

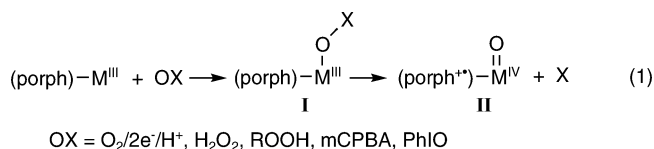
## Catalytic Sulfoxidation and Epoxidation with a Mn(III) Triazacorrole: Evidence for A "Third Oxidant" in High-Valent Porphyrinoid Oxidations

Sheena Hailin Wang, Beaven S. Mandimutsira, Ryan Todd, Bobby Ramdhanie, Joseph P. Fox, and David P. Goldberg\*

Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

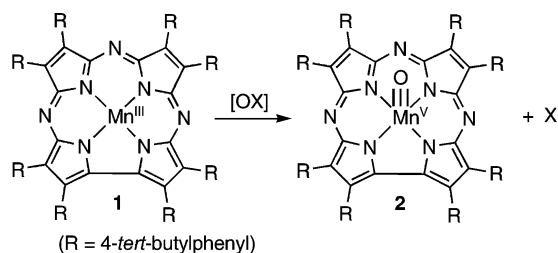
Received October 8, 2003; E-mail: dpg@jhu.edu

A major goal in understanding the mechanism of synthetic and naturally occurring metalloporphyrin-catalyzed oxidations has been to identify the structures of the reactive intermediates, with particular attention given to cytochrome P450-type processes such as sulfoxidation, epoxidation, and hydroxylation. The importance of high-valent metal-oxo species (e.g. Fe=O, Mn=O) in such oxygenation chemistry is well-established,<sup>1</sup> although typically these species are short-lived and difficult to observe directly. A generalized scheme depicting the formation of possible reactive intermediates is shown in eq 1.



The consensus view has pointed to the metal-oxo intermediate II as being the active oxidant, but recently there is mounting evidence that the (porph)metal-oxidant intermediate I can also serve as an oxidizing agent under certain conditions, functioning as a possible "second oxidant".<sup>2</sup> A similar type I intermediate has recently been suggested to compete with the established (salen)-Mn(V)(O) species in the Jacobsen-Katsuki epoxidation.<sup>3</sup> In this communication we provide evidence for a new, third type of intermediate by examination of oxygen-atom-transfer (OAT) reactions catalyzed by a Mn-porphyrinoid complex.

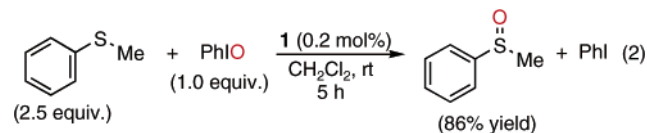
The ring-contracted analogues of porphyrins, known as corroles, have come under intense investigation in part because of their ability to stabilize high-valent metal-oxo species such as Cr(V)O and Mn(V)O.<sup>4</sup> We have recently described the room-temperature isolation of a stable Mn(V)O corrolazine (Cz) complex, which is a *meso*-N-substituted version of a corrole.<sup>5</sup>



We had previously found that this complex rapidly reacts with PPh<sub>3</sub> to give OPPh<sub>3</sub> and regeneration of the Mn(III) complex 1. This result prompted us to examine 1 under catalytic conditions in which an appropriate oxygen atom donor (OX) could be coupled with a suitable organic substrate, presumably going through 2 as the active oxidant. We report herein the catalytic oxidation of

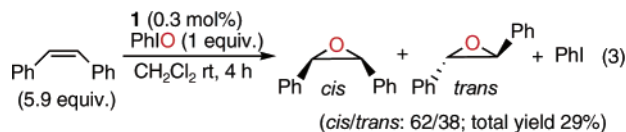
thioanisole (PhSMe) to sulfoxide (PhS(O)Me) with iodosylbenzene (PhIO) as the oxygen source and 1 as added catalyst. However, instead of 2 serving as the active intermediate, we show that a novel PhIO-Mn(V)O adduct is most likely the active oxidizing species in the catalytic mechanism. In addition, 1 is capable of catalyzing the selective epoxidation of *cis*-stilbene via the same intermediate.

Previously, the Mn(III) complex 1 was oxidized to 2 by mCPBA in CH<sub>2</sub>Cl<sub>2</sub>, and 2 was then isolated by column chromatography.<sup>5</sup> We speculated that other oxidants should be competent to convert 1 to 2. Both PhIO and *p*-cyanodimethylaniline-*N*-oxide (CDMANO)<sup>6</sup> quantitatively convert 1 to 2 as shown by UV-vis and <sup>1</sup>H NMR spectroscopy (Figures S1-S4). We then examined the oxidation of PhSMe under catalytic conditions using both PhIO and CDMANO as the oxygen atom source. With PhIO as oxidant, sulfoxidation was catalyzed according to eq 2, and good yield and turnover (TON = 165) were observed after 5 h.



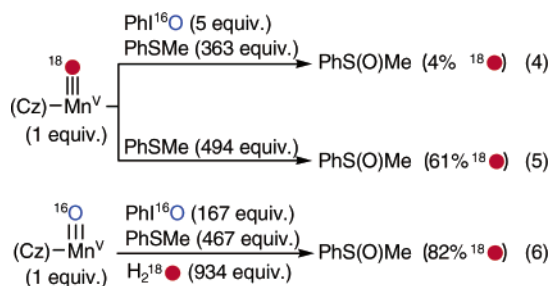
In contrast, when CDMANO was employed in place of PhIO in eq 2, less than 4% sulfoxide product was observed after 5 h, although the Mn(V)-oxo complex 2 was clearly present by UV-vis spectroscopy. These data suggest that 2 by itself cannot be the active OAT agent in the catalytic reaction with PhIO. In addition, the reaction between isolated 2 and PhSMe gave only a 14% yield (0.14 turnovers) of PhS(O)Me after 5 h, and 45% yield (0.45 turnovers) after 24 h. This reaction appears to be far too slow for the Mn(V)-oxo species to be the reactive intermediate in the catalytic reaction. If isolated 2 is added directly to the reaction in eq 2 in place of the Mn(III) complex 1, sulfoxidation proceeds with the same yield, and TON as found when 1 is added as catalyst. We considered the possibility that the iodobenzene generated during the catalytic reaction could react with 2 to give Mn(III)-OIPh (a type I intermediate), or even potentially activate 2 toward OAT by axial coordination trans to the oxo group. The former reaction is preceded by a recent study which describes an equilibrium between (porph)<sup>+</sup>Fe<sup>IV</sup>(O) (intermediate II) and (porph)Fe<sup>III</sup>-OIPh (intermediate I) with excess PhI.<sup>2a</sup> Thus, the reaction between PhSMe and 2 was run in the presence of a large excess of PhI (PhSMe:PhI:2, 464:98:1), but the yield of PhS(O)Me after 5 and 24 h was the same as that found in the absence of PhI.<sup>7</sup>

The catalytic epoxidation of *cis*-stilbene with PhIO proceeds as shown in eq 3. The *cis*-epoxide is preferentially formed over the *trans*, and the total yield of epoxides corresponds to 18 turnovers. In contrast, less than 5% *trans*-epoxide (and no *cis*-epoxide) is observed for *trans*-stilbene under the same conditions.



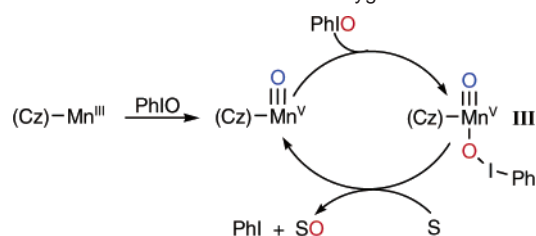
When isolated **2** was combined with excess *cis*-stilbene in the absence of PhIO, no epoxidation was observed after 24 h, clearly ruling out **2** as the reactive intermediate. A proposed mechanism for the catalytic reactions (eqs 2–3) is shown in Scheme 1. The first step involves rapid formation of the Mn(V)–oxo complex, followed by coordination and Lewis acid activation of PhIO.<sup>8</sup> The coordinated PhIO then directly transfers an O atom to the substrate. Thus, the active oxidant **III** is a hybrid of intermediates **I** and **II** in eq 1. This mechanism accounts for all observations regarding the catalytic reactivity. Even the diastereoselectivity of *cis*-stilbene and the lack of reactivity of *trans*-stilbene is taken into account by this mechanism, since stilbene epoxidations involving previously proposed M–OX Lewis acid catalysts have shown the same patterns of reactivity.<sup>2a,e,3,9</sup>

To bolster the support for this mechanism, we conducted <sup>18</sup>O-labeling experiments (eqs 4–6). Complex **2** was labeled with <sup>18</sup>O by addition of H<sub>2</sub><sup>18</sup>O as described previously,<sup>5</sup> and the label was quantitated by reaction of **2** with PPh<sub>3</sub> to give labeled OPPh<sub>3</sub> (84% <sup>18</sup>O incorporation). Catalytic sulfoxidation with **2**-<sup>18</sup>O (eq 4) gave only a small amount of <sup>18</sup>O incorporation in the PhS(O)Me product. Importantly, the <sup>18</sup>O label in **2** remains intact throughout the catalytic process; at the end of this reaction quenching **2**-<sup>18</sup>O with PPh<sub>3</sub> gave <sup>18</sup>OPPh<sub>3</sub> with quantitative recovery of the <sup>18</sup>O label. The direct reaction between **2**-<sup>18</sup>O and PhSMe in the absence of PhIO (under noncatalytic conditions) led to significant <sup>18</sup>O incorporation in PhS(O)Me (eq 5). Interestingly, when H<sub>2</sub><sup>18</sup>O was added directly to the catalytic reaction, high <sup>18</sup>O incorporation was observed (eq 6). Studies by Valentine<sup>10</sup> and others<sup>2a</sup> have shown that efficient <sup>18</sup>O exchange occurs between H<sub>2</sub><sup>18</sup>O and metal-bound PhIO, with the labeled O atom ultimately being transferred to substrate (hydrocarbon or alkene). Thus, the <sup>18</sup>O-labeling results are in excellent agreement with the proposed mechanism (Scheme 1), in which the high-valent metal–oxo species **2** serves only as a Lewis acid catalyst for the activation of PhIO, and the O atom in the coordinated PhIO is preferentially transferred to substrate.



To our knowledge this study provides the first evidence for a high-valent metal–oxo porphyrinoid species acting as a Lewis acid catalyst in the same way as the proposed (porph)–M(III) species **I** does in eq 1. In fact, much of the evidence for **I** in the synthetic porphyrin and salen-catalyzed oxidations comes from the observa-

**Scheme 1.** Consensus Mechanism of Oxygen Atom Transfer



tion that product distributions are dependent on the nature of the oxidant (OX).<sup>2,3</sup> Intriguingly, it may be possible to rationalize many of these previous observations by invoking an intermediate similar to **III** as the active oxidant, rather than **I**, even though the high-valent metal–oxo porphyrin or salen complex is typically more reactive than the analogous corrole or corrolazine complex. In addition, similar catalytic reactivity was observed in the epoxidation of alkenes by manganese corrole complexes and PhIO,<sup>4b,c</sup> and it was suggested that the active catalytic species may be a higher valent complex produced by disproportionation of the (corrole)–Mn(V)O complex.<sup>4c</sup> We suggest that the corrole analogue of **III** may be responsible for the observed reactivity instead of a disproportionation product.

**Acknowledgment.** We thank the NSF (CHE0094095 and CHE0089168 to D.P.G.) for financial support. R.C.T. is grateful for a Howard Hughes Summer Fellowship through the Johns Hopkins University. D.P.G. also acknowledges the Alfred P. Sloan Jr., Foundation for support.

**Supporting Information Available:** Experimental details, UV–vis and <sup>1</sup>H NMR (Figures S1–S5), and representative GC data (Figure S6) (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

## References

- McLain, J. L.; Lee, J.; Groves, J. T. In *Biomimetic Oxidations Catalyzed by Transition Metal Complexes*; Meunier, B., Ed.; Imperial College Press: 2000; pp 91–169.
- (a) Nam, W.; Choi, S. K.; Lim, M. H.; Rohde, J.-U.; Kim, I.; Kim, J.; Kim, C.; Que, L., Jr. *Angew. Chem., Int. Ed.* **2003**, *42*, 109–111. (b) Newcomb, M.; Hollenberg, P. F.; Coon, M. J. *Arch. Biochem. Biophys.* **2003**, *409*, 72–79. (c) Ogliaro, F.; de Visser, S. P.; Cohen, S.; Sharma, P. K.; Shaik, S. *J. Am. Chem. Soc.* **2002**, *124*, 2806–2817. (d) Collman, J. P.; Chien, A. S.; Eberspacher, T. A.; Brauman, J. I. *J. Am. Chem. Soc.* **2000**, *122*, 11098–11100. (e) Nam, W.; Lim, M. H.; Lee, H. J.; Kim, C. *J. Am. Chem. Soc.* **2000**, *122*, 6641–6647. (f) Machii, K.; Watanabe, Y.; Morishima, I. *J. Am. Chem. Soc.* **1995**, *117*, 6691–6697.
- Adam, W.; Roschmann, K. J.; Saha-Möllner, C. R.; Seebach, D. *J. Am. Chem. Soc.* **2002**, *124*, 5068–5073.
- (a) Mahammed, A.; Gray, H. B.; Meier-Callahan, A. E.; Gross, Z. *J. Am. Chem. Soc.* **2003**, *125*, 1162–1163. (b) Liu, H.-Y.; Lai, T.-S.; Yeung, L.-L.; Chang, C. K. *Org. Lett.* **2003**, *5*, 617–620. (c) Gross, Z.; Golubkov, G.; Simkhovich, L. *Angew. Chem., Int. Ed.* **2000**, *39*, 4045–4047.
- Mandimutsira, B. S.; Ramdhanie, B.; Todd, R. C.; Wang, H.; Zareba, A. A.; Czernuszewicz, R. S.; Goldberg, D. P. *J. Am. Chem. Soc.* **2002**, *124*, 15170–15171.
- CDMANO has been used in (porph)Fe oxidations. Woon, T. C.; Dicken, C. M.; Bruce, T. C. *J. Am. Chem. Soc.* **1986**, *108*, 7990–7995.
- Mixing excess PhI and isolated **2** in CH<sub>2</sub>Cl<sub>2</sub> showed no reaction by UV–vis spectroscopy (see Figure S5).
- (Porph)Mn<sup>IV</sup>–OIPh species have been described. Smegal, J. A.; Scharadt, B. C.; Hill, C. L. *J. Am. Chem. Soc.* **1983**, *105*, 3510–3515.
- Yang, Y.; Diederich, F.; Valentine, J. S. *J. Am. Chem. Soc.* **1991**, *113*, 7195–7205.
- Nam, W.; Valentine, J. S. *J. Am. Chem. Soc.* **1993**, *115*, 1772–1778.

JA038951A