

## Radical Autoxidation and Autogenous O<sub>2</sub> Evolution in Manganese–Porphyrin Catalyzed Alkane Oxidations with Chlorite

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Received January 18, 2004

A manganese porphyrin catalyst employing chlorite (ClO<sub>2</sub><sup>-</sup>) as a “shunt” oxidant displays remarkable activity in alkane oxidation, oxidizing cyclohexane to cyclohexanol and cyclohexanone with >800 turnover numbers. The ketone is apparently formed without the intermediacy of alcohol and accounts for an unusually large fraction of the product (~40%). Radical scavenging experiments indicate that the alkane oxidation mechanism involves both carbon-centered and oxygen-centered radicals. The carbon-radical trap CBrCl<sub>3</sub> completely suppresses cyclohexanone formation and reduces cyclohexanol turnovers, while the oxygen-radical trap Ph<sub>2</sub>NH inhibits all oxidation until it is consumed. These observations are indicative of an autoxidation mechanism, a scenario further supported by TEMPO inhibition and <sup>18</sup>O<sub>2</sub> incorporation into products. However, similar cyclohexane oxidation activity occurs when air is excluded. This is explained by mass spectrometric and volumetric measurements showing catalyst-dependent O<sub>2</sub> evolution from the reaction mixture. The catalytic disproportionation of ClO<sub>2</sub><sup>-</sup> into Cl<sup>-</sup> and O<sub>2</sub> provides sufficient O<sub>2</sub> to support an autoxidation mechanism. A two-path oxidation scheme is proposed to explain all of the experimental observations. The first pathway involves manganese–porphyrin catalyzed decomposition of ClO<sub>2</sub><sup>-</sup> into both O<sub>2</sub> and an unidentified radical initiator, leading to classical autoxidation chemistry providing equal amounts of cyclohexanol and cyclohexanone. The second pathway is a “rebound” oxygenation involving a high-valent manganese–oxo intermediate, accounting for the excess of alcohol over ketone. This system highlights the importance of mechanistic studies in catalytic oxidations with highly reactive oxidants, and it is unusual in its ability to sustain autoxidation even under apparent exclusion of O<sub>2</sub>.

### Introduction

Metalloporphyrin-catalyzed oxidations of alkanes have been intensely investigated as mechanistic models for the cytochrome P-450 family of monooxygenases.<sup>1</sup> A greatly simplified catalytic cycle and potential applications in fine chemicals synthesis have been made possible by the use of “shunt reagents”:<sup>2</sup> oxygen atom donors such as PhIO, NaOCl, RO<sub>3</sub>H, and KHSO<sub>5</sub> which circumvent the two-electron reduction per oxygen atom required for oxidation catalysis

with O<sub>2</sub>. The mechanistic evidence is consistent with high-valent metal–oxo complexes functioning as the active oxidizing intermediates in the majority of these “shunt” systems,<sup>3</sup> implying that the selectivity of catalytic oxidation should depend only on the intrinsic reactivity of the metal–oxo moiety regardless of the “shunt” oxidant employed. However, a few notable examples of metalloporphyrin-catalyzed oxidations in which reaction selectivity is oxidant-dependent have appeared, including alkane hydroxylations<sup>4,5</sup> as well as alkene epoxidations.<sup>6–8</sup> These results have been

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interpreted as evidence for the participation of low-valent metal complexes of the iodolylarene<sup>4,7</sup> or peroxide<sup>5,6</sup> terminal oxidant as active oxidizing intermediates. P-450 mutant<sup>9</sup> and kinetic isotope effect<sup>10</sup> studies by Coon, Vaz, Newcomb, and co-workers demonstrated that peroxo–iron(III) species can effect some of the oxidations commonly attributed to the high-valent iron–oxo intermediate, suggesting that multiple active oxidants may exist even in enzymatic systems. An important implication of these findings is that variation of the “shunt” oxidant can alter the catalytic mechanism, thereby providing a potential means of tuning the selectivities of oxidations. Investigations of the selectivity and mechanisms of catalytic oxidations with novel or unusual “shunt” oxidants are clearly warranted.

In 1990 we reported a highly active catalytic system for the oxidation of alkanes based on a manganese tetraarylporphyrin catalyst with sodium chlorite (NaClO<sub>2</sub>) as the terminal oxidant.<sup>11</sup> This system exhibited unprecedented activity for a manganese porphyrin catalyst in cyclohexane oxidation, with >1000 turnover numbers under some conditions and parallel formation of both 2e<sup>−</sup> (alcohol) and 4e<sup>−</sup> (ketone) oxidation products. The apparent production of ketone without the intermediacy of alcohol led us to postulate the involvement of a unique active oxidant, perhaps containing coordinated ClO<sub>2</sub><sup>−</sup>, that is capable of delivering two oxygen atom equivalents. Apart from our initial report and a few instances of its use in P-450 oxygenations,<sup>12</sup> the development of ClO<sub>2</sub><sup>−</sup> as a “shunt” oxidant remains unexplored.

The recent revelations of oxidant-dependent catalytic mechanisms in metalloporphyrin systems have prompted us to revisit the mechanism of catalytic alkane oxidation with chlorite. The previous results suggested that the manganese–porphyrin/ClO<sub>2</sub><sup>−</sup> system could potentially be optimized for selective 4e<sup>−</sup> oxidation reactions, and a thorough understanding of the mechanism is crucial for pursuit of this goal. Herein we present evidence that the oxygenation activity of this system results primarily from free-radical chemistry arising from metal-catalyzed decomposition of chlorite. We also report our discovery that this system can sustain alkane autoxidation even in the absence of air due to an unusual O<sub>2</sub>-generating reaction involving metal-catalyzed decomposition of chlorite.

## Experimental Section

**Materials.** Sodium chlorite (Acros, 80%) was purified by recrystallization from water, giving 97.6% pure material (by

iodometric titration), which was stored in a freezer. Chlorite solutions were prepared in aqueous Na<sub>3</sub>PO<sub>4</sub>/NaHCO<sub>3</sub> buffer (pH = 11, Micro Essential Laboratory, Brooklyn, NY) immediately prior to use. BDTAC<sup>13</sup> (Fluka, anhydrous >99%) was used as received. Other materials were purchased from Aldrich (cyclohexane, 4-*tert*-butylpyridine, CBrCl<sub>3</sub>, Ph<sub>2</sub>NH, Ph-Cl) or Fisher (CH<sub>2</sub>Cl<sub>2</sub>, CH<sub>3</sub>CN), purified by standard procedures,<sup>14</sup> and kept in a freezer or in amber bottles under argon. For CH<sub>2</sub>Cl<sub>2</sub> and cyclohexane, this included washing with concentrated H<sub>2</sub>SO<sub>4</sub>, then NaHCO<sub>3</sub>, prior to distillation. Mn(TDCPP)Cl was prepared by literature methods.<sup>15</sup> Catalyst samples were taken from stock solutions prepared with Mn(TDCPP)Cl samples of at least 5 mg, massed on a Mettler balance with ±0.1 mg accuracy.

**Product Analyses.** Products were analyzed on a Hewlett-Packard 6850 gas chromatograph with a (5% phenyl)-methyl siloxane capillary column (HP5-MS, Agilent Technologies, 0.25 mm i.d. × 30 m) and a flame ionization detector. A chlorobenzene internal standard (1 μL/reaction) was used for quantification, and concentrations were determined using multilevel calibration plots with stock solutions of product standards which approximated experimental concentrations.

**Catalytic Cyclohexane Oxidation (Reference Reaction).** A solution of Mn(TDCPP)Cl (0.13 μmol), 4-*tert*-butylpyridine (13.5 μmol, 2 μL), benzyldimethyltetradecylammonium chloride (BDTAC, 20.1 μmol, 7.4 mg), cyclohexane (740 μmol, 80 μL), and chlorobenzene (GC standard, 1 μL) in 2 mL of 50% CH<sub>3</sub>CN/CH<sub>2</sub>-Cl<sub>2</sub> was added to 5 mL of a 0.5 M solution of NaClO<sub>2</sub> in aqueous buffer (phosphate–bicarbonate, pH = 11) in a round-bottom flask. The biphasic mixture was stirred vigorously, and aliquots were withdrawn for periodic GC analysis.

**Cyclohexane Oxidations under Argon.** Aqueous and organic phases were prepared in separate flasks (same conditions as reference reaction), and additives (CBrCl<sub>3</sub>, TEMPO) were introduced into the organic phase at this point. In the case of CBrCl<sub>3</sub>, 0.2 mL of CH<sub>2</sub>Cl<sub>2</sub> was substituted with CBrCl<sub>3</sub>. The organic layer was degassed by three freeze–pump–thaw cycles and then placed under argon, while the aqueous layer was purged with argon for 15 min by a needle inserted through a Suba-Seal septum (Aldrich). The organic layer was then transferred onto the aqueous layer under argon counterflow using a gastight Sample-Lock syringe. Stirring was commenced, and aliquots were withdrawn from the organic phase through the septum for GC analysis. Argon was purified by passage through a 5 × 100 cm column of Q5 catalyst and 4 Å molecular sieves. Reactions were conducted in darkened hoods and further protected from light with aluminum foil.

**Cyclohexane Oxidation under <sup>18</sup>O<sub>2</sub>.** A 14 mL Schlenk tube containing a stir bar was evacuated on a vacuum line, and 200 Torr of <sup>18</sup>O<sub>2</sub> (ICON, 99% labeled) was admitted from a glass bulb. The organic phase was prepared as in the reference reaction, degassed by three freeze–pump–thaw cycles, and transferred to the Schlenk tube via a gastight Sample-Lock syringe. The aqueous layer was purged with argon for 15 min and then transferred into the Schlenk tube via syringe. An aliquot of the organic phase was withdrawn at 25 min and analyzed immediately using a Hewlett-Packard GC with a HP 5973 mass selective detector.

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- (13) Abbreviations used: TDCPP, *meso*-tetrakis-2,6-dichlorophenylporphyrin; BDTAC, benzyldimethyltetradecylammonium chloride; TEMPO, 2,2,6,6-tetramethyl-1-piperidinyloxy radical; DBMPH, 2,6-di-*tert*-butyl-4-methylphenol; <sup>t</sup>BuPy, 4-*tert*-butylpyridine; (Por), generalized porphyrin dianion.  
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


**UV–Vis Analysis of Mn(TDCPP)Cl + NaClO<sub>2</sub>.** A solution of Mn(TDCPP)Cl (0.05 mg, 10 μM) and 4-*tert*-butylpyridine (1 μL, 1350 μM) in a 1:9 mixture of H<sub>2</sub>O and CH<sub>3</sub>CN (5 mL) was placed in a quartz cuvette capped with a septum. The solution was purged with N<sub>2</sub> by a steel needle inserted through the septum, and an initial UV–visible spectrum was acquired on a Hewlett-Packard 8452A diode array spectrophotometer. Twenty microliters of a 50 mM solution of NaClO<sub>2</sub> (20 equiv/Mn) was added via microsyringe, the cuvette was briefly shaken, and UV–visible monitoring commenced. This procedure was repeated with 60 μL (0.56 mmol) of cyclohexane added. The initial rate of disappearance of the putative Mn–oxo species was estimated by fitting the absorbance of the Soret peak at 432 nm to a first-order exponential decay.

**EPR Analysis of Mn(TDCPP)Cl + NaClO<sub>2</sub>.** A solution of Mn(TDCPP)Cl (2.0 mg, 2.0 μmol), 4-*tert*-butylpyridine (10 μL, 68 μmol), and H<sub>2</sub>O (8 μL) in 270 μL of CH<sub>3</sub>CN was purged with N<sub>2</sub> in a septum-capped vial. A solution of 62 mg of NaClO<sub>2</sub> in 1 mL of H<sub>2</sub>O was purged separately with N<sub>2</sub>. The CH<sub>3</sub>CN solution was syringed into a 3 mm o.d. quartz tube which had been fitted with a septum, evacuated, and backfilled with N<sub>2</sub>. Sixty microliters (41 μmol) of the NaClO<sub>2</sub> solution was then syringed into the tube, the tube was briefly shaken, and the one-phase solution was quickly frozen in liquid N<sub>2</sub>. The EPR spectrum was recorded on a Bruker EMX spectrometer (X-band, 9.399 GHz) at 77 K.

**O<sub>2</sub> Evolution by Mass Spectrometry.** A custom 100 mL flask with one 14/20 ground glass joint and two #9 O-ring joints was set up with one O-ring joint connected to a modified Schlenk line and bubbler, and the second connected via a 1 mm i.d. stainless steel capillary to a mass spectrometric gas analyzer (Stanford Research Systems residual gas analyzer model RGA200). The system was evacuated with a Suba-Seal septum in the 14/20 joint and then placed under a slow, steady stream of argon (780 Torr total pressure). Flask headspace gas was drawn through the capillary and a series of pressure reduction valves to achieve a pressure of  $5 \times 10^{-6}$  Torr in the analyzer. Mass spectrometric signals for N<sub>2</sub>, O<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>, and H<sub>2</sub>O were recorded every 15 s. A small but constant N<sub>2</sub> signal and a noisy O<sub>2</sub> baseline were measured by the analyzer, attributed to argon impurities. Argon-purged aqueous buffer (5 mL), CH<sub>2</sub>Cl<sub>2</sub> (1 mL), and CH<sub>3</sub>CN (1 mL) were introduced via gastight syringe, and the mixture was stirred vigorously until the H<sub>2</sub>O and CH<sub>2</sub>Cl<sub>2</sub> signals had stopped changing. In separate flasks, the chlorite solution (5 mL, 1.0 M) and catalyst solution (0.26 μmol of Mn(TDCPP)Cl, 27 μmol of 4-*tert*-butylpyridine, and 40.2 μmol of BDTAC in 2 mL of 1:1 CH<sub>2</sub>Cl<sub>2</sub>/CH<sub>3</sub>CN) were degassed and placed under argon and then transferred sequentially to the reaction flask in gastight syringes. Upon addition of the catalyst solution, all monitored signals (CH<sub>2</sub>Cl<sub>2</sub>, H<sub>2</sub>O, N<sub>2</sub>) were observed to increase slightly, though their ratios stayed constant, while the O<sub>2</sub> signal increased significantly. The O<sub>2</sub>/N<sub>2</sub> ratio was recorded to follow the time course of O<sub>2</sub> evolution (Expt trace, vide infra). No increase in this ratio or in any signals occurred in an identically performed control experiment with the catalyst omitted from the last added solution (Control trace). To probe the effect of added substrate, the Expt and Control runs were repeated along with a third trial using identical conditions to Expt with 80 μL (0.74 mmol) of cyclohexane added to the organic phase (Expt 2, Figure S1, Supporting Information).

**Gas Buret Measurements.** Twenty milliliters of 0.5 M NaClO<sub>2</sub> in aqueous buffer was placed in a two-neck, 50 mL flask. The catalyst solution (0.51 μmol of Mn(TDCPP)Cl, 54 μmol of 4-*tert*-butylpyridine, and 80.4 μmol of BDTAC in 8 mL of 1:1 CH<sub>2</sub>Cl<sub>2</sub>/CH<sub>3</sub>CN) was placed in a closed-end 90° addition tube that was attached to one neck with a silicone grease seal. The other neck

**Table 1.** Catalytic Turnover Numbers for Cyclohexane Oxidation at 3 h

Conditions	TN <sup>a</sup>		
			
Reference reaction	606	236	27
1 M CBrCl <sub>3</sub> <sup>b,c</sup>	199	13	3
500 equiv. Ph <sub>2</sub> NH	435	201	61
500 equiv. TEMPO <sup>c</sup>	101	55	0
Under Ar, no additive <sup>c</sup>	611	227	181

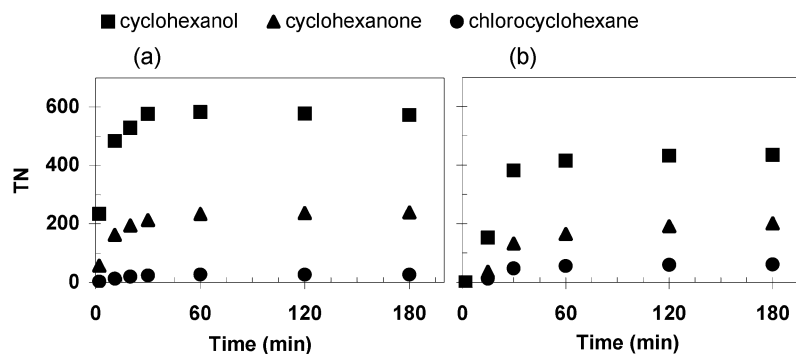
<sup>a</sup> TN = moles of product/mole of catalyst. <sup>b</sup> Bromocyclohexane produced in 161 TN. <sup>c</sup> Carried out under argon.

was fitted with an adapter connected via 2.4 mm i.d. Tygon tubing to a 3 mm o.d. glass tube inserted through a Suba-Seal septum into the top of a water-filled 50 mL buret. The bottom of the buret was connected via tubing to a water-filled leveling bulb to allow pressure equalization. The catalyst and chlorite solutions were mixed by rotating the addition tube and vigorously stirring the resulting mixture, and the increase in headspace volume was measured from the buret over time. Prior to each experiment, a zero point volume was measured by attaching the addition tube containing 8 mL of buffer instead of catalyst solution. The volume increase due to solvent vapor pressure was determined at each time point in a control reaction with catalyst omitted from the organic layer and the chlorite solution replaced with 0.5 M NaCl in buffer. Three replicate experimental and control measurements were obtained, and errors are given at the 95% confidence level.

## Results and Discussion

Mn(TDCPP)Cl<sup>13</sup> proved to be the most suitable catalyst for mechanistic investigations of chlorite oxidations because of its relative resistance to oxidative degradation compared with nonhalogenated tetraarylporphyrins. Catalytic oxidation of cyclohexane in a biphasic aqueous/organic solvent system was examined as the reference reaction (see Experimental Section), with Mn(TDCPP)Cl catalyst present in 0.018 mol % relative to substrate and an excess of NaClO<sub>2</sub> (3.4 equiv/substrate) in the aqueous layer. Under these conditions, cyclohexanol, cyclohexanone, and chlorocyclohexane are produced with turnover numbers (TN) of 606, 236, and 27, respectively (Table 1). Significant oxidation activity is observed only with added nitrogen base (4-*tert*-butylpyridine),<sup>16–18</sup> a phase transfer agent (BDTAC), and buffering of the aqueous layer at pH > 10. The observed turnover numbers exceed those reported for manganese–porphyrin catalyzed cyclohexane oxidations with PhIO,<sup>19</sup> H<sub>2</sub>O<sub>2</sub>,<sup>18</sup> KHSO<sub>5</sub>,<sup>15</sup> or hypochlorite<sup>11</sup> by a factor of 40 or more, with at least double the ketone/alcohol ratio.

- (16) Addition of imidazoles or pyridines has been reported to drastically enhance the catalytic activity of Mn–porphyrins in alkene epoxidations<sup>15,17,18</sup> and alkane hydroxylations,<sup>11,15,18</sup> presumably by activating the “shunt” oxidant through a trans-axial ligand effect.
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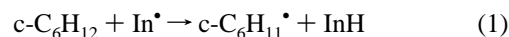
**Figure 1.** Turnover numbers vs time for cyclohexane oxidation with  $\text{ClO}_2^-$  catalyzed by  $\text{Mn}(\text{TDCPP})\text{Cl}/\text{BuPy}$ : (a) reference reaction; (b) with 500 equiv of  $\text{Ph}_2\text{NH}$ . First data point is at 2 min.

Monitoring the time course of the reaction revealed that the catalysis proceeds in a rapid “burst” in which 35% of the oxidation occurs within 2 min (Figure 1a), followed by gradual loss of activity over  $\sim 2$  h concomitant with catalyst bleaching. Initial spiking of the reaction mixture with a quantity of cyclohexanol equivalent to that produced in 2 min (250 equiv/catalyst) results in only a minor increase in cyclohexanone TN from 57 to 66 after 2 min. This confirms our previous proposal that ketone is not formed by stepwise two-electron oxidations, since at least a doubling of the cyclohexanone TN should result in the latter experiment if ketone is produced exclusively by oxidation of alcohol. 4-Methylcyclohexane gives a similar result (11 TN 4-methylcyclohexanone after 2 min with 250 equiv added) and does not inhibit cyclohexane oxidation.

New insight into the catalytic mechanism comes from radical trapping experiments, which implicate the involvement of both carbon-centered and oxygen-centered radicals in the cyclohexane oxidation system. Addition of 1 M  $\text{CBrCl}_3$  under careful exclusion of air almost completely shuts down ketone formation, reduces cyclohexanol formation by 67%, and produces 161 TN of bromocyclohexane. This provides strong evidence for the intermediacy of cyclohexyl radicals.<sup>20,21</sup> In reactions under air, addition of 500 equiv/catalyst of  $\text{Ph}_2\text{NH}$ , an efficient scavenger of alkylperoxyl radicals,<sup>21–23</sup> completely suppresses cyclohexane oxidation for the first few minutes, after which catalysis resumes to give cyclohexanol and cyclohexanone in a similar ratio to the reference reaction and with 25% fewer TN (Figure 1b). The resumption of catalytic activity corresponds roughly to the time ( $\sim 5$  min) when 500 TN of cyclohexane oxidation are attained in the reference reaction.<sup>24</sup> Additional evidence for radical processes

comes from inhibition of cyclohexane oxidation by the carbon-radical trap TEMPO and increased amounts of chlorocyclohexane side product in reactions with oxygen excluded (Table 1).

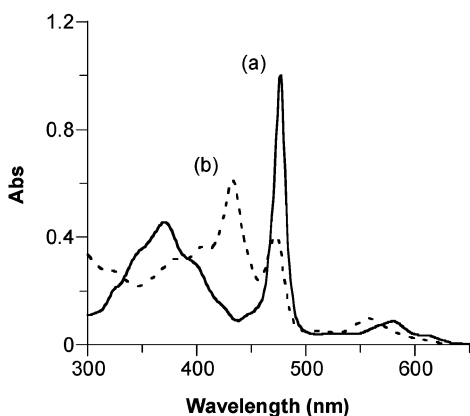
The preceding evidence points to an autoxidation-type mechanism involving initiation to form cyclohexyl radicals (eq 1),  $\text{O}_2$  trapping to form cyclohexylperoxyl radicals (eq 2), and combination/disproportionation to form alcohol and ketone (eq 3). This type of mechanism is prevalent in metal-catalyzed hydrocarbon oxidations using molecular oxygen<sup>23,27</sup> and has been implicated in  $\text{Fe}^{\text{II}}(\text{Por})$  catalyzed examples.<sup>28</sup>



The radical trapping results do not rule out the possibility of a manganese–oxo intermediate which could produce some of the alcohol product via a “rebound” mechanism involving transient, caged cyclohexyl radicals.<sup>29</sup> Addition of 20 equiv of  $\text{NaClO}_2$  to a solution of  $\text{Mn}(\text{TDCPP})\text{Cl}$  (0.01 mM) and 4-*tert*-butylpyridine (1.4 mM) in 10%  $\text{H}_2\text{O}/\text{CH}_3\text{CN}$  results in appearance of a new Soret peak at 432 nm in the visible spectrum (Figure 2), consistent with a high-valent (Por) $\text{Mn}$ –oxo;<sup>30,31</sup> the EPR spectrum of a similarly prepared solution exhibits signals at  $g \sim 4$  and  $g \sim 2$  characteristic of  $\text{Mn}^{\text{IV}}$ .<sup>30,32</sup> Participation of this species or a more reactive  $\text{Mn}^{\text{V}}$ –oxo<sup>31</sup>

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- (24) We previously reported<sup>11</sup> that the radical scavenger DBMPH does not significantly affect product yield or distribution in this system, and this was confirmed under the present conditions using 100–500 equiv DBMPH/ $\text{Mn}$ .  $\text{CyOO}^\bullet$  is scavenged more slowly by DBMPH ( $1 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ )<sup>25</sup> than by  $\text{Ph}_2\text{NH}$  ( $3 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ ),<sup>26</sup> suggesting that DBMPH may be consumed in side reactions with  $\text{ClO}_2^-$  or its decomposition products.

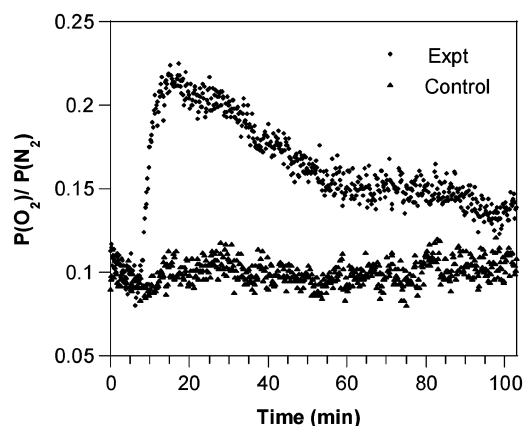
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**Figure 2.** UV-visible spectrum of Mn(TDCPP)Cl ( $\sim 10 \mu\text{M}$ ) in 1:9  $\text{H}_2\text{O}/\text{CH}_3\text{CN}$  before (a) and immediately after (b) addition of 20 equiv of  $\text{NaClO}_2$ .

in cyclohexane hydroxylation would be consistent with chlorite reactivity in P-450 oxygenations<sup>12</sup> and electrocatalytic studies with metalloporphyrins,<sup>33</sup> and might explain the lack of complete suppression of cyclohexanol production in the presence of  $\text{CBrCl}_3$ . However, it is likely that a large fraction of the oxidation in the present system depends on *freely diffusing* cyclohexylperoxyl radicals given the following considerations: (1) added cyclohexane does not accelerate the disappearance ( $k = 4 \times 10^{-4} \text{ s}^{-1}$ ) of the putative (Por)Mn<sup>IV</sup>=O absorbance at 432 nm; (2)  $\text{Ph}_2\text{NH}$  reacts rapidly with oxygen-centered rather than carbon-centered radicals;<sup>21</sup> (3) cyclohexane oxidation performed under  $^{18}\text{O}_2$  (200 Torr) showed significant incorporation (9%) of  $^{18}\text{O}$  into both alcohol and ketone products.

An important question is the identity of the radical initiator. The lack of an induction period and the absence of oxidation without catalyst present require that the initiating species be produced rapidly by reaction of chlorite with the Mn(Por) catalyst. One-electron oxidation of  $\text{ClO}_2^-$  to the radical  $\text{ClO}_2$  ( $E^\circ = 0.936 \text{ V}$ ) via inner-sphere electron transfer to certain transition metal ions is known to be rapid,<sup>34</sup> even in cases with unfavorable thermodynamics such as  $\text{Fe}^{\text{III}}$  ( $E^\circ = 0.77 \text{ V}$ ).<sup>35</sup> Hydrogen atom abstraction by  $\text{ClO}_2$  has been observed for benzylic alcohols,<sup>36</sup> but this seems unlikely in the present case because H atom abstraction from Cy-H should be quite endergonic ( $\Delta G^\circ \approx +14.7 \text{ kcal/mol}$ ).<sup>37</sup> Furthermore, no traces of  $\text{ClO}_2$  could be observed spectroscopically in either reaction phase ( $\epsilon = 1250 \text{ M}^{-1} \text{ cm}^{-1}$  at 359 nm).<sup>34</sup> Other possible initiators are  $\text{Cl}(\text{II})$ , which has been postulated in several metal-catalyzed  $\text{ClO}_2^-$  decompositions,<sup>34</sup> and  $\text{Cl}^\bullet$ , which is produced in photochemical decompositions of  $\text{ClO}_2$ <sup>38</sup> and possibly in acid-catalyzed  $\text{ClO}_2^-$  degradation.<sup>39</sup> Although no reports of  $\text{Cl}^\bullet$  formation by metal-catalyzed



**Figure 3.**  $\text{O}_2/\text{N}_2$  ratios in mass spectrometric detection of headspace gases in the biphasic reaction of Mn(TDCPP)Cl/BuPy with  $\text{ClO}_2^-$  (Expt) and Control with catalyst omitted. Injection of catalyst (or blank) solution was at 6 min.

decomposition of  $\text{ClO}_2^-$  or  $\text{ClO}_2$  have appeared,  $\text{Cl}^\bullet$  is thermodynamically competent to abstract  $\text{H}^\bullet$  from  $\text{Cy-H}$ ,<sup>40</sup> and the observed initial turnover frequency of 28 TN/min for ketone production requires a pseudo-first-order rate constant of only  $\sim 10^{-4} \text{ s}^{-1}$  for  $\text{Cl}^\bullet$  production from  $\text{ClO}_2^-$ .<sup>41</sup> The noted complexity of  $\text{ClO}_2^-/\text{I}^-$  oscillating reaction,<sup>42</sup> may render definitive identification of the initiator in this system quite challenging, and such a task is beyond the scope of this study.

Termination in autoxidations of secondary alkanes occurs primarily by a Russell-type bimolecular reaction of two alkylperoxyl radicals (eq 3) when  $p(\text{O}_2) > 100 \text{ Torr}$ ,<sup>27,43</sup> as is the case in the reference reaction. However, reactions under argon showed essentially no difference in alcohol and ketone TN (Table 1, last entry), demonstrating that termination does not depend on exogenous  $\text{O}_2$ . Mass spectrometric analysis of headspace gases revealed that  $\text{O}_2$  is *catalytically produced in this system* (Figure 3). Precedent for  $\text{O}_2$  formation by catalytic decomposition of  $\text{ClO}_2^-$  (eq 4) exists in recent reports of a heme-containing chlorite dismutase enzyme<sup>44</sup> in perchlorate-reducing bacteria.<sup>45</sup> This unusual reaction provides an intriguing parallel to known  $\text{O}_2$ -evolving disproportionations of peroxidic reagents by heme catalase models (with  $\text{H}_2\text{O}_2$ )<sup>46</sup> and some alkane oxidation catalysts (with  $\text{RO}_2\text{H}$ ).<sup>47</sup> However, it is remarkable in being a rare

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(41) Assuming propagation by  $\text{CyOO}^\bullet$  is slow,  $d[\text{ketone}]/dt = 1/2k_{\text{init}}[\text{ClO}_2^-]$ .<sup>27</sup>  $[\text{Mn}(\text{TDCPP})\text{Cl}]$  is assumed constant at  $61 \mu\text{M}$ .

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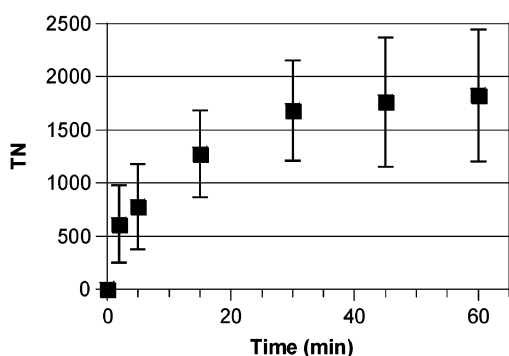
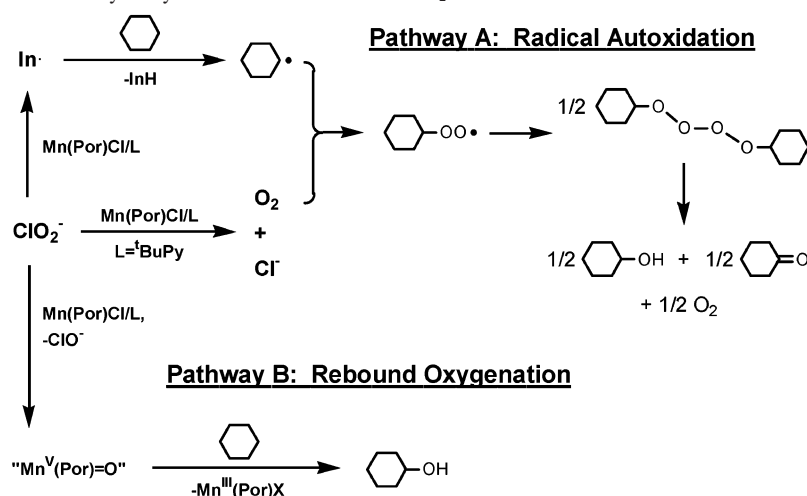
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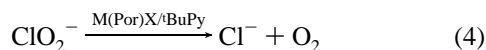
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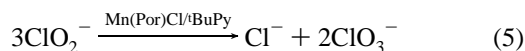
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**Scheme 1.** Two-Path Scheme for Catalytic Cyclohexane Oxidation with  $\text{ClO}_2^-$ **Figure 4.** Turnover numbers of catalytic  $\text{O}_2$  production in the biphasic reaction of  $\text{Mn}(\text{TDCPP})\text{Cl}/\text{BuPy}$  with  $\text{ClO}_2^-$ , measured volumetrically by gas buret. Error bars are at the 95% confidence level.

example of catalytic oxygen–oxygen bond formation with a mechanism that is presently unknown.



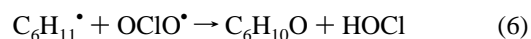
In our initial study,<sup>11</sup> catalytic  $\text{ClO}_2^-$  decomposition was noted and attributed to the disproportionation shown in eq 5. This reaction may occur parallel to the  $\text{O}_2$ -forming disproportionation in eq 4, but it cannot contribute to the observed alkane oxygenation since  $\text{ClO}_3^-$  is completely inactive as an oxidant in this system.



Because the mass spectrometric technique used to identify  $\text{O}_2$  evolution did not allow quantification of the amount produced, catalytic disproportionation of  $\text{ClO}_2^-$  was examined in a closed system attached to a gas buret. These measurements revealed that  $\text{O}_2$  is evolved in the  $\text{ClO}_2^-/\text{Mn}(\text{TDCPP})\text{Cl}/\text{BuPy}$  system in 1800 ( $\pm 600$ ) TN in 1 h, with 610 ( $\pm 360$ ) TN within 2 min (Figure 4). This should be sufficient to produce a  $p(\text{O}_2)$  of 120 Torr within 2 min in the 3 mL headspace of a typical reaction, resulting in an  $\text{O}_2$  concentration high enough to sustain autoxidation with Russell termination.

The relatively small (9%) incorporation of  $^{18}\text{O}$  into oxygenated products in the reaction under 200 Torr of  $^{18}\text{O}_2$

is a point that needs to be addressed. One plausible explanation is that rapid oxygen evolution from  $\text{ClO}_2^-$  results in a higher-than-equilibrium concentration of  $^{16}\text{O}_2$  in solution. Alternatively, some ketone-forming termination could occur by reaction of cyclohexyl radicals with catalytically evolved  $\text{ClO}_2$  (eq 6). The latter reaction has a greater thermodynamic driving force than Russell termination,<sup>48</sup> and a similar termination has been implicated in benzylic C–H oxidations with  $\text{ClO}_2$ .<sup>36</sup> However, the former scenario is more likely given that drastically reduced levels of headspace  $\text{O}_2$  were detected in experiments with added cyclohexane compare to those without (Figure S1), consistent with rapid consumption of evolved  $\text{O}_2$  in autoxidation processes.



On the basis of the preceding evidence, cyclohexane oxygenation by the  $\text{Mn}(\text{Por})\text{Cl}/\text{BuPy}/\text{ClO}_2^-$  catalyst system is best explained by a two-path scheme (Scheme 1). In pathway A, the function of the manganese–porphyrin complex is to catalytically decompose  $\text{ClO}_2^-$  into both  $\text{O}_2$  and an unidentified radical initiator, leading to  $\text{CyOO}\cdot$  radicals which dimerize and form cyclohexanol and cyclohexanone via Russell termination. Product formation by metal-catalyzed decomposition of  $\text{CyOOH}$  is also a possibility,<sup>28</sup> but it is unlikely to be significant in this scheme provided that production of the initiator is faster than  $\text{H}\cdot$  abstraction from cyclohexane by  $\text{CyOO}\cdot$ .<sup>27</sup> Some cyclohexanol also arises from a “rebound” pathway (pathway B) involving a high-valent manganese–oxo intermediate formed by oxygen atom transfer from  $\text{ClO}_2^-$ . We postulate a transient  $\text{Mn}^{\text{V}}$ -oxo based on the lack of reactivity of the observed  $\text{Mn}^{\text{IV}}$ -oxo species toward cyclohexane. Pathway B is necessary to account for the excess of cyclohexanol over cyclohexanone and the formation of significant amounts of alcohol even in the presence of 1 M  $\text{CBrCl}_3$ .

The above scheme does not address the chlorocyclohexane side product, which may result from reaction of cyclohexyl

(48)  $\Delta G^\circ = -113$  kcal/mol for  $\text{C}_6\text{H}_{11}\cdot + \text{ClO}_2 \rightarrow \text{C}_6\text{H}_{10}\text{O} + \text{HOCl}$ ;  $\Delta G^\circ = -71$  kcal/mol for  $\text{C}_6\text{H}_{11}\cdot + 1/2\text{O}_2 \rightarrow 1/2\text{C}_6\text{H}_{11}\text{OH} + 1/2\text{C}_6\text{H}_{10}\text{O}$ ; see Supporting Information.

radicals with  $\text{CH}_2\text{Cl}_2$  or from a  $\text{ClO}_2^-$ -derived chlorinating agent. Catalytic cyclohexane oxidation performed under argon in 10%  $\text{H}_2\text{O}/\text{CH}_3\text{CN}$  with 0.24 equiv  $\text{NaClO}_2$ /substrate still produces significant chlorocyclohexane (30 TN, along with 99 TN cyclohexanol and 84 TN cyclohexanone), indicating that the latter scenario accounts for at least some of the chloroalkane side product. This is consistent with reports of chlorination reactions catalyzed by heme peroxidases in the presence of  $\text{ClO}_2^-$ ,<sup>49</sup> which are thought to proceed via catalytic decomposition of  $\text{ClO}_2^-$  into  $\text{ClO}^-$  or  $\text{ClO}_2$ .<sup>50</sup>

### Conclusion

The present evidence clearly shows that rapid oxidation of secondary alkanes by the chlorite/ $\text{Mn}(\text{Por})\text{Cl}/^t\text{BuPy}$  catalyst system depends largely on its ability to initiate and sustain free-radical autoxidation. The formation of ketone without the intermediacy of alcohol is readily explained if most of the cyclohexanone is generated by free-radical chemistry. This system illustrates that the nature of the “shunt” oxidant can dramatically affect the mechanism of a metal-catalyzed hydrocarbon oxidation reaction, in this case

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leading to autoxidation chemistry even under apparently anaerobic conditions. Thus, careful mechanistic studies are critically important, especially in catalyst systems employing oxidants such as  $\text{ClO}_2^-$  that are prone to disproportionation or radical decomposition.<sup>51</sup> In addition, we have discovered that metal-catalyzed production of  $\text{O}_2$  from  $\text{ClO}_2^-$  is facile in this system, providing an unusual example of catalytic oxygen–oxygen bond formation.

**Acknowledgment.** This material is based upon work supported by the National Science Foundation under Grant No. CHE0131206. We thank Peng Chen (Solomon group) for providing a sample of  $^{18}\text{O}_2$ . David Hodson of Freshminds Design (Stillwater, OK) is acknowledged for assistance in designing the cover artwork.

**Supporting Information Available:** Thermochemical calculations supporting discussions in the text; plot of mass spectrometric detection of headspace  $\text{O}_2$  in catalytic  $\text{ClO}_2^-$  decomposition with cyclohexane present; EPR spectrum of putative  $(\text{Por})\text{Mn}^{\text{IV}}\text{-oxo}$  species. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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