

Oxygen transfer involving nonheme iron: The influence of leaving group ability on the rate constant for oxygen transfer to (EDTA)Fe(III) from peroxycarboxylic acids and hydroperoxides

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ABSTRACT Ethylenediaminetetraacetato iron(III) [(EDTA)Fe(III)] has been shown to react with a series of four peroxycarboxylic acids and four alkyl hydroperoxides (YOOH; dry methanol solvent, 30°C) by heterolytic O-O bond scission that accompanies the transfer of an oxygen atom to the iron(III) moiety $\{(\text{EDTA})\text{Fe}(\text{III}) + \text{YOOH} \rightarrow [(\text{EDTA})\text{Fe}(\text{O})]^+ + \text{YOH}\}$. A single linear free-energy relationship exists for both peroxycarboxylic acids and alkyl hydroperoxides when the logarithm of the second-order rate constant (k_{YOOH}) for reaction of YOOH species with (EDTA)Fe(III) is plotted vs. the $\text{p}K_{\text{a}}$ of the YOH leaving group.

Nonheme iron containing enzymes as the pterin-requiring mammalian aromatic amino acid hydroxylases (1) and α -ketoglutarate-dependent mixed function oxidases (2-5) act as efficient catalysts in the enzymatic oxidation of organic substrates. Little attention has been afforded the nonheme iron enzymes and very little experimental data of a chemical nature has been generated upon which the relevant enzyme mechanisms may be based. Iron(III) ethylenediaminetetraacetato [(EDTA)Fe(III)] serves as a convenient model for an iron(III) complexed to a nonheme and nonconjugated ligand. We have shown (6) that (EDTA)Fe(III) reacts with phenyl peroxyacetic acid and *m*-chloroperoxybenzoic acid (MCPBA) by heterolytic O-O bond scission to provide [(EDTA)-(FeO)]⁺. The second-order rate constants (k_{YOOH}) for the reaction of (EDTA)Fe(III) with a number of peroxycarboxylic acids and alkyl hydroperoxides (YOOH) have been determined in dry methanol solvent. It is established that $\log k_{\text{YOOH}}$ is a linear function of the $\text{p}K_{\text{a}}$ values of YOH. This result supports heterolytic O-O bond scission for oxygen transfer to (EDTA)Fe(III) from both peroxycarboxylic acids and alkyl hydroperoxides.

MATERIALS AND METHODS

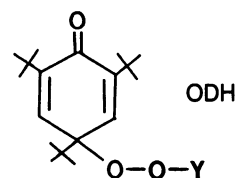
Materials employed in this study have been described (6-8).

Kinetic Studies. All the reactions were carried out under anaerobic conditions (either nitrogen or argon atmosphere in methanol, $30 \pm 0.2^\circ\text{C}$) as described (6). The kinetics of the oxygen transfer reactions from the various peroxycarboxylic acids and alkyl hydroperoxides to (EDTA)Fe(III) were followed spectrophotometrically by trapping the reaction iron-oxo intermediate with 2,4,6-tri-*t*-butylphenol (TBPH). Reactions were generally followed under pseudo-first-order conditions of $[\text{TBPH}] \gg [\text{YOOH}] > [(\text{EDTA})\text{Fe}(\text{III})]$, by monitoring the appearance of 2,4,6-tri-*t*-butylphenoxyl radical (TBP•) at 400 nm. Each reported rate constant is an average of at least two different determinations. For the peroxycarboxylic acid reactions, each kinetic trace was analyzed as a combination of consecutive pseudo-first-order

and zero-order reactions with the help of a computer program written for this purpose using a Hewlett-Packard Model 9825A computer. In the case of the alkyl hydroperoxide reactions, the oxygen transfer reactions were inconveniently slow and, therefore, the method of initial rates was employed to determine the rate constant from the absorbance vs. time kinetic trace for the oxygen transfer reactions as given (8, 9). Further, it should be noted that, since each equivalent of alkyl hydroperoxide results in the oxidation of two equivalents of TBPH, the rate constant obtained by the method of initial rates is 2-fold greater than the absolute rate constant for the oxygen transfer reaction and the necessary adjustment was made for the alkyl hydroperoxide reactions.

RESULTS

The plots of A_{400} vs. time for the reaction of (EDTA)Fe(III) with peroxycarboxylic acids are biphasic, as reported (6) for MCPBA. The initial 90% of the appearance of TBP• follows the first-order rate law, and this is followed by a very slow zero-order component of TBP• radical formation. It has been established (3), using MCPBA, that the pseudo-first-order component of TBP• radical formation corresponds to the oxygen transfer reaction from peroxycarboxylic acids to (EDTA)Fe(III), and the slow zero-order component is due to the breakdown of a peroxidic component (ODH; 1,3,5-tri-*t*-butyl-4-oxycyclohexa-2,5-dienyl-hydroperoxide) formed during the oxidation reaction (10-12). Therefore, all the plots of A_{400} vs. time for



the reaction of the various peroxycarboxylic acids with (EDTA)Fe(III) were analyzed as a combination of sequential first-order and zero-order reactions. A complete kinetic analysis that accounts for the percentage yields of product and the rates of their formation has been reported (6). In the present study our only concern is with the second-order rate constants for oxygen transfer to (EDTA)Fe(III) so that we have restricted the kinetic analysis to the major pseudo-first-order component of the TBP• radical formation. For the reaction of the most reactive alkyl hydroperoxides, diphenylhydroperoxyacetone and methyl diphenylhydroperoxyacetate, pseudo-first-order rate constants were determined

from initial rates as a function of the initial concentration of (EDTA)Fe(III) [(EDTA)Fe(III)]_i. For the least reactive alkyl hydroperoxides, cumene hydroperoxide (6.0 mM) and *t*-BuOOH (6.0 mM), the kinetic measurement was restricted to a single [(EDTA)Fe(III)]_i (0.6 mM) in the presence of TBPH (95 mM). The concentration of reactants employed in these experiments were maximal due to the restrictions in solubility of TBPH and the finding that these oxidants react very sluggishly with (EDTA)Fe(III). Therefore, on the basis of both peroxycarboxylic acid and alkyl hydroperoxide reactions with (EDTA)Fe(III), the rate law for the oxidation may be given as follows:

$$\frac{d[\text{TBP}\cdot]}{dt} = -\frac{d[\text{RCO}_3\text{H}]}{dt} \\ = k_A[(\text{EDTA})\text{Fe}(\text{III})]_i[\text{RCO}_3\text{H}], \quad [1]$$

and

$$k_{\text{obs}} = k_A[(\text{EDTA})\text{Fe}(\text{III})]_i.$$

$$\frac{d[\text{TBP}\cdot]}{dt} = v_i = -\frac{d[\text{ROOH}]}{dt} \\ = k_B[(\text{EDTA})\text{Fe}(\text{III})]_i[\text{ROOH}]_i[\text{TBPH}], \quad [2]$$

and

$$k_B[(\text{EDTA})\text{Fe}(\text{III})]_i = k_{\text{obs}} = v_i[\text{ROOH}]_i^{-1}[\text{TBPH}]^{-1}.$$

In Eq. 1 and 2, v_i [= $\Delta A_{400}/(\Delta \epsilon)(\Delta t)$] is the initial rate, k_A is the second-order rate constant for the reaction of peroxycarboxylic acids, k_B is the second-order rate constant for the alkyl hydroperoxide reactions, and ROOH is an alkyl hydroperoxide.

It has been shown (6) that the rate of reaction of MCPBA with (EDTA)Fe(III) is independent of the concentration of the trapping reagent TBPH and, therefore, the reaction order with TBPH is zero. The value of k_{obs} is independent of the initial concentration of peroxycarboxylic acid and is linearly dependent upon [(EDTA)Fe(III)]_i. By these criteria the reaction is first order in both peroxycarboxylic acids and (EDTA)Fe(III).

Analysis of the various products shows that in the presence of (EDTA)Fe(III) and any peroxycarboxylic acid (1.50 mM), and TBPH at 95 mM, provides 20% of TBP· radical and ≈65% of formaldehyde, due to the oxidation of CH₃OH solvent. Invariably, for all the peroxycarboxylic acid reactions, at [TBPH] = 95 mM, there exists a peroxo-active species (ODH) that, by an iodometric method (6), has been estimated to account for nearly 10% of the initial concentration of peroxycarboxylic acids. This result is in accord with our previous finding with MCPBA (6). The reaction of diphenylhydroperoxyacetone, the most reactive alkyl hydroperoxide, could be monitored to 40% consumption of alkyl hydroperoxide. It was found that nearly 4% of TBP· and 35% of CH₂O are formed on the basis of the initial concentration of alkyl hydroperoxide. For the other alkyl hydroperoxide reactions, there is a very small amount of TBP·, and no formaldehyde is detected for a reaction period of more than 24 hr. This result does not reflect a lack of formation of products but only that the reactions could not be followed to sufficient completion for product analysis.

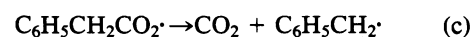
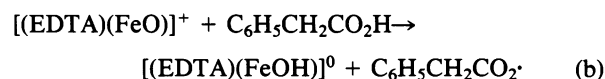
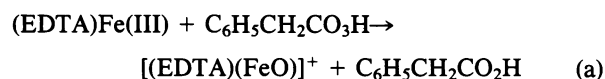
DISCUSSION

Pertinent observations are as follows: (i) With phenyl peroxyacetic acid and MCPBA (6), the pseudo-first-order rate constants for oxygen transfer to (EDTA)Fe(III) are independent of the initial concentration of peroxycarboxylic acids at constant [(EDTA)Fe(III)]_i and constant concentration of the

trap TBPH. (ii) The rate is independent of the initial concentration of TBPH (6). (iii) The pseudo-first-order rate constant exhibits a first-order dependence upon [(EDTA)Fe(III)]_i. (iv) At constant [peroxycarboxylic acid] and [TBPH] the molar ratio of the products CH₂O/TBP·/ODH, 62:20:10, is independent of the concentrations of (EDTA)Fe(III) and the structure of the peroxycarboxylic acid. (v) In the case of the most reactive alkyl hydroperoxide (diphenylhydroperoxyacetone), the reaction could be followed to *ca.* one half-life, and both CH₂O and TBP· could be established as products. These results show that the rate-determining step is the transfer of oxygen from peroxycarboxylic acids or alkyl hydroperoxides to (EDTA)Fe(III) to form the reactive iron-oxo species [(EDTA)(FeO)]⁺. Further reaction of [(EDTA)(FeO)]⁺ with TBPH and CH₃OH results in the formation of products, TBP·, CH₂O, and ODH. The relative constancy of the percentage yields of the various products when using all the peroxycarboxylic acids establishes that the same iron-oxo species is formed by each peroxycarboxylic acid.

A plot of the logarithm of the second-order rate constants for the oxygen transfer (k_{YOOH}) from YOOH to (EDTA)Fe(III) vs. the corresponding $\text{p}K_a$ of the leaving group YOH (i.e., YOH = Alkyl-OH, RCO₂H) is shown in Fig. 1. It should be noted that the determination of the second-order rate constants for the less-reactive cumene hydroperoxide (6.0 mM) and *t*-BuOOH (6.0 mM) were calculated from initial rates taken at a few percent of reaction. The calculated second-order rate constants for cumene hydroperoxide and *t*-BuOOH can only be considered as approximate and represent the maximum values. The slope of the linear free-energy plot is $\beta_g = -0.42$. Since oxygen transfer from phenyl peroxyacetic acid to (EDTA)Fe(III), in the presence of TBPH, is accompanied by 100% heterolytic cleavage of the peroxycarboxylic acid O-O bond (6), it is reasonable to assume that the other peroxycarboxylic acids also transfer an oxygen to (EDTA)Fe(III) via a heterolytic mechanism. Because the linear plot of $\log k_{\text{YOOH}}$ vs. the $\text{p}K_a$ of YOH accommodates both peroxycarboxylic acids and alkyl hydroperoxides, it is most likely that oxygen transfer from the alkyl hydroperoxides to (EDTA)Fe(III) also involves a heterolytic O-O bond scission.

Walling and his coworkers (13, 14) have shown that H₂O₂ reacts with (EDTA)Fe(III) in aqueous solution via a homolytic mechanism that involves reduction of the iron(III) moiety but was not able to see any reaction of *t*-BuOOH with (EDTA)Fe(III) in water. A homolytic mechanism could not apply to the present study (CH₃OH solvent) since, with peroxycarboxylic acids, it would lead to the formation of carboxyl radicals, and, as we have shown, phenyl peroxyacetic acid does not undergo decarboxylation on reaction with (EDTA)Fe(III) in the presence of concentrations of TBPH sufficient to trap the [(EDTA)(FeO)]⁺ species (6). In the reaction of phenyl peroxyacetic acid with (EDTA)Fe(III) in the absence of the TBPH trap, there is seen to be ≈40% decarboxylation of phenyl acetic acid product (6). This must be due to the reactions of Eq. 3. Oxidation of carboxylic acid product,



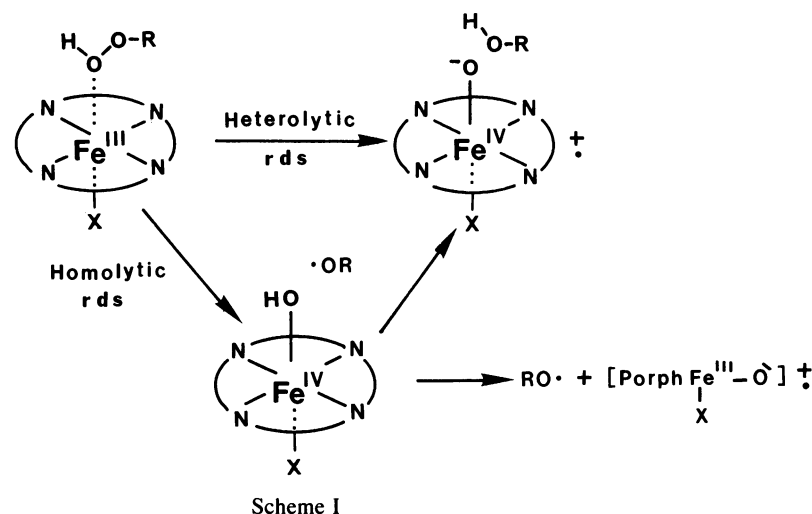
and formation of bibenzyl (Eq. 3), in the absence of a trapping agent for $[(\text{EDTA})(\text{FeO})]^+$, establish that the latter if not trapped oxidizes carboxylic acid.

Sugimoto and Sawyer (15–17) have studied the reaction of ferrous perchlorate and ferric chloride with H_2O_2 in dry acetonitrile and were able to show that the formation of a ferryl like species occurs. Rush and Bielski (18) report that $\text{Fe}(\text{III})(\text{OH})_4^-$ can be converted by pulse radiolysis at high pH in H_2O to the iron(IV) species $\text{FeO}(\text{OH})_n^{2-n}$ and FeO_4^{2-} to the iron(V) species FeO_4^{3-} .

The second-order rate constants for the reaction of peroxycarboxylic acids and alkyl hydroperoxides with *meso*-tetrakis(tetraphenyl)porphinato iron(III) chloride $[(\text{TPP})\text{Fe}(\text{III})\text{Cl}]$ have been determined under the same reaction conditions as employed in the present investigation (7). A plot of $\log k_{\text{YOOH}}$ vs. the pK_a of YOH (included in Fig. 1) was found to have a break at $\text{pK}_a \approx 9.5$. The $\log k_{\text{YOOH}}$ values for the peroxycarboxylic acids and the more acidic alkyl hydroperoxides form a straight line with a slope $\beta_{\text{lg}} = -0.35$, whereas the $\log k_{\text{YOOH}}$ values for the less acidic hydroperoxides fall on a straight line with a less negative slope ($\beta_{\text{lg}} = -0.15$). This finding suggests a change in reaction mechanism for the reaction of YOOH species with $(\text{TPP})\text{Fe}(\text{III})\text{Cl}$ in methanol solvent from one involving heterolytic O-O bond cleavage for peroxycarboxylic acids to homolytic cleavage for the less acidic alkyl hydroperoxides (Scheme I). There-

exhibits (8) a change of slope at *ca.* $\text{pK}_a = 9.5$, and the product is the cobalt(III) porphyrin dication $[(^{2+}\text{TPP})\text{Co}(\text{III})\text{X}]$, whereas the like reaction of $(\text{TPP})\text{Cr}(\text{III})\text{Cl}$ with YOOH species (in dry CH_2Cl_2) is characterized (21) by a linear free-energy plot that shows no break in slope, and the product is the chromium(V)-oxo porphyrin $[(\text{TPP})\text{Cr}(\text{V})\text{O}]$. Whatever the correct electronic interpretation of the structure of the $[(\text{EDTA})(\text{FeO})]^+$ species [the (FeO) moiety representing, in the extreme cases, $\text{Fe}(\text{III})$ (oxygen atom) (15–17) or $\text{Fe}(\text{V})\text{O}$], it is most likely that the electron deficiency is not in the ligand EDTA. The reaction of $(\text{EDTA})\text{Fe}(\text{III})$ and $(\text{TPP})\text{Cr}(\text{III})\text{Cl}$ share in common, therefore, both localization of the $2e^-$ oxidation at the metal-oxo center and a single linear plot of $\log k_{\text{YOOH}}$ vs. pK_a of the leaving group, which encompasses both peroxycarboxylic acids and hydroperoxides.

From the little that is presently known it would appear clear that peroxycarboxylic acids, and the most acidic alkyl hydroperoxides, react with the TPP- and EDTA-ligated metal ions via a $2e^-$ oxidation involving heterolytic O-O bond scission and oxygen transfer to the metal center. The question arises as to what features determine the importance of the homolytic reaction. The importance of the homolytic reaction as compared to the heterolytic reaction is indicated by the intersection of the linear free energy plots. For $(\text{TPP})\text{Fe}(\text{III})\text{Cl}$ and $(\text{TPP})\text{Co}(\text{III})\text{Cl}$, the two lines intersect at



fore, when the ligand is changed from TPP to EDTA, there is a change in mechanism for the weakly acidic alkyl hydroperoxides from homolytic to heterolytic O-O bond scission. The slopes of the plots of $\log k_{\text{YOOH}}$ vs. pK_a of Fig. 1 for the reaction of peroxycarboxylic acids in methanol with both $(\text{EDTA})\text{Fe}(\text{III})$ and $(\text{TPP})\text{Fe}(\text{III})\text{Cl}$ are within experimental error equal at $\beta_{\text{lg}} \approx -0.4$. With the porphyrin as a ligand, peroxycarboxylic acids react at the iron(III) center with rate constants ≈ 60 -fold greater than when EDTA is the ligand. This may be attributed to the greater π conjugation in the case of the iron(III)porphyrin.

The difference in the mechanisms of reaction of weakly acidic alkyl hydroperoxides with $(\text{TPP})\text{Fe}(\text{III})\text{Cl}$ and $(\text{EDTA})\text{Fe}(\text{III})$ begs explanation. Two electron ($2e^-$) oxidation of an oxo-ligated tetraphenylporphinato iron(III) provides as product an iron(IV)-oxo porphyrin π -cation radical. This shows the oxidation to be partially ligand centered (19, 20). Also, the linear free-energy plot of $\log k_{\text{YOOH}}$ vs. pK_a for the reaction of YOOH species with $(\text{TPP})\text{Co}(\text{III})\text{Cl}$ (in dry CHCl_3)

a pK_a of YOH of ≈ 9.5 ; while with the imidazole-ligated tetraphenylporphinato manganese(III) $[(\text{TPP})\text{Mn}(\text{III})\text{ImH}-\text{Cl}]$ (22), the intersection is at ≈ 11 . In the latter case, the most acidic hydroperoxides reside on the plot for the heterolytic reaction. Since a homolytic mechanism is not observed with $(\text{EDTA})\text{Fe}(\text{III})$ or $(\text{TPP})\text{Cr}(\text{III})\text{Cl}$, the intersections of their linear free-energy plots must occur at a pK_a of $\text{YOH} > 17$ (essentially beyond the limit of pK_a values of alcohol leaving groups). The $2e^-$ oxidation potentials for the *meso*-tetrakis(2,4,6-trimethylphenyl)porphinato iron(III) hydroxide and *meso*-tetrakis(2,4,6-trimethylphenyl)porphinato iron(III) methoxide to give the iron(IV) porphyrin π -cation radical is +1.14 V (SCE), whereas the $2e^-$ oxidation potential for $(\text{TPP})\text{Fe}(\text{III})\text{OMe}$ is +1.16 V suggesting that the methyl substituents on the phenyl rings do not influence the oxidation potentials to yield the iron(IV) porphyrin π -cation radical (19, 20). If one compares this $2e^-$ oxidation potential to generate the iron(IV)-oxo porphyrin π -cation radical with the $2e^-$ oxidation potential to generate $(\text{TPP})\text{Cr}(\text{V})\text{O}$ from (TPP)

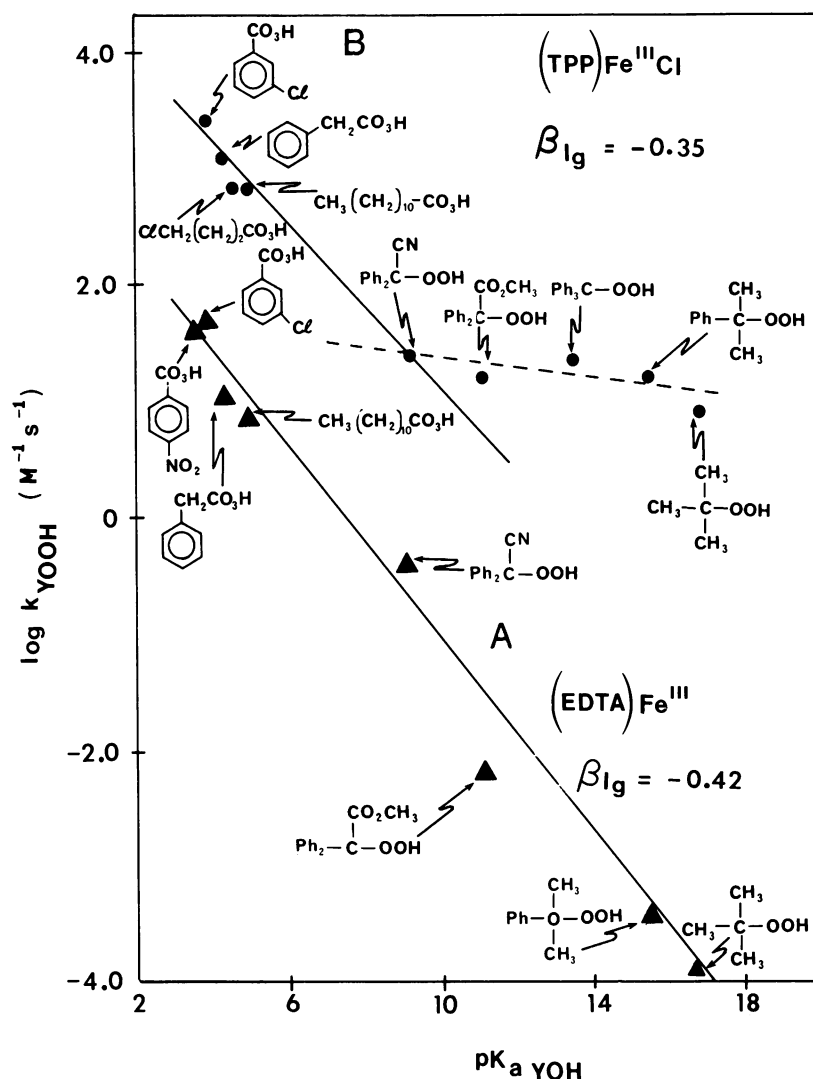


FIG. 1. A plot of the logarithm of the second-order rate constants for the reaction of various peroxycarboxylic acids and alkyl hydroperoxides with (EDTA)Fe(III) (curve A) and (TPP)Fe(III)Cl (curve B) vs. the pK_a of the leaving groups (YOH). The reactions were carried out in anhydrous methanol and at $T = 30 \pm 0.2^\circ\text{C}$ under an oxygen-free atmosphere. The data and plotting of the results with (TPP)Fe(III)Cl were taken from ref. 7.

Cr(III)OH (which is $+0.84\text{ V}$) (23), the oxidation of [(TPP)-Cr(III)] $^+$ by a given hydroperoxide is thermodynamically favored by $\approx 14\text{ kcal}\cdot\text{M}^{-1}$ ($1\text{ Cal} = 4.18\text{ J}$) over the oxidation of [(TPP)Fe(III)] $^+$. For this reason alkyl hydroperoxides can most easily enter into a $2e^-$ oxidation of the Cr(III) porphyrin. The difference in the potentials for the $1e^-$ and $2e^-$ oxidation of porphyrato iron(III) hydroxide salts is $\approx 100\text{ mV}$ (19, 20). Therefore, the $1e^-$ oxidation is thermodynamically favored over the $2e^-$ oxidation by $\approx 2.3\text{ kcal}\cdot\text{M}^{-1}$ so that a homolytic $1e^-$ oxidation by alkyl hydroperoxides is observed with the iron(III)porphyrin. The overlap of the d_{xy} - d_{yz} orbitals of the metal moiety with the porphyrin π system differentiates [(TPP)Fe(III)] $^+$ from (EDTA)Fe(III) since in the former a conjugation of metal ion with the porphyrin ring creates a unifying electron cloud resulting in the [(TPP)Fe(III)] $^+$ being a poorer Lewis acid than is (EDTA)Fe(III). It is known that increase in Lewis acid acidity increases the tendency of metal ion centers to react with hydroperoxides by way of heterolytic O-O bond scission (24).

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