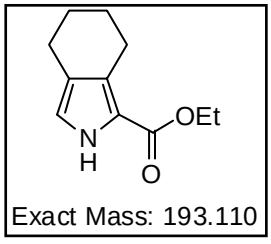
Supporting Information For

Manganese(III) Complexes of Bis-Hydroxyphenyldipyrromethenes are Potent Orally Active Peroxynitrite Decomposition Catalysts

General Methods

Analytical thin layer chromatography (TLC) was performed on Analtech 0.15 mm silica gel 60-GF_{254} plates. Visualization was accomplished with exposure to UV light, exposure to Iodine. Solvents for extraction were HPLC or ACS grade. Chromatography was performed by the method of Still with Merck silica gel 60 (230-400 mesh) with the indicated solvent system. NMR spectra were collected on a JEOL ECS 400. ^{1}H NMR spectra were reported in ppm from tetramethylsilane on the δ scale. Data are reported as follows: Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broadened, obs = obscured), coupling constants (Hz), and assignments or relative integration. ^{13}C NMR spectra were reported in ppm from the central deuterated solvent peak. Data are reported as follows: Chemical shift, multiplicity, coupling information, integration. Grouped shifts are provided where an ambiguity has not been resolved. LCMS were run on a Waters Alliance – SQ 3100 system using Agilent Eclipse (XDB-C18, 4.6 x 150 mm, 5-Micron) column. UV-Vis spectra were recorded using an Ocean Optics Red Tide UV-VIS Spectrometer. Magnetic susceptibilities were measured using a Johnson Matthey Mark I magnetic susceptibility balance.

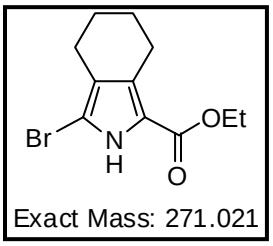
Ethyl 4,5,6,7-tetrahydro-*2H*-isoindole-1-carboxylate (5).[1] A mixture of 1-nitrocyclohexene (5.00 g, 4.43 mL, 0.04 mmol), ethyl isocyanoacetate (4.44 g 4.29 mL, 0.04 mmol) and DBU (5.98 g, 5.87 mL, 0.04 mmol) in THF (50 mL) was stirred at room temperature under argon atmosphere for 16 h. The reaction mixture was partitioned with CH_2Cl_2 (200 mL) and brine (200 mL). The organic layer was separated, dried with anhydrous sodium sulfate and filtered. The solvent was removed under reduced pressure and residue was purified by flash chromatography (silica gel/ CH_2Cl_2) to give **5** (6.70 g, 87% yield) as white solid. ^{1}H NMR ($CDCl_3$) δ 1.32 (m, 3 H), 1.72 (m, 4 H), 2.79 (m, 2 H), 4.28 (m, 2 H), 6.62 (s, 1 H), 8.9 (br s, 1 H). ^{13}C NMR ($CDCl_3$) δ 14.6, 21.9, 23.2, 23.4, 23.5, 59.8, 117.7, 119.0, 122.1, 128.2, 162.0. LCMS (50-95% acetonitrile in 0.05% TFA over 8 minutes) retention time = 5.75 min, $C_{11}H_{15}NO_2$, $(M + H)^+$ = 194.0.



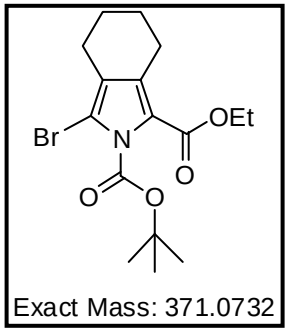
Exact Mass: 193.110

[1] May, Jr., D. A., Lash, T. D. *J. Org. Chem.* **1992**, *57*, 4820-4828

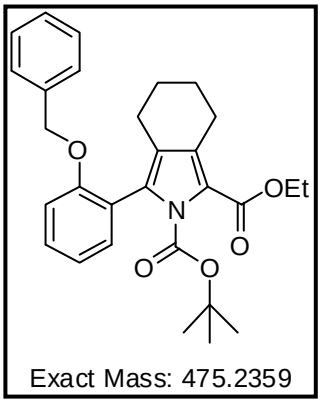
Ethyl 3-bromo-4,5,6,7-tetrahydro-*2H*-isoindole-1-carboxylate (5.1) Compound **5** (4.00 g, 20.7 mmol) in anhydrous THF (150 mL) was treated with N-bromosuccinimide (3.68 g, 20.7 mmol). The resulting reaction was allowed to stir at room temperature for 30 minutes. The mixture was then diluted with CH_2Cl_2 (200 mL), and washed with water (100 mL) and brine (100 mL). The layers were separated and the CH_2Cl_2 solution was dried (Na_2SO_4), filterd and concentrated to afford **5.1** (5.60 g, 100 % yield) as light yellow solid. TLC (silica plate) R_f = 0.52 (4:1 Hexanes/Ethyl Acetate). ^{1}H NMR ($CDCl_3$) δ 1.32 (t, J = 7.2 Hz, 3 H), 1.70 (m, 4 H), 2.37 (m, 2 H), 2.75 (m, 2 H), 4.29 (q, J = 7.2 Hz, 2 H), 9.39 (br s, 1 H). ^{13}C NMR ($CDCl_3$) δ 14.6, 21.7, 22.9, 23.3, 29.6, 60.2, 102.7, 118.8, 121.9, 129.7, 160.2. LCMS (50-95% acetonitrile in 0.05% TFA over 8 minutes) retention time = 6.67 min, $C_{11}H_{14}BrNO_2$ $(M + H)^+$ = 272.15. HRMS (ESI) m/z = 272.0281 (272.0286 calcd for $C_{11}H_{15}{}^{78.9}BrNO_2$, $(M + H^+)$); 274.0260 (274.0266 calcd for $C_{11}H_{15}{}^{80.9}BrNO_2$, $(M + H^+)$).



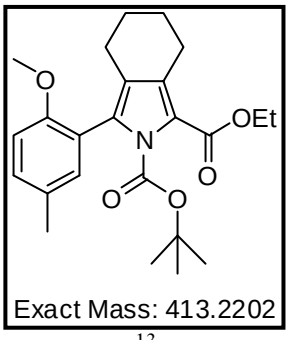
2-*tert*-butyl 1-ethyl 3-bromo-4,5,6,7-tetrahydro-*2H*-isoindole-1,2-dicarboxylate 6: To a solution of 1.00 g (3.68 mmol), of **5.1** in 25.0 mL of acetonitrile was added 67.4 mg (0.55 mmol) of DMAP and 1.04 g (4.78 mmol) of di-tert-butyl dicarbonate and the resulting mixture was stirred for 16h at room temperature. The reaction mixture was partitioned with diethyl ether (80 mL) and 1 M aqueous $KHSO_4$ (40 mL). The organic layer was separated and washed sequentially with aqueous $KHSO_4$ (100 mL), water (100mL), saturated $NaHCO_3$ (100mL), and brine (50mL) and then dried (Na_2SO_4), filtered and concentrated. Purification by flash chromatography (silica gel/4:96 EtOA/Hexane), afforded **6** as yellow viscous oil (1.29 g, 94% yield). TLC (silica plate) R_f = 0.66 (4:1 Hexanes/Ethyl Acetate). ^{1}H NMR ($CDCl_3$) δ 1.31 (t, J = 7.2 Hz, 3 H), 1.59 (m, 4 H), 1.69 (m, 2 H), 2.36 (m, 2 H), 2.71 (m, 4 H), 4.27 (q, J = 7.2 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 14.5, 22.0, 22.6, 22.9, 23.3, 27.4, 60.4, 85.2, 85.5, 104.8, 120.9, 123.1, 131.9, 146.8, 148.6, 160.2. LCMS (50-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 9.15 min, $C_{16}H_{22}BrNO_4$ $(M + 1)^+$ = 372.29. HRMS (ESI) m/z = 372.0806 (372.0810 calcd for $C_{16}H_{23}{}^{78.9}BrNO_4$, $(M + H^+)$); 374.0786 (374.0790 calcd for $C_{16}H_{23}{}^{80.9}BrNO_4$, $(M + H^+)$).



General Synthesis of Compounds 7a.1-7c.1: Boc-protected bromopyrrole (**6**) (2.50 g, 6.73 mmol), the desired boronic acid (13.4 mmol), and tetrakis(triphenylphosphine)palladium(0) (80.8 mg, 0.07 mmol) were added to a round bottom flask fitted with a vacuum adapter and a temperature control thermocouple. The apparatus/mixture was subjected to 5 vacuum/argon cycles and a solution of degassed 2.0 M (aq) Na_2CO_3 (6.70 mL, 13.4 mmol) was added via syringe. Degassed toluene (100 mL) and methanol (20.0 mL) were added and the reaction mixtures were stirred at 80°C for 16 h under argon atmosphere. The reaction mixtures were cooled, filtered through a plug of silica gel or Celite using EtOAc as eluant, and concentrated. Residues were purified by flash chromatography (silica gel/5-8% EtOAc/Hexanes) to afford products **7a.1**, **7b.1** and **7c.**

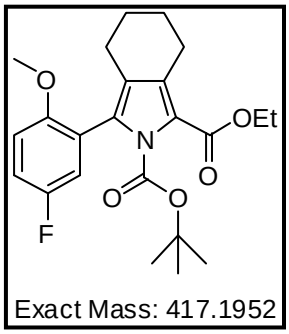


2-*tert*-butyl 1-ethyl 3-(2-(benzyloxy)phenyl)-4,5,6,7-tetrahydro-*2H*-isoindole-1,2-dicarboxylate 7a.1: TLC (silica plate) R_f = 0.55 (4:1 Hexanes/Ethyl Acetate). **(**2.24 g, 70 %), clear viscous oil, ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 9 H), 1.35 (t, J = 7.2 Hz, 3 H), 1.65 (m, 4 H), 2.27 (m, 2 H), 2.80 (m, 2 H), 4.30 (q, J = 7.2 Hz, 2 H), 5.02 (q, J = 7.2 Hz, 2H), 6.95 (m, 2H), 7.25 (m, 7H). ^{1}H ^{13}C NMR ($CDCl_3$) δ 14.6, 23.1, 23.2, 23.5, 27.2, 60.2, 70.3, 83.4, 113.1, 119.7, 120.8, 121.9, 122.5, 126.7, 127.6, 128.5, 129.7, 130.8, 131.7, 137.1, 149.2, 156.7, 161.5. LCMS (50-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 9.45 min, $(M + H)^+$ = 476.47. HRMS (Q-TOF) m/z = 476.24143 (476.24316 calcd for $C_{29}H_{34}NO_5$, $(M + H)^+$).

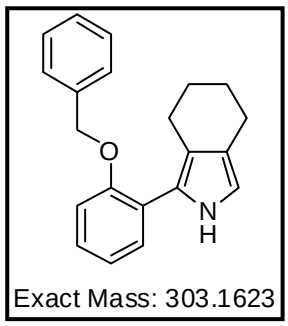


2-*tert*-butyl 1-ethyl 3-(2-methoxy-5-methylphenyl)-4,5,6,7-tetrahydro-*2H*-isoindole-1,2-dicarboxylate 7b.1: TLC (silica plate) R_f = 0.42 (4:1 Hexanes/Ethyl Acetate). (2.24g, 81 %), clear viscous oil, ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 9 H), 1.31 (m, 3 H), 1.70 (m, 4H),2.23-2.35 (m, 2 H), 2.27 (s, 3 H) (m, 5H [2 H cyclohexyl + 3 H CH_3]), 2.78 (m, 2 H), 3.68 (s, 3 H), 4.28 (m, 2 H), 6.78 (d, J = 8.0 Hz, 1 H), 6.98 (m, 1 H), 7.11 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 14.6, 20.5, 21.7, 23.1, 23.2, 23.4, 27.3, 55.5, 60.2, 83.4, 110.3,

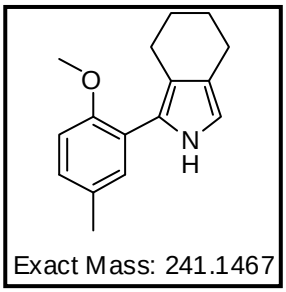
111.3, 119.4, 120.9, 121.6, 129.3, 129.6, 129.9, 130.9, 131.6, 131.9, 149.3, 155.4, 161.3. LCMS (50-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 9.07 min, $(M + H)^+$ = 414.37. HRMS (Q-TOF) m/z = 414.22616 (414.22751 calcd for $C_{24}H_{32}NO_5$, $(M + H)^+$).



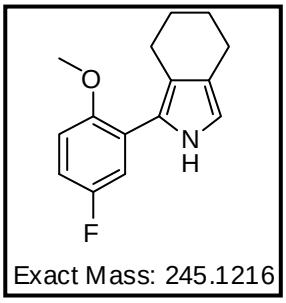
2-*tert*-butyl 1-ethyl 3-(5-fluoro-2-methoxyphenyl)-4,5,6,7-tetrahydro-*2H*-isoindole-1,2-dicarboxylate 7c.1: TLC (silica plate) R_f = 0.50 (4:1 Hexanes/Ethyl Acetate). (2.49g, 89 %), white solid, ^{1}H NMR ($CDCl_3$) δ 1.31 (s, 9 H), 1.32-1.35 (m, 3 H), 1.66 (m, 4 H), 2.29 (m, 2 H), 2.76 (m, 2 H), 3.68 (s, 3 H), 4.29 (q, J = 7.2 Hz, 2 H), 6.79 (m, 1 H), 6.93 (m, 1 H), 7.01 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 14.6, 23.0, 23.1, 23.2, 27.3, 55.9, 60.3, 83.7, 111.0, 111.1, 115.2, 115.4, 118.3, 120.0, 122.1, 122.7, 129.2, 131.4, 149.0, 153.5, 155.4, 157.7, 161.3. LCMS (50-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 8.48 min, $(M + H)^+$ = 418.42. HRMS (Q-TOF) m/z = 418.20101 (418.20244 calcd for $C_{23}H_{29}FNO_5$ $(M + H)^+$).



1-(2-(benzyloxy)phenyl)-4,5,6,7-tetrahydro-*2H*-isoindole 8a: A mixture of KOH (0.84 g, 15.0 mmol) and ethylene glycol (100 mL) was refluxed under argon for 1 h. At this time **7a.1** (1.50 g, 3.15 mmol) was added. The progress of the reaction was followed by LCMS. After 30 min the mixture was cooled to room temperature, diluted with CH_2Cl_2 (100 mL), washed with water (200 mL) and brine (50 mL). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (silica gel/ CH_2Cl_2) to afford **8a** (0.67 g, 70%) as light yellow solid. TLC (silica plate) R_f = 0.64 (4:1 Hexanes/Ethyl Acetate). ^{1}H NMR ($CDCl_3$) δ 1.79 (m, 4 H), 2.64 (m, 2 H), 2.80 (m, 2 H), 5.14 (s, 2 H), 6.48 (br s, 1 H), 7.02 (m, 2 H), 7.13 (m, 1 H), 7.40 (m, 5 H), 7.57 (m, 1 H), 9.42 (br s, 1 H). ^{13}C NMR ($CDCl_3$) δ 22.4, 23.6, 24.5, 24.9, 71.0, 113.1, 121.5, 126.2, 127.6, 128.1, 128.3, 128.8, 136.8, 154.5. LCMS (50-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 8.45 min, $(M + H)^+$ = 304.33. HRMS (ESI) m/z = 304.1697 (304.1701 calcd for $C_{21}H_{22}NO$ $(M + H^+)$).

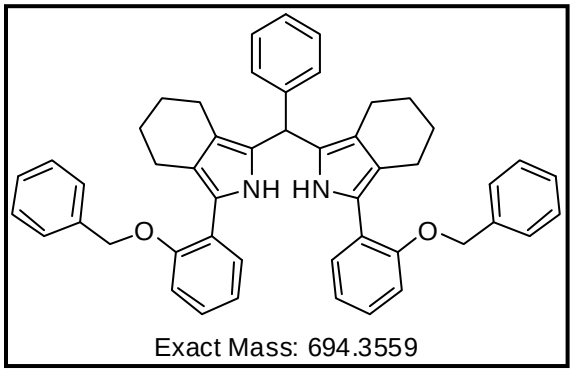


1-(2-methoxy-5-methylphenyl)-4,5,6,7-tetrahydro-*2H*-isoindole 8b: A mixture of KOH (1.17 g, 21.0 mmol) and ethylene glycol (100 mL) was refluxed under argon for 1 h. At this time **7b.1** (1.80 g, 4.35 mmol) was added. The reaction was followed by LCMS and after 30 min there was a $(M+H)^+$ peak for the desired compound **8b**. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (100 mL), washed with water (200 mL) and brine (50 mL). The solvent was removed under reduced pressure and residue was purified by flash chromatography (silica gel/ CH_2Cl_2) to give **5b** (0.80 g, 76%) as light purple viscous oil. TLC (silica plate) $R_f = 0.68$ (4:1 Hexanes/Ethyl Acetate). ^{1}H NMR ($CDCl_3$) δ 1.78 (m, 4 H), 2.31 (s, 3 H), 2.65 (m, 2 H), 2.77 (m, 2 H), 3.85 (s, 3 H), 6.58 (br s, 1 H), 6.85 (d, J = 8.0 Hz, 1 H), 6.97 (m, 1 H), 7.31 (m, 1 H), 9.26 (br s, 1 H). ^{13}C NMR ($CDCl_3$) δ 20.2, 22.0, 23.6, 24.4, 25.2, 56.3, 110.8, 112.2, 116.4, 121.8, 126.0, 128.4, 129.8, 130.2, 152.8, 156.2. LCMS (50-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 8.03 min, $C_{16}H_{20}NO$ $(M + H)^+ = 242.29$.



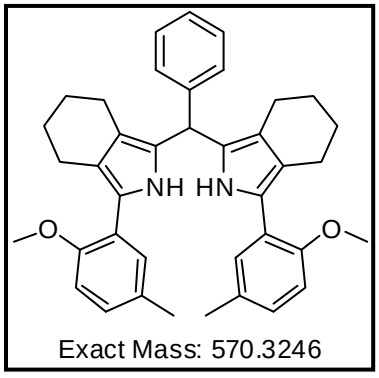
1-(5-fluoro-2-methoxyphenyl)-4,5,6,7-tetrahydro-*2H*-isoindole 8c: A mixture of KOH (0.78 g, 14.0 mmol) and ethylene glycol (100 mL) was refluxed under argon for 1 h. At this time **7c.1** (1.20 g, 2.87 mmol) was added. The reaction was followed by LCMS and after 30 min there was a $(M+H)^+$ peak for the desired compound **8c**. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (100 mL), washed with water (200 mL) and brine (50 mL). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (silica gel/ CH_2Cl_2) to give **8c** (0.60 g, 85% yield) as an olive-colored viscous oil. TLC (silica plate) $R_f = 0.52$ (4:1 Hexanes/Ethyl Acetate). ^{1}H NMR ($CDCl_3$) δ 1.78 (m, 4 H), 2.63 (m, 2 H), 2.77 (m, 2 H), 3.87 (s, 3 H), 6.60 (br s, 1 H), 6.83 (m, 2 H), 7.23 (m, 1 H), 9.48 (s, 1 H). ^{13}C NMR ($CDCl_3$) δ 22.3, 22.7, 23.6, 24.3, 24.7, 31.7, 56.3, 100.0, 112.2, 112.3, 114.0, 114.3, 151.4, 156.1, 158.5. LCMS (50-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 7.63 min, $(M + H)^+ = 246.21$. HRMS (ESI) m/z = 246.1289 (246.1294 calcd for C15H17FNO $(M + H^+)$).

3,3'-(phenylmethylene)bis(1-(2-(benzyloxy)phenyl)-4,5,6,7-tetrahydro-*2H*-isoindole) 8a.1:



Compound **8a** (0.60 g, 2.00 mmol) and benzaldehyde (0.10 mL, 1.00 mmol) were dissolved in CH_2Cl_2 (20.0 mL) at 0^oC under argon. The mixture was stirred for 5 min and then a catalytic amount of trifluoroacetic acid (TFA) was added (2-3 drops). The resulting mixture was stirred for an additional 10 min. The progress of the reaction was followed by LCMS (e.g. after 10 min a sample was withdrawn from the reaction mixture, oxidized by treatment with a small quantity of DDQ, and analyzed for presence of the dipyrromethene derivative; an $(M+H)^+$ peak for dipyrromethene of **8a.1** was the major product). The reaction mixture was diluted with CH_2Cl_2 (50 mL), and washed with saturated $NaHCO_3$ (50 mL), water (100 mL) and brine (50 mL). The layers were separated and the CH_2Cl_2 solution was dried (Na_2SO_4), filtered and concentrated to afford **8a.1** (0.70 g, 99 %) as a orange crystalline solid. ^{1}H NMR ($CDCl_3$) δ 1.72 (s, 8 H), 2.26 (s, 4 H), 2.78 (s, 4 H), 4.93 (s, 4 H), 5.29 (s, 1 H), 6.84 (m, 2 H), 6.91 (m, 2 H), 6.98 (m, 4 H), 7.10 (m, 2 H), 7.28 (m, 11 H), 7.52 (m, 2 H), 9.14 (br s, 2 H). ^{13}CNMR ($CDCl_3$) δ 21.8, 23.6, 24.5, 25.3, 41.6, 53.5, 70.2, 70.4, 113.0, 117.1, 119.1, 120.8, 121.3, 121.5, 122.8, 125.3, 125.8, 126.3, 126.6, 127.2, 127.4, 127.5, 127.9, 128.3, 128.4, 128.6, 128.7, 129.1, 129.8, 131.7, 134.6, 136.8, 137.7, 141.5, 154.0, 156.3. LCMS (85-95% acetonitrile in 0.05% TFA over 8 minutes) retention time = 5.55 min, $C_{49}H_{45}N_2O_2$ $(M + H)^+$ = 693.70 (The sample was again oxidized with DDQ to check LCMS for dipyrromethene due to acid instability of dipyrromethane).

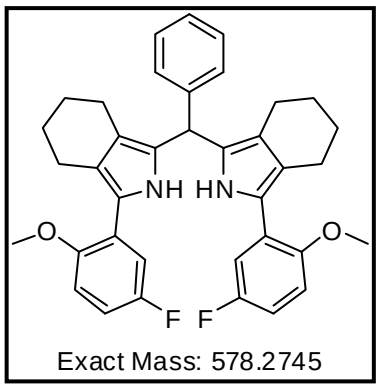
3,3'-(phenylmethylene)bis(1-(2-methoxy-5-methylphenyl)-4,5,6,7-tetrahydro-*2H*-isoindole)



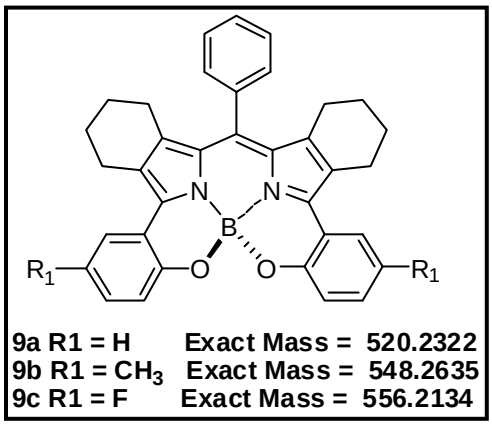
8b.1: Compound **8b** (0.80 g, 3.30 mmol) and benzaldehyde (0.16 mL, 1.60 mmol) were dissolved in CH_2Cl_2 (20 mL). To this stirred solution was added a catalytic amount of TFA following the same procedure as in **8a.1**. The progress of the reaction was again followed by LCMS. After 10 min a sample was withdrawn from the reaction mixture and oxidized with DDQ. LCMS confirmed the presence of the desired dipyrromethene derivative of **8b.1**. The reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with saturated $NaHCO_3$

(50 mL), water (100 mL) and brine (50 mL). The layers were separated and the CH_2Cl_2 solution was dried (Na_2SO_4), filtered and concentrated to afford **8b.1** (0.92 g, 97 %) as a orange crystalline solid. ^{1}H NMR ($CDCl_3$) δ 1.72 (m, 8H), 2.26 (s, 6 H), 2.32 (m, 4 H), 2.79 (m, 4 H), 3.54 (s, 6 H), 5.46 (s, 1 H), 6.71 (d, J = 8.0 Hz, 2 H), 6.84 (m, 2 H), 7.24 (m, 2 H), 7.26 (m, 4 H), 7.32 (m, 2 H), 9.08 (br s, 2 H). ^{13}C NMR ($CDCl_3$) δ 20.8, 21.7, 23.6, 24.5, 25.1, 41.3, 55.4, 111.2, 116.9, 118.8, 121.4, 122.1, 125.7, 125.8, 126.5, 127.8, 128.6, 130.0, 141.8, 152.9. LCMS (85-95% acetonitrile in 0.05% TFA over 8 minutes) retention time = 5.08 min, $C_{39}H_{40}N_2O_2$ $(M + H)^+$ = 569.60 (The sample was again oxidized with DDQ to check LCMS for dipyrromethene due to acid instability of dipyrromethane).

3,3'-(phenylmethylene)bis(1-(5-fluoro-2-methoxyphenyl)-4,5,6,7-tetrahydro-*2H*-isoindole)

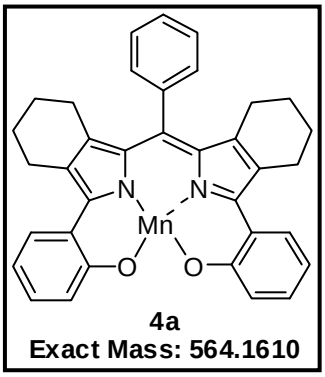


8c.1: Compound **8c** (0.40 g, 1.60 mmol) and benzaldehyde (0.08 mL, 0.80 mmol) were dissolved in CH_2Cl_2. To this stirred solution was added a catalytic amount of TFA following the same procedure as in **8a.1**. The progress of the reaction was again followed by LCMS. After 10 min a sample was withdrawn from the reaction mixture and oxidized with DDQ. LCMS confirmed the presence of the desired dipyrromethene derivative of **8c.1**. The reaction mixture was diluted with with CH_2Cl_2 (50 mL), washed with saturated $NaHCO_3$ (50 mL), water (100 mL) and brine (50 mL). The layers were separated and the CH_2Cl_2 solution was dried (Na_2SO_4), filtered and concentrated to afford **8c.1** (0.47 g, 99 %) as a orange crystalline solid. ^{1}H NMR ($CDCl_3$) δ 1.69 (m, 4 H), 1.77 (m, 4 H), 2.31 (m, 4 H), 2.78 (m, 4 H), 3.53 (m, 6 H), 5.47 (s, 1 H), 6.72 (m, 4 H), 6.97 (m, 1 H), 7.18 (m, 1 H), 7.21 (m, 1 H), 7.35 (m, 2 H), 7.58 (m, 2 H), 9.23 (br s, 2 H). ^{13}C NMR ($CDCl_3$) δ 21.6, 23.3, 24.3, 25.1, 41.2, 55.8, 100.0, 110.6, 110.8, 112.2, 112.3, 113.0, 113.2, 117.4, 120.0, 120.6, 123.5, 123.6, 126.3, 126.8, 127.4, 128.6, 128.8, 141.4, 150.9, 156.2. LCMS (85-95% acetonitrile in 0.05% TFA over 8 minutes) retention time = 3.15 min, $C_{37}H_{34}F_2N_2O_2$ $(M + H)^+$ = 577.50 (The sample was again oxidized with DDQ to check LCMS for dipyrromethene due to acid instability of dipyrromethane).



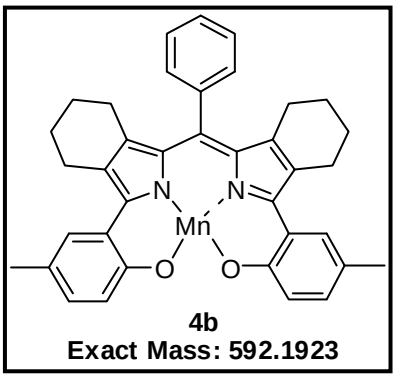
9a R1 = H **Exact Mass = 520.2322**
9b R1 = CH_3 **Exact Mass = 548.2635**
9c R1 = F **Exact Mass = 556.2134**

BODIPY Analogues 9a-c: Compounds **8a.1-8c.1** (1.0 mmol) were dissolved in CH_2Cl_2 (50 mL) and oxidized by treatment with chloranil (1.0 mmol) for 1 h at room temperature under argon. The progress of the reaction was followed by LCMS. At this time the solvent was removed under reduced pressure to give **8a.2-8c.2**. Compounds **8a.2-8c.2** in dichloromethane were cooled to 0°C, treated with BBr_3 dropwise (10 mmol), and stirred overnight. The mixtures were then quenched with sat. NH_4Cl at 0°C, and extracted with ethyl acetate (100 mL). The combined organic layers were washed with sat. NH_4Cl (200 mL), dried over sodium sulfate, filtered and concentrated to afford dark purple crystalline solids **9a-c**.



4a
Exact Mass: 564.1610

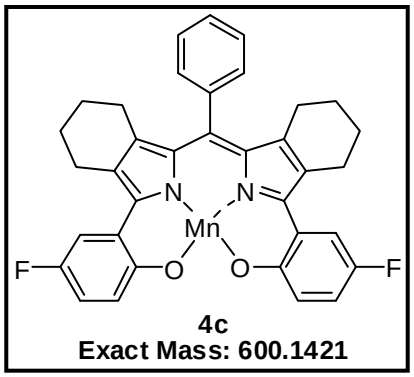
Complex 4a: A mixture of **9a** in $CHCl_3$/MeOH (3:1, 60mL) was treated with 16 equivalents of $MnCl_2$ and catalytic amount of 2,6-lutidine (5 drops). The resulting mixture was stirred at 50 °C in the air for 16 h. The mixture was partitioned with CH_2Cl_2 (100 mL) and brine (50 mL). The layers were separated and the CH_2Cl_2 solution was dried (Na_2SO_4), filtered and concentrated. The crude reaction mixture was purified by flash chromatography (neutral alumina /CH_2Cl_2/CH_3OH 99:1) to afford complex **4a** as a green solid (0.41 g, 72.1%). TLC (silica plate) R_f = 0.65 (3:1 Hexanes/Ethyl Acetate). Anal. Calcd for $C_{35}H_{31}MnN_2O_3$ (**4a**•H_2O): C, 72.16; H, 5.36, N, 4.81. Found: C, 71.73; H, 5.13; N, 4.79. LCMS (85-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 4.53 min, $(M)^+$ = 564.47, $(M + H)^+$ = 565.42, $(M + H + ACN)^+$ = 606.47. HRMS (Q-TOF) m/z = 564.15833 (564.16093 calcd for $C_{35}H_{29}MnN_2O_2$ (M^+)). UV-vis (in CH_2Cl_2, λ_{max}): 227, 307, 370,437, 596 (sh), 648.



4b
Exact Mass: 592.1923

Complex 4b: Prepared from **9b** following the above method. Purification by flash chromatography (SiO_2/ CH_2Cl_2/MeOH/TEA 6/0.1/0.05)) afforded complex **4b** as a green solid (0.71 g, 68%). TLC (silica plate) R_f = 0.60 (3:1 Hexanes/Ethyl Acetate). Anal. Calcd for $C_{37}H_{37}MnN_2O_4$

(**4b**•2H_2O): C, 70.69; H, 5.93, N, 4.46. Found: C, 70.08; H, 6.65; N, 4.37. LCMS (85-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 4.50 min, $(M)^+$ = 592.56, $(M + H)^+$ = 593.50, $(M + H + ACN)^+$ = 634.49. HRMS (Q-TOF) m/z = 592.19013 (592.19223 calcd for $C_{37}H_{33}MnN_2O_2$ (M^+)). UV-vis (in CH_2Cl_2, λ_{max}): 229, 312, 376, 445, 602 (sh), 656.



4c
Exact Mass: 600.1421

Complex 4c: Prepared from **9c** following the above method. Purification by flash chromatography (neutral alumina/ CH_2Cl_2/MeOH 98:2) afforded complex **4c** as a green solid (0.50 g, 80%). TLC (silica plate) R_f = 0.58 (3:1 Hexanes/Ethyl Acetate). Anal. Calcd for $C_{35}H_{29}F_2MnN_2O_3$ (**4c**•H_2O): C, 67.96; H, 4.73, N, 4.53. Found: C, 67.90; H, 4.91; N, 4.16. LCMS (85-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 4.77 min, $(M)^+$ = 600.39, $(M + H)^+$ = 601.40, $(M + H + ACN)^+$ = 642.39. HRMS (Q-TOF) m/z = 600.13961 (600.14209 calcd for $C_{35}H_{27}F_2MnN_2O_2$ (M^+)). UV-vis (in CH_2Cl_2, λ_{max}): 228, 312, 371, 441, 602 (sh), 654.

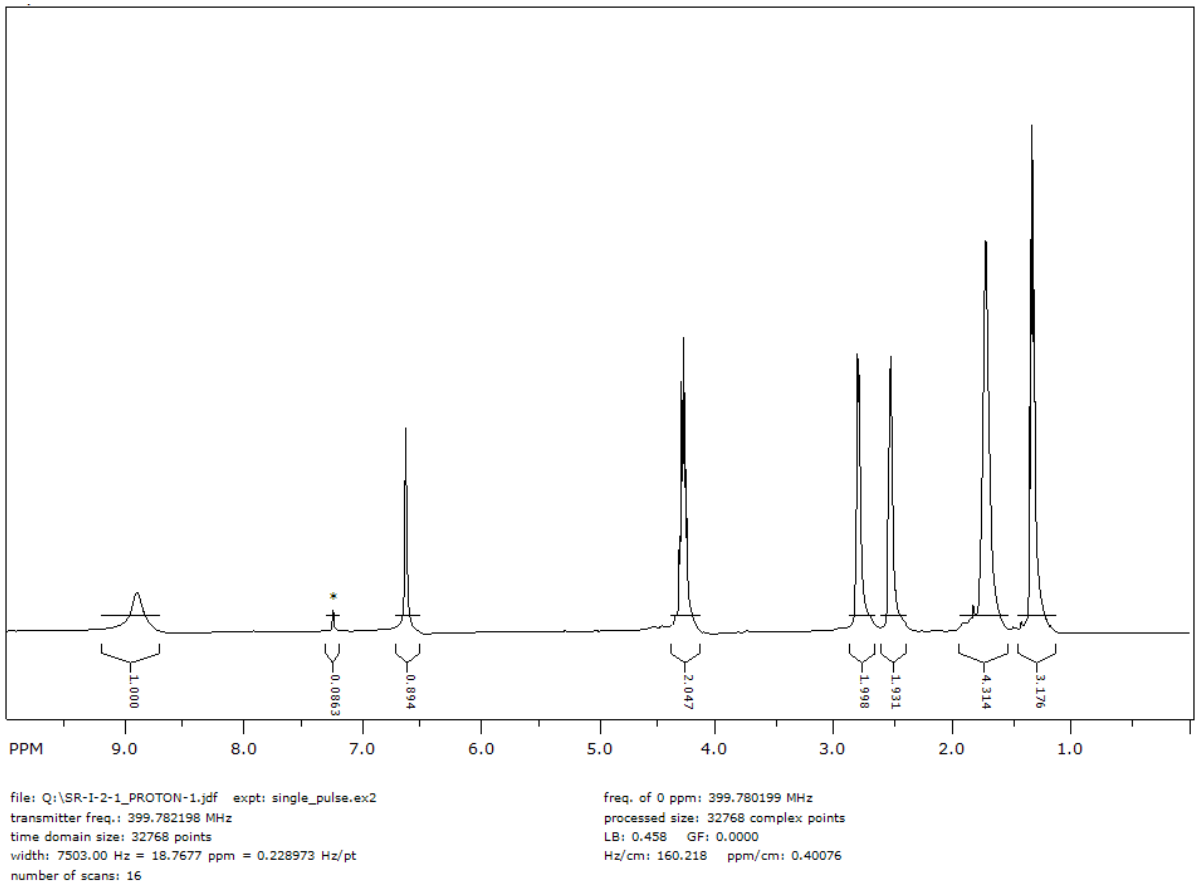
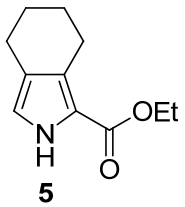


Figure S1a: ^{1}H NMR spectrum of compound **5.**



5

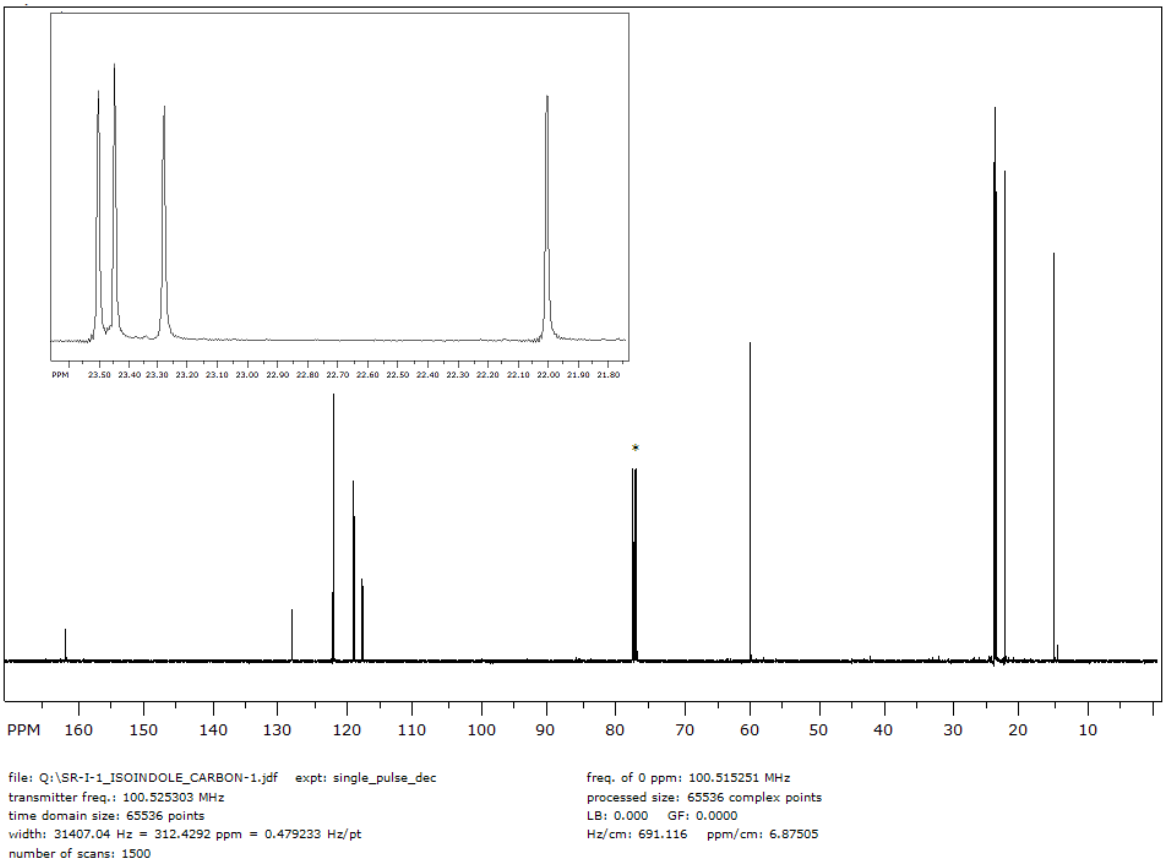
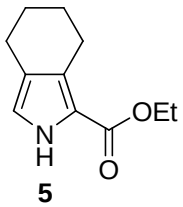


Figure S1b: ^{13}C NMR spectrum of compound **5.**



5

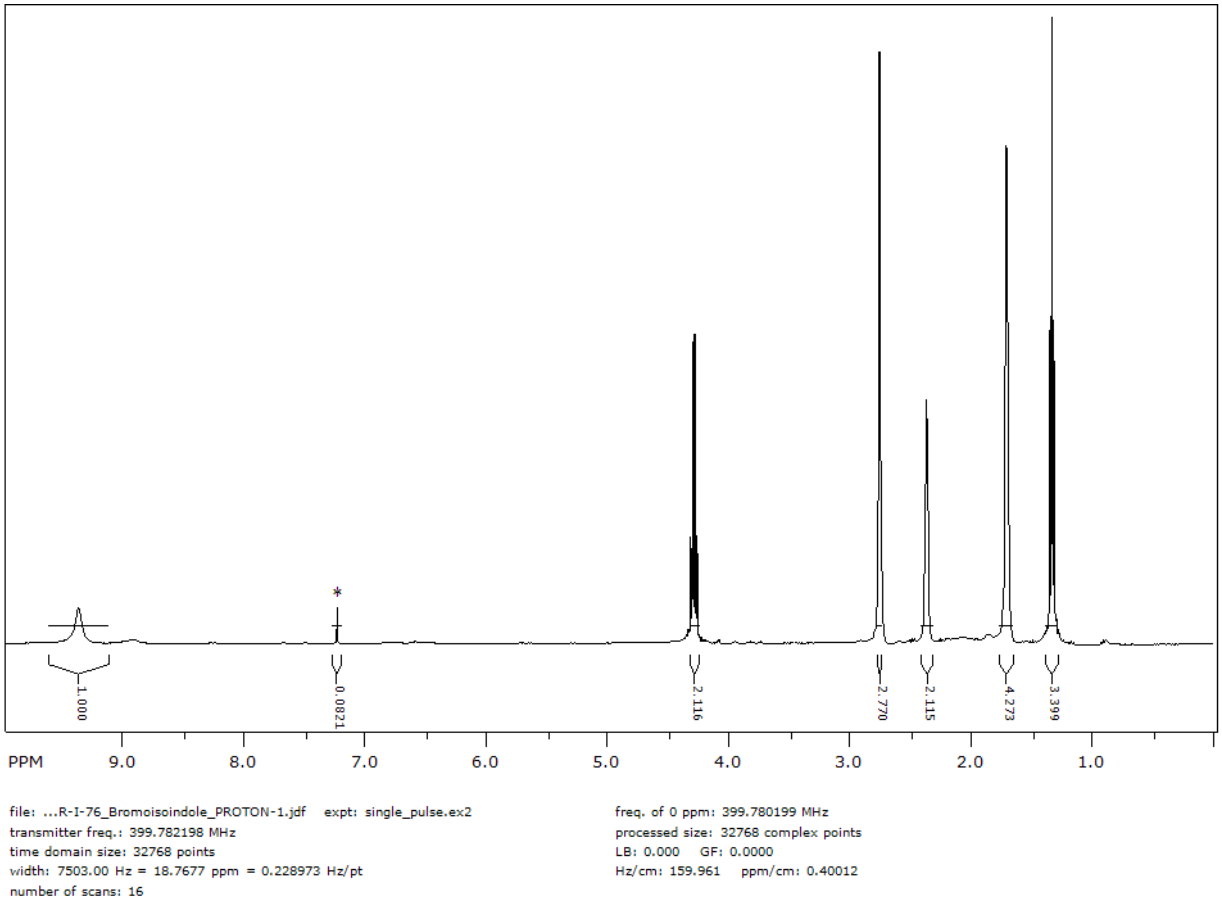
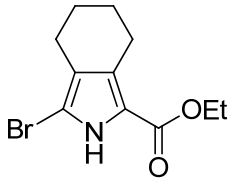


Figure S2a: ^{1}H NMR spectrum of compound **5.1.**



5.1

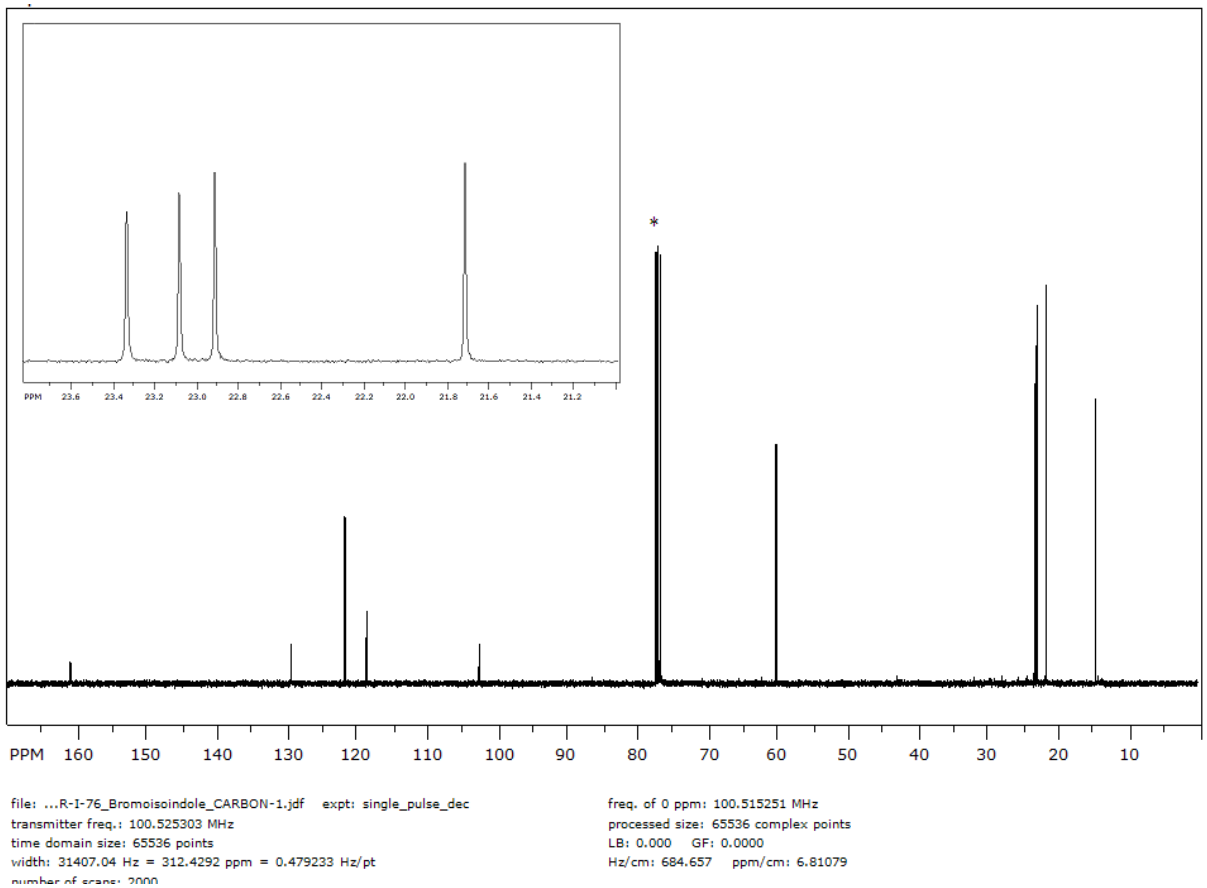
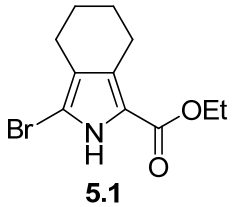


Figure S2b: ^{13}C NMR spectrum of compound **5.1.**



5.1

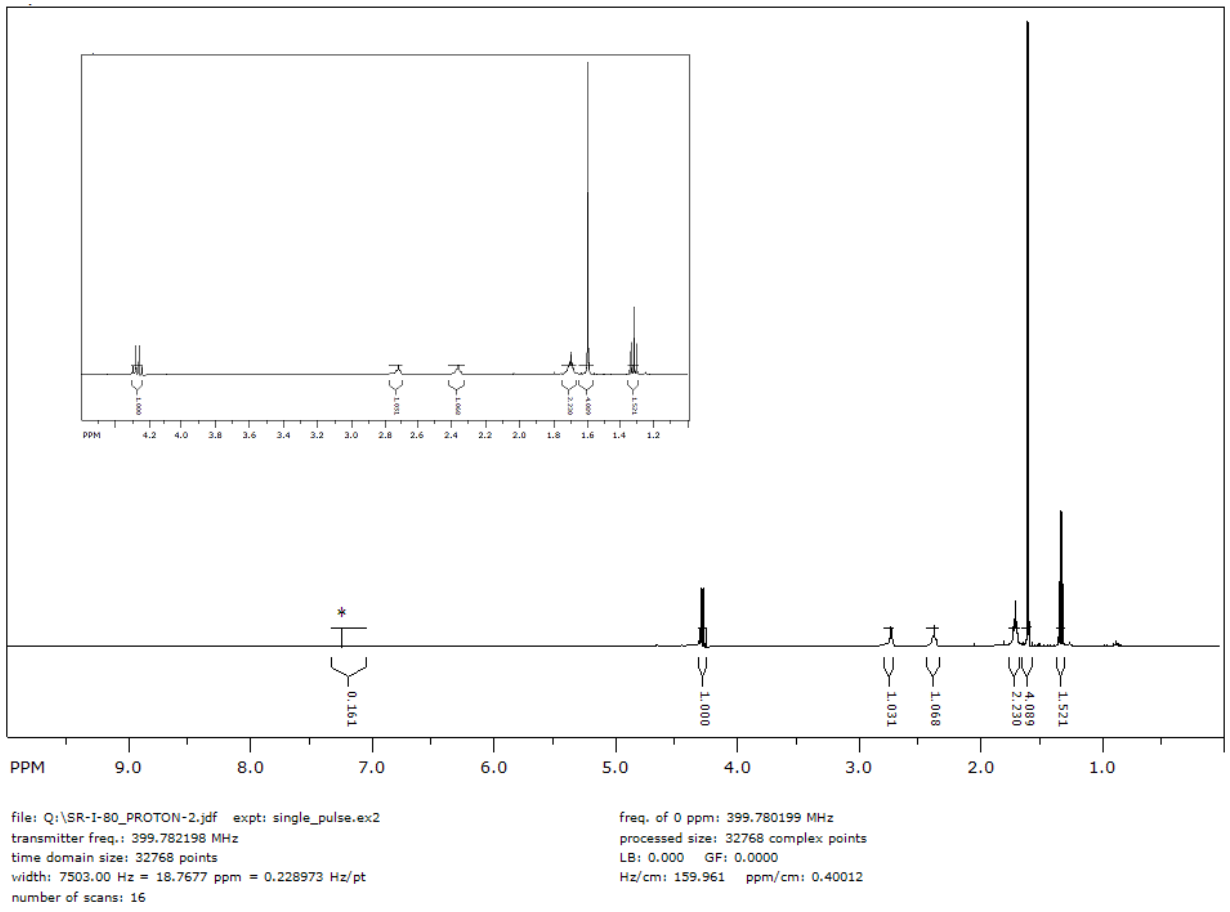
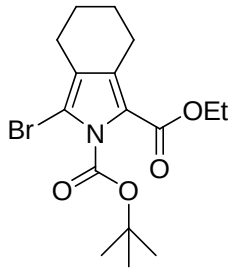


Figure S3: ^{1}H NMR spectrum of compound **6.**



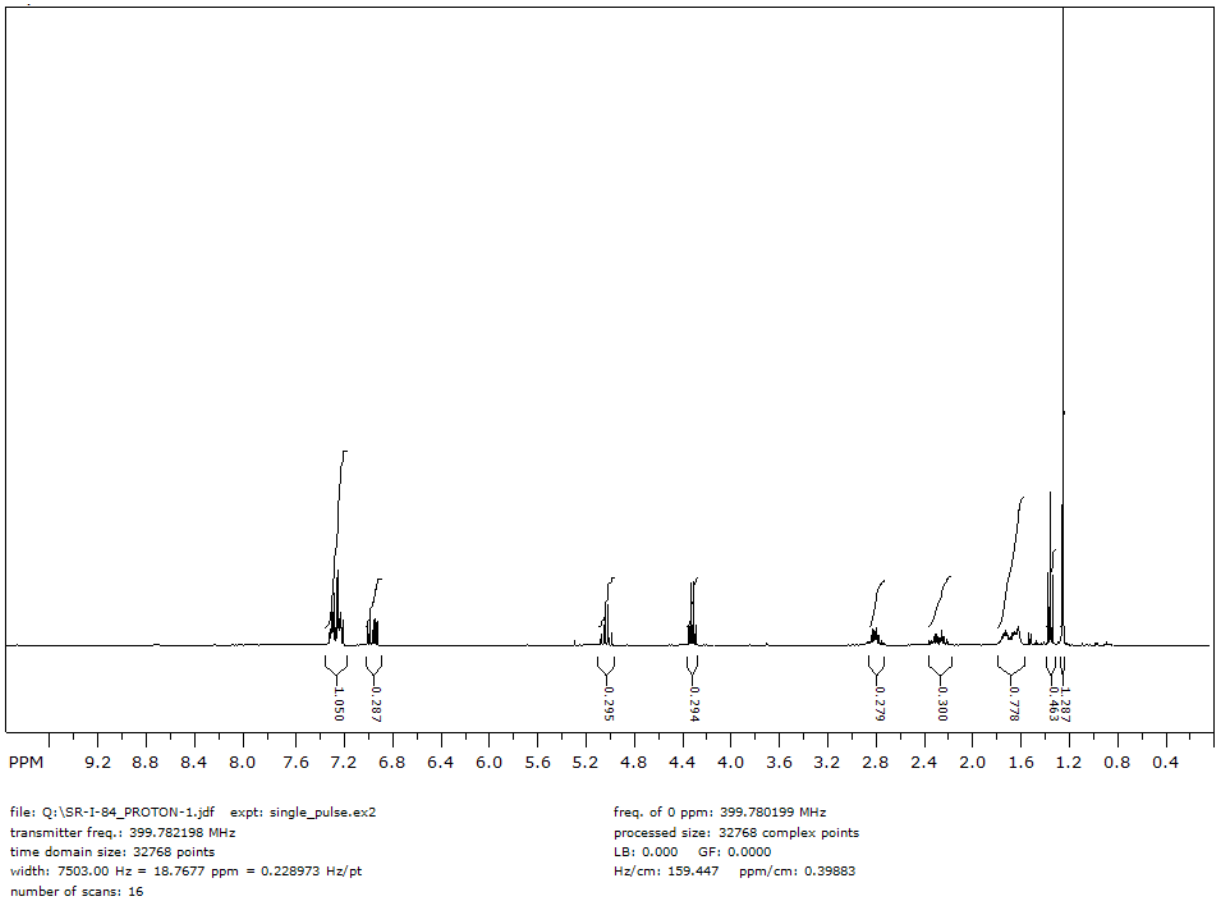
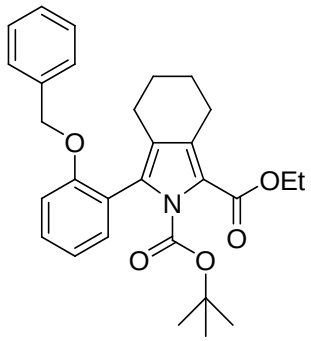


Figure S4a: ^{1}H NMR spectrum of compound **7a.1.**



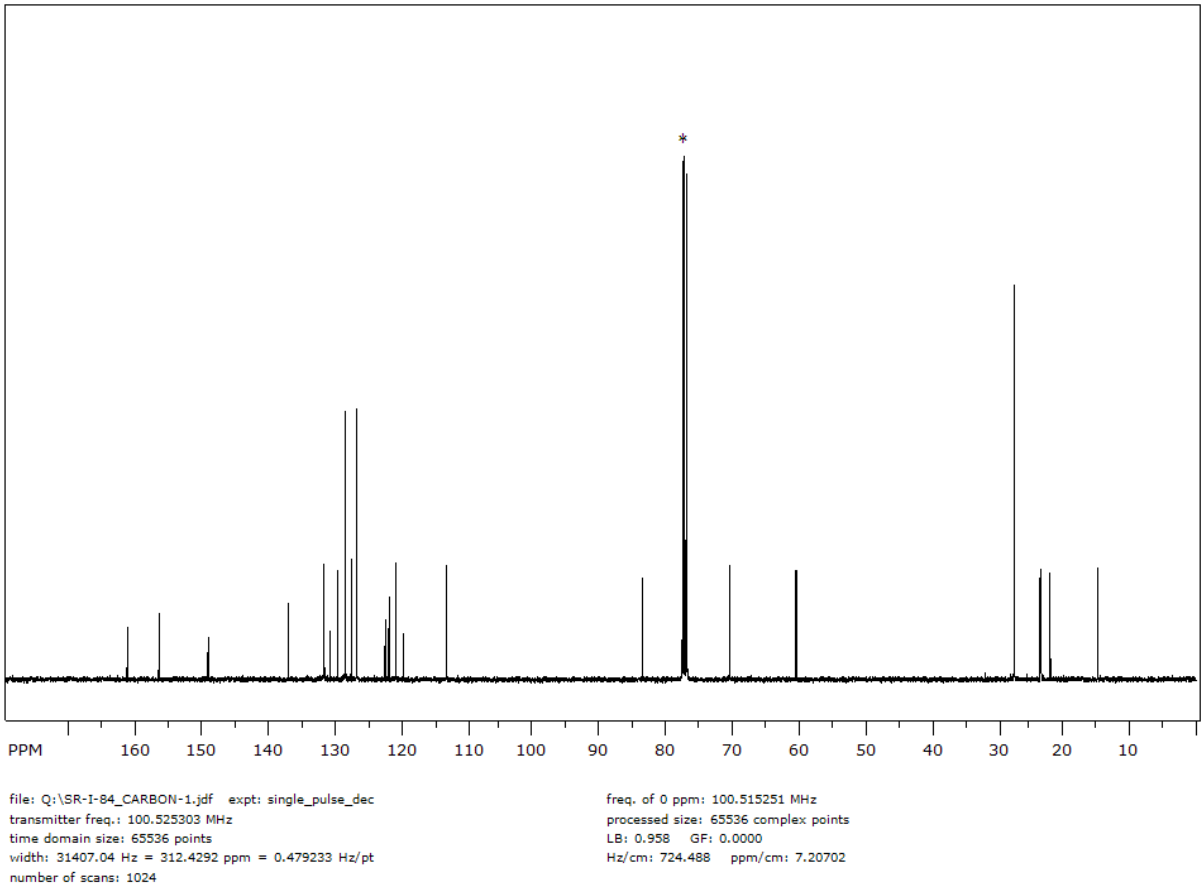
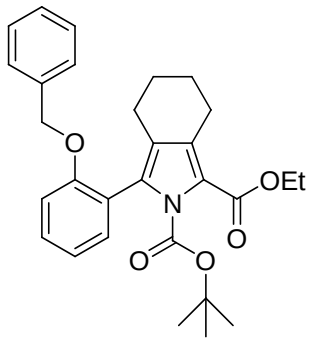


Figure S4b: ^{13}C NMR spectrum of compound **7a.1.**



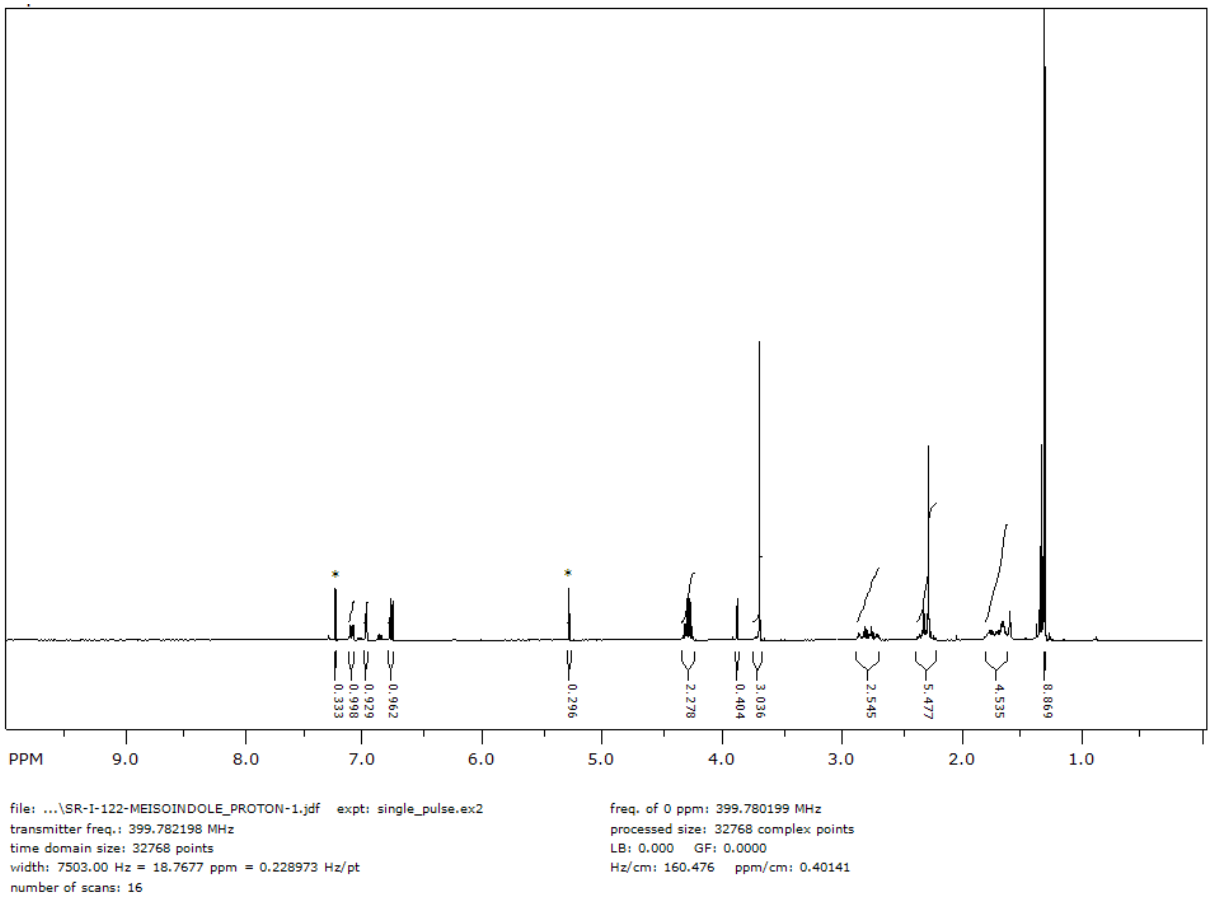
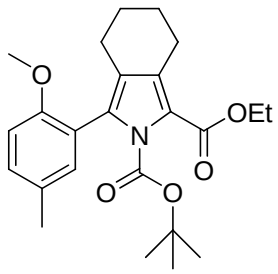


Figure S5a: ^{1}H NMR spectrum of compound **7b.1.** The mark with * is due to solvent impurity.



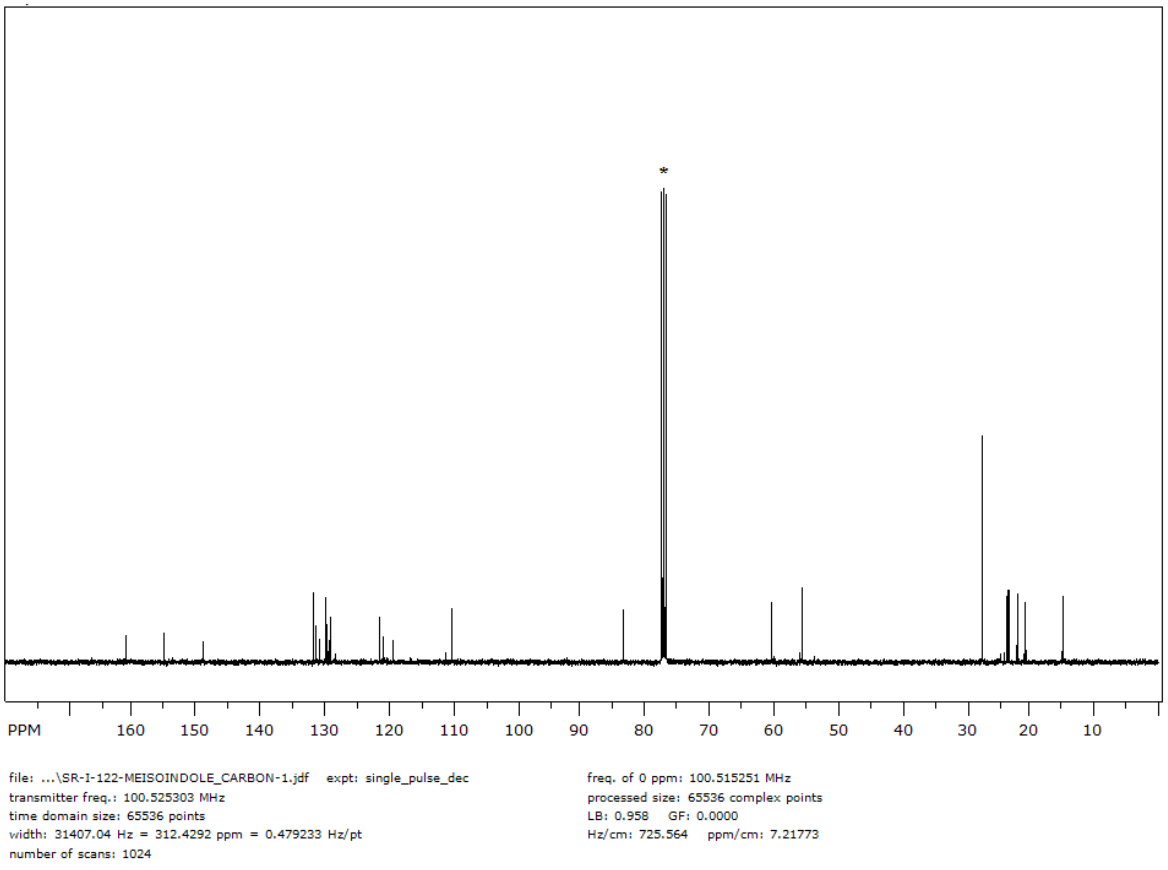
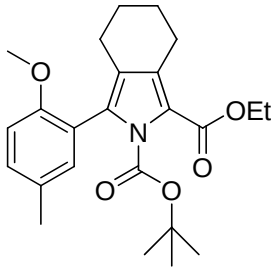


Figure S5b: ^{13}C NMR spectrum of compound **7b.1.**



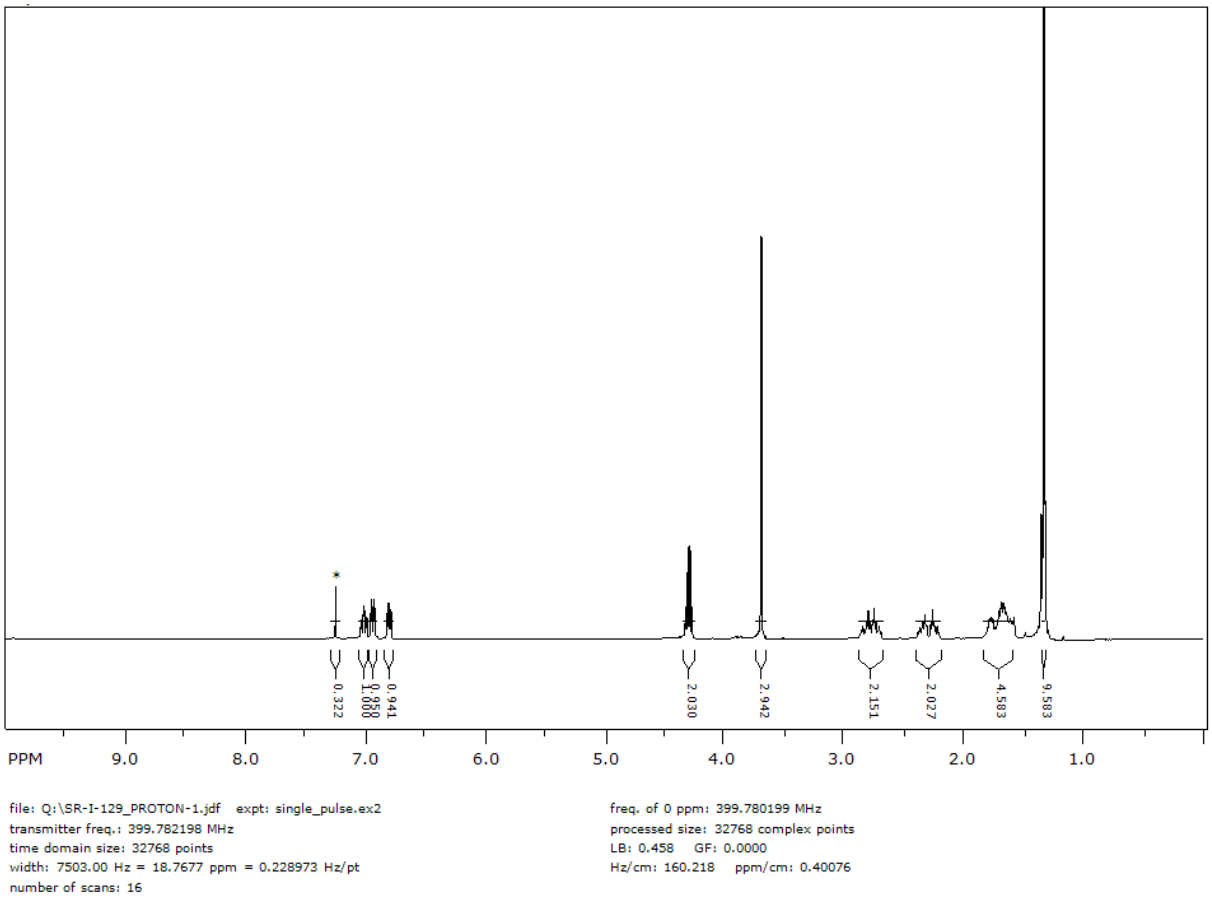
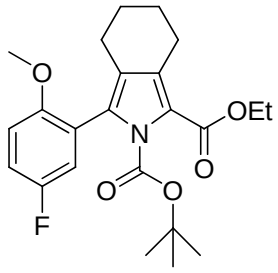


Figure S6a: ^{1}H NMR spectrum of compound **7c.1**.



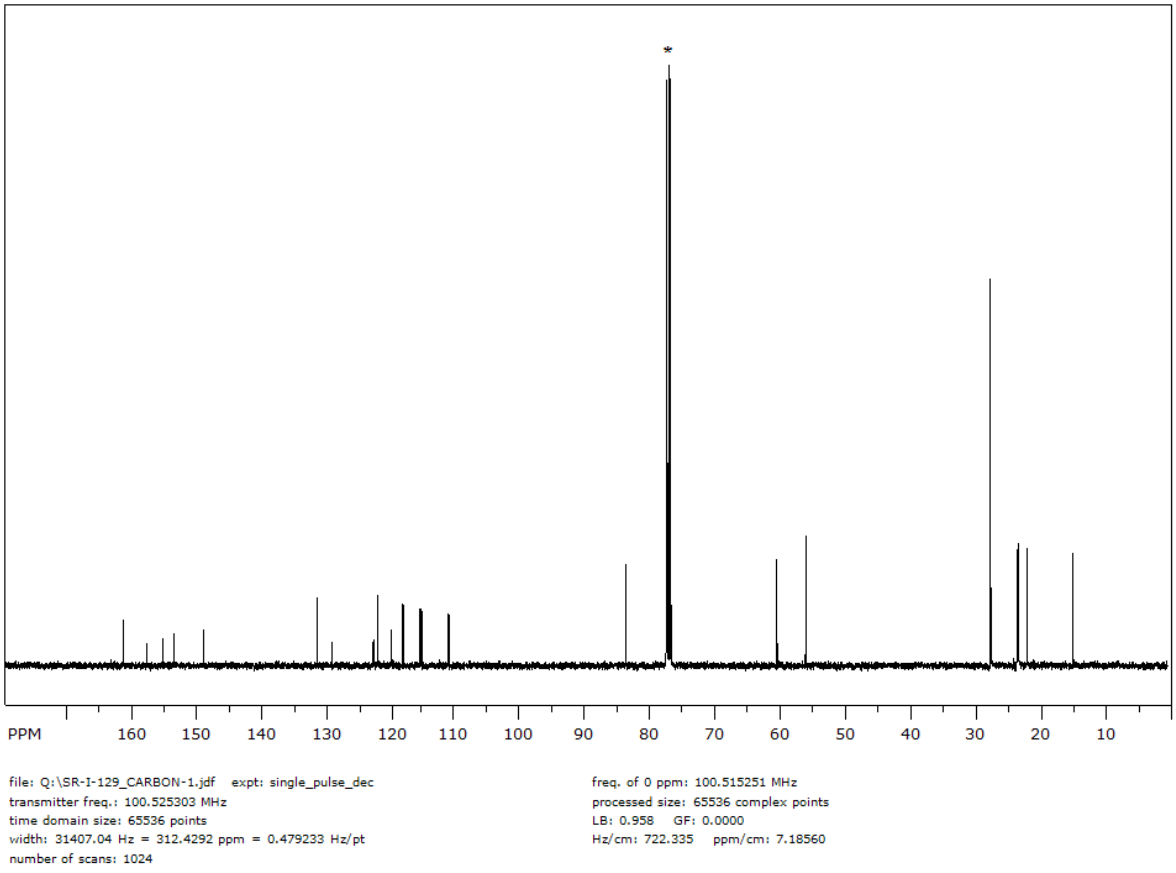
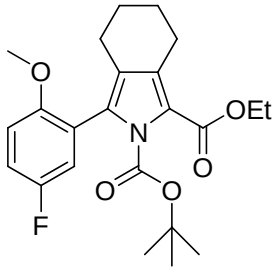


Figure S6b: ^{13}C NMR spectrum of compound **7c.1**.



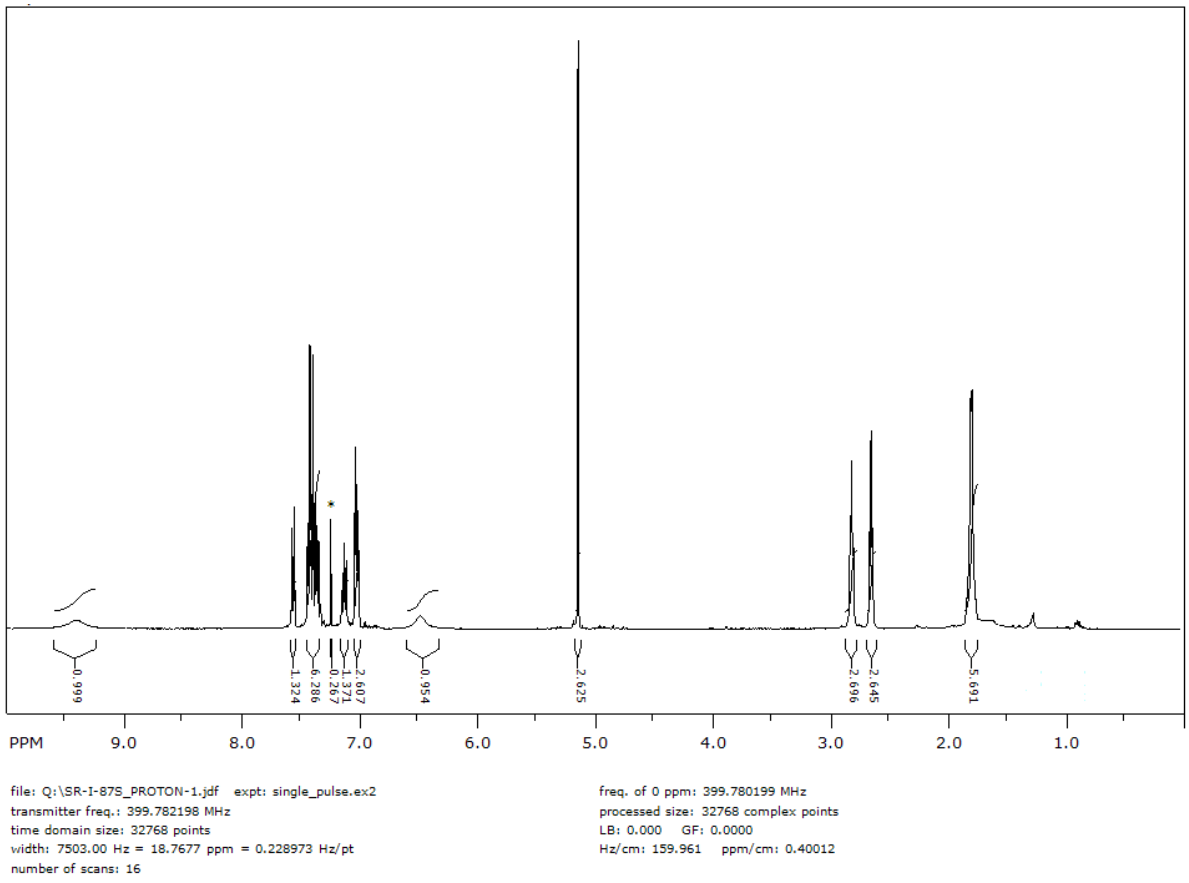
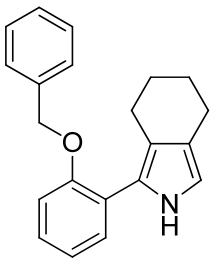


Figure S7a: ^{1}H NMR spectrum of compound **8a**.



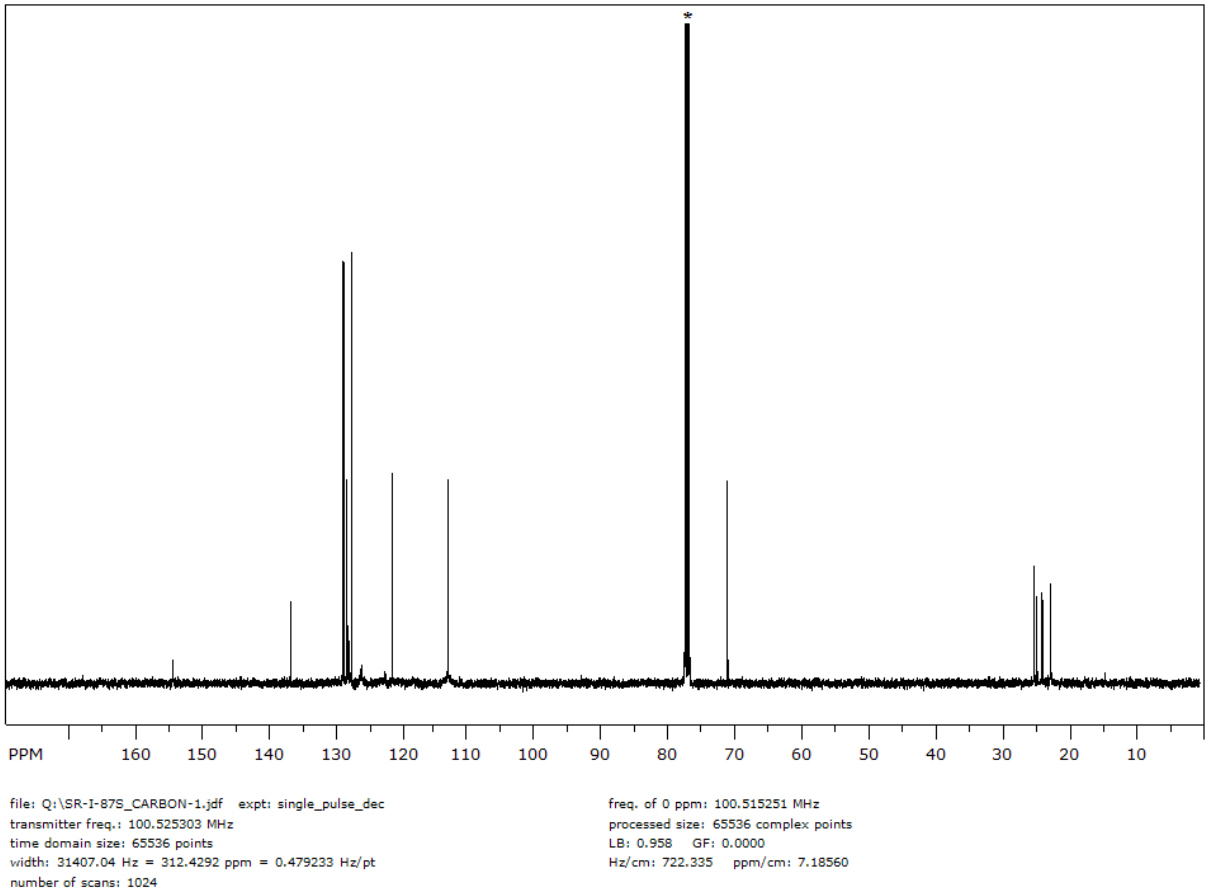
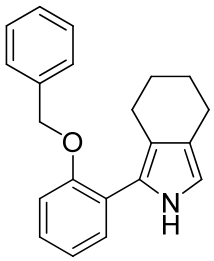


Figure S7b: ^{13}C NMR spectrum of compound **8a**.



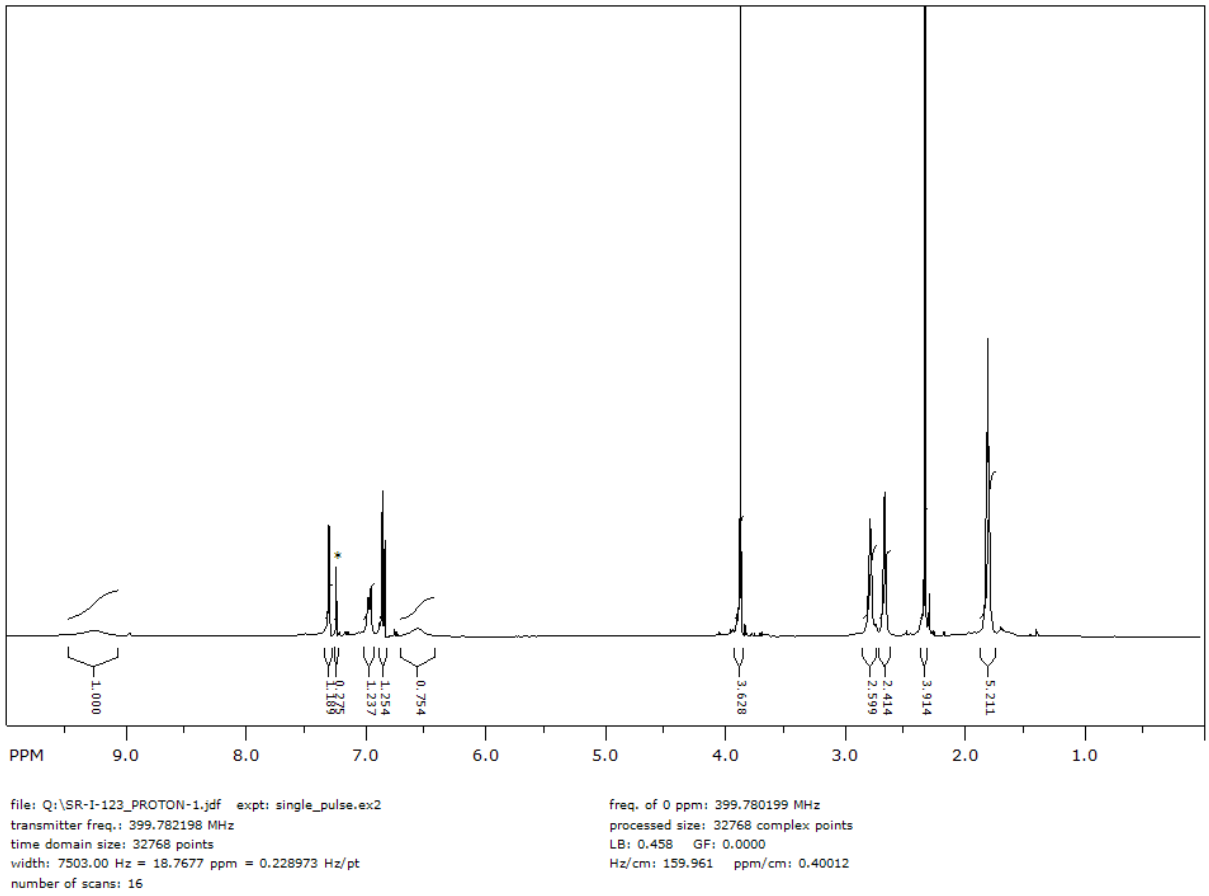
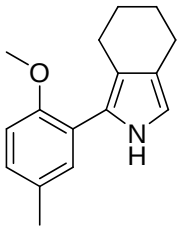


Figure S8: 1H NMR spectrum of compound **8b**.



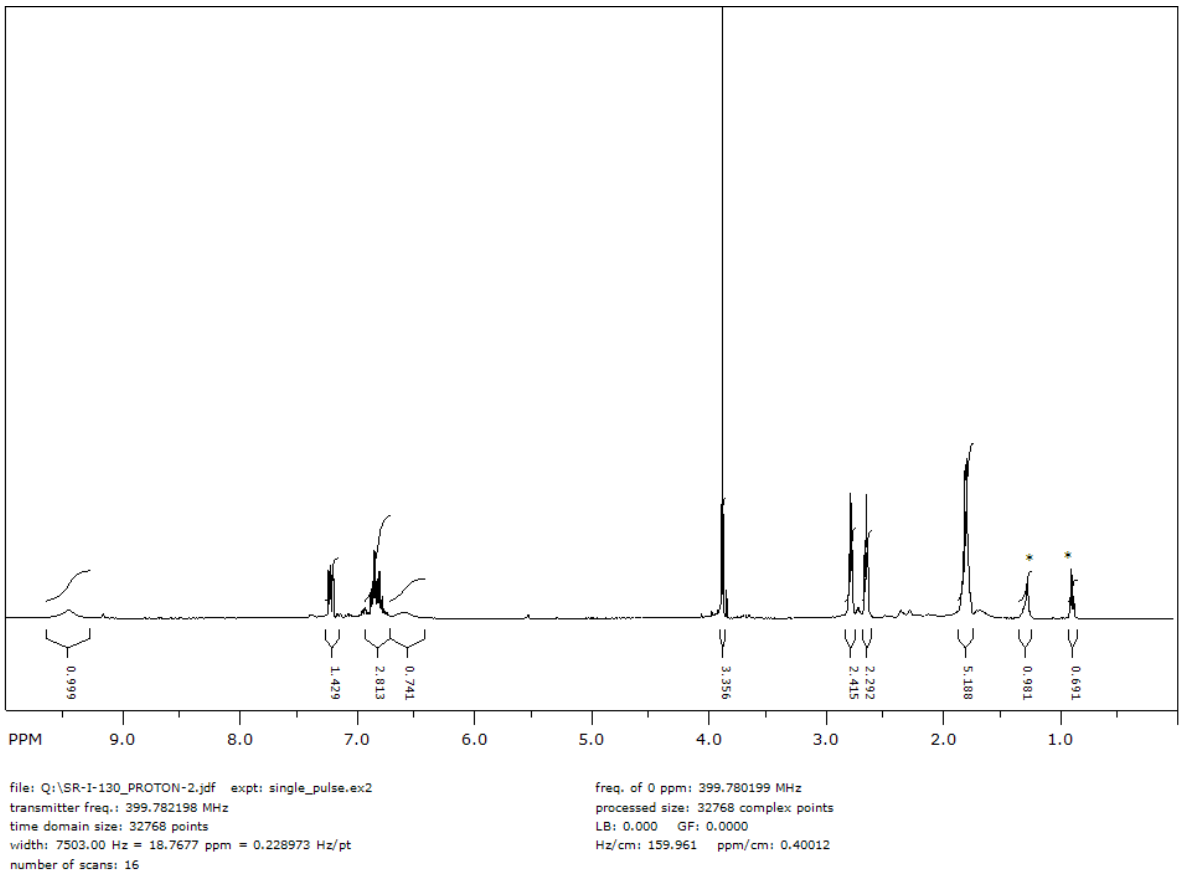
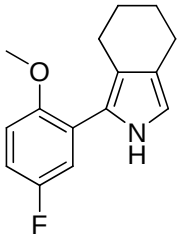


Figure S9a: ^{1}H NMR spectrum of compound **8c**. The marks with * is due to solvent impurity.



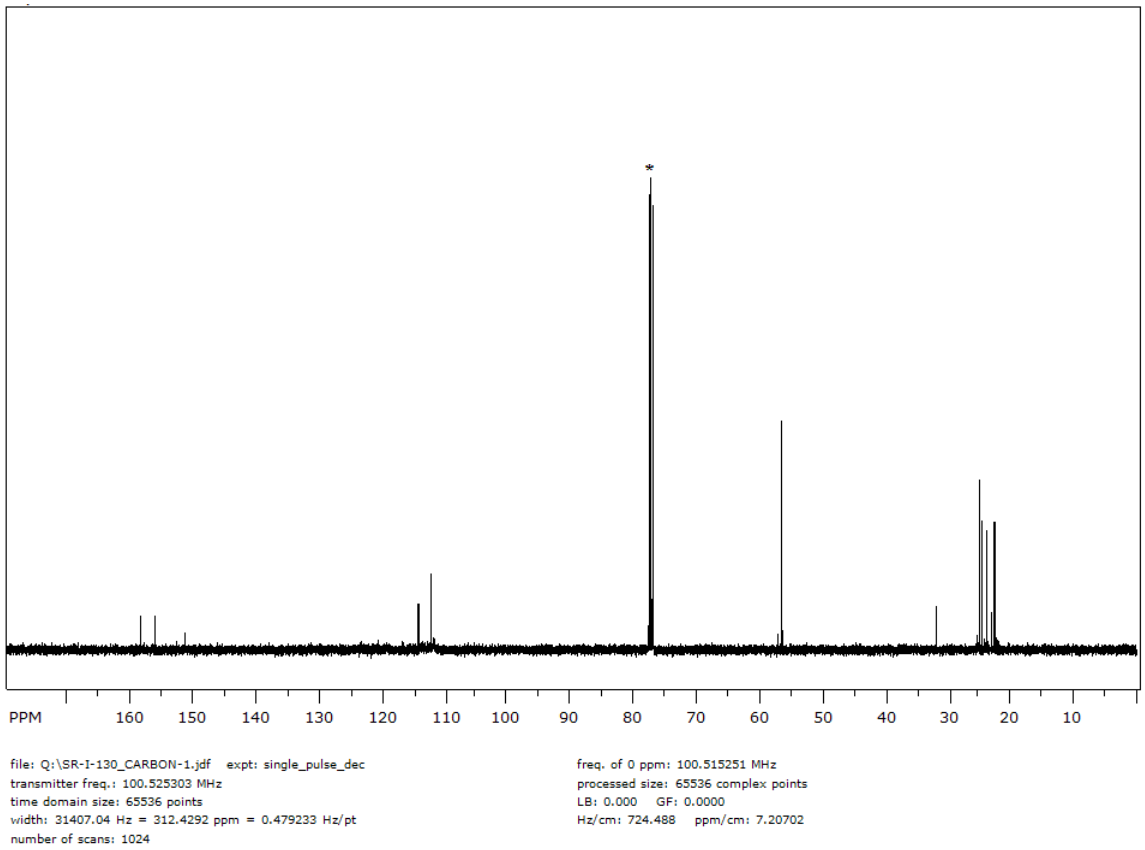
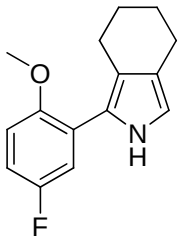


Figure S9b: ^{13}C NMR spectrum of compound **8c**.



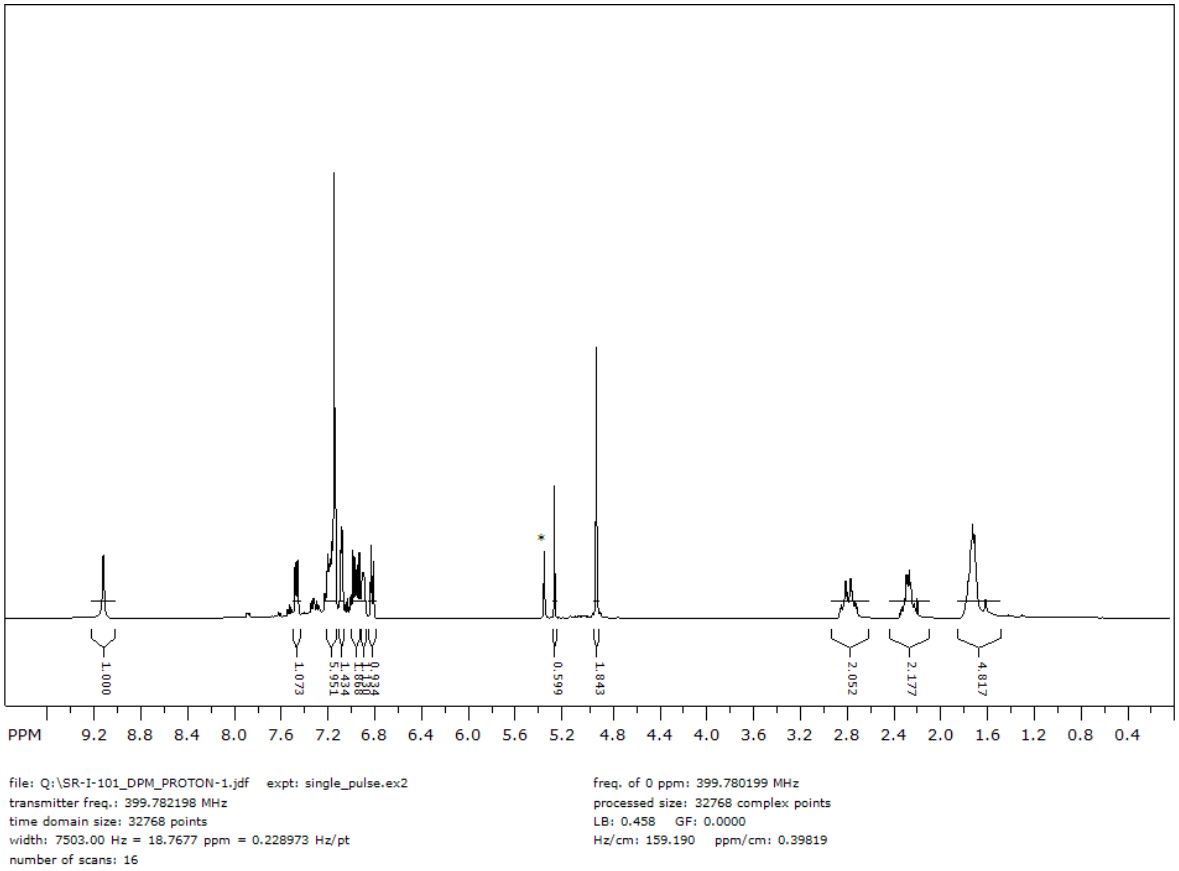
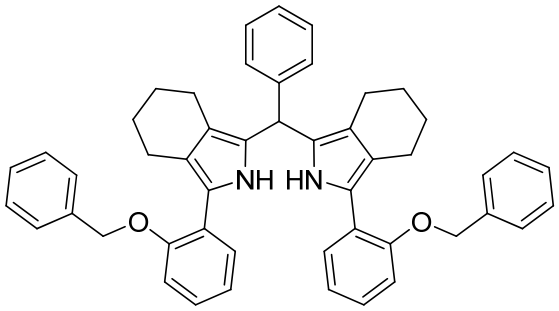


Figure S10a: ^{1}H NMR spectrum of compound **8a.1**. The mark with * is due to solvent impurity.



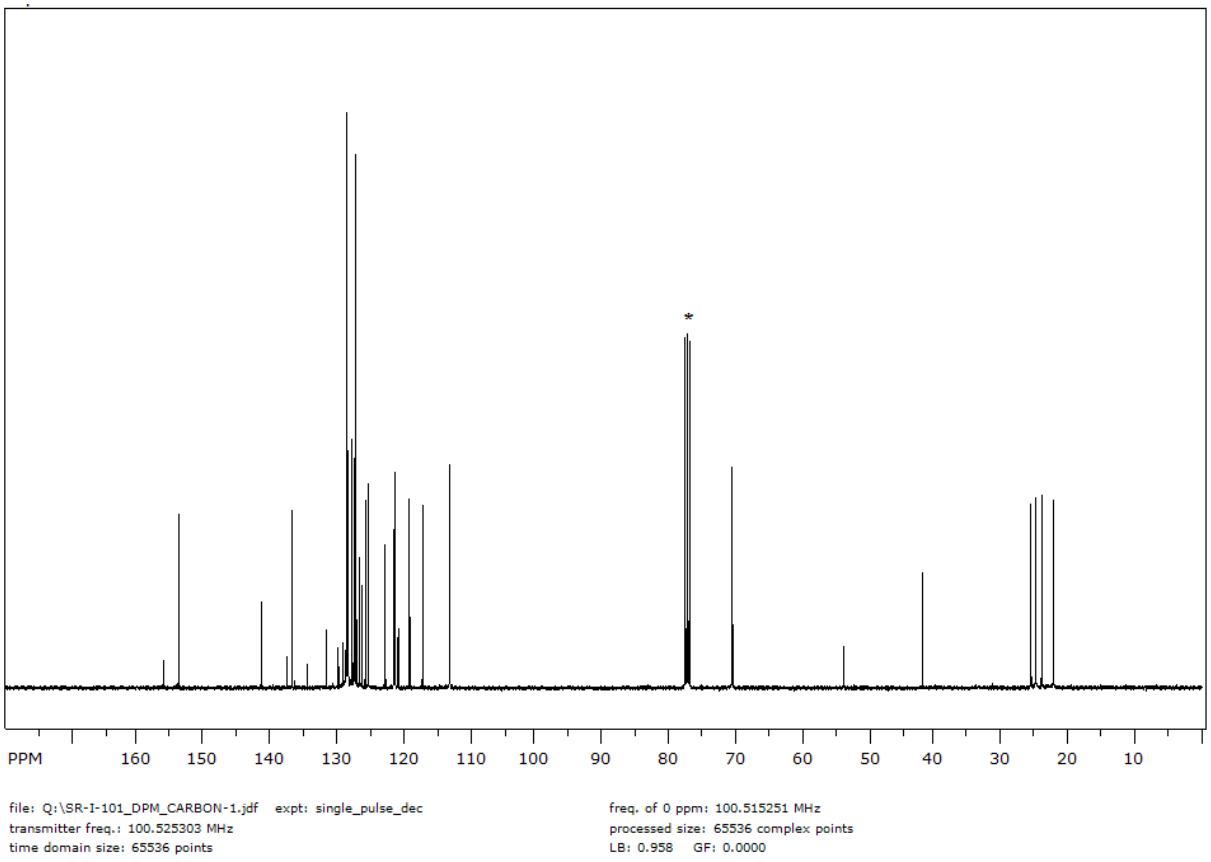
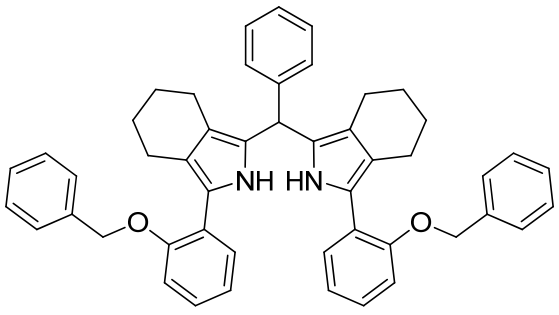


Figure S10b: ^{13}C NMR spectrum of compound **8a.1**.



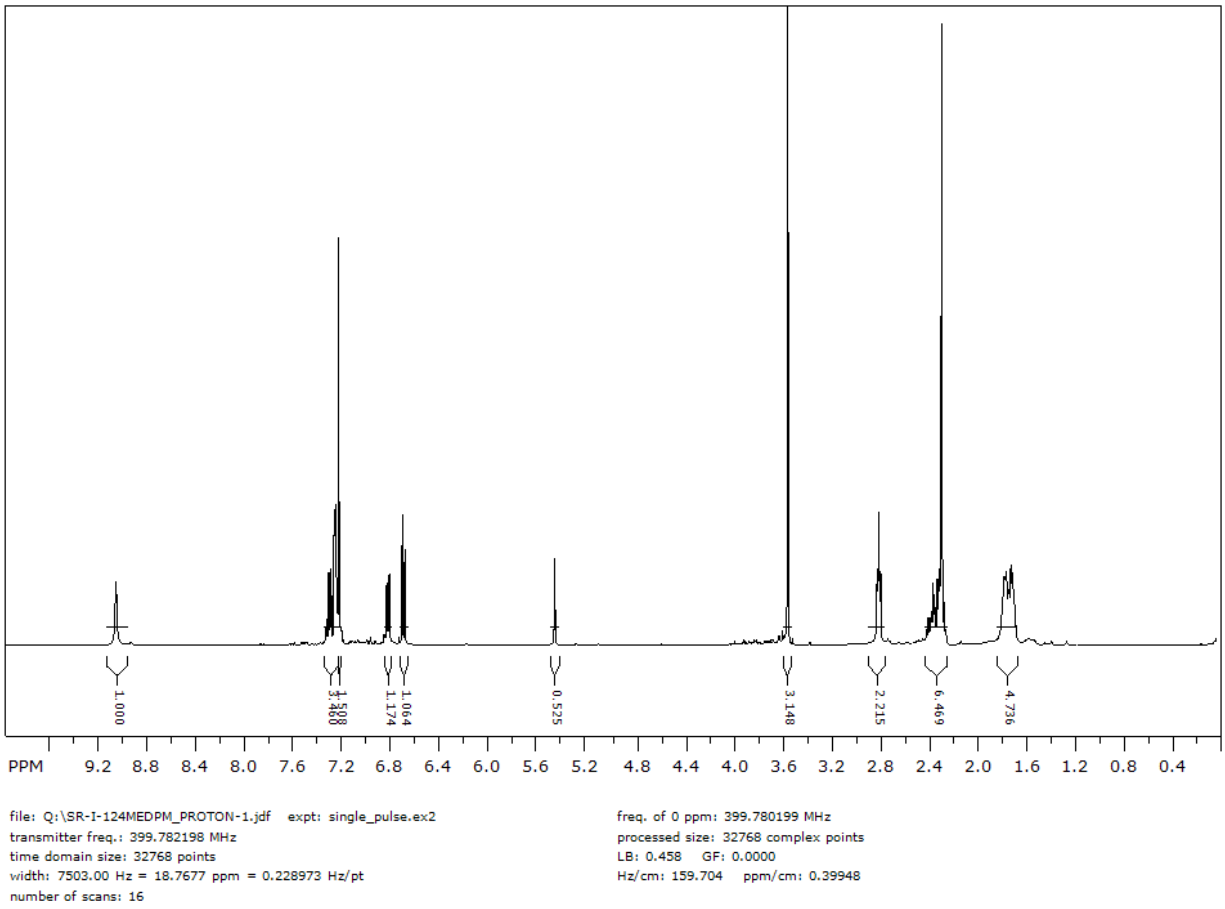
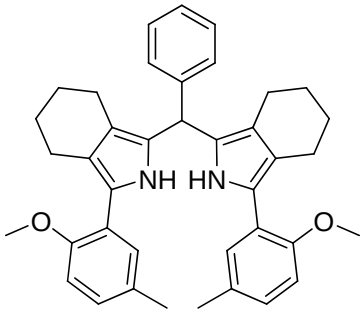


Figure S11a: ^{1}H NMR spectrum of compound **8b.1**.



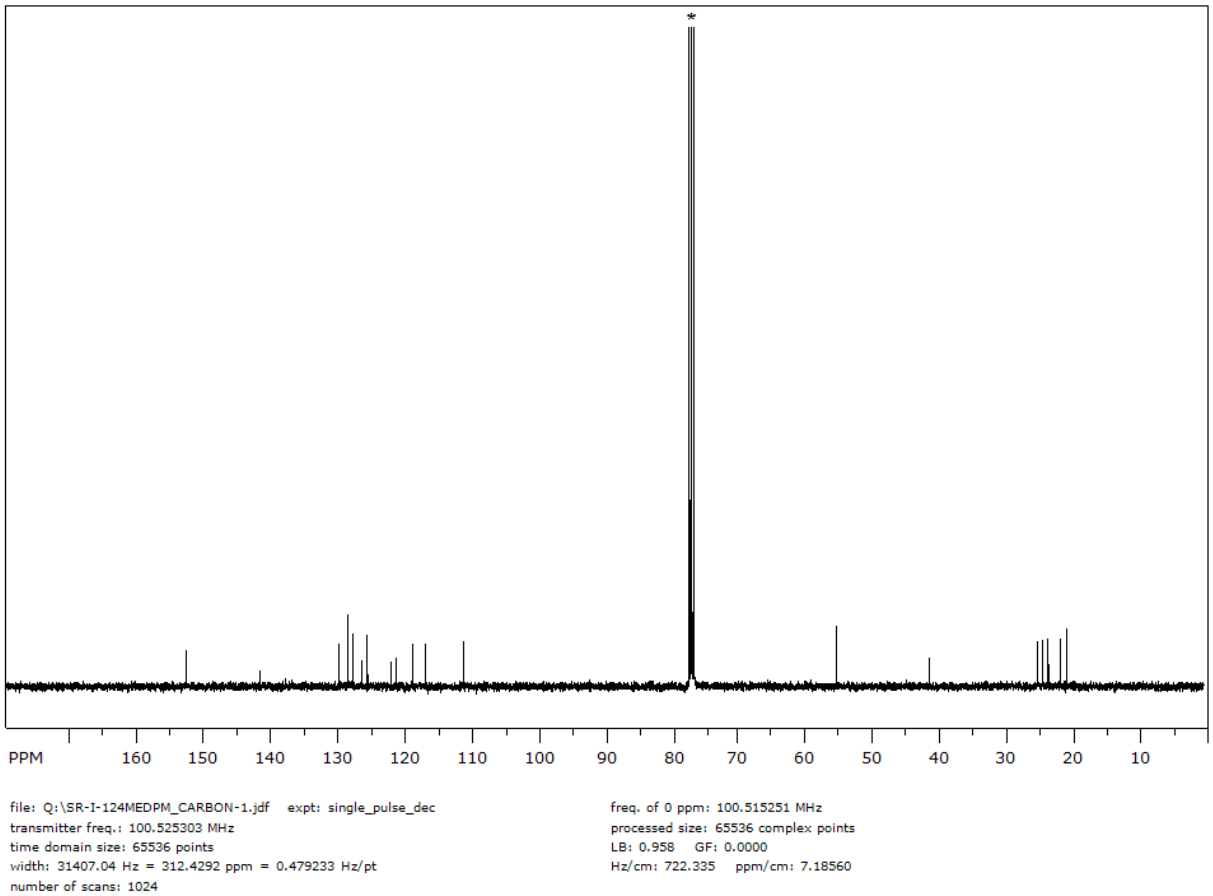
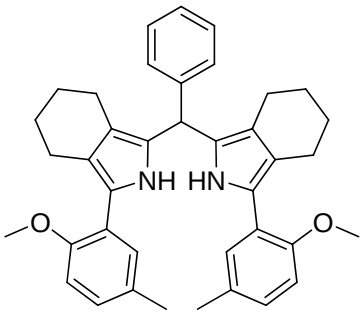


Figure S11b: ^{13}C NMR spectrum of compound **8b.1**



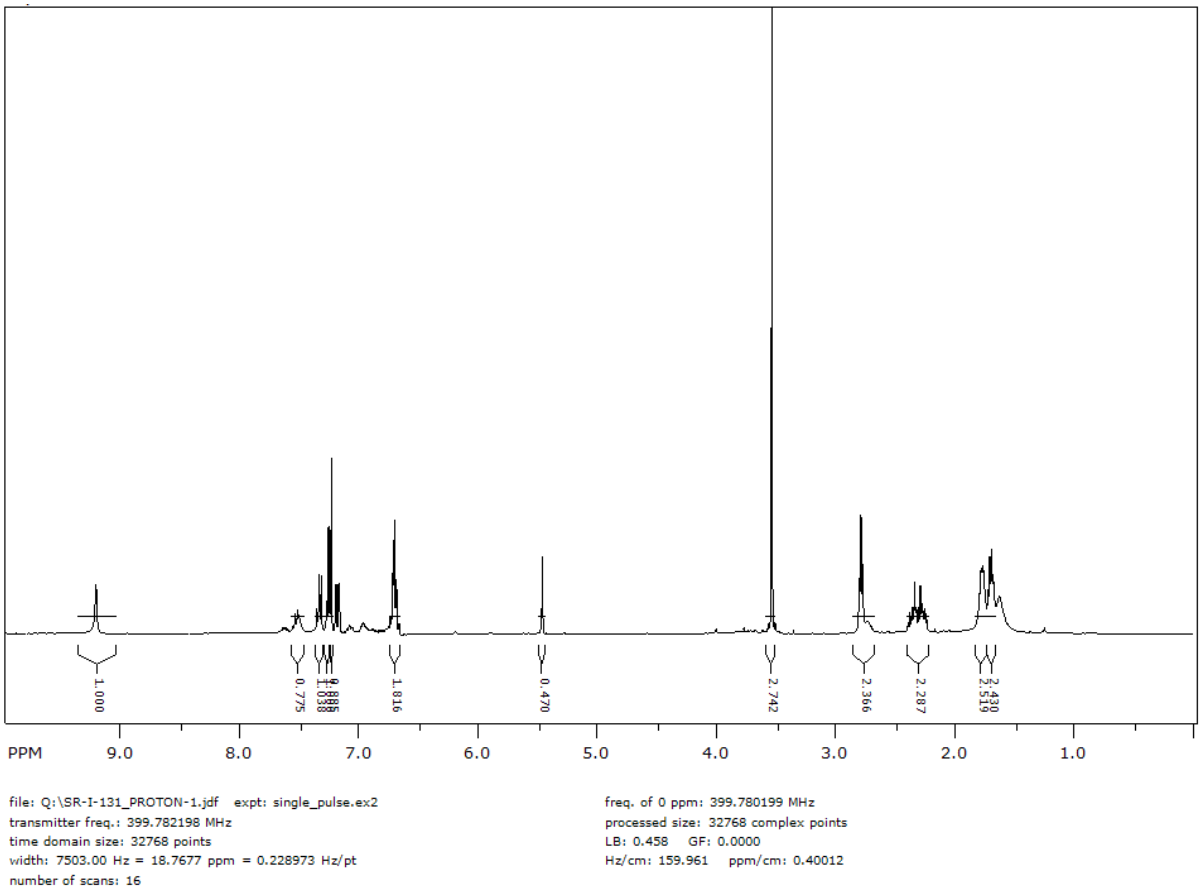
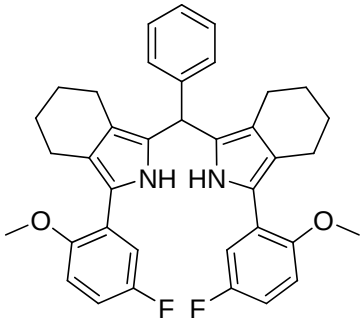


Figure S12a: ^{1}H NMR spectrum of compound **8c.1**.



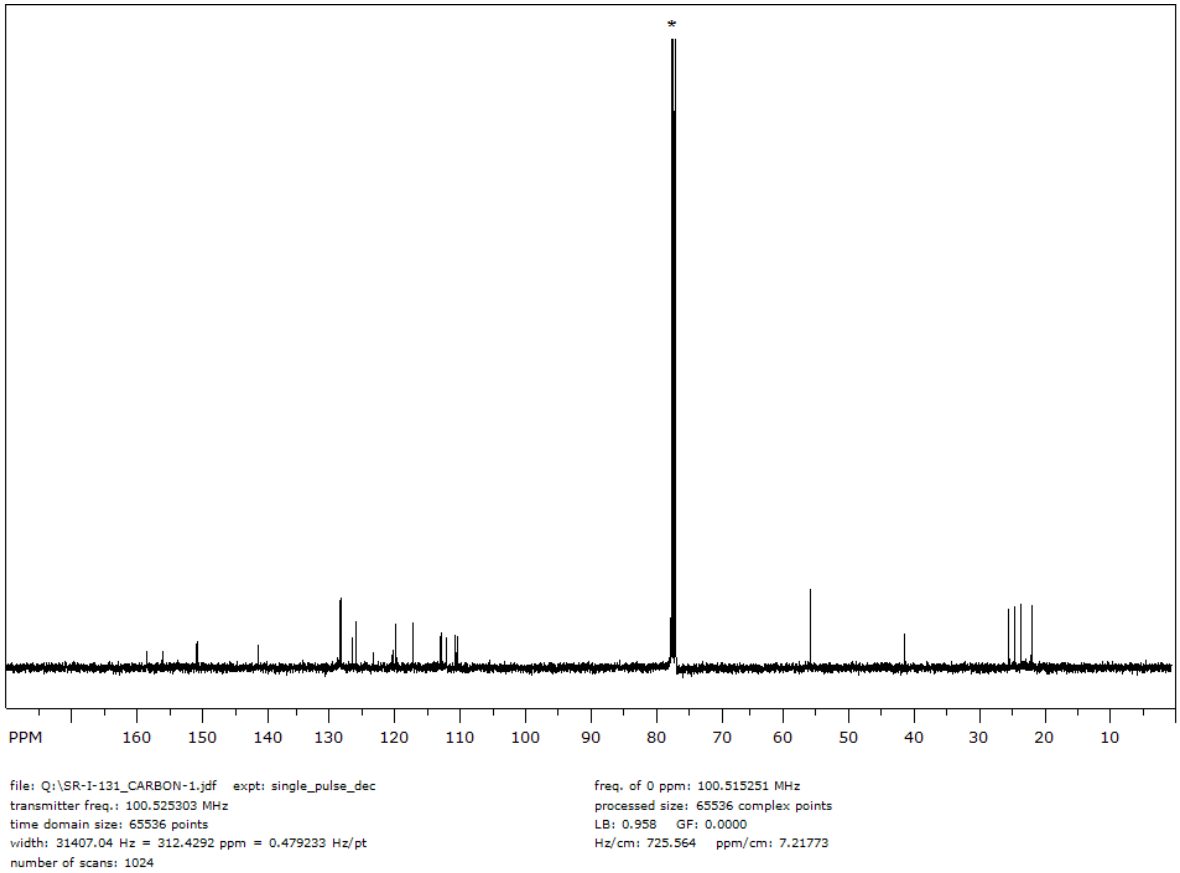
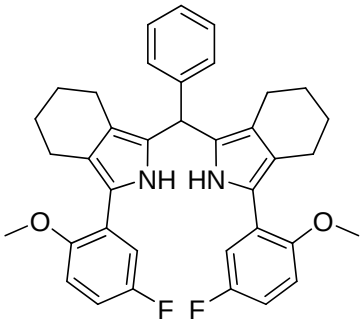


Figure S12b: ^{13}C NMR spectrum of compound **8c.1**.



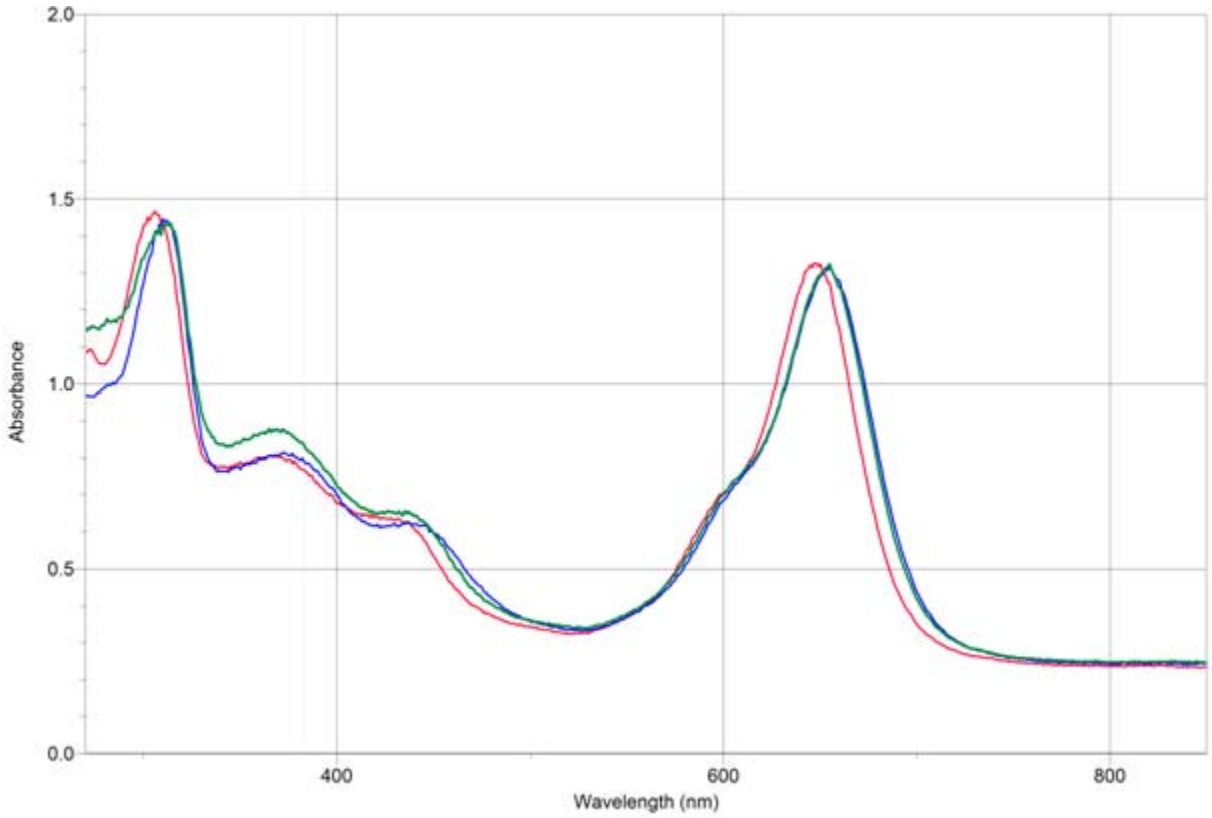


Figure S13: Comparison of absorption spectra of **4a** (———), **4b** (———), **4c** (———) recorded in dichloromethane.

Table S1: Absorption Data for Mn(III) Complexes **4a-4c** and Their Corresponding Mn(V)O Complexes **10a-10c**. The concentrations used for Q and Soret band spectra were 5×10^{-5} M (in methanol). Molar extinction coefficients are expressed as log ε.

Complexes	Soret band λ_{abs}, nm (log ε)	absorption Q-bands λ, nm (log ε)			
4a	307 (4.2)	370 (4.0)	437{sh}	596 {sh}	648 (4.2)
10a	304 (4.3)	-	373 {sh}	-	583 (3.7)
4b	312 (4.5)	376 (4.2)	445 {sh}	602 {sh}	656 (4.4)
10b	304 (4.6)	-	384 {sh}	-	582 (4.1)
4c	312 (4.3)	371 (4.0)	441 {sh}	602 {sh}	654 (4.2)
10c	307 (4.4)	-	388 {sh}	-	577 (3.9)

{sh = shoulder}

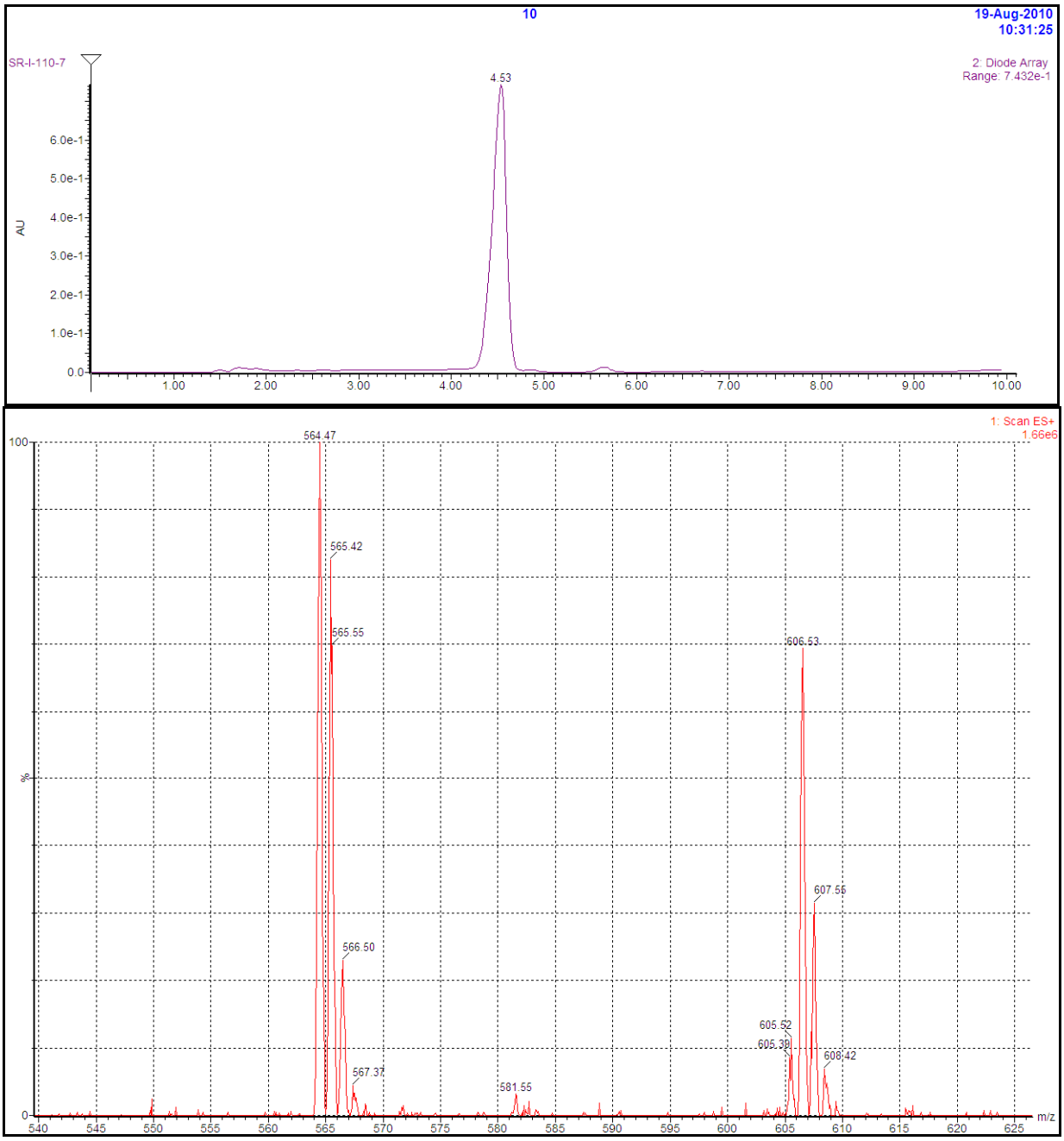


Figure S14: LCMS of complex **4a**.

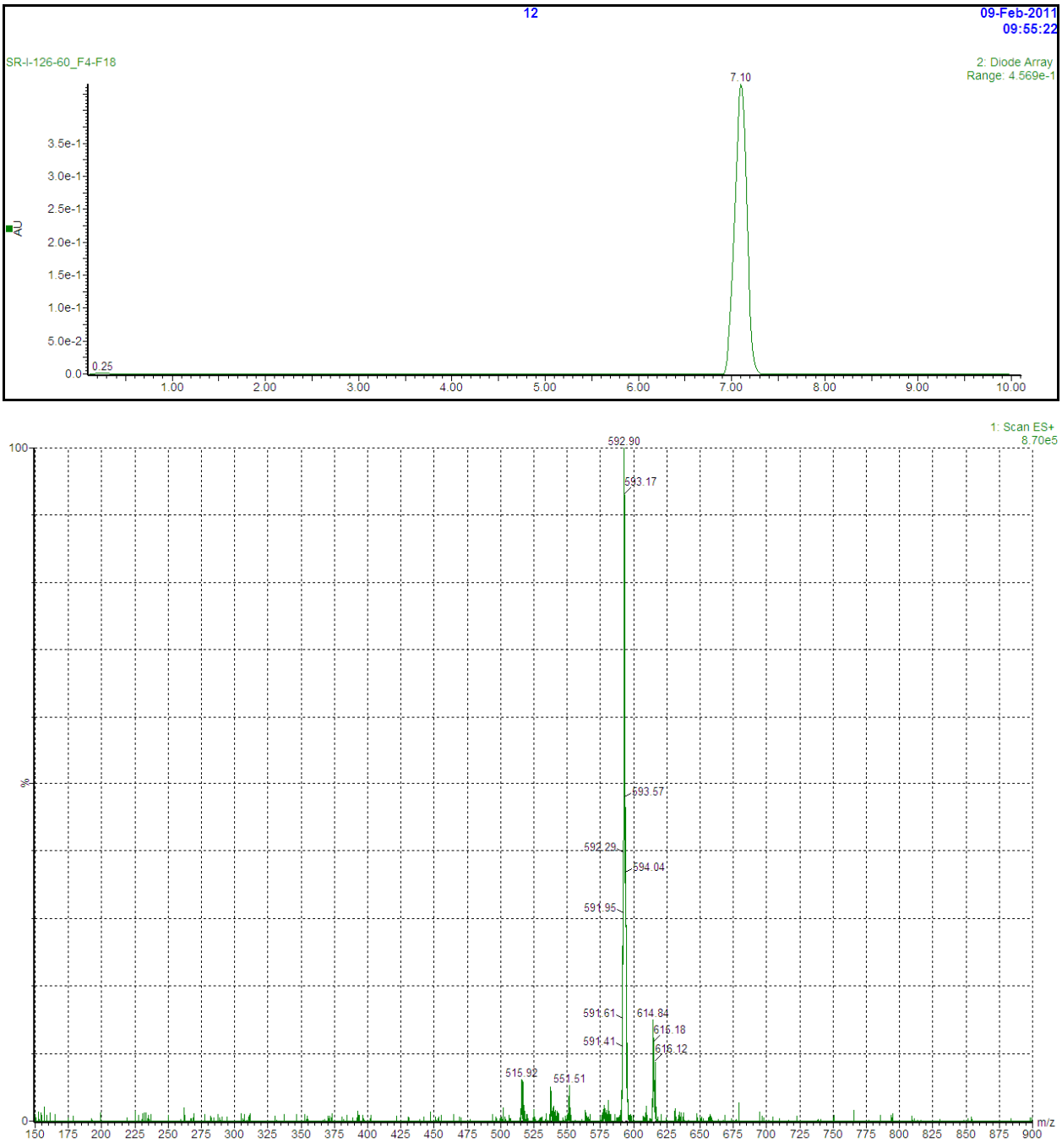


Figure S15: LCMS of complex **4b**.

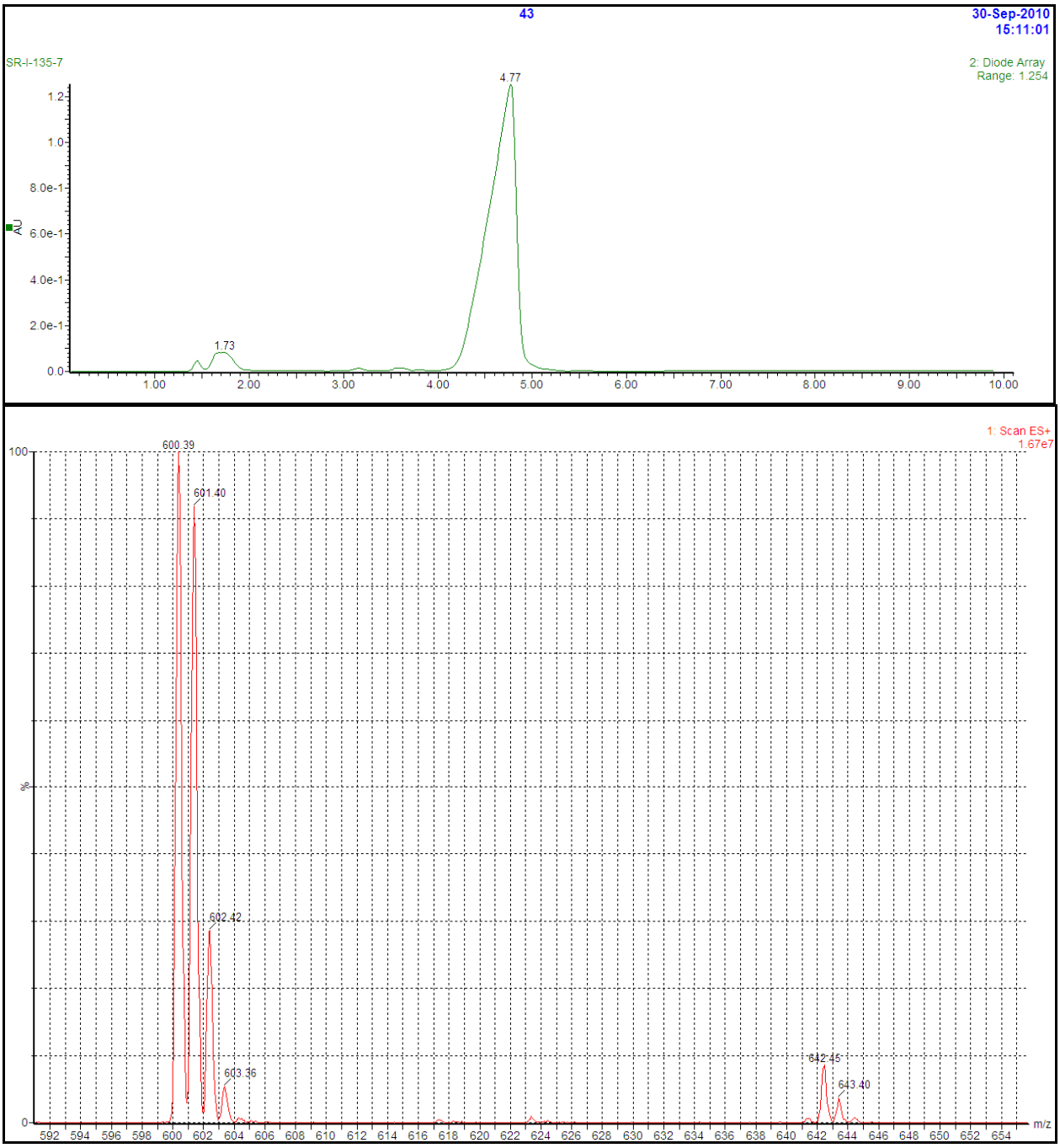
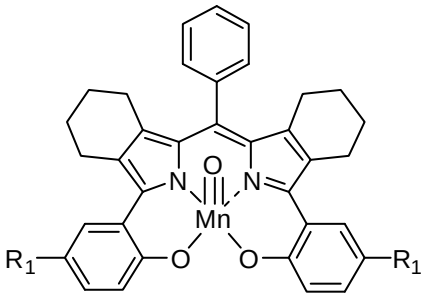


Figure S16: LCMS of complex **4c**.



10a R1 = H **Exact Mass =** 580.1559
10b R1 = CH_3 **Exact Mass =** 608.1872
10c R1 = F **Exact Mass =** 616.1370

Mn(V)O Complexes 10a-c from reaction of 4a-c with peroxynitrite: Complexes **4a-c** were dissolved in methanol to afford 3.3 x 10^{-5}M solutions (e.g. 2 mg **4c**, 3.3 x 10^{-6} moles, dissolved in 100 mL MeOH in a volumetric flask). Aliquots of 3 mL of each solution were removed and then treated with 20 equivalents of peroxynitrite (from a 0.05 M solution in 0.1N NaOH). Within 1 min the formation of the Mn(V)O species could be observed by a color change from green to red-brown. In each case the reaction was simultaneously followed by UV/Vis and LCMS to confirm complete formation of the Mn(V)O complexes. Similar results were obtained using oxone® in 4 different solvents; methanol, ethanol, isopropanol and acetone. Similar results were also obtained with m-CPBA in CH_2Cl_2 and with iodosylbenzene in $CHCl_3$.

10a: LCMS (75-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 1.73 min, $(M + H)^+$ = 581.42.

10b: LCMS (75-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 2.07 min, $(M + H)^+$ = 609.44.

10c: LCMS (75-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 1.70 min, $(M + H)^+$ = 617.34.

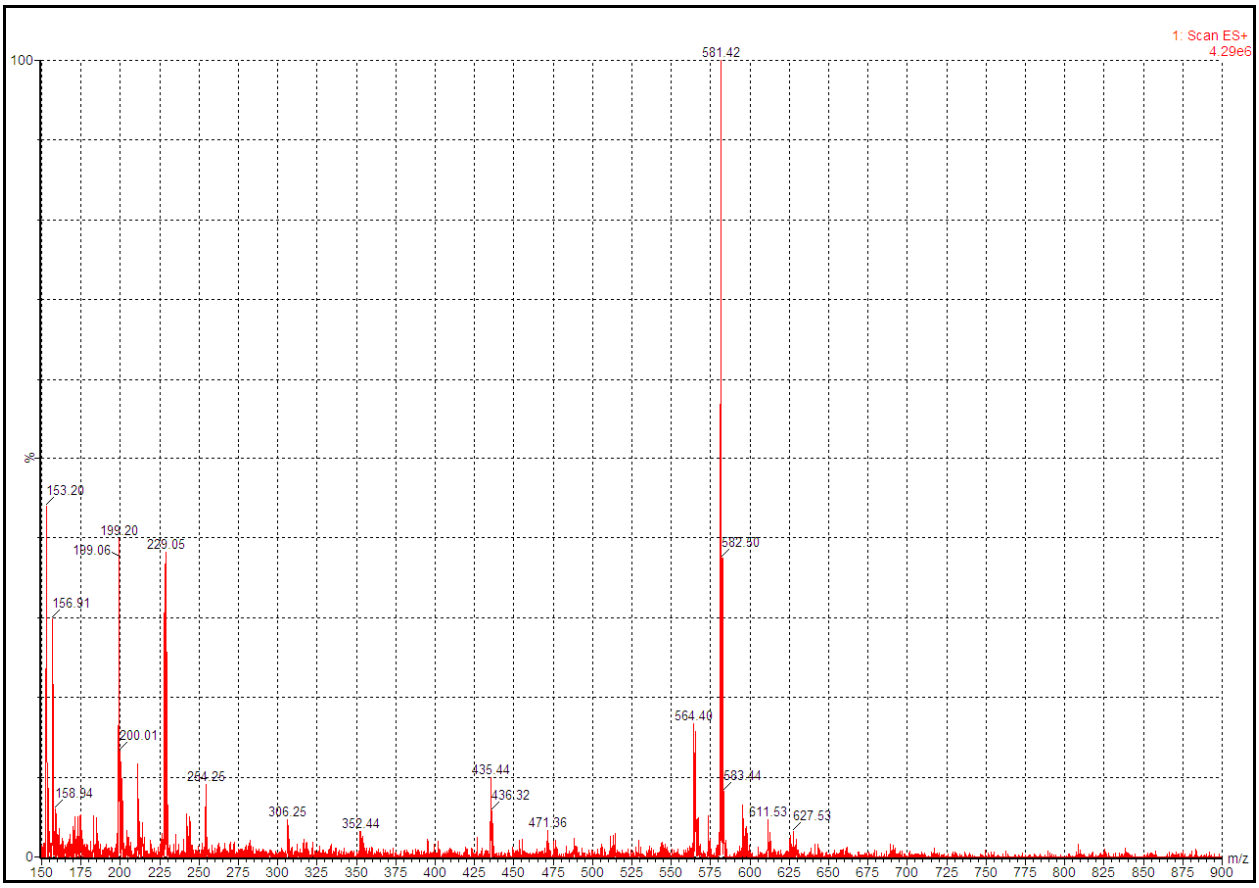


Figure S17: LCMS spectrum of **10a**.

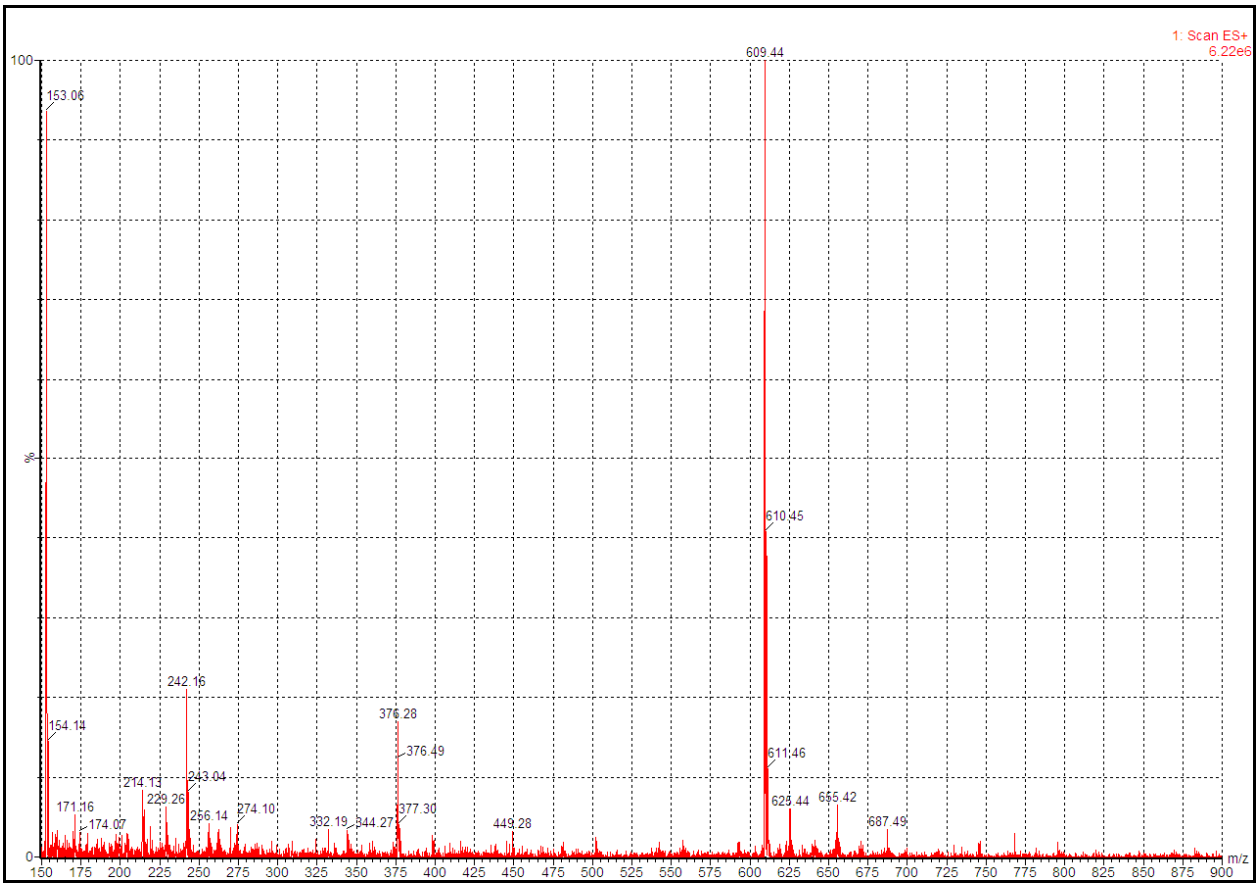


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Figure S18: LCMS spectrum of **10b**.

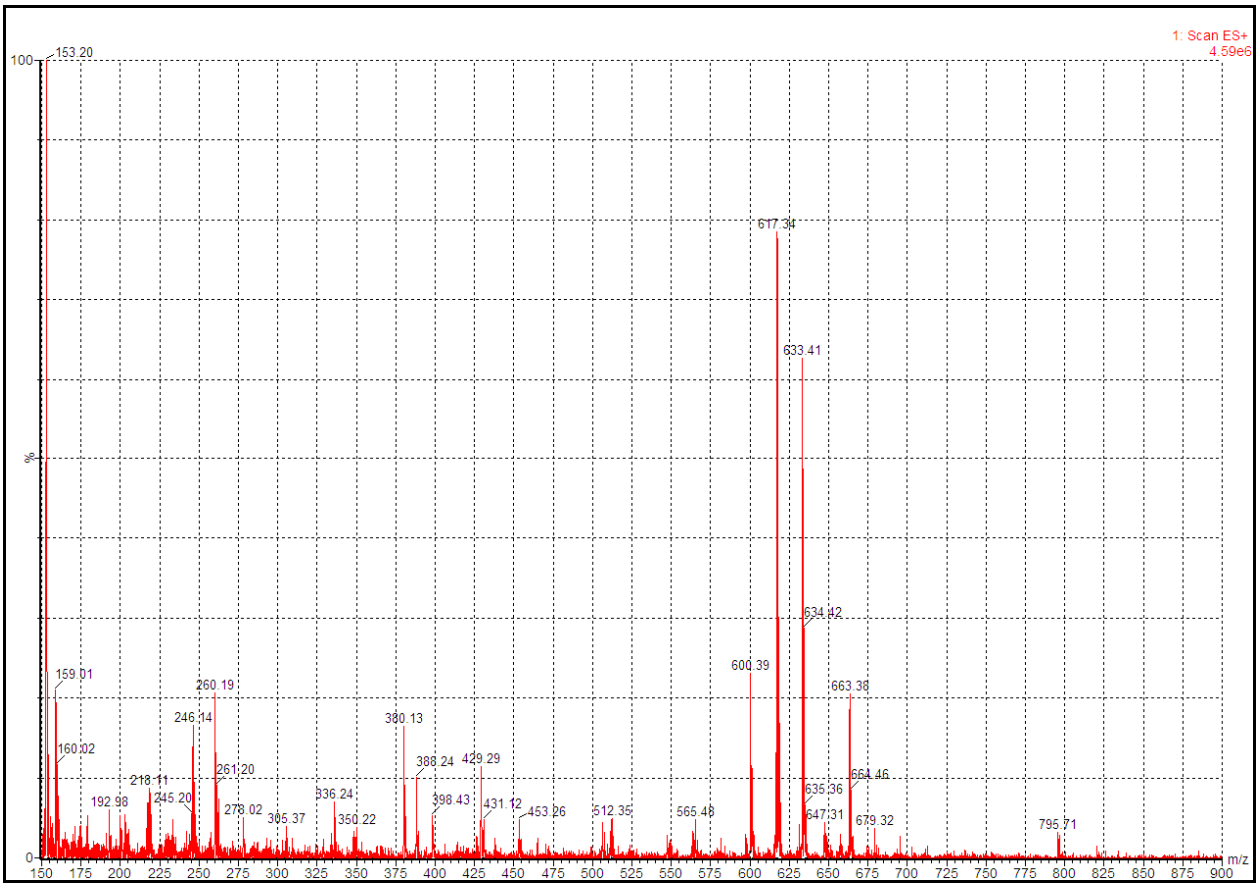


Figure S19: LCMS spectrum of **10c**.

A solution of complex **4c** (3 mL of a 3.3 x 10^{-5}M solution in methanol) was treated with 10 equivalents of peroxynitrite (from a 0.05 M solution in 0.1N NaOH). Within 1 min the formation of the Mn(V)O species **10c** could be observed by a color change from green to red-brown. Under these conditions, UV/Vis indicated a ~50/50 mixture of Mn(III) and Mn(V)O and LCMS of this mixture confirms mainly these two species (see Figure S19a-c). After 5 min, the mixture was treated with 100 mM phosphate buffer (100 μL) and the color instantaneously changed from red to green. A gas was evolved during this process (possibly O_2). LCMS at this time confirms the return to Mn(III) complex **4c** (Figure S20a-b).

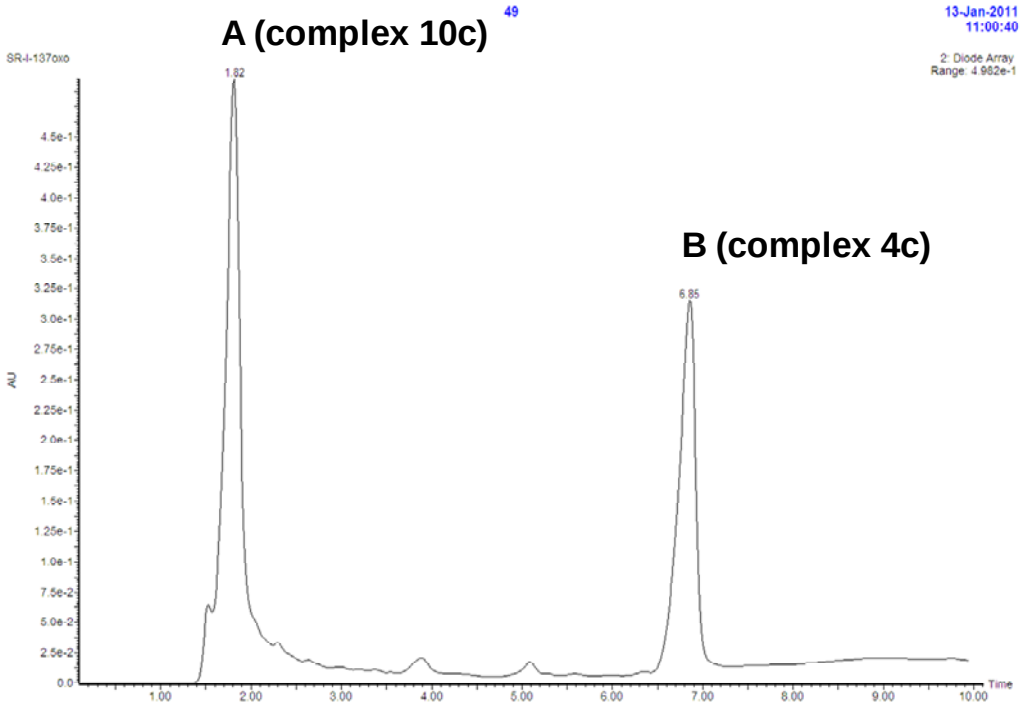


Figure S20a. LC trace for treatment of **4c** with 10 equivalents of peroxynitrite

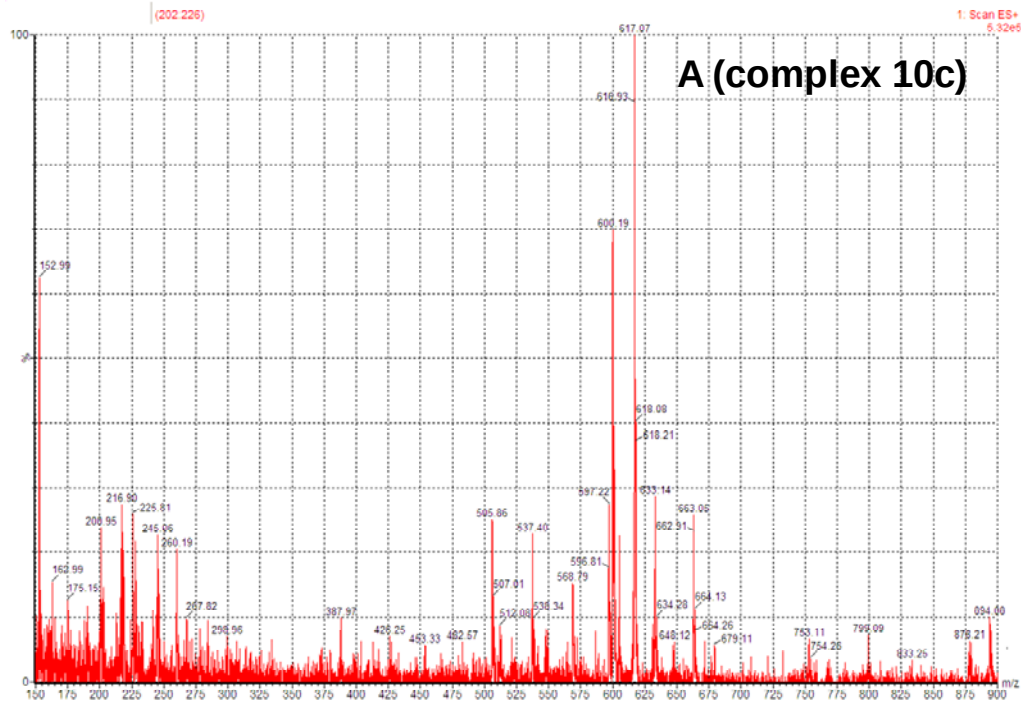


Figure S20b. Mass Spectrum for peak A (complex **10c**) in LC trace of Figure S19a.

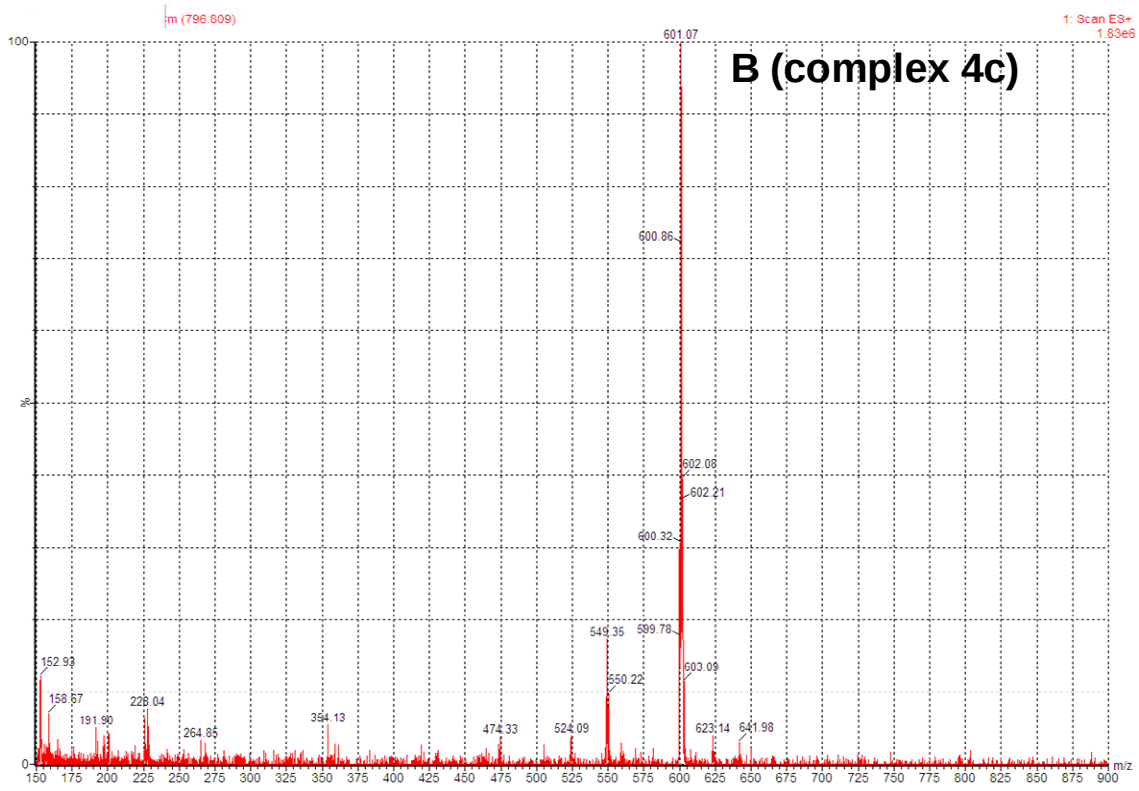


Figure S20c. Mass Spectrum for peak B (complex **4c**) in LC trace of Figure S19a.

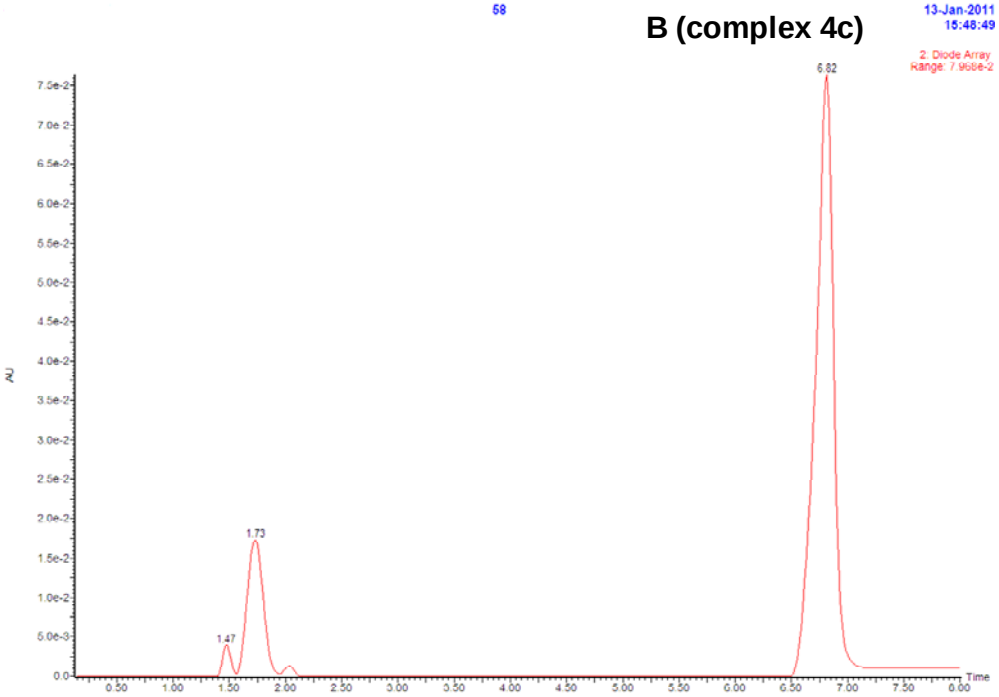


Figure S20a. LC trace for treatment of the mixture of **4c** and **10c** (Figure S19a) with 100 µL phosphate buffer.

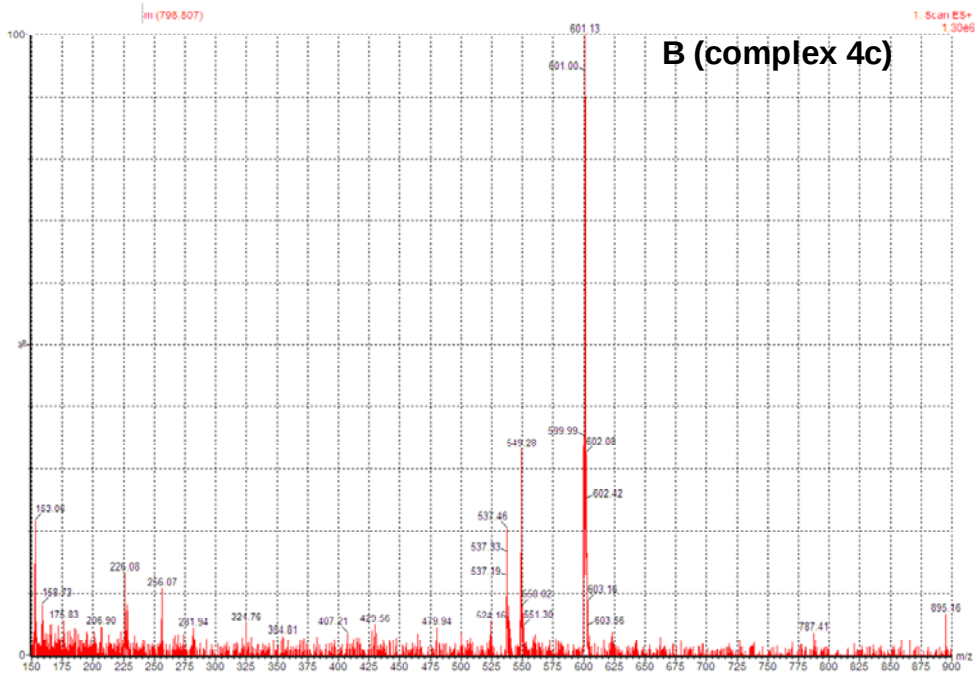
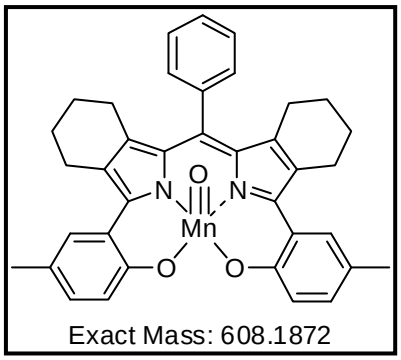


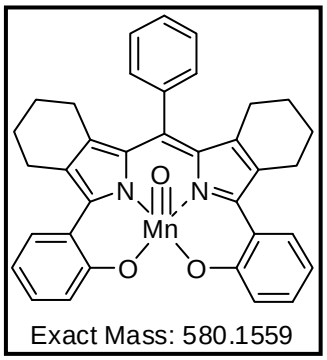
Figure S20b. Mass Spectrum for peak B (complex **4c**) in LC trace of Figure S20a.



Exact Mass: 608.1872

Mn(V)O Complex 10b from reaction with m-CPBA: To a green solution of **4b** (10.0 mg, 0.016 mmol) in 10 mL of CH_2Cl_2 was added *m*-CPBA (3.05 mg, 0.017 mmol). Within 1 min a color change from deep green to red-brown was observed. The reaction was followed closely by UV-vis and LCMS. LCMS confirmed the formation of **10b** as the major product after 1 min reaction time. LCMS (75-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 2.07 min, $(M + H)^+ = 609.44$. UV-vis (in CH_2Cl_2, λ_{max}): 304, 384, 582.

Mn(V)O Complex 10a from reaction with m-CPBA: To a green solution of **4a** (10.0 mg, 0.017 mmol) in 10 mL of CH_2Cl_2 was added *m*-CPBA (3.05 mg, 0.017 mmol). Within 1 min a color change from deep green to red-brown was observed. The reaction was monitored by UV-vis and LCMS. LCMS confirmed the formation of **10a** as the major product after 1 min reaction time. Attempted purification of **10a** by flash chromatography (silica gel/CH_2Cl_2) resulted in decomposition products (some conversion back to the green Mn(III) species was also observed). The reaction was repeated in CD_2Cl_2 and the ^1H NMR of the diamagnetic Mn(V)O species was recorded for the reaction mixture. Figure S22 compares the ^1H NMR for the upfield region (focusing on the cyclohexyl proton absorptions) for the paramagnetic high-spin Mn(III) complex **4a** and the diamagnetic low-spin d_2 Mn(V)O complex **10a**: ^1H NMR (CD_2Cl_2): δ 1.70 (m, 8 H), 2.26 (m, 4 H), 2.71 (m, 4 H). LCMS (75-95% acetonitrile in 0.05% TFA over 10 minutes) retention time = 1.73 min, $(M + H)^+ = 581.42$.UV-vis (in CH_2Cl_2, λ_{max}): 304, 373, 583.



Exact Mass: 580.1559

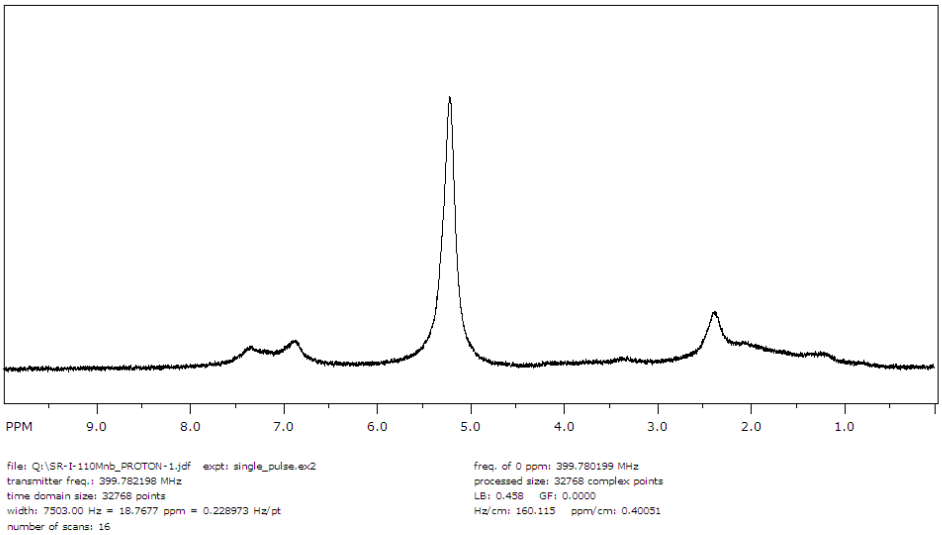


Figure S21a: ^{1}HNMR spectra of **4a** recorded in CD_2Cl_2.

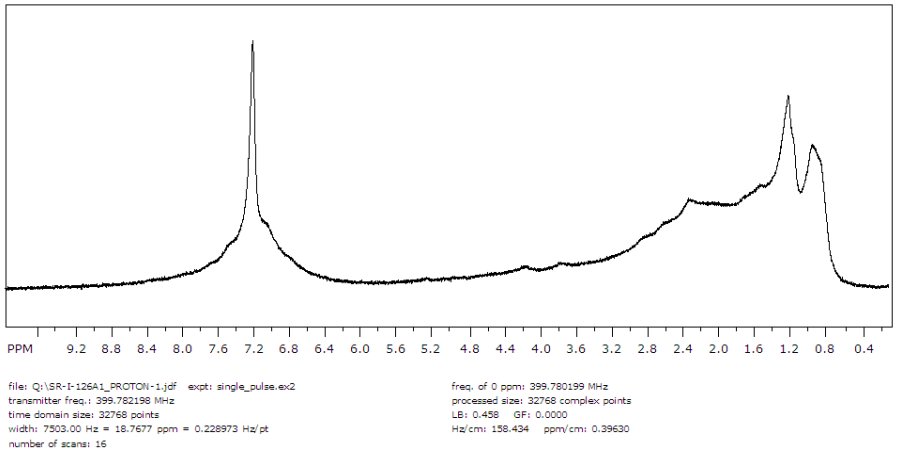


Figure S21b: ^{1}HNMR spectra of **4b** recorded in $CDCl_3$.

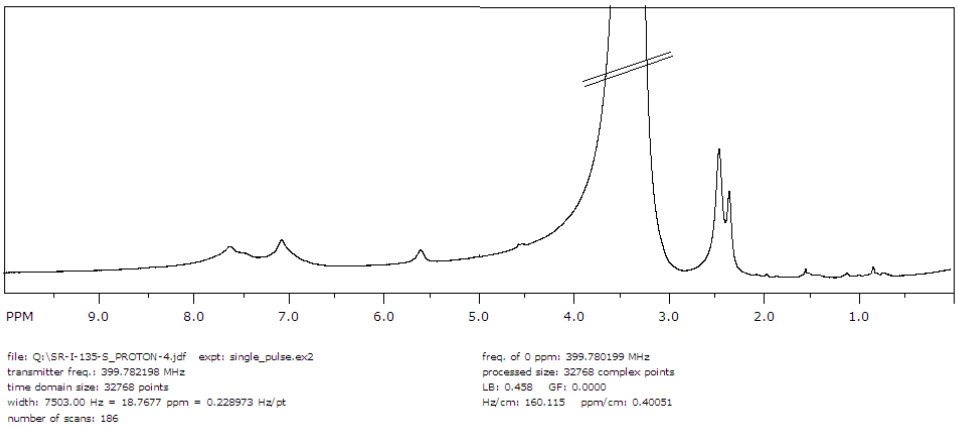


Figure S21c: ^{1}HNMR spectra of **4c** recorded in DMSO-d_6.

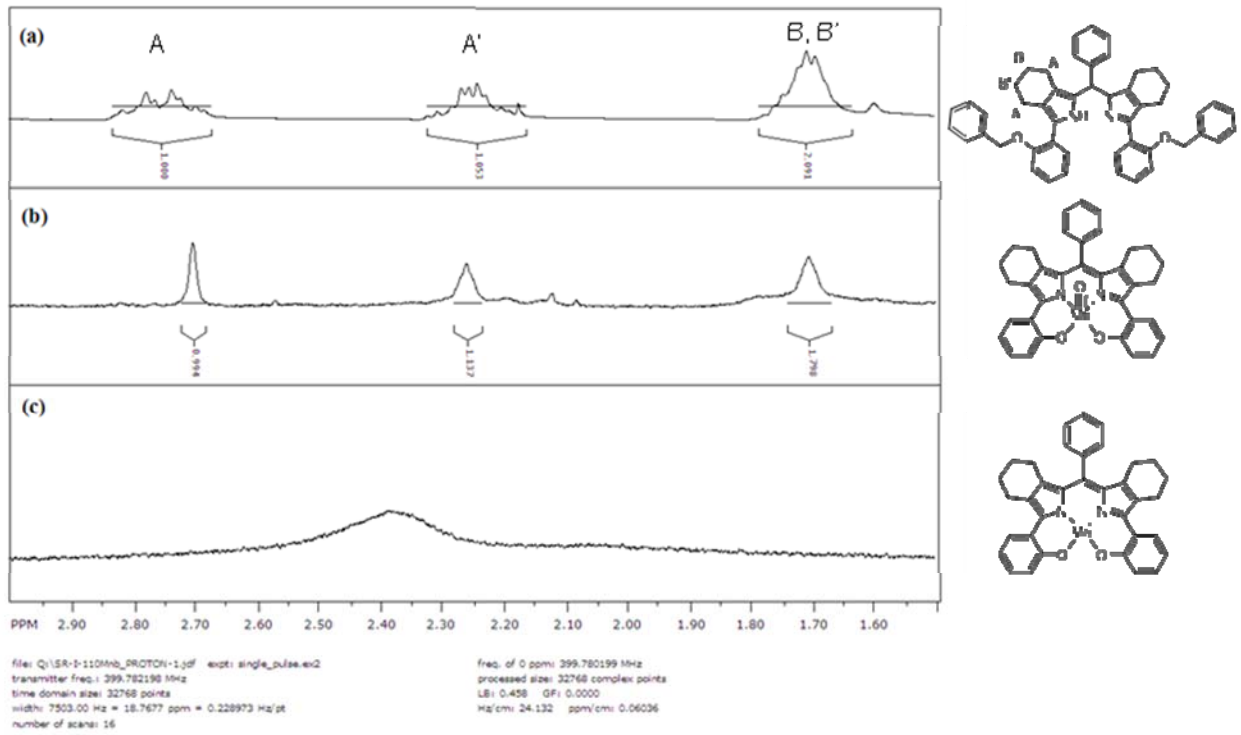


Figure S22. Comparison of ^{1}HNMR spectra of (a) **8a.1**, (b) **10a** and (c) **4a** recorded in CD_2Cl_2.

(a) Dipyrromethane compound **8a.1** (included for reference chemical shift values for the cyclohexenyl protons in a similar diamagnetic system). The spin system "A" is tentatively assigned to the downfield multiplet due to its proximity to the deshielding region of the adjacent phenyl group. (b) The diamagnetic Mn(V)O complex **10a** showing similar cyclohexenyl absorptions. (c) The broadened and paramagnetically shifted upfield region for Mn(III) complex **4a**.

Magnetic Susceptibility Measurement. A representative magnetic susceptibility for compound **4b** was measured using the Johnson-Matthey Mark I magnetic susceptibility balance. The temperature was 25°C (298 °K). The Johnson-Matthey balance is similar to the Gouy balance but, instead of measuring the force that a magnet exerts on a sample, the opposite force that the sample exerts on a suspended magnet is observed.

Mass Susceptibility of **4b**:

$$\chi_g = \frac{C_{bal} l (R-R_o)}{10^9\, m} = \frac{(1.063)(1.0)(650)}{10^9(0.0491)} = 1.41 \times 10^{-5}\ \text{c.g.s.}$$

l = sample length (cm)

m = sample mass (g)

R = reading for tube plus sample

R_o = empty tube reading

C_{bal} = balance calibration constant

Molar Susceptibility of **4b**:

$$\chi_m = \chi_g \times \text{Molecular weight} = 1.41 \times 10^{-5} \times 592.19 = 8.35 \times 10^{-3}\ \text{cm}^3/\text{mol}$$

Uncorrected Spin only μ_{eff} of **4b**:

$$\mu_{eff} = \sqrt{8\,\chi T} = \sqrt{8(8.35 \times 10^{-3})(298)} = 4.46\ \text{BM}$$

Number of unpaired electrons for **4b**:

$\mu_{eff} = \sqrt{n(n+2)}$ for n = 4 unpaired electrons:

$$\mu_{eff} = \sqrt{4(4+2)} = \sqrt{4(4+2)} = 4.9\text{BM}$$

Peroxynitrite Decomposition via Inhibition of Aryl Boronate Oxidation Assay. Stock solutions of 4-acetylphenylboronic acid and the catalyst were prepared in DMSO (in the 5-50 mM range). Peroxynitrite in 0.1 N NaOH solution was prepared by the method of Pryor[2] and frozen at -80 °C until needed). Small aliquots of the PN solution were thawed, kept on ice and the concentration was measured by UV spectroscopy just before measurements were made. Peroxynitrite concentrations ranged from 58-77 mM for these studies. In a typical procedure 9.5 x 10^{-7} moles of 4-acetylphenylboronic acid (24.0 µL of stock) was dispensed into a small vial equipped with a magnetic stir bar. 2.00 mL of 100 mM phosphate buffer (pH = 7.2) which contained 0.7% sodium dodecyl sulphate and 100 µM DTPA was added followed by 9.5 x 10^{-7} moles of the catalyst (aliquot from DMSO stock). To this rapidly stirred mixture was added 9.5 x 10^{-7} moles peroxynitrite by rapid injection. The mixture was stirred for one minute and analyzed by LCMS (Waters Alliance-MS3100 system; 15% acetonitrile/H_2O to 95% acetonitrile (0.05% TFA) over 10 minutes; Agilent Eclipse XD8-C18 column, 5 µM, 4.6 x 150 mm, UV detection 280 nm for 4-hydroxyacetophenone oxidation product). Reactions were run in mulitplets (n = 5) and compared to controls (also n=5) which contained everything except the catalyst (amounts of DMSO which were equivalent to those from aliquoted catalyst solutions were added to the controls to compensate for the very small effect of DMSO). The peak areas for phenol oxidation products were compared for catalyst vs control runs to determine percent inhibition.

Calculations:

% Inhibition

$$(1 - \frac{OX_{cat}}{OX_{control}}) * 100$$

$$\%\ RSD^2 = (\%\ RSD\ OX_{cat})^2 + (\%\ RSD\ OX_{control})^2$$

$$\Delta\ \%I = \sqrt{\left(\frac{\Delta\ OX_{cat}}{OX_{cat}}\right)^2 + \left(\frac{\Delta\ OX_{control}}{OX_{control}}\right)^2} \times\ \%I$$

Estimated k for oxidation of Mn(III) to Mn(V)O

$$k_{est} = \left(\frac{\%I}{100-\%I}\right) \cdot 1.6 \times 10^6$$ (2^{nd} order rate constant for oxidation of boronic acid by peroxynitrite)

$$\%\ RSD^2 = (\%\ RSD\ Ox)^2 + (\%\ RSD\ Reduced)^2$$

$$\Delta\ k_{est} = \sqrt{\left(\frac{\Delta\ \%I}{\%I}\right)^2 + \left(\frac{\Delta\ \%I}{100-\%I}\right)^2} \times\ k_{est}$$

[2] Uppu, R. M.; Pryor, W. A. *Anal. Biochem.* **1996**, *236*, 242-9.

Experimental animals. Male Sprague Dawley rats (200-220 g) were purchased from Harlan (Indianapolis IN), housed 3-4 per cage, and maintained in a controlled environment (12 h light/dark cycles) with food and water available *ad libitum*. All experiments were performed in accordance with the International Association for the Study of Pain and the National Institutes of Health guidelines on laboratory animal welfare and the recommendations by Saint Louis University Institutional Animal Care and Use Committee.

Drug administration and induction of thermal hyperalgesia. 4a or its vehicle DMSO was given by gavage (0.2 ml) 30 minutes before intraplantar injection of carrageenan (50 μl of a 1% solution in saline) into the right hindpaw of lightly anesthetized rats [CO_2 (80%)/O_2 (20%)]. Hyperalgesic responses to heat were determined by the Hargreaves' Method using a Basile Plantar Test (Ugo Basile; Comeria, Italy) (Hargreaves et al., 1988) with a cut-off latency of 20 s employed to prevent tissue damage. Rats were individually confined to Plexiglas chambers. A mobile infrared generator was positioned to deliver a thermal stimulus directly to an individual hindpaw from beneath the chamber. The withdrawal latency period of injected paws was determined with an electronic clock circuit and thermocouple. Results are expressed as Paw-Withdrawal Latency (s). Experiments were conducted with the experimenters blinded to treatment conditions

Statistical Analysis. All data are expressed as a mean ± SEM. The differences in levels of thermal hyperalgesia were assessed by two-way analysis of variance (ANOVA) with Bonferroni *post hoc* comparisons to vehicle where significance is defined at $P<0.05$.