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Article

Olefin Epoxidation by Alkyl Hydroperoxide with a Novel Cross-Bridged Cyclam Manganese Complex: Demonstration of Oxygenation by Two Distinct Reactive Intermediates

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Olefin epoxidation provides an operative protocol to investigate the oxygen transfer process in nature. A novel manganese complex with a cross-bridged cyclam ligand, $Mn^{IV}(Me_2EBC)(OH)_2^{2+}$ (Me_2EBC = 4,11-dimethyl-1,4,8,-11-tetraazabicyclo[6.6.2]hexadecane), was used to study the epoxidation mechanism with biologically important oxidants, alkyl hydroperoxides. Results from direct reaction of the freshly synthesized manganese(IV) complex, $[Mn(Me_2EBC)(OH)_2](PF_6)_2$, with various olefins in neutral or basic solution, and from catalytic epoxidation with oxygen-labeled solvent, $H_2{}^{18}O$, eliminate the manganese oxo moiety, $Mn^{IV}{=}O$, as the reactive intermediate and obviate an oxygen rebound mechanism. Epoxidations of norbornylene under different conditions indicate multiple mechanisms for epoxidation, and *cis*-stilbene epoxidation under atmospheric $^{18}O_2$ reveals a product distribution indicating at least two distinctive intermediates serving as the reactive species for epoxidation. In addition to alkyl peroxide radicals as dominant intermediates, an alkyl hydroperoxide adduct of high oxidation state manganese(IV) is suggested as the third kind of active intermediate responsible for epoxidation. This third intermediate functions by the Lewis acid pathway, a process best known for hydrogen peroxide adducts. Furthermore, the *tert*-butyl peroxide adduct of this manganese(IV) complex was detected by mass spectroscopy under catalytic oxidation conditions.

Introduction

Heme- and non-heme-containing metal complexes have long attracted interest for two reasons: their contributions to the understanding of the enzyme mechanisms of, for example, cytochromes P-450 and insights into mechanisms of oxygenation that are useful in industry.[1] In the case of the P-450 enzymes, it is commonly accepted that, iron−oxo species, $Fe^{IV}{=}O^{+\cdot}$, transfer oxygen atoms to substrates by an *oxygen rebound mechanism* in the key mechanistic step in hydroxylation and epoxidation reactions.[2] In reactions using such chemical oxidants as PhIO, NaClO, and peracids, it has also been established that the metal−oxo species are the reactive intermediates for catalytic epoxidations mediated by iron, manganese, and chromium porphyrin and salen complexes. The definitive experiments establishing these metal−oxo species as the reactive intermediates include the use of isotopically labeled water, $H_2{}^{18}O$, and involve two sequential reactions. In the first reaction, the ^{18}O label confirmed the equilibration of the metal−oxo moiety with the labeled water, $H_2{}^{18}O$, to form the labeled catalyst intermediate $LM{=}^{18}O$ (L = porphyrin). In the second step, the labeled metal complex $LM{=}^{18}O$ was identified as the source of the oxygen atom that is transferred to the olefin, thereby supporting the oxygen rebound mechanism (Scheme 1).[3,4]

The situation has been less clear for the cases in which biologically important oxidants, hydrogen peroxide and alkyl

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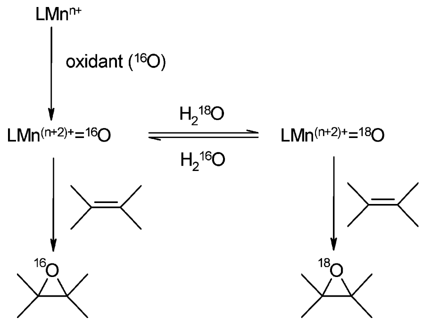
Scheme 1



hydroperoxide, were used as the terminal oxidants. Heterolysis and homolysis of the O−O bond become competitive with oxygen atom transfer under varying reaction conditions. Heterolytic two-electron cleavage of the O−O bond leads to formation of highly reactive metal−oxo species, $LFe^{IV}{=}O^{+\cdot}$ and $LMn^{V}{=}O$, which serve as the reactive intermediates in synthetic systems, as well as in P-450 enzymes. On the other hand, one-electron homolytic cleavage leads to formation of $LFe^{IV}{=}O$ or $LMn^{IV}{=}O$ species, which are less active or inactive as oxygen transfer reagents. Formation of these tetravalent metal−oxo species initiates predominant radical reactions. In protic solvents, iron porphyrin complexes are found to catalyze acid-assisted heterolytic cleavage of the O−O bond, while homolytic cleavage of the O−O bond occurs in neutral aqueous media and in aprotic solvents.[5,6] In the presence of imidazole or other heterocyclic bases, iron and manganese porphyrin complexes catalyze heterolytic cleavage of the O−O bond to form $Fe^{IV}{=}O^{+\cdot}$ and $Mn^{V}{=}O$ in both aqueous and aprotic solvents.[6a,7]

Recent investigations in these laboratories have shown that the hydrogen peroxide adduct of the oxidized manganese complex can transfer an oxygen atom directly to the substrate from the peroxide molecule by a Lewis acid pathway, rather than involving a redox change at the metal atom.[8] This recent result has confirmed the suggestions that Mn^{4+} and Fe^{3+} complexes might react in the same way as early transition metal ions, such as titanium(IV), vanadium(V), tungsten(IV), molybdenum(IV), and rhenium(VII), for which the accepted intermediate is the metallo-organic peracid,[9] in this case, $Mn^{n+}OOH$.[8] Similar transition metal species have been detected and proposed to serve as the active intermediates for oxygen transfer in hydroxylation and epoxidation processes.[10] The iodosylbenzene (PhIO) adduct of a manganese complex has been proposed as the reactive intermediate for epoxidation,[11] in a pathway competing with the well-known manganese−oxo intermediates. Our recent work clearly demonstrated that the hydrogen peroxide adduct of a novel manganese(IV) complex, $Mn^{IV}(Me_2EBC)(O)(OOH)^+$ (Me_2EBC = 4,11-dimethyl-1,4,8,11-tetraazabicyclo[6.6.2]hexadecane), serves as the main reactive intermediate for olefin epoxidation using the biologically important oxidant, hydrogen peroxide, as the terminal oxidant.[8] Previous to the work reported here, there has been no demonstration that the equally important family of oxidants, alkyl hydroperoxides, form adducts with manganese that are capable of direct oxygen transfer to olefinic double bonds by heterolytic O−O bond cleavage. Herein, we report our new results for olefin epoxidation using *tert*-butyl hydroperoxide as the terminal oxidant with the $Mn(Me_2EBC)Cl_2$ catalyst. Our data reveal multiple mechanisms for olefin epoxidation. In addition to the radical intermediates that predominate in this oxidation reaction, the alkyl hydroperoxide adduct of manganese(IV) also transfers oxygen directly to olefins by a Lewis acid pathway.

Experimental Section

$Mn^{II}(Me_2EBC)Cl_2$ (+99.9%) was generously supplied by the Procter and Gamble Company. $[Mn^{III}(Me_2EBC)Cl_2]PF_6$ and $[Mn^{IV}(Me_2EBC)(OH)_2](PF_6)_2$ were synthesized as reported.[12,13] Reagents containing ^{18}O were purchased from Isotope Services.

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Other reagents were purchased from Aldrich or Lancaster. Elemental analysis was performed by Quantitative Technologies, Inc. Mass spectra were measured by the Analytical Service of The University of Kansas on a VG ZAB HS spectrometer equipped with a xenon gun.

Quantitative Epoxidation of Norbornylene with [Mn^{IV}(Me$_2$EBC)(OH)$_2$](PF$_6$)$_2$·H$_2$O. In a typical reaction, 0.3255 g (0.50 mmol) of [Mn^{IV}(Me$_2$EBC)(OH)$_2$](PF$_6$)$_2$ ·H$_2$O was dissolved in a 5 mL of acetone/water (ratio 4:1). After 1 mmol of norbornylene was added, the reaction mixture was stirred in a controlled atmosphere wet box at room temperature for at least 2 days in the absence of oxygen. Quantitative analysis of products was performed using gas chromatography.

Catalytic Epoxidation of Olefins. In a typical reaction, a solution of 0.1 mL of 50 mM (0.0050 mmol) Mn^{II}(Me$_2$EBC)Cl$_2$ was prepared in 5 mL of acetone/water (ratio 4:1). After 0.2 mL of 2.5 M (0.50 mmol) norbornylene in acetone was added to the solvent mixture containing the catalyst, 0.34 mL of 70% *tert*-BuOOH (2.65 mmol) was added to produce the reaction. The reaction mixture was stirred for 14 h at room temperature. The quantitative analysis of products was performed using chromatography by the internal standard method, and the identities of the products were confirmed by GC-MS. A parallel experiment without catalyst was run as a control.

Isotope Labeling: Epoxidation with $H_2{}^{18}O$. In a typical reaction, 0.019 g (0.0050 mmol) of Mn(Me$_2$EBC)Cl$_2$ and 0.047 g (0.50 mmol) of norbornylene were added to 1.25 mL acetone/water (4:1, ^{18}O, 95 atom %). The reaction was initiated by adding 2.7 mmol of *t*-BuOOH in decane. Then the reaction mixture was stirred for 14 h at room temperature. Product analysis was performed by GC-MS. All determinations were repeated three times to evaluate reproducibility. A parallel experiment with no isotopic labeling was run as a control.

Isotope Labeling: Epoxidation under $^{18}O_2$. In a typical reaction, 5 mL of degassed acetone containing 1.9 mg (0.0050 mmol) of Mn^{II}(Me$_2$EBC)Cl$_2$ and 0.047 g (0.50 mmol) of norbornylene were injected into a 50 mL flask under atmospheric $^{18}O_2$. The reaction was initiated by injecting 0.34 mL of 70% *tert*-BuOOH (2.65 mmol). The reaction mixture was stirred for 14 h at room temperature. Product analysis was performed by GC-MS. All determinations were repeated three times to evaluate reproducibility. A parallel experiment with no isotopic labeling was run as a control.

ESI Mass Spectrometry. An acetone solution of 20 mM Mn(Me$_2$EBC)Cl$_2$ was first treated with 2 equiv of AgPF$_6$ to remove chloride. The resulting solution (1 mL) was mixed with excess 70% TBHP to initiate the oxidation, and the reaction mixture was examined by the ESI mass spectrometer in minutes. Skipping the removal of chloride prior to TBHP addition produced a weaker signal attributable to Mn(Me$_2$EBC)(O)(*t*-OOBu)$^+$. The mass spectrometer used in these experiments is the instrument identified at the beginning of the Experimental Section.

Results and Discussion

Attempted Direct Epoxidation of Olefins Using [Mn^{IV}(Me$_2$EBC)(OH)$_2$](PF$_6$)$_2$. The manganese(II) complex of a cross-bridged cyclam ligand, 4,11-dimethyl-1,4,8,11-tetraazabicyclo[6.6.2]hexadecane (Me$_2$EBC), Mn^{II}(Me$_2$EBC)Cl$_2$, has been explored extensively as a potential catalyst for selective oxidation reactions, and its novel behavior in epoxidation reactions constitutes a significant example of selectivity.[8,12−15] Probing the oxidation mechanism of this catalyst attracted our interest because its potential industrial applications rest on its distinctive selectivity. In the literature, manganese(V)−oxo species[3c,4,16] and, to a lesser extent, manganese(IV)−oxo species[17] are commonly proposed to be the active intermediates for oxygen transfer in reactions mediated by compounds of manganese. Successful synthesis of [Mn^{IV}(Me$_2$EBC)(OH)$_2$](PF$_6$)$_2$ provided the opportunity to determine whether that particular manganese−oxo species can epoxidize olefins directly and provide additional insights into the mechanism of catalytic oxidations with hydrogen peroxide and alkyl hydroperoxides. We specifically address the question “does this catalytic reaction proceed by the oxygen rebound mechanism as described in the literature for other manganese systems?” Our recent publication demonstrated that, when hydrogen peroxide is used as the terminal oxidant, the hydrogen peroxide adduct of the manganese(IV) complex, Mn^{IV}(Me$_2$EBC)(O)(OOH)$^+$, serves as the main reactive intermediate for olefin epoxidation.[8] Surprisingly, that critical intermediate was not the expected manganese(IV)−oxo or manganese(V)−oxo species. Here, we address the same question but using another important oxidant, *tert*-butyl hydroperoxide, as the terminal oxidant. [Mn^{IV}(Me$_2$EBC)(OH)$_2$](PF$_6$)$_2$ is conveniently synthesized by oxidation of Mn^{II}(Me$_2$EBC)Cl$_2$ with hydrogen peroxide in the presence of NH$_4$PF$_6$ in aqueous solution, and the structure has been confirmed by X-ray analysis (Figure 1).[12]

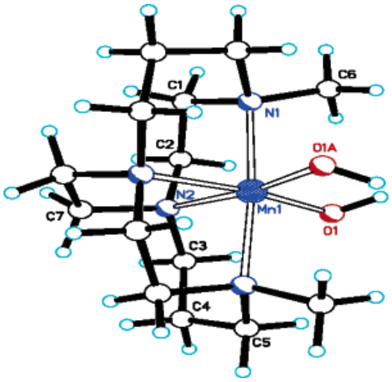

Figure 1. X-ray crystal structure of [Mn^{IV}(Me$_2$EBC)(OH)$_2$]$^{2+}$. Selected bond lengths (Å) and angles (deg): Mn1−O1 = 1.811(2), Mn1−N1 = 2.110(3), Mn1−N2 = 2.090(2), O1−Mn1−O1A = 97.44(14), N1−Mn1−N2(#1) = 171.90(10).[12]

Direct reaction between substrates such as norbornylene, styrene, and *cis*-stilbene and either the manganese(III) or the

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manganese(IV) complex does not occur in solution even after the mixture is left standing for days at room temperature. Under these conditions, no norbornylene is consumed, and no epoxide can be detected. Clearly the Mn^{IV} complex alone is not capable of epoxidation of norbornylene even though substantial amounts of $[Mn^{IV}(Me_2EBC)(OH)_2]^{2+}$, whose p$K_a$ is 6.86, would be expected to exist as the oxo complex $[Mn^{IV}(Me_2EBC)(O)OH]^+$.

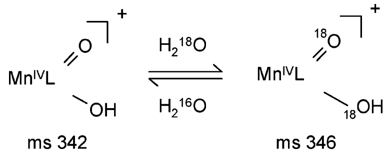
Because the manganese(IV) complex is unstable in base, slowly degrading to $Mn^{III}(Me_2EBC)$ species, a disproportionation mechanism for decompostion was suspected. The erstwhile Mn(V) complex might well be unstable and decompose spontaneously.

$$2\text{Mn(IV)} \leftrightarrow \text{Mn(III)} + \text{Mn(V)} \rightarrow \text{decompose}$$

As stated earlier, $Mn^V{=}O$[3c,4,16] (and in a few cases $Mn^{IV}{=}O$)[17] is frequently proposed to be the active intermediate for epoxidation, and several $Mn^V{=}O$ complexes have been isolated from solution and characterized, with the disappointing result that these particular manganese(V) complexes are inactive for direct oxygen transfer from manganese(V)=O to olefins.[18] We have shown that $[Mn^{IV}(Me_2EBC)(OH)_2]^{2+}$ does not epoxidize olefins, for example, norbornylene. The possibility still exists that a $Mn^V{=}O$ derivative, produced by disproportionation in basic solution, might reveal its presence by epoxidation of a substrate. We suggest that the presence or absence of manganese(V) should be distinguished by experiments designed to produce the epoxidation of norbornylene by the manganese(V) formed during disproportionation of Mn(IV) in basic media. Those experiments were conducted: no epoxide product could be detected, and no conversion of norbornylene was observed upon dissolution of the manganese(IV) complex in basic solution in the presence of norbornylene.

Further, treatment of the Mn(II), Mn(III) or Mn(IV) complexes with various oxidants, such as PhIO, H_2O_2, and *t*-BuOOH, in aqueous solution, failed to provide evidence supporting the existence of $Mn^V{=}O$ species. In fact, $[Mn^{IV}(Me_2EBC)(OH)_2]^{2+}$ has been confirmed to be the dominant species by UV−vis spectroscopy. In this context, it should be recalled that the synthesis of $[Mn^{IV}(Me_2EBC)(OH)_2](PF_6)_2$ was performed by oxidation of $Mn^{II}(Me_2EBC)Cl_2$ with aqueous H_2O_2.[12] The presence in the main ligand of π-systems that transmit electron density to the $Mn^V{=}O$ moiety, as in the cases of porphyrins and salen ligands, may be necessary to stabilize those $Mn^V{=}O$ species. From that perspective, it is not surprising that stable $Mn^V{=}O$ species do not exist with these bridged cyclam ligands since they contain only tertiary nitrogen donors and no π-electron systems except for the hydroxo and oxo ligands.

Scheme 2



Probing the Epoxidation Mechanism with $H_2^{18}O$. Isotopically labeled water, $H_2^{18}O$, is used in a well-established protocol to implicate a metal−oxo intermediate in the oxygen transfer process of, for example, epoxidation.[4] For metal−oxo species that equilibrate with the solvent water, when ^{18}O-labeled oxygen is found in the epoxide product, it is generally concluded that a metal−oxo function performed the oxygen-transfer process.

The basis of this conclusion is the usual rapid exchange of ^{18}O between $H_2^{18}O$ and metal−oxo groups. In the present work, the exchange of ^{18}O was observed between the $Mn^{IV}{=}O$ species containing the cross-bridged cyclam and $H_2^{18}O$ (Scheme 2). When $[Mn^{IV}(Me_2EBC)(OH)_2]^{2+}$ was dissolved in $H_2^{18}O$ (95% ^{18}O), the original MS peak for $[Mn^{IV}(Me_2EBC)(O)(OH)]^+$ at *m*/*z* 342, observed for normal aqueous solutions, disappeared, and a new MS peak for $[Mn^{IV}(Me_2EBC)(^{18}O)(^{18}OH)]^+$ appeared immediately at *m*/*z* 346. This confirmed the ^{18}O exchange between the bridged cyclam manganese−oxo complex and water. Furthermore, this kind of rapid ^{18}O exchange has also been demonstrated by low-frequency resonance Raman spectroscopy (rR).[12]

The ^{18}O-labeling experiment for the oxygen-transfer reaction used *t*-BuOOH in decane as the terminal oxidant for the epoxidation of norbornylene with $[Mn^{II}(Me_2EBC)(OH_2)_2]^{2+}$ in 4:1 acetone/$H_2^{18}O$ (95% ^{18}O). The product analysis by GC-MS shows that no ^{18}O from $H_2^{18}O$ is introduced into the epoxide product. The results of these ^{18}O-labeling experiments strongly support the conclusion that manganese−oxo or −hydroxo species, including $Mn^{IV}(Me_2EBC)(OH)_2^{2+}$, $Mn^{IV}(Me_2EBC)(O)(OH)^+$, and $Mn^V(Me_2EBC)(O)_2^+$, are not responsible for the oxygen-transfer process in this manganese complex-catalyzed reaction. This is consistent with the results described in the preceding section involving the failed attempt at direct epoxidation of norbornylene with $[Mn^{IV}(Me_2EBC)(OH)_2]^{2+}$ in aqueous solution, as well as additional experiments seeking to demonstrate the disproportionation of that complex with concurrent generation of what might have been a more reactive Mn^V complex.

Catalytic Epoxidation Implicates Multiple Mechanisms. Catalytic epoxidation of various olefins using *t*-BuOOH as the terminal oxidant with $Mn(Me_2EBC)Cl_2$ as the catalyst was performed in an acetone/water solvent mixture (ratio 4:1) in the presence of air for 14 h at room temperature. The results are summarized in Table 1. The color of the reaction mixture turns to purple upon addition of *t*-BuOOH, and UV−vis spectrophotometry shows that the manganese is present predominantly in the tetravalent state. No dioxygen evolution was observed under the reaction conditions explored in our studies. The reaction of cyclohexene produces

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Table 1. Epoxidation of Various Olefins by $Mn(Me_2EBC)Cl_2$ with *t*-BuOOH[a]

substrate	product	yield (%)
cyclohexene	cyclohexene oxide	1.4
	cyclohexen-1-one	32.3
styrene	styrene oxide	4.8
	benzaldehyde	24
norbornylene	norbornylene oxide	36.0
cis-stilbene	*cis*-stilbene oxide	0.8
	trans-stilbene oxide	13.5
	benzaldehyde	6.1

[a] Reaction conditions: solvent, acetone/water (4:1), catalyst 1 mM, olefin 0.1 M, 0.53 M *t*-BuOOH, room temp, 14 h, yield determined by GC with internal standard.

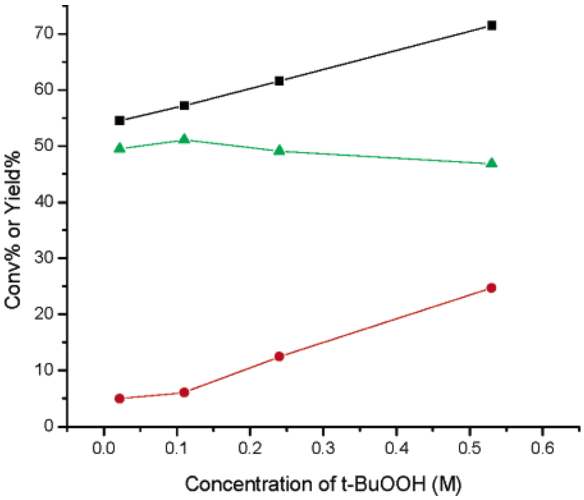

Figure 2. Influence of concentration of oxidant on norbornylene epoxidation: ■, conversion of norbornylene; ●, yield of norbornylene epoxide; ▲, yield of other products. Reaction conditions: 4:1 acetone/H_2O, 1 mM catalyst, 0.1 M norbornylene, room temp, 14 h.

Table 2. Oxygen Source in Epoxide (% ^{18}O) for Epoxdation of Norbornylene with $Mn^{II}(Me_2EBC)Cl_2$ and *tert*-Butyl Hydroperoxide (TBHP)

run	oxygen source	incorporation of ^{18}O in norbornylene oxide (%)
1	TBHP/air (blank)	4.4 ± 0.1
2	TBHP/$^{18}O_2$	74.6 ± 2
3[a]	TBHP/$^{18}O_2$	71.8 ± 1.8

[a] TBHP was used in low concentration as initiator as described in literature.[19d]

mainly the allylic hydrogen abstraction product, cyclohexen-1-one (yield 32.3%), along with cyclohexene oxide (yield 1.4%) as the minor epoxidation product. With styrene, the dominant reaction involves C−C bond breaking, yielding benzaldehyde (24%) with only small amounts of styrene oxide (yield 4.8%). *cis*-Stilbene produces mostly *trans*-stilbene oxide (yield 13.5%) and minor amounts of *cis*-stilbene oxide (yield 0.8%) plus a 6.1% yield of benzaldehyde. The reaction mixture also contains unreacted olefin and traces of undetermined oxidation products. These results strongly suggest a dominate radical pathway for this oxidation reaction, as should be expected on the basis of earlier literature reports.[6d,19] Clearly, the manganese complex catalyzes the homolytic cleavage of the O−O bond of *t*-BuOOH to initiate a dominant radical process,.

Table 3. Oxygen Source in Epoxide (% ^{18}O) for Epoxdation of *cis*-Stilbene with $Mn^{II}(Me_2EBC)Cl_2$ and *tert*-Butyl Hydroperoxide (TBHP)

run	oxygen source	incorporation of ^{18}O in *cis*-epoxide (%)	incorporation of ^{18}O in *trans*-epoxide (%)
1	TBHP/air (blank)	1.7 ± 0.3	2.6 ± 1
2	TBHP/$^{18}O_2$	25 ± 0.3	55.1 ± 1

Significantly, the reaction of norbornylene with *t*-BuOOH in the presence of $Mn(Me_2EBC)Cl_2$, provides a relatively high yield of norbornylene oxide (36%), and the results of detailed studies on the effect of oxidant concentration on product distribution are in disagreement with a single radical pathway. In a typical radical process, as described by Pecoraro,[19d] $ROO^{\cdot}$ radicals participate in both hydrogen abstraction and oxygen-atom transfer, while $RO^{\cdot}$ is strictly a hydrogen-abstracting agent. In a kinetic epoxidation process produced solely by this radical process, one can expect the yield of hydrogen abstraction products to increase in proportion with the increase in yield of the epoxidation product. However, such parallel yield increases do not occur during norbornylene epoxidation (Figure 2). As the initial concentration of *t*-BuOOH is increased, the conversion of norbornylene and the yield of epoxide increase, while the total percentage yield of products formed by radical hydrogen abstraction changes very little, apparently decreasing slowly. These results imply multiple oxygen-transfer mechanisms in this manganese/*t*-BuOOH system. That is, in addition to the alkoxy radical initiated by homolytic cleavage of O−O bond of *t*-BuOOH, at least one additional reactive intermediate participates in this olefin epoxidation system. Further, the additional intermediate or intermediates do not include the manganese−oxo species itself.

Mechanistic Insights from Isotopic Labeling of Dioxygen, $^{18}O_2$. As mentioned above, ^{18}O-labeling experiments are commonly used in studies of reaction mechanism to address the origin of oxygen atoms found in oxidation products. For example, isotopic ^{18}O-labeled water, $H_2{}^{18}O$, is used to clarify whether oxygen was incorporated from solvent water into the product by the oxygen rebound mechanism,[4] while isotopic ^{18}O-labeled dioxygen, $^{18}O_2$, is used to address whether a radical process is involved in the reaction.[19d]

To confront this issue, the atmospheric $^{18}O_2$-labeling experiment was conducted, using *t*-BuOOH as the terminal oxidant and $Mn(Me_2EBC)Cl_2$ as the catalyst, during the epoxidation of norbornylene in 4:1 acetone/water (Table 2). The product analysis by GC-MS shows substantial ^{18}O incorporation into norbornylene oxide from $^{18}O_2$ (74.6 ± 2% ^{18}O incorporation vs 4.4 ± 0.1% ^{18}O incorporation in the control experiment),[20] strongly indicating that the dioxygen

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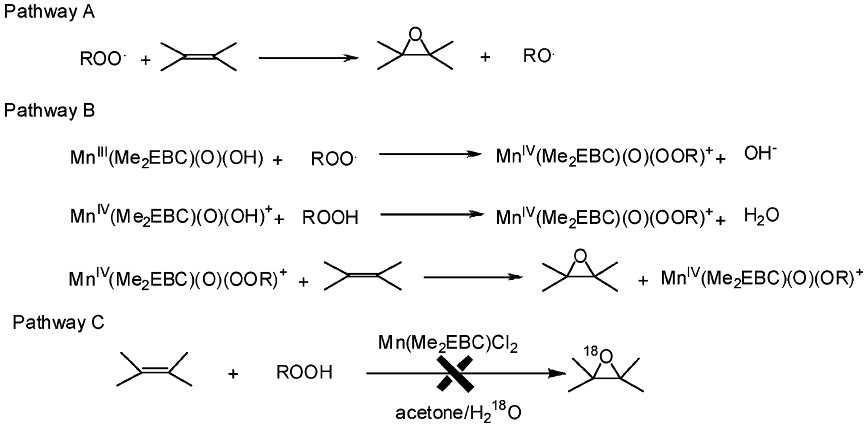
(19) (a) Brill, W. F. *J. Am. Chem. Soc.* **1963**, *85*, 141. (b) Birnbaum, E. R.; Labinger, J. A.; Bercaw, J. E.; Gray, H. B. *Inorg. Chim. Acta* **1998**, *270*, 433. (c) Weiner, H.; Trovarelli, A.; Finke, R. G. *J. Mol. Catal. A: Chem.* **2003**, *191*, 217. (d) Caudle, M. T.; Riggs-Gelasco, P.; Gelasco, A. K.; Penner-Hahn, J. E.; Pecoraro, V. L. *Inorg. Chem.* **1996**, *35*, 3577.

(20) The ^{18}O signal in the control experiment with normal water is a background signal of MS.

Scheme 3. Proposed Mechanisms for Olefin Epoxidation[a]



[a] Pathways B and C have been implicated for the system using Mn(Me_2EBC)Cl_2 and *t*-BuOOH.

oxidation reaction involves a radical process. However, it also reveals that there are two oxygen sources in the epoxide: 74.6 ± 2% of the oxygen comes from atmospheric dioxygen by a radical process and 25.4 ± 2% of the oxygen, from the added oxidant, *t*-BuOOH, either by a radical or a non-radical process. One might argue that this 25.4 ± 2% oxygen could be derived from the *t*-BuOO$^{\cdot}$ radical, either through its direct reaction or through the unlabeled dioxygen, $^{16}O_2$, it produced. The later would simply dilute the labeled dioxygen. In this way, both the *t*-BuOO$^{\cdot}$ radical and its derived dioxygen, $^{16}O_2$, could serve as oxygen sources for ^{16}O-epoxide.

A typical radical reaction has been demonstrated by Pecoraro,[19d] in which cyclohexene oxidation was performed with a small amount of *t*-BuOOH as the initiator and Mn_2-(2-OHsalphen)$_2$ as the catalyst under an $^{18}O_2$ atmosphere. The product analysis showed that the oxygen sources in the cyclohexene oxidation products were exclusively derived from $^{18}O_2$, in general agreement with an exclusively radical oxidation reaction. Our isotopically labeled $^{18}O_2$ experiment for norbornylene oxidation with *t*-BuOOH as the initiator and Mn(Me_2EBC)Cl_2 as the catalyst has also been carried out under conditions identical to those described by Pecoraro. The results reveal that, even though the concentration of *t*-BuOOH is as low as that described in literature, the norbornylene oxide product still contains only 71.8 ± 1.8% ^{18}O incorporation from isotopic dioxygen, $^{18}O_2$, with 28.2 ± 1.8% ^{16}O traceable to the initiator, *t*-BuOOH. This suggests a mechanistic difference between this system and the catalyst system described by Pecoraro. It is concluded that data both from the isotopic labeling of dioxygen and from the previously discussed kinetic analysis require at least two pathways for the olefin epoxidation in this manganese complex-catalyzed reaction. One of these pathways proceeds to the olefin epoxide by the expected peroxy radical mechanism. The other pathway appears to require direct transfer of an oxygen atom from the oxidant, *t*-BuOOH, to the olefin but not by the familiar rebound, since the oxygen has not equilibrated with the water in the solvent.

cis-Stilbene is a frequently used substrate for the study of olefin epoxidation mechanisms because of the stereochemistry associated with the transformation.[11a,16a,21] Unlike other olefins, such as norbornylene, cyclohexene, and styrene, epoxidation of *cis*-stilbene provides two epoxidation products, *cis*-stilbene oxide and *trans*-stilbene oxide. Thus, the study of *cis*-stilbene can provide additional mechanistic information through the simple act of determining the ratio of the cis and trans isomers of the stilbene oxide produced. Catalytic epoxidation of *cis*-stilbene was performed with our Mn(Me_2EBC)Cl_2 catalyst, under atmospheric $^{18}O_2$ using *t*-BuOOH as the terminal oxidant in 4:1 acetone/water (Table 3). The product analysis by GC-MS shows that *cis*-stilbene oxide contains 25 ± 0.3% incorporation of ^{18}O from atmospheric $^{18}O_2$ versus 1.7 ± 0.3% ^{18}O in a control experiment using ordinary air,[20] whereas *trans*-stilbene oxide contains 55.1 ± 1% incorporation of ^{18}O from atmospheric $^{18}O_2$ versus 2.6 ± 1% ^{18}O incorporation in a control experiment. One could rationally expect to find similar ^{18}O incorporation ratios for the *cis*- and *trans*-stilbene oxides if there were only one reaction pathway and a single reactive intermediate for epoxidation. However, the incorporation of ^{18}O in *cis*-stilbene oxide (25 ± 0.3%) is definitely different from that in *trans*-stilbene oxide (55.1 ± 1%). This result leads to the conclusion that at least two distinct reactive intermediates occur in these epoxidation reactions. This is also consistent with the results described above for norbornylene epoxidation.

As shown in Table 3, the epoxidation of *cis*-stilbene provides mostly *trans*-stilbene oxide (yield of 13.5%), and that isomer contains excess ^{18}O derived from $^{18}O_2$ (55.1 ± 1%); this is consistent with the radical pathway in which ROO$^{\cdot}$ is the reactive intermediate (Scheme 3, pathway A.[6d,19d] The substantially greater yield of cyclohexen-1-one over cyclohexene oxide in cyclohexene oxidation and the dominance of products resulting from C−C bond cleavage in the case of styrene oxidation suggest the same mechanism. The remaining viable model for the second reactive intermediate leading to this minor epoxidation product from *cis*-stilbene, which displays a lower ^{18}O incorporation (25 ± 0.3%), is

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(21) (a) Linde, C.; Koliai, N.; Norrby, P.-O.; Akermark, B. *Chem.*−*Eur. J.* **2002**, *8* (11), 2568. (b) Castellino, A. J.; Bruice, T. C. *J. Am. Chem. Soc.* **1988**, *110*, 158. (c) Heimbrook, D. C.; Mulholland, R. L.; Hecht, S. M. *J. Am. Chem. Soc.* **1986**, *108*, 7839.

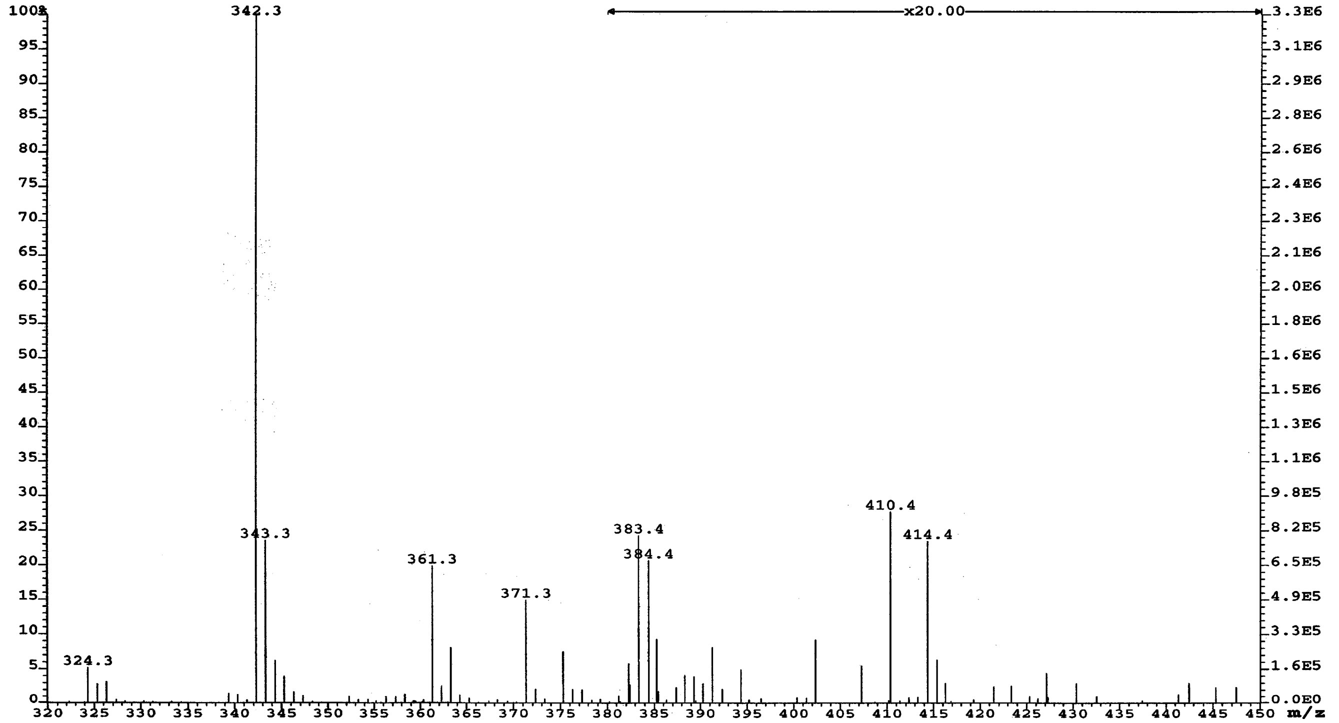

Figure 3. Electrospray ionization mass spectrum identifying $Mn^{IV}(Me_2EBC)(O)(\textit{tert}\text{-}OOBu)^+$ at *m*/*z* 414 (acetone solution containing aqueous *tert*-butyl hydroperoxide).

the Lewis acid pathway in which an oxygen atom is transferred directly from the alkyl hydroperoxide adduct of the manganese(IV) complex to the olefinic double bond. Recently, we provided strong support for the corresponding mechanism for olefin epoxidation by the hydrogen peroxide adduct of the manganese(IV) complex $Mn^{IV}(Me_2EBC)(O)(OOH)^+$ (Scheme 3, pathway B).[8] The manganese(IV) complex is the dominant manganese species in solution during the oxidation reaction (vide supra). The alkyl hydroperoxide adduct of that manganese(IV) complex, $Mn^{IV}(Me_2EBC)(O)(OOR)^+$, should be formed by simple ligand exchange in which *t*-$BuOO^-$ replaces the hydroxo ligand in $Mn^{IV}(Me_2EBC)(O)(OH)^+$ or by oxidation of $Mn^{III}(Me_2EBC)(O)(OH)$ by the $ROO^{\cdot}$ radical, again replacing the hydroxo ligand. Within the adduct, the high charge of manganese(IV) and its potent Lewis acid character polarizes the O−O bond of the bound alkyl peroxide, making it susceptible to nucleophilic attack by the olefinic double bond, a process well-known for high oxidation state early transition element species, including titanium(IV), vanadium(V), molybdenum(VI), tungsten(VI), and rhenium(VII).[9,22] For completeness, Scheme 3 includes pathway C, the oxygen rebound mechanism. However, as shown earlier, pathway C does not occur in the system under study here.

To detect the expected second reactive intermediate, $Mn^{IV}(Me_2EBC)(O)(OOR)^+$, MS spectra were determined for solutions in which $[Mn^{II}(Me_2EBC)(OH_2)_2]^{2+}$, its oxidized derivatives, and its partially deprotonated forms were making use of *tert*-BuOOH and actively catalyzing the epoxidation reaction (Figure 3). Indeed, a weak MS peak at *m*/*z* 414 can be attributed to $[Mn^{IV}(Me_2EBC)(O)(t\text{-}OOBu)]^+$. A strong peak at *m*/*z* 342 is assigned to $Mn^{IV}(Me_2EBC)(O)(OH)^+$. Furthermore, accurate mass measurement proves that the peak at *m*/*z* 414 corresponds precisely to $[Mn^{IV}(Me_2EBC)(O)(\textit{t}\text{-}OOBu)]^+$ (M^+ calcd, 414.2403; found, 414.2402). This provides the first direct evidence for the existence of the alkyl hydroperoxide adduct of high oxidation state manganese species. In heme and non-heme iron monoxygenase models, Fe−OOR species (R = H, alkyl) have been proposed as the reactive intermediates in certain oxygenation processes, and MS and Raman spectra have also provided evidence for the existence of Fe−OOH species.[10] In retrospect, one should expect the alkyl peroxide adduct of manganese(IV) to be an active intermediate for epoxidation in this and other manganese systems in which the Mn(IV)/Mn(III) couple has a modest potential because the manganese(IV) ion is reminiscent of titanium(IV). The early transition metals, Ti, V, W, Mo, and Re, are, as stated above, well-known to form metallo-peracid species when they function as epoxidation catalysts.[9,22] Although the alkyl peroxide adduct of this manganese(IV) complex plays only a minor role in the chemically catalyzed oxygen-transfer process studied here, we suggest that the same process could be much more important in highly selective systems such as those of biological origin.

Recently, we first identified the hydroperoxide adduct of this manganese complex, $Mn^{IV}(Me_2EBC)(O)(OOH)^+$, as the main reactive intermediate responsible for olefin oxygenation in the $Mn(Me_2EBC)Cl_2/H_2O_2$ catalytic system.[8] Various ^{18}O isotopically labeled experiments, including $^{18}O_2$, $H_2{}^{18}O$, and $H_2{}^{18}O_2$ as reactants, and experimental detection of $Mn^{IV}(Me_2$-

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(22) (a) Brill, W. F. *J. Am. Chem. Soc.* **1963**, *85*, 141. (b) Birnbaum, E. R.; Labinger, J. E.; Gray, H. B. *Inorg. Chim. Acta* **1998**, *270*, 433. (c) Weiner, H.; Trovarelli, A.; Finke, R. G. *J. Mol. Catal. A: Chem.* **2003**, *191*, 217.

EBC)(O)(OOH)$^+$ by MS provide strong evidence for this mechanism. Here, with the use of *t*-BuOOH as the terminal oxidant, the alkyl hydroperoxide adduct of the manganese complex, $Mn^{IV}(Me_2EBC)(O)(OOR)^+$, has also been detected and identified as one of the reactive intermediates for olefin epoxidation, while the ROO$^\cdot$ radical is the main reactive intermediate for epoxidation. (Note that *trans*-stilbene oxide is the main epoxidation product as shown in Table 1.) This contrasting mechanistic behavior can be rationalized on the basis of the physical parameters of the O−O bonds in these two oxidants. The bond dissociation energy (BDE) of the O−O bond in H_2O_2 is 213.8 kJ/mol, which is 21.8 kJ/mol higher than that of the O−O bond in *t*-BuOOH (192 kJ/mol).[23] Further, the activation energy for O−O bond cleavage in H_2O_2 is also higher than that in *t*-BuOOH (48 kcal/mol vs 42 kcal/mol).[24] The Mn−O−O−*t*-Bu moiety more easily undergoes homolytic O−O bond cleavage than does the Mn−O−O−H group, and this favors a radical pathway for the *t*-BuOOH derivative. Consequently, it is easy to understand why in some H_2O_2-based manganese-catalyzed epoxidation reactions, exemplified by this $Mn(Me_2EBC)Cl_2$ system, the hydrogen peroxide adduct of the manganese complex serves as the dominant intermediate leading to epoxidation, accompanied by only a minor radical process, while, in contrast, with *t*-BuOOH as the oxidant, a radical process dominates with minor participation by the alkyl peroxide/manganese adduct.

Conclusions

In summary, we have demonstrated unambiguously that at least two distinct reactive intermediates, the alkyl peroxy radical, ROO$^\cdot$, and the Mn(IV)/alkyl peroxo adduct, $Mn^{IV}(Me_2EBC)(O)(OOR)^+$, serve as epoxidizing reagents in $Mn(Me_2EBC)Cl_2$-mediated oxygen-transfer reaction using alkyl hydroperoxide as the terminal oxidant. Labeling experiments using $H_2{}^{18}O$ and $^{18}O_2$ provide compelling evidence for this conclusion. In agreement with our recent reports in which the hydrogen peroxide adduct of the manganese complex, $Mn^{IV}(Me_2EBC)(O)(OOH)^+$, was identified as the reactive intermediate in the transfer of oxygen atoms directly to the olefinic double bond from the hydroperoxide unit, the *t*-BuOO$^-$ adduct, $Mn^{IV}(Me_2EBC)(O)(OOR)^+$, is the first example demonstrating that manganese can catalyze the direct transfer of an oxygen atom to an olefin from that biologically important oxidant. In combination, this work shows that both hydrogen peroxide and alkyl peroxides can transfer oxygen atoms to substrates under Lewis acid catalysis, a pathway independent of both the commonly recognized oxygen rebound mechanism and the peroxy radical pathway. This provides a new insight into the roles manganese can play in oxygenation processes in the laboratory, industry, and nature.

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Supporting Information Available: GC/MS graphs for epoxidation of olefins under various reaction conditions. This material is available free of charge via the Internet at http://pubs.acs.org.

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