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Review

Mechanistic insights into iron porphyrin-catalyzed olefin epoxidation by hydrogen peroxide: Factors controlling activity and selectivity

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Abstract

Iron porphyrins are well known for their ability to catalyze the oxidation of hydrocarbons by hydrogen peroxide and by organic peroxides in general. While many mechanistic studies have been reported, a complete description of the reaction pathway by which the olefin epoxidation occurs has emerged only recently as a result of the work reported by the authors. The aim of this review is to present a summary of the authors' research and to place it into perspective with previously published studies. What emerges is a complete mechanistic picture for the epoxidation of olefins by hydrogen peroxide catalyzed by iron porphyrins that is consistent with all experimental evidence. Rate parameters associated with elementary processes in the reaction mechanism have been determined from experimental measurements of cyclooctene epoxide formation and hydrogen peroxide consumption as a function of the composition of the solvent, axial ligand, porphyrin, and substrate. Several notable findings emerge from this effort. The first is that only iron(III) porphyrin cations are catalytically active. These species are formed by dissociation of the neutral complex, consisting of an iron(III) porphyrin cation and an anion serving as the axial ligand, into solvated cations and anions. Weakly bound axial ligands, such as triflate anions, dissociate in aprotic solvent, whereas a protic solvent is necessary to dissociate strongly bound ligands such as chloride anions. The role of solvent composition on the dissociation of iron porphyrin complex is fully described by a model of the thermodynamics of the process. The selectivity of hydrogen peroxide towards epoxidation versus decomposition is determined by two competitive processes, heterolytic and homolytic cleavage of the O–O bond of the iron(III)-coordinated hydrogen peroxide molecule. The former process leads to the production of an iron(IV) pi-radical cation which is active for olefin epoxidation, while the later process leads to an iron(IV)-hydroxo species that is active exclusively for peroxide decomposition. A competition also occurs between olefin and hydrogen peroxide for reaction with the iron(IV) pi-radical cation species. Substrate composition does not affect the individual rate parameters as long as the olefin does not interact electronically with the iron porphyrin. Solvent alcohol coordinates to the iron(III) porphyrin in the axial position, thereby modifying the electronic properties of the iron. A second effect of alcohols is to facilitate the heterolytic cleavage of the oxygen–oxygen bond of hydrogen peroxide. The quantity, position, and electronegativity of halogen substituents attached to the phenyl groups at the meso-position of the porphyrin ring also affect the activity and selectivity of the porphyrin for olefin epoxidation. All of these effects are well explained by the mechanism that we have proposed. The rate parameters associated with the proposed mechanism vary in a systematic and physically meaningful fashion with changes in the composition of the porphyrin, the axial ligand associated with the porphyrin, and the solvent in which the porphyrin is dissolved.

Keywords: Porphyrin; Peroxide; Epoxidation; Mechanism; Iron

Contents

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1. Introduction

Iron porphyrins are effective catalysts for both the hydroxylation of hydrocarbons and the epoxidation of olefins by a number of different oxidants [1–3]. When hydrogen peroxide is used as the oxidant, iron porphyrins catalyze two primary reactions, the transfer of an oxygen atom from hydrogen peroxide to the organic substrate [4–20] and the decomposition of hydrogen peroxide to water and oxygen [5,7–10,20–24]. The activity and selectivity of such catalysts for hydrocarbon oxidation as opposed to hydrogen peroxide decomposition is affected strongly by the composition of the porphyrin catalyst [5,7–9,12–14,21,25–27], the substrate concentration [10,28,29], and the solvent composition [7,14,29]. While the literature provides a good description of the qualitative effects of these variables, there have been only very limited attempts to describe their influence on the individual rate parameters associated with elementary steps comprising the reaction mechanism [10].

The greatest clarity and consensus regarding reaction mechanism has come from studies of olefin epoxidation and in particular cyclooctene epoxidation, since only one organic product is produced [10,30–32]. In a recent series of studies, we have shown that the reaction mechanism shown in Fig. 1 can be written for the iron(III) [tetrakis(pentafluorophenyl)] porphyrin-catalyzed epoxidation of cyclooctene by hydrogen peroxide in a methanol-containing solvent that is valid for a wide range of reaction conditions [28,29,33]. This mechanism has also been shown to be valid for other porphyrins [27] (see Fig. 2) and solvents [34] compositions. The aim of this review is to summarize our findings, to discuss the effects of porphyrin and solvent composition on the equilibrium and rate parameters appearing in the mechanism, and to draw inferences about what is required in order to achieve high epoxidation activity and hydrogen peroxide selectivity.

2. Proposed reaction mechanism

We have proposed the reaction mechanism shown in Fig. 1 based on ideas reported in the literature and on evidence derived from our own mechanistic studies [27–29,33,34]. Reaction 1 involves the dissociation of the catalytically inactive iron(III) chloride porphyrin species to produce a catalytically active solvent-coordinated cation species. In Fig. 1, a generic alcohol is shown as the solvent that enables dissociation of the porphyrin salt. However, only small alcohols result in dissociation, as steric hindrance prevents the coordination of bulky alcohols, such as *t*-butanol, to the iron cation [29]. Consistent with the work of Traylor and Ciccone, hydrogen peroxide is shown to coordinate reversibly to the iron(III) porphyrin cation in Reaction 2 in Fig. 1. Bruice and coworkers have proposed that the oxygen–oxygen

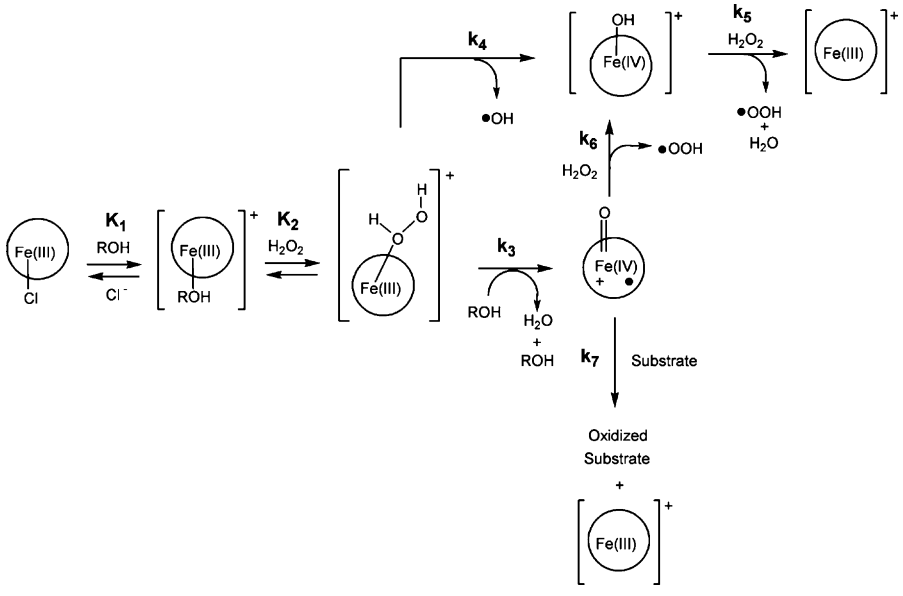
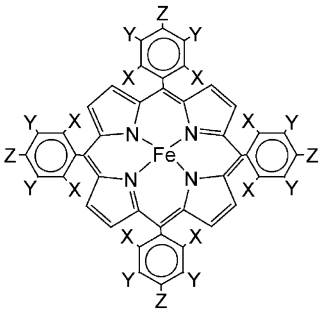


Fig. 1. Proposed mechanism for the epoxidation of olefins by iron(III)-chloride porphyrins using H_2O_2 as oxidant.



Porphyrin Catalyst	Symbol	X	Y	Z
iron (III) [tetrakisphenyl] porphyrin	(TPP)Fe	H	H	H
iron(III) [tetrakis(4-fluorophenyl)] porphyrin	(4-F_4TPP)Fe	H	H	F
iron(III) [tetrakis(2,6-difluorophenyl)] porphyrin	(2,6-F_8TPP)Fe	F	H	H
iron(III) [tetrakis(3,5-difluorophenyl)] porphyrin	(3,5-F_8TPP)Fe	H	F	H
iron(III) [tetrakis(pentafluorophenyl)] porphyrin	(F_{20}TPP)Fe	F	F	F
iron(III) [tetrakis(2,6-dichlorophenyl)] porphyrin	(2,6-Cl_8TPP)Fe	Cl	H	H

Fig. 2. Structure and terminology used for various iron(III) porphyrin catalysts.

bond of the coordinated hydrogen peroxide then undergoes homolytic cleavage to produce a hydroxyl radical and a one-electron oxidized iron(IV) porphyrin species [4,16,17,35,36]. On the other hand, Traylor and coworkers have proposed that acid-catalyzed heterolytic cleavage of the oxygen–oxygen bond occurs to produce an equivalent of water and a two-electron oxidized iron(IV) pi-radical cation species [5–8,15,21,37]. More recently, Nam et al. have reported evidence indicating that heterolytic and homolytic cleavage can occur simultaneously and that the partitioning between the two pathways depends upon the composition of the porphyrin catalyst, the axial ligand, and the oxidant [9]. We have, therefore, included both reaction pathways in the proposed mechanism as Reactions 3 and 4. Consistent with literature, the one-electron oxidized iron(IV) species formed by homolytic cleavage in Reaction 4 is shown to contribute exclusively to peroxide decomposition via Reaction 5 [9,10]. Pathways for both the decomposition of hydrogen peroxide, Reaction 6, and epoxidation of olefin, Reaction 7, by the iron(IV) pi-cation radical species are also included in the proposed mechanism [8–10,26]. Hydroxyl and hydroperoxyl radicals are shown to form in Reactions 3, 5, and 6. These species are believed to be involved in porphyrin degradation [10,33] and the production of dioxygen [38–40]. A pathway for the reaction of the iron-coordinated hydrogen peroxide with the substrate has not been included in the mechanism, since this type of reaction has been shown to be unlikely based on both experimental [37] and theoretical studies [41,42].

2.1. Evaluation of the mechanism

Expressions for the rate of hydrogen peroxide consumption, the rate of cyclooctene epoxidation, and the yield of cyclooctene epoxide can be derived based on the mechanism shown in Fig. 1 [33]. The assumptions underlying these expressions are that: (1) the chloride-coordinated iron(III) porphyrin is catalytically inactive, whereas the alcohol-coordinated iron(III) porphyrin cation is catalytically active; (2) Reactions 1 and 2 are equilibrated; (3) the relative rates of heterolytic to homolytic cleavage are time-independent and the final yield of epoxide relative to the total amount of hydrogen peroxide consumed is determined by this ratio; (4) the cleavage of the oxygen–oxygen bond of coordinated hydrogen peroxide limits the overall rate of hydrogen peroxide consumption; (5) heterolytic cleavage of the oxygen–oxygen bond of coordinated hydrogen peroxide is facilitated by a protic solvent, whereas homolytic cleavage of this bond is not; and (6) free radical species do not contribute to the oxidation of the substrate. As shown by Eq. (1), the overall rate of hydrogen peroxide consumption is first-order in hydrogen peroxide concentration. The apparent rate constant for hydrogen peroxide consumption, $k_{H_2O_2}$, is defined by Eq. (2). In Eq. (2), [Fe–ROH] is the concentration of alcohol-coordinated porphyrin species, as defined by Reaction 1, and Y_∞ is the final yield of epoxide relative to the initial concentration of hydrogen peroxide. As a consequence of the third assumption (see above), the concentration of hydrogen peroxide can be approximated by Eq. (3), where [C_8–O] is the concentration of cyclooctene epoxide as a function of time. It then follows that the final cyclooctene epoxide yield can be related to the rate parameters k_3K_2 and k_4K_2 by Eq. (4). The observed rate of epoxidation is given by Eq. (5), where k_{EPX} is defined as the product of Y_∞ and $k_{H_2O_2}$.

$$\frac{d[H_2O_2]}{dt} = -k_{H_2O_2}[H_2O_2] \quad (1)$$

$$k_{H_2O_2} = \frac{k_3K_2[ROH][Fe-ROH]}{Y_\infty} \quad (2)$$

$$[H_2O_2] = [H_2O_2] - \frac{[C_8-O]}{Y_\infty} \quad (3)$$

$$Y_\infty = \frac{k_3K_2[ROH]}{k_3K_2[ROH] + 2k_4K_2} \quad (4)$$

$$\frac{d[C_8-O]}{dt} = k_{EPX}[H_2O_2] \quad (5)$$

Each of the assumptions underlying Eqs. (1)–(5) has been validated experimentally [28,29,33]. ^{1}H NMR and UV–vis spectroscopies were used to confirm that the chloride-coordinated porphyrin and the methanol-coordinated cation appearing in Reaction 1 are at equilibrium with each other [28]. The observation of a linear relationship between the observed rate coefficient and the concentration of alcohol-coordinated species confirms that only the alcohol-coordinated species are catalytically active and that Reaction 1 is equilibrated under reaction conditions [28,29,33]. The assumption that Reaction 2 is equilibrated is consistent with the observation of a first-order rate in hydrogen peroxide concentration and the independence of the rate constant and final yield on the concentration of hydrogen peroxide. The third assumption was verified by using ^{1}H NMR to measure the concentration of hydrogen peroxide as a function of time under reaction conditions [33,43]. The independence of the reaction rate and the epoxide yield on the concentration of cyclooctene at high concentrations is consistent with the assumption that Reactions 3 and 4 are rate determining and that the rate of Reac-

Table 1
Effects of alcohol composition on reaction parameters for the mechanism shown in Fig. 1 as follows

Variable	Methanol	Ethanol	*n*-Propanol	*n*-Butanol	*Iso*-propanol
pK_a	15.3	15.9	16.1	16.1	17.1
Gutmann donor number	19.1	19.2	19.8	21.8	21.1
Porphyrin degradation with olefin (%)	10	10	18	24	30
Porphyrin degradation without olefin (%)	21	23	44	53	100
Epoxide yield w.r.t. H_2O_2	88%	86%	79%	79%	74%
[Fe–ROH] (μM)	46	49	59	57	44
$k_{H_2O_2}$(min^{-1})	0.25	0.23	0.15	0.14	0.09
k_{EPX}(min^{-1})	0.22	0.20	0.12	0.11	0.07
K_1 from GC	1.2×10^{-5}	1.5×10^{-5}	3.5×10^{-5}	3.0×10^{-5}	1.0×10^{-5}
K_1 from NMR	1.0×10^{-5}	1.5×10^{-5}	3.3×10^{-5}	2.8×10^{-5}	0.9×10^{-5}
k_3K_2 (M^{-2} s^{-1})	13	11	5.3	5.1	4.1
k_4K_2 (M^{-1} s^{-1})	5.3	5.7	4.4	4.2	4.5
k_3/k_4 (M^{-1})	2.5	1.9	1.2	1.2	0.9
k_6/k_7	0.30	0.45	0.60	0.65	0.95

All data is for an alcohol concentration of 5.6 M.

tion 7 is much greater than that of Reaction 6 [33]. The faster rate of Reaction 7 relative to Reaction 6 holds as long as olefin is present in moderate concentration. The observed rate of reaction and the epoxide yield are also unaffected by the nature of the olefin, provided that the olefin does not coordinate with the iron porphyrin [34]. The involvement of alcohol in the heterolytic cleavage of the O–O bond of coordinated H_2O_2 is supported by experiments showing that the rate of heterolytic cleavage is first-order in alcohol concentration, whereas the rate of homolytic cleavage is independent of the concentration and composition of the alcohol [29,33]. No evidence was seen for organic oxidation products produced via a radical mechanism [33]. Finally, the mechanism shown in Fig. 1 explained well the rates of hydrogen peroxide consumption and olefin epoxidation as a function of the composition and concentration of porphyrin, substrate, hydrogen peroxide, and solvent. Similar mechanistic studies have shown that the mechanism shown in Fig. 1 also applies to other porphyrin and solvent compositions. The remainder of this review discusses the effects of these parameters on each step of the reaction mechanism.

2.2. Reaction 1: dissociation of iron(III) porphyrin chloride

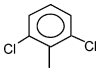
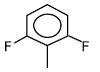
A number of studies have shown that the extent of iron(III) porphyrin chloride dissociation is a function of solvent composition [29,44–56]. The first evidence for the ionic dissociation of (TPP)FeCl in ethanol was obtained from conductivity measurements and UV–vis spectroscopy [48]. Detailed thermodynamic studies of the dissociation of (F_{20}TPP)FeCl in MeOH/MeCN mixtures have revealed that the dissociation of this salt is an endothermic process that becomes more favorable as the concentration of methanol increases [28]. The composition of the alcohol solvent also affects the degree of (F_{20}TPP)FeCl dissociation. As shown in Table 1, K_1 becomes more favorable as the electron-density on the alcoholic oxygen atom, indicated by the Gutmann donor number, increases [29]. Steric effects are observed for branched alcohols, such as *iso*-propanol and *iso*-butanol. In these cases, the value of K_1 decreases, since the alcohol cannot access the Fe(III) cation without steric interference by the porphyrin ring [29]. Similar steric effects are also seen for other ligands [46,54]. The solvent affects the extent of (F_{20}TPP)FeCl dissociation not only through its role in solvating the resulting cation but also by micro-solvation of the Cl^- anion. A recent theoretical study suggests that the latter effect of the solvent is more important than the former in promoting the dissociation of (F_{20}TPP)FeCl [57]. Here too, steric effects can be important, since the number of alcohol molecules that can interact with a Cl^- anion is less for branched than for linear alcohols.

The composition of the porphyrin ligand also influences the ease with which (F_{20}TPP)FeCl dissociates. For example, halogen substituents on the phenyl rings of tetra-aryl porphyrins influence the Lewis acidity of the iron(III) cation, as evidenced by changes in the $Fe^{III/II}$ reduction potential (see Table 2) [27,58,59]. As the Lewis acidity of the iron(III) cation increases, so does the strength of the iron-chloride bond, making dissociation of (F_{20}TPP)FeCl more difficult [27,44]. Table 2 shows that halogen substitution at the *meta*- and *para*-positions of the phenyl rings results exclusively in withdrawal of electron-density from the porphyrin ring and the iron cation, thereby increasing the Lewis acidity of the iron cation and making the release of chloride anions more difficult. This trend is seen clearly in the variation of K_1 with porphyrin composition, as shown in Table 2 [27,44,46,47]. On the other hand, halogen substitution at the *ortho*-positions of the phenyl rings results in overlap between the electron cloud of the halogen atoms and the pi-electron cloud of the porphyrin ring. These interactions lead to a decrease in the Lewis acidity of the iron(III) cation, a weakening of the iron-chloride bond, and, hence, a facilitation in the dissociation (F_{20}TPP)FeCl (see Table 2) [27,44]. In summary, dissociation of (F_{20}TPP)FeCl increases as the Lewis basicity of the alcohol solvent increases and as the Lewis acidity of the iron(III) porphyrin cation decreases.

2.3. Reaction 2: coordination of hydrogen peroxide

The inability to isolate the H_2O_2-coordinated porphyrin species has made it difficult to determine the extent to which

Table 2
Effects of porphyrin composition on reaction parameters for the mechanism shown in Fig. 1 as follows

Variable	 (F$_{20}$TPP)Fe in MeCN	 (F$_{20}$TPP)Fe in CH_2Cl_2	 (TPP)Fe	 (2,6-Cl$_8$TPP)Fe	 (2,6-F$_8$TPP)Fe	 (3,5-F$_8$TPP)Fe	 (4-F$_4$TPP)Fe
E_0[Porp]FeCl (V)[a,b]	–	−0.09	−0.22	−0.25	−0.23	–	–
E_0[Porp]Fe$^+$ (V)[c,d]	–	0.12	−0.11	−0.05	0.00	–	–
Porphyrin degradation (%)	10	3	100	56	13	100	100
Epoxide yield w.r.t. H_2O_2 (%)	88	88	45	78	88	–	–
K_1	1.0×10^{-5}	1.3×10^{-5}	1.3×10^{-5}	60×10^{-5}	12×10^{-5}	0.4×10^{-5}	0.7×10^{-5}
[Fe–MeOH] (μM)	46	46	47	73	68	–	–
$k_{H_2O_2}$ (min^{-1})	0.25	1.41	0.02	0.03	0.25	–	–
k_{EPX}(min^{-1})	0.22	1.24	0.01	0.02	0.22	–	–
k_3K_2 (M^{-2} s^{-1})	13	82	0.6	1.0	10	–	–
k_4K_2 (M^{-1} s^{-1})	5.5	31	2.1	0.8	3.7	–	–
k_3/k_4 (M^{-1})	2.4	2.6	0.29	1.3	2.6	–	–
k_5 (M^{-1} s^{-1})	225	n.d.	>300	Large	Large	–	–
k_6/k_7	0.30	0.50	300	∼10	1.1	–	–

[a] Taken from Refs. [55,56].
[b] (TPP)FeCl in CH_2Cl_2 other porphyrins in 1:1 CH_2Cl_2:CH_3CN. All relative to SCE.
[c] Taken from Ref. [9] and converted from Fc/Fc$^+$ to SCE.
[d] Porphyrin cations formed by dissociation of chloride ligand in a 3:1 mixture of CH_3OH:CH_2Cl_2.

hydrogen peroxide coordinates to the iron(III) cation. Density functional theory has been used to calculate the dissociation energy of the hydrogen peroxide-coordinated iron(III) species for cytochrome P450 [60]. However, this methodology has not been extended to investigate the effects of changes to the local environment around the iron(III) cation. Experimental studies completed in our laboratory have provided a qualitative understanding of solvent effects on the extent of hydrogen peroxide coordination to the iron(III) cation. At low alcohol concentrations, K_2 is not affected significantly by the concentration or composition of the alcohol. For a constant molar alcohol concentration of 5.6 M, the value of k_4K_2, as shown in Table 1, is independent of alcohol composition, suggesting that both k_4 and K_2 are independent of alcohol composition [29]. Furthermore, the linearity of $k_{H_2O_2}$ with k_3K_2[Fe–MeOH]/Y_∞ for MEOH/MeCN and MeOH/CH_2Cl_2 mixtures indicate that K_2 is not affected significantly at methanol concentrations below 12 M and 8 M, respectively [27,28]. At high methanol concentrations, the observation of a non-linear increase in $k_{H_2O_2}$ with k_3K_2[Fe–MeOH]/Y_∞ has been attributed to an increase of intermolecular interactions between hydrogen peroxide and the alcohol, which result in a solvent-dependent value for K_2 [27]. Larger values of k_3K_2 and k_4K_2 are observed in MeOH/CH_2Cl_2 versus MeOH/MeCN for cyclooctene epoxidation using (F$_{20}$TPP)FeCl (see Table 2) [27]; however, k_3/k_4 is independent of the aprotic solvent. This indicates that the difference in k_3K_2 and k_4K_2 is due to a difference in K_2 in the two solvents. ^{1}H NMR also indicates that hydrogen peroxide is more nucleophilic in methylene chloride than in acetonitrile, which is consistent with the value of K_2 being smaller in MeOH/MeCN than in MeOH/CH_2Cl_2 [27]. Together, the kinetic and NMR data indicate that the nucleophilicity of hydrogen peroxide and the value of K_2 increase in the order of MeOH < MeCN < CH_2Cl_2. The extent of hydrogen peroxide coordination is also expected to increase as the iron(III) cation becomes more Lewis acidic, which can be accomplished by adding electronegative substituents to the porphyrin ligand [27]. It is important to note here that *ortho*-halogens, as evidenced by changes in the reduction potential, have a net electron-withdrawing effect after the chloride ligand is dissociated from the iron cation (see Table 2) [27].

2.4. Reactions 3 and 4: heterolytic versus homolytic cleavage of the O–O bond of coordinated H_2O_2

Solvent and porphyrin composition affect the selectivity between the heterolytic and homolytic cleavage of the O–O bond of coordinated H_2O_2. Comparison of reactions carried out in MeOH/MeCN and MeOH/CH_2Cl_2 solutions have shown that the selectivity of H_2O_2 consumption for olefin epoxidation is unaffected by the composition of the aprotic component of the solvent [27]. However, the rate of heterolytic cleavage decreases with decreasing alcohol acidity (see k_3K_2 in Table 1) [29]. As shown in Table 1, the rate of homolytic cleavage (see k_4K_2) is independent of alcohol composition [29]. Therefore, the selectivity towards heterolytic cleavage of the O–O bond of coordinated H_2O_2 increases with increasing alcohol acidity. Nam and coworkers have shown that the selectivity towards heterolytic cleavage increases as the iron cation becomes more electron-deficient as a consequence of changes in the composition of the phenyl substituents [9] and the axial ligand [12]. In agreement with these qualitative observations, we have found that electronegative substituents on the porphyrin ring promote heterolytic cleavage relative to homolytic cleavage, as evidenced by an increase in the value of k_3/k_4 (see Table 2) [27]. The activity and selectivity of iron(III) porphyrins may

be influenced as well by the conformation of the porphyrin ring, which is affected by the size of substituents, particularly *ortho* substituents, on the phenyl groups [27]. Changes in the porphyrin structure are expected to influence the coordination of hydrogen peroxide (Reaction 2), as well as the subsequent alcohol-assisted heterolytic cleavage of the coordinated hydrogen peroxide (Reaction 3). Therefore, the extent of heterolytic cleavage versus homolytic cleavage is maximized by increasing the acidity of the alcohol and by reducing the electron-density on the iron cation.

2.5. Reaction 5: peroxide decomposition via Fe^{IV}–OH

The product of homolytic cleavage (see Reaction 4) is commonly represented in the literature as either an iron(IV)-oxo species or an iron(IV)-hydroxo species. Theoretical calculations even suggest that there may be as many as six different isomers of the one-electron oxidized species, including two different spin states of an iron(III)-hydroxo pi-radical cation species [61]. On the other hand, experimental studies have suggested only iron(IV)-oxo or iron(IV)-hydroxo species for enzymatic and model porphyrin systems. We have shown the one-electron oxidized product of Reaction 4 to be an iron(IV)-hydroxo species (see Fig. 1) for the following reasons. First, the iron(IV)-hydroxo species is what would be expected for homolytic cleavage of hydrogen peroxide coordinated to the iron(III) porphyrin, whereas the iron(IV)-oxo species would only be expected for homolytic cleavage of an iron(III)-hydroperoxo species. Deprotonation of hydrogen peroxide prior to homolytic cleavage would likely involve proton transfer to a solvent alcohol molecule, and the kinetics that follow from such a scheme are not consistent with the observed rate of hydrogen peroxide consumption as a function of methanol concentration [29,33]. On the other hand, a mechanism involving homolytic cleavage of the iron-coordinated hydrogen peroxide molecule is consistent with the observed kinetics.

We note further that Bruice and coworkers have suggested that iron(IV)-hydroxo species are likely to exist in solutions containing water [62]. Water is known to be present in the reaction mixture from various sources: un-dried solvents, aqueous (30 wt%/wt%) hydrogen peroxide, and as a product of Reaction 3. Further evidence for the protonated form of the iron(IV) porphyrin comes from reactivity studies. Iron(IV)-oxo species have been documented to epoxidize olefins at room temperature [62,63]. However, protonation of the iron(IV)-oxo species is expected to shift reactivity from oxygen transfer to mere electron transfer [64]. Consistent with this idea, iron(IV)-hydroxo species have been proposed to be inactive for olefin epoxidation or alkane hydroxylation [65]. Moreover, reactivity studies have revealed that $(F_{20}TPP)Fe(IV)O$ readily epoxidizes cyclooctene in the absence of water; however, this reactivity diminishes in the presence of microliter aliquots of water, suggesting that even small amounts of water may convert the iron(IV)-oxo species to an iron(IV)-hydroxo species [36]. Therefore, based upon consistency with the proposed mechanism and evidence suggested by reactivity studies, the product of Reaction 4 is represented as an iron(IV)-hydroxo species in the mechanism shown in Fig. 1.

The one-electron oxidized iron(IV)-hydroxo species has been proposed to react with hydrogen peroxide via Reaction 5 to regenerate the iron(III) porphyrin and release water [8,10]. We have determined a value of $225\,M^{-1}\,s^{-1}$ for k_5 at 298 K for $(F_{20}TPP)Fe^{IV}OH$ in methanol/acetonitrile from a fit to rate data [29,33]. In situ UV–vis spectroscopy experiments for the reaction of H_2O_2 in the presence and absence of cyclooctene have shown that the steady-state concentration of iron(IV)-hydroxo species is consistent qualitatively with the reported value of k_5 [29,33]. Experiments with other porphyrin ligands, all less electronegative than $(F_{20}TPP)Fe$, have shown that the rate of Reaction 5 is much greater than that of Reaction 4 in $MeOH/CH_2Cl_2$ (i.e. k_5 increases). This effect may be attributed to changes either in the porphyrin or solvent composition. The absence of spectral features for iron(IV) species in steady-state UV–vis spectra also indicates that the rate coefficient for Reaction 5 is large under these conditions [27]. A value for k_5 could not be determined when k_5 was greater than $\sim 300\,M^{-1}\,s^{-1}$ because the contribution of Reaction 5 to the rate of hydrogen peroxide decomposition can no longer be isolated.

2.6. Reactions 6 and 7: selectivity for epoxidation

As originally proposed by Traylor [5,7,8,21], pi-radical cations are consumed in competitive reactions between olefin epoxidation (Reaction 7) and hydrogen peroxide decomposition (Reaction 6). Several studies have shown that electron-rich porphyrins favor reaction with hydrogen peroxide, while electron-poor porphyrins favor reaction with olefins [8,9,21,26]. Research in our laboratory has confirmed these findings and has quantified the effect of meso-phenyl substituents on the ratio of k_6/k_7 (see Table 2) [27]. The composition of the alcohol solvent, also affects the selectivity between Reactions 6 and 7. In addition to serving as an acid catalyst in Reaction 3, the alcohol coordinates to the iron porphyrin cation as an axial ligand, resulting in electron donation from the coordinated alcohol to the iron(IV) pi-radical cation [29]. As seen in Table 1, the value of k_6/k_7 increases with increasing electron donation, as indicated by a larger Gutmann donor number, resulting in less selective utilization of H_2O_2 for epoxidation. Therefore, increased electron donation, either from the axial ligand or from the porphyrin, results in a decreased selectivity towards epoxidation.

Two reasons have been offered to explain the decrease in k_6/k_7 with increasing electronegativity of the porphyrin. First, it has been proposed that iron(IV) pi-radical cations of electron-deficient porphyrins may exhibit a greater propensity for electron transfer to an olefin than for hydrogen abstraction from a peroxide molecule [8]. Alternatively, the reaction with hydrogen peroxide may be diffusion controlled, while the reaction with olefin is limited by kinetics [8]. The second explanation seems more likely and is consistent with our finding that the ratio of k_6/k_7 is greater in dichloromethane than in acetonitrile [27]; stronger interactions between acetonitrile and hydrogen peroxide are expected to slow the rate of diffusion.

2.7. Additional factors affecting activity and selectivity

Several additional factors can affect the activity and selectivity of iron(III) porphyrins for olefin epoxidation by H_2O_2. First, under some circumstances, the substrate molecule may coordinate axially to the iron cation, resulting in a change to the local environment of the iron cation [34]. Second, oxidative degradation of the porphyrin ring can occur during reaction, resulting in a loss of activity [10,33,66]. Finally, isolated porphyrin species may dimerize to form μ-oxo dimers, which exhibit different activity and selectivity than do monomeric species [27]. We have shown that all three of these effects result in decreased activity and selectivity for olefin epoxidation.

Kinetic studies have demonstrated that the mechanism shown in Fig. 1 is independent of the substrate composition for olefins that do not coordinate to the iron cation (e.g., cyclooctene, styrene, and cis-stilbene) [34]. However, lower selectivities and reactivities were observed for the epoxidation of cyclohexene and norbornene [34]. Coordination of the smaller olefins to the iron cation results in increased electron donation to the iron cation, thus decreasing activity and selectivity to epoxidation versus hydrogen peroxide decomposition. Evidence for olefin coordination to the iron cation was verified by UV–vis and ^{1}H NMR spectroscopies [34].

Catalyst degradation is a serious concern in porphyrin-catalyzed oxidation reactions, since decreasing catalyst concentration can result in underestimation of catalyst activity. In addition, complete porphyrin degradation prior to complete oxidant consumption can lead to a misinterpretation of yield and selectivity data. The major pathway for porphyrin degradation is believed to be attack of the porphyrin ring by hydroxyl radicals [10,33] generated via homolytic cleavage of coordinated hydrogen peroxide (Reaction 4). Consistent with this hypothesis, we have observed that the extent of porphyrin degradation increases with increasing rate of hydroxyl radical generation. Thus, factors which decrease the ratio of k_3/k_4 contribute to porphyrin degradation, as can be seen from Tables 1 and 2.

The extent of porphyrin degradation also depends on the initial concentrations of porphyrin catalyst and hydrogen peroxide [33]. As the initial concentration of porphyrin is increased, the rate at which radicals are produced increases as well. However, since porphyrin degradation is first-order in free radical concentration, whereas radical–radical recombination is second-order in radical concentration, the rate of radical recombination increases faster than the observed rate of porphyrin decomposition as the initial porphyrin concentration is increased. Therefore, a smaller fraction of the initial porphyrin is degraded in the period during which all of the hydrogen peroxide is consumed as the initial porphyrin concentration is increased. On the other hand, the extent of porphyrin degradation increases with increasing initial concentration of hydrogen peroxide, since a larger concentration of free radical are produced over the period during which hydrogen peroxide is consumed [33].

Another reaction that can lead to a misinterpretation of rate data is the formation of μ-oxo dimers. We have shown that the formation of μ-oxo dimers can result in diminished yield, since μ-oxo dimers are inefficient for epoxidation but can decompose hydrogen peroxide at a rate comparable to that of iron(III) cation monomers [27]. The extent of dimerization was found to increase in the order of (3,5-F_8TPP)FeCl > (4-F_4TPP)FeCl > (TPP)FeCl, indicating that dimerization occurs more readily for electronegative porphyrin species [27]. However, halogen substituents located at the *ortho*-positions of the phenyl rings offer steric protection against dimerization. For example, it is well documented that (2,6-Cl_8TPP)FeCl dose not dimerize [2,67]. In addition, our studies have shown no evidence

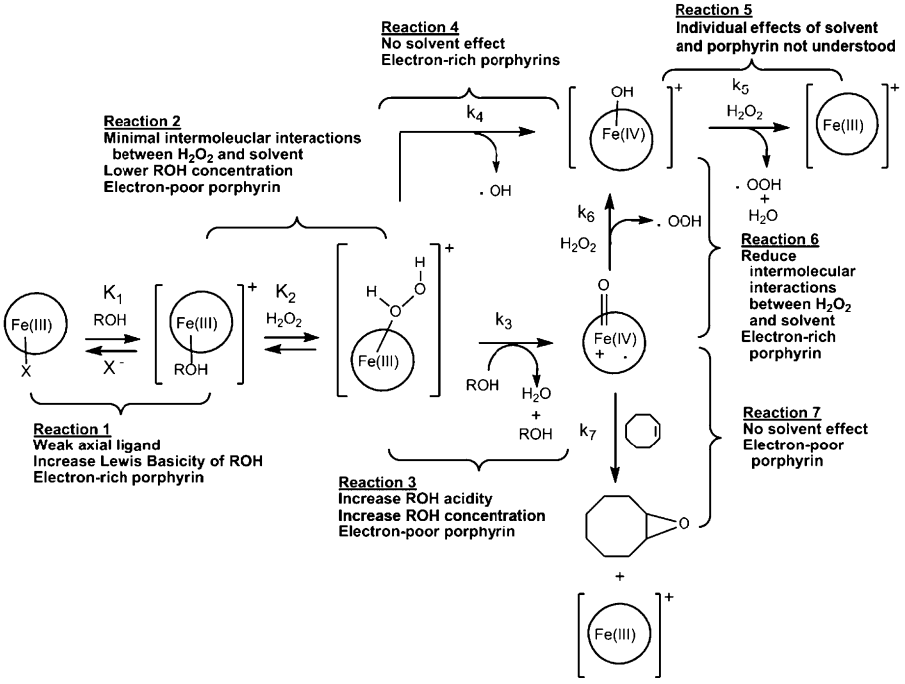


Fig. 3. Qualitative explanations for the effects of solvent and porphyrin composition on individual reactions.

for the formation of μ-oxo dimers by either (F_{20}TPP)FeCl or (2,6-F_8TPP)FeCl, suggesting that the fluorine atoms located at the *ortho* positions on the phenyl rings may also offer some protection against dimerization.

3. Conclusions

Fig. 3 summarizes the effects of local environment around the iron(III) cation in the porphyrin for each elementary reaction. Dissociation of the chloride ligand (Reaction 1) can be promoted by increasing the Lewis basicity of the protic solvent or by decreasing the Lewis acidity of the iron(III) cation. Hydrogen peroxide coordinates to the iron(III) cation (Reaction 2) more readily when the iron(III) cation is more Lewis acidic and when intermolecular interactions between the solvent and hydrogen peroxide are minimized. Increasing the electron-withdrawing ability of the porphyrin ligand or axial ligand promotes heterolytic (Reaction 3) relative to homolytic (Reaction 4) cleavage of the hydrogen peroxide oxygen–oxygen bond. The rate of homolytic cleavage is unaffected by the solvent, but the rate of heterolytic cleavage increases with the concentration and acidity of the protic solvent. The effects of solvent and porphyrin composition on the reactivity of iron(IV)-hydroxo species and hydrogen peroxide (Reaction 5) could not be determined. Selectivity towards epoxidation (Reactions 6 versus 7) is favored by increasing the electronegativity of the porphyrin or the axial ligand. Increased intermolecular interactions between hydrogen peroxide and the solvent also improve selectivity by reducing the rate of Reaction 6. Porphyrin degradation is minimized by increasing reaction rate and selectivity for heterolytic cleavage. Degradation can also be reduced by halogenation of the phenyl groups attached to the porphyrin ring. The formation of μ-oxo dimers, another process contributing to a loss in expoxidation activity, is more favorable for electron-poor porphyrins, but *ortho*-fluoro and *ortho*-chloro substituents offer steric protection from the formation of dimers under reaction conditions. The analysis presented in this review also demonstrates that high catalyst activity for cyclooctene epoxidation by hydrogen peroxide, i.e., a high value of k_{EPX} is achieved by a complex trade-off of the effects of porphyrin and solvent composition. For the materials studied, the highest value of k_{EPX} is for (F_{20}TPP)FeCl dissolved in a mixture of MeOH and CH_2Cl_2, as shown in Table 2.

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