Rh(III)-Catalyzed C(sp^2)-H Functionalization/[4+2] Annulation of Oxadiazolones with Iodonium Ylides to Access Diverse Fused-Isoquinolines and Fused-Pyridines

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1. General information

Unless otherwise noted, all reactions were carried out at room temperature under an atmosphere of nitrogen with flame-dried glassware. If reaction was not conducted at room temperature, reaction temperatures are reported as the temperature of the bath surrounding the vessel unless otherwise stated. The dry solvents used were purified by distillation over the drying agents indicated in parentheses and were transferred under nitrogen: 1,2-dichloroethane (CaH_2), dichloromethane (CaH_2). Anhydrous CF_3CH_2OH, HFIP, DCE, 1,4-dioxane, ethyl alcohol and MeOH were purchased from Acros Organics and stored under nitrogen atmosphere. Commercially available chemicals were obtained from commercial suppliers and used without further purification unless otherwise stated.

Proton NMR (^1H) were recorded at 400 MHz, and Carbon NMR (^{13}C) at 101 MHz NMR spectrometer unless otherwise stated. The following abbreviations are used for the multiplicities: s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet, br s: broad singlet for proton spectra. Coupling constants (*J*) are reported in Hertz (Hz).

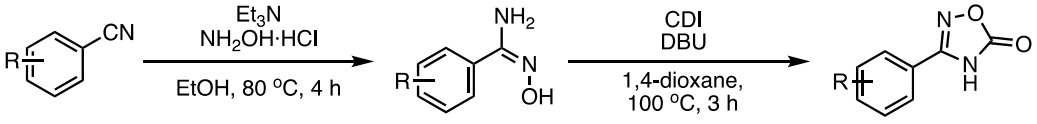
High-resolution mass spectra HRMS-ESI (Quadrupole) were recorded on a BRUKER VPEXII spectrometer with EI and ESI mode unless otherwise stated.

Analytical thin layer chromatography was performed on Polygram SIL G/UV_{254} plates. Visualization was accomplished with short wave UV light, or $KMnO_4$ staining solutions followed by heating. Flash column chromatography was performed using silica gel (200-300 mesh) with solvents distilled prior to use.

No attempts were made to optimize yields for substrate synthesis.

2. Synthesis of substrates

2.1 Synthesis of 3-aryl-1,2,4-oxadiazolones (**1a**-**1u**):

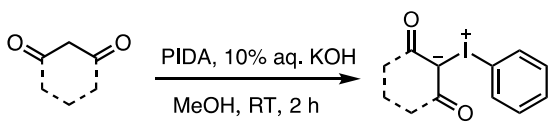


1a-1u

Following a modified literature procedure[1], taking **1a** as an example, to a round bottom flask (100.0 mL) containing benzonitrile (5.15 g, 50.0 mmol) was added hydroxylamine hydrochloride (5.21 g, 75.0 mmol) and Et_3N (7.59 g, 75.0 mmol). Then, ethyl alcohol (50.0 mL) was sequentially added to the system and the reaction mixture was stirred at 80 °C for 4 h. After cooling to ambient temperature, the mixture was concentrated in vacuo. EtOAc was used to extract the product from the aqueous layer. The combined organic layer was washed with water (3 × 50 mL), dried over Na_2SO_4, filtered and concentrated to afford the crude product. This residue was pure enough for the further reaction as white solid.

To a round bottom flask (100.0 mL) containing substituted (*Z*)-*N*′-hydroxybenzimidamide (for example, (Z)-*N*′-hydroxybenzimidamide, 4.08 g, 30.0 mmol) were added CDI (*N*,*N*′-carbonyldiimidazole, 5.84 g, 36.0 mmol) and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene, 5.02 g, 33.0 mmol). Then, 1,4-dioxane (30.0 mL) was sequentially added to the system and the reaction mixture was stirred at 100 °C for 3 h. After cooling to ambient temperature, the mixture was diluted with water, and adjusted to pH ≈ 2 with 3 M HCI and extracted with EtOAc (3× 100 mL). The combined organic layers were washed with water (3× 50 mL), dried over Na_2SO_4, filtered and concentrated to affordthe crude product. The crude product was filtered and the precipitate was washed with cold CH_2CI_2 (3 × 10 mL). This residue was pure enough for the further reaction.

2.2 Synthesis of hypervalent iodonium ylides **2a**-**2f**:

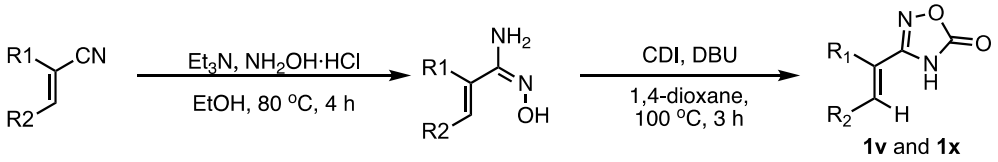


2a-2f

Following a modified literature procedure[2], in a 100 mL oven dried reaction tube with a magnetic stir bar, 5,5-dimethylcyclohexane -1,3-dione (5.0 mmol,1.0 equiv) and MeOH (15 mL)

was subjected and kept the solution at RT. Then, 10.0 mL of 10% aq. KOH solution was added to the reaction mixture at RT. The tube was capped with septa. Further, iodoxybenzene diacetate (6.0 mmol, 1.2 equiv) was dissolved in 20.0 mL MeOH and slowly added to the above reaction mixture via syringe. The resulting mixture was stirred at room temperature for the period of 2 h and evaporated the solvent under reduced pressure, quenched with saturated NaCl (10.0 mL). Then, the mixture was extracted with CH_2Cl_2 and dried over Na_2SO_4. The product was obtained by recrystallization of dichloromethane and petroleum ether. (**2a-2f**, white solid, 68-89%)

2.3 Synthesis of **1v** and **1x**:



1v and **1x**

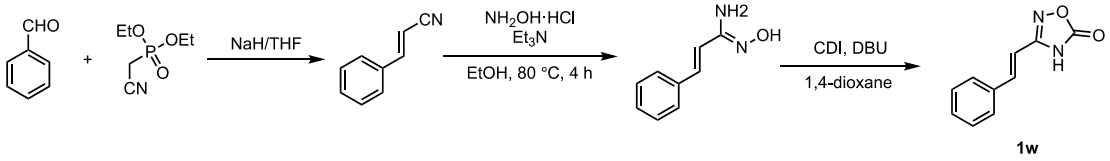
Taking **1v** as an example[3], to a round bottom flask (100 mL) containing methacrylonitrile (1.0 equiv, 20.0 mmol) was added hydroxylamine hydrochloride (1.5 equiv, 30.0 mmol) and Et_3N (1.5 equiv, 30.0 mmol). Then, ethyl alcohol (20.0 mL) was sequentially added to the system and the reaction mixture was stirred at 80 °C for 4 h. After cooling to ambient temperature, the mixture was concentrated in vacuo. EtOAc was used to extract the product from the aqueous layer. The combined organic layer was washed with water (3 × 50 mL), dried over Na_2SO_4, filtered and concentrated to afford the crude product. This residue was pure enough for the further reaction as white solid.

To a round bottom flask (50 mL) containing substituted (*E*)*N'*-hydroxymethacrylimidamide, (1.0 equiv, 10.0 mmol) were added CDI (*N*,*N*'-Carbonyldiimidazole, 1.2 equiv, 12.0 mmol) and DBU (1,8-Diazabicyclo[5.4.0]undec-7-ene, 1.1 equiv, 11.0 mmol). Then, 1,4-dioxane (10.0 mL) was sequentially added to the system and the reactionmixture was stirred at 100 °C for 3 h. After cooling to ambient temperature, the mixture was dilutedwith water, and adjusted to pH ≈ 2 with 3 M HCI and extracted with EtOAc. The combined organiclayer was washed with water (3× 50.0 mL), dried over Na_2SO_4, filtered and concentrated to affordthe crude product. The crude product was filtered and the precipitate was washed with cold CH_2Cl_2 (3 × 10.0 mL). This residue was pure enough for the further reaction.

3-(prop-1-en-2-yl)-1,2,4-oxadiazol-5(4*H*)-one (**1v**), 73%, white solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71 (s, 1H), 5.58 (s, 1H), 2.06 (s, 3H). HRMS (ESI) *m/z* calcd. for $C_5H_6N_2O_2Na$ $[M+Na]^+$ 149.0327; Found 149.0323.

(*E*)-3-(but-2-en-2-yl)-1,2,4-oxadiazol-5(4*H*)-one (**1x**), 35%, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.10 (q, *J* = 7.2 Hz, 1H), 2.03 (s, 3H), 1.98 (d, *J* = 7.5 Hz, 3H). HRMS (ESI) *m/z* calcd. for $C_6H_8N_2O_2Na$ $[M+Na]^+$ 163.0484; Found 163.0482.

2.4 Synthesis of (*E*)-3-styryl-1,2,4-oxadiazol-5(4*H*)-one (**1w**):



1w

Following a modified literature procedure[3], NaH (1.8 g, 45 mmol, 1.50 equiv) was placed in an over-dried 250 mL two-neck round bottom flask. THF (50.0 mL) was added under nitrogen. The reaction mixture was cooled and diethyl cyanomethylphosphonate(6.37 g, 36.0 mmol, 1.20 equiv) was added dropwise with stirring at 0 °C. The solution was stirred at room temperature for 1.0 h until gas evolution had ceased. And then, the benzaldehyde (30 mmol, 1.00 equiv) were added to the solution dropwise. The solution was stirred at room temperature until no starting material was detected by TLC. The reaction mixture was quenched with water and extracted with ethyl acetate.

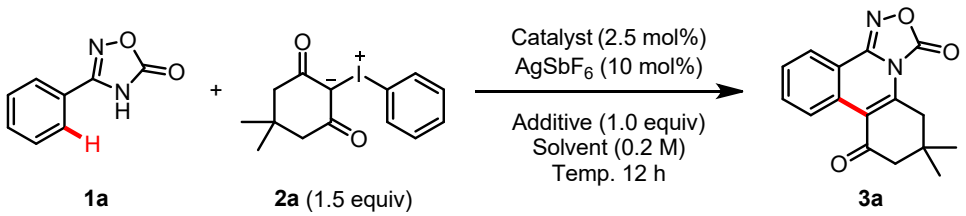
To a round bottom flask (100 mL) containing substituted cinnamonitrile (1.0 eq, 30 mmol) were added hydroxylamine hydrochloride (3.13 g, 45.0 mmol, 1.5 equiv) and Et_3N (4.55 g, 45 mmol, 1.5 equiv). Then, ethyl alcohol (50.0 mL) was sequentially added to the system and the reaction mixture was stirred at 80 °C for 4 h. After cooling to ambient temperature, the mixture was concentrated in vacuo. EtOAc was used to extract the product from the aqueous layer. The combined organic layer was washed with water (3 × 50 mL), dried over Na_2SO_4, filtered and concentrated to afford the crude product. This residue was pure enough for the further reaction.

To a round bottom flask (100 mL) containing substituted (*Z*)-*N*'-hydroxycinnamimidamide (30.0 mmol, 1.0 equiv) were added CDI (*N*, *N*'-carbonyldiimidazole, 5.83 g, 36.0 mmol, 1.2 equiv) and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene, 5.02 g, 33.0 mmol, 1.1 equiv). Then, 1,4-dioxane (30.0 mL) was sequentially added to the system and the reaction mixture was stirred at 100 °C for

3 h. After cooling to ambient temperature, the mixture was diluted with water, and adjusted to pH≈ 2 with 3 M HCl and extracted with EtOAc. The combined organic layer was washed with water (3×50 mL), dried over Na_2SO_4, filtered and concentrated to afford the crude product. The crude product was filtered and the precipitate was washed with cold CH_2Cl_2 (3 × 5 mL). This residue was pure enough for the further reaction. 76%, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.51 (m, 2H), 7.41 (dd, *J* = 5.0, 2.0 Hz, 3H), 7.28 (d, *J* = 16.7 Hz, 1H), 6.72 (d, *J* = 16.7 Hz, 1H). HRMS (ESI) *m/z* calcd. for $C_{10}H_8N_2O_2Na$ $[M+Na]^+$ 211.0484 ; Found 211.0479.

3. Optimization of Reaction Conditions

Table S1. Optimization of the Reaction Conditions[a]



1a **2a** (1.5 equiv) **3a**

Entry	Catalyst	Additives	Solvent	Temp (°C)	Yields[b]
1	$[Cp^*RhCl_2]_2$	-	DCE	60	46
2	$[Cp^*IrCl_2]_2$	-	DCE	60	ND[c]
3[d]	$[Ru(p\text{-}cym)Cl_2]_2$	-	DCE	60	ND
4	$[Cp^*RhCl_2]_2$	-	DCM	60	29
5	$[Cp^*RhCl_2]_2$	-	HFIP	60	34
6	$[Cp^*RhCl_2]_2$	-	CF_3CH_2OH	60	43
7	$[Cp^*RhCl_2]_2$	Cs_2CO_3	DCE	60	ND
8	$[Cp^*RhCl_2]_2$	PivOH	DCE	60	41
9	$[Cp^*RhCl_2]_2$	$B(OH)_3$	DCE	60	51
10	$[Cp^*RhCl_2]_2$	HOAc	DCE	60	57
11	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	60	75
12	$[Cp^*RhCl_2]_2$	AdCOOH	H_2O	60	ND
13	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	50	53
14	**$[Cp^*RhCl_2]_2$**	**AdCOOH**	**DCE**	**80**	**82**
15	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	100	68
16[e]	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	80	67
17[f]	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	80	76
18[g]	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	80	57
19[h]	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	80	9
20[i]	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	80	0
21[j]	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	80	32

22[k]	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	80	83
23[l]	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	80	64
24[d]	$[Cp^*RhCl_2]_2$	AdCOOH	DCE	80	34
25	-	AdCOOH	DCE	80	0

[a]Reaction Conditons: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst (2.5 mol%), additives (1.0 equiv), solvent (0.2 M), Temp., 60 °C, 12 h.

[b]Isolated yield.

[c]ND: Not detected.

[d]No $AgSbF_6$.

[e]Under N_2 atmosphere.

[f]Under O_2 atmosphere.

[g]$AgBF_4$ instead of $AgSbF_6$.

[h]Ag_2CO_3 instead of $AgSbF_6$.

[i]$Cu(OAc)_2$ instead of $AgSbF_6$.

[j]2.0 equiv AdCOOH was used.

[k]4% $[Cp^*RhCl_2]_2$ was used.

[l]1% $[Cp^*RhCl_2]_2$ was used.

4. General procedure and characterization of products

General procedure A

In an oven-dried Schlenk tube under air, a mixture of the 3-aryl-1,2,4-oxadiazol-5(4*H*)-ones **1**(0.20 mmol, 1.0 equiv), 2-(phenyl-λ3-iodaneylidene)cyclohexane-1,3-diones **2** (0.30 mmol, 1.5 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), $AgSbF_6$ (6.9 mg, 0.02 mmol, 10.0 mol%), AdCOOH (36.0 mg, 0.2 mmol, 1.0 equiv), and DCE or CH_3CH_2OH (1.0 mL, 0.2 M) was stirred at 80 °C for 8-12 h. Then the reaction mixture was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product **3a**-**3t**, **4a**-**4e**.

General procedure B

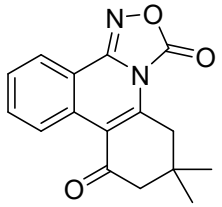
In an oven-dried Schlenk tube under air, a mixture of the 3-alkenyl-1,2,4-oxadiazol-5(4*H*)-ones **1** (0.20 mmol, 1.0 equiv), 2-(phenyl-λ3-iodaneylidene)cyclohexane-1,3-diones **2** (0.30 mmol, 1.5 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), $AgSbF_6$ (6.9 mg, 0.02 mmol, 10.0 mol%), AdCOOH (36.0 mg, 0.2 mmol, 1.0 equiv), and CH_3CH_2OH (1.0 mL, 0.20 M) was stirred at rt for 0.33-2 h. Then the reaction mixture was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product **5a**-**5f**.

General procedure C

In an oven-dried Schlenk tube under air, a mixture of the (*E*)-3-styryl-1,2,4-oxadiazol-5(4*H*)-one **1w** (0.20 mmol, 1.0 equiv), 5,5-dimethyl-2-(phenyl-λ3-iodaneylidene)cyclohexane-1,3-dione **2a** (0.40 mmol, 2.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), $AgSbF_6$ (6.9 mg, 0.02 mmol, 10.0 mol%), $AgBF_4$(7.8 mg, 0.04 mmol, 20.0 mol%), PivOH (20.4 mg, 0.2 mmol, 1.0 equiv), and DCM (1.0 mL, 0.2 M) was stirred at 50 °C for 8 h. Then the reaction mixture was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product **5g**.

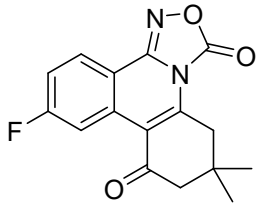
Characterization of products

6,6-dimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3a)



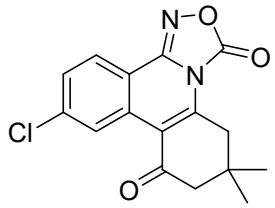
Following the general procedure A, the product **3a** was obtained in 82% yield (46.1 mg, 0.160 mmol) as a whitesolid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). Rf (Petroleum ether/EtOAc 16:1): 0.21. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (d, *J* = 8.4 Hz, 1H), 8.18 – 8.16 (m, 1H), 7.75 – 7.71 (m, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 3.45 (s, 2H), 2.56 (s, 2H), 1.20 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.9, 154.9, 152.0, 145.1, 133.6, 129.6, 128.9, 127.5, 123.4, 116.9, 115.1, 52.8, 37.8, 32.2, 28.2. HRMS (ESI) *m/z* calcd. for $C_{16}H_{15}N_2O_3$ $[M+H]^+$ 283.1082; Found 283.1081.

10-fluoro-6,6-dimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3b)



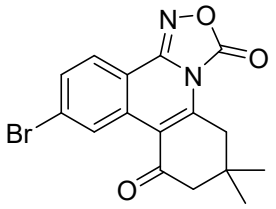
Following the general procedure A, the product **3b** was obtained in 96% yield (57.8 mg, 0.192 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). Rf (Petroleum ether/EtOAc 16:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (dd, *J* = 11.9, 2.5 Hz, 1H), 8.17 (dd, *J* = 8.8, 5.8 Hz, 1H), 7.29 (s, 1H), 3.46 (s, 2H), 2.56 (s, 2H), 1.20 (s, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 196.6, 165.7 (d, *J* = 253.3 Hz), 154.7, 151.5, 146.4, 132.2 (d, *J* = 11.3 Hz), 125.9 (d, *J* = 9.7 Hz), 117.2 (d, *J* = 24.0 Hz), 114.4 (d, *J* = 26.8 Hz), 114.3 (d, *J* = 3.4 Hz), 113.3 (d, *J* = 2.8 Hz), 52.6, 37.8, 32.1, 28.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.6. HRMS (ESI) *m/z* calcd. for $C_{16}H_{14}FN_2O_3$ $[M+H]^+$ 301.0988; Found 301.0992.

10-chloro-6,6-dimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3c)



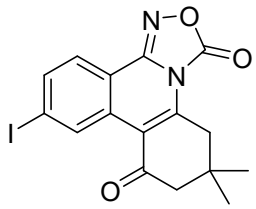
Following the general procedure A, the product **3c** was obtained in 29% yield (18.2 mg, 0.057 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). Rf (Petroleum ether/EtOAc 16:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.22 (s, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.54 (d, *J* = 8.5 Hz, 1H), 3.46 (s, 2H), 2.58 (s, 2H), 1.21 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.8, 154.6, 151.5, 146.4, 140.3, 130.9, 129.4, 127.4, 124.7, 115.1, 114.1, 52.6, 37.7, 32.1, 28.1. HRMS (ESI) *m/z* calcd. for $C_{16}H_{14}ClN_2O_3$ $[M+H]^+$ 317.0693; Found 317.0699.

10-bromo-6,6-dimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3d))



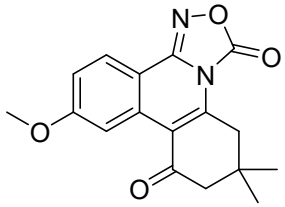
Following the general procedure A, the product **3d** was obtained in 41% yield (29.8 mg, 0.082 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). Rf (Petroleum ether/EtOAc 16:1): 0.21. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (s, 1H), 8.02 (d, *J* = 8.5 Hz, 1H), 7.67 (d, *J* = 1.8 Hz, 1H), 3.45 (s, 2H), 2.56 (s, 2H), 1.20 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.5, 154.6, 151.6, 146.3, 132.2, 131.0, 130.5, 128.9, 124.7, 115.6, 114.0, 52.7, 37.8, 32.2, 28.2. HRMS (ESI) *m/z* calcd. for $C_{16}H_{14}BrN_2O_3$ $[M+H]^+$ 361.0188; Found 361.0179.

10-iodo-6,6-dimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3e)



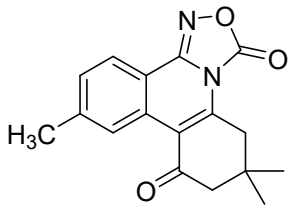
Following the general procedure A, the product **3e** was obtained in 43% yield (35.1 mg, 0.086 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). Rf (Petroleum ether/EtOAc 16:1): 0.21. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.58 (s, 1H), 7.87 (dd, *J* = 15.8, 8.2 Hz, 2H), 3.45 (s, 2H), 2.55 (s, 2H), 1.19 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.5, 151.8, 147.2, 146.1, 138.0, 136.5, 130.7, 124.4, 116.1, 113.9, 101.5, 52.7, 37.8, 32.2, 28.2. HRMS (ESI) *m/z* calcd. for $C_{16}H_{14}IN_2O_3$ $[M+H]^+$ 409.0049; Found 409.0054.

10-methoxy-6,6-dimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3f)



Following the general procedure A, the product **3f** was obtained in 63% yield (39.7 mg, 0.127 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). Rf (Petroleum ether/EtOAc 16:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.73 (d, *J* = 2.2 Hz, 1H), 8.03 (d, *J* = 8.8 Hz, 1H), 7.09 (dd, *J* = 8.8, 2.3 Hz, 1H), 3.94 (s, 3H), 3.45 (s, 2H), 2.56 (s, 2H), 1.20 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 197.2, 163.3, 154.9, 151.8, 145.9, 131.7, 125.0, 117.4, 114.7, 110.1, 109.6, 55.7, 52.8, 37.8, 32.1, 28.2. HRMS (ESI) *m/z* calcd. for $C_{17}H_{17}N_2O_4$ $[M+H]^+$ 313.1188; Found 313.1190.

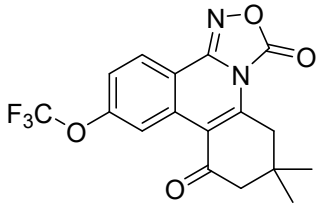
6,6,10-trimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3g)



Following the general procedure A, the product **3g** was obtained in 84% yield (49.8 mg, 0.168 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). RF (Petroleum ether/EtOAc 16:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.94 (s, 1H),

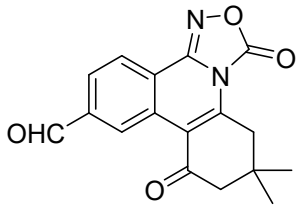
8.04 (d, *J* = 8.1 Hz, 1H), 7.37 (dd, *J* = 8.1, 1.0 Hz, 1H), 3.44 (s, 2H), 2.55 (s, 2H), 2.51 (s, 3H), 1.19 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 197.1, 155.0, 152.1, 145.0, 144.6, 130.1, 129.6, 127.6, 123.3, 115.1, 114.3, 52.9, 37.8, 32.2, 28.2, 22.5. HRMS (ESI) *m/z* calcd. for $C_{17}H_{17}N_2O_3$ $[M+H]^+$ 297.1239; Found 297.1236.

6,6-dimethyl-10-(trifluoromethoxy)-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3h)



Following the general procedure A, the product **3h** was obtained in 50% yield (36.6 mg, 0.099 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). RF (Petroleum ether/EtOAc 16:1): 0.21. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm)9.14 (s, 1H), 8.21 (d, *J* = 8.8 Hz, 1H), 7.40 (dd, *J* = 8.7, 0.9 Hz, 1H), 3.46 (s, 2H), 2.57 (s, 2H), 1.20 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm)δ 196.6, 154.6, 152.9 (d, J = 1.8 Hz), 151.3, 146.6, 131.7, 125.4, 121.3, 120.3 (q, *J* = 259.5 Hz), 119.3, 115.2, 114.1, 52.6, 37.8, 32.2, 28.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.5. HRMS (ESI) *m/z* calcd. for $C_{17}H_{14}F_3N_2O_4$ $[M+H]^+$ 367.0905; Found 367.0908.

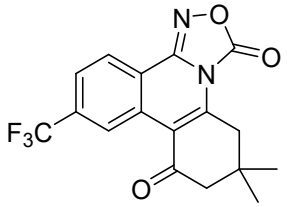
6,6-dimethyl-3,8-dioxo-5,6,7,8-tetrahydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-10-carbaldehyde (3i)



Following the general procedure A, the product **3i** was obtained in 41% yield (39.5 mg, 0.127 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). RF (Petroleum ether/EtOAc 16:1): 0.19. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.59 (s, 1H), 8.28 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 3.46 (s, 2H), 2.59 (s, 2H), 1.21 (s, 6H). ^{13}C NMR

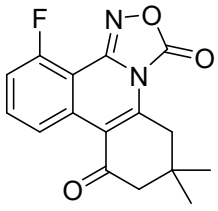
(101 MHz, $CDCl_3$) δ (ppm) 196.3, 154.3, 151.0, 147.0, 132.0, 131.3, 130.3, 124.3, 120.2, 117.7, 117.3, 113.7, 52.5, 37.8, 32.2, 28.2. HRMS (ESI) *m/z* calcd. for $C_{17}H_{15}N_2O_4$ $[M+H]^+$ 311.1032; Found 311.1029.

6,6-dimethyl-10-(trifluoromethyl)-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3j)



Following the general procedure A, the product **3j** was obtained in 40% yield (28.3 mg, 0.081 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). Rf (Petroleum ether/EtOAc 16:1): 0.20. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.54 (s, 1H), 8.29 (d, *J* = 8.3 Hz, 1H), 7.79 (dd, *J* = 8.3, 1.2 Hz, 1H), 3.47 (s, 2H), 2.59 (s, 2H), 1.21 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) 196.4, 154.5, 151.3, 146.4, 135.1 (q, *J* = 32.9 Hz), 130.2, 125.3 (q, *J* = 3.3 Hz), 124.9 (q, *J* = 4.2 Hz), 124.2, 123.4 (d, *J* = 273.3 Hz), 119.6, 114.3, 52.6, 37.8, 32.2, 28.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) -63.2. HRMS (ESI) *m/z* calcd. for $C_{17}H_{14}F_3N_2O_3$ $[M+H]^+$ 351.0956; Found 351.0954.

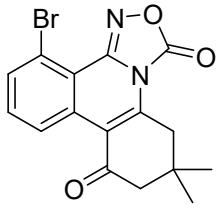
12-fluoro-6,6-dimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3k)



Following the general procedure A, the product **3k** was obtained in 89% yield (53.2 mg, 0.177 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). Rf (Petroleum ether/EtOAc 16:1): 0.21. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.97 (d, *J* = 8.4 Hz, 1H), 7.70 (td, *J* = 8.4, 5.9 Hz, 1H), 7.33 – 7.27 (m, 1H), 3.47 (s, 2H), 2.57 (s, 2H), 1.20 (s,

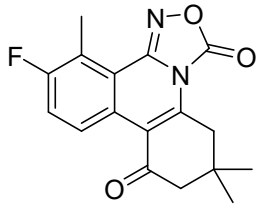
6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.5, 159.7 (d, *J* = 262.3 Hz), 154.2, 149.9 (d, *J* = 6.7 Hz), 146.1, 134.6 (d, *J* = 8.8 Hz), 131.5, 123.2 (d, *J* = 4.0 Hz), 115.9 (d, *J* = 18.7 Hz), 114.7(d, *J* = 1.7 Hz), 106.5 (d, *J* = 13.1 Hz), 52.8, 37.9, 32.1, 28.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) -103.4. HRMS (ESI) *m/z* calcd. for $C_{16}H_{14}FN_2O_3$ $[M+H]^+$ 301.0988; Found 301.0989.

12-bromo-6,6-dimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3l)



Following the general procedure A, the product **3l** was obtained in 60% yield (42.8 mg, 0.118 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). Rf (Petroleum ether/EtOAc 16:1): 0.21. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.51 (t, *J* = 8.2 Hz, 1H), 3.48 (s, 2H), 2.56 (s, 2H), 1.19 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.5, 154.5, 151.3, 145.6, 135.3, 133.2, 132.6, 126.3, 120.0, 117.3, 115.0, 52.9, 37.9, 32.1, 28.2. HRMS (ESI) *m/z* calcd. for $C_{16}H_{13}BrN_2O_3Na$ $[M+Na]^+$ 383.0008 ; Found 382.9998.

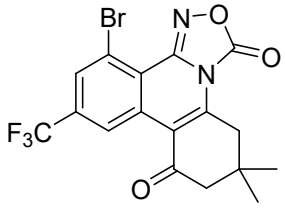
11-fluoro-6,6,12-trimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3m)



Following the general procedure A, the product **3m** was obtained in 37% yield (23.1 mg, 0.073 mmol) as a pale yellow liquid after column chromatography (eluent = Petroleum ether/EtOAc 4:1 v/v). Rf (Petroleum ether/EtOAc 4:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.02 (dd, *J* = 9.2, 5.4 Hz, 1H), 7.37 (t, *J* = 9.1 Hz, 1H), 3.44 (s, 2H), 2.67 (s, 3H), 2.54 (s, 2H),

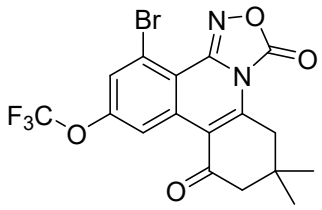
1.18 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm)197.0, 160.3 (d, *J* = 247.7 Hz), 154.5, 152.9, 144.0, 127.0 (d, *J* = 3.4 Hz), 126.8 (d, *J* = 8.7 Hz), 124.8 (d, *J* = 18.9 Hz), 120.1 (d, *J* = 24.1 Hz), 118.5 (d, *J* = 5.2 Hz), 115.2, 52.9, 37.7, 32.1, 28.2, 13.8 (d, *J* = 6.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) -113.3. HRMS (ESI) *m/z* calcd. for $C_{17}H_{16}FN_2O_3$ $[M+H]^+$ 315.1145; Found 315.1148.

12-bromo-6,6-dimethyl-10-(trifluoromethyl)-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3n)



Following the general procedure A, the product **3n** was obtained in 96% yield (77.2 mg, 0.180 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 14:1 v/v). Rf (Petroleum ether/EtOAc 14:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 8.03 (s, 1H), 3.48 (s, 2H), 2.58 (s, 2H), 1.20 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ196.1, 154.1, 150.7, 147.1, 134.6 (q, *J* = 33.5 Hz), 133.2, 131.5 (q, *J* = 3.5 Hz), 123.4 (q, *J* = 4.0 Hz), 122.5 (q, *J* = 273.8 Hz), 120.5, 120.0 (d, *J* = 0.6 Hz), 114.1, 52.7, 37.9, 32.1, 28.2.^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4. HRMS (ESI) *m/z* calcd. for $C_{17}H_{12}BrF_3N_2O_3Na$ $[M+Na]^+$ 450.9881; Found 450.9874.

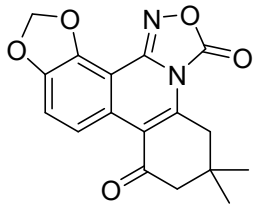
12-bromo-6,6-dimethyl-10-(trifluoromethoxy)-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (3o)



Following the general procedure A, the product **3o** was obtained in 64% yield (57.2 mg, 0.128 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 16:1 v/v). Rf (Petroleum ether/EtOAc 16:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (dd, *J* = 2.2, 0.9

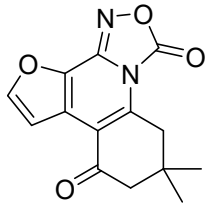
Hz, 1H), 7.69 (d, *J* = 1.5 Hz, 1H), 3.48 (s, 2H), 2.57 (s, 2H), 1.20 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.2, 154.2, 151.5, 150.7, 147.2, 134.0, 127.0(d, *J* = 0.9 Hz), 121.5, 120.2 (d, *J* = 260.6 Hz), 117.7, 115.7, 113.9, 52.7, 37.9, 32.0, 28.2.^{19}F NMR (376 MHz, $CDCl_3$) δ -57.5. HRMS (ESI) *m/z* calcd. for $C_{17}H_{13}BrF_3N_2O_4$ $[M+H]^+$ 445.0011; Found 445.0013.

2,2-dimethyl-2,3-dihydro-12H-[1,3]dioxolo[4,5-i][1,2,4]oxadiazolo[4,3-f]phenanthridine-4,12(1H)-dione (3p)



Following the general procedure A, the product **3p** was obtained in 74% yield (48.2 mg, 0.148 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 8:1 v/v). Rf (Petroleum ether/EtOAc 8:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.77 (d, *J* = 8.2 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 1H), 6.14 (s, 2H), 3.38 (s, 2H), 2.59 (s, 2H), 1.21 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 193.7, 154.9, 152.3, 152.0, 143.6, 142.9, 119.3, 116.3, 112.1, 111.4, 110.3, 101.9, 51.8, 37.1, 33.2, 28.6. HRMS (ESI) *m/z* calcd. for $C_{17}H_{11}N_2O_5Na$ $[M+Na]^+$ 349.0801; Found 349.0798.

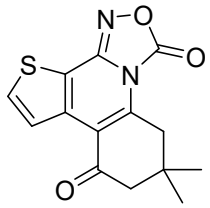
6,6-dimethyl-6,7-dihydro-3H-furo[2,3-c][1,2,4]oxadiazolo[4,3-a]quinoline-3,8(5H)-dione (3q)



Following the general procedure A, the product **3q** was obtained in 81% yield (44.2 mg, 0.162 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 10:1 v/v). Rf (Petroleum ether/EtOAc 10:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.82 (s, 1H), 7.54 (d, *J* = 1.6 Hz, 1H), 3.44 (s, 2H), 2.51 (s, 2H), 1.19 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ

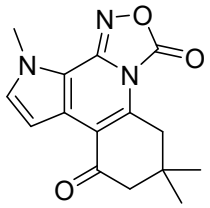
(ppm) 195.0, 154.6, 149.3, 145.5, 144.6, 134.2, 126.3, 113.7, 109.9, 50.93, 36.8, 32.9, 28.3. HRMS (ESI) *m/z* calcd. for $C_{14}H_{13}N_2O_4$ $[M+H]^+$ 273.0875; Found 273.0875.

6,6-dimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-a]thieno[2,3-c]quinoline-3,8(5*H*)-dione (3r)



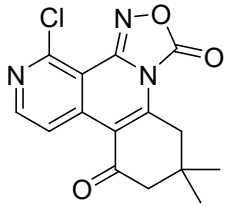
Following the general procedure A, the product **3r** was obtained in 95% yield (55.1 mg, 0.191 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 12:1 v/v). Rf (Petroleum ether/EtOAc 12:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.41 (d, *J* = 5.2 Hz, 1H), 7.77 (d, *J* = 5.2 Hz, 1H), 3.47 (s, 2H), 2.54 (s, 2H), 1.20 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 195.2, 154.7, 150.3, 145.2, 138.6, 132.8, 126.8, 118.3, 115.1, 51.6, 37.1, 32.6, 28.3. HRMS (ESI) *m/z* calcd. for $C_{14}H_{13}N_2O_3S$ $[M+H]^+$ 289.0647; Found 289.0646.

6,6,11-trimethyl-5,6,7,11-tetrahydro-3H,8H-[1,2,4]oxadiazolo[4,3-a]pyrrolo[2,3-c]quinoline-3,8-dione (3s)



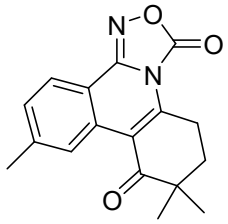
Following the general procedure A, the product **3s** was obtained in 87% yield (50.2 mg, 0.176 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 12:1 v/v). Rf (Petroleum ether/EtOAc 12:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.20 (d, *J* = 2.7 Hz, 1H), 7.07 (d, *J* = 2.7 Hz, 1H), 4.01 (s, 3H), 3.38 (s, 2H), 2.47 (s, 2H), 1.16 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.1, 155.0, 147.5, 140.7, 131.6, 123.1, 114.9, 113.7, 107.2, 51.3, 36.7, 36.4, 32.8, 28.3. HRMS (ESI) *m/z* calcd. for $C_{15}H_{16}N_3O_3$ $[M+H]^+$ 286.1191; Found 286.1194.

12-chloro-6,6-dimethyl-6,7-dihydro-3*H*-benzo[*c*][1,2,4]oxadiazolo[3,4-*a*][2,7]naphthyridine-3,8(5*H*)-dione (3t)



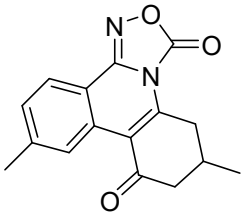
Following the general procedure A, the product **3t** was obtained in 22% yield (13.8 mg, 0.043 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 4:1 v/v). Rf (Petroleum ether/EtOAc 4:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.04 (d, *J* = 5.7 Hz, 1H), 8.61 (d, *J* = 5.7 Hz, 1H), 3.50 (s, 2H), 2.57 (s, 2H), 1.20 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 195.6, 153.9, 151.9, 150.2, 149.9, 149.5, 139.7, 118.9, 113.3, 112.3, 52.5, 38.1, 32.1, 28.2. HRMS (ESI) *m/z* calcd. for $C_{15}H_{13}ClN_3O_3$ $[M+H]^+$ 318.0645; Found 318.0649.

7,7,10-trimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (4a)



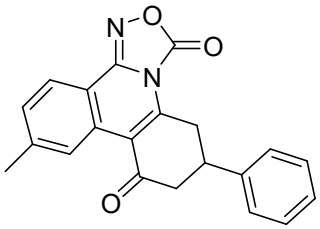
Following the general procedure A, the product **4a** was obtained in 98% yield (58.2 mg, 0.196 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 10:1 v/v). Rf (Petroleum ether/EtOAc 10:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.78 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 3.49 (t, *J* = 6.3 Hz, 2H), 2.47 (s, 3H), 2.03 (t, *J* = 6.3 Hz, 2H), 1.23 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 201.9, 155.0, 151.8, 144.7, 144.3, 130.1, 129.9, 127.7, 123.3, 114.4, 114.3, 42.0, 33.4, 24.2, 22.4, 21.3. HRMS (ESI) *m/z* calcd. for $C_{17}H_{17}N_2O_3$ $[M+H]^+$ 297.1239; Found 297.1235.

6,10-dimethyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (4b)



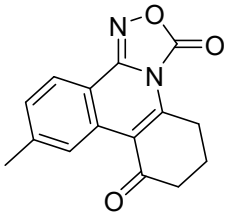
Following the general procedure A, the product **4b**was obtained in 57% yield (31.9 mg, 0.113 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 12:1 v/v). Rf (Petroleum ether/EtOAc 12:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 3.94 – 3.88 (m, 1H), 2.92 – 2.90 (m, 1H), 2.74 – 2.72 (m, 1H), 2.50 (s, 3H), 2.40 – 2.38 (m, 2H), 1.23 (d, *J* = 5.9 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 197.1, 154.9, 151.9, 146.3, 144.5, 130.0, 129.6, 127.6, 123.3, 115.6, 114.1, 47.2, 32.0, 28.1, 22.4, 20.9. HRMS (ESI) *m/z* calcd. for $C_{16}H_{15}N_2O_3$ $[M+H]^+$ 283.1082; Found 283.1082.

10-methyl-6-phenyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (4c)



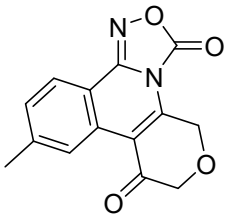
Following the general procedure A, the product **4c** was obtained in 90% yield (62.3 mg, 0.181 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 8:1 v/v). Rf (Petroleum ether/EtOAc 8:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm) 8.96 (s, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.42 – 7.37 (m, 3H), 7.32 (d, *J* = 2.6 Hz, 2H), 7.31 (d, *J* = 2.5 Hz, 1H), 4.19 – 4.13 (m, 1H), 3.37 – 3.32 (m, 1H), 2.97 – 2.92 (m, 2H), 2.51 (s, 3H), 1.65– 1.63 (m, 1H).^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm)196.1, 154.8, 151.8, 146.0, 144.6, 141.3, 130.2, 129.6, 129.1, 127.7, 127.6, 126.7, 123.4, 115.8, 114.3, 45.8, 38.4, 31.8, 22.5. HRMS (ESI) *m/z* calcd. for $C_{21}H_{17}N_2O_3$ $[M+H]^+$ 345.1239; Found 345.1239.

10-methyl-6,7-dihydro-3H-[1,2,4]oxadiazolo[4,3-f]phenanthridine-3,8(5H)-dione (4d)



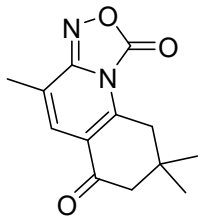
Following the general procedure A, the product **4d** was obtained in 96% yield (51.6 mg, 0.192 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 8:1 v/v). Rf (Petroleum ether/EtOAc 8:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.86 (s, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 3.50 (t, *J* = 6.2 Hz, 2H), 2.68 – 2.63 (m, 2H), 2.48 (s, 3H), 2.22 – 2.15 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.8, 154.9, 151.7, 146.8, 144.5, 129.9, 129.7, 127.7, 123.3, 115.9, 114.2, 39.1, 24.4, 22.5, 20.4. HRMS (ESI) *m/z* calcd. for $C_{15}H_{13}N_2O_3$ $[M+H]^+$ 269.0926; Found 269.0927.

10-methyl-7-hydro-3H,5H-[1,2,4]oxadiazolo[3,4-a]pyrano[3,4-c]isoquinoline-3,8-dione (4e)



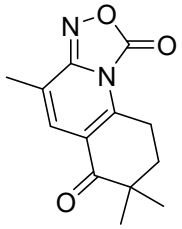
Following the general procedure A, the product **4e** was obtained in 92% yield (49.8 mg, 0.184 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 8:1 v/v). Rf (Petroleum ether/EtOAc 8:1): 0.20. ^{1}H NMR (400 MHz, DMSO) δ(ppm) 7.95 (s, 1H), 7.18 (d, *J* = 8.1 Hz, 1H), 6.68 (d, *J* = 8.1 Hz, 1H), 4.47 (s, 2H), 3.52 (s, 2H), 1.64 (s, 3H).^{13}C NMR (101 MHz, DMSO) δ(ppm) 192.7, 154.6, 151.6, 146.9, 144.6, 130.7, 129.1, 127.2, 123.7, 114.5, 112.1, 72.1,62.6,22.4. HRMS (ESI) *m/z* calcd. for $C_{14}H_{11}N_2O_4$ $[M+H]^+$ 271.0719; Found 271.0718.

4,8,8-trimethyl-8,9-dihydro-1H-[1,2,4]oxadiazolo[4,3-a]quinoline-1,6(7H)-dione (5a)



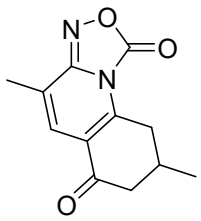
Following the general procedure B, the product **5a** was obtained in 92% yield (45.4mg, 0.184 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 8:1 v/v). Rf (Petroleum ether/EtOAc 8:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.38 (s, 1H), 3.34 (s, 2H), 2.42 (s, 2H), 2.21 (s, 3H), 1.14 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 193.9, 155.2, 154.3, 145.4, 127.9, 121.3, 118.1, 50.3, 36.3, 32.7, 28.3, 14.9. HRMS (ESI) *m/z* calcd. for $C_{13}H_{15}N_2O_3$ $[M+H]^+$ 247.1082; Found 247.1081.

4,7,7-trimethyl-8,9-dihydro-1H-[1,2,4]oxadiazolo[4,3-a]quinoline-1,6(7H)-dione (5b)



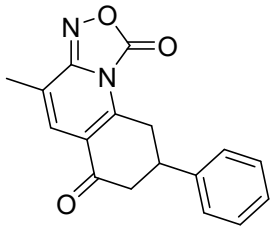
Following the general procedure B, the product **5b** was obtained in 96% yield (47.1 mg, 0.191 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 8:1 v/v). Rf (Petroleum ether/EtOAc 8:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.40 (s, 1H), 3.47 (t, *J* = 6.1 Hz, 2H), 2.22 (s, 3H), 1.99 (t, *J* = 6.3 Hz, 2H), 1.18 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.8, 155.3, 154.0, 145.4, 128.9, 121.4, 117.1, 40.5, 34.1, 23.9, 20.2, 14.9. HRMS (ESI) *m/z* calcd. for $C_{13}H_{15}N_2O_3$ $[M+H]^+$ 247.1082; Found 247.1077.

4,8-dimethyl-8,9-dihydro-1H-[1,2,4]oxadiazolo[4,3-a]quinoline-1,6(7H)-dione (5c)



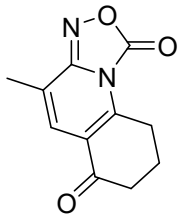
Following the general procedure B, the product **5c** was obtained in 97% yield (43.2 mg, 0.195 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 8:1 v/v). Rf (Petroleum ether/EtOAc 8:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H), 3.91 – 3.85 (m, 1H), 2.91 – 2.89 (m, 1H), 2.71 – 2.62 (m, 1H), 2.32 – 2.25 (m, 1H), 2.23 (s, 3H), 1.67 – 1.66 (m, 1H), 1.21 (d, *J* = 5.8 Hz,3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 155.2, 154.1, 146.4, 128.1, 121.4, 118.7, 44.7, 30.6, 28.7, 21.0, 14.8. HRMS (ESI) *m/z* calcd. for $C_{12}H_{13}N_2O_3$ $[M+H]^+$ 233.0926; Found 233.0926.

4-methyl-8-phenyl-8,9-dihydro-1H-[1,2,4]oxadiazolo[4,3-a]quinoline-1,6(7H)-dione (5d)



Following the general procedure B, the product **5d** was obtained in 69% yield (40.8 mg, 0.139 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 8:1 v/v). Rf (Petroleum ether/EtOAc 8:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.45 (s, 1H), 7.38 (d, *J* = 7.0 Hz, 1H), 7.31 (dd, *J* = 18.1, 11.1 Hz, 4H), 4.15 - 4.09 (m, 1H), 3.48 - 3.40 (m, 1H), 3.35 – 3.30 (m, 1H), 2.88– 2.82 (m, 2H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 193.3, 155.1, 154.1, 146.1, 141.3, 129.1, 128.0, 127.7, 126.7, 121.8, 118.8, 43.4, 39.0, 30.5, 14.9. HRMS (ESI) *m/z* calcd. For$C_{17}H_{15}N_2O_3$ $[M+H]^+$ 295.1082; Found 295.1088.

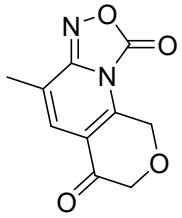
4-methyl-8,9-dihydro-1H-[1,2,4]oxadiazolo[4,3-a]quinoline-1,6(7H)-dione (5e)



Following the general procedure B, the product **5e** was obtained in 79% yield (34.6 mg, 0.159 mmol) as a pale white solid after column chromatography (eluent = Petroleum ether/EtOAc 8:1 v/v). Rf (Petroleum ether/EtOAc 8:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.44 (s, 1H),

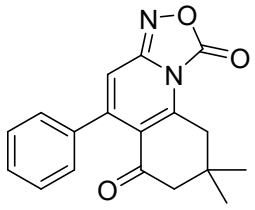
3.51 (t, *J* = 6.2 Hz, 2H), 2.62 – 2.59 (m, 2H), 2.25 (d, *J* = 1.1 Hz, 3H), 2.20 (dd, *J* = 13.0, 6.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 155.2, 154.0, 147.0, 128.2, 121.4, 119.0, 36.6, 22.9, 20.8, 14.9. HRMS (ESI) *m/z* calcd. for $C_{11}H_{11}N_2O_3$ $[M+H]^+$ 219.0769; Found 219.0771.

4-methyl-9-hydro-1H,7H-[1,2,4]oxadiazolo[4,3-a]pyrano[4,3-e]pyridine-1,6-dione (5f)



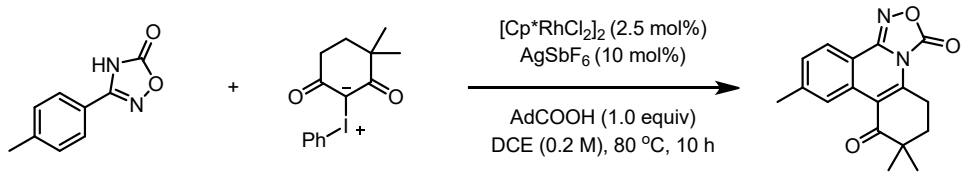
Following the general procedure B, the product **5f** was obtained in 79% yield (34.6 mg, 0.157 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 8:1 v/v). Rf (Petroleum ether/EtOAc 8:1): 0.20. ^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) 7.38 (s, 1H), 5.36 (s, 2H), 4.30 (s, 2H), 2.27 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ(ppm) 189.4, 154.5, 153.3, 144.1, 126.4, 123.1, 116.4, 71.5, 61.8, 14.9. HRMS (ESI) *m/z* calcd. for $C_{10}H_8N_2O_4Na$ $[M+Na]^+$ 243.0382 ; Found 243.0381.

8,8-dimethyl-5-phenyl-8,9-dihydro-1H-[1,2,4]oxadiazolo[4,3-a]quinoline-1,6(7H)-dione(5g)



Following the general procedure C, the product **5g** was obtained in 32% yield (19.8 mg, 0.064 mmol) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 8:1 v/v). Rf (Petroleum ether/EtOAc 8:1): 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 5.0, 1.8 Hz, 3H), 7.15 (dd, *J* = 6.4, 3.1 Hz, 2H), 6.68 (s, 1H), 3.49 (s, 2H), 2.45 (s, 2H), 1.19 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.4, 154.5, 152.6, 148.6, 147.9, 138.6, 128.4, 128.1, 127.0, 118.1, 111.7, 52.1, 37.5, 32.5, 28.3. HRMS (ESI) *m/z* calcd. for $C_{18}H_{16}N_2O_3Na$ $[M+Na]^+$ 331.1059; Found 331.1067.

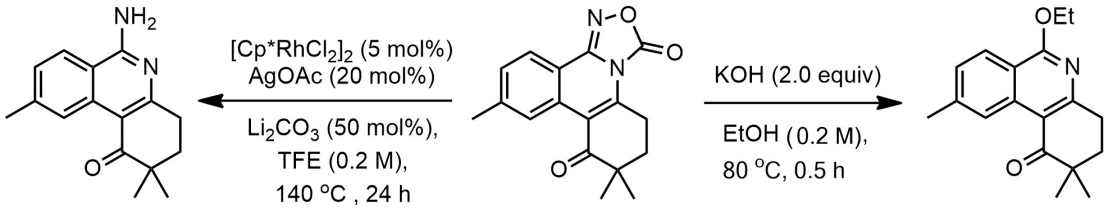
5. Gram-Scale Synthesis:



1g (3.0 mmol) **2b** (1.5 equiv) **4a**, 821.3 mg, 92 %

In an oven-dried Schlenk tube under air, a mixture of the substrates **1g** (3.0 mmol, 1.0 equiv), 4,4-dimethyl-2-(phenyl-λ^3-iodaneylidene)cyclohexane-1,3-dione **2b** (4.5 mmol, 1.5 equiv), $[Cp^*RhCl_2]_2$ (0.075 mmol, 2.5 mol%), $AgSbF_6$ (0.3 mmol, 10 mol%), AdCOOH (3.0 mmol, 1.0 equiv) and DCE (0.20 M) was stirred at 80 °C for 10 h. Then the reaction mixture was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product (PE : EA = 16:1) to give **4a** (821.3 mg, 92%).

6. Synthetic application of the product 4g:



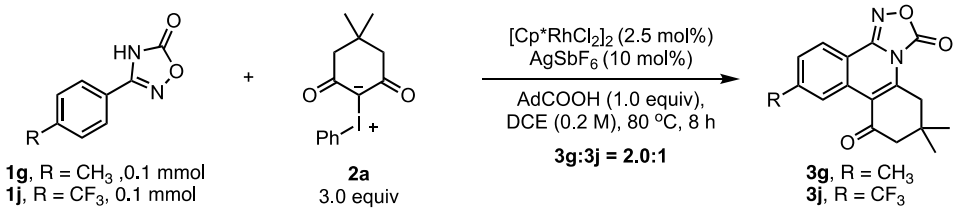
6, 21.3 mg, 84 % **4a**, 0.1 mmol **7**, 21.7 mg, 77 %

Product **6** was prepared following a modified literature procedure[4]. In an oven-dried Schlenk tube under air, a mixture of the substrate **4a** (0.10 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.0050 mmol), AgOAc (0.02 mmol, 20 mol%), $LiCO_3$ (0.05 mmol, 50 mol%), and TFE (0.5 mL, 0.20 M) was stirred at 140 °C for 24 h. The pure product was purified by flash column chromatography on silica gel to afford the pure product (petroleum ether : ethyl acetate = 2:1) to give **6** (21.3 mg, 84%), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.05 (s, 1H), 9.13 (s, 1H), 8.30 (d, *J* = 8.2 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 3.08 (t, *J* = 6.3 Hz, 2H), 2.52 (s, 3H), 2.05 (t, *J* = 6.3 Hz, 2H), 1.27 (s, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 201.9, 164.4, 151.4, 145.0, 136.2, 128.2, 127.1, 126.4, 122.2, 108.9, 42.1, 34.3, 26.9, 25.0, 22.5. HRMS (ESI) *m/z* calcd. for

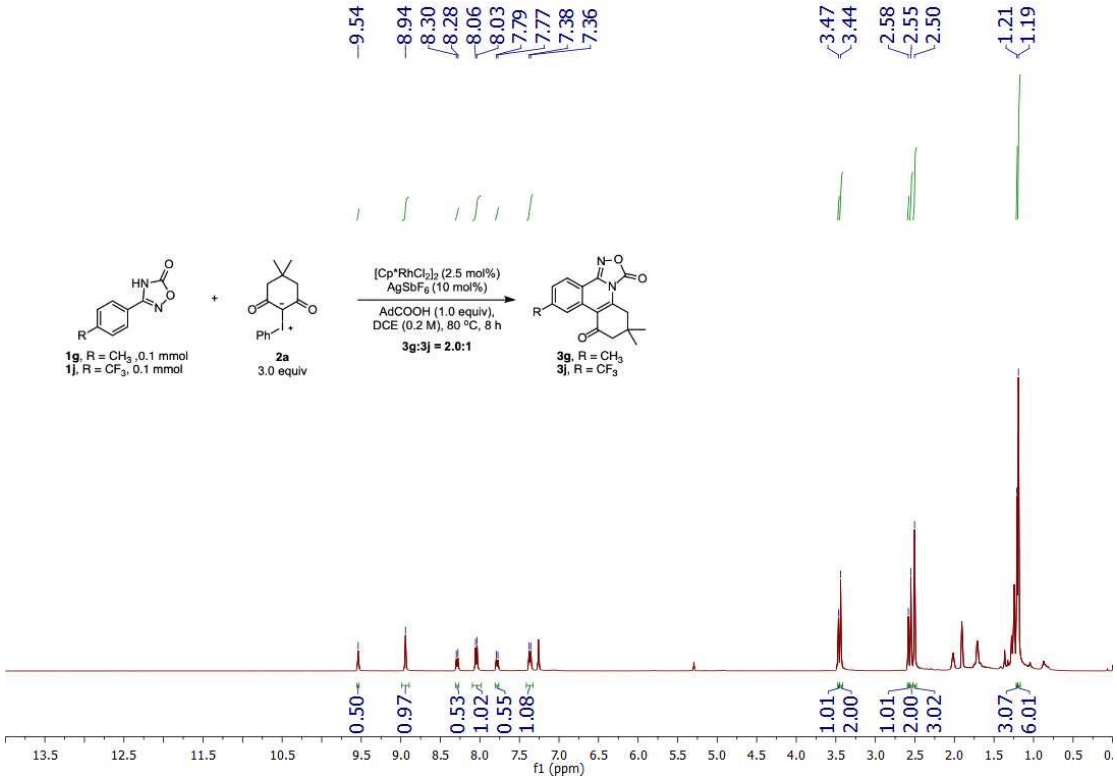
$C_{16}H_{19}N_2O$ $[M+H]^+$ 255.1497; Found 255.1497.

Product **7** was prepared as followed. In an oven-dried Schlenk tube under air, a mixture of the substrates **4a** (0.10 mmol, 1.0 equiv), KOH (0.20 mmol, 2.0 equiv), and EtOH (0.5 mL, 0.20 M) was stirred at 80 °C for 0.5 h. The pure product was purified by flash column chromatography on silica to afford the pure product (petroleum ether : ethyl acetate = 64:1) to give **7** (21.7 mg, 77%), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.33 (dd, *J* = 8.4, 1.4 Hz, 1H), 4.61 (q, *J* = 7.1 Hz, 2H), 3.12 (t, *J* = 6.4 Hz, 2H), 2.54 (s, 3H), 2.02 (t, *J* = 6.4 Hz, 2H), 1.49 (d, *J* = 7.1 Hz, 3H), 1.26 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.8, 162.4, 160.5, 143.0, 136.9, 128.0, 125.4, 124.1, 117.0, 114.9, 62.6, 42.4, 35.2, 30.4, 24.9, 22.5, 14.5. HRMS (ESI) *m/z* calcd. for $C_{18}H_{22}NO_2$ $[M+H]^+$ 284.1650; Found 284.1653.

7. Competitive experiment:

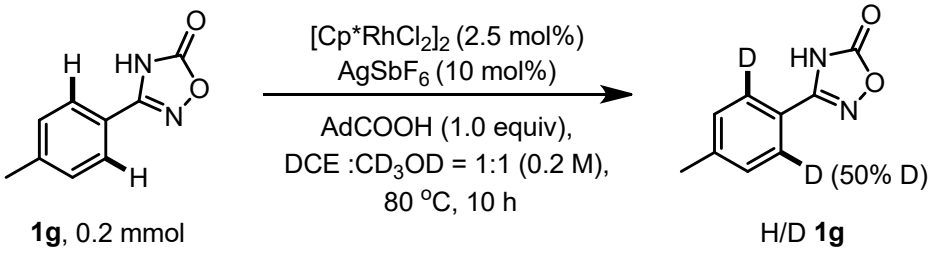


In an oven-dried Schlenk tube under air, a mixture of the substrates **1g** (0.1 mmol), **1j** (0.1 mmol), **2a** (0.3 mmol), $(Cp^*RhCl_2)_2$ (2.5 mol%), $AgSbF_6$ (10.0 mol%), AdCOOH (0.2 mmol) and DCE (0.2 M) was stirred at 80 °C for 8 h. Thenthe reaction mixture was purified by flash column chromatography onsilica with an appropriate solvent (petroleum ether : ethyl acetate = 16:1) toafford the product **3g: 3j** = 2.0:1.



8. Mechanistic studies

(1) Reversibility of C−H bond cleavage

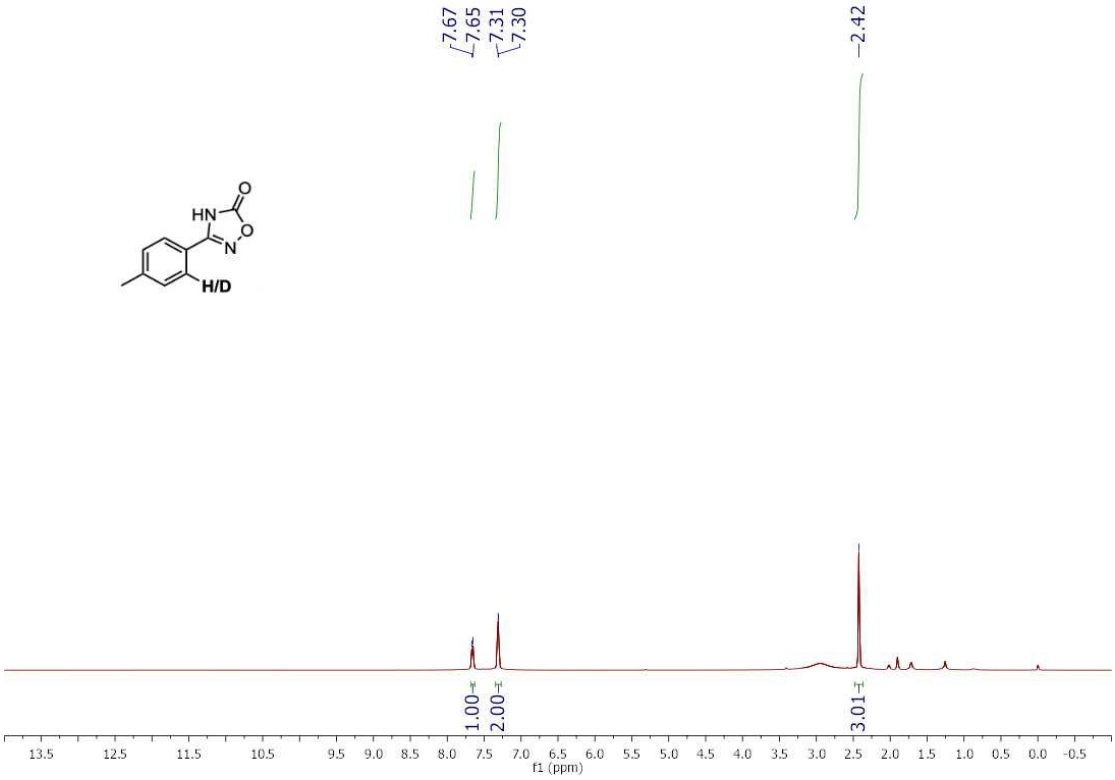


1g, 0.2 mmol

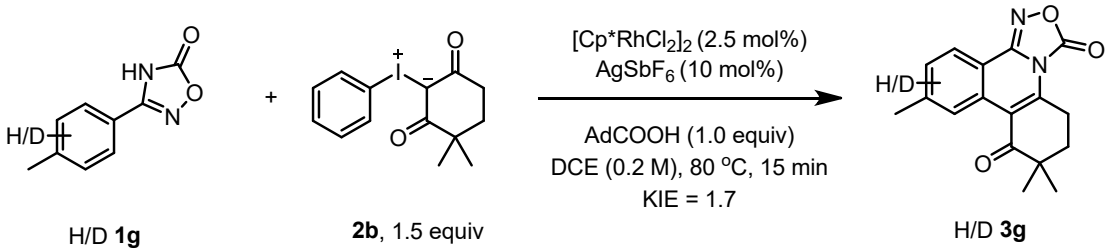
H/D **1g**

To a reaction tube equipped with a stir bar were charged with 3-(*p*-tolyl)-1,2,4-oxadiazol-5(4*H*)-one (**1g**, 35.2 mg, 0.20 mmol), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.0050 mmol), $AgSbF_6$ (6.8 mg, 10 mol%), AdCOOH (36.1 mg, 0.2 mmol), CD_3OD (0.5 mL) and DCE (0.5 mL). The resulting mixture was stirred at 80 °C for 10 h. Afterwards, cooled to room temperature, quenched with saturated brine (5.0 mL), and extracted with EtOAc (10 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel chromatography using PE/EA (2:1) as eluent to afford H/D **1g**. ^1H NMR

analysis revealed 50% deuteration at the *ortho*-position of phenyl ring based on the double doublet at δ: 7.66.



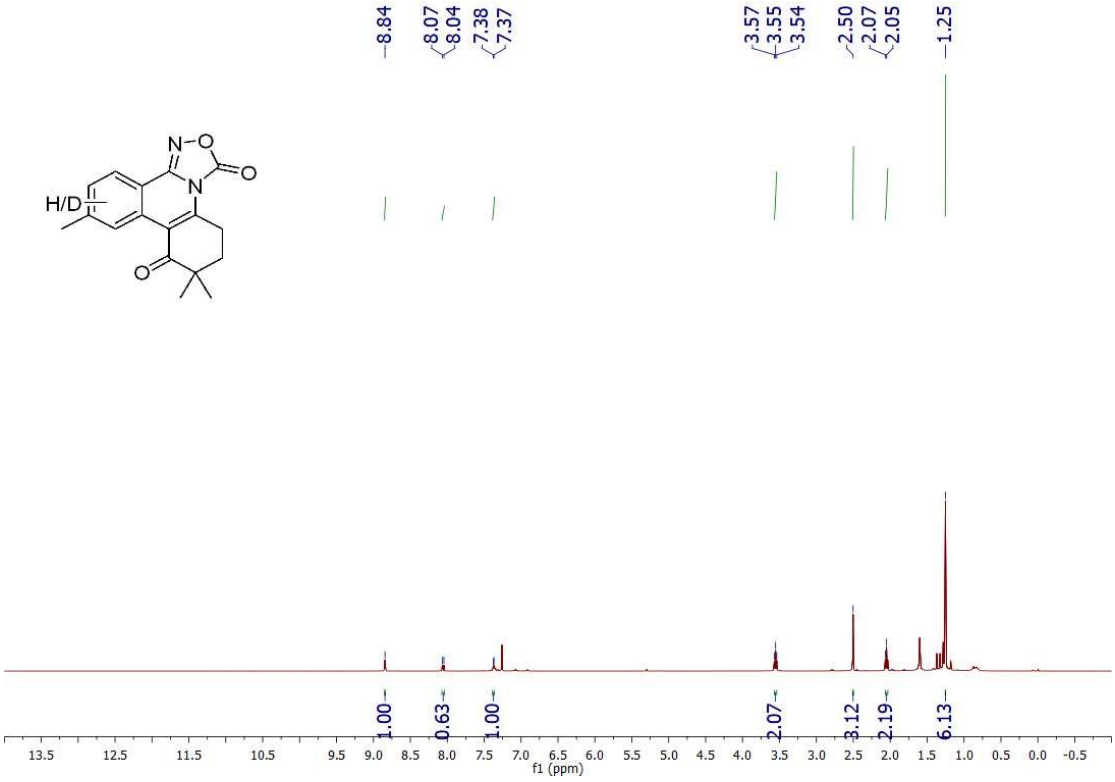
(2) An intermolecular KIE experiment



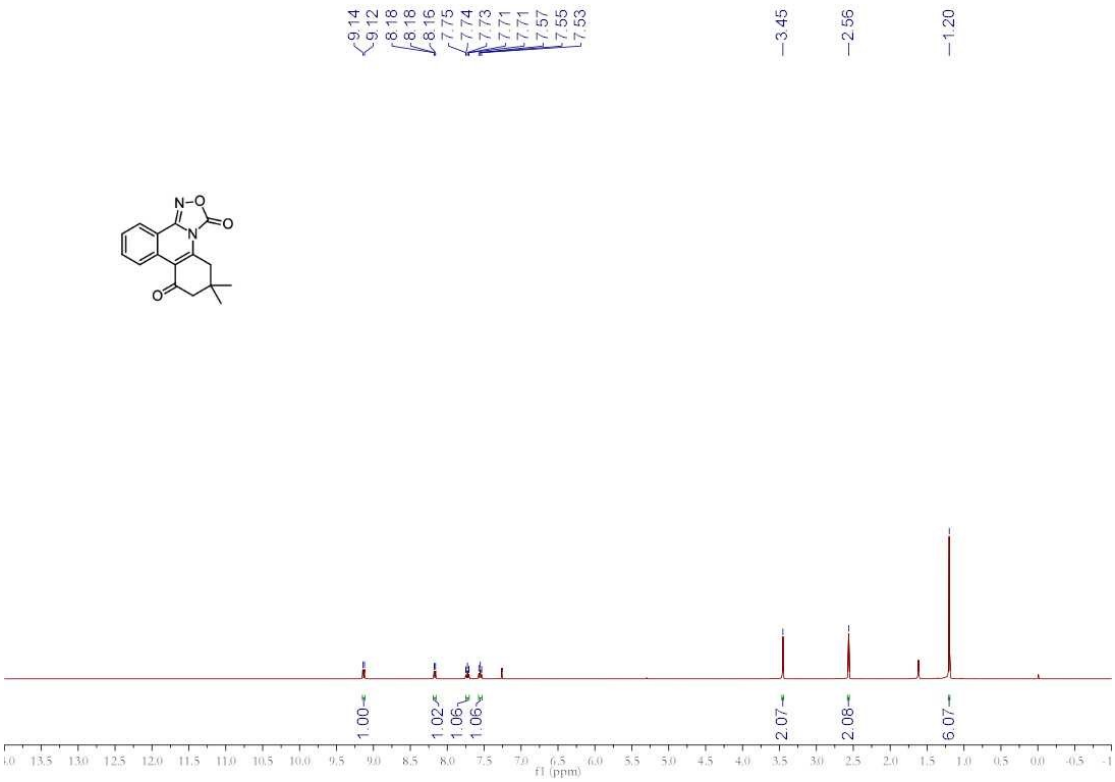
H/D **1g** **2b**, 1.5 equiv H/D **3g**

To a reaction tube equipped with a stir bar were added 3-(*p*-tolyl)-1,2,4-oxadiazol-5(4*H*)-one (**1g**, 17.6 mg, 0.10 mmol), 4,4-dimethyl-2-(phenyl-λ^3-iodaneylidene)cyclohexane-1,3-dione(**2b**, 51.3 mg, 0.15 mmol), $[Cp^*RhCl_2]_2$ (1.6 mg, 0.025 mmol), $AgSbF_6$ (3.4 mg, 10 mol%), AdCOOH (18.0 mg, 0.10 mmol) and DCE (0.5 mL). The resulting mixture was then stirred at 80 °C for 15 min. Afterwards, cooled to room temperature, quenched with saturated brine (5.0 mL), and extracted with EtOAc (10 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure.The residue was purified by silica gel

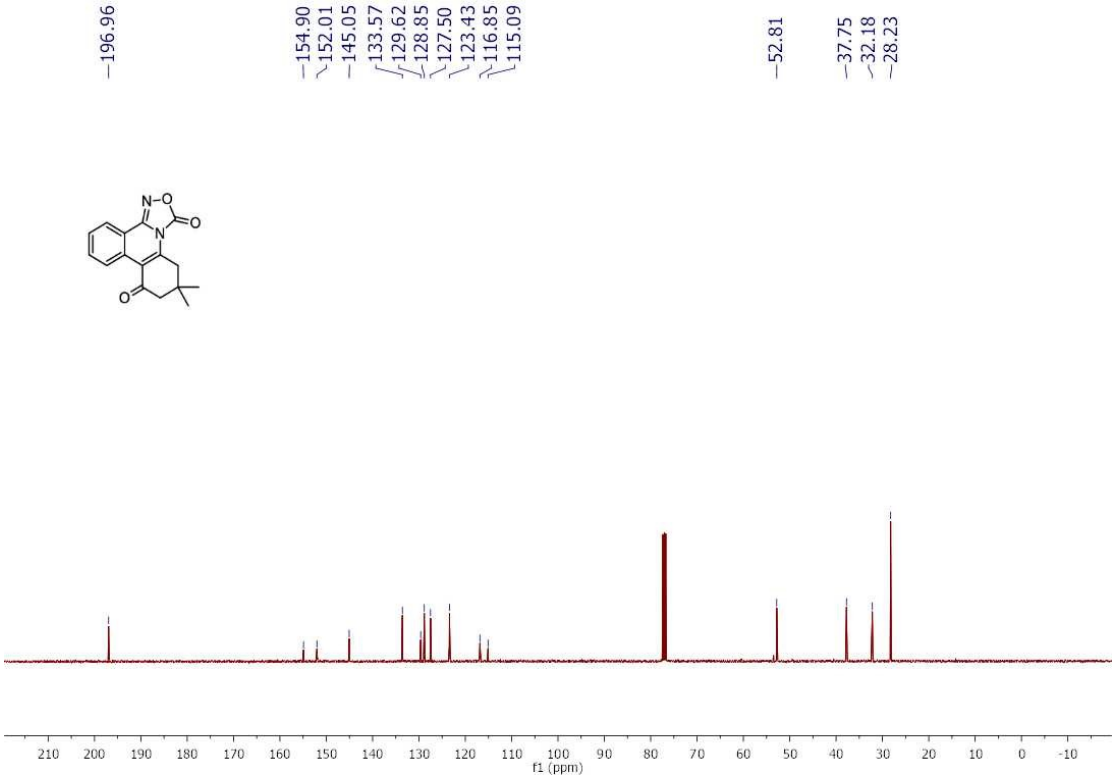
chromatography using PE/EA (16:1) as eluent to afford a mixture of **3g**. Upon analyzing the corresponding ^{1}H NMR spectrum, the average intermolecular *KIE* (K_H/K_D) was determined as 1.7 (K_H/K_D = 0.63/0.37) based on the double doublet at δ: 8.04.



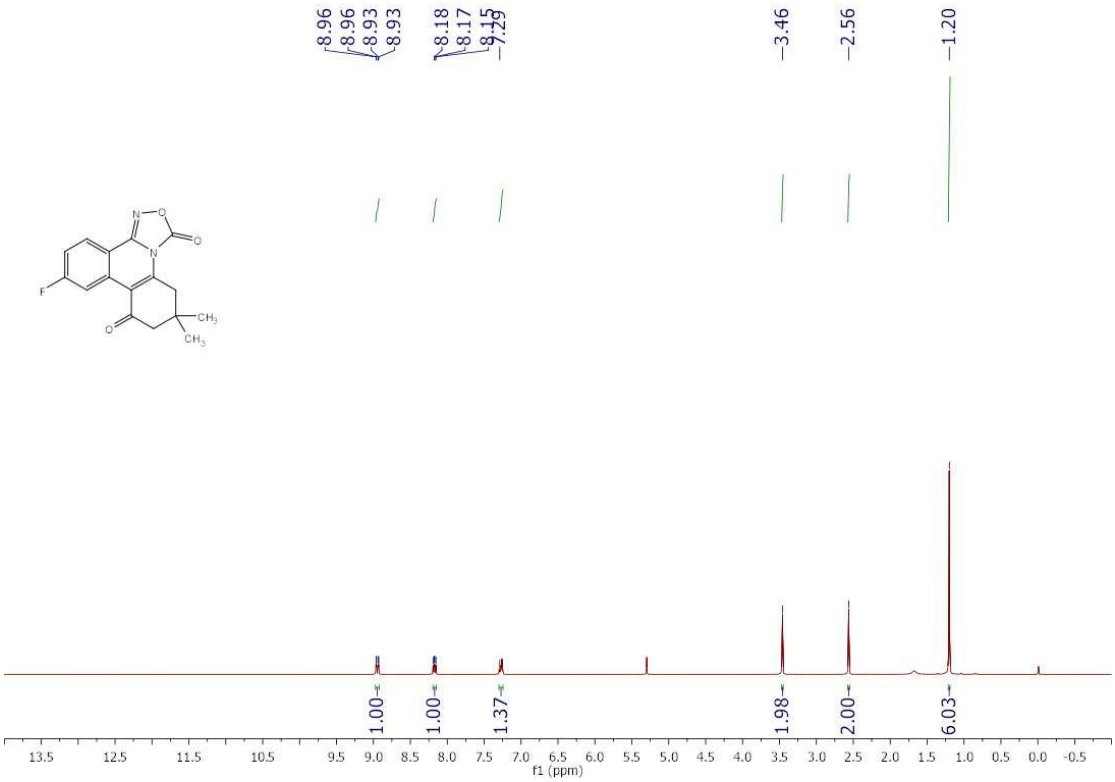
9. NMR Spectra for New Compounds



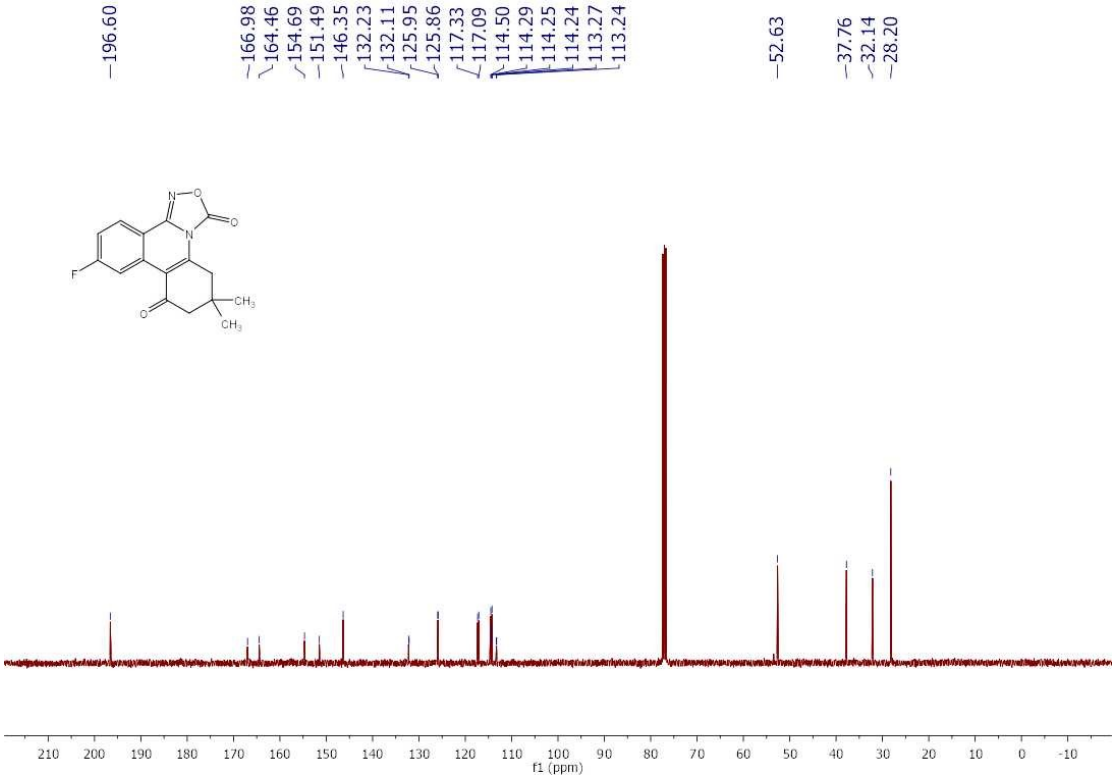
^{1}H NMR spectrum of **3a** (400 MHz, $CDCl_3$)



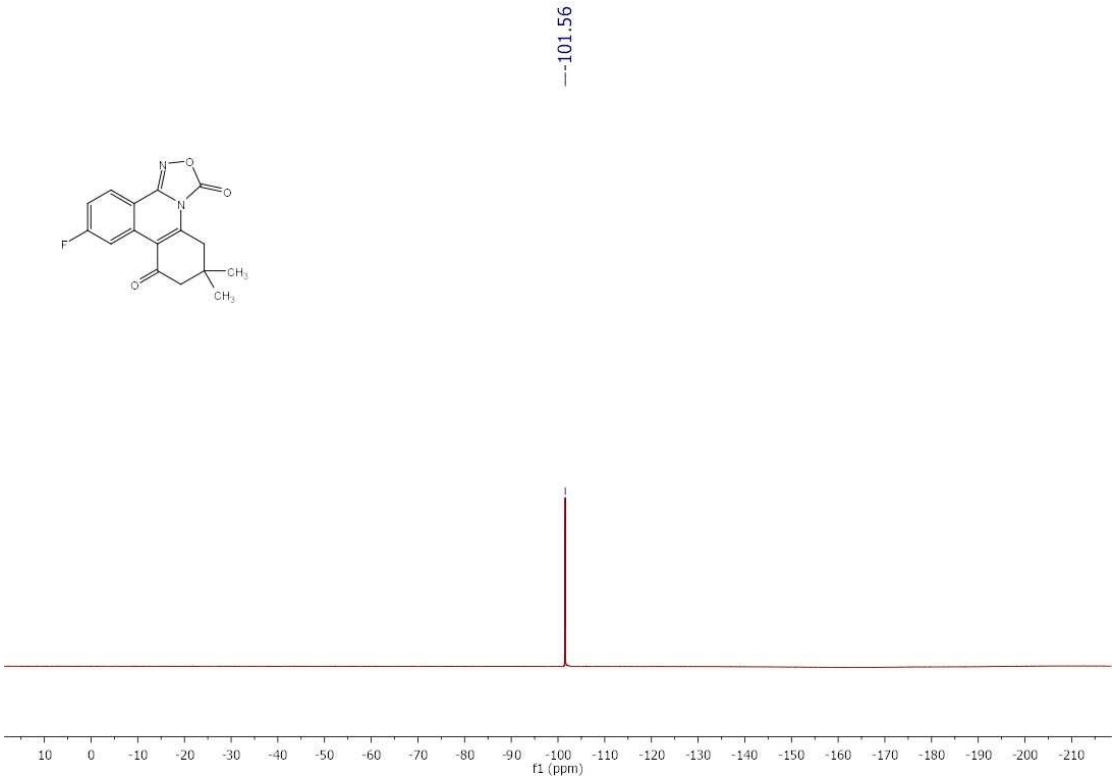
^{13}C NMR spectrum of **3a** (101 MHz, $CDCl_3$)



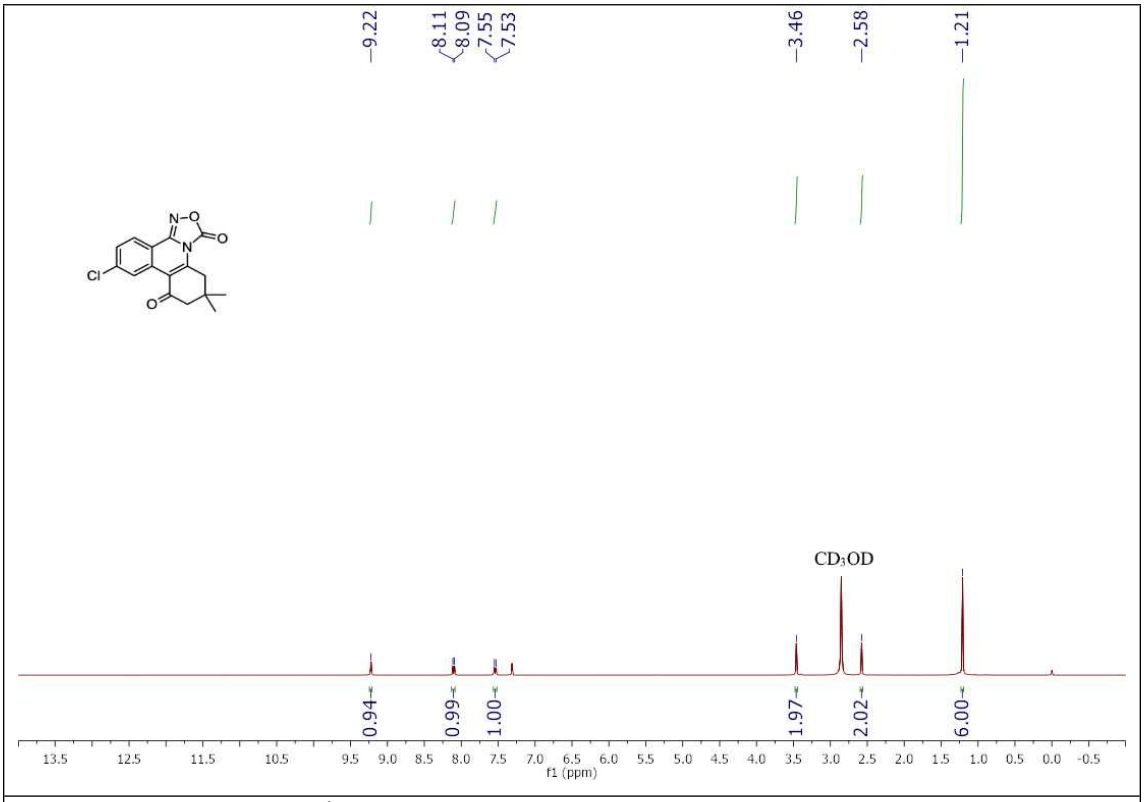
^{1}H NMR spectrum of **3b** (400 MHz, $CDCl_3$)



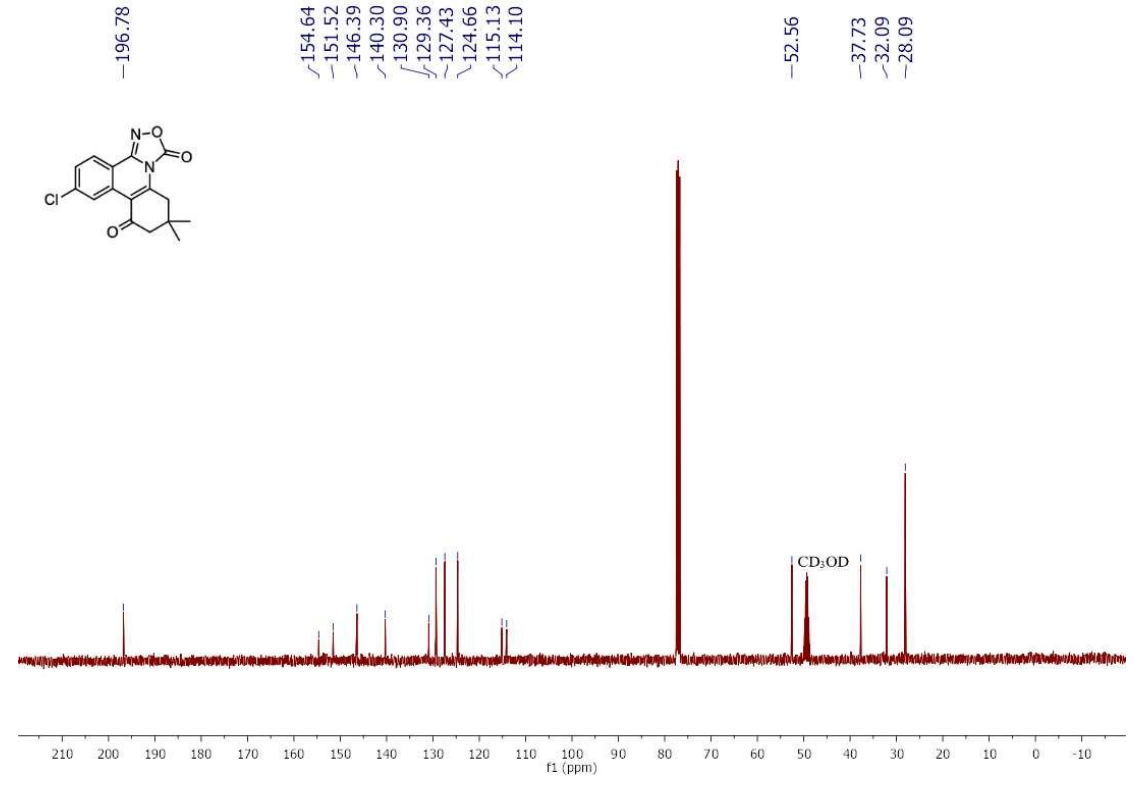
^{13}CNMR spectrum of **3b** (101 MHz, $CDCl_3$)



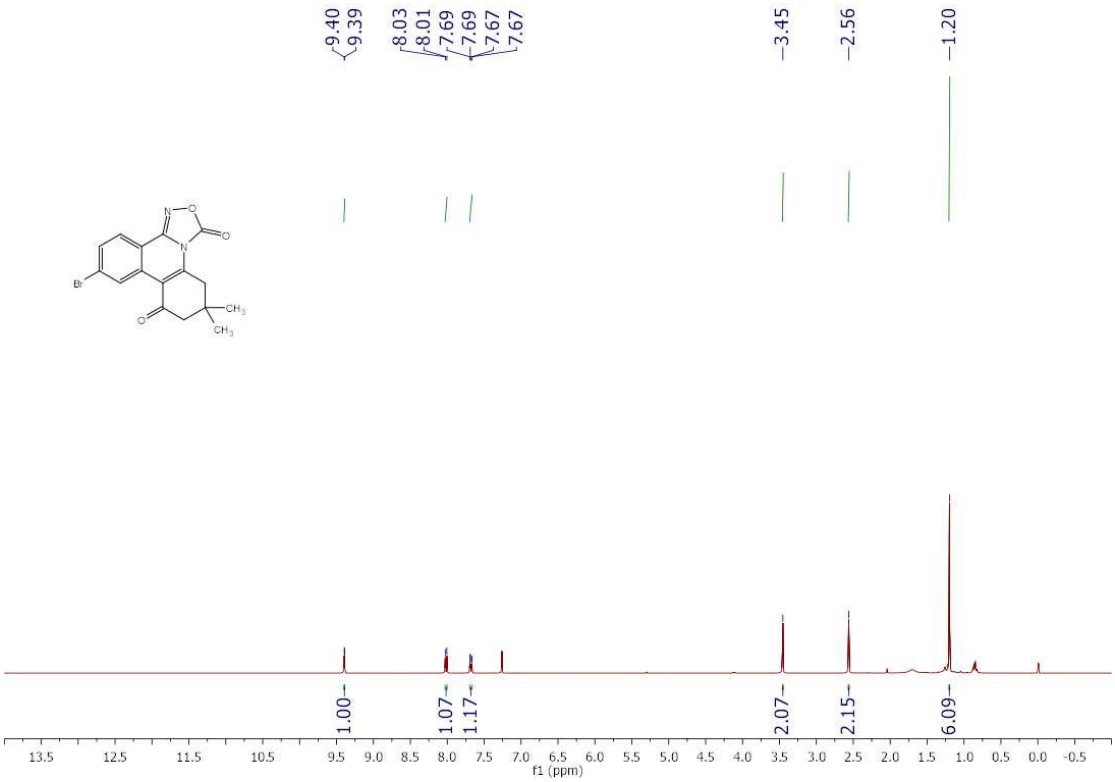
^{19}F NMR spectrum of **3b** (376 MHz, $CDCl_3$)



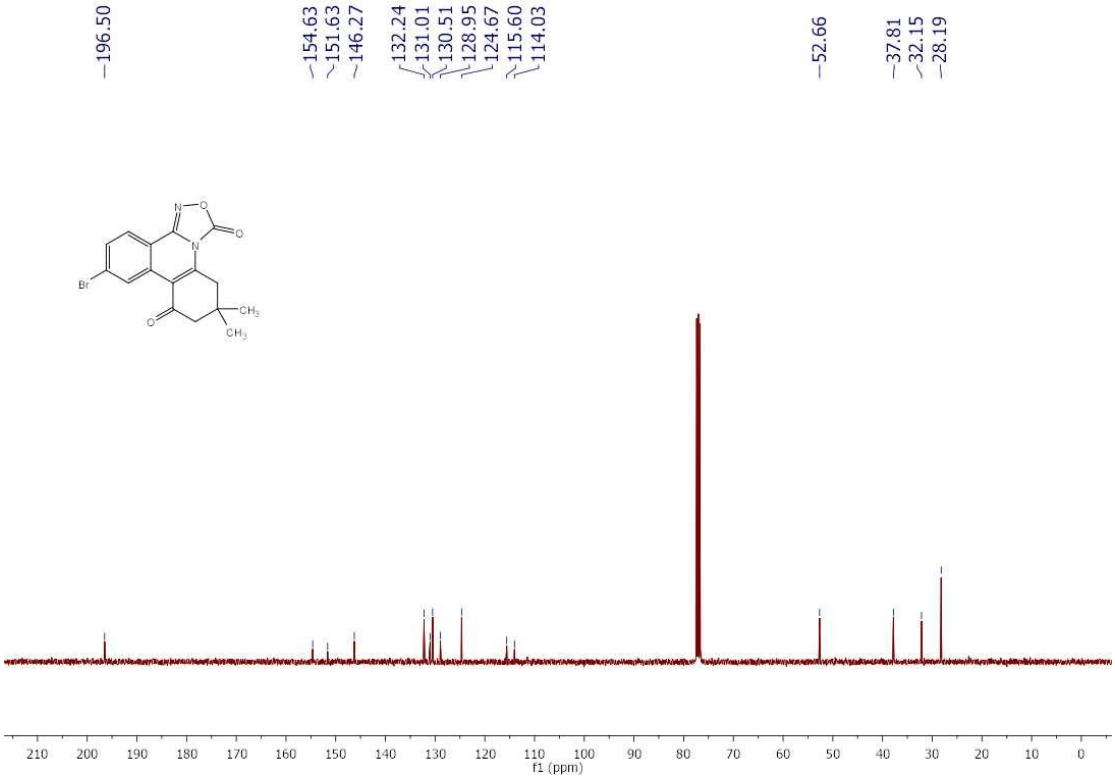
^{1}H NMR spectrum of **3c** (400 MHz, $CDCl_3$)



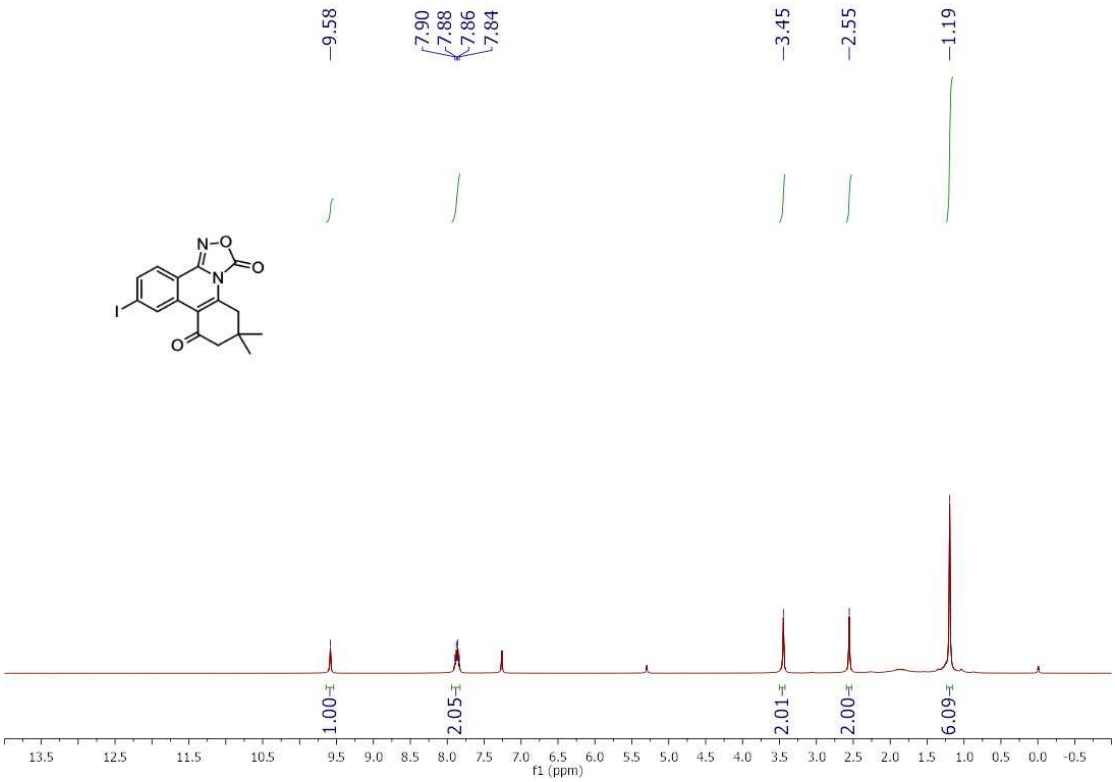
^{13}C NMR spectrum of **3c** (101 MHz, $CDCl_3$)



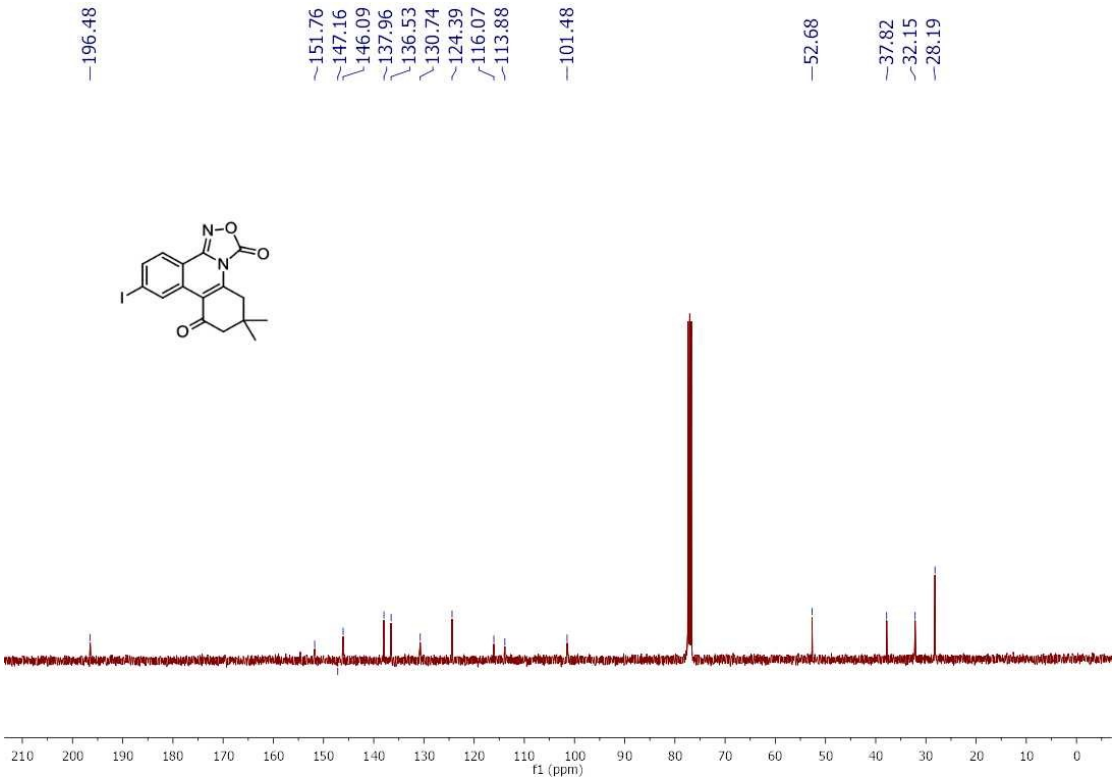
^{1}H NMR spectrum of **3d** (400 MHz, $CDCl_3$)



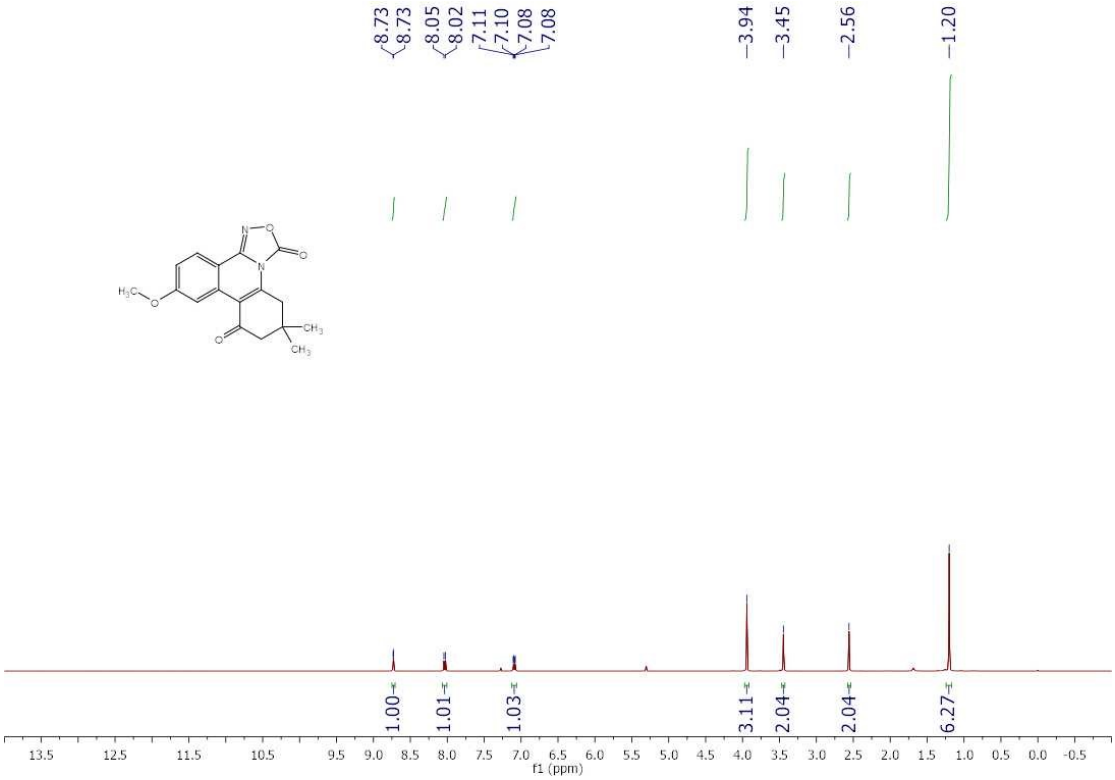
^{13}C NMR spectrum of **3d** (101 MHz, $CDCl_3$)



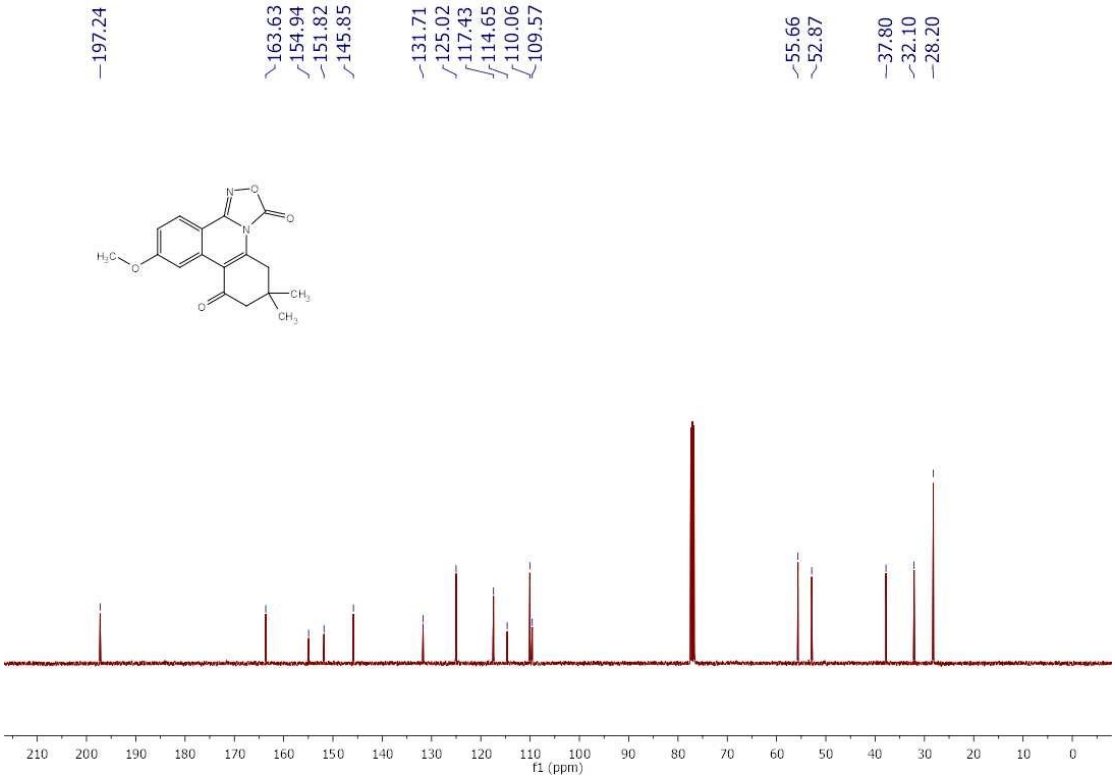
^{1}H NMR spectrum of **3e** (400 MHz, $CDCl_3$)



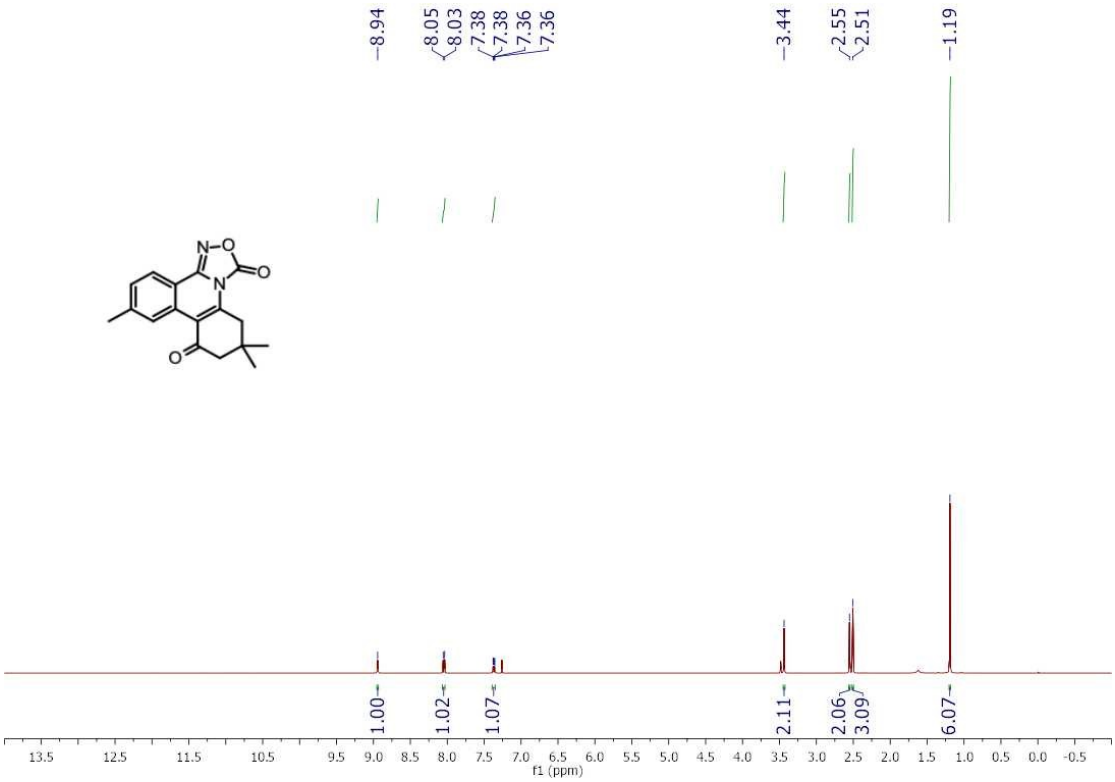
^{13}C NMR spectrum of **3e** (101 MHz, $CDCl_3$)



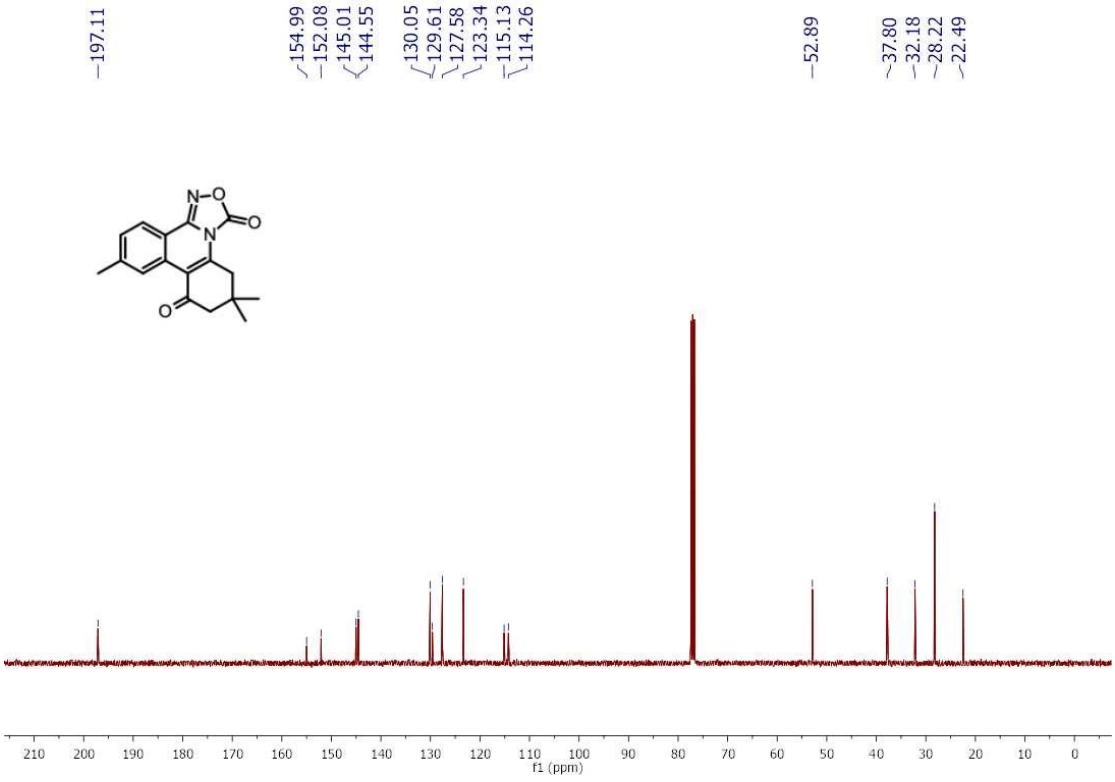
^{1}H NMR spectrum of **3f** (400 MHz, $CDCl_3$)



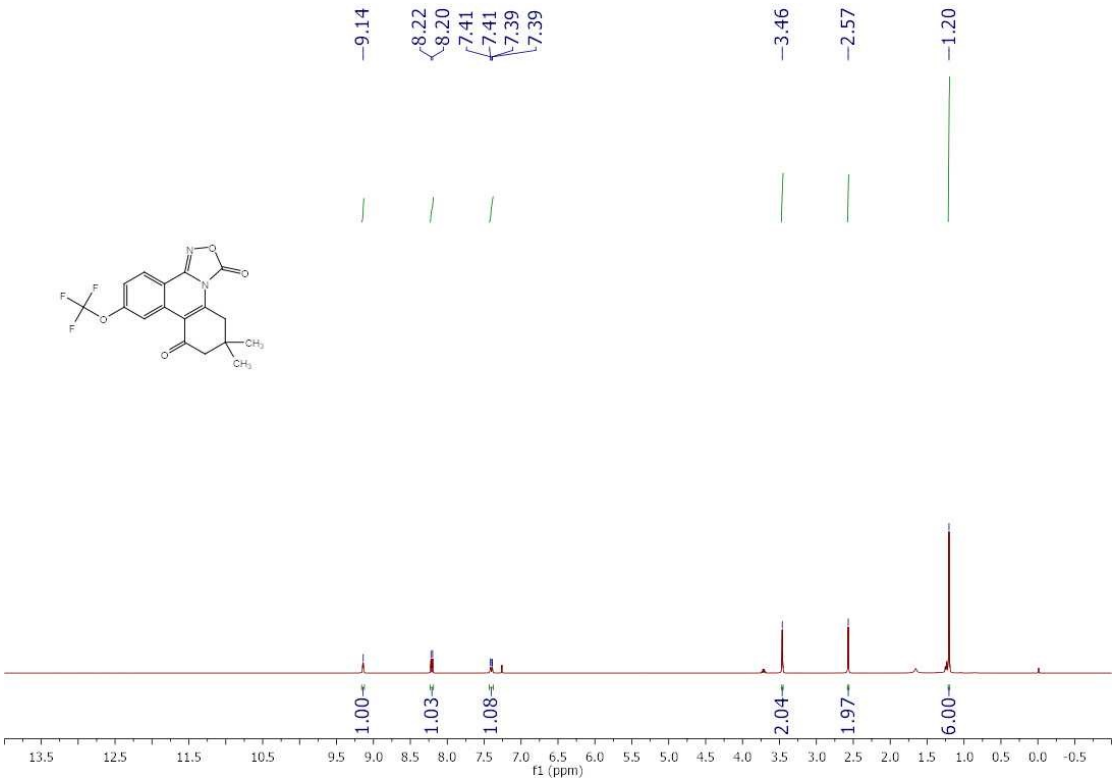
^{13}C NMR spectrum of **3f** (101 MHz, $CDCl_3$)



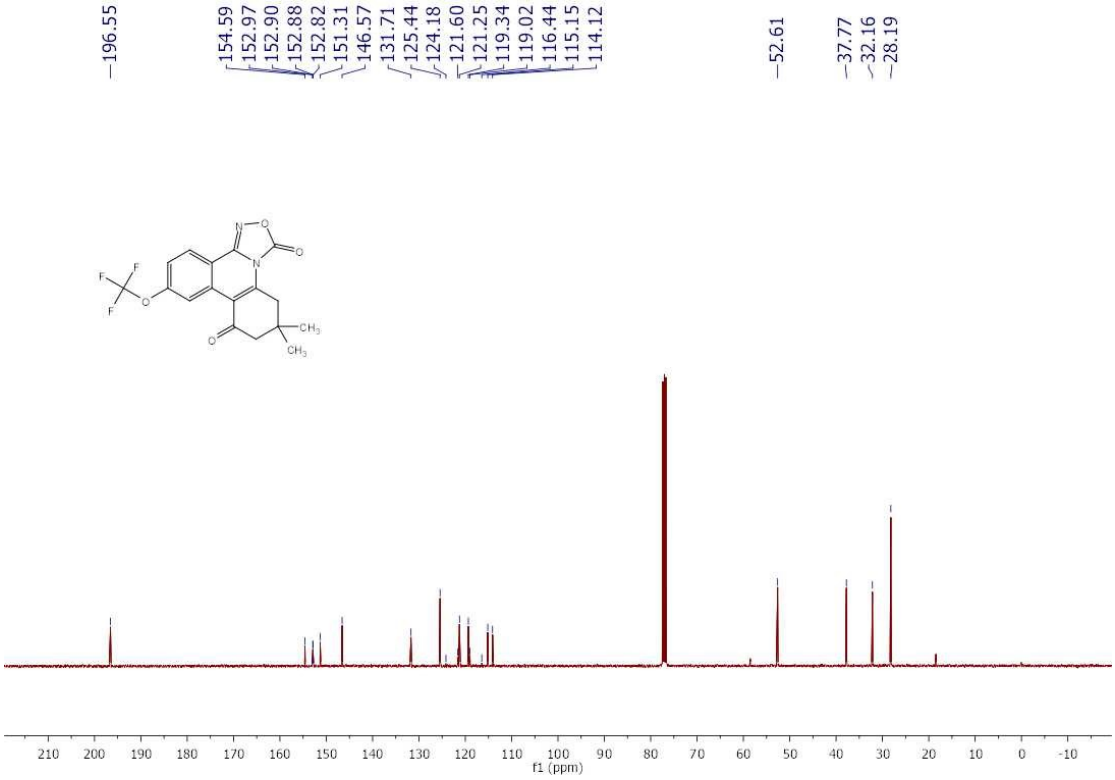
^{1}H NMR spectrum of **3g** (400 MHz, $CDCl_3$)



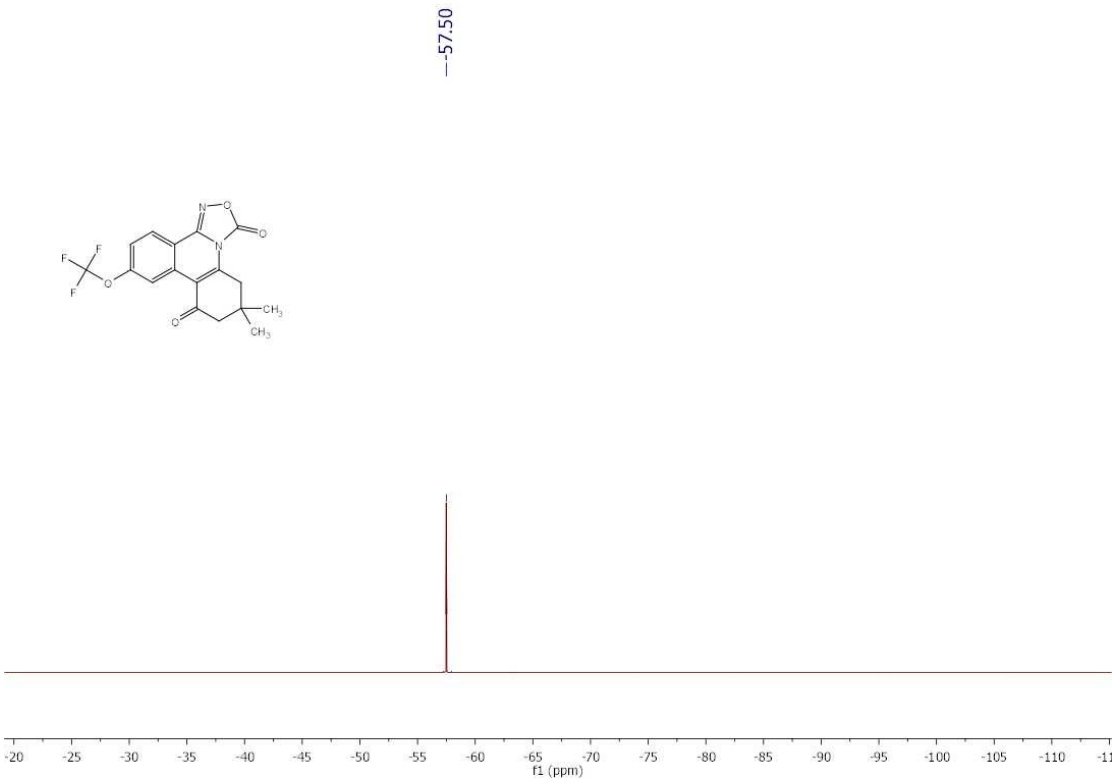
^{13}C NMR spectrum of **3g** (101 MHz, DMSO)



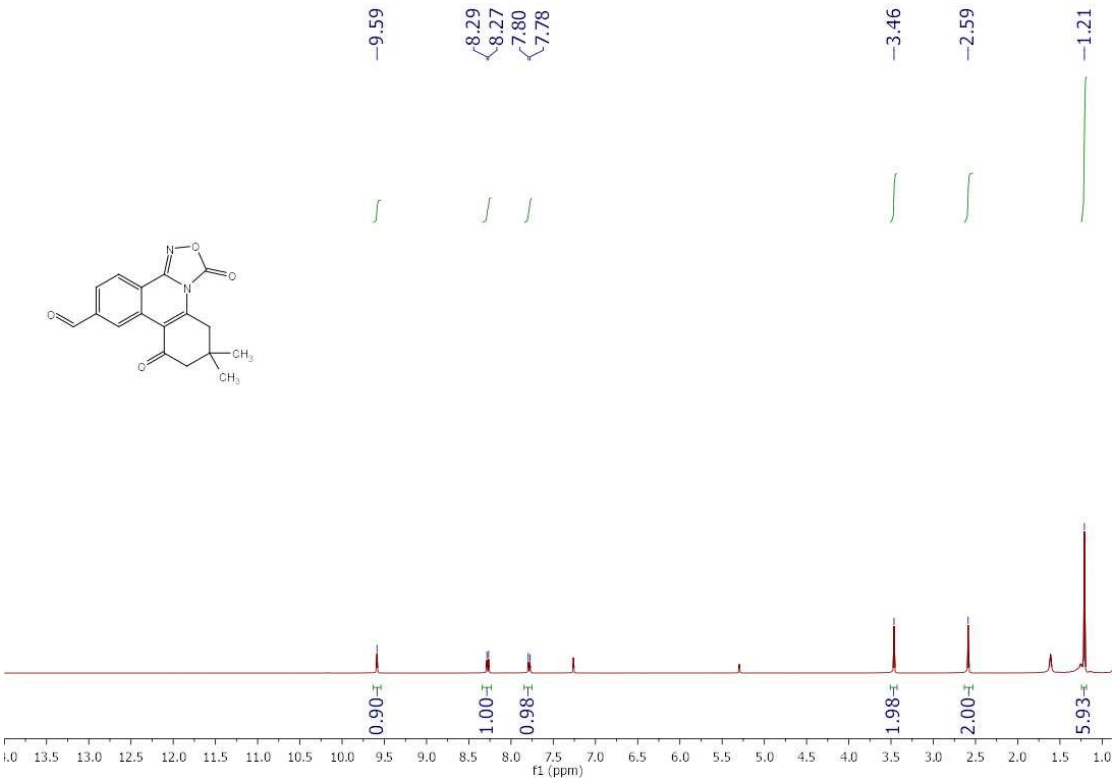
^{1}H NMR spectrum of **3h** (400 MHz, $CDCl_3$)



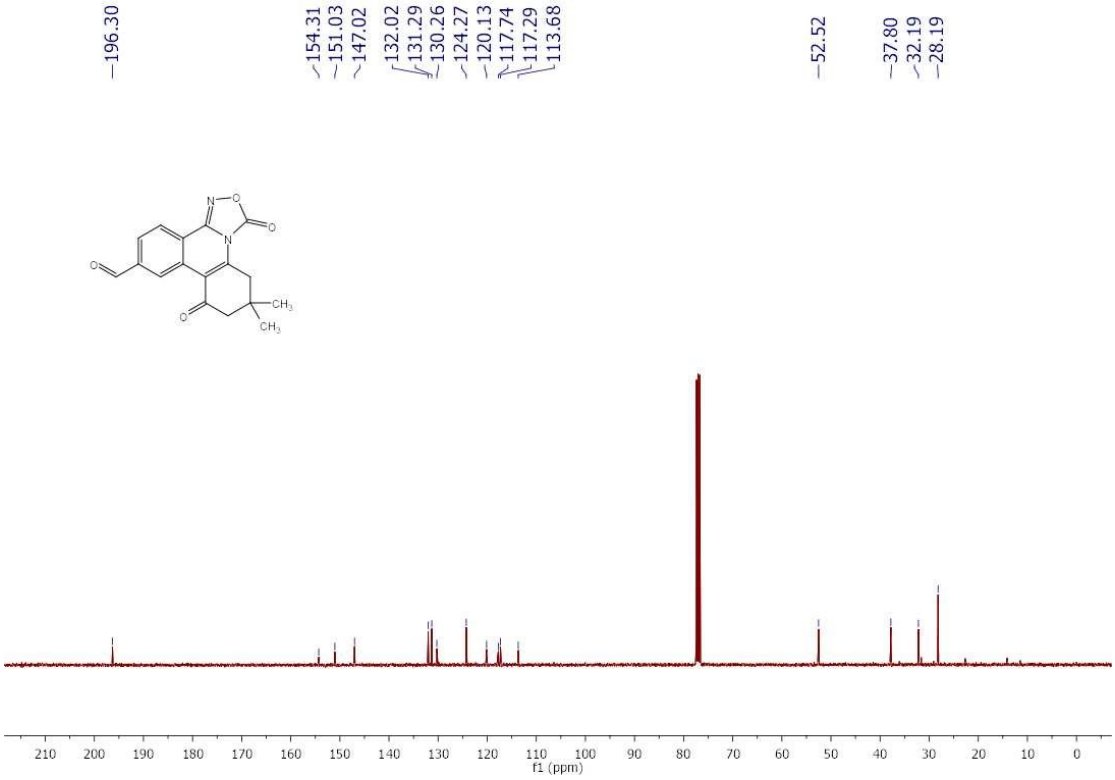
^{13}C NMR spectrum of **3h** (101 MHz, $CDCl_3$)



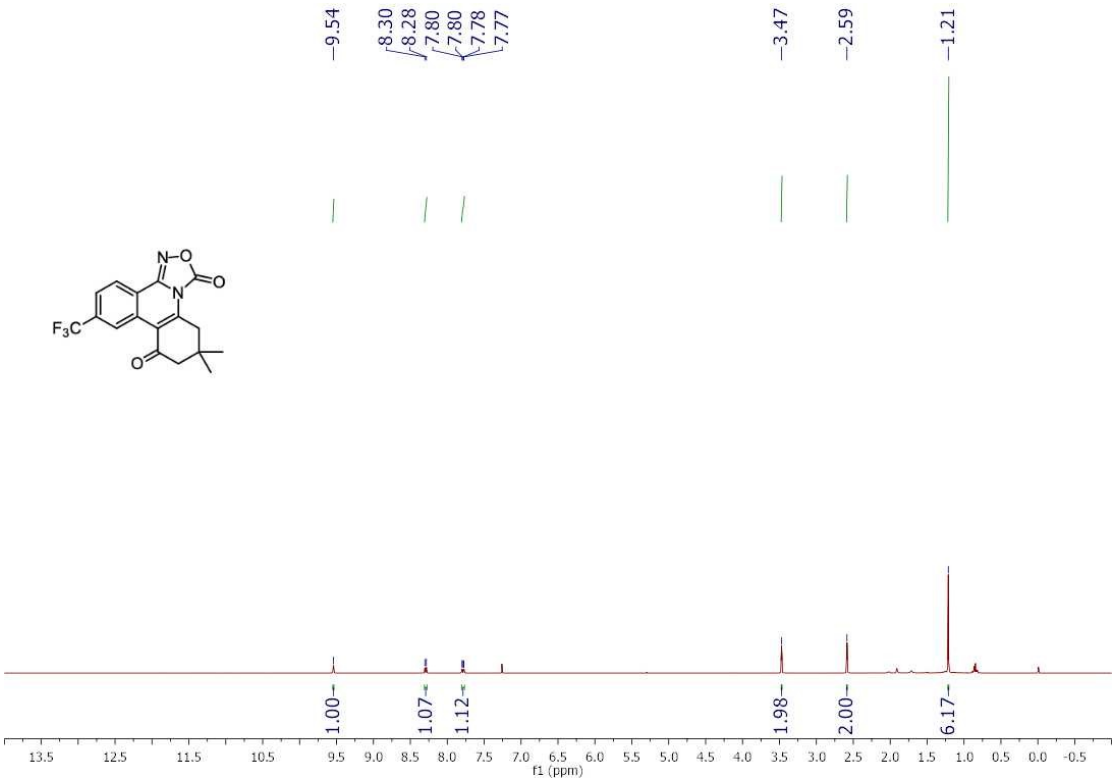
^{19}F NMR spectrum of **3h** (376 MHz, $CDCl_3$)



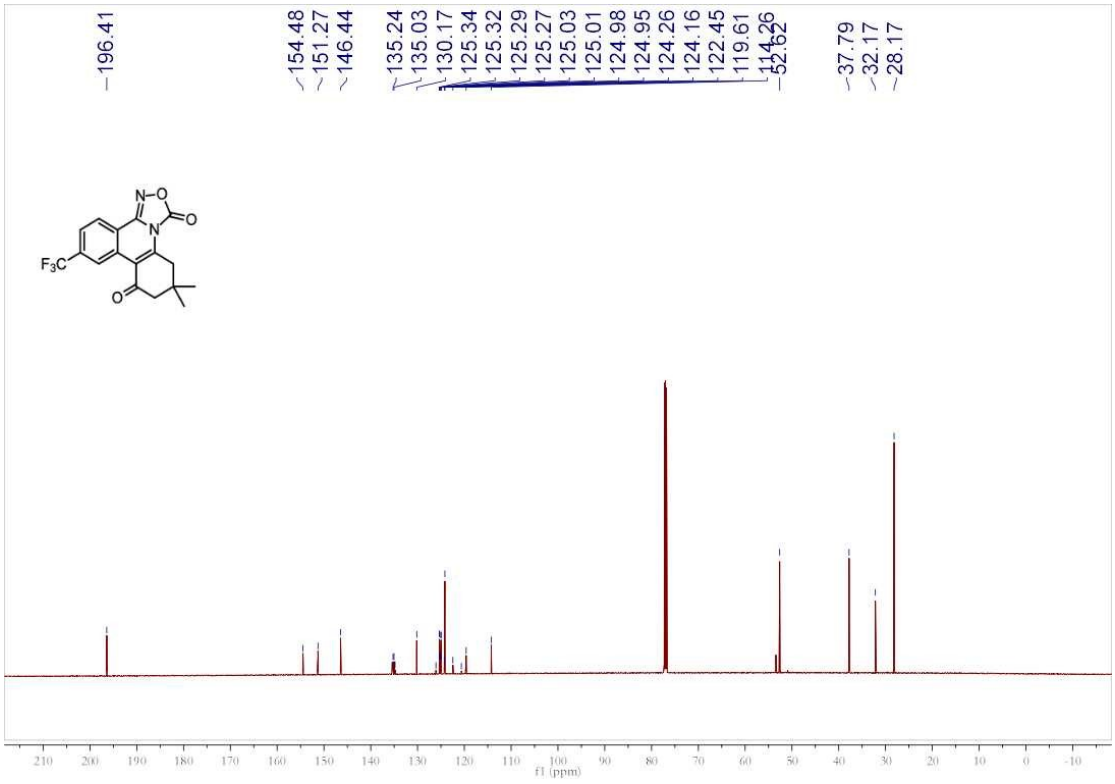
^{1}H NMR spectrum of **3i** (400 MHz, $CDCl_3$)



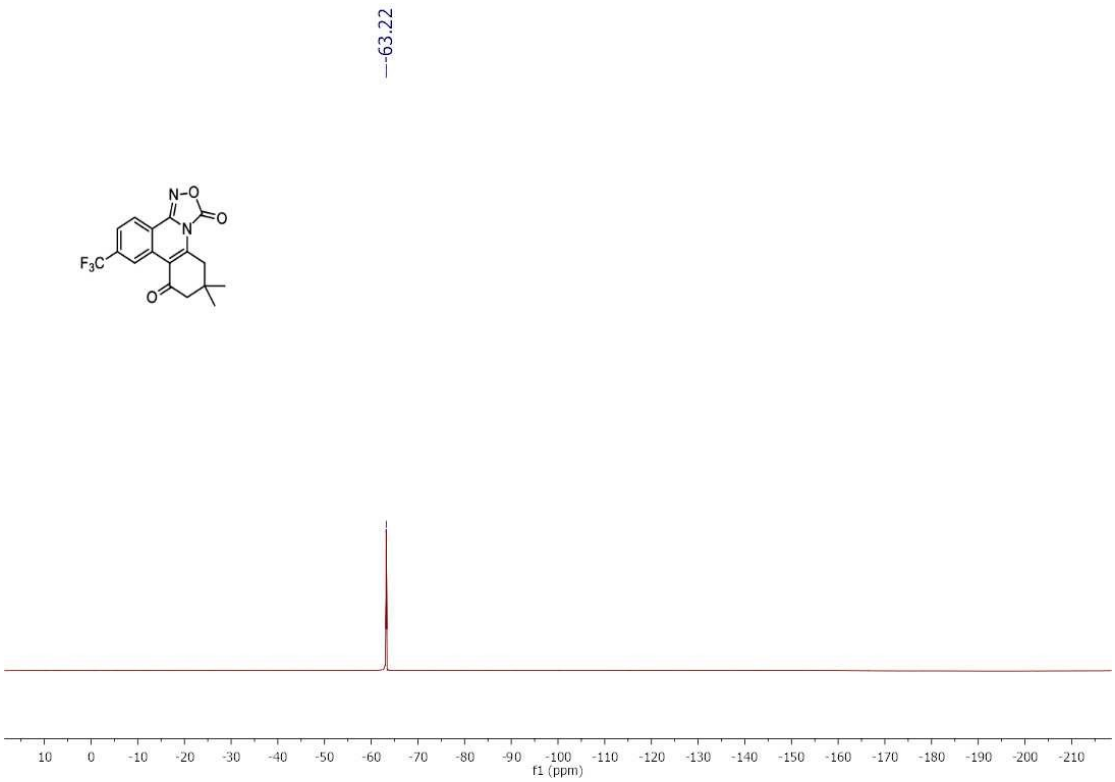
^{13}C NMR spectrum of **3i** (101 MHz, $CDCl_3$)



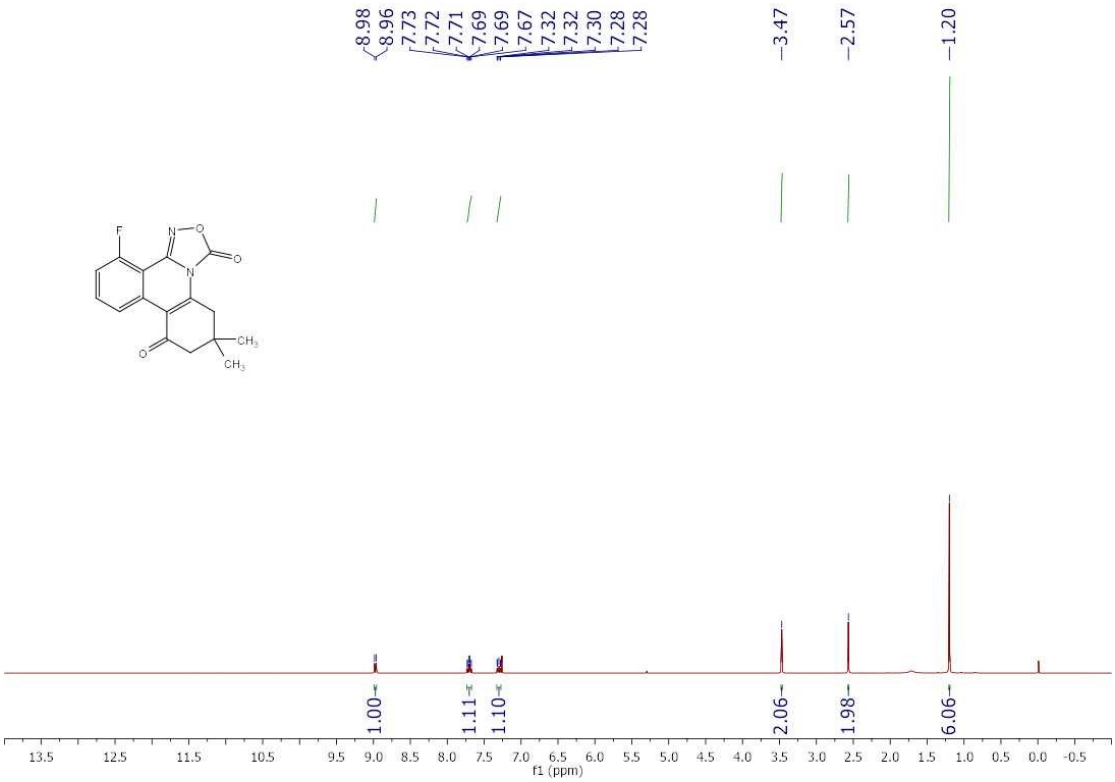
^{1}H NMR spectrum of **3j** (400 MHz, $CDCl_3$)



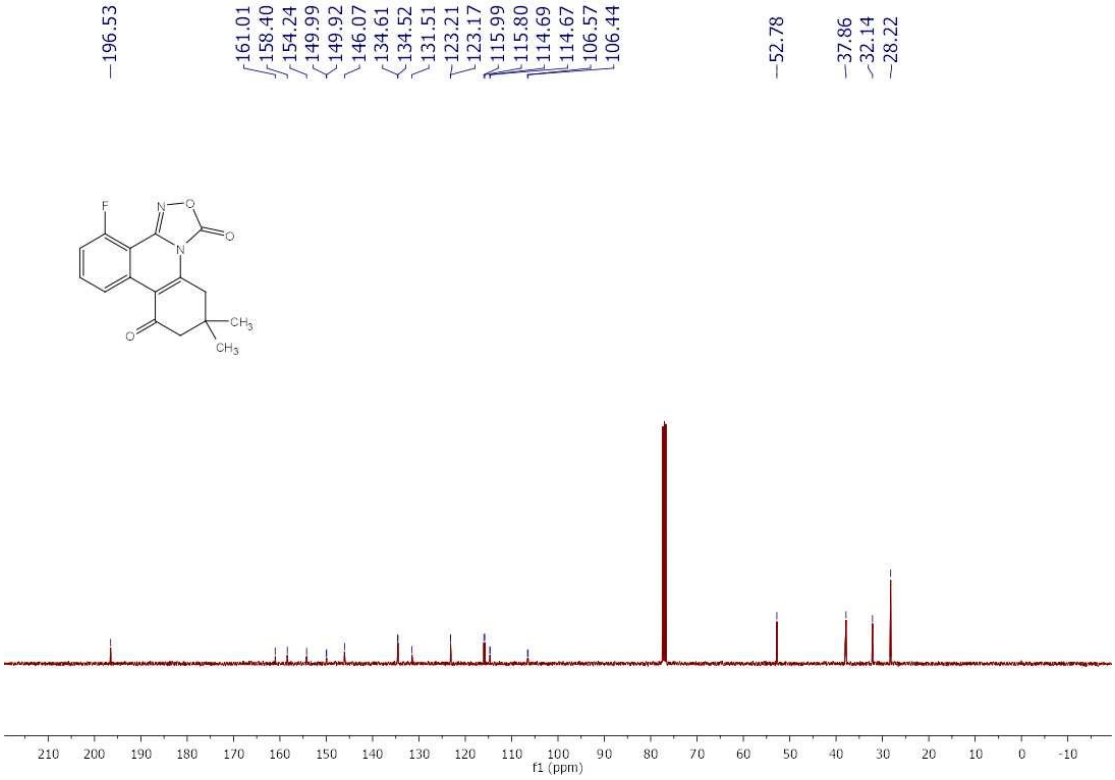
^{13}C NMR spectrum of **3j** (101 MHz, $CDCl_3$)



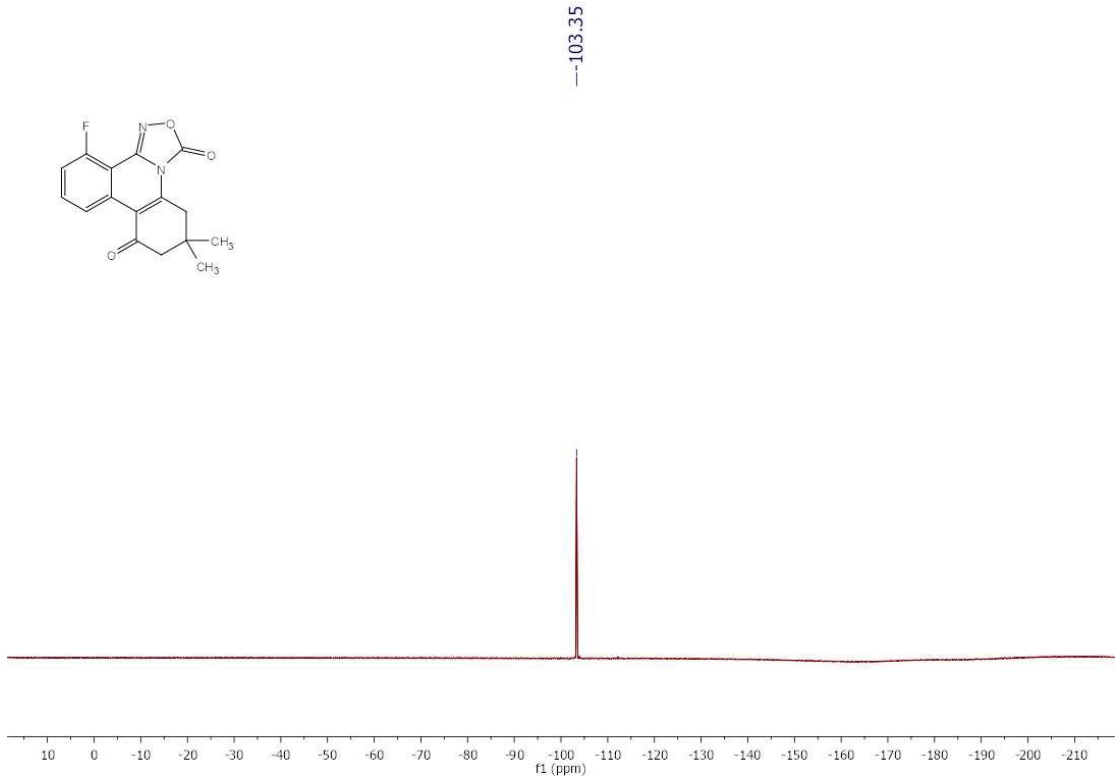
^{19}F NMR spectrum of **3j** (376 MHz, $CDCl_3$)



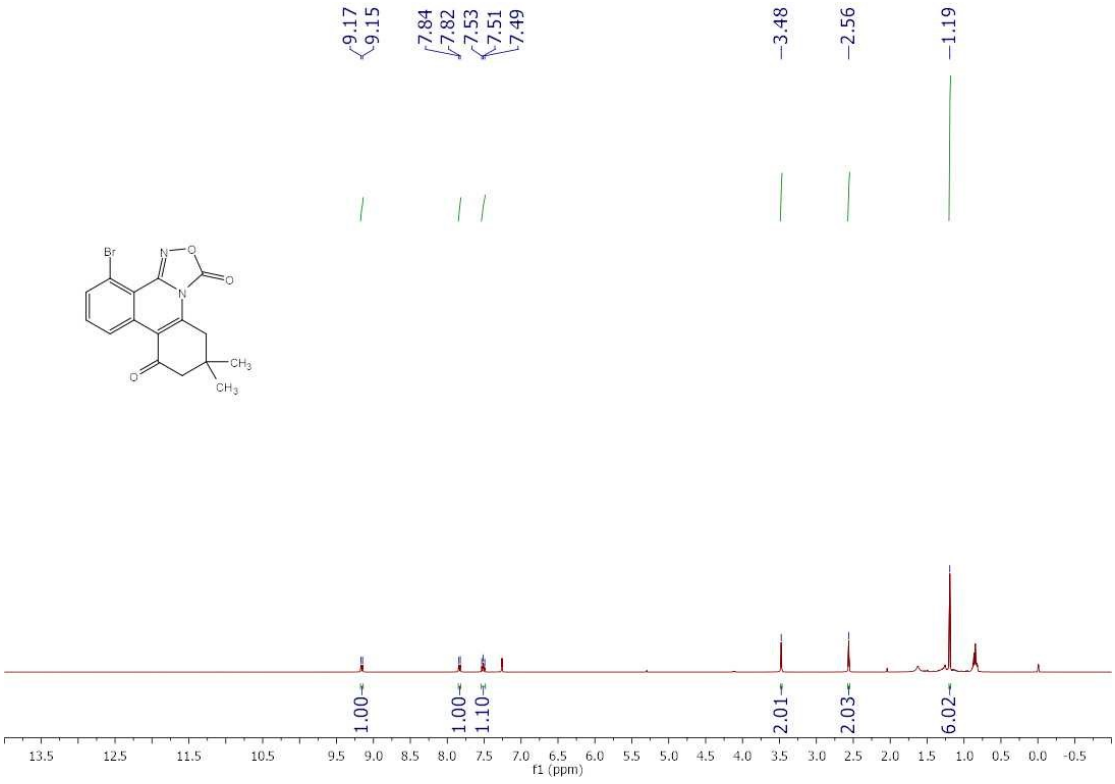
^{1}H NMR spectrum of **3k** (400 MHz, $CDCl_3$)



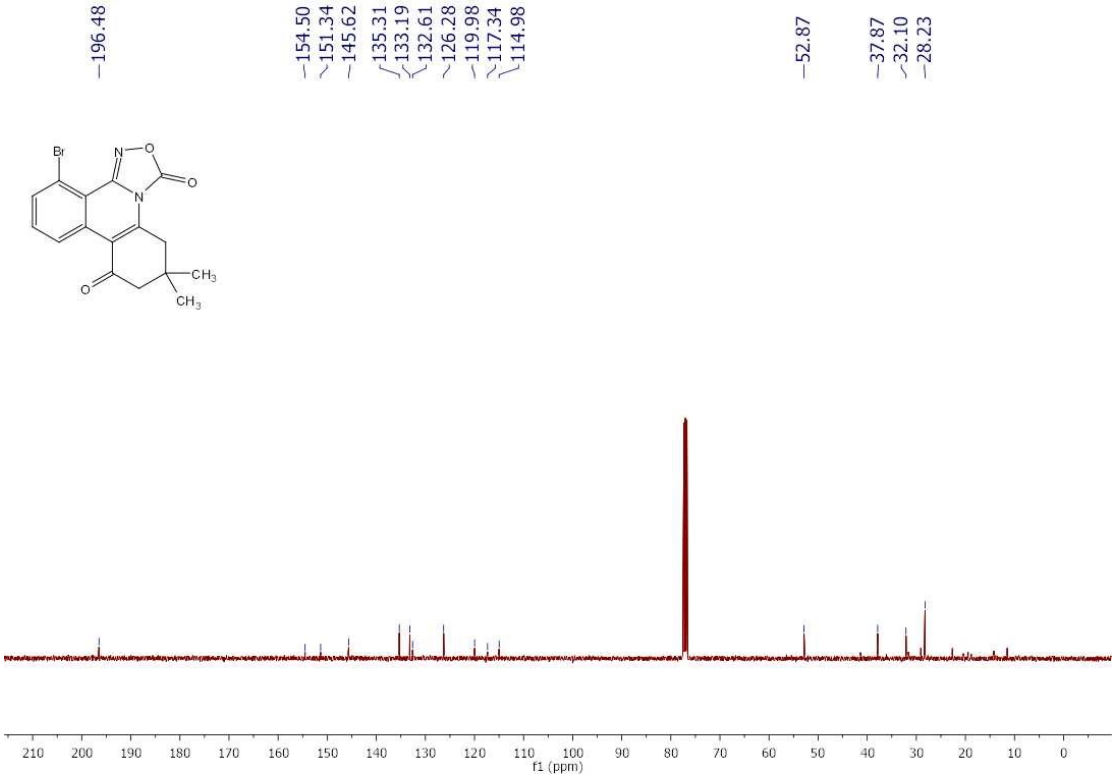
^{13}C NMR spectrum of **3k** (101 MHz, $CDCl_3$)



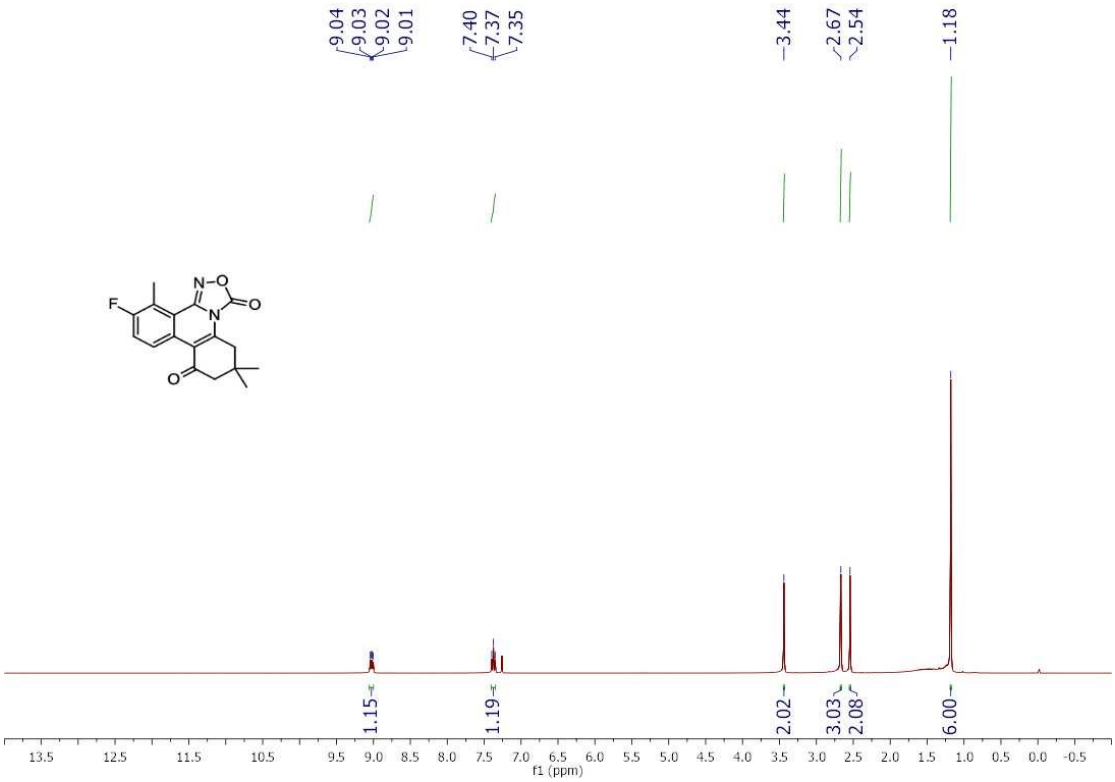
^{19}F NMR spectrum of **3k** (376 MHz, $CDCl_3$)



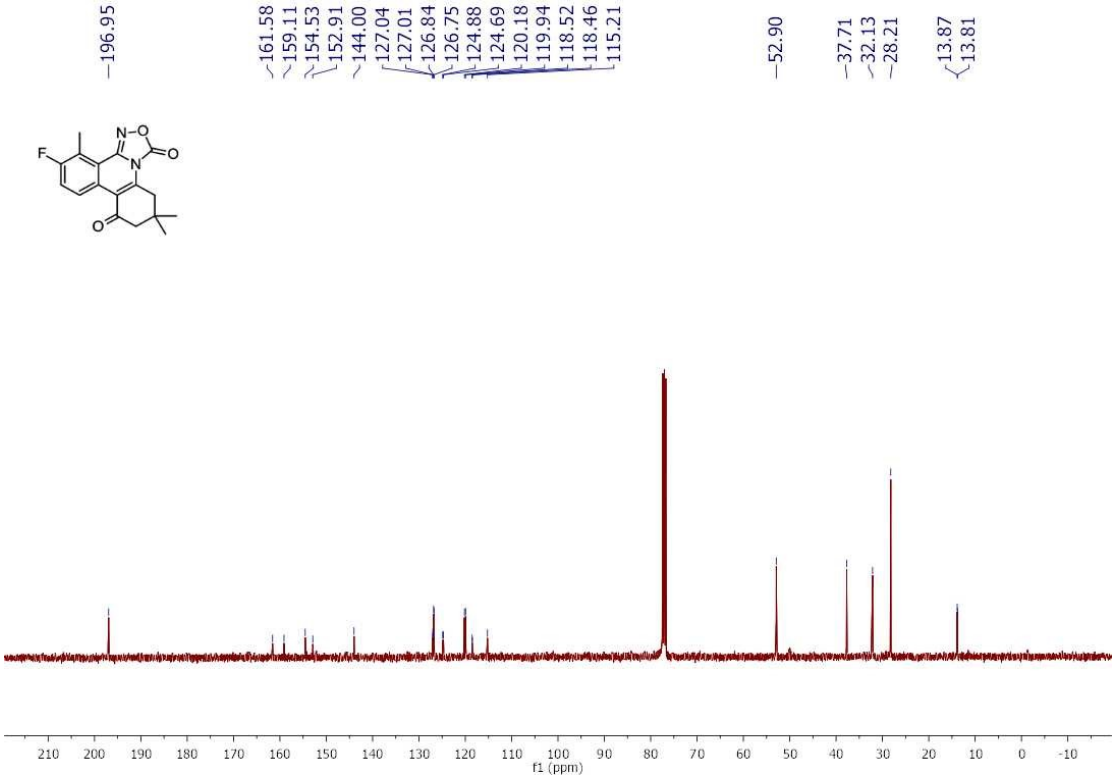
^{1}H NMR spectrum of **3l** (400 MHz, $CDCl_3$)



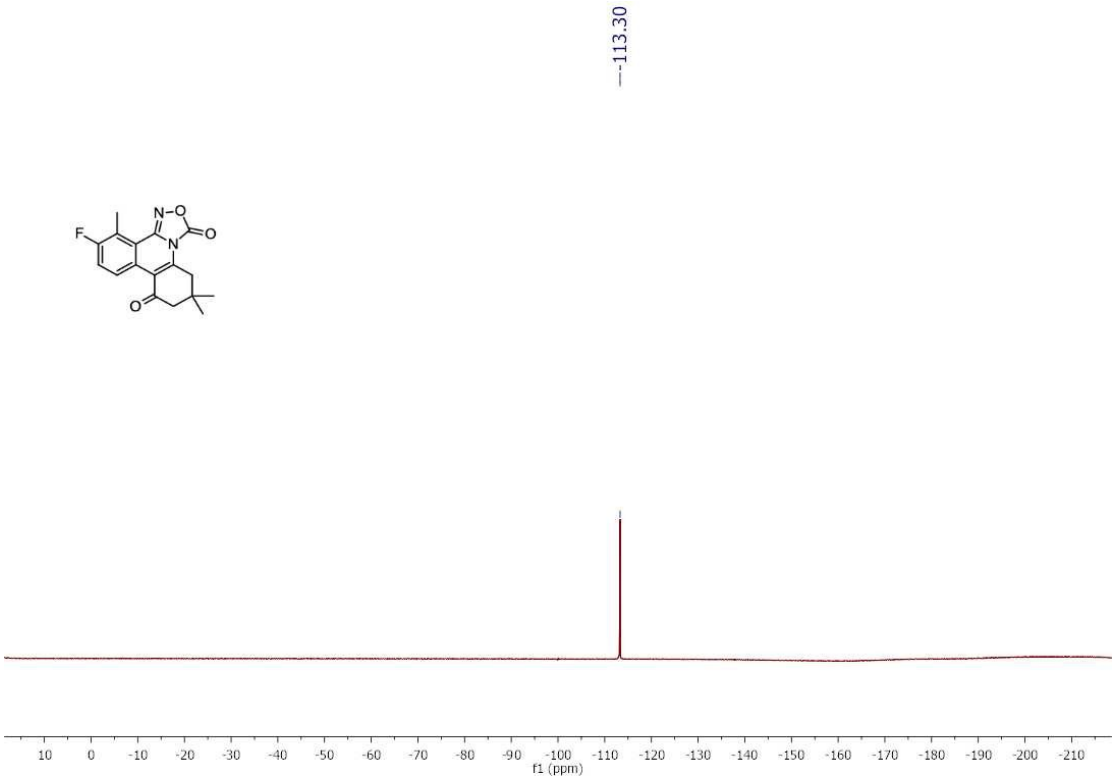
^{13}C NMR spectrum of **3l** (101 MHz, $CDCl_3$)



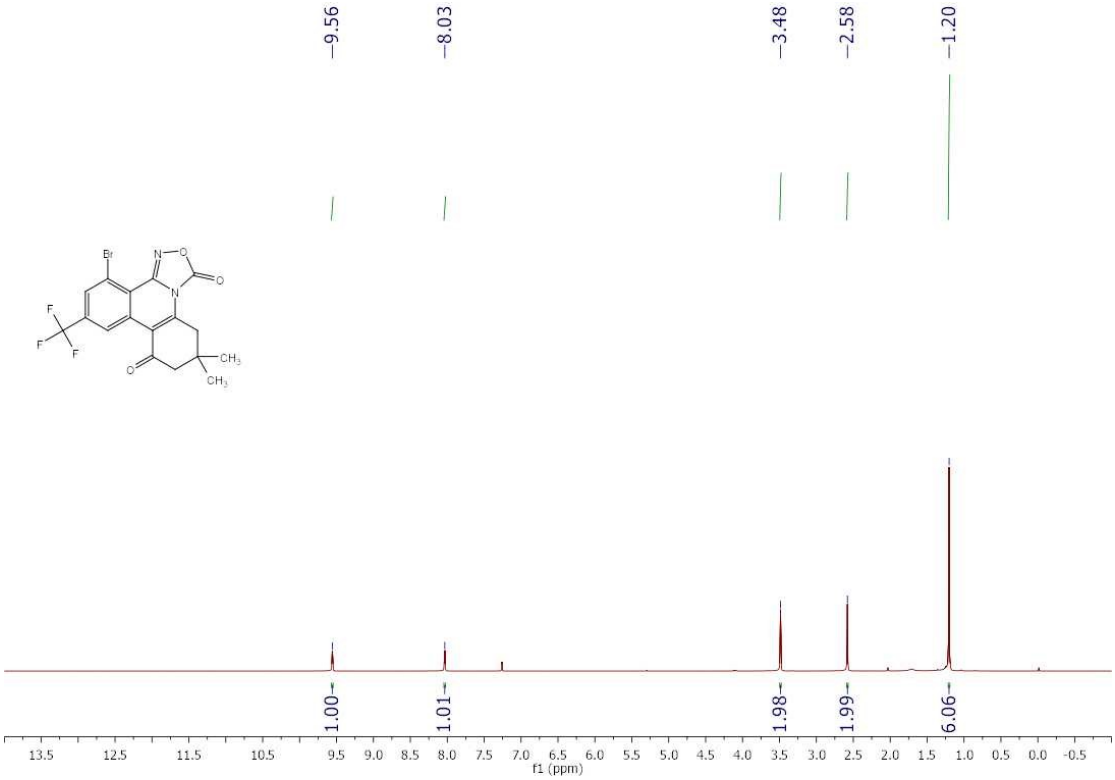
^{1}H NMR spectrum of **3m** (400 MHz, $CDCl_3$)



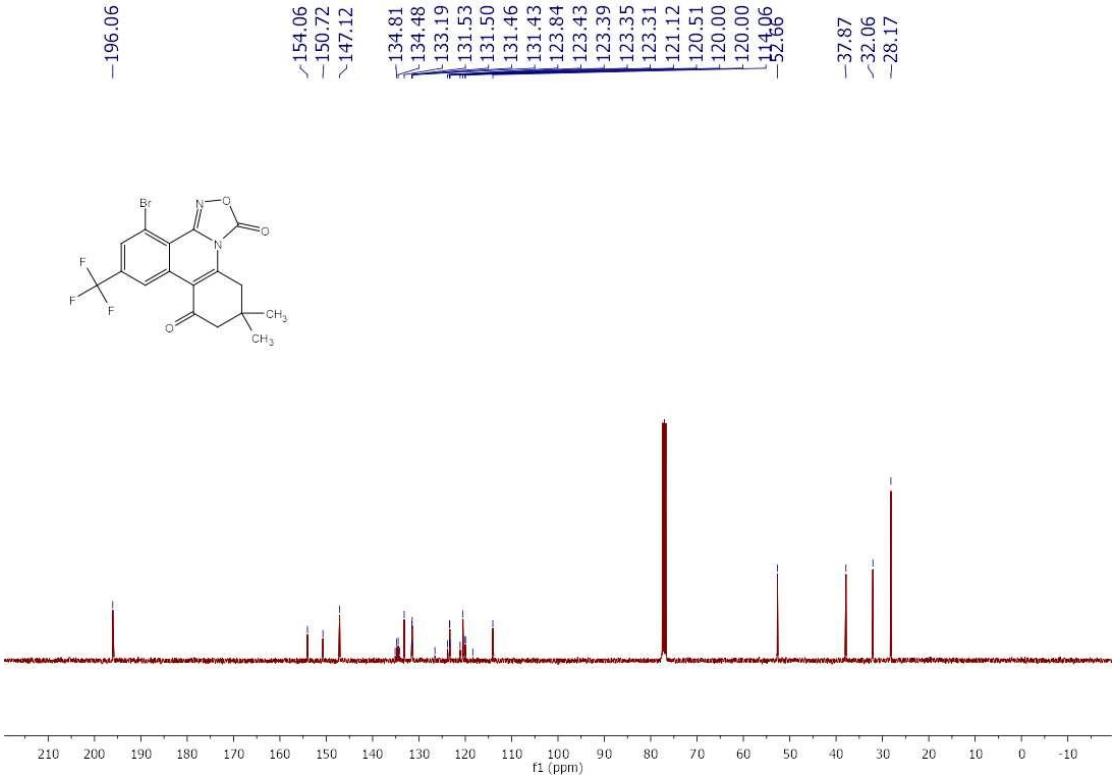
^{13}C NMR spectrum of **3m** (101 MHz, $CDCl_3$)



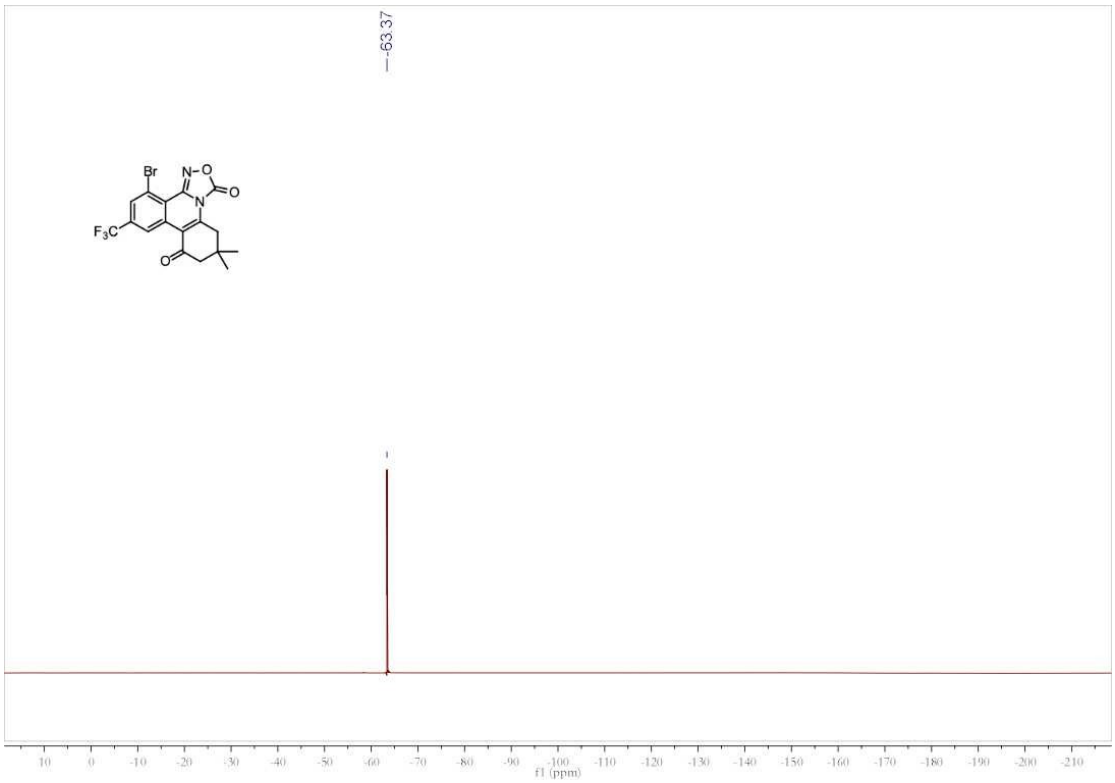
^{19}F NMR spectrum of **3m** (376 MHz, $CDCl_3$)



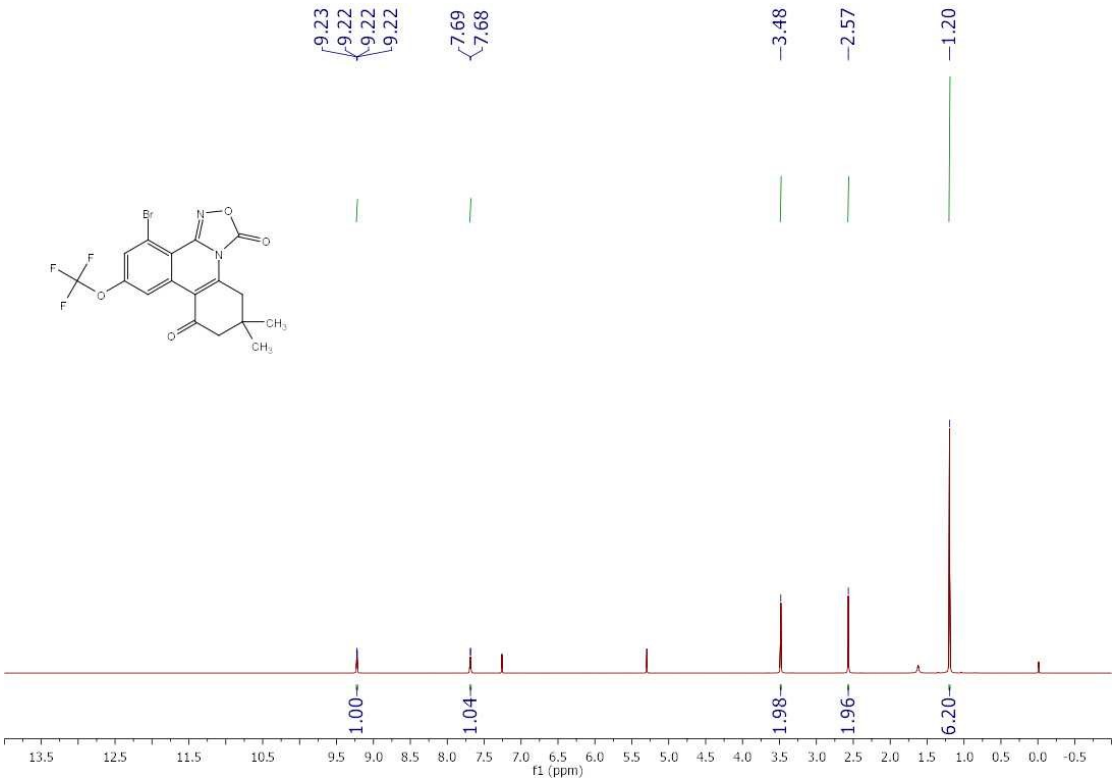
^{1}H NMR spectrum of **3n** (400 MHz, $CDCl_3$)



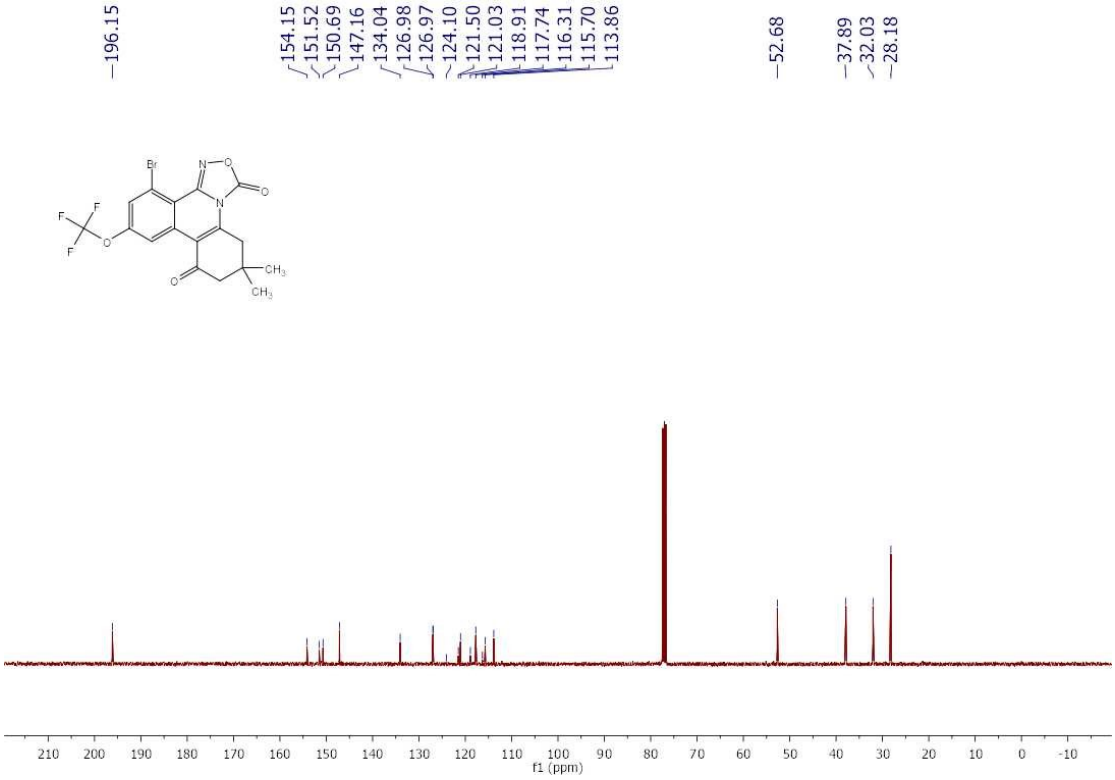
^{13}C NMR spectrum of **3n** (101 MHz, $CDCl_3$)



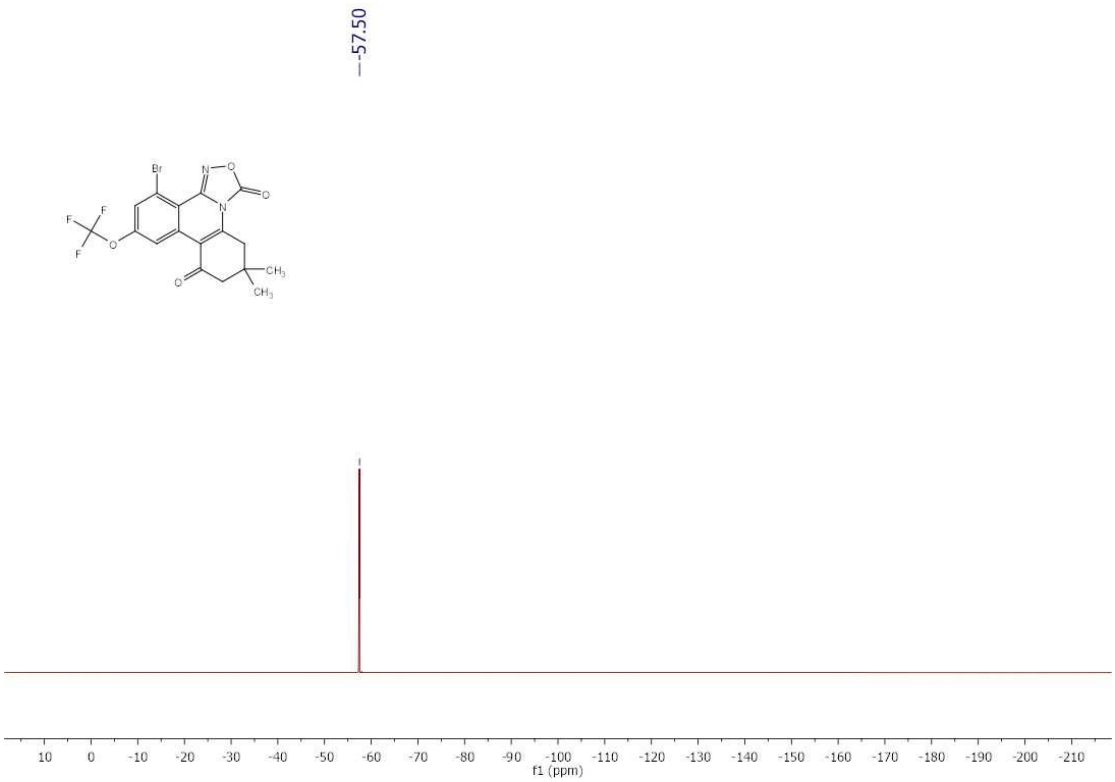
^{19}F NMR spectrum of **3n** (376 MHz, $CDCl_3$)



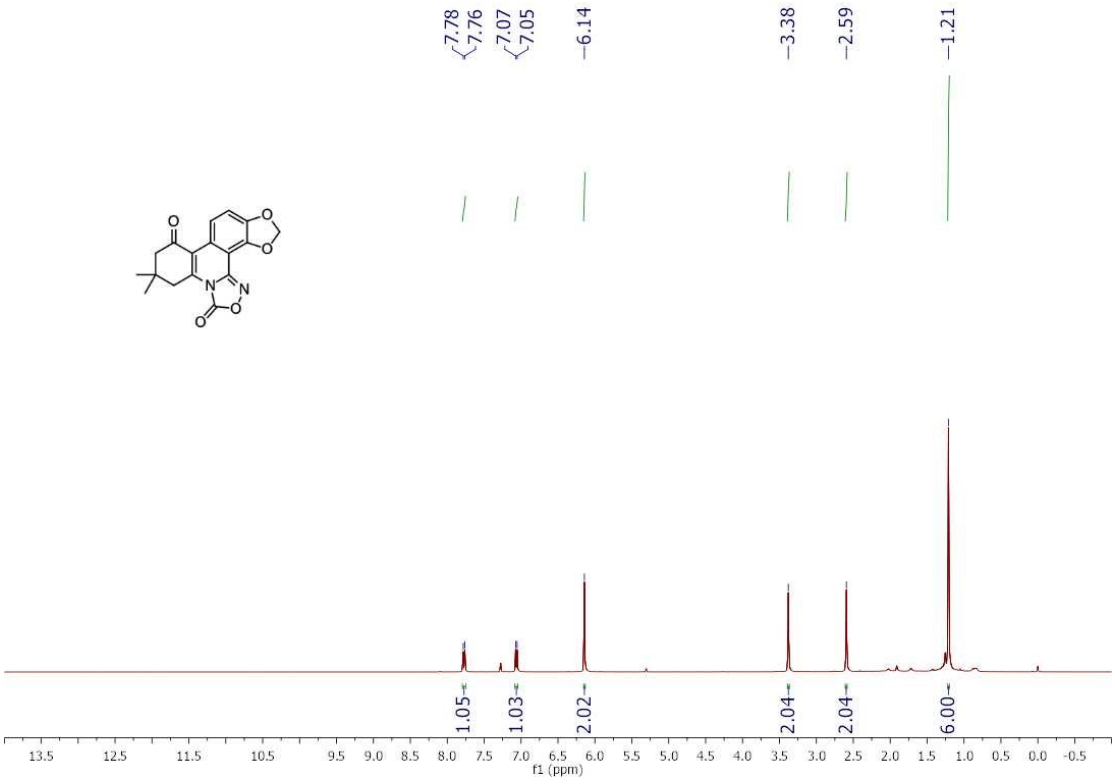
^{1}H NMR spectrum of **3o** (400 MHz, $CDCl_3$)



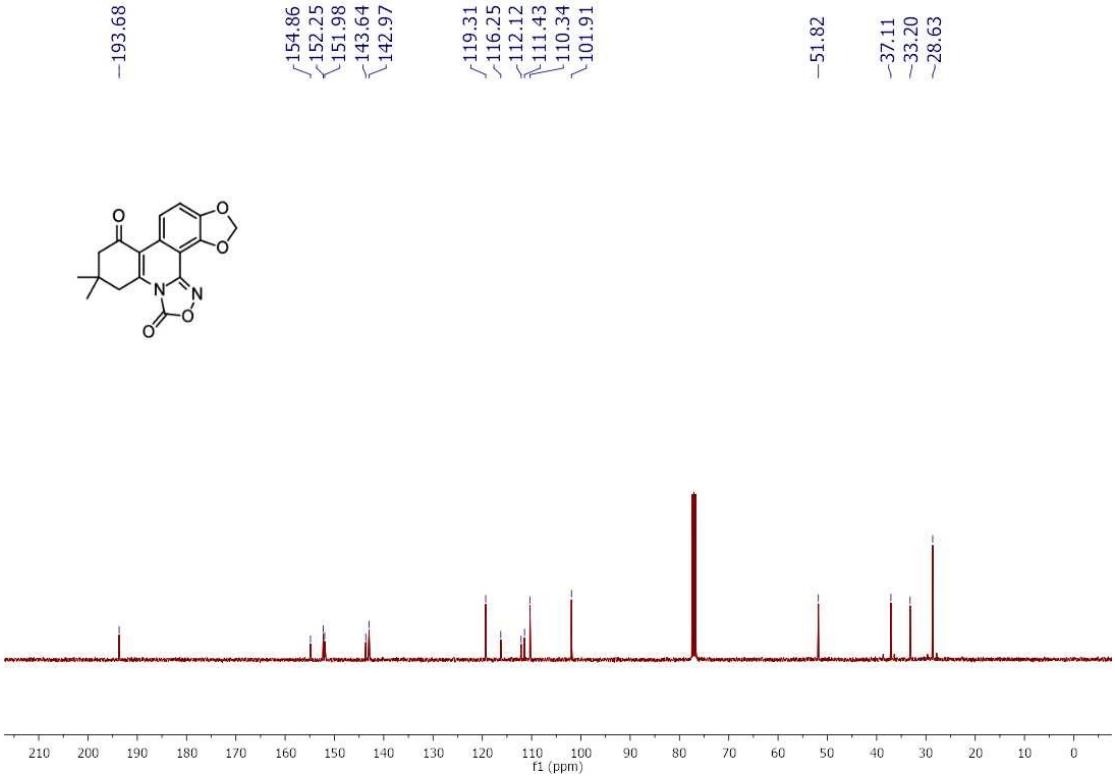
^{13}C NMR spectrum of **3o** (101 MHz, $CDCl_3$)



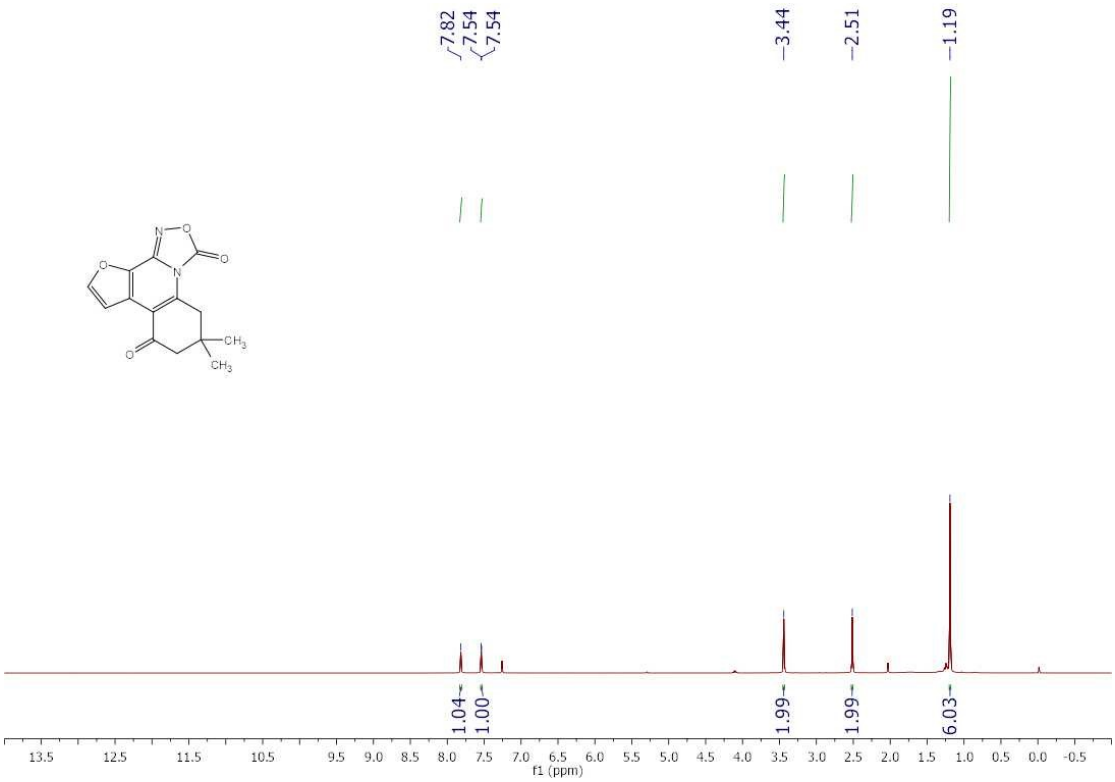
^{19}F NMR spectrum of **3o** (376 MHz, $CDCl_3$)



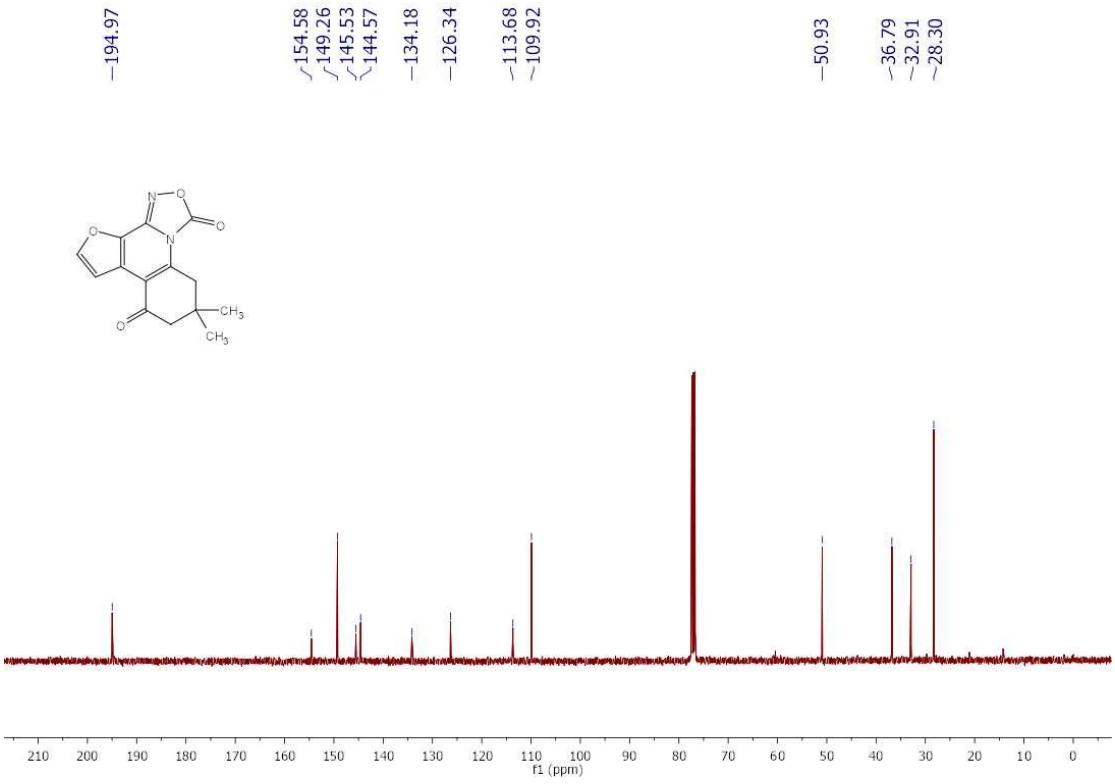
^{1}H NMR spectrum of **3p** (400 MHz, $CDCl_3$)



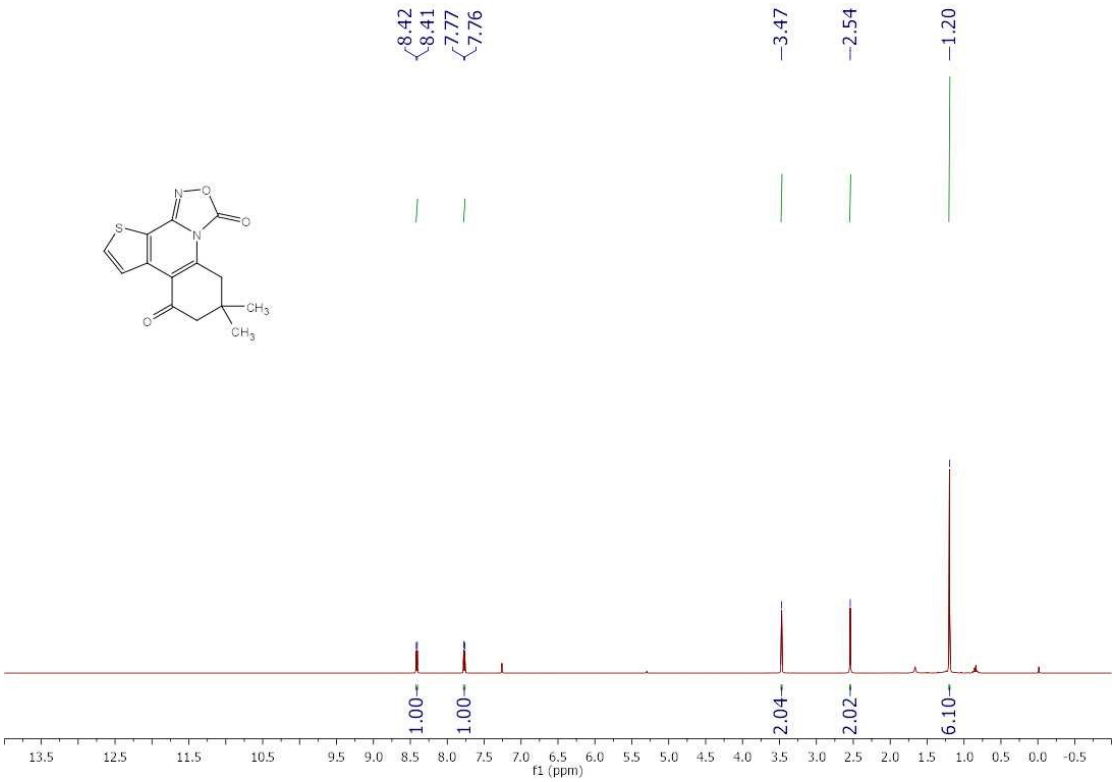
^{13}C NMR spectrum of **3p** (101 MHz, $CDCl_3$)



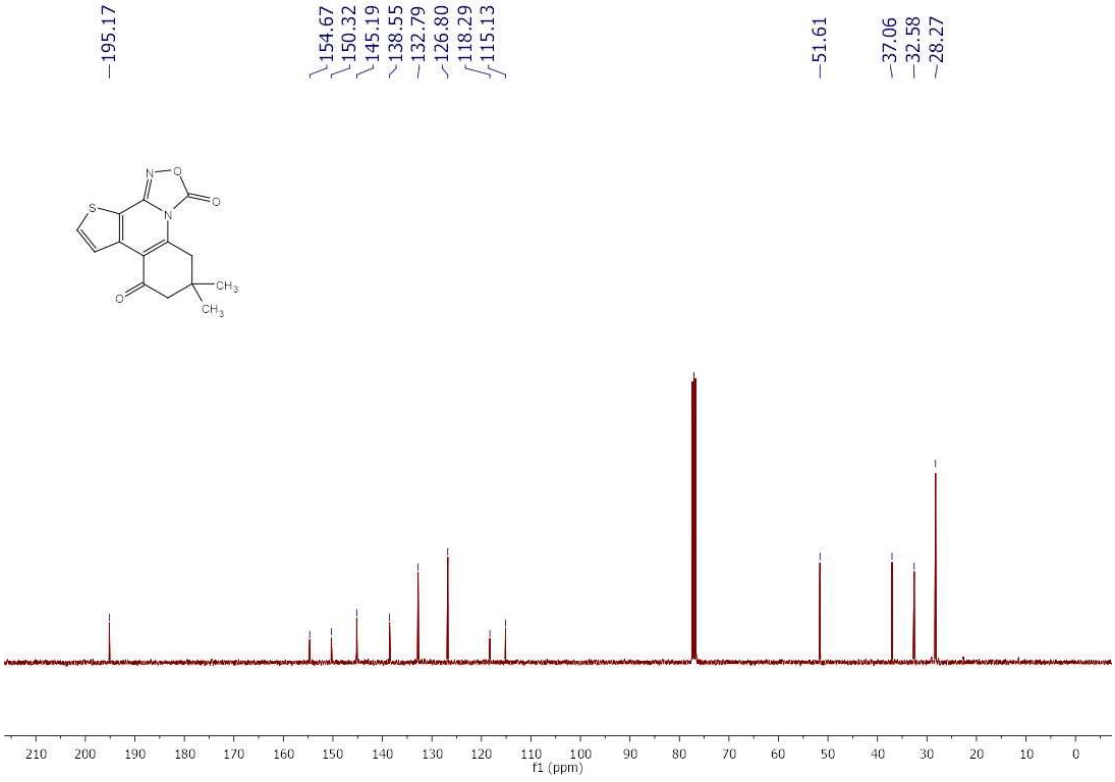
^{1}H NMR spectrum of **3q** (400 MHz, $CDCl_3$)



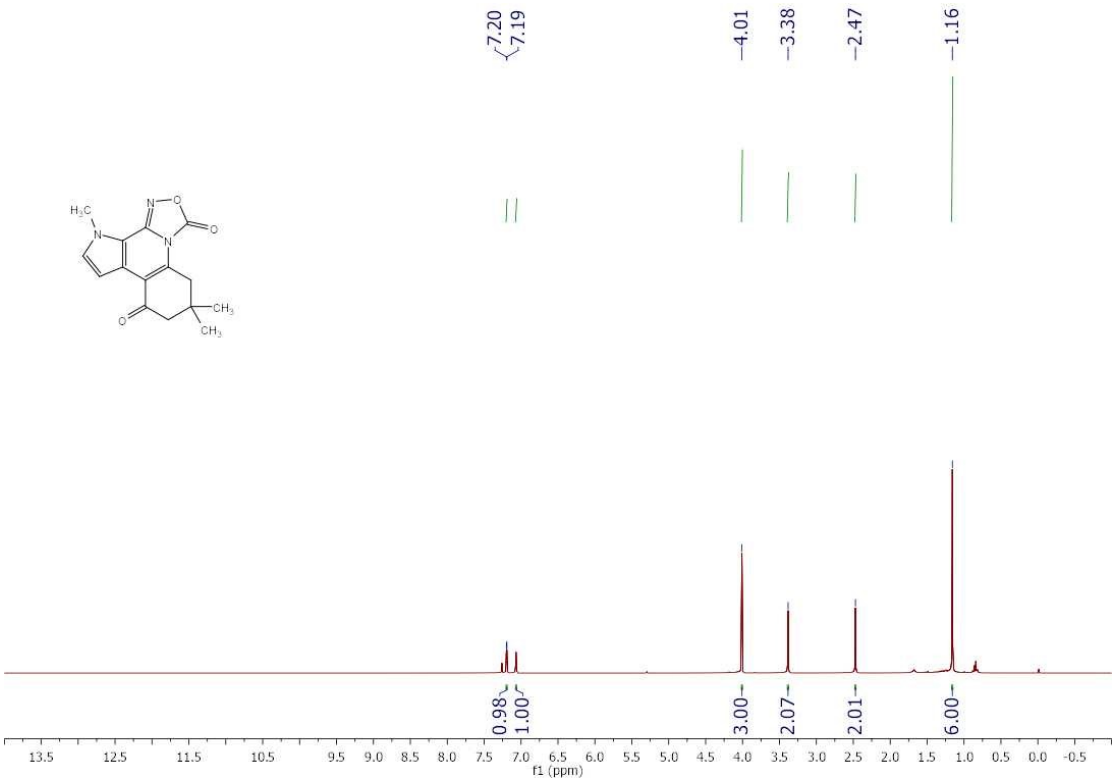
^{13}C NMR spectrum of **3q** (101 MHz, $CDCl_3$)



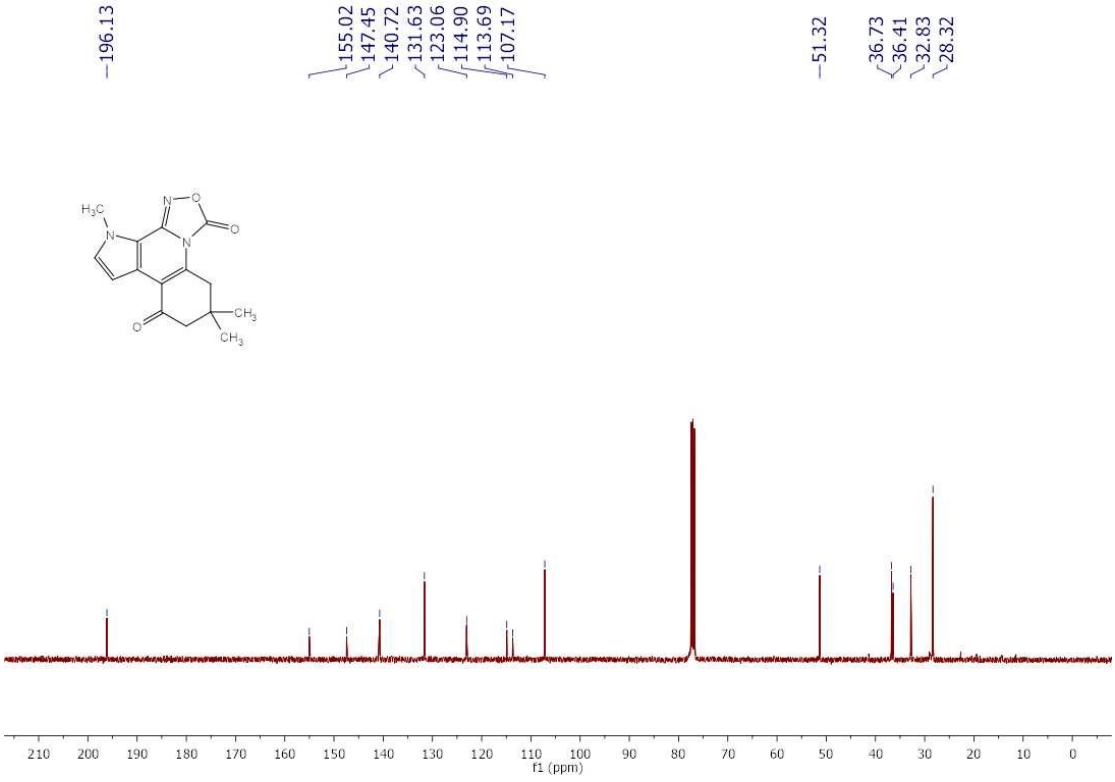
^{1}H NMR spectrum of **3r** (400 MHz, $CDCl_3$)



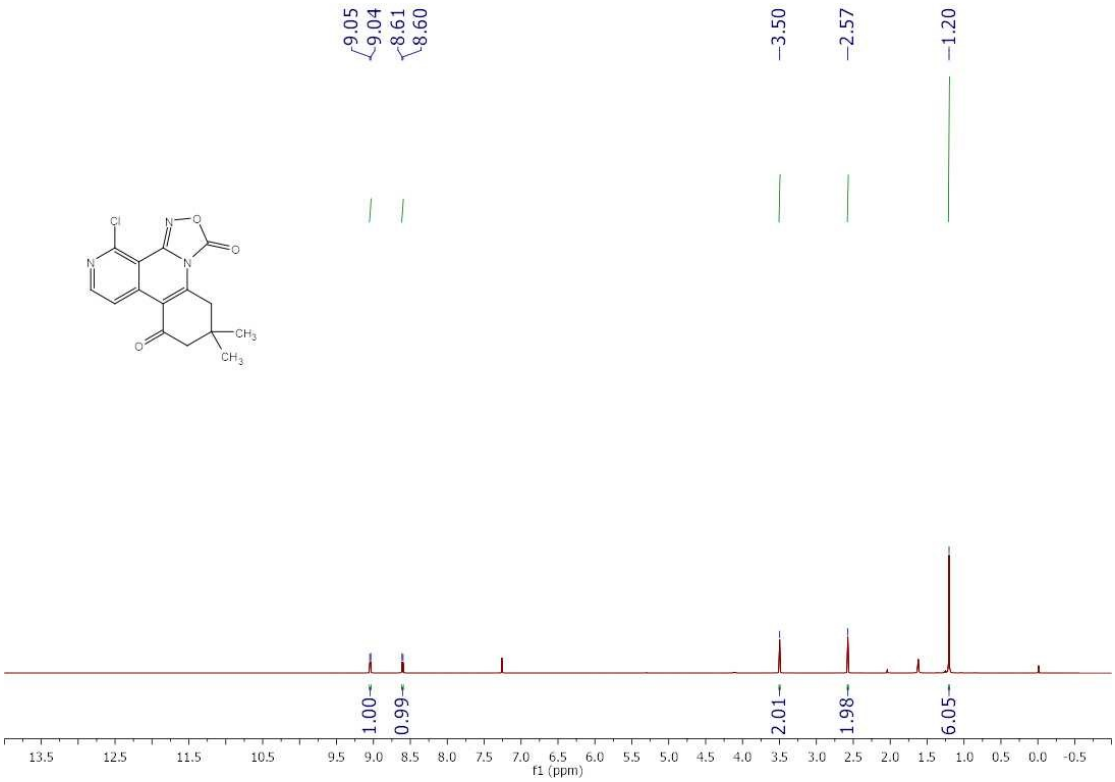
^{13}C NMR spectrum of **3r** (101 MHz, $CDCl_3$)



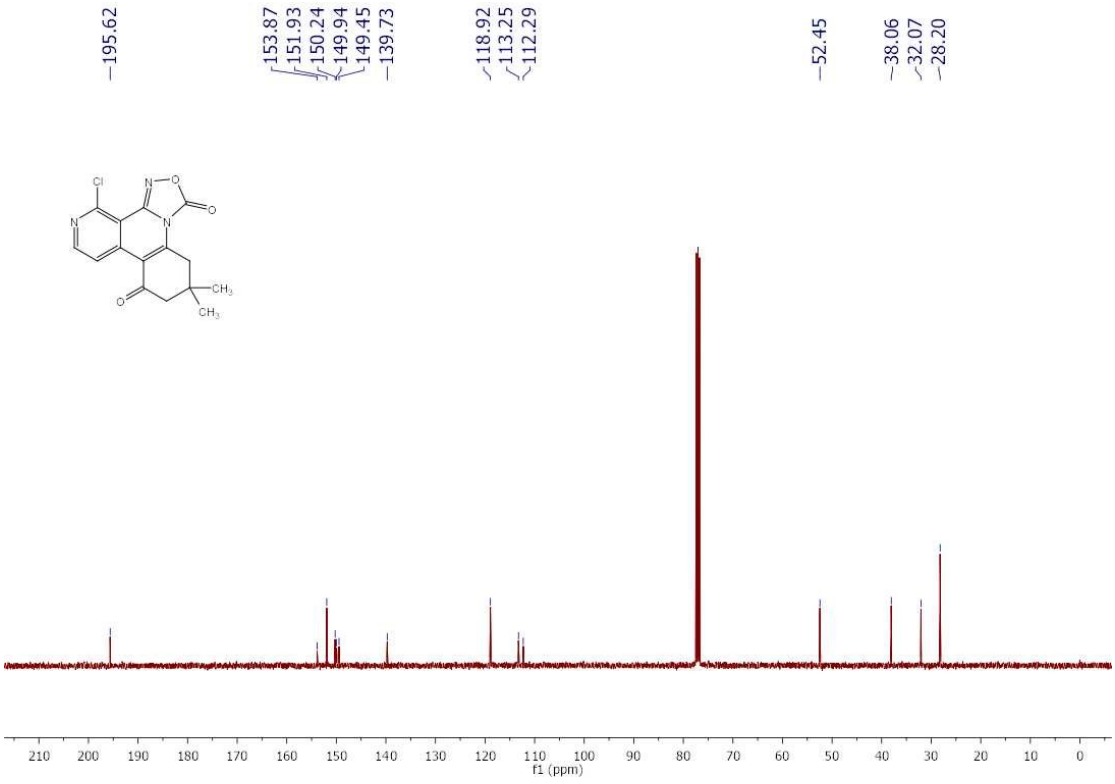
^{1}H NMR spectrum of **3s** (400 MHz, $CDCl_3$)



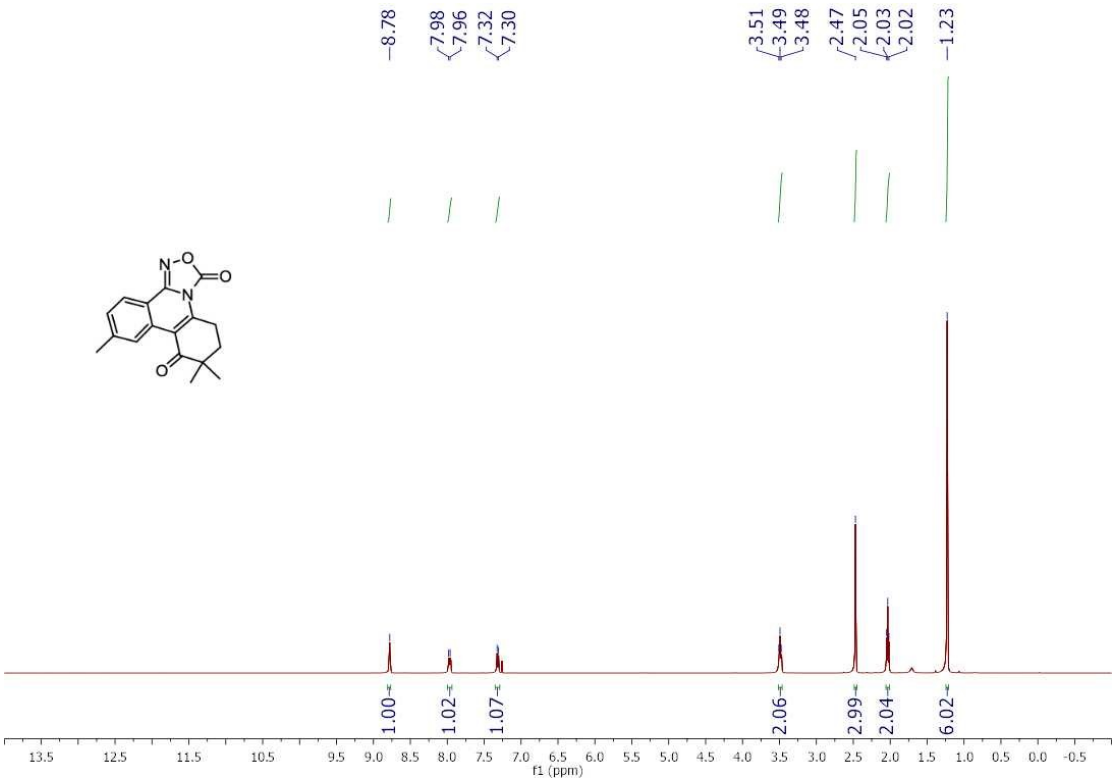
^{13}C NMR spectrum of **3s** (101 MHz, $CDCl_3$)



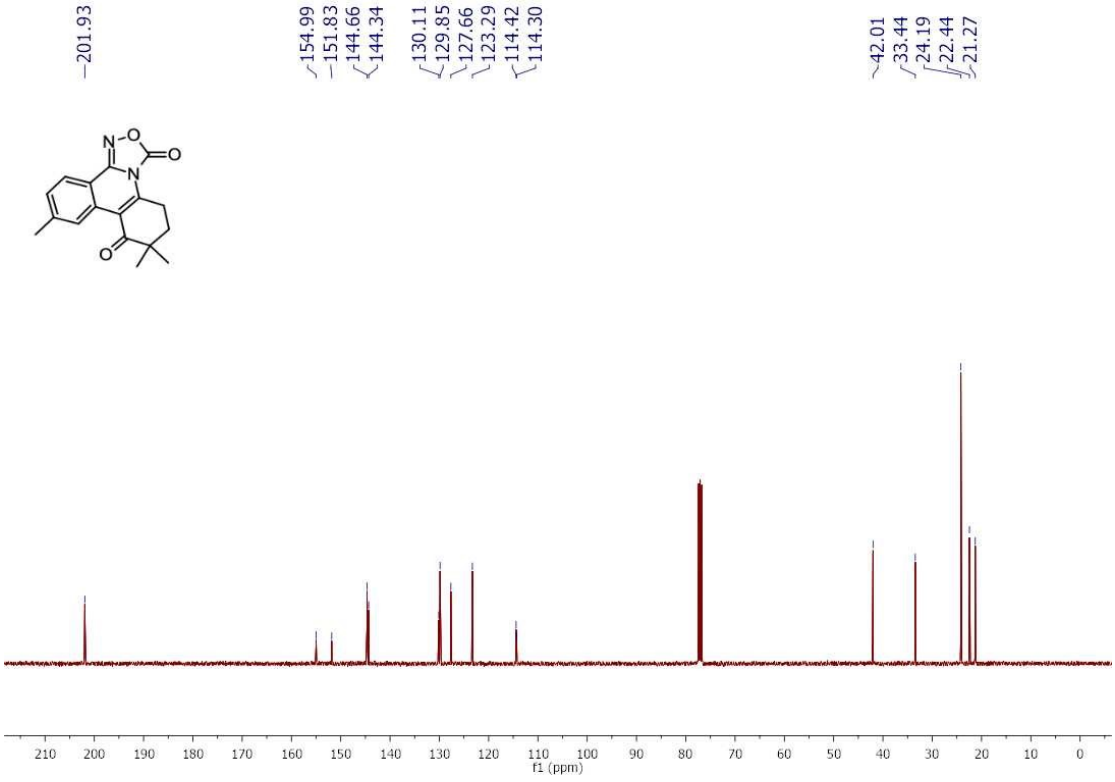
^{1}H NMR spectrum of **3t** (400 MHz, $CDCl_3$)



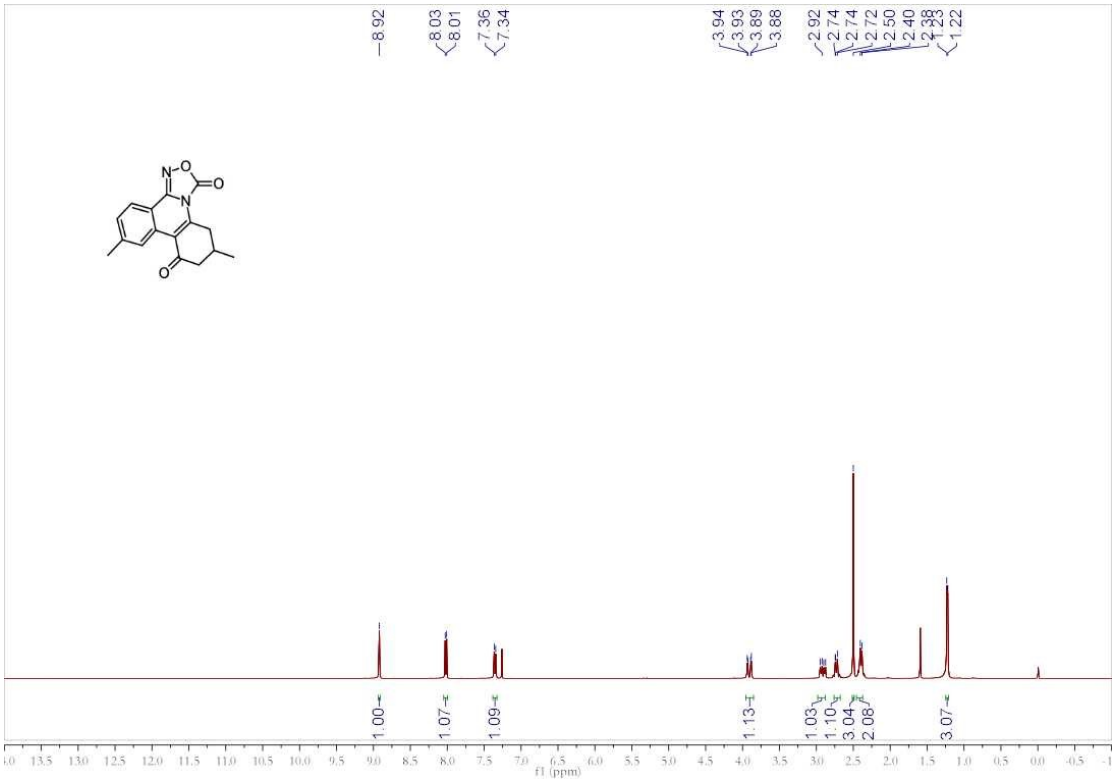
^{13}C NMR spectrum of **3t** (101 MHz, $CDCl_3$)



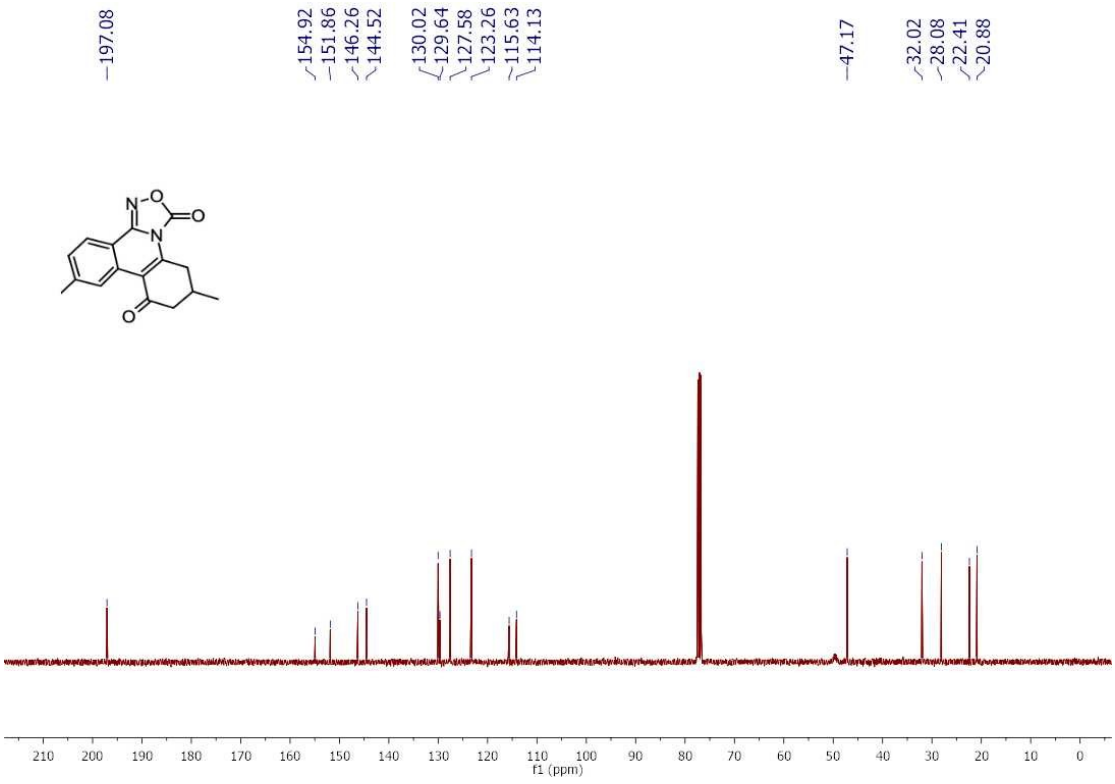
^{1}H NMR spectrum of **4a** (400 MHz, $CDCl_3$)



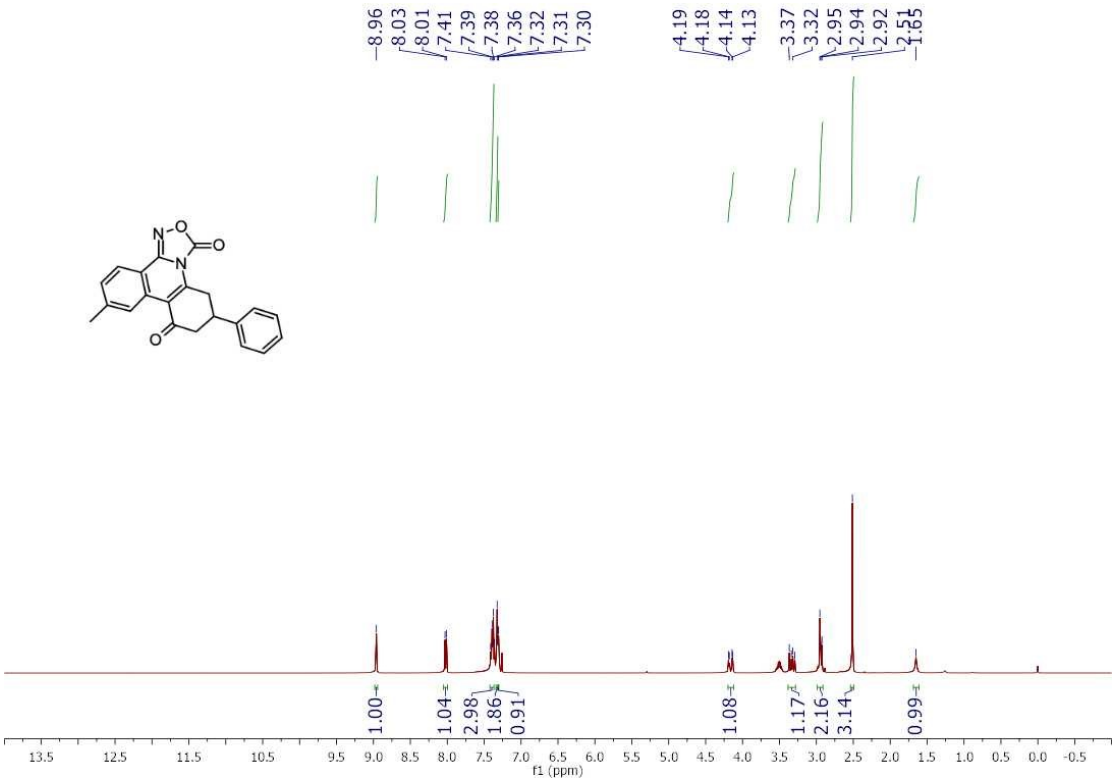
^{13}C NMR spectrum of **4a** (101 MHz, $CDCl_3$)



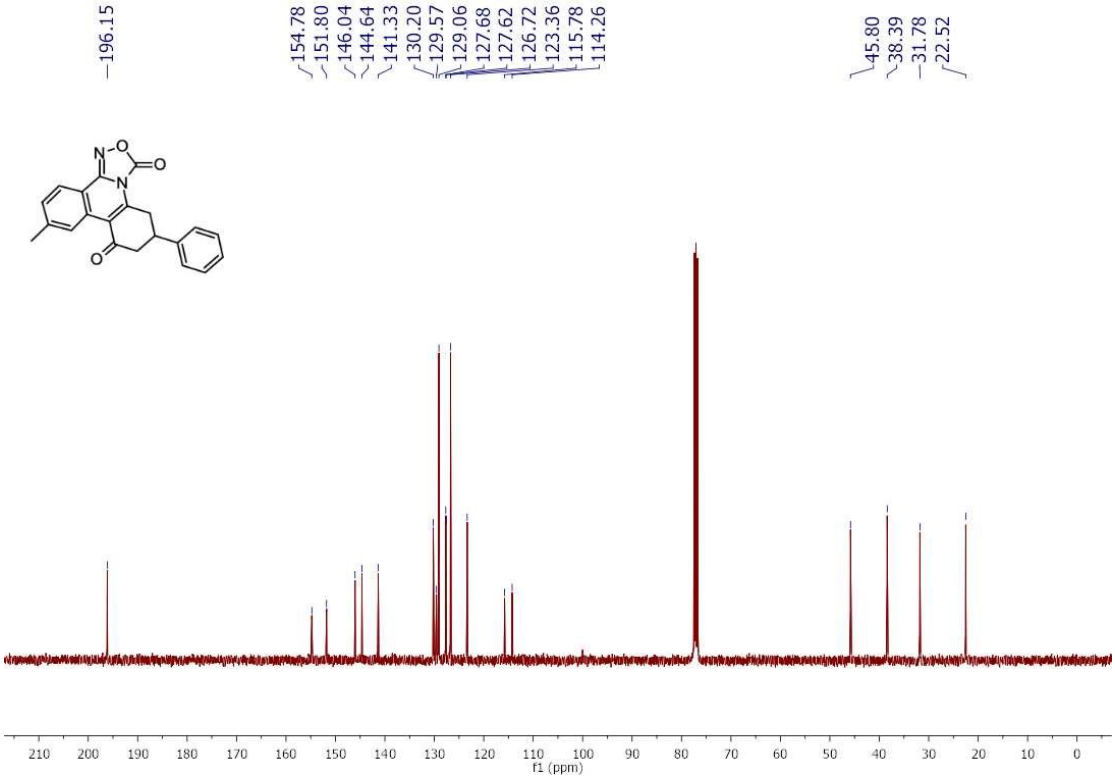
^{1}H NMR spectrum of **4b** (400 MHz, $CDCl_3$)



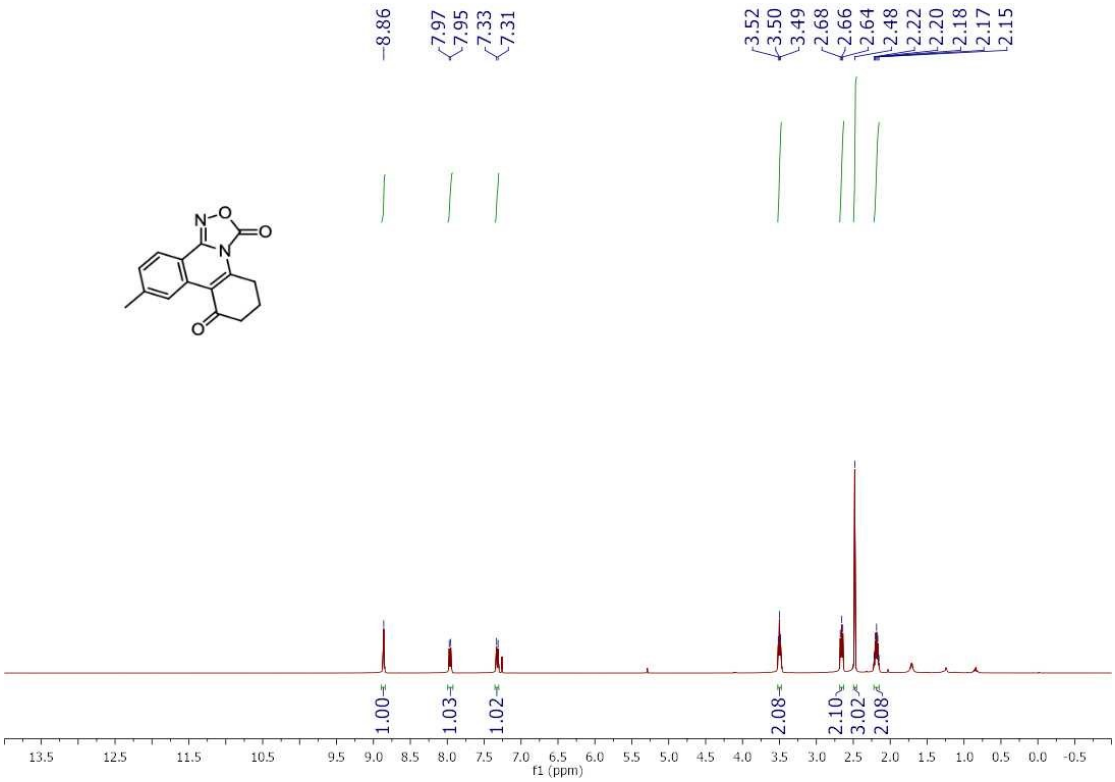
^{13}C NMR spectrum of **4b** (101 MHz, $CDCl_3$)



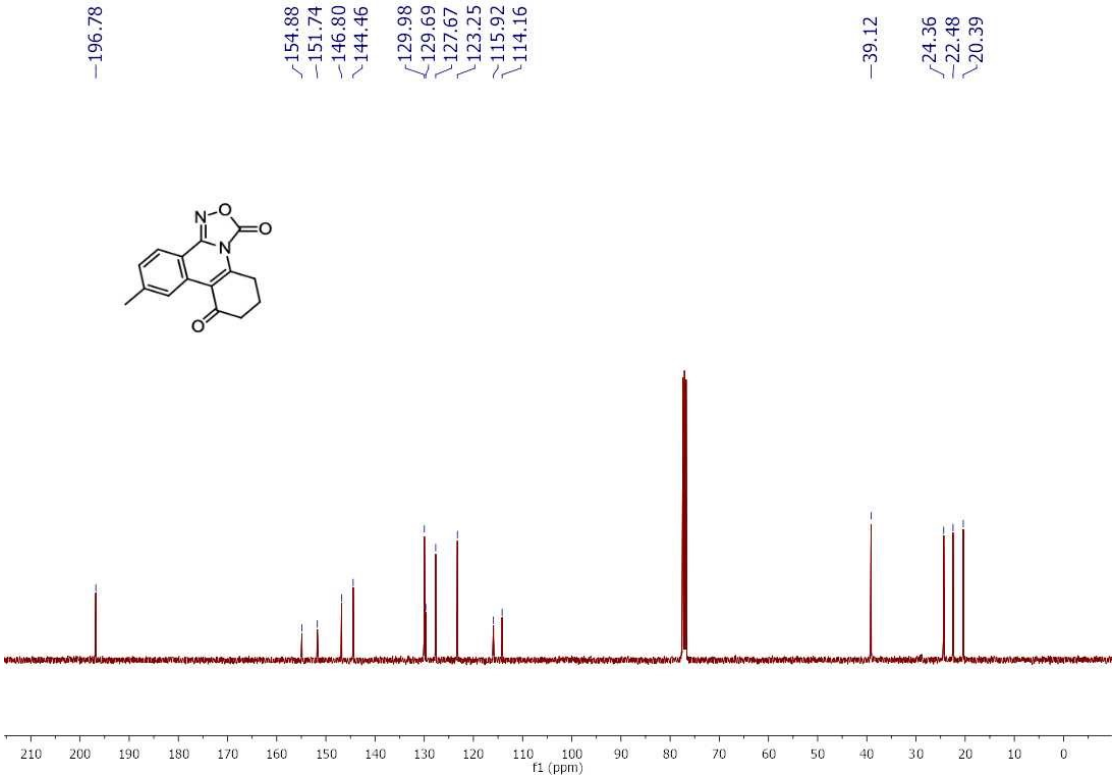
^{1}H NMR spectrum of **4c** (400 MHz, $CDCl_3$)



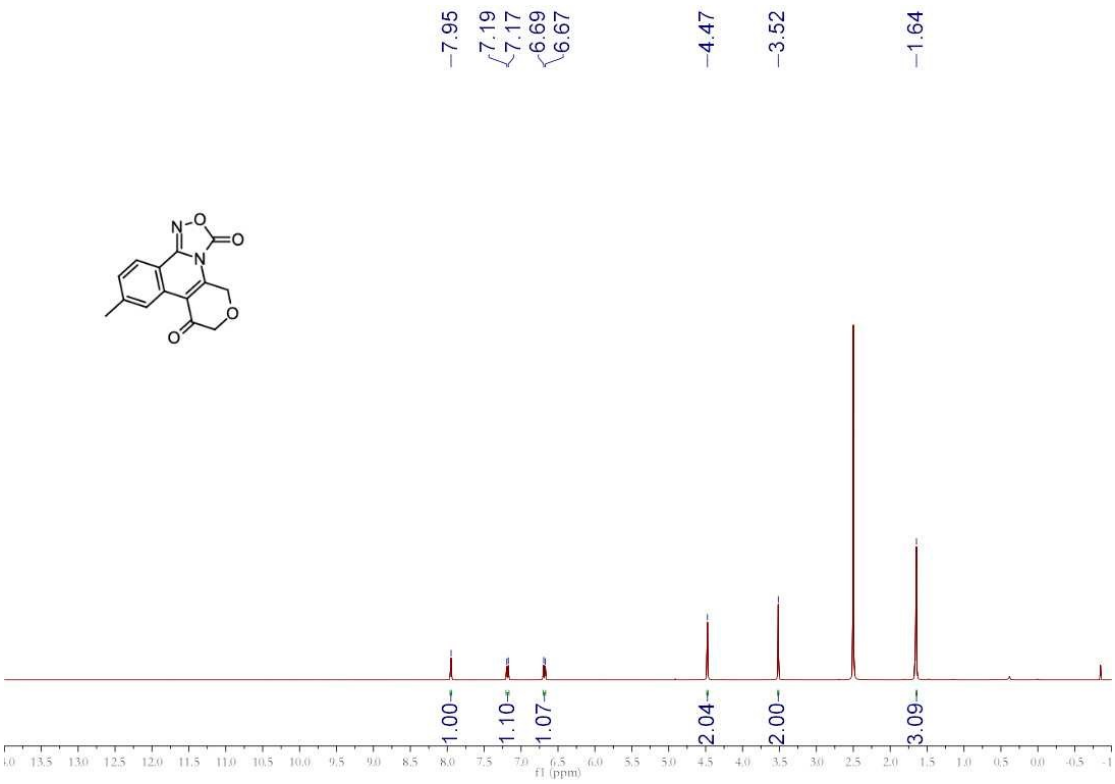
^{13}C NMR spectrum of **4c** (101 MHz, $CDCl_3$)



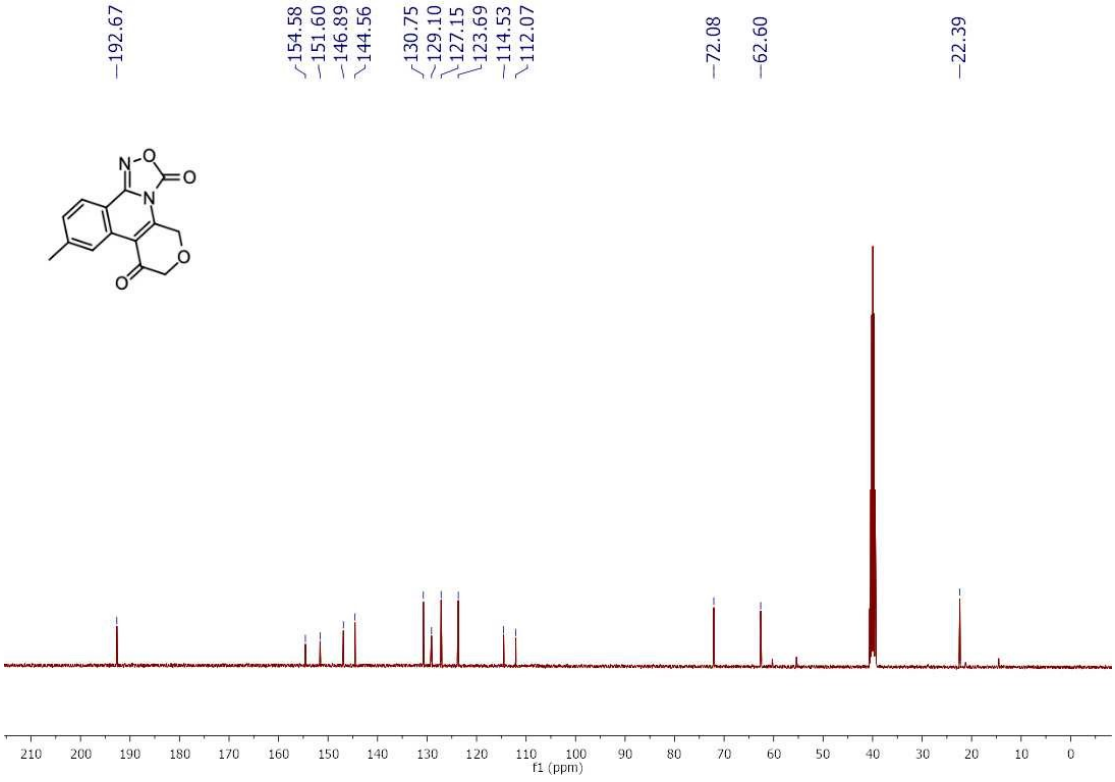
^{1}H NMR spectrum of **4d** (400 MHz, $CDCl_3$)



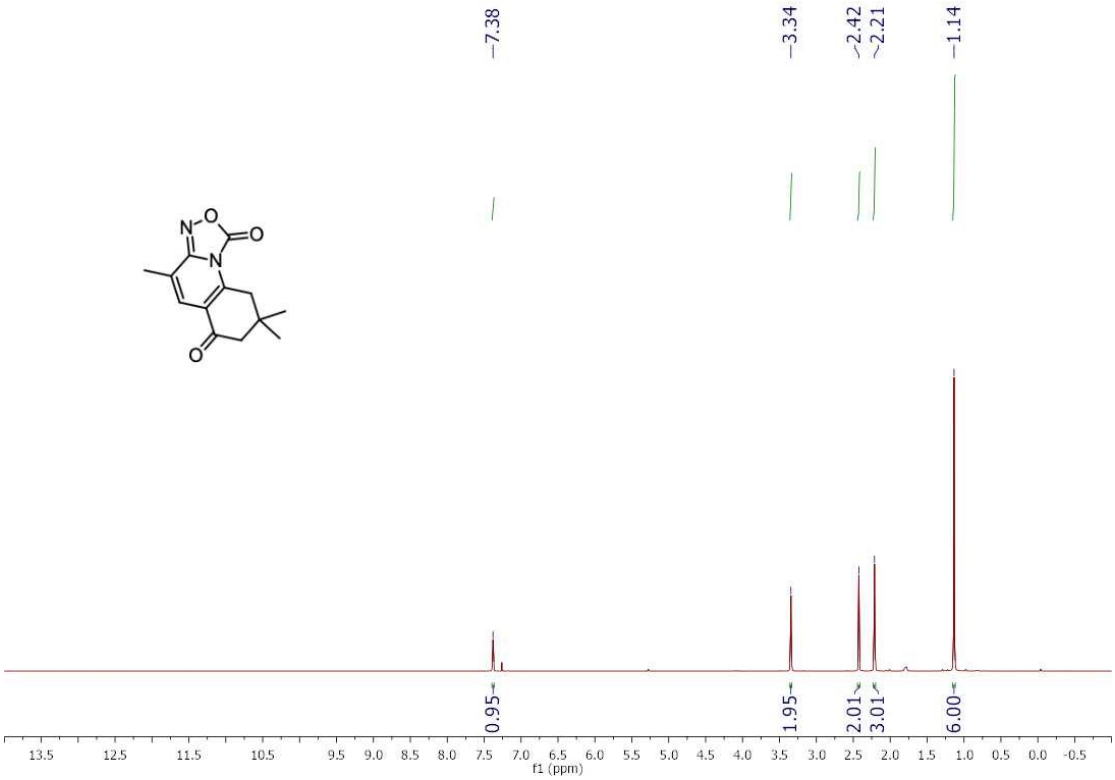
^{13}C NMR spectrum of **4d** (101 MHz, $CDCl_3$)



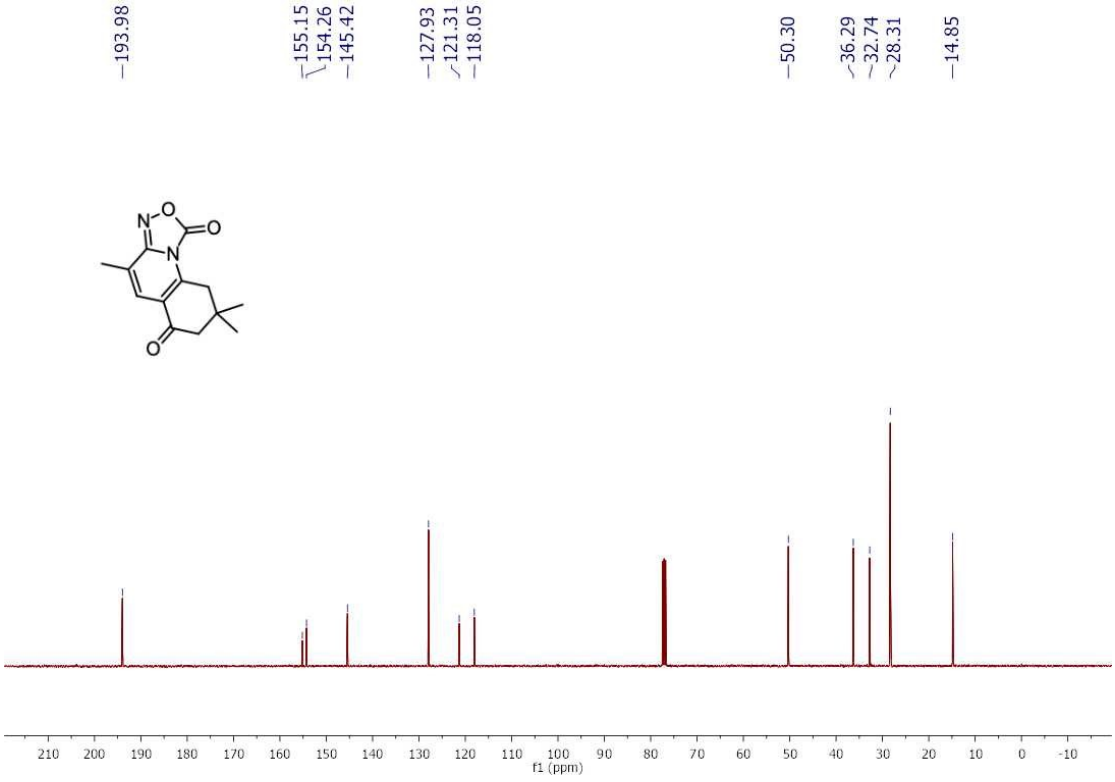
^{1}H NMR spectrum of **4e** (400 MHz, DMSO)



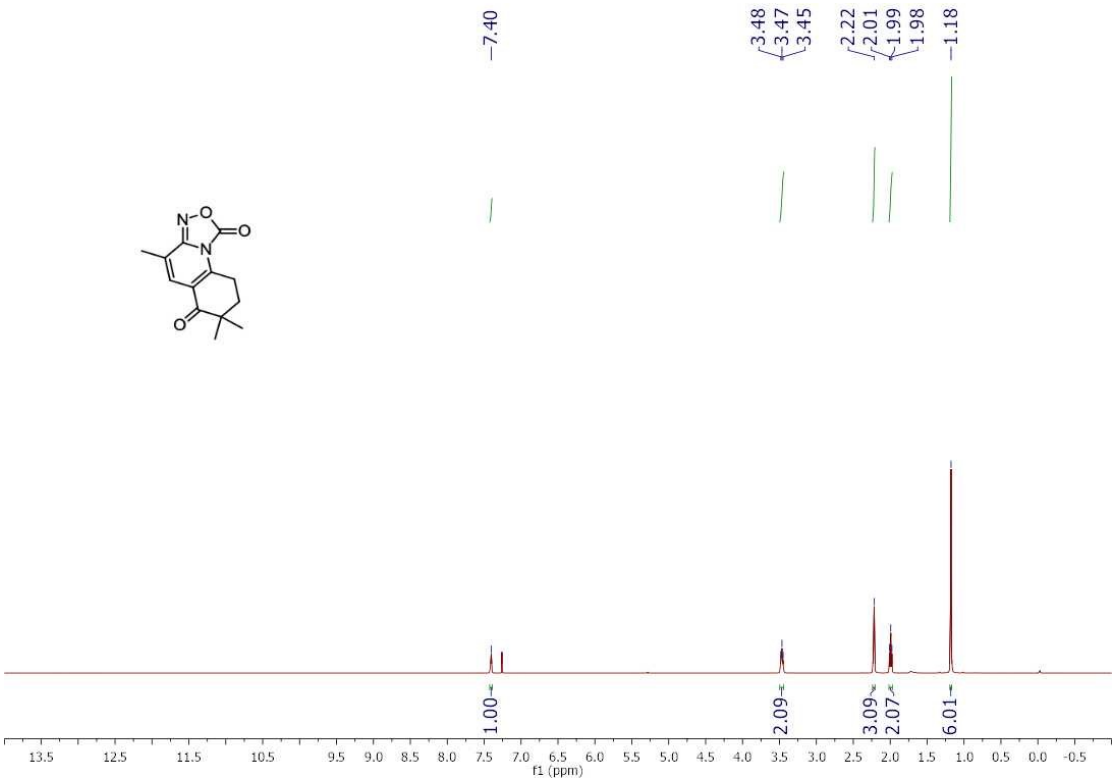
^{13}C NMR spectrum of **4e** (101 MHz, DMSO)



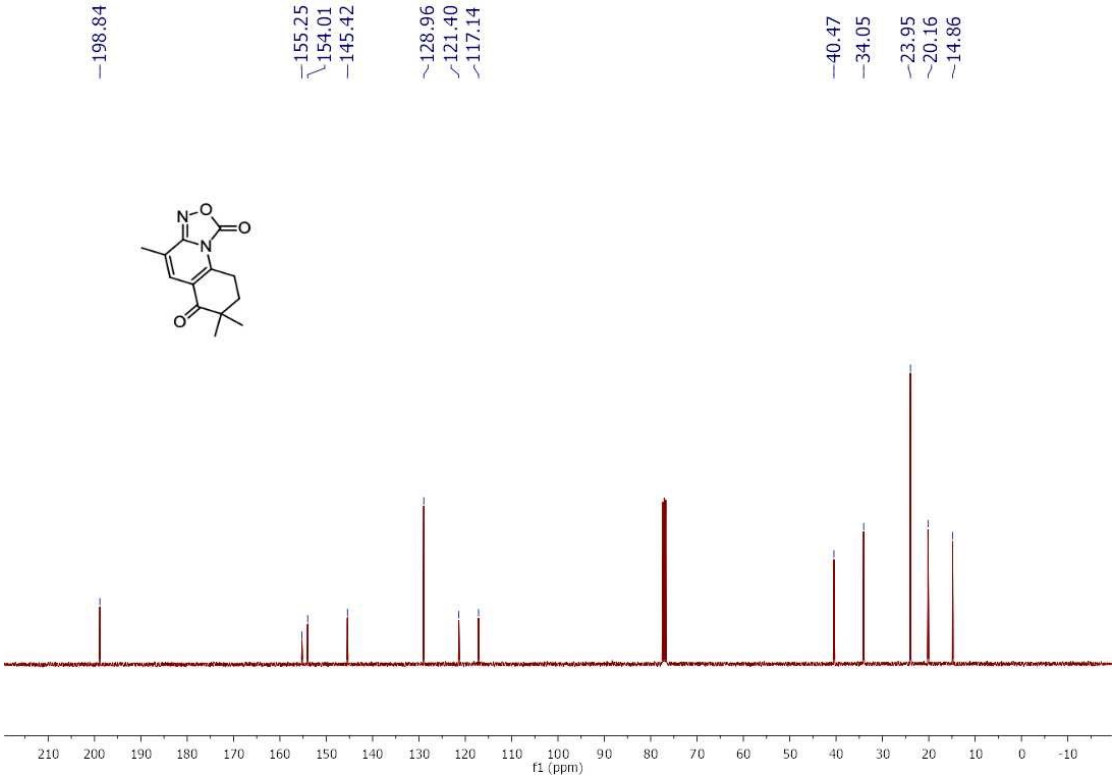
^{1}H NMR spectrum of **5a** (400 MHz, $CDCl_3$)



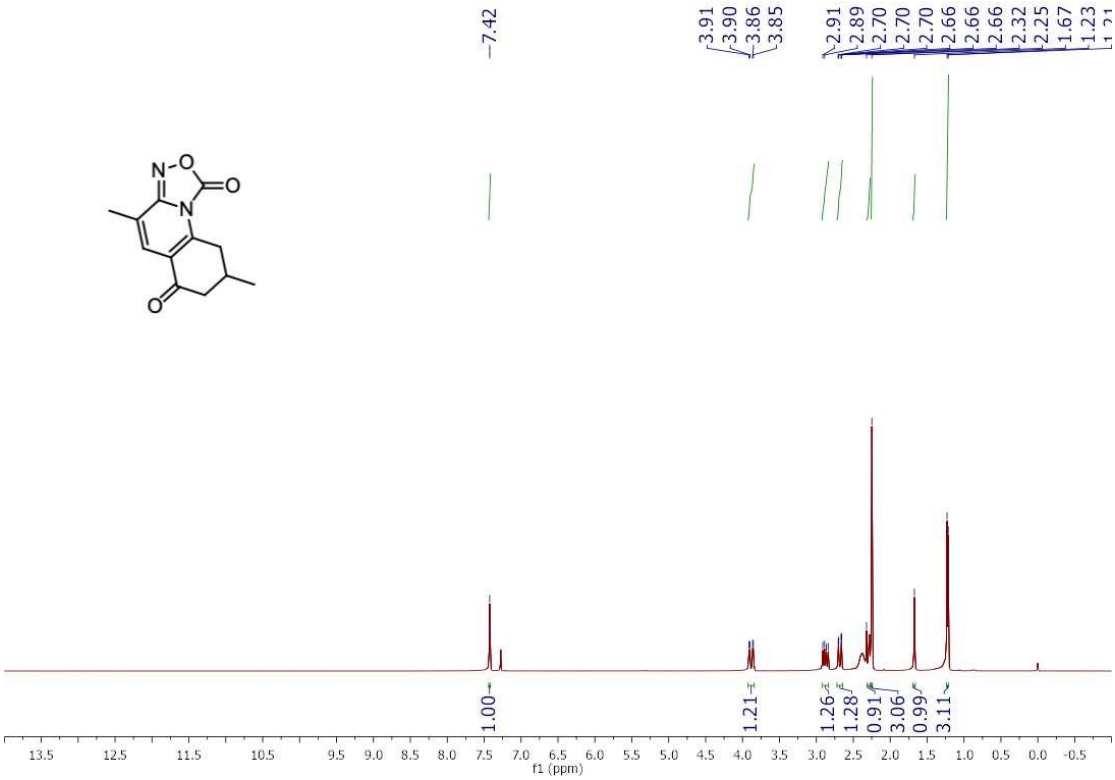
^{13}C NMR spectrum of **5a** (101 MHz, $CDCl_3$)



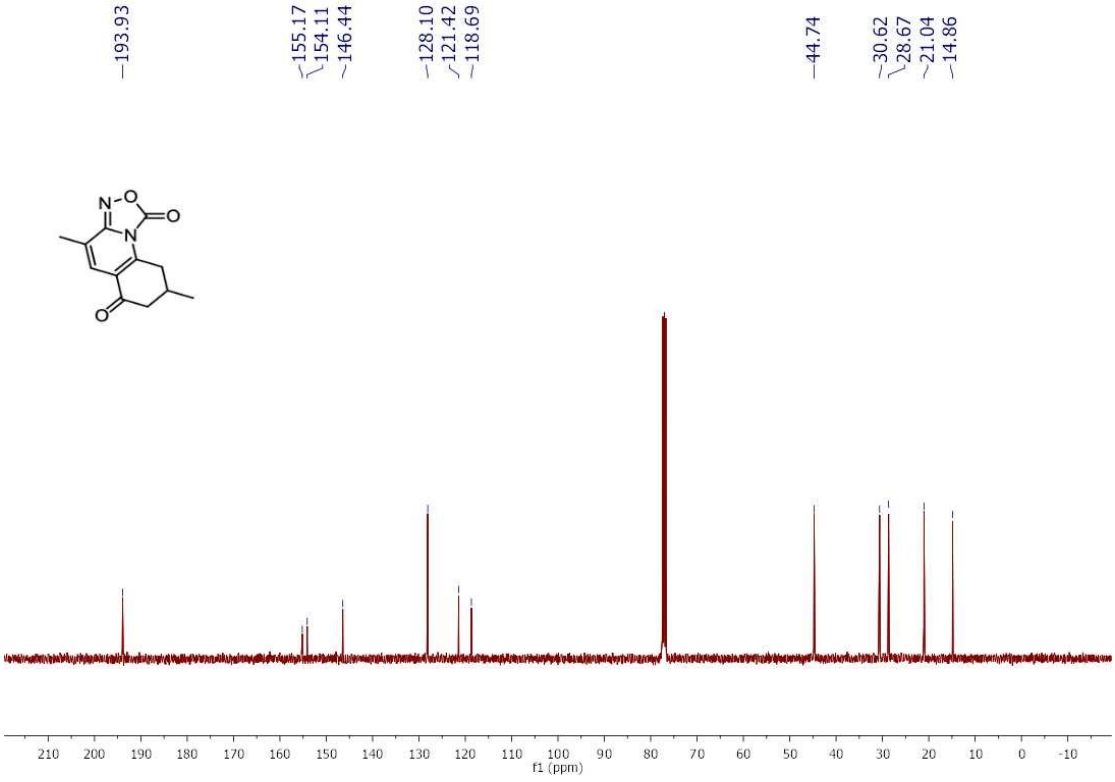
^{1}H NMR spectrum of **5b** (400 MHz, $CDCl_3$)



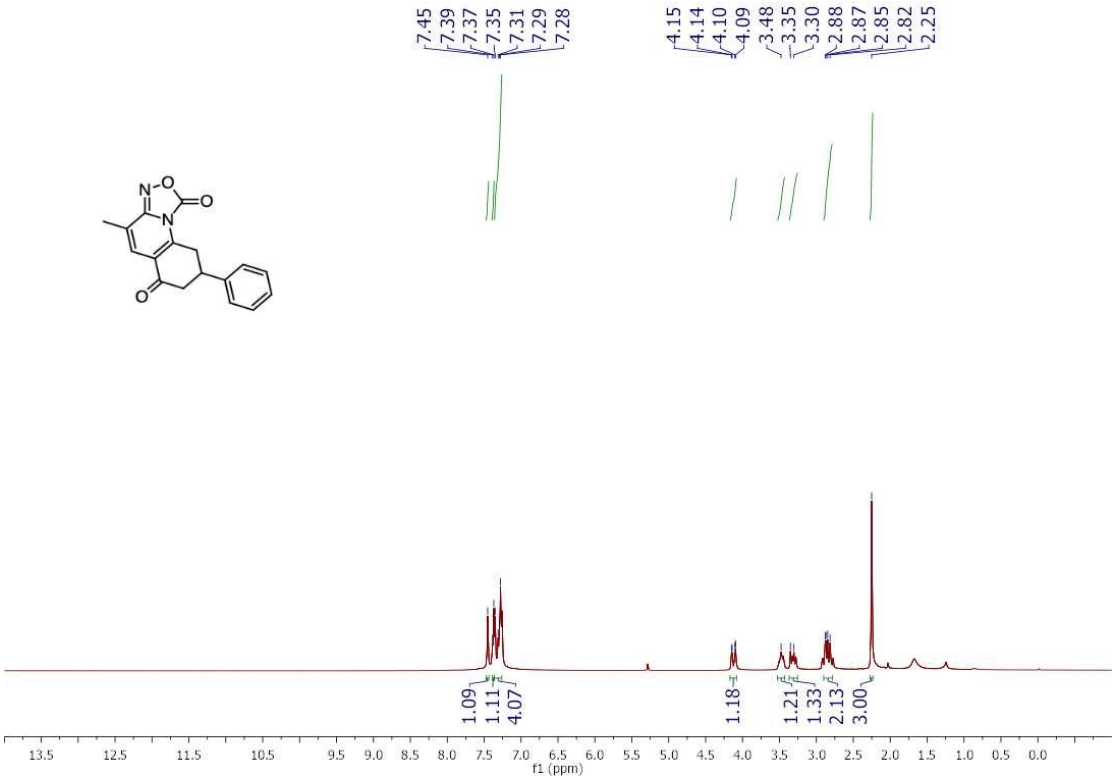
^{13}C NMR spectrum of **5b** (101 MHz, $CDCl_3$)



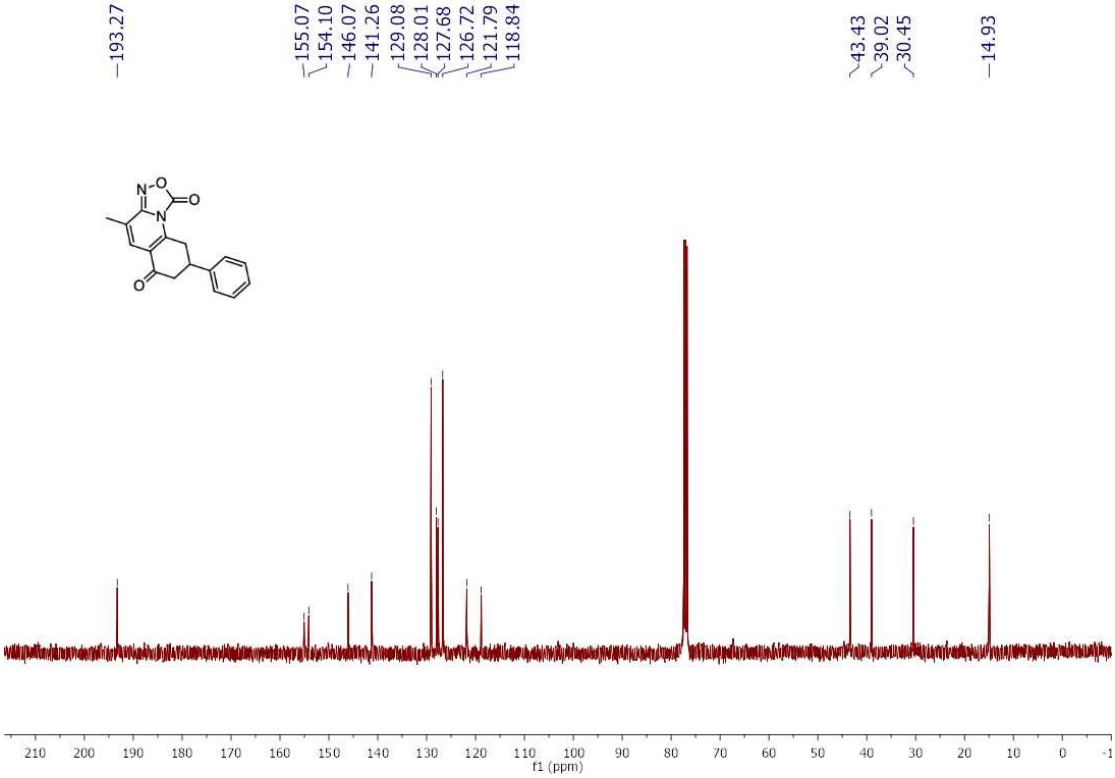
^{1}H NMR spectrum of **5c** (400 MHz, $CDCl_3$)



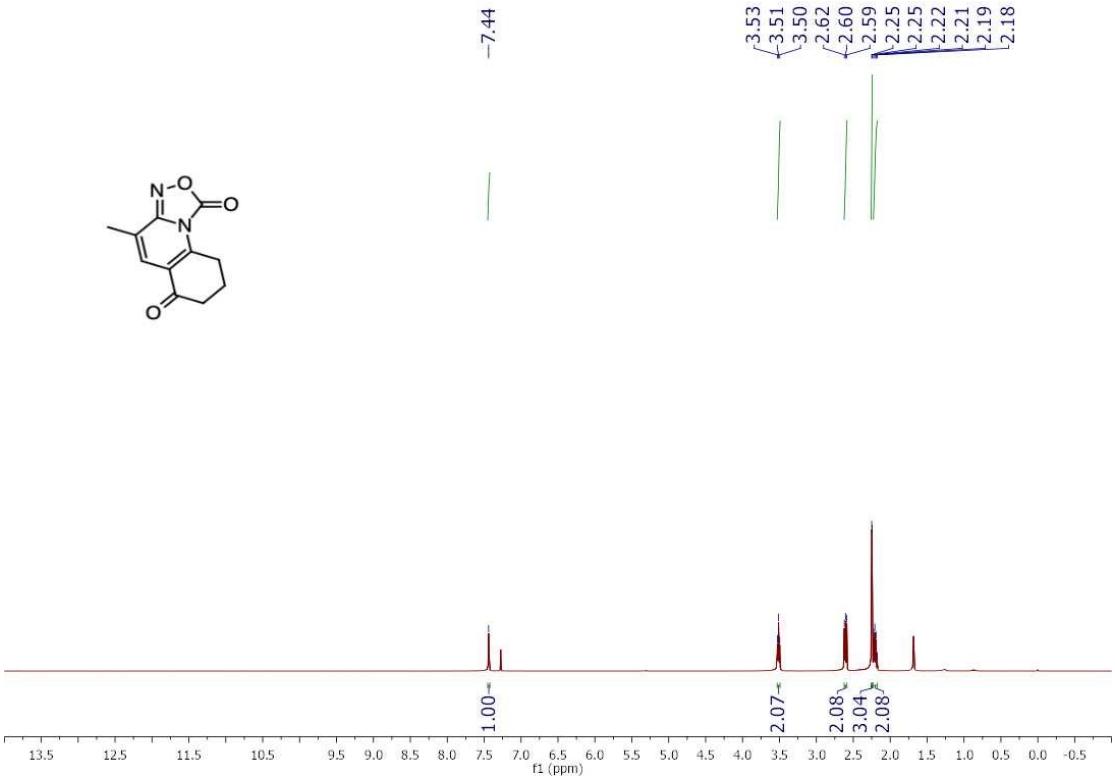
^{13}C NMR spectrum of **5c** (101 MHz, $CDCl_3$)



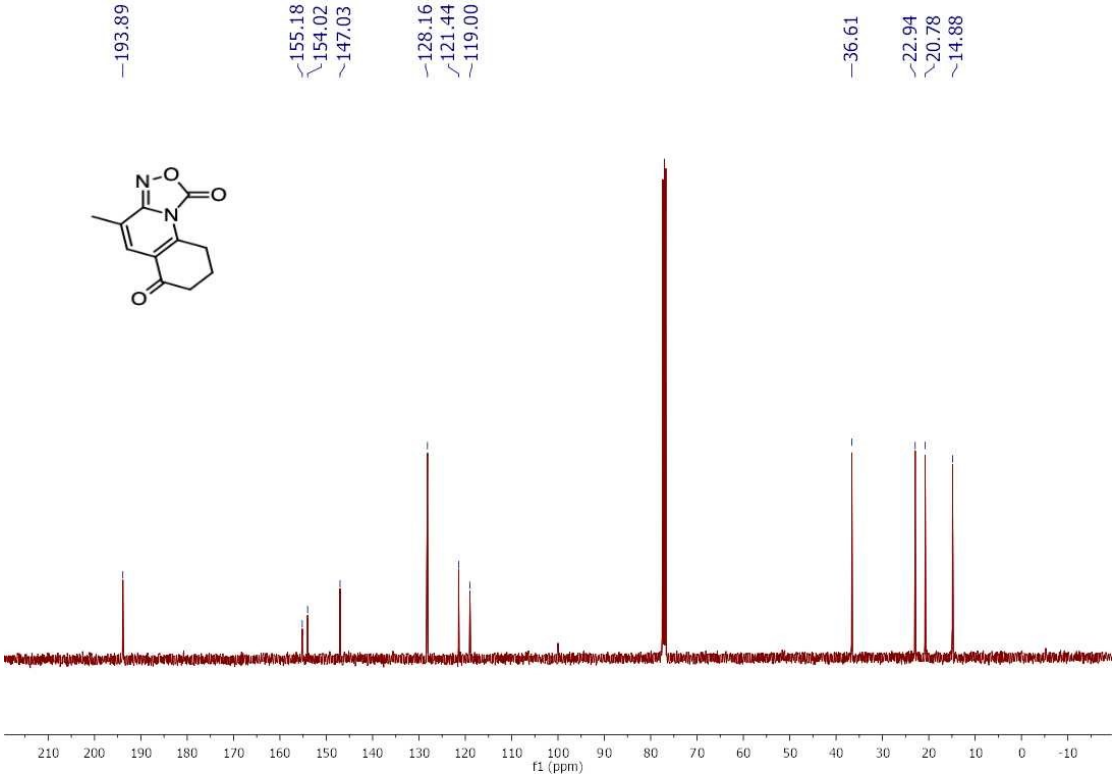
^{1}H NMR spectrum of **5d** (400 MHz, $CDCl_3$)



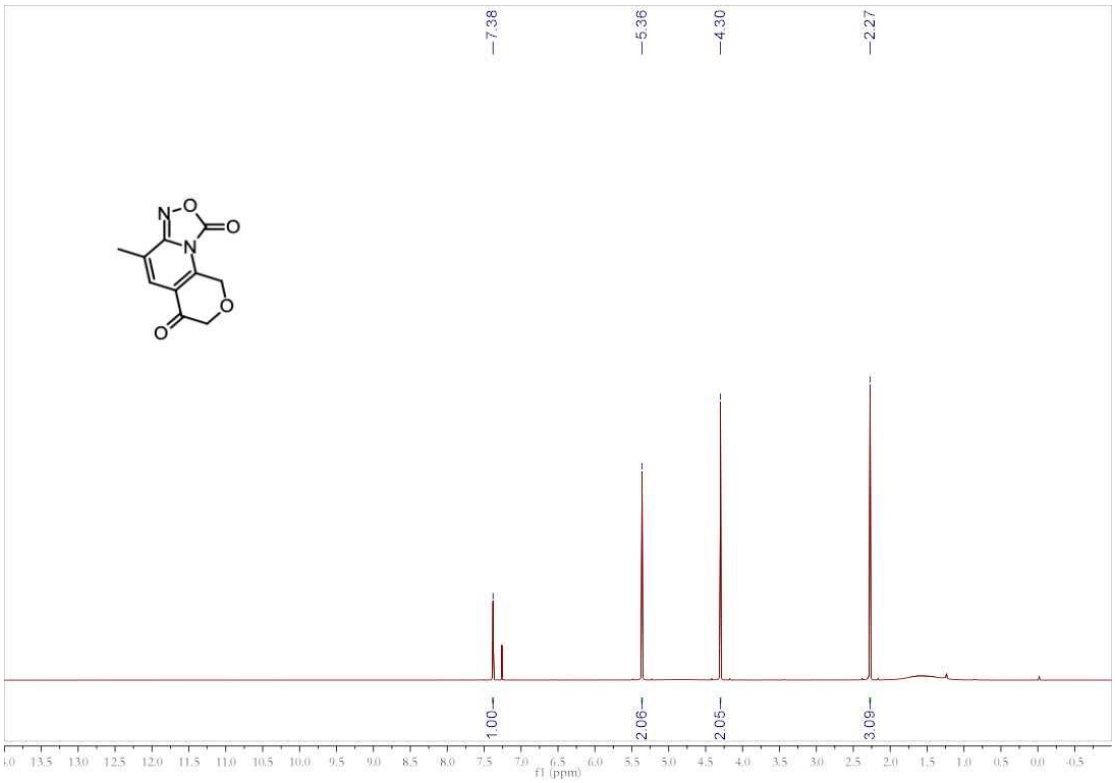
^{13}C NMR spectrum of **5d** (101 MHz, $CDCl_3$)



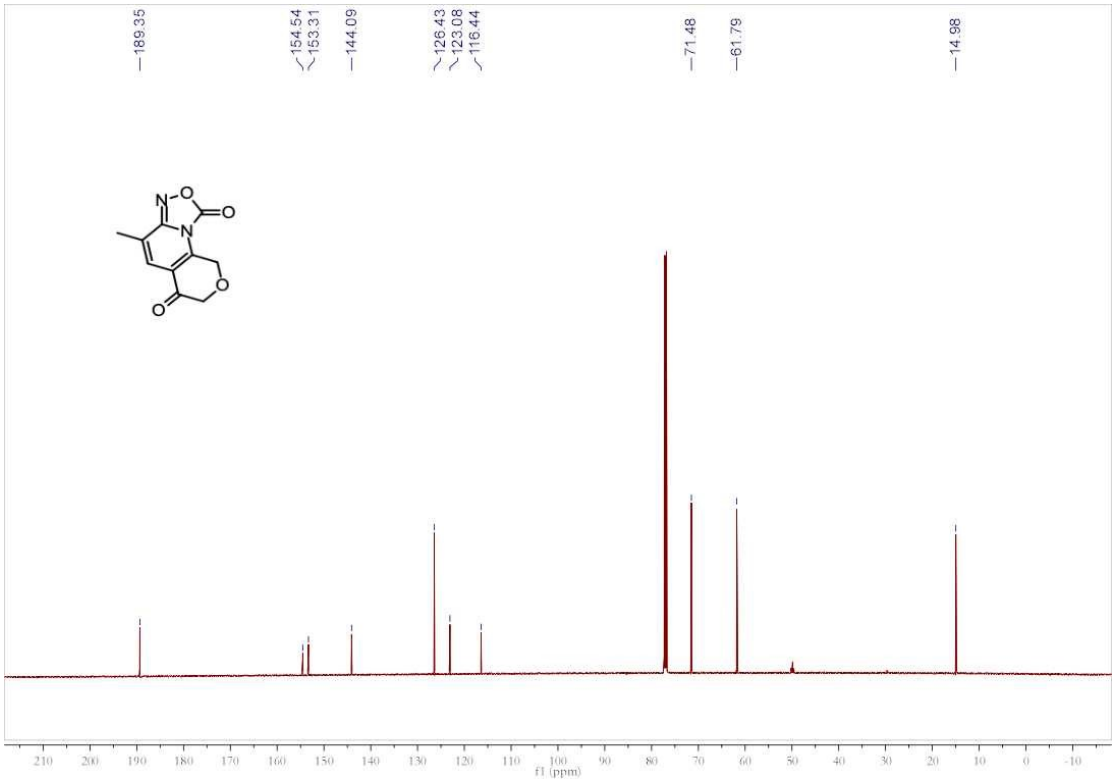
^{1}H NMR spectrum of **5e** (400 MHz, $CDCl_3$)



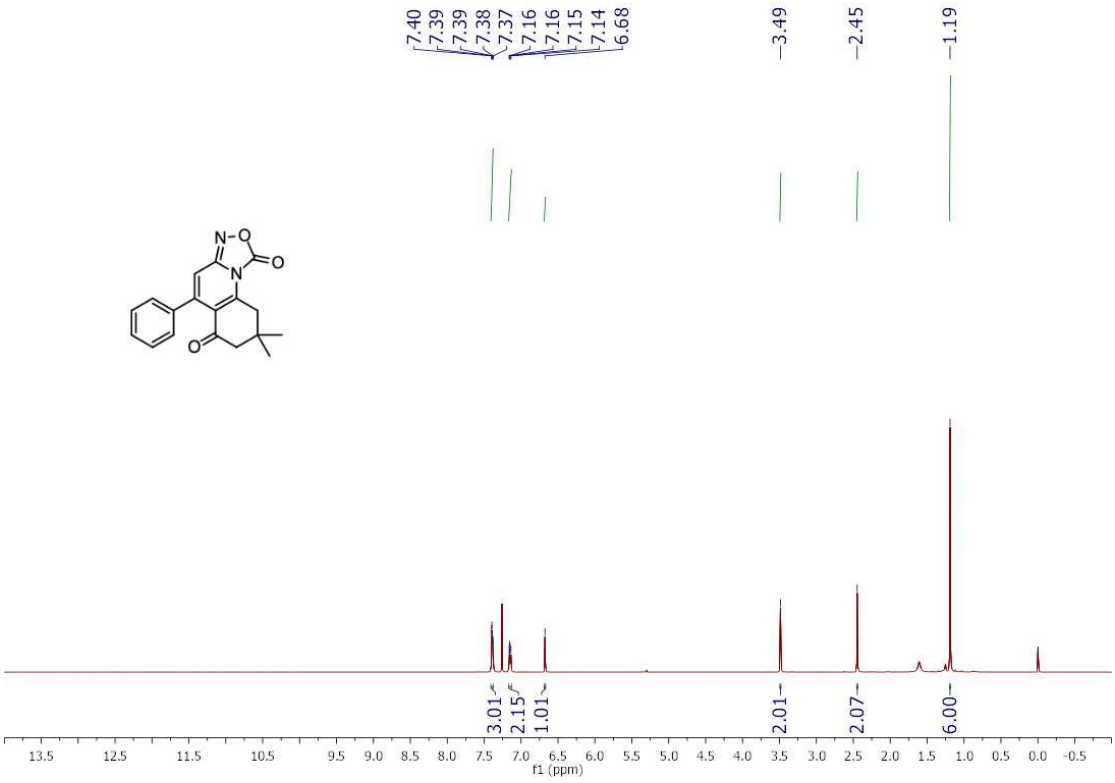
^{13}C NMR spectrum of **5e**(101 MHz, $CDCl_3$)



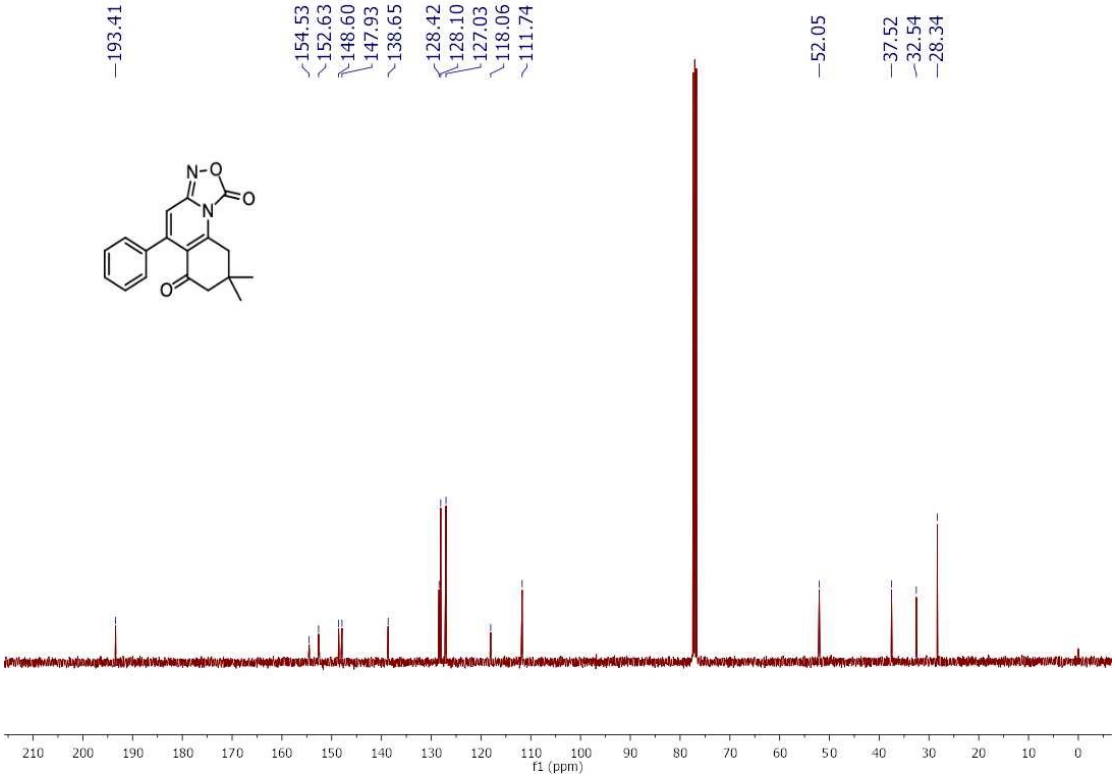
^{1}H NMR spectrum of **5f** (600 MHz, $CDCl_3$)



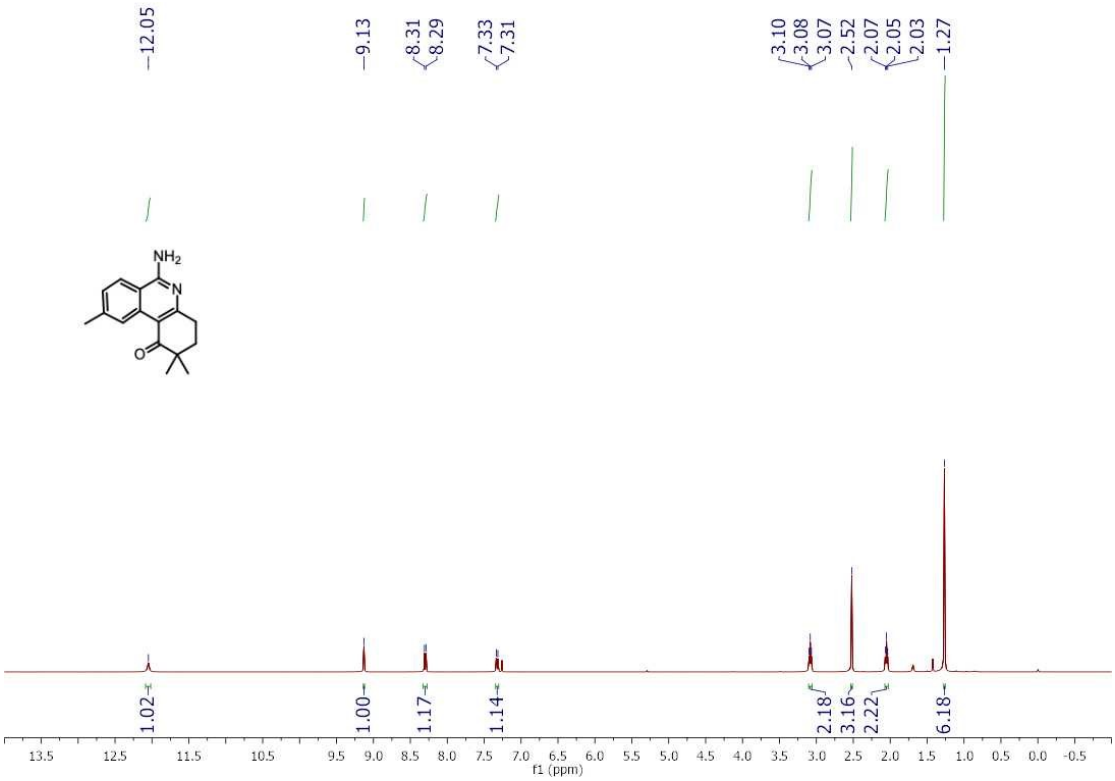
^{13}C NMR spectrum of **5f** (151 MHz, $CDCl_3$)



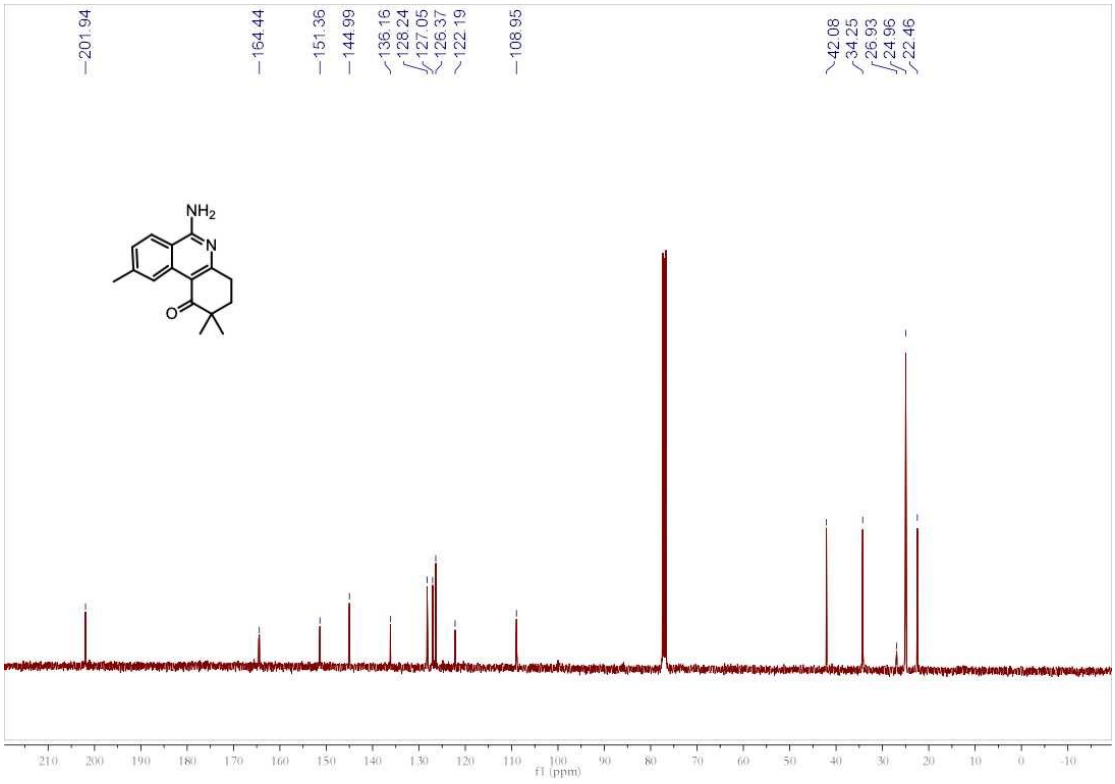
^{1}H NMR spectrum of **5g** (400 MHz, $CDCl_3$)



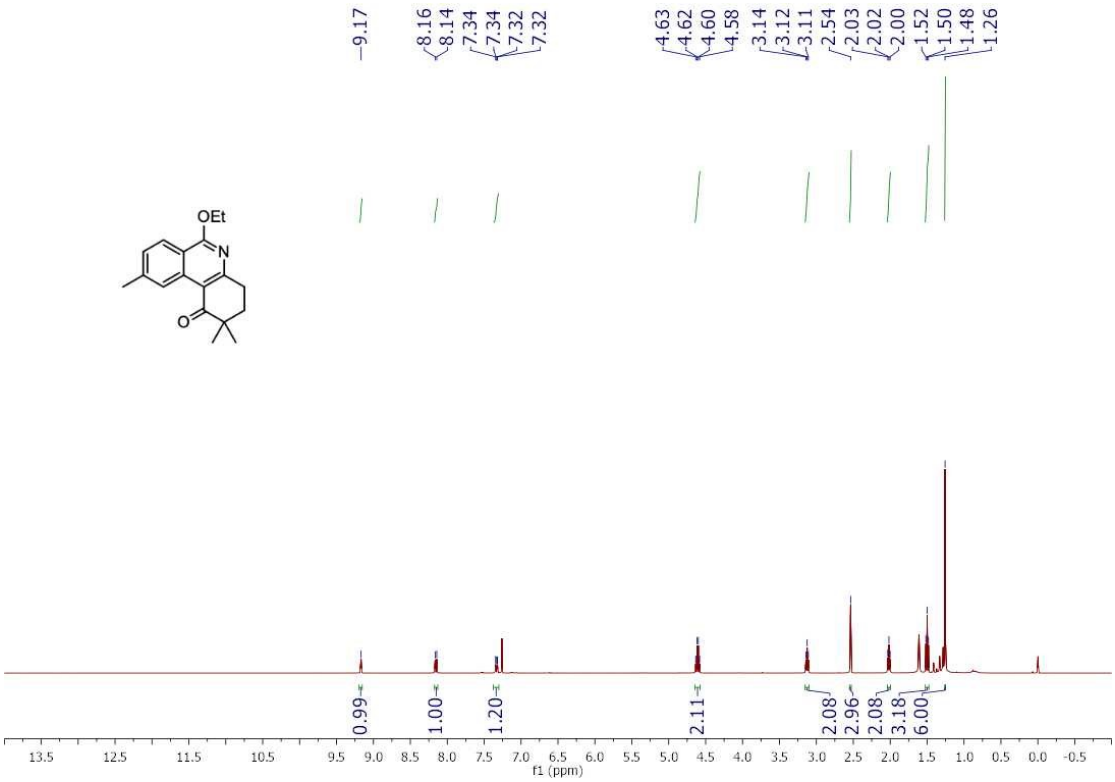
^{13}C NMR spectrum of **5g** (101 MHz, $CDCl_3$)



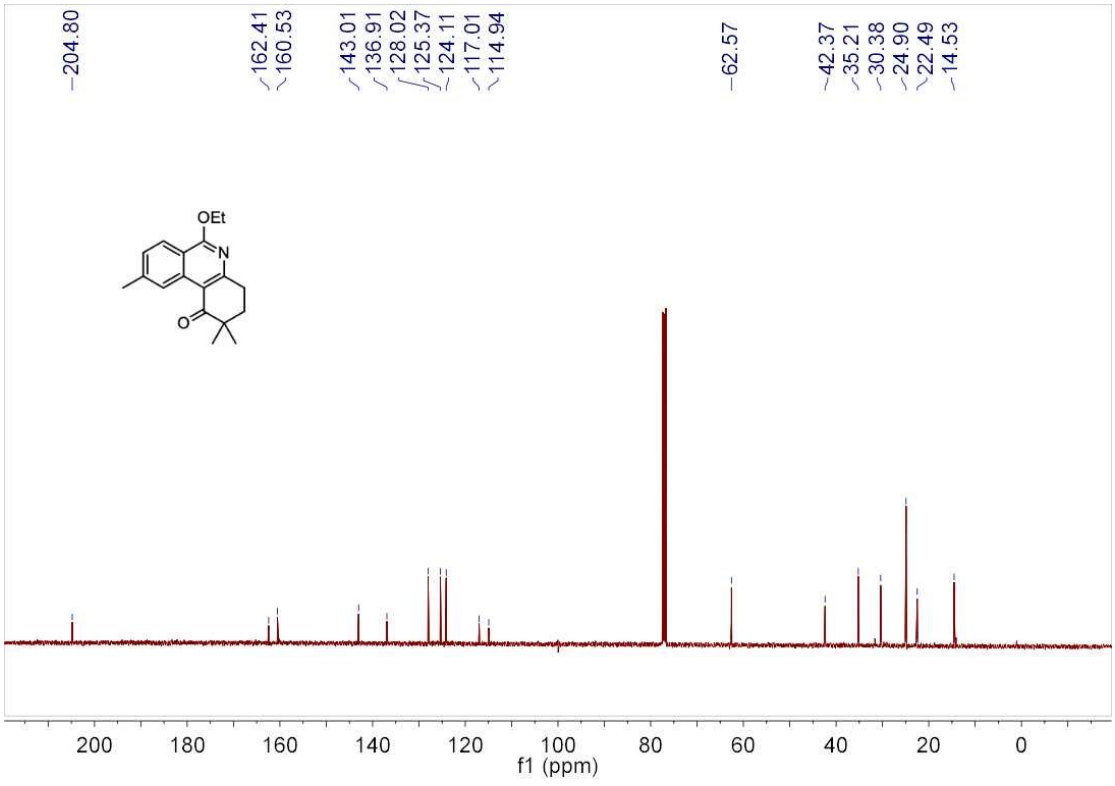
^{1}H NMR spectrum of **6** (400 MHz, $CDCl_3$)



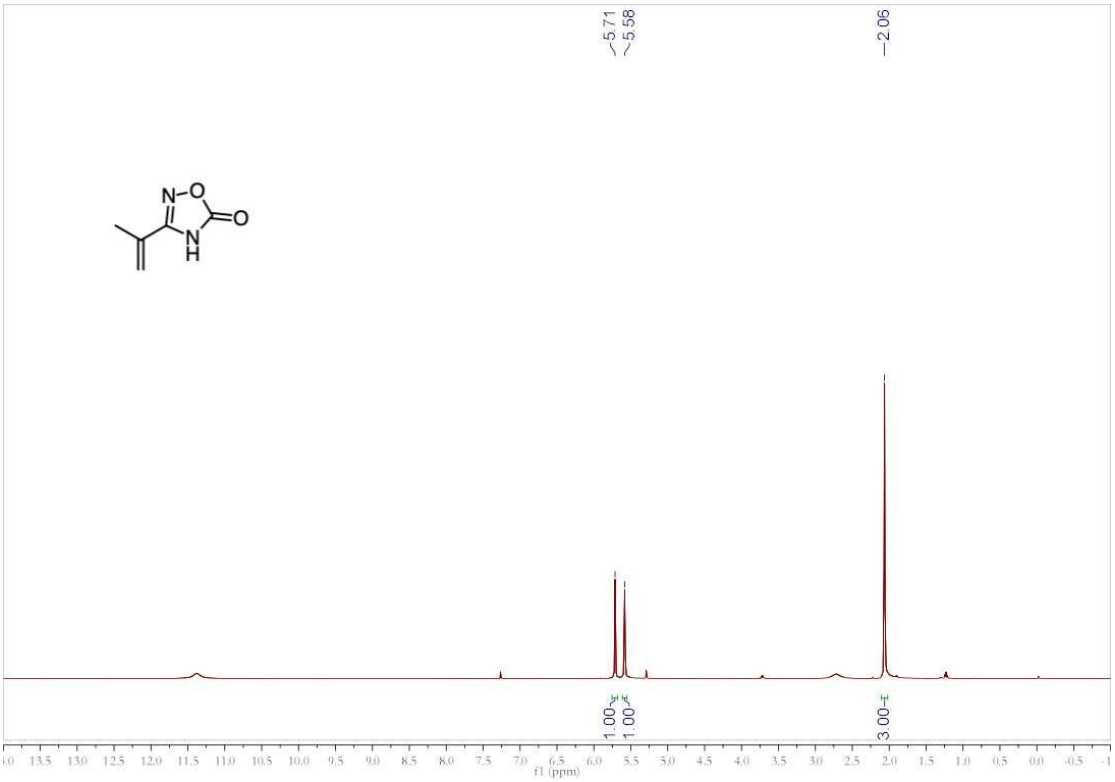
^{13}C NMR spectrum of **6** (101 MHz, $CDCl_3$)



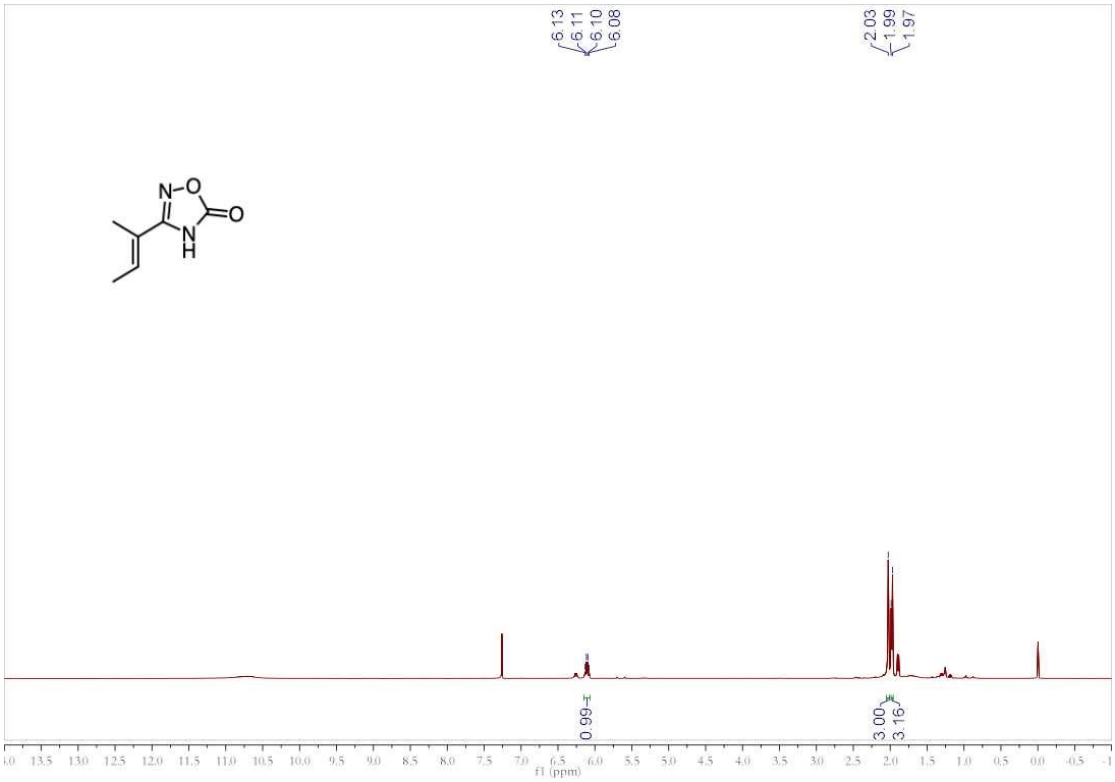
^{1}H NMR spectrum of **7** (400 MHz, $CDCl_3$)



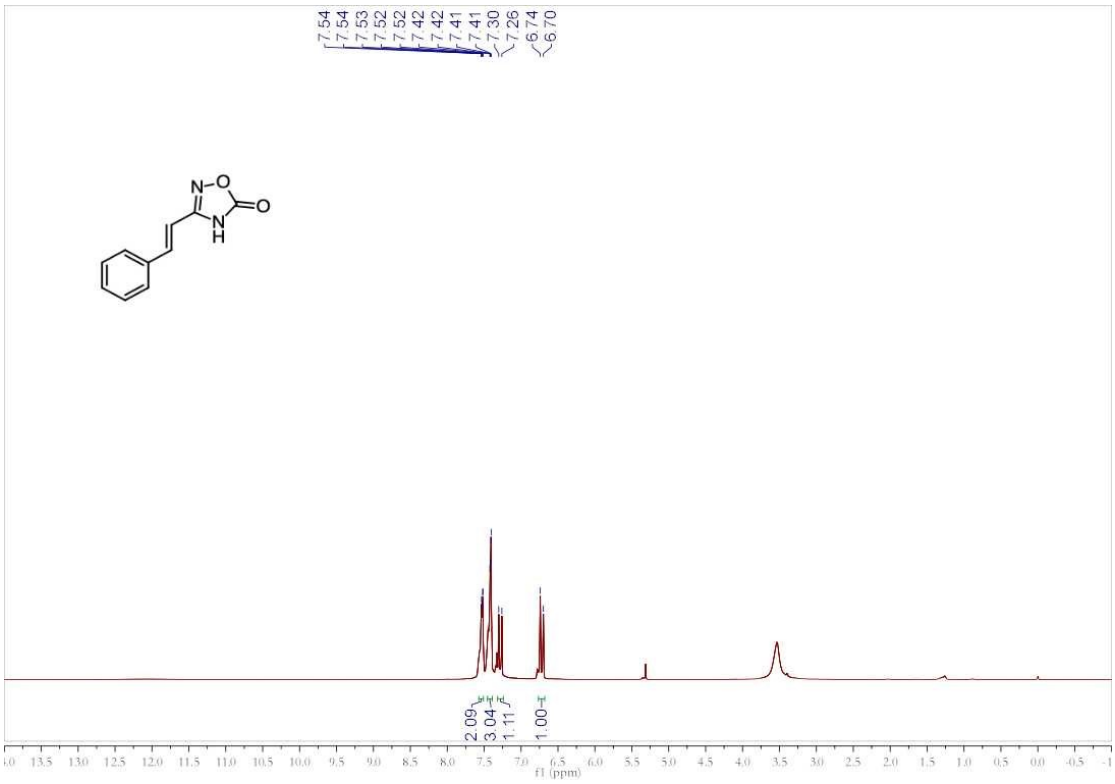
^{13}C NMR spectrum of **7** (101 MHz, $CDCl_3$)



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



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



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

10. References

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3. Yu X, Chen K, Wang Q, Guo S, Zha S, Zhu J. Associative Covalent Relay: An Oxadiazolone Strategy for Rhodium(III)-Catalyzed Synthesis of Primary Pyridinylamines. Angew Chem Int Ed Engl 2017, **56**(19)**:** 5222-5226.
4. Wang Y, Zhang Q, Hao Y, Luo C, Huang X, Guo L, Wu Y. C-H Activation-Engaged Synthesis of Diverse Fused-Heterocycles from the Reactions of 3-Phenyl-1,2,4-oxadiazol-5(2H)-ones with Vinylene Carbonate. Organometallics 2022, **41**(17)**:** 2494-2507.