Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Directed C8-H allylation of quinoline *N*-oxides with vinylcyclopropanes *via* sequential C-H/C-C activation

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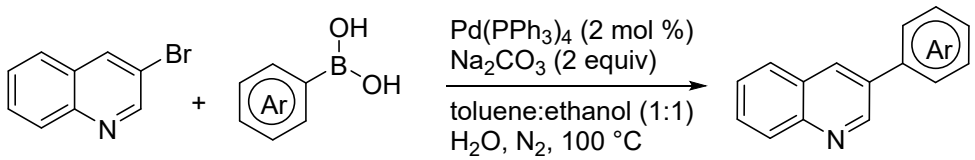
General Information. Quinolines, $[RhCp^*Cl_2]_2$ (97%), $[Ru(p\text{-cymene})Cl_2]_2$, $AgSbF_6$ (99%), $AgNTf_2$ (97%), Ag_2O (99%), Ag_2CO_3 (99%), Cu_2O ((≥99.9%), $Cu(OAc)_2•H_2O$ (98%), PivOH (99%), AgOAc (≥99.9%), $NaOPiv•H_2O$ (99%), *m*-CPBA (≥77%), AcOH (≥99%), NaOAc (≥99%), CsOAC (≥99.9%) and CsOPiv (98%) of Aldrich and TFE of TCI chemicals were used as received. Quinoline *N*-oxides[1] and vinylcyclopropanes[2] were prepared according to the reported procedure. $[CoCp^*(CO)I_2]$ was synthesized as per the reported literature.[3] All the heating reactions were performed using oil bath as heating source. SRL silica gel G/GF 254 plates were used for analytical TLC and SRL silica gel (230-400 mesh) was used for column chromatography. Bruker Avance III 600, 500 and 400 MHz spectrometers used for NMR spectra using tetramethylsilane (Me_4Si) as an internal standard. Chemical shifts (δ) and spin-spin coupling constant (*J*) are reported in parts per million (ppm) and hertz (Hz), respectively, and other data are reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet, dd = double doublet. Melting points were determined using a Büchi B-540 apparatus and are uncorrected. IR spectra were collected on a PerkinElmer Fourier transform infrared (FTIR) spectrometer. Quadrupole time-of-flight electrospray ionization (ESI) mass spectrometer used for recording HRMS.

General Procedure for the 3-Substituted Quinolines[4]



In an oven dried sealed tube, 3-bromoquinoline (1 mmol, 208 mg), aryl boronic acid (2 mmol), $Pd(PPh_3)_4$ (0.02 mmol, 23 mg), Na_2CO_3 (2 mmol, 212 mg), H_2O (10 µL) and toluene : ethanol (1:1, 4 mL) were stirred at 100 °C under nitrogen atmosphere. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and passed through a short pad of celite with CH_2Cl_2 (20 ml). Evaporation of the solvent gave a residue that was purified on silica gel column chromatography using hexane and EtOAc as an eluent to give the substituted quinolines.

Synthesis of *tert*-Butyl quinolin-5-ylcarbamate[5]

To a stirred solution of 5-aminoquinoline (1 mmol, 144 mg) in ethanol (2 mL), $(Boc)_2O$ (1.1 mmol, 240 mg) was added at room temperature. Reaction was monitored by TLC and after

completion of the reaction, the solution was concentrated under vacuum to afford the target compound in high yield. Protected aminoquinoline was used for the next step without further purification.

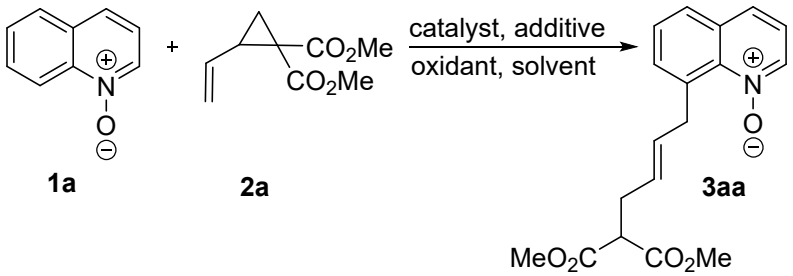
Synthesis of Quinolin-6-yl benzoate[6]

In a round-bottomed flask, 6-hydroxyquinoline (1 mmol, 145 mg) and 4-(dimethylamino) pyridine (0.05 mmol, 6 mg) were dissolved in Et_3N (3 mL) and CH_2Cl_2 (15 mL). Benzoyl chloride (1 mmol, 0.14 mL) was added dropwise at room temperature and the resulting mixture was left for stirring. Reaction was monitored by the TLC using EtOAc and hexane as the eluent. After completion, the reaction was quenched by adding water (5 mL) and extracted using CH_2Cl_2 (2 x 20 mL). Drying (Na_2SO_4) and evaporation of the solvent provided a residue that was purified by column chromatography using hexane and EtOAc as an eluent (80/20, v/v) to afford the target quinoline.

General Procedure for the Synthesis of Quinoline *N*-oxide

To a stirred solution of quinoline (1 mmol) in $CHCl_3$ (5 mL), *m*-CPBA (2.5 mmol, 431 mg) was added and the reaction mixture was allowed to reflux for 4 h. Then the reaction mixture was cooled to room temperature and quenched with aqueous $NaHCO_3$ (5 mL) and extracted using CH_2Cl_2 (3 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue which was purified by silica gel column chromatography using hexane and EtOAc as the eluent to afford the quinoline *N*-oxides **1**.

Optimization of Reaction Conditions[a]



1a **2a** **3aa**

entry	catalyst	additive	oxidant	solvent	yield (%)[b]	*E/Z*[c]
1	$[RhCp^*Cl_2]_2$/ $AgBF_4$	-	-	TFE	25	4:1
2	$[RhCp^*Cl_2]_2$/ $AgBF_4$	AcOH	-	TFE	n.d.	-

3	$[RhCp^*Cl_2]_2$/ $AgBF_4$	PivOH	-	TFE	22	6:1
4	$[RhCp^*Cl_2]_2$/ $AgBF_4$	AgOAc	-	TFE	45	11:1
5	$[RhCp^*Cl_2]_2$/ $AgBF_4$	NaOAc	-	TFE	36	8:1
6	$[RhCp^*Cl_2]_2$/ $AgBF_4$	CsOAC	-	TFE	38	10:1
7	$[RhCp^*Cl_2]_2$/ $AgBF_4$	$NaOPiv•H_2O$	-	TFE	49	16:1
8	$[RhCp^*Cl_2]_2$/ $AgBF_4$	CsOPiv	-	TFE	12	5:1
9	**$[RhCp^*Cl_2]_2$/ $AgBF_4$**	**$NaOPiv•H_2O$**	**Ag_2O**	**TFE**	**78**	**16:1**
10	$[RhCp^*Cl_2]_2$/ $AgSbF_6$	$NaOPiv•H_2O$	Ag_2O	TFE	63	16:1
11	$[RhCp^*Cl_2]_2$/ $AgNTf_2$	$NaOPiv•H_2O$	Ag_2O	TFE	65	8:1
12	$[RhCp^*Cl_2]_2$/ $AgBF_4$	$NaOPiv•H_2O$	Ag_2O	EtOH	trace	-
13	$[RhCp^*Cl_2]_2$/ $AgBF_4$	$NaOPiv•H_2O$	Ag_2O	HFIP	trace	-
14	$[RhCp^*Cl_2]_2$/ $AgBF_4$	$NaOPiv•H_2O$	Ag_2O	THF	trace	-
15	$[RhCp^*Cl_2]_2$/ $AgBF_4$	$NaOPiv•H_2O$	Ag_2O	Toluene	n.d.	-
16	$[RhCp^*Cl_2]_2$/ $AgBF_4$	$NaOPiv•H_2O$	Ag_2O	DCE	trace	-
17[d]	$[RhCp^*Cl_2]_2$/ $AgBF_4$	$NaOPiv•H_2O$	Ag_2O	TFE	43	16:1
18[e]	$[RhCp^*Cl_2]_2$/ $AgBF_4$	$NaOPiv•H_2O$	Ag_2O	TFE	60	16:1
19[f]	$[RhCp^*Cl_2]_2$/	$NaOPiv•H_2O$	Ag_2O	TFE	59	12:1

	$AgBF_4$					
20	$[CoCp^*(CO)I_2]$/ $AgBF_4$	-	-	TFE	n.d.	-
21	$[Ru(p\text{-cymene})Cl_2]_2$/ $AgBF_4$	-	-	TFE	n.d.	-

[a]Reaction condition: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst (5 mol %) and silver source (20 mol %), additive (20 mol %), oxidant (0.2 mmol), solvent (1 mL) rt, N_2, 18 h. [b]Isolated yield. [c]Determined by ^1H NMR. [d]24 h reaction time. [e]16 h reaction time. [f]50 °C temp. n.d. = not detected.

General Procedure for Rh-Catalyzed C8-Allylation of Quinoline *N*-oxide

Quinoline *N*-oxides **1** (0.2 mmol), vinylcyclopropanes **2** (0.3 mmol), $[RhCp^*Cl_2]_2$ (0.01 mmol, 6 mg), $AgBF_4$ (0.04 mmol, 7.8 mg), $NaOPiv•H_2O$ (0.04 mmol, 6 mg) and Ag_2O (0.2 mmol, 46 mg) were stirred in TFE (1 mL) for 18 h at room temperature under N_2 atmosphere. After completion, the reaction mixture was extracted with EtOAc (3 x 10 mL). The combined organic layer was washed with saturated $NaHCO_3$ (2 x 5 mL) and water (2 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using hexane and EtOAc as an eluent to afford C8-allyl quinoline *N*-oxides **3**.

Scale-up Synthesis of 3aa

Quinoline *N*-oxide **1a** (3.44 mmol, 500 mg), vinylcyclopropane **2a** (5.16 mmol, 950 mg), $[RhCp^*Cl_2]_2$ (5 mol %, 104 mg), $AgBF_4$ (0.688 mmol, 134.16 mg), $NaOPiv•H_2O$ (0.688 mmol, 98 mg) and Ag_2O (0.2 mmol, 795 mg) were stirred in TFE (12 mL) for 18 h at room temperature under N_2 atmosphere. After completion, the reaction mixture as passed through a short pad of celite using EtOAc (50 mL) and the evaporation of the solvent gave a residue which was purified by silica gel column chromatography using hexane and EtOAc as an eluent (40/60, v/v) to afford **3aa** in 70% (793 mg) yield.

Post-Synthetic Modifications

Synthesis of 4aa and 4ha[7]

To an oven dried sealed tube, respective quinoline *N*-oxide (0.1 mmol) **3** and $PhB(OH)_2$ (0.15 mmol, 18 mg) were stirred in 1,2-dichloroethane (1 mL) for 12 h at 120 °C. After the completion, the reaction mixture was cooled to room temperature and diluted with CH_2Cl_2 (30

mL) and washed with water (2 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified by silica gel column chromatography to afford the target compounds **4aa** and **4ha**.

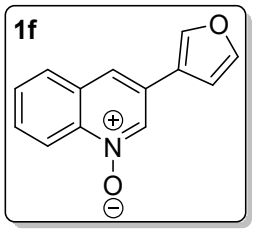
Synthesis of 5[8]

To an oven dried sealed tube, **3aa** (0.1 mmol, 32 mg), Me_3SiCN (0.12 mmol, 16 µL) and DBU (0.23 mmol, 34 µL) were stirred in THF (1 mL) for 12 h under reflux. The reaction mixture was cooled to room temperature and extracted with EtOAc (2 x 10 mL) and washed with water (2 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent residue gave a residue which was purified by silica column chromatography using hexane and EtOAc as an eluent (90/10, v/v) to afford **5** in 86% yield (29 mg).

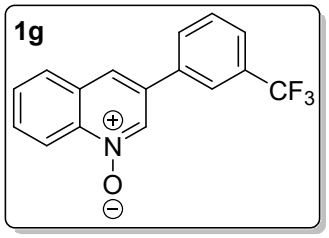
Synthesis of 6[9]

In an oven dried round bottom flask, **3aa** (0.1 mmol, 32 mg) and LiCl (0.5 mmol, 21 mg) were stirred in DMSO (1 mL) and H_2O (0.5 mmol, 10 µL) for 12 h at 130 °C under N_2 atmosphere. After the completion, reaction mixture was cooled to room temperature and extracted using EtOAc (2 x 10 mL) and washed with water (2 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified by silica column chromatography using hexane and EtOAc as an eluent (90/10, v/v) to afford **6** in 65% yield (16.5 mg).

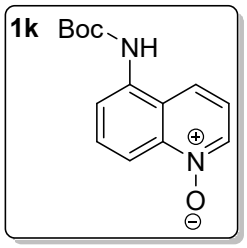
Characterization data of *N*-oxides



3-(Furan-3-yl)quinoline 1-oxide 1f. Analytical TLC on silica gel, 3:2 ethyl acetate/hexane R_f = 0.3; brown solid; mp 85-86 °C; yield 85% (179 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.70 (d, *J* = 8.5 Hz, 1H), 7.87-7.85 (m, 2H), 7.80 (s, 1H), 7.74-7.71 (m, 1H), 7.66-7.63 (m, 1H), 7.56-7.55 (m, 1H), 6.77 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.8, 140.3, 139.8, 134.3, 130.5, 130.1, 129.3, 128.1, 126.8, 122.2, 122.1, 119.8, 108.4; FT-IR (neat) 2925, 1652, 1608, 1583, 1395, 1347, 1260, 1222, 1162, 874, 825, 765, 594 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{13}H_{10}NO_2$: 212.0706, found 212.0706.

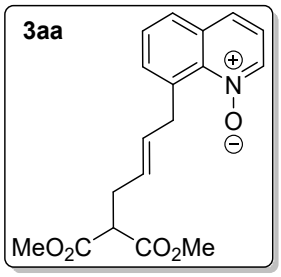


3-(3-(Trifluoromethyl)phenyl)quinoline 1-oxide 1g. Analytical TLC on silica gel, 3:2 ethyl acetate/hexane R_f = 0.4; brown solid; mp 183-184 °C; yield 80% (230 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.77 (d, *J* = 9 Hz, 1H), 7.96-7.91 (m, 3H), 7.84-7.78 (m, 2H), 7.74-7.65 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.8, 136.9, 134.7, 133.6, 132.2 (J_{C-F} = 32.3 Hz), 130.8, 130.4, 130.3, 130.1, 129.5, 128.6, 125.8 (J_{C-F} = 3.75 Hz), 125.0 (J_{C-F} = 271 Hz), 124.1 (J_{C-F} = 3.75 Hz), 123.7, 119.9; ^{19}F NMR (377 MHz, CDCl3) δ -62.74; FT-IR (neat) 3064, 1583, 1493, 1369, 1316, 1171, 1110, 934, 766, 684 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{16}H_{11}F_3NO$: 290.0787, found 290.0785.



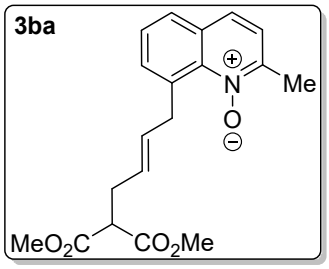
5-((*tert*-Butoxycarbonyl)amino)quinoline 1-oxide 1k. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.2; colorless solid; mp 185-186 °C; yield 77% (200 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.55-8.52 (m, 2H), 8.01-8.00 (m, 1H), 7.88-7.85 (m, 1H), 7.74-7.71 (m, 1H), 7.35-7.28 (m, 1H), 7.15 (s, 1H), 1.55 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.3, 142.3, 135.6, 134.2, 130.5, 124.7, 121.8, 120.4, 119.9, 115.9, 81.6, 28.4; FT-IR (neat) 3200, 2978, 1721, 1536, 1404, 1364, 1304, 1237, 1152, 1054, 879, 784 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{14}H_{17}N_2O_3$: 261.1234, found 261.1229.

Characterization Data of the Products

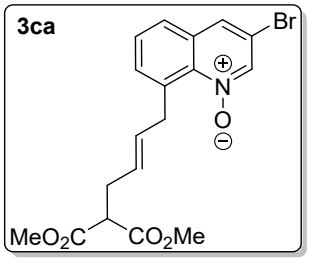


(*E*)-8-(6-Methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)quinoline 1-oxide 3aa. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.30; brown solid; mp 75-76 °C; yield 78% (51 mg); *E/Z* = 16:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (d, *J* = 6 Hz, 1H), 7.68 (t, *J* = 9 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.43 (d, *J* =

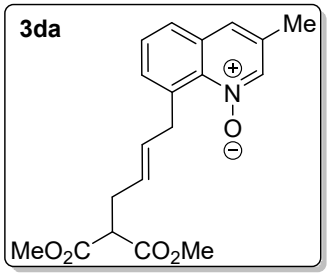
6.6 Hz, 1H), 7.22-7.20 (m, 1H), 5.99-5.95 (m, 1H), 5.46-5.41 (m, 1H), 4.36 (d, *J* = 6.6 Hz, 2H), 3.66 (s, 6H), 3.41 (t, *J* = 7.8 Hz, 1H), 2.60 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 140.6, 137.7, 135.7, 134.2, 133.0, 132.6, 128.3, 127.5, 126.8, 126.2, 120.7, 52.5, 52.0, 39.7, 32.0; FT-IR (neat) 2953, 1732, 1572, 1435, 1274, 1219, 1156, 815, 751 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{18}H_{20}NO_5$: 330.1336, found 330.1337.



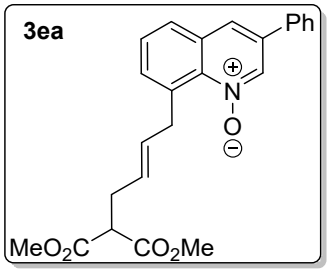
(*E*)-8-(6-Methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)-2-methylquinoline 1-oxide 3ba. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.30; brown solid; mp 99-100 °C; yield 77% (53 mg); *E/Z* = 13:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.2 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.41-7.39 (m, 2H), 7.25 (d, *J* = 8.4 Hz, 1H), 6.01-5.96 (m, 1H), 5.44-5.39 (m, 1H), 4.37 (d, *J* = 6.6 Hz, 2H), 3.63 (s, 6H), 3.39 (t, *J* = 7.8 Hz, 1H), 2.61-2.58 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 147.2, 140.7, 135.2, 134.5, 132.9, 131.3, 127.4, 127.3, 125.8, 125.5, 122.7, 52.4, 52.0, 39.9, 32.0, 19.3; FT-IR (neat) 2953, 1731, 1567, 1435, 1239, 1151, 1023, 821, 765 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{22}NO_5$: 344.1492, found 344.1495.



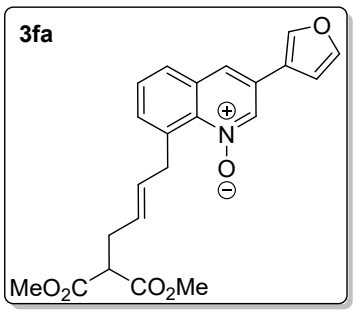
(*E*)-3-Bromo-8-(6-methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)quinoline 1-oxide 3ca. Analytical TLC on silica gel, 2:3 ethyl acetate/hexane R_f = 0.30; brown solid; mp 134-135 °C; yield 75% (61 mg); *E/Z* = 19:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.79 (s, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 7.8, 1H), 7.41 (d, *J* = 6.6 Hz, 1H), 5.95-5.90 (m, 1H), 5.44-5.39 (m, 1H), 4.29 (d, *J* = 6.6 Hz, 2H), 3.67 (s, 6H), 3.40 (t, *J* = 7.8 Hz, 1H), 2.60 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 139.7, 138.8, 135.9, 133.7, 132.9, 132.4, 129.2, 128.0, 126.7, 126.5, 114.0, 52.5, 52.0, 39.4, 32.0; FT-IR (neat) 2953, 1732, 1557, 1435, 1355, 1275, 1213, 1156, 877, 764 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{18}H_{19}BrNO_5$: 408.0441, found 408.0449.



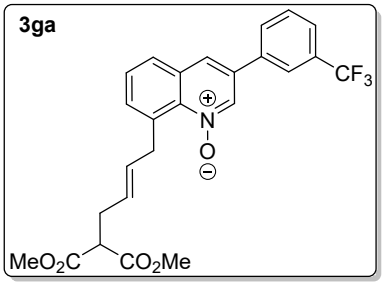
(*E*)-8-(6-Methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)-3-methylquinoline 1-oxide 3da. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f= 0.40; brown solid; mp 70-71 °C; yield 76% (52 mg); *E/Z* > 23:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.57 (d, *J* = 8 Hz, 1H), 7.41-7.38 (m, 2H), 7.32 (d, *J* = 6.5 Hz, 1H), 5.98-5.92 (m, 1H), 5.44-5.38 (m, 1H), 4.33 (d, *J* = 6 Hz, 2H), 3.64 (s, 6H), 3.39 (t, *J* = 7.5 Hz, 1H), 2.58 (t, *J* = 7.0 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 139.0, 138.7, 135.4, 134.2, 132.3, 131.8, 130.8, 128.2, 126.8, 126.2, 126.0, 52.4, 52.0, 39.5, 32.0, 18.3; FT-IR (neat) 2953, 1727, 1579, 1434, 1214, 1149, 1025, 848, 763 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{22}NO_5$: 344.1492, found 344.1491.



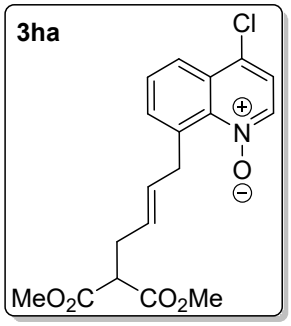
(*E*)-8-(6-Methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)-3-phenylquinoline 1-oxide 3ea. Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f= 0.30; brown solid; mp 100-101 °C; yield 73% (59 mg); *E/Z* = 19:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.83 (s, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.65-7.64 (m, 2H), 7.53-7.48 (m, 3H), 7.45 (t, *J* = 7.8, 1H), 7.42 (d, *J* = 7.2 Hz, 1H), 6.03-5.98 (m, 1H), 5.49-5.44 (m, 1H), 4.39 (d, *J* = 6.6 Hz, 2H), 3.67 (s, 6H), 3.43 (t, *J* = 7.8 Hz, 1H), 2.62 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 139.4, 136.8, 135.7, 134.5, 134.2, 132.7, 132.5, 129.4, 129.0, 128.6, 127.7, 127.0, 126.2, 124.0, 52.5, 52.0, 39.6, 32.0; FT-IR (neat) 2952, 1731, 1580, 1434, 1217, 1152, 1022, 860, 758, 694 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{24}NO_5$: 406.1649, found 406.1653.



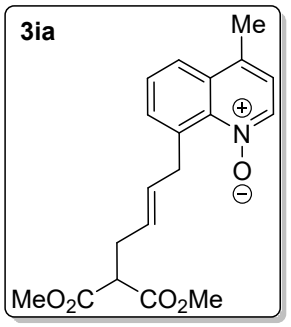
(*E*)-3-(Furan-3-yl)-8-(6-methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)quinoline 1-oxide 3fa. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.40; light brown solid; mp 144-145 °C; yield 64% (50.5 mg); *E/Z* > 23:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.85 (s, 1H), 7.70-7.67 (m, 2H), 7.556 (s, 1H), 7.47 (t, *J* = 8 Hz, 1H), 7.38 (d, *J* = 7 Hz, 1H), 6.75 (s, 1H), 6.00-5.95 (m, 1H), 5.48-5.42 (m, 1H), 4.35 (d, *J* = 6.5 Hz, 2H), 3.67 (s, 6H), 3.42 (t, *J* = 8 Hz, 1H), 2.61 (t, *J* = 7 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 144.7, 139.8, 139.2, 136.0, 135.7, 134.1, 132.56, 132.50, 128.7, 127.4, 126.37, 126.32, 122.5, 121.8, 108.4, 52.5, 52.0, 39.5, 32.0; FT-IR (neat) 2953, 1731, 1611, 1583, 1435, 1217, 1156, 1022, 874, 761, 597 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{22}NO_6$: 396.1442, found 396.1442.



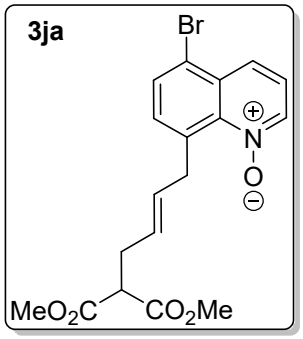
(*E*)-8-(6-Methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)-3-(3-(trifluoromethyl)pheny l)quinoline 1-oxide 3ga. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.40; grey solid; mp 134-135 °C; yield 65% (61.5 mg); *E/Z* > 23:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.90 (s, 1H), 7.83-7.81 (m, 2H), 7.77 (d, *J* = 8 Hz, 1H), 7.72 (d, *J* = 8 Hz, 1H), 7.65 (t, *J* = 8 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 7.5 Hz, 1H), 6.02-5.96 (m, 1H), 5.49-5.43 (m, 1H), 4.38 (d, *J* = 6.5 Hz, 2H), 3.68 (s, 6H), 3.42 (t, *J* = 7.5 Hz, 1H), 2.62 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 139.7, 136.6, 136.5, 135.8, 134.0, 133.2, 133.1, 132.4, 132.1 (J_{C-F} = 32.5 Hz), 130.3, 130.0, 128.9, 127.9, 126.4, 125.7 (J_{C-F} = 3.6 Hz), 124.8 (J_{C-F} = 270.9 Hz), 124.1, 123.9 (J_{C-F} = 3.9 Hz), 52.5, 52.0, 39.5, 32.0; ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.74; FT-IR (neat) 2954, 1732, 1581, 1436, 1343, 1316, 1159, 1123, 804, 763, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{25}H_{23}F_3NO_5$: 474.1523, found 474.1530.



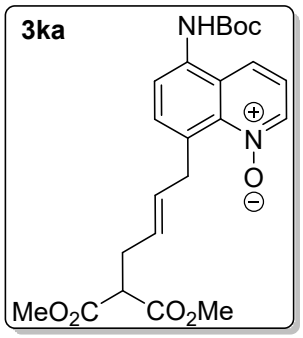
(*E*)-4-Chloro-8-(6-methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)quinoline 1-oxide 3ha. Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f = 0.30; brown solid; mp 118-119 °C; yield 72% (52.5 mg); *E/Z* = 19:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (d, *J* = 6.6 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 6 Hz, 1H), 7.31 (d, *J* = 6.6 Hz, 1H), 5.97-5.92 (m, 1H), 5.45-5.40 (m, 1H), 4.34 (d, *J* = 6.6 Hz, 2H), 3.67 (s, 6H), 3.40 (t, *J* = 7.8 Hz, 1H), 2.60 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 141.3, 136.9, 136.4, 133.9, 133.8, 129.9, 129.8, 129.2, 126.5, 124.3, 121.1, 52.5, 52.0, 39.6, 32.0; FT-IR (neat) 2954, 1730, 1561, 1435, 1372, 1296, 1208, 1150, 757 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{18}H_{19}ClNO_5$: 364.0946, found 364.0951.



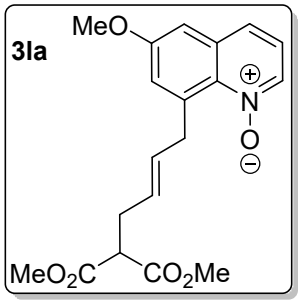
(*E*)-8-(6-Methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)-4-methylquinoline 1-oxide 3ia. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.30; brown solid; mp 58-59 °C; yield 65% (44.5 mg); *E/Z* = 23:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (d, *J* = 6 Hz, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.05 (d, *J* = 6 Hz, 1H), 6.00-5.95 (m, 1H), 5.44-5.39 (m, 1H), 4.37 (d, *J* = 6.6 Hz, 2H), 3.65 (s, 6H), 3.40 (t, *J* = 7.8 Hz, 1H), 2.59-2.58 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 140.0, 136.9, 136.2, 134.5, 134.3, 132.8, 131.7, 128.0, 126.0, 123.7, 121.6, 52.4, 52.0, 39.9, 32.0, 19.3; FT-IR (neat) 2953, 1730, 1567, 1394, 1218, 1151, 974, 830, 759 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{22}NO_5$: 344.1492, found 344.1491.



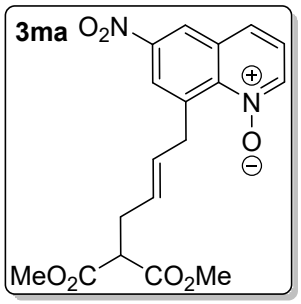
(*E*)-5-Bromo-8-(6-methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)quinoline 1-oxide 3ja. Analytical TLC on silica gel, 3:2 ethyl acetate/hexane R_f = 0.30; brown sticky liquid; yield 74% (60 mg); *E/Z* = 23:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (d, *J* = 6 Hz, 1H), 8.08 (d, *J* = 9 Hz, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.31-7.28 (m, 1H), 7.25 (d, *J* = 7.8 Hz, 1H), 5.94-5.89 (m, 1H), 5.44-5.39 (m, 1H), 4.27 (d, *J* = 6.6 Hz, 2H), 3.66 (s, 6H), 3.39 (t, *J* = 7.8 Hz, 1H), 2.59 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.4, 141.6, 137.9, 135.8, 133.5, 132.6, 132.3, 131.4, 126.6, 125.6, 121.6, 120.8, 52.5, 51.9, 39.7, 31.9; FT-IR (neat) 2953, 1730, 1568, 1510, 1435, 1393, 1262, 850, 750 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{18}H_{19}BrNO_5$: 408.0441, found 408.0446.



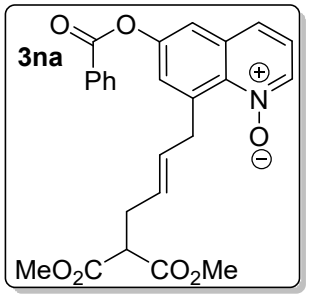
(*E*)-5-((tert-Butoxycarbonyl)amino)-8-(6-methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)quinoline 1-oxide 3ka. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.30; dark brown sticky liquid; yield 68% (60.5 mg); *E/Z* > 23:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (d, *J* = 6 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.68 (s, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.14-7.11 (m, 1H), 5.91-5.87 (m, 1H), 5.40-5.35 (m, 1H), 4.23 (d, *J* = 6 Hz, 2H), 3.64 (s, 6H), 3.37 (t, *J* = 7.8 Hz, 1H), 2.56 (t, *J* = 7.2 Hz, 2H), 1.48 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.4, 153.7, 140.8, 137.5, 134.0, 132.7, 132.5, 132.0, 127.3, 126.1, 122.9, 120.5, 120.2, 81.2, 52.4, 51.9, 39.6, 31.9, 28.3; FT-IR (neat) 3198, 2977, 1727, 1538, 1436, 1239, 1156, 1054, 881, 750 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{29}N_2O_7$: 445.1969, found 445.1977.



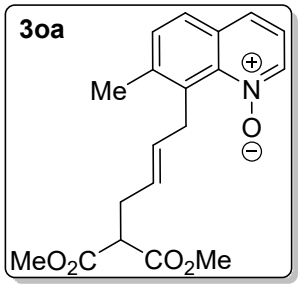
(*E*)-6-Methoxy-8-(6-methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)quinoline 1-oxide 3la. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f= 0.30; brown liquid; yield 60% (43 mg); *E/Z* = 16:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (d, *J* = 4.8 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.14-7.11 (m, 1H), 7.03-7.02 (m, 1H), 6.91-6.90 (m, 1H), 5.95-5.90 (m, 1H), 5.46-5.42 (m, 1H), 4.31 (d, *J* = 6 Hz, 2H), 3.87 (s, 3H), 3.66 (s, 6H), 3.41 (t, *J* = 7.8 Hz, 1H), 2.60 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 158.3, 137.7, 136.5, 135.8, 134.2, 133.6, 126.6, 125.6, 124.5, 121.2, 104.8, 55.5, 52.5, 51.9, 39.5, 32.0; FT-IR (neat) 2955,1726, 1610, 1430, 1277, 1200, 1032, 831, 749 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{22}NO_6$: 360.1442, found 360.1441.



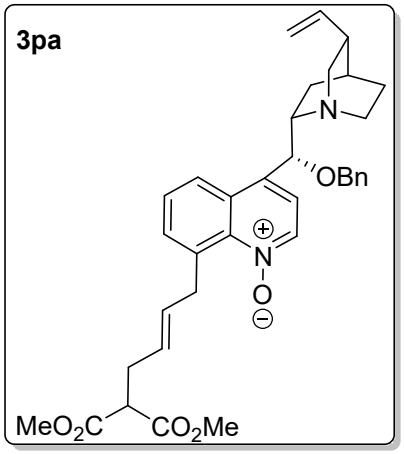
(*E*)-8-(6-Methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)-6-nitroquinoline 1-oxide 3ma. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f= 0.30; dark brown solid; mp 120-121 °C; yield 43% (32 mg); *E/Z* = 16:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 (d, *J* = 2.4 Hz, 1H), 8.57 (d, *J* = 6 Hz, 1H), 8.16 (d, *J* = 2.4 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.41-7.38 (m, 1H), 5.97-5.92 (m, 1H), 5.54-5.50 (m, 1H), 4.43 (d, *J* = 6.6 Hz, 2H), 3.70 (s, 6H), 3.43 (t, *J* = 7.8 Hz, 1H), 2.64 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.4, 146.3, 142.7, 140.4, 139.5, 132.3, 132.2, 128.1, 127.6, 125.0, 123.3, 122.9, 52.6, 51.8, 39.8, 31.9; FT-IR (neat) 3080, 2925, 2853, 1734, 1542, 1436, 1348, 1214, 792 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{18}H_{19}N_2O_7$: 375.1187, found 375.1188.



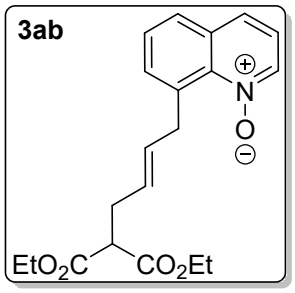
(*E*)-8-(6-Methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)-6-(2-phenylacetoxy)quinoline 1-oxide 3na. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f= 0.30; colorless liquid; yield 74% (68.5 mg); *E/Z* > 23:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 6 Hz, 1H), 8.22 (d, *J* = 8 Hz, 2H), 7.67-7.61 (m, 3H), 7.53 (t, *J* = 8 Hz, 2H), 7.29-7.29 (d, *J* = 2.5 Hz, 1H), 7.23-7.20 (m, 1H), 5.98-5.92 (m, 1H), 5.51-5.46 (m, 1H), 4.40 (d, *J* = 6.5 Hz, 2H), 3.65 (s, 6H), 3.42 (t, *J* = 7.5 Hz, 1H), 2.62 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 164.8, 149.7, 138.8, 138.5, 137.4, 134.1, 133.4, 133.2, 130.3, 129.0, 128.8, 127.2, 127.1, 126.2, 121.5, 118.1, 52.5, 51.9, 39.5, 32.0; FT-IR (neat) 3075, 3006, 1731, 1574, 1375, 1249, 1151, 1049, 1024, 750, 708 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{26}H_{26}NO_7$: 450.1547, found 450.1554.



(*E*)-8-(6-Methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)-7-methylquinoline 1-oxide 3oa. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f= 0.30; brown solid; mp 65-66 °C; yield 54% (37 mg); *E/Z* = 4:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 6 Hz, 1H), 7.58 (t, *J* = 9.5 Hz, 2H), 7.37 (d, *J* = 8 Hz, 1H), 7.12 (t, *J* = 7.2 Hz, 1H), 5.98-5.93 (m, 1H), 5.36-5.28 (m, 1H), 4.38 (d, *J* = 7.2 Hz, 2H), 3.62 (s, 6H), 3.36 (t, *J* = 8 Hz, 1H), 2.56 (t, *J* = 7.5 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 140.9, 138.1, 133.1, 131.99, 131.90, 131.2, 126.68, 126.60, 125.2, 123.9, 119.9, 52.4, 52.1, 34.0, 32.0, 20.9; FT-IR (neat) 2953, 1730, 1557, 1435, 1229, 1151, 1023, 828, 752 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{22}NO_5$: 344.1492 , found 344.1492.

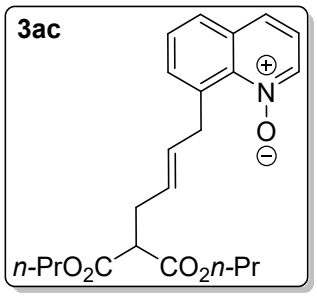


4-((R)-(Benzyloxy)((1S,2R,4S,5R)-5-vinylquinuclidin-2-yl)methyl) -8-((*E*)-6-methoxy-5-(methoxycarbonyl)-6-oxohex-2-en-1-yl)quinoline 1-oxide 3pa. Analytical TLC on silica gel, 1:9 methanol/dichloromethane R_f= 0.70; light brown liquid; yield 64% (75 mg); *E/Z* = 11:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.39 (d, *J* = 6.0 Hz, 1H), 8.07 (d, *J* = 4.8 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.2 Hz, 1H), 7.36-7.33 (m, 3H), 7.31-7.28 (m, 3H), 6.01-5.96 (m, 1H), 5.74-5.69 (m, 1H), 5.50-5.45 (m, 1H), 5.33 (s, 1H), 4.97-4.93 (m, 2H), 4.44 (s, 2H), 4.37 (d, *J* = 6.6 Hz, 2H), 3.67 (s, 6H), 3.44-3.41 (m, 2H), 3.13-3.10 (m, 2H), 2.73-2.65 (m, 2H), 2.62 (t, *J* = 7.2 Hz, 2H), 2.33-2.31 (m, 1H), 1.84-1.73 (m, 4H), 1.56-1.52 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 141.1, 140.6, 137.5, 136.9, 136.6, 135.5, 134.2, 132.8, 130.4, 128.66, 128.61, 128.0, 127.8, 126.2, 122.7, 118.9, 114.9, 71.5, 60.5, 56.6, 52.69, 52.68, 52.5, 52.0, 43.2, 40.1, 39.5, 32.0, 27.8, 27.3; FT-IR (neat) 2927, 2863, 1732, 1565, 1435, 1265, 1150, 1044, 731, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{35}H_{41}N_2O_6$: 585.2959, found 585.2971.

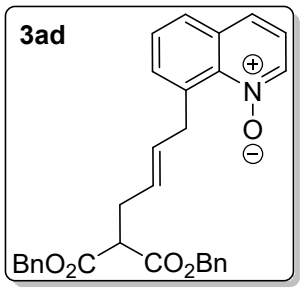


(*E*)-8-(6-Ethoxy-5-(ethoxycarbonyl)-6-oxohex-2-en-1-yl)quinoline 1-oxide 3ab. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f= 0.40; colourless liquid; yield 73% (52 mg); *E/Z* = 23:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, *J* = 6.0 Hz, 1H), 7.67-7.62 (m, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 6.5 Hz, 1H), 7.19-7.17 (m, 1H), 6.00-5.94 (m, 1H), 5.48-5.42 (m, 1H), 4.36 (d, *J* = 6.5 Hz, 2H), 4.14-4.08 (m, 4H), 3.36 (t, *J* = 7.5 Hz, 1H), 2.59 (t, *J* = 7.5 Hz, 2H), 1.18 (t, *J* = 7.5 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.1, 140.6, 137.6, 135.7, 134.0, 132.9, 132.6, 128.30, 127.4, 126.5, 126.3,

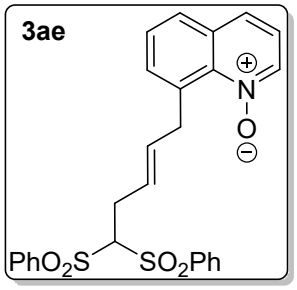
120.7, 61.3, 52.3, 39.7, 31.9, 14.1; FT-IR (neat) 2982, 2926, 1727, 1572, 1369, 1274, 1219, 1153, 1031, 815, 751 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{24}NO_5$: 358.1649, found 358.1649.



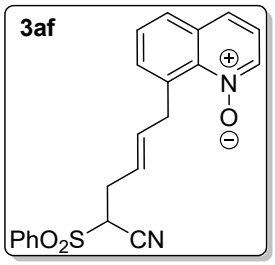
(*E*)-8-(6-Oxo-6-propoxy-5-(propoxycarbonyl)hex-2-en-1-yl) quinoline 1-oxide 3ac. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.50; colourless liquid; yield 71% (54.5 mg); *E/Z* > 23:1 mixture of diastereomers; ^1H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, *J* = 6 Hz, 1H), 7.64 (t, *J* = 8.5 Hz, 2H), 7.44-7.38 (m, 2H), 7.18-7.15 (m, 1H), 5.98-5.92 (m, 1H), 5.46-5.40 (m, 1H), 4.33 (d, *J* = 6 Hz, 2H), 4.03-3.95 (m, 4H), 3.37 (t, *J* = 7.5 Hz, 1H), 2.58 (t, *J* = 7.0 Hz, 2H), 1.59-1.52 (m, 4H), 0.84 (t, *J* = 7.5 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.1, 140.5, 137.6, 135.6, 133.9, 132.9, 132.5, 128.2, 127.4, 126.7, 126.3, 120.6, 66.8, 52.2, 39.6, 31.8, 21.8, 10.3; FT-IR (neat) 2967, 1726, 1571, 1383, 1300, 1268, 1219, 1147, 1058, 814, 756 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{28}NO_5$: 386.1962, found 386.1967.



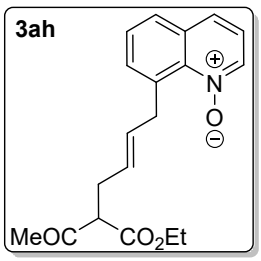
(*E*)-8-(6-(Benzyloxy)-5-((benzyloxy)carbonyl)-6-oxohex-2-en-1-yl) quinoline 1-oxide 3ad. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.40; colourless liquid; yield 72% (69.3 mg); *E/Z* > 23:1 mixture of diastereomers; ^1H NMR (600 MHz, $CDCl_3$) δ 8.40 (d, *J* = 6.0 Hz, 1H), 7.66-7.62 (m, 2H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 6.6 Hz, 1H), 7.30-7.28 (m, 6H), 7.25-7.23 (m, 4H), 7.18-7.16 (m, 1H), 6.00-5.95 (m, 1H), 5.45-5.40 (m, 1H), 5.08 (d, *J* = 3 Hz, 4H), 4.33 (d, *J* = 6.6 Hz, 2H), 3.50 (t, *J* = 7.8 Hz, 1H), 2.65 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.7, 140.6, 137.6, 135.6, 135.4, 134.3, 132.9, 132.6, 128.5, 128.3, 128.2, 128.1, 127.4, 126.5, 126.0, 120.7, 67.0, 52.3, 39.6, 31.9; FT-IR (neat) 3033, 2922, 1729, 1571, 1455, 1217, 1145, 973, 813,749, 696 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{30}H_{28}NO_5$: 482.1962, found 482.1965.



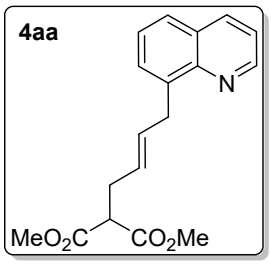
(*E*)-8-(5,5-bis(Phenylsulfonyl)pent-2-en-1-yl)quinoline 1-oxide 3ae. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.30; light yellow liquid; yield 82% (81 mg); *E/Z* = 12:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (d, *J* = 6 Hz, 1H), 7.92-7.91 (m, 4H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.64-7.61 (m, 2H), 7.54-7.46 (m, 5H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.24-7.21 (m, 1H), 5.89-5.84 (m, 1H), 5.40-5.36 (m, 1H), 4.45 (t, *J* = 6 Hz, 1H), 4.27 (d, *J* = 6.6 Hz, 2H), 2.86 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.6, 138.1, 137.7, 135.6, 135.3, 134.6, 133.4, 132.7, 129.8, 129.7, 128.4, 127.9, 126.7, 121.6, 120.9, 113.8, 57.8, 39.8, 30.2; FT-IR (neat) 3060, 2923, 1660, 1573, 1447, 1329, 1155, 1078, 750, 687, 553 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{26}H_{24}NO_5S_2$: 494.1090, found 494.1097.



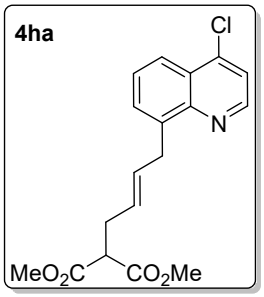
(*E*)-8-(5-Cyano-5-(phenylsulfonyl)pent-2-en-1-yl)quinoline 1-oxid e 3af. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.40; colourless liquid; yield 42% (32 mg); *E/Z* = 12:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (d, *J* = 6.0 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 2H), 7.75-7.73 (m, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.22-7.20 (m, 1H), 6.21-6.16 (m, 1H), 5.41-5.36 (m, 1H), 4.37 (d, *J* = 6 Hz, 2H), 3.92 (dd, J = 10.8, 4.2 Hz, 1H), 2.92-2.87 (m, 1H), 2.58-2.53 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.6, 138.1, 137.7, 135.7, 135.0, 134.6, 133.3, 132.7, 129.8, 129.1, 128.4, 127.7, 126.6, 124.2, 120.9, 84.0, 39.7, 29.0; FT-IR (neat) 2923, 2853, 1712, 1465, 1275, 1260, 1157, 1082 750 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{21}H_{19}N_2O_3S$: 379.1111, found 379.1112.



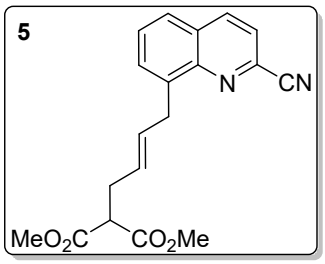
(*E*)-8-(5-(Ethoxycarbonyl)-6-oxohept-2-en-1-yl)quinoline 1-oxide 3ah. Analytical TLC on silica gel, 7:3 ethyl acetate/hexane R_f = 0.35; colourless liquid; yield 70% (46 mg); *E/Z* = 13:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (d, *J* = 6 Hz, 1H), 7.68-7.64 (m, 2H), 7.46 (t, *J* = 8 Hz, 1H), 7.40 (d, *J* = 7 Hz, 1H), 7.21-7.18 (m, 1H), 5.99-5.93 (m, 1H), 5.42-5.37 (m, 1H), 4.34 (d, *J* = 7.5 Hz, 2H), 4.13-4.09 (m, 2H), 3.46 (t, *J* = 7.5 Hz, 1H), 2.56-2.52 (m, 2H), 2.17 (s, 3H), 1.18 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.0, 169.4, 140.6, 137.6, 135.6, 134.0, 133.0, 132.6, 128.3, 127.5, 126.5, 126.4, 120.7, 61.3, 59.8, 39.7, 31.3, 29.2, 14.1; FT-IR (neat) 2981, 2922, 1711, 1572, 1423, 1383, 1300, 1217, 1151, 1015, 815, 757 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{22}NO_4$: 328.1543, found 328.1547.



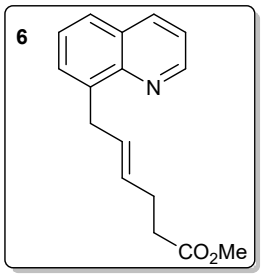
Dimethyl (*E*)-2-(4-(quinolin-8-yl)but-2-en-1-yl)malonate 4aa. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.30; light brown liquid; yield 78% (24.5 mg); *E/Z* > 23:1 mixture of diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93-8.92 (m, 1H), 8.14-8.12 (m, 1H), 7.69-7.66 (m, 1H), 7.52-7.44 (m, 2H), 7.41-7.38 (m, 1H), 5.95-5.88 (m, 1H), 5.56-5.49 (m, 1H), 4.00 (d, *J* = 6.8 Hz, 2H), 3.66 (s, 6H), 3.43 (t, *J* = 7.6 Hz, 1H), 2.63 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 149.5, 146.6, 139.4, 136.4, 132.5, 128.8, 128.5, 126.9, 126.5, 126.3, 121.0, 52.5, 52.0, 34.1, 32.0; FT-IR (neat) 3004, 2952, 1731, 1497, 1434, 1275, 1149, 1025, 971, 793, 750 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{18}H_{20}NO_4$: 314.1387, found 314.1384.



Dimethyl (*E*)-2-(4-(4-chloroquinolin-8-yl)but-2-en-1-yl)malonate 4ha. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.30; light brown liquid; yield 77% (26.8 mg); *E/Z* = 19:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76-8.74 (m, 1H), 8.09-8.05 (m, 1H), 7.54-7.51 (m, 2H), 7.47-7.43 (m, 1H), 5.90-5.85 (m, 1H), 5.54-5.48 (m, 1H), 3.97 (d, *J* = 4.5 Hz, 2H), 3.65 (s, 6H), 3.42 (t, *J* = 7.5 Hz, 1H), 2.62 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.4, 148.7, 147.4, 142.8, 139.8, 132.2, 129.7, 127.4, 127.1, 126.5, 122.5, 121.1, 52.4, 51.8, 34.3, 31.9; FT-IR (neat) 2953, 1732, 1584, 1489, 1435, 1386, 1230, 1149, 971, 763 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{18}H_{19}ClNO_4$: 348.0997, found 348.0992.



Dimethyl (*E*)-2-(4-(2-cyanoquinolin-8-yl)but-2-en-1-yl) malon ate 5. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.30; light brown liquid; yield 75% (25.5 mg); *E/Z* > 23:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.4 Hz, 1H), 7.74-7.73 (m, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.62-7.60 (m, 2H), 5.86-5.82 (m, 1H), 5.58-5.54 (m, 1H), 3.97 (d, *J* = 7.2 Hz, 2H), 3.68 (s, 6H), 3.44 (t, *J* = 7.8 Hz, 1H), 2.63 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 146.6, 140.5, 137.7, 132.5, 131.8, 130.4, 129.5, 128.9, 127.5, 126.1, 123.3, 117.9, 52.6, 51.8, 33.9, 31.9. FT-IR (neat) 2924, 2235, 1731, 1434, 1261, 1150, 971, 841, 765 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{19}H_{18}NaN_2O_4$: 361.1159, found 361.1160.



Methyl (*E*)-6-(quinolin-8-yl)hex-4-enoate 6. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.50; colorless liquid; yield 68% (17.5 mg); *E/Z* > 23:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.94 (d, *J* = 2.4 Hz 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 6.6 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.41-7.39 (m, 1H), 5.88-5.84 (m, 1H), 5.59-5.54 (m, 1H), 4.01 (d, *J* = 6.6 Hz, 2H), 3.63 (s, 3H), 2.40-2.36 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8, 149.5, 146.6, 139.6, 136.5, 130.2, 129.7, 128.9, 128.5, 126.5, 126.3, 121.0, 51.6, 34.2, 34.1, 28.0; FT-IR (neat) 2949, 2915, 1732, 1596, 1497, 1435, 1365, 1151, 970, 826, 793 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{16}H_{18}NO_2$: 256.1332, found 256.1331.

Mechanistic Investigations

H/D-Exchange Studies

To a stirred solution of quinoline *N*-oxide **1a** (0.1 mmol, 14.5 mg), $[RhCp^*Cl_2]_2$ (0.005 mmol, 3 mg), $AgBF_4$ (0.02 mmol, 4 mg), $NaOPiv.H_2O$ (0.02 mmol, 2.8 mg), Ag_2O (0.1 mmol, 23 mg) and TFE (0.5 mL), deuterated solvent (30 equiv) was added. The resulting mixture was stirred for 18 h at room temperature under N_2 atmosphere and extracted using EtOAc (3 x 10 mL). The combined organic layer was washed with aqueous $NaHCO_3$ (5 mL) and water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified according to general procedure. Deuterium incorporation of the recovered starting material was confirmed by ^{1}H NMR.

Preparation of Deuterated 8-d$_1$ Quinoline *N*-oxide [D$_1$]-1a[10]

A round bottom flask was charged with magnetic bar and Quinoline *N*-oxide **1a** (1 mmol, 145 mg), $[RhCp^*Cl_2]_2$ (0.02 mmol, 12 mg), PivOH (0.1 mmol, 11 mg), $AgSbF_6$ (0.08 mmol, 28 mg) and DCE:CD_3COOD (1:1, 4 mL). The mixture was stirred for 36 h at 110 °C and cooled to room temperature. The mixture was extracted using EtOAc (3 x 15 mL) and evaporation of solvent gave a residue that was purified as shown in the general procedure. The deuterium incorporation of the recovered starting material was found 87% using ^{1}H NMR.

Kinetic Isotope Effect

Quinoline *N*-oxide **1a** (0.05 mmol, 7.3 mg), quinoline 1-oxide-8-d_1 [D_1]-**1a** (0.05 mmol, 7.3 mg), vinylcyclopropane **2a** (0.15 mmol, 28 mg), $[RhCp^*Cl_2]_2$ (0.005, 3 mg), $AgBF_4$ (0.02 mmol, 4 mg), NaOPiv•H_2O (0.02 mmol, 3 mg), Ag_2O (0.1 mmol, 23 mg) and TFE (0.5 mL) were stirred for 40 minutes at room temperature under N_2 atmosphere. ^1H NMR was taken of the recovered *N*-oxide to calculate the intermolecular k_H/k_D and found to be 2.75.

References

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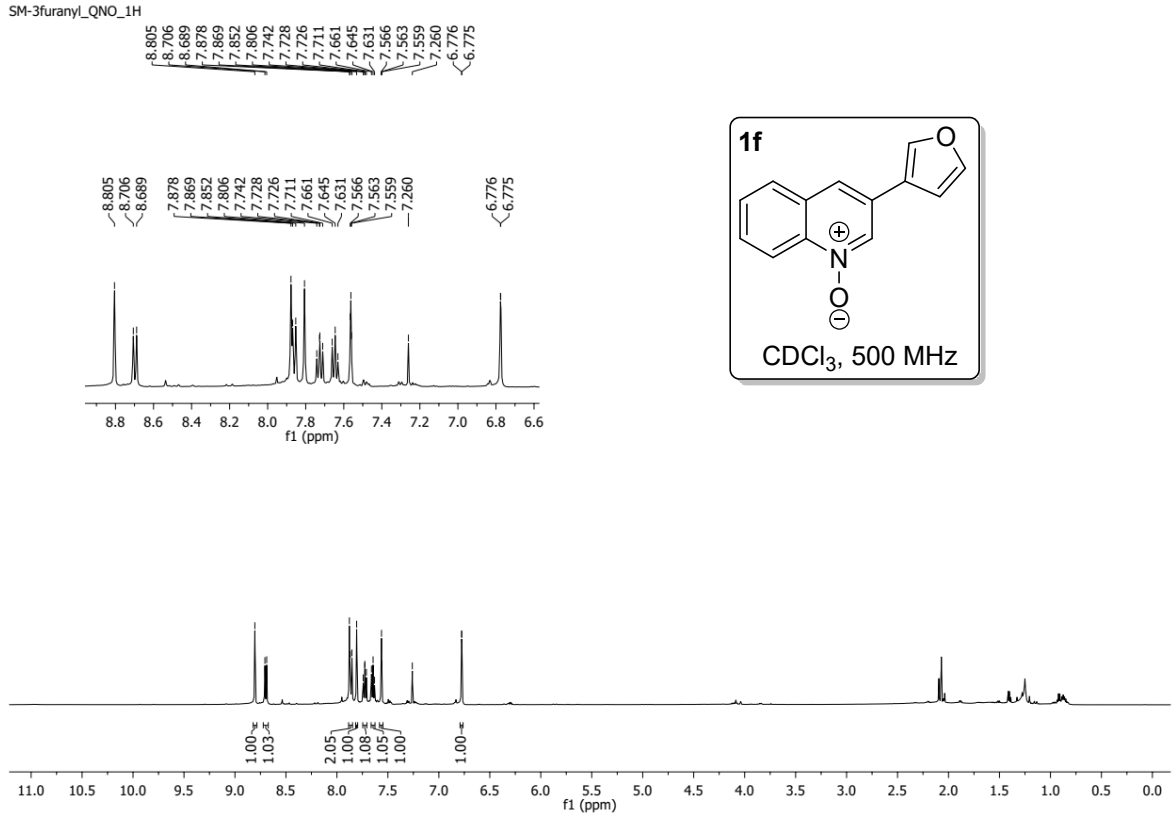
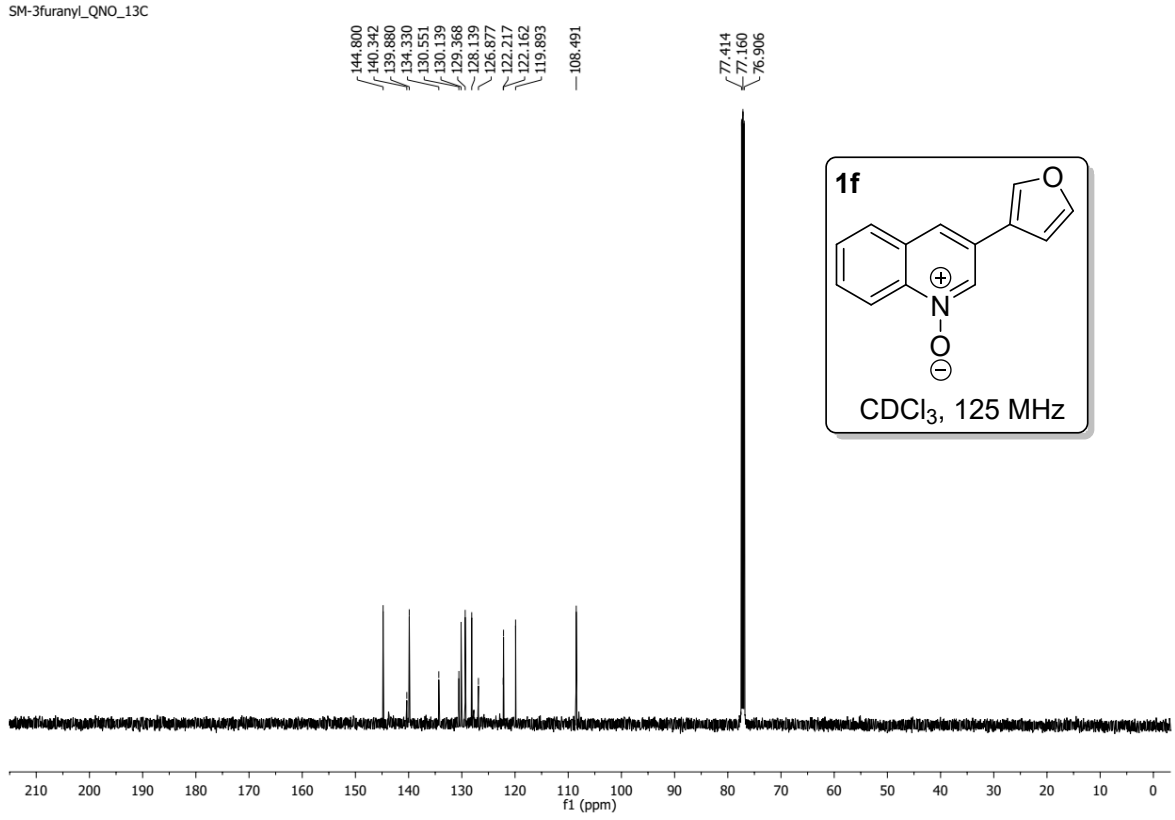
NMR (^{1}H, ^{13}C, ^{19}F and NOESY) Spectra





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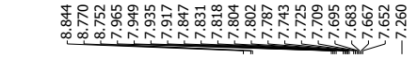

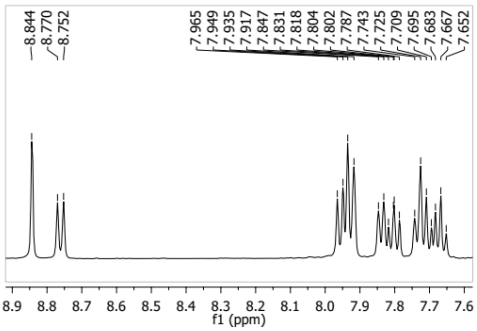

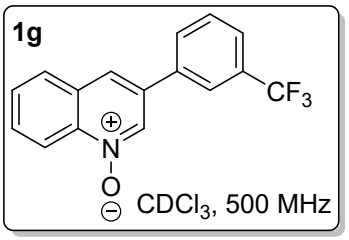

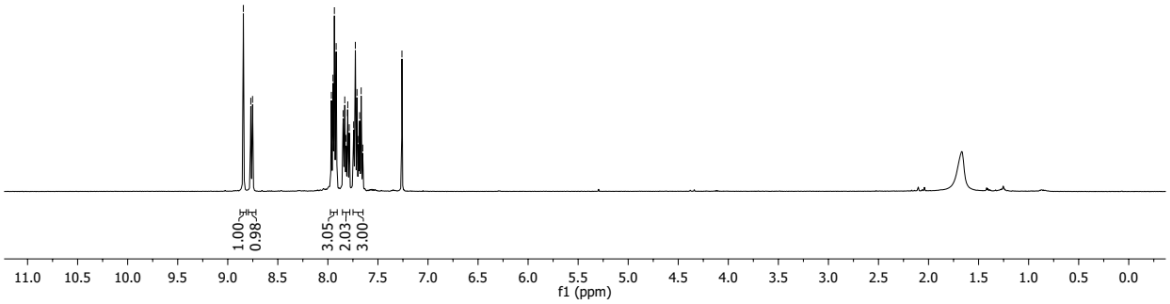

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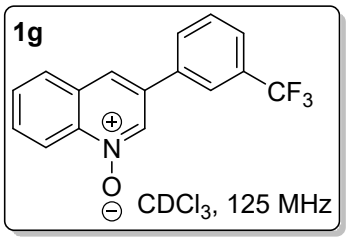

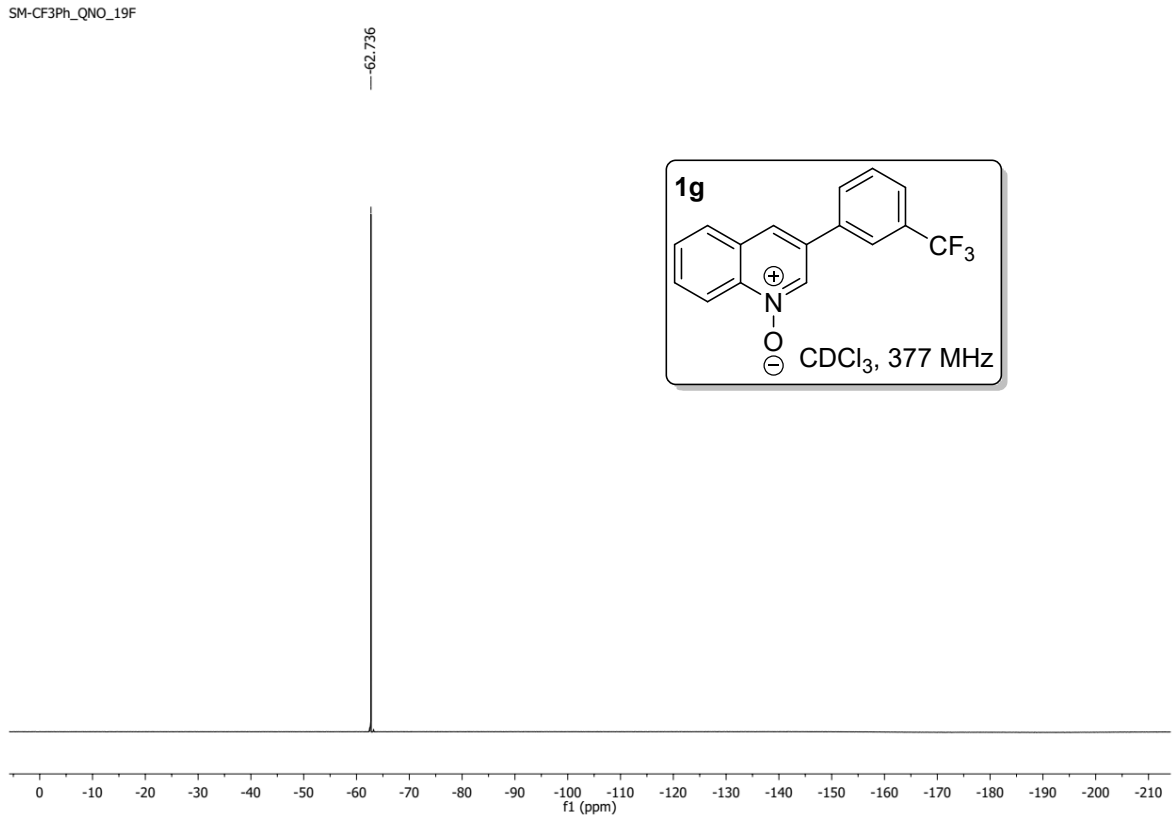
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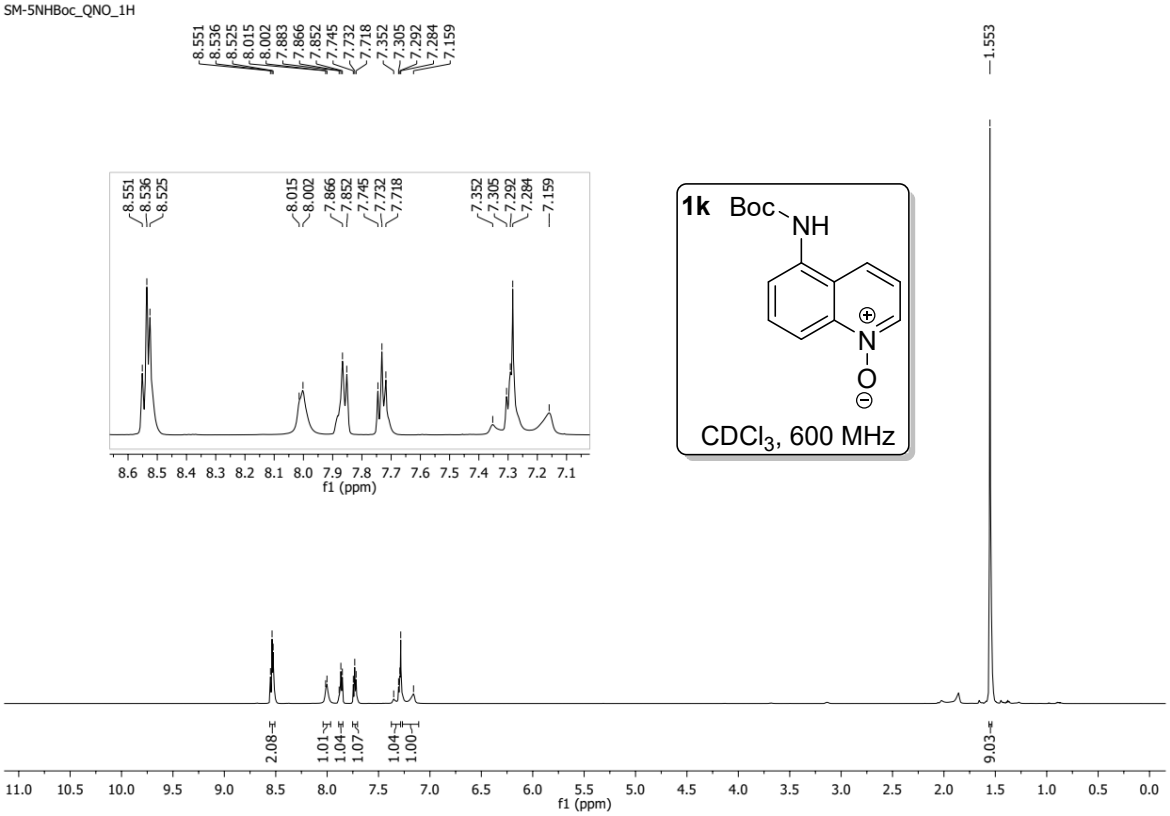
f1 (ppm)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f1 (ppm)
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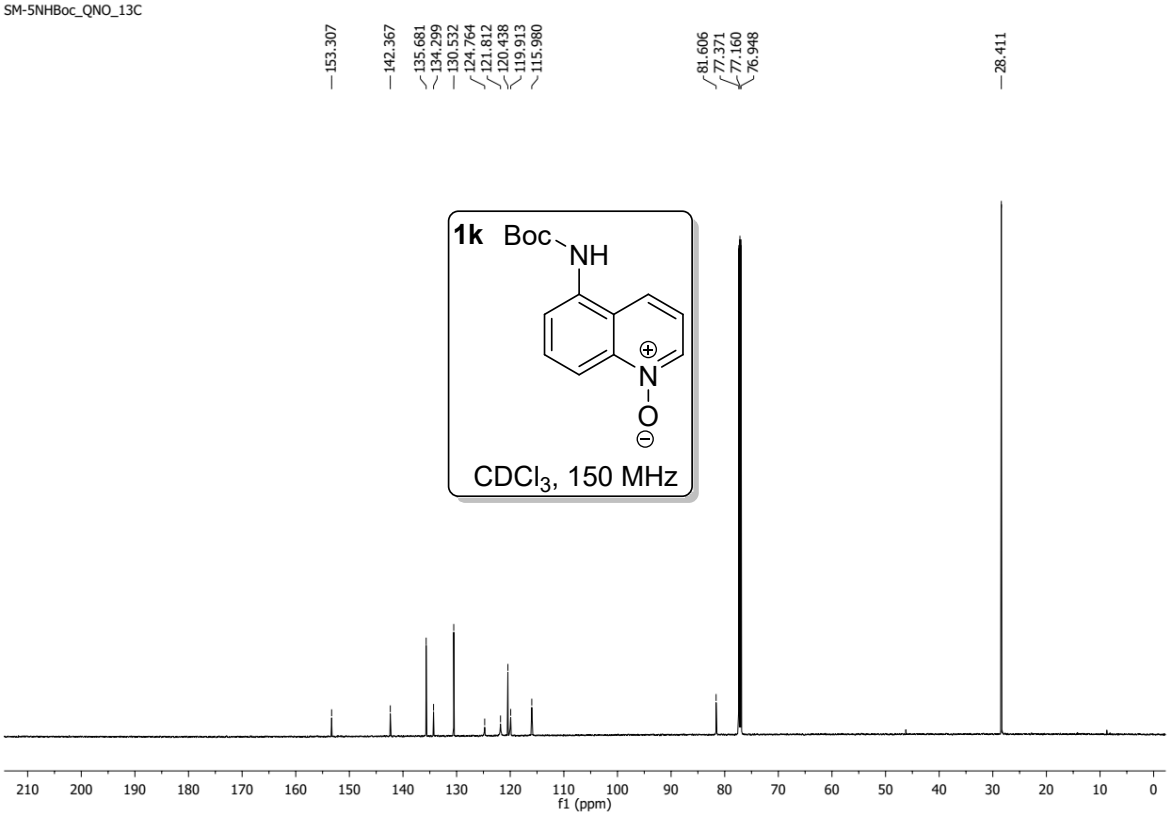
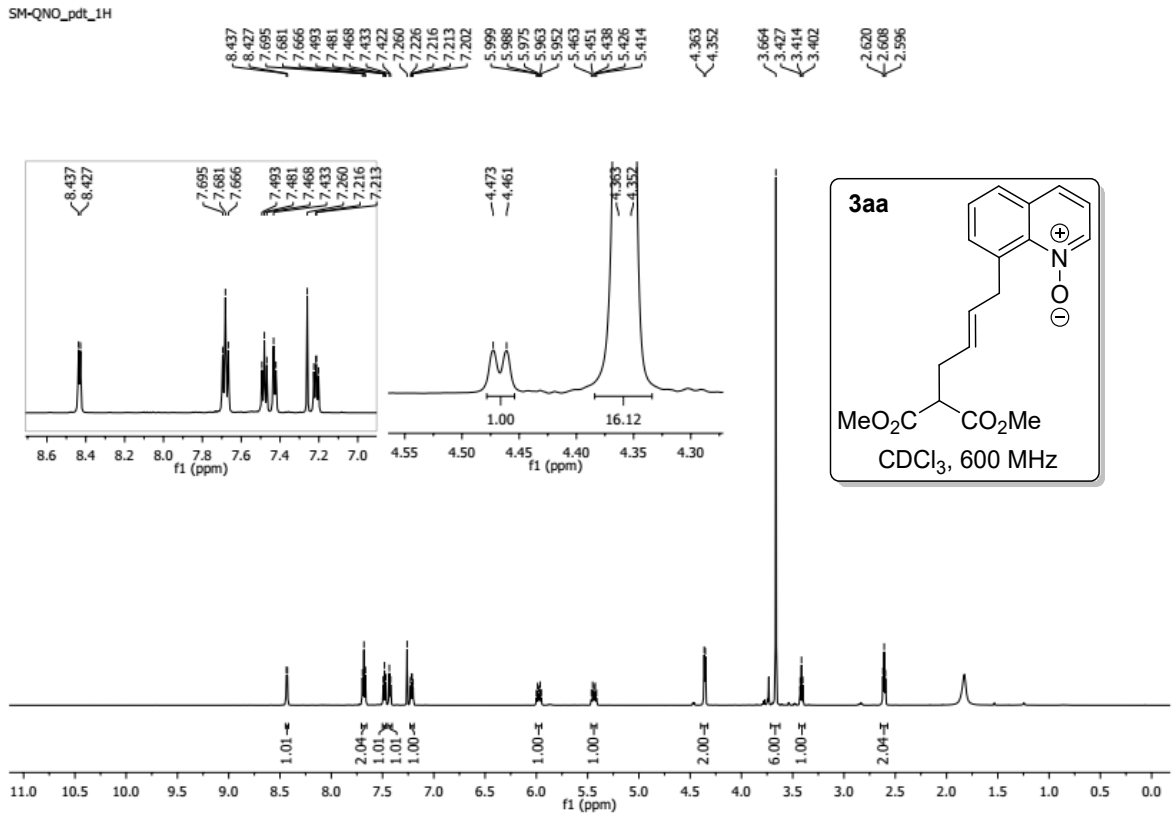
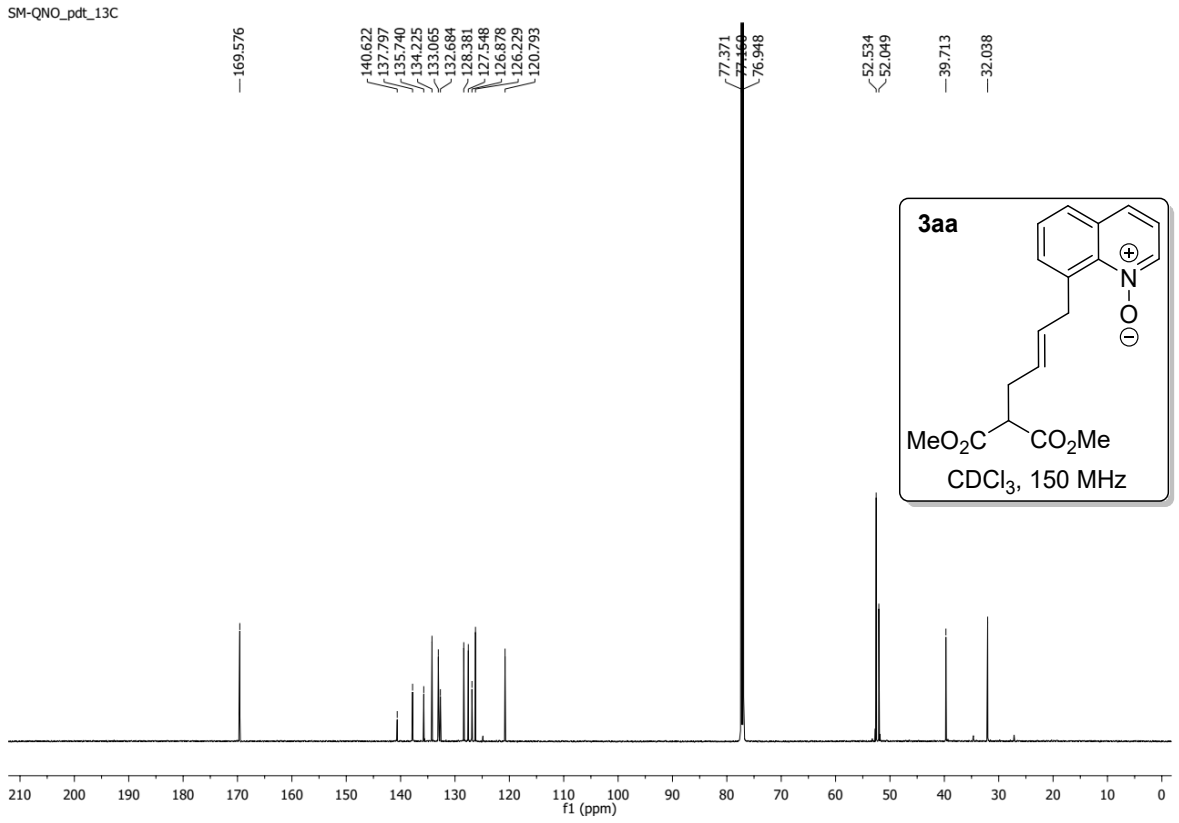
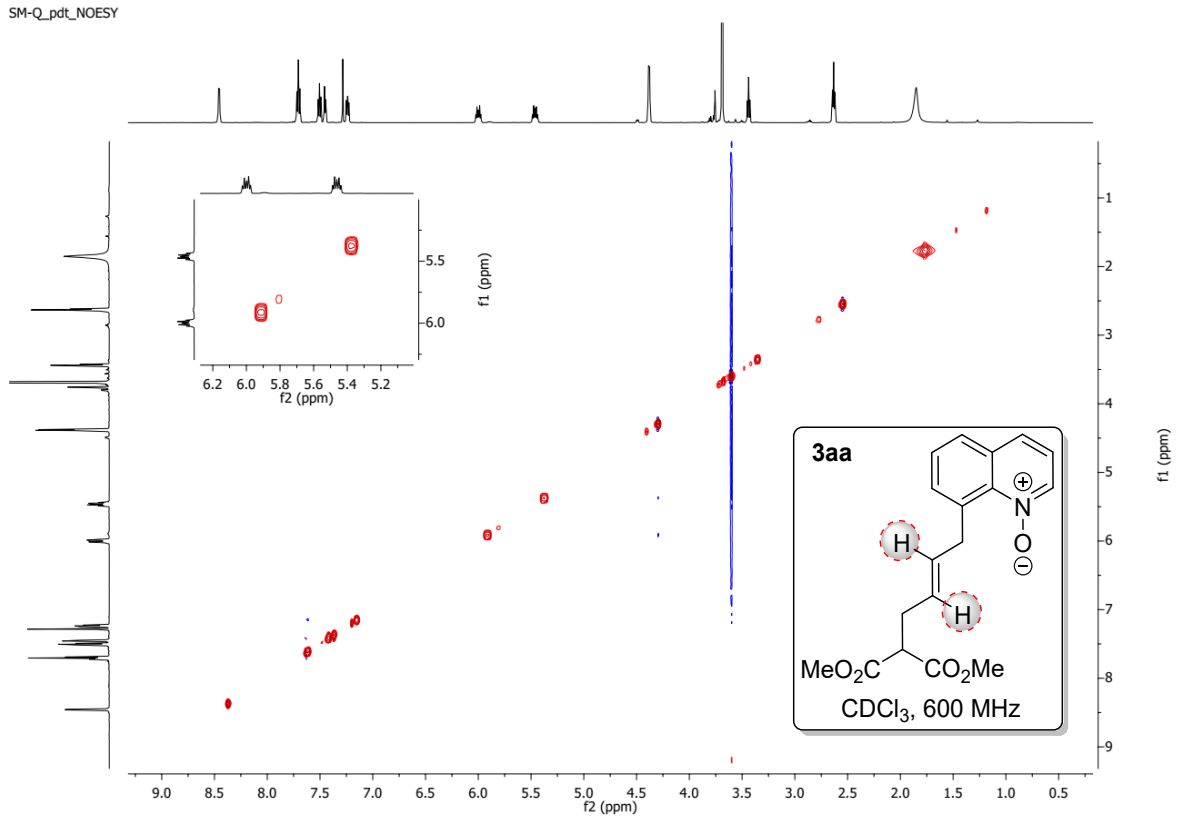
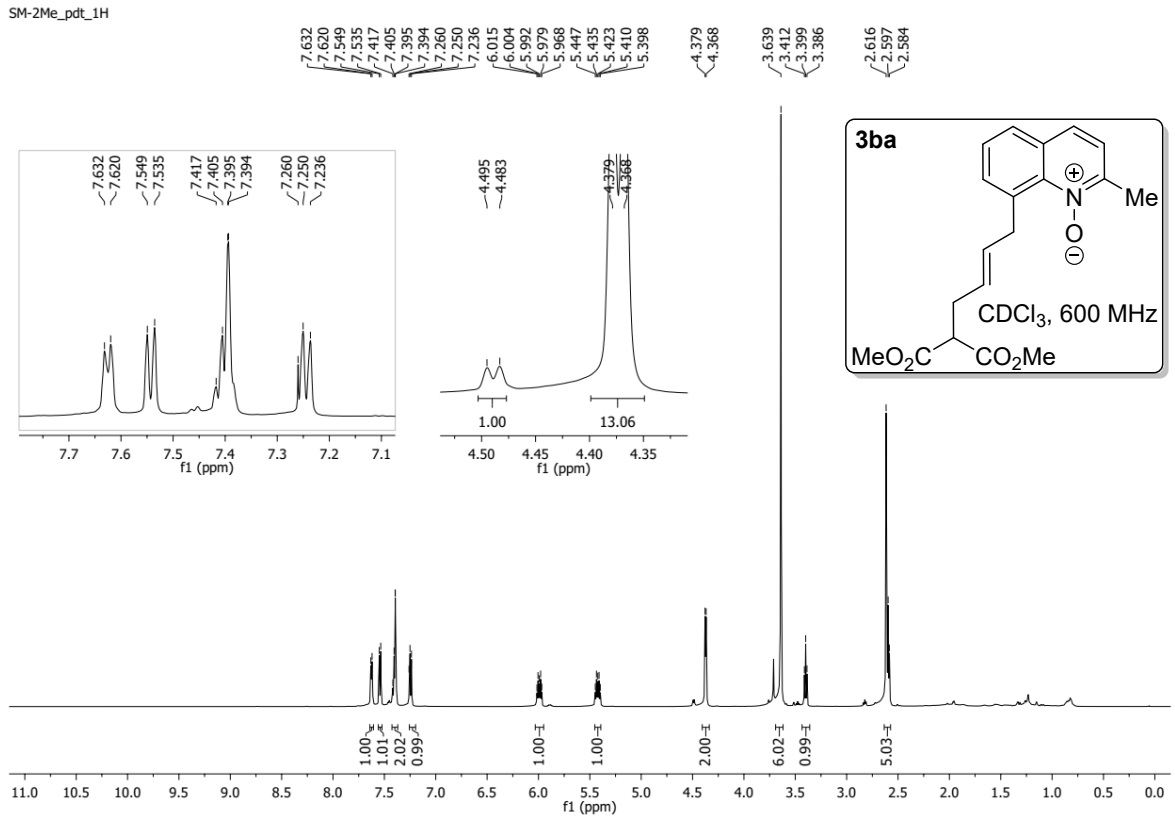
1.00
9.03

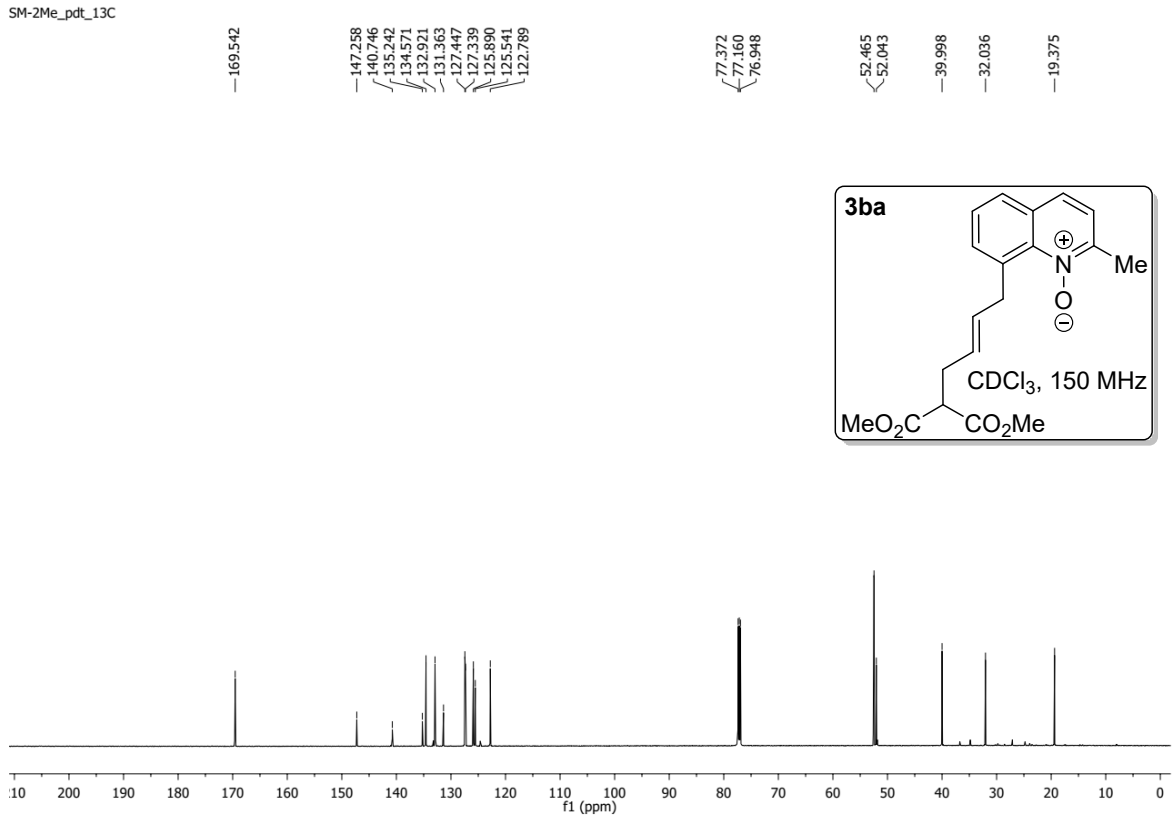

SM-5NHBoc_QNO_13C
153.307
142.367
135.681
134.299
130.532
124.764
121.812
120.438
119.913
115.980
81.606
77.371
77.160
76.948
28.411
1k Boc NH
CDCl3, 150 MHz
f1 (ppm)

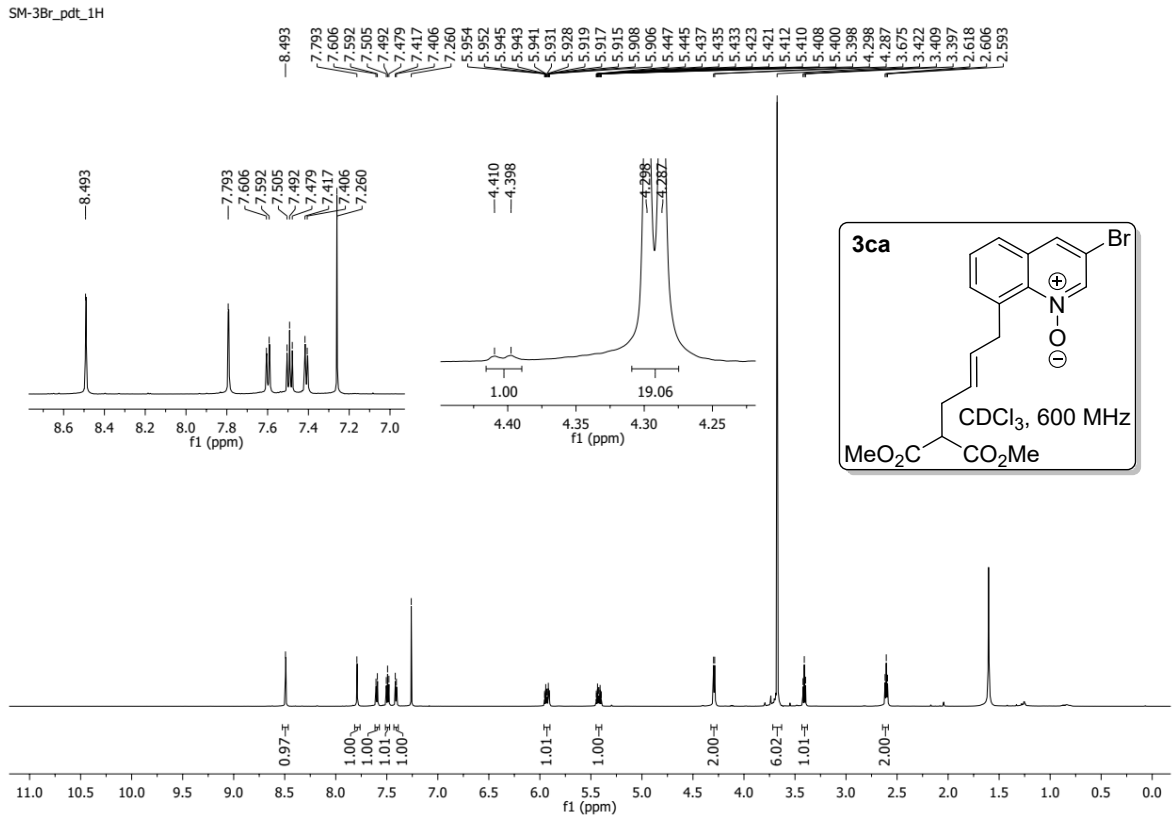

SM-QNO_pdt_1H
3aa
MeO2C CO2Me
CDCl3, 600 MHz
f1 (ppm)

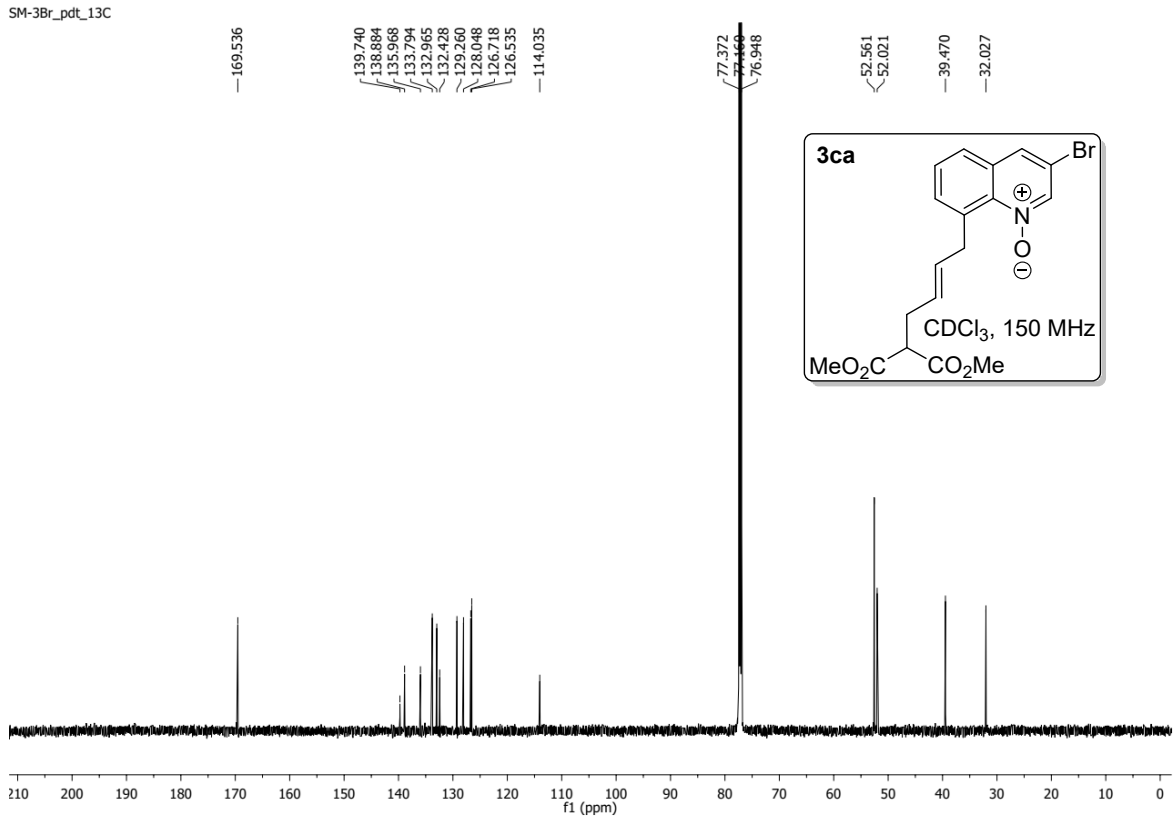

SM-QNO_pdt_13C
3aa
MeO2C CO2Me
CDCl3, 150 MHz
f1 (ppm)


SM-Q_pdt_NOESY
f2 (ppm)
f1 (ppm)
3aa
MeO2C
CO2Me
CDCl3, 600 MHz

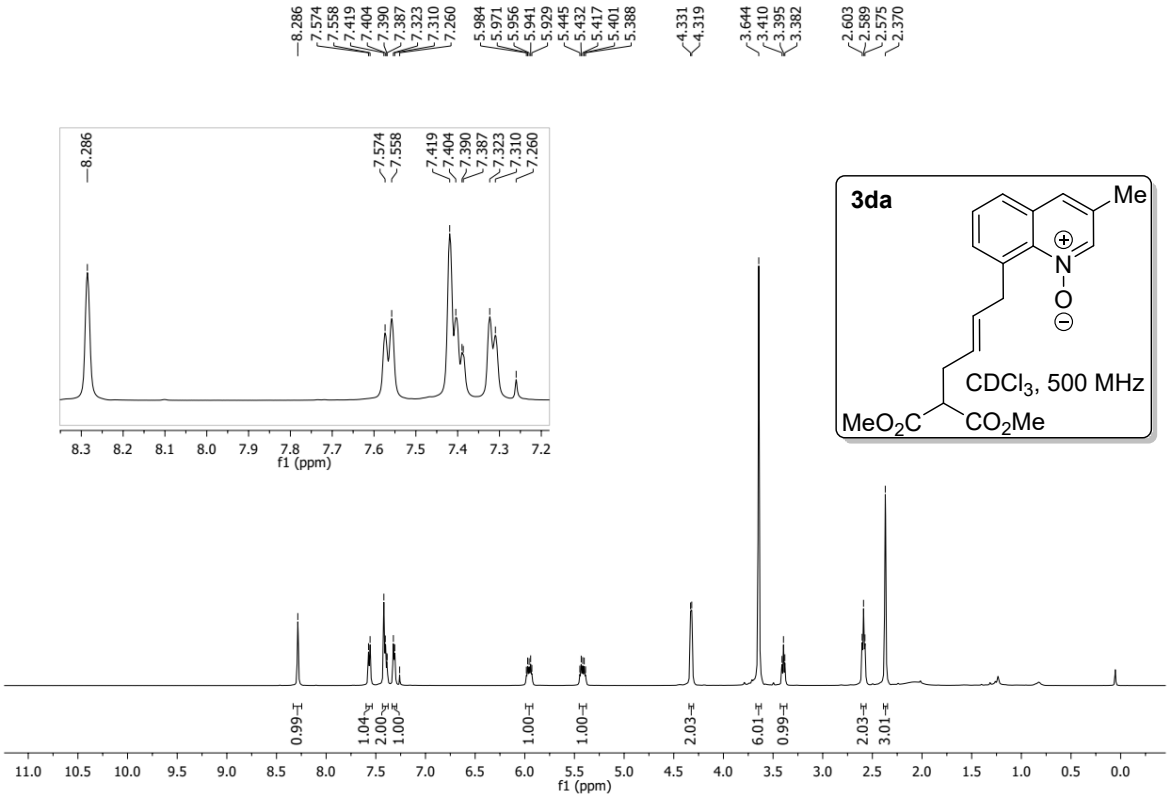

SM-2Me_pdt_1H
3ba
CDCl3, 600 MHz
MeO2C
CO2Me
Me
f1 (ppm)


SM-2Me_pdt_13C
3ba
CDCl3, 150 MHz
MeO2C
CO2Me
Me
f1 (ppm)

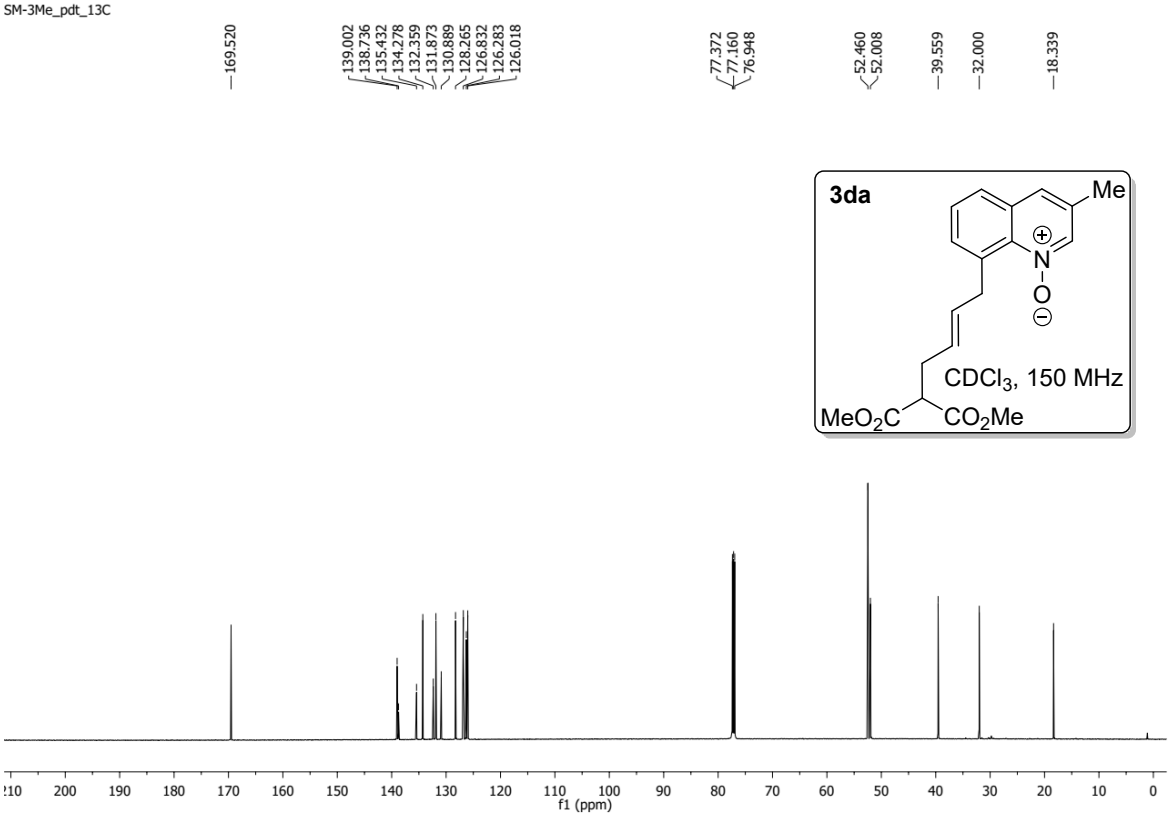

SM-3Br_pdt_1H
3ca
Br
N
O
CDCl3, 600 MHz
MeO2C
CO2Me
f1 (ppm)


SM-3Br_pdt_13C
3ca
Br
N
O
CDCl3, 150 MHz
MeO2C
CO2Me
f1 (ppm)

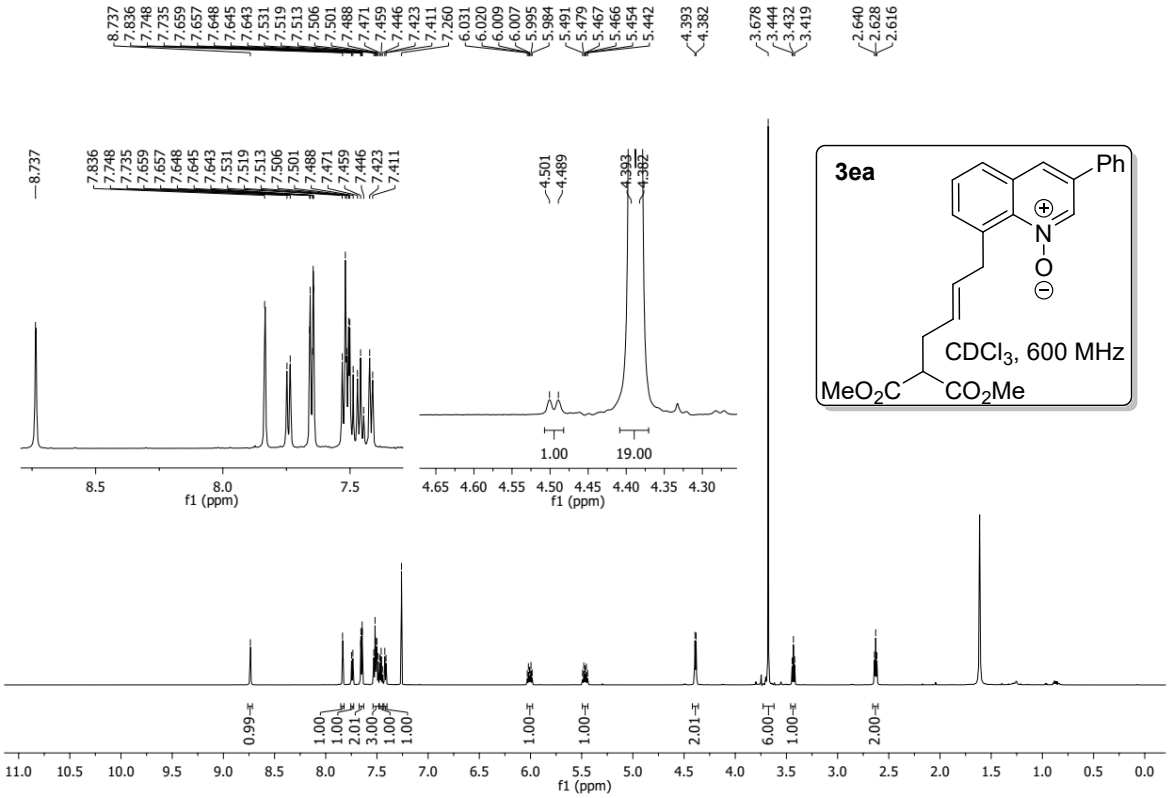
SM-3Me_pdt_1H



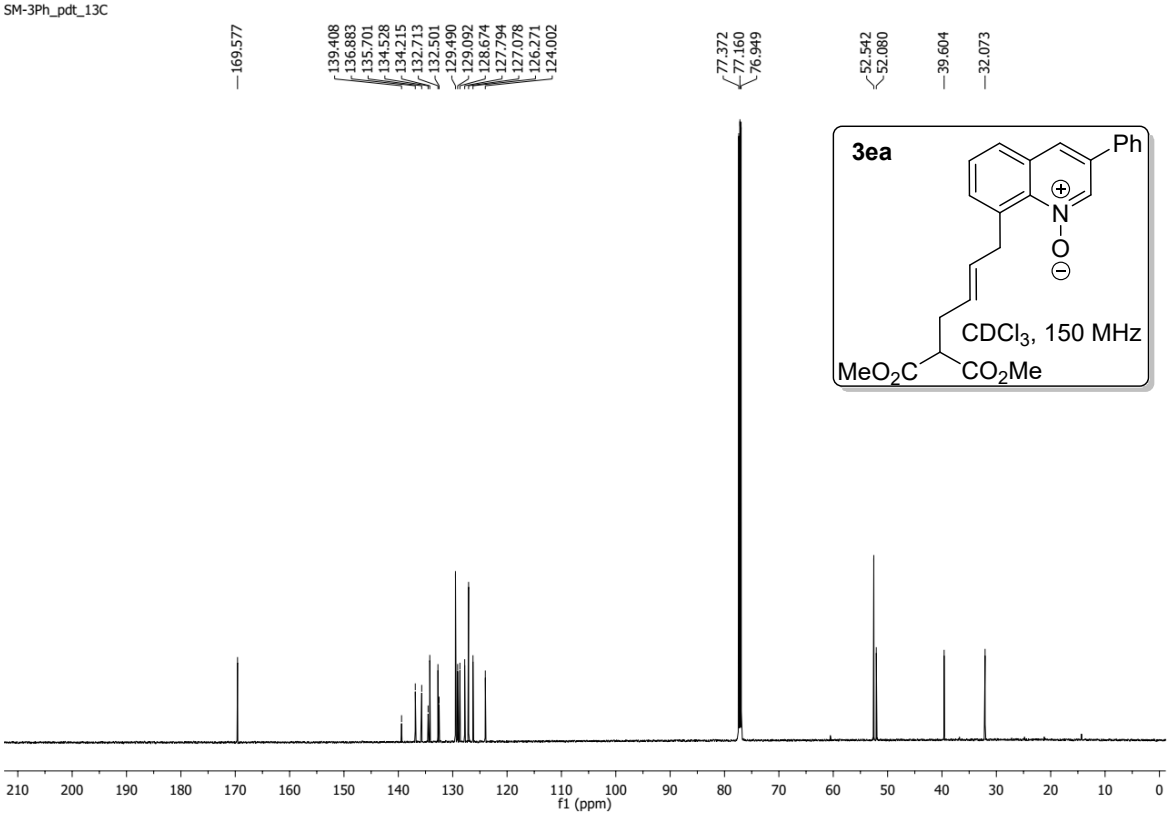
SM-3Me_pdt_13C

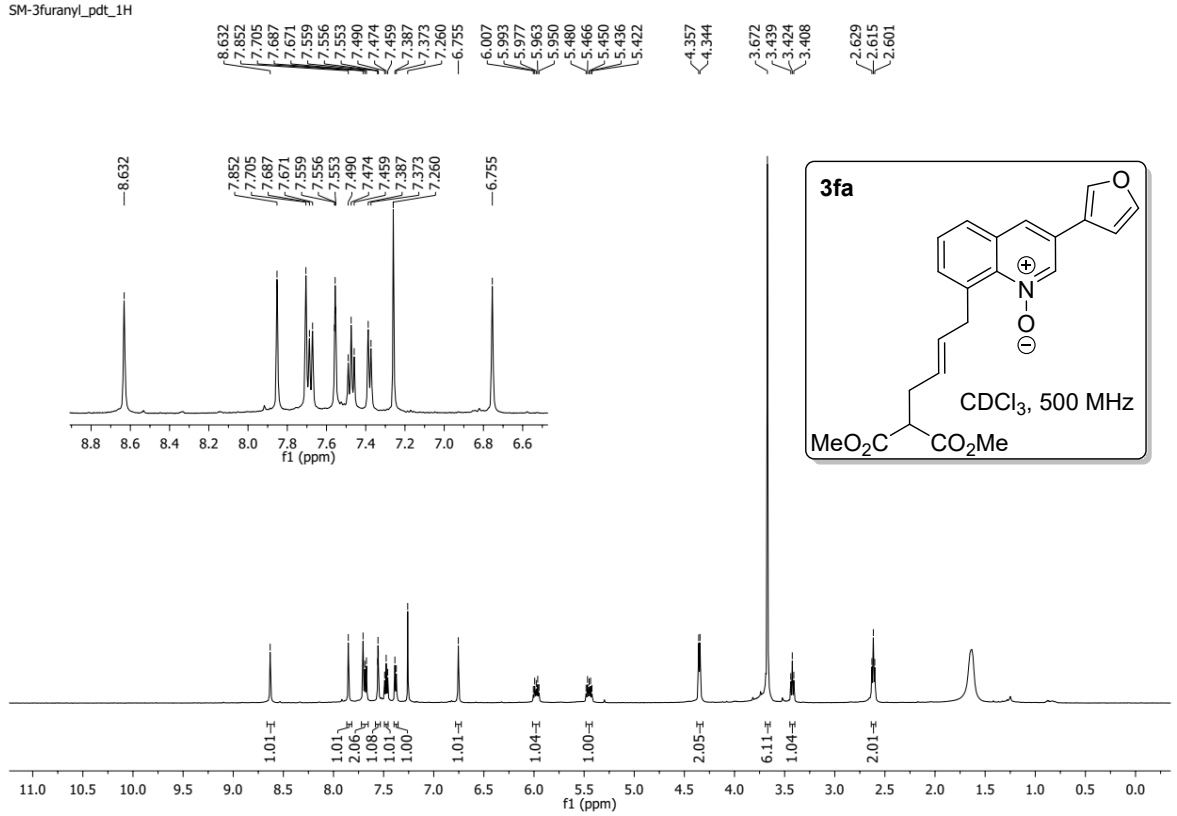


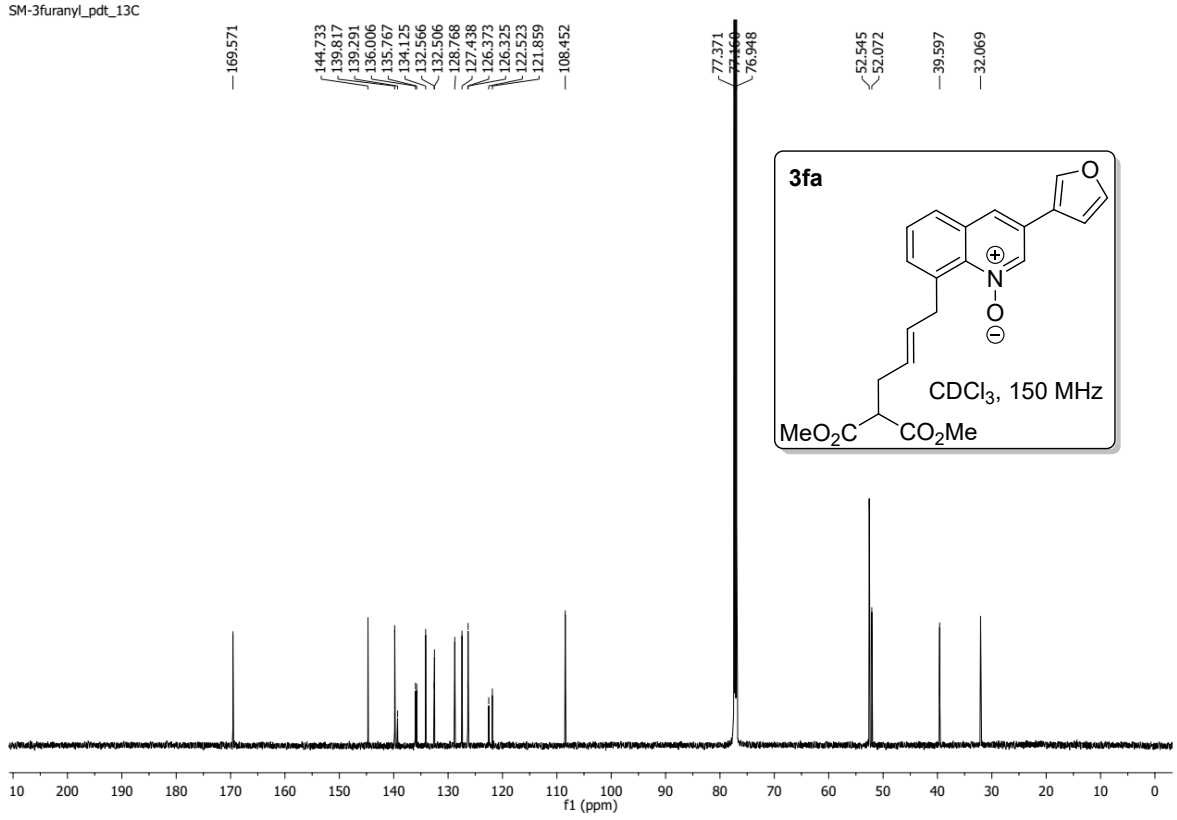
SM-3Ph_pdt_1H

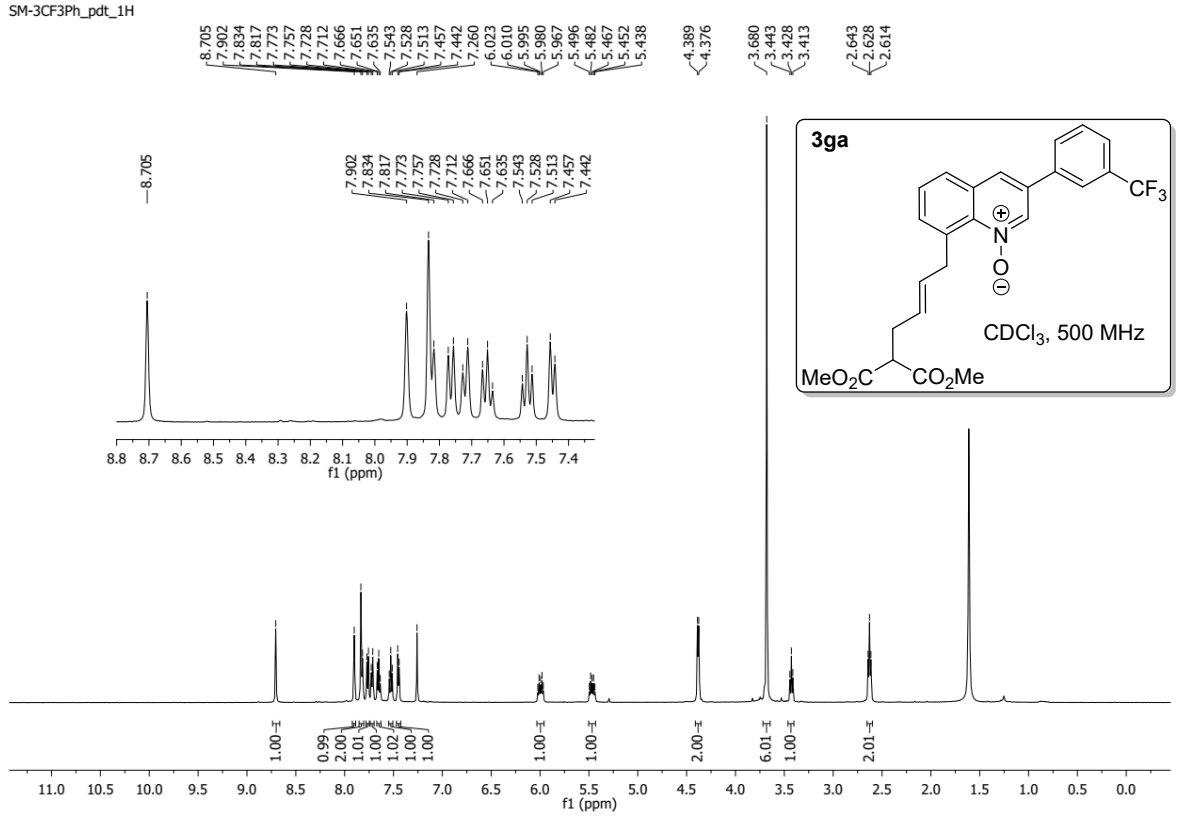


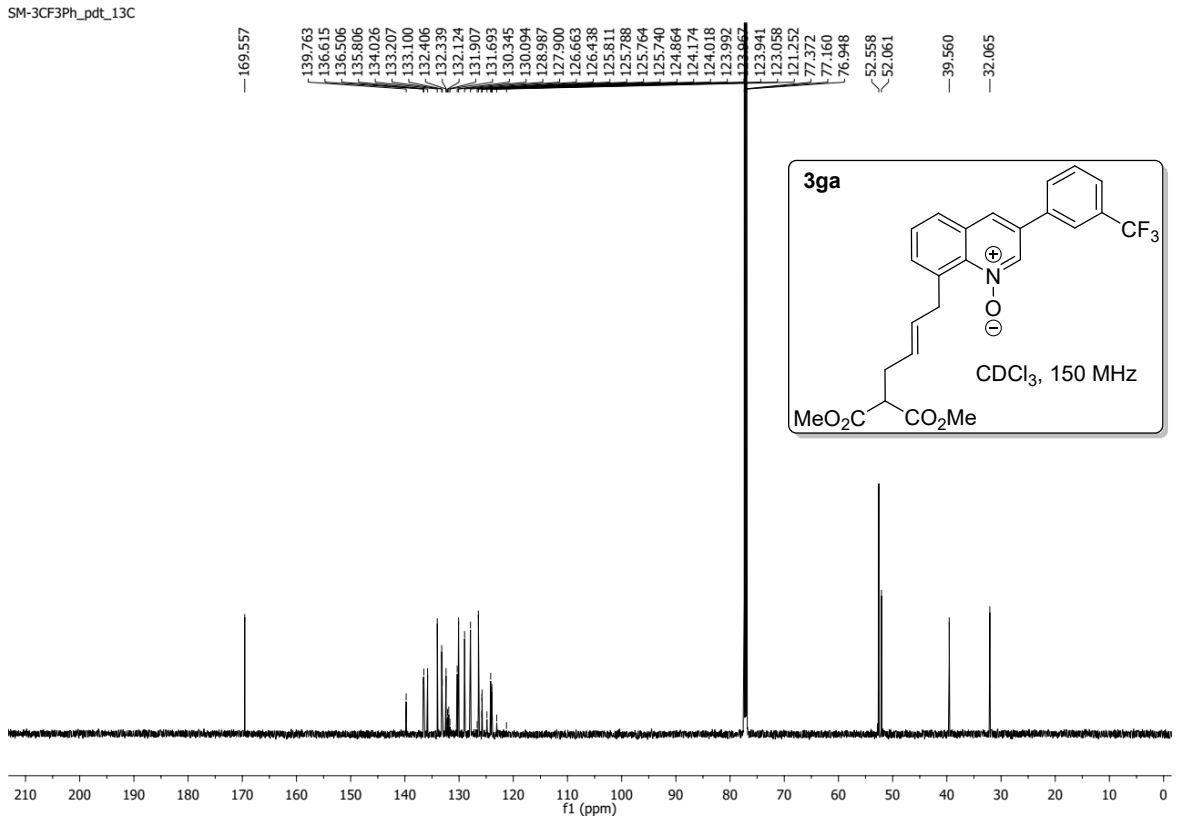
SM-3Ph_pdt_13C



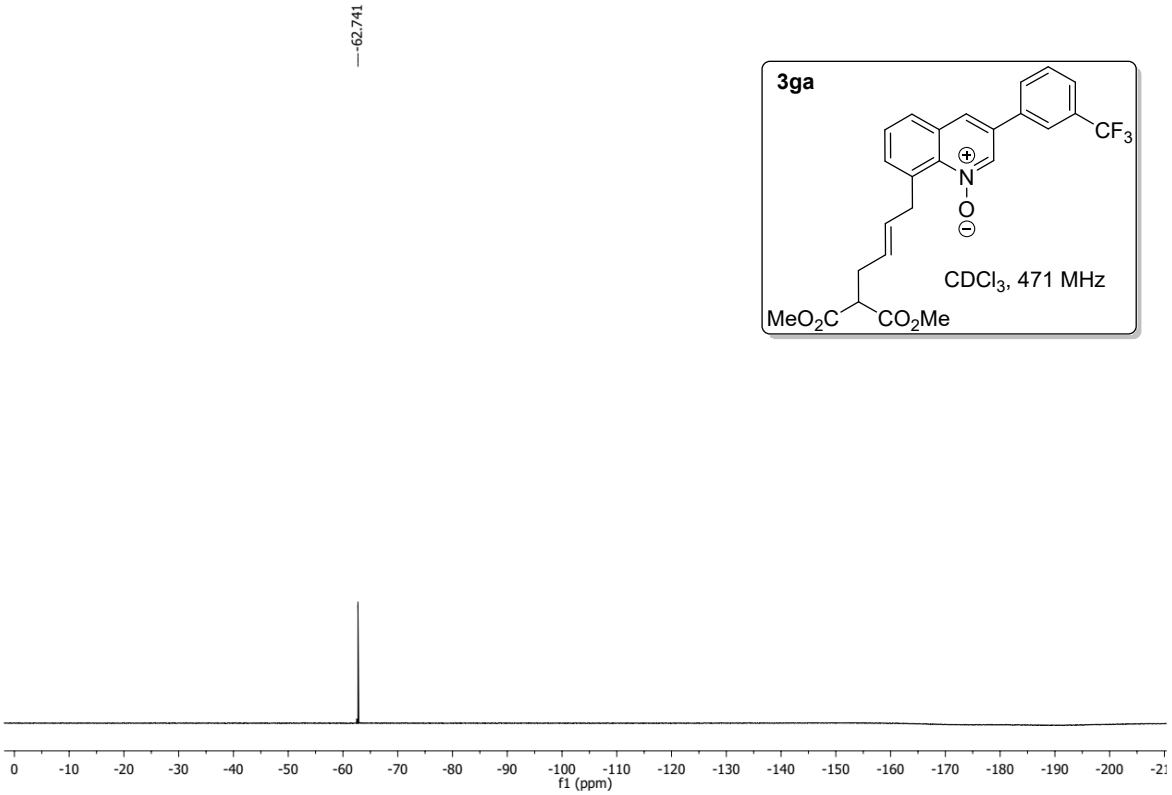

SM-3furanyl_pdt_1H
3fa
CDCl3, 500 MHz
MeO2C
CO2Me
f1 (ppm)

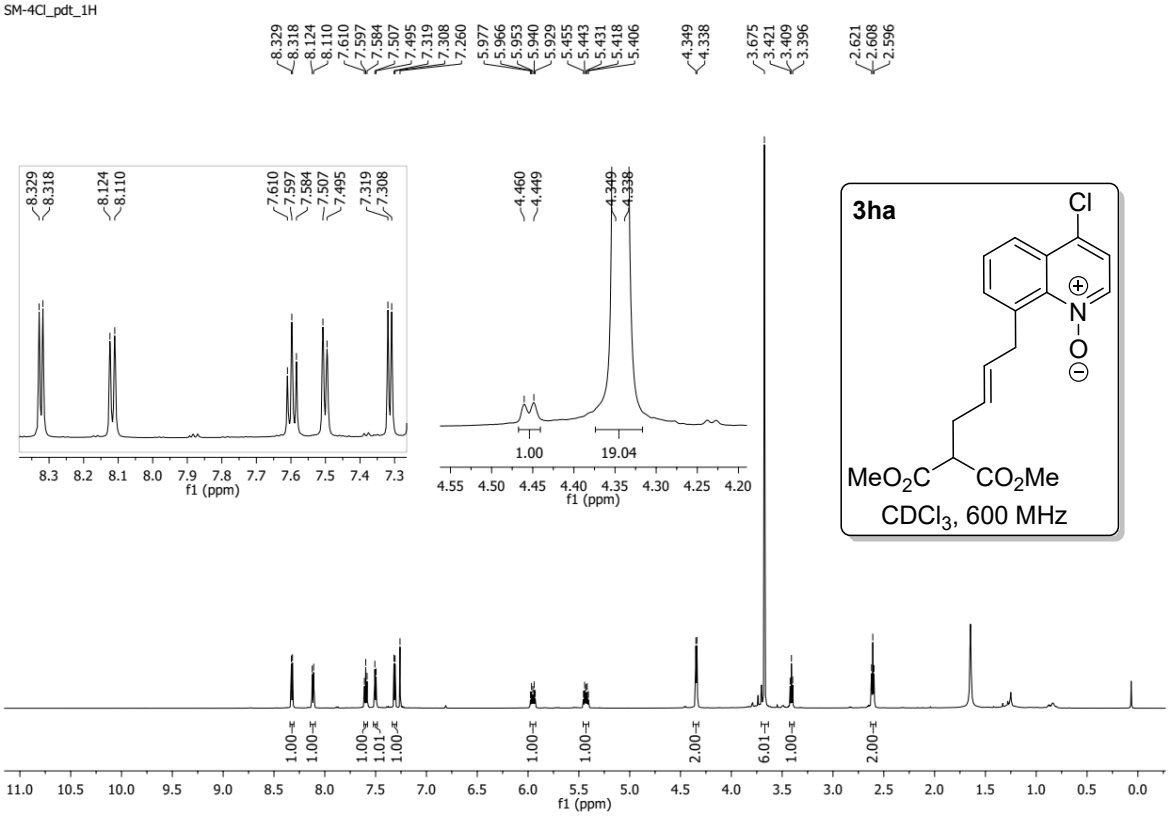

SM-3furanyl_pdt_13C
3fa
CDCl3, 150 MHz
MeO2C
CO2Me
f1 (ppm)

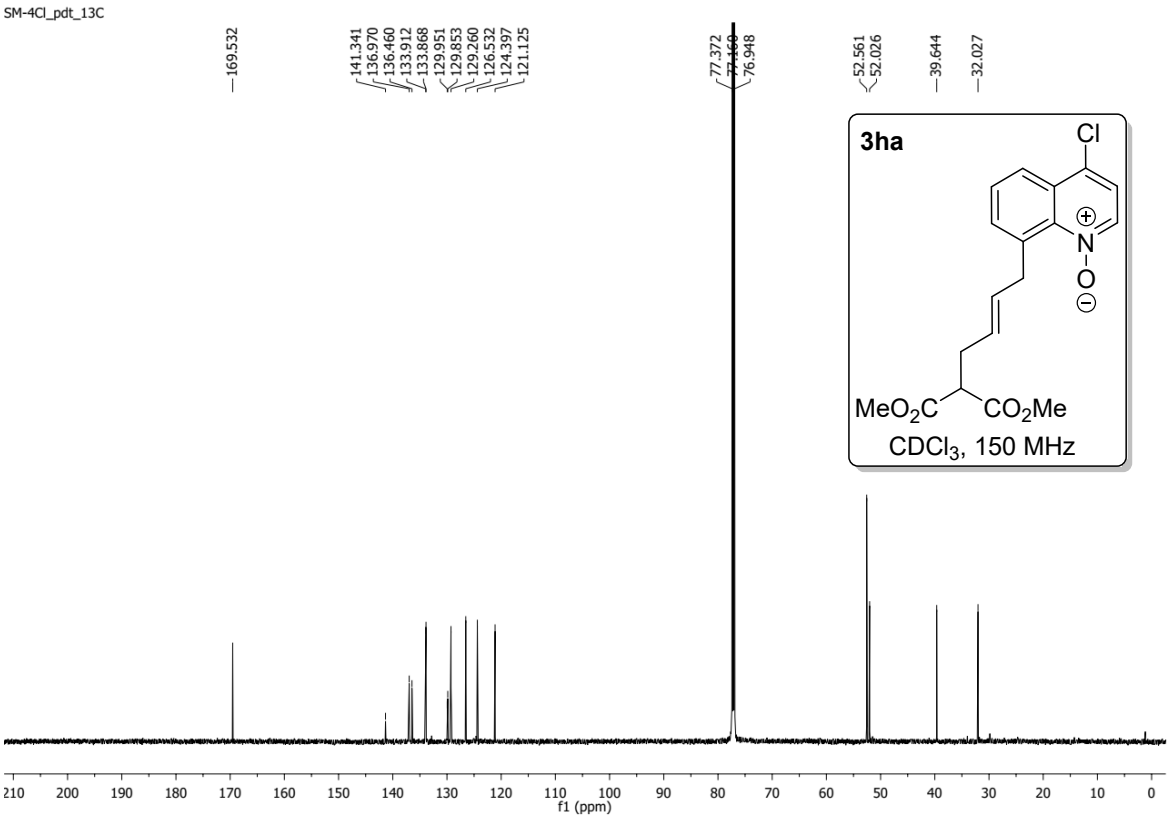

SM-3CF3Ph_pdt_1H
3ga
CF3
CDCl3, 500 MHz
MeO2C
CO2Me
f1 (ppm)


SM-3CF3Ph_pdt_13C
3ga
CF3
CDCl3, 150 MHz
MeO2C
CO2Me
f1 (ppm)

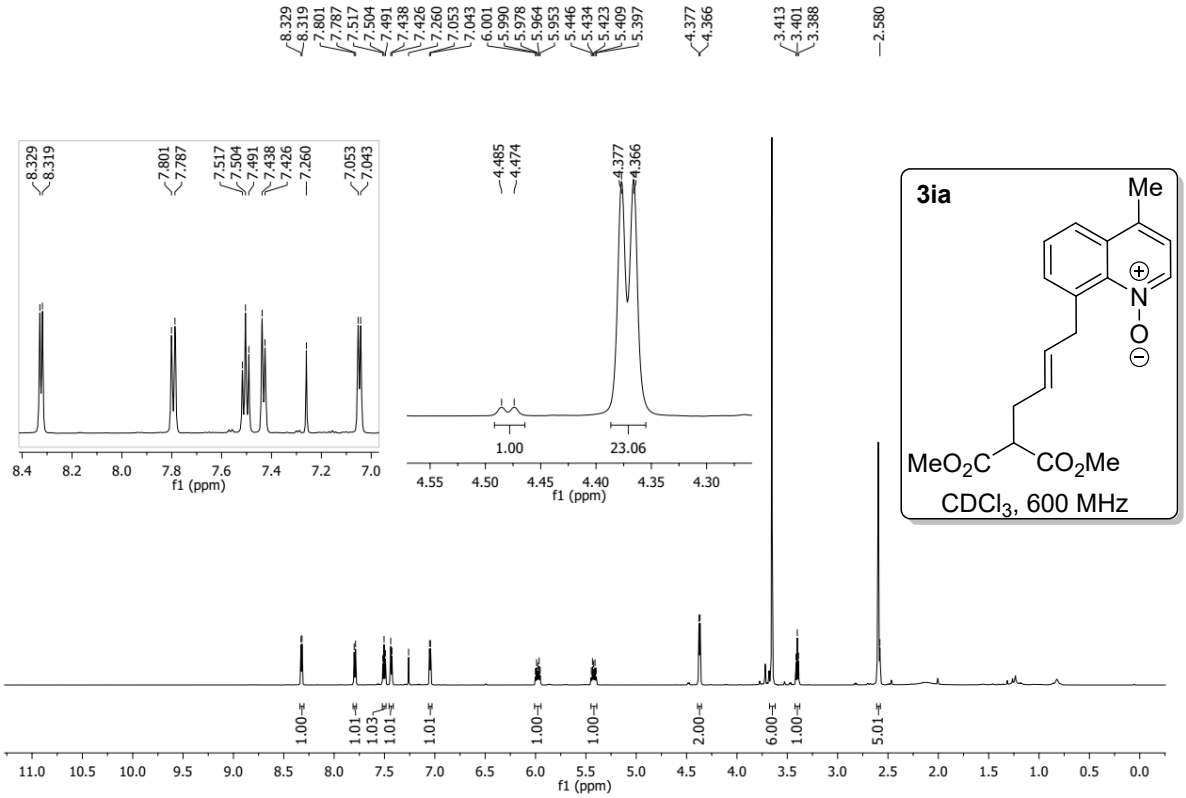
SM-3CF3Ph_pdt_19F



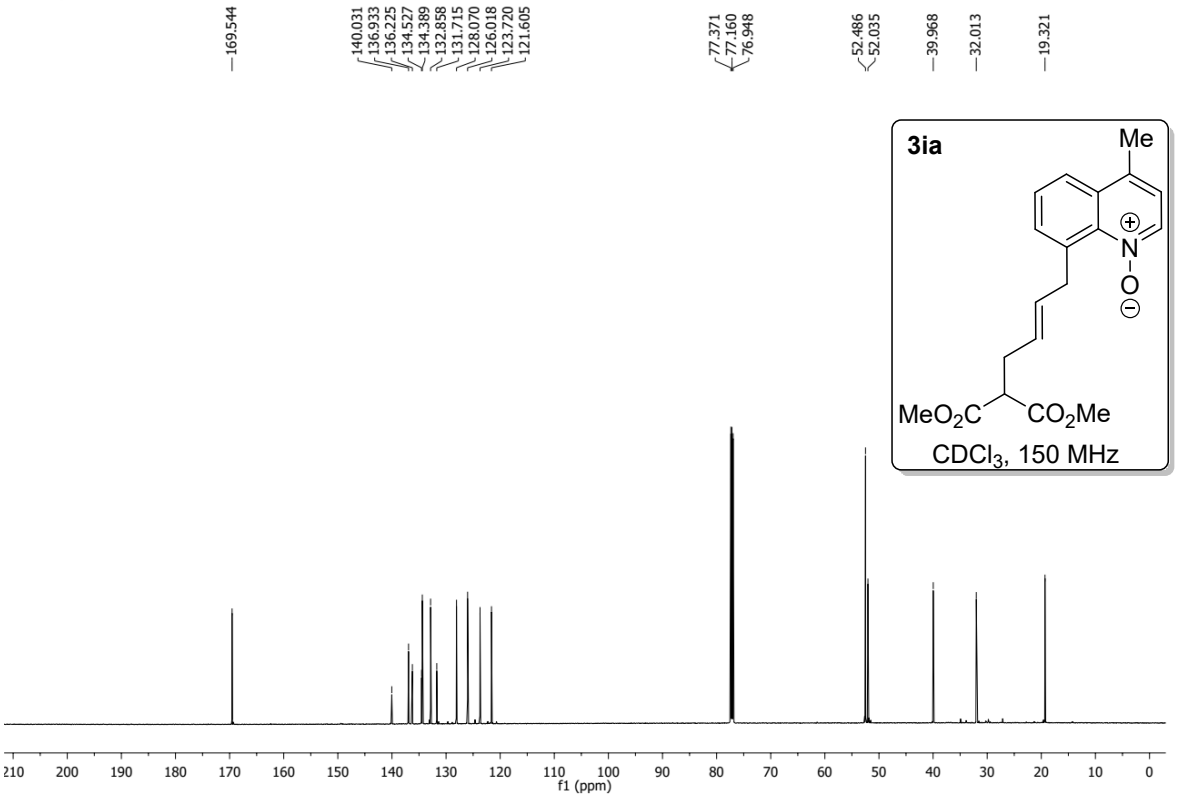

SM-4Cl_pdt_1H
3ha
Cl
N
O
MeO2C
CO2Me
CDCl3, 600 MHz
1.00
19.04
f1 (ppm)

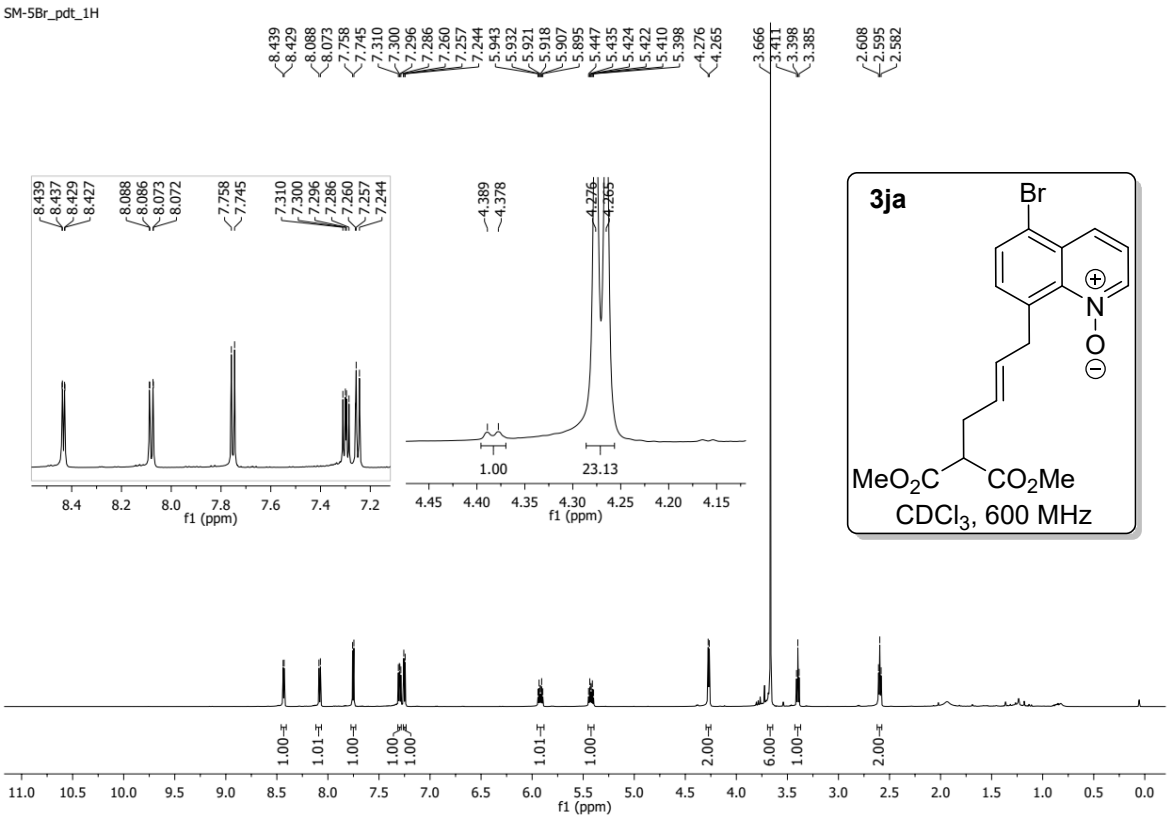

SM-4Cl_pdt_13C
3ha
Cl
N
O
MeO2C
CO2Me
CDCl3, 150 MHz
f1 (ppm)

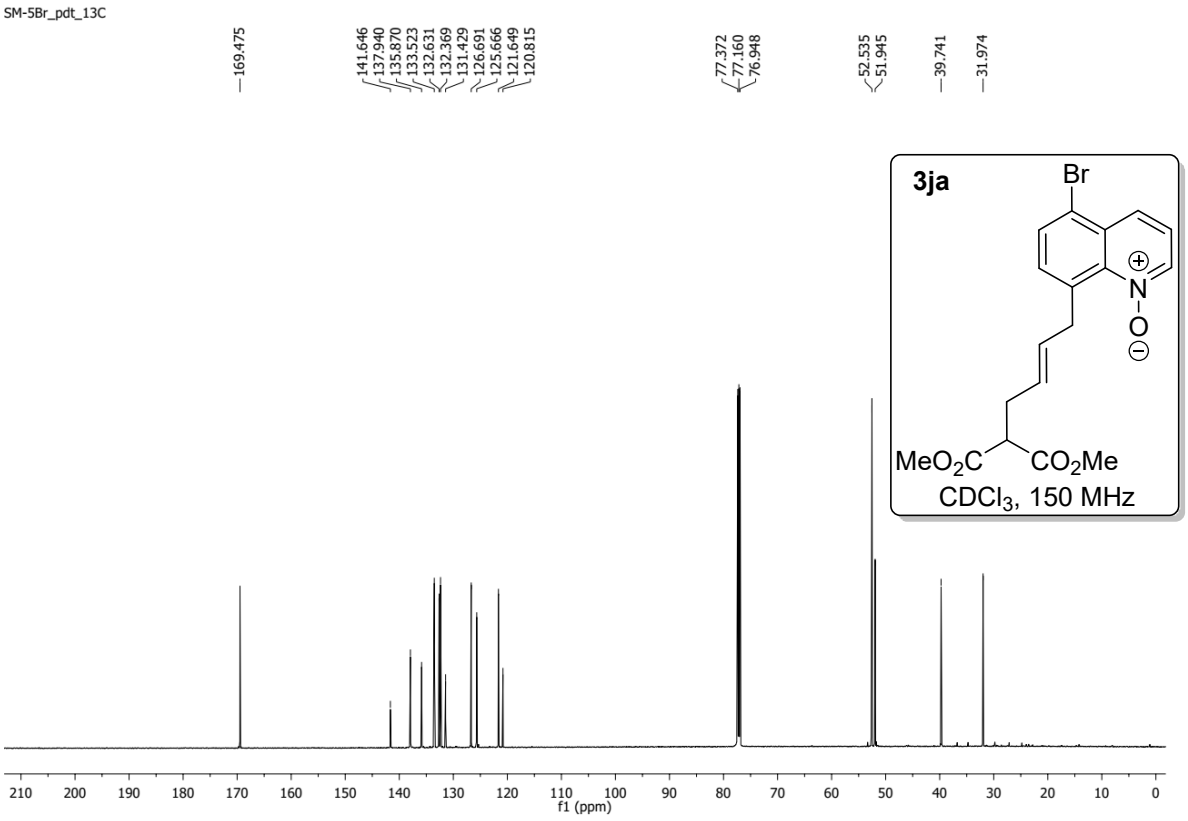
SM-4Me_pdt_1H

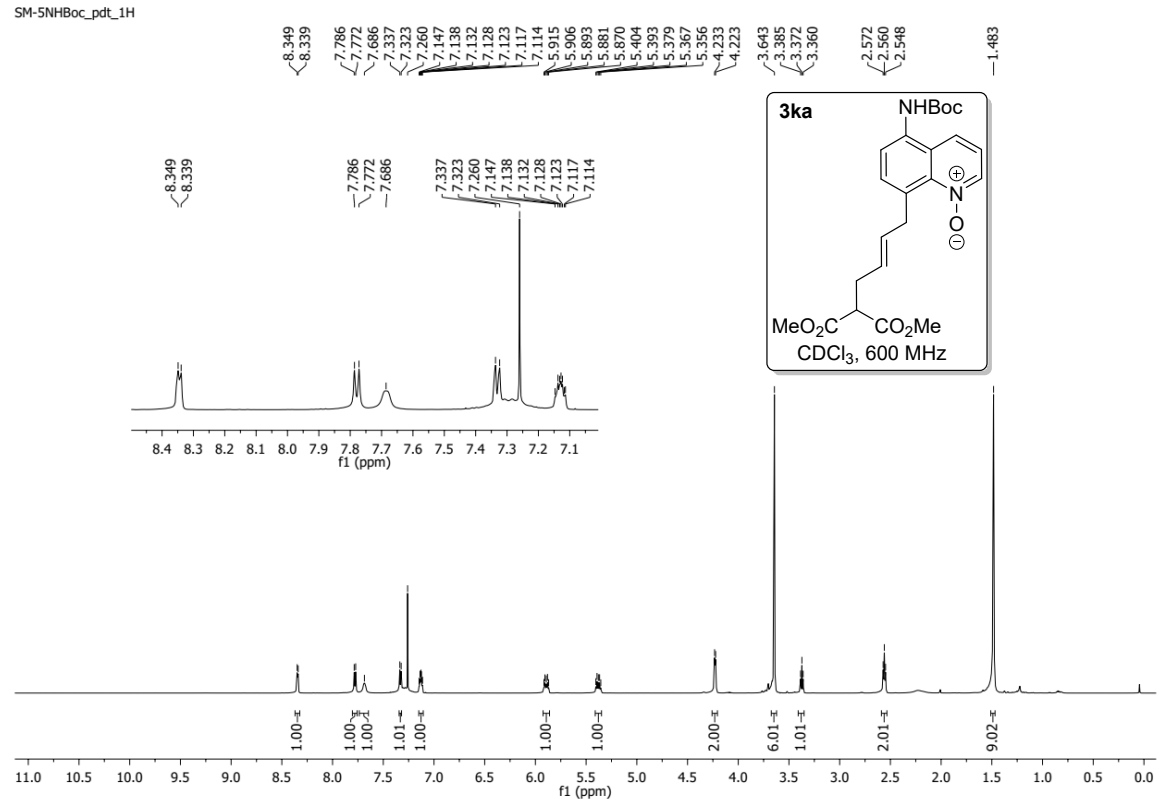


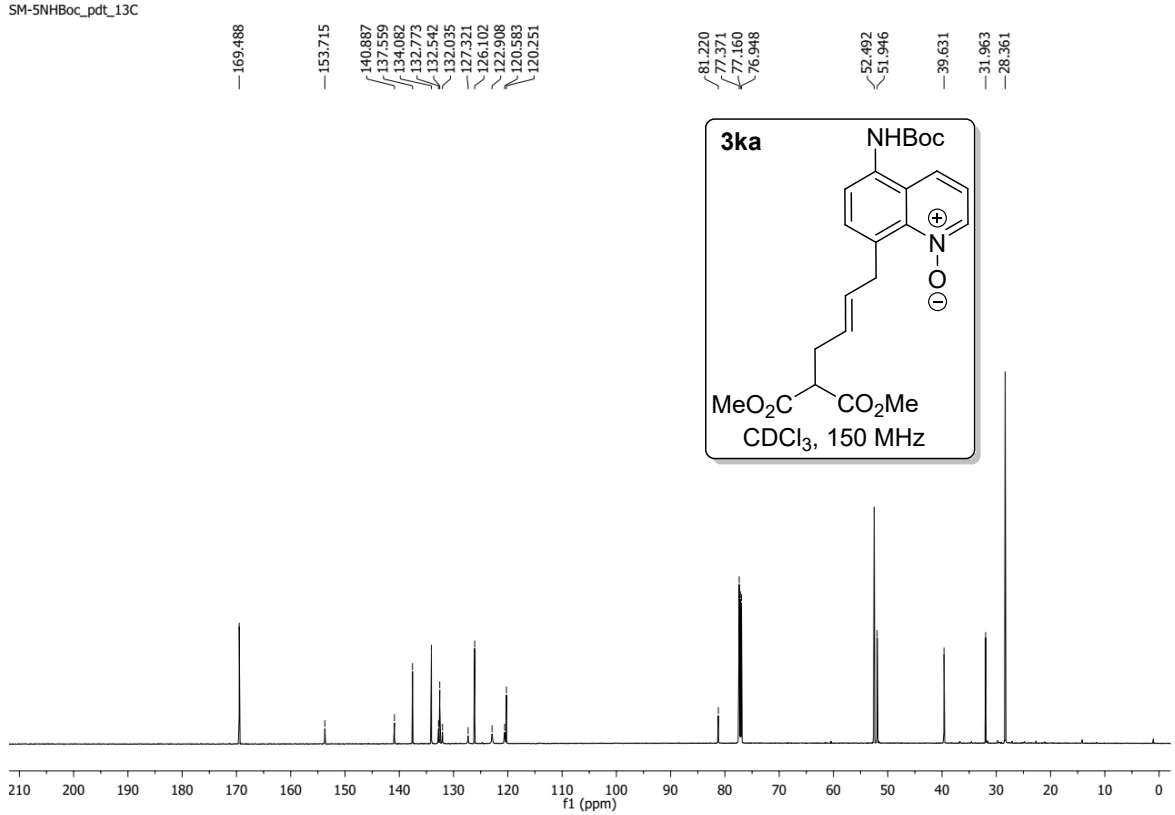
SM-4Me_pdt_13C



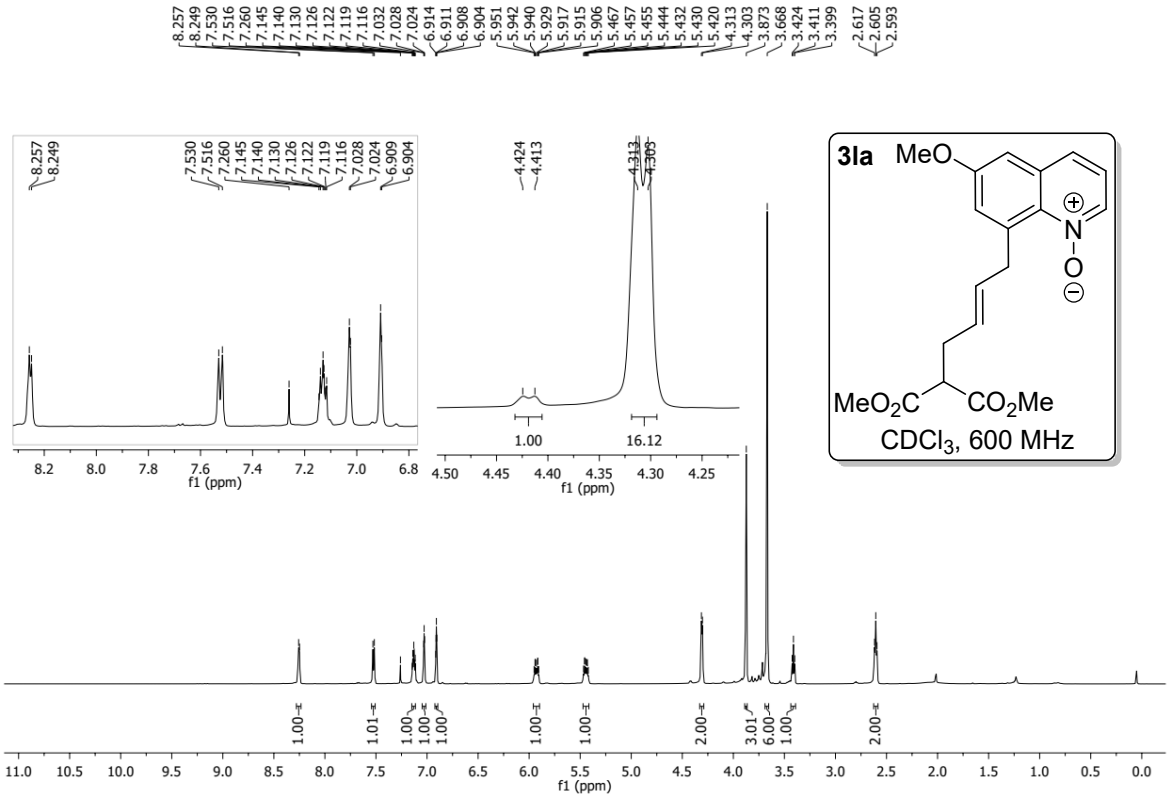

SM-5Br_pdt_1H
3ja
Br
MeO2C
CO2Me
CDCl3, 600 MHz
f1 (ppm)


SM-5Br_pdt_13C
3ja
Br
MeO2C
CO2Me
CDCl3, 150 MHz
f1 (ppm)

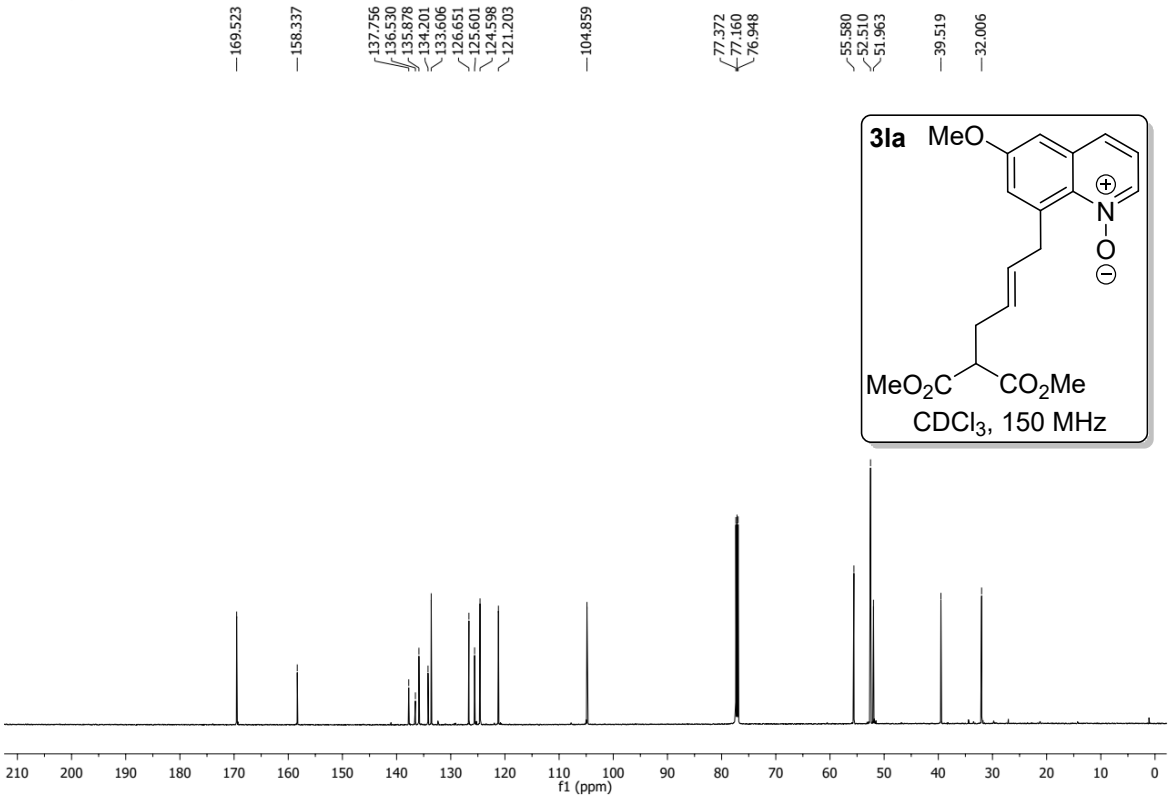

SM-5NHBoc_pdt_1H
3ka
NHBoc
MeO2C
CO2Me
CDCl3, 600 MHz
f1 (ppm)

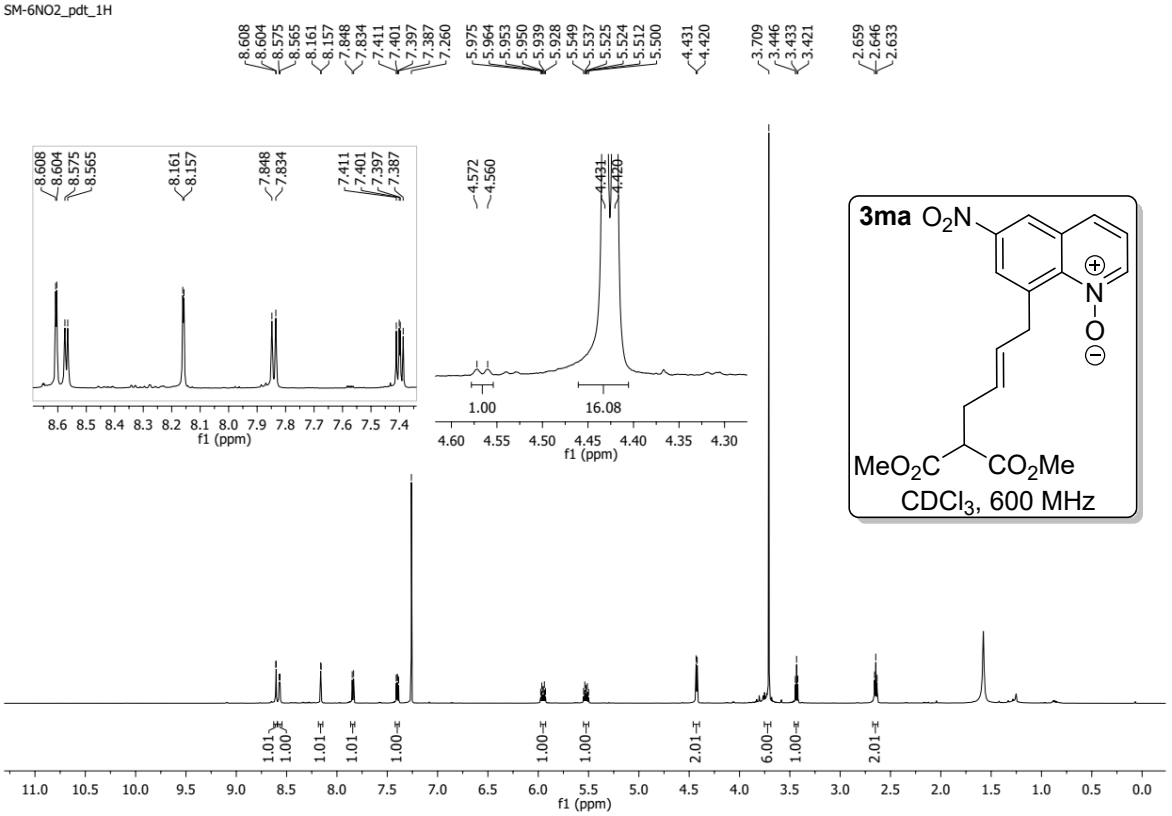

SM-5NHBoc_pdt_13C
3ka
NHBoc
MeO2C
CO2Me
CDCl3, 150 MHz
f1 (ppm)

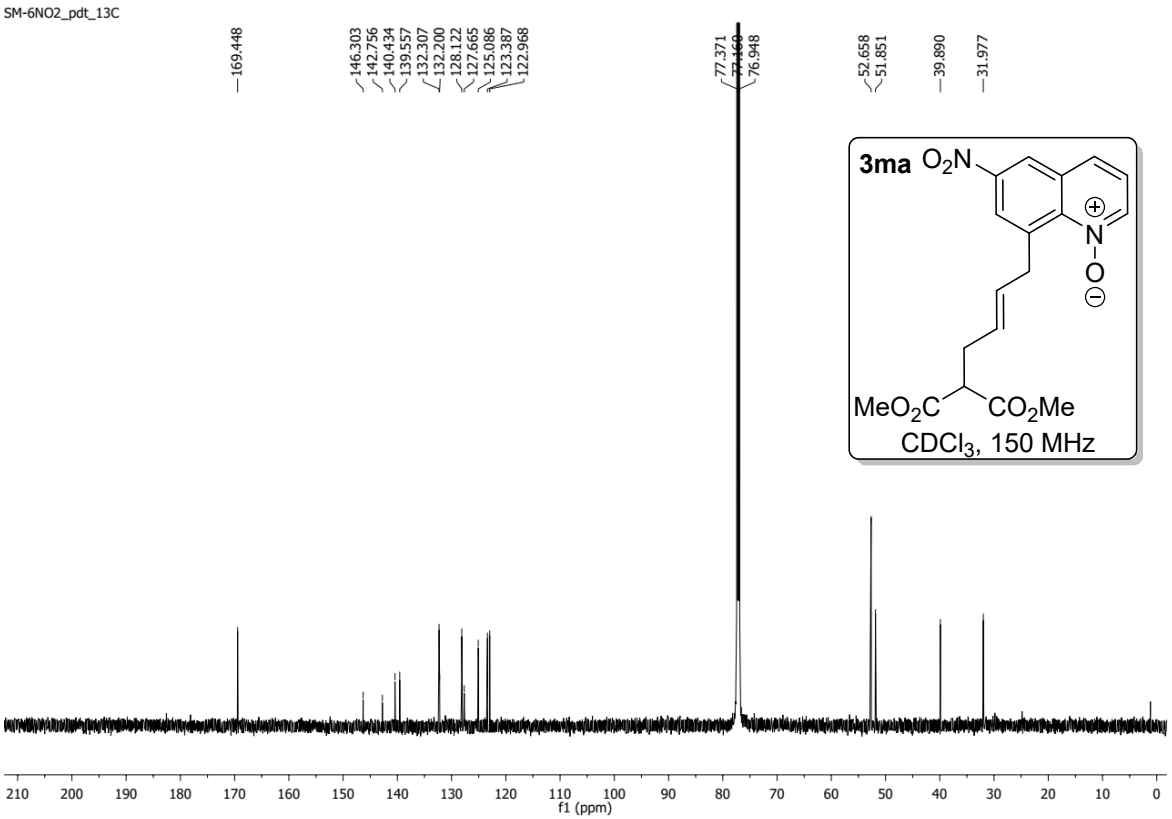
SM-6OMe_pdt_1H

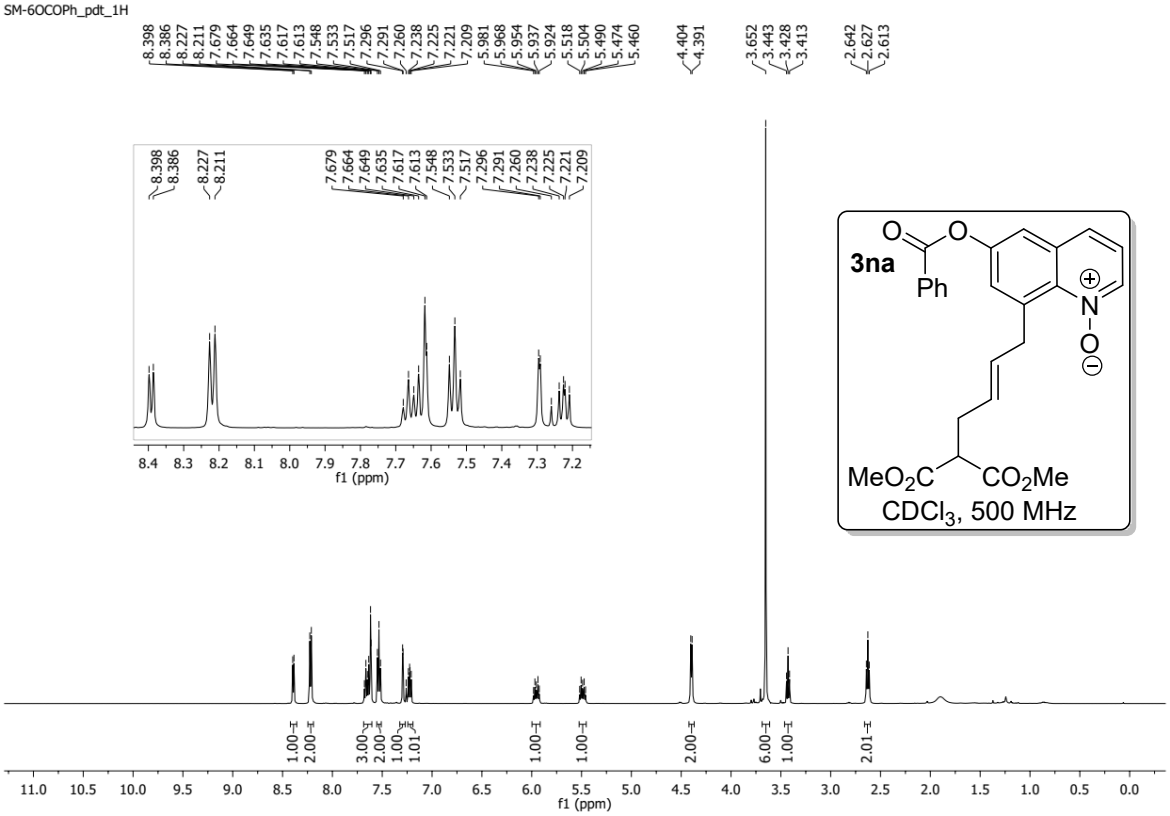


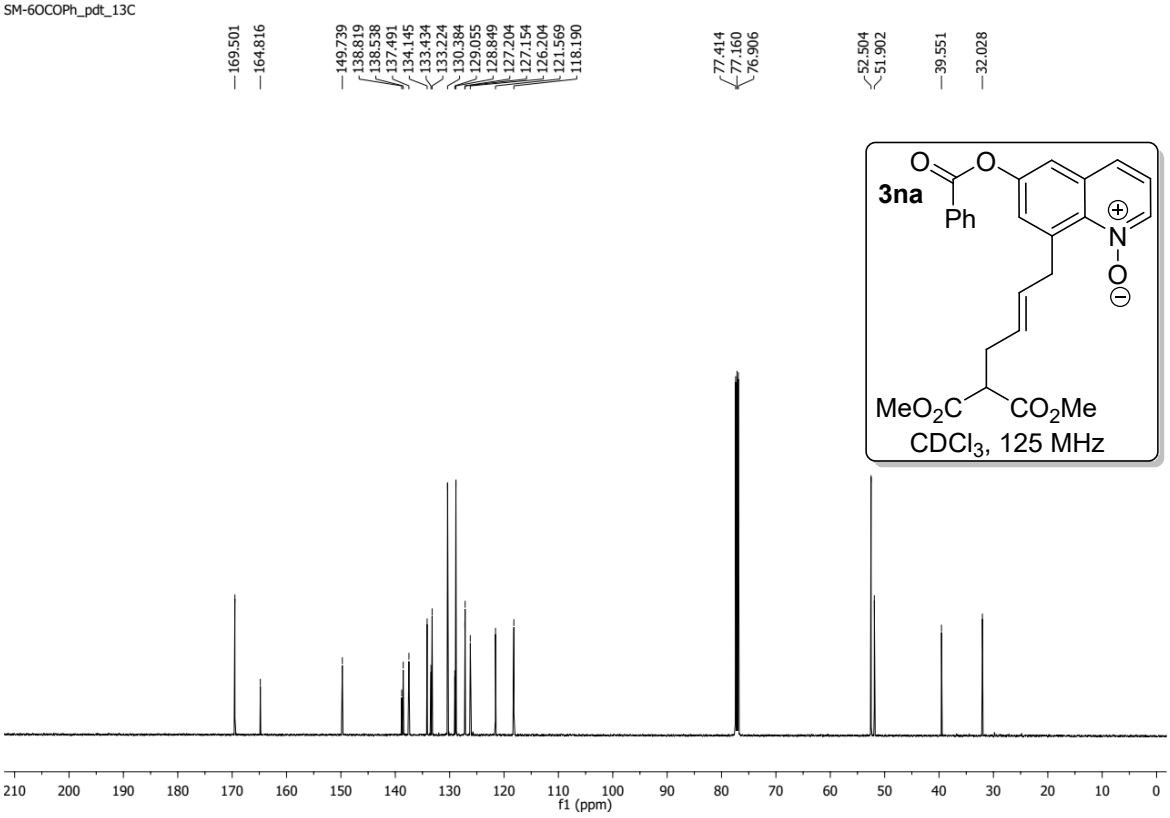
SM-6OMe_pdt_13C

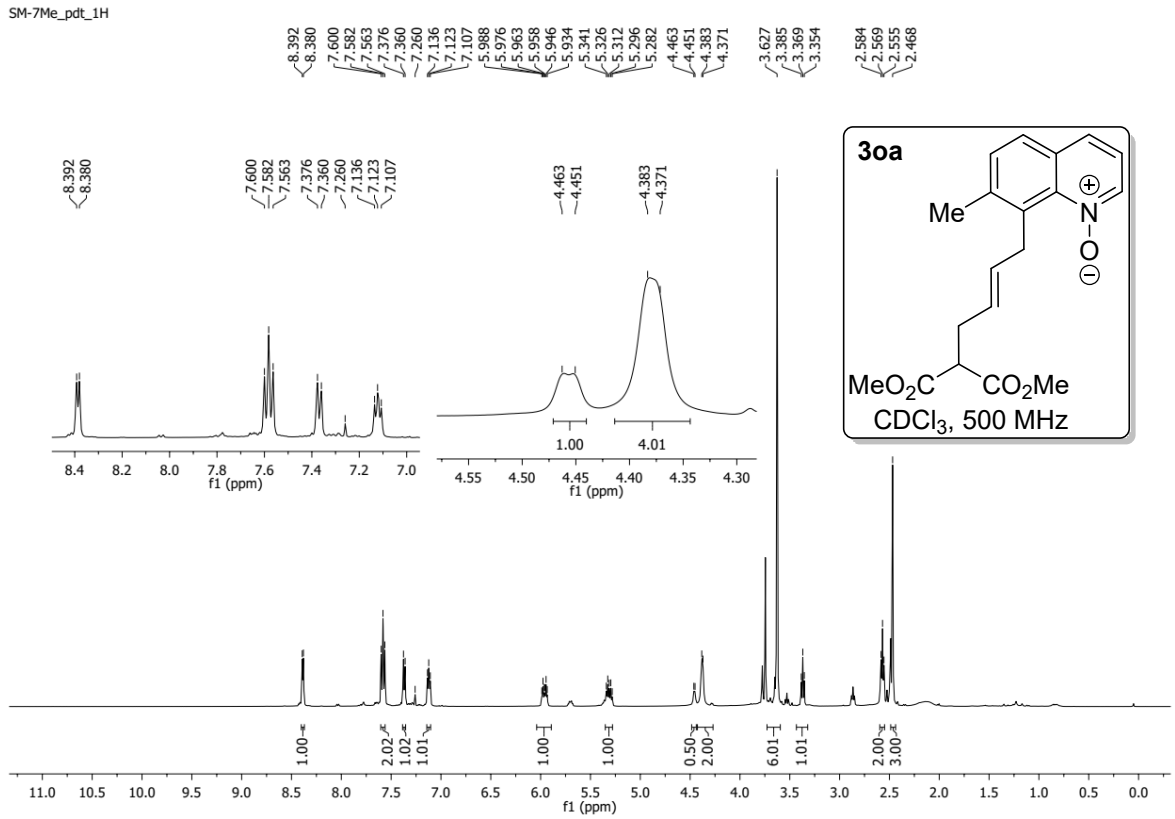


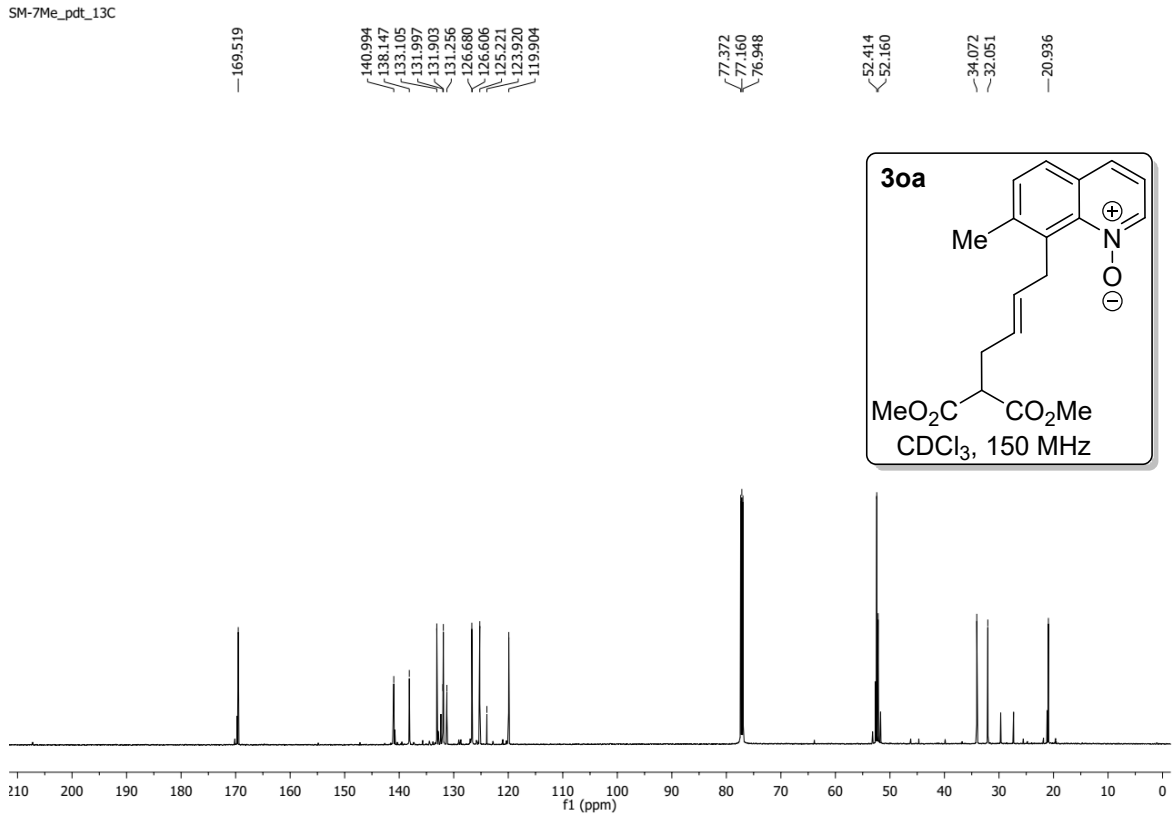

SM-6NO2_pdt_1H
3ma
CDCl3, 600 MHz
f1 (ppm)

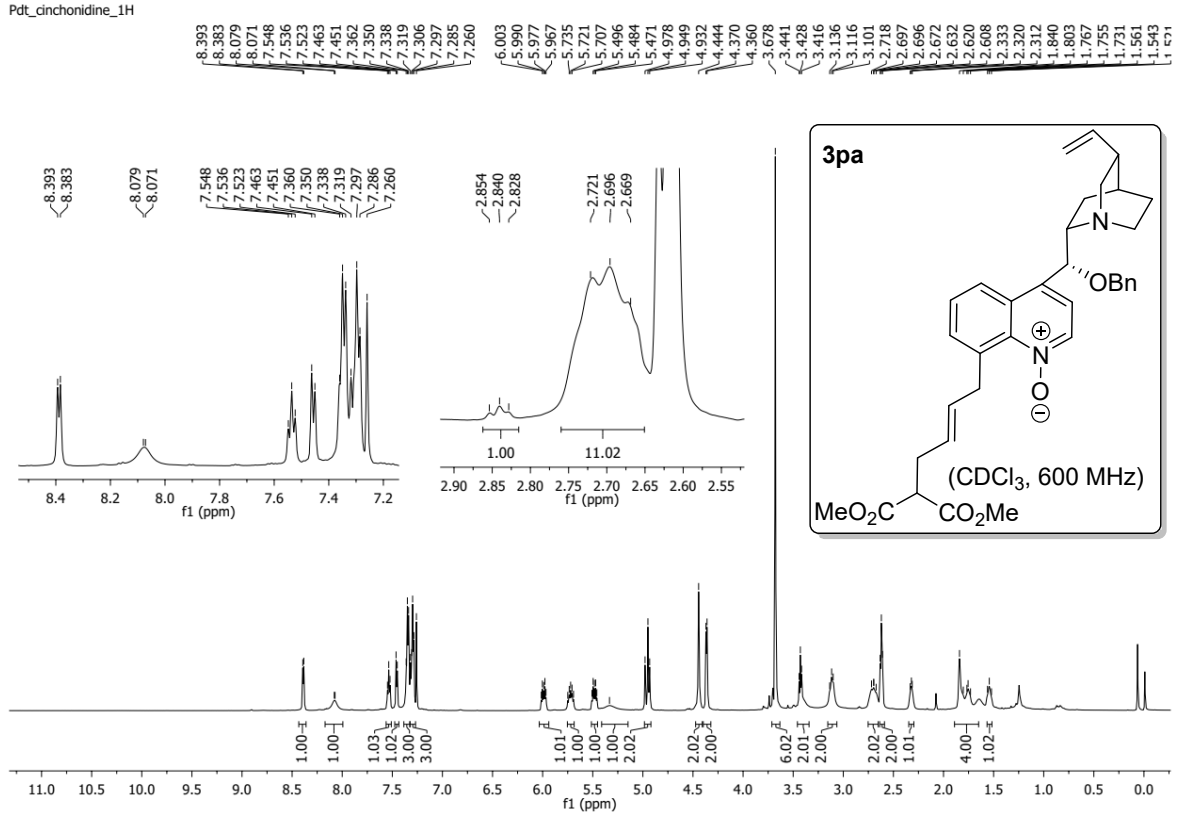

SM-6NO2_pdt_13C
3ma
CDCl3, 150 MHz
f1 (ppm)

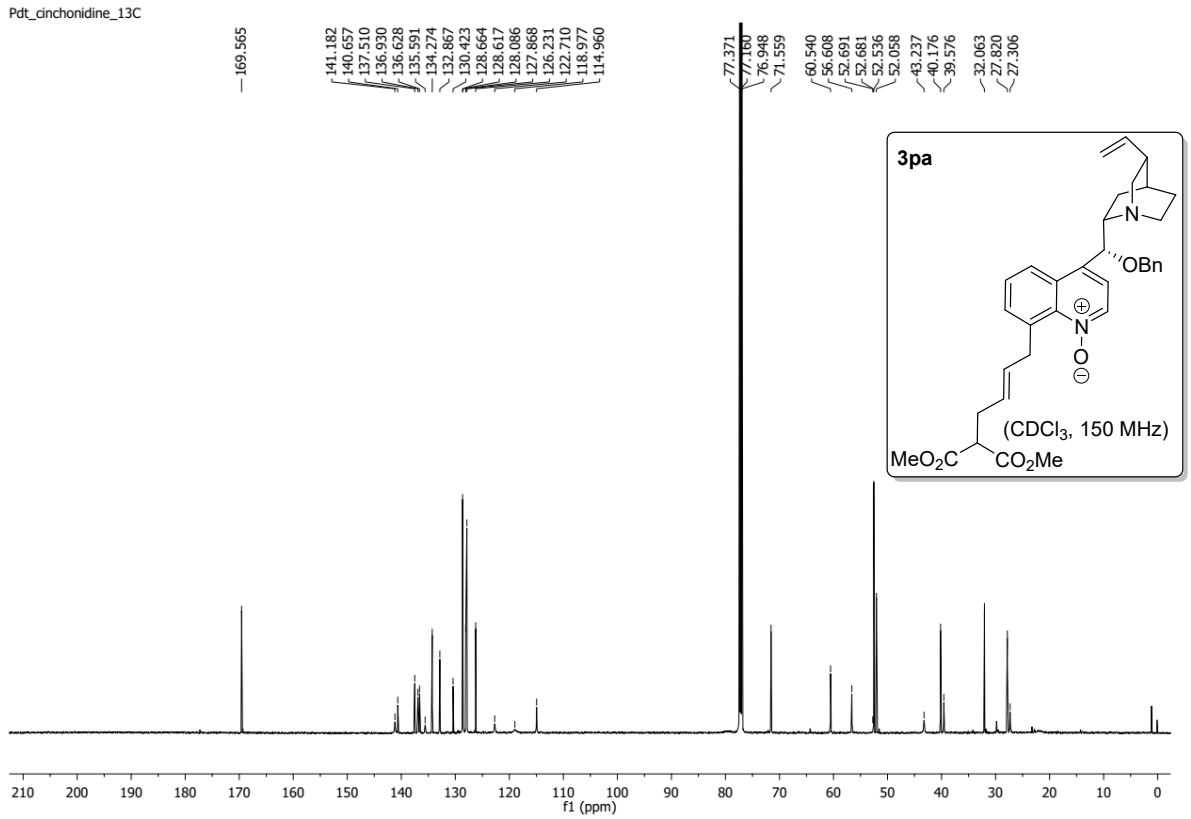

SM-6OCOPh_pdt_1H
3na
Ph
MeO2C
CO2Me
CDCl3, 500 MHz
f1 (ppm)

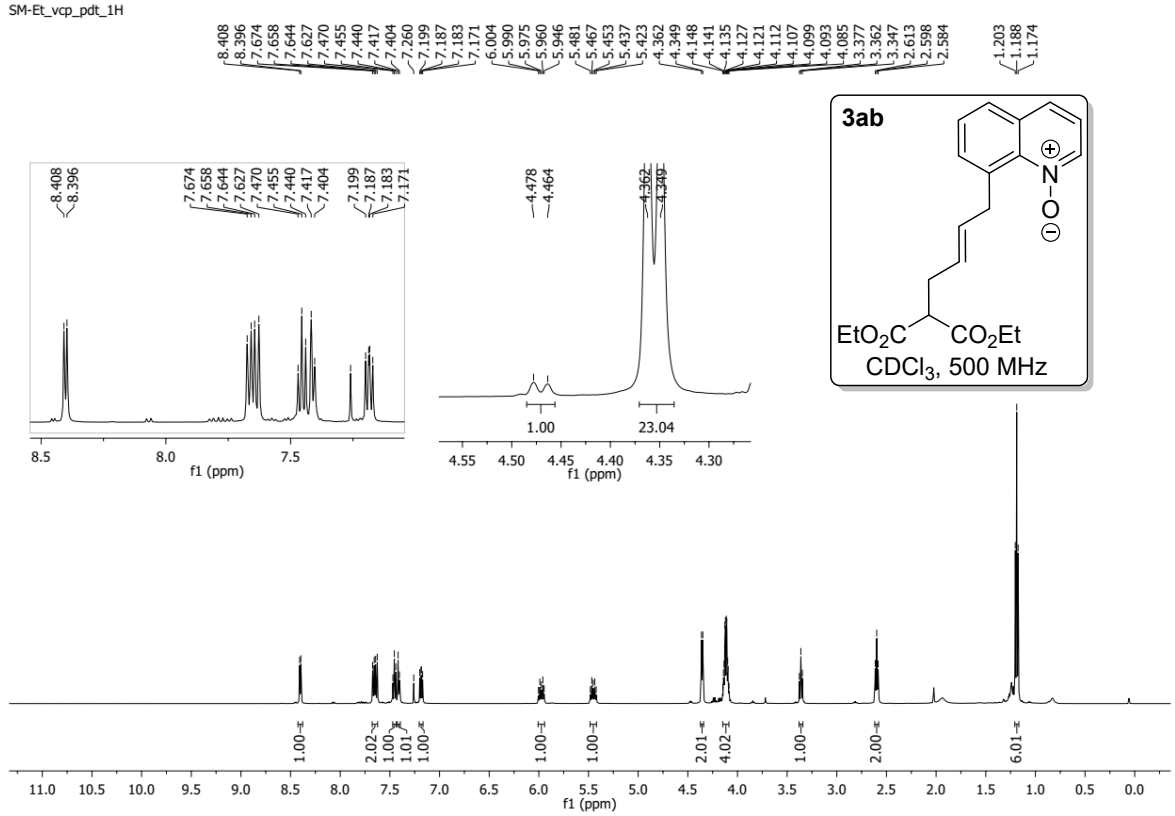

SM-6OCOPh_pdt_13C
3na
Ph
MeO2C
CO2Me
CDCl3, 125 MHz
f1 (ppm)

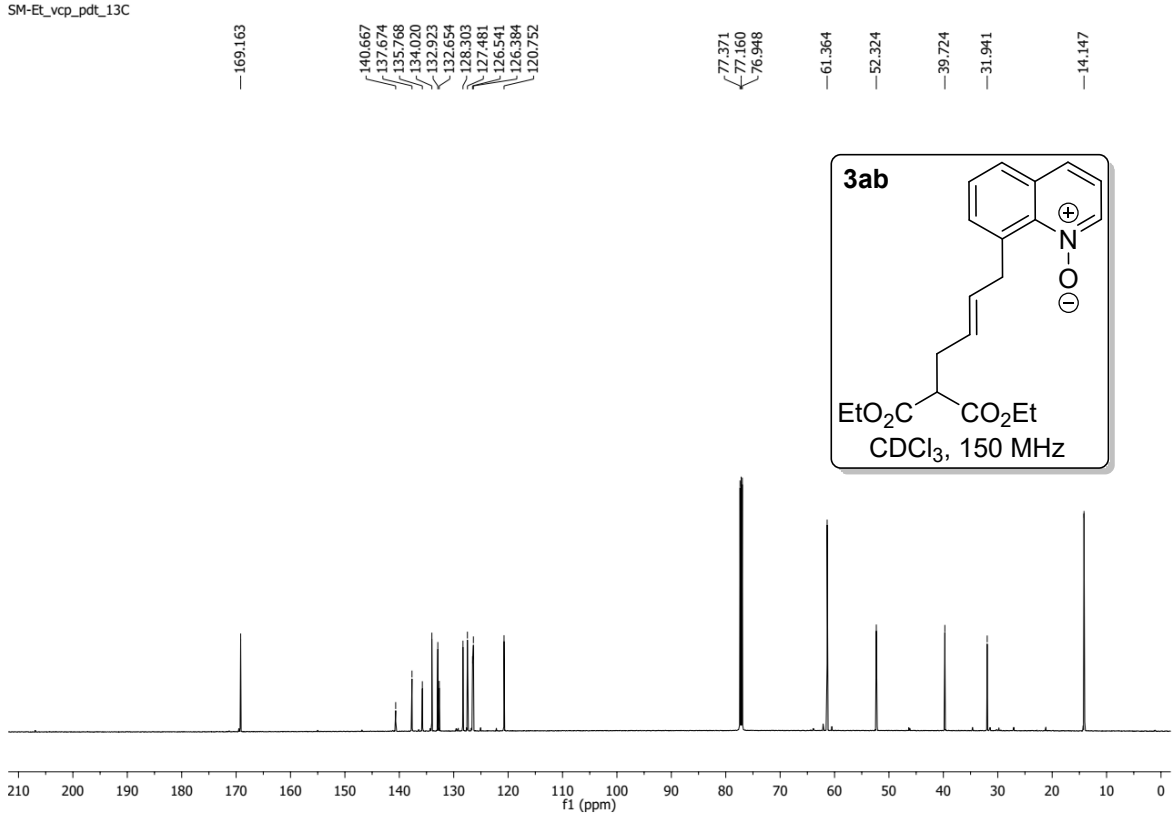

SM-7Me_pdt_1H
3oa
Me
N
O
MeO2C
CO2Me
CDCl3, 500 MHz
f1 (ppm)


SM-7Me_pdt_13C
3oa
Me
N
O
MeO2C
CO2Me
CDCl3, 150 MHz
f1 (ppm)

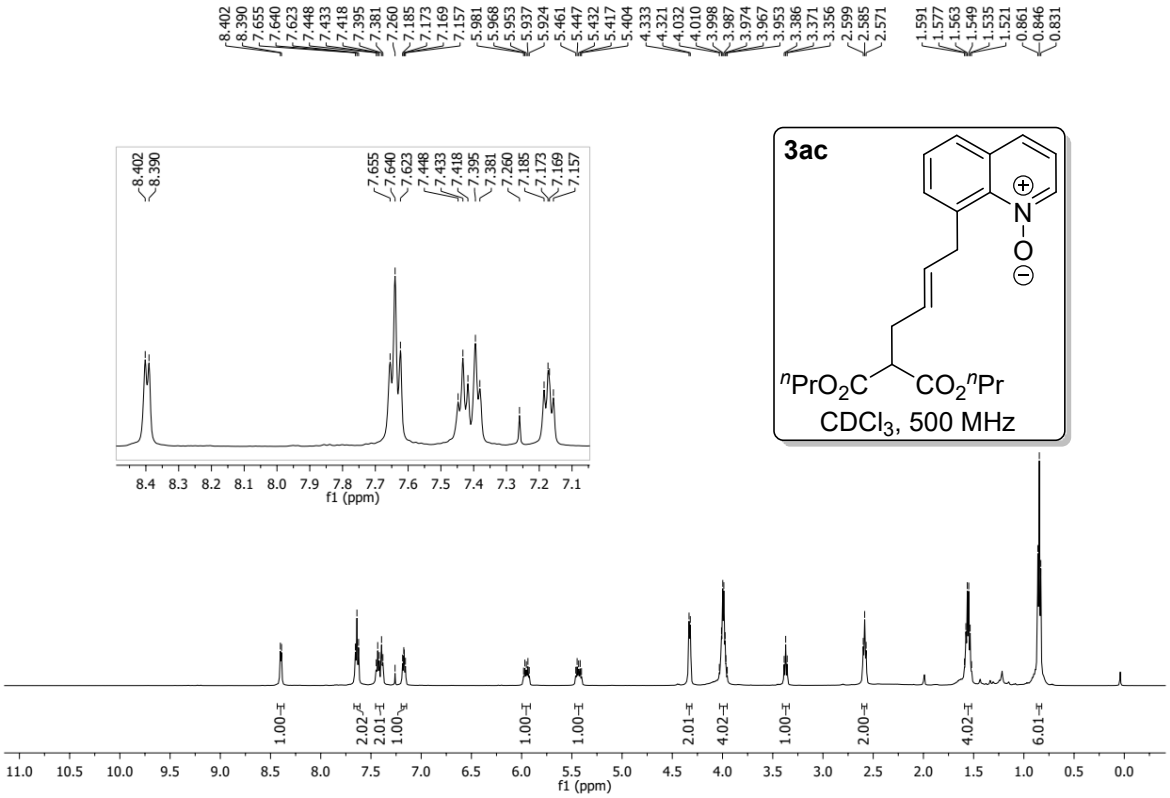

Pdt_cinchonidine_1H
3pa
(CDCl3, 600 MHz)
MeO2C
CO2Me
OBn
f1 (ppm)


Pdt_cinchonidine_13C
3pa
(CDCl3, 150 MHz)
MeO2C
CO2Me
OBn
f1 (ppm)

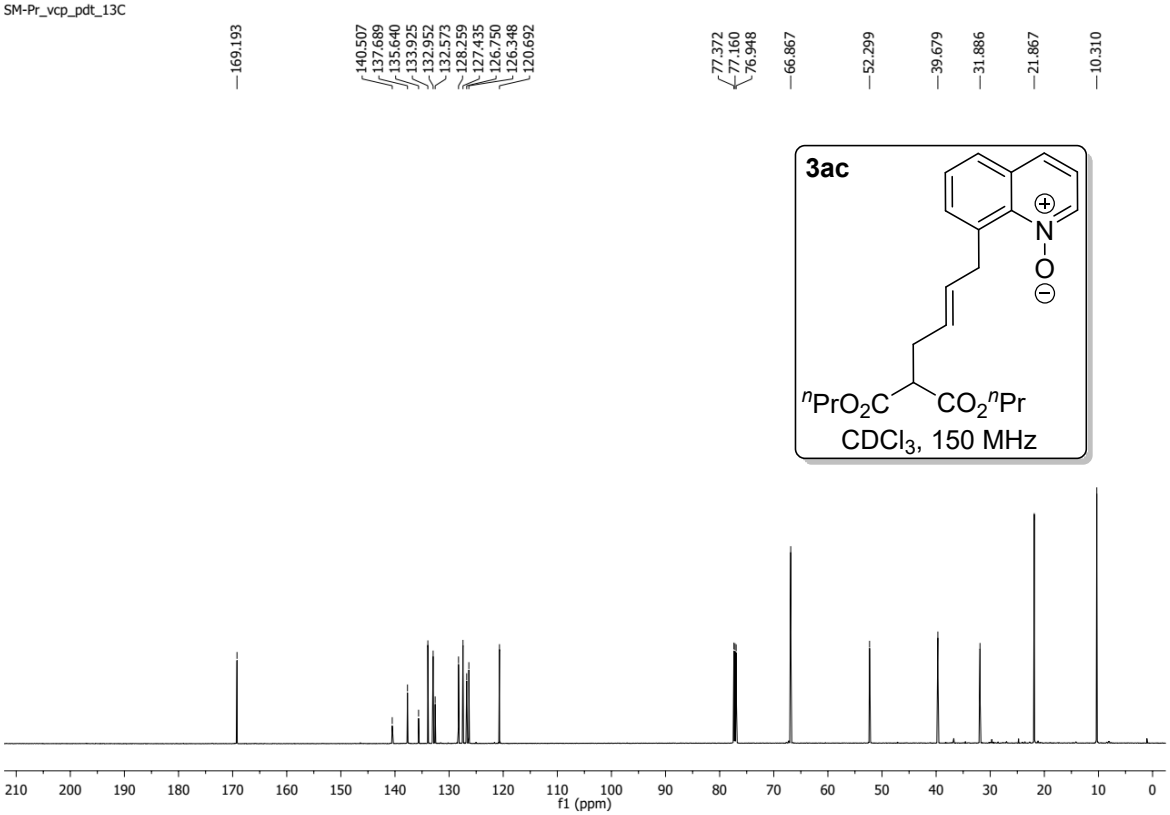

SM-Et_vcp_pdt_1H
3ab
EtO2C CO2Et
CDCl3, 500 MHz
f1 (ppm)

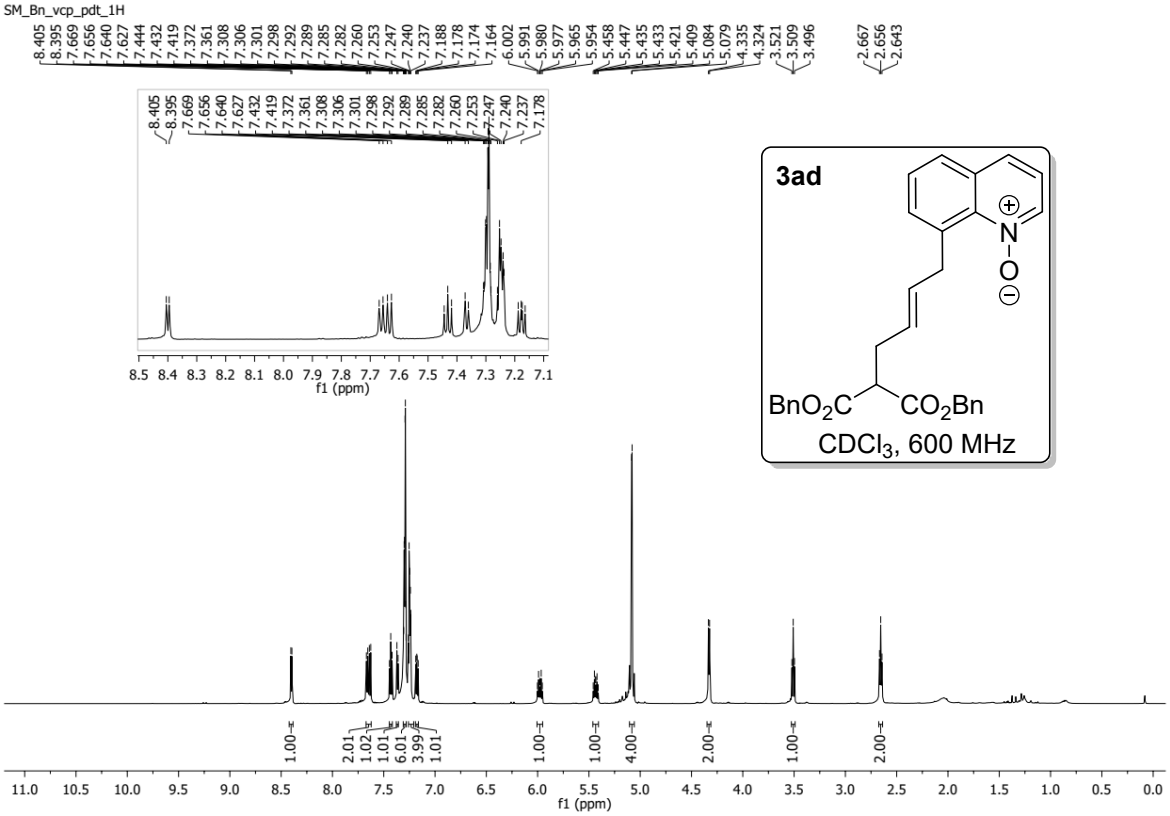

SM-Et_vcp_pdt_13C
3ab
EtO2C CO2Et
CDCl3, 150 MHz
f1 (ppm)

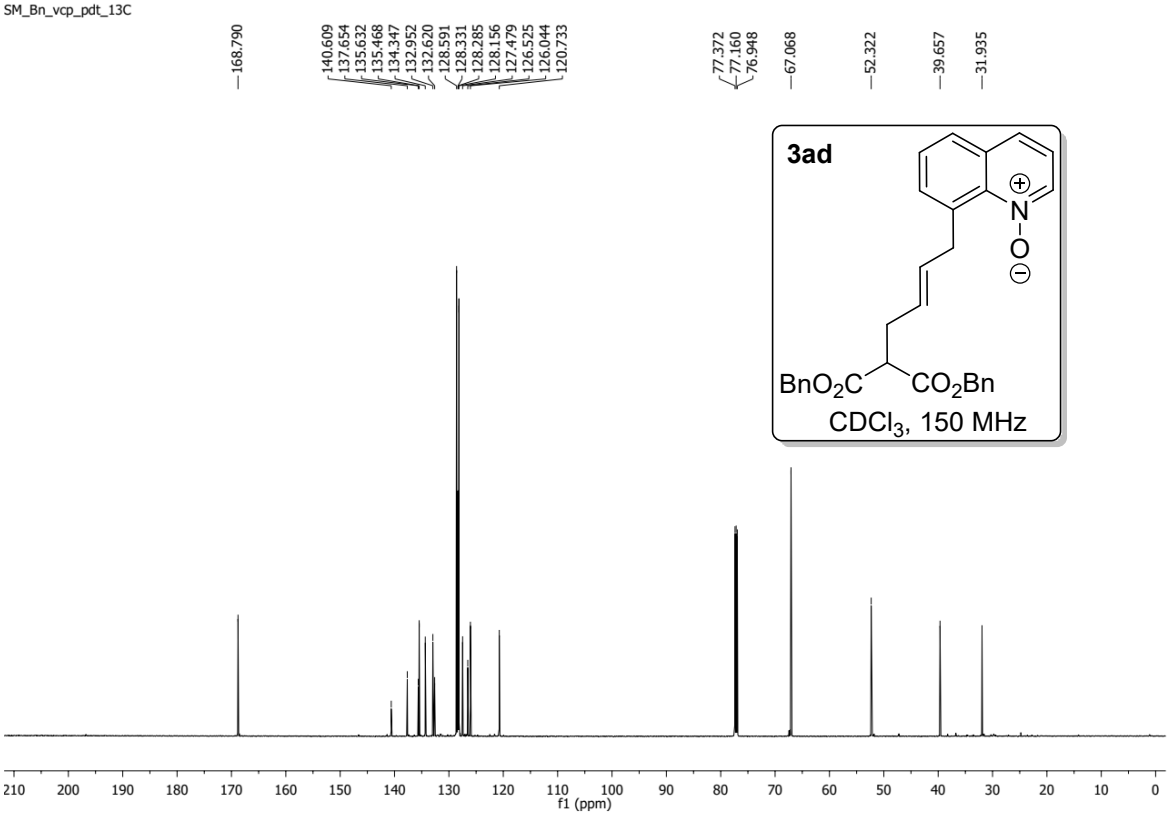
SM-Pr_vcp_pdt_1H

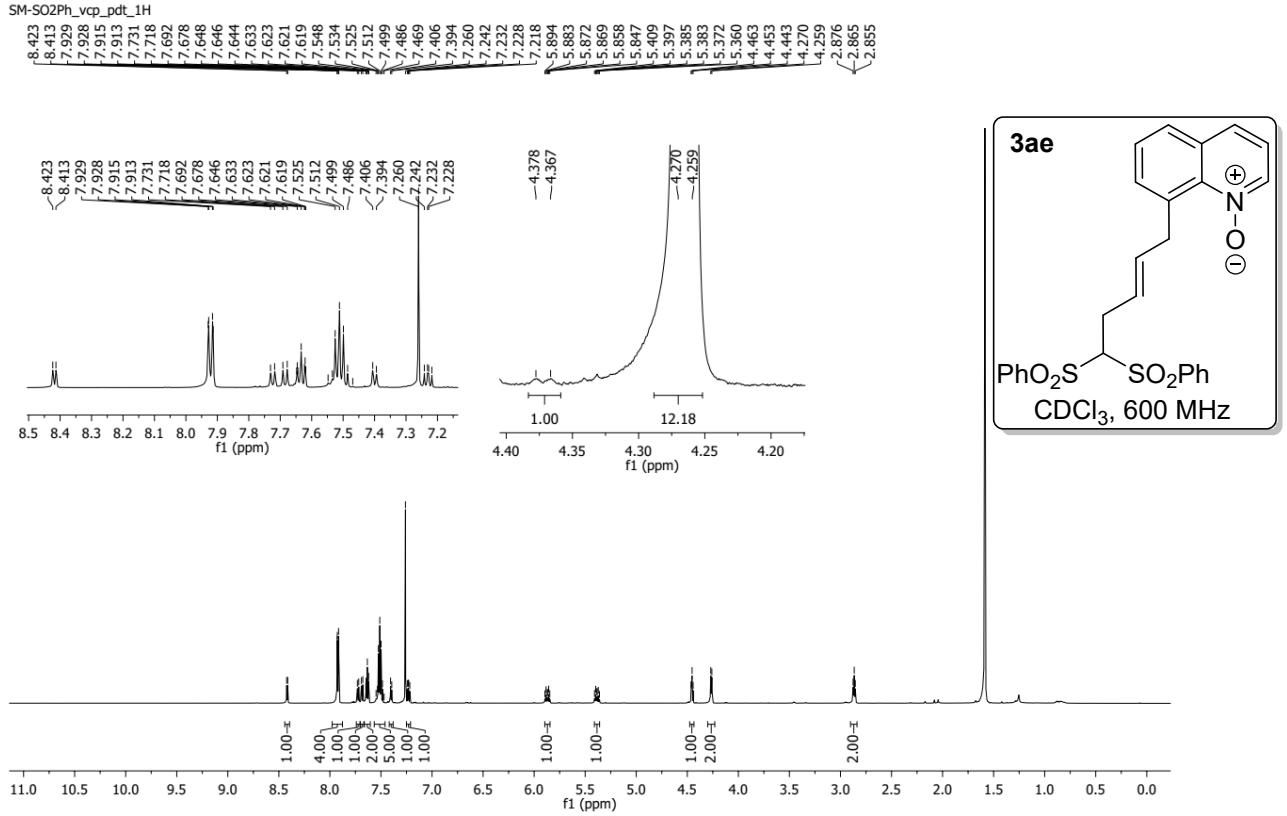


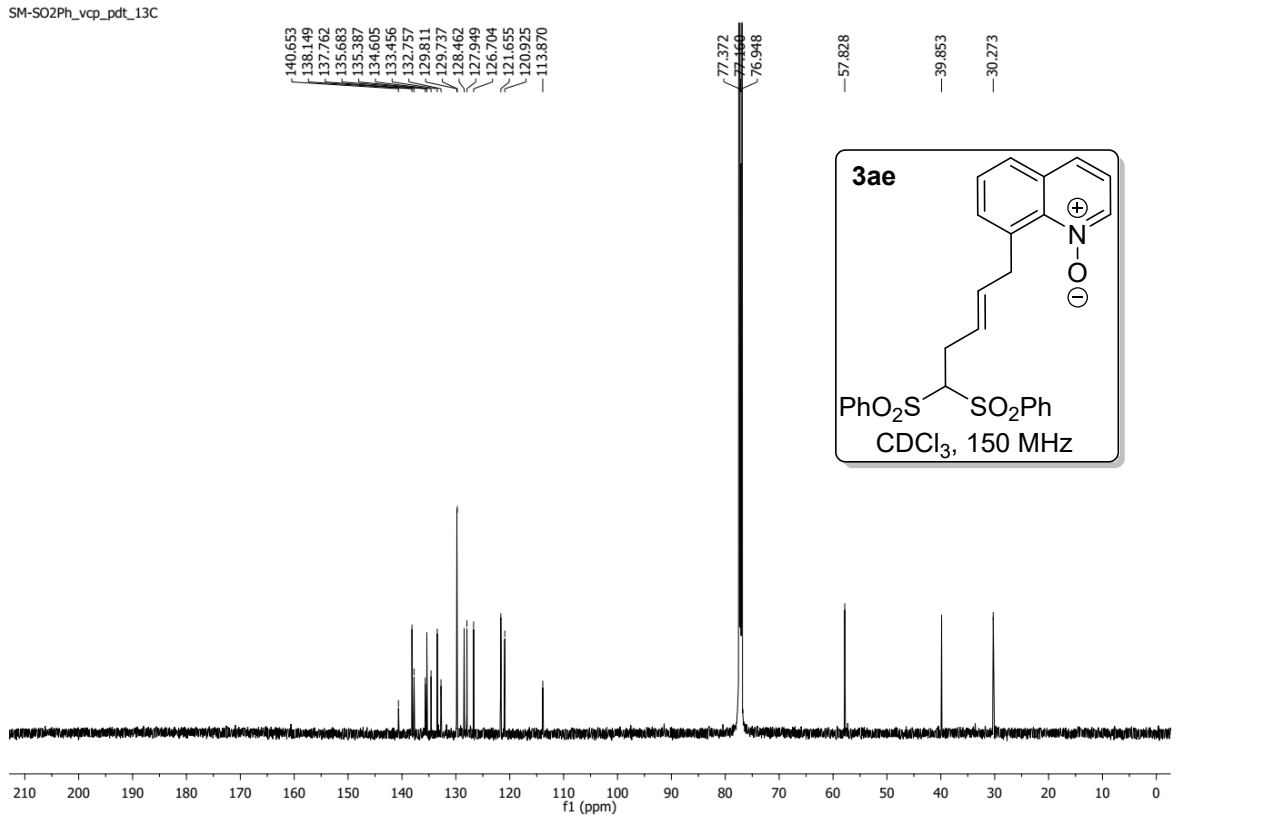
SM-Pr_vcp_pdt_13C

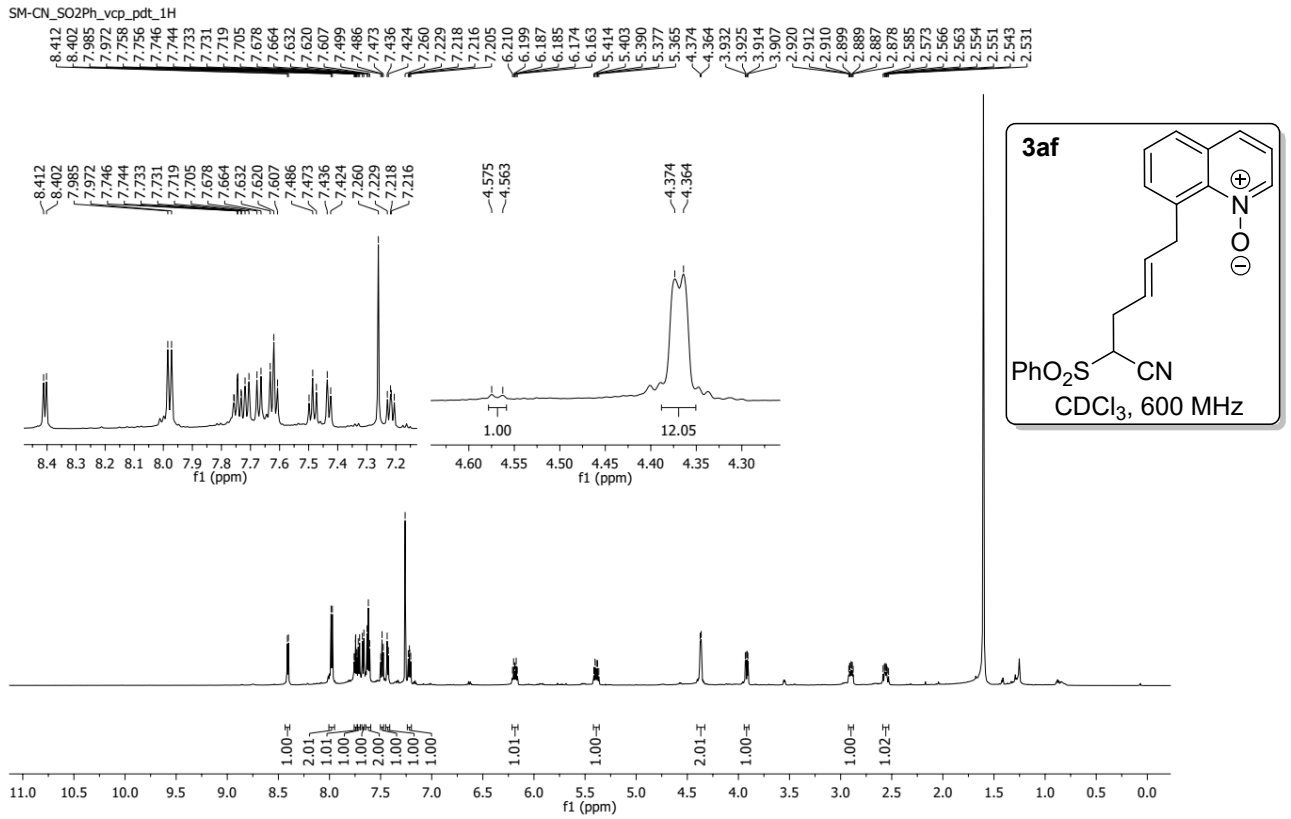


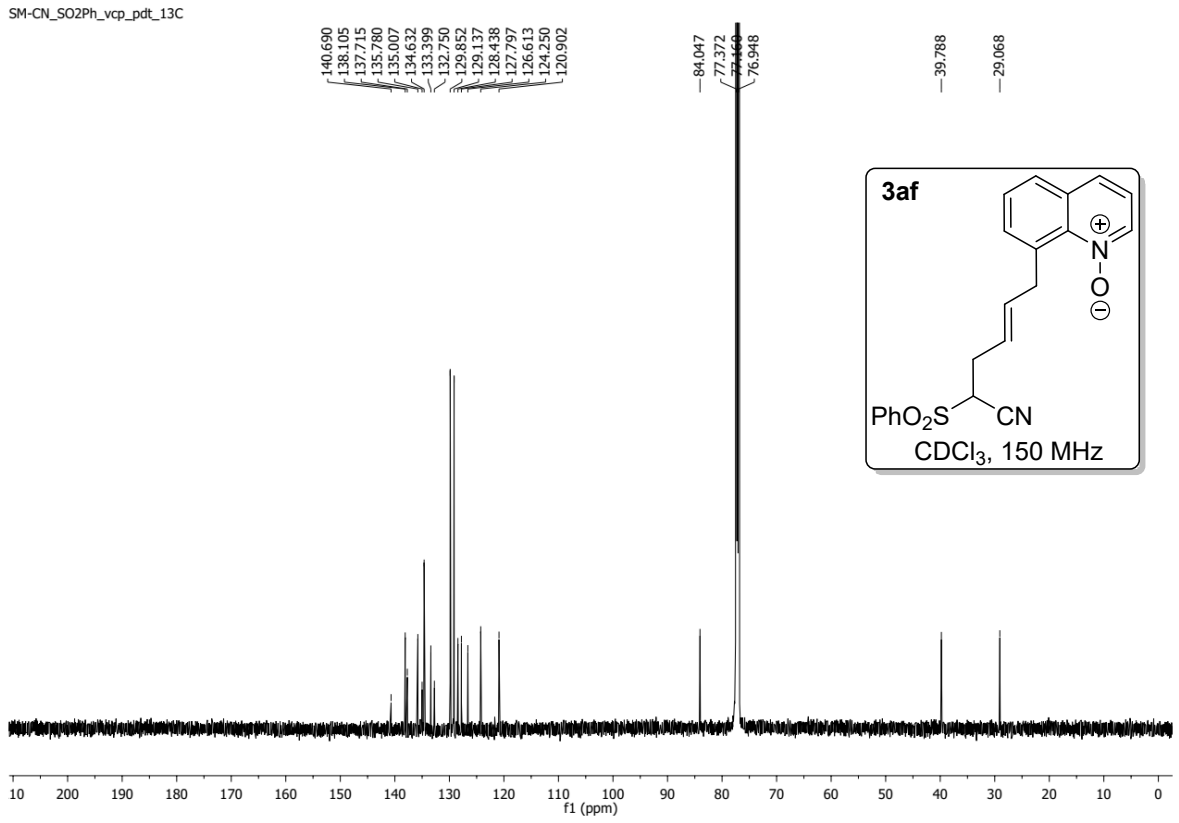

SM_Bn_vcp_pdt_1H
3ad
BnO2C
CO2Bn
CDCl3, 600 MHz
f1 (ppm)

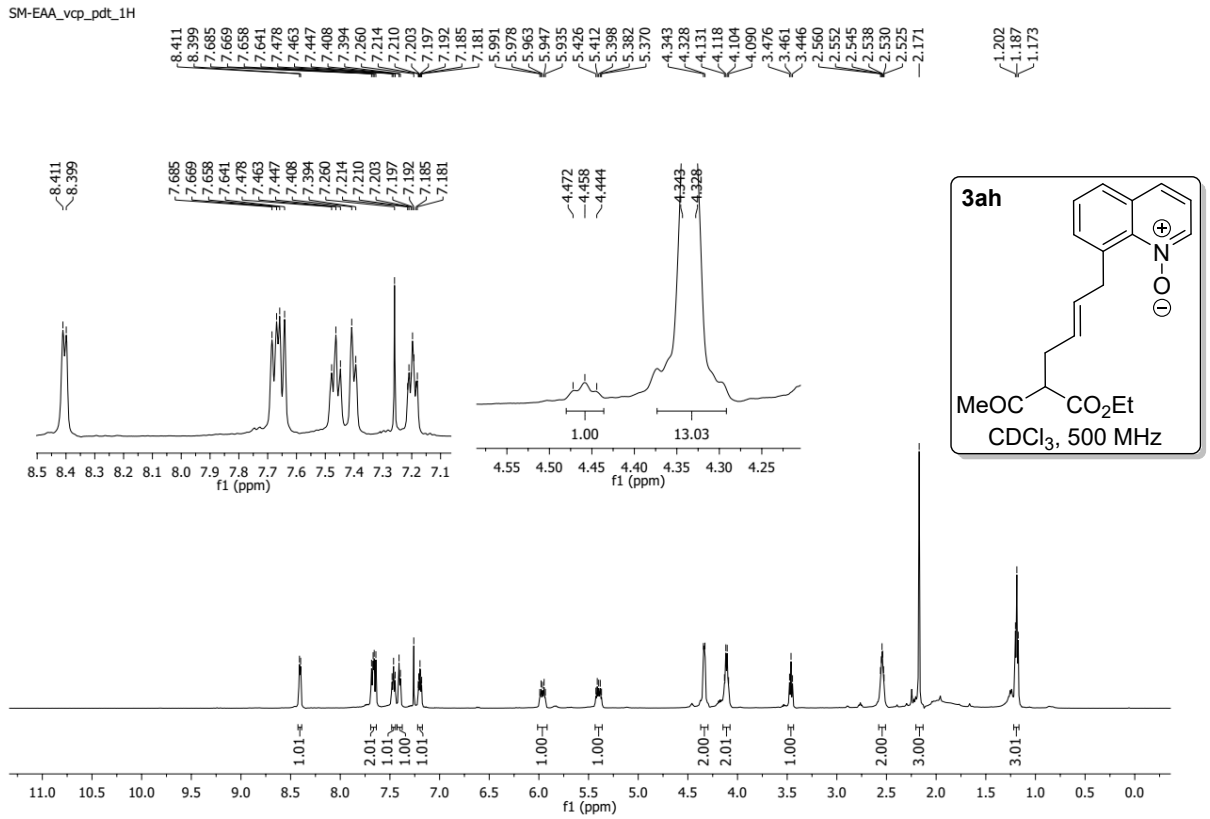

SM_Bn_vcp_pdt_13C
3ad
BnO2C
CO2Bn
CDCl3, 150 MHz
f1 (ppm)

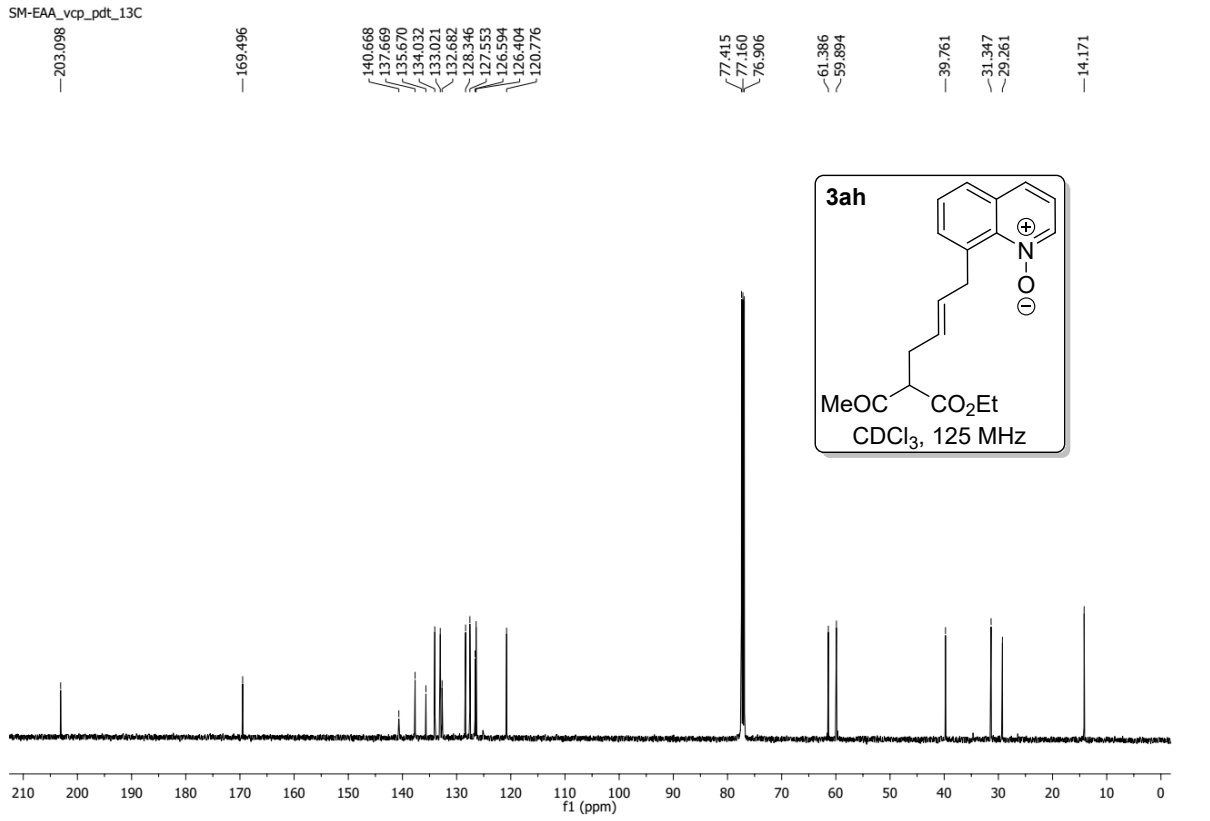

SM-SO2Ph_vcp_pdt_1H
3ae
PhO2S SO2Ph
CDCl3, 600 MHz
f1 (ppm)


SM-SO2Ph_vcp_pdt_13C
3ae
PhO2S SO2Ph
CDCl3, 150 MHz
f1 (ppm)

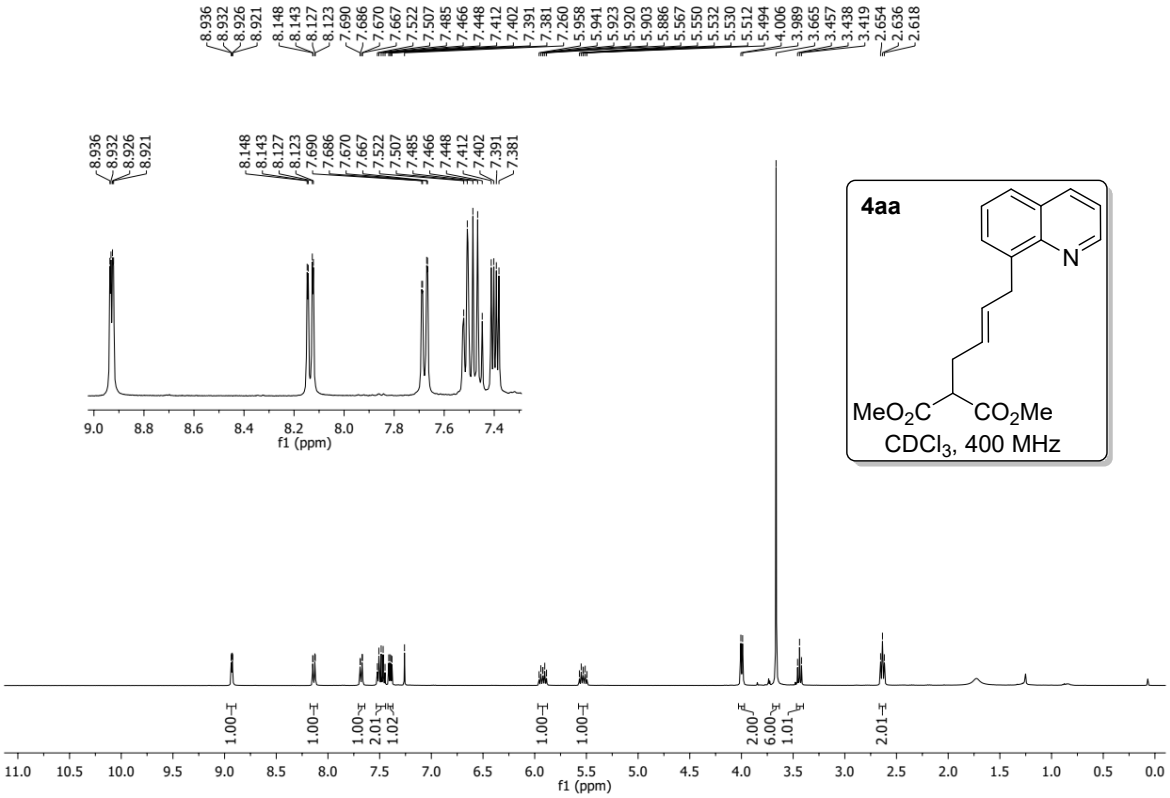

SM-CN_SO2Ph_vcp_pdt_1H
3af
PhO2S
CN
CDCl3, 600 MHz
1.00
12.05
f1 (ppm)


SM-CN_SO2Ph_vcp_pdt_13C
3af
PhO2S
CN
CDCl3, 150 MHz
f1 (ppm)

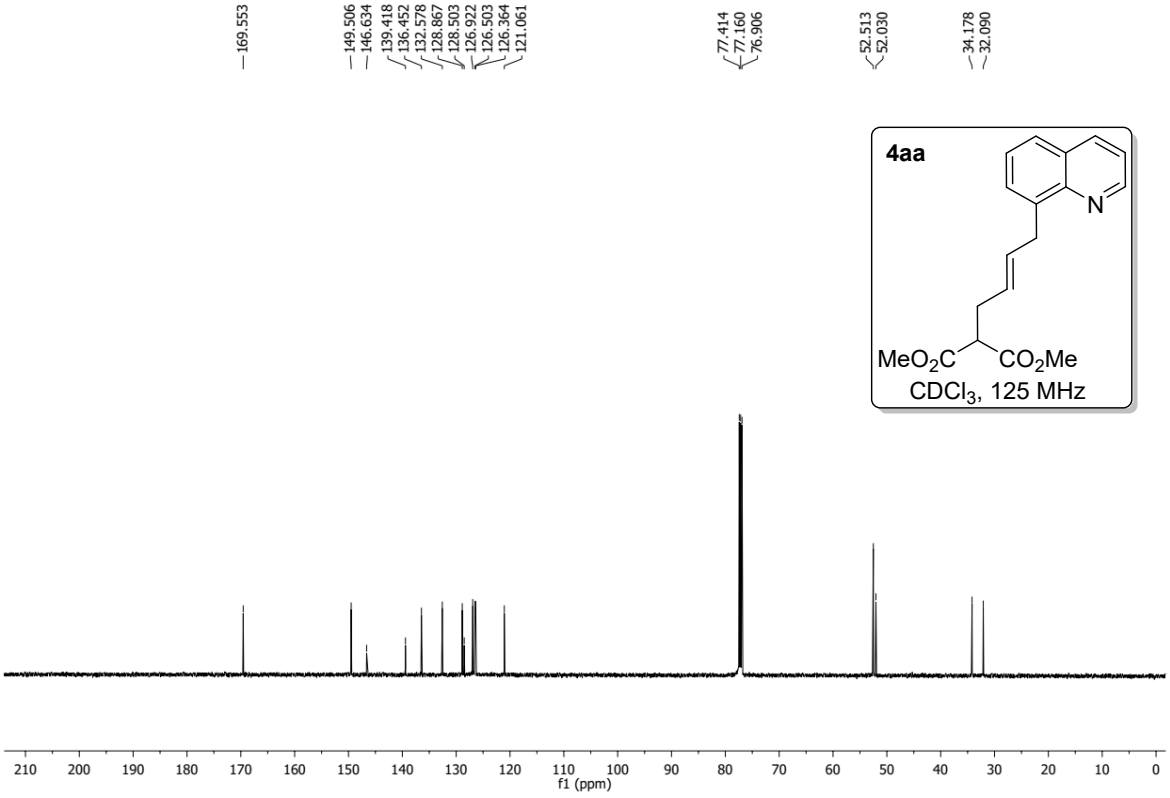

SM-EAA_vcp_pdt_1H
3ah
MeOC
CO2Et
CDCl3, 500 MHz
1.00
13.03
f1 (ppm)


SM-EAA_vcp_pdt_13C
3ah
MeOC
CO2Et
CDCl3, 125 MHz
f1 (ppm)

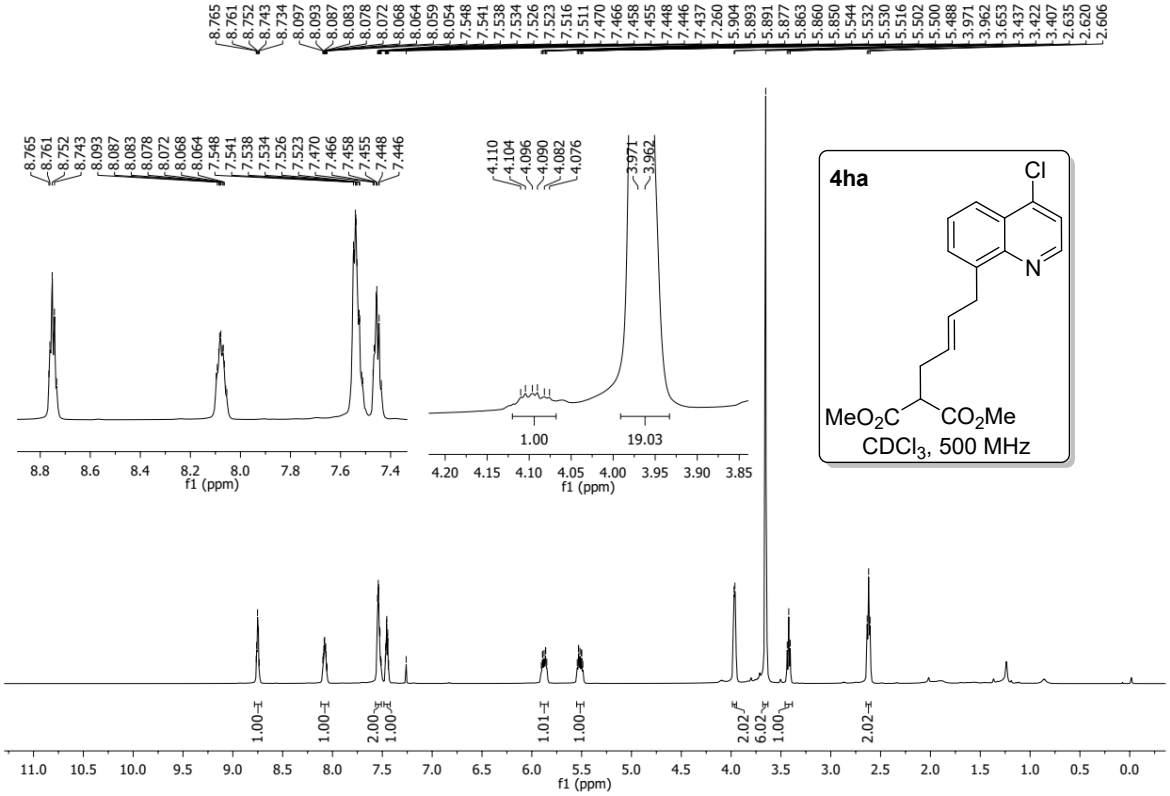
SM-Q_pdt_1H



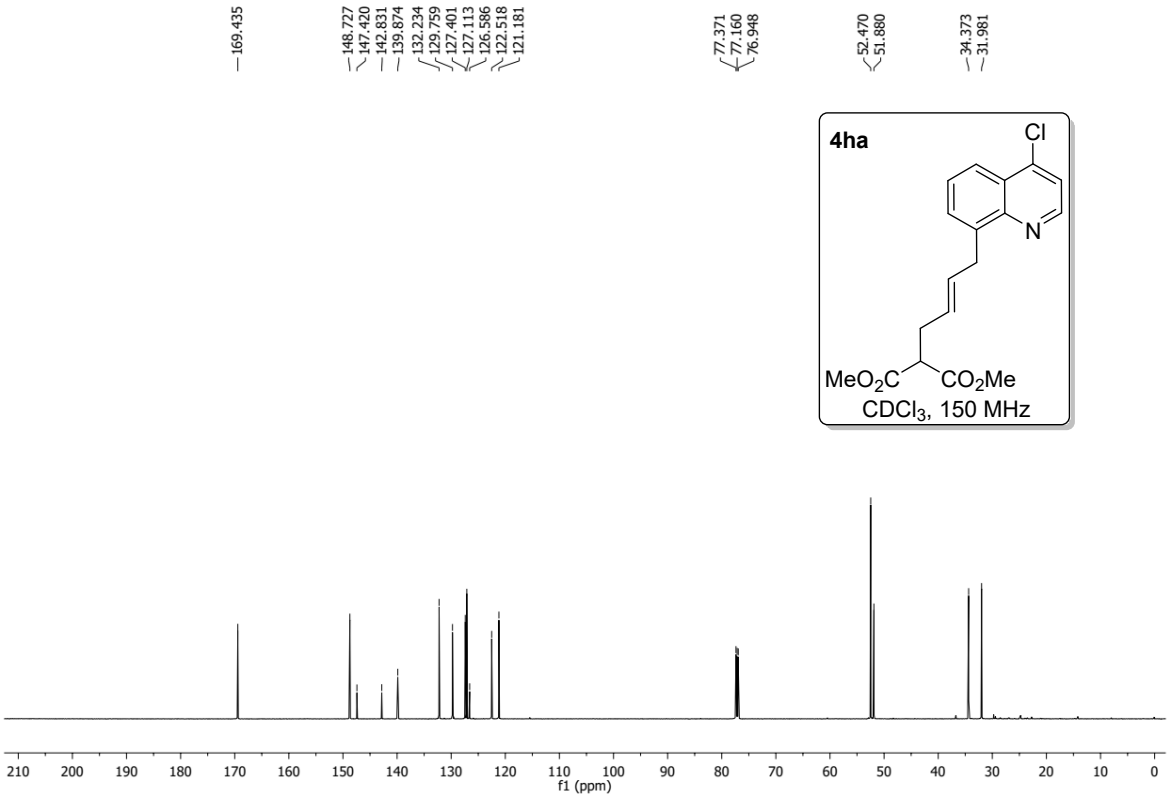
SM-Q_pdt_13C

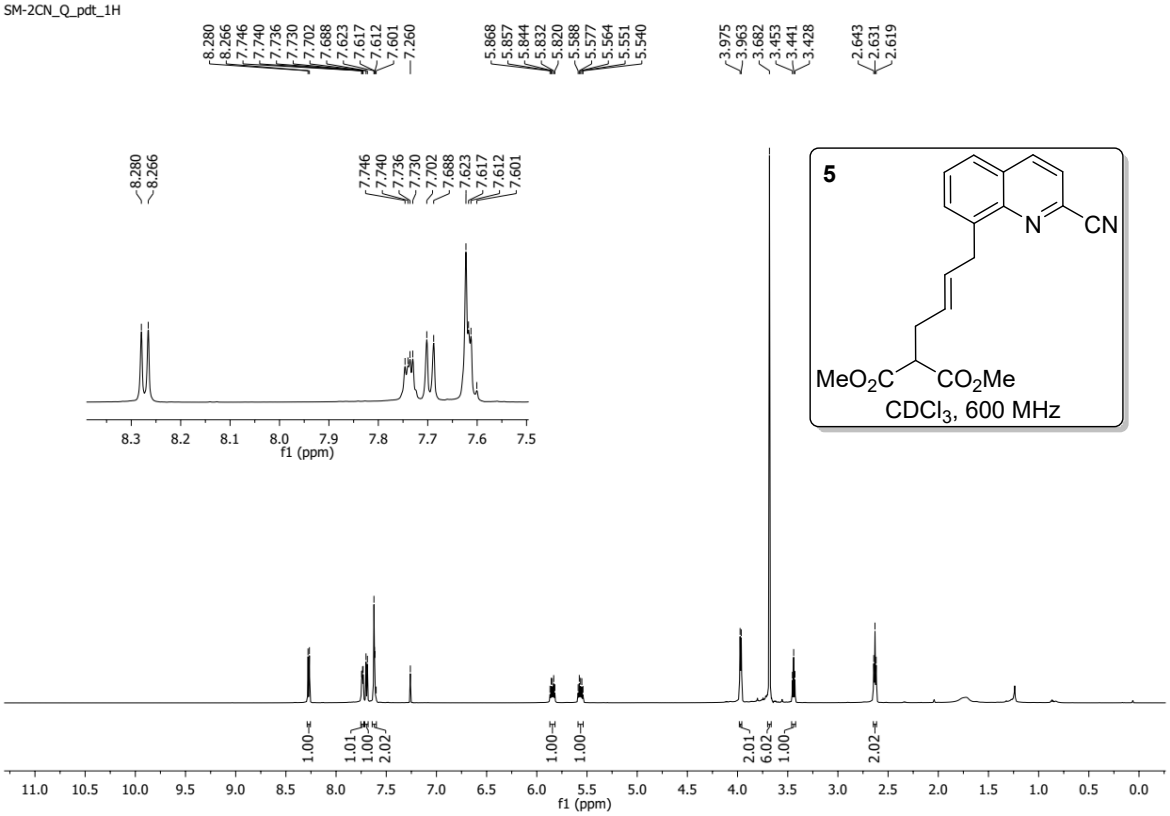


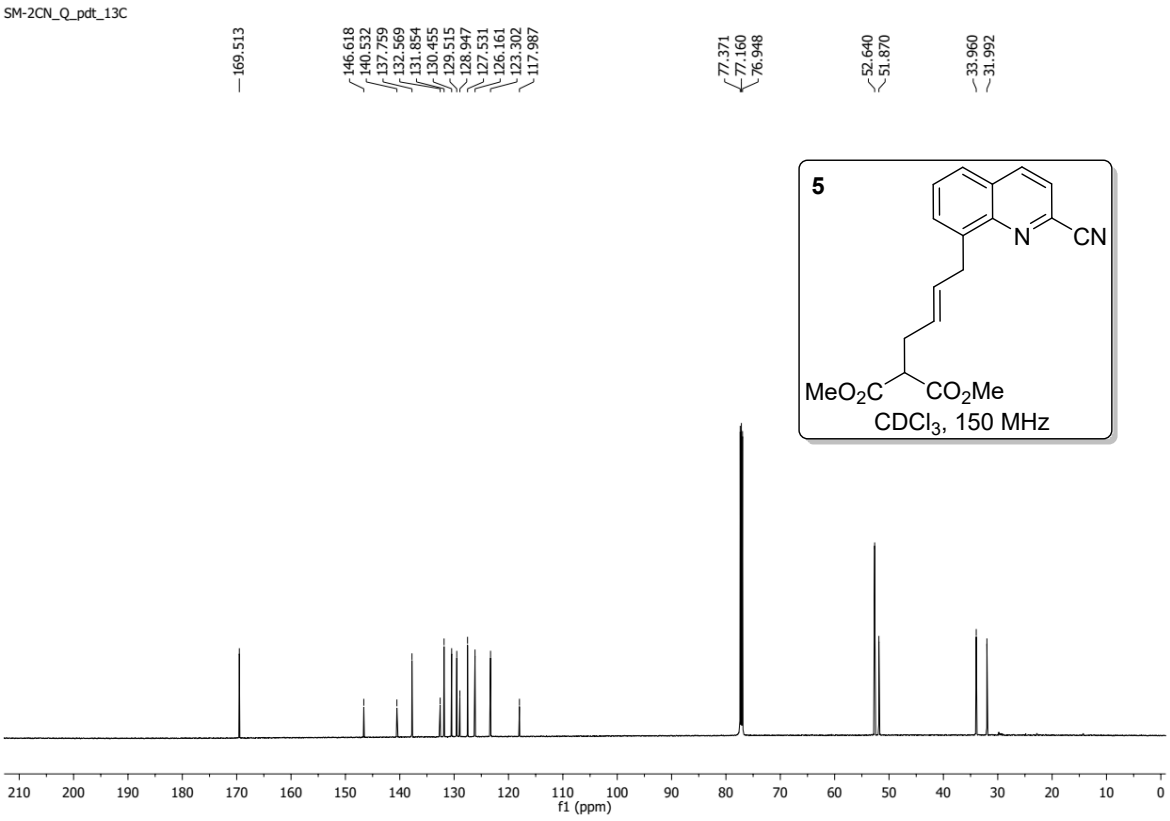
SM-4Cl_Q_pdt_1H

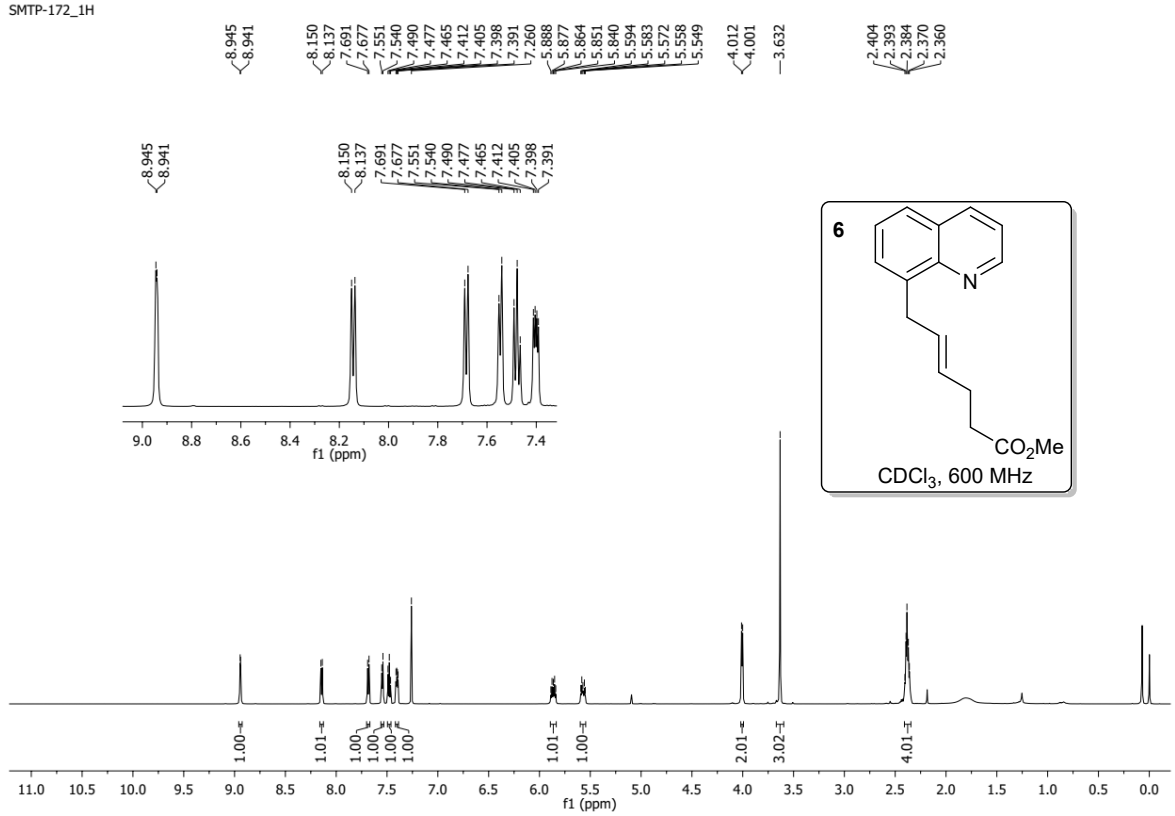


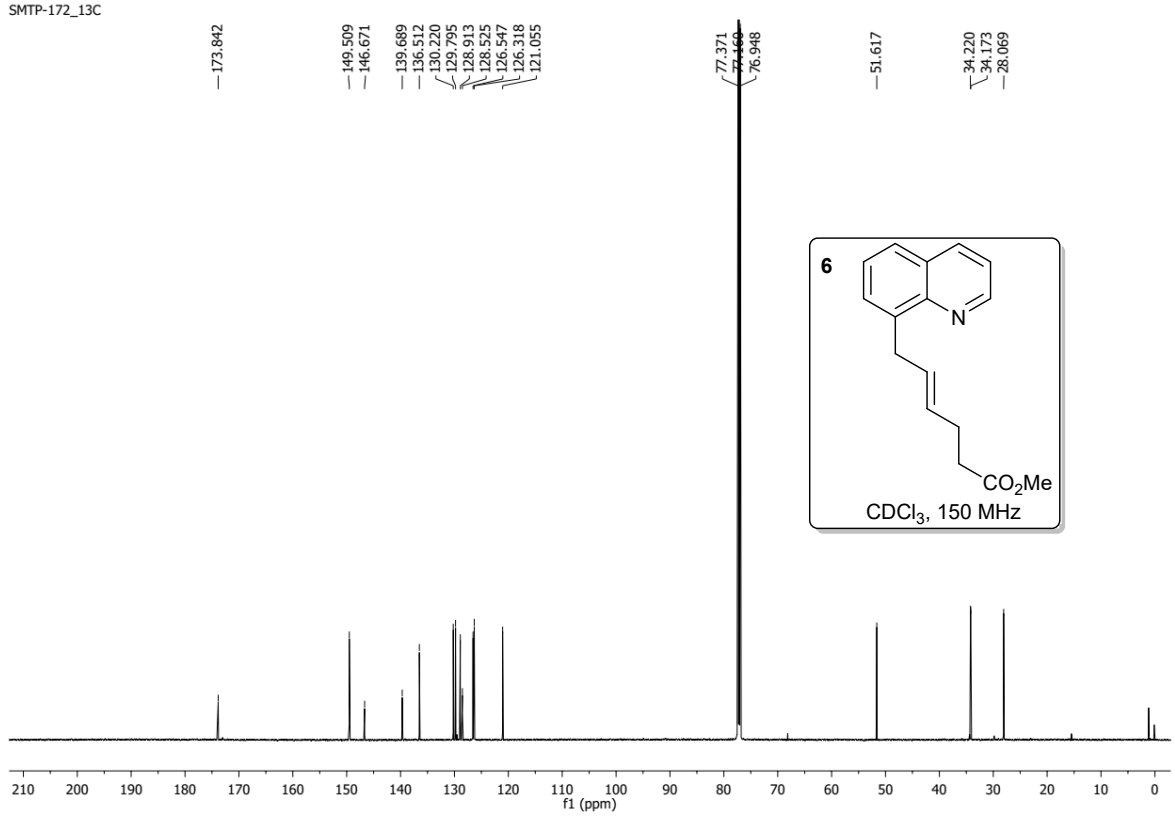
SM-4Cl_Q_pdt_13C



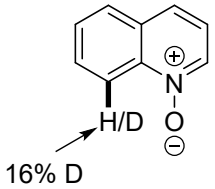

SM-2CN_Q_pdt_1H
8.280
8.266
7.746
7.740
7.736
7.730
7.702
7.688
7.623
7.617
7.612
7.601
7.260
5.868
5.857
5.844
5.832
5.820
5.588
5.577
5.564
5.551
5.540
3.975
3.963
3.682
3.453
3.441
3.428
2.643
2.631
2.619
5
N
CN
MeO2C
CO2Me
CDCl3, 600 MHz
f1 (ppm)


SM-2CN_Q_pdt_13C
169.513
146.618
140.532
137.759
132.569
131.854
130.455
129.515
128.947
127.531
126.161
123.302
117.987
77.371
77.160
76.948
52.640
51.870
33.960
31.992
5
N
CN
MeO2C
CO2Me
CDCl3, 150 MHz
f1 (ppm)


SMTP-172_1H
8.945
8.941
8.150
8.137
7.691
7.677
7.551
7.540
7.490
7.477
7.465
7.412
7.405
7.398
7.391
7.260
5.888
5.877
5.864
5.851
5.840
5.594
5.583
5.572
5.558
5.549
4.012
4.001
3.632
2.404
2.393
2.384
2.370
2.360
f1 (ppm)
6
N
CO2Me
CDCl3, 600 MHz
1.00
1.01
1.00
1.00
1.00
1.00
1.01
1.00
2.01
3.02
4.01


SMTP-172_13C
173.842
149.509
146.671
139.689
136.512
130.220
129.795
128.913
128.525
126.547
126.318
121.055
77.371
77.160
76.948
51.617
34.220
34.173
28.069
f1 (ppm)
6
N
CO2Me
CDCl3, 150 MHz

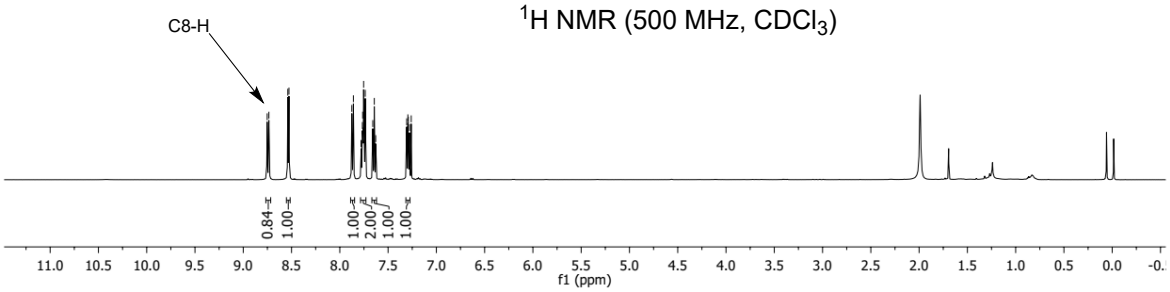
SM-H/D_exchange_D2O_1H



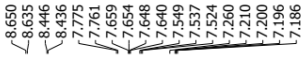
16% D

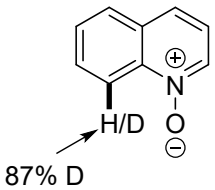
[D_1]-**1a**

^{1}H NMR (500 MHz, $CDCl_3$)



8-d1_quinoline_1H

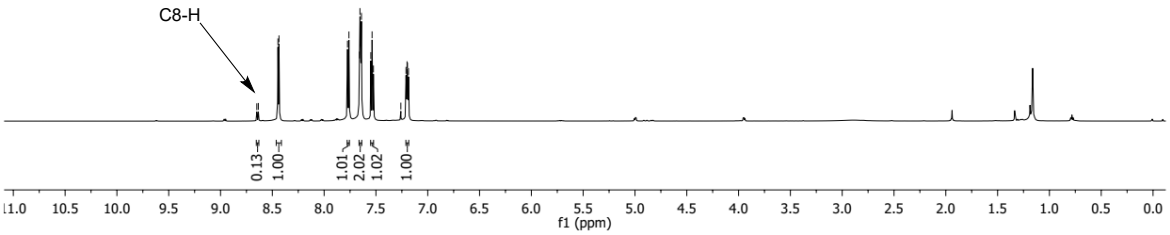




87% D

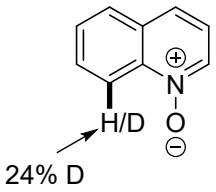
[D_1]-**1a**

^{1}H NMR (600 MHz, $CDCl_3$)



SM-KH/KD_1H

8.762
8.740
8.555
8.540
7.886
7.866
7.791
7.768
7.747
7.671
7.652
7.633
7.322
7.307
7.301
7.286
7.260



24% D

Recovered **1a**/[D_1]-**1a**

^{1}H NMR (400 MHz, $CDCl_3$)