New Insights into the Mechanisms of O−O Bond Cleavage of Hydrogen Peroxide and *tert*-Alkyl Hydroperoxides by Iron(III) Porphyrin Complexes

Wonwoo Nam,*,† Hui Jung Han,† So-Young Oh,† Yoon Jung Lee,† Mee-Hwa Choi,† So-Yeop Han,† Cheal Kim,‡ Seung Kyun Woo,§ and Woonsup Shin§

Contribution from the Department of Chemistry and Division of Molecular Life Sciences, Ewha Womans University, Seoul 120-750, Korea, Department of Fine Chemistry, Seoul National Polytechnic University, Seoul 139-743, Korea, and Department of Chemistry, Sogang University, Seoul 121-742, Korea

Received December 16, 1999

Abstract: The mechanisms of heterolytic versus homolytic O−O bond cleavage of H_2O_2, *tert*-butyl hydroperoxide (*t*-BuOOH), 2-methyl-1-phenyl-2-propyl hydroperoxide (MPPH), and *m*-chloroperoxybenzoic acid (*m*-CPBA) by iron(III) porphyrin complexes have been studied by carrying out catalytic epoxidations of cyclohexene in protic solvent. In these reactions, various iron(III) porphyrin complexes containing electron-withdrawing and -donating substituents on phenyl groups at the meso position of the porphyrin ring were employed to study the electronic effect of porphyrin ligands on the heterolytic versus homolytic O−O bond cleavage of the hydroperoxides. In addition, various imidazoles were introduced as axial ligands to investigate the electronic effect of axial ligands on the pathways of hydroperoxide O−O bond cleavage. Unlike the previous suggestions by Traylor, Bruice, and co-workers, the hydroperoxide O−O bonds were found to be cleaved both heterolytically and homolytically and partitioning between heterolysis and homolysis was significantly affected by the electronic nature of the iron porphyrin complexes (i.e., electronic properties of porphyrin and axial ligands). Electron-deficient iron porphyrin complexes show a tendency to cleave the hydroperoxide O−O bonds heterolytically, whereas electron-rich iron porphyrin complexes cleave the hydroperoxide O−O bonds homolytically. The heterolytic versus homolytic O−O bond cleavage of the hydroperoxides was also found to be significantly affected by the substituent of the hydroperoxides, ROOH (R = C(O)R′, H, $C(CH_3)_3$, and $C(CH_3)_2CH_2Ph$ for *m*-CPBA, H_2O_2, *t*-BuOOH, and MPPH, respectively), in which the tendency of O−O bond heterolysis was in the order of *m*-CPBA > H_2O_2 > *t*-BuOOH > MPPH. This result indicates that the O−O bond of hydroperoxides containing electron-donating *tert*-alkyl groups such as *t*-BuOOH and MPPH tends to be cleaved homolytically, whereas electron-withdrawing substituents such as an acyl group in *m*-CPBA facilitates O−O bond heterolysis. Since we have observed that the homolytic O−O bond cleavage of hydroperoxides prevails in the reactions performed with electron-rich iron porphyrin complexes and with hydroperoxides containing electron-donating substituents such as the *tert*-alkyl group, we suggest that the homolytic O−O bond cleavage is facilitated when more electron density resides on the O−O bond of (Porp)Fe(III)-OOR intermediates. We also present convincing evidence that the previous assertion that the reactions of iron(III) porphyrin complexes with hydrogen peroxide and *tert*-alkyl hydroperoxides *invariably* proceed by heterolytic O−O bond cleavage in protic solvent and that the failure to obtain high epoxide yields in iron porphyrin complex-catalyzed epoxidation of olefins by hydroperoxides is due to the mechanism of heterolytic O−O bond cleavage followed by a fast hydroperoxide oxidation is highly unlike.

Introduction

Heme-containing enzymes such as cytochromes P-450, peroxidases, and catalases utilize dioxygen and its partially reduced forms in a variety of enzymatic reactions such as the incorporation of oxygen atoms into organic substrates (cytochrome P-450) and the oxidation of substrates (peroxidase and catalase).[1] A unique feature of these enzymes is to cleave O−O bonds of putative iron(III) hydroperoxide porphyrin intermediates heterolytically, forming high-valent iron(IV) oxo porphyrin cation radical intermediates.[1] Anionic proximal ligands such as thiolate in cytochrome P-450, imidazolate in peroxidase, and phenolate in catalase have been considered to be crucial to facilitate the heterolytic O−O bond cleavage process by serving as a strong internal electron donor ("push effect").[2,3]

As biomimetic models for the heme-containing enzymes, the reactions of iron(III) porphyrin complexes with various oxidants

† Ewha Womans University.
‡ Seoul National Polytechnic University.
§ Sogang University.

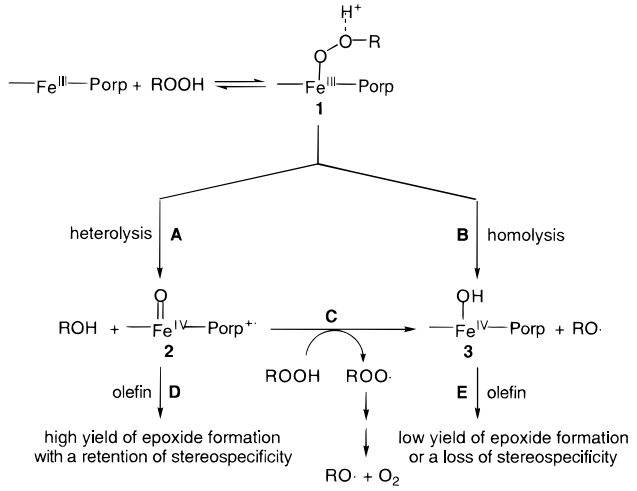
(1) (a) Ortiz de Montellano, P. R. *Cytochrome P450: Structure, Mechanism, and Biochemistry*, 2nd ed.; Plenum Press: New York, 1995. (b) Sono, M.; Roach, M. P.; Coulter, E. D.; Dawson, J. H. *Chem. Rev.* **1996**, *96*, 2841−2887. (c) Shimada, H.; Sligar, S. G.; Yeom, H.; Ishimura, Y. In *Oxygenases and Model Systems*; Funabiki, T., Ed.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1997; pp 195−221. (d) Erman, J. E.; Hager, L. P.; Sligar, S. G. *Adv. Inorg. Biochem.* **1994**, *10*, 71−118.

(2) (a) Franzen, S.; Roach, M. P.; Chen, Y.-P.; Dyer, R. B.; Woodruff, W. H.; Dawson, J. H. *J. Am. Chem. Soc.* **1998**, *120*, 4658−4661. (b) Dawson, J. H. *Science* **1988**, *240*, 433−439.

(3) (a) Poulos, T. L. *J. Biol. Inorg. Chem.* **1996**, *1*, 356−359. (b) Goodin, D. B. *J. Biol. Inorg. Chem.* **1996**, *1*, 360−363. (c) Rietjens, I. M. C. M.; Osman, A. M.; Veeger, C.; Zakharieva, O.; Antony, J.; Grodzicki, M.; Trautwein, A. X. *J. Biol. Inorg. Chem.* **1996**, *1*, 372−376.

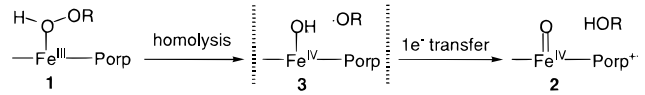
10.1021/ja994403e CCC: $19.00
Published on Web 08/26/2000

Scheme 1



such as peroxyacids and hydroperoxides have been extensively studied, with the intention of elucidating the mechanisms of O−O bond activation and oxygen atom transfer reactions.[4] Our current understanding of such mechanisms is quite advanced in the case where peroxyacids are used as oxidants. The O−O bond of peroxyacids is cleaved heterolytically by the iron porphyrin complexes in solvents such as CH_2Cl_2 and CH_3OH, resulting in the formation of high-valent iron(IV) oxo porphyrin cation radical intermediates, **2** (Scheme 1, pathway A).[5,6] However, the situation is less clear in the cases where biologically important oxidants such as hydrogen peroxide and *tert*-alkyl hydroperoxides are used. Traylor and co-workers proposed that the O−O bond of an intermediate complex, **1**, is heterolytically cleaved to give the formation of **2** as reactive species in the epoxidation of olefins by hydrogen peroxide and *tert*-alkyl hydroperoxides in protic solvents such as a solvent mixture of CH_3OH and CH_2Cl_2 (Scheme 1, pathway A).[7] The role of the protic alcohol solvents has been suggested to be general-acid catalysis.[8] In contrast, Bruice and co-workers provided evidence that the initial step of the hydroperoxide O−O bond

Scheme 2



cleavage of **1** is homolysis in aqueous and aprotic solvents, resulting in the formation of a ferryl-oxo complex, **3**, and an alkoxyl (or hydroxyl) radical (Scheme 1, pathway B).[9,10] They suggested later that the generation of **2** in enzymes such as catalases and peroxidases and in the reactions of iron porphyrin complexes with hydroperoxides may arise via homolytic O−O bond cleavage followed by oxidation of **3** by another ROOH[10] or an electron transfer from **3** to RO• "in the cage" (Scheme 2).[9a] Several other groups also proposed that the reactions of iron porphyrins with alkyl hydroperoxides involve O−O bond homolysis in aqueous and aprotic solvents.[11,12] In other studies such as the hemoprotein-mediated O−O bond cleavage of alkyl hydroperoxides, partitioning between heterolysis and homolysis was observed and the ratios of heterolysis to homolysis were found to depend on the identity of the proximal axial ligand.[13] Very recently, we presented strong evidence that the hydroperoxide O−O bond is cleaved both heterolytically and homolytically in aqueous solution, depending on the reaction conditions such as the pH of reaction solutions and the nature of iron porphyrin complexes.[14] Despite the intensive study for the last two decades, the mechanisms of the O−O bond cleavage of hydrogen peroxide and *tert*-alkyl hyeroperoxides by iron porphyrin complexes have been controversial and still remain unclear.

One of the frequently used mechanistic tools to differentiate the types of O−O bond cleavage of hydroperoxides is to analyze the products obtained in the epoxidation of olefins by iron porphyrin complexes and hydroperoxides.[7,9−11] A high yield of epoxide formation with the retention of stereospecificity is the indication of the formation of **2** via heterolytic O−O bond cleavage of **1** (Scheme 1, pathway A followed by pathway D),[7] whereas the generation of **3** via O−O bond homolysis of **1** affords a low epoxide yield with the formation of allylic oxidation products or a loss of stereospecificity (Scheme 1, pathway B followed by pathway E).[9−11] However, Traylor and co-workers proposed an alternative mechanism for the product distributions of O−O bond homolysis. They suggested that the reactions of iron porphyrin complexes with hydroperoxides initially proceed by heterolytic O−O bond cleavage but that a subsequent side reaction between **2** and ROOH takes place at

(4) (a) Watanabe, Y. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic: New York, 2000; Vol. 4, Chapter 30, pp 97−117. (b) Ingold, K. U.; MacFaul, P. A. In *Biomimetic Oxidations Catalyzed by Transition Metal Complexes*; Meunier, B., Ed.; Imperial College Press: London, 2000; pp 45−89. (c) McLain, J. L.; Lee, J.; Groves, J. T. In *Biomimetic Oxidations Catalyzed by Transition Metal Complexes*; Meunier, B., Ed.; Imperial College Press: London, 2000, pp 91−169. (d) Watanabe, Y. In *Oxygenases and Model Systems*; Funabiki, T., Ed.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1997; pp 223−282. (e) Traylor, T. G.; Traylor, P. S. In *Active Oxygen in Biochemistry*; Valentine, J. S., Foote, C. S., Greenberg, A., Liebman, J. F., Eds.; Blackie Academic and Professional, Chapman and Hall: London, 1995; pp 84−187. (f) Montanari, F.; Casella, L. *Metalloporphyrins Catalyzed Oxidations*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1994. (g) Meunier, B. *Chem. Rev.* **1992**, *92*, 1411−1456.

(5) (a) Groves, J. T.; Haushalter, R. C.; Nakamura, M.; Nemo, T. E.; Evans, B. J. *J. Am. Chem. Soc.* **1981**, *103*, 2884−2886. (b) Groves, J. T.; Watanabe, Y. *J. Am. Chem. Soc.* **1986**, *108*, 7834−7836. (c) Groves, J. T.; Watanabe, Y. *J. Am. Chem. Soc.* **1988**, *110*, 8443−8452.

(6) (a) Traylor, T. G.; Lee, W. A.; Stynes, D. V. *J. Am. Chem. Soc.* **1984**, *106*, 755−764. (b) Lee, W. A.; Bruice, T. C. *J. Am. Chem. Soc.* **1985**, *107*, 513−514. (c) Mandon, D.; Weiss, R.; Jayaraj, K.; Gold, A.; Terner, J.; Bill, E.; Trautwein, A. X. *Inorg. Chem.* **1992**, *31*, 4404−4409. (d) Fujii, H. *Chem. Lett.* **1994**, 1491−1494.

(7) (a) Traylor, T. G.; Kim, C.; Fann, W.-P.; Perrin, C. L. *Tetrahedron* **1998**, *54*, 7977−7986. (b) Traylor, T. G.; Kim, C.; Richards, J. L.; Xu, F.; Perrin, C. L. *J. Am. Chem. Soc.* **1995**, *117*, 3468−3474. (c) Traylor, T. G.; Tsuchiya, S.; Byun, Y.-S.; Kim, C. *J. Am. Chem. Soc.* **1993**, *115*, 2775−2781. (d) Traylor, T. G.; Fann, W.-P.; Bandyopadhyay, D. *J. Am. Chem. Soc.* **1989**, *111*, 8009−8010. (e) Traylor, T. G.; Ciccone, J. P. *J. Am. Chem. Soc.* **1989**, *111*, 8413−8420. (f) Traylor, T. G.; Xu, F. *J. Am. Chem. Soc.* **1987**, *109*, 6201−6202.

(8) Traylor, T. G.; Xu, F. *J. Am. Chem. Soc.* **1990**, *112*, 178−186.

(9) (a) Almarsson, O.; Bruice, T. C. *J. Am. Chem. Soc.* **1995**, *117*, 4533−4544 and references therein. (b) Arasasingham, R. D.; Bruice, T. C. In *The Activation of Dioxygen and Homogeneous Catalytic Oxidation*; Barton, D. H. R., Martell, A. E., Sawyer, D. T., Eds., Plenum Press: New York, 1993; pp 147−169. (c) Bruice, T. C. *Acc. Chem. Res.* **1991**, *24*, 243−249.

(10) He, G.-X.; Bruice, T. C. *J. Am. Chem. Soc.* **1991**, *113*, 2747−2753.

(11) (a) Minisci, F.; Fontana, F.; Araneo, S.; Recupero, F.; Banfi, S.; Quici, S. *J. Am. Chem. Soc.* **1995**, *117*, 226−232. (b) Arasasingham, R. D.; Cornman, C. R.; Balch, A. L. *J. Am. Chem. Soc.* **1989**, *111*, 7800−7805. (c) Labeque, R.; Marnett, L. J. *J. Am. Chem. Soc.* **1989**, *111*, 6621−6627. (d) Labeque, R.; Marnett, L. J. *Biochemistry* **1988**, *27*, 7060−7070.

(12) (a) Colclough, N.; Lindsay Smith, J. R. In *The Activation of Dioxygen and Homogeneous Catalytic Oxidation*; Barton, D. H. R., Martell, A. E., Sawyer, D. T., Eds.; Plenum Press: New York, 1993; pp 171−182. (b) Bell, S. E. J.; Cooke, P. R.; Inchley, P.; Leanord, D. R.; Lindsay Smith, J. R.; Robbins, A. *J. Chem. Soc., Perkin Trans. 2* **1991**, 549−559.

(13) (a) Matsui, T.; Ozaki, S.; Watanabe, Y. *J. Am. Chem. Soc.* **1999**, *121*, 9952−9957. (b) Adachi, S.; Nagano, S.; Ishimori, K.; Watanabe, Y.; Morishima, I.; Egawa, T.; Kitagawa, T.; Makino, R. *Biochemistry* **1993**, *32*, 241−252. (c) Allentoff, A. J.; Bolton, J. L.; Wilks, A.; Thompson, J. A.; Ortiz de Montellano, P. R. *J. Am. Chem. Soc.* **1992**, *114*, 9744−9749.

(14) (a) Nam, W.; Choi, H. J.; Han, H. J.; Cho, S. H.; Lee, H. J.; Han, S.-Y. *Chem. Commun.* **1999**, 387−388. (b) Yang, S. J.; Nam, W. *Inorg. Chem.* **1998**, *37*, 606−607.

a fast rate (Scheme 1, pathway A followed by pathway C), resulting in the product distribution of O−O bond homolysis.[7a,c] Indirect evidence for the mechanism of heterolysis followed by a fast reaction of ROOH with **2** was provided by carrying out olefin epoxidations with an electron-rich iron(III) porphyrin complex, (*meso*-tetramesitylporphinato)iron(III) chloride [Fe(TMP)Cl], and fast-reacting PFIB (pentafluoroiodosylbenzene) or *m*-CPBA in the presence of *tert*-alkyl hydroperoxides.[7a,c] Drastic reduction in product yields with the loss of epoxide stereochemistry was observed in these reactions, demonstrating that **2** initially formed in the reactions of iron(III) porphyrins with PFIB or *m*-CPBA at a rapid rate[6a] reacted faster with alkyl hydroperoxides (Scheme 1, pathway C) than with olefins (Scheme 1, pathway D).[7a−c] Although the results of using oxidant mixtures clearly indicate that **2** containing electron-rich porphyrin ligand indeed reacts fast with ROOH, we cannot rule out the possibility that the low epoxide formation is due to the homolytic O−O bond cleavage of hydroperoxides (Scheme 1, pathway B followed by pathway E). Recently, we provided evidence that the lack of epoxide formation in the catalytic epoxidation of cyclohexene by hydrogen peroxide and *tert*-butyl hydroperoxide catalyzed by electron-deficient iron(III) porphyrin complexes in aprotic solvent was caused by homolytic O−O bond cleavage of the hydroperoxides (Scheme 1, pathway B).[15]

Since the elucidation of the mechanisms of O−O bond cleavage of biologically relevant oxidants such as hydrogen peroxide and alkyl hydroperoxides by iron complexes is extremely important in understanding the chemistry of heme- and nonheme-containing monooxygenase enzymes [16,17] and is still the subject of high interest in the communities of bioinorganic and oxidation chemistry, the controversial mechanisms remaining in the reactions of iron porphyrin complexes with the hydroperoxides need to be clarified (i.e., heterolysis by Traylor and co-workers versus homolysis by Bruice and co-workers). Moreover, although it has been generally believed that the electronic nature of heme iron plays an important role in the O−O bond cleavage of putative iron(III) hydroperoxide porphyrin intermediates in heme-containing enzymes (i.e., "push-effect"),[2,3] no systematic studies have been carried out to demonstrate the significance of the electronic effect of iron(III) porphyrin complexes on the heterolytic versus homolytic O−O bond cleavage of hydrogen peroxide and alkyl hydroperoxides in iron porphyrin models.[18] In this paper, we report that (1) the O−O bond of hydroperoxides such as hydrogen peroxide and *tert*-alkyl hydroperoxides is cleaved both heterolytically and homolytically in protic solvent, (2) the ratio of heterolysis to homolysis is significantly affected by the electronic nature of iron(III) porphyrin complexes (i.e., the electronic properties of porphyrin and axial ligands), and (3) there is also a significant substituent effect of hydroperoxides on the heterolytic versus homolytic O−O bond cleavage of (Porp)Fe^{III}-OOR species [i.e., R = C(O)R′, H, $C(CH_3)_3$, and $C(CH_3)_2CH_2Ph$ for the reactions of *m*-CPBA, H_2O_2, *t*-BuOOH, and MPPH, respectively]. These results are discussed in light of the electronic effect of heme iron on the O−O bond cleavage of iron(III) hydroperoxide porphyrin intermediates in heme-containing enzymes. We also demonstrate here that the previous assertion[7] that the failure to obtain high epoxide yields in iron porphyrin complex-catalyzed epoxidation of olefins by hydroperoxides is always due to the mechanism of heterolytic O−O bond cleavage followed by a fast hydroperoxide oxidation is highly unlike.

Experimental Section

Materials. Methanol (anhydrous) and dichloromethane (anhydrous) were obtained from Aldrich Chemical Co. and purified by distillation over CaH_2 prior to use. All reagents purchased from Aldrich Chemical Co. were the best available purity and used without further purification unless otherwise indicated. 2-Methyl-1-phenyl-2-propyl hydroperoxide (MPPH) was prepared according to literature procedures and the purity of MPPH was determined to be 100% by NMR.[19] *m*-Chloroperoxybenzoic acid (*m*-CPBA) purchased from Aldrich Chemical Co. was purified by washing with phosphate buffer (pH 7.4) followed by water and then dried under reduced pressure. H_2O_2 (30% aqueous) and *tert*-butyl hydroperoxide (*t*-BuOOH, 70% aqueous) were purchased from Fluka and Sigma, respectively. Iron(III) porphyrin complexes such as (*meso*-tetrakis(2,3,5,6-tetrafluoro-*N*,*N*,*N*-trimethyl-4-aniliniumyl)porphinato)iron(III) triflate [Fe(TF_4TMAP)(CF_3SO_3)$_5$, **4a**], (*meso*-tetrakis(2,6-difluorophenyl)porphinato)iron(III) chloride [Fe(TDFPP)Cl, **4c**], (*meso*-tetrakis(2,6-dichlorophenyl)porphinato)iron(III) chloride [Fe(TDCPP)Cl, **4d**], and (*meso*-tetramesitylporphinato)iron(III) chloride [Fe(TMP)Cl, **4f**] were obtained from Mid-Century Chemicals. Other iron(III) porphyrin complexes such as (*meso*-tetrakis(pentafluorophenyl)porphinato)iron(III) chloride [Fe(TPFPP)Cl, **4b**] and (*meso*-tetraphenylporphinato)iron(III) chloride [Fe(TPP)Cl, **4e**] were purchased from Aldrich Chemical Co.

Instrumentation. Product analyses for the cyclohexene epoxidation reactions were performed on either a Hewlett-Packard 5890 II Plus gas chromatograph interfaced with a Hewlett-Packard Model 5989B mass spectrometer or a Donam Systems 6200 gas chromatograph equipped with a FID detector using a 30-m capillary column (Hewlett-Packard, HP-1 and HP-5). Products obtained in the reactions of MPPH and in the epoxidations of *cis*-stilbene were analyzed by Orom Vintage 2000 HPLC equipped with a variable-wavelength UV-200 detector. Detection was made at 215 or 254 nm. Products were separated on a Waters Symmetry C18 reverse phase column (4.6 × 250 mm), eluted first with 50% methanol in water for 15 min and then with 85% methanol in water for 10 min at a flow rate of 1 mL/min. The retention times of benzyl alcohol, benzaldehyde, MPPOH, MPPH, and *cis*-stilbene oxide were 6.0, 8.1, 12.6, 13.8, and 17.8 min, respectively. UV−vis spectra were recorded on a Hewlett-Packard 8453 spectrophotometer. ^{1}H NMR were recorded on a Bruker 250 spectrometer.

Reaction Conditions. Reactions were performed at ambient temperature under argon atmosphere unless otherwise indicated. All reactions were run at least triplicate, and the data reported represent the averages of these reactions.

In general, an iron porphyrin complex (1.25×10^{-3} mmol) was dissolved in a solvent mixture (2.5 mL) of CH_3OH/CH_2Cl_2 (3:1) containing cyclohexene (1.0 mmol). After oxidant (0.10 mmol) was added to the reaction mixture, the reaction solution was stirred for 20 min unless otherwise indicated. The reactions of Fe(TDCPP)Cl, **4d**, and Fe(TMP)Cl, **4f**, with *t*-BuOOH and MPPH were run for 4 h due to slow reaction rate, and the disappearance of MPPH was monitored

(15) Goh, Y. M.; Nam, W. *Inorg. Chem.* **1999**, *38*, 914−920.

(16) (a) Deeth, R. J.; Dalton, H. *J. Biol. Inorg. Chem.* **1998**, *3*, 302−306. (b) Whittington, D. A.; Valentine, A. M.; Lippard, S. J. *J. Biol. Inorg. Chem.* **1998**, *3*, 307−313. (c) Shteinman, A. A. *J. Biol. Inorg. Chem.* **1998**, *3*, 325−330. (d) Lipscomb, J. D.; Que, L., Jr. *J. Biol. Inorg. Chem.* **1998**, *3*, 331−336.

(17) (a) Valentine, A. M.; Stahl, S. S.; Lippard, S. J. *J. Am. Chem. Soc.* **1999**, *121*, 3876−3887. (b) Basch, H.; Mogi, K.; Musaev, D. G.; Morokuma, K. *J. Am. Chem. Soc.* **1999**, *121*, 7249−7256. (c) Que, L., Jr.; Ho, R. Y. N. *Chem. Rev.* **1996**, *96*, 2607−2624. (d) Wallar, B. J.; Lipscomb, J. D. *Chem. Rev.* **1996**, *96*, 2625−2657.

(18) It has been shown with peracids that the pathways and rates of O−O bond cleavage of acylperoxo-iron(III) porphyrin intermediates, (Porp)Fe^{III}-OOC(O)R, are significantly affected by the electronic nature of iron porphyrin complexes and solvents: (a) Yamaguchi, K.; Watanabe, Y.; Morishima, I. *J. Am. Chem. Soc.* **1993**, *115*, 4058−4065. (b) Higuchi, T.; Shimada, K.; Maruyama, N.; Hirobe, M. *J. Am. Chem. Soc.* **1993**, *115*, 7551−7552.

(19) (a) MacFaul, P. A.; Wayner, D. D. M.; Ingold, K. U. *Acc. Chem. Res.* **1998**, *31*, 159−162. (b) MacFaul, P. A.; Ingold, K. U.; Wayner, D. D. M.; Que, L., Jr. *J. Am. Chem. Soc.* **1997**, *119*, 10594−10598. (c) Oldroyd, R. D.; Thomas, J. M.; Maschmeyer, T.; MacFaul, P. A.; Snelgrove, D. W.; Ingold, K. U.; Wayner, D. D. M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2787−2790. (d) Arends, I. W. C. E.; Ingold, K. U.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1995**, *117*, 4710−4711.

by analyzing the amount of MPPH remaining in the reaction solutions with HPLC. After the given stirring time, the resulting solution was directly analyzed by GC/MS or GC to determine the yields of products formed in the cyclohexene epoxidations and by HPLC to calculate the yields of products derived from MPPH decomposition. Product yields were determined by comparison against standard curves.

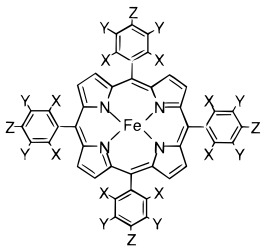
For the studies of the imidazole ligand effect, imidazole (0.1 mmol) was added to a reaction solution containing Fe(TPFPP)Cl, **4b**, and the binding of imidazoles to **4b** was monitored by taking UV−vis spectra of the reaction solution.[20a,21] Other reaction procedures were the same as described above.

For the studies of cyclohexene epoxidation using mixtures of *m*-CPBA and ROOH (ROOH = H_2O_2, *t*-BuOOH, or MPPH), an oxidant mixture of *m*-CPBA (0.02 mmol) and ROOH (0.1 mmol) dissolved in a solvent mixture (0.3 mL) of CH_3OH/CH_2Cl_2 (3:1) was added to a reaction solution containing an iron porphyrin complex (1.25×10^{-3} mmol) and cyclohexene (1.0 mmol) in a solvent mixture (2.2 mL) of CH_3OH/CH_2Cl_2 (3:1). The resulting solution was stirred for 20 min except for the reactions of Fe(TDCPP)Cl, **4d**, and Fe(TMP)Cl, **4f**, with oxidants containing *t*-BuOOH and MPPH. The latter reactions were stirred for 4 h. Product analyses were performed as described above.

Electrochemical Measurements. All electrochemical experiments were performed under N_2 atmosphere in a glovebox at room temperature using a BAS 50W voltammetric analyzer. The cyclic voltammetry measurements were carried out in a solvent mixture of CH_3OH/CH_2Cl_2 (3:1) containing iron porphyrin complexes (1 mM) and *t*-Bu_4NBF_4 (0.1 M) as a supporting electrolyte in one compartment cell. The working electrode was a glassy carbon (area = 0.07 cm^2) disk and the counter electrode was a platinum wire. The reference was a Ag/Ag^+ electrode (0.01 M $AgNO_3$ in CH_3OH/CH_2Cl_2 (3:1) containing 0.1 M *t*-Bu_4NBF_4) with a porous Vycor glass tip junction. The measured potentials were converted and reported versus a Fc/Fc^+ (ferrocene/ferrocinium ion) couple. The reduction potentials ($E^{o\prime}$) were determined from the midpoint of the cathodic and anodic peak potentials of the reversible or quasireversible wave of Fe(III)/Fe(II) of the iron porphyrin complexes. The cyclic voltammograms were run at scan rate of 50 mV/s.

Results and Discussion

Effects of the Electronic Nature of Iron Porphyrin Complexes and the Substituent of Hydroperoxides on the O−O Bond Cleavage of Hydroperoxides. We have studied the electronic effect of iron(III) porphyrin complexes and the substituent effect of hydroperoxides on the heterolytic versus homolytic O−O bond cleavage of (Porp)Fe^{III}-OOR species by carrying out the epoxidations of cyclohexene with various oxidants such as H_2O_2, *t*-BuOOH, MPPH, and *m*-CPBA (i.e., substituent effect of hydroperoxides) in the presence of iron(III) porphyrin complexes containing electron-withdrawing and -donating substituents at the meso position of the porphyrin ring (i.e., electronic effect of porphyrin ligands) and binding various imidazoles as axial ligands (i.e., electronic effect of axial ligands). The epoxidation reactions were performed in protic solvents such as solvent mixtures of CH_3OH and CH_2Cl_2,[7] since it has been demonstrated previously that high-valent iron(IV) oxo porphyrin cation radical complexes are generated as reactive epoxidizing intermediates in the reactions of iron porphyrin complexes with the oxidants in the solvent system.[7d,20] In all of the cyclohexene epoxidation reactions, cyclohexene oxide was obtained as the major product with no or only small amounts of allylic oxidation products such as cyclohexenol and cyclohexenone, demonstrating that the involvement of radicals such as $ROO^\bullet$ and $RO^\bullet$ as reactive oxygenating species is ruled out under the conditions employed in the reactions.[22,23] Further evidence for ruling out the involvement of radical-type oxidation reactions was obtained in the studies of *cis*-stilbene epoxidations.[10,22] *cis*-Stilbene was predominantly oxidized to *cis*-stilbene oxide with no or trace amounts of *trans*-stilbene oxide or benzaldehyde formation (data not shown). The heterolytic versus homolytic O−O bond cleavage of hydroperoxides and the ratios of heterolysis to homolysis were determined by analyzing the yields of cyclohexene oxide formed in the epoxidations of cyclohexene by iron porphyrin complexes and hydroperoxides, since the formation of **2** via O−O bond heterolysis yields the epoxide product (Scheme 1, pathway A followed by pathway D) and the generation of **3** via O−O bond homolysis affords no epoxide formation (Scheme 1, pathway B followed by pathway E).



Iron(III) porphyrins	X	Y	Z
4a, $Fe(TF_4TMAP)(OTf)_5$	F	F	$N^+(CH_3)_3$
4b, Fe(TPFPP)Cl	F	F	F
4c, Fe(TDFPP)Cl	F	H	H
4d, Fe(TDCPP)Cl	Cl	H	H
4e, Fe(TPP)Cl	H	H	H
4f, Fe(TMP)Cl	CH_3	H	CH_3

Figure 1. Structures of iron(III) porphyrin complexes used in this study.

We first explored the porphyrin ligand effect of iron(III) porphyrin complexes on the heterolytic versus homolytic O−O bond cleavage of hydroperoxides such as H_2O_2, *t*-BuOOH, MPPH, and *m*-CPBA with various iron(III) porphyrin complexes containing a series of substituents at the meso position of the porphyrin ring (i.e., electron-withdrawing and -donating substituents on phenyl groups) (see Figure 1 for the structures of iron porphyrin complexes). The electronic nature of the iron(III) porphyrin complexes used in this study was determined by measuring the $Fe^{III/II}$ reduction potentials of the iron(III) porphyrin complexes with cyclic voltammetry under the identical reaction conditions employed in the epoxidation reactions.[24] Electron-withdrawing substituents on phenyl groups of the porphyrin ligands shift the $Fe^{III/II}$ reduction potentials to more positive values and electron-donating substituents such as methyl groups on phenyl groups shift the $Fe^{III/II}$ potentials to more negative values. On the basis of the $Fe^{III/II}$ reduction potentials of the iron(III) porphyrin complexes (see $E^{o\prime}$ values in Figure 2), the electron-deficiency of the iron(III) porphyrin complexes was determined to be in the order of **4a** ≈ **4b** > **4c** > **4d** > **4e** > **4f** under our reaction conditions. As the results of the epoxidation of cyclohexene by various oxidants catalyzed by the iron(III) porphyrin complexes are shown in Figure 2, the yields of cyclohexene oxide formed in the *m*-CPBA reactions were high and not dependent on the electronic nature of the iron porphyrin complexes, indicating that all of the iron porphyrin complexes react with *m*-CPBA to form **2** as a reactive epoxidizing intermediate (Scheme 1, pathway A followed by pathway D).[7] In contrast to the *m*-CPBA reactions, the amounts of cyclohexene oxide obtained in the reactions of H_2O_2,

(20) (a) Lee, K. A.; Nam, W. *J. Am. Chem. Soc.* **1997**, *119*, 1916−1922. (b) Nam, W.; Lee, H. J.; Lim, M. H.; Kim, C. *J. Am. Chem. Soc.* **2000**, *122*, 6641−6647.

(21) Quinn, R.; Nappa, M.; Valentine, J. S. *J. Am. Chem. Soc.* **1982**, *104*, 2588−2595.

(22) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, 1981.

(23) Minisci, F.; Fontana, F.; Araneo, S.; Recupero, F.; Zhao, L. *Synlett* **1996**, 119−125.

(24) (a) Kadish, K. M. In *Iron Porphyrins, Part II*; Lever, A. B. P., Gray, H. B., Eds; Addison-Wesley Publishing Company: London, 1983; pp 161−249. (b) Wijesekera, T.; Matsumoto, A.; Dolphin, D.; Lexa, D. *Angew. Chem., Int. Ed.* **1990**, *29*, 1028−1030. (c) Chen, H. L.; Ellis, P. E., Jr.; Wijesekera, T.; Hagan, T. E.; Groh, S. E.; Lyons, J. E.; Ridge, D. P. *J. Am. Chem. Soc.* **1994**, *116*, 1086−1089. (d) Grinstaff, M. W.; Hill, M. G.; Labinger, J. A.; Gray, H. B. *Science* **1994**, *264*, 1311−1313.

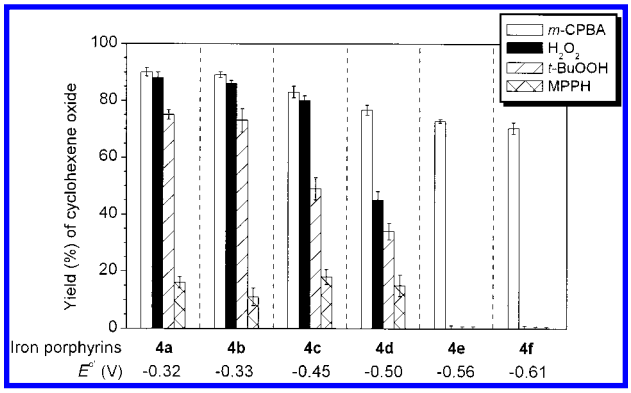


Figure 2. Porphyrin ligand effect of iron(III) porphyrin complexes on the yields of cyclohexene oxide formed in the epoxidations of cyclohexene by *m*-CPBA, H_2O_2, *t*-BuOOH, and MPPH catalyzed by various iron porphyrin complexes containing a series of electron-rich and -poor porphyrin ligands. The yields are based on the oxidants used and the $Fe^{III/II}$ reduction potentials ($E^{o\prime}$) of iron porphyrin complexes are reported versus the Fc/Fc^+ (ferrocene/ferrocinium ion) couple. See the Experimental Section for detailed reaction procedures.

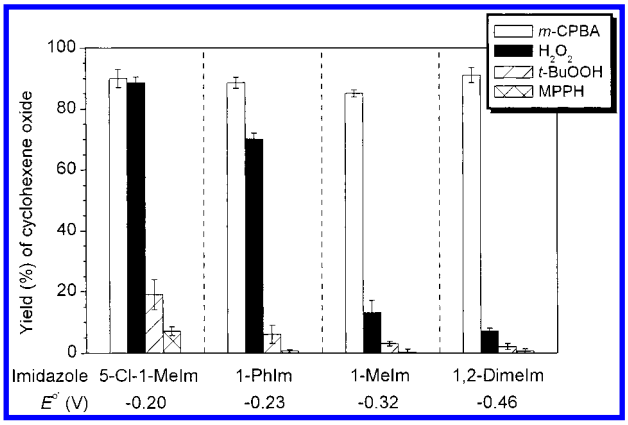
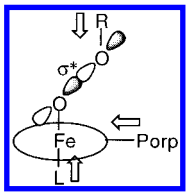


Figure 3. Axial ligand effect of iron(III) porphyrin complexes on the yields of cyclohexene oxide formed in the epoxidations of cyclohexene by *m*-CPBA, H_2O_2, *t*-BuOOH, and MPPH catalyzed by Fe(TPFPP)-$(Im)_2$ complexes binding a series of imidazole axial ligands. The yields are based on the oxidants used and the $Fe^{III/II}$ reduction potentials ($E^{o\prime}$) of the low-spin Fe(TPFPP)$(Im)_2$ complexes are reported versus the Fc/Fc^+ (ferrocene/ferrocinium ion) couple. See the Experimental Section for detailed reaction procedures.

t-BuOOH, and MPPH were found to depend significantly on the electronic nature of the iron porphyrin complexes. The results suggest that there are competitive heterolytic and homolytic O−O bond cleavages of the hydroperoxides and that the ratio of heterolysis to homolysis is a sensitive function of the electronic nature of the iron porphyrin complexes. A striking observation was that iron complexes containing halogenated electron-deficient porphyrin ligands show a tendency to cleave the O−O bond of H_2O_2 and *t*-BuOOH heterolytically, whereas relatively electron-rich iron porphyrin complexes such as **4e** and **4f** cleave the hydroperoxide O−O bonds homolytically. Among the halogenaged electron-deficient iron porphyrin complexes, the more electron-deficient iron porphyrins such as **4a** and **4b** cleave the hydroperoxide O−O bonds more heterolytically than the less electron-deficient iron porphysins such as **4c** and **4d**. These results are contrary to the classical "push effect", in which anionic proximal ligands bound to heme iron in heme-containing enzymes serve as a strong electron donor to facilitate O−O bond heterolysis.[2,3,18a] According to the "push effect", electron-rich iron porphyrin complexes should yield more epoxide product than electron-deficient iron porphyrins; however, we observed the opposite trend in this study (vide infra). In addition to the electronic effect of iron porphyrin complexes on the yields of cyclohexene oxide formed in the epoxidation of cyclohexene, we found that there was a significant substituent effect of hydroperoxides on the oxide yields as well. The substituents of ROOH are C(O)R′, H, $C(CH_3)_3$, and $C(CH_3)_2CH_2Ph$ for *m*-CPBA, H_2O_2, *t*-BuOOH, and MPPH, respectively, and the amounts of cyclohexene oxide obtained by the oxidants are in the order of *m*-CPBA > H_2O_2 > *t*-BuOOH > MPPH (e.g., see the yields of cyclohexene oxide product formed by **4d** in Figure 2). Since the formation of **2** via O−O bond heterolysis yields cyclohexene oxide product, the tendency of O−O bond heterolysis of the hydroperoxides is in the order *m*-CPBA > H_2O_2 > *t*-BuOOH > MPPH. This result suggests that the O−O bond of hydroperoxides containing electron-donating *tert*-alkyl groups such as *t*-BuOOH and MPPH tends to be homolytically cleaved, whereas an electron-withdrawing substituent such as an acyl group in *m*-CPBA facilitates O−O bond heterolysis.

Further evidence for the significant electronic effect of iron porphyrin complexes on the heterolytic versus homolytic O−O bond cleavage of hydroperoxides has been obtained from the studies of the axial ligand effect (Figure 3).[13,18] The reactions have been performed by adding excess amounts of imidazoles[18a] such as 5-chloro-1-methylimidazole (5-Cl-1-MeIm), 1-phenylimidazole (1-PhIm), 1-methylimidazole (1-MeIm), and 1,2-dimethylimidazole (1,2-DimeIm) to the reaction solutions containing Fe(TPFPP)Cl, **4b**. The binding of the imidazoles to the iron porphyrin complex was confirmed by taking UV−vis spectra of the reaction solutions (data not shown),[20a,21] and the $Fe^{III/II}$ reduction potentials of the imidazole-bound low-spin iron(III) porphyrins, Fe(TPFPP)$(Im)_2$, were measured with cyclic voltammetry. As the electron-donating ability of the imidazoles bound to **4b** increased, the $Fe^{III/II}$ reduction potentials of the low-spin Fe(TPFPP)$(Im)_2$ complexes were shifted to more negative values (see $E^{o\prime}$ values in Figure 3). The epoxidation of cyclohexene by H_2O_2, *t*-BuOOH, MPPH, and *m*-CPBA catalyzed by the Fe(TPFPP)$(Im)_2$ complexes was performed under the identical reaction conditions employed in the studies of the porphyrin ligand effect (i.e., in a solvent mixture of CH_3OH and CH_2Cl_2), and the yields of cyclohexene oxide formed in the reactions are reported in Figure 3. As we have observed in the studies of porphyrin ligand effect, the yields of cyclohexene oxide formed in the *m*-CPBA reactions were high and not dependent on the electronic nature of the iron porphyrin catalysts (i.e., no axial ligand effect on the oxide yields in the *m*-CPBA reactions), whereas the amounts of cyclohexene oxide formed in the reactions of H_2O_2, *t*-BuOOH, and MPPH were significantly affected by the nature of imidazoles bound to **4b**. The general trend appears to be that as the electron-donating ability of the imidazoles bound to iron increased, the yields of cyclohexene oxide formed in the reactions of H_2O_2, *t*-BuOOH, and MPPH decreased and the diminution of the yields of oxide product were greater in the reactions of *tert*-alkyl hydroperoxides than those of H_2O_2. These results demonstrate again that partitioning between the heterolytic and homolytic O−O bond cleavages of H_2O_2 and *tert*-alkyl hydroperoxides is sensitive to the electronic environment of iron porphyrin complexes and the substituents of hydroperoxides. Iron porphyrins binding less electron-donating imidazoles such as 5-Cl-1-MeIm show a tendency to cleave the hydroperoxide O−O bonds heterolytically (Scheme 1, pathway A), whereas iron porphyrins binding more electron-donating imidazoles such as 1-MeIm and 1,2-DimeIm cleave the hydroperoxide O−O bonds homolytically (Scheme 1, pathway B). Also, the results of the substituent effect of hydroperoxides indicate that, as we have observed in the studies of porphyrin ligand effect, the tendency of O−O bond het-

Scheme 3



erolysis of the hydroperoxides is in the order of *m*-CPBA > H_2O_2 > *t*-BuOOH > MPPH, demonstrating again that hydroperoxides containing electron-donating *tert*-alkyl groups such as *t*-BuOOH and MPPH prefer O−O bond homolysis to heterolysis.

Then, how do the electronic nature of iron(III) porphyrin complexes and the substituent of hydroperoxides affect the types of O−O bond cleavage of (Porp)Fe^{III}-OOR intermediates, **1** (Scheme 1, pathway A versus pathway B)? It has been shown previously that the σ^* orbital of the iron-bound hydroperoxide is overlapping with the iron d_{xz}, d_{yz}, and d_{z^2} orbitals,[18a,25] implying that the electronic nature of iron porphyrin complexes influences the electron density in the σ^* orbital of the hydroperoxide O−O bond (Scheme 3). Also, the electron density in the σ^* orbital of the hydroperoxide O−O bond should be influenced by the substituent of hydroperoxides (Scheme 3). Therefore, the electron density in the σ^* orbital of the hydroperoxide O−O bond is expected to be controlled by both the electronic nature of iron porphyrin complexes (i.e., the electronic properties of porphyrin and axial ligands) and the substituent of hydroperoxides. Since we have observed that the homolytic O−O bond cleavage of hydroperoxides prevails in the reactions performed with electron-rich iron porphyrin complexes and with hydroperoxides containing electron-donating substituents such as the *tert*-alkyl group, we suggest that the homolytic character of the transition state for the O−O bond cleavage is enhanced upon increasing the electron density residing on the O−O bond of (Porp)Fe(III)-OOR intermediates.[25b] This argument is contrary to the classical "push effect", in which the role of the proximal ligands of heme enzymes is to donate electron density into the hydroperoxide O−O bond through iron(III), thereby weakening the O−O bond and facilitating O−O bond heterolysis.[2,3] For instance, the "push effect" is provided by the proximal histidine ligand in peroxidases, whose electron donor capability is enhanced via hydrogen bonding to a neighboring carboxylate group.[2b] In cytochrome P-450 enzymes, the more nucleophilic thiolate ligand is required to promote O−O bond heterolysis due to the lack of distal machinery present in the peroxidases.[2b,26] However, recent results from site-directed mutagenesis studies emphasized the importance of secondary interactions between the proximal ligands and protein.[3,27] The thiolate ligand in cytochrome P-450 forms two hydrogen bonds with peptide NH groups, resulting in a decrease in the negative charge on the thiolate ligand and a positive shift of the $Fe^{III/II}$ reduction potential of heme iron.[28] Also, it has been demonstrated in iron(III) porphyrin models that the presence of NH···S hydrogen bonds positively shifts the $Fe^{III/II}$ reduction potential of iron porphyrin complexes.[28a,b] Since we have observed in this study that the O−O bond of (Porp)Fe(III)-OOR intermediates is homolytically cleaved when the electron density residing on the O−O bond is too large, we postulate that one of the possible functions of the NH···S hydrogen bonds in cytochrome P-450 is to decrease the amount of electron donation from the proximal thiolate ligand to heme iron, thereby controlling the electron density on the iron(III)-bound hydroperoxide O−O bond to ensue O−O bond heterolysis, not homolysis.[29] Also, it should be pointed out here that, to our knowledge, no evidence has been obtained in iron porphyrin models that the "push effect" indeed facilitates the O−O bond heterolysis of hydrogen peroxide and alkyl hydroperoxides. Previous studies used peracids such as *m*-CPBA as an oxidant, not hydrogen peroxide or alkyl hydroperoxides, in demonstrating the "push effect" on the heterolytic versus homolytic O−O bond cleavage.[18,25a] Since we clearly showed in this study that the reactivities of hydrogen peroxide and alkyl hydroperoxides are different from that of *m*-CPBA and that the O−O bond of peracids tends to be cleaved heterolytically under any reaction circumstances, we therefore suggest that some prior evidence for supporting the "push effect" with the results of peracids should be reevaluated and that oxidants such as hydrogen peroxide and alkyl hydroperoxides rather than peracids should be used in investigating the "push effect" on the mechanism of O−O bond cleavage of iron(III) hydroperoxide porphyrin intermediates.[30]

Reevaluation of the Mechanism of Heterolytic O−O Bond Cleavage Followed by Hydroperoxide Oxidation. The second part of the present study concerns the mechanism of heterolytic O−O bond cleavage followed by hydroperoxide oxidation, proposed by Traylor and co-workers to explain the failure of obtaining high epoxide yields in the catalytic epoxidation of olefins by iron(III) porphyrin complexes and hydroperoxides in protic solvent.[7] In the previous section, we differentiated the types of O−O bond cleavage of hydroperoxides by analyzing the oxide yields formed in the epoxidations of cyclohexene by iron porphyrin complexes and hydroperoxides, with the assumption that the formation of **2** via O−O bond heterolysis yields the epoxide product (Scheme 1, pathway A followed by pathway D) and the generation of **3** via O−O bond homolysis affords no epoxide formation (Scheme 1, pathway B followed by pathway E). However, Traylor and co-workers proposed that the failure to give epoxide formation is not due to the O−O bond homolysis of the hydroperoxides but due to a fast side reaction between **2** and hydroperoxides after **2** is initially formed via O−O bond heterolysis (Scheme 1, pathway A followed by

(25) (a) Yamaguchi, K.; Watanabe, Y.; Morishima, I. *Inorg. Chem.* **1992**, *31*, 156−157. (b) Groves, J. T.; Watanabe, Y. *Inorg. Chem.* **1986**, *25*, 4808−4810.

(26) Liu, H. I.; Sono, M.; Kadkhodayan, S.; Hager, L. P.; Hedman, B.; Hodgson, K. O.; Dawson, J. H. *J. Biol. Chem.* **1995**, *270*, 10544−10550.

(27) Choudhury, K.; Sundaramoorthy, M.; Hickman, A.; Yonetani, T.; Woehl, E.; Dunn, M. F.; Poulos, T. L. *J. Biol. Chem.* **1994**, *269*, 20239−20249.

(28) (a) Suzuki, N.; Higuchi, T.; Urano, Y.; Kikuchi, K.; Uekusa, H.; Ohashi, Y.; Uchida, T.; Kitagawa, T.; Nagano, T. *J. Am. Chem. Soc.* **1999**, *121*, 11571−11572. (b) Ueno, T.; Kousumi, Y.; Yoshizawa-Kumagaye, K.; Nakajima, K.; Ueyama, N.; Okamura, T.; Nakamura, A. *J. Am. Chem. Soc.* **1998**, *120*, 12264−12273. (c) Ueyama, N.; Nishikawa, N.; Yamada, Y.; Okamura, T.; Nakamura, A. *J. Am. Chem. Soc.* **1996**, *118*, 12826−12827.

(29) We do not know at this moment how much electron density needs to be on the hydroperoxide O−O bond to facilitate O−O bond heterolysis. Nonetheless, we venture to suggest that the amount of electron density on the hydroperoxide O−O bond should be optimized for the process of O−O bond heterolysis (i.e., neither too much nor too little). More detailed mechanistic studies including theoretical investigation should be attempted to understand the correlation between the amount of electron density on the O−O bond of (Porp)Fe^{III}-OOR species and the pathways of the O−O bond cleavage. Some examples showing theoretical approach for explaining the formation of compound I in heme-containing enzymes are as follows: (a) Wirstam, M.; Blomberg, M. R. A.; Siegbahn, P. E. M. *J. Am. Chem. Soc.* **1999**, *121*, 10178−10185. (b) Harris, D. L.; Loew, G. H. *J. Am. Chem. Soc.* **1998**, *120*, 8941−8948. (c) Woon, D. E.; Loew, G. H. *J. Phys. Chem. A* **1998**, *102*, 10380−10384.

(30) As Watanabe et al. clearly demonstrated with peracids that the rate of O−O bond cleavage of acylperoxo-iron(III) porphyrin complexes is significantly affected by the electronic nature of iron porphyrin complexes,[18a] we suggest here that the role of the "push effect" (i.e., electron-rich iron porphyrin complexes) may increase the rate of O−O bond cleavage of (Porp)Fe^{III}-OOR species but not facilitate O−O bond heterolysis.

Table 1. Epoxidation of Cyclohexene by *m*-CPBA, H_2O_2, *t*-BuOOH, and Mixtures of These Oxidants Using Fe(TMP)Cl, **4f**, as the Catalyst[a]

	concn of oxidants (mmol × 10^2)			yields (mmol × 10^2) of products		
entry	H_2O_2	*t*-BuOOH	*m*-CPBA	cyclohexene oxide	cyclohexenol	cyclohexenone
1	10			0	0	0
2		10		0	0	0
3			2	0.51 ± 0.08	0	0
4	10		2	0.05 ± 0.03	0	0
5		10	2	0.07 ± 0.03	0	0

[a] See the Experimental Section for detailed reaction procedures. All reactions were run at least triplicate, and the data reported represent the average of these reactions.

pathway C).[7a,c] We therefore reexamined whether the heterolytic O−O bond cleavage followed by hydroperoxide oxidation is a valid mechanism to explain the phenomenon of the low yields of epoxide formation in iron porphyrin complex-catalyzed epoxidation of olefins by hydroperoxides in protic solvent.

The reactions of an electron-rich iron(III) porphyrin complex (e.g., Fe(TMP)Cl, **4f**) with hydroperoxides such as H_2O_2 and *t*-BuOOH did not yield the cyclohexene oxide product in a solvent mixture of CH_3OH and CH_2Cl_2 (Figure 2 and entries 1 and 2 in Table 1). Since the lack of the epoxide formation might result from the fast reaction of **2** with ROOH as Traylor and co-workers proposed, we carried out the epoxidation of cyclohexene using oxidant mixtures of *m*-CPBA and hydroperoxides such as H_2O_2 and *t*-BuOOH under our reaction conditions.[7a,c] The presence of hydroperoxides in the epoxidation reactions by *m*-CPBA caused drastic reduction in the yields of cyclohexene oxide product (compare the yield of cyclohexene oxide in entry 3 with that in entries 4 and 5 in Table 1), confirming the proposal of Traylor and co-workers that **2**, which was initially generated in the reactions of Fe(TMP)Cl with *m*-CPBA at a fast rate,[6a] reacted with ROOH (Scheme 1, pathway C) faster than with cyclohexene (Scheme 1, pathway D).[7a,c] However, although the results of using oxidant mixtures clearly indicate that **2** containing electron-rich porphyrin ligands indeed reacts fast with ROOH (Scheme 1, pathway C),[15] such results cannot rule out the possibility that the failure to obtain high epoxide yields in the catalytic epoxidations of olefins by hydroperoxides is due to the occurrence of O−O bond homolysis (Scheme 1, pathway B). Since we observed in this study that the yields of cyclohexene oxide formed in the reactions of electron-deficient iron porphyrins with hydroperoxides were low in some reactions (see Figures 2 and 3) and we demonstrated previously that high-valent iron(IV) oxo porphyrin cation radical complexes containing electron-withdrawing porphyrin ligands react faster with olefins than ROOH in a competitive reaction of cyclohexene and ROOH in aprotic solvent,[15] the low epoxide yields formed in the epoxidation reactions by the halogenated electron-deficient iron porphyrins such as **4a**, **4b**, **4c**, and **4d** should not be due to the fast reaction of **2** with ROOH (Scheme 1, pathway A followed by pathway C) but due to the O−O bond homolysis (Scheme 1, pathway B). Evidence for supporting this argument is presented below.

The yields of cyclohexene oxide formed in the reactions of MPPH with highly electron-deficient iron porphyrin complexes, **4a** and **4b**, were much lower than those formed in the reactions of H_2O_2 and *t*-BuOOH (Figure 2 and entries 1 and 4 in Table 2). If **2** was formed as a common intermediate via O−O bond heterolysis in all of the reactions of H_2O_2, *t*-BuOOH, and MPPH, the low epoxide formation in the MPPH reactions suggests that the reaction rate of **2** with MPPH should be much faster than that of **2** with H_2O_2 and *t*-BuOOH. However, it is hard to imagine that the reaction rates of the two alkyl hydroperoxides, MPPH and *t*-BuOOH, with **2** are so much different. We also found in the MPPH reactions that the products derived from MPPH decomposition were mainly those formed from the alkoxy-radical intermediate, $MPPO^{\bullet}$ radical (entries 1 and 4 in Table 2), and that the amounts of cyclohexene oxide and MPPOH, the products of O−O bond heterolysis, were similar (see Scheme 4 for the mechanism of MPPH decomposition and the products derived from heterolysis and homolysis).[19,31] Also, **2** containing such highly electron-withdrawing porphyrin ligands should react faster with cyclohexene than with another MPPH;[7b,15] therefore, the low epoxide yields and the products derived from the alkoxy-radical intermediate in the reactions of electron-deficient iron porphyrins with MPPH should be the result of O−O bond homolysis. To obtain more strong evidence to rule out an involvement of a fast reaction of **2** with another MPPH in protic solvent, we carried out the epoxidations of cyclohexene with the highly electron-deficient iron porphyrin complexes **4a** and **4b**, using an oxidant mixture of *m*-CPBA and MPPH. We made an assumption that if the low epoxide yields obtained in the MPPH reactions were due to the mechanism of heterolytic O−O bond cleavage followed by a fast reaction of **2** with another MPPH (Scheme 1, pathway A followed by pathway C), then we would observe the diminution of the oxide yields in the reactions using the oxidant mixture of *m*-CPBA and MPPH. The results shown in Table 2 indicate that the yields of cyclohexene oxide formed in the reactions using the oxidant mixture of *m*-CPBA and MPPH were not diminished but became the sum of the oxide yields formed in each of the *m*-CPBA and MPPH reactions within experimental error (e.g., compare the oxide yield in entry 3 with the sum of the oxide yields in entries 1 and 2 and the oxide yield in entry 6 with the sum of the oxide yields in entries 4 and 5). These results clearly demonstrate that **2**, formed in the reactions of the electron-deficient iron(III) porphyrin complexes with *m*-CPBA at a fast rate,[7b] reacts faster with cyclohexene than with MPPH and that the low epoxide yields obtained in the epoxidation reactions by MPPH are not due to a fast reaction of **2** with MPPH. Another example that shows that the low epoxide formation in the epoxidations of cyclohexene by hyroperoxides such as H_2O_2 and *t*-BuOOH results from the O−O bond homolysis is presented in Table 3. The yields of cyclohexene oxide formed in the reactions of Fe(TDCPP)Cl, **4d**, with H_2O_2 and *t*-BuOOH were not high; however, when we carried out the epoxidation of cyclohexene using oxidant mixtures of *m*-CPBA and hydroperoxides such as H_2O_2 and *t*-BuOOH, the yields of cyclohexene oxide formed in the reactions using the oxidant mixtures were not diminished but became the sum of the oxide yields formed in each oxidant reaction (e.g., compare the oxide yield in entry 5 with the sum of the oxide yields in entries 2 and 3). We therefore conclude on the basis of the results presented above that the proposal of Traylor and co-workers[7] that the failure to obtain high epoxide yields in the catalytic olefin epoxidations by hydroperoxides is *always* due to a fast side reaction between **2** and ROOH is highly unlike. Furthermore, such results suggest that the previous assertion[7] that the reactions of iron(III) porphyrin complexes with hydrogen peroxide and *tert*-alkyl hydroperoxides *invariably* proceed by heterolytic O−O bond cleavage in protic solvent is *incorrect*.

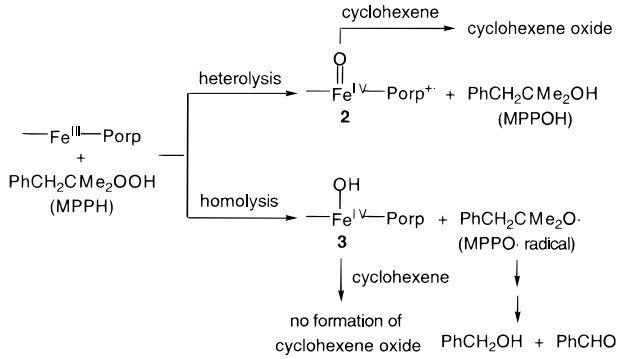
(31) (a) MacFaul, P. A.; Arends, I. W. C. E.; Ingold, K. U.; Wayner, D. D. M. *J. Chem. Soc., Perkin Trans. 2* **1997**, 135−145. (b) Ingold, K. U.; Snelgrove, D. W.; MacFaul, P. A.; Oldroyd, R. D.; Thomas, J. M. *Catal. Lett*. **1997**, *48*, 21−24. (c) Snelgrove, D. W.; MacFaul, P. A.; Ingold, K. U.; Wayner, D. D. M. *Tetrahedron Lett*. **1996**, *37*, 823−826.

Table 2. Products Obtained in the Epoxidation of Cyclohexene by *m*-CPBA, MPPH, and Mixtures of These Oxidants Using Electron-Deficient Iron(III) Porphyrins as the Catalyst[a]

entry	iron(III) porphyrins	concn of oxidants (mmol × 10^2)		yields of products (mmol × 10^2)			
		MPPH	*m*-CPBA	epoxide[b]	MPPOH	$PhCH_2OH$	PhCHO
1	**4a**	10		1.6 ± 0.2	1.9 ± 0.2	6.4 ± 0.3	0.2 ± 0.1
2	**4a**		2	1.8 ± 0.1			
3	**4a**	10	2	3.3 ± 0.2	1.8 ± 0.2	6.4 ± 0.3	0.3 ± 0.1
4	**4b**	10		1.1 ± 0.3	1.3 ± 0.2	6.4 ± 0.3	0.5 ± 0.1
5	**4b**		2	1.8 ± 0.1			
6	**4b**	10	2	2.7 ± 0.4	1.2 ± 0.2	6.3 ± 0.3	0.3 ± 0.1

[a] See the Experimental Section for detailed reaction procedures. All reactions were run at least triplicate, and the data reported represent the average of these reactions. [b] No or only small amounts of allylic oxidation products such as cyclohexenol and cyclohexenone were formed.

Scheme 4



Conclusions

The present results with our previous communications[14] clearly indicate that the O−O bond of hydroperoxides such as hydrogen peroxide and alkyl hydroperoxides is cleaved both heterolytically and homolytically by iron(III) porphyrin complexes in aqueous and organic solvents and that the ratio of heterolysis to homolysis is significantly affected by the electronic nature of iron porphyrin complexes and the substituent of hydroperoxides. The observation that both heterolysis and homolysis can occur depending on reaction conditions rationalizes the long-standing dichotomy of the interpretation for the mechanisms of hydroperoxide O−O bond cleavage by iron porphyrin complexes, mainly suggested by Traylor, Bruice, and their co-workers. Traylor and co-workers proposed that only the heterolysis mechanism occurs in protic solvent, whereas Bruice and co-workers insisted that only homolysis takes place in aqueous and aprotic solvents.[7,9−12]

We also present conclusive evidence that the mechanism of heterolytic O−O bond cleavage followed by hydroperoxide oxidation should not be generalized to explain the failure of obtaining high epoxide yields in the catalytic olefin epoxidations by hydroperoxides such as H_2O_2 and *t*-BuOOH.[7] However, we should not exclude the possibility of O−O bond heterolysis in the cases where no or only small amounts of oxygenated product are formed in the catalytic oxygenations of hydrocarbons by hydroperoxides, since some high-valent iron oxo intermediates containing electron-rich porphyrin ligands indeed react faster with hydroperoxides than with hydrocarbons. We therefore suggest that care should be taken in determining the pathways of hydroperoxide O−O bond cleavage by analyzing the yields of products formed in the catalytic oxygenation of hydrocarbons by hydroperoxides.

Last, we believe that the observation of the significant electronic effect of iron porphyrin complexes on the pathways of the O−O bond cleavage of (Porp)Fe^{III}-OOR sepcies in iron porphyrin models may provide clues not only to elucidate the electronic effect of heme iron on the O−O bond activation of putative iron(III) hydroperoxide porphyrin intermediates in heme-containing enzymes but also to develop efficient biomimetic oxygenation systems using environmentally clean oxidants such as hydrogen peroxide. Moreover, we believe that the present results may provide some useful information for understanding the mechanisms of the O−O bond activation of hydroperoxides by non-porphyrin iron complexes and nonheme iron monooxygenase enzymes.[32,33]

Table 3. Epoxidation of Cyclohexene by H_2O_2, *t*-BuOOH, *m*-CPBA, and Mixtures of ROOH and *m*-CPBA Using Fe(TDCPP)Cl, **4d**, as the Catalyst[a]

entry	concn of oxidants (mmol × 10^2)			yields of products (mmol × 10^2)		
	H_2O_2	*t*-BuOOH	*m*-CPBA	cyclohexene oxide	cyclohexenol	cyclohexenone
1	10			4.5 ± 0.3	0	0
2		10		3.4 ± 0.3	0	0
3			2	1.7 ± 0.2	0	0
4	10		2	5.8 ± 0.7	0	0
5		10	2	5.1 ± 0.4	0	0

[a] See the Experimental Section for detailed reaction procedures. All reactions were run at least triplicate, and the data reported represent the average of these reactions.

Acknowledgment. Financial support for this research from the Korea Science and Engineering Foundation (96-0501-01-01-3, 1999-2-122-002-4), Korea Research Foundation (1997-001-D00214), Center for Cell Signaling Research, and the Ministry of Education of Korea (BSRI-98-3412) is gratefully acknowledged. H.J.H., S.-Y.O, and M.-H.C. are the recipients of a research fellowship (Brain Korea 21 Project). We thank Professor Matthias Selke (California State University, Los Angeles) for helpful suggestions in revising this manuscript.

JA994403E

(32) (a) Neimann, K.; Neumann, R.; Rabion, A.; Buchanan, R. M.; Fish, R. H. *Inorg. Chem*. **1999**, *38*, 3575−3580. (b) Menage, S.; Galey, J.-B.; Dumats, J.; Hussler, G.; Seite, M.; Luneau, I. G.; Chottard, G.; Fontecave, M. *J. Am. Chem. Soc*. **1998**, *120*, 13370−13382. (c) Rabion, A.; Chen, S.; Wang, J.; Buchanan, R. M.; Seris, J.-L.; Fish, R. H. *J. Am. Chem. Soc*. **1995**, *117*, 12356−12357. (d) Nam, W.; Ho, R.; Valentine, J. S. *J. Am. Chem. Soc*. **1991**, *113*, 7052−7054.

(33) It has been reported by Que and co-workers that the reactions of some non-porphyrin iron complexes such as $[Fe(TPA)(CH_3CN)_2](ClO_4)_2$ with H_2O_2 generate Fe^V═O intermediates via O−O bond heterolysis, whereas the non-porphyrin iron complexes cleave the O−O bond of *tert*-alkyl hydroperoxides such as *t*-BuOOH and MPPH homolytically to form Fe^{IV}═O intermediates: (a) Lange, S. J.; Miyake, H.; Que, L., Jr. *J. Am. Chem. Soc*. **1999**, *121*, 6330−6331. (b) Chen, K.; Que, L., Jr. *Chem. Commun*. **1999**, 1375−1376. (c) Kim, C.; Chen, K.; Kim, J.; Que, L., Jr. *J. Am. Chem. Soc*. **1997**, *119*, 5964−5965.