Supporting Information

One flask cascade approach to complex pyrano[2,3-c]pyrazole-pyrazolone hybrid heterocyclic system and its initiatory neurobiological profiling

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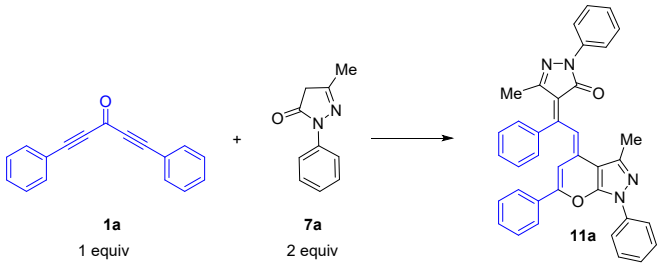
Table 1. Optimization of reaction conditions[a]



S. No	Base	Base equiv	Solvent	Temp (°C)	Time (min)	Isolated Yield (%)
1	DBU	0.2	THF	26	60	35[b]
2	DBU	0.2	THF	26	60	68
3	DABCO	0.2	THF	26	60	52
4	*i*-Pr_2NEt	0.2	THF	26	60	60
5	K_2CO_3	0.2	THF	26	60	42
6	^tBuOK	0.2	THF	26	60	45
7	NaOH	0.2	THF	26	60	33
8	**DBU**	**0.5**	**THF**	**26**	**30**	**80**
9	DBU	1	THF	26	30	72
10	DBU	0.5	toluene	26	30	75
11	DBU	0.5	ACN	26	30	66
12	DBU	0.5	DMF	26	30	59
13	DBU	0.5	1,4-dixoane	26	30	70
14	DBU	0.5	2-MeTHF	26	30	68
15	DBU	0.5	THF	-10	180	52
16	DBU	0.5	THF	-78	180	ND
17	Blank	Blank	THF	26	120	Trace

[a]General conditions are as follows**: 1a** (1 equiv), **7a** (2 equiv), base, solvent (2 mL); [b] Reaction carried out with **1a** (1 equiv), **7a** (1 equiv). ND (No reaction occurred)

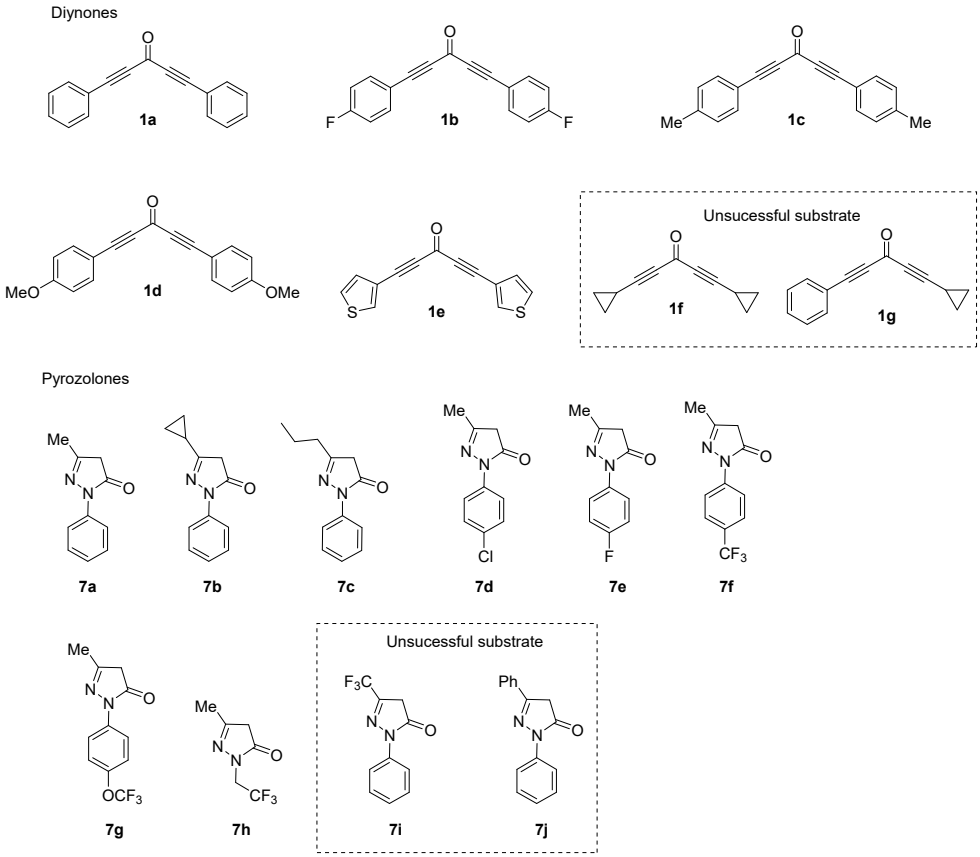
Table 2. IC50 (μM) values for SRB assay and 50% inhibition of enzyme activity by AChE assay.

Compound	IC50 ± SD (μM) for SRB assay	IC50 ± SD (μM) for 50% AChE enzyme inhibition
7a	0.0099 ± 0.0070	0.092 ± 0.0034
7e	0.0824 ± 0.0074	0.1482 ± 0.0862
11a	0.0059 ± 0.0051	0.0682 ± 0.0321
11b	0.8909 ± 0.0051	0.1852 ± 0.1634
11f	0.1046 ± 0.0086	0.0980 ± 0.0441
11l	0.0022 ± 0.0054	0.0858 ± 0.0523
11n	0.0817 ± 0.0040	0.0820 ± 0.0442
11o	0.0924 ± 0.0077	0.5337 ± 0.1446

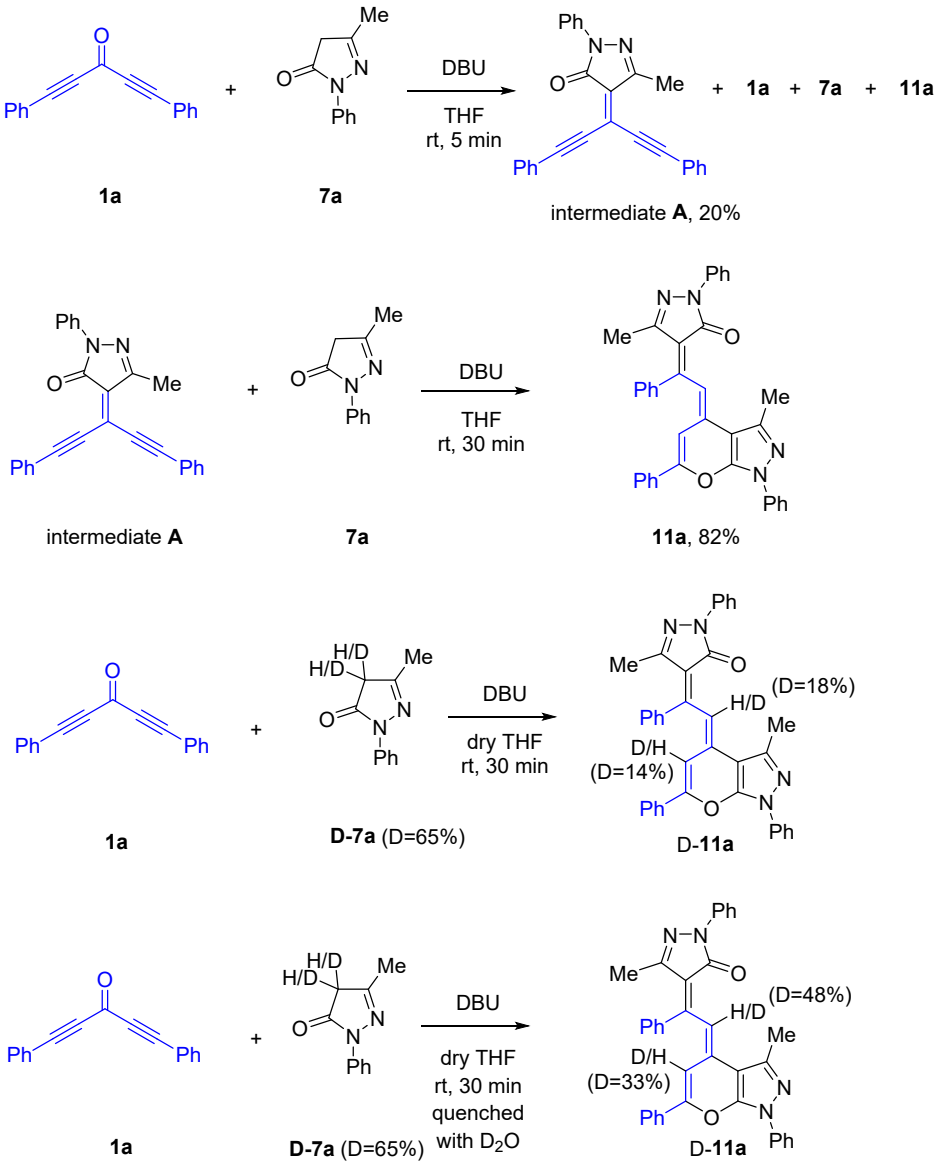
Table 3. *Insilco* logBB values for Blood brain permeability assessment

Compound	Results	logBB-pkCSM[1] https://biosig.lab.uq.edu.au/pkcsm/	logBB-AlzPlatform[2] https://www.cbligand.org/
7a	BBB+	0.354	0.090
7e	BBB+	0.304	0.081
11a	BBB+	0.07	0.061
11b	BBB+	-0.508	0.082
11f	BBB+	0.001	0.055
11l	BBB+	-0.181	0.046
11n	BBB+	-0.993	0.025
11o	BBB+	0.032	0.042

Figure 1. List of starting materials used in this project



Scheme 1. Control experiments and deuterium labelling



Deuteration experiments revealed that the protonation source can be from H_2O/D_2O generated after Knoevenagel condensation or from the external quencher. The deuterium incorporation occurred at vinylic position of **11a** when the reaction was carried with deuterated pyrazolone or after quenching with D_2O. The deuterium location is supportive of the mechanistic proposal that also validates the intermediacy of allene or vinyl anion intermediate.

EXPERIMENTAL SECTION

General Information. All reagents and chemicals were used as obtained from commercial sources, unless specified. Air and moisture sensitive reactions were performed under positive N_2 or a blanket in flame- or oven-dried glassware. Melting points were determined on a capillary melting point apparatus and uncorrected. IR spectra were recorded neat on a Bruker Alpha FT-IR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded (400/500 and 100/125 MHz, respectively) on a Bruker Avance DPX 400/500 MHz using $CDCl_3$. Chemical shifts for proton and carbon resonances are reported for the major isomer in parts per million (δ) relative to tetramethylsilane (δ 0.00) and chloroform (*δ* 77.7), respectively. Multiplicities are indicated by singlet (*s*), doublet (*d*), triplet (*t*), quartet (*q*), multiplet (*m*), broad singlet (*brs*). Coupling constants (*J*) were reported in hertz (*Hz*). High resolution mass analyses were performed using ESI-TOF technique. Single-crystal X-ray data was collected on a Bruker APEX-II CCD and XtaLAB Synergy diffractometer, using Mo Kα radiation at 298 K. Structure solution and refinements were performed in Olex2 using SHELX program. Thin layer chromatography (TLC) was performed using pre-coated silica gel 60 F_{254} (Merck) and visualized through UV light, iodine and *p*-anisaldehyde stain. Column chromatography was performed using silica gel (100-200 mesh). Diynones **1a**-**e** were prepared using reported literature procedure.[3] Pyrazolones (**7a**) were used from commercial sources or synthesized (**7b**-**h**) following literature procedures[4a,b]. Deuterated pyrazolone (D-**7a**)[4c] was prepared following literature procedure.

General procedure for synthesis of 11

To a solution of diynone **1** (0.2 mmol) and pyrazolone **7** (0.4 mmol) in THF (3 mL) at 25-30 °C was added DBU (0.1 mmol). The reaction mixture was stirred at same temperature under open air atmosphere and monitored by TLC until the disappearance of pyrazolone **7**. After the appropriate period, the reaction mixture was quenched with water (5 mL) and diluted with EtOAc (10 mL). The organic phase was separated and the aqueous layer was washed with EtOAc (10 mL). Concentration of the combined organic layer under reduced pressure afforded the crude product, which was purified by column chromatography (Ethyl acetate: hexane 5:95) to afford the corresponding product **11**.

Scale-up procedure for synthesis of 11a

To a solution of diynone **1a** (2 mmol) and pyrazolone **7a** (4 mmol) in THF (10 mL) at 0 °C was added DBU (1 mmol). The reaction mixture was stirred at 0 °C under open air atmosphere

and monitored by TLC until the disappearance of pyrazolone **7**. After the appropriate period, the reaction mixture was quenched with water (10 mL) and diluted with EtOAc (30 mL). The organic phase was separated and the aqueous layer was washed with EtOAc (30 mL). Concentration of the combined organic layer under reduced pressure afforded the crude product, which was purified by silica gel column chromatography (ethyl acetate: hexane 5:95) to afford the corresponding product **11a**.

(E)-5-methyl-4-((E)-2-(3-methyl-1,6-diphenyl-3a,7a-dihydropyrano[2,3-c]pyrazol-4(1H)-ylidene)-1-phenylethylidene)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (**11a**)

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2 to 95:5).

Compound description: Reddish brown solid.

R_f: 0.3 (10% EtOAc/Hexane)

Yield: 90 mg (80%)

Melting point: 142-144 °C

FT-IR (neat): ν_{max} 2923, 1626, 1515, 1004 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.02-8.00 (m, 2H), 7.81-7.79 (m, 2H), 7.63-7.61 (m, 3H), 7.54-7.46 (m, 4H), 7.43-7.31 (m, 6H), 7.18-7.14 (m, 3H), 5.92 (s, 1H), 2.90 (s, 3H), 1.50 (s, 3H) ppm

^{13}C NMR (151 MHz, $CDCl_3$) δ 164.3, 158.0, 152.7, 149.1, 148.9, 146.7, 141.9, 139.7, 139.0, 137.1, 131.2, 130.6, 129.5, 129.2, 129.0, 128.78, 128.76, 127.2, 125.4, 124.3, 121.0, 119.4, 118.7, 111.6, 105.2, 103.9, 17.2, 16.5 ppm

HRMS (ESI) Calcd for $C_{37}H_{28}N_4O_2$ $[M+H]^+$ 561.2291; found, 561.2297.

(E)-5-cyclopropyl-4-((E)-2-(3-cyclopropyl-1,6-diphenyl-3a,7a-dihydropyrano[2,3-c]pyrazol-4(1H)-ylidene)-1-phenylethylidene)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one **(11b)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2)

Compound description: Reddish brown solid

R_f: 0.4 (10% EtOAc/Hexane)

Yield: 95 mg (78%)

Melting point: 161-163 °C

FT-IR (neat): ν_{max} 2924, 1626, 1509, 749 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.01 (dd, *J* = 8.6, 0.9 Hz, 2H), 7.80-7.78 (m, 2H), 7.59-7.55 (m, 5H), 7.52-7.49 (m, 2H), 7.40-7.31 (m, 6H), 7.16-7.10 (m, 3H), 5.94 (s, 1H), 2.67-2.62 (m, 1H), 1.31-1.27 (m, 2H), 1.16-1.13 (m, 2H), 0.87-0.84 (m, 2H), 0.61-0.56 (m, 1H), 0.36-0.32 (m, 2H) ppm

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4, 157.9, 152.8, 152.3, 151.2, 149.0, 141.6, 140.0, 139.2, 137.3, 131.4, 130.4, 129.5, 129.4, 129.2, 129.1, 128.7, 128.6, 127.0, 125.4, 124.0, 121.0, 119.0, 112.4, 105.6, 104.2, 11.4, 10.4, 7.9, 7.3 ppm

HRMS (ESI) Calcd for $C_{41}H_{32}N_4O_2$ $[M+H]^+$ 613.2604; found, 613.2627.

(E)-4-((E)-2-(1,6-diphenyl-3-propyl-3a,7a-dihydropyrano[2,3-c]pyrazol-4(1H)-ylidene)-1-phenylethylidene)-2-phenyl-5-propyl-2,4-dihydro-3H-pyrazol-3-one **(11c)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2)

Compound description: Reddish brown solid

R_f: 0.4 (10% EtOAc/Hexane)

Yield: 86 mg (70%);

Melting point: 160-162 °C;

FT-IR (neat): ν_{max} 2922, 1714, 1505, 833 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.15-7.97 (m, 2H), 7.80 (dd, *J* = 8.6, 1.0 Hz, 2H), 7.68-7.56 (m, 3H), 7.55-7.45 (m, 4H), 7.44-7.27 (m, 6H), 7.20-7.08 (m, 3H), 5.90 (s, 1H), 3.35-3.13 (m, 2H), 2.03-1.86 (m, 2H), 1.74-1.65 (m, 2H), 1.45-1.32 (m, 2H), 1.19 (t, *J* = 7.3 Hz, 3H), 0.64 (t, *J* = 7.3 Hz, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 157.4, 152.3, 152.2, 150.6, 149.1, 141.5, 139.7, 139.2, 137.2, 131.3, 130.4, 129.4, 129.3, 129.2, 128.7, 128.7, 127.1, 125.3, 124.0, 121.1, 119.1, 118.4, 112.4, 104.5, 104.2, 32.3, 31.6, 22.1, 21.4, 14.0, 13.9 ppm

HRMS (ESI) Calcd for $C_{41}H_{36}N_4O_2$ $[M+H]^+$ 617.2917; found, 617.2933.

(E)-2-(4-chlorophenyl)-4-((E)-2-(1-(4-chlorophenyl)-3-methyl-6-phenyl-3a,7a-dihydropyrano [2,3-c]pyrazol-4(1H)-ylidene)-1-phenylethylidene)-5-methyl-2,4-dihydro-3H-pyrazol-3-one **(11d):**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2 to 95:5)

Compound description: Reddish brown solid

R_f: 0.3 (10% EtOAc/Hexane)

Yield: 98 mg (78%)

Melting point: 162-164 °C

FT-IR (neat): ν_{max} 2923, 1625, 1491, 828 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.11-7.91 (m, 2H), 7.84-7.68 (m, 2H), 7.68-7.58 (m, 3H), 7.53-7.43 (m, 4H), 7.43-7.38 (m, 1H), 7.38-7.31 (m, 4H), 7.18-7.08 (m, 2H), 5.91 (s, 1H), 2.88 (s, 3H), 1.48 (s, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$) *δ* 164.2, 158.2, 152.9, 149.2, 147.0, 141.9, 139.5, 137.6, 135.7, 132.7, 131.1, 130.7, 129.6, 129.5, 129.3, 129.2, 128.9, 128.9, 128.7, 125.3, 122.0, 120.2, 118.6, 111.7, 105.3, 104.0, 17.2, 16.4 ppm

HRMS (ESI) Calcd for $C_{37}H_{26}Cl_2N_4O_2$ $[M+H]^+$ 629.1511; found, 629.1541.

(E)-2-(4-fluorophenyl)-4-((E)-2-(1-(4-fluorophenyl)-3-methyl-6-phenyl-3a,7a-dihydropyrano [2,3-c]pyrazol-4(1H)-ylidene)-1-phenylethylidene)-5-methyl-2,4-dihydro-3H-pyrazol-3-one **(11e)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2)

Compound description: Reddish brown solid

R_f: 0.35 (10% EtOAc/Hexane)

Yield: 81 mg (68%)

Melting point: 159-161 °C

FT-IR (neat): ν_{max} 2925, 1715, 1508, 835 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.04-7.89 (m, 2H), 7.87-7.69 (m, 2H), 7.69-7.57 (m, 3H), 7.51-7.42 (m, 2H), 7.39 (t, *J* = 7.3 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 8.5 Hz, 2H), 7.15-7.02 (m, 4H), 5.91 (s, 1H), 2.87 (s, 3H), 1.48 (s, 3H) ppm

^{13}C NMR (150 MHz, $CDCl_3$) δ 164.08, 161.3 (d, *J* = 257.1 Hz), 159.7 (d, *J* = 252.9 Hz), 158.2, 152.8, 149.0, 148.9, 146.7, 141.9, 139.6, 135.1, 133.2, 131.1, 130.7, 129.5, 129.3, 128.9, 128.8, 125.3, 122.9 (d, *J* = 8.4 Hz), 121.1 (d, *J* = 7.7 Hz), 118.6, 116.4 (d, *J* = 22.0 Hz), 115.3 (d, *J* = 22.3 Hz), 111.7, 105.1, 103.9, 17.2, 16.4 ppm

^{19}F NMR (377 MHz, $CDCl_3$) δ -114.0, -118.5 ppm

HRMS (ESI) Calcd for $C_{37}H_{26}F_2N_4O_2$ $[M+H]^+$ 597.2102; found, 597.2119.

(E)-5-methyl-4-((E)-2-(3-methyl-6-phenyl-1-(4-(trifluoromethyl)phenyl)-3a,7a-dihydropyrano [2,3-c]pyrazol-4(1H)-ylidene)-1-phenylethylidene)-2-(4-(trifluoromethyl)phenyl)-2,4-dihydro-3H-pyrazol-3-one **(11f)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2 to 95:5)

Compound description: Reddish brown solid

Yield: 78 mg (56%)

R_f: 0.3 (10% EtOAc/Hexane)

Melting point: 187-189 °C

FT-IR (neat): ν_{max} 2924, 1714, 1512, 757 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.20 (d, *J* = 8.5 Hz, 2H), 7.98 (d, *J* = 8.5 Hz, 2H), 7.78 (d, *J* = 8.6 Hz, 2H), 7.70-7.59 (m, 5H), 7.49-7.45 (m, 2H), 7.42 (t, *J* = 7.3 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.16-7.13 (m, 2H), 5.92 (s, 1H), 2.90 (s, 3H), 1.50 (s, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 158.4, 153.4, 153.1, 151.8, 149.8, 149.5, 147.5, 146.0, 141.8, 139.9, 139.4, 133.2, 131.0, 130.8, 129.6, 129.4, 128.9, 128.9, 128.7, 126.77, 126.75, 126.0, 125.9, 125.4, 124.8 (q, *J* = 269.8 Hz), 123.8 (q, *J* = 270.6 Hz), 120.4, 118.6, 118.3, 115.2, 113.9, 111.9, 105.7, 104.2, 99.8, 17.2, 16.4 ppm

^{19}F NMR (377 MHz, $CDCl_3$) δ -61.9, -62.4 ppm

HRMS (ESI) Calcd for $C_{39}H_{26}F_6N_4O_2$ $[M+H]^+$ 697.2038; found, 697.2057.

(E)-5-methyl-4-((E)-2-(3-methyl-6-phenyl-1-(4-(trifluoromethoxy)phenyl)-3a,7a-dihydro pyrano[2,3-c]pyrazol-4(1H)-ylidene)-1-phenylethylidene)-2-(4-(trifluoromethoxy)phenyl)-2,4-dihydro-3H-pyrazol-3-one **(11g)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2 to 90:10)

Compound description: Reddish brown solid

Yield: 95 mg (65%)

R_f: 0.2 (10% EtOAc/Hexane)

Melting point: 192-194 °C

FT-IR (neat): ν_{max} 2922, 1626, 1505, 756 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.09-8.02 (m, 2H), 7.88-7.82 (m, 2H), 7.67-7.58 (m, 3H), 7.49-7.43 (m, 2H), 7.43-7.31 (m, 5H), 7.25-7.24 (m, 2H), 7.16-7.10 (m, 2H), 5.91 (s, 1H), 2.88 (s, 3H), 1.49 (s, 3H) ppm

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 158.3, 152.9, 149.3, 149.2, 147.6, 147.1, 145.4, 141.9, 139.5, 137.6, 135.6, 131.1, 130.7, 129.5, 129.3, 128.9, 125.4, 122.1, 122.0, 121.9, 121.7, 121.5, 120.6 (q, *J* = 255.3 Hz), 120.5 (q, *J* = 258.2 Hz), 120.2, 118.5, 111.8, 105.4, 104.0, 17.2, 16.4 ppm

^{19}F NMR (377 MHz, $CDCl_3$) δ -57.95, -58.01 ppm

HRMS (ESI) Calcd for $C_{39}H_{26}F_6N_4O_4$ $[M+H]^+$ 729.1936; found, 729.1963.

(E)-5-methyl-4-((E)-2-(3-methyl-6-phenyl-1-(2,2,2-trifluoroethyl)-3a,7a-dihydropyrano[2,3-c]pyrazol-4(1H)-ylidene)-1-phenylethylidene)-2-(2,2,2-trifluoroethyl)-2,4-dihydro-3H-pyrazol-3-one **(11h)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2)

Compound description: Reddish brown solid

Yield: 83 mg (72%)

R_f: 0.4 (10% EtOAc/Hexane)

Melting point: 145-147 °C

FT-IR (neat): ν_{max} 2930, 1627, 1517, 754 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.66-7.54 (m, 3H), 7.46-7.34 (m, 3H), 7.36-7.29 (m, 2H), 7.17-7.05 (m, 2H), 5.84 (s, 1H), 4.71 (q, *J* = 8.2 Hz, 2H), 4.40 (q, *J* = 8.7 Hz, 2H), 2.78 (s, 3H), 1.40 (s, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 158.7, 152.8, 150.8, 148.9, 147.0, 141.8, 139.3, 130.9, 130.7, 129.5, 129.3, 128.8, 128.7, 125.3, 123.7 (q, *J* = 278.9 Hz), 122.6 (q, *J* = 278.2 Hz), 117.3, 111.7, 104.1, 103.8, 48.5 (q, *J* = 35.8 Hz), 45.1 (q, *J* = 34.7 Hz), 17.1, 16.1 ppm

^{19}F NMR (377 MHz, $CDCl_3$) δ -70.7, -70.8 ppm

HRMS (ESI) Calcd for $C_{29}H_{22}F_6N_4O_2$ $[M+H]^+$ 573.1725; found, 573.1754.

(E)-4-((E)-1-(4-fluorophenyl)-2-(6-(4-fluorophenyl)-3-methyl-1-phenyl-3a,7a-dihydropyrano [2,3-c]pyrazol-4(1H)-ylidene)ethylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one **(11i)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2 to 95:5)

Compound description: Reddish brown solid

Yield: 98 mg (82%)

R_f: 0.3 (10% EtOAc/Hexane)

Melting point: 158-160 °C

FT-IR (neat): ν_{max} 2958, 1626, 1494, 752 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.01 (d, *J* = 7.6 Hz, 2H), 7.79 (d, *J* = 7.7 Hz, 2H), 7.55 (t, *J* = 8.0 Hz, 2H), 7.51-7.44 (m, 3H), 7.44-7.40 (m, 2H), 7.40-7.32 (m, 2H), 7.24-7.14 (m, 3H), 7.13-7.03 (m, 2H), 5.77 (s, 1H), 2.90 (s, 3H), 1.56 (s, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.08, 164.06 (d, *J* = 251.7 Hz),163.5 (d, *J* = 249.4 Hz), 156.4, 152.0, 149.0, 148.4, 146.7, 141.6, 138.9, 137.0, 135.6, 131.03 (d, *J* = 7.8 Hz), 129.5, 128.8, 127.4 (d, *J* = 2.8 Hz), 127.33 (d, *J* = 3.1 Hz), 127.27, 124.4, 121.0, 119.4, 119.1, 116.54 (d, *J* = 21.3 Hz), 116.25 (d, *J* = 22.0 Hz), 111.8, 105.0, 103.6, 17.5, 16.4 ppm

^{19}F NMR (471 MHz, $CDCl_3$) δ -108.3, -111.4 ppm

HRMS (ESI) Calcd for $C_{37}H_{26}F_2N_4O_2$ $[M+H]^+$ 597.2102; found, 597.2099.

(E)-5-cyclopropyl-4-((E)-2-(3-cyclopropyl-6-(4-fluorophenyl)-1-phenyl-3a,7a-dihydropyrano [2,3-c]pyrazol-4(1H)-ylidene)-1-(4-fluorophenyl)ethylidene)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one **(11j)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2 to 95:5)

Compound description: Reddish brown solid

Yield: 98 mg (78%)

R_f: 0.25 (10% EtOAc/Hexane)

Melting point: 164-166 °C

FT-IR (neat): ν_{max} 2974, 1627, 1516, 730 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.03-7.95 (m, 2H), 7.81-7.71 (m, 2H), 7.58-7.46 (m, 4H), 7.43-7.34 (m, 3H), 7.34-7.27 (m, 2H), 7.22-7.16 (m, 3H), 7.10-7.02 (m, *J* = 8.6 Hz, 2H), 5.77 (s, 1H), 2.67-2.54 (m, 1H), 1.30-1.23 (m, 2H), 1.16-1.09 (m, 2H), 0.92-0.84 (m, 2H), 0.63 (m, 1H), 0.44-0.36 (m, 2H) ppm

^{13}C NMR (125 MHz, $CDCl_3$) δ 163.4 (d, *J* = 247.3 Hz), 163.3 (d, *J* = 240.1 Hz), 156.3, 152.4, 151.6, 151.2, 148.8, 141.3, 139.1, 137.2, 136.0, 131.5 (d, *J* = 7.6 Hz), 129.4, 128.6, 127.6 (d, *J* = 2.3 Hz), 127.3, 127.2 (d, *J* = 3.0 Hz), 124.1, 121.0, 119.4, 119.0, 116.3 (d, *J* = 21.1 Hz), 116.2 (d, *J* = 21.9 Hz), 112.6, 105.5, 103.9, 11.6, 10.3, 7.9, 7.3 ppm

^{19}F NMR (377 MHz, $CDCl_3$) δ -108.6, -111.6 ppm

HRMS (ESI) Calcd for $C_{41}H_{30}F_2N_4O_2$ $[M+H]^+$ 649.2415; found, 649.2445.

(E)-4-((E)-1-(4-fluorophenyl)-2-(6-(4-fluorophenyl)-1-phenyl-3-propyl-3a,7a-dihydropyrano [2,3-c]pyrazol-4(1H)-ylidene)ethylidene)-2-phenyl-5-propyl-2,4-dihydro-3H-pyrazol-3-one **(11k)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2 to 95:5)

Compound description: Reddish brown solid

Yield: 98 mg (78%)

R_f: 0.3 (10% EtOAc/Hexane)

Melting point: 161-163 °C

FT-IR (neat): ν_{max} 2957, 1630, 1493, 753 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.04 (d, *J* = 7.8 Hz, 2H), 7.80-7.73 (m, 2H), 7.56-7.44 (m, 4H), 7.44-7.35 (m, 3H), 7.35-7.28 (m, 2H), 7.21-7.12 (m, 3H), 7.09-7.02 (m, 2H), 5.72 (s, 1H), 3.27-3.15 (m, 2H), 2.00-1.85 (m, 2H), 1.78-1.68 (m, 2H), 1.49-1.33 (m, 2H), 1.17 (t, *J* = 7.3 Hz, 3H), 0.69 (t, *J* = 7.3 Hz, 3H) ppm

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 164.0 (d, *J* = 253.3 Hz), 163.5 (d, *J* = 251.7 Hz), 155.8, 151.8, 151.6, 150.6, 149.0, 141.2, 139.1, 137.1, 135.7, 131.3 (d, *J* = 7.8 Hz), 129.5, 128.7, 127.5 (d, *J* = 2.3 Hz), 127.3, 127. 2 (d, *J* = 3.3 Hz), 124.1, 121.2, 119.0, 118.8, 116.4 (d, *J* = 21.4 Hz), 116.2 (d, *J* = 22.0 Hz), 112.5, 104.4, 103.8, 32.5, 31.6, 22.1, 21.2, 14.0, 13.9 ppm

^{19}F NMR (377 MHz, $CDCl_3$) δ -108.5, -111.3 ppm

HRMS (ESI) Calcd for $C_{41}H_{34}F_2N_4O_2$ $[M+H]^+$ 653.2728; found, 653.2737.

(E)-4-((E)-2-(1,6-bis(4-fluorophenyl)-3-methyl-3a,7a-dihydropyrano[2,3-c]pyrazol-4(1H)-ylidene)-1-(4-fluorophenyl)ethylidene)-2-(4-fluorophenyl)-5-methyl-2,4-dihydro-3H-pyrazol-3-one **(11l)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2 to 90:10)

Compound description: Reddish brown solid

Yield: 83 mg (65%)

R_f: 0.2 (10% EtOAc/Hexane)

Melting point: 162-164 °C

FT-IR (neat): ν_{max} 2928, 1599, 1507, 835 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.03-7.89 (m, 2H), 7.82-7.66 (m, 2H), 7.49-7.40 (m, 2H), 7.38-7.29 (m, 2H), 7.25-7.19 (m, 2H), 7.18-7.13 (m, 2H), 7.12-7.04 (m, 4H), 5.74 (s, 1H), 2.86 (s, 3H), 1.53 (s, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.1 (d, *J* = 251.7 Hz), 163.9, 163.5 (d, *J* = 249.3 Hz), 161.4 (d, *J* = 246.7 Hz), 159.7 (d, *J* = 241.6 Hz), 156.6, 152.1, 148.9, 148.5, 146.7, 141.6, 135.5, 135.0, 133.1, 131.0 (d, *J* = 7.8 Hz), 127.3 (d, *J* = 8.8 Hz), 123.0 (d, *J* = 8.4 Hz), 121.1 (d, *J* =

7.8 Hz), 119.0, 116.6 (d, *J* = 21.2 Hz), 116.5 (d, *J* = 22.3 Hz), 116.3 (d, *J* = 21.2 Hz), 115.4 (d, *J* = 22.3 Hz), 111.9, 104.9, 103.6, 17.4, 16.3 ppm

^{19}F NMR (377 MHz, $CDCl_3$) δ -108.1, -111.2, -113.7, -118.4 ppm

HRMS (ESI) Calcd for $C_{37}H_{24}F_4N_4O_2$ $[M+H]^+$ 633.1914; found, 633.1934.

(E)-5-methyl-4-((E)-2-(3-methyl-1-phenyl-6-(p-tolyl)-3a,7a-dihydropyrano[2,3-c]pyrazol-4(1H)-ylidene)-1-(p-tolyl)ethylidene)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one **(11m)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2)

Compound description: Reddish brown solid

Yield: 85 mg (72%)

R_f: 0.4 (10% EtOAc/Hexane)

Melting point: 155-157 °C

FT-IR (neat): ν_{max} 2920, 1624, 1497, 757 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.53 (t, *J* = 8.0 Hz, 2H), 7.47-7.31 (m, 7H), 7.22-7.10 (m, 3H), 7.07 (d, *J* = 8.3 Hz, 2H), 5.83 (s, 1H), 2.90 (s, 3H), 2.59 (s, 3H), 2.40 (s, 3H), 1.58 (s, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 158.5, 152.9, 149.2, 149.1, 146.7, 142.1, 141.1, 139.4, 139.0, 137.2, 136.8, 130.0, 129.6, 129.4, 129.0, 128.7, 128.5, 127.1, 125.3, 124.2, 121.0, 119.4, 118.4, 111.7, 105.2, 103.4, 21.4, 17.4, 16.5 ppm

HRMS (ESI) Calcd for $C_{39}H_{32}N_4O_2$ $[M+H]^+$ 589.2604; found, 589.2621.

(E)-4-((E)-1-(4-methoxyphenyl)-2-(6-(4-methoxyphenyl)-3-methyl-1-phenyl-3a,7a-dihydropyrano[2,3-c]pyrazol-4(1H)-ylidene)ethylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one **(11n)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2 to 90:10).

Compound description: Reddish brown solid

Yield: 93 mg (75%)

R_f: 0.4 (15% EtOAc/Hexane)

Melting point: 172-174 °C

FT-IR (neat): ν_{max} 2960, 1623, 1493, 755 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.01 (d, *J* = 7.6 Hz, 2H), 7.79 (dd, *J* = 8.6, 1.0 Hz, 2H), 7.58-7.46 (m, 2H), 7.45-7.30 (m, 5H), 7.21-7.06 (m, 5H), 6.91-6.75 (m, 2H), 5.78 (s, 1H), 3.95 (s, 3H), 3.84 (s, 3H), 2.87 (s, 3H), 1.59 (s, 3H) ppm

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 161.6, 160.7, 158.3, 152.8, 149.2, 149.1, 146.7, 142.4, 139.1, 137.2, 131.9, 130.5, 129.5, 128.7, 127.1, 127.0, 124.2, 123.7, 121.0, 119.4, 118.4, 114.8, 114.2, 111.7, 105.1, 102.7, 55.54, 55.48, 17.5, 16.4 ppm

HRMS (ESI) Calcd for $C_{39}H_{32}N_4O_4$ $[M+H]^+$ 621.2502; found, 621.2524.

(E)-5-methyl-4-((E)-2-(3-methyl-1-phenyl-6-(thiophen-3-yl)-3a,7a-dihydropyrano[2,3-c]pyrazol-4(1H)-ylidene)-1-(thiophen-3-yl)ethylidene)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one **(11o)**

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent hexane:ethyl acetate (98:2 to 90:10)

Compound description: Reddish brown solid

Yield: 68 mg (60%)

R_f: 0.3 (15% EtOAc/Hexane)

Melting point: 149-151 °C

FT-IR (neat): ν_{max} 2924, 1623, 1495, 754 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.00-7.98 (m, 2H), 7.80-7.78 (m, 2H), 7.64-7.63 (m, 1H), 7.54-7.49 (m, 3H), 7.43-7.33 (m, 5H), 7.20 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.17-7.13 (m, 1H), 6.87 (dd, *J* = 5.2, 1.3 Hz, 1H), 5.81 (s, 1H), 2.87 (s, 3H), 1.63 (s, 3H) ppm

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 152.5, 149.5, 148.9, 148.8, 146.7, 141.8, 139.7, 138.9, 137.1, 133.7, 129.5, 129.1, 128.7, 127.3, 127.2, 124.9, 124.7, 124.6, 124.3, 121.0, 119.4, 111.9, 104.9, 103.1, 16.5, 16.4 ppm

HRMS (ESI) Calcd for $C_{33}H_{24}N_4O_2S_2$ $[M+H]^+$ 573.1419; found, 573.1441.

<u>Intermediate A:</u> ***4-(1,5-Diphenylpenta-1,4-diyn-3-ylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one*** (**A**)

Following the general procedure and purified by column chromatography on silica gel (100-200 mesh), eluent 100% hexane

Compound description: Reddish brown solid

R_f: 0.6 (10% EtOAc/Hexane)

FT-IR (neat): ν_{max} 3067, 2188, 1689, 1496 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 1H NMR (400 MHz, $CDCl_3$) δ 7.99-7.95 (m, 2H), 7.79-7.77 (m, 2H), 7.64-7.62 (m, 2H), 7.51-7.39 (m, 8H), 7.20-7.16 (m, 2H), 2.64 (s, 3H) ppm
^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 147.7, 138.2, 133.2, 132.2, 130.7, 130.6, 128.8, 128.6, 124.8, 121.8, 121.2, 119.0, 117.6, 106.6, 103.7, 88.2, 87.5, 16.8 ppm
HRMS (ESI) Calcd for $C_{27}H_{18}N_2O$ $[M+H]^+$ 387.1497; found, 387.1479.

Procedure for the synthesis of D-11a:

To a solution of diynone **1** (0.2 mmol) and deuterated pyrazolone D-**7a** (0.4 mmol) in dry THF (3 mL) at 25-30 °C was added DBU (0.1 mmol). The reaction mixture was stirred at same temperature under nitrogen atmosphere for 30 min. After the appropriate period, the reaction mixture was quenched with D_2O (5 mL) and diluted with EtOAc (10 mL). The organic phase was separated and the aqueous layer was washed with EtOAc (10 mL). Concentration of the combined organic layer under reduced pressure afforded the crude product, which was purified by column chromatography (Ethyl acetate: hexane 5:95) to afford the corresponding product D-**11a**.

Compound description: Reddish brown solid.
R_f: 0.3 (10% EtOAc/Hexane)
Yield: 90 mg (80%)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 0.52H), 8.11-7.91 (m, 2H), 7.87-7.69 (m, 2H), 7.69-7.57 (m, 3H), 7.52 (t, *J* = 8.0 Hz, 2H), 7.49-7.45 (m, 2H), 7.44-7.30 (m, 6H), 7.23-7.06 (m, 3H), 5.92 (s, 0.77H), 2.90 (s, 3H), 1.50 (s, 3H) ppm
HRMS (ESI) Calcd for $C_{37}H_{26}D_2N_4O_2$ $[M+H]^+$ 563.2416; found, 563.2426.

Biological experiments

The SRB assay was performed by known protocol[5] to assess cytotoxicity. Briefly cytotoxicity against the Neuro2A (N2A) cell line was performed by using three different concentrations (1μM, 0.1μM, 0.01μM) of hybrid pyrano[2,3-c]pyrazole-pyrazolone/pyrazolone and galantamine. N2A cells were passaged and seeded in 96-well plates at a density of 3200 cells per well. Following a 24-hour incubation, cells were treated with ice-cold 50% TCA and incubated at 4°C for 1 hour. Subsequently, plates were washed with distilled water, dried, and subjected to incubation with 0.04% SRB dye at room temperature for 1 hour. After rinsing with

1% acetic acid and drying, 10mM Tris base was added to each well, and absorbance was measured at 510 nm using a microplate reader.

The Neurite outgrowth assay and imaging commenced with seeding Neuro2A cells at a density of 96000 cells per well in 6-well plates. Following a 24-hour incubation period, cells were subjected to serum-deprivation (0.1% serum) for 6 hours before exposure to compounds at three distinct non-toxic concentrations (1μM, 0.1μM, 0.01μM). Following the incubation period, cellular imaging was conducted using a Motic microscope (Moticam Pro 282A) at 20×magnification. Neurite outgrowth was quantified by utilizing ImageJ software to calculate the average length.

For AChE inhibitory property studies followed Ellman et al[6] protocol; In this assay, 60 μL of Tris-HCl and 10 μL of acetylcholine enzyme (0.01 units) were added to each well of a 96-well plate. This was followed by the addition of 1.5 μL of the hybrid pyrano[2,3-c]pyrazole-pyrazolone/ pyrazolone compound and 3.5 μL of Tris-HCl. The plate was then incubated for 20 minutes at room temperature on a shaker. After incubation, 10 μL of acetylthiocholine (0.075 M) and 60 μL of DTNB (0.001 M) were added to the wells. Spectrophotometric measurements were taken at 405 nm, and the percentage of enzyme inhibition was calculated.

IC50 calculation[7]

The most popular and useful method of determining a drug effectiveness is by calculating its half-maximal inhibitory concentration (IC50). The four-parameter logistic regression model is used to model dose-response relationships. The equation for this model is:

$$Y = \text{Min} + \frac{\text{Max} - \text{Min}}{1 + \left(\frac{X}{IC_{50}}\right)^{\text{Hill coefficient}}}$$

here:

- Y is the response variable (e.g., cell viability or % of inhibition).
- Min is the minimum response value.
- Max is the maximum response value.
- X is the concentration of the drug or substrate.
- IC50 is the concentration of the drug or substrate at which 50% inhibition is observed.
- Hill coefficient describes the steepness of the curve.

This model typically produces a sigmoid (S-shaped) curve, where the IC50 represents the midpoint of the curve, indicating the drug concentration that produces 50% of its maximum effect.

Steps to Calculate IC50 Using AAT Bioquest

1. The cell viability of all drugs were measured at three different concentrations: 1 μM, 0.1 μM, and 0.01 μM.
2. The measured viability responses, along with the corresponding drug concentrations, were input into the AAT Bioquest IC50 calculator.
3. The tool uses the four-parameter logistic regression model to fit the data points. This involves estimating the Min, Max, IC50, and Hill coefficient values that best describe the observed data.
4. Curve Generation:
   The calculator generates a dose-response curve based on the fitted model. The curve visually represents how the cell viability changes with varying concentrations of the drug.
5. IC50 Determination:
   The IC50 value is extracted from the model. It is the concentration at which the response is halfway between the Min and Max values.

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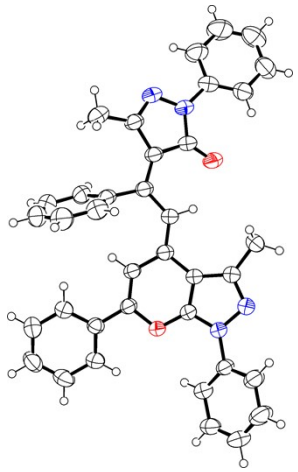
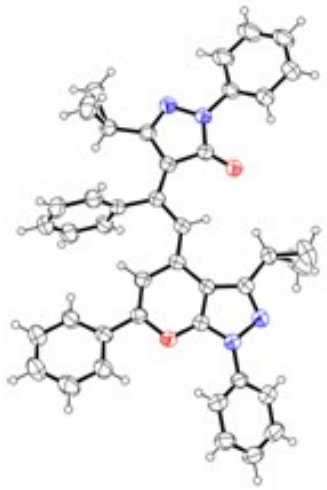
Figure S1. ORTEP view (30% probability ellipsoid) and crystallographic data for **11a** (CCDC 2324618)



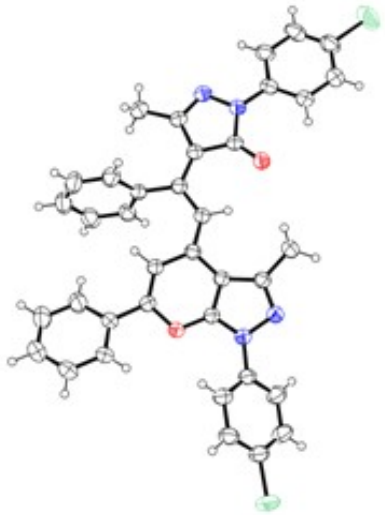
Compound	**11a**
Emp form.	$C_{37}H_{28}N_4O_2$
Form wt.	560.63
Sp. Grp.	*P -1*
T (K)	294
a (Å)	9.5486(18)
b (Å)	9.8277(19)
c (Å)	16.757(3)
α (º)	103.234(6)
β (º)	103.776(5)
γ (º)	97.299(6)
Z	2
V (Å^3)	1459.0(5)
ρcalcd (g/cm3)	1.276
Rflns. collect	8901
Unique rflns.	8710
Obsd. Rflns.	5031
R_1	0.0464
wR_2	0.1388
Diffractometer	Bruker APEX-II CCD

Figure S2. ORTEP view (30% probability ellipsoid) and crystallographic data for **11b** (CCDC 2324619)

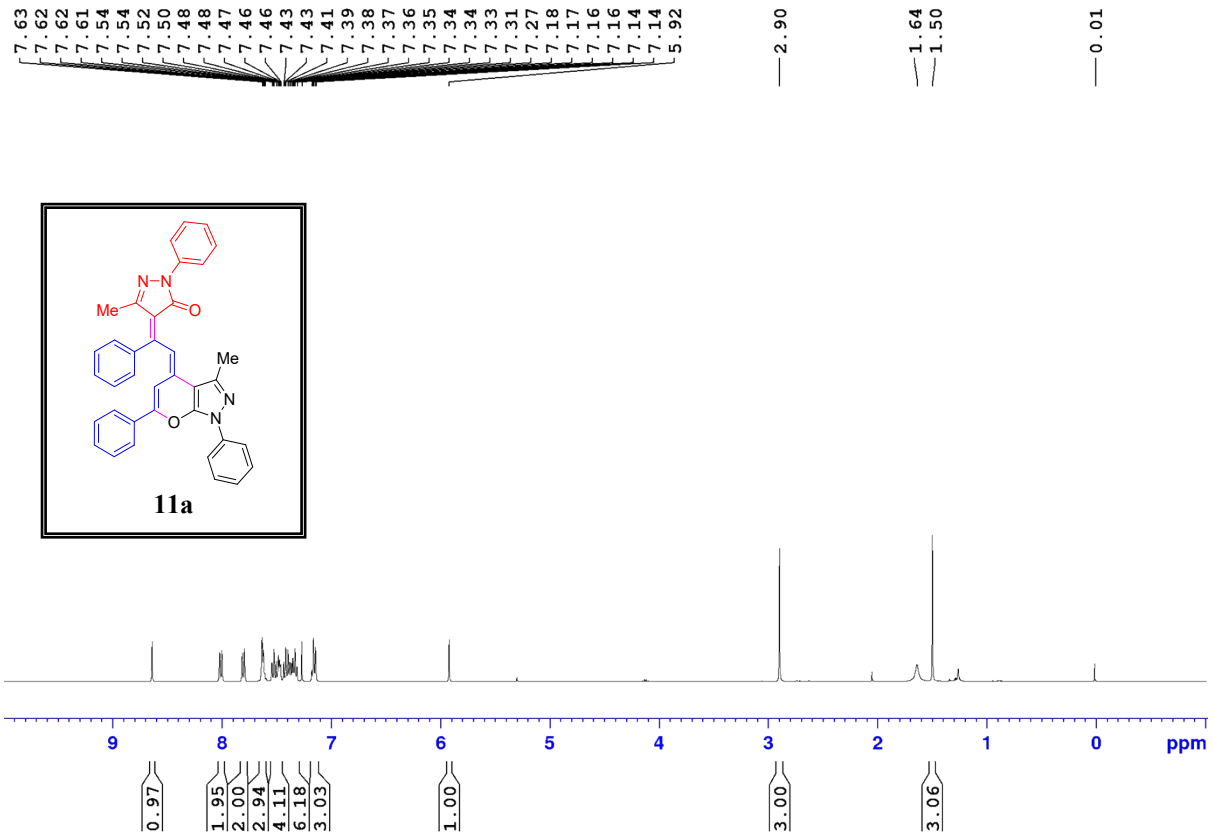


Compound	**11b**
Emp form.	$C_{41}H_{32}N_4O_2$
Form wt.	612.70
Sp. Grp.	*P -1*
T (K)	293
a (Å)	9.341(7)
b (Å)	11.471(8)
c (Å)	15.177(11)
α (º)	88.237(13)
β (º)	77.033(15)
γ (º)	83.309(13)
Z	2
V (Å^3)	1573.9(19)
ρcalcd (g/cm3)	1.293
Rflns. collect	9637
Unique rflns.	9447
Obsd. Rflns.	3876
R_1	0.0665
wR_2	0.2147
Diffractometer	Bruker APEX-II CCD

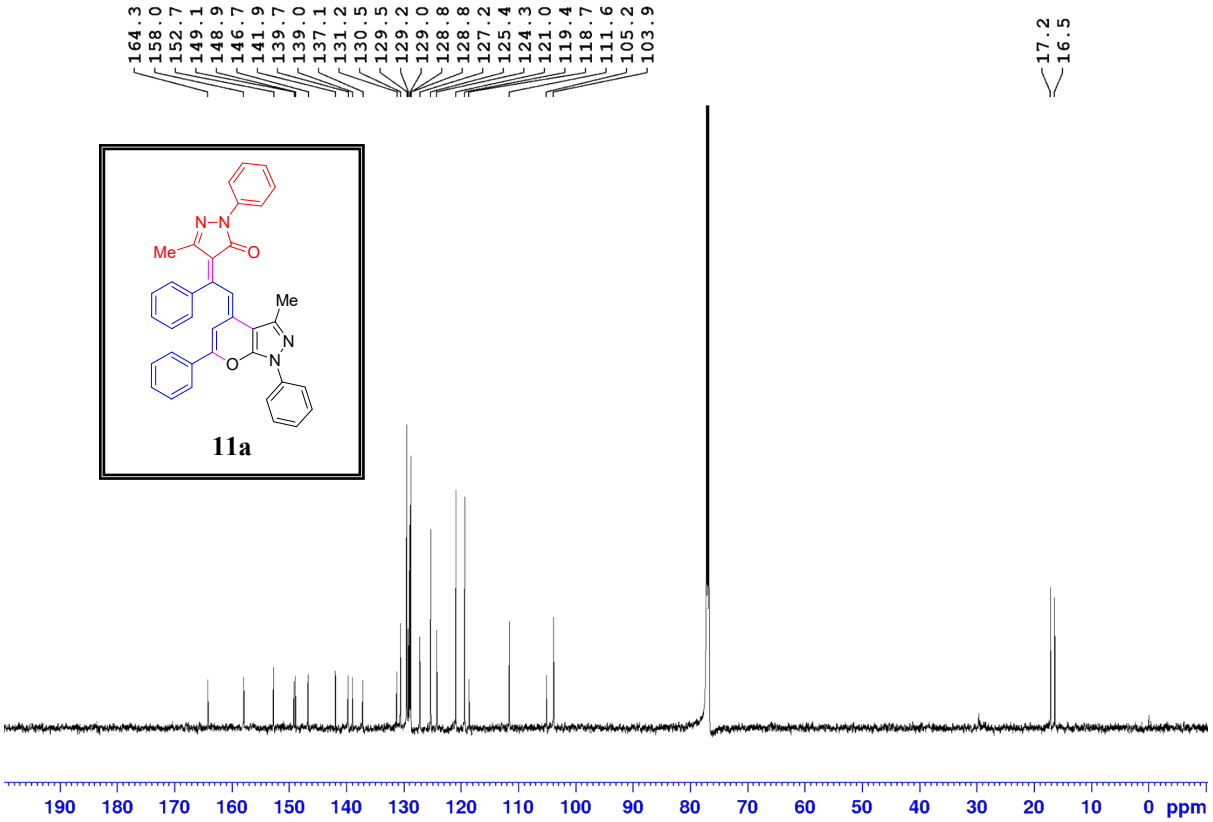
Figure S3. ORTEP view (30% probability ellipsoid) and crystallographic data for **11d** (CCDC 2324620)



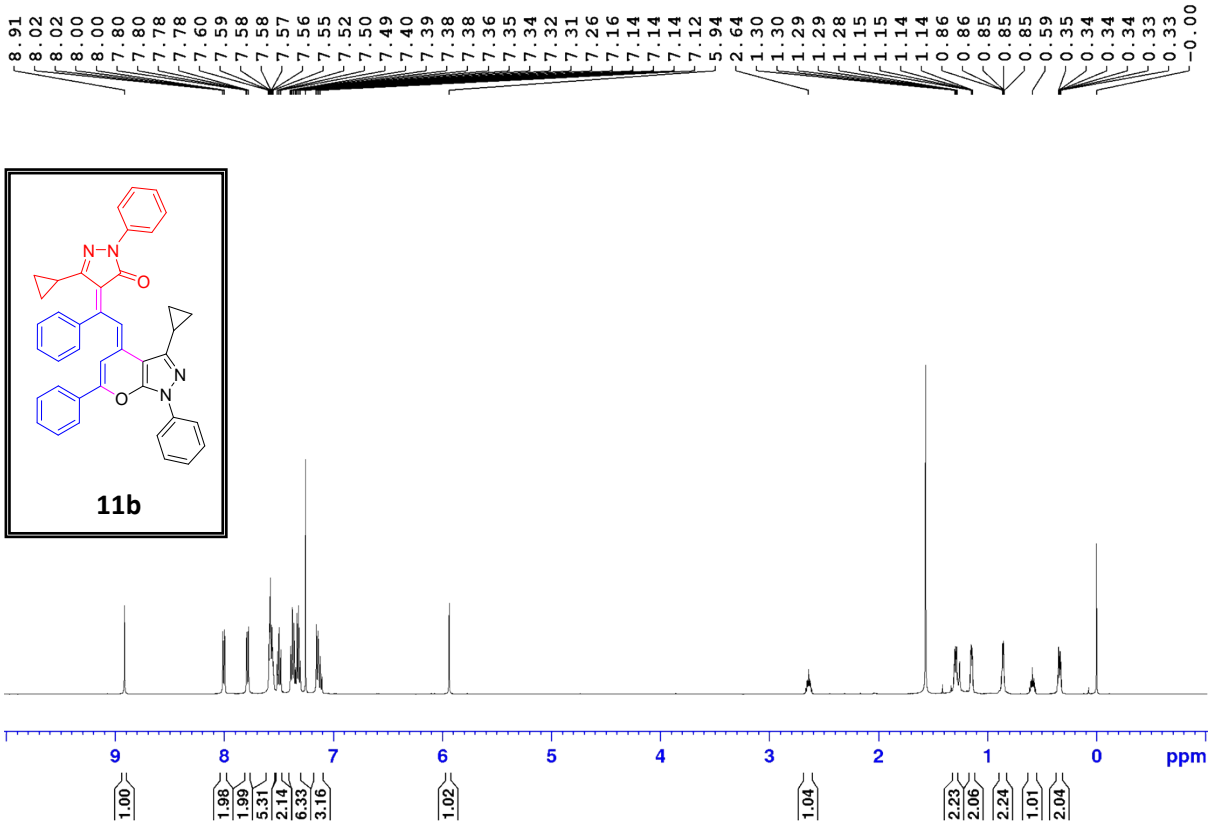
Compound	**11d**
Emp form.	$C_{37}H_{26}Cl_2N_4O_2$
Form wt.	629.52
Sp. Grp.	*P -1*
T (K)	293
a (Å)	9.724(7)
b (Å)	12.297(9)
c (Å)	13.872(10)
α (º)	103.225(15)
β (º)	106.099(14)
γ (º)	98.327(16)
Z	2
V (Å^3)	1512.5(18)
ρcalcd (g/cm3)	1.382
Rflns. collect	7603
Unique rflns.	7527
Obsd. Rflns.	4613
R_1	0.0476
wR_2	0.1355
Diffractometer	Bruker APEX-II CCD



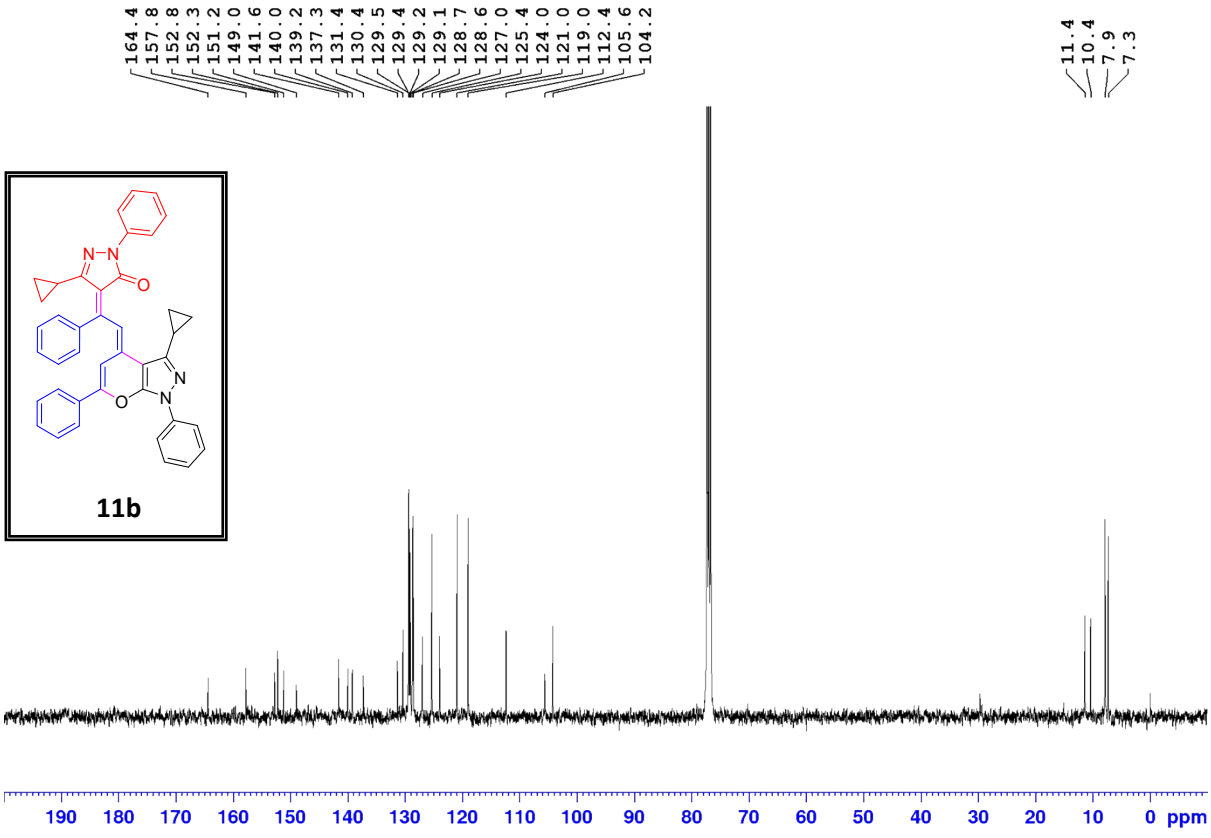
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11a**



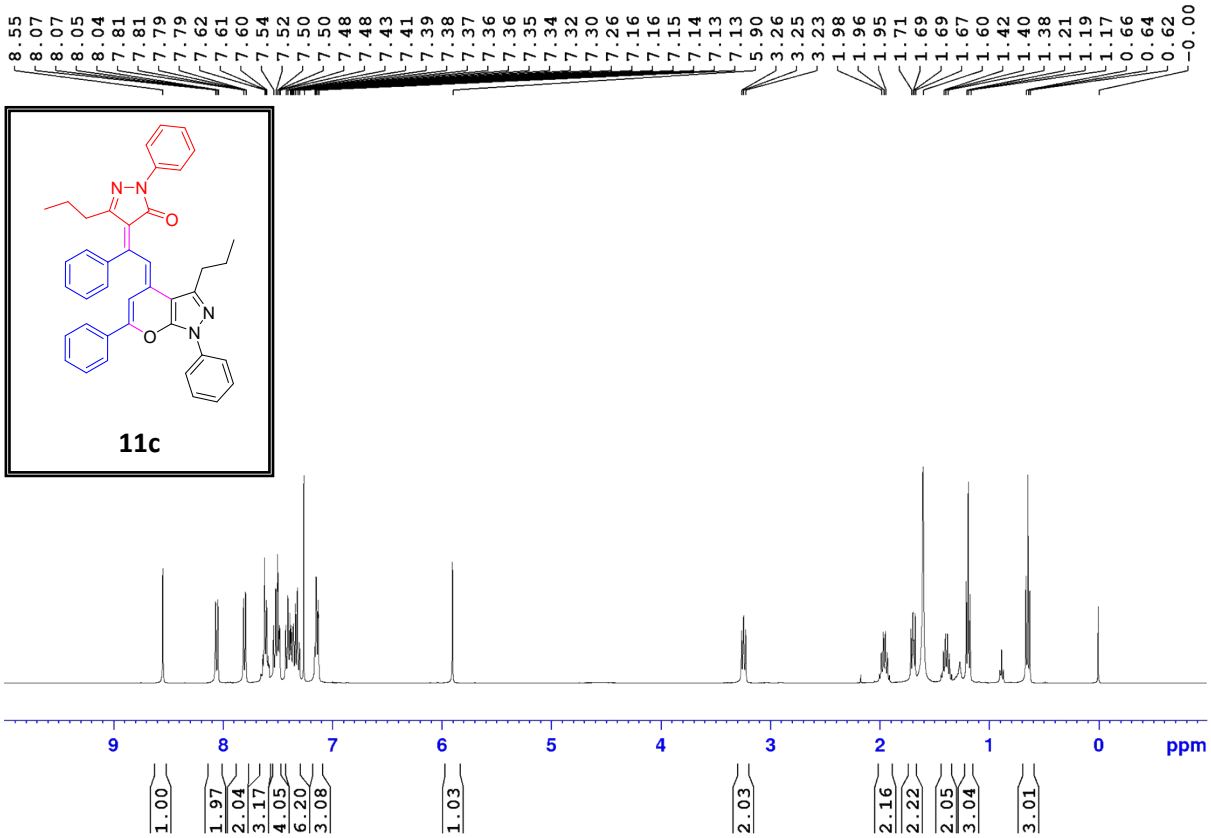
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11a**



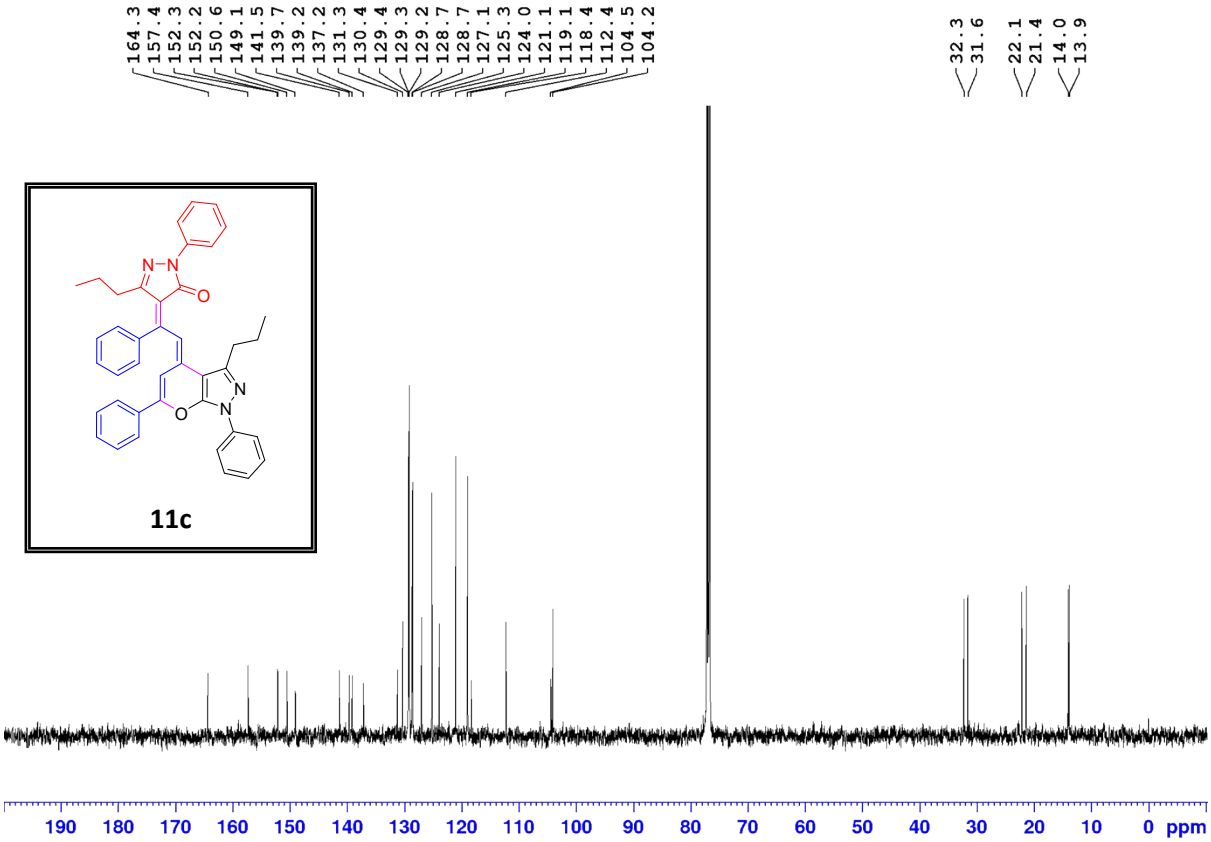
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11b**



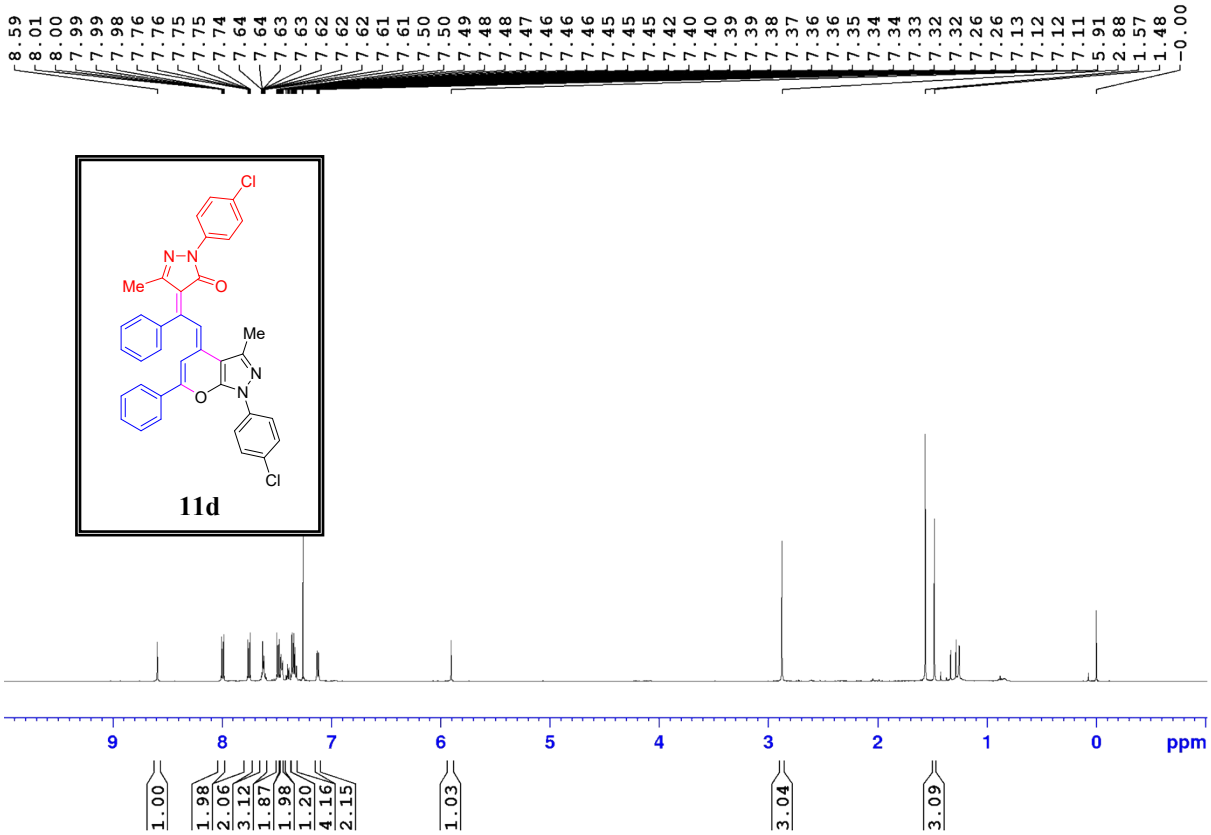
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11b**



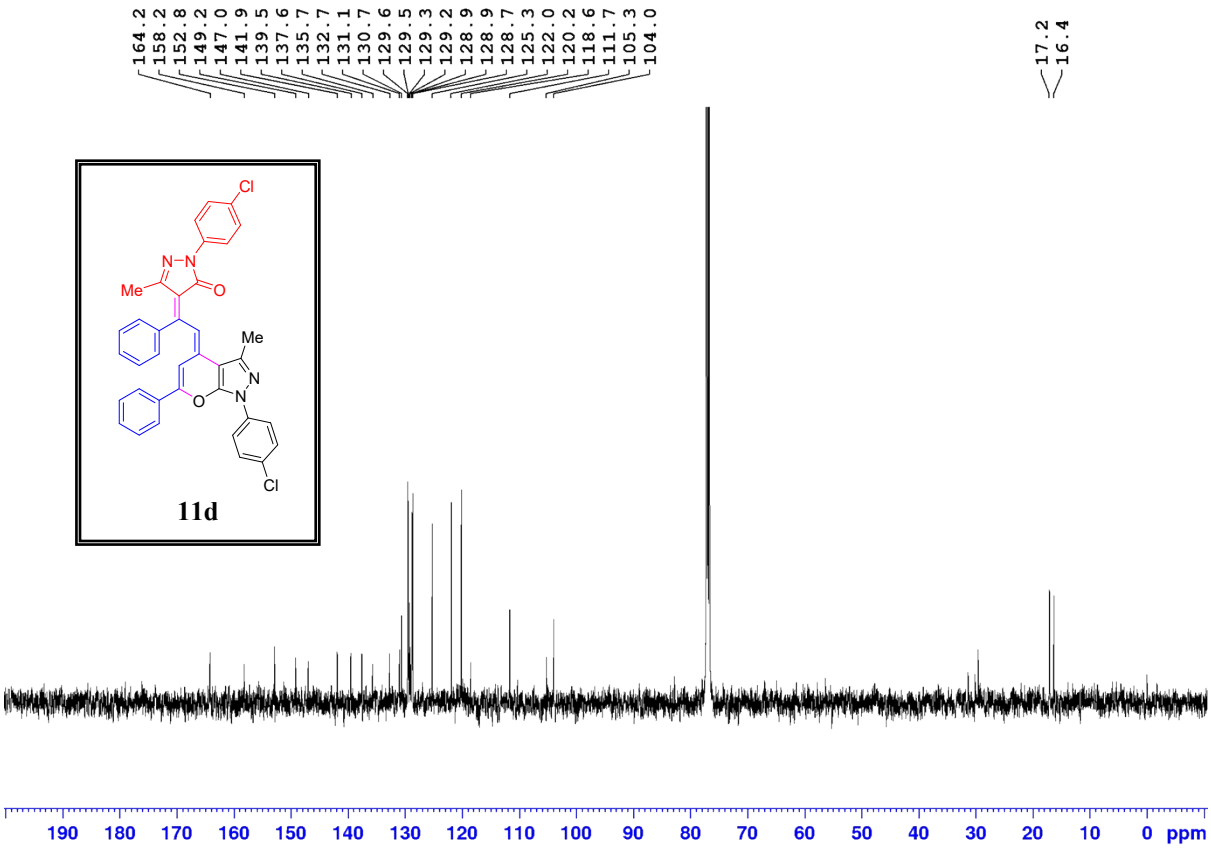
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11c**



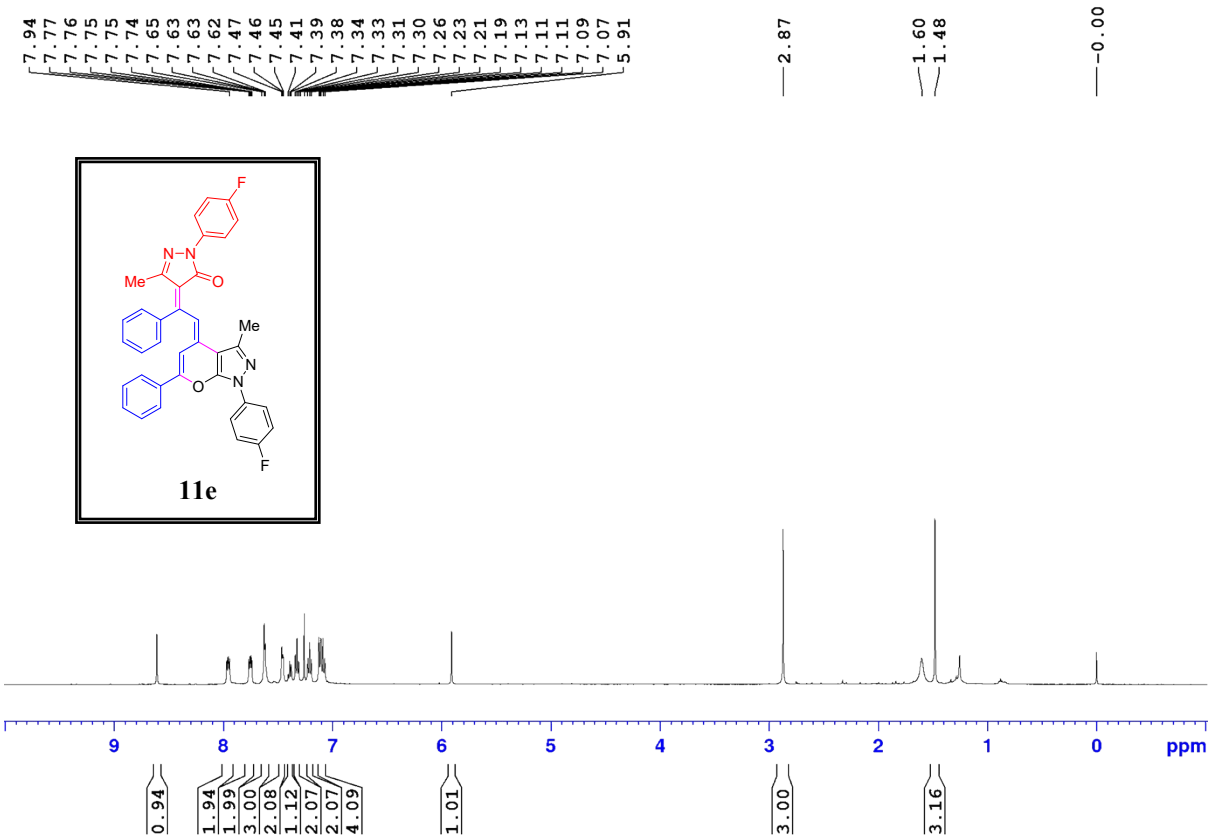
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11c**



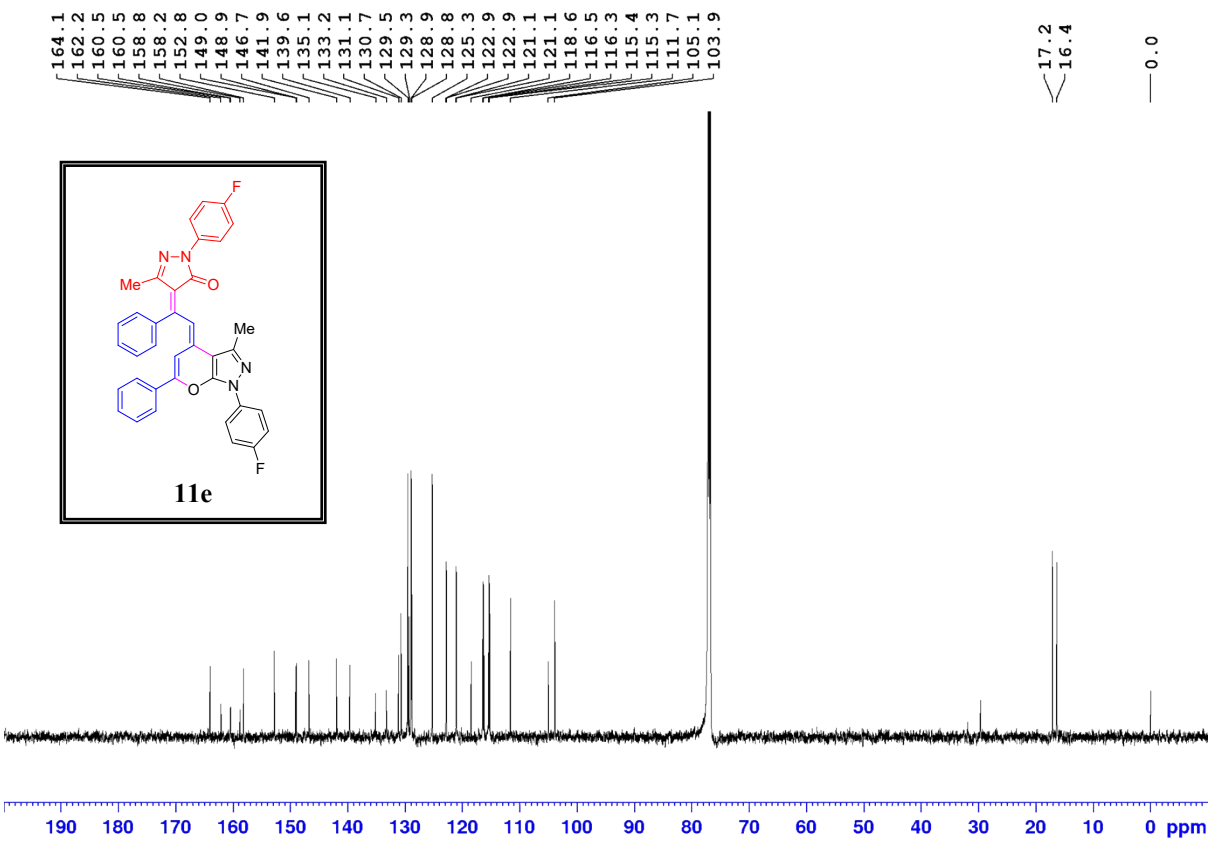
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11d**



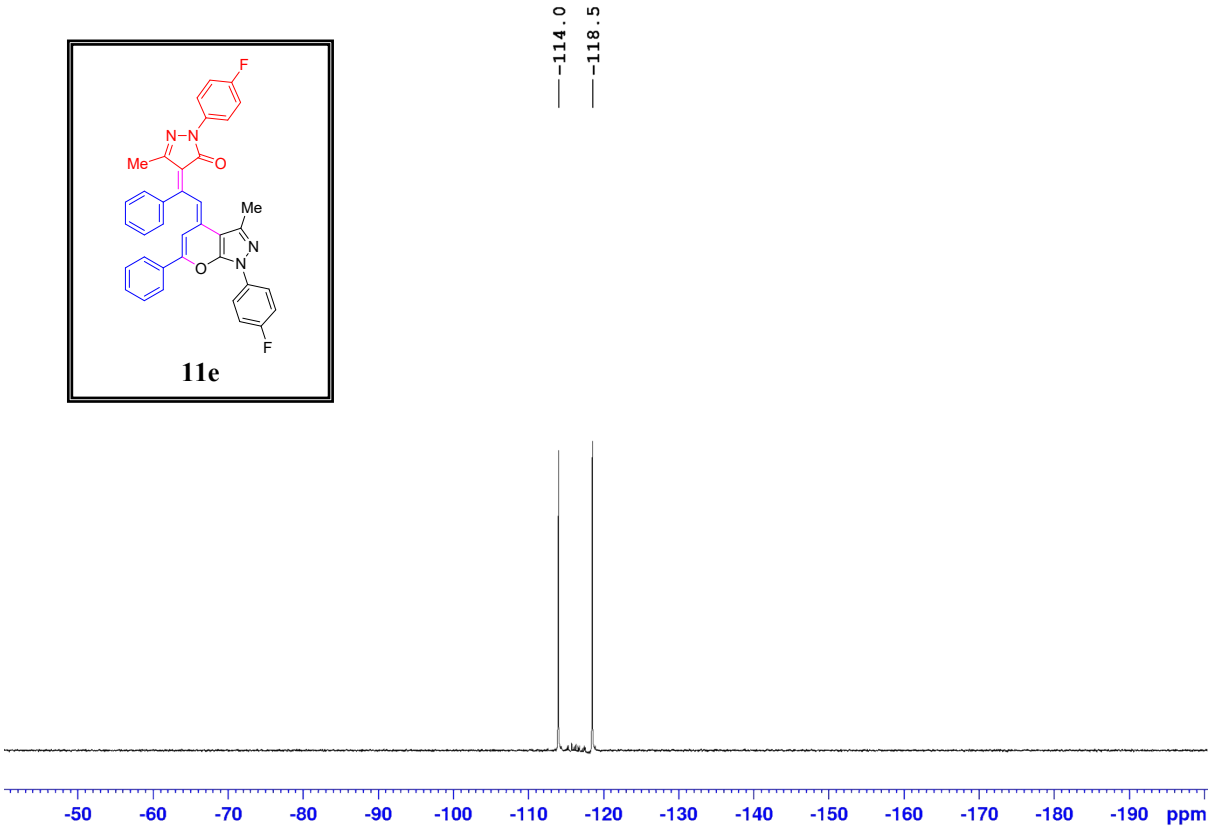
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11d**



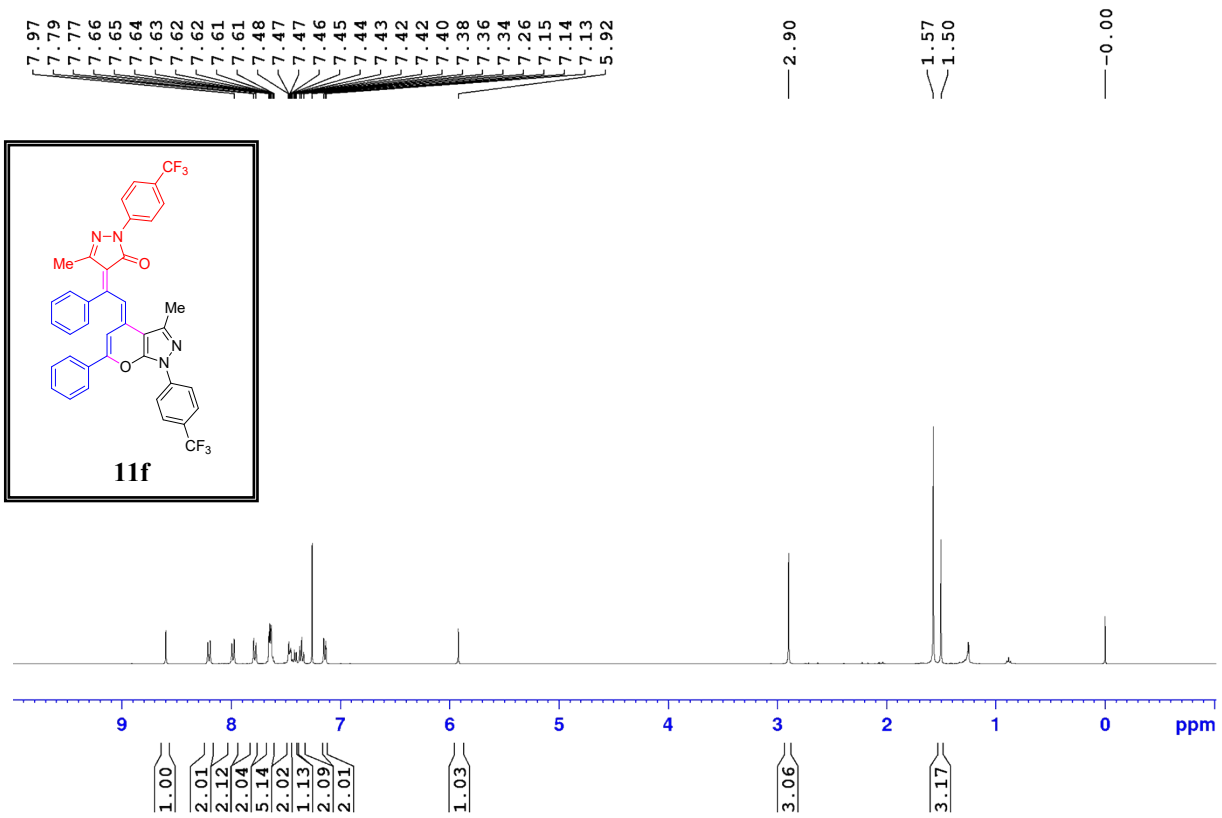
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11e**



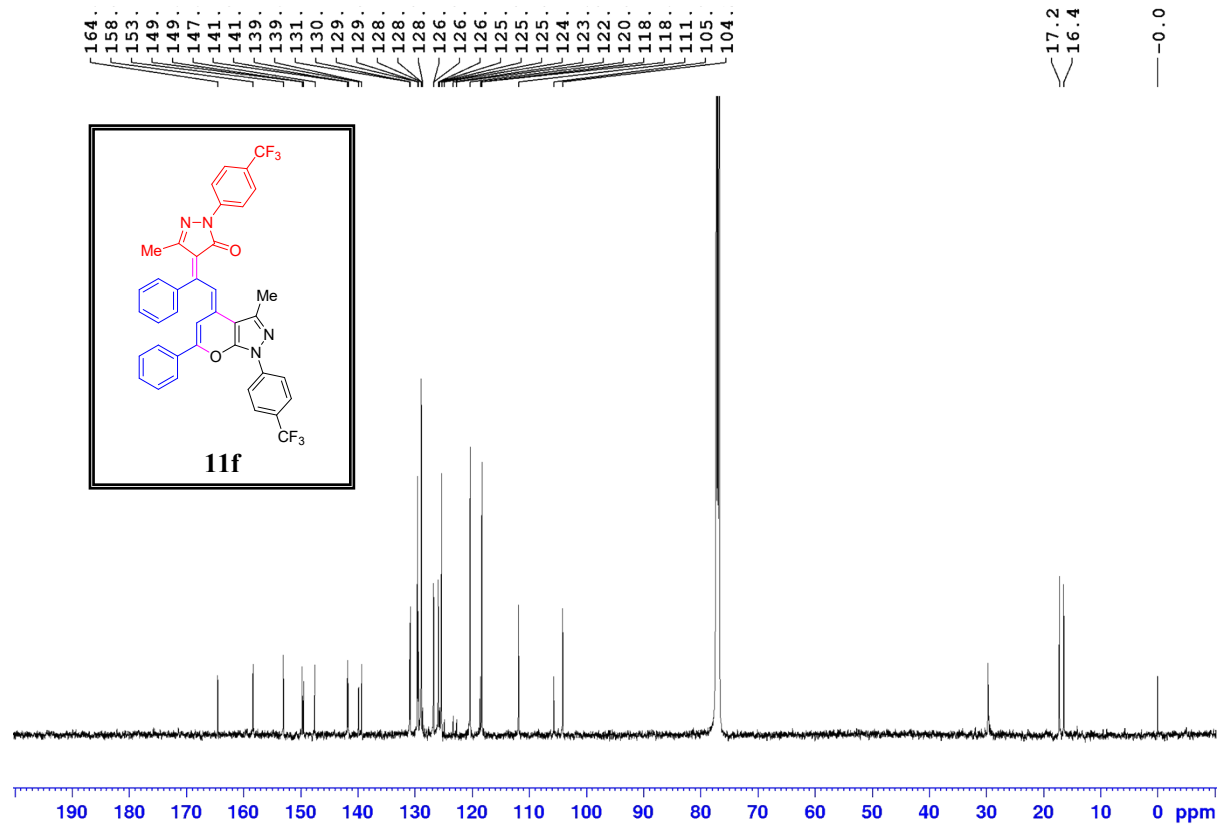
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11e**



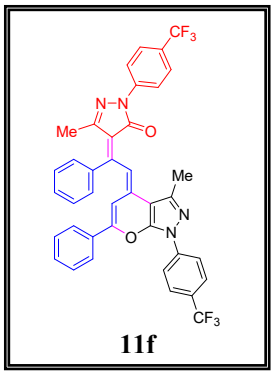
^{19}F NMR ($CDCl_3$, 377 MHz) spectrum of **11e**



^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11f**

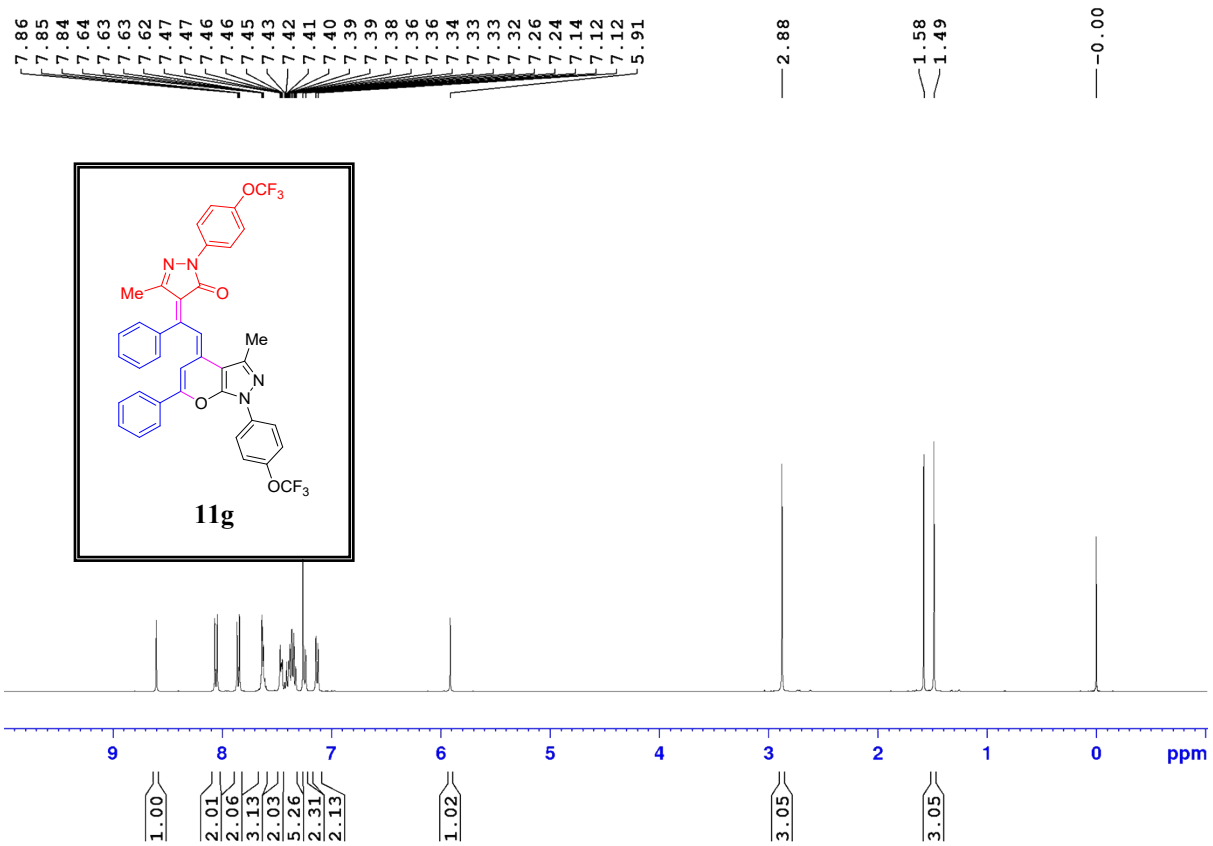


^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11f**

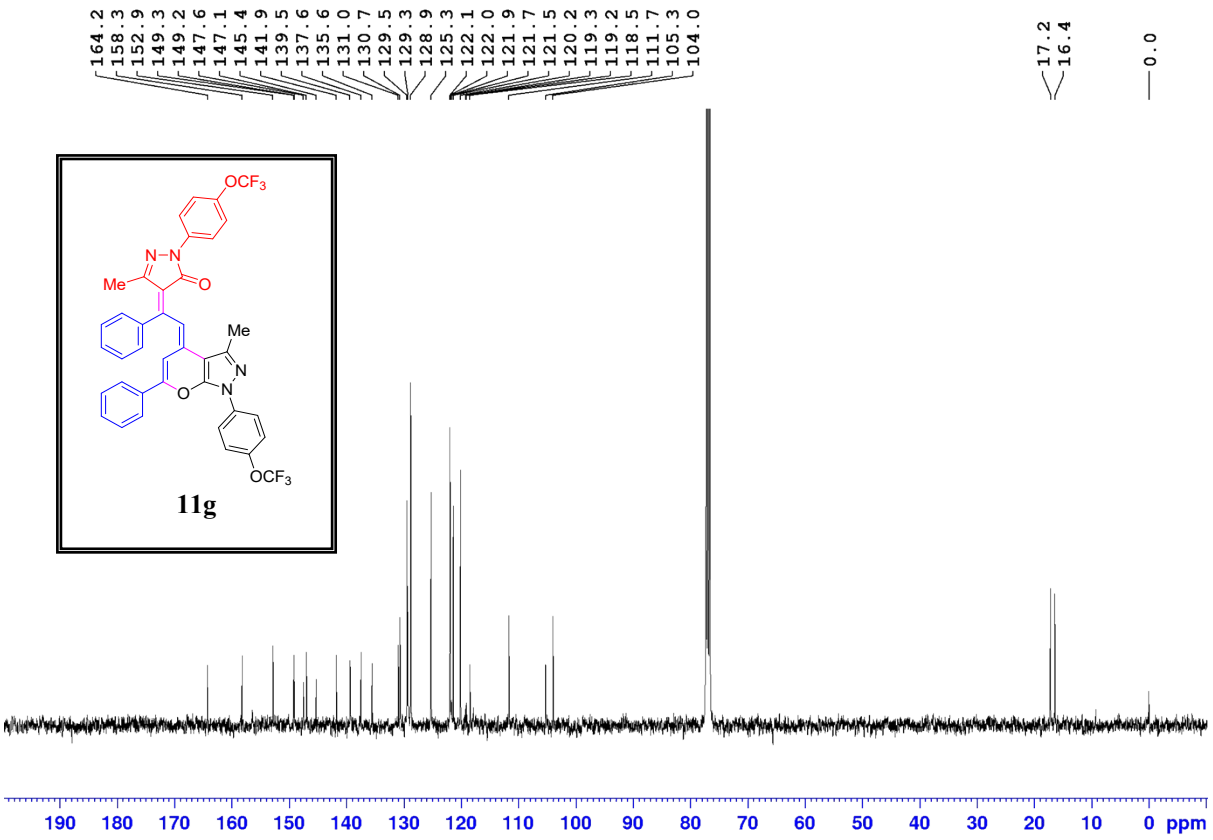


11f

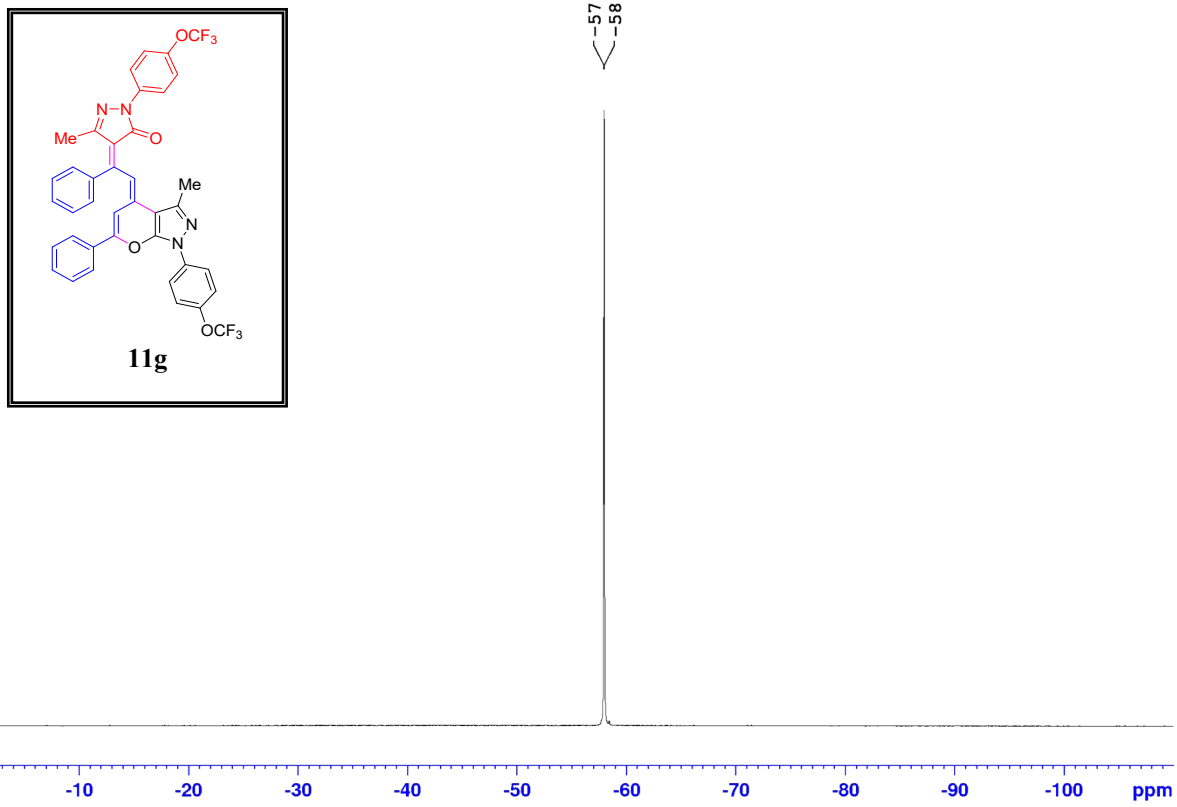
^{19}F NMR ($CDCl_3$, 377 MHz) spectrum of **11f**



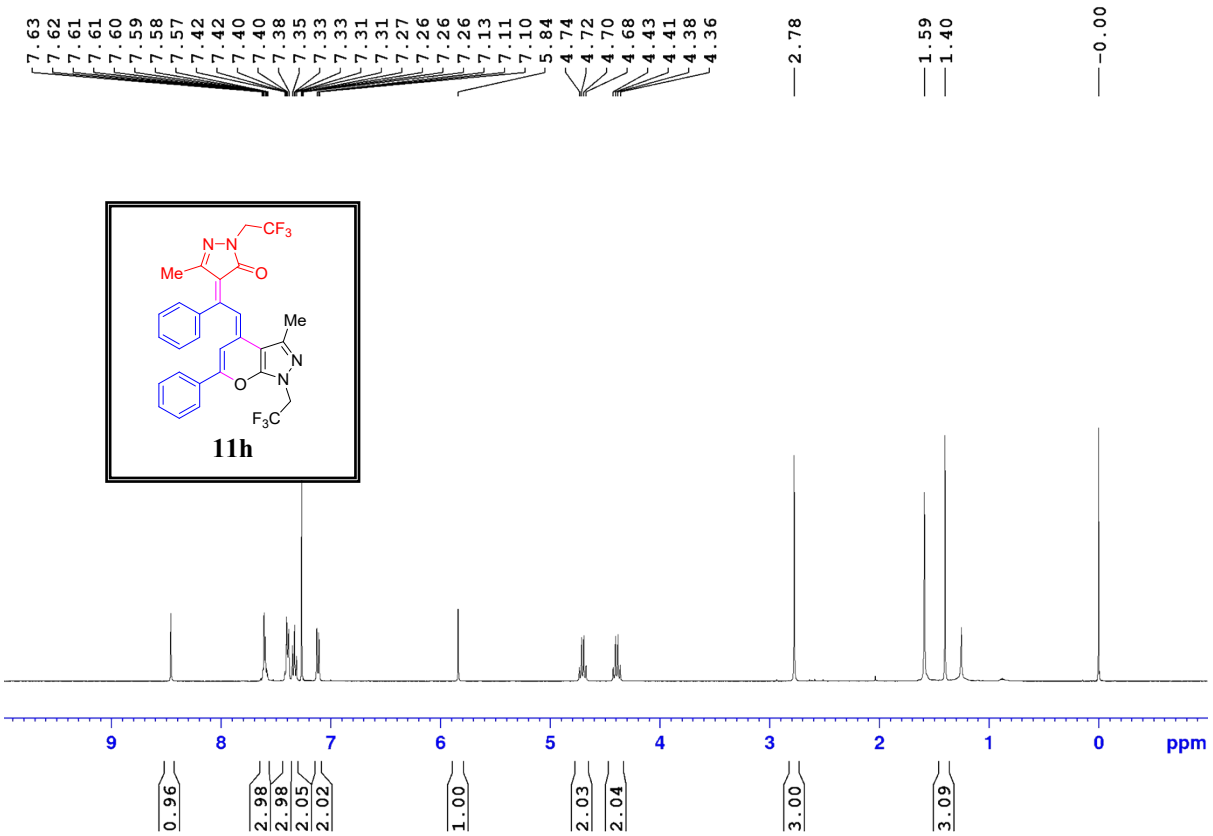
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11g**



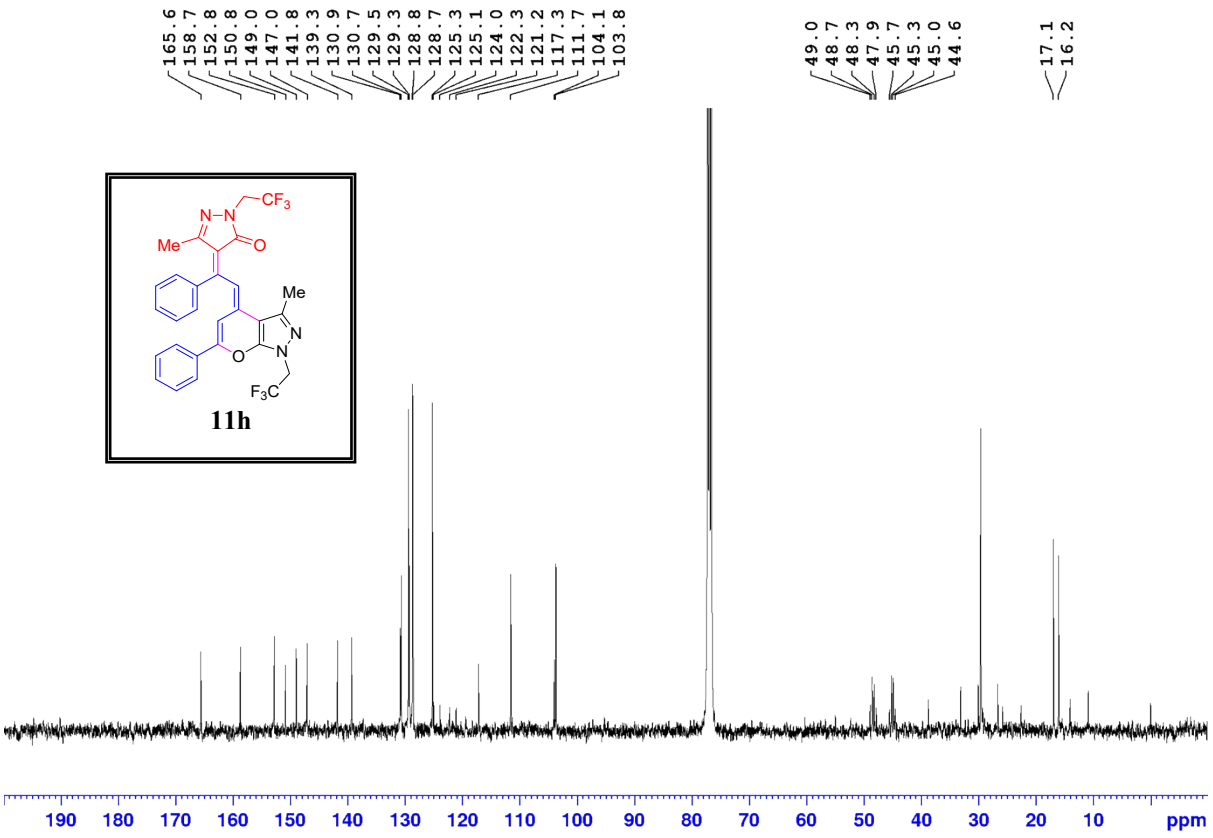
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11g**



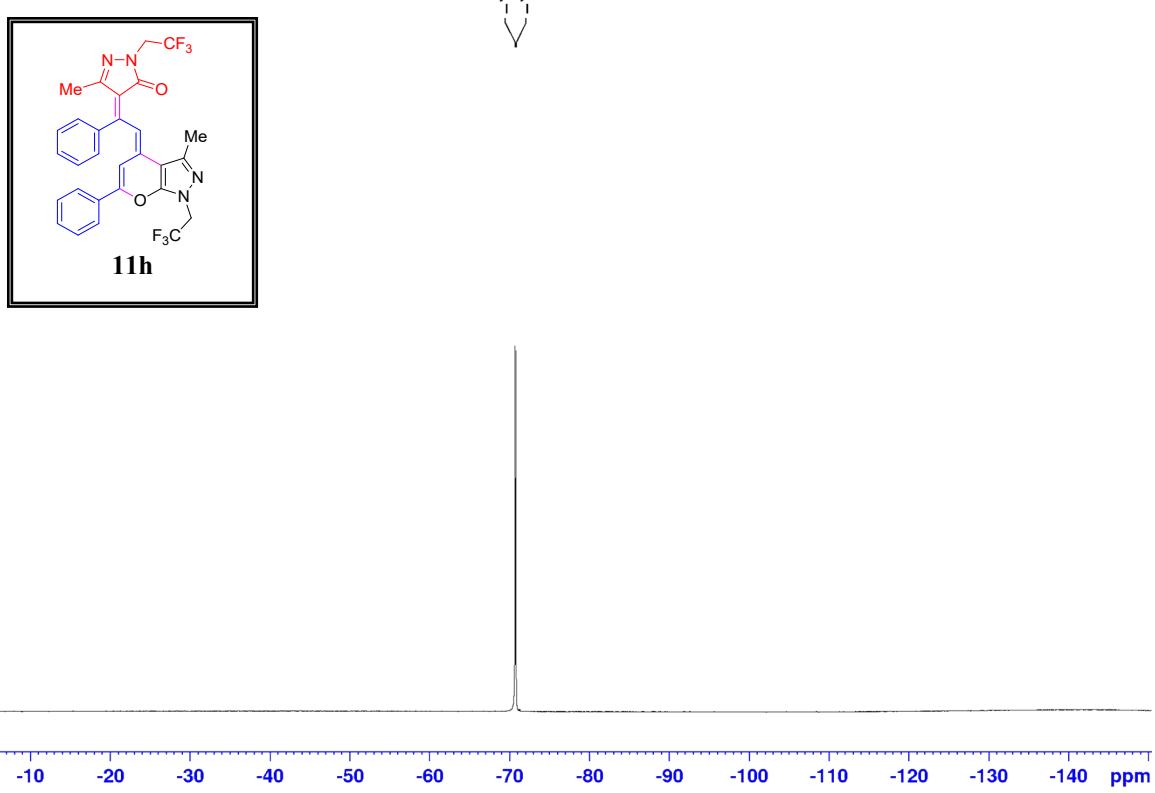
^{19}F NMR ($CDCl_3$, 377 MHz) spectrum of **11g**



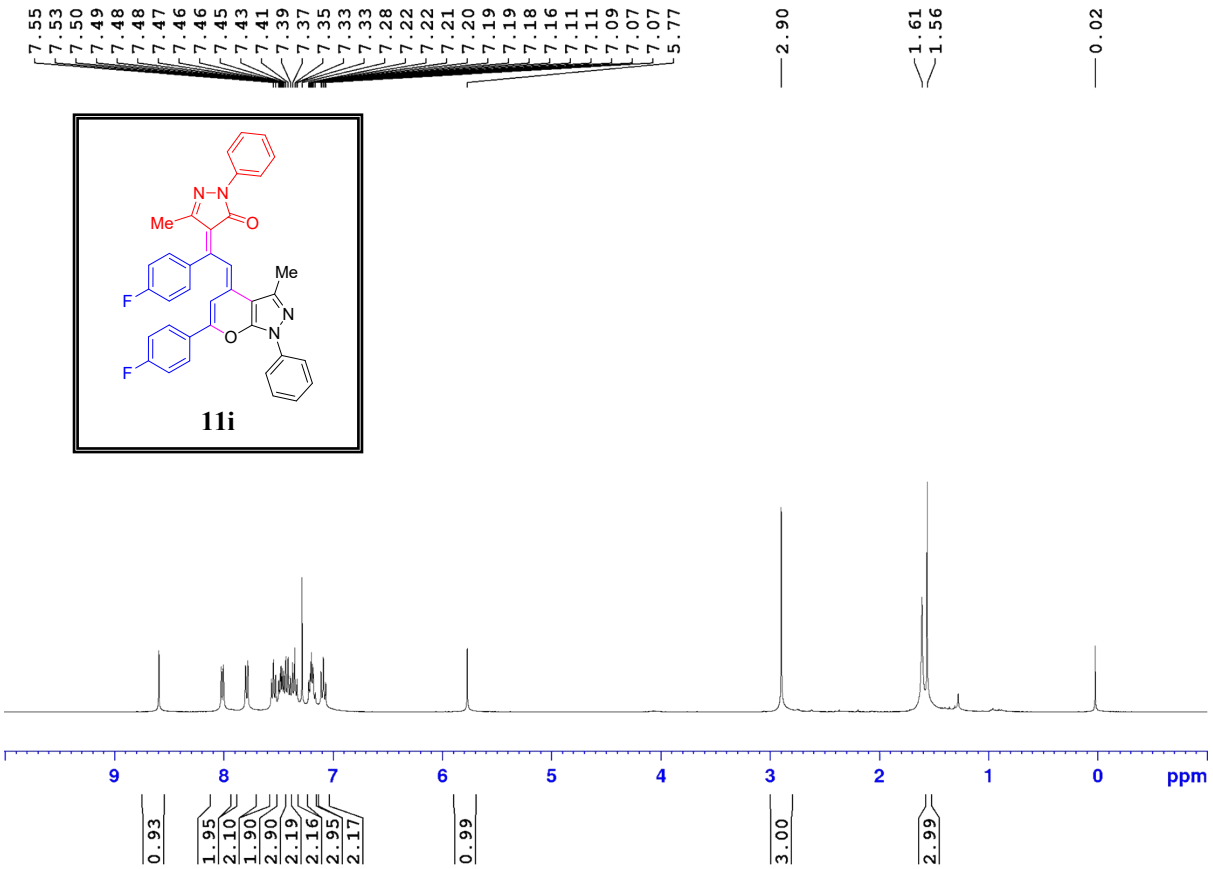
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of **11h**



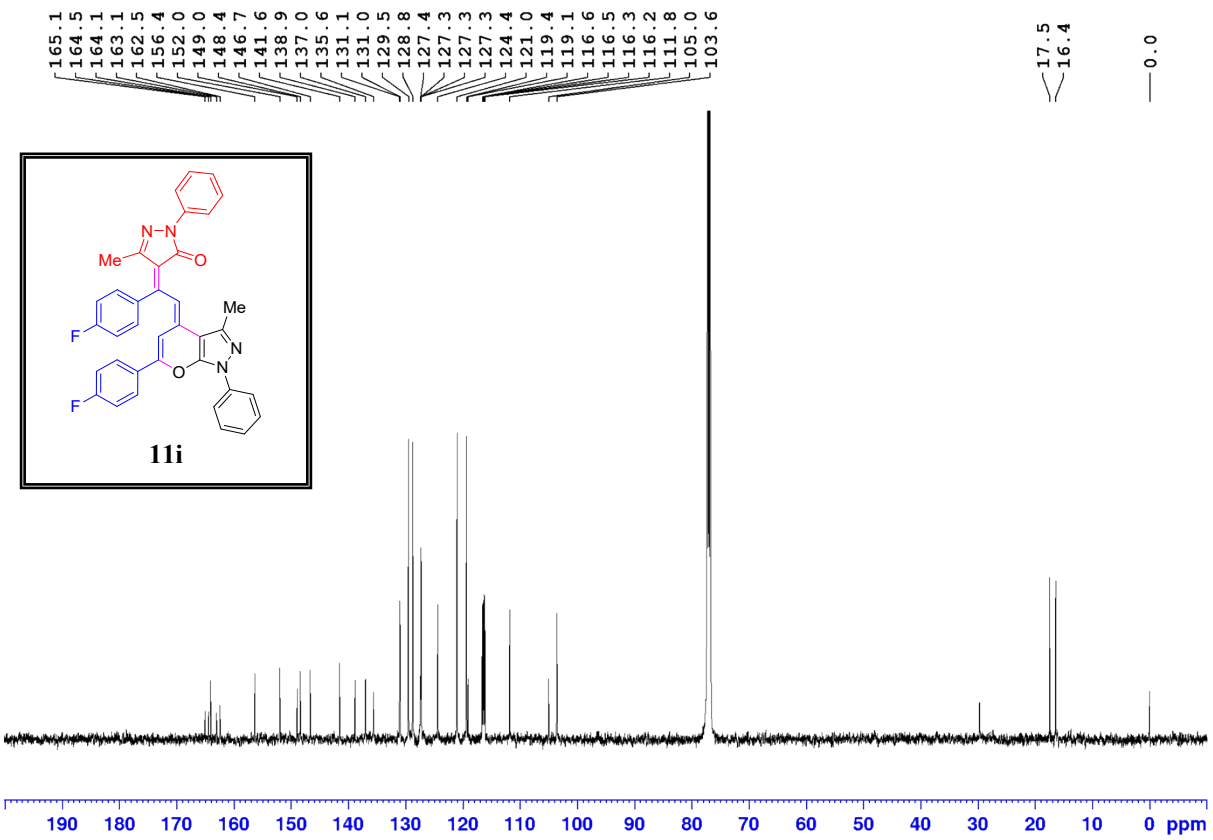
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11h**



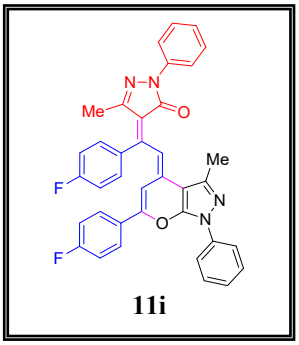
^{19}F NMR ($CDCl_3$, 377 MHz) spectrum of **11h**



^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11i**

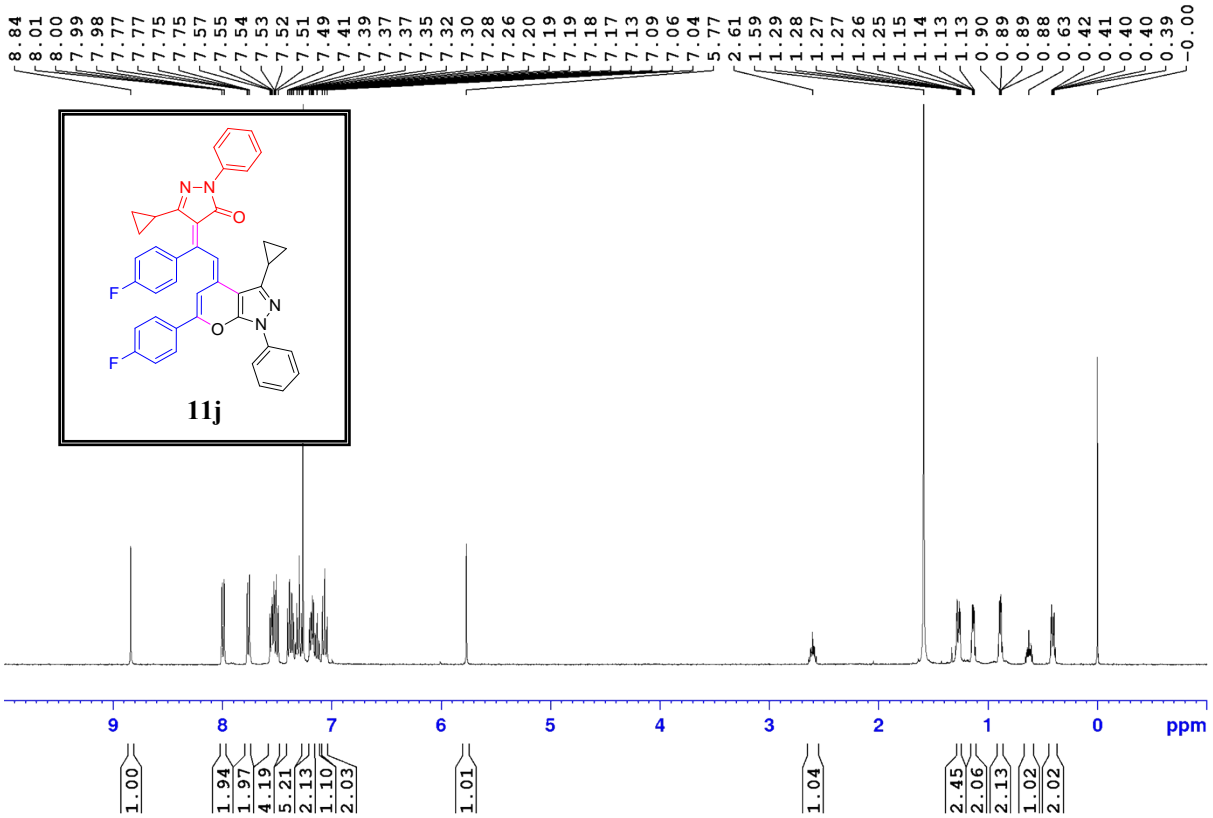


^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11i**

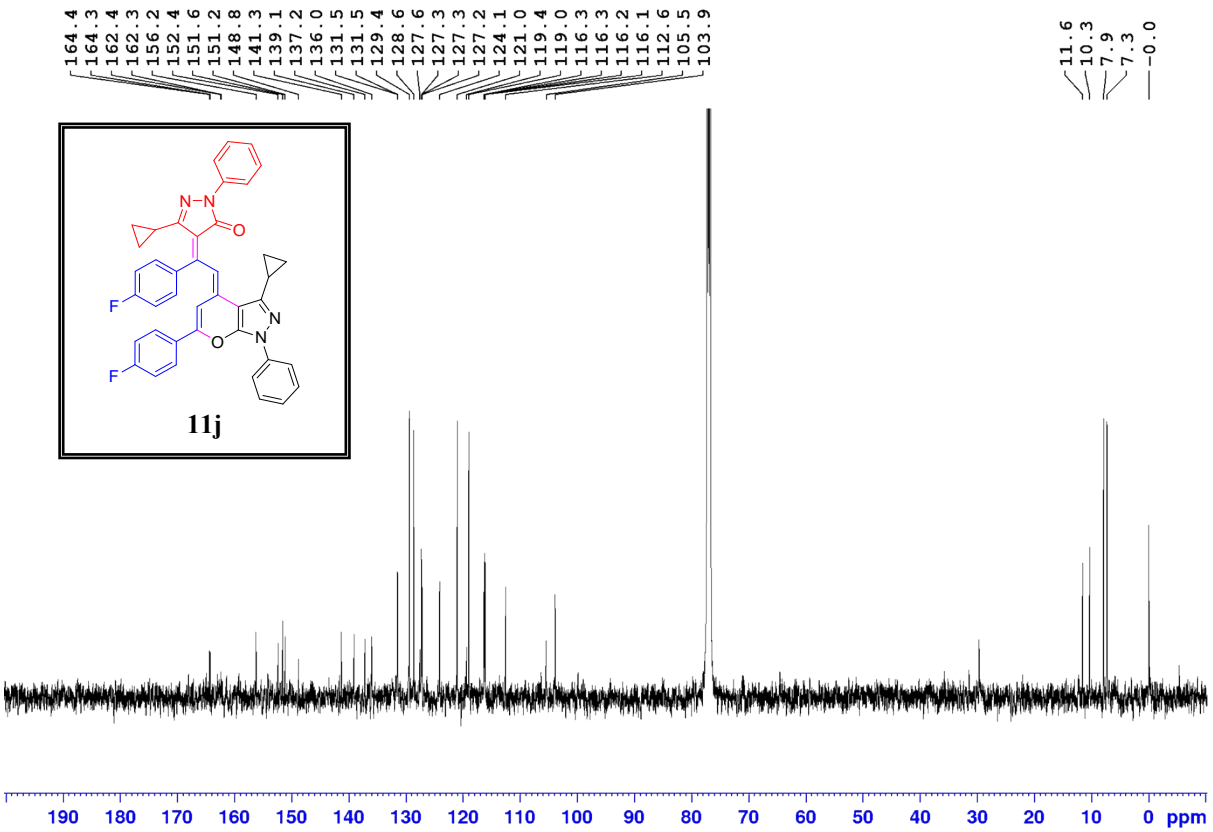


11i

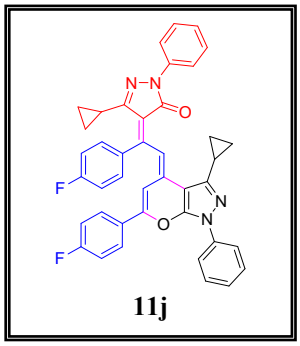
^{19}F NMR ($CDCl_3$, 470 MHz) spectrum of **11i**



^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11j**

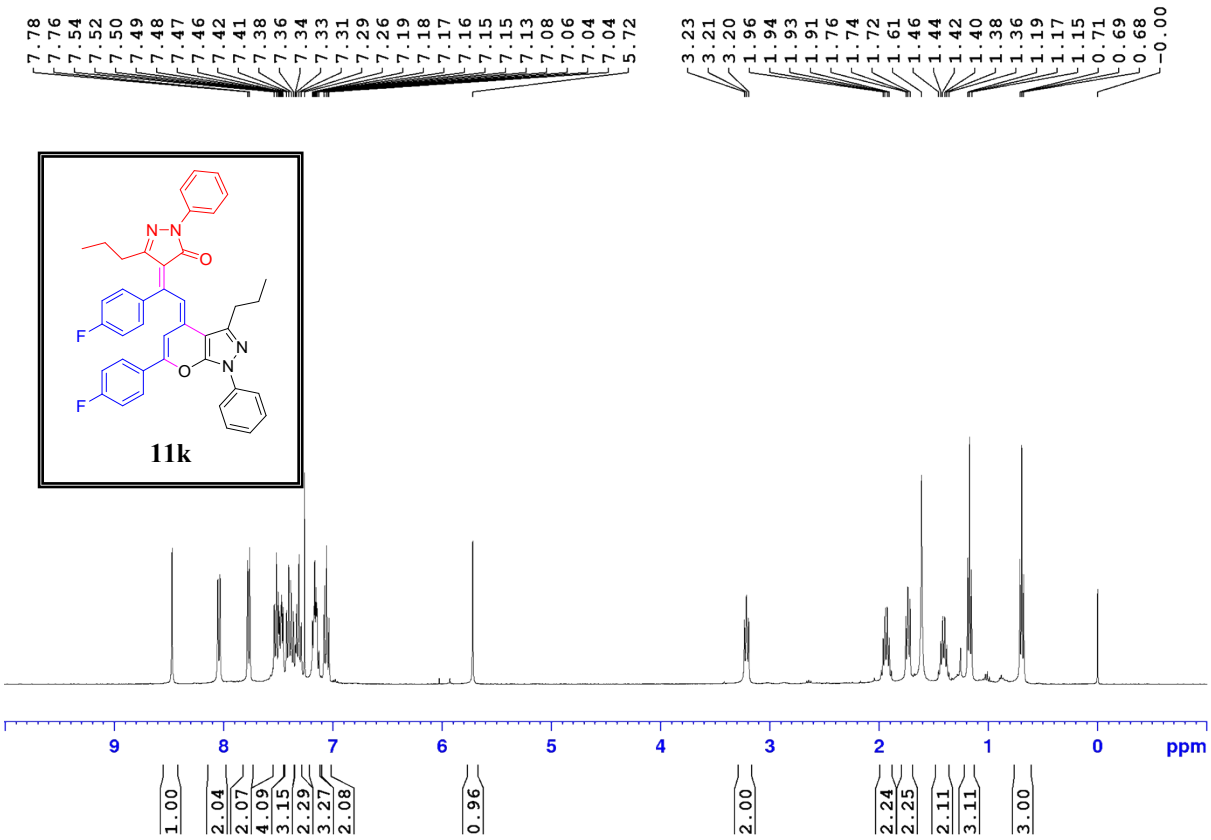


^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11j**

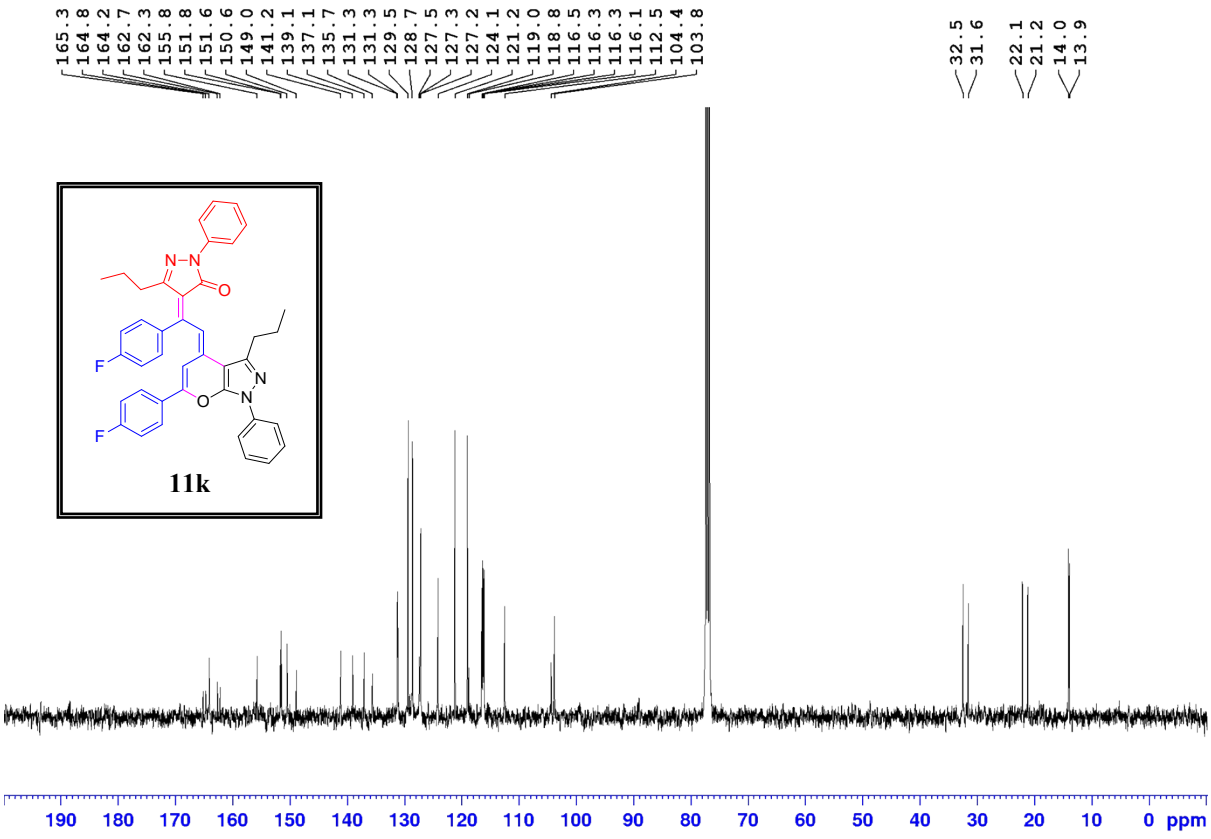


11j

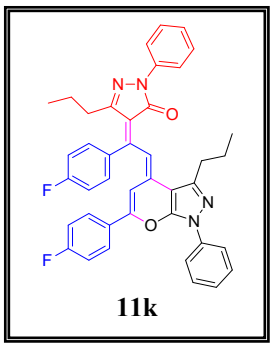
^{19}F NMR ($CDCl_3$, 377 MHz) spectrum of **11j**



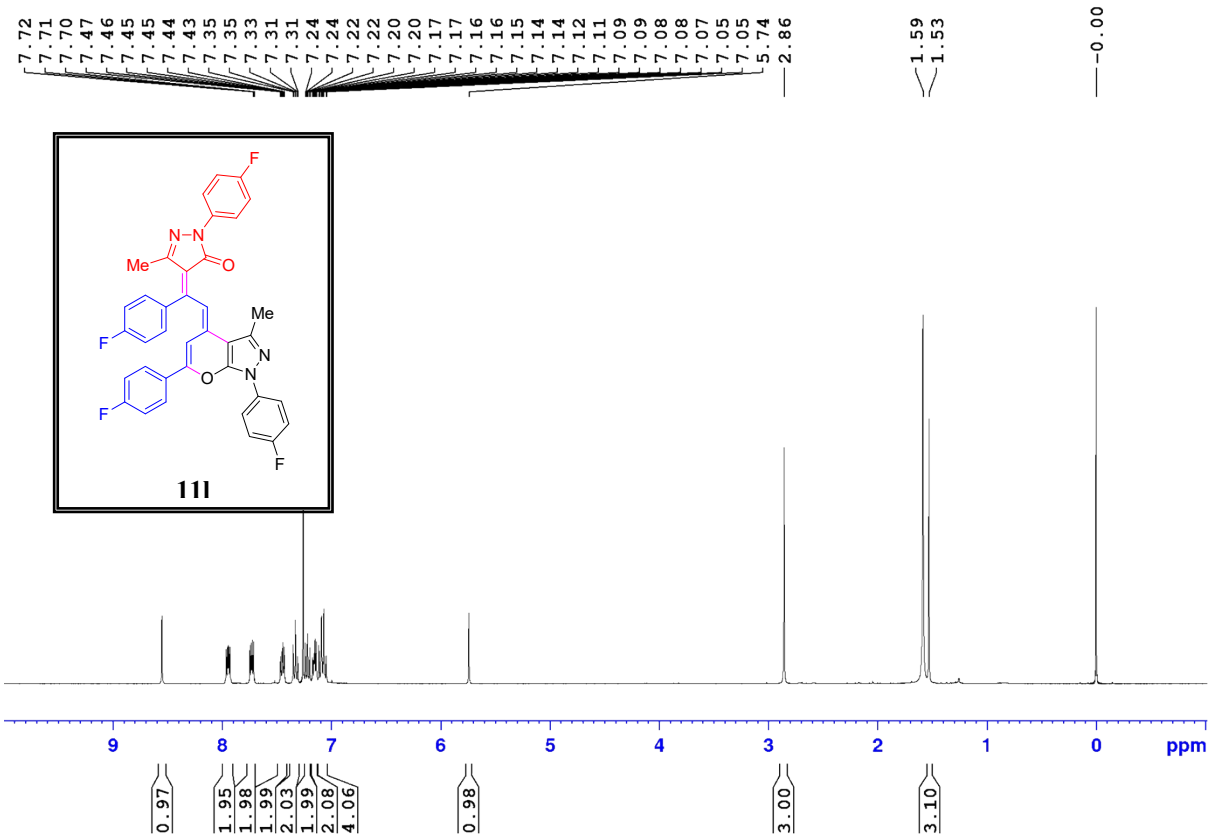
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11k**



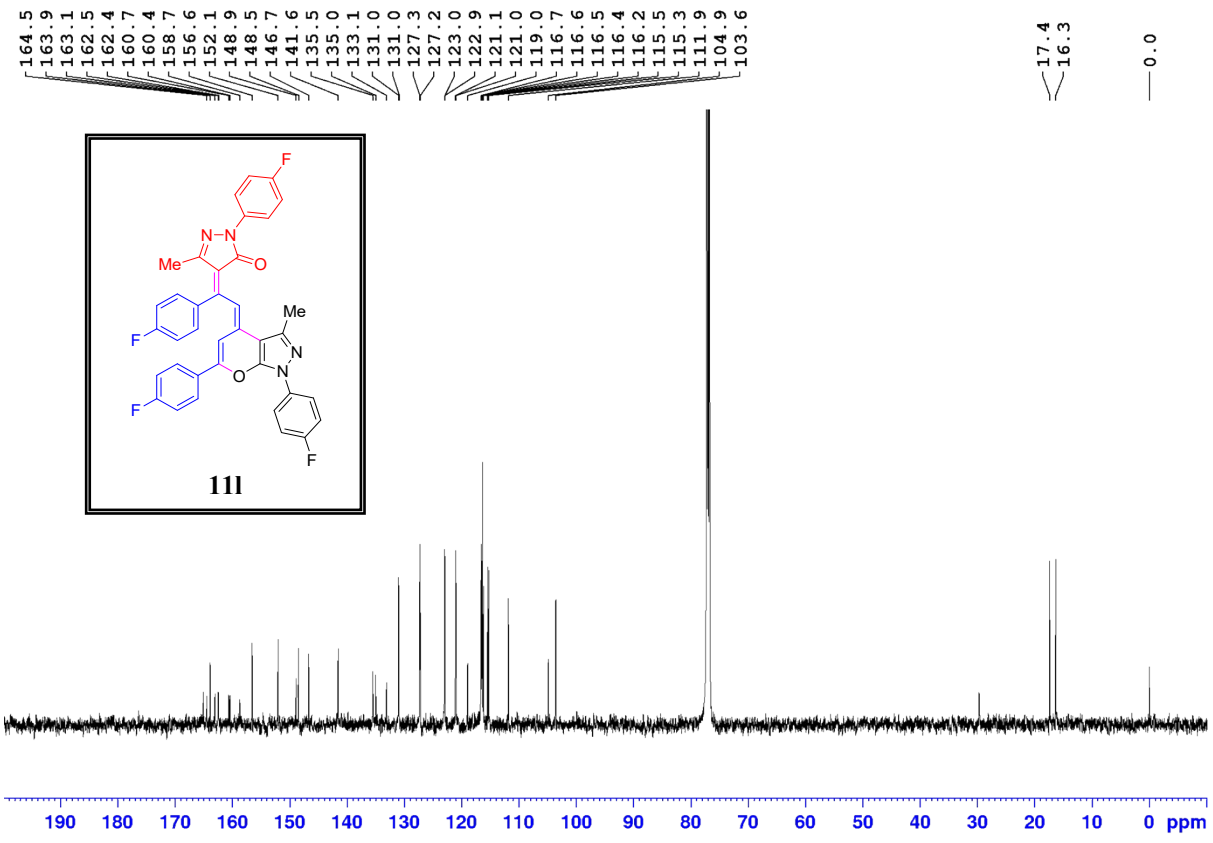
^{13}C{^{1}H} NMR ($CDCl_3$, 101MHz) spectrum of **11k**



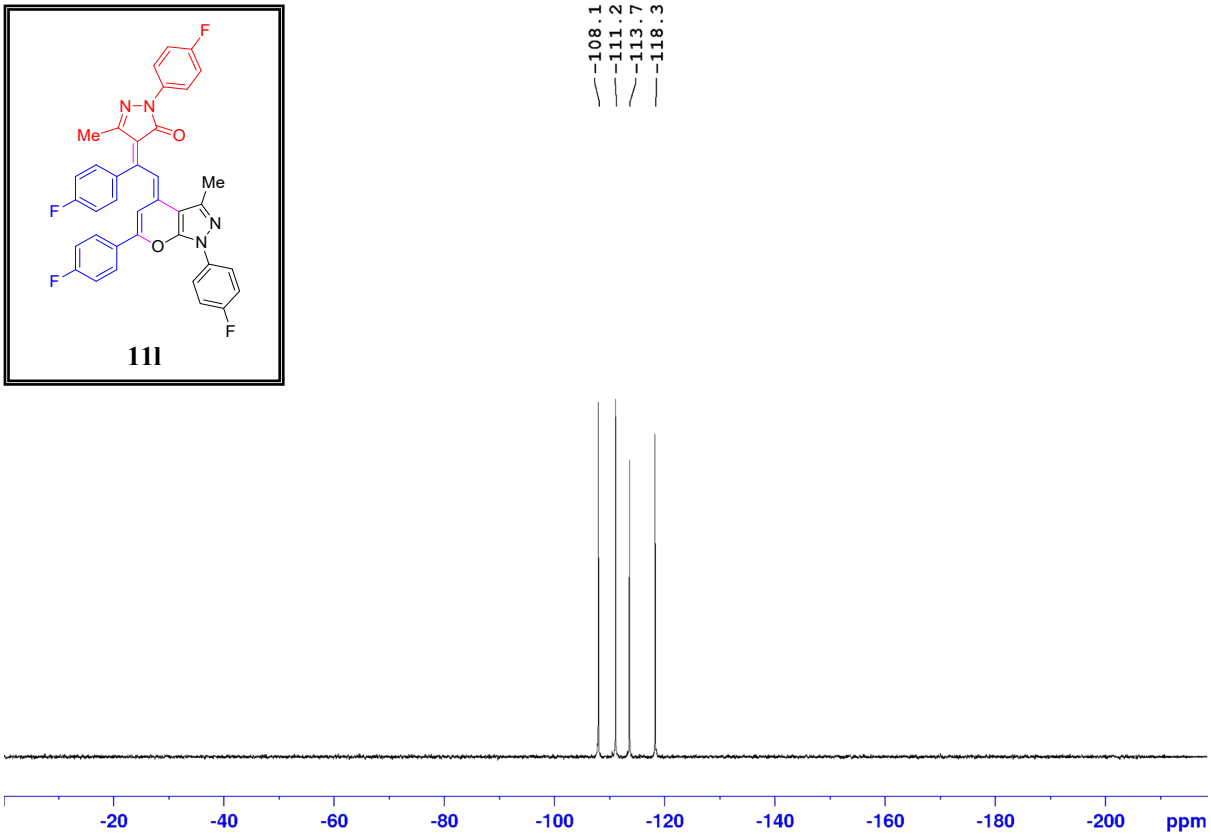
^{19}F NMR ($CDCl_3$, 377 MHz) spectrum of **11k**



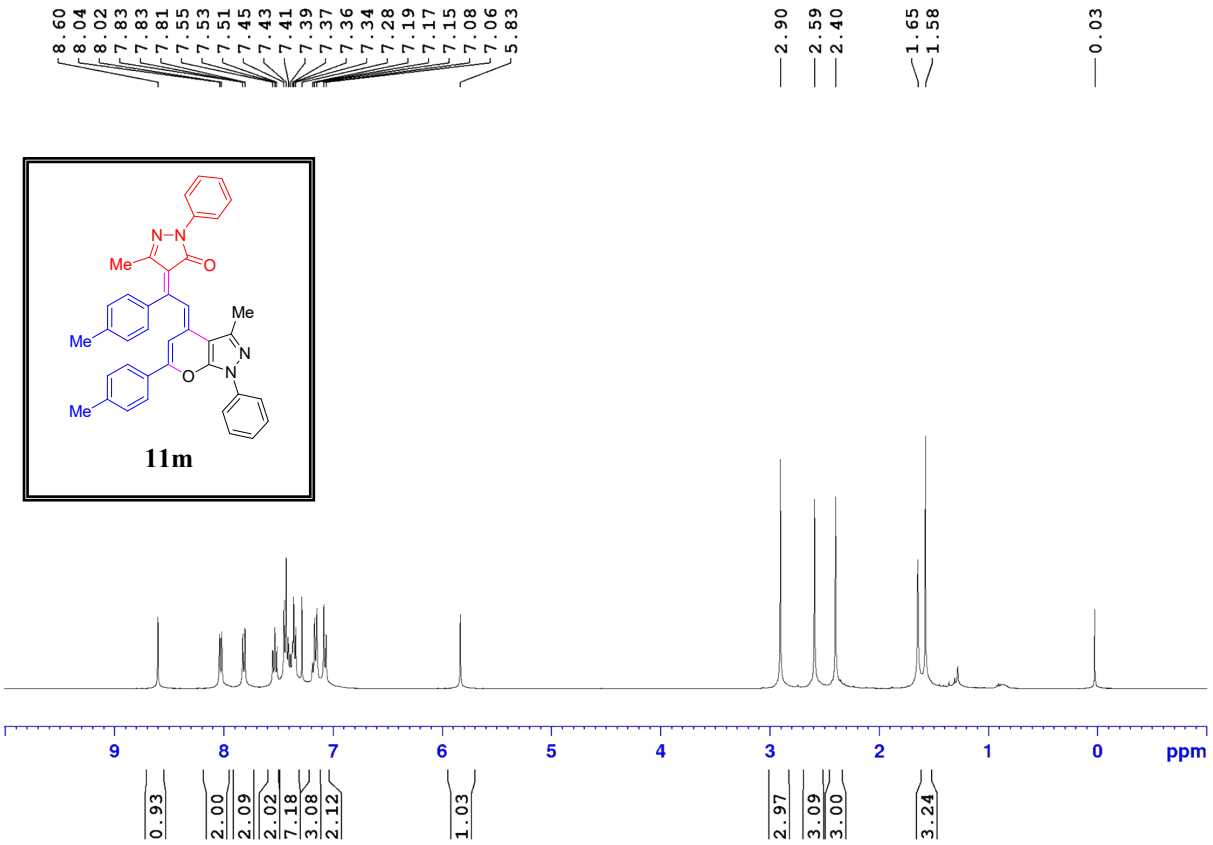
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11l**



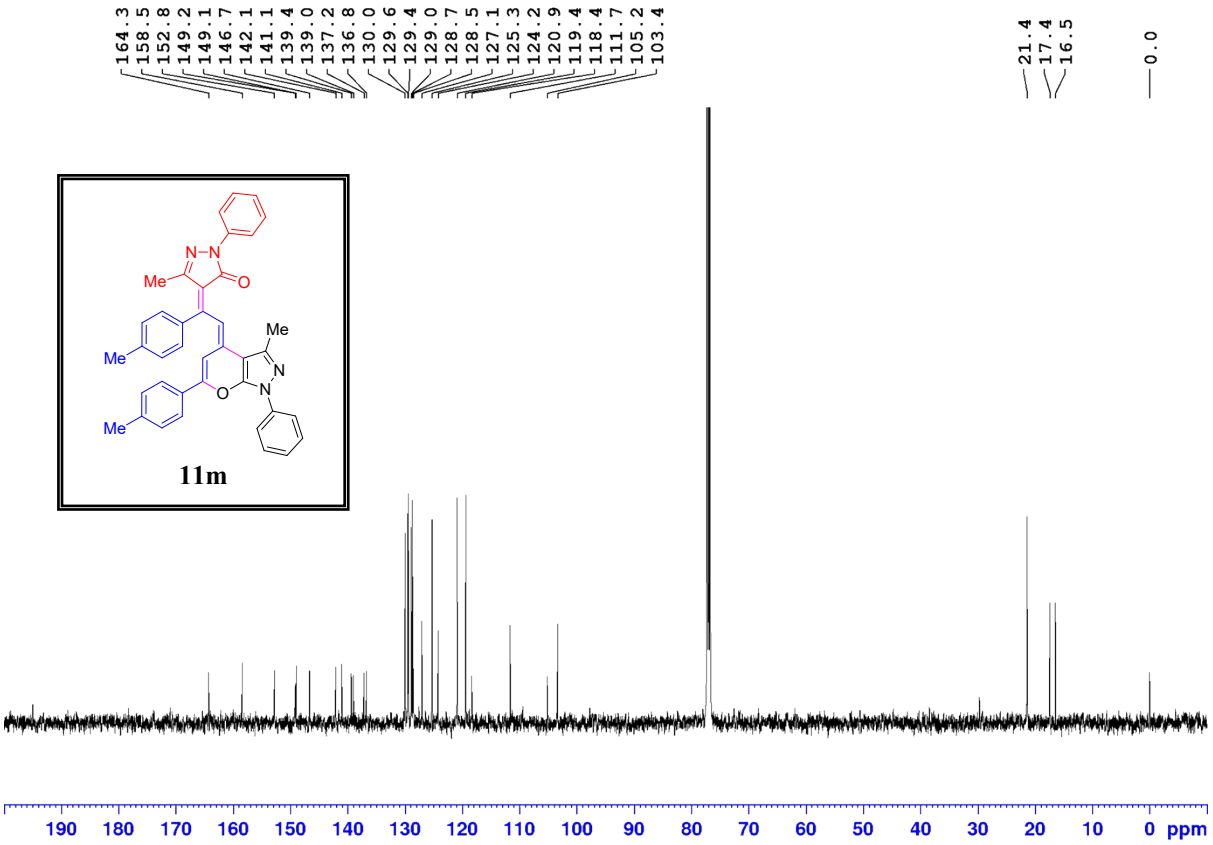
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11l**



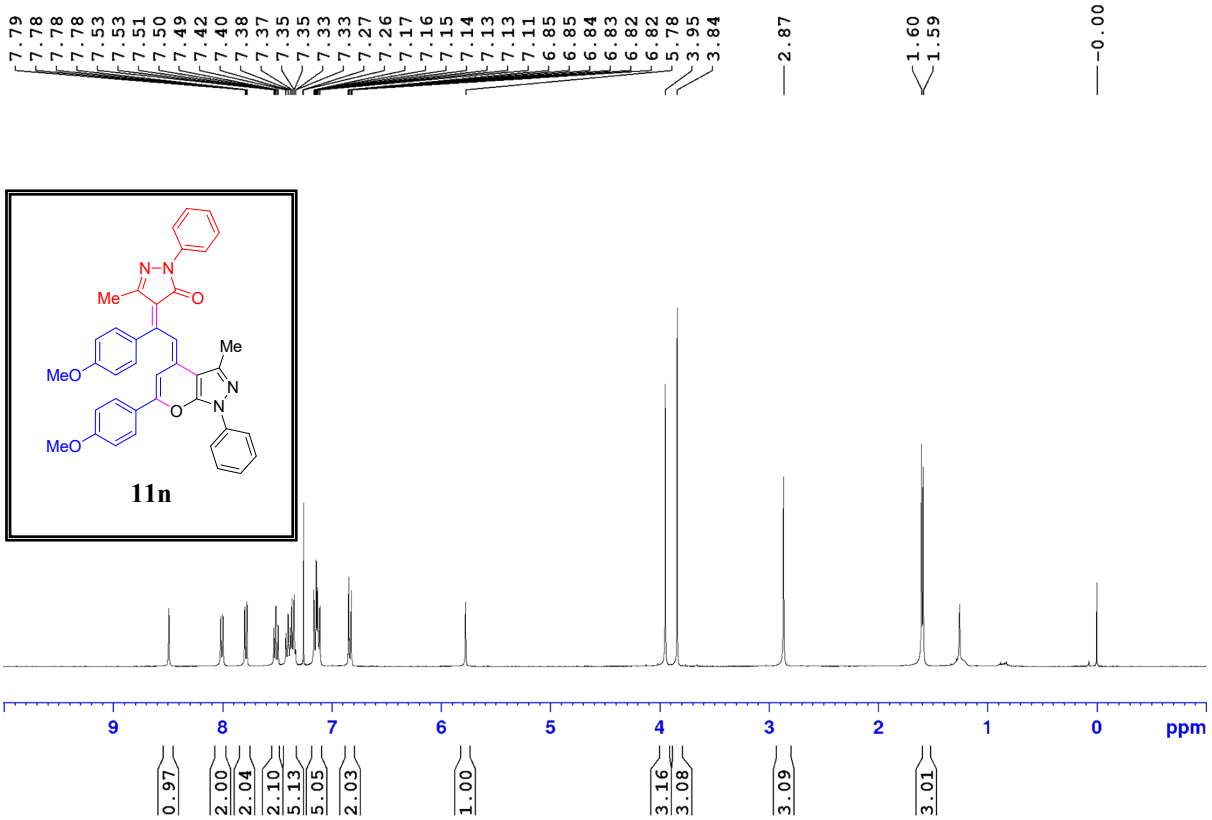
^{19}F NMR ($CDCl_3$, 377 MHz) spectrum of **11l**



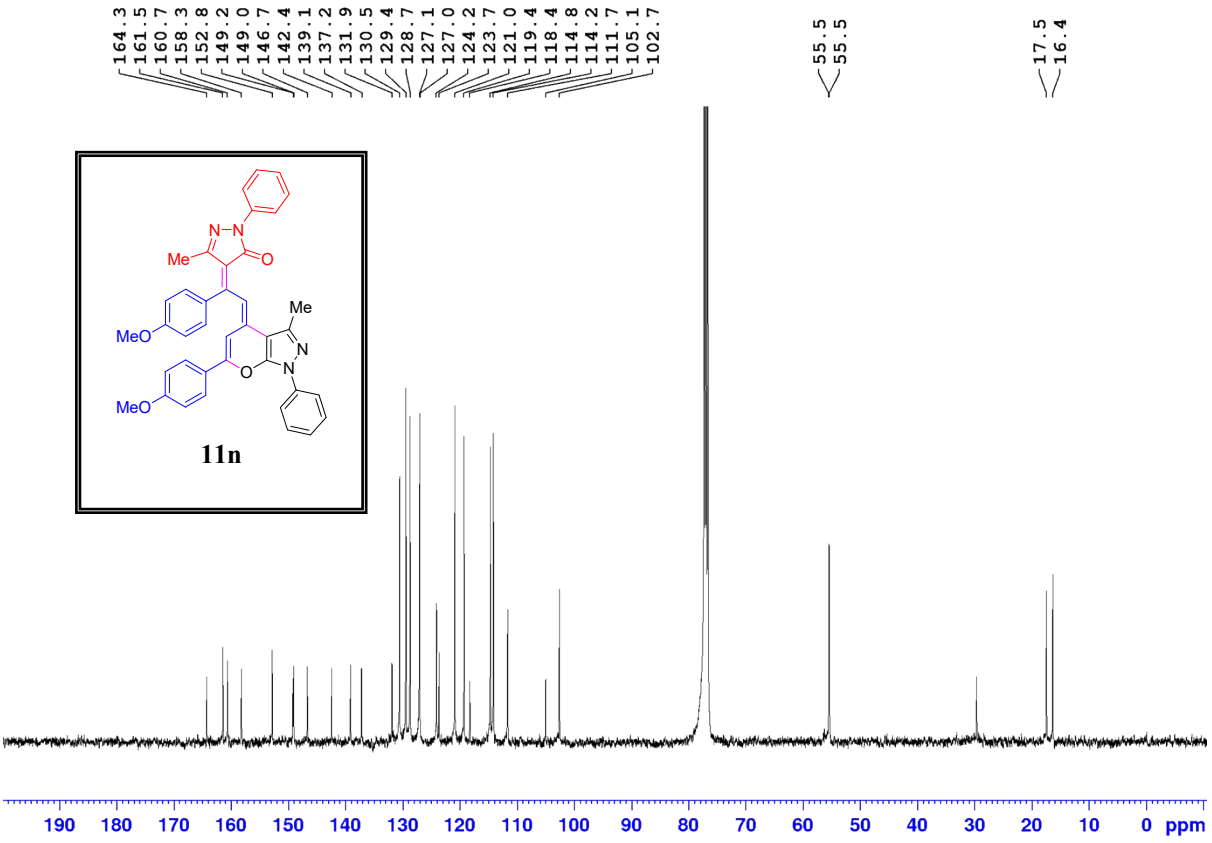
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11m**



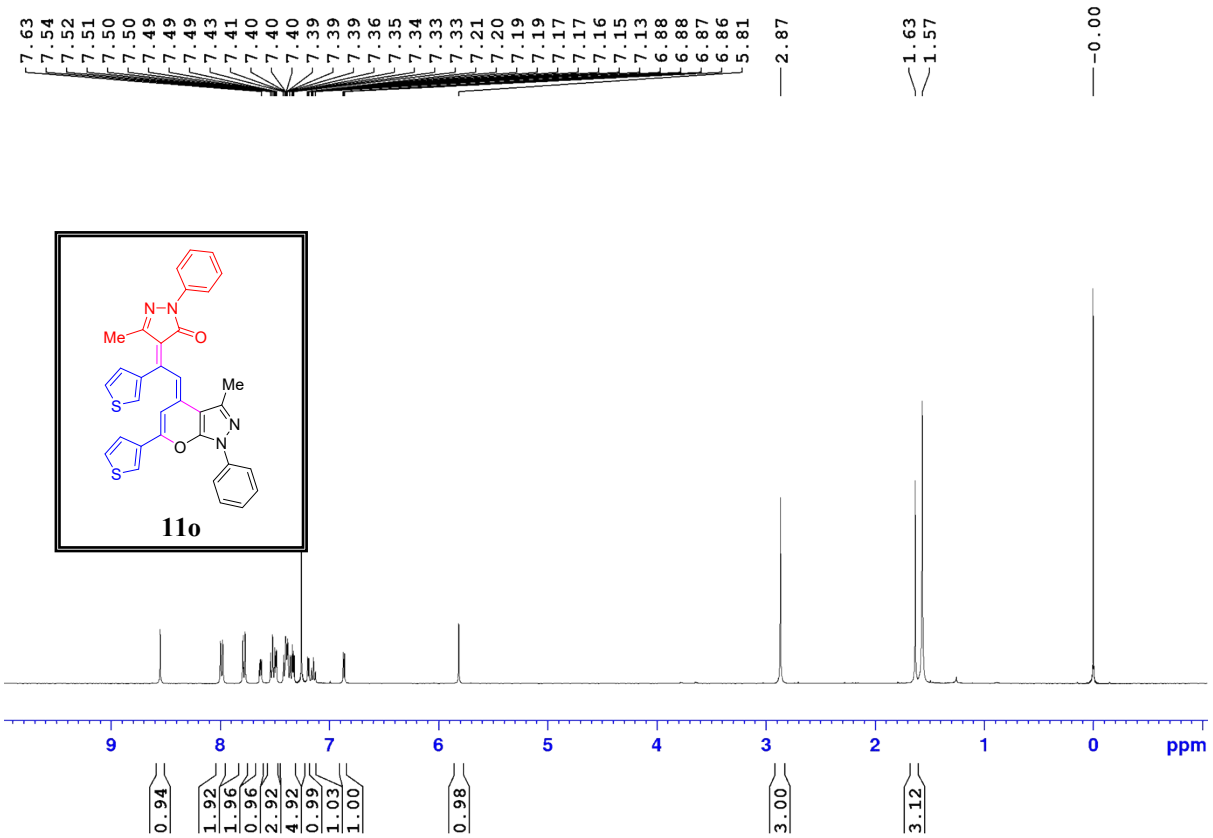
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11m**



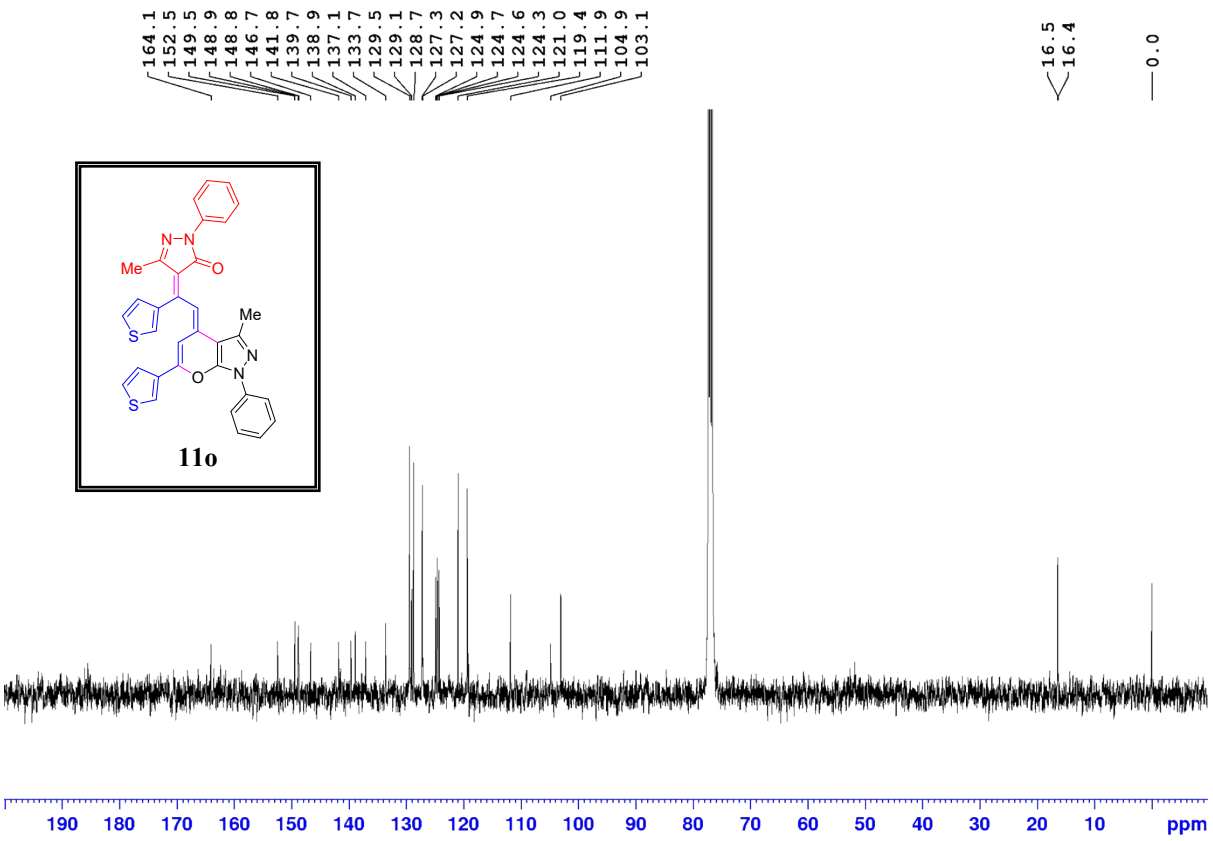
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of **11n**



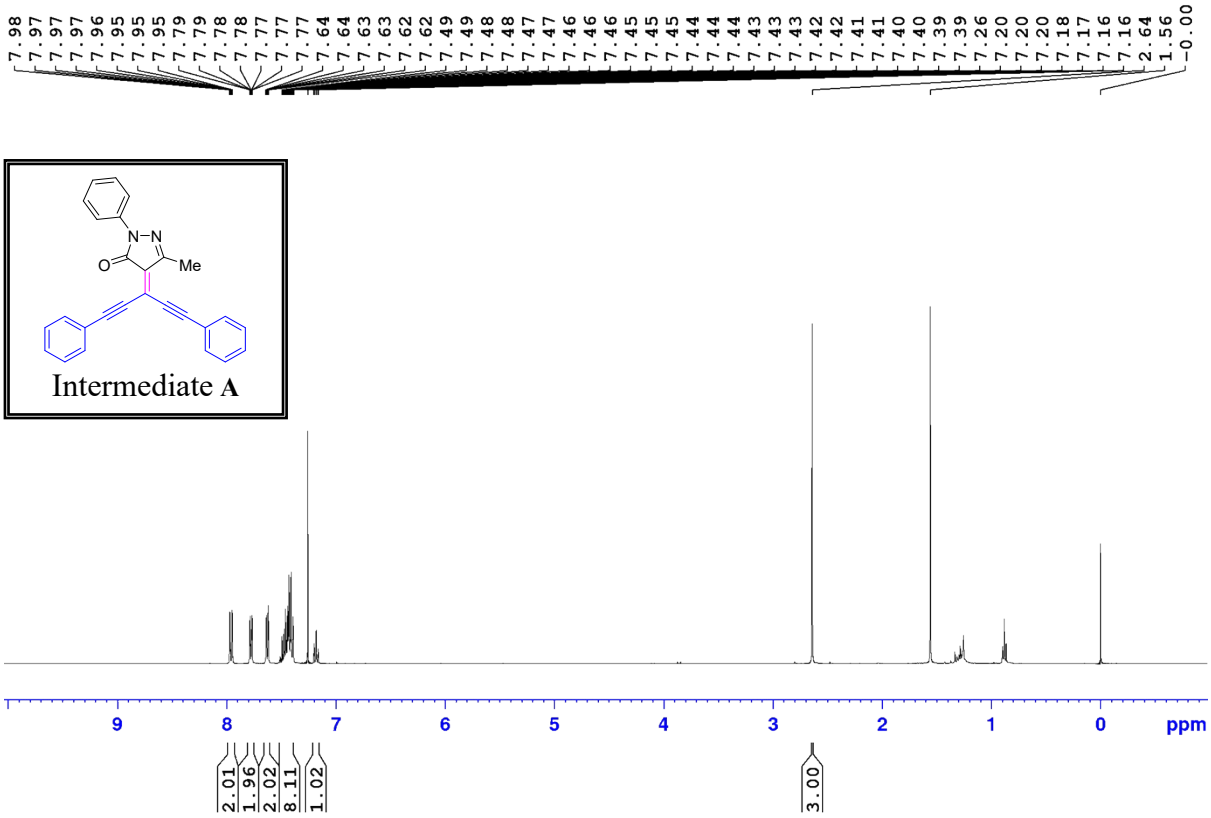
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11n**



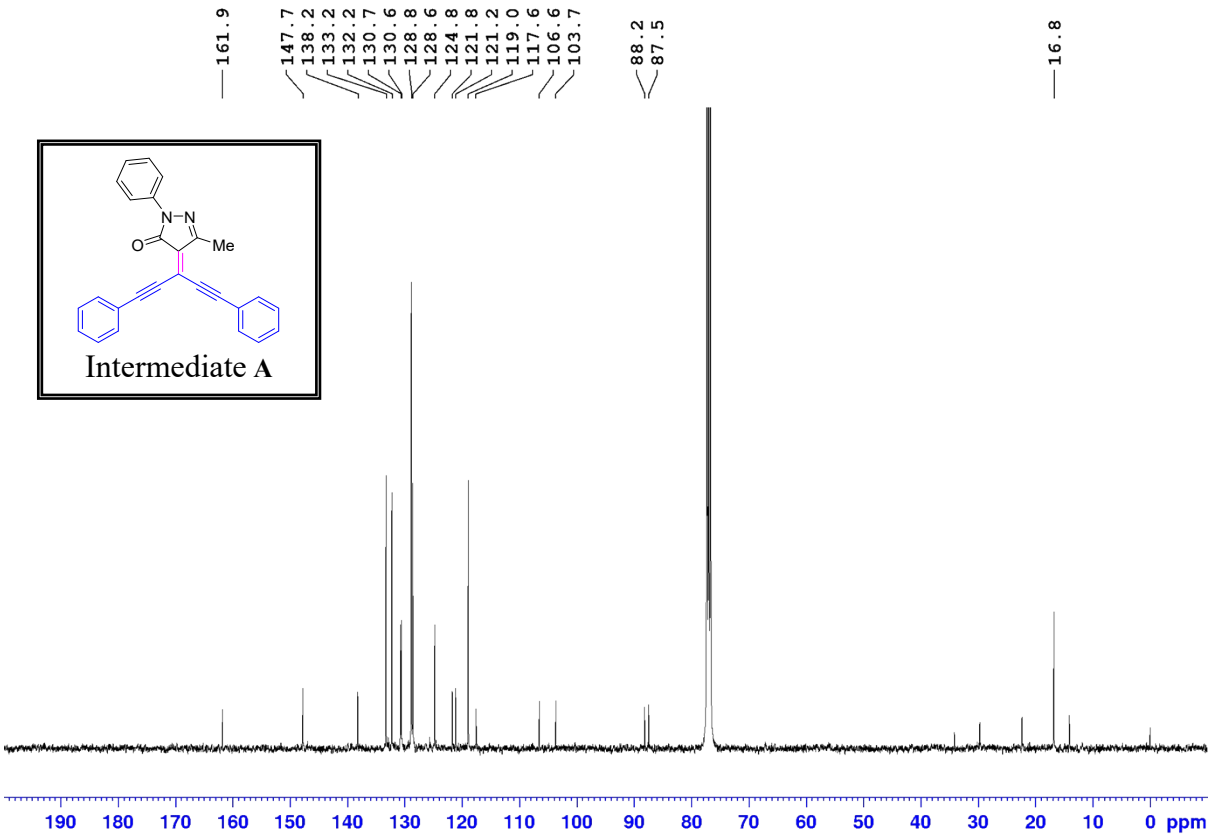
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of **11o**



^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) spectrum of **11o**

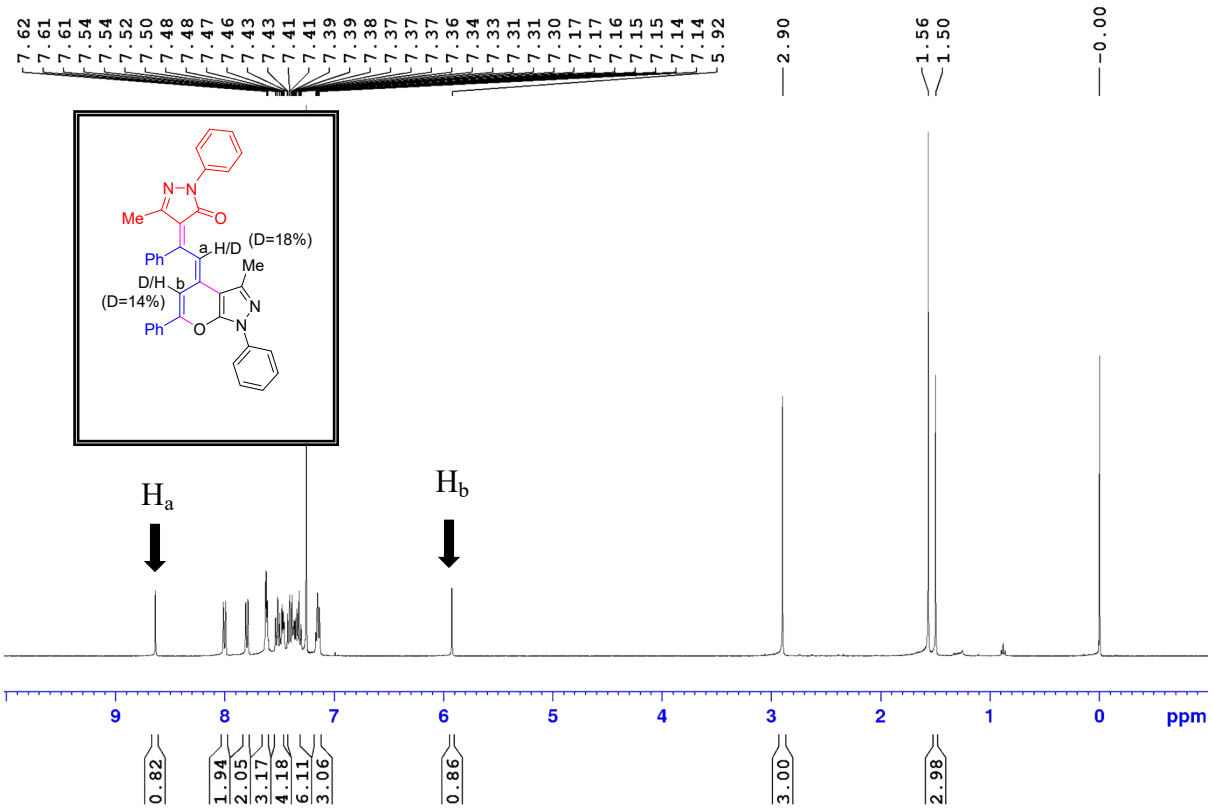


^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of intermediate **A**

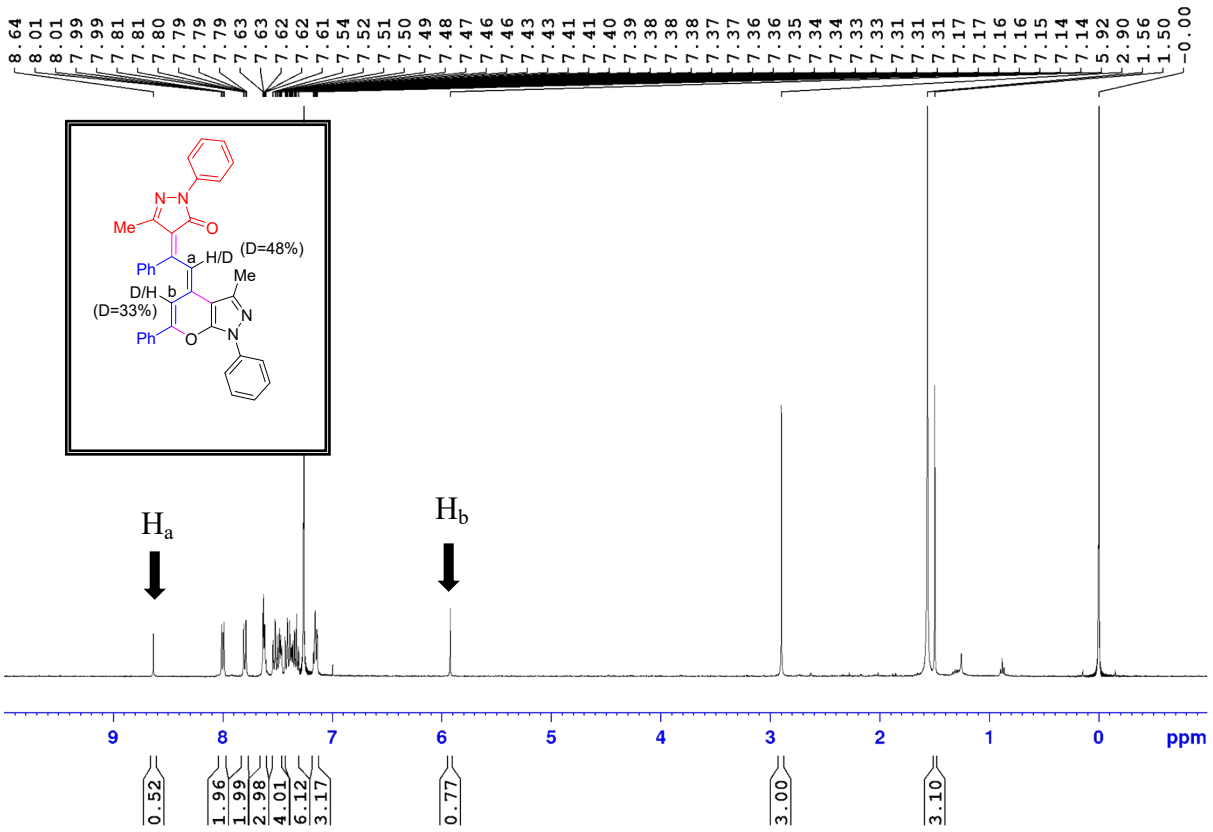


^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) spectrum of intermediate **A**

(Note: Peaks at δ 14.1, 22.4, 34.1 ppm due to n-pentane and 29.7 ppm due to grease)



^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of D-**11a**



^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of D-**11a**