Catalytic and Asymmetric Epoxidation of Olefins with Iron Complexes of "Twin-Coronet" Porphyrins. A Mechanistic Insight into the Chiral Induction of Styrene Derivatives

Yoshinori Naruta,* Fumito Tani, Nobuo Ishihara, and Kazuhiro Maruyama*

Contribution from the Department of Chemistry, Faculty of Science, Kyoto University, Sakyo-ku, Kyoto 606, Japan. *Received November 14, 1990*

Abstract: As a cytochrome-P-450-modeling asymmetric-oxidation system we designed and synthesized novel chiral C_2-symmetric "twin-coronet" porphyrins, which have chiral biaryl auxiliaries (i.e. binaphthyl and bitetralin derivatives) linked by ethereal bonds on both faces. Each face of these porphyrins forms a chiral substrate-binding site and is sterically protected from oxidative catalyst deterioration. In the catalytic oxidation of styrene derivatives with the iron porphyrins and iodosobenzene, we observed the highest ee (89%) for 2-nitrostyrene. We also found that the substituent σ^+ values correlated well with both the obtained log k_{rel} and the optical yields of the epoxides produced. The existence of a possible intermediate and the mechanism of chiral induction are discussed. Charge-transfer (CT) interactions between the substrates and the binaphthalene moieties over the catalysts at the oxo-transfer stage seem to function cooperatively with steric interactions in the fixation of the substrates and the recognition of their prochiral faces. We propose a new guideline for achieving high enantioselectivity through appropriate CT interactions in the catalytic asymmetric oxidation of simple substrates.

Asymmetric reactions have not been entirely exploited in modern synthetic organic chemistry; the field is still full of promise. In general, chemical amplification of the asymmetry of homogeneous chiral catalysts offers the most advantageous solution to this problem. Fair success has been obtained in enantioselective hydrogenation[1] and C–C bond formation.[2] Nevertheless, there has been relatively little progress in catalytic asymmetric oxidation (or oxygenation), especially for substrates not bearing coordinative functional groups.[3] In the successful catalytic systems, for example Sharpless oxidation,[4] the substrates should bear specific polar groups in order to form the precoordination site for the active metal center. If this restriction were removed, the pool of available substrates could be infinite in principle. Thus, it is desirable to design and synthesize novel oxidizing chiral catalysts that will be able to accomplish prochiral atom (or face) selection of simple substrates solely dependent upon weak nonbonding interactions. Moreover, to construct such a molecular architecture performing two coupled functions, i.e. catalysis and chiral recognition, has been one of the major challenging targets in host–guest chemistry.

By contrast, some natural oxygenases such as cytochrome P-450s[5] catalyze oxygen transfer to various organic compounds with high efficiency and stereospecificity. These enzymes provide hints for both the creation of active oxidizing species and the stereospecific recognition of substrate molecules.[6] Several modified chiral porphyrins[7] have been synthesized, and some of them, such as cytochrome P-450 models, have been reported to exhibit catalytic enantioselective oxygenation.[8] Detailed analysis of asymmetric induction in the catalytic process, however, has not been fully attained in the reported examples. Only steric interaction between substrates and chiral auxiliaries of catalysts was proposed. For further development of highly efficient catalytic systems, it is indispensable to construct a rational base deduced from detailed mechanistic analysis.

We describe first the synthesis and characterization of "twin-coronet" porphyrins (Figure 1) and next the catalytic asymmetric oxidation of olefins with their iron complexes and iodosobenzene as oxidants.[9] On the basis of the results obtained, we discuss the mechanisms of oxygen transfer and chiral induction. It is demonstrated that the combination of rationally introduced steric and CT interactions between substrates and chiral catalysts could cooperatively function to accomplish prochiral atom (or face) selection in catalytic asymmetric oxidation, an area in which the current applicable methodology is limited.

Results and Discussion

Design and Synthesis of Chiral Porphyrins. As depicted in Scheme I, a strategy for the preparation of chiral ligands is to create bridging between the ortho positions of adjacent aryl rings by biaryl derivatives through an ethereal linkage. Hence, 5,10,15,20-tetrakis(2,6-dihydroxyphenyl)porphine (**6**) and the optically active bis(bromomethyl)binaphthalene **12** or -bitetralin **17** are required for the desired condensation reaction.

The porphyrin (**6**), which differs from 5,10,15,20-tetrakis(2-hydroxyphenyl)porphine[10] or the analogous 2-aminophenyl derivatives,[11] is highly symmetrical, does not show atropisomerism arising from the rotation around its C_{meso}–$C_{aryl\text{-}1}$ axes, and can be modified on both its faces. The biaryl chiral auxiliaries linked to the ortho positions can afford chiral cavities near the central metal.

To avoid the formation of many stereoisomers, enantiomerically pure 2,2′-dimethoxy-1,1′-binaphthalene (**12**) or bitetralin derivatives (**17**) are used as chiral auxiliaries. Both compounds are

(1) Halpern, J. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, Chapter 2.
(2) Noyori, R.; Kitamura, M. In *Modern Synthetic Chemistry*; Scheffold, R., Ed.; Springer-Verlag: Berlin, 1989; p 155.
(3) Typical reactions: (a) Wai, J. S. M.; Markó, I. E.; Svendsen, J. S.; Finn, M. G.; Jacobsen, E. N.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989**, *111*, 1123. (b) Corey, E. J.; Jardine, P. D.; Virgil, S.; Yuen, P. W.; Connell, R. D. *J. Am. Chem. Soc.* **1989**, *111*, 9243. (c) Tomioka, K.; Nakajima, M.; Iitaka, Y.; Koga, K. *Tetrahedron Lett.* **1988**, *29*, 573. (d) Yamada, T.; Narasaka, K. *Chem. Lett.* **1986**, 131. (e) Hirama, M.; Oishi, T.; Itô, S. *J. Chem. Soc., Chem. Commun.* **1989**, 665. (f) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801.
(4) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, Chapter 8.
(5) *Cytochrome P-450*; Ortiz de Motellano, P. R., Ed.; Plenum Press: New York, 1986.
(6) (a) Morgan, B.; Dolphin, D. In *Metal Complexes with Tetrapyrrole Ligands. I.*; Buchler, J. W., Ed.; Springer-Verlag: Berlin, 1987; p 115. (b) Mansuy, D.; Battioni, P.; Battioni, J.-P. *Eur. J. Biochem.* **1989**, *184*, 267 and references cited therein.
(7) (a) Aoyama, Y.; Saita, K.; Toi, H.; Ogoshi, H. *Tetrahedron Lett.* **1987**, *28*, 4853. (b) Boitrel, B.; Lecas, A.; Rose, E. *J. Chem. Soc., Chem. Commun.* **1989**, 349. (c) Konishi, K.; Miyazaki, K.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1990**, *112*, 5639.
(8) (a) Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5791. (b) Groves, J. T.; Viski, P. *J. Am. Chem. Soc.* **1989**, *111*, 8537. (c) Groves, J. T.; Viski, P. *J. Org. Chem.* **1990**, *55*, 3628. (d) Mansuy, D.; Battioni, P.; Renaud, J.-P.; Guerin, P. *J. Chem. Soc., Chem. Commun.* **1985**, 155. (e) O'Malley, S.; Kodadek, T. *J. Am. Chem. Soc.* **1989**, *111*, 9116. (f) Collman, J. P.; Zhang, X.; Hembre, R. T.; Brauman, J. I. *J. Am. Chem. Soc.* **1990**, *112*, 5356.
(9) Preliminary report: Naruta, Y.; Tani, F.; Maruyama, K. *Chem. Lett.* **1989**, 1269.
(10) Gottwald, L. K.; Ullman, E. F. *Tetrahedron Lett.* **1969**, 3071.
(11) Lindsey, J. *J. Org. Chem.* **1980**, *45*, 5215.

0002-7863/91/1513-6865$02.50/0

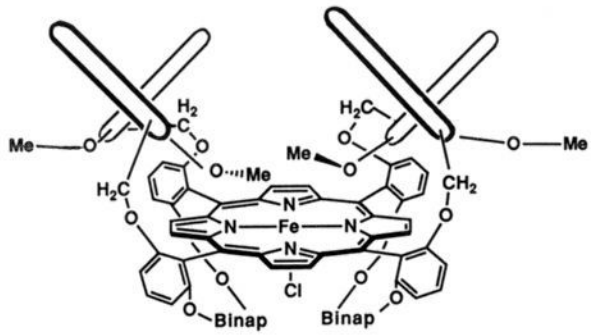


Figure 1. Structure of a "twin-coronet" porphyrin (eclipsed form).

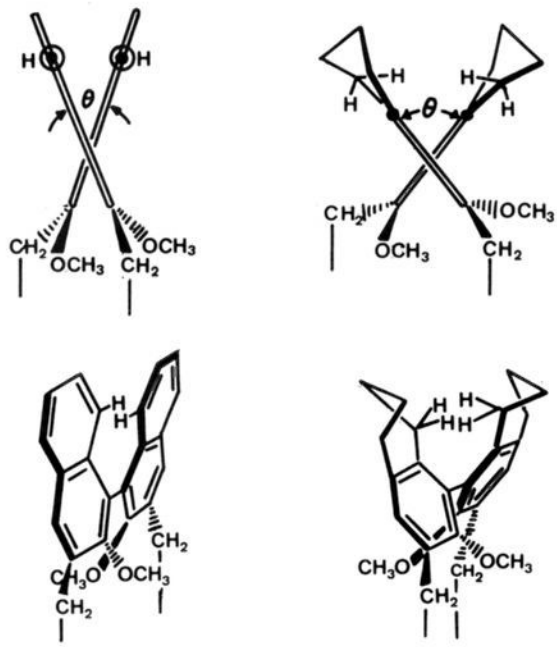


Figure 2. Comparison between the molecular conformations of the binaphthalene and the bitetralin derivatives.

prepared from optically active 1,1′-bi-2-naphthol (**7**)[12] in several steps with satisfactory chemical yields and complete preservation of its optical purity (Scheme II). In addition, chiral bitetralindiol **13** can be obtained quantitatively by simple hydrogenation of 1,1′-bi-2-naphthol (**7**) without any loss of its optical purity.[13]

The binaphthalene and the bitetralin compounds have rigid chiral frameworks that are composed of sufficiently bulky aromatic rings and whose electronic properties can be controlled by a variety of substituents on the aromatic rings. Furthermore, the dihedral angles between two naphthalene or tetralin mean planes are allowed to have flexibility (60–120°), and to some degree, the molecules can avoid possible steric repulsion (Figure 2).

The binaphthalene-modified twin-coronet porphyrins were synthesized and characterized as follows. Almost identical methods could be applied to the case of the bitetralin-modified ones. A THF–acetone solution of the octahydroxylated porphyrin **6** and (*S*)-3,3′-bis(bromomethyl)-2,2′-dimethoxy-1,1′-binaphthyl

(12) (a) Pummer, R.; Prell, E.; Rieche, A. *Ber. Dtsch. Chem. Ges.* **1926**, *59*, 2159. (b) Jacques, J.; Fouquey, C.; Viterbo, R. *Tetrahedron Lett.* **1971**, 4617. (c) Kyba, E. P.; Gokel, G. W.; de Jong, F.; Koga, K.; Sousa, L. R.; Siegel, M. G.; Kaplan, L.; Sogah, G. D. Y.; Cram, D. J. *J. Org. Chem.* **1977**, *42*, 4173. (d) Miyano, S.; Tobita, M.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3522. (e) Jacques, J.; Fouquey, C. *Org. Synth.* **1988**, *67*, 1.

(13) Cram, D. J.; Helgeson, R. C.; Peacock, S. C.; Kaplan, L. J.; Domeier, L. A.; Moreau, P.; Koga, K.; Mayer, J. M.; Chao, Y.; Siegel, M. G.; Hoffman, D. H.; Sogah, G. D. Y. *J. Org. Chem.* **1978**, *43*, 1930.

Table I. ^{1}H NMR Chemical Shifts of Selected Protons of Twin-Coronet Porphyrins

compd	pyrrole β-H	benzyl CH_2	OCH_3
		Eclipsed	
1a	8.68, 8.38	5.30, 4.96, 4.85, 4.38 (16 H, each d, J = 9, 11 Hz)	2.90, **−1.62**
3a	8.60, 8.31 (8 H, each s)	5.30, 4.73, 4.71, 4.32 (16 H, each d, J = 9, 12 Hz)	3.15, **−1.16** (24 H, each s)
		Staggered	
2a	8.52, 8.38	5.28, 4.88, 4.71, 4.63 (16 H, each d, J = 10, 11 Hz)	2.78, **−1.75**
4a	8.48, 8.37 (8 H, each d, J = 4 Hz)	5.22, 4.76, 4.58, 4.50 (16 H, each d, J = 10, 11 Hz)	2.86, **−1.05** (24 H, each s)

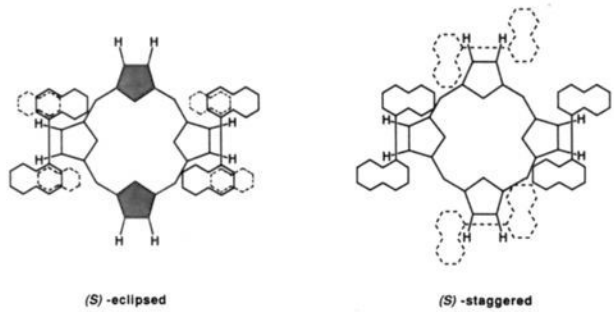


Figure 3. Schematic drawings of the twin-coronet porphyrins (top view). Binaphthalenes above (—) and below (---) the porphyrin ring are shown. For clarity, the phenyl rings at meso positions and other substituents on the binaphthalenes are omitted.

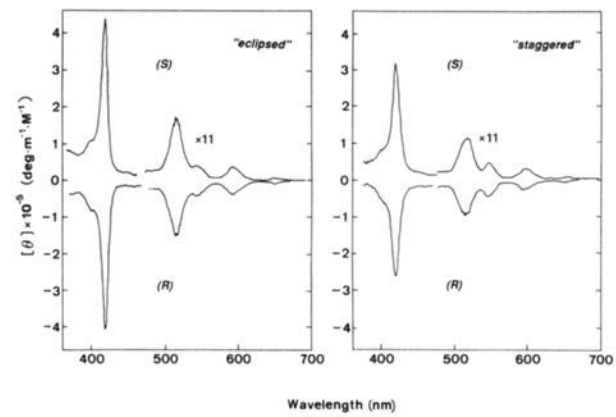
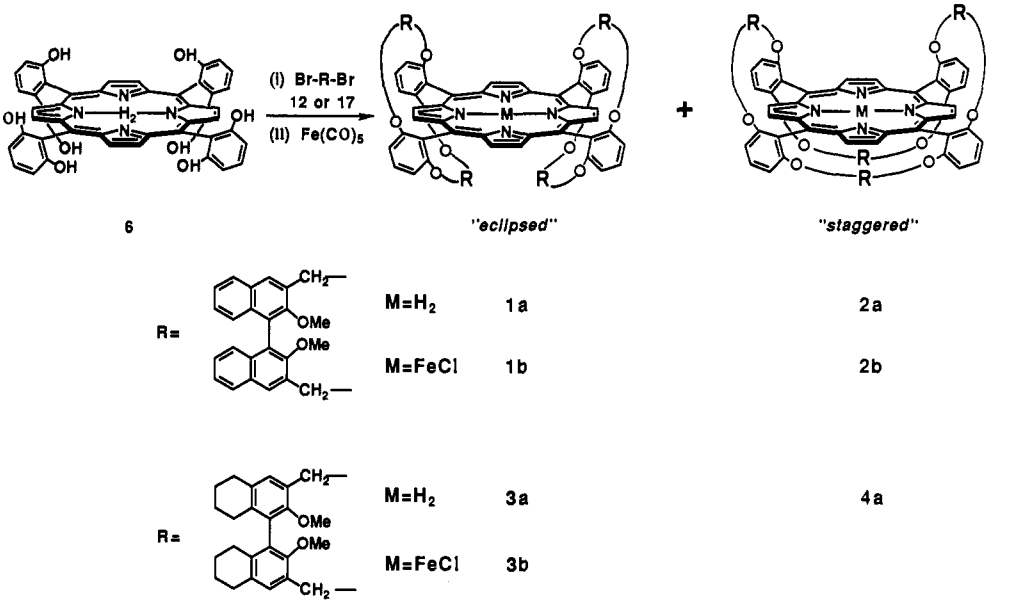


Figure 4. CD spectra of the binaphthalene-modified twin-coronet porphyrins (**1a**, **2a**) in CH_2Cl_2.

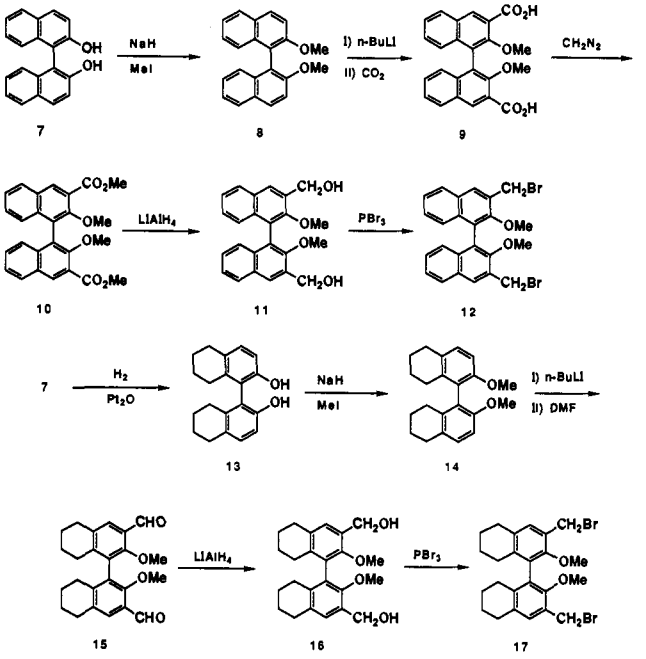
((*S*)-**12**) was heated to reflux in the presence of excess K_2CO_3 under high-purity Ar atmosphere (O_2 < 0.2 ppm),[14] to give two isomeric porphyrins, (*S*)-**1a** and (*S*)-**2a**, which were separated by silica-gel column chromatography. From their ^{1}H NMR spectra (Table I), the less polar isomer and the polar one were determined to be H_2[(*S*)-Binap$(OMe)_2]_4$TPP-eclipsed ((*S*)-**1a**) and H_2-[(*S*)-Binap$(OMe)_2]_4$TPP-staggered ((*S*)-**2a**), respectively. The two isomers were distinguished by ^{1}H NMR signals of the pyrrole β-protons. In (*S*)-**1a**, two β-protons on one pyrrole ring are equivalent, and there are two sets of equivalent pyrrole rings (Figure 3). Thus, the β-protons are observed as a pair of singlets. On the other hand, the four pyrrole rings of (*S*)-**2a** are all

(14) The polyhydroxylated porphyrin **6** is very sensitive to O_2 under basic conditions, and a trace amount of O_2 causes its oxidative decomposition. Related chemistry has been reported in the following literature: Milgrom, L. R.; Jones, C. O. C.; Harriman, A. *J. Chem. Soc., Perkin Trans. 2* **1988**, 71 and references cited therein.

Scheme I



Scheme II



equivalent, but the two β-protons on one pyrrole ring are in different environments. Hence, two doublet peaks are observed. On the basis of these spectroscopic features, the structures of the two obtained diastereomers were determined.

Bis(bromomethyl)-(*R*)-binaphthyl (*R*)-**12** in place of (*S*)-**12** afforded the corresponding (*R*)-binaphthyl twin-coronet porphyrins, (*R*)-**1a** and (*R*)-**2a**. The two enantiomers of the *eclipsed* porphyrin showed intense CD spectra in the range 400–700 nm that are mirror images of each other, in the same manner as the enantiomeric pair of the *staggered* porphyrin (Figure 4). These results imply the absence of racemization in the coupling stage of the twin-coronet porphyrins and that both faces of the obtained porphyrins have chiral cavities. To the best of our knowledge,[7a,c,15] this is the first example of such a clear CD spectrum of Q-bands caused by vicinal effects[16] of the chiral auxiliaries in the porphyrin chromophore.

The ^{1}H NMR chemical shift of a group above the porphyrin ring is diagnostic of its proximity due to its strong magnetic anisotropy.[17] The two singlets of the methoxy protons of each porphyrin are considerably shifted to high field, compared to those of the corresponding binaphthalene (δ 3.30) or bitetralin derivative (δ 3.44) (Table I). Especially shifted are the high-field methoxy groups (δ −1.05 to −1.75) that exist just above the porphyrin ring inside the cavities. These distinguished signals of the bitetralin-modified isomers, (*S*)-**3a** and (*S*)-**4a**, are substantially shifted to lower field relative to those of the binaphthalene-modified ones (δ −1.16 to −1.62 and δ −1.05 to −1.75, respectively), in sharp contrast to the small differences in the signals of the pyrrole β-protons. The inner methoxy groups in (*S*)-**1a** and (*S*)-**2a** could be closer to the porphyrin ring than those in (*R*)-**3a** and (*R*)-**4a**. The spectroscopic evidence is in accord with the steric properties of the auxiliaries. Because of the more severe steric hindrance between the saturated bulky rings of the bitetralin moieties, the dihedral angles (θ) of the benzene rings would be larger than those of the naphthalene rings, and so, the methoxy groups might be elevated with respect to the porphyrin planes (Figure 2).

These chiral twin-coronet porphyrins and their iron complexes have C_2 symmetry.[18] The two binaphthalene (or bitetralin) groups facing each other over the macrocycles can create rigid chiral cavities on both identical sides and block the formation of an unreactive μ-oxo dimer and the oxidative degradation of the porphyrin rings themselves, permitting the approach of olefinic substrates and iodosobenzene to the central iron atom.

Catalytic Epoxidations. A typical epoxidation by the catalyst and iodosobenzene was performed according to the following procedure: The chiral catalyst (1 μmol), an olefin (500 μmol), and a GLC internal standard were dissolved in deaerated dry CH_2Cl_2 (1 mL). Reaction was initiated by the addition of PhIO (100 μmol) and stirring at a constant speed under an Ar atmosphere at 0 °C in the dark. At appropriate intervals, aliquots taken from the reaction mixture were quenched by a CH_2Cl_2 solution of a slight excess of PPh_3 and then analyzed by GLC. The isolation of oxidation products was done by silica-gel column chromatography. Results are summarized in Table II. Besides epoxides, the corresponding arylacetoaldehydes were concomitantly produced.[19] Without any iron porphyrin catalysts, the olefin

(15) (a) Ogoshi, H.; Saita. K.; Sakurai, K.: Watanabe, T.; Toi. H.: Aoyama. Y.; Okamoto, Y. *Tetrahedron Lett.* **1986**, *27*, 6365. (b) Kubo, H.; Aida, T.; Inoue. S.; Okamoto, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 1015.

(16) Hawkins, C. J. *Absolute Configuration of Metal Complexes*: Wiley: New York, 1970.

(17) Abraham, R. J.; Bedford, G. R.; McNeillie, D.; Wright, B. *Org. Magn. Reson.* **1980**, *14*, 418.

(18) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581.

(19) The ratio of aldehyde to epoxide was determined by ^{1}H NMR spectroscopy because of the difficulty of their GLC separation and the thermal rearrangement of epoxides to the corresponding aldehydes in the GLC injection port (240 °C).

Table II. Asymmetric Epoxidation Catalyzed by Iron Twin-Coronet Porphyrins

run	X	catalyst	reacn time, h	turnover no. epoxide	turnover no. aldehyde	ee, %	config[a]
1	H	(*S*)-**1b**	3.5	49	5	20	*R*
2	H	(*R*)-**1b**	3.5	50	5	22	*S*
3	2-NO_2	(*S*)-**1b**	3	26	tr	80	(*R*)
4	2-NO_2	(*S*)-**2b**	3	26	tr	54	(*R*)
5	3-NO_2	(*S*)-**1b**	2	57	tr	60	(*R*)
6	4-NO_2	(*S*)-**1b**	2	38	tr	54	(*R*)
7	2,4-$(NO_2)_2$	(*S*)-**1b**	3	20	tr	68	(*R*)
8	3,5-$(NO_2)_2$	(*S*)-**1b**	2	20	tr	74	(*R*)
9	F_5	(*S*)-**1b**	2	36	tr	74	*R*
10	4-CF_3	(*R*)-**1b**	3	42	tr	41	(*S*)
11	4-Br	(*S*)-**1b**	2	31	5	28	(*R*)
12	4-CH_3	(*R*)-**1b**	5	48	12	11	(*S*)
13	2-OCH_3	(*S*)-**1b**	2.5	32	16	0	
14	3-OCH_3	(*S*)-**1b**	2.5	35	6	45	(*R*)
15	4-OCH_3	(*S*)-**1b**	1.5	0	58		
16	1-vinylnaphthalene	(*S*)-**1b**	1.5	30	6	46	(*R*)
17	2-vinylnaphthalene	(*S*)-**1b**	1	47	3	17	(*R*)
18	H	(*R*)-**3b**[b]	8	84	tr	54	*S*
19	2-NO_2	(*R*)-**3b**[c]	7	46	tr	89	(*S*)

[a] Major configurations of the epoxides of styrene and pentafluorostyrene were determined by comparison with the authentic optically pure oxides. Others in parentheses were deduced from analogy with the spectroscopic behavior of (*R*)-styrene oxide. [b] 0.2 μmol of the catalyst was used. [c] 0.6 μmol of the catalyst was used.

substrates were hardly oxygenated by iodosobenzene alone under the identical reaction conditions.

Enantiomeric excesses for the resulting epoxides were determined by ^1H NMR spectroscopy performed in the presence of a chiral shift reagent, tris[3-((heptafluoropropyl)hydroxymethylene)-(+)-camphorato]europium(III), $Eu(hfc)_3$.

When (*S*)-**1b** was used as a catalyst, (*R*)-epoxides were preferably obtained in the oxidation of all the substrates applied. The employment of the antipode, (*R*)-**1b**, surely resulted in the formation of (*S*)-styrene oxide as a dominant enantiomer in a similar ee (runs 1 and 2).

Good optical yields were obtained in the oxidation of electron-deficient styrene derivatives (runs 3–9), and excellent enantiomeric excesses were recorded in the case of 2-nitrostyrene, 80% (catalyzed by (*S*)-**1b**, run 3) and 89% (catalyzed by (*S*)-**3b**, run 19). These values are the highest reported so far in epoxidation with related chiral porphyrin catalysts.[8] By the use of (*R*)-**3b** in place of (*S*)-**1b**, ee was greatly improved from 20% to 54% even in the case of styrene (run 18). The bitetralin-modified catalyst ((*R*)-**3b**) was found to be superior to the binaphthalene one with respect to enantioselection. The bitetralin moieties, which are bulkier than the binaphthalene ones, would inhibit olefins from adopting the sterically unfavorable arrangement at their oxo-transfer stage, as shown in Figure 8A.

The *staggered* catalyst (*S*)-**2b** exhibited only modest enantioselection compared to its diastereomer, *eclipsed* (*S*)-**1b** (run 4). The degree of recognition of the prochiral face could actually be influenced by a microscopic change of the porphyrin structure in the vicinity of the iron center. For this and synthetic reasons, the iron complexes of the *eclipsed* isomers were mainly employed in the catalytic oxidation in preference to the *staggered* ones.

Catalyst decomposition in oxidation reactions using porphyrin-based catalysts is a serious problem, especially for catalysts derived from *meso*-tetrakis(2-aminophenyl)porphyrin.[20] To verify that the reaction rates and ee's were sufficiently reliable for a discussion of the reaction mechanism, we measured the time course of epoxide ee in the oxidation of 2-nitrostyrene. During the reaction time examined (<3 h), the observed ee's were almost constant within experimental error and 90% of the initially charged catalyst (*R*)-**1b** survived after 3 h, which was confirmed by the absorbance of the Soret band. These results indicate that both ee's and reaction rates are reliable for mechanistic analysis of the present reaction system and that the modification of porphyrins through ethereal linkages is far superior to that through amide linkages.

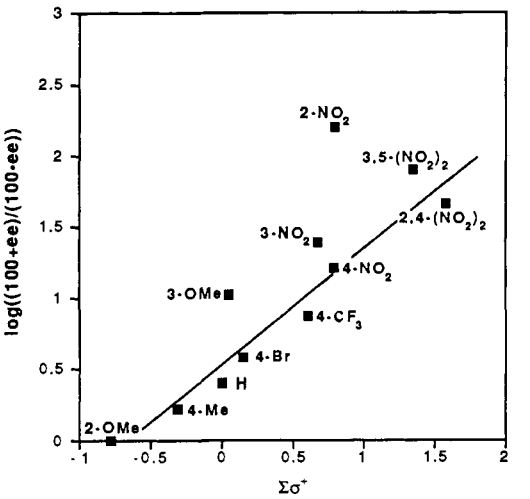


Figure 5. Plot of the optical yields of epoxides vs $\sum\sigma^+$ of the substituents.

The binap-*eclipsed* catalyst (*S*)-**1b** was applied to the oxidation of a series of styrene derivatives with respect to their electronic and steric properties (Table II). From the plot of log ((100 + ee)/(100 + ee))[21] versus $\sum\sigma^+$ of the substituents, a clear trend was recognized (Figure 5). The more easily oxidized substrates gave the lower enantiomeric excesses. On the other hand, effective chiral differentiation was realized in the oxidation of the electron-deficient substrates. The degree of enantioselection was principally dependent upon the electronic character of the substrates, not upon the steric factors; e.g., compare runs 1 and 9 as typical examples. In order to clarify this point, consideration should be paid at first to the mechanism of oxygen transfer from the high-valent metal–oxo center to the double bonds of the substrates.

Various mechanisms have been proposed for epoxide formation catalyzed by metalloporphyrins (Scheme III): concerted oxygen

(20) El-Kasmi, A.; Lexa, D.; Maillard, P.; Momenteau, M.; Savéant, J. M. *J. Am. Chem. Soc.* **1991**, *113*, 1586.

(21) The term log ((100 + ee)/(100 − ee)) is proportional to $-\Delta\Delta G^*$ according to the following equation:

$$\log((100 + ee)/(100 - ee)) = -\Delta\Delta G^*/RT$$

Here, $-\Delta\Delta G^*$ is free energy difference between two diastereomeric transition states leading to enantiomeric products.

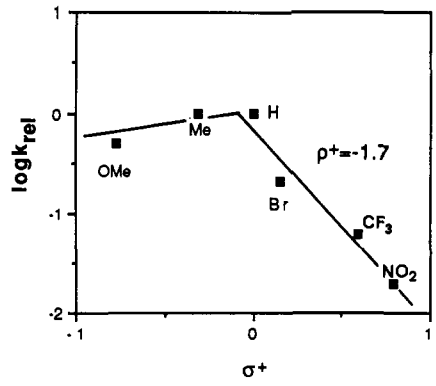
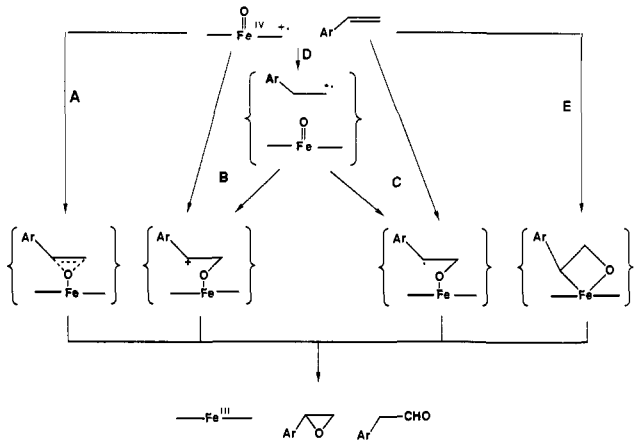


Figure 6. Hammet plot of para-substituted styrenes in the catalytic epoxidation by (*S*)-**1b** and iodosobenzene.

Scheme III



addition (A),[22a] acyclic cation formation (B),[22b,c] acyclic radical formation (C),[22d] electron transfer (D),[22b] and oxametallacycle formation (E).[22e,f] The concerted addition (A) and the formation of an acyclic cationic intermediate via electron transfer followed by ionic collapse (B, D) are most consistent with the following evidence obtained.

From the measurement of the total amount of epoxide and aldehyde produced by (*S*)-**1b** at the initial stage of the reaction, the relative pseudo-first-order rate constants k_{rel} of para-substituted styrene derivatives were plotted vs σ^+ values (Figure 6). A profile of two phases was observed. In the region of electron-withdrawing groups, a large negative ρ^+ (−1.7) was seen, which implies electrophilic character of the rate-determining step, possibly initial electron transfer from the olefin to the iron–oxo center. On the other hand, ρ^+ is nearly zero in the negative-σ^+ region, and other steps, presumably oxygen attack, would be the rate-determining ones in this reaction.

Both Traylor[23] and Lindsay-Smith[24] have reported a small negative ρ^+ value ($\simeq$−0.9) in the oxidation of styrene derivatives, and the former has proposed an electron-transfer mechanism followed by the formation of an acyclic cationic intermediate together with other supporting evidence.[25] In addition, Groves[26]

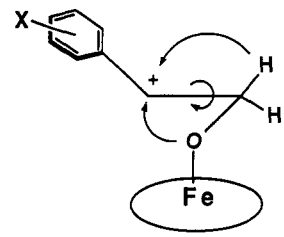


Figure 7. Possible pathways of product formation from the carbocationic intermediate.

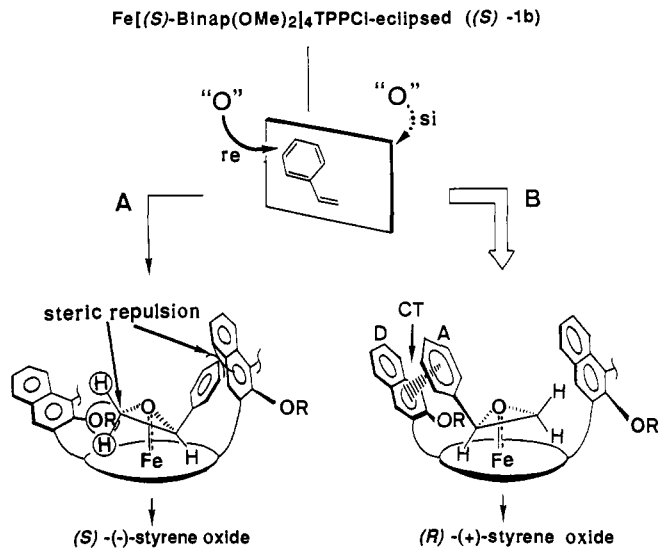


Figure 8. Geometry of styrene in the cavity over the catalyst ((*S*)-**1b**) in the transition state of oxygen transfer.

and Bruice[27] independently reported the same ρ^+ (−1.9), suggesting the existence of an initial electron (or partial charge) transfer process, regardless of the kind of metalloporphyrins used.

Further, it is worthy of note that in the present system the formation of arylacetoaldehydes was apparently enhanced in the oxidation of the electron-rich substrates (Table II). These aldehydes are the primary products in the oxidation, not the secondary ones formed through the subsequent rearrangement of epoxides.[22f,8a] The formation of aldehydes as the major products predicts the presence of an acyclic cationic intermediate, i.e. a cation center on the C_α of styrenes formed after electron transfer and ionic collapse (oxygen attack on C_β), as suggested by Traylor[23,25] (Figure 7). Such an intermediate could preserve the stereochemistry of the starting olefin in epoxidation, if the rate of ring closure is rapid enough and its lifetime is short in comparison with the rates of bond rotation and hydrogen rearrangement. However, an olefin with an electron-donating group will cause relatively fast electron transfer as an initial event, and the resultant cationic intermediate, which is stabilized by the electron-donating π-substituents and should have a long lifetime, reacts in the following three routes: oxygen attack (to give epoxide), C_α–C_β bond rotation (to give racemic product), or H-rearrangement (to give aldehyde). Hence, the optical yields become low, and the electron-transfer step is not rate-determining ($\rho^+ \simeq 0$). In the oxidation of the electron-deficient substrates, on the contrary, slow electron transfer and the subsequent rapid oxygen attack on the very unstable cation radical occur as a major pathway of the oxidation reaction. These olefins will give the corresponding epoxides in good ee's. Thus, the correlation between the optical yields and the electronic character of the substrates can be rationally explained.

Concerted oxygen addition to olefins can be considered as the extreme case of slow electron transfer and competitive oxo transfer

(22) (a) Ortiz de Montellano, P. R.; Mangold, B. L. K.; Wheeler, C.; Kunze, K. L.; Reich, N. O. *J. Biol. Chem.* **1983**, *258*, 4208. (b) Traylor, T. G.; Miksztal, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 2770. (c) Castellino, A. J.; Bruice, T. C. *J. Am. Chem. Soc.* **1988**, *110*, 158. (d) Fontecave, M.; Mansuy, D. *J. Chem. Soc., Chem. Commun.* **1984**, 879. (e) Collman, J. P.; Kodadek, T.; Brauman, J. I. *J. Am. Chem. Soc.* **1986**, *108*, 2588. (f) Collman, J. P.; Kodadek, T.; Raybuck, S. A.; Brauman, J. I.; Papazian, L. M. *J. Am. Chem. Soc.* **1985**, *107*, 4343.

(23) Traylor, T. G.; Xu, F. *J. Am. Chem. Soc.* **1988**, *110*, 1953.

(24) Lindsay-Smith, J. R.; Sleath, P. R. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1009.

(25) (a) Traylor, T. G.; Nakano, T.; Dunlap, B. E.; Traylor, P. S.; Dolphin, D. *J. Am. Chem. Soc.* **1986**, *108*, 2782. (b) Traylor, T. G.; Nakano, T.; Miksztal, A. R.; Dunlap, B. E. *J. Am. Chem. Soc.* **1987**, *109*, 3625.

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

(27) Garrison, J. M.; Ostovic, D.; Bruice, T. C. *J. Am. Chem. Soc.* **1989**, *111*, 4960.

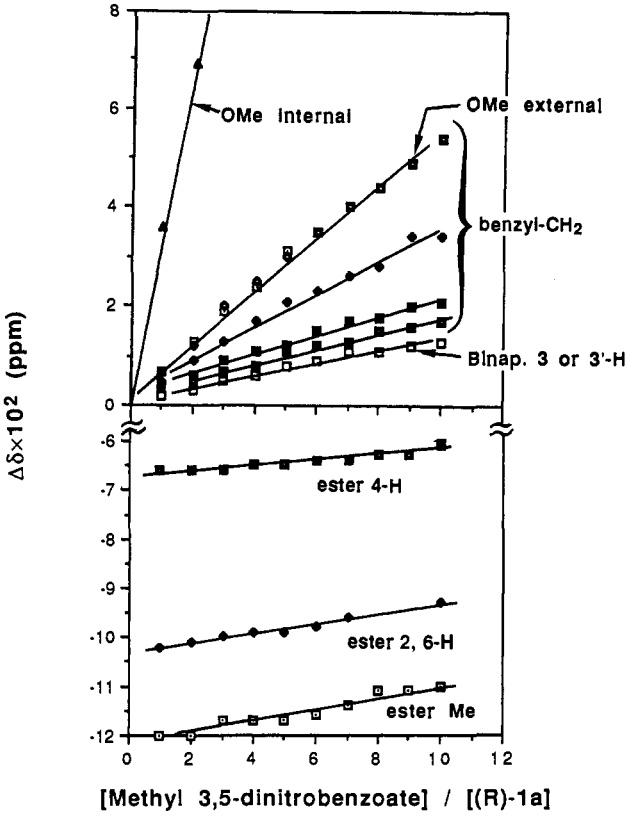


Figure 9. Plot of ^{1}H NMR shift differences vs relative concentration of methyl 3,5-dinitrobenzoate. Conditions: [(*R*)-**1a**] = 8.7 × 10^{-4} M in $CDCl_3$-$(CDCl_2)_2$ (10:1, v/v) at 25 °C.

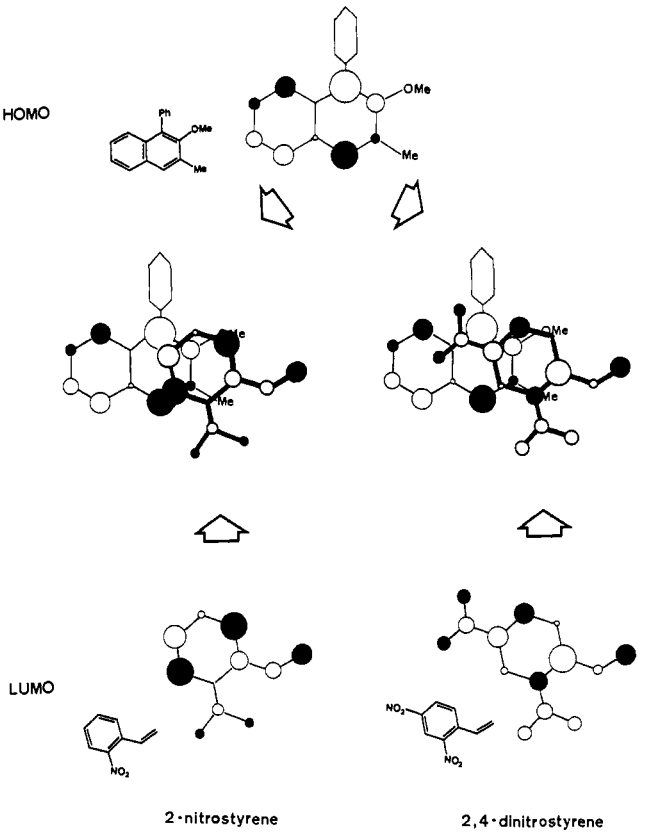


Figure 10. Investigation on the symmetry of the frontier orbitals of electron-deficient substrates and a model compound of the binaphthalene auxiliary.

with cationic intermediate formation. This could be the case in electron-deficient styrene derivatives such as nitro- or pentafluoro-substituted ones. The reaction mechanism could continuously alternate between B, D and A (in Scheme III) depending mainly on the degree of the electronic properties of the substrates given.

A mechanism determining absolute configurations of produced epoxides (e.g, (*S*)-**1b** gave (*R*)-epoxides) can be understood according to the following picture. From an examination using CPK models, an olefin molecule will approach the putative oxo–iron center from the side opening of the biaryl walls with the olefin double bond remaining parallel to the plane of the porphyrin ring so as to minimize steric interaction. The terminal carbon atom of the olefins would sterically interact with a methoxy group pointed toward the central metal inside the cavity (Figure 8). In the geometry A (*re*-addition), the phenyl ring of the substrates cannot be situated in an orientation parallel to the tilted naphthalene moiety fixed over the macrocycle, and the steric repulsion between the β-carbon of the substrates and the inner methoxy group cannot be avoided. In the geometry B (*si*-addition), on the other hand, the parallel orientation of naphthalene and the phenyl ring can be allowed to develop an effective π–π* interaction (frontier-orbital interaction between a donor and an acceptor), and the β-carbon does not collide with the methoxy group outside the cavity. Hence, the oxygen atom of the oxo–iron center attacks favorably from the *si*-face of the substrates to give the (*R*)-epoxides as major enantiomers. Moreover, the fixation of a substrate molecule in this geometry at the transition state would be promoted by the charge-transfer interaction between an electron-deficient phenyl ring of a styrene derivative and the electron-donating naphthalene ring, the latter being electron-rich on account of both the methoxy and methylene groups appendant to it.

To examine the possibility of the expected host–guest CT interaction inside the cavity, a solution of the free-base twin-coronet porphyrin (*R*)-**1a** in $CDCl_3$-$(CDCl_2)_2$ was titrated with methyl 3,5-dinitrobenzoate as a representative electron-deficient aromatic guest and the shift value $\Delta\delta$ ($=\delta_{mix} - \delta_{original}$) was monitored by ^{1}H NMR spectroscopy (Figure 9). According to the addition of the benzoyl ester, some of the porphyrin protons showed positive $\Delta\delta$. Their shift differences were proportional to the concentration of the benzoyl ester added. Especially, the methoxy groups inside the cavity showed large positive $\Delta\delta$'s (2.84 × 10^{-2} ppm/equiv of guest molecule). Other protons proximal to the active site of the porphyrin also showed appreciable positive $\Delta\delta$'s. On the other hand, the protons of the guest benzoyl ester exhibited relatively large negative $\Delta\delta$'s. These phenomena of the observed shift changes can be explained by the benzoate complexation inside the cavity of the host porphyrin molecule with a high formation constant. In similar experiments with 2,4- or 3,5-dinitrostyrene, similar interactions also occurred, while their shift differences were small. This evidence indicates that an electron-deficient substrate selectively forms a complex in the cavity built on the porphyrin plane.

In Figure 5, the optical yield of 2-nitrostyrene is much higher than the expected values from the correlated line. In contrast, that of 2,4-dinitrostyrene is reasonable regardless of its larger electron-deficiency and expected to cause an effective CT interaction. In these substrates, steric interactions between the substrate in the para position and the auxiliary are not essential, because 4-nitrostyrene is oxidized in a reasonable ee. These anomalous results can be explained by taking into account the symmetry of the molecular orbitals of both the substrates and the binaphthalene auxiliary. The symmetry of the molecular orbitals contributing to π–π* CT stacking is considered to be significant as well as the overall electronic character of molecules. CNDO MO calculations were performed on the styrene derivatives and a naphthalene derivative closely analogous to the chiral auxiliary (Figure 10). The LUMO of a substrate is overlapped onto the HOMO of the naphthalene in the most likely geometry of the oxygen-transfer step, and the symmetry of the two orbitals is compared. The most important interaction develops between (i) C_1 and C_2 of the naphthalene and C_4 of the substrate and (ii) C_3 and C_4 of the naphthalene and C_3 of the substrate. As a typical example, much favorable stacking is obtained in the case of 2-nitrostyrene but not in the case of 2,4-dinitrostyrene (Figure 10). These CNDO

MO results are consistent with the experimental results for all other electron-deficient substrates examined.

There are some known examples that apply such $\pi-\pi^*$ interactions to the chromatographic resolution of optical isomers[28] but, to the best of our knowledge, no precedent for the actual asymmetric reactions in our oxidation systems.

Concluding Remarks

In this paper, we have presented systems for the catalytic and asymmetric oxidation of olefins by using a series of novel chiral biaryl-modified iron–porphyrin complexes and iodosobenzene, and we have achieved efficient chiral induction in the oxidation of electron-deficient styrene derivatives. The maximum ee (89%) was recorded for 2-nitrostyrene.

From the survey of the catalytic reactions of the styrene derivatives, we suggested the reaction mechanism, the intermediate of the oxygen-transfer step, and the origin of the chiral induction. Formation of an acyclic cation intermediate through initial electron transfer and concerted oxygen addition are the most possible candidates consistent with the obtained results. The correlation between the optical yields and the electronic properties of the substrates used can be reasonably explained with respect to the proposed reaction mechanism. Symmetry-regulated CT interactions between the substrates and the chiral auxiliaries were shown to function cooperatively with steric interactions between the substrates and the chiral auxiliaries in the fixation of the substrates in an appropriate geometry and prochiral face recognition. We propose this type of $\pi-\pi^*$ interaction between substrate and catalyst as a useful approach for successful catalytic asymmetric oxidation of simple organic molecules.

In the present catalytic oxidation systems, electron-rich olefins are oxidized preferentially through an electron-transfer process. For electron-deficient olefins, on the other hand, their $\pi-\pi^*$ interaction with the electron-donating chiral auxiliaries is highlighted as a major interaction because of the difficult electron transfer from the substrates to form cation intermediates.

The reported examples with chiral metalloporphyrin catalysts,[8a-c] however, have rather electron-withdrawing binaphthalene moieties because of their amide linkages. In such cases, $\pi-\pi^*$ interaction of the auxiliaries with electron-rich olefins would be capable of fixing the geometry in the transition state of oxo transfer to some extent. Thus, it would enhance the prochiral face recognition. The electron-transfer process, however, would be dominant in the case of electron-rich olefins. So, these two modes, i.e. electron transfer and $\pi-\pi^*$ interaction, have opposite effects on their optical yields. These phenomena make the analysis of the substrate–catalyst interaction difficult from the standpoint of product analysis.

Experimental Section

All reagents or solvents were of the commercial reagent grade and were used without further purification except where noted. Dry dichloromethane was obtained by refluxing and distilling over P_2O_5 or CaH_2. Dry toluene was obtained by refluxing and distilling over Na. Dry THF was obtained by refluxing and distilling over benzophenone ketyl. ^1H NMR spectra (400 MHz) were recorded on a JEOL JNM-GX400 spectrometer, chemical shifts being reported on the δ scale relative to TMS. Mass spectra were obtained on a JEOL JMS-DX-300 mass spectrometer. FAB mass spectra of the porphyrins were recorded on a JEOL JMS-HX-110 or a JEOL JMS-DX-300 mass spectrometer, with 3-nitrobenzyl alcohol as the FAB matrix. UV–vis absorption spectra were measured on a Shimadzu UV-3000 spectrophotometer. Infrared spectra were recorded on a JASCO IRA-1 or a Horiba FT-300 spectrometer. Optical rotations were measured on a JASCO DIP-181 spectropolarimeter at ambient temperature. Melting points were obtained on a Yanagimoto micro melting point apparatus and not corrected. Circular dichroism spectra were taken on a JASCO J-20 spectrophotometer. Gas chromatography was performed on a Shimadzu GC-8A chromatograph using a Shimadzu CBP-1-520-050 capillary column (0.33 mm × 25 m) and a FID detector.

Synthesis of Twin-Coronet Porphyrins and Their Iron Complexes. H_2[(*S*)-Binap(OMe)$_2$]$_4$TPP-eclipsed ((*S*-1a) and -staggered ((*S*)-2a). A suspension of finely ground anhydrous K_2CO_3 (5.4 g) in acetone (100 mL) and THF (100 mL) was vigorously bubbled with high-purity argon gas. To this were added dropwise both a solution of the octahydroxylporphyrin **6** (360 mg, 0.485 mmol) in acetone–THF (25 mL/150 mL) and a solution of the bis(bromomethyl)binaphthalene (*S*)-**11** (1.2 g, 2.40 mmol) in acetone–THF (25 mL/25 mL) under refluxing conditions. The reaction mixture was heated for 3 days under anaerobic conditions, and then the solvent was evaporated. The residue was poured into H_2O and CH_2Cl_2, and the mixture was suction-filtered to remove insoluble solids. The filtrate was separated and extracted with additional CH_2Cl_2. The combined organic phases were dried over Na_2SO_4 and evaporated to dryness in vacuo. The residue was separated by flash chromatography on a silica-gel column and eluted successively with benzene, benzene–CH_2Cl_2 (2:1, v/v), and CH_2Cl_2. The less polar red band and the polar one contained (*S*)-**1a** and (*S*)-**2a**, respectively. These fractions were separately purified by column chromatography on activated alumina (CH_2Cl_2).

(*S*)-**1a**: yield 43.3 mg (0.021 mmol, 4.3%); ^1H NMR ($CDCl_3$) δ 8.68 (4 H, s, pyrrole β-H), 8.38 (4 H, s, pyrrole β-H), 7.84 (4 H, s), 7.78–7.73 (8 H, m), 7.45 (4 H, s), 7.32 (4 H, d, J = 8 Hz), 7.24–7.18 (12 H, m), 7.02 (4 H, t, J = 7 Hz), 6.84 (4 H, d, J = 9 Hz), 6.64 (4 H, t, J = 7 Hz), 6.23 (4 H, t, J = 7 Hz), 6.13 (4 H, d, J = 8 Hz), 5.30 (4 H, d, J = 9 Hz), 4.96 (4 H, d, J = 9 Hz), 4.85 (4 H, d, J = 11 Hz), 4.38 (4 H, d, J = 11 Hz), 2.90 (12 H, s, OCH_3), -1.62 (12 H, s, OCH_3), -3.20 (2 H, s, NH); MS (FAB) m/e 2096 ($M + H^+$); UV–vis (CH_2Cl_2) λ_{max} 420, 513, 540, 587, 641 nm.

(*S*)-**2a**: yield 53.5 mg (0.026 mmol, 5.3%); ^1H NMR ($CDCl_3$) δ 8.52 (4 H, d, J = 4 Hz, pyrrole β-H), 8.38 (4 H, d, J = 4 Hz, pyrrole β-H), 7.84 (4 H, s), 7.81–7.73 (12 H, m), 7.40 (4 H, d, J = 9 Hz), 7.25 (4 H, t, J = 7 Hz), 7.22 (4 H, s), 7.12 (8 H, d, J = 8 Hz), 7.03 (4 H, t, J = 7 Hz), 6.82 (4 H, d, J = 8 Hz), 6.54 (4 H, t, J = 7 Hz), 6.13 (4 H, d, J = 8 Hz), 5.91 (4 H, t, J = 8 Hz), 5.28 (4 H, d, J = 10 Hz), 4.88 (4 H, d, J = 11 Hz), 4.71 (4 H, d, J = 10 Hz), 4.63 (4 H, d, J = 11 Hz), 2.78 (12 H, s, OCH_3), -1.75 (12 H, s, OCH_3), -3.23 (2 H, s, NH); MS (FAB) m/e 2096 ($M + H^+$); UV–vis (CH_2Cl_2) λ_{max} 420, 513, 540, 587, 643 nm.

The corresponding compounds (*R*)-**1a** and (*R*)-**2a** were also prepared by the same method in yields of 3.8% and 6.1%, respectively.

The bitetralin-modified twin-coronet porphyrins were synthesized in a similar manner.

(*R*)-**3a**: yield 1.0%; ^1H NMR ($CDCl_3$) δ 8.60 (4 H, s, pyrrole β-H), 8.31 (4 H, s, pyrrole β-H), 7.71 (4 H, t, J = 9 Hz), 7.16 (4 H, d, J = 9 Hz), 7.13 (4 H, d, J = 9 Hz), 7.01 (4 H, s), 6.66 (4 H, s), 5.30 (4 H, d, J = 9 Hz), 4.73 (4 H, d, J = 9 Hz), 4.71 (4 H, d, J = 12 Hz), 4.32 (4 H, d, J = 12 Hz), 3.15 (12 H, s, OCH_3), 2.76–2.63 (8 H, m), 2.28–2.21 (16 H, m), 2.00–1.96 (4 H, m), 1.66–1.45 (16 H, m), 1.26–1.04 (20 H, m), -1.16 (12 H, s, OCH_3), -3.29 (2 H, s, NH); MS (FAB) m/e 2129 ($M + H^+$); UV–vis (CH_2Cl_2) λ_{max} 421, 513, 539, 586, 642 nm.

(*R*)-**4a**: yield 1.1%; ^1H NMR ($CDCl_3$) δ 8.48 (4 H, d, J = 4 Hz, pyrrole β-H), 8.37 (4 H, d, J = 4 Hz, pyrrole β-H), 7.72 (4 H, t, J = 8 Hz), 7.26 (4 H, d, J = 8 Hz), 7.09 (4 H, d, J = 8 Hz), 7.04 (4 H, s), 6.44 (4 H, s), 5.22 (4 H, d, J = 10 Hz), 4.76 (4 H, d, J = 11 Hz), 4.58 (4 H, d, J = 11 Hz), 4.50 (4 H, d, J = 10 Hz), 2.86 (12 H, s, OCH_3), 2.86–2.75 (4 H, m), 2.71–2.61 (4 H, m), 2.34–2.12 (16 H, m), 2.06–1.93 (8 H, m), 1.70–1.40 (16 H, m), 1.30–0.80 (16 H, m), -1.05 (12 H, s, OCH_3), -3.15 (2 H, s, NH); MS (FAB) m/e 2129 ($M + H^+$); UV–vis (CH_2Cl_2) λ_{max} 423, 514, 545, 589, 644 nm.

Fe(Cl)[(*S*)-Binap(OMe)$_2$]$_4$TPP-eclipsed ((*S*)-1b). A mixture of (*S*)-**1a** (42.3 mg, 0.020 mmol), $Fe(CO)_5$ (0.070 mL, 0.53 mmol), and iodine (18 mg, 0.071 mmol) in dry toluene (40 mL) was heated at 55 °C under N_2 for 4 h and stirred at room temperature under aerobic conditions overnight. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 and water. The separated organic phase was dried over Na_2SO_4 and evaporated, followed by silica-gel flash column chromatography. The unreacted porphyrin (*S*)-**1a** was first eluted with dichloromethane, and then the metalated one was removed with CH_2Cl_2–ethanol (50:1 v/v). The effluent was washed with 5% HCl, dried over NaCl, and freed from solvent, affording (*S*)-**1b**: yield 33 mg (0.015 mmol, 75%); high MS (FAB) m/e calcd for $^{12}C_{139}{}^{13}CH_{100}N_4O_{16}{}^{56}Fe$ 2149.652, found 2149.644 ($(M - Cl)^+$); IR (KBr) 3050 (w), 2927 (m), 2858 (w), 1724 (m), 1591 (m), 1457 (s), 1371 (m), 1257 (s), 1078 (s), 1003 (m) cm^{-1}; UV–vis (CH_2Cl_2) λ_{max} 419, 508, 580, 648 nm.

The other iron complexes of twin-coronet porphyrins were obtained from the corresponding free-base porphyrins by using the same procedure. The preparation of the iron complex of (*R*)-**4a** was unsuccessful.

(*S*)-**2b**: yield 19%; high MS (FAB) m/e calcd for $^{12}C_{139}{}^{13}CH_{100}N_4O_{16}{}^{56}Fe$ 2149.652, found 2149.646 ($(M - Cl)^+$); IR (KBr) 3062 (w), 2927 (m), 2864 (w), 1628 (w), 1587 (m), 1456 (s), 1412

(28) Pirkle, W. H.; Pochapsky, T. C. *Chem. Rev.* **1989**, *89*, 347.

(w), 1363 (w), 1243 (s), 1076 (s), 996 (m) cm^{-1}; UV-vis (CH_2Cl_2) λ_{max} 422, 508, 577, 650 nm.

(*R*)-**3b**: yield 52%; high MS (FAB) *m/e* calcd for $^{12}C_{139}{}^{13}CH_{132}N_4O_{16}{}^{56}Fe$ 2181.902, found 2181.896 ($(M - Cl)^+$); IR (KBr) 2925 (s), 2854 (m), 1732 (w), 1650 (w), 1590 (m), 1458 (s), 1286 (w), 1252 (m), 1072 (s), 1003 (m) cm^{-1}; UV-vis (CH_2Cl_2) λ_{max} 421, 506, 580 nm.

Epoxidation of Styrene by Fe(Cl)[(*S*)-Binap(OMe)$_2$]$_4$TPP-eclipsed ((*S*)-1b) and Iodosobenzene. To a mixture of the catalyst (1 μmol), styrene (500 μmol), and *n*-tridecane (50 μmol) as a GLC internal standard in deaerated dry CH_2Cl_2 (1 mL) was added at once solid iodosobenzene (22 mg, 100 μmol), and the reaction mixture was stirred at a constant speed under an argon atmosphere. Aliquots (5 μL) were taken at appropriate intervals and quenched with a CH_2Cl_2 solution of PPh_3 (1.3 μmol). The formation of oxidized products was monitored by GLC, and their isolation was accomplished by silica-gel flash column chromatography, followed by identification by ^1H NMR spectroscopy. The optical yield (ee) was determined by the following method.

The trans β-proton of styrene oxide was analyzed by ^1H NMR spectroscopy in the presence of the chiral shift reagent tris[3-((heptafluoropropyl)hydroxymethylene)-(+)-camphorato]europium(III) (Eu(hfc)$_3$).[29] The proton showing the larger shift value was determined to be that of the *R* isomer.

Oxidation and analysis of the other olefins and oxidation by other catalysts were performed in the same manner with the exceptions noted in the text and Table II.

Acknowledgment. We thank Professor S. Takahashi of the Chemical Institute of Kyoto University for his technical assistance in recording the CD spectra. We also thank Dr. F. Imashiro of Kyoto University for his advice on the CNDO MO calculations, which were performed on a FACOM M-780 at the Data Processing Center of Kyoto University. We thank Professor I. Yamashina of Kyoto Industrial University for his permission to use the HX-110 mass spectrometer. We are grateful to Ono Pharmaceutical Co. Ltd. for their gift of the chiral binaphthalene derivative. This work was supported by a Grants-in-Aid for Scientific Research (63470015, 63607516, and 01607003) from the Ministry of Education, Science, and Culture of Japan.

Supplementary Material Available: A textual presentation of the experimental procedure for the preparation of compounds **5** and **6** and **8-17** (8 pages). Ordering information is given on any current masthead page.

(29) Fraser, P. R.; Petit, M. A.; Saunders, J. K. *J. Chem. Soc. D* **1971**, 1450.
(30) Tuschida, E.; Hasegawa, E.; Komatsu, T.; Nakata, T.; Nishide, H. *Chem. Lett.* **1990**, 389.
(31) Akimoto, H.; Yamada, S. *Tetrahedron* **1971**, *27*, 5999.
(32) Moneta, W.; Baret, P.; Pierre, J.-L. *Bull. Soc. Chim. Fr.* **1988**, 995.

Electrochemically Induced Nucleophilic Substitution of Perfluoroalkyl Halides. An Example of a Dissociative Electron-Transfer-Induced Chemical Reaction

Maurice Mędebielle, Jean Pinson, and Jean-Michel Savéant*

Contribution from the Laboratoire d'Electrochimie Moléculaire de l'Université de Paris 7, Unité Associée au CNRS No. 438, 2 place Jussieu, 75251 Paris Cedex 05, France.
Received March 1, 1991

Abstract: Nucleophilic substitution of perfluoroalkyl halides can be induced electrochemically. The reaction mechanism is a slightly modified version of the classical $S_{RN}1$ mechanism in which the reaction is triggered by dissociative electron transfer, not involving the intermediacy of the anion radical of the substrate. Direct electrochemical induction is possible in principle with the iodides but not with the bromides because the reduction potentials of the substrate and of the perfluoroalkyl radical are too close in the latter case. This impossibility can be overcome by using as inductor an electrochemically generated outer-sphere electron donor. Thiolates react at the sulfur atom whereas phenoxide as well as imidazolate ions react at ring carbons rather than at the negatively charged heteroatom.

The work described in the following had two objectives. One was to contribute to the search of methods for introducing perfluoroalkyl groups into organic molecules. The second objective is of mechanistic nature. Electrochemically induced nucleophilic substitutions have been thoroughly investigated in the case of aromatic substrates.[1] This allowed the precise establishment of the reaction mechanisms of $S_{RN}1$[2a-c] aromatic nucleophilic substitution,[2d] of the nature of the competing side-reactions, and of the mechanics of the competition. In this case, the electron transfer that catalytically triggers the reaction is an outer-sphere process producing as the first intermediate the anion radical of the substrate. The aryl radical formed upon decomposition of this anion radical is the object of the nucleophilic attack but, at the same time, is a very good electron acceptor. Both facts—the intermediacy of the substrate anion radical and the high reducibility of the aryl radical—are the key ingredients that govern the outcome of the competition between substitution and hydrogenolysis of the substrate. As will be shown in the following discussion, in the present case, the electron transfer that triggers the reaction is dissociative, and therefore the feasibility of the substitution reaction directly depends upon the reducibility of the ensuing perfluoroalkyl free radical. In the case where the latter radical is not rapidly reduced by the electron donor used to trigger the reaction, other reactions, for example, H-atom abstraction from the solvent, may compete with the substitution process.

Introduction of fluoro substituents into organic molecules appears as an increasingly important goal in view of the applications of the resulting species as pharmaceutical and agrochemical agents or as precursors of tensioactive compounds. As regards more specifically the introduction of perfluoroalkyl groups, most of the reactions described so far seem to proceed via the prior formation

(1) (a) Pinson, J.; Savéant, J.-M. *J. Chem. Soc., Chem. Commun.* **1974**, 933. (b) For reviews, see ref 18c-e. (c) Savéant, J.-M. *Acc. Chem. Res.* **1980**, *13*, 323. (d) Savéant, J.-M. *Adv. Phys. Org. Chem.* **1990**, *26*, 1. (e) Pinson, J.; Savéant, J.-M. In *Festschrift in Honour of Manuel Baizer*; Little, R. D., Ed.; Marcel Dekker, New York, in press.
(2) (a) Kornblum, N.; Michel, R. E.; Kerber, R. C. *J. Am. Chem. Soc.* **1966**, *88*, 5662. (b) Russell, G. A.; Danen, W. C. *J. Am. Chem. Soc.* **1966**, *88*, 5663. (c) Kim, J. K.; Bunnett, J. F. *J. Am. Chem. Soc.* **1970**, *92*, 7463. (d) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.

0002-7863/91/1513-6872$02.50/0