Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Selective synthesis of pyridazin-fused chromones and 3-pyridazinyl chromones through intermolecular chromone annulation of *o*-hydroxyphenylenaminones with aryldiazonium salts

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1. General information.

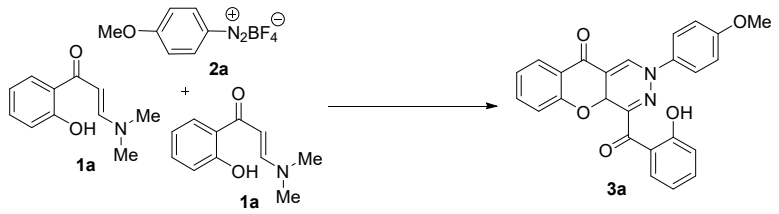
All compounds were fully characterized by spectroscopic data. The NMR spectra were recorded on a DRX600 (^{1}H: 600 MHz, ^{13}C: 150 MHz) and a AV500 (^{1}H: 500 MHz, ^{13}C: 125 MHz), chemical shifts (δ) are expressed in ppm, and J values are given in Hz, and deuterated $CDCl_3$, DMSO-d_6 were used as solvent. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on XT-4A melting point apparatus and are uncorrected. HRMs were performed on an Agilent LC/MS TOF instrument.

All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on silica gel (200–300 mesh).

o-Hydroxyphenylenaminones **1** were prepared according to the literature[1], aryldiazonium salts **2** were prepared according to the literature[2]. Other reagents were purchased from Energy Chemical and Adamas-beta®.

2. Optimization of reaction conditions.

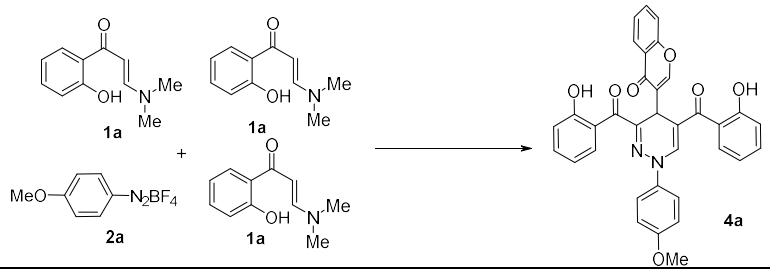
Table S1. Optimization of the Pyridazin-fused Chromones.[a]



Entry	Additive (eq.)	Solvent	T (°C)	Atmosphere	Yield[b] (%)
1	-	MeCN	r.t.	N_2	48
2	CuI (1.0)	MeCN	r.t.	N_2	43
3	$NaIO_3$ (1.0)	MeCN	r.t.	N_2	51
4	CuCl (1.0)	MeCN	r.t.	N_2	22
5	$(CF_3SO_3)_3Fe$ (1.0)	MeCN	r.t.	N_2	32
6	I_2 (1.0)	MeCN	r.t.	N_2	55
7	AcOH (1.0)	MeCN	r.t.	N_2	31
8	TFA (1.0)	MeCN	r.t.	N_2	18
9	$TsOH·H_2O$ (1.0)	MeCN	r.t.	N_2	49
10	Adipic acid (1.0)	MeCN	r.t.	N_2	33
11	Trifluoroacetic anhydride (1.0)	MeCN	r.t.	N_2	39
12	TfOH (1.0)	MeCN	r.t.	N_2	51
13	Benzoic anhydride (1.0)	MeCN	r.t.	N_2	63
14	Difluoroacetic anhydride (1.0)	MeCN	r.t.	N_2	38
15	Chloroacetic anhydride (1.0)	MeCN	r.t.	N_2	42
16	4-Nitrobenzoic acid (1.0)	MeCN	r.t.	N_2	n.d.
17	H_2SO_4 (1.0)	MeCN	r.t.	N_2	n.d.
18	Isobutyric acid (1.0)	MeCN	r.t.	N_2	53
19	Isobutyric anhydride (1.0)	MeCN	r.t.	N_2	92
20	Succinic anhydride (1.0)	MeCN	r.t.	N_2	93
21	Diethylamine (1.0)	MeCN	r.t.	N_2	32
22	Succinic anhydride (0.2)	MeCN	r.t.	N_2	51
23	Succinic anhydride (0.5)	MeCN	r.t.	N_2	54
24	Succinic anhydride (0.8)	MeCN	r.t.	N_2	86
25	Succinic anhydride (1.2)	MeCN	r.t.	N_2	91
26	Succinic anhydride (1.0)	DCM	r.t.	N_2	81
27	Succinic anhydride (1.0)	1,4-dioxane	r.t.	N_2	46
28	Succinic anhydride (1.0)	DMSO	r.t.	N_2	48
29	Succinic anhydride (1.0)	Toluene	r.t.	N_2	42
30	Succinic anhydride (1.0)	THF	r.t.	N_2	n.r.
31	Succinic anhydride (1.0)	Xylene	r.t.	N_2	n.r.
32	Succinic anhydride (1.0)	MeCN	r.t.	Air	90
33	Succinic anhydride (1.0)	MeCN	r.t.	O_2	84
34	Succinic anhydride (1.0)	MeCN	40	N_2	67

[a]Reacion conditions: **1a** (0.21 mmol), **2a** (0.1 mmol), catalyst and additive in 2 ml of solvent for 8.0 h. [b]Isolated yields.

Table S2. Optimization of the 3-Pyridazinyl-chromones.[a]

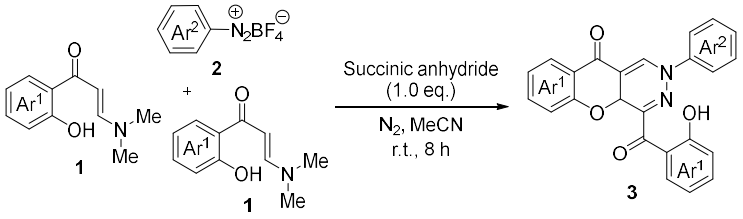


Entry	Additive (eq.)	1a (eq.)	Solvent	T (°C)	Atmosphere	Yield[b] (%)
1	-	3.0	MeCN	r.t.	Air	n.d.
2	Isobutyric acid (1.0)	3.0	MeCN	r.t.	Air	14
3	$TsOH·H_2O$ (1.0)	3.0	MeCN	r.t.	Air	24
4	TfOH (1.0)	3.0	MeCN	r.t.	Air	39
5	AcOH (1.0)	3.0	MeCN	r.t.	Air	38
6	TFA (1.0)	3.0	MeCN	r.t.	Air	trace
7	Benzoic anhydride (1.0)	3.0	MeCN	r.t.	Air	32
8	Trifluoroacetic anhydride (1.0)	3.0	MeCN	r.t.	Air	19
9	Caproic anhydride (1.0)	3.0	MeCN	r.t.	Air	trace
10	Isobutyric anhydride (1.0)	3.0	MeCN	r.t.	Air	16
11	Ac_2O (1.0)	3.0	MeCN	r.t.	Air	trace
12	Difluoroacetic anhydride (1.0)	3.0	MeCN	r.t.	Air	21
13	Chloroacetic anhydride (1.0)	3.0	MeCN	r.t.	Air	43
14	Succinic anhydride (1.0)	3.0	MeCN	r.t.	Air	48
15	Succinic anhydride (1.0)	3.0	MeCN	50	Air	53
16	Succinic anhydride (1.0)	3.0	MeCN	80	Air	72
17	Succinic anhydride (1.0)	3.0	MeCN	110	Air	60
18	Succinic anhydride (0.5)	3.0	MeCN	80	Air	39
19	Succinic anhydride (1.5)	3.0	MeCN	80	Air	65
20	Succinic anhydride (1.0)	3.0	Toluene	80	Air	31
21	Succinic anhydride (1.0)	3.0	EA	80	Air	35
22	Succinic anhydride (1.0)	3.0	DCM	80	Air	28
23	Succinic anhydride (1.0)	3.0	Acetone	80	Air	n.d.
24	Succinic anhydride (1.0)	3.0	EtOH	80	Air	n.d.
25	Succinic anhydride (1.0)	3.0	THF	80	Air	n.d.
26	Succinic anhydride (1.0)	3.0	1,4-dioxane	80	Air	43
27	Succinic anhydride (1.0)	3.0	Et_2O	80	Air	50
28	Succinic anhydride (1.0)	3.0	DMSO	80	Air	31
29	Succinic anhydride (1.0)	3.0	DMF	80	Air	46
30	Succinic anhydride (1.0)	3.0	MeCN	80	N_2	75
31	Succinic anhydride (1.0)	3.0	MeCN	80	O_2	63
32	Succinic anhydride (1.0)	3.5	MeCN	80	N_2	79
33	Succinic anhydride (1.0)	4.0	MeCN	80	N_2	81
34	Succinic anhydride (1.0)	4.5	MeCN	80	N_2	80
35	-	4.5	MeCN	80	N_2	51

[a]Reacion conditions: **1a** (x mmol), **2a** (0.1 mmol), catalyst and additive in 2 ml of solvent for 15.0 h. [b]Isolated yields.

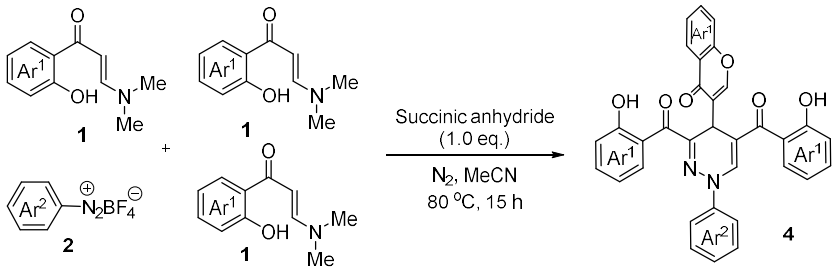
3. General procedure.

3.1 Synthesis of Pyridazin-fused Chromones 3.



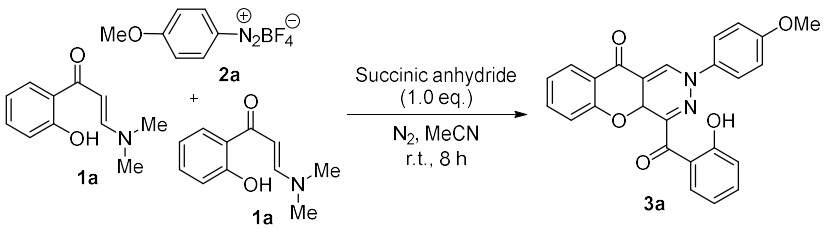
o-Hydroxyarylenaminones **1** (0.21 mmol), aryldiazonium salts **2** (0.1 mmol), Succinic anhydride (0.1 mmol), and MeCN (2.0 mL) were charged into a 10 mL Ace Glass pressure tubes, and the mixture was stirred at r.t. for 8.0 h until aryldiazonium salts were completely consumed. Then EtOAc (15 mL × 2) were added. The organic phase was washed with water (10 mL), dried over Na_2SO_4, concentrated and purified by flash column chromatography to afford pyridazin-fused chromones **3**. (The separation can also be obtained by filtration, but the purity is not satisfactory).

3.2 Synthesis of 3-Pyridazinyl-chromones 4.



o-Hydroxyarylenaminones **1** (2.0 mmol), aryldiazonium salts **2** (0.5 mmol), Succinic anhydride (0.5 mmol), and MeCN (2.0 mL) were charged into a 10 mL Ace Glass pressure tubes, and the mixture was stirred at 80 ºC for 15.0 h until aryldiazonium salts were completely consumed. The mixture was cooled to room temperature, and then EtOAc (15 mL × 2) were added. The organic phase was washed with water (10 mL), dried over Na_2SO_4, concentrated and purified by flash column chromatography to afford 3-Pyridazinyl-chromones **4**. (The separation can also be obtained by filtration, but the purity is not satisfactory).

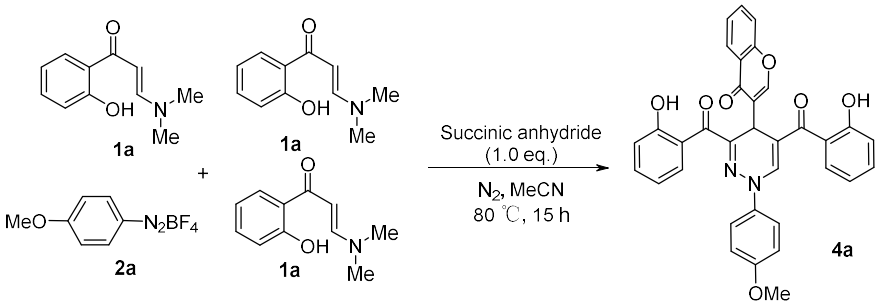
3.3 Gram-scale synthesis of Pyridazin-fused Chromones 3a.



o-Hydroxyarylenaminones **1a** (6.3 mmol), aryldiazonium salts **2a** (3.0 mmol), Succinic anhydride (3.0 mmol), and MeCN (20.0 mL) were charged into a 100 mL Ace Glass

pressure tubes, and the mixture was stirred at r.t. for 8.0 h until aryldiazonium salts were completely consumed. Then EtOAc (15 mL × 2) were added. The organic phase was washed with water (10 mL), dried over Na_2SO_4, concentrated and purified by flash column chromatography to afford pyridazin-fused chromone **3a**.

3.4 Gram-scale synthesis of 3-Pyridazinyl-chromones 4a.



o-Hydroxyarylenaminones **1a** (12.0 mmol), aryldiazonium salts **2a** (3.0 mmol), Succinic anhydride (3.0 mmol), and MeCN (20.0 mL) were charged into a 100 mL Ace Glass pressure tubes, and the mixture was stirred at 80 ºC for 15.0 h until aryldiazonium salts were completely consumed. The mixture was cooled to room temperature, and then EtOAc (15 mL × 2) were added. The organic phase was washed with water (10 mL), dried over Na_2SO_4, concentrated and purified by flash column chromatography to afford 3-pyridazinyl-chromone **4a**.

3.5 Antiviral activity against HCoV-OC43.

Drugs

ARB tablets (0.1 g per tablet) were purchased from CSPC Ouyi Pharmaceutical Co., Ltd. ARB and candidate drugs were dissolved in dimethyl sulfoxide (DMSO) and stored at – 20℃ before use.

Cell lines and virus

The human rectal carcinoma cell line HRT-18 (ATCC CCL-244) was cultured in Roswell Park Memorial Institute 1640 medium (RPMI 1640, Hyclone, USA). The lung adenocarcinoma cell line A549 (ATCC CCL-185) was cultured in Dulbecco's modified Eagle's medium (DMEM, Gibco, USA). All cells were cultured in medium supplemented with 10% fetal bovine serum (FBS), 100 U/ml penicillin, and 100 μg/ml streptomycin (Gibco, USA). HCoV-OC43 (VR-1558) was propagated in HRT-18 cell and the 50% tissue culture infective dose ($TCID_{50}$) was calculated by using the Reed-Muench method as previously described.[3] Viral stocks were stored at – 80℃. This viral infection was conducted in BSL-2 laboratory.

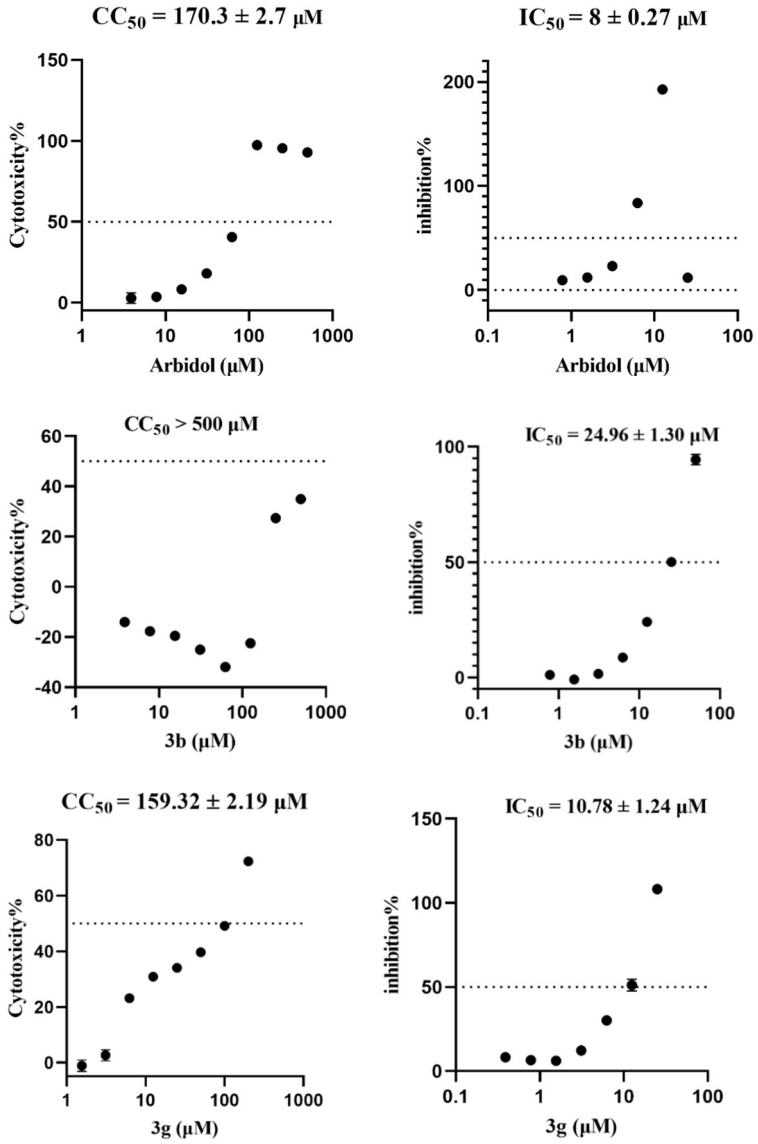
Cytotoxicity assay

The cytotoxic effects of drugs on A549 cells were measured by cell counting Kit-8 (CCK-8) (Beyotime, China). Cell monolayer grown in 96-well plates was incubated

with indicated concentrations of drugs. After 48 h, 10 μL of CCK-8 reagent was added into each well and culture at 37 ℃ for 40 min. The absorbance at 450 nm was measured by using a Multiskan GO Microplate Spectrophotometer (Thermo Fisher, USA). The 50% cytotoxic concentration (CC_{50}) of drugs to cells was calculated by the GraphPad Prism 8.0 software.

Cytopathic effect (CPE) inhibition assay

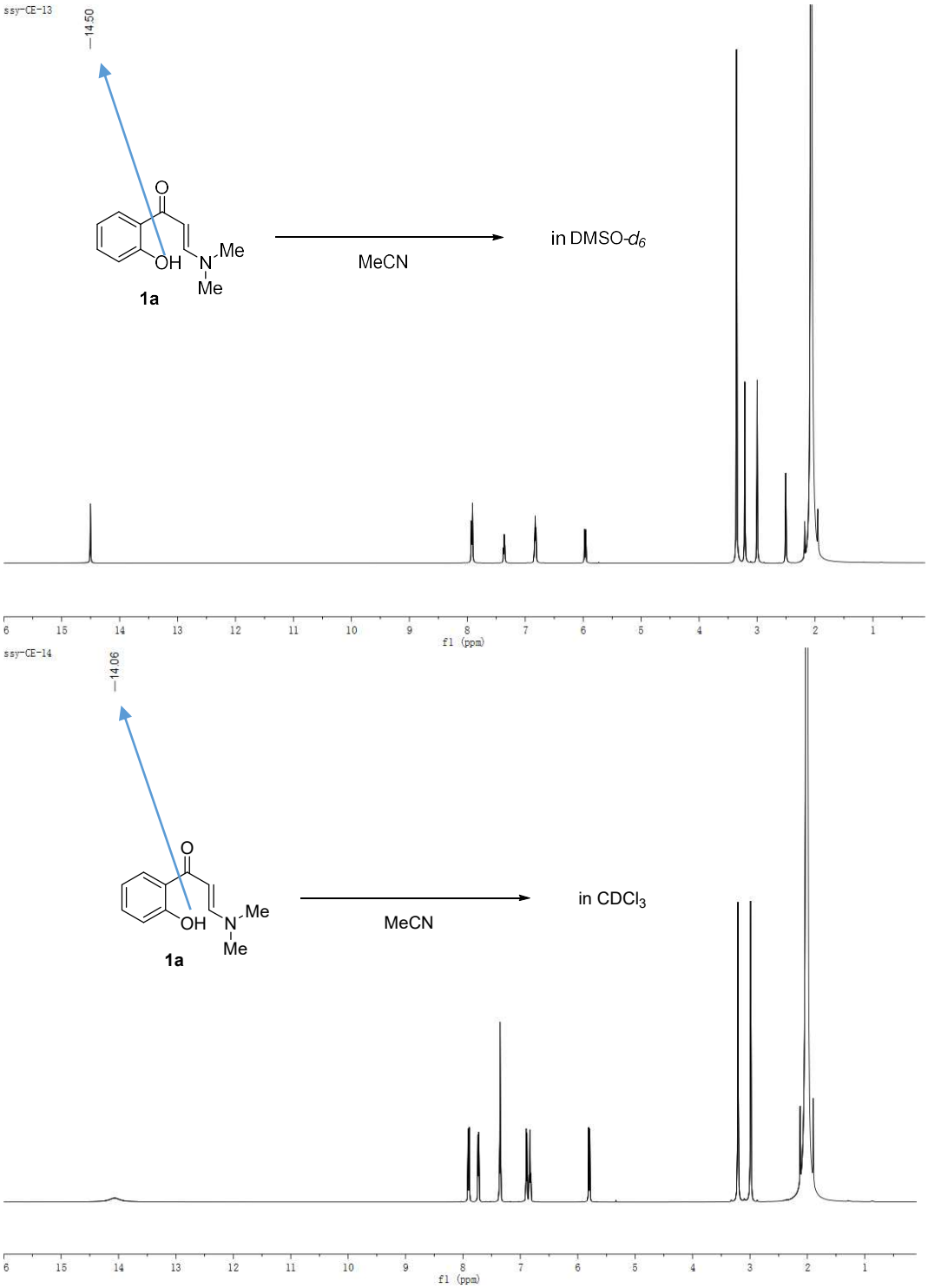
The cell monolayer cultured in 96-well plates was inoculated with 100 $TCID_{50}$ of HCoV-OC43 at 34℃ for 3 h. After removing the inoculums, cells were treated with indicated concentrations of drugs in culture medium with 2%FBS at 34℃ in a 5%CO_2 incubator. At 7 dpi, the cell viability was detected by CCK-8 assay to calculate the 50% inhibitory concentration (IC50) of agents against CPE via the Reed-Muench method. The cytotoxicity and antiviral effects of **3b** and **3g** in A549 cells infected with HCoV-OC43 are shown in the figure below.



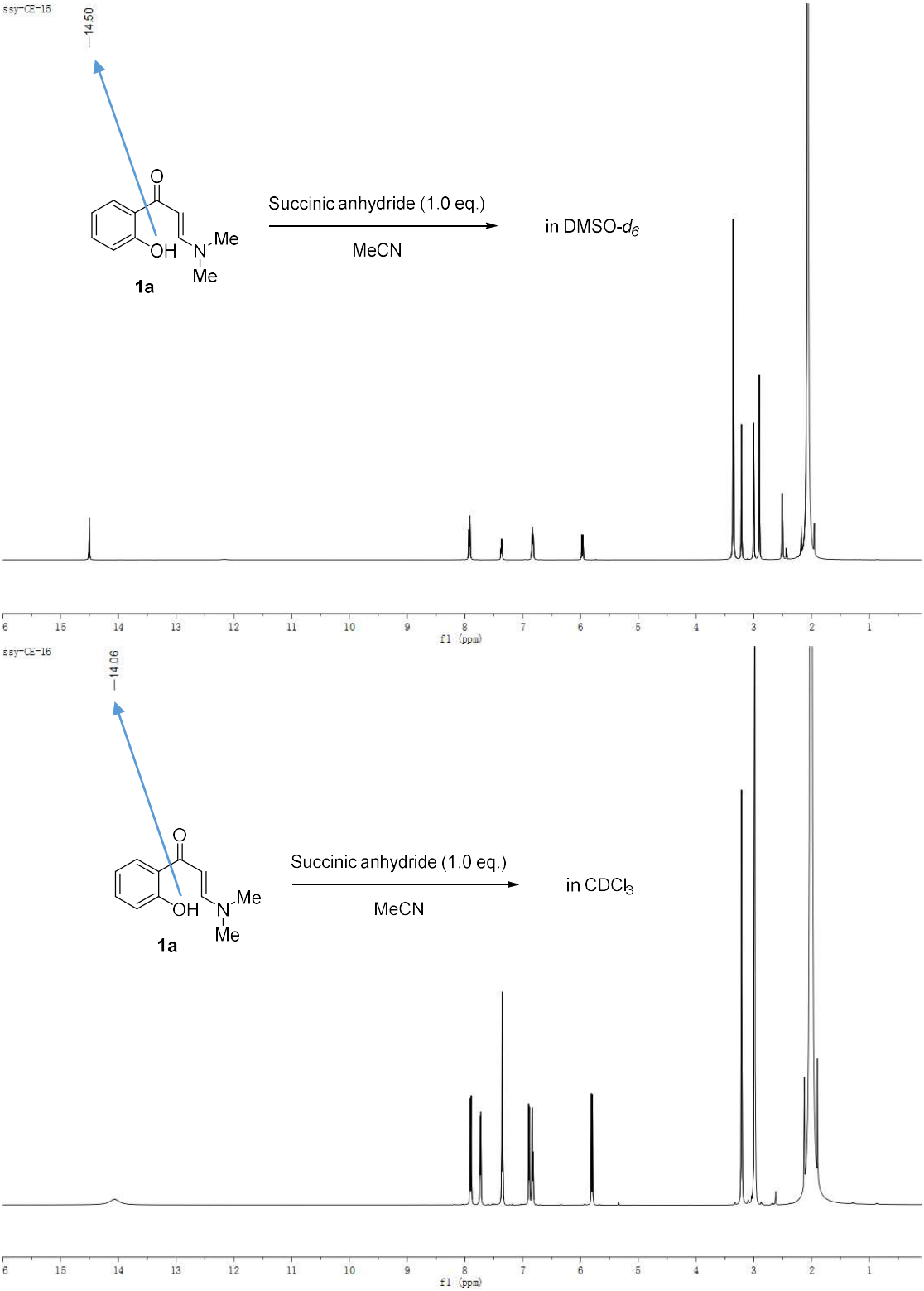
3.6 The NMR A value for OH groups in o-hydroxyarylenaminones.

$\Delta\delta = \delta(\text{DMSO}) - \delta(\text{CDCl}_3)$; $A_{\text{NMR}} = 0.0065 + 0.133\Delta\delta$

There is a clear distinction between aromatic OH groups that do not form an intraHB, which have $A_{\text{NMR}} > 0.5$, and OH groups that form a strong intraHB, which have $A_{\text{NMR}} < 0.1$.[4]



$\Delta\delta = 14.50 - 14.06 = 0.44$; $A_{\text{NMR}} = 0.0065 + 0.133 * 0.44 = 0.06502$ (< 0.1), the OH group form a strong intraHB.

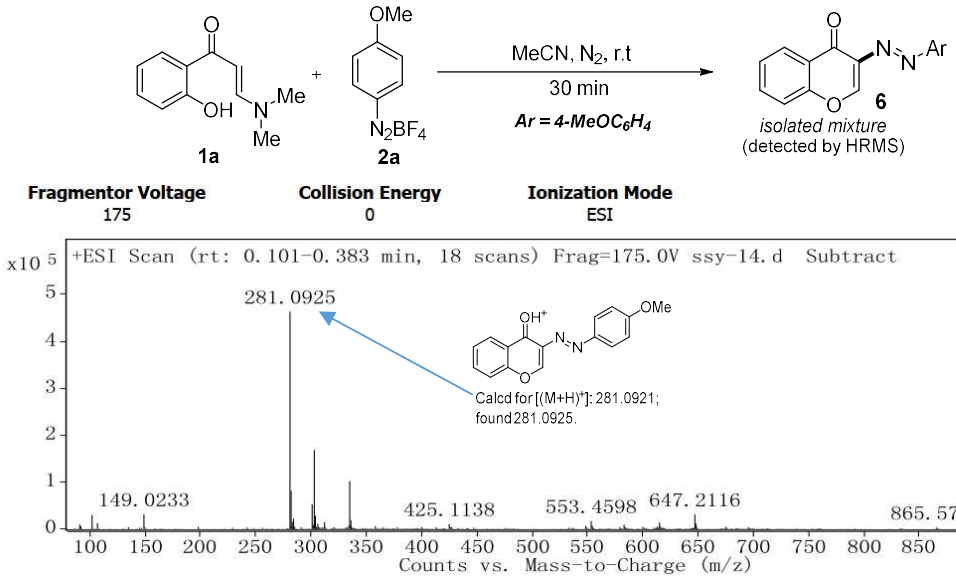


$\Delta\delta$ = 14.50 - 14.06 = 0.44; A_{NMR} = 0.0065 + 0.133 * 0.47 = 0.06502 (< 0.1), the OH group form a strong intraHB.

The ANMR value did not change by the addition of SA, suggesting that the strong intramolecular hydrogen bond of o-HPEs would not be affected by SA.

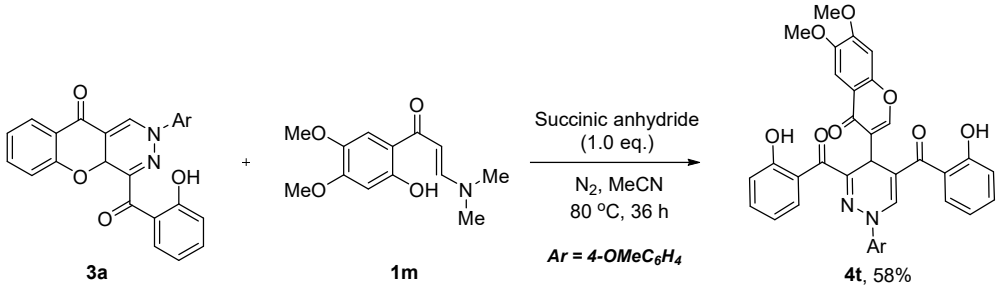
3.7 Synthesis of 3-diazenyl chromone 6.

o-Hydroxyarylenaminones **1a** (0.1 mmol), aryldiazonium salts **2a** (0.1 mmol), and MeCN (1.0 mL) were charged into a 10 mL Ace Glass pressure tubes, and the mixture was stirred at room remperature for 30 min. The reaction mixture contained solid sediment and the 3-diazenyl chromone product **6** was obtained by filtration. 3-Diazenyl chromone product **6** is an unstable mixture that can be detected by HRMS.



3.8 Synthesis of 3-pyridazinyl chromone 4t.

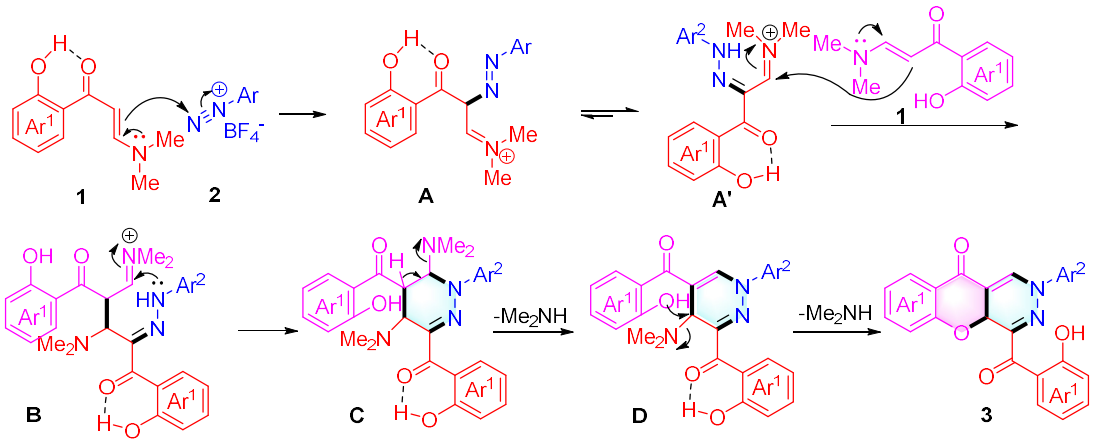
Pyridazin-fused chromone **3a** (0.4 mmol), *o*-hydroxyarylenaminones **1m** (0.4 mmol), Succinic anhydride (0.4 mmol), and MeCN (2.0 mL) were charged into a 10 mL Ace Glass pressure tubes, and the mixture was stirred at 80 ºC for 36 h until pyridazin-fused chromone **3a** were completely consumed. Then EtOAc (15 mL × 2) were added. The organic phase was washed with water (10 mL), dried over Na_2SO_4, concentrated and purified by flash column chromatography to afford 3-pyridazinyl chromone **4t**.



3.9 Another proposed mechanism.

The intermolecular addition reaction of *o*-HPEs **1** and aryldiazonium salts **2** was initiated to give intermediates **A**, which follwed to isomerize to form **A'**. Next, the intermolecular nucleophilic addition of intermediate **A'** with another molecular **1** was executed to give intermediate **B**, followed by the intramolecular cyclization lead to the formation of pyridazin-precursor intermediate **C**. The subsequent deamination,

intramolecular cyclization, and deamination-dehydrogenation were performed sequentially, leading to the formation of desired pyridazin-fused chromanones **3**.

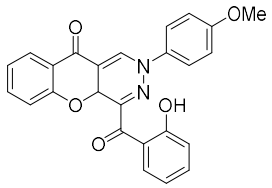


Scheme S1. Proposed mechanism.

4. Spectroscopic data.

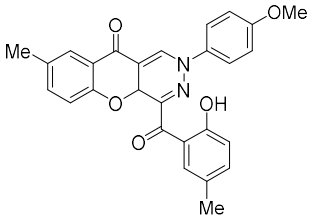
4.1 Spectroscopic data of Pyridazin-fused Chromones.

4-(2-Hydroxybenzoyl)-2-(4-methoxyphenyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3a)



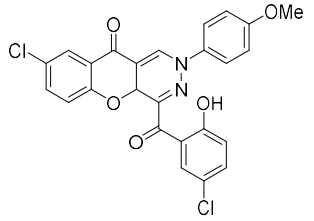
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 40 mg (93%); mp = 143–144 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.82 (s, 1H, ArOH), 8.20 (s, 1H, C=CH), 7.99 (s, 2H, ArH), 7.57 (t, *J* = 7.4 Hz, 1H, ArH), 7.52 (t, *J* = 7.3 Hz, 1H, ArH), 7.37 (d, *J* = 8.8 Hz, 2H, ArH), 7.09 (t, *J* = 8.9 Hz, 2H, ArH), 6.99–6.93 (m, 4H, ArH), 6.41 (s, 1H, C–CH), 3.83 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 193.2, 181.2, 163.8, 158.3, 157.6, 140.3, 137.1, 136.6, 136.0, 133.2, 129.0, 127.3, 123.4, 122.3, 120.3, 120.3, 118.9, 118.5, 118.5, 118.4, 114.7, 114.7, 109.5, 64.2, 55.6; HRMS (TOF ES+): m/z calcd for $C_{25}H_{19}N_2O_5$ [$(M+H)^+$], 427.1288, found, 427.1309.

4-(2-Hydroxy-5-methylbenzoyl)-2-(4-methoxyphenyl)-8-methyl-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3b)



$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 42 mg (92%); mp = 178–179°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.63 (s, 1H, ArOH), 8.00 (d, *J* = 13.4 Hz, 2H, ArH), 7.78 (s, 1H, C=CH), 7.39–7.35 (m, 3H, ArH), 7.32 (d, *J* = 6.1 Hz, 1H, ArH), 6.98 (d, *J* = 7.0 Hz, 1H, ArH), 6.96–6.92 (m, 2H, ArH), 6.84 (d, *J* = 7.1 Hz, 1H, ArH), 6.34 (s, 1H, C–CH), 3.83 (s, 3H, $ArOCH_3$), 2.34 (s, 6H, $ArCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.2, 181.3, 161.8, 158.3, 155.7, 140.5, 138.1, 137.6, 136.2, 132.9, 131.8, 128.9, 127.9, 126.9, 123.1, 120.2, 120.2, 118.3, 118.3, 118.2, 114.8, 114.8, 109.7, 64.2, 55.6, 20.6, 20.5; HRMS (TOF ES+): m/z calcd for $C_{27}H_{23}N_2O_5$ [$(M+H)^+$], 455.1601, found, 455.1603.

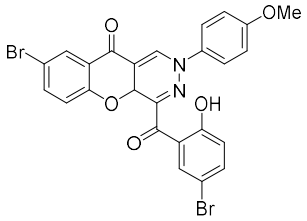
8-Chloro-4-(5-chloro-2-hydroxybenzoyl)-2-(4-methoxyphenyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3c)



$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 33 mg (67%); mp = 140–141°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 11.66 (s, 1H, ArOH), 8.28 (s, 1H, C=CH), 7.97 (s, 1H, ArH), 7.94 (s, 1H, ArH), 7.50 (d, *J* = 7.4 Hz, 1H, ArH), 7.45 (d, *J* = 7.0 Hz, 1H, ArH), 7.37 (d, *J* = 8.6 Hz, 2H, ArH),

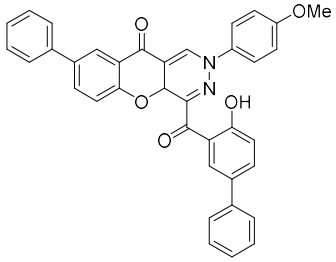
7.03 (d, J = 8.9 Hz, 1H, ArH), 6.97 (d, J = 8.7 Hz, 2H, ArH), 6.91 (d, J = 8.7 Hz, 1H, ArH), 6.37 (s, 1H, C–CH), 3.84 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 191.7, 180.0, 162.2, 158.6, 155.9, 139.8, 136.8, 136.5, 135.8, 132.4, 129.6, 127.9, 126.8, 124.1, 123.7, 120.6, 120.6, 120.3, 120.1, 118.8, 114.9, 114.9, 109.4, 64.1, 55.7; HRMS (TOF ES+): m/z calcd for $C_{25}H_{17}Cl_2N_2O_5$ [$(M+H)^+$], 495.0509, found, 495.0507.

8-Bromo-4-(5-bromo-2-hydroxybenzoyl)-2-(4-methoxyphenyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3d)



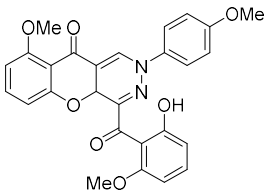
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 24 mg (41%); mp = 201–202°C; ^1H NMR (600 MHz, $CDCl_3$): δ = 11.68 (s, 1H, ArOH), 8.45 (s, 1H, C=CH), 8.04 (d, J = 73.8 Hz, 2H, ArH), 7.59 (s, 2H, ArH), 7.38 (s, 2H, ArH), 6.98 (s, 3H, ArH), 6.85 (s, 1H, ArH), 6.38 (s, 1H, C–CH), 3.84 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.8, 178.2, 160.9, 156.9, 154.6, 137.9, 137.7, 137.5, 134.0, 133.7, 128.1, 127.8, 122.8, 118.8, 118.8, 118.8, 118.7, 117.7, 113.4, 113.1, 113.1, 108.8, 107.7, 62.3, 53.9; HRMS (TOF ES+): m/z calcd for $C_{25}H_{17}Br_2N_2O_5$ [$(M+H)^+$], 582.9499, found, 582.9494.

4-(4-Hydroxy-[1,1'-biphenyl]-3-carbonyl)-2-(4-methoxyphenyl)-8-phenyl-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3e)



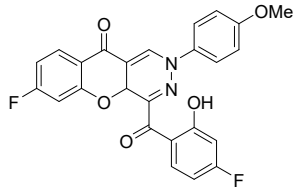
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 45 mg (77%); mp = 195–196°C; ^1H NMR (600 MHz, $CDCl_3$): δ = 11.91 (s, 1H, ArOH), 8.58 (s, 1H, ArH), 8.23 (s, 1H, ArH), 8.00 (s, 1H, C=CH), 7.83–7.77 (m, 2H, ArH), 7.61 (d, J = 7.3 Hz, 2H, ArH), 7.52 (d, J = 7.3 Hz, 2H, ArH), 7.44 (t, J = 7.4 Hz, 2H, ArH), 7.41–7.33 (m, 6H, ArH), 7.17 (d, J = 8.6 Hz, 1H, ArH), 7.04 (d, J = 8.5 Hz, 1H, ArH), 6.89 (d, J = 8.6 Hz, 2H, ArH), 6.46 (s, 1H, C–CH), 3.82 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.7, 181.3, 163.3, 158.4, 157.0, 140.3, 139.9, 139.5, 136.1, 135.8, 135.3, 135.3, 132.2, 131.8, 129.2, 128.9, 128.9, 128.9, 128.9, 127.5, 127.2, 126.8, 126.8, 126.7, 126.7, 125.4, 123.5, 120.7, 120.7, 119.1, 118.9, 118.5, 114.7, 114.7, 110.1, 64.2, 55.7; HRMS (TOF ES+): m/z calcd for $C_{37}H_{27}N_2O_5$ [$(M+H)^+$], 579.1914, found, 579.1917.

4-(2-Hydroxy-6-methoxybenzoyl)-9-methoxy-2-(4-methoxyphenyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3f)



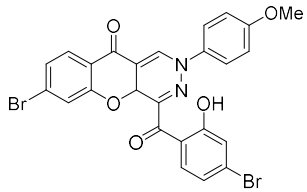
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 35 mg (72%); mp = 165–166°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.26 (s, 1H, ArOH), 8.79 (s, 1H, C=CH), 7.75 (s, 1H, ArH), 7.71 (s, 1H, ArH), 7.46 (t, *J* = 8.3 Hz, 1H, ArH), 7.36 (t, *J* = 8.3 Hz, 1H, ArH), 6.90 (d, *J* = 8.4 Hz, 1H, ArH), 6.85 (d, *J* = 8.9 Hz, 1H, ArH), 6.70 (d, *J* = 8.2 Hz, 1H, ArH), 6.61 (s, 1H, ArH), 6.49 (d, *J* = 8.3 Hz, 1H, ArH), 6.35 (d, *J* = 8.2 Hz, 1H, ArH), 5.61 (s, 1H, C–CH), 3.84 (s, 3H, $ArOCH_3$), 3.77 (s, 3H, $ArOCH_3$), 3.59 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 195.3, 192.9, 176.3, 160.8, 159.9, 158.4, 157.8, 157.5, 152.9, 138.8, 137.1, 136.5, 133.6, 123.4, 119.8, 119.8, 114.5, 114.5, 110.6, 109.9, 106.4, 102.8, 101.8, 56.3, 55.9, 55.6, 29.9; HRMS (TOF ES+): m/z calcd for $C_{27}H_{23}N_2O_7$ [$(M+H)^+$], 487.1500, found, 487.1500.

7-Fluoro-4-(4-fluoro-2-hydroxybenzoyl)-2-(4-methoxyphenyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3g)



$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Red solid: 40 mg (86%); mp = 196–197 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 12.15 (s, 1H, ArOH), 8.27–8.23 (m, 1H, ArH), 8.03–8.00 (m, 1H, ArH), 7.98 (s, 1H, C=CH), 7.35 (d, *J* = 8.9 Hz, 2H, ArH), 6.96 (d, *J* = 8.9 Hz, 2H, ArH), 6.81 (t, *J* = 7.3 Hz, 1H, ArH), 6.76 (d, *J* = 10.2 Hz, 1H, ArH), 6.69 (t, *J* = 8.5 Hz, 1H, ArH), 6.65 (d, *J* = 9.6 Hz, 1H, ArH), 6.43 (s, 1H, C–CH), 3.83 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 191.7, 179.9, 167.9 (*J* = 258.2 Hz), 167.9(*J* = 256.7 Hz), 166.5(*J* = 15.1 Hz), 159.3(*J* = 13.6 Hz), 158.4, 139.9, 135.9, 135.7 (*J* = 11.7 Hz), 129.9 (*J* = 11.4 Hz), 129.2, 120.4, 120.4, 120.2 (*J* = 2.5 Hz), 115.5(*J* = 1.5 Hz), 114.8, 114.8, 110.7 (*J* = 22.7 Hz), 109.1, 107.5 (*J* = 22.6 Hz), 105.4(*J* = 24.5 Hz), 105.1 (*J* = 23.6 Hz), 64.7, 55.6; HRMS (TOF ES+): m/z calcd for $C_{25}H_{17}F_2N_2O_5$ [$(M+H)^+$], 463.1100, found, 463.1104.

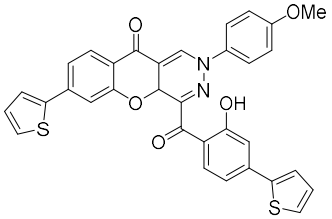
7-Bromo-4-(4-bromo-2-hydroxybenzoyl)-2-(4-methoxyphenyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3h)



$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 27 mg (47%); mp = 210–211°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.87 (s, 1H, ArOH), 8.07 (d, *J* = 8.6 Hz, 1H, ArH), 7.97 (s, 1H, C=CH), 7.83 (d, *J* = 8.3 Hz, 1H, ArH), 7.34 (d, *J* = 8.6 Hz, 2H, ArH), 7.28 (s, 1H, ArH), 7.23 (d, *J* = 8.4 Hz, 1H, ArH), 7.16 (s, 1H, ArH), 7.11 (d, *J* = 8.4 Hz, 1H, ArH), 6.96 (d, *J* = 8.6 Hz, 2H, ArH), 6.40 (s, 1H, C–CH), 3.83 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.3, 180.4, 164.2, 158.5,

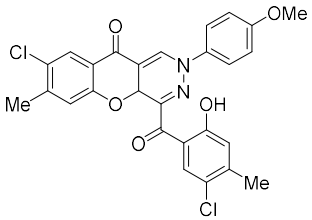
157.7, 139.9, 135.8, 134.0, 131.9, 131.1, 129.3, 128.6, 125.9, 122.7, 122.3, 121.7, 121.7, 120.4, 120.4, 117.3, 114.9, 114.9, 109.3, 64.5, 55.7; HRMS (TOF ES+): m/z calcd for $C_{25}H_{17}Br_2N_2O_5$ [$(M+H)^+$], 582.9499, found, 582.9493.

4-(2-Hydroxy-4-(thiophen-2-yl)benzoyl)-2-(4-methoxyphenyl)-7-(thiophen-2-yl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3i)



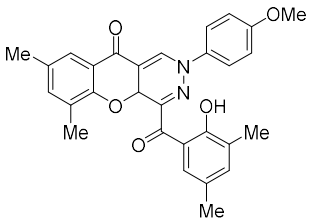
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 7:1, R_f = 0.25; Yellow solid: 22 mg (37%); mp = 194–195°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 12.03 (s, 1H, ArOH), 8.23 (d, J = 9.7 Hz, 1H, C=CH), 8.01 (s, 1H, C=CH), 8.00 (d, J = 8.5 Hz, 1H, C=CH), 7.52 (d, J = 2.8 Hz, 1H, C=CH), 7.43 (s, 2H, ArH), 7.39 (d, J = 8.9 Hz, 2H, ArH), 7.37 (s, 1H, ArH), 7.34 (d, J = 8.2 Hz, 2H, ArH), 7.24 (d, J = 6.7 Hz, 1H, C=CH), 7.21 (s, 1H, ArH), 7.15 (t, J = 3.0 Hz, 1H, C=CH), 7.11 (t, J = 4.5 Hz, 1H, C=CH), 6.97 (d, J = 9.1 Hz, 2H, ArH), 6.45 (s, 1H, C–CH), 3.84 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.2, 180.5, 164.4, 158.3, 157.9, 142.5, 142.5, 142.5, 142.3, 140.3, 136.1, 133.9, 128.9, 128.5, 128.4, 128.1, 127.5, 127.1, 125.7, 125.3, 122.1, 120.3, 120.3, 119.8, 117.4, 116.6, 114.8, 114.8, 114.7, 114.5, 109.5, 64.4, 55.7; HRMS (TOF ES+): m/z calcd for $C_{33}H_{23}N_2O_5S_2$ [$(M+H)^+$], 591.1043, found, 591.1049.

8-Chloro-4-(5-chloro-2-hydroxy-4-methylbenzoyl)-2-(4-methoxyphenyl)-7-methyl-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3j)



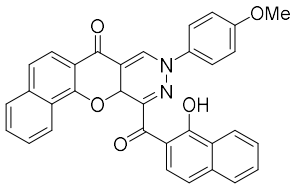
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 44 mg (84%); mp = 200–201°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.69 (s, 1H, ArOH), 8.28 (s, 1H, C=CH), 7.95 (d, J = 19.8 Hz, 2H, ArH), 7.38 (d, J = 9.2 Hz, 2H, ArH), 6.98–6.96 (m, 3H, ArH), 6.86 (s, 1H, ArH), 6.34 (s, 1H, C–CH), 3.84 (s, 3H, $ArOCH_3$), 2.42 (s, 3H, $ArCH_3$), 2.37 (s, 3H, $ArCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 191.3, 179.9, 162.2, 158.5, 155.7, 146.4, 145.9, 139.9, 135.9, 132.7, 129.3, 128.5, 127.0, 124.4, 122.3, 120.5, 120.4, 120.4, 120.4, 117.1, 114.8, 114.8, 109.5, 64.1, 55.6, 20.9, 20.9; HRMS (TOF ES+): m/z calcd for $C_{27}H_{21}Cl_2N_2O_5$ [$(M+H)^+$], 523.0822, found, 523.0829.

4-(2-Hydroxy-3,5-dimethylbenzoyl)-2-(4-methoxyphenyl)-6,8-dimethyl-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3k)



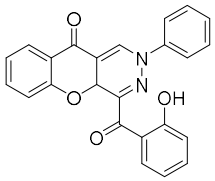
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 42 mg (87%); mp = 186–187°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.95 (s, 1H, ArOH), 7.98 (s, 1H, C=CH), 7.87 (s, 1H, ArH), 7.62 (s, 1H, ArH), 7.37 (d, J = 9.0 Hz, 2H, ArH), 7.27 (s, 1H, ArH), 7.19 (s, 1H, ArH), 6.96–6.92 (m, 2H, ArH), 6.29 (s, 1H, C–CH), 3.83 (s, 3H, $ArOCH_3$), 2.32 (s, 3H, $ArCH_3$), 2.30 (s, 6H, $ArCH_3$), 2.07 (s, 3H, $ArCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 179.0, 176.5, 156.3, 155.4, 154.3, 153.2, 138.0, 136.3, 136.1, 134.8, 131.2, 127.7, 127.4, 127.3, 124.4, 123.7, 123.0, 122.7, 122.5, 116.0, 116.0, 114.7, 114.7, 75.0, 55.6, 20.9, 20.6, 15.7, 15.5; HRMS (TOF ES+): m/z calcd for $C_{29}H_{27}N_2O_5$ [$(M+H)^+$], 483.1914, found, 483.1911.

11-(1-Hydroxy-2-naphthoyl)-9-(4-methoxyphenyl)-9,11a-dihydro-7*H*-benzo[7,8]chromeno[2,3-*d*]pyridazin-7-one (3l)



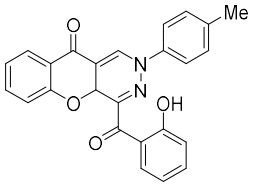
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 48 mg (91%); mp = 180–181°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.57 (d, J = 8.3 Hz, 1H, ArH), 8.26 (d, J = 8.9 Hz, 1H, ArH), 8.18 (s, 1H, C=CH), 8.09 (d, J = 8.3 Hz, 1H, ArH), 7.99 (d, J = 8.8 Hz, 1H, ArH), 7.83–7.78 (m, 2H, ArH), 7.70 (t, J = 7.7 Hz, 1H, ArH), 7.60 (s, 2H, ArH), 7.49 (d, J = 8.7 Hz, 1H, ArH), 7.45 (t, J = 7.7 Hz, 1H, ArH), 7.35 (d, J = 8.4 Hz, 2H, ArH), 7.10 (s, 2H, ArH), 6.83 (d, J = 8.4 Hz, 1H, ArH), 6.57 (s, 1H, C–CH), 3.84 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.5, 180.8, 164.9, 160.7, 155.7, 143.6, 140.1, 137.8, 137.6, 130.8, 130.5, 129.9, 128.1, 127.8, 127.5, 126.7, 126.5, 126.1, 125.2, 124.9, 124.6, 123.8, 122.0, 121.9, 118.3, 117.9, 112.4, 112.1, 110.1, 109.6, 104.2, 65.1, 55.5; HRMS (TOF ES+): m/z calcd for $C_{33}H_{23}N_2O_5$ [$(M+H)^+$], 527.1601, found, 527.1597.

4-(2-Hydroxybenzoyl)-2-phenyl-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3m)



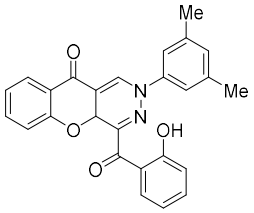
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 33 mg (82%); mp = 163–164°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 11.79 (s, 1H, ArOH), 8.21 (d, J = 7.6 Hz, 1H, ArH), 8.09 (s, 1H, C=CH), 8.00 (d, J = 7.3 Hz, 1H, ArH), 7.60–7.56 (m, 1H, ArH), 7.53–7.50 (m, 1H, ArH), 7.47–7.43 (m, 4H, ArH), 7.28 (s, 1H, ArH), 7.11–7.07 (m, 2H, ArH), 7.01–6.97 (m, 1H, ArH), 6.94 (d, J = 8.1 Hz, 1H, ArH), 6.39 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.3, 181.1, 163.9, 157.7, 142.4, 140.7, 137.2, 136.7, 133.3, 129.8, 129.8, 128.5, 127.4, 126.6, 123.4, 122.4, 119.1, 118.6, 118.5, 118.5, 118.3, 118.3, 109.9, 64.2; HRMS (TOF ES+): m/z calcd for $C_{24}H_{17}N_2O_4$ [$(M+H)^+$], 397.1183, found, 397.1188.

4-(2-Hydroxybenzoyl)-2-(*p*-tolyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3n)



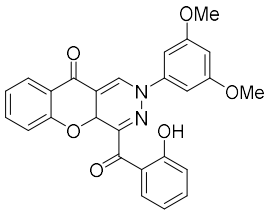
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 23 mg (56%); mp = 175–176°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.82 (s, 1H, ArOH), 8.21 (d, *J* = 7.4 Hz, 1H, ArH), 8.05 (s, 1H, C=CH), 8.00 (d, *J* = 7.1 Hz, 1H, ArH), 7.58–7.55 (m, 1H, ArH), 7.53–7.50 (m, 1H, ArH), 7.34 (d, *J* = 7.3 Hz, 2H, ArH), 7.23 (d, *J* = 7.3 Hz, 2H, ArH), 7.10–7.07 (m, 2H, ArH), 6.97 (d, *J* = 7.0 Hz, 1H, ArH), 6.94 (d, *J* = 8.1 Hz, 1H, ArH), 6.40 (s, 1H, C–CH), 2.37 (s, 3H, $ArCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.2, 181.2, 163.8, 157.6, 140.4, 140.2, 137.1, 136.6, 136.6, 133.3, 130.2, 130.2, 128.6, 127.4, 123.4, 122.3, 118.9, 118.5, 118.5, 118.4, 118.4, 118.4, 109.7, 64.2, 20.9; HRMS (TOF ES+): m/z calcd for $C_{25}H_{19}N_2O_4$ [$(M+H)^+$], 411.1339, found, 411.1332.

2-(3,5-Dimethylphenyl)-4-(2-hydroxybenzoyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3o)



$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 30 mg (70%); mp = 166–167°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.83 (s, 1H, ArOH), 8.23 (d, *J* = 7.8 Hz, 1H, ArH), 8.05 (s, 1H, C=CH), 8.00 (d, *J* = 7.5 Hz, 1H, ArH), 7.57 (t, *J* = 7.5 Hz, 1H, ArH), 7.51 (t, *J* = 7.3 Hz, 1H, ArH), 7.23 (s, 1H, ArH), 7.18 (s, 2H, ArH), 7.10 (t, *J* = 7.7 Hz, 2H, ArH), 6.98 (t, *J* = 7.6 Hz, 1H, ArH), 6.94 (d, *J* = 8.3 Hz, 1H, ArH), 6.40 (s, 1H, C–CH), 2.30 (s, 3H, $ArCH_3$), 2.27 (s, 3H, $ArCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.3, 181.2, 163.8, 157.6, 140.4, 140.3, 138.2, 137.1, 136.6, 135.3, 133.4, 130.6, 128.8, 127.3, 123.39, 122.3, 119.6, 118.9, 118.5, 118.5, 118.4, 115.9, 109.6, 64.3, 20.1, 19.3; HRMS (TOF ES+): m/z calcd for $C_{26}H_{21}N_2O_4$ [$(M+H)^+$], 425.1496, found, 425.1496.

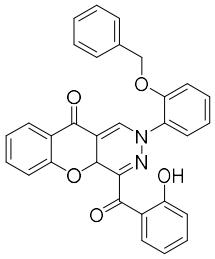
2-(3,5-Dimethoxyphenyl)-4-(2-hydroxybenzoyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3p)



$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 33 mg (72%); mp = 130–131°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.84 (s, 1H, ArOH), 8.27 (d, *J* = 9.0 Hz, 1H, ArH), 7.99 (d, *J* = 7.7 Hz, 1H, ArH), 7.85 (s, 1H, C=CH), 7.56–7.49 (m, 2H, ArH), 7.10–7.05 (m, 2H, ArH), 6.97–6.92 (m, 4H, ArH), 6.89–6.86 (m, 1H, ArH), 6.41 (s, 1H,C–CH), 3.88 (s, 3H, $ArOCH_3$), 3.77 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.4, 181.3, 163.8, 157.7, 153.7, 146.5, 140.4, 137.0,

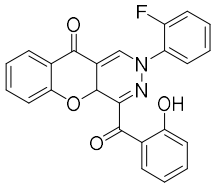
136.5, 133.5, 132.8, 132.0, 127.4, 123.6, 122.2, 118.8, 118.6, 118.5, 118.4, 114.3, 113.2, 111.0, 108.1, 63.9, 56.4, 55.9; HRMS (TOF ES+): m/z calcd for $C_{26}H_{21}N_2O_6$ [$(M+H)^+$], 457.1394, found, 457.1398.

2-(2-(Benzyloxy)phenyl)-4-(2-hydroxybenzoyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3q)



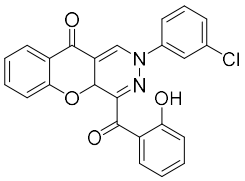
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 18 mg (35%); mp = 200–201°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.30 (d, J = 7.5 Hz, 1H, ArH), 8.09 (s, 1H, C=CH), 8.03 (d, J = 7.3 Hz, 1H, ArH), 7.70 (t, J = 7.4 Hz, 1H, ArH), 7.57 (d, J = 7.4 Hz, 2H, ArH), 7.49 (d, J = 8.4 Hz, 2H, ArH), 7.45–7.42 (m, 3H, ArH), 7.37–7.32 (m, 2H, ArH), 7.11 (t, J = 7.5 Hz, 1H, ArH), 7.00 (d, J = 8.2 Hz, 1H, ArH), 6.90 (d, J = 6.9 Hz, 2H, ArH), 6.84–6.80 (m, 1H, ArH), 6.57 (s, 1H, C–CH), 5.25 (s, 2H, CH_2); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 178.3, 176.1, 159.1, 156.3, 154.9, 146.0, 136.7, 135.8, 133.9, 132.3, 128.8, 128.7, 128.7, 127.9, 127.6, 126.9, 126.9, 126.2, 125.5, 124.1, 123.5, 123.2, 122.9, 122.4, 121.7, 118.3, 118.3, 113.9, 112.4, 75.5, 70.4; HRMS (TOF ES+): m/z calcd for $C_{31}H_{23}N_2O_5$ [$(M+H)^+$], 503.1601, found, 503.1604.

2-(2-Fluorophenyl)-4-(2-hydroxybenzoyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3r)



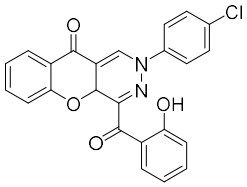
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 16 mg (39%); mp = 202–203°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.78 (s, 1H, ArOH), 8.21 (d, J = 7.8 Hz, 1H, ArH), 7.99 (d, J = 7.5 Hz, 1H, ArH), 7.84 (s, 1H, C=CH), 7.57–7.54 (m, 1H, ArH), 7.51 (t, J = 7.5 Hz, 1H, ArH), 7.44 (t, J = 7.6 Hz, 1H, ArH), 7.35–7.32 (m, 1H, ArH), 7.25–7.21 (m, 2H, ArH), 7.12–7.05 (m, 2H, ArH), 6.99–6.93 (m, 2H, ArH), 6.40 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.3, 181.0, 163.9, 157.8, 155.1(J = 251.3 Hz), 141.2, 137.4, 136.7, 133.4, 131.6(J = 5.0 Hz), 130.9(J = 9.8 Hz), 129.4(J = 7.7 Hz), 127.5, 125.2(J = 3.8 Hz), 125.0, 123.5, 122.5, 119.2, 118.8, 118.6, 118.5, 117.4(J = 19.9 Hz), 109.2, 63.9; HRMS (TOF ES+): m/z calcd for $C_{24}H_{16}FN_2O_4$ [$(M+H)^+$], 415.1089, found, 415.1090.

2-(3-Chlorophenyl)-4-(2-hydroxybenzoyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3s)



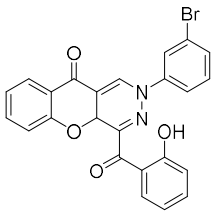
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 35 mg (81%); mp = 215–216°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.30 (d, J = 7.6 Hz, 1H, ArH), 8.13 (s, 1H, C=CH), 8.00 (d, J = 7.5 Hz, 1H, ArH), 7.72 (t, J = 7.3 Hz, 1H, ArH), 7.52 (t, J = 8.0 Hz, 2H, ArH), 7.46 (t, J = 7.6 Hz, 1H, ArH), 7.16–7.11 (m, 3H, ArH), 7.03 (d, J = 8.2 Hz, 1H, ArH), 6.93 (d, J = 7.0 Hz, 2H, ArH), 6.48 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 179.2, 176.1, 159.5, 156.3, 154.6, 143.7, 136.4, 135.3, 134.1, 130.3, 129.3, 127.5, 126.2, 125.6, 124.0, 123.4, 122.8, 122.7, 122.6, 118.3, 118.3, 114.7, 112.9, 75.8; HRMS (TOF ES+): m/z calcd for $C_{24}H_{16}ClN_2O_4$ [$(M+H)^+$], 431.0793, found, 431.0787.

2-(4-Chlorophenyl)-4-(2-hydroxybenzoyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3t)



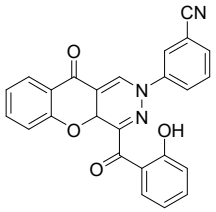
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 34 mg (78%); mp = 194–195°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.75 (s, 1H, ArOH), 8.15 (d, J = 7.6 Hz, 1H, ArH), 8.05 (s, 1H, C=CH), 7.99 (d, J = 7.1 Hz, 1H, ArH), 7.61–7.58 (m, 1H, ArH), 7.53–7.50 (m, 1H, ArH), 7.40 (s, 4H, ArH), 7.13–7.09 (m, 2H, ArH), 7.00–6.97 (m, 1H, ArH), 6.94 (d, J = 8.2 Hz, 1H, ArH), 6.37 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 179.0, 175.9, 159.4, 156.3, 154.7, 141.1, 136.3, 134.0, 129.4, 129.4, 128.9, 128.5, 127.5, 126.1, 125.6, 123.9, 122.8, 122.7, 122.5, 118.3, 118.3, 115.8, 115.8, 75.6; HRMS (TOF ES+): m/z calcd for $C_{24}H_{16}ClN_2O_4$ [$(M+H)^+$], 431.0793, found, 431.0793.

2-(3-Bromophenyl)-4-(2-hydroxybenzoyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3u)



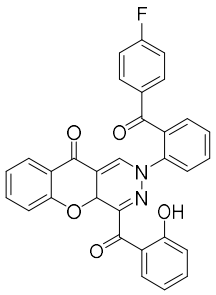
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 42 mg (88%); mp = 174–175°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.74 (s, 1H, ArOH), 8.15 (s, 1H, ArH), 8.05 (s, 1H, C=CH), 8.00 (s, 1H, ArH), 7.62 (d, J = 24.8 Hz, 2H, ArH), 7.52 (s, 1H, ArH), 7.40 (s, 2H, ArH), 7.30 (s, 1H, ArH), 7.11 (s, 2H, ArH), 7.02–6.94 (m, 2H, ArH), 6.36 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.0, 180.9, 163.9, 157.7, 143.3, 141.1, 137.4, 136.7, 133.1, 130.9, 129.4, 127.8, 127.4, 123.4, 123.2, 122.5, 121.3, 119.1, 118.5, 118.5, 118.4, 116.5, 110.2, 64.1; HRMS (TOF ES+): m/z calcd for $C_{24}H_{16}BrN_2O_4$ [$(M+H)^+$], 475.0288, found, 475.0294.

3-(4-(2-Hydroxybenzoyl)-10-oxo-10*H*-chromeno[2,3-*d*]pyridazin-2(4a*H*)-yl)benzonitrile (3v)



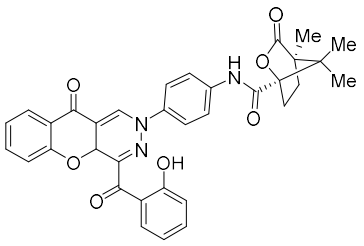
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 5:1, R_f = 0.25; Yellow solid: 37 mg (89%); mp = 186–187°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 13.76 (s, 1H, ArOH), 8.29 (d, *J* = 7.7 Hz, 1H, ArH), 8.16 (s, 1H, C=CH), 8.00 (d, *J* = 7.5 Hz, 1H, ArH), 7.73 (t, *J* = 7.4 Hz, 1H, ArH), 7.53 (t, *J* = 8.1 Hz, 2H, ArH), 7.48 (t, *J* = 7.4 Hz, 1H, ArH), 7.34 (s, 1H, ArH), 7.31–7.28 (m, 1H, ArH), 7.24–7.20 (m, 2H, ArH), 7.14 (t, *J* = 7.3 Hz, 1H, ArH), 7.03 (d, *J* = 8.1 Hz, 1H, ArH), 6.43 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 178.4, 174.9, 158.7, 155.3, 153.6, 142.3, 135.6, 133.2, 129.4, 129.1, 126.6, 125.5, 124.9, 124.8, 122.9, 121.6, 121.5, 121.5, 117.7, 117.4, 117.3, 117.2, 116.4, 112.3, 74.9; HRMS (TOF ES+): m/z calcd for $C_{25}H_{16}N_3O_4$ [$(M+H)^+$], 422.1135, found, 422.1129.

2-(2-(4-Fluorobenzoyl)phenyl)-4-(2-hydroxybenzoyl)-2,4a-dihydro-10*H*-chromeno[2,3-*d*]pyridazin-10-one (3w)



$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 7:1, R_f = 0.25; Yellow solid: 21 mg (40%); mp = 203–204°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 7.6 Hz, 1H, ArH), 8.13 (d, *J* = 7.8 Hz, 1H, ArH), 8.11 (s, 1H, C=CH), 7.80–7.77 (m, 2H, ArH), 7.71 (d, *J* = 7.3 Hz, 1H, ArH), 7.65 (d, *J* = 8.3 Hz, 1H, ArH), 7.52–7.44 (m, 4H, ArH), 7.37 (t, *J* = 7.5 Hz, 1H, ArH), 7.16–7.09 (m, 3H, ArH), 7.01 (d, *J* = 8.2 Hz, 1H, ArH), 6.96 (t, *J* = 7.3 Hz, 1H, ArH), 6.56 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.3, 178.2, 176.0, 165.2 (*J* = 253.8 Hz), 159.5, 156.3, 154.8, 144.8, 136.3, 135.0 (*J* = 3.0 Hz), 134.1 (*J* = 14.6 Hz), 133.1, 132.63 (*J* = 9.1 Hz), 131.2, 128.2, 126.2, 125.6, 124.0, 122.9 (*J* = 26.9 Hz), 122.6, 121.2, 121.1, 118.3, 118.3, 115.3 (*J* = 21.8 Hz), 115.3, 75.8; HRMS (TOF ES+): m/z calcd for $C_{31}H_{20}FN_2O_5$ [$(M+H)^+$], 519.1351, found, 519.1353.

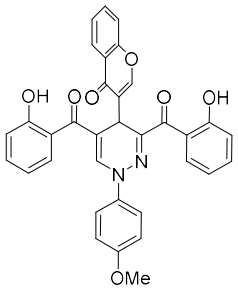
(1*S*,4*S*)-*N*-(4-(4-(2-Hydroxybenzoyl)-10-oxo-10*H*-chromeno[2,3-*d*]pyridazin-2(4a*H*)-yl)phenyl)-4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxamide (3x)



$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 5:1, R_f = 0.25; Yellow solid: 20 mg (33%); mp = 196–198 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 13.97 (s, 1H, ArOH), 8.28 (d, J = 7.9 Hz, 1H, ArH), 8.12 (s, 1H, NH), 8.04 (s, 1H, C=CH), 7.99 (d, J = 7.8 Hz, 1H, ArH), 7.72 (s, 1H, ArH), 7.53–7.42 (m, 4H, ArH), 7.16–6.99 (m, 5H, ArH), 6.50 (s, 1H, C–CH), 2.58 (d, J = 8.9 Hz, 1H, CCH_2), 1.98 (t, J = 11.6 Hz, 2H, CCH_2), 1.74 (d, J = 11.3 Hz, 1H, CCH_2), 1.14 (s, 6H, CCH_3), 0.95 (s, 3H, CCH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 178.8, 177.9, 175.9, 164.9, 159.3, 156.3, 154.7, 139.4, 136.1, 133.9, 132.6, 128.4, 127.4, 126.1, 125.5, 123.9, 122.9, 122.7, 122.5, 121.0, 121.0, 118.2, 118.2, 115.2, 115.2, 92.4, 75.5, 55.4, 54.4, 30.4, 29.0, 16.7, 16.6, 9.7; HRMS (TOF ES+): m/z calcd for $C_{34}H_{30}N_3O_7$ [$(M+H)^+$], 592.2078, found, 592.2077.

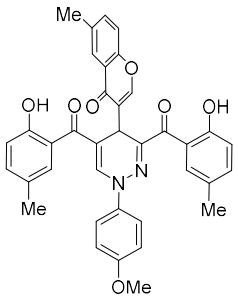
4.2 Spectroscopic data of 3-Pyridazinyl-chromones.

(1-(4-Methoxyphenyl)-4-(4-oxo-4*H*-chromen-3-yl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4a)



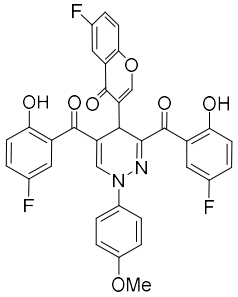
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 232 mg (81%); mp = 246–247 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.74 (s, 1H, ArOH), 10.94 (s, 1H, ArOH), 8.23–8.21 (m, 1H, ArH), 8.12 (d, J = 3.3 Hz, 2H, ArH), 7.65 (s, 1H, C=CH), 7.61 (t, J = 6.5 Hz, 2H, ArH), 7.42 (d, J = 10.0 Hz, 4H, ArH), 7.40 (s, 1H, C=CH), 7.33 (t, J = 7.5 Hz, 1H, ArH), 7.00 (d, J = 8.2 Hz, 1H, ArH), 6.97–6.94 (m, 3H, ArH), 6.89 (t, J = 7.5 Hz, 1H, ArH), 6.84 (t, J = 7.6 Hz, 1H, ArH), 5.69 (s, 1H, C–CH), 3.83 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.5, 194.8, 177.4, 163.3, 161.1, 158.1, 156.3, 155.4, 143.6, 137.6, 137.2, 136.5, 135.0, 134.1, 133.8, 130.8, 125.6, 125.4, 124.7, 121.3, 120.6, 120.6, 120.2, 119.0, 119.0, 118.9, 118.5, 118.4, 118.1, 114.8, 114.8, 110.4, 55.8, 30.6; HRMS (TOF ES+): m/z calcd for $C_{34}H_{24}N_2NaO_7$ [$(M+Na)^+$], 595.1476, found, 595.1472.

(1-(4-Methoxyphenyl)-4-(6-methyl-4-oxo-4*H*-chromen-3-yl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxy-5-methylphenyl)methanone) (4b)



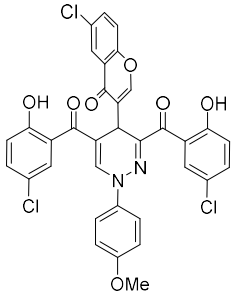
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 243 mg (79%); mp = 231–232 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.59 (s, 1H, ArOH), 10.71 (s, 1H, ArOH), 8.10 (s, 2H, ArH), 7.93 (s, 1H, C=CH), 7.66 (s, 1H, C=CH), 7.43–7.39 (m, 3H, ArH), 7.38 (s, 1H, ArH), 7.31 (d, J = 8.5 Hz, 1H, ArH), 7.26–7.21 (m, 2H, ArH), 6.95 (d, J = 8.9 Hz, 2H, ArH), 6.91 (d, J = 8.4 Hz, 1H, ArH), 6.87 (d, J = 8.4 Hz, 1H, ArH), 5.67 (s, 1H, C–CH), 3.83 (s, 3H, $ArOCH_3$), 2.39 (s, 3H, $ArCH_3$), 2.29 (s, 3H, $ArCH_3$), 2.25 (s, 3H, $ArCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.5, 194.3, 177.5, 161.2, 158.8, 157.9, 155.4, 154.6, 143.8, 137.5, 137.2, 137.1, 135.9, 135.3, 135.0, 133.7, 130.6, 128.2, 127.9, 124.9, 124.4, 121.2, 120.2, 120.2, 119.9, 118.7, 118.2, 118.1, 117.8, 114.8, 114.8, 110.7, 55.8, 30.6, 21.0, 20.8, 20.7; HRMS (TOF ES+): m/z calcd for $C_{37}H_{30}N_2NaO_7$ [$(M+Na)^+$], 637.1945, found, 637.1944.

(4-(6-Fluoro-4-oxo-4*H*-chromen-3-yl)-1-(4-methoxyphenyl)-1,4-dihydropyridazine-3,5-diyl)bis((5-fluoro-2-hydroxyphenyl)methanone) (4c)



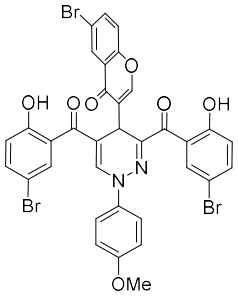
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 229 mg (73%); mp = 229–230 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.54 (s, 1H, ArOH), 10.52 (s, 1H, ArOH), 8.15 (s, 1H, C=CH), 8.08–8.04 (m, 1H, ArH), 7.80–7.77 (m, 1H, ArH), 7.64 (s, 1H, C=CH), 7.44–7.42 (m, 3H, ArH), 7.38–7.33 (m 1H, ArH), 7.27 (d, J = 5.2 Hz, 1H, ArH), 7.21–7.14 (m, 2H, ArH), 7.00 (d, J = 9.1 Hz, 2H, ArH), 6.99–6.95 (m, 1H, ArH), 6.95–6.91 (m, 1H, ArH), 5.65 (s, 1H, C–CH), 3.85 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 194.9, 192.8, 176.4, 159.4 (J = 247.6 Hz), 159.4, 158.3, 156.8, 155.5, 154.8 (J = 240.1 Hz), 154.5 (J = 237.1 Hz), 152.3, 143.1, 137.7, 136.7, 125.6 (J = 7.2 Hz), 123.9 (J = 23.8 Hz), 122.1 (J = 22.7 Hz), 122.0 (J = 25.7 Hz), 120.8, 120.8, 120.5, 120.3 (J = 8.1 Hz), 119.6 (J = 6.2 Hz), 119.6 (J = 7.4 Hz), 119.1 (J = 7.3 Hz), 118.5 (J = 25.0 Hz), 118.1 (J = 7.6 Hz), 115.8 (J = 23.8 Hz), 114.8, 114.8, 110.5 (J = 23.8 Hz), 109.9, 55.6, 29.9; HRMS (TOF ES+): m/z calcd for $C_{34}H_{21}F_3N_2NaO_7$ [$(M+Na)^+$], 649.1193, found, 649.1194.

(4-(6-Chloro-4-oxo-4*H*-chromen-3-yl)-1-(4-methoxyphenyl)-1,4-dihydropyridazine-3,5-diyl)bis((5-chloro-2-hydroxyphenyl)methanone) (4d)



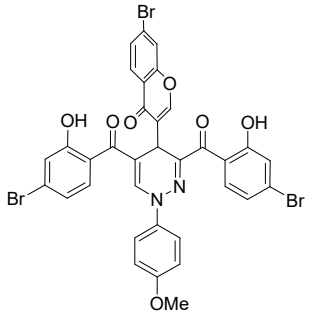
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Red solid: 229 mg (68%); mp = 175–176 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.65 (s, 1H, ArOH), 10.70 (s, 1H, ArOH), 8.42 (d, J = 2.7 Hz, 1H, ArH), 8.15 (s, 1H, C=CH), 8.13 (d, J = 2.6 Hz, 1H, ArH)), 7.65 (s, 1H, C=CH), 7.58–7.55 (m, 1H, ArH), 7.53 (d, J = 2.6 Hz, 1H, ArH), 7.44 (d, J = 8.7 Hz, 2H, ArH), 7.40–7.36 (m, 3H, ArH), 7.01 (d, J = 8.7 Hz, 2H, ArH), 6.96 (d, J = 8.8 Hz, 1H, ArH), 6.92 (d, J = 8.9 Hz, 1H, ArH), 5.63 (s, 1H, C–CH), 3.85 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 194.9, 192.5, 176.2, 161.8, 159.4, 158.5, 155.7, 154.6, 143.1, 137.8, 136.7, 136.3, 134.9, 134.2, 133.0, 131.5, 129.7, 125.6, 125.3, 123.9, 123.7, 121.5, 120.8, 120.8, 120.8, 120.1, 120.1, 119.8, 119.3, 115.1, 115.1, 110.3, 55.8, 30.1; HRMS (TOF ES+): m/z calcd for $C_{34}H_{21}Cl_3N_2NaO_7$ [$(M+Na)^+$], 697.0307, found, 697.0303.

(4-(6-Bromo-4-oxo-4*H*-chromen-3-yl)-1-(4-methoxyphenyl)-1,4-dihydropyridazine-3,5-diyl)bis((5-bromo-2-hydroxyphenyl)methanone) (4e)



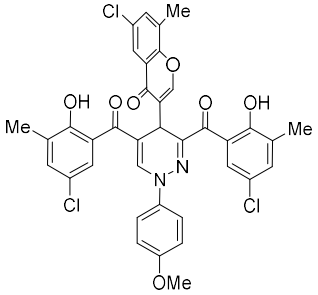
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Red solid: 262 mg (65%); mp = 209–210 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.66 (s, 1H, ArOH), 10.71 (s, 1H, ArOH), 8.61 (d, J = 2.3 Hz, 1H, ArH), 8.30 (d, J = 2.3 Hz, 1H, ArH), 8.16 (s, 1H, C=CH), 7.72–7.68 (m, 1H, ArH), 7.67 (s, 1H, ArH), 7.66 (s, 1H, C=CH), 7.54–7.48 (m, 2H, ArH), 7.45 (d, J = 8.9 Hz, 2H, ArH), 7.33 (d, J = 8.9 Hz, 1H, ArH), 7.02 (d, J = 9.0 Hz, 2H, ArH), 6.91 (d, J = 8.8 Hz, 1H, ArH), 6.87 (d, J = 8.8 Hz, 1H, ArH), 5.61 (s, 1H, C–CH), 3.86 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 194.8, 192.2, 176.1, 162.2, 159.9, 158.5, 155.7, 155.0, 143.0, 138.9, 137.8, 137.7, 136.9, 136.7, 136.1, 132.7, 128.5, 125.9, 121.6, 121.4, 120.6, 120.6, 120.6, 120.3, 120.2, 119.9, 118.9, 115.1, 115.1, 110.8, 110.6, 110.4, 55.8, 30.1; HRMS (TOF ES+): m/z calcd for $C_{34}H_{22}Br_3N_2O_7$ [$(M+H)^+$], 806.8972, found, 806.8972.

(4-(7-Bromo-4-oxo-4*H*-chromen-3-yl)-1-(4-methoxyphenyl)-1,4-dihydropyridazine-3,5-diyl)bis((4-bromo-2-hydroxyphenyl)methanone) (4f)



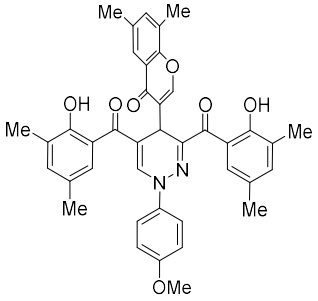
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 266 mg (66%); mp = 254–255 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.80 (s, 1H, ArOH), 11.03 (s, 1H, ArOH), 8.09 (s, 1H, ArH), 8.07 (s, 1H, C=CH), 7.96 (d, J = 8.6 Hz, 1H, ArH), 7.61 (s, 1H, C=CH), 7.58 (s, 1H, ArH), 7.48–7.44 (m, 1H, ArH), 7.42 (d, J = 8.4 Hz, 1H, ArH), 7.38 (d, J = 8.8 Hz, 2H, ArH), 7.20–7.15 (m, 2H, ArH), 7.04–7.00 (m, 1H, ArH), 6.99–6.95 (m, 3H, ArH), 5.61 (s, 1H, C–CH), 3.84 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 195.6, 193.8, 176.8, 163.7, 161.7, 158.4, 156.3, 155.5, 143.3, 137.6, 136.9, 134.9, 131.6, 131.3, 129.5, 129.2, 128.3, 127.0, 123.5, 122.6, 122.5, 121.8, 121.5, 121.5, 121.4, 120.7, 120.7, 118.9, 117.8, 114.9, 114.9, 110.1, 55.8, 30.4; HRMS (TOF ES+): m/z calcd for $C_{34}H_{21}Br_3N_2NaO_7$ [$(M+Na)^+$], 828.8791, found, 828.8800.

6-Chloro-3-(3-(5-chloro-2-hydroxy-3-methylbenzoyl)-5-(5-chloro-2-hydroxy-4-methylbenzoyl)-1-(4-methoxyphenyl)-1,4-dihydropyridazin-4-yl)-7-methyl-4*H*-chromen-4-one (4g)



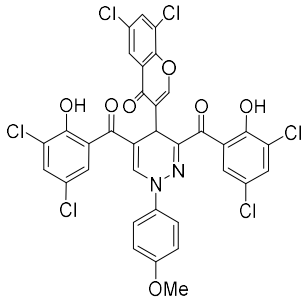
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 279 mg (78%); mp = 198–199 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.71 (s, 1H, ArOH), 10.83 (s, 1H, ArOH), 8.43 (s, 1H, ArH), 8.10 (s, 1H, ArH), 8.07 (s, 1H, C=CH), 7.64 (s, 1H, C=CH), 7.54 (s, 1H, ArH), 7.44 (d, J = 8.9 Hz, 2H, ArH), 7.28 (s, 1H, ArH), 7.00 (d, J = 8.9 Hz, 2H, ArH), 6.86 (d, J = 23.6 Hz, 2H, ArH), 5.60 (s, 1H, C–CH), 3.85 (s, 3H, $ArOCH_3$), 2.43 (s, 3H, $ArCH_3$), 2.34 (s, 6H, $ArCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 194.8, 192.1, 176.1, 161.8, 159.5, 158.3, 155.4, 154.5, 145.7, 144.1, 143.2, 143.2, 137.3, 136.9, 133.4, 132.1, 130.2, 125.5, 124.4, 124.4, 123.7, 121.4, 120.6, 120.5, 120.5, 120.1, 120.0, 118.9, 117.6, 115.0, 115.0, 110.4, 55.8, 30.2, 20.9, 20.9, 20.8; HRMS (TOF ES+): m/z calcd for $C_{37}H_{28}Cl_3N_2O_7$ [$(M+H)^+$], 717.0957, found, 717.1123.

(4-(6,8-Dimethyl-4-oxo-4*H*-chromen-3-yl)-1-(4-methoxyphenyl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxy-3,5-dimethylphenyl)methanone) (4h)



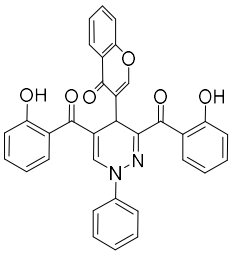
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Red solid: 230 mg (70%); mp = 272–273 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.90 (s, 1H, ArOH), 11.00 (s, 1H, ArOH), 8.11 (s, 1H, ArH), 7.91 (s, 1H, C=CH), 7.76 (s, 1H, ArH), 7.65 (s, 1H, C=CH), 7.38 (d, J = 8.9 Hz, 2H, ArH), 7.24 (d, J = 16.2 Hz, 2H, ArH), 7.13 (d, J = 18.2 Hz, 2H, ArH), 6.93 (d, J = 8.9 Hz, 2H, ArH), 5.69 (s, 1H, C–CH), 3.83 (s, 3H, $ArOCH_3$), 2.37 (s, 3H, $ArCH_3$), 2.34 (s, 3H, $ArCH_3$), 2.25 (s, 3H, $ArCH_3$), 2.22 (s, 3H, $ArCH_3$), 2.21 (s, 6H, $ArCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 197.0, 194.9, 177.8, 159.7, 157.8, 157.2, 154.9, 153.2, 144.0, 138.6, 137.3, 137.0, 136.9, 135.9, 134.7, 131.3, 128.3, 127.5, 127.4, 127.2, 127.1, 126.6, 124.3, 122.5, 120.9, 120.1, 120.1, 119.2, 117.9, 114.7, 114.7, 110.8, 55.8, 30.9, 20.9, 20.8, 20.7, 15.8, 15.8, 15.6; HRMS (TOF ES+): m/z calcd for $C_{40}H_{36}N_2NaO_7$ [$(M+Na)^+$], 679.2415, found, 679.2479.

(4-(6,8-Dichloro-4-oxo-4*H*-chromen-3-yl)-1-(4-methoxyphenyl)-1,4-dihydropyridazine-3,5-diyl)bis((3,5-dichloro-2-hydroxyphenyl)methanone) (4i)



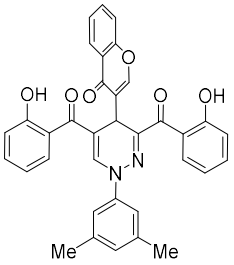
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 7:1, R_f = 0.25; Red solid: 295 mg (76%); mp = 172–173 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 12.11 (s, 1H, ArOH), 10.90 (s, 1H, ArOH), 8.35 (d, J = 2.6 Hz, 1H, ArH), 8.25 (s, 1H, C=CH), 8.03 (d, J = 2.5 Hz, 1H, ArH), 7.68 (d, J = 2.6 Hz, 1H, ArH), 7.63 (s, 1H, C=CH), 7.56–7.50 (m, 2H, ArH), 7.43–7.40 (m, 3H, ArH), 7.01 (d, J = 8.8 Hz, 2H, ArH), 5.63 (s, 1H, C–CH), 3.86 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 194.0, 192.0, 175.7, 158.8, 157.5, 155.7, 155.0, 150.7, 142.8, 138.3, 136.5, 135.9, 134.5, 134.2, 131.6, 131.3, 128.2, 126.3, 124.7, 124.2, 123.9, 123.9, 123.7, 123.5, 121.6, 121.5, 120.9, 120.9, 119.8, 115.1, 115.1, 110.1, 55.8, 30.1; HRMS (TOF ES+): m/z calcd for $C_{34}H_{18}Cl_6N_2NaO_7$ [$(M+Na)^+$], 798.9137, found, 798.9140.

(4-(4-Oxo-4*H*-chromen-3-yl)-1-phenyl-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4j)



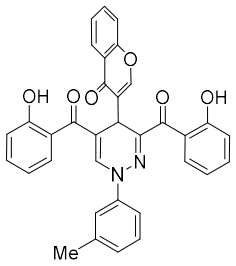
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 192 mg (71%); mp = 243–244 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 10.43 (s, 1H, ArOH), 10.11 (s, 1H, ArOH), 8.34 (s, 1H, C=CH), 7.99 (d, J = 7.7 Hz, 1H, ArH), 7.78 (t, J = 7.9 Hz, 1H, ArH), 7.68 (s, 1H, C=CH), 7.62 (d, J = 8.4 Hz, 1H, ArH), 7.53 (d, J = 7.7 Hz, 1H, ArH), 7.45 (t, J = 7.6 Hz, 1H, ArH), 7.41–7.39 (m, 3H, ArH), 7.35–7.32 (m, 3H, ArH), 7.30 (d, J = 7.6 Hz, 1H, ArH), 7.21 (t, J = 7.3 Hz, 1H, ArH), 6.93 (d, J = 8.2 Hz, 1H, ArH), 6.91–6.88 (m, 2H, ArH), 6.87–6.85 (m, 1H, ArH), 5.49 (s, 1H, C–CH); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 193.5, 192.9, 175.7, 158.5, 155.6, 155.6, 155.2, 145.4, 142.9, 138.4, 134.3, 134.2, 131.9, 131.2, 129.7, 129.7, 125.7, 125.7, 125.7, 125.2, 123.5, 123.1, 121.9, 121.9, 119.2, 118.8, 118.5, 117.9, 117.9, 116.9, 116.6, 110.7, 28.3; HRMS (TOF ES+): m/z calcd for $C_{33}H_{23}N_2O_6$ [$(M+H)^+$], 543.1551, found, 543.1594.

(1-(3,5-Dimethylphenyl)-4-(4-oxo-4*H*-chromen-3-yl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4k)



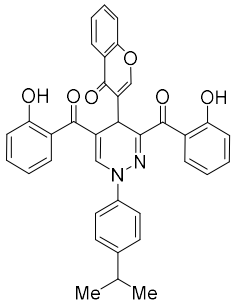
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 9:1, R_f = 0.25; Yellow solid: 237 mg (83%); mp = 160–161 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.75 (s, 1H, ArOH), 10.98 (s, 1H, ArOH), 8.26–8.23 (m, 1H, ArH), 8.14–8.12 (m, 1H, ArH), 8.11 (s, 1H, C=CH), 7.71 (s, 1H, C=CH), 7.64–7.59 (m, 2H, ArH), 7.46–7.42 (m, 2H, ArH), 7.40 (d, J = 8.4 Hz, 1H, ArH), 7.33 (t, J = 7.5 Hz, 1H, ArH), 7.09 (s, 2H, ArH), 7.01 (d, J = 8.2 Hz, 1H, ArH), 6.97 (d, J = 8.2 Hz, 1H, ArH), 6.92–6.88 (m, 2H, ArH), 6.85 (t, J = 7.5 Hz, 1H, ArH), 5.68 (s, 1H, C–CH), 2.34 (s, 6H, $ArCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.6, 194.8, 177.3, 163.3, 161.2, 156.3, 155.4, 143.7, 143.4, 139.6, 139.6, 137.2, 136.6, 135.1, 134.2, 133.8, 130.9, 127.9, 125.7, 125.3, 124.7, 121.3, 120.2, 119.0, 118.9, 118.9, 118.5, 118.4, 118.1, 116.5, 116.5, 110.6, 30.7, 21.7, 21.7; HRMS (TOF ES+): m/z calcd for $C_{35}H_{26}N_2NaO_6$ [$(M+Na)^+$], 593.1683, found, 593.1686.

(4-(4-Oxo-4*H*-chromen-3-yl)-1-(m-tolyl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4l)



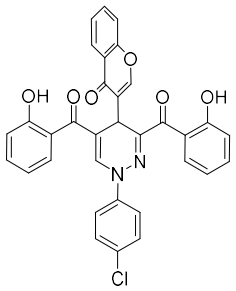
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 228 mg (82%); mp = 226–227 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.73 (s, 1H, ArOH), 10.96 (s, 1H, ArOH), 8.26–8.22 (m, 1H, ArH), 8.14–8.11 (m, 2H, C=CH and ArH), 7.73 (s, 1H, C=CH), 7.64–7.59 (m, 2H, ArH), 7.46–7.42 (m, 2H, ArH), 7.41 (d, J = 8.4 Hz, 1H, ArH), 7.35–7.30 (m, 2H, ArH), 7.29 (s, 1H, ArH), 7.27 (s, 1H, ArH), 7.07 (d, J = 7.3 Hz, 1H, ArH), 7.01 (d, J = 8.2 Hz, 1H, ArH), 6.97 (d, J = 8.3 Hz, 1H, ArH), 6.92–6.88 (m, 1H, ArH), 6.86–6.83 (m, 1H, ArH), 5.69 (s, 1H, C–CH), 2.39 (s, 3H, $ArCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.6, 194.8, 177.4, 163.3, 161.2, 156.3, 155.4, 143.9, 143.4, 139.9, 137.1, 136.6, 135.2, 134.2, 133.8, 130.9, 129.6, 126.9, 125.7, 125.4, 124.7, 121.2, 120.2, 119.3, 119.1, 118.9, 118.9, 118.5, 118.4, 118.1, 115.7, 110.8, 30.8, 21.8; HRMS (TOF ES+): m/z calcd for $C_{34}H_{24}N_2NaO_6$ [$(M+Na)^+$], 579.1527, found, 579.1517.

(1-(4-Isopropylphenyl)-4-(4-oxo-4*H*-chromen-3-yl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4m)



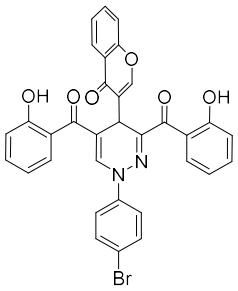
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 10:1, R_f = 0.25; Yellow solid: 213 mg (73%); mp = 231–232 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 11.72 (s, 1H, ArOH), 10.92 (s, 1H, ArOH), 8.25–8.22 (m, 1H, ArH), 8.14–8.10 (m, 2H, C=CH and ArH), 7.72 (s, 1H, C=CH), 7.63–7.58 (m, 2H, ArH), 7.46–7.42 (m, 2H, ArH), 7.41–7.39 (m, 3H, ArH), 7.33 (t, J = 7.5 Hz, 1H, ArH), 7.28 (d, J = 8.5 Hz, 2H, ArH), 7.01 (d, J = 8.2 Hz, 1H, ArH), 6.97 (d, J = 8.3 Hz, 1H, ArH), 6.89 (t, J = 7.5 Hz, 1H, ArH), 6.85 (t, J = 7.6 Hz, 1H, ArH), 5.70 (s, 1H, C–CH), 2.98–2.89 (m, 1H, CH), 1.27 (s, 3H, CCH_3), 1.25 (s, 3H, CCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 196.6, 194.9, 177.3, 163.3, 161.2, 156.3, 155.4, 147.1, 143.8, 141.4, 137.3, 136.5, 135.1, 134.1, 133.8, 130.9, 127.7, 127.7, 125.7, 125.3, 124.7, 121.4, 120.3, 119.1, 119.0, 118.9, 118.8, 118.8, 118.5, 118.4, 118.1, 110.7, 33.8, 30.7, 24.1, 24.1; HRMS (TOF ES+): m/z calcd for $C_{36}H_{28}N_2NaO_6$ [$(M+Na)^+$], 607.1840, found, 607.1846.

(1-(4-Chlorophenyl)-4-(4-oxo-4*H*-chromen-3-yl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4n)



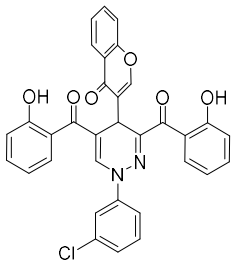
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 207 mg (72%); mp = 214–215 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.65 (s, 1H, ArOH), 10.91 (s, 1H, ArOH), 8.18–8.15 (m, 1H, ArH), 8.13 (s, 1H, C=CH), 8.12–8.09 (m, 1H, ArH), 7.67 (s, 1H, C=CH), 7.63–7.59 (m, 2H, ArH), 7.47–7.43 (m, 2H, ArH), 7.41 (d, J = 2.6 Hz, 1H, ArH), 7.41–7.36 (m, 4H, ArH), 7.34 (t, J = 7.5 Hz, 1H, ArH), 7.01 (d, J = 8.2 Hz, 1H, ArH), 6.97 (d, J = 8.2 Hz, 1H, ArH), 6.91 (t, J = 7.5 Hz, 1H, ArH), 6.84 (t, J = 7.6 Hz, 1H, ArH), 5.67 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.6, 194.8, 177.4, 163.3, 161.2, 156.3, 155.6, 144.2, 141.9, 136.7, 136.4, 135.3, 133.9, 133.9, 131.4, 130.8, 129.8, 129.8, 125.6, 125.5, 124.6, 120.9, 120.1, 119.6, 119.6, 119.1, 119.0, 118.9, 118.6, 118.4, 118.2, 111.3, 30.8; HRMS (TOF ES+): m/z calcd for $C_{33}H_{21}ClN_2NaO_6$ [$(M+Na)^+$], 599.0980, found, 599.0997.

(1-(4-Bromophenyl)-4-(4-oxo-4*H*-chromen-3-yl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4o)



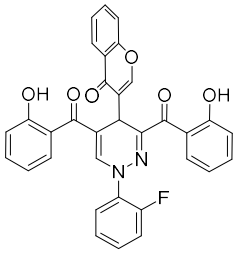
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 248 mg (80%); mp = 176–177 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.65 (s, 1H, ArOH), 10.91 (s, 1H, ArOH), 8.18–8.14 (m, 1H, ArH), 8.13 (s, 1H, C=CH), 8.12–8.09 (m, 1H, ArH), 7.67 (s, 1H, C=CH), 7.63–7.60 (m, 2H, ArH), 7.53 (d, J = 8.8 Hz, 2H, ArH), 7.47–7.43 (m, 2H, ArH), 7.41 (d, J = 8.4 Hz, 1H, ArH), 7.36–7.32 (m, 3H, ArH), 7.01 (d, J = 8.2 Hz, 1H, ArH), 6.97 (d, J = 8.3 Hz, 1H, ArH), 6.91 (t, J = 7.5 Hz, 1H, ArH), 6.84 (t, J = 7.6 Hz, 1H, ArH), 5.67 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.6, 194.7, 177.4, 163.3, 161.2, 156.3, 155.6, 144.2, 142.4, 136.8, 136.2, 135.4, 133.9, 133.9, 132.7, 132.7, 130.8, 125.6, 125.5, 124.6, 120.9, 120.0, 119.9, 119.9, 119.1, 119.0, 119.0, 118.9, 118.6, 118.4, 118.2, 111.4, 30.8; HRMS (TOF ES+): m/z calcd for $C_{33}H_{21}BrN_2NaO_6$ [$(M+Na)^+$], 643.0475, found, 643.0477.

(1-(3-Chlorophenyl)-4-(4-oxo-4*H*-chromen-3-yl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4p)



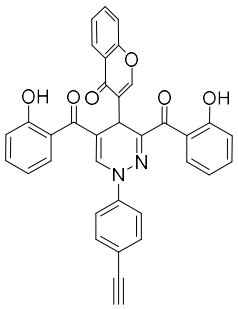
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 176 mg (61%); mp = 228–229 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.65 (s, 1H, ArOH), 10.92 (s, 1H, ArOH), 8.18 (d, J = 8.0 Hz, 1H, ArH), 8.13 (s, 1H, C=CH), 8.11 (d, J = 8.2 Hz, 1H, ArH), 7.68 (s, 1H, C=CH), 7.64–7.59 (m, 2H, ArH), 7.49 (s, 1H, ArH), 7.49–7.43 (m, 2H, ArH), 7.41 (d, J = 8.4 Hz, 1H, ArH), 7.37–7.33 (m, 3H, ArH), 7.22 (d, J = 7.0 Hz, 1H, ArH), 7.02 (d, J = 8.2 Hz, 1H, ArH), 6.98 (d, J = 8.3 Hz, 1H, ArH), 6.93 (t, J = 7.5 Hz, 1H, ArH), 6.87 (t, J = 7.6 Hz, 1H, ArH), 5.67 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.7, 194.7, 177.4, 163.4, 161.3, 156.3, 155.6, 144.3, 144.2, 136.8, 136.0, 135.6, 135.4, 133.9, 133.9, 130.8, 130.8, 125.9, 125.6, 125.5, 124.6, 120.9, 120.0, 119.2, 119.1, 118.9, 118.6, 118.6, 118.4, 118.2, 116.1, 111.5, 30.9; HRMS (TOF ES+): m/z calcd for $C_{33}H_{21}ClN_2NaO_6$ [$(M+Na)^+$], 599.0980, found, 599.0972.

(1-(2-Fluorophenyl)-4-(4-oxo-4*H*-chromen-3-yl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4q)



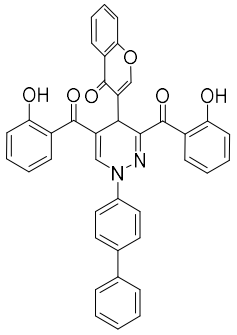
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Yellow solid: 176 mg (63%); mp = 223–224 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.71 (s, 1H, ArOH), 11.02 (s, 1H, ArOH), 8.17 (t, J = 8.3 Hz, 2H, ArH), 8.12 (s, 1H, C=CH), 7.65 (d, J = 7.6 Hz, 1H, ArH), 7.64–7.60 (m, 2H, ArH), 7.59 (s, 1H, C=CH), 7.43–7.40 (m, 3H, ArH), 7.34 (t, J = 7.4 Hz, 1H, ArH), 7.26–7.18 (m, 3H, ArH), 7.00–6.94 (m, 2H, ArH), 6.88 (t, J = 7.4 Hz, 1H, ArH), 6.81 (t, J = 7.5 Hz, 1H, ArH), 5.71 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.6, 194.9, 177.3, 163.4, 161.2, 156.3, 154.6 (J = 249.2 Hz), 144.6, 139.7, 139.7, 136.7, 135.3, 133.9 (J = 31.3 Hz), 131.8 (J = 9.0 Hz), 131.2, 128.1 (J = 7.6 Hz), 125.8, 125.4, 125.2 (J = 3.8 Hz), 124.7, 124.5, 124.5, 121.1, 119.9, 119.0, 118.9, 118.9, 118.4, 118.4, 118.1, 117.2 (J = 19.9 Hz), 110.0, 30.5; HRMS (TOF ES+): m/z calcd for $C_{33}H_{21}FN_2NaO_6$ [$(M+Na)^+$], 583.1276, found, 583.1280.

(1-(4-Ethynylphenyl)-4-(4-oxo-4*H*-chromen-3-yl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4r)



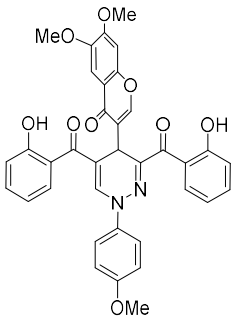
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 5:1, R_f = 0.25; Yellow solid: 190 mg (67%); mp = 236–237 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.65 (s, 1H, ArOH), 10.92 (s, 1H, ArOH), 8.18 (d, J = 8.1 Hz, 1H, ArH), 8.13 (s, 1H, C=CH), 8.10 (d, J = 8.0 Hz, 1H, ArH), 7.72 (s, 1H, C=CH), 7.64–7.60 (m, 2H, ArH), 7.54 (d, J = 8.5 Hz, 2H, ArH), 7.47–7.44 (m, 2H, ArH), 7.42–7.40 (m, 3H, ArH), 7.34 (t, J = 7.5 Hz, 1H, ArH), 7.02 (d, J = 8.2 Hz, 1H, ArH), 6.98 (d, J = 8.3 Hz, 1H, ArH), 6.92 (t, J = 7.5 Hz, 1H, ArH), 6.85 (t, J = 7.6 Hz, 1H, ArH), 5.67 (s, 1H, C–CH), 3.12 (s, 1H, C≡CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.7, 194.8, 177.4, 163.4, 161.3, 156.3, 155.6, 144.4, 143.2, 136.8, 135.9, 135.4, 134.0, 133.9, 133.6, 133.6, 130.8, 125.6, 125.5, 124.6, 120.9, 120.0, 119.4, 119.2, 119.1, 118.9, 118.6, 118.4, 118.2, 117.8, 117.8, 111.6, 82.9, 78.1, 30.9; HRMS (TOF ES+): m/z calcd for $C_{35}H_{22}N_2NaO_6$ [$(M+Na)^+$], 589.1370, found, 589.1360.

(1-([1,1'-Biphenyl]-4-yl)-4-(4-oxo-4*H*-chromen-3-yl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4s)



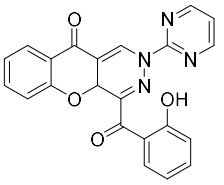
$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 8:1, R_f = 0.25; Red solid: 238 mg (77%); mp = 252–253 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.72 (s, 1H, ArOH), 10.96 (s, 1H, ArOH), 8.27–8.24 (m, 1H, ArH), 8.14 (s, 1H, C=CH), 8.15–8.11 (m, 1H, ArH), 7.79 (s, 1H, ArH), 7.68–7.65 (m, 2H, ArH), 7.65 (s, 1H, C=CH), 7.63–7.60 (m, 1H, ArH), 7.59 (d, J = 7.3 Hz, 2H, ArH), 7.54 (d, J = 8.6 Hz, 2H, ArH), 7.48–7.43 (m, 4H, ArH), 7.41 (d, J = 8.4 Hz, 1H, ArH), 7.37 (t, J = 7.4 Hz, 1H, ArH), 7.34 (t, J = 7.6 Hz, 1H, ArH), 7.03 (d, J = 8.1 Hz, 1H, ArH), 6.99 (d, J = 8.1 Hz, 1H, ArH), 6.93 (t, J = 7.3 Hz, 1H, ArH), 6.88 (t, J = 7.4 Hz, 1H, ArH), 5.71 (s, 1H, C–CH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.6, 194.8, 177.4, 163.3, 161.2, 156.3, 155.5, 144.1, 142.5, 140.1, 138.9, 136.7, 136.6, 135.2, 134.1, 133.9, 130.9, 129.0, 129.0, 128.4, 128.4, 127.6, 127.1, 127.1, 125.7, 125.4, 124.7, 121.1, 120.2, 119.1, 119.0, 118.9, 118.7, 118.7, 118.5, 118.4, 118.2, 111.1, 30.8; HRMS (TOF ES+): m/z calcd for $C_{39}H_{26}N_2NaO_6$ [$(M+Na)^+$], 641.1683, found, 641.1491.

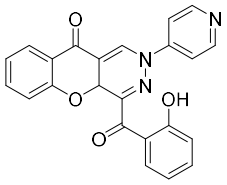
(4-(6,7-dimethoxy-4-oxo-4*H*-chromen-3-yl)-1-(4-methoxyphenyl)-1,4-dihydropyridazine-3,5-diyl)bis((2-hydroxyphenyl)methanone) (4t)



$V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 2:1, R_f = 0.25; Yellow solid: 238 mg (58%); mp = 241–242 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.73 (s, 1H, ArOH), 10.93 (s, 1H, ArOH), 8.22 (s, 1H, ArH), 8.05 (s, 1H, C=CH), 7.65 (s, 1H, ArH), 7.62 (s, 1H, C=CH), 7.44–7.40 (m, 5H, ArH), 7.01–6.88 (m, 5H, ArH), 6.82 (d, J = 21.8 Hz, 2H, ArH), 5.67 (s, 1H, C–CH), 3.92 (s, 3H, $ArOCH_3$), 3.91 (s, 3H, $ArOCH_3$), 3.82 (s, 3H, $ArOCH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 196.4, 194.8, 176.3, 163.1, 160.9, 157.9, 154.5, 154.4, 152.4, 147.6, 143.7, 137.5, 137.1, 136.3, 134.9, 134.0, 130.7, 120.6, 120.4, 120.4, 120.2, 118.9, 118.9, 118.8, 118.3, 118.1, 117.9, 114.7, 114.7, 110.4, 104.0, 99.6, 56.5, 56.4, 55.7, 30.5; HRMS (TOF ES+): m/z calcd for $C_{36}H_{28}N_2NaO_9$ [$(M+Na)^+$], 655.1687, found, 655.1681.

Failed examples:





5. X-ray Structure and Data.

5.1 X-ray Structure and Data[5] of 3s (CCDC 2286041).

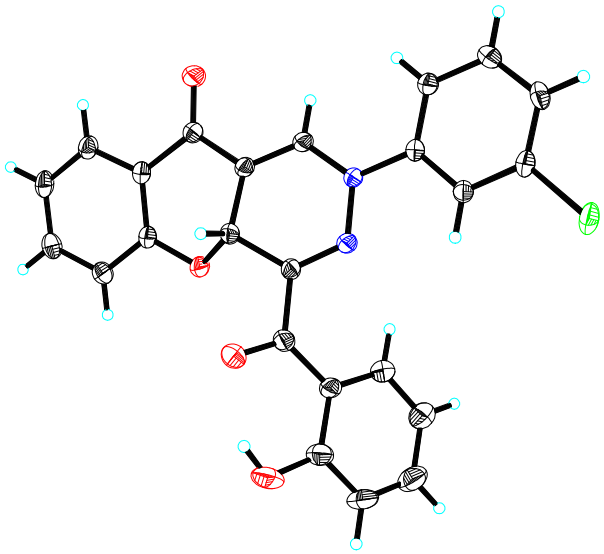


Figure S1 X-Ray crystal structure of **3s.**

Table S3 Crystal data and structure refinement for **3s.**

Empirical formula	$C_{24}H_{15}ClN_2O_4$	
Formula weight	430.83	
Temperature	296.15 K	
Crystal system, space group	Monoclinic, P2(1)/c	
Unit cell dimensions	a = 7.4673(10) A	alpha = 90 deg.
	b = 34.647(5) A	beta = 100.3200(10) deg.
	c = 7.6160(17) A	gamma = 90 deg.
Volume	1938.5(6) A^3	
Z, Calculated density	4, 1.476 Mg/m^3	
Absorption coefficient	0.234 mm^-1	
F(000)	888.0	
Theta range for data collection	2.35 to 55.108 deg.	
Limiting indices	-9<=h<=9, -44<=k<=44, -9<=l<=8	
Reflections collected / unique	11555 / 4363 [R(int) = 0.0274]	
Data/restraints/parameters	4363 / 0 / 281	
Goodness-of-fit on F^2	1.085	
Final R indices [I>2sigma(I)]	R1 = 0.0519, wR2 = 0.1209	
R indices (all data)	R1 = 0.0761, wR2 = 0.1361	
Largest diff. peak and hole	0.25 and -0.37 e.A^-3	

5.2 X-ray Structure and Data[6] of 4j (CCDC 2312821).

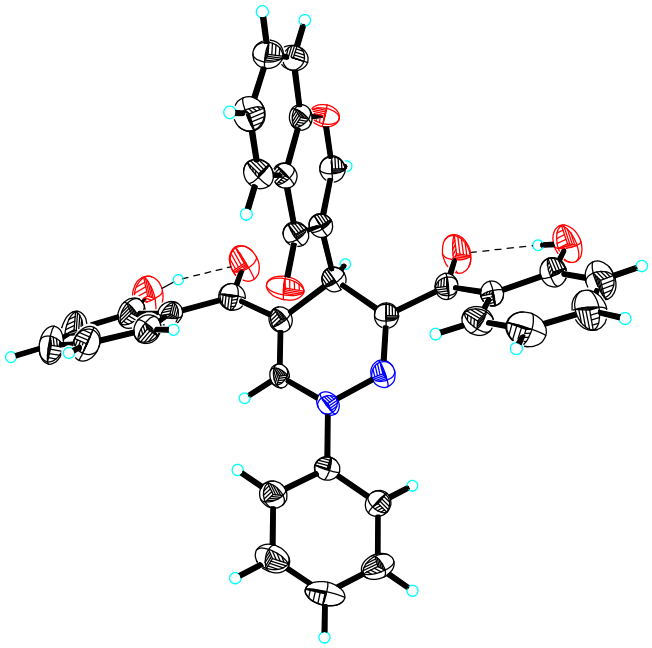


Figure S2 X-Ray crystal structure of **4j.**

Table S4 Crystal data and structure refinement for **4j.**

Empirical formula	$C_{33}H_{22}N_2O_6$
Formula weight	542.52
Temperature	296.15 K
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 10.784(3) A alpha = 90 deg.
	b = 19.095(6) A beta = 92.648(7) deg.
	c = 12.933(4) A gamma = 90 deg.
Volume	2660.4(14) A^3
Z, Calculated density	4, 1.355 Mg/m^3
Absorption coefficient	0.094 mm^-1
F(000)	1128.0
Theta range for data collection	5.262 to 55.16 deg.
Limiting indices	-11<=h<=14, -24<=k<=24, -16<=l<=16
Reflections collected / unique	15919 / 6029 [R(int) = 0.1040]
Data/restraints/parameters	6029 / 0 / 372
Goodness-of-fit on F^2	0.930
Final R indices [I>2sigma(I)]	R1 = 0.0731, wR2 = 0.1301
R indices (all data)	R1 = 0.2365, wR2 = 0.1797
Largest diff. peak and hole	0.27 and -0.24 e.A^-3

6. ^{1}H NMR and ^{13}C NMR spectra for spectroscopic data.

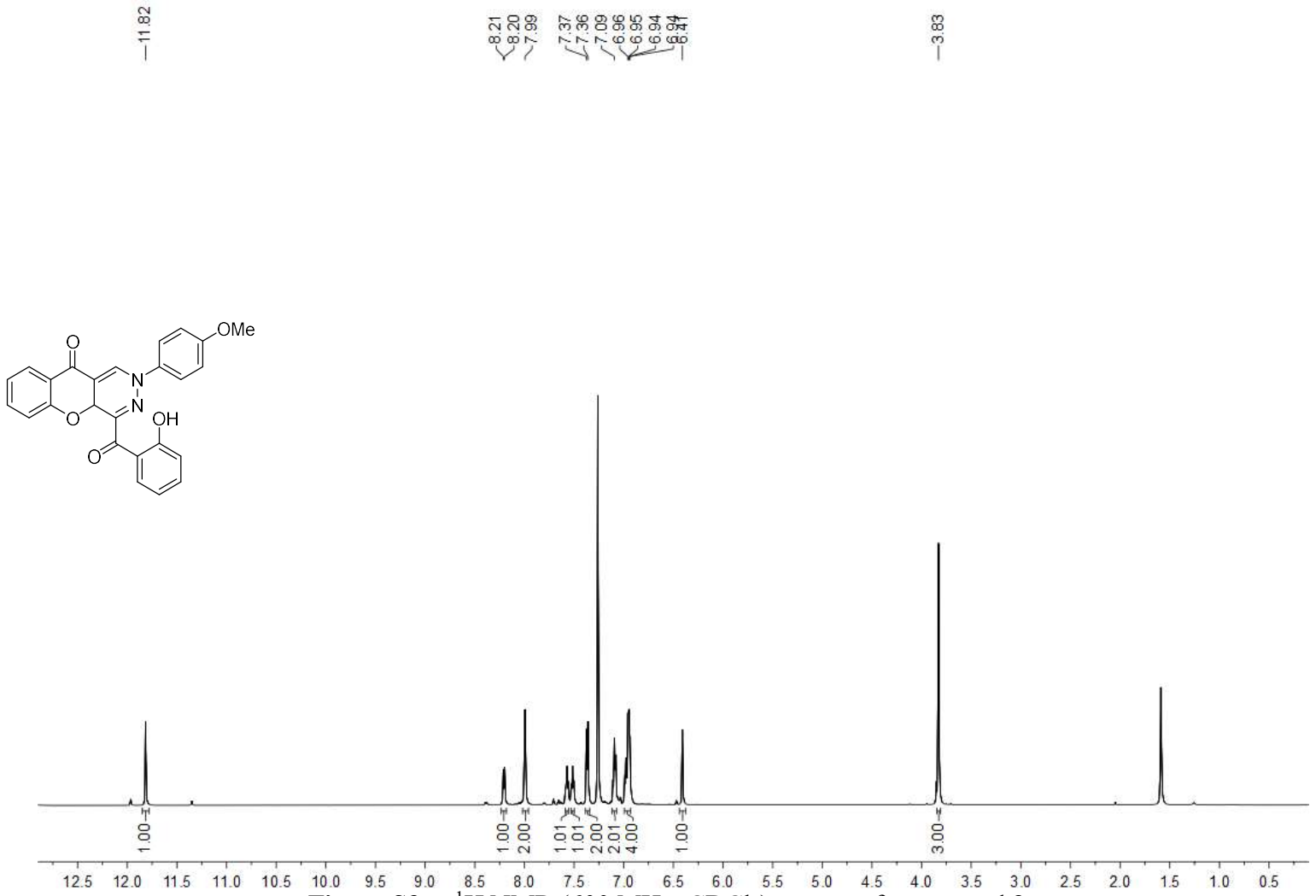


Figure S3. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3a**

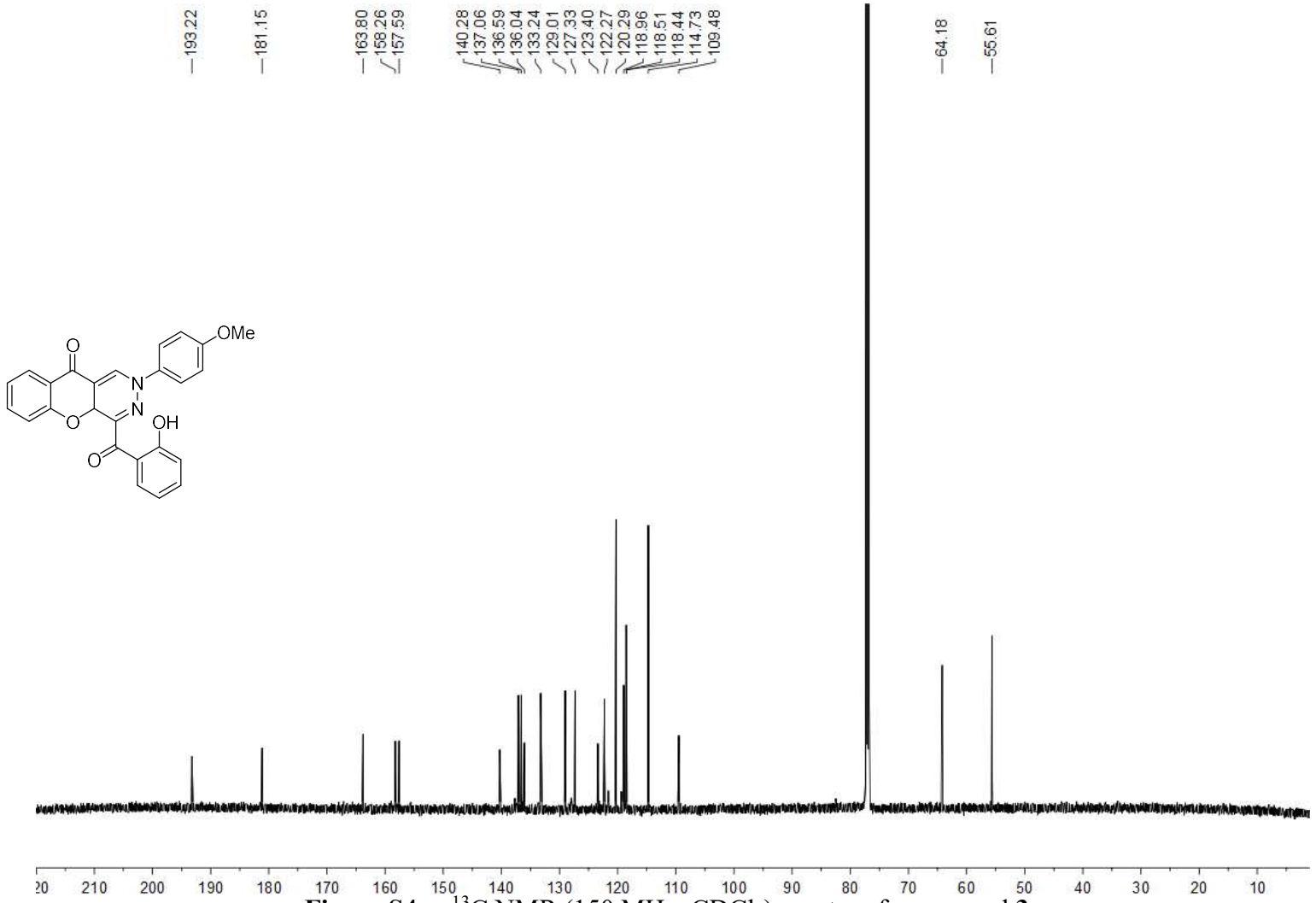


Figure S4. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3a**

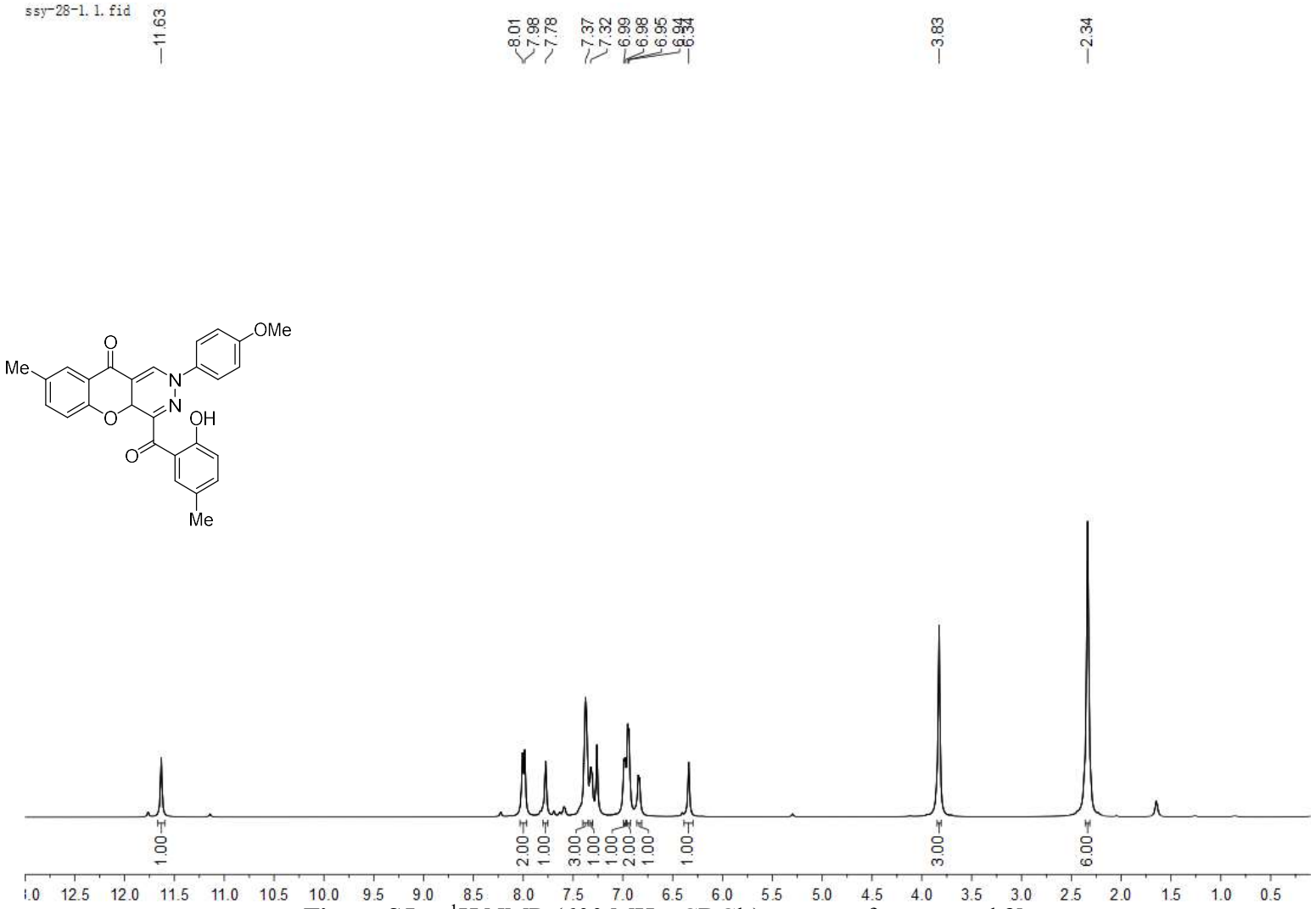


Figure S5. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3b**

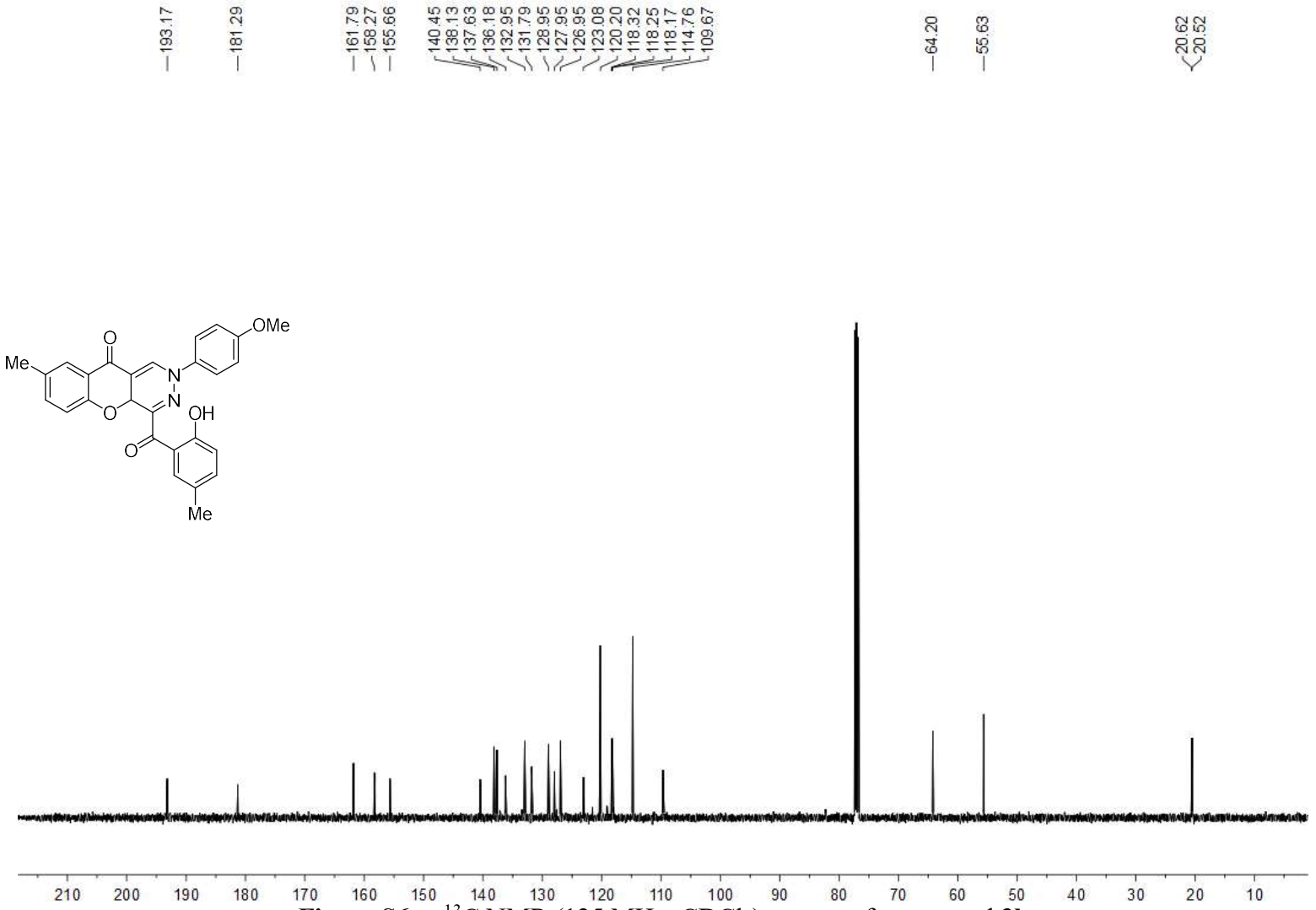


Figure S6. ^{13}C NMR (125 MHz, $CDCl_3$) spectra of compound **3b**

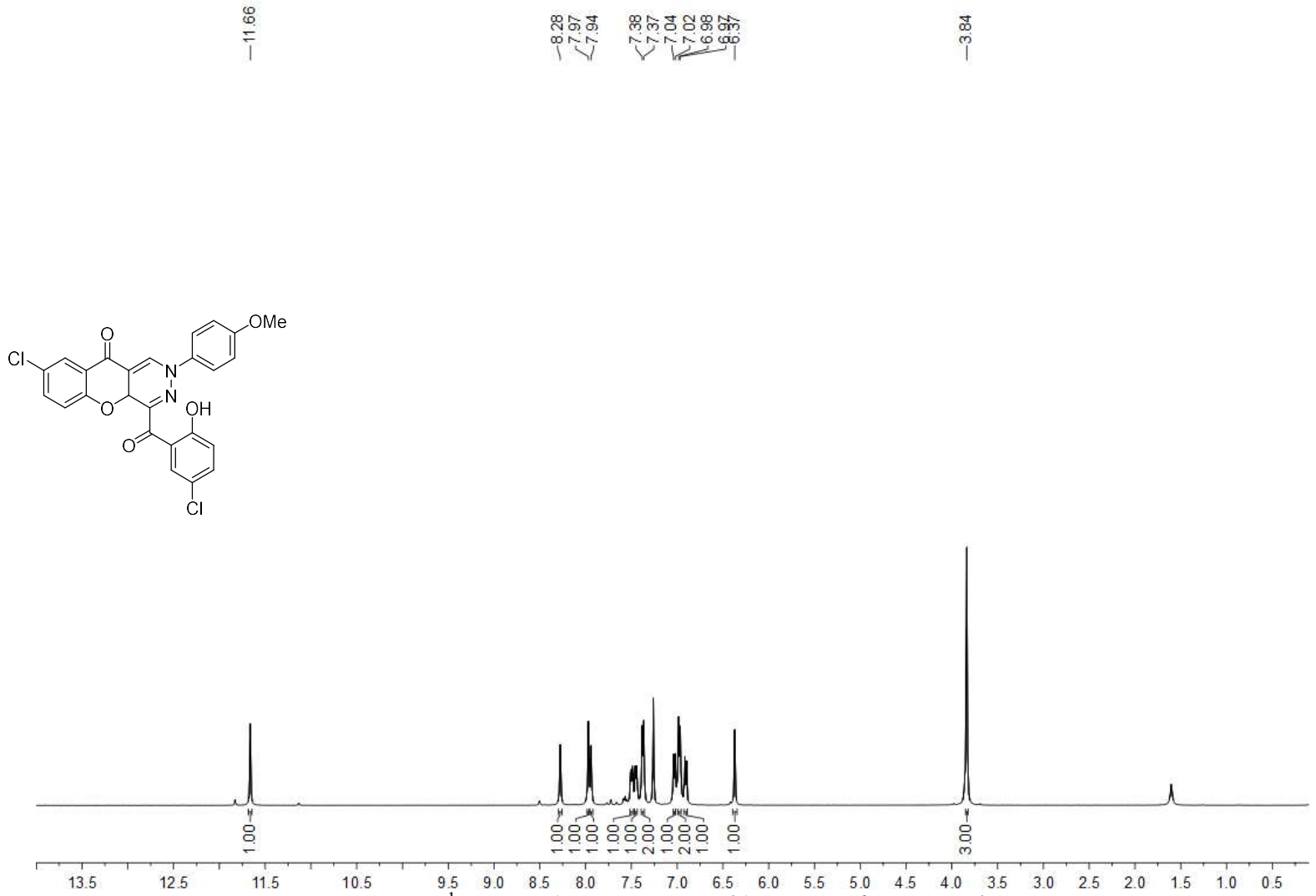


Figure S7. ^{1}H NMR (500 MHz, $CDCl_3$) spectra of compound **3c**

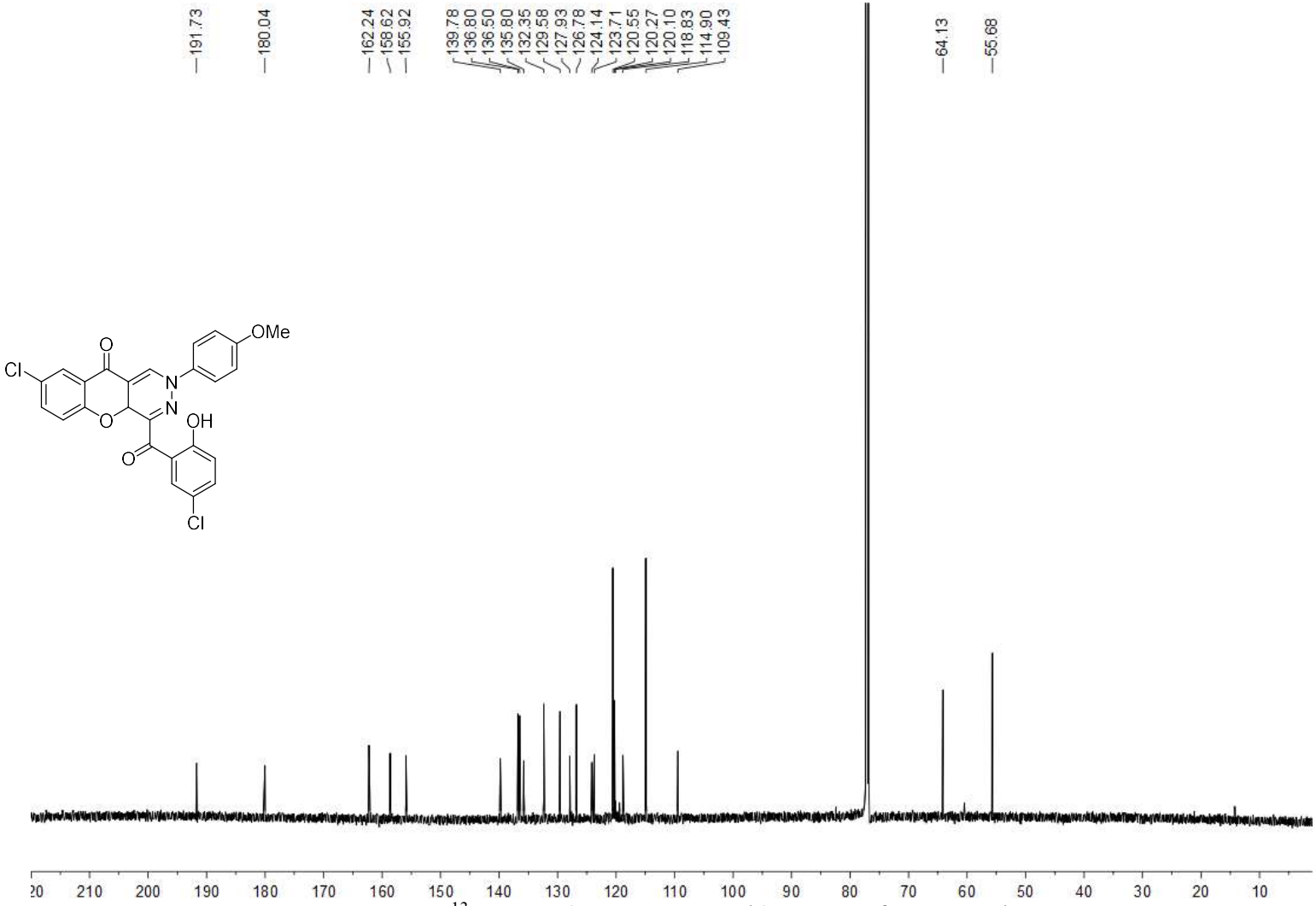


Figure S8. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3c**

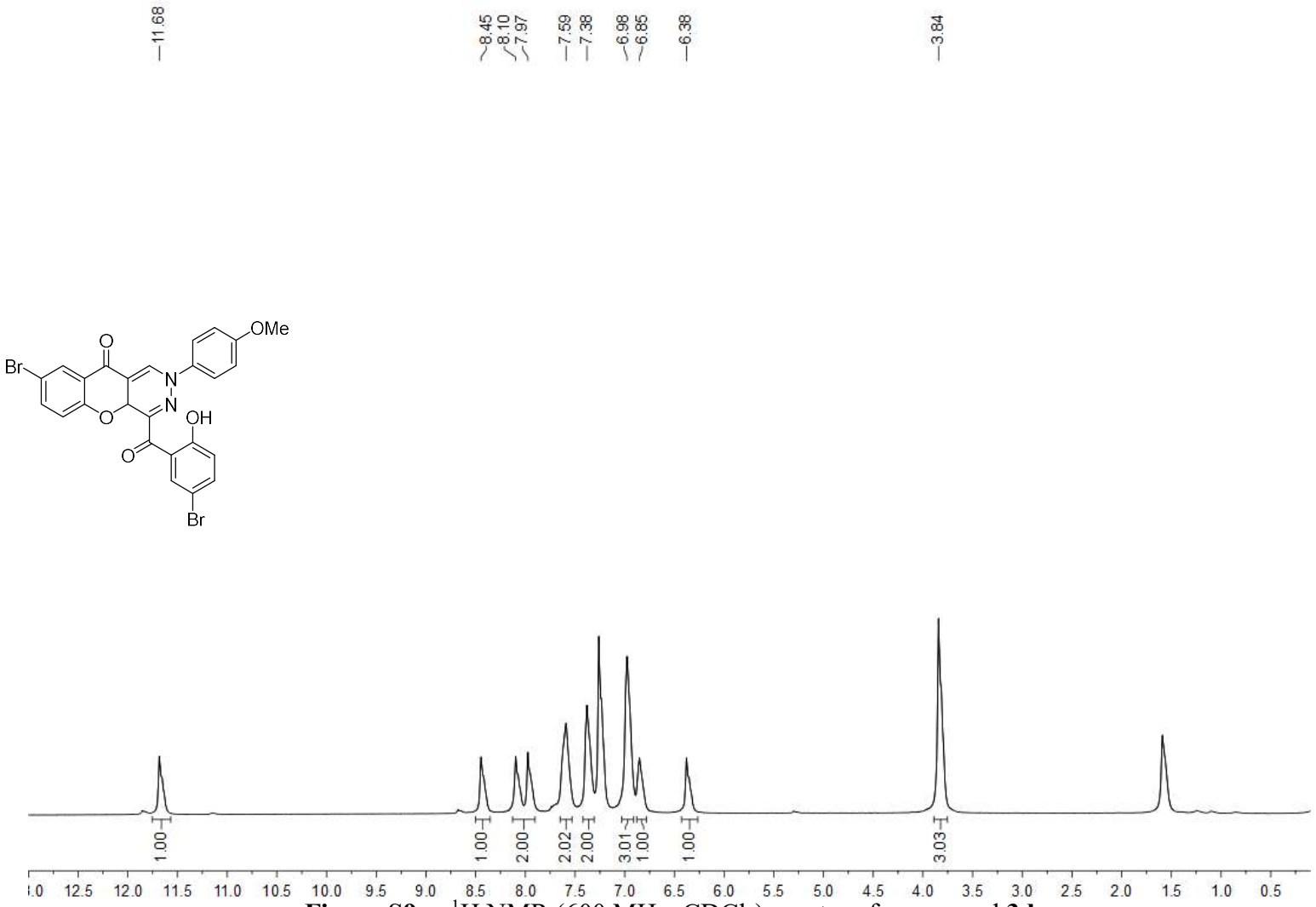


Figure S9. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3d**

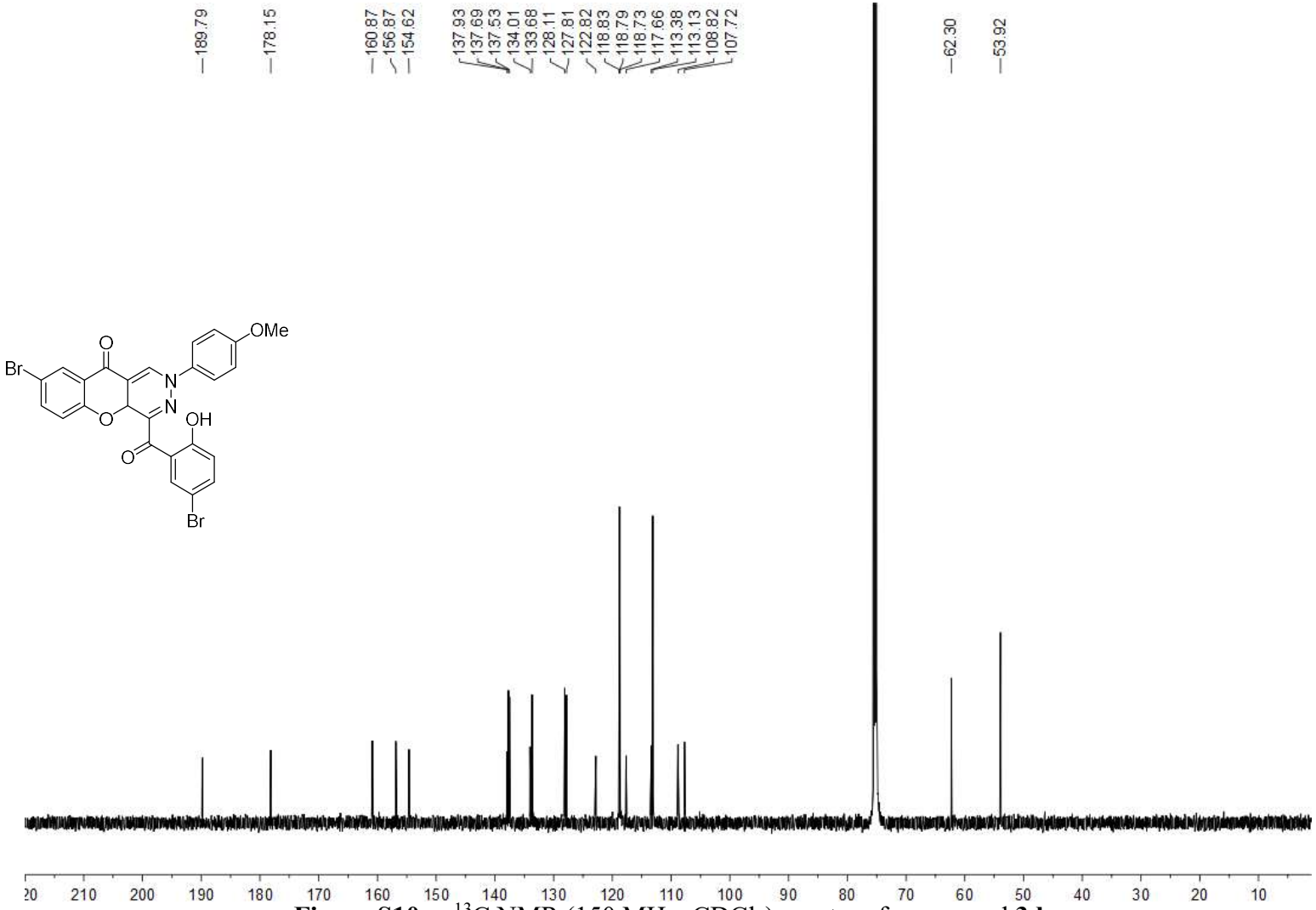


Figure S10. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3d**

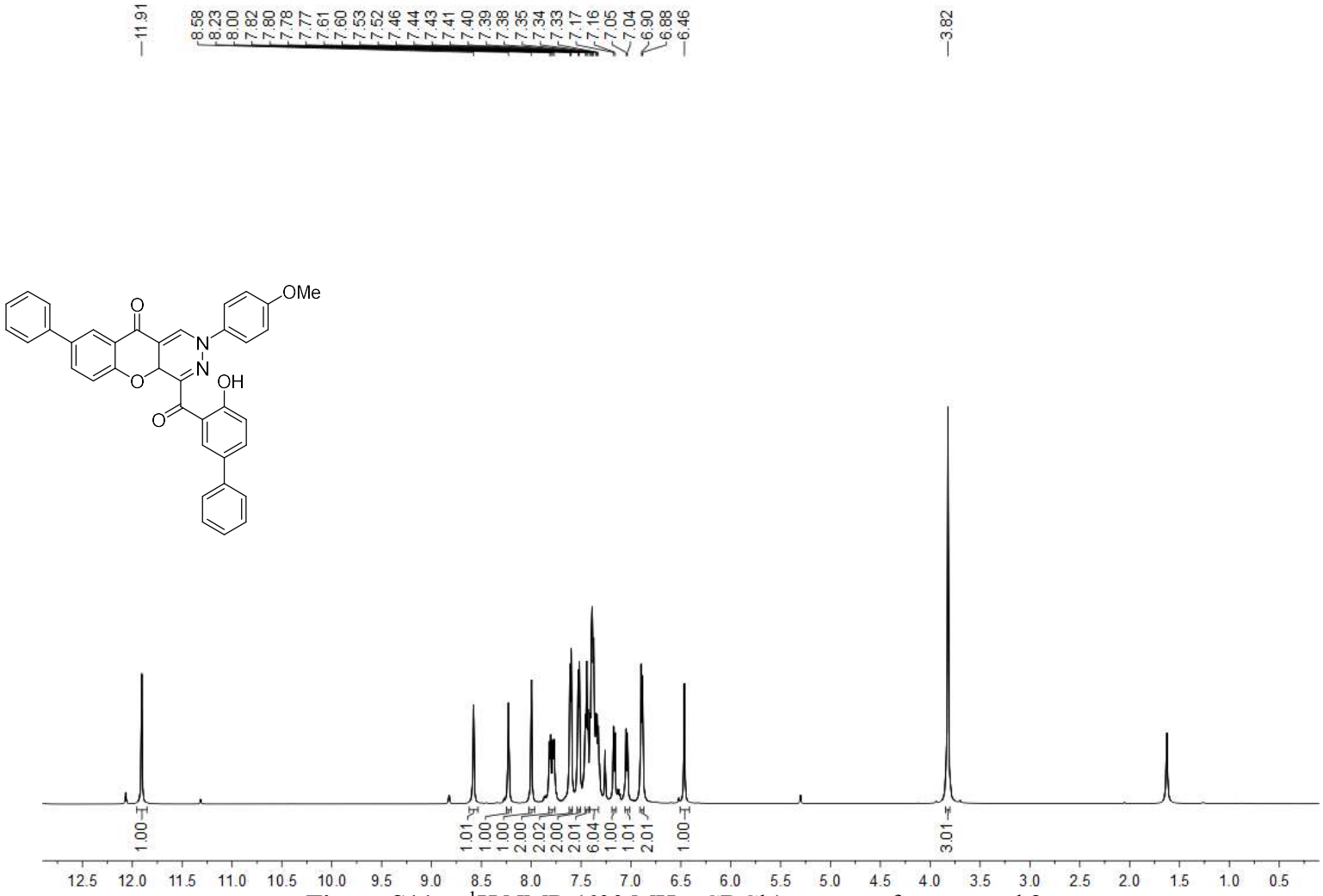


Figure S11. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3e**

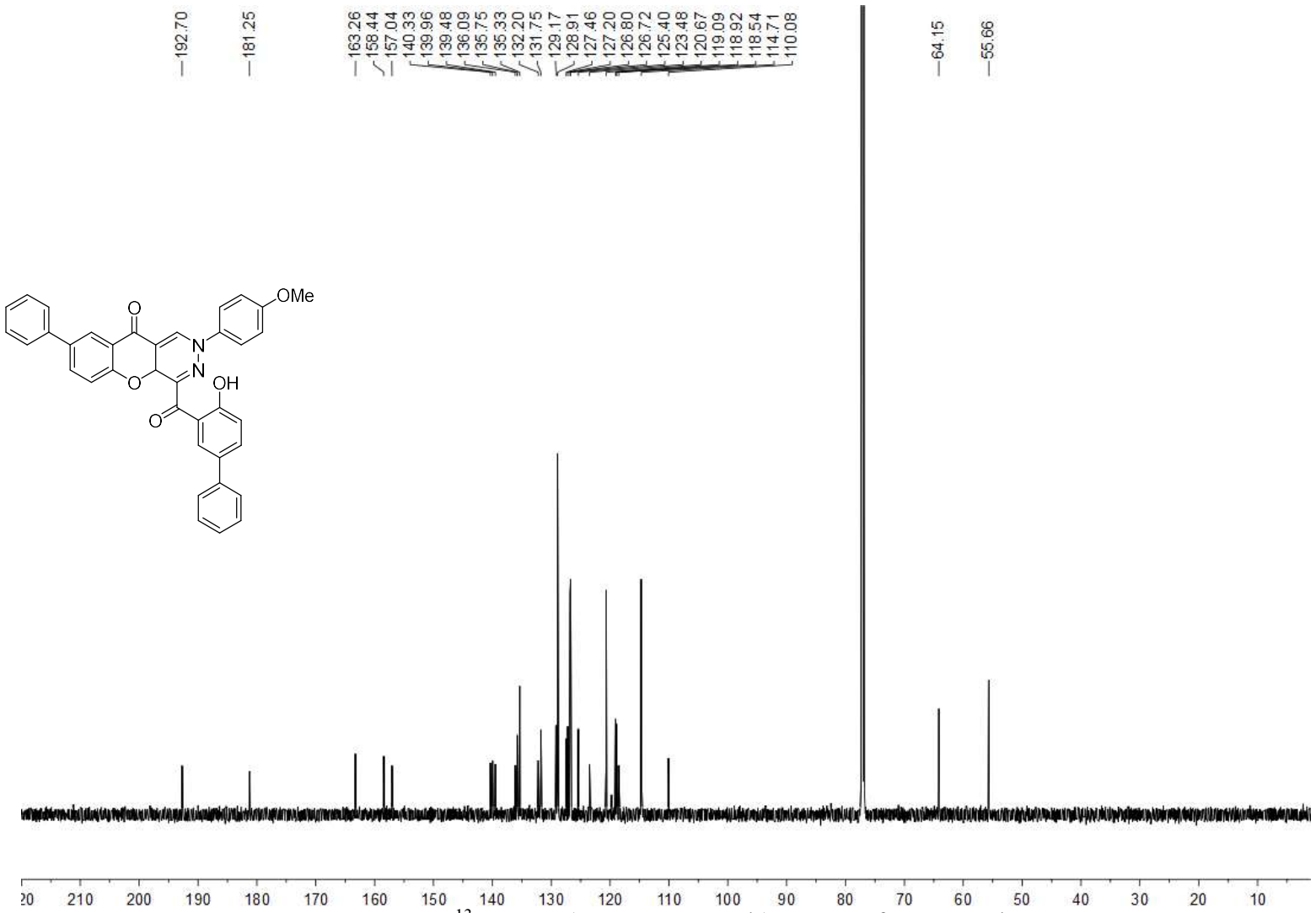


Figure S12. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3e**

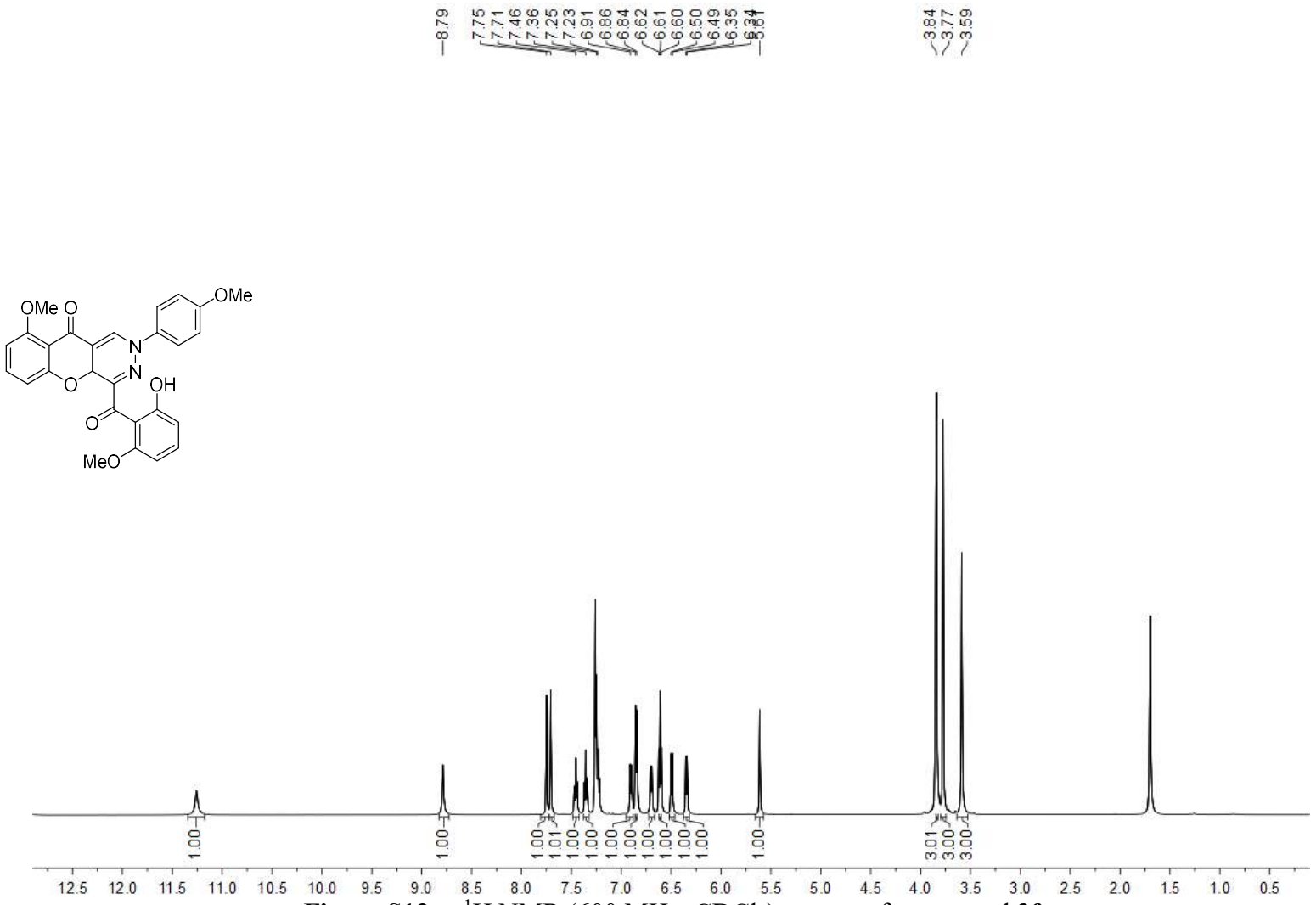


Figure S13. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3f**

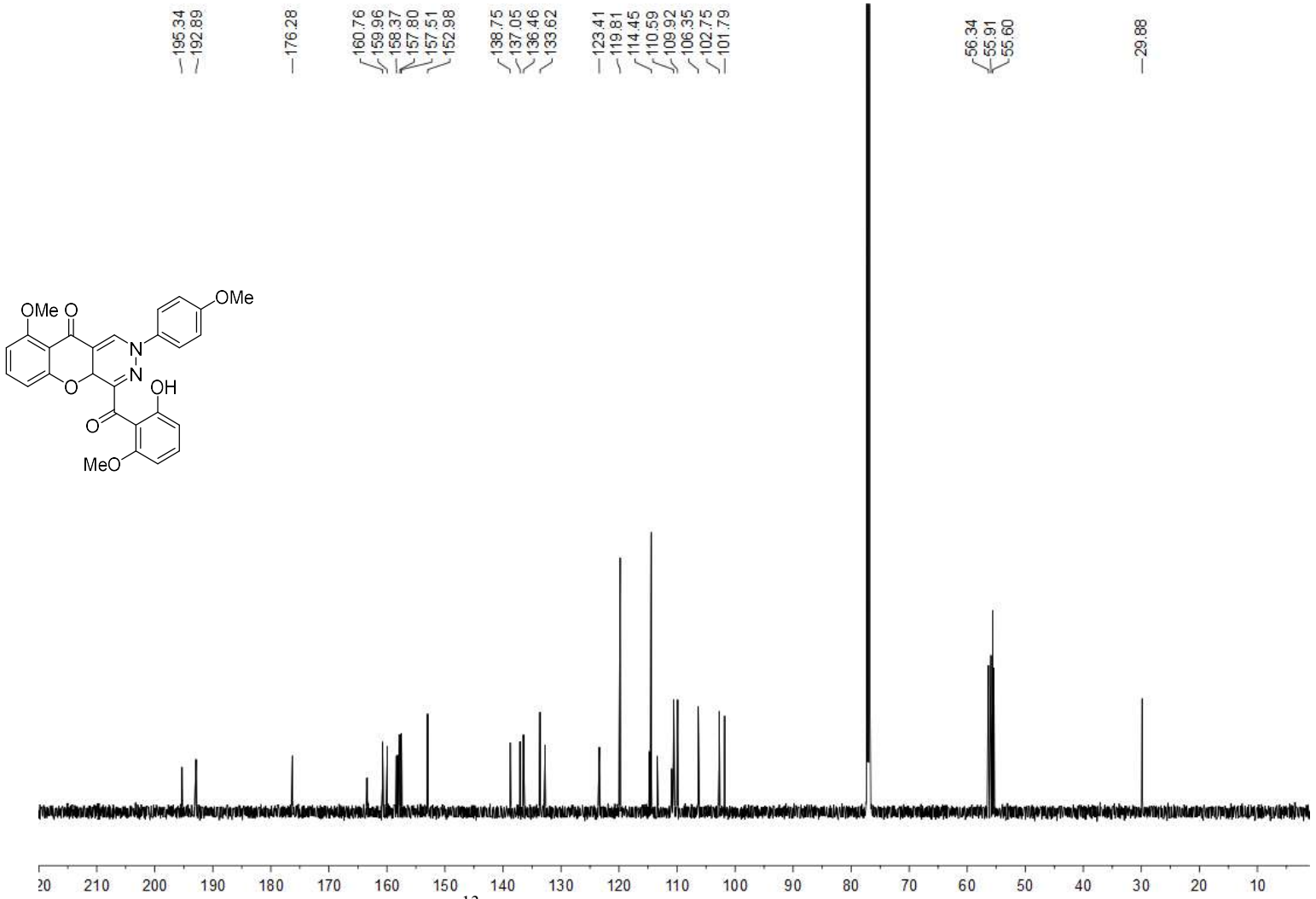


Figure S14. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3f**

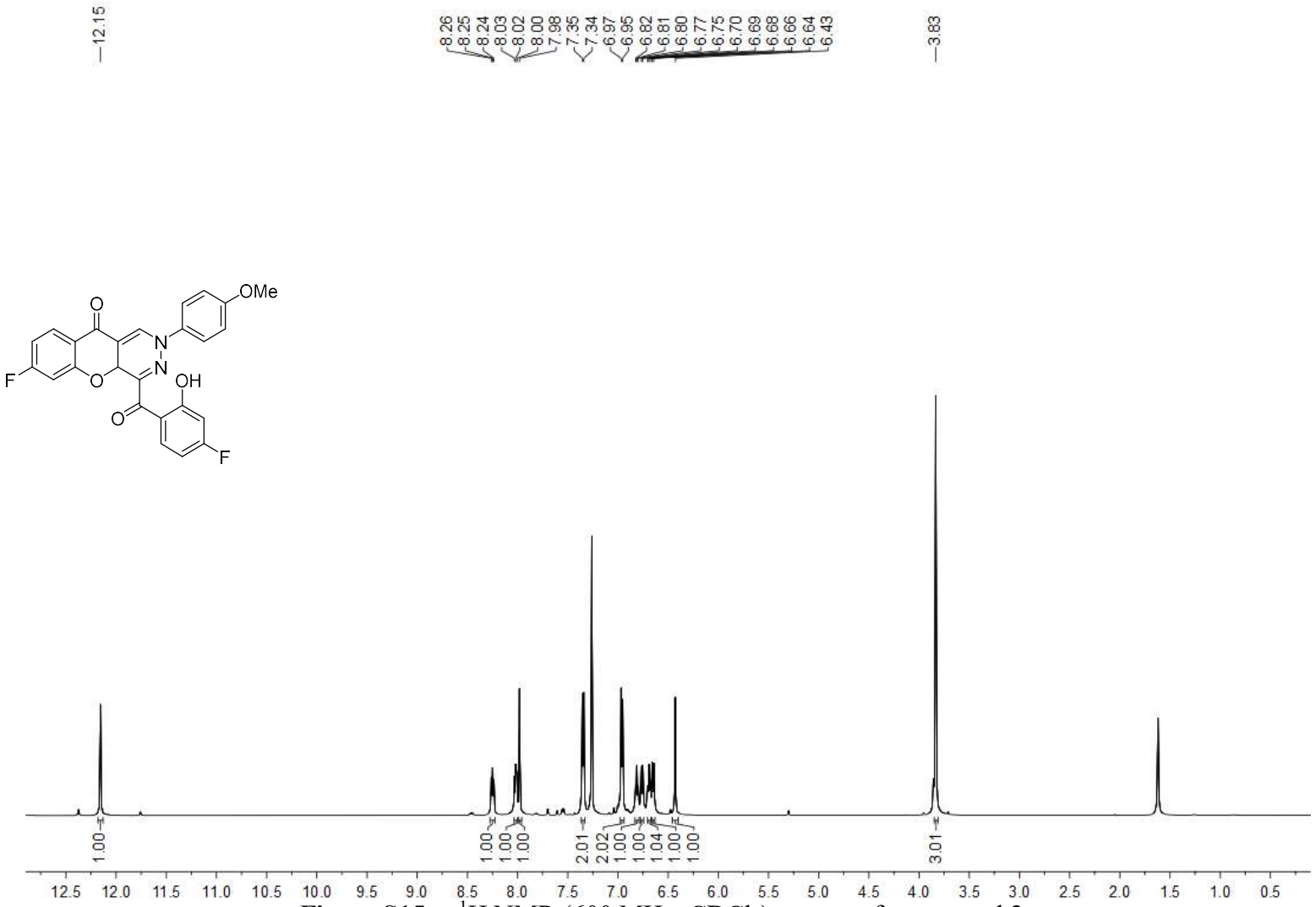


Figure S15. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3g**

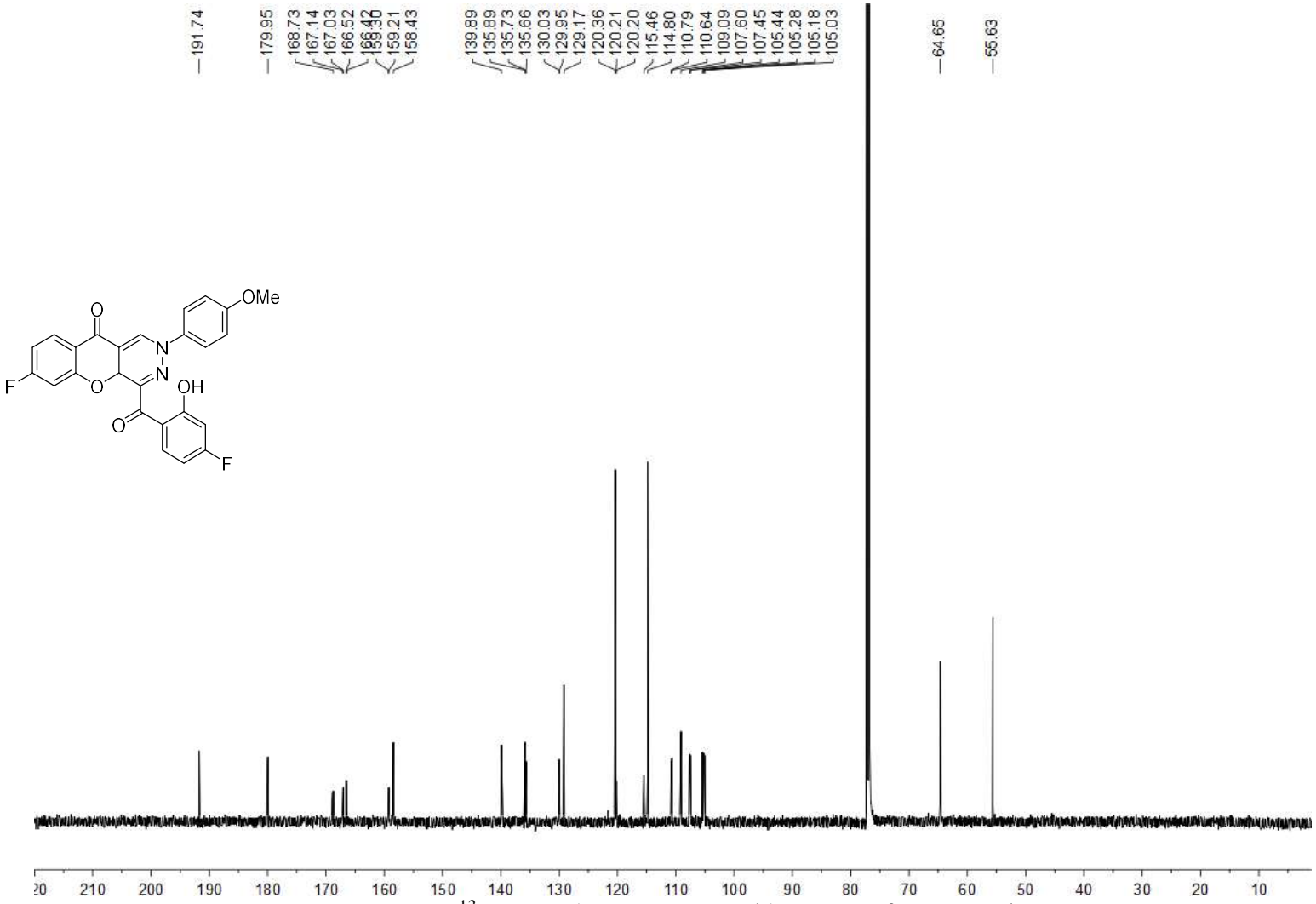


Figure S16. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3g**

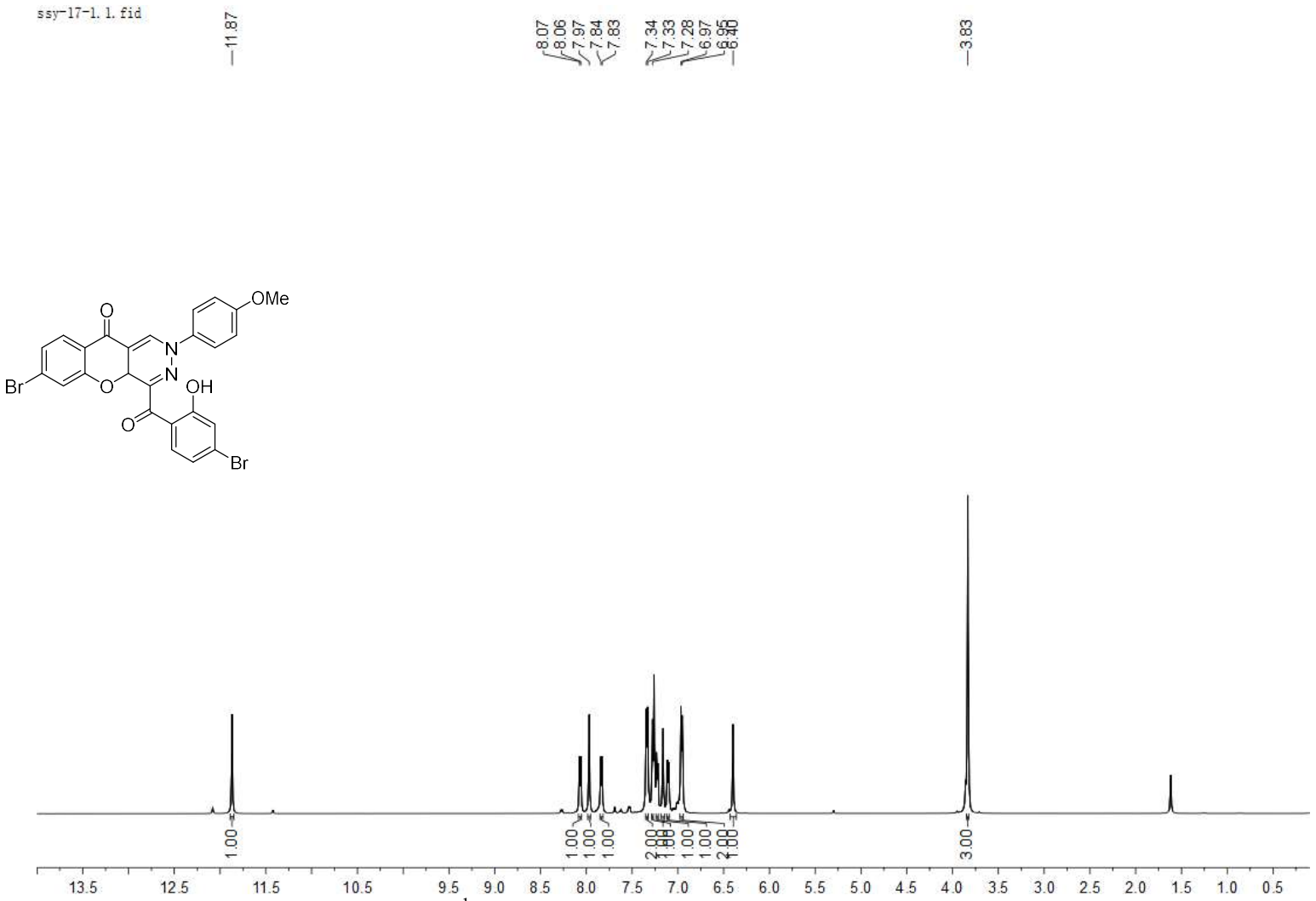


Figure S17. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3h**

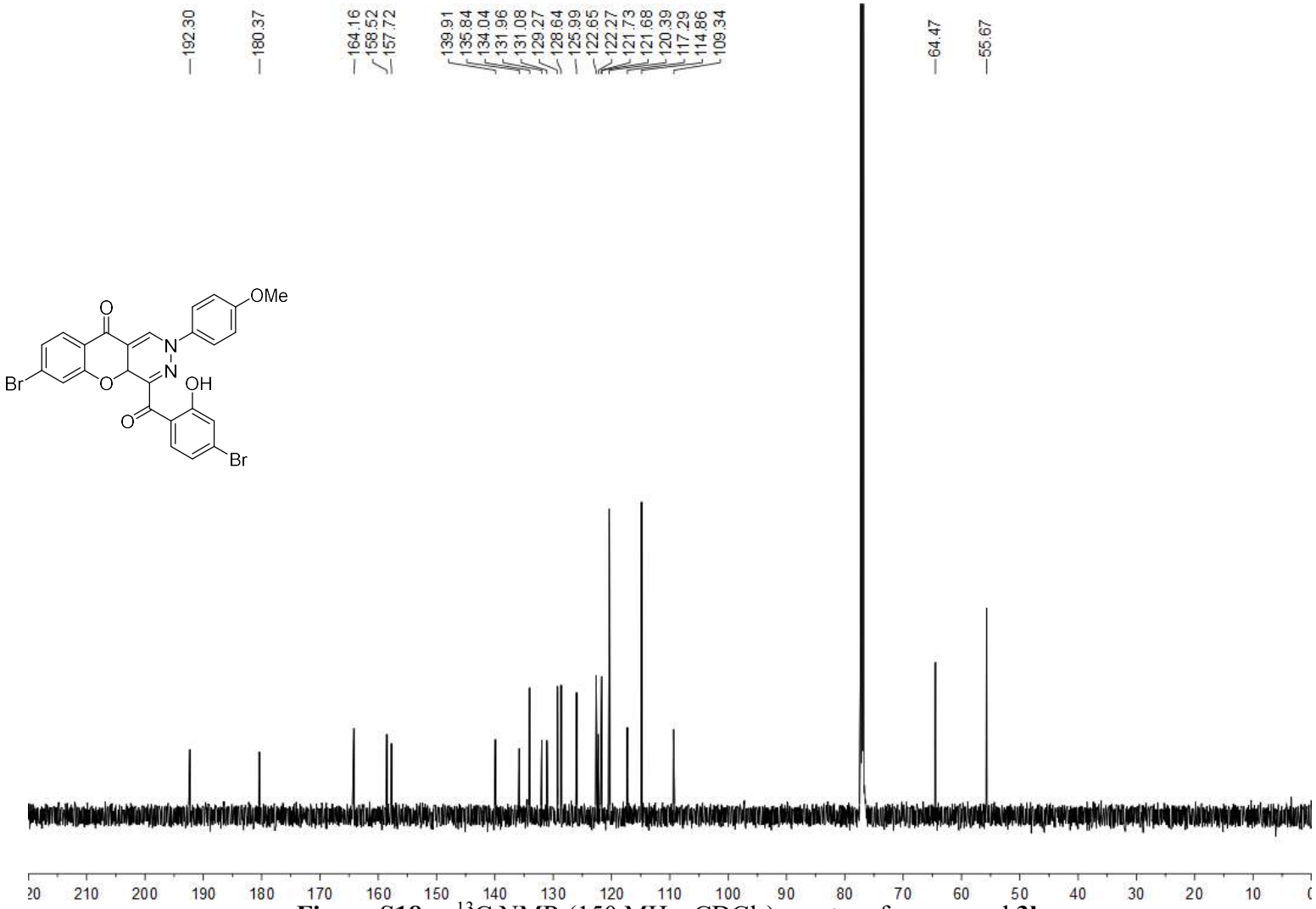


Figure S18. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3h**

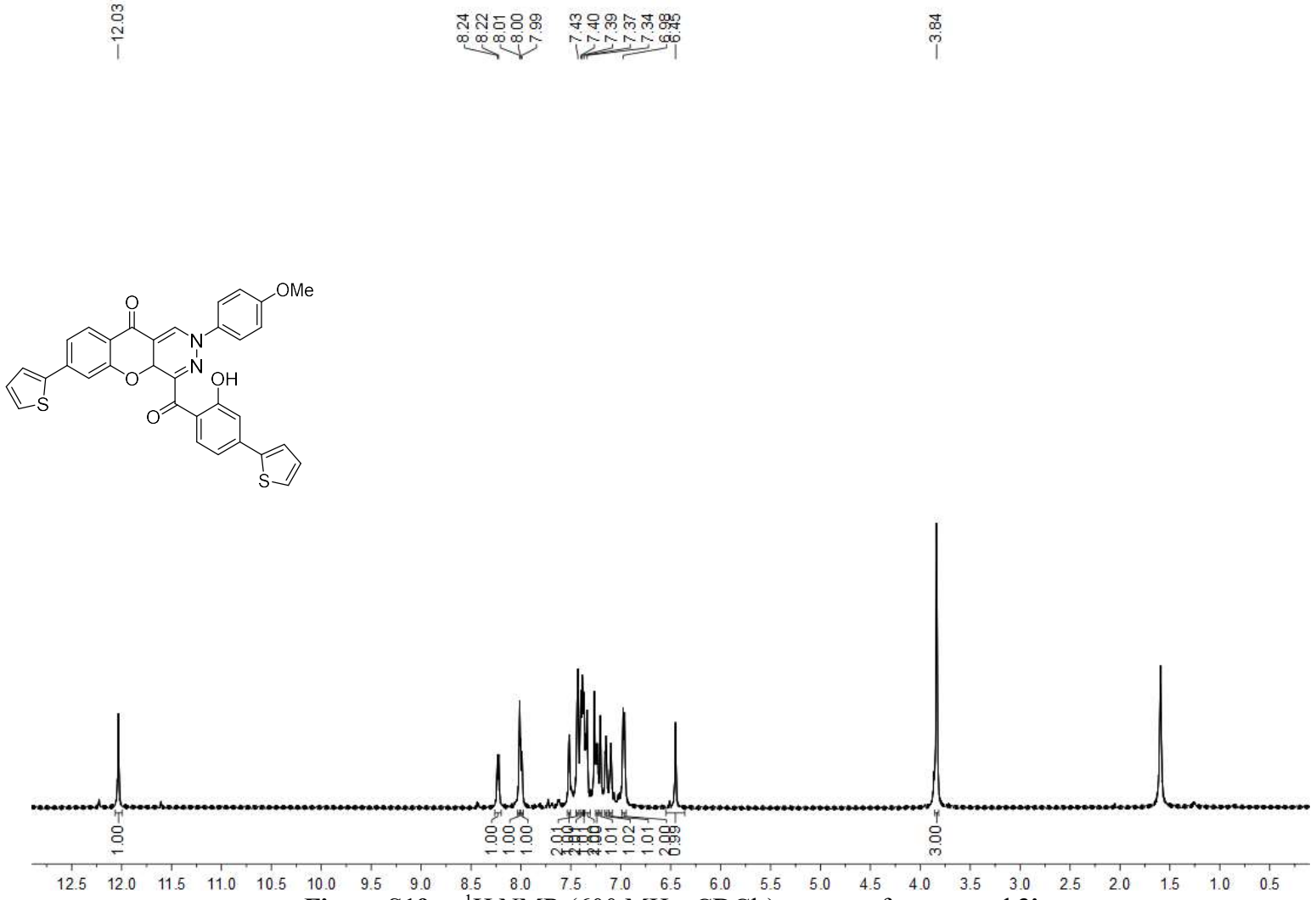


Figure S19. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3i**

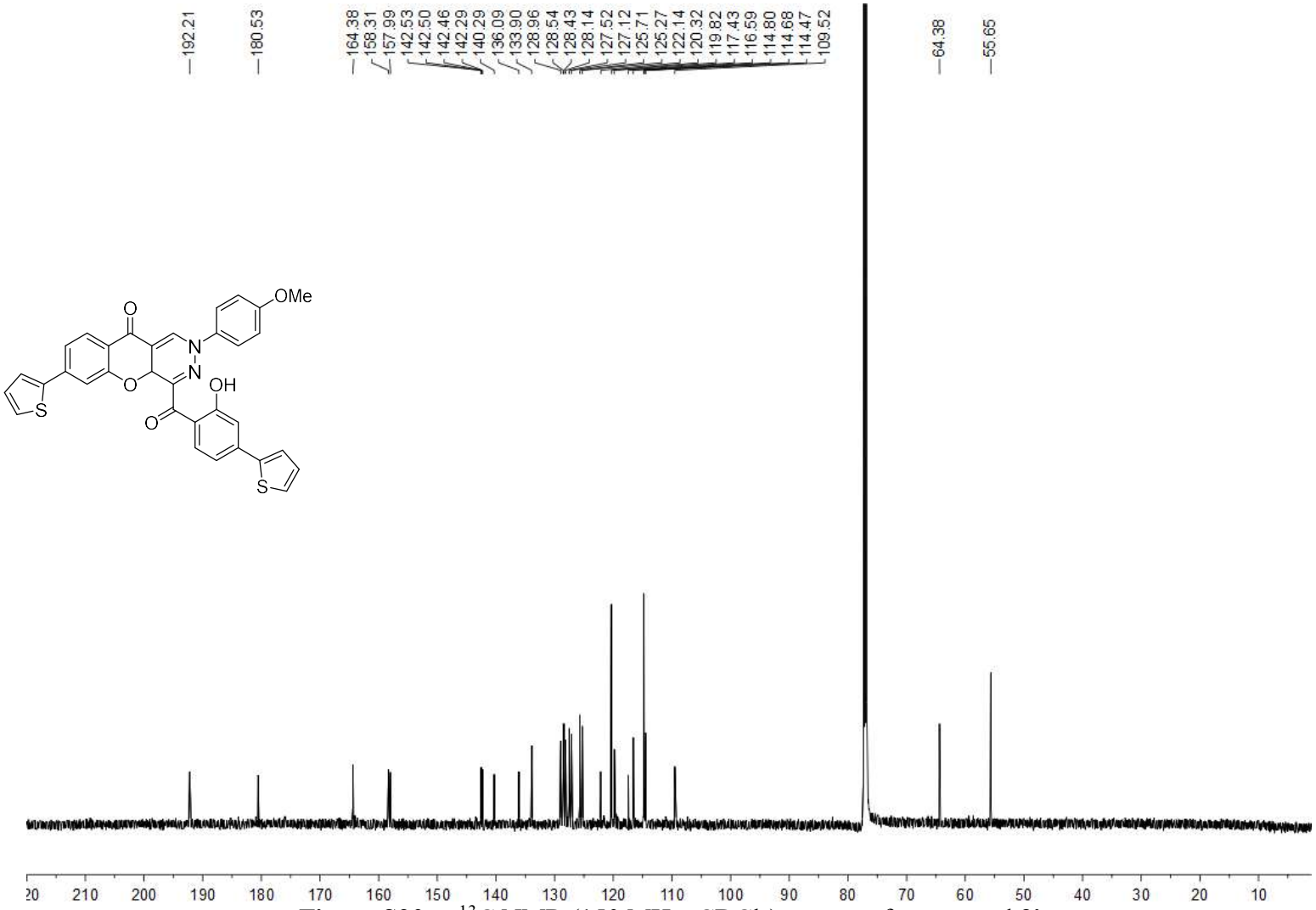


Figure S20. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3i**

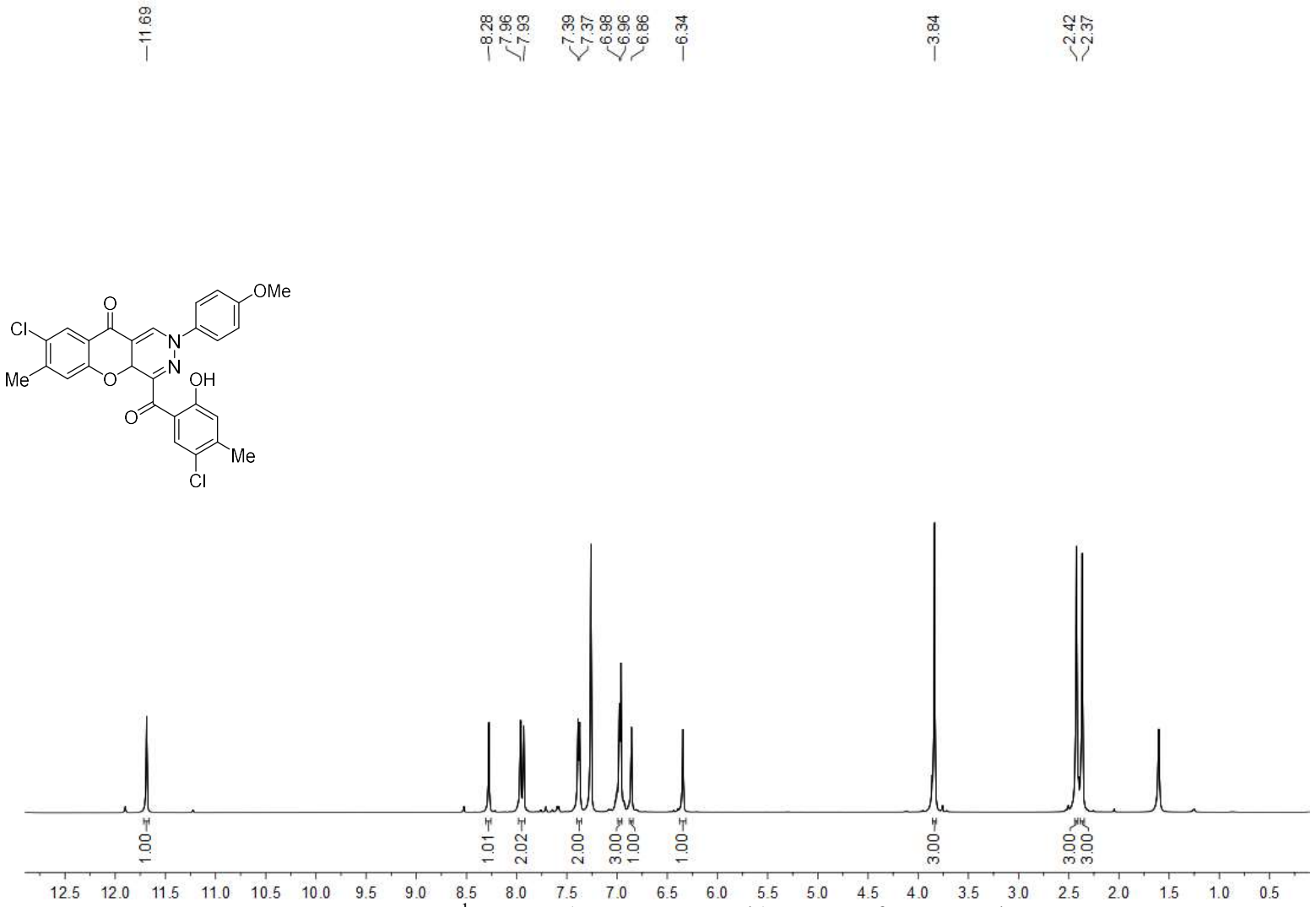


Figure S21. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3j**

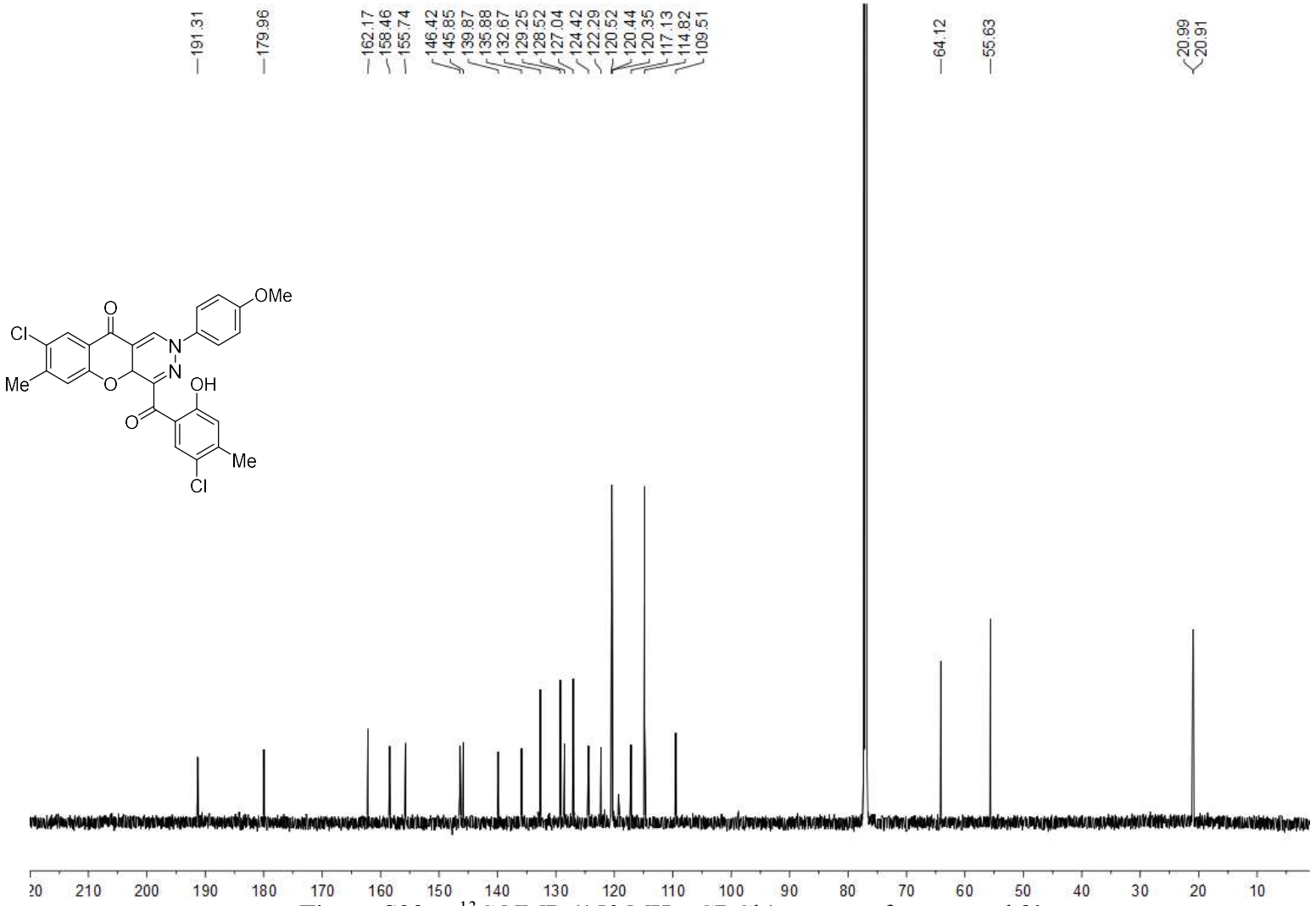


Figure S22. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3j**

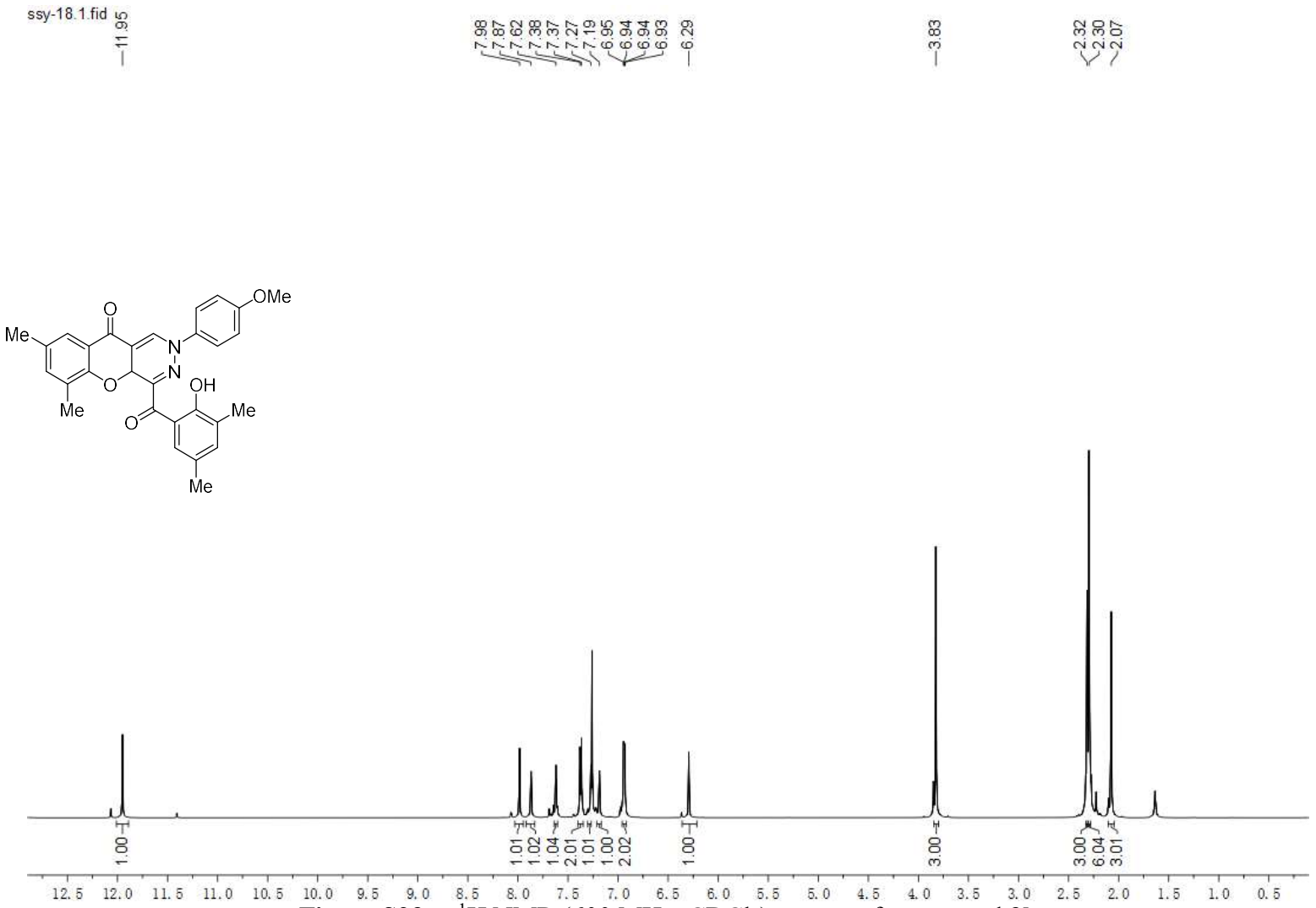


Figure S23. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3k**

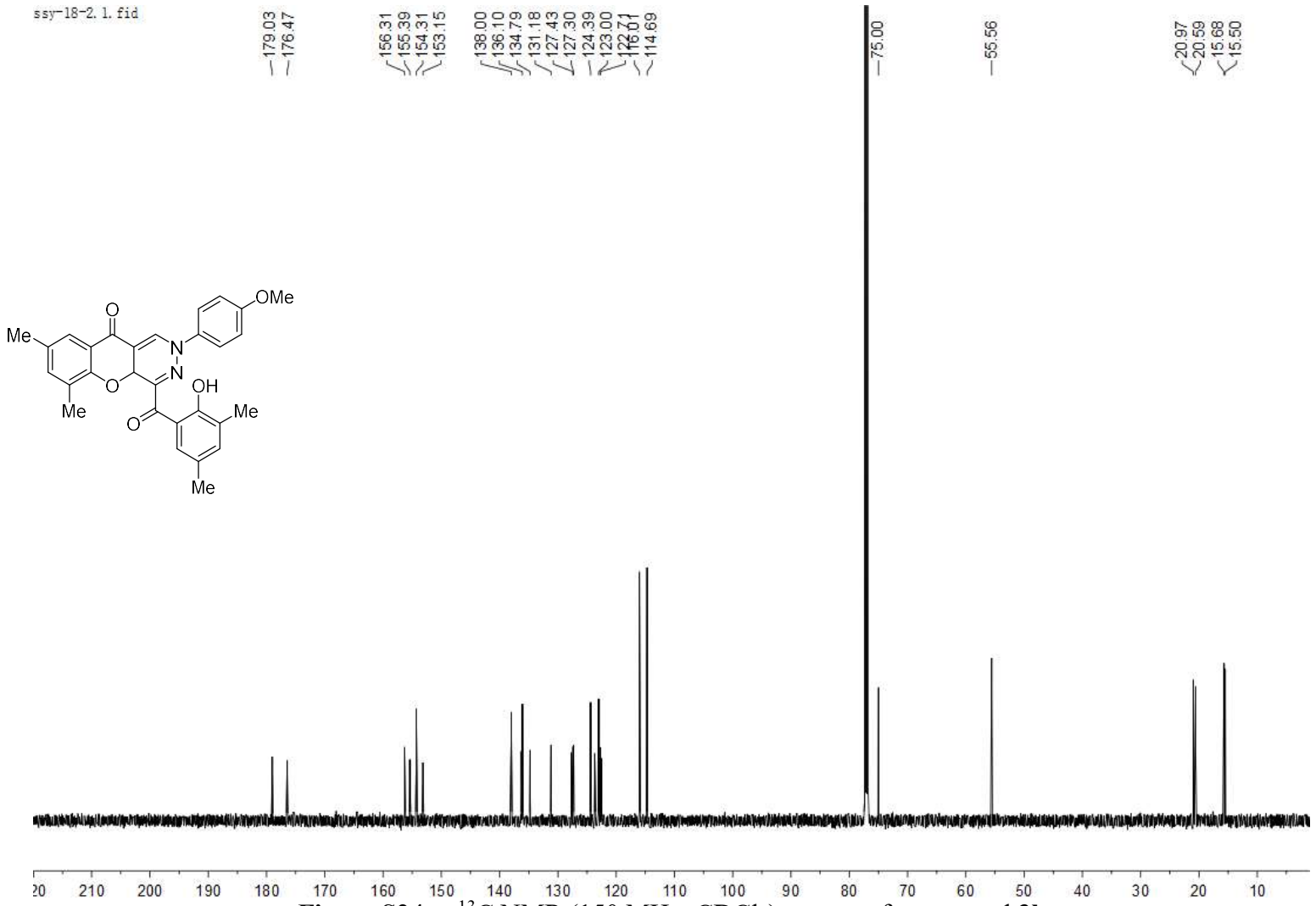


Figure S24. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3k**

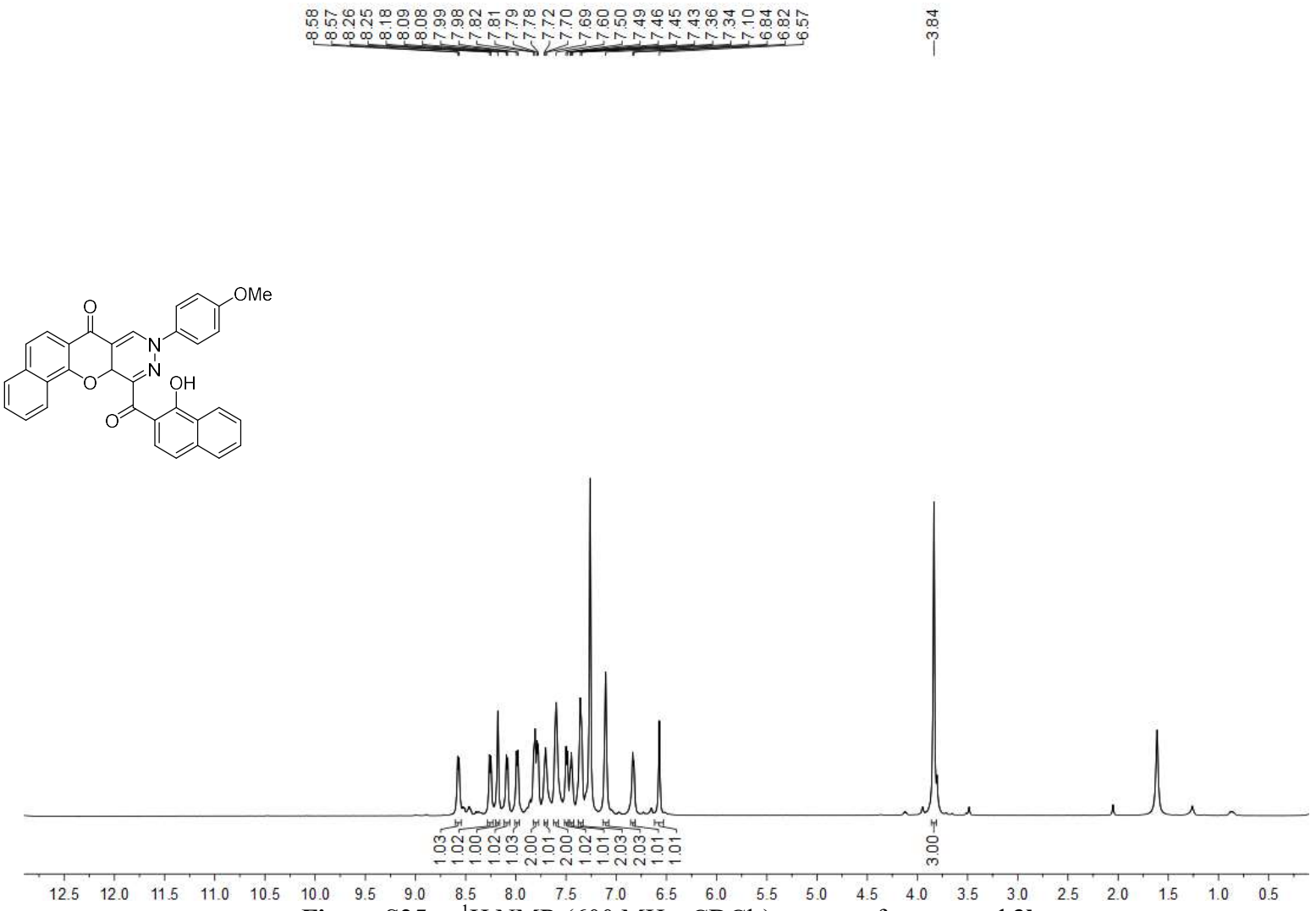


Figure S25. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3l**

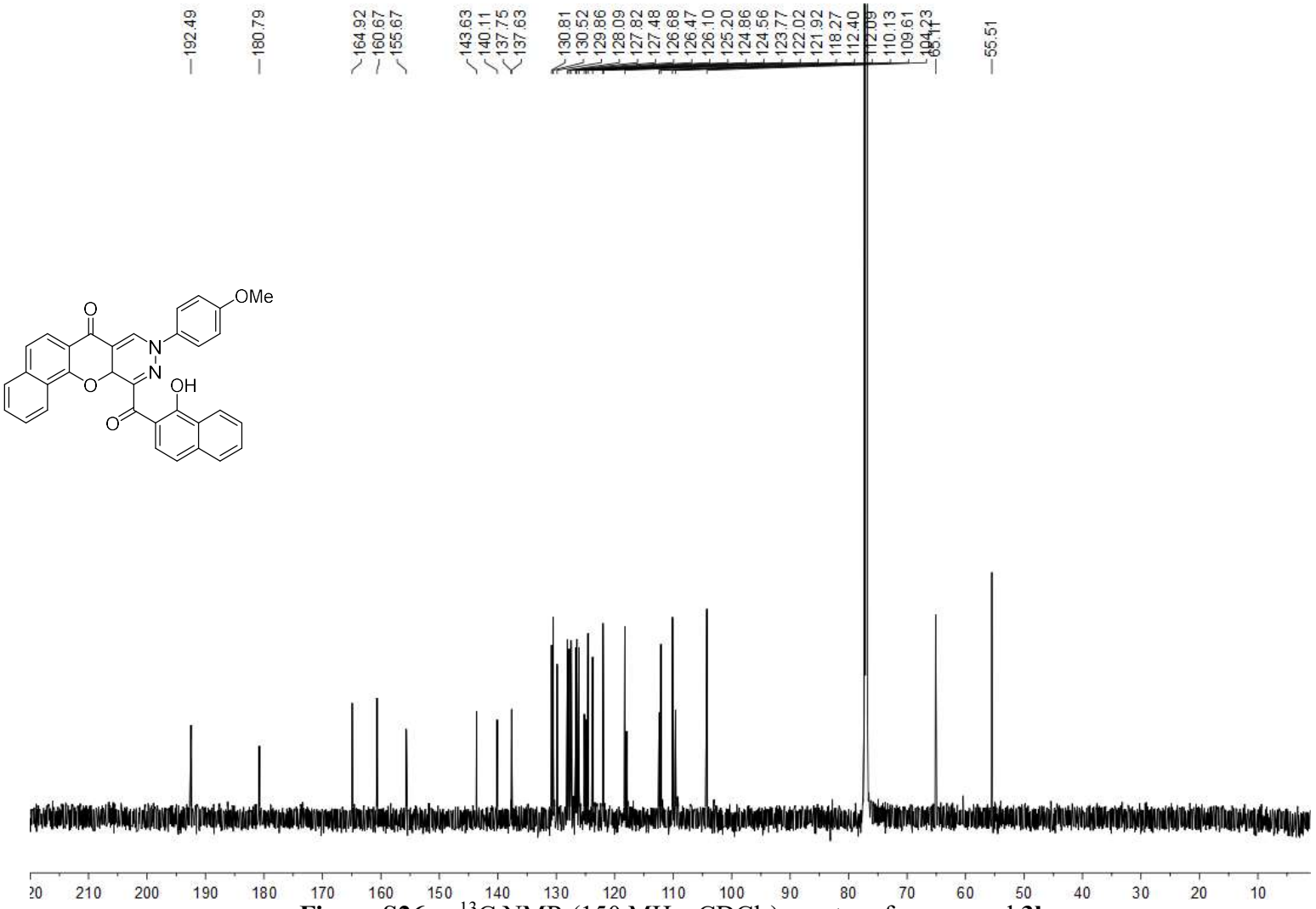


Figure S26. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3l**

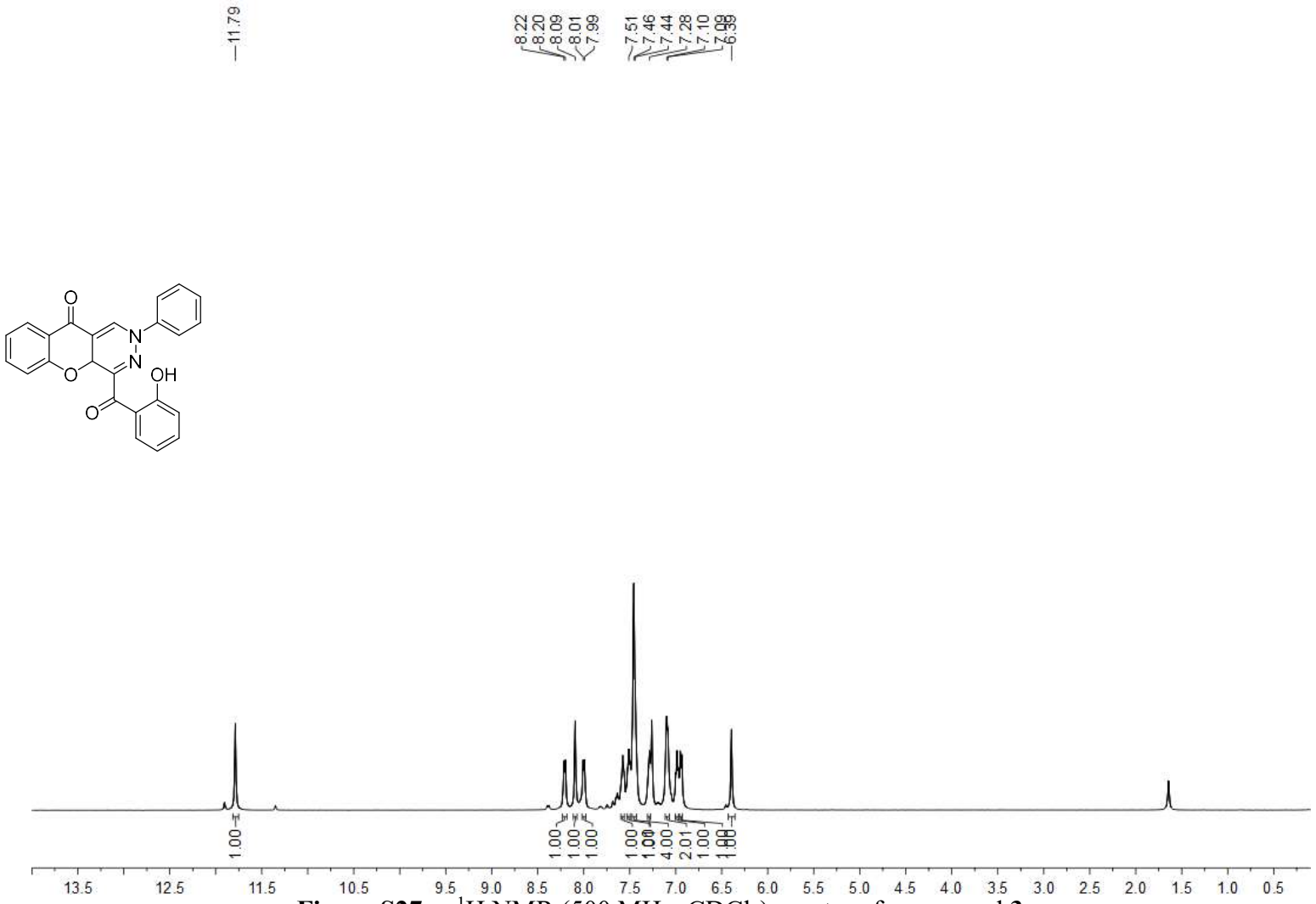


Figure S27. ^{1}H NMR (500 MHz, $CDCl_3$) spectra of compound **3m**

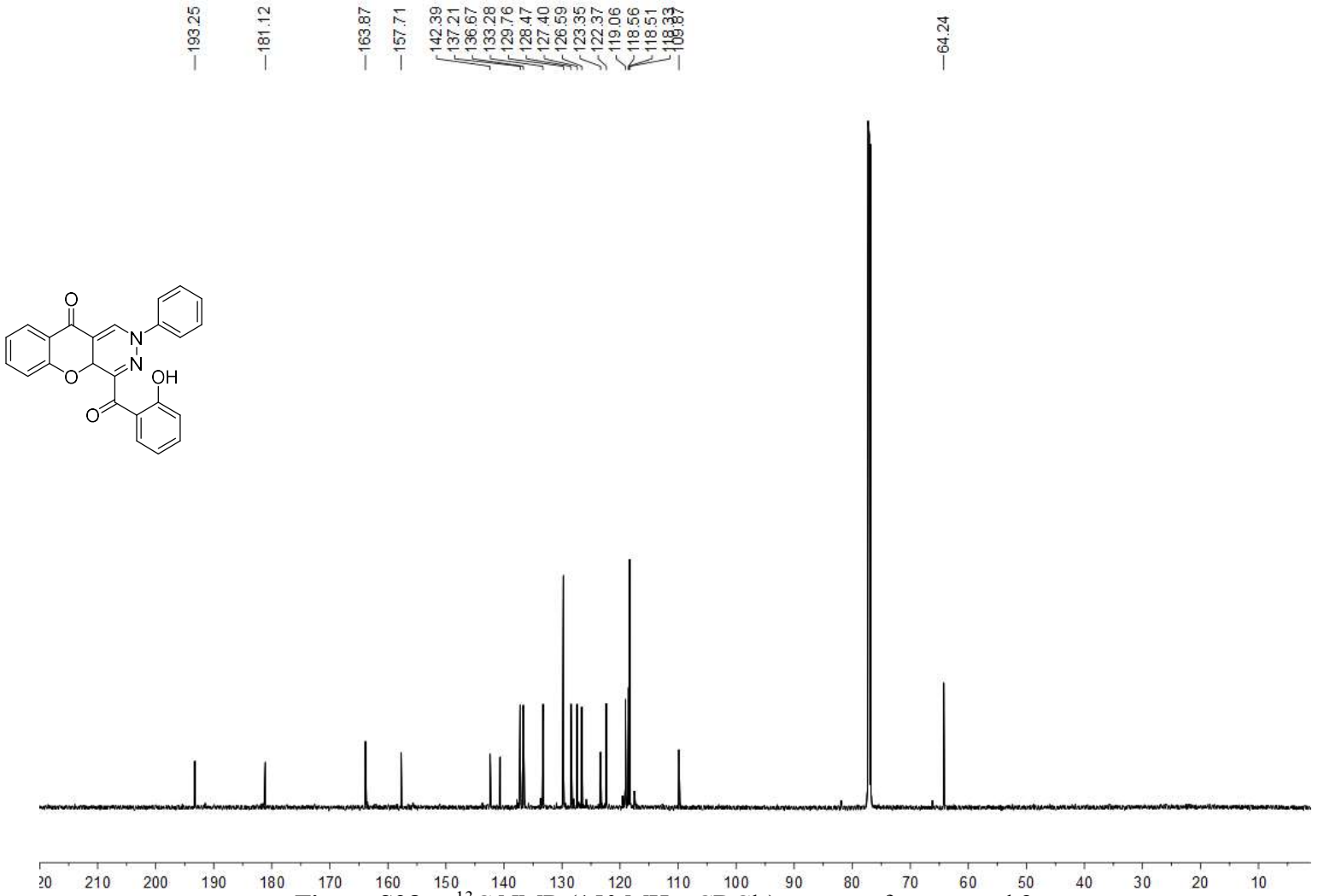


Figure S28. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3m**

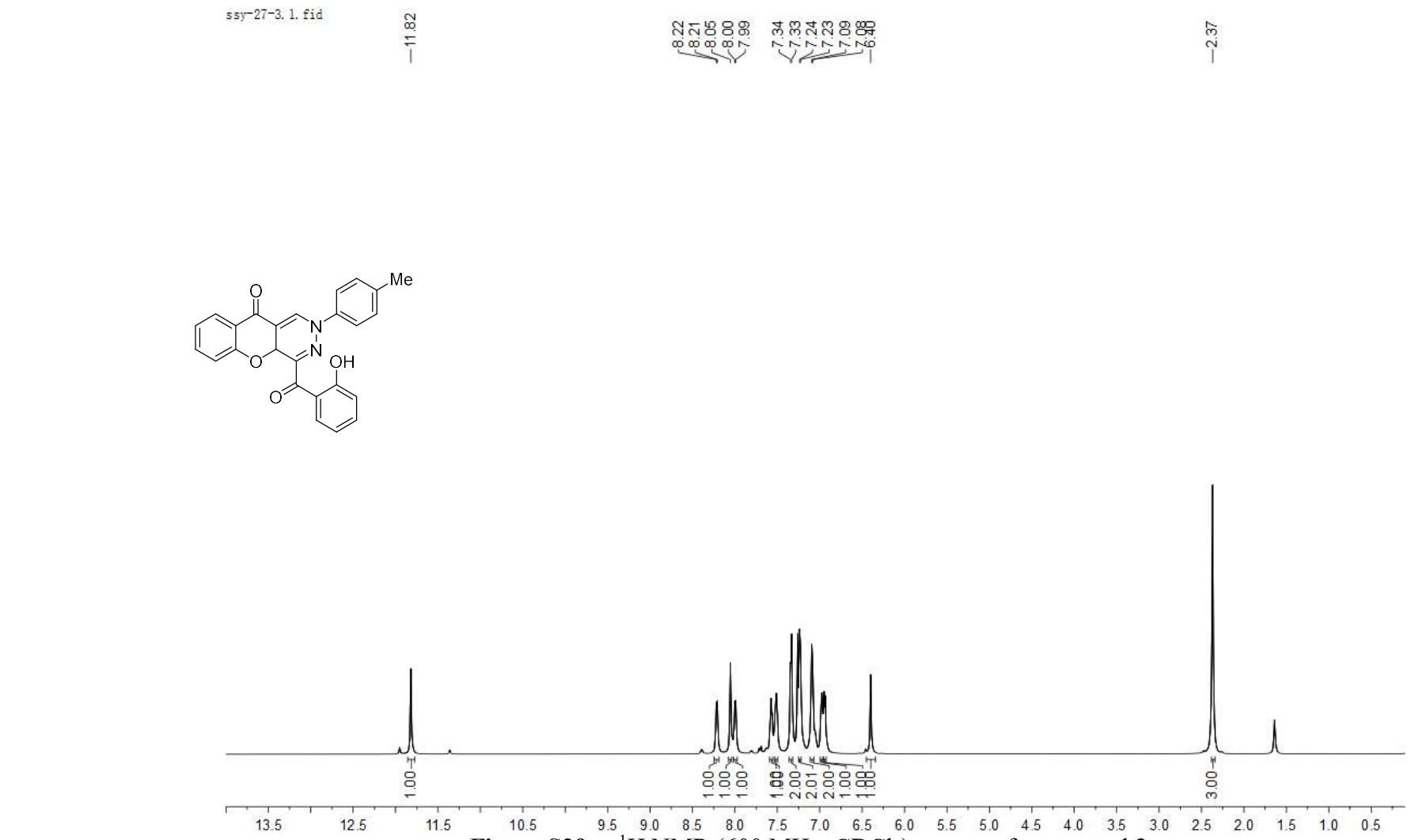


Figure S29. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3n**

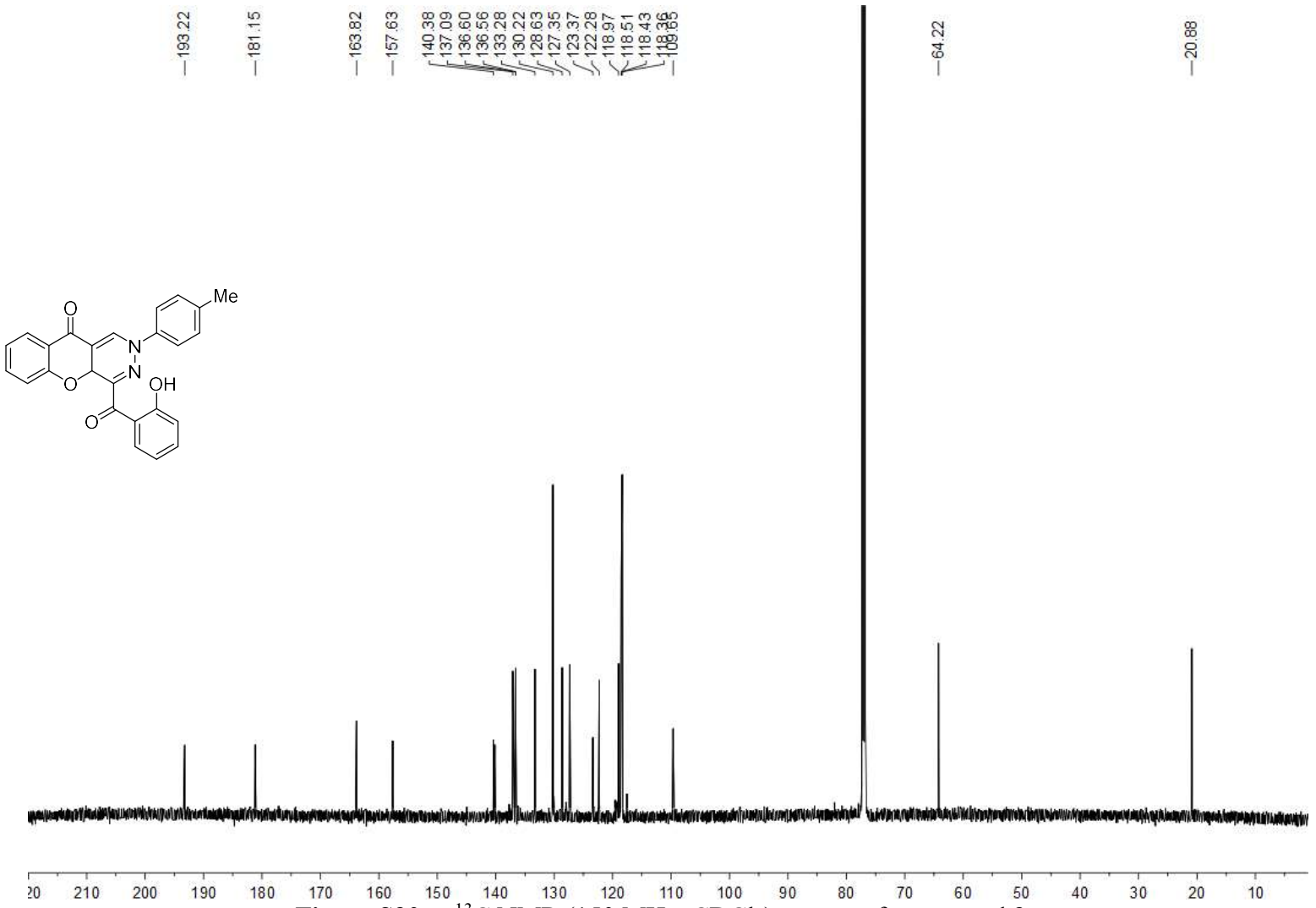


Figure S30. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3n**

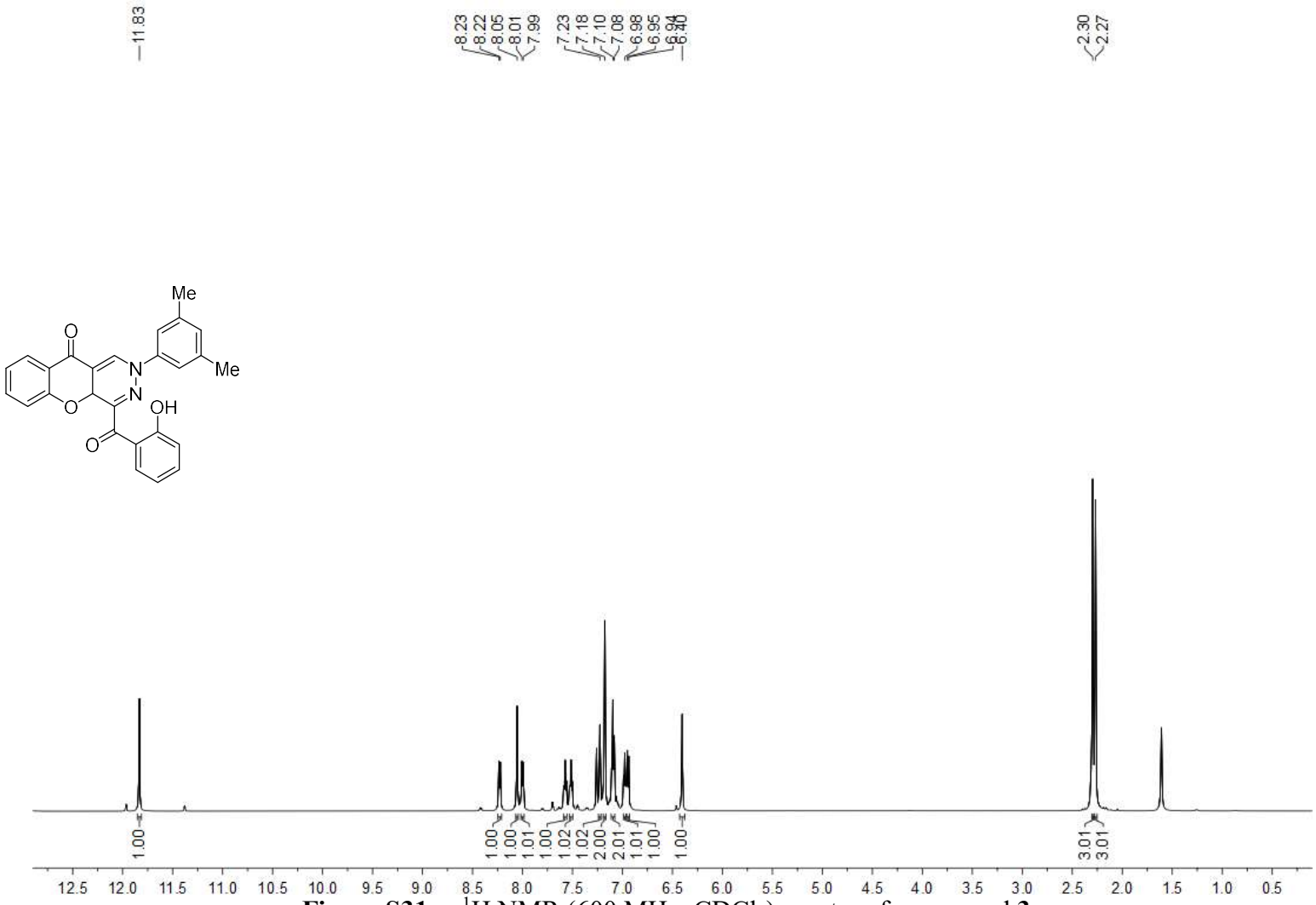


Figure S31. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3o**

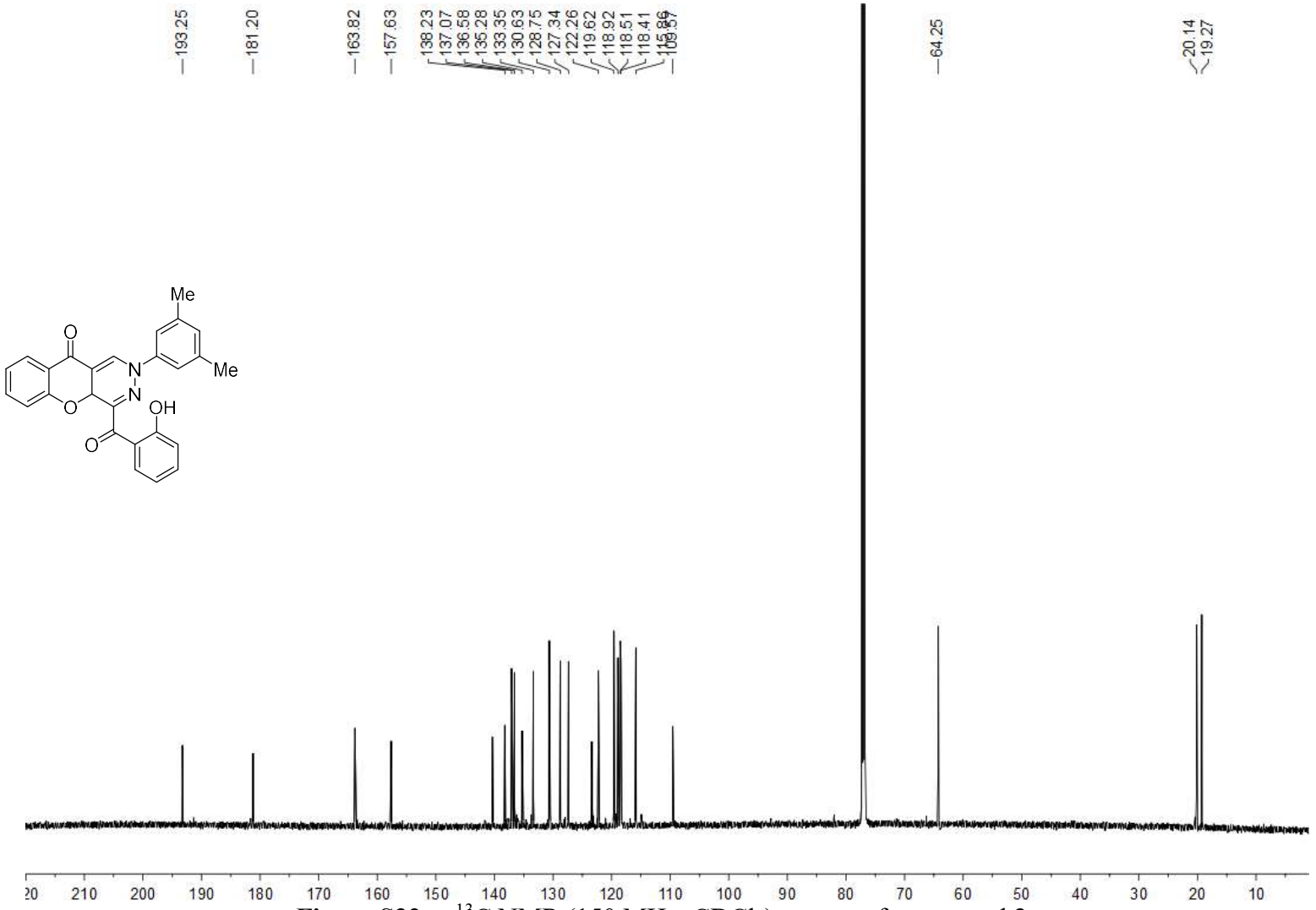


Figure S32. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3o**

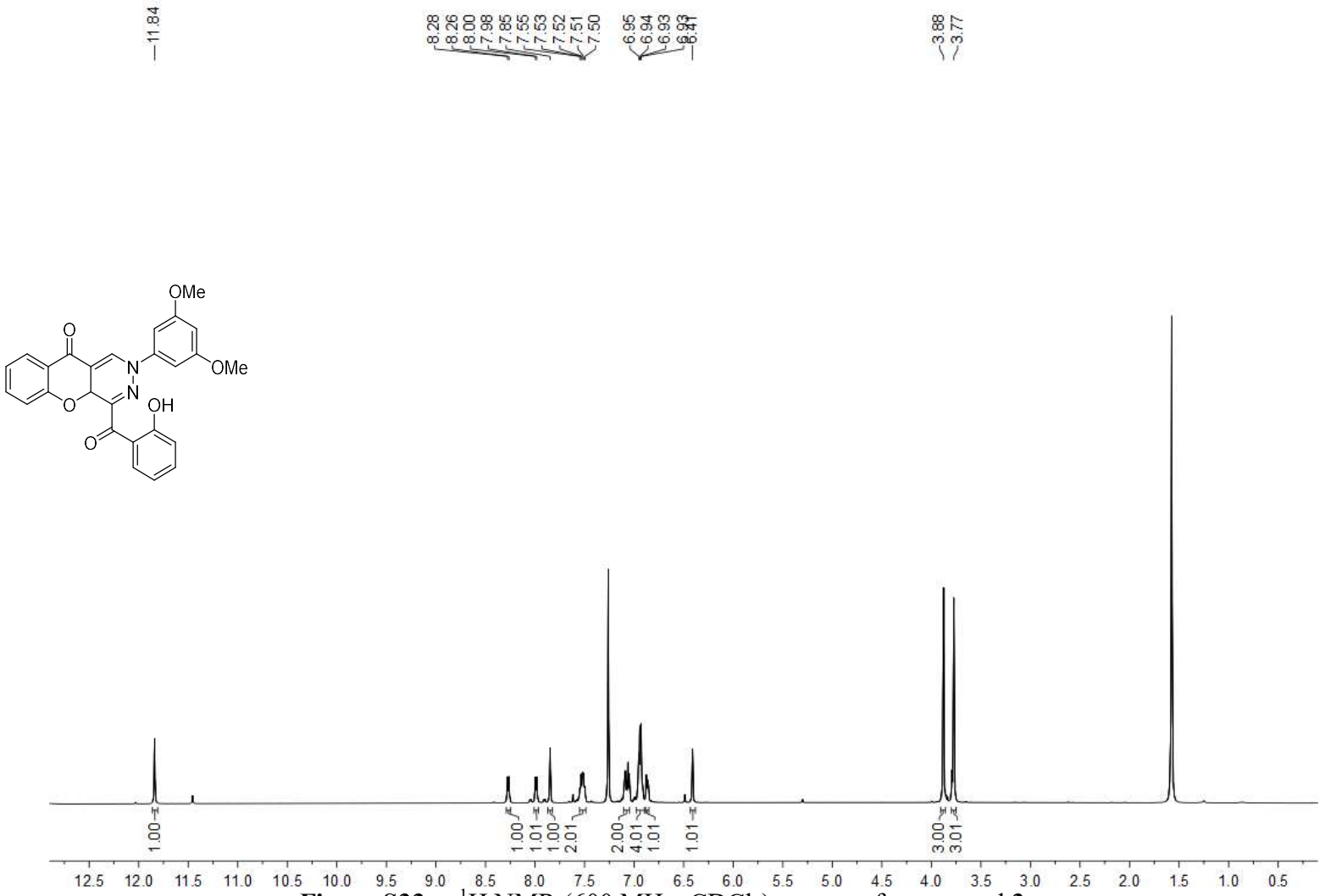


Figure S33. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3p**

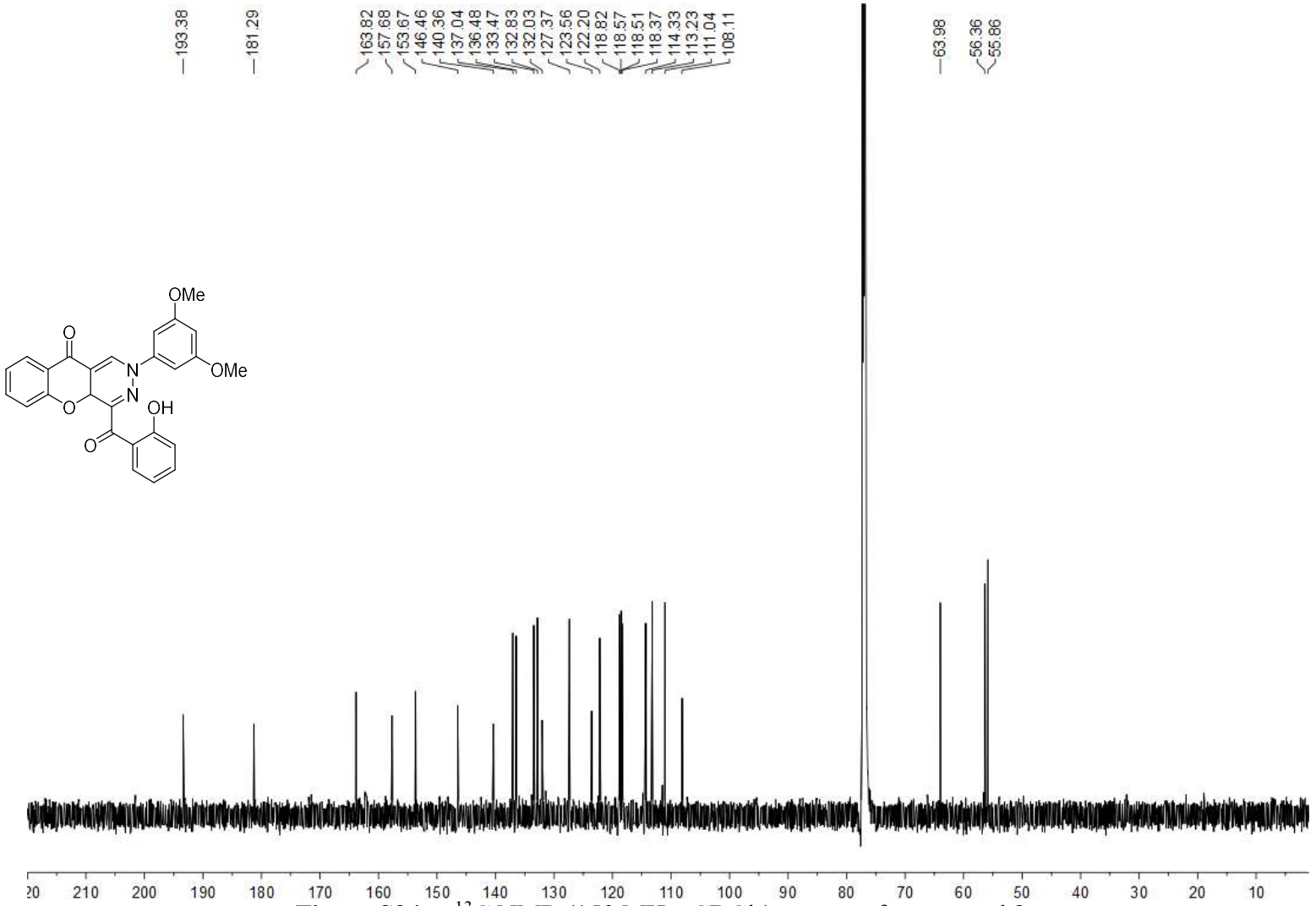


Figure S34. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3p**

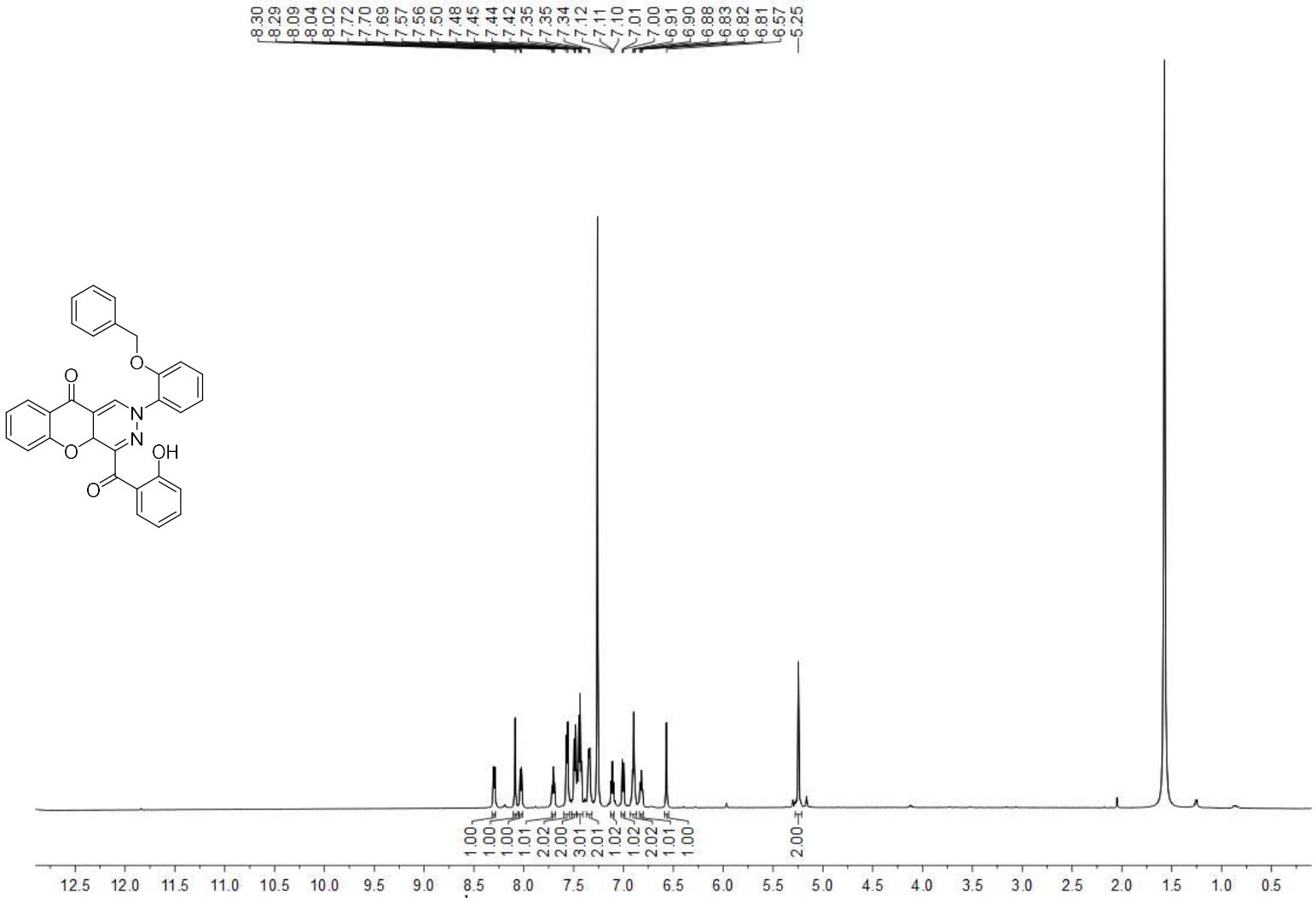


Figure S35. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3q**

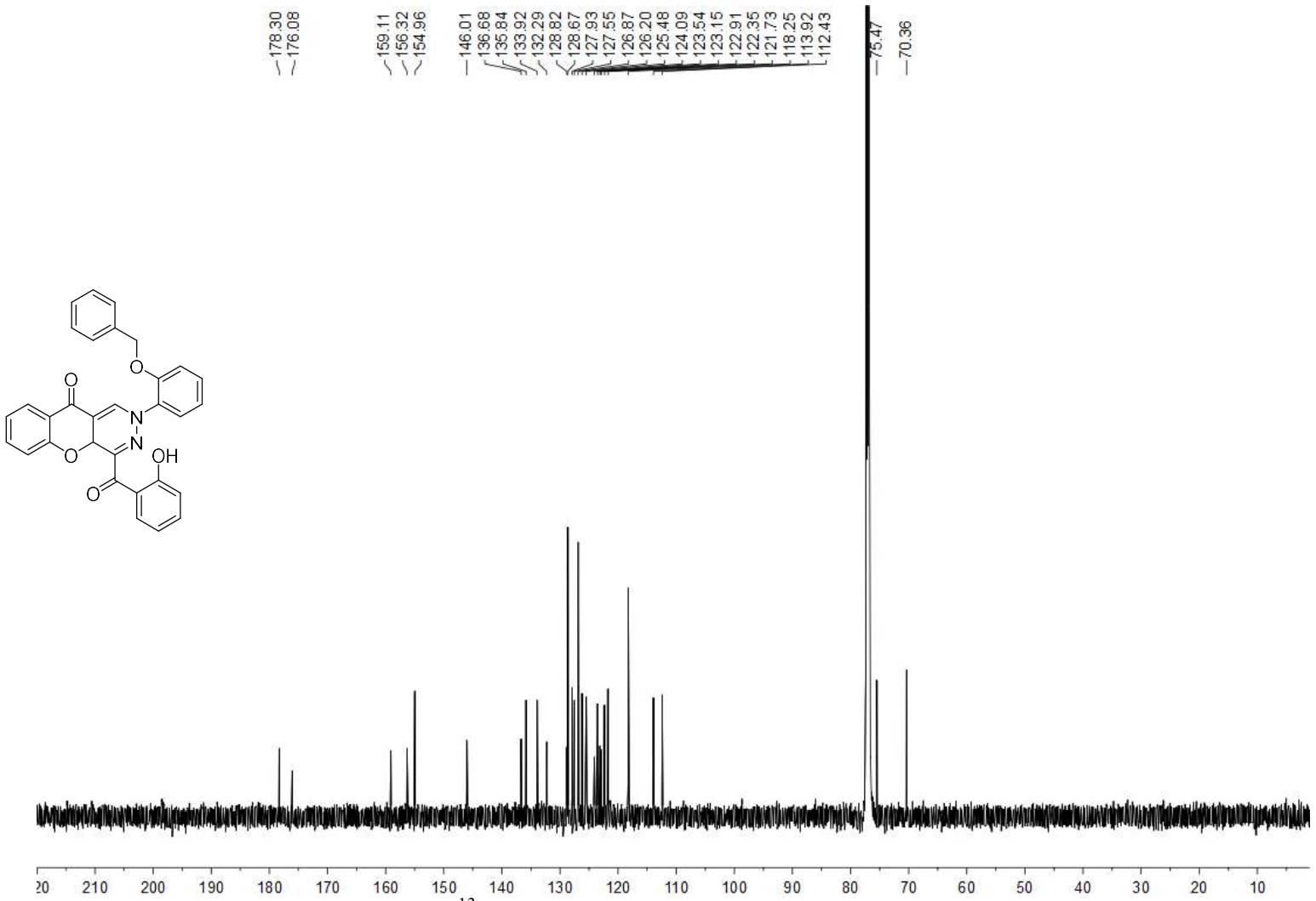


Figure S36. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3q**

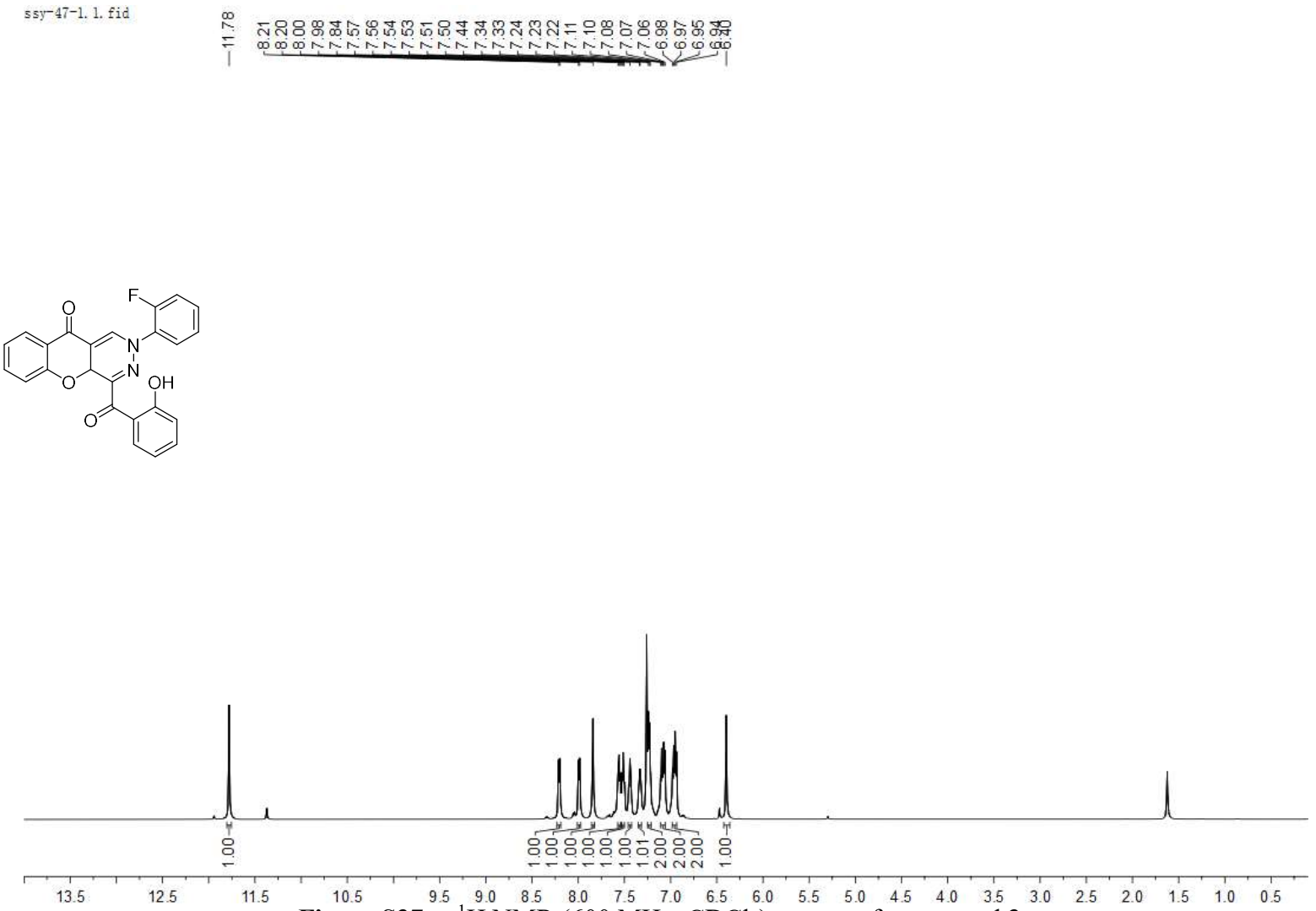


Figure S37. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3r**

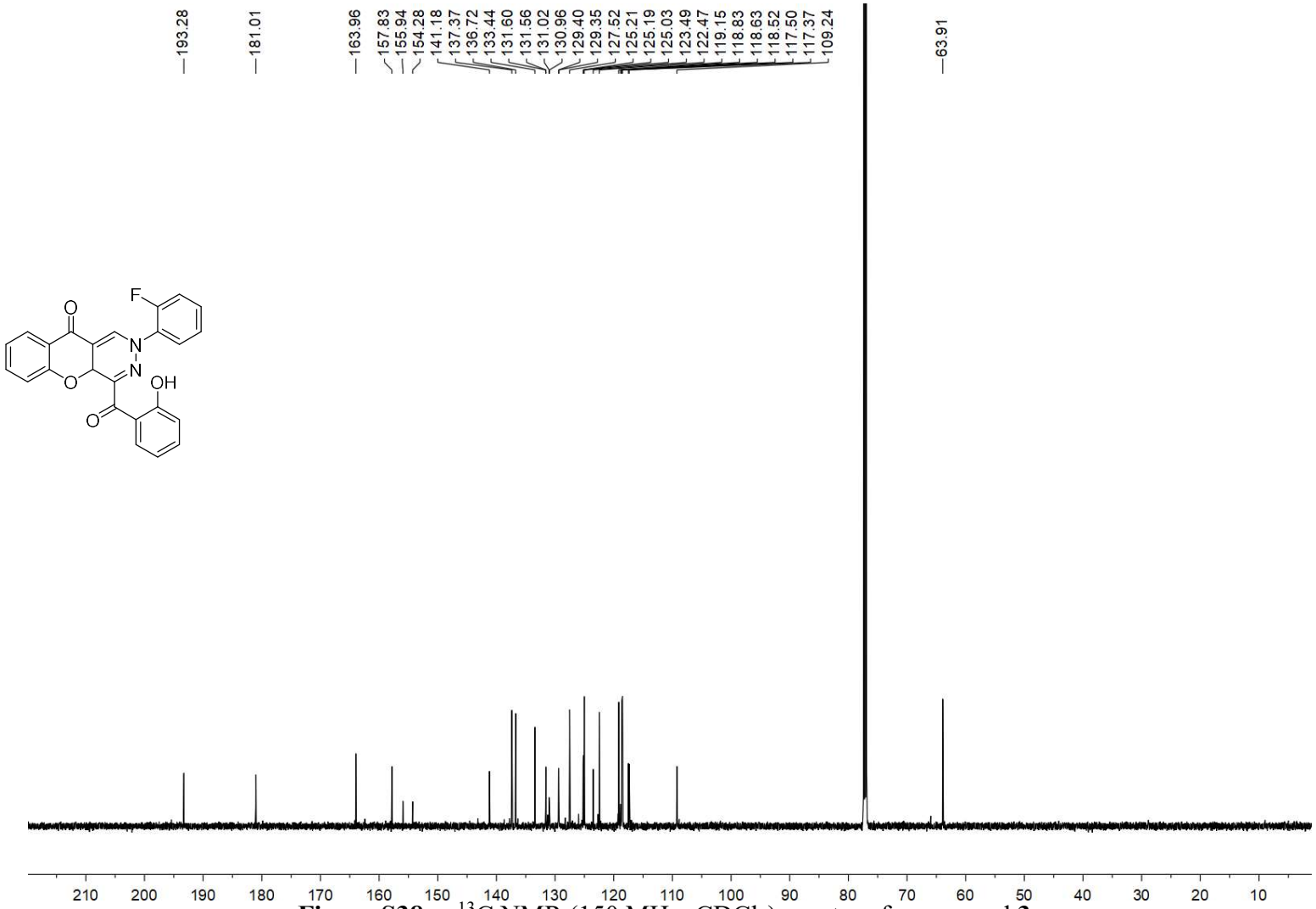


Figure S38. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3r**

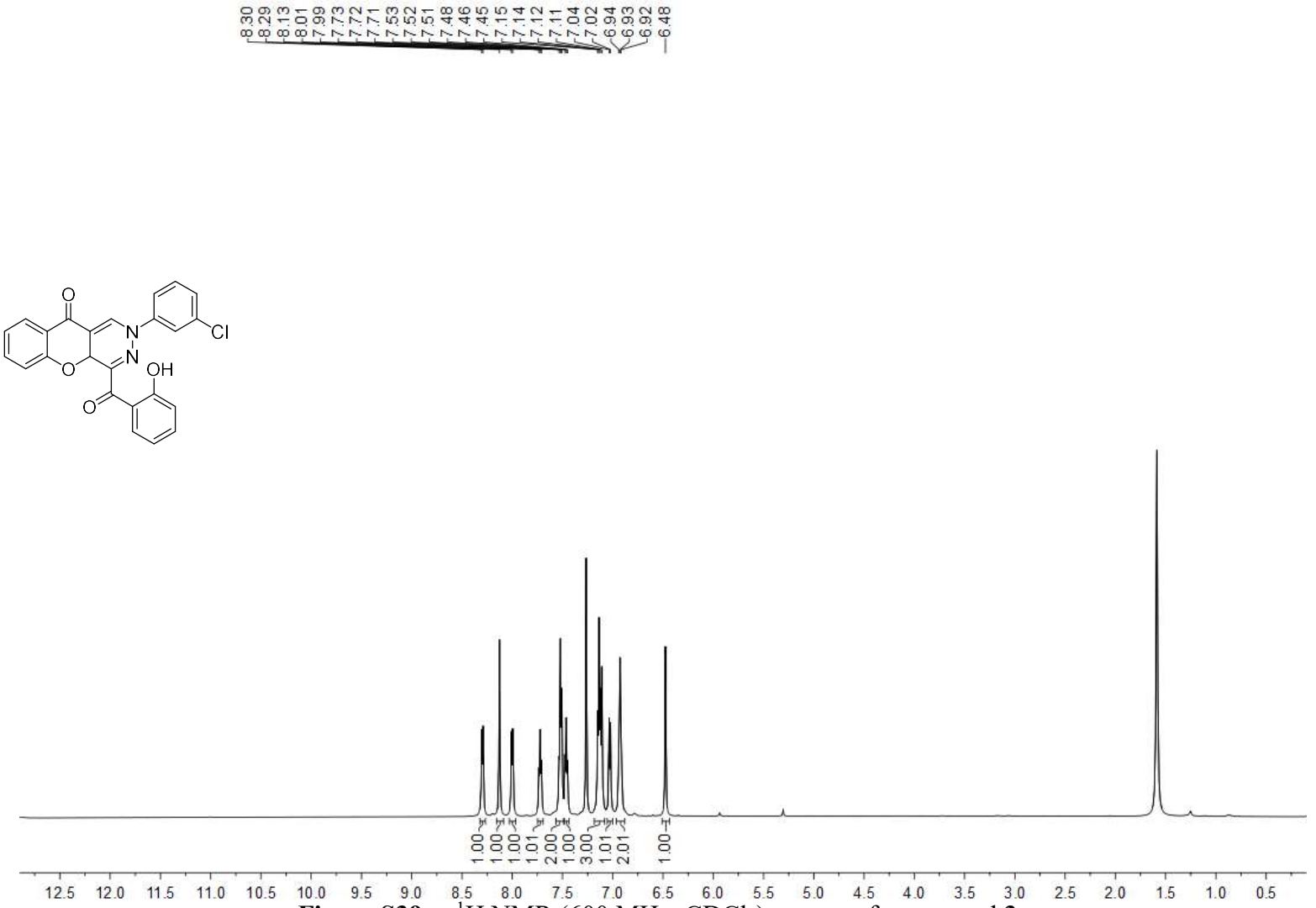


Figure S39. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3s**

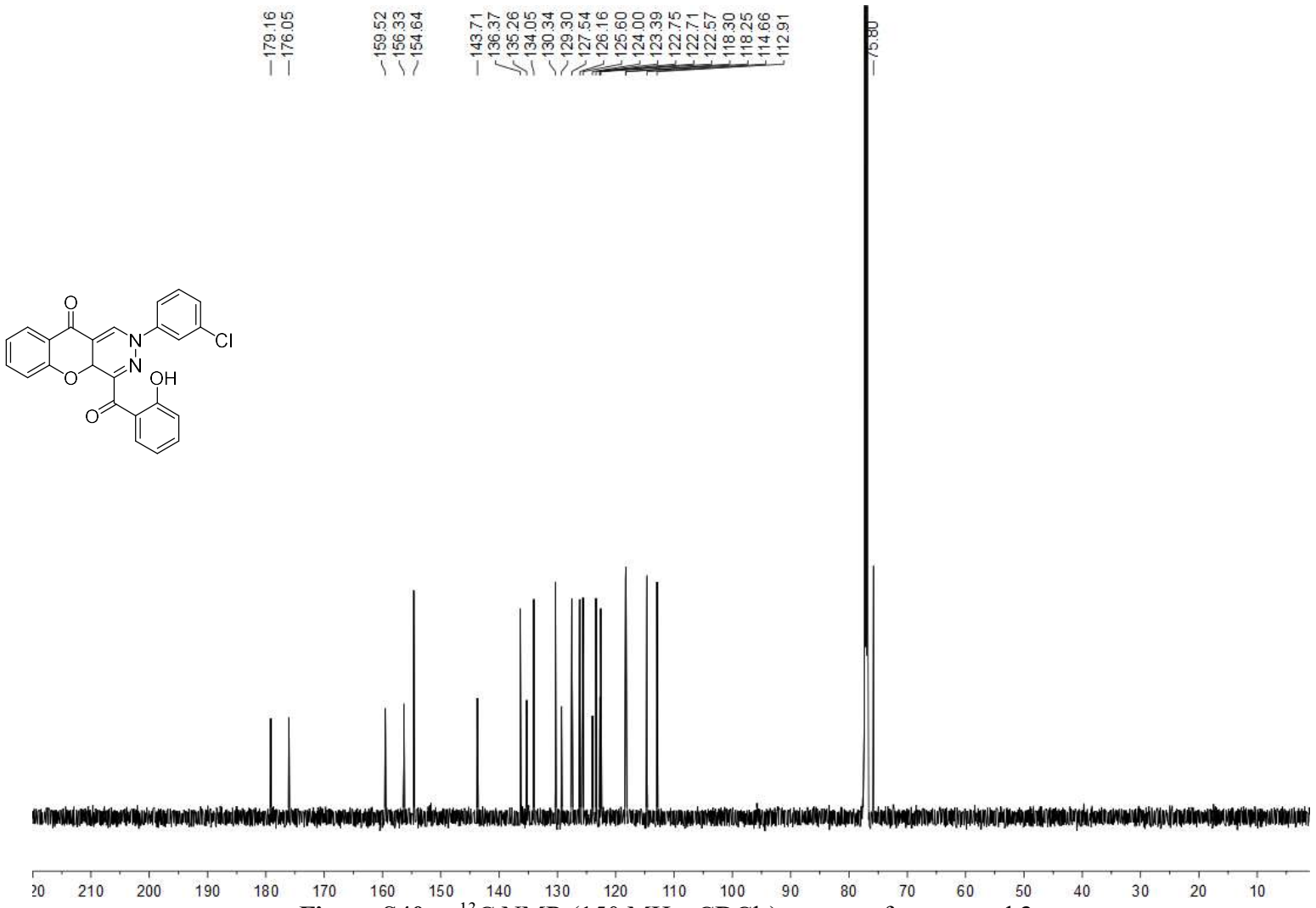


Figure S40. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3s**

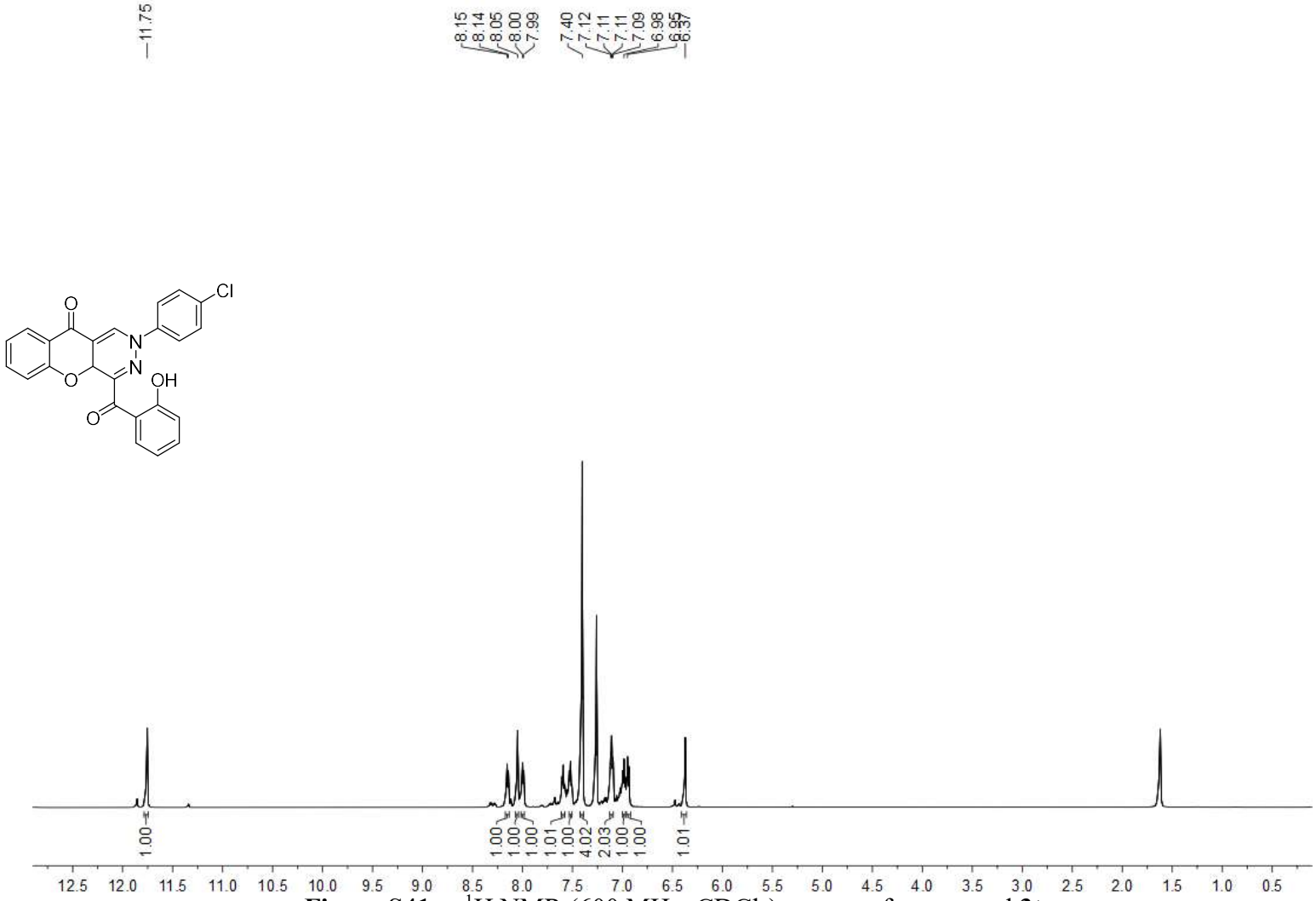


Figure S41. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3t**

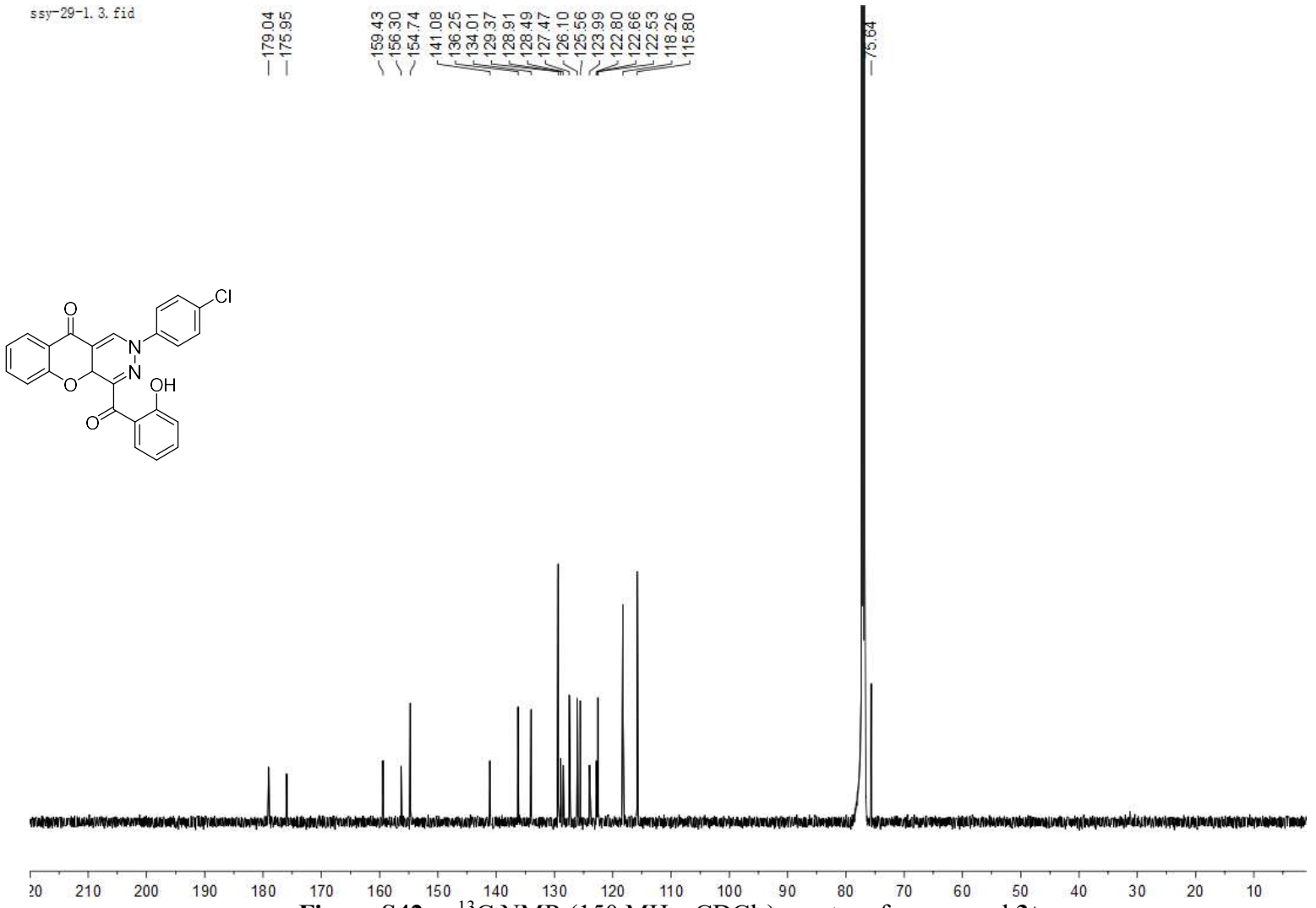


Figure S42. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3t**

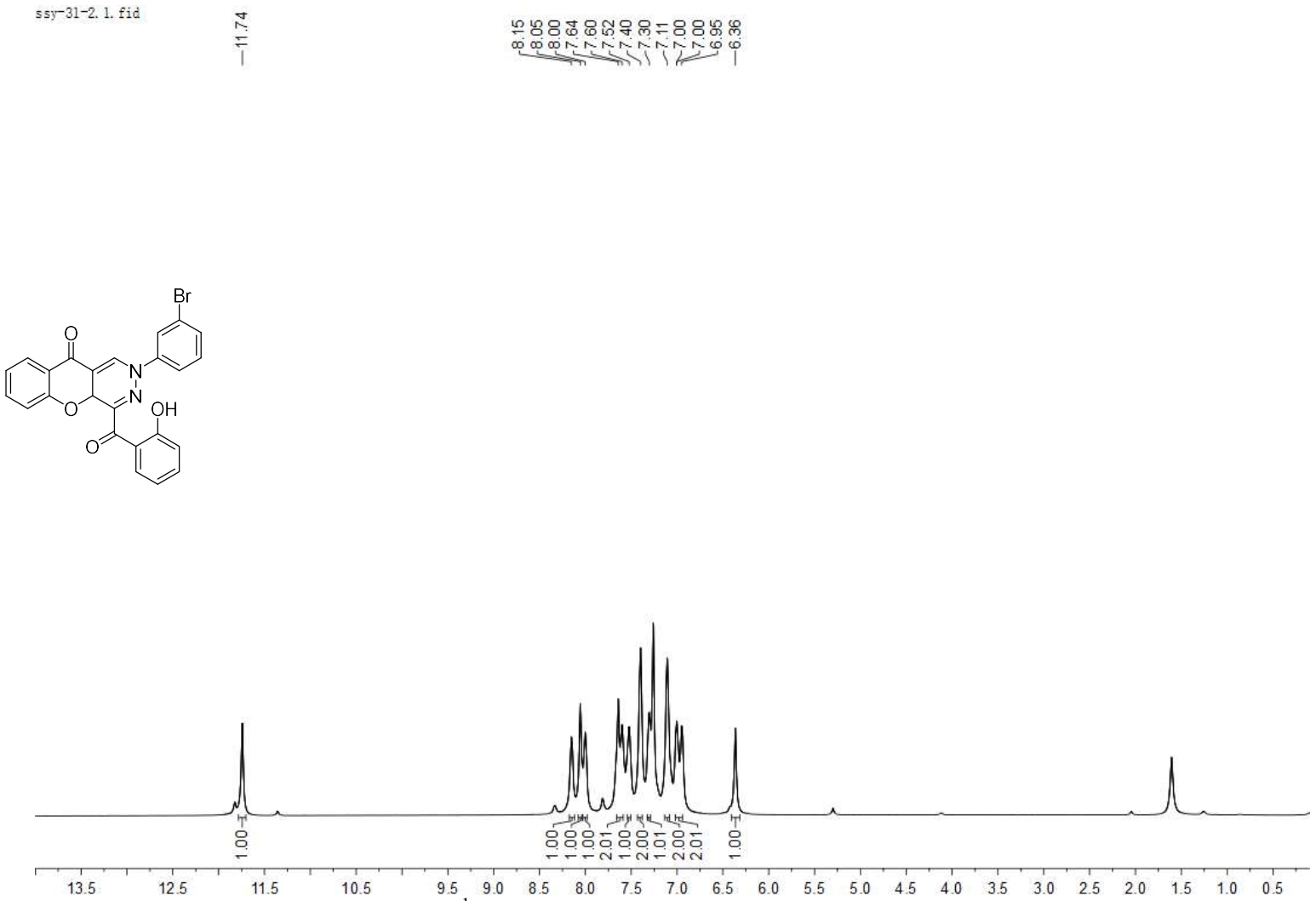


Figure S43. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3u**

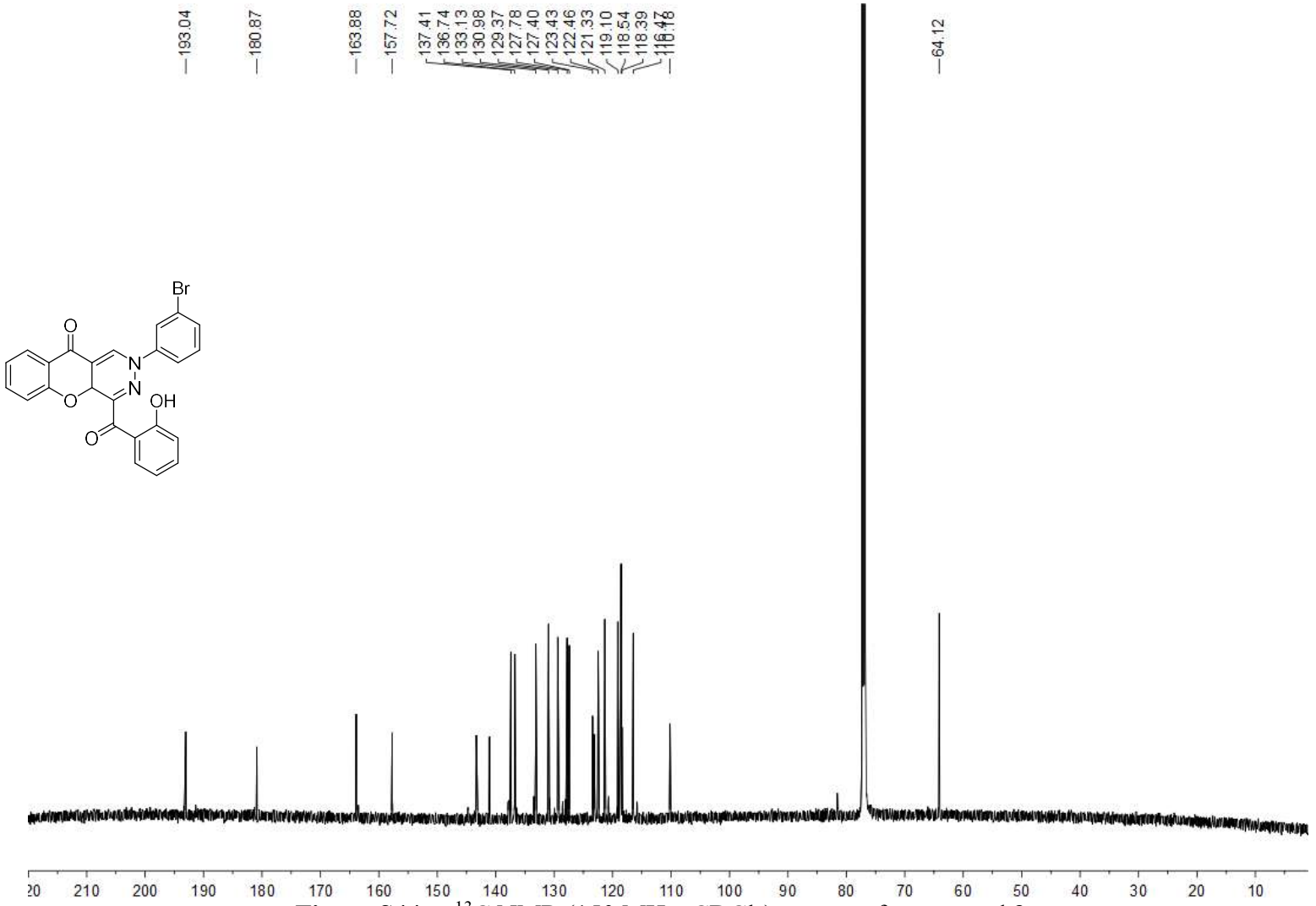


Figure S44. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3u**

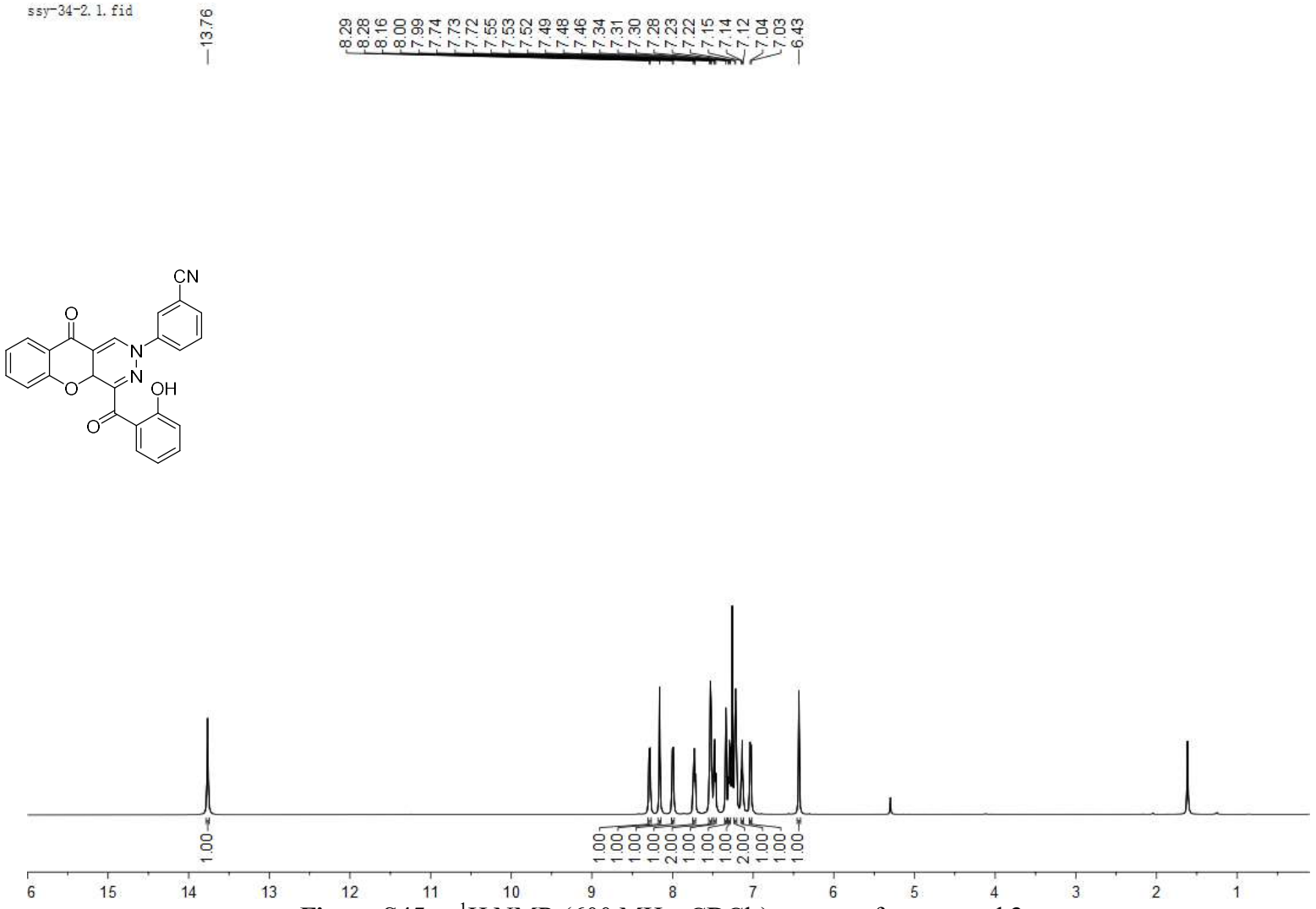


Figure S45. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3v**

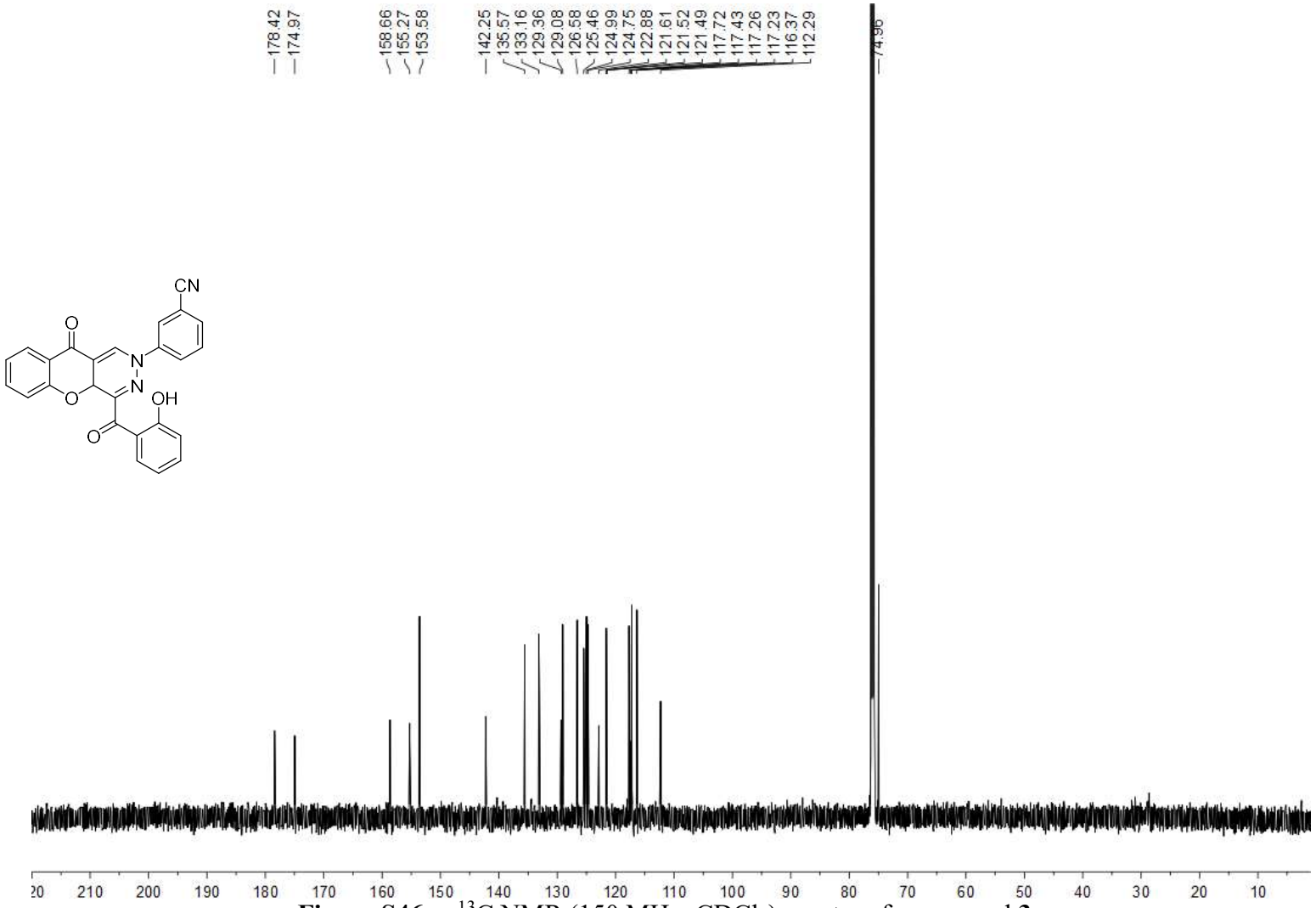


Figure S46. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3v**

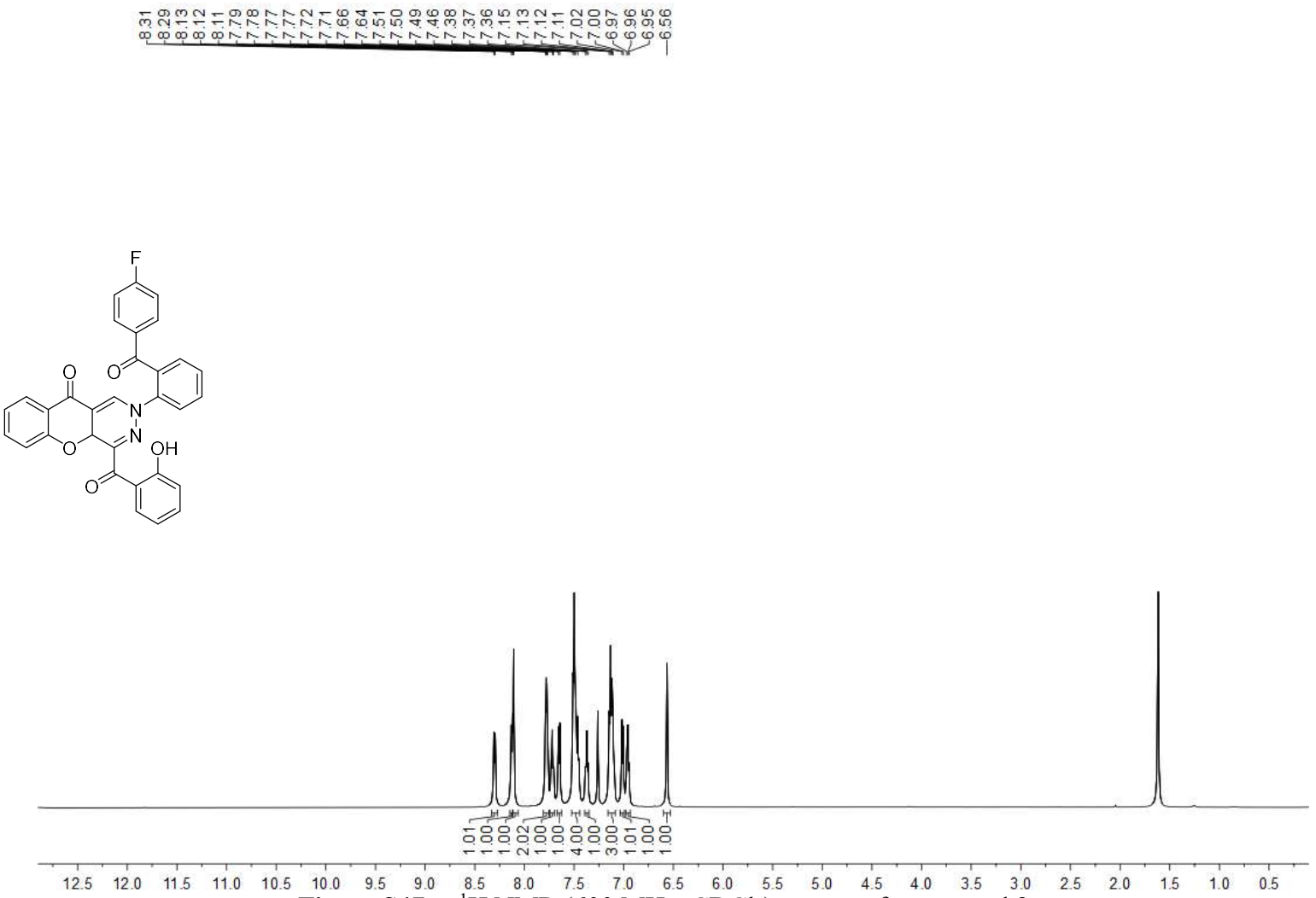


Figure S47. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3w**

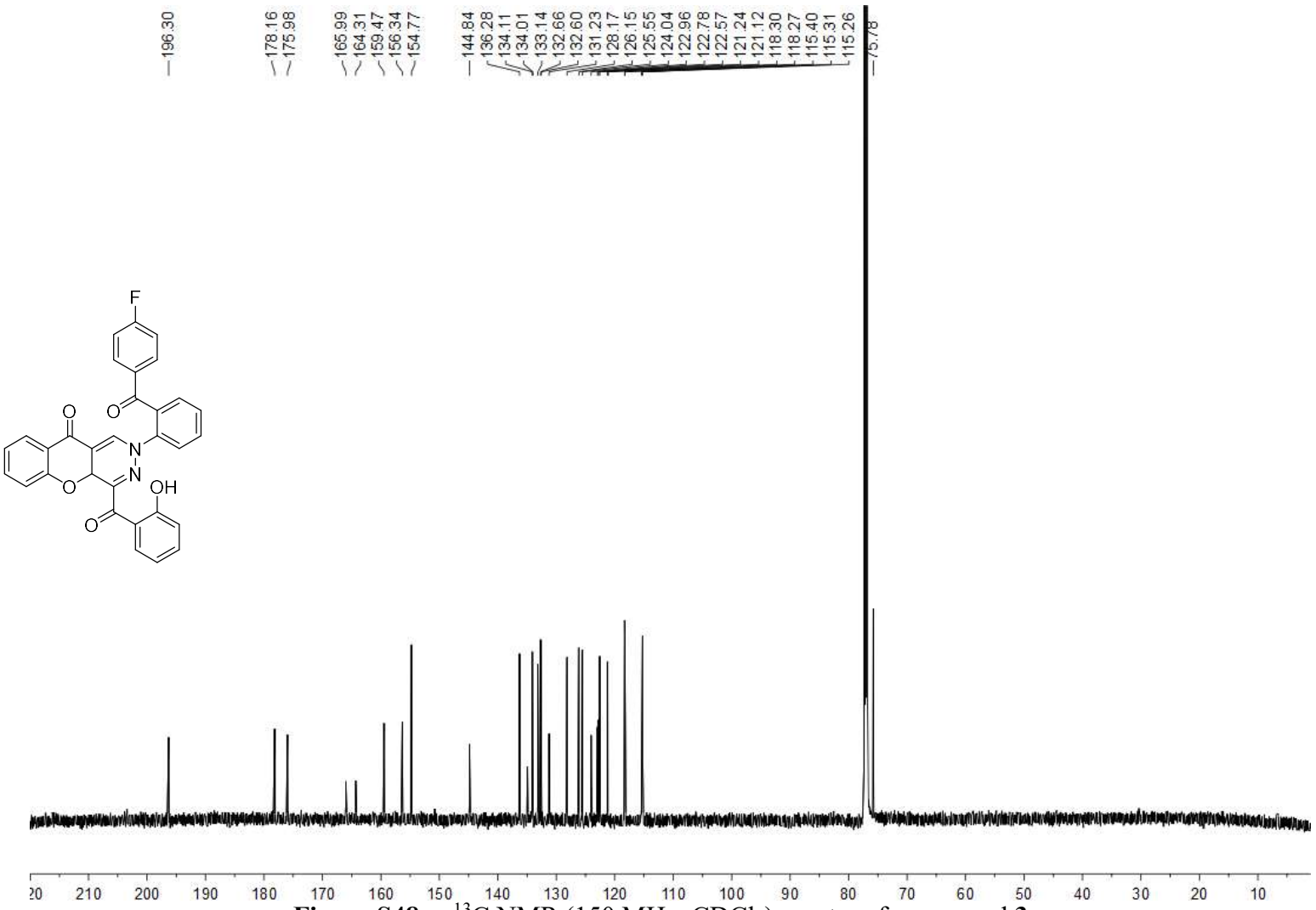


Figure S48. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3w**

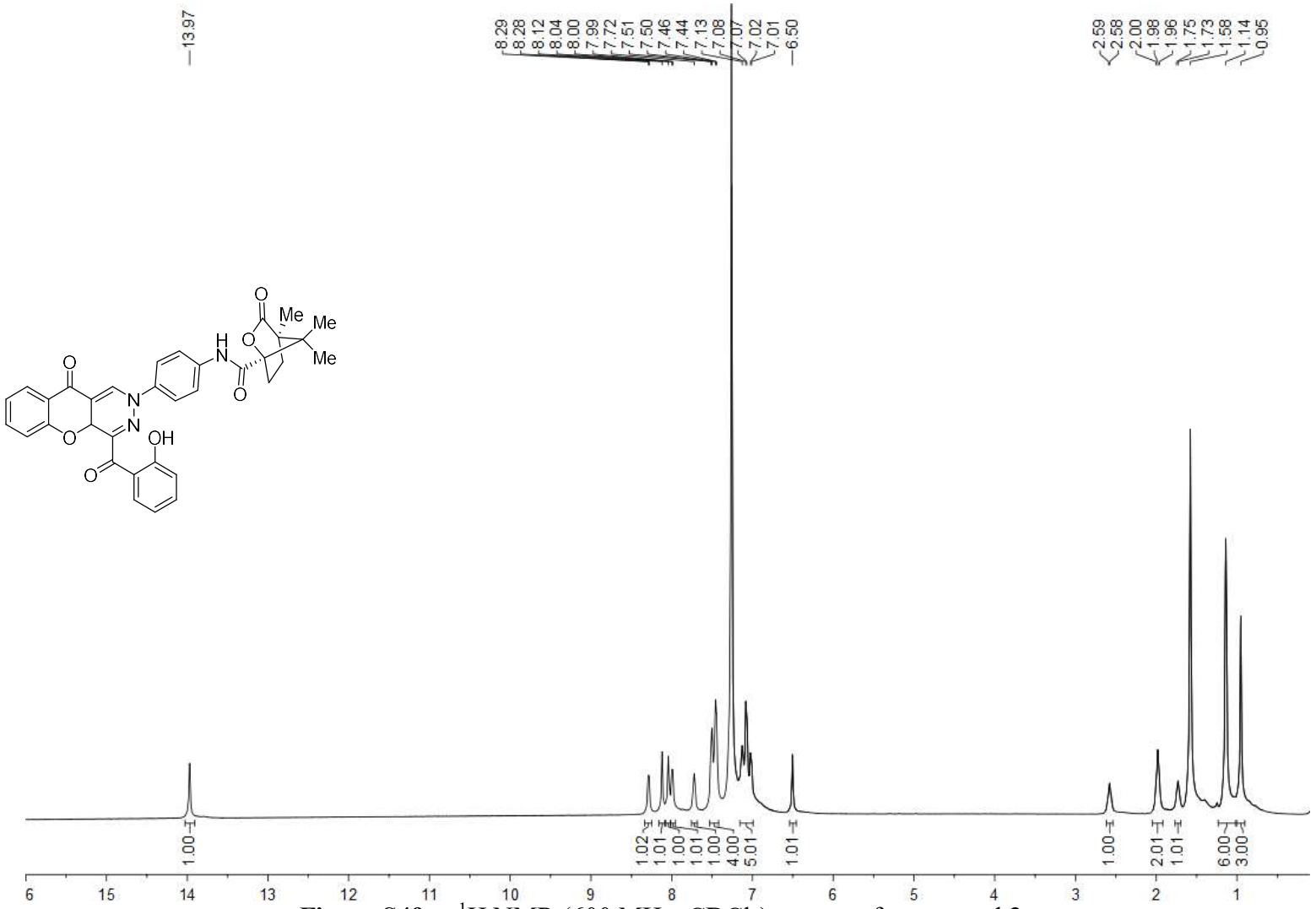


Figure S49. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **3x**

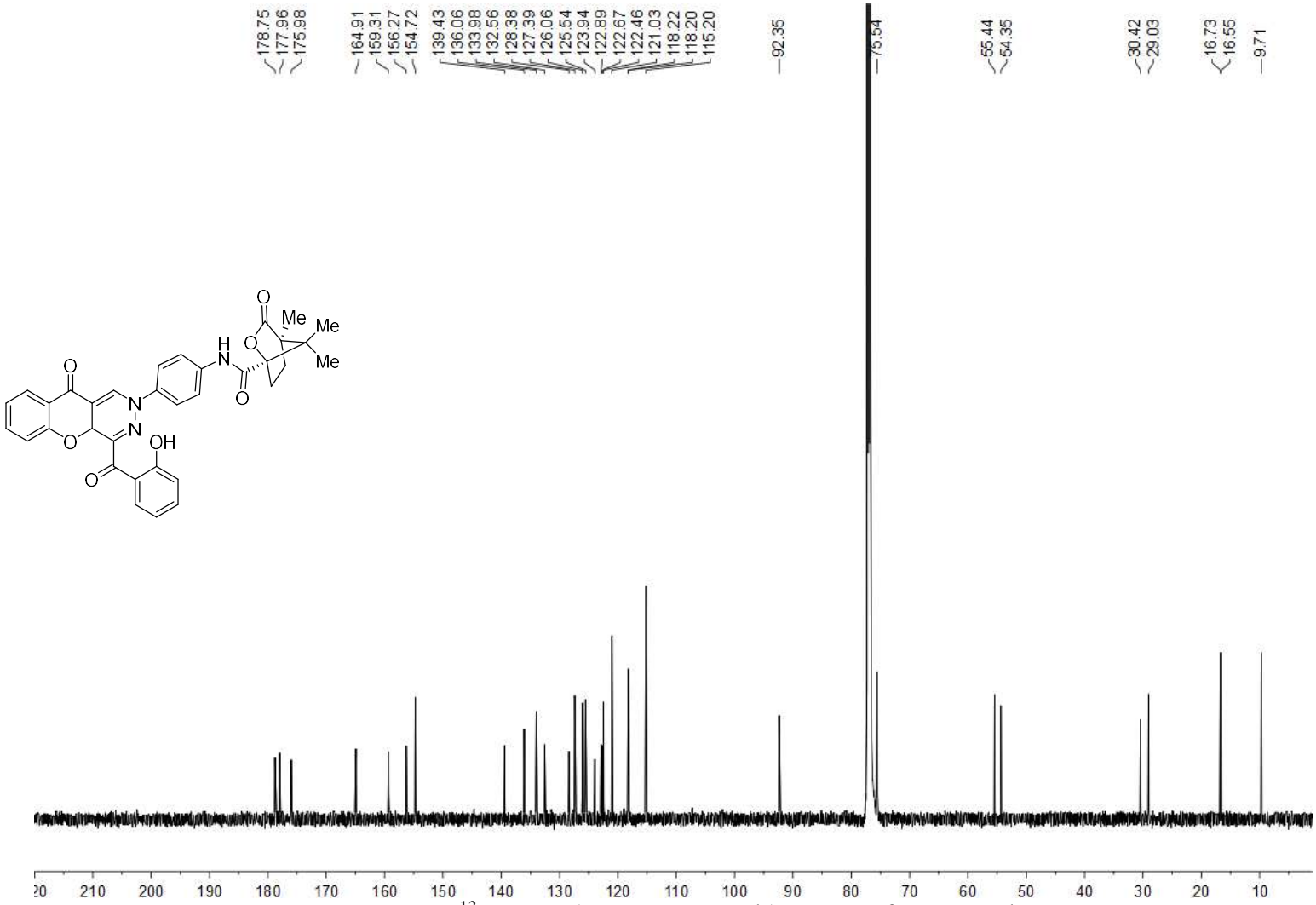


Figure S50. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **3x**

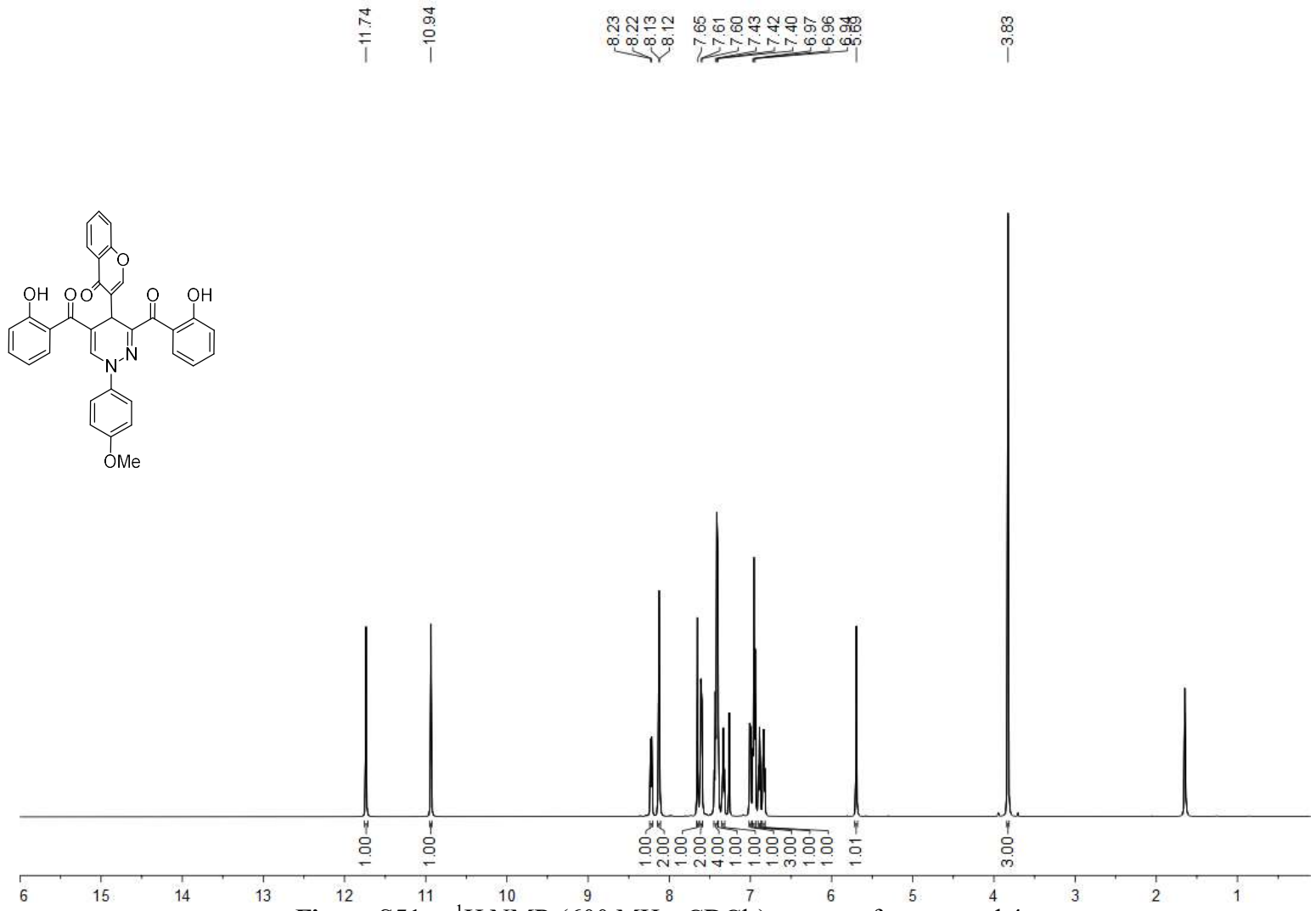


Figure S51. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4a**

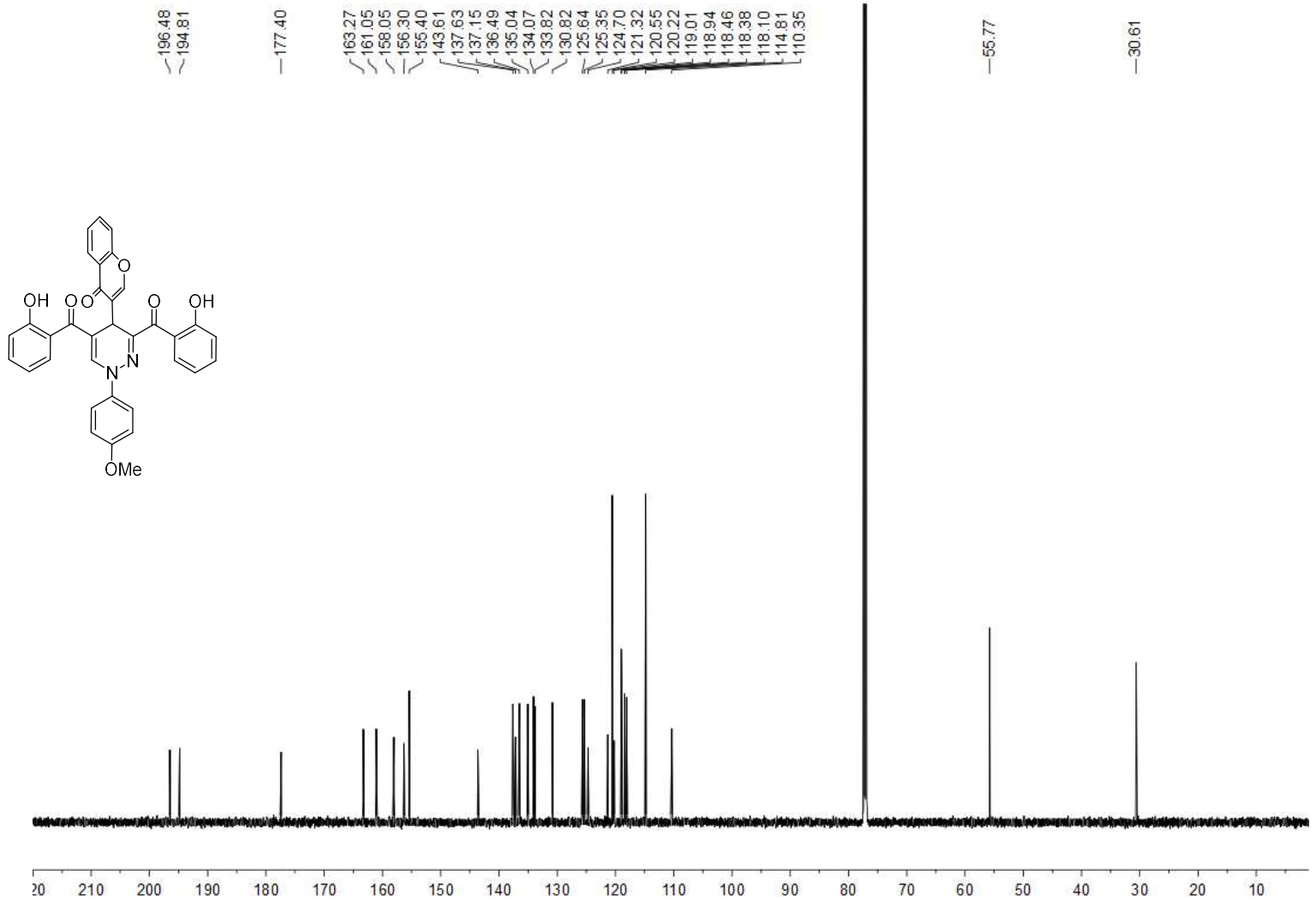


Figure S52. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4a**

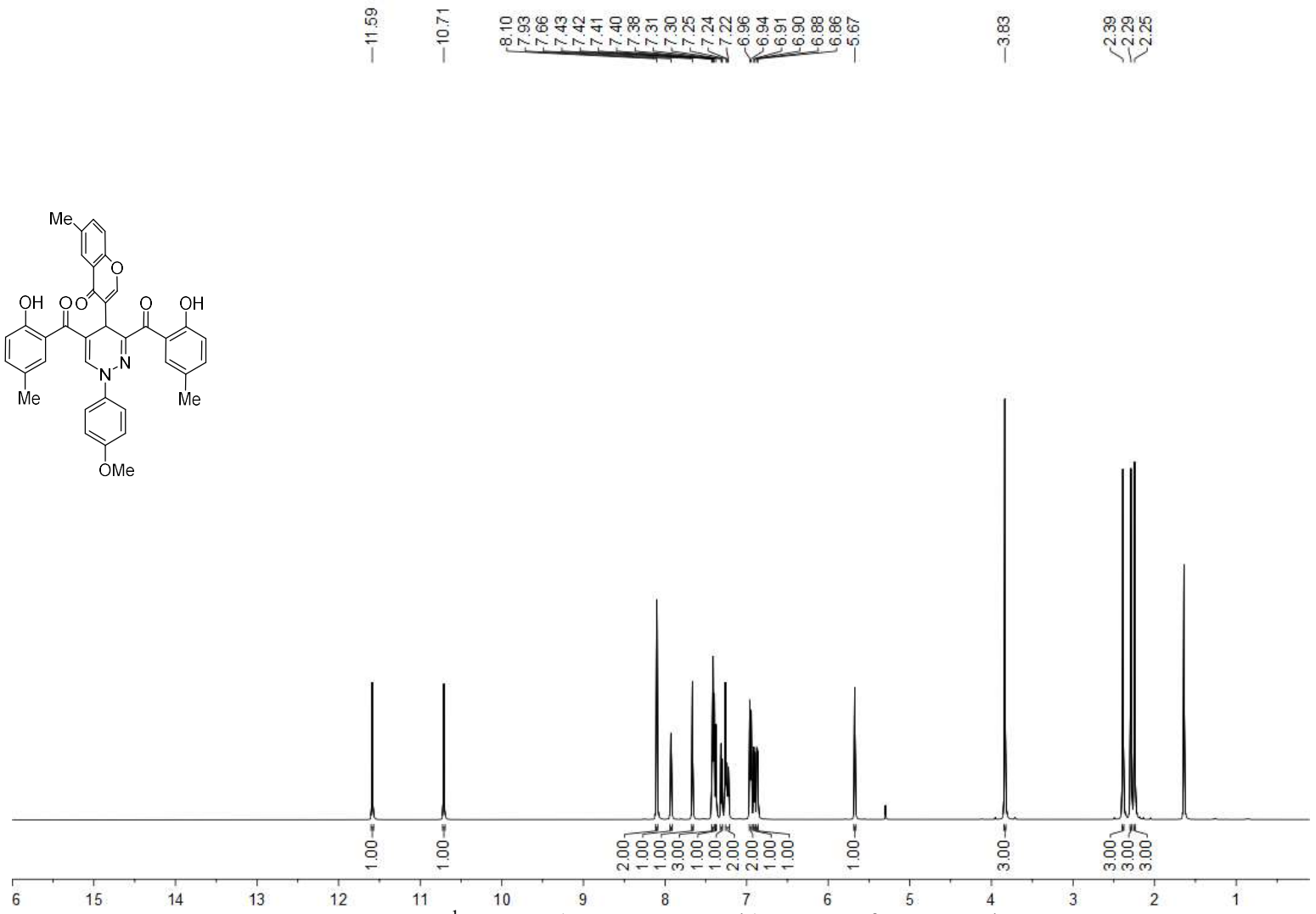


Figure S53. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4b**

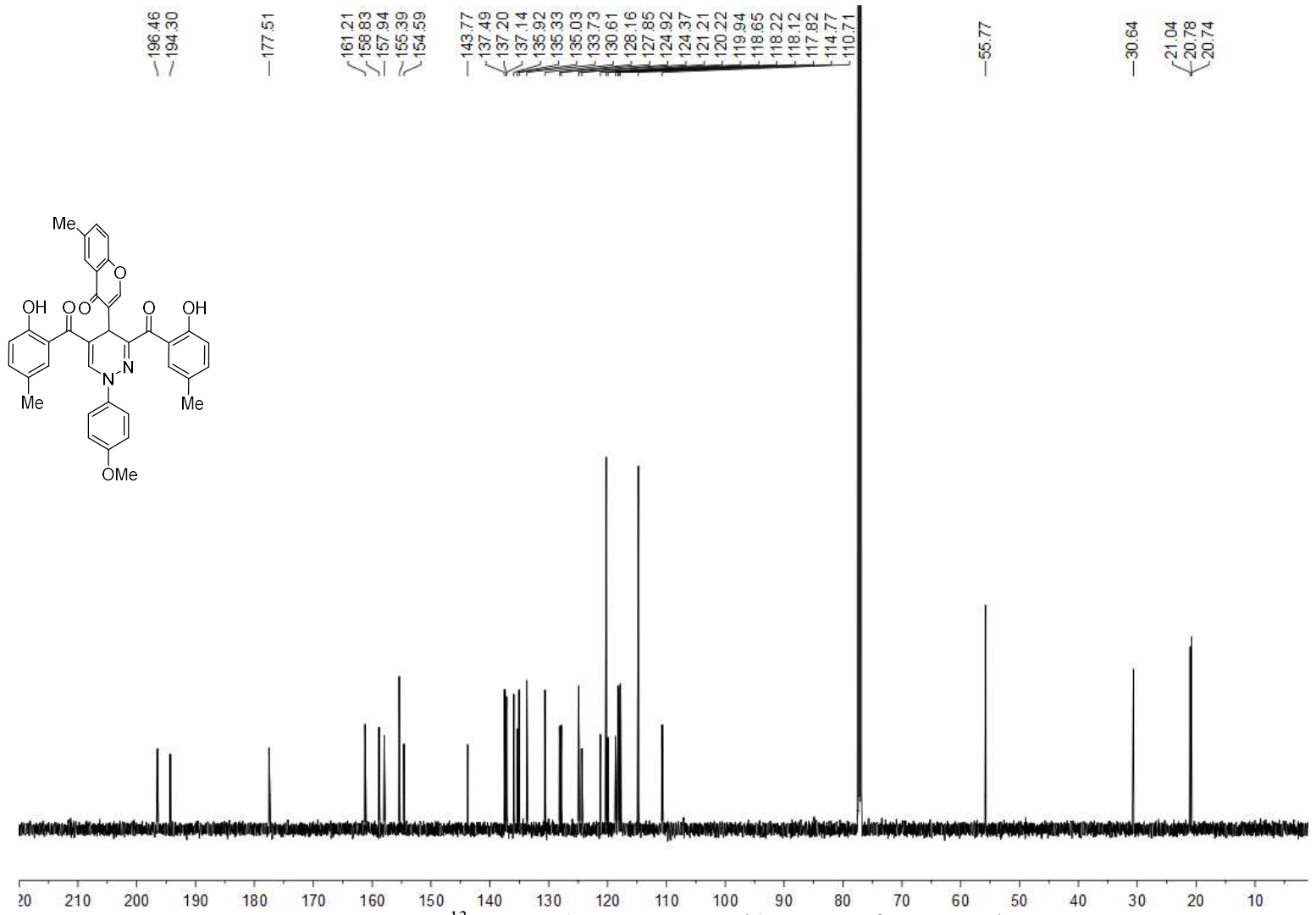


Figure S54. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4b**

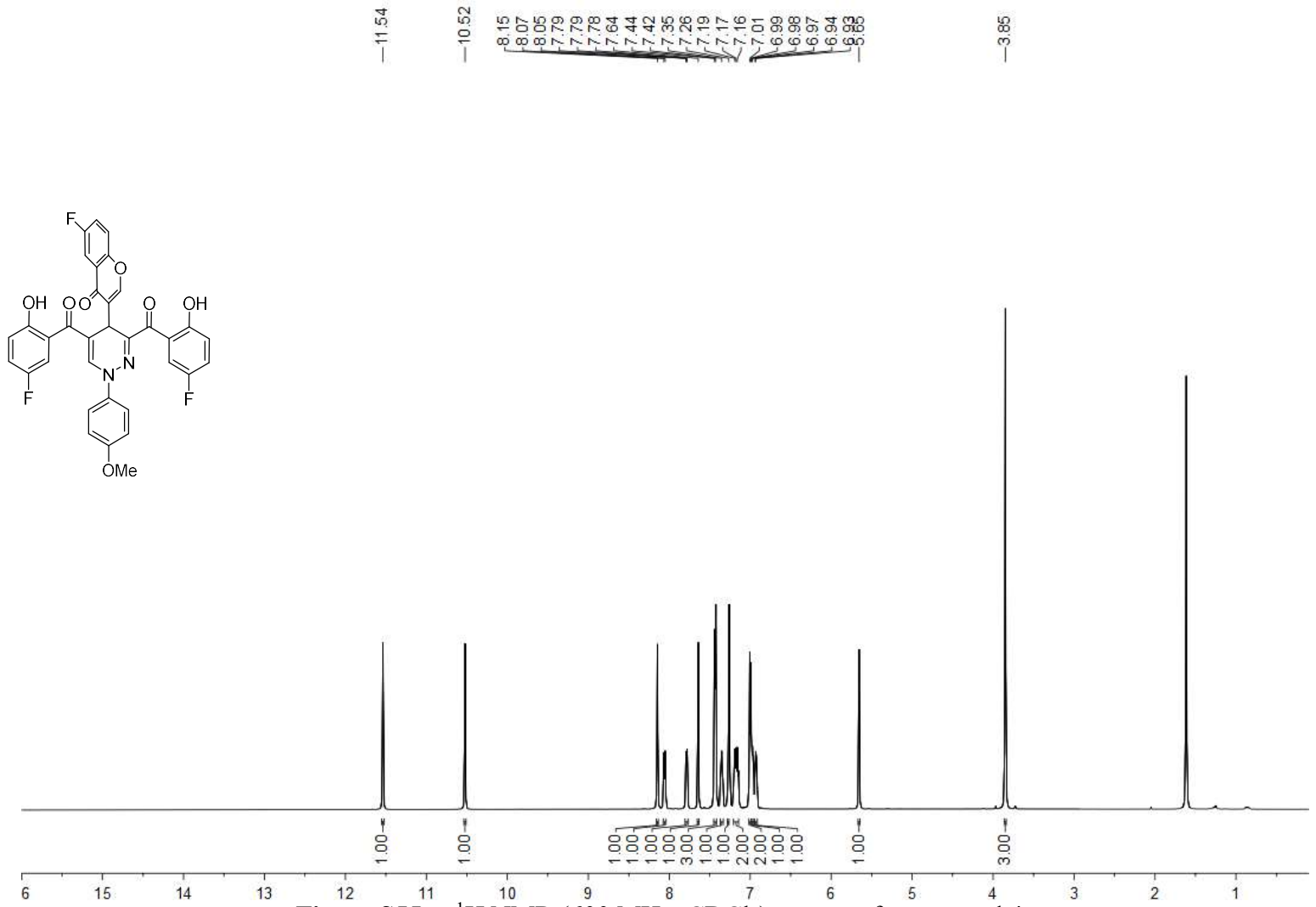


Figure S55. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4c**

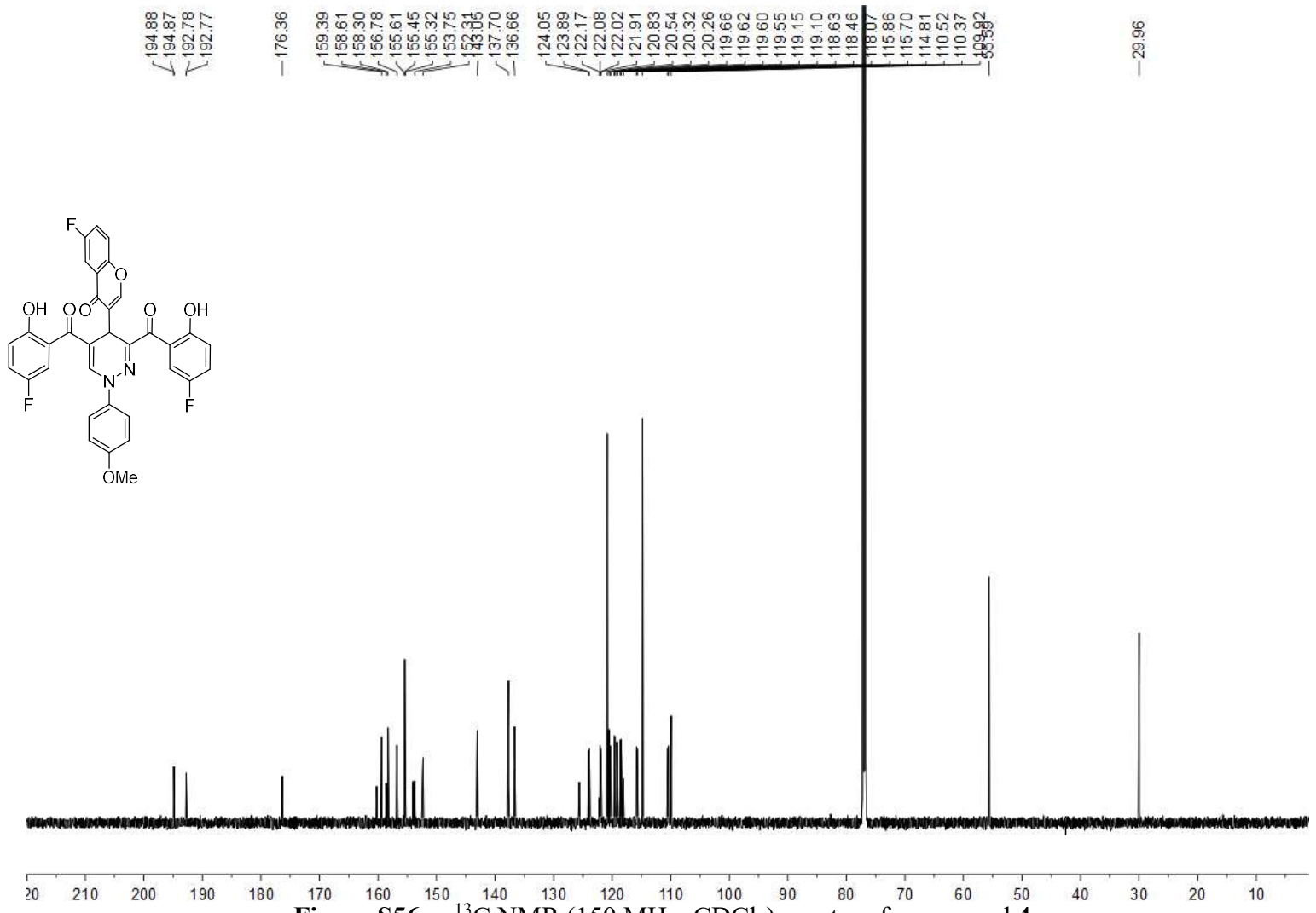


Figure S56. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4c**

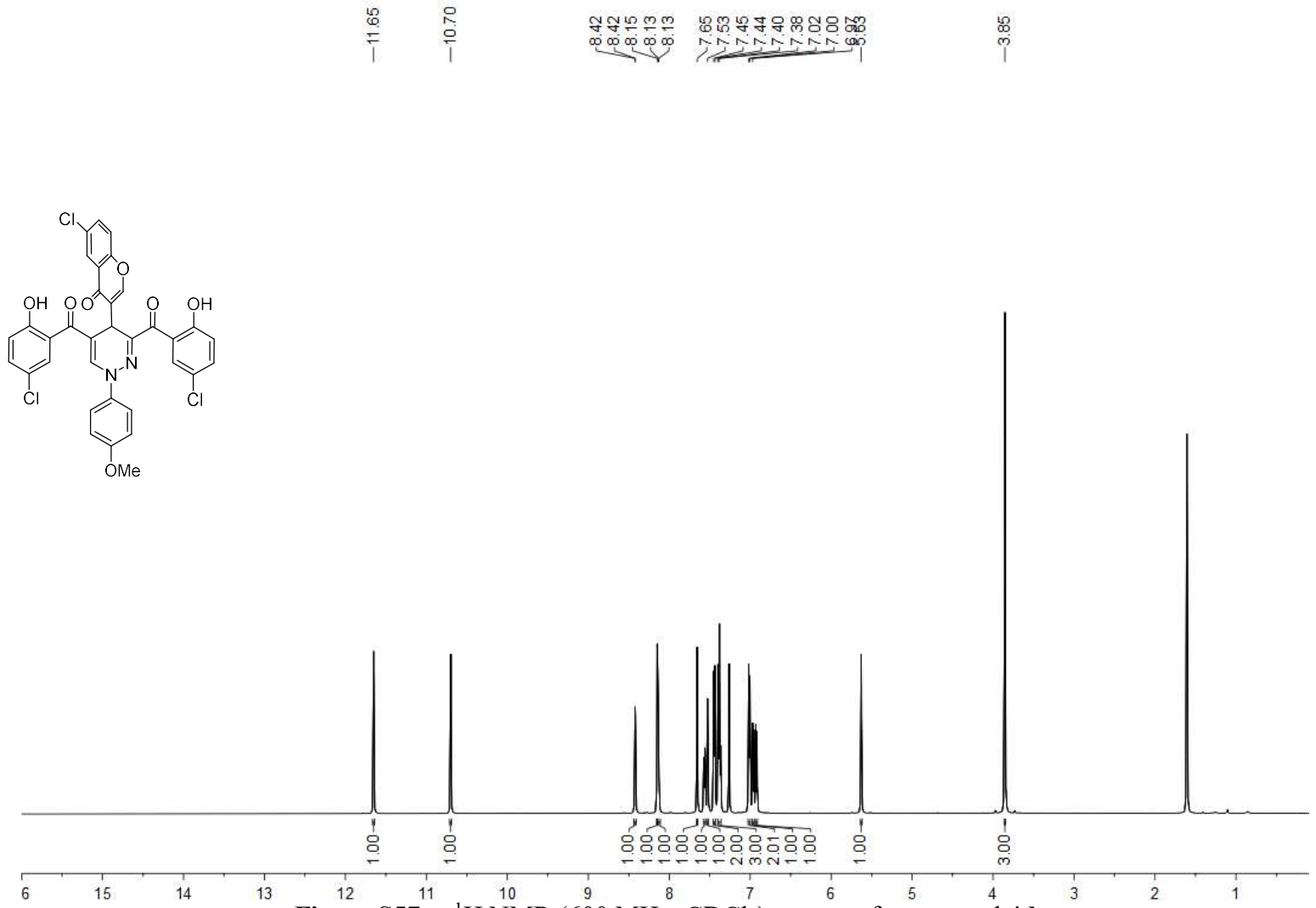


Figure S57. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4d**

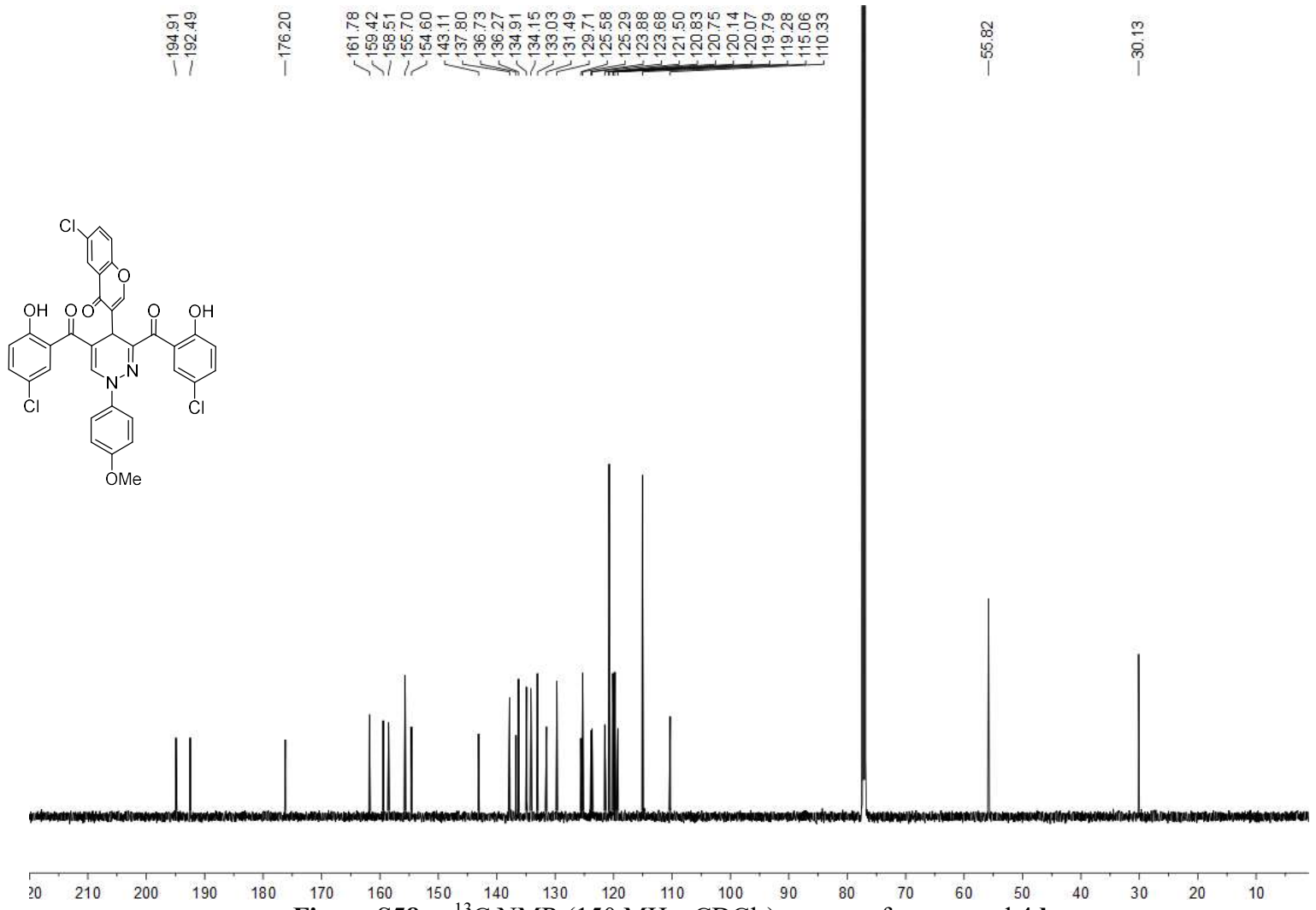


Figure S58. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4d**

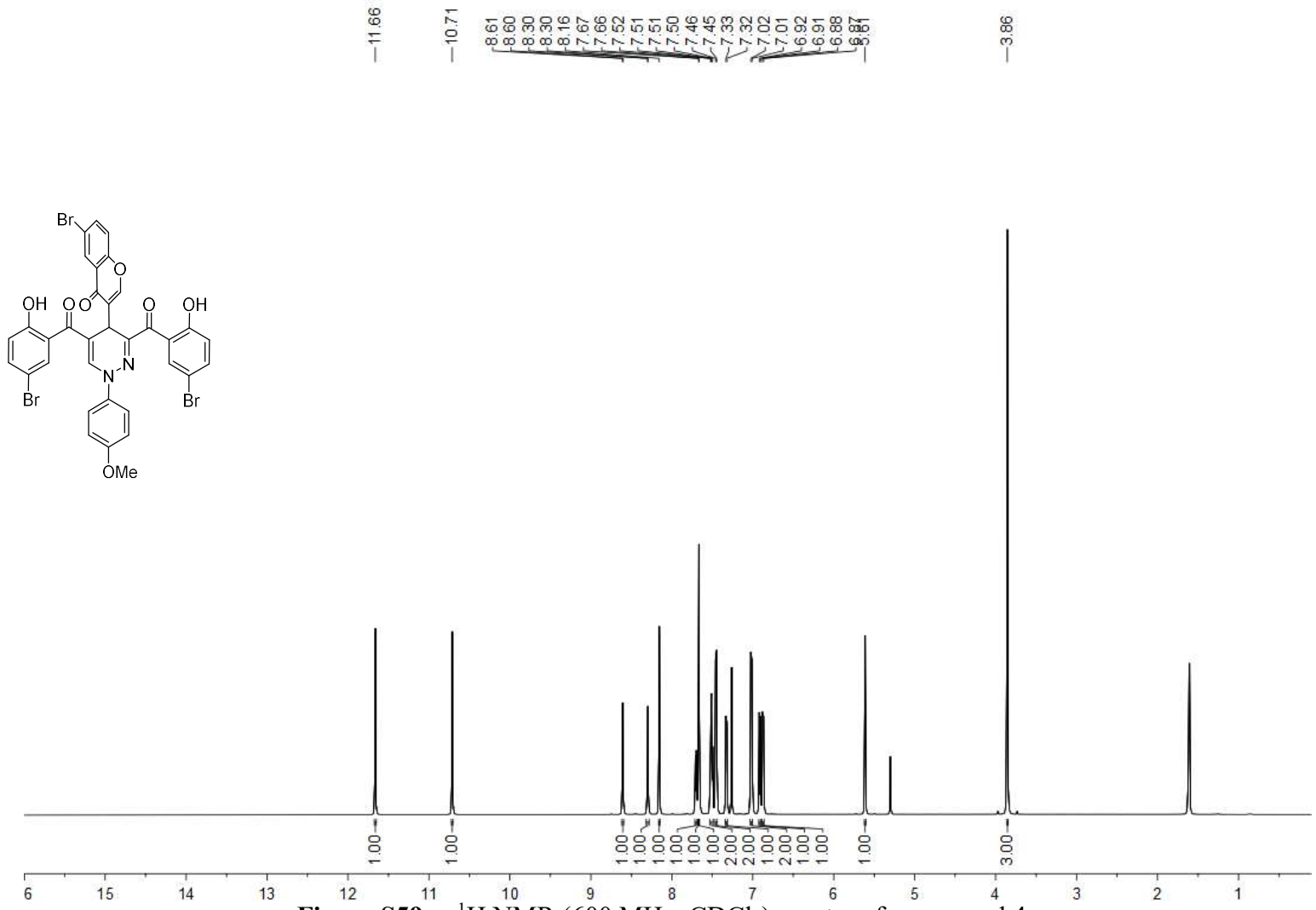


Figure S59. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4e**

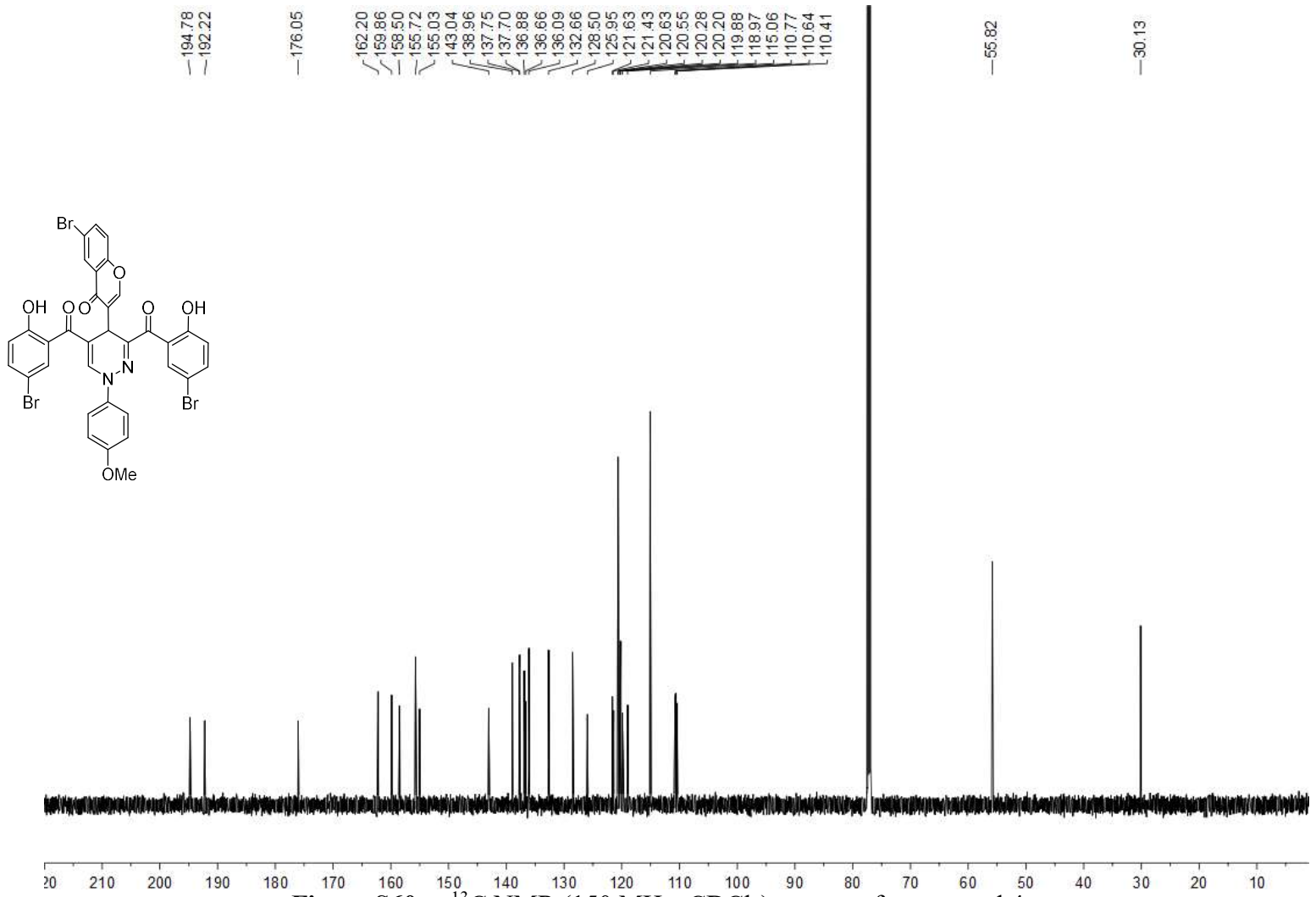


Figure S60. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4e**

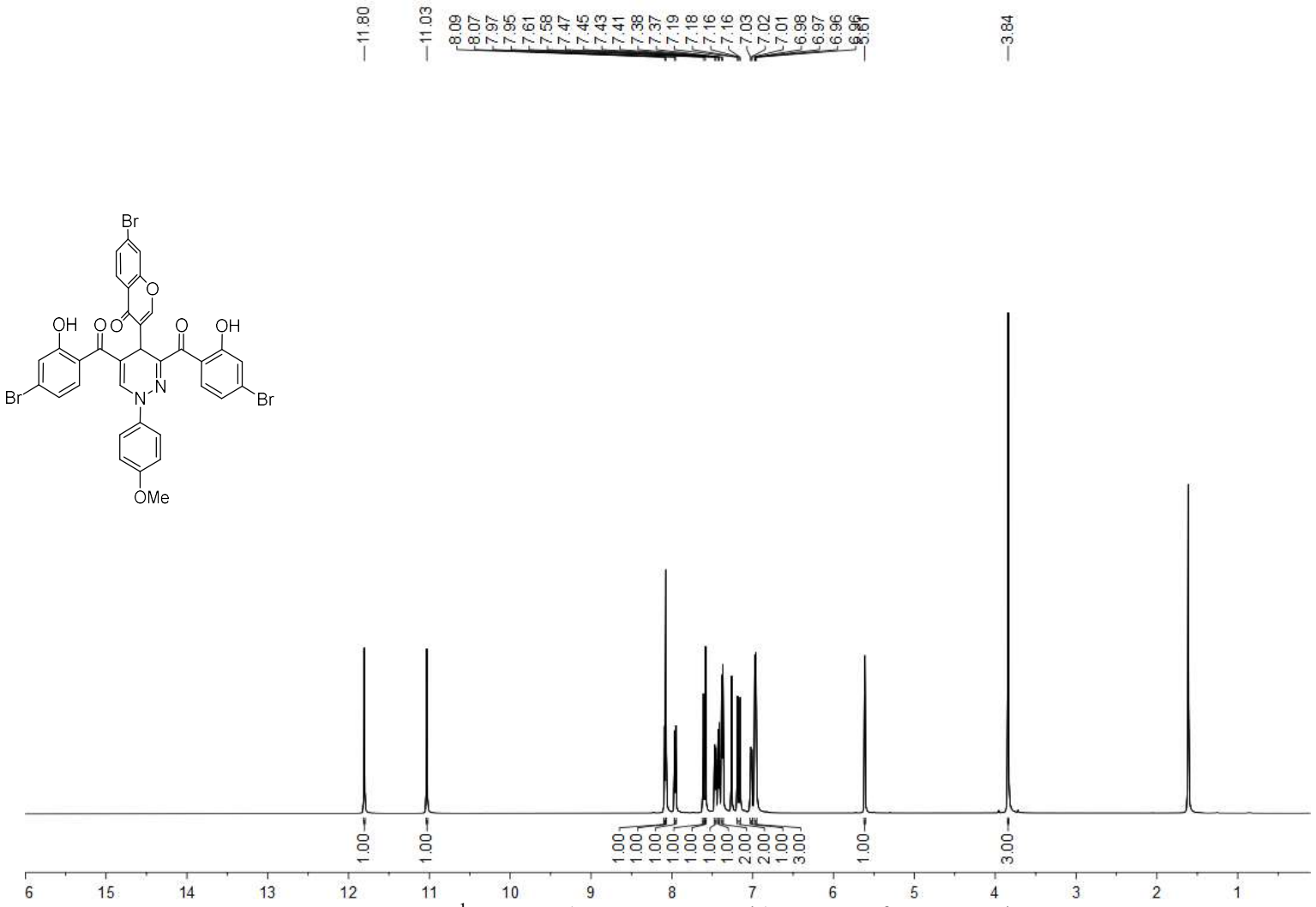


Figure S61. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4f**

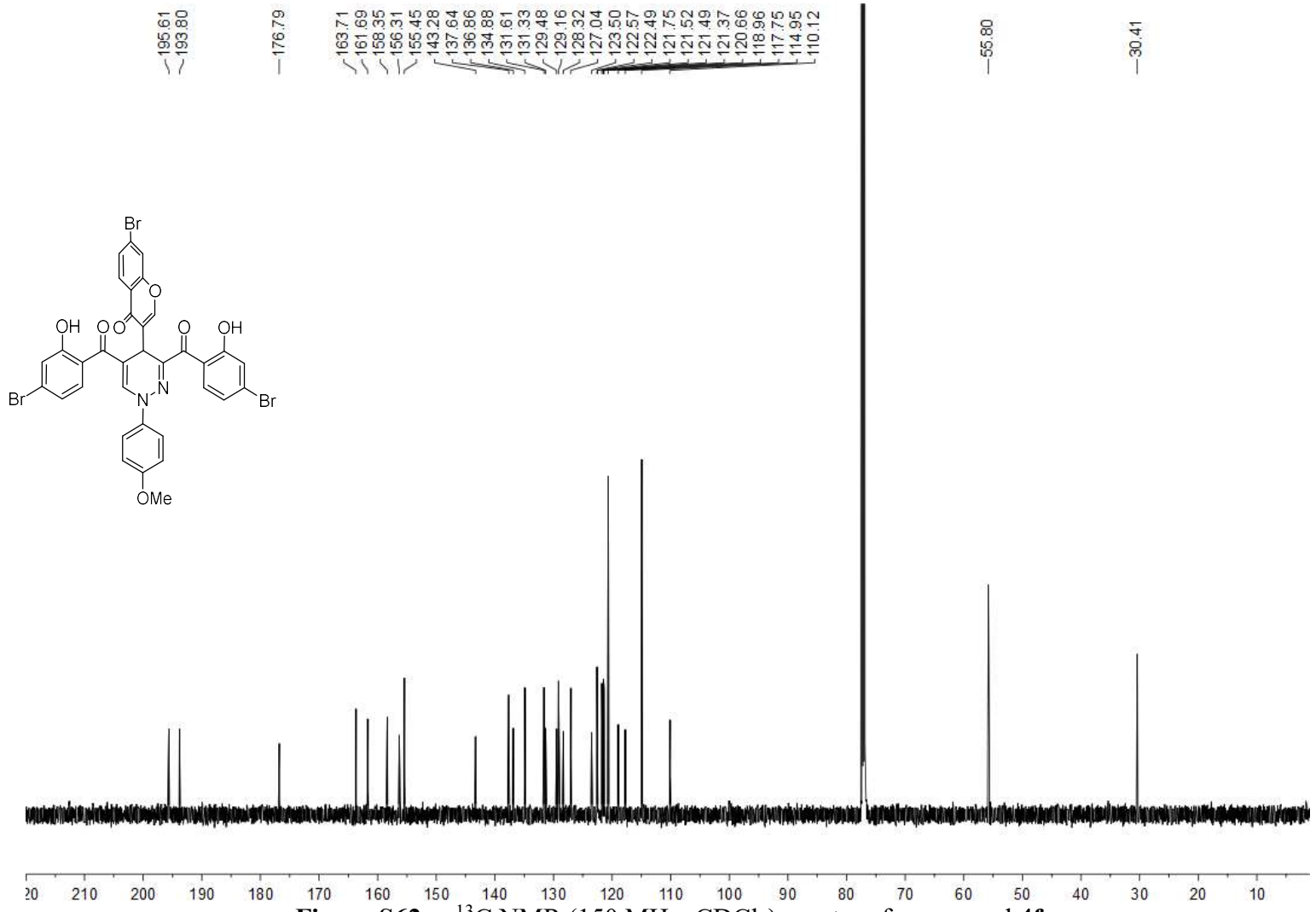


Figure S62. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4f**

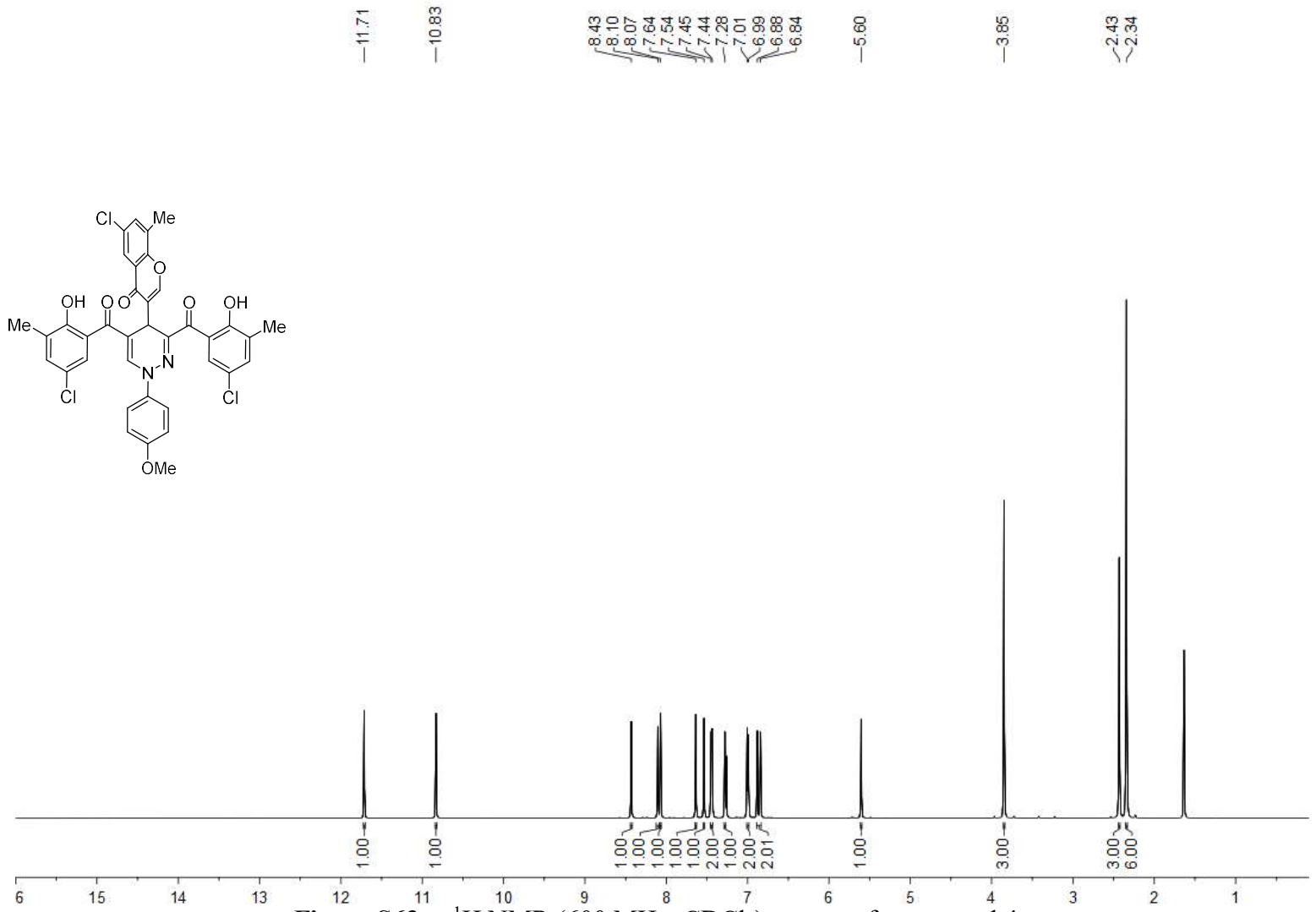


Figure S63. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4g**

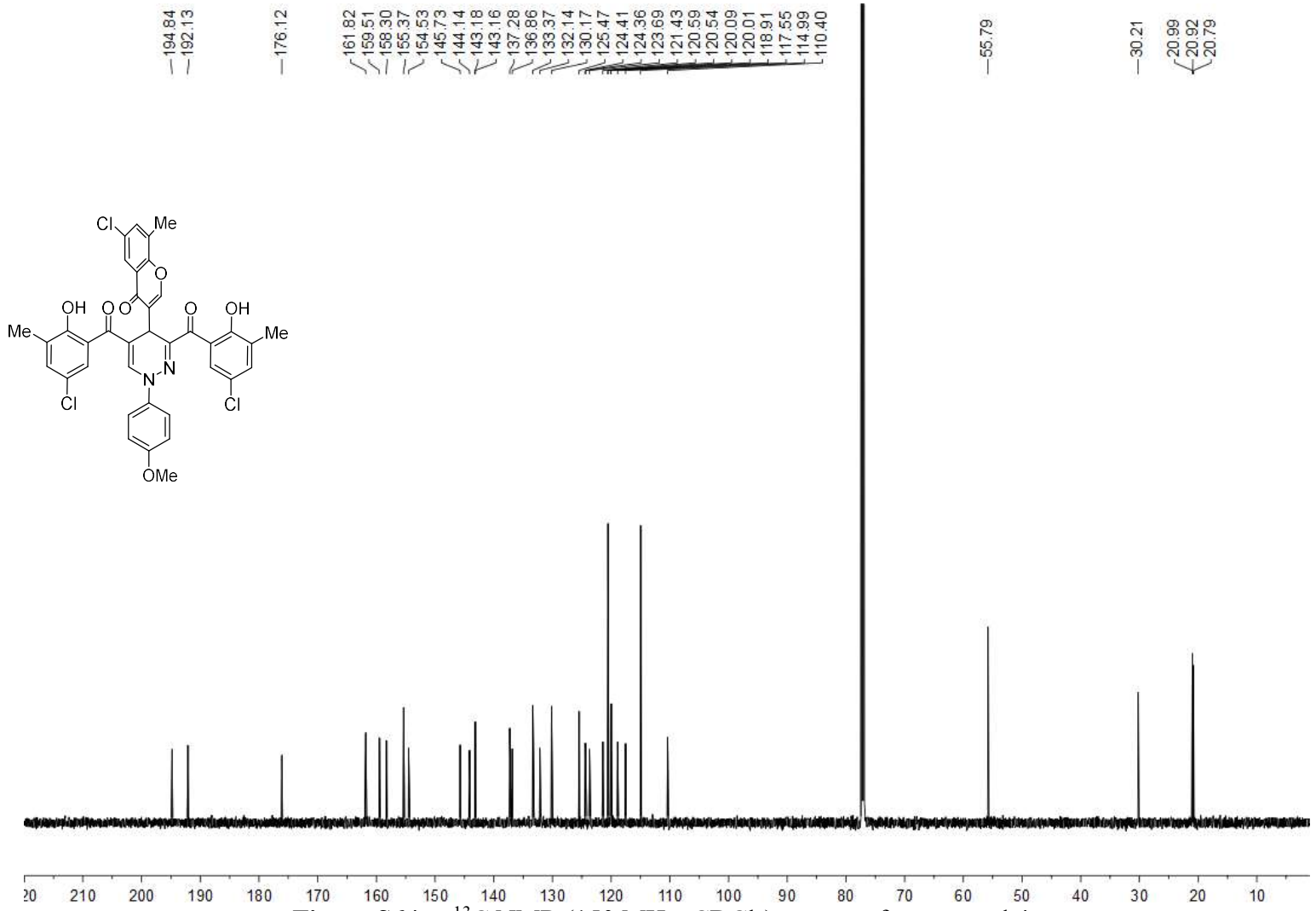


Figure S64. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4g**

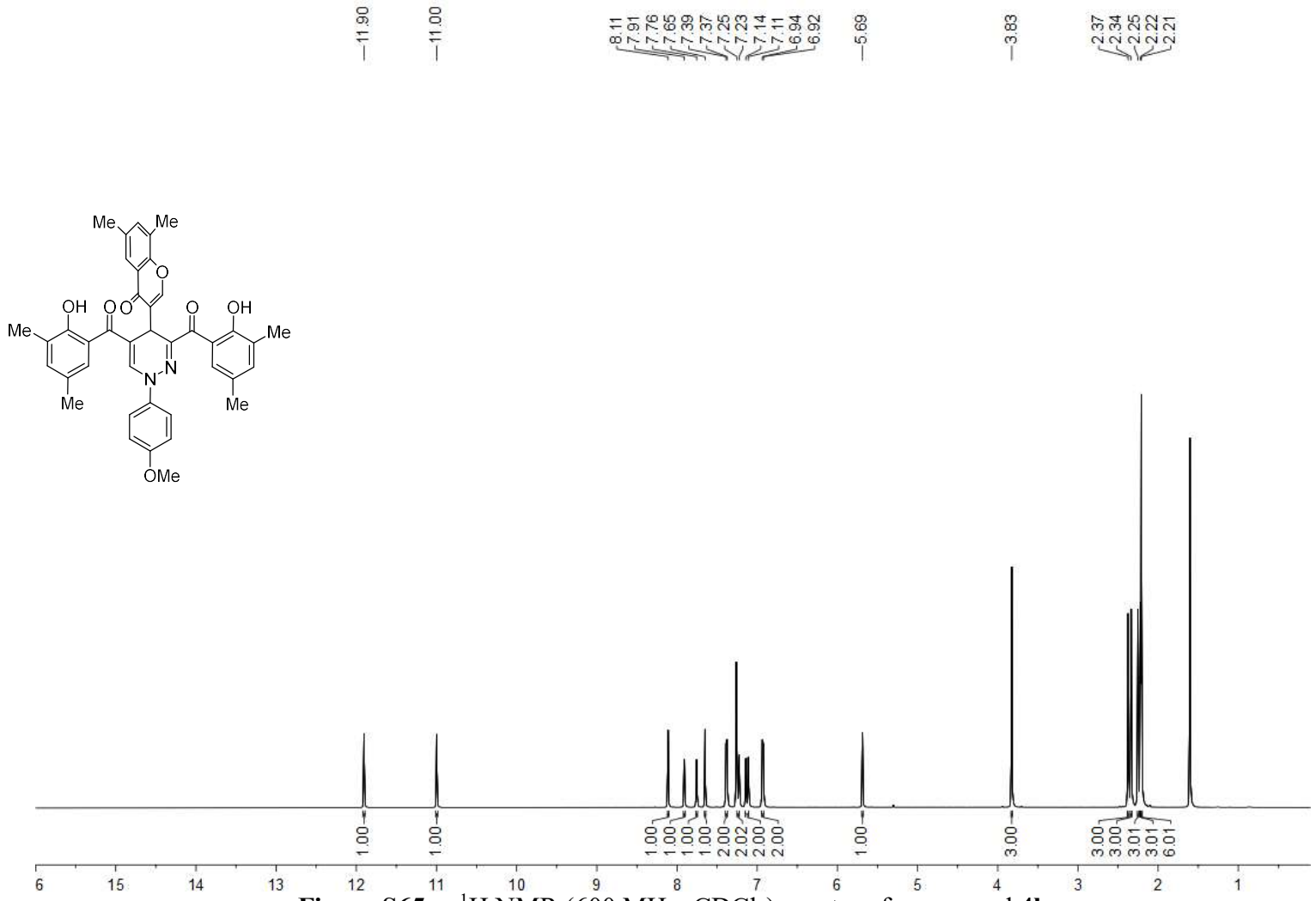


Figure S65. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4h**

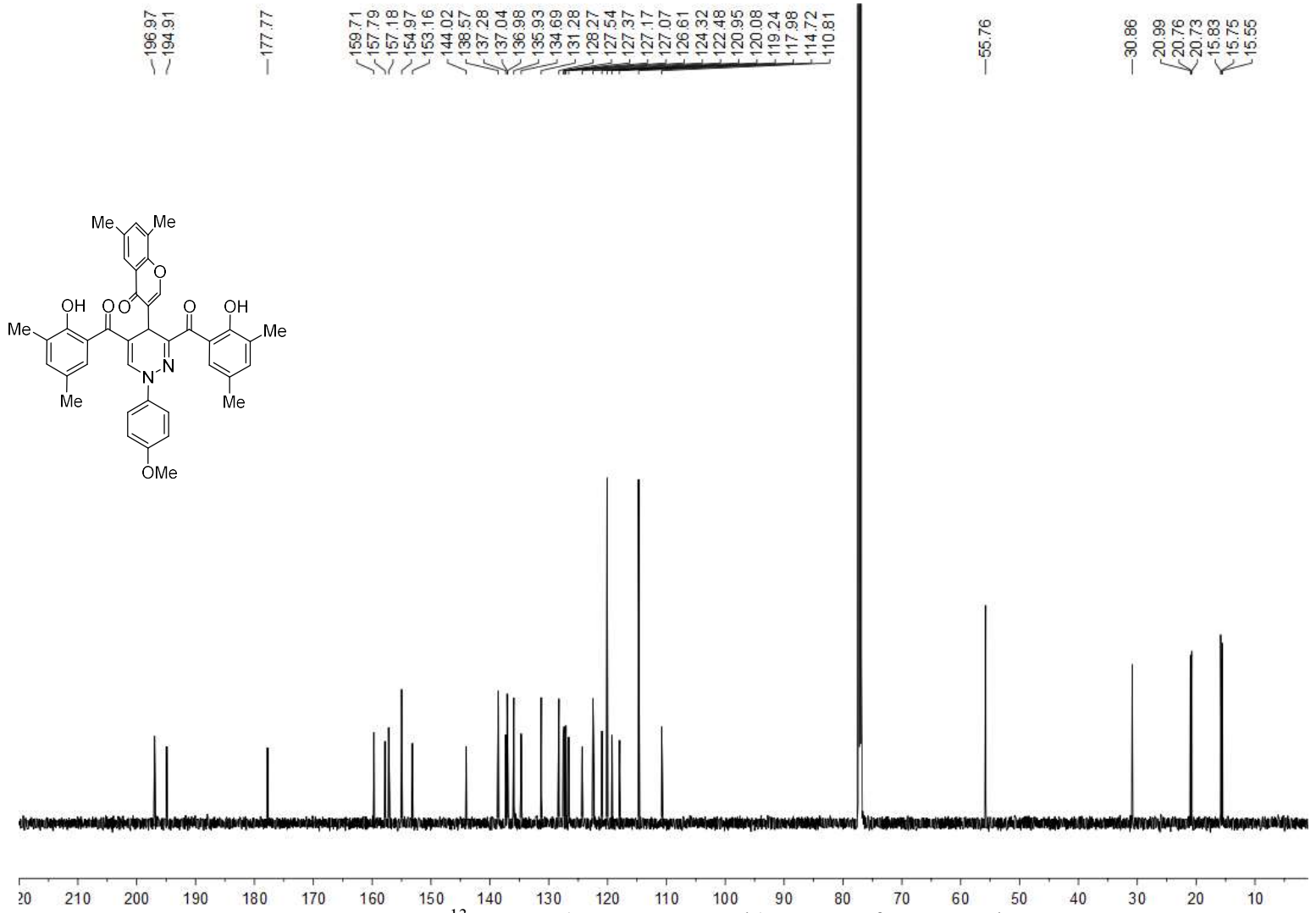


Figure S66. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4h**

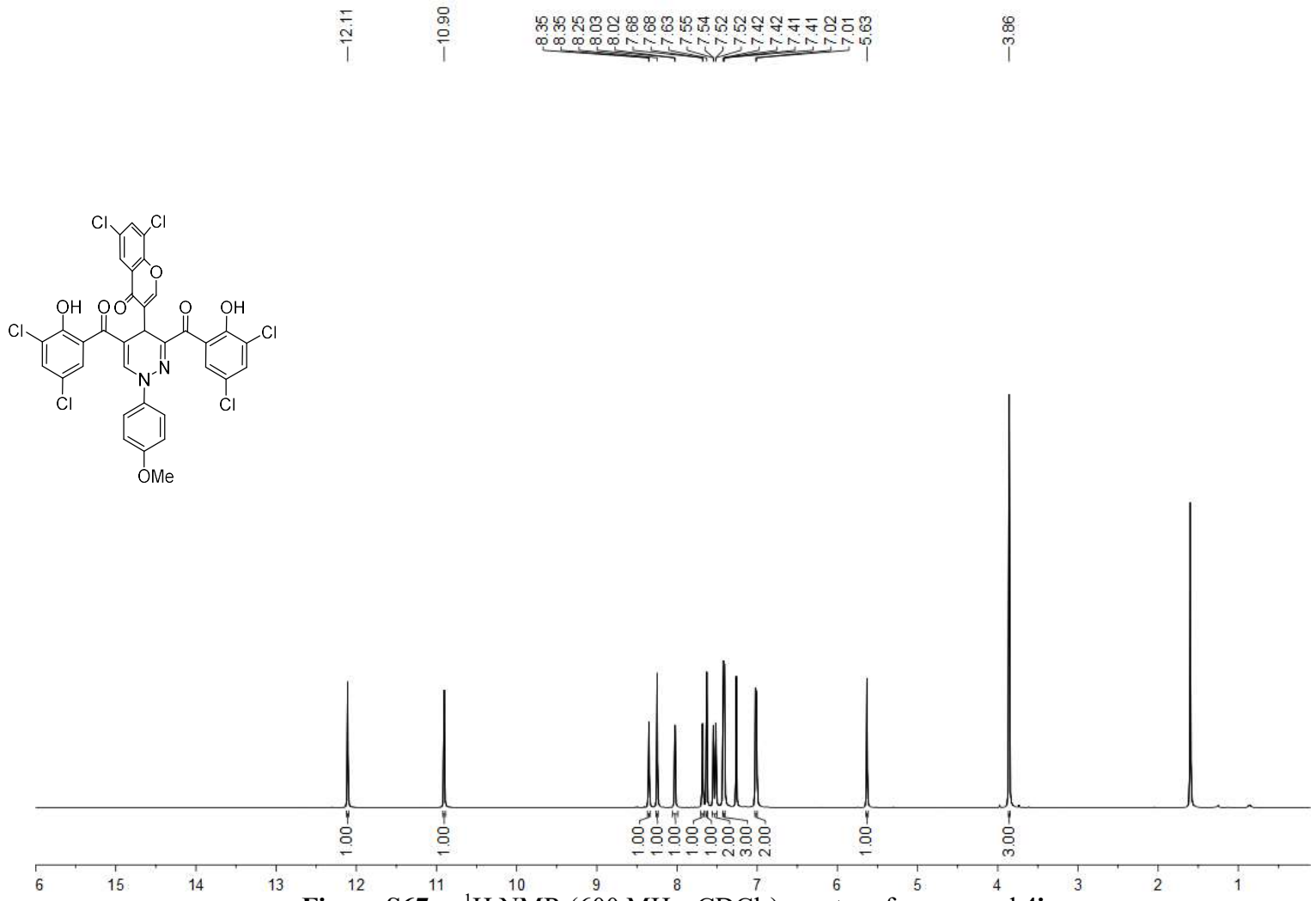


Figure S67. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4i**

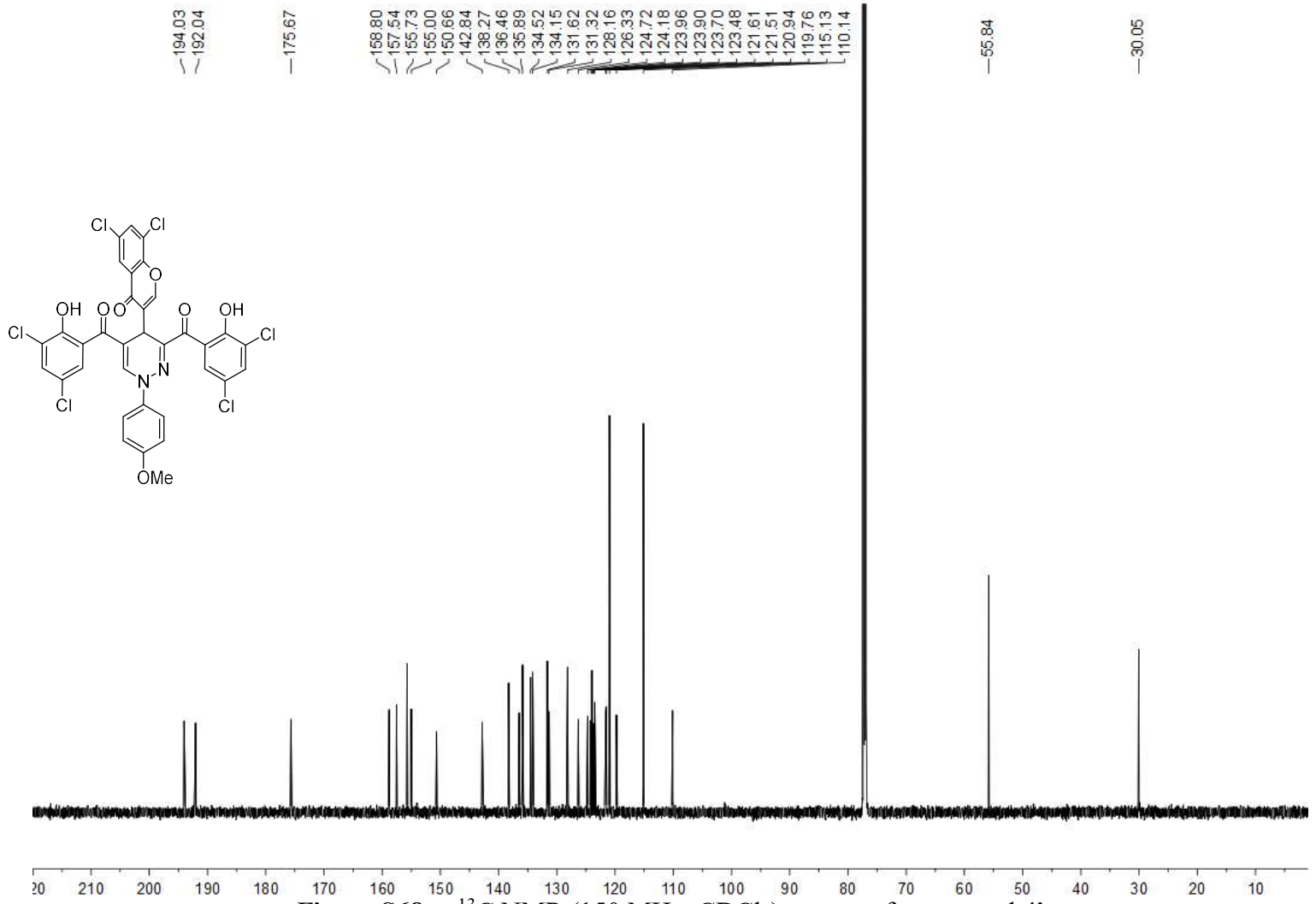


Figure S68. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4i**

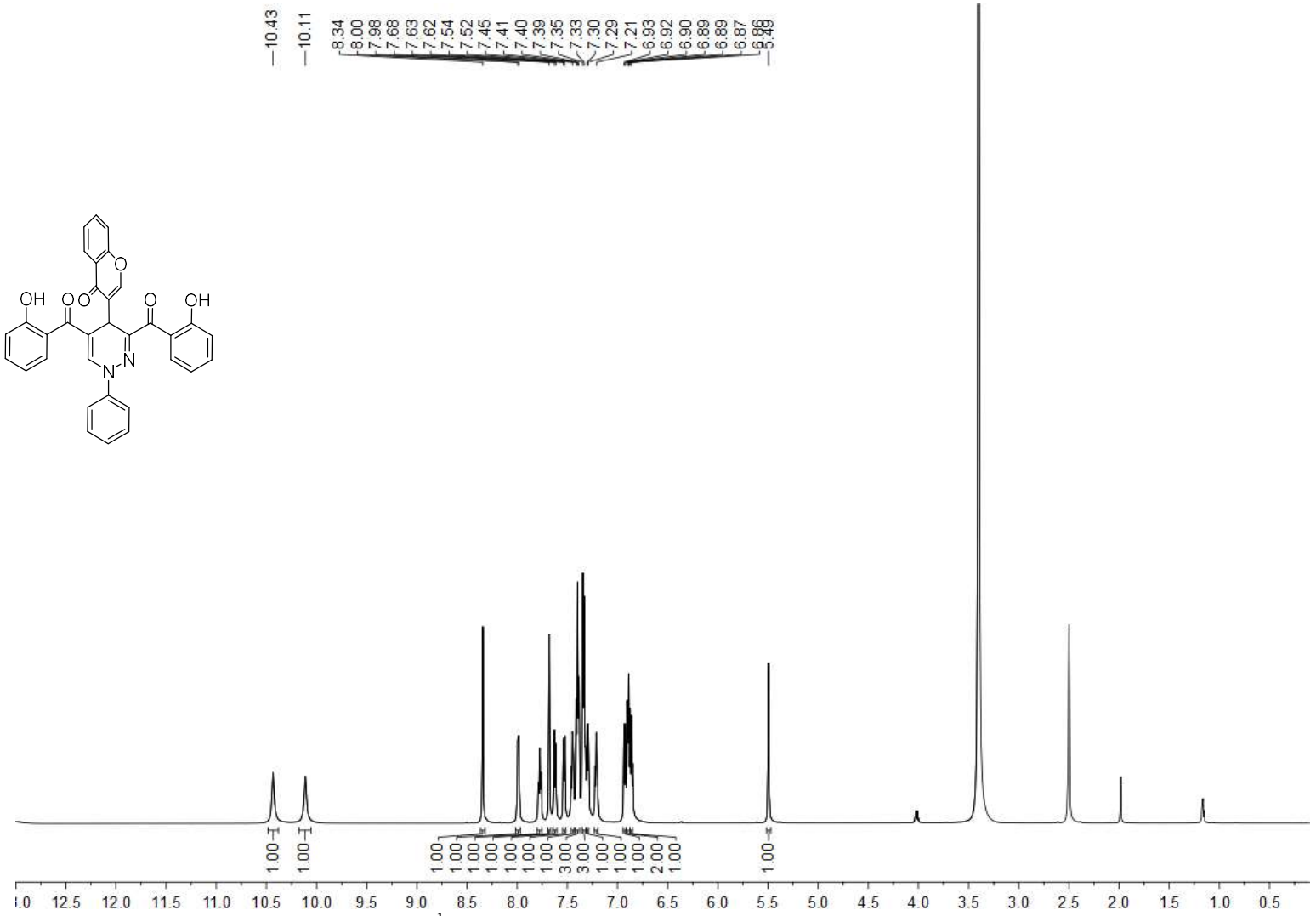


Figure S69. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **4j**

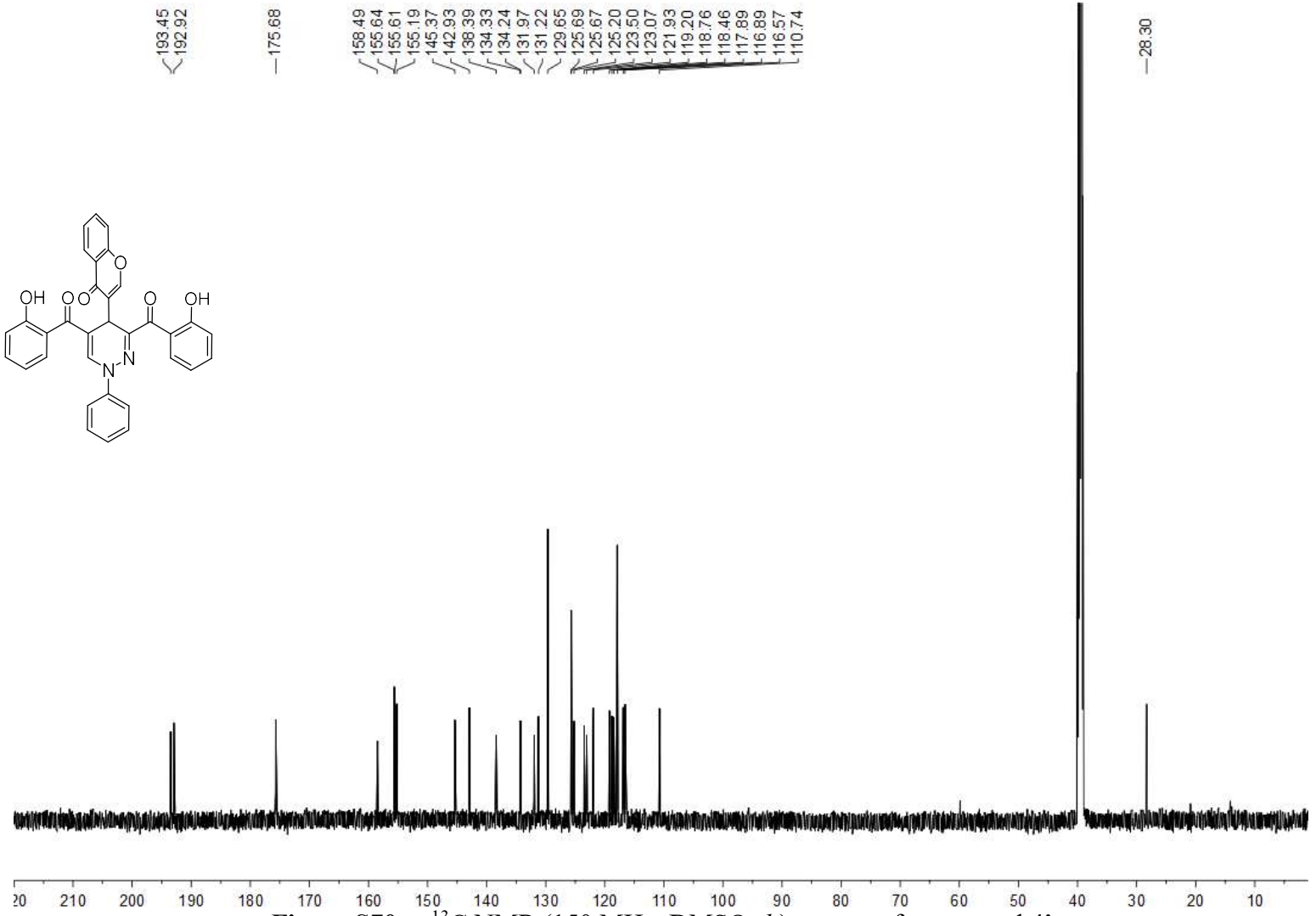


Figure S70. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **4j**

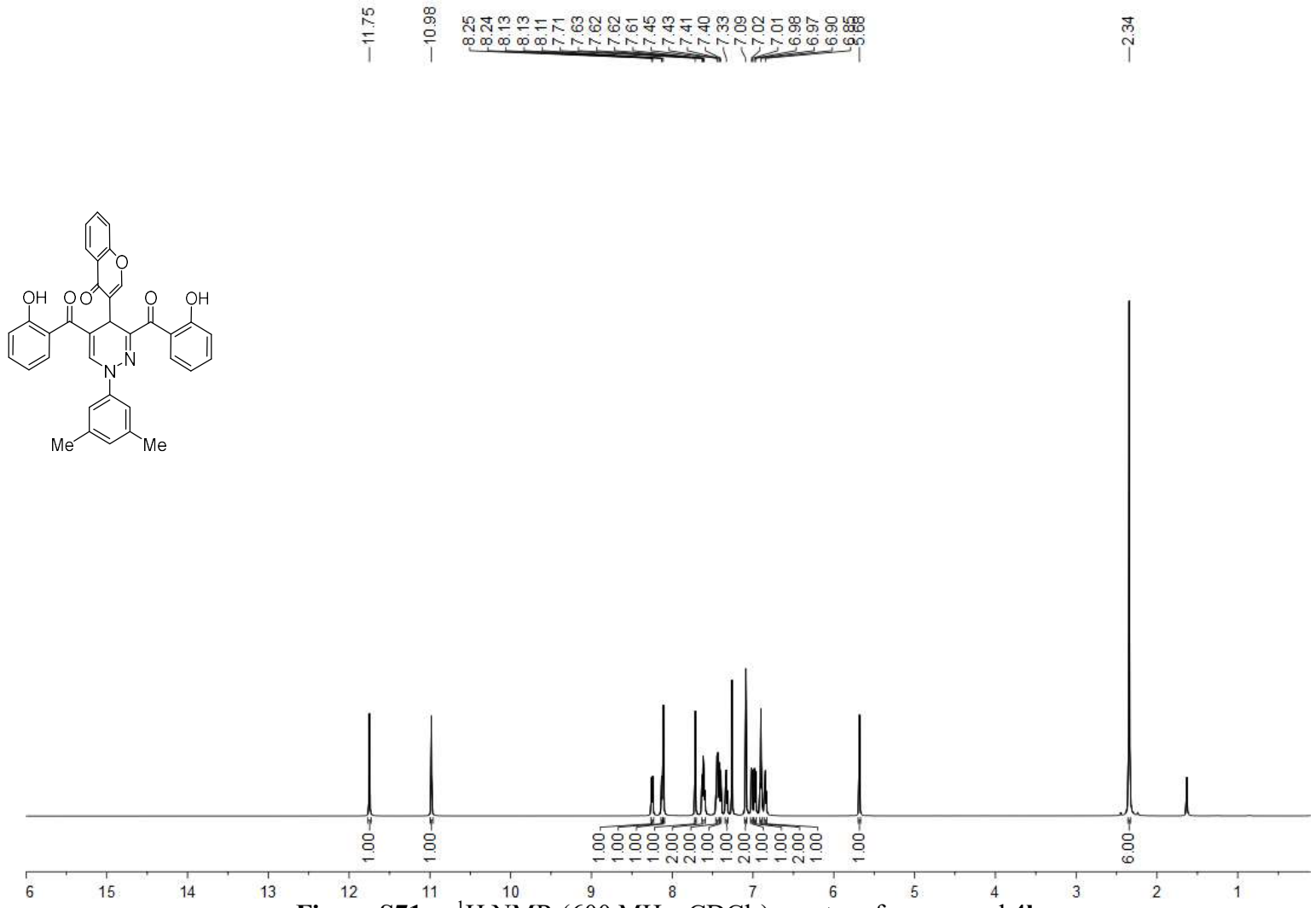


Figure S71. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4k**

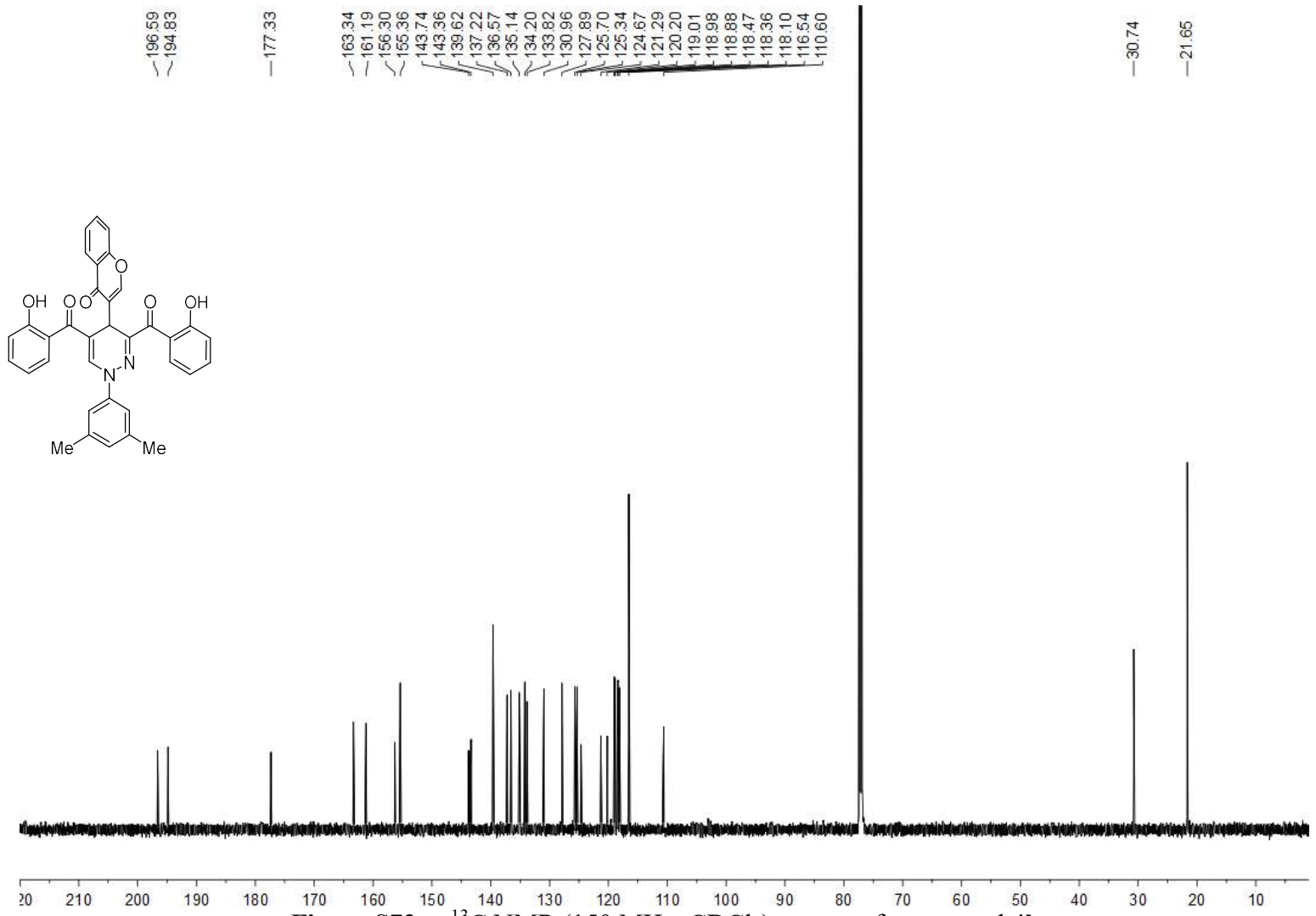


Figure S72. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4k**

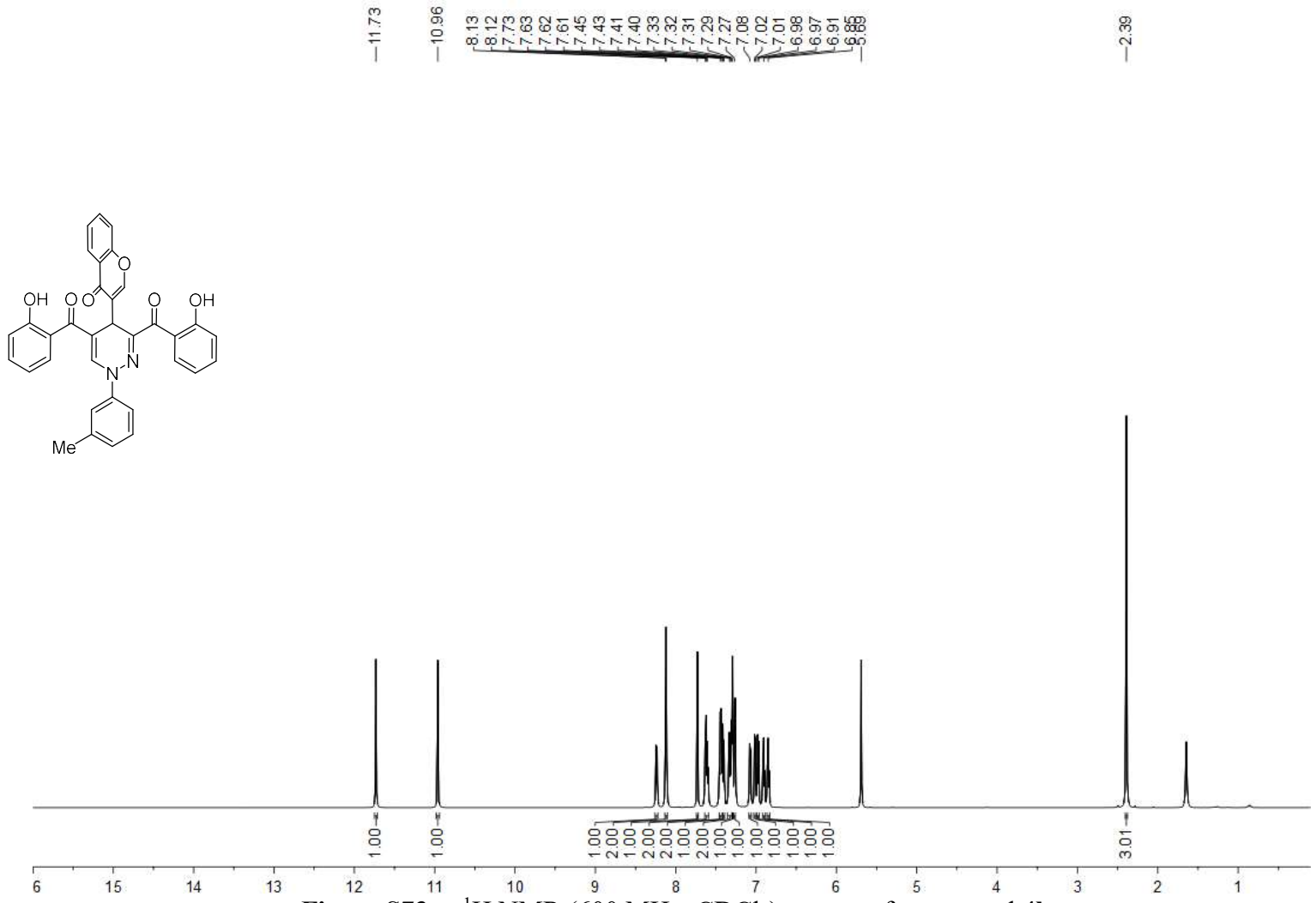


Figure S73. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4l**

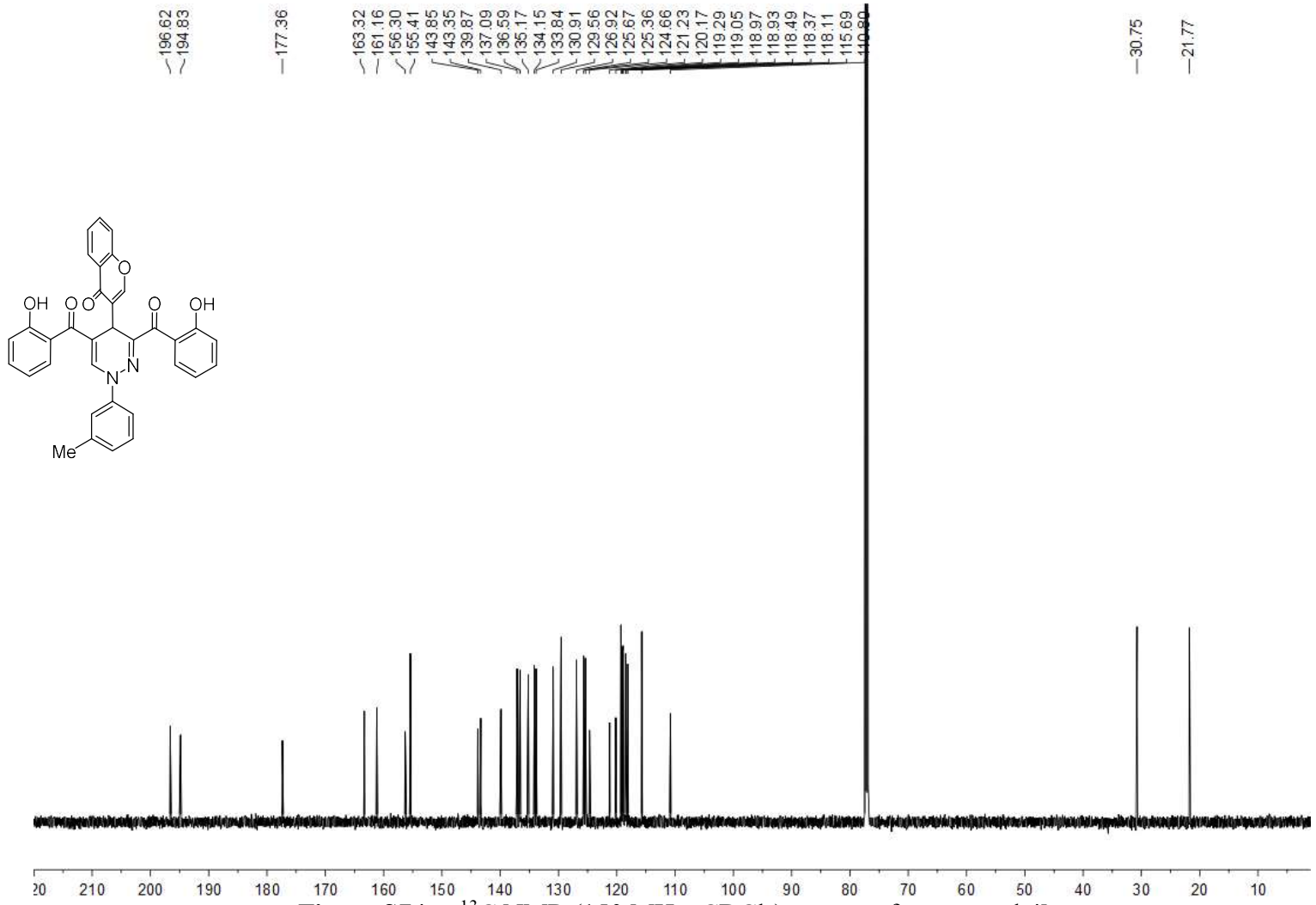


Figure S74. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4l**

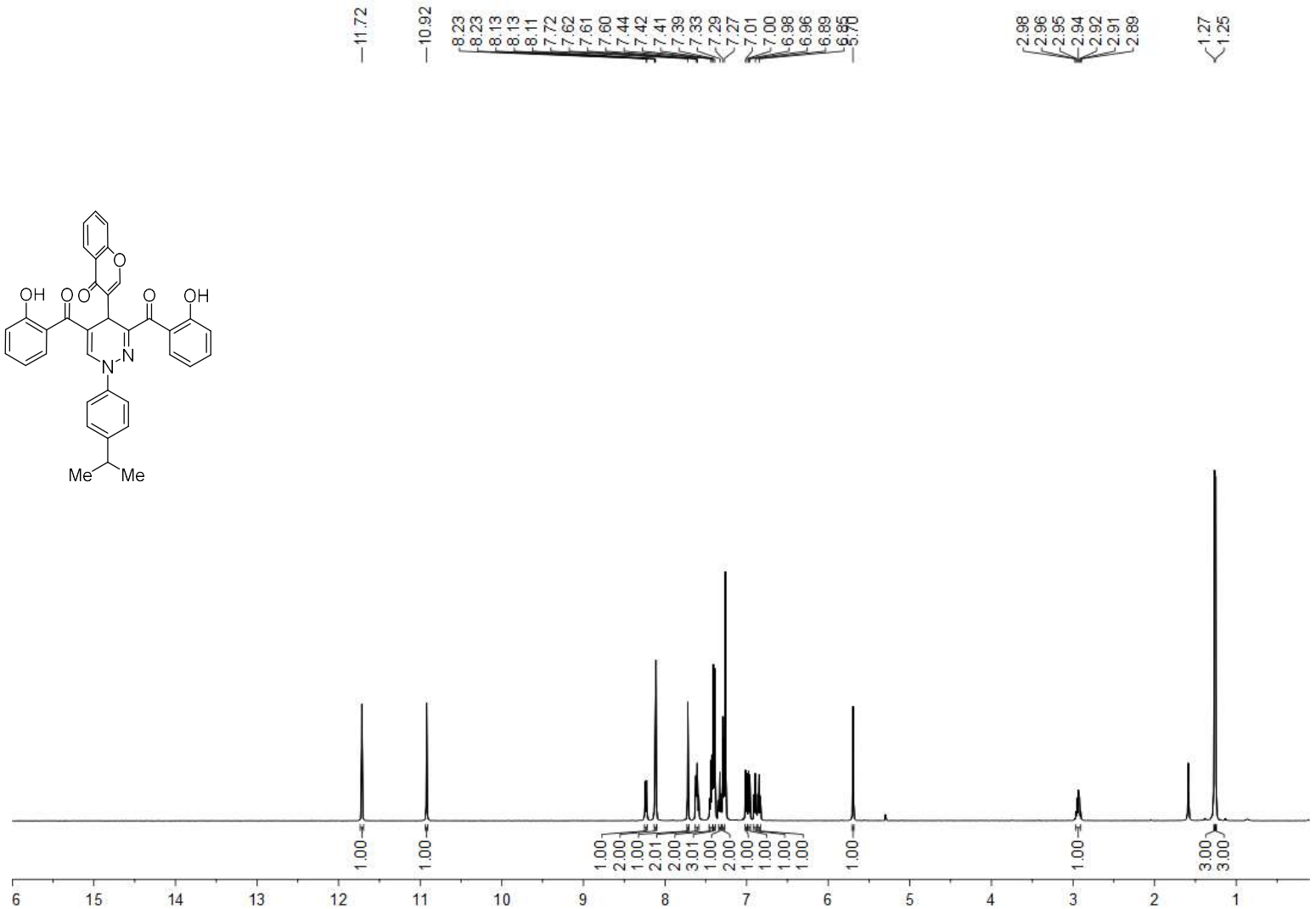


Figure S75. ^{1}H NMR (500MHz, $CDCl_3$) spectra of compound **4m**

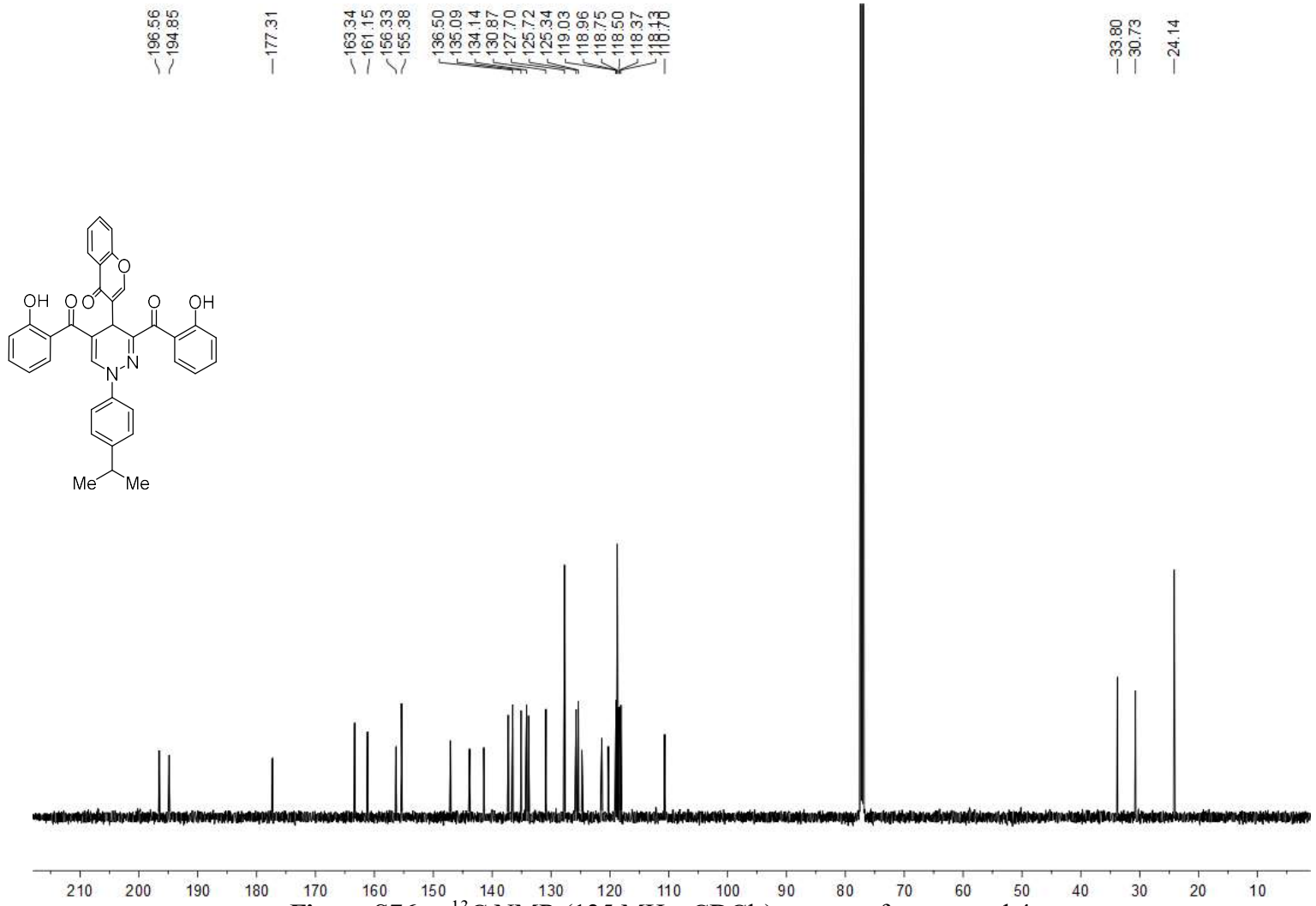


Figure S76. ^{13}C NMR (125 MHz, $CDCl_3$) spectra of compound **4m**

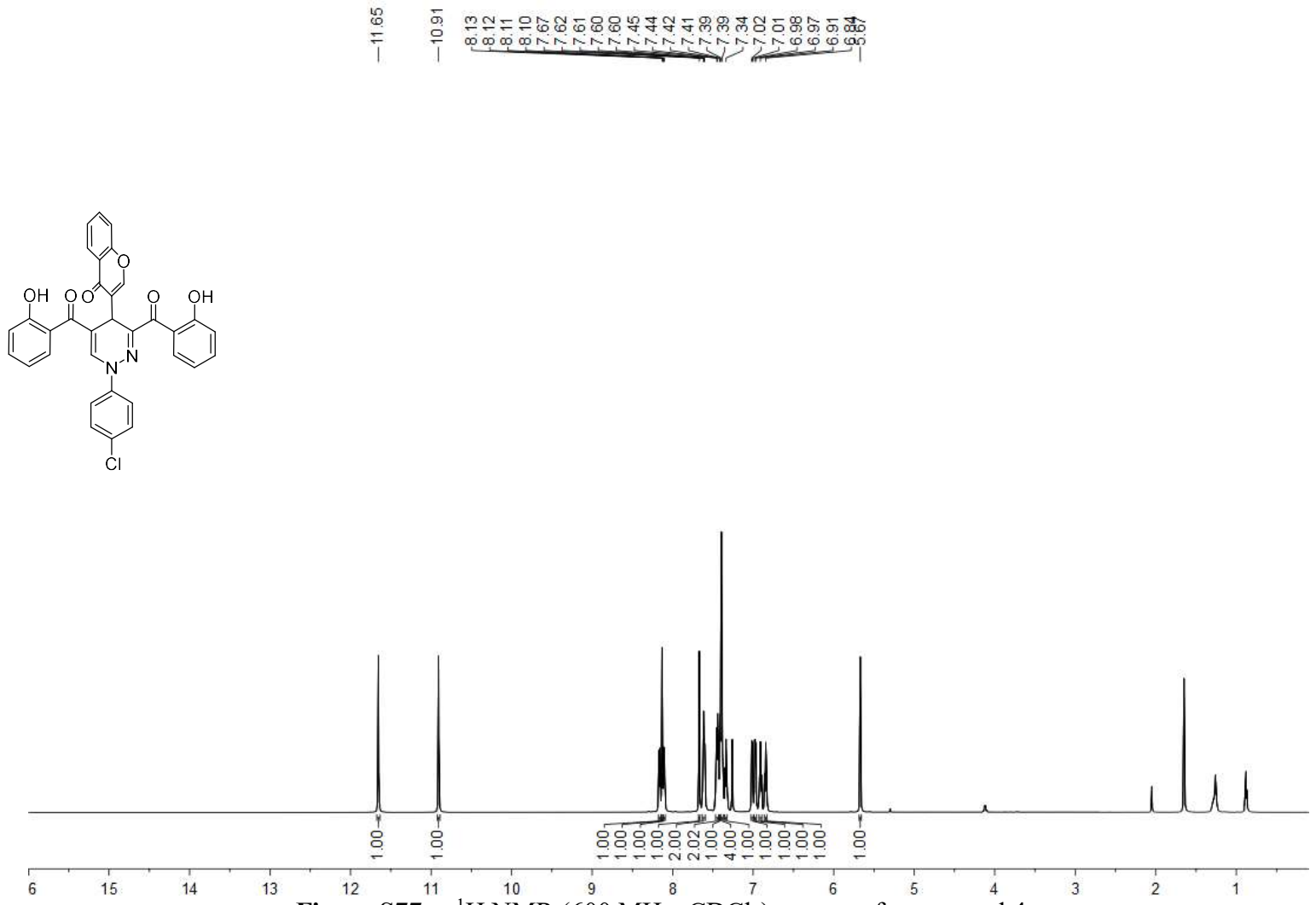


Figure S77. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4n**

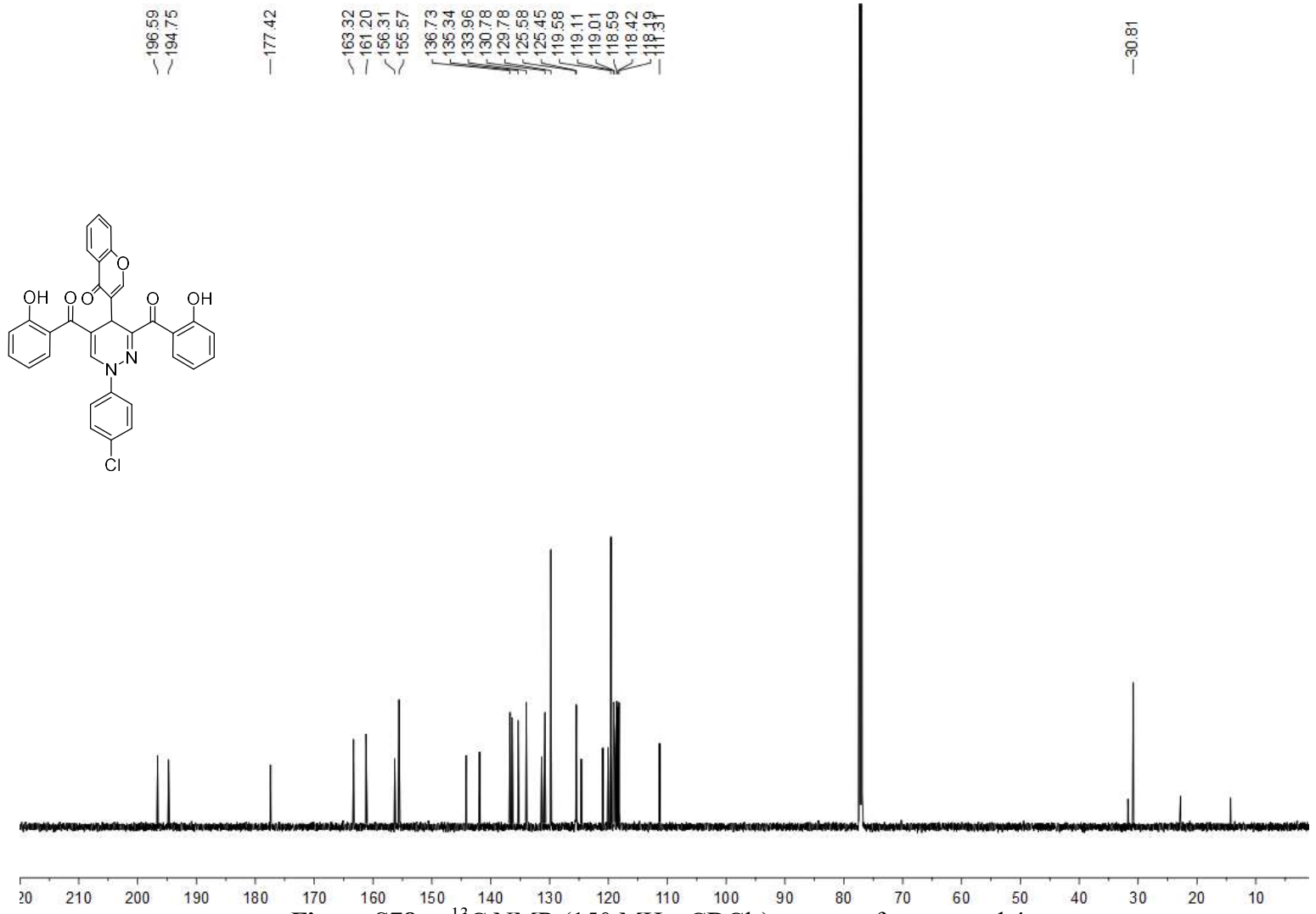


Figure S78. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4n**

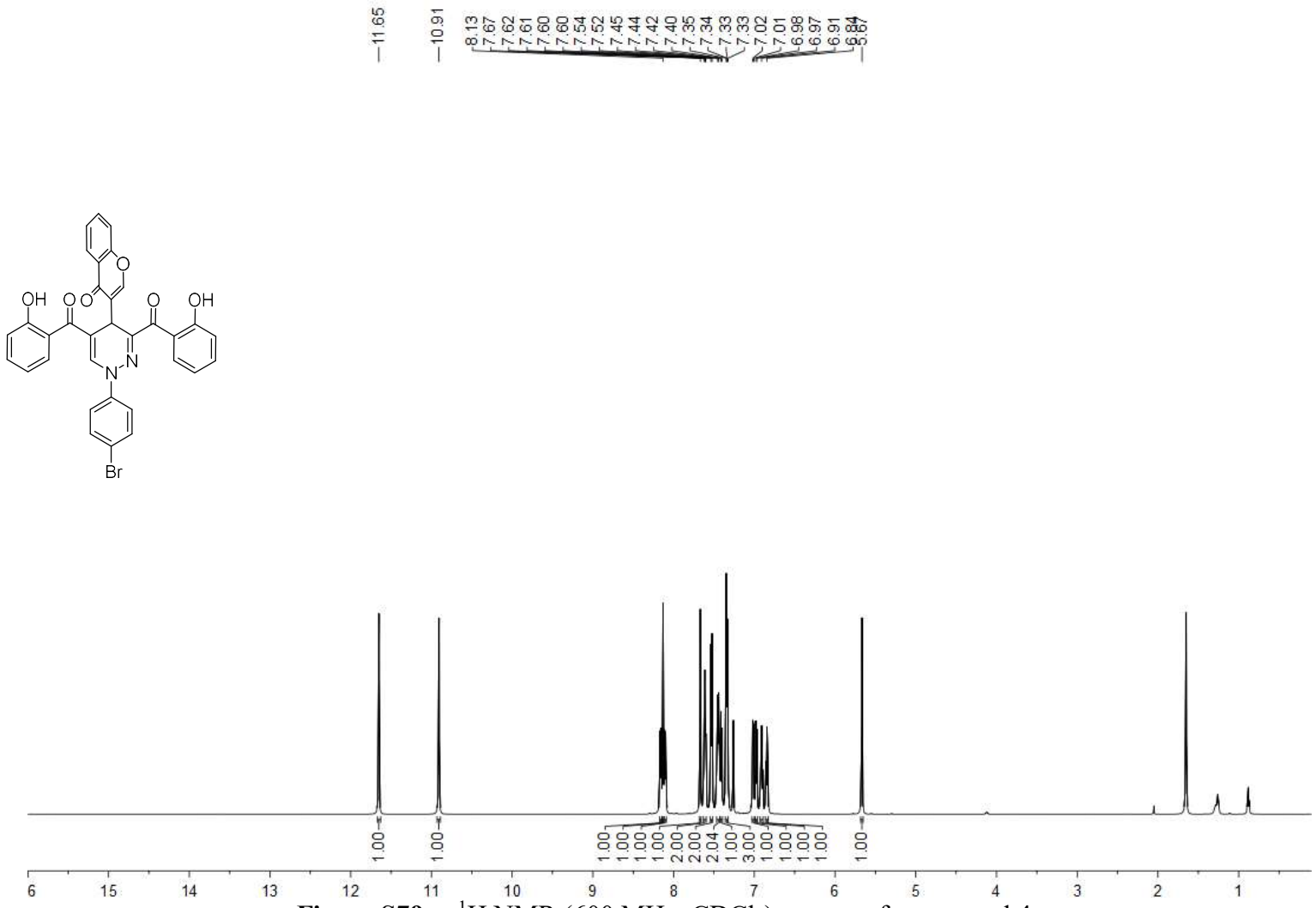


Figure S79. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4o**

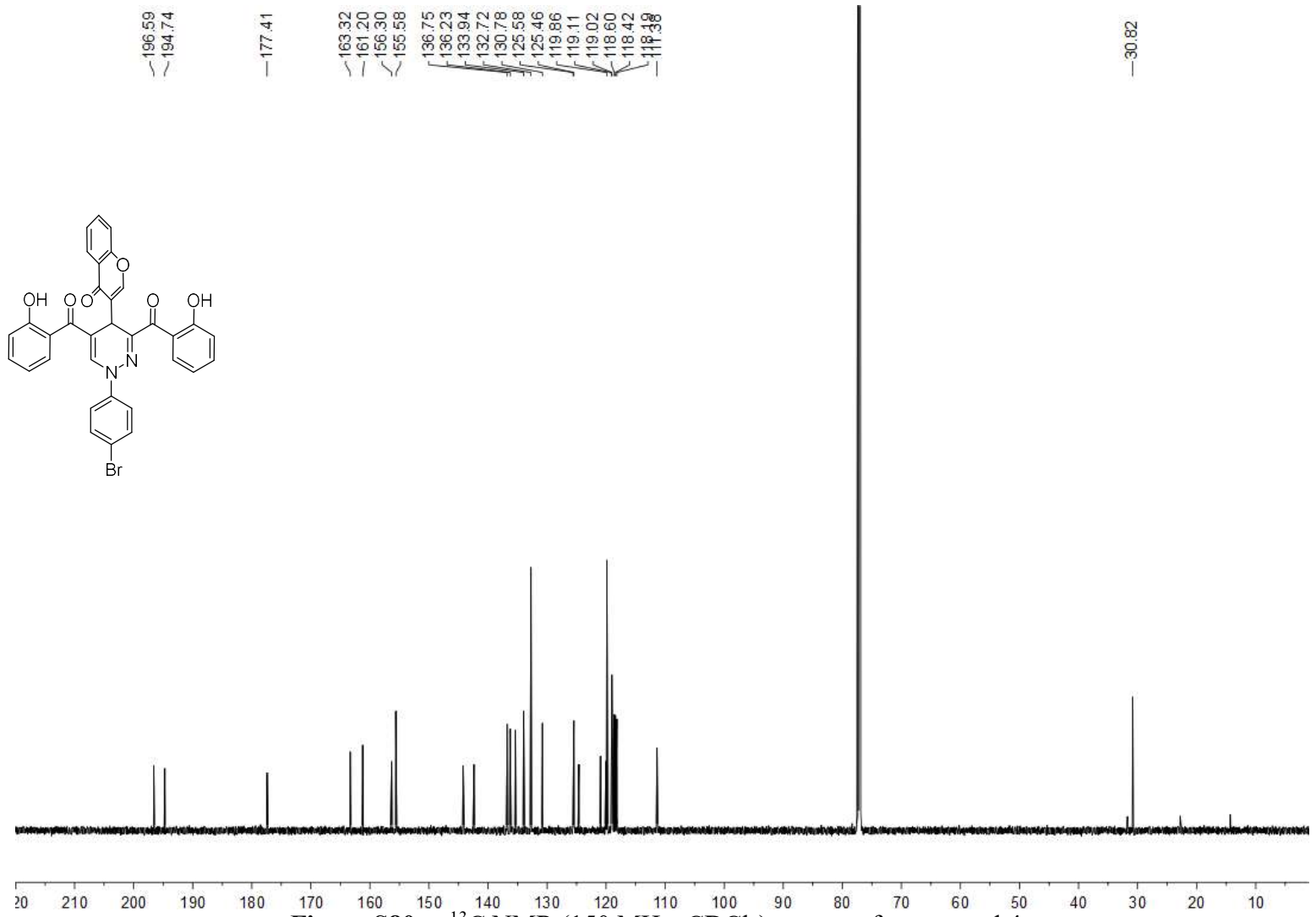


Figure S80. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4o**

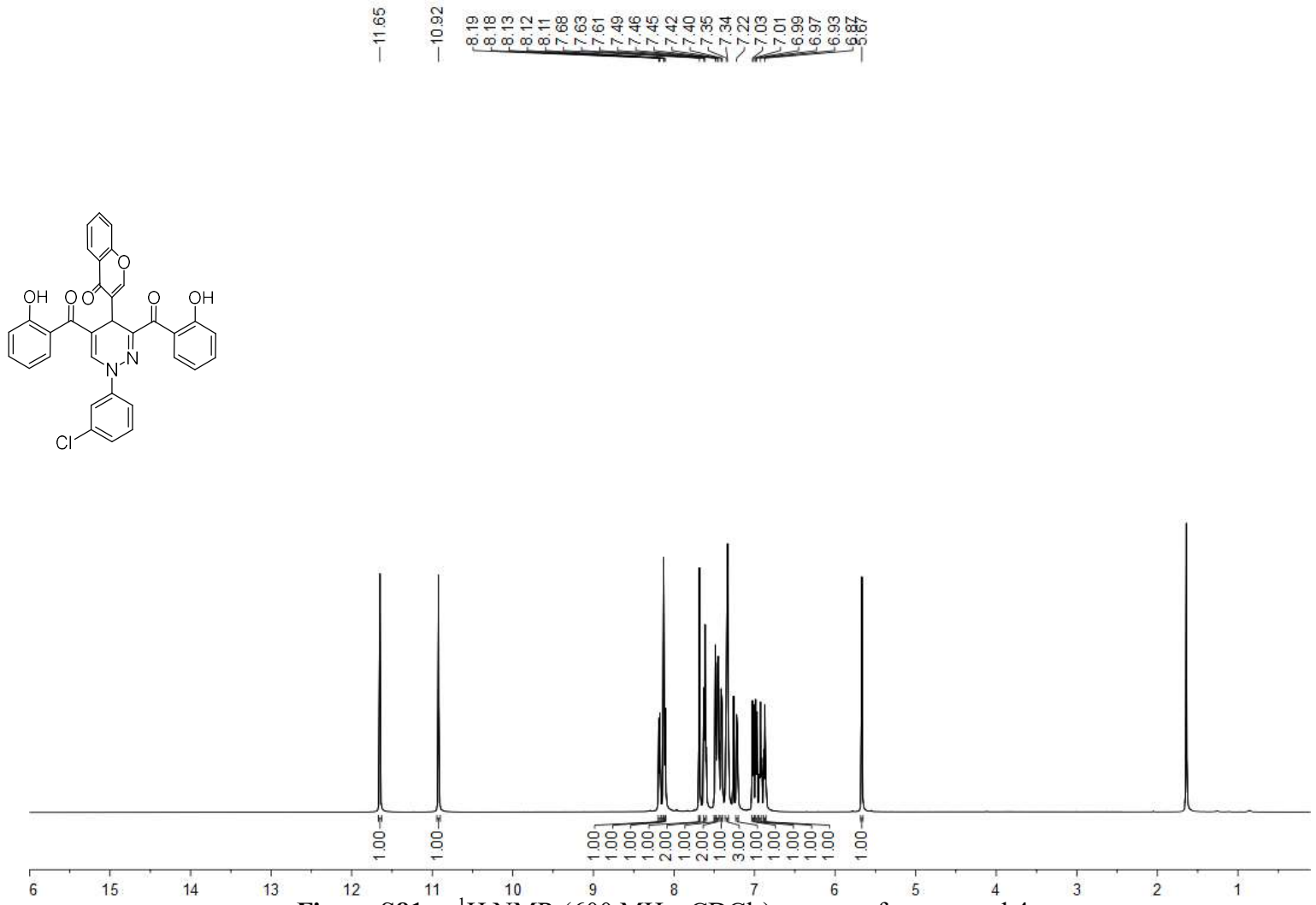


Figure S81. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4p**

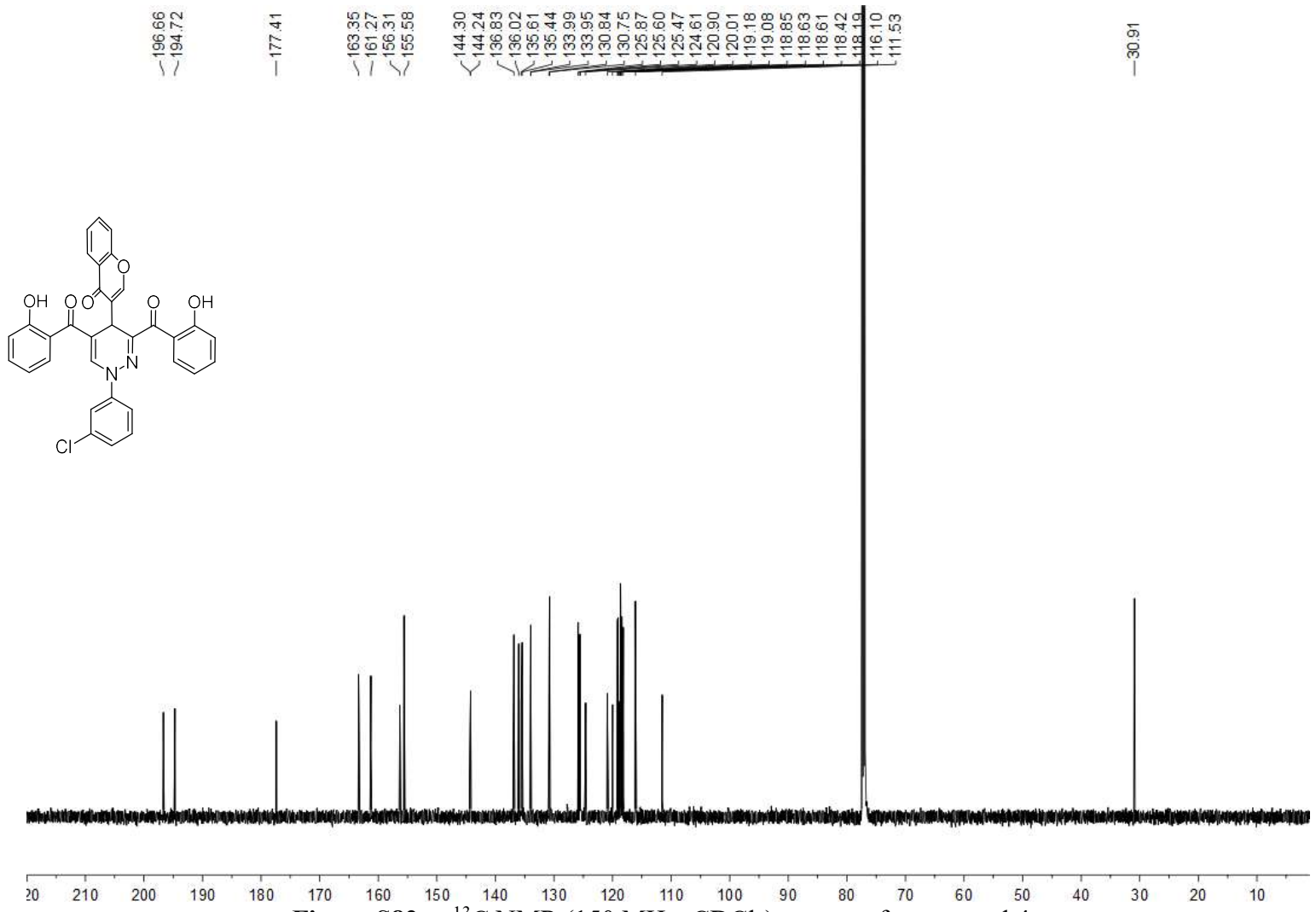


Figure S82. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4p**

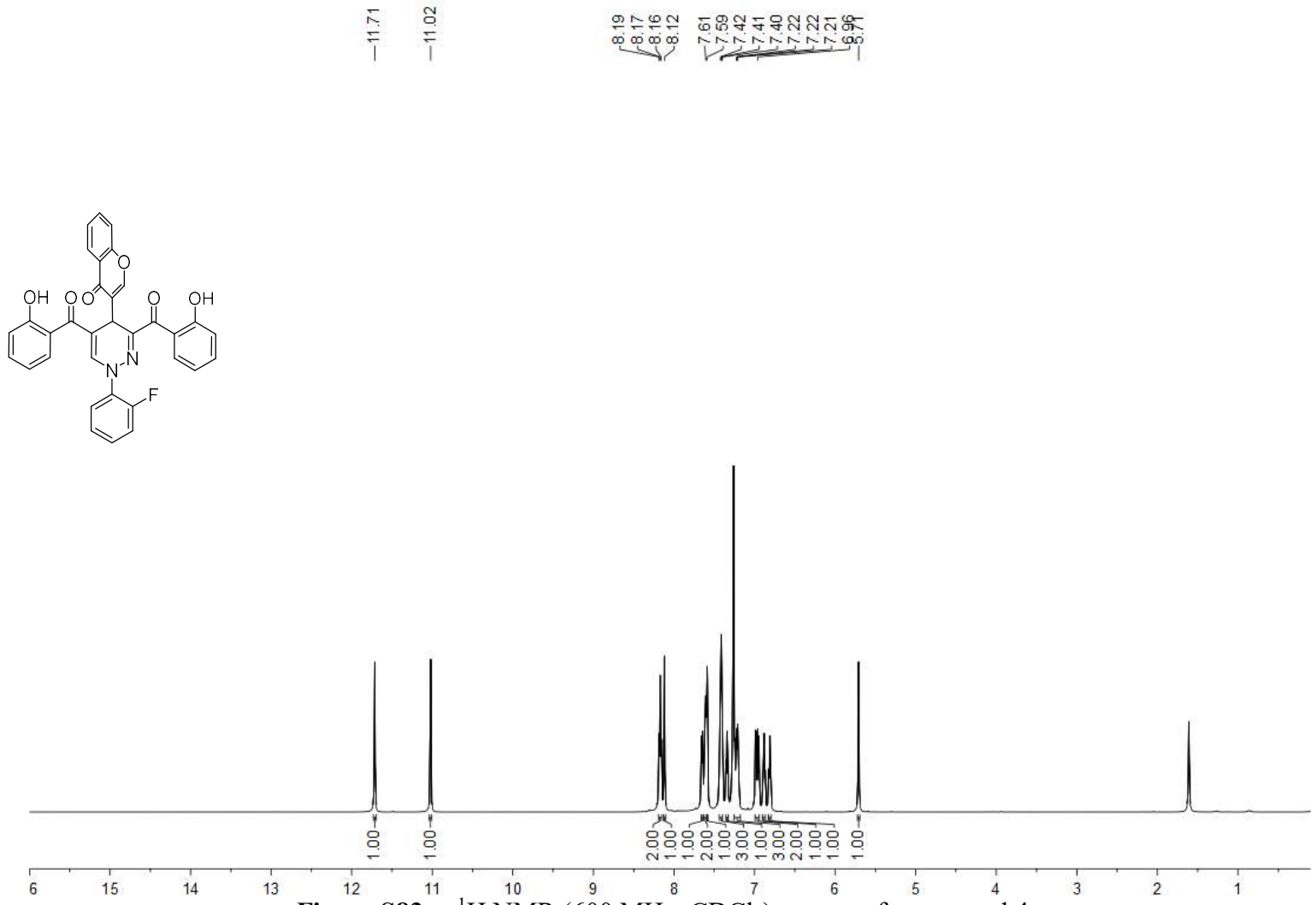


Figure S83. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4q**

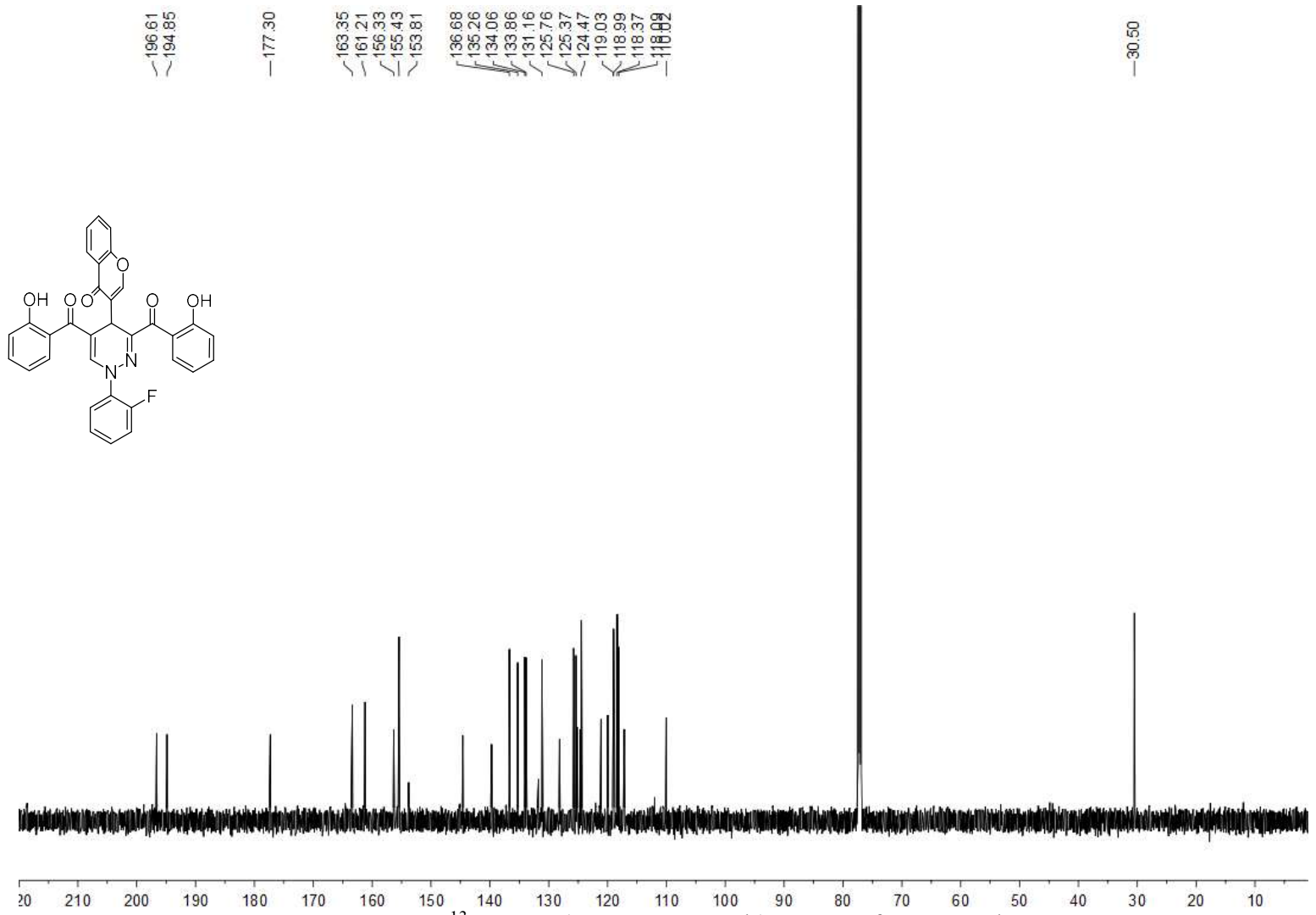


Figure S84. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4q**

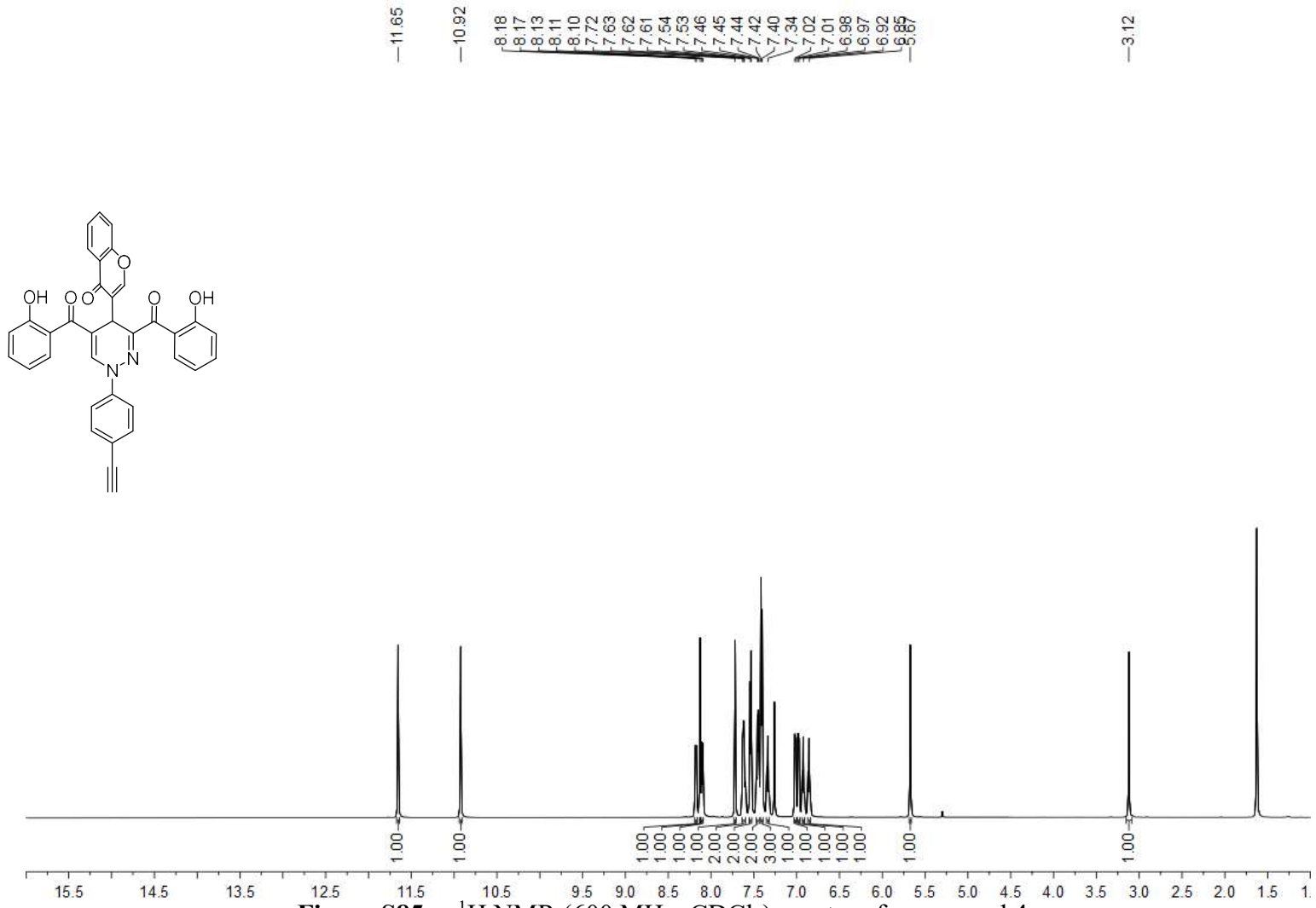


Figure S85. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4r**

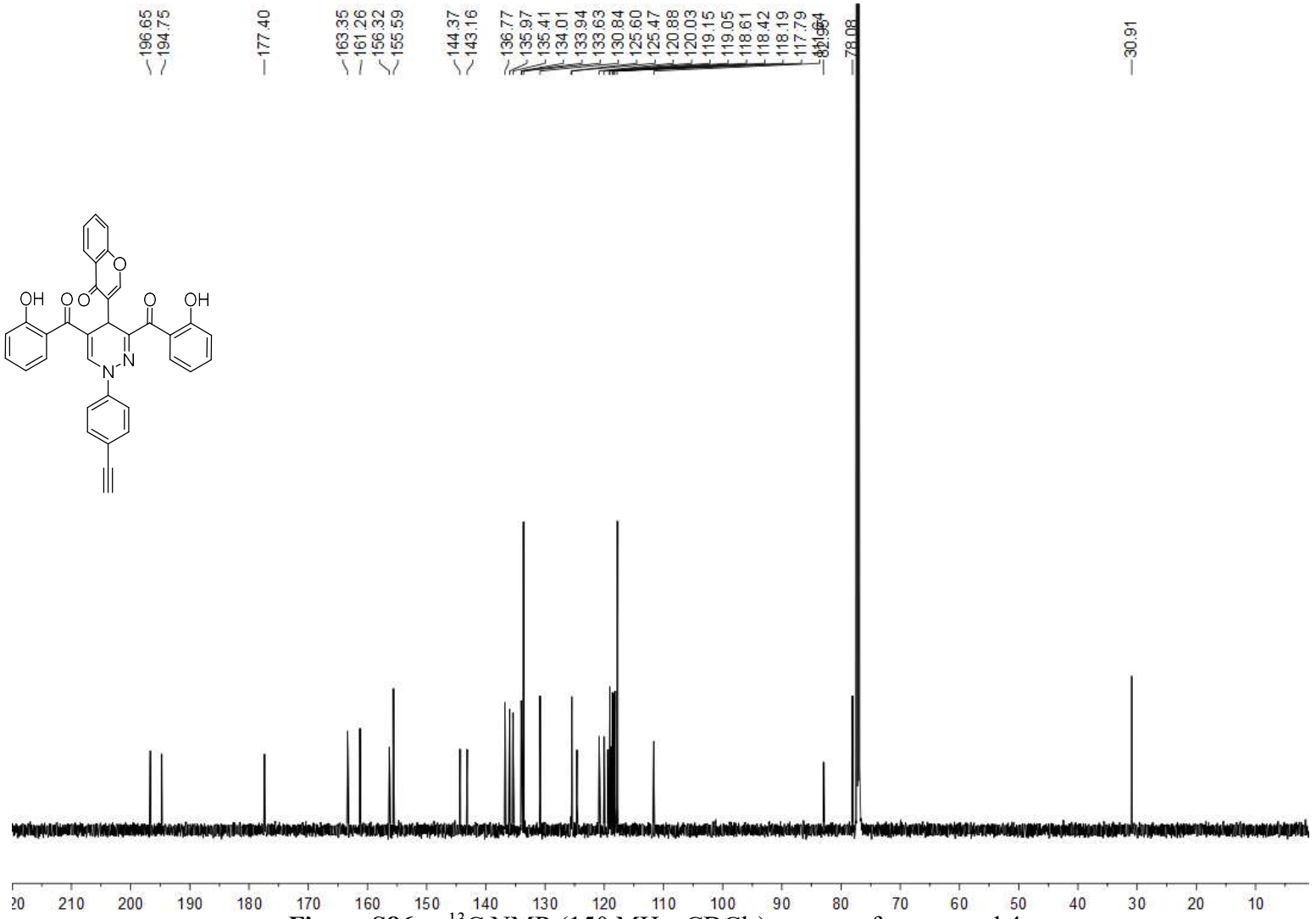


Figure S86. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4r**

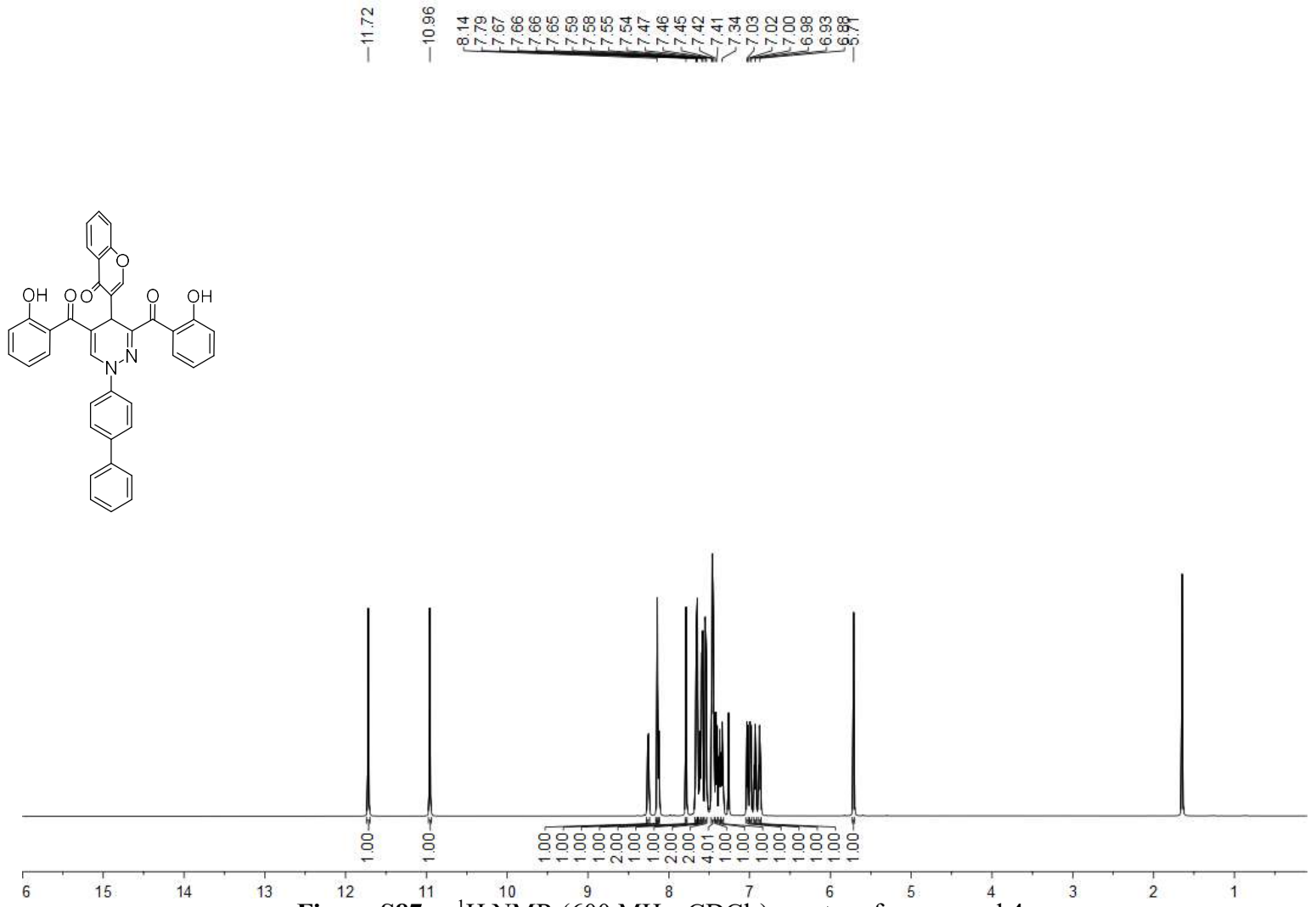


Figure S87. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4s**

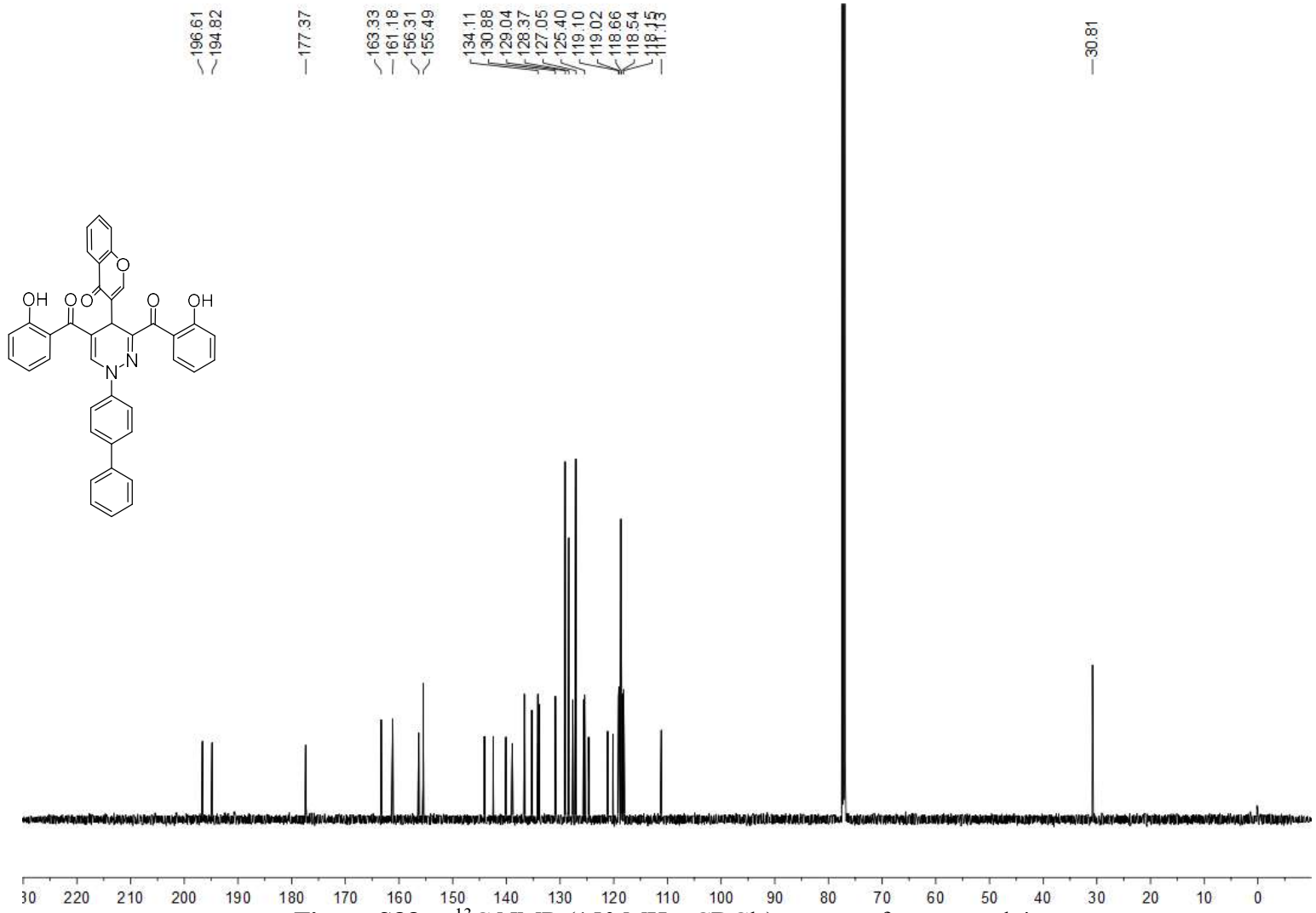


Figure S88. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4s**

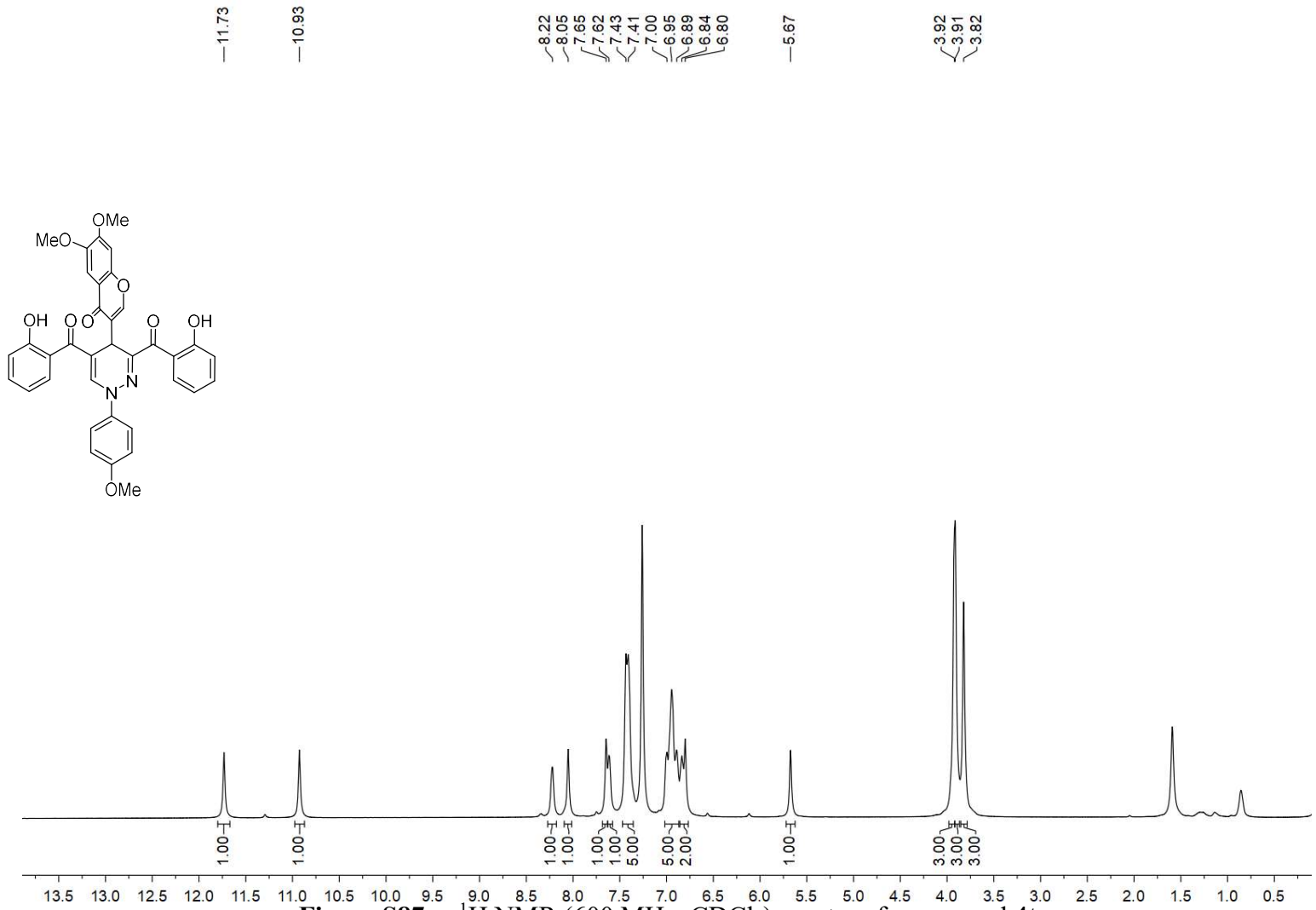


Figure S87. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4t**

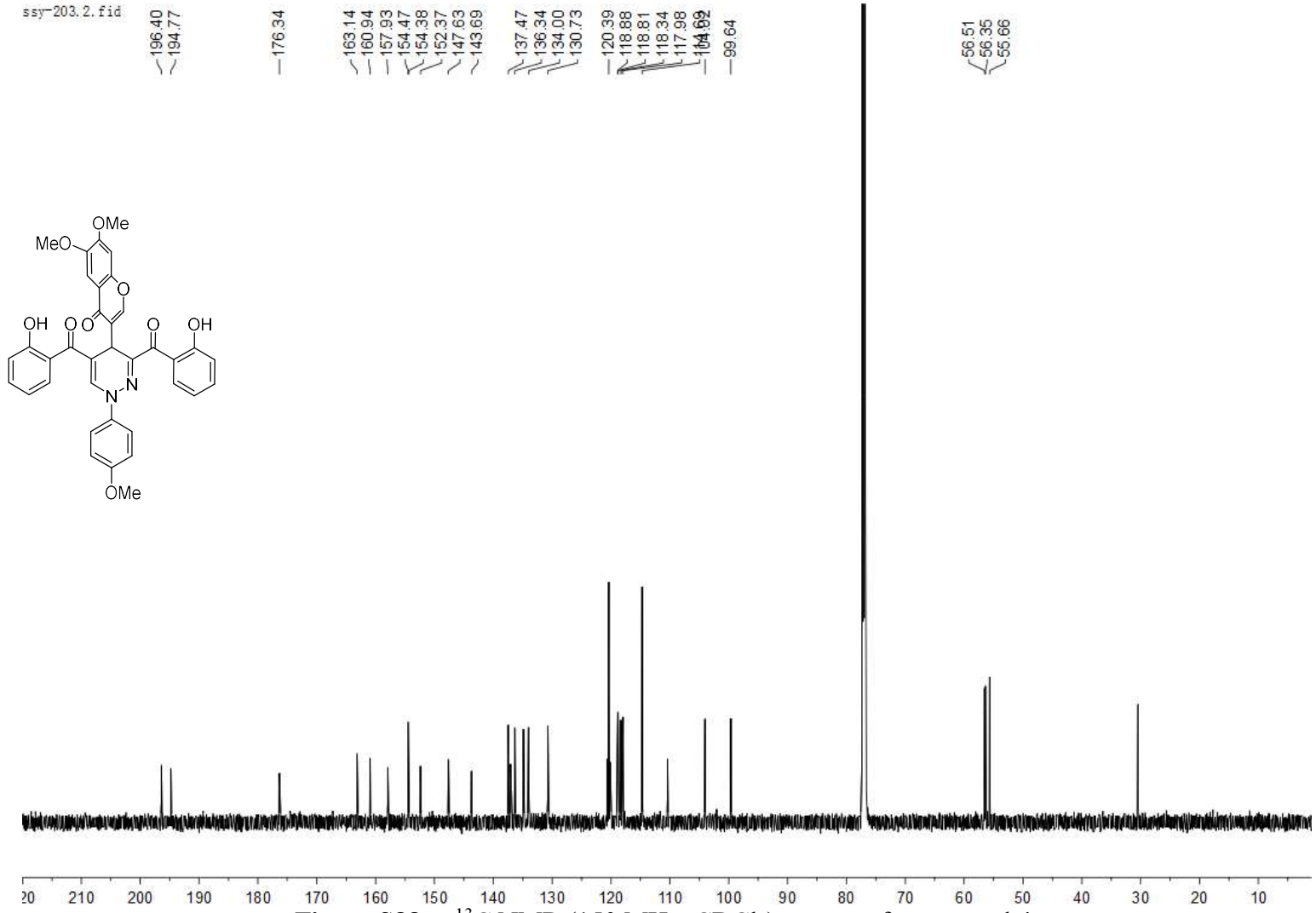


Figure S88. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4t**

7. References and notes.

1. (*a*) Tingoli, M.; Mazzella, M.; Panunzi, B.; Tuzi, A. L-Proline-catalyzed activation of methyl ketones or active methylene compounds and DMF-DMA for syntheses of (2E)-3-dimethylamino-2-propen-1-ones. *Eur. J. Org. Chem.* **2011**, *2011*, 399. (*b*) Das, B.; enkateswarlu, K.; Majhi, V.; Reddy, M. R.; Reddy, K. N.; Yerra Rao, K.; Ravikumar, K.; Sridhar, B. Highly efficient, mild and chemo- and stereoselective synthesis of enaminones and enamino esters using silica supported perchloric acid under solvent-free conditions. *J. Mol. Catal. A: Chem.* **2006**, *246*, 276. (c) Liu, Y.; Zhou, R. Wan, J.-P. Water-promoted synthesis of enaminones. Mechanism investigation and application in multicomponent reactions. *Synth. Commun.* **2013**, *43*, 2475.

2. Wu, J.; Gu, Y.; Leng, X.; Shen, Q. Copper-promoted sandmeyer difluoromethylthiolation of aryl and heteroaryl diazonium salts. *Angew. Chem. Int. Ed.* **2015**, *54*, 7648.

3. Xie, P.; Fang Y.; Shen, Z.; Shao, Y.; Ma, Q.; Yang, Z.; Zhao, J.; Li, H.; Li, R.; Dong, S.; Wen, W.; Xia, X. Broad antiviral and anti-inflammatory activity of Qingwenjiere mixture against SARS-CoV-2 and other human coronavirus infections. *Phytomedicine* **2021**, *93*, 153808.

4. Abraham, M. H.; Abraham, R. J.; Acree Jr, W. E.; Aliev, A. E.; Leo, A. J.; Whaley, W. L. An NMR method for the quantitative assessment of intramolecular hydrogen bonding; application to physicochemical, environmental, and biochemical properties. *J. Org. Chem.* **2014**, *79*, 11075−11083.

5. CCDC 2286041 contain the supplementary crystallographic data for compound **3s**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif.

6. CCDC 2312821 contain the supplementary crystallographic data for compound **4j**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif.