A Biomimetic Model for Catalase: The Mechanisms of Reaction of Hydrogen Peroxide and Hydroperoxides with Iron(III) Porphyrins

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The reactions of metalloporphyrin complexes with oxygen-atom transfer agents such as hydroperoxides, peracids, iodosylbenzenes, and hypochlorite have been actively studied in recent years.[1-5] The major pathway of these reactions is considered to be the heterolytic cleavage exemplified in eq 1.[6,7] The oxidation of

$$>Fe^{+} + RC(=O)OOH \longrightarrow >Fe^{+}{=}O + RC(=O)OH \qquad (1)$$

phenols, alkenes, and hydrocarbons by the intermediate "oxene" indicates that these compounds are biomimetic model systems for peroxidases and for cytochrome P-450.[1-7] While there has been some indication that hydrogen peroxide or hydroperoxides react with hemins differently from other oxidants[8,9] sometimes evolving dioxygen,[10,11] the mechanisms of reactions of these oxidants have not been studied in detail, and no model system for catalase[12] has been presented.

Because compound I, the iron(IV) radical cation, has been observed with catalase, the mechanism of hydrogen peroxide decomposition must proceed in at least two steps.[12] We now report two experiments which reveal separately the mechanisms of each of these steps in a model system.

$$>Fe^{+} + H_2O_2 \rightarrow >Fe^{+}{=}O + H_2O \qquad (2)$$

$$>Fe^{+}{=}O + H_2O_2 \rightarrow >Fe^{+} + H_2O + O_2 \qquad (3)$$

First, we make use of the discovery by Balch et al. that $>Fe{=}O$ (i.e., a model compound for compound II of HRP and an Fe(IV) system) does not epoxidize alkenes.[13,14] Previous studies of the reaction of *tert*-butyl hydroperoxide with iron(III) porphyrins and alkenes revealed no epoxidation, a result interpreted as homolytic cleavage[7-9,15] producing Fe(IV) (reaction 4).

$$>Fe^{+} + ROOH \rightarrow >Fe^{+}{-}OH + RO^{\bullet} \qquad (4)$$

Finding that *t*-BuOOH is a substrate for $>Fe^{+}{=}O$ (see below), we reinvestigated this reaction with different ratios of hydroperoxide to norbornene. Figure 1 shows a plot of epoxide yield (direct and reciprocal) as a function of the concentration ratio, *t*-BuOOH/norbornene. The reciprocal plot extrapolates to 100% epoxide yield at a zero value of this ratio. Clearly, with use of the Balch result, this means that the cleavage is heterolytic as we had previously suggested from kinetic studies.[6a] Previous failures to find epoxide[8] resulted from the rapid reaction of the $>Fe^{+}{=}O$ with the hydroperoxide.

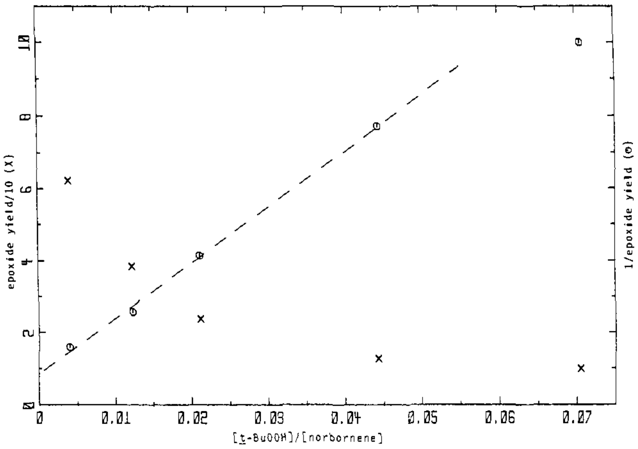

Figure 1. Plots of % yield (X) and 100/yield (O) vs. ratio of concentrations of *t*-BuOOH and norbornene for reactions in solutions containing 5 M norbornene, 10^{-3} M FeClTMP, and varying concentrations of *t*-BuOOH in methylene chloride after complete reaction. The reciprocal plot only approximates the kinetic descriptions but becomes more exact at low *t*-BuOOH concentrations.

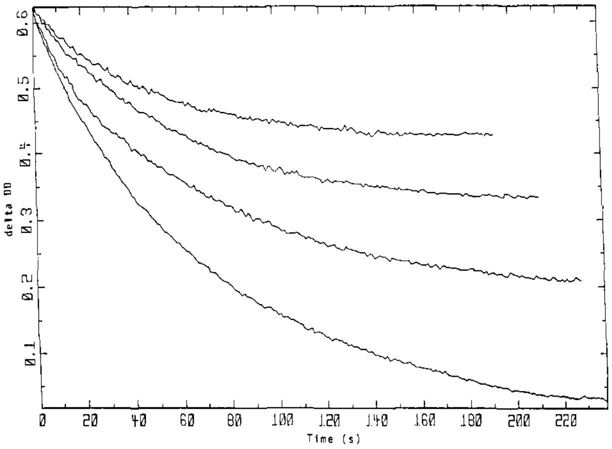

Figure 2. Plots of absorbance at 348 nm vs. time for solutions of 10^{-5} M FeClTMP, 3×10^{-4} M F_5PhIO, and 3×10^{-4} M, 1,4-diphenylbutadiene in $CH_2Cl_2/CH_3OH/H_2O$ (80:18:2) at 25 °C. Beginning with lower plot, solutions contained 0, 3×10^{-4}, 4.6×10^{-4}, and 8.8×10^{-4} M *t*-BuOOH.

In order to observe the second reaction (reaction 3), we took advantage of the rate constants shown below and measured by previously published methods.[16]

$$F_5PhIO + t\text{-}BuOOH \xrightarrow{k\,=\,30\ M^{-1}\,s^{-1}} F_5PhI + t\text{-}BuOH + t\text{-}BuOO\text{-}t\text{-}Bu \qquad (5)$$

$$t\text{-}BuOOH + >Fe^{+} \xrightarrow{k\,=\,9\ M^{-1}\,s^{-1}} >Fe^{+}{=}O + t\text{-}BuOH \qquad (6)$$

$$F_5PhIO + >Fe^{+} \xrightarrow[CH_2Cl_2/MeOH/H_2O]{k\,\cong\,10^{4}\ M^{-1}\,s^{-1}} F_5PhI + >Fe^{+}{=}O \qquad (7)$$

At the proper concentrations reaction 7 is the only direct reaction of the $>Fe^{+}$. Therefore in the presence of *t*-BuOOH, its reaction with the "oxene" ($>Fe^{+}{=}O$) can be independently observed. Interestingly, although Fe(III) tetramesitylporphyrin (FeClTMP) is instantly destroyed by pentafluoroiodosylbenzene,[16]

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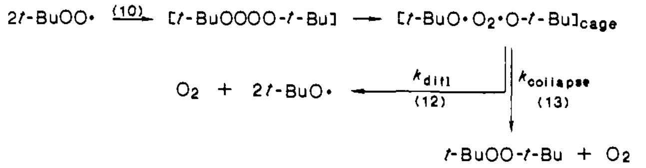
addition of 0.2 M t-BuOOH or H_2O_2 completely protects the hemin, affording *tert*-butyl alcohol, di-*tert*-butyl peroxide, and dioxygen from the hydroperoxide and dioxygen from hydrogen peroxide.[17] These products are diagnostic for hydroperoxy radical production, showing that the sequence of reactions for t-BuOOH is as shown below.[18]

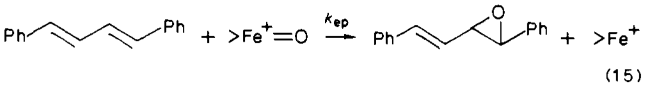
$$F_5PhIO + {>}Fe^{+} \rightarrow {>}Fe^{+}{=}O + F_5PhI \quad (8)$$

$$>Fe^{+}{=}O + t\text{-BuOOH} \rightarrow t\text{-BuOO}\cdot + {>}Fe^{+}{-}OH \quad (9)$$



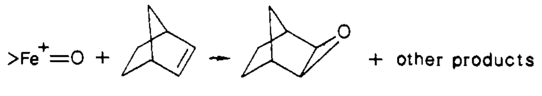
$$t\text{-BuO}\cdot + t\text{-BuOOH} \rightarrow t\text{-BuOH} + t\text{-BuOO}\cdot \quad (14)$$

To measure the rates of these reactions relative to rates of epoxidation, we have used a kinetic technique developed for relative epoxidation rates.[19] We follow the disappearance of the 348-nm peak of 1,4-diphenylbutadiene as an indication of epoxidation.



(15)

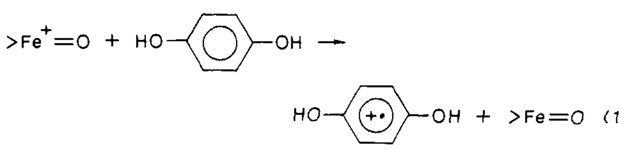
The pseudo-first-order rate constant is identical with that obtained by observing RIO disappearance.[16] However, addition of a second alkene, t-BuOOH or H_2O_2, results in a reduction of consumption of 1,4-diphenylbutadiene as seen in Figure 2. Kinetic analysis of this figure[19] reveals $k_9/k_{15} = 1.1$, the ratio of bimolecular rate constants for reactions of t-BuOOH and 1,4-diphenylbutadiene. By using the previously determined value[19] of k_{15}/k_{16} we calculate $k_9/k_{16} = 70$ and a similar ratio with hydrogen peroxide. This explains previous failures to observe epoxidation. From previous estimates of a minimum value[16c] of $k_{16} \geq 10^5$ M^{-1} s^{-1} we tentatively estimate that k_9 is near 10^7 M^{-1} s^{-1}. The catalase reaction is naturally efficient.



(16)

By using the same kinetic technique in deuteriated solvents (where hydroperoxides and hydroquinone are deuteriated) we observe the primary isotope effects for reactions 9, 17, and 18 to be 4.1, 3.1, and 1.3, respectively. These isotope effects suggest electron transfer for oxidation of hydroquinone[20] and hydrogen abstraction for reactions 9 and 17.

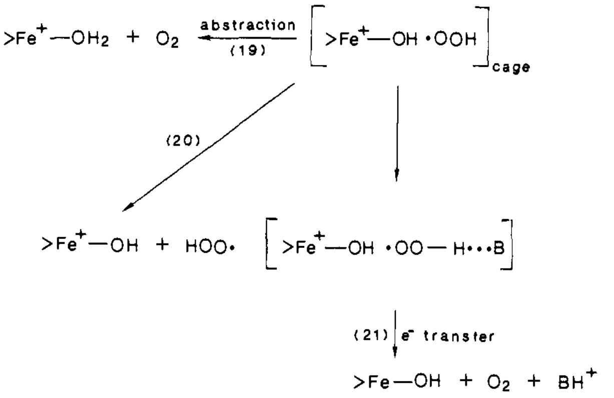
$$>Fe^{+}{=}O + H_2O_2 \rightarrow HOO\cdot + {>}Fe^{+}{-}OH \quad (17)$$



(18)

The rapid rate of hydrogen abstraction (9) suggests that the acid catalysis of this step conjectured from the catalase crystal structure[21] is unnecessary. The ionic and hydrogen-bonding groups on the distal side of the heme in catalase,[21] as in peroxidase,[22] are probably needed for the general acid catalysis of the first step,[22] already demonstrated in model compound studies.[6a,10]

We can therefore write the first and second steps in the model catalase reactions as reaction 2 followed by reaction 17. The third step in the catalase reaction might be cage abstraction, cage electron transfer, or diffusion followed by either of these. Details of this step are under study.



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A New Low-Temperature Route to Metal Polychalcogenides: Solid-State Synthesis of $K_4Ti_3S_{14}$, a Novel One-Dimensional Compound

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During the last few years a large number of new *molecular* sulfides have been reported.[1] These compounds are of interest as models for biologically and catalytically important sulfides.[1a,b] They exhibit a variety of polysulfide ligands (S_x^{2-}, $x = 1,2...$) and a number of sulfur-bonding modes.[1d] Concomitant with this work on molecular sulfides has been an increased activity in *nonmolecular* (i.e., extended structure) sulfides. This work has been fueled by the catalytic and electronic properties of these materials.[2] We report here a new synthetic approach that allows for the low-temperature synthesis of new low-dimensional polychalcogenides, a class of compounds that bridges the chemistry of the molecular and solid-state compounds.

Molten alkali metal polysulfides have previously been used as fluxes in the crystal growth of solid-state sulfides.[3-5] These previous reports have involved syntheses at high temperatures (>800 °C), and none of the compounds prepared contains polysulfide ions. We have used A_2Q/Q melts (A = alkali metal, Q = S or Se) for the synthesis at low temperatures of new low-

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