Electronic Supplementary Information for

Phenylalanine Iminoboronates as New Phenylalanine Hydroxylase Modulators

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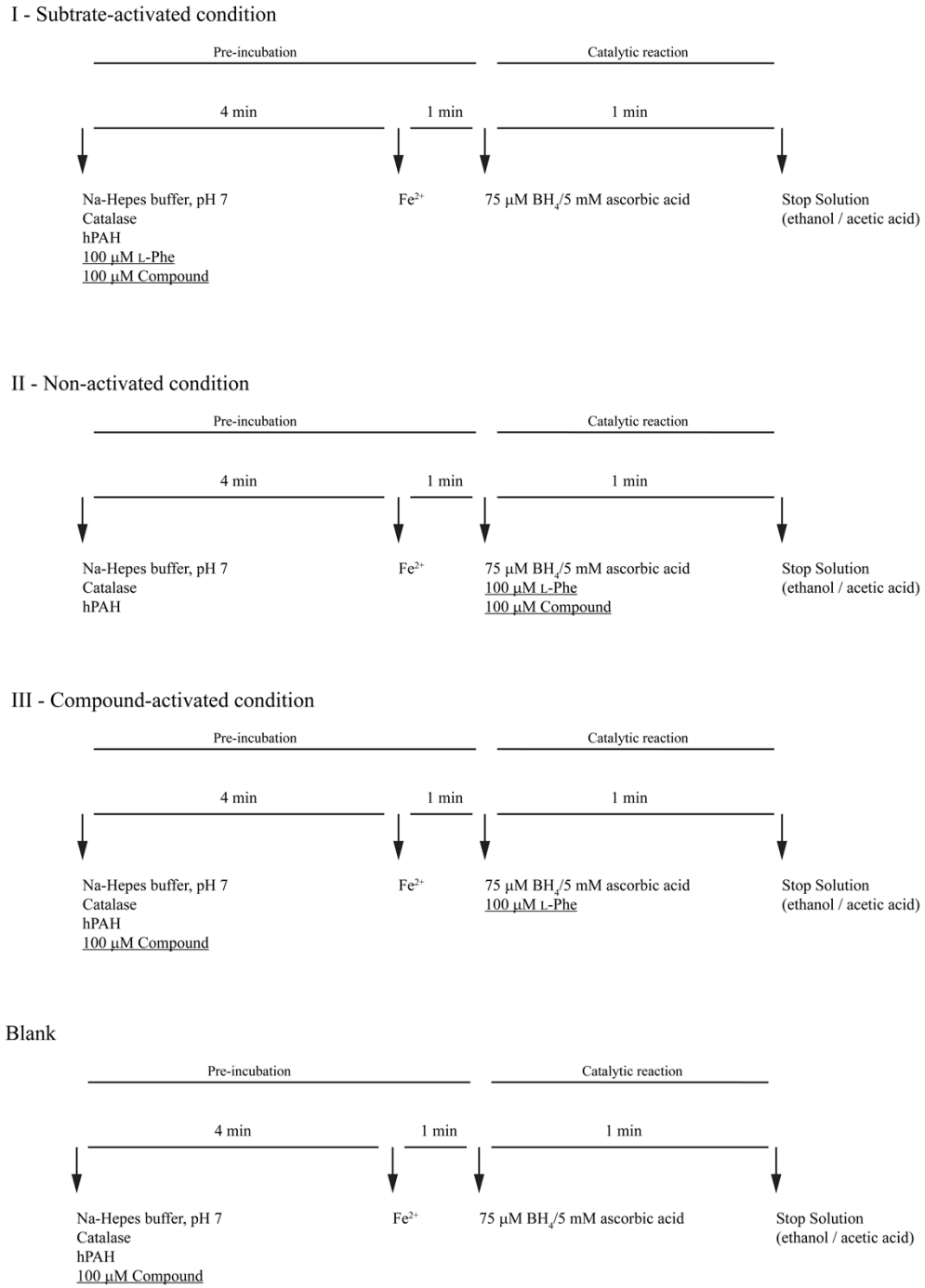

Scheme S1. Depiction of the enzymatic reactions used in this study for evaluation of competition between substrate and compound (I - Substrate-activated condition), and activation by the compound (II - Non-activated *versus* III – Compound-activated condition). A blank reaction without the substrate was included and subtracted for each condition in order to rule out contribution of the compound to tyrosine formation.

Differential Scanning Fluorimetry

To monitor the binding properties of the regulatory (RD) and catalytic domain (CD) of hPAH towards each compound, DSF assays[1] were run in the presence of increased compound concentrations (0–2.56 mM), L-Phe and 1% DMSO (vehicle control) (Fig. S1).

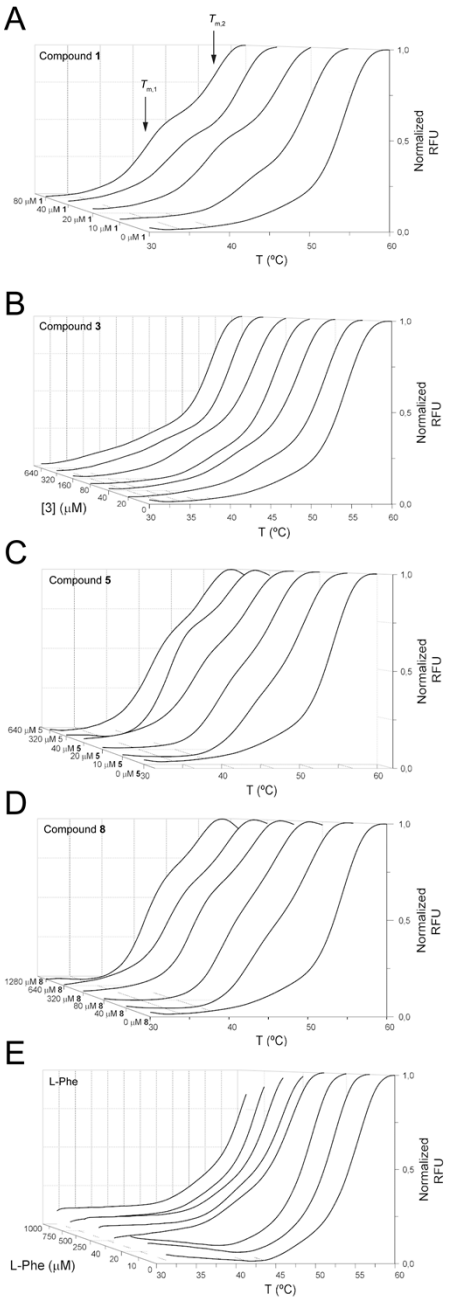

Fig. S1. Curves obtained from variation in SYPRO Orange fluorescence with temperature of increased compound concentrations (0–2.56 mM) for **1**, **3**, **5** and **8** (A-D), L-Phe (E) and 1% DMSO (vehicle control). The melting temperature for the first transition, $T_{m,1}$ (regulatory domain) and for the second transition, $T_{m,2}$ (catalytic domain) are indicated for compound **1**. The curves were normalized and are representative of three independent experiments.

A careful analysis of Fig. S1 reveals a clear effect of the compounds on the RD domain of the protein, namely on the contribution of the RD domain to the overall unfolded process. Temperature scan curves were fitted to a biphasic dose-response function and the T_m values were obtained from the midpoint of the first and second transitions. $C_{0.5}$ values provide apparent binding affinities and are best-fit parameters obtained from the effect of the compound on the contribution of the regulatory domain to the overall unfolded process (Fig. S2). The former effect was observed with compounds able to activate the protein (e.g. the non-activator compound **3** did not reveal such behavior (Fig. S2B)), and it is most likely related to substrate(compound)-induced conformational transition[2] that leads to activation of hPAH with global conformational changes throughout the entire protein. This reversible L-Phe induced conformational transition has been study by different methods, e.g surface plasmon resonance ($[\text{L-Phe}]_{0.5}$ = 98 ± 7 μM) and by intrinsic tryptophan fluorescence ($[\text{L-Phe}]_{0.5}$ = 145 ± 5 μM).[2,3] The different values of the two methods revealed the contribution of different elements of the transition.[2] Here, by using DSF and analyzing the effect of L-Phe on the contribution of the RD domain to the overall unfolded process, a $[\text{L-Phe}]_{0.5}$ = 16.3 ± 6.3 μM was obtained which reflects an additional analysis of the activated enzyme.

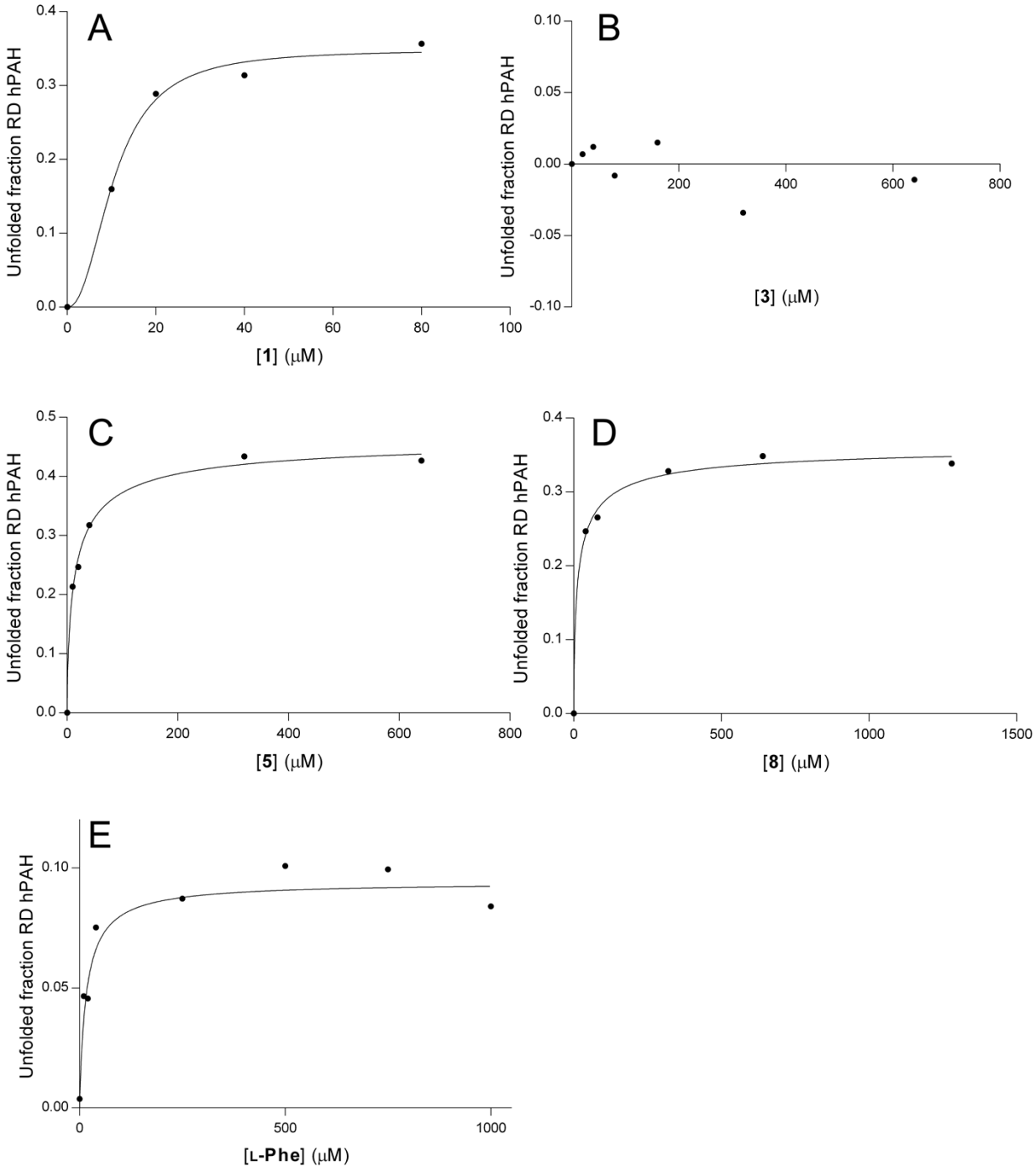

Fig. S2. Apparent binding affinities of compounds **1** (A), **3** (B), **5** (C), **8** (D) and L-Phe (E) to hPAH. Compound **3** did not reveal affinity for hPAH. Assays were performed in triplicate and the curves fit to a one site specific binding with Hill slope (GraphPad Prism 6).

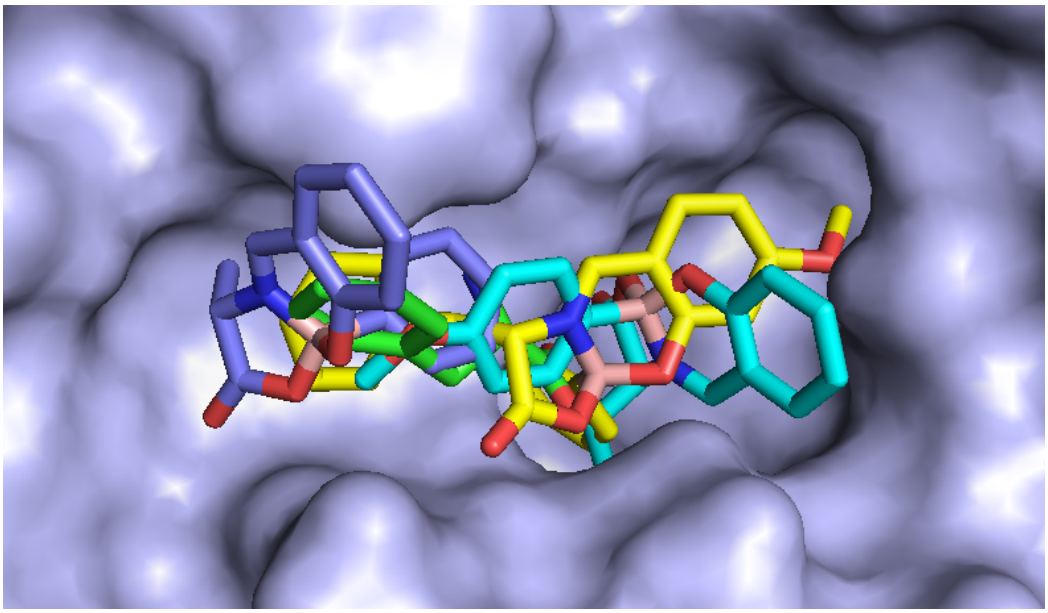

Fig. S3. Superposition of best docking poses obtained for L-Phe (green), compounds 3 (blue), 6 (cyan) and 8 (yellow), resulting from docking of the compound onto the hPAH structure (PDB code 1MMT).

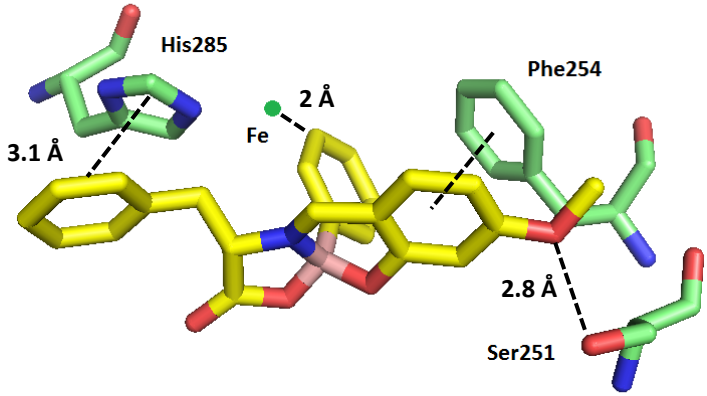

Fig. S4. Principal interactions between compound **8** (yellow) and some residues at the active site (green) resulting from docking of the compound onto the hPAH structure (PDB code 1MMT).

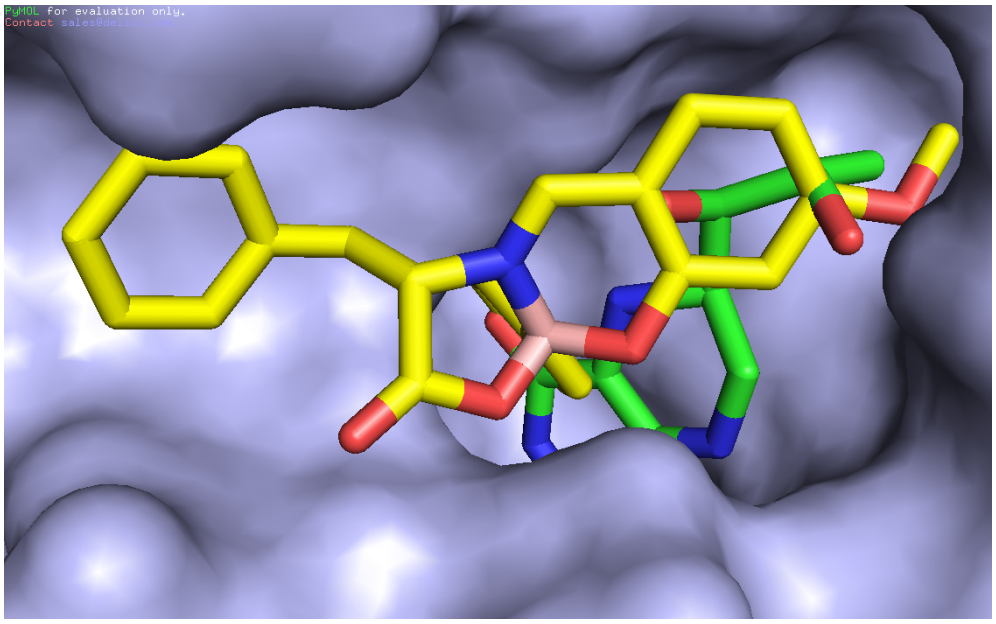

Fig. S5. Compound **8** (yellow) and BH_4 (green) superposition, resulting from docking of the compound onto the hPAH structure (PDB code 1MMT).

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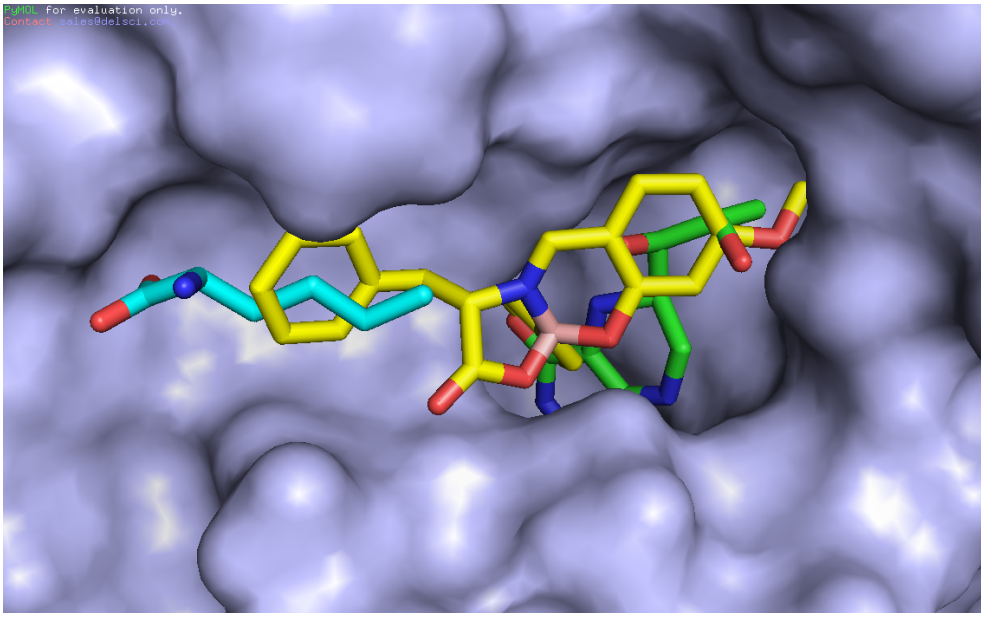

Fig. S6. Compound **8** (yellow), BH_4 (green) and norleucine (cyan) superposition, resulting from docking of the compound onto the hPAH structure (PDB code 1MMT).

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References

1. F. H. Niesen, H. Berglund and M. Vedadi, *Nat. Protoc.*, 2007, 2, 2212-2221.
2. A. J. Stokka and T. Flatmark, *Biochem. J.*, 2003, 369, 509-518.
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General Remarks

The aldehydes, boronic acids and amino acids were purchased from Aldrich and used without further purification. Reaction mixtures were analysed by TLC using F_{254} from Merck (Ref. 105554, silica gel 60), and visualisation of TLC spots was effected using UV and phosphomolybdic acid solution. Proton and carbon nuclear magnetic resonance spectra (^{1}H/^{13}C NMR) were recorded on Bruker AMX 400, spectrophotometer with $CDCl_3$ as solvent, ^{11}boron nuclear magnetic resonance (^{11}B NMR) were recorded on Bruker AMX 300, spectrophotometer with $CDCl_3$ as solvent. Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform (δ 7.26, singlet). Multiplicities are given as: s (singlet), d (doublet), t (triplet), q (quartet), dd (double of doublet), td (triplet of doublets) or m (multiplets). The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a *J* value in Hertz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform (δ 77.16, triplet). The *dr*s were determined based on the ^{1}H, ^{13}C and NOESY NMR spectroscopy and by comparison with the x-rays obtained for compounds: **3**, **5** and **6**[1].

General procedure for preparation of boron heterocycles using water as solvent

A round bottom flask equipped with a magnetic stirrer was charged with amino acid (2.0 equiv.), aldehyde (1.5 equiv.) and distilled water (2.0 mL). This suspension was stirred at 90ºC for 1 h after which the boronic acid (0.41 mmol) was added, the mixture was then stirred at 90ºC for 20 h. The reaction mixture, which appears as a biphasic composition of precipitate and a supernatant liquid, was filtered and the solid retained in the filter was then washed with water followed by hexane. The desired compound was recovered with dichloromethane, which was subsequently removed under reduced pressure.

Compounds characterization

Compound 1[1] was obtained in 86% yield, *d.r.* 100%, after 20 h at 90ºC (0.125 g). **^{1}H NMR** (400 MHz, CDCl3, 25ºC, TMS): δ 2.71 (t, 1H, *J* = 13.2, –CHC*H*$_2$Ph), 3.41 (dd, 1H, *J* = 3.6, 14.0, –CHC*H*$_2$Ph), 4.34 (dd, 1H, *J*= 3.6, 12.4, –NC*H*CH2Ph), 6.87–6.95 (m, 3H, Ar), 7.02–7.05 (m, 1H, Ar), 7.11– 7.16 (m, 2H, Ar), 7.27–7.34 (m, 6H, Ar), 7.43–7.55 (m, 3H, Ar). **^{13}C-NMR** (100 MHz, CDCl3, 25ºC, TMS): δ 37.73 (–CH*C*H$_2$Ph), 66.92(–N*C*HCOCH$_2$–),117.57, 120.19,120.32,127.79,127.90,128.58, 129.16, 129.21, 130.55, 131.45, 135.11, 139.04 (Ar),

159.95 (-N*C*HAr-), 160.43(Ar, quaternary), 170.22 (–CH*C*OO–). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 6.71. **ESI$^+$**: 394, 378,356, 270, 248.

Compound 2[2] was obtained in 50 % yield, *d.r.*100%, after 20 h at 90 ºC (0.142 g). **^{1}H NMR** (400 MHz, $CDCl_3$, 25ºC, TMS): δ 1.05 (dd, 6H, *J* = 12.9, 6.4 Hz, -CHCH$_2$CH(C*H$_3$*)$_2$), 1.77–1.96 (m, 1H, -CHCH$_2$C*H*(C*H$_3$*)$_2$), 2.03– 2.27 (m, 2H, -NCHC*H$_2$*CH(C*H$_3$*)$_2$), 4.53 (td, 1H, *J* = 5.7, 2.3 Hz, -NC*H*CH$_2$CH(CH$_3$)$_2$),6.96 – 7.07 (m, 1H, Ar), 7.16 (d, 1H, *J* = 8.4 Hz, Ar), 7.21 - 7.35 (m, 4H, Ar), 7.39 (dd, 2H, *J* = 7.5, 1.8 Hz, Ar), 7.44 (dd, 1H, *J* = 7.8, 1.6 Hz,Ar), 7.62 (td, 1H, *J* = 8.7, 7.4, 1.7 Hz, Ar). **^{13}C-RMN** (100MHz, $CDCl_3$, 25ºC, TMS): δ 22.50 (-CH*C*H$_2$(*C*H3)$_2$), 22.93 (-CH*C*H$_2$(*C*H3)$_2$), 25.16 (-NCHCH$_2$*C*H-), 37.16 (-NCH*C*H$_2$-), 60.64 (-N*C*HCH$_2$ -), 117.49, 120.21, 120.27, 125.98, 127.83, 128.43, 130.89, 131.65 (Ar), 139.02 (-N*C*HAr-), 156.70, 159.70 (Ar, quaternary), 170.79 (-CH*C*OO-). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 6.73.**ESI$^+$**: 360, 344, 322, 274, 236.

Compound 3[2] was obtained in 52 % yield, *d.r.*100%, after 20 h at 90 ºC (0.142 g). **^{1}H NMR** (400 MHz, $CDCl_3$, 25ºC, TMS): δ 1.73 (d, 3H, *J* = 6.8 Hz, -CHC*H$_3$*), 4.62 (qd, 1H, *J* = 6.7, 2.3 Hz, -C*H*CH$_3$), 6.93 –7.08 (m, 1H, Ar), 7.16 (d, 1H, *J* = 8.4 Hz, Ar), 7.20 – 7.33 (m, 3H, Ar), 7.40 (dd, 2H, *J* = 7.5, 1.7 Hz, Ar), 7.45 (dd, 1H, *J* = 7.8, 1.6 Hz, Ar), 7.55– 7.71 (m, 1H, Ar), 8.17 (d, 1H, *J* = 2.2 Hz, Ar). **^{13}C-RMN** (100MHz, $CDCl_3$, 25ºC, TMS): δ 12.98 (-CH*C*H$_3$), 58.59 (-N*C*HCH$_3$-), 117.30, 120.22, 120.35, 125.83, 127.83, 128.48, 130.74, 131.60, 139.07 (Ar), 156.61 (Ar, quaternary), 159.79 (Ar*C*HN-), 170.66 (-CH*C*OO-). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 6.99. **ESI$^+$**: 318, 302, 280, 122.

Compound 4[1] was obtained in 83 % yield, *d.r.* 100%, after 20 h at 90 ºC (0.126 g). **^{1}H NMR** (400 MHz, $CDCl_3$, 25ºC, TMS): δ 2.34 (s, 3H, -ArC*H$_3$*), 2.73 (t, 1H, *J*= 12.0, -CHC*H$_2$*Ph), 3.42 (dd, 1H, *J*= 4.0, 14.0, -CHC*H$_2$*Ph), 4.35 (dd, 1H, *J*= 4.0, 12.0, -NC*H*CH$_2$Ph), 6.91 (t, 1H, *J*= 8.0, Ar), 6.99-7.04 (m, 3H, Ar), 7.12-7.16 (m, 4H, Ar), 7.28-7.38 (m, 5H, Ar), 7.50-7.56 (m, 1H, Ar). **^{13}C-RMN** (100MHz, $CDCl_3$, 25ºC, TMS): δ 21.44 (-Ar*C*H$_3$), 37.78 (-CH*C*H$_2$Ph), 66.90 (-N*C*HCH$_2$Ph-), 117.62, 120.14, 120.32, 127.80, 128.67, 129.16, 129.28, 130.61, 131.46, 135.21, 138.19, 138.94 (Ar), 159.94 (Ar, quaternary), 160.35 (Ar*C*HN-), 170.35 (-CH*C*OO-). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 6.97. **ESI$^+$**: 392, 370, 300, 188.

Compound 5[1] was obtained in 80 % yield, *d.r.* 100%, after 20 h at 90 ºC (0.122 g). **^{1}H NMR** (400 MHz, $CDCl_3$, 25ºC, TMS): δ 2.68 (t, *J*= 13.2,, 1H -CHC*H$_2$*Ph), 3.45 (dd, 1H, *J*= 3.4, 13.8, -CHC*H$_2$*Ph), 4.36 (dd, 1H, *J*= 3.2, 12.4, -NC*H*CH$_2$Ph_), 6.80-7.71 (m, 14H, Ar). **^{13}C-RMN** (100MHz, $CDCl_3$, 25ºC, TMS): δ 37.79 (-CH*C*H$_2$Ph), 66.87 (-N*C*HCH$_2$-), 114.74, 114.94, 117.47, 120.32, 120.38, 127.91, 129.16, 129.24, 131.53,132.34, 132.41, 134.97, 139.23 (Ar), 159.84 (Ar, quaternary), 160.56 (Ar, quaternary), 170.13 (-H*C*OO). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 6.50.**ESI$^+$**: 412, 374, 270.

Compound 6[1] was obtained in 31 % yield, *d.r*. 100 %, after 20 h at 90 ºC (0.048 g). **^{1}H NMR** (400 MHz, $CDCl_3$, 25ºC, TMS): δ 2.72 (t, *J*= 13.0, 1H, -CHC*H*$_2$Ph), 3.42 (dd, 1H, *J*= 3.2, 13.6, -CHC*H*$_2$Ph), 3.81 (s, 3H, -ArOC*H*$_3$), 4.34 (dd, 1H,*J*= 3.2, 12.4, -NC*H*COCH$_2$-), 6.80-7.35 (m, 14H, Ar). **^{13}C-RMN** (100MHz, $CDCl_3$, 25ºC, TMS): δ 37.87 (-CH*C*H$_2$Ph), 55.04 (-ArO*C*H$_3$), 66.82 (-N*C*HCOCH$_2$-), 113.42, 117.55, 120.15, 120.27, 127.80, 129.16, 129.28, 131.48, 131.96, 135.14, 138,92 (Ar), 159.94(Ar*C*HN-), 159.98, 160.22 (Ar, quaternary), 170.42 (-CH*C*OO-). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 6.95. **ESI$^+$**: 408, 386, 288, 270.

Compound 7[1] was obtained in 64 % yield, *d.r*. 100%, after 20 h at 90 ºC (0.095 g). **^{1}H NMR** (400 MHz, $CDCl_3$, 25ºC, TMS): δ 2.35 (s, 3H, -ArC*H*$_3$), 2.70 (t, 1H, *J*= 12.0, -CHC*H*$_2$Ph), 3.41 (dd, 1H, *J*= 2.0, 14.0, -CHC*H*$_2$Ph), 4.34 (dd, 1H, *J*= 4.0, 12.0, -C*H*CH$_2$Ph), 6.73 (d, 1H, *J*= 8.0Hz, Ar), 6.85 (s, 1H, Ar), 6.97-7.03 (m, 3H, Ar), 7.12 (s, 1H, AR), 7.28-7.38 (m, 6H, Ar), 7.45-7.47 (m, 2H, Ar). **^{13}C-RMN** (100MHz, $CDCl_3$, 25ºC, TMS): δ 22.50 (-Ar*C*H$_3$), 37.75(-CH*C*H$_2$Ph), 66.75 (-N*C*HCOCH$_2$-), 115.41, 120.38, 121.74, 127.74, 127.88, 128.48, 129.14, 129.24, 130.58, 131.23, 135.28 (Ar), 151.41 (Ar, quaternary), 159.95 (Ar, quaternary), 159.99 (Ar*C*HN-), 170.58 (-CH*C*OO-). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 6.94. **ESI$^+$**: 408, 392, 370, 284.

Compound 8[1] was obtained in 87 % yield, *d.r*. 100%, after 20 h at 90 ºC (0.133 g). **^{1}H NMR** (400 MHz, $CDCl_3$, 25ºC, TMS): δ 2.69 (t, 1H, *J*= 13.0, -CHC*H*$_2$Ph), 3.39 (dd, 1H, *J*= 3.6, 14.0, -CHC*H*$_2$Ph), 3.84 (s, 3H, -ArOC*H*$_3$), 4.31 (dd, 1H, *J*= 3.2, 12.4, -NC*H*CH$_2$Ph-), 6.45-6.50 (m, 2H, Ar), 6.97-7.09 (m, 4H, Ar), 7.28-7.48 (m, 6H, Ar), 7.49-7.50 (m, 2H, Ar). **^{13}C-RMN** (100MHz, $CDCl_3$, 25ºC, TMS): δ 37.78 (-CH*C*H$_2$Ph), 55.87 (-ArO*C*H$_3$), 66.54 (-N*C*HCOCH$_2$-), 102.62, 110.12, 111.47, 127.65, 127.88, 128.42, 129.10, 129.24, 130.57, 132.88, 135.47 (Ar), 158.98 (Ar*C*HN-), 162.65 (Ar, quaternary), 168.80 (Ar, quaternary), 170.91 (-CH*C*OO-). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 7.62. **ESI$^+$**: 424, 408, 386, 300.

Stability assay (50% DMSO) – 300 µL of a solution 10^{-2} M of the compound in DMSO + 1200 µL DMSO + 1500 µL of ammonium acetate buffer (I = 150 mM; pH 7.4)

The assay was performed at 37ºC and aliquots of 200 µL were collected at different times and were analysed by HPLC (solvent gradient: 10% CH_3CN, 30min up to, 95% CH_3CN). The absorbance was measured at 256nm. Determined compound $t_{1/2}$ = 1.7 horas

Compound 9[1] was obtained in 78 % yield, *d.r*. 100 %, after 20 h at 90 ºC (0.125 g). **^{1}H NMR** (400 MHz, $CDCl_3$, 25ºC, TMS): δ 2.73 (t, 1H, *J*= 13.0, -CHC*H*$_2$Ph), 3.44 (dd, 1H. *J*= 3.6, 14.0, -CHC*H*$_2$Ph), 3.85 (s, 3H, -ArOC*H*$_3$), 4.31 (dd, 1H, *J*= 3.4, 12.2, -NC*H*CH$_2$Ph.), 6.47-6.52 (m, 2H, Ar), 6.95-7.04 (m, 5H, Ar), 7.28-7.40 (m, 5H, Ar). **^{13}C-RMN** (100MHz, $CDCl_3$, 25ºC, TMS): δ 38.22 (-CH*C*H$_2$Ph), 55.89 (-ArO*C*H$_3$), 66.02 (-N*C*HCOCH$_2$-), 102.72, 110.19, 111.50, 125.71, 127.70, 127.75, 129.11, 129.34, 129.80, 132.82, 135.32 (Ar), 158.24 (Ar*C*HN-), 162.34 (Ar,

quaternary), 168.70 (Ar, quaternary), 171.05 (-CH*C*OO-). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 5.70. **ESI$^+$**: 430, 392, 338, 300.

Compound 10[2] was obtained in 84% yield, *d.r*. 96%, after 20 h at 90 ºC (144 mg). **^{1}H NMR** (400 MHz, CDCl3, 25ºC, TMS): δ 2.62 (t, 1H, *J*= 13.2 Hz, -NCHCOC*H*$_2$-), 3.38 (d, 1H, *J*= 13.9 Hz, -CHC*H*$_2$Ph-), 3.82 (s, 3H, -OC*H*$_3$), 4.28 (d, 1H, *J*= 11.7 Hz, -C*H*CH$_2$Ph-), 6.36 – 7.45 (m, 14H, Ar). **^{13}C NMR** (100 MHz, CDCl3) δ38.1 (-CH*C*H2Ph-), 56.2 (-O*C*H3), 66.8 (-N*C*HCH$_2$Ph-), 102.9, 110.7, 111.7, 128.1, 128.4, 129.5, 132.3, 133.3, 134.6, 135.6 (Ar), 159.5 (Ar, quaternary), 162.8 (Ar, quaternary), 169.3 (Ar, quaternary), 171.0 (-CHCO). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 6.48. **ESI$^+$**: 442, 322, 300, 166.

Compound 11[2] was obtained in 50 % yield, *d.r*. 92 %, after 20 h at 90 ºC (0.08 g). **^{1}H NMR** (400 MHz, $CDCl_3$, 25ºC, TMS): δ 2.54 (dd, 1H, *J*= 14.1, 12.3 Hz, -NC*H*CH$_2$Ph), 3.23 (dd, 1H, *J* = 14.2, 3.0 Hz, -CHC*H*$_2$Ph), 3.83 (s, 3H, -OC*H*$_3$), 4.32 (dd, 1H, *J* = 12.2, 3.1 Hz, -CHC*H*$_2$Ph), 6.39 – 6.46 (m, 2H, Ar), 6.99 (d, 1H, *J* = 8.7 Hz, Ar), 7.03 – 7.17 (m, 2H, Ar), 7.07-7.39 (m, 5H, Ar), 7.61 (dd, 1H, *J* = 7.9, 0.9 Hz, Ar), 7.68 (dd, 1H, *J* = 7.5, 1.7 Hz, Ar). **^{13}C-RMN** (100MHz, $CDCl_3$, 25ºC, TMS): δ 37.82 (-CH*C*H$_2$Ph), 55.89 (-O*C*H$_3$), 66.49 (-N*C*HCOCH$_2$-), 102.60, 110.27, 114.76, 127.73, 127.63, 129.15, 129.5, 132.34, 132.25, 132.89, 135.32, 158.99 (Ar), 162.57 (-CH*C*OO-). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 6.48. **ESI$^+$**: 442, 426, 360, 300.

Compound 12[2] was obtained in 66 % yield, *d.r*. 81%, after 20 h at 90 ºC (0.111 g). **^{1}H NMR** (400 MHz, $CDCl_3$, 25ºC, TMS): δ3.08 – 3.18 (m, 1H, -NC*H*CH$_2$Ph-), 3.55 (dt, 1H, *J*= 8.6, 4.3 Hz, -CHC*H*$_2$Ph), 3.85 (s, 3H, -OC*H*$_3$), 4.34 (dd, 1H, *J*= 11.9, 3.7 Hz, -CHC*H*$_2$Ph), 7.46 – 6.71 (m, 16H, Ar). **^{13}C-RMN** (100MHz, $CDCl_3$, 25ºC, TMS): δ 38.8 (-CH*C*H$_2$Ph), 56.2 (-O*C*H$_3$), 66.0 (-N*C*HCOCH$_2$-), 103.0, 110.3, 112.0, 126.8, 127.8, 128.1, 128.7, 129.5, 129.7, 133.2, 135.7, 138.9, 158.6 (Ar, quaternary), 162.8 (Ar, quaternary), 168.9 (Ar, quaternary), 171.4 (-CH*C*OO-). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ = 6.36. **ESI$^+$**: 300, 188, 166, 120.

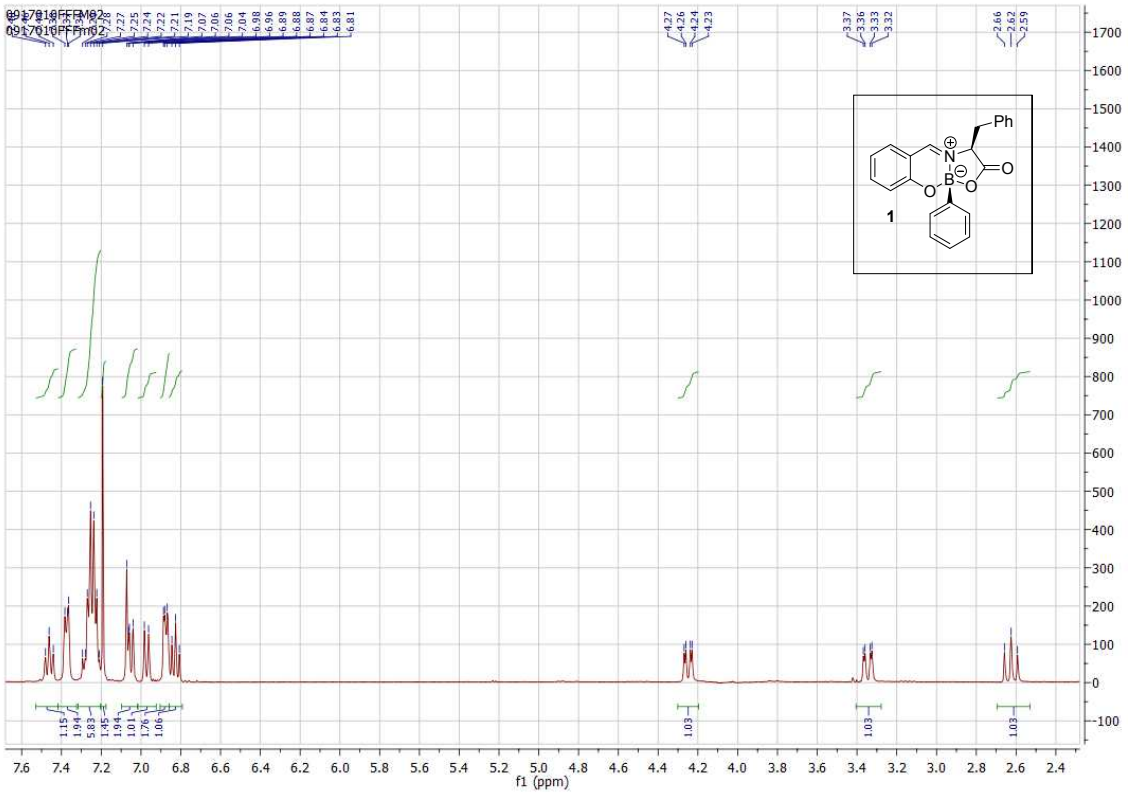
Compound 13[2] was obtained in 50 % yield, *d.r*. 77 %, after 20 h at 90 ºC (0.09 g). **^{1}H NMR** (400 MHz, $CDCl_3$, 25ºC, TMS): δ 2.54 (dd, 1H, *J* = 14.1, 12.4 Hz, -NC*H*CH$_2$Ph-), 3.24 (dd, 1H, *J* = 14.1, 2.9 Hz, -CHC*H*$_2$Ph), 3.84 (s, 3H, -OC*H*$_3$), 4.30 (dd, 1H, *J*= 12.3, 3.3 Hz, -CHC*H*$_2$Ph), 6.43-6.46 (m, 2H, Ar), 7.07 – 7.30 (m, 3H, Ar), 7.28-7.40 (m, 5H, Ar), 7.61 (dd, 1H, *J* = 7.9, 1.0 Hz, Ar), 7.70 (dd,1H, *J* = 7.5, 1.7 Hz, Ar). **^{13}C-RMN** (100MHz, $CDCl_3$, 25ºC, TMS): δ 37.26 (-CH*C*H$_2$Ph), 55.9 (-O*C*H$_3$), 68.38 (-N*C*HCOCH$_2$-), 101.78, 110.33, 112.6, 126.8, 127.8, 129.0, 129.3, 129.86, 133.0, 134.2, 133.5, 135.6, 161.7, 169.41 (Ar, quaternary), 162.8 (Ar, quaternary), 169.7 (Ar, quaternary), 170.4 (-CH*C*OO-). **^{11}B NMR** (300 MHz, $CDCl_3$, 25°C): δ =6.29. **ESI$^+$**: 502, 486, 464, 256.

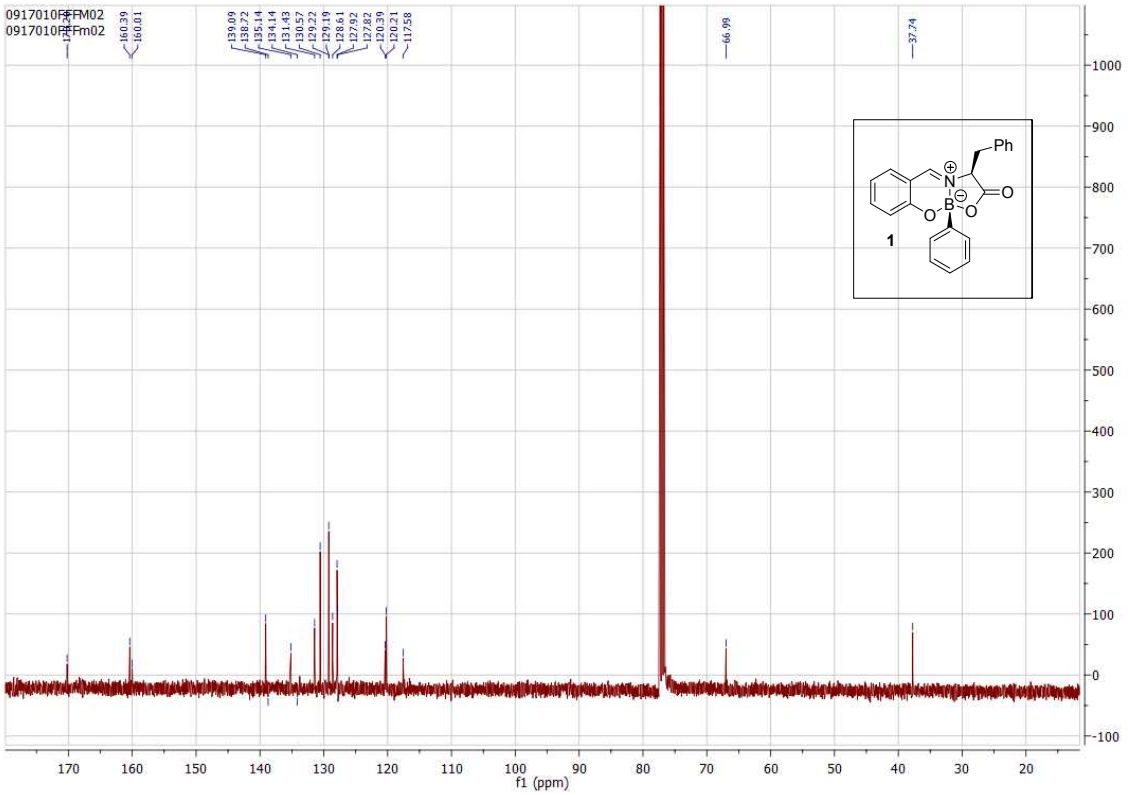
References:

1- N. R. Candeias, P. M.S.D. Cal, V. André, M. T. Duarte, L. F. Veiros, P. M.P. Gois, *Tetrahedron,* 2010, 66, 2736–2745.

2- F. Montalbano, P. M. Cal, M. A. Carvalho, L. M. Goncalves, S. D. Lucas, R. C. Guedes, L. F. Veiros, R. Moreira and P. M. Gois, *Org. Biomol. Chem.*, 2013, 11, 4465-4472.

Compounds NMRs

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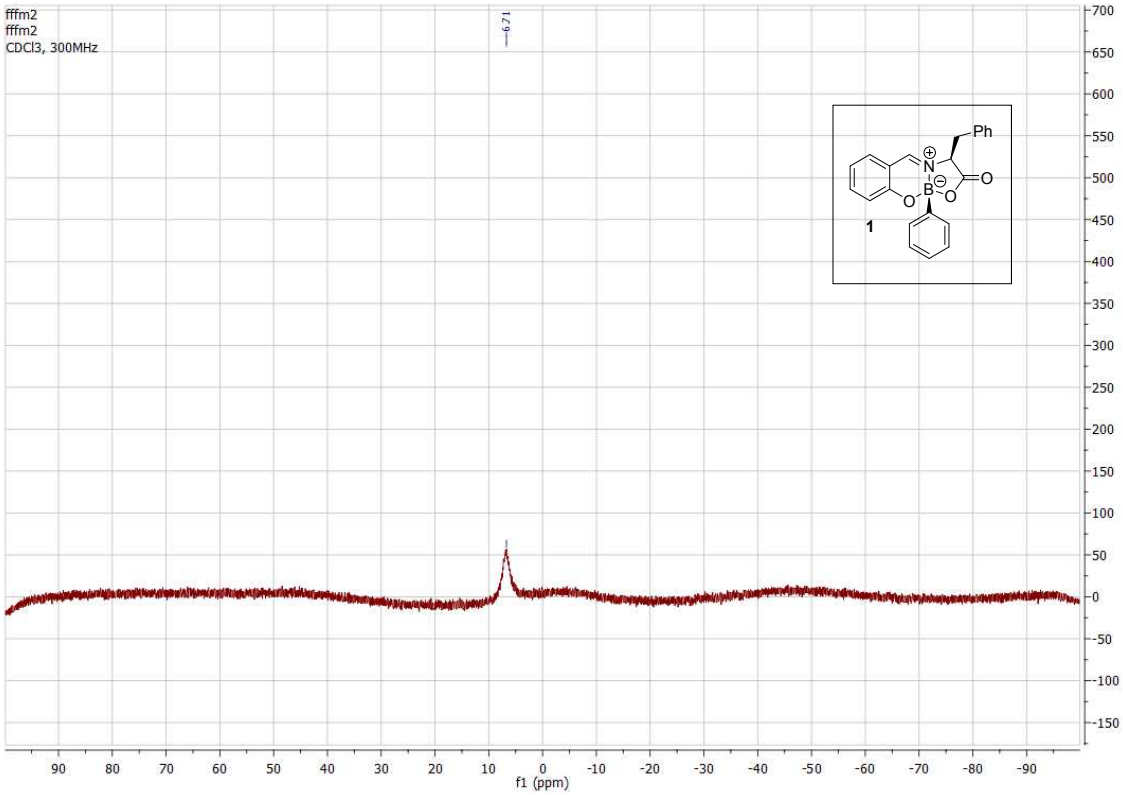
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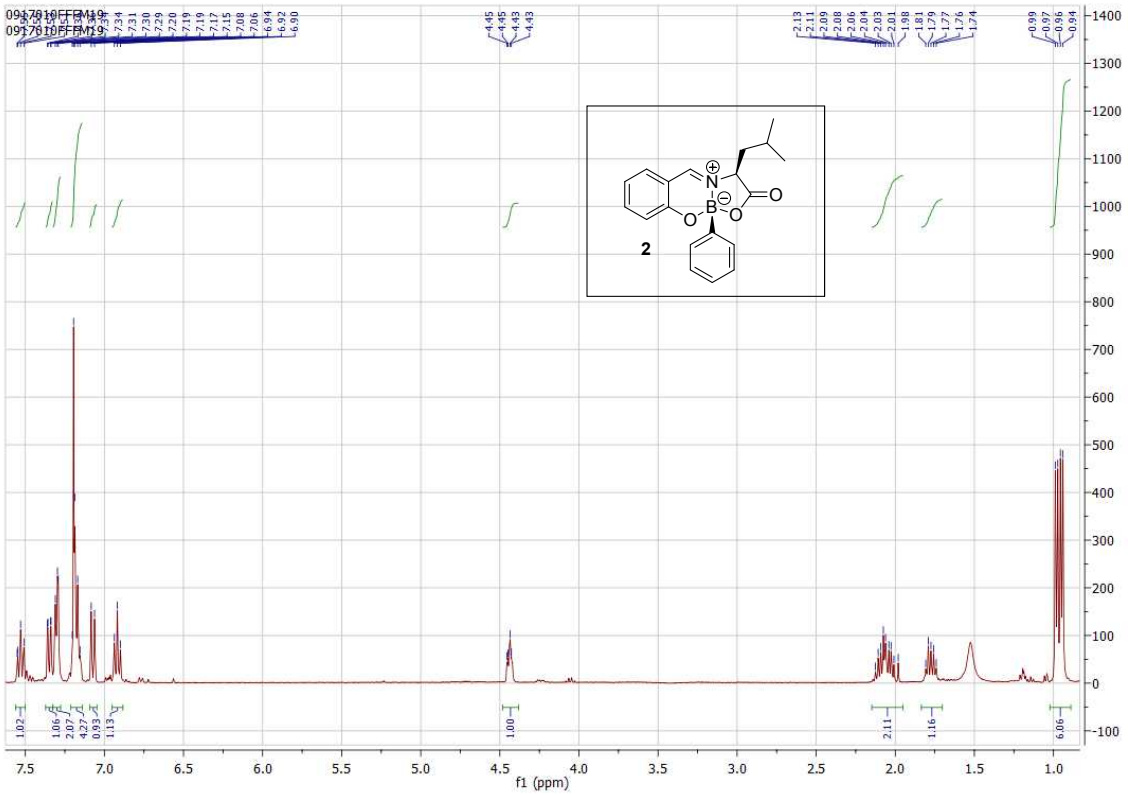
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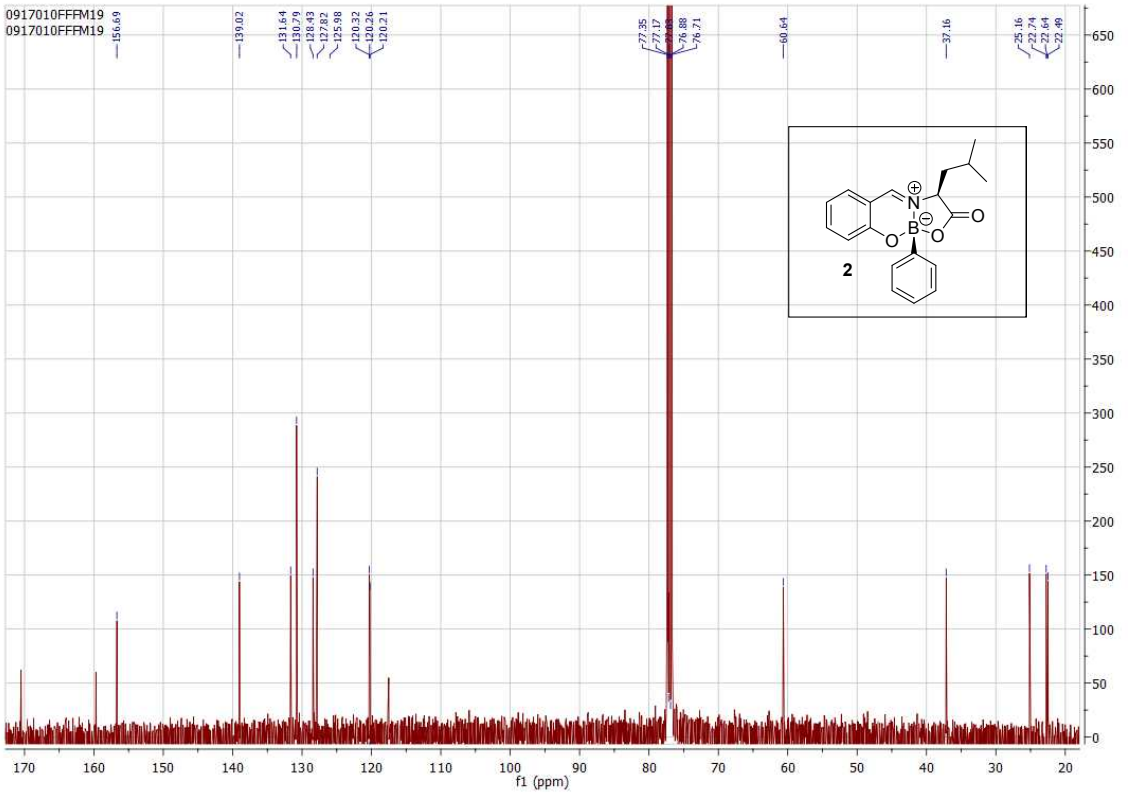
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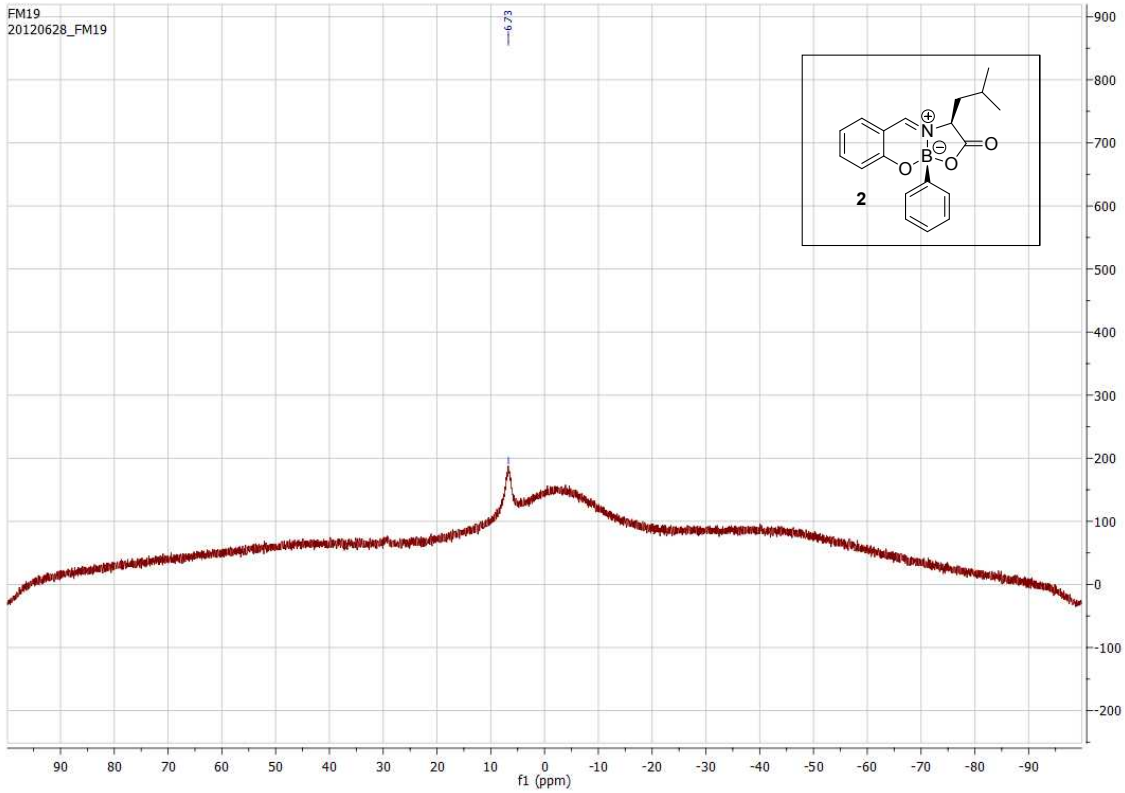
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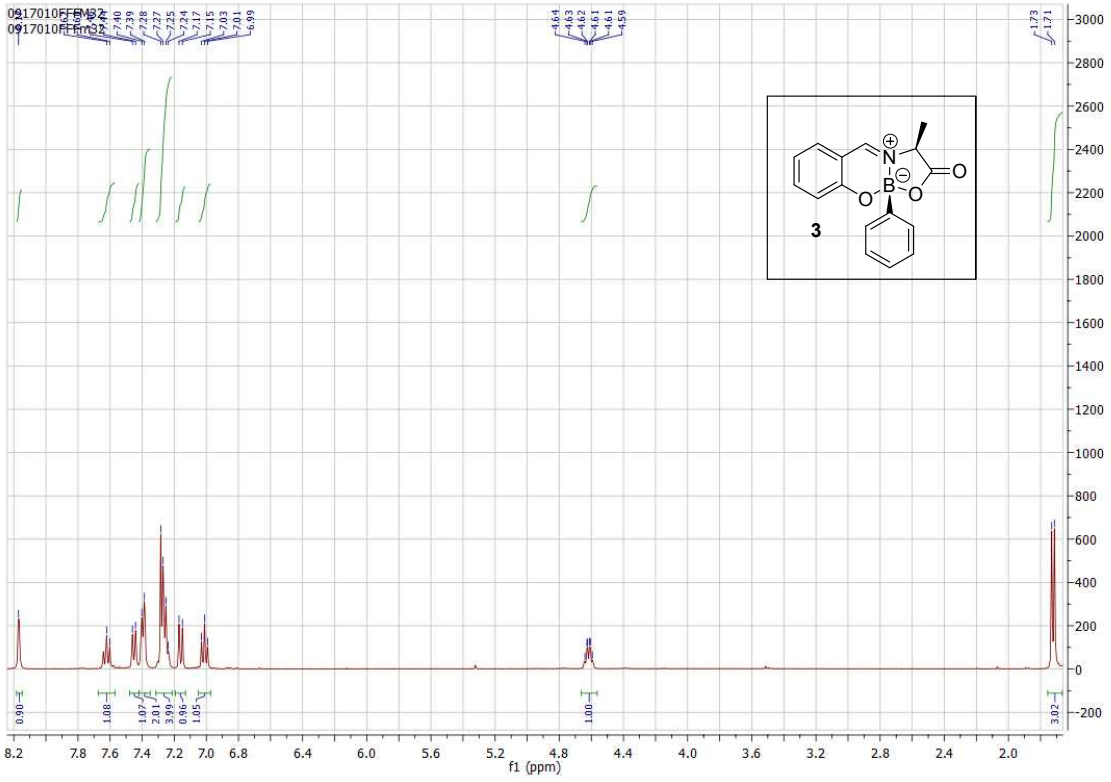
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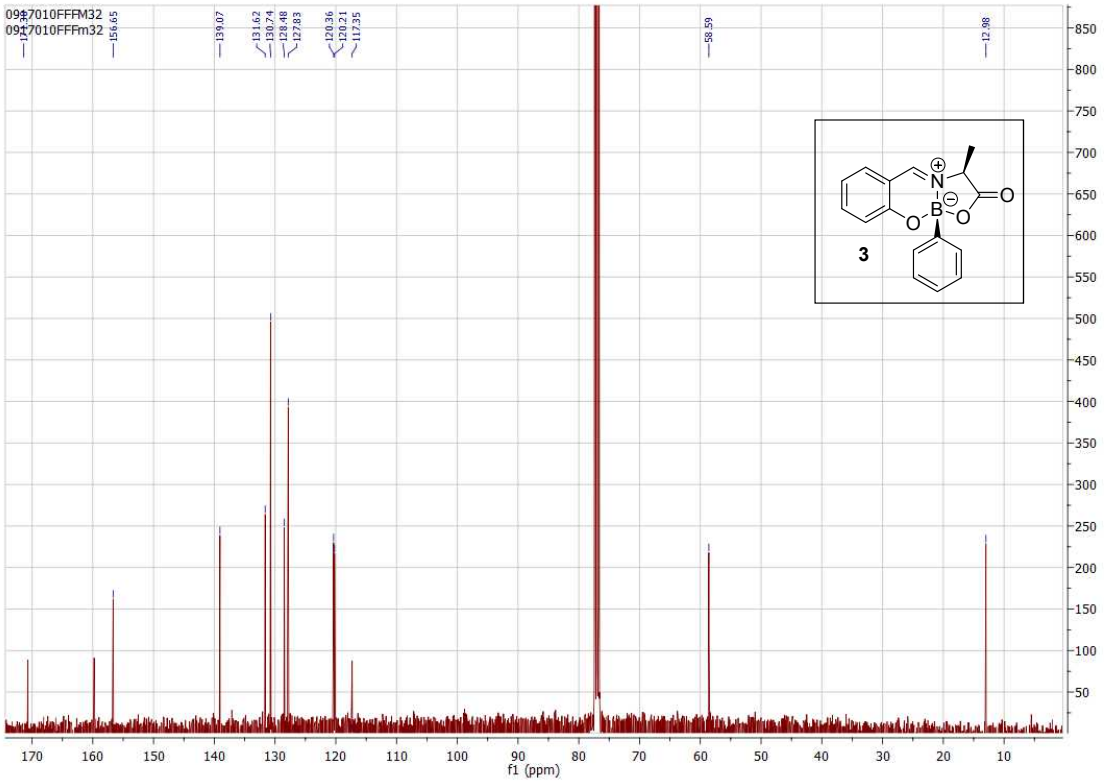
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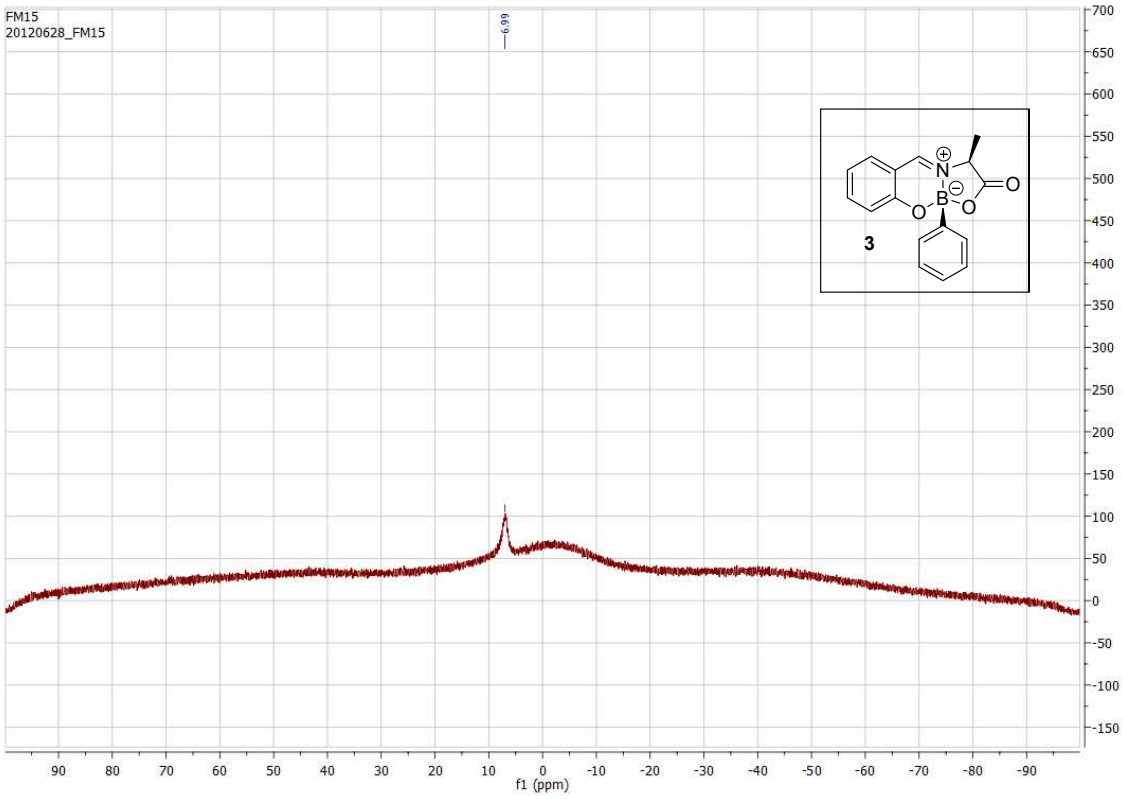
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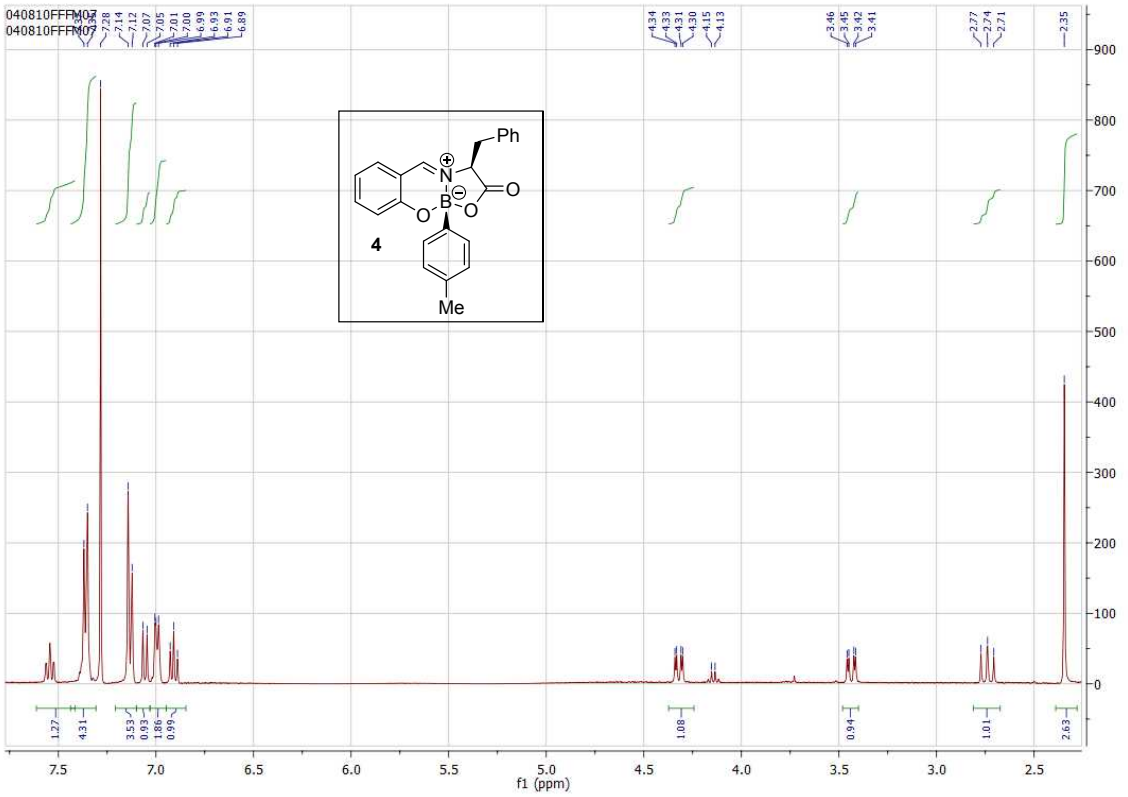
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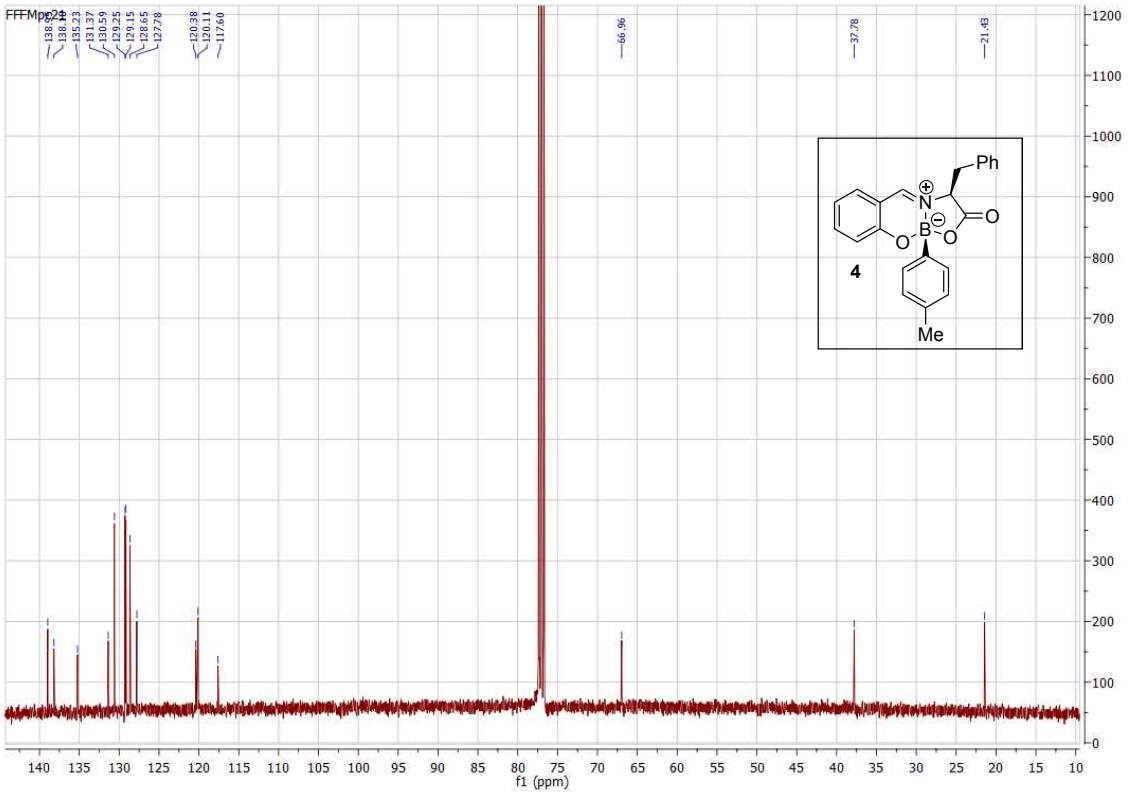
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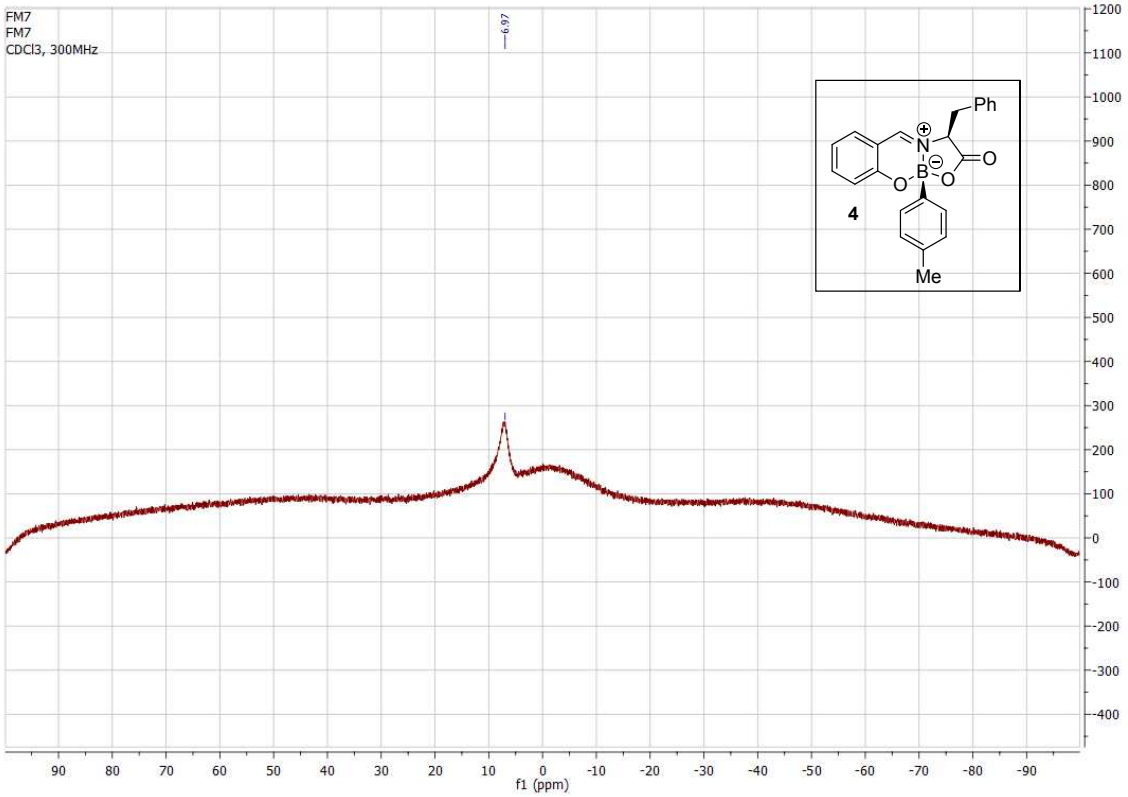
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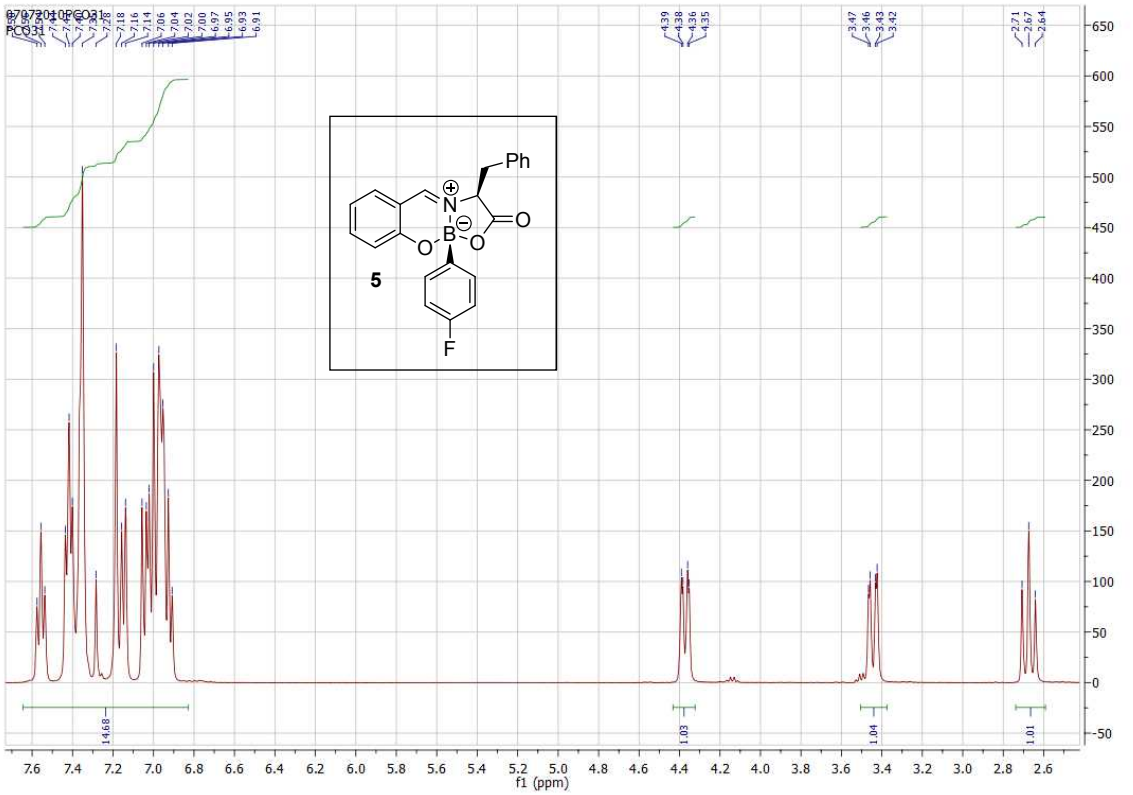
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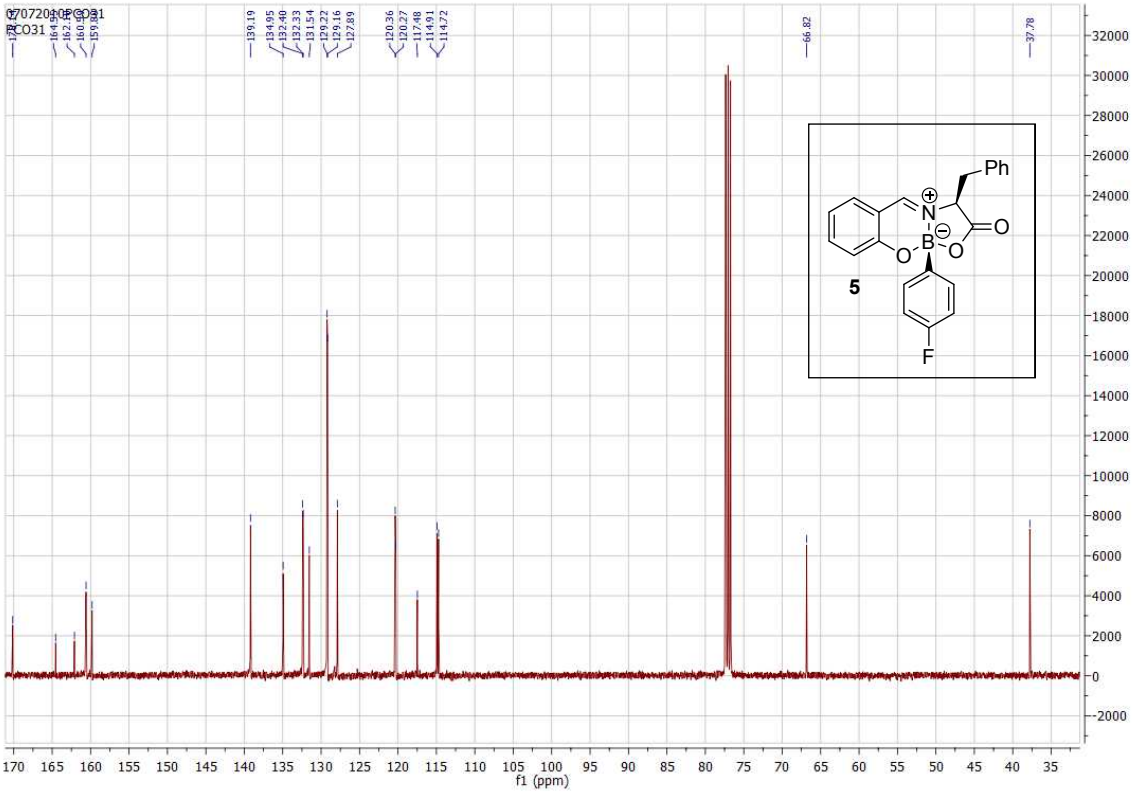
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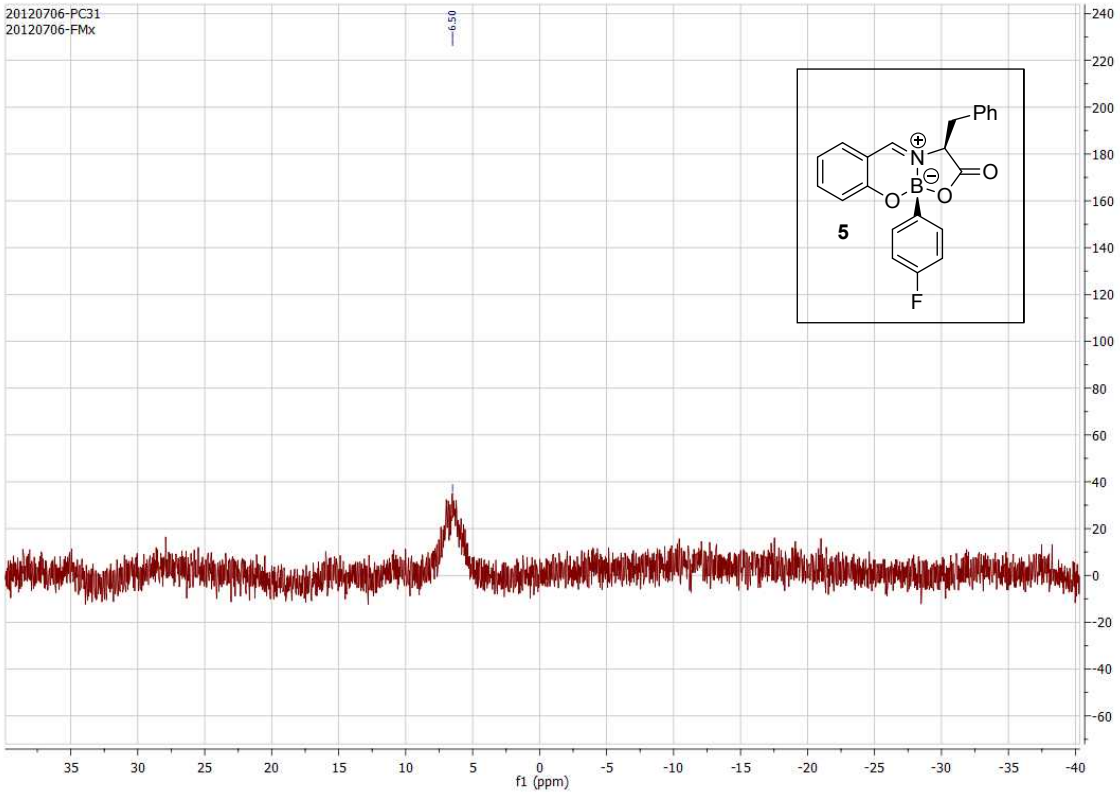
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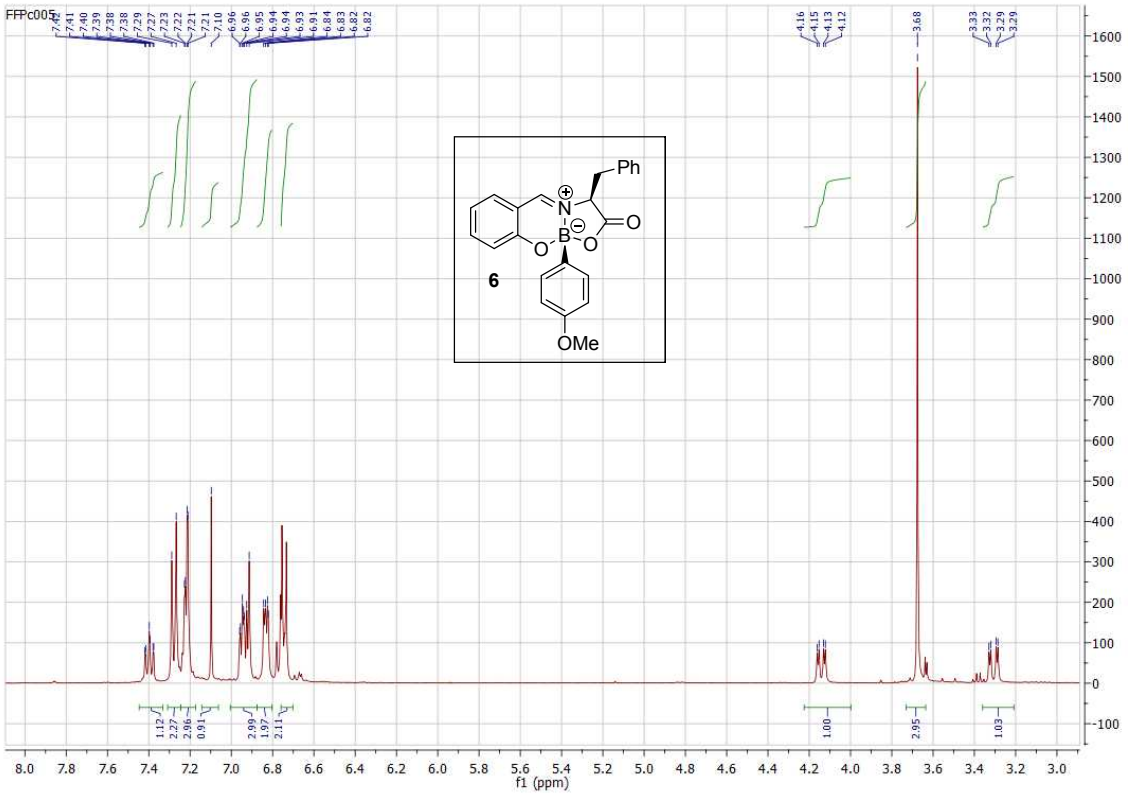
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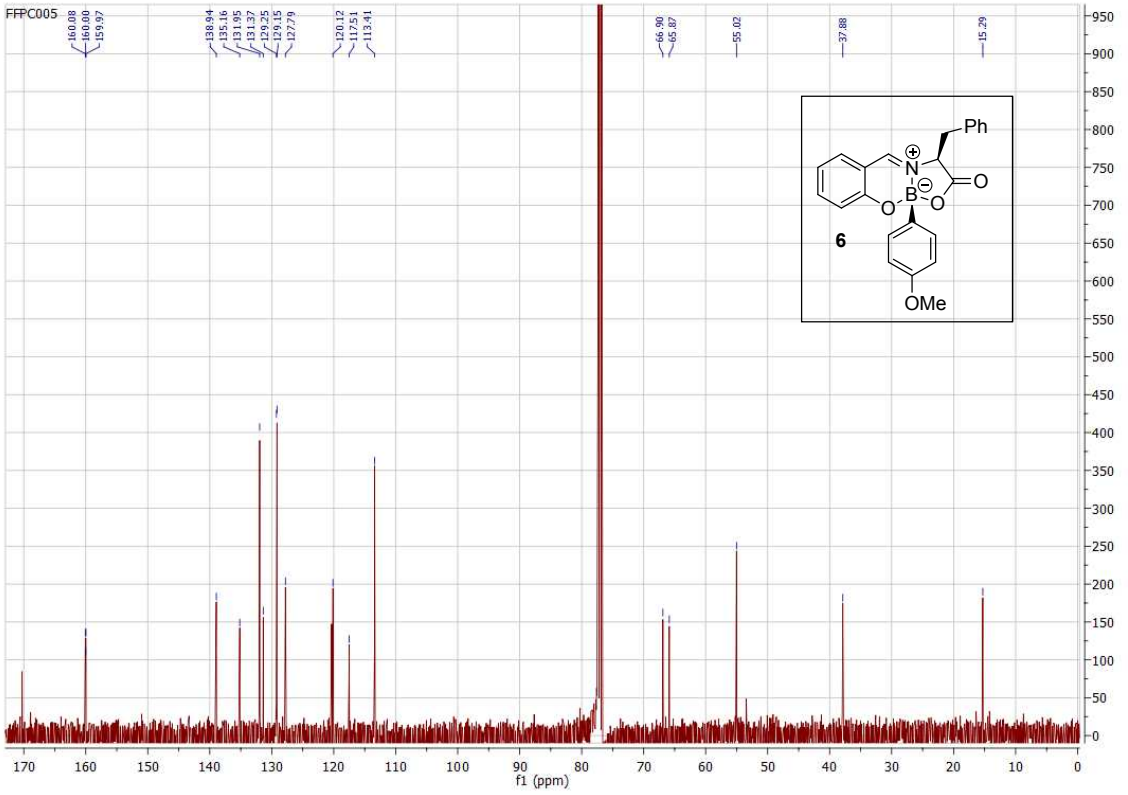
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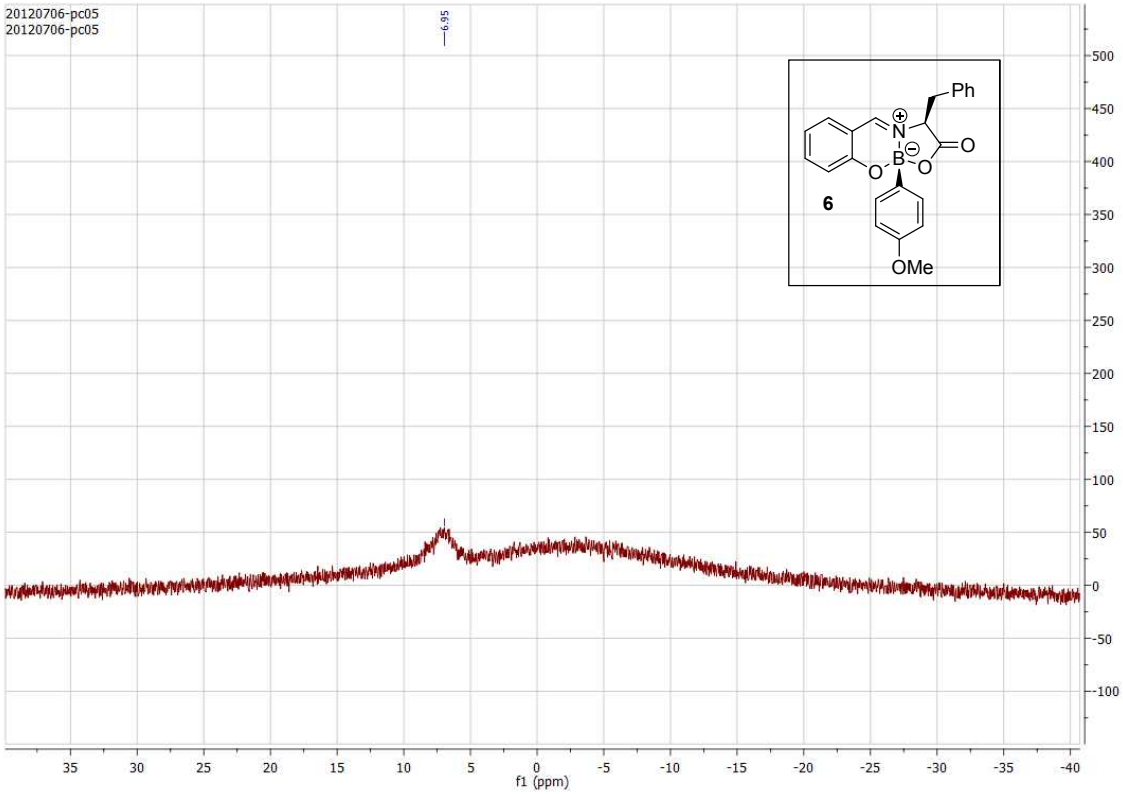
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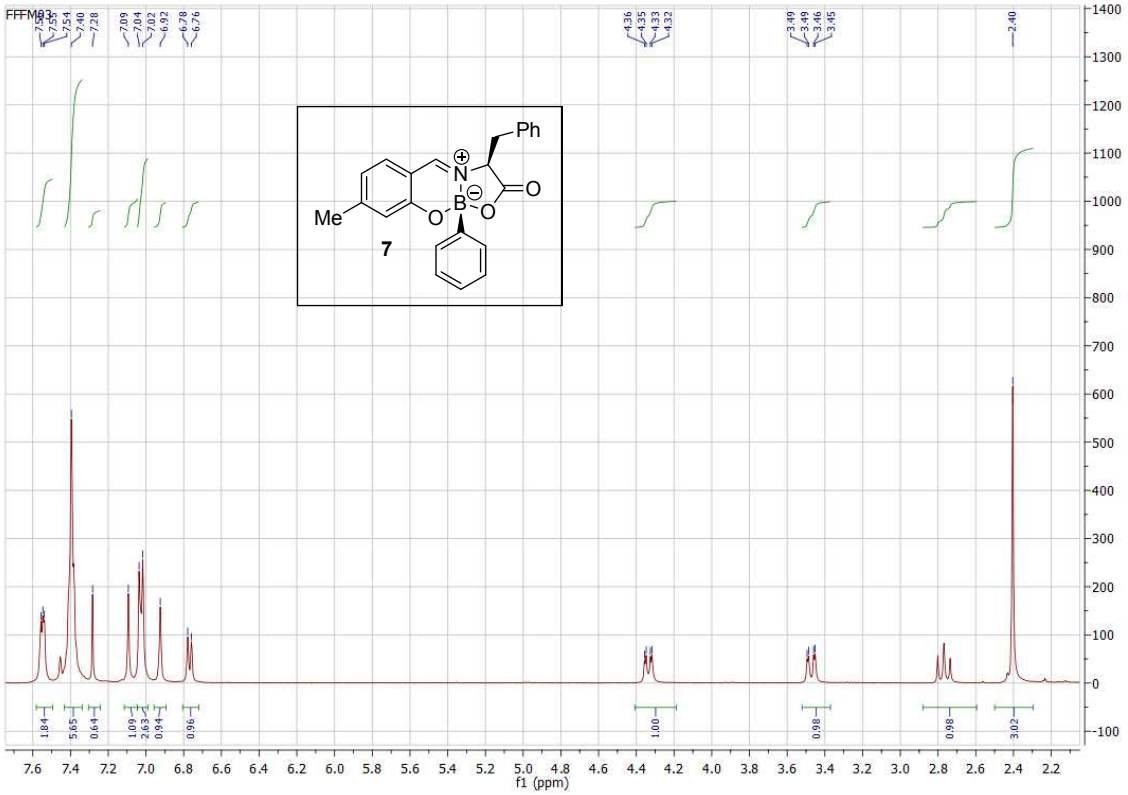
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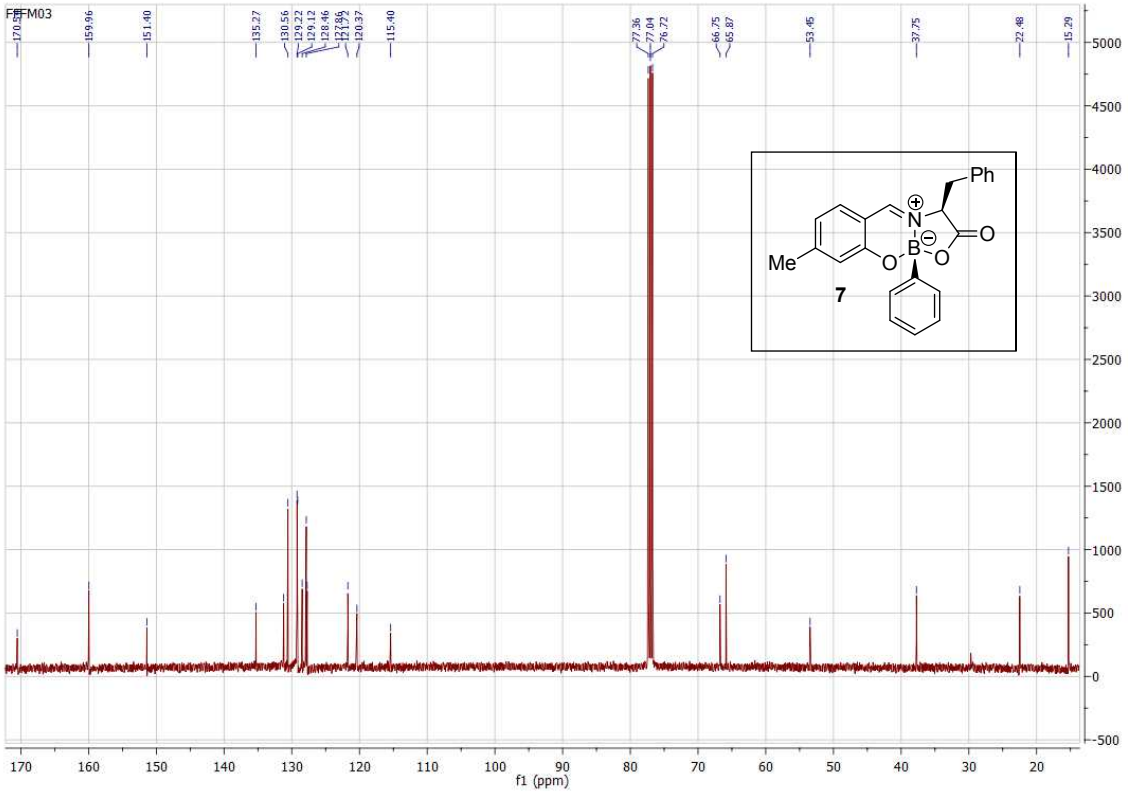
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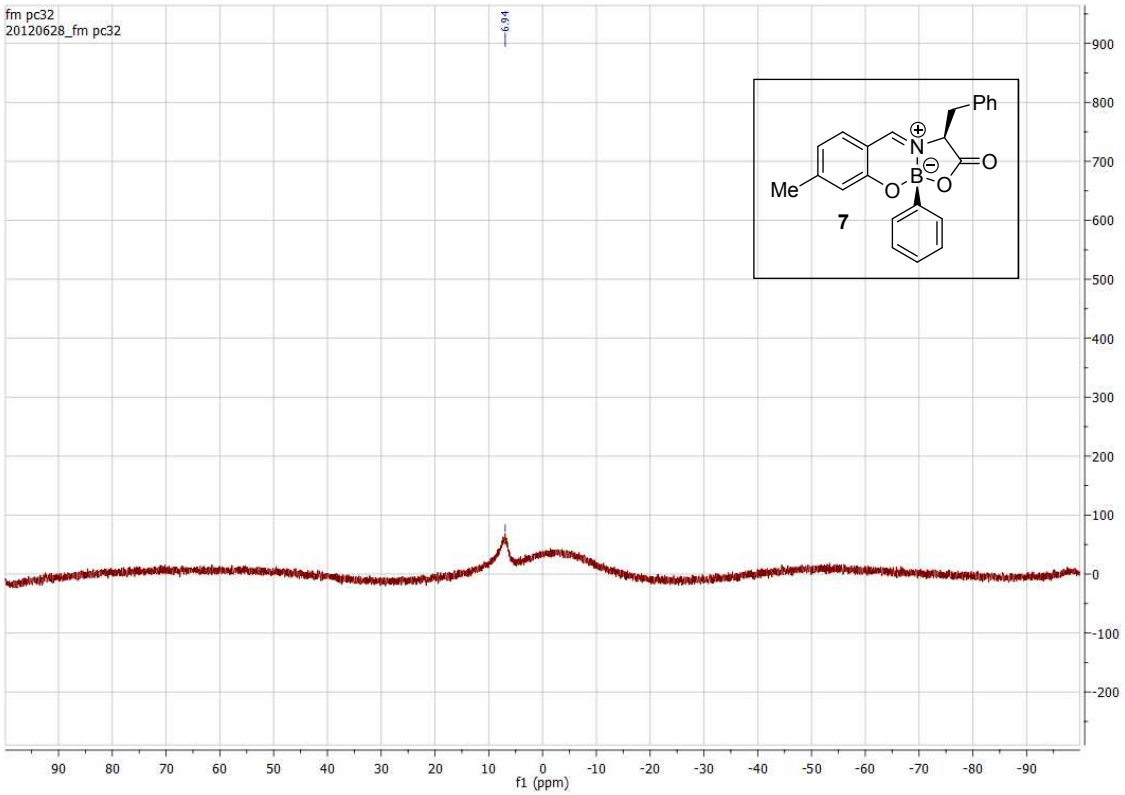
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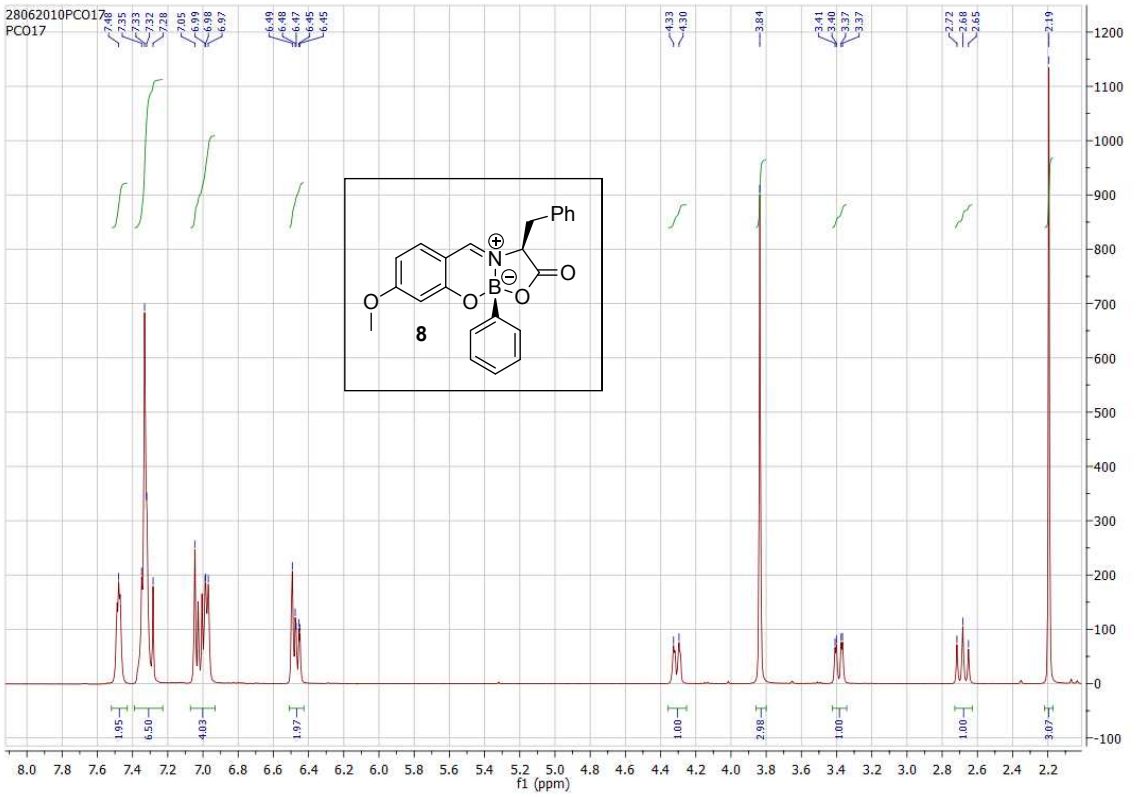
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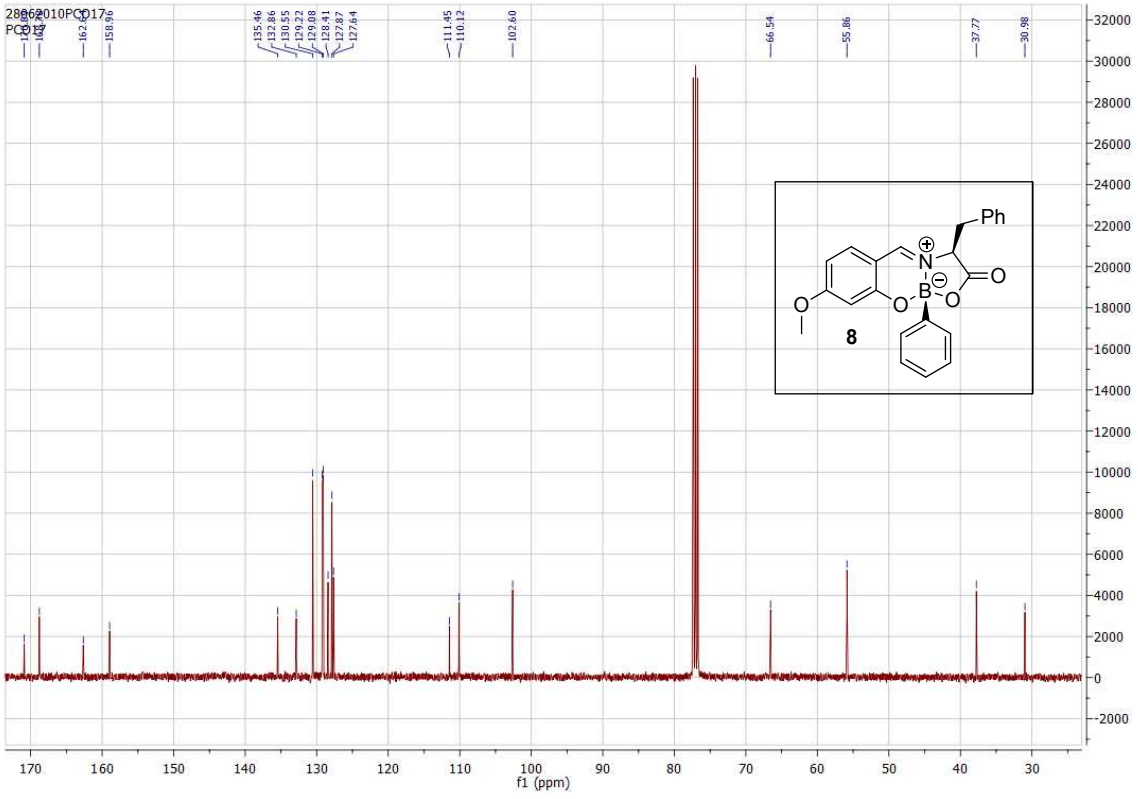
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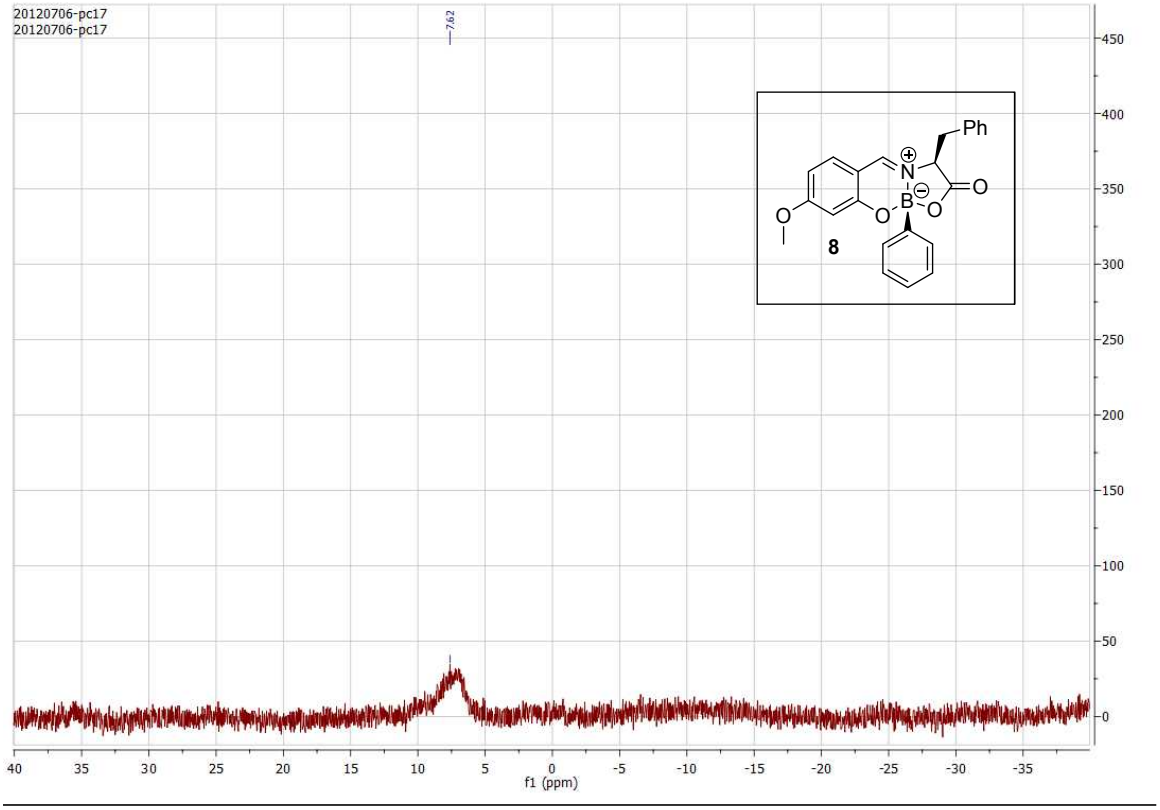
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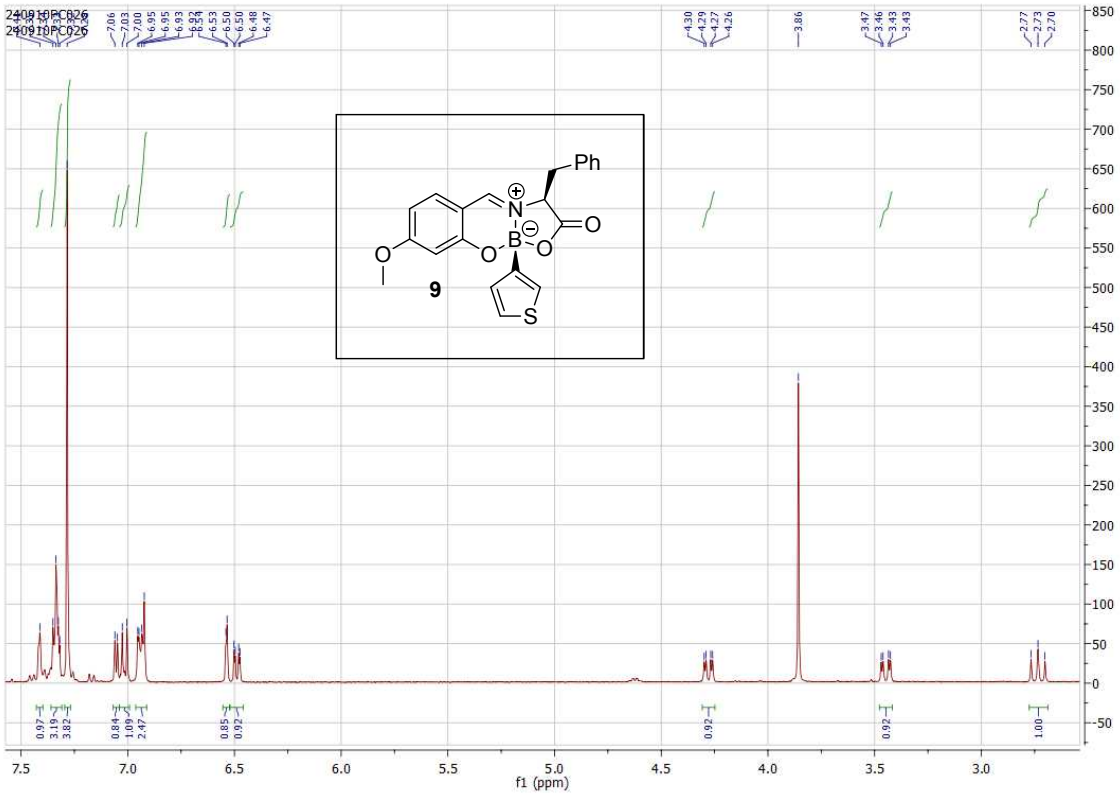
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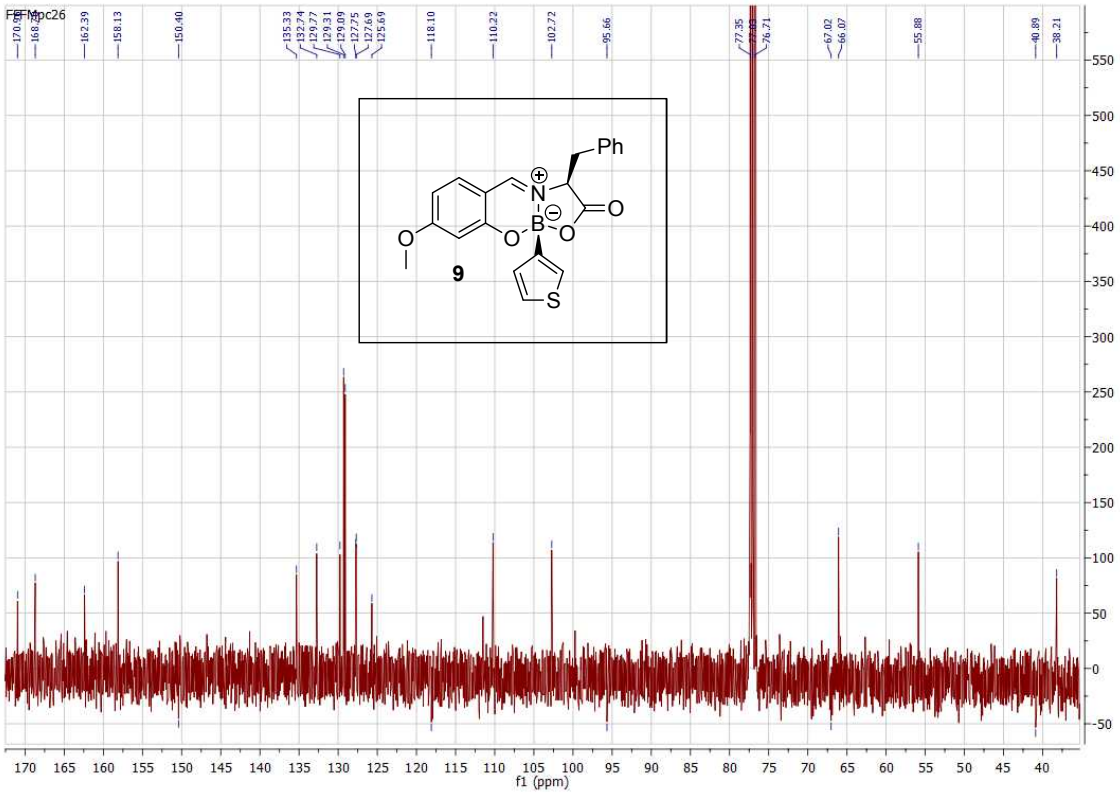
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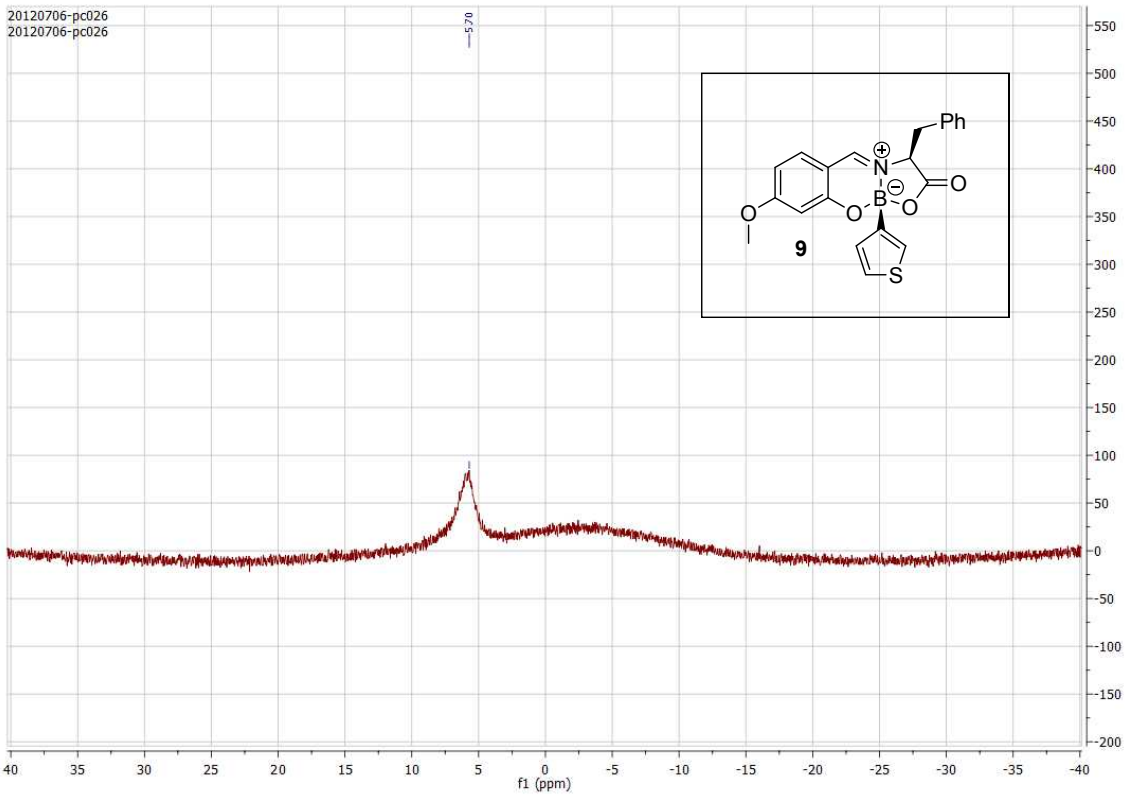
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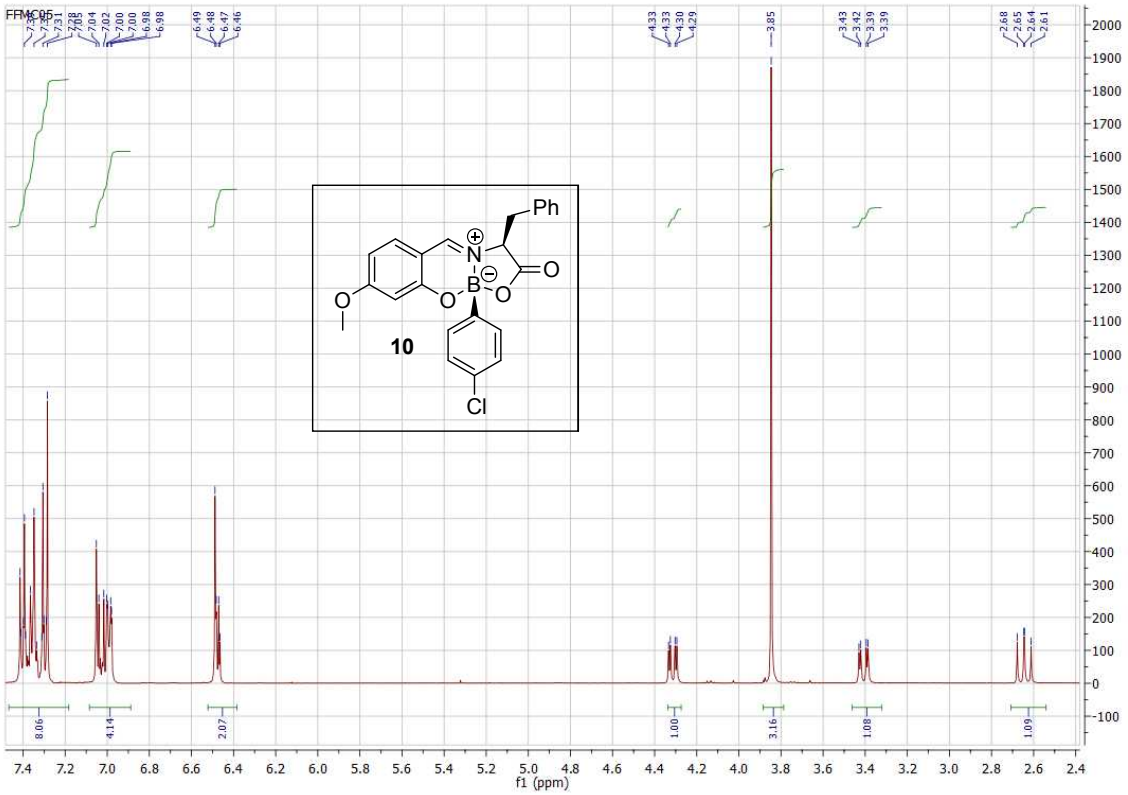
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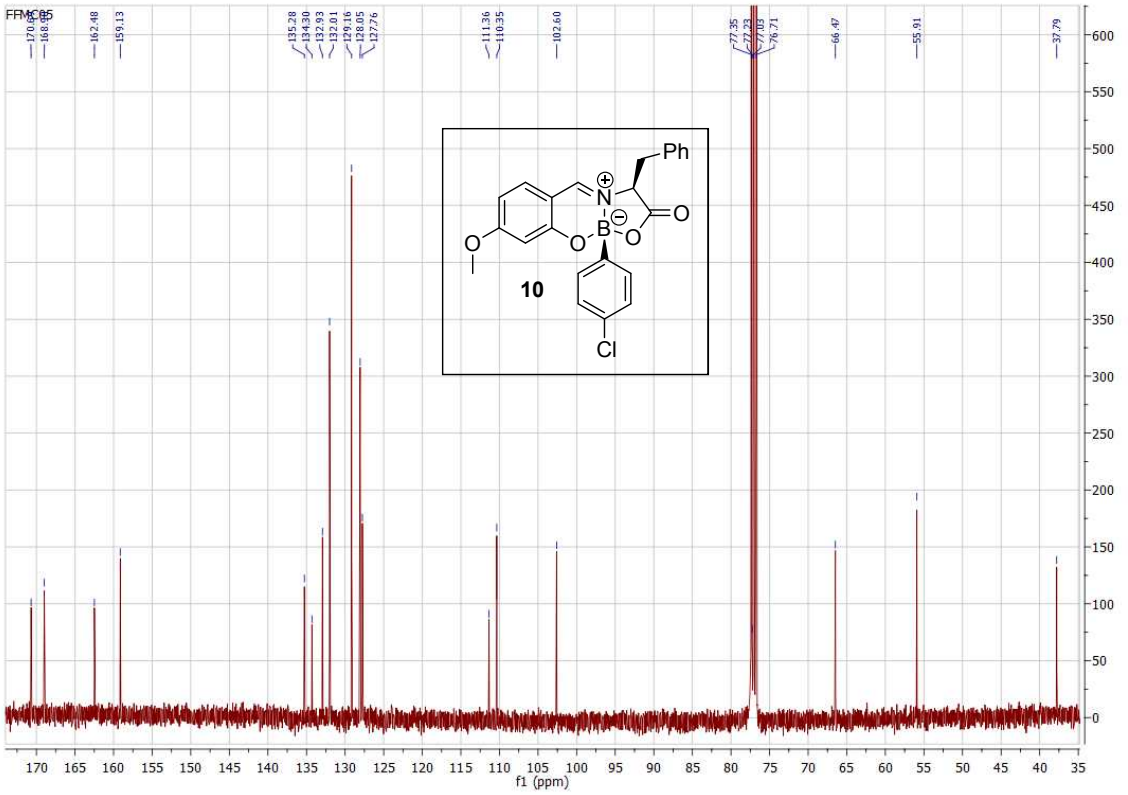
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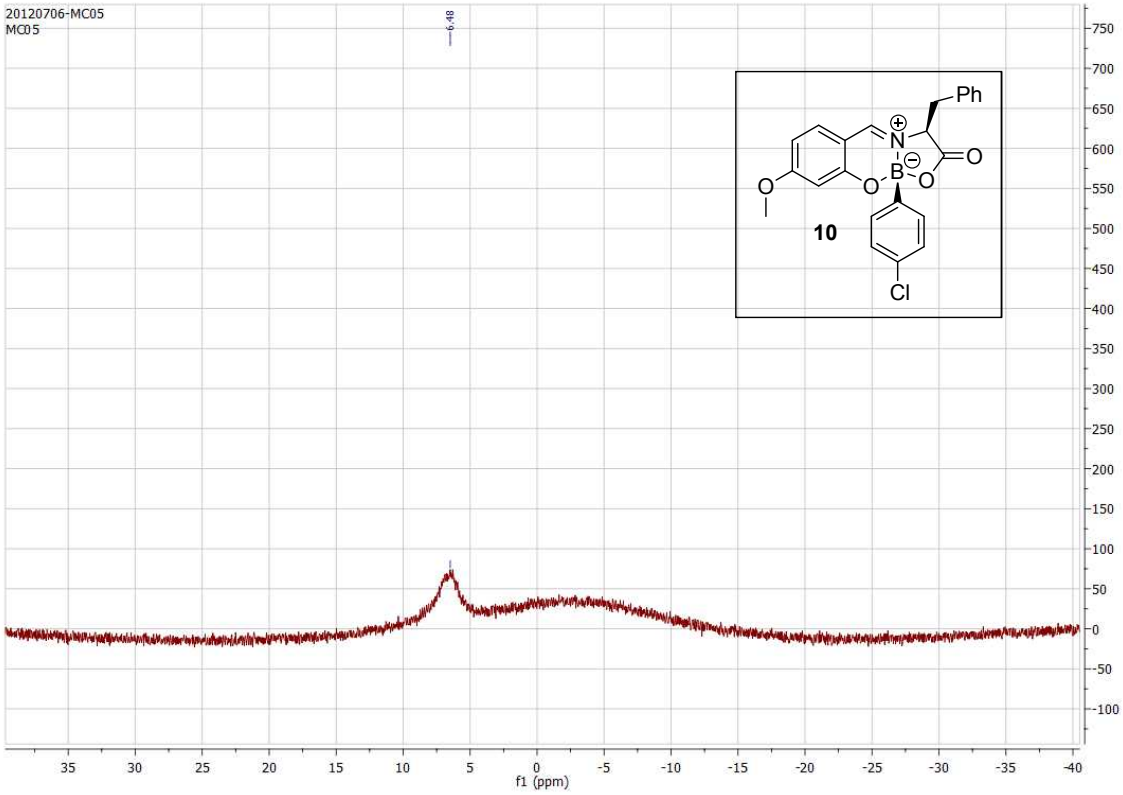
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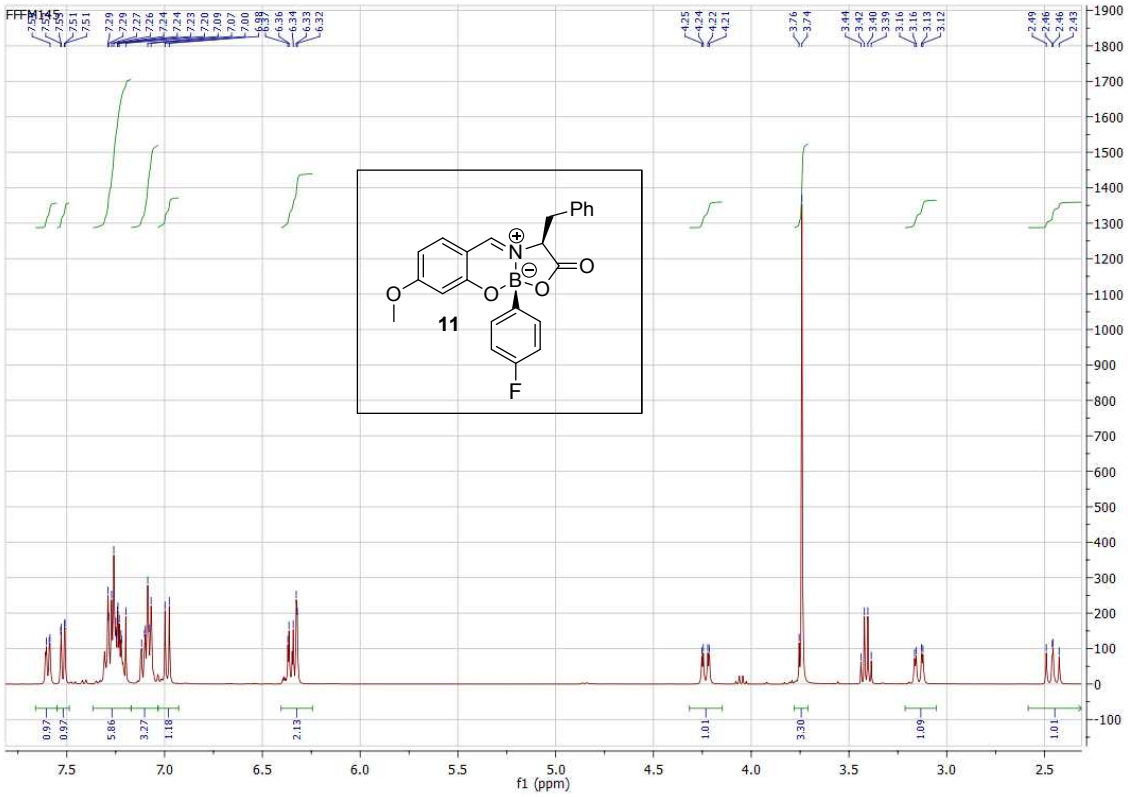
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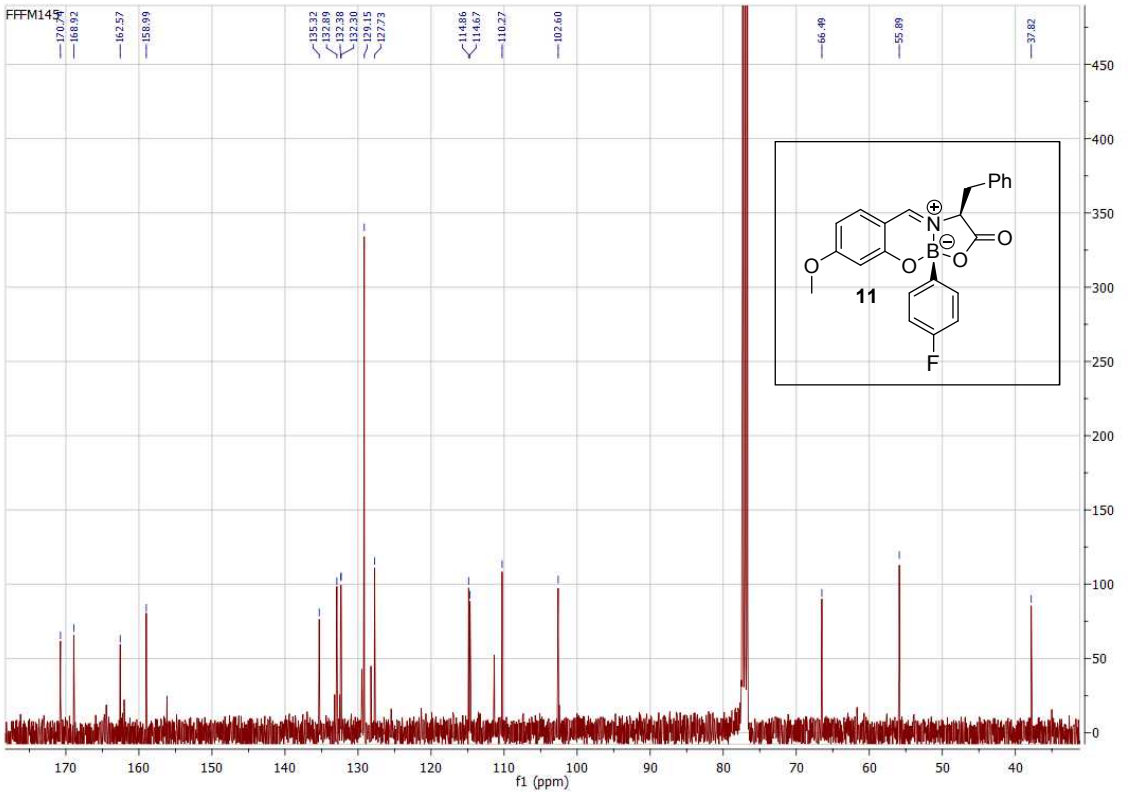
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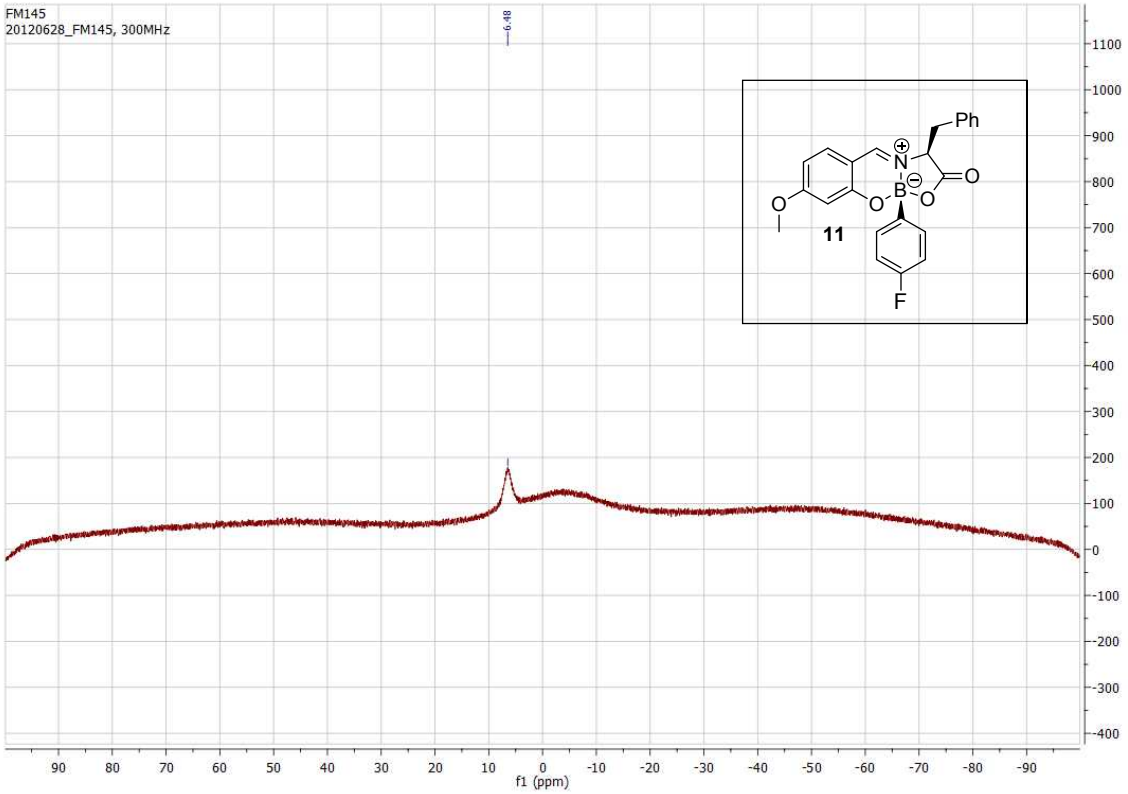
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11
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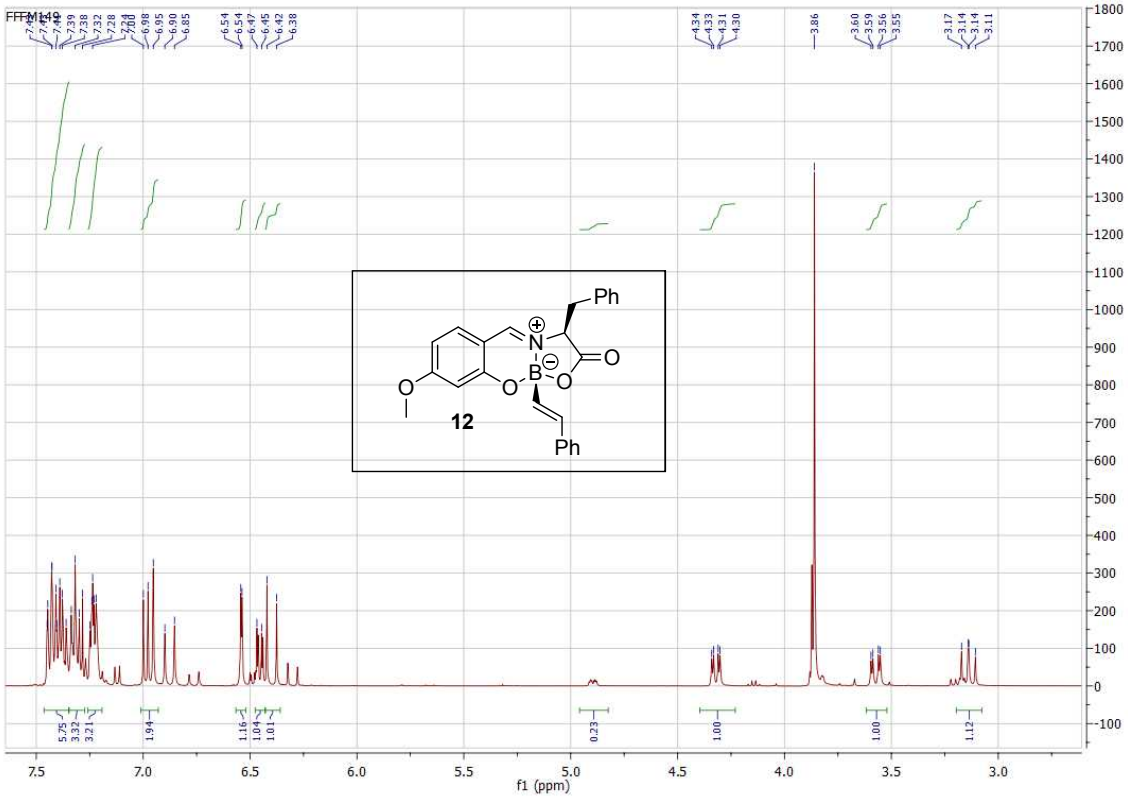
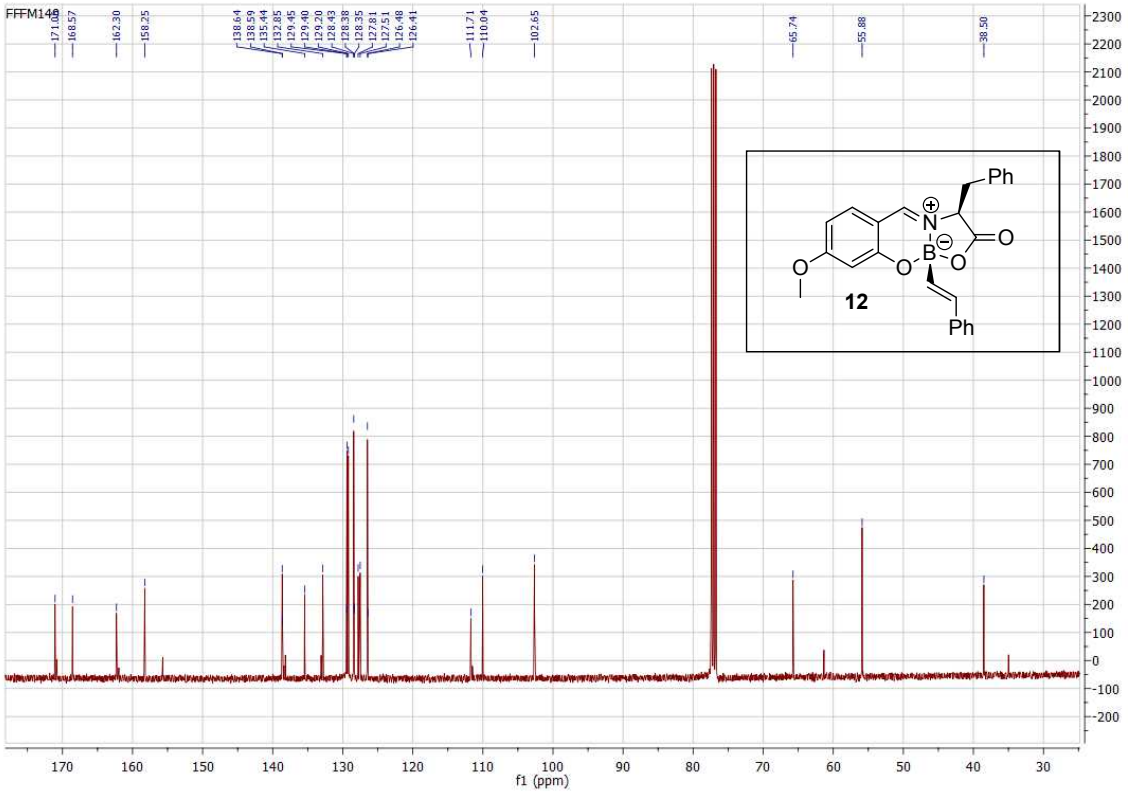
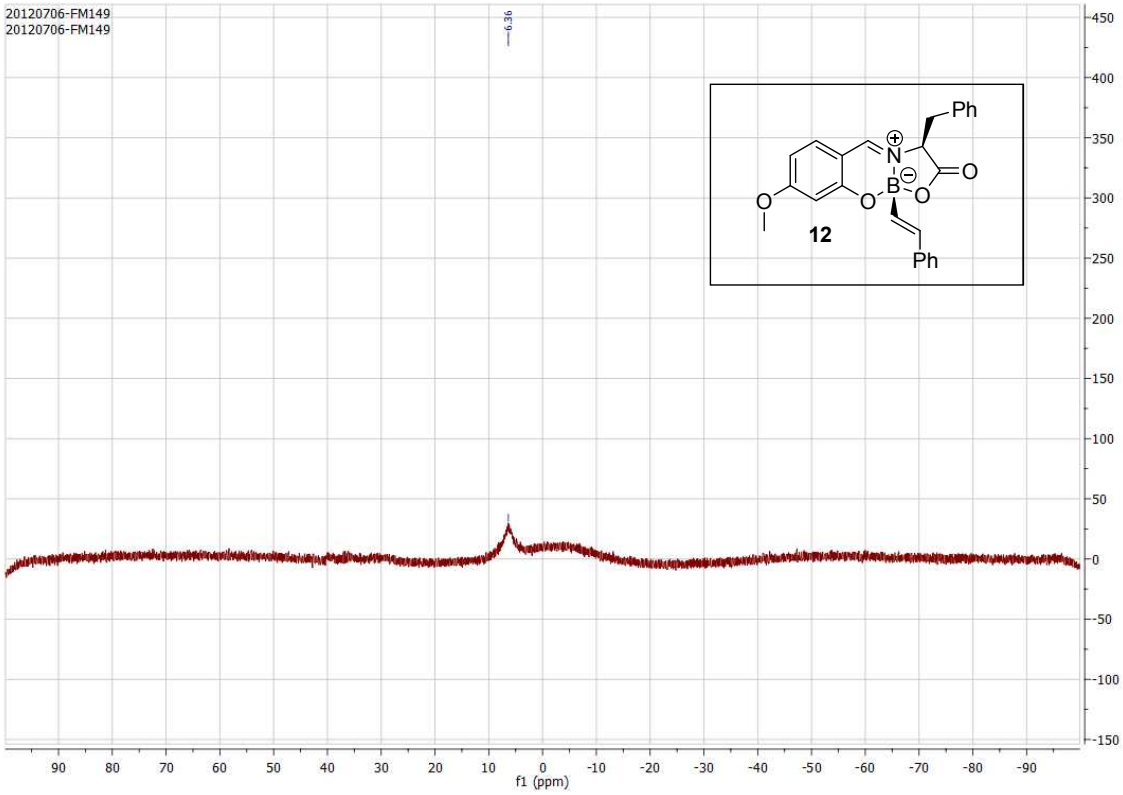
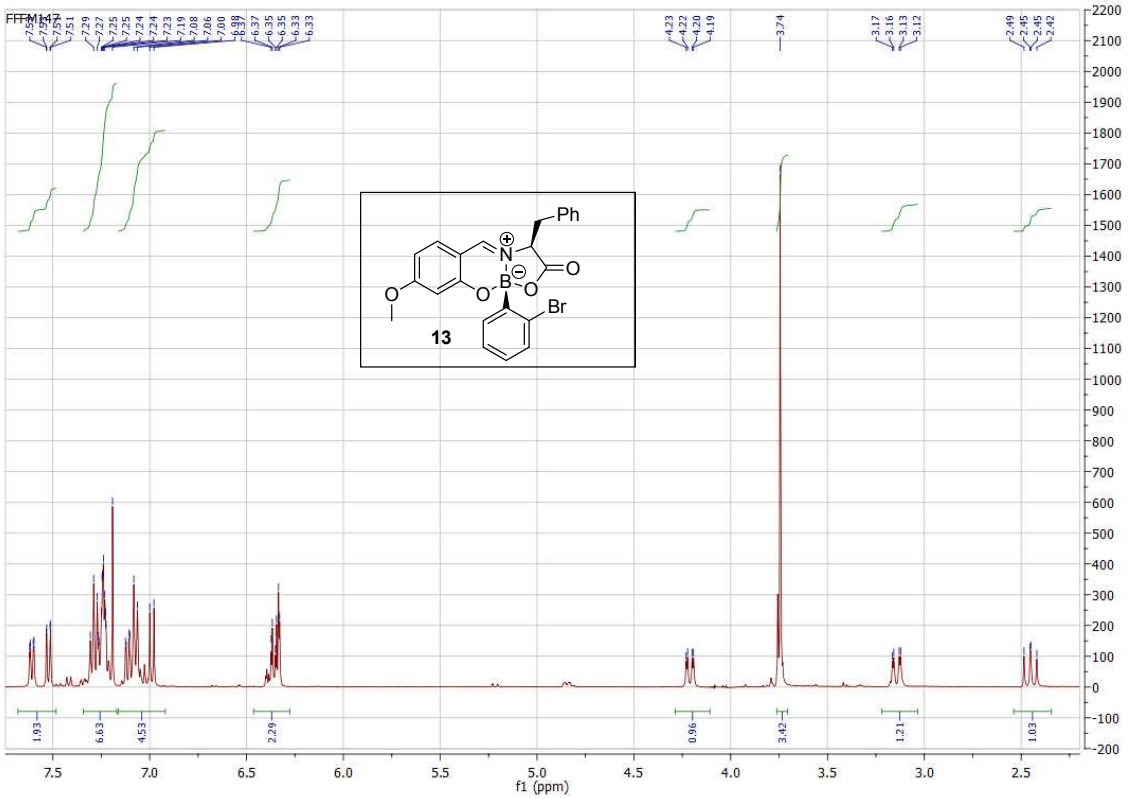
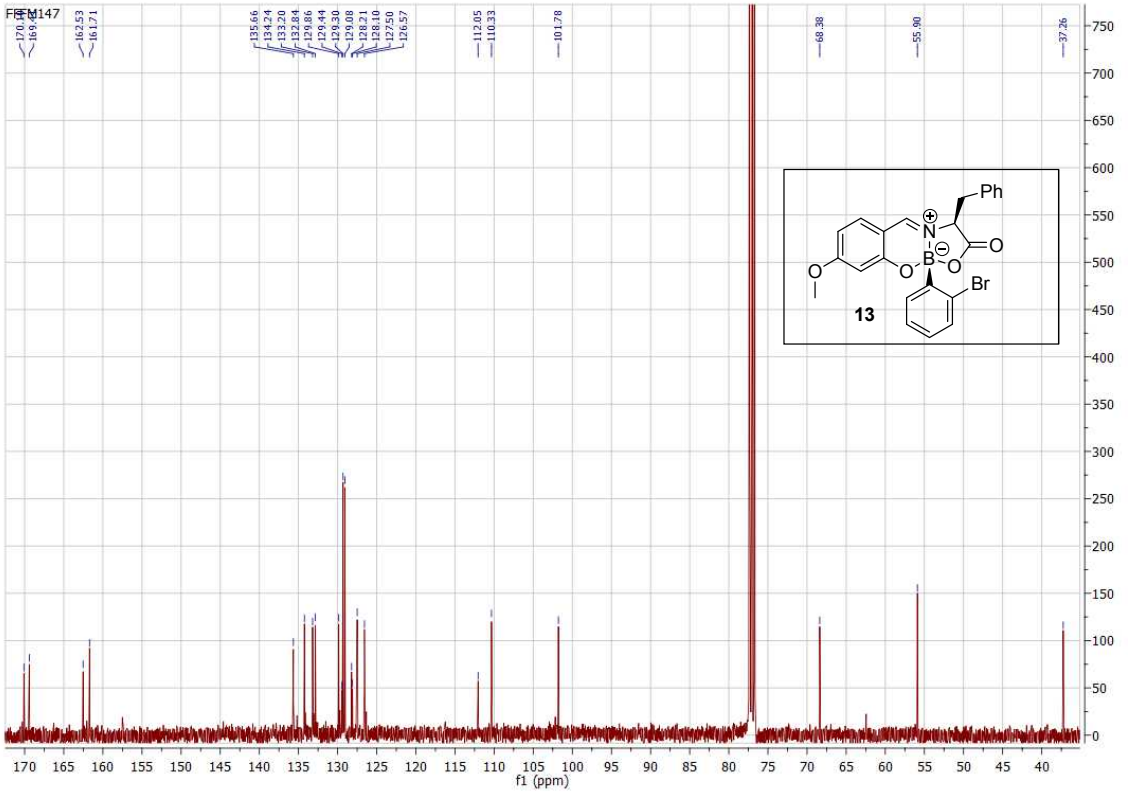
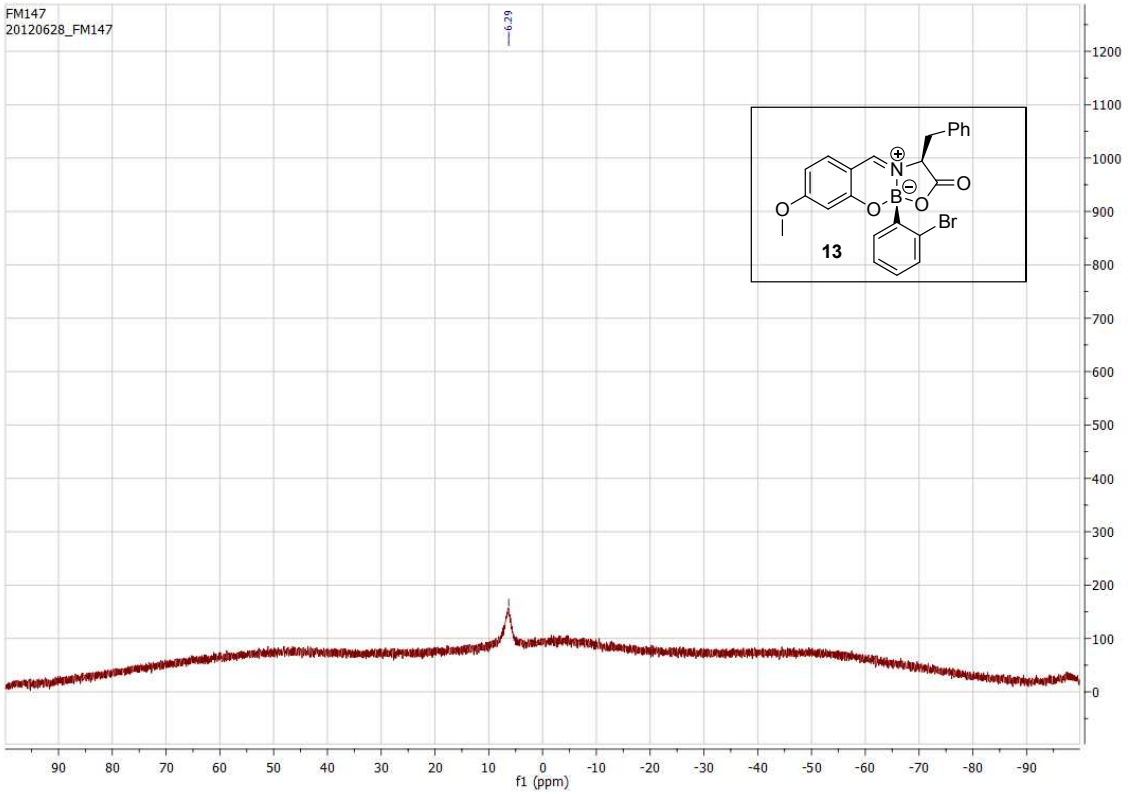

FFFM149
7.74
7.44
7.39
7.38
7.32
7.28
7.00
6.98
6.95
6.90
6.85
6.54
6.54
6.47
6.45
6.42
6.38
4.34
4.33
4.31
4.30
3.86
3.60
3.59
3.56
3.55
3.17
3.14
3.14
3.11
Ph
N
O
B
O
O
O
12
Ph
5.75
3.32
3.21
1.94
1.16
1.04
1.01
0.23
1.00
1.00
1.12
f1 (ppm)


FFFM149
171.08
168.57
162.30
158.25
138.64
138.59
135.44
132.85
129.45
129.40
129.20
128.43
128.38
128.35
127.81
127.51
126.48
126.41
111.71
110.04
102.65
65.74
55.88
38.50
Ph
N
O
B
O
O
O
12
Ph
f1 (ppm)


20120706-FM149
20120706-FM149
6.36
Ph
N
O
B
O
O
O
Ph
12
450
400
350
300
250
200
150
100
50
0
-50
-100
-150
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)


FFM147
Ph
N
O
B
O
O
O
Br
13
f1 (ppm)


FFM147
Ph
N
O
B
O
O
O
Br
13
f1 (ppm)


FM147
20120628_FM147
6.29
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)
Ph
N
O
B
O
O
O
Br
13