Photocatalytic Asymmetric Epoxidation of Terminal Olefins Using Water as an Oxygen Source in the Presence of a Mononuclear Non-Heme Chiral Manganese Complex

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S Supporting Information

ABSTRACT: Photocatalytic enantioselective epoxidation of terminal olefins using a mononuclear non-heme chiral manganese catalyst, [(R,R-BQCN)Mn^{II}]$^{2+}$, and water as an oxygen source yields epoxides with relatively high enantioselectivities (e.g., up to 60% enantiomeric excess). A synthetic mononuclear non-heme chiral Mn(IV)−oxo complex, [(R,R-BQCN)Mn^{IV}(O)]$^{2+}$, affords similar enantioselectivities in the epoxidation of terminal olefins under stoichiometric reaction conditions. Mechanistic details of each individual step of the photoinduced catalysis, including formation of the Mn(IV)−oxo intermediate, are discussed on the basis of combined results of laser flash photolysis and other spectroscopic methods.

The development of highly efficient and environmentally benign catalytic oxidation reactions using bioinspired metal complexes under mild conditions is of current interest in the communities of synthetic organic, oxidation, and bioinorganic chemistry.[1] Recently, enantioselective epoxidation of olefins using bioinspired metal catalysts has attracted much attention[2] since the resulting epoxides are important building blocks and intermediates that can be used in fine chemical and pharmaceutical industries and understanding mechanistic details of the biomimetic catalysis may provide clues for the development of biologically relevant and catalytically efficient and selective oxidation systems. Indeed, it has been shown recently that non-heme manganese (and iron) complexes supported by chiral tetradentate aminopyridine ligands are highly promising catalysts in the enantioselective epoxidation of electron-deficient olefins, affording excellent enantioselectivities of up to 99% enantiomeric excess (*ee*);[2−5] it is notable that an environmentally benign oxidant, H$_2$O$_2$, has been used in those asymmetric olefin epoxidation reactions. However, to the best of our knowledge, no photocatalytic oxidation reactions using water as the environmentally benign oxygen source have been attempted for the asymmetric expoxidation of olefins. Further, although high-valent manganese(V)−oxo species have been proposed as reactive epoxidizing intermediates in the asymmetric epoxidation of olefins invariably,[4,5a] direct evidence

for the intermediacy of such Mn(V)−oxo species under catalytic and/or stoichiometric reaction conditions has yet to be obtained. Thus, the nature of the asymmetric epoxidizing intermediate(s) (e.g., Mn(V)−oxo, Mn(IV)−oxo, or Mn−OX (X = OH or OR)) remains to be clarified.[6] In addition, although the formation of a non-heme Mn(IV)−oxo complex (and non-heme Fe(IV)−oxo and Ru(IV)−oxo complexes) under photocatalytic oxidation conditions has been demonstrated recently,[7−10] a detailed mechanism of the photoinduced generation of the M(IV)−oxo complex has yet to be addressed.

Herein we report the photocatalytic enantioselective epoxidation of terminal olefins using a chiral manganese catalyst, [(R,R-BQCN)Mn^{II}(OTf)$_2$] (**1**) (BQCN = N,N′-dimethyl-N,N′-bis(8-quinolyl)cyclohexanediamine; OTf = CF$_3$SO$_3^-$),[11] [Ru^{II}(bpy)$_3$]$^{2+}$ (bpy = 2,2′-bipyridine) as a photocatalyst, [Co^{III}(NH$_3$)$_5$Cl]$^{2+}$ as a one-electron oxidant, and water as an oxygen source (Scheme 1); it should be noted

Scheme 1. Enantioselective Epoxidation of Terminal Olefins by a Mn(IV)−Oxo Complex under Photocatalytic and Stoichiometric Reaction Conditions
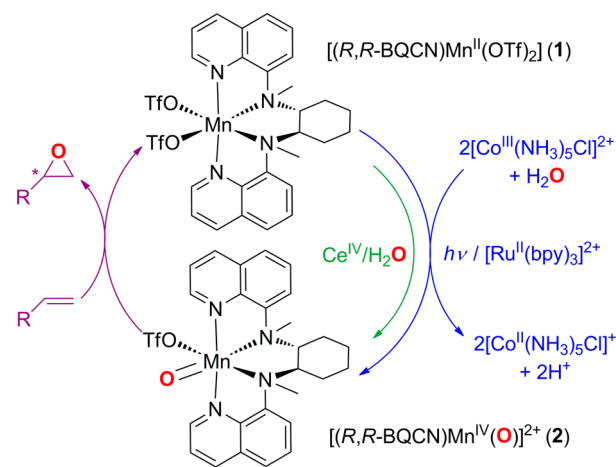
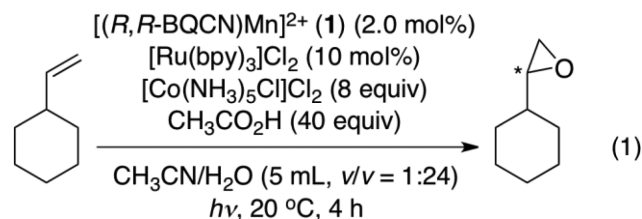that terminal olefins are challenging substrates in (asymmetric) epoxidation reactions.[12] We also report the first direct evidence for the involvement of a high-valent Mn(IV)−oxo complex as an epoxidizing intermediate in the asymmetric epoxidation of olefins; a mononuclear non-heme Mn(IV)−oxo complex, $[(R,R\text{-BQCN})Mn^{IV}(O)]^{2+}$ (**2**), synthesized using cerium(IV) ammonium nitrate (CAN) as an oxidant,[11] afforded moderately high *ee* values in the asymmetric epoxidation of olefins (Scheme 1). The photocatalytic formation mechanism and kinetics of the Mn(IV)−oxo complex were elucidated using a combination of nanosecond laser flash photolysis and other spectroscopic measurements.

The chiral Mn(II) complex **1** was synthesized by reacting $Mn(OTf)_2$ with the chiral *R,R*-BQCN ligand (see the Supporting Information). Photoirradiation ($\lambda > 420$ nm) of a CH_3CN/H_2O solvent mixture (1:24 v/v) containing vinylcyclohexane (0.030 mmol), **1** (2.0 mol %), $[Ru^{II}(bpy)_3]^{2+}$ (10 mol %), $[Co^{III}(NH_3)_5Cl]^{2+}$ (8 equiv relative to the substrate), and acetic acid (40 equiv relative to the substrate) yielded the epoxide product, 2-cyclohexyloxirane (59 ± 4% yield, turnover number = 30 ± 2) with moderately high enantioselectivity (>50% *ee*) (eq 1 and Table 1, entry 1; see Table S1 for

$$[(R,R\text{-BQCN})Mn]^{2+} \text{ (1) (2.0 mol\%)}$$
$$[Ru(bpy)_3]Cl_2 \text{ (10 mol\%)}$$
$$[Co(NH_3)_5Cl]Cl_2 \text{ (8 equiv)}$$
$$CH_3CO_2H \text{ (40 equiv)}$$
$$CH_3CN/H_2O \text{ (5 mL, } v/v = 1:24)$$
$$h\nu, 20\ ^\circ C, 4\ h \qquad (1)$$

optimization of the reaction conditions; also see Table S2). When the photocatalytic epoxidation of vinylcyclohexane was

**Table 1. Photocatalytic Enantioselective Epoxidation of Terminal Olefins by 1**[a]

entry	substrate	product	yield (%)[b]	ee (%)[b]
1			59 ± 4	53 ± 2
2			68 ± 5	50 ± 2
3			24 ± 3	57 ± 1
4			26 ± 3	60 ± 2
5			35 ± 4	56 ± 2
6			65 ± 5	43 ± 2

[a]A CH_3CN/H_2O solvent mixture (1:24 v/v) containing substrate (0.030 mmol), **1** (2.0 mol %), $[Ru^{II}(bpy)_3]^{2+}$ (10 mol %), $[Co^{III}(NH_3)_5Cl]^{2+}$ (8 equiv), and acetic acid (40 equiv) was photoirradiated at 20 °C for 4 h. [b]Determined by GC with a Chirasil-Dex CB column.

performed using $H_2^{18}O$ (97% ^{18}O-enriched) instead of $H_2^{16}O$, the epoxide product contained 94 ± 2% ^{18}O (Figure S1) in the absence or presence of air, indicating that the oxygen in the epoxide product was derived from water. Other terminal olefins were also oxidized to the corresponding epoxides in moderate yields and enantioselectivities (Tables 1 and S2); the highest yield (68 ± 5%) was obtained for vinylpentane with 50 ± 2% *ee* (Table 1, entry 2), whereas the highest enantioselectivity (60 ± 2% *ee*) but with a lower yield (26 ± 3%) was obtained for 1-heptene (Table 1, entry 4). No or negligible amounts of epoxides were formed when the photocatalytic oxidation reactions were performed in the absence of **1**, $[Ru^{II}(bpy)_3]^{2+}$, $[Co^{III}(NH_3)_5Cl]^{2+}$, or acetic acid,[13] indicating that all of these components are required for the formation of the epoxide products.

What is the nature of the intermediate responsible for the asymmetric epoxidation of olefins? As proposed for most of the catalytic asymmetric epoxidation reactions,[4,5a] a Mn(V)−oxo species can be considered as a plausible intermediate generated in the photocatalytic oxidation reactions. A Mn(IV)−oxo species is also a viable intermediate; however, such a Mn(IV)−oxo complex has rarely been suggested as an epoxidizing intermediate in catalytic asymmetric epoxidation reactions. Since it has been shown recently that mononuclear non-heme Mn(IV)−oxo complexes are capable of epoxidizing olefins,[14] we synthesized a Mn(IV)−oxo complex bearing the *R,R*-BQCN ligand, $[(R,R\text{-BQCN})Mn^{IV}(O)]^{2+}$ (**2**), according to the published procedures[11] and investigated its reactivity in asymmetric epoxidation of terminal olefins (Figures 1 and
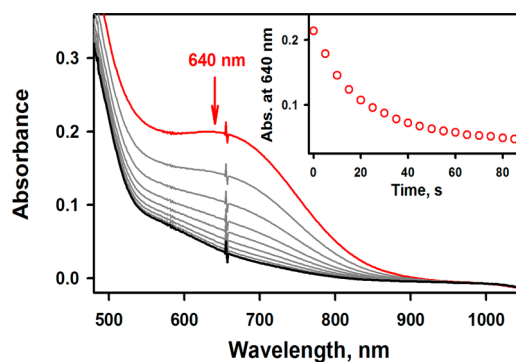

Figure 1. Absorption spectral changes observed in the reaction of **2** with vinylcyclohexane (50 mM) in CH_3CN/H_2O (9:1 v/v) at 20 °C. **2** was prepared by reacting **1** (0.50 mM) with CAN (3.0 mM). The inset shows the decay of the peak at 640 nm.

S2). Upon addition of vinylcyclohexane to a solution of **2**, the absorption band at 640 nm due to **2** disappeared, and the decay rate obeyed first-order kinetics (Figure 1, inset). The pseudo-first-order rate constant increased linearly with increasing vinylcyclohexane concentration (Figure S3), giving a second-order rate constant of 1.1(1) $M^{-1} s^{-1}$ at 20 °C. Importantly, analysis of the reaction solution revealed the formation of the epoxide product, 2-cyclohexyloxirane (70 ± 4% yield based on the amount of **2** with 62 ± 2% *ee*). Similarly, a second-order rate constant of 2.6(2) × $10^{-1}\ M^{-1} s^{-1}$ at 20 °C was obtained in the reaction of **2** with 1-heptene, which yielded 1,2-epoxyheptane as the product (80 ± 4% yield based on the amount of **2**) with 63 ± 2% *ee* (Figure S4; also see Table S3). In these reactions, a Mn(II) species was formed as the decay product of **2** (Figure S5). Thus, the present results demonstrate

that a chiral Mn(IV)−oxo complex indeed epoxidizes terminal olefins to give the corresponding epoxides with moderately high enantioselectivities (Scheme 1). Further, on the basis of the present results, we suggest that Mn(IV)−oxo species should be considered as active oxidants responsible for the asymmetric epoxidation of olefins reported in previous studies.[2−5]

We then investigated each individual step of the photo-catalytic oxidation of **1** carried out in the presence of $[Ru^{II}(bpy)_3]^{2+}$ and $[Co^{III}(NH_3)_5Cl]^{2+}$. The initial steps of the photocatalytic cycle were too fast to be followed using a photodiode array spectrophotometer. Thus, nanosecond laser flash photolysis was used to examine the kinetics and the reaction mechanism (see Scheme 2). Laser excitation ($\lambda_{ex} = 430$

Scheme 2. Mechanistic Details for the Photoinduced Generation of 2 and Its Reaction with Olefin
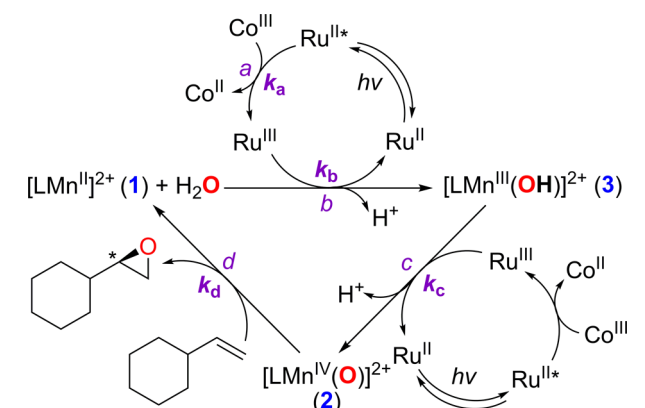
nm) of a CH$_3$CN/H$_2$O (1:1 v/v) solution of $[Ru^{II}(bpy)_3]^{2+}$ resulted in the formation of the triplet excited state species, $[Ru(bpy)_3]^{2+*}$, which decayed back to the starting $[Ru^{II}(bpy)_3]^{2+}$ complex with a rate constant of $k_T = 1.2(1) \times 10^6$ s^{-1} (lifetime = 830(40) μs)[7a,9a] at 20 °C, as indicated by the full recovery of the bleaching at 450 nm (Figure S6; also see the black line in Figure S7). In the presence of $[Co^{III}(NH_3)_5Cl]^{2+}$, the recovery was faster but not complete (Figure S7, red line), indicating that electron transfer (ET) from $[Ru(bpy)_3]^{2+*}$ to $[Co^{III}(NH_3)_5Cl]^{2+}$ occurred to give $[Ru^{III}(bpy)_3]^{3+}$ and $[Co^{II}(NH_3)_5Cl]^{+}$ (Scheme 2, reaction a); the latter is known to decompose irreversibly to release NH$_3$.[9a] The ET rate, as monitored by the recovery of the bleaching at 450 nm, obeyed first-order kinetics, and the pseudo-first-order rate constant increased linearly with increasing concentration of $[Co^{III}(NH_3)_5Cl]^{2+}$ (Figure S8). The second-order rate constant (k_a in Scheme 2) was determined to be $6.2(5) \times 10^7$ M^{-1} s^{-1}. The intercept was 1.1×10^6 s^{-1}, which agrees well with the decay rate constant of $[Ru(bpy)_3]^{2+*}$ in the absence of $[Co^{III}(NH_3)_5Cl]^{2+}$ ($k_T = 1.2(1) \times 10^6$ s^{-1}) (vide infra).

The fast dynamics of the first ET of Mn^{II} to give Mn^{III} was also examined with laser flash photolysis (Scheme 2, reaction b). In contrast to the case without **1**, complete recovery of the bleaching at 450 nm was observed within 180 μs after nanosecond laser excitation of a CH$_3$CN/H$_2$O (1:1 v/v) solution of $[Ru^{II}(bpy)_3]^{2+}$ and $[Co^{III}(NH_3)_5Cl]^{2+}$ with **1** as a result of the full regeneration of $[Ru^{II}(bpy)_3]^{2+}$ (Figure 2; also see the blue line in Figure S7). The recovery rate obeyed first-order kinetics, and the rate constant for ET from **1** to $[Ru^{III}(bpy)_3]^{3+}$ (k_b in Scheme 2) was determined to be 3.7(3)
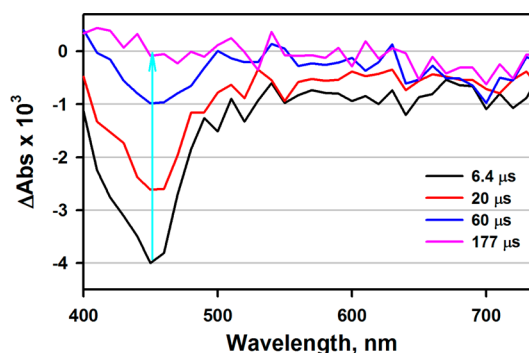
Figure 2. Representative transient absorption spectra observed at 6.4, 20, 60, and 177 μs after nanosecond laser pulse excitation ($\lambda_{ex} = 430$ nm) of a CH$_3$CN/H$_2$O (1:1 v/v) solution of $[Ru^{II}(bpy)_3]^{2+}$ (40 μM), $[Co^{III}(NH_3)_5Cl]^{2+}$ (4.0 mM), and **1** (0.80 mM) at 20 °C.

$\times 10^7$ M^{-1} s^{-1} at 20 °C from the slope of the linear plot of the pseudo-first-order rate constant versus concentration of **1** (Figure S9).

The second ET from **3** to $[Ru^{III}(bpy)_3]^{3+}$ was slow (Scheme 2, reaction c); therefore, the reaction was followed using a photodiode array spectrophotometer. As reported previously,[8] **3** was produced in the one-electron oxidation of **1** with 1.1 equiv of $[Ru^{III}(bpy)_3]^{3+}$ in CH$_3$CN/H$_2$O (1:1 v/v). Further addition of 1.1 equiv of $[Ru^{III}(bpy)_3]^{3+}$ to the solution of **3** resulted in ET from **3** to $[Ru^{III}(bpy)_3]^{3+}$, yielding **2** and $[Ru^{II}(bpy)_3]^{2+}$ after deprotonation (Figures S10 and S11). The second-order rate constant for the second ET (k_c in Scheme 2) was then determined under second-order kinetics conditions to be $1.6(1) \times 10^3$ M^{-1} s^{-1} in CH$_3$CN/H$_2$O (1:1 v/v) at 20 °C (Figure S10), where the same k_c value was obtained using different concentrations of **3** and $[Ru^{III}(bpy)_3]^{3+}$ (1:1). In the final step of the reaction cycle (Scheme 2, reaction d), **2** oxygenated vinylcyclohexane to give the epoxide product with the rate constant (k_d in Scheme 2) of 1.1(1) M^{-1} s^{-1} at 20 °C (Figure S3).

In conclusion, photocatalytic enantioselective epoxidation of terminal olefins with a chiral manganese complex has been achieved using H$_2$O as an oxygen source, $[Ru^{II}(bpy)_3]^{2+}$ as a photocatalyst, and $[Co^{III}(NH_3)_5Cl]^{2+}$ as a weak one-electron oxidant. The present study has paved a new way to use water as the most environmentally benign oxygen source in asymmetric epoxidation reactions. We have also provided the first example of the use of a synthetic chiral Mn(IV)−oxo complex in the asymmetric epoxidation of olefins. We are currently synthesizing more chiral Mn−oxo complexes with different ligands and will investigate their reactivities in various asymmetric oxidation reactions to understand the detailed mechanisms as well as the ligand effect on the enantioselectivity in the asymmetric epoxidation of olefins.

■ ASSOCIATED CONTENT

ⓢ Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b10836.

Experimental details, Figures S1−S11, Tables S1−S4, and GC chromatograms (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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(13) Replacement of acetic acid by other acids (e.g., HOTf, HClO$_4$, trifluoroacetic acid, and 2-ethylhexanoic acid) and acetate anions (e.g., CH$_3$CO$_2$Na) failed to yield epoxide in the photocatalytic oxidation of vinylcyclohexane (Table S4). However, using propionic acid instead of acetic acid afforded the same amount of epoxide product (e.g., 59 ± 4%) but with low enantioselectivity (e.g., 25 ± 2% *ee*; Table S4). Thus, acetic acid plays an important role in the photocatalytic enantioselective epoxidation of terminal olefins. However, its exact role has yet to be clarified.

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