because of 2-fold ruthenium participation; however, even these data are clearly compatible[7a] with an overwhelming ligand character of the singly occupied MO. Major anisotropy effects appear, however, if carbonyl-containing radical ligands with strong mixing of ligand and metal orbitals are employed.[26-28]

The results from this ESR study support the interpretation of spectroscopic and electrochemical differences between the redox series involving compounds **1-16**.[6] Furthermore, the results support the hopping model[3a-f] for homoleptic tris(ligand) systems on the time scale of the ESR experiment and show the effects of localization for heteroleptic systems. In spite of the limited information available from poorly resolved ESR spectra with very little g anisotropy, even the isotropic g factors of the radical complexes have proven valuable for analysis of the electronic structure: As has been demonstrated in previous studies,[12,14] the presence of more than one low-lying unoccupied orbital in nonreduced precursor complexes (and corresponding photoreactivity)[12,14] may be correlated via Chart II to small g values of the singly reduced complexes.

Acknowledgment. This work has been generously supported by Deutsche Forschungsgemeinschaft and Stiftung Volkswagenwerk. We also thank Degussa AG for a donation of chemicals and Dipl.-Chem. E. Roth and Dr. J. Jordanov (CENG, Grenoble, France) for assistance with the low-temperature ESR measurements.

Mechanisms of Reactions of Iron(III) Porphyrins with Hydrogen Peroxide and Hydroperoxides: Solvent and Solvent Isotope Effects

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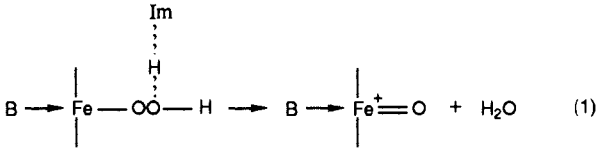
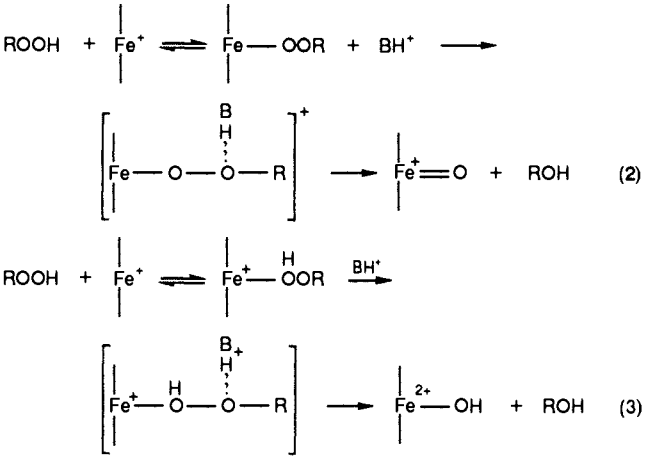
Abstract: The effect of solvent polarity and acidity and the solvent isotope effects on the reaction of iron(III) porphyrins with hydrogen peroxide, *tert*-butyl hydroperoxide, and peracids have been investigated. Both the solvent and solvent isotope effects on the reactions of hydroperoxides with hemins are almost identical with these effects on the reactions of hydroperoxides with dialkyl sulfides and the effects on the reaction of peracids with iron(III) porphyrins. Since both of the latter reactions are known to involve heterolytic cleavage of the O-O bond, this similarity provides strong evidence for heterolytic cleavage of hydroperoxide by reaction with hemins. The strong alcohol catalysis of the studied reactions provides a mechanistic rationale for the O-O bond cleavage in cytochrome P-450 in terms of general-acid catalysis by water in the enzyme site.

The reactions of hydrogen peroxide with peroxidases and catalase result in heterolytic cleavage of the oxygen-oxygen bond to produce a two-electron-oxidized "oxene" species,[1,2] also recently identified by using model hemin compounds.[3] Crystal structures of cytochrome c peroxidase[4] and catalase[5] reveal a general-acid/general-base apparatus in proper juxtaposition to assist the hydroxide leaving group, proposed to occur as shown.



(1)

This general-acid/general-base process has been mimicked in model systems with the demonstration that cleavage of peracids and hydroperoxides by simple hemins is catalyzed by added buffers[6-8] and by covalently attached bases or carboxylic acids[6a] as well as by electron donation by hemin substituents[6a] and by hydrogen bonding to the proximal imidazole.[6c,7c] Mechanisms for the general-base- and general-acid-catalyzed processes have therefore been concluded to occur as follows.[6-8]



A simplified form of the transition state in eq 2 is often written[6,7] as

(1) (a) Dunford, H. B.; Stillman, J. S. *Coord. Chem. Rev.* **1976**, *19*, 187. (b) Hewson, W. D.; Hager, L. P. In *The Porphyrins*; Dolphin, D., Ed.; Academic: New York, 1979; Vol. VII.

(2) (a) Deisseroth, A.; Douce, A. L. *Physiol. Rev.* **1970**, *50*, 319. (b) Schonbaum, G. R.; Chance, B. In *The Enzymes* (3rd Ed.); Boyer, P. D., Ed.; Academic: New York, 1976; Vol. 13, p 363.

(3) Groves, J. T.; Haushalter, R. C.; Nakamura, M.; Nemo, T. E.; Evans, B. J. *J. Am. Chem. Soc.* **1981**, *103*, 2884.

(4) (a) Poulos, T. L.; Freer, S. T.; Alden, R. A.; Edwards, S. L.; Skogland, U.; Takio, K.; Eriksson, B.; Xuong, N.; Yonetani, T.; Kraut, J. *J. Biol. Chem.* **1980**, *255*, 575. (b) Poulos, T. L.; Kraut, J. *Ibid.* **1980**, *255*, 8199.

(5) Vainshtein, B. K.; Melik-Adamyan, W. R.; Barynin, V. V.; Vagin, A. A.; Grebenko, A. I.; Borisov, V. U.; Bartels, K. S.; Fita, I.; Rossmann, M. G. *J. Mol. Biol.* **1986**, *88*, 49.

(6) (a) Traylor, T. G.; Lee, W. A.; Stynes, D. V. *J. Am. Chem. Soc.* **1984**, *106*, 755. (b) Traylor, T. G.; Popovitz-Biro, R. *Ibid.* **1988**, *110*, 239. (c) Traylor, T. G.; Ciccone, J. P. *J. Am. Chem. Soc.*, in press. (d) Ciccone, J. P.; Fann, W. P.; Xu, F., unpublished.

(7) (a) Zipplies, M. F.; Lee, W. A.; Bruice, T. C. *J. Am. Chem. Soc.* **1986**, *108*, 4433. (b) Bruice, T. C.; Zipplies, M. F.; Lee, W. A. *Proc. Natl. Acad. Sci. U.S.A.* **1986**, *83*, 4646. (c) Lee, W. A.; Yuan, L. C.; Bruice, T. C. *J. Am. Chem. Soc.* **1988**, *110*, 4277. (d) Balasubramanian, P. N.; Schmidt, E. S.; Bruice, T. C. *Ibid.* **1987**, *109*, 7865. (e) Zipplies, M. F.; Lee, W. A.; Bruice, T. C. *Ibid.* **1986**, *108*, 4443. (f) Bruice, T. C.; Balasubramanian, P. N.; Lee, R. W.; Lindsay Smith, J. R. *Ibid.* **1988**, *110*, 7891. (g) Lindsay Smith, J. R.; Balasubramanian, P. N.; Bruice, T. C. *Ibid.* **1988**, *110*, 7411.

(8) Groves, J. T.; Watanabe, Y. *J. Am. Chem. Soc.* **1986**, *108*, 507, 7834.

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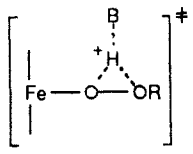


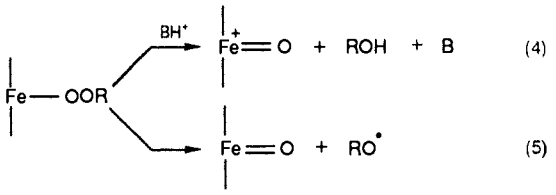
A

Therefore the model hemin studies are in accord with the mechanistic conclusions based upon the heme protein crystal structures.[3,4]

Because the ubiquitous enzyme, cytochrome P-450,[9] involves at some point the breaking of the O–O bond, it was expected that a similar catalytic apparatus for this process might be present, an expectation not realized when the crystal structure of P-450$_{cam}$ was determined.[10] The pocket in this protein contains no general acids or bases. The only group that might function in this way is water, which partially fills the site.

It is therefore of some importance to determine whether water or alcohols can function in this catalytic manner and to establish the relative importance of heterolytic and homolytic cleavage in the absence of efficient general acids or bases.

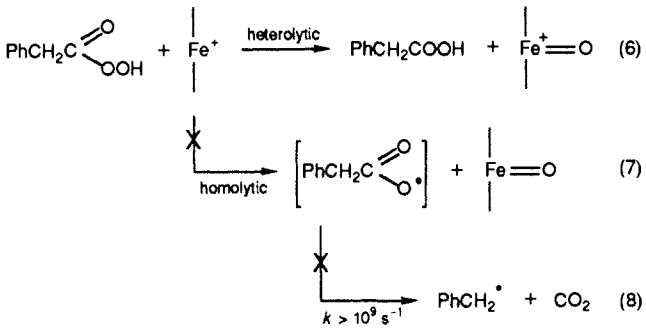
The species Fe–OOR in which R is hydrogen or an alkyl group is not likely to cleave to RO$^-$ in the absence of an acid. It therefore might take one of two pathways:



(4)

(5)

We have provided definitive evidence for heterolytic cleavage of peracids in this reaction by demonstrating that no carbon dioxide is evolved upon reaction of phenylperacetic acid.[6a,c,11]



(6)

(7)

(8)

The phenylacetoxy radical is known to decompose faster than diffusion rates and perhaps to have no individual lifetime.[12] Therefore, peracids react according to eq 4 in these solvents.

Finding that peracids and hydroperoxides display similar buffer catalyses and react with rates that increase with increasing stability of the RO$^-$ leaving group, we suggested that all these oxidants could be accommodated by reaction 4.[6a] Examples of general-acid/general-base catalyses of heterolytic processes abound, whereas buffer catalyses of homolytic bond cleavages are rare if they occur at all. This interpretation has also been adopted by Bruice et al. for the buffer-catalyzed reaction.[7e,13]

Several groups have reported product studies in the reactions of alkyl hydroperoxides with hemins that require the intermediacy of alkoxy radicals.[14-16] The source of these alkoxy radicals was generally suggested to be the homolytic cleavage of reaction 5. The alternative induced chain decomposition of hydroperoxides was not ruled out. In addition, our studies of rates of reaction as a function of ROOH structure, which we had interpreted as heterolytic cleavage,[6a] have been extended and interpreted in terms of homolytic cleavage of ROOH when the pK_a of ROH exceeds 11 or 12.[7a-f]

Therefore, although there are attractive alternatives to the suggested homolytic processes, there does not seem to be any unanimity of interpretation. Unfortunately, the definitive test for homolytic cleavage in terms of cage fragmentation of RO$^\bullet$, which we had applied to peracids, is not applicable to alkyl hydroperoxides since alkoxy radicals do not fragment in the cage.[17]

We have therefore chosen a less direct approach of determining the effects of solvent polarity or acidity, solvent isotope change, and buffer catalysis on rates of reactions of hemins with hydroperoxides and comparing these effects with those on known heterolytic processes involving similar reactions. The two heterolytic reactions are (1) reactions of peracids with hemins and (2) reactions of hydroperoxides with dialkyl sulfides.

Reaction 5, producing an alkoxy or hydroxy radical, will display rates of reaction that follow this stability and thus correlate with, for example, ROOH bond strengths.[18] However, homolytic processes producing alkoxy or other radicals are sensitive to neither solvent effects nor buffer catalysis.[19] Therefore, the general properties of polar solvent effects, dependence upon alcohol acidities or solvent isotope effects, will not be seen for this process (eq 5) unless there is an isotope-dependent preequilibrium. The homolytic reaction will not involve proton transfer in the rate-limiting step since the leaving group, i.e., the alkoxy radical, is not a strong base.

By contrast, reaction 4 involves charge separation and, more importantly, includes a proton transfer at the transition state. This suggests that the reaction, even in alcohols or water, could involve a proton transfer from either the solvent or the buffer. We have therefore studied the reaction in alcohol/methylene chloride mixtures using alcohols of varying pK_a values and have determined the pH dependence and the solvent deuterium isotope effect on the reaction of *tert*-butyl hydroperoxide, hydrogen peroxide, and peracetic acid. Additionally, solvent isotope effects for the buffer-catalyzed and extrapolated zero buffer rates in aqueous methanol solutions have been studied. Our results are inconsistent

Table I. Basicity Constants of Buffer Components

solvent[a]	*p*-nitrophenol (1) pK_b	*p*-nitrophenol (1) ΔpK_b[b]	collidine (2) pK_b	collidine (2) ΔpK_b[b]	hexafluoroacetone (3) pK_b	hexafluoroacetone (3) ΔpK_b[b]
H_2O/CH_3OH (80/20)	4.7	0.5	5.5	0.5		
H_2O/CH_3OH (40/60)	4.7	0.2			4.7	0.2
$CH_2Cl_2/CH_3OH/H_2O$ (80/18/2)	5.0	0.3	4.0	0.3		

[a] In H_2O, the pK_b values were found to be 6.8, 6.8, and 7.5, respectively, for **1**–**3**, in good agreement with literature values of 6.74–8.76,[20a] 6.57,[20b] and 7.5.[20c] [b] ΔpK_b = pK_b (protic solvent) − pK_b (deuterated solvent).

(9) *Cytochrome P-450*; Ortiz de Mongellano, P. R., Ed.; Plenum: New York, 1986.

(10) Poulos, T. L. In *Cytochrome P-450*; Ortiz de Montellano, P. R., Ed.; Plenum: New York, 1986; p 505.

(11) This finding has been confirmed elsewhere with Fe(III) tetraphenylporphyrin.[7c]

(12) (a) *Free Radicals*; Kochi, J., Ed.; Wiley: New York, 1973; Vol. 1, p 113. (b) Bartlett, P. D.; Hiatt, R. *J. Am. Chem. Soc.* **1958**, *80*, 1398.

(13) Recently the buffer-catalyzed reaction has been suggested to proceed by homolysis, but no evidence was provided for this suggestion.[7f]

(14) (a) Dix, T. A.; Marnett, L. *J. Am. Chem. Soc.* **1983**, *105*, 7001. (b) Lebeque, R.; Marnett, L. *Biochemistry* **1988**, *27*, 7060.

(15) (a) Renaud, J.-P.; Battioni, P.; Bartoli, J. F.; Mansuy, D. *J. Chem. Soc., Chem. Commun.* **1985**, 888. (b) Mansuy, D.; Devocelle, L.; Artrand, I.; Battioni, J. P. *Nouv. J. Chim.* **1985**, 9711.

(16) Balch, A. L., private communication.

(17) The suggestion that *tert*-butoxy radical cleaves in the cage in aqueous solution with a rate constant of $\sim 1.4 \times 10^6$ s^{-1} [7g] is unreasonable in view of the known diffusion rates of $>10^9$ s^{-1} in low-viscosity solvents.[12]

(18) *Free Radicals*; Kochi, J., Ed.; John Wiley and Sons: New York, 1973; Vol. II, p 697.

(19) Martin, J. C. In *Free Radicals*; Kochi, J., Ed.; John Wiley and Sons: New York, 1973; Vol. II, p 493.

(20) (a) *Solute–Solvent Interactions*; Coetzee, J. F., Ritchie, C. D., Eds.; M. Peliker: New York, 1969; Vol. 1, p 411. (b) *Handbook of Chemistry and Physics*, 5th ed.; CRC: Cleveland, OH, 1972; p D119. (c) *The Proton: Application to Organic Chemistry*; Stewart, R., Ed.; Academic, New York, 1985; p 43.

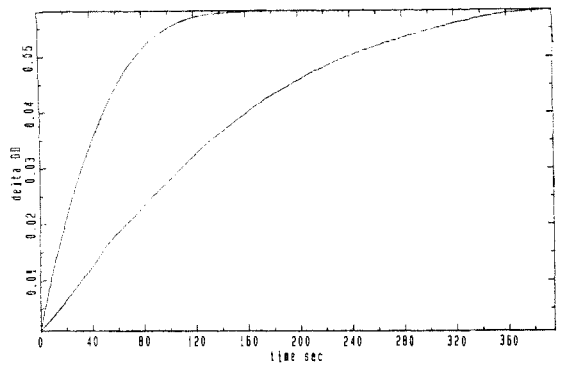


Figure 1. Increases of absorbance at 630 nm (first-order kinetic behavior) due to the formation of the phenoxy radical in H_2O/CH_3OH (upper curve) or D_2O/CH_3OD (lower curve) (4:1 volume ratio). "Water-soluble phenol", 7.2×10^{-3} M; H_2O_2, 1.5×10^{-4}; collidine/collidine HCl, 0.02/0.02 M; microperoxidase, 5.6×10^{-6} and 3.0×10^{-6} M in the protiated and deuterated solutions, respectively.

with homolytic cleavage of the O–O bond in these reactions. Additionally these studies provide a likely mechanism for the O–O bond cleavage in cytochrome P-450 through catalysis by the water that is present in the site.

Experimental Section

Materials. The following chemicals were used without purification: *p*-nitrophenol (Matheson), collidine (Aldrich, 99%), tetrabutylammonium hydroxide (Aldrich, 40%), hexafluoroacetone trihydrate (Aldrich, 98%), methanol (Fisher, spectra grade), microperoxidase (Sigma), deuterium oxide (Aldrich, 99%), CH_3OD (Aldrich, 99%), 2-propanol (Fisher, spectra grade), *tert*-butyl alcohol (Mallinckrodt, HPLC grade), 2,2,2-trifluoroethanol (Aldrich, 99%), 1,1,1,3,3,3-hexafluoro-2-propanol (Aldrich, 99%), *tert*-butyl hydroperoxide (Aldrich, 3 M in toluene), peracetic acid (FMC, 40%), hydrogen peroxide (Fisher, 30%). Protohemin mono-3-(1-imidazolyl)propanamide chloride monomethyl ester (chelated protohemin chloride), collidine hydrochloride, and [2-methyl-2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propyl]ammonium chloride ("water-soluble phenol") were obtained from previous studies.[6a] Octaethylporphyrin (Aldrich) was converted to the iron(III) complex as previously described.[6a] Dichloromethane (Fisher, spectra grade) was distilled over calcium hydride. The 2,4,6-tri-*tert*-butylphenol (Aldrich) was recrystallized from $EtOH/H_2O$.

Methods. The pK_b values of buffer components collidine and hexafluoroacetone in the two protic and deuterated solvents were determined by first titrating *p*-nitrophenol in each solvent by standard techniques and subsequently using *p*-nitrophenol as an indicator of the pH or pD of solutions buffered by various ratios of base to acid with the two buffer components above. Table I lists the pK_b values of the buffers employed.

Polarities of the mixed solvents (CH_2Cl_2/ROH) were determined by the method of Taft et al.[21] using the $\lambda_{max} \sim 430$ nm of *o*-nitro-*N*-methylaniline. The relative λ_{max} shift $(\lambda_{mixture} - \lambda_{alc})/(\lambda_{CH_2Cl_2} - \lambda_{alc})$ as a function of alcohol concentration will be presented in the Results section.

In the solvent studies, solutions in dichloromethane or alcohol/dichloromethane mixtures of 10^{-2} M tri-*tert*-butylphenol and 10^{-6}–10^{-5} M chelated protohemin chloride (concentration determined by absorption at the Soret peak ($\lambda = 405$ nm, $\epsilon = 10^5$ M^{-1} cm^{-1}) were used.[6a,c] The initial rates were determined by the appearance of the 630-nm absorbance of the tri-*tert*-butylphenoxyl radical after addition of *tert*-butyl hydroperoxide.[6a,c] Varying original concentrations revealed the reactions to be first order in the hemin, first order in *tert*-butyl hydroperoxide, and independent of phenol concentration as previously reported.[6c] The second-order rate constants were obtained by dividing the zero-order rates by the concentrations of *tert*-butyl hydroperoxide and hemin. Similar methods were employed in the study of octaethylhemin chloride in dichloromethane/methanol/water mixtures.

The hexafluoroacetone buffer studies were carried out by preparing solutions in mixtures containing 1 volume of water (or D_2O) to 1.5 volumes of methanol (or CH_3OD) containing 10^{-3}–10^{-2} M [2-methyl-2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propyl]ammonium chloride, 10^{-3}–10^{-2} M hexafluoroacetone, 10^{-3}–10^{-2} M tetrabutylammonium hydroxide, and 10^{-6}–10^{-5} M chelated protohemin. The oxidant, *t*-BuOOH or CH_3CO_3H, was added to start the reaction, which was followed by the increase in the phenoxyl radical absorption at 630 nm. Pseudo-first-order decays, typified by that of Figure 1, were observed in these reactions. Second-order rate constants were determined by dividing the first-order rate constants by hemin concentrations.

Similar methods were used in the microperoxidase studies in solvent mixtures containing 4 volumes of water (or D_2O) to 1 volume of methanol (or CH_3OD). The oxidants H_2O_2 or CH_3CO_3H ($\sim 10^{-4}$ M) were added to solutions of 10^{-7}–10^{-6} M microperoxidase (assayed by its Soret absorption), 10^{-3}–10^{-2} M of [2-methyl-2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propyl]ammonium chloride, 10^{-3}–10^{-2} M collidine, and 10^{-3}–10^{-2} M collidine hydrochloride to start the reaction, and the pseudo-first-order decay of the oxidant was measured and converted to second-order rate constants as described above. Concentrations of oxidants, hemin, and buffer were varied in order to determine dependencies on concentration of each. In all cases, in all three studies, no appreciable reaction occurs without the hemin catalyst. Data will be presented in the plots described below.

(21) Kamlet, M. J.; Abboud, J. L.; Taft, R. W. *J. Am. Chem. Soc.* **1977**, *99*, 6027.

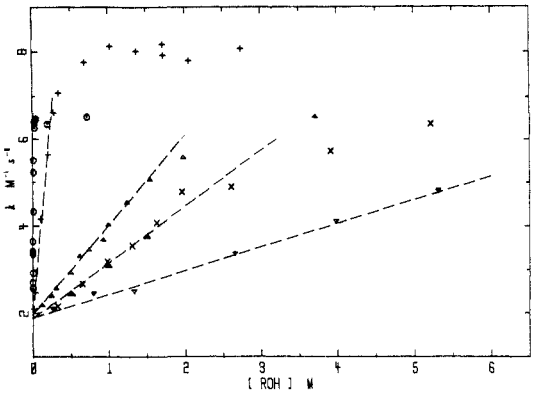


Figure 2. Plots of the second-order rate constants for the reaction of chelated protohemin with *tert*-butyl hydroperoxide in dichloromethane against varying concentrations of added alcohols. ⊙, $(CF_3)_2CHOH$; +, CF_3CH_2OH; △, CH_3OH; ▲, CH_3OD; ×, $(CH_3)_2CHOH$; ▽, *t*-BuOH.

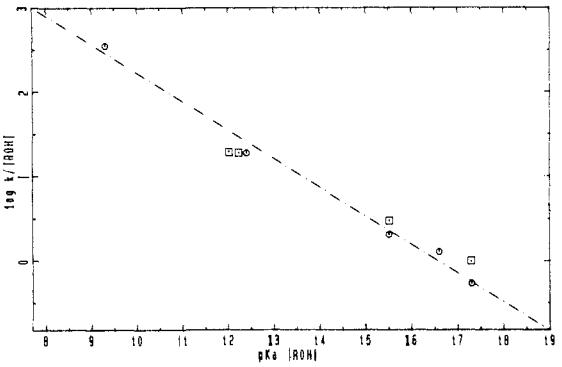


Figure 3. Plot of the log (slope) of the lines in Figure 2 (log k_{ROH}) against the pK_a of the added alcohols. Squares refer to the R_2S reaction. See the text.

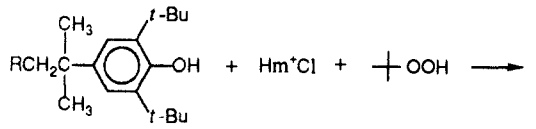
Table II. Slopes and Intercepts of the Plots of Figure 2 ($k_{obsd} = k_i + k_s[ROH]$)

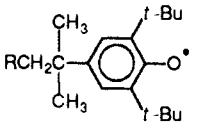
ROH	pK_a	k_s	k_i
t-BuOH	17.3[a]	0.54	1.9
i-PrOH	16.6[a]	1.29	1.9
CH_3OH	15.5[a,b]	2.05	2.0
CF_3CH_2OH	12.4[b]	18.9	1.9
$(CF_3)_2CHOH$	9.3[b]	35.0	1.9

[a] Reference 22. [b] Reference 20c, p 24.

Results

Effects of Alcohol Concentration and Structure on Rates of ROOH Reactions. The reaction of chelated protohemin chloride with *tert*-butyl hydroperoxide was studied in methylene chloride/alcohol solvent mixtures by observing the appearance of phenoxyl radical **4a**. Rates were first order in hydroperoxide as previously reported[6a] and were converted to second-order rate constants by dividing by the hemin concentration. Plots of sec-





(9)

4A, R = H
4B, R = NH_3^+

ond-order rate constants for this reaction in varying concentrations of several alcohols are seen in Figure 2 where the dashed lines are correlations of rates with concentrations. Table II gives the low concentration slopes and intercepts of these correlations. Figure 3 shows a plot of the log (slope) against the published pK_a values of the alcohols.[6a,22]

In order to ascertain whether these increases in rate constants with increasing alcohol concentration were due to changes in solvent polarity, we determined the solvent polarity in these mixtures using the wavelength shift of *o*-nitro-*N*-methylaniline as described by Taft et al.[21] Plots of wavelength shift against percentage of alcohol are shown in Figure 4 on the same scale as that of Figure 2. It can be seen by comparing Figures 2 and 4 that the increase in rate upon addition of small amounts of alcohols are not a function of solvent polarity but of alcohol acidity. Consistent with this conclusion is the observation that the rates become independent of alcohol concentration at high alcohol concentrations (Figure 2).

In order to determine the effect of added hydroxylic solvents on the rate of reaction of hemin with hydroperoxides in the absence of the proximal imidazole, we have determined rates of reaction of *tert*-butyl hydroperoxide with iron(III) octaethylporphyrin chloride in dichloromethane and in mixtures of dichloromethane and added quantities of a 9:1 (by volume) mixture of methanol/water. The constants are plotted as a function of methanol concentration in these mixtures in Figure 5. The rate constant in pure dichloromethane is 3×10^{-2} M^{-1} s^{-1}. For the iron(III) tetraphenylporphyrin chloride the rate constant is 2×10^{-2} M^{-1} s^{-1}. A similar plot for the reaction of *m*-chloroperbenzoic acid is shown in Figure 6.

Solvent Isotope Effects. We have used two different hemins, three different solvent systems, and two different buffers, one of which does not display appreciable buffer catalysis of the reaction. Having previously shown that ionic strength has a negligible effect upon these rates,[6a] we did not maintain constant ionic strength.

A. Chelated Protohemin Chloride in Aqueous Methanol with Hexafluoroacetone (p$K_a^{H_2O}$ = 6.5) as Buffer. After the pK_b of *p*-nitrophenoxide ion was determined in a given solvent (60:40 CH_3OH/H_2O by volume), this value was used to determine the pK_b of $(CF_3)_2(OH)O^-$ (pK_b = 4.7) in the same solvent. The pK_b values of this and other buffer components in three of the solvents used in this study are shown in Table I. Deuterated solvents are also included in this table. Plots of second-order rate constants for the reaction of *t*-BuOOH and CH_3CO_3H with chelated protohemin in CH_3OH/H_2O and CH_3OD/D_2O against buffer concentrations are shown in Figures 7 and 8. Summaries of slopes and intercepts from such plots are given in Tables III and IV. Since the rates are relatively independent of either buffer concentration or pH in the range studied, the solvent isotope effects for the reactions not catalyzed by buffer are easily established to be $k_H^0/k_D^0 \sim 2$ for both peracid and hydroperoxide.

B. Microperoxidase in Methanol/Water with Collidine Buffers. Microperoxidase, the undecapeptide obtained from cytochrome *c*,[23] was used as catalyst at 10^{-6}–10^{-7} M concentration in 20:80 $MeOH/H_2O$ (by volume). In this solvent, the pK_b of *p*-nitrophenoxide was found to be 4.7 and that of collidine to be 5.5. Both increased by 0.5 pK unit in CH_3OD/D_2O. Kinetics of reaction were determined by using the same phenol and the same method as that described in A. Phenol concentrations were maintained around $(7–9) \times 10^{-3}$ M to ensure complete trapping of the iron intermediate. Hydrogen peroxide concentrations ranged from 1×10^{-4} to 4×10^{-4} M and buffer ratios ranged from 1:1 to 10:1 BH^+/B with one study at a 1:10 ratio. Plots of second-order rate constants versus total buffer concentrations are shown in Figure 9 for hydrogen peroxide and Figure 10 for peracetic acid. The slopes and intercepts of these plots are given in Table V. Clearly, both reactions are similarly buffer catalyzed and both reactions have solvent isotope effects $k_H/k_D \sim 2$.

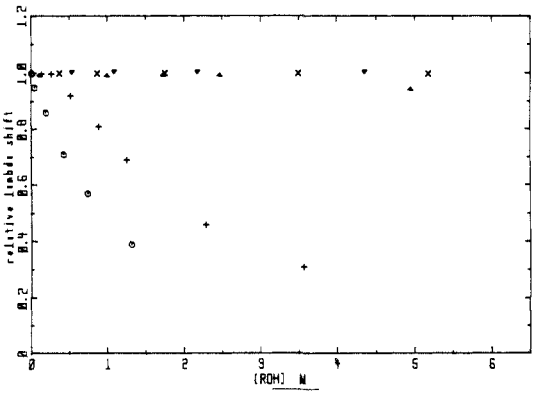


Figure 4. Plots of the λ_{max} shift of the 430-nm peak of *o*-nitroaniline $(\lambda_{max} - \lambda_{alc})/(\lambda_{CH_2Cl_2} - \lambda_{alc})$ against varying concentrations of alcohols in dichloromethane. ⊙, $(CF_3)_2CHOH$; +, CF_3CH_2OH; △, CH_3OH, ×, $(CH_3)_2CHOH$; ▽, *t*-BuOH.

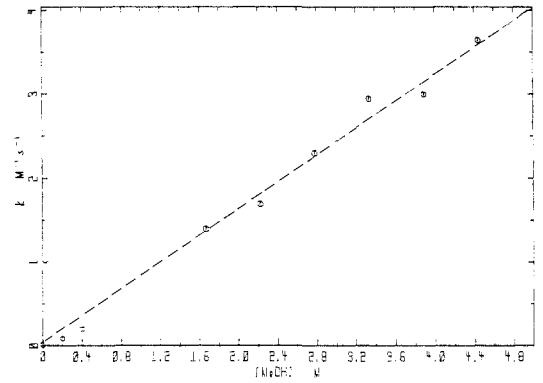


Figure 5. Plot of the second-order rate constants for the reaction of *tert*-butyl hydroperoxide with iron(III) octaethylporphyrin chloride (based upon the production of 2,4,6-tri-*tert*-butylphenoxyl radical at 25 °C) in dichloromethane containing various amounts of a 90:10 mixture of methanol/water calculated as molarity of methanol.

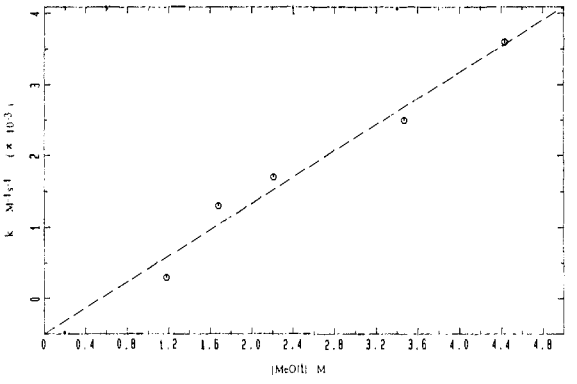


Figure 6. Plot of second-order rate constants for the reaction of *m*-chloroperbenzoic acid with iron(III) octaethylporphyrin, as in Figure 5.

Discussion

We have previously observed a linear increase in the rates of reaction of hydroperoxides, hydrogen peroxide, and peracids with

(22) Ballinger, P.; Long, F. A. *J. Am. Chem. Soc.* **1960**, *82*, 795.
(23) (a) Tuppy, H.; Paleus, S. *Acta Chem. Scand.* **1955**, *9*, 353. (b) Paleus, S.; Ehrenberg, A.; Tuppy, H. *Ibid.* 363.

Table III. Slopes (k_c), Intercepts (k_0), and Solvent and Buffer Isotope Effects Calculated from Figure 7 for the Reaction with *tert*-Butyl Hydroperoxide ($k_{obsd} = k_0 + k_c$[buffer])[a]

	H solvent[c]			D solvent[c]				
B^-/BH^b	pOH[d]	k_0	k_c	pOD[d]	k_0	$(k_H/k_D)_0$[e]	k_c	$(k_H/k_D)_c$[e]
0.2	5.42	5.3×10^2	7.3×10^3					
0.5	5.02	4.9×10^2	7.1×10^3	4.82	2.2×10^2	2.2	3.3×10^3	2.5
1	4.72	4.7×10^2	7.0×10^3	4.52	2.0×10^2	2.3 (2.2)[f]	3.3×10^3	2.1 (2.2)[f]
2	4.52	$\sim 4.4 \times 10^2$	$\sim 7.3 \times 10^3$	4.22	1.7×10^2	2.5	3.8×10^3	1.9

[a] Units: k_{obsd}, k_0, $M^{-1}\ s^{-1}$; k_c, $M^{-2}\ s^{-1}$. [b] B^-, $(CF_3)_2C(OH)O^-$; BH, $(CF_3)_2C(OH)_2$. [c] CH_3OH/H_2O (60:40) or CH_3OD/D_2O (60:40), volume ratio. [d] Calculated from pOH = pK_b + log $[B^-]/[BH]$. pK_b, $(CF_3)_2C(OH)O^-$, 4.72 and 4.52 in CH_3OH/H_2O (60:40) and CH_3OD/D_2O, respectively. [e] k(H solvent)/k(D solvent). [f] Ratio of k(pOH = 4.52)/k(pOD = 4.52).

Table IV. Slopes (k_c), Intercepts (k_0), and Solvent and Buffer Isotope Effects Calculated from Figure 8[a,g]

	H solvent[c]			D solvent[c]		
B^-/BH^b	pOH[d]	k_0	k_c	pOD	k_0	$(k_H/k_D)_0$[e]
0.5	5.02	3.6×10^4	8.1×10^4	4.82	1.8×10^4	2.0
1	4.72	3.4×10^4	9.6×10^4	4.52	1.6×10^4	2.2 (2.1)[f]
2	4.52	3.3×10^4	7.0×10^3	4.22	1.4×10^4	2.3

[g] Footnotes are given in Table III.

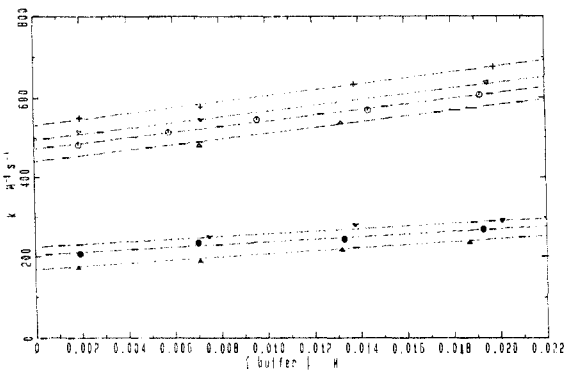


Figure 7. Plots of second-order rate constants for the reaction of *t*-BuOOH with chelated protohemin chloride in 60:40 (volume ratio) methanol/water (upper lines) and CH_3OD/D_2O (lower lines) against total buffer concentration. The buffer is $(CF_3)_2C(OH)_2$. Buffer ratios (B^-/BH), top to bottom, 0.2, 0.5, 1.0, 2.0, 0.5, 1.0, and 2.0. The trap phenol is **4B** at 0.01 M.

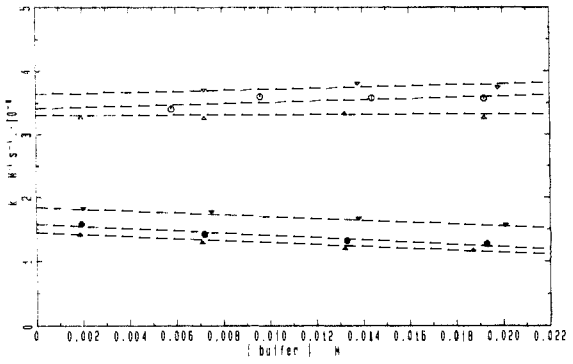


Figure 8. Plots of second-order rate constants for the reaction of peracetic acid with chelated protohemin chloride against total buffer concentration, as in Figure 7. Buffer ratios, top to bottom, 0.5, 1.0, 2.0, 0.5, 1.0, and 2.0.

iron(III) porphyrins with increasing collidine or acetate buffer concentrations.[6a,c] Bruice et al. have further shown that there can be both general-acid and general-base components to this catalysis.[7a] These results can be summarized in the following equation, where k_B and k_{BH^+} are the acid and base forms of general catalysis and k_{ROH} is the rate at zero buffer concentration in an alcohol or water solvent.

$$k_{obsd} = [Hm^+][ROOH][k_{ROH}[ROH] + k_B[B] + k_{BH^+}[BH^+]] \quad (10)$$

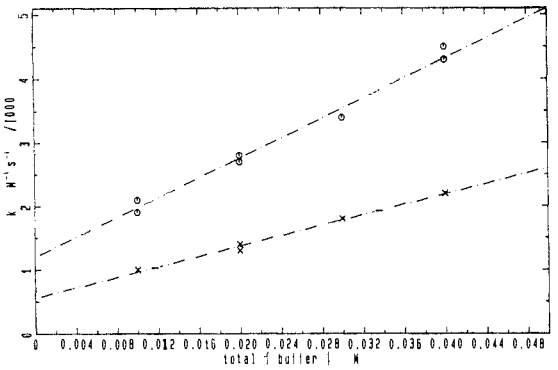


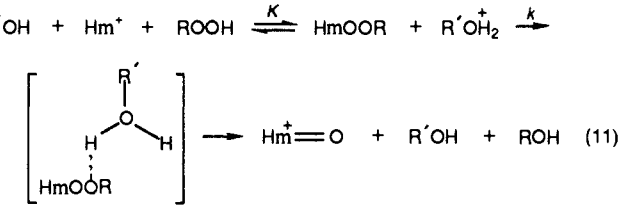
Figure 9. Plots of second-order rate constants for the reaction of microperoxidase with hydrogen peroxide (2×10^{-4} M) (followed by phenoxyl radical appearance) as a function of total buffer concentration. (pH = 7.5, pD = 8.2) Microperoxidase, 3×10^{-7} M; solvent, water/methanol (D_2O/CH_3OD) 80:20 volume ratio. Phenol (**4B**), 8×10^{-3} M. Protic solvent, ⊙; deuterated solvent, ×. Collidine/collidine hydrochloride ratio: 1.0 (data for 0.1 ratio not shown).

Table V. Slopes, Intercepts, and Solvent and Buffer Isotope Effects Calculated from Figures 9 and 10 ($k_{obsd} = k_0 + k_c$[buffer])[a]

		H_2O_2		CH_3CO_3H	
solvent	pH	k_0	k_c	k_0	k_c
H	6.5	1.2×10^3	3.7×10^4	1.5×10^5	1.5×10^6
D	7	6.1×10^2	1.4×10^4	5.8×10^4	5.6×10^5
k_H/k_D		2.0	2.6	2.6	2.6
H	7.5	1.2×10^3	7.9×10^4	7.7×10^4	2.0×10^6
D	8	5.6×10^2	4.1×10^4	3.0×10^4	9.7×10^5
k_H/k_D		2.1	1.9	2.6	2.0

[a] Microperoxidase (MP-11), 10^{-6}–10^{-5} M. "Water-soluble phenol", 7×10^{-3} M. Buffer, 10^{-2}–10^{-1} M. H_2O_2 and CH_3CO_3H, 1.3×10^{-4} M. H_2O/CH_3OH (80:20).

Solvent Effects. We now find that the k_{ROH}[ROH] term is, in fact, dependent upon concentration and type of ROH solvent at low concentrations of ROH. This effect might operate in either the preequilibrium or the O–O bond-breaking step. Because more acidic R'OHs accelerate the rate to a greater extent, whereas, according to eq 11,



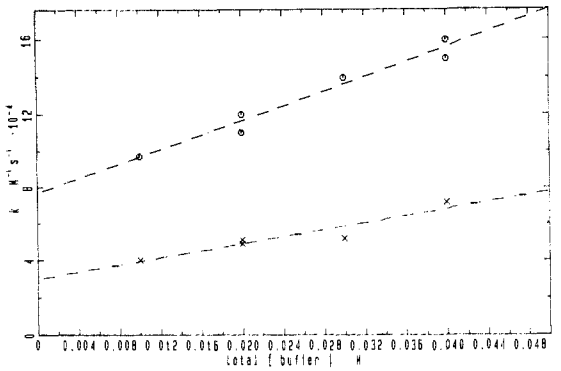
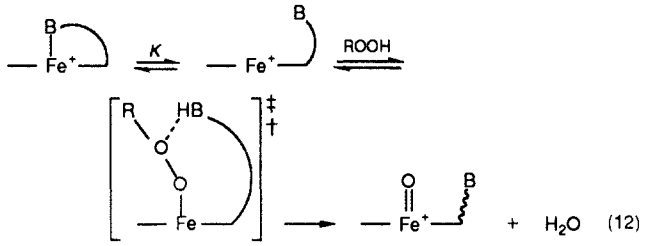


Figure 10. Plots of second-order rate constants against total buffer concentration for the reaction of microperoxidase with peracetic acid (2×10^{-4} M). Symbols and conditions are the same as in Figure 9.

the opposite effect should accrue from changes in K, we attribute the alcohol effect to a general catalysis of the rate-limiting bond cleavage, k, just as in the case of the buffer catalysis.

The increase in rate with alcohol concentration in dichloromethane is linear in alcohol concentration at low concentrations of alcohols, as seen in Figure 2. Furthermore, a plot of the initial slopes log $[d(k_{R'OH})/d[R'OH]]$ versus $pK_a^{R'OH}$ (Figure 3) shows a reasonable Brønsted relationship with a slope of −0.34. These results predict that the slope should have a solvent deuterium isotope effect. This was observed (Figure 2) and will be discussed below. The increase in alcohol acidity is expected to shift K of eq 11 to the left, thus reducing the rate. The alcohol acidity effect is therefore one of general-acid catalysis.

The acceleration provided by added methanol ($k_{slope}/k_{intercept}$) is not large ($k_{slope}/k_{intercept} = 1$) for the case of chelated protoheme, which already has an accelerated rate (1.9 M^{-1} s^{-1}) compared to octaethylhemin chloride (2×10^{-2} M^{-1} s^{-1}) (Table II). This acceleration of 100-fold by the proximal base accrues at least in part from proximal basicity. However, some of the base could be free and would then act as an internal general base.



(12)

Therefore it is of interest to determine the acceleration of rates of reaction of simple hemin. Figure 5 shows the increase in rate with increase in methanol (and water) concentration. The $k_{slope}/k_{intercept}$ value is 40, indicating a much greater acceleration in the absence of proximal imidazole. For the MCPBA reaction the slope/intercept value is ~10. This substantial acceleration of the rate by alcohols is consistent with heterolytic cleavage in alcohol or aqueous solvents.

Solvent Isotope Effects. A further indication of acid catalysis by alcohols (or water) derives from the solvent deuterium isotope effects. With both collidine buffers, which show large slopes, and hexafluoroacetone buffers, which show small slopes, the rates extrapolated to zero buffer concentration show a solvent deuterium isotope effect near 2.0 for *t*-BuOOH reaction with chelated protohemin (see Tables III and IV). Furthermore, this isotope effect is similar to that obtained with peracetic acid where heterolytic cleavage is well established. In addition, the isotope effect on the buffer term (k_{Buff}) is also near 2. It can also be seen in Figure 2 that the slope of the plot of the second-order rate constants against alcohol concentration is 1.9 times greater for CH_3OH than for CH_3OD, confirming the conclusion that this acceleration involves proton transfer.

We interpret these data to mean that hydroperoxides, like peracids, are cleaved by hemins in a heterolytic manner with general-acid/general-base catalysis as long as the reactions are in polar solvents. Solvent isotope effects in the range of 2.0 are typical of reactions involving proton transfer.[24]

This catalysis by alcohols requires that eq 10 be expanded to

$$k_{obsd} = [Hm^+][ROOH][k_0 + k_{ROH}[ROH] + k_B[B] + k_{BH^+}[BH^+]] \quad (13)$$

An equation that would describe the reaction over a wide pH range, such as that reported by Bruice et al.,[7] would require terms in the lyate and/or lyonium ions. We omit these here because in the neutral pH range of interest to us (pH = 5–8) there is only a small pH dependence and because at high pH values hydroxyhemin might be involved.[7]

Although the buffer-catalyzed reactions are, by definition, processes involving some kind of proton transfer in the rate-limiting step consistent with the isotope effect, $(k_H/k_D) \cong 2$, the solvent-catalyzed process could conceivably involve changes in preequilibrium. Thus, the solvent isotope effect could result from the 0.5 difference between pH and pD, the pD buffer being more basic. However, as can be seen from the figures and from previous studies in our laboratories[6a] and those of Bruice,[7] these cleavage reactions increase in rates slightly in the pH range studied as the pH is increased. Therefore, since the deuterated buffer solution is more basic than the protiated solution, the pH effect should give $k_H/k_D < 1$. This means that the solvent isotope effects, $k_H/k_D \cong 2$, are actually minimum isotope effects. The k_{ROH}/k_{ROD} for the HFA-buffered system can be calculated at pH = pD by using the data in Table IV. A slight pH extrapolation to afford rates under these conditions gives $(k_{ROH}/k_{ROD})_{pH=pD} \cong 2.1$. It is also satisfying that this isotope effect is about the same as k_B^H/k_B^D (Tables III and IV) calculated from the slopes of Figures 7 and 8.

Comparisons with Known Heterolytic Cleavage Reactions. Reactions of hydroperoxides with dialkyl sulfides

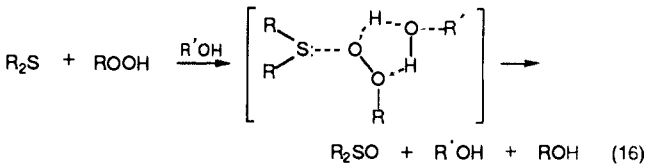
$$ROOH + R_2S \xrightarrow{k} ROH + R_2S\text{-}O \quad (14)$$

and the reactions of peracids with hemins

$$RC(O)OOH + Hm^+ \rightarrow Hm^+O + RCO_2H \quad (15)$$

have been firmly established as heterolytic reactions.[6a,25,26] It is therefore of some interest to compare the responses of these reactions to changes in structure, solvent, etc. with those of the reaction in question here, that of hydroperoxides with hemins.

First, it can be seen from the intercepts in Figures 2 and 5 that the rate of reaction of chelated prothemin with *tert*-butyl hydroperoxide increases from ~2 M^{-1} s^{-1} in methylene chloride to 400 M^{-1} s^{-1} in 60% aqueous methanol. Similar increases are seen with peracids. The plot in Figure 3 also illustrates the large effect of protic solvents. The reaction of sulfides with alkyl hydroperoxides is very sensitive to solvent polarity and autoprotolysis constant. The mechanism of this reaction discussed in terms of general-acid catalysis by Edwards et al.[25] and by Bruice et al.[26,27] is



(16)

The similarities of structure and solvent effects reported for reaction 16 by Edwards et al.[25] to those reported here are striking. For example, hydrogen peroxide reacts about ~20 times faster than does *tert*-butyl hydroperoxide with R_2S. With chelated protohemin this ratio is ~10.[28] This is the expected result for

(24) Wiberg, K. B. *Chem. Rev.* **1955**, *55*, 713.
(25) Dankleff, M. A. P.; Curci, R.; Edwards, J. O.; Pyun, H. *J. Am. Chem. Soc.* **1968**, *90*, 3209.
(26) Ball, S.; Bruice, T. C. *J. Am. Chem. Soc.* **1980**, *102*, 6498.
(27) Buffer catalysis of the reaction of thio ethers with iodide ion is under investigation.

OH^- as a leaving group. However, any reaction producing *t*-BuO• or HO• radicals would be much slower in producing the unstable HO• than that producing *t*-BuO•.[19] More strikingly, a plot of the log of the alcohol catalysis constant of the sulfide oxidation against pK_a of the alcohol gives a slope similar to that which we find for the reaction with hemins. This point is made convincingly by the inclusion of log k^{ROH} + 6 for R_2S oxidation (squares) taken from Edwards et al.[25] in Figure 3. The alcohol catalysis of the two reactions responds to alcohol acidity in essentially an identical fashion. Equally important to this discussion is the observation that the heterolytic cleavage of peracids in reaction with hemins shows a similar effect of alcohol concentration on rate (Figure 6) as well as similar behavior toward general catalysis.

Edwards et al.[25] also report a solvent isotope effect for R_2S oxidation of ~1.7. We find solvent isotope effects near 2.0 for several solvents as well as for the k^{ROH} we obtained from Figure 2. They interpreted their isotope effect in terms of a proton transfer to the leaving group in the transition state (eq 16). This is exactly the interpretation that we have given the general-base catalysis and now the solvent isotope effect in our reaction of hydrogen peroxide with iron(III) porphyrins.[6a-c]

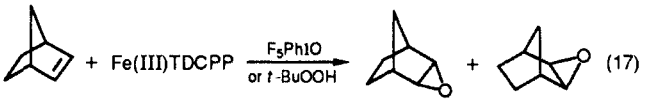
The one apparent difference between the reaction of hydrogen peroxide with dialkyl sulfides on the one hand and hemins on the other is the failure to observe the expected acetate buffer catalysis in the dialkyl sulfide oxidation. As Edwards et al. pointed out, water is a very good general acid and a low Brønsted coefficient would cause a small buffer catalysis to be negligible. We have observed that buffer catalysis of our reactions is much poorer for acetate[6c] or hexafluoroacetone than for collidine buffers and it decreases as the solvent becomes more polar and more acidic.[7c] Indeed, although we observe collidine buffer catalysis in all our studies, including an 80% H_2O/20% MeOH solvent, we find little or no catalysis by hexafluoroacetone hydrate in an 80:20 mixture of water and methanol. Bruice et al. reported similarly negligible acetate catalysis of hydrogen peroxide reaction with a water-soluble hemin in water.[7b] The reaction of hemins with alkyl hydroperoxide, hydrogen peroxide, and peracids are all buffer catalyzed in most cases. The same is probably true for sulfide oxidation, as Edwards has suggested.[25] Under some conditions this catalysis is not observable.

The remarkable similarities of these two reactions (as well as the reaction of peracids with hemins) with regard to salt effects, solvent effects, and isotope effects can be taken as evidence for similarities in their mechanisms. Because R_2S oxidation by alkyl hydroperoxides or hydrogen peroxide has been shown to involve heterolytic breaking of the O–O bond, this similarity means that the hemin oxidation very probably proceeds by a similar mechanism, i.e., heterolytic cleavage.

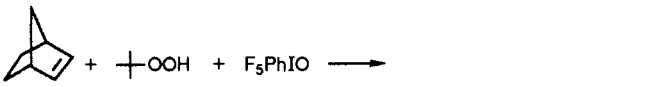
General Catalysis of Peracid and Hydroperoxide Reactions. We have shown here and elsewhere[6a,c,d] that reactions of hemins with peracids, hydroperoxides, and hydrogen peroxide are subject to general catalysis by collidine or acetate buffers. We have also demonstrated internal general-acid/general-base catalyses of both peracid and hydroperoxide reactions with hemins.[6a,d] Furthermore, the magnitude of this catalysis does not differ greatly between peracids and hydroperoxides. In addition, this general catalysis shows similar isotope effects in the cases of peracids and hydroperoxides.

Although all these similarities might be fortuitous, it is much more reasonable to conclude that they indicate similarities in mechanisms of reaction. Since the reaction of peracids with hemins involves heterolytic O–O bond cleavage under these conditions, we must conclude that hydroperoxides do the same.

Epoxide Products as Diagnostic Tests for >Fe⁺=O. As a probe for the oxene (>Fe⁺=O), peroxy radicals, or >Fe=O reactions, we recently studied the epoxidation of norbornene with *t*-BuOOH and 2,6-dichlorophenylhemin at low hydroperoxide concentrations.[29] The exo/endo epoxide ratio is very similar for hemin-catalyzed epoxidations using either *tert*-butyl hydroperoxide or pentafluoroiodosylbenzene. This ratio is very sensitive to the nature of the oxidizing intermediate, going from 1000 when electron-rich porphyrin chromium(III) catalysts are used to 3 when electron-deficient porphyrin iron(III) catalysts are used.[30] No appreciable endo epoxide is produced by reaction of norbornene with *t*-BuOO• radicals[31] and Fe = 0 does not epoxidize alkenes.[6d,16,32]

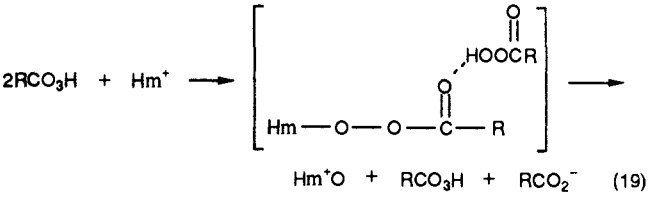


(17)



(18)

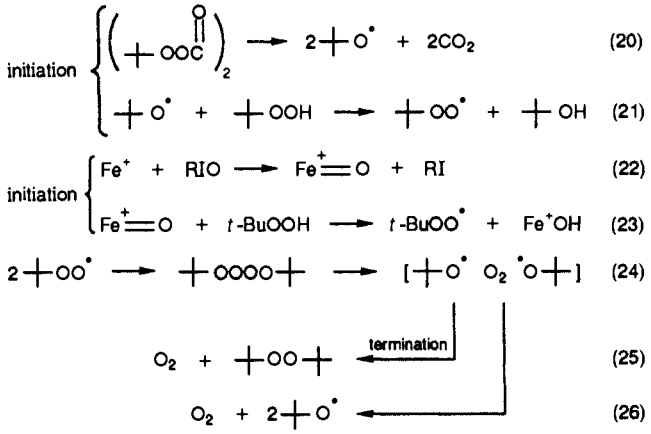
Reactions in Aprotic Solvents. Having implied that general-acid catalysis by buffer or hydroxylic solvent is required for heterolytic cleavage, we must ask what brought about heterolytic cleavage in methylene chloride solvent. One possibility is suggested by the finding of Groves et al.[8] that peracids act both as oxidant and as general catalyst in their reaction with hemin at low temperature. Similarly, Edwards et al.[25] found the reaction of hydroperoxides with dialkyl sulfides to be second order in hydroperoxide in some solvents. Both cases were interpreted as general-acid catalyses, exemplified for the peracid reaction.



(19)

Such a process is also conceivable for hydroperoxides that are similar to trifluoroethanol in their acidities.

Alkoxy Radicals and Their Cleavage Products. Iron porphyrin or phthalocyanine catalyzed decomposition of hydroperoxides has been known for a long time.[33] The products of *tert*-butyl hydroperoxide decomposition show that this reaction involves the same chain process as does that which is initiated with common free-radical initiators. We have recently shown[29] that the oxene species Fe^+=O is an excellent initiator for this reaction, and the evolution of dioxygen from hemin reactions with hydroperoxides has often been reported.[7a,33] The facile chain decomposition reaction is known to occur as follows.[29,34,35]



(28) We find that H_2O_2 reacts at least 10 times faster than does *t*-BuOOH with Fe(III) tetraphenylporphyrin in methanol.

(29) (a) Traylor, T. G.; Fann, W.-P.; Bandyopadhyay, D. *J. Am. Chem. Soc.*, in press. (b) Traylor, T. G.; Xu, F. *J. Am. Chem. Soc.* **1987**, *109*, 6201.

(30) Traylor, T. G.; Miksztal, A. R. *J. Am. Chem. Soc.* **1989**, *111*, 7443.

(31) Generation of *tert*-butylperoxy radicals by addition of pentafluoroiodosylbenzene to solutions of *tert*-butyl hydroperoxide and norbornene, under conditions where *t*-BuOOH and the hemin afforded epoxides,[29] gave *tert*-butyl peroxide and *tert*-butyl alcohol but no endo epoxide.

(32) Peterson, M. W.; Rivers, D. S.; Richman, R. M. *J. Am. Chem. Soc.* **1985**, *107*, 2907.

(33) Hopf, H.; Spangenberg, J.; Gunst, A.; Hinrichsen, J. *Liebigs Ann. Chem.* **1980**, 1923.

Since *tert*-butoxy radicals do not combine in solution unless they are created as a geminate pair,[34] the presence of *tert*-butyl peroxide is definitive evidence for the sequence of eq 24–26. We invariably find *tert*-butyl peroxide in hemin reactions with *tert*-butyl hydroperoxide unless a very good trap for $Fe^+{=}O$ is present.

Recently the formation of products derived from alkoxy radicals, either ketones from alkoxy radical cleavage or abstraction products, has been reported.[14-16]

$$>Fe^+ + R_3COOH \rightarrow R_3CO^\bullet \quad (27)$$

$$R_3CO^\bullet + R'H \rightarrow R'^\bullet + R_3COH \quad (28)$$

$$R_3CO^\bullet \rightarrow R_2CO + R^\bullet \quad (29)$$

Such products have sometimes been taken as evidence for homolytic cleavage of the O–O bond in the first step (reaction 5). However, in many cases[7a-f] oxygen evolution was observed even in the presence of supposedly good traps for high-valent iron intermediates, indicating that reaction 23 was competing successfully with the trap. Additionally, cleavage of cumyloxy and *tert*-butoxy radicals was observed, providing strong evidence for insufficient trapping of intermediates.

It must therefore be concluded that the facile reactions 22–26 must be rigorously excluded before alkoxy radical products can be taken as evidence for homolytic cleavage reaction 5. Since hydroperoxides react with hemins to bring about epoxidation, providing strong evidence for heterolytic cleavage under these conditions, the source of the alkoxy radicals should be carefully reinvestigated.

Peracids versus Hydroperoxides. Differences in the behavior of peracids and hydroperoxides toward hemins have led to the postulate of a change in mechanism from heterolytic to homolytic cleavage upon changes from peracids to hydroperoxides.

$$RCO_3H + >Fe^+ \rightarrow >Fe^+{=}O \quad (30)$$

$$ROOH + >Fe^+ \rightarrow >Fe{=}O \quad (31)$$

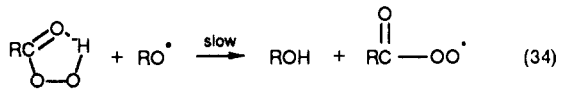
It is instructive to consider the fundamental behavior of peracids and peroxides and their derivatives in this context. First, as to the cleavage of an oxygen–oxygen bond, reactions 32 and 33 reveal

$$t\text{-BuOOC(O)CH}_3 \rightarrow t\text{-BuO}^\bullet + CH_3C(O)\text{-}O^\bullet \quad (32)$$

$$t\text{-BuOO-}t\text{-Bu} \rightarrow 2t\text{-BuO}^\bullet \quad (33)$$

a much greater rate of homolysis to produce the resonance-stabilized acyloxy radical.[12b] Therefore, if homolysis reaction 5 is to occur, it is more likely to be accelerated with peracids than with hydroperoxides.[36]

The second consideration is the propensity toward hydrogen abstraction from peracids versus that from hydroperoxides. We investigated these reactions in some detail.[34,35,38,39] The abstraction of hydrogen from hydroperoxides (reaction 21) in the chain-induced reaction sequence (20, 21, 23–26) is very facile, accounting for the oxygen evolution mentioned above. Similarly, we find that the oxene ($Fe^+{=}O$) abstracts this hydrogen or that of hydroquinone with about the same rate. By contrast the free radical chain induced decomposition of peracids (replace *t*-BuOOH with CH_3CO_3H in the same sequence) is difficult to achieve because the hydrogen abstraction is slow, presumably due to hydrogen bonding.



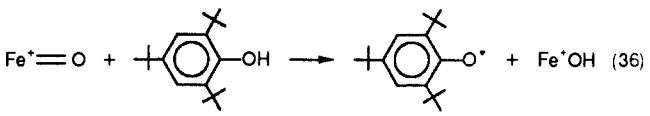
(34)

Therefore a major difference between peracids and hydroperoxides is in the hydrogen abstraction step.

$$Fe^+{=}O + ROOH \rightarrow ROO^\bullet + Fe^+OH \quad (35)$$

We have shown that this reaction does not occur to any appreciable extent with peracids. Therefore, the "catalase" reaction 35 is facile with hydroperoxides and very poor for peracids.

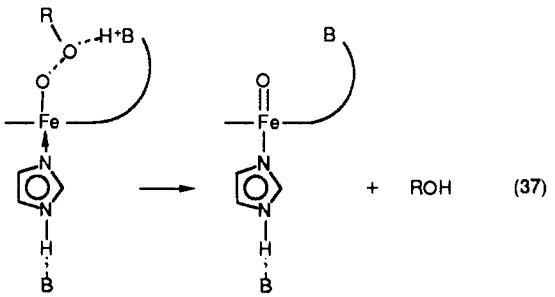
This difference can be seen in the uniformly high yield of phenoxy radical or epoxide production in hemin-catalyzed peracid oxidations and the low yield of these products with hydroperoxides. This competition between the "catalase" reaction and the reaction of interest, which is not problematical with peracid oxidations, causes great difficulty in determining the rates of reactions of hemins with hydroperoxides. This is further exacerbated by the possibility that changes in either the hydroperoxide or the hemin can cause variations in the competition between the "catalase" reaction (35) and, e.g., the trapping reaction (36).



(36)

Thus, whereas quantitative yields of the phenoxy radical are obtained with peracids,[6a] it is common to obtain as little as 10–30% yield with *tert*-butyl hydroperoxides.[6d,7c-e] It is probable that these difficulties account at least in part for the differences in the relative rates of hydroperoxide reactions observed in different laboratories.[6,7]

Catalysis of the O–O Bond Cleavage in Cytochrome P-450. The internal and external buffer catalysis, the increase in rate with basicity of the proximal group, and the increase in rate with hydrogen bonding and thus further increase in basicity of the proximal imidazole in model compounds have been interpreted to explain the catalysis in peroxidases where distal general buffer groups, proximal bases, and proximal hydrogen bonding are present.[6,7] These effects on a peroxidase model are summarized in reaction 37.



(37)

Although cytochrome P-450 has a thiolate proximal base, furnishing electron density, it has none of the buffer groups (imidazole, carboxylate, etc.) on the distal side. The pocket does contain water in varying amounts, depending upon the presence of the substrate.[10] Since protons are required to produce water from O_2 (i.e., to cleave the O–O bond), water has been suggested as the only possible source of these protons.

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(35) Traylor, T. G.; Kenley, R. A. *J. Am. Chem. Soc.* **1975**, *97*, 4700.
(36) Homolytic cleavage of peracid anions by iron(III) porphyrins has recently been observed.[37]
(37) Groves, J. T.; Yoshihito, W. *J. Am. Chem. Soc.* **1988**, *110*, 8443.
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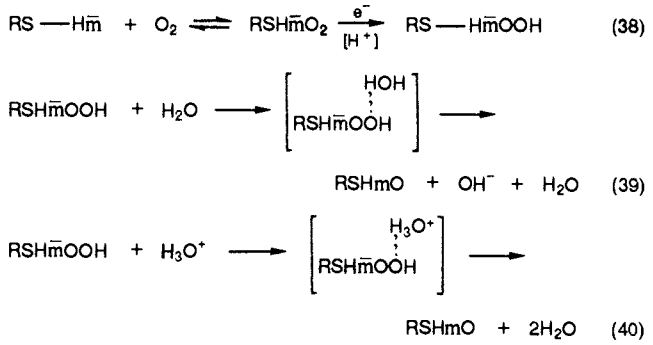
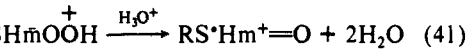
(39) Clinton, N. A.; Kenley, R. A.; Traylor, T. G. *J. Am. Chem. Soc.* **1975**, *97*, 3757.
(40) **Added in Proof**: The rates of reactions of hemin, F_5C_6IO, and *tert*-butyl hydroperoxide are such that the reaction of the first two, producing $Fe^+{=}O$, can be made to dominate.[29b] Under these conditions, $Fe^+{=}O$ reacts with norbornene (1 M) in preference to *tert*-butyl hydroperoxide (0.01 M) to produce an exo/endo epoxide mixture (eq 17) indicative[30] of direct epoxidation of $Fe^+{=}O$ if the catalyst is iron(III) tetrakis(2,6-dichlorophenyl)-porphyrin chloride.[29a] However, when the catalyst is iron(III) tetrakis(mesityl)porphyrin chloride only *exo epoxide* is produced under these conditions, indicating diversion of the process by reaction 23 leading to epoxidation by *tert*-butylperoxy radicals, a process known to give exo epoxide.[29] This demonstrates that heterolytic cleavage to give $Fe^+{=}O$ nevertheless leads to the production of peroxy and thence alkoxy radicals and further weakens the conclusion that such radicals and derived products provide evidence for reaction 5.

The present results put this idea on very solid ground, demonstrating that alcohols or water can serve as general acids/bases for catalysis of O–O bond cleavage. Therefore, we have provided viable mechanisms for cytochrome P-450 catalysis.



An attractive alternative process would use the thiolate as a reductant.



Conclusions. The effect of concentration and acidities of protic solvents on the rate of reactions of hydroperoxides with iron(III) porphyrins and the solvent isotope effects on these rates have been investigated and shown to be almost identical with those effects on the reaction of hydroperoxides with R_2S as well as with reactions of peracids with hemins. These and previously reported data allow two conclusions to be drawn. First, the reactions of hydrogen peroxide, hydroperoxides, and peracids with iron(III) porphyrins in protic solvents all proceed by heterolytic cleavage whether buffer catalyzed or solvent catalyzed. In the absence of efficient solvent buffer catalysis, the complex HmOOR is likely to cleave in a homolytic fashion.[14b,37] Second, alcohol and water catalyses of this reaction have been demonstrated, providing a rational mechanism for water-catalyzed breaking of the O–O bond in the cytochrome P-450 catalytic cycle.

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Molybdenum-Mediated Imido Group Transfer: Stoichiometric and Catalytic Reactions and Structures

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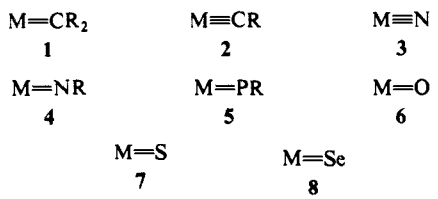
Abstract: The isoelectronic relationship $O^{2-} = RN^{2-}$ implies imido group transfer chemistry related to oxygen atom transfer reactivity, which is extensive for certain elements. This matter has been subjected to its first systematic examination, using the *N,N*-diethyldithiocarbamate (Et_2dtc) complexes of molybdenum and the *N*-tosylimido (NTs) group. The imido group transfer reactions to Mo, $MoO(Et_2dtc)_2$ + XNR and $Mo(CO)_2(Et_2dtc)_2$ + XNR, afford $MoO(NTs)(Et_2dtc)_2$ and $Mo(NTs)_2(Et_2dtc)_2$, respectively, in high yield with the imido group transfer reagents XNR = C_5H_5NNTs, PhMeSNTs, Ph_3SbNTs, PhINTs, and TsN_3. $MoO(NTs)(Et_2dtc)_2 \cdot {}^1/_2PhMe$ crystallizes in triclinic space group $P\bar{1}$ with a = 9.212 (2) Å, b = 12.080 (4) Å, c = 14.310 (4) Å, α = 115.02 (2)°, β = 95.51 (2)°, γ = 100.34 (2)°, and Z = 2; the structure was refined to R = 4.8%. $Mo(NTs)_2(Et_2dtc)_2$ was obtained in monoclinic space group $P2_1/n$ with a = 10.632 (2) Å, b = 16.307 (3) Å, c = 19.023 (5) Å, β = 101.29 (2)°, and Z = 4; the structure was refined to R = 4.0%. The two compounds have a distorted octahedral structure with the multiply bonded groups O and NTs in cis positions. Comparison of these structures with that of $MoO_2(Et_2dtc)_2$ reveals that the NTs group is a nearly isostructural replacement for oxo. The imido group transfer reactions from Mo, $MoO(NTs)(Et_2dtc)_2$ + R_3P, proceed but with the more basic phosphines favoring imido (R_3PNTs) rather than oxo (R_3PO) transfer. Imido transfers to and from Mo involve the purple intermediates $Mo_2O_2(NTs)(Et_2dtc)_4$ and $MoO(NTs)_2(Et_2dtc)_4$, respectively, which are in presumed equilibrium with Mo(IV,VI) complexes. The complex $Mo(NTs)(Et_2dtc)_2$, resulting from imido group transfer, was too unstable to be isolated. Group transfers to and from Mo were coupled to form the catalytic reactions XNTs + $R_3P \rightarrow X + R_3PNTs$, which did not proceed at a measurable rate in the absence of $Mo(NTs)_2(Et_2dtc)_2$. The system based on PhMeSNTs + Ph_2MeP showed 28 turnovers in 7.5 h in chloroform at 35 °C. The reaction PhMeSNTs + 2PhSH → PhSMe + PhSSPh + $TsNH_2$, in which benzenethiol acts as an electron donor, was also catalyzed by $Mo(NTs)_2(Et_2dtc)_2$. All known imidometal groups are tabulated, and oxo and imido group transfer reactions of Mo are schematically summarized.

A rapidly expanding research area is that including the preparations, structures, and reactions of compounds containing the metal–ligand multiple bond groups **1–8**. This set encompasses



oxo, alkylidene, alkylidyne, nitrido, imido, phosphido, sulfido, and selenido ligands that interact as four- or six-electron donors with metals in their high oxidation states to afford groups whose bond lengths are indicative of multiple bonding. Properties of compounds containing groups **1** and **2**,[1,2] **3**,[3] **4**,[1,4,5] **6**,[1,6,7] and **7**[8] have been summarized. The newest group is **5**, of which there are only several examples.[9] Of these groups, by far the greatest amount

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