Iron-Catalyzed Olefin Epoxidation in the Presence of Acetic Acid: Insights into the Nature of the Metal-Based Oxidant

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Abstract: The iron complexes [(BPMEN)Fe(OTf)$_2$] (**1**) and [(TPA)Fe(OTf)$_2$] (**2**) [BPMEN = N,N'-bis-(2-pyridylmethyl)-N,N'-dimethyl-1,2-ethylenediamine; TPA = tris-(2-pyridylmethyl)amine] catalyze the oxidation of olefins by H$_2$O$_2$ to yield epoxides and *cis*-diols. The addition of acetic acid inhibits olefin *cis*-dihydroxylation and enhances epoxidation for both **1** and **2**. Reactions carried out at 0 °C with 0.5 mol % catalyst and a 1:1.5 olefin/H$_2$O$_2$ ratio in a 1:2 CH$_3$CN/CH$_3$COOH solvent mixture result in nearly quantitative conversions of cyclooctene to epoxide within 1 min. The nature of the active species formed in the presence of acetic acid has been probed at low temperature. For **2**, in the absence of substrate, [(TPA)Fe^{III}(OOH)(CH$_3$COOH)]$^{2+}$ and [(TPA)Fe^{IV}O(NCCH$_3$)]$^{2+}$ intermediates can be observed. However, neither is the active epoxidizing species. In fact, [(TPA)Fe^{IV}O(NCCH$_3$)]$^{2+}$ is shown to form in competition with substrate oxidation. Consequently, it is proposed that epoxidation is mediated by [(TPA)Fe^{V}(O)(OOCCH$_3$)]$^{2+}$, generated from O–O bond heterolysis of the [(TPA)Fe^{III}(OOH)(CH$_3$COOH)]$^{2+}$ intermediate, which is promoted by the protonation of the terminal oxygen atom of the hydroperoxide by the coordinated carboxylic acid.

Introduction

The discovery of efficient methods for catalytic epoxidation is an important goal in synthetic chemistry. Furthermore, developing systems that achieve high selectivity using environmentally friendly conditions and inexpensive terminal oxidants remains as an important challenge.[1] To address these questions, inspiration can be found in nature. For instance, cytochromes P450 (P450) constitute a family of heme enzymes that catalyze oxygenation reactions of a variety of substrates, including epoxidation of olefins.[2] In addition, the non-heme iron enzyme methane monooxygenase (MMO) is an excellent catalyst for the selective hydroxylation of small hydrocarbons, which also can catalyze olefin epoxidation.[3] Inspired by these enzymes, much effort has been invested in developing biomimetic iron porphyrin catalysts[4] and, more recently, in the design of new families of non-heme iron catalysts.[5,6] The main feature that distinguishes non-heme catalysts from their heme analogues is their ability to catalyze not only epoxidation but also olefin *cis*-dihydroxylation.[7] Previous studies reveal a surprisingly complex reaction landscape for non-heme iron catalysts[8] and suggest that olefin epoxidation and *cis*-dihydroxylation are in fact closely related transformations that can be carried out by a common HO–Fe^{V}=O oxidant.[9] Furthermore, the mechanisms and catalytic activities of non-heme iron complexes can be modified by additives such as acetone, water, or acetic acid.[10]

Addition of acetic acid to some non-heme iron-catalyzed olefin oxidation reactions resulted in an increase in both catalytic activity and selectivity toward epoxidation. This effect was originally observed for [(BPMEN)Fe(NCCH$_3$)$_2$]$^{2+}$ (**1**) by Jacobsen and co-workers,[11] and a later extension to [(TPA)Fe(NCCH$_3$)$_2$]$^{2+}$ (**2**) (Chart 1) indicated that the preference of this catalyst for *cis*-dihydroxylation was inhibited to clearly favor epoxidation upon addition of CH$_3$COOH.[12] In addition, Stack and co-workers also demonstrated that the Fe–phenanthroline complex, [((phen)$_2$(H$_2$O)Fe^{III})$_2$(μ-O)](ClO$_4$)$_4$, is an efficient

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Chart 1. Representation of the Structures of $[LFe^{II}(NCCH_3)_x]^{2+}$ Complexes Used in This Study

$[(BPMEN)Fe^{II}(CH_3CN)_2]^{2+}$ $[(TPA)Fe^{II}(CH_3CN)_2]^{2+}$ $[(N4Py)Fe^{II}(CH_3CN)]^{2+}$
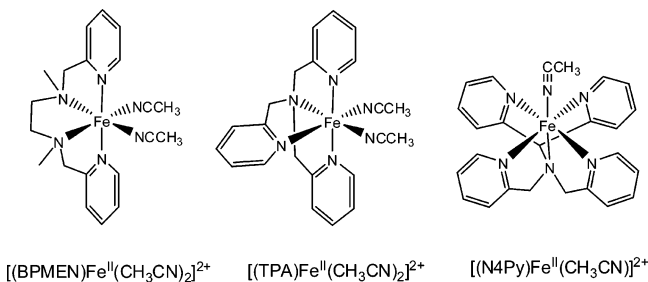
epoxidation catalyst with peracetic acid as the oxidant.[13] This observation raised the possibility that iron-catalyzed *in situ* formation of peracetic acid from CH_3COOH and H_2O_2 could rationalize the effect of acetic acid on olefin oxidation catalyzed by complexes **1** or **2**.[12] Interestingly, results reported for **1** suggest that the presence of acetic acid sufficiently enhances its catalytic activity to envisage synthetic applications of these bioinspired systems.[11] However, despite the potential practical implications of these observations, the mechanism of olefin epoxidation catalyzed by non-heme iron complexes in the presence of acetic acid remains unexplored. To fill this gap, identification of intermediate species generated under catalysis conditions would be very helpful. In the past decade, a large amount of data has been accumulated concerning the spectroscopic characterization of Fe(TPA)-derived intermediates such as $Fe^{III}OOH$[5,14] and $Fe^{III}OOR$[15] complexes as well as $Fe^{IV}O$ species.[16] However, less is known about Fe(BPMEN)-derived intermediates, but some information has recently become available.[17] Taking advantage of the knowledge accumulated on the oxidation chemistry exhibited by $Fe^{II}TPA$, this work explores the mechanistic implications of adding acetic acid to **1** and **2**. Furthermore, this work reports experimental conditions where the presence of acetic acid allows nearly 100% conversion of olefin to epoxide using 0.5 mol % catalyst.

Experimental Section

Materials and Methods. All reagents were purchased from Aldrich and used as received unless noted otherwise. CH_3CN solvent was distilled over CaH_2 before use. $H_2^{18}O_2$ (90% ^{18}O-enriched, 2% or 10% solutions in $H_2^{16}O$) was obtained from Cambridge Isotope Laboratories Inc., and $H_2^{18}O$ (95% ^{18}O-enriched) was purchased from ICON isotopes. The olefin substrates were purified by passing through basic alumina immediately before the reactions. The syntheses of complexes **1** and **2** were carried out in a glove box under a dry N_2 atmosphere following procedures previously reported.[16,18] Electrospray ionization mass spectral experiments were carried out on a Bruker BioTOF II mass spectrometer using the following conditions: spray chamber voltage = 4000 V; gas carrier temperature = 200 °C. GC product analyses were performed on a Perkin-Elmer Sigma 3 gas chromatograph (AT-1701 column, 30 m) with a flame ionization detector. GC mass spectral analyses were

performed on a HP 5898 GC (DB-5 column, 60 m) with a Finnigan MAT 95 mass detector or a HP 6890 GC (HP-5 column, 30 m) with an Agilent 5973 mass detector. A 4% NH_3/CH_4 mix was used as the ionization gas for chemical ionization analyses. Electronic absorption spectra were recorded on a Hewlett-Packard (Agilent) 8452 diode array spectrophotometer over a 190–1100 nm range in quartz cuvettes cooled to the desired temperature by liquid nitrogen in a Unisoku cryostat. X-band EPR spectra were obtained at 2 K on a Bruker E-500 spectrometer equipped with an Oxford ESR-10 liquid-helium cryostat.

Reaction Conditions for Catalysis Experiments with Limiting Oxidant. A total of 0.287 mL of a 70 mM H_2O_2 solution (diluted from a 35% H_2O_2 solution) in CH_3CN was delivered by syringe pump over 25 min at 25 °C in air to a CH_3CN solution (2.0 mL) containing iron 1 mM catalyst and 200 mM olefin substrate. In various experiments, acetic acid was added to the initial solution such that the final concentration of acid was 85 mM. The solution was stirred for another 5 min after syringe pump addition was complete. In all cases, the resulting solutions were treated with acetic anhydride (1 mL) together with 1-methylimidazole (0.1 mL) to esterify the diol products. Naphthalene was added as an internal standard. Organic products were extracted with $CHCl_3$ and the solution was subjected to GC analysis. All experiments were run at least in duplicate, the reported data being the average of these reactions.

Reaction Conditions for Catalysis Experiments with Limiting Olefin Substrate. A total of 0.3 mL of a 2.0 M H_2O_2 solution (300 equiv) was delivered by syringe pump over 60 min or added all at once to a CH_3CN solution (2.0 mL) containing iron 1 mM catalyst and 200 mM olefin substrate. The solution was stirred for another 30 min after H_2O_2 addition was complete by syringe pump or for 90 min if the H_2O_2 was added all at once. These experiments were carried out either at room temperature or at 0 °C (in ice/water bath) with variable amounts of acetic acid or $HClO_4$. Samples were analyzed by GC following the acetylation work up explained above. Epoxide production was monitored by adding all at once the H_2O_2 solution to a pure CH_3-CN solvent, a 1:2 mixture CH_3CN/CH_3COOH, or a 1 mM solution of $HClO_4$ in CH_3CN at room temperature containing iron catalyst and cyclooctene. To aliquots extracted from reaction mixtures at different reaction times were added a solution containing 1-methylimidazole (0.1 mL) and naphthalene and passed through a silica gel column before GC analysis. The products were identified by their GC retention times. Analogous experiments were carried out at 0 °C in a 1:2 CH_3CN/CH_3-COOH mixture.

^{18}O-Labeling Experiments. For experiments with labeled water, $H_2^{18}O$, 42 μL of $H_2^{18}O$ (1000 equiv) were added to the catalyst solution containing 1000 equiv of CH_3COOH prior to the injection of H_2O_2. In the comparable experiment with labeled hydrogen peroxide, 70 mM $H_2^{18}O_2$ (diluted in CH_3CN from a 2% $H_2^{18}O_2/H_2O$ solution) was added, instead of H_2O_2, to a solution containing the iron complex and CH_3-COOH (1000 equiv). In a subsequent experiment carried out with the goal of determining if the label from H_2O_2 was incorporated to a fraction of the acetic acid, 70 mM $H_2^{18}O_2$ (diluted in CH_3CN from a 10% $H_2^{18}O_2/H_2O$ solution) was added, instead of H_2O_2, to a solution containing the iron complex and CH_3COOH (50 equiv). In all cases, the organic products were subjected to GC/CI–MS analyses.

Spectroscopic Experiments. Spectroscopic experiments were carried out using 1 mM solutions of $[Fe(TPA)(OTf)_2]$ (**2**) in 2.0 mL of CH_3-CN in a 1 cm UV–visible cuvette precooled to −20 °C. A total of 43 μL of 0.7 M H_2O_2 (15 equiv) was added to a solution containing the iron(II) complex and variable amounts of CH_3COOH. In another set of experiments the metastable $Fe^{III}OOH$ species was first generated by adding 43 μL of H_2O_2 0.7 M (15 equiv) to a 1 mM solution of [Fe-(TPA)(OTf)$_2$] at −30 °C. After maximal formation of the $Fe^{III}OOH$ species, variable amounts of CH_3COOH or CH_3COOD were added. Both procedures resulted in the formation of the $Fe^{IV}O$ intermediate with yields up to 65%. Quantitative obtention of $Fe^{IV}O$ species from **2** was achieved by addition of 1 equiv of AcO_2H (0.004 mmol, 32 wt %

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Table 1. Olefin Oxidations by H_2O_2 Catalyzed by **1** or **2** in CH_3CN at Room Temperature in the Presence of 100 equiv of $CH_3COOH^{a,b}$

catalyst	olefin	no acid		100 equiv CH_3COOH	
		epoxide	diol	epoxide	diol
1	cyclooctene	7.5	0.5	8.5	0.2
	cis−2-heptene	6.5	0.4	7.4	0.1
		(R.C. 90%)^c	(R.C. 83%)^c	(R.C. 98%)^c	(R.C. 50%)^c
	1-octene	3.6	0.8	5.8	0.2
	t-butyl acrylate	0.6	0.9	3.8	0.7
2	cyclooctene	3.1	4.4	7.6	0.7
	cis−2-heptene	1.9	3.5	4.2	1.2
		(R.C. 81%)^c	(R.C. 95%)^c	(R.C. 97%)^c	(R.C. 83%)^c
	1-octene	1.3	6.1	4.2	0.6
	t-butyl acrylate	<0.1	2.6	<0.1	1.3
$[(N4Py)Fe^{II}(NCMe)]^{2+}$	cyclooctene	0.4	<0.1	0.4	<0.1

^{a} Values are expressed in turnover numbers ^{b} Reaction conditions: 287 μL of a 70-mM H_2O_2 solution in CH_3CN (10 equiv with respect the iron(II) catalyst) delivered by syringe pump over 25 min to 2 mL CH_3CN containing 1 mM iron catalyst, 100 mM carboxylic acid, and 200 mM olefin (Fe/H_2O_2/substrate = 1/10/200). Five extra minutes of stirring were allowed before work up. ^{c} %RC = 100 × (cis − trans)/(cis + trans).

AcO$_2$H) in 0.05 mL of CH_3CN to a CH_3CN solution containing the starting iron(II) complex at −20 °C.

Results and Discussion

Catalysis Results. Complexes [(BPMEN)Fe^{II}(OTf)$_2$] (**1**) and [(TPA)Fe^{II}(OTf)$_2$] (**2**) (Chart 1) have been shown to be excellent iron catalysts for the oxidation of olefins in CH_3CN solvent with H_2O_2 as the oxidant.[7] Under conditions wherein the olefin is in excess, as much as 95% of the H_2O_2 oxidant can be converted into a combination of epoxide and *cis*-diol products.[10] Complex **1** is an epoxide-selective catalyst, whereas **2** favors *cis*-dihydroxylation. The reason for this difference in reactivity is not clear at the present time, but it seems likely that the topology of the tetradentate ligand about the iron center plays a significant role in determining this outcome.[8] The linear BPMEN ligand in **1** wraps around the iron center in a *cis*-α topology with the two labile sites trans to the tertiary amines,[18] whereas the tripodal TPA ligand in **2** coordinates to the iron in such a way as to give rise to one labile site trans to the tertiary amine and the other trans to one of the pyridines (Chart 1).[19] Complex **1** catalyzes olefin oxidation to afford epoxide/diol ratios of ≥15:1 for electron-rich cyclooctene and *cis*-2-heptene, but these values decrease to 4.5:1 for 1-octene and 1:1.5 for *tert*-butyl acrylate. In contrast, oxidations catalyzed by **2** exhibit epoxide/diol ratios ranging from ∼1:1.5 for cyclooctene and *cis*-2-heptene, to 1:5 for 1-octene and 1:>30 for *t*-butyl acrylate. As illustrated in Table 1, the addition of 100 equiv (relative to catalyst) of acetic acid to the reaction mixture suppresses the formation of *cis*-diol, enhances the selectivity for epoxidation, and increases the epoxide yield. Of note are the observations that the epoxide/diol ratio in cyclooctene oxidation by **1** increases from 15:1 to 43:1, with 85% of the H_2O_2 converted to epoxide, whereas for **2** the epoxide/diol ratio in cyclooctene oxidation goes from 1:1.4 to 11:1 with a comparable conversion of H_2O_2 into products. Also worth noting is the oxidation of *tert*-butyl acrylate by **1**, where addition of acetic acid converts **1** from a dihydroxylation-selective agent (epoxide/diol = 1:1.5) to one that is much more epoxide-selective (epoxide/diol = 5:1). Interestingly, the effect of adding 100 equiv of acetic acid to a reaction catalyzed by **2** can be mitigated by the addition of water. The diol fraction in the product mixture derived from cyclooctene oxidation increases as more water is added, achieving an epoxide/diol ratio of 1.5/1

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when 1000 equiv of water are added (Figure S1, Supporting Information). This observation suggests that acetic acid and water compete in an equilibrium that affects the outcome of the oxidation reactions.

The experiments discussed above involved H_2O_2 as the limiting reagent (Fe/CH_3COOH/H_2O_2/substrate = 1:100:10: 200). However, Jacobsen and co-workers previously reported excellent epoxidation yields using 3 mol % **1** at 4 °C in CH_3-CN and limiting substrate (Fe/CH_3COOH/H_2O_2/substrate = 1:10:50:33.3).[11] The epoxide yield for cyclooctene oxidation obtained under these conditions was 86% (29 turnovers), making such reaction conditions potentially useful for synthetic transformations. Considering this precedent, we investigated similar reaction conditions in which the H_2O_2/olefin ratio was maintained at 1.5:1 and found that the catalyst was still effective even at 0.5 mol % (Fe/H_2O_2/substrate = 1:300:200) with the H_2O_2 oxidant introduced by syringe pump over a period of an hour. These results are summarized in Tables 2 and 3. At room temperature and in pure acetonitrile, cyclooctene was oxidized by **1** with 69% efficiency (136 turnovers) and an epoxide/diol ratio of 10.5:1 and by **2** with 69% efficiency (138 turnovers) and an epoxide/diol ratio of 0.9:1. Both epoxide yield and selectivity improved significantly in the presence of acetic acid. Optimal conditions were found using a 1:2 mixture of CH_3CN and acetic acid, affording epoxide yields of 90% (180 turnovers) for both catalysts with epoxide/diol ratios of 180:1 for **1** and 45:1 for **2** (Table 2). These excellent yields improved to nearly 100% by carrying out the reactions at 0 °C (Table 2). As illustrated graphically in Figure 1 for cyclooctene oxidation at 0 °C, the diol yield, particularly for **2**, decreased as a function of acetic acid concentration, but the epoxide yield did not improve significantly until at least 1000 equiv of acetic acid were present.

With *cis*-2-heptene as a substrate, the epoxide product derived from both catalysts in a 1:2 CH_3CN/CH_3COOH mixture showed a very high degree of retention of configuration (99%), whereas the very minor (≤1%) diol product reflected a significant loss of configuration, particularly at ambient temperature. The high stereoselectivity of *cis*-2-heptene epoxidation excludes an autoxidation pathway and argues strongly for a metal-based oxidation mechanism. In the case of the very minor diol products, it seems likely that a very small fraction of epoxide formed may be hydrolyzed to the *trans*-diol under these conditions, accounting for the decreased %R.C. values.

Table 2. Olefin Oxidations Catalyzed by **1** or **2** in a 1:2 CH_3CN/CH_3COOH Mixture with 0.5 mol % Catalyst (Fe/H_2O_2/substrate = 1/300/200)[a]

		0 °C		room temperature	
catalyst	olefin	epoxide[b]	diol[b]	epoxide[b]	diol[b]
1	cyclooctene	99% (198 TON)	0.3% (0.6 TON)	90% (180 TON)	0.5% (1.0 TON)
	cis-2-heptene[c]	77% (153 TON)	0.3% (0.6 TON)	64% (127 TON)	0.8% (1.6 TON)
		(R.C. 99%)	(R.C. 50%)	(R.C. 99%)	(R.C. −23%)
2	cyclooctene	98% (195 TON)	1.0% (2.0 TON)	89% (178 TON)	2.0% (4.0 TON)
	cis-2-heptene[c]	44% (88 TON)	1.0% (2.0 TON)	28.0% (56 TON)	1.0% (2.0 TON)
		(R.C. 99%)	(R.C. 66%)	(R.C. 99%)	(R.C. 35%)

[a] H_2O_2 was delivered by syringe pump over 60 min and 30 extra minutes of stirring were allowed before workup. [b] TON = Turnover number. [c] %RC = $100 \times$ (cis − trans)/(cis + trans).

Table 3. Cyclooctene Oxidations Catalyzed by **1** or **2** (0.5 mol % Catalyst) at Room Temperature in CH_3CN (Fe/H_2O_2/substrate = 1/300/200)

catalyst	acid content	H_2O_2 addition	epoxide	*cis*-diol
1	none added	a	63%	6%
	none added	b	24%	4%
	0.1 equiv of $HClO_4$	a	74%	6%
	1 equiv of $HClO_4$	a	84%	4%
	1 equiv of $HClO_4$	b	85%	5%
	10 equiv of $HClO_4$	a	64%	0.7%
	1:2 CH_3CN/CH_3COOH	a	90%	0.4%
	1:2 CH_3CN/CH_3COOH	b,c	90%	0.5%
2	none added	a	32%	37%
	none added	b	2%	3%
	0.1 equiv of $HClO_4$	a	33%	39%
	1 equiv of $HClO_4$	a	39%	38%
	1 equiv of $HClO_4$	b	8%	9%
	10 equiv of $HClO_4$	a	9%	4%
	1:2 CH_3CN/CH_3COOH	a	89%	2%
	1:2 CH_3CN/CH_3COOH	b,c	85%	3%
$[Fe(L1)]^{2+}$	none added	d	4%	−
	5 equiv of HOTf	d	66%	−
$[Fe(L2)]^{2+}$	none added	d	9%	−
	5 equiv of HOTf	d	86%	−
$[Fe(L3)]^{2+}$	none added	d	6%	−
	5 equiv of HOTf	d	89%	−

[a] H_2O_2 was delivered by syringe pump over 60 min, and 30 extra minutes of stirring were allowed before workup. [b] H_2O_2 added all at once, products analyzed after 90 min of stirring. [c] No change in product yields with only 3 min of stirring [d] L1, L2, and L3 ligands correspond to pyridine-containing macrocycles bearing an aminopropyl pendant arm as described in reference 6a. Reactions were carried out at room temperature with 5 mol % catalyst (Fe/H_2O_2/substrate = 1/30/20) in CH_3CN with H_2O_2 added all at once and products analyzed 5 min after H_2O_2 addition.

The data presented above, together with previously reported results,[11,12] suggest that the addition of acetic acid can be a good strategy to design efficient and synthetically useful systems for epoxidation of olefins using catalysts **1** or **2**. To determine whether the acetic acid merely acts as a source of protons, further experiments were carried out by replacing the acetic acid with 0.1, 1, and 10 equiv of $HClO_4$ at room temperature (Table 3). The addition of 1 equiv of $HClO_4$ did show a similar effect as CH_3COOH in enhancing the conversion of olefin into epoxide for catalyst **1** but did not dramatically change the results obtained for **2**. On the other hand, 10 equiv of $HClO_4$ was too much of an amount to add as the conversion efficiency of **1** dropped to a level comparable to that with no acid added, whereas the conversion efficiency of **2** decreased significantly.

The experiments presented above were carried out by adding the H_2O_2 with a syringe pump. In the absence of acid, the all-at-once addition of H_2O_2 resulted in the disproportionation of H_2O_2 and dramatically reduced the yield of epoxide and diol products. At room temperature, all-at-once addition of 300 equiv
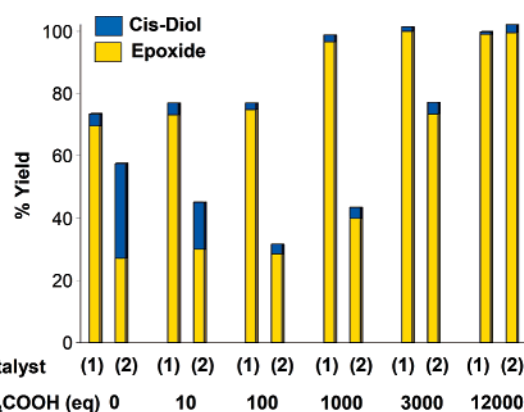
Figure 1. Cyclooctene oxidation by H_2O_2 at 0 °C catalyzed by **1** or **2** with 0.5 mol % catalyst (Fe/H_2O_2/substrate = 1/300/200) in the presence of variable amounts of acetic acid. H_2O_2 was delivered by syringe pump over 60 min, and 30 extra minutes of stirring were allowed before work up procedure.

of H_2O_2 to a solution containing **1** and 200 equiv of cyclooctene afforded a maximum yield of 24% of epoxide and 4% of diol, which was less than half of the yield obtained by adding the H_2O_2 by syringe pump over 1 h. This decrease of activity was even more dramatic for **2**, where the yields observed adding the H_2O_2 all at once were 10 times lower than those observed using a syringe pump. To determine whether adding CH_3COOH or $HClO_4$ affected the disproportionation of H_2O_2, the experiments summarized in Figure 2 were carried out. A comparison of the epoxide yields in **1**-catalyzed reactions obtained at different reaction times in the absence of additives and in the presence of CH_3COOH (1:2 CH_3CN/CH_3COOH mixture) or $HClO_4$ (1 equiv relative to catalyst) showed that both CH_3COOH and $HClO_4$ enhanced the epoxidation process (conversions of epoxide 85−90%). However, whereas epoxidation by **1** in the presence of acetic acid is almost complete within the initial 30 s at room temperature, epoxidation in the presence of $HClO_4$ required 90 min for maximal conversion. The high retention of configuration for the epoxide product (>96%) observed in analogous experiments using *cis*-2-heptene as substrate under these conditions indicated that the epoxidation must be a metal-based process and not due to autoxidation. Thus, the presence of either perchloric or acetic acid suppressed the disproportionation of H_2O_2 by **1**, allowing efficient oxidation to proceed without the use of a syringe pump. Acetic acid had the same effect for **2**-catalyzed epoxidation, but $HClO_4$ did not, the latter resulting in combined yields for epoxide and diol of less than 20%. For both **1** and **2**, adding acetate (1.2 M) to the catalysis experiments in 1:2 CH_3CN/CH_3COOH resulted in a > 90% drop in epoxide turnovers.
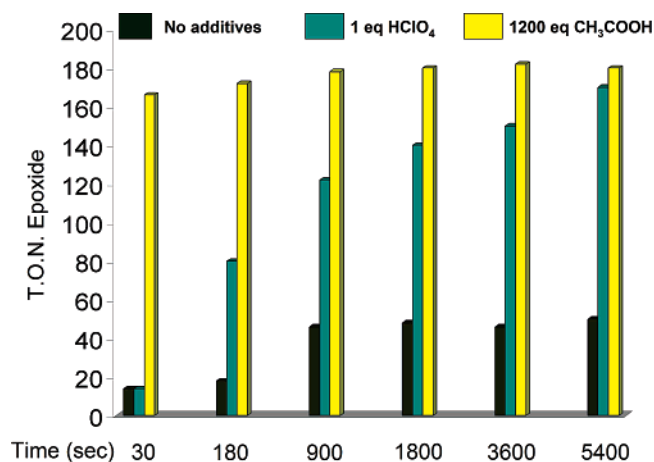
Figure 2. Epoxide yield as a function of the reaction time during the oxidation of cyclooctene by H_2O_2 catalyzed by **1** at room temperature in pure CH_3CN (dark green), in the presence of 1 equiv of $HClO_4$ (light green), and in a 1:2 mixture of CH_3CN/CH_3COOH, with 0.5 mol % catalyst (Fe/H_2O_2/substrate = 1/300/200) (yellow). H_2O_2 was delivered all at once with a micropipette.
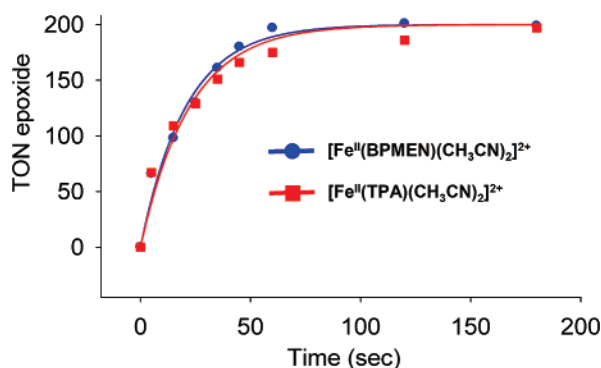

Figure 3. Epoxide yield as a function of reaction time during the oxidation of cyclooctene by H_2O_2 at 0 °C in a 1:2 mixture of CH_3CN/CH_3COOH catalyzed by **1** or **2** with 0.5 mol % catalyst (Fe/H_2O_2/substrate = 1/300/200). H_2O_2 was delivered all at once with a micropipette.

Since the oxidant can be added all at once in the presence of acetic acid, we monitored the epoxidation of cyclooctene catalyzed by **1** and **2** as a function of time at 0 °C (Figure 3). In both cases, epoxide formation appeared to be exponential and nearly complete within 1 min. An exponential fit of the data afforded k_{obs} values of 0.048 and 0.045 s^{-1}, respectively (or approximately 3 min^{-1}), comparable to those reported by Stephenson and Bell[20] for the epoxidation of cyclooctene by H_2O_2 catalyzed by [$Fe^{III}(F_{20}TPP)(OMe)$] ($H_2F_{20}TPP$ = tetrakis-(pentafluorophenyl)porphin) in 3:1 CH_3CN/CH_3OH at room temperature. Within the context of bio-inspired iron catalysis, the preliminary kinetic results suggest that both **1** and **2** are efficient catalysts for olefin epoxidation in the presence of acetic acid. With 200 equiv of cyclooctene at 0 °C, half of the olefin was oxidized during the first 14 s, which corresponds to a turnover frequency of 7 s^{-1}. These results merit a detailed kinetic investigation that will be reported subsequently.

From the results presented above it is clear that acetic acid affects the nature of the iron oxidant that is generated. The effect of acetic acid is more complex than a simple intermolecular protonation and the carboxylic group is somehow needed to both accelerate and favor the epoxidation process. In the
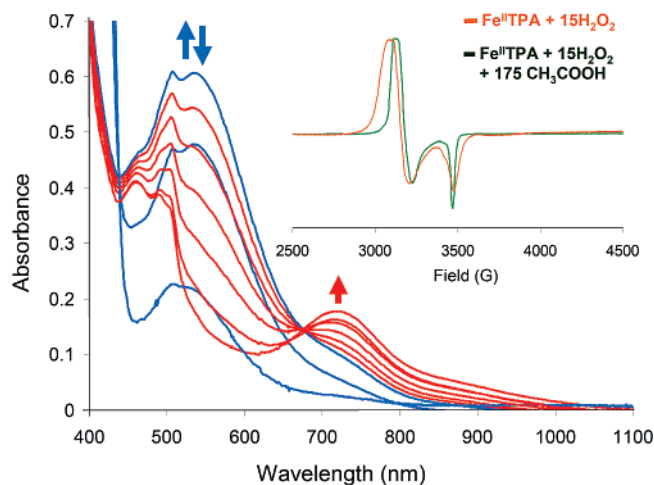
(20) Stephenson, N. A.; Bell, A. T. *J. Am. Chem. Soc.* **2005**, *127*, 8635.

Figure 4. UV−vis spectral evolution of 1 mM **2** in CH_3CN (at −20 °C) in the presence of acetic acid (175 equiv) after addition of 15 equiv of H_2O_2. Time interval between spectra is 2 seconds.
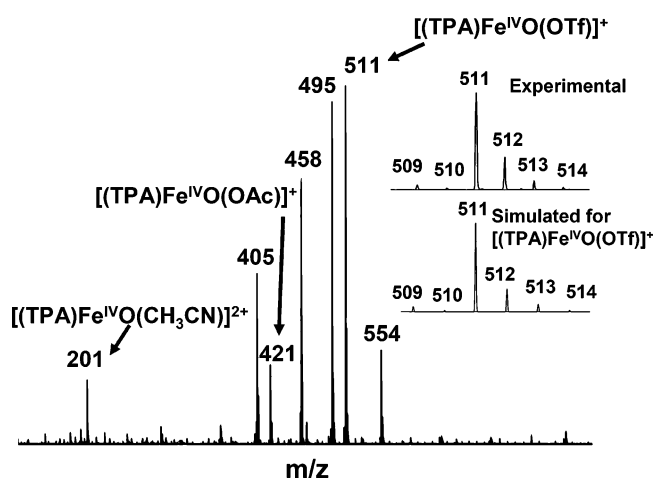

Figure 5. ESI-MS spectrum of the solution resulting from the reaction with 15 equiv of H_2O_2 with **2** in CH_3CN (1 mM, at −20 °C) in the presence of acetic acid (175 equiv). Peaks at m/z = 405, 458, 495, and 554 correspond to the [$(TPA)Fe(OOCCH_3)$]$^+$, [$(TPA)_2Fe_2(O)(OOCCH_3)(OTf)$]$^{2+}$, [$(TPA)$-$Fe(OTf)$]$^+$, and [$(TPA)Fe(OOCCH_3)(OTf)$]$^+$ cations, respectively.

following sections we discuss experiments that were carried out to gain mechanistic insight into the dramatic effect of acetic acid on the behavior of our bio-inspired non-heme iron catalysts.

Iron Intermediates Observed in the Presence of Acetic Acid. The changes in outcome effected by the addition of acetic acid on **1**- and **2**-catalyzed olefin oxidations, particularly dramatic in the case of the latter, suggest a potential change in the mechanism by which H_2O_2 is activated to carry out the epoxidation of the olefin. The top half of Scheme 1 summarizes the proposed mechanistic landscape that currently rationalizes the observations in the absence of carboxylic acid. A key intermediate is a low-spin Fe^{III}−OOH species that has been characterized by several spectroscopic methods in the case of **2** (L = TPA).[7,14,21] This intermediate, formulated as [(TPA)-$Fe^{III}(OOH)(NCCH_3)$]$^{2+}$ (**2a**), has been shown to be a sluggish oxidant,[22] so it cannot itself be the oxidant but serves as the precursor to a putative $Fe^V(O)(OH)$ oxidant that forms via a water-assisted mechanism (Scheme 1).[7,23] Indirect support for

(21) Ho, R. Y. N.; Roelfes, G.; Feringa, B. L.; Que, L., Jr. *J. Am. Chem. Soc.* **1999**, *121*, 264.
(22) Park, M. J.; Lee, J.; Suh, Y.; Kim, J.; Nam, W. L. *J. Am. Chem. Soc.* **2006**, *128*, 2630.

Scheme 1 Mechanistic Landscape Proposed for Oxidation of Olefins by Non-Heme Iron Catalysts
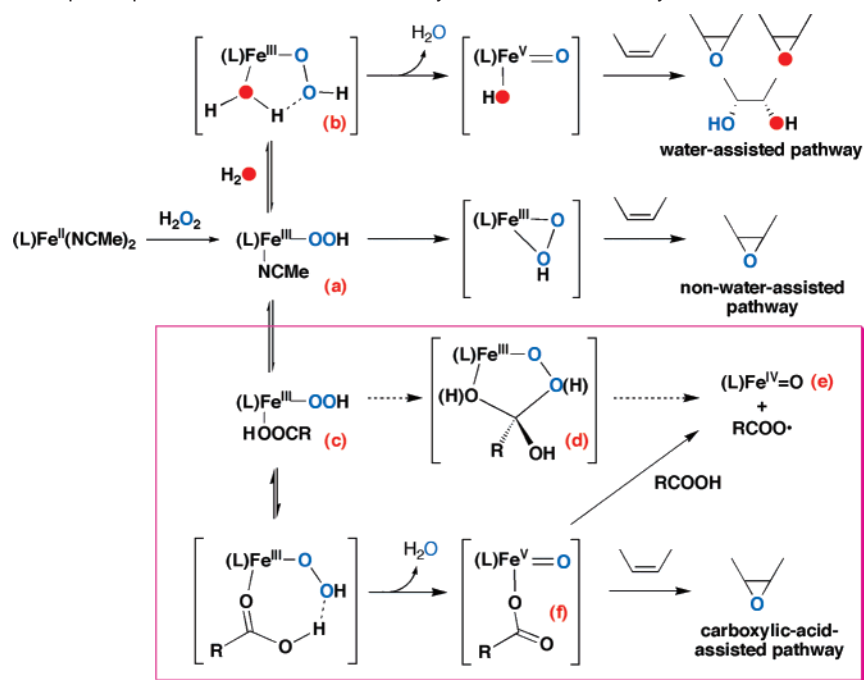
the latter was obtained from the observed incorporation of ^{18}O into the epoxide and *cis*-diol products when the reactions were carried out in the presence of $H_2^{18}O$.[7] However, when labeling studies of **1**- and **2**-catalyzed reactions were conducted in the presence of acetic acid, the oxygen of the epoxide products solely derived from H_2O_2. These observations suggest that the mechanistic landscape in Scheme 1 must be modified or augmented to account for the acetic acid results.

Our efforts to deduce the active species in the acetic-acid-promoted epoxidations by **1** and **2** were influenced by our earlier success in trapping and characterizing the Fe^{III}-OOH and Fe^{IV}=O intermediates generated from **2**,[7,14,16] so we have focused on the reaction of **2** with H_2O_2 in the presence of acetic acid. Figure 4 shows the UV−vis spectral evolution of a solution of **2** (1 mM) and 175 equiv of CH_3COOH in CH_3CN at −20 °C upon addition of 15 equiv of H_2O_2. The rapid formation and decay of a transient species with a maximum absorbance at 540 nm were observed, followed by the appearance of a new weaker feature at 722 nm. The 540 nm species has a visible absorption maximum essentially identical to that associated with **2a** (Scheme 1), but its EPR spectrum differs. Intermediate **2a** has been described as a rhombic low-spin iron(III) species with *g* values at 2.19, 2.15, and 1.97 in 1:1 CH_3CN/CH_2Cl_2;[14] its spectrum is broader in pure CH_3CN, but its *g* values are consistent with those from the better-resolved spectrum in 1:1 CH_3CN/CH_2Cl_2 (Figure 4 inset). On the other hand, the low-spin Fe^{III}−OOH intermediate formed in CH_3CN in the presence of 175 equiv of CH_3COOH, designated **2c**, has a more axial EPR spectrum with *g* values at 2.15, 2.15, and 1.97 (Figure 4 inset).

The 722 nm species that derived from the decay of **2c** can easily be identified as $[(TPA)Fe^{IV}O(NCCH_3)]^{2+}$ (**2e**), which was previously obtained from the reaction of $[(TPA)Fe^{II}(NCCH_3)_2]^{2+}$ with 1 equiv of peracid.[16] ESI-MS analysis of this solution

showed the presence of three different cations that originate from the $[(TPA)Fe^{IV}O]^{2+}$ species: $[(TPA)Fe^{IV}O(NCCH_3)]^{2+}$ (m/z = 201.6; intensity = 20%), $[(TPA)Fe^{IV}O(OOCCH_3)]^+$ (m/z = 421.1; intensity = 25%), and $[(TPA)Fe^{IV}O(OTf)]^{2+}$ (m/z = 511.1; intensity = 100%) (Figure 5). The yield of $[(TPA)-Fe^{IV}O]^{2+}$ estimated from the optical spectra depended on the amount of added CH_3COOH, with a maximum yield of ∼70% obtained after addition of 175 or more equivalents of acetic acid (Figure 6).

Decay of the 540 nm band occurred concomitantly with an increase of the absorption at 722 nm with an isosbestic point found at 677 nm (Figure 4). Thus, decomposition of **2c** afforded **2e** without an observable intermediate. Further confirmation was obtained by first generating **2a** *in situ* by reaction of **2** with 15 equiv of H_2O_2 at −20 °C and then adding 175 equiv of CH_3-COOH, which initiated the rapid conversion of the 540-nm intermediate to **2e** (Figure S2). This transformation was not effected by adding 2, 4, or 8 equiv of $HClO_4$ diluted in CH_3CN to *in situ* generated solutions of **2a**; the addition of strong acid merely increased the rate of decay of the Fe^{III}−OOH intermediate with no $Fe^{IV}O$ formation detected by UV−vis spectroscopy. The addition of acetate anion in place of CH_3COOH to *in situ* generated solutions of **2a** also failed to promote the formation of the $Fe^{IV}O$ complex but instead caused decay of **2a** to form $[(TPA)Fe^{III}(\mu-O)(\mu-CH_3COO)Fe^{III}(TPA)]^{3+}$, as evidenced by its characteristic UV−vis spectrum.[24] Since the conversion of the Fe^{III}−OOH intermediate to **2e** was promoted neither by strong acid nor acetate ion, the remaining logical alternative that rationalizes the observed transformation is the displacement of the CH_3CN solvent-derived in **2a** by acetic acid to form **2c**.

Nature of the Epoxidizing Agent. Since the intitial report of Jacobsen on the effect of acetic acid on **1**-catalyzed epoxidation,[11] several possibilities have been raised for the nature of the active oxidant. The crystallization of $[Fe^{III}_2O(O_2-$

(23) Bassan, A.; Blomberg, M. R. A.; Siegbahn, P. E. M.; Que, L., Jr. *J. Am. Chem. Soc.* **2002**, *124*, 11056.

(24) Norman, R. E.; Yan, S.; Que, L., Jr.; Backes, G.; Ling, J.; Sanders-Loehr, J.; Zhang, J. H.; O'Connor, C. J. *J. Am. Chem. Soc.* **1990**, *112*, 1554.
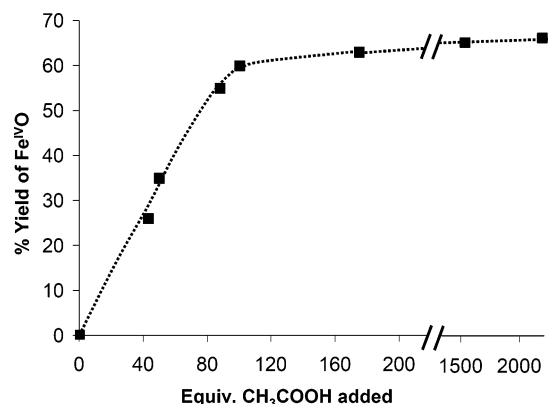
**Figure 6.** Dependence of yield of $[(TPA)Fe^{IV}O]^{2+}$ (calculated from its absorption in the near IR region) on the amount of acetic acid added.

Figure 7. Comparison of the rate of formation of $[(TPA)Fe^{IV}O]^{2+}$ (generated from reaction with 15 equiv of H_2O_2 of complex **2** in CH_3CN (1 mM, at -20 °C) in the presence of acetic acid (175 equiv) and its rate of decay by reaction with 200 equiv of cyclooctene or *cis*-2-heptene.

$CCH_3)(BPMEN)_2]X_3$ from the reaction mixture led Jacobsen and co-workers to suggest that this complex was in fact the actual catalyst. However, our earlier work with this and related $(\mu\text{-oxo})(\mu\text{-carboxylato})$diiron(III) complexes showed that such complexes were thermodynamic sinks,[24] so their stability and coordinative saturation made them unlikely to participate in catalysis. Experiments carried out subsequent to Jacobsen's 2001 report using isolated $(\mu\text{-oxo})(\mu\text{-carboxylato})$diiron(III) complexes as catalyst and H_2O_2 as oxidant consistently led to the conclusion that such complexes are catalytically inactive for olefin epoxidation.[25]

An alternative mechanistic hypothesis proposed by Fujita and Que involved iron-catalyzed formation of peracetic acid from H_2O_2 and acetic acid.[12] This notion derived from the observation that the same products and yields were obtained for **1**- and **2**-catalyzed olefin oxidation with either peracetic acid as oxidant or H_2O_2 in the presence of acetic acid. In the context of the present study, the peracetic acid thus formed could then react with the iron complex to give rise to an $Fe^{IV}=O$ oxidant.[16] We considered this hypothesis to be quite attractive, since it could rationalize the shift away from *cis*-dihydroxylation and toward epoxidation (particularly for **2**) in the presence of acetic acid.

To evaluate the ability of $[(TPA)Fe^{IV}O]^{2+}$ (**2e**) to epoxidize olefins, the reactivity of preformed **2e** with cyclooctene and *cis*-2-heptene was tested. As previously reported, the reaction of **2** with exactly 1 equiv of peracetic acid resulted in its stoichiometric conversion to **2e**.[16] Subsequent addition of 200 equiv of cyclooctene or *cis*-2-heptene under argon induced the decay of the $[(TPA)Fe^{IV}O]^{2+}$ species. GC analysis of the reaction mixture indicated an epoxide yield of less than 10% relative to $Fe^{IV}O$, which is lower than the 30% yield reported earlier for the oxidation of cyclooctene by **2e** carried out in air.[16] Similarly low yields for cyclooctene oxidation were observed by adding an excess of acetic acid to the **2e** solution prior to the addition of olefin or by generating **2e** by the reaction of **2** with H_2O_2 in the presence of acetic acid. Furthermore, addition of 1 equiv of $(Bu_4N)(O_2CCH_3)$ to a 1 mM $[(TPA)Fe^{IV}O]$ solution accelerated the rate of decay of the oxoiron(IV) species ($t_{1/2} = 5$ min at -20 °C vs >30 h in the absence of acetate), but did not result in the oxidation of cyclooctene to either epoxide or diol. The decay of the $Fe^{IV}O$ species led to its conversion to $[Fe^{III}_2(\mu\text{-}O)(\mu\text{-}CH_3COO)(TPA)_2]^{3+}$, as indicated by the appearance of
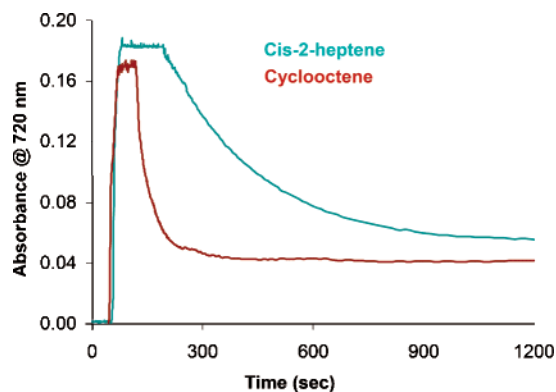
the characteristic UV−vis spectrum of the latter (Figure S3, Supporting Information). Taken together, the collective data make it very unlikely for **2e** to be the active species in the highly efficient catalytic epoxidation observed in the presence of acetic acid.

What then is the active oxidant? As can be noted from Figure 7, the rate of formation of **2e** from the reaction of H_2O_2 with **2** in the presence of acetic acid was considerably higher than its rate of decay by reaction with 200 equiv of cyclooctene or *cis*-2-heptene. Thus, significant accumulation of **2e** should be expected even when the substrate is present in the starting solution. However, in experiments where 200 equiv of cyclooctene or *cis*-2-heptene were added to a solution of 1 mM **2** and 175 mM acetic acid, formation of intermediate **2c** upon addition of H_2O_2 was observed, but its decay did not result in the formation of **2e**. These results suggest that substrate epoxidation and $[(TPA)Fe^{IV}O]^{2+}$ formation are competitive processes and that **2e** is formed by an unproductive pathway.

As precursors of **2e** that may be responsible for the epoxidation activity, we considered **2c** and **2d**, the latter being derived from **2c** via nucleophilic attack of the acetic acid carbonyl by the bound hydroperoxo moiety (Scheme 1). Similar to the behavior previously noted by Nam and co-workers for **2a**, the rate of decay of intermediate **2c**, generated from reaction of **2** with 15 equiv of H_2O_2 in the presence of 175 equiv of CH_3-COOH ($k_{obs} = 0.19(1)$ sec^{-1} at -20 °C), was not affected by the addition of 200 equiv olefin. Thus, **2c** cannot itself be the epoxidizing species.

Proposed intermediate **2d** is the hydrated form of a peroxyacetatoiron(III) complex and could conceivably be the precursor to **2e** as well as the epoxidizing agent. In the course of the proposed epoxidation, acetic acid would be regenerated, and this acetic acid should incorporate oxygen from H_2O_2. However, when a catalysis experiment was carried out by adding 10 equiv of $H_2^{18}O_2$ (from a 10% solution in water) to an acetonitrile solution of 1 mM $[(TPA)Fe^{II}(NCCH_3)_2]^{2+}$, 50 mM CH_3COOH, and 200 mM cyclooctene, the acetic acid in the reaction mixture showed absolutely no ^{18}O incorporation when analyzed by GC-MS. Consistent with this result, ESI-MS analysis of the resulting iron products showed that the two cationic species observed, $[(TPA)_2Fe^{III}_2(\mu\text{-}O)(\mu\text{-}O_2CCH_3)]^{3+}$ and $[(TPA)Fe^{II}(O_2CCH_3)]^+$, also did not incorporate any label. Thus, **2d** is not an intermediate in acetic-acid-promoted epoxidation pathway.

(25) (a) Ryu, J. Y.; Kim, J.; Costas, M.; Chen, K.; Nam, W.; Que, L., Jr. *Chem. Commun.* **2002**, 1288. (b) Taktak, S.; Kryatov, S. V.; Haas, T. E.; Rybak-Akimova, E. V. *J. Mol. Cat. A.* **2006**, *259*, 24.

The above experiments thus exclude most of the plausible epoxidizing species except for one remaining possibility, species **2f**, which is derived from O—O bond heterolysis of **2c** that is promoted by the bound acetic acid. A closely related [(TPA)-Fe^V(O)(O$_2$CAr)]$^{2+}$ species has been proposed as the oxidant responsible for self-hydroxylation of *m*-chloroperbenzoic acid by Fe(TPA).[26] Conversion of **2c** to **2f** is analogous to the proposed protonation of the bound hydroperoxo group by the coordinated water molecule in [(TPA)Fe^{III}(OOH)(OH$_2$)]$^{2+}$ (**2b**) that leads to the [(TPA)Fe^V(O)(OH)]$^{2+}$ oxidant in the water-assisted mechanism.[23] Coordination of the carboxylic acid to the iron center appears to be required, as adding acetic acid did not enhance the epoxidation ability of [(N4Py)Fe^{II}(NCMe)]$^{2+}$ (N4Py = *N,N*-bis(2-pyridylmethyl)-bis(2-pyridyl)methylamine), a structurally related non-heme iron complex with only one labile site (see Chart 1).[27] These experiments emphasize the importance of two cis labile sites to observe the enhancing effect of carboxylic acids on the epoxidation activity of these non-heme iron catalysts. As proposed for the bound water of **2c** in the water-assisted pathway, coordination of the carboxylic acid to the metal center both enhances its acidity and brings it in close proximity to the target hydroperoxide. Other related epoxidation systems that also take advantage of an intramolecular proton source to promote O—O bond heterolysis and significantly enhance the conversion efficiency of substrate to product include the "hangman" porphyrin system of Nocera[28] and an iron complex of a macrocyclic N$_4$ ligand with an alkylammonium tail recently reported by Rybak-Akimova.[6a] Such a proton-assisted O—O bond heterolysis is also generally accepted to be the key feature in generating the active oxidant in the cytochrome P450 mechanism.[2,29]

Once formed, species **2f** is proposed to be a powerful enough oxidant to carry out olefin epoxidation or, in the absence of olefin, the oxidation of the bound carboxylate.[30] Whereas epoxidation is a two-electron oxidation and regenerates Fe^{III}-(TPA) to bind for more H$_2$O$_2$ to maintain the catalytic cycle, the oxidation of the carboxylate is a one-electron process that generates **2e** and the corresponding carboxyl radical. Support for the latter was obtained by using phenylacetic acid in place of acetic acid. Like acetic acid, phenylacetic acid also enhanced epoxide selectivity in catalytic experiments at 25 °C. GC analysis of the reaction mixture consisting of 1 mM Fe^{II}TPA, 100 mM phenylacetic acid, and 10 mM H$_2$O$_2$ revealed the formation of 0.9 equiv of benzaldehyde (relative to catalyst), presumably resulting from the formation of the phenylacetoxy radical, its decarboxylation, and trapping of the resulting benzyl
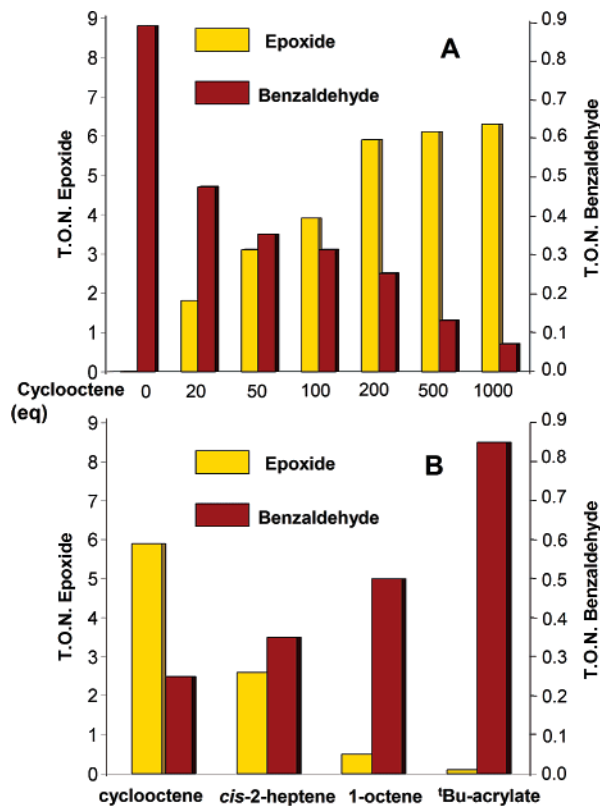

Figure 8. Yields of epoxide and benzaldehyde obtained from reactions of H$_2$O$_2$ catalyzed by **2** in CH$_3$CN in the presence of phenylacetic acid (Fe/H$_2$O$_2$/phenylacetic acid = 1/10/100) with variable amounts of cyclooctene (**A**) or 200 equiv of diverse olefins (**B**). H$_2$O$_2$ was delivered by syringe pump over 25 min, and 5 extra minutes of stirring were allowed before workup procedure.

radical by O$_2$.[31] Formation of the phenylacetoxyl radical is competitive with olefin epoxidation, as shown in Figure 8A, where the yields of epoxide and benzaldehyde clearly depend on the concentration of olefin but in opposite ways. Higher concentrations of cyclooctene afforded more epoxide and less benzaldehyde. The fact that the maximum yield of benzaldehyde approached a value comparable to the catalyst concentration strongly implies that formation of **2e** is a dead end that leads to the catalytically inactive [Fe^{III}$_2$O(O$_2$CCH$_3$)(TPA)$_2$]$^{3+}$ byproduct. Thus, intermediate **2c** must evolve in the presence of acetic acid into a species that epoxidizes olefins catalytically or, in the absence of olefins, undergoes stoichiometric conversion to **2e** and carboxyl radical to terminate catalysis (see Scheme 1 box).

A similar inverse correlation was observed in experiments carried out with different olefins, with the yield of epoxide being highly dependent on the nature of the olefin (Figure 8B). The reactivity of olefins followed the order: cyclooctene > *cis*-2-heptene > 1-octene > *tert*-butyl acrylate. The more electron-rich the olefin, the more epoxide is produced and the less benzaldehyde is observed. These results also support the notion of competing epoxidation and generation of **2e** (Scheme 1).

From the foregoing discussion, it is clear that the carboxylic acid plays a crucial role in promoting epoxidation by serving as both base and acid. It needs to be basic enough to bind to the iron(III) center of **2a** but also acidic enough to be able to

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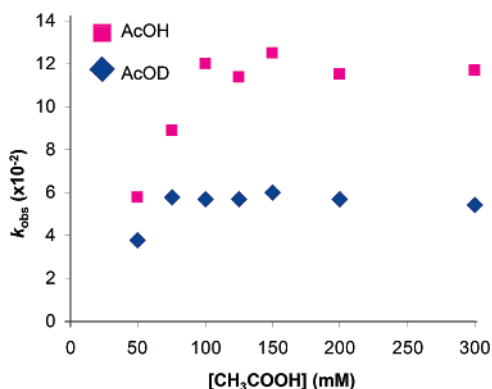
Figure 9. Rate constants calculated from the decay of the absorption at 540 nm at −30 °C after addition of variable amounts of CH₃COOH or CH₃COOD to a solution of intermediate **2a** preformed from reaction of 1 mM **2** with 15 equiv of H₂O₂.

promote O−O bond heterolysis of the bound hydroperoxo moiety. Acetic acid seems well positioned to play both roles, as demonstrated in the experiments presented in Figure 9. In a solution containing **2** and 15 equiv of H_2O_2 at −30 °C, the rate of decay of the generated **2c** intermediate was measured as a function of acetic acid concentration by monitoring the disappearance of its band at 540 nm. At concentrations of acetic acid up to 0.1 M, the rates of decay increased linearly with acetic acid concentration. Above 0.1 M, the decay rate plateaued. This saturation behavior reflects the required pre-equilibrium for the ligand exchange between CH_3CN and CH_3COOH that results in generation of **2c** from **2a**. According to the proposed mechanistic scheme, the decay of **2c** is initiated by the protonation of the hydroperoxo group by the coordinated acid and generates **2e** in the absence of olefin substrate, the yield of which depends on the acetic acid concentration (Figure 6). Furthermore, as shown in Figure 9, addition of CH_3COOD instead of CH_3COOH slowed the decomposition of **2c** by a factor of 2. We attribute this kinetic isotope effect on the decay of **2c** to the weaker acidity of CH_3COOD ($pK_a = 5.3$ vs 4.8 for CH_3COOH), which would be expected to be less effective at promoting the rate determining O−O cleavage step.

Finally, the high epoxidation selectivity of the putative $[(TPA)Fe^V O(OOCCH_3)]^{2+}$ oxidant formed in this manner can be understood in light of the DFT calculations carried out by Bassan et al.[9] on the reactivity of the $[(TPA)Fe^V O(OH)]^{2+}$ oxidant proposed for the water-assisted mechanism. From these calculations, epoxidation derives from attack of the olefin on the oxo group, whereas *cis*-dihydroxylation results from attack of the olefin on the hydroxo moiety. The latter has an activation barrier lower by 1.6 kcal/mol. With acetate replacing hydroxide in the Fe^V−oxidant of the acetic-acid-promoted pathway, attack of the olefin on the bound acetate may be much less favored than attack on the oxo group, so epoxidation becomes the dominant reaction in the presence of acetic acid.

To what extent does Scheme 1 apply to olefin oxidation catalysis by **1**? In previous work, the main evidence supporting the involvement of water-assisted and non-water-assisted pathways in the action of **1** derived only from ¹⁸O labeling experiments and associated DFT calculations.[32] Although our efforts to observe intermediates for **1** analogous to the Fe^{III}-OOH and $Fe^{IV}O$ species identified for **2** at temperatures down to −40 °C were unsuccessful, Talsi and co-workers recently reported NMR evidence for the formation of an $Fe^{IV}O$ intermediate from **1** in reactions at −50 °C in 1:1 CD_2Cl_2/CD_3CN with either peracetic acid or H_2O_2/CH_3COOH.[17a] To ascertain whether this pathway might be operating during catalysis despite our inability to observe the $Fe^{IV}O$ intermediate, we carried out experiments with phenylacetic acid in place of acetic acid and looked for evidence for the formation of benzyl radical, which would be a byproduct of $Fe^{IV}O$ formation under these conditions (see Scheme 1). Unlike for **2**, we found no evidence for the formation of benzaldehyde, which supports our earlier conclusion that an $Fe^{IV}O$ species is not on the olefin epoxidation catalysis pathway but instead leads to a dead-end product. The fact that no benzaldehyde was observed for **1** under these conditions shows that **1** is less susceptible than **2** to inactivation via this route.

In summary, we have investigated the chemistry of two non-heme iron complexes that are effective as epoxidation catalysts using H_2O_2 as oxidant in 1:2 CH_3CN/CH_3COOH. With 0.5 mol % catalyst, nearly quantitative conversion of cyclooctene to its epoxide (200 turnovers) can be achieved at 0 °C within 1 min. After exclusion of two intermediates observable at low temperature, namely species **c** and **e** in Scheme 1, we propose the most likely epoxidizing agent to be $[(L)Fe^V(O)(OOCCH_3)]^{2+}$ (species **f** in Scheme 1).

Supporting Information Available: Cyclooctene oxidation at room-temperature catalyzed by **2** in the presence of 100 equiv of acetic acid as a function of added water (Figure S1). Evolution of the $[(TPA)Fe^{III}OOH]^{2+}$ intermediate monitored by UV−vis spectroscopy after addition of 175 equiv of CH_3COOH (Figure S2). Evolution of the $[(TPA)Fe^{IV}O(NCCH_3)]^{2+}$ (generated *in situ* by reaction with 1 equiv of CH_3COOOH) as monitored by UV−vis spectroscopy after addition of 200 equiv of cyclooctene (Figure S3). This material is available free of charge via the Internet at http://pubs.acs.org.

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