Hydrogen Peroxide Complex of Zinc

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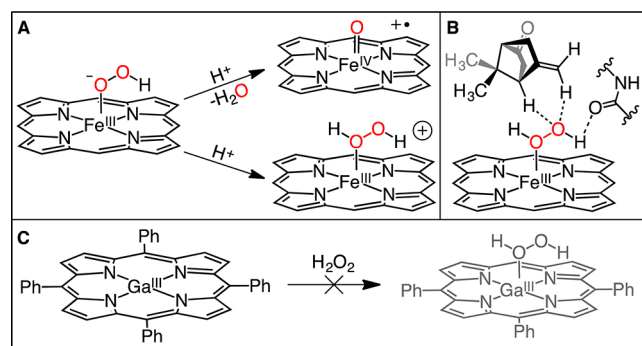
S *Supporting Information*

ABSTRACT: Metal(H_2O_2) complexes have been implicated in kinetic and computational studies but have never been observed. Accordingly, H_2O_2 has been described as a very weak ligand. We report the first metal(H_2O_2) adduct, which is made possible by incorporating intramolecular hydrogen-bonding interactions with bound H_2O_2. This $Zn^{II}(H_2O_2)$ complex decays in solution by a second-order process that is slow enough to enable characterization of this species by X-ray crystallography. This report speaks to the intermediacy of metal(H_2O_2) adducts in chemistry and biology and opens the door to exploration of these species in oxidation catalysis.

Hydrogen peroxide is a readily accessible and "green" oxidant,[1] with major industrial applications including bleaching of raw cotton and wood pulp, textile bleaching,[2] and propylene epoxidation.[3] These industrial processes are improved by the use of metal catalysts that activate H_2O_2. Remarkably, metal(H_2O_2) adducts that may be important intermediates in H_2O_2 activation have never been observed, although they have been kinetically implicated.[4] In cytochromes P450, an $Fe^{III}(H_2O_2)$ adduct may be the "second oxidant" or a precursor to the second oxidant (Figure 1a) and is likely the source of free H_2O_2 formed via "uncoupling."[5] The intermediacy of $Fe^{III}(H_2O_2)$ complexes in cytochromes P450 has been contentious, and Mayer demonstrated that related (porphyrin)-Ga^{III} complexes do not interact with H_2O_2 in anhydrous CH_2Cl_2 solutions despite the availability of open coordination sites on Ga^{III} and a strong interaction between Ga^{III} and added H_2O

Figure 1. (a) Proposed $Fe^{III}(H_2O_2)$ adduct in cytochromes P450.[5] (b) Shaik's computed $Fe^{III}(H_2O_2)$ adduct demonstrating the importance of second-sphere hydrogen-bonding interactions with bound H_2O_2 for preventing "uncoupling."[7] (c) Demonstration by Mayer that H_2O_2 is a very poor ligand for Ga^{III}.[6a]

(Figure 1c).[6] However, a recent computational study by Shaik supported H_2O_2 coordination in cytochromes P450, not as the "second oxidant" but as an alternative route to the reactive $Fe^{IV}(oxo)$ species (Compound 1, Figure 1a),[7] where hydrogen bonding between the coordinated H_2O_2 ligand and the surrounding environment was critical to the accessibility and longevity of this $Fe^{III}(H_2O_2)$ species (Figure 1b). Related computational studies of M/H_2O_2 oxidation catalysts (M = Mn, Os) also implicate the intermediacy of $M(H_2O_2)$ adducts that benefit from intramolecular hydrogen bonding involving bound H_2O_2.[8] Herein, we report the first coordination compound of H_2O_2, a $Zn^{II}(H_2O_2)$ species that features hydrogen bonding between bound H_2O_2 and the ancillary ligand.

Ligands that engage in second-sphere hydrogen bonding have been utilized extensively by Borovik, with highlights including the sole report of a high-spin $Fe^{III}(oxo)$ species stabilized by intramolecular hydrogen-bond donors[9] and O_2 activation at Co^{II} centers that was dependent on the presence and number of second-sphere hydrogen-bond donors.[10] Recognizing the higher acidity of H_2O_2 compared to H_2O and the corresponding demonstration by Prikhodchenko that H_2O_2 is a more effective hydrogen-bond donor than H_2O,[11] we targeted ligands that would provide second-sphere hydrogen-bond acceptors. We were particularly attracted by trianionic trisulfonamido derivatives of tren (tren = tris(2-aminoethyl)amine) that have been demonstrated by Borovik to provide an electron-rich coordination environment well suited for hydrogen bonding with H_2O and HO^- ligands.[12] Reasoning that diamagnetic metals would enable the study of metal(H_2O_2) interactions by ^1H NMR spectroscopy, we targeted Zn^{II} complexes supported by trisulfonamido derivatives of tren.
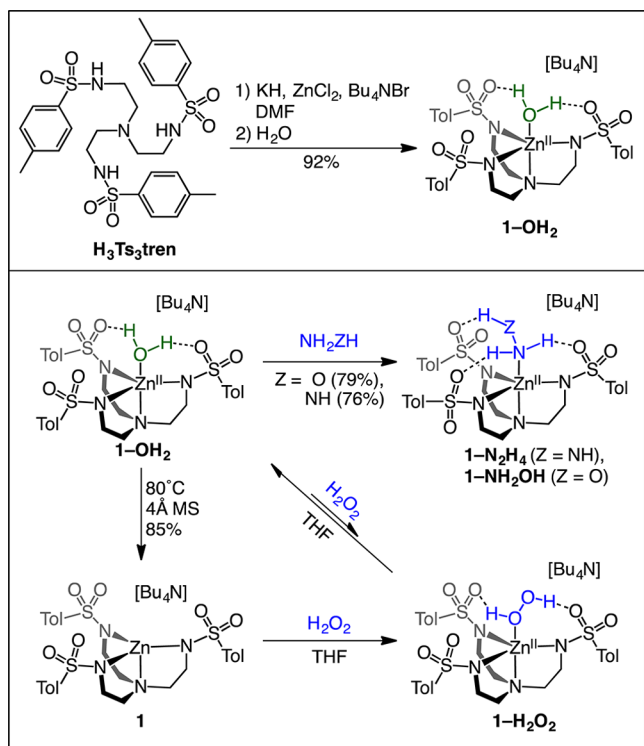
Combining H_3Ts_3tren, KH, and $ZnCl_2$ in DMF, followed by addition of $[nBu_4N][Br]$ and H_2O, provides access to $[nBu_4N]$-$[(Ts_3tren)Zn^{II}(OH_2)]$ in 92% crystalline yield (**1-OH$_2$**, Scheme 1). X-ray crystallographic characterization of **1-OH$_2$** shows hydrogen-bonding interactions between the bound H_2O protons and the sulfonyl oxygens (Figure 2) similar to what Borovik observed with other metals.[12] Displacement of water from **1-OH$_2$** was readily accomplished with both hydrazine and hydroxylamine, which are structurally analogous to H_2O_2 (Scheme 1). The X-ray crystal structures of **1-N$_2$H$_4$** and **1-NH$_2$OH** also exhibit second-sphere hydrogen bonding interactions, in these cases demonstrating hydrogen bonding with the terminal ZH group (Figure 2). While crystallographically characterized metal−(N_2H_4) complexes are abundant, we are aware of only five other metal−(NH_2OH) species that have been crystallographically characterized.[13]

Scheme 1. Synthesis of Compounds Examined[a]

[a]Yields of crystalline products shown.

We next turned to exploring coordination of H_2O_2 to Zn^{II}. We found that H_2O_2 can be readily extracted from solid $H_2O_2 \cdot$ urea into anhydrous d_8-THF to provide up to 500 mM H_2O_2 solutions with <5% H_2O relative to H_2O_2. Addition of this solution of H_2O_2 (1 equiv) to a d_8-THF solution of **1-H_2O** resulted in a 0.72 ppm upfield shift of bound water toward the free-H_2O resonance of 2.54 ppm with concomitant 0.05 ppm downfield shift of the H_2O_2 resonance away from free H_2O_2 (9.40 ppm) (Figure S8). This was the first indication that H_2O_2 interacts with **1-OH_2** and reveals that K_{eq} for H_2O displacement by H_2O_2 is less than unity (Scheme 1). This contrasts the observation that both N_2H_4 and NH_2OH quantitatively displace H_2O from **1-OH_2** and is consistent with H_2O_2 being the weakest ligand of this series.

Encouraged by the interaction of H_2O_2 with **1-OH_2** in d_8-THF, we turned to dehydration of **1-OH_2** to probe coordination of H_2O_2 to **1** in the absence of H_2O. Formation of anhydrous **1** was accomplished by heating **1-OH_2** in glyme to 80 °C overnight in the presence of 4 Å molecular sieves, followed by precipitation

with pentane. Dehydration was verified by the disappearance of any resonance associated with bound or free H_2O by ^1H NMR spectroscopy. Addition of one equivalent of anhydrous H_2O_2 to **1** in d_8-THF resulted in a 0.45 ppm downfield shift of the H_2O_2 proton resonance, consistent with interaction between H_2O_2 and **1** to form **1-H_2O_2**, although the nature of the interaction (coordination, hydrogen bonding, electrostatic interaction) could not be established from these data (Figure 3). Importantly,
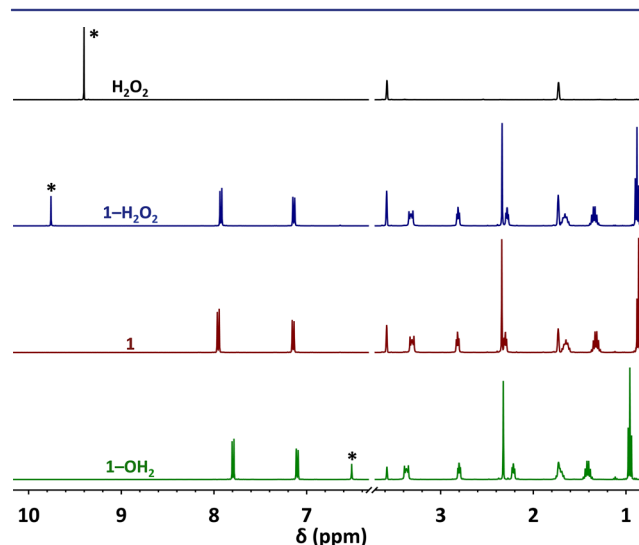

Figure 3. From top to bottom, ^1H NMR spectra (d_8-THF) of H_2O_2, **1-H_2O_2**, **1**, and **1-OH_2**. Free (top) and bound H_2O_2 (second from top) and bound H_2O positions (bottom) are marked with an asterisk. Free H_2O in d_8-THF appears at 2.54 ppm.

no interaction between H_2O_2 and H_3Ts_3tren or between H_2O_2 and $ZnCl_2$ in d_8-THF is observed by ^1H NMR spectroscopy (Table S1). The H_2O_2 proton resonance in **1-H_2O_2** shifts linearly downfield with decreasing temperature with a slope that is steeper than that of free H_2O_2 or that of bound H_2O in **1-OH_2** (Figure S7). This large temperature dependence is indicative of strong intramolecular hydrogen bonding in **1-H_2O_2**.[14]

1-H_2O_2 decomposes in solution to **1-OH_2** by a second order pathway ($k = 3.8 \times 10^{-3}$ M^{-1} s^{-1}, Figure S3). Precipitation of **1-H_2O_2** resulted in a 1:1 mixture of **1-OH_2** and **1-H_2O_2** in the solid state. This solid was explored by thermogravimetric analysis (TGA) to probe the strength of the H_2O_2 interaction with **1** in the solid state by comparison to crystalline and powdered samples of **1-OH_2** (Figure 4). These data show that H_2O_2 is the first ligand to be lost upon heating solid samples of **1-OH_2/1-**
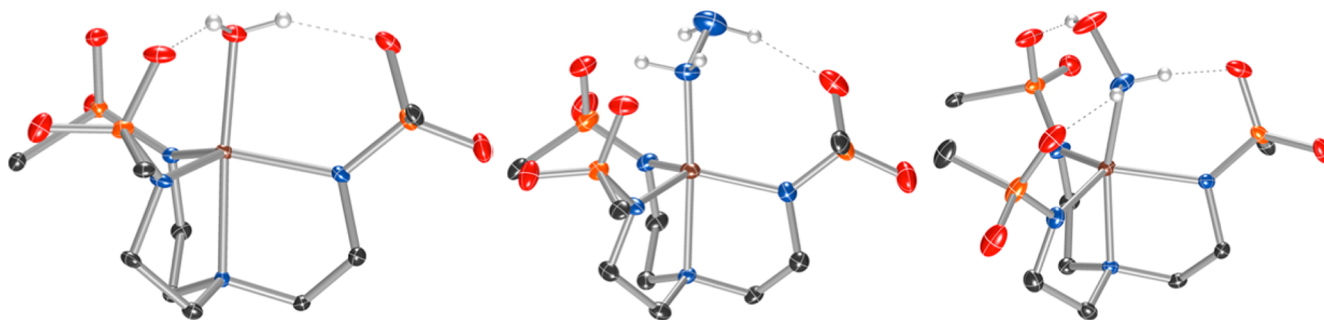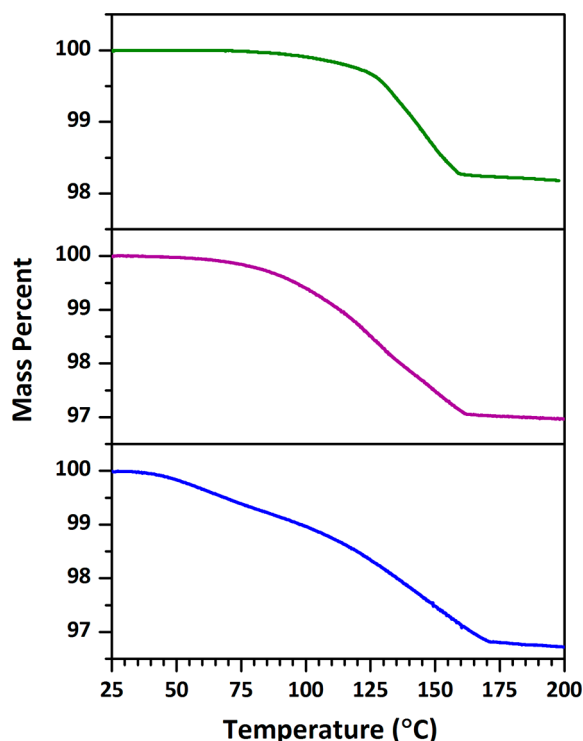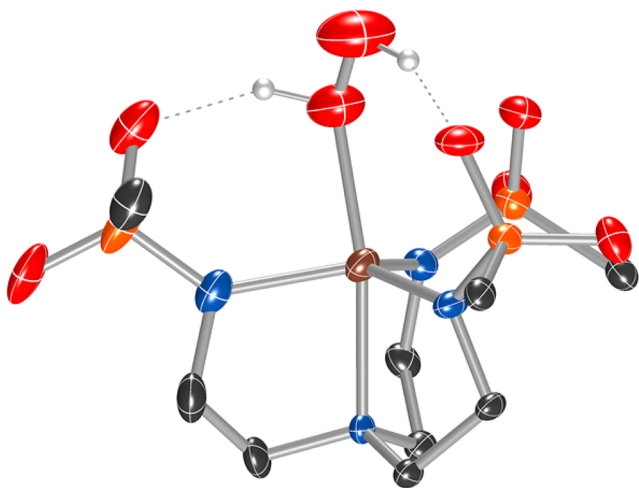

Figure 2. X-ray crystal structures of the anions in **1-OH_2** (left), **1-N_2H_4** (middle), and **1-NH_2OH** (right), highlighting intramolecular hydrogen bonding. Aryl groups truncated for clarity.

Figure 4. TGA traces of crystalline **1-OH₂** (top), powdered **1-OH₂** (middle), and powdered 1:1 mixture of **1-H₂O₂** and **1-OH₂** (bottom). Mass loss experimental/theoretical: 0.74 mg/0.82 mg (top), 0.67 mg/0.63 mg (middle), and 0.70 mg/0.82 mg (bottom).

H_2O_2 because there is a lower-temperature mass-loss event than observed in powdered samples of **1-OH₂**. Therefore, in both the solid state and in solution, H_2O_2 is a weaker ligand than H_2O for **1**.

Encouraged by the isolation of solid samples containing **1-H₂O₂** despite the bimolecular decay pathway of this species, we explored whether crystalline samples of **1-H₂O₂** could be obtained. Rapid crystallization of **1-H₂O₂** from THF with MTBE provided crystals with varying amounts of bound H_2O and H_2O_2, with the best crystal examined having a 50:50 disorder of **1-H₂O₂** (Figure 5) and **1-OH₂**, each refined as a distinct

Figure 5. X-ray crystal structure of the anion in **1-H₂O₂** from a 1:1 crystal of **1-OH₂:1-H₂O₂**. Aryl groups truncated for clarity.

component. The H_2O_2 and H_2O ligands share the same apical position. The electron density of **1-OH₂/1-H₂O₂** (see Supporting Information) unambiguously establishes the presence of a bent H_2O_2 ligand coordinated to Zn^{II}. **1-H₂O₂** is the first structurally characterized H_2O_2 coordination compound. H_2O_2 coordination to Zn^{II} is analogous to coordination of N_2H_4 and NH_2OH, where intramolecular hydrogen bonding between both H_2O_2 protons and the sulfonyl oxygens is observed in the solid state. The Zn−O bond lengths of **1-OH₂** and **1-H₂O₂** (2.185(10) Å and 2.171(10) Å, respectively) fall within 1σ of one another, consistent with formation of a direct Zn−O bond in each case. The O−O bond length in **1-H₂O₂** is 1.445(14) Å, indicative of an O−O single bond.

While H_2O_2 has been described as a very poor ligand,[6a,15] H_2O is a common ligand in coordination chemistry. Both of these ligands can engage in hydrogen bonding, so we probed the extent to which coordination of H_2O to **1** was favored over coordination of H_2O_2. As described above, addition of one equivalent of H_2O_2 to **1-OH₂** in d_8-THF results in a 0.05 ppm downfield shift of H_2O_2 from its uncoordinated position with a concomitant 0.72 ppm upfield shift of H_2O from its coordinated position (Figure S8), enabling us to measure the equilibrium constant for H_2O vs H_2O_2 coordination to **1** by comparing these exchange-averaged chemical shifts to their corresponding free and bound shifts (see Supporting Information for details; exchange of H_2O and H_2O_2 is fast on the NMR time scale even at −100 °C, Figure S4). We calculate that $K_{eq} = 37$ ($\Delta G° = -2.1$ kcal/mol) in favor of H_2O coordination to **1** over H_2O_2.

$$K_{eq} = \frac{[\mathbf{1-OH_2}][\mathbf{H_2O_2}]}{[\mathbf{1-H_2O_2}][\mathbf{H_2O}]} \approx 37$$

H_2O remains a better ligand than H_2O_2 even with supporting ligands that facilitate second-sphere hydrogen-bonding interactions, but the preference is not particularly stark: the ratio of bound H_2O to bound H_2O_2 at equal concentrations of these two species and **1** is ~6:1.

We have demonstrated the first H_2O_2 coordination complex, where the M−(H_2O_2) interaction is facilitated by second-sphere hydrogen-bonding interactions. Coordination of H_2O_2 speaks to the viability of metal(H_2O_2) adducts as intermediates in catalysis,[4,8] particularly in reference to the "second oxidant" in cytochromes P450.[5,7] Furthermore, an understanding of how to facilitate formation of metal(H_2O_2) adducts opens a new pathway for exploring H_2O_2 activation for substrate oxidation reactions, a goal that we are currently pursuing.

■ ASSOCIATED CONTENT

ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b10450.

> Synthesis and characterization of compounds, experimental details, description of TGA, and equilibrium calculations (PDF)
> Crystallographic information (CIF)

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Notes

The authors declare no competing financial interest.

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