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The Prime Reactive Intermediate in the Iron(III) Porphyrin Complex Catalyzed Oxidation Reactions by *tert*-Butyl Hydroperoxide

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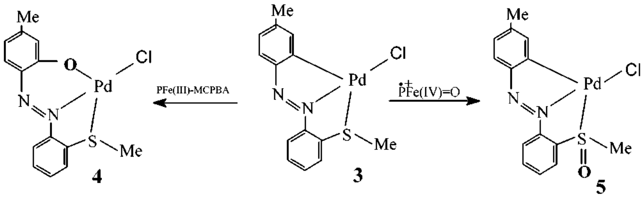
The heme and non-heme enzyme-catalyzed oxygenation reactions of organic substrates have been a subject of considerable interest for the last few decades.[1] In heme-containing enzymes and in the iron(III)porphyrin model compounds, it has been generally believed for a long time that oxo-iron(IV)porphyrin cation radical(**2**) is the only reactive intermediate responsible for the oxygenation of hydrocarbons (eq 1).[2]

$$\mathrm{PFe(III)} + \mathrm{Oxidant} \longrightarrow \underset{\mathbf{1}}{\mathrm{PFe(III)\text{-}Oxidant}} \longrightarrow \underset{\mathbf{2}}{\overset{+\bullet}{\mathrm{P}}\mathrm{Fe(IV){=}O}} \qquad (1)$$

Newcomb, Coon, Vaz, and co-workers have, however, demonstrated the oxidation of hydrocarbons by the catalyst−oxidant adduct (**1**) in native and mutant cytochrome P-450 enzymes.[3] Oxygenation of hydrocarbons by **1** prior to its conversion to **2** in aprotic solvent has been proposed recently in model compounds.[4] In the alkane hydroxylation and alkene epoxidation reactions one oxygen atom is incorporated into the C−H and C═C bonds, respectively. Recently we have reported one such oxygen atom insertion reaction into a C−Pd bond by MCPBA where the involvement of a reactive intermediate of type-**1** has been indicated. The reactive intermediate **2** has, however, selectively oxidized the thioether fragment of **3** (Scheme 1).[5] The nature of the reactive intermediate(s) in these oxygenation reactions are well understood where MCPBA and iodosylbenzenes are the oxidants, but it is less defined for hydroperoxides.[6] Compound **3** has been found to be more reactive than norbornene, and under constrained reagent concentrations **3** has been made to react more slowly than 2,4,6-tri-*tert*-butylphenol (TTBP) with *t*-BuOOH where F_{20}TPPFeCl (F_{20}TPP= *meso*-tetrakis (pentafluorophenyl) porphinato dianion) has been used as a catalyst. This unique reactivity difference of these three substrates and the results of some crucial experiments described herein have clearly demonstrated that **1** is the most plausible reactive intermediate in this oxidizing system and that neither **2** nor its secondary reaction product *t*-BuOO$^\bullet$ radical is important.

Scheme 1



Regiospecific and quantitative oxygenation of the C−Pd bond has been observed when 34−36 mM of **3** was reacted with 5.5 mM of *t*-BuOOH in the presence of F_{20}TPPFeCl as a catalyst in MeOH−CH_2Cl_2(1:2) at 25 °C. The same oxidizing system has produced 90% of *exo*-norborneneoxide when **3** was replaced by excess of norbornene (500 mM). In the latter reaction small quantities of endo-epoxide and aldehyde/ketone were also formed; the total yield of these minor products was 6−8%. On the other hand when TTBP (500−600 mM) was reacted with this oxidizing system, 93% of the corresponding radical (TTBP$^\bullet$) was formed.[7] The accountability of the total *t*-BuOOH observed in these reactions is the highest in the literature to the best of our knowledge. At lower substrate concentrations the yields of the products were lower in all cases (Table S-1). The competitive oxidation reactions of these substrates were then studied under the identical substrate and reagent concentrations. These results are given in Table 1. Compound **3** did not perturb the oxidation of TTBP (entry 3 vs 6); however the oxidation of TTBP was seriously inhibited by norbornene, and in this reaction no norbornene-oxidized products were detected (entry 3 vs 5).[9] Interestingly there is a clean competition in the oxygen atom-transfer reaction between **3** and norbornene (entry 4). The substrate concentrations in this reaction, however, suggest that the reactive intermediate transfers the oxygen atom to C−Pd bond more efficiently than it does to the C═C bond (entry 4).[10]

Either of the two reactive intermediates **1** or **2** could be responsible for these oxidation reactions. In case **2** is the reactive intermediate; authentically generated **2** should generate an equivalent data set observed in Table 1. We, along with others have noted that the F_{20}TPPFe(III)−MCPBA adduct(**1**) oxidizes substrates before its transformation to **2**.[4b,c,5] Therefore, an unequivocal sample of **2** has been generated by the reaction of F_{20}TPPFeCl and C_6F_5IO, and it has been identified by its selective

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[7] In a typical reaction, the substrate and the catalyst were dissolved in argon-saturated MeOH−CH_2Cl_2 (1:2) at 25 °C and a μL quantity of *t*-BuOOH was injected into the reaction mixture to initiate the reaction. The yields of **4**, **5**, and TTBP radicals were measured spectrophotometrically.[2b,5,8] The norbornene oxidized products were monitored by GC, and the yields of *exo*-norborneneoxide were measured from the calibration curve. All of these reactions progressed slowly, and the yields were measured after 2.5 h.

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[9] In this reaction the rate of the oxidation of TTBP was slowed by norbornene, and the reaction was not followed after 2.5 h.

[10] The quantitative oxygenation reaction of **3** was unperturbed when a nearly equimolar mixture of **3** (34 mM) and norbornene (<50 mM) were oxygenated by this oxidizing system.

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Table 1. Products from the F_{20}TPPFe(III)Cl-Catalyzed Oxidation of Substrates by *t*-BuOOH in MeOH−CH_2Cl_2 (1:2) at 25 °C[a]

	substrate concentrations (mM)			product yields (%)[b]			
entry	**3**	NB[c]	TTBP	**4**	**5**	*exo*-NBO[d]	$\text{TTBP}^\bullet$
1	35	0	0	100	−	−	−
2	0	500	0	−	−	90	−
3	0	0	500	−	−	−	93
4	35	500	0	65	−	32	−
5	0	500	500	−	−	−	40
6	36	0	500	−	−	−	91

[a] Concentrations of F_{20}TPPFe(III)Cl: 13 ± 2 μM; *t*-BuOOH = 5.5 mM in all the reactions. [b] Yields are based on total oxidant. Averages of duplicate sets of experiments with concordant readings are given. [c] Norbornene. [d] *exo*-Norbornene epoxide. The (−) marks indicate that these products are either not detected or are not expected in that run.

Table 2. Products from the F_{20}TPPFe(III)Cl-Catalyzed Oxidation of Substrates by C_6F_5IO in MeOH−CH_2Cl_2 (1:2) at 25 °C[a]

	substrate concentrations (mM)			product yields (%)[b]			
entry	**3**	NB[c]	TTBP	**4**	**5**	*exo*-NBO[d]	$\text{TTBP}^\bullet$
1	34	0	0	<2	95	−	−
2	0	500	0	−	−	87	−
3	0	0	500	−	−	−	68
4	35	500	0	<1	−	88	−
5	0	500	500	−	−	−	62
6	36	0	500	−	−	−	65

[a] Concentrations of F_{20}TPPFe(III)Cl: 12 ± 4 μM; C_6F_5IO = 4.5 ± 0.5 mM in all the reactions. [b] Yields are based on total oxidant. The yields are measured after 2 min of the addition of the oxidant to the reaction mixture. Averages of duplicate sets of experiments with concordant readings are given. [c] Norbornene. [d] *exo*-Norbornene epoxide. The (−) marks indicate that these products are either not detected or are not expected in that run.

Table 3. Products from the Oxidation of Substrates by **2** in Presence of *t*-BuOOH in MeOH−CH_2Cl_2 (1:2) at 25 °C[a]

	substrate concentrations (mM)			product yields (%)[b]			
entry	**3**	NB[c]	TTBP	**4**	**5**	*exo*-NBO[d]	$\text{TTBP}^\bullet$
1	35	0	0	82	<2	−	−
2	0	500	0	−	−	65	−
3	0	0	500	−	−	−	15
4	34	500	0	16	−	32	−
5	0	500	500	−	−	19	15
6	36	0	500	−	−	−	15

[a] Concentrations of F_{20}TPPFe(III)Cl: 12 ± 2 μM; C_6F_5IO = 4.4 ± 0.2 mM and *t*-BuOOH = 11.1 mM in all the reactions. Solid C_6F_5IO was added to the solution of the substrate(s), catalyst, and *t*-BuOOH under argon at 25 °C. The yields of the products were measured after allowing the reactions to proceed for 2 min. [b] Yields are based on total C_6F_5IO. Averages of duplicate sets of experiments with concordant readings are given. [c] Norbornene. [d] *exo*-norbornene oxide. The (−) marks indicate that these products are either not detected or are not expected in that run.

reaction with **3**.[5,11] Expectedly, **5** has been the exclusive product (Table 2, entry1) and this reaction was over in 2 min. This reaction was then repeated by sequentially replacing **3** with norbornene, TTBP, and the three binary mixtures of the three substrates, and the product profiles were analyzed after 2 min. These results are summarized in Table 2. The striking observations were: (i) the oxidation of norbornene has not been perturbed by **3** (entry 2 vs 4) and (ii) the oxidation of TTBP has not been dramatically inhibited by norbornene (entry 3 vs 5 of Table 1 and 2). These observations suggest that **2** may not be the prime reactive intermediate in the oxidation reactions of *t*-BuOOH. Now we have repeated these reactions of **2** in the presence of *t*-BuOOH. These experiments test whether **2** (if generated by the reaction of the catalyst and *t*-BuOOH) abstracts a hydrogen atom from *t*-BuOOH to give *t*-$\text{BuOO}^\bullet$ radical as the major reactive intermediate.[12] If this has been the case, the entire reaction might be radical-derived, and such a reaction mixture should reproduce the data set of Table 1. The results of these reactions are presented in Table 3. When **3** was reacted with such a reaction mixture, the *t*-$\text{BuOO}^\bullet$ radical-derived product **4** was formed in high yields in 2 min (Table 3, entry 1).[5] Surprisingly the yield of $\text{TTBP}^\bullet$ radical was only 15%, and this reaction was unaffected by other two substrates (Table 3, entries 3, 5, 6). It also appears that the *t*-$\text{BuOO}^\bullet$ radical is more reactive with norbornene than with **3** (Table 3, entry 4). These results and consistently lower yields of all the products from this oxidizing system do not conform with the results presented in Table 1. Thus, we believe that neither **2** nor *t*-$\text{BuOO}^\bullet$ radical are the important reactive intermediates in the oxidizing system of F_{20}TPPFeCl and *t*-BuOOH in methanolic solvent. The high-to-quantitative yields of *exo*-epoxide and **4** (Table 1, entry 2,1) reject the possible involvement of PFe(IV)═O too.[5]

We believe that **1** is the most plausible reactive intermediate in the F_{20}TPPFeCl-catalyzed oxidation of **3**, norbornene, and TTBP by *t*-BuOOH. It is possible that at higher concentrations of norbornene appreciable numbers of this molecule have been positioned above the iron(III) center like camphor in cytochrome P-450 and that this might inhibit the formation of **1** (Table 1, entry 5). Oxidation of TTBP to the $\text{TTBP}^\bullet$ radical is a one-electron and one-proton-transfer reaction on the other hand the oxygenation of **3** and norbornene are the inner-sphere oxygen atom-transfer reactions. Thus, it is very much expected that in the competition reaction, TTBP should always win as has been observed. The competitive reactions of **1** with alkenes of variable size are under investigation. This should give further insight about the structure of the proposed intermediate.

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Supporting Information Available: Experimental details and date collection (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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