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FACTORS AFFECTING THE OXYGEN ATOM TRANSFER IN METALLOPORPHYRIN-CATALYZED EPOXIDATION OF CYCLOHEXENE, A MODEL FOR P-450 CATALYZED OXIDATION

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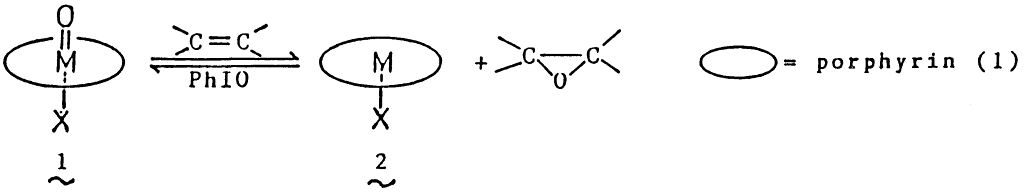
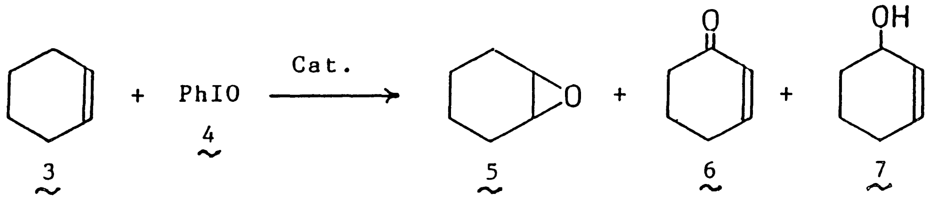
The effects of metals, substituents on porphyrin and axial ligands on the metalloporphyrin-catalyzed epoxidation of cyclohexene with iodosobenzene were examined. The results suggested that the oxo ligand in the ferryl porphyrin intermediate functions as an electrophile to olefins.

The cytochrome P-450 is a heme-containing monooxygenase which catalyzes the hydroxylation of alkanes and the epoxidation of alkenes. In these enzymic reactions oxygen atom transfer to organic substrates has been postulated to proceed through high-valent iron porphyrin intermediates.1) Since Groves and coworkers2) found that oxygen atom transfer from iodosobenzene to olefins was catalyzed by Fe(TPP)Cl complex,3) metalloporphyrin-catalyzed oxidations employing a various kinds of oxidants(iodosobenzene,2) hypochlorite,11) peroxycarboxylic acids,12) hydroperoxides,13) and N,N-dimethylaniline N-oxides14)) have been reported as model reactions for the P-450 catalyzed oxidation. In these reactions formation of metal oxo porphyrin complexes and subsequent oxo ligand transfer to olefins have been confirmed spectroscopically12)(see Eq.1). Factors governing the epoxidations, however, are not well understood at present. Especially the role of axial ligands(X) in **1** has scarcely been discussed. Here we wish to describe the effects of the central metal ions, the substituents on a porphyrin ligand, and the axial ligands on the matalloporphyrin-catalyzed epoxidation of cyclohexene with iodosobenzene and to discuss the reactivity of the oxo ligand in ferryl porphyrins **1**(M = Fe).



(1)

Cyclohexene(**3**)(1 ml, 10 mmol) was treated with iodosobenzene(**4**)(88 mg, 0.40 mmol) in the presence of a metalloporphyrin(0.02 mmol) in dichloromethane(15 ml) at ambient temperature under nitrogen for 6 h and the reaction products were analyzed by GLC on a PEG-20M column; cyclohexanone was employed as an internal standard. Cyclohexene oxide(**5**), cyclohexenone(**6**) and cyclohexenol(**7**) were detected in the product(Eq. 2) and the yields were calculated based on **4**. Since compounds **6** and **7** formed from **3** and **4** even in the absence of the catalysts, we employed the yield of cyclohexene oxide **5** as a measure of the catalytic activity of oxygen atom transfer.



(2)

Effects of metal ions in M(TPP)X on the catalytic epoxidation of **3** were summarized in Table 1. Mn(TPP)Cl, Fe(TPP)Cl and Co(TPP) showed moderate catalytic activity. It is known that these metal complexes are also effective catalysts for the hydroxylation of cyclohexane with cumylhydroperoxide.13) Cr(TPP)Cl15) and Cu(TPP)Cl were totally inactive. TiO(TPP), VO(TPP), and Ni(TPP) showed only poor catalytic activity. The stability of the metal oxo bonding may be responsible for the catalytic activity of the porphyrin complexes.16,17) Very stable metal oxo bonding in TiO(TPP) or VO(TPP) may prevent the oxygen atom transfer to **3**, whereas Ni(TPP) or Cu(TPP) may be difficult to form the metal(IV) oxo porphyrins.

Table 1. Effects of Metal Ions on Formation of Cyclohexene oxide **5** Catalyzed by M(TPP)X

MX	TiO	VO	CrCl	MnCl	FeCl	Co	Ni	Cu
Yield of **5** /%	2	3	0	46	37	11	2	0

Substituents on porphyrin markedly affected the yields of **5** as shown in Table 2. The β-substituted porphyrinato iron complexes such as Fe(PPIXDME)Cl are less catalytically active than the meso substituted ones such as Fe(TPP)Cl. This can be understood by considering that the oxidant **4** easily attacks the meso position of the porphyrin ligand leading to the decomposition of the complex. Actually the destruction of the complex was spectroscopically confirmed during Fe(PPIXDME)Cl-catalyzed epoxidation of **3** with **4**. It has been reported9,12) that porphyrinato iron complexes bearing bulky substituents at the meso position of the porphyrin was stable to iodosobenzene and thereby showed high catalytic activity in the epoxidations. The higher catalytic activity shown by Fe(TMP)Br and Fe(TAP)Br, compared with Fe(TPP)Cl, would be explained on the basis of the steric effect. The catalytic activity of Fe(TDCPP)Cl and Fe(TMOPP)Cl can, however, not be interpreted in terms of the steric factors. Fe(TMOPP)Cl bearing bulkier and more electron donating methoxy groups exhibited the lowest activity among Fe(TPP)X congeners. On the contrary Fe(TDCPP)Cl which has less bulky but electron withdrawing chlorides showed the highest catalytic activity. Thus the electron withdrawing substituents promoted the oxygen atom transfer to olefins, whereas the electron donating substituents

Table 2. Effects of Porphyrin's Substituents on Epoxidation Catalyzed by Porphyrinato Iron(III) Chloride Complexes

P	MPIXDME	PPIXDME	ADIXDME	TPP	TMP$^{a)}$	TAP$^{a)}$	TMOPP	TDCPP	$T_{piv}PP^{a)}$
Yield of **5** /%	8	15	19	37	52	45	27	77	70

a) Fe(P)Br.

retarded it. It has turned out that the electronic effects of the substituents as well as their steric effects play an important role in the epoxidations of 3 catalyzed by iron(III) porphyrin complexes. Similar electronic effects were also observed in β-substituted porphyrinato iron complexes; electron withdrawing ability of porphyrins is in the order ADIXDME> PPIXDME> MPIXDME as estimated from their pK_3 values.[18] Fig. 1 shows that the yields of 5 in the meso-substituted porphyrinato iron(III) complexes-catalyzed epoxidation are correlated well with the near infrared absorption bands of the porphyrin complexes which relate to the degree of the elctron transfer from porphyrin to iron(III).[19] Although a few reports[20,21] described that the electron withdrawing substituents on porphyrins increase the catalyst lifetime by suppressing the oxidative destruction of hemin, such decomposition of porphyrins was not observed for Fe(TPP)Cl-catalyzed reaction under the present conditions. The electron withdrawing groups may decrease electron density on the central iron atom and then that on the oxo ligand in the ferryl porphyrin intermediate. This reduction of electron density may enhance the electrophilicity of the oxo ligand toward olefins and consequently the porphyrin complex becomes the active catalyst for olefin epoxidation.[22] The electrophilicity of the oxo ligand serves also the regioselective epoxidation of limonene.[24]

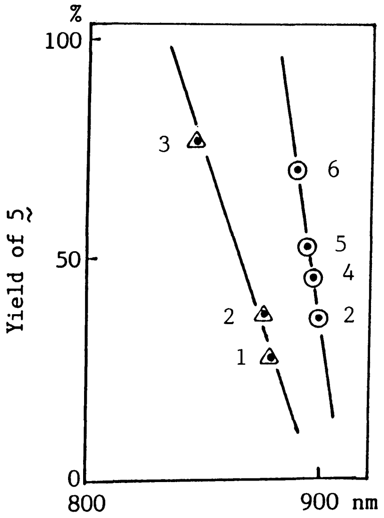


Fig. 1. Plot of the yield of 5 vs. the near infrared absorption band of Fe(P)Cl (▲) and Fe(P)Br (⊙). P: 1=TMOPP, 2=TPP, 3=TDCPP, 4=TAP, 5=TMP, 6=T_{piv}PP.

The effects of the axial ligand X on the catalytic activity were examined by using Fe(TPP)X as a catalyst(Table 3). The iodide axial ligand, the weakest electron withdrawing halogen, gave the lowest yield of 5 in the halogen complexes. Analogously replacing the OAc group in Fe(TPP)(OAc) with a more electronegative CF_3COO increases the catalytic activity considerably. A weak coordinating ligand such as perchlorate or fluoroborate may similarly increase the electrophilicity of oxo ligand leading to the higher yield of 5. Fe(TPP)OMe showed a similar activity to that of Fe(TPP)Cl but μ-oxo dimer $[Fe(TPP)]_2O$ exhibited a lower activity. Although the effect of halogens on the yield of 5 is hardly compared with that of MeO ligand due to their different bonding nature to iron, it can be mentioned that within a series of homologous ligands, e.g. halogens, enhancement of electron accepting ability of axial ligands(X) in 1(M = Fe) increases the elecrophilicity of the trans oxo ligand just as substituents on porphyrins do. Concerning axial ligands, it has been claimed[11,25] that addition of imidazole or pyridine increases

Table 3. Effects of Axial Ligands in Fe(TPP)X on Catalytic Epoxidation

X	F	Cl	Br	I	CF_3COO	CH_3COO	ClO_4	BF_4	MeO	1/2O	Cl+Im[a]	ClO_4+Im[a]
Yield of 5 /%	35	37	36	23	45	38	55	47	33	28	37	53

a) Im(Imidazole)/Fe = 10.

the yield in the epoxidation with Mn(TPP)Cl derivatives-$NaClO_4$ or H_2O_2 systems. In the present oxidation, however, addition of imidazole did not affect the epoxide formation. Thus, the reaction mechanism of epoxidation would be different in both catalytic systems. Contrary to our results, a recent paper21) on hydroxylation of alkanes with 4 catalyzed by Fe(TPP)X has described that a perchlorate as an axial ligand gave a lower activity than halogens or methoxy ligand. Two model reactions for P-450 catalyzed oxidation, epoxidation and hydroxylation seem to proceed via different mechanisms.

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3) Abbrevations used in this paper: TPP,4) meso-tetraphenylporphyrin dianion; MPIXDME,5) mesoporphyrin IX dimethylester dianion; PPIXDME,5) protoporphyrin IX dimethylester dianion; ADIXDME,5) 2,4-diacetyldeuteroporphyrin IX dimethylester dianion; TMP,6) meso-tetramesitylporphyrin dianion; TAP,7) meso-tetrakis(9-anthryl)porphyrin dianion; TMOPP,8) meso-tetrakis(2,4,6-trimethoxyphenyl) porphyin dianion; TDCPP,9) meso-tetrakis(2,6-dichlorophenyl)porphyrin dianion; $T_{piv}PP$,10) meso-α,α,α,α-tetrakis(o-pivalamidophenyl)pophyrin dianion
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