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Selective Oxygenation of Cyclohexene by Dioxygen via an Iron(V)-Oxo Complex-Autocatalyzed Reaction

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S Supporting Information

ABSTRACT: An iron complex with a tetraamido macrocyclic ligand, $[(TAML)Fe^{III}]^-$, was found to be an efficient and selective catalyst for allylic oxidation of cyclohexene by dioxygen (O₂); cyclohex-2-enone was obtained as the major product along with cyclohexene oxide as the minor product. An iron(V)-oxo complex, $[(TAML)Fe^V(O)]^-$, which was formed by activating O₂ in the presence of cyclohexene, initiated the autoxidation of cyclohexene with O₂ to produce cyclohexenyl hydroperoxide, which reacted with $[(TAML)Fe^{III}]^-$ to produce $[(TAML)Fe^V(O)]^-$ by autocatalysis. Then, $[(TAML)Fe^V(O)]^-$ reacted rapidly with $[(TAML)Fe^{III}]^-$ to produce a μ -oxo dimer, $[(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-}$, which was ultimately converted to $[(TAML)Fe^V(O)]^-$ when



 $[(TAML)Fe^{III}]^-$ was not present in the reaction solution. An induction period was observed in the autocatalytic production of $[(TAML)Fe^{V}(O)]^-$. The induction period was shortened with increasing catalytic amounts of $[(TAML)Fe^{V}(O)]^-$ and cyclohexenyl hydroperoxide, whereas the induction period was prolonged by adding catalytic amounts of a spin trapping reagent such as 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO). The allylic oxidation of cycloalkenes was also found to depend on the allylic C–H bond dissociation energies, suggesting that the hydrogen atom abstraction from the allylic C–H bonds of cycloalkenes is the rate-determining radical chain initiation step. In this study, we have shown that an iron(III) complex with a tetraamido macrocyclic ligand is an efficient catalyst for the allylic oxidation of cyclohexene via an autocatalytic radical chain mechanism and that $[(TAML)Fe^{V}(O)]^-$ acts as a reactive intermediate for the selective oxygenation of cyclohexene with O₂ to produce cyclohex-2-enone predominantly.

INTRODUCTION

Allylic oxidation reactions are fundamental and important for C-H bond functionalizations, accompanied by a significant increase in the synthetic and/or commercial value of the target molecules, because the resulting oxidation products are attractive synthetic intermediates for pharmaceuticals.^{1–} Classically, allylic oxidations are performed with stoichiometric amounts of chromium reagents.³ Due to the high toxicity of the chromium reagents, however, the stoichiometric use of toxic oxidants should be avoided and replaced by environmentally friendly methods whenever possible.4-14 Among various oxidants, dioxygen (O_2) is an ideal oxidant because it is ubiquitous and environmentally totally benign. Thus, a number of metal-catalyzed methods have been developed for allylic oxidations by O_2 .¹⁵⁻¹⁸ However, the catalytic oxidation of alkenes by O₂ is normally not selective.¹⁸ For example, the catalytic oxidation of cyclohexene by O2 afforded mixtures of cyclohex-2-enol, cyclohex-2-enone, cyclohexene oxide, and other products, including cyclohexenyl hydroperoxide and 1,2-cyclohexanediol (Scheme 1).¹⁹ Thus, there has been no report on the selective, catalytic oxidation of cyclohexene by O₂

Scheme 1. Oxidation Products of Cyclohexene



under mild conditions. In addition, the mechanism of the catalytic oxidation of cyclohexene by O_2 has yet to be clearly clarified.

We report herein the catalytic and selective allylic oxidation of cyclohexene by O₂ to produce cyclohex-2-enone as the major product together with cyclohexene oxide as the minor product in the presence of an iron complex bearing a tetraamido macrocyclic ligand, Na[(TAML)Fe^{III}], in O₂-saturated acetonitrile (MeCN) at 298 K (Scheme 2a for the structure of [(TAML)Fe^{III}]⁻ and Scheme 2b for the products formed in the autoxidation of cyclohexene by [(TAML)Fe^{III}]⁻). The catalytic mechanism is proposed on the basis of a detailed kinetics study

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Scheme 2. (a) Molecular Structure of Iron(III) Tetraamido Macrocyclic Complex ($[(TAML)Fe^{III}]^-$) and (b) Allylic Oxidation Products Formed in the Oxidation of Cyclohexene with $[(TAML)Fe^{III}]^-$ in O₂-Saturated Acetonitrile (MeCN) at 298 K



and the detection of intermediates in the catalytic oxidation reactions. This is the first time the catalytic and selective oxidation of cyclohexene by O_2 has been achieved under ambient temperature and pressure with the elucidation of the autocatalytic reaction mechanisms.

RESULTS AND DISCUSSION

Catalytic Oxidation of Cyclohexene by Dioxygen in the Presence of [(TAML)Fe^{III}]⁻. The [(TAML)Fe^{III}]⁻ complex with Na⁺ countercation^{20,21} exhibited no reactivity toward oxygen in acetonitrile, although the [(TAML)- $Fe^{III}(H_2O)]^-$ complex with PPh₄⁺ countercation was reported to be oxidized by oxygen to produce the μ -oxo dimer in dichloromethane.²² In this study, the oxidation reaction was carried out with Na[(TAML)Fe^{III}] (2.0 mM) and cyclohexene (50 mM) in an O₂-saturated MeCN solution at 298 K, yielding cyclohex-2-enone (90%) and cyclohexene oxide (10%) without the formation of cyclohex-2-enol, cyclohexenyl hydroperoxide, or cyclohexanediol (Figure 1 and Table 1). The solvent MeCN molecule may be coordinated to $[(TAML)Fe^{III}]^{-}$. The products were identified and quantified by ¹H NMR as well as gas chromatography (GC) and gas chromatography linked to a mass spectrometer (GC-MS); the yields of products were within experimental errors ($\pm 10\%$) in the ¹H NMR and GC



Figure 1. Reaction time profiles for the formation of cyclohex-2-enone (green) and cyclohexene oxide (red) and for the consumption of cyclohexene (black) in the oxidation of cyclohexene (50 mM) in the presence of $[(TAML)Fe^{III}]^-$ (2.0 mM) in O₂-saturated MeCN at 298 K.

Table 1. Catalytic Oxidation	of Cyclohexene by O_2 in the
Presence of [(TAML)Fe ^{III}] ⁻	in O ₂ -Saturated Acetonitrile ^a

catalyst	\bigcirc	product (%)			
(mM)	(mM)	O	OH		ООН
2.0	30	11(1)	0	89(2)	0
2.0	50	11(1)	0	89(2)	0
2.0	100	10(1)	11(1)	79(2)	0
2.0	200	10(1)	23(2)	67(2)	trace
1.0	200	8.4(6)	28(2)	64(2)	trace
0.50	200	8.9(7)	32(2)	56(2)	3.0(3)
0.020	200	5.9(6)	33(3)	52(3)	9.0(5)
0.010	200	3.0(3)	31(3)	54(3)	12(1)

^{*a*}Reaction conditions: the catalytic activity of $[(TAML)Fe^{III}]^-$ toward cyclohexene was examined by bubbling O₂ into the reaction solution of deuterated acetonitrile (CD₃CN) for 4 h at 298 K. Products were analyzed and quantified by taking ¹H NMR spectra of the reaction solution.

analyses (see Figure S1 in the Supporting Information for the analysis of products using ¹H NMR).

As shown in Table 1, an increase in the substrate concentration to 200 mM resulted in the formation of cyclohex-2-enone as the major product together with cyclohexene oxide and cyclohex-2-enol as the oxygenated products. Then, the decrease of the catalyst (20 μ M) in an O₂-saturated MeCN solution containing cyclohexene (200 mM) resulted in the formation of cyclohex-2-enone as the major product together with cyclohex-2-enol, cyclohexene oxide, and cyclohexenyl hydroperoxide as the oxygenated products. The formation of cyclohex-2-enone, cyclohex-2-enol, cyclohexenyl hydroperoxide, and cyclohexene oxide was confirmed by ¹H NMR measurements (Figure S1 in the Supporting Information). The turnover number (TON) reached $>10^4$ by a decrease in the catalyst concentration, although the selectivity of the allylic oxidation products was somewhat diminished (Table 1). We have also examined the effect of concentrations of the catalyst and substrates (Table 1): the concentration of cyclohexenyl hydroperoxide decreased with increasing concentration of [(TAML)Fe^{III}]⁻, because cyclohexenyl hydroperoxide reacts with [(TAML)Fe^{III}]⁻ to produce an iron(V)-oxo complex, $[(TAML)Fe^{V}(O)]^{-}$ (vide infra). In the absence of the [(TAML)Fe^{III}]⁻ catalyst, no formation of the oxygenated products was observed. In addition, iron salts (e.g., Fe- $(CF_3SO_3)_2$) and iron complexes, such as $[Fe(TMC)]^{2+}$ (TMC = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane),²³ $[Fe(N4Py)]^{2+}$ (N4Py = N,N-bis(2-pyridylmethyl)-Nbis(pyridyl)methylamine),²⁴ and [Fe(Bn-TPEN)]²⁺ (Bn-TPEN = N-benzyl-N,N',N'-tris(2-pyridylmethyl)-1,2-diaminoethane),²⁵ did not yield the oxygenated products under the catalytic conditions described above. These results demonstrate that [(TAML)Fe^{III}]⁻ is a highly efficient catalyst for the oxidation of cyclohexene by O2. We have also performed the catalytic reaction in the presence of isotopically labeled $H_2^{18}O_2^{26}$ In the reaction mixture, nearly 50% incorporation of ¹⁸O-labeled cyclohexene oxide was observed (Figure S2 in the Supporting Information).

Autocatalytic Formation of $[(TAML)Fe^{V}(O)]^{-}$ in the Reaction of $[(TAML)Fe^{III}]^{-}$ with Cyclohexene and Dioxygen. Addition of $[(TAML)Fe^{III}]^{-}$ (0.10 mM) to an O₂-saturated MeCN solution containing cyclohexene (2.5 mM) resulted in UV-vis spectral changes of the iron complex (Figure 2a), where the absorption band at 400 nm due to



Figure 2. UV–visible absorption spectral changes observed in the oxygenation of $[(TAML)Fe^{III}]^-$ (0.10 mM) with O₂ in the presence of cyclohexene (2.5 mM) in O₂-saturated MeCN at 298 K. The two-step changes are separated by the time regions of (a) 0–720 s and (b) 720–800 s.

[(TAML)Fe^{III}]⁻ decreased with isosbestic points at 372 and 415 nm, accompanied by the formation of a μ -oxo dimer, $[(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-,27-29}$ with an induction period (Figure 2a, inset). The latter species was then converted rapidly to an iron(V)-oxo complex, $[(TAML)Fe^{V}(O)]^{-}$, with isosbestic points at 572 and 692 nm in the time region of 720-780 s (Figure 2b). The yield of the iron(V)-oxo complex was determined to be >95% on the basis of the extinction coefficient at 630 nm.^{21,27-29} The formation of the iron(V)oxo complex has also been confirmed by electron paramagnetic resonance (EPR) spectroscopy and cold spray ionization timeof-flight mass (CSI-MS) spectrometry. The major anisotropic EPR signals with $g_{xx} = 1.98$, $g_{yy} = 1.97$, and $g_{zz} = 1.76$ in the EPR spectrum recorded in acetone at 77 K belong to S = 1/2 $[(TAML)Fe^{V}(O)]^{-}$ species (Figure S3 in the Supporting Information). A simulated EPR spectrum using the anisotropic **g**-tensors of $g_{xx} = 1.979$, $g_{yy} = 1.973$, and $g_{zz} = 1.763$ was also represented (Figure S3a, pink dotted line). The spin amount of the iron(V)-oxo complex (78(4)%) was determined by a comparison of the doubly integrated value of the EPR signal with that of 2,2-diphenyl-1-picrylhydrazyl radical (DPPH[•]) species as a reference (Figure S3). The signals with g values of 2.06 and 2.03 originated from the minor species.²⁷ The CSI-MS spectrum of $[(TAML)Fe^{V}(O)]^{-}$ exhibits a prominent ion peak at a mass to charge ratio of m/z 442.1 (Figure S4 in the Supporting Information), whose mass and isotope distribution pattern corresponds to $[(TAML)Fe^{V}(O)]^{-}$ (calculated m/z442.1). When the reaction was carried out with isotopically labeled H₂¹⁸O, a mass peak appeared corresponding to $[(TAML)Fe^{V}(^{18}O)]^{-}$ (m/z 444.1) (Figure S4), indicating that the intermediate contains only one oxygen atom. Thus, the stability of $[(TAML)Fe^{V}(O)]^{-}$ at 298 K increased under our reaction conditions, such as using O₂ as an oxidant. It should be also noted that the $[(TAML)Fe^{V}(O)]^{-}$ complex generated by other oxidants, such as cumene hydroperoxide and cyclohexenyl hydroperoxide, at 298 K (see Figures S5 and S6 in the Supporting Information) is much more stable than that produced by *m*-CPBA,^{21,27} probably indicating that the presence of H⁺ derived from *m*-CPBA may decrease the stability of $[(TAML)Fe^{V}(O)]^{-}$.

Addition of a catalytic amount of $[(TAML)Fe^{V}(O)]^{-}$ to an MeCN solution of $[(TAML)Fe^{III}]^{-}$ containing cyclohexene resulted in a significant decrease in the induction period, which became shorter with an increase in the catalytic amount of $[(TAML)Fe^{V}(O)]^{-}$ (Figure 3a). Because $[(TAML)Fe^{V}(O)]^{-}$ is the product of the oxidation of $[(TAML)Fe^{III}]^{-}$ with O₂ in the presence of cyclohexene, the decrease in the induction period in Figure 3a indicates an autocatalytic behavior; an autocatalytic reaction is defined as one in which the product acts as the catalyst for its own formation.³⁰ Because the rate of reaction is proportional to the concentration of product, the time course of the reaction exhibits an induction period with a sigmoidal curvature, as shown in Figure 3a.³⁰ Autocatalysis has been extensively studied because it is central to the propagation of living systems.³¹⁻³⁸

Addition of a catalytic amount of the μ -oxo dimer $([(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-})$ to an MeCN solution of [(TAML)Fe^{III}]⁻ containing cyclohexene decreased the induction period in a similar way (Figure 3b). The induction period was also reduced by addition of a catalytic amount of cyclohexenyl hydroperoxide (Figure 3c), which was independently prepared by photoinduced autoxidation of cyclohexene by O_2 with xyloquinone,³⁹ and the concentration was determined on the basis of iodometric titration (Figures S1e and S7 in the Supporting Information).⁴⁰ Addition of a catalytic amount of cumene hydroperoxide also resulted in the reduction of the induction period with an increase in the concentration of cumene hydroperoxide (Figure S8 in the Supporting Information), because cumene hydroperoxide reacted with $[(TAML)Fe^{III}]^-$ to produce $[(TAML)Fe^V(O)]^-$ (Figure S5 in the Supporting Information). The induction period was also reduced by increasing the concentration of cyclohexene (Figure 4a). In contrast, the induction period increased with increasing concentration of [(TAML)Fe^{III}]⁻ (Figure 4b). Since the $[(TAML)Fe^{V}(O)]^{-}$ complex rapidly reacts with $[(TAML)^{-}$ Fe^{III}]⁻ to yield [(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]²⁻, which is in equilibrium with $[(TAML)Fe^{V}(O)]^{-}$ and the equilibrium shifted to the right-hand side for the formation of the μ -oxo dimer,^{41,42} the concentration of $[(TAML)Fe^{V}(O)]^{-}$, which acted as the autocatalyst, decreased with increasing concentration of [(TAML)Fe^{III}]⁻ when the induction period increased (Figure 4b). These autocatalytic behaviors suggest that a radical chain autoxidation is responsible for the formation of $[(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-}$ and $[(TAML)Fe^{V}(O)]^{-}$ in the oxidation of $[(TAML)Fe^{III}]^{-}$ by O_2 in the presence of cyclohexene, as shown in Scheme 3 for the autocatalytic radical chain reaction induced by the $[(TAML)Fe^{V}(O)]^{-}$ complex (see below).



Figure 3. Time profiles monitored for the change of absorbance at 630 nm due to $[(TAML)Fe^{V}(O)]^{-}$ in the autocatalytic oxygenation of $[(TAML)Fe^{III}]^{-}$ (0.10 mM) with O₂ in the presence of cyclohexene (2.5 mM) with catalytic amounts of (a) $[(TAML)Fe^{V}(O)]^{-}$ (0–10%), (b) $[(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-}$ (0–15%), and (c) cyclohexenyl hydroperoxide (0–1.5%) in aerated MeCN at 298 K.

It has been known that the initiation of autoxidation of cyclohexene by O₂ occurs without any catalyst.⁴³ The radical chain reaction is then started by hydrogen atom abstraction of the allylic C–H bonds of cyclohexene by $[(TAML)Fe^{V}(O)]^{-1}$ to produce [(TAML)Fe^{IV}(OH)]⁻ and cyclohexenyl radical (Scheme 3, reaction a), which readily reacts with O_2 to afford cyclohexenylperoxyl radical (Scheme 3, reaction b). The produced [(TAML)Fe^{IV}(OH)]⁻ may be dimerized to produce the μ -oxo dimer. The cyclohexenylperoxyl radical is the chain carrier, which abstracts a hydrogen atom from cyclohexene to produce cyclohexenyl hydroperoxide and the regeneration of cyclohexenyl radical (Scheme 3, reaction c), constituting the radical chain reactions.⁴⁴ Cyclohexenyl hydroperoxide oxygen-ates [(TAML)Fe^{III}]⁻ to produce cyclohex-2-enol and $[(TAML)Fe^{V}(O)]^{-}$ (Scheme 3, reaction d). It was confirmed that addition of cyclohexenyl hydroperoxide to an MeCN solution of [(TAML)Fe^{III}]⁻ resulted in the generation of $[(TAML)Fe^{V}(O)]^{-}$ (Figure S6 in the Supporting Information). In the presence of $[(TAML)Fe^{III}]^-$, $[(TAML)Fe^V(O)]^-$ is known to react rapidly with $[(TAML)Fe^{III}]^-$ to produce the μ -



Figure 4. (a) Time profiles monitored for the change of absorbance at 630 nm due to $[(TAML)Fe^{V}(O)]^{-}$ in the autocatalytic oxygenation of $[(TAML)Fe^{III}]^{-}$ (0.10 mM) with O₂ in the presence of cyclohexene (2.5–10.0 mM). (b) Time profiles monitored for the change of absorbance at 630 nm due to $[(TAML)Fe^{V}(O)]^{-}$ in the reaction of cyclohexene (5.0 mM) with $[(TAML)Fe^{III}]^{-}$ (0.10–0.25 mM) in aerated MeCN at 298 K.

Scheme 3. Autocatalytic Radical Chain Mechanism for Catalytic Oxidation of Cyclohexene by O_2 in the Presence of $[(TAML)Fe^{III}]^-$



oxo dimer $[(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-}$ (Scheme 3, reaction *e*).^{21,27–29,41,42} When $[(TAML)Fe^{III}]^-$ was completely consumed, $[(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-}$ was rapidly converted to $[(TAML)Fe^{V}(O)]^-$ (Scheme 3, reaction *f*), as shown in Figure 2b.

The overall chain reaction is given in eq 1, where cyclohexene reacts with O_2 and $[(TAML)Fe^{III}]^-$ to yield $[(TAML)Fe^V(O)]^-$. Then, cyclohexene is directly oxygenated by $[(TAML)Fe^V(O)]^-$ to produce cyclohex-2-enol (Scheme 4, reaction *a*), which is further oxidized by $[(TAML)Fe^V(O)]^-$ to



$$[(L)Fe^{V}(O)]^{-} L = TAML$$

$$[(L)Fe^{III}]^{-} + [(L)Fe^{V}(O)]^{-} [(L)Fe^{IV}(O)Fe^{IV}(L)]^{2^{-}}$$

$$[(L)Fe^{V}(O)]^{-}$$

$$[(L)Fe^{III}]^{-} + [(L)Fe^{V}(O)]^{-} [(L)Fe^{IV}(O)Fe^{IV}(L)]^{2^{-}}$$

$$+ H_{2}O$$

$$[(L)Fe^{III}]^{-} + H_{2}O$$

yield cyclohex-2-enone (Scheme 4, reaction *b*), accompanied by the regeneration of $[(TAML)Fe^{III}]^-$, which is in equilibrium with $[(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-}$ in the presence of $[(TAML)Fe^{V}(O)]^{-}$ (Scheme 4). The rapid oxidation of cyclohex-2-enol by $[(TAML)Fe^{V}(O)]^{-}$ was independently confirmed (Figure 5a; see also Figure S9 in the Supporting Information), in which the rate of the reaction of [(TAML)- $Fe^{V}(O)$ with cyclohex-2-enol was about 10 times faster than that of $[(TAML)Fe^{V}(O)]^{-}$ with cyclohexene at 233 K (Figure 5b). As a minor reaction pathway, cyclohexene was epoxidized by $[(TAML)Fe^{V}(O)]^{-}$ to give cyclohexene epoxide (Scheme 5). Once the autocatalytic radical chain reaction starts, the initiation step by $[(TAML)Fe^{V}(O)]^{-}$ produced in an autocatalytic pathway (Scheme 3) becomes dominant in comparison with the O_2 activation pathway. Previously we have reported the formation of $[Fe^{IV}(O)(TMC)]^{2+}$ by reacting $[Fe^{II}(TMC)]^{2+}$ with dioxygen in the presence of cycloalkenes.^{23c} In the case of dioxygen activation by [Fe^{II}(TMC)]²⁺, however, no autocatalytic pathway was involved, in contrast to the present study of [(TAML)Fe^{III}]⁻.

The UV–vis spectral changes were also monitored under the same conditions as in Figure 1 to clarify the rate-determining step in Scheme 3. The results are shown in Figure S10 in the Supporting Information, where spectral changes were observed similar to those seen in Figure 2. When the cyclohexene concentration was 50 mM, which was much larger than that in Figure 2 (2.5 mM), no induction period was observed (Figure S10a). The nearly complete formation of $[(TAML)Fe^{V}(O)]^{-}$ via the formation of $[(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-}$ from $[(TAML)Fe^{V}(O)]^{-}$ and $[(TAML)Fe^{III}]^{-}$ indicates that the oxygenation of cyclohexene with $[(TAML)Fe^{V}(O)]^{-}$ is the rate-determining step (Scheme 3, reaction *a*). After the completion of the oxidation of cyclohexene, $[(TAML)Fe^{III}]^{-}$ was regenerated (Figure S10b). The regenerated $[(TAML)Fe^{III}]^{-}$ was confirmed by EPR and CSI-MS (Figure S11 in the Supporting Information).

Inhibition of the Radical Chain Reaction. The chain carrier radical (cylcohexenylperoxyl radical) was trapped by



Figure 5. (a) UV–visible spectral changes observed in the reaction of $[(TAML)Fe^V(O)]^-$ (0.20 mM) with cyclohex-2-enol (5.0 mM) in MeCN at 233 K. $[(TAML)Fe^V(O)]^-$ was generated by the O₂-activation reaction of $[(TAML)Fe^{III}]^-$ (0.20 mM) with cyclohexene (5.0 mM) in O₂-saturated MeCN. (b) UV–visible spectral changes observed in the reaction of $[(TAML)Fe^V(O)]^-$ (0.20 mM) with cyclohexene (5.0 mM) in O₂-saturated MeCN at 233 K. Insets show the time courses monitored at 840 nm.

Scheme 5. Epoxidation of Cyclohexene with [(TAML)Fe^{III}]⁻ (Minor Pathway)

$$[(L)Fe^{V}(O)]^{-} L = TAML$$

$$[(L)Fe^{III}]^{-} + [(L)Fe^{V}(O)]^{-} - [(L)Fe^{V}(O)]^{-} [(L)Fe^{IV}(O)Fe^{IV}(L)]^{2-}$$

$$0$$

5,5'-dimethyl-1-pyrroline N-oxide (DMPO), which is a typical spin-trapping reagent. $^{45-47}$ The addition of only 0.001% DMPO to an aerated MeCN solution of [(TAML)Fe^{III}]⁻ and cyclohexene resulted in an increase in the induction period, and the addition of 2% DMPO inhibited the reaction completely, as shown in Figure 6. Such a strong inhibition of the reaction by DMPO suggests a long radical chain length. Since the rate constants of the spin-trapping reactions of peroxyl radicals with DMPO $(10^3 - 10^4 \text{ M}^{-1} \text{ s}^{-1})^{48}$ are much larger than those of allylic hydrogen atom abstraction from alkenes by peroxyl radicals (e.g., 2.7 $M^{-1} s^{-1}$ for the reaction of *tert*-butylperoxyl radical with tetralin),^{49,50} the rate of consumption of DMPO in the induction period ([DMPO]/ $(t_4 - t_2)$) corresponds to the initiation rate. The propagation rate is obtained as the fast rate after the induction period (i.e., $[[(TAML)Fe^{III}]^-]/(t_3 - t_1))$ (see Figure 7). Then, the chain length of the propagation step in Scheme 3 is evaluated as the ratio of the propagation rate to the initiation rate, $\{[(TAML)Fe^{III}]^{-}]/(t_3 - t_1)\}/\{[DMPO]/$



Figure 6. Time profiles monitored for the change of absorbance at 630 nm due to $[(TAML)Fe^{V}(O)]^{-}$ in the oxidation of $[(TAML)Fe^{III}]^{-}$ (0.10 mM) with O₂ in the presence of cyclohexene (2.5 mM) with $[(TAML)Fe^{III}]^{-}$ (0.10 mM) and a catalytic amount of DMPO (0–2.0%) with O₂ in aerated MeCN at 298 K.



Figure 7. Chain length evaluated as the ratio of the propagation rate to the initiation rate. The initiation rate is equal to $[DMPO]/(t_4 - t_2)$, whereas the propagation rate is equal to $[[(TAML)Fe^{III}]^-]/(t_3 - t_1)$: $t_1 = 580$ s; $t_2 = 630$ s; $t_3 = 830$ s; $t_4 = 2240$ s. The chain length was calculated from $\{[[(TAML)Fe^{III}]^-]/(t_3 - t_1)\}/\{[DMPO]/(t_4 - t_2)\}$ to be 650.

 $(t_4 - t_2)$, which is ca. 650 (Figure 7). Thus, the chain length is long enough to obtain large TONs in Table 1. It should be noted that the autocatalytic radical chain reaction is for the formation of $[(TAML)Fe^V(O)]^-$, which acts as an efficient catalyst for the selective oxidation of cyclohexene to cyclohex-2enone as the major oxidized product, in contrast with the autoxidation pathway to produce cyclohexenyl hydroperoxide.

Interconversion between $[(TAML)Fe^{V}(O)]^{-}$ and $[(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-}$ Depending on Temperature. The balance for the autocatalytic formation of $[(TAML)Fe^{V}(O)]^{-}$ in Scheme 3 and the oxidation of cyclohexene with $[(TAML)Fe^{V}(O)]^{-}$ (eq 1) is changed depending on the temperature. When the reaction temperature was lowered to 233 K after the formation of $[(TAML)Fe^{V}(O)]^{-}$ at 298 K, the absorbance at 630 nm due to $[(TAML)Fe^{V}(O)]^{-}$ at 298 K, the absorbance at 630 nm due to $[(TAML)Fe^{V}(O)]^{-}$ decreased, accompanied by the appearance of an absorption band at 840 nm due to the formation of the μ -oxo dimer $[(TAML)Fe^{IV}(O)]^{-}$ and $[(TAML)Fe^{III}]^{-}$ (Figure 8);^{21,27-29,41,42} cyclohexene is oxidized by $[(TAML)Fe^{V}(O)]^{-}$ to produce cyclohex-2-enol and $[(TAML)Fe^{III}]^{-}$, which reacts with $[(TAML)Fe^{V}(O)]^{-}$ rapidly to yield the μ -oxo dimer species $[(TAML)Fe^{V}(O)]^{-}$ rapidly to yield the μ -oxo dimer species $[(TAML)Fe^{V}(O)]^{-}$ and $[(TAML)Fe^{III}]^{-}$ (Schemes 4 and 5). The reaction of $[(TAML)Fe^{V}(O)]^{-}$ and $[(TAML)Fe^{III}]^{-}$ is faster than the autocatalytic formation of $[(TAML)Fe^{V}(O)]^{-}$



Figure 8. (a) UV–vis spectral changes observed in the reversible interconversion between $[(TAML)Fe^{V}(O)]^{-}$ and $[(TAML)Fe^{IV}(O)-Fe^{IV}(TAML)]^{2-}$ by changing the temperature between 253 and 233 K. Initially, $[(TAML)Fe^{V}(O)]^{-}$ was generated by an O₂ activation reaction of $[(TAML)Fe^{III}]^{-}$ (0.20 mM) with cyclohexene (5.0 mM) in O₂-saturated MeCN at 298 K. (b) Time profiles monitored at 840 nm due to $[(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-}$ by changing the reaction temperature between 253 and 233 K.

(Scheme 3). When the temperature was increased to 253 K, however, the absorbance at 840 nm due to $[(TAML)Fe^{IV}(O)-Fe^{IV}(TAML)]^{2-}$ decreased, accompanied by an increase in absorbance at 630 nm due to $[(TAML)Fe^{V}(O)]^{-}$. This result indicates that, at a higher temperature, the autocatalytic formation of $[(TAML)Fe^{V}(O)]^{-}$ (Scheme 3) is faster than the oxidation of cyclohexene by $[(TAML)Fe^{V}(O)]^{-}$ (Schemes 4 and 5). Such interconversion between $[(TAML)Fe^{V}(O)]^{-}$ and $[(TAML)Fe^{IV}(O)Fe^{IV}(TAML)]^{2-}$ can be repeated by changing the temperature between 233 and 253 K (Figure 8).

Catalytic Oxygenation of Other Cycloalkenes by O₂. Other cycloalkenes, such as cycloheptene, were also oxygenated by O_2 in the presence of a catalytic amount of $[(TAML)Fe^{III}]^$ to produce the corresponding allylic oxidation products with epoxides (Table 2). In the case of cyclooctene and deuterated

Table 2. Products Formed in the Catalytic Oxidation of Cycloalkenes by O₂ in the Presence of $[(TAML)Fe^{III}]^-$ in O₂-Saturated Acetonitrile at 298 K^{*a*}

		product (%)	
substrate	alcohol	ketone	epoxide
cyclohexene	0	89(2)	11(1)
cycloheptene	10(1)	22(2)	22(1)
cyclooctene	0	0	0

"Reaction conditions: the oxygenation of cycloalkenes was performed by bubbling O_2 into a CD_3CN solution containing [(TAML)Fe^{III}]⁻ (2.0 mM) and cycloalkenes (50 mM) at 298 K for 4 h. Products were analyzed and quantified by taking ¹H NMR spectra and comparing them with those of authentic samples.

cyclohexene (cyclohexene- d_{10}), however, the oxidation by O_2 with [(TAML)Fe^{III}]⁻ did not occur under the identical reaction conditions (Table 2). No $[(TAML)Fe^{V}(O)]^{-}$ was produced in the reaction of $[(TAML)Fe^{III}]^-$ (0.10 mM) with O₂ in the presence of cyclooctene (50 mM) in O2-saturated MeCN at 298 K for 4 h due to the much slower autoxidation to start the autocatalytic reaction (Figure S12 in the Supporting Information). The reactivity of cycloalkenes was correlated with the allylic C-H bond dissociation energies (BDEs) of cycloalkenes, since the yields of oxygenated products decrease with an increase in the C-H BDEs, such as cyclohexene $(100\%, BDE = 81.0 \text{ kcal mol}^{-1})$, cycloheptene (54%, BDE = 83)kcal mol⁻¹), and cyclooctene (0%, BDE = $85.0 \text{ kcal mol}^{-1}$) (Table 2).⁵¹ Thus, the hydrogen atom abstraction from cycloalkenes by $[(TAML)Fe^{V}(O)]^{-}$ is the initiation step in the autoxidation radical chain reactions, as proposed in Scheme 3.

CONCLUSION

The selective catalytic oxidation of cyclohexene by O_2 has been achieved by using an iron complex bearing a tetraamido macrocyclic ligand, $[(TAML)Fe^{III}]^{-1}$, which is oxidized by O₂ in the presence of cyclohexene to yield $[(TAML)Fe^{V}(O)]^{-}$ and the corresponding allylic oxidation products via an autocatalytic radical chain mechanism.⁵² The nonselectivity in the oxidized products in Scheme 1 results mainly from free radical decomposition reactions of the autoxidation product (i.e., cyclohexenyl hydroperoxide). Cyclohexenyl hydroperoxide rapidly oxygenates [(TAML)Fe^{III}]⁻ to produce [(TAML)- $Fe^{V}(O)$]⁻, which can selectively oxygenate cyclohexene to yield mainly cyclohex-2-enone, which would otherwise be difficult to obtain selectively. Thus, the present study provides a unique autocatalytic reaction mechanism for the selective catalytic oxygenation of substrates by O2 without the involvement of free radical decomposition of alkyl hydroperoxides.

EXPERIMENTAL SECTION

Materials. Commercially available chemicals and solvents were used without further purification unless otherwise indicated. The complex Na(H₂O)_x[(TAML)Fe^{III}] was purchased from GreenOx Catalyst, Inc. (Pittsburgh, PA, USA), and recrystallized from an isopropyl alcohol/H₂O mixture before use.²⁰ Acetonitrile, cyclohexene, cyclohex-2-enone, cyclohex-2-enol, cyclohexene oxide, cycloheptene, cyclooctene, and 5,5'-dimethyl-1-pyrroline *N*-oxide were purchased from Aldrich Chemical Co. 2,5-Dimethyl-4-benzoquinone was purchased from Alfa-Aesar Chemical Co. Olefins were refluxed and distilled under Ar and filtered through an active alumina column prior to use.⁵³ H₂¹⁸O (95% ¹⁸O enriched) was purchased from ICON Services Inc. (Summit, NJ, USA).

Instrumentation. UV-vis spectra were recorded on a Hewlett-Packard 8453 diode array spectrophotometer equipped with a UNISOKU Scientific Instruments USP-203A Cryostat for lowtemperature experiments. X-band electron paramagnetic resonance (EPR) spectra were recorded at 5 K using an X-band Bruker EMXplus spectrometer equipped with a dual mode cavity (ER 4116DM). Low temperature was achieved and controlled with an Oxford Instruments ESR900 liquid He quartz cryostat with an Oxford Instruments ITC503 temperature and gas flow controller. The experimental parameters for EPR measurement were as follows: microwave frequency, 9.647 GHz; microwave power, 1.0 mW; modulation amplitude, 10 G; gain, 1×10^4 ; modulation frequency, 100 kHz; time constant, 40.96 ms; conversion time, 81.00 ms. Nuclear magnetic resonance (NMR) spectra were measured with a Bruker model digital AVANCE III 400 FT-NMR spectrometer. The cold spray ionization time-of-flight mass (CSI-MS) spectral data were

collected on a JMS-T100CS (JEOL) mass spectrometer equipped with a CSI source. Typical measurement conditions are as follows: needle voltage, 2.2 kV; orifice 1 current, 50-500 nA; orifice 1 voltage, 0-20 V; ring lens voltage, 10 V; ion source temperature, 5 °C; spray temperature, -40 °C. The product analyses were also performed with an Agilent 6890N gas chromatograph (GC) and a FOCUS DSQ (dual-stage quadrupole) mass spectrometer (Thermo Finnigan, Austin, TX, USA) interfaced with a Finnigan FOCUS gas chromatograph (GC-MS).

Formation of Fe(V)-Oxo Intermediate. Reactions were run in a 1 cm UV cuvette by monitoring UV–vis spectral changes of reaction solutions. Addition of a catalytic amount of $[(TAML)Fe^{III}]^-$ (0.10 mM) to an O₂-saturated MeCN solution containing cyclohexene (2.5 mM) resulted in the formation of $[(TAML)Fe^V(O)]^-$ at 298 K in a good yield, which was determined using the extinction coefficient at 630 nm due to $[(TAML)Fe^V(O)]^-$. An authentic $[(TAML)Fe^V(O)]^-$ complex was synthesized by reacting $[(TAML)Fe^{III}]^-$ with *m*-chloroperbenzoic acid (*m*-CPBA) according to the published procedure.²⁷

Catalytic Oxygenation of Cycloalkenes by O_2 in the Presence of [(TAML)Fe^{III}]⁻. The catalytic activity of [(TAML)Fe^{III}]⁻ toward cycloalkenes was examined by bubbling dioxygen into the reaction solution of acetonitrile (MeCN or CD₃CN). Oxygenated products were identified by ¹H NMR and GC and then compared with those of authentic samples to determine product yields.

Synthesis and Characterization of Cyclohexenyl Hydroperoxide. Cyclohexenyl hydroperoxide was generated using cyclohexene (450 μ L, 9.8 M) and xyloquinone (2.0 mM) after 15 h of irradiation using a xenon lamp (300 W) at 298 K according to the literature method for the photocatalytic production of hydroperoxides.³⁹ It was confirmed by ¹H NMR spectroscopy; the hydroperoxide peaks match with the previously reported literature.⁵⁴

Iodometric Titration of Cyclohexenyl Hydroperoxide. The amount of cyclohexenyl hydroperoxide was determined by titration with iodide ion;⁴⁰ 10 μ L of the reaction solution containing cyclohexenyl hydroperoxide generated by cyclohexene (450 μ L, 9.8 M) and xyloquinone (2.0 mM) with irradiation was taken and diluted up to 2.0 mL with MeCN. The reaction solution was then treated with an excess of sodium iodide under an Ar atmosphere. The amount of I₃⁻ formed was quantified by absorbance at 361 nm due to I₃⁻ (λ_{max} 361 nm, $\varepsilon = 2.5 \times 10^4$ M⁻¹ cm⁻¹).⁴⁰

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorg-chem.7b00220.

Figures S1–S12 as described in the text (PDF)

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