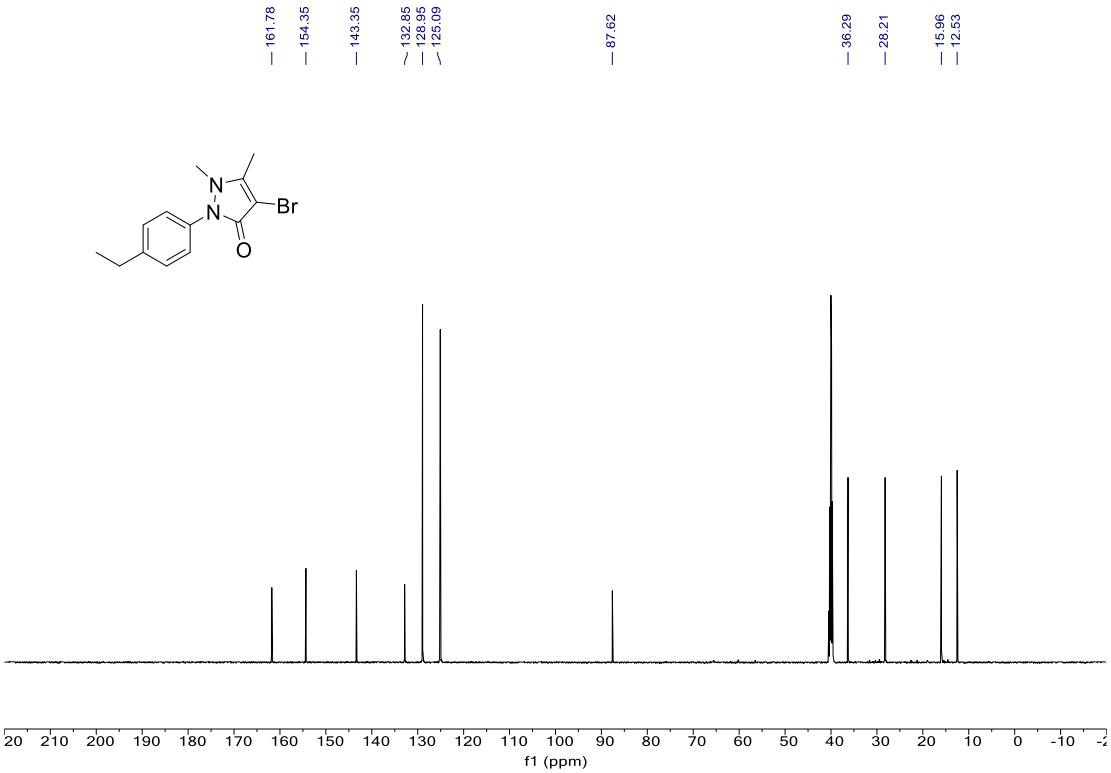
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3b**



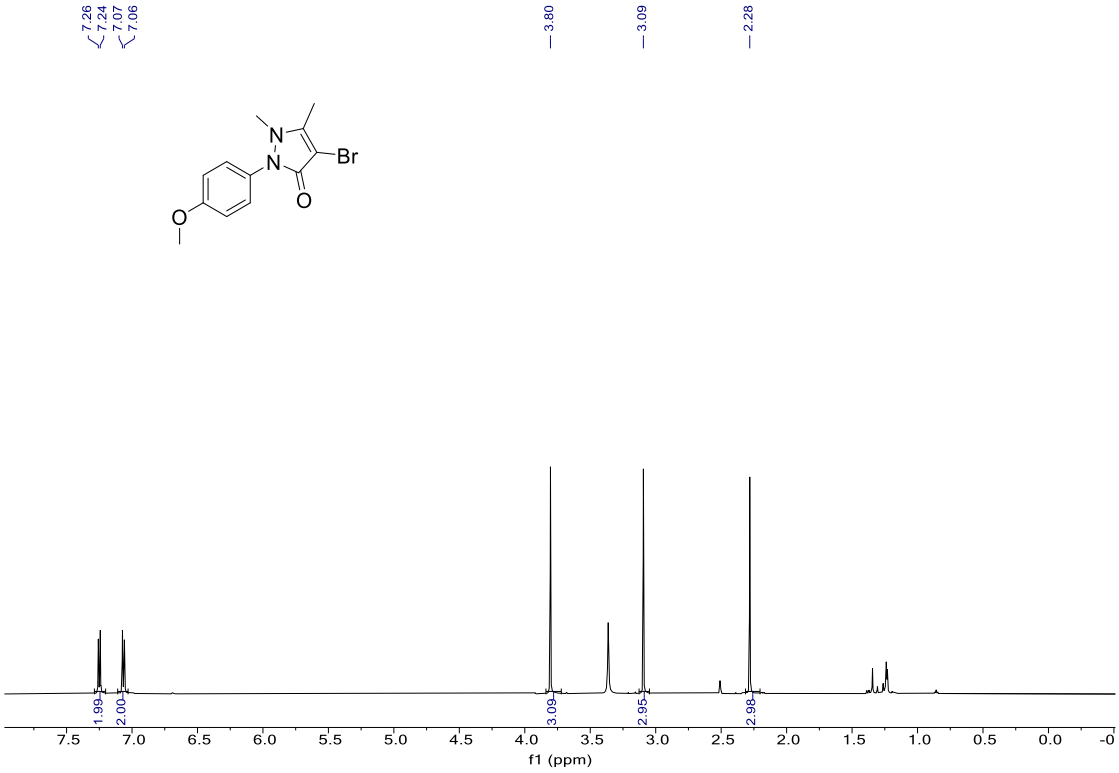
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3c**



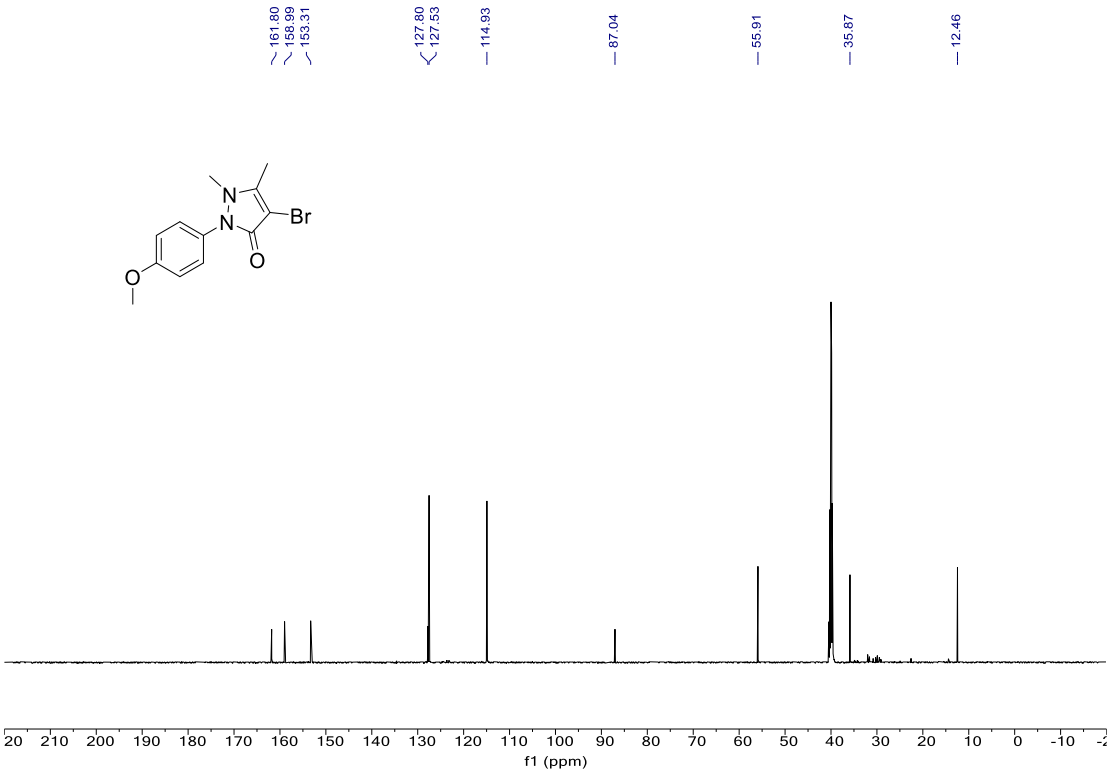
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3c**



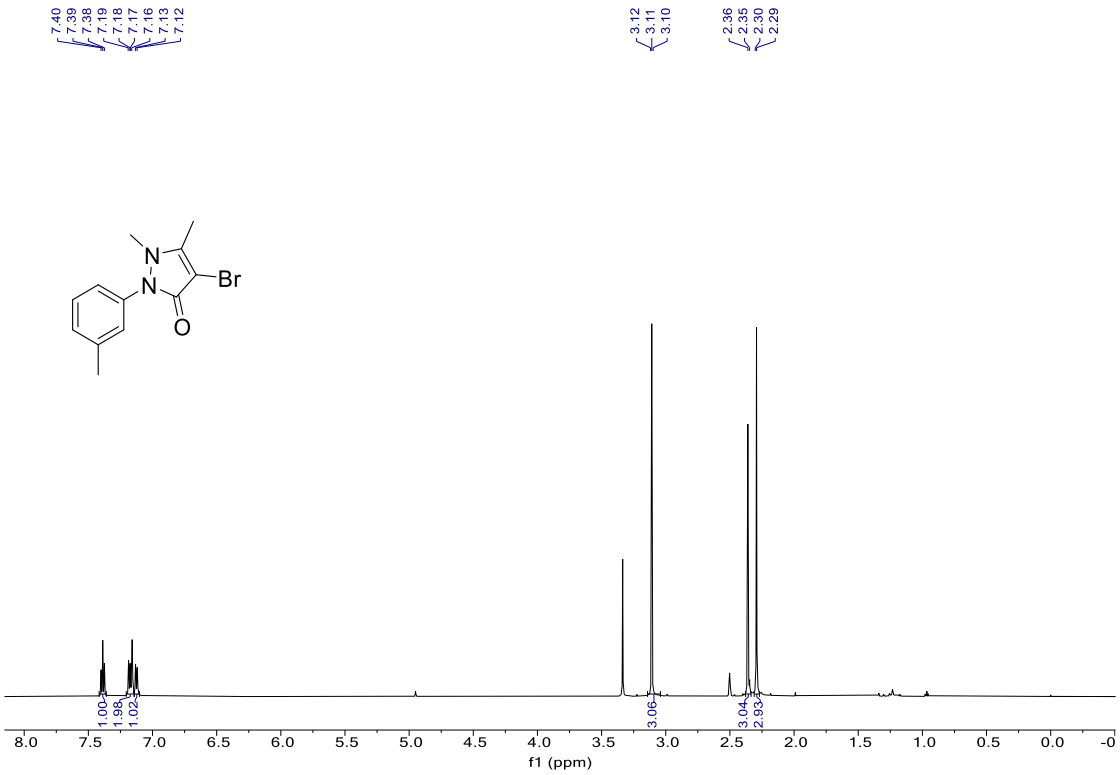
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3d**



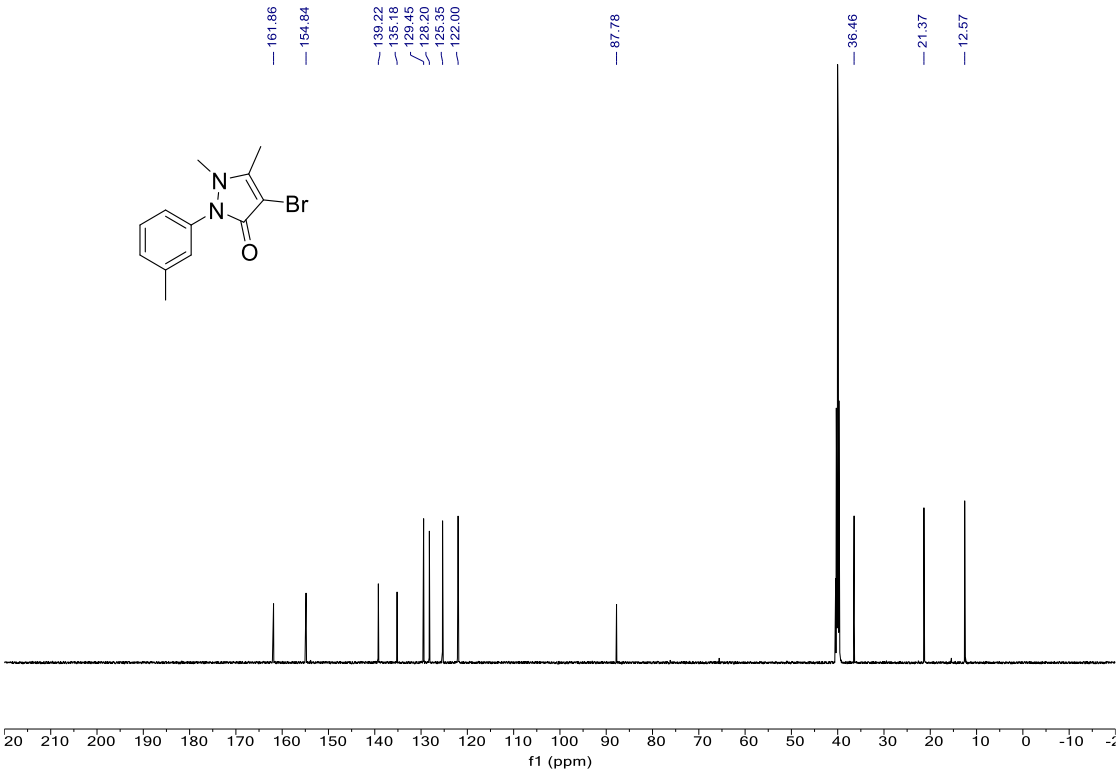
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3d**



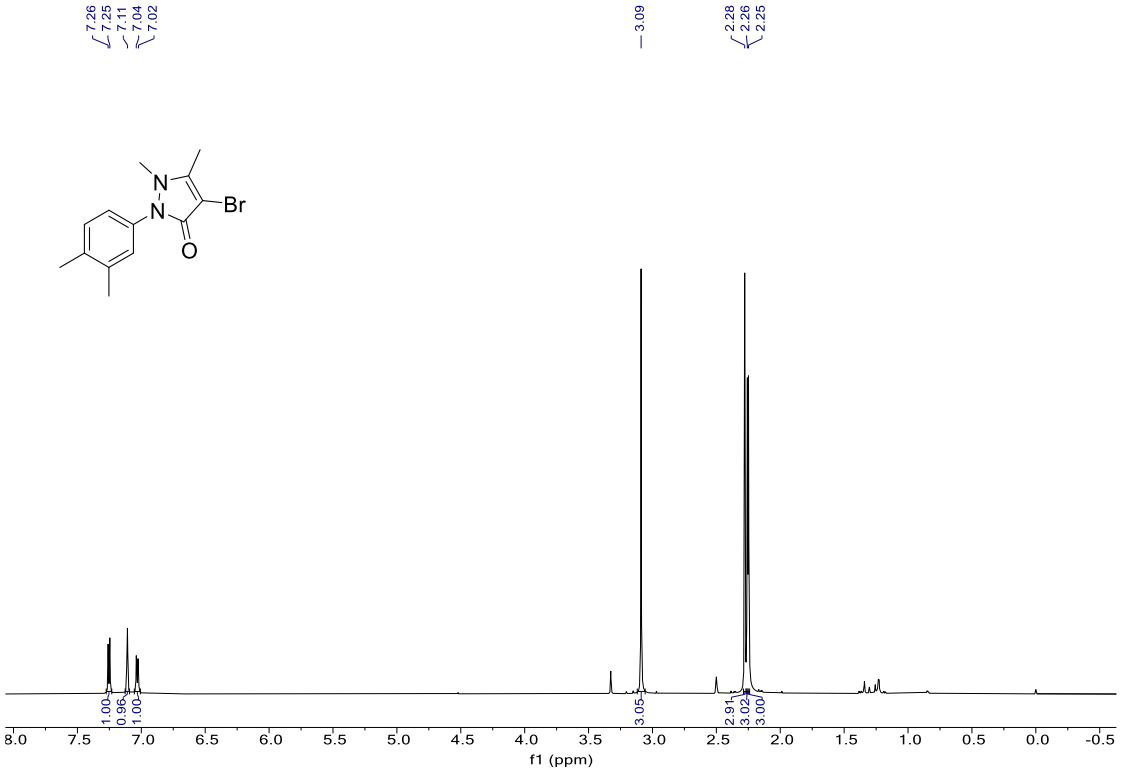
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3e**



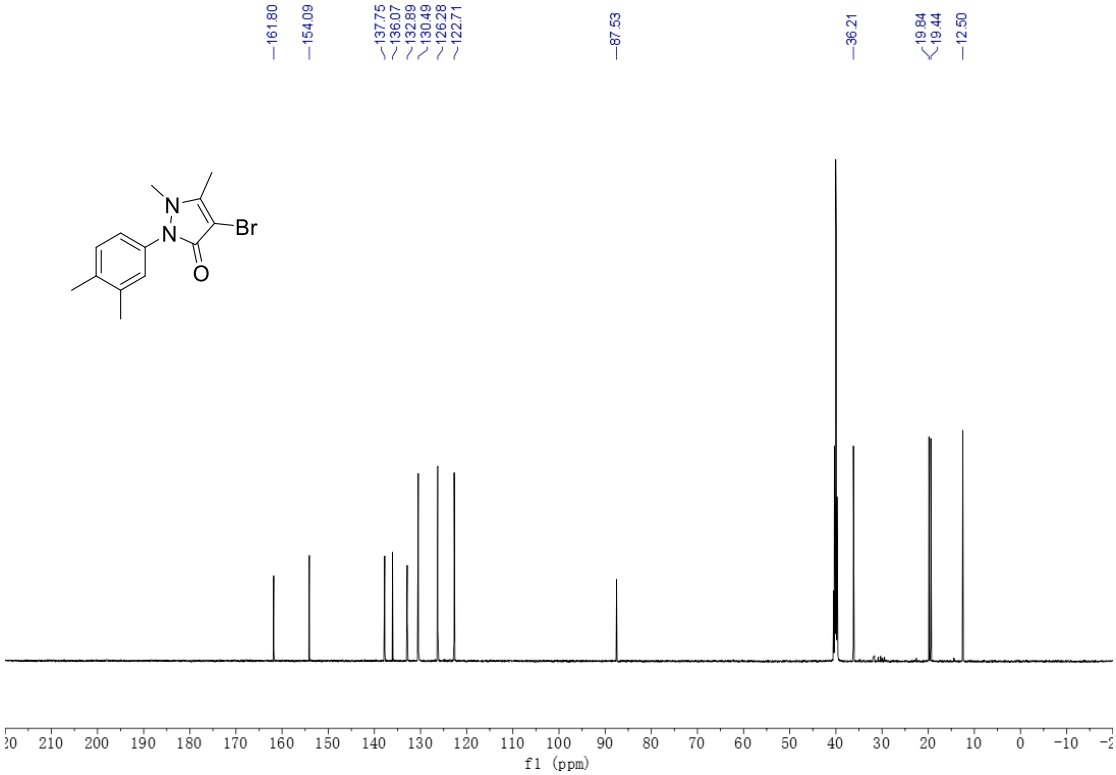
^{13}C NMR (600 MHz, DMSO- d_6) of compound **3e**



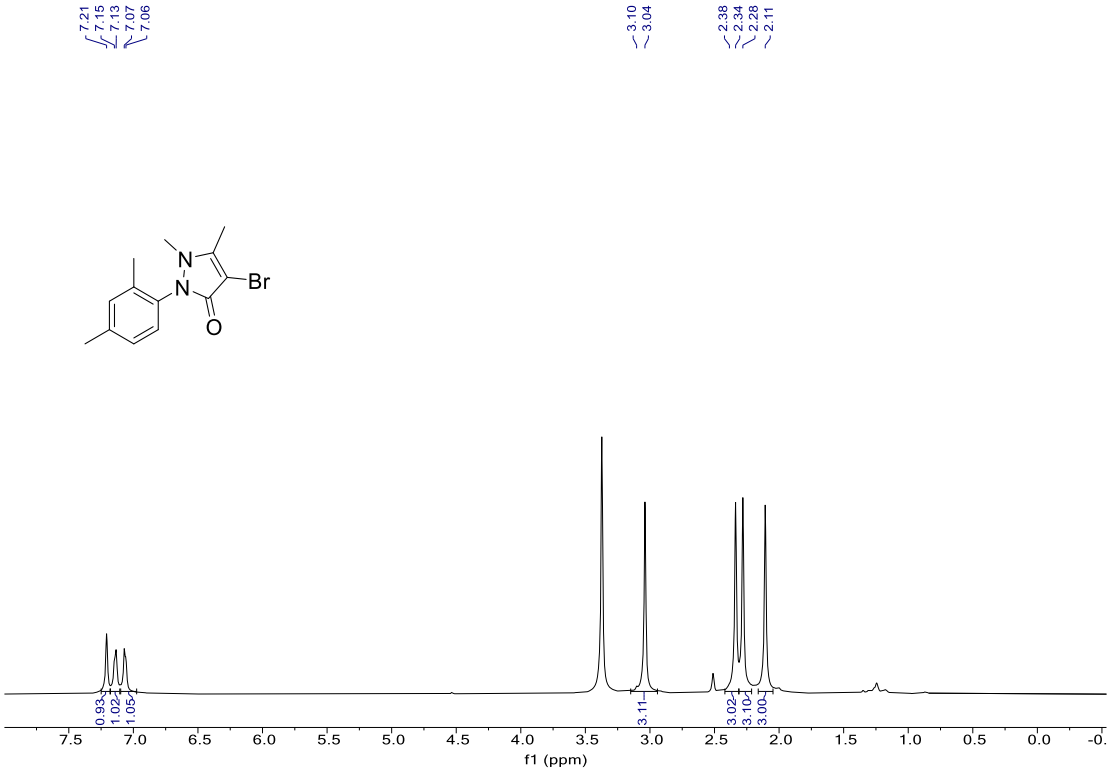
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3f**



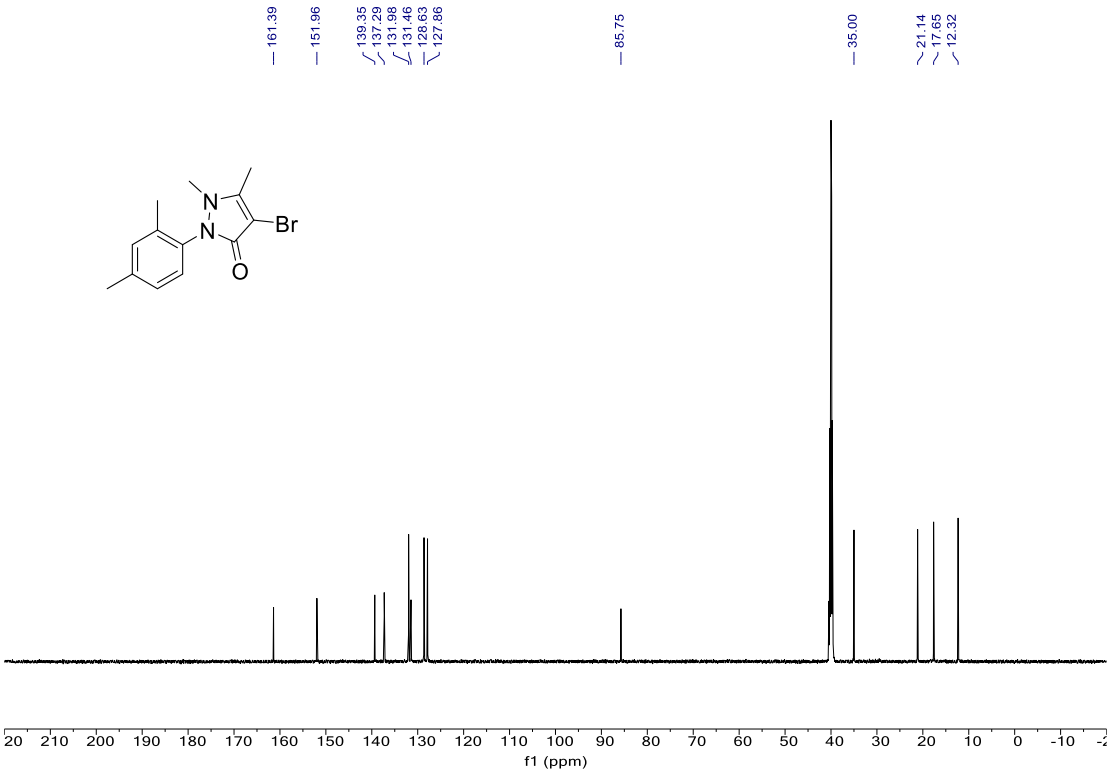
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3f**



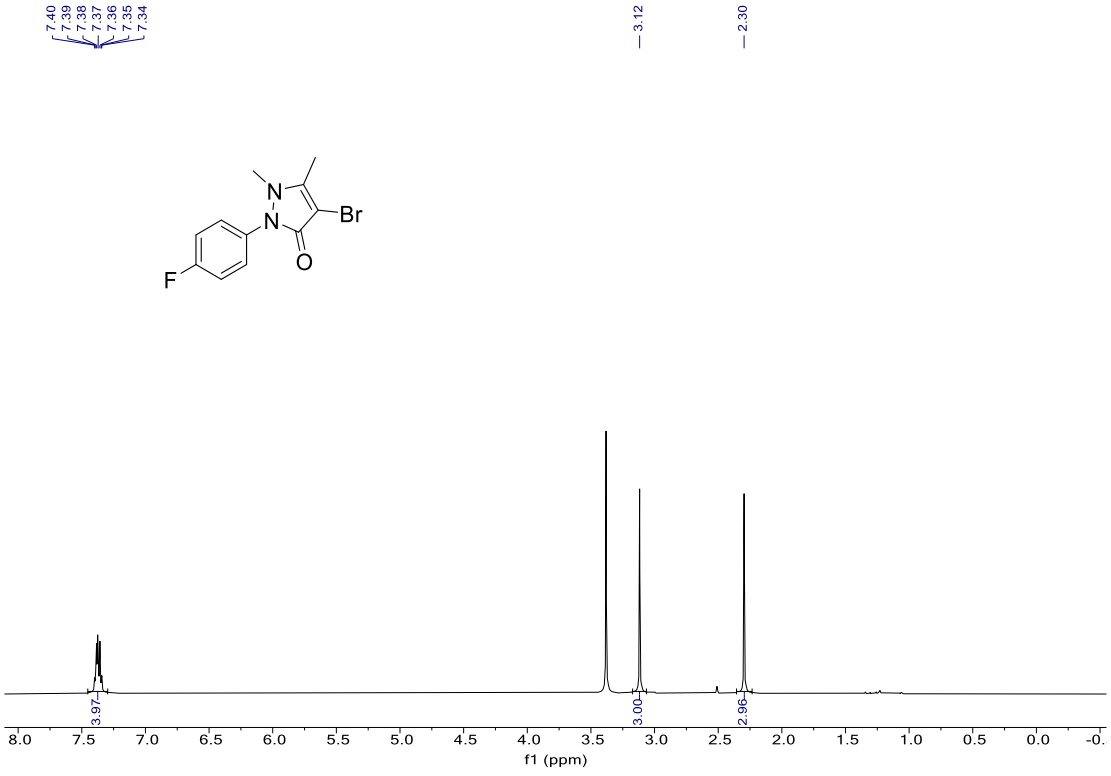
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3g**



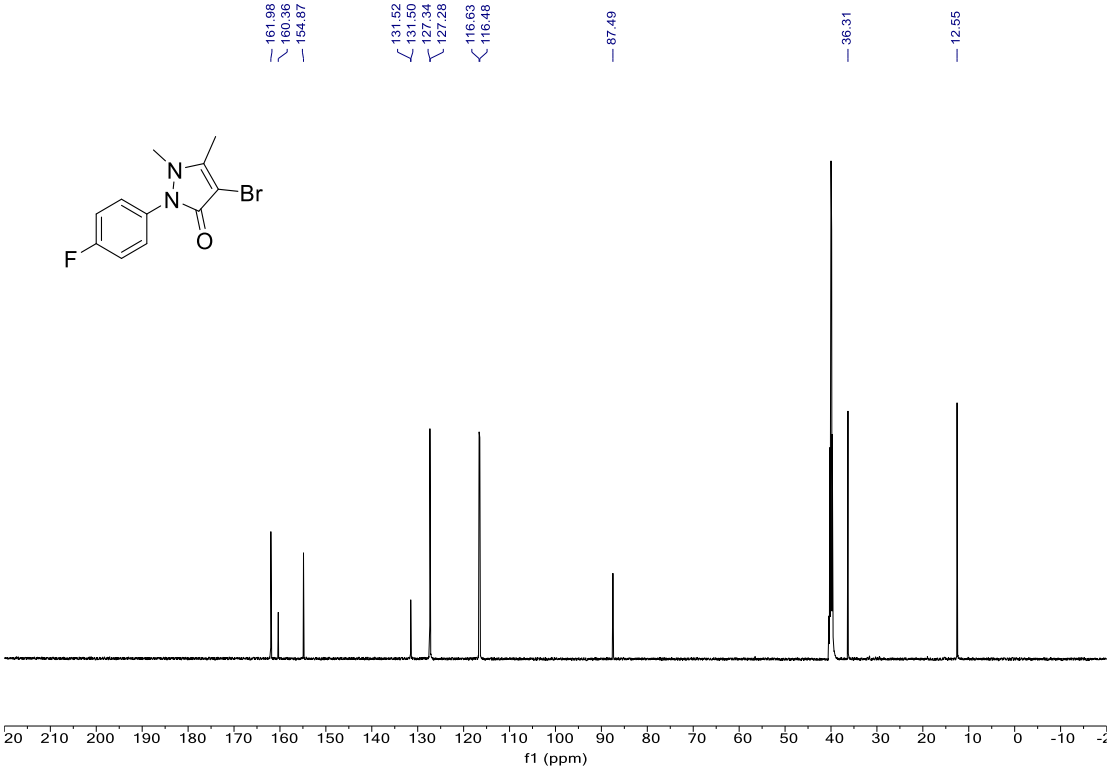
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3g**



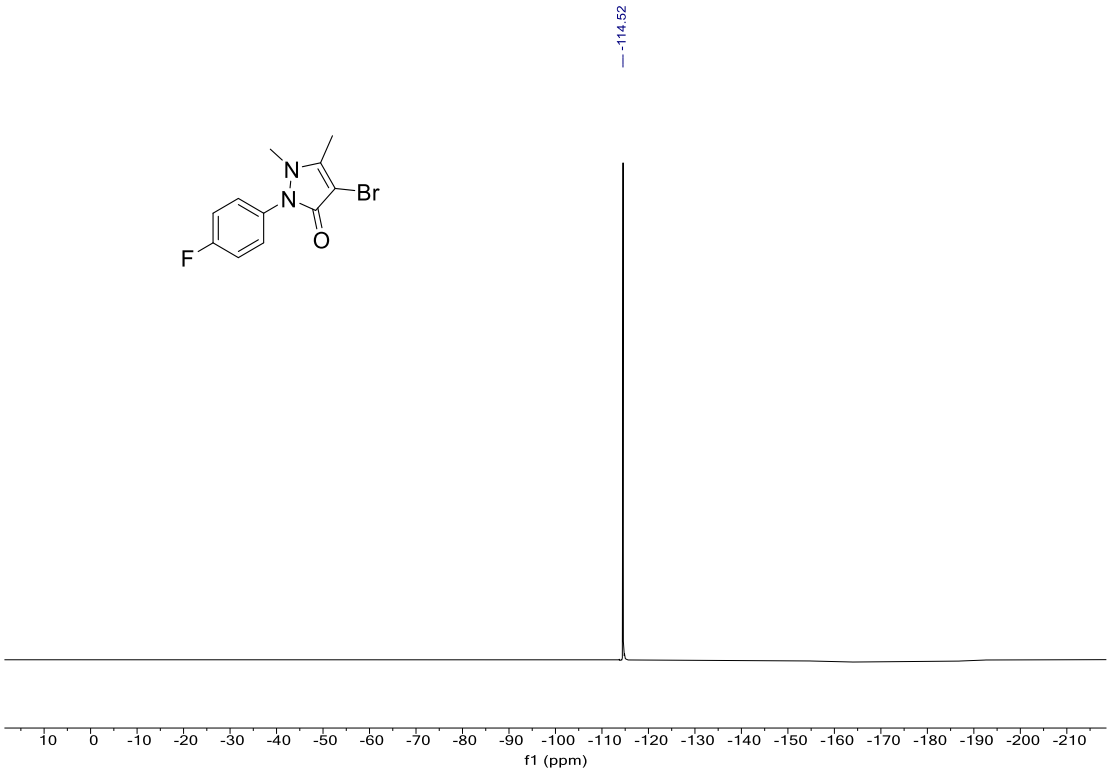
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3h**



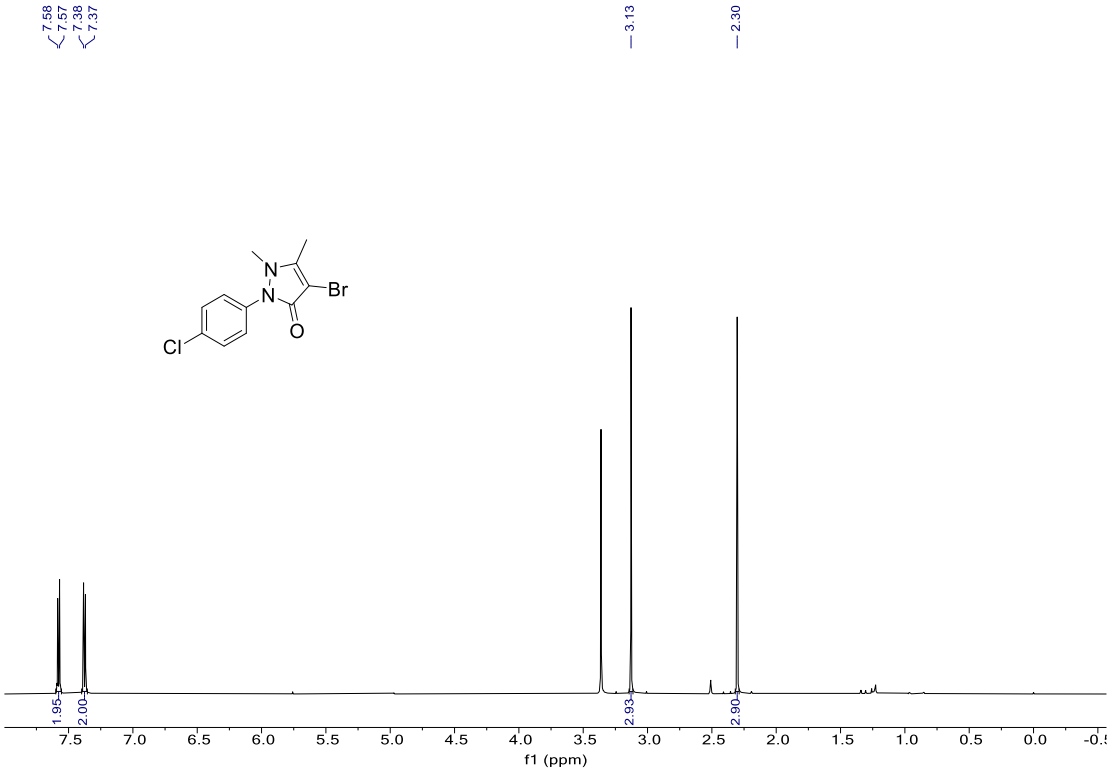
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3h**



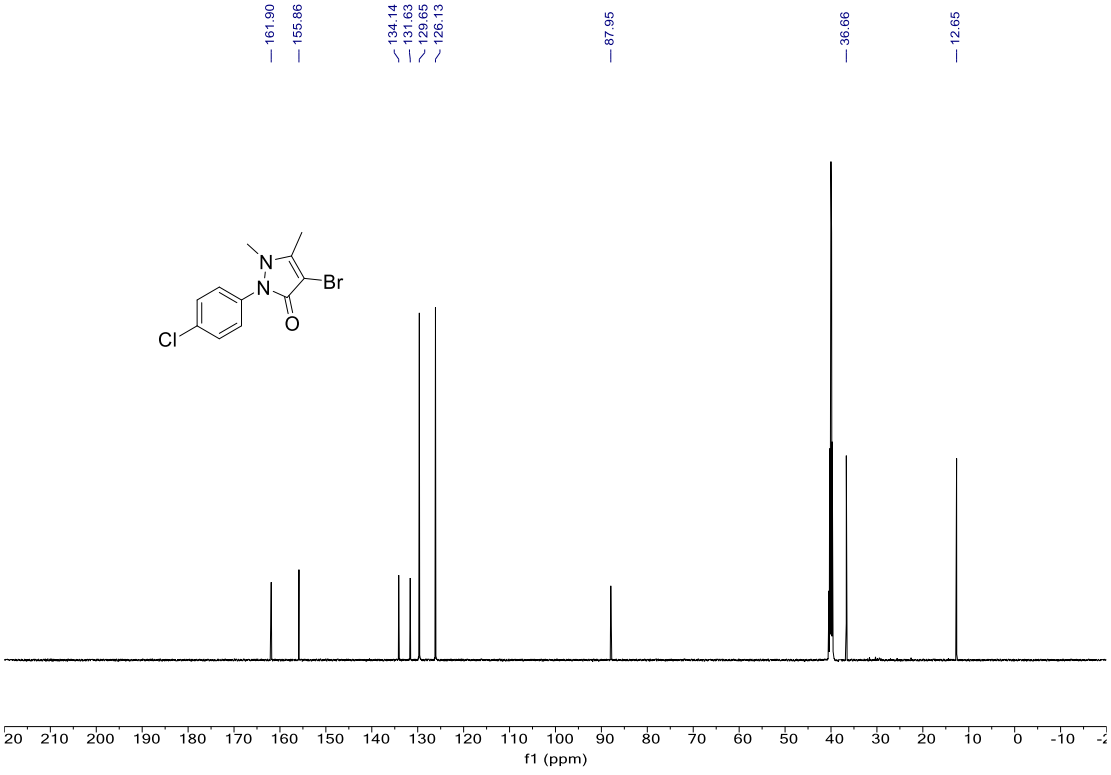
^{19}F NMR (565 MHz, DMSO- d_6) of compound **3h**



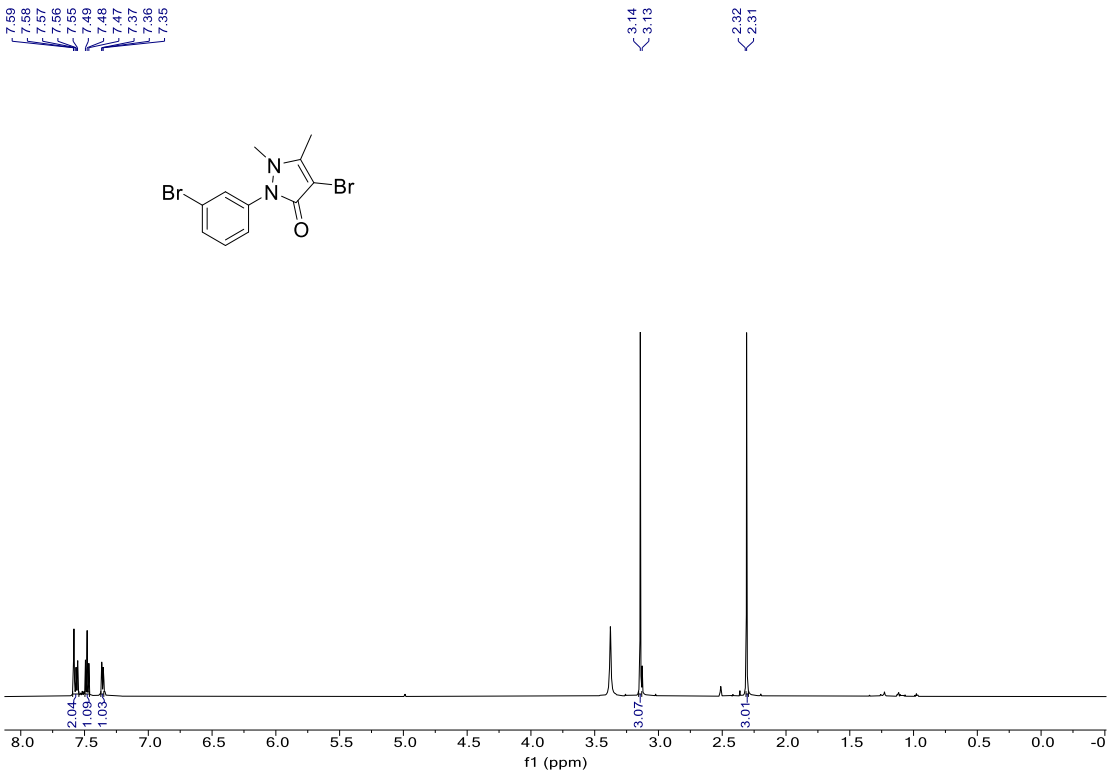
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3i**



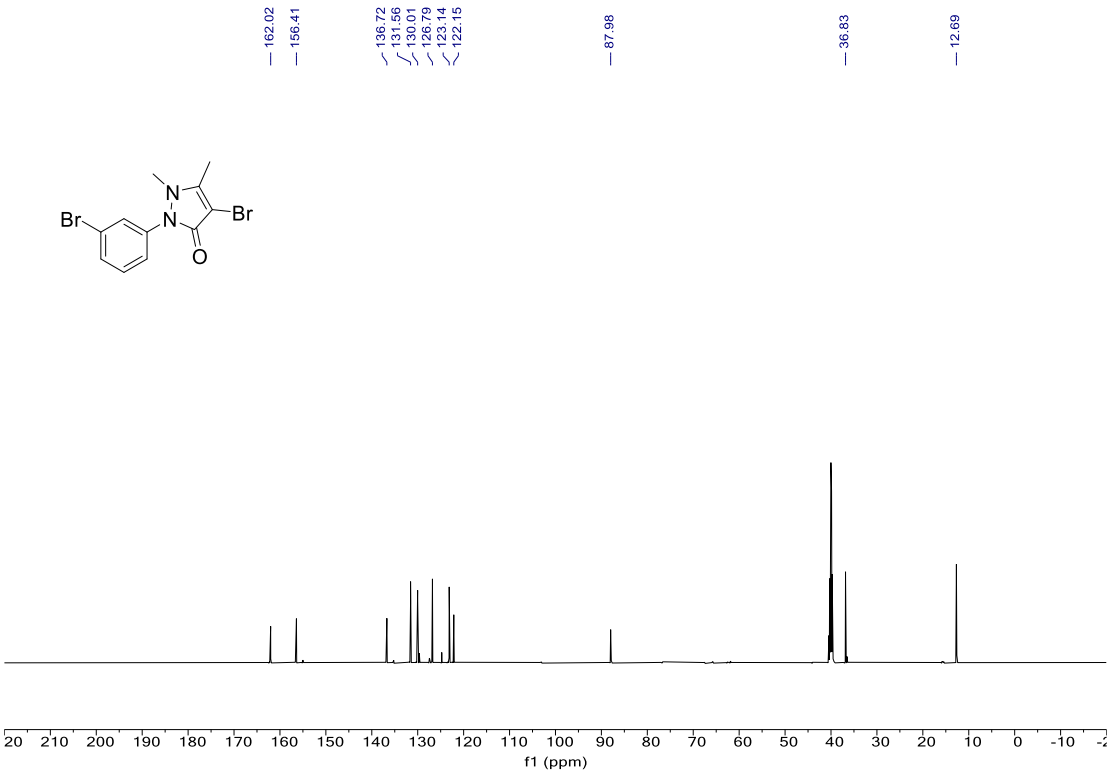
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3i**



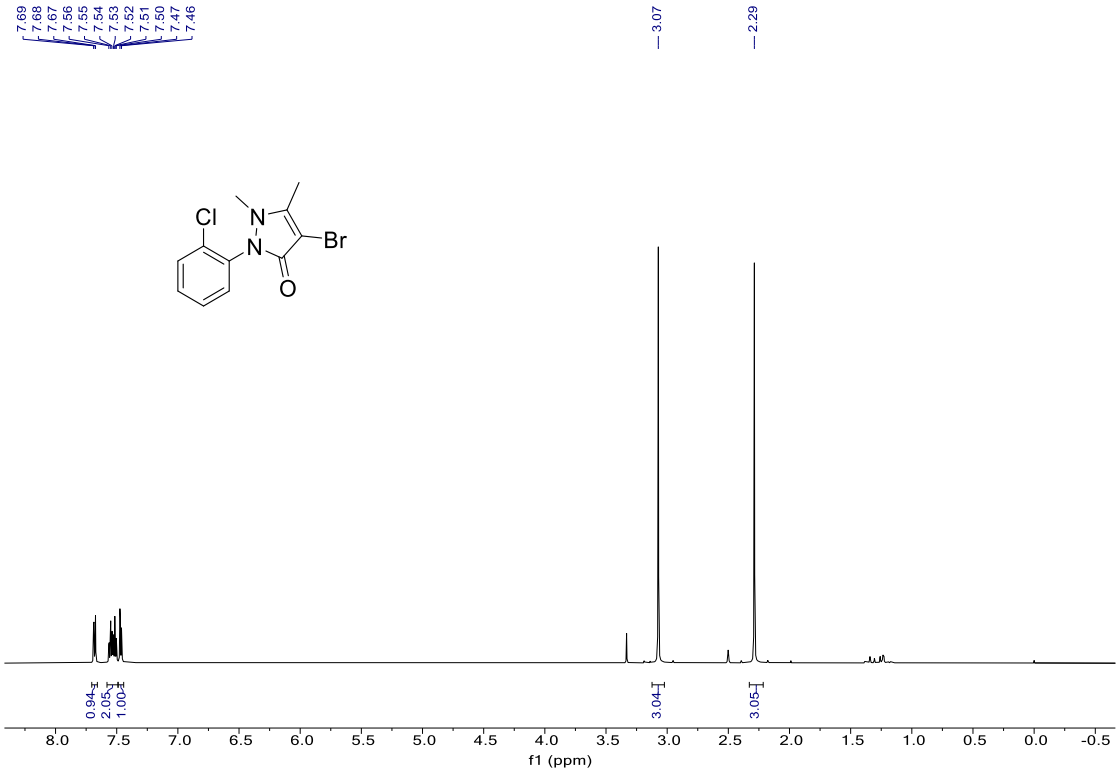
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3j**



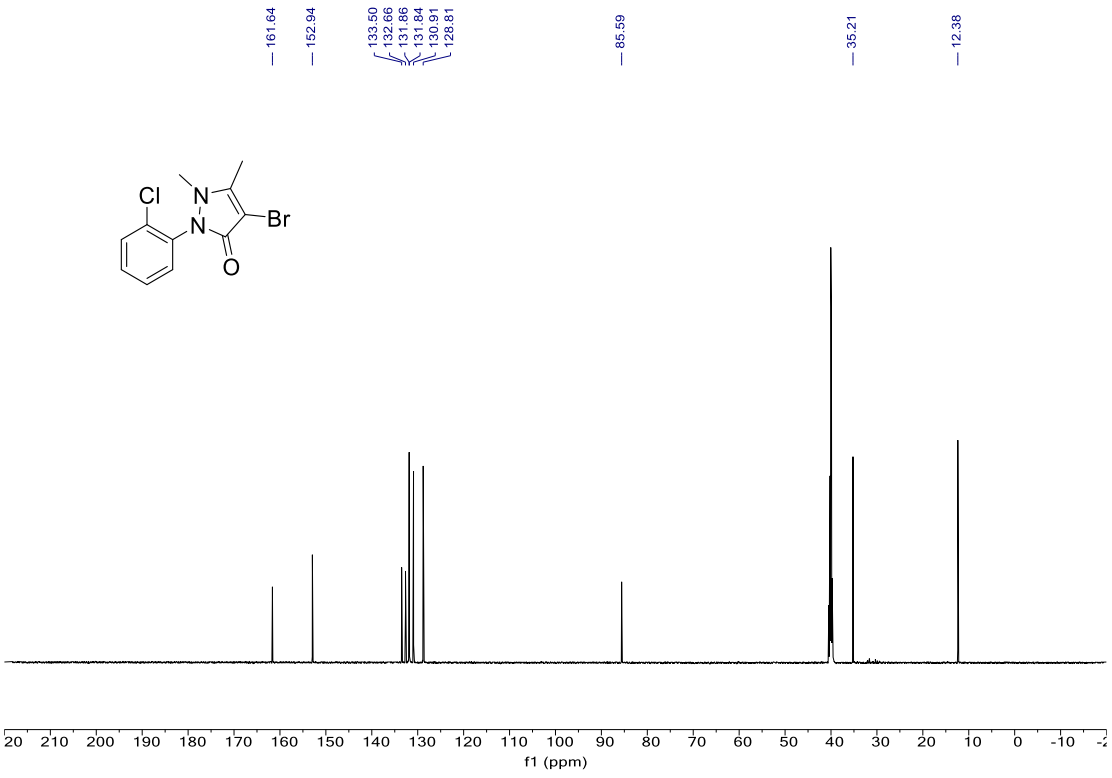
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3j**



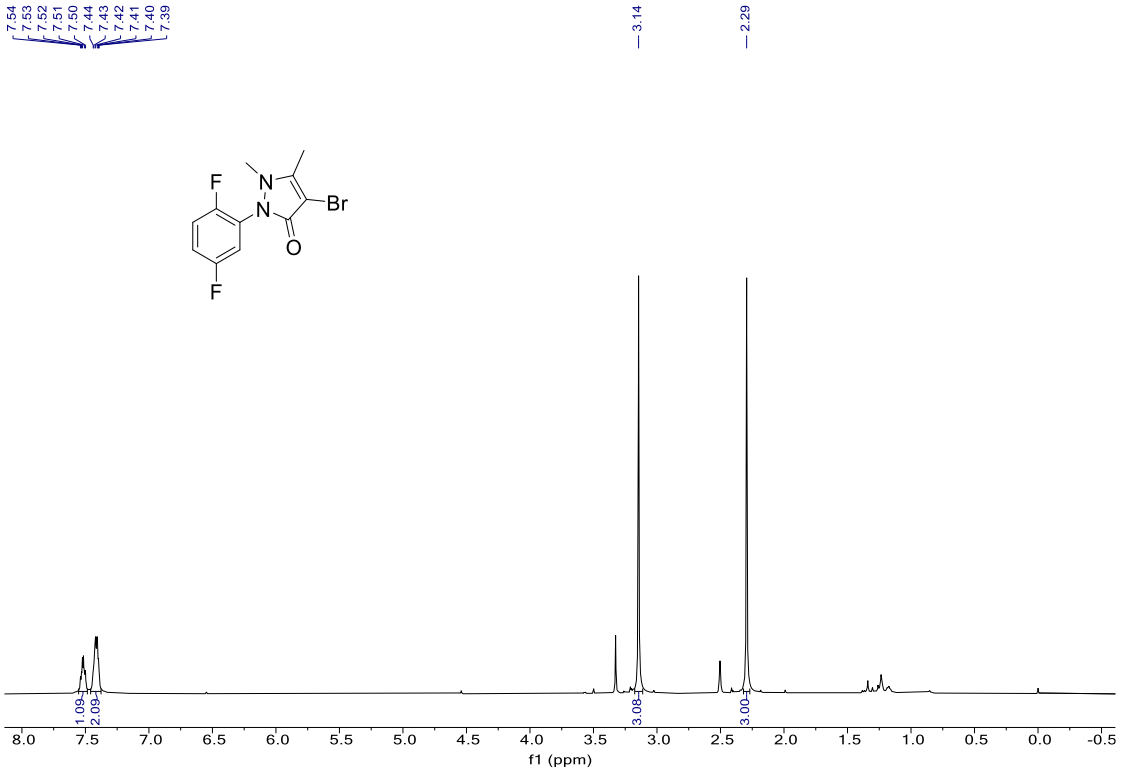
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3k**



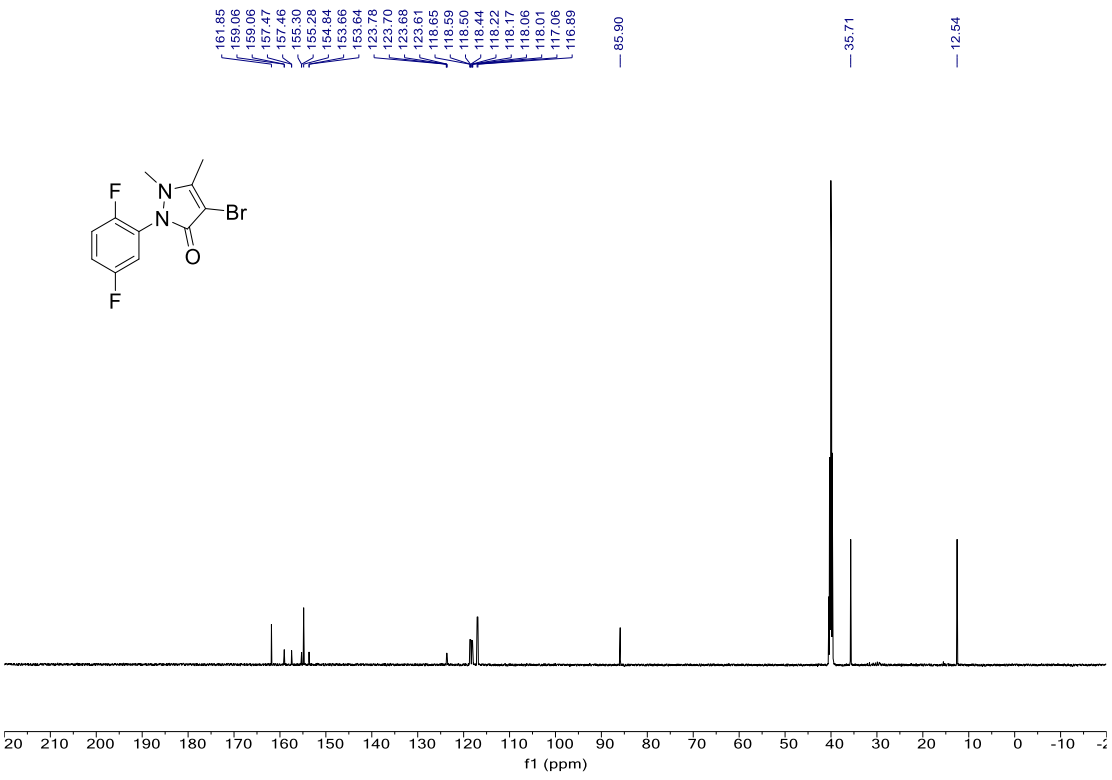
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3k**



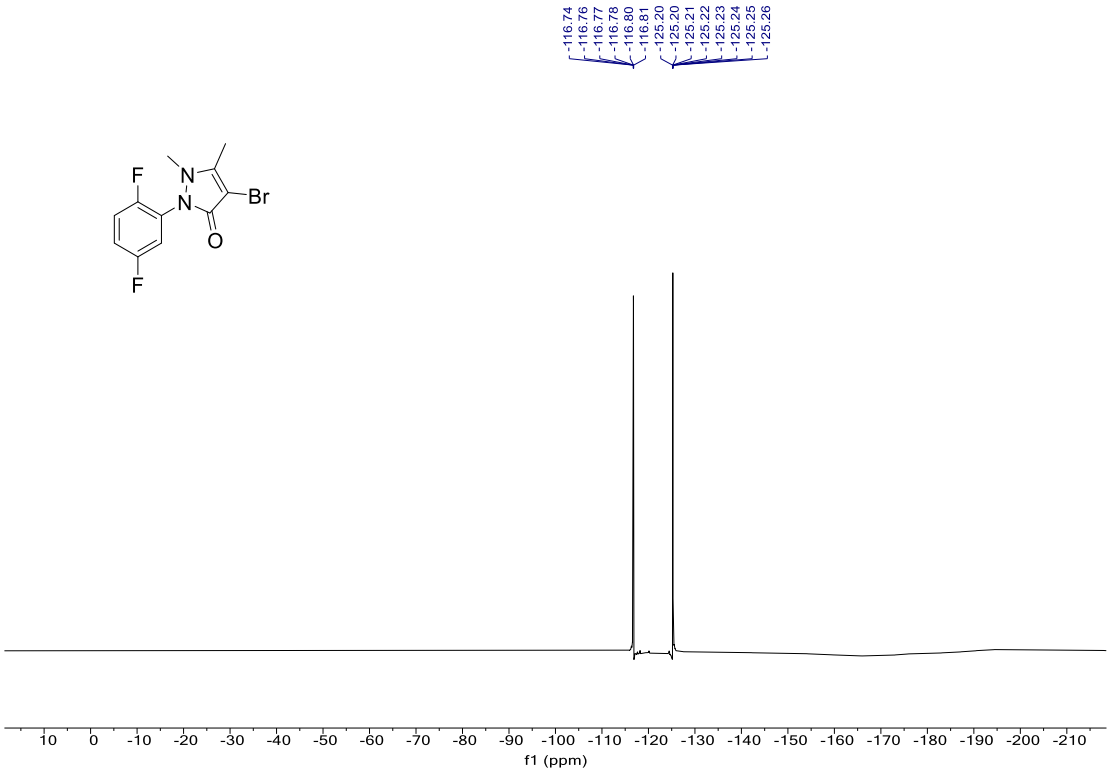
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3l**



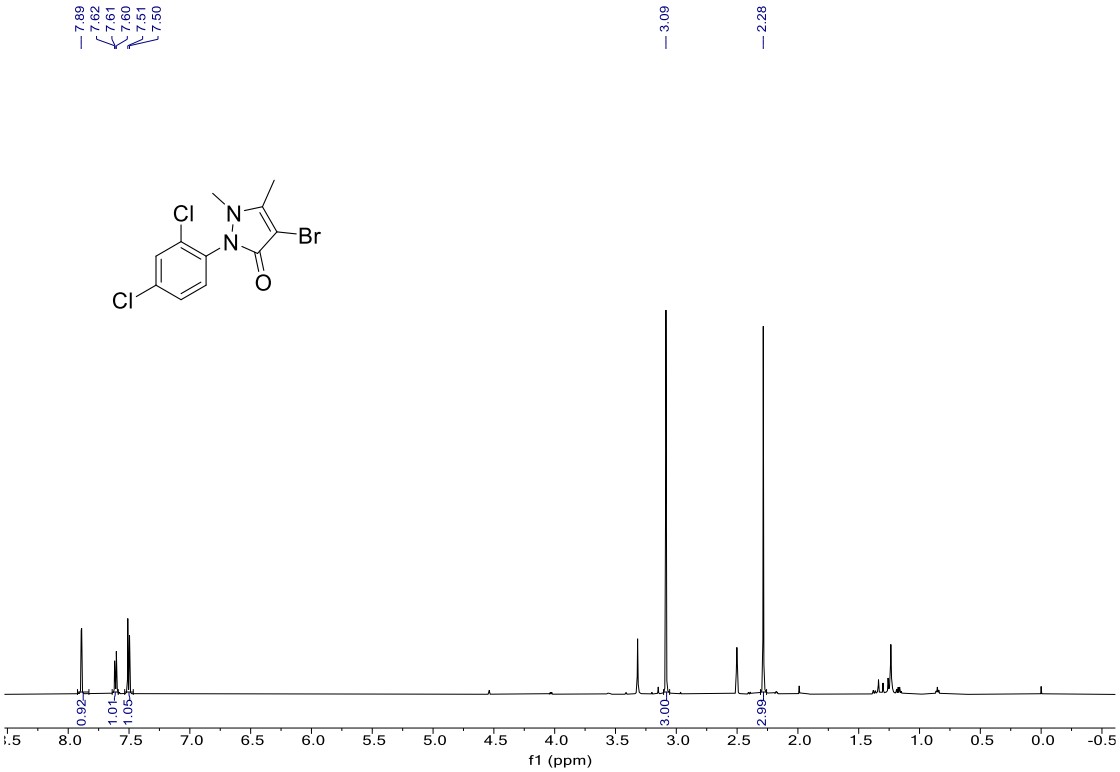
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3l**



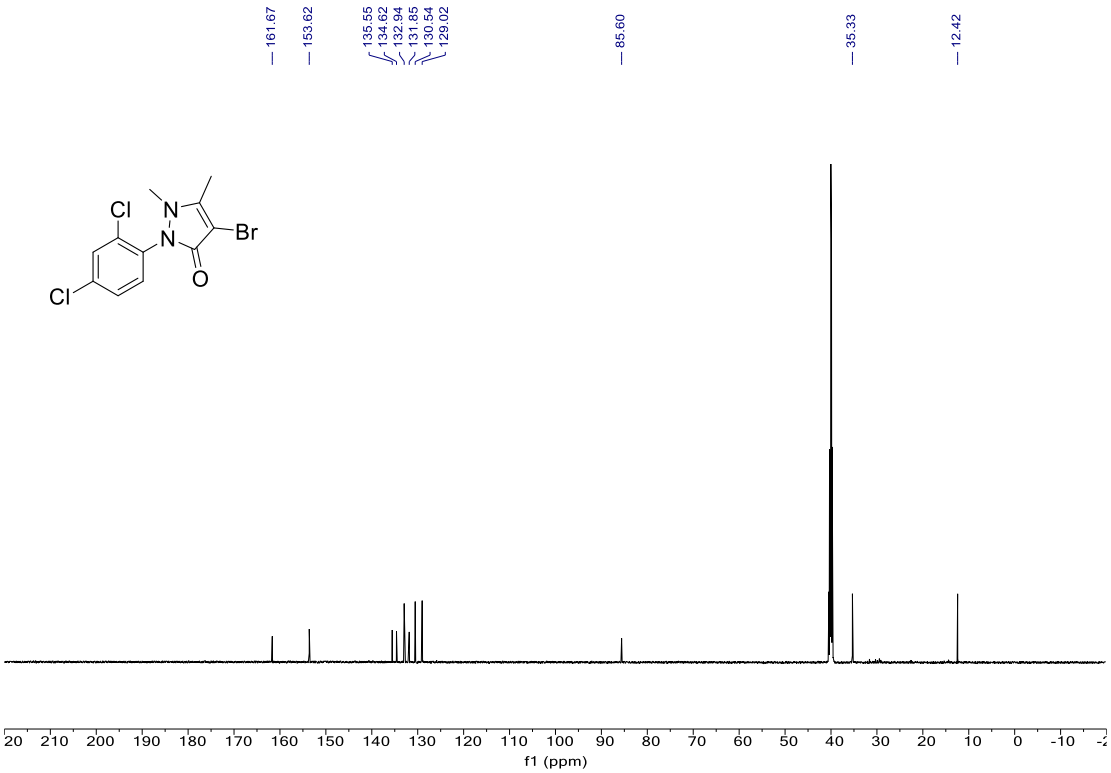
^{19}F NMR (565 MHz, DMSO- d_6) of compound **3l**



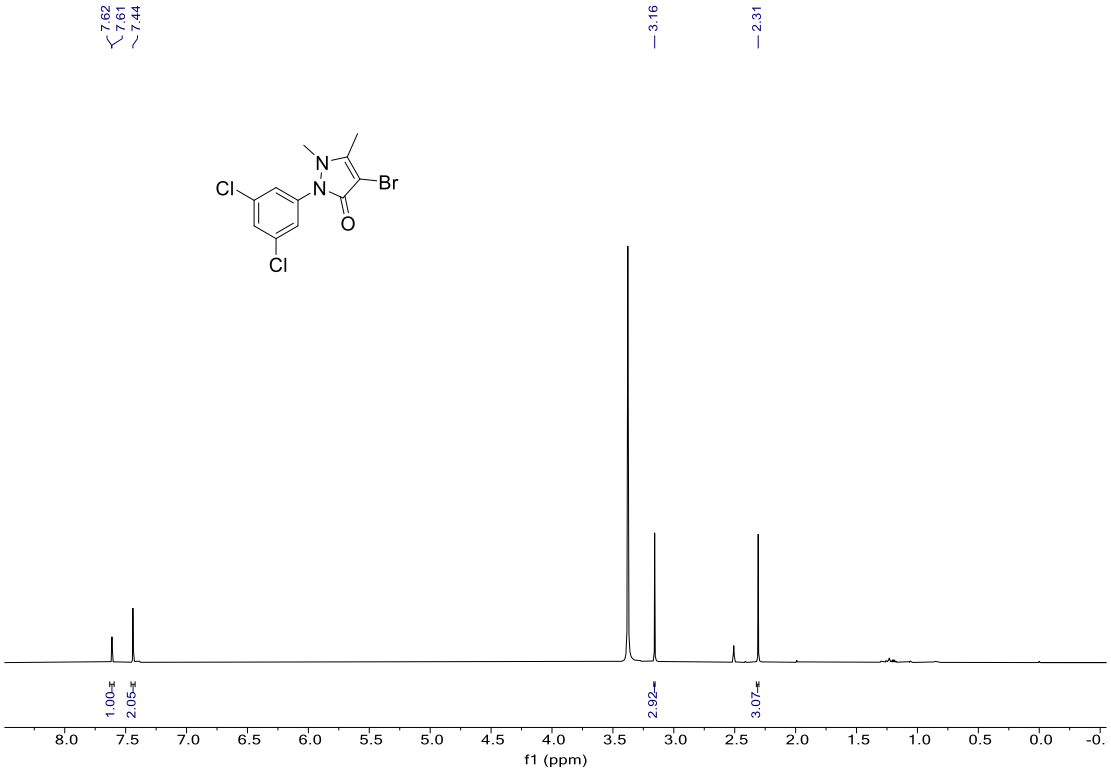
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3m**



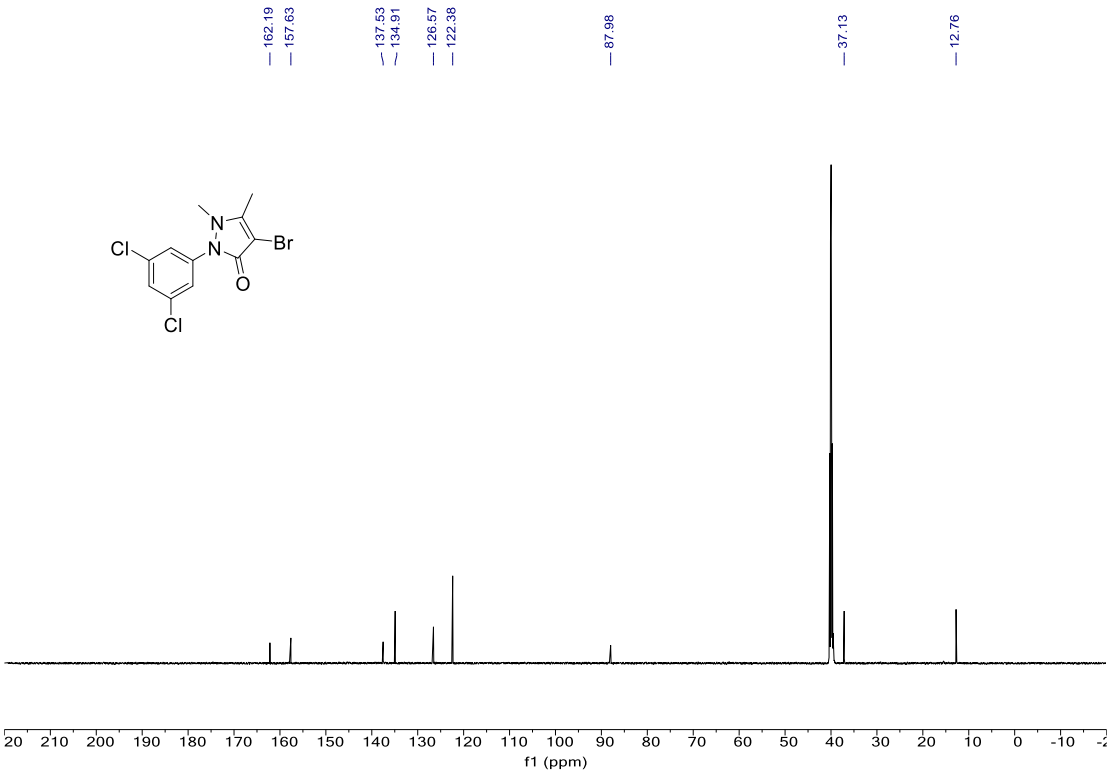
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3m**



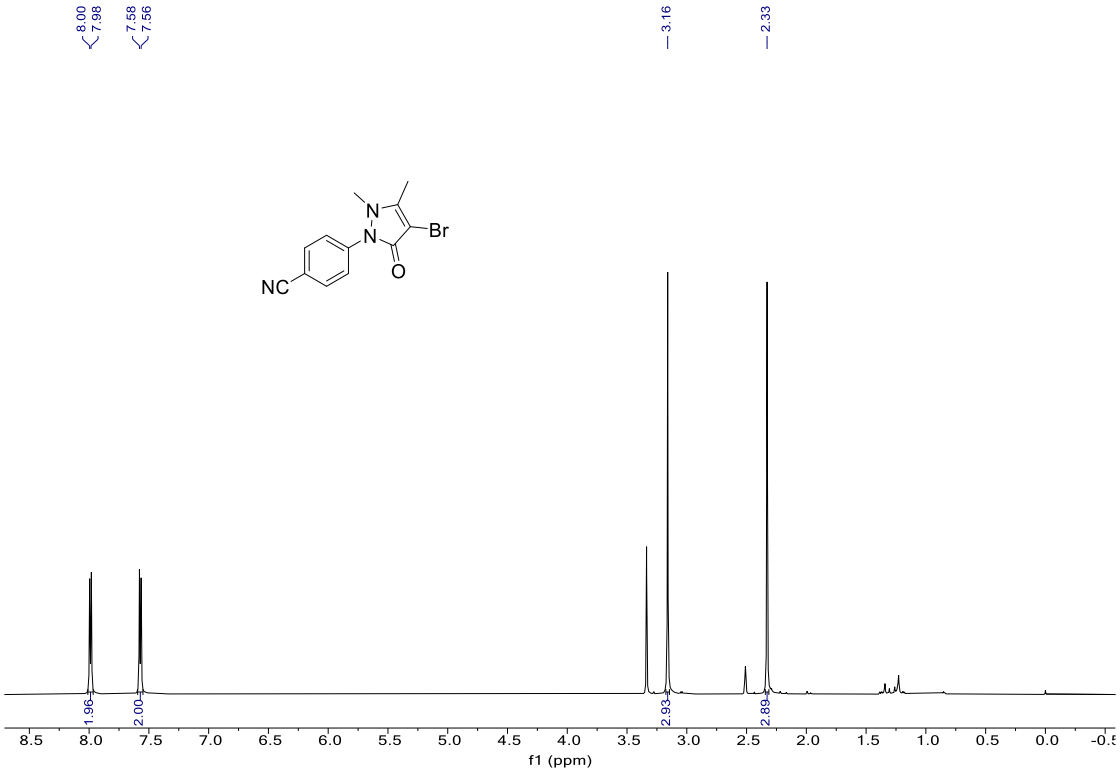
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3n**



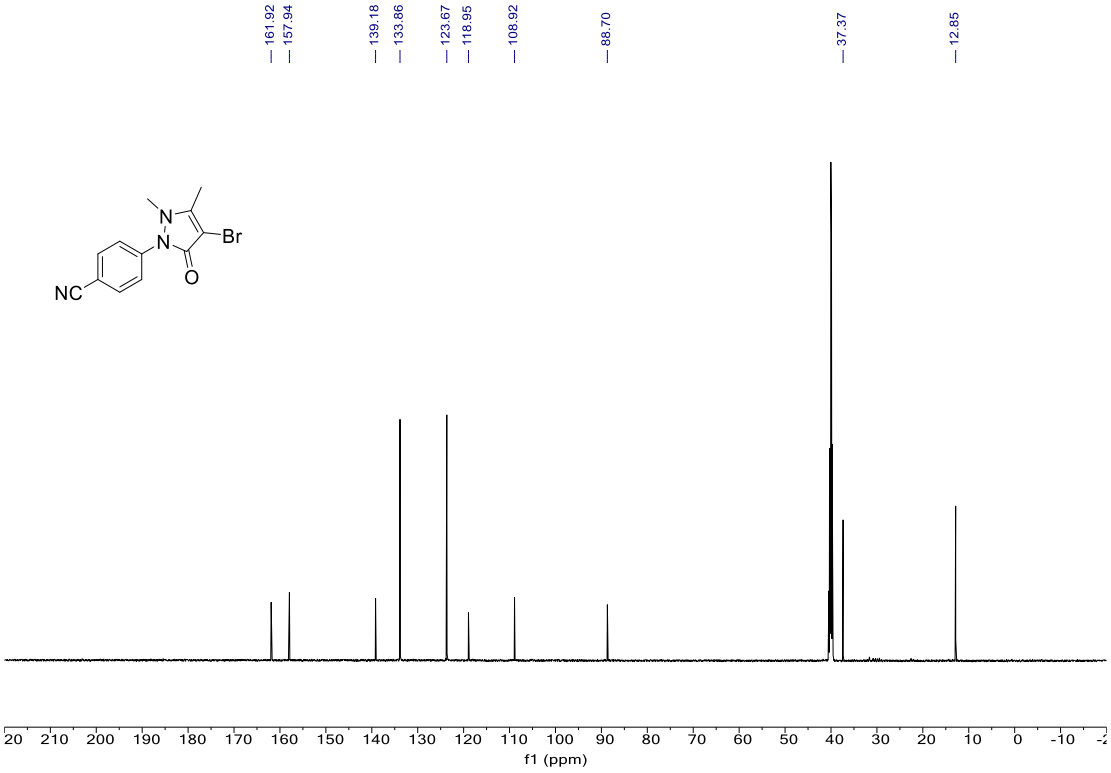
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3n**



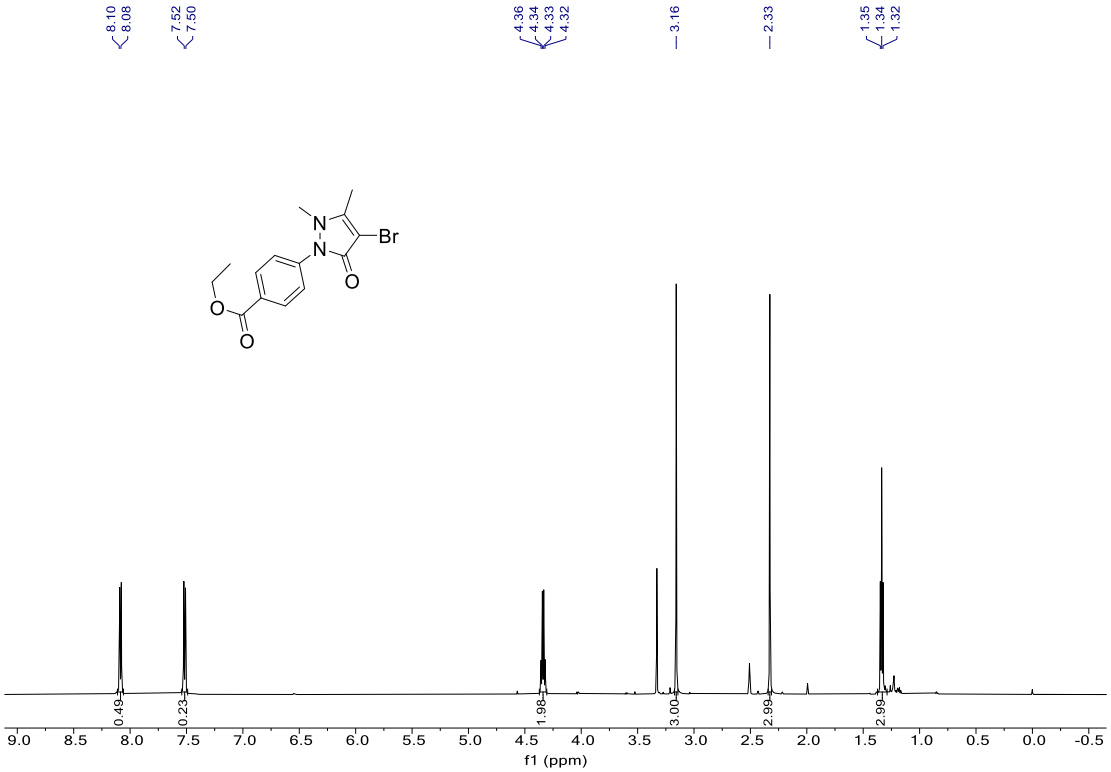
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3o**



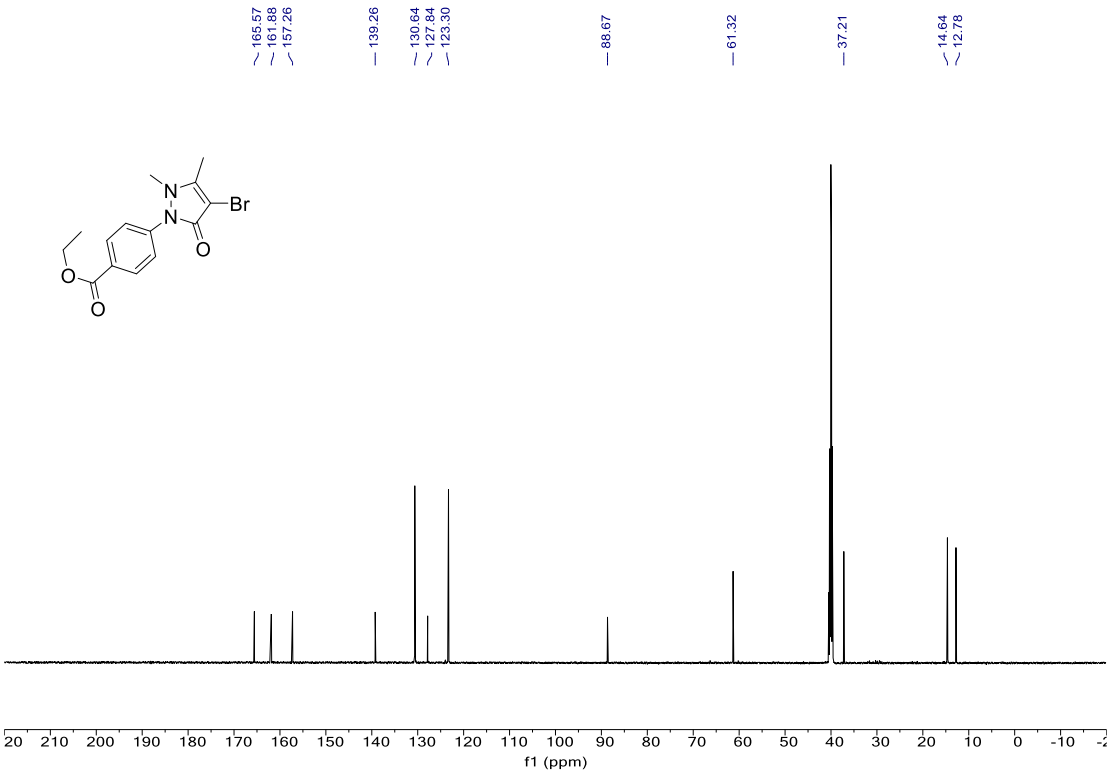
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3o**



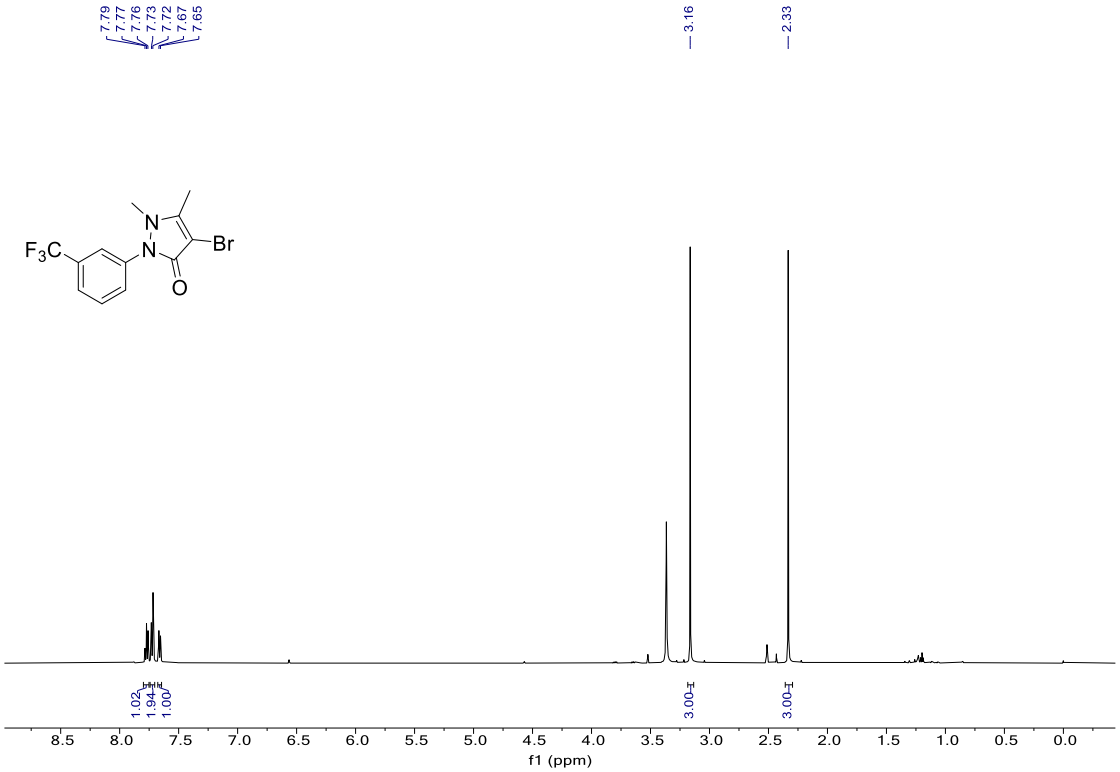
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3p**



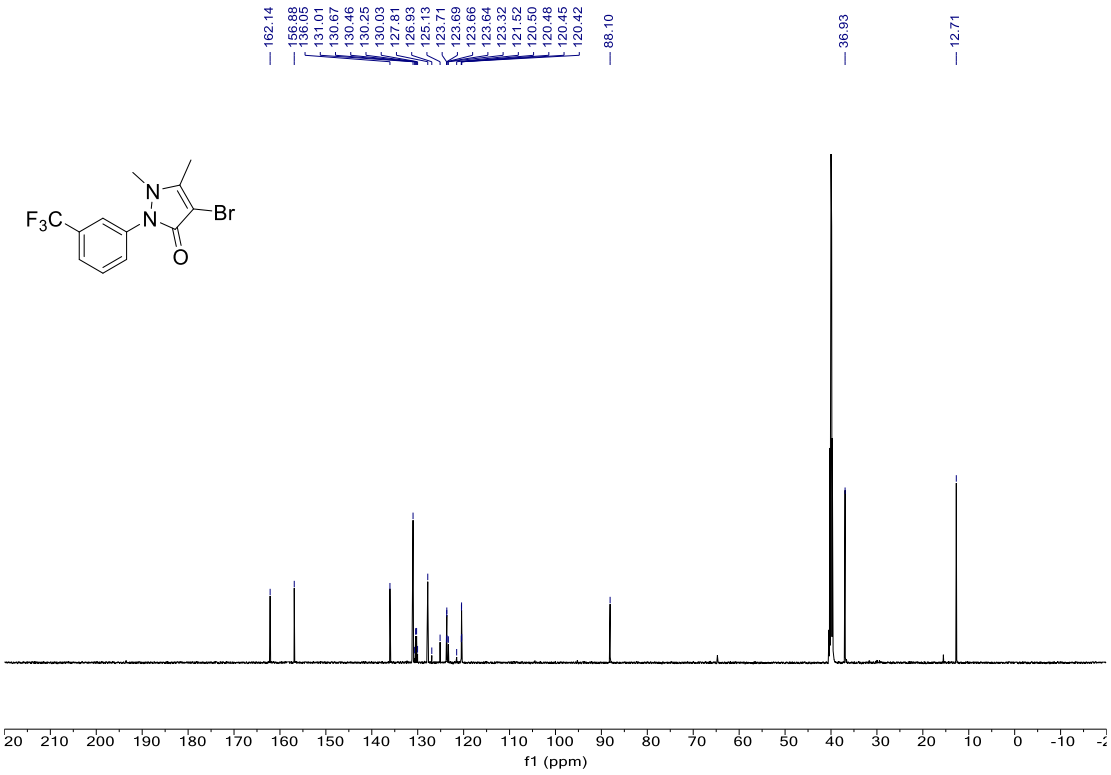
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3p**



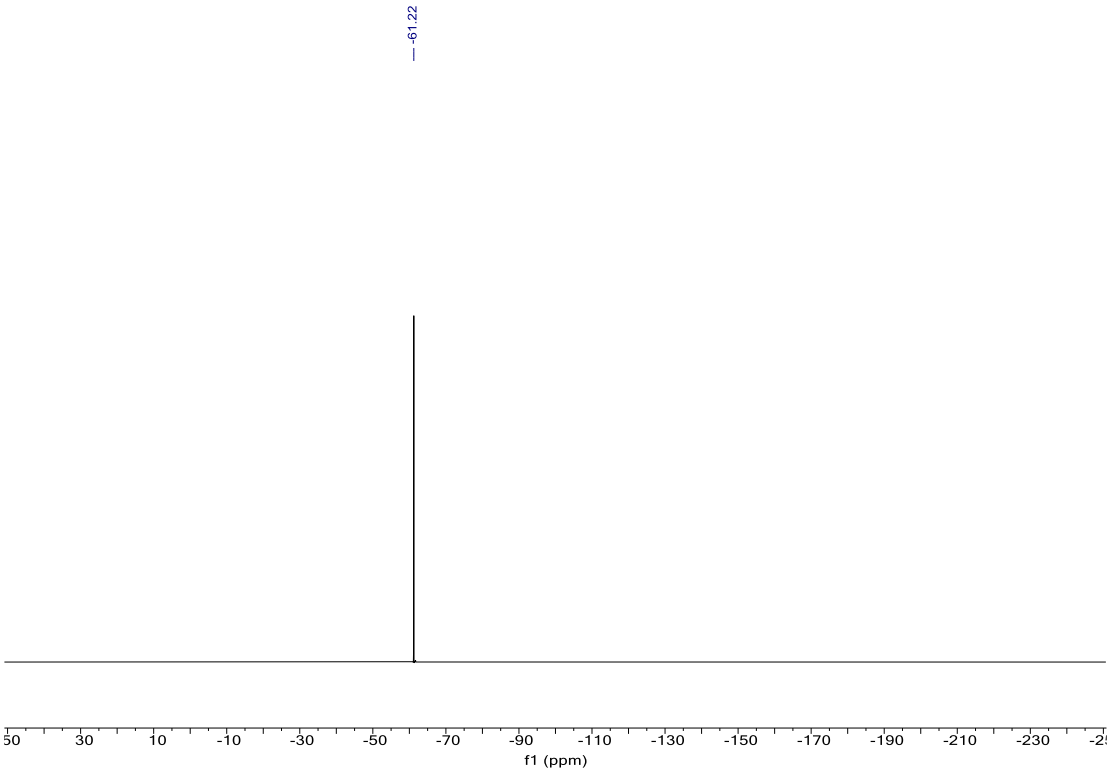
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3q**



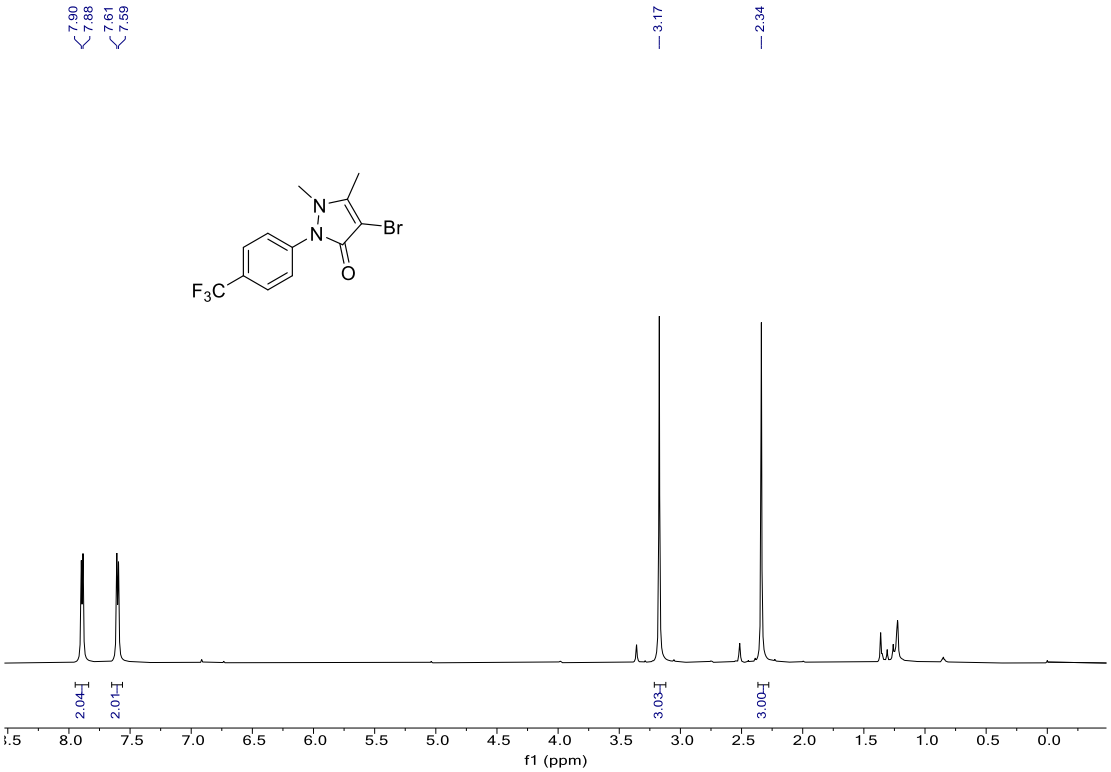
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3q**



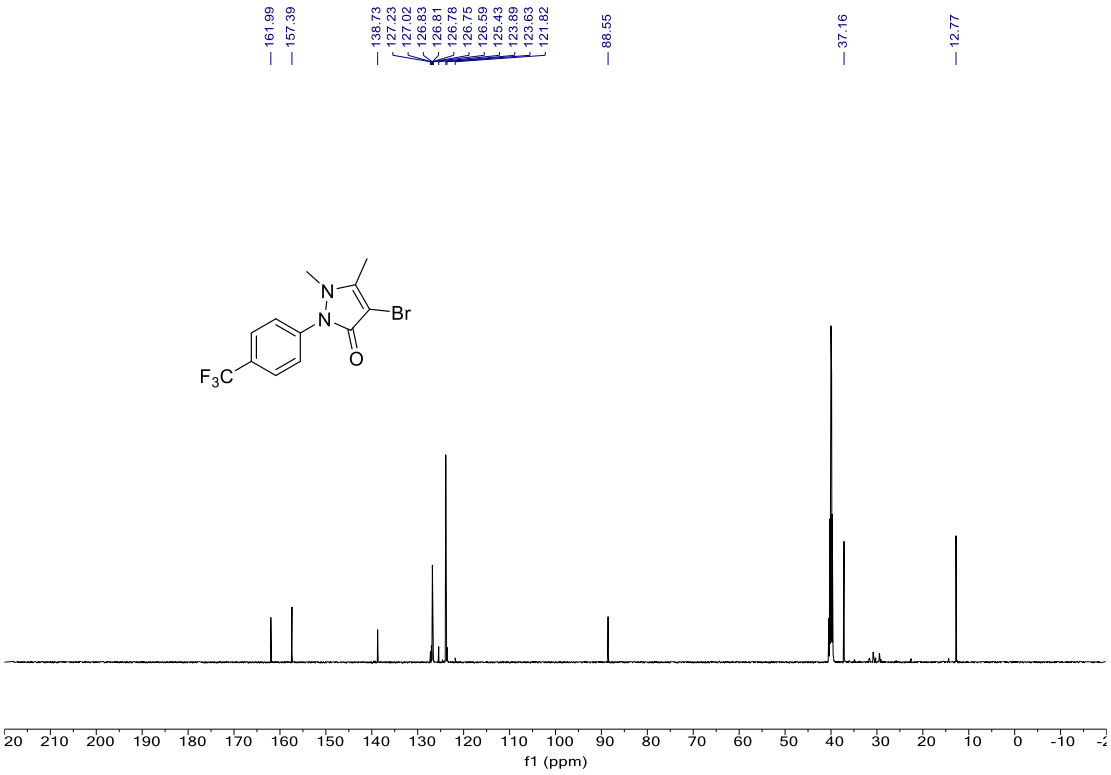
^{19}F NMR (565 MHz, DMSO- d_6) of compound **3q**



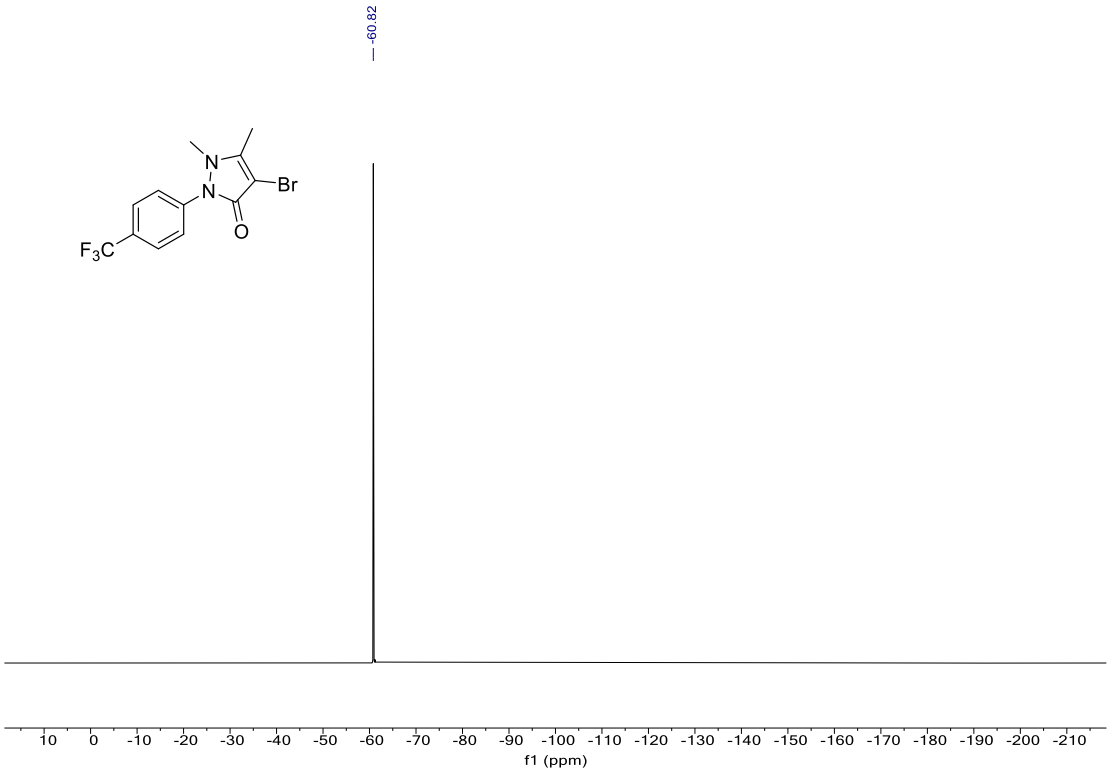
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3r**



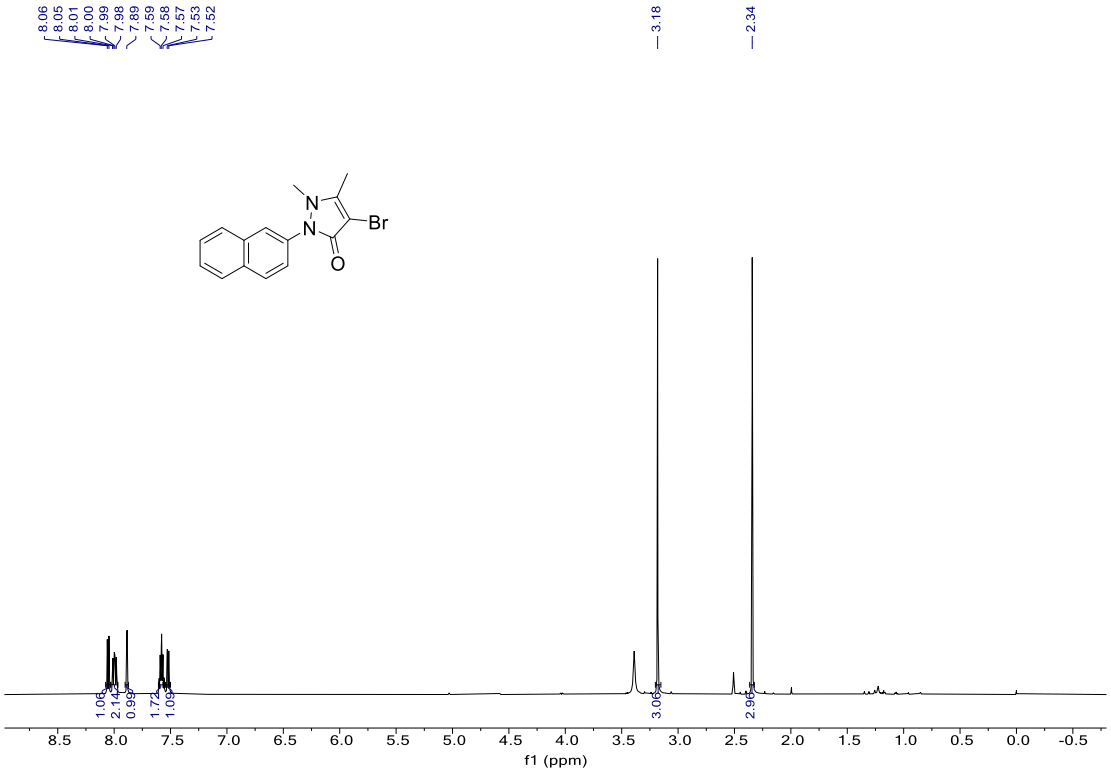
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3r**



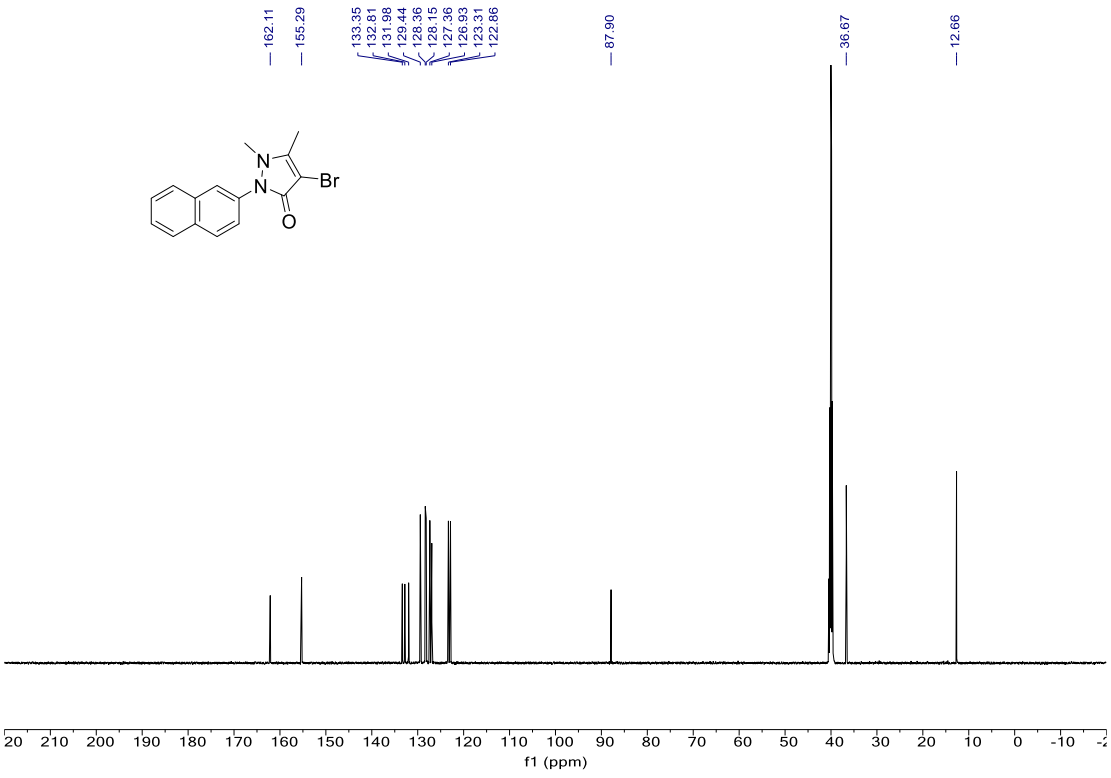
^{19}F NMR (565 MHz, DMSO- d_6) of compound **3r**



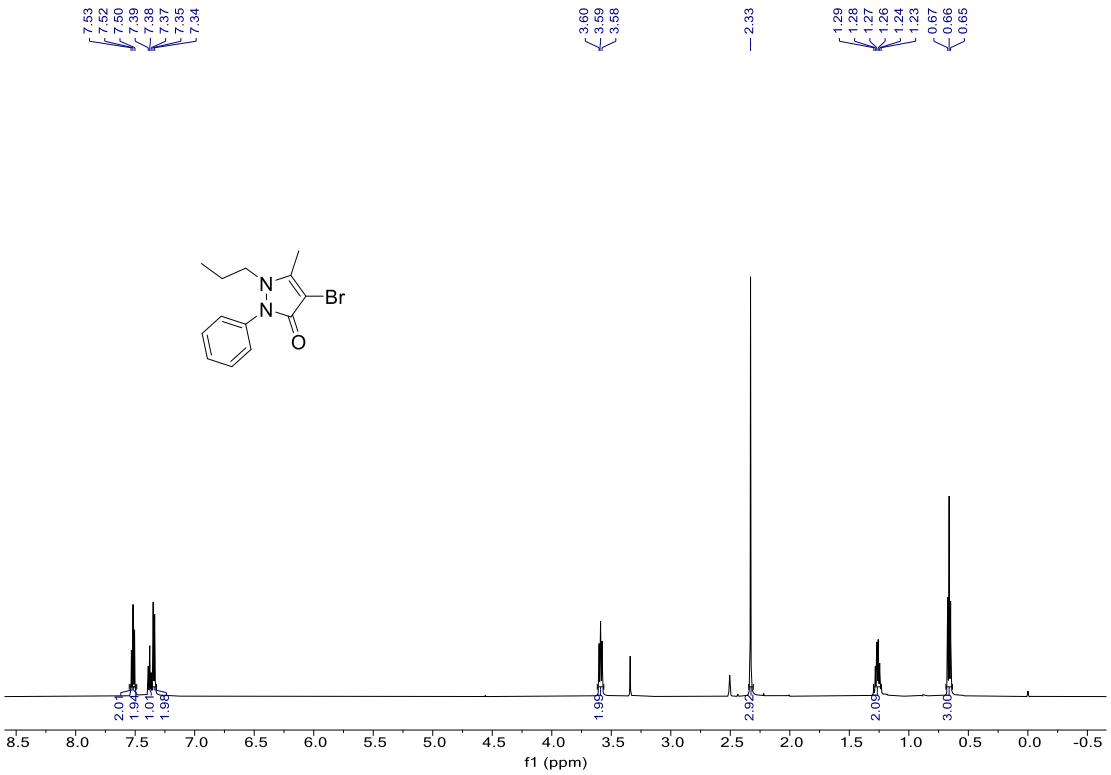
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3s**



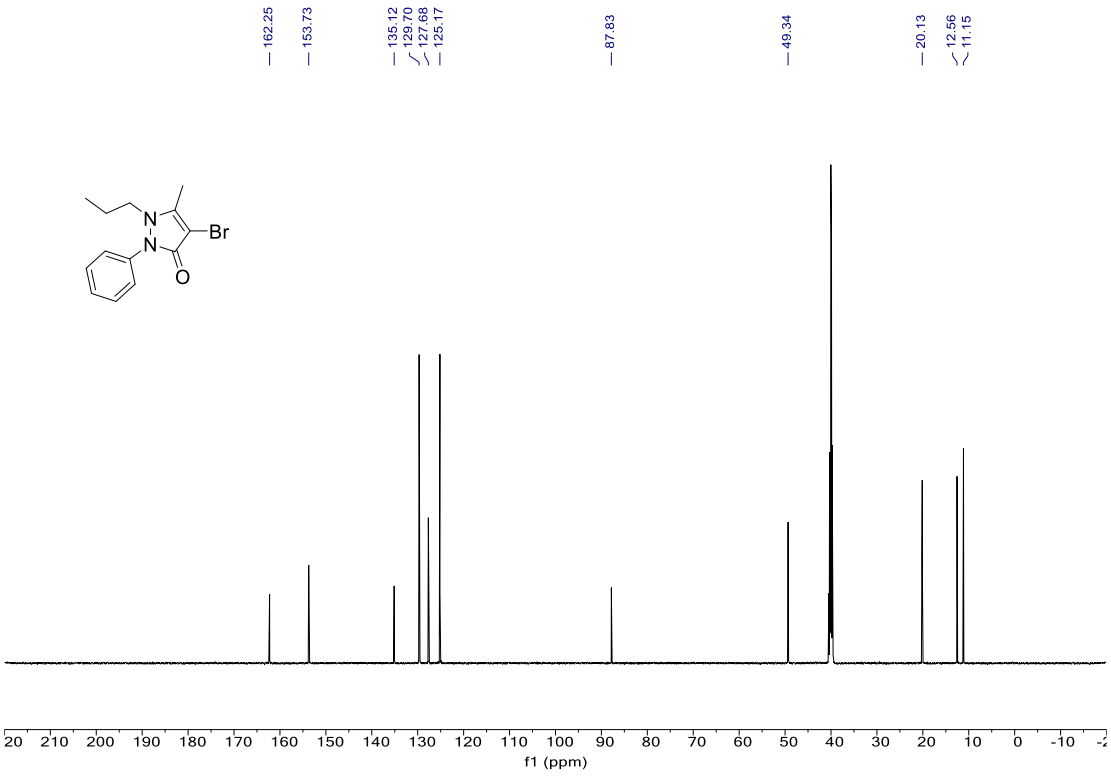
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3s**



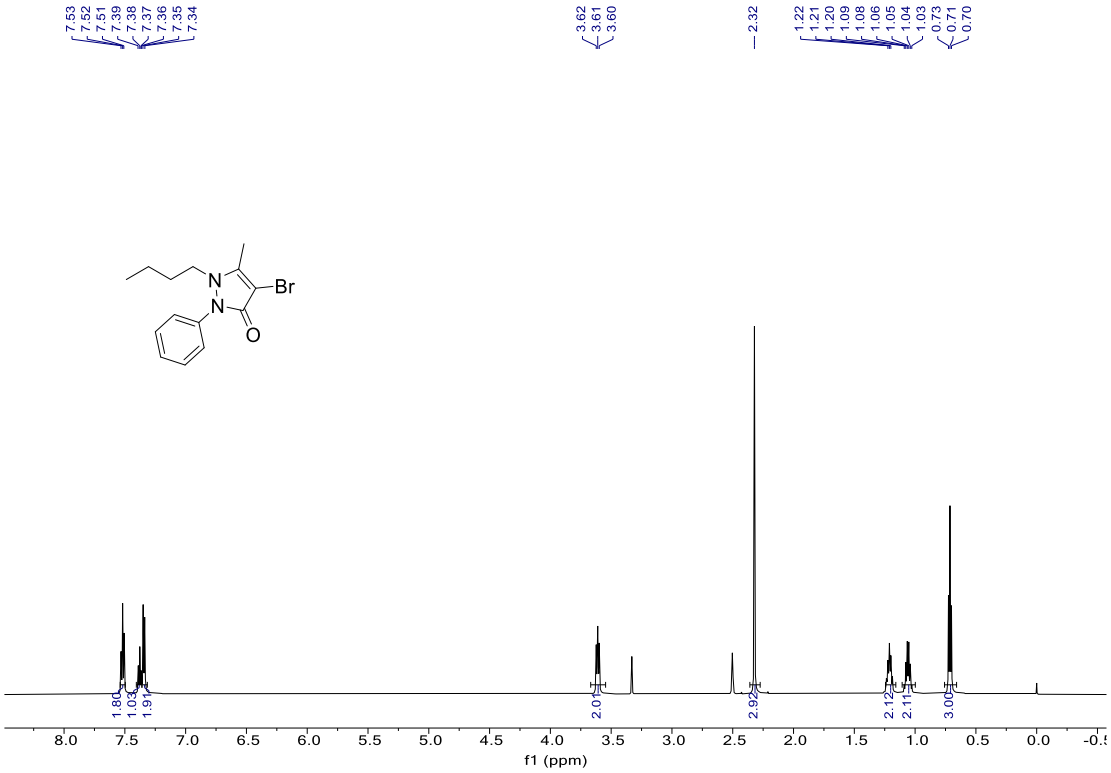
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3t**



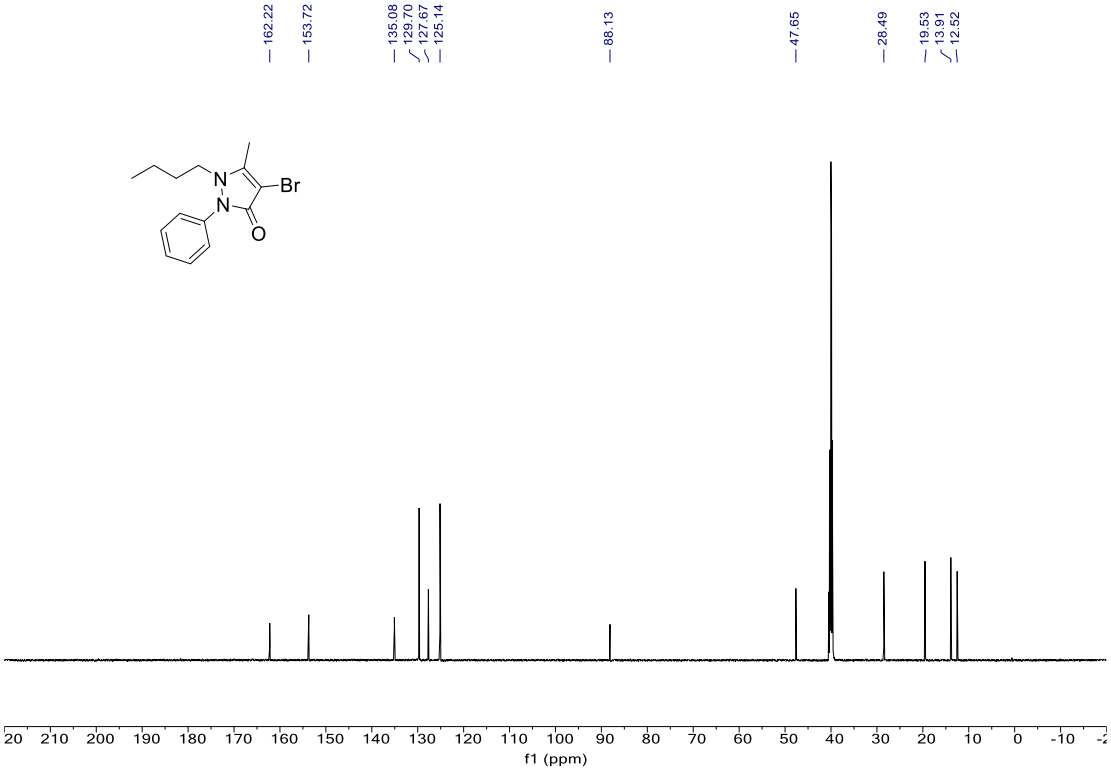
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3t**



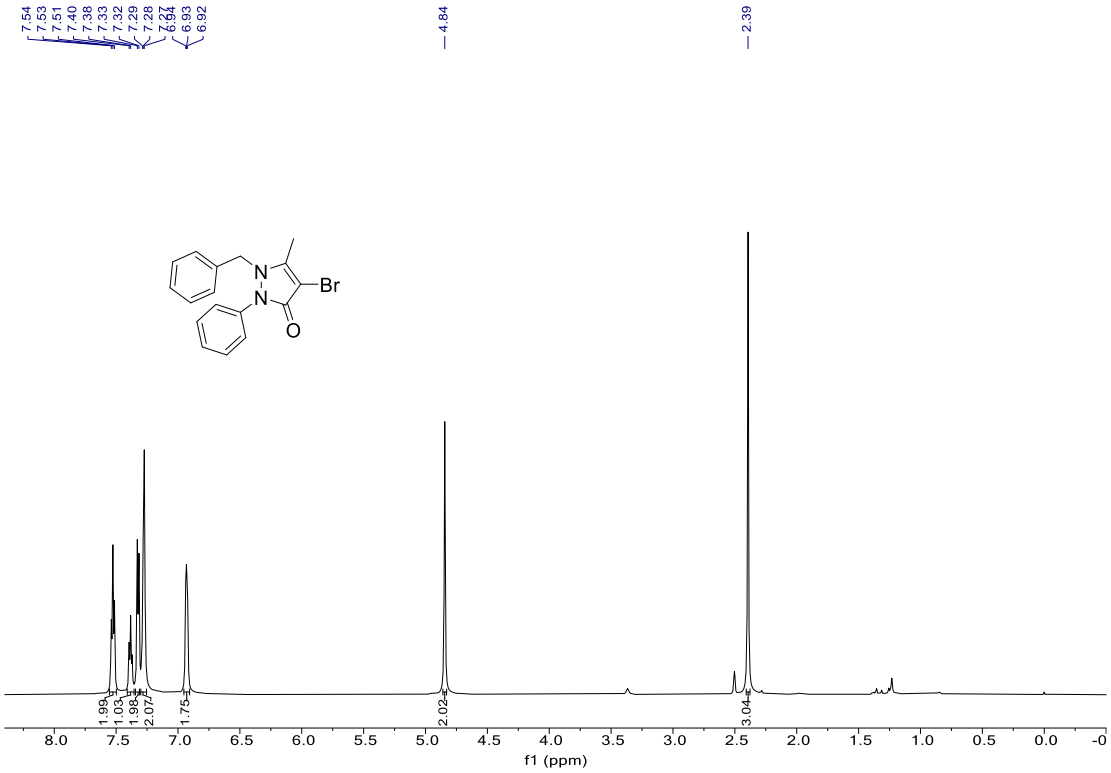
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3u**



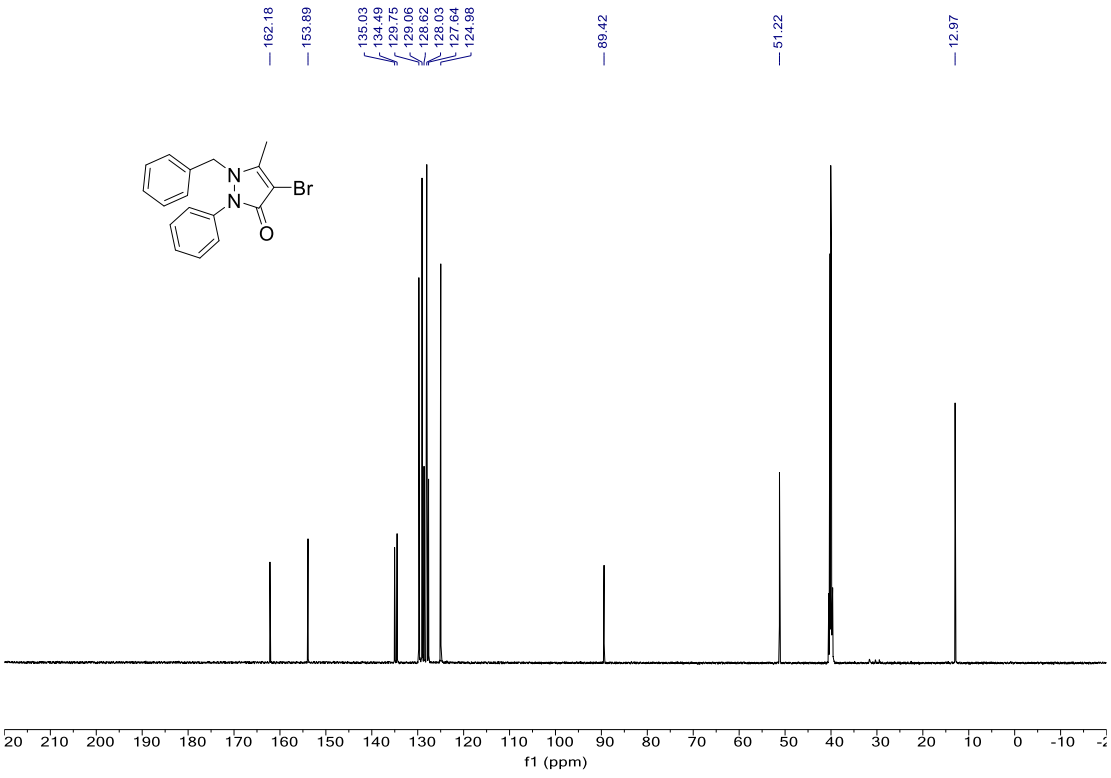
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3u**



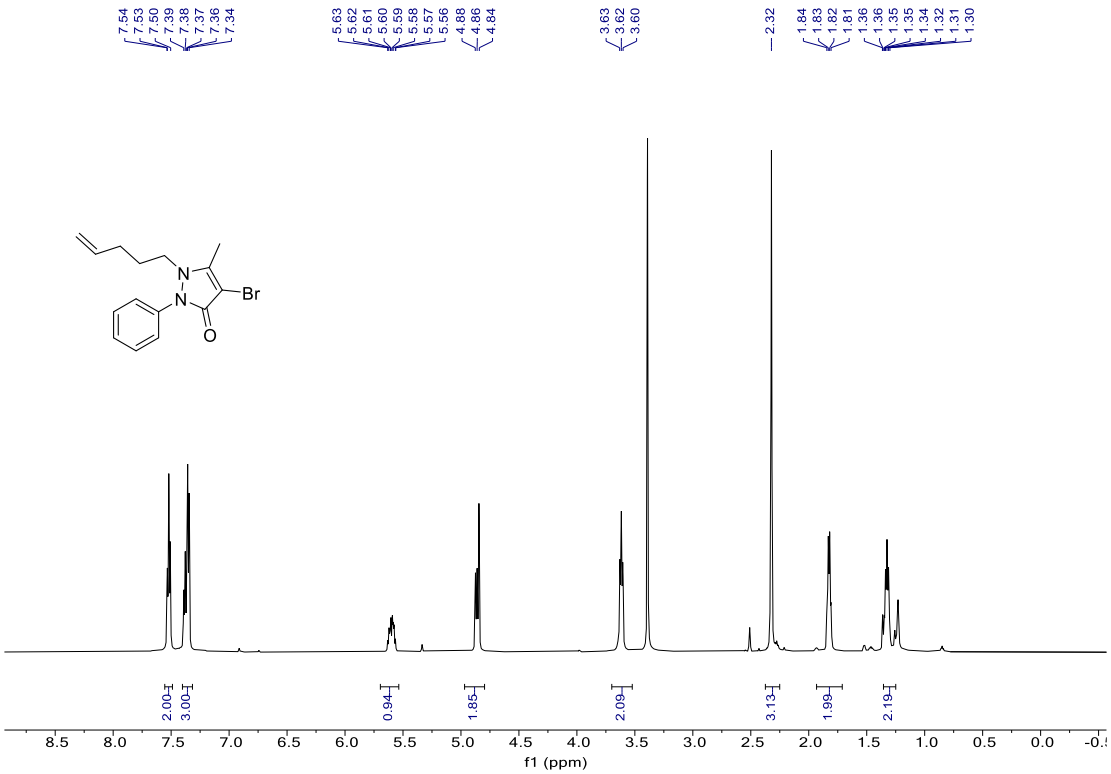
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3v**



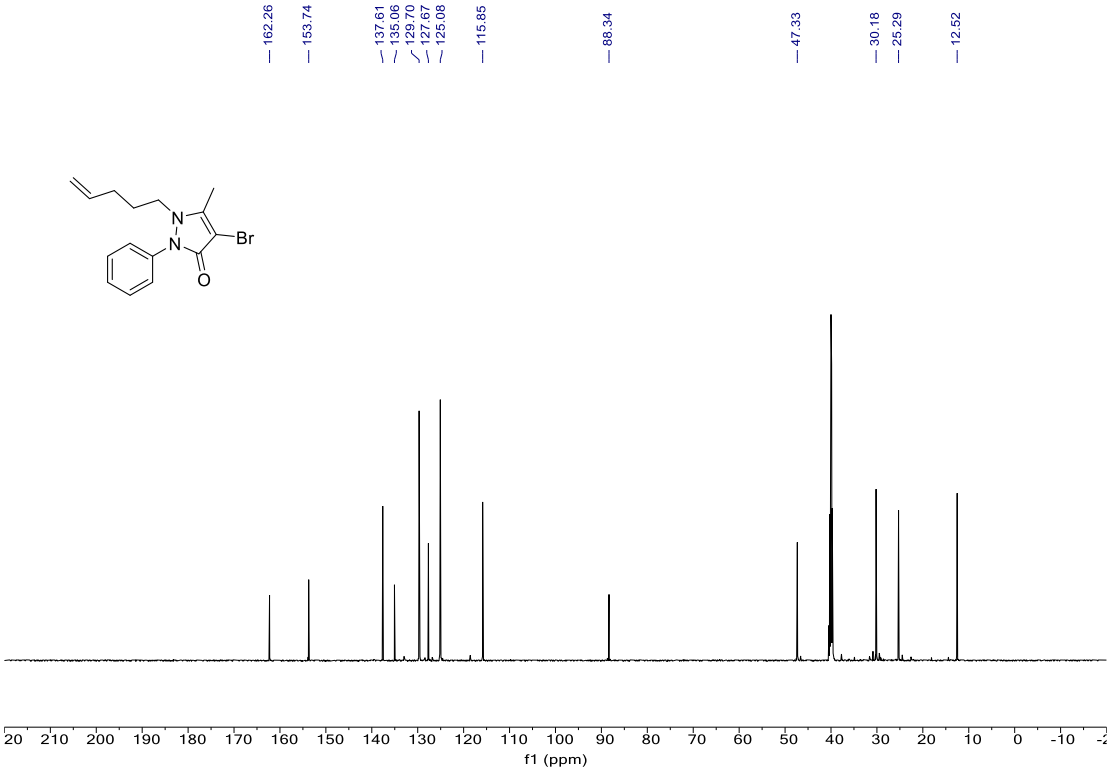
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3v**



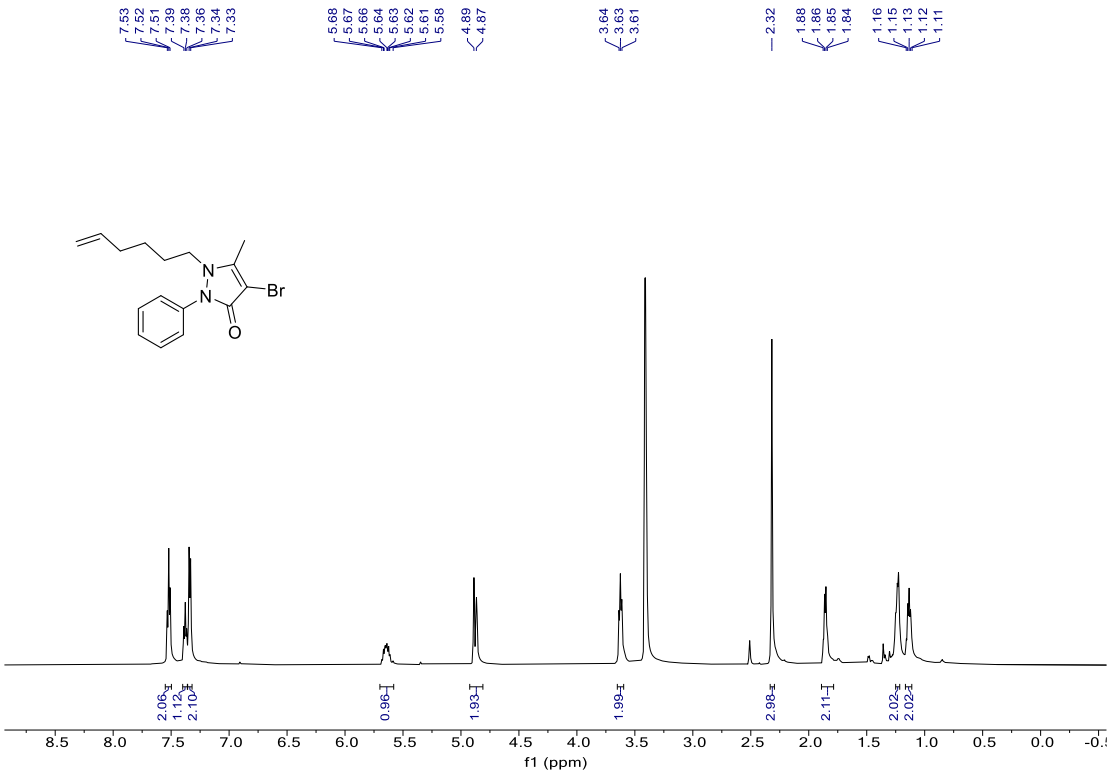
^{1}H NMR (600 MHz, DMSO- d_6) of compound **3w**



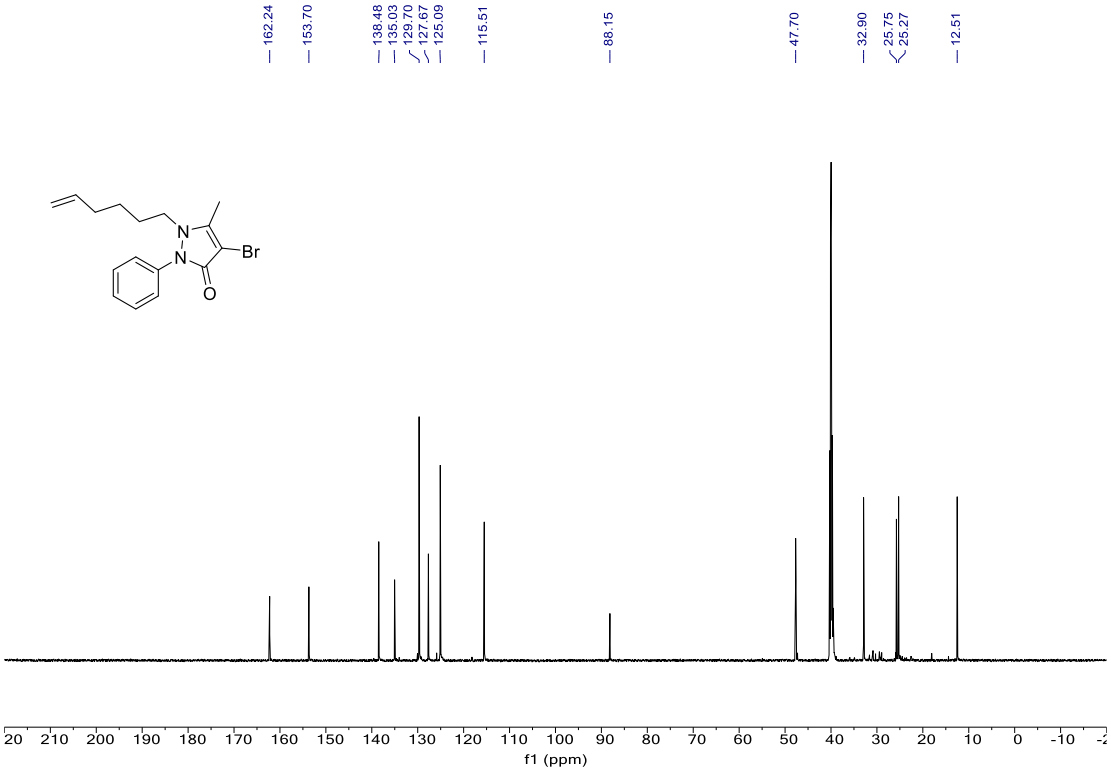
^{13}C NMR (151 MHz, DMSO- d_6) of compound **3w**



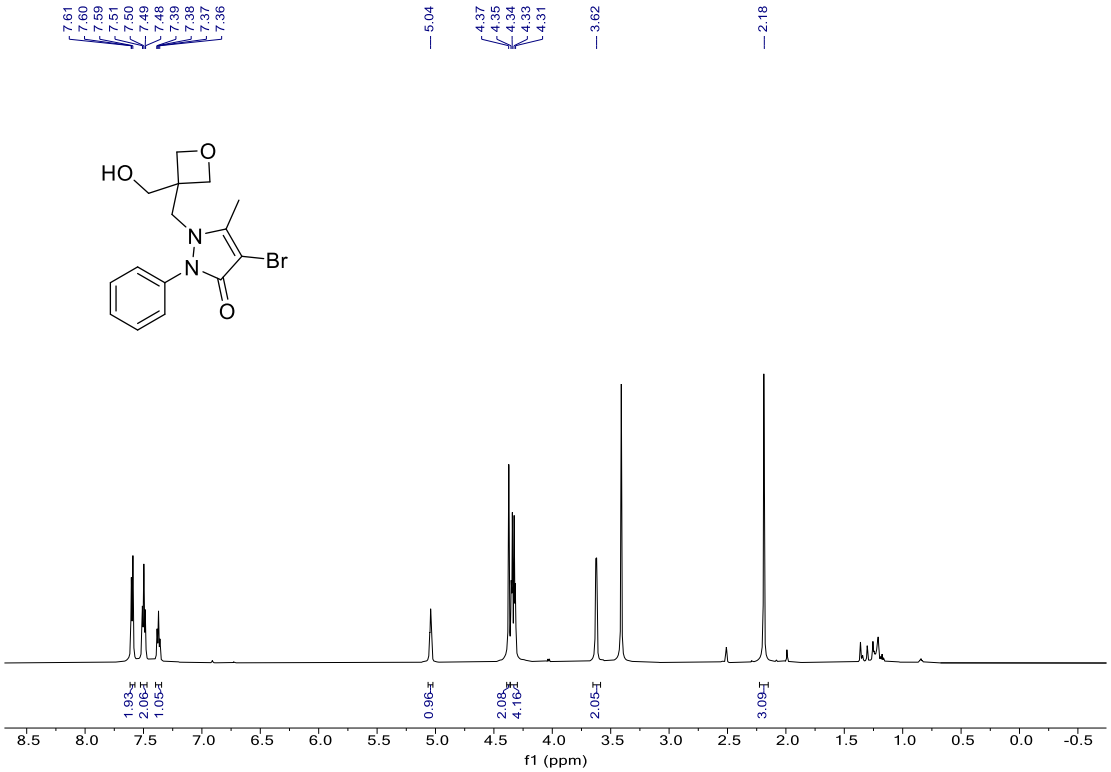
^{1}H NMR (600 MHz, DMSO-d_6) of compound **3x**



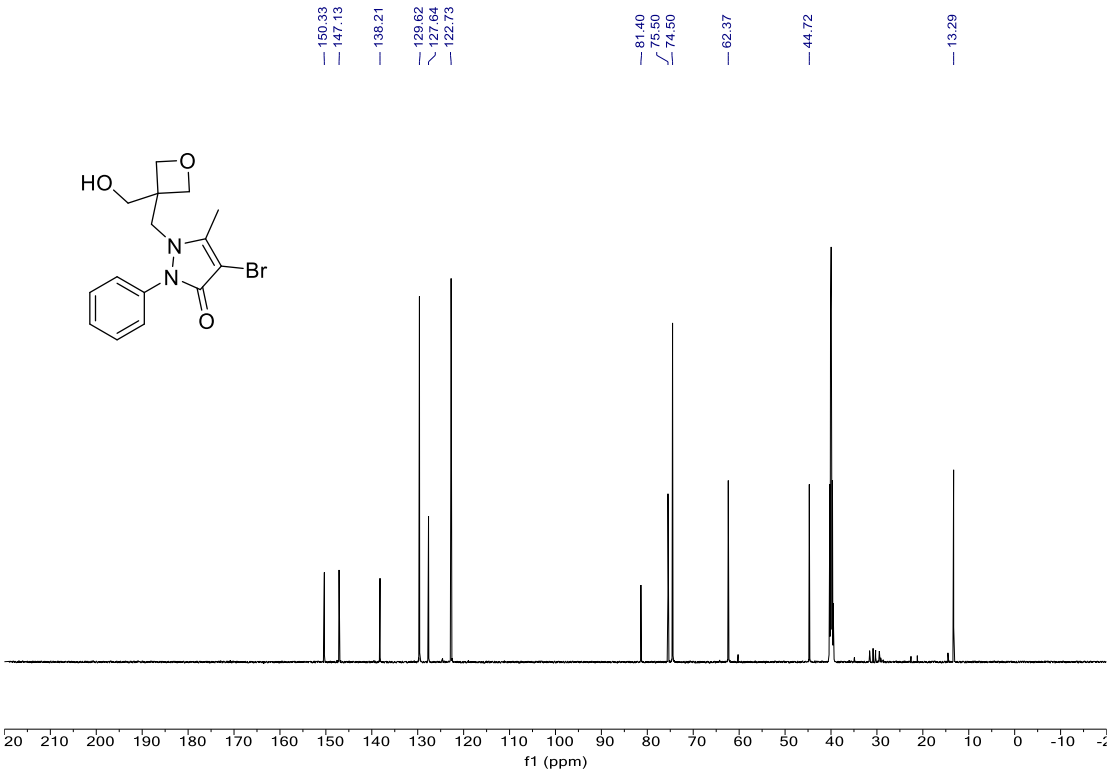
^{13}C NMR (151 MHz, DMSO-d_6) of compound **3x**



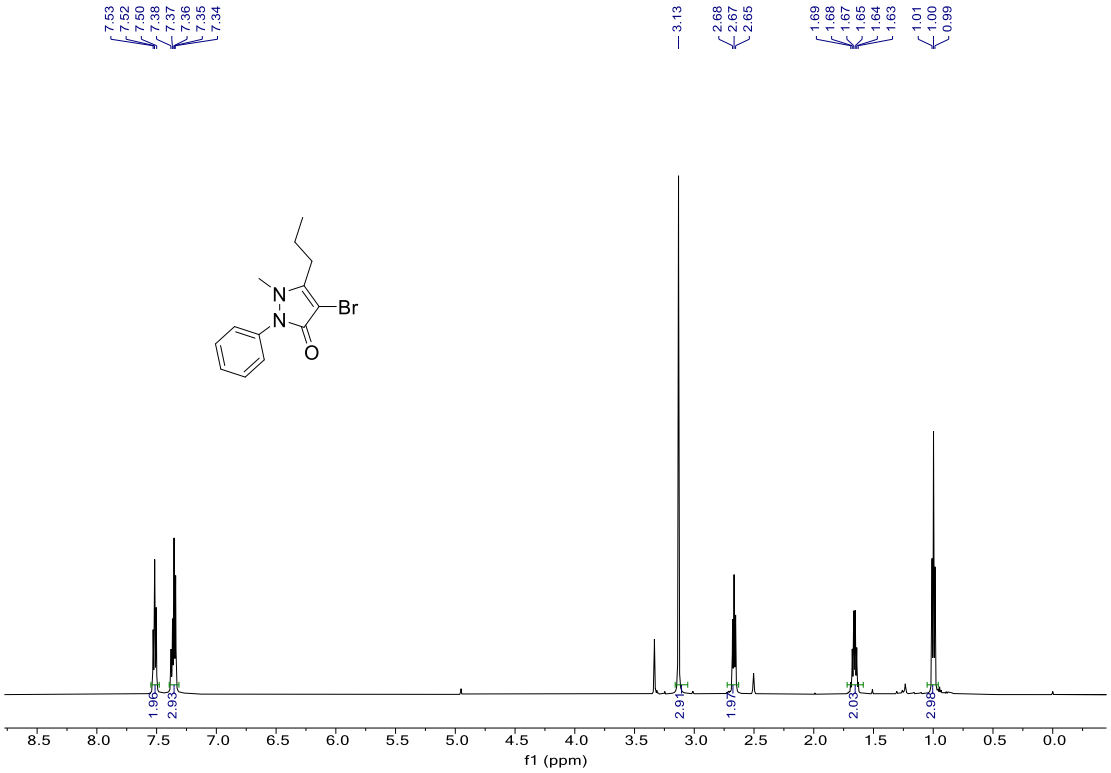
^{1}H NMR (600 MHz, DMSO-d_6) of compound **3y**



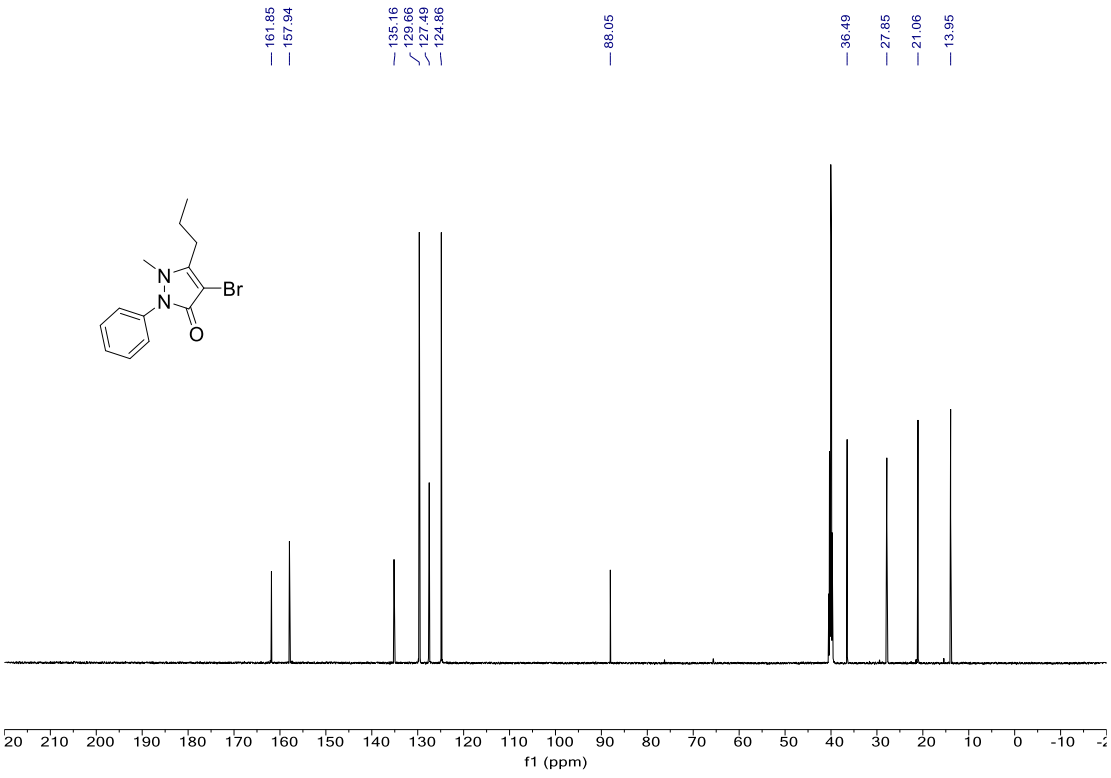
^{13}C NMR (151 MHz, DMSO-d_6) of compound **3y**



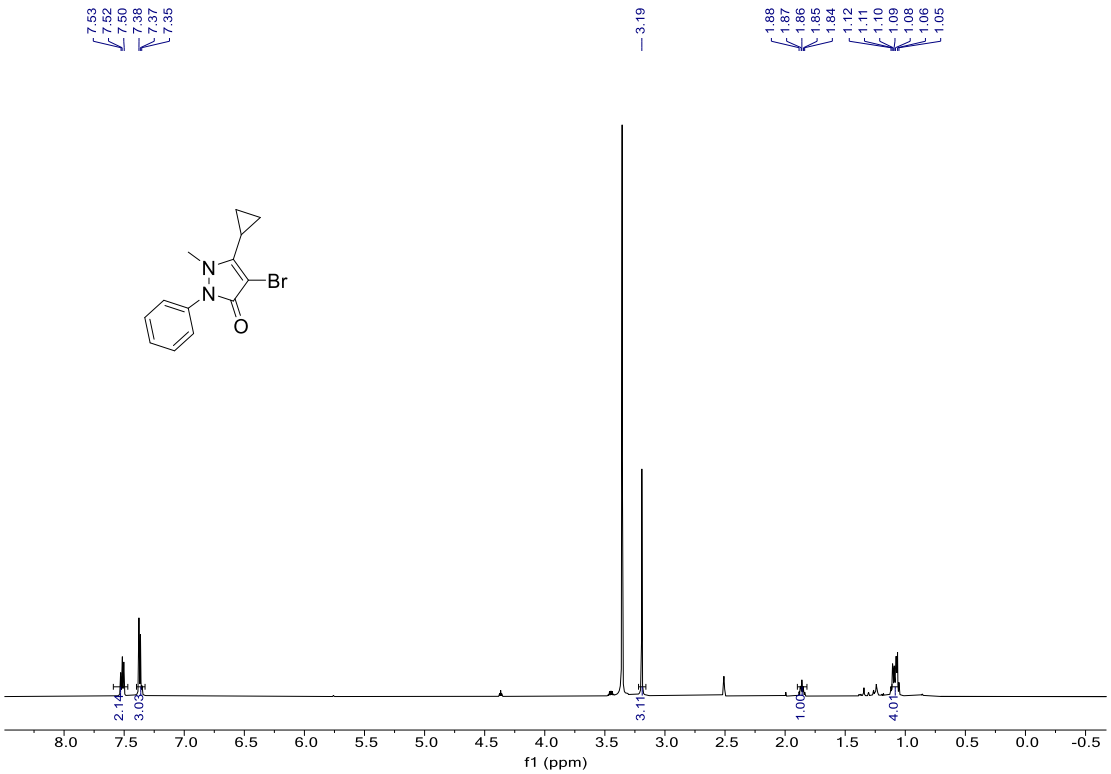
^{1}H NMR (600 MHz, DMSO-d_6) of compound **3z**



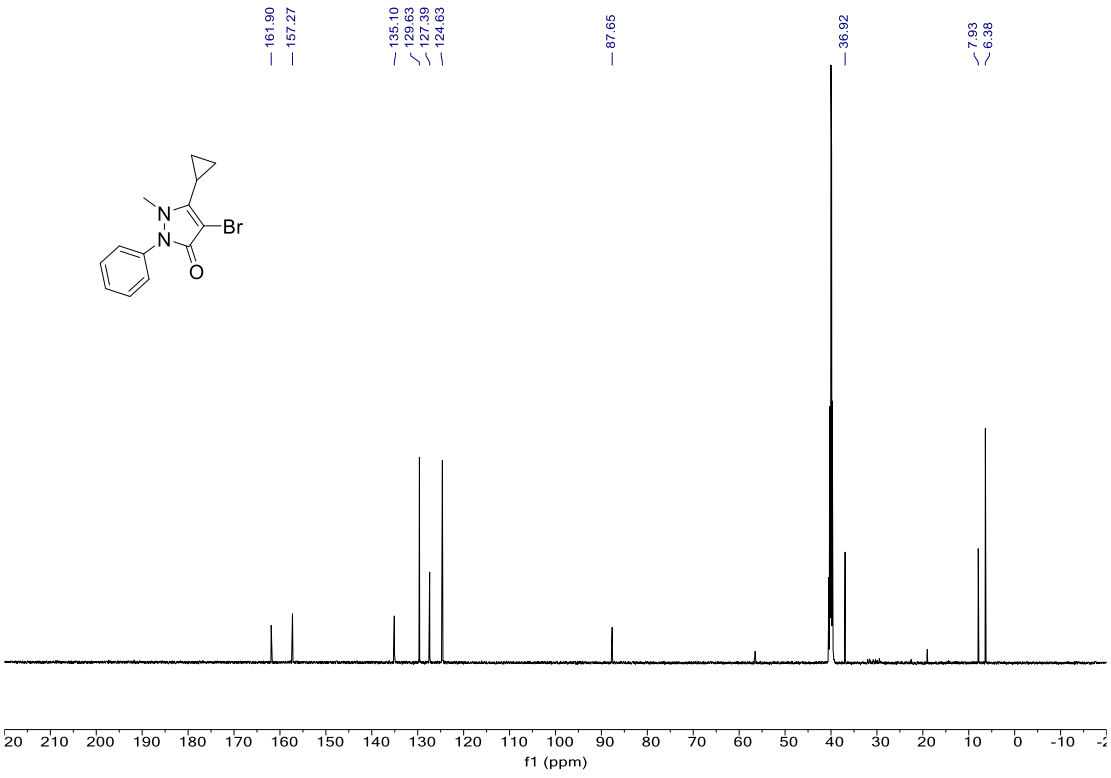
^{13}C NMR (151 MHz, DMSO-d_6) of compound **3z**



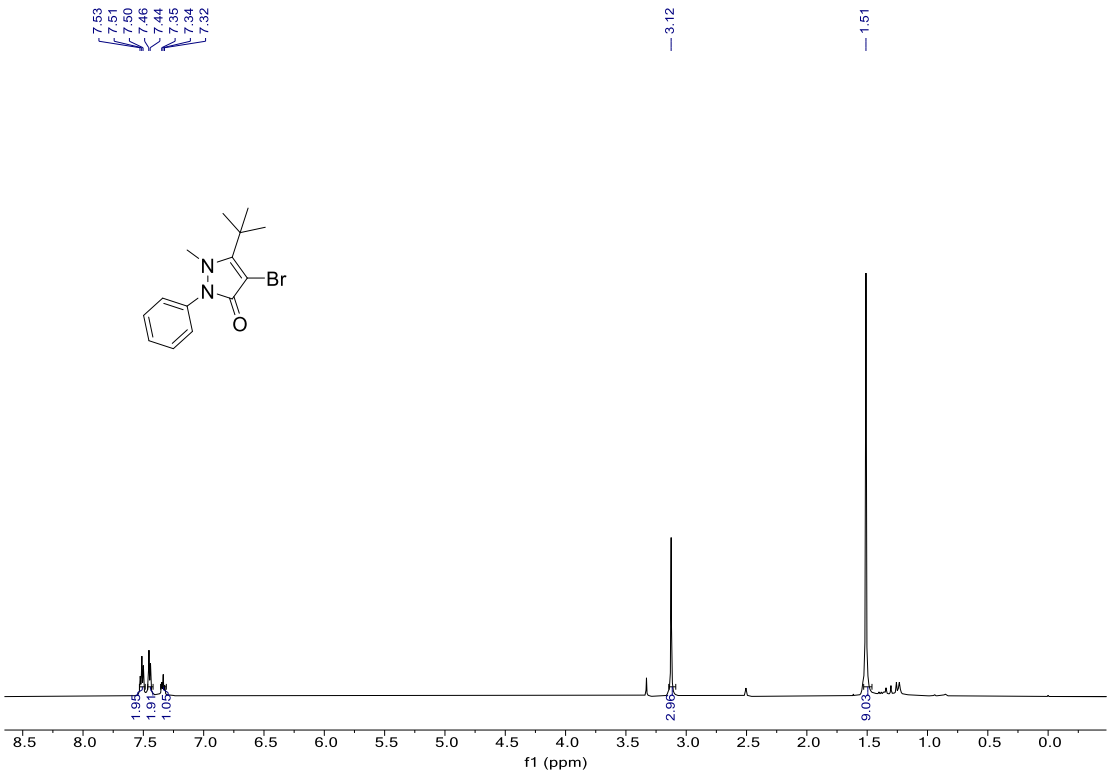
^{1}H NMR (600 MHz, DMSO-d_6) of compound **3za**



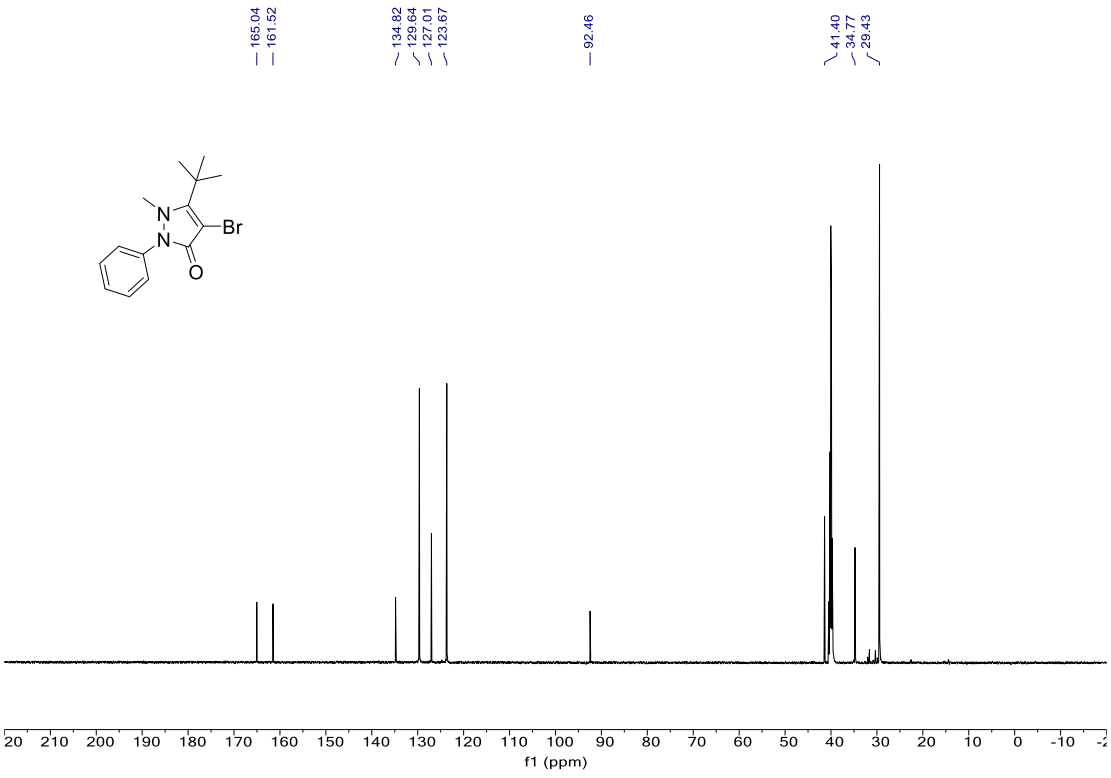
^{13}C NMR (151 MHz, DMSO-d_6) of compound **3za**



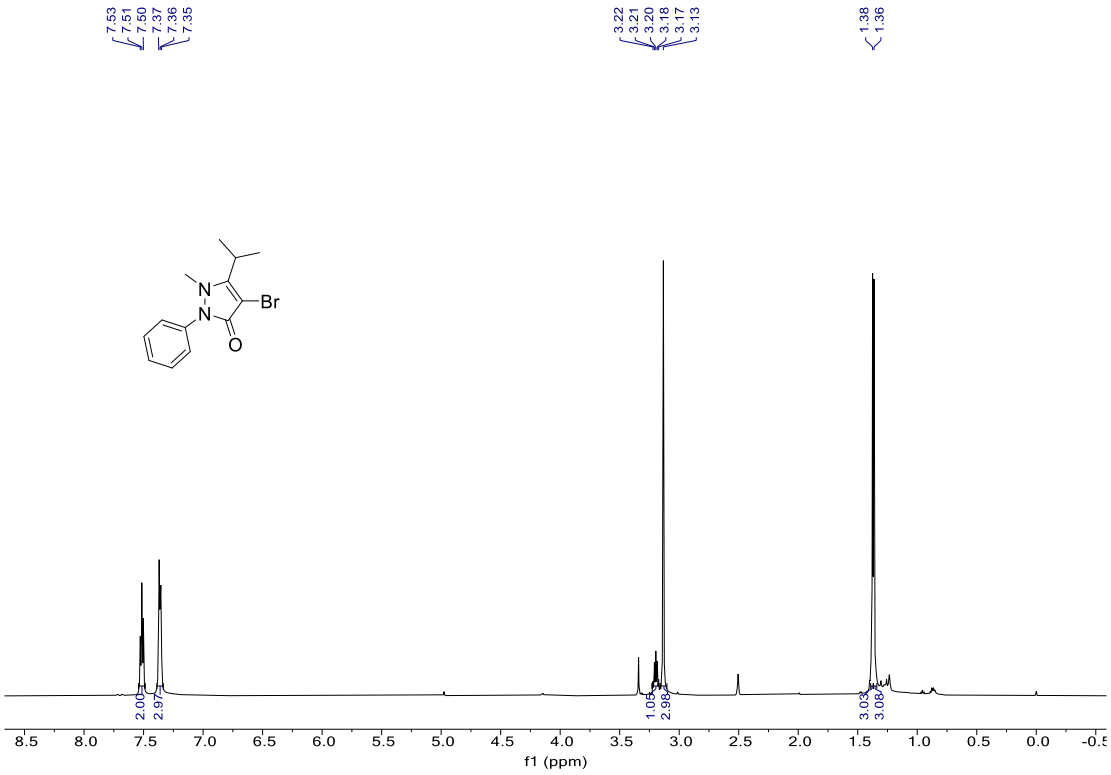
^{1}H NMR (600 MHz, DMSO-d_6) of compound **3zb**



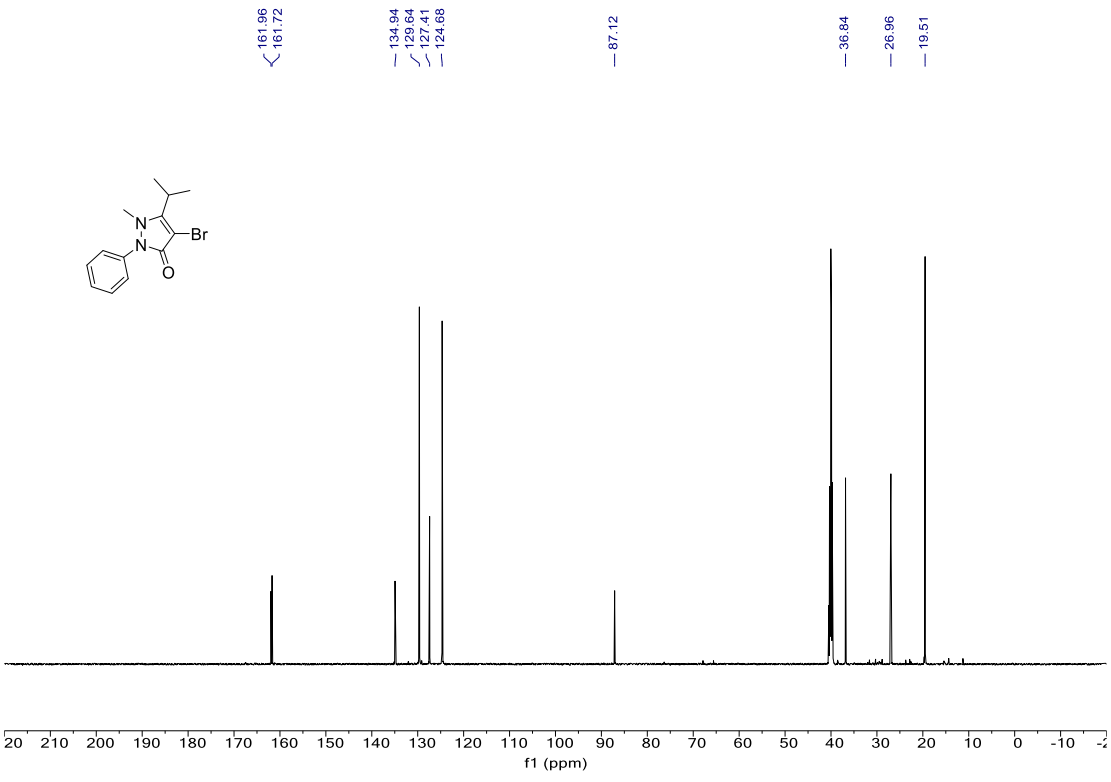
^{13}C NMR (151 MHz, DMSO-d_6) of compound **3zb**



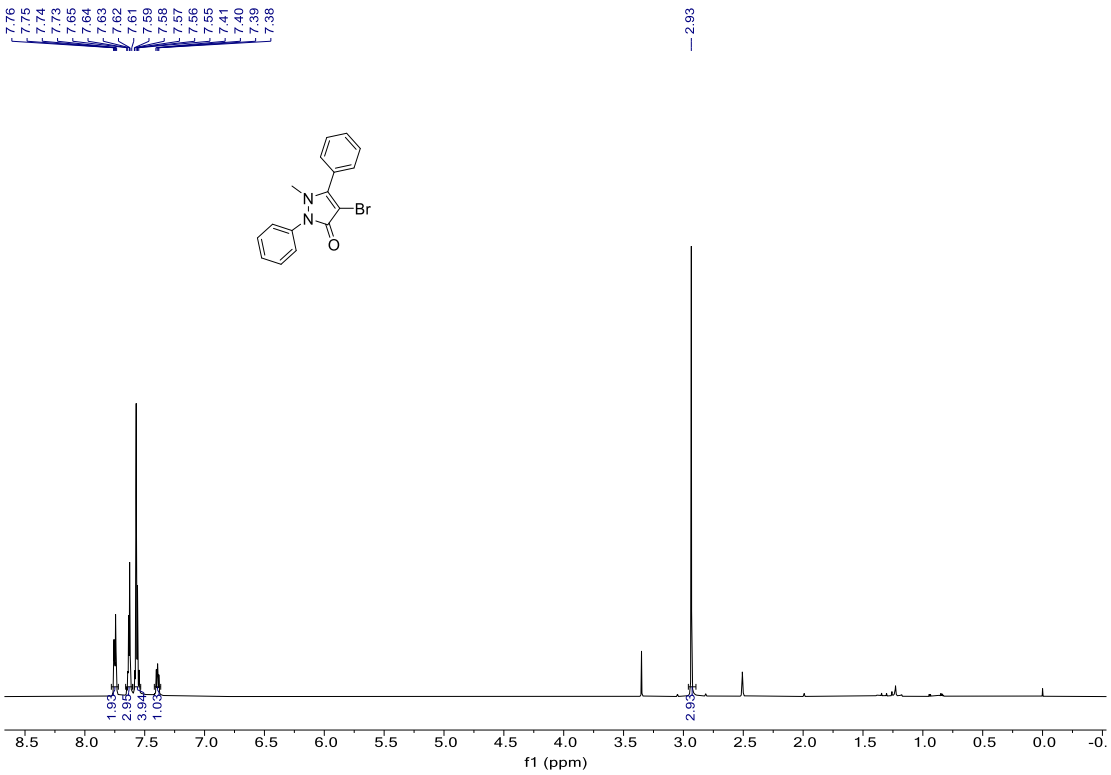
\[1]H NMR (600 MHz, DMSO-d_6) of compound **3zc**



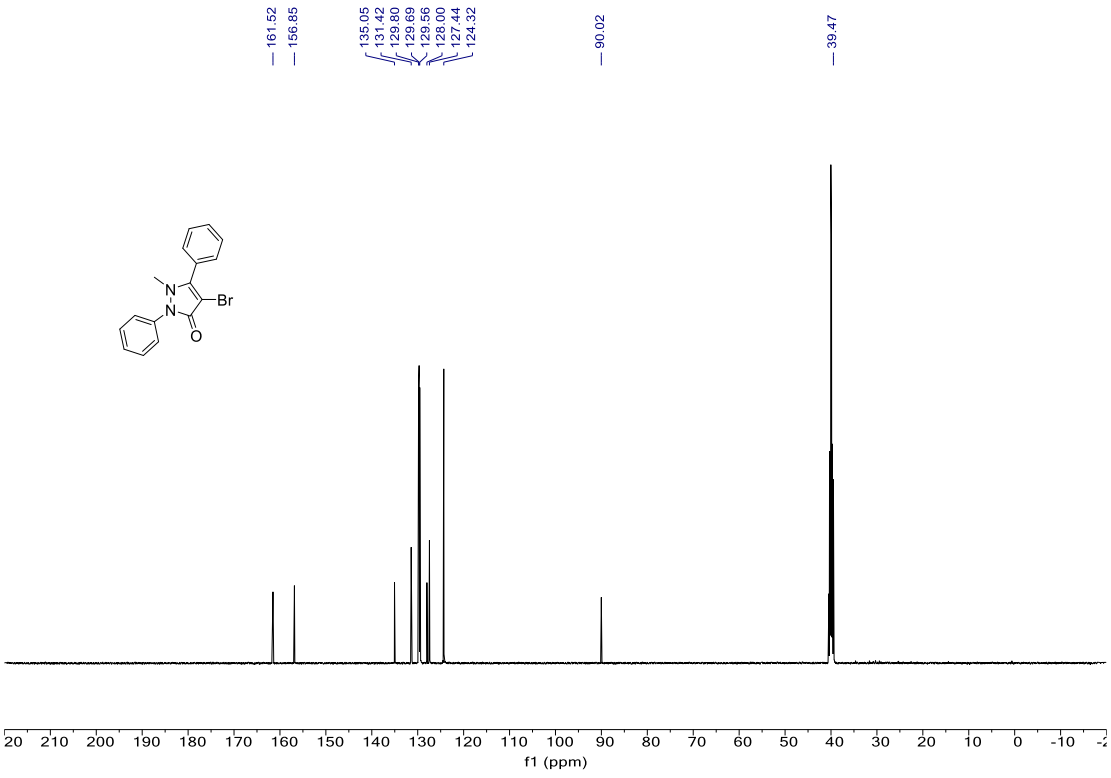
^{13}C NMR (151 MHz, DMSO-d_6) of compound **3zc**



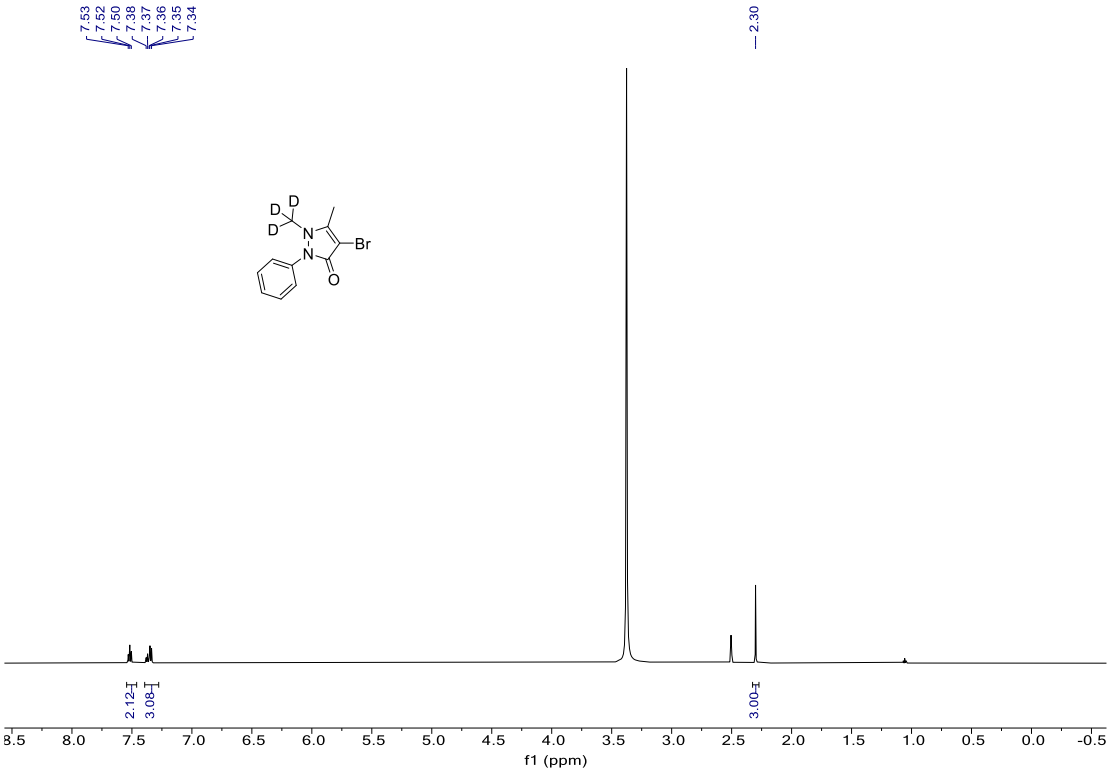
^{1}H NMR (600 MHz, DMSO-d_6) of compound **3zd**



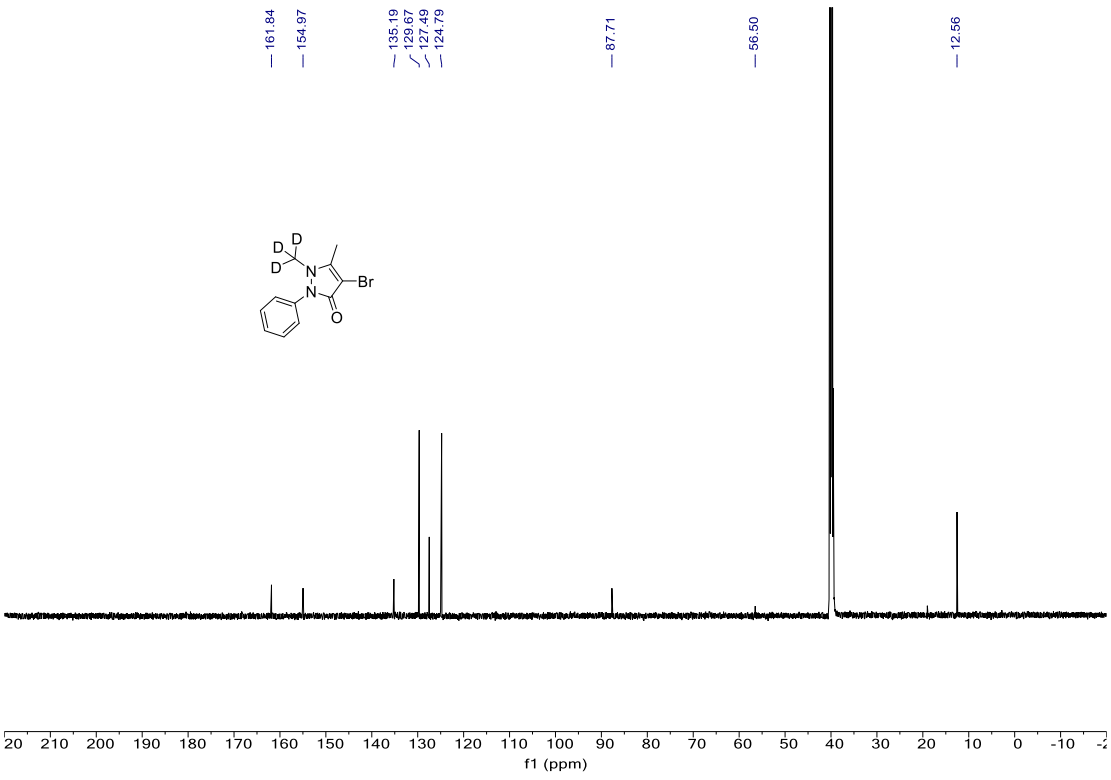
^{13}C NMR (151 MHz, DMSO-d_6) of compound **3zd**



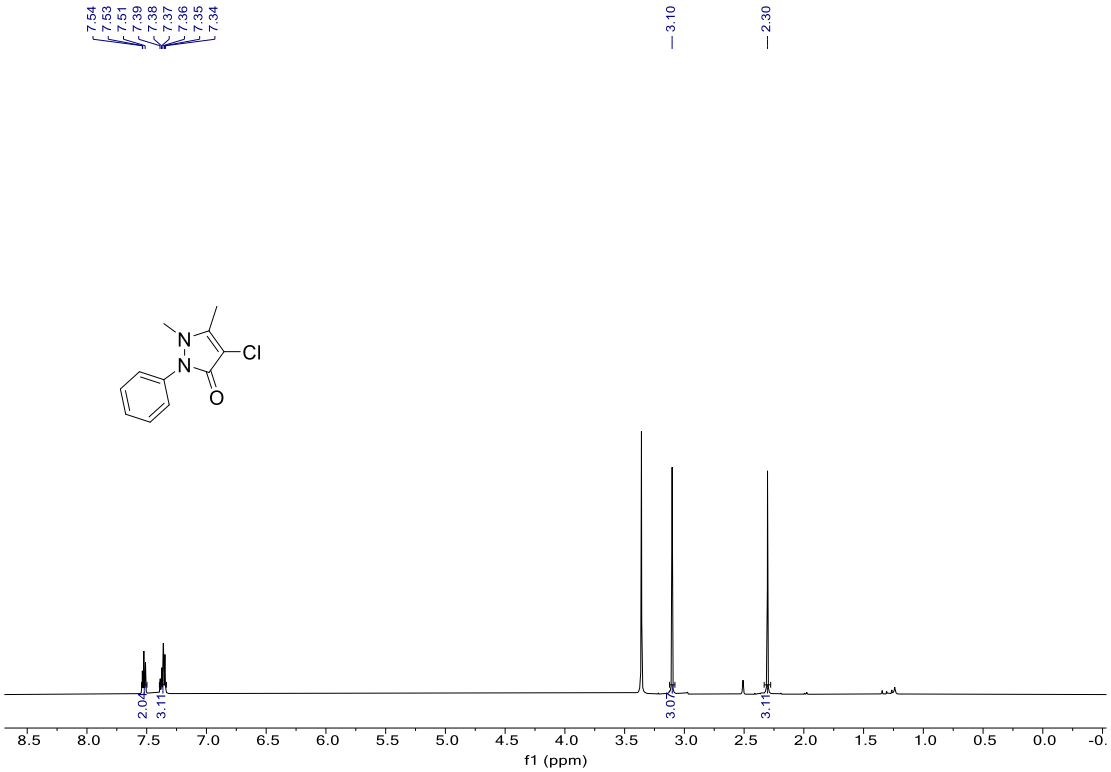
^{1}H NMR (600 MHz, DMSO-d_6) of compound **3ze**



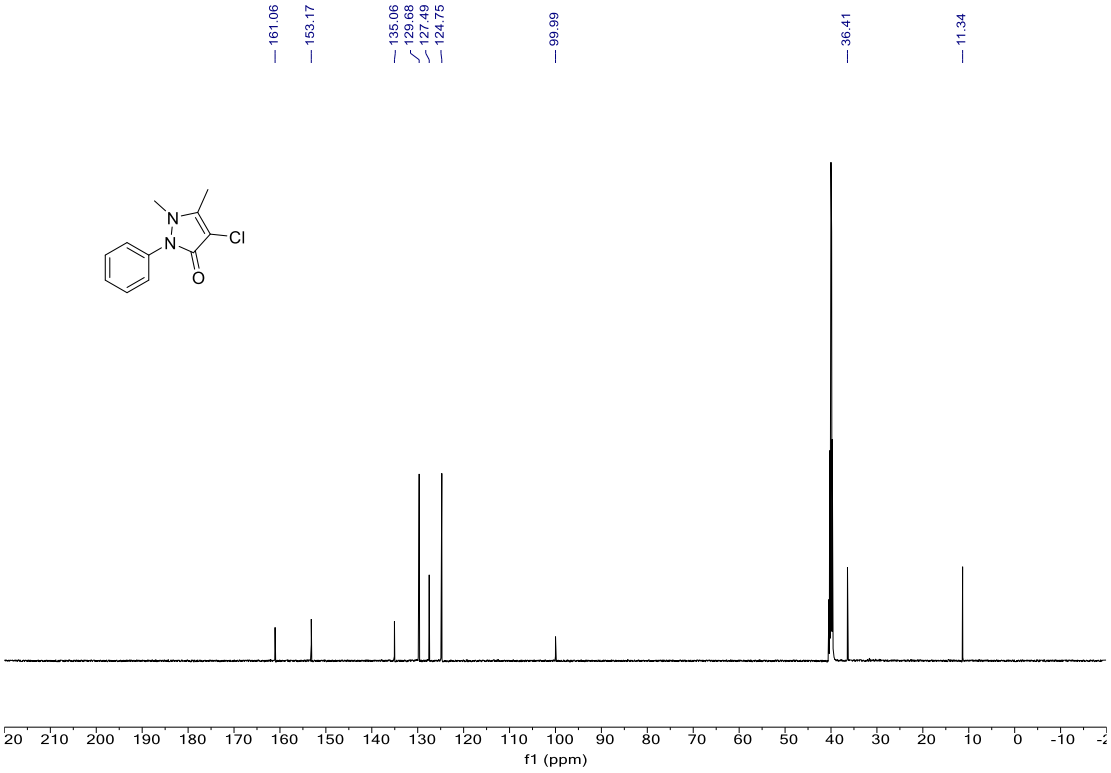
^{13}C NMR (151 MHz, DMSO-d_6) of compound **3ze**



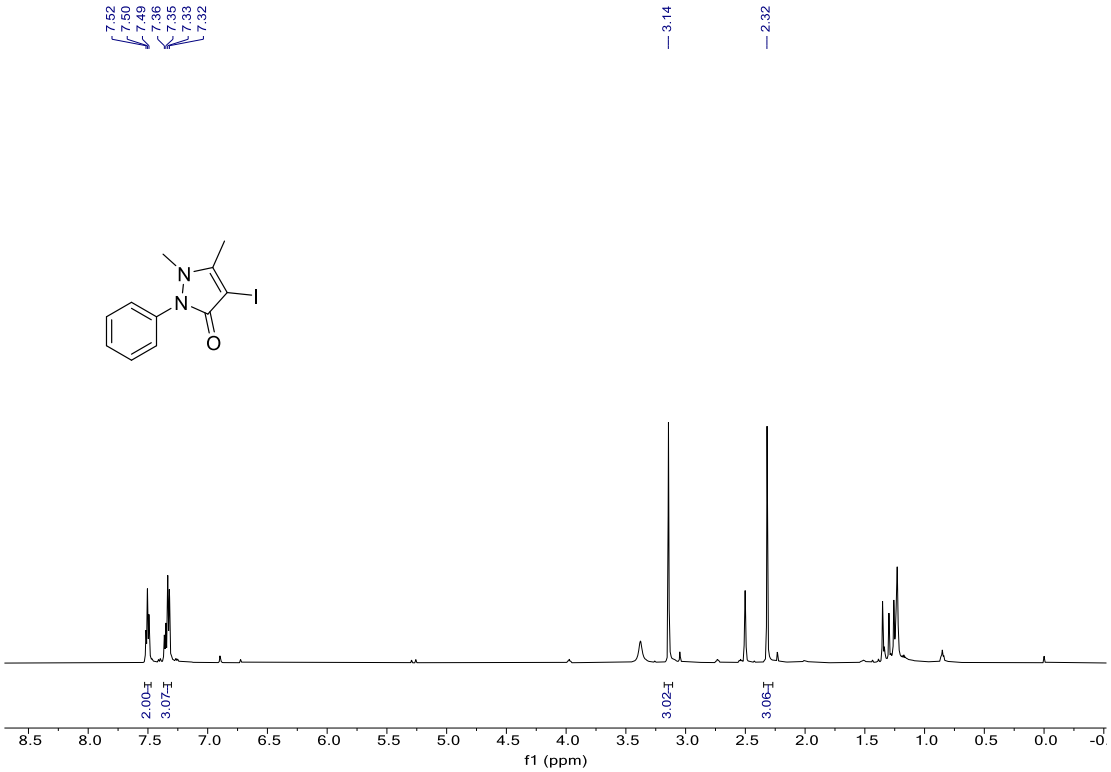
^{1}H NMR (600 MHz, DMSO-d_6) of compound **3zf**



^{13}C NMR (151 MHz, DMSO-d_6) of compound **3zf**



^{1}H NMR (600 MHz, DMSO-d_6) of compound **3zg**



^{13}C NMR (151 MHz, DMSO-d_6) of compound **3zg**