# Asymmetric Epoxidation of Olefins Catalyzed by Manganese Complexes of Chiral "Strapped" Porphyrins with Diastereotopic Faces. A Novel Strategy for Stereochemical Modeling of the Active Site of Cytochrome P-450

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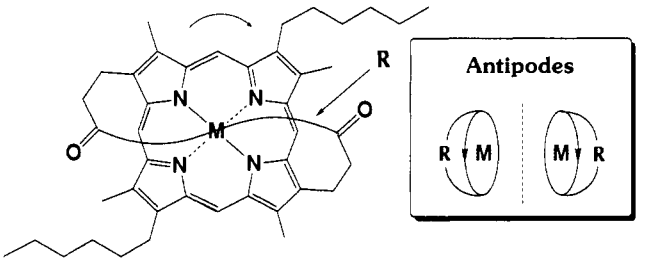
**Abstract:** The optical antipodes of chiral *p*-xylylene-, *m*-xylylene-, and dodecamethylene-strapped porphyrins were resolved by HPLC. Asymmetric epoxidation of prochiral olefins such as styrene derivatives and vinylnaphthalene by iodosobenzene was achieved by using the manganese complexes of the antipodes of *p*-xylylene-strapped porphyrin as catalysts in the presence of imidazole, and the optically active epoxides were obtained in 42–58% ee (enantiomeric excess). When imidazole was absent, the epoxides with the opposite configuration were formed in lower ee. In the presence of imidazole, the enantioselectivity of the reaction depended on the structure of the strap in the catalyst, while no such dependence was observed in the absence of imidazole. When imidazole was present in the competitive oxidation of styrene with more substituted olefins, the *p*-xylylene-strapped catalyst showed higher selectivity for styrene than (EtioP)MnCl, while the selectivity decreased in the absence of imidazole.

## Introduction

Cytochrome P-450 is one of the most attractive metalloenzymes, which catalyze metabolic oxygen-transfer processes. The active site of cytochrome P-450 is an iron porphyrin bound to a cysteine thiolate group of the chiral protein molecule.[1] It has been also noted that the epoxidation of prochiral olefins mediated by cytochrome P-450 takes place enantioselectively under appropriate conditions.[2] In relation to the mechanism of this interesting asymmetric oxygen transfer, various chiral metalloporphyrin catalysts have been exploited.[3] The representative catalysts bear chiral groups such as binaphthyl and peptide groups covalently linked to achiral porphyrin moieties, which model the essential role of the chiral protein molecule of cytochrome P-450 in the stereochemical course of the oxygen-transfer process.

In the present paper, we propose a fundamentally new strategy for structurally modeling the active site of cytochrome P-450 in asymmetric epoxidation of prochiral olefins. The porphyrin ligand of P-450 is protoporphyrin IX, which has enantiotopic faces, and therefore, the active site has a diastereoisomeric structure upon coordination with the chiral cysteine thiolate group (Figure 1, I). In connection with this, the coordinated protoheme has been proposed to exist as either of two possible optically active diastereoisomers as a result of a stereospecific discrimination between the faces of the heme by the chiral thiolate group. Thus, the oxygen transfer in the metabolic process has been considered to occur predominantly on either of the two chemically inequivalent, diastereotopic faces of the active site.[1] The catalysts exploited here are the manganese complexes of chiral strapped porphyrins **2c–4c**. Since the precursor dihexyldeuteroporphyrin II (**1**) is of $C_{2h}$ symmetry and has enantiotopic faces (prochiral), the strapped




**1** M = $H_2$, R = OH (x 2); Diacid

**2a** M = $H_2$
**2b** M = Zn
**2c** M = MnCl
} R = —NHCH$_2$–⟨benzene⟩–CH$_2$NH—

**3a** M = $H_2$
**3c** M = MnCl
} R = ⟨benzene⟩(—NHCH$_2$, —CH$_2$NH—)

**4a** M = $H_2$
**4c** M = MnCl
} R = —NH–(CH$_2$)$_{12}$–NH—

porphyrins derived from **1** are chiral due to the presence of the "strap" on either side of the two faces. Thus, the catalysts **2c–4c** have two chemically inequivalent, diastereotopic faces, and model the stereochemical structure of the P-450 active site. When an axially coordinating ligand is present on the nonstrapped face, the oxygen-transfer reaction is expected to occur exclusively on the strapped face of the catalyst (Figure 1, II) (Scheme I).

By using these novel P-450 model catalysts (**2c–4c**), we have attempted asymmetric epoxidation of prochiral olefins and discussed the effects of coordinating base on the enantioselectivity of the reaction, taking into account also the results of competitive oxidation of olefin pairs with different steric bulks.

## Results

**Optical Resolution of Chiral Strapped Porphyrin.**[5] The antipodes of a series of chiral strapped porphyrins (**2a–4a**) were obtained in optically pure forms by means of HPLC on silica gel coated with cellulose tris[(3,5-dimethylphenyl)carbamate]. For example, zinc complex of *p*-xylylene-strapped porphyrin ((*p*-XYSP)Zn, **2b**) showed two peaks (fractions I and II) with comparable peak areas when chromatographed with hexane/ethanol/diethylamine (96/3/1 v/v) as eluent (Figure 2). The compounds corresponding to these two peaks were fractionated, both of which were found to be identical to the original **2b** in terms of the absorption spectra, while the circular dichroism (CD) spectra were perfect mirror

(1) (a) Ortiz de Montellano, P. R.; Kunze, K. L.; Belian, H. S. *J. Biol. Chem.* **1983**, *258*, 45. (b) Kunze, K. L.; Mangold, B. L. K.; Wheeler, C.; Belian, H. S.; Ortiz de Montellano, P. R. *J. Biol. Chem.* **1983**, *258*, 4202.

(2) (a) Miwa, G. T.; Lu, A. Y. H. The Topology of the Mammalian Cytochrome P-450 Active Site. In *Cytochrome P-450, Structure, Mechanism, and Biochemistry*; Ortiz de Montellano, P. R., Ed.; Plenum Press: New York and London, 1986; pp 77–88. (b) Harris, C.; Philpot, R. M.; Hernandez, O.; Bend, J. R. *J. Pharmacol. Exp. Ther.* **1989**, *248*, 492. (c) Foureman, G. L.; Harris, C.; Guengerich, F. P.; Bend, J. R. *J. Pharmacol. Exp. Ther.* **1986**, *236*, 144. (d) Ortiz de Montellano, P. R.; Fruetel, J. A.; Collins, J. R.; Camper, D. L.; Loew, G. H. *J. Am. Chem. Soc.* **1991**, *113*, 3195.

(3) (a) Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5791. (b) Mansuy, D.; Battioni, P.; Renaud, J. P.; Guerin, P. *J. Chem. Soc., Chem. Commun.* **1985**, 155. (c) Naruta, Y.; Tani, F.; Maruyama, K. *Chem. Lett.* **1989**, 1269. (d) O'Malley, S.; Kodadek, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 9116. (e) Collman, J. P.; Zhang, X.; Hembre, R. T.; Brauman, J. I. *J. Am. Chem. Soc.* **1990**, *112*, 5356. (f) Groves, J. T.; Viski, P. *J. Org. Chem.* **1990**, *55*, 3628.

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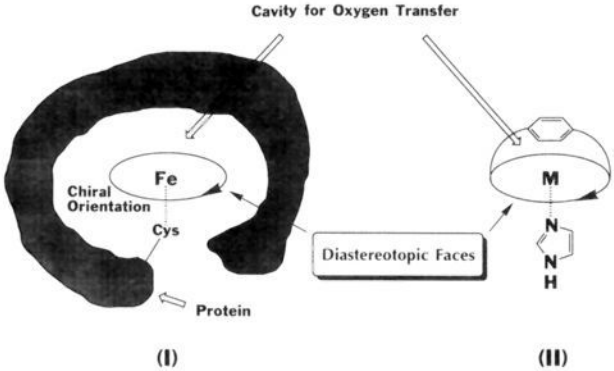



**Figure 1**. Schematic representations of the structures of the active site of cytochrome P-450 (I) and the metal complex of chiral strapped porphyrin coordinated by imidazole (II).

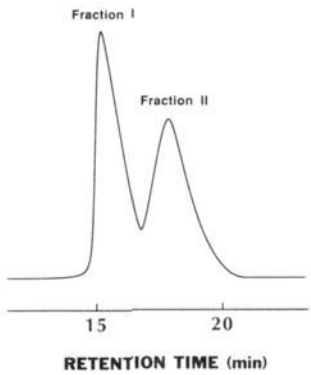
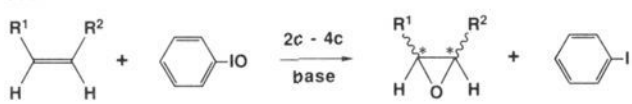



**Figure 2**. HPLC profile of **2b** using the analytical column (see Experimental Section) with hexane/ethanol/diethylamine (96/3/1 v/v) as eluent at room temperature monitored at 390 nm.

**Scheme I**




images of each other (Figure 3A).[4] Fraction I provided a positive CD band in the Soret region (410 nm) and fraction II a negative band. Thus, these two antipodes are denoted here as (+)- and (−)-**2b**, respectively. The free-base porphyrin **2a** derived from (+)-**2b** also exhibited a positive CD band at the Soret region (401 nm) ((+)-**2a**), and that from (−)-**2b** a negative band ((−)-**2a**). The same was true for the CD profiles of the antipodes of the chloromanganese complex **2c** ((+)- and (−)-**2c**) derived from (+)- and (−)-**2a**, respectively (Figure 3A). The antipodes of **2a** in the free-base forms could not be directly resolved by HPLC due to the poor peak separation under similar HPLC conditions. An attempted HPLC resolution of the manganese complex **2c** also failed due to its too strong affinity toward the column pack. In sharp contrast to **2a**, the antipodes of the free-base *m*-xylylene-strapped porphyrin ((*m*-XYSP)$H_2$, **3a**) and dodecamethylene-strapped porphyrin ((DMSP)$H_2$, **4a**) could be directly resolved by HPLC with the same column pack and showed strong CD bands at the Soret regions (401 nm) (Figure 3B,C). However, as for **3a**, the antipode obtained as the first fraction showed a negative CD band at the Soret region (401 nm) ((−)-**3a**), and the second fraction a positive band. ((+)-**3a**). Thus, the order of elution of the (+)- and (−)-antipodes of **3a** was opposite to that of **4a**.

(4) We have recently reported the optical resolution of the antipodes of chiral porphyrins and metalloporphyrins derived from etioporphyrin I with $C_{4h}$ symmetry using similar HPLC techniques: (a) N-substituted porphyrins: Kubo, H.; Aida, T.; Inoue, S.; Okamoto, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 1015. (b) Meso-substituted porphyrins: Konishi, K.; Miyazaki, K.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1990**, *112*, 5639. (c) Cobalt(III) porphyrins: Konishi, K.; Sugino, T.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1991**, *113*, 6487.

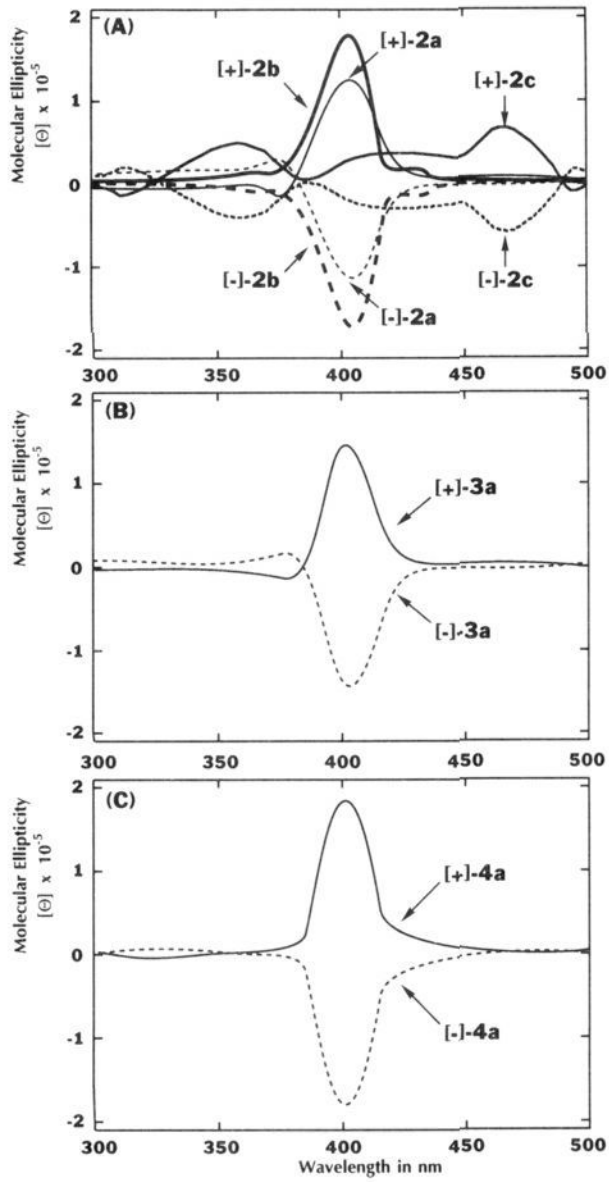



**Figure 3**. CD spectra of the antipodes of **2a**, **2b**, and **2c** (A), **3a** (B), and **4a** (C) in $CHCl_3$ at room temperature.

**Asymmetric Epoxidation of Olefins.** Typically, epoxidation of olefins was carried out under nitrogen in $CH_2Cl_2$ at −20 to −10 °C using the antipodes of the chloromanganese complexes **2c**–**4c** as chiral catalysts, 100 equiv of iodosobenzene as oxidant, and 500 equiv of olefin. As shown in Table I, the epoxidation occurred with satisfactory enantioselectivities when the antipodes of *p*-xylylene-strapped catalyst **2c** were used as catalysts in the presence of imidazole. For example, use of (+)-**2c** as a catalyst with 10 equiv of imidazole for the epoxidation of styrene resulted in the formation of optically active styrene oxide in 43% yield (determined on the basis of the initial amount of iodosobenzene)[5] with (*R*) configuration in 49% enantiomeric excess (ee) (run 1). As expected, using the catalyst with the opposite configuration ((−)-**2c**), (*S*)-styrene oxide was preferentially formed (45% yield) in a comparable enantiomeric excess (48% ee) under the same conditions (run 2). Similarly, 4-chloro- and 4-methylstyrenes, 2-vinylnaphthalene, indene, and 1,2-dihydronaphthalene were enantioselectively epoxidized in the presence of imidazole in 42–58% ee with yields based on the initial amount of iodosobenzene ranging from 32% to 65% (runs 7 and 11–14). Substituted imidazoles such as 1-ethyl- and 2-methylimidazoles worked

(5) The yield of styrene oxide, as determined on the basis of the amount of the converted styrene (10.2%, by GC), was 84%.

Table I. Asymmetric Epoxidation of Olefins by Chiral Manganese Porphyrins[a]

| run | olefin | catalyst | base | yield, %[b,c] | ee, % | confign |
|---|---|---|---|---|---|---|
| 1 | styrene | (+)-**2c** | imidazole | 43[d] | 49 | (*R*)-(+) |
| 2 | | (−)-**2c** | imidazole | 45 | 48 | (*S*)-(−) |
| 3 | | (+)-**2c** | none | 72 | 18 | (*S*)-(−) |
| 4 | | (+)-**2c** | imidazole[e] | 32 | 49 | (*R*)-(+) |
| 5 | | (+)-**2c** | 1-ethylimidazole | 68 | 50 | (*R*)-(+) |
| 6 | | (−)-**2c** | 1-ethylimidazole[f] | 55 | 48 | (*S*)-(−) |
| 7 | 4-chlorostyrene | (−)-**2c** | imidazole | 41 | 42 | (*S*)-(−) |
| 8 | | (−)-**2c** | imidazole[g] | 8 | 23 | (*S*)-(−) |
| 9 | | (−)-**2c** | 2-methylimidazole | 40 | 42 | (*S*)-(−) |
| 10 | | (−)-**2c** | 2-phenylimidazole | 36 | 8 | (*S*)-(−) |
| 11 | 4-methylstyrene | (+)-**2c** | imidazole | 56 | 47 | (*R*)-(+)[h] |
| 12 | 2-vinylnaphthalene | (+)-**2c** | imidazole | 65 | 42 | (*R*)-(+)[h] |
| 13 | indene | (+)-**2c** | imidazole | 58 | 58 | (1*R*,2*S*)-(−) |
| 14 | 1,2-dihydronaphthalene | (+)-**2c** | imidazole | 32 | 52 | (1*R*,2*S*)-(+) |
| 15 | styrene | (+)-**3c** | 1-ethylimidazole | 27 (5) | 30 | (*R*)-(+) |
| 16 | | (+)-**3c** | none | 18 (4) | 16 | (*S*)-(−) |
| 17 | styrene | (+)-**4c** | 1-ethylimidazole | 33 (14) | 17 | (*R*)-(+) |
| 18 | | (+)-**4c** | none | 30 (10) | 16 | (*S*)-(−) |

[a] $[Olefin]_0/[PhIO]_0/[base]_0/[catalyst]_0$ = 900 μmol/180 μmol/18 μmol/1.8 μmol in $CH_2Cl_2$ (1.0 mL) at −20 to −10 °C under $N_2$ for 3 h. [b] By GC based on the amount of iodosobenzene charged. [c] No carbonyl compounds were detected unless otherwise noted. The numbers in parentheses are the yields of phenylacetaldehyde. [d] 84%, as determined on the basis of the amount of the converted styrene (10.2%, by GC). [e] $[Imidazole]_0/[catalyst]_0$ = 100. [f] In acetonitrile (1.0 mL). [g] In toluene/$CH_2Cl_2$ (0.5 mL/0.5 mL). [h] From analogy of the $^1H$ NMR profile with that of (*R*)-styrene oxide in the presence of $Eu(hfc)_3$.

similarly to nonsubstituted imidazole for the asymmetric epoxidation (runs 5 and 9), while use of 2-phenylimidazole resulted in a remarkable decrease in enantioselectivity (run 10). In a more polar solvent such as acetonitrile under similar conditions, asymmetric epoxidation of styrene also occurred with a comparable enantioselectivity to that in $CH_2Cl_2$ (run 6). On the other hand, use of a less polar solvent such as toluene/$CH_2Cl_2$ (50/50) resulted in lowering the chemical yield and enantiomeric excess of the product (run 8). When the chiral *m*-xylylene-strapped catalyst (−)-**3c** was used coupled with 1-ethylimidazole, (*R*)-styrene oxide was formed in 30% ee (27% yield) under similar conditions (run 15). Use of the chiral catalyst bearing dodecamethylene strap (+)-**4c** resulted in a significant decrease in enantiomeric excess of the epoxide (17% ee; (*R*), 33% yield) along with the formation of a considerable amount of phenylacetaldehyde (run 17). Thus, in the presence of imidazole, the enantioselectivity of the reaction varies with the structure of the strap in the catalyst. However, it should be also noted that (*R*)-epoxides were always formed predominantly using as catalysts the (+)-antipodes of **2c**–**4c**, providing positive CD bands in the Soret regions, while the formation of (*S*)-epoxides was favored when the catalysts with the opposite configuration ((−)-antipodes) were employed.

In sharp contrast, when styrene was epoxidized in the absence of imidazole using **2c** as catalyst (run 3), the epoxide with the opposite configuration to that in the presence of imidazole (run 1) was formed. The same was true for the reactions using **3c** and **4c** as catalysts (runs 16 and 18, runs 15 and 17). Furthermore, the observed percent ee of the products were all low in the range of 16–18%, indicating that the strap part of the catalyst does not affect the enantioselectivity of the reaction.

**Competitive Epoxidation.** In connection with the mechanism of the above asymmetric oxygen transfer, styrene and more substituted olefins were competitively oxidized using **2c** as catalyst in the presence or absence of imidazole, and the substrate selectivities were compared with those of (EtioP)MnCl[6] as a non-strapped catalyst. As shown in Table II, **2c** coupled with 1-ethylimidazole showed substrate selectivities for styrene competing with other olefins. For example, the oxidation of an equimolar mixture of styrene and *trans*-β-methylstyrene (250 equiv of each) with iodosobenzene (100 equiv) catalyzed by racemic **2c** in the presence of 1-ethylimidazole (10 equiv) at −10 °C resulted in the conversion ratio of styrene to *trans*-β-methylstyrene of 3.2:1 (run 1). In contrast, in the absence of 1-ethylimidazole, the preference for styrene was reduced to give the ratio of 0.5:1 (run 2), which is very close to that observed with the (EtioP)MnCl/1-ethylimidazole system (0.4:1, run 3). Similarly, in the competitive oxidation of styrene with β,β-dimethylstyrene (runs 4 and 5), *cis*-2-octene (runs 6–8) or 2-methyl-2-pentene (runs 9 and 10) using **2c**/1-ethylimidazole system, the selectivity for styrene was higher than those observed with **2c** alone (run 7) and the (EtioP)MnCl/1-ethylimidazole system (runs 5, 8 and 10). These observations again indicate the essential effect of imidazole on the oxygen-transfer process mediated by the manganese strapped porphyrin catalyst **2c**.

**Coordination of Imidazole to Manganese Strapped Porphyrin 2c.** The spectral changes upon titration of a $CH_2Cl_2$ solution of **2c** with imidazole were linear with the concentration of imidazole to the first power,[7] indicating that only one imidazole molecule can coordinate to **2c**.[8] The molecular model study indicated that the coordination of imidazole to **2c** is likely to occur specifically on the open face of **2c**, since imidazole is too large to be incorporated into the strap cavity. In connection with the low enantioselectivity in run 10 in Table I, the binding constants of imidazole and 2-phenylimidazole to **2c** were determined in $CH_2Cl_2$ at 20 °C to be $2.1 \times 10^2$ and $0.49 \times 10^2$ $L \cdot mol^{-1}$, respectively. Thus, the coordinating ability of 2-phenylimidazole to **2c** is lower than that of imidazole.

**NMR Studies on the Structures of Xylylene-Strapped Porphyrins 2a and 3a.** In relation to the difference in enantioselectivity between two xylylene-strapped catalysts (**2c** and **3c**) in the presence of imidazole (runs 5 and 15), the $^1H$ NMR spectra of the free-base porphyrins **2a** and **3a** were measured in $CDCl_3$, where **2a** showed a single 1,4-phenylene signal at δ 2.44 ppm, indicating a parallel conformation of the phenylene moiety with the porphyrin plane on the NMR time scale. On the other hand, as for the 1,3-phenylene moiety of **3a**, the notable upfield shift for the signal of the proton at the 2-position (δ 0.30) compared with those for the protons at the 4- and 6-positions (δ 5.81) and 5-position (δ 6.14) was observed, which indicates a perpendicular conformation of the phenylene moiety with the porphyrin plane.

## Discussion

The asymmetric oxygen transfer achieved with the chiral manganese strapped porphyrin catalyst/imidazole systems is

(6) (EtioP)MnCl: chloro(2,7,12,17-tetraethyl-3,8,13,18-tetramethylporphinato)manganese.

(7) Ariel, S.; Dolphin, D.; Domazeits, G.; James, B. R.; Leung, T. W.; Rettig, S. J.; Trotter, J.; Williams, G. M. *Can. J. Chem.* **1984**, *62*, 755.

(8) A similar observation has been reported by Collman et al. for the coordination of 1-methylimidazole to a bromomanganese(III) complex of picnic basket porphyrin, where only one imidazole binds to form a five-coordinate manganese complex: Collman, J. P.; Brauman, J. I.; Fitzgerald, J. P.; Hampton, P. D.; Naruta, Y.; Michida, T. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 47.

Table II. Competitive Epoxidation of Olefins by Manganese Porphyrins[a]

| run | olefin A | olefin B | catalyst system[b] | yield, %[c,d] epoxide A | yield, %[c,d] epoxide B | conversn of olefin A[e] / conversn of olefin B[e] |
|---|---|---|---|---|---|---|
| 1 | styrene | *trans*-β-methylstyrene | **2c**/NEIm | 58 | 18 | 3.2 |
| 2 | | | **2c** | 21 | 42 | 0.5 |
| 3 | | | (EtioP)MnCl/NEIm | 13 (13) | 62 | 0.4 |
| 4 | styrene | β,β-dimethylstyrene | **2c**/NEIm | 50 | 21 | 2.3 |
| 5 | | | (EtioP)MnCl/NEIm | 12 (17) | 55 | 0.5 |
| 6 | styrene | *cis*-2-octene | **2c**/NEIm | 55 | 6 | 9.1 |
| 7 | | | **2c** | 37 | 16 | 2.4 |
| 8 | | | (EtioP)MnCl/NEIm | 16 (26) | 40 | 1.0 |
| 9 | styrene | 2-methyl-2-pentene | **2c**/NEIm | 64 | 10 | 6.6 |
| 10 | | | (EtioP)MnCl/NEIm | 20 (26) | 40 | 1.2 |

[a] $[\text{Olefin A}]_0/[\text{olefin B}]_0/[\text{PhIO}]_0/[\text{base}]_0/[\text{catalyst}]_0$ = 250 μmol/250 μmol/100 μmol/10 μmol/1 μmol in $CH_2Cl_2$ (0.5 mL) at −10 °C under $N_2$ for 1 h. [b] NEIm: 1-ethylimidazole. [c] By GC based on the amount of iodosobenzene charged. [d] No carbonyl compounds were detected unless otherwise noted. The numbers in parentheses are the yields of phenylacetaldehyde. [e] By GC.

considered a result of the epoxidation predominantly occurring on the strapped face of the catalyst. In the presence of imidazole, the unstrapped face of the active site is considered to be blocked by the coordination with imidazole, so that the access of olefins and/or iodosobenzene is prohibited. Therefore, the enantioselectivity of the reaction in the presence of imidazole is affected by the structure of the strap in the catalyst (runs 5, 15, and 17) but not affected in the absence of imidazole (runs 3, 16, and 18). When imidazole is coordinated to the catalyst, the enantioselectivity increased in the order **4c**, **3c**, and **2c**, where the catalyst **4c** bearing the longest and relatively flexible strap exhibited the lowest enantioselectivity (run 17). The difference in enantioselectivity of the two xylylene-strapped catalysts **2c** and **3c** (runs 5 and 15) may be ascribed to the conformational difference of the phenylene moieties, where the phenylene moiety in **2c** oriented in parallel with the porphyrin plane may provide a sterically more hindered cavity on the active site than the vertically oriented phenylene group in **3c**.

In the absence of imidazole, the reaction on the unstrapped open face of the catalyst is allowed, which preferentially affords the epoxides with the opposite configurations. Taking into account the inversion of the stereochemistry of reaction and the decrease in percent ee of the products (runs 3, 16, and 18), the epoxidation in the absence of imidazole is considered to occur predominantly on the sterically less hindered unstrapped face of the catalyst with a low steric requirement. When an imidazole with a low coordinating ability such as 2-phenylimidazole is used, the epoxidation on the unstrapped face is less efficiently suppressed, so that the percent ee of the product decreases (run 10).

The results of the competitive oxidation of styrene with more substituted olefins can also support the above mechanistic understanding on the oxygen-transfer reaction. In the presence of a coordinating imidazole, the reaction predominantly occurs on the sterically hindered strapped face of the catalyst, so styrene having a nonsubstituted olefinic carbon atom is preferred to the 1,2-di- and 1,1,2-trisubstituted olefins (runs 1, 4, 6, and 9 in Table II). On the other hand, in the absence of imidazole, the reaction occurs predominantly on the sterically less hindered unstrapped face. Therefore, the selectivity for styrene (runs 2 and 7) is almost comparable to the case using the nonstrapped catalyst system (EtioP)MnCl/1-ethylimidazole (runs 3 and 8). Thus, the results of competitive oxidation again indicate the difference in steric requirement between the strapped and nonstrapped faces of the catalyst.

## Conclusion

In the present paper, the conceptually new chiral metalloporphyrin catalysts **2c**–**4c** which mediate asymmetric oxygen-transfer reaction have been presented. The catalysts are derived from an enantiotopic porphyrin by introducing a strap on one side, and have diastereotopic faces (II in Figure 1) analogous to the chirally oriented protoheme in the active center of cytochrome P-450 (I) having enantiotopic protoporphyrin IX. The reaction proceeds with satisfactory enantioselectivity using the catalyst **2c** having a parallel-oriented phenylene strap and a coordinating imidazole on the opposite side.

## Experimental Section

**Materials.** Acetonitrile, triethylamine, and dichloromethane ($CH_2Cl_2$) were distilled over calcium hydride under dry nitrogen. Toluene and tetrahydrofuran (THF) were distilled over sodium benzophenone ketyl just before use. Dihexyldeuteroporphyrin II dimethyl ester (2,12-bis-[2′-(methoxycarbonyl)ethyl]-3,8,13,18-tetramethyl-7,17-dihexylporphine) was synthesized from 4-ethyl-3-[(methoxycarbonyl)ethyl]-5-methylpyrrole-2-carboxylic acid[9] and 4-ethyl-5-formyl-3-hexylpyrrole-2-carboxylic acid[10] by a similar procedure reported by Collman et al.[11]

**Hydrolysis of Dihexyldeuteroporphyrin II Dimethyl Ester.** Dihexyldeuteroporphyrin II dimethyl ester (1.0 g, 1.41 mmol) was dissolved in a mixture of THF (100 mL) and concentrated hydrochloric acid (100 mL), and stirred at room temperature in the dark for 20 h. The solvents were removed under reduced pressure, and the residue was taken up in $CHCl_3$ (100 mL). The organic phase was washed with water until the aqueous phase was neutralized, dried over anhydrous $Na_2SO_4$, and evaporated to dryness to give dihexyldeuteroporphyrin II (**1**) as a purple powder, which was used in the next reaction without further purification.

***p*-Xylylene-Strapped Porphyrin ((*p*-XYSP)$H_2$, 2a).**[12] To a THF solution (200 mL) of dihexyldeuteroporphyrin II (**1**) (960 mg, 1.41 mmol) in a 1-L round-bottom flask equipped with a dropping funnel were successively added triethylamine (1.0 mL, 7.4 mmol) and isobutyl chloroformate (0.5 mL, 3.4 mmol) by means of hypodermic syringes under dry nitrogen at room temperature to convert **1** into the corresponding mixed anhydride. After the mixture was stirred for 1 h at room temperature, a THF solution (500 mL) of 1,4-xylylenediamine (584 mg, 4.29 mmol) was introduced to the dropping funnel by a syringe and added dropwise to the mixed anhydride solution for a period of 5 h. The mixture was then stirred for 36 h at room temperature under dry nitrogen and evaporated to dryness. The residue dissolved in $CH_2Cl_2$ (100 mL) was filtered from insoluble fractions by passing through Cerite, and the filtrate was concentrated to a small volume, which was chromatographed on silica gel (Wakogel C-300). After a brown band was eluted with $CH_2Cl_2$, a red band was eluted with $CHCl_3$/ethyl acetate (90/10 v/v), which was collected and evaporated to dryness, and the residue was recrystallized from $CH_2Cl_2$/hexane to give **2a** as a red-purple powder (382.3 mg, 35% yield). FAB-HRMS: calcd for $C_{50}H_{63}O_2N_6$ ($MH^+$) $m/z$ 779.5013, obsd 779.5071. UV-vis: $\lambda_{max}$ (log ε) 401 nm (5.18), 500 (4.05), 536 (3.97), 566 (3.78), 620 (3.49). $^1$H NMR: δ 10.13 and 10.03 (s × 2, 4 H, meso), 4.70 (td, 2 H, diastereotopic porph-C$H_2$CH$_2$CO), 4.24–3.96 (m, overlapped, 6 H, diastereotopic porph-C$H_2$CH$_2$CO (2 H) and porph-C$H_2C_5H_{11}$ (4 H)), 3.76 and 3.55 (s × 2, 12 H, porph-$CH_3$), 3.29 (br, 2 H, CONH), 2.97 and 2.36 (m × 2, 4 H, diastereotopic porph-CH$_2$C$H_2$CO), 2.58 (d, 4 H, C$H_2C_6H_4$), 2.44 (s, 4 H, $C_6H_4$), 2.27 (m, 4 H, porph-CH$_2$C$H_2C_4H_9$), 1.77–1.32 (m, overlapped, 12 H, porph-$C_2H_4$C$H_2C_3H_7$, -$C_3H_6$C$H_2C_2H_5$, and -$C_4H_8$C$H_2$CH$_3$), 0.91 (t, 6 H, porph-$C_5H_{10}$C$H_3$), −3.55 (br, 2 H, core NH). These assignments were supported by 2D NMR.

**Preparation and Demetalation of Zinc Complex of *p*-Xylylene-Strapped Porphyrin ((*p*-XYSP)Zn, 2b).** **2b** was obtained quantitatively by the reaction of **2a** with zinc acetate in $CHCl_3$/MeOH.[13] Demetalation was

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carried out by shaking a $CHCl_3$ solution of **2b** with 10% HCl followed by neutralization with aqueous $NaHCO_3$.

***m*-Xylylene-Strapped Porphyrin ((*m*-XYSP)$H_2$, 3a).** To a 50-mL round-bottom flask containing a THF solution (25 mL) of **1** (483 mg, 0.71 mmol) were successively added triethylamine (0.51 mL, 3.77 mmol) and isobutyl chloroformate (0.22 mL, 1.7 mmol) under dry nitrogen at room temperature. After stirring for 1 h at room temperature, the resulting mixed anhydride solution was transferred in a nitrogen stream by a syringe to a dropping funnel connected to a 500-mL round-bottom flask containing THF (75 mL). The above mixed anhydride solution was added dropwise to the flask for a period of 10 h, with a simultaneous addition of a THF solution (25 mL) of 1,3-xylylenediamine (140 μL, 1.16 mmol) by a syringe pump through a rubber septum. The reaction mixture was then stirred for 12 h and evaporated to dryness. The residue dissolved in $CH_2Cl_2$ (100 mL) was filtered through Cerite, and the filtrate was chromatographed on silica gel (Wakogel C-300). A red fraction eluted with $CH_2Cl_2$ was collected and concentrated to a small volume (5 mL), to which hexane (30 mL) was then added, and the mixture was slowly evaporated under reduced pressure to give **3a** as a purple powder (130 mg, 23% yield). FAB-HRMS: calcd for $C_{50}H_{63}O_2N_6$ ($MH^+$) *m/z* 779.5013, obsd 779.5034. UV-vis: $\lambda_{max}$ (log ε) 401 nm (5.14), 501 (3.98), 538 (3.96), 566 (3.75), 620 (3.42). $^1H$ NMR: δ 10.06 and 10.03 (s × 2, 4 H, meso), 6.14 (t, 1 H, 5-H of $C_6H_4$), 5.81 (dd, 2 H, 4- and 6-H of $C_6H_4$), 4.67 (td, 2 H, diastereotopic porph-$CH_2CH_2CO$), 4.19–4.06 (m, overlapped, 6 H, diastereotopic porph-$CH_2CH_2CO$ (2 H) and porph-$CH_2C_5H_{11}$ (4 H)), 3.75 and 3.53 (s × 2, 12 H, porph-$CH_3$), 2.80 and 2.11 (m × 2, 4 H, diastereotopic porph-$CH_2CH_2CO$), 2.36–2.31 (m, overlapped, 6 H, porph-$CH_2CH_2C_4H_9$ and diastereotopic $CH_2C_6H_4$), 2.19 (br, 2 H, NHCO), 1.76–1.34 (m, overlapped, 12 H, porph-$C_2H_4CH_2C_3H_7$, -$C_3H_6CH_2C_2H_5$, and -$C_4H_8CH_2CH_3$), 0.92 (t, 6 H, porph-$C_5H_{10}CH_3$), 0.30 (s, 1 H, 2-H of $C_6H_4$), −0.64 (d, 2 H, diastereotopic $CH_2C_6H_4$), −3.58 (br, 2 H, core NH). These assignments were supported by 2D NMR.

**Dodecamethylene-Strapped Porphyrin ((DMSP)$H_2$, 4a).** **4a** was prepared in 27% yield from **1** and dodecamethylenediamine in a manner similar to that described for the preparation of **2a**. FAB-HRMS: calcd for $C_{54}H_{79}O_2N_6$ ($MH^+$) *m/z* 843.6264, obsd 843.6264. UV-vis: $\lambda_{max}$ (log ε) 401 nm (5.18), 500 (4.05), 536 (3.97), 566 (3.78), 620 (3.49). $^1H$ NMR: δ 10.13 and 10.09 (s × 2, 4 H, meso), 4.81 (t, 2 H, CONH), 4.67 (dd, 2 H, diastereotopic porph-$CH_2CH_2CO$), 4.24–4.07 (m, overlapped, 6 H, diastereotopic porph-$CH_2CH_2CO$ (2 H) and porph-$CH_2C_5H_{11}$ (4 H)), 3.69 and 3.55 (s × 2, 12 H, porph-$CH_3$), 3.28 and 3.10 (td × 2, 4 H, diastereotopic porph-$CH_2CH_2CO$), 2.27 (m, 4 H, porph-$CH_2CH_2C_4H_9$), 1.82–1.37 (m, overlapped, 12 H, porph-$C_2H_4CH_2C_3H_7$, -$C_3H_6CH_2C_2H_5$, and -$C_4H_8CH_2CH_3$), 0.95 (t, 6 H, porph-$C_5H_{10}CH_3$), 0.57 (m, 8 H, $CONHCH_2$ and $CONHCH_2CH_2$), 0.11 (m, 8 H, $CONH(CH_2)_2CH_2$ and $CONH(CH_2)_3CH_2$), −0.22 (br, 8 H, $CONH(CH_2)_4CH_2$ and $CONH(CH_2)_5CH_2$), −3.55 (br, 2 H, core NH).

**Optical Resolutions by HPLC.** Resolutions of the optical antipodes of **2b**, **3a**, and **4a** were carried out by using a 0.46 × 250 mm (analytical) or 20 × 500 mm (preparative) HPLC column packed with silica gel coated with cellulose tris[(3,5-dimethylphenyl)carbamate] as a chiral stationary phase. HPLC experiments with the analytical column were performed on a JASCO Type TWINCLE equipped with a JASCO Type 875-UV variable wavelength detector at a flow rate of 1.0 mL·min$^{-1}$ at room temperature and monitored at 390 nm. HPLC experiments with the preparative column were performed on a JASCO Type 887-PU pump equipped with a JASCO Type 875-UV variable wavelength detector, a JASCO Type 802-SC system controller, and a JASCO Type 892-01 column selector at a flow rate of 10.0 mL·min$^{-1}$ at room temperature and monitored at 410 nm. The HPLC column packs were prepared by the method reported by Okamoto et al.[14]

**Resolution of the Antipodes of 2b.** **2b** (2 mg) was dissolved in $CCl_4$ (20 mL) containing diethylamine (1 drop), and an aliquot (20 μL) of the solution was subjected to HPLC with the analytical column using hexane/ethanol/diethylamine (96/3/1 v/v) as eluent. Two peaks were observed at 15.2 and 18.6 min. For milligram-scale resolution, 3-mL portions of a $CCl_4$ solution (50 mL) of **2b** (50 mg) containing diethylamine (2 drops) were loaded on the preparative column with hexane/ethanol/diethylamine (84/15/1 v/v) as eluent.

**Resolution of the Antipodes of 3a.** **3a** (2 mg) was dissolved in $CCl_4$ (20 mL), and an aliquot (20 μL) of the solution was subjected to HPLC with the analytical column using hexane/ethanol (92/8 v/v) as eluent. Two peaks were observed at 8.4 and 9.6 min. For milligram-scale resolution, 3-mL portions of a $CCl_4$ solution (50 mL) of **3a** (50 mg) were loaded on the preparative column with hexane/ethanol (88/12 v/v) as eluent.

**Resolution of the Antipodes of 4a.** Under similar conditions as for **3a**, two peaks were observed at 19.7 and 24.8 min, using hexane/2-propanol/$CHCl_3$ (70/20/10 v/v) as eluent. In this case, the analytical column was also used for a milligram-scale resolution.

**Preparation of Chiral Chloromanganese Complexes.**[15] To a 50-mL round-bottom flask containing an acetic acid/acetic anhydride solution (5 mL/1 mL) of an optically active free-base porphyrin (**2a**, **3a**, or **4a**) (20 mg) was added $MnCl_2{\cdot}4H_2O$ (10 mg), and the mixture was refluxed for 10 h. Then, the reaction mixture was poured into a mixture of saturated aqueous $NaHCO_3$ and $CHCl_3$. The organic layer was separated and washed twice with saturated aqueous NaCl, dried over anhydrous $Na_2SO_4$, and evaporated to dryness. Recrystallization of the residue from $CH_2Cl_2$/hexane gave an optically active manganese complex (**2c**, **3c**, or **4c**) as a brown powder in a quantitative yield.

**Epoxidation Reactions. Asymmetric Epoxidation.** In a standard experiment, to a 20-mL Schlenk flask containing a stirring bar were successively added a dry $CH_2Cl_2$ solution (1 mL) of a manganese porphyrin (1.8 μmol), imidazole (10 equiv), and biphenyl or naphthalene (4–5 mg, GC standard). After the solution was degassed and cooled to −10 to −20 °C, an olefin (500 equiv) and iodosobenzene (100 equiv) were added, and the mixture was stirred for 3 h. An aliquot of the reaction mixture was subjected to GC analysis to determine the yield of epoxide. The residue was evaporated and subjected to flash column chromatography on silica gel with hexane/ether (80/20 v/v) as eluent, affording the analytically pure epoxide, which was analyzed by $^1H$ NMR in $CDCl_3$ containing a chiral shift reagent, tris[3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato]europium(III) (Eu(hfc)$_3$), to determine the enantiomeric excess. The absolute configuration was determined by polarimetry with sodium D-line.[16]

**Competitive Epoxidation.** To a 20-mL Schlenk flask containing a stirring bar were successively added a dry $CH_2Cl_2$ solution (0.5 mL) of a manganese porphyrin (1.0 μmol), 1-ethylimidazole (10 μmol), and naphthalene (4–5 mg, GC standard). To this solution were added two olefins (250 μmol of each), and then iodosobenzene (100 μmol), and the mixture was stirred at −10 °C under nitrogen for 1 h. The yields of epoxides and the conversions of olefins were determined by GC analysis of an aliquot of the reaction mixture.

**Measurements.** $^1H$ NMR spectra were measured in $CDCl_3$ on a JEOL Type GSX-270 spectrometer operating at 270 MHz, where the chemical shifts were determined with respect to internal $CHCl_3$ (δ 7.28). Absorption and circular dichroism spectra were measured in $CH_2Cl_2$ on a JASCO Type U-best 50 spectrometer and a JASCO Type J-500 spectropolarimeter, respectively, by using a quartz cell of 1-cm path length. Gas chromatographic analyses were performed on an Ohkura gas chromatograph, model-103, equipped with a RASCOT stainless capillary column (OV-101, 0.25 mm × 25 m), or a Shimadzu gas chromatograph, model GC-14A, equipped with a Shimadzu fused silica capillary column (CBP20-M25-025, 0.2 mm × 25 m). FAB-HRMS measurements were performed on a JEOL JMS-HX110 spectrometer. Optical rotation measurements were performed on a JASCO Model DIP-360 digital polarimeter.

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**Registry No. 1**, 63183-04-0; **2a**, 138260-17-0; (+)-**2a**, 138260-18-1; (−)-**2a**, 138260-19-2; **2b**, 138260-25-0; (+)-**2b**, 138332-62-4; (−)-**2b**, 138332-63-5; **2c** (isomer 1), 138260-26-1; **2c** (isomer 2), 138332-61-3; **3a**, 138260-20-5; (+)-**3a**, 138260-21-6; (−)-**3a**, 138260-22-7; (+)-**3c**, 138260-27-2; **4a**, 135327-80-9; (+)-**4a**, 138260-23-8; (−)-**4a**, 138260-24-9; (+)-**4c**, 138260-28-3; dihexyldeuteroporphyrin II dimethyl ester, 65486-04-6; 1,4-xylylenediamine, 539-48-0; 1,3-xylylenediamine, 1477-55-0; dodecamethylenediamine, 2783-17-7; styrene, 100-42-5; 4-chlorostyrene, 1073-67-2; 4-methylstyrene, 622-97-9; 2-vinylnaphthalene, 827-54-3; indene, 95-13-6; 1,2-dihydronaphthalene, 447-53-0; (*R*)-(+)-epoxystyrene, 20780-53-4; (*S*)-(−)-epoxystyrene, 20780-54-5; (*S*)-(−)-4-chloroepoxystyrene, 97466-49-4; (*R*)-(+)-4-methylepoxystyrene, 86457-69-4; (*R*)-(+)-2-(epoxyvinyl)naphthalene, 86457-71-8; (1*R*,2*S*)-epoxyindene, 85354-35-4; (1*R*,2*S*)-(+)-epoxy-1,2-dihydronaphthalene, 58800-12-7; cytochrome P-450, 9035-51-2.

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