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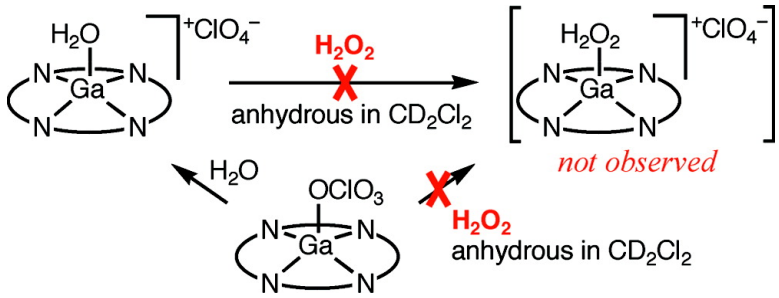

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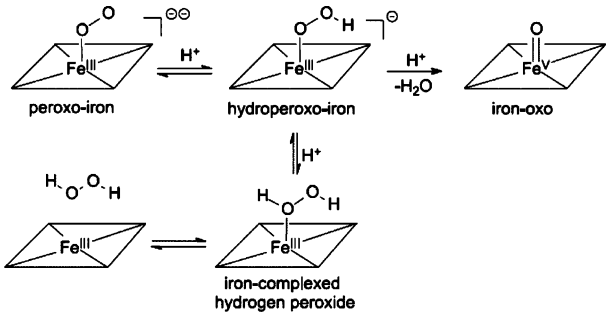
Hydrogen Peroxide: A Poor Ligand to Gallium Tetraphenylporphyrin

Antonio G. DiPasquale† and James M. Mayer*
Department of Chemistry, Campus Box 351700, University of Washington, Seattle, Washington 98195-1700
Received October 2, 2007; E-mail: mayer@chem.washington.edu

Hydrogen peroxide is a thermodynamically potent oxidant that is an important "reactive oxygen species" in biology and is being increasingly used as an industrial reagent.[1] H_2O_2 is typically kinetically activated by a metal catalyst. For instance, it forms active oxidants when reacted with heme enzymes or iron porphyrin complexes [(por)Fe].[2] The possible involvement of a [(por)Fe^{III}-(H_2O_2)] complex in catalysis by cytochrome P450 enzymes has been debated and such a complex could be involved in H_2O_2 loss from the enzyme (Scheme 1[3a]).[2−4] A recent thermochemical analysis suggests that H_2O_2 could be strongly bound to the Fe^{III}-heme in P450.[5] Despite this interest, much is uncertain about the interaction of H_2O_2 with metal ions. To our knowledge there are no observations of metal−H_2O_2 complexes (although they have been implicated in kinetic studies[6]). We report here efforts to generate a gallium−porphyrin peroxide complex which suggest that H_2O_2 is a very poor ligand. A simple procedure to prepare dilute solutions of anhydrous H_2O_2 in CD_2Cl_2 is also described.

When an H_2O_2 complex acts directly as an oxidant, for example, in the suggested $[Fe^{III}(H_2O_2)]^+ + RH \rightarrow [Fe^{III}(OH)] + ROH_2^+$,[3] redox change at the metal is not involved. Therefore it is attractive to model this process with redox-inactive Ga^{3+}, which has been used as an analogue of Fe^{3+}, particularly similarly sized high-spin Fe^{3+}.[7] (Por)Fe^{III}(OOH) species are most often low spin,[8] although a five-coordinate high spin form has been described.[8c] [(Por)Fe^{III}-(H_2O_2)] species have not been observed but one form is calculated to have closely lying doublet and quartet states.[4b] (OEP)Ga(SR) has been used as models for P450[7a,b] and Balch et al. have reported tetraphenylporphyrin gallium peroxide complexes (TPP)GaOOR.[9]

Scheme 1. Suggested Intermediates in Cytochrome P450 Oxidations (from ref 3a)



As a possible route to an H_2O_2 adduct, (TPP)Ga^{III} complexes with weakly coordinating anions have been prepared. (TPP)GaCl reacts with 1 equiv of AgOTf (OTf = $CF_3SO_3^-$) or $AgClO_4$ in CH_2Cl_2 to give (TPP)GaOTf (**1**) or (TPP)$GaClO_4$ (**2**, eq 1; X =

$$(TPP)GaCl + AgX \rightarrow (TPP)GaX + AgCl \qquad (1)$$

OTf (**1**), ClO_4 (**2**)). Reactions with $AgPF_6$ and $AgBF_4$ gave multiple products, and the anions BPh_4^- and $B[3,5\text{-}C_6H_3(CF_3)_2]_4^-$ are not stable to H_2O_2. The hydroxide complex (TPP)GaOH (**3**) precipitates

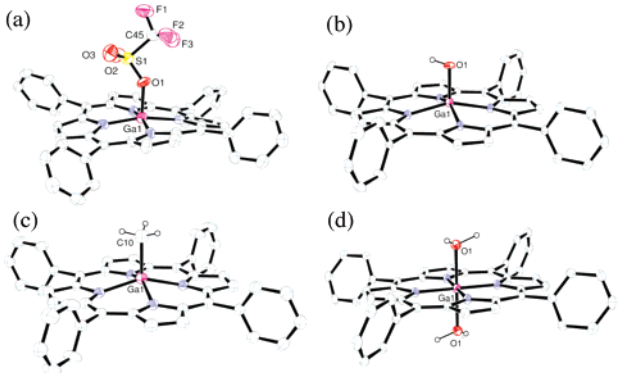


Figure 1. ORTEP drawings of the Ga complexes in (a) (TPP)GaOTf·C_7H_8 (**1**), (b) (TPP)GaOH (**3**), (c) (TPP)$GaCH_3$ (**4**), and (d) [(TPP)Ga-(OH_2)$_2$]ClO_4.

upon the addition of water to THF solutions of (TPP)Ga(OO^tBu)[9] or (TPP)Ga(O^tBu) or when using "wet" solvent (eq 2). The related (TPP)GaOH·H_2O has been reported.[10] Treatment of (TPP)GaCl with CH_3Li in Et_2O gives the methyl derivative (TPP)GaMe (**4**, eq 3).

$$(TPP)Ga(O_x{}^tBu) + H_2O \rightarrow (TPP)GaOH\ (\mathbf{3}) + {}^tBuO_xH\ (x = 1,2) \qquad (2)$$

$$(TPP)GaCl + CH_3Li \rightarrow (TPP)GaCH_3\ (\mathbf{4}) + LiCl \qquad (3)$$

Compounds **1**−**4** have been characterized by ^1H and $^{13}C\{^1H\}$ NMR spectroscopy and elemental analyses.[11] X-ray crystal structures for **1**, **3**, and **4** show five-coordinate complexes with Ga displaced as much as 0.530(3) Å from the porphyrin plane for **4** (Figure 1).[11] The structures of **3** and **4** contain a crystallographic mirror plane co-incident with the porphyrin, with the Ga and axial ligand disordered above and below the plane. Crystals of **2** have not been obtained but the related iron derivative, (TPP)Fe(κ^1-ClO_4), has been structurally characterized.[12] Small amounts of water convert (TPP)Ga(ClO_4) in CD_2Cl_2 to the mono-aquo complex [(TPP)Ga(OH_2)]ClO_4 (**5**) (eq 4), characterized by ^1H NMR especially integration of the coordinated H_2O signal at δ −14.2. Excess water precipitates the insoluble bis(aquo) complex, whose X-ray structure is shown in Figure 1d.

$$(TPP)Ga(ClO_4) + H_2O \rightarrow [(TPP)Ga(OH_2)]ClO_4\ (\mathbf{5}) \qquad (4)$$

One challenge of preparing hydrogen peroxide complexes is that H_2O_2 is commercially available only as an aqueous solution. Pure H_2O_2 has been described but is extremely hazardous.[1b] We have focused on preparing dilute solutions of H_2O_2 in an aprotic, anhydrous, and oxidation resistant organic solvent. Literature routes to such solutions have been problematic in our hands but key to our success were the reports that $Mg(ClO_4)_2$ is a selective sorbent for H_2O that does not decompose H_2O_2.[13] CD_2Cl_2 gave the best results of the solvents examined.[11] A fresh bottle of CD_2Cl_2 (25 g) was treated with ∼5 g $Mg(ClO_4)_2$ (anhydrous desiccant grade from Fisher Scientific) and cooled at −4 °C for 30 min. Approximately 3 mL of 50% H_2O_2 was added dropwise over a 10 min period,

† Current address: Department of Chemistry and Biochemistry, University of California-San Diego, California. E-mail: adipasqu@chem.ucsd.edu.

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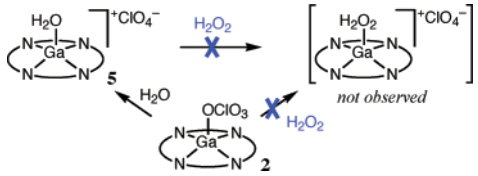
Scheme 2. Experiments Indicating the Lack of Binding of H_2O_2 to (TPP)Ga^{III} Complexes in CD_2Cl_2



maintaining −4 °C, and the mixture was stored overnight. Only glassware cleaned with Caro's acid (H_2O_2/H_2SO_4) was used. Aliquots of such solutions removed with a glass pipet have ^{1}H NMR spectra that show only a single resonance at δ 7.55 (other than the residual $CHDCl_2$ peak) and thus have $[H_2O] < 3\%\ [H_2O_2]$. The addition of small amounts of H_2O results in the appearance of a second resonance, at δ 1.57 for H_2O, without affecting the H_2O_2 resonance (Figure S1). The addition of Ph_3P to the H_2O_2/CD_2Cl_2 solutions results in rapid and quantitative formation of Ph_3PO and H_2O. While *caution* must be exercised in any procedure using either perchlorate salts or 50% H_2O_2, we have experienced no difficulties with these solutions, which are stable for months at −4 °C. Solutions of 1−100 mM H_2O_2 have been prepared (measured by ^{1}H NMR using an internal standard); typical procedures have used ~10 mM solutions.

Surprisingly, the gallium triflate complex **1** does not react with H_2O_2/CD_2Cl_2 as determined by ^{1}H NMR. The resonances for **1** and H_2O_2 remain unperturbed and no new peaks appear. Adding PPh_3 to solutions of **1** and H_2O_2 causes rapid quantitative formation of $OPPh_3$ and H_2O (^{1}H NMR), showing that H_2O_2 is still present. Similarly, successive additions of H_2O_2/CD_2Cl_2 to purified samples of the perchlorate complex **2** causes no change in the ^{1}H NMR chemical shifts. (Multiply recrystallized **2** is required because trace $AgClO_4$ appears to disproportionate H_2O_2.) Some broadening and then sharpening of the resonances for **2** are observed with increasing H_2O_2 (Figure S2), perhaps because of changes in solvation. The addition of PPh_3 to solutions of **2** + H_2O_2 quantitatively yield $OPPh_3$ and the H_2O generated in this reaction forms **5**. In sum, H_2O_2 does not bind significantly to the gallium triflate or perchlorate complexes.

The aquo complex **5** was generated *in situ* by dissolving **2** in CD_2Cl_2 saturated with H_2O, yielding a mixture of **2** and **5** (by ^{1}H NMR), together with some precipitated bis(aquo) complex. The addition of H_2O_2/CD_2Cl_2, such that there was roughly twice as much H_2O_2 as H_2O, caused only very minor changes in the ^{1}H NMR spectra. The H_2O resonance of **5** shifted downfield very slightly (<0.02 ppm) and the concentration of **5** actually increased slightly (Figure S3), possibly as a result of the greater solubility of the bis(aquo) complex in the presence of H_2O_2. Thus, as summarized in Scheme 2, H_2O_2 does not displace the water ligand in **5**.

(TPP)Ga(OO^{t}Bu), (TPP)GaOH (**3**), and (TPP)$GaCH_3$ (**4**) are also inert to H_2O_2/CD_2Cl_2 at 25 °C. Complex **4** does react with HOTf to form **1** but is unreactive with H_2O. Solutions containing (TPP)$GaClO_4$ and H_2O_2 in CD_2Cl_2 did not show any reactivity with cyclohexene, norbornene, or *trans*-stilbene by NMR or GC−MS.[11] If a small amount of an H_2O_2 complex is present under these conditions, it is not highly reactive.

In sum, H_2O_2 is a very poor ligand to (TPP)Ga^{III}. An excess of H_2O_2 in CD_2Cl_2 does not displace H_2O or ClO_4^- from the gallium center. While tetraphenylporphyrin-gallium salts in CD_2Cl_2 are distant models for the heme-iron(III) center in P450, these results do not lend support to the suggestions of a hydrogen peroxide complex as an important oxidant. To our knowledge there are no reports of observable M(H_2O_2) or M(ROOH) complexes. Gas-phase calculations indicate that η^2-binding of H_2O_2 to Li^+ and Na^+ is about 5 kcal mol^{-1} weaker than binding of H_2O,[14] which is consistent with our calculations on (TPP)Ga^+.[15] The gas-phase proton affinity of H_2O_2 is 4 kcal mol^{-1} less than that that of H_2O (161 vs 165 kcal mol^{-1}).[16] Very weak binding of H_2O_2 to Co^{III} has previously been suggested on the basis of kinetic studies.[6] That H_2O_2 is poorer ligand than H_2O may be understood by considering that changing from H_2O to H_2O_2 involves replacing H by the more electron-withdrawing OH. Weak binding of H_2O_2 is likely a general feature of its chemistry, in the absence of a base to form hydroperoxo or peroxo complexes.

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Supporting Information Available: Full experimental details and CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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