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Iron Catalyzed Competitive Olefin Oxidation and *ipso*-Hydroxylation of Benzoic Acids: Further Evidence for an $Fe^{V}{=}O$ Oxidant

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The iron complex $[Fe^{II}(TPA)(CH_3CN)_2](OTf)_2$ (**1**) [TPA = tris(2-pyridylmethyl)amine] with H_2O_2 as an oxidant performs *ipso*-hydroxylation of electron-withdrawing benzoic acids at room temperature, leading to multiple turnovers of corresponding phenols. *ipso*-Hydroxylation competes with olefin epoxidation and *cis*-dihydroxylation in the presence of olefins, with the product ratios being modulated by the relative amounts of benzoic acid, olefin, and water. It is proposed that benzoic acid and water compete for the available sixth site on the $[(TPA)Fe^{III}(OOH)]$ intermediate, which undergoes O−O bond heterolysis to form, respectively, the $Fe^{V}(O)(O_2CAr)$ and $Fe^{V}(O)(OH)$ oxidants that determine the product outcome. The putative $Fe^{V}(O)(O_2CAr)$ oxidant decays either by undergoing oxidative decarboxylation and subsequent *ipso*-hydroxylation to form the observed phenol product or by oxo-transfer to olefins to form epoxide. The observed higher yield of phenol over epoxide or *cis*-diol in all cases studied, where an electron-withdrawing benzoic acid is present in the reaction mixture, suggests that intramolecular decay of the putative $Fe^{V}(O)(O_2CAr)$ oxidant is favored over intermolecular olefin oxidation. These results support the mechanistic framework postulated for Fe(TPA) oxidative catalysis and further strengthens the notion that oxoiron(V) species are the key oxidants in these reactions.

Introduction

Nonheme iron oxygenases have emerged as a very important group of enzymes that perform a variety of interesting oxidative transformations.[1−3] Of particular interest is the family of Rieske dioxygenases[4,5] that catalyze the *cis*-dihydroxylation of arene double bonds in the biodegradation of aromatic molecules by soil bacteria.[1,6,7] Such a transformation was unique to a biological iron center, until quite recently. We initiated an effort more than ten years ago to develop bioinspired nonheme iron complexes that can carry out the *cis*-dihydroxylation of C═C double bonds and found a family of complexes exemplified by $[Fe^{II}(TPA)(MeCN)_2]^{2+}$(**1**) that represented the first examples of catalysts for olefin *cis*-dihydroxylation by a nonbiological iron center. These catalysts used H_2O_2 as oxidant in place of the combination of O_2, electrons, and protons required in the enzyme reactions. Complex **1** and other nonheme iron complexes have also been shown to use H_2O_2 as oxidant for a variety of other reactions[8] including the hydroxylation of alkanes,[9−15] the epoxidation of olefins,[12,16−20] and

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the hydroxylation of arenes.[21−25] Very recently the **1**/H_2O_2 combination was shown to carry out the *cis*-dihydroxylation of naphthalene to *cis*-1,2-dihydro-1,2-naphthalenediol, making it the first functional model of the enzyme naphthalene 1,2-dioxygenase.[21]

In this paper, we focus on the *ipso*-hydroxylation of benzoic acids catalyzed by **1**, its relationship with olefin epoxidation and *cis*-dihydroxylation, and mechanistic insights derived therefrom. Complex **1** has been shown to hydroxylate benzoic acids regioselectively with H_2O_2 as an oxidant. Depending on the position of the substituent in the arene ring, the benzoic acid can undergo either *ortho*-hydroxylation (forming salicylates) or oxidative decarboxylation followed by hydroxylation at the *ipso*-carbon (making phenols).[22] The salicylates obtained from *ortho*-hydroxylation are excellent bidentate ligands and form stable iron(III) complexes that exclude the possibility of catalytic turnover. However, as reported in this paper, the phenolates obtained from *ipso*-hydroxylation are more susceptible to displacement by substrate, and multiple turnovers of phenol formation are observed for benzoic acids with electron withdrawing substituents. Furthermore, experiments in the presence of 1-octene or *tert*-butyl acrylate show that *ipso*-hydroxylation and olefin oxidation are competitive reactions and provide further support for the $Fe^{V}{=}O$ oxidant proposed for **1**-catalyzed oxidations.

Experimental Section

Materials and Methods. All chemicals and solvents were purchased from Aldrich and were used without additional purification unless otherwise noted. CH_3CN solvent was dried over CaH_2 before use. $H_2{}^{18}O$ (97% ^{18}O-enriched) was obtained from Cambridge Isotope Laboratories Inc. (Andover, MA). $H_2{}^{18}O_2$ (90% ^{18}O-enriched) was obtained from Isotec (Sigma-Aldrich) Inc. The complex $[Fe^{II}(TPA)(CH_3CN)_2](OTf)_2$ (**1**) was prepared in an anaerobic glovebox according to the published procedures.[26] Product analyses were performed on a Perkin-Elmer Sigma 3 gas chromatograph (AT-1701 column, 30 m) with a flame ionization detector. GC-MS experiments were carried using an HP 6890 gas chromatograph (HP-5 column, 30 m) with an Agilent 5973 mass detector.

Catalytic Studies. Catalytic studies were performed using 0.2 mL of a 10 mM solution of **1** along with 0.287 mL of a 70 mM solution of H_2O_2 (10 equiv) at room temperature in acetonitrile where the final concentration of **1** in the solution was 1 mM. H_2O_2 was added using a syringe pump over 25 min with an additional 5 min of stirring. Ten, 25, or 50 equivalents (relative to **1**) of perfluorobenzoic, 2-nitrobenzoic, or 2-chlorobenzoic acid were added in various experiments. For competition experiments with olefins, various amounts of olefin were added prior to the introduction of H_2O_2. Each catalytic result reported represented the average of at least three experiments.

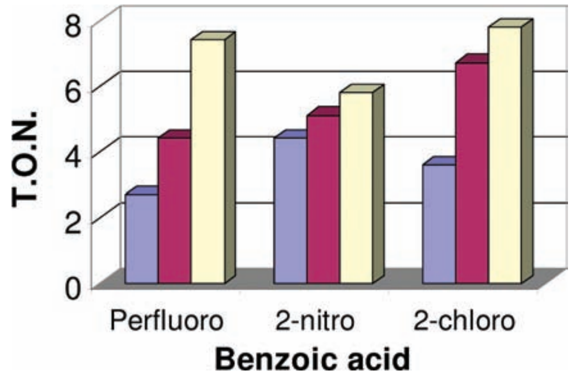

Figure 1. Phenol formation catalyzed **1** (1 mM) with 10 equivalents of H_2O_2 as oxidant in the presence of 10 (lavender-blue), 25 (maroon), or 50 (yellow) equivalents of benzoic acids at room temperature. TON (turn over number) was calculated as moles of product/mol of the catalyst.

Results and Discussion

$[Fe^{II}(TPA)(CH_3CN)_2](OTf)_2$ (**1**) has been shown to be an effective olefin oxidation catalyst to produce *cis*-diol and epoxide with H_2O_2 as the oxidant.[17] The **1**/H_2O_2 combination has also been shown to attack a variety of benzoic acids and effect either *ortho*-hydroxylation (producing salicylates) or *ipso*-hydroxylation (producing phenolates),[22] depending on the position of the substituent in the aromatic ring. 3-Substituted benzoic acids are converted to salicylates, while 2- and 4-substituted ones produce phenolates as a result of oxidative decarboxylation and *ipso*-hydroxylation. Further explorations of this chemistry, presented in this paper with benzoic acids having electron-withdrawing substituents, reveal that *ipso*-hydroxylation can be catalytic.

Figure 1 shows the results of experiments with **1** as catalyst, 10 equiv of H_2O_2, and varying amounts of benzoic acid. We chose to study the oxidations of perfluoro-, 2-nitro-, and 2-chlorobenzoic acids, which have respective pK_a's of 1.88, 2.19, and 2.92. The yields of the corresponding *ipso*-hydroxylated products increased with a larger excess of the benzoic acid. As much as 75% of the H_2O_2 was converted to phenol product. The phenol products were readily identified by their characteristic GC retention times and their mass spectral patterns from GC-MS analysis. This is the first example of the catalytic production of phenol from benzoic acids from an iron catalyst and the environmentally friendly oxidant H_2O_2 at ambient temperature and pressure. However, much lower phenol yields were observed for benzoic acids with electron donating substituents due to overoxidation of the resulting phenols. For example, in the **1**-catalyzed oxidation of 2,6-dimethylbenzoic acid, the products found were 0.5 equiv of 2,6-dimethylphenol and 1 equiv of 2,6-dimethylbenzoquinone. As a consequence, our subsequent experiments focused only on the benzoic acids with electron withdrawing substituents. The observed increased yield of phenol products in Figure 1 with higher concentrations of benzoic acid reflects pre-equilibrium binding of the benzoic acid to iron(III)-hydroperoxo species **A** prior to O−O bond cleavage that leads to the formation of **C**, as proposed in Scheme 1.

To gain further insight into the relative reactivities of the electron withdrawing benzoic acids with respect to **1**/H_2O_2, reactions were performed involving pairwise combinations of perfluoro-, 2-nitro-, and 2-chlorobenzoic acids. These competition experiments (Figure 2, Table 1) showed that 2-chlorobenzoic acid was the easiest to oxidize and perfluorobenzoic

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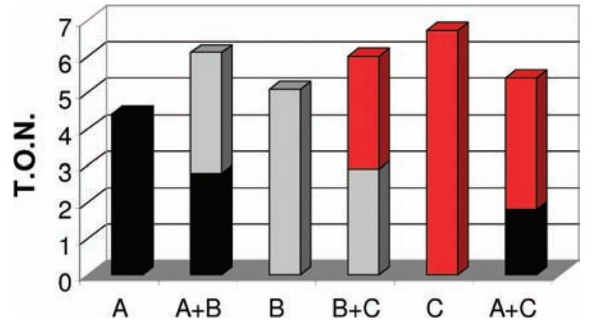

Figure 2. Competition reactions between any two of perfluoro- (A), 2-nitro- (B), and 2-chlorobenzoic acid (C) (25 equiv each with respect to **1**) and **1**/H_2O_2 (1/10) at room temperature. Data for the reactions of **1**/H_2O_2 and the individual benzoic acids (25 equiv with respect to **1**) are also shown for comparison. Black, gray, and red blocks depict amounts of perfluorophenol, 2-nitrophenol, and 2-chlorophenol, respectively.

Scheme 1. Proposed Pre-Equilibrium Binding of the Benzoic Acid to the $Fe^{III}-OOH$ Intermediate

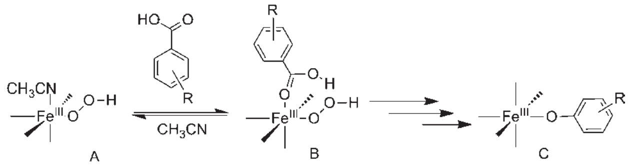

Table 1. **1**-Catalyzed Competitive *ipso*-Hydroxylation of Benzoic Acids[a]

benzoic acid	perfluorophenol	2-nitrophenol	2-chlorophenol
A	4.4 (1)		
A + B	2.8 (2)	3.3 (2)	
B		5.1 (1)	
B + C		2.9 (1)	3.1 (3)
C			6.7 (4)
A + C	1.8 (1)		3.6 (3)

[a] Reaction conditions: **1** (1 mM), 10 equiv H_2O_2, 25 equiv of each benzoic acid designated in acetonitrile at room temperature. A, B, and C represent perfluoro-, 2-nitro-, and 2-chlorobenzoic acid, respectively.

acid was the hardest, consistent with the cumulative electron-withdrawing abilities of the substituents, as reflected by the pK_a's of the three acids. This trend may be rationalized by either (a) a lower affinity of the stronger acid for $Fe^{III}-OOH$ (Scheme 1) and/or (b) a greater difficulty in oxidizing the benzoate with more electron withdrawing substituents.

Competition between Olefin Oxidation and *ipso*-Hydroxylation. Complex 1 has been previously shown to be an effective catalyst for olefin epoxidation and *cis*-dihydroxylation using H_2O_2 as an oxidant.[17,27,28] Furthermore, the addition of acetic acid to the aforementioned catalytic system led to significantly increased formation of epoxide at the expense of *cis*-diol.[27,29] It was proposed that the presence of acetic acid changed the nature of the active oxidant in the catalytic reaction from $Fe^V(O)(OH)$, where one or both oxygen atoms could be transferred to the olefin substrate, to $Fe^V(O)(OAc)$, where only oxo-atom transfer could occur.[29] However, the effect of aromatic acids (e.g., benzoic acids) on olefin oxidation catalysis has not been investigated. It would be interesting to know how the addition of benzoic acids might affect the epoxide/*cis*-diol ratio and whether the oxidation of the arene ring was competitive with olefin oxidation.

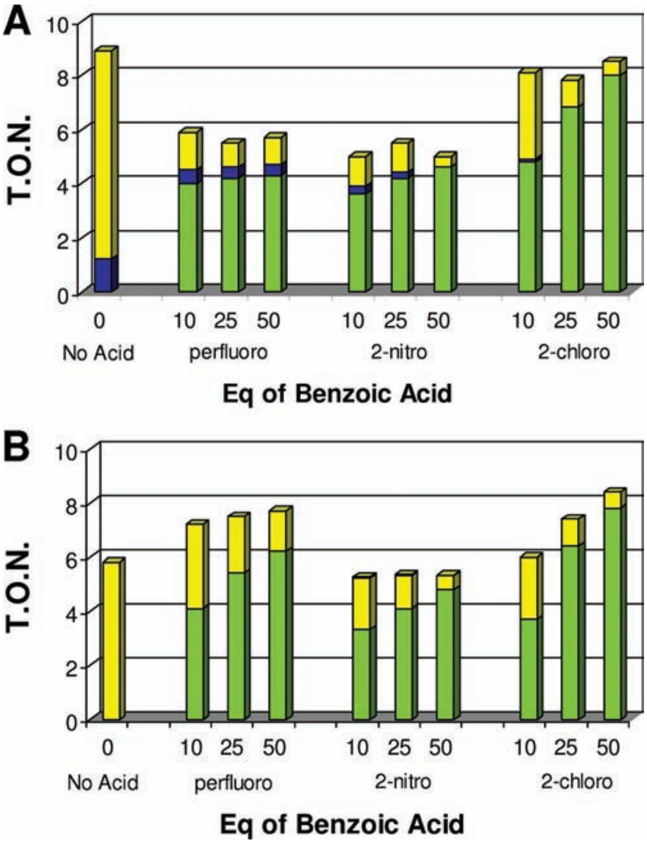

Figure 3. 1-Octene (A) and *tert*-butyl acrylate (B) oxidation by H_2O_2 with 1 mM **1** as catalyst at room temperature (**1**/H_2O_2/1-octene = 1/10/100) in the presence of different amounts of substituted benzoic acids. Green, blue, and yellow blocks represent phenol, epoxide, and *cis*-diol products, respectively.

Figure 3 presents the results of catalytic olefin oxidation experiments by **1**/H_2O_2 carried out with different amounts of added benzoic acid in the presence of a 100-fold excess of 1-octene or *tert*-butyl acrylate (relative to **1**); these results are also tabulated in Table 2. Olefin oxidation products (*cis*-diol and epoxide for 1-octene and *cis*-diol for *tert*-butyl acrylate) were observed in the reactions along with multiple turnovers of phenol, clearly suggesting that *ipso*-hydroxylation of the benzoic acids competes with olefin oxidation. Adding more benzoic acid increased the yield of phenol at the expense of the olefin oxidation products. The results of the competition experiments are similar for both 1-octene and *tert*-butyl acrylate (Figure 3), despite the fact that two olefins are quite different in terms of their electronic properties. Indeed, in a previously reported competitive oxidation of 1-octene and *tert*-butyl acrylate in the absence of added benzoic acid, 1-octene oxidation products were favored by 4:1 over those of *tert*-butyl acrylate, indicating that 1-octene is the olefin more preferably oxidized by the 1/H_2O_2 combination.[28] However, in all experiments presented in Figure 3, phenols were the dominant products. These results demonstrate that *ipso*-hydroxylation of the benzoic acids

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Table 2. Competitive Olefin Oxidation and *ipso*-Hydroxylation Experiments Catalyzed by **1**[a]

		10 equiv acid			25 equiv acid			50 equiv acid		
benzoic acid	1-octene	phenol	epoxide	diol	phenol	epoxide	diol	phenol	epoxide	diol
perfluoro	0	2.7 (2)			4.4 (1)			7.4 (3)		
	100	4.0 (2)	0.5 (1)	1.4 (1)	4.2 (3)	0.4 (1)	0.9 (1)	4.3 (3)	0.4 (1)	1.0 (4)
	250				3.4 (3)	1.2 (1)	2.1 (2)			
	500				2.6 (2)	1.8 (4)	1.7 (2)			
	1000				1.8 (2)	2.0 (3)	1.5 (5)			
2-nitro	0	4.4 (2)			5.1 (1)			5.8 (1)		
	100	3.6 (2)	0.3 (2)	1.1 (4)	4.2 (3)	0.2 (1)	1.1 (2)	4.6 (2)	0	0.4 (2)
	250				3.8 (4)	0.6 (2)	1.0 (3)			
	500				3.3 (3)	1.2 (3)	1.0 (3)			
	1000				2.9 (4)	1.5 (5)	0.9 (3)			
2-chloro	0	3.6 (2)			6.7 (4)			7.8 (1)		
	100	4.8 (2)	0	3.2 (4)	6.8 (2)	0	1.0 (2)	8.0 (3)	0	0.5 (1)
	250				7.1 (5)	0	1.0 (1)			
	500				7.2 (3)	0	1.3 (2)			
	1000				6.8 (4)	0	1.5 (3)			

		10 equiv acid			25 equiv acid			50 equiv acid		
	tert-butyl acrylate	phenol	epoxide	diol	phenol	epoxide	diol	phenol	epoxide	diol
perfluoro	0	2.7 (2)			4.4 (1)			7.4 (3)		
	100	4.1 (1)	0	3.1 (4)	5.4 (3)	0	2.1 (1)	6.2 (2)	0	1.5 (1)
2-nitro	0	4.4 (2)			5.1 (1)			5.8 (1)		
	100	3.3 (1)	0	1.9 (4)	4.1 (2)	0	1.2 (5)	4.8 (1)	0	0.5 (2)
2-chloro	0	3.6 (2)			6.7 (4)			7.8 (1)		
	100	3.7 (4)	0	2.3 (5)	6.4 (4)	0	1.0 (5)	7.8 (2)	0	0.6 (3)

[a] Competitive oxidations carried out in acetonitrile at room temperature with 1 mM **1**, 10 equiv H_2O_2, and 100 equiv olefin in the presence of various amounts of the listed benzoic acid. H_2O_2 was delivered by a syringe pump over 25 min with an additional 5 min of stirring before the reaction was worked up. Values listed reflect the average of at least three experiments. A TON value of 0 is listed for experiments where the actual TON is <0.1.

is favored over olefin oxidation, despite the lower concentration of the benzoic acid. This advantage may derive from the likely intramolecular nature of the *ipso*-hydroxylation versus the intermolecular nature of the olefin oxidation.

Figure 4 and Table 2 present results of experiments where the amount of olefin added was varied from 100 to 1000 equivalents in the presence of 25 equiv benzoic acid, resulting in an increase in the yields of olefin oxidation products. For 2-chlorobenzoic acid (Figure 4C), the amount of 2-chlorophenol formed remained constant at about 6.9 TON, while the amount of *cis*-diol product increased from 1 to 1.5 TON; however, less than 0.1 TON epoxide was observed. For 2-nitrobenzoic acid (Figure 4B), the amount of *cis*-diol product remained approximately constant at 1 TON, but the yield of epoxide increased at the expense of phenol, with the combined amount of phenol and epoxide holding constant at about 4.4 TON. In this series of experiments, the diol-to-epoxide ratio of 7 observed in the absence of added acid decreased to 0.6 upon addition of 1000 equiv 1-octene (Table 2). A similar behavior was observed for perfluorobenzoic acid (Figure 4A), with epoxide yield increasing at the expense of phenol and the combined amount of phenol and epoxide remaining at about 4 TON. Interestingly for this acid, the amount of *cis*-diol formed increased from 0.9 TON at 100 equiv 1-octene to 2.1 TON at 250 equiv, which then decreased with more added olefin. Similar to that observed for 2-nitrobenzoic acid, the diol-to-epoxide ratio in the presence of 1000 equiv of 1-octene decreased from 7 in the absence of acid to 0.8 in its presence. These results demonstrate the likely participation of multiple equilibria and oxidation pathways that determine the outcome of the catalysis experiments.

The preference of **1**-catalyzed oxidation for *ipso*-hydroxylation could be counteracted by the addition of water. Experiments carried out by introducing varying amounts of water at a fixed concentration of acid and olefin (Figure 5) showed that water competed with the benzoic acid in determining the nature of the products. The results indicated that higher amounts of water in the medium increased the yield of *cis*-diol at the expense of phenol formation, while epoxide yield remained relatively low in all experiments, unlike the results presented in Figure 4. There would appear to be multiple equilibria that affect the outcome of these catalytic oxidation experiments.

Labeling Studies. ^{18}O labeling experiments have previously provided important insights into the mechanism of olefin oxidation by the Fe^{II}TPA catalyst family[17] and are also useful in the present case for discerning the reaction pathways available. We showed previously that **1**-catalyzed olefin oxidations afforded epoxide products, where about 10% of the incorporated oxygen atom was derived from H_2O and the other 90% was from H_2O_2, and *cis*-diol products where one O atom was derived from H_2O and the other was from H_2O_2.[17] The incorporation of label from H_2O implicated a water-assisted mechanism for O−O bond cleavage. By comparing the ^{18}O labeling results in the presence or absence of perfluorobenzoic acid, it should be possible to discern what effect the added benzoic acid has on the mechanism of **1**-catalyzed oxidation.

The ^{18}O labeling results are listed in Table 3. As previously reported, the addition of increasing amounts of $H_2{}^{18}O$ resulted in a greater incorporation of ^{18}O into the *cis*-diol and epoxide products in the absence of added benzoic acid. In the presence of 25 equiv of $C_6F_5CO_2H$, the labeling outcome for the *cis*-diol was similar; however, much less ^{18}O from $H_2{}^{18}O$ was incorporated into the epoxide product, as previously reported for **1**-catalyzed epoxidations in the presence of acetic acid.[29] Interestingly, in the

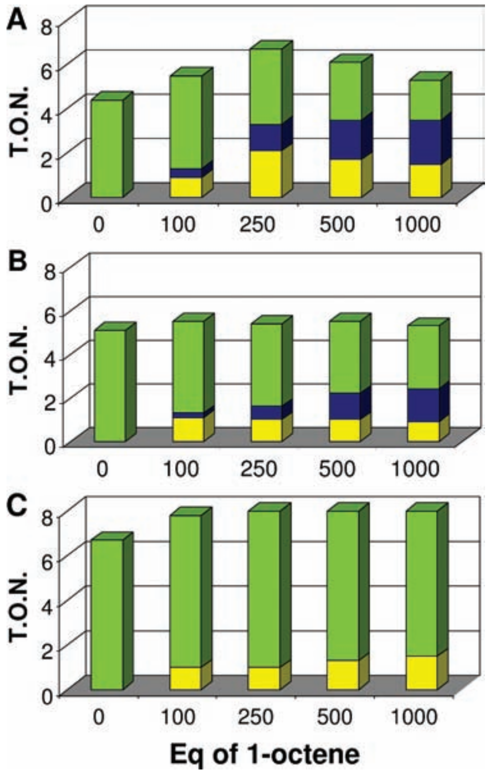

Figure 4. Oxidation of perfluorobenzoic acid (A), 2-nitrobenzoic acid (B), and 2-chlorobenzoic acid (C) catalyzed by **1** (1 mM) with H_2O_2 as oxidant in the presence of variable amounts of 1-octene at room temperature (**1**/H_2O_2/substituted benzoic acid = 1/10/25). Yellow, blue, and green blocks represent *cis*-diol, epoxide, and phenol, respectively.

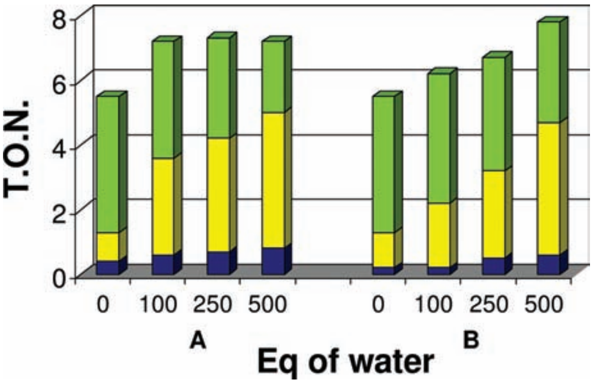

Figure 5. 1-Octene oxidation catalyzed by **1** (1 mM) with H_2O_2 as oxidant at room temperature (**1**/1-octene/substituted benzoic acid/H_2O_2 = 1/100/25/10) in the presence of variable amounts of water. The left side (A) represents the results for perfluorobenzoic acid, while the right side (B) depicts the study with 2-nitrobenzoic acid. Blue, yellow, and green blocks represent epoxide, *cis*-diol, and phenol, respectively.

complementary labeling experiment performed with 10 equiv of $H_2{}^{18}O_2$ in the presence of 1000 equiv from $H_2{}^{16}O$, there was almost no change in the extent of label incorporation for *cis*-diol in the presence and absence of added perfluorobenzoic acid, but the fraction of ^{18}O-labeled epoxide increased from 82% in the absence of added acid to 92% in the presence of 25 equiv of $C_6F_5CO_2H$. The same extent of ^{18}O label incorporation was also observed for perfluorophenol. Given that the H_2O_2 used was 90% ^{18}O labeled, the labeling of epoxide and phenol by $H_2{}^{18}O_2$ was essentially quantitative, implicating a common oxidant that effects these two oxidative transformations but is different from the oxidant that carries out the *cis*-dihydroxylation.

Mechanistic Insights. Scheme 2 depicts our current understanding of the mechanistic landscape for **1**-catalyzed olefin oxidation and *ipso*-hydroxylation, which takes into account the results from this paper and from our previous work on olefin oxidation[17,29] and arene ring oxidation.[22] The iron(III)-hydroperoxo species (**P1**), generated from the reaction of **1** and H_2O_2, has been trapped and characterized in detail by various spectroscopic techniques, namely UV−vis,[30] electrospray ionization (ESI)-MS,[30] EPR,[30,31] and resonance Raman spectroscopy.[31,32] We propose that intermediate **P1** is the branching point in the reaction of **1** and H_2O_2 leading to the formation of various high-valent iron oxidants. The eventual fate of **P1** is dependent on what is bound at the labile sixth site and can be tracked by monitoring the percent ^{18}O incorporation into the products. The addition of a large excess of H_2O results in the displacement of the CH_3CN ligand on **P1** to form the aquated intermediate **P2**. Decay of **P2** via a water-assisted heterolytic O−O bond cleavage step affords the $Fe^V(O)(OH)$ (**O2**) oxidant where the oxo atom derives from H_2O_2 and the hydroxo O atom derives from H_2O. These notions are corroborated by ^{18}O-labeling experiments (Table 3). Olefin oxidation in the presence of 1000 equiv $H_2{}^{18}O$ results in the incorporation of ^{18}O label into the oxidation products with 9% into the epoxide and 77% into one oxygen atom of the *cis*-diol. The complementary labeling experiment carried out with a 2% solution of $H_2{}^{18}O_2$ (containing 100 equiv $H_2{}^{16}O$ per equiv $H_2{}^{18}O_2$ added) confirms the $H_2{}^{18}O$ result, where the epoxide product is 82% labeled and 92% of the *cis*-diol is singly labeled.

As the amount of excess H_2O is decreased, the extent of water incorporation into the olefin oxidation products diminishes, as expected. For example, with 20 equiv added $H_2{}^{18}O$ (per H_2O_2 used), there is a significant fraction (~45%) of the *cis*-diol that is unlabeled (Table 3), implying that both oxygen atoms of H_2O_2 must be incorporated into the *cis*-diol for this subpopulation. Thus, **P1** itself must be involved in *cis*-dihydroxylation via a nonwater-assisted mechanism that cleaves the O−O bond of the iron(III)-hydroperoxo intermediate and delivers both the O atoms to the *cis*-diol product. In fact, such a nonwater-assisted O−O bond cleavage to form a $Fe^V(O)(OH)$ species (**O1**) has been proposed on the basis of density-functional theory (DFT) calculations for the related FeBPMEN [BPMEN = *N*,*N*′-dimethyl-*N*,*N*′-bis(2-pyridylmethyl)ethane-1,2-diamine] complex and found to be energetically viable.[33] Thus, both **P1** and **P2** participate in this mechanistic landscape, with their respective involvement being determined by the extent of solvent exchange between MeCN and H_2O.

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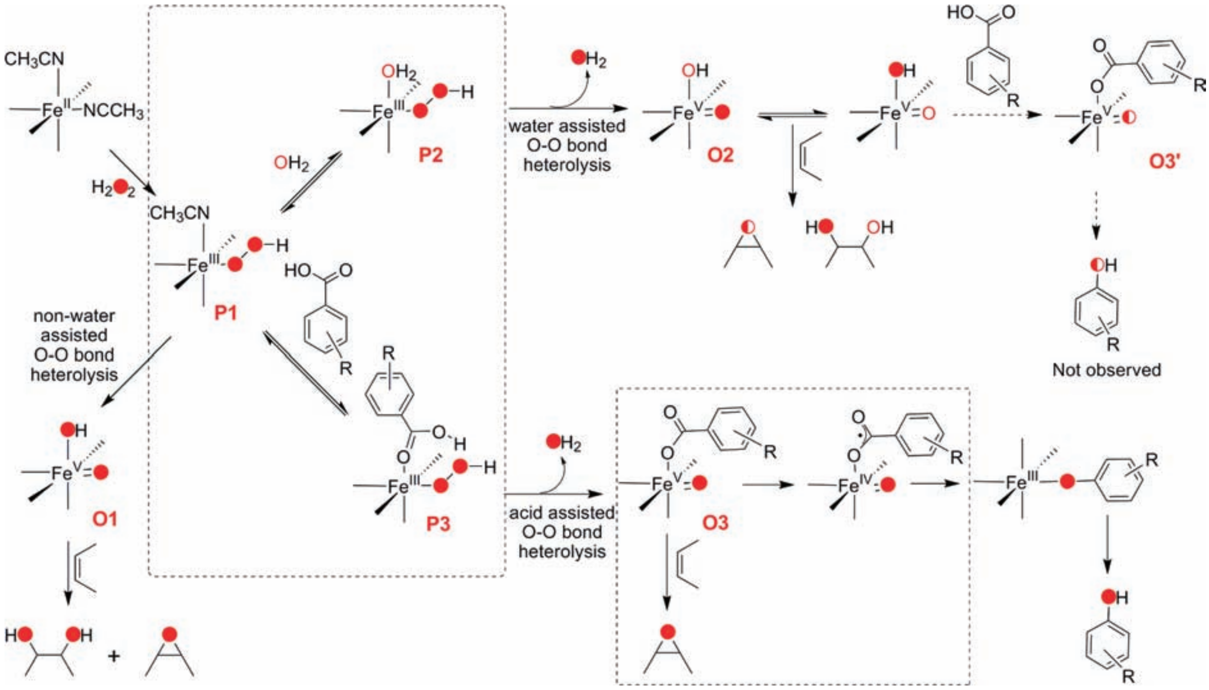
Table 3. Effect of Added $C_6F_5CO_2H$ on the ^{18}O-Label Distributions in the Products of **1**-Catalyzed Oxidation of 1-Octene by H_2O_2[a]

equiv of added $H_2{}^{18}O$ or $H_2{}^{18}O_2$	no acid					25 equiv $C_6F_5CO_2H$						
	1,2-epoxyoctane		1,2-octanediol			1,2-epoxyoctane		1,2-octanediol			phenol	
	^{16}O	^{18}O	$^{16}O^{16}O$	$^{16}O^{18}O$	$^{18}O^{18}O$	^{16}O	^{18}O	$^{16}O^{16}O$	$^{16}O^{18}O$	$^{18}O^{18}O$	^{16}O	^{18}O
200 $H_2{}^{18}O$	96	4	43	57		100		46	54		100	
500 $H_2{}^{18}O$	93	7	32	68		98	2	38	62		100	
1000 $H_2{}^{18}O$	91	9	23	77		98	2	31	69		100	
10 $H_2{}^{18}O_2$[b]	18	82	5	92	3	8	92	5	93	2	9	91

[a] Reaction conditions: **1**(1 mM)/H_2O_2/1-octene = 1/10/1000 in acetonitrile at room temperature. [b] The commercially available 2% aqueous solution of $H_2{}^{18}O_2$ contains a 1:100 molar ratio of $H_2{}^{18}O_2$ and $H_2{}^{16}O$.

Scheme 2. Mechanistic Landscape for Oxidations by the Nonheme Iron Catalyst **1** with H_2O_2 as Oxidant[a]



[a] P and O represent the various proposed iron-hydroperoxo and iron-oxo intermediates, respectively.

The addition of carboxylic acids complicates this mechanistic landscape by introducing yet another potential ligand that can displace the CH_3CN solvate from **P1**. In the case of added acetic acid, olefin oxidation yields predominantly epoxide, with the epoxide O-atom derived exclusively from H_2O_2.[29] These results can be rationalized by the formation of an $Fe^V(O)(O_2CR)$ (**O3**) oxidant from **P3** in a carboxylic-acid-assisted pathway. This oxidant acts mainly as an oxo transfer agent, converting the olefin substrate into epoxide. Lacking a bound hydroxo group, **O3** cannot effect olefin *cis*-dihydroxylation, although a small amount of a novel byproduct has been identified that derives from the transfer of both the oxo and acetato groups to the substrate, resulting in the *cis*-hydroxyacetoxylation of the olefin.[34]

This same carboxylic-acid-assisted pathway can also be invoked to rationalize the results presented in this paper on the effect of adding benzoic acids with electron withdrawing substituents. With benzoate replacing acetate in **O3**, an additional wrinkle to the mechanism is introduced, as the benzoate can undergo oxidative decarboxylation and *ipso*-hydroxylation to afford phenol as a product. In fact, electron withdrawing benzoic acids are catalytically converted to phenols. The catalytic results presented in this paper demonstrate the existence of an equilibrium among **P1**, **P2**, and **P3**, as indicated by an increase in the yields of phenol products as more benzoic acid is added to the catalytic oxidation system (Figure 1) and a corresponding decrease when water is added (Figure 5). When olefin is present in the reaction mixture, there is a competition between *ipso*-hydroxylation and olefin epoxidation that is affected by the relative amounts of benzoic acid and olefin (Figures 3 and 4) and the phenol and epoxide products exhibit the same extent of label incorporation from $H_2{}^{18}O_2$ (Table 3), suggesting that they share a common oxidant.

The observed oxidative decarboxylation and *ipso*-hydroxylation of electron withdrawing benzoic acids is postulated to occur via intermediate **O3**. Internal electron transfer from the bound benzoate to the $Fe^V{=}O$ center generates a carboxyl radical and an $Fe^{IV}{=}O$ species, which then

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recombine after loss of CO_2 to form the *ipso*-hydroxylated product. However, it is also plausible for the decay of **P3** to bypass **O3** entirely and proceed directly by O−O bond homolysis to generate the carboxyl radical and the $Fe^{IV}=O$ species. Figure 4 shows data that strongly disfavor the homolysis alternative. With the amount of perfluorobenzoic acid held constant at 25 equiv, the introduction of 1-octene resulted in the formation of the corresponding epoxide and diol products. Interestingly, as the 1-octene concentration increased, the yield of *cis*-diol changed by a factor of 2, but the amount of epoxide formed grew 5- to 7-fold. Thus, the diol-to-epoxide ratio decreased from 7:1 in the absence of the acid to 0.8:1 in its presence. Furthermore, the epoxide appeared to form at the expense of the phenol product. In our interpretation of the data, the amount of diol formed reflects the extent to which the water-assisted pathway is operating, consistent with the amount of label incorporation into the diol from $H_2{}^{18}O$ (Table 3). However, in the presence of perfluorobenzoic acid, label incorporation into the epoxide decreased from $H_2{}^{18}O$ and increased from $H_2{}^{18}O_2$. Both observations are consistent with a switch in the oxidant that forms epoxide from **O2** in the absence of added perfluorobenzoic acid to **O3** in its presence (Table 3). Thus, there is a competition between *ipso*-hydroxylation of the bound perfluorobenzoate and the epoxidation of added 1-octene, an outcome that can only be rationalized by the involvement of **O3**, which is derived from the carboxylic-acid-assisted heterolysis of the O−O bond of **P3**. A similar reactivity pattern was observed for 2-nitrobenzoic acid (Figure 4B). In the case of 2-chlorobenzoic acid (Figure 4C), less than 0.1 equiv of epoxide could be detected under all conditions studied; the very low yield of epoxide may be attributed to the greater ease of oxidizing 2-chlorobenzoate versus perfluoro- or 2-nitrobenzoate. A similar competition between olefin epoxidation and oxidative decarboxylation has been noted previously for the catalysis of olefin epoxidation by **1**/H_2O_2 in the presence of phenylacetic acid, where the yield of epoxide was correlated inversely with the yield of benzaldehyde, which was derived from oxidative decarboxylation of the acid.[29] In the case of acetic acid, **O3** appears directed only toward the olefin epoxidation.

Lastly, the absence of any label incorporation from $H_2{}^{18}O$ into C_6F_5OH (Table 3) excludes the participation of the $Fe^V=O$ oxidant **O2** in *ipso*-hydroxylation. Were the water-assisted pathway also involved in *ipso*-hydroxylation, the phenol would have been partially ^{18}O labeled, resulting from the formation of **O3′** from **O2** by ligand exchange after the oxo/hydroxo tautomerization of **O2** had occurred (Scheme 2). That the water-assisted pathway is not involved is supported by the essentially quantitative incorporation of label from $H_2{}^{18}O_2$ into the C_6F_5OH product (91% from 90% labeled peroxide). Also, the almost identical ^{18}O label distribution in *cis*-diol with $H_2{}^{18}O_2$ in the presence or absence of added perfluorobenzoic acid further emphasizes that *cis*-dihydroxylation is derived purely from the water-assisted pathway (via **P2** and **O2**). The clear difference in labeling outcomes for the diol and the phenol products demonstrates that olefin *cis*-dihydroxylation and *ipso*-hydroxylation must result from two related but distinct reaction pathways that involve two different $Fe^V=O$ oxidants.

These mechanistic speculations are supported by recent EPR evidence reported by Talsi and co-workers that suggest the trapping of an $Fe^V=O$ oxidant in the reaction of **1** and peracids at −70 °C.[35] This transient $S = 1/2$ species was shown to decay at a rate dependent on the concentration of the added olefin and found to yield epoxide, demonstrating its involvement in olefin epoxidation. However, direct proof of the iron oxidation state of the epoxidizing species was not obtained; such proof will be essential to place the mechanistic landscape of Scheme 2 on even firmer ground.

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