

SUPPLEMENTARY INFORMATION

Effect of Coordination Dissymmetry on the Catalytic Activity of Manganese Catalase Mimics

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Synthesis of secondary amines and ligand intermediates 1 - 5

Bis(2-pyridylmethyl)amine, prepared as described in reference [1]. 2-Picolylamine (488 μ L, 4.67 mmol) was added drop by drop to an ice bath cooled solution of 2-pyridinecarboxaldehyde (0.44 mL, 4.67 mmol) in MeOH (15 mL). The yellow solution was allowed to stir at room temperature for 3 h. The mixture was cooled in an ice bath and NaBH₄ (353.3 mg, 4.67 mmol) was added while stirring. The mixture was stirred overnight at room temperature and then the solvent evaporated under vacuum. The residue was diluted with 10 mL water and neutralized with 2 M HCl (added drop by drop) up to pH \approx 7.0. The resulting mixture was extracted with Cl₂CH₂ (3 \times 15 mL), washed with brine (10 mL) and dried over Na₂SO₄. After solvent evaporation bis(2-pyridylmethyl)amine was obtained as a yellow oil. Yield: 0.7520 g, 80.7 %. ¹H NMR spectrum (δ , CDCl₃, ppm): 8.56(d, 2H, Ar-H); 7.64 (td, 2H, Ar-H); 7.37 (d, 2H, Ar-H); 7.15 (t, 2H, Ar-H); 3.99 (s, 4H, -CH₂); 3.09 (1H, -NH). ¹³C NMR spectrum (δ , CDCl₃, ppm): 159.51, 149.18, 136.32, 122.15, 121.61, 54.6.

N-(2-hydroxybenzyl)benzylamine, prepared as described in reference [2]. Salicylaldehyde (1.09 mL, 9.33 mmol) was added dropwise to a solution of benzaldehyde (1.02 mL, 9.33 mmol) in 30 mL EtOH. The deep yellow solution was stirred at reflux for 5 h and then allowed to cool to room temperature. Solid NaBH₄ (0.4235 g, 11.2 mmol) was added in portions to the reaction solution cooled in an ice bath with stirring. The colorless mixture was stirred overnight and concentrated under reduced pressure. The residue was diluted with 10 mL water, neutralized with 2 M HCl (pH \approx 7.0), extracted with CH₂Cl₂ (3 \times 15 mL), washed with brine (10 mL) and dried over Na₂SO₄. After solvent evaporation the oily product was obtained. Yield: 1.72 g, 86.4 %. ¹H NMR spectrum (δ , CDCl₃, ppm): 7.38-7.24 (m, 5H, Bz-H); 7.17 (t, 1H, Ar-H); 6.99 (d, 1H, Ar-H); 6.87-6.75 (m, 2H, Ar-H); 3.99 (s, 2H, -CH₂); 3.80 (s, 2H, -CH₂). ¹³C NMR spectrum (δ , CDCl₃, ppm): 158.10, 138.19, 128.81, 128.67, 128.51, 128.36, 127.58, 122.11, 119.10, 116.40, 52.50, 51.75.

***N*-(2-hydroxybenzyl)glycine chlorohydrate.** The procedure is described in ref. [3]. A mixture of glycine (0.75 g, 0.01 mmol) and an aqueous solution of KOH (0.56 g, 0.01 mmol, in 10 mL water) was stirred for 5 min. Then a solution of salicylaldehyde (1.22 g, 0.01 mmol) in 10 mL ethanol was added. The yellow mixture was kept with stirring for 30 min at room temperature and then cooled in an ice bath. NaBH₄ (0.46 g, 0.012 mmol in 5 mL of 1% NaOH) was added to the reaction mixture and the yellow solution bleached to colorless. The reaction mixture was allowed to stir for 20 min. Then, conc. HCl was added drop by drop until the pH 3.5 and the white solid separated from solution was filtered under reduced pressure, washed with ethanol and dried under vacuum. The solid was recrystallized from 1:1 ethanol:water mixture. Yield: 0.728 g, 33.5%. mp: 210 °C. ¹H NMR spectrum (δ , D₂O/NaOD, ppm): 7.11 (m, 2H, Ar-H); 6.65 (m, 2H, Ar-H); 3.96 (s, 2H, Ar-CH₂); 3.36 (s, 2H, -CH₂CO₂Na). ¹³C NMR spectrum (δ , D₂O/NaOD, ppm) 179,81, 164,94, 129,40, 128,69, 127,93, 119,00, 113,84, 51,83, 48,07.

(6-Methyl-2-phenyl-2,4-dihydro-1,3-benzodioxin-8-yl)methanol (1). This compound was synthesized following a reported procedure [4]. 2,6-Bis(hydroxymethyl)-4-methylphenol (10 g, 59.5 mmol), benzaldehyde dimethyl acetal (11 g, 71.4 mmol) and *p*-toluene sulfonic acid monohydrate (200 mg) were mixed in 50 mL DMF. The yellow solution was stirred for 6 h at 50 °C under reduced pressure. Reaction mixture was diluted with 50 mL CHCl₃. The pale-yellow solution was washed with NaHCO₃ (20 mL \times 2) and brine (20 mL \times 2). The organic layer was collected, dried over Na₂SO₄ and filtered. After evaporation of solvent a thick mass was obtained, which turned into a white solid after addition of 10 mL hexane. The solid was filtered, washed with hexane and dried under vacuum. Yield: 12.12 g, 79.4 %. The crystalline compound was recovered as long needles after recrystallizing from 8:1 EtOAc:hexane. mp = 83 °C. ¹H NMR spectrum (δ , CDCl₃, ppm): 7.60-7.57(m, 2H, Ar-H); 7.46-7.42 (m, 3H, Ar-H); 7.03 (s, 1H, Ar-H); 6.78 (s, 1H, Ar-H); 6.01 (s, 1H, -CH); 5.14 (d, 1H, -CH₂); 4.98 (s, 2H, -CH₂); 4.68 (s, 2H, -CH₂);

2.29 (s, 3H, CH₃). ¹³C NMR spectrum (δ , CDCl₃, ppm): 148.6, 136.9, 130.5, 129.4, 128.5, 128.4, 127.8, 126.2, 124.5, 120.4, 99.6, 66.7, 61.0, 20.6.

8-(bromomethyl)-6-methyl-2-phenyl-2,4-dihydro-1,3-benzodioxine (2). This compound was synthesized following a reported procedure [4]. Compound **1** (4.8146 g, 18.8 mmol) was charged in a round bottom flask sealed with a rubber septum purged with N₂. Anhydrous DMF (15 mL) was injected through the septum and the solution cooled in an ice bath. Solutions of CBr₄ (9.34 g, 37.6 mmol) in 15 mL DMF and PPh₃ (7.39 g, 37.6 mmol) in 15 mL DMF were prepared separately and injected into the reaction flask. The reaction mixture was stirred overnight at room temperature. The reaction was quenched with MeOH and the solvent removed under vacuum. The brown red residue was dissolved in CH₂Cl₂ (25 mL), and washed with 5% NaHCO₃ solution (15 mL \times 3). The organic layer was collected and dried over Na₂SO₄. After solvent evaporation, the resulting solid was stirred in 40 mL of 9:1 hexane:CH₂Cl₂ mixture for 10 min. After decantation, the liquid was poured away and the solid dried under reduced pressure. The white solid was purified by flash column chromatography using hexane:CH₂Cl₂ (9:1) as mobile phase. Yield: 3.423 g, 57.1%. mp: 93 °C. ¹H NMR spectrum (δ , CDCl₃, ppm): 7.67-7.63(m, 2H, Ar-H); 7.48-7.41(m, 3H, Ar-H); 7.07(s, 1H, Ar-H); 6.79(s, 1H, Ar-H); 6.04(s, 1H, -CH); 5.12(d, 1H, -CH₂); 4.96(s, 1H, -CH₂); 4.55 (dd, 2H, -CH₂Br); 2.28(s, 3H, CH₃). ¹³C NMR spectrum (δ , CDCl₃, ppm): 148.81, 136.99, 130.51, 129.84, 129.34, 128.44, 126.34, 125.91, 125.43, 120.95, 98.93, 66.48, 27.78, 20.56.

8-(bis(2-pyridylmethyl)aminomethyl)-6-methyl-2-phenyl-2,4-dihydro-1,3-benzodioxine (3). This compound was synthesized following a classic procedure [4,5]. To bis(2-pyridylmethyl)amine (1.6756 g, 88.41 mmol) dissolved in 10 mL CH₂Cl₂, NaH (3 equiv.) was added in portions during 5 min with stirring at room temperature. A solution of **2** (2.6844 g, 8.41 mmol) in 15 CH₂Cl₂ was added to this mixture and left stirring at room temperature for 4 days. The reaction progress was monitored by TLC. The brown

red mixture was diluted with 15 mL CHCl_3 and washed with NaHCO_3 (15 mL), water (15 mL) and brine (15 mL). The organic layer was collected, dried over Na_2SO_4 and filtered. After solvent evaporation the crude product was purified by silica gel column chromatography using CH_2Cl_2 :hexane (1:1) as mobile phase. Yield: 3.0738 g, 83.5%. ^1H NMR spectrum (δ , CDCl_3 , ppm): 8.47 (d, 2H, $\text{Ar}_{\text{py}}\text{-H}$); 7.61-7.57 (m, 4H, $\text{Ar}_{\text{py}}\text{-H}$); 7.47-7.42 (m, 5H, Ar-H); 7.18 (s, 1H, Ar-H); 7.07 (t, 2H, Ar-H); 6.72 (s, 1H, Ar-H); 5.94 (s, 1H, -CH); 5.18 (d, 1H, $-\text{CH}_2$); 4.96 (d, 1H, $-\text{CH}_2$); 3.84 (dd, 4H, $-\text{CH}_2\text{-Ar}_{\text{py}}$); 3.73 (dd, 2H, $-\text{CH}_2\text{-N}$); 2.28 (s, 3H, CH_3). ^{13}C NMR spectrum (δ , CDCl_3 , ppm): 160.02, 149.46, 148.82, 137.3, 136.32, 130.14, 130.03, 129.35, 128.48, 126.56, 124.12, 122.59, 121.76, 120.39, 120.06, 99.07, 66.85, 60.33, 52.30, 20.80.

2-(N,N-bis(2-(pyridylmethyl)aminomethyl)-6-(hydroxymethyl)-4-methylphenol (4).

This compound was synthesized following a classic procedure [6]. To a solution of **3** (3.0738 g, 7.0253 mmol) in 20 mL THF, 1 N HCl (20 mL) was added dropwise at 0 °C and the reaction mixture was stirred for 48 h at room temperature. The reaction mixture was allowed to cool to 0 °C and neutralized with NaHCO_3 . THF was evaporated under vacuum and the aqueous layer was extracted with CH_2Cl_2 (15 mL \times 2). The organic extracts were collected and washed with 10 % NaHSO_3 (10 mL \times 2), water (10 mL \times 2) and brine (15 mL), dried over Na_2SO_4 and filtered. After solvent evaporation the product was obtained as an oil. Yield: 1.9087 g, 77.6%. ^1H NMR spectrum (δ , CDCl_3 , ppm): 8.56 (d, 2H, Ar-H_{py}); 7.66-7.60 (m, 2H, Ar-H_{py}); 7.30 (d, 2H, Ar-H); 7.16 (dt, 2H, Ar-H); 6.95 (d, 1H, Ar-H); 6.82 (d, 1H, Ar-H); 4.72 (s, 2H, $-\text{CH}_2\text{OH}$); 3.87 (s, 4H, $-\text{CH}_2\text{-Ar}_{\text{py}}$); 3.76 (s, 2H, $-\text{CH}_2\text{N}$); 2.23 (s, 3H, CH_3). ^{13}C NMR spectrum (δ , CDCl_3 , ppm): 158.18, 153.43, 148.91, 136.81, 130.20, 128.83, 127.78, 127.70, 123.25, 122.50, 122.26, 62.95($-\text{CH}_2\text{OH}$), 59.09, 56.79, 20.36.

2-(N,N-bis(2-(pyridylmethyl)aminomethyl)-6-(chloromethyl)-4-methylphenol (5).

This compound was synthesized following a reported procedure [2]. A solution of **4** (1.4878 g, 4.2578 mmol) in freshly distilled SOCl_2 (20 mL) was left with stirring for 3 h

at 35 °C. Thionyl chloride was removed by rotary evaporation and the product washed with CH₂Cl₂ (5 mL × 3) and hexane (5 mL × 2). The resulting residue was dried under vacuum. Yield: 100 %. ¹H NMR spectrum (δ, MeOD, ppm): 8.79 (dd, 2H, Ar-H_{py}); 8.49 (dt, 2H, Ar-H); 8.02 (d, 2H, Ar-H); 7.92 (dt, 2H, Ar-H); 6.96 (d, 1H, Ar-H); 6.83 (d, 1H, Ar-H); 4.54 (s, 2H, -CH₂Cl); 4.46 (s, 4H, -CH₂-Ar_{py}); 3.77 (s, 2H, -CH₂N); 2.11 (s, 3H, CH₃). ¹³C NMR spectrum (δ, MeOD, ppm): 154.79, 152.54, 147.98, 142.40, 134.71, 133.09, 131.31, 128.35, 127.28, 126.39, 125.33, 58.75, 56.87, 42.91(-CH₂Cl), 20.26.

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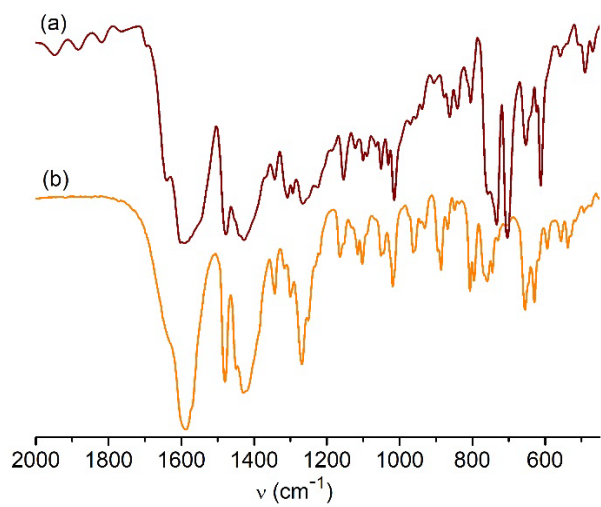


Figure S1. IR spectra of complexes (a) **6** and (b) **7**

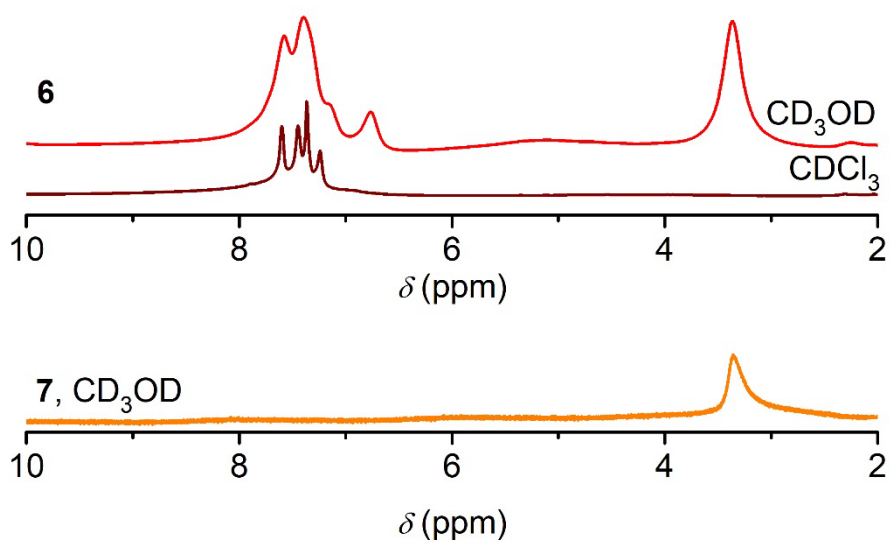


Figure S2. Diamagnetic region of the ^1H NMR spectra of complexes **6** and **7**

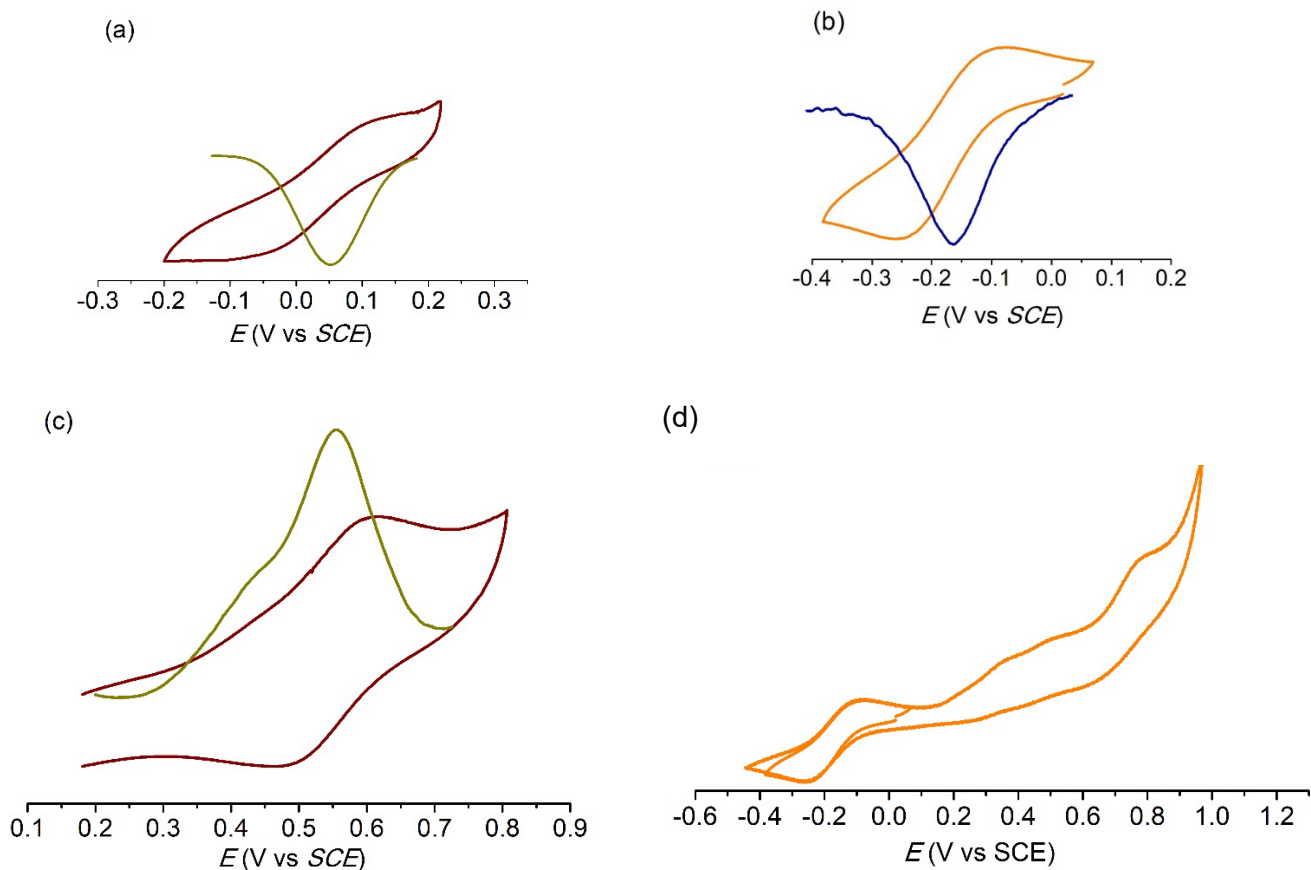


Figure S3. Cyclic (wine and orange lines) and square-wave voltammogram (dark yellow and blue lines) of **6** (a) and (c), and **7** (b) and (d), in DMF. Conditions: C/Pt/SCE; conc. = 1 mM; supporting electrolyte: Bu_4NPF_6 . Scan rate (CV) = 10 mV/s. Scan frequency (SWV) = 1 Hz.

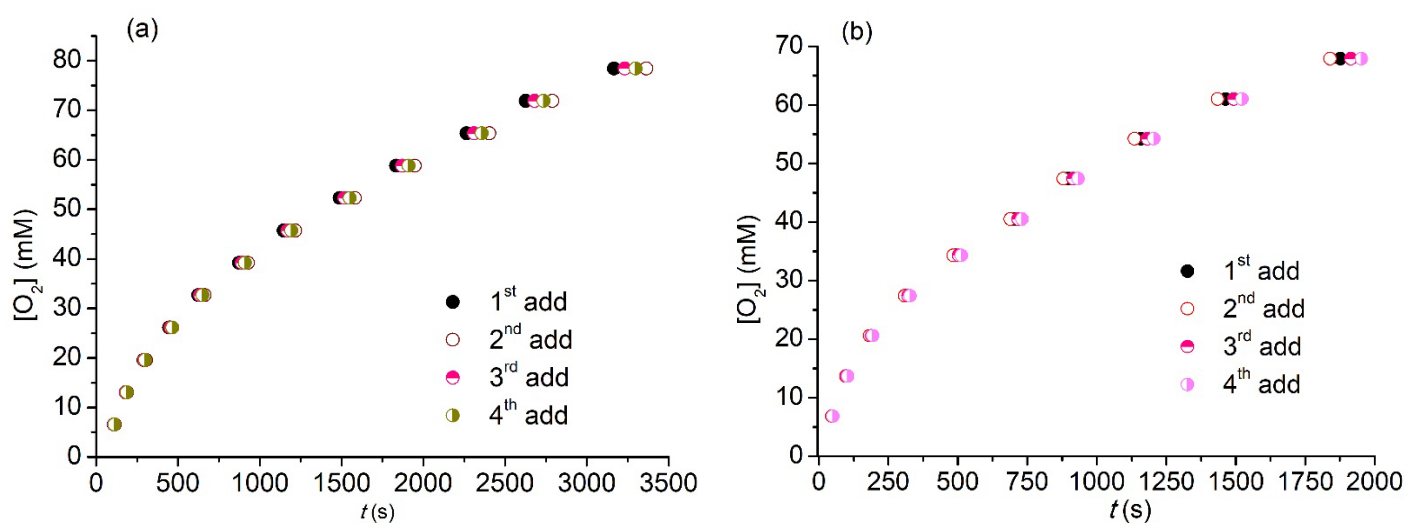


Figure S4. Oxygen evolved from successive additions of 800 equiv. of H_2O_2 on (a) 0.25 mM **6** and (b) 0.25 mM **7**, DMF solutions. $T = 25\text{ }^\circ\text{C}$.

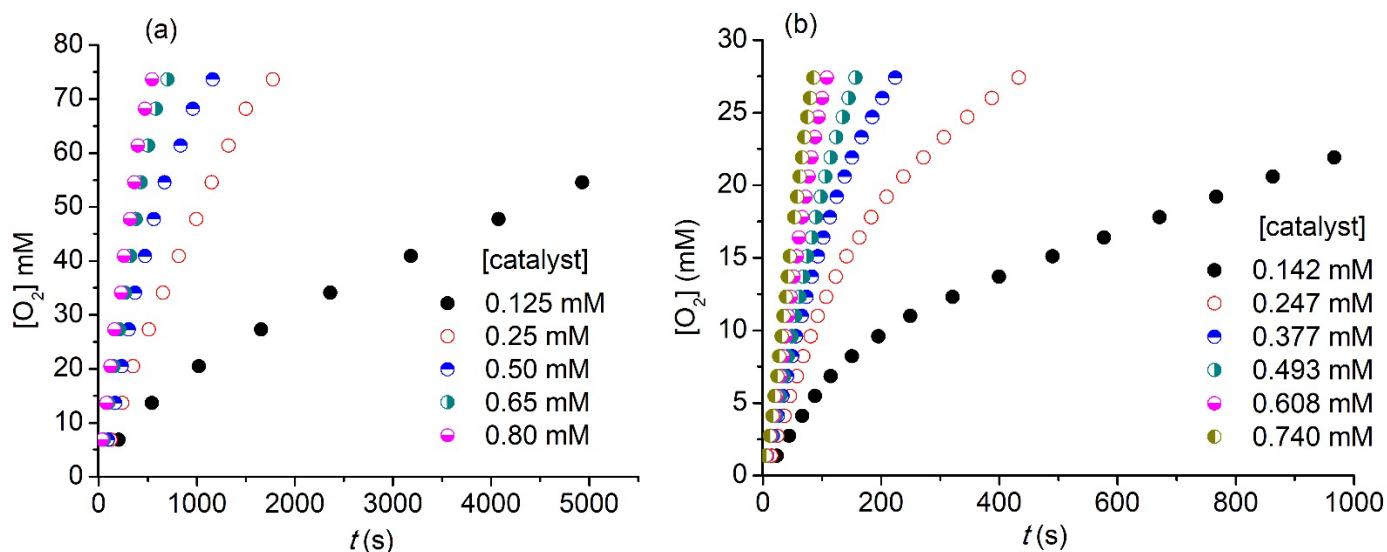


Figure S5. Time-evolution of $[O_2]$ from mixtures of H_2O_2 (148 mM) and various concentrations of (a) **6** and (b) **7**, in 3.0 mL DMF, $T = 25\text{ }^\circ\text{C}$. Experimental data are the mean of at least three determinations.

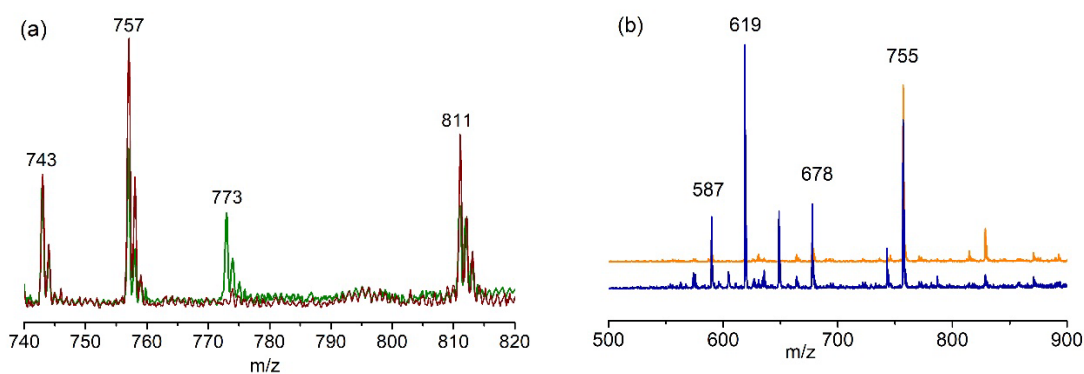


Figure S6. Mass spectra of **6** (a) and **7** (b) before (wine and orange lines) and after (green and blue lines) reaction with 100 equiv. H_2O_2 in DMF. Solutions were diluted to c.a. 10^{-5} M with CH_3CN

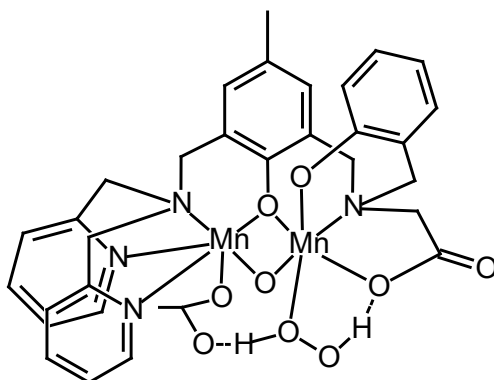


Figure S7. Schematic hydrogen bond of H₂O₂ to the terminally bound carboxylate group of the ligand and acetate within the catalyst-H₂O₂ adduct for the oxidized form of complex **7**