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Hydrogen Peroxide Mediated Oxidation of Manganese Carbonyls in Alkaline Solution

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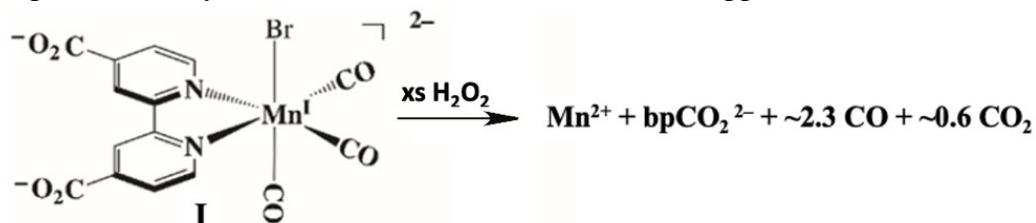
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Abstract:

Reported are stopped-flow kinetics studies of the hydrogen peroxide reaction with the water-soluble manganese(I) carbonyl complex. *fac*-[Mn(CO)₃(Br)(bpCO₂)]²⁻ (**I**, bpCO₂²⁻ = 2,2'-bipyridine-4,4'-dicarboxylate dianion) in alkaline solution. In an earlier study, the H₂O₂ oxidation of **I** was shown to be accompanied by the release of more than two equivalents of carbon monoxide. The stopped-flow studies here confirm the strongly pH dependence of the reaction rate, and a revised mechanism for this kinetics behavior is proposed. The larger interest in these systems derives from evaluating redox mechanisms for CO delivery from metal-based carbon monoxide releasing moieties (CORMs) under physiologically relevant conditions.

Introduction:

An earlier study from this laboratory investigated the products and kinetics of the reaction between the water-soluble manganese carbonyl complex *fac*-[Mn(CO)₃(Br)(bpCO₂)]²⁻, (**I**, bpCO₂²⁻ = 2,2'-bipyridine-4,4'-dicarboxylate dianion) and hydrogen peroxide (eq. 1) in near neutral, aqueous solutions.¹ The incentive for that study was drawn from earlier reports that manganese carbonyl complexes release CO in tumor cells owing to oxidation by endogenous H₂O₂,² which is known to be present in hypoxic tumors at elevated concentrations.³ ~~Notably, s~~Such hydrogen peroxide has also been targeted in other strategies for cancer chemotherapy.⁴ ~~Redox-In addition,~~ redox pathways are ~~also~~ relevant to mechanisms by which ~~CO-releasing moieties (~~potentially therapeutic CO releasing moieties (CORMs)~~CORMs)~~ are activated at sites of inflammation,⁵ a ~~topic-subject~~ of continuing considerable interest.⁶⁻⁸ Notably, several other manganese carbonyls have been investigated as CORMs a topic that has recently been reviewed.^{8f} Unraveling the pathways occurring under oxidative stress has the potential to provide important insight regarding the therapeutic delivery of CO for anticancer or antimicrobial applications.⁹



(1)

As indicated by eq. 1, Barrett et al.¹ demonstrated that H₂O₂ oxidation of **I** results in the release of nearly two and a half equivalents of carbon monoxide, along with the formation of Mn(II) and roughly half an equivalent of carbon dioxide. In near-neutral, aqueous media the reaction rate proved to be first-order in the concentrations of both **I** and H₂O₂ (eq. 2) and sufficient to generate physiologically relevant concentrations of CO.¹

$$-\left(\frac{d[\text{I}]}{dt}\right)_{\square} = k'[\text{H}_2\text{O}_2]_{\text{tot}}[\text{I}] \quad (2)$$

Here, $[H_2O_2]_{tot}$ indicates the total concentration of peroxide species. Under these conditions, the reaction rate was also shown to be pH dependent, with the rate constant k' increasing markedly as the pH was raised within the buffered range (pH 5 to 8) as characterized by eq. 3.^{1,2}

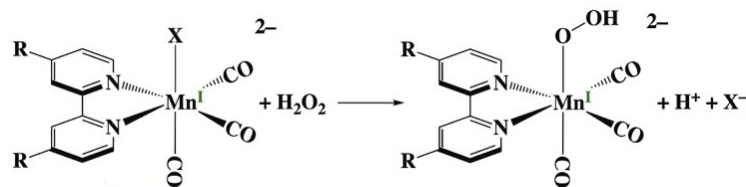
$$k' = k_1 + k_2 \quad (3)$$

Given that H_2O_2 is a weak acid with a K_a of 2.4×10^{-12} M (eq. 4),¹⁰ the second term of this relationship was attributed to greater direct reactivity of the hydroperoxide anion HO_2^- with **I** represented by the rate constant k_2 (eq. 5). In near neutral solutions, k_2' would approximately equal $k_2 K_a$, with k_2 being several orders of magnitude greater than k_1 .

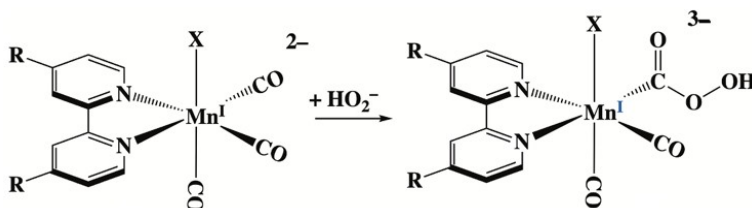


$$\frac{-d[I]}{dt} = (k_1[H_2O_2] + k_2) \quad (5)$$

Although this scenario is a reasonable explanation of the kinetics behavior within the studied pH range, it does not address the nature of the initial step in the cascade of reactions leading to CO release from this CORM. Mechanistically, one can envision several prospective schemes, outer sphere electron transfer, ligand substitution of H_2O_2 for Br^- (Scheme 1) or formation of a hydroperoxyl-carbonyl complex (Scheme 2), as the first-initial step in the reaction sequence leading to the products of eq. 1. The outer sphere electron transfer pathway was discarded owing to the thermodynamic considerations,¹ but it has been much more difficult to differentiate the latter two pathways. Either first-initial step would be followed by oxidation of the metal center and CO labilization. Indeed, it was deemed likely that both were playing roles in the overall reaction. In these contexts, the present study was initiated employing stopped-flow kinetics techniques to probe the reaction kinetics of this reaction at much higher pH values where the reaction with HOO^- should be dominant. Perhaps not surprisingly, the new perspectives gained under these conditions require a reevaluation of the mechanistic arguments.



Scheme 1. Ligand substitution initial step (R = the carboxylate group $-\text{CO}_2^-$)



Scheme 2. Attack on coordinated CO initial step.

Experimental Section:

Materials: Bromopentacarbonylmanganese(I) ($\text{Mn}(\text{CO})_5\text{Br}$, 98%) was purchased from Strem Chemicals. The H_2O_2 stock solution (30%, Certified ACS), NaOH stock solution, 2,2'-bipyridine-4,4'-dicarboxylic acid (bpCO_2H , 98%), silver trifluoromethanesulfonate ($\text{Ag}(\text{CF}_3\text{SO}_3)$, 98%), and trifluoromethanesulfonic (triflic) acid (98%) were purchased from Fischer Scientific. The hydrogen peroxide was titrated using potassium permanganate, standardized against sodium oxalate, to determine the exact concentration. All deuterated solvents were purchased from Cambridge Isotope Laboratories. In all cases, diluted solutions were made using 18 $\text{M}\Omega\text{-cm}$ resistivity deionized water.

Instrumentation: Absorbance spectra were recorded on a Shimadzu UV-2401PC spectrophotometer. Infrared spectra were obtained on a Jasco FT/IR-4100 spectrometer via solid-state KBr pellets. A Bruker Avance NEO 500 MHz was used to acquire NMR spectra. Kinetics studies at higher pH values were performed using an upgraded Applied Photophysics model SX-18 MV stopped-flow spectrophotometer with either a photomultiplier tube (PMT) or a photodiode array (PDA) used as the detector. However, solutions studied using the PDA method suffered from some photochemical decomposition in the reaction cell that affected the kinetics results. For this reason, all rate constants reported here were obtained using single wavelength monitoring with the PMT detector, where control experiments showed that no significant photochemistry occurred within the timeframe of the kinetics studies. Temperature control was performed by a thermostatic,

circulating water bath. In several experiments at low pH, time-resolved absorbance data were obtained on a Jasco V-730 spectrophotometer with internal temperature control. The pH values of solutions were measured using a Hanna edge pH meter. with a Ag/AgCl reference electrode.

Syntheses: The diprotonated form of **I**, *fac*-[Mn(CO)₃(Br)(bpCO₂H)] was prepared from Mn(CO)₅Br and bpCO₂H as previously described¹¹ and characterized by optical, FTIR, and ¹H-NMR spectroscopy. The optical spectrum in aqueous solution displayed the expected metal to ligand charge transfer (MLCT) band at ~409 nm ($\epsilon = 3.1 \times 10^3 \text{ M}^{-1} \text{ cm}^{-1}$) plus strong UV absorptions characteristic of ligand π - π^* transitions, while the FTIR spectrum (KBr, Supporting Information Fig. S1) displayed ν_{CO} bands at 1942 (broad) and 2033 cm^{-1} . The ¹H-NMR spectrum (500 MHz, D₂O, SI Fig. S2) displayed δ (ppm) 8.01 (dd, 2H), 8.78 (s, 2H), 9.39 (d, 2H).

The aqua complex salt [*fac*-Mn(CO)₃(H₂O)(bpCO₂H)](CF₃SO₃) was synthesized via reaction of protonated **I** with Ag(CF₃SO₃). A 50.0 mg (0.108 mmol) sample of *fac*-Mn(CO)₃(Br)(bpCO₂H) was added to 25 mL H₂O, and to this mixture, a 2.16 mL volume of 0.1 M NaOH solution was added to aid in dissolving the starting material. The Ag(CF₃SO₃), 35.4 mg, 0.138 mmol) was weighed inside a glove box, owing to its being highly hygroscopic, then was transferred out and dissolved in a minimal amount of water. After both solutions were homogeneous, the silver triflate was added to the manganese solution. Upon mixing, the reaction solution immediately changed from a deep transparent orange to a cloudy light orange solution. The mixture was stirred for approximately 30 min., after which it was centrifuged to remove the AgBr precipitate, and the supernatant was isolated. The latter was acidified by adding ~2 mL (heavy excess) of 0.2 M CF₃SO₃H, and the resulting solution was left undisturbed overnight to allow the product to precipitate. A light orange powder was isolated via vacuum filtration (yield 85%). The UV-visible spectrum of the product in aqueous solution displayed a MLCT band at 408 nm ($\epsilon = 2.9 \times 10^3 \text{ M}^{-1} \text{ cm}^{-1}$). The FTIR spectrum (KBr, SI Fig. S3) displayed ν_{CO} bands at 1898, 1952 and 2041 cm^{-1} and the ¹H-NMR spectrum (500 MHz, D₂O, SI Fig. S4) displayed δ (ppm) resonances at 8.01 (dd, 2H), 8.77 (s, 2H), 9.38 (d, 2H).

Kinetics Experiments: All solution samples of manganese carbonyls were protected from exposure to ambient light, owing to the demonstrated photolability of such complexes.^{1,12} For each kinetics experiment, quantitative solutions of *fac*-Mn(CO)₃(Br)(bpCO₂H) (or [*fac*-Mn(CO)₃(H₂O)

(bpCO₂H)(CF₃SO₃)) and H₂O₂ were prepared and each brought as nearly as possible to the desired pH via addition of NaOH solution. The amount of NaOH necessary was calculated beforehand, and the final pH of each solution was recorded. Stopped-flow experiments with added pyridine were performed approximately 45 min. after the quantitative addition of pyridine to the solution of **I**. All reactions were carried out under pseudo first-order conditions with the concentration of H₂O₂ being approximately three orders of magnitude greater than the concentration of **I**. The solutions were loaded into the stopped-flow spectrometer via syringes, and the temporal absorbance of the solutions post-mixing was monitored at a single wavelength. The symmetrical mixing operation mode was used in all experiments. In most cases, reactions were observed at 408 nm, corresponding to the λ_{max} of the metal-to-ligand charge transfer band of **I**. For the experiments performed under less basic conditions for which the reaction rate would be too slow to monitor via stopped-flow mixing, a conventional UV/Vis spectrophotometer was used. In that case, The-the prepared solutions of **I** and of H₂O₂, both at same pH, were quantitatively added to the-a quartz cuvette in a 1:1 ratio. The resulting solution was mixed -and-mixed by shaking the cuvette, which was-and immediately placed in the spectrophotometer, wheree the temporal absorbance at a single wavelength (usually 408 nm) over-time was monitored. However, Under-under this reaction set-up, formation of CO and CO₂ bubbles allowed—interfered with recording the final absorbancesmonitoring only up to the point that this interference occurs. For this reason, The data for-eachaccumulated under these conditions -of these experimental methods was thereforewere also analyzed using initial rate techniques in the manner also used in reference 1.

Data Analysis: The time-resolved absorbance data for each of the reactions studied here were analyzed using Jupyter Notebook. Using this program, the raw data from each trial were plotted and fit to the desired function. Most of the reactions were observed under conditions for which the rates were fast enough to be monitored via stopped-flow spectroscopy and displayed an exponential decay corresponding to a first-order reaction. These data were fit to the parameters of a single exponential decay using the formula $y = a \cdot e^{-kt} + c$, where y is the absorbance, t is time, k is the first-order rate constant, and a and c are constants. The exponential decay was fit in the range of $t = 0$ to $t \cong 4\tau$ (four lifetimes, approximately) for each experiment. From this fit, the first-first-order rate constant of the reaction, k , can be determined. Some experimental conditions slowed the

reaction beyond what is ideal for the stopped-flow method, and in these cases, the initial stages of the reaction were monitored until the bubble formation caused interference in the absorbance measurement. The absorbance versus time data from these trials appear somewhat parabolic in shape, initially decreasing in a linear fashion followed by an increase in absorbance due to bubble formation in the cuvette. From the slope of the initial linear region, one can determine the first-first-order rate constant for the reaction. Accordingly, the initial rate of the reaction can be determined by the relationship $\frac{\Delta c}{t} = \frac{\Delta A}{t} \frac{1}{\Delta \epsilon \cdot l}$ where $\frac{\Delta c}{t}$ is the change in concentration over time, or the rate, $\frac{\Delta A}{t}$ is the change in absorbance over time corresponding to the slope of the initial linear region, $\Delta \epsilon$ is the change in extinction coefficient over the course of the reaction, and l is the path length of the cuvette. This treatment will yield the rate of the reaction in the units of $\text{M} \cdot \text{s}^{-1}$. To obtain the first-first-order rate constant, this value is divided by the initial concentration of the manganese complex.

The proposed reaction mechanism (see below) was modeled using Wolfram Mathematica in conjunction with the experimental data according to the following procedure. The differential equations obtained from the proposed mechanism were inputted alongside the predicted rate constants according to assumptions made within the model which could be varied to achieve the best fit. The experimental data as k_{obs} versus pH as well as the initial conditions for the set of experiments were also entered. Due to limitations of the model, only the experiments performed at 25 °C with an initial hydrogen peroxide concentration of 100 mM, which make up the majority of the data set, were included. The program was then set to solve the set of differential equations using the initial conditions and predict the change in concentration over time. A subsequent exponential fit to the predicted data allowed for the determination of k_{obs} for a given pH. This procedure was then looped over the pH range of 5 to 13 in 0.01 increments to produce a model data set of k_{obs} versus pH. The experimental data were then plotted against this result, and the chi-squared value of the fit was obtained.

Results

Under neutral or alkaline conditions, **I** is moderately soluble in aqueous solutions owing to deprotonated carboxylate groups ($\text{p}K_{\text{a}} = 2.25, 2.6$).^{11b} The broad MLCT band at 408 nm is

characteristic of polypyridine complexes of Mn(I) while the strong UV bands can be attributed to π - π^* transitions of the bpCO_2^{2-} ligand. As noted previously, this spectrum is stable for hours in aerobic buffered solution at 37 °C;¹ however, it was observed that the complex is less stable when the pH is greater than ~10.0. Furthermore, the complex is unstable under pH conditions greater than ~11.8, where it apparently decomposed. For this reason, fresh solutions were made up for each set of experiments, and no kinetics data were gathered above pH 11.7.

Figure 1 illustrates the temporal spectra changes resulting from mixing solutions of **I** and H_2O_2 at pH 11 in the stopped flow spectrometer using photodiode array detection. The decreases in the MLCT band and of the π - π^* absorption between 300 and 340 nm qualitatively parallel the similar, but much slower, spectral changes observed at near neutral pH values.¹ However, as described in the Experimental Section, quantitative temporal measurements using this method were unreliable, since **I** is sufficiently photoreactive such that the more intense light source used with diode detection compromises kinetics analysis. For this reason, kinetics measurements were based on single wavelength detection, where photolysis contributions, if any, were insignificant.

Figure 2 is an example of the temporal absorbance changes using the stopped-flow spectrophotometer in the single wavelength detection mode at 408 nm. The absorbance decay at pH 11.15 can be fit to a single exponential, which is consistent with the rate being first-order in

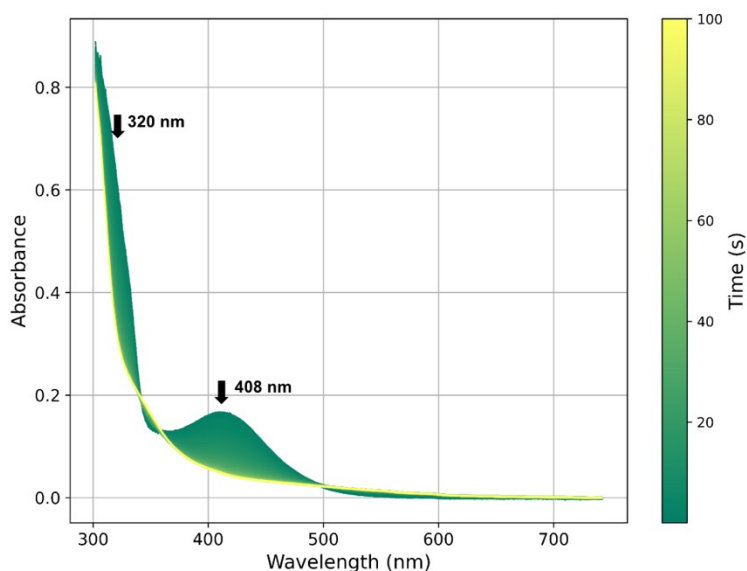


Figure 1: Spectral changes following stopped-flow mixing of solutions of **I** and H_2O_2 using diode array detection with initial concentrations of $[\text{I}] = 71.3 \mu\text{M}$ and $[\text{H}_2\text{O}_2] = 25.4 \text{ mM}$ at pH 11.02 and 25 °C.

[I]. Experiments in which only the concentration of **I** was varied did not result in any significant change in the observed rate constant k_{obs} , validating the pseudo first-order approximations. The inset of Figure 2 illustrates the linear dependence of k_{obs} on $[\text{H}_2\text{O}_2]_{\text{tot}}$, behavior consistent with the second order nature of the reaction observed at near neutral pH (eq. 2, where $k_{\text{obs}} = k'[\text{H}_2\text{O}_2]$).¹ The temperature dependence of the reaction rate was monitored at pH 11.01 with $[\text{H}_2\text{O}_2]$ held constant at 50 mM. Eyring analysis of the kinetics data over the temperature range of 25 – 40 °C gave the apparent activation parameters $\Delta H^\ddagger = 12.8 \pm 1 \text{ kcal mol}^{-1}$ and $\Delta S^\ddagger = -20 \pm 3 \text{ cal mol}^{-1} \text{ K}^{-1}$ (SI Fig. S5). (Arrhenius analysis gave $E_a = 13.4 \text{ kcal/mol}$). For comparison, the apparent activation parameters measured at pH 7.4¹ were $\Delta H^\ddagger = 22 \pm 3 \text{ kcal mol}^{-1}$ and $\Delta S^\ddagger = 7 \pm 3 \text{ cal mol}^{-1} \text{ K}^{-1}$.

As expected from the earlier analysis of the rates measured in buffered, near neutral, aqueous solutions, the kinetics measured by the stopped-flow mixing method in more strongly alkaline solution increased dramatically at higher pH. Furthermore, at pH values $> \sim 11$ the rates become independent of pH, as shown in Figure 23, display first-order dependence on $[\text{H}_2\text{O}_2]_{\text{tot}}$. Figure 3 displays this pattern as a plot of $k_{\text{obs}}/[\text{H}_2\text{O}_2]$ (i.e, k') vs. pH including data points recorded at lower pH values and reported previously.¹ However, as discussed below, the rates determined at the higher pH values proved to be much smaller than predicted by the earlier analysis. The numerical values measured over a range of different solution conditions are summarized in SI Table S1.

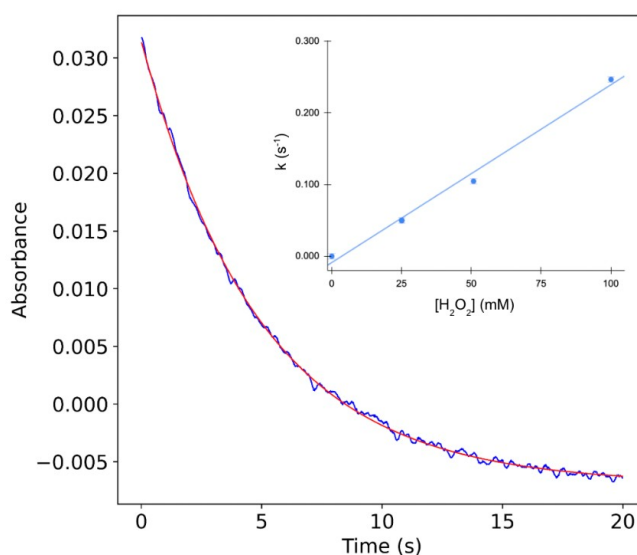


Figure 2. Temporal absorbance changes at 408 nm (in blue) for the reaction of **I** (130 μM) with H_2O_2 ($[\text{H}_2\text{O}_2]_{\text{tot}} = 99.9 \text{ mM}$) at pH = 11.10, T = 25.0 °C. The red line is the exponential fit to the experimental data ($k_{\text{obs}} = 0.202 \text{ s}^{-1}$). *Inset:* Plot of k_{obs} vs $[\text{H}_2\text{O}_2]_{\text{tot}}$ fit to the equation $k_{\text{obs}} = k'[\text{H}_2\text{O}_2]_{\text{tot}} + b$ ($k' = 2.48 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$, $b = -8.77 \times 10^{-3} \text{ s}^{-1}$).

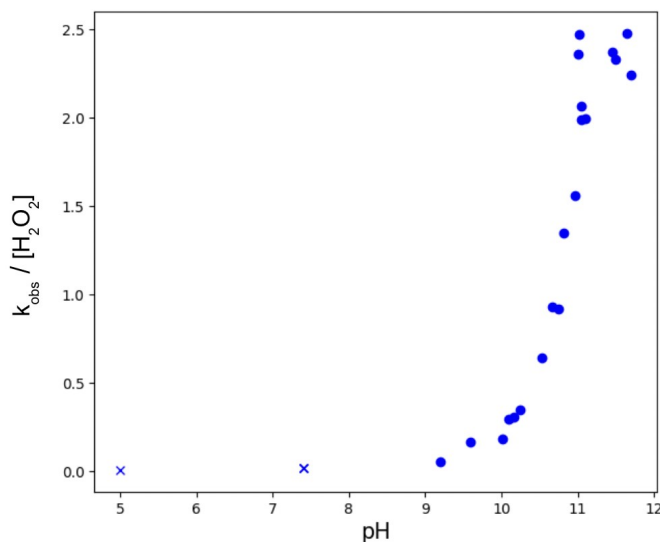


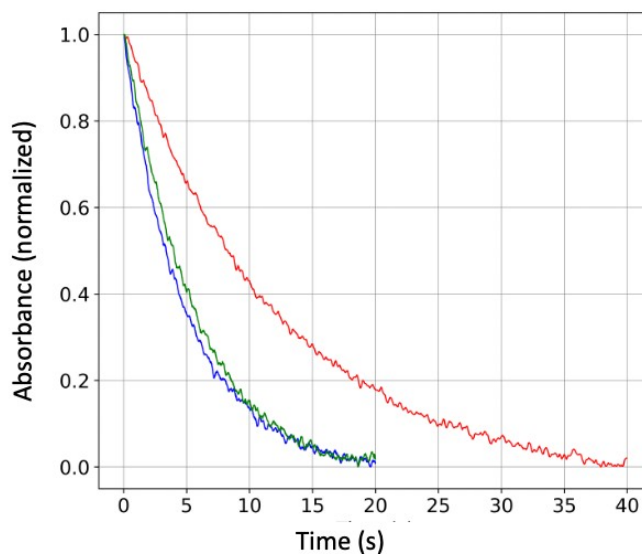
Figure 3. Plot of $k_{\text{obs}}/[\text{H}_2\text{O}_2]$ values monitored at 408 nm in 25.0 ± 0.3 °C aqueous solutions. (x's indicate data-rate constants previously reported in reference 1 obtained from Barret et. al.⁴).

Notably, when reactions initiated by stopped-flow mixing of comparable solutions were monitored by absorbance changes of the bipyridyl ligand $\pi\pi^*$ band at 320 nm, exponential decay was also observed (SI Fig. S6). However, the absorbance decay at this wavelength often did not appear to reach an asymptote and continued to decrease slowly over time after the completion of the reaction, possibly reflecting decomposition of the oxidized complex or further reaction of the ligand. The pH dependence of the rates so measured was qualitatively in agreement with that found for disappearance of the MLCT band at 408 nm under the same conditions, although there were some quantitative differences and these exponential fits (SI Table 2) are not considered to be as reliable as those at 408 nm. No clear evidence of intermediates was detected at either wavelength.

Since the substitution lability of **I** (e.g. Scheme 1) may play a major role in the reaction with H_2O_2 , the aquo complex $[\text{fac-Mn}(\text{CO})_3(\text{H}_2\text{O})(\text{bpCO}_2\text{H})](\text{CF}_3\text{SO}_3)$ was prepared by removing the bromide from $\text{fac-Mn}(\text{CO})_3(\text{Br})(\text{bpCO}_2\text{H})$ upon reaction with $\text{Ag}(\text{CF}_3\text{SO}_3)$. The visible spectrum of the aquo complex in solution, presumably as the anion $\text{fac-}[\text{Mn}(\text{CO})_3(\text{H}_2\text{O})(\text{bpCO}_2)]^-$ (**II**) (MLCT $\lambda_{\text{max}} = 409$ nm, $\epsilon = 3.0 \times 10^3 \text{ M}^{-1} \text{ cm}^{-1}$) proved to be qualitatively the same as that of **I** under comparable conditions (SI Fig. S7). This observation as well as the kinetics results described below are consistent with the claim by Walsh et al that **I** undergoes aquation of the bromide in aqueous solution.^{9a}

The reaction between **II** and H₂O₂ was studied under conditions comparable to the analogous experiments with **I**. Figure 4 illustrates the stopped-flow kinetics for reactions of **I** and of **II** with H₂O₂ at ~pH 11.1. The k_{obs} values (0.20 and 0.18 s⁻¹, see also SI Fig. S8) are effectively the same within realistic experimental uncertainties. Furthermore, the activation parameters for the latter system ($\Delta H^\ddagger = 13.2 \pm 1$ kcal mol⁻¹, $\Delta S^\ddagger = 18 \pm 3$ cal mol⁻¹K⁻¹, $E_a = 13.8 \pm 1$ kcal/mol) measured for **II** over the temperature range 24.9-39.9 °C (SI Table S3, Fig. S9) proved to be effectively the same as observed for the analogous reaction of **I**. These observations strongly suggest that Mn(I) substrate is the same in both cases, presumably as the result of the labilization of the bromide ion from **I** once the solutions have been prepared for rate measurements.

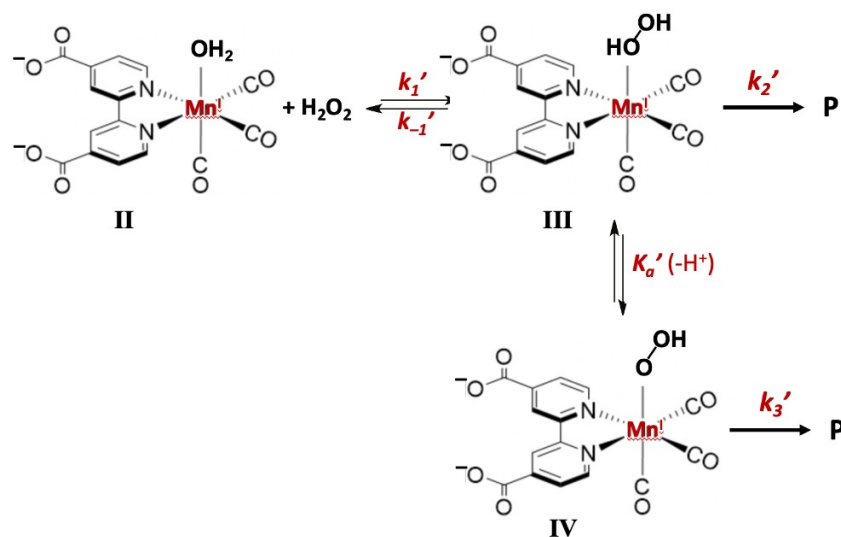
The kinetics were also studied via *in situ* experiments in which pyridine (100 mM) was added to the solution of **I** before mixing with the H₂O₂ solution ([H₂O₂]_{tot} = 100 mM). The key observation is that the resulting rate ($k_{\text{obs}} = 0.081$ s⁻¹) was significantly slower (Fig. 4). Increasing [py] to 200 mM suppressed k_{obs} further to 0.057 s⁻¹ (SI Table S2). This result parallels experiments at lower pH where addition of pyridine led to considerable suppression of the rate of the redox reaction presumably by competing with H₂O₂ for coordination at the manganese center.¹ Solutions to which py had been added displayed a modest blue shift in the MLCT absorption band consistent with competitive coordination of py at the labile site.



Discussion:

$$k_{\text{obs}} = k' [\text{H}_2\text{O}_2]_{\text{tot}} = k_1 \quad (6)$$

A second point is that the reactivities of **I** and **II** were shown to be nearly identical, at least under the high pH conditions studied. Furthermore, the addition of py significantly suppressed the reaction rate. Thus, we conclude that, in the absence of py coordination, complex **II** is the likely reactive manganese carbonyl species regardless of the initial Mn(I) substrate under the conditions studied here. This conclusion leads one to consider the mechanism described by Scheme 3 where, the key initial first step is substitution of H₂O₂ into the Mn^I coordination sphere. In this mechanism the pK_a of the H₂O₂ ligand would play a key role in the overall kinetics; however, one can readily accept that it should be moderately more acidic than solution phase -free hydrogen peroxide. Based on this model the reaction rate should respond to the solution variables according to Eq. 7, where [Mn^I] represents all manganese(I) species and K₁' equals k₁'/k₋₁' (see SI Scheme S1 for derivation).



Scheme 3: Proposed mechanism for the oxidation of **II** by H₂O₂ in alkaline aqueous solutions. The products P are presumed to be those observed previously found at lower pH (eq. 1).¹

$$\frac{-d[\text{Mn}^{\text{I}}]}{dt} = \frac{(k_2' + k_3' K_a' [\text{H}^+]^{-1}) K_1' [\text{H}_2\text{O}_2]}{1 + K_1' [\text{H}_2\text{O}_2] (1 + K_a' [\text{H}^+]^{-1})} [\text{Mn}^{\text{I}}] = k_{\text{obs}} [\text{Mn}^{\text{I}}] \quad (7)$$

However, closer examination of equation 7 suggests that at sufficiently high pH, the reaction rate should be independent of both pH and [H₂O₂] (see SI Scheme S2 for a more detailed analysis). While the former is apparently true, the latter is not (Fig. 2). The explanation may lie in the assumption that species **III** is in rapid equilibrium with **II**, depending on the peroxide concentration, and that the redox steps of Scheme 3 indicated by the constants k₂' and k₃' are rate

limiting. However, at sufficiently high pH, the depletion of **III** via rapid deprotonation to **IV** and subsequent reaction may be faster than formation of **III** via substitution of H_2O_2 for the coordinated H_2O of **II**. Under such conditions, the reaction rate would simplify to $k_1'[\text{II}][\text{H}_2\text{O}_2]$, therefore, would be first-order in $[\text{H}_2\text{O}_2]$ but independent of pH. Figure 5 is an attempt to fit the experimental data reported in Figure 3 to this model with the pH dependence defined by the $\text{p}K_a$ of the coordinated hydrogen peroxide of complex **III** but with the limiting rate at higher pH defined by the rate limiting formation of **III** from **II** ($k_1' = 2.5 \text{ M}^{-1}\text{s}^{-1}$). SI Scheme S2 discusses this analysis in greater detail.

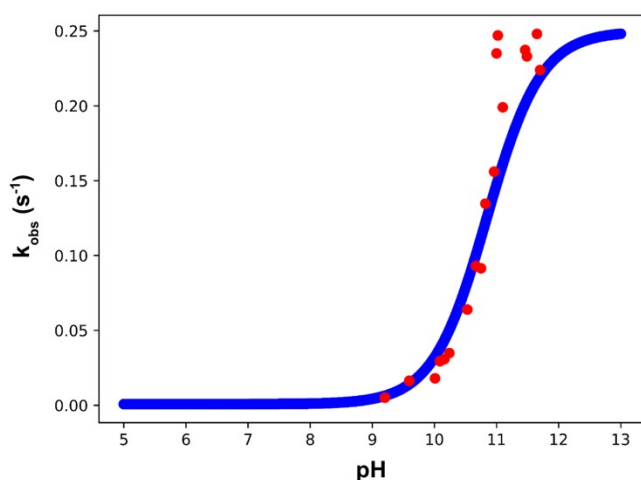


Figure 5. The blue curve represents the calculated k_{obs} as a function of pH at 25 °C and $[\text{H}_2\text{O}_2] = 100 \text{ mM}$ according to the differential equation model based on the proposed kinetic scheme. The red dots are the experimental values of k_{obs} determined by kinetics studies under these conditions. The curve was based on the following parameters: $k_1' = 2.5 \text{ M}^{-1}\text{s}^{-1}$, $k_{-1} = 139 \text{ s}^{-1}$, $k_2' = 0.44 \text{ s}^{-1}$, $K_a' = 10^{-11} \text{ M}$, $k_3 = 200 \text{ s}^{-1}$ ($\chi^2 = 0.0235$). See SI Scheme S2 for an explanation of these choices.

The **first-key** point of discussion regarding this model is that the numbers used for the fit shown in Figure 5 are not **unique** solutions. As described in SI Scheme S2, the values of k_{-1}' and k_2' are directly dependent on the estimated value of K_1' , i.e. k_1'/k_{-1}' . While the kinetics data clearly point to K_1' having a value $\ll 1 \text{ M}^{-1}$, there appear to be few precedents in the literature establishing the coordinating strength of H_2O_2 relative to H_2O , although it is concluded that such bonding is weak.¹³ The K_1' estimate of 0.018 M^{-1} in SI Scheme S2 was based on the assumption that H_2O_2 would have approximately equal affinity for the Mn(I) center as H_2O , thus the much greater concentration of the latter in aqueous solution gives it a statistical advantage. (This estimate is supported by DFT computation indicating the energy change in replacing the H_2O of **II** with H_2O_2

to form **III** to be very small, but slightly endoergic. See SI Scheme S3.) In addition, the magnitude of k_3' depends on the estimated values both of K_1' and of K_a' (10^{-11} M), although the K_a' can be reliably estimated given the shape of the data presented in Figure 3 (as well as poorer fits when this was changed to a higher or lower value). Other pH dependent issues, not addressed in this model, would be the possible role of the free-hydroperoxide ion and potential dissociation of a proton from the coordinated H_2O of compound **II**. It is likely that the latter would inhibit the reaction since the hydroxy form of **II** should be less susceptible to ligand exchange than the aqua form. With regard to the hydroperoxide ion, this species was viewed as the likely contributor to the pH dependent pathways in the earlier study¹ given the suggestion that it might attack coordinated carbonyls as illustrated in Scheme 2. However, that model can apparently be dispelled by the very poor fits to the kinetics data reported here (SI Fig. S10).

According to the model in Scheme 3, the activation enthalpy measured at pH 11 (13.2 kcal mol⁻¹) represents the $\Delta H^\ddagger$ for the rate limiting k_1' at this pH (SI Scheme S2). While this is significantly lower than $\Delta H^\ddagger$ (apparent) for the kinetics measured at pH 7.4 (22 kcal mol⁻¹), the latter has a major component from the limiting low pH rate behavior. According to the model described by Scheme 3, the contribution from the pH independent component to k_{obs} would equal $K_1'k_2'[\text{H}_2\text{O}_2]$ with a $\Delta H^\ddagger$ being the sum of ΔH° for K_1' plus the $\Delta H^\ddagger$ for k_2' .

In summary, the stopped-flow kinetics studies reported here confirm the strong pH dependence of the oxidative decomposition of compound **I** in aqueous media reported previously.¹ However, in this case, the evidence points towards an inner sphere mechanism where the predominant pathway involves initial coordination of H_2O_2 to the Mn(I) center. The marked pH dependence is thus attributed to the dissociation of a proton to give the corresponding hydroperoxide complex, which undergoes oxidative decomposition and CO release.

Associated Contents

Supporting Information: ten figures, three tables summarizing rate constants measured at different pH values and temperatures, two schemes delineating rate law derivation for the proposed mechanism and estimated key rate constants. This material is available free of charge on the ACS Publications website.

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Conflict of interest statement:

The authors have no conflict of interest to declare.

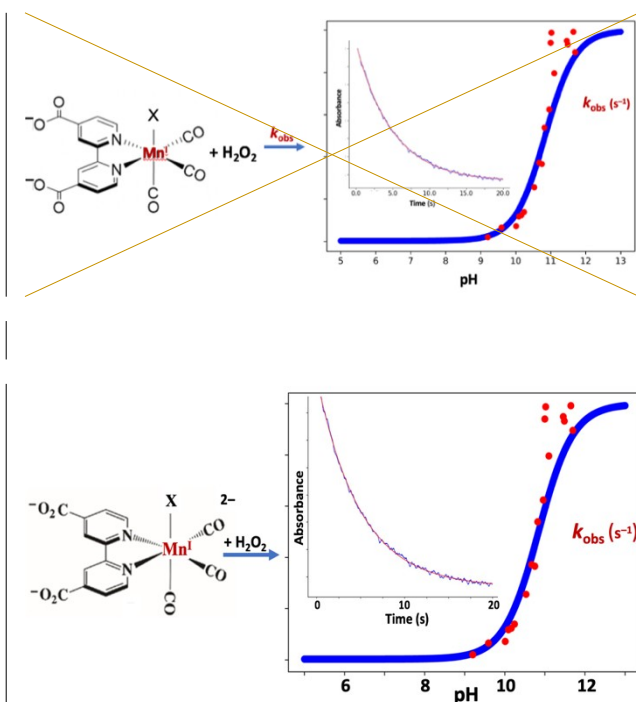
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For Table of Contents Illustration Only:



Supporting Information

Hydrogen Peroxide Mediated Oxidation of Manganese Carbonyls in Aqueous Solution

Claudia Robison, Madalyn Phan, Leroy Laverman, Peter C. Ford

Figures:

Figure S1. Solid-state FTIR spectrum of Mn(CO)₃(Br)(bpCO₂H) in KBr.

Figure S2. 500 MHz ¹H-NMR spectrum of [Mn(CO)₃(Br)(bpCO₂)]²⁻ (**I**) in D₂O.

Figure S3. Solid-state FTIR spectrum of solid [Mn(CO)₃(H₂O)(bpCO₂H)](CF₃SO₃) in KBr.

Figure S4. 500 MHz ¹H-NMR spectrum of Mn(CO)₃(H₂O)(bpCO₂)⁻ (**II**) in D₂O.

Figure S5. Eyring plot for k_{obs} values for reaction of **I** with H₂O₂ at pH 11.0.

Figure S6. Temporal absorbance changes at 320 nm for reaction of **I** with H₂O₂ at pH 11.08.

Figure S7. Optical spectra in aqueous solution of **I** & **II** and of **I** with excess py.

Figure S8. Temporal absorbance changes at 408 nm for reaction of **II** with H₂O₂ at pH 11.15.

Figure S9. Eyring plot of k_{obs} values for the reaction of **II** with H₂O₂ at pH 11.15.

Figure S10. Comparison of experimental values $k_{obs}/[H_2O_2]$ to values predicted by Schemes 1 & 2.¹

Tables:

Table S1. Kinetics data for the reaction of **I** with H₂O₂ as monitored at 408 nm.

Table S2. Comparison of k_{obs} values from exponential fits at 408 or 320 nm for reaction of **I** with H₂O₂

Table S3. Temperature effects on the reaction of **II** with H₂O₂ in aqueous solution.

Schemes:

Scheme S1. Rate law implied by manuscript Scheme 3.

Scheme S2. Analysis of kinetics predicted by manuscript Scheme 3 and eq. 7.

Scheme S3. DFT analysis of the equilibrium between complexes II and III.

References

FIGURES

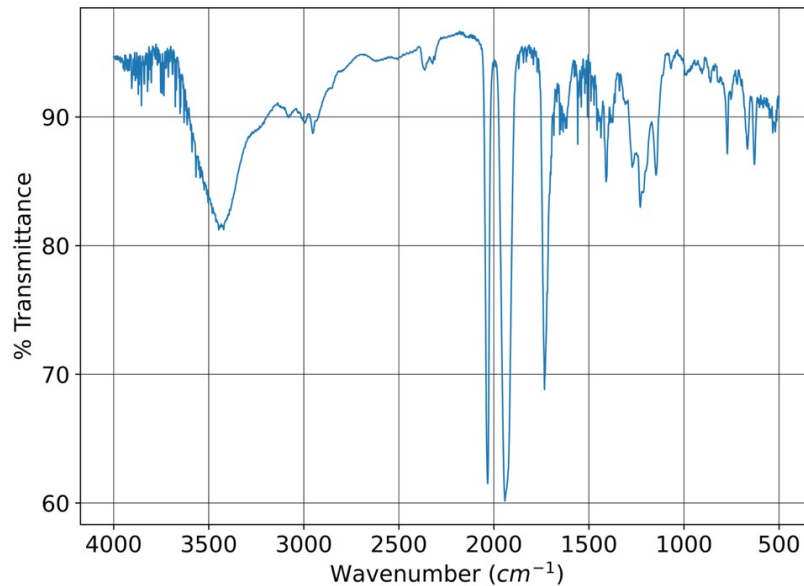


Figure S1. Solid-state FTIR spectrum of $\text{Mn}(\text{CO})_3(\text{Br})(\text{bpCO}_2\text{H})$ taken in KBr.

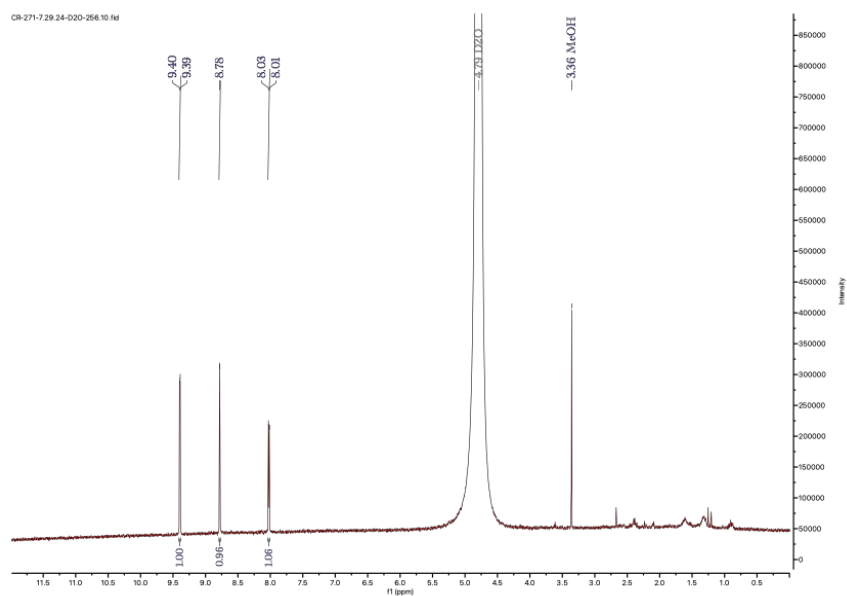


Figure S2. 500 MHz ^1H -NMR spectrum of $[\text{Mn}(\text{CO})_3(\text{Br})(\text{bpCO}_2)]^{2-}$ (**I**) in D_2O . 8.01 (dd, 2H), 8.78 (s, 2H), 9.39 (d, 2H). Solvent peak at 4.79 ppm. (Note: There is a methanol impurity at 3.36 ppm. This solvent was used during the synthetic procedure.)

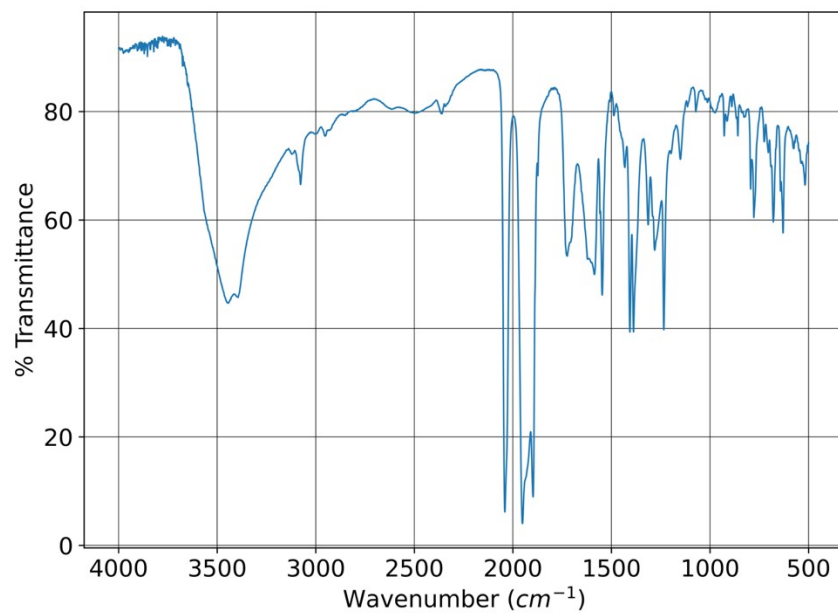


Figure S3. FTIR spectrum of solid $[\text{Mn}(\text{CO})_3(\text{H}_2\text{O})(\text{bpCO}_2\text{H})](\text{CF}_3\text{SO}_3)$ in KBr.

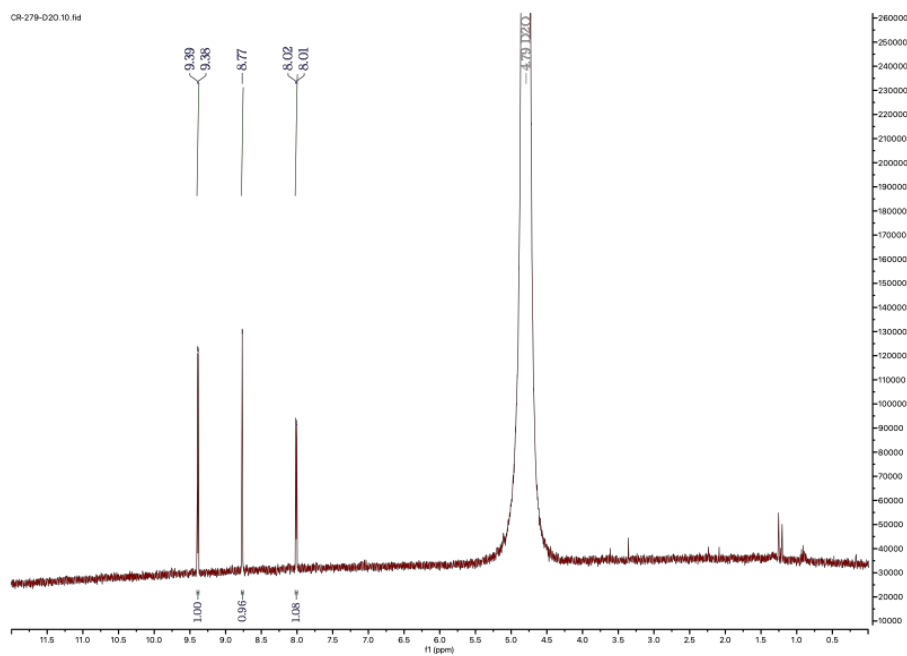


Figure S4. 500 MHz ^1H -NMR spectrum of $\text{Mn}(\text{CO})_3(\text{H}_2\text{O})(\text{bpCO}_2)^-$ (**II**) in D_2O . δ (ppm): 8.01 (dd, 2H), 8.77 (s, 2H), 9.38 (d, 2H). Solvent peak at 4.79 ppm.

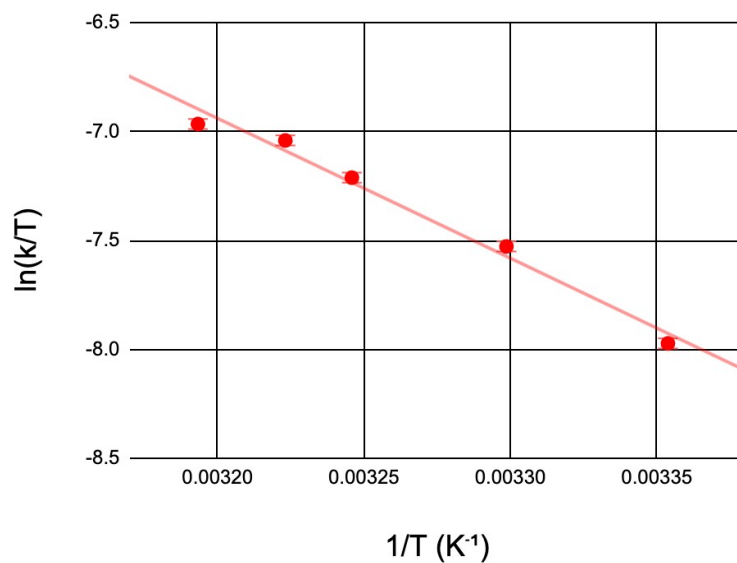


Figure S5. Eyring plot for k_{obs} values determined over the temperature range 298-313 K for the reaction of **I** (avg. conc. 258 μ M) with H_2O_2 (ave. conc. 50 mM) at pH 11.01(ave). Reaction was observed at 408 nm. $\Delta H^\ddagger = 12.8 \pm 1$ kcal/mol, $\Delta S^\ddagger = -20 \pm 3$ kcal/mol*K.

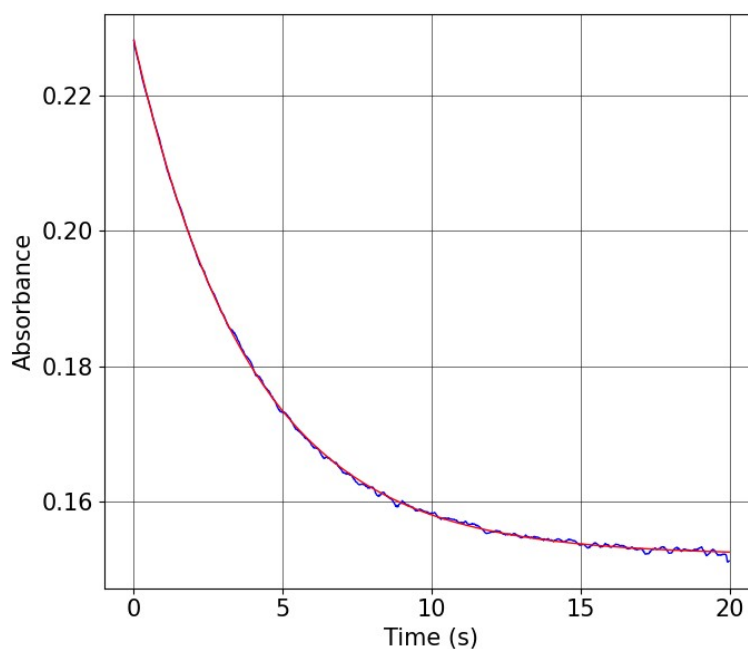


Figure S6. Temporal absorbance change at 320 nm for the reaction of **I** (130 μ M) with H_2O_2 (99.9 μ M) (pH 11.10, 25.0 $^\circ\text{C}$, $k_{obs} = 0.256$ s⁻¹; blue=data, red=fit).

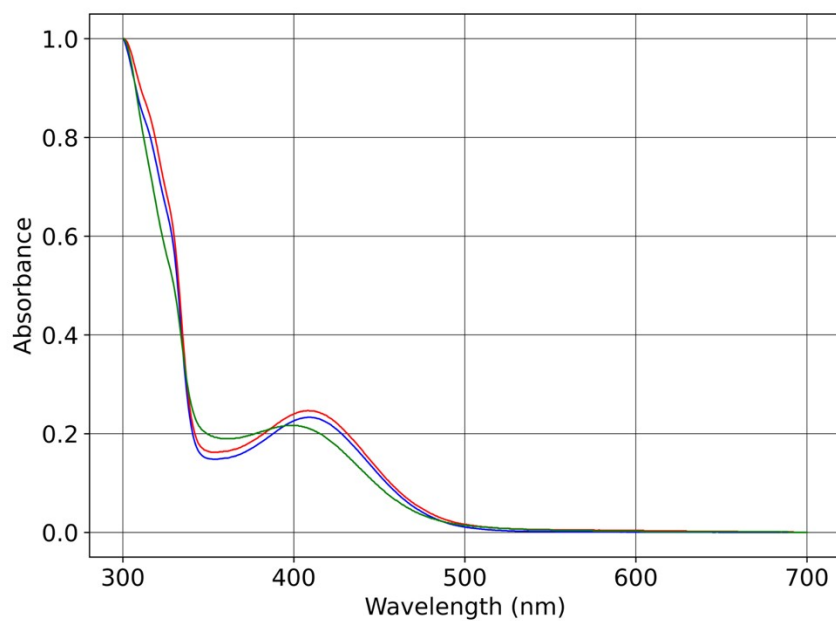


Figure S7. Optical spectra in aqueous solution of $\text{Mn}(\text{CO})_3(\text{Br})\text{bp}(\text{COOH})_2$ (blue, $\epsilon_{\text{max}} = 3.1 \times 10^3 \text{ M}^{-1}\text{cm}^{-1}$ at 408 nm), $\text{Mn}(\text{CO})_3(\text{H}_2\text{O})\text{bp}(\text{COOH})_2$ (red, $\epsilon_{\text{max}} = 2.9 \times 10^3 \text{ M}^{-1}\text{cm}^{-1}$ at 408 nm), and a solution of $\text{Mn}(\text{CO})_3(\text{Br})\text{bp}(\text{COOH})_2$ and excess pyridine (green, $\epsilon_{\text{max}} = 3.2 \times 10^3 \text{ M}^{-1}\text{cm}^{-1}$ at 399 nm).

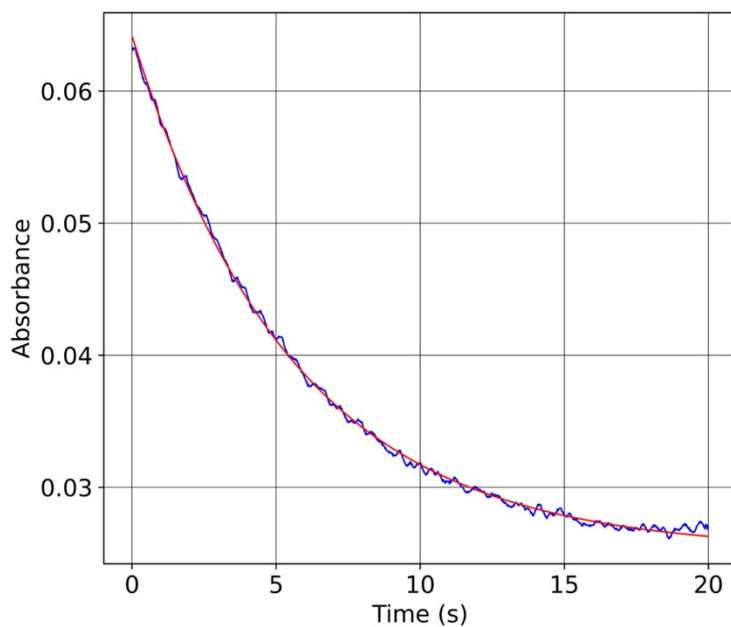


Figure S8. Temporal absorbance changes at 408 nm (blue) for the reaction of **II** (125 μM) with H_2O_2 (100 mM) at pH 11.15 & 24.9 $^\circ\text{C}$. ($k_{obs} = 0.180 \text{ s}^{-1}$, red=fit)

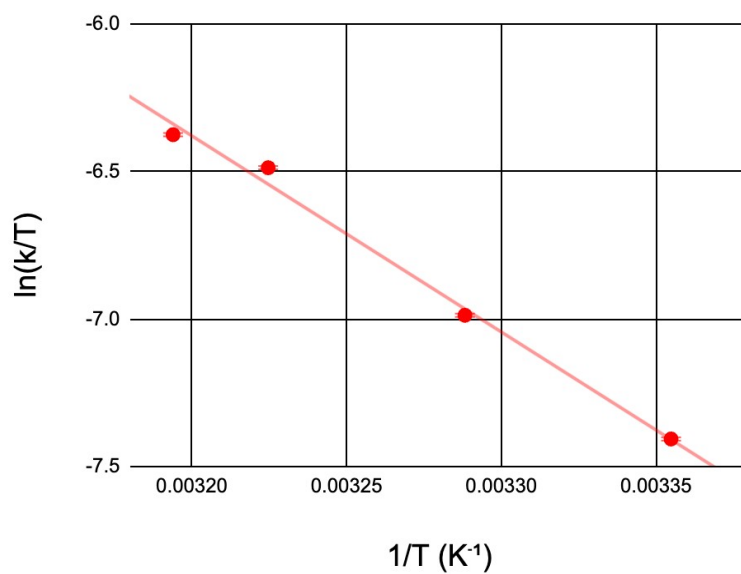


Figure S9. Eyring plot of k_{obs} values determined over the temperature range 298-313 K for the reaction of **II** (125 μ M) with H_2O_2 (100 mM) at pH 11.15. Reaction was observed at 408 nm. $\Delta H^\ddagger = 13.2 \pm 1$ kcal/mol, $\Delta S^\ddagger = -18 \pm 3$ kcal/mol*K.

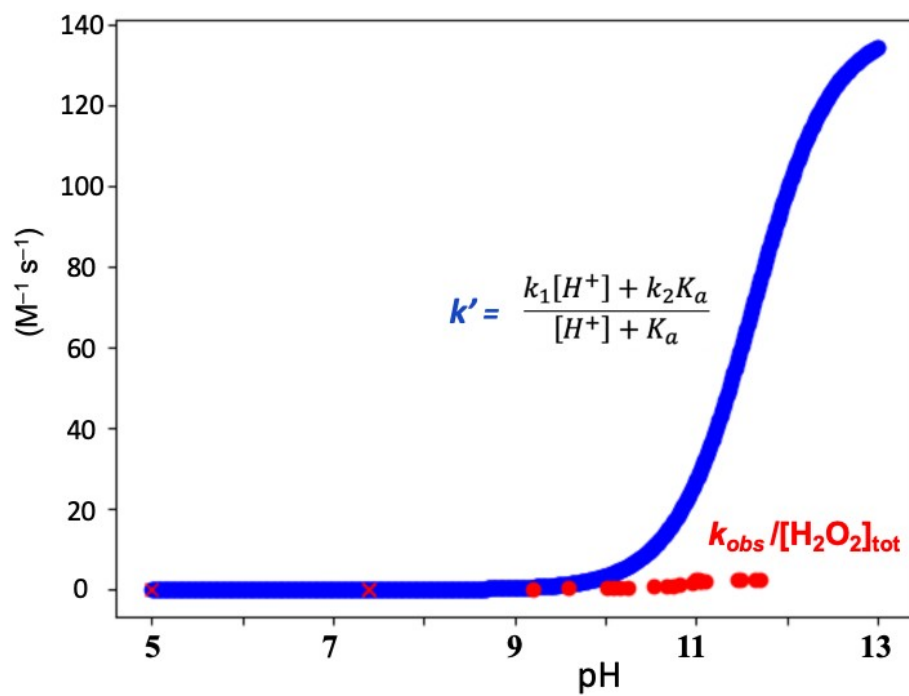


Figure S10. Predicted pH behavior of the second order rate constant k' (**blue**) at 25 °C calculated from eq. 6 using values of $k_1 = 0.010 \text{ M}^{-1} \text{ s}^{-1}$ and $k_2 = 140 \text{ M}^{-1} \text{ s}^{-1}$ drawn from ref. 1 and $K_a = 2.4 \times 10^{-12} \text{ M}$. The experimental values $k_{obs}/[\text{H}_2\text{O}_2]$ are shown in **red**.

TABLES

Table S1. Kinetics data for the reaction of **I** with H₂O₂ as monitored at 408 nm. Reported concentrations are after stopped-flow mixing. pH values are averages of the reactant solutions.

pH	T (°C)	[I] (μM)	[H ₂ O ₂] (mM)	k_{obs} (s ⁻¹)	Standard deviation	k_{obs}/H_2O_2 (M ⁻¹ s ⁻¹)	# trials averaged
9.20	24.9	128	100.	0.00506	0.0003	0.0506 ± 0.003	7*
9.59	25.1	248	100.	0.0164	0.004	0.164 ± 0.04	14*
10.01	25.2	125	100.	0.0180	0.0002	0.180 ± 0.002	5*
10.09	25.0	125	100.	0.0295	0.0005	0.295 ± 0.005	6
10.11	25.3	251	100.	0.139 [‡]	0.005	1.39 [‡] ± 0.05	6
10.16	25.3	124	100.	0.0308	0.0005	0.308 ± 0.005	6
10.24	24.8	296	101	0.0349	0.001	0.345 ± 0.01	5
10.53	25.0	125	100.	0.0639	0.0003	0.639 ± 0.003	4
10.67	24.9	125	100.	0.0930	0.003	0.930 ± 0.03	6
10.75	24.9	124	100.	0.0915	0.001	0.915 ± 0.01	6
10.82	24.8	128	100.	0.135	0.002	1.35 ± 0.02	4
10.96	24.9	125	100.	0.156	0.003	1.56 ± 0.03	4
11.00	24.2	121	99.7	0.235	0.01	2.36 ± 0.1	9
11.02	24.7	242	100.	0.247	0.008	2.47 ± 0.08	9
11.04	25.2	259	25.1	0.0499	0.0006	1.99 ± 0.02	6
11.05	25.0	264	50.8	0.105	0.003	2.07 ± 0.06	6
11.10	25.0	130	99.9	0.199	0.003	1.99 ± 0.03	7
11.46	24.9	123	100.	0.237	0.006	2.37 ± 0.06	6
11.49	25.0	125	100.	0.233	0.004	2.33 ± 0.04	6
11.65	25.6	246	100.	0.248	0.009	2.48 ± 0.09	7
11.70	25.1	124	99.8	0.224	0.004	2.24 ± 0.04	6
11.07	30.0	261	50.1	0.163	0.005	3.26 ± 0.10	6
10.97	34.9	253	50.2	0.227	0.004	4.53 ± 0.08	7
11.01	37.0	253	100	0.557	0.007	5.57 ± 0.07	5
10.98	37.1	257	50.0	0.272	0.003	5.43 ± 0.06	7
10.98	40.0	257	50.0	0.296	0.004	5.91 ± 0.08	6
11.11 ^a	25.1	127	H ₂ O ₂ : 99.9 py: 100 mM	0.0806	0.001	0.807 ± 0.01	9
11.11 ^a	25.0	126	H ₂ O ₂ : 100 py: 200 mM	0.0571	0.0004	0.571 ± 0.004	6
7.4 ^b	25.5	75	Various			0.017 ± 0.004	12*
5.0 ^b	25.0	80	32.0	0.000245		0.008	2*

*Rate constants obtained by initial rates method.

[‡]After multiple experiments at a similar pH, this data point was concluded to be an outlier and was not included in the data fitting.

^a reactions carried out with added pyridine.

^b reference 1.

Table S2. Comparison of k_{obs} values determined by exponential fits to absorbance decay at 408 nm (black) or 320 nm (blue) or by the initial rates method (red).

pH	T (°C)	[Mn] (mM)	[H ₂ O ₂] _{tot} (mM)	k_{obs} (s ⁻¹) (#runs) ^a
11.70	25.1	124	99.8	0.224±0.004 (6) ^b
				0.215±0.002 (6) ^c
11.49	25.0	125	100	0.233±0.003 (6) ^b
				0.279±0.004 (6) ^c
11.46	24.9	123	100	0.237±0.006 (6) ^b
				0.295±0.012 (6) ^c
11.10	25.0	130	100	0.199±0.003 (7) ^b
				0.257±0.007 (6) ^c
10.96	24.9	125	100	0.156±0.003 (4) ^b
				0.193±0.004 (4) ^c
10.82	24.9	126	100	0.135±0.002 (4) ^b
				0.126±0.005 (4) ^c
10.75	25.0	124	100	0.092±0.001 (6) ^b
				0.091±0.002 (6) ^c
10.67	25.0	125	100	0.093±0.002 (6) ^b
				0.099±0.002 (6) ^c
10.53	25.0	125	100	0.064±0.003 (4) ^b
				0.054±0.001 (4) ^c
10.22	25.0	128	100	0.030±0.001 (4) ^b
				0.032±0.001 (8) ^d
10.16	25.3	124	100	0.031±0.001 (6) ^b
				0.028±0.001 (8) ^d
10.16	25.1	124	100	0.028±0.001 (6) ^c
10.09	25.0	125	100	0.029±0.001 (6) ^b
				0.027±0.001 (8) ^d
				0.026±0.001 (6) ^c

^a Average value for a sequence of stopped flow runs under identical conditions. Number of runs in parentheses

^b Rate constants determined from fits to the exponential decay of the MLCT absorbance of **I** at 408 nm.

^c Rate constants determined from exponential fits to the absorbance changes at 320 nm

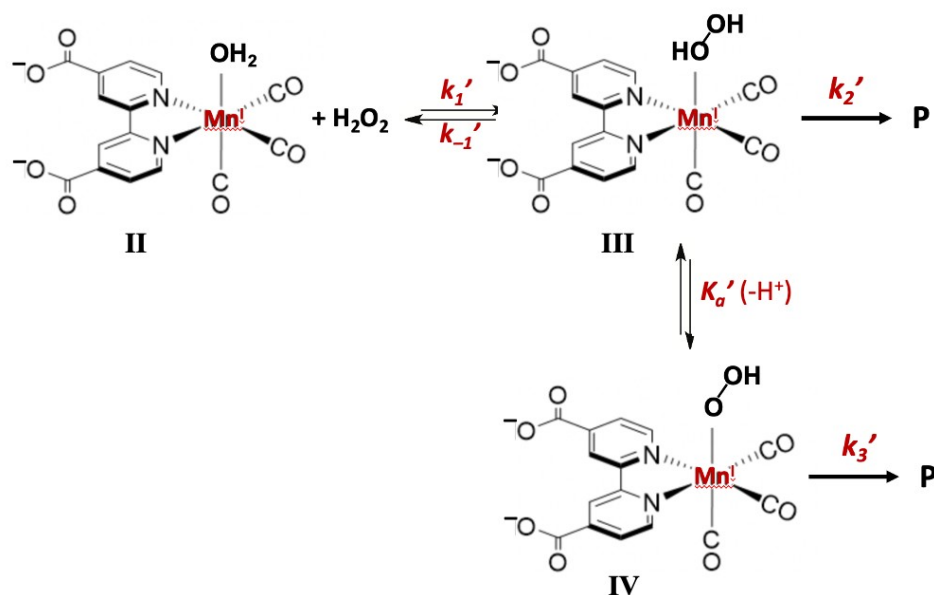
^d First order rate constants determined by dividing the initial rate by [Mn]_{initial}.

Table S3. Temperature effects on the reaction of **II** with H₂O₂ in aqueous solution.

pH	T (°C)	[I] (μM)	[H ₂ O ₂] (mM)	k_{obs} (s ⁻¹)	Standard deviation	k_{obs}/H_2O_2 (M ⁻¹ s ⁻¹)	# trials averaged
10.22	25.0	128	100.	0.0297	0.0008	0.297±0.008	4
11.15	24.9	125	100.	0.181	0.002	1.81 ± 0.02	4
11.15	31.0	125	100.	0.281	0.007	2.81 ± 0.07	8
11.15	37.0	125	100.	0.472	0.009	4.72 ± 0.09	7
11.15	39.9	125	100.	0.534	0.005	5.34 ± 0.05	5

SCHEMES

Scheme S1. Kinetics analysis of manuscript Scheme 3.



$$d[\text{P}]/dt = -d[\text{Mn}^{\text{I}}]/dt$$

Assuming fast equilibria

$$d[\text{P}]/dt = k_2'[\text{III}] + k_3'[\text{IV}] = (k_2' + k_3'K_a'[\text{H}^+]^{-1})[\text{III}] \quad (1\text{-i})$$

if

$$[\text{III}] = K_1'[\text{II}][\text{H}_2\text{O}_2], \text{ where } K_1' = k_1'/k_{-1}' \quad (1\text{-ii})$$

then

$$d[\text{P}]/dt = (k_2' + k_3'K_a'[\text{H}^+]^{-1})K_1'[\text{II}][\text{H}_2\text{O}_2] \quad (1\text{-iii})$$

Exponential decay of absorbance at 408 nm implies kinetics are first order in $[\text{Mn}^{\text{I}}]$

$$\text{Where } [\text{Mn}^{\text{I}}] = [\text{II}] + [\text{III}] + [\text{IV}] \quad (1\text{-iv})$$

$$= [\text{II}] + K_1' [\text{H}_2\text{O}_2] [\text{III}] + K_1' [\text{H}_2\text{O}_2] K_a' [\text{H}^+]^{-1} [\text{IV}] \quad (1\text{-v})$$

$$= (1 + K_1' [\text{H}_2\text{O}_2] (1 + K_a' [\text{H}^+]^{-1})) [\text{II}] \quad (1\text{-vi})$$

$$[\text{II}] = [\text{Mn}^{\text{I}}] / (1 + K_1' [\text{H}_2\text{O}_2] (1 + K_a' [\text{H}^+]^{-1})) \quad (1\text{-vii})$$

These relationships give eq. 7

$$-d[\text{Mn}^{\text{I}}]/dt = \frac{(k_2' + k_3' K_a' [\text{H}^+]^{-1}) K_1' [\text{H}_2\text{O}_2]}{1 + K_1' [\text{H}_2\text{O}_2] (1 + K_a' [\text{H}^+]^{-1})} [\text{Mn}^{\text{I}}] = k_{obs} [\text{Mn}^{\text{I}}]$$

Scheme S2: Analysis of kinetics predicted by manuscript Scheme 3 and eq. 7.

$$k_{obs} = \frac{(k_2' + k_3' K_a' [\text{H}^+]^{-1}) K_1' [\text{H}_2\text{O}_2]}{1 + K_1' [\text{H}_2\text{O}_2] (1 + K_a' [\text{H}^+]^{-1})} \quad (2\text{-i})$$

At low pH, $[\text{H}^+] \gg K_a'$, and reaction is first order in $[\text{H}_2\text{O}_2]$, thus $1 \gg K_1' [\text{H}_2\text{O}_2]$

$$\text{giving } k_{obs} = (k_2' + k_3' K_a' [\text{H}^+]^{-1}) K_1' [\text{H}_2\text{O}_2] \quad (2\text{-ii})$$

and at very low pH,

$$k_{obs} = k_2' K_1' [\text{H}_2\text{O}_2] \quad (2\text{-iii})$$

At very high pH, $[\text{H}^+] \ll K_a'$, thus eq. 2-i can be rewritten as

$$k_{obs} = \frac{k_3' K_a' K_1' [\text{H}_2\text{O}_2]}{[\text{H}^+] + K_a' K_1' [\text{H}_2\text{O}_2]} \quad (2\text{-iv})$$

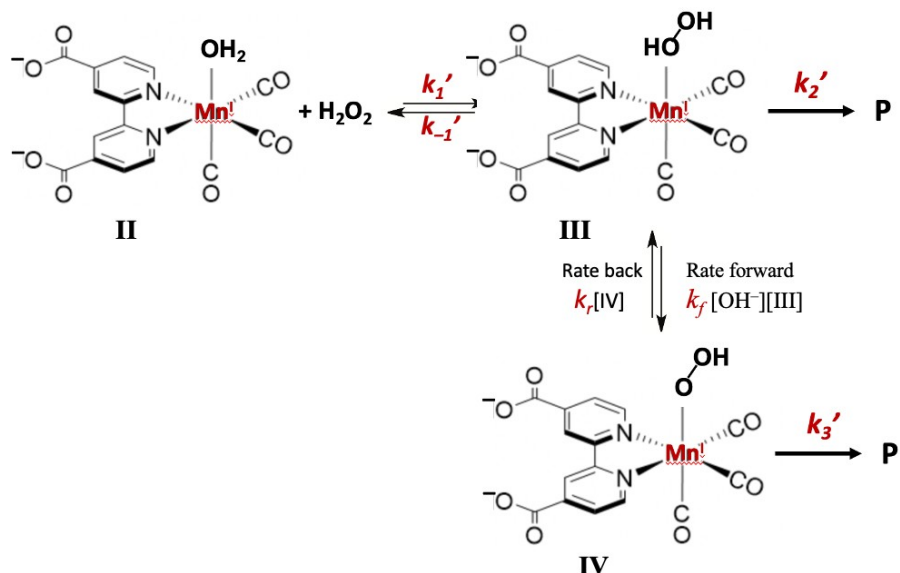
Thus, according to this model, at sufficiently high pH,

$$k_{obs} = k_3'$$

and should be independent both of $[\text{H}^+]$ and $[\text{H}_2\text{O}_2]$

However, while k_{obs} becomes pH independent, it is not independent of $[\text{H}_2\text{O}_2]$ at high pH. Thus, this mechanism can be revised by lifting the assumptions that the steps between **II** and **III** and between **III** and **IV** are equilibria rapidly established relative to the redox steps indicated by rate constants k_2' and k_3' . While these assumptions may be valid at low pH where the reaction is

quite slow, that may not be the case at higher pH. Instead, the kinetics may be simulated by differential equations treating the forward and back rates as shown in the following model:



Scheme S2: continued

Limiting high pH

The pH independent but $[H_2O_2]$ dependent behavior of k_{obs} at high pH can then be interpreted in terms of this scheme if the $II \rightarrow III$ step becomes rate limiting with

$$k_{obs} = \sim k_1' [H_2O_2].$$

Thus, according to the data shown in manuscript Fig. 3, k_1' would equal $2.5 \pm 0.1 \text{ M}^{-1}\text{s}^{-1}$

For further analysis, it is important to note that, at high pH, **IV** is formed by the hydroxide promoted deprotonation of **III**, the forward rate being $k_f[OH^-][III]$. In this context, the following analysis applies:

$$k_f/k_r = K_{OH} = [IV]/([III][OH^-]) = K_a' K_w^{-1}$$

The rate of the deprotonation of a weak acid by hydroxide ion in aqueous solution generally approaches diffusion limits,² so we estimate k_f as follows:

$$k_f(\text{est}) = 10^{10} \text{ M}^{-1}\text{s}^{-1}$$

This leads to

$$k_r(\text{est}) = k_f(\text{est}) K_w (K_a')^{-1} = (10^{-4} \text{ s}^{-1} \text{ M})(K_a')^{-1}$$

So $k_r(\text{est})$ can be derived from the value of K_a' implied by the inflection of the rate data illustrated in Figure 3; for example, if $K_a' = 10^{-11} \text{ M}$,

$$k_r(\text{est}) \text{ would be } 10^7 \text{ s}^{-1}.$$

Limiting low pH

At very low pH, where deprotonation of **III** is too slow to affect the overall rate,

$$k_{obs}/[\text{H}_2\text{O}_2] = (k_2' + k_3' K_a' [\text{H}^+]^{-1}) K_I' = \sim k_2' K_I'$$

The reported value of $k_{obs}/[\text{H}_2\text{O}_2]$ at pH 5 and 25 C is $0.008 \text{ M}^{-1}\text{s}^{-1}$ (Table S1)

The question is whether one can estimate the value of K_I' ? There is surprisingly little quantitative data regarding the binding constants for H_2O_2 coordination of metal complexes in aqueous solution although it is considered a very weak ligand if not stabilized by hydrogen bonding in the second coordination sphere.³ Furthermore, it was noted above that at all H_2O_2 concentrations studied $K_I' \ll 1 \text{ M}^{-1}$. In this context, we will estimate that H_2O_2 and H_2O would have similar affinities for the Mn(I) center (see also Scheme S3), and that would statistically give an estimated

$$K_I'(\text{est}) = 0.018 \text{ M}^{-1}$$

from which the value

$$k_2'(\text{est}) = 0.44 \text{ s}^{-1}$$

would be derived.

Scheme S2: continued

Furthermore, the K_I' estimate of 0.018 M^{-1} and the k_I' value noted above ($2.5 \text{ M}^{-1}\text{s}^{-1}$) gives

$$k_{-I}'(\text{est}) = k_I' / K_I' = 139 \text{ s}^{-1}$$

Intermediate but low pH

With the above estimates one can extrapolate further to discern working estimates for the other parameters in this model by examining the k_{obs} values measured at pH values, where raising the pH begins to have a significant affect on the reaction rate.

$$\text{At pH 9.2, } k_{obs}/[\text{H}_2\text{O}_2] = 0.051 \text{ M}^{-1} \text{ s}^{-1} = 0.008 \text{ M}^{-1} \text{ s}^{-1} + K_I' K_a' k_3' [\text{H}^+]^{-1}$$

$$\text{Then, } K_I' K_a' k_3' [\text{H}^+]^{-1} = 0.043 \text{ M}^{-1} \text{ s}^{-1}, K_a' k_3' = [\text{H}^+] (0.043 \text{ M}^{-1} \text{ s}^{-1} / K_I') = 1.36 \times 10^{-9} \text{ M s}^{-1}$$

$$\text{If } K_a' = 10^{-11} \text{ then } k_3' = \sim 1.4 \times 10^2 \text{ s}^{-1}$$

At pH 9.59, $k_{obs}/[\text{H}_2\text{O}_2] = 0.164 \text{ M}^{-1} \text{ s}^{-1} = 0.008 \text{ M}^{-1} \text{ s}^{-1} + K_I' K_a' k_3' [\text{H}^+]^{-1}$

Then, $K_I' K_a' k_3' [\text{H}^+]^{-1} = 0.156 \text{ M}^{-1} \text{ s}^{-1}$, $K_a' k_3' = [\text{H}^+] (0.156 \text{ M}^{-1} \text{ s}^{-1}) / K_I' = 2.00 \times 10^{-9} \text{ M s}^{-1}$

If $K_a' = 10^{-11}$ then $k_3' = \sim 2.0 \times 10^2 \text{ s}^{-1}$

The above arguments lead to the following rate constants based in part on the estimates of K_I' (**0.018 M^{-1}**) and K_a' (**10^{-11} M^{-1}**). These were used as initial guesses in testing the fit of Scheme 3 to the pH dependence of the experimental k_{obs} values recorded.

$$k_I' = 2.5 \pm 0.1 \text{ M}^{-1} \text{ s}^{-1}$$

$$k_{-I}' = k_I' / K_I' = 139 \text{ s}^{-1}$$

$$k_2' = 0.44 \text{ s}^{-1}$$

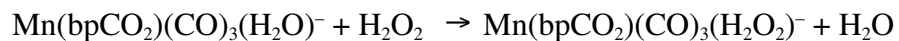
$$k_3' = \sim 2.0 \times 10^2 \text{ s}^{-1}$$

$$k_f = 10^{10} \text{ M}^{-1} \text{ s}^{-1}$$

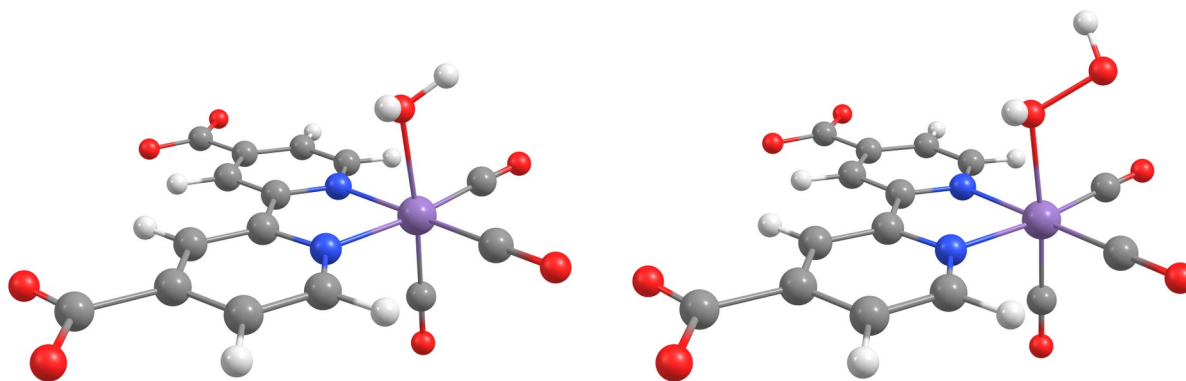
$$k_r = 10^7 \text{ s}^{-1}.$$

Scheme S3: Density functional analysis of the **II** + H₂O₂ → **III** + H₂O energetics.

Electronic energy DFT calculations were performed using ORCA version 6.0.1.⁴ The geometries of all species for the reaction shown were optimized independently using the ω B97M-V functional⁵ including DFT-NL dispersion corrections^{6,7} with the def2-TZVPP basis set⁸ and def2/J auxiliary basis set.⁹ Implicit solvent was included using a universal solvent model, SMD, for water.¹⁰



The optimized geometries of the reactant and product Mn complexes are shown below. The difference in energy for the reaction was calculated to be +1.35 kcal/mol.



Optimized geometries of Mn(bpCO₂)(CO)₃(OH₂)⁻ (**II**) and Mn(bpCO₂)(CO)₃(H₂O₂)⁻ (**III**)

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