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A biomimetic oxidation catalyzed by manganese(III) porphyrins and iodobenzene diacetate: Synthetic and mechanistic investigations



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ABSTRACT

With iodobenzene diacetate [PhI(OAc)₂] as the oxygen source, manganese(III) porphyrin complexes exhibit remarkable catalytic activity toward the selective oxidation of alkenes and activated hydrocarbons. Conspicuous is the fact that the readily soluble PhI(OAc)₂ in the presence of a small amount of water is more efficient than the commonly used PhIO and other oxygen sources under same catalytic conditions. High selectivity for epoxides and excellent catalytic efficiency with up to 10,000 TON have been achieved in alkene epoxidations. It was found that the reactivity of manganese(III) porphyrin catalysts was greatly affected by axial ligand and the weakly binding perchlorate gave the highest catalytic activity in the epoxidation of alkenes. A manganese(IV)-oxo porphyrin was detected in the reaction of the manganese(III) porphyrin and PhI(OAc)₂. However, our catalytic competition and Hammett studies have suggested that the more reactive manganese(V)-oxo intermediate was favored as the premier active oxidant, even it is too short-lived to be produced in detectable concentrations.

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1. Introduction

Catalytic oxidation is a pivotal synthetic transformation in organic laboratories and chemical industries [1]. As the demand for greener processing increases [2,3], the transition metal catalyzed oxidations of hydrocarbons to oxygenated products with environmentally friendly oxygen sources such as molecular oxygen are becoming the most important and rewarding protocols in chemical industries [4,5]. In Nature, the ubiquitous cytochrome P-450 enzymes (P450s) [6] can catalyze a wide variety of oxidation reactions with exceptionally high reactivity and selectivity [7,8]. In this context, many transition metal catalysts with a core structure closely resembling that of the iron porphyrin core of P450s, have been synthesized as models to invent enzyme-like oxidation catalysts as well as to probe the sophisticated mechanism of molecular oxygen activation [9,10]. Among the most extensively studied systems are the epoxidation of alkenes and hydroxylation of alkanes catalyzed by transition metals in macrocyclic ligands, including those containing chiral auxiliaries for enantioselective oxidations [11]. Historically, synthetic manganese porphyrin complexes have shown catalytic promise as P450s enzyme model in oxidation reactions over decades [9,12]. The sacrificial oxidants compatible with manganese porphyrins were mostly restricted to PhIO, NaOCl, H_2O_2 , ^tBuOOH (*tert*-butylhydroperoxide), KHSO₅ and oxaziridines [9]. Molecular oxygen can also be used in the presence of an electron source [13]. The use of H_2O_2 often results in oxidative degradation of the catalyst due to the potency of this oxidant [9]. In contrast to epoxidations catalyzed by other metals, the manganese porphyrin-catalyzed oxidation gave low stereospecificity. For example, the epoxidation of *cis*-stilbene catalyzed by Mn^{III}(TPP)Cl (TPP = tetraphenylporphyrin) and PhIO generated *cis*- and *trans*-stilbene oxide in a ratio of 35:65 [14].

Identifying the kinetically competent oxidants could lead to better control of the catalytic oxidation reactions, especially in terms of selectivities. In general, high-valent transition metal-oxo transients are invoked as the active oxidizing species in many metal-catalyzed oxidations [15]. However, in most catalytic reactions, the concentrations of active metal-oxo oxidants do not build up to detectable amounts. For example, highly reactive porphyrinmanganese(V)-oxo derivatives were proposed as the key intermediates in catalytic processes for decades [14,16], but they eluded detection until 1997 when Groves and co-workers reported the synthesis of the first manganese(V)-oxo porphyrin complex [17]. Subsequently, additional examples of manganese(V)-oxo porphyrins were reported [18,19]. In contrast, the well characterized manganese(IV)-oxo derivatives are less reactive than manganese(V)-oxo species and unlikely to be the dominant oxidants in manganese porphyrin-catalyzed oxidations [20-22]. In previous laser flash photolysis (LFP) studies reported by Newcomb and coworkers, both porphyrin-manganese(IV)-oxo







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species and porphyrin-manganese(V)-oxo species were photochemically produced as a function of the identity of the counterions binding to the metal of the manganese(III) [23,24]. For homogeneous catalysts, where catalytic species have ready access to one another, high-valent metal-oxo species might be detected, but these species might not be reactive enough to be the true oxidants. Moreover, as reported studies of porphyrin-manganese(IV)-oxo species [24], and corrole-manganese(V)-oxo species [25], indicate, a high-valent metal-oxo species detected in a reaction might not be the true oxidant in the system. Specifically, the observable less reactive porphyrin-manganese(IV)-oxo intermediate that is the true oxidant but is not produced in detectable amounts [24].

Our group initiated a general program that aims to fully exploit the potential of metalloporphyrin complexes toward oxidation reactions, with an ultimate goal of developing practical metalloporphyrin oxidation catalysts for organic synthesis. In contrast to the sacrificial oxidants in common use for metal-catalyzed reactions, iodobenzene diacetate, i.e. PhI(OAc)₂, has been less often employed for porphyrin-manganese-catalyzed oxidations due to its mild oxidizing ability. Of note, PhI(OAc)₂ is readily soluble in organic media and safe to use. In particular, it does not show appreciable reactivity toward organic substrates nor damage the metal catalysts under the usual catalytic conditions. Collman and Nam reported, respectively, the use of $PhI(OAc)_2$ as terminal oxidant for the iron(III) porphyrin catalyzed oxidation of hydrocar-[26,27]. Xia and coworkers also described bons the manganese(III) porphyrin catalyzed epoxidation of several alkenes with $PhI(OAc)_2$ in the ionic liquid/ CH_2Cl_2 mixed solvent [12,13]. Adam et al. described a highly selective oxidation of alcohols by chromium(III) salen with PhI(OAc)₂ [28]. In addition, Nishiyama showed that PhI(OAc)₂ is a better oxidant than PhIO in ruthenium-pyridine-2,6-dicarboxylate complex-catalyzed epoxidation of *trans*-stilbene [29]. We recently employed PhI(OAc)₂ as an efficient oxygen source for the selective catalytic sulfoxidations by ruthenium porphyrins under visible light irradiation [30]. In our unpublished work, we have discovered that the electron-deficient corrole-iron(III) complex catalyzed efficient oxidation of alkenes with PhI(OAc)₂ as a promising oxygen source. The inherent unstable corrole-catalyst against degradation was much improved owing to the mild oxidizing power of PhI(OAc)₂. In this study, we present our detailed findings on the usefulness of PhI(OAc)₂ for the highly efficient catalytic oxidation of alkenes and activated benzylic hydrocarbons by porphyrin-manganese(III) catalysts (1a-c in Scheme 1). In most cases, quantitative conversions of substrates, excellent selectivities and high turnovers of up to 10,000 TON were obtained. Meanwhile, we show that a low-reactivity manganese(IV)-oxo porphyrin intermediate which was detected by the oxidation of the manganese(III) porphyrin with PhI(OAc)₂, is not likely the sole oxidant. Instead, a more reactive porphyrinmanganese(V)-oxo species is favored as the premier active oxidant.

2. Results and discussions

2.1. Screening studies

Table 1

The potential of PhI(OAc)₂ as an oxygen source was first evaluated in the catalytic epoxidation of *cis*-cyclooctene (**2a**) by different manganese(III) porphyrin catalysts (**1a–c** in Scheme 1). Under mild homogeneous conditions, the epoxidations were carried out with a catalyst: substrate: PhI(OAc)₂ ratio of 1:200:300 (Table 1). After 30 min of reaction in CH₃CN, *cis*-cyclooctene oxide (**3a**) was obtained as the only identifiable oxidation product (>99% by GC)

Manganese(III) porphyrin-catalyzed epoxidation of cis-cyclooctene with PhI(OAc)₂.^a

Mn ^{III} (Por)X (0.01-0.5 mol%)					
2a Phl(OAc) ₂ (1.5 equiv.) 3a					
Entry	Cataluct	Columnt	t (min)	Conum	Violdo(%) ^C
EIIUY	Calalysi	Solvent	t (mm)	(%) ^b	fields(%)
1 ^d	Mn ^{III} (TPFPP)Cl	CH ₃ CN	30	22	100
2			30	100	100
3			10	100	100 (93) ^e
			(50 °C)		
4^{f}			200	100	100
			(50 °C)		
5		CH₃OH	30	37	99
6		CH_2Cl_2	30	67	100
7		CH ₂ Cl ₂ /CH ₃ CN	30	90	100
		(v/v = 1)			
8	Mn ^{III} (TPP)Cl	CH ₃ CN	30	7	100
9	Mn ^{III} (TMP)Cl	CH₃CN	30	8	100
10		CH₃CN	10	23	100
			(50 °C)		

^a Unless otherwise specified, all reactions were carried out in solvent (0.5 mL) with H_2O (5 μ L) at 23 °C with *cis*-cyclooctene (0.20 mmol), 1.5 equiv. of PhI(OAc)₂ and 0.5 mol% of manganese(III) porphyin catalysts.

^b Determined by GC–MS analysis of the crude reaction mixture with a capillary column (J&W Scientific Cyclodex B).

^c Based on the amount of substrate consumed; material balances > 95%.

^d Without H₂O.

^e Isolated yield after column chromatography (silica gel).

f 0.01 mol% catalyst loading.



Scheme 1. Biomimetic oxidations catalyzed by manganese(III) porphyrins (1) with PhI(OAc)₂.

with ca. 22% conversion (Table 1, entry 1). The most striking feature of these catalytic epoxidations by Mn^{III}(TPFPP)Cl (1a; TPFPP = *tetrakis*(pentafluorophenyl)porphyrin) is the remarkable enhancement of the reaction rate by addition of H₂O. Thus, the same epoxidation proceeded much more rapidly with a small amount of H_2O (5 μ L), and quantitative conversions were obtained within 30 min at 23 °C (entry 2) or 10 min at 50 °C (entry 3). Fig. 1 depicts the time courses for the epoxidation in the presence and absence of water with 1a and 1c, respectively. The effect of water amounts on the epoxidation of cis-cyclooctene 2a with 1a in acetonitrile was further investigated (see Fig. S1 in Supporting Information). Clearly, addition of 5–10 µL of water resulted in a maximum acceleration in the rate of catalytic reaction, whereas addition of over 100 µL water slowed the reaction. Similar water accelerating effect observed in the previously reported iron(III) porphyrin/corrole-catalyzed oxidations was rationalized in terms of the formation of more oxidizing PhIO [27]. Another striking catalytic enhancement caused by the addition of water was observed in the alkene expoxidation with IO_4^- catalyzed by 2-methylimidazole and Mn^{III}(TPFPP)(OAc), where deprotonation of imidazoles to imidazolate may play a significant role in the presence of water [11]. These findings indicate that the access of the oxygen source to the metal center might be crucial. Water is a dissociating solvent and helps removal of the axial ligand and efficiently binding oxygen source.

To test the synthetic utility of the method, the epoxidation of *cis*-cyclooctene was scaled up to 4.0 mmol and 100% conversion and 95% isolated yield exclusively for epoxide were still obtained. Remarkably, the catalyst loading of **1a** can be as low as of 0.01 mol% (entry 4) without significant loss of activity, illustrating an unequivocally the high efficiency (10,000 TON!). The use of CH₃OH or CH₂Cl₂ as solvent instead of CH₃CN resulted in reduced activity (entries 5 and 6). When the non-halogenated Mn^{III}(TPP)Cl (**1b**) and Mn^{III}(TMP)Cl (**1c**; TMP = tetramesityl-porphyrin) were used as catalyst, poor activities were obtained within 30 min at ambient temperature (entries 8 and 9). Control experiments demonstrated that no epoxide was formed in the absence of either the catalyst or PhI(OAc)₂ even at elevated temperature (50 °C).



Fig. 1. Time courses of epoxidation of *cis*-cyclooctene (0.2 mmol) with PhI(OAc)₂ (0.30 mmol) in CH₃CN (0.5 mL) at room temperature catalyzed by Mn^{III}(TPFPP)Cl without water (cube); Mn^{III}(TMP)Cl with 5 μ L of water (diamond); Mn^{III}(TPFPP)Cl with 5 μ L of water (circle). Aliquots were taken at selected time intervals for GC analyses.

2.2. Comparison of various oxygen sources

The promising results with the $PhI(OAc)_2$ in Table 1 prompted us to evaluate other common oxygen sources in the manganese(III) porphyrin-catalyzed epoxidation of cyclohexene for the intended purpose of comparison. Cyclohexene not only is common substrate for epoxidation reactions but also offers the opportunity to test the chemoselectivity of the oxidation in terms of epoxide versus allylic alcohol formation, that is, oxygen transfer to the double bond or oxygen insertion into the allylic C-H bond. A screening of diverse oxygen source under identical experimental conditions disclosed that the mild oxygen source PhI(OAc)₂ was especially effective for selective oxidation of cyclohexene to the corresponding epoxide, as representative results are shown in Table 2. Although iodosobenzene (PhIO) is a more common oxygen source used for metalloporphyrin-catalyzed oxidations, it was found that the use of the soluble PhI(OAc)₂ under the same conditions led to the epoxide in higher substrate conversion and selectivity for epoxide (Table 2, entries 1 and 3). The use of more oxidizing NaOCl gave lower conversion and selectivities (entry 4). With ^tBuOOH and H₂O₂, significant amounts of allylic oxidation products, i.e. 2-cyclohexenol (4b) and 2-cyclohexenone (5b) were obtained with minor epoxide (entries 5 and 6). Using heterocyclic additives such as pyrazole can improve the chemoselectivity for epoxide (entry 7). The most likely explanation is that these oxygen sources might generate different reactive oxidizing intermediates and/or reaction mechanisms with manganese porphyrin catalyst than that with PhI(OAc)₂. Besides the high selectivity and catalytic efficiency, an additional advantage of the PhI(OAc)₂ compared to the other oxidants, is the fact that it will not cause the degradation of the porphyrin catalysts. Again, a very high catalytic activity with a TON of 9400 was achieved at the very low catalyst loading of only 0.01 mol% (entry 2).

2.3. Substrate scope

In view of the efficient epoxidation of cyclohexene and *cis*cyclooctene with $PhI(OAc)_2$ catalyzed by manganese(III) porphyrins, the catalytic activity of $Mn^{III}(TPFPP)Cl$ (**1a**) toward oxidations of a variety of organic substrates were investigated in

Table 2

Catalytic oxidation of cyclohexene by the $\mathsf{Mn}^{III}(\mathsf{TPFPP})\mathsf{CI}$ (1a) with various oxygen sources.^a



Entry	Oxygen source (OS)	<i>t</i> (h)	Convn (%) ^b	Product ratio ^b (3b:4b:5b)
1	PhI(OAc) ₂	2	95	93:7:0
2 ^c		3	94	86:2:12
		(50 °C)		
3	PhIO	2	86	90:2:8
4	NaOCl (8% aq.)	2	61	85:4:11
5	^t BuOOH (70% aq.)	2	53	2:85:13
6	H ₂ O ₂ (30% aq.)	6	5	11:63:26
7 ^d		2	14	86:7:7

 a Unless otherwise specified, all reactions were carried out in CH₃CN (0.5 mL) with H₂O (5 μ L) at 23 °C with cyclohexene (0.20 mmol), 1.5 equiv. of Phl(OAc)_2 and 0.5 mol% of manganese(III) porphyrin (**1a**). b Determined by GC–MS analysis of the crude reaction mixture with a capillary

^o Determined by GC-MS analysis of the crude reaction mixture with a capillary column (J&W Scientific Cyclodex B); material balances > 95%.

0.01 mol% of catalyst loading and 92% isolated yield.

^d With 5 mg of pyrazole.

the presence of a small amount of H₂O at elevated temperature (50 °C). Table 3 lists the oxidized products and corresponding substrate conversions and product yields including isolated yields using **1a** as catalyst with PhI(OAc)₂. As evident in Table 3, in most cases, quantitative conversions, excellent selectivity and rapid turnovers (up to 20 TOF min⁻¹) were observed within a short reaction time. In the oxidation of alkenes, epoxides were afforded as the major products with high efficiency. For example, epoxidation of norbornene was completed within 10 min, giving primarily exo epoxide with negligible amounts of endo products (Table 3, entry 1). Significant for preparative purposes, most reactions gave comparable yields in isolated products (entries 1-3, 8, 10, 11, 13 and 14). In the epoxidation of styrene and substituted styrene, 100% conversions were observed albeit with small amounts of aldehyde products (entries 2–7). Epoxidation of *cis*-stilbene gave epoxide product with a ratio of *cis/trans* = 91:9 (entry 8). In contrast, *trans*-alkenes afforded corresponding trans-epoxides exclusively with complete

Table 3 Catalytic oxidation with PhI(OAc)₂ in the presence of H₂O by Mn^{III}(TPFPP)Cl.^a.

stereoretention (entries 10 and 11). This catalytic activity and product selectivity is a major improvement over previously reported oxygen sources including PhIO and NaOCl [9,12]. Remarkably, the Mn^{III}(TPFPP)Cl effectively catalyzes the epoxidation of the allylic alcohol mainly to the epoxy alcohol with a ratio of *cis/trans* = 1:4 in a quantitative conversion (entry 12). Although the rate of oxidation reactions was markedly influenced by the presence of water, the product yields and distributions in most cases were not affected by the presence and absence of H₂O. Similarly, the oxidation of secondary benzylic alcohols gave the corresponding ketones with excellent catalytic activities (entries 13 and 14), similar to the alkene epoxidation. Activated alkanes including triphenylmethane, ethylbenzene and diphenylmethane were oxidized to the corresponding alcohols and/or ketones from over-oxidation with lowest activity (entries 15–17). It is noteworthy that monitoring catalytic reactions by UV-Vis spectroscopy indicated no appreciable catalyst bleaching in the end of reactions.

Entry	Substrate	Products	t (min)	Convn. (%) ^b	Yields (%) ^c (isolated yield)	TOF^{d} (min ⁻¹)
1	٨	Δ	10	100	100 ^e (88)	20
		$\Box D^{0}$				
2		$\langle \rangle \land \rangle$	10	100	91 (85)	20
3	O ₂ N	O ₂ N	10	100	92 ^f (90)	20
4	F-	F-CO	10	100	87 ^f	18
5			10	100	92 ^f	19
6	Me	Me	10	100	95 ^f	20
7	MeO	MeO	10	100	100	20
8	Ph, Ph	Ph Ph	10	100	91(<i>cis</i>):9(<i>trans</i>) (82)	20
		\bigtriangledown				
9	\bigwedge	\sim	10	100	90	18
10	Ph	Ph	20	100	99 (<i>trans</i>) (91)	20
11	`Ph	Ph	10	100	00 (04)	20
11		Pn	10	100	33 (34)	20
12	ŎН	QH Q	10	100	78 ^g :22	20
	\square					
13	ОН	$\sim \sim \sim$	10	97	100 (92)	19
	Ph-<	Ph				
14	OH Ph─	O Ph-√	10	100	100 (95)	20
	Ph	Ph				
15	Ph Ph→	Ph Ph—←OH	24 (h)	43	100	0.06
	Ph	Ph				
16	Ph		24 (h)	82	24:76	0.1
17	Ph-		24 (h)	86	67:33	0.1
.,	F'' \ Ph	Ph-(^{OH} Ph-(21(11)		0	0.1
		, Ph Ph				

^a All reactions were carried out at 50 °C with 0.5 mol% catalyst of Mn^{III}(TPFPP)Cl in 0.5 mL of CH₃CN containing 0.2 mmol of substrate, 0.3 mmol of PhI(OAc)₂ and 5 µL H₂O.

^b Determined by GC–MS analysis of the crude reaction mixture with an internal standard (1,2,4-trichlorobenzene); material balances > 95%.

^c Based on 100% conversion of substrate; isolated yields listed in the parenthesis.

^d TOF = turnovers frequency (min⁻¹).

^e Isomeric ratio (*exo:endo*) > 95:5.

^f A trace amount of benzaldehyde was detected (<5%).

^g A diastereomeric ratio of *cis/trans* = 1:4.

2.4. Axial ligand effect

It is literature known that axial ligand has a marked influence on the reactivity of the high-valent metal-oxo porphyrin intermediate [31,32]. It has been shown that axial ligands of iron(III) porphyrin complexes play an important role in the catalytic oxidation of hydrocarbons by various terminal oxidants, in which the yields of oxidized products were markedly dependent on the axial ligands of the iron(III) porphyrin catalysts [33]. In this regard, the effect of axial ligand on the catalytic reactivity of Mn^{III}(TPFPP)X $(X = Cl^{-}, ClO_{4}^{-}, ClO_{3}^{-}, NO_{3}^{-}, and NO_{2}^{-})$ had been investigated in the epoxidation of cis-cyclooctene and cis-stilbene (Table 4). Reactions of the porphyrin-manganese(III) chloride with corresponding silver salts, i.e. AgX ($X = ClO_4^-$, ClO_3^- , NO_3^- , and NO_2^-), gave solutions of the corresponding $Mn^{III}(TPFPP)X$ salts; the formation of these species was indicated by the UV-Vis spectra, matching those literature reported values [24]. To make a quantitative comparison, epoxidations were catalyzed under identical conditions. The results in Table 4 reveal that the axial ligand of the manganese catalysts has a significant effect on the rate of products formation. The Mn^{III}(TPFPP)(ClO₄) was the best catalyst, which gave a complete conversion of *cis*-cyclooctene within 10 min. Slower conversions were observed when $Mn^{III}(TPFPP)X$ (X = ClO₃, NO_3^- , and NO_2^-) were used instead. The lowest conversion was obtained with Cl⁻ as the axial ligand. It should be pointed out that, among all axial ligands that we studied, ClO_4^- has the weakest, albeit the Cl⁻ has the strongest coordinating ability to the metal of manganese. Thus, the effect of axial ligand is likely due to a rapid reaction of Mn^{III}(TPFPP)(ClO₄) with PhI(OAc)₂ to generate the active oxidizing species. The dependence of the oxidation rates product ratios on the axial ligands of manganese(III) porphyrin catalysts may also suggest the involvement of different reactive species in olefin epoxidation reactions [33].

2.5. Mechanistic investigations

Prior to the present studies, conspicuous is the fact that use of $PhI(OAc)_2$ for manganese porphyrin-catalyzed oxidation has not been well studied before [12,13]. We now show that manganese(III) porphyrins catalyze the highly efficient oxidation of alkenes and activated hydrocarbons by $PhI(OAc)_2$ in the presence of a small amount of H_2O . The preparative utility and synthetic value of the new catalytic system presented above are indisputable, but mechanistic understanding of the complex oxygen-transfer processes is important for the design of still more effective and selective oxidants with general applicability.

It is known that the reactions of manganese(III) porphyrin complexes with more oxidizing oxidants such as m-chloroperoxybenzoic acid (m-CPBA), iodosylarenes and H₂O₂, produced high-

Table 4

Effect of axial ligand on the manganese(III) porphyrin-catalyzed *cis*-alkene epoxidations.^a.

Entry	Mn ^{III} (TPFPP)X X ⁻	cis-Cyclooctene		cis-Stilbene	
		Convn (%) ^b	Yields (%) ^b	Convn (%) ^b	Epoxides (%) ^b cis:trans
1	ClO_4^-	100	100	74	91:9
2	ClO_3^-	82	100	45	86:14
3	NO_3^-	65	100	24	92:8
4	NO_2^-	76	100	57	93:7
5	Cl^{-}	18	100	17	90:10

^a All reactions were carried out in CH_3CN (0.5 mL) over 10 min at 23 °C with substrate (0.20 mmol), 1.5 equiv. of $PhI(OAc)_2$ and 0.5 mol% of manganese(III) porphyin (**1a**).

^b Determined by GC–MS analysis of the crude reaction mixture with an internal standard (1,2,4-trichlorobenzene); material balances > 95%.

valent manganese(V)-oxo porphyrins (6) in aqueous solutions or organic solvents in the presence of base [17,19]. To probe the identity of the active oxidizing species, we conducted the chemical oxidation reaction of manganese(III) catalyst **1a** by PhI(OAc)₂ in CH₃CN or CD₃CN in the absence of substrate (Fig. 2A). As shown in Fig. 2A, with 5–10 equivalent of PhI(OAc)₂, the precursor (1a) was converted to a species **7a** which then slowly decayed back to Mn^{III} precursor with clearly resolved isosbestic points. The absorption spectrum of **7a** with a strong Soret band at 418 nm and weak absorption band around 538 nm was essentially identical to that of the known manganese(IV) mono-oxo porphyrin, which was independently prepared from a reported method (Fig. 2S in Supporting Information) [24]. In principle, Mn^{IV}-oxo derivatives might have been formed by comproportionation reactions of the Mn^V-oxo porphyrin with the residual Mn^{III} products. Previous studies with manganese-oxo species found that porphyrinmanganese(V)-oxo species comproportionate rapidly with manganese(III) species [24], and corrole-manganese(V)-oxo species reacted with corrole-manganese(III) species to give manganese(IV) species [25]. As thermodynamically favored, the comproportionation reactions were important under our condition with the mild oxidizing PhI(OAc)₂. Since the chemical conversions of **1a** by mild oxidizing $PhI(OAc)_2$ to Mn^V -oxo was relatively slow process, therefore, the Mn^{IV}-oxo derivative was formed from the fast reactions of Mn^V-oxo with residual Mn^{III} to give Mn^{IV}-oxo species.

The Mn^{IV}-oxo species (**7a**) in the presence of substrates decayed to give Mn^{III} product with no evidence for formation of Mn^{II} species in any of our studies, similar to that of self-decay shown in Fig. 2A. The asymmetric nature of the Soret absorbance at 470 nm indicates that the products are a mixture of manganese(III) porphyrin species containing different axial ligands.

The isosbestic points at 384, 442, 492 and 595 nm demonstrate that the conversion of Mn^{IV} -oxo (**7a**) to Mn^{III} species (**1a**) does not involve the accumulation of any intermediates.

The observed rate constants for decay of **7a** with the substrates such as ethylbenzene were fit reasonably well by pseudo-first-order solutions. The rate constants increased as a function of substrate concentration, and plots of k_{obs} versus substrate concentration were linear (Fig. 2B). As solved by Eq. (1), where k_{obs} is the observed rate constant, k_0 is rate constant of background reaction and k_{ox} is second-order rate constant for oxidation of substrate, reactions of **7a** gave a $k_{ox} = (7.12 \pm 0.03) \times 10^{-1} \text{ M}^{-1} \text{ s}^{-1}$ for ethylbenzene, and $k_{ox} = (7.16 \pm 0.01) \times 10^{-2} \text{ M}^{-1} \text{ s}^{-1}$ for ethylbenzene- d_{10} , thus revealing a kinetic isotope effect (KIE) of $k_{\text{H}}/k_{\text{D}} = 9.9 \pm 0.2$ at 298 K.

(1)	
	(1	(1)

2.6. Competitive kinetics

The directly observed Mn^{IV}-oxo species (**7a**) in above kinetic studies is not necessarily the active oxidant under catalytic turnover conditions. One method to evaluate whether the same species is active in the two sets of conditions is to compare the ratios of products formed under catalytic turnover conditions to the ratios of rate constants measured in the direct kinetic studies [34]. If the same oxidant is present in both cases, the ratios of absolute rate constants from direct measurements and relative rate constants from the competition studies should be similar, although a coincident similarity for two different oxidants cannot be excluded. When the ratios are not similar, however, the active oxidants under the two sets of conditions must be different.

To evaluate the identity of the active oxidant during the catalytic conditions, the competition studies with $Mn^{III}(TPFPP)X$ with different axial ligands (CI^- and CIO_4^-) and $PhI(OAc)_2$ were



Fig. 2. (A) Time-resolved spectrum following the self-decay of **7a** generated by reacting **1a** $(1.0 \times 10^{-5} \text{ M})$ with PhI(OAc)₂ (*ca.* 5 equiv.) over 300 s in CH₃CN at 23 ± 2 °C; (B) observed rate constants for reactions of **7a** with ethylbenzenes in CH₃CN at 23 ± 2 °C, monitored at 418 nm.

Table 5

Relative ratios from absolute rate constants of kinetic studies and from competition catalytic oxidations.^a.

Substrate	Oxidant	Method	$k_{\rm rel}$
PhEt/PhEt-d ₁₀	Mn ^v (TPFPP)O	Kinetic ratio	2.3 ^b
	Mn ^{IV} (TPFPP)O	Kinetic ratio	9.9 ^c
	Mn ^{III} (TPFPP)Cl/PhI(OAc) ₂	Competition	3.3
	Mn ^{III} (TPFPP)(ClO ₄)/	Competition	2.9
	$PhI(OAc)_2$		
cis-stilbene/Ph ₂ CH ₂	Mn ^v (TPFPP)O	Kinetic ratio	4.7 ^b
	Mn ^{III} (TPFPP)Cl/PhI(OAc) ₂	Competition	5.2
	Mn ^{III} (TPFPP)(ClO ₄)/	Competition	4.9
	$PhI(OAc)_2$		
4-fluorostyrene/styrene	Mn ^{III} (TPFPP)Cl/PhI(OAc) ₂	Competition	1.1
	Mn ^{III} (TPFPP)(ClO ₄)/	Competition	1.0
	PhI(OAc) ₂		
4-chlorostyrene/styrene	Mn ^{III} (TPFPP)Cl/PhI(OAc) ₂	Competition	1.1
	Mn ^{III} (TPFPP)(ClO ₄)/	Competition	1.0
	$PhI(OAc)_2$		
4-methylstyrene/styrene	Mn ^{III} (TPFPP)Cl/PhI(OAc) ₂	Competition	1.4
	Mn ^{III} (TPFPP)(ClO ₄)/	Competition	1.3
	PhI(OAc) ₂		
4-methoxystyrene/	Mn ^{III} (TPFPP)Cl/PhI(OAc) ₂	Competition	1.6
styrene	Mn ^{III} (TPFPP)(ClO ₄)/	Competition	1.5
	$PhI(OAc)_2$		
3-nitrotyrene/styrene	Mn ^{III} (TPFPP)Cl/PhI(OAc) ₂	Competition	0.7
	Mn ^{III} (TPFPP)(ClO ₄)/	Competition	0.6
	PhI(OAc) ₂		

 a All competition reactions were conducted in CH_3CN (0.5 mL) in the presence of H_2O (5 μ L) containing equal amounts of two substrates, e.g., PhEt (0.2 mmol) and PhEt-d_{10} (0.2 mmol), PhI(OAc)_2 (0.1 mmol) and catalyst Mn^{III}(TPFPP)X (X = CI and ClO_4) (1.0 μ mol). Ratios of relative rate constants from competition reactions were determined based on the conversions of substrates. All competition ratios are averages of 2–3 determinations with standard deviations smaller than 5% of the reported values.

^b From LFP kinetic studies (see Ref. [24]).

^c From kinetic studies of this work.

conducted. Table 5 contains the relative ratios of absolute rate constant of manganese(V)-oxo porphyrin complex, i.e. Mn^{V} (TPFPP)O, from our previous laser flash photolysis (LFP) studies[24], whereas irradiation of Mn^{III} (TPFPP)(OCIO₃) perchlorate resulted in heterolytic cleavage of O–Cl bonds to give porphyrin-manganese(V)-oxo cations. The inherent good temporal resolution of LFP methods permits the production, spectral characterization, and kinetic studies of highly reactive Mn^{V} (TPFPP)O intermediates that cannot be



Fig. 3. Hammett correlation studies ($\log k_{rel} vs \sigma^+$) for the Mn^{III}(TPFPP)Cl-catalyzed epoxidation of substituted styrenes by PhI(OAc)₂ in CH₃CN at 23 ± 2 °C.

observed by chemical oxidations in mixing experiments [24]. Table 5 also includes the ratios of absolute rate constant of less reactive manganese(IV)-oxo porphyrin (7a) that was observed from the reaction of **1a** and PhI(OAc)₂ (this work), and competition reactions where PhI(OAc)₂ was employed as sacrificial oxygen source. In competition studies, a limiting amount of PhI(OAc)₂ was used to keep the conversion less than 25% to avoid the effect of substrate concentration on the product ratios. As evident in Table 5, the results of the competition reactions between ethylbenzene and ethlybenzene- d_{10} and between *cis*-stilbene and diphenylmethane are in close agreement with the ratios of the absolute rate constants found in direct kinetic studies of the Mn^V(TPFPP)O from LFP studies. Notably, the competitive catalytic oxidation of PhEt- d_0 and PhEt- d_{10} revealed a kinetic isotope effect (KIE) of $k_{\rm H}/k_{\rm D}$ = 3.3 (X = CI) and 2.9 $(X = CIO_4^-)$ at 298 K, much smaller than the KIE of $k_{\rm H}/k_{\rm D}$ = 9.9 for the same reaction with the observed Mn^{IV}-oxo species (7a). From standard reactivity-selectivity considerations, a more reactive porphyrin-manganese(V)-oxo species would be expected to display smaller ratios of substrate selectivity than the less reactive manganese(IV)-oxo porphyrin. The similarity in relative rate constants suggests that Mn^V(TPFPP)O species (**6a**) were the primary active oxidants in the catalytic reactions, as



Scheme 2. Proposed catalytic cycle.

commonly assumed, and demonstrates that the kinetic results can be used in a predictive manner for estimating the relative reactivities of substrates under catalytic conditions. Differences in inherent reactivities of the reductants obviously influence the ratio of products, but the close match between the ratios of absolute rate constants and the ratios of products from the competition experiment strongly suggests that manganese(V)-oxo species were the active oxidants in the catalytic oxidation reactions, even though they could not be detected during the reactions.

2.7. Hammett correlation

A further reflection of the more reactive manganese(V)-oxo intermediate involved in the catalytic oxidations instead of manganese(IV)-oxo complex is seen in the linear Hammett plot for competitive oxidations of the series of substituted styrenes (Y-styrene, Y = 4-MeO, 4-Me, 4-F, 4-Cl, and 3-NO₂). Fig. 3 depicts a linear correlation (R = 0.996) of log $k_{rel}[k_{rel} = k(Y-styrene)/k(styr$ ene)] versus Hammett σ^+ substituent constant (Table 5). The slope (ρ^{+}) of the plot is -0.42, which indicates transition states for ratelimiting steps which involve very little charge separation. Again, this observed ρ^+ value is about 2-fold smaller in magnitude than the previously reported value (-0.99) found for a related porphyrin-manganese(IV)-oxo complex [35]. Apparently, the competitive product analysis and Hammett correlation studies strongly suggest that the observed manganese(IV)-oxo species is unlikely to be the sole oxidant. Instead, the highly reactive porphyrinmanganese(V)-oxo species as the premier reactive intermediate is plausible, even though it could not be detected during the catalvtic reactions.

On the basis of the present experimental facts, a catalytic cycle is proposed with a high-valent manganese(V)-oxo species as the active oxidant that might describe catalytic oxidation reactions under turnover conditions (Scheme 2). Reaction of the porphyrin-manganese(III) salt with the sacrificial PhI(OAc)₂ might give a porphyrin-manganese(V)-oxo species (6) that is the major oxidant of substrate. In a fast competing process, the porphyrin-manganese(V)-oxo species might react with residual manganese(III) salt to form a manganese(IV)-oxo complex (7) that also serves as a sluggish oxidant [35]. When reactive substrates were not present, porphyrin-manganese(IV)-oxo derivatives might be the only observable products because the porphyrinmanganese(V)-oxo species are too short-lived and do not accumulate to detectable concentrations.

If this proposed reaction mechanism is reasonable, then it is possible that catalytic oxidations could involve two active oxidants that have different reactivities and selectivities in, for example, competition reactions [36,37]. Thus, the competition results in Table 5 are consistent with a multiple oxidant model [38,39]. Involvement of the less reactive manganese(IV)-oxo species may explain the loss of stereoselectivity as we observed in the epoxidation of *cis*-stilbene (Table 5). Much evidence has accumulated in recent years that multiple oxidants can be involved in oxidations by ligand–metal catalysts under turnover conditions, although the

identities of the multiple oxidants are speculative points [26,38–40]. The relative populations of manganese(V)-oxo (**6**) and manganese(IV)-oxo species (**7**) were determined by the rates of the subsequent comproportionation reactions. Of note, the manganese(V)-oxo porphyrin does react rapidly with the chloride salt of its manganese(III) precursor, but the comproportionation reaction of the manganese(V)-oxo species with the perchlorate salt is slower [24]. This apparently reflects the observed axial ligand effect (Table 3) that a weak-binding ligand perchlorate is more active catalyst, whereas a tight-binding ligand chloride is less effective.

3. Conclusions

In summary, we have demonstrated that manganese(III) porphyrins catalyze the highly efficient oxidation of alkenes and activated hydrocarbons with PhI(OAc)₂ in the presence of small amount of water. A variety of alkenes and activated hydrocarbons were oxidized to afford epoxides or alcohols and ketones with excellent yields of up to 100% and high selectivities. It was found that the reactivity of Mn^{III}(TPFPP)X was greatly affected by axial ligand and the weakly binding perchlorate gave the highest catalytic activity in the epoxidation of *cis*-alkenes. The catalytic competition and Hammett correlation studies have suggested that the observed Mn^{IV} -oxo species (**7a**) in direct kinetic studies is not likely the sole oxidant under catalytic turnover conditions. A high-valent manganese(V)-oxo intermediate was indicated as the premier active oxidant, even it does not accumulate to detectable concentrations due to its high reactivity. A catalytic mechanism involving two possible oxidants with different reactivities and selectivities, i.e. manganese(V)-oxo and manganese(IV)-oxo complexes, has been suggested.

4. Experimental

4.1. Materials and methods

Acetonitrile was obtained from Fisher Scientific and distilled over P_2O_5 prior to use. All reactive substrates for catalytic reactions were from Sigma–Aldrich Chemical Co. and purified by passing through a dry column of active alumina (Grade I) before use. Iodobenzene diacetate or (diacetoxyiodo)benzene, i.e. PhI(OAc)₂, H₂O₂ (30%) and *tert*-butyl hydroperoxide (^tBuOOH, 70%) were purchase from Aldrich Chemical Co. and used as such. Iodosylbenzene (PhIO) was purchased from the TCI America Co. and was used as obtained.

Free porphyrin ligand, 5,10,15,20-*tetrakis*(pentafluorophenyl)porphyrin (H₂TPFPP) was purchased from Sigma–Aldrich and used as received. 5,10,15,20-tetramesitylporphyrin (H₂TMP) was prepared according to the known methods [41]. Mn^{III}(TPFPP) Cl and Mn^{III}(TMP)Cl were prepared according to the literature procedure [42] and purified by chromatography on silica-gel. Mn^{III}(TPP)Cl was obtained from Aldrich Chemical Co. and used without further purification. All perchlorate salts, chlorate salts, nitrate and nitrite salts of manganese(III) porphyrin complexes were prepared by stirring equimolar amounts of Mn^{III}(TPFPP)Cl with AgClO₄. AgClO₃, AgNO₃, and AgNO₂, respectively. The resulting mixtures were filtered and used for catalytic studies immediately after preparation.

UV-Vis spectra were recorded on an Agilent 8453 diode array spectrophotometer. ¹H NMR was performed on a JEOL ECA-500 MHz spectrometer at 298 K with tetramethylsilane (TMS) as internal standard. Gas Chromatograph analyses were conducted on an Agilent GC7820A/MS5975 equipped with a flame ionization detector (FID) using a J&W Scientific capillary column. The above GC/MS system is also coupled with an auto sample injector. Reactions of Mn^{III}(TPFPP) with excess of PhI(OAc)₂ were conducted in a anaerobic acetonitrile solution at 23 ± 2 °C.

4.2. General procedure for catalytic oxidations

Unless otherwise indicated, all catalytic reactions were typically carried out in the presence of a small amount of H_2O (5 μ L) with 1 µmol of catalyst (approximate 0.5 mol%), 0.2 mmol of organic substrate and 1.5 equivalent of PhI(OAc)₂ (0.3 mmol) in 0.5 mL of acetonitrile at 23 °C or 50 °C in a water bath. Aliquots of the reaction solution at constant time interval were analyzed by GC/MS to determine the conversions, formed products and yields with an internal standard. The pure products were isolated by a flash column chromatography (silica gel with CH₂Cl₂ and hexane mixture) to give isolated yields (Table 1, entry 3, Table 2, entry 2; and Table 3, entries 1–3, 8, 10, 11, 13 and 14). All reactions were run 2 to 3 times, and the data reported represent the average of these reactions. Since the epoxidation and hydroxylation reactions were not affected by molecular oxygen, all the reactions presented in this study were performed in air.

4.3. Catalytic competitive oxidations and kinetic isotope effect (KIE) studv

A CH₃CN solution containing equal amounts of two substrates. e.g. styrenes (0.2 mmol) and substituted styrenes (0.2 mmol), manganese(III) porphyrin catalyst (1.0 µmol) and an internal standard of 1,2,4-trichlorobezene (0.1 mmol) was prepared (final volume = 0.5 mL). The internal standard was shown to be stable to the oxidation conditions in control reactions. PhI(OAc)₂ (0.1 mmol) as limiting reagent was added, and the mixture was stirred at ambient temperature $(23 \pm 2 \circ C)$ for 10 min. Relative rate ratios for catalytic oxidations were determined based on the amounts of substrates by GC (FID) as measured against an internal standard. In this work, all the catalytic epoxidation proceeded with good epoxide yields (>80%) and mass balance (>95%), and in all cases no traces of polymers or oligomers were detected. Thus, the rate of alkene disappearance should reasonably reflect the alkene reactivity toward the porphyrin-manganese(III)-catalyzed epoxidation. The values reported in Table 5 are the averages of 2–3 runs with standard deviations (1 σ).

Abbreviations used in this work

TPFPP = 5,10,15,20-tetrapentafluorophenylporphyrin dianion; TMP = 5,10,15,20-tetramesitylporphyrin dianion; TPP = 5,10,15,

20-tetraphenylporphyrin dianion; *m*-CPBA = *meta*-chloroperoxybenzoic acid; TON = turnover number; KIE = kinetic isotope effect; LFP = laser flash photolysis.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ica.2015.03.003.

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