Supporting information

New prodrugs and analogs of the phenazine 5,10-dioxide natural products iodinin and myxin promote selective cytotoxicity towards human acute myeloid leukemia cells

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PAMPA (Parallel Artificial Membrane Permeability Assay)

Table S-1: Shows the permeability of analogs

Cmpd	$LogP_{eff}$[1]	Deviation[2]	Permeability[3]	Cmpd	$LogP_{eff}$[1]	Deviation[2]	Permeability[3]
3	-5.64*	0.33	Intermediate	**27**	-4.85	0.02	High
4	-4.94	0.35	High	**28**	-4.95	0.02	High
7	-4.84*	0.15	High	**29**	-4.91	0.02	High
11	-6.06	0.20	Low	**44**	-5.45	0.08	Intermediate
12	-7.74	0.92	Impermeable	**45**	-7.23	0.81	Impermeable
13	-7.32*	0.17	Impermeable	**48**	-4.93	0.02	High
14	-4.75	0.06	High	**50**	-5.16	0.26	High
15	-5.96*	0.38	Low	**51**	-5.24	0.23	High
16	-4.74	0.06	High	**52**	-4.97	0.13	High
17	-5.06	0.06	High	**53**	-5.26*	0.17	High
18	-5.74	0.15	Low	**54**	-4.97*	0.24	High
19	-5.1	0.03	High	**55**	-4.88	0.14	High
20	-5.3	0.05	High	**56**	-5.18	0.24	High
21	-4.74	0.01	High	**57**	-4.85	0.47	High
24	-4.93	0.04	High	**60**	-4.35	0.02	High
25	-4.76	0.11	High	**61**	-4.48	0.06	High
26	-5.2	0.08	High	**62**	-4.65	0.22	High

1: Asterisks denote that n ≥ 3. For all other samples, n=2.

2: Deviation is calculated either as STD (n≥3) or high value minus average (n=2)

3: As defined in: Bennion BJ, Be NA, McNerney MW, Lao V, Carlson EM, Valdez CA, et al. Predicting a Drug's Membrane Permeability: A Computational Model Validated With in Vitro Permeability Assay Data. The journal of physical chemistry B. 2017;121(20):5228-37

Membrane permeability were classified by the range defined by Bennion et al., allowing us to divide the compounds into four groups, compounds with high permeability (LogPeff > -5.33), intermediate permeability (LogPeff > -5.66 and < -5.33), low permeability (LogPeff > -6.14 and < -5.66) impermeable (LogPeff < -6.14).

General information for synthesis

1-hydroxyphenazine (**25**) was purchased from Aurum Pharmatech. Iodinin (**3**) and myxin (**4**) were prepared in accordance with procedure published in prior by this group.[1] 3-amino-2-nitrophenol was purchased from AK Scientific. All other reagents were purchased from Sigma Aldrich or TCI Chemicals Europe unless stated otherwise and used without further purification. All solvents were purchased from Sigma Aldrich and used without further purification. Yields that are stated are based on isolated material and are uncorrected. Thin layer chromatography (TLC) analysis was performed using silica gel 60 F_{254} plates (aluminum backed) supplied by Merck. For column chromatography, Merck silica 60 mesh (35-70 µm) was used. TLC plates were visualized by UV-light at 254 or 366 nm. ^{1}H- and ^{13}C-NMR were recorded on Bruker DPX300, Bruker AVII 400 and Bruker AVII 600 instruments at 300 MHz, 400 MHz and 600 MHz for ^{1}H-NMR and at 101 MHz and 151 MHz for ^{13}C-NMR respectively. All experiments were measured at 25 °C in DMSO-d_6 or $CDCl_3$. The DMSO-d_6 utilized was purchased from VWR and is supplied with 0.03% (v/v) TMS-internal standard. Chemical shifts (**δ)** are reported as parts per million (ppm) and coupling constants (*J*) are reported in Hz. The chemical shifts are reported in relation to residual protio-solvent within the spectra: 7.26 ppm/77.16 ppm for ^{1}H- and ^{13}C-NMR in $CDCl_3$ and 2.50 ppm/39.52 ppm for ^{1}H- and ^{13}C-NMR in DMSO-d_6. Mass spectra were recorded using ESI as the method of ionization. HRMS-ESI spectra were measured with a QTOF instrument. Before submitting compounds to biological testing, samples were dried for a minimum of 3 hours on a high vacuum pump at pressure below 1 mbar.

Synthetic procedures

General procedure 1 – Carbamoylation of myxin (4) and 1-hydroxyphenazine 5,10-dioxides (synthesis of compounds 18-20, 27-29, 52-55, 57 and 61-62)

A dry round bottomed flask was charged with any type of 1-hydroxyphenazine 5,10-dioxide, compound **60** or myxin (**4**) (0.28 mmol, 1.0 eq.), DABCO (1.67 mmol, 3-6 eq.)* and a magnetic stir bar under argon atm. The mixture of solids was dispersed in THF (5-10 mL, anhydrous) and the resulting mixture cooled to 0 °C on ice water-bath. A carbamoyl chloride was added (0.84 mmol, 3 eq)* before the cooling source was removed and the mixture allowed to stir for a period of 90-180 min. If starting material was still observed after 3 hours from start (judged by TLC analysis typically using 2-5% MeOH/DCM as eluent), DABCO (1.12 mmol, 2.0 eq) and a carbamoyl chloride (0.56 mmol, 1.0 eq) were added and the mixture allowed to rotate at rt for additional period of 1-2 hours. The resulting mixture was diluted with 50 mL $NaHCO_3$ (saturated aqueous sol.) and the aqueous layer extracted with DCM (4 x 20 mL). The pooled organic phases were washed with brine, dried over $MgSO_4$ and filtered before solvents were removed *in vacuo*. The obtained crude materials were further purified as stated for each individual compound below.
**If the carbamoyl chloride was 4-Methyl-1-piperazinecarbonyl chloride hydrochloride salt, 6 eq. of DABCO were used*

General procedure 2 - alkylation of 1-hydroxyphenazines and analogs (synthesis of compounds 24-26, 48-51 and 56)

A dry round bottomed flask was charged with any type of 1-hydroxyphenazine 5,10-dioxide (0.30 mmol, 1.0 eq), K_2CO_3 (62 mg, 0.45 mmol, 1.5 eq) and 18-Crown-6 (119 mg, 0.45 mmol, 1.5 eq) and a magnetic stir bar at rt under argon atm. The mixture of solids was dispersed in DMF (5-10 mL, anhydrous) and allowed to stir for 15 min before a corresponding electrophile (3 eq, 0.90 mmol of either ethyl bromoacetate, *tert*butyl-bromoacetate or 2-chloro-*N*,*N*-diethylacetamide) was added. In cases where 2-chloro-*N*,*N*-diethylacetamide was used (synthesis of **26** and **56**), KI (15 mg, 0.09 mmol, 0.3 eq) was also added and the mixture left to stir overnight. In cases where bromoacetates were used (synthesis of **24-25** and **48-51**), the resulting mixture was left stirring for 2-5 h at room temperature (depending on TLC). If starting material was still present after 3-4 hours (TLC analysis, 2-5% MeO), K_2CO_3 (31 mg, 0.23 mmol, 0.75 eq), 18-Crown-6 (60 mg, 0.23 mmol, 0.75 eq) and a corresponding bromoacetate (0.45 mmol, 1.5 eq) were added and the resulting mixture left to stir for 1-2 additional hours. The mixture was diluted with H_2O (50 mL) and 1M HCl (aqueous sol. ~1 mL). The aqueous phase was extracted with DCM (3 x 30 mL or until no color was extracted from the aqueous phase). Pooled organic phases were washed with brine (100-200 mL), dried over $MgSO_4$ and filtered before concentrated *in vacuo*. Further purification was undertaken as stated below for each individual compound.

General procedure 3 - Oxidation of 1-hydroxyphenazines and analogs (synthesis of compounds 44-47 and 60)

These compounds were synthesized in accordance with a published procedure by this group for the synthesis of iodinin (**3**).[1] A dry round bottomed flask (with an attached reflux condenser) was charged with the corresponding 7,8-disubstituted-1-hydroxyphenazine (**40**-**43**) or 2,3-dimethylquinoxalin-5-ol (**60**) (1-2 mmol, 1 eq). The corresponding solid was dissolved in toluene (30-60 mL, anhydrous) at rt and *m*CPBA (2-4 mmol, 2 eq, Sigma Aldrich, <77%) was added before the resulting mixture was gradually warmed to 80 °C. *m*CPBA was added again 1 hour from the initial portion (1 mmol, 1 eq) and this step was repeated after 2 hrs, 3hrs and 4 hrs (a total reaction time of 5 hours; adding a total of 5 eq of *m*CPBA in pulses). If not stated otherwise, the reaction mixture was cooled on ice bath, transferred to a 1L round bottomed flask and carefully concentrated to a dark slur *in vacuo*. The crude afforded was purified further as stated for each individual compound below.

General procedure for the Synthesis of 7.8 substituted 1-methoxyphenazines 36-39

This method was performed in accordance to previous work published by Conda-Sheridan *et al*[2] and later by Huigens RW *et al*.[3] A dry round bottomed flask was charged with 3-methoxychatechol (1.4 -2.6g , 10-18.5 mmol, 1.0 equiv.) under argon atm. Anhydrous Et_2O was added (30-60 mL) at room temp and stirred until a clear solution was obtained. The solution afforded was cooled to -78° C before *o*-chloranil (3.07-5.69g, 12.5-23.1 mmol, 1.25 equiv) was added. The temperature (-78° C) was kept for

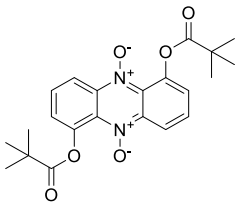
4h. The crude mixture was filtered twice using a Büchner funnel and a filter paper. The dark crude material retained was washed with 30-60 mL of ice-cold ether and left to dry for 10 minutes. The solid crude was then transferred to 250 mL round bottom flask containing a solution of the corresponding *ortho*diphenylamine **32**-**35** (0.5 equiv) in 1:1 PhMe/AcOH (70-140 mL). The obtained mixture was stirred for 24h at room temperature before it was *concentrated in vacuo* to a dark slurry material which was carefully neutralized with $NaHCO_3$ (sat. aqueous sol.). Before transferring to a separatory funnel for extraction, the obtained solution was filtered through a sinter under vacuum and the remaining residues on top washed with DCM until no yellow color was observed in the solution running through the filter. The organic layer was separated and the aqueous phase extracted with DCM (4x50 mL). Combined organic phases were dried over $MgSO_4$ and filtered. The resulting crude solution was absorbed onto silica gel.

General procedurefor the synthesis of 7.8 substituted 1-hydroxyphenazines 40-43

Unless stated otherwise, Boron tribromide (5g ampule, 20 mmol) was transferred to a dry round bottom flask containing a corresponding 1-methoxyphenazine **36-39** (0.8-3.9 mmol, 1 eq) under argon atm. The mixture was gradually warmed up to 90 °C and refluxed for 5 hrs. The mixture was cooled down on ice bath and quenched *very slowly and carefully* allowing one H_2O drop at a time to slide down the walls of the round bottom flask.* The pH of the aqueous mixture was adjusted to ~7 by 1M NaOH aqueous sol using standard pH paper as reference. The precipitated crude product was filtered and washed with cold H_2O. Further purification for each individual compound is stated below.

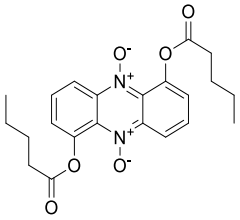
**This step produces fume as water reacts violently with* BBr_3

Experimental procedures for final compounds



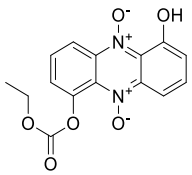
1,6-bis(pivaloyloxy)phenazine 5,10-dioxide (11)

A dry round bottomed flask was charged with iodinin (**3**)(50 mg, 0.20 mmol) under argon atm and dispersed in anhydrous toluene (4 mL). The dispersion was cooled down to -40 °C. Pivaloyl chloride was added drop wise (0.15 mL, 1.23 mmol) followed by Et_3N (0.17 mL, 1.23 mmol) and the resulting mixture stirred for 1 hour. DMAP (10 mg, 0.08 mmol) was added upon which the color of the mixture started immediately to turn from from dark purple towards brown/yellow. The mixture was stirred for 30 min or until no starting material observed by TLC and then quenched with H_2O (50 mL). The aqueous phase was extracted by EtOAc (3 x 25mL). Pooled organic phases were washed with HCl (0.1 M aqueous sol.), dried over $MgSO_4$ and filtered before solvents were removed *in vacuo*. Flash column chromatography on silica (20% EtOAc in heptane) afforded 33 mg (39%) of an orange solid. R_f: 0.28 (20% EtOAc in heptane). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.55 (dd, *J* = 9.1, 1.3 Hz, 2H), 7.65 (dd, *J* = 9.1, 7.5 Hz, 2H), 7.28 (dd, *J* = 7.5, 1.3 Hz, 2H), 1.50 (s, 18H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.9, 143.7, 139.2, 131.1, 130.2, 124.5, 118.7, 39.2, 27.4. HRMS (TOF ES$^+$): Exact mass calculated for $C_{22}H_{24}N_2O_6Na$ $[M+Na]^+$: 435.1532, found 435.1540 (1.82 ppm).



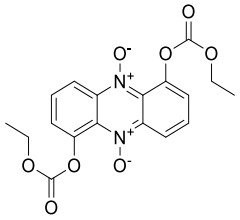
1,6-bis(pentanoyloxy)phenazine 5,10-dioxide (12)

A dry round bottomed flask was charged with iodinin (**3**)(45 mg, 0.18 mmol) under argon atm and dispersed in anhydrous toluene (5 mL). The deep purple dispersion was cooled down to 0 °C before valeric anhydride (218 µL, 1.11 mmol) was added dropwise. The mixture was stirred for 10 minutes before DMAP (4.5 mg, 0.04 mmol) was added, followed by Et_3N (102 µL, 0.74 mmol) upon which the mixture started to change color rapidly from purple towards more yellow/orange. The mixture was left stirring for a period of 16 hours and gradually reaching room temperature before it was quenched with NH_4Cl (50 mL 10% aqueous sol.) The aqueous layer was extracted with DCM (2 x 30 mL) and the pooled organic phases were washed with HCl (50 mL 0.1M aqueous sol.), brine (50 mL), dried over $MgSO_4$ and filtered. Flash column chromatography on silica (10-50% EtOAc/heptane) afforded 30 mg (39%) of an orange solid. R_f: 0.33 (30% EtOAc in heptane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (dd, *J* = 9.2, 1.3 Hz, 2H), 7.69 (dd, *J* = 9.1, 7.6 Hz, 2H), 7.34 (dd, *J* = 7.5, 1.3 Hz, 2H), 2.81 (t, *J* = 7.6 Hz, 4H), 1.84 (p, *J* = 7.6 Hz, 4H), 1.57 – 1.47 (m, 4H), 1.01 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 143.3, 139.2, 130.9, 130.6, 124.7, 118.6, 34.1, 26.7, 22.5, 14.0. HRMS (TOF ES+): Exact mass calculated for $C_{22}H_{24}N_2O_6$ Na [M+Na]+: 435.1532, found 435.1530 (-0.47 ppm).



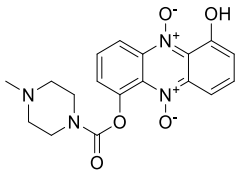
1-hydroxy-6-((ethoxycarbonyl)oxy)-phenazine 5,10-dioxide (13)

Iodinin (**3**) (160 mg, 0.66 mmol) was placed in a dry round bottomed flask and dispersed in anhydrous toluene (10 mL) and cooled down to -40 °C. Ethyl chloroformate (88 µL, 0.92 mmol) was added followed by DMAP (16 mg, 0.13 mmol). The resulting mixture was allowed to stir for 10 min before Et_3N (128 µL, 0.92 mmol) was added. After 1 hour, another portion of ethyl chloroformate (38 µL, 0.39 mmol, 0.6 eq) was added and the dry ice-acetone bath removed and the mixture stirred for a period of 30 min. The resulting mixture was diluted by Et_2O (30 mL) and filtered through a sintered funnel. The retained sediment (unreacted iodinin) on top washed with diethyl ether (20 mL) and MeOH (20 mL). The obtained crude solution was concentrated *in vacuo* and re-dissolved in EtOAc (50 mL). The organic phase was washed with HCl (1M aqueous sol., 2 x 30 mL), dried over $MgSO_4$, filtered and absorbed onto silica gel. Flash column chromatography (20-50% EtOAc in heptane) afforded 51 mg (25%) of a deep-red solid. R_f: 0.39 (1:1 EtOAc/Heptane). ^1H NMR (600 MHz, $CDCl_3$) δ 14.32 (s, 1H), 8.59 (dd, *J* = 9.1, 1.3 Hz, 1H), 7.98 (dd, *J* = 9.0, 1.1 Hz, 1H), 7.74 (dd, *J* = 9.1, 7.6 Hz, 1H), 7.65 (dd, *J* = 9.0, 7.9 Hz, 1H), 7.44 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.13 (dd, *J* = 7.9, 1.1 Hz, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.9, 153.0, 143.1, 138.6, 135.5, 133.2, 130.9, 130.9, 126.2, 124.0, 117.9, 115.3, 108.8, 65.9, 14.4. HRMS (EI^+): Exact mass calculated for $C_{15}H_{12}N_2O_6$: 316.0695, found 316.0686 (2.9 ppm).



1,6-bis((ethoxycarbonyl)oxy)phenazine 5,10-dioxide (14)

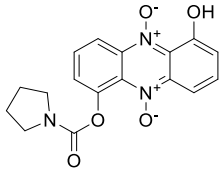
A dry round bottomed flask was charged with iodinin (**3**)(60 mg, 0.25 mmol) and dispersed in anhydrous toluene (4 mL). The purple dispersion was cooled down to 0 °C before ethyl chloroformate (105 µL, 1.10 mmol) was added. The mixture was stirred for 10 minutes before DMAP (15 mg, 0.12 mmol) was added followed by Et_3N (30 µL, 0.20 mmol) upon which the mixture starting to change color. The resulting mixture was left stirring for 30 min before another addition of ethyl chloroformate (50 µL, 0.52 mmol) and Et_3N (30 µL, 0.20 mmol) was added. The mixture was stirred at 0 °C for 90 min before filtered through a sinter and the retained material on top (mostly unreacted iodinin) washed with ice-cold Et_2O and MeOH (30 mL each). The filtered solution was concentrated *in vacuo,* dispersed in H_2O (50 mL) and the aqueous layer extracted with EtOAc (4 x 30 mL). The combined organic phases were washed with 1M HCl (aqueous sol., 150 mL), brine (150 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash column chromatography on silica (20-50% EtOAc in heptane) afforded 64 mg (67%) of an orange solid. R_f: 0.39 (50% EtOAc in heptane). ^1H NMR (600 MHz, $CDCl_3$) δ 8.59 (dd, *J* = 9.1, 1.3 Hz, 2H), 7.70 (dd, *J* = 9.1, 7.5 Hz, 2H), 7.46 (dd, *J* = 7.6, 1.3 Hz, 2H), 4.44 (q, *J* = 7.1 Hz, 4H), 1.47 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.1, 143.4, 139.1, 130.8, 130.6, 124.4, 119.0, 65.9, 14.4. HRMS (EI): Exact mass calculated for $C_{18}H_{16}N_2O_8$: 388.0907, found 388.0900 (1.8 ppm).



1-hydroxy-6-((4-methylpiperazine-1-carbonyl)oxy)phenazine 5,10-dioxide (15)

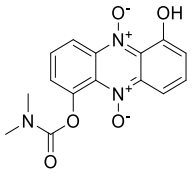
A dry round bottomed flask was charged with iodinin (**3**)(137 mg, 0.56 mmol, 1 eq), 4-methyl-1-piperazinecarbonyl chloride hydrochloride (553 mg, 2.78 mmol, 5 eq) and DABCO (261 mg, 2.22 mmol, 4 eq) under argon atm. Anhydrous THF (4 mL) was added at room temp upon which the color of the dispersion instantly started to turn from dark/purple towards brown/red. The mixture was left stirring for 90 min and then diluted with H_2O (100 mL). The aqueous phase was extracted by DCM (4 x 25 mL) before the pooled organic phases were extracted by 0.1M HCl (aqueous sol. 3 x 25 mL or until no red color was extracted). The aqueous phase was washed with DCM (2 x 20 mL) before the pH was adjusted to ~8 using K_2CO_3 (1M aqueous sol.). The resulting aqueous phase was then extracted with DCM (3 x 25 mL). The pooled organic phases were dried over $MgSO_4$ and filtered before concentrated *in vacuo*. Flash column chromatography on silica (0-2% MeOH/DCM) afforded 68 mg (33%) of a cherry red

solid. R*f*: 0.14 (5% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.39 (s, 1H), 8.50 (dd, *J* = 9.2, 1.3 Hz, 1H), 7.92 (dd, *J* = 9.0, 1.1 Hz, 1H), 7.69 (dd, *J* = 9.2, 7.6 Hz, 1H), 7.59 (dd, *J* = 9.0, 7.9 Hz, 1H), 7.35 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.08 (dd, *J* = 7.9, 1.1 Hz, 1H), 3.92 – 3.72 (m, 2H), 3.72 – 3.55 (m, 2H), 2.70 – 2.46 (m, 4H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.8, 153.3, 143.8, 138.5, 135.4, 132.7, 131.4, 130.9, 126.0, 124.6, 117.0, 115.0, 108.8, 54.8, 54.7, 46.4, 45.1, 44.4. HRMS (ESI$^+$): Exact mass calculated for $C_{18}H_{19}N_4O_5$ $[M+H]^+$: 371.1350, found 371.1348 (0.5 ppm).



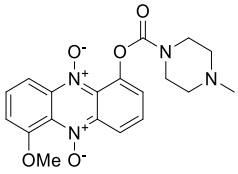
1-hydroxy-6-((pyrrolidine-1-carbonyl)oxy)phenazine 5,10-dioxide (16)

A dry round bottomed flask was charged with iodinin (**3**) (150 mg, 1.04 mmol) and DABCO (150 mg, 1.28 mmol) under argon atm. The solids were dispersed in THF (10 mL, anhydrous). The resulting mixture was cooled on ice bath for 10 min before 1-Pyrrolidinecarbonyl chloride (0.14 mL, 1.28 mmol) was added and mixture left stirring for 2 hours. The reaction mixture was diluted with H_2O (50 mL) and 0.1 M HCl (aqueous sol., 20 mL) and the aqueous layer extracted with DCM (3 x 30 mL). The combined organic phases were dried over $MgSO_4$ and filtered. The afforded crude solution was eluted through a plug of silica gel (5% MeOH in DCM) only collecting solution of intense dark-red color which subsequently was concentrated *in vacuo*. Flash column chromatography on silica (0-5% MeOH in DCM) gave 24 mg (11%) of a deep-red solid. R$_f$: 0.63 (3% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.46 (s, 1H), 8.53 (dd, *J* = 9.2, 1.3 Hz, 1H), 7.95 (dd, *J* = 9.1, 1.1 Hz, 1H), 7.72 (dd, *J* = 9.2, 7.5 Hz, 1H), 7.61 (dd, *J* = 9.0, 7.9 Hz, 1H), 7.38 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.10 (dd, *J* = 7.9, 1.1 Hz, 1H), 3.76 (t, *J* = 6.7 Hz, 2H), 3.55 (t, *J* = 6.7 Hz, 2H), 2.14 – 1.96 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 152.8, 143.9, 138.7, 135.5, 132.7, 131.7, 131.0, 126.0, 124.8, 116.9, 115.0, 108.9, 46.9, 46.8, 26.0, 25.3. HRMS (TOF ES+): Exact mass calculated for $C_{17}H_{15}N_3O_5Na$ [M+Na]+: 364.364.0904, found 364.0896 (2.1 ppm).



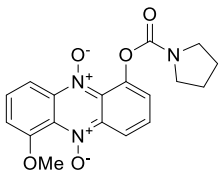
1-hydroxy-6-((dimethylcarbamoyl)oxy)phenazine 5,10-dioxide (17)

A dry round bottomed flask was charged with iodinin (**3**) (250 mg, 1.02 mmol), DABCO (359 mg, 3.06 mmol) and a magnetic stir bar. The mixture of solids was dispersed in THF (7 mL, anhydrous) and stirred for 10 min. Thereafter, dimethylcarbamoyl chloride (141 µL, 1.53 mmol) was added. The resulting mixture was left stirring overnight before it was filtered (filter paper and Büchner funnel) and the retained filtrate on top washed with DCM (50 mL) and H_2O (100 mL). The filtered aqueous and organic phases were transferred to a separatory funnel and separated. The aqueous phase was extracted further with DCM (3x40 mL). The combined organic phases were washed with brine (300 mL), dried over $MgSO_4$, filtered and absorbed onto silica gel *in vacuo*. Flash column chromatography on silica (1% MeOH in DCM) afforded 30 mg (9%) of a cherry red solid. R*f*: 0.09 (1% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.44 (s, 1H), 8.54 (dd, *J* = 9.1, 1.3 Hz, 1H), 7.96 (dd, *J* = 9.0, 1.1 Hz, 1H), 7.72 (dd, *J* = 9.2, 7.6 Hz, 1H), 7.62 (dd, *J* = 9.0, 7.9 Hz, 1H), 7.38 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.11 (dd, *J* = 7.9, 1.1 Hz, 1H), 3.27 (s, 3H), 3.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.6, 153.9, 144.0, 138.7, 135.5, 132.8, 131.6, 131.0, 126.1, 124.8, 117.0, 115.0, 108.9, 37.2, 37.0. HRMS (ESI$^+$): Exact mass calculated for $C_{15}H_{13}N_3O_5$ $[M+K]^+$: 354.0487, found 354.0487 (-0.1 ppm).



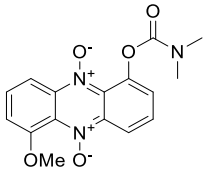
1-((4-methylpiperazine-1-carbonyl)oxy)-6-methoxyphenazine 5,10-dioxide (18)

Prepared in accordance with general procedure 1 from myxin (**4**) (72 mg scale). Flash column chromatography on silica (2-5% MeOH in DCM) afforded 92 mg (86%). R_f: 0.19 (5% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (dd, *J* = 9.2, 1.3 Hz, 1H), 8.22 (dd, *J* = 9.1, 1.1 Hz, 1H), 7.65 (dd, *J* = 9.1, 7.6 Hz, 1H), 7.59 (dd, *J* = 9.1, 8.0 Hz, 1H), 7.06 (dd, *J* = 8.1, 1.1 Hz, 1H), 4.06 (s, 3H), 3.93 – 3.76 (m, 2H), 3.73 – 3.53 (m, 2H), 2.79 – 2.47 (m, 4H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 153.5, 143.8, 139.6, 139.2, 131.0, 131.0, 130.0, 129.6, 124.9, 118.5, 112.1, 110.4, 57.4, 54.8, 54.7, 46.3, 45.1, 44.3. HRMS (ESI$^+$): Exact mass calculated for $C_{19}H_{21}N_4O_5$ $[M+H]^+$: 385.1506, found 385.1506 (0.0 ppm).



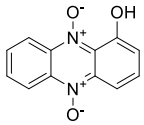
1-((pyrrolidine-1-carbonyl)oxy)-6-methoxyphenazine 5,10-dioxide (19)

Prepared in accordance to general procedure 1 from myxin (**4**) (55 mg scale). Flash column chromatography on silica (0-2% MeOH in DCM) afforded 44 mg (59%) of an orange solid. R_f: 0.13 (3% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (dd, *J* = 9.2, 1.3 Hz, 1H), 8.22 (dd, *J* = 9.1, 1.1 Hz, 1H), 7.65 (dd, *J* = 9.1, 7.5 Hz, 1H), 7.57 (dd, *J* = 9.1, 8.0 Hz, 1H), 7.37 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.05 (dd, *J* = 8.1, 1.1 Hz, 1H), 4.06 (s, 3H), 3.76 (t, *J* = 6.7 Hz, 2H), 3.54 (t, *J* = 6.6 Hz, 2H), 2.12 – 1.93 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.95, 153.0, 143.8, 139.7, 139.2, 131.3, 130.9, 130.1, 129.6, 125.0, 118.4, 112.1, 110.4, 57.4, 46.8, 26.0, 25.2. HRMS (ESI$^+$): Exact mass calculated for $C_{18}H_{17}N_3O_5Na$ $[M+Na]^+$: 378.1060, found 378.1061 (-0.2 ppm).



1-((dimethylcarbamoyl)oxy)-6-methoxyphenazine 5,10-dioxide (20)

Prepared in accordance to general procedure 1 from myxin (**4**) (48 mg scale). Flash column chromatography (1% MeOH in DCM) afforded 29 mg (46%) of an orange solid. R_f: 0.24 (3% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (dd, *J* = 9.1, 1.3 Hz, 1H), 8.24 (dd, *J* = 9.1, 1.1 Hz, 1H), 7.65 (dd, *J* = 9.1, 7.5 Hz, 1H), 7.59 (dd, *J* = 9.1, 8.0 Hz, 1H), 7.36 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.06 (dd, *J* = 7.9, 1.1 Hz, 1H), 4.07 (s, 3H), 3.26 (s, 3H), 3.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8, 154.0, 144.0, 139.7, 139.3, 131.2, 131.0, 130.0, 129.7, 125.0, 118.5, 112.2, 110.5, 57.4, 37.1, 37.0. HRMS (ESI$^+$): Exact mass calculated for C16$H_{15}N_3O_5Na$ $[M+Na]^+$: 352.0904, found 352.0904 (-0.1 ppm).



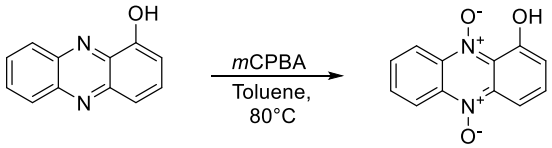
1-Hydroxyphenazine 5,10-dioxide (21) from benzofuroxane

The compound was synthesized according to the published procedure by Haddadin *et al*.[4] with small modifications. Benzofuroxan (6.0 g, 44 mmol) dissolved in diethylamine (60 mL) was added drop wise to a stirring solution of 1.2-cyclahexanedione (2.47 g, 22.0 mmol) in diethylamine (25 mL) at 0 °C under open air. Upon complete addition, the mixture was stirred for 30 min before the ice bath was removed. The resulting mixture was then stirred for additional 60 min gradually reaching room temperature before the mixture was pored over ice and neutralized with AcOH (drop-wise, ~60 mL). The precipitated red crude compound was filtered (filter paper and Büchner funnel) and the retained filter cake was washed with cold H_2O and then dried. The red crude material was collected in a 250 mL round bottomed flask, attached to a reflux condenser and subsequently dispersed in toluene (150 mL). *m*CPBA (2.5g, Sigma Aldrich, < 77%) was added and the mixture gradually warmed up to 80 °C. *m*CPBA (1.5 g) was added again 1 hr from start, 2 hrs from start and 3 hrs from start. The resulting mixture was left stirring for 60 min after addition of the 3rd portion of *m*CPBA. After cooldown on ice-bath, the mixture was transferred to a 1L round bottomed flask and carefully concentrated to a dark slur *in vacuo*. The crude afforded was re-dissolved in minimum amount of DCM and the crude mixture absorbed onto silica gel. The silica-absorbed crude material was placed on top of a silica plug (8 cm high, 5 cm in

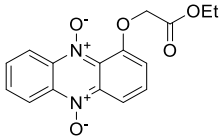
diameter) and eluted trough silica under vacuum using 0-50% EtOAc in DCM, only collecting solution of intense brown-red color. The dark-red solution was further concentrated *in vacuo* and the obtained crude material dispersed in MeOH and filtered (Büchner funnel and filter paper). The retained filter cake on top was washed further in the following order; H_2O (100 mL), MeOH (50 mL), sat. $NaHCO_3$ (aqueous sol., 100 mL), H_2O (100 mL) and MeOH (50 mL). The brown-red filter cake was dried before the material on top was collected, dissolved in minimum amount of $CHCl_3$ and concentrated *in vacuo* affording 2.0 g (40% over 2 steps) of a brown-red powder. No further purification proved to be necessary. R_f: 0.74 (1% MeOH/DCM). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 14.48 (s, 1H), 8.69 – 8.59 (m, 2H), 8.06 (dd, *J* = 9.0, 1.1 Hz, 1H), 7.89 – 7.77 (m, 2H), 7.68 (dd, *J* = 9.0, 7.9 Hz, 1H), 7.14 (dd, *J* = 7.9, 1.1 Hz, 1H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 154.1, 137.5, 136.1, 133.8, 133.0, 131.8, 131.7, 126.6, 120.1, 119.4, 114.7, 108.7. HRMS (ESI+): Exact mass calculated for $C_{12}H_8N_2O_3$ Na [M+Na]+: 251.0427, found 251.0427 (0.1 ppm).

******An alternative preparation of this compound from 1-hydroxyphenazine (compound **22**) is described within the supplementary information.*

1-Hydroxyphenazine 5.10-dioxide (21) from 1-hydroxyphenazine (22)

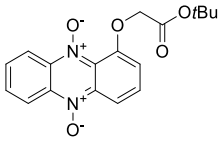


A dry round bottomed flask (with a reflux condenser) was loaded with 1-hydroxyphenazine (694 mg, 3.54 mmol) at rt under argon atm. The yellow solid was suspended in 80 mL of anhydrous toluene and stirred for 10 min at rt. *m*CPBA (1.55 g, ≤77% purity; Sigma-Aldrich) was added before the mixture was shielded from light and gradually warmed to 80 °C and added 0.8 g *m*CPBA in pulses every hour from addition of the first portion (repeated 4 times). After 5 h at 80 °C, the reaction mixture cooled down on ice bath before toluene was carefully removed *in vacuo*. The resulting dark crude material was dispersed in DCM and dry-loaded on silica gel. The silica absorbed crude material was eluted through a plug of silica using DCM, only collecting product of intense dark-red color. The afforded red solution was concentrated *in vacuo* before the crude material was dispersed in MeOH/Et_2O (1:1). The dispersion was filtered and the retained crude material on top washed with MeOH, $NaHCO_3$ (sat. aqueous sol.), H_2O and dried. The collected crude material was further purified by flash column chromatography on silica (0-1% MeOH/DCM) affording 399 mg (49%) of the dark red solid. R_f: 0.74 (1% MeOH/DCM). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 14.48 (s, 1H), 8.69 – 8.59 (m, 2H), 8.06 (dd, *J* = 9.0, 1.1 Hz, 1H), 7.89 – 7.77 (m, 2H), 7.68 (dd, *J* = 9.0, 7.9 Hz, 1H), 7.14 (dd, *J* = 7.9, 1.1 Hz, 1H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 154.1, 137.5, 136.1, 133.8, 133.0, 131.8, 131.7, 126.6, 120.1, 119.4, 114.7, 108.7. HRMS (ESI+): Exact mass calculated for $C_{12}H_8N_2O_3$ Na [M+Na]+: 251.0427, found 251.0427 (0.1 ppm).



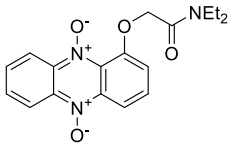
1-(2-ethoxy-2-oxoethoxy)phenazine 5,10-dioxide (24)

Prepared in accordance to general procedure 2 from **21** (64 mg scale). Flash column chromatography (dry-load) on silica (2-5% MeOH in DCM) gave 71 mg (81%) of an orange solid. R_f: 0.46 (5% MeOH/DCM). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.66 (td, *J* = 8.2, 1.8 Hz, 2H), 8.41 (dd, *J* = 9.1, 1.2 Hz, 1H), 7.84 – 7.72 (m, 2H), 7.62 (dd, *J* = 9.1, 7.8 Hz, 1H), 7.14 (dd, *J* = 7.8, 1.2 Hz, 1H), 4.88 (s, 2H), 4.29 (q, *J* = 7.2 Hz, 2H), 1.31 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 168.1, 151.9, 138.4, 137.6, 135.7, 131.7, 131.1, 130.8, 130.8, 120.7, 120.2, 115.1, 114.3, 68.6, 61.7, 14.3. HRMS (ESI^+): Exact mass calculated for $C_{16}H_{14}N_2O_5Na$ $[M+Na]^+$: 337.0795, found 337.0795 (-0.1 ppm).



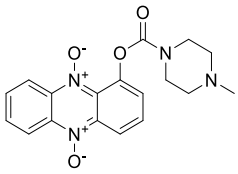
1-(2-(tert-butoxy)-2-oxoethoxy)phenazine 5,10-dioxide (25)

Prepared in accordance with general procedure 2 from **21** (47 mg scale). Flash column chromatography (dry-load) on silica (60-100% EtOAc/heptane) gave 58 mg (82%) of an orange solid. R_f: 0.41 (100% EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 – 8.60 (m, 2H), 8.38 (dd, *J* = 9.1, 1.2 Hz, 1H), 7.86 – 7.73 (m, 2H), 7.61 (dd, *J* = 9.1, 7.9 Hz, 1H), 7.08 (dd, *J* = 7.9, 1.2 Hz, 1H), 4.77 (s, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 152.2, 138.4, 137.6, 135.7, 131.7, 131.0, 130.8, 130.6, 120.7, 120.1, 113.9, 113.7, 82.9, 68.4, 28.2. HRMS (ESI$^+$): Exact mass calculated for $C_{18}H_{18}N_2O_5Na$ [M+Na]$^+$: 365.1108, found 365.1107 (0.4 ppm).



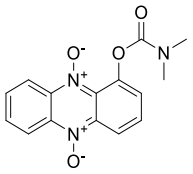
1-(2-(diethylamino)-2-oxoethoxy)phenazine 5,10-dioxide (26)

Prepared in accordance with general procedure 2 from **21** (200 mg scale). Flash column chromatography on silica (2-5% MeOH/DCM) and subsequent recrystallization from hot EtOH afforded 75 mg (25%) of the orange solid. R_f: 0.22 (5% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 – 8.61 (m, 2H), 8.39 (dd, *J* = 9.1, 1.2 Hz, 1H), 7.85 – 7.73 (m, 2H), 7.64 (dd, *J* = 9.0, 7.9 Hz, 1H), 7.33 (dd, *J* = 7.9, 1.2 Hz, 1H), 4.98 (s, 2H), 3.55 (q, *J* = 7.1 Hz, 2H), 3.42 (q, *J* = 7.1 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 152.4, 138.5, 137.6, 135.8, 131.7, 131.2, 131.0, 130.6, 120.7, 120.3, 114.7, 113.6, 70.6, 41.7, 40.5, 14.5, 13.0. HRMS (ESI$^+$): Exact mass calculated for $C_{18}H_{19}N_3O_4Na$ [M+Na]$^+$: 364.1268, found 364.1267 (0.1 ppm).



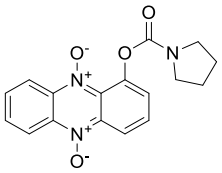
1-((4-methylpiperazine-1-carbonyl)oxy)phenazine 5,10-dioxide (27)

Prepared in accordance with general procedure 1 from **21** (74 mg scale). Flash column chromatography on silica (2-5% MeOH/DCM) afforded 83 mg (73%) of the yellow solid. R_f: 0.13 (5% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 – 8.59 (m, 3H), 7.84 – 7.74 (m, 2H), 7.71 (dd, *J* = 9.1, 7.6 Hz, 1H), 7.38 (dd, *J* = 7.6, 1.3 Hz, 1H), 3.88 (s, 2H), 3.68 (s, 2H), 2.75 – 2.53 (m, 4H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.5, 144.1, 138.0, 137.3, 135.8, 131.7, 131.5, 131.2, 130.5, 124.6, 120.5, 120.2, 118.3, 54.8, 54.7, 46.4, 45.1, 44.3. HRMS (ESI$^+$): Exact mass calculated for $C_{18}H_{19}N_4O_4$ [M+H]$^+$: 355.1401, found 355.1401 (0.0 ppm).



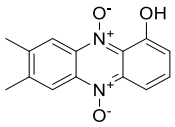
1-((dimethylcarbamoyl)oxy)phenazine 5,10-dioxide (28)

Prepared in accordance with general procedure 1 from **21** (78 mg scale). The reaction mixture was diluted with H_2O (30 mL) which gave a dispersion of orange particles which were filtered and washed with cold HCl (0.1 M aqueous sol.) and H_2O (50 mL). The obtained crude material from filtration was re-dissolved in DCM and absorbed onto silica. Flash column chromatography on silica (0-2% MeOH/DCM) afforded 79 mg (77%) of an orange solid. R_f: 0.39 (5% MeOH/DCM).^{1}H NMR (400 MHz,$CDCl_3$) δ 8.72 – 8.60 (m, 3H), 7.83 – 7.74 (m, 2H), 7.71 (dd, *J* = 9.1, 7.5 Hz, 1H), 7.39 (dd, *J* = 7.5, 1.3 Hz, 1H), 3.28 (s, 3H), 3.11 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8, 144.3, 138.0, 137.5, 135.9, 131.7, 131.7, 131.2, 130.5, 124.7, 120.6, 120.3, 118.2, 37.2, 37.1. HRMS (ESI$^+$): Exact mass calculated for $C_{15}H_{13}N_3O_4Na$ [M+Na]$^+$: 322.0798, found 322.0798 (-0.1 ppm).



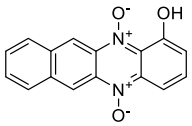
1-((pyrrolidine-1-carbonyl)oxy)phenazine 5,10-dioxide (29)

Prepared in accordance to general procedure 1 from **21** (51 mg scale). Flash column chromatography on silica (0-1% MeOH/DCM) afforded 63 mg (87%) of an orange solid. R_f: 0.05 (2% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 – 8.54 (m, 3H), 7.81 – 7.64 (m, 3H), 7.37 (dd, *J* = 7.5, 1.3 Hz, 1H), 3.75 (t, *J* = 6.7 Hz, 2H), 3.54 (t, *J* = 6.6 Hz, 2H), 2.13 – 1.94 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.9, 144.1, 137.9, 137.4, 135.7, 131.7, 131.6, 131.0, 130.5, 124.6, 120.5, 120.1, 118.0, 46.8, 46.8, 26.0, 25.2. HRMS (ESI$^+$): Exact mass calculated for $C_{17}H_{15}N_3O_4Na$ [M+Na]$^+$: 348.0955, found 348.0953 (0.4 ppm).



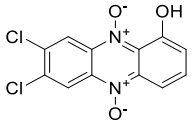
1-hydroxy-7,8-dimethylphenazine 5,10-dioxide (44)

Prepared in accordance with general procedure 3 from **40** (202 mg scale). Upon cooldown. the crude mixture was diluted with $NaHCO_3$ (sat. aqueous sol., 200 mL) and the phases separated. The aqueous layer was further extracted with DCM (2 x 40 mL). The pooled organic phases were dried over $MgSO_4$ and filtered through a plug of silica (0-1% MeOH/DCM) under vacuum, only collecting solution of intense red color. The obtained crude solution was absorbed onto silica gel. Flash column chromatography (dry-load) on silica (0-1% MeOH/DCM) afforded 185 mg (79 %) of a red-brown solid. R_f: 0.22 (1% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.52 (broad s, 1H), 8.40 (s, 1H), 8.38 (s, 1H), 8.05 (dd, *J* = 9.0, 1.1 Hz, 1H), 7.65 (dd, *J* = 8.9, 7.9 Hz, 1H), 7.11 (dd, *J* = 7.9, 1.1 Hz, 1H), 2.57 – 2.51 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 143.9, 143.7, 137.0, 134.7, 132.5, 132.4, 126.0, 118.7, 117.8, 114.2, 108.6, 20.8, 20.8. HRMS (ESI$^+$): Exact mass calculated for $C_{14}H_{12}N_2O_3Na$ [M+Na]$^+$: 279.0740, found 279.0741 (-0.2 ppm).



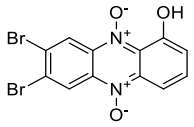
1-hydroxybenzo[b]phenazine 5,12-dioxide (45)

Prepared in accordance with general procedure 3 from **41** (370 mg scale). After solvent removal *in vacuo,* the obtained crude material was dissolved in minimum amount of DCM and absorbed onto silica gel. The silica-absorbed crude material was placed on top of a silica plug and eluted through with DCM as solvent. Only solution of intense dark-blue color was collected and concentrated *in vacuo*. The obtained crude material was dispersed in ice-cold MeOH, filtered and washed with ice-cold MeOH (40 mL). The retained crude material was collected, dissolved in a minimum amount of DCM and absorbed onto silica gel. Flash column chromatography (dry-load) on silica afforded 126 mg (30%) of a dark-blue solid. R_f: 0.22 (DCM). ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 14.80 (s, 1H), 9.30 (s, 1H), 9.24 (s, 1H), 8.38 (dt, *J* = 6.8, 3.6 Hz, 2H), 7.92 (dd, *J* = 9.1, 1.0 Hz, 1H), 7.77 – 7.66 (m, 3H), 7.09 (dd, *J* = 7.7, 1.0 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 152.9, 136.5, 133.8, 133.8, 133.5, 132.2, 131.3, 129.0, 128.8, 128.8, 126.6, 118.5, 118.1, 112.8, 108.2. HRMS (ESI$^+$): Exact mass calculated for $C_{16}H_{10}N_2O_3Na$ [M+Na]$^+$: 301.0584, found 301.0583 (0.4 ppm).



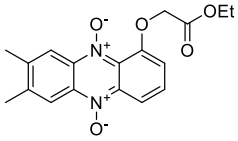
7,8-dichloro-1-hydroxyphenazine 5,10-dioxide (46)

Prepared in accordance with general procedure 3 from **42** (340 mg scale). The resulting dark crude-slur was dispersed in sat. $NaHCO_3$ (aqueous sol., 100 mL) and filtered (Büchner funnel and filter paper) where the retained crude material was further washed with ice-cold H_2O and MeOH (50 mL each). Upon drying, the material was collected, dissolved in DCM and absorbed onto silica gel. Flash column chromatography (DCM) afforded crude material which was further purified by a wash on a filter paper (using a Büchner funnel) in the following order: sat. $NaHCO_3$ (aqueous sol., 50 mL), H_2O (50 mL), MeOH (25 mL) and Et_2O (25 mL). This procedure gave 120 mg (31%) of a deep purple solid which used for synthesis of derivatives without further purification. R_f: 0.35 (DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.10 (s, 1H), 8.78 (s, 1H), 8.77 (s, 1H), 8.03 (dd, *J* = 9.0, 1.1 Hz, 1H), 7.71 (dd, *J* = 8.9, 7.9 Hz, 1H), 7.17 (dd, *J* = 8.0, 1.1 Hz, 1H). HRMS (ESI$^+$): Exact mass calculated for $C_{12}H_6Cl_2N_2O_3Na$ $[M+Na]^+$: 318.9648, found 318.9647 (0.4 ppm).



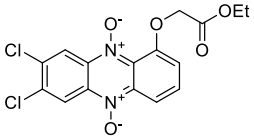
7,8-dibromo-1-hydroxyphenazine 5,10-dioxide (47)

Prepared in accordance to general procedure 3 from **43** (293 mg scale). After the reaction mixture was concentrated to a slur *in vacuo*, the obtained crude material was re-dissolved in DCM and eluted through a plug of silica (100% DCM) with a Na_2SO_4 and celite on top (1 cm layer each). Only solution of intense dark-purple colour was collected. The afforded DCM solution was transferred to a separatory funnel and washed with sat $NaHCO_3$ (aqueous sol., 300 mL) before concentrated *in vacuo*. The obtained crude material was dispersed in ice-cold mixture of MeOH and Et_2O (1:1) and filtered (Büchner funnel and filter paper) before dried. Flash column chromatography on silica (100% DCM) afforded 143 mg (45%) of a deep-purple solid. R_f: 0.60 (2% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.10 (s, 1H), 8.95 (s, 1H), 8.93 (s, 1H), 8.03 (dd, *J* = 8.9, 1.1 Hz, 1H), 7.71 (dd, *J* = 9.0, 7.9 Hz, 1H), 7.17 (dd, *J* = 8.0, 1.1 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.1, 137.8, 134.7, 133.6, 132.5, 130.2, 130.0, 126.7, 124.3, 123.7, 115.6, 109.0. HRMS (ESI$^+$): Exact mass calculated for $C_{12}H_6BrN_2O_3{}^{81}BrNa$ $[M+Na]^+$: 408.8617, found 408.8617 (0.0 ppm).



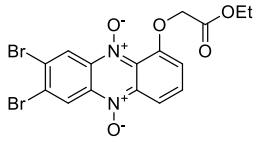
1-(2-ethoxy-2-oxoethoxy)-7,8-dimethylphenazine 5,10-dioxide (48)

Prepared in accordance with general procedure 2 from **44** (33 mg scale). Flash column chromatography on silica (EtOAc) afforded 34 mg (80%) of an orange solid. R_f: 0.24 (5% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 – 8.33 (m, 3H), 7.59 (dd, *J* = 9.1, 7.8 Hz, 1H), 7.14 (dd, *J* = 7.8, 1.2 Hz, 1H), 4.87 (s, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.55 – 2.44 (m, 6H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 151.9, 143.7, 142.9, 138.0, 136.3, 134.5, 130.5, 130.4, 119.5, 119.0, 115.5, 114.6, 69.0, 61.7, 20.7, 20.6, 14.3. HRMS (ESI$^+$): Exact mass calculated for $C_{18}H_{18}N_2O_5Na$ $[M+Na]^+$: 365.1108, found 365.1109 (-0.2 ppm).



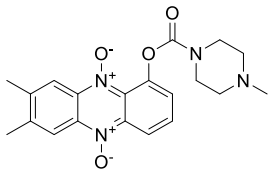
7,8-dichloro-1-(2-ethoxy-2-oxoethoxy)phenazine 5,10-dioxide (50)

Prepared in accordance to general procedure 2 from **46** (34 mg scale). Flash column chromatography on silica (0-10% EtOAc in DCM) afforded 42 mg (95%) of a red solid. R_f: 0.27 (10% EtOAc in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.78 (s, 1H), 8.37 (dd, *J* = 9.1, 1.2 Hz, 1H), 7.66 (dd, *J* = 9.1, 7.9 Hz, 1H), 7.15 (dd, *J* = 7.9, 1.2 Hz, 1H), 4.88 (s, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 152.0, 138.8, 137.8, 137.1, 135.9, 134.1, 131.5, 131.0, 121.9, 121.4, 115.2, 114.2, 68.4, 61.9, 14.3. HRMS (ESI$^+$): Exact mass calculated for $C_{16}H_{12}Cl_2N_2O_5Na$ $[M+Na]^+$: 405.0015, found 405.0015 (0.0 ppm).



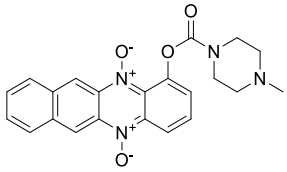
7,8-dibromo-1-(2-ethoxy-2-oxoethoxy)phenazine 5,10-dioxide (51)

Prepared in accordance to general procedure 2 from **47** (55 mg scale). Flash column chromatography on silica (10% EtOAc in DCM) afforded 65 mg (97%) of a red solid. R_f: 0.36 (10% EtOAc/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (s, 1H), 8.95 (s, 1H), 8.37 (dd, *J* = 9.1, 1.2 Hz, 1H), 7.66 (dd, *J* = 9.1, 7.9 Hz, 1H), 7.15 (dd, *J* = 7.9, 1.2 Hz, 1H), 4.31 (q, *J* = 7.2 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 152.1, 138.8, 136.3, 134.5, 131.5, 131.0, 130.0, 129.1, 125.2, 124.6, 115.3, 114.2, 68.5, 61.9, 14.3. HRMS (ESI$^+$): Exact mass calculated for $C_{16}H_{12}N_2O_5{}^{79}Br^{81}BrNa$ [M+Na]$^+$: 494.8985, found 494.8985 (-0.2 ppm).



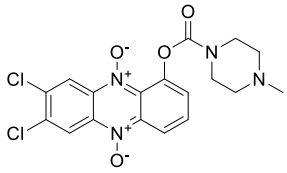
7,8-dimethyl-1-((4-methylpiperazine-1-carbonyl)oxy)phenazine 5,10-dioxide (52)

Prepared in accordance to general procedure 1 from **44** (23 mg scale). Flash column chromatography on silica (0-5% MeOH in DCM) afforded 34 mg (99 %) of an orange solid. R_f: 0.12 (5% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 9.1, 1.3 Hz, 1H), 8.41 (s, 1H), 8.37 (s, 1H), 7.67 (dd, *J* = 9.1, 7.5 Hz, 1H), 7.35 (dd, *J* = 7.5, 1.3 Hz, 1H), 3.88 (s, 2H), 3.68 (s, 2H), 2.72 – 2.54 (m, 4H), 2.54 – 2.47 (m, 6H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.6, 144.0, 143.5, 143.0, 137.5, 136.0, 134.5, 131.0, 130.0, 124.2, 119.3, 119.0, 118.2, 54.8, 54.7, 46.4, 45.0, 44.3, 20.6. HRMS (ESI$^+$): Exact mass calculated for $C_{20}H_{23}N_4O_4$ [M+H]$^+$: 383.1714, found 383.1715 (-0.2 ppm).



1-((4-methylpiperazine-1-carbonyl)oxy)benzo[b]phenazine 5,12-dioxide (53)

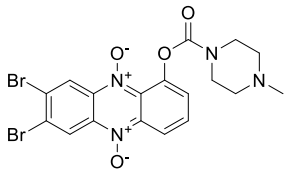
Prepared in accordance to general procedure 1 from **45** (20 mg scale). Flash column chromatography on silica (2-5% MeOH in DCM) afforded 28 mg (97%) of the dark purple solid. R_f: 0.23 (5% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (s, 1H), 9.19 (s, 1H), 8.63 (dd, *J* = 9.2, 1.3 Hz, 1H), 8.18 – 8.06 (m, 2H), 7.71 – 7.60 (m, 3H), 7.34 (dd, *J* = 7.5, 1.3 Hz, 1H), 3.97 (s, 2H), 3.76 (s, 2H), 2.99 – 2.59 (m, 5H), 2.51 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.6, 143.9, 137.4, 134.7, 134.5, 134.3, 133.3, 131.2, 130.0, 129.1, 129.0, 129.0, 128.9, 124.0, 119.9, 119.5, 118.3, 54.8, 54.7, 46.3, 45.0, 44.3. HRMS (ESI$^+$): Exact mass calculated for $C_{22}H_{21}N_4O_4$ [M+H]$^+$: 405.1557, found 405.1557 (0.1 ppm).



7,8-dichloro-1-((4-methylpiperazine-1-carbonyl)oxy)phenazine 5,10-dioxide (54)

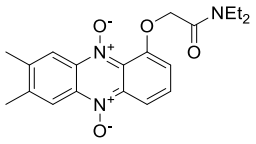
Prepared in accordance to general procedure 1 from **46** (25 mg scale). Flash column chromatography on silica (0-5% MeOH in DCM) afforded 23 mg (65%) of an orange solid. R_f: 0.13 (5% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.73 (s, 1H), 8.58 (dd, *J* = 9.2, 1.3 Hz, 1H), 7.74 (dd, *J* = 9.1, 7.6 Hz, 1H), 7.41 (dd, *J* = 7.6, 1.3 Hz, 1H), 3.88 (s, 2H), 3.70 (s, 2H), 2.85 – 2.53 (m, 4H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 144.2, 138.4, 137.7, 137.3, 135.6, 134.2, 131.9, 131.2, 125.3,

121.7, 121.4, 118.3, 54.7, 53.6, 46.3, 44.9, 44.2. HRMS (ESI$^+$): Exact mass calculated for $C_{18}H_{17}Cl_2N_4O_4$ [M+H]$^+$: 423.0621, found 423.0621 (0.1 ppm).



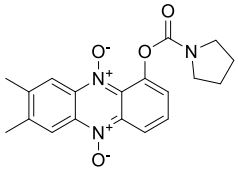
7,8-dibromo-1-((4-methylpiperazine-1-carbonyl)oxy)phenazine 5,10-dioxide (55)

Prepared in accordance to general procedure 1 from **47** (62 mg scale). Flash column chromatography on silica (1-5% MeOH in DCM) afforded 63 mg (77%) of a red solid. R_f: 0.08 (3% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.87 (s, 1H), 8.54 (dd, *J* = 9.2, 1.3 Hz, 1H), 7.72 (dd, *J* = 9.1, 7.6 Hz, 1H), 7.39 (dd, *J* = 7.6, 1.3 Hz, 1H), 3.90 – 3.75 (m, 2H), 3.70 – 3.56 (m, 2H), 2.73 – 2.59 (m, 2H), 2.55 (t, *J* = 5.0 Hz, 2H), 2.41 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 144.2, 138.3, 136.0, 134.5, 131.9, 131.1, 129.8, 129.3, 125.2, 124.9, 124.5, 118.2, 54.8, 54.7, 46.4, 45.1, 44.4. HRMS (ESI$^+$): Exact mass calculated for $C_{18}H_{17}N_4O_4{}^{79}Br^{81}Br$ [M+H]$^+$: 512.9591, found 512.9590 (0.2 ppm).



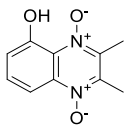
1-(2-(diethylamino)-2-oxoethoxy)-7,8-dimethylphenazine 5,10-dioxide (56)

Prepared in accordance to general procedure 2 from **44** (69 mg scale). Flash column chromatography on silica (0-5% MeOH in DCM) and subsequent recrystallization from hot EtOH afforded 51 mg (51 %) of an orange solid. R_f: 0.30 (5% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 – 8.41 (m, 2H), 8.39 (dd, *J* = 9.1, 1.2 Hz, 1H), 7.61 (dd, *J* = 9.0, 7.8 Hz, 1H), 7.32 (dd, *J* = 7.9, 1.2 Hz, 1H), 4.97 (s, 2H), 3.56 (q, *J* = 7.1 Hz, 2H), 3.42 (q, *J* = 7.1 Hz, 2H), 2.57 – 2.45 (m, 6H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 152.3, 143.6, 142.8, 138.0, 136.2, 134.4, 130.8, 130.1, 119.4, 119.0, 114.6, 113.7, 70.8, 41.7, 40.5, 20.7, 20.6, 14.5, 13.0. HRMS (ESI$^+$): Exact mass calculated for $C_{20}H_{23}N_3O_4Na$ [M+Na]$^+$: 392.1581, found 392.1581 (-0.2 ppm).



7,8-dimethyl-1-((pyrrolidine-1-carbonyl)oxy)phenazine 5,10-dioxide (57)

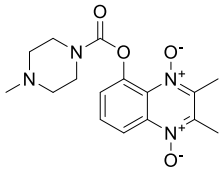
Prepared in accordance to general procedure 1 from **44** (69 mg scale). Flash column chromatography on silica (0-5% MeOH in DCM) and subsequent recrystallization from hot EtOH afforded 35 mg (37%) of orange flakes. R_f: 0.52 (5% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (dd, *J* = 9.1, 1.4 Hz, 1H), 8.43 (s, 1H), 8.39 (s, 1H), 7.68 (dd, *J* = 9.1, 7.5 Hz, 1H), 7.36 (dd, *J* = 7.5, 1.4 Hz, 1H), 3.78 (t, *J* = 6.7 Hz, 2H), 3.57 (t, *J* = 6.7 Hz, 2H), 2.53 (s, 3H), 2.50 (s, 3H), 2.13 – 1.94 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 144.1, 143.4, 142.9, 137.6, 136.2, 134.5, 131.4, 130.0, 124.4, 119.4, 119.0, 118.1, 46.8, 26.1, 25.3, 20.6, 20.6. HRMS (ESI$^+$): Exact mass calculated for $C_{19}H_{19}N_3O_4Na$ [M+Na]$^+$: 376.1268, found 376.1267 (0.1 ppm).



5-hydroxy-2,3-dimethylquinoxaline 1,4-dioxide (60)

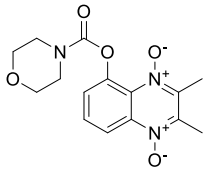
Prepared in accordance to general procedure 3 from **59** (1.32g scale). Upon cooldown, the reaction mixture was diluted with sat. $NaHCO_3$ (aqueous sol., 400 mL) and the phases separated. The aqueous layer was extracted using toluene (4 x 40 mL).

The pooled organic phases were washed with $NaHCO_3$ (sat. aqueous sol, 3 x 100 mL) and concentrated *in vacuo*. Flash column chromatography on silica (20% EtOAc in Heptane) gave 1.24 g (80%) of an orange-yellow solid. R_f: 0.23 (50% EtOAc in Heptane) ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.41 (broad s, 1H), 7.86 (dd, *J* = 8.7, 1.2 Hz, 1H), 7.58 (t, *J* = 8.4 Hz, 1H), 7.08 (dd, *J* = 8.0, 1.2 Hz, 1H), 2.67 (s, 3H), 2.66 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 141.3, 139.6, 138.1, 132.6, 124.8, 116.3, 108.5, 14.8, 14.1. HRMS (ESI^+): Exact mass calculated for $C_{10}H_{10}N_2O_3Na$ $[M+Na]^+$:229.0584, found 229.0584 (-0.1 ppm).



2,3-dimethyl-5-((4-methylpiperazine-1-carbonyl)oxy)quinoxaline 1,4-dioxide (61)

Prepared in accordance to general procedure 1 from **60** (147 mg scale). Flash column chromatography on silica (5% MeOH in DCM) afforded 201 mg (85%) of a light-yellow oil. R_f: 0.05 (5% MeOH in DCM). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 – 8.46 (m, 1H), 7.68 (t, *J* = 8.3 Hz, 1H), 7.39 – 7.30 (m, 1H), 3.88 – 3.69 (m, 2H), 3.68 – 3.49 (m, 2H), 2.66 (s, 3H), 2.59 (s, 3H), 2.58 – 2.52 (m, 3H), 2.52 – 2.45 (m, 2H), 2.35 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 143.8, 142.8, 141.4, 138.6, 131.4, 130.5, 125.4, 118.0, 54.7, 54.6, 46.3, 45.0, 44.3, 14.9, 14.8. HRMS (ESI^+): Exact mass calculated for $C_{16}H_{21}N_4O_4$ $[M+H]^+$: 333.1558, found 333.1557 (-0.3 ppm).

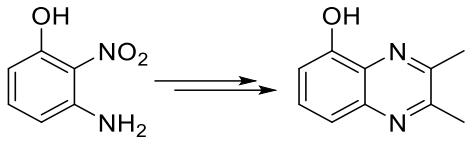


2,3-dimethyl-5-((morpholine-4-carbonyl)oxy)quinoxaline 1,4-dioxide (62)

Prepared in accordance to general procedure 1 from **60** (152 mg scale). Flash column chromatography on silica (0-3% MeOH in DCM) afforded 79 mg (34%) of a light-yellow oil. R_f: 0.30 (5% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 8.8, 1.4 Hz, 1H), 7.71 (dd, *J* = 8.8, 7.8 Hz, 1H), 7.40 (dd, *J* = 7.8, 1.4 Hz, 1H), 3.91 – 3.77 (m, 6H), 3.63 – 3.56 (m, 2H), 2.69 (s, 3H), 2.62 (s, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 153.6, 143.8, 142.9, 141.5, 138.7, 131.3, 130.6, 125.4, 118.1, 77.5, 77.4, 77.2, 76.8, 66.6, 45.6, 44.7, 14.9, 14.9. HRMS (ESI^+): Exact mass calculated for $C_{15}H_{17}N_3O_5Na$ $[M+Na]^+$: 342.1060, found 342.1062 (-0.3 ppm).

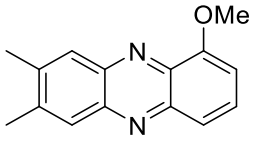
Experimental procedures for synthetic intermediates

Synthesis of 2,3-dimethylquinoxalin-5-ol (59)



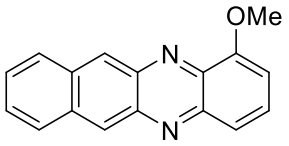
2,3-dimethylquinoxalin-5-ol (59)

3-amino-2-nitrophenol (1.5g, 9.7 mmol) was added to a mixture of $Na_2S_2O_4$ (25 mL saturated aq. solution), MeOH (20 mL) and Na_2CO_3 (5.0 g). The resulting dispersion was gradually warmed up to 100 °C and refluxed for 2 h. Upon cooling, the mixture was concentrated *in vacuo* before the chuncky crude mixture was dispersed in AcOH (40 mL) and toluene (30 ml). Diacetyl (1.2 mL, 13.80 mmol) was added and the resulting dispersion left stirring for 20 h before concentrated *in vacuo*. The solid crude was dispersed in $NaHCO_3$ (300 mL saturated aqueous solution) and the aqueous layer extracted with DCM (4x40 mL). The pooled organic phases were concentrated *in vacuo* and the afforded crude material recrystallized from hot EtOH to afford 693 mg of pure compound. The remaining liquid after filtration of crystals was concentrated and filtered through a plug of silica (100% DCM) to afford more of the product. Total yield of 1.33g (79% over 2 steps) was afforded of a beige colored solid. R_f: 0.63 (100% DCM). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 – 7.80 (m, 1H), 7.57 – 7.51 (m, 1H), 7.51 – 7.46 (m, 1H), 7.10 (dd, *J* = 7.4, 1.4 Hz, 1H), 2.71 (d, *J* = 2.4 Hz, 3H), 2.67 (d, *J* = 3.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.4, 151.6, 151.3, 141.4, 131.0, 129.9, 118.8, 110.1, 23.2, 22.9. NMR data match published literature. [2]



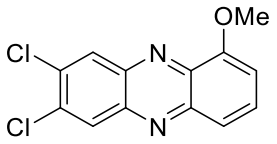
1-methoxy-7,8-dimethylphenazine (36)

Synthesized according to general procedure S-1. Flash column chromatography on silica (100% DCM) afforded 280 mg (24%) of the yellow solid. R_f: 0.47 (10% EtOAc/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.92 (s, 1H), 7.77 (dd, *J* = 8.9, 1.1 Hz, 1H), 7.66 (dd, *J* = 8.8, 7.5 Hz, 1H), 6.99 (dd, *J* = 7.6, 1.1 Hz, 1H), 4.13 (s, 3H), 2.51 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 143.9, 143.0, 142.3, 141.8, 141.5, 136.5, 129.8, 128.7, 127.7, 121.4, 106.1, 56.5, 20.8, 20.7. ^{1}H og ^{13}C NMR data are in accordance with litterature.[2]



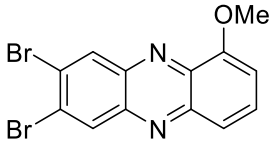
1-methoxybenzo[b]phenazine (37)

Synthesized according to general procedure S-1. Flash column chromatography on silica (0-10% EtOAc/DCM) afforded 1551 mg (78%) of red solid. R_f: 0.13 (DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.86 (s, 1H), 8.16 – 8.04 (m, 2H), 7.80 (dd, *J* = 9.0, 1.2 Hz, 1H), 7.70 (dd, *J* = 9.0, 7.4 Hz, 1H), 7.55 – 7.45 (m, 2H), 6.97 (d, *J* = 7.4 Hz, 1H), 4.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 145.3, 140.1, 139.0, 138.7, 135.0, 134.5, 131.0, 128.9, 128.7, 128.6, 127.4, 127.2, 126.9, 121.9, 105.9, 56.6. ^{1}H og ^{13}C NMR data are in accordance with litterature.[2]



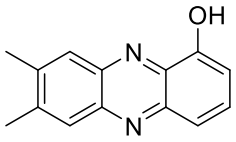
7,8-dichloro-1-methoxyphenazine (38)

Synthesized according to general procedure S-1. Flash column chromatography on silica (100% DCM) afforded 953 mg 45% of a yellow solid. R_f: 0.17 (100% DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.37 (s, 1H), 7.83 – 7.75 (m, 2H), 7.10 (dd, *J* = 5.7, 3.0 Hz, 1H), 4.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 144.6, 142.0, 140.7, 137.4, 136.1, 135.3, 131.8, 130.5, 129.6, 121.5, 107.4, 56.7. ^{1}H og ^{13}C NMR data are in accordance with litterature.[2]



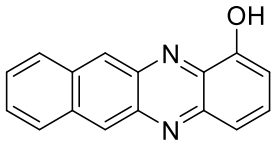
7,8-dibromo-1-methoxyphenazine (39)

Synthesized according to general procedure S-1. Flash column chromatography on silica (0-10% EtOAc/DCM) affording 1.34g 73% of a yellow solid. R_f: 0.68 (10% EtOAc/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.56 (s, 1H), 7.85 – 7.73 (m, 2H), 7.09 (dd, *J* = 5.0, 3.6 Hz, 1H), 4.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 144.8, 142.5, 141.1, 137.4, 134.0, 133.2, 131.8, 128.1, 127.3, 121.6, 107.4, 56.7. ^{1}H og ^{13}C NMR data are in accordance with litterature.[2]



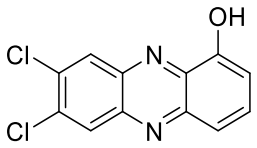
7,8-dimethylphenazin-1-ol (40)

This compound was demethylated using 1M BBr_3 solution in DCM (8 mL) overnight at 40° C under argon atm. The resulting mixture was quenched with drop wise addition of ice-cold H_2O and the pH of the aqueous mixture was adjusted to ~7 by 1M NaOH aqueous sol. The mixture was transferred to a separatory funnel and the aqueous layer extracted with DCM (4x20 mL). The pooled organic phases were dried over $MgSO_4$, filtered and dried *in vacuo*. The afforded crude material was further purified by flash column chromatography on silica (0-10% EtOAC/DCM) afforded 202 mg (87%) of a yellow solid. R_f: 0.56 (15% EtOAc/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.99 (s, 1H), 7.93 (s, 1H), 7.80 – 7.64 (m, 2H), 7.19 (dd, *J* = 7.1, 1.5 Hz, 1H), 2.55 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8, 143.5, 143.2, 142.5, 142.1, 140.7, 134.3, 131.2, 128.0, 127.6, 119.8, 108.6, 20.9, 20.8. This compound was earlier prepared by Haddadin *et al*.[4]



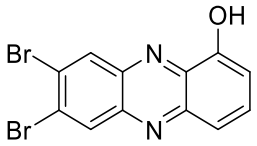
benzo[b]phenazin-1-ol (41)

Synthesized according to general procedure S-2. After the filtrate was obtained, the crude product was washed with H_2O and filtered. Flash column chromatography on silica (0-10% EtOAc/DCM) afforded 837 mg (88%) of cherry-red solid. R_f: 0.40 (100% DCM). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.63 (s, 1H), 9.03 (d, *J* = 1.1 Hz, 1H), 8.97 (d, *J* = 1.1 Hz, 1H), 8.36 – 8.19 (m, 2H), 7.77 (dd, *J* = 9.0, 7.3 Hz, 1H), 7.68 (dd, *J* = 8.9, 1.2 Hz, 1H), 7.66 – 7.55 (m, 2H), 7.14 (dd, *J* = 7.3, 1.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 153.3, 144.8, 139.5, 137.9, 137.6, 134.2, 133.8, 132.5, 128.5, 128.3, 127.5, 127.1, 127.1, 126.9, 119.4, 109.6.[3]



7,8-dichlorophenazin-1-ol (42)

Synthesized according to general procedure S-2. After the filtrate was obtained according to general procedure 2**,** it was washed with H_2O and EtOH before dried under vacuum. Orange solid was obtained (510 mg, >99 %).^{1}H NMR (600 MHz, DMSO-*d6*) δ 10.79 (s, 1H), 8.58 (s, 1H), 8.55 (s, 1H), 7.85 (dd, *J* = 8.8, 7.5 Hz, 1H), 7.69 (dd, *J* = 8.8, 1.1 Hz, 1H), 7.24 (dd, *J* = 7.5, 1.2 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 153.7, 144.2, 141.5, 139.8, 136.3, 134.0, 133.2, 133.2, 130.0, 129.8, 119.0, 111.4



7,8-dibromophenazin-1-ol (43)

Synthesized according to general procedure S-2. After the filtrate was obtained according to general procedure 2, the crude product was filtered and washed with H_2O and dried affording a beige solid (721 mg, 93 %). For characterization, small amount was recrystallized from boiling $CHCl_3$ and filtered. ^{1}H NMR (600 MHz, DMSO-d6) δ 10.77 (s, 1H), 8.69 (s, 1H), 8.67 (s, 1H), 7.84 (dd, *J* = 8.8, 7.5 Hz, 1H), 7.67 (dd, *J* = 8.8, 1.2 Hz, 1H), 7.24 (dd, *J* = 7.5, 1.2 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 153.7, 144.2, 141.9, 140.2, 136.3, 133.2, 133.2, 133.0, 126.9, 126.1, 119.0, 111.4.

^{1}H- and ^{13}C-NMR spectra of final compounds

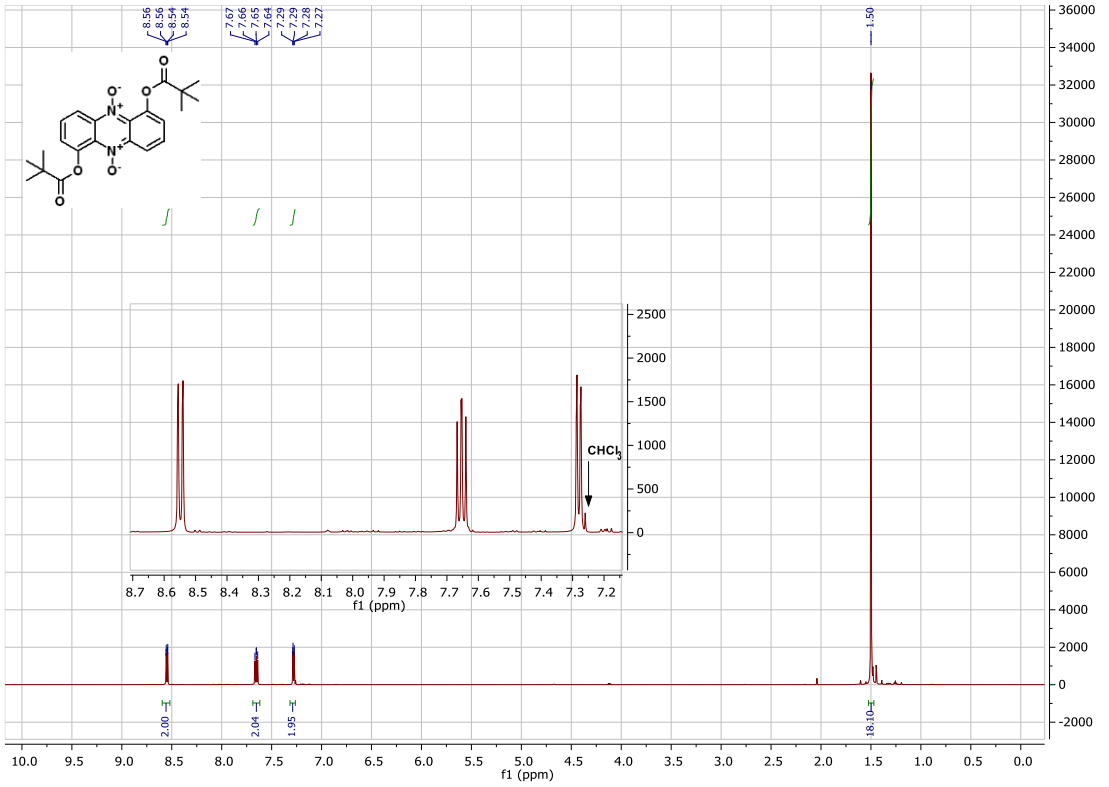


Figure S-1: ^{1}H-NMR spectra of compound **11**

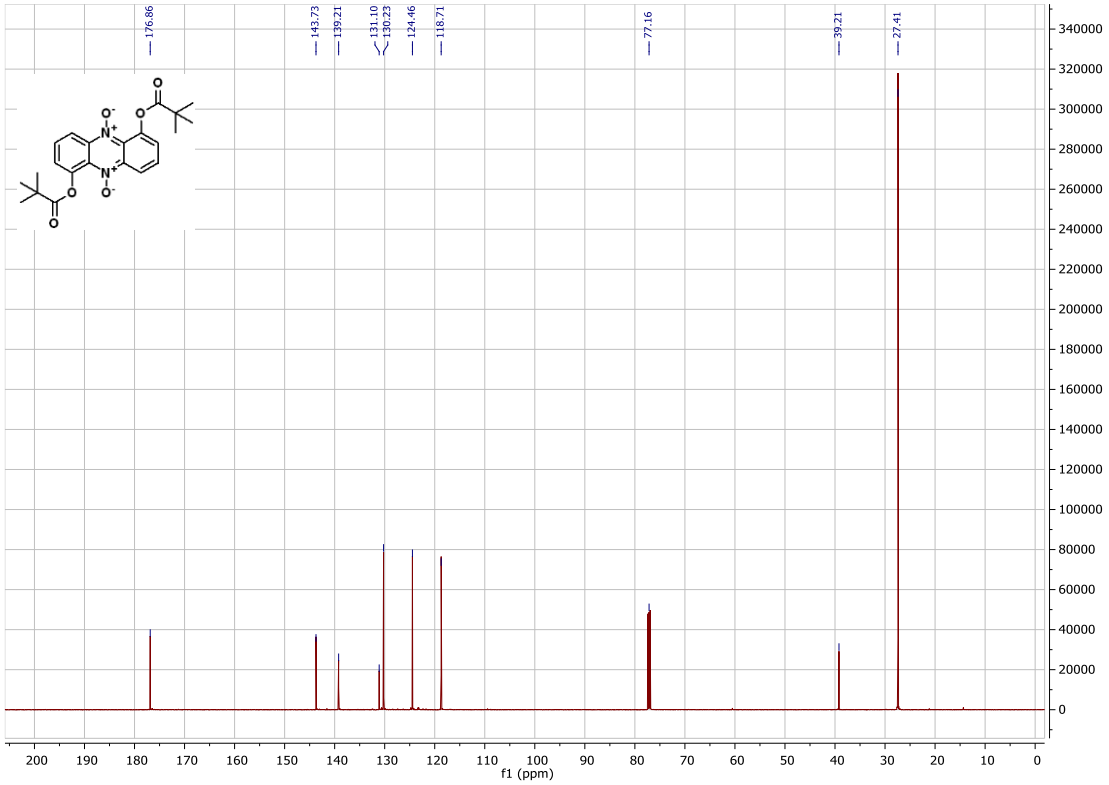


Figure S-2: ^{13}C-NMR spectra of compound **11**

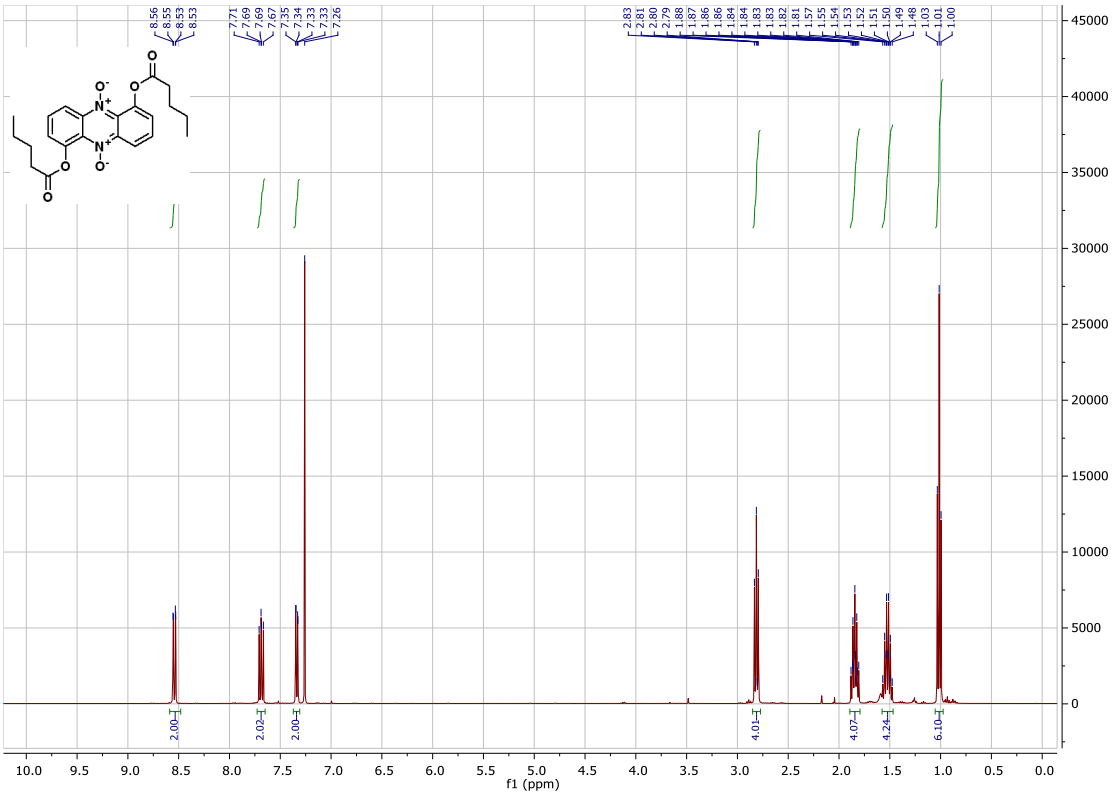


Figure S-3: ^{1}H-NMR spectra of compound **12**

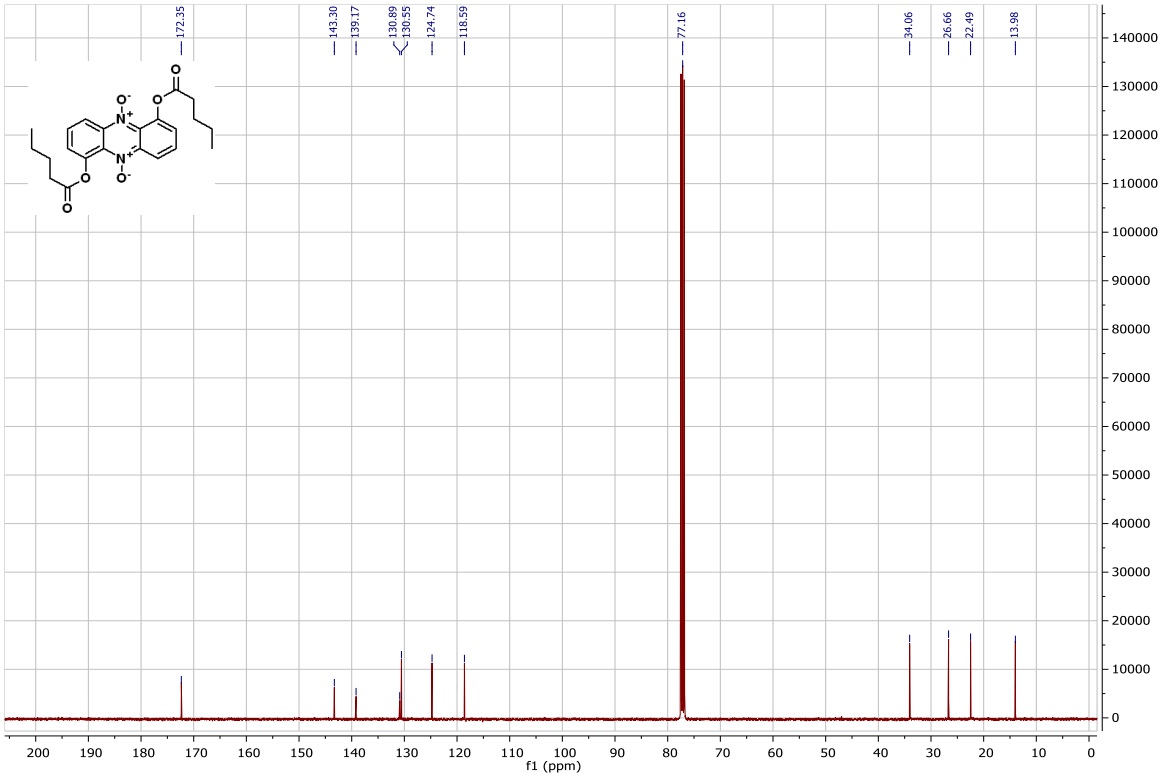


Figure S-4: ^{13}C-NMR spectra of compound **12**

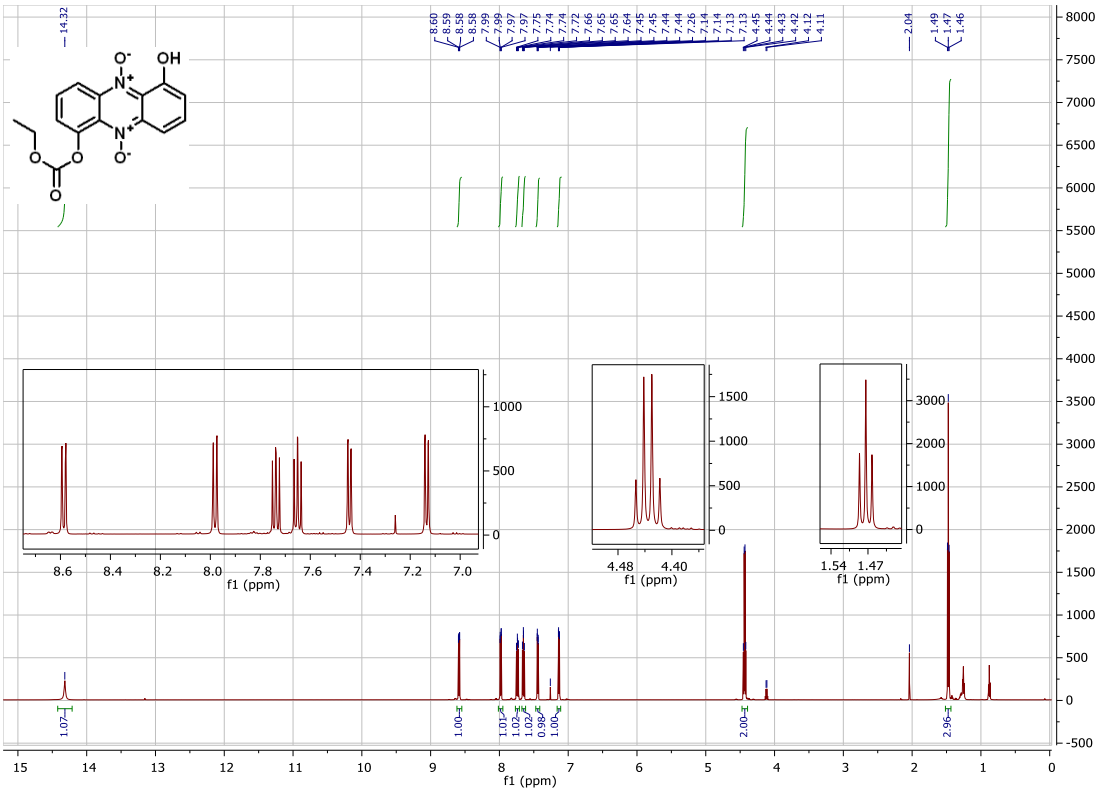


Figure S-5: ^{1}H-NMR spectra of compound **13**

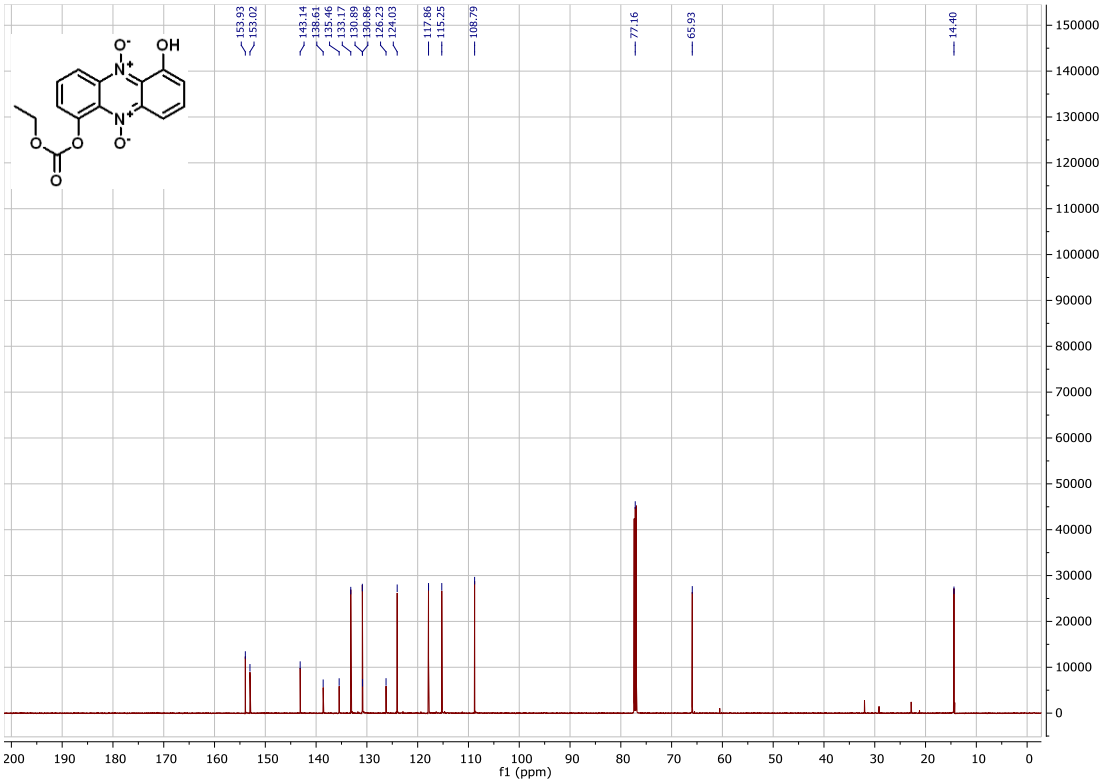


Figure S-6: ^{13}C-NMR spectra of compound **13**

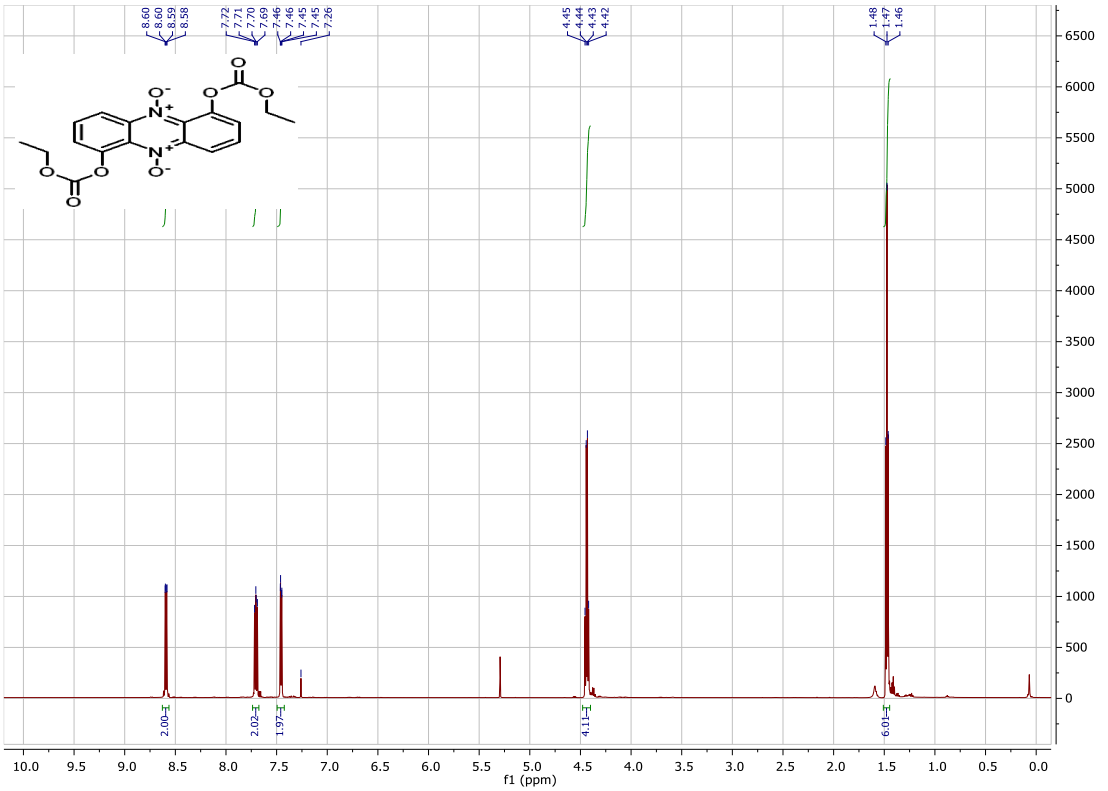


Figure S-7: ^{1}H-NMR spectra of compound **14**

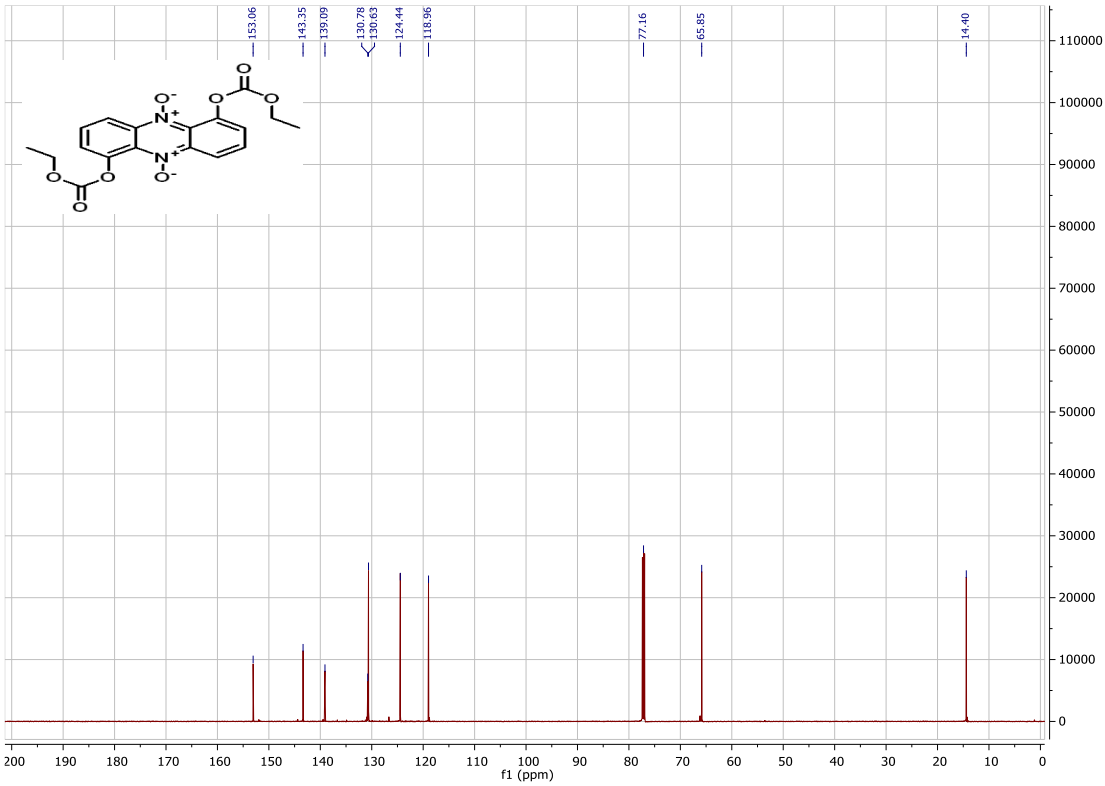


Figure S-8: ^{13}C-NMR spectra of compound **14**

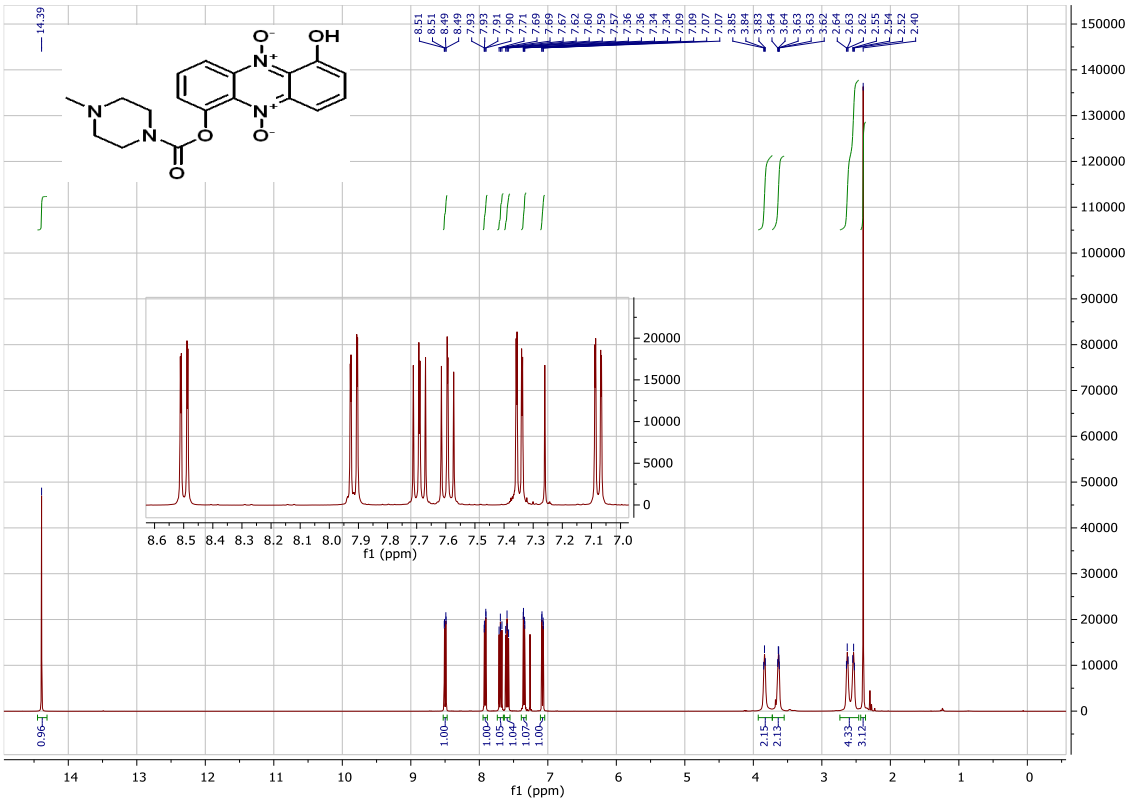


Figure S-9: ^{1}H-NMR spectra of compound **15**

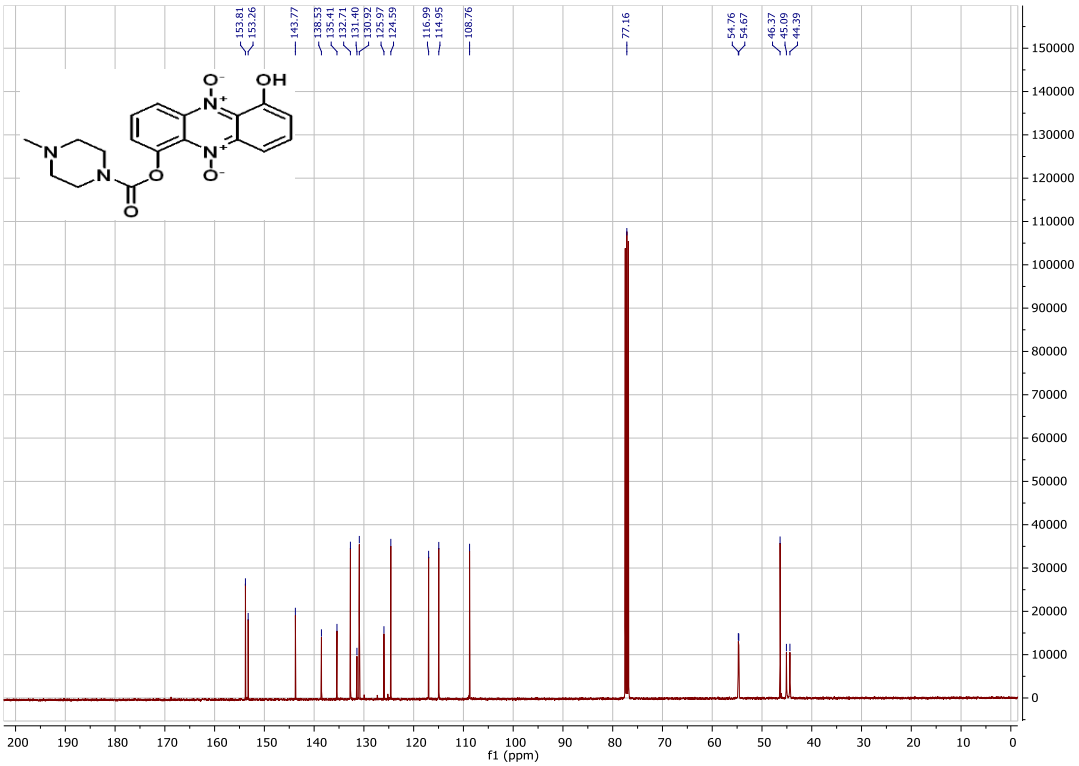


Figure S-10: ^{13}C-NMR spectra of compound **15**

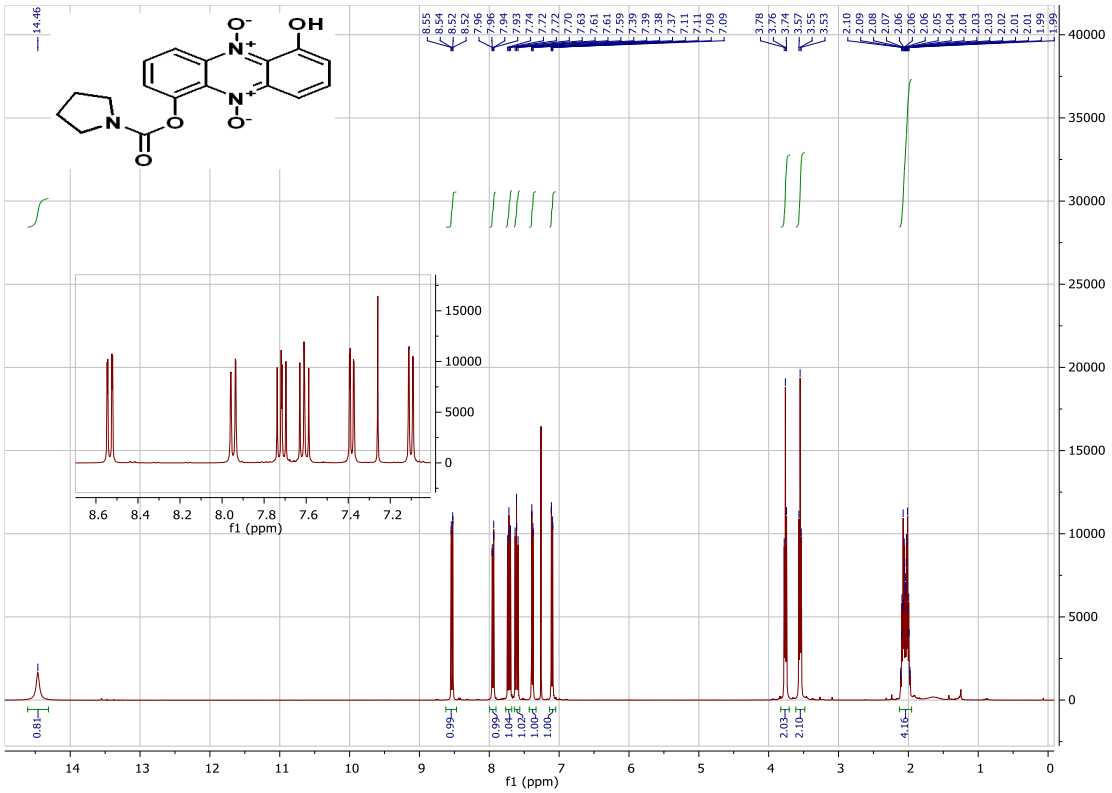


Figure S-11: ^{1}H-NMR spectra of compound **16**

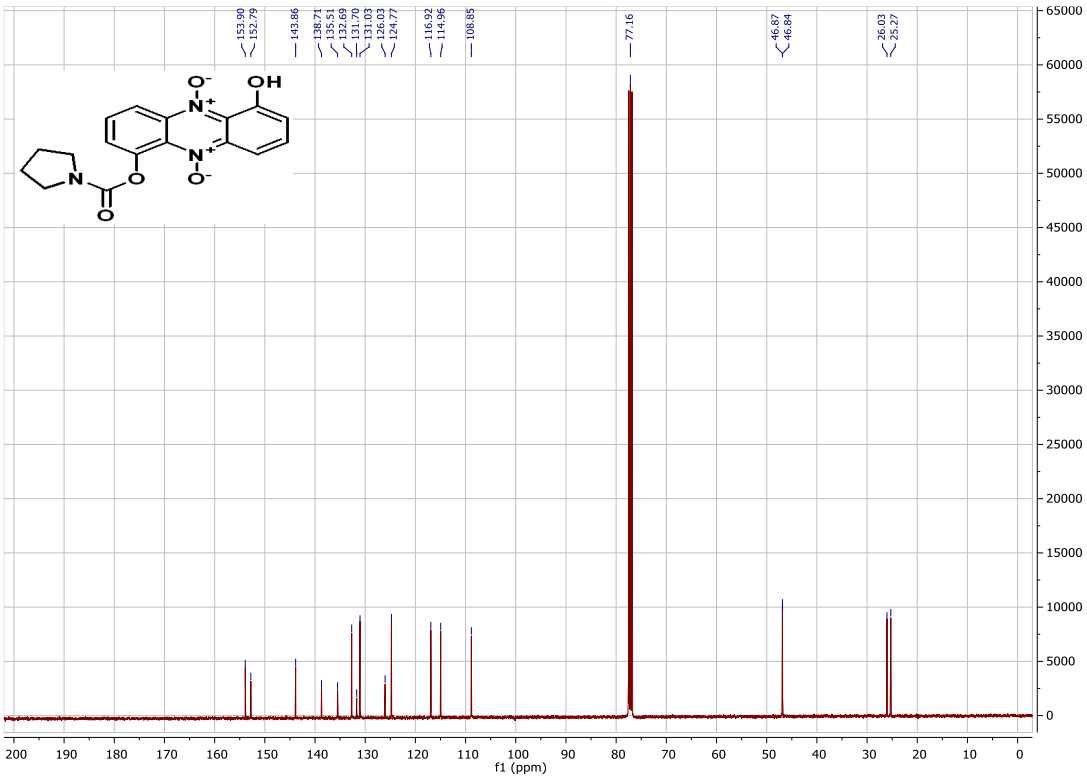


Figure S-12: ^{13}C-NMR spectra of compound **16**

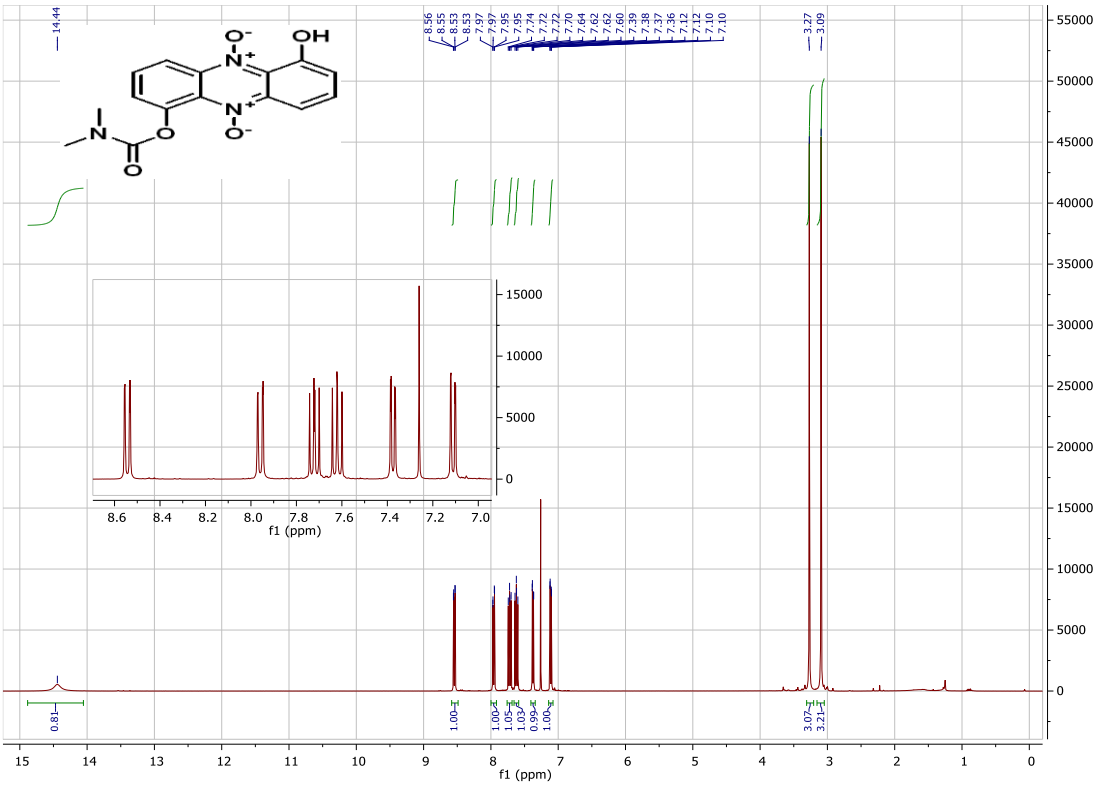


Figure S-13: ^{1}H-NMR spectra of compound **17**

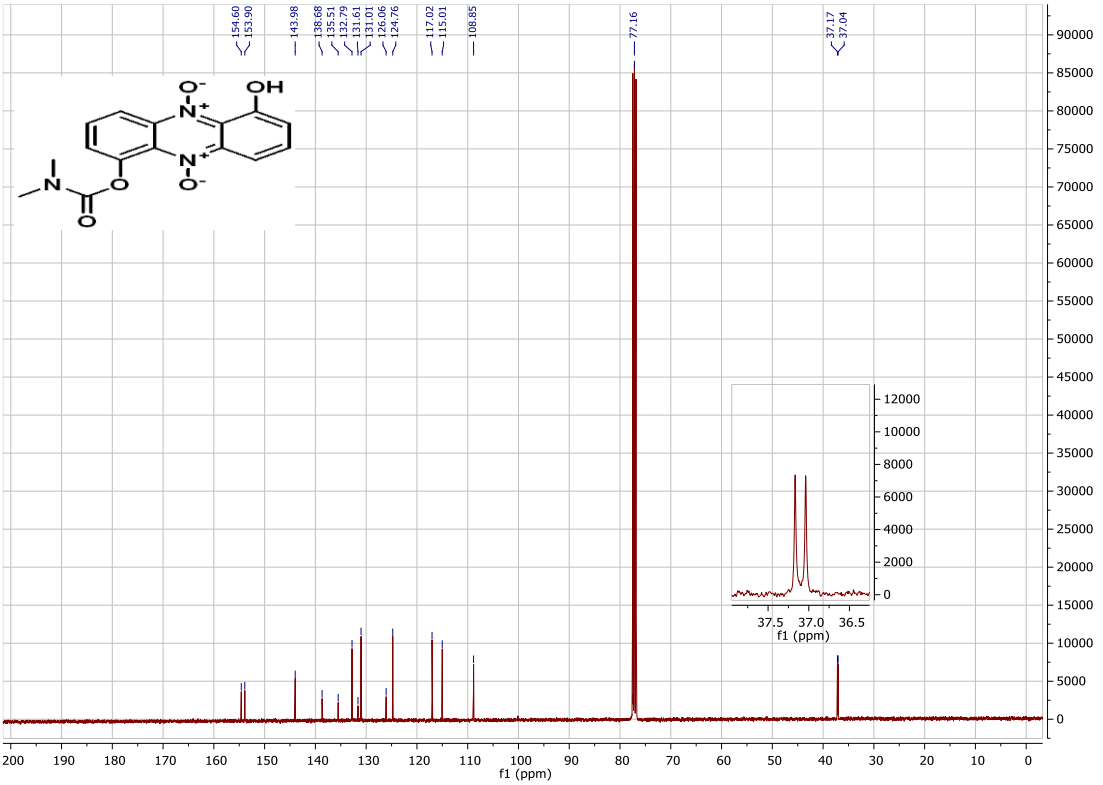


Figure S-14: ^{13}C-NMR spectra of compound **17**

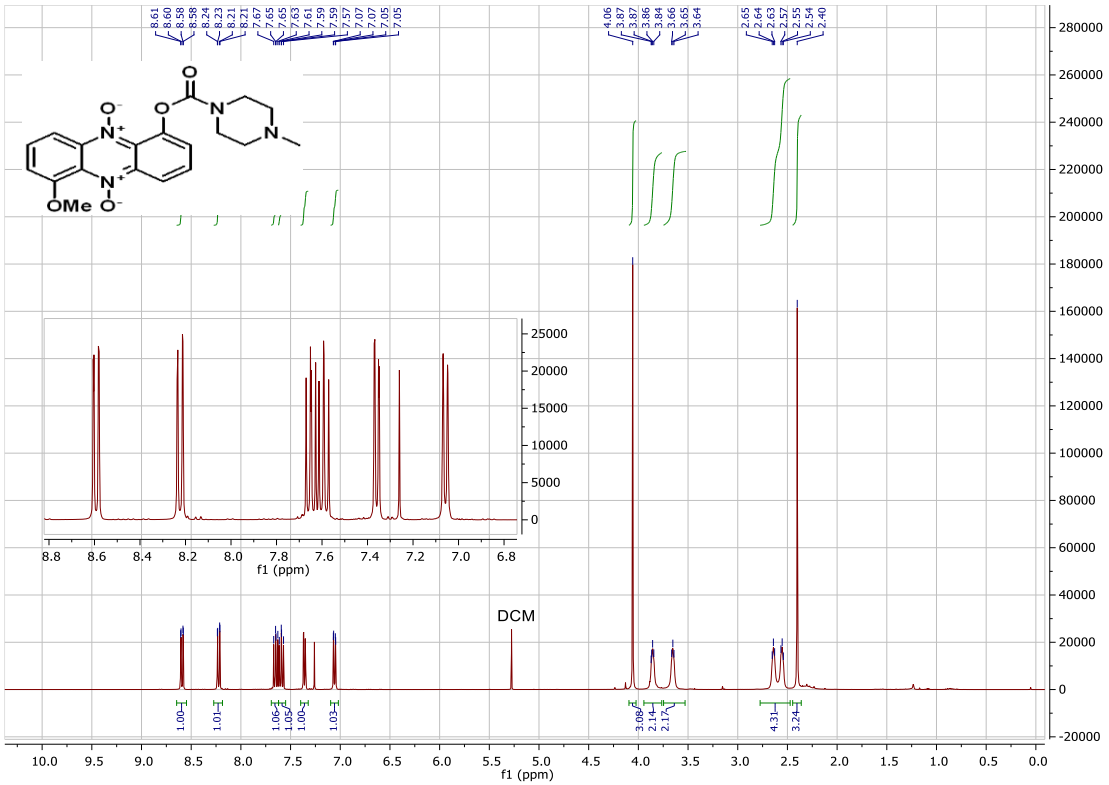


Figure S-15: ^{1}H-NMR spectra of compound **18**

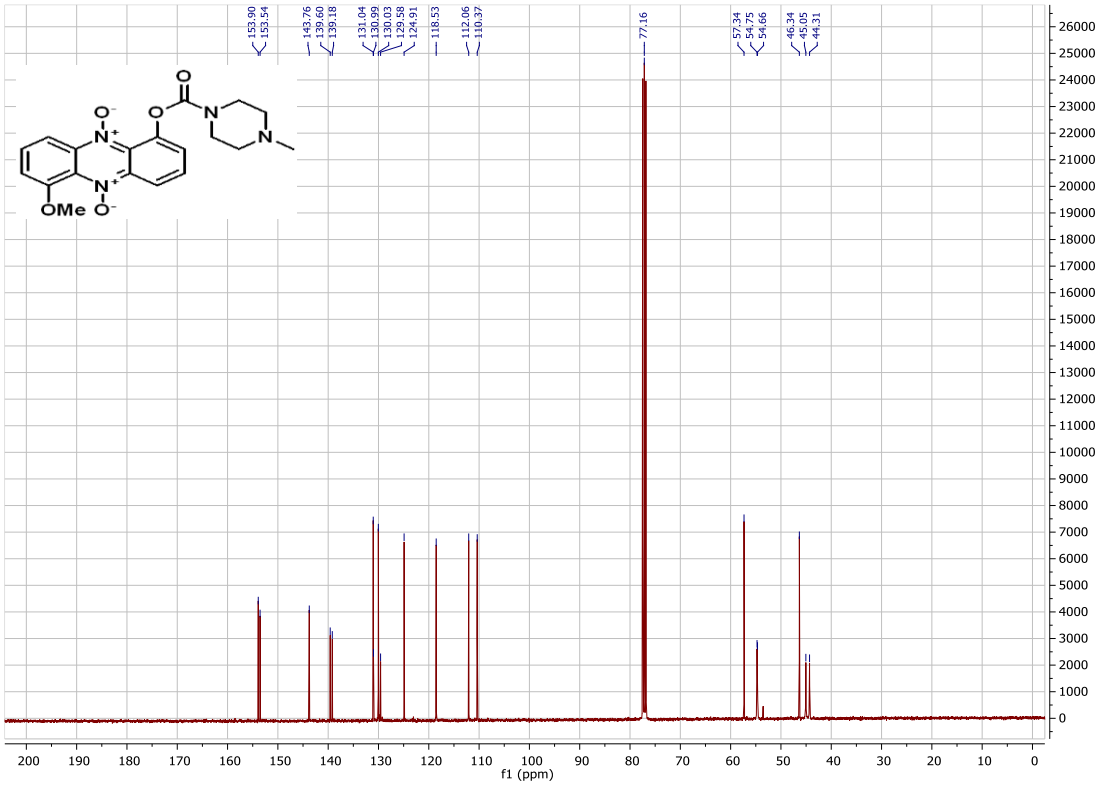


Figure S-16: ^{13}C-NMR spectra of compound **18**

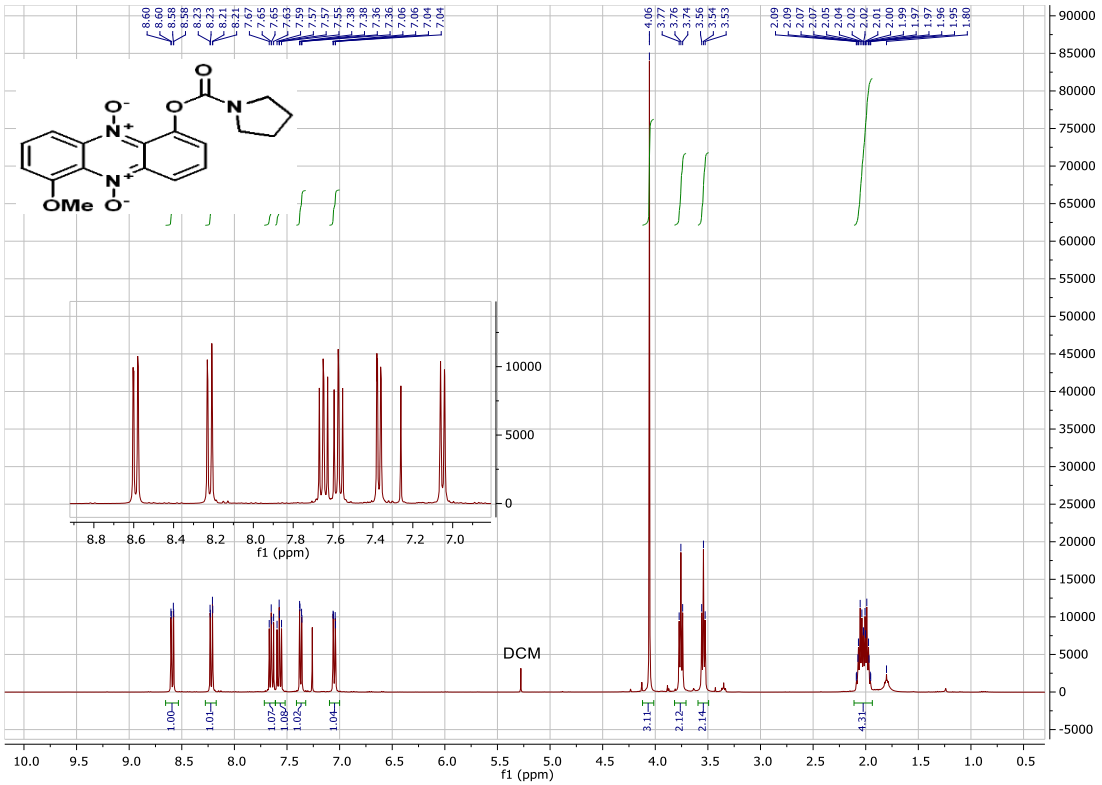


Figure S-17: ^{1}H-NMR spectra of compound **19**

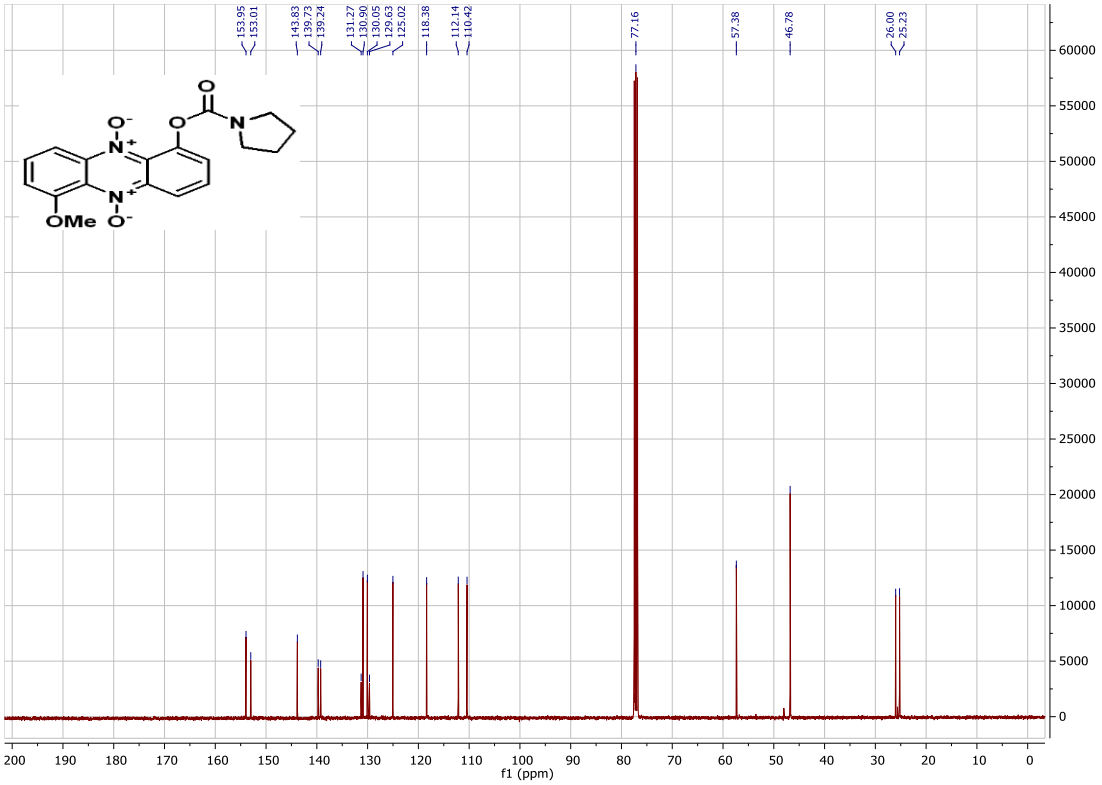


Figure S-18: ^{13}C-NMR spectra of compound **19**

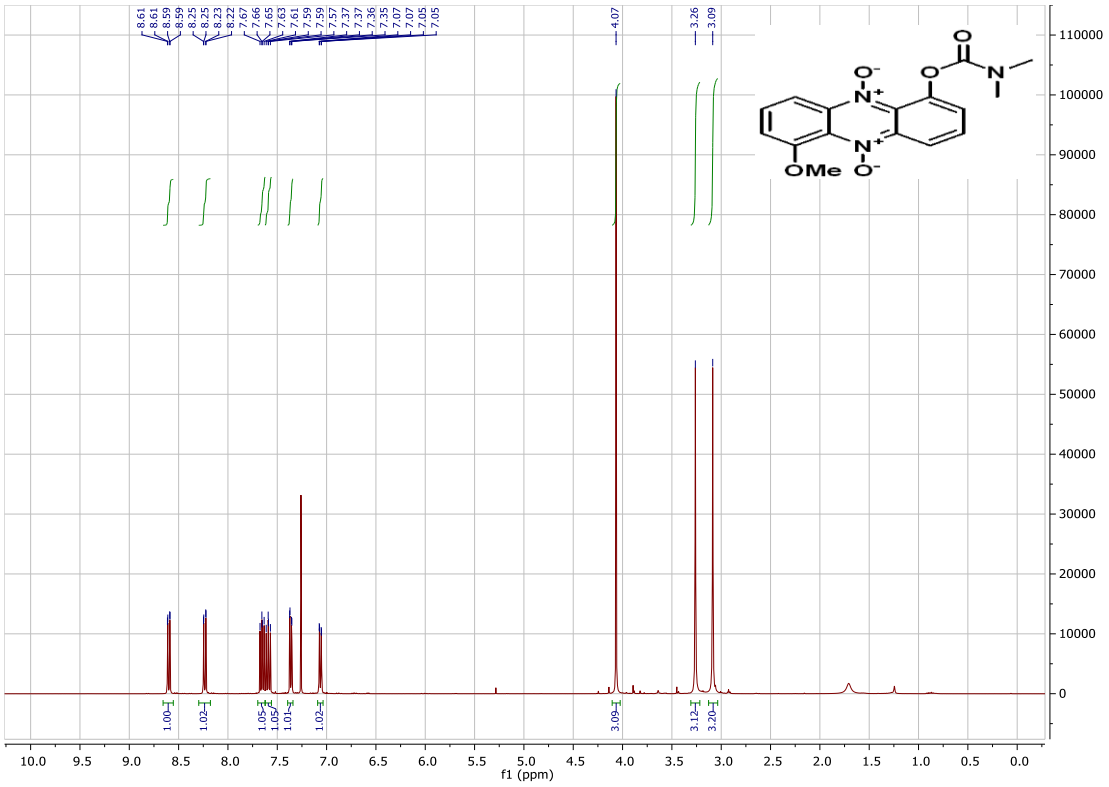


Figure S-19: ^{1}H-NMR spectra of compound **20**

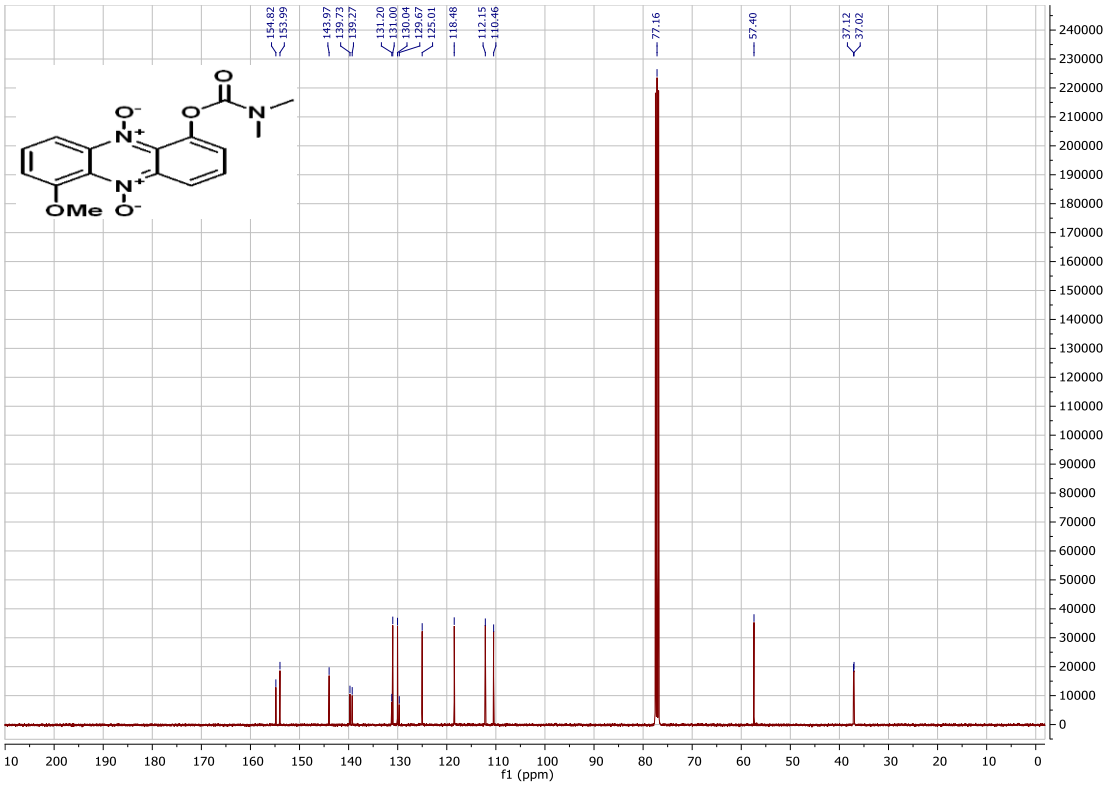


Figure S-20: ^{13}C-NMR spectra of compound **20**

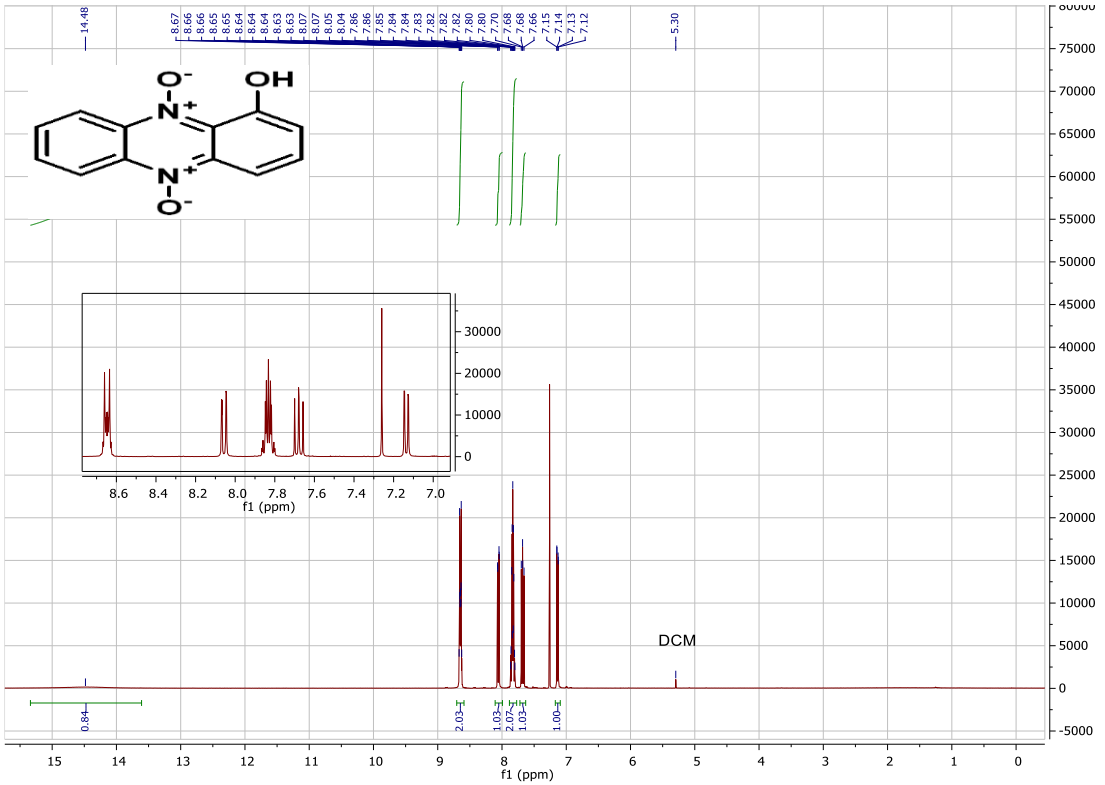


Figure S-21: ^{1}H-NMR spectra of compound **21**

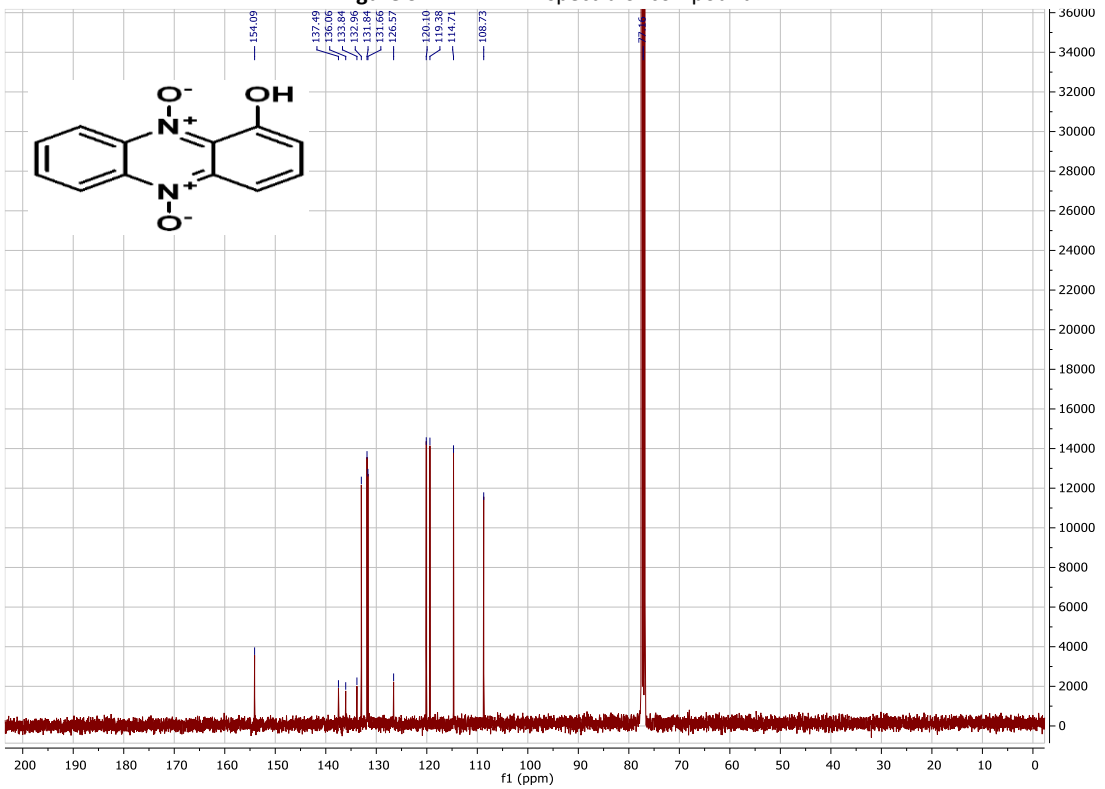


Figure S-22: ^{13}C-NMR spectra of compound **21**

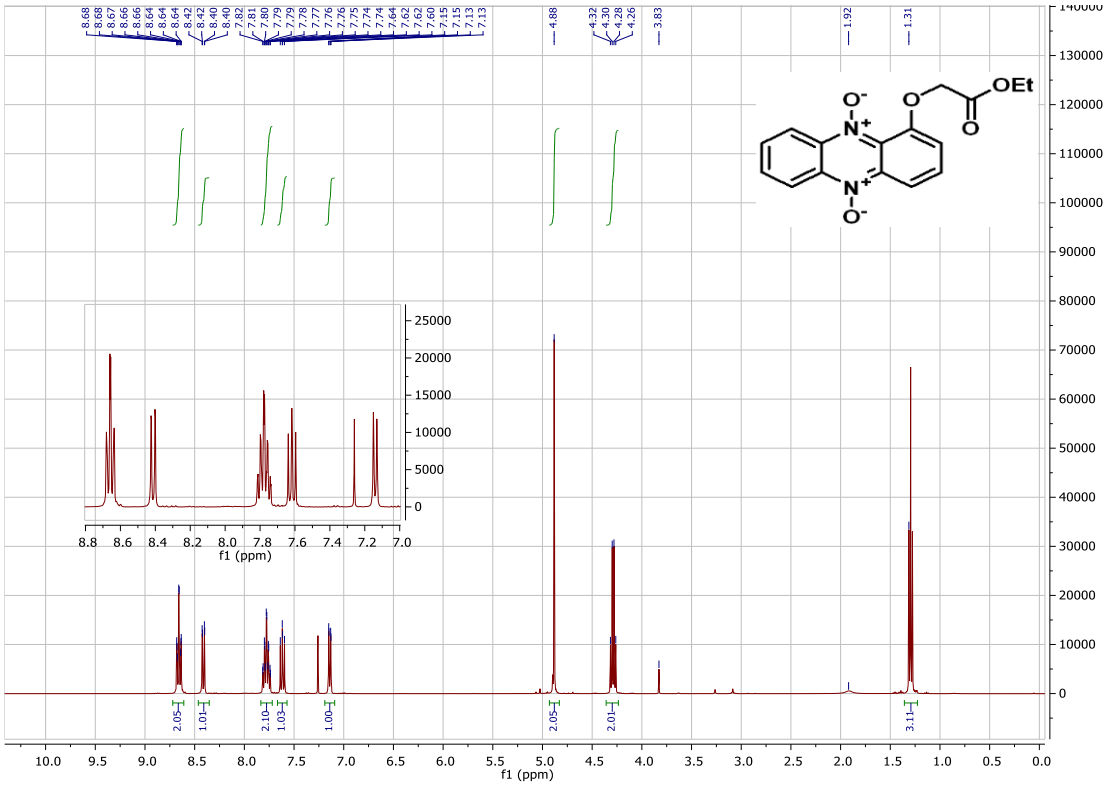


Figure S-23: ^{1}H-NMR spectra of compound **24**

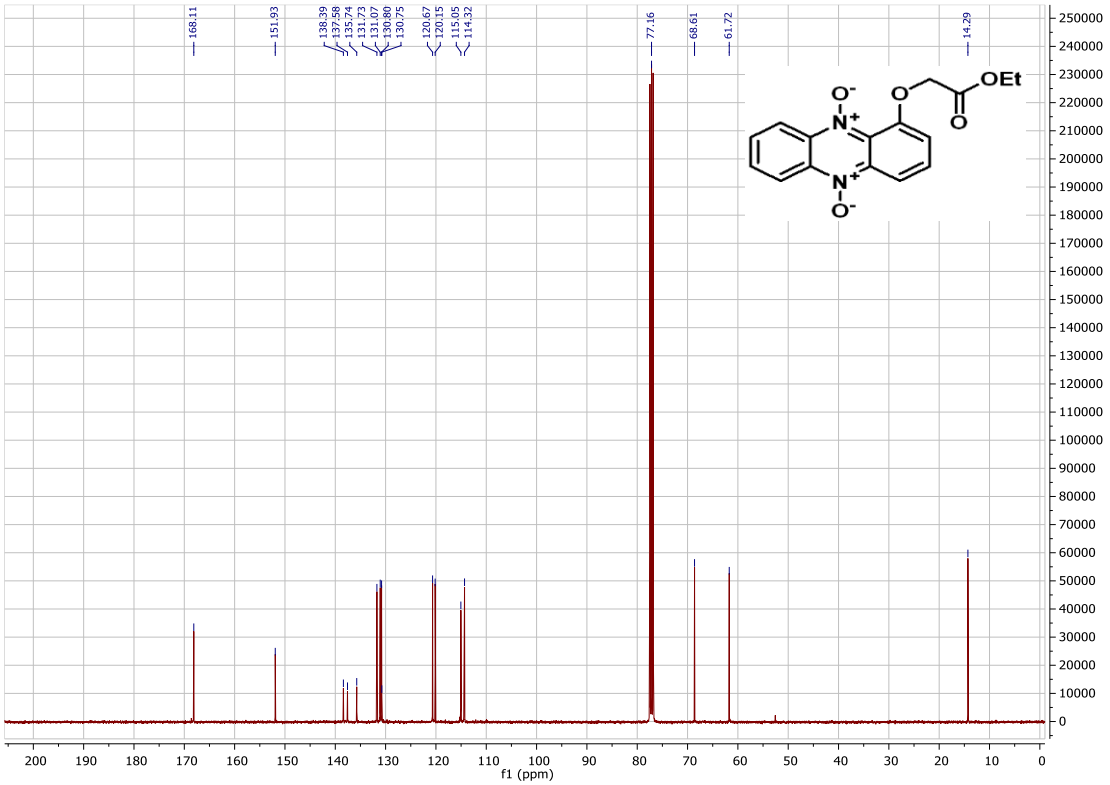


Figure S-24: ^{13}C-NMR spectra of compound **24**

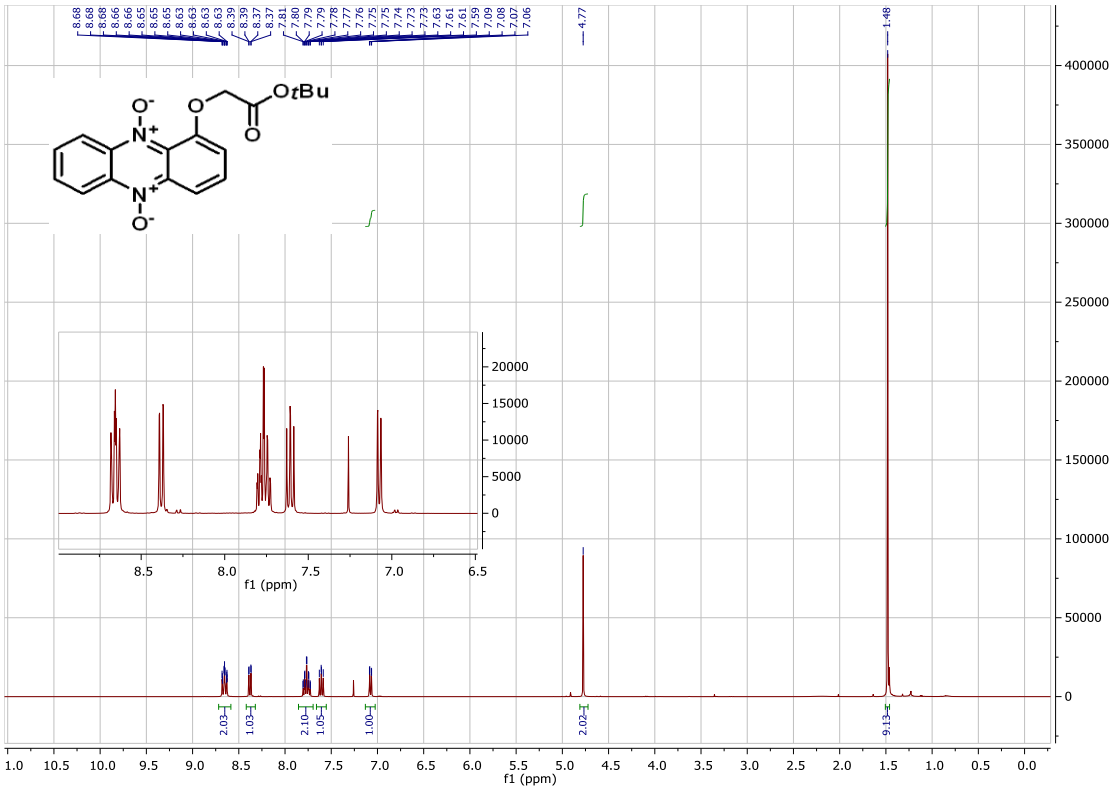


Figure S-25: ^{1}H-NMR spectra of compound **25**

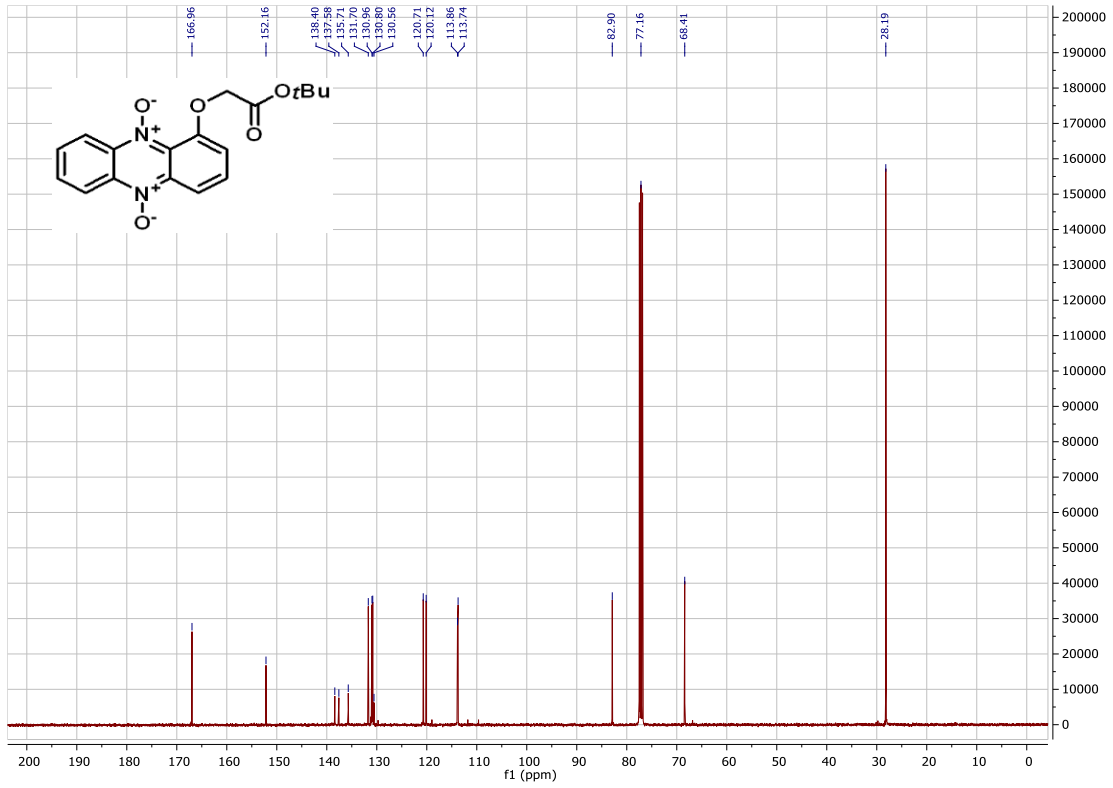


Figure S-26: ^{13}C-NMR spectra of compound **25**

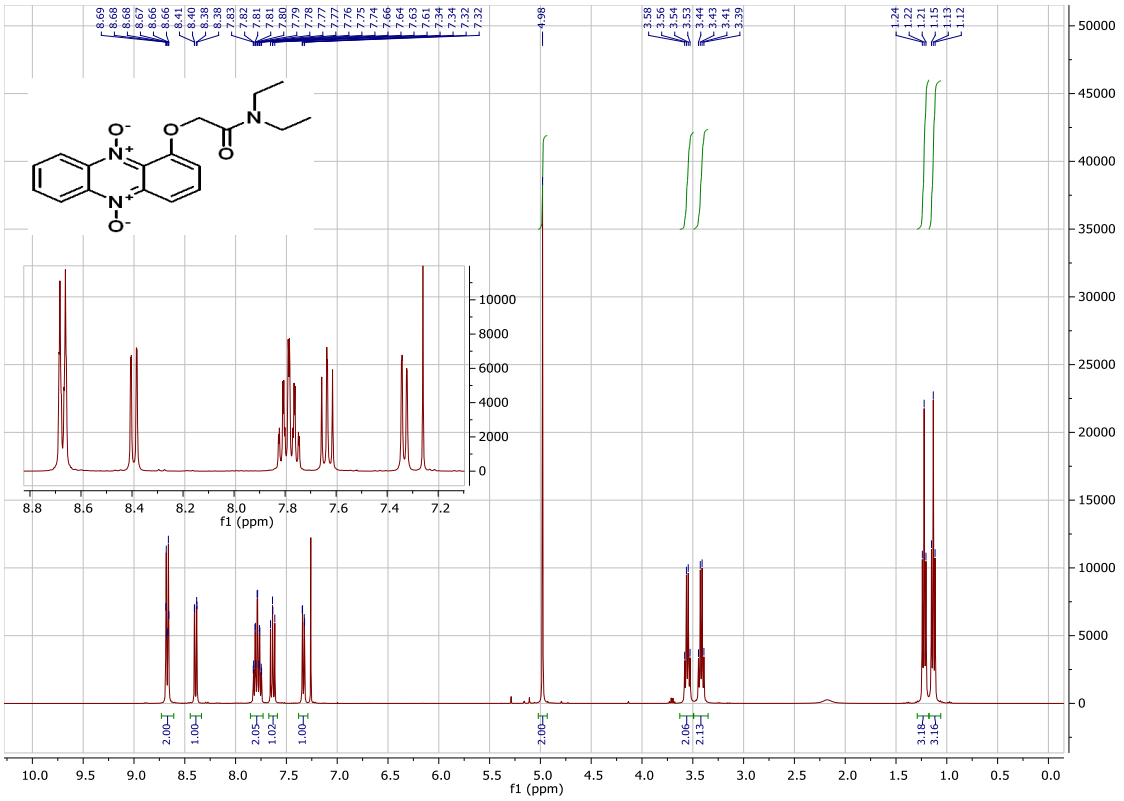


Figure S-27: ^{1}H-NMR spectra of compound **26**

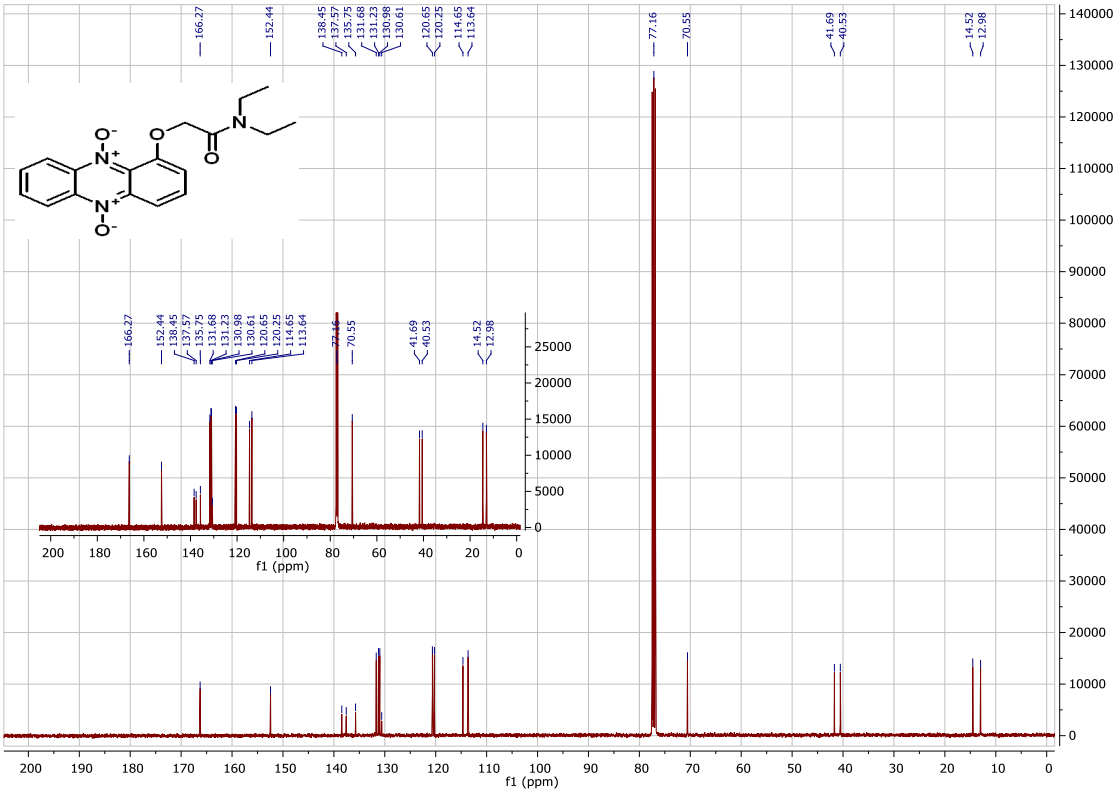


Figure S-28: ^{13}C-NMR spectra of compound **26**

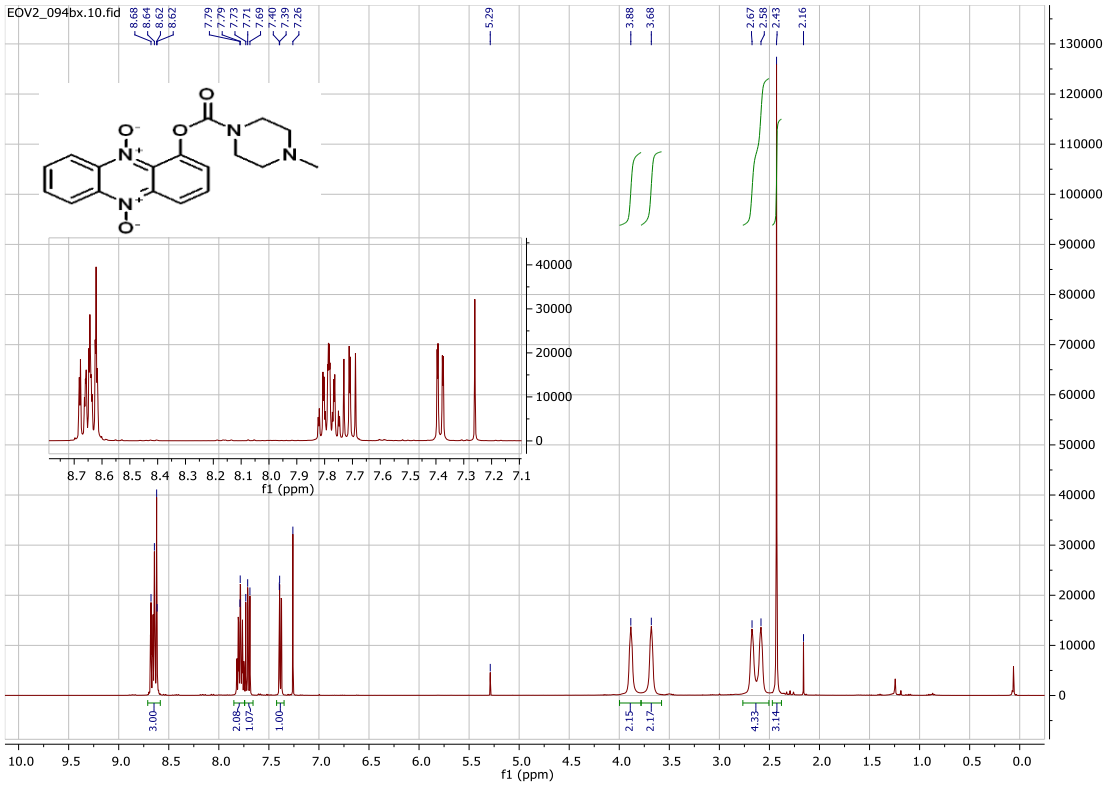


Figure S-29: ^{1}H-NMR spectra of compound **27**

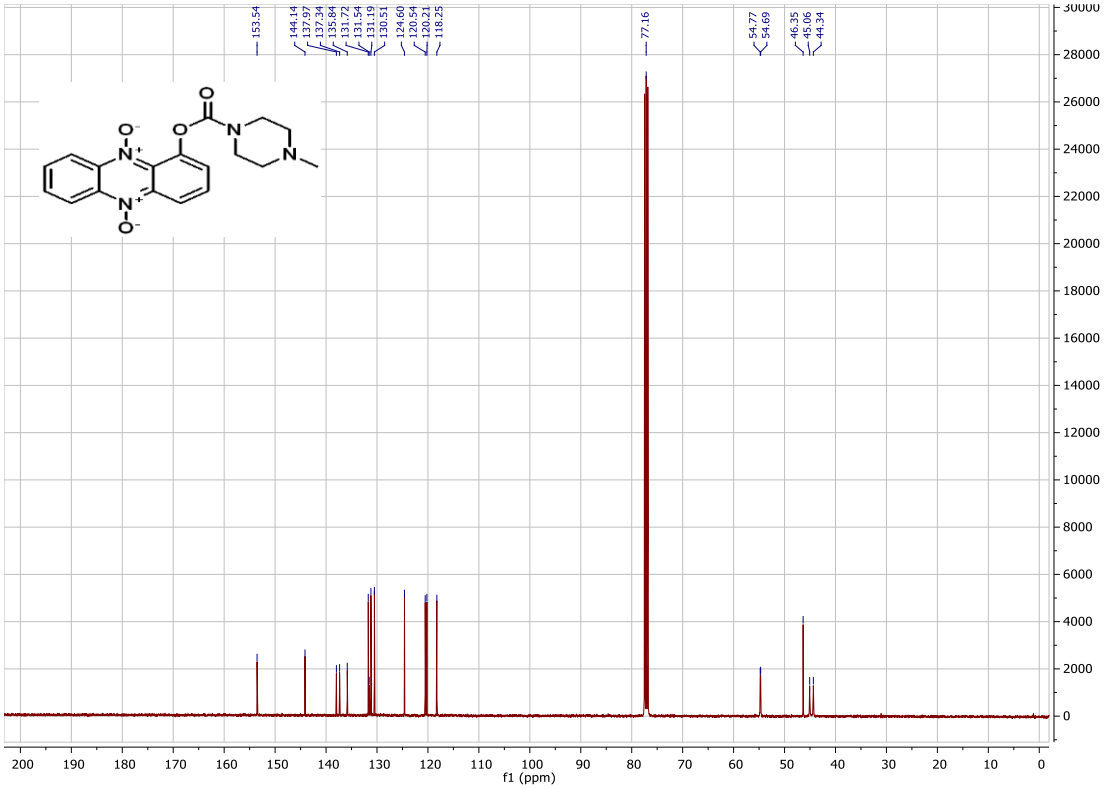


Figure S-30: ^{13}C-NMR spectra of compound **27**

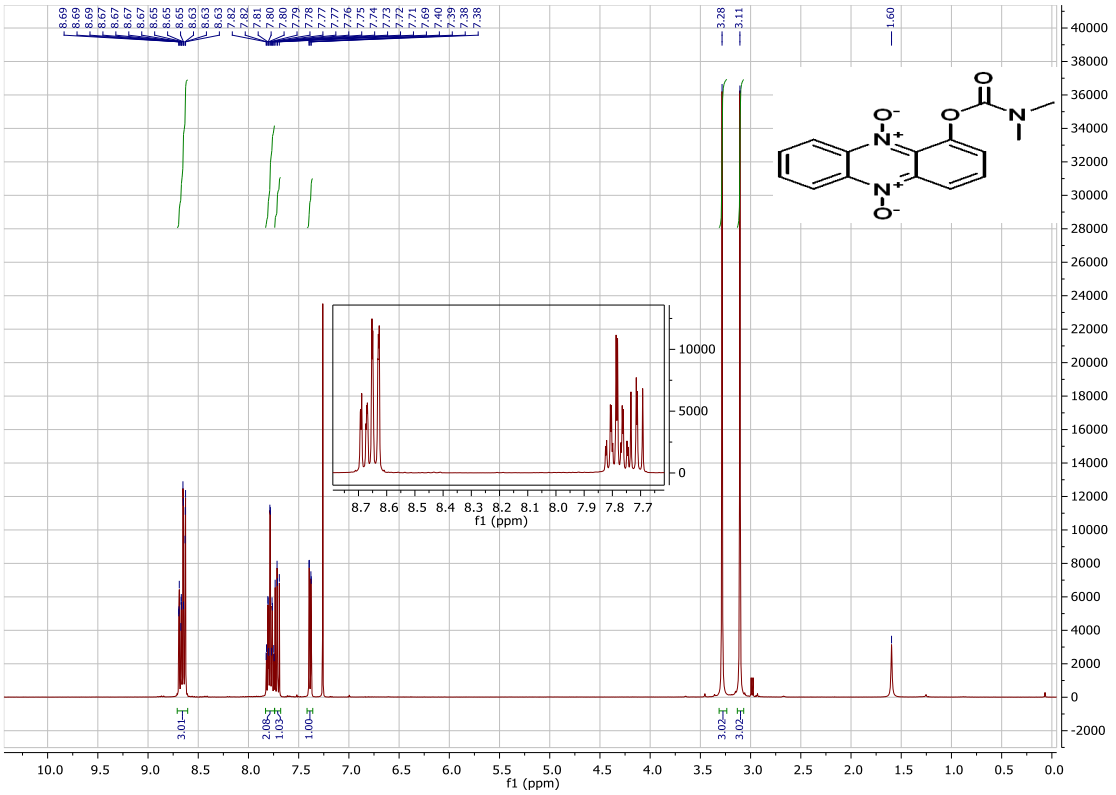


Figure S-31: ^{1}H-NMR spectra of compound **28**

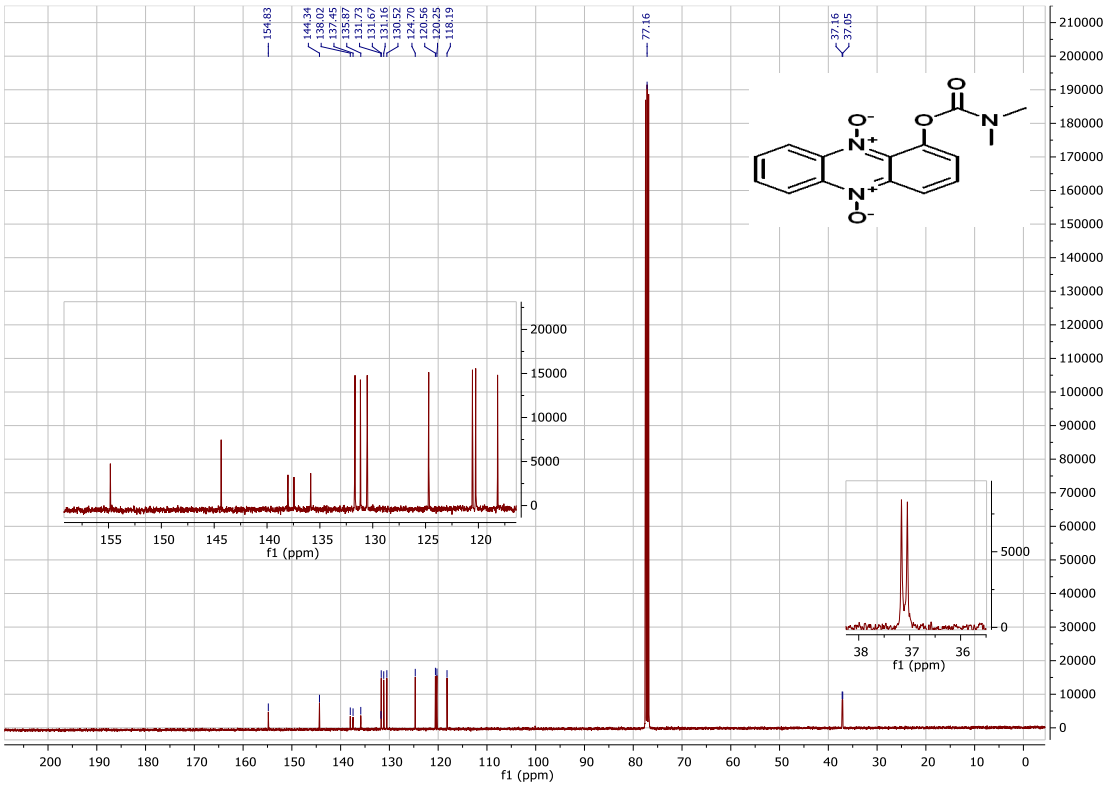


Figure S-32: ^{13}C-NMR spectra of compound **28**

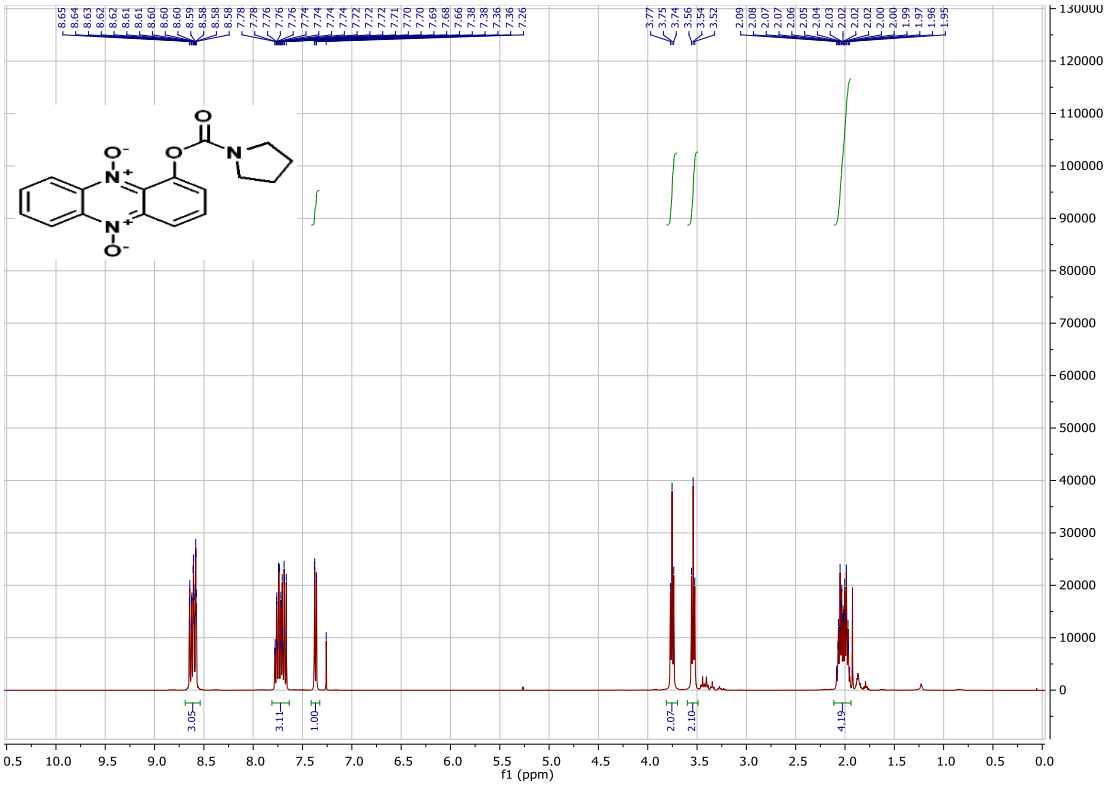


Figure S-33: ^{1}H-NMR spectra of compound **28**

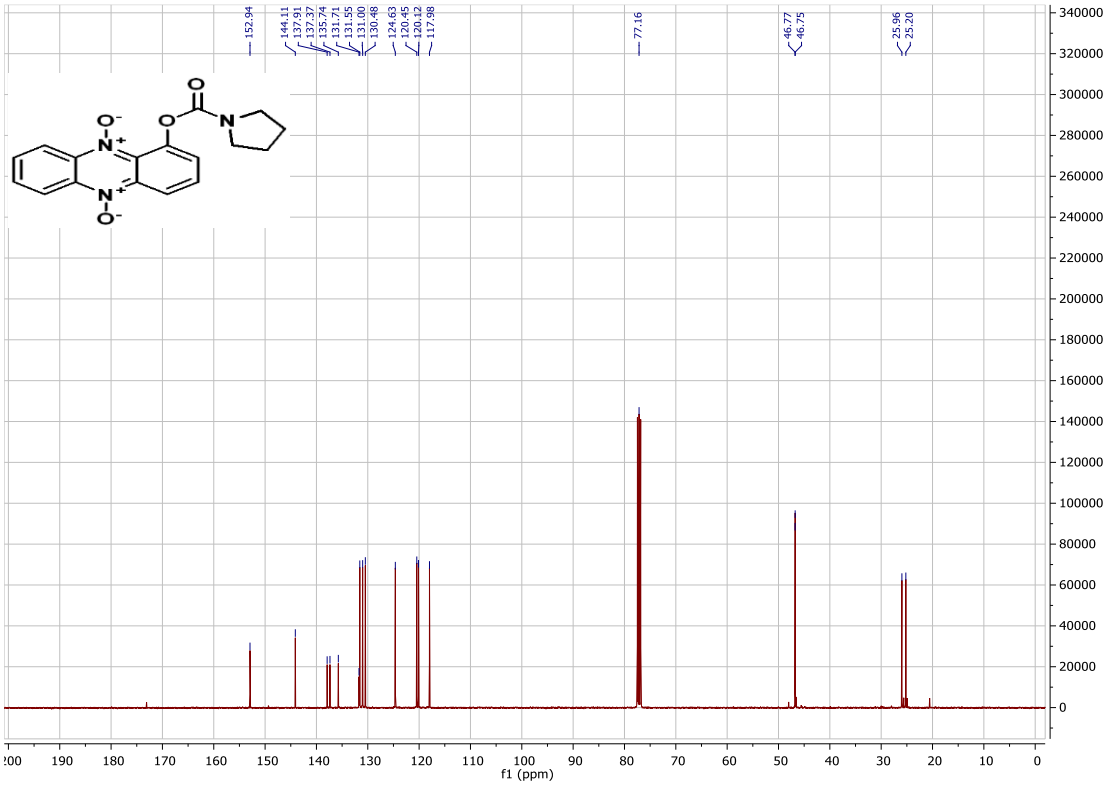


Figure S-34: ^{13}C-NMR spectra of compound **28**

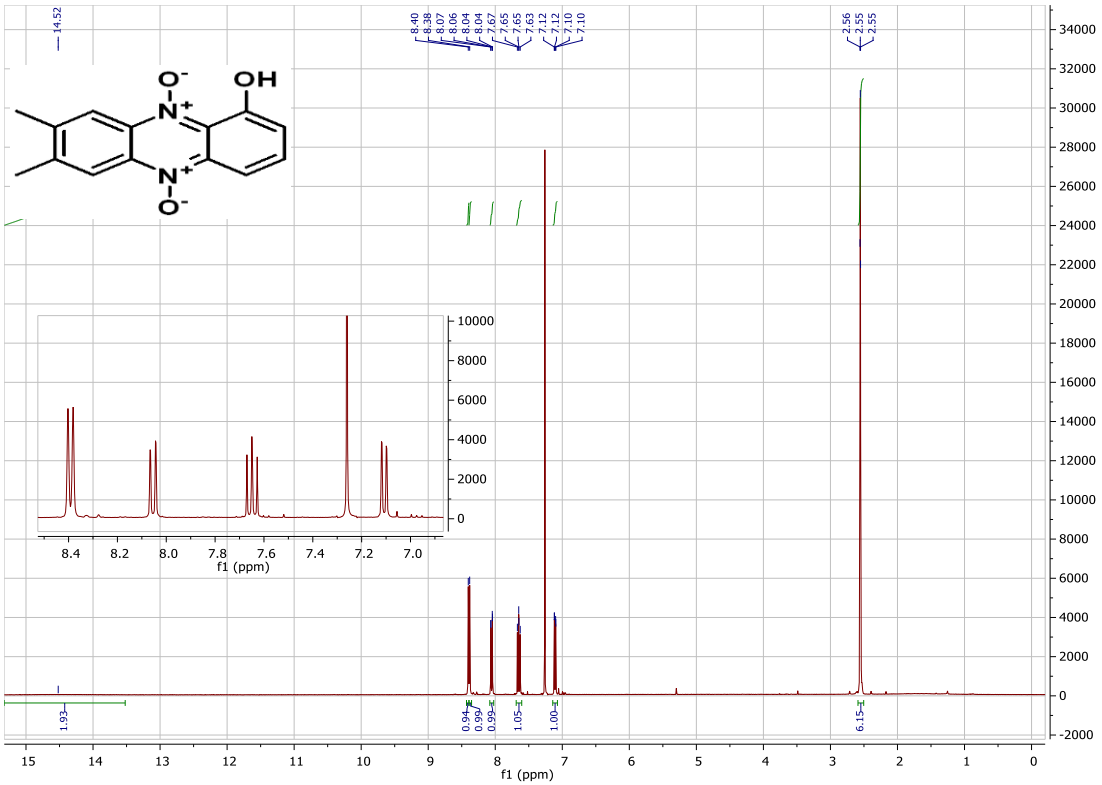


Figure S-35: ^{1}H-NMR spectra of compound **44**

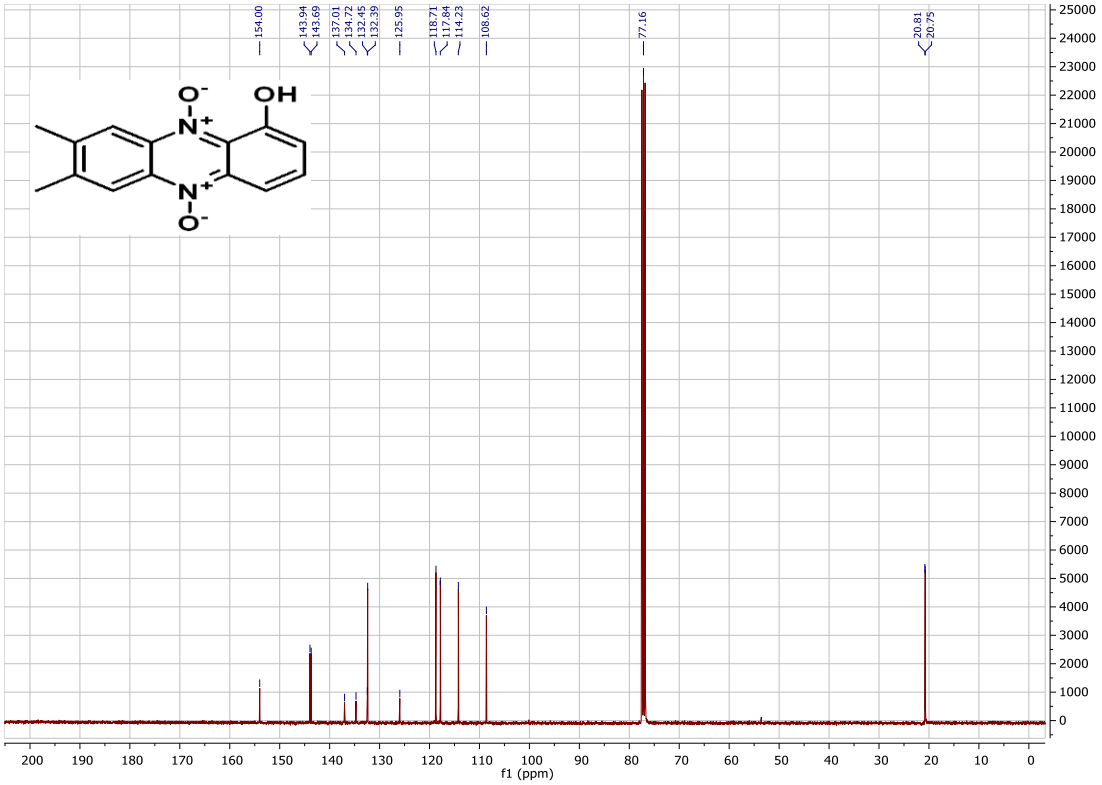


Figure S-36: ^{13}C-NMR spectra of compound **44**

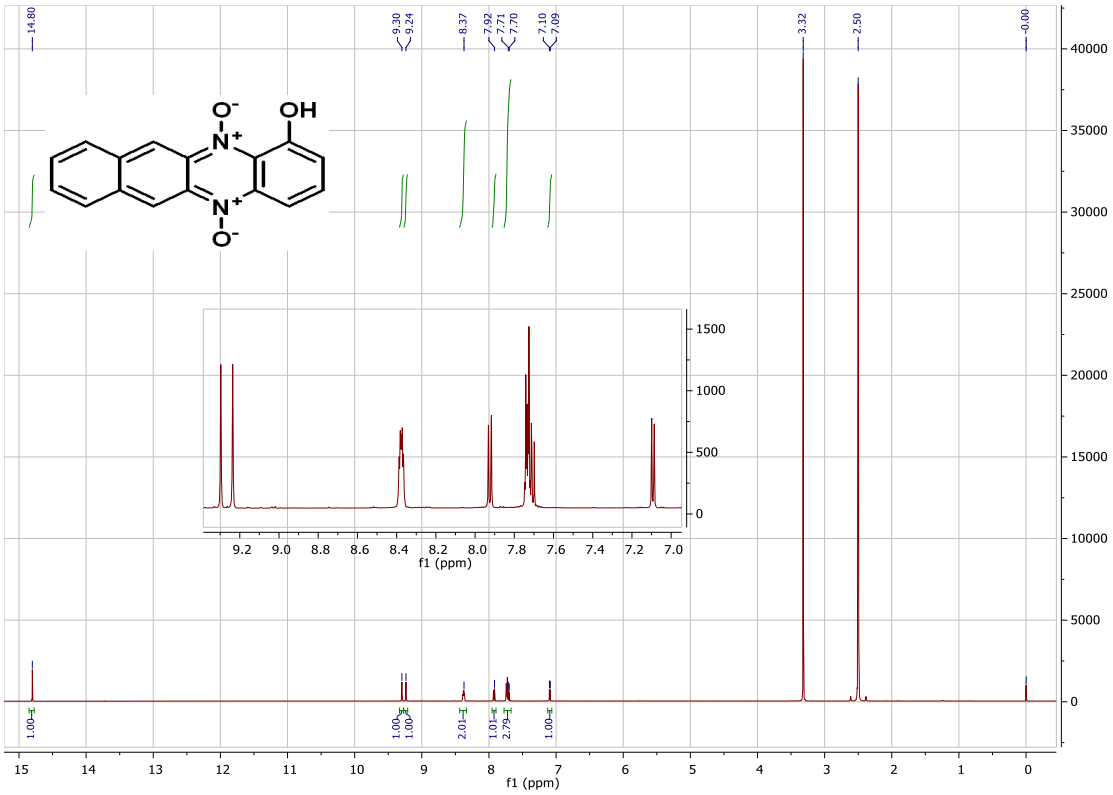


Figure S-37: ^{1}H-NMR spectra of compound **45**

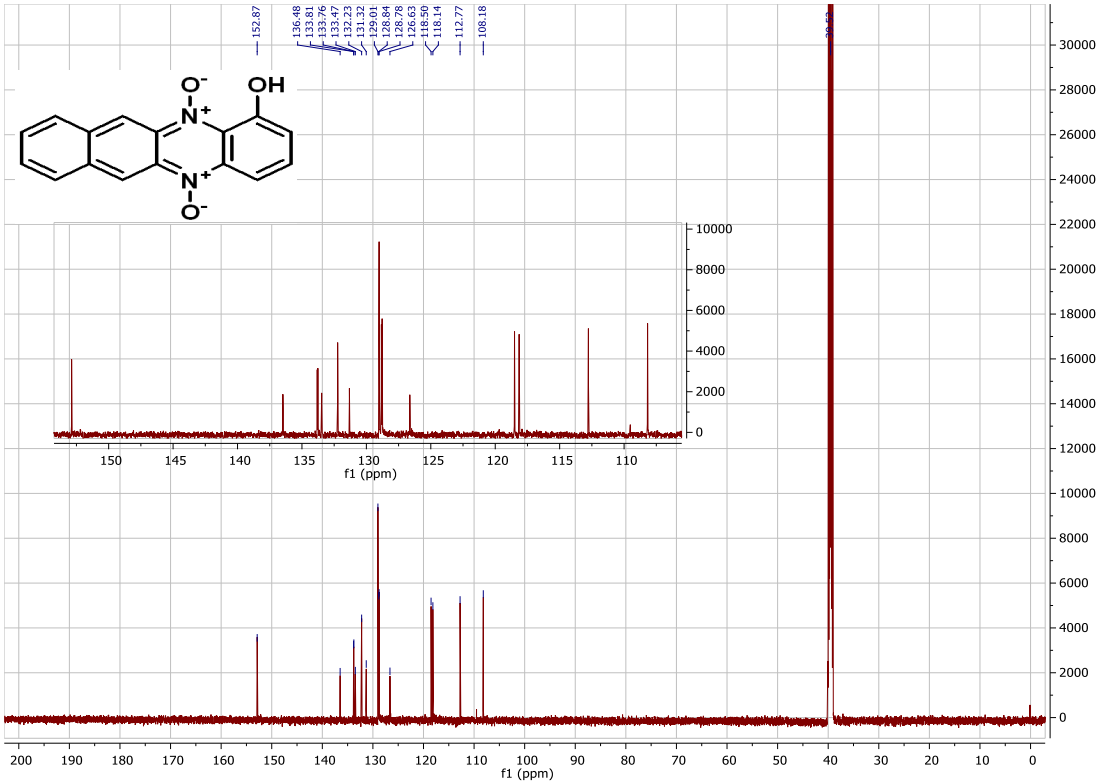


Figure S-38: ^{13}C-NMR spectra of compound **45**

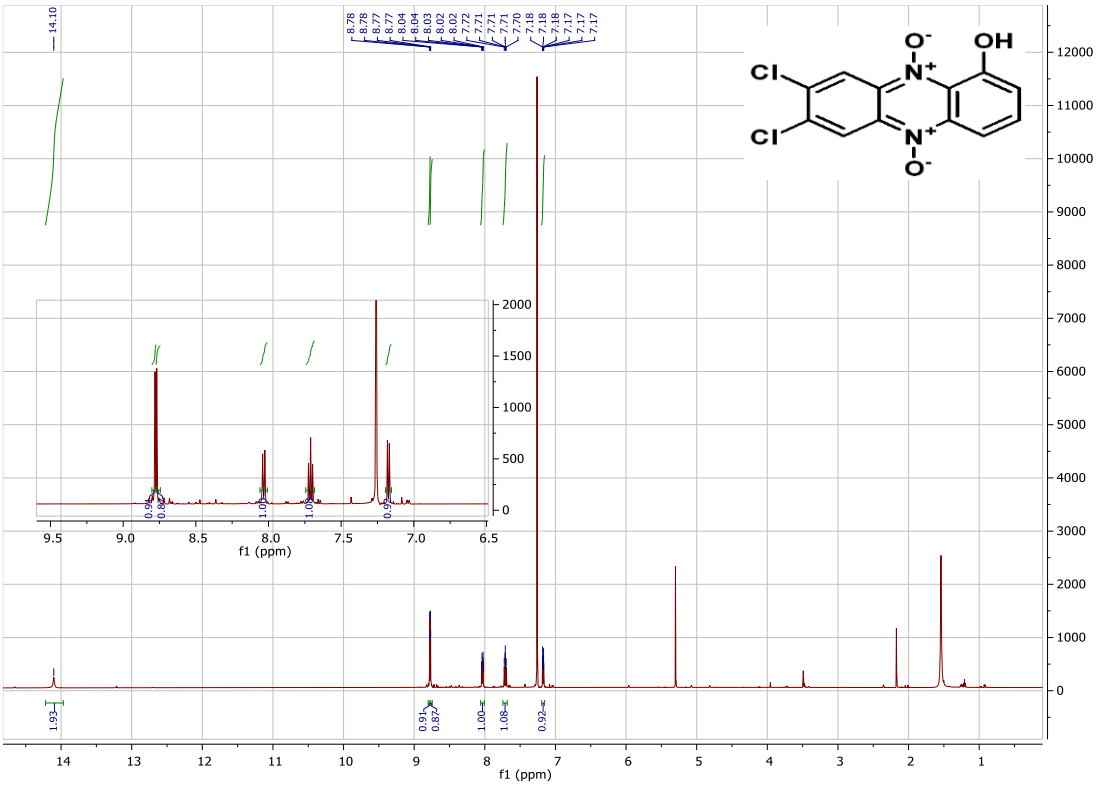


Figure S-39: ^{1}H-NMR spectra of compound **46**

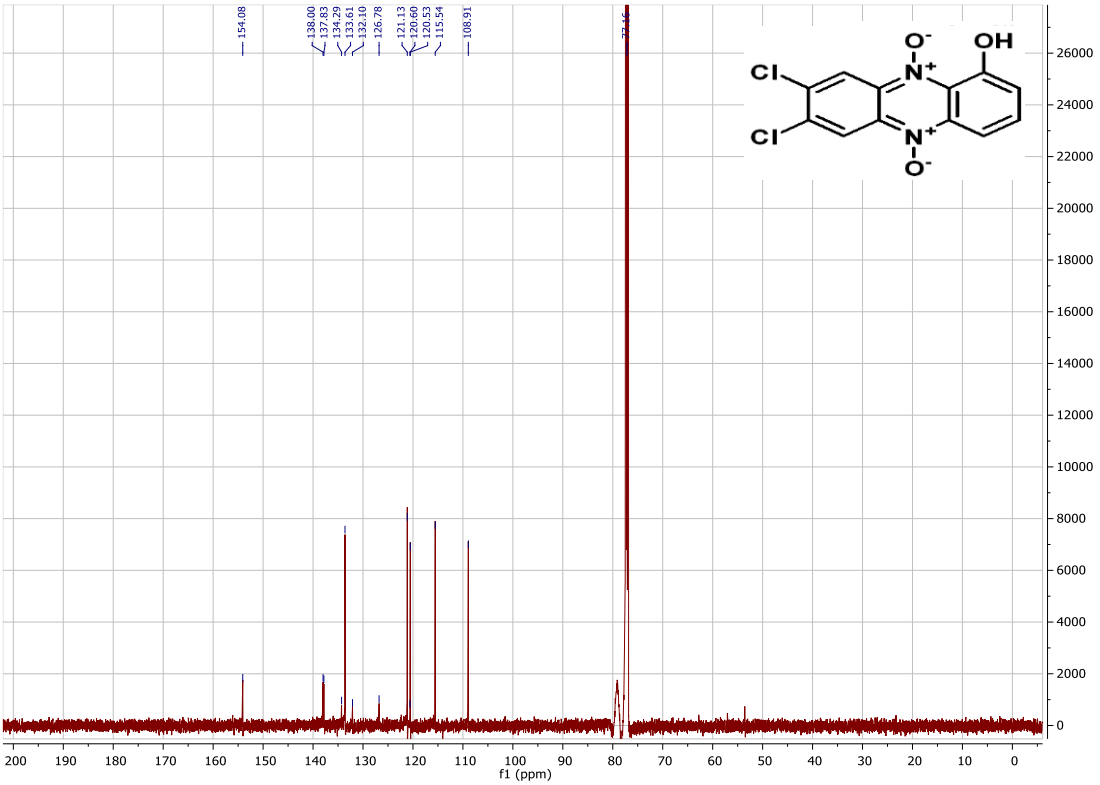


Figure S-40: ^{13}C-NMR spectra of compound **46**

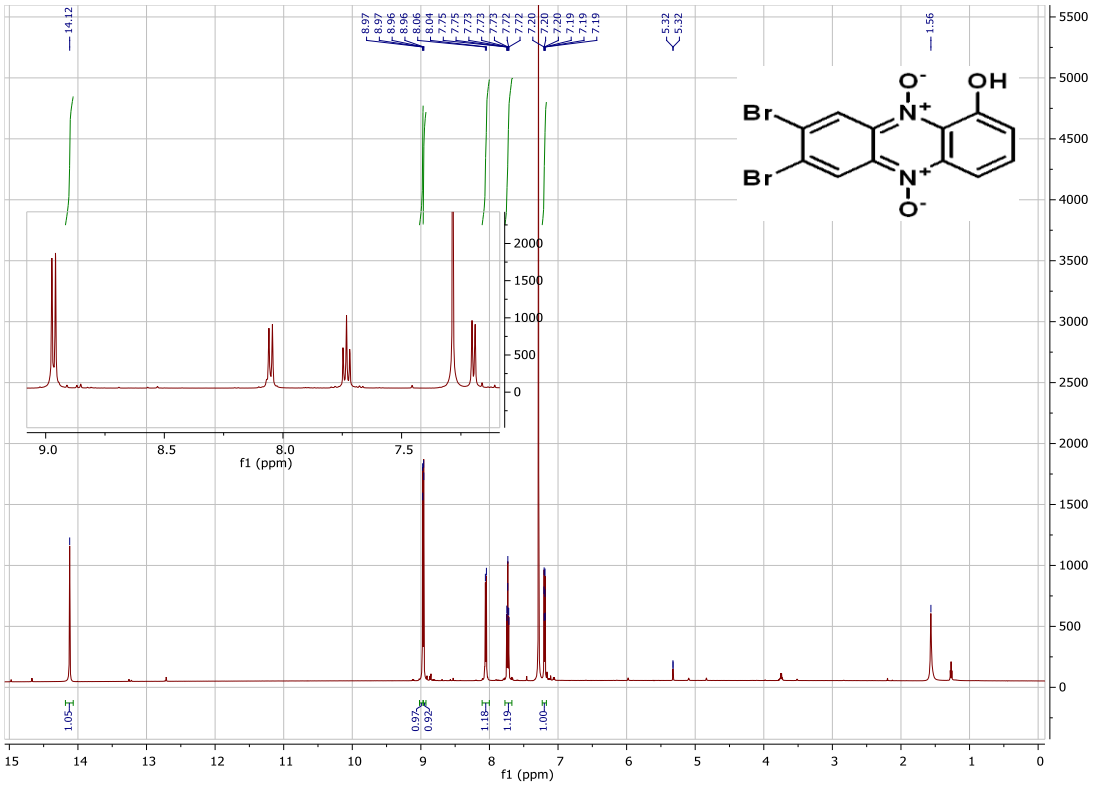


Figure S-41: ^{1}H-NMR spectra of compound **47**

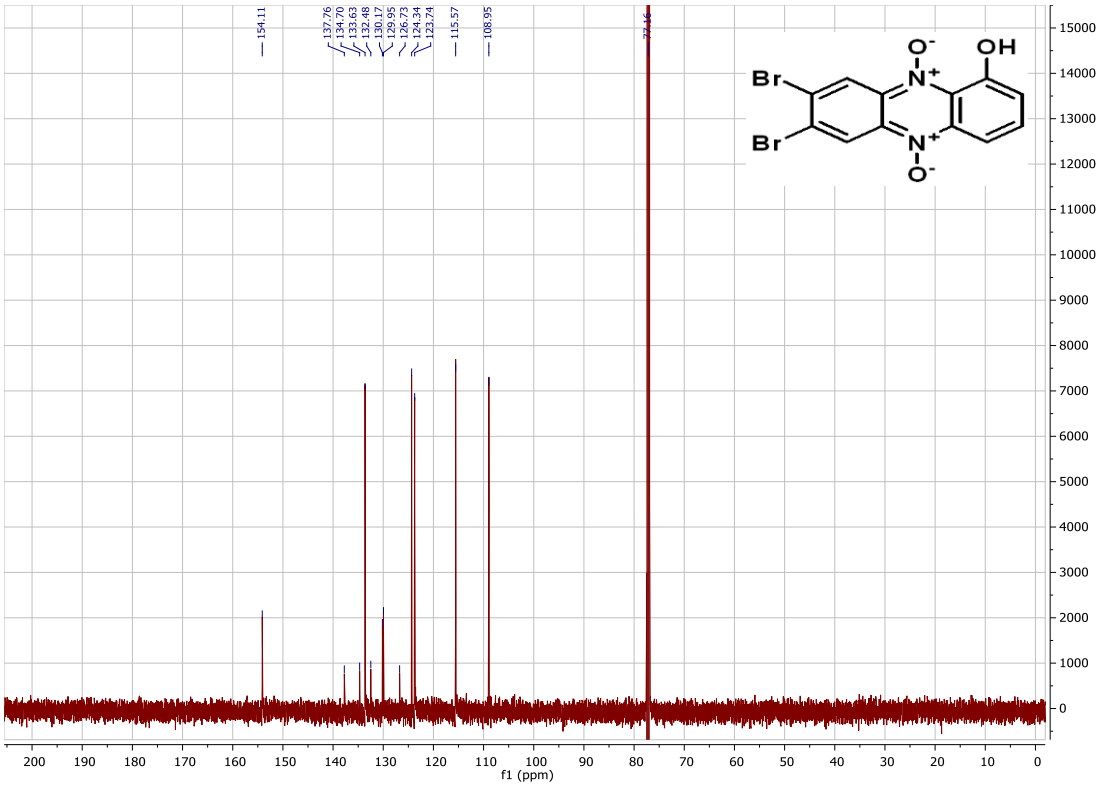


Figure S-42: ^{13}C-NMR spectra of compound **47**

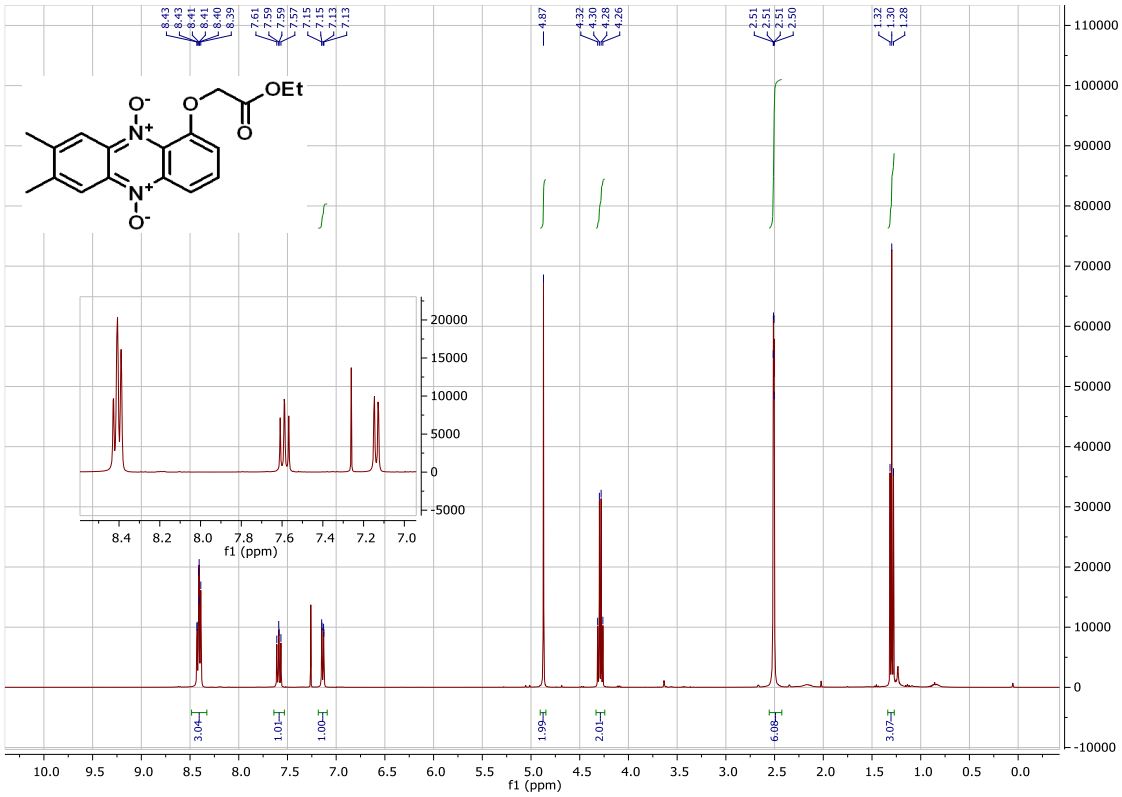


Figure S-43: ^{1}H-NMR spectra of compound **48**

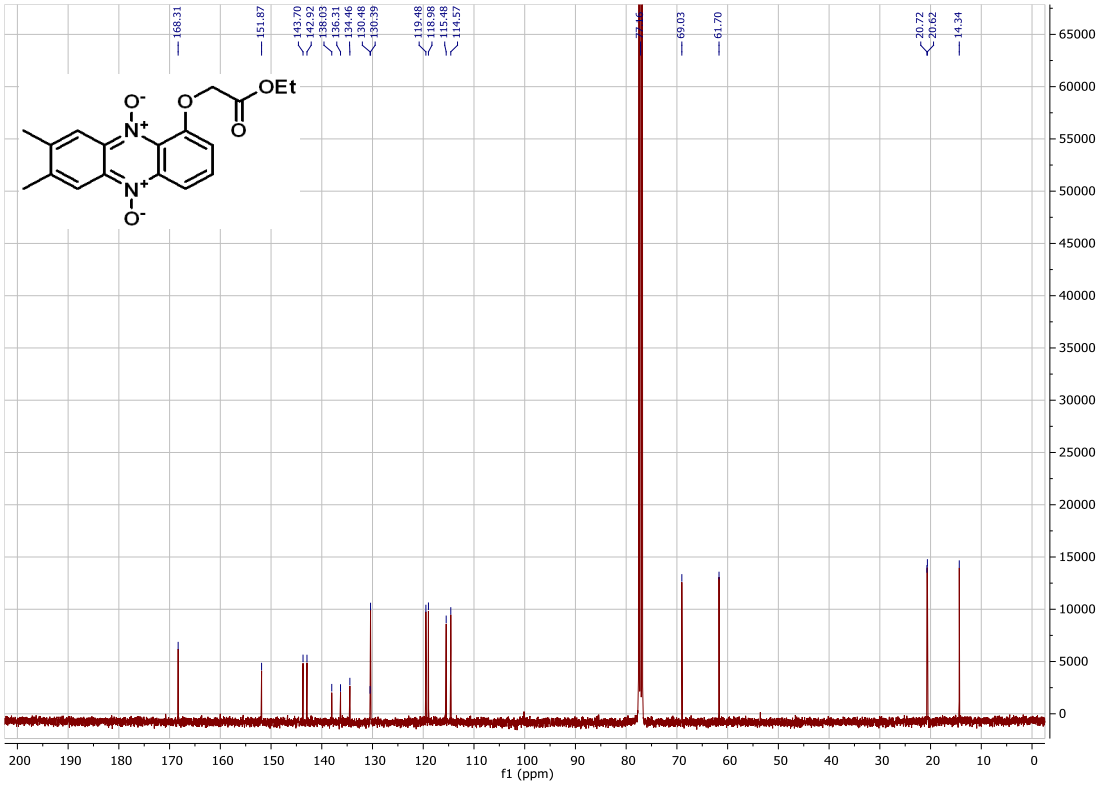


Figure S-44: ^{13}C-NMR spectra of compound **48**

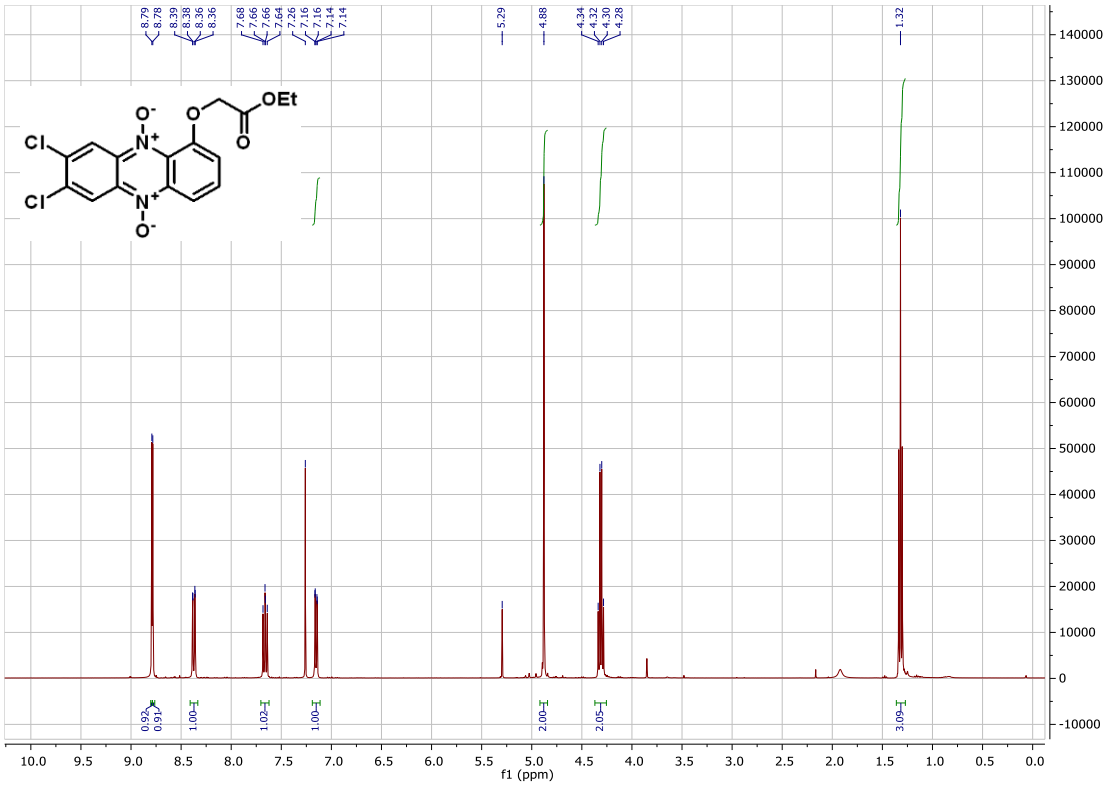


Figure S-45: ^{1}H-NMR spectra of compound **50**

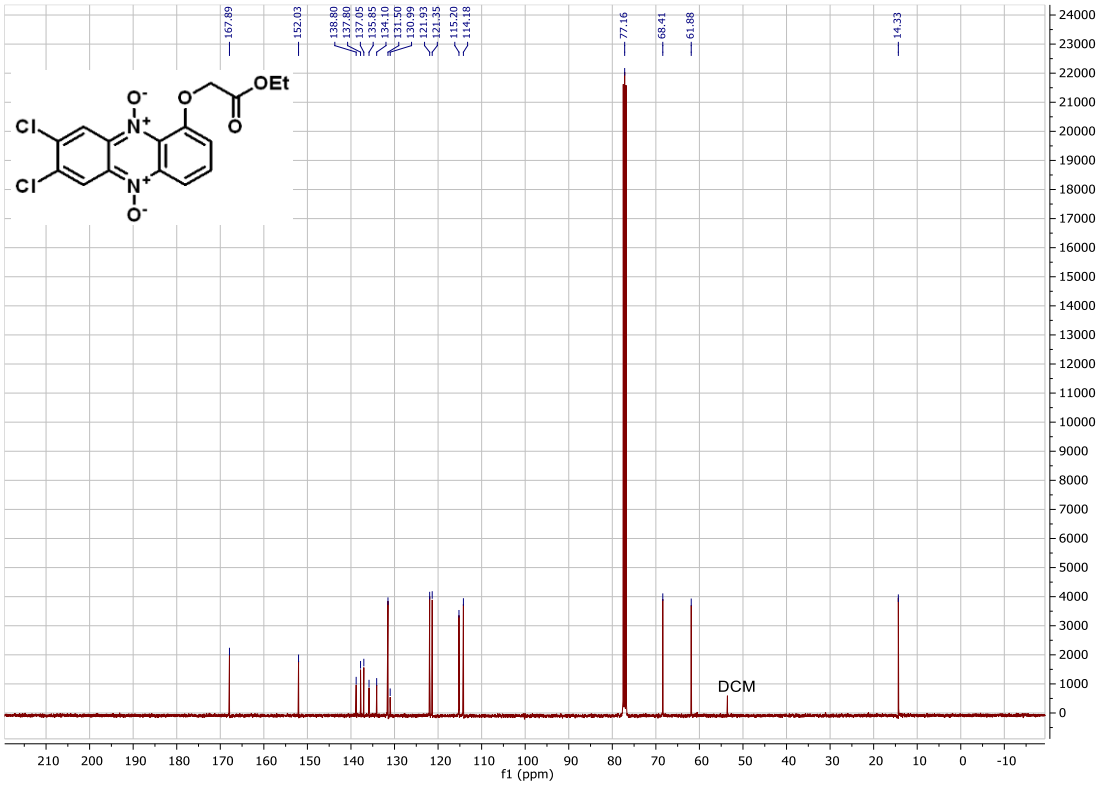


Figure S-46: ^{13}C-NMR spectra of compound **50**

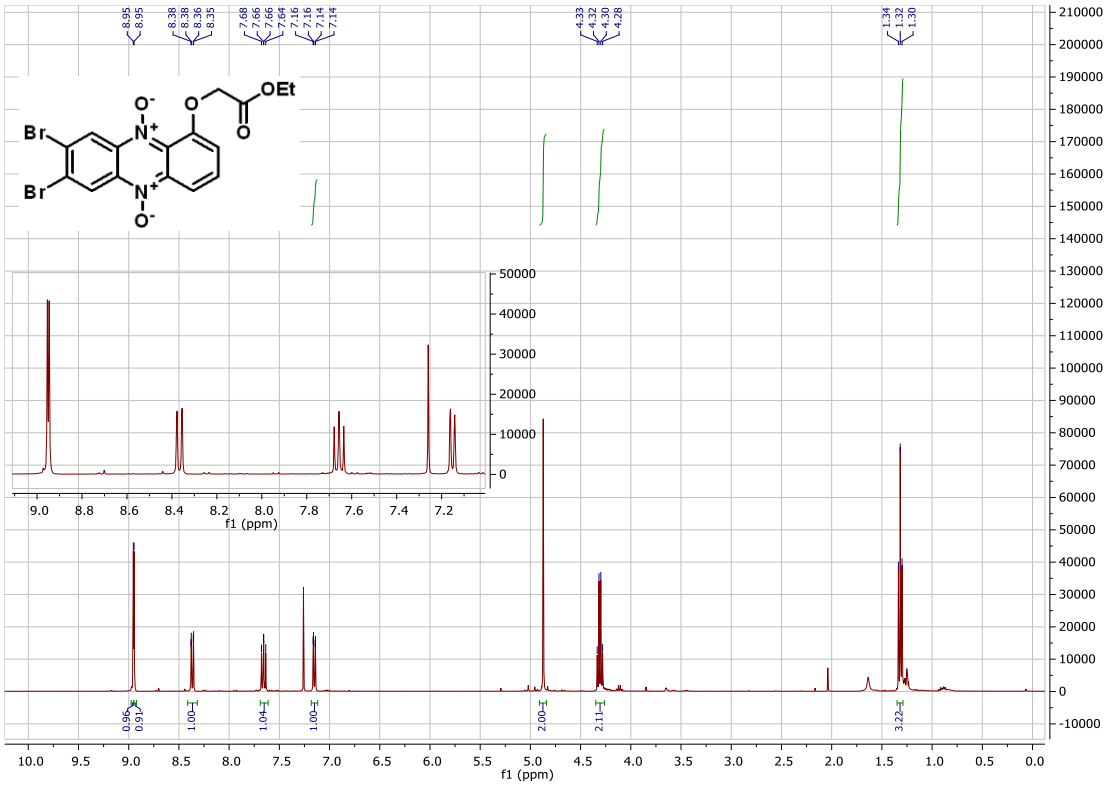


Figure S-47: ^{1}H-NMR spectra of compound **51**

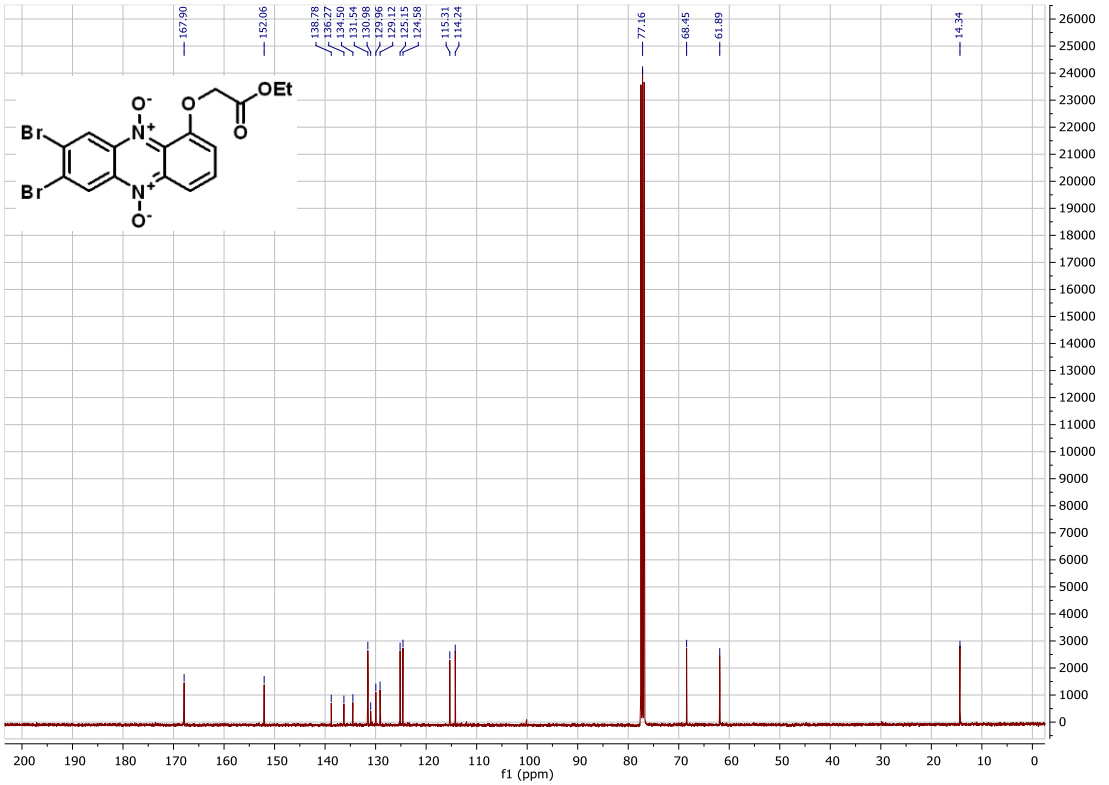


Figure S-48: ^{13}C-NMR spectra of compound **51**

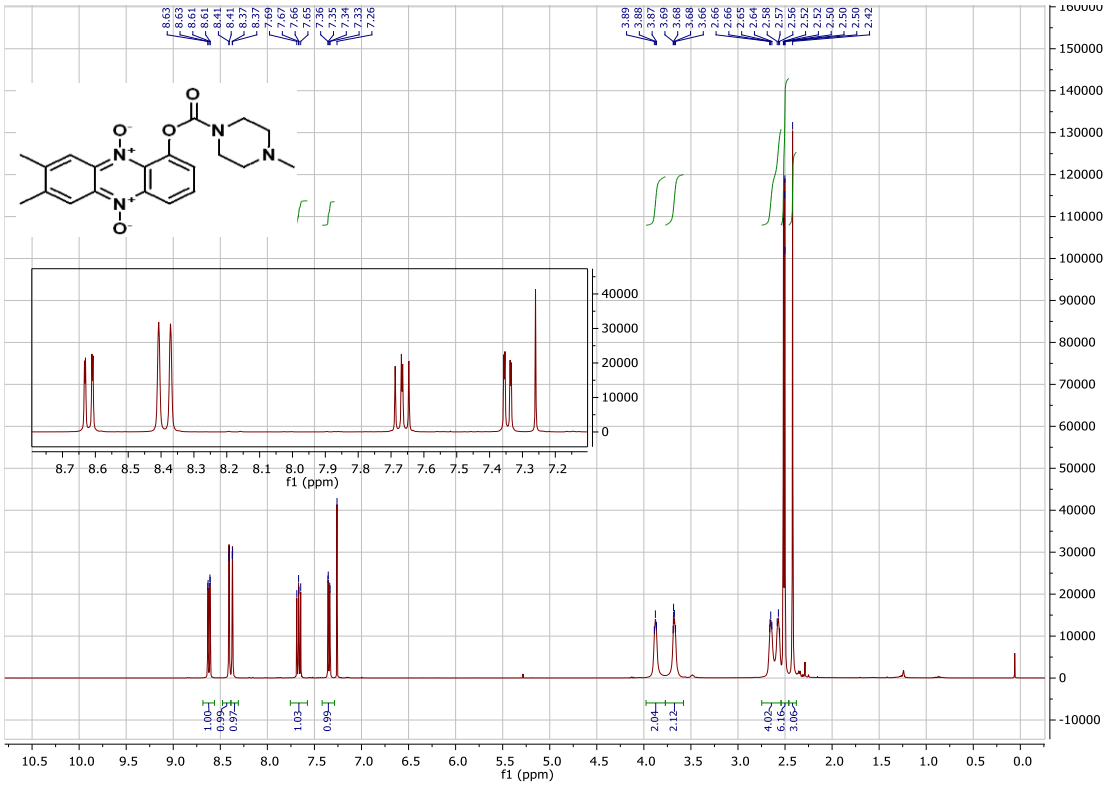


Figure S-49: ^{1}H-NMR spectra of compound **52**

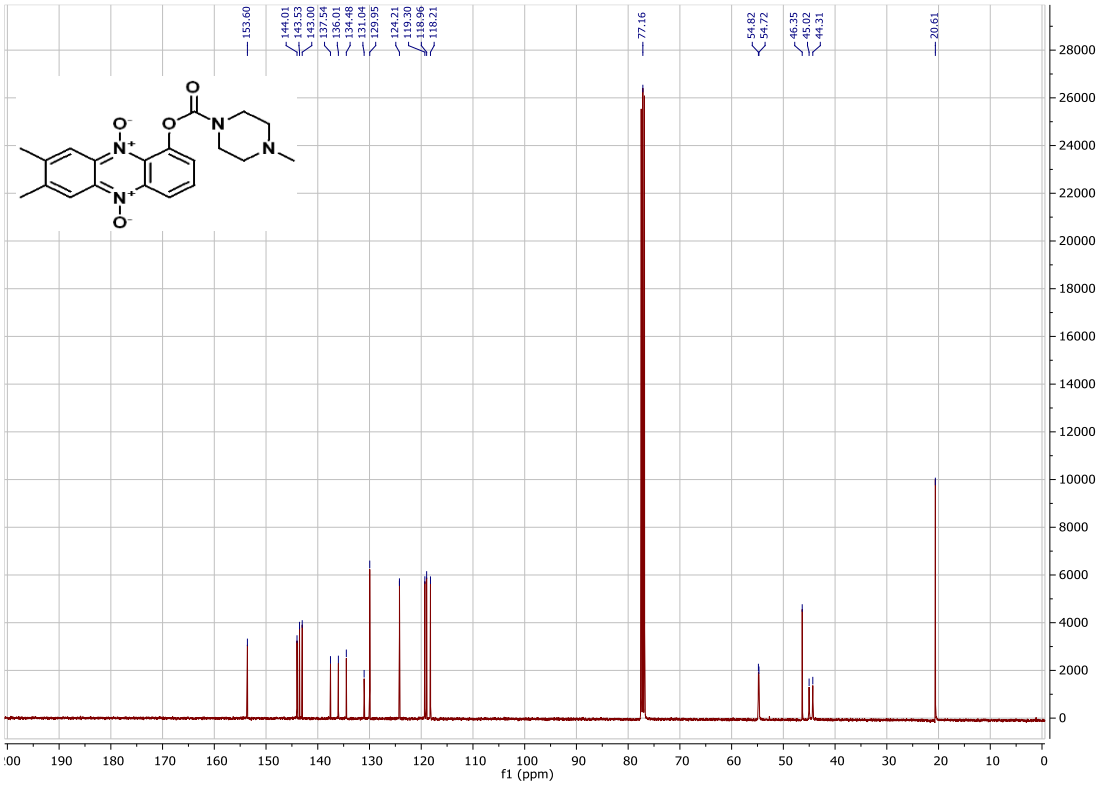


Figure S-50: ^{13}C-NMR spectra of compound **52**

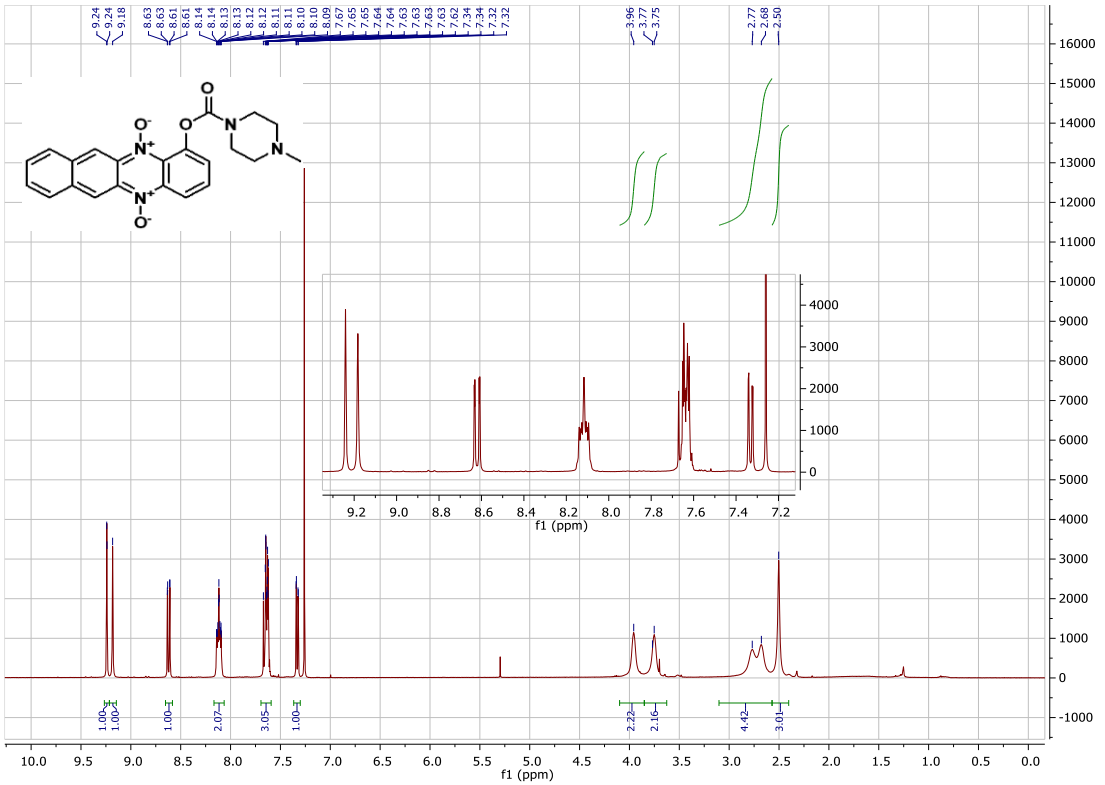


Figure S-51: ^{1}H-NMR spectra of compound **53**

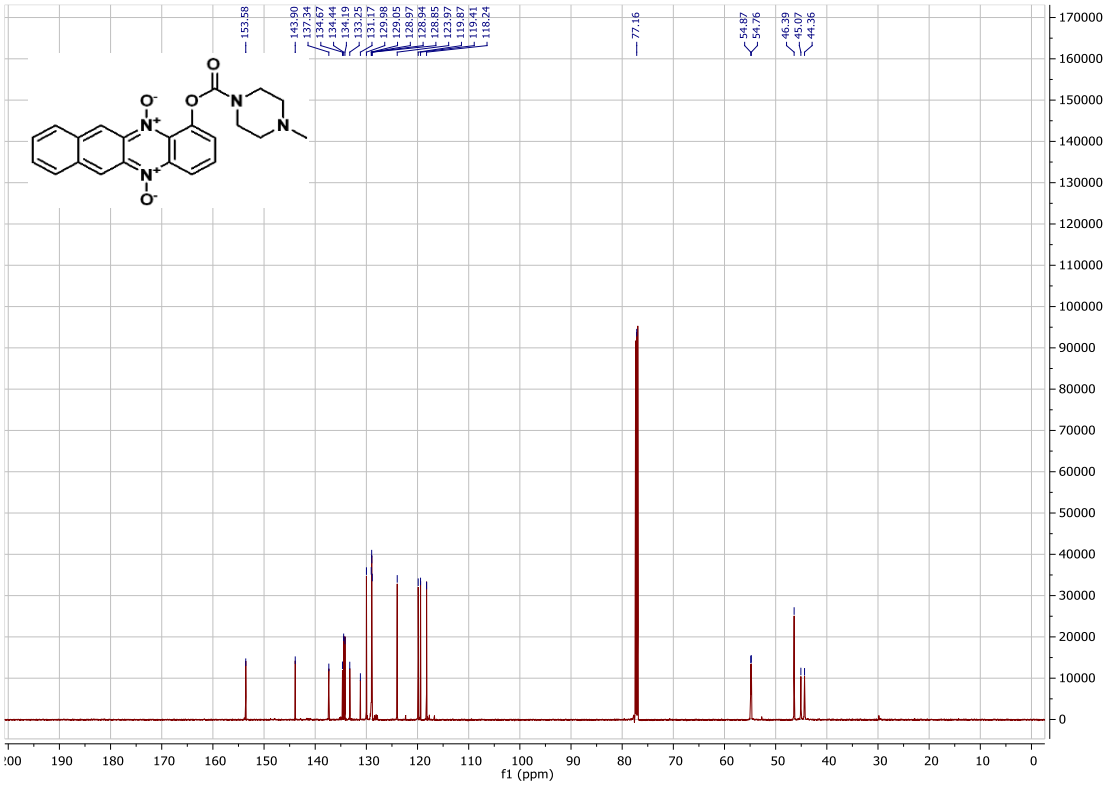


Figure S-52: ^{13}C-NMR spectra of compound **53**

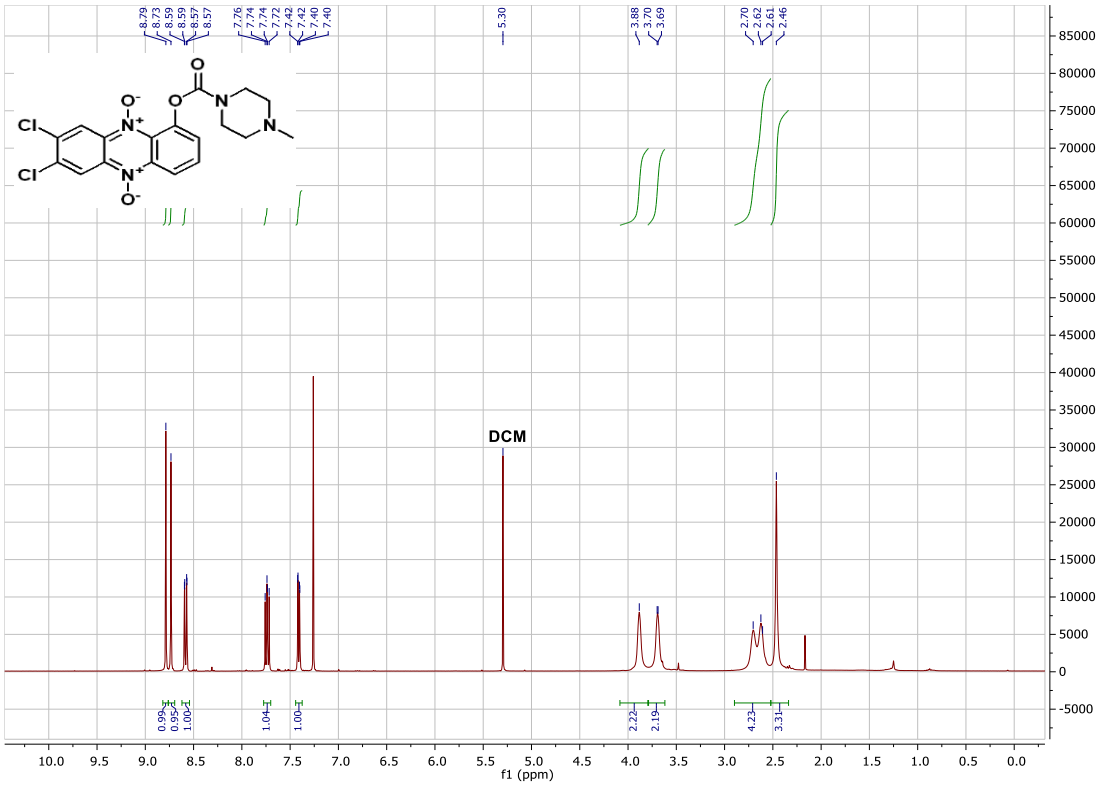


Figure S-53: ^{1}H-NMR spectra of compound **54**

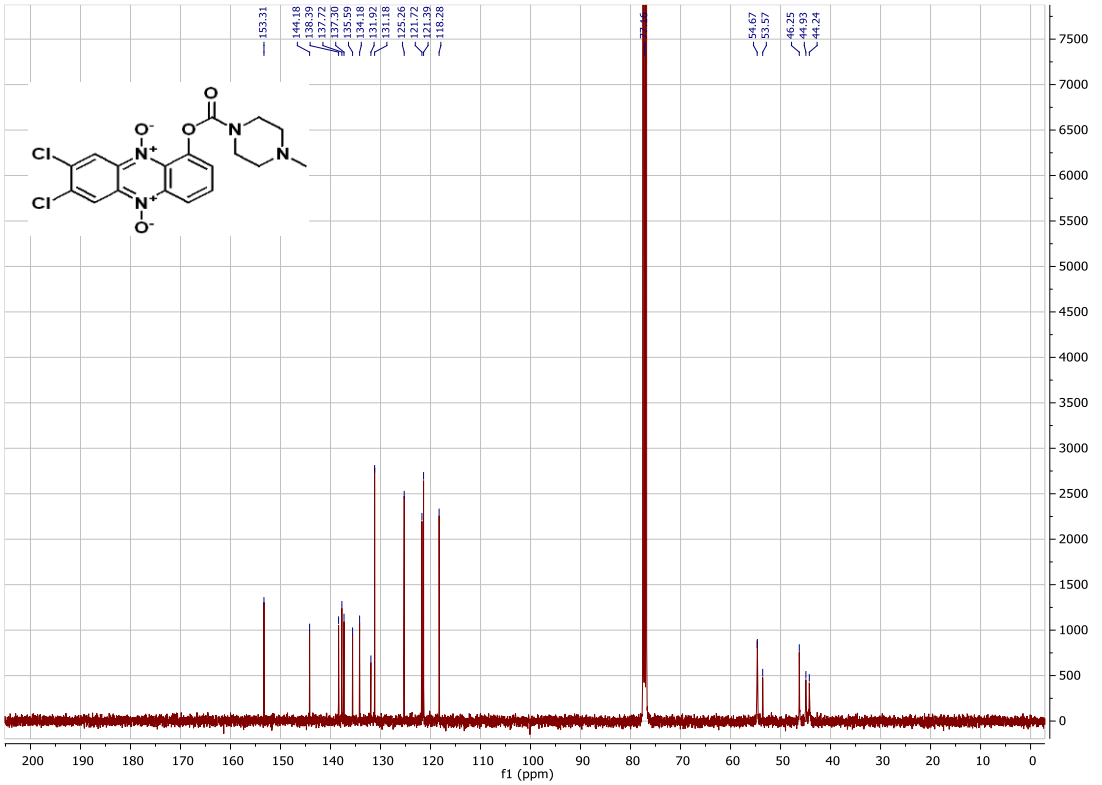


Figure S-54: ^{13}C-NMR spectra of compound **54**

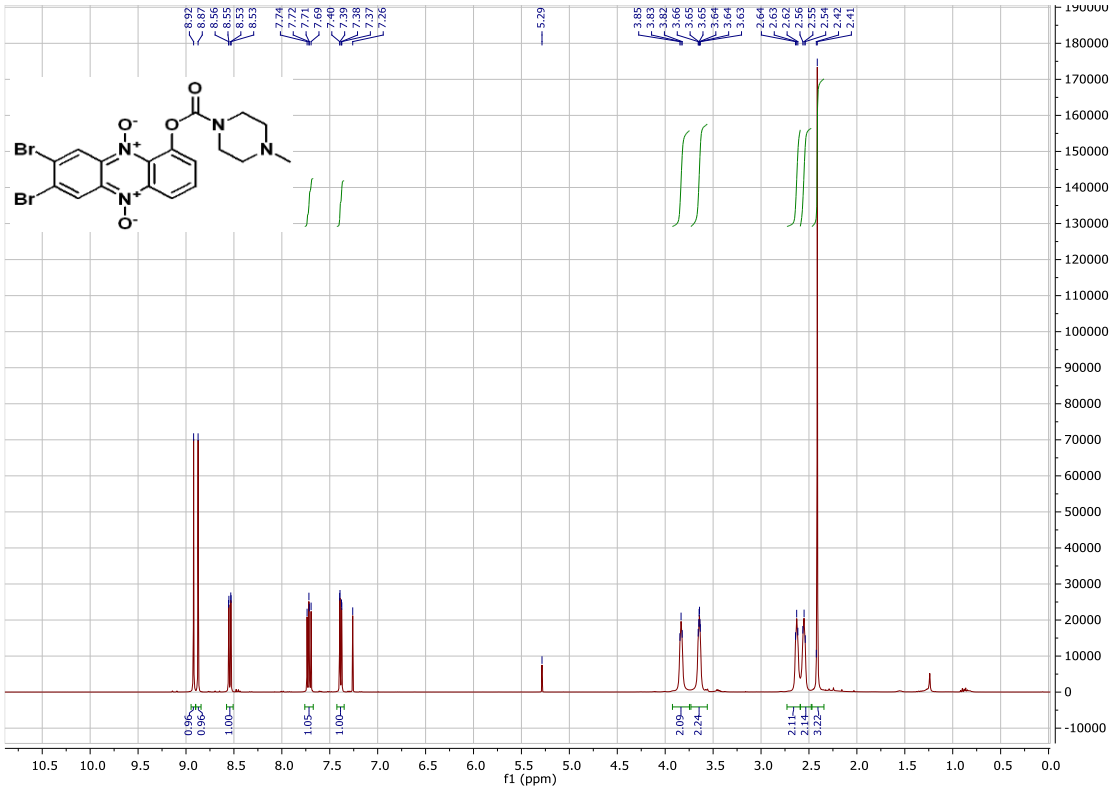


Figure S-55: ^{1}H-NMR spectra of compound **55**

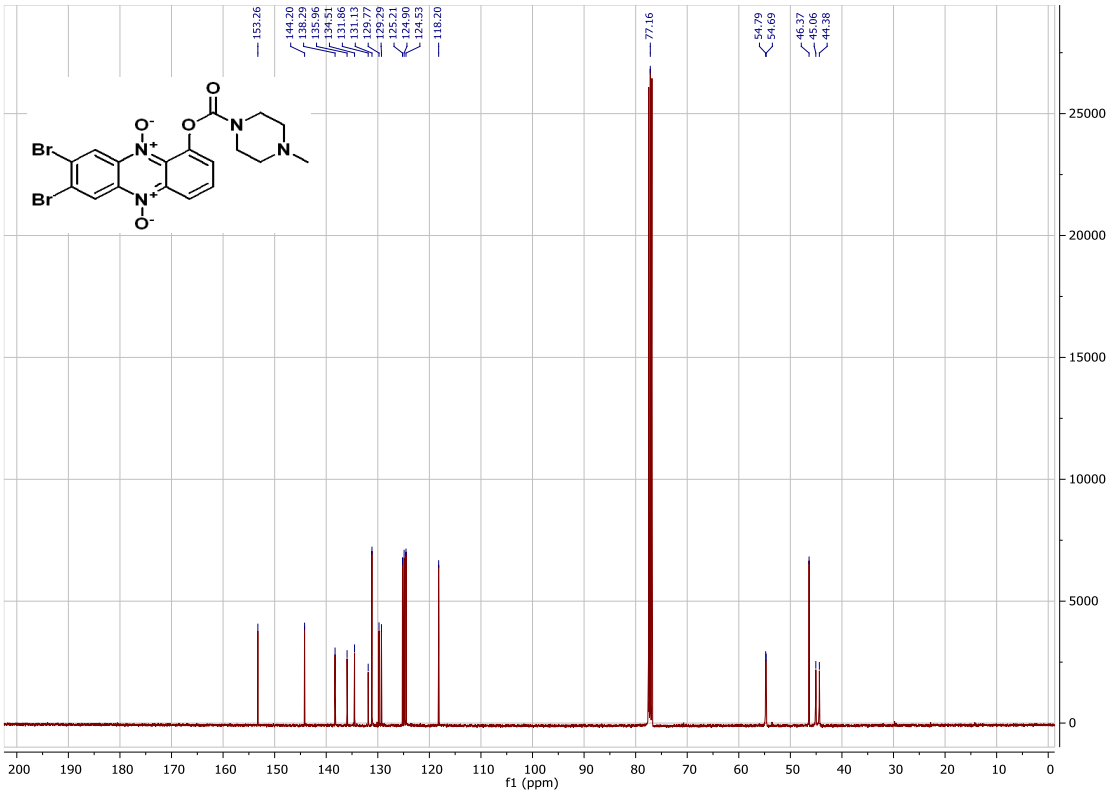


Figure S-56: ^{13}C-NMR spectra of compound **55**

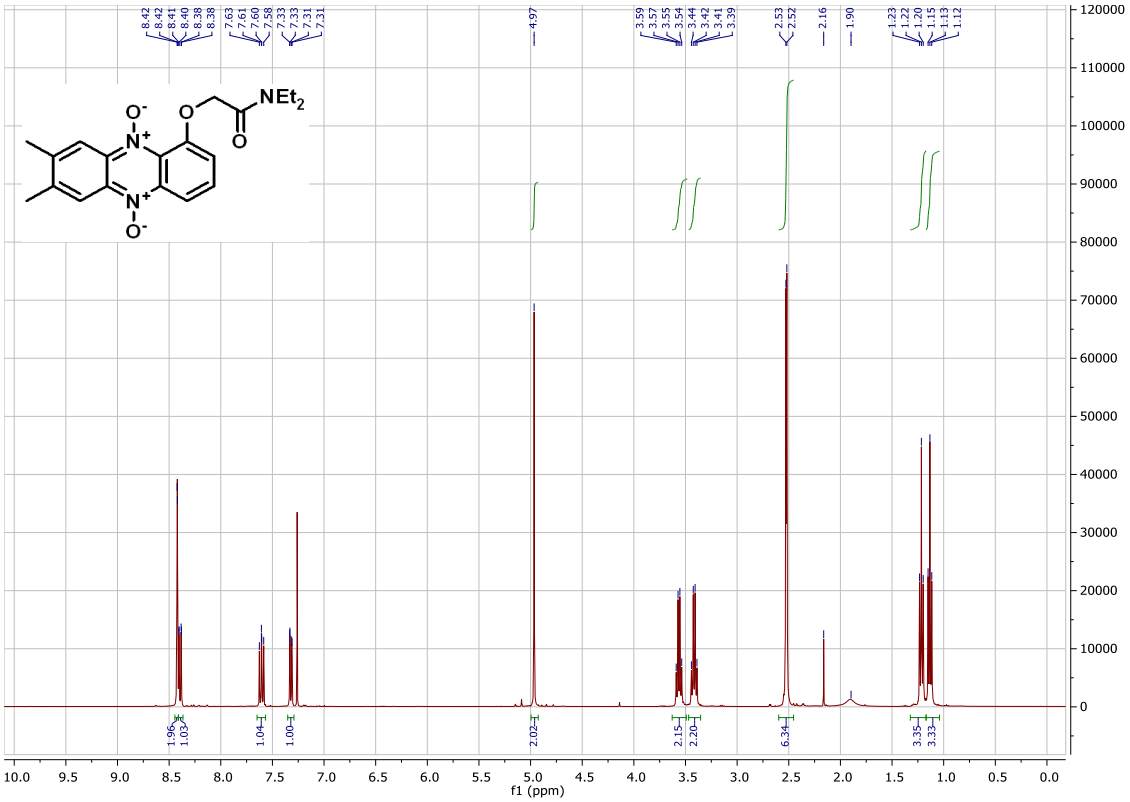


Figure S-57: ^{1}H-NMR spectra of compound **56**

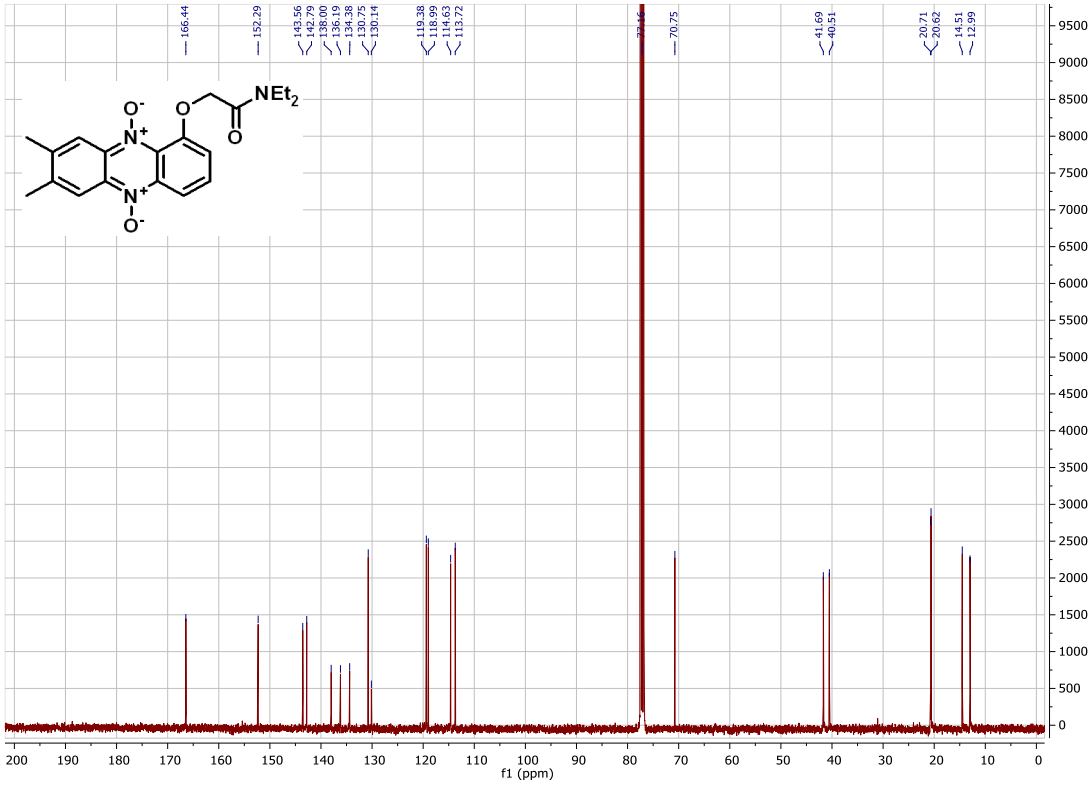


Figure S-58: ^{13}C-NMR spectra of compound **56**

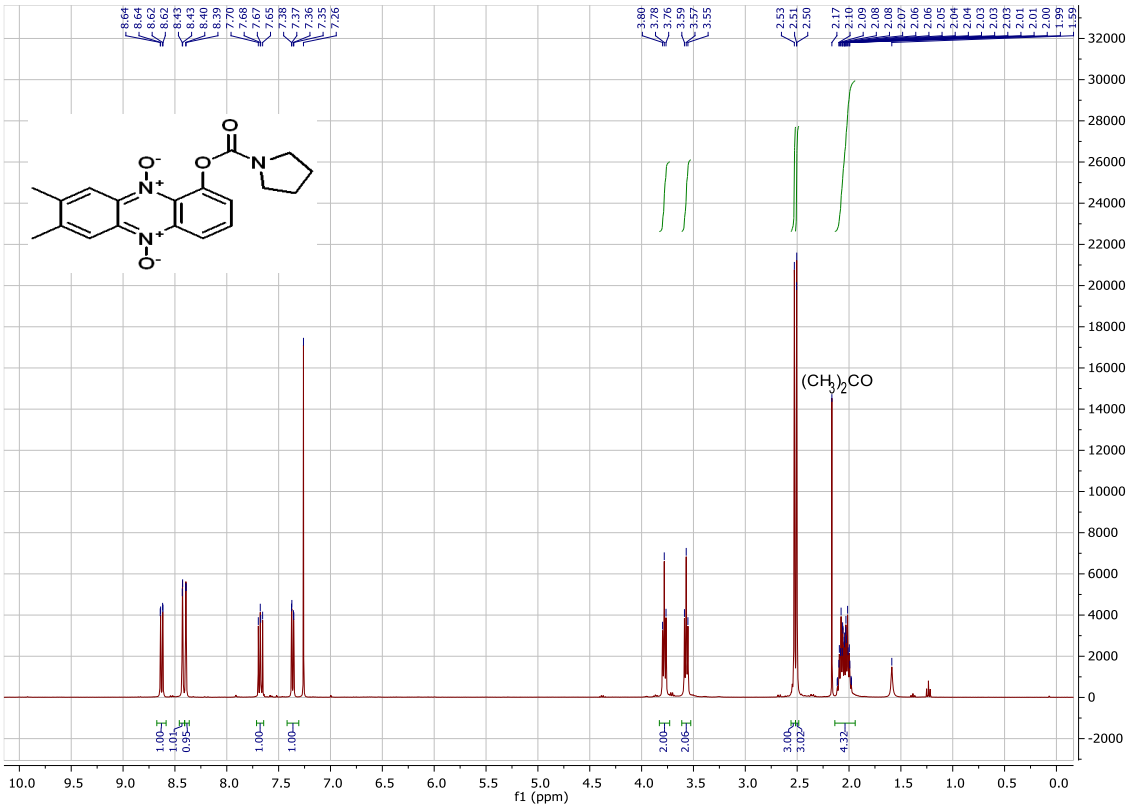


Figure S-59: ^{1}H-NMR spectra of compound **57**

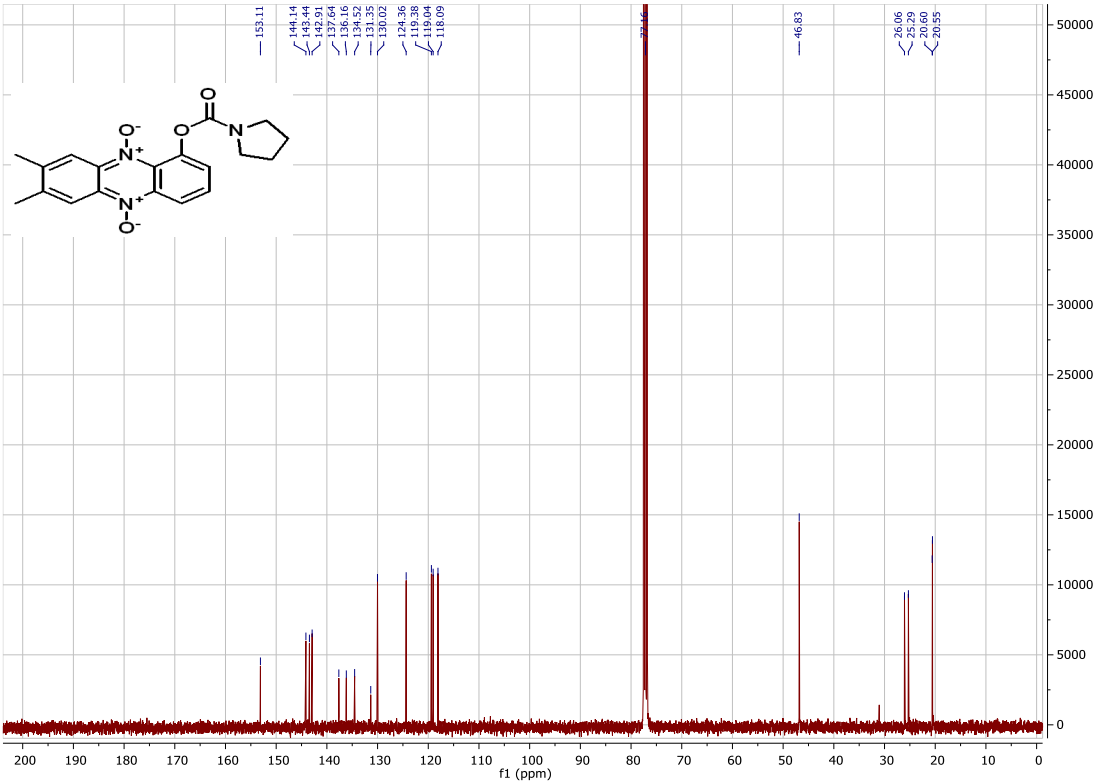


Figure S-60: ^{13}C-NMR spectra of compound **56**

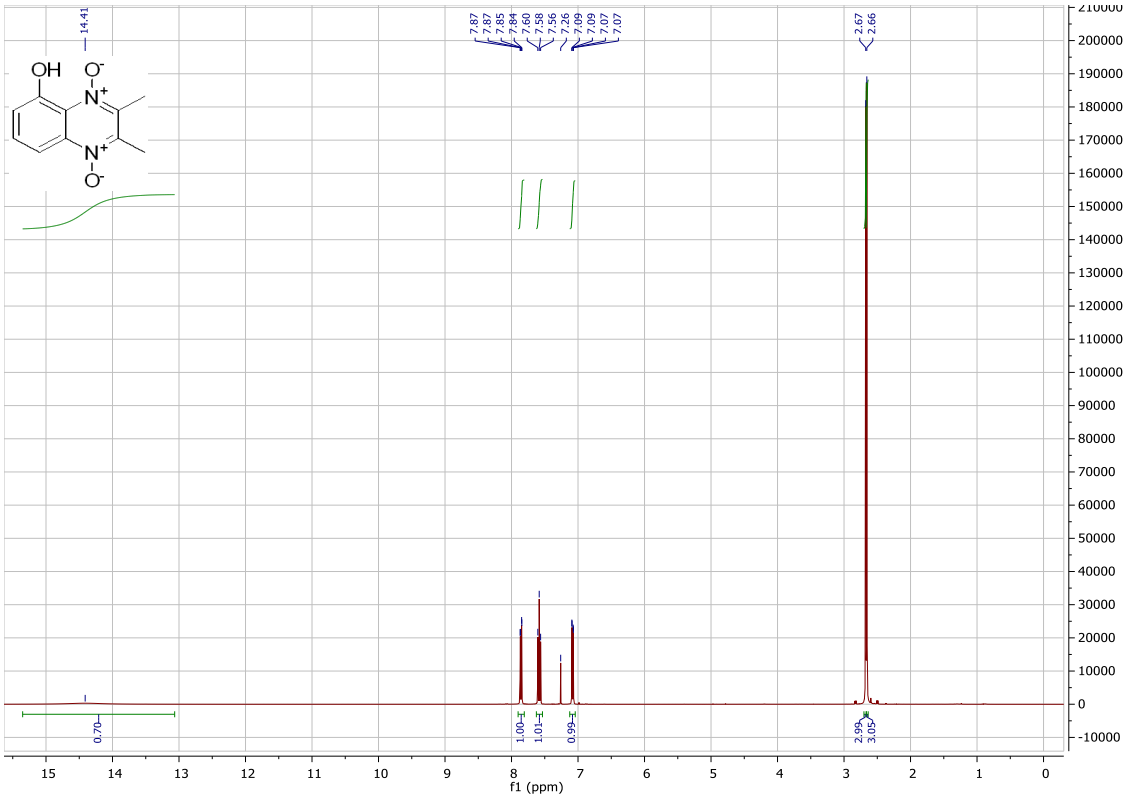


Figure S-61: ^{1}H-NMR spectra of compound **60**

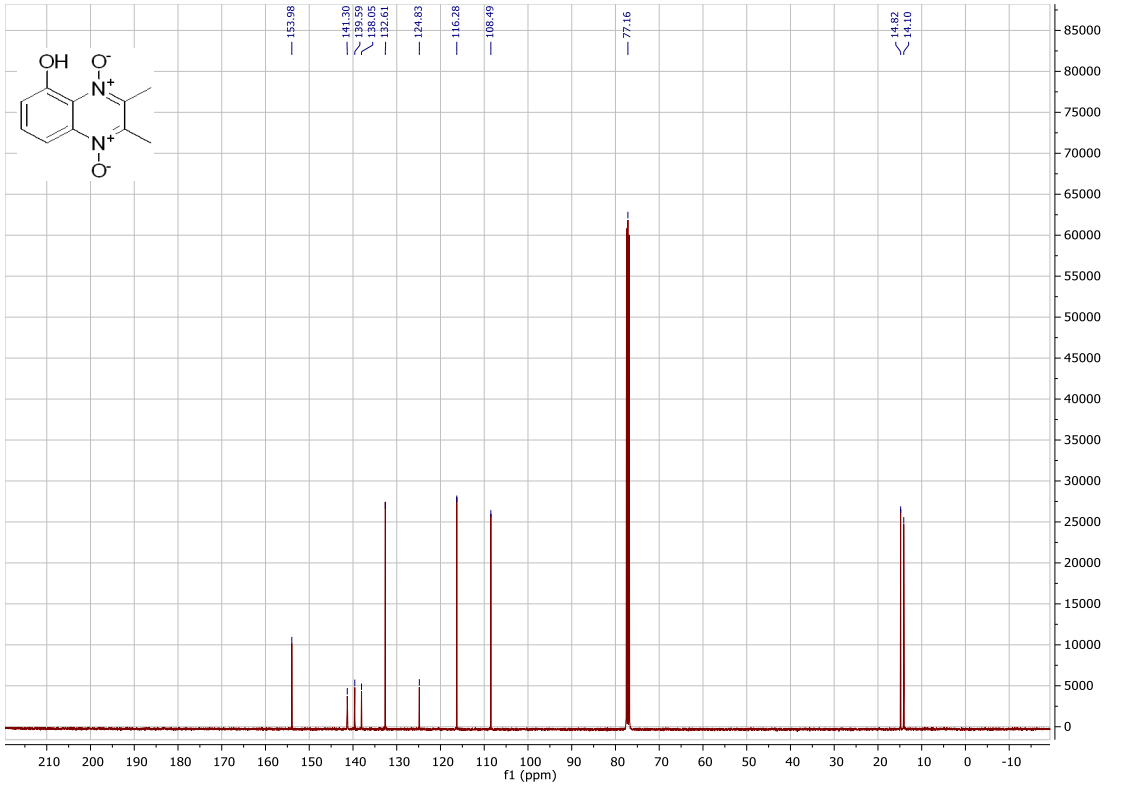


Figure S-62: ^{13}C-NMR spectra of compound **60**

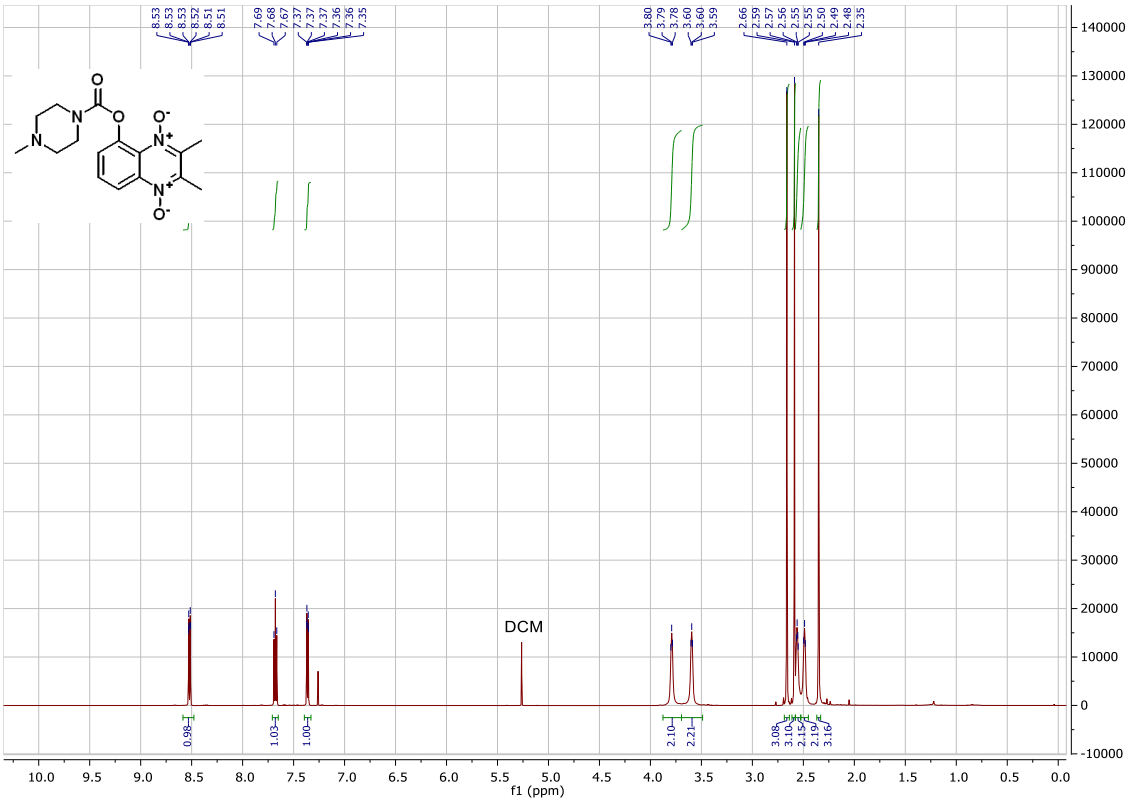


Figure S-63: ^{1}H-NMR spectra of compound **61**

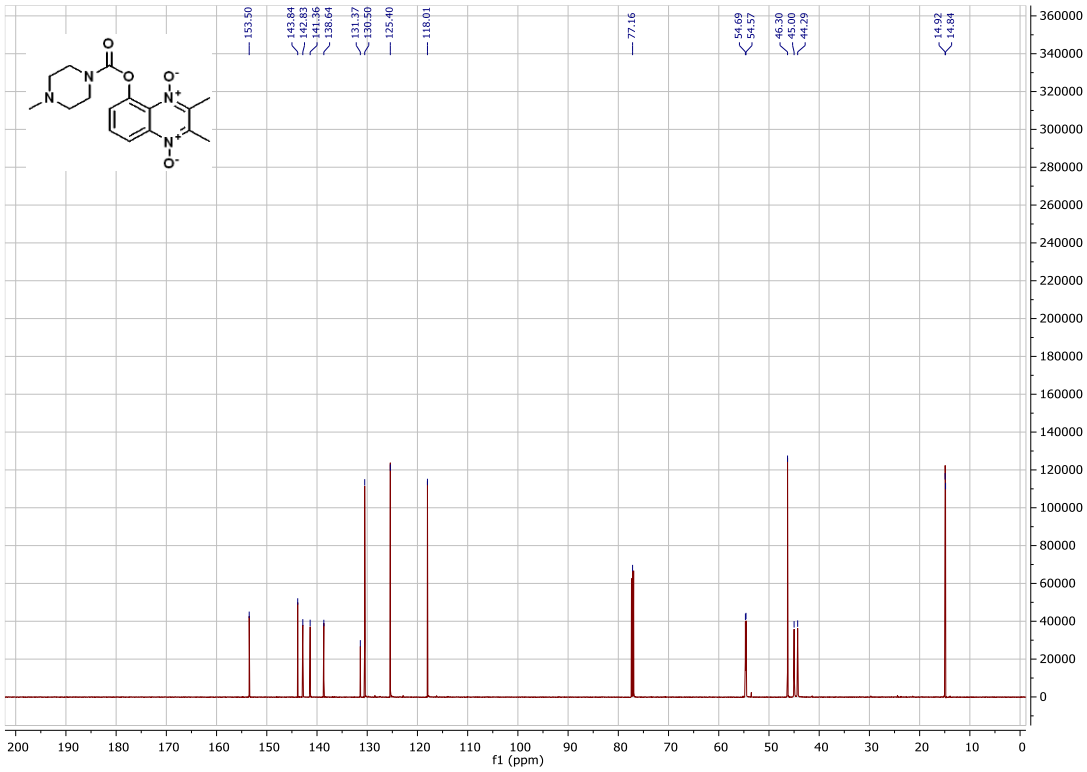


Figure S-64: ^{13}C-NMR spectra of compound **61**

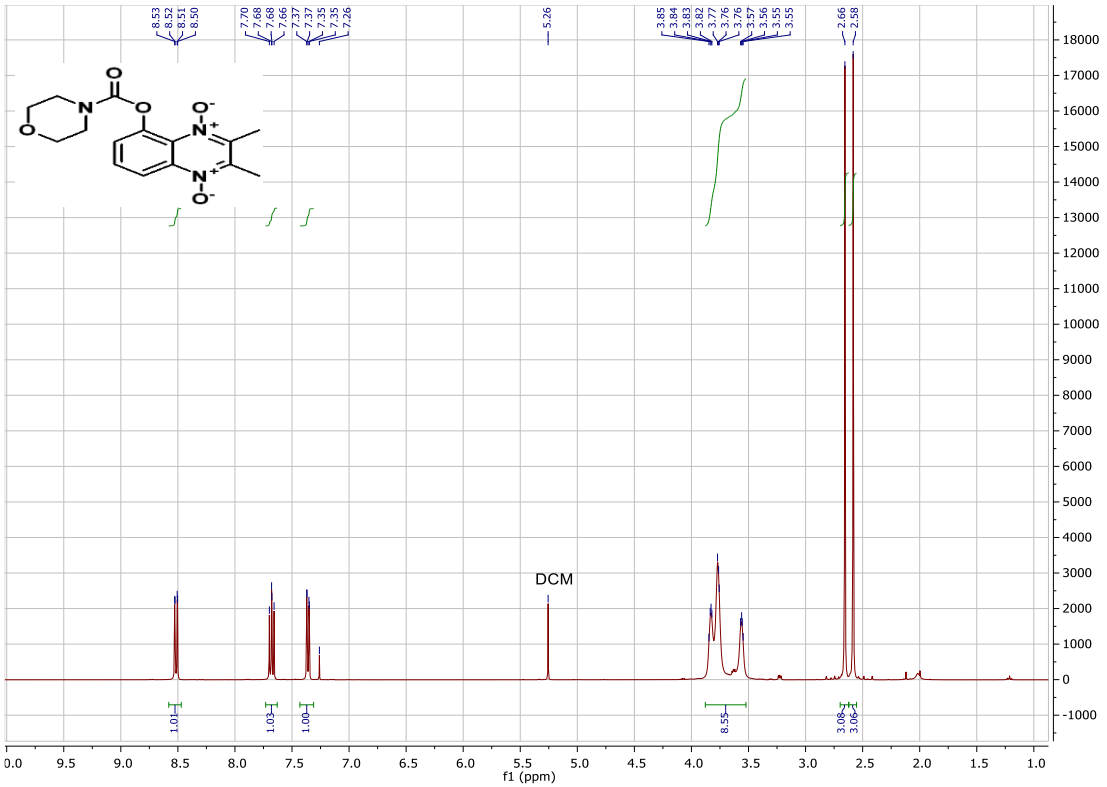


Figure S-65: ^{1}H-NMR spectra of compound **62**

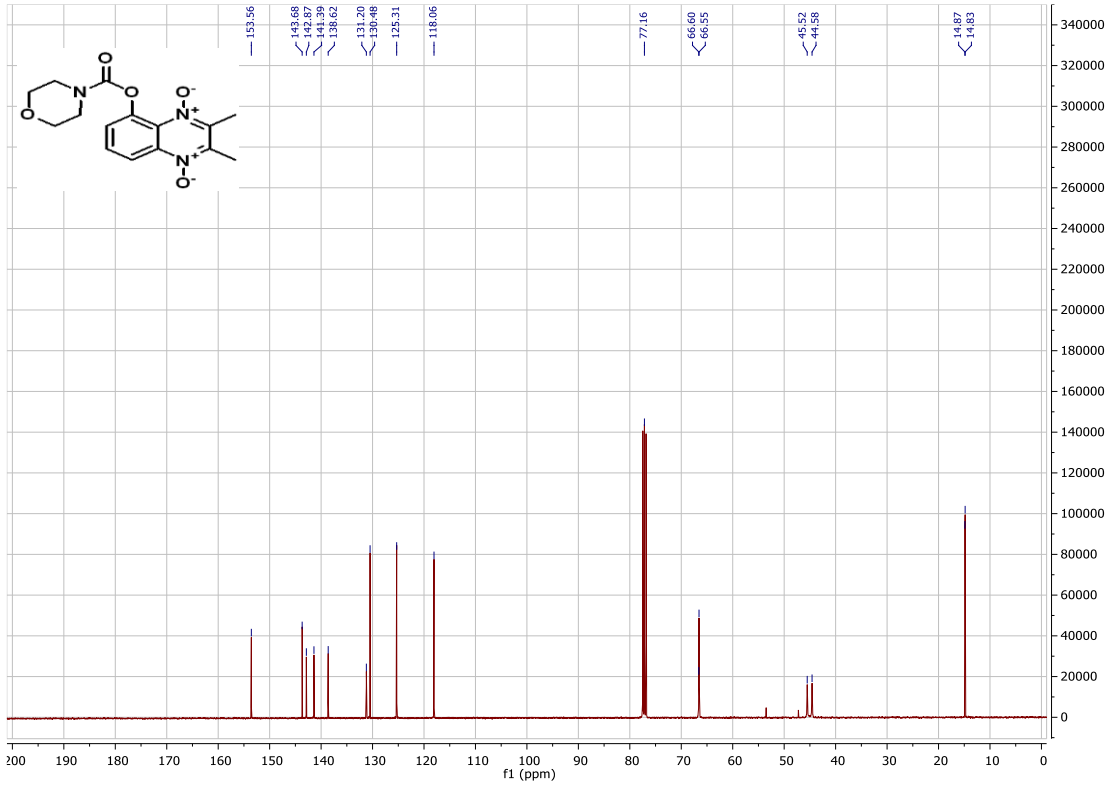


Figure S-66: ^{13}C-NMR spectra of compound **62**

^{1}H- and ^{13}C-NMR spectra of synthetic intermediates

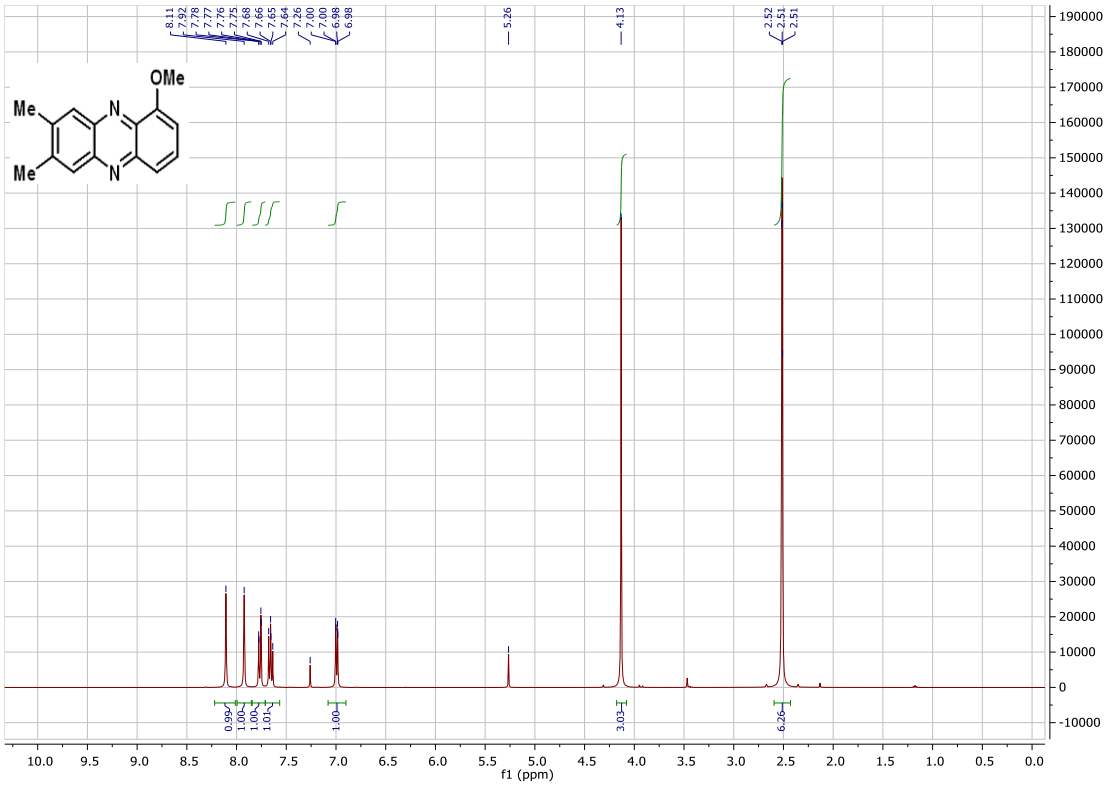


Figure S-67: ^{1}H-NMR spectra of compound **36**

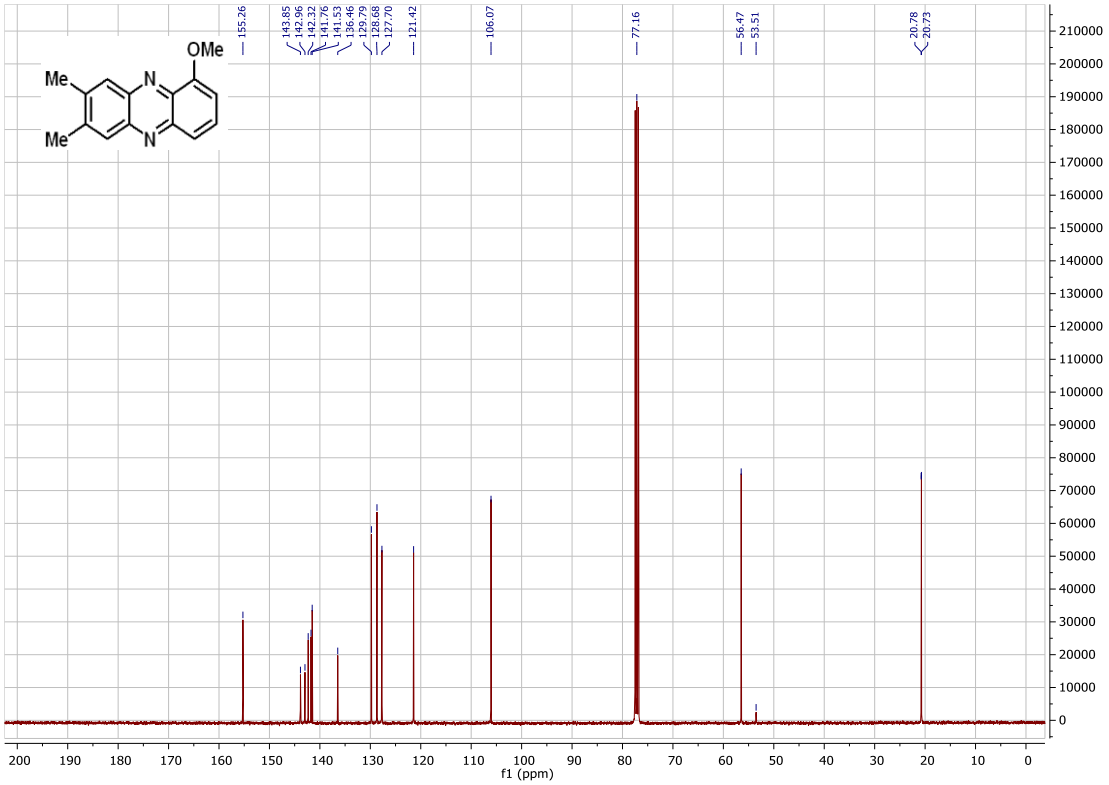


Figure S-68: ^{13}C-NMR spectra of compound **36**

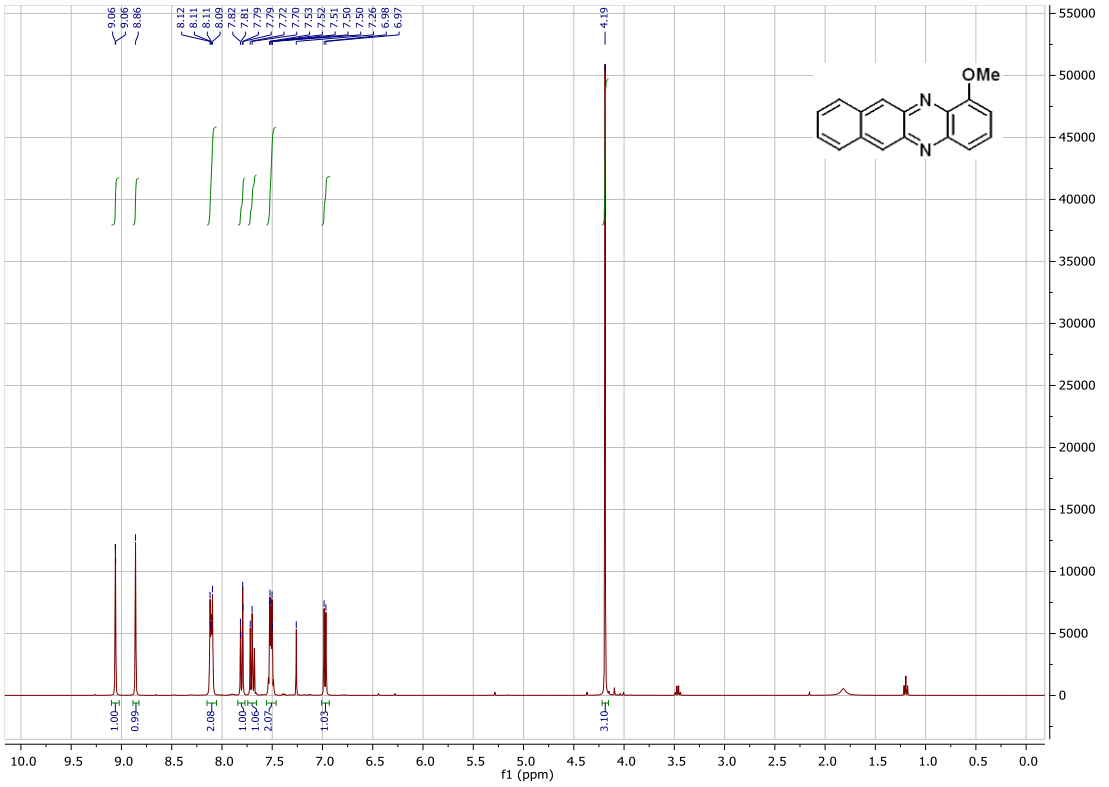


Figure S-69: ^{1}H-NMR spectra of compound **37**

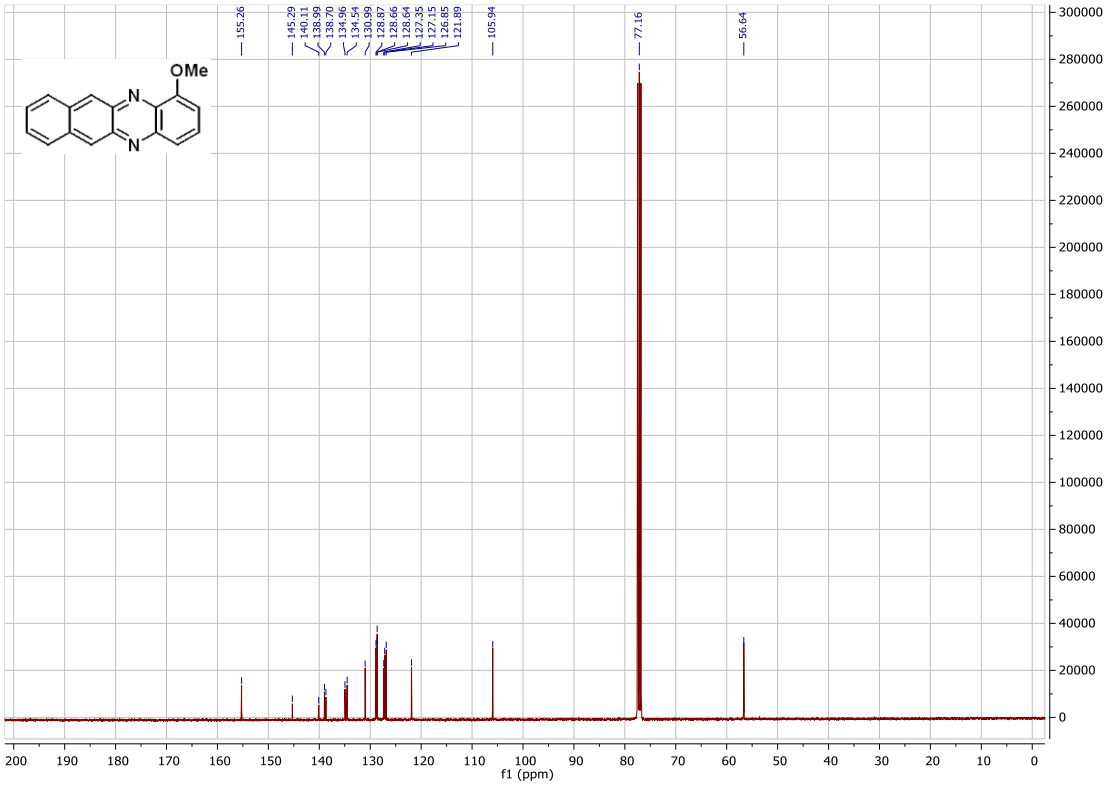


Figure S-70: ^{13}C-NMR spectra of compound **37**

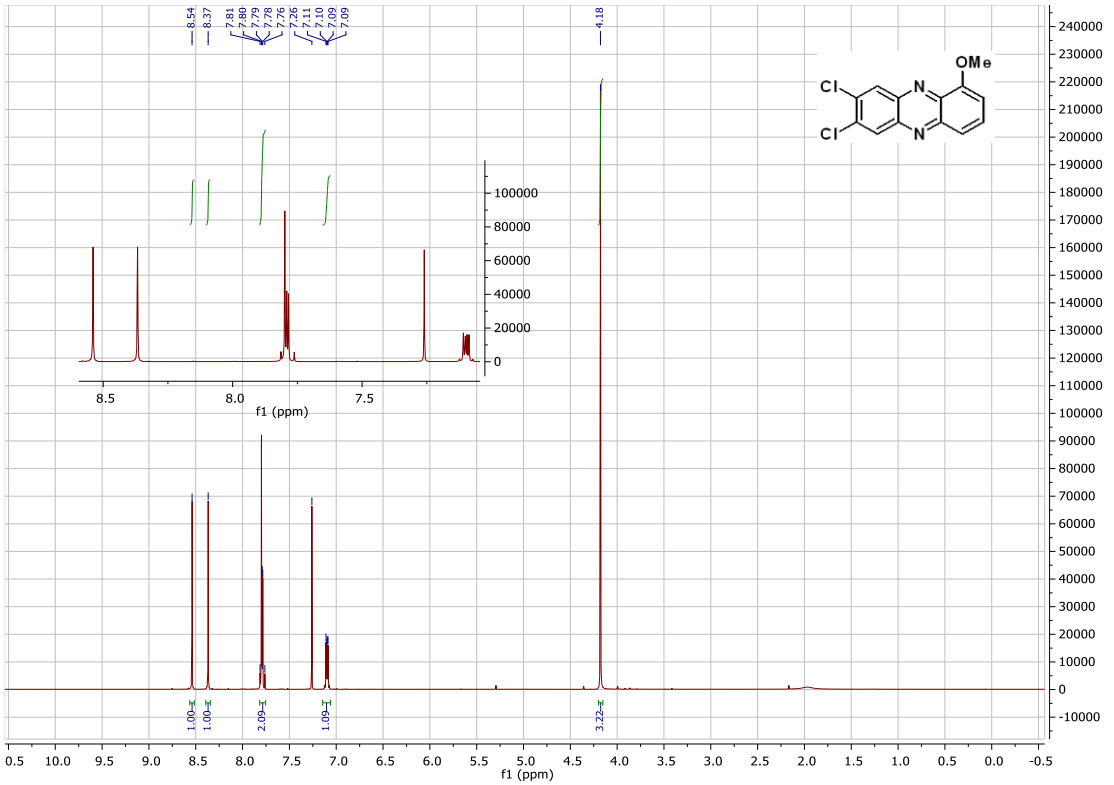


Figure S-71: ^{1}H-NMR spectra of compound **38**

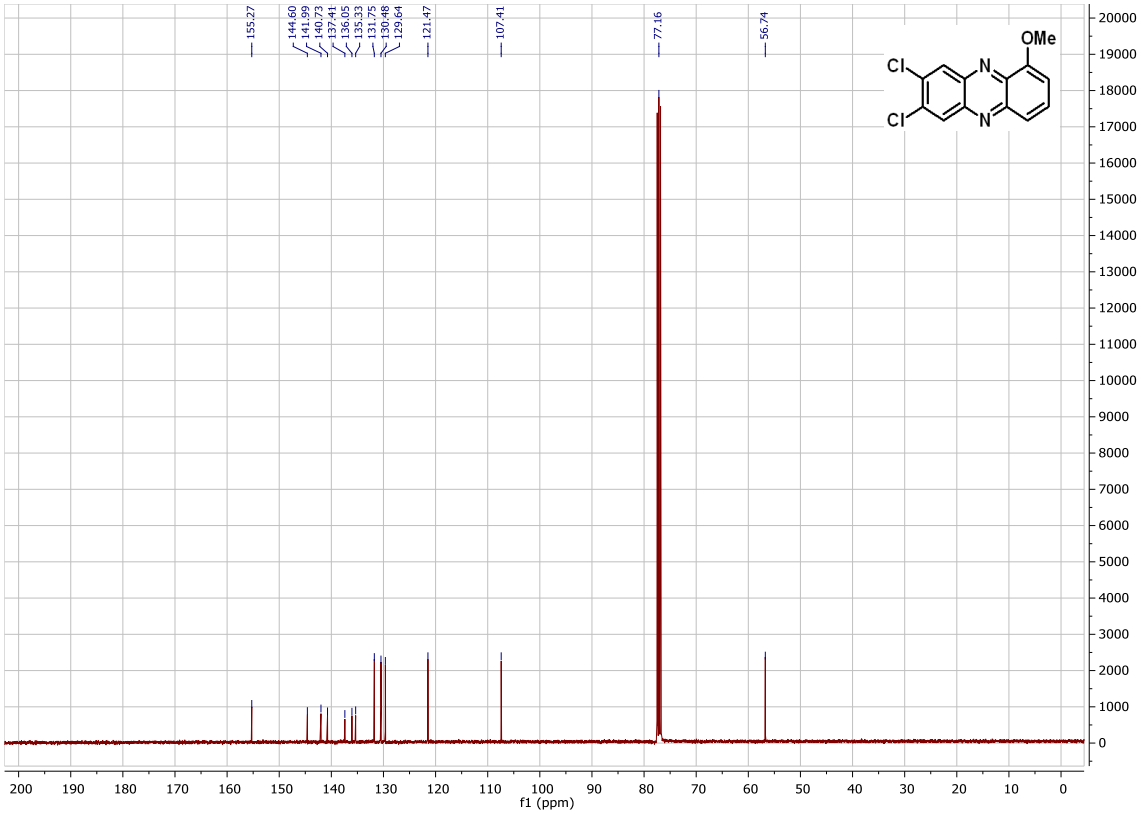


Figure S-72: ^{13}C-NMR spectra of compound **38**

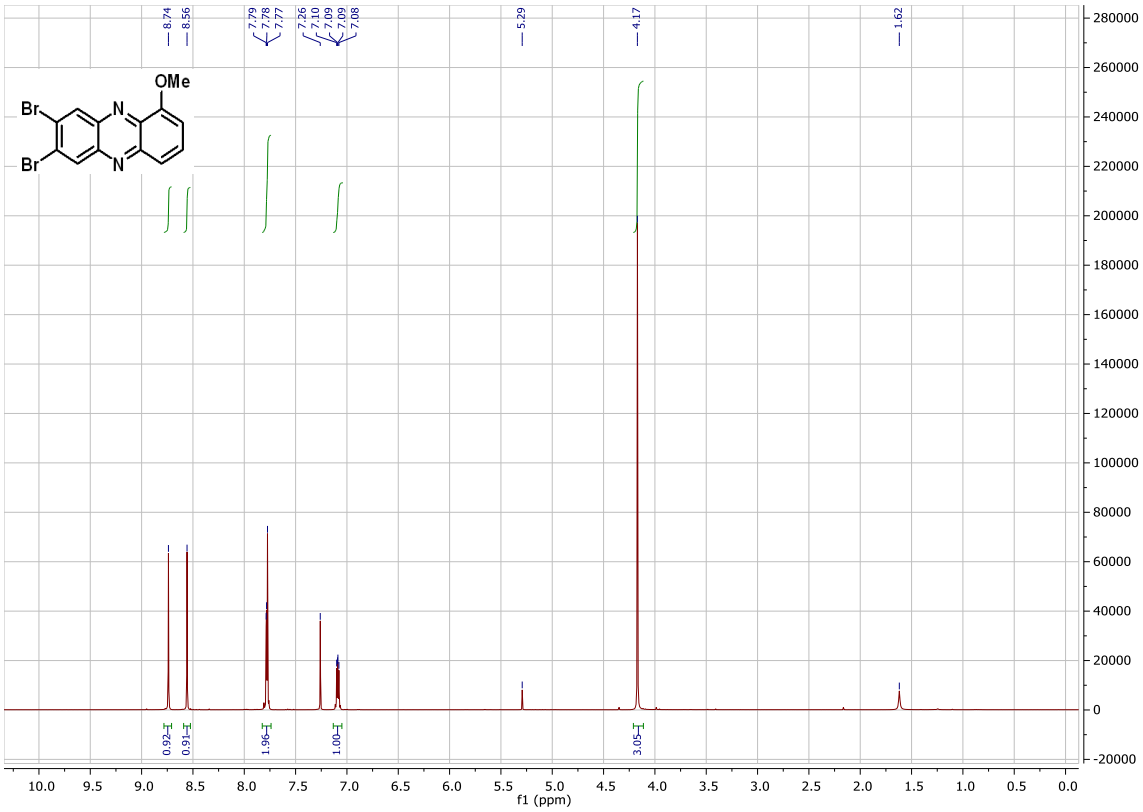


Figure S-73: ^{1}H-NMR spectra of compound **39**

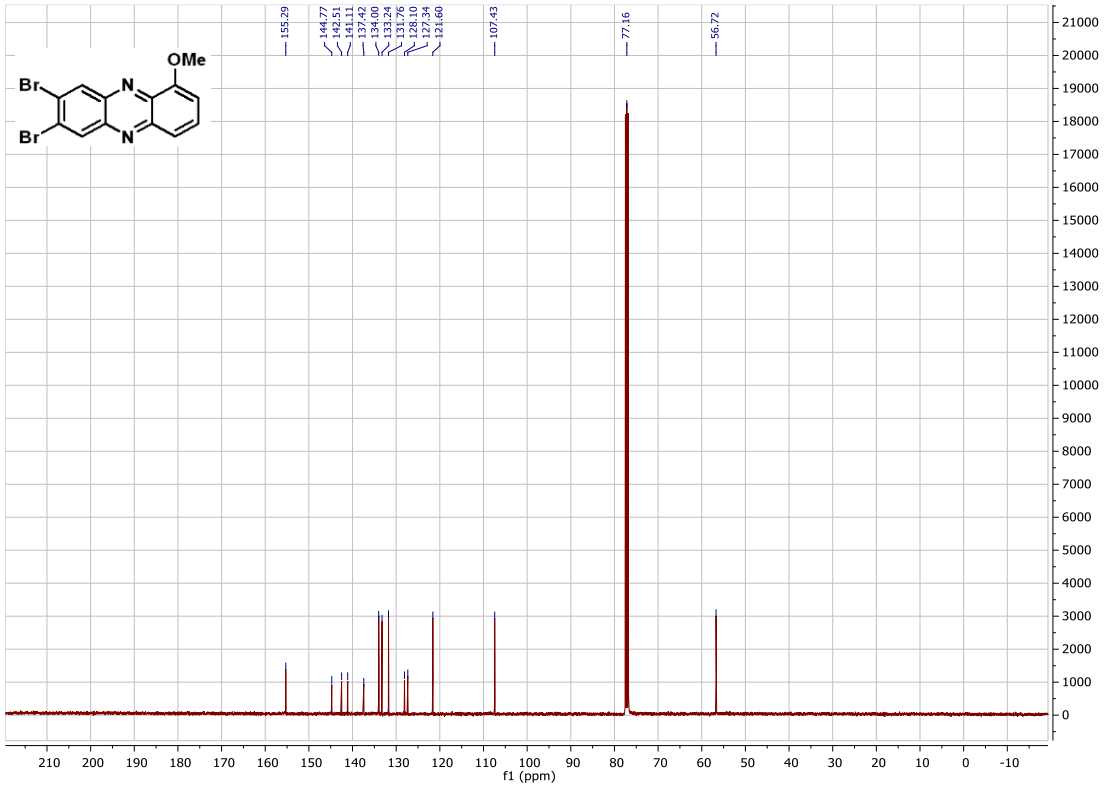


Figure S-74: ^{13}C-NMR spectra of compound **39**

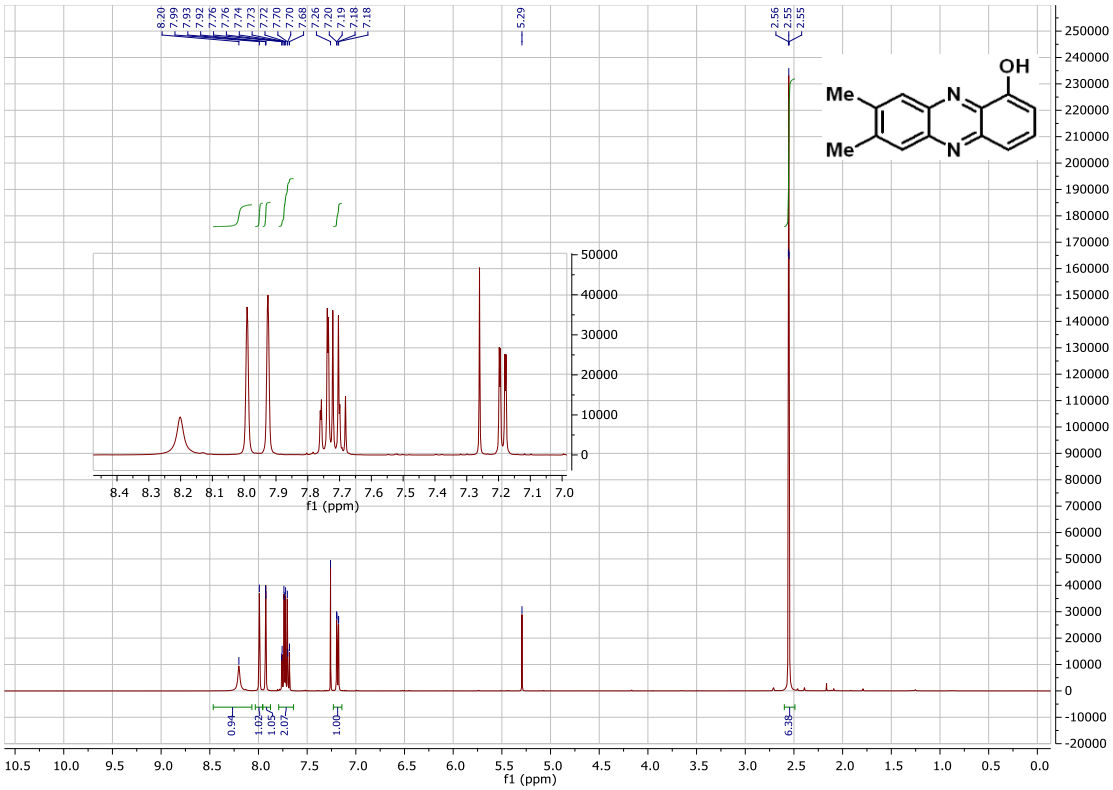


Figure S-75: ^{1}H-NMR spectra of compound **40**

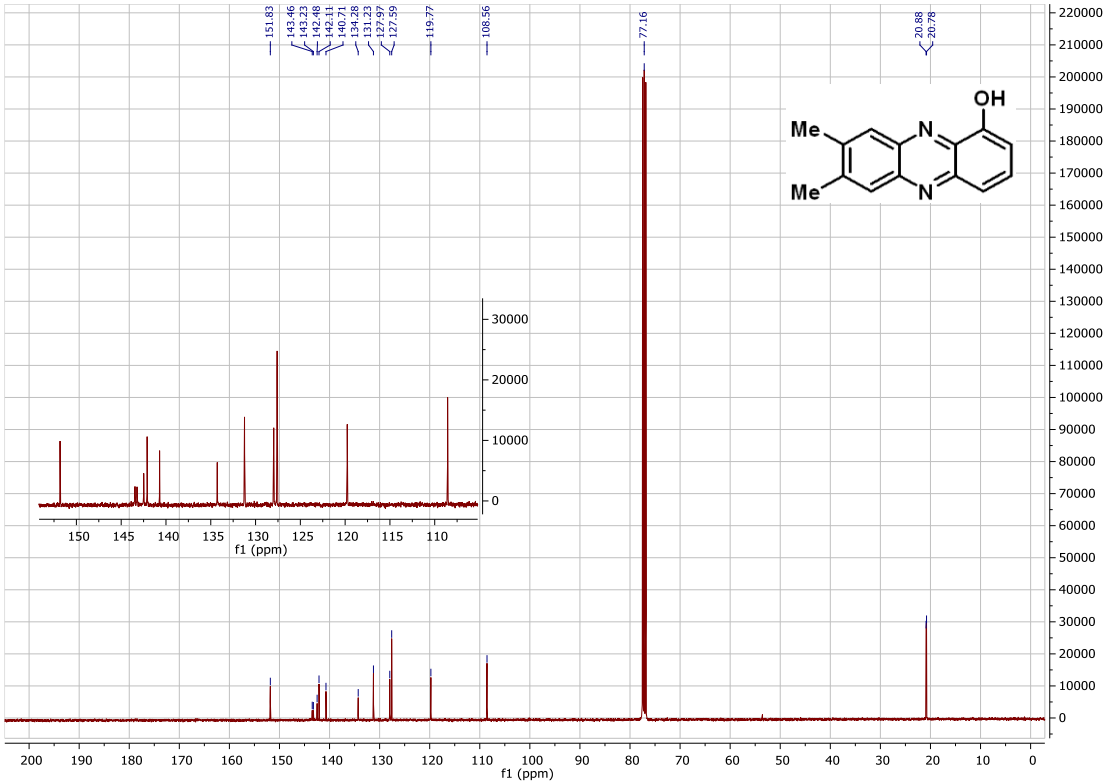


Figure S-76: ^{13}C-NMR spectra of compound **40**

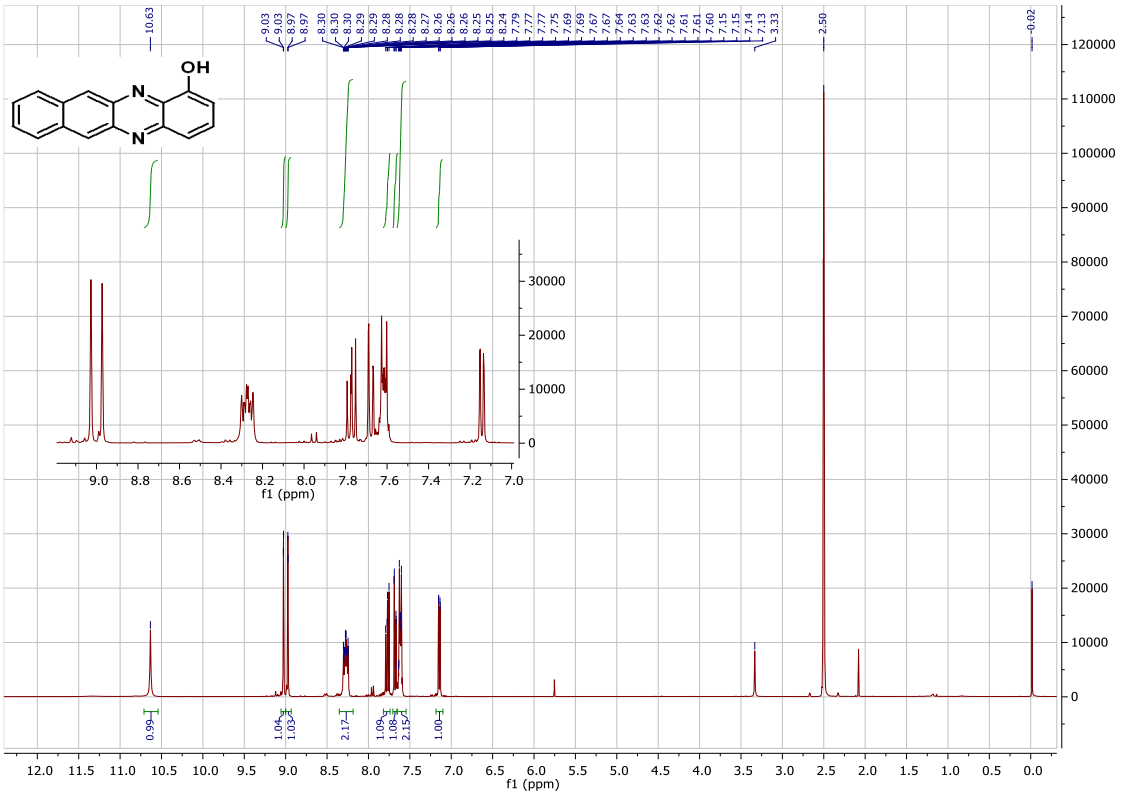


Figure S-77: ^{1}H-NMR spectra of compound **41**

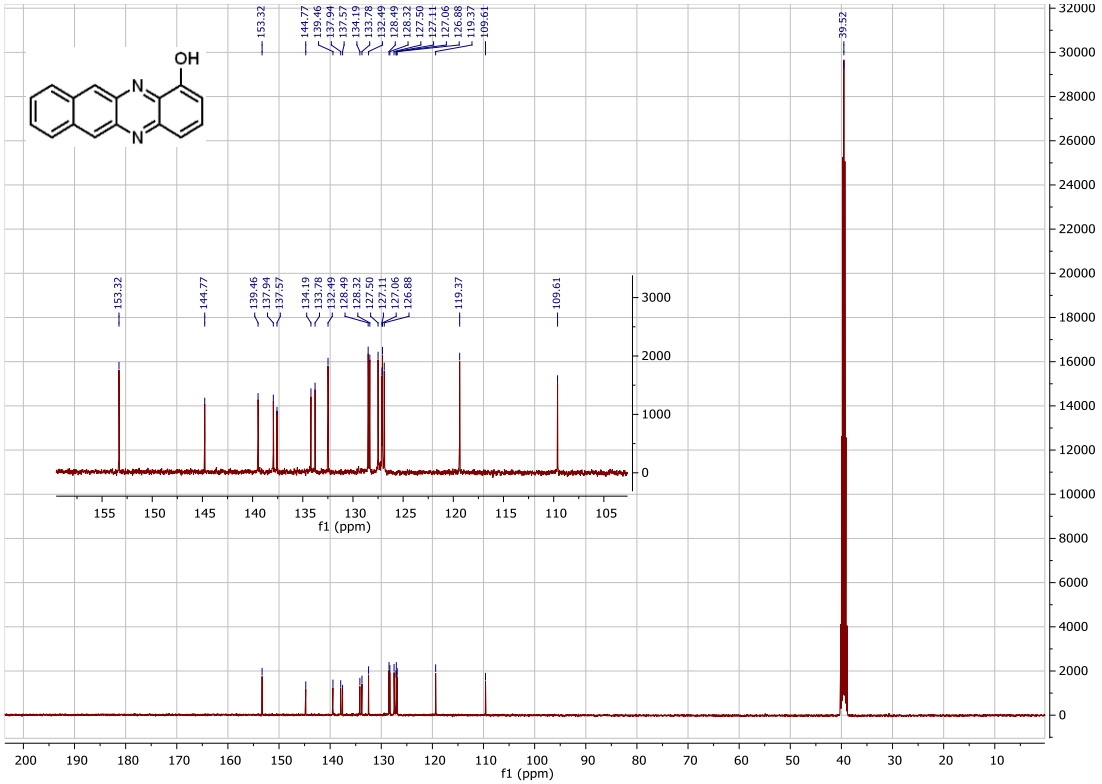


Figure S-78: ^{13}C-NMR spectra of compound **41**

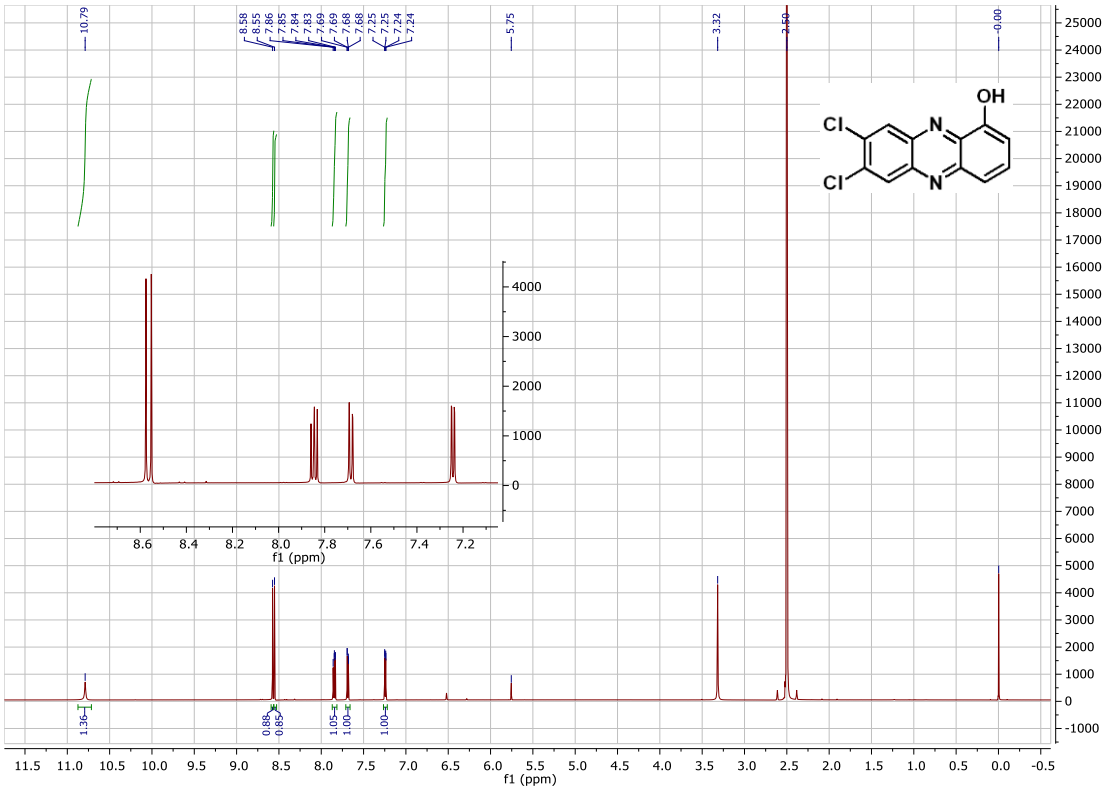


Figure S-79: ^{1}H-NMR spectra of compound **42**

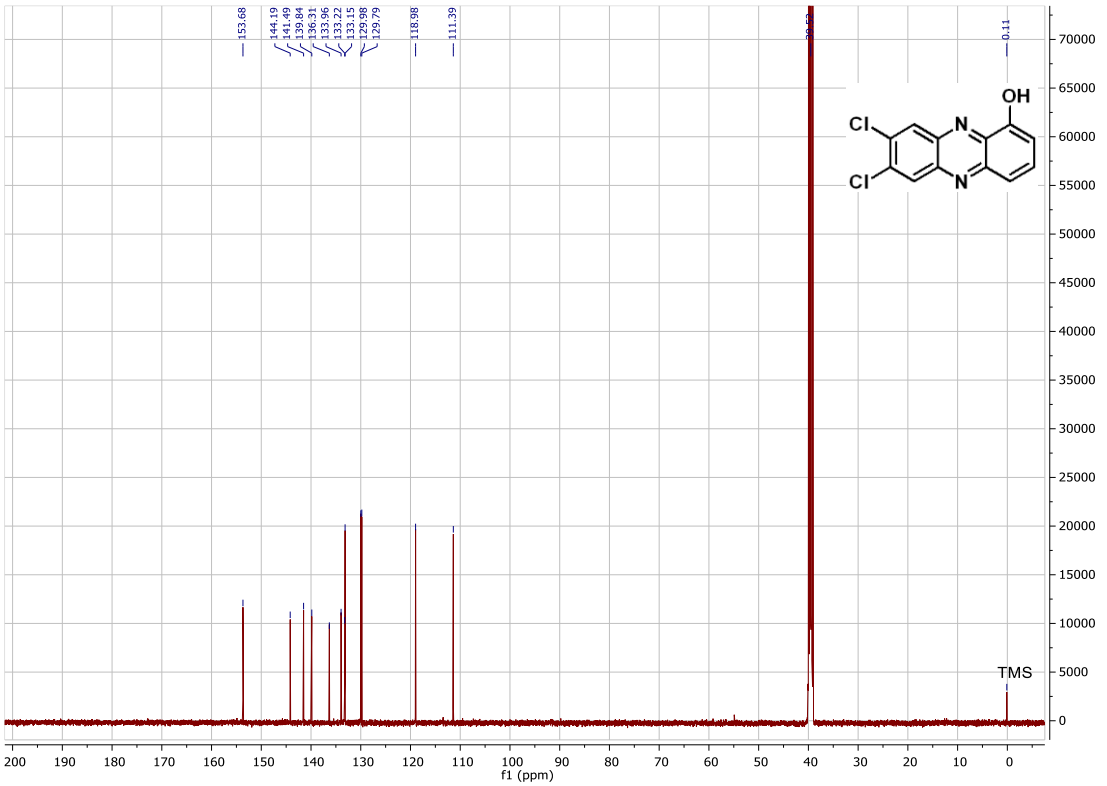


Figure S-80: ^{13}C-NMR spectra of compound **42**

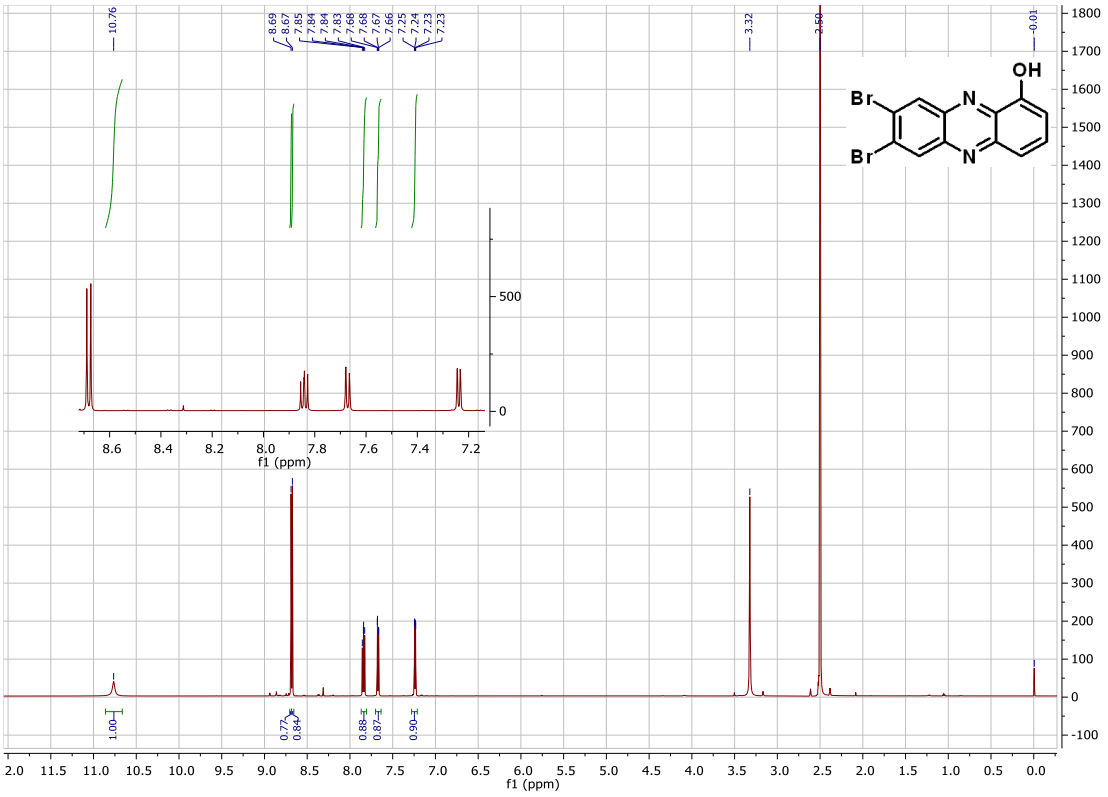


Figure S-81: ^{1}H-NMR spectra of compound **42**

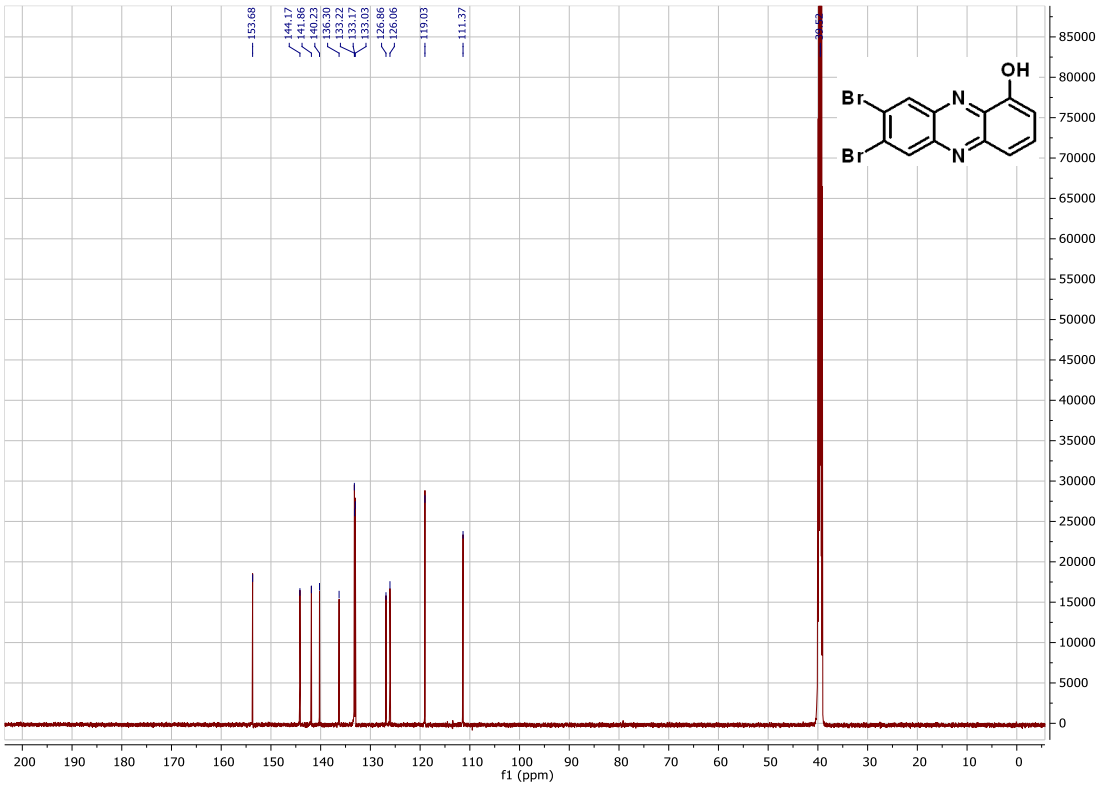


Figure S-82: ^{13}C-NMR spectra of compound **42**

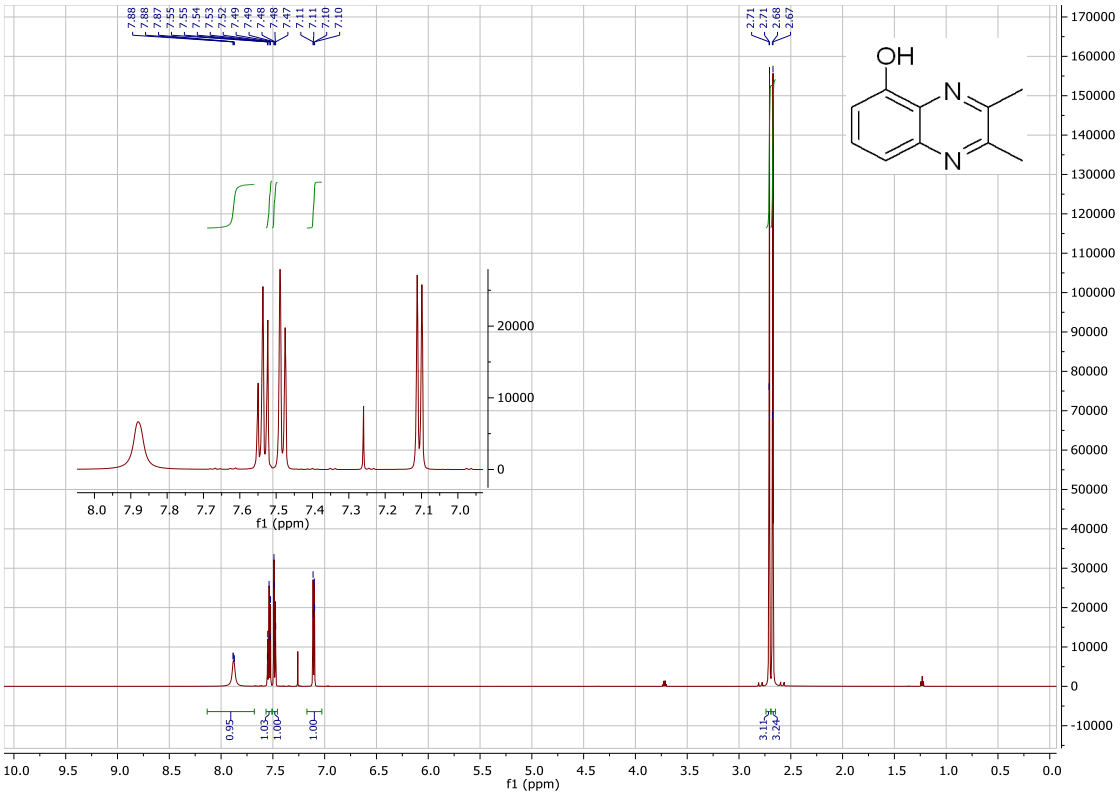


Figure S-83: ^{1}H-NMR spectra of compound **59**

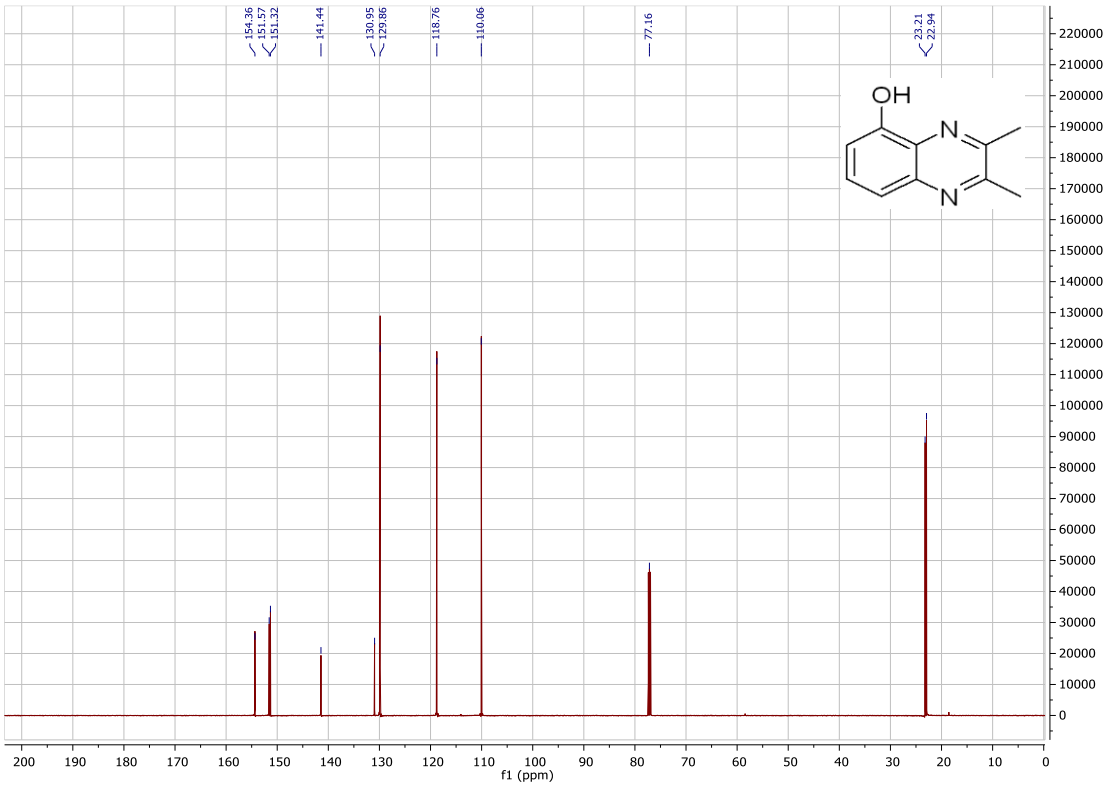


Figure S-84: ^{13}C-NMR spectra of compound **59**

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