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Hydrocarbon oxidation catalyzed by manganese and iron complexes with the hexadentate ligand *N,N'*-di(ethylacetate)-*N,N'*-bis(2-pyridyl-methyl)-1,2-ethanediamine

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ABSTRACT

Analogs of recently reported manganese and iron catalysts for alkene and alkane oxidation reactions have been prepared with the potentially hexadentate ligand *N,N'*-di(ethylacetate)-*N,N'*-bis(2-pyridylmethyl)-1,2-ethanediamine (debpn). The Mn(II) and Fe(II) complexes, which were previously found to be hepta-coordinate in the solid state, are capable of catalyzing alkene epoxidation and aliphatic C–H activation reactions, although these activities are inferior to those of related complexes with less coordinating ligands. The hydrocarbon oxidation catalyzed by iron is more severely disrupted. Cyclic voltammetry indicates that the +2 oxidation states for both debpn complexes' metal ions are stabilized by the two additional chelate arms. Product analysis of the C–H activation and olefin epoxidation chemistries suggest that ligand-substrate steric interactions may exert additional inhibitory effects on the reactivity for the manganese catalysts.

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1. Introduction

Manganese(II) and iron(II) complexes with tetradentate, neutral N-donor ligands have found application as homogeneous catalysts for the oxidation of hydrocarbons. The Mn(II) compounds have been used to catalyze the epoxidation of alkenes by peracids and other two-electron oxidants; [1–6] whereas, the Fe(II) complexes have been found to facilitate the oxidation of both alkenes [7,8] and alkanes [9–15]. The chemistry is widely believed to proceed through higher-valent metal oxidants that are produced from initial reactions between the M(II) complexes and the terminal oxidants [4,6,7,13–18]. The structurally characterized M(II) complexes with the aforementioned tetradentate ligands contain hexacoordinate centers with two readily exchangeable coordination sites capable of allowing inner-sphere oxidation of the metal ions to proceed.

One disadvantage that is commonly encountered with such catalysts is their limited stability. Removal of the metal from the tetradentate ligand often halts or greatly diminishes the catalysis [1–3]. In manganese-catalyzed alkene epoxidation, the use of ligands that are less highly coordinating, through either the removal of donor atoms or the installation of steric bulk, generally decreases the activity [3]. Most of the metal complexes are unstable in water, which limits the potential "greenness" of their

reactions. The use of a more highly coordinating ligand may sufficiently stabilize such compounds to allow oxidative catalysis in water. The additional chelate arms necessary for this stability, however, could hinder or preclude the coordination of the terminal oxidant required for the catalysis.

Earlier work from our laboratory involved the synthesis and characterization of two heptacoordinate metal complexes with the ligand *N,N'*-di(ethylacetate)-*N,N'*-bis(2-pyridylmethyl)-1,2-ethanediamine (debpn, Scheme 1) [19]. The Mn(II) complex with debpn was sufficiently stable in water to serve as a contrast agent for magnetic resonance imaging. Although the optical spectrum of the Fe(II) complex resembles those of other known heptacoordinate ferrous compounds [19,20], it is difficult to tell for certain whether the heptacoordination of the Mn(II) and Fe(II) complexes is maintained in solution. The debpn ligand resembles the tetradentate *N,N'*-dimethyl-*N,N'*-bis(2-pyridylmethyl)-1,2-ethanediamine (bpmen, Scheme 1) which has been used to prepare hexacoordinate first-row transition metal catalysts for both alkene epoxidation and alkane hydroxylation [1–3,8,10–13]. Electronically, the two organic ligands are similar. The ester groups of the debpn ligand interact weakly with the metal center and do not impact the overall charge of either the ligand or its metal complexes [19]. More importantly, the debpn complexes with Mn(II) and Fe(II) each contain a readily exchangeable coordination site that can accommodate an inner-sphere oxidant, such as hydrogen peroxide or peracetic acid. The O-donors from the esters are not fully bound to the Co(II) and Ni(II) ions in other structures [19],

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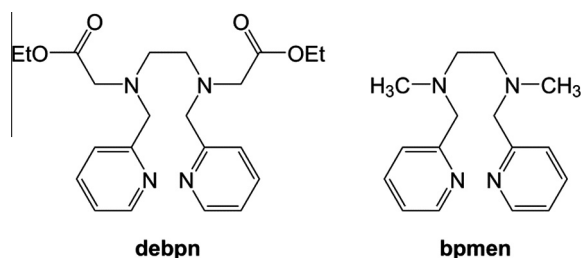
Scheme 1.
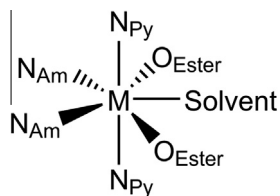
Scheme 2. Inner-sphere coordination of $[Mn(debpn)(H_2O)]^{2+}$ and $[Fe(debpn)(H_2O)]^{2+}$.

suggesting that these groups are weakly coordinating and can detach from the Mn(II) and Fe(II) to provide additional coordination sites for inner-sphere oxidants.

In the present work, we have assessed the catalytic capabilities of the Mn(II) and Fe(II) complexes with debpn (Scheme 2). Specifically, we have studied their abilities to accelerate the activation of aliphatic C–H bonds and the conversion of olefins to epoxides and compared these to the catalytic activities of analogous complexes with the less highly coordinating bpmen.

2. Experimental

2.1. Materials

Unless otherwise stated, all chemicals were bought from Sigma–Aldrich and used without further purification. cis-Cyclooctene, 1-octene, ethyl sorbate, and anhydrous acetonitrile (MeCN) were purchased from Acros. Hydrogen peroxide (H_2O_2, 30% or 50% in water) was purchased from Fisher and stored in a refrigerator when not in use. Glacial acetic acid (CH_3CO_2H) was bought from Pharmco-Aaper. The peracetic acid (PAA_R, 7.5%) was custom-made through a previously described process [3]. In this procedure, 50% H_2O_2 and CH_3CO_2H react in the presence of the acidic resin Amberlite IR-120. This synthesis produces a less acidic grade of peracetic acid that lacks the H_2SO_4 impurity found in commercial sources (PAA_C). The concentration of the peracid was determined by periodically checked by ^{13}C NMR. The compounds $[Mn(debpn)(H_2O)](ClO_4)_2$ and $[Fe(debpn)(H_2O)](OTf)_2$ were prepared as previously described [19]. Crystalline samples of these two compounds were used for all catalytic reactions.

Caution: Although no accidents occurred in the described studies, peracids, peroxides, and metal perchlorate salts, such as $[Mn(debpn)(H_2O)](ClO_4)_2$, are potentially explosive. As precautionary measures, most reactivity assays involving peracids were performed at 0 °C behind a blast shield, using minimal amounts of these reagents. The peracetic acid was stored in a freezer when not in use.

2.2. Instrumentation

All ^1H magnetic resonance (NMR) spectra were acquired on a 400 MHz AV Bruker NMR spectrometer at 294 K; all observed resonance peaks were assigned relative to known internal standards. Gas chromatography (GC) was obtained on a ThermoScientific Trace GC Ultra spectrometer with a flame ionization detector (FID). All cyclic voltammetry was performed under N_2 at 294 K using a Pine Instrument Co. AFCBP1 bipotentiostat, a glassy carbon working electrode, a platinum wire auxiliary electrode, a silver wire reference electrode, and tetrabutylammonium perchlorate as a supporting electrolyte. Since all electrochemistry was done in MeCN, ferrocene was added as an internal reference [21].

2.3. Reactivity

All reactions were run under N_2. The protocols for the alkene epoxidation reactions were adapted from previously reported procedures [1–3,8]. In the reactions with the Mn(II) catalyst, [Mn(debpn)(H_2O)]^{2+}, the substrate and oxidant were combined in a glass vial and dissolved in MeCN. The internal standard, 1,2-dichlorobenzene, was added and the solution was cooled to 0 °C with an ice bath. The terminal oxidant, PAA_R, was added over the course of 2 min. Aliquots of the reaction mixture were taken for GC analysis at set time points after the reaction began (the start of the addition of the oxidant). Each aliquot was run through a plug of silica gel prior to analysis; this removed the metal salts and the excess oxidant without removing the organic products [22,23]. After the samples were diluted with ether, the identities and quantities of the products were assessed by GC. All products were identified through comparison of their GC retention times to those of known standards. ^1H NMR spectroscopy was used to confirm the identities of isolated products. All reactions were repeated at least three times; the provided yields are the averages of those independent runs.

The alkene epoxidation protocol with the Fe(II) catalyst, $[Fe(debpn)(H_2O)]^{2+}$, was similar to that corresponding to the Mn(II) catalysis with two modifications. First, CH_3CO_2H was added to the initial MeCN solution of the catalyst and substrate. Second, H_2O_2 was used as the terminal oxidant instead of PAA_R. The isolated yields on Table 3 were obtained from reactions between 232 mg cis-cyclooctene (2.0 mmol), 23.5 mg [Fe(debpn)(H_2O)](OTf)_2 (0.060 mmol), 34 μL CH_3CO_2H (0.60 mmol), and 173 μL H_2O_2 (50 wt%, 3.0 mmol) in 14 mL of MeCN. After 5, 30, or 60 min, 40 mL of a saturated solution of Na_2CO_3 in water was added to quench the reaction. The product was extracted with CH_2Cl_2 (3 × 30 mL). The extracts were dried over $MgSO_4$ and filtered. The solvent and starting material were removed from the mixture through rotavaporation, yielding the cyclooctene oxide as a colorless oil.

The protocol for the alkane oxidation reactions was based on previously reported procedures in order to facilitate comparison to prior research [10–12,14]. The Fe(II) catalyst and alkane substrate were dissolved in MeCN, with initial concentrations of 1.0 mM and 1.0 M, respectively, unless noted otherwise. The terminal oxidant, H_2O_2, was diluted in MeCN and added dropwise over the course of 1 min in order to minimize changes to the reaction temperature. The final volume of each reaction solution was 2.50 mL. At various time points, aliquots of the solution were taken via syringe, filtered through silica gel, and analyzed via GC. Prior to GC analysis, 1,2-dichlorobenzene was added as an internal standard.

3. Result

3.1. Alkene epoxidation-manganese

The heptacoordinate $[Mn(debpn)(H_2O)]^{2+}$ complex (**1**) was tested as a catalyst for the epoxidation of various olefins by peracetic acid
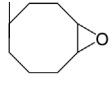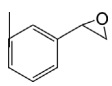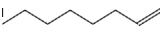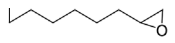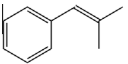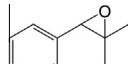
Table 1
Epoxidation of 1-octene catalyzed by $[Mn(debpn)(H_2O)]^{2+}$ (**1**) and $[Mn(bpmen)(OTf)_2]$ (**3**).

Catalyst	Loading (mol%)	Time (s)	GC Yield (%)
1	0.1	15	1
		300	38
	1.0	15	9
		300	77
3	0.1	15	2
		300	49
	1.0	15	83
		300	87

All reactions were run at 298 K in MeCN under N_2, with initial concentrations of 100 mM 1-octene and 150 mM PAA_R. The reported yields are the averages of at least three independent reactions. The only observed product is 1-octene oxide; no other oxidized organic products were observed above the limit of detection. The data for **3** are from Ref. [3] these were reproduced by our laboratory.

(PAA_R). The reaction protocol was chosen to facilitate comparison to the previously reported catalytic capabilities of $[Mn(bpmen)(OTf)_2]$ (**3**), although in most instances the reactions using **1** were run at 0 °C, rather than 25 °C [1,2]. Although **1** catalyzes the reaction between alkenes and peracetic acid, the activity is inferior to that of the bpmen compound, as assessed by the lower conversions of 1-octene (Table 1). With both ligands, the epoxide is the only observed organic product; the yields of epoxides and conversions of alkene starting material are equal within error. The observed reactivity is unusual in that 1-octene and cis-cyclooctene are oxidized to similar extents, with essentially identical yields of the corresponding epoxides at 5 min (Table 2). This is noteworthy since the more electron deficient C=C bond in 1-octene is generally less reactive. [1,2,7,17,23,24] Styrene is also more reactive than one might otherwise anticipate, for the measured yields at 5 and 30 min are not much lower than their counterparts for dimethylstyrene. The catalyst is not stable under the reaction conditions; over 30 min, the debpn ligand is oxidized, as evidenced by mass spectrometry (Fig. S5). Further, the reaction mixture changes color from light yellow to brown, indicating that the manganese is oxidized as well.

Table 2
Epoxidation of alkenes by 7.5% peracetic acid catalyzed by $[Mn(debpn)(H_2O)]^{2+}$ (**1**).

Substrate	Product	Catalyst loading (mol%)	Time (min)	GC Yield (%)
		1.0	5	78
			30	79
		0.10	5	52
			30	78
		0.0	5	3
			30	8
		1.0	5	44
			30	62
		0.0	5	0
			30	0
		1.0	5	75
			30	77
		0.0	5	0
			30	0
		1.0	5	62
			30	78
		0.0	5	0
			30	0

All reactions were run at 273 K in MeCN under N_2, with initial concentrations of substrate and PAA_R equal to 100 and 150 mM, respectively. The initial concentrations of **1** in the 1.0 and 0.10 mol% catalyst loadings were 1.0 and 0.10 mM respectively. The shown epoxides are the only observed organic products; the remaining material is non-oxidized starting material. All reported yields are the averages of at least three independent reactions.

3.2. Alkene epoxidation-iron

The epoxidation of alkenes by H_2O_2 proceeds more slowly and to a lesser extent with $[Fe(debpn)(H_2O)]^{2+}$ (**2**) as the catalyst relative to similar reactions reported by White, Doyle, and Jacobsen using $[Fe(bpmen)(MeCN)_2](SbF_6)_2$ (**4**) [8]. cis-Cyclooctene is oxidized to half the extent (40% isolated yield) and requires 60 min, rather than 5 min, for this maximum yield to be reached (Table 3). The ferrous debpn complex also appears to catalyze the oxidation of terminal alkenes less avidly relative to both **1** and its bpmen analog **4**. 1-Octene is converted to 1-octene oxide in 47% yield over 30 min with a 5 mol% loading of **2**; with **4**, conversely, non-functionalized terminal alkenes are oxidized to epoxides in yields of 76–90% within 5 min [8]. As with the aforementioned **1**, **2** is itself oxidized under the reaction conditions. Mass spectrometry reveals that the debpn ligand is oxidized over the 30 min allowed for the reactions (Fig. S6). The solutions also discolor, suggesting that the iron oxidizes as well.
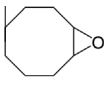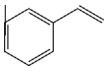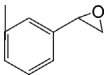
3.3. Alkane oxidation-iron
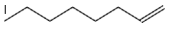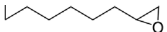
Compound **2** also catalyzes the oxidation of alkanes by H_2O_2 to alcohols and ketones (Table 4). As with the alkene epoxidation, this activity is not as extensive as that previously observed with the bpmen ligand. Cyclohexane is oxidized to a mixture of cyclohexanol and cyclohexanone. When 10 equiv. of H_2O_2 are provided as the terminal oxidant, the catalyst only turns over 2.1 times; this activity is exceptionally mild relative to the catalysis reported for other non-heme iron compounds [10–14]. $[Fe(bpmen)(MeCN)_2]$ $(OTf)_2$, for instance, can catalyze 7.0 turnovers under identical reaction conditions (5.6 TON for cyclohexanol, 0.7 TON for cyclohexanone which requires two equiv. of H_2O_2) [12,13]. Additionally, the selectivity for the alcohol product is lost; the products of cyclohexane oxidation promoted by **2** contain nearly equal amounts of cyclohexanol and cyclohexanone. A kinetic isotope effect of 2.4 was measured from a competition experiment with protonated and deuterated cyclohexane (C_6D_{12}), suggesting that C–H bond cleavage is involved in the product-determining step of the reaction. Compound **2** catalyzes 1.3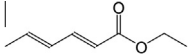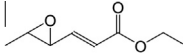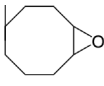 turnovers over 30 min when C_6D_{12} is the sole substrate with a 3:1 ratio of alcohol to ketone products. This reactivity is more extensive than one would expect from the KIE and the TON reported for the protonated cyclohexane.

In order to assess the potential impact of steric repulsions between the catalyst and the substrate on the C-H activation, the more sterically complex alkanes cis- and trans-1,2-dimethylcyclohexane were investigated as substrates using a protocol first employed by White [25] and subsequently by ourselves [14]. In these experiments, the ratio of secondary to tertiary carbon oxidation is used as a measure of the accessibility of the metal-based oxidant to substrates. More sterically congested catalysts will direct the oxidation to the thermodynamically stronger but more accessible C–H bonds on secondary carbons [10,14,25]. The ratios of secondary/tertiary oxidation observed for **2** are similar to those observed for reactions catalyzed by other non-heme iron compounds but are lower than those of $[Fe(bbpc)(MeCN)_2]^{2+}$ (bbpc = N,N′-bis(phenylmethyl)-N,N′-bis(2-pyridinylmethyl)-1,2-cyclohexanediamine), which is a markedly superior catalyst for cyclohexane oxidation (4.5 TON, 7.3:1 alcohol:ketone (A:K) ratio with 10 equiv. H_2O_2) [14].

3.4. Electochemistry

Cyclic voltammetry (CV) was performed for compounds **1**–**4** in anaerobic MeCN. Each debpn and bpmen compound except for **4** has a single irreversible redox feature, which we assign to the M(III/II) couple. The manganese complexes have oxidation peaks

Table 3
Epoxidation of alkenes by hydrogen peroxide catalyzed by [Fe(debpn)(H$_2$O)]$^{2+}$ (**2**) and [Fe(bpmen)(MeCN)$_2$](SbF$_6$)$_2$ (**4**).

Catalyst	Substrate	Product	Catalyst loading (mol%)	Time (min)	Yield (%)	TON
2			3.0	5	33, 29[a]	11.0
				30	38, 33[a]	12.7
				60	44, 40[a]	14.7
			5.0	5	68	13.6
				30	82	16.4
				60	87	17.4
			5.0	5	5	1.0
				30	5	1.0
				60	6	1.2
			5.0	5	35	7.0
				30	47	9.4
				60	47	9.4
			5.0	5	27	5.4
				30	27	5.4
				60	27	5.4
4			3.0	5	86[a,b]	28.3[b]

All reactions were run in MeCN at 273 K under N$_2$. The initial concentrations of substrate, H$_2$O$_2$, and acetic acid were 100 mM, 150 and 50 mM. The reported yields are the averages of at least three independent reactions. The epoxides are the sole observed organic products. All yields are GC yields unless stated otherwise.
[a] Isolated yield.
[b] Data from Ref. [8]; these results were independently reproduced by our laboratory.

Table 4
Oxidation of alkanes by hydrogen peroxide catalyzed by [Fe(debpn)(H$_2$O)]$^{2+}$ (**2**).

Substrate	Products[a]	TON[b]	Notes
cyclohexane	cyclohexanol	0.76	1.1:1 A:K ratio
	cyclohexanone	0.67	
1-hexane	2-hexanol	0.049	1.1:1 A:K ratio, no primary carbon oxidation
	3-hexanol	0.19	
	2-hexanone	0.074	
	3-hexanone	0.15	
cis-1,2-dimethylcyclohexane	trans-1,2-dimethylcyclohexanol	3.3	modified procedure[c]
	cis-1,2-dimethylcyclohexanol	0.3	
	cis-2,3-dimethylcyclohexanone	2.2	
	cis-3,4-dimethylcyclohexanone	0.1	
trans-1,2-dimethylcyclohexane	trans-1,2-dimethylcyclohexanol	0.9	modified procedure[c]
	cis-1,2-dimethylcyclohexanol	1.5	
	trans-2,3-dimethylcyclohexanol	1.8	
	trans-2,3-dimethylcyclohexanone	2.8	
	cis-3,4-dimethylcyclohexanone	1.7	

Standard reaction conditions: All reactions were run at 298 K in MeCN under N$_2$. For cyclohexane and hexane, the starting concentrations of **2** and the substrate were 1.0 and 1.0 M, respectively. A solution of H$_2$O$_2$ diluted in MeCN was added dropwise over the course of 1 min. The final volume of each reaction solution was 2.50 mL. The duration of each reaction was 30 min. After this time, the solution was filtered through silica gel and analyzed via GC.
[a] The products were identified by GC/MS and comparison of the retention times with those of authentic samples. The concentrations of each organic product were calibrated relative to that of an internal standard (dichlorobenzene) with a known concentration.
[b] Turnover number, defined as the number of moles of cyclohexanol and cyclohexanone generated per mole of **2**.
[c] Modified procedure reaction conditions: the general protocol was adapted from Ref. [25] in order to facilitate direct comparison of the data to previously reported results. The substrate (0.056 g, 0.50 mmol, 1 equiv) was dissolved in 1.0 mL of MeCN. The iron catalyst and the terminal oxidant, H$_2$O$_2$, were added to this solution in three portions. For each addition, the H$_2$O$_2$ was added dropwise over the course of 90 s. After the first additions, the concentrations were as follows: [Fe] = 4.26 μM, [substrate] = 85.2 μM, [H$_2$O$_2$] = 0.102 mM. 10 min after the first portion of H$_2$O$_2$ was added, further equivalents of catalyst and oxidant were added, yielding the following concentrations: [Fe] = 4.65 μM, [substrate] = 46.5 μM, [H$_2$O$_2$] = 0.112 mM. 20 min after the first portion of H$_2$O$_2$ was added, the third portions of catalyst and oxidant were added, yielding the following concentrations: [Fe] = 4.80 μM, [substrate] = 32.0 μM, [H$_2$O$_2$] = 0.115 mM.

at 1020 mV (debpn) and 960 mV (bpmen); whereas, the iron complexes have similar features at 1010 mV (debpn) and 835 mV (bpmen). The feature for [Fe(bpmen)(MeCN)$_2$]$^{2+}$ is quasi-reversible. Although the ΔE of 60 mV is consistent with a reversible process, the current of the cathodic peak is much less than that of the anodic. The +2 oxidation state is stabilized by the additional ester arms of the debpn ligand, with Fe(II) being stabilized to a much greater extent.

4. Discussion

The use of a more highly coordinating ligand can potentially impact the catalytic properties of a bound metal ion in several ways.

First, the additional donor atoms can alter the fundamental electronic structure through a change in the coordination geometry, which could better stabilize certain oxidation states over others. Second, a more highly chelating ligand can stabilize metal–ligand adducts crucial to the desired reactivity. Third, the ligand could hinder the ability of inner-sphere terminal oxidants to ligate the metal, due to the more crowded coordination sphere. Fourth, the extra binding groups can block substrates from interacting with the generated metal-based oxidants, which remain nebulous in many instances [3,4,18,26].

In their investigation of alkene epoxidation catalyzed by manganese complexes with bidentate, tridentate, and tetradentate ligands, Murphy and Stack found that ligands with higher

denticities tend to promote superior reactivity, with respect to both the ultimate yield and speed of the reaction [3]. The better activity of the complexes with the tetradentate ligands was attributed to the greater stability of the manganese complexes; the use of a less highly chelating ligand or the introduction of steric modifications that lengthened and weakened the Mn–L bonds generally led to a pronounced loss of catalytic activity [3]. The Mn(II) complex with the debpn ligand promotes slightly less active epoxidation than the Mn(II) complexes with most tetradentate ligands, using the epoxidation of 1-octene as the basis for comparison (Table 1). The yield of the 1-octene epoxide is ~90% of that of the reaction catalyzed by its most closely related six-coordinate analog [Mn(bpmen)(OTf)$_2$]. The reactivity promoted by **1** also proceeds more slowly, evidenced most clearly by the yields measured at 15 s. The results demonstrate that factors other than the stability of the manganese-ligand adduct influence the catalysis of alkene epoxidation by peracetic acid. That 1-octene and *cis*-cyclooctene are oxidized to essentially the same extent (Table 1) suggests that steric interactions between the catalyst's ligand and the organic substrate may hinder the oxidation of more sterically congested olefins; normally, *cis*-cyclooctene is far more reactive than 1-octene [1,7,17,23,24]. The similar reactivities of styrene and dimethylstyrene also support this conclusion. With the latter two substrates, the reactions are substantially slower, requiring 30 min for completion instead of 5 min.

Slower alkene epoxidation activity is also observed when the Fe(II) complex **2** is used as a catalyst using a protocol developed by White, Doyle, and Jacobsen in their analysis of [Fe(bpmen)(MeCN)$_2$]$^{2+}$ (**4**) [8]. Epoxidations catalyzed by **4** finish within 5 min; whereas, analogous reactions catalyzed by **2** need 30 min to reach their optimal yields. The final yield of the *cis*-cyclooctene epoxidation catalyzed by **2** is lower, being approximately 50% of that reported for the reaction promoted by [Fe(bpmen)(MeCN)$_2$]$^{2+}$. Compared to its Mn(II) analog **1**, **2** is not as effective at catalyzing the oxidation of terminal olefins, and the reactivity with styrene, in particular, is negligible. The loss of epoxidation activity associated with the use of a hexadentate ligand in place of a tetradentate one is greater for iron than it is for manganese. Steric effects are not as evident for the iron-catalyzed epoxidation. The yields of 1-octene oxide from 1-octene are about half those of cyclooctene oxide from *cis*-cyclooctene.

The Fe(II) complex **2** was also tested as a catalyst for the oxidation of alkanes by H$_2$O$_2$ (Table 4). Iron complexes with bpmen have been explored extensively as catalysts for these reactions [10–13]. The addition of the ethyl esters to the ligand framework reduces the activity to a greater extent than the previously described epoxidation reactions. Using the oxidation of cyclohexane by 10 equiv. of H$_2$O$_2$ as a comparative standard, about 70% of the catalytic activity is lost upon switching the catalyst from [Fe(bpmen)(OTf)$_2$] to **2**. The debpn ligand does appear to be relatively bulky, as assessed by the retention of configuration (RC) for the oxidation of *cis*-1,2-dimethylcyclohexane. RC has been previously defined as $[([(1R,2R + 1S,2S) - (1R,2S + 1S,2R)]/(\text{total amount of tertiary alcohol})$, where (1R,2R), (1S,2S), (1R,2S), and (1S,2R) are the various isomers of 1,2-dimethylcyclohexanol [10]. The RC for *cis*-1,2-dimethylcyclohexane oxidation has been found to decrease upon switching to an iron catalyst with a bulkier ligand. The 83% RC for **2** is significantly lower than the 96% value for [Fe(bpmen)(OTf)$_2$] but is higher than those associated with more catalytically active iron complexes with doubly and triply methylated tris(picolylamine) ligands [10].

The reduced C–H activation catalysis therefore cannot be solely attributed to increased steric interactions between **2** and potential substrates. The ratios of secondary to tertiary carbon oxidation for the two 1,2-dimethylcyclohexane substrates provide an alternative means of assessing the steric hindrance between the substrate and

catalysts. The ratios observed for **2** are similar to those reported for other non-heme iron catalysts with bulky N-donor ligands [14,25]. Further, another Fe(II) complex of ours, [Fe(bbpc)(MeCN)$_2$]$^{2+}$, shows much stronger preferences for secondary over tertiary carbon oxidation (a ratio of 4.8:1 with *trans*-1,2-dimethylcyclohexane) without as marked a decrease in the catalysis [14]. The installation of the weakly binding ethyl esters also eliminates the selectivity for the alcohol over the ketone product that was observed for both the bpmen and bbpc systems [12–14].

Cyclic voltammetry (CV) measurements suggest that the +2 oxidation state is better stabilized by the debpn ligand than by the bpmen, with the iron being particularly stabilized by the additional chelate arms. In each of the CV of compounds **1–4**, a single irreversible or quasi-reversible feature is observed, which we assign to the divalent metal ion's oxidation to the +3 state. The CV of **1** has a redox feature 60 mV higher than that observed for **3**. The redox event observed for **2** is 175 mV higher than that of **4**. The comparative increased difficulty in converting the Fe(II) to higher oxidation states may explain why the iron loses more of its activity than the Mn(II) upon the bpmen-for-debpn switch. For the alkane hydroxylation, the oxidation of the iron does not appear to be fully rate-limiting, however. The measured KIE for cyclohexane is consistent with C–H bond cleavage in the product-determining step. More turnovers are observed with C$_6$H$_{12}$ than with C$_6$D$_{12}$ suggesting that C–H bond cleavage is still relevant to the rate-determining step. The ratio of these turnover numbers (1.4:1), however, is much less than what one would expect based on the KIE of 2.4. An alternative explanation for the reduced activity may be that the higher reduction potentials destabilize the higher-valent iron oxidant responsible for alkane oxidation. This oxidant may consequently exhibit faster rates of intramolecular ligand oxidation [6], thereby eliminating opportunities for the oxidant to react with exogenous substrates. The observed debpn ligand degradation may be consistent with this alternative explanation.

Although the additional chelate arms of debpn were previously found to stabilize and solubilize ligand–metal adducts in water [19], neither the Mn(II) nor the Fe(II) compound is a competent catalyst for hydrocarbon oxidation in aqueous solutions. Reactions were run in anaerobic distilled water; otherwise the reaction conditions were identical to those of the MeCN reactions. Due to the immiscibility of the substrate with water, the reactions were stirred quickly to ensure that the reaction proceeded [27], The yields of cyclohexene oxide from cyclohexene for the uncatalyzed reactions with peracetic acid and H$_2$O$_2$ are equal to those with a debpn compound present. The [Fe(debpn)(H$_2$O)]$^{2+}$ complex fails to catalyze the oxidation of cyclohexane by H$_2$O$_2$ in water. Although the debpn ligand should remain more tightly bound to the metals due to their potential hexadenticity, the Mn(II) and Fe(II) complexes are still susceptible to degradation through side reactions with the terminal oxidants used for hydrocarbon oxidation.

Although the use of a neutral ligand that promotes heptacoordination appears to be a poor design feature for a first-row transition metal catalyst for hydrocarbon oxidation, such ligands may be beneficial for other applications. One concern in using transition metal ions for biological imaging, for instance, is that they often catalyze unwanted redox activity. Preparing a biological imaging agent with a more highly coordinating ligand may significantly limit these reactions by better stabilizing the metals in lower oxidation states.

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.2013.06.009.

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