Electronic Effect of Iron(III) Porphyrin Complexes on the Epoxidation of Cyclohexene: Epoxidation *versus* Hydroxylation

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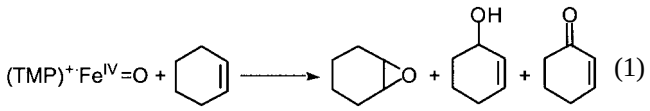
Since the selective oxidations of hydrocarbons are of importance in both synthetic chemistry and industrial processes, biomimetic oxidation reactions by iron(III) porphyrin complexes have attracted much attention over the past two decades.[1] Groves and co-workers were the first to report that a simple iron porphyrin complex (*e.g.*, Fe(TPP)Cl, TPP = *meso*-tetraphenylporphinato dianion) catalyzes the epoxidation and hydroxylation of hydrocarbons by iodosylbenzene (PhIO).[2] Since then, much effort has been taken to improve the catalytic reactivity of iron porphyrin complexes.[3] An important finding for this was that the introduction of electron-withdrawing substituents into the phenyl groups of porphyrin ligands enhanced the reactivity of the iron porphyrins greatly and diminished the oxidative degradation of the porphyrin ligands dramatically.[4] Even more effective iron porphyrin catalysts were achieved when the porphyrin ring was fully halogenated.[5] The highly electron-deficient iron porphyrins turned out to be remarkable catalysts with fast rates and high product yields in the oxidation reactions.[5a]

It has been shown previously that Fe(TMP)Cl (TMP = *meso*-tetramesitylporphinato dianion) is able to epoxidize olefins *via* the formation of an oxoiron(IV) porphyrin cation radical intermediate (*e.g.*, $(TMP)^{+\cdot}Fe^{IV}=O$).[6] Recently, Groves and Gross reported that the epoxidation of cyclohexene by Fe(TMP)X with oxidants such as PhIO or *m*-chloroperoxybenzoic acid (*m*-CPBA) yielded products derived from epoxidation (*i.e.*, cyclohexene oxide) and allylic hydroxylation (*i.e.*, cyclohexen-3-ol and cyclohexen-3-one) (eq 1).



(1)

The ratio of the products of the epoxidation and hydroxylation was found to depend on the axial ligand X in $(TMP)^{+\cdot}Fe^{IV}=O(X)$ and reaction temperature in an unusual way.[7] Based on the observation, they suggested that more than one reaction pathway must be involved in the oxidation of cyclohexene and further, that while the epoxidation proceeds *via* the formation of a complex between the intermediate and the olefin, the hydroxylation reaction proceeds by a non-intersecting reaction pathway not involving this complex.[7] In contrast, in the case of cyclohexene epoxidations by electron-deficient iron(III) porphyrin complexes, it has been shown that cyclohexene oxide was the sole or predominant product with trace amounts of allylic oxidation products.[8] Therefore, in order to understand the different product distributions observed in the epoxidations of cyclohexene by electron-rich and -deficient iron porphyrin complexes, we have conducted the cyclohexene epoxidation with *m*-CPBA in a solvent mixture of CH_3OH and CH_2Cl_2 at various reaction temperatures, using iron(III) porphyrins containing different substituents on the phenyl groups at the meso position of the porphyrin ring. We report in this study that the reactions of electron-deficient iron porphyrins with *m*-CPBA selectively epoxidize cyclohexene to give cyclohexene oxide product solely without showing the temperature effect, whereas an electron-rich iron porphyrin [*i.e.*, Fe(TMP)Cl] oxidizes cyclohexene to give two products, epoxide and allylic alcohol. In addition, the product distiributions were found to vary depending on the reaction temperatures in the latter reaction, as Groves and Gross have reported previously.[7] We also report the results of ^{18}O-labeled water, $H_2{}^{18}O$, experiments obtained in the epoxidation of cyclohexene by Fe(TMP)Cl and *m*-CPBA at various reaction temperatures.

Experimental Section

Materials. Dichloromethane (anhydrous) and methanol (anhydrous) were purchased from Aldrich Chemical Co. and used without further purification. All chemicals obtained from Aldrich were the best available purity and used without further purification unless otherwise indicated. The purity of *m*-CPBA purchased from Aldrich was determined to be 65% by iodometric analysis.[9] Iron(III) porphyrin complexes such as (*meso*-tetramesityl-porphinato)iron(III) chloride [Fe(TMP)Cl], (*meso*-tetrakis(2,6-dichlorophenyl)porphinato)-iron(III) chloride [Fe(TDCPP)Cl], (*meso*-tetrakis(2,6-difluorophenyl)porphinato)iron(III) chloride [Fe(TDFPP)Cl], and (*meso*-tetrakis(pentafluorophenyl)porphinato)iron(III) chloride [Fe(F_{20}-TPP)Cl] were obtained from Mid-Century Chemicals.

Instrumentation. Product analyses were performed on either a Hewlett-Packard 5890 II Plus gas chromatograph interfaced with Hewlett-Packard Model 5989B mass spectrometer or a Donam Systems 6200 gas chromatograph equipped with a FID detector using 30-m capillary column (Hewlett-Packard, HP-5 and Ultra 2). UV-vis spectra were recorded on a Hewlett Packard 8453 spectrophotometer.

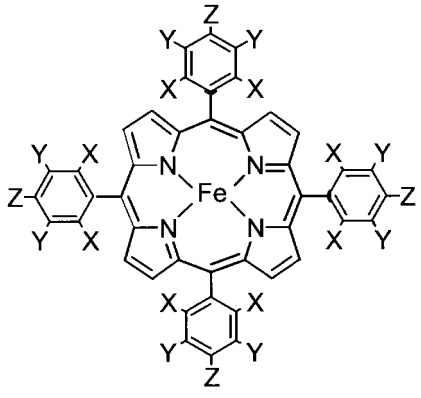
Cyclohexene Epoxidation Reactions. Since the product yields and product distributions obtained in the epoxidation

reactions were not affected by the presence of molecular oxygen, all the reactions were performed in air. *m*-CPBA (2.4×10^{-3} mmol, diluted in 20 μL of CH_2Cl_2) was added to a solution containing iron(III) porphyrin complex (2×10^{-3} mmol) and cyclohexene (0.2 mmol) in a solvent mixture (0.5 mL) of CH_3OH and CH_2Cl_2 (3 : 1). The reaction mixture was stirred for 10 min at room temperature and then directly analyzed by GC and GC/MS. The stirring time for low temperature reactions was 0.5 hr at 0 °C and -25 °C and 1 hr at -50 °C and -78 °C.

^{18}O-Labeled $H_2{}^{18}O$ Experiments. *m*-CPBA (2.4×10^{-3} mmol, diluted in a solvent mixture (20 μL) of CH_3OH and CH_2Cl_2 (3 : 1)) was added to a solution containing Fe(TMP)Cl (2×10^{-3} mmol), cyclohexene (0.2 mmol), and $H_2{}^{18}O$ (5 μL, 0.26 mmol, 95% ^{18}O enriched, obtained from Aldrich Chemical Co.) in a solvent mixture (0.5 mL) of CH_3OH and CH_2Cl_2 (3 : 1). The reaction mixture was stirred for 10 min at room temperature and then directly analyzed by GC/MS. The reaction time for low temperature reactions was 0.5 hr at 0 °C and -25 °C and 1 hr at -50 °C and -78 °C. ^{16}O and ^{18}O compositions in cyclohexene oxide and cyclohexen-3-ol were determined by the relative abundance of mass peaks at *m*/*z* = 57 and *m*/*z* = 59 for cyclohexene oxide and *m*/*z* = 83 and *m*/*z* = 85 for cyclohexen-3-ol.

Results and Discussion

Epoxidation *versus* Hydroxylation in Iron Porphyrin Complex-Catalyzed Epoxidation of Cyclohexene at Various Reaction Temperatures. The epoxidation of cyclohexene by *m*-CPBA was carried with four different iron(III) porphyrin complexes such as Fe(TMP)Cl, Fe(TDCPP)Cl, Fe(TDFPP)Cl, and Fe(F_{20}TPP)Cl (see Figure 1 for the structures of iron porphyrin complexes) in a mixture of CH_3OH and CH_2Cl_2. As the results are shown in Table 1, the electron-rich iron porphyrin complex, Fe(TMP)Cl, yielded two products, cyclohexene oxide (80%) and cyclohexe-3-ol (9%), at room temperature (entry 1), whereas the electron-deficient iron porphyrins yielded quantitative amounts of cyclohexene oxide with trace amounts of allylic oxidation products (entries 6, 9, 12). Then, we carried out the cyclohexene epoxidations by varying the reaction temperature. In Fe(TMP)Cl-catalyzed epoxidation reactions, as the reaction temperature became lower, the yields of epoxide product decreased but the yields of cyclohexen-3-ol increased (see entries 1-5 in Table 1).[7] However, in the epoxidations of cyclohexene by electron-deficient iron porphyrins, the dependence of the product distributions on the reaction temperature was not observed (see entries 6-14 in Table 1). Cyclohexene oxide was always the sole product with only trace amounts of allylic oxidation product formation in the latter reactions.



Iron(III) porphyrins	X	Y	Z
Fe(TMP)Cl	CH_3	H	CH_3
Fe(TDCPP)Cl	Cl	H	H
Fe(TDFPP)Cl	F	H	H
Fe(F_{20}TPP)Cl	F	F	F

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

Table 1. Catalytic Epoxidation of Cyclohexene by Iron(III) Porphyrin Complexes and *m*-CPBA at Various Reaction Temperatures[a]

Entry	Iron porphyrins	Temp (°C)	Yields (%) of products[b]		
			Cyclohexene oxide	Cyclohexen-3-ol	Cyclohexen-3-one
1	Fe(TMP)Cl	25	80 ± 2	9 ± 2	trace[d]
2		0	77 ± 3	12 ± 1	7 ± 2
3		-25	75 ± 5	10 ± 1	7 ± 2
4		-50	75 ± 4	14 ± 2	3 ± 1
5		-78	50 ± 2	23 ± 2	6 ± 2
6	Fe(TDCPP)Cl	25	96 ± 4	trace[c]	trace[c]
7		-25	96 ± 4	trace[c]	trace[c]
8		-78	82 ± 5 [d]	trace[c]	trace[c]
9	Fe(TDFPP)Cl	25	96 ± 4	trace[c]	trace[c]
10		-25	96 ± 4	trace[c]	trace[c]
11		-78	96 ± 4	trace[c]	trace[c]
12	Fe(F_{20}TPP)Cl	25	96 ± 4	trace[c]	trace[c]
13		-25	96 ± 4	trace[c]	trace[c]
14		-78	96 ± 4	trace[c]	trace[c]

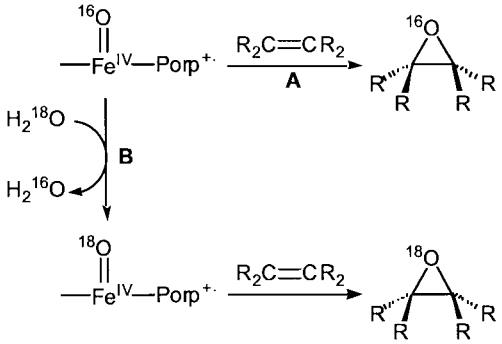
[a]See Experimental Section for detailed experimental procedures. All reactions were run at least in triplicate, and the data reported represent the average of these reactions. [b]Based on *m*-CPBA used. [c]Yields were less than 3% based on *m*-CPBA. [d]The low yields might be due to the low solubility of Fe(TDCPP)Cl at -78 °C.

In order to confirm that a common intermediate (*e.g.*, $(TMP)^{+\cdot}Fe^{IV}$=O) is responsible for the formation of both cyclohexene oxide and cyclohexen-3-ol in Fe(TMP)Cl-catalyzed epoxidation reactions, we performed ^{18}O-labeled water experiments in the epoxidation of cyclohexene by Fe(TMP)Cl and *m*-CPBA at various reaction temperatures.[10,11] When labeled ^{18}O is incorporated from $H_2{}^{18}O$ into the oxygenated products, an involvement of a high-valent iron(IV) oxo porphyrin cation radical intermediate can be suggested, since it has been unambiguously shown that the oxygen of the iron oxo intermediate exchanges with $H_2{}^{18}O$.[10,11] As the results are shown in Table 2, the percentages of ^{18}O found in the epoxide and alcohol products were high and similar, suggesting that $(TMP)^{+\cdot}Fe^{IV}$=O was the reactive intermediate responsible for the formation of epoxide and alcohol prod-

Table 2. Percentages of ^{18}O Incorporated from $H_2{}^{18}O$ into Products Formed in the Epoxidation of Cyclohexene by Fe(TMP)Cl and *m*-CPBA[a]

Temp (°C)	Percentages of ^{18}O in products	
	Cyclohexene oxide	Cyclohexen-3-ol
25	30 ± 3	22 ± 2
0	39 ± 4	31 ± 3
-25	46 ± 4	36 ± 3
-50	52 ± 4	45 ± 4
-78	52 ± 4	46 ± 4

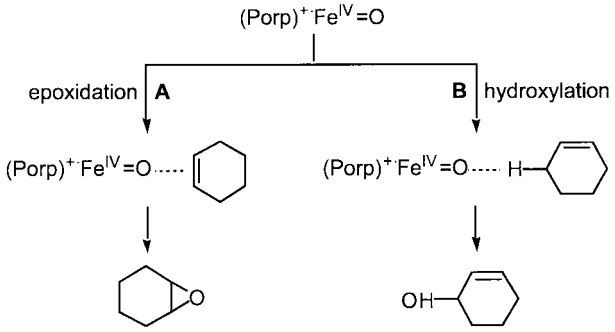
[a]See Experimental Section for detailed experimental procedures. All reactions were run at least duplicate, and the data reported represent the average of these reactions.



Scheme 1

ucts. We also found in the labeled water experiments that the amounts of ^{18}O incorporated into the oxygenated products depended on the reaction temperature and that the extent of ^{18}O-incorporation gradually increased as the reaction temperature became lower. The dependence of the ^{18}O-incorporation on the reaction temperature might be due to that the rate of the reaction of the oxoiron(IV) porphyrin cation radical intermediate with olefin (Scheme 1, pathway A) is slower than that of oxygen exchange between the intermediate and labeled water (Scheme 1, pathway B) at low temperature.

On the Mechanism of Epoxidation *versus* Hydroxylation. Unusual reactivity of cyclohexene with the electron-rich iron porphyrin complex at low temperature reveals a significant fact concerning a mechanistic insight into the iron porphyrin-catalyzed epoxidation *versus* hydroxylation of olefins. The variation in product ratios observed in the epoxidations of cyclohexene by electron-rich and -deficient iron(III) porphyrin complexes indicates that oxygen transfer from reactive species to olefins must have taken place by two different mechanisms, although they have not been proved clearly yet.[7] One possible explanation for the selectivity of epoxidation *versus* hydroxylation is that the epoxidation of olefins by reactive intermediates has more electron-transfer characteristics than does the allylic hydroxylation of olefins by the intermediates. Therefore, the decrement of the electron density on iron porphyrin complexes (*e.g.*, electron-deficient iron porphyrins) makes the reactive intermediates (*i.e.*, $(Porp)^{+\cdot}Fe^{IV}=O$) more reactive toward the double bond of olefins (Scheme 2, pathway A). As a result, the electron-



Scheme 2

rich double bond moiety of olefins has an easy accessibility by the iron porphyrin intermediates containing electron-deficient porphyrin ligands. Therefore, the epoxidation reaction becomes more facile by the electron-deficient porphyrins (Scheme 2, pathway A), resulting in giving high yields of epoxide product. In contrast, the increment of the electron density on the porphyrin ligand (*e.g.*, electron-rich iron porphyrin such as $Fe^{III}(TMP)$) makes the intermediate (*e.g.*, $(TMP)^{+\cdot}Fe^{IV}=O$) less reactive toward the double bond of olefins. Also, by decreasing the reaction temperature, we propose that the rate of the olefin epoxidation by the oxoiron (IV) porphyrin cation radical intermediate might become even more slower, thereby reducing the yield of epoxide product (Scheme 2, pathway A) and increasing the yield of allylic alcohol product (Scheme 2, pathway B). This observation seems to be closely related to the proposal of Traylor and co-workers, in which the selectivity of epoxidation *versus* hydroperoxide decomposition (k_{ep}/k_{per}) by oxene intermediates is significantly affected by the electronic nature of iron porphyrin complexes.[12]

Conclusion

In conclusion, we have shown here that the reactive intermediates generated in the reactions of electron-deficient iron porphyrins and *m*-CPBA prefer epoxidation over allylic oxidation in the epoxidation of cyclohexene without showing the dependence of reaction temperature, whereas an oxoiron(IV) porphyrin cation radical intermediate containing an electron-rich porphyrin ligand [*i.e.*, $(TMP)^{+\cdot}Fe^{IV}=O$] epoxidizes cyclohexene to give two products, epoxide as a major product and a good amount of allylic alcohol product. In addition, the product distributions were found to very significantly depending on the reaction temperature in the latter case, as Groves and Gross have reported previously.[7] We suggest that the different selectivity of epoxidation *versus* hydroxylation by the electron-deficient and -rich iron porphyrin complexes might be caused by the preference of two-electron reduction process (*i.e.*, epoxidation) over one-electron reduction process (*i.e.*, allylic hydroxylation), depending the electronic nature of iron porphyrin complexes.

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