Supporting information

Ruthenium(II) catalyzed oxidative-dehydrogenation and hydroarylation of maleimides with phthalazinones - Insights into additive controlled product selectivity

Alagumalai Ramkumar,[a] Ramdas Sreedharan,[a] Purushothaman Rajeshwaran,[a] and Thirumanavelan Gandhi*[a]

[a]Department of Chemistry, School of Advanced Sciences, Vellore Institute of Technology, Vellore, Tamil Nadu-632014, India.

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1. General experimental methods and materials.

Unless otherwise mentioned all the reactions were carried out in screw capped reaction tubes (10 mL). Anhydrous CH_3CN, DCE, TFE, EtOAc and DCM were purchased from commercial sources and used without further purification. Chemicals were purchased from Sigma-Aldrich, Alfa Aesar and AVRA. Thin layer chromatography was carried out on 250 mm diameter aluminium supported silica gel TLC plates (MERCK TLC Plates) and with narrow tip capillary. The products were purified by column chromatography using 100-200 mesh silica gel. ^{1}H NMR spectra were recorded on Bruker spectrometer (400 MHz) and reported in units ppm (parts per million) relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent. ^{13}C NMR spectra were recorded on Bruker spectrometer (100 MHz) and are reported in ppm relative to deuterated chloroform (77.23 ppm) with tetramethyl silane as an internal standard. Coupling constants (*J*) are reported in Hz; splitting patterns are assigned *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *dd* = doublet of doublet, *td* = triplet of doublet, *br* = broad signal. High-resolution mass spectra (HRMS) were performed on TOF-Q analyser.

1.1 X-ray crystallography of compounds 3h and 4a.

Single crystal X-ray structural data of the compounds **3h** and **4a** were collected on a CMOS based Bruker D8 Venture PHOTON 100 diffractometer equipped with a INCOATEC microfocus source with graphite monochromated Mo Kα radiation (λ = 0.71073 Å) operating at 50 kV and 30mA. The SAINT[1] program was used for the integration of diffraction profiles and absorption correction was applied with the SADABS[2] program. Both the structures were initially solved by SIR 92[3] and refined by the full matrix least squares method using SHELXL 2013[4] WinGX system, Ver2013.3.[5] The non-hydrogen atoms in all the structures were located using the difference Fourier map and refined anisotropically. The hydrogen atoms were fixed by HFIX and placed in ideal positions and included in the refinement process using a riding model with isotropic thermal parameters. All the crystallographic and structure refinement data of the compounds are summarized in section 5.

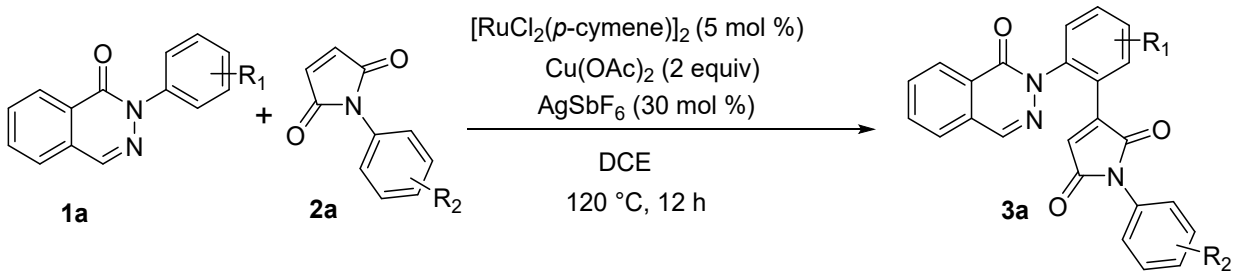
2. General procedure for synthesis of phthalazinones and 2-phenylisoquinolin-1(2H)-one.

Phthalazinones were synthesized using reported procedure.[6] 2-phenylisoquinolin-1(2H)-one was synthesized using reported procedure.[7]

3. General Synthetic procedure.

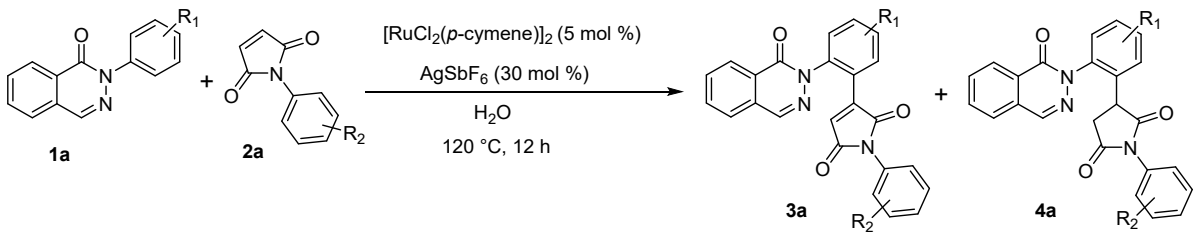
3.1 General procedure for Heck type product (Condition A).

In an oven-dried vial equipped with stir bar was charged with corresponding phthalazinone **1a** (0.45 mmol), corresponding maleimide **2a** (0.90 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), $AgSbF_6$ (30 mol %) and copper(II) acetate (2 equiv) in DCE and it was placed in a preheated oil bath at 120 °C and stirred for 12 h. After the mentioned time the reaction mixture was cooled to the ambient temperature and it was diluted with DCM and concentrated under reduced pressure. The crude was then purified by column chromatography on silica gel 100-200 mesh using hexane/ethyl acetate as the eluent.



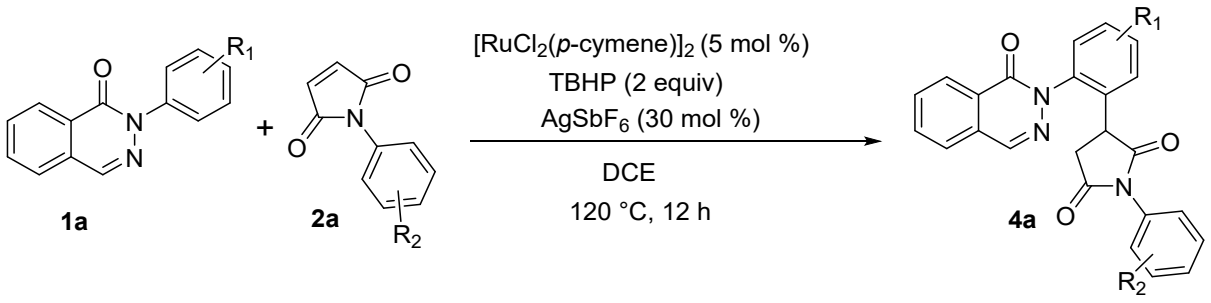
3.2 General procedure for alkylated product in water (Condition B).

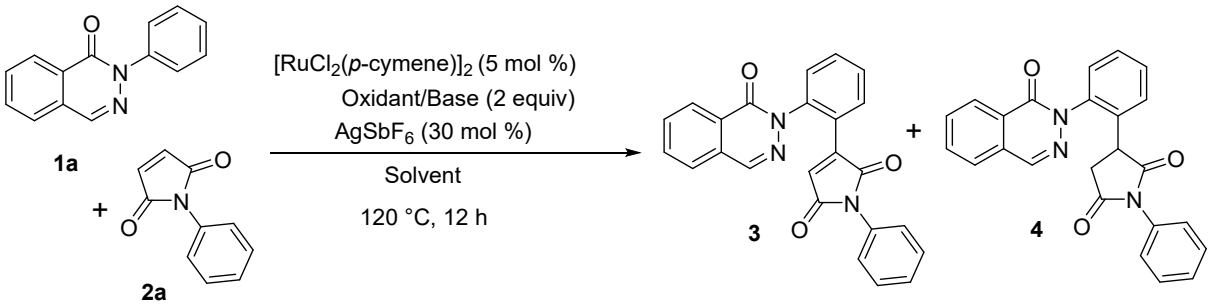
In an oven-dried vial equipped with stir bar was charged with corresponding phthalazinone **1a** (0.45 mmol), corresponding maleimide **2a** (0.90 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %) and $AgSbF_6$ (30 mol %) in H_2O and it was placed in a preheated oil bath at 120 °C and stirred for 12 h. After the mentioned time the reaction mixture was cooled to the ambient temperature and it was extracted with DCM and concentrated under reduced pressure. The crude was then purified by column chromatography on silica gel 100-200 mesh using hexane/ethyl acetate as the eluent.



3.3 General procedure for exclusive alkylated product (Condition C).

In an oven-dried vial equipped with stir bar was charged with corresponding phthalazinone **1a** (0.45 mmol), corresponding maleimide **2a** (0.90 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %) and $AgSbF_6$ (30 mol %) and TBHP (2 equiv) in DCE and it was placed in a preheated oil bath at 120 °C and stirred for 12 h. After the mentioned time the reaction mixture was cooled to the ambient temperature and it was diluted with DCM and concentrated under reduced pressure. The crude was then purified by column chromatography on silica gel 100-200 mesh using hexane/ethyl acetate as the eluent.





4. Optimization table

No	Catalyst	Oxidant/Base	Additive	Solvent	Yield %[b]	
					3	4
1	$[RuCl_2(p\text{-cymene})]_2$	KOAc	$AgSbF_6$	DCE	30	34
2	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OTf)_2$	$AgSbF_6$	DCE	33	34
3	$[RuCl_2(p\text{-cymene})]_2$	CuO	$AgSbF_6$	DCE	30	33
4	$[RuCl_2(p\text{-cymene})]_2$	O_2	$AgSbF_6$	DCE	25	25
5	**$[RuCl_2(p\text{-cymene})]_2$**	**$Cu(OAc)_2$**	**$AgSbF_6$**	**DCE**	**60**	**0**
6	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$	$AgSbF_6$	DCE	64[c]	0
7	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$	$AgSbF_6$	DCE	58[d]	0
8	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$	$AgSbF_6$	TFE	0	0
9	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$	$AgSbF_6$	EtOAc	0	0
10	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$	$AgSbF_6$	DCM	0	0
11	**$[RuCl_2(p\text{-cymene})]_2$**	**TBHP**	**$AgSbF_6$**	**DCE**	**0**	**65**
12	**$[RuCl_2(p\text{-cymene})]_2$**	**---------**	**$AgSbF_6$**	**H_2O**	**15**	**45**

[a] Until and otherwise mentioned all the reactions were carried out with **1a** (0.45 mmol), **2a** (0.90 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), $AgSbF_6$ (30 mol %) in solvent 2 mL at 120 °C for 12 h. [b] Isolated yields. [c] Reaction stirred for 24 h. [d] Reaction carried out at 150 °C.

5.1. Crystallographic data for 3h

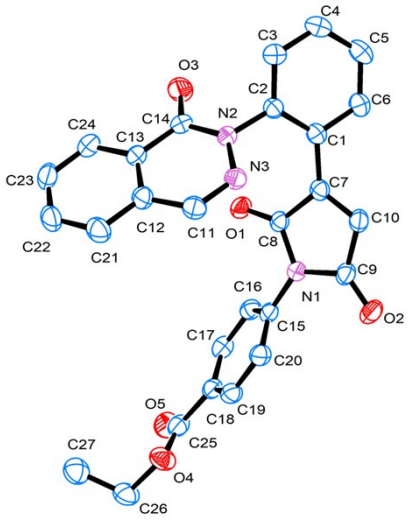


Fig S1. Perspective view of the X-ray structure of **3h**. Hydrogen atoms are omitted for clarity.

Compound	**3h**
CCDC No.	2216957
Empirical formula	$C_{27}H_{19}N_3O_5$
Formula weight	465.46 g/mol
Temperature/K	293(2)
Crystal system	Monoclinic
Wavelength	0.71073
Space group	P 1 21/n 1
a/Å	13.934(4)
b/Å	7.1249(19)
c/Å	23.124(6)
α /°	90
β/°	102.776(8)

γ/°	90
Volume	2238.9(10)
Z	4
Calculated density g/cm3	1.375
Absorption coefficient (μ/mm-1)	0.095
F(000)	964
	-16<=h<=16,
Index ranges	-8<=k<=8,
	-27<=l<=27
Reflections collected	50858
Independent reflections	3981
Data/restraint/parameters	3981 / 0 / 317
Goodness of fit on F2	0.943
Final R indices[I>2σ(I)]	R1 = 0.0459
	wR2 = 0.1107
Final R indices [all data]	R1 = 0.0549
	wR2 = 0.1178

Bond distance

Atom	**Atom**	**Distance Å**	**Atom**	**Atom**	**Distance Å**
O1	C8	1.206(2)	O2	C9	1.201(2)
O3	C14	1.206(2)	O4	C25	1.335(3)
O4	C26	1.451(2)	O5	C25	1.205(2)
N1	C8	1.395(2)	N1	C9	1.403(2)
N1	C15	1.426(2)	N2	C14	1.382(2)

N2	N3	1.388(2)	N2	C2	1.438(2)
N3	C11	1.291(2)	C1	C2	1.396(3)
C1	C6	1.395(3)	C1	C7	1.474(3)
C2	C3	1.383(3)	C3	C4	1.375(3)
C4	C5	1.380(3)	C5	C6	1.381(3)
C7	C10	1.329(3)	C7	C8	1.502(3)
C9	C10	1.475(3)	C11	C12	1.432(3)
C12	C13	1.392(3)	C12	C21	1.407(3)
C13	C24	1.383(3)	C13	C14	1.465(3)
C15	C16	1.388(3)	C15	C20	1.384(3)
C16	C17	1.383(3)	C17	C18	1.387(3)
C18	C19	1.388(3)	C18	C25	1.495(3)
C19	C20	1.376(3)	C21	C22	1.368(3)
C22	C23	1.380(4)	C23	C24	1.367(3)
C26	C27	1.496(3)			

Bond angles

Atom	**Atom**	**Atom**	**Angle [^{0}]**	**Atom**	**Atom**	**Atom**	**Angle [^{0}]**
O5	C25	O4	124.2(2)	O5	C25	C18	124.0(2)
O4	C26	C27	111.37(19)	O4	C25	C18	111.75(17)
O3	C14	N2	120.69(17)	O3	C14	C13	124.12(19)
O2	C9	N1	125.32(17)	O2	C9	C10	128.16(17)
O1	C8	N1	125.59(17)	O1	C8	C7	128.16(17)
N3	N2	C2	113.69(14)	N3	C11	C12	125.10(18)
N2	C14	C13	115.19(17)	N1	C9	C10	105.78(15)

N1	C8	C7	106.24(15)	C9	N1	C15	125.59(15)
C8	N1	C9	110.07(15)	C8	N1	C15	124.33(14)
C7	C10	C9	110.21(17)	C6	C1	C7	118.14(16)
C4	C5	C6	119.35(19)	C4	C3	C2	120.41(19)
C3	C4	C5	120.3(2)	C3	C2	N2	118.38(16)
C3	C2	C1	120.51(17)	C2	C1	C7	123.86(16)
C2	C1	C6	117.88(17)	C25	O4	C26	117.17(18)
C24	C23	C22	121.2(2)	C24	C13	C14	120.95(19)
C23	C24	C13	119.4(2)	C23	C22	C21	120.2(2)
C22	C21	C12	119.8(2)	C21	C12	C11	122.76(19)
C20	C15	N1	119.42(2)	C1	C7	C8	124.45(16)
C1	C6	C5	121.57(19)	C1	C2	N2	121.08(16)
C19	C18	C25	121.80(19)	C19	C18	C17	119.24(18)
C18	C19	C20	120.42(19)	C18	C17	C16	120.71(18)
C17	C18	C25	118.83(18)	C16	C15	N1	120.02(17)
C16	C15	C20	120.53(18)	C15	C20	C19	119.81(18)
C15	C16	C17	119.24(18)	C14	N3	N3	126.24(15)
C14	N2	C2	119.66(15)	C13	C12	C21	119.12(15)
C13	C12	C11	118.11(17)	C12	C13	C24	120.15(19)
C12	C13	C14	118.88(17)	C11	N3	N2	116.19(16)
C10	C7	C8	107.54(16)				

5.2. Crystallographic data for 4a

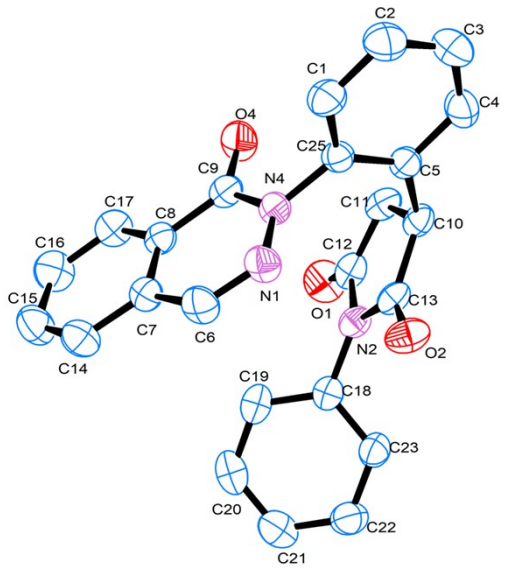


Fig S2. Perspective view of the X-ray structure of **4a**. Hydrogen atoms are omitted for clarity.

Compound	**4a**
CCDC No.	2232967
Empirical formula	$C_{24}H_{17}N_3O_3$
Formula weight	395.40 g/mol
Temperature/K	300(2)
Crystal system	Monoclinic
Wavelength	0.71073
Space group	P 1 21/c 1
a/Å	10.4045(9)
b/Å	8.8690(8)
c/Å	21.6415(17)
α /°	90

β/°	102.176(2)
γ/°	90
Volume	1952.1(3)
Z	4
Calculated density g/cm3	1.345
Absorption coefficient (μ/mm-1)	0.091
F(000)	824
	-11<=h<=13,
Index ranges	-11<=k<=11,
	-28<=l<=28
Reflections collected	36983
Independent reflections	4825
Data/restraint/parameters	4825 / 0 / 271
Goodness of fit on F2	1.047
Final R indices[I>2σ(I)]	R1 = 0.0501
	wR2 = 0.1004
Final R indices [all data]	R1 = 0.1012
	wR2 = 0.1224

Bond distance

Atom	**Atom**	**Distance Å**	**Atom**	**Atom**	**Distance Å**
O1	C12	1.212(2)	O2	C13	1.203(2)
O4	C9	1.220(2)	N1	C6	1.285(2)
N1	N4	1.3919(19)	N2	C13	1.391(2)
N2	C12	1.393(2)	N2	C18	1.436(2)

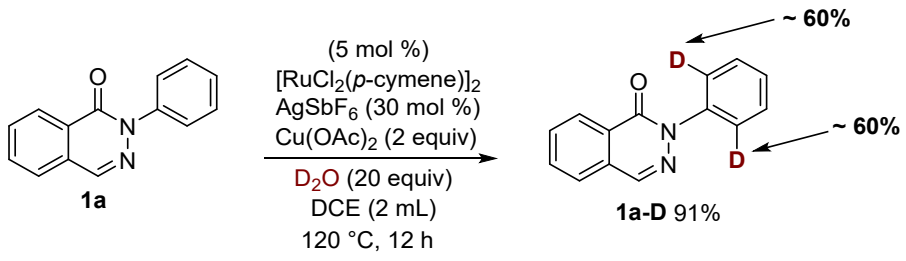
N4	C9	1.374(2)	N4	C25	1.446(2)
C1	C2	1.373(3)	C1	C25	1.382(2)
C2	C3	1.366(3)	C3	C4	1.382(3)
C4	C5	1.392(2)	C5	C25	1.389(2)
C5	C10	1.515(2)	C6	C7	1.432(2)
C7	C8	1.389(2)	C7	C14	1.400(3)
C8	C17	1.379(2)	C8	C9	1.465(2)
C10	C13	1.513.2)	C10	C11	1.529(2)
C11	C12	1.482(3)	C14	C15	1.374(3))
15	C16	1.380(3)	C16	C17	1.371(3)
C18	C23	1.373(2)	C18	C19	1.381(2)
C19	C20	1.386(3)	C20	C21	1.376(3)
C20	C22	1.368(3)	C22	C23	1.381(3)

Bond angle

Atom	**Atom**	**Atom**	**Angle [^{0}]**	**Atom**	**Atom**	**Atom**	**Angle [^{0}]**
C6	N1	N4	116.44(14)	C13	N2	C12	112.40(15)
C13	N2	C18	123.40(14)	C12	N2	C18	124.09(15)
C9	N4	N1	125.62(14)	C9	N4	C25	119.17(15)
N1	N4	C25	113.73(13)	C2	C1	C25	120.53(18)
C3	C2	C1	119.18(19)	C2	C3	C4	120.6(2)
C3	C4	C5	121.41(19)	C25	C5	C4	116.93(16)
C25	C2	C10	124.22(16)	C4	C5	C10	118.81(16)
N1	C6	C7	125.15(17)	C8	C7	C14	119.31(17
C8	C7	C6	118.11(16)	C14	C7	C6	122.58(17)

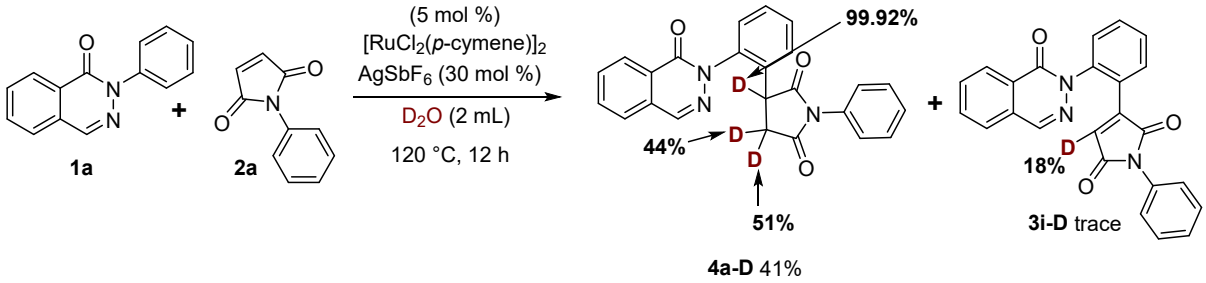
C17	C8	C7	120.63(17)	C17	C8	C9	120.68(16)
C7	C8	C9	118.67(15)	O4	C9	N4	120.55(17)
O4	C9	C8	123.69(16)	N4	C9	C8	115.76(15)
C13	C10	C5	115.02(14)	C13	C10	C11	104.40(14)
C5	C10	C11	115.76(14)	C12	C11	C10	105.73(14)
O1	C12	N2	123.48(18)	O1	C12	C11	127.77(59)
N2	C12	C11	108.74(15)	O2	C13	N2	124.59(17)
O2	C13	C10	127.12(16)	N2	C13	C10	108.26(14)
C15	C14	C7	119.47(19)	C14	C15	C16	120.3(2)
C17	C16	C15	120.8(2)	C16	C17	C8	119.40(19)
C23	C18	C19	120.50(18)	C23	C18	N2	119.40(16)
C19	C18	N2	120.10(16)	C18	C19	C20	119.22(19)
C21	C20	C19	120.14(19)	C22	C21	C20	120.2(2)
C21	C22	C123	120.21(19)	C18	C23	C22	119.76(18)
C1	C25	C5	121.33(16)	C1	C25	N4	116.44(15)
C5	C25	N4	122.23(15)				

6.1. Mechanistic studies (H/D exchange reaction):

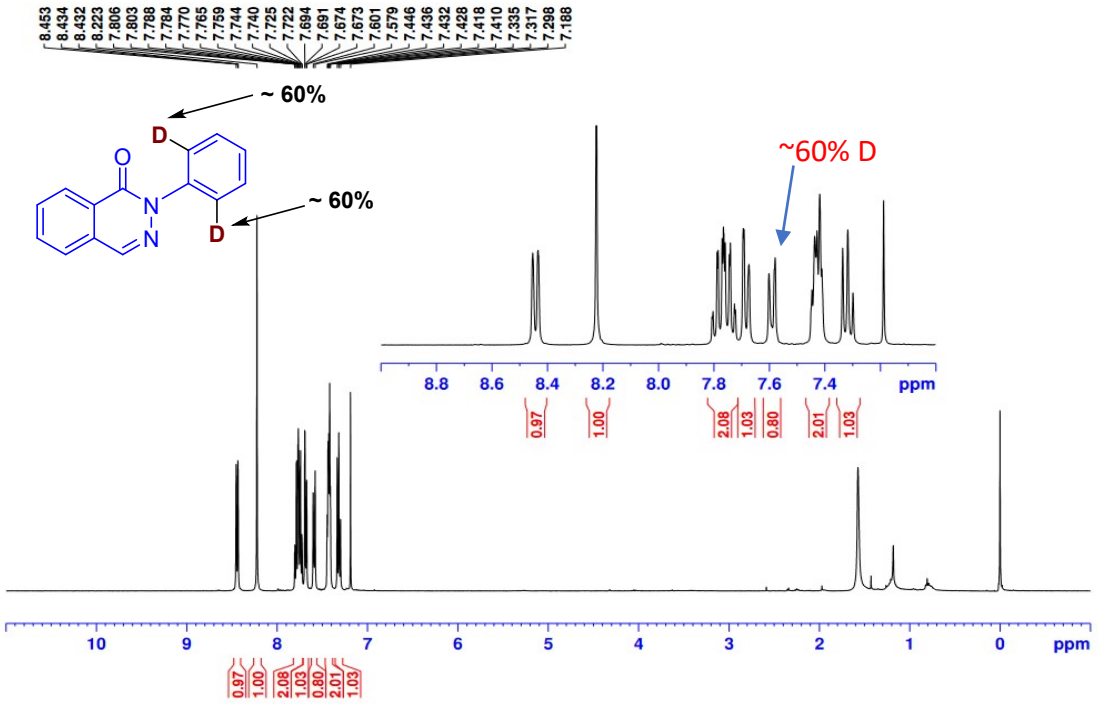


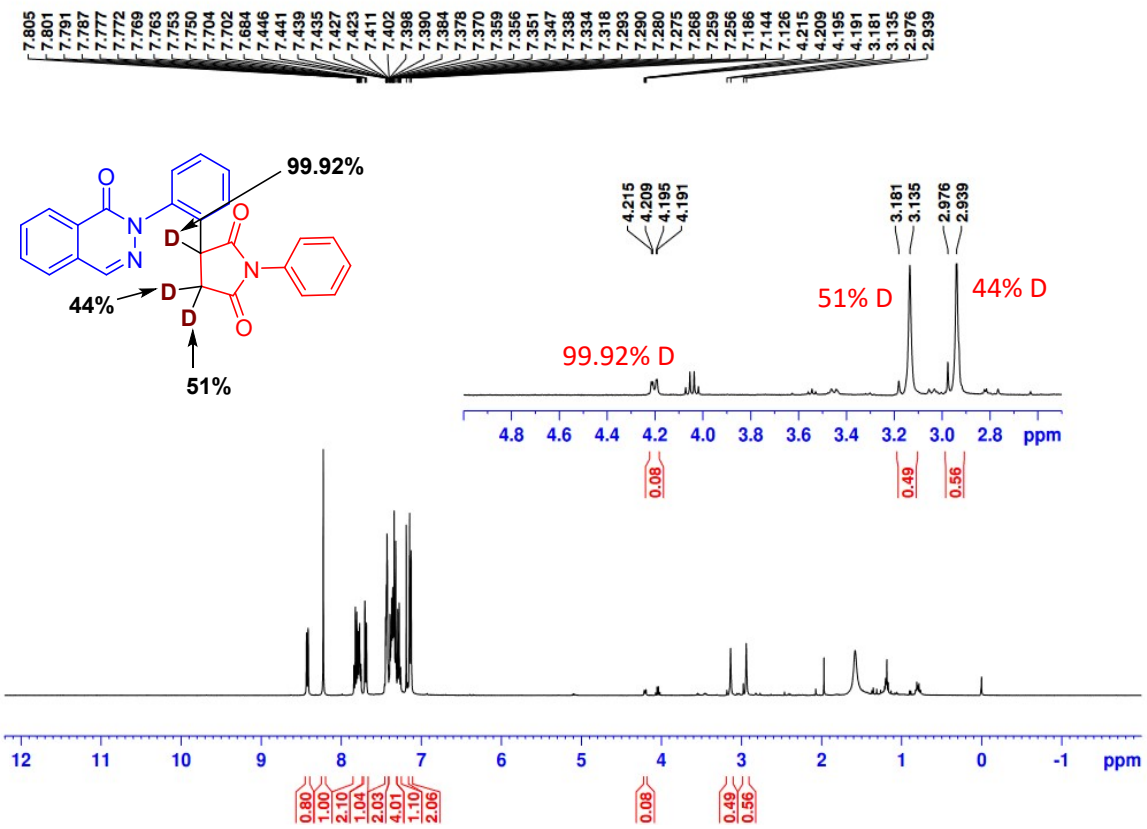
In an oven-dried vial equipped with stir bar was charged with phthalazinone **1a** (0.45 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), $AgSbF_6$ (30 mol %), $Cu(OAc)_2$ (2 equiv) and D_2O (20 equiv). To this mixture DCE (2 mL) was added. The vial was tightly capped and placed in a pre-heated oil bath at 120 °C. After 12 h, the reaction mixture was cooled to the ambient temperature and it was diluted with DCM and concentrated under reduced pressure. The crude was then purified by column chromatography on silica gel 100-200 mesh using hexane/ethyl acetate as the eluent.

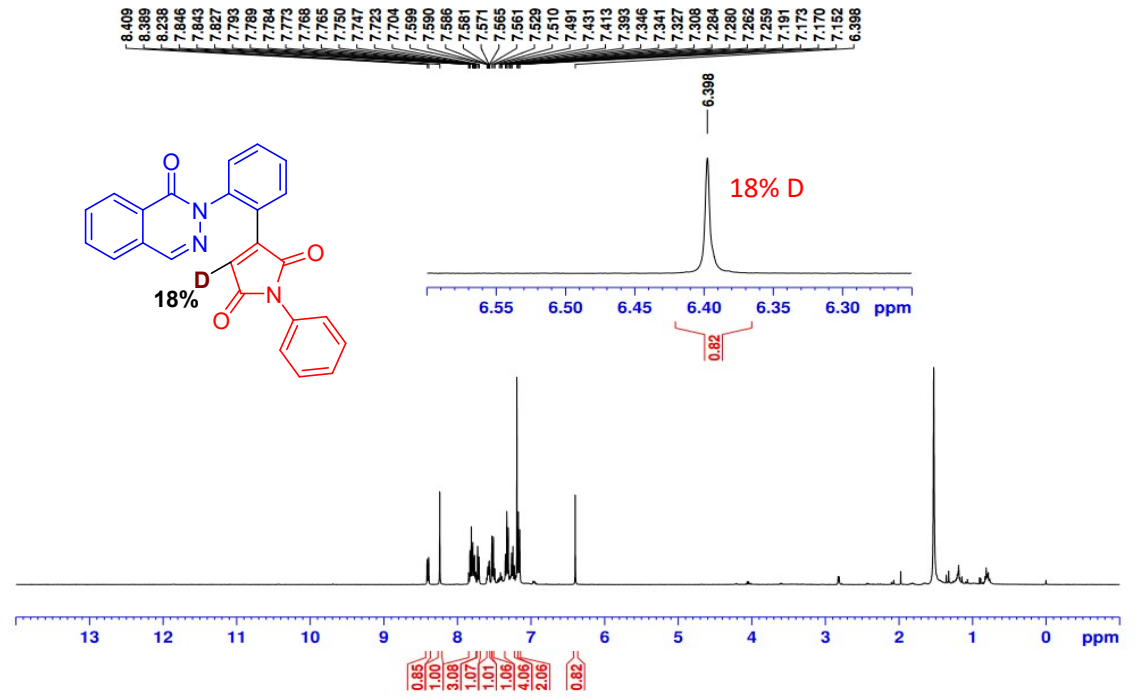
6.2. Deuterium incorporation reaction



In an oven-dried vial equipped with stir bar was charged with phthalazinone **1a** (0.45 mmol), maleimide **2a** (0.90 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), $AgSbF_6$ (30 mol %). To this mixture D_2O (2 mL) was added. The vial was tightly capped and placed in a pre-heated oil bath at 120 °C. After 12 h, the reaction mixture was cooled to the ambient temperature and it was diluted with DCM and concentrated under reduced pressure. The crude was then purified by column chromatography on silica gel 100-200 mesh using hexane/ethyl acetate as the eluent.




99.92%
D
D
D
44%
51%
51% D
44% D
99.92% D
ppm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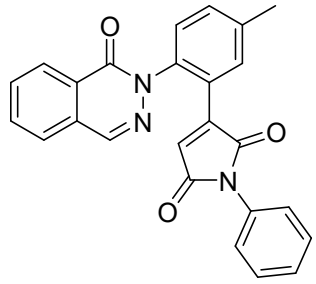
7. Characterization Data

3-(5-methyl-2-(1-oxophthalazin-2(1H)-yl)phenyl)-1-phenyl-1H-pyrrole-2,5-dione (3a)



Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

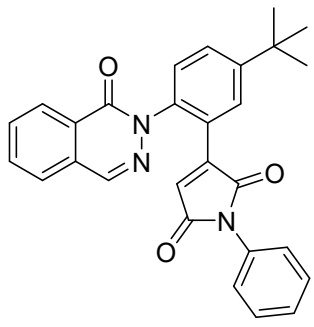
Yield: 60% from Condition A**,** Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (d, *J* = 7.8 Hz, 1H), 8.21 (s, 1H), 7.82–7.72 (m, 2H), 7.70 (d, *J* = 7.72 Hz, 1H), 7.60 (s, 1H), 7.39–7.36 (m, 2H), 7.33–7.29 (m, 2H), 7.25–7.21 (m, 1H), 7.18–7.15 (m, 2H), 6.35 (s, 1H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.1, 168.6, 159.4, 142.9, 139.0, 138.8, 138.3, 133.8, 132.3, 132.1, 131.5, 131.4, 129.6, 128.9, 128.5, 128.1, 127.7, 127.3, 127.0, 126.4, 126.0, 125.8, 21.2.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{25}H_{17}N_3O_3Na$, 430.1162; Found 430.1172.

3-(5-(tert-butyl)-2-(1-oxophthalazin-2(1H)-yl)phenyl)-1-phenyl-1H-pyrrole-2,5-dione (3b)



Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

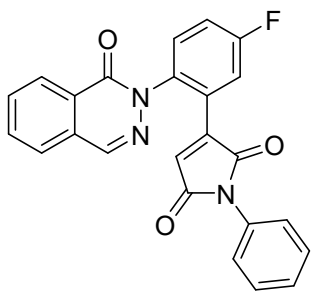
Yield: 50% from Condition A, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.48 (d, *J* = 7.76 Hz, 1H), 8.29 (s, 1H), 7.90–7.81 (m, 3H), 7.78 (d, *J* = 7.64 Hz, 1H), 7.66 (d, *J* = 8.28 Hz, 1H), 7.51 (d, *J* = 8.44 Hz, 1H), 7.42–7.38 (m, 2H), 7.33–7.31 (m, 1H), 7.26–7.24 (m, 2H), 6.44 (s, 1H), 1.40 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.2, 168.7, 159.4, 152.0, 143.1, 138.8, 138.2, 133.8, 132.3, 131.4, 129.6, 129.0, 128.6, 128.3, 128.2, 128.2, 127.7, 127.3, 126.8, 126.4, 126.0, 125.4, 34.9, 31.2.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{28}H_{23}N_3O_3Na$, 472.1632; Found 472.1647.

3-(5-fluoro-2-(1-oxophthalazin-2(1H)-yl)phenyl)-1-phenyl-1H-pyrrole-2,5-dione (3c)



Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

Yield: 45% from Condition A, Off-white coloured solid

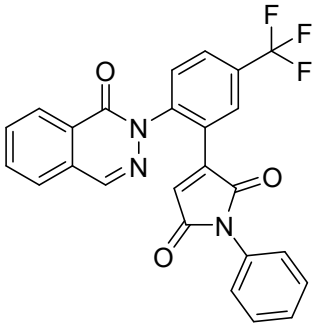
^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.40 (d, *J* = 7.84 Hz, 1H), 8.23 (s, 1H), 7.84 (dt, *J* = 7.46 Hz 1H), 7.78 (dt, *J* = 7.6 Hz 1H), 7.73 (d, *J* = 7.84 Hz, 1H), 7.59–7.56 (m, 1H), 7.50–7.7.47 (m, 1H), 7.36–7.32 (m, 2H), 7.28–7.24 (m, 2H), 7.19–7.16 (m, 2H), 6.38 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.7, 168.2, 159.4, 141.3, 139.2, 134.1, 132.6, 131.2, 130.7, 130.6, 129.6, 129.0, 128.0, 127.9, 127.8, 127.3, 126.6, 126.0, 118.4, 118.2, 118.1, 117.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.06

HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{24}H_{15}FN_3O_3$, 412.1092; Found 412.1098.

3-(2-(1-oxophthalazin-2(1H)-yl)-5-(trifluoromethyl)phenyl)-1-phenyl-1H-pyrrole-2,5-dione(3d)



Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

Yield: 34% from Condition A, Off-white coloured solid

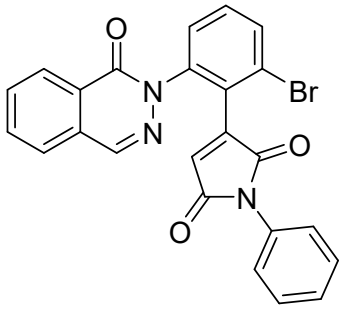
^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.50 (d, *J* = 7.8 Hz, 1H), 8.34 (s, 1H), 8.12 (s, 1H), 7.96–7.86 (m, 3H), 7.80 (t, *J* = 8.44 Hz, 2H), 7.42 (t, *J* = 7.18 Hz, 2H), 7.36–732 (m, 1H), 7.25 (d, *J* = 7.36 Hz, 2H), 6.59 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.6, 168.0, 159.2, 143.5, 142.0, 139.4, 134.3, 132.7, 131.1, 129.5, 129.4, 129.0, 128.1, 127.9, 127.4, 126.9, 126.6, 125.9, 121.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ: -62.53

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{25}H_{14}F_3N_3O_3Na$, 484.0879; Found 484.0895.

3-(2-bromo-6-(1-oxophthalazin-2(1H)-yl)phenyl)-1-phenyl-1H-pyrrole-2,5-dione (3e)



Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

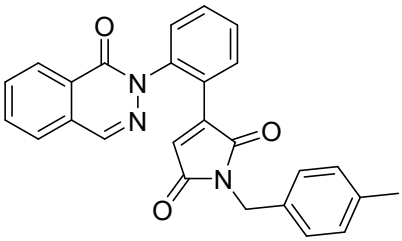
Yield: 58% from Condition A, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (d, *J* = 7.8 Hz, 1H), 8.23 (s, 1H), 7.83 (t, *J* = 7.26 Hz, 1H), 7.77 (t, *J* = 7.28 Hz, 1H), 7.72–7.68 (m, 3H), 7.65–7.62 (m, 1H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.24 (t, *J* = 7.36 Hz, 1H), 7.16 (d, *J* = 7.6 Hz, 2H), 6.38 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.8, 168.3, 159.2, 141.8, 141.6, 139.3, 134.2, 132.6, 132.1, 132.1, 132.0, 131.3, 129.5, 129.0, 128.0, 127.9, 127.3, 127.2, 126.6, 126.0, 125.2, 125.1.

HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{24}H_{15}BrN_3O_3$, 472.0291; Found 472.0279.

1-(4-methylbenzyl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)-1H-pyrrole-2,5-dione (3f)



Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

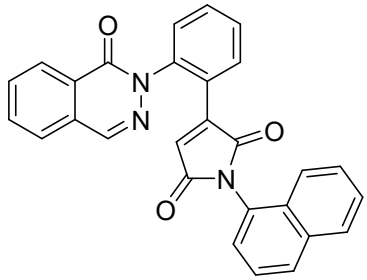
Yield: 56% from Condition A, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.35 (d, *J* = 7.8 Hz, 1H), 8.06 (s, 1H), 7.79 (t, *J* = 7.06 Hz, 1H), 7.73 (t, *J* = 7.28 Hz, 1H), 7.67 (d, *J* = 7.64 Hz, 1H), 7.62 (d, *J* = 7.68 Hz, 1H), 7.54–7.48 (m, 2H), 7.46–7.42 (m, 1H), 7.03 (d, *J* = 7.96 Hz, 2H), 6.95 (d, *J* = 7.92 Hz, 2H), 6.28 (s, 1H), 4.46 (s, 2H), 2.23 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.9, 169.3, 159.3, 143.5, 140.5, 138.7, 137.3, 133.7, 133.2, 132.3, 131.2, 130.9, 129.5, 129.2, 128.7, 128.6, 128.3, 128.1, 127.3, 127.1, 126.4, 126.3, 41.1, 29.1.

HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{26}H_{20}N_3O_3$, 422.1499; Found 422.1491.

1-(naphthalen-1-yl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)-1H-pyrrole-2,5-dione (3g)



Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

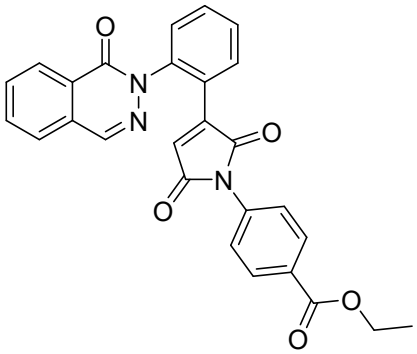
Yield: 32% from Condition A, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.44 (d, *J* = 7.2 Hz, 1H), 8.26 (s, 1H), 7.83–7.74 (m, 5H), 7.69 (dd, *J* = 7.84 Hz, 1H), 7.61–7.54 (m, 2H), 7.51 (dt, *J* = 7.28 Hz, 1H), 7.43–7.38 (m, 3H), 7.30 (dt, *J* = 7.64 Hz, 1H), 7.22 (d, *J* = 7.24 Hz, 1H), 6.56 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.6, 168.9, 159.3, 144.1, 140.6, 139.0, 134., 133.9, 132.4, 131.5, 130.8, 130.3, 129.8, 129.6, 128.8, 128.6, 128.4, 128.1, 127.8, 127.2, 127.2, 126.9, 126.9, 126.5, 126.4, 126.2, 125.3, 122.2.

HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{28}H_{18}N_3O_3$, 444.1343; Found 444.1343.

Ethyl 4-(2,5-dioxo-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)-2,5-dihydro-1H-pyrrol-1-yl)benzoate (3h)



Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

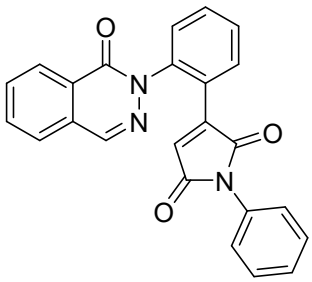
Yield: 36% from Condition A, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (d, *J* = 7.24 Hz, 1H), 8.23 (s, 1H), 7.99 (d, *J* = 7.92 Hz, 2H), 7.82 (d, *J* = 6.96 Hz, 1H), 7.78 (d, *J* = 6.88 Hz, 2H), 7.71 (d, *J* = 7.24 Hz, 1H), 7.58 (d, *J* = 6.84 Hz, 1H), 7.54–7.50 (m, 2H), 7.30 (d, *J* = 8.04 Hz, 2H), 6.42 (s, 1H), 4.30 (q, *J* = 6.92 Hz, 2H), 1.30 (t, *J* = 6.48 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.5, 168.0, 165.8, 159.3, 143.2, 140.7, 139.0, 135.4, 134.0, 132.5, 131.6, 130.9, 130.3, 129.6, 129.3, 128.9, 128.8, 128.1, 127.3, 127.2, 126.5, 125.9, 125.1, 61.1, 14.3.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{27}H_{19}N_3O_5Na$, 488.1217; Found 488.1241.

3-(2-(1-oxophthalazin-2(1H)-yl) phenyl)-1-phenyl-1H-pyrrole-2,5-dione (3i)



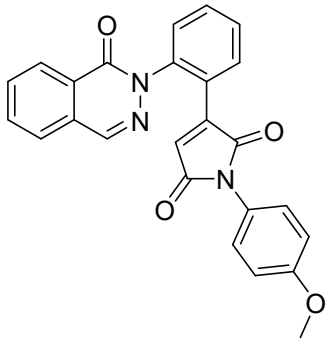
Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

Yield: 15% from Condition B, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (d, *J* = 7.8 Hz, 1H), 8.23 (s, 1H), 7.83–7.73 (m, 3H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.59–7.55 (m, 1H), 7.52–7.47 (m, 2H), 7.33–7.29 (m, 2H), 7.25 (d, *J* = 7.64 Hz, 1H), 7.16 (d, *J* = 7.48 Hz, 2H), 6.39 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.1, 168.5, 159.4, 142.9, 140.8, 138.9, 133.9, 132.7, 131.4, 131.4, 131.0, 129.6, 129.0, 128.9, 128.8, 128.1, 127.8, 127.3, 127.1, 126.5, 126.1, 126.0.

HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{24}H_{16}N_3O_3$, 394.1186; Found 394.1189.



1-(4-methoxyphenyl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)-1H-pyrrole-2,5-dione (3k)

Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

Yield: 4% from condition B, sticky white oil

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.41 (d, *J* = 7.52 Hz, 1H), 8.22 (s, 1H), 7.82–7.73 (m, 3H), 7.70 (d, *J* = 7.36 Hz, 1H), 7.56–7.47 (m, 3H), 7.27 (t, *J* = 7.74 Hz, 1H), 7.00 (d, *J* = 7.48 Hz, 1H), 6.90–6.85 (m, 2H), 6.41 (s, 1H), 3.62 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.3, 168.6, 159.3, 155.3, 143.2, 140.7, 138.8, 133.8, 132.3, 131.3, 131.1, 130.5, 130.0, 129.7, 128.8, 128.7, 128.2, 127.5, 127.3, 126.4, 120.7, 112.0, 55.7.

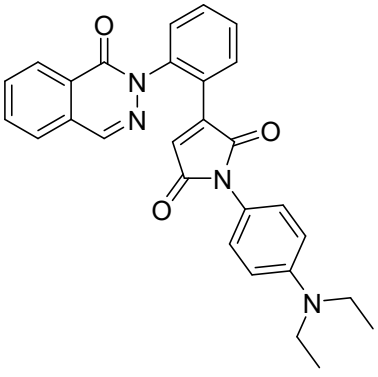
HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{25}H_{17}N_3O_4Na$, 446.1111; Found 446.1136.

1-(4-(diethylamino)phenyl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)-1H-pyrrole-2,5-dione (3l)

Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

Yield: 6% from condition B, sticky pale yellow oil

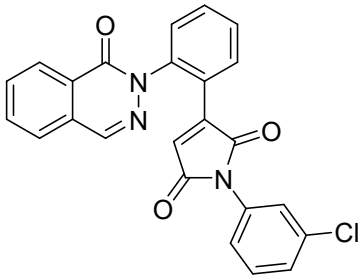
^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (d, *J* = 7.2 Hz, 1H), 8.22 (s, 1H), 7.82–7.75 (m, 4H), 7.70 (d, *J* = 6.84 Hz, 1H), 7.55–7.48 (m, 3H), 6.92 (d, *J* = 7.92 Hz, 2H), 6.55 (d, *J* = 7.8 Hz, 2H), 6.34 (s, 1H), 3.26–3.24 (m, 4H), 1.06 (m, 6H).



^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.0, 169.3, 159.4, 147.4, 142.4, 140.7, 139.9, 133.9, 132.4, 131.2, 131.1, 129.6, 128.9, 128.7, 128.1, 127.5, 127.3, 127.1, 126.5, 126.4, 118.5, 111.5, 44.43, 12.5.

HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{28}H_{25}N_4O_3$, 465.1921; Found 465.1943.

1-(3-chlorophenyl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)-1H-pyrrole-2,5-dione (3m)



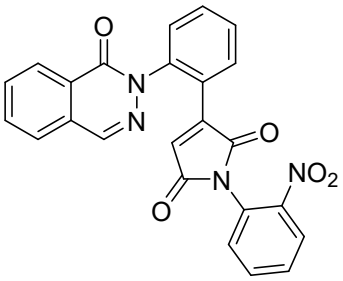
Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

Yield: 5% from condition B, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.40 (d, *J* = 7.48 Hz, 1H), 8.24 (s, 1H), 7.83–7.75 (m, 3H), 7.73 (d, *J* = 7.26 Hz, 1H), 7.59 (d, *J* = 7.24 Hz, 1H), 7.54–7.49 (m, 2H), 7.25–7.22 (m, 2H), 7.15 (s, 1H), 7.11 (d, *J* = 7.44 Hz, 1H), 6.41 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.5, 167.0, 158.3, 142.2, 139.7, 137.9, 133.4, 133.0, 131.5, 131.4, 130.6, 129.9, 128.8, 128.5, 127.8, 127.7, 127.0, 126.8, 126.2, 126.0, 125.5, 125.0, 124.8, 122.9.

HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{24}H_{14}ClN_3O_3Na$, 450.0616; Found 450.0634.



1-(2-nitrophenyl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)pyrrolidine-2,5-dione (3n)

Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

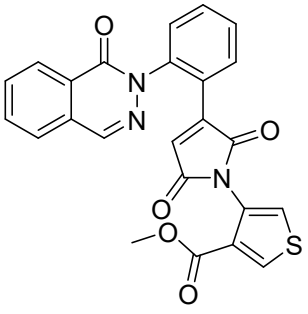
Yield: 5% from condition B, pale yellow coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.42 (d, *J* = 7.4 Hz, 1H), 8.26 (s, 1H), 8.01 (d, *J*= 8.16 Hz, 1H), 7.80–7.75 (m, 2H), 7.71 (d, *J* = 7.48 Hz, 2H), 7.60–7.57 (m, 3H), 7.49–7.44 (m, 1H), 7.26 (d, *J* = 7.4 Hz, 1H), 6.60 (s, 1H), 6.53 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.0, 167.5, 159.5, 145.4, 144.8, 140.6, 139.2, 134.0, 133.8, 132.3, 131.5, 131.0, 130.9, 129.6, 129.6, 128.8, 128.7, 127.8, 128.7, 128.1, 127.8, 127.3, 126.6, 125.8, 125.7, 116.1.

HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{24}H_{15}N_4O_5$, 439.1037; Found 439.1039.

Methyl4-(2,5-dioxo-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)-2,5-dihydro-1H-pyrrol-1-yl)thiophene-3-carboxylate (3o)



Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

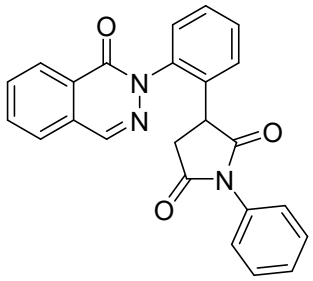
Yield: 5% from condition B, pale yellow coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.40 (d, *J* = 7.56 Hz, 1H), 8.24 (s, 1H), 7.80–7.74 (m, 3H), 7.70 (d, *J* = 7.44 Hz, 1H), 7.56–7.50 (m, 4H), 6.87 (d, *J* = 3.08 Hz, 1H), 6.42 (s, 1H), 3.66 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.2, 167.7, 160.6, 159.3, 143.7, 140.7, 139.0, 133.9, 133.0, 132.3, 131.4, 131.1, 130.2, 129.7, 128.8, 128.7, 128.2, 128.0, 127.6, 127.3, 127.2, 126.5, 126.2, 52.1.

HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{24}H_{16}N_3O_5S$, 458.0805; Found 458.0795.

3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)-1-phenylpyrrolidine-2,5-dione (4a)



Purified by column chromatography on silica gel using hexane/ethylacetate (65/35)

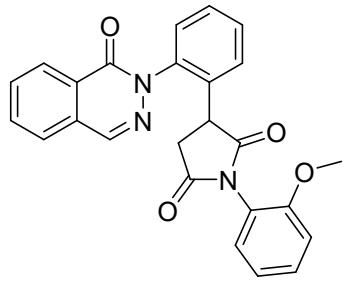
Yield: 45% from condition B, 60% from condition C, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.44 (d, *J* = 7.76 Hz, 1H), 8.23 (s, 1H), 7.83 (dt, *J* = 7.36 Hz, 1H), 7.78 (dt, *J* = 7.58 Hz, 1H), 7.71 (d, *J* = 7.84 Hz, 1H), 7.45–7.43 (m, 2H), 7.39–7.32 (m, 4H), 7.30 (d, *J* = 7.16 Hz, 1H), 7.15 (d, *J* = 7.32 Hz, 2H), 4.23–4.19 (m, 1H), 3.20–3.13 (m, 1H), 2.99–2.93 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.1, 175.1, 159.5, 140.9, 138.9, 134.9, 133.9, 132.4, 131.8, 131.2, 129.8, 129.6, 129.1, 129.0, 128.9, 128.5, 128.1, 127.3, 126.4, 126.2, 42.4, 37.3.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{24}H_{17}N_3O_3Na$, 418.1162; Found 418.1190.

1-(2-methoxyphenyl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)pyrrolidine-2,5-dione (4b)

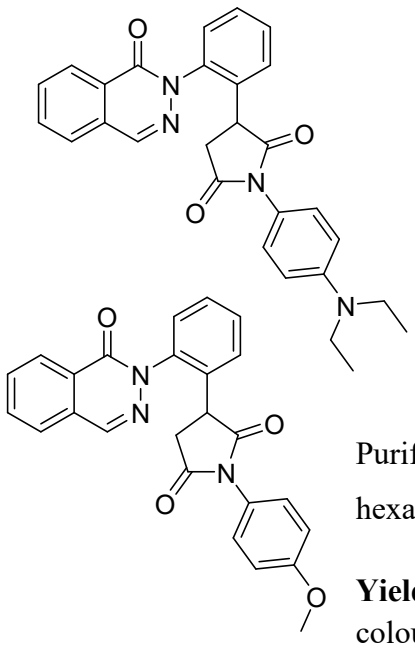


Purified by column chromatography on silica gel using hexane/ethylacetate (65/35)

Yield: 20% from condition B, 50% from condition C, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.45 (d, *J* = 9.24 Hz, 2.41H), 8.26 (s, 1.27H), 8.25 (s, 0.98H), 7.86–7.77 (m, 4.78H), 7.73 (d, *J* = 7.68 Hz, 2.40H), 7.51–7.27 (m, 11.81H), 7.02–6.88 (m, 7.08H), 4.26–4.22 (m, 1H), 4.15–4.12 (m, 1.53H), 3.80 (s, 4.52H), 3.65 (s, 3H), 3.21–3.19 (m, 1H), 3.16–3.13 (m, 1.52H), 2.95–2.91 (m, 1H), 2.91–2.86 (m, 1.56H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.3 (C), 175.8 (C*), 175.3 (C), 175.0 (C*), 159.5 (CC*), 154.6 (CC*), 141.0 (C), 140.9 (C*), 138.8 (C), 138.8 (C*), 136.1 (C), 135.2 (C*), 133.9 (CC*), 132.3 (C), 132.3 (C*), 130.8 (C), 130.7 (C*), 129.8 (C), 129.8 (C*), 129.7 (CC*), 129.1 (CC*), 128.9 (C), 128.8 (C*), 128.3 (CC*), 128.2 (C), 128.1 (C*), 127.9 (C), 127.4 (C*), 127.3 (C),



127.2 (C*), 126.4 (C), 126.4 (C*), 121.0 (C), 120.9 (C*), 120.8 (C), 120.7 (C*), 112.1 (C), 112.1 (C*), 55.9 (C), 55.7 (C*), 42.5 (C), 42.0 (C*), 38.2 (C), 37.6 (C*).

HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{25}H_{20}N_3O_4$, 426.1448; Found 426.1458.

1-(4-methoxyphenyl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)pyrrolidine-2,5-dione (4c)

Purified by column chromatography on silica gel using hexane/ethylacetate (65/35)

Yield: 40% from condition B, 57% from condition C, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.43 (d, *J* = 7.72 Hz, 1H), 8.22 (s, 1H), 7.84–7.75 (m, 2H), 7.71 (d, *J* = 8.28 Hz, 1H), 7.45–7.40 (m, 2H), 7.39–7.34 (m, 2H), 7.06 (d, *J* = 8.96, 2H), 6.85 (d, *J* = 8.96, 2H), 4.20–4.17 (m, 1H), 3.73 (s, 3H), 3.17–3.10 (m, 1H), 2.96–2.90 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.2, 175.3, 159.5, 159.4, 140.9, 138.9, 135.0, 133.9, 132.3, 129.8, 129.6, 129.0, 128.8, 128.1, 128.1, 127.4, 127.3, 126.4, 124.5, 114.4, 55.4, 42.4, 37.2.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{25}H_{19}N_3O_4Na$, 448.1268; Found 448.1289.

1-(4-(diethylamino)phenyl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)pyrrolidine-2,5-dione (4d)

Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

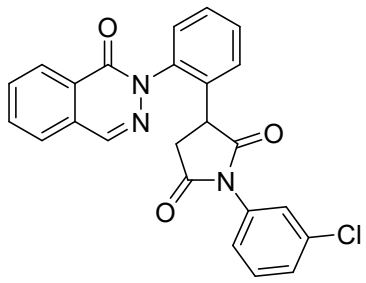
Yield: 35% from condition B, 54% from condition C, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.52 (d, *J* = 7.76 Hz, 1H), 8.32 (s, 1H), 7.91–7.86 (m, 2H), 7.80 (d, *J* = 7.2 Hz, 1H), 7.51–7.46 (m, 4H), 7.03 (d, *J* = 8.52 Hz, 2H), 6.66 (d, *J* = 8.24 Hz, 2H), 4.27–4.24 (m, 1H), 3.36–3.34 (m, 4H), 3.23–3.16 (m, 1H), 3.00–2.95 (m, 1H), 1.16 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.6, 175.8, 159.5, 147.7, 140.9, 138.9, 135.3, 133.9, 132.3, 129.8, 129.6, 128.9, 128.7, 128.1, 128.0, 127.3, 127.1, 126.4, 119.0, 111.4, 44.4, 42.2, 37.3, 12.5.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{28}H_{26}N_4O_3Na$, 489.1897; Found 489.1908.

1-(3-chlorophenyl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)pyrrolidine-2,5-dione (4e)



Purified by column chromatography on silica gel using hexane/ethylacetate (65/35)

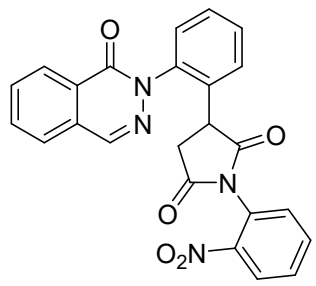
Yield: 23% from condition B, 58% from condition C, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.43 (d, *J* = 7.64 Hz, 1H), 8.22 (s, 1H), 7.85–7.76 (m, 2H), 7.71 (d, *J* = 7.36 Hz, 1H), 7.44–7.35 (m, 4H), 7.25 (s, 2H), 7.12–7.06 (m, 2H), 4.21 (m, 1H), 3.21–3.14 (m, 1H), 3.03–2.98 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.5, 174.6, 159.5, 140.8, 139.0, 134.5, 134.0, 132.8, 132.4, 129.9, 129.8, 129.6, 128.7, 128.4, 128.0, 127.3, 127.3, 126.4, 124.3.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{24}H_{16}ClN_3O_3Na$, 452.0772; Found 452.0794.

1-(2-nitrophenyl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)-1H-pyrrole-2,5-dione (4f)



Purified by column chromatography on silica gel using hexane/ethylacetate (65/35)

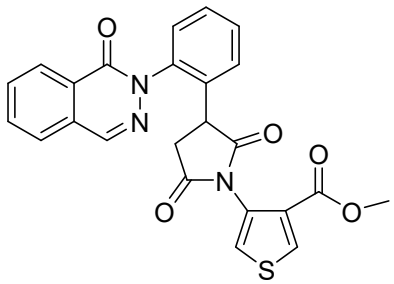
Yield: 76% from condition B, 54% from condition C, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.44 (d, *J* = 7.44 Hz, 2.34H), 8.25 (s, 2.36H), 8.13–8.06 (m, 2.78H), 7.84–7.78 (m, 5.29H), 7.73 (d, *J* = 7.28 Hz, 3H), 7.64 (d, *J* = 6.84 Hz, 3.18H), 7.54–7.49 (m, 6.35H), 7.43–7.35 (m, 7.50H), 7.23–7.21 (m, 2.84H), 4.28 (m, 1H), 4.20 (m, 1.28H), 3.28–3.20 (m, 2.22H), 3.02–2.97 (m, 2.30H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.2 (C), 174.2 (C*), 159.5 (CC*), 139.1 (C), 139.0 (C*), 134.3 (CC*), 133.9 (CC*), 133.1 (CC*), 132.4 (C), 132.4 (C*), 132.3 (CC*), 130.4 (CC*), 130.3 (CC*), 130.1 (CC*), 129.8 (C), 129.6 (C*), 129.2 (C), 129.1 (C*), 129.0 (CC*), 128.1 (C), 128.1 (C*), 128.0 (C), 127.5 (C*), 127.3 (CC*), 126.8 (C), 126.5 (C*), 126.4 (CC*), 126.1 (C), 126.0 (C*), 125.9 (CC*), 42.9 (C), 42.1 (C*), 38.4 (C), 37.5 (C*).

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{24}H_{16}N_4O_5Na$, 463.1013; Found 463.1033.

Methyl 4-(2,5-dioxo-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)pyrrolidin-1-yl)thiophene-3-carboxylate (4g)



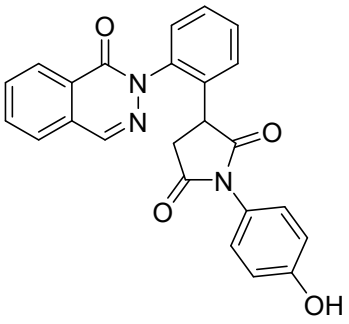
Purified by column chromatography on silica gel using hexane/ethylacetate (65/35)

Yield: 34% from condition B, 53% from condition C, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.43 (d, *J* = 7.76 Hz, 1H), 8.24 (s, 1H), 7.83 (dt, *J* = 7.12 Hz, 1H), 7.78 (dt, *J* = 7.58 Hz, 1H), 7.73 (d, *J* = 7.84 Hz, 1H), 7.52 (d, *J* = 7.4 Hz, 1H), 7.47–7.40 (m, 3H), 7.37–7.35 (m, 1H), 6.84 (d, *J* = 5.28 Hz, 1H), 4.22–4.18 (m, 1H), 3.73 (s, 3H), 3.23–3.19 (m, 1H), 2.99–2.93 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.5, 174.3, 160.5, 159.5, 141.0, 138.9, 135.1, 134.1, 133.9, 132.3, 130.4, 129.9, 129.6, 129.0, 128.4, 128.2, 128.1, 127.4, 127.3, 126.4, 52.2, 42.4, 38.0.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{24}H_{17}N_3O_5SNa$, 482.0781; Found 482.0802.



1-(4-hydroxyphenyl)-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)pyrrolidine-2,5-dione (4h)

Purified by column chromatography on silica gel using hexane/ethylacetate (65/35)

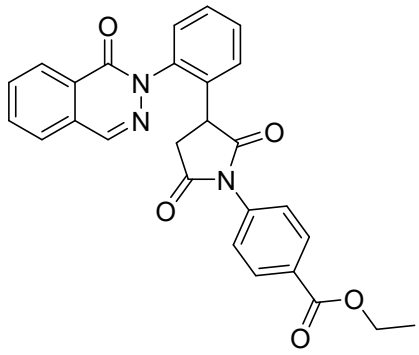
Yield: 56% from condition C, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.41 (d, *J* = 7.72 Hz, 1H), 8.23 (s, 1H), 7.83–7.74 (m, 2H), 7.70 (d, *J* = 7.44 Hz, 1H), 7.41–7.32 (m, 4H), 6.86 (d, *J* = 7.68 Hz, 2H), 6.64 (d, *J* = 7.6 Hz, 2H), 4.18–4.14 (m, 1H), 3.15–3.08 (m, 1H), 2.94–2.88 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.6, 175.5, 159.7, 156.2, 140.8, 139.1, 134.8, 134.1, 132.5, 129.9, 129.6, 129.1, 128.8, 128.2, 128.0, 127.5, 127.2, 126.5, 123.8, 116.0, 42.3, 37.2.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{24}H_{17}N_3O_4Na$, 434.1111; Found 434.1133.

Ethyl 4-(2,5-dioxo-3-(2-(1-oxophthalazin-2(1H)-yl)phenyl)pyrrolidin-1-yl)benzoate (4i)



Purified by column chromatography on silica gel using hexane/ethylacetate (65/3)

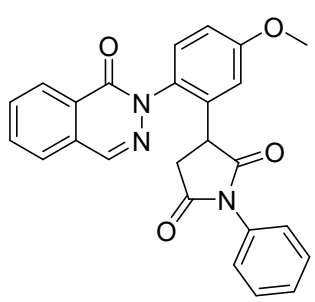
Yield: 58% from condition C, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.42 (d, *J* = 7.68 Hz, 1H), 8.21 (s, 1H), 8.00 (d, *J* = 7.44 Hz, 2H), 7.84–7.77 (m, 2H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.45–7.42 (m, 2H), 7.39–7.34 (m, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 4.31 (q, *J* = 7.09 Hz, 2H), 4.23–4.20 (m, 1H), 3.22–3.15 (m, 1H), 3.03–2.96 (m, 1H), 1.31 (t, *J* = 7.14 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.5, 174.5, 165.6, 159.5, 140.9, 138.9, 135.6, 134.6, 134.0, 132.4, 130.2, 129.8, 129.6, 129.2, 129.0, 128.4, 128.0, 127.3, 126.4, 125.8, 125.1, 61.2, 42.6, 37.2, 14.3.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{27}H_{21}N_3O_5Na$, 490.1373; Found 490.1396.

3-(5-methoxy-2-(1-oxophthalazin-2(1H)-yl)phenyl)-1-phenylpyrrolidine-2,5-dione (4j)



Purified by column chromatography on silica gel using hexane/ethylacetate (65/35)

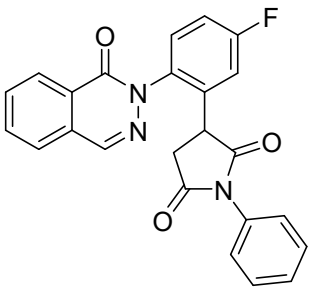
Yield: 51% from condition B, 56% from condition C, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.41 (d, *J* = 7.72 Hz, 1H), 8.19 (s, 1H), 7.82–7.73 (m, 2H), 7.68 (dd, *J* = 7.8 Hz, 1H), 7.35–7.25 (m, 4H), 7.13–7.11 (m, 2H), 6.93 (dd, *J* = 8.76 Hz, 1H), 6.86 (d, *J* = 2.76 Hz, 1H), 4.17–4.13 (m, 1H), 3.78 (s, 3H), 3.15–3.07 (m, 1H), 2.98–2.92 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.7, 174.9, 160.1, 159.7, 138.8, 136.0, 133.8, 133.7, 132.3, 131.8, 129.9, 129.6, 129.0, 128.5, 128.1, 127.3, 126.4, 126.2, 114.0, 113.7, 55.6, 42.5, 37.2.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{25}H_{19}N_3O_4Na$, 448.1268; Found 448.1293.

3-(5-fluoro-2-(1-oxophthalazin-2(1H)-yl)phenyl)-1-phenylpyrrolidine-2,5-dione (4k)



Purified by column chromatography on silica gel using hexane/ethylacetate (65/35)

Yield: 43% from condition B, 52% from condition C, Off-white coloured solid

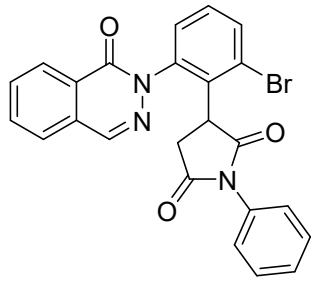
^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.43 (d, *J* = 7.76 Hz, 1H), 8.23 (s, 1H), 7.86–7.77 (m, 2H), 7.71 (d, *J* = 7.4 Hz, 1H), 7.39–7.33 (m, 3H), 7.31 (d, *J* = 7.2 Hz, 1H), 7.15–7.08 (m, 4H), 4.23–4.19 (m, 1H), 3.17–3.10 (m, 1H), 2.96–2.90 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.3, 174.5, 163.8 (d, *J* = 248 Hz), 159.6, 139.1, 137.1 (d, *J* = 8 Hz), 137.0, 136.9, 134.1, 132.5, 131.6, 130.8 (d, *J* = 9.1 Hz), 129.6, 129.1, 128.6, 128.0, 127.3 (d, *J* = 81 Hz), 126.2, 116.2 (d, *J* = 22.53 Hz), 115.3 (d, J = 24 Hz), 42.4, 36.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.41

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{24}H_{16}FN_3O_3Na$, 436.1068; Found 436.1098.

3-(2-bromo-6-(1-oxophthalazin-2(1H)-yl)phenyl)-1-phenylpyrrolidine-2,5-dione (4l)



Purified by column chromatography on silica gel using hexane/ethylacetate (65/35)

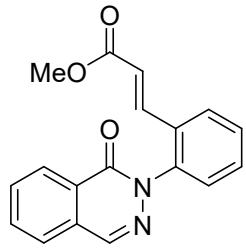
Yield: 24% from condition B, 46% from condition C, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.41 (d, *J* = 7.68 Hz, 1H), 8.22 (s, 1H), 7.85–7.76 (m, 2H), 7.70 (d, *J* = 7.44 Hz, 1H), 7.56–7.54 (m, 2H), 7.35– 7.22 (m, 4H), 7.12 (d, *J* = 8.88 Hz, 3H), 4.18–4.15 (m, 1H), 3.18–3.11 (m, 1H), 2.95–2.88 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.5, 174.7, 159.4, 141.9, 139.3, 134.2, 134.0, 132.8, 132.6, 132.1, 131.6, 129.5, 129.1, 128.6, 127.9, 127.3, 126.5, 126.2, 122.1, 42.2, 37.0.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{24}H_{16}BrN_3O_3Na$, 496.0267; Found 496.0266.

methyl (*E*)-3-(2-(1-oxophthalazin-2(1*H*)-yl)phenyl)acrylate (3p)



Purified by column chromatography on silica gel using hexane/ethylacetate (70/30)

Yield: 51% from condition A, Off-white coloured solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.42 (d, *J* = 7.76 Hz, 1H), 8.22 (s, 1H), 7.81 (td, *J* = 7.36 Hz, 1H), 7.75 (td, *J* = 7.56 Hz, 1H), 7.72 (d, *J* = 8.12 Hz, 2H), 7.47–7.40 (m, 3H), 7.37 (td, *J* = 7.6 Hz, 1H), 6.39 (d, *J* = 15.92 Hz, 1H), 3.61 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.9, 159.5, 141.1, 139.6, 138.8, 133.8, 132.2, 131.8, 130.9, 129.7, 129.2, 128.4, 128.2, 127.3, 127.2, 126.4, 120.2, 51.6.

HRMS (ESI) m/z: $[M+Na]^+$ Calculated for $C_{18}H_{14}N_2O_3Na$, 329.0897; Found 329.0897.

8. References

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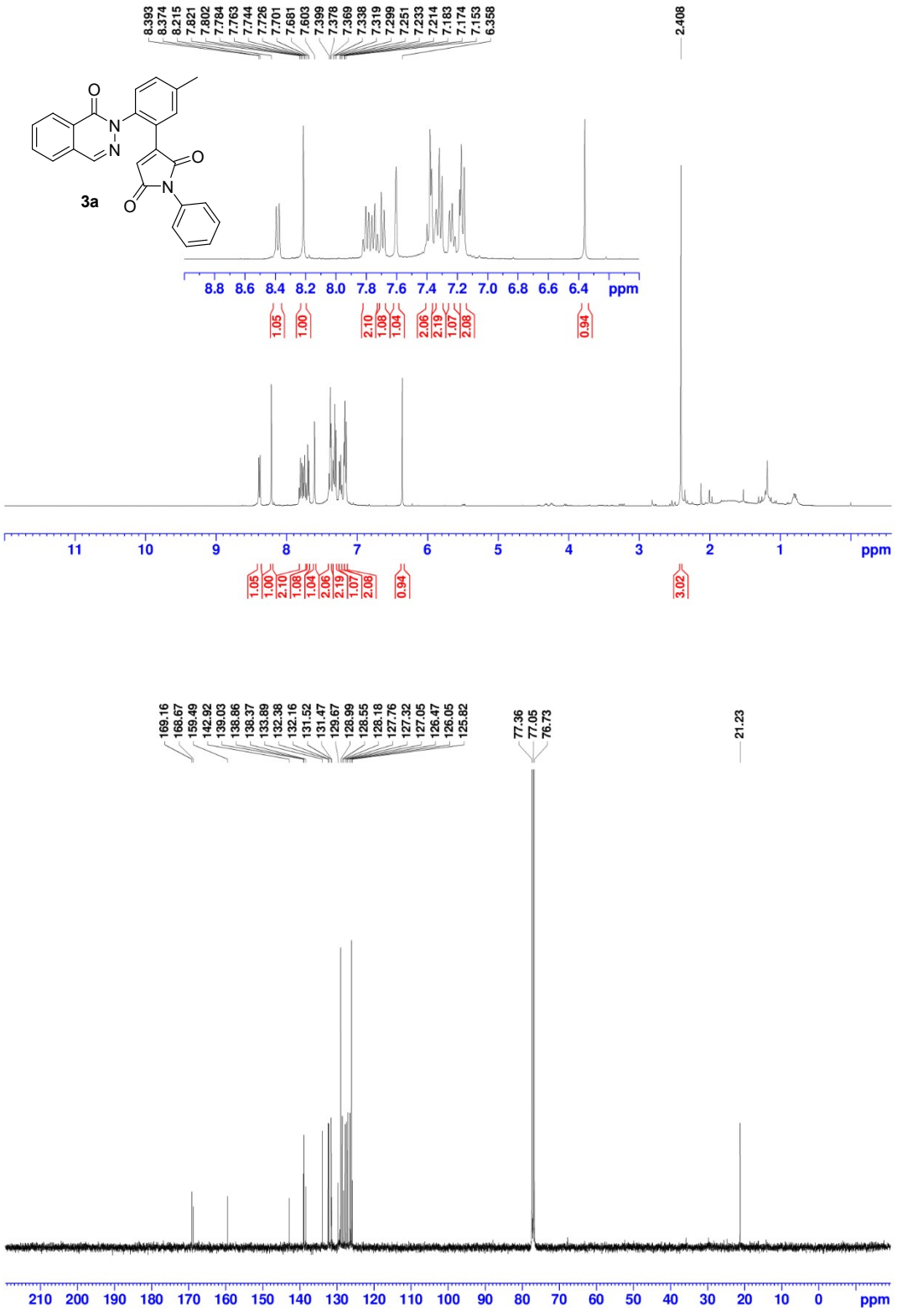
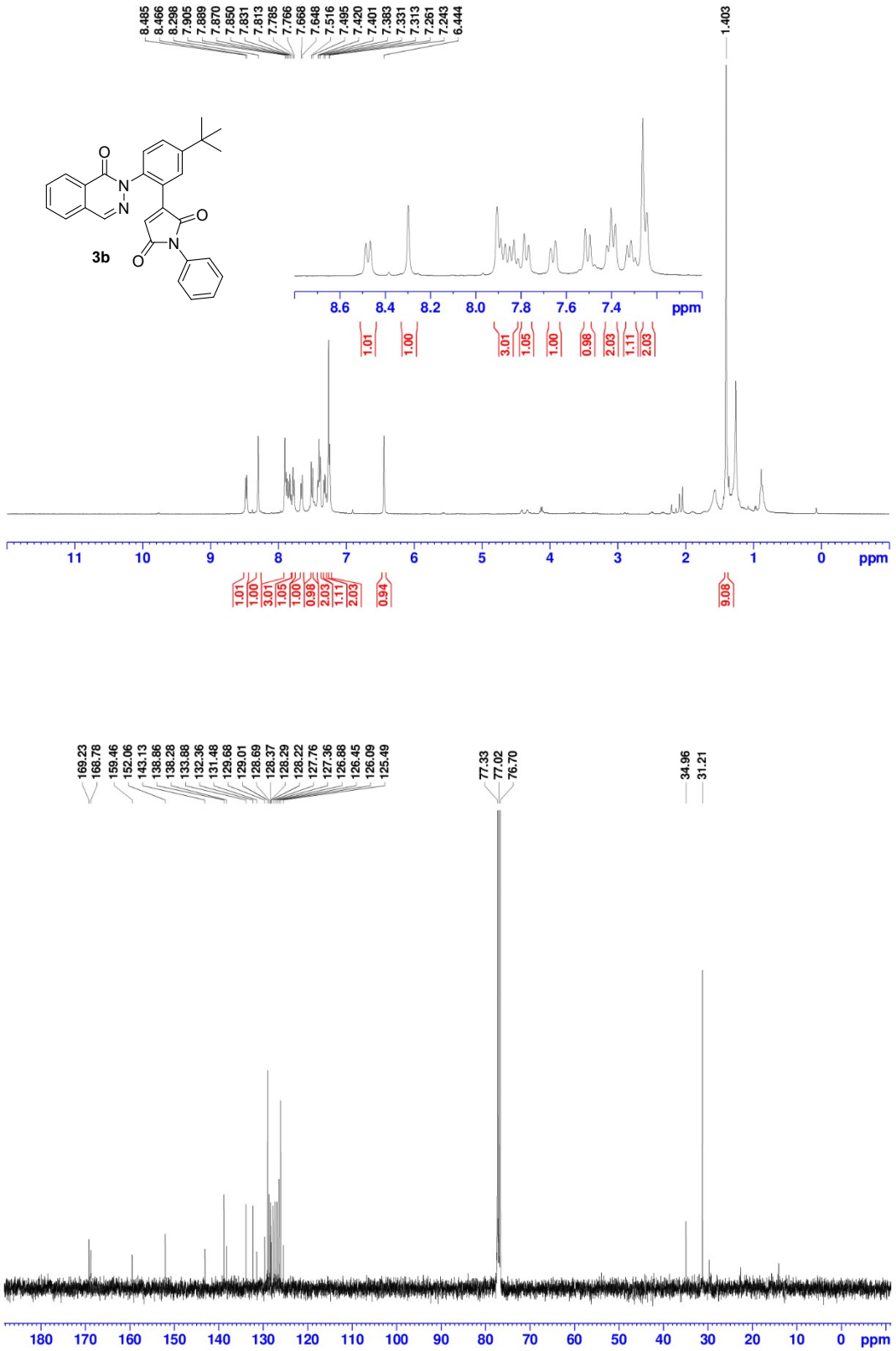
9. Copies of ^{1}H, ^{13}C and ^{19}F NMR spectra of synthesized derivatives

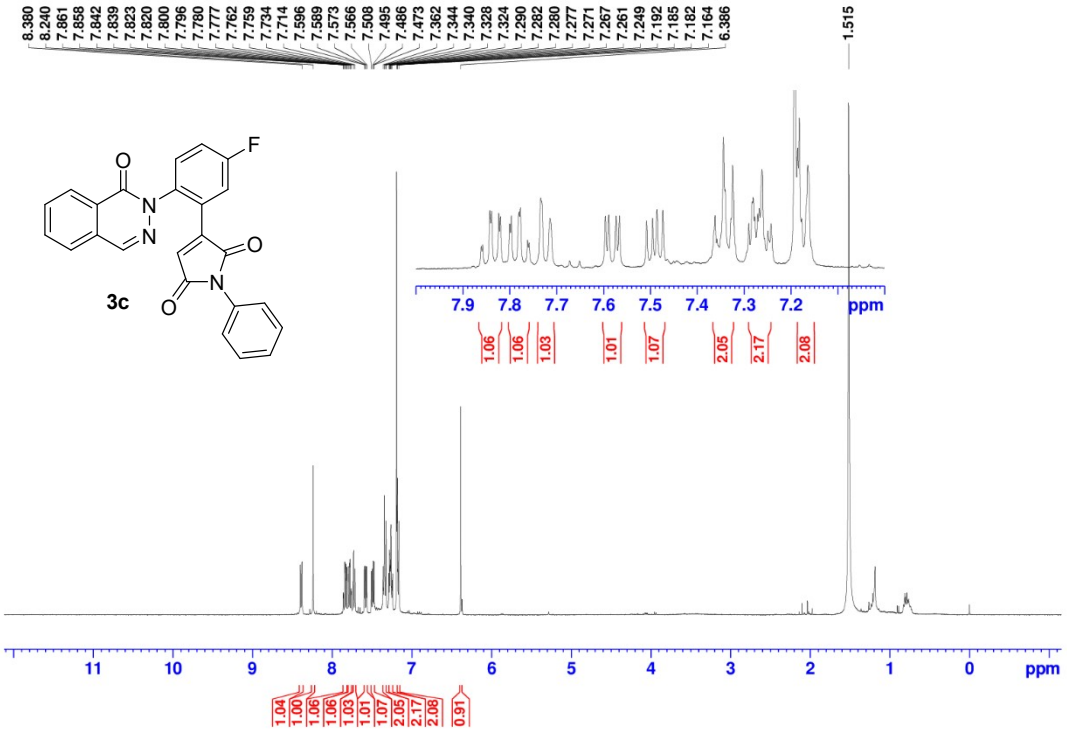
^{1}H and ^{13}C NMR spectrum of 3a



^{1}H and ^{13}C NMR spectrum of 3b



^{1}H, ^{13}C NMR and ^{19}F spectrum of 3c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1.06 1.06 1.03 1.01 1.07 2.05 2.17 2.08
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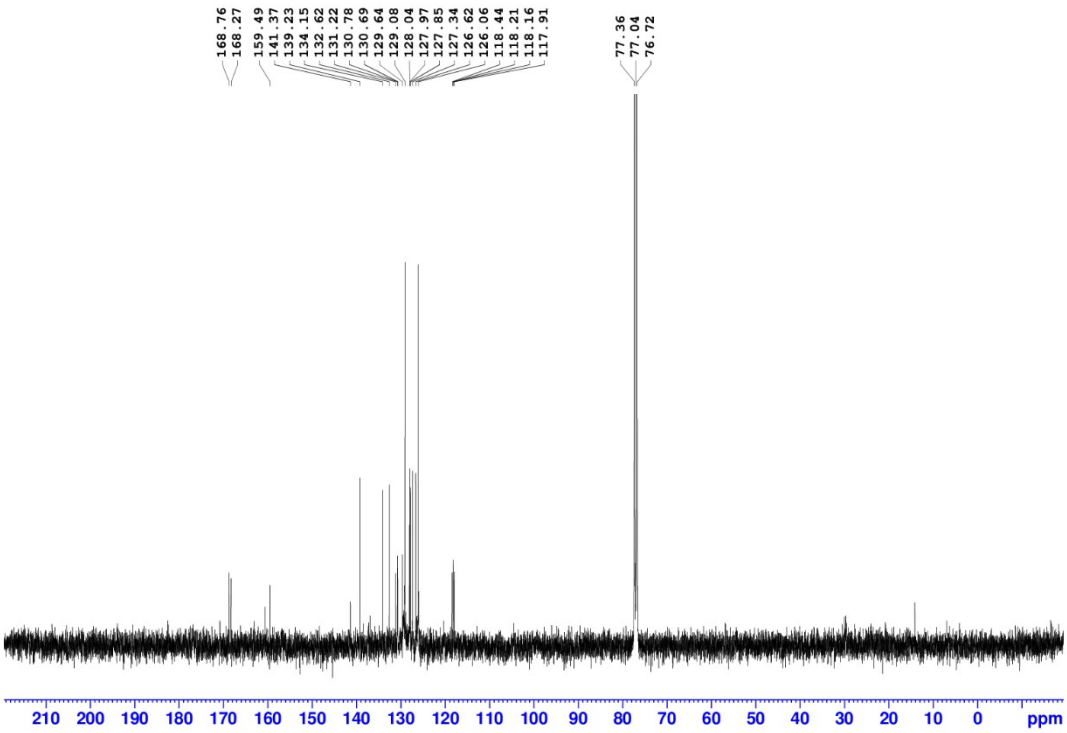
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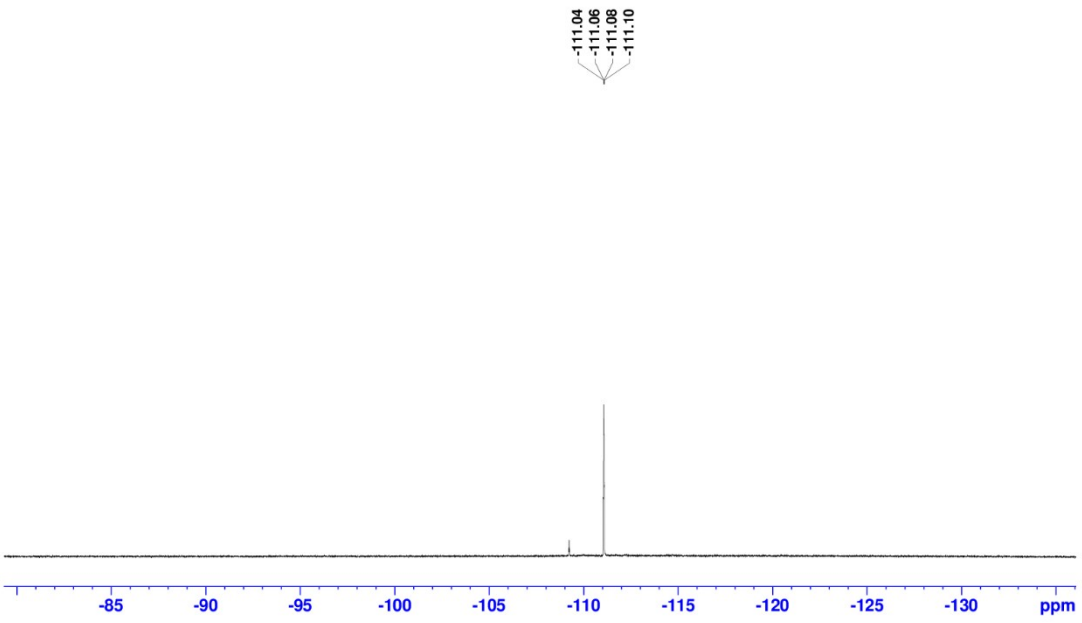
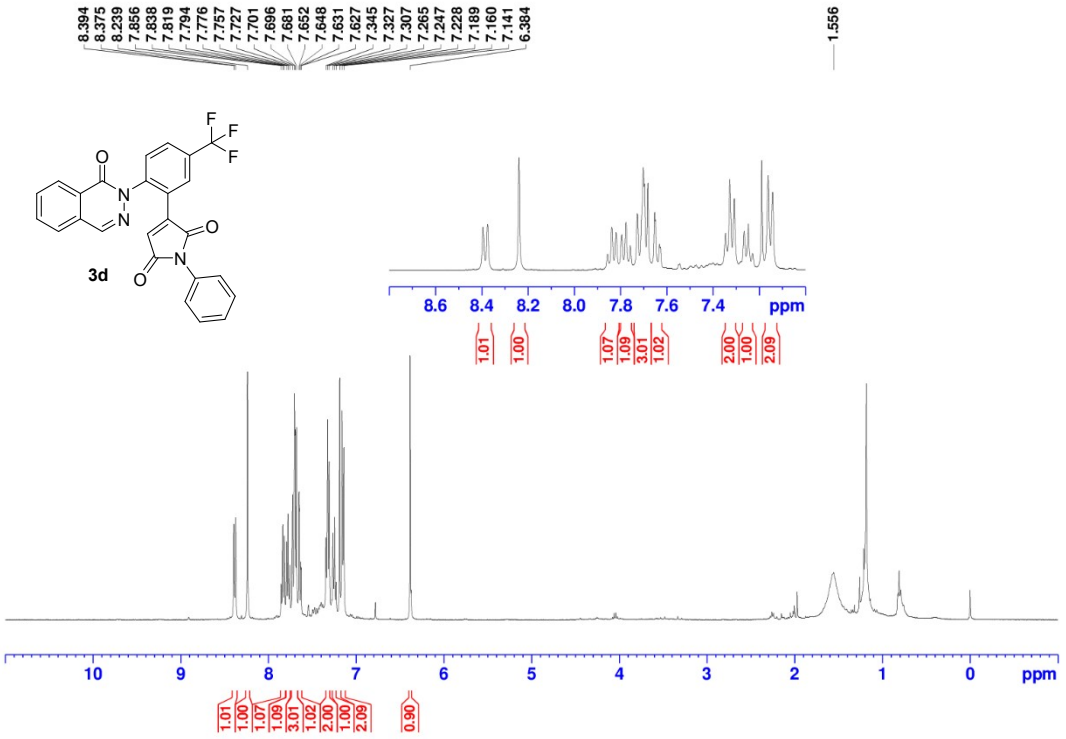
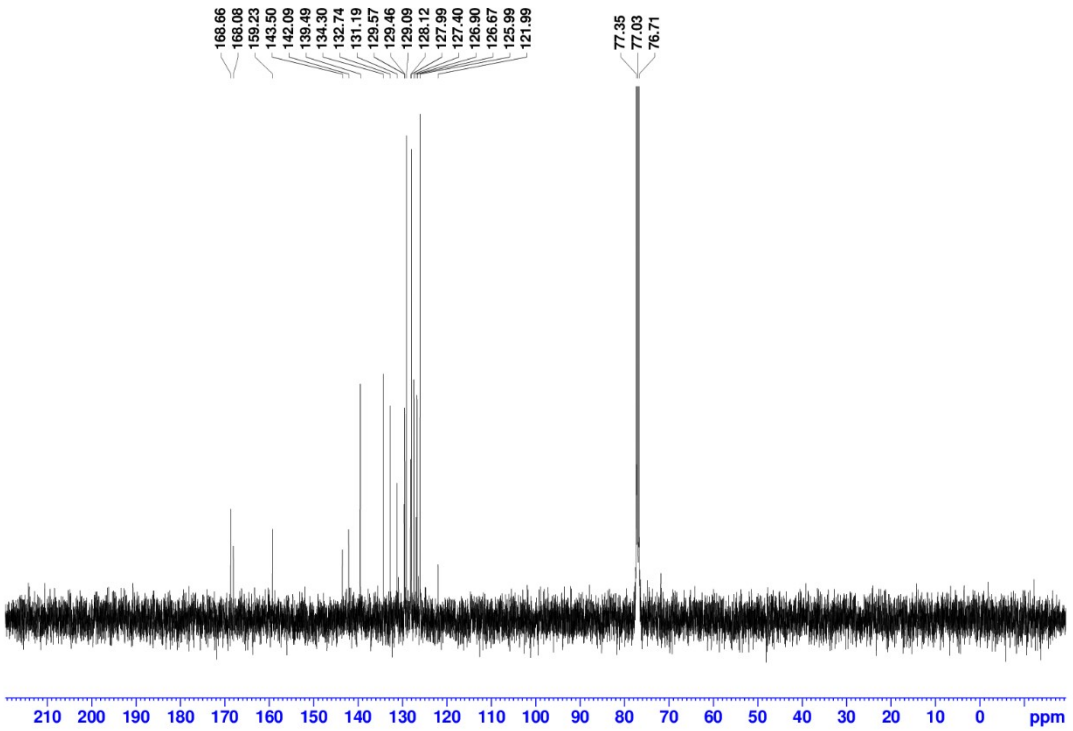
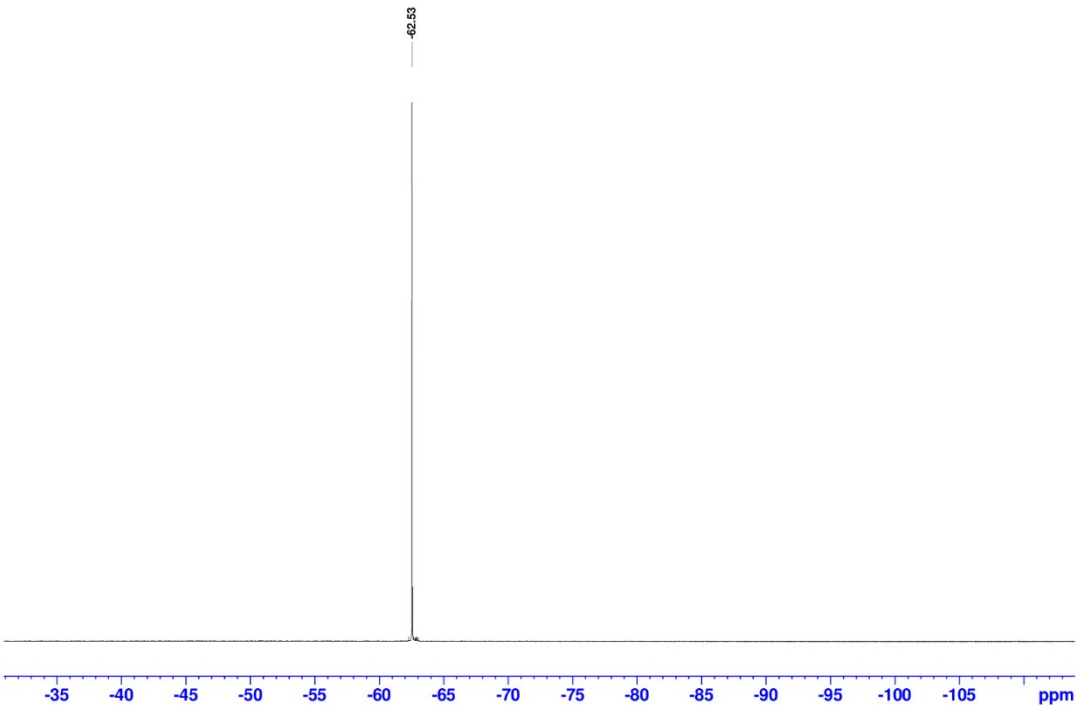
126.62
126.06
118.44
118.21
118.16
117.91
77.36
77.04
76.72
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


-111.04
-111.06
-111.08
-111.10
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
ppm

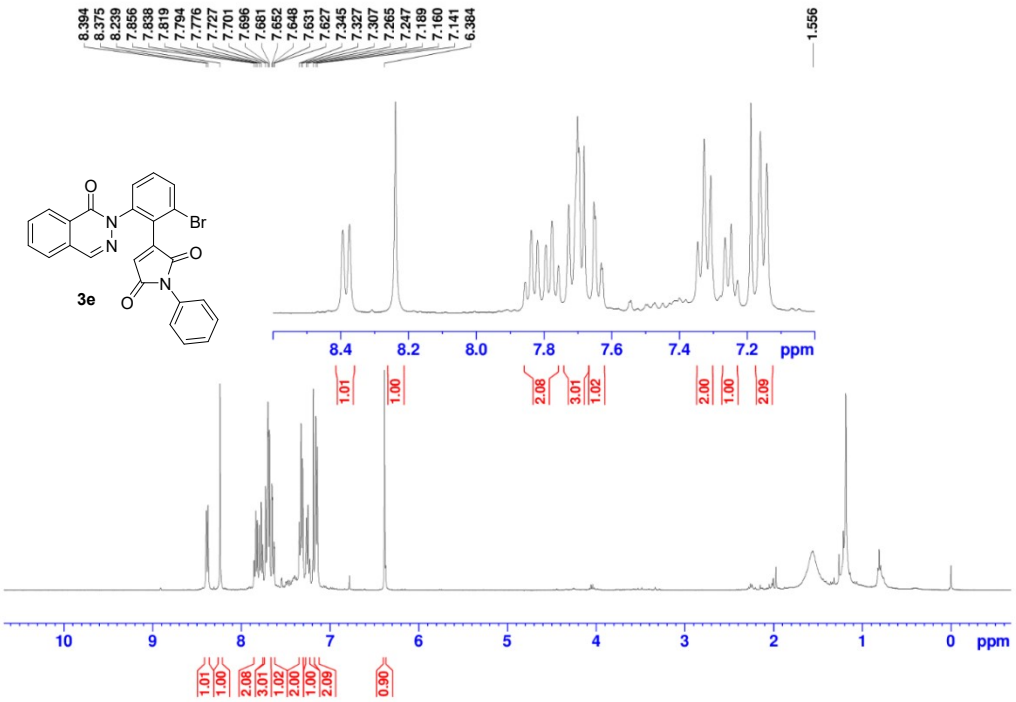
^{1}H, ^{13}C NMR and ^{19}F spectrum of 3d

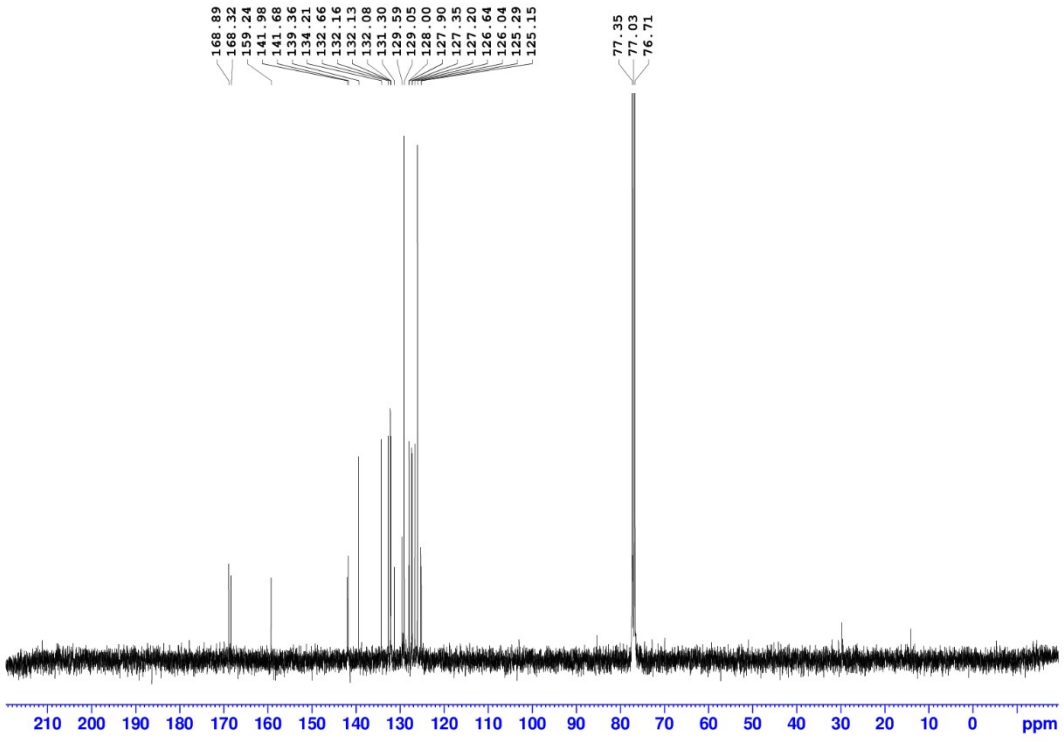




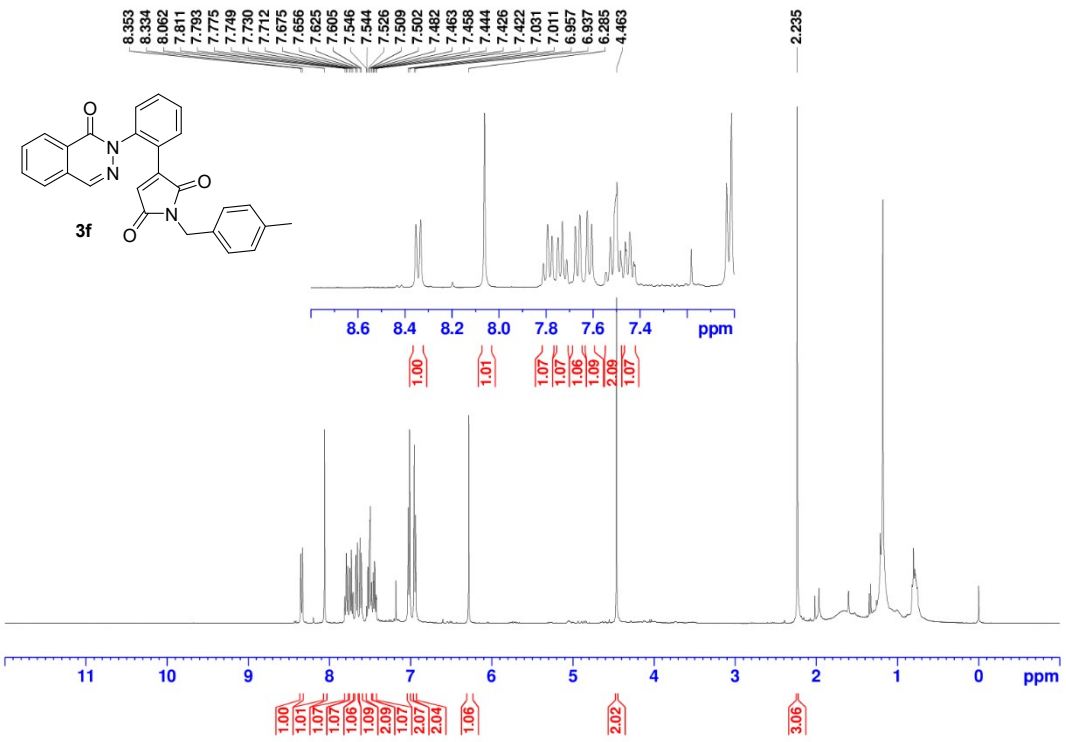

-62.53
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
ppm

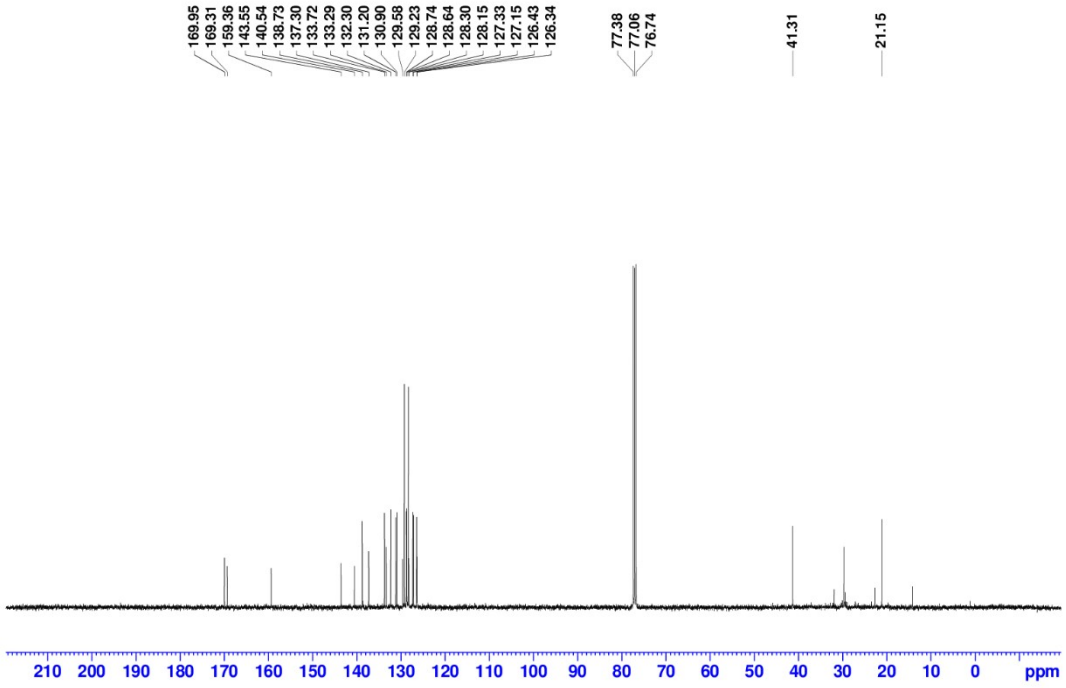
^{1}H and ^{13}C NMR spectrum of 3e



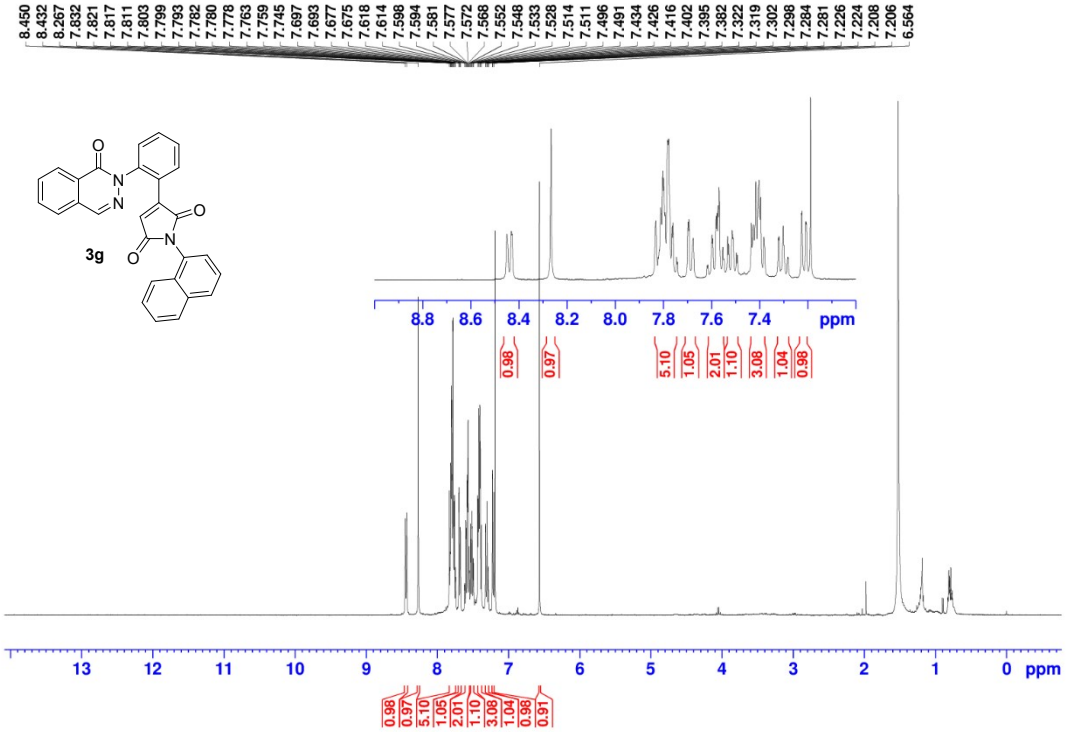


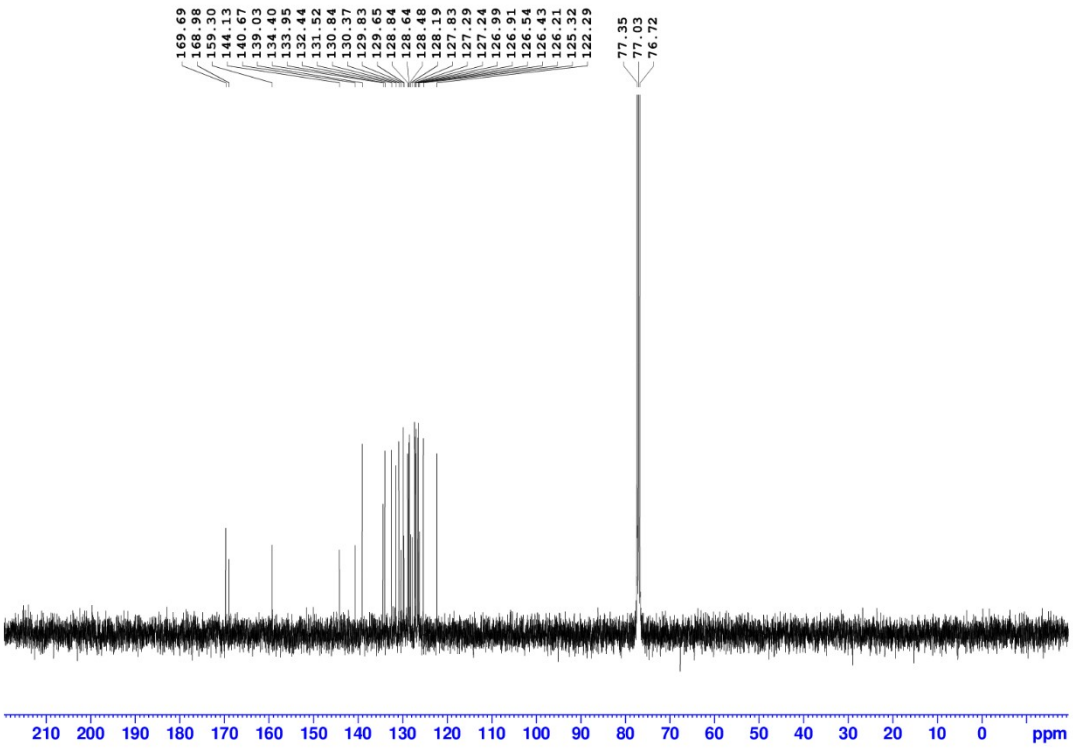
^{1}H and ^{13}C NMR spectrum of 3f



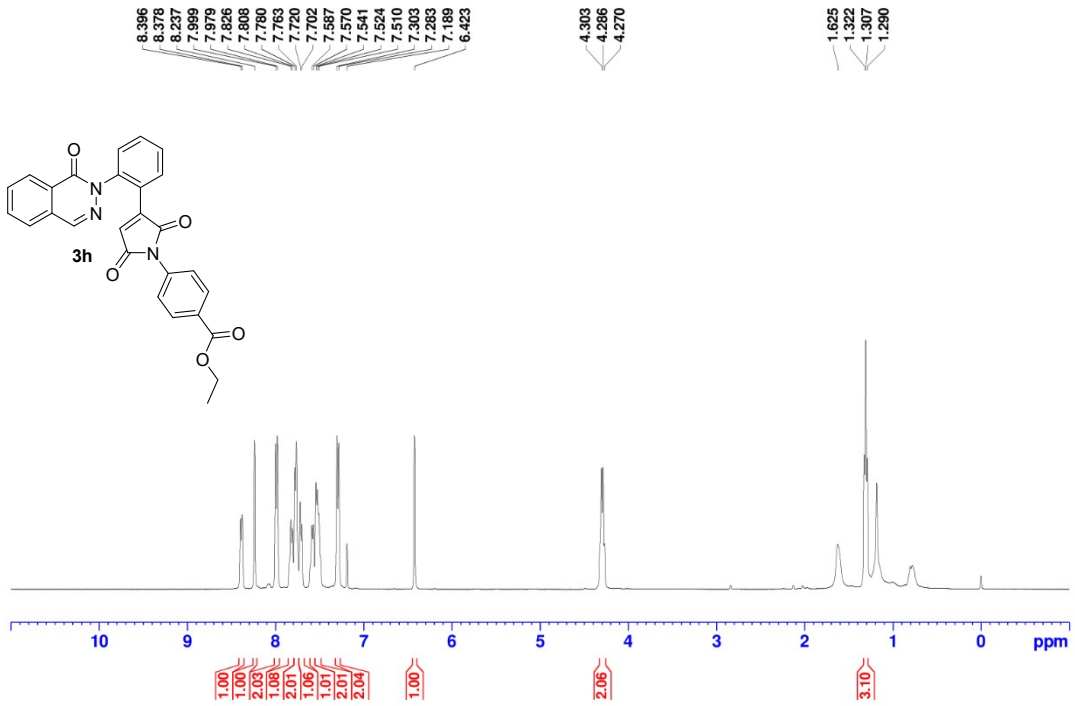


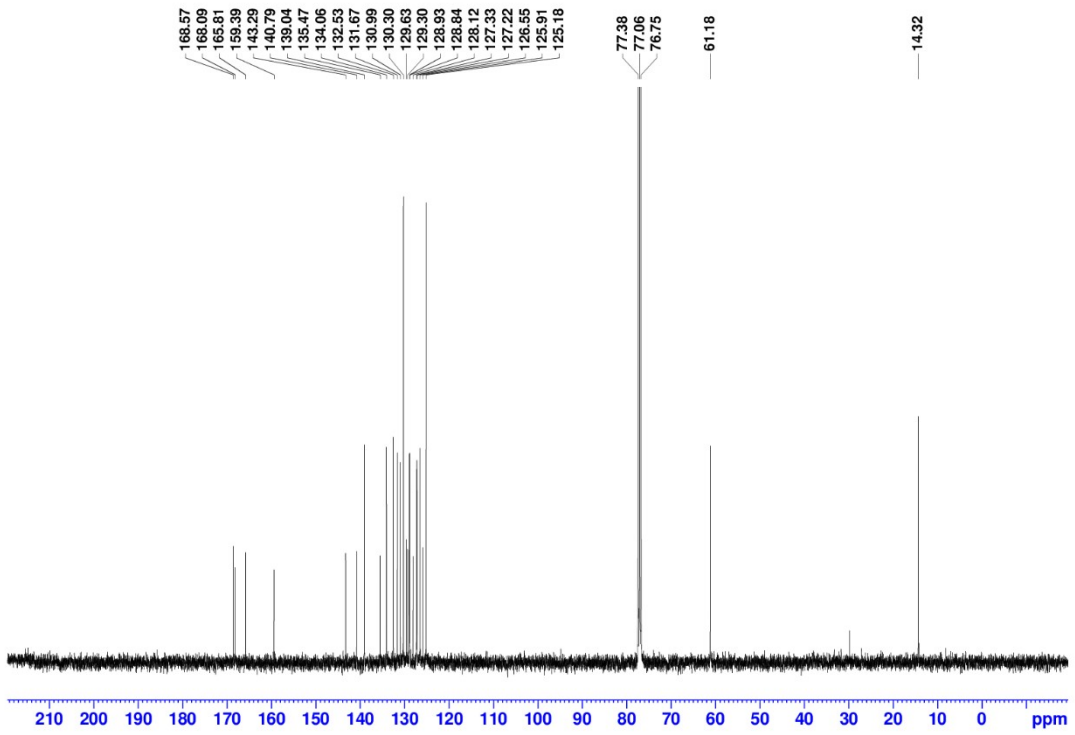
^{1}H and ^{13}C NMR spectrum of 3g



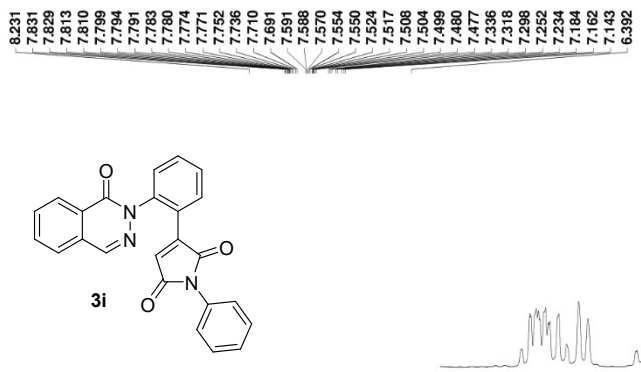


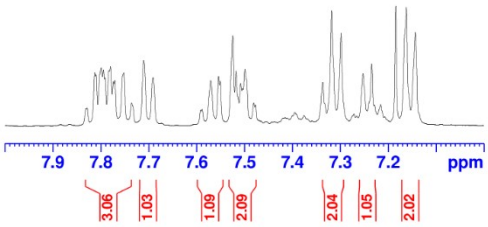
^{1}H and ^{13}C NMR spectrum of 3h

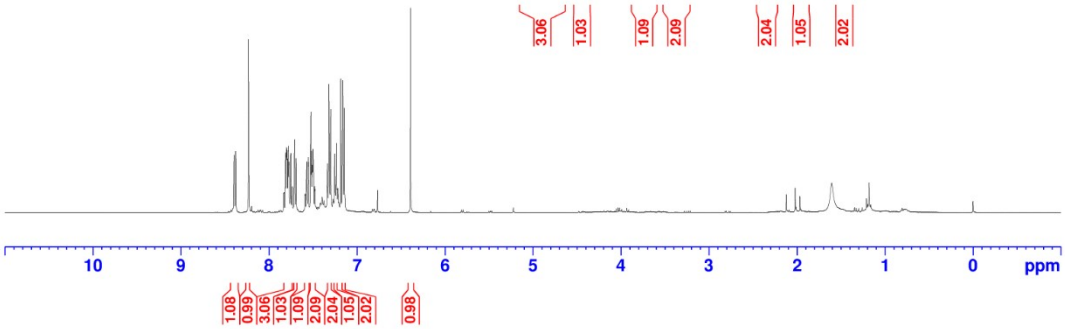


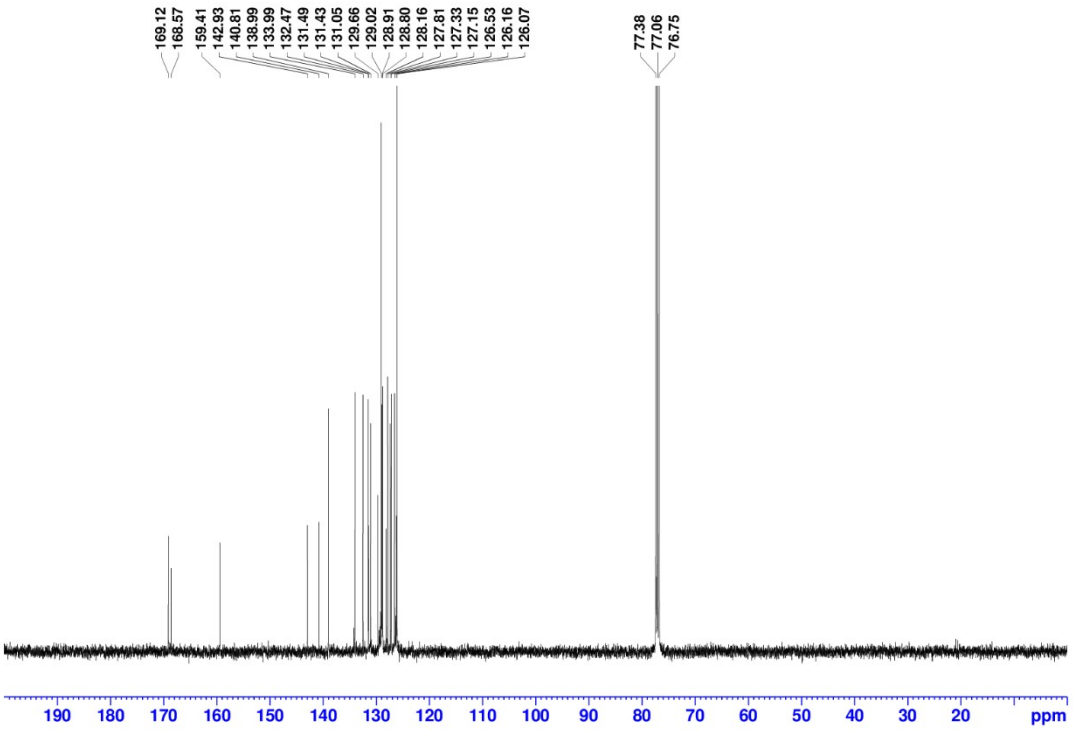


^{1}H and ^{13}C NMR spectrum of 3i

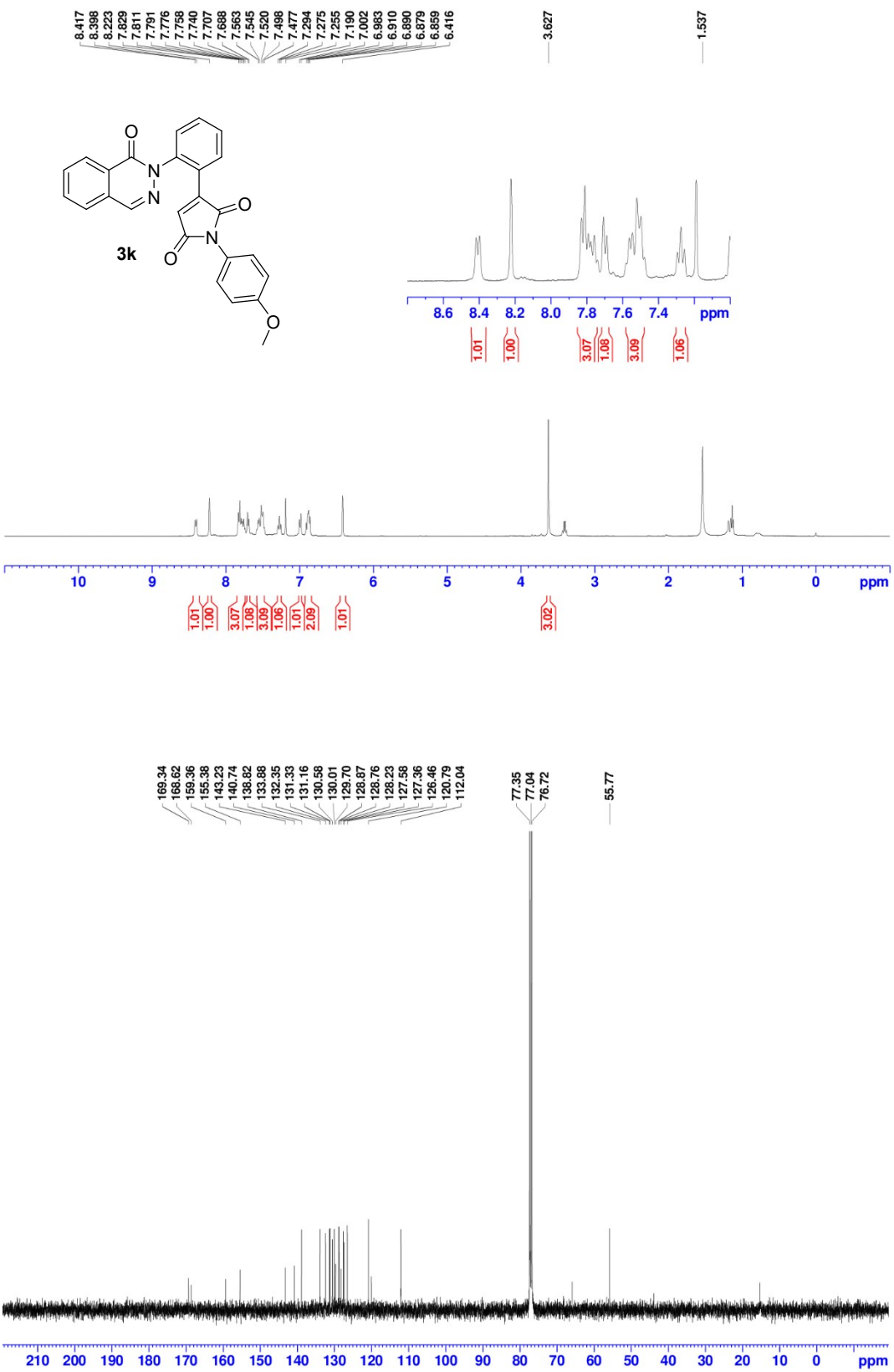




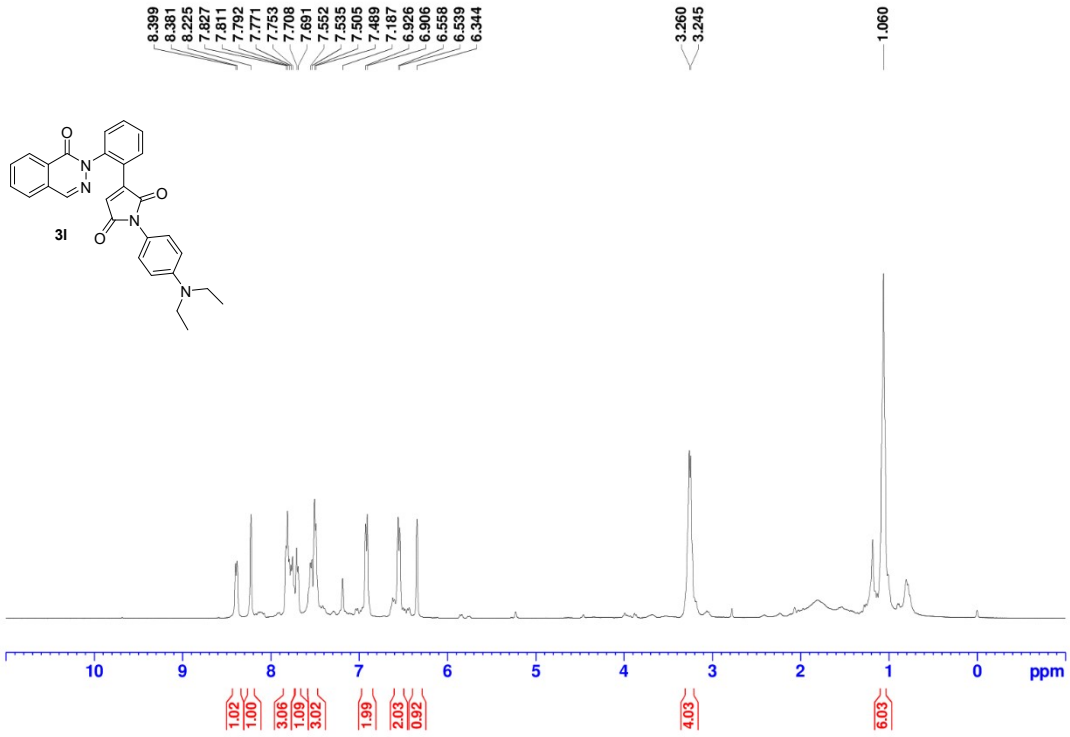


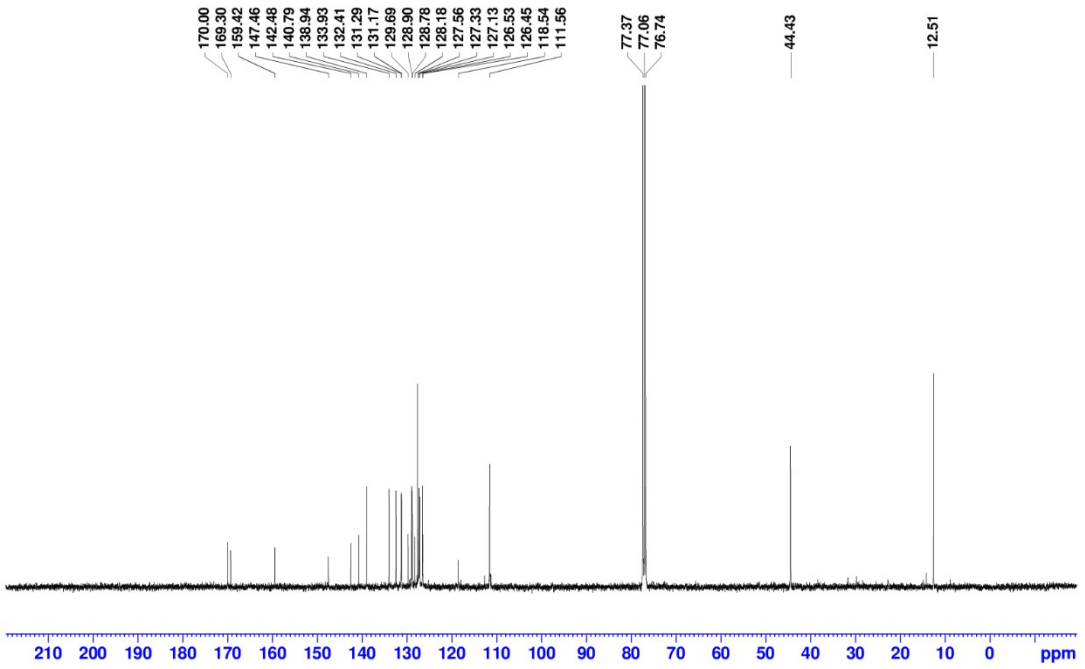


^{1}H and ^{13}C NMR spectrum of 3k

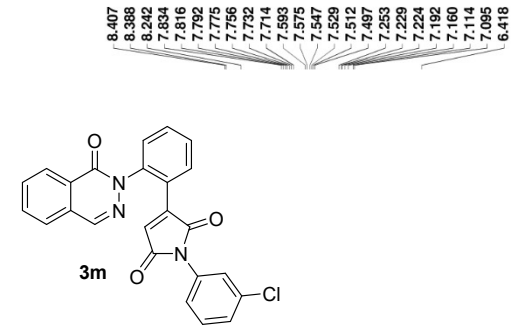


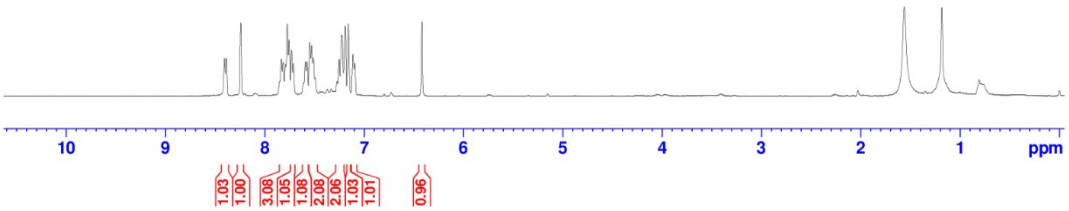
^{1}H and ^{13}C NMR spectrum of 3l

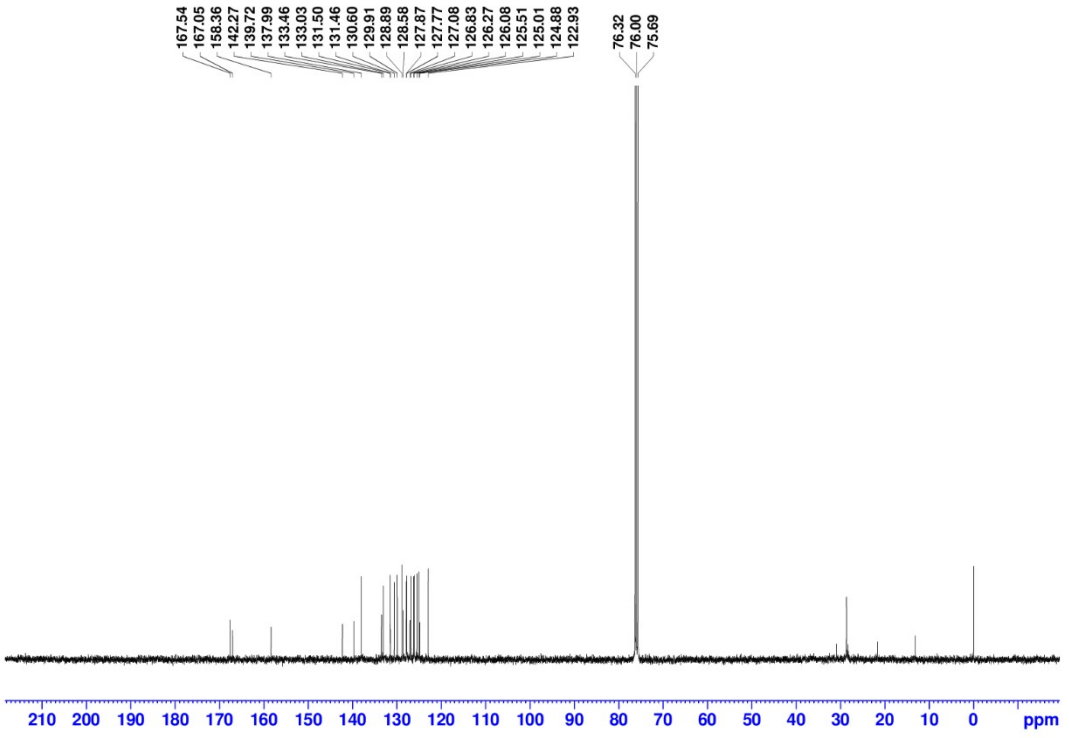




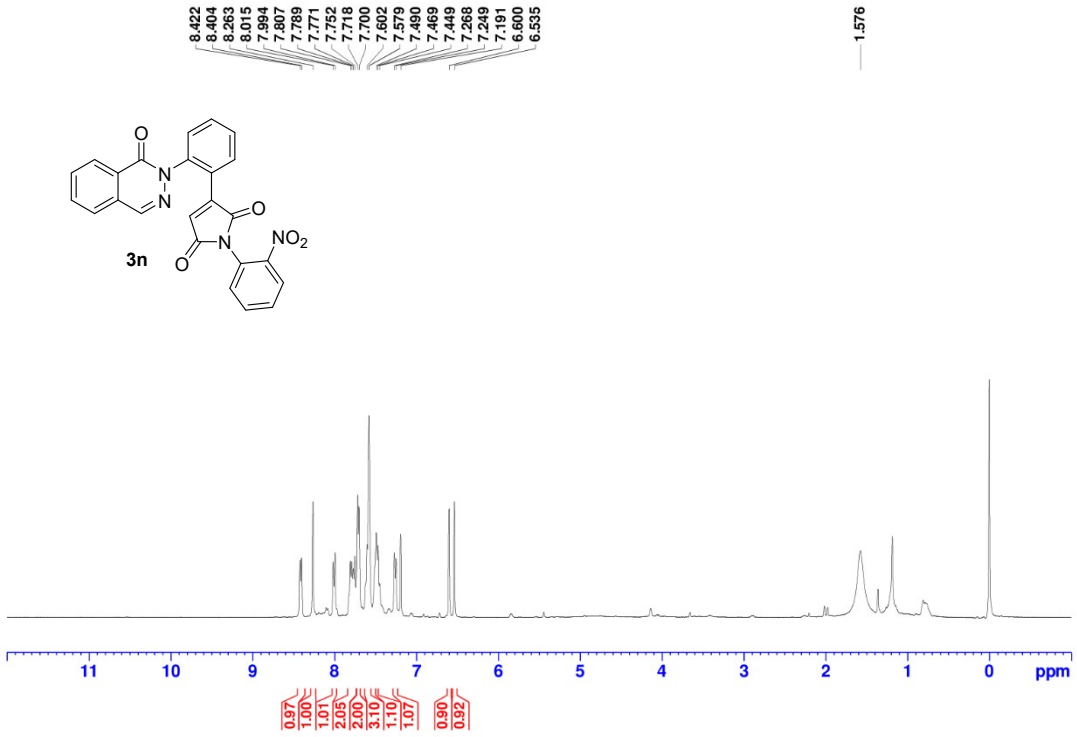
^{1}H and ^{13}C NMR spectrum of 3m

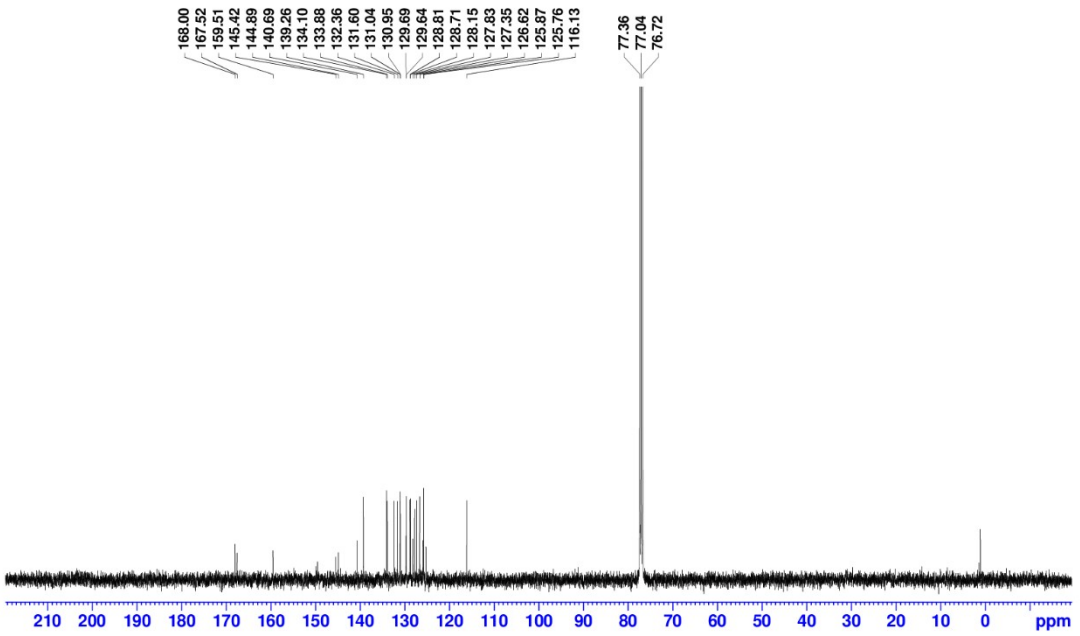




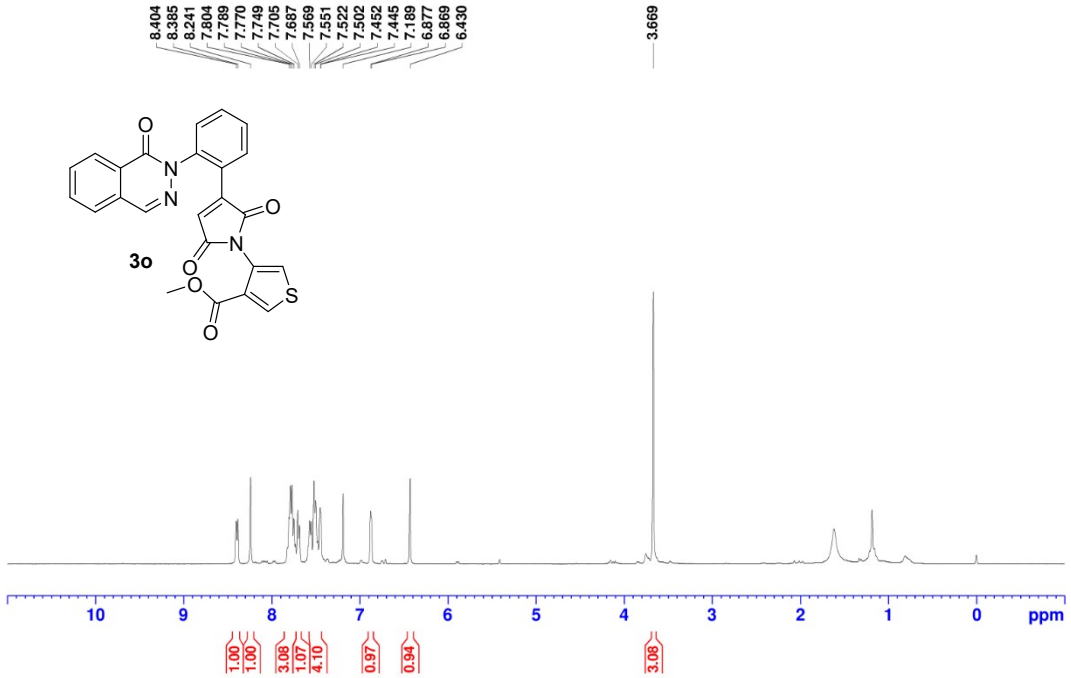


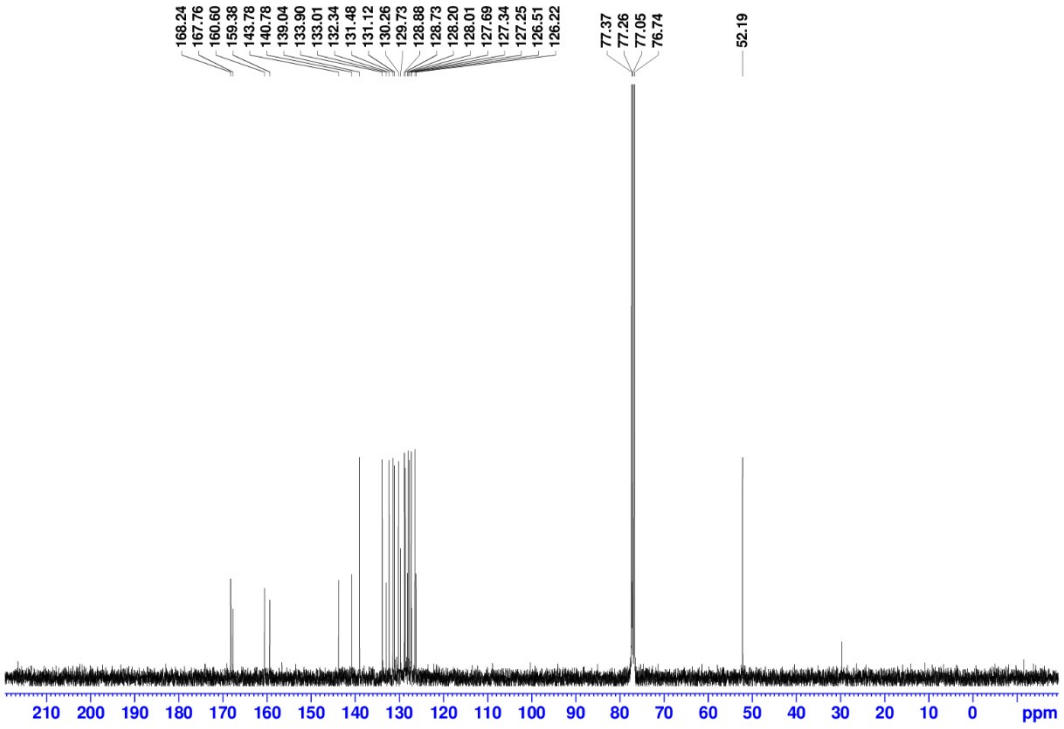
^{1}H and ^{13}C NMR spectrum of 3n



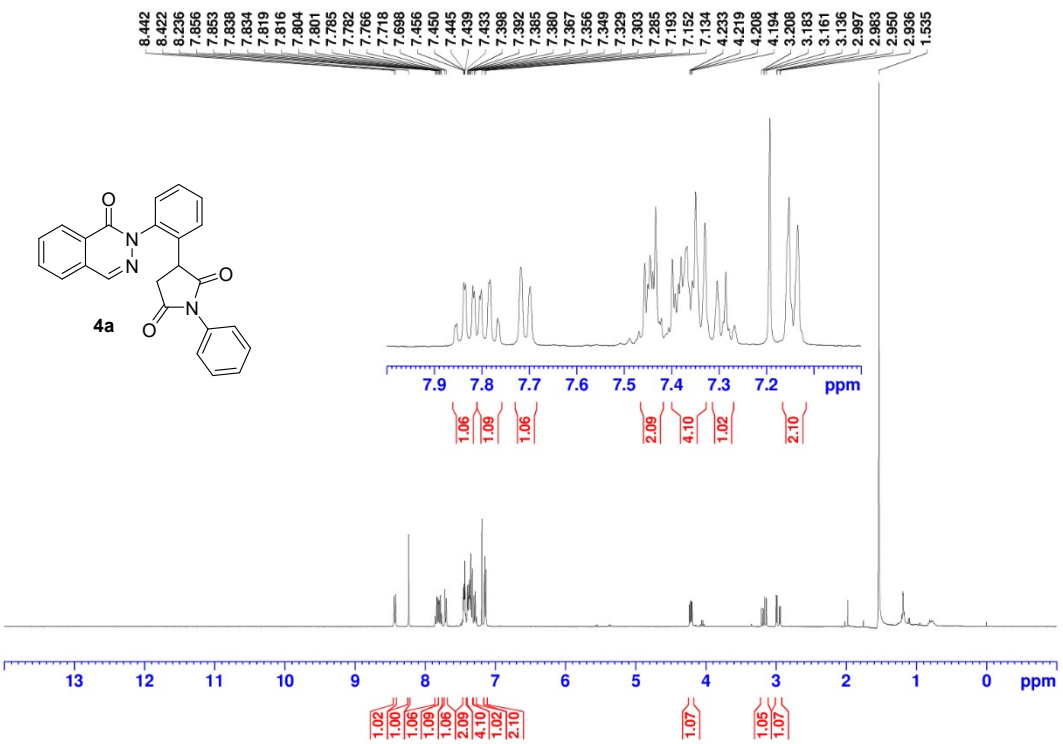


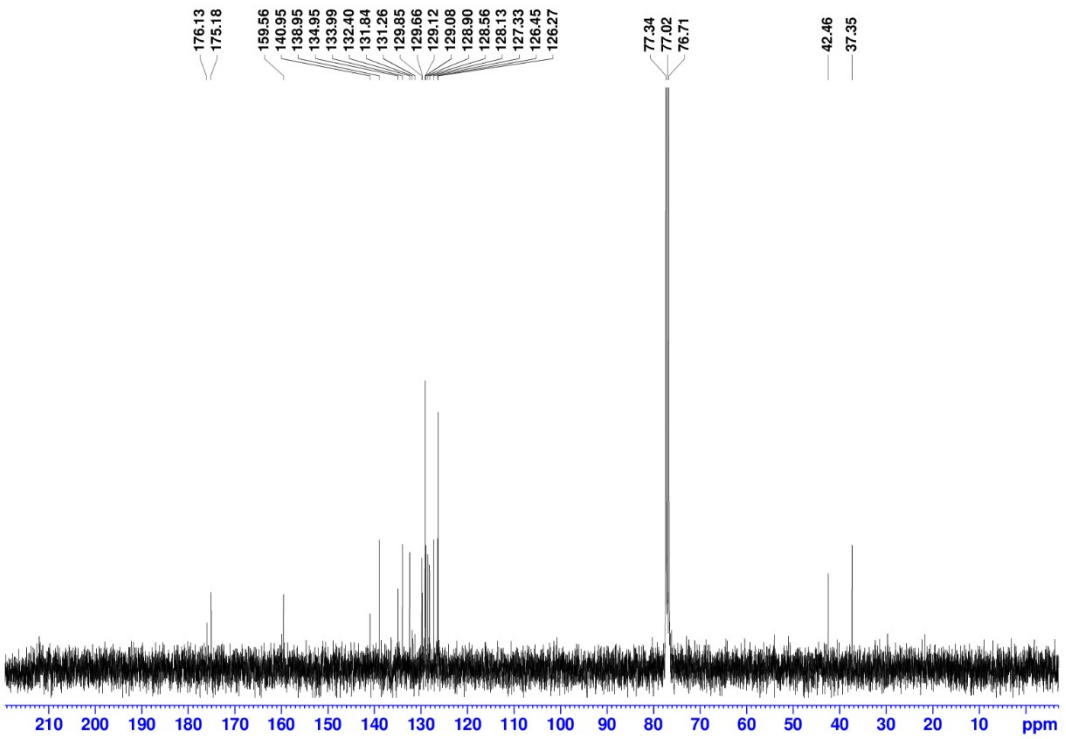
^{1}H and ^{13}C NMR spectrum of 3o



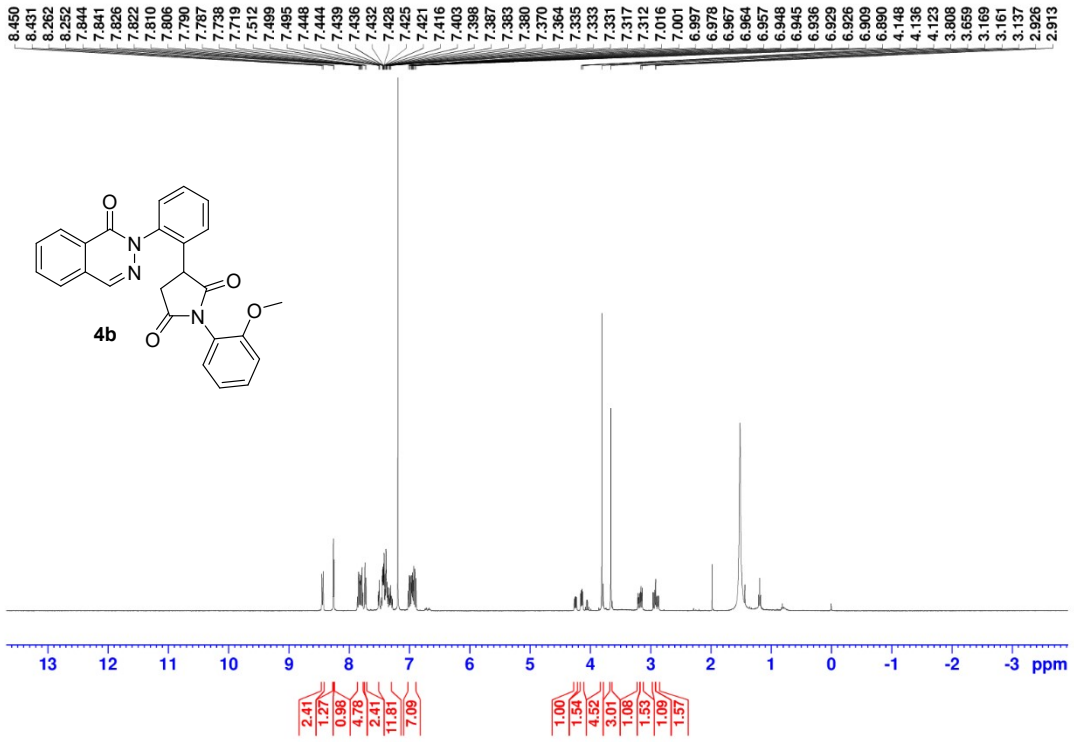


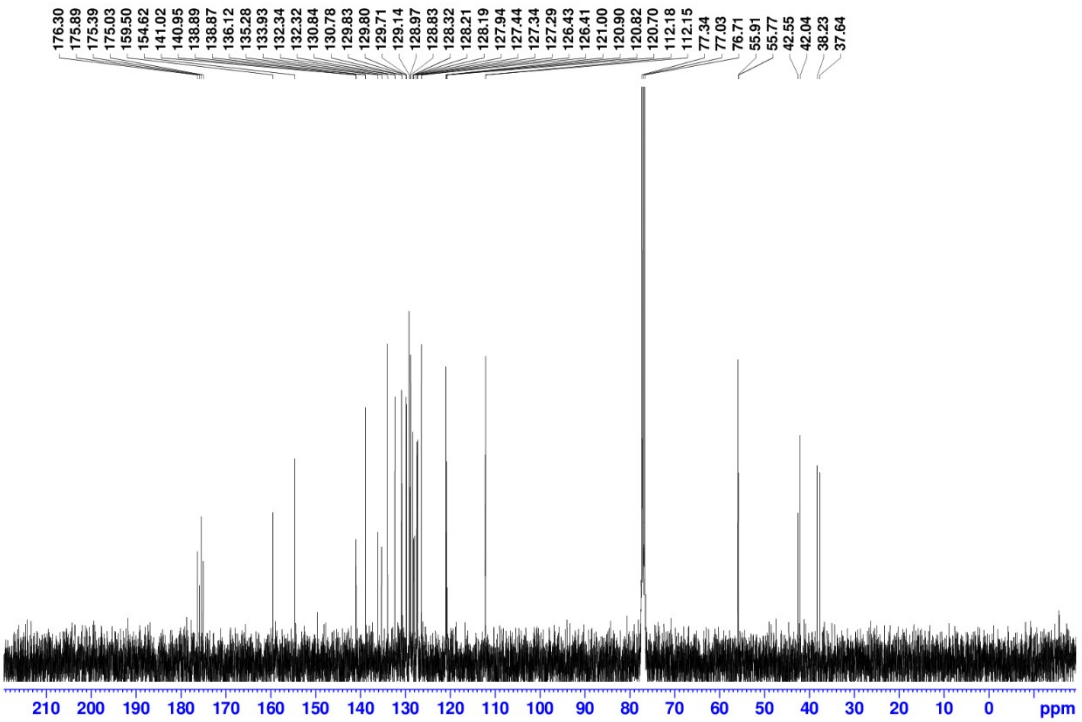
^{1}H and ^{13}C NMR spectrum of 4a



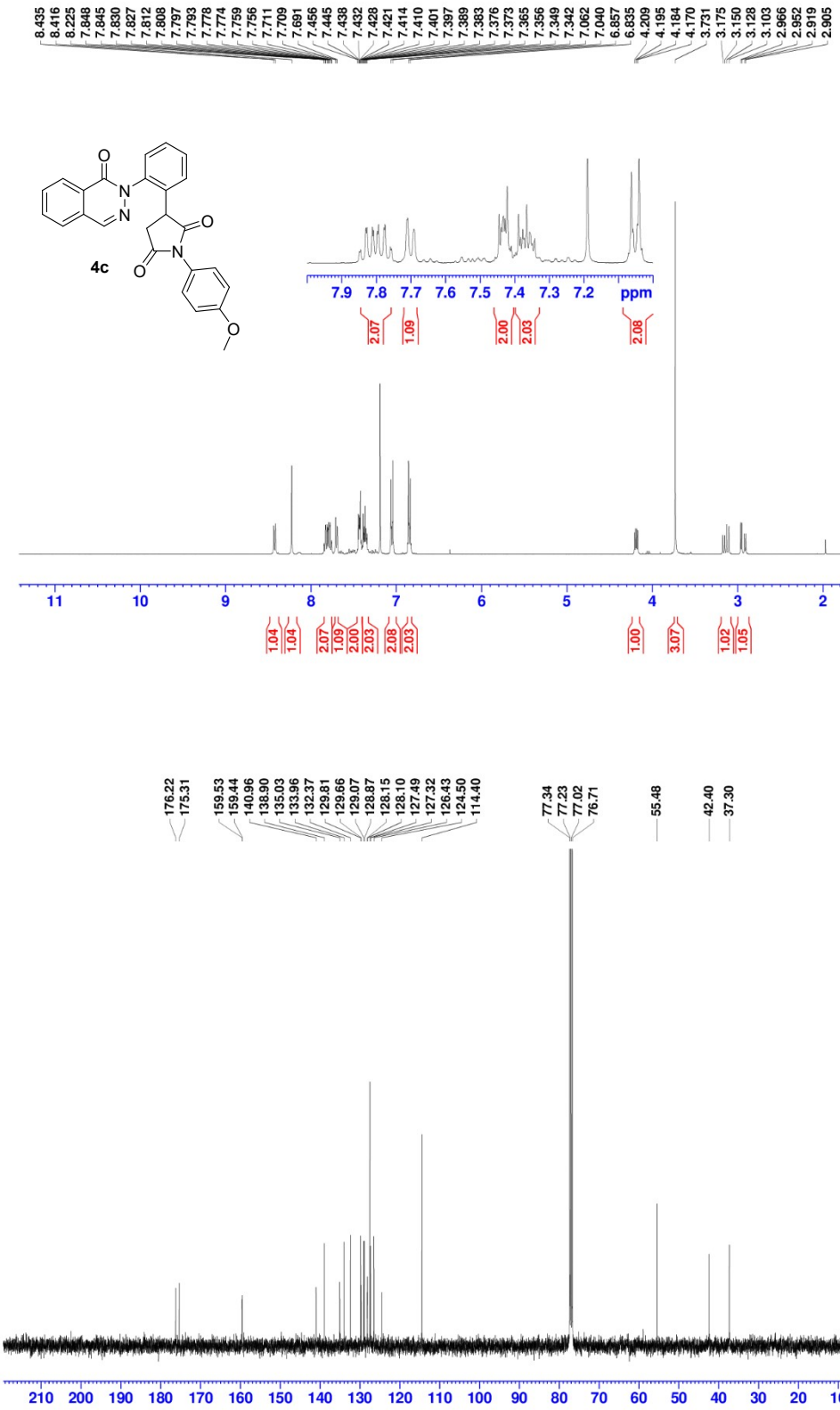


^{1}H and ^{13}C NMR spectrum of 4b

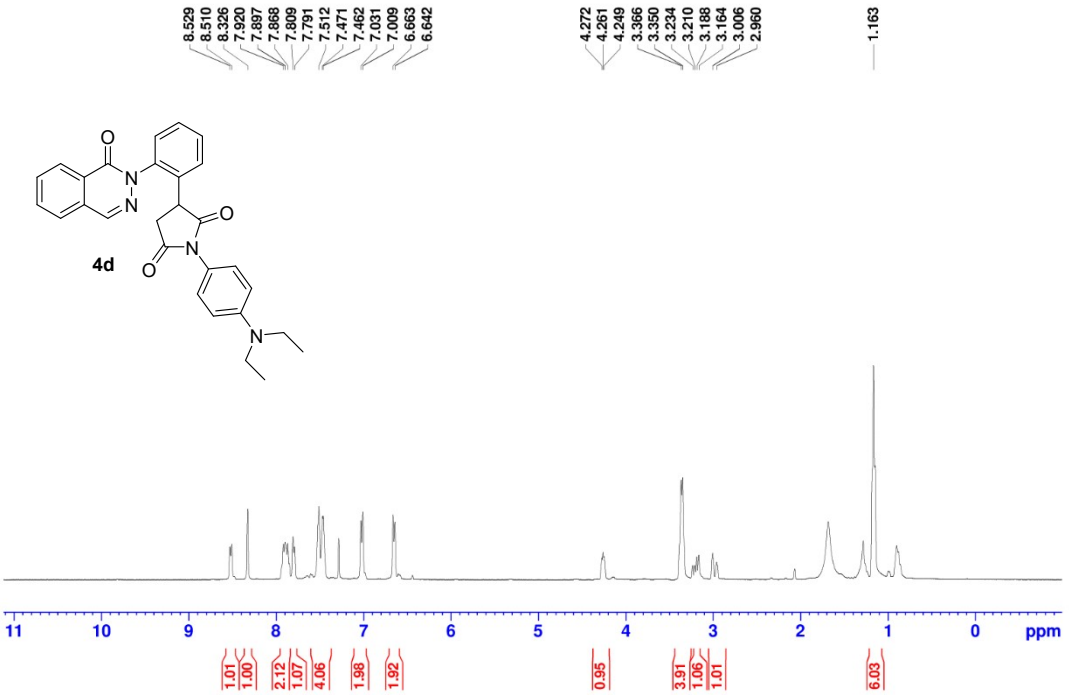


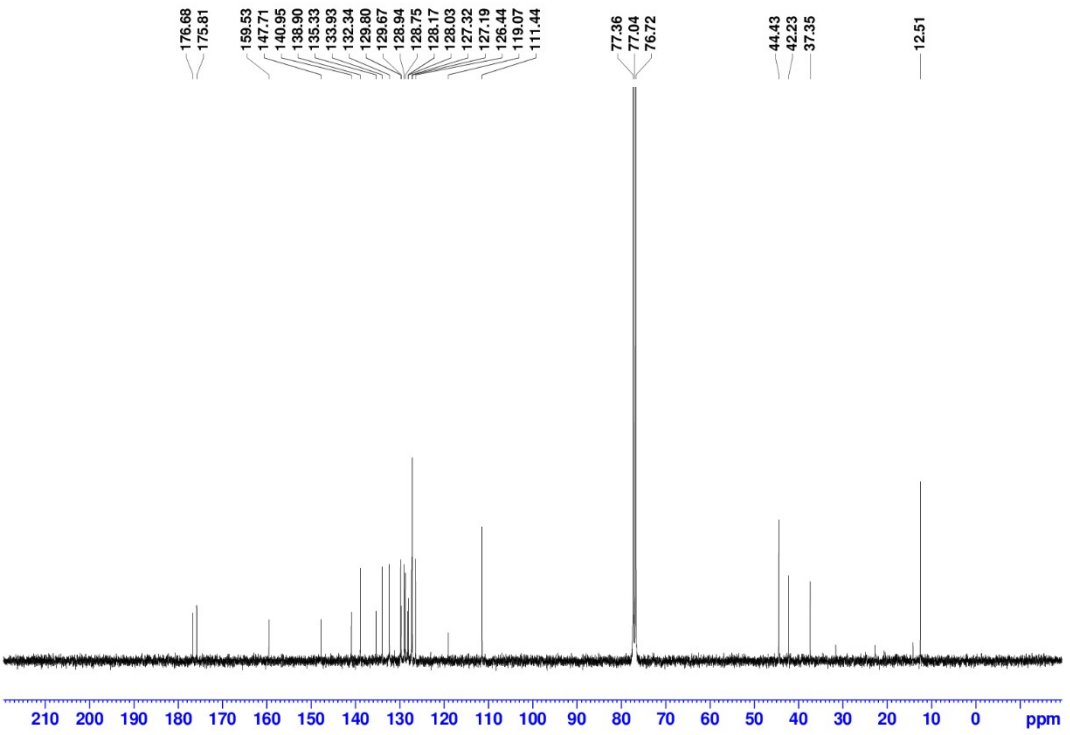


^{1}H and ^{13}C NMR spectrum of 4c

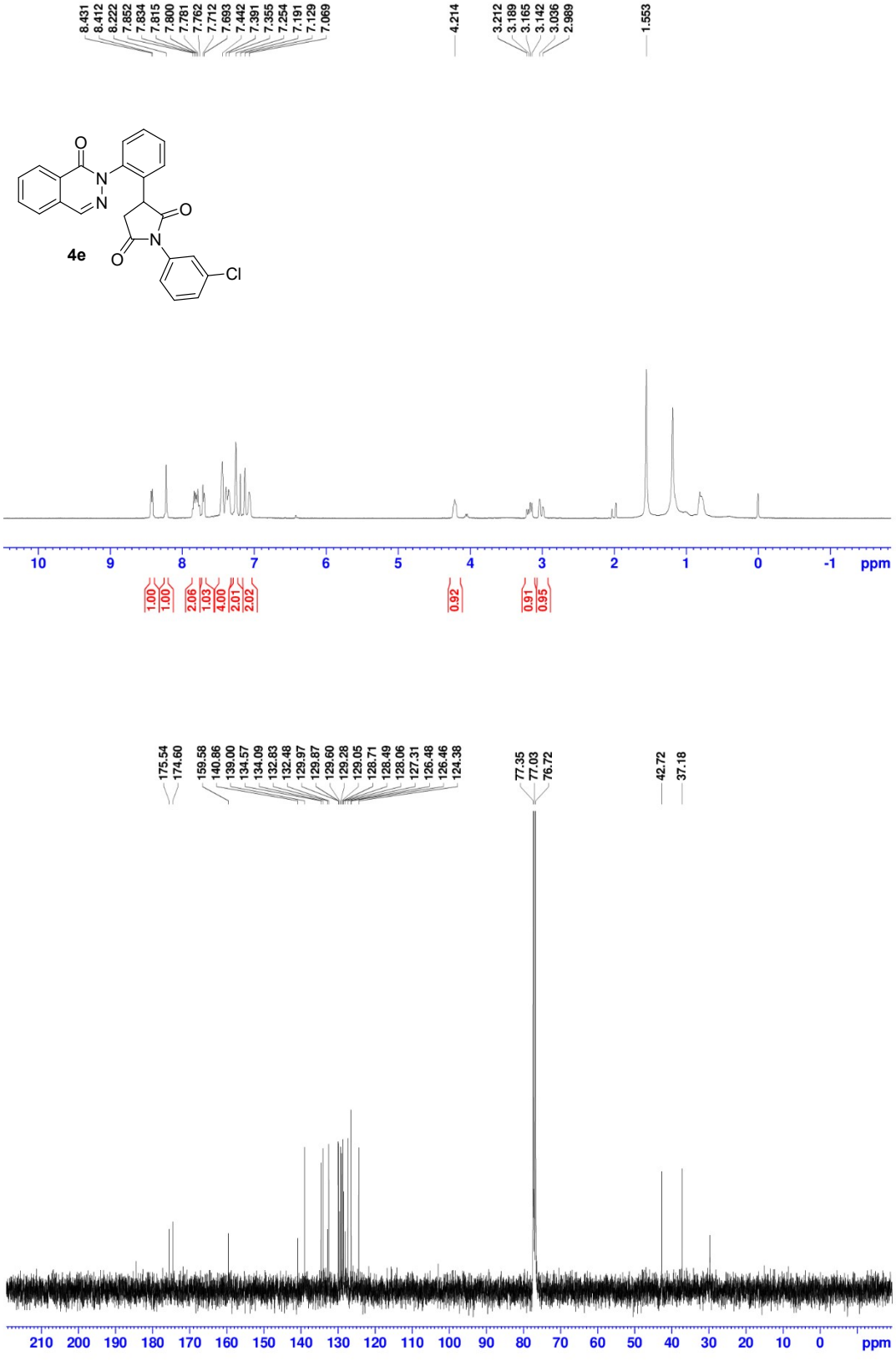


^{1}H and ^{13}C NMR spectrum of 4d

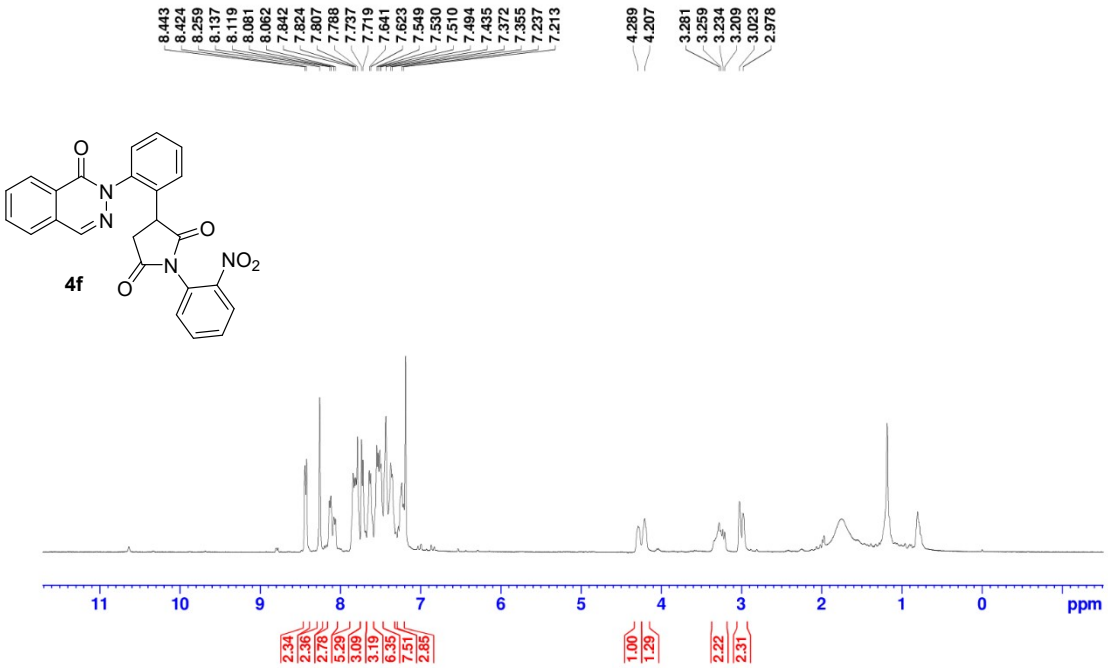


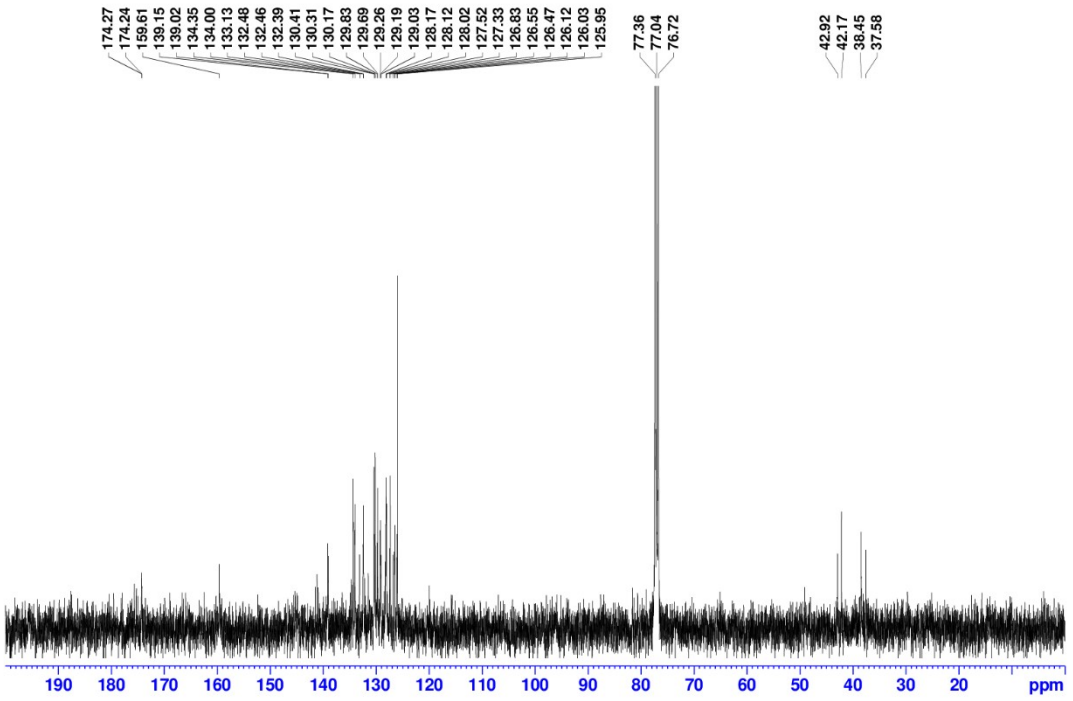


^{1}H and ^{13}C NMR spectrum of 4e

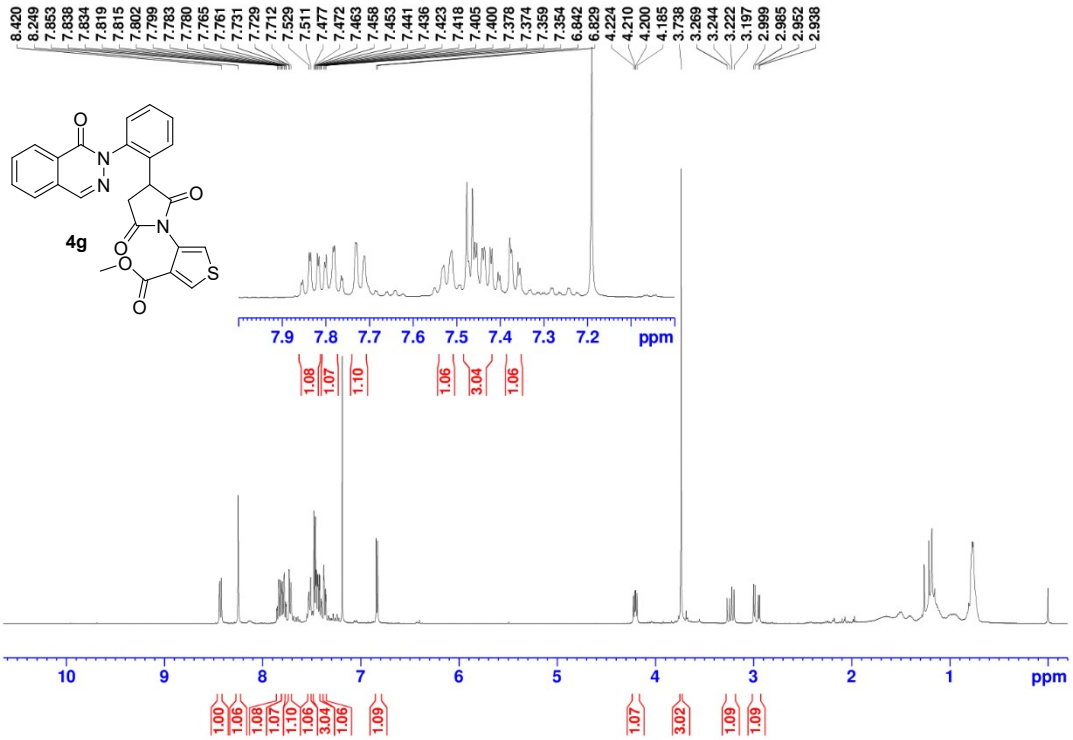


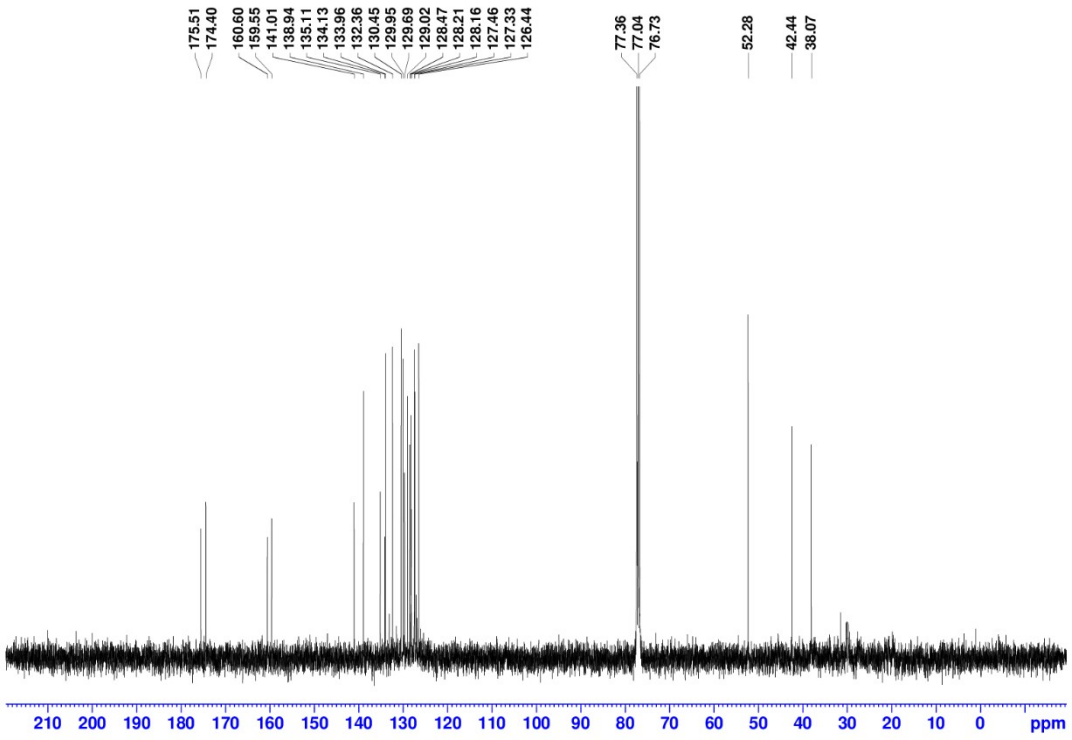
^{1}H and ^{13}C NMR spectrum of 4f



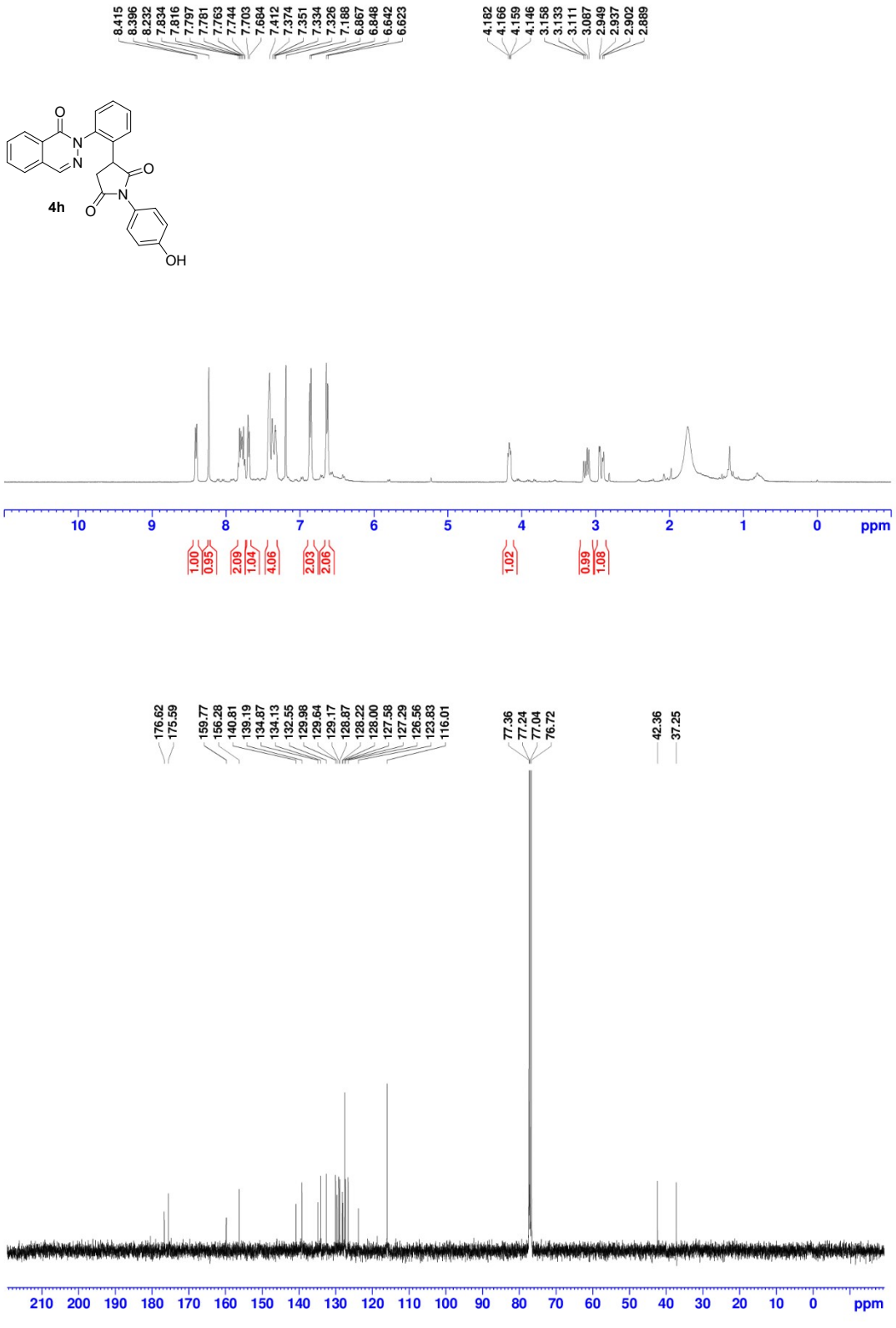


^{1}H and ^{13}C NMR spectrum of 4g

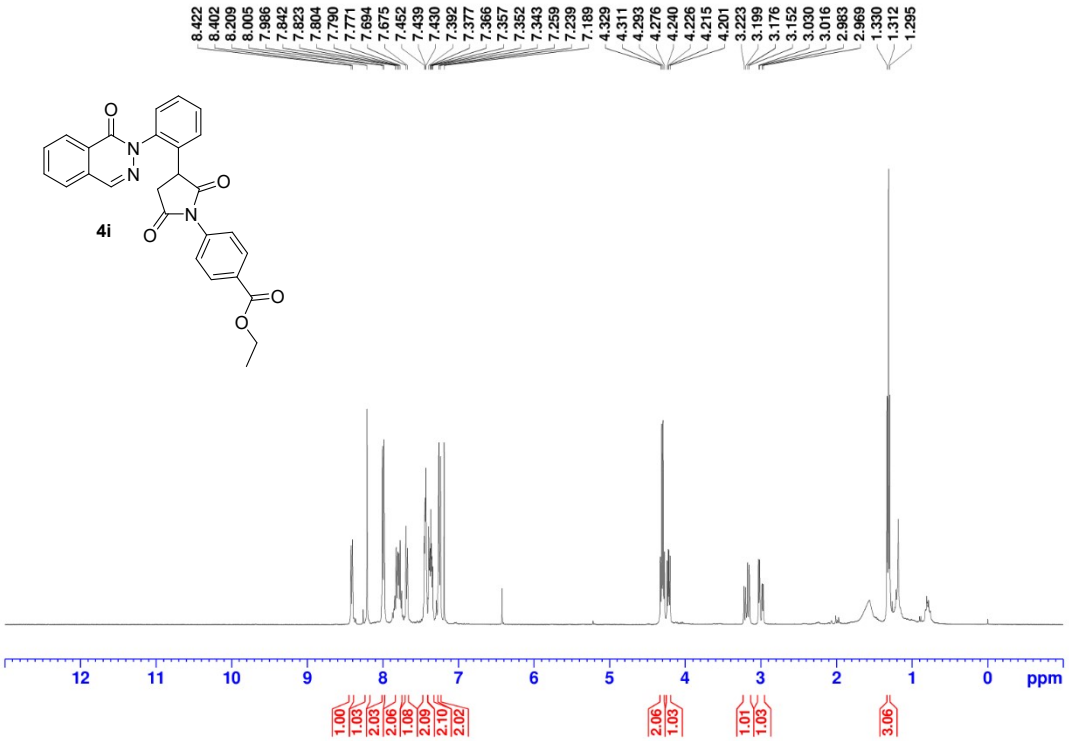


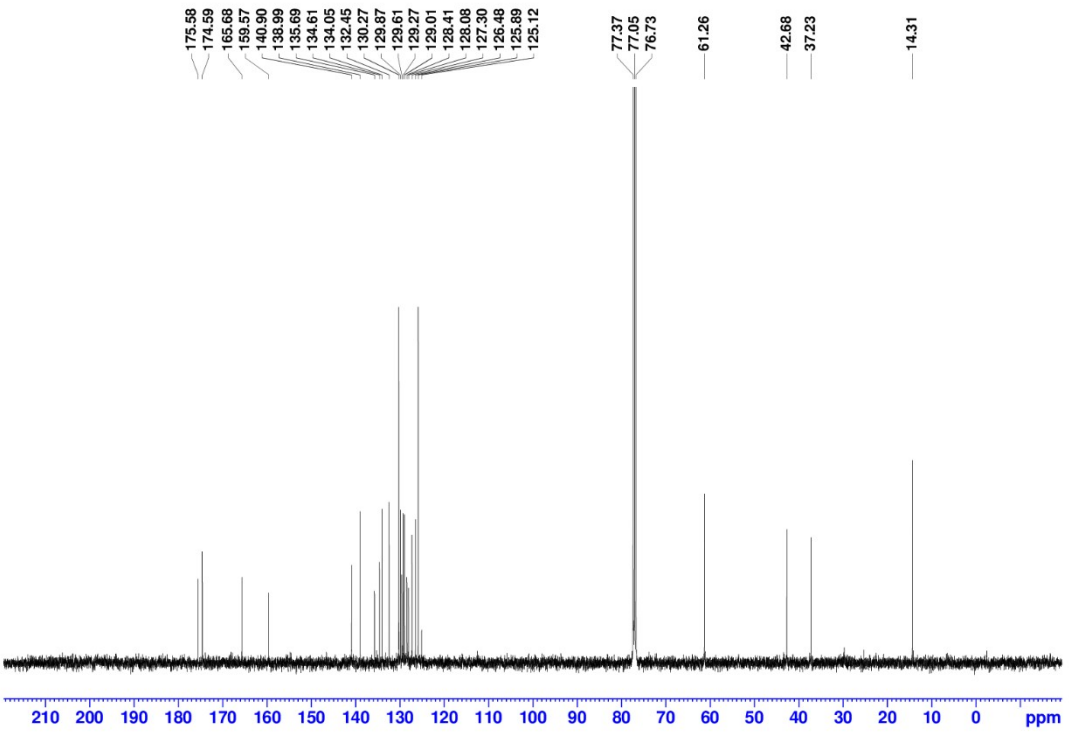


^{1}H and ^{13}C NMR spectrum of 4h

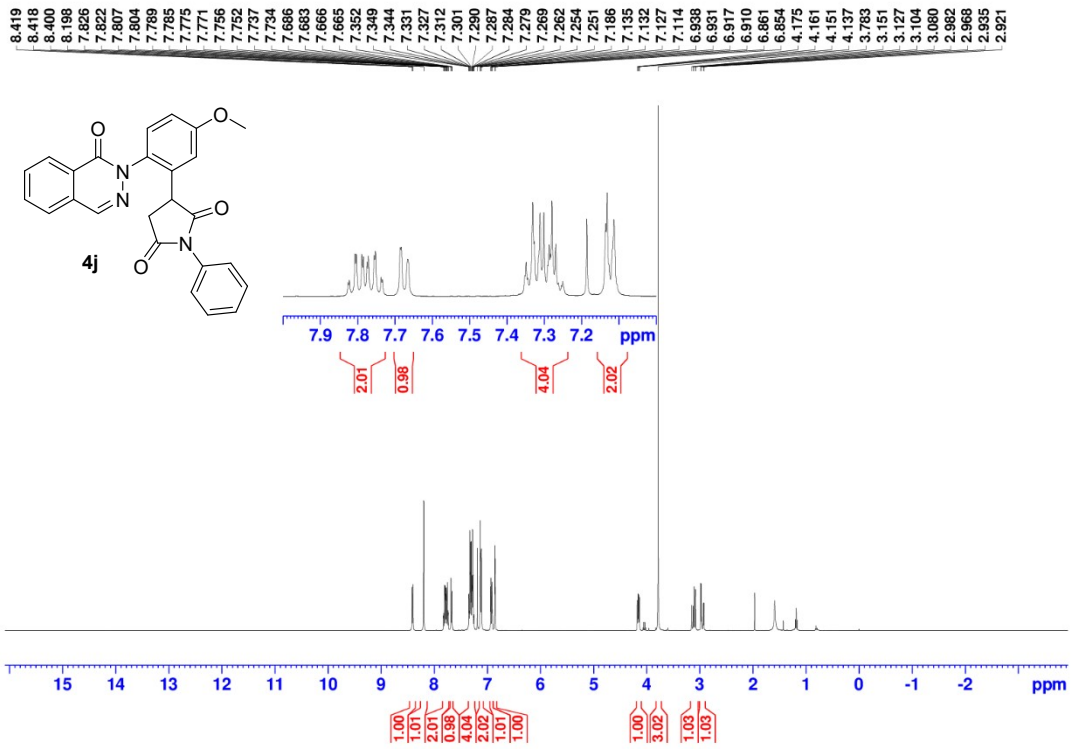


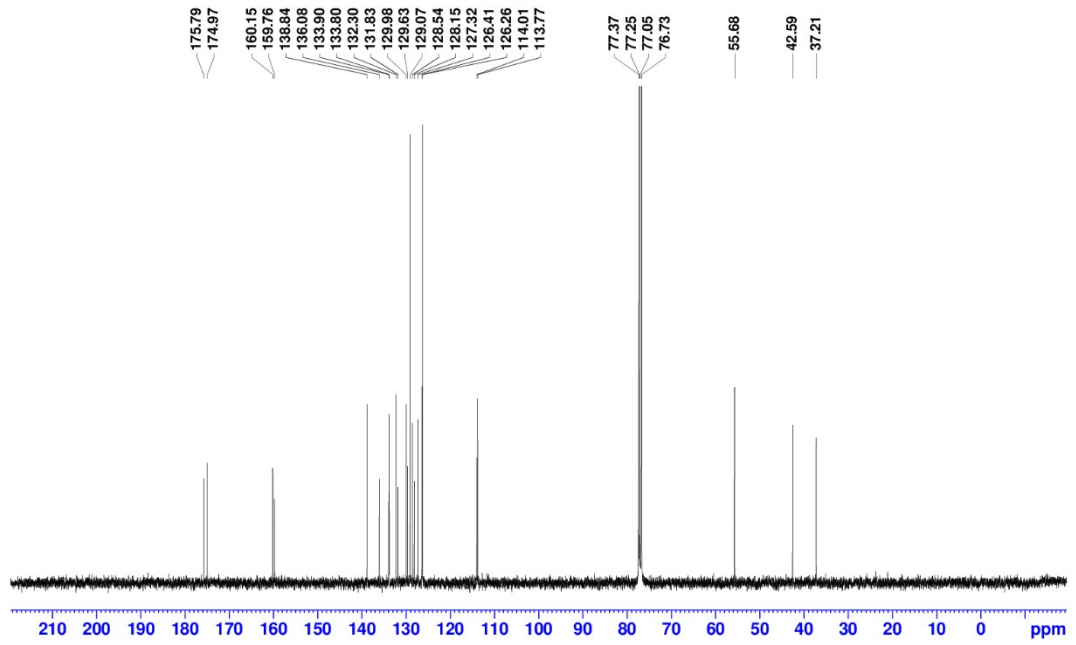
^{1}H and ^{13}C NMR spectrum of 4i



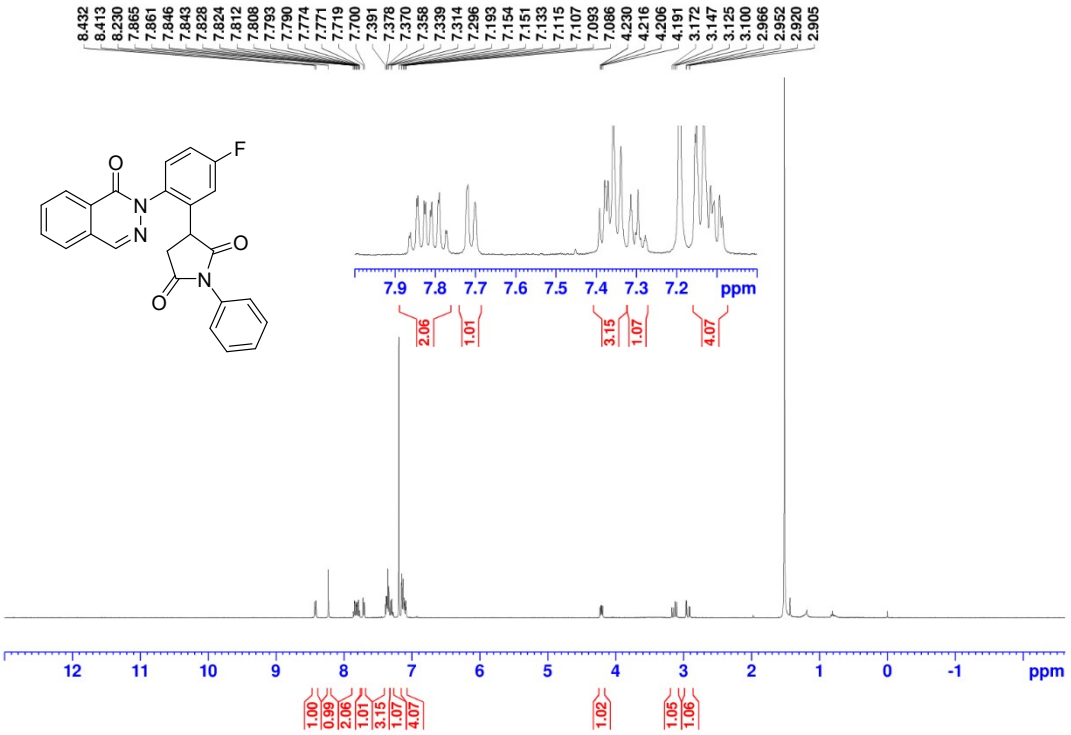


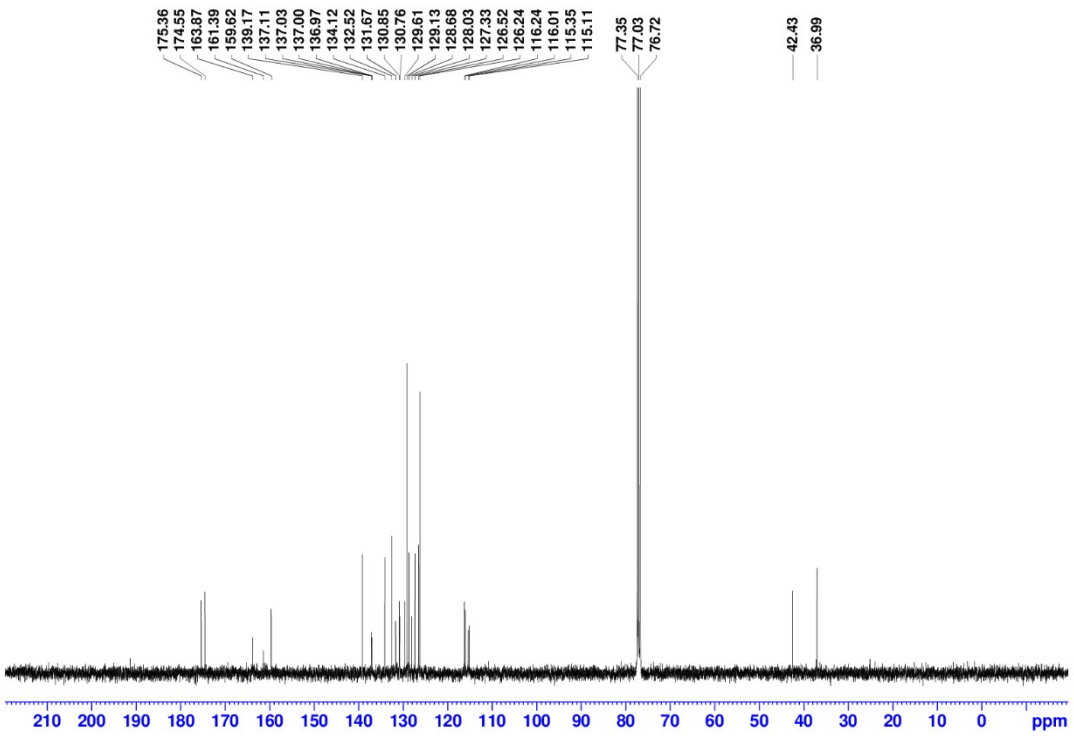
^{1}H and ^{13}C NMR spectrum of 4j

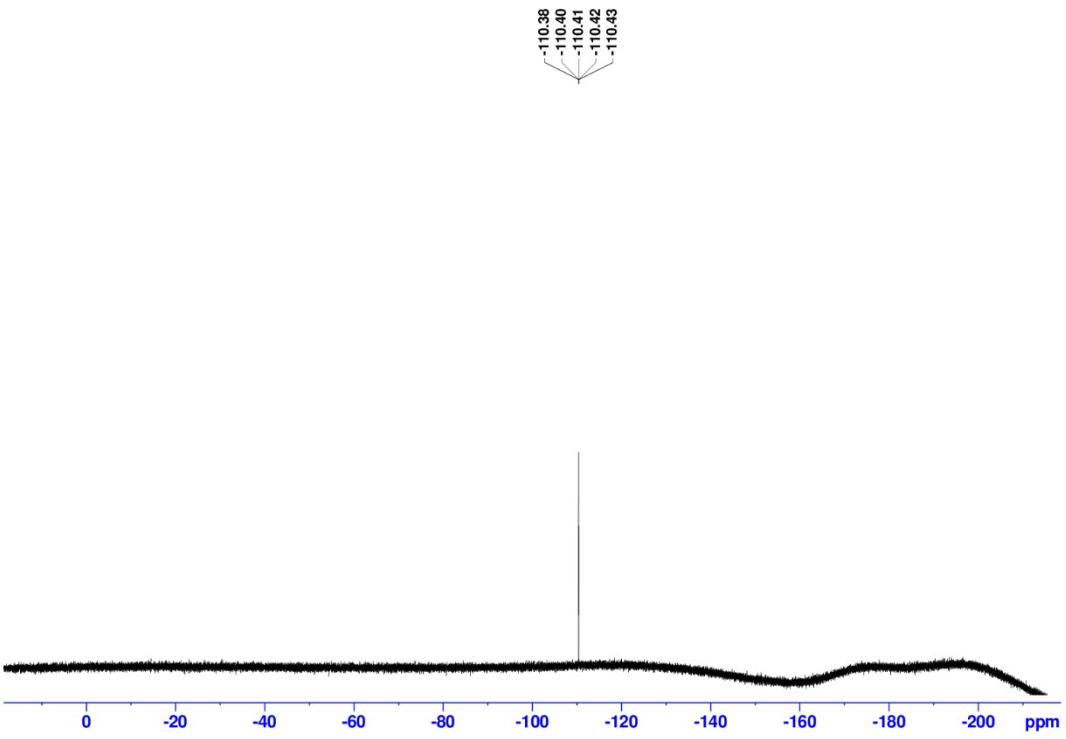




^{1}H and ^{13}C NMR spectrum of 4k



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-110.43
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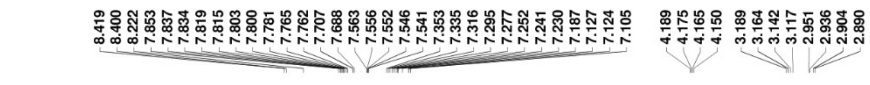
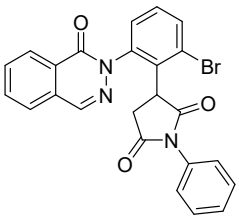
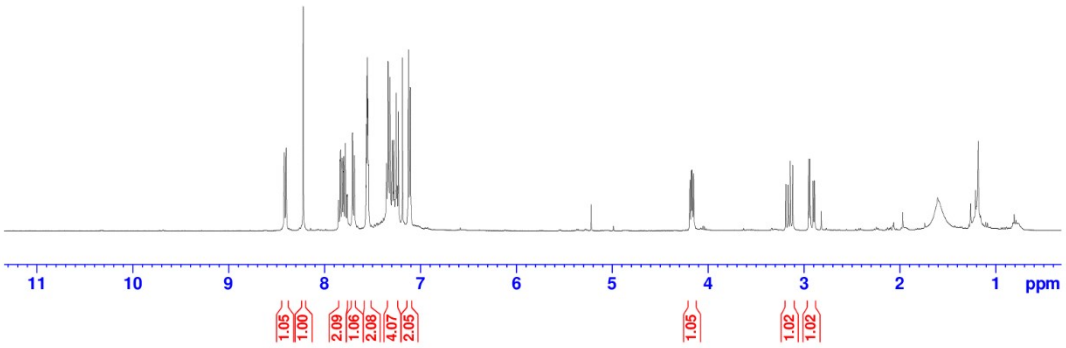
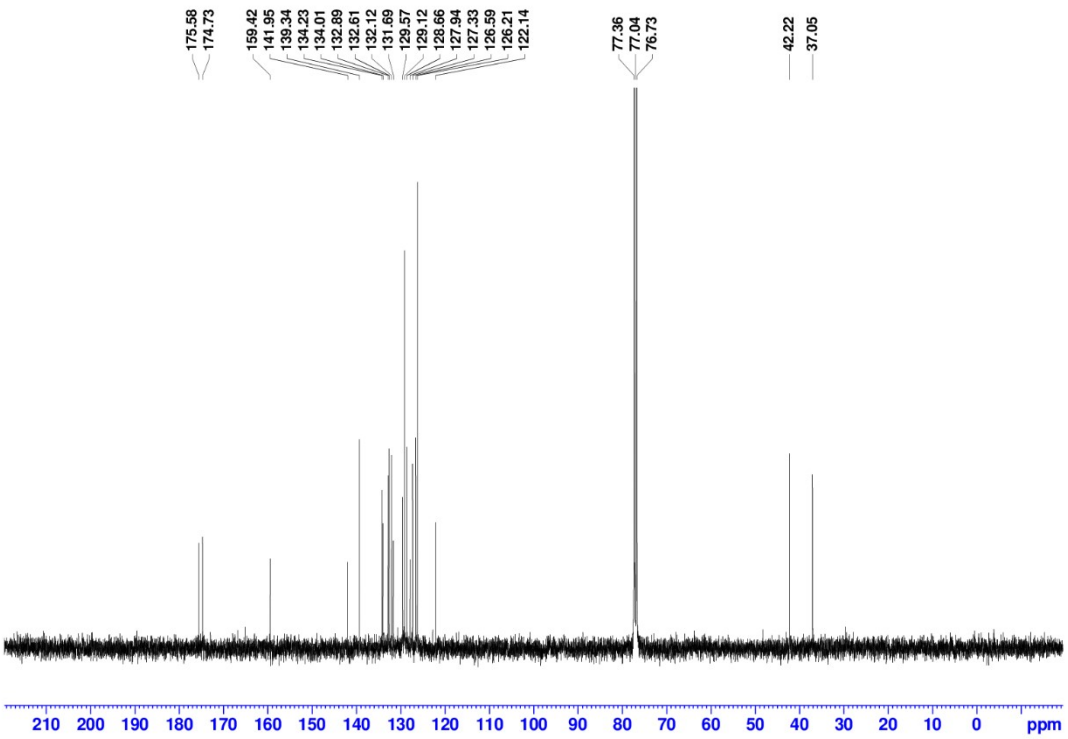
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

^{1}H and ^{13}C NMR spectrum of 4l









^{1}H and ^{13}C NMR spectrum of 3p