Epoxidation of Olefins with H_2O_2 Catalyzed by an Electronegatively-Substituted Iron Porphyrin Complex in Aprotic Solvent

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Catalytic epoxidation of olefins by hydrogen peroxide in the presence of an electronegatively-substituted iron porphyrin complex yielded epoxide products in acetonitrile solution. An iron(III) hydroperoxide porphyrin complex was proposed as a reactive intermediate responsible for the olefin epoxidations.

Olefin epoxidation reactions by iron(III) porphyrin complexes with oxidizing agents such as iodosylbenzenes and peracids have been intensively studied with the purpose of understanding the structure of reactive intermediates and the mechanism of oxygen atom transfer occurring in cytochrome P-450 enzymes.[1] High-valent iron(IV) oxo porphyrin cation radicals have been characterized in some cases[2] and generally proposed as reactive intermediates responsible for the olefin epoxidations. However, the oxidants used in the studies were biologically irrelevant; therefore, use of biologically important oxidants such as hydrogen peroxide and alkyl hydroperoxides has drawn particular attention in recent years.[3] Traylor and co-workers first succeeded in using hydrogen peroxide and *tert*-butyl hydroperoxide in the iron porphyrin complex-catalyzed epoxidation of olefins.[3] In the reactions, hydroxylic solvents such as methanol were required to cleave the O-O bond of (Porp)Fe^{III}-OOR complex heterolytically. In the absence of the alcohol solvent, no or nonstereospecific epoxidations took place.[4,5] In this communication, we report that an electronegatively-substituted iron(III) porphyrin complex catalyzes the epoxidation of olefins by hydrogen peroxide *via* non-radical type of oxidation reactions in aprotic solvent and that an iron(III) hydroperoxide porphyrin complex rather than a high-valent iron(IV) oxo porphyrin cation radical is proposed as a reactive intermediate responsible for the olefin epoxidations.

Table 1. Epoxidation of olefins by 30% H_2O_2 catalyzed by $Fe(TF_4TMAP)^{5+}$ in CH_3CN[a]

Substrate	Products	Yield/%[b]
cyclooctene	cyclooctene oxide	90
cyclohexene	cyclohexene oxide	60
	cyclohexen-2-ol	3
	cyclohexen-2-one	<0.5
1-octene	1,2-epoxyoctane	33
cis-stilbene	*cis*-stilbene oxide	50
	trans-stilbene oxide	4
	benzaldehyde	3

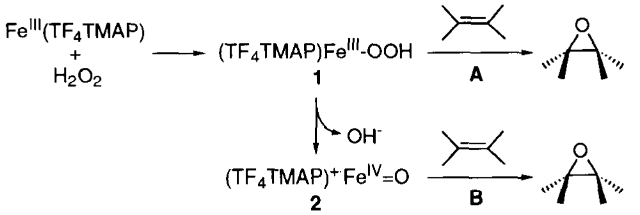
[a]Reactions were run in a solution containing $Fe(TF_4TMAP)^{5+}$ (1×10^{-3} mmol) and substrate (0.6 mmol) in CH_3CN (1.5 mL) at room temperature in air. Hydrogen peroxide (0.05 mmol, 30% aqueous, diluted in 0.2 mL of CH_3CN) was slowly added to the reaction solution over a period of 3 min, and the solution was stirred for 10 min at room temperature. An aliquot of the reaction mixture was analyzed by GC or HPLC with known authentic samples. [b]Based on the amount of H_2O_2 added.

The reactions of $Fe(TF_4TMAP)^{5+}$ [TF_4TMAP = tetrakis(2,3,5,6-tetrafluoro-*N,N,N*-trimethyl-4-aniliniumyl)porphyrinato][6] with aqueous 30% H_2O_2 in the presence of olefins yielded the corresponding oxide products in acetonitrile (Table 1). In the epoxidation of cyclohexene, only trace amounts of allylic oxidation products such as cyclohexenol and cyclohexenone were formed, indicating that Fenton-type oxidation reactions were not involved in the olefin epoxidation reactions.[7] Moreover, *cis*-stilbene was predominantly oxidized to *cis*-stilbene oxide with small amounts of *trans*-stilbene oxide and benzaldehyde formation, suggesting that neither hydroperoxyl radical (HOO·) nor oxoiron(IV) porphyrin [(Porp)Fe^{IV}=O] is responsible for the olefin epoxidation since these species show no stereospecificity in the epoxidation of *cis*-stilbene or *cis*-β-methylstyrene.[7,8] More interestingly, when the epoxidation of cyclooctene was performed with ^{18}O-labeled $H_2{}^{18}O_2$ (92% ^{18}O enriched) in air, we found that the oxygen atom in cyclooctene oxide came from the oxidant $H_2{}^{18}O_2$, not from molecular oxygen (eq 1), demonstrating again that the epoxidation occurs *via* non-radical type of oxidation reactions.

$$\text{cyclooctene} \xrightarrow[\text{CH}_3\text{CN}]{\text{Fe(TF}_4\text{TMAP)}^{5+}\,/\,\text{H}_2{}^{18}\text{O}_2} \underset{92\%\ ^{18}\text{O}}{\text{cyclooctene oxide-}^{18}\text{O}} \quad (1)$$

We then focused our efforts to elucidate the nature of the reactive intermediate responsible for the olefin epoxidation. Since we ruled out the involvement of a hydroperoxyl radical and an oxoiron(IV) porphyrin complex in the olefin epoxidation (*vide supra*), remained two active oxidants that we should consider are an iron(III) hydroperoxide porphyrin **1** and a high-valent iron(IV) oxo porphyrin cation radical **2** (see Scheme 1).

Scheme 1



We therefore generated complex **2** by reacting $Fe(TF_4TMAP)^{5+}$ with MCPBA at -40 °C in acetonitrile[9] and compared its reactivity patterns to those obtained from the reactions of $Fe(TF_4TMAP)^{5+}$ and H_2O_2, with the assumption that similar reactivity patterns should be observed if the intermediate generated in the reactions of $Fe(TF_4TMAP)^{5+}$ and H_2O_2 is complex **2** (Scheme 1, pathway B). If complex **1** is the active

Table 2. Reactivity comparisons for the olefin epoxidation reactions by $(TF_4TMAP)^{+\cdot}Fe^{IV}{=}O$ and by $Fe(TF_4TMAP)^{5+}$ with H_2O_2

		Labeled $H_2{}^{18}O$ experiment		Competitive epoxidation,[d] yield/%[e]	
	Temperature	^{18}O (%) in added water	^{18}O (%) in product[c]	1,2-epoxyoctane	cyclooctene oxide
$(TF_4TMAP)^{+\cdot}Fe^{IV}{=}O$[a]	-40 °C	95	15	25	40
$Fe(TF_4TMAP)^{5+}$ + H_2O_2[b]	-40 °C	95	0	8	38
$Fe(TF_4TMAP)^{5+}$ + H_2O_2[b]	25 °C	95	0	7	35

[a] $(TF_4TMAP)^{+\cdot}Fe^{IV}{=}O$ was prepared by reacting $Fe(TF_4TMAP)^{5+}$ (2.0×10^{-3} mmol) and MCPBA (2.4×10^{-3} mmol) in CH_3CN (0.5 mL) at -40 °C. For the $H_2{}^{18}O$ experiments, a mixture of cyclooctene (5×10^{-4} mmol) and $H_2{}^{18}O$ (5 μL, 95% ^{18}O enrichment, 0.26 mmol of $H_2{}^{18}O$) in a solvent mixture (0.2 mL) of CH_3CN/CH_2Cl_2 (1:1) was added to the $(TF_4TMAP)^{+\cdot}Fe^{IV}{=}O$ solution. The reaction mixture was stirred for 5 min at -40 °C, and then directly analyzed by GC/MS (Hewlett-Packard 5890 II Plus gas chromatograph interfaced with Hewlett-Packard Model 5989B mass spectrometer). For the competitive epoxidation reactions, a mixture of 1-octene (0.2 mmol) and cyclooctene (0.01 mmol) in a solvent mixture (0.2 mL) of CH_3CN/CH_2Cl_2 (1:1) was added to the $(TF_4TMAP)^{+\cdot}Fe^{IV}{=}O$ solution. The reaction mixture was analyzed by GC after 5 min stirring at -40 °C. [b] Reaction conditions and procedures were the same as described in footnote a except that H_2O_2 (2.4×10^{-3} mmol, diluted in 0.2 mL of CH_3CN/CH_2Cl_2 (1:1)) was added to a reaction solution containing $Fe(TF_4TMAP)^{5+}$, cyclooctene, and $H_2{}^{18}O$ (for $H_2{}^{18}O$ experiments) or 1-octene (for competitive epoxidations). [c] The ^{16}O and ^{18}O compositions in cyclooctene oxide were determined by the relative abundances of mass peaks at m/z = 111 for ^{16}O and m/z = 113 for ^{18}O. [d] In order to improve the accuracy for measuring the amount of the 1,2-epoxyoctane product, an 1:20 mixture of 1-octene and cyclooctene was used. [e] Based on the amounts of oxidants used.

epoxidizing intermediate (Scheme 1, pathway A), then different reactivity patterns would be expected. We studied isotopically labeled water experiments[10] and intermolecular competitive epoxidations,[11] and these results are discussed below.

When a mixture of cyclooctene and $H_2{}^{18}O$ was added to a solution containing complex **2**, we found that a moderate amount of ^{18}O was incorporated from $H_2{}^{18}O$ into the oxide product (see Table 2).[12] In contrast, when the epoxidation of cyclooctene by H_2O_2 was performed in the presence of identical amount of $H_2{}^{18}O$, we found no ^{18}O-incorporation from $H_2{}^{18}O$ into the oxide product at -40 °C and 25 °C. In the competitive epoxidations performed with 1-octene and cyclooctene, the ratios of the oxygenated products, 1,2-epoxyoctane and cyclooctene oxide, were identical in the reactions of H_2O_2 performed at low and room temperatures, whereas the ratio of the oxide products formed by the complex **2** was different from those obtained in the H_2O_2 reactions (see Table 2). Therefore, the results of the mechanistic studies discussed above lead us to suggest that the intermediate formed in the reaction of $Fe(TF_4TMAP)^{5+}$ and H_2O_2 is not the high-valent iron(IV) oxo porphyrin cation radical **2** but the iron(III) hydroperoxide porphyrin complex **1**.

Iron(III) hydroperoxide complexes have been proposed as epoxidizing intermediates in non-porphyrin iron[13] and iron bleomycin systems.[14] In iron porphyrin-catalyzed epoxidation reactions, as far as we have been able to discern, this study presents the first strong evidence that an iron(III) hydroperoxide porphyrin complex is able to transfer an oxygen atom to olefins prior to the O-O bond cleavage at low and room temperatures.

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12 We have shown previously[10] that the oxygen exchange between the high-valent iron oxo species and labeled water is competing with the oxygen transfer from the high-valent iron oxo intermediate to olefin. Also, we have unpublished results that a high-valent iron oxo intermediate with highly electron-withdrawing substituents on the porphyrin ligand exchanges its oxygen atom with labeled water slowly. This is the reason why only 15% ^{18}O-labeled oxygen was incorporated into the oxide product when the epoxidation of cyclooctene by $(TF_4TMAP)^{+\cdot}Fe^{IV}{=}O$ was performed with only a small amount of cyclooctene.
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