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Bioinspired Olefin *cis*-Dihydroxylation and Aliphatic C−H Bond Hydroxylation with Dioxygen Catalyzed by a Nonheme Iron Complex

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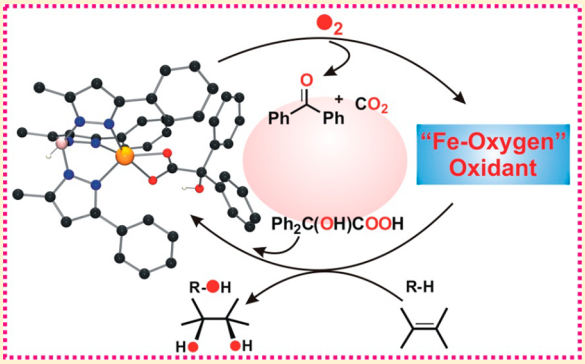
Supporting Information

ABSTRACT: A mononuclear iron(II)-α-hydroxy acid complex [$(Tp^{Ph,Me})Fe^{II}$(benzilate)] ($Tp^{Ph,Me}$ = hydrotris(3-phenyl-5-methylpyrazol-1-yl)borate) of a facial tridentate ligand has been isolated and characterized to explore its catalytic efficiency for aerial oxidation of organic substrates. In the reaction between the iron(II)-benzilate complex and O_2, the metal-coordinated benzilate is stoichiometrically converted to benzophenone with concomitant reduction of dioxygen on the iron center. Based on the results from interception experiments and labeling studies, different iron-oxygen oxidants are proposed to generate in situ in the reaction pathway depending upon the absence or presence of an external additive (such as protic acid or Lewis acid). The five-coordinate iron(II) complex catalytically *cis*-dihydroxylates olefins and oxygenates the C−H bonds of aliphatic substrates using O_2 as the terminal oxidant. The iron(II) complex exhibits better catalytic activity in the presence of a Lewis acid.



INTRODUCTION

Selective oxyfunctionalization of hydrocarbons is an important step in the synthesis of useful materials in chemical industries.[1] Traditional oxidants, such as heavy-metal oxides/oxo-hydroxides, chlorine, periodate, peroxides, and so on, are commonly used for oxidation of alkanes and alkenes.[2] In these reactions, the oxidant-derived products are often hazardous and the reactions are not selective. Despite extensive research in this field,[3,4] development of sustainable methods for oxidation reactions with high efficiency and selectivity still remains a challenge. In biological systems, metalloenzymes are involved in catalyzing these challenging oxidations under mild conditions using dioxygen as the terminal electron acceptor.[5−9] Taking lessons from nature, bioinspired approaches toward development of sustainable oxidation catalysts have attracted considerable attention. While significant progress has been made in bioinspired catalysis using peroxides or peracids for the oxidation of hydrocarbon substrates by metal complexes,[10−18] use of dioxygen in catalytic oxidations remains less explored. The reductive activation of dioxygen by bioinspired complexes and subsequent generation of metal−oxygen oxidants for substrate oxidation requires electron and proton sources.[19−27] In biomimetic chemistry, cosubstrate-assisted activation of O_2 by transition metal complexes offers attractive alternatives for bioinspired catalysis.[5,28−33] In spite of a few reports on oxygen-dependent transformation of hydrocarbon substrates by nonheme iron complexes in the presence of sacrificial reductants[26,34,35] the crisis of selective and catalytic systems prevail.

In our endeavor to develop bioinspired catalysts for oxidations with O_2, we have been pursuing systematic studies on the reductive activation of dioxygen by biomimetic iron(II) complexes using α-hydroxy acids as sacrificial reductants.[36−40] The iron(II)−benzilate complexes have been reported to oxidize substrates through in situ generation of iron−oxygen oxidants (Scheme 1). Unfortunately, there is no direct experimental evidence yet for such iron−oxygen oxidants. We have proposed different iron−oxygen oxidants generated under different experimental conditions based on indirect evidence such as interception and mechanistic studies. Among the reported complexes, the iron(II)−benzilate complex of the Tp^{Ph2} (hydrotris(3,5-diphenylpyrazolyl)borate)) ligand exhibits better reactivity in stoichiometric oxidation compared to those supported by tetradentate ligands. However, the tendency of the ligand (Tp^{Ph2}) to undergo intramolecular hydroxylation[21,41] under oxidizing conditions is expected to make the iron complexes of this ligand less active for catalytic oxidation. Recently, we demonstrated that the iron(II) complex [$(Tp^{Ph,Me})Fe^{II}$(BF)] (BF = monoanionic benzoylformate, $Tp^{Ph,Me}$ = hydrotris(3-phenyl-5-methylpyrazolyl)borate) was capable of performing the catalytic aerobic oxidation of alcohols and oxygen atom transfer reactions without detectable

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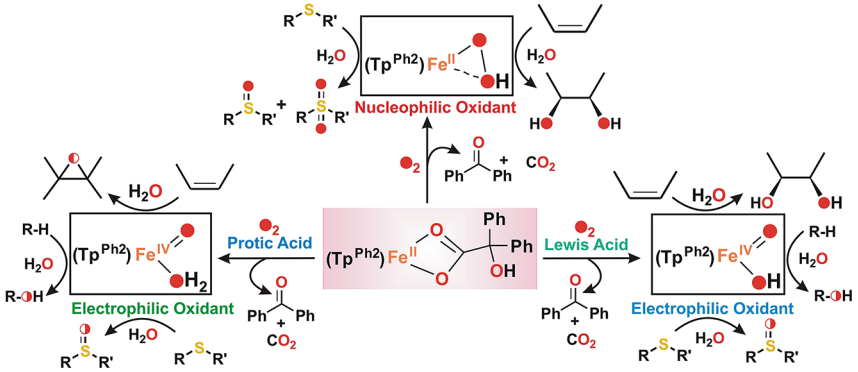
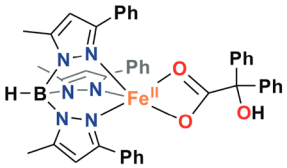
Scheme 1. Proposed Iron−Oxygen Oxidants Generated In Situ upon Reductive Activation of Dioxygen from [(Tp^{Ph2})Fe^{II}(benzilate)] Complex under Different Reaction Conditions[36−38]

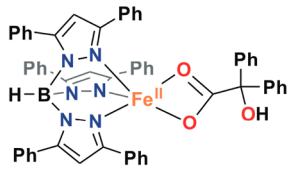


intraligand hydroxylation.[42] This motivated us to isolate the iron(II)−benzilate complex [(Tp^{Ph,Me})Fe^{II}(benzilate)] (**1**) and explore its efficiency in the aerobic oxidation of substrates. In the present investigation, we found that complex **1** not only displayed selective oxygenation of substrates under stoichiometric condition, but also exhibited catalytic oxidation of alkanes, alkenes and sulfides. The catalytic ability of **1** in the O_2-dependent oxidation reactions and its comparison with that of [(Tp^{Ph2})Fe^{II}(benzilate)] (**2**; Chart 1) are presented in this manuscript.

Chart 1. Iron(II)−Benzilate Complexes of Facial N_3 Ligands



[(Tp^{Ph,Me})Fe^{II}(Ph$_2$C(OH)COO)] (**1**)



[(Tp^{Ph2})Fe^{II}(Ph$_2$C(OH)COO)] (**2**)

RESULTS AND DISCUSSION

Synthesis and Characterization. Complex **1** was isolated from the reaction of KTp^{Ph,Me} with iron(II) chloride and sodium benzilate in a solvent mixture of dichloromethane and methanol at room temperature under nitrogen atmosphere (Experimental Section). The ^{1}H NMR spectrum of **1** displaying paramagnetically shifted proton resonances in the range between +70 and −25 ppm supported the high spin nature of the complex in solution (Figure S1, SI). The ESI-mass spectrum of **1** in acetonitrile exhibits an ion peak at m/z 767.3 with the isotope distribution pattern calculated for [(Tp^{Ph,Me})Fe(benzilate) + H$^+$] along with other mass fragments (Figure S2 and Experimental Section). The composition of the complex was further confirmed by single crystal X-ray diffraction studies (Table 1). The X-ray crystal structure of the neutral complex displays a five-coordinate iron center coordinated by the facial tridentate Tp^{Ph,Me} ligand and the carboxylate oxygen atoms of benzilate monoanion (Figure 1). In the ternary complex, the iron center adopts a distorted square pyramidal coordination geometry. Two nitrogen donors (N1 and N3) from the Tp^{Ph,Me} ligand, and two carboxylate oxygen atoms (O1 and O2) from benzilate constitute the basal plane of the distorted square pyramid (τ = 0.46)[43] The apical position is occupied by N5 nitrogen from the Tp^{Ph,Me} ligand with the Fe1−N5 distance of 2.076(6) Å (Table 2). The

Table 1. Crystallographic Data for [(Tp^{Ph,Me})Fe^{II}(benzilate)] (1)

	1
empirical formula	$C_{44}H_{39}BFeN_6O_3$
formula weight	766.47
crystal system	triclinic
space group	*P*-1
a, Å	11.878(4)
b, Å	14.847(5)
c, Å	15.937(6)
α, deg	100.607(8)
β, deg	100.605(8)
γ, deg	101.476(8)
volume, Å^3	2635.2(16)
Z	2
D_{calcd}, Mg/m^3	0.967
μ Mo K$_\alpha$, mm^{-1}	0.322
F(000)	800.96
θ range, deg	1.34−28.44
reflections collected	12086
reflns unique	8208
R(int)	0.0453
data ($I > 2\sigma(I)$)	6826
parameters refined	504
goodness-of-fit on F^2	1.153
R_1 [$I > 2\sigma(I)$]	0.0782
wR_2	0.2132

average Fe−N bond length of 2.105 Å is comparable to those of other Fe^{II}(Tp^{Ph,Me}) complexes,[44] while the iron−oxygen distances (r(Fe1−O1), 2.338(6) and r(Fe1−O2), 2.020(5) Å) indicate asymmetric bidentate binding mode of carboxylate. The geometry of the five-coordinate iron center and the binding mode of benzilate is very similar to those of the reported complex of the Tp^{Ph2} ligand.[36] The hydroxy group of benzilate remains noncoordinated in both the complexes. The Fe−O2(carboxylate) and the Fe−N1 bonds in **1** are slightly elongated compared to those in **2** (Table 2). Additionally, the phenyl rings at 3-position of each pyrazole ring in **1** are slightly tilted away from the metal center (Figure S3). These slight structural variations likely prevent the intraligand hydroxylation.

Dioxygen Reactivity. The iron(II) complex (**1**) reacted with pure dioxygen in benzene to convert the colorless solution to light yellow (Figure S4). Time-dependent product analyses revealed the quantitative conversion of iron-coordinated

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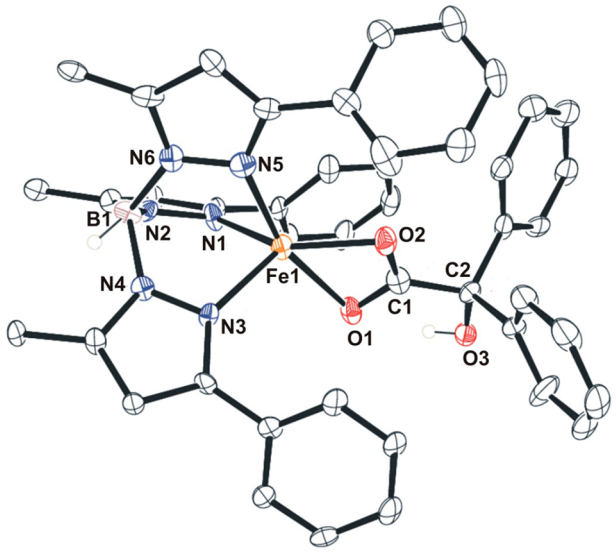

Figure 1. ORTEP plot of $[(Tp^{Ph,Me})Fe^{II}(benzilate)]$ (**1**). All the hydrogen atoms other than those on B1 and O3 are omitted for clarity.

Table 2. Selected Bond Lengths (Å) and Bond Angles (deg) for $[(Tp^{Ph,Me})Fe^{II}(benzilate)]$ (1) and $[(Tp^{Ph2})Fe^{II}(benzilate)]$ (2)

	$[(Tp^{Ph,Me})Fe^{II}(benzilate)]$ (**1**)	$[(Tp^{Ph2})Fe^{II}(benzilate)]$ (**2**)[39]
Fe(1)–N(1)	2.147(7)	2.075(3)
Fe(1)–N(3)	2.095(6)	2.082(3)
Fe(1)–N(5)	2.076(6)	2.120(3)
Fe(1)–O(2)	2.020(5)	2.008(3)
Fe(1)–O(1)	2.338(6)	2.346(3)
C(1)–O(1)	1.251(10)	1.248(4)
C(1)–O(2)	1.275(9)	1.273(5)
C(1)–C(2)	1.520(11)	1.534(5)
C(2)–O(3)	1.430(10)	1.421(5)
N(1)–Fe(1)–O(1)	107.74(2)	98.23(10)
N(1)–Fe(1)–O(2)	131.22(2)	134.82(11)
N(3)–Fe(1)–O(1)	98.23(2)	107.88(10)
N(3)–Fe(1)–O(2)	134.94(2)	131.04(11)
N(5)–Fe(1)–O(1)	162.8(2)	162.16(11)
N(5)–Fe(1)–O(2)	104.3(2)	103.85(12)
O(1)–Fe(1)–O(2)	60.00(2)	59.83(10)
N(1)–Fe(1)–N(3)	91.57(2)	91.87(11)
N(1)–Fe(1)–N(5)	87.7(2)	88.75(11)
N(3)–Fe(1)–N(5)	88.5(2)	88.16(11)
τ	0.46	0.46

benzilate to benzophenone in 45 min (Figure 2). The ESI-mass spectrum of the oxidized solution showed an ion peak at m/z 539.2 attributable to $[(Tp^{Ph,Me})Fe]^+$ ion. Unlike that observed with **2**, no peak corresponding to the iron complex of the hydroxylated form of $Tp^{Ph,Me}$ was observed in the mass spectrum of the oxidized solution of **1** (Figure S5, inset).

The two-electron oxidative decarboxylation of benzilate to benzophenone suggests that dioxygen can undergo two-electron reduction on the iron center. In the absence of any observable intermediate in the reaction pathway, the in situ formed iron–oxygen oxidant from **1** was intercepted using external substrates as probes (Table 3, Experimental Section). Complex **1** reacted with thioanisole (10 equiv) to afford a

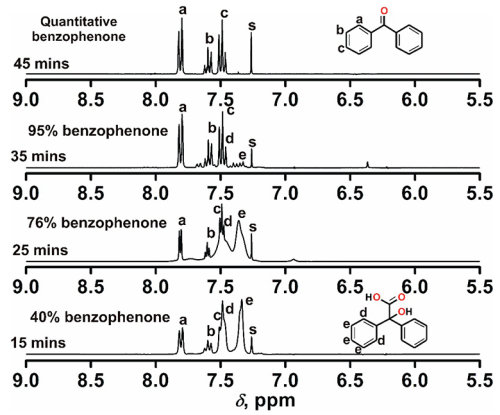

Figure 2. Time-dependent ^1H NMR (500 MHz, $CDCl_3$, 295 K) spectra monitoring the formation of benzophenone in the reaction between complex **1** and O_2.

mixture of methyl phenyl sulfoxide (93%) and methyl phenyl sulfone (4%; Figure S6). The oxidized solution of **1** after the reaction with thioanisole was found to be X-band EPR silent and exhibited paramagnetically shifted proton resonances in the NMR spectrum indicating the formation of an iron(II) species (Figure S7). Thus, the in situ formed species was a two-electron reduced iron–oxygen oxidant which after oxidation of thioanisole generated an iron(II) complex. Hammett analyses using 1:1 mixtures of thioanisole and different *para*-substituted thioanisoles (p-$XC_6H_4SCH_3$, where X = NO_2, Br, H, Me, OMe) resulted in a ρ value of +1.04 (Figure S8) supporting the nucleophilic nature of the iron–oxygen oxidant from **1**. Nucleophilic iron–oxygen oxidants from H_2O_2 have been reported to *cis*-dihydroxylate alkenes.[15,45] Reaction of **1** with cyclohexene yielded around 80% *cis*-cyclohexane-1,2-diol as the only product (Figure S9). Cyclooctene afforded 86% *cis*-cyclooctane-1,2-diol (Figure S10) and 1-octene was selectively converted to octane-1,2-diol with about 92% yield (Figure S11). Electron-deficient olefin, *tert*-butyl acrylate showed very high yield of the corresponding diol (96%; Figure S12).

As observed with complex **2**,[37] an electrophilic oxidant was generated from **1** in the presence of $Sc(OTf)_3$ (Figure S13). In the reaction condition, thioanisole was selectively oxidized to thioanisole oxide with the incorporation of one ^{18}O atom from $H_2{}^{18}O$ into the sulfoxide product (Figure S14). The electrophilic oxidant selectively oxidized alkenes to the corresponding *cis*-diols, in which partial incorporation of oxygen atom from water took place (Figure 3, Scheme 2). The product profile and the results of labeling experiments clearly support that the oxidant from **1** and O_2 with Sc^{3+} can exchange its oxygen atoms with water.

Aliphatic C–H bonds were oxygenated with high selectivity by the electrophilic oxidant (Scheme 2). Cyclohexane formed cyclohexanol (60%) and cyclohexanone (5%) with high A/K (12) ratio (Figure S15). Labeling experiments with $^{16}O_2$ and $H_2{}^{18}O$ showed about 38% incorporation of ^{18}O into cyclohexanol (Figure S16). Adamantane and methylcyclohexane were selectively transformed to 1-adamantanol (70% yield; Figure S17) and 1-methylcyclohexanol (63% yield), respectively (Figure S18). Except for the electron-deficient alkene (*tert*-butyl acrylate), the yields of oxygenated products were found to be higher compared to that found with complex **2** under similar experimental conditions (Table 3).

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Table 3. Reactivity of Iron(II)-Benzilate Complexes (1 and 2) of Monoanionic N_3 Ligands toward Different Substrates[a]

substrate	product(s)	yield (%) of products with $[(Tp^{Ph,Me})Fe^{II}(benzilate)]$ (1)[c] without additive	with $Sc(OTf)_3$	with $PyHClO_4$	yield (%) of products with $[(Tp^{Ph2})Fe^{II}(benzilate)]$ (2)[b] without additive	with $Sc(OTf)_3$	with $PyHClO_4$
thioanisole (10 equiv)	$PhSOCH_3$	93 ± 1	96 ± 2	97 ± 1	84	90	90
	$PhSO_2CH_3$	4 ± 1	0	0	7	0	0
cyclooctene (100 equiv)	*cis*-cyclooctane-1,2-diol	86 ± 1	87 ± 3	0	80	80	0
	cyclooctene oxide	0	0	58 ± 1	0	0	70
1-octene (100 equiv)	octane-1,2-diol	92 ± 2	93 ± 1	0	85	85	0
	1,2-epoxy-octane	0	0	56 ± 2	0	0	67
cyclohexene (100 equiv)	*cis*-cyclohexane-1,2-diol	80 ± 1	82 ± 2	0	60	60	0
	2-cyclohexen-1-one	0	0	31 ± 2	0	0	35
	2-cyclohexen-1-ol	0	0	20 ± 2	0	0	22
	cyclohexene oxide	0	0	5 ± 1	0	0	5
tert-butyl acrylate (100 equiv)	*tert*-butyl 2,3-dihydroxypropanoate	96 ± 2	8 ± 1		96	10	
cyclohexane (100 equiv)	cyclohexanol	0	60 ± 1	58 ± 3	0	50	45
	cyclohexanone	0	5 ± 1	6 ± 1	0	5	8
1-methyl-cyclohexane (100 equiv)	1-methyl-cyclohexanol	10 ± 1	63 ± 2	60 ± 2	12	45	44
	2-methyl-cyclohexanol	0	0	4 ± 1	3	13	15
adamantane (50 equiv)	1-adamantanol	20 ± 2	70 ± 4	65 ± 4	20	70	47
	2-adamantanol	4 ± 1	0	<2	4	0	18
	2-adamantanone	5 ± 1	0	<4	5	0	0

[a]Reaction conditions: 0.02 mmol complex dissolved in dry benzene. [b]Reaction time = 15 min. [c]Reaction time = 45 min.

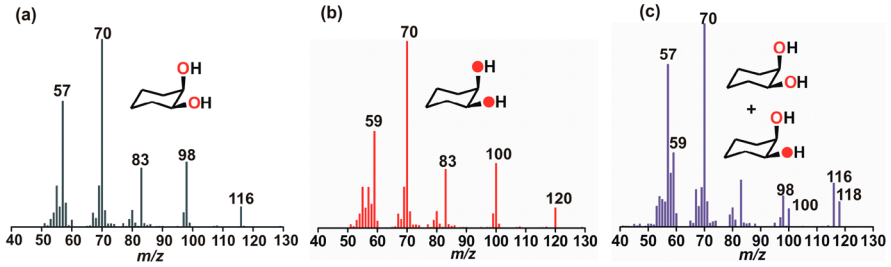
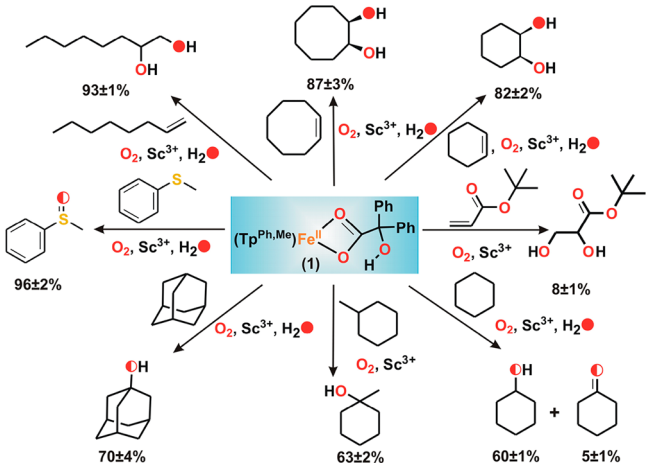
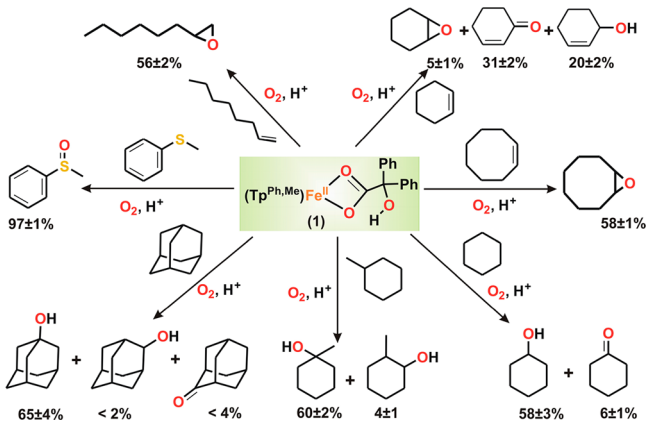


Figure 3. GC-mass spectrum of *cis*-cyclohexane-1,2-diol product formed in the reaction of **1** with cyclohexene and (a) $^{16}O_2$, (b) $^{18}O_2$, and (c) $^{16}O_2/H_2{}^{18}O$ in the presence of Sc^{3+} (1 equiv).

Scheme 2. Oxidation of Substrates by Complex 1 in the Presence of $Sc(OTf)_3$



Scheme 3. Oxidation of Substrates by Complex 1 with Dioxygen in the Presence of Pyridinium Perchlorate (2 equiv)



The effect of protic acid on the reactivity of **1** toward different substrates was also investigated (Scheme 3). The reaction of **1** with thioanisole and pyridinium perchlorate (2 equiv) afforded thioanisole oxide. As in the case with Sc^{3+}, the oxidant here hydroxylated adamantane to form 1-adamantanol (65%) and trace amounts of 2-adamantanol and 2-adamantanone (<4% each). Cyclohexane was converted to cyclohexanol (58%) and cyclohexanone (6%). Methylcyclohexane was oxygenated to 1-methylcyclohexanol (60%) along with a small amount of 2-methylcyclohexanol (4%). The

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Table 4. Catalytic Oxidation of Substrates by 1 and Its Comparison with 2

			[(Tp^{Ph,Me})Fe^{II}(benzilate)] (**1**)		[(Tp^{Ph2})Fe^{II}(benzilate)] (**2**)	
substrate	external additive	products (S^{Ox})	TON (S^{Ox})[h]	TON (Ph_2CO)[i]	TON (S^{Ox})[h]	TON (Ph_2CO)[i]
1-octene[b]		octane-1,2-diol	17 ± 1	20 ± 0.5	1.3 ± 0.1	1.6 ± 0.1
	$Sc(OTf)_3$[f]	octane-1,2-diol	21 ± 1	25 ± 1	2 ± 0.2	2.3 ± 0.2
	$PyNH^+$[g]	1,2-epoxyoctane	6 ± 1	20 ± 1	nd	nd
cyclooctene[b]		*cis*-cyclooctane-1,2-diol	15 ± 0.5	20 ± 0.5	nd	nd
	$Sc(OTf)_3$[f]	*cis*-cyclooctane-1,2-diol	19 ± 0.6	23 ± 1	nd	nd
	$PyNH^+$[g]	cyclooctene oxide	14 ± 0.7	18 ± 1	nd	nd
cyclohexene[b]		*cis*-cyclohexane-1,2-diol	14 ± 0.5	19 ± 1	nd	nd
	$Sc(OTf)_3$[f]	*cis*-cyclohexane-1,2-diol	19 ± 1	21 ± 1	nd	nd
	$PyNH^+$[g]	cyclohexene oxide	4 ± 1	20 ± 0.5	nd	nd
		2-cyclohexenol	8 ± 1			
		2-cyclohexenol	6 ± 1			
thioanisole[c]		thioanisole oxide	5 ± 0.5	13 ± 0.5	1 ± 0.1	2.4 ± 0.1
	$Sc(OTf)_3$[f]	thioanisole oxide	10 ± 1	16 ± 1	3 ± 0.2	7 ± 0.2
	$PyNH^+$[g]	thioanisole oxide	8 ± 0.4	14 ± 0.5	nd	nd
adamantane[d]	$Sc(OTf)_3$[f]	1-adamantanol	12 ± 1	18 ± 1	nd	nd
		2-adamantanol	1.2 ± 1			
		2-adamantanone	1.9 ± 1			
	$PyNH^+$[g]	1-adamantanol	8 ± 1	15 ± 0.5	nd	nd
		2-adamantanol	1.1 ± 1			
		2-adamantanone	1.4 ± 1			
cyclohexane[e]	$Sc(OTf)_3$[f]	cyclohexanol	10 ± 0.5	16 ± 0.5	0.6 ± 0.1	1.1 ± 0.1
		cyclohexanone	0.9 ± 0.5		0.05	
	$PyNH^+$[g]	cyclohexanol	7 ± 0.5	14 ± 1	nd	nd
		cyclohexanone	0.5 ± 0.5			
methyl-cyclohexane[e]	$Sc(OTf)_3$[f]	1-methylcyclo-hexanol	11 ± 2	15 ± 1	nd	nd
		2-methylcyclo-hexanol	4 ± 1			
		2-methylcyclo-hexanone	1.3 ± 1			
	$PyNH^+$[g]	1-methylcyclo-hexanol	9 ± 2	15 ± 0.5	nd	nd
		2-methylcyclo-hexanol	5 ± 0.5			
		2-methylcyclo-hexanone	2 ± 1			
				1.06[j]	nd	nd
	$Sc(OTf)_3$			9.0[k]	nd	nd

[a]Reaction conditions: Dry benzene-acetonitrile (4:1) solvent mixture (4 h for **1** and 1 h for **2**) with 0.02 mmol (0.0153 g) catalyst, and 30 equiv (0.150 g, 0.6 mmol) of sodium benzilate. [b]Concentration of alkenes (1-octene, cyclooctene and cyclohexene): 100 equiv with respect to catalyst. [c]100 equiv of thioanisole. [d]50 equiv adamantane. [e]100 equiv of cyclohexane/methylcyclohexane. [f]20 equiv of $Sc(OTf)_3$ with respect to catalyst; [g]10 equiv of pyridinium perchlorate was added. [h]TON (S^{Ox}) = mol of product formed/mol of catalyst used. [i]TON (benzilate) = (mol of benzophenone formed−mol of catalyst used)/mol of catalyst. [j]reaction with complex **1** and sodium benzilate (30 equiv). [k]reaction with complex **1** and sodium benzilate (30 equiv) in the presence of 20 equiv of $Sc(OTf)_3$. nd: not determined.

oxidant from **1** in the presence of protic acid oxidized alkenes to the corresponding epoxides. With cyclooctene as substrate, cyclooctene oxide was formed in 58% yield. The oxidant converted 1-octene to 1,2-epoxyoctane in 56% yield (Figure S19). When cyclohexene is used, the corresponding allylic oxidation products were formed along with a small amount of epoxide (Scheme 3 and Figure S20). Therefore, a different electrophilic oxidant was generated from **1** in the presence of protic acid which could carry out epoxidation of alkenes instead of *cis*-dihydroxylation.

Catalytic Activity. The high yields in substrate oxidations without detectable intraligand hydroxylation under stoichiometric conditions encouraged us to explore the catalytic activity of complex **1** in O_2-dependent oxidations using excess benzilate. After several experimental trials with 1-octene, the reaction condition was optimized (Experimental Section). The catalytic reactions were then separately performed: (i) without any external additive, (ii) with Sc^{3+}, and (iii) with a proton source in a solvent mixture of dry benzene and acetonitrile (4:1) for 4 h (Table 4). For catalytic reactions with additives, maximum catalytic activity of **1** was obtained with 20 equiv of Sc^{3+} (Figures S21 and S22) and 10 equiv of protic acid (Figure S23). With increasing concentration of sodium benzilate, the turnovers number (TON) of benzophenone increased and reached a maximum value with 30 equiv of sodium benzilate (Figure 4). However, the TON of the oxidized product from 1-

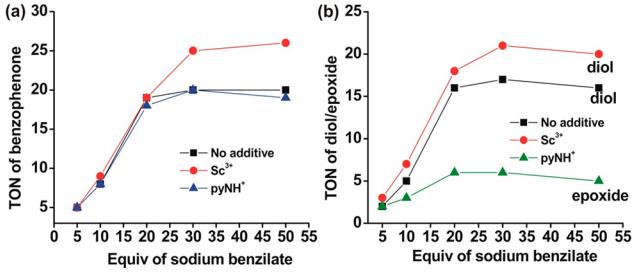

Figure 4. Plot of (a) TON for benzophenone vs equiv of sodium benzilate added and (b) TON of oxidized product(s) from 1-octene vs equiv of sodium benzilate by complex **1** and O_2.

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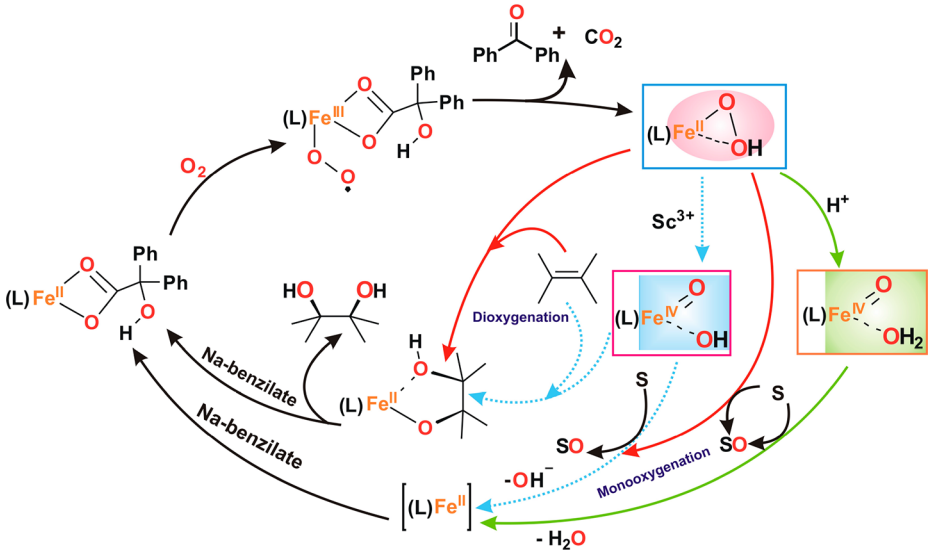
Scheme 4. Proposed Catalytic Cycle for the Oxygenation of Substrates with O_2 by a Nonheme Iron(II)−Benzilate Complex



octene (diol/epoxide) was found to be additive dependent (Figure 4b). In the experimental conditions, highest catalytic activity was observed with Sc^{3+}, affording 25 turnovers for the conversion of benzilate to benzophenone and 21 turnovers for octane-1,2-diol. Without any external additive, 20 turnovers for benzophenone and 17 turnovers for octane-1,2-diol were achieved (Table 4). With the protic acid, the TON of benzophenone was maximized at 20 but the TON for 1,2-epoxyoctane was found to be 6 (Table 4). Catalytic reactions with 1-octene in the presence of Sc^{3+} revealed that the TONs of octane-1,2-diol increased with substrate concentration and achieved a maximum TON at 100 equiv of substrate (Figure S24). For cyclohexene, 14 turnovers of *cis*-diol were achieved as quantified by acetylation of the oxidized product (Figure S25). The TON for benzophenone not only depends on additives but also on the nature of substrates; alkenes display better reactivity compared to other substrates.

With aliphatic substrates, catalytic reactions were performed separately with Sc^{3+} and protic acid (Table 4). Adamantane was oxidized to 1-adamantanol with a TON of 12 in the presence of Sc^{3+} and a TON of 8 in the presence of protic acid. In both the cases, 2-adamantanol and 2-adamantanone were observed but with very low yields. Moreover, complex **1** catalyzed the hydroxylation of strong C−H bonds of cyclohexane in the presence a Lewis acid or a protic acid (as the case may be) with multiple TON. Methylcyclohexane was catalytically oxidized to 1-methylcyclohexanol with a TON of 11 with Sc^{3+} and a TON of 9 with protic acid. Additionally, complex **1** is active in catalytic oxo transfer reaction to convert thioanisole to thioanisole oxide (Table 4). From the experimental results, it is evident that Lewis acid enhances the catalytic efficiency of **1** toward olefin *cis*-dihydroxylation, aliphatic C−H bond oxygenation, and oxo transfer reaction. It is important to mention here that these substrates were not catalytically oxidized under the reaction conditions of control experiments using a combination of the $Tp^{Ph,Me}$ ligand and iron(II) chloride/perchlorate (Experimental Section). These results clearly demonstrated the role of benzilate in directing the catalytic oxidation of substrates.

For comparison, the catalytic reactivity of [(Tp^{Ph2})-Fe^{II}(benzilate)] (**2**) was investigated (Table 4). Here, the reactions took about an hour to attain maximum yield. The activity of the complex, however, was found to be low. The complex did not show catalytic turnover for benzophenone in the absence of substrate. The oxidation of thioanisole or 1-octene in the presence of Sc^{3+} showed very low TON but the complex underwent intraligand hydroxylation. The tendency of the ligand to undergo intraligand hydroxylation was responsible for low catalytic activity of **2**. Among all other reported iron(II)−benzilate complexes,[36−40] complex **1** is not only a better system for stoichiometric oxidation, but also for selective and catalytic oxidation of substrates (Tables 3, 4, and S1).

On the basis of the above experimental results and by analogy with the mechanistic proposal reported for the Tp^{Ph2} system,[36−38] a side-on bound nucleophilic iron(II)-hydroperoxide is proposed to form initially in the reductive activation of dioxygen by complex **1** (Scheme 4). With a Lewis acid, the iron(II)-hydroperoxide undergoes heterolytic O−O bond cleavage to generate an electrophilic iron(IV)-oxo-hydroxo oxidant where two oxygen atoms are disposed *cis* to each other and can exchange with water. With protic acid, an iron(IV)-oxo-aqua species is proposed as the active oxidant.[38] While both iron(II)-hydroperoxide and iron(IV)-oxo-hydroxo can perform *cis*-dihydroxylations of alkenes, the iron(IV)-oxo species generated with protic acid participates in olefin epoxidation reaction instead of *cis*-dihydroxylation. In the case of aliphatic C−H bond hydroxylation, only the electrophilic high-valent iron-oxo species are involved. After oxidation of substrates, the iron(II)−benzilate complex is regenerated from sodium benzilate. The ESI-mass spectrum (positive ion mode in benzene−acetonitrile) of the oxidized solution of **1** after the reaction with cyclohexene revealed an ion peak at m/z 655.3 corresponding to the iron(II)-alkoxide (monodeprotonated diol) complex of $Tp^{Ph,Me}$ ligand (Figure S26). Although the same complex could not be isolated, the addition of excess sodium benzilate to the above solution resulted in catalytic turnovers of cyclohexene. This result indicates that iron(II)-coordinated monodeprotonated diols are labile enough to be replaced by anionic carboxylate donor of benzilate, thereby regenerating the catalyst.

Thus, complex **1** displays moderate activity as an oxidation catalyst which makes use of O_2 as the terminal oxidant to

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catalyze selective oxygenation of a number of substrates. While the TON for diols (dioxygenation) from alkenes are high compared to monooxygenated products, there is a clear mismatch for the TON of benzophenone and thioanisole, and of benzophenone and monooxygenated products with protic acid. It is important to mention here that neither benzilic acid nor a combination of benzilic acid and scandium(III) triflate exhibited catalytic oxidation. Additionally, the complex (**1**) in the reaction with sodium benzilate (30 equiv) displayed only stoichiometric conversion of benzilate in the absence of both substrate and Sc^{3+}. Interestingly, a combination of sodium benzilate (30 equiv) and scandium(III) triflate (20 equiv) was able to convert benzilate to benzophenone with a TON of 9 even in the absence of thioanisole (Table 4). In the presence of thioanisole, the TON of benzophenone was increased to 16 along with 10 turnovers for thioanisole oxide. Therefore, the electrophilic oxidants from **1** can oxidize noncoordinated benzilate, causing the mismatch in benzilate and substrate TONs. For monooxygenation reactions with or without Sc^{3+}, 1 equiv of hydroxide ion is expected to generate after each cycle. The hydroxide ion either remains coordinated to the iron center or in free form in solution. All attempts to isolate an iron(II)−hydroxide complex of the $Tp^{Ph,Me}$ ligand failed, but the addition of tetrabutylammonium hydroxide (3 equiv) almost completely inhibited the catalytic conversion of thioanisole by complex **1**. Similarly, no turnover for substrate oxidation was observed in the presence of pyridine (10 equiv). The formation of pyridine in the reaction with pyridinium perchlorate and the gradual accumulation of hydroxide in the catalysis without any additive possibly cause low turnovers in monooxygenation reactions. The hydroxide ion can be partially quenched by Lewis acid showing relatively better activity in the catalytic reactions with Sc^{3+}. The formation of catalytically inactive complexes (hydroxide/pyridine-coordinated iron complex, diiron(III) species) likely contribute to limiting the turnovers (Scheme S1).

SUMMARY AND CONCLUSIONS

In conclusion, the catalytic efficiency of a nonheme iron(II)-α-hydroxy acid complex of a hydrotris(3-phenyl-5-methylpyrazolyl)borate ligand toward selective oxygenation of organic substrates using O_2 as the terminal oxidant has been explored. The complex catalyzes selective oxidation of organic substrates with multiple turnovers. Based on interception and labeling experiments, involvement of iron−oxygen oxidants such as iron(II)-hydroperoxide (with no external additive), iron(IV)-oxo-hydroxo (with a Lewis acid) and iron(IV)-oxo-aqua (with a protic acid) has been proposed in the oxidation reactions. Lewis acid enhances the catalytic efficiency of the iron(II)-benzilate toward oxygenation reactions. Thus, a "proof of concept" of using sacrificial reductant for sustainable catalytic oxidation with O_2 by a bioinspired iron complex has been established. The results presented here would provide useful information in developing oxidatively robust and efficient catalytic systems for O_2-dependent oxidations of organic substrates.

EXPERIMENTAL SECTION

Materials and Methods. All chemicals and reagents were obtained from commercial sources and were used as such unless otherwise noted. Solvents were distilled and dried before use. Preparation and handling of air-sensitive materials were carried out under an inert atmosphere in a glovebox. *Although no problem was encountered during the synthesis of the complexes, perchlorate salts are potentially explosive and should be handled with care.* The ligand $KTp^{Ph,Me}$ was prepared according to a procedure reported in the literature.[46] Complex **2** was prepared according to the reported procedure.[39]

Fourier transform infrared spectroscopy on KBr pellets was performed on a Shimadzu FT-IR 8400S instrument. Elemental analyses were performed on a PerkinElmer 2400 series II CHN analyzer. Electrospray ionization (ESI) mass spectra were recorded with a Waters QTOF Micro YA263 instrument. Solution electronic spectra (single and time-dependent) were measured on an Agilent 8453 diode array spectrophotometer. All room temperature NMR spectra were collected on a Bruker Avance 500 MHz spectrometer. X-band EPR measurements were performed on a JEOL JES-FA 200 instrument. GC-MS measurements were carried out with a PerkinElmer Clarus 600 using Elite 5 MS (30 m × 0.25 mm × 0.25 μm) column with a maximum temperature of 300 °C. Labeling experiments were carried out with $^{18}O_2$ gas (99 atom %) or $H_2{}^{18}O$ (98 atom %) purchased from Icon Services Inc., U.S.A.

*Synthesis of [($Tp^{Ph,Me}$)Fe^{II}(benzilate)] (**1**).* Anhydrous iron(II) chloride (0.06 g, 0.50 mmol) was added to a solution of the ligand $KTp^{Ph,Me}$ (0.26 g, 0.50 mmol) in dichloromethane (5 mL). The resulting mixture was stirred for 10 min to form a white suspension. To the resulting solution was added a methanolic solution of sodium benzilate (0.13 g, 0.50 mmol) and was stirred at room temperature under nitrogen atmosphere for 2 h. The solution was then concentrated under vacuum, washed with dichloromethane, and filtered. The resulting filtrate was concentrated, washed with acetonitrile, and filtered. The filtrate was further concentrated and washed with hexane to isolate an off-white solid. The solid was further purified by recrystallization from a solvent mixture of dichloromethane and methanol (1:1). Yield: 0.11 g (30%). Elem. anal. Calcd (%) for $C_{44}H_{40}BFeN_6O_3{\cdot}CH_3OH$ (799.52 g mol^{-1}): C, 67.60; H, 5.55; N, 10.51. Found: C, 67.56; H, 5.38; N, 10.67. IR (KBr): 3434(br), 3137−2962, 2551, 1728, 1618(br), 1546(m), 1485(m), 1448(m), 1413, 1344 (s) 1280, 1188(s), 1176(s), 1066(s) 975, 761(vs), 696(vs) cm^{-1}. ESI-MS (positive ion mode, benzene-CH_3CN) m/z (%): 789.3 (3%), {[($Tp^{Ph,Me}$)Fe(benzilate)] + Na}$^+$; 767.3 (6%), {[($Tp^{Ph,Me}$)Fe(benzilate)] + H}$^+$; 697.3 (20%), [($Tp^{Ph,Me}$)Fe + (3Ph,5MePzH)]$^+$; 557.2 (10%), {[($Tp^{Ph,Me}$)Fe] + H_2O}$^+$; 539.2 (90%), [($Tp^{Ph,Me}$)Fe]$^+$; 485.4 (20%), {($Tp^{Ph,Me}$) + 2H}$^+$; 327.2 (100%), {[($Tp^{Ph,Me}$)-3Ph,5MePzH] + H}$^+$.

*Reaction of **1** with Dioxygen.* The iron(II)−benzilate complex (0.02 mmol) was dissolved in 10 mL of dioxygen-saturated benzene. The solution was allowed to stir at room temperature for 45 min. After the reaction, the solution was concentrated and the residue was treated with 5 M HCl solution (10 mL). The organic products were extracted with diethyl ether (3 × 15 mL), and the organic layer was dried over anhydrous sodium sulfate. After removal of the solvent, the colorless residue was analyzed by GC-MS and ^{1}H NMR spectroscopy. For dioxygen reactivity in the presence of Lewis acid or protic acid, the required amount of acid was dissolved in acetonitrile and added to the reaction solution immediately after purging dioxygen to the iron(II)−benzilate complex.

*Reactions of **1** with Substrates.* The iron(II)−benzilate complex (0.02 mmol) was dissolved in benzene (10 mL) under a nitrogen atmosphere. To the solution was added the substrate, and dry dioxygen was purged through the solution for 2 min. For the reactions in the presence of additive, the dioxygen-saturated solution was treated with a Lewis acid/protic acid dissolved in acetonitrile followed by the addition of external substrate. The reaction solution was allowed to stir at room temperature for 40−45 min. After oxidation, the solvent was removed under reduced pressure and the iron complex was decomposed with 10 mL of 5 M HCl solution. Organic products were then extracted either with diethyl ether or with chloroform (3 × 15 mL), and the organic layer was dried over anhydrous sodium sulfate. After removal of the solvent, organic products were analyzed by GC-MS and ^{1}H NMR spectroscopy. For reactions with alkenes, the products were analyzed by ^{1}H NMR or injected to GC-MS after esterification with acetic anhydride following

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the literature procedure.[47] Quantification of organic products by NMR was done by comparing the peak area of four aromatic *ortho* protons (7.81 ppm) of benzoquinone. For reactions with alkenes in the presence of protic acid, the solution after reaction with dioxygen was passed through 15 cm silica (60−120 mesh size) column using dichloromethane as eluent. The combined organic phase was then analyzed by GC-mass spectrometry. For GC analyses, naphthalene was used as an internal standard and the products were identified by comparison of their GC retention times and GC-MS with those of authentic compounds. For mixed labeling experiment, $H_2{}^{18}O$ (12 μL) water was added to the solution of the complex prior to exposure to dioxygen. All the products were quantified by ^{1}H NMR spectroscopy except for cyclohexanol, cyclohexanone, 1-methylcyclohexanol, 2-methylcyclohexanol, 2-methylcyclohexanone,2-cyclohexenone, 2-cyclohexenol, and the epoxides derived from alkenes (cyclohexene oxide, 1,2-epoxyoctane, and cyclooctene oxide), which were quantified by GC-MS.

Catalytic Reactions. For catalytic experiments, the iron(II) complex (0.02 mmol) was dissolved in 10 mL of benzene-acetonitrile solvent mixture (4:1) under nitrogen atmosphere. To the solution, sodium benzilate (30 equiv, 0.15 g) was added followed by addition of excess substrate (100 equiv/50 equiv for adamantane). Then dioxygen was purged through the solution for 2 min. The reaction solution was allowed to stir at room temperature for 4 h. For catalysis in the presence of Lewis acid, 20 equiv of scandium(III) triflate was added in four equal portions at an interval of 10 min. Similarly for catalytic experiments in the presence of protic acid, 10 equiv of pyridinium perchlorate was added in four equal portions at an interval of 10 min. After the reaction, the solvent was removed under reduced pressure and the iron complex was decomposed by addition of 5 M HCl solution (10 mL). The organic products were extracted either by diethyl ether or by chloroform (3 × 15 mL), and the organic layer was dried over anhydrous sodium sulfate. After removal of the solvent, organic products were analyzed by GC-MS and ^{1}H NMR spectroscopy. For catalytic experiments, quantification of the products were done by adding 3,5-di-*tert*-butyl benzoquinone as a standard (to the organic layer after acidic work up). All experiments were performed in triplicate and the average values are reported.

Control Experiments. For control experiments, iron(II) perchlorate hydrate (0.007 g, 0.02 mmol) was added to a solution of the ligand $KTp^{Ph,Me}$ (0.01 g, 0.02 mmol) in 10 mL benzene-acetonitrile (4:1) solvent mixture. To the resulting solution, substrate (100 equiv or 50 equiv for adamantane) was added and dioxygen was purged to the solution for 2 min. The solution was allowed to stir for 4 h. After the reaction, the solvent was removed under reduced pressure and the iron compound was decomposed by addition of 5 M HCl solution (10 mL). The organic products were extracted by diethyl ether (3 × 15 mL), and the organic layer was dried over anhydrous sodium sulfate. After removal of the solvent, organic products were analyzed by GC-MS and ^{1}H NMR spectroscopy.

For reactions with alkenes in the presence of protic acid, the solution after reaction with O_2 was passed through 15 cm silica (60−120 mesh size) column using dichloromethane as eluent. The combined organic phase was then analyzed by GC-mass spectrometry.

All the substrates (thioanisole, 1-octene, cyclooctene and cyclohexene, cyclohexane, methylcyclohexane and adamantane) were tested for control experiments used in catalytic experiments. For most of the substrates, no oxidized product was observed under the reaction conditions of control experiments. Trace amounts of 2-adamantanone (5%), cyclohexanone (<2%), and 2-methyl cyclohexanone (3%) were detected from adamantane, cyclohexane, and methylcyclohexane, respectively. Similar results were observed in control experiments using the in situ generated iron(II)−chloro complex from the $Tp^{Ph,Me}$ ligand and $FeCl_2$.

Control experiments were also performed with cyclohexanol and $Sc(OTf)_3$ or pyridinium perchlorate using $H_2{}^{18}O$ in benzene−acetonitrile solvent mixture in the presence and absence of iron(II) salt. In both the cases, no exchange of water with alcohols was observed.

^{1}H NMR (500 MHz, $CDCl_3$) Data of Organic Products. Benzophenone: δ 7.80 (d, 4H), 7.59 (t, 2H), 7.50 (t, 4H). Thioanisole oxide: δ 7.66 (m, 2H), 7.52 (m, 3H), 2.73 (s, 3H). Methyl phenyl sulfone: δ 7.96 (d, 2H), 7.60 (m, 3H), 3.06 (s, 3H). *cis*-Cyclohexane-1,2-diol: δ 3.77−3.82 (m, 2H), 1.73−1.82 (m, 2H), 1.51−1.64 (m, 4H), 1.27−1.35 (m, 2H). Octane-1,2-diol: δ 3.80−3.63 (m, 2H), 3.49 (m, 1H), 1.44−1.40 (m, 2H), 1.30−1.24 (m, 6H), 0.920 (m, 3H). *cis*-Cyclooctane-1,2-diol: δ 3.94 (d, 2H), 1.93−1.86 (m, 2H), 1.70−1.63 (m, 4H), 1.55−1.49 (m, 6H). 1-Adamantanol: δ 2.14 (s, 3H), 1.72−1.71 (m, 6H), 1.62−1.61 (m, 6H). 2-Adamantanol: δ 4.5 (s, 1H), 2.06 (s, 2H), 1.72−1.71 (m, 6H), 1.62−1.61 (m, 6H). (1*R*, 2*R*)-Cyclohexane-1,2-diyl diacetate: δ 5.14 (d, 2H), 2.24 (s, 6H), 2.04 (m, 2H), 1.81−1.78 (m, 2H), 1.71−1.76 (m, 2H), 1.33−1.23 (m, 2H). 3-*tert*-Butoxy-3-oxopropane-1,2-diyl diacetate: δ 4.15 (m, 2H), 3.65 (m, 1H), 2.72 (s, 3H), 2.58 (s, 3H), 1.44 (s, 9H).

X-ray Crystallographic Data Collection and Refinement of the Structures. X-ray single-crystal data were collected at 120 K using MoKα (λ = 0.7107 Å) radiation on a SMARTAPEX diffractometer equipped with CCD area detector. Data collection, data reduction, structure solution and refinement were carried out using the software package of APEX II.[48] The structure was solved by direct method and subsequent Fourier analyses and refined by the full-matrix least-squares method on F^2 with all observed reflections.[49] The nonhydrogen atoms were treated anisotropically for complex **1**. Routine SQUEEZE was applied to data intensities of compound **1** in order to take into account the disordered solvent molecules.[50] The hydrogen atoms on oxygen (O1) and that on N(7) could not be assigned. CCDC 1508424 (for **1**) contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.8b01353.

Spectroscopic data of oxygenated compounds (PDF).

Accession Codes

CCDC 1508424 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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