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Electronic effects on enantioselectivity in epoxidation catalyzed by D_4-symmetric chiral porphyrins

Hiroshi Nakagawa,[a] Yoshihisa Sei,[b] Kentaro Yamaguchi,[b] Tetsuo Nagano[a] and Tsunehiko Higuchi[c,*]

[a]*Graduate School of Pharmaceutical Sciences, The University of Tokyo, Bunkyo-ku, Tokyo 113-0033, Japan*
[b]*Chemical Analysis Center, Chiba University, Yayoi-cho, Inage-ku, Chiba 263-8522, Japan*
[c]*Graduate School of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467-8603, Japan*

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Abstract—Asymmetric epoxidation of various aromatic olefins was examined with our D_4-symmetric chiral porphyrin. The enantioselectivity was greatly improved upon when the substrates contained electron-deficient groups. Moreover, examination of electronic effects in the porphyrin catalyst revealed that electron-deficient groups lowered and electron-donating groups raised the enantioselectivity. Hammett plot analysis suggested that these electronic effects could be interpreted in terms of the Hammond postulate.

1. Introduction

Metalloporphyrins are of great interest as oxidation catalysts, for example, for epoxidation or hydroxylation. Since application of chiral metalloporphyrins to asymmetric epoxidation was first reported in 1983,[1] many chiral porphyrins designed to catalyze asymmetric reactions have been synthesized,[2] with some of them showing high enantioselectivity. In these asymmetric reactions, electronic features have an important influence on the enantioselectivity. The addition of amines as axial ligands is a convenient method for modifying the electronic features, while the enantioselectivity was enhanced by the addition of axial ligands in some porphyrins.[3–6] In addition, the enantioselectivity was greatly improved with Naruta's catalyst by utilizing the π-stacking effect between porphyrin and substrate.[7] We were interested in the electronic effect in the epoxidation catalyzed by our D_4-symmetric chiral porphyrin **1**[8] (Fig. 1), because **1** showed much higher enantioselectivity in the case of substrates with electron-deficient groups. The electronic effects were examined in detail by utilizing various styrene derivatives and porphyrins **1**–**5**. Herein, we focus on how the electronic features of the porphyrin rings affect the enantioselectivity. Our findings should lead to the development of superior catalysts offering improved levels of asymmetric induction.

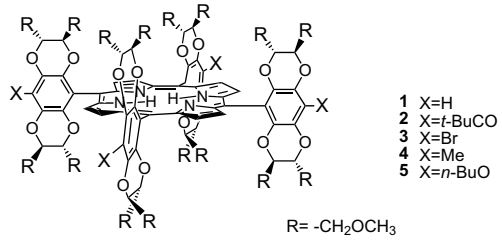

Figure 1. D_4-symmetric porphyrins with electron-withdrawing or donating groups.

2. Results and discussion

Table 1 shows the results of the epoxidation of substituted styrenes with the **1**–Fe(Br)/PhIO system.[9] The presence of electron-deficient substituents greatly increased the enantioselectivity, with the highest enantiomeric excess achieved in the case of 3-nitrostyrene (78% ee, run 11). To evaluate the effects of the substituents, the results in Table 1 were analyzed by means of a Hammett plot (Fig. 2). A linear correlation was

* Corresponding author. Tel.: +81 52 836 3435; fax: +81 52 836 3435; e-mail: higuchi@phar.nagoya-cu.ac.jp

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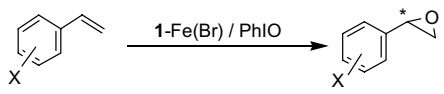
Table 1. Epoxidation of substituted styrenes with **1**–Fe(Br)



Run	X	Ee (%)	Yield (%)
1	H	47	68
2	3-F[a]	66	66
3	4-F	52	59
4	4-Cl	51	67
5	4-Br	48	67
6	2-Me[a]	31	58
7	3-Me	42	53
8	4-Me	28	51
9	3-CF_3	74	53
10	4-CF_3	52	66
11	3-NO_2[a]	78	62

Ees and yields (based on PhIO) were determined by HPLC analysis.
[a] Isolated yields. Ees were determined by ^{1}H NMR with (+)-Eu(hfc)$_3$.

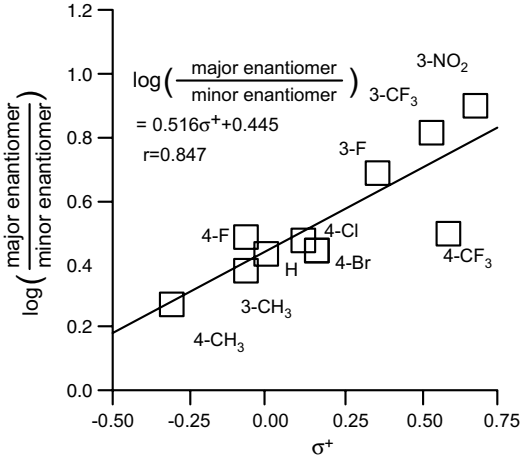


Figure 2. Correlation of optical yields of epoxides versus σ^+ of substituents of styrenes.

observed between log(major enantiomer/minor enantiomer) and σ^+ values. This suggests the existence of a benzyl cation intermediate, which is subject to racemization (Fig. 3).[10,11] Thus, the improvement of the enantioselectivity by electron-deficient groups might be rationalized in terms of a shortening of the lifetime of this benzyl cation intermediate. To investigate the role of the putative benzyl cation intermediate, 3-trifluoromethyl-*trans*-β-methylstyrene was used, because the influence of C_α–C_β bond rotation could be quantified from the amounts

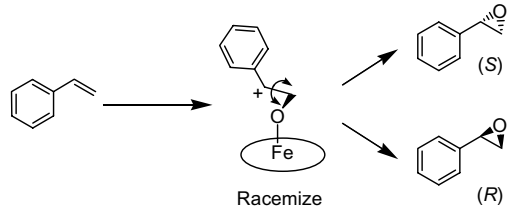


Figure 3. Effect of carbocationic intermediate.

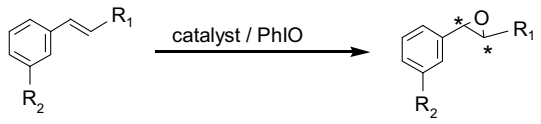
of *cis*-oxide and *trans*-oxide formed. In the epoxidation of 3-trifluoromethyl-*trans*-β-methylstyrene, the ratio of *cis*-oxide/*trans*-oxide was slightly lower than in that of *trans*-β-methylstyrene (0.05–0.01), while the enantiofacial selectivity[12] was markedly increased (2.3–3.7). Therefore the main effect of these electron-deficient groups is not due to shortening of the lifetime of the benzyl cation intermediate. π-Stacking effects between porphyrins and substrates may explain the improvement of the ees, but such interaction would be sterically difficult and lead to deviation from the linear correlation of Figure 2.[7] The reason for the high enantioselectivity is discussed later.

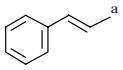
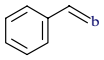
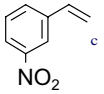
Next, we focused on the electronic features of the porphyrin ring, and examined the electronic effects on the enantioselectivity of the catalysts. Substituents, which could influence the electronic features of the catalysts, were placed at the *p*-positions of the *meso*-phenyl groups of **1** (Fig. 1) and the effects on the enantioselectivity were examined. *n*-Butoxy, methyl, bromo, and pivaloyl groups were introduced as substituents.

Styrene, 3-nitrostyrene, and *trans*-β-methylstyrene were epoxidized in the presence of these iron porphyrins with PhIO as the oxidant (Table 2).[9] While electron-deficient groups on the porphyrin lowered the enantiomeric excesses, electron-donating groups increased the enantioselectivity (for example, the *n*-butoxy-substituted catalyst **5** gave 52% ee for styrene, 79% ee for 3-nitrostyrene and 45% ee for *trans*-β-methylstyrene) with the difference between **2**–Fe(Br) and **5**–Fe(Br) being 6–10% ee. The *cis*-oxide was obtained in the epoxidation of *trans*-β-methylstyrene with low yield (2–3%), and no correlation was observed among the substituents, the enantiomeric excesses [(1*S*,2*R*), 8–10% ee] and chemical yields.[13]

The results in Table 2 were plotted against the σ_p values. As shown in Figure 4, linear relationships were observed between the σ_p values of the substituents of the porphyrins and log(major enantiomer/minor enantiomer) for all three substrates. This can be rationalized in terms of the Hammond postulate, as demonstrated for Jacobsen catalysts.[12] That is, lower reactivity leads to a comparatively late transition state and concomitantly higher selectivity. The electron-donating groups of **4**–Fe(Br) and **5**–Fe(Br) attenuate the reactivity of the catalysts,[14] and the transition states would be more product-like according to the Hammond postulate. Thus, catalysts and substrates would have a more effective interaction and the enantioselectivity with **4**–Fe(Br) and **5**–Fe(Br) becomes higher. The $|\rho|$ values of these substrates, which are useful for investigating the Hammond postulate, were slightly different. The $|\rho|$ value of 3-nitrostyrene was the largest, suggesting that the interaction between catalyst and substrate was the greatest, because the lower reactivity of 3-nitrostyrene leads to a transition state with the most product-like conformation. Higher enantioselectivity of styrenes with electron-deficient groups in Table 1 can also be explained by the Hammond postulate.[6,7] The $|\rho|$ values in Figure 4 are smaller than the $|\rho^+|$ value in Figure 2, because the substituents of the

Table 2. Epoxidation of olefins catalyzed by bromo-[tetrakis(*p*-substituted phenyl)porphyrinato]iron



Substrate	Ee (%), yield (%)				
	2–Fe(Br)	**3**–Fe(Br)	**1**–Fe(Br)	**4**–Fe(Br)	**5**–Fe(Br)
	39 (48)	40 (43)	42 (45)	44 (46)	45 (49)
	42 (72)	44 (65)	47 (68)	49 (65)	52 (66)
	71 (68)	74 (70)	78 (61)	78 (70)	79 (63)

Ees and yields (based on PhIO) were determined by HPLC analysis except for 3-nitrostyrene.
[a] (1*S*,2*S*)-Epoxide was obtained as the major enantiomer. The *cis*-epoxide was also obtained in 2–3% yield (1*S*,2*R*), 8–10% ee.
[b] (*S*)-Epoxide was obtained.
[c] Isolated yields. Ees were determined by ^{1}H NMR with (+)-Eu(hfc)$_3$. Absolute configuration of epoxide was not determined.

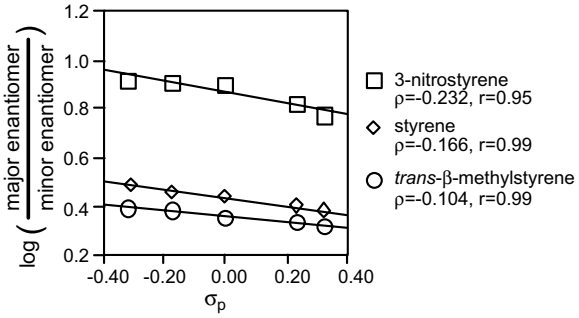


Figure 4. Correlation of optical yields of epoxides versus σ_p of substituents of porphyrins. Log(enantiofacial selectivity) was used as the vertical axis for *trans*-β-methylstyrene. Enantiofacial selectivity = [(1*S*,2*S*) + (1*R*,2*S*)]/[(1*R*,2*R*) + (1*S*,2*R*)].[10]

porphyrins **1**–**5** are far from the central metal and the electronic effect would be smaller. In general, porphyrins with electron-deficient groups would be preferable as oxidation catalysts, since their reactivity is higher and the porphyrins become more resistant to self-oxidation.[15] However these groups also lower the selectivity. Modifications that lead to milder reactivity, such as introduction of electron-donating groups into the catalyst, would be expected to yield higher enantioselectivity.

3. Experimental

All solvents were purified by standard methods. Unless otherwise noted, reagents were obtained from commercial suppliers and used without further purification. Melting points were determined on a cover glass with an electrothermal melting point apparatus and are uncorrected. ^{1}H NMR chemical shifts in $CDCl_3$ were reported relative to internal TMS. ^{1}H NMR chemical shifts in CD_2Cl_2 and ^{13}C NMR chemical shifts were reported relative to the solvent peak. HPLC was performed on a chiral column (CHIRALPAK AS, 46 mm × 250 mm, Daicel Chemical Industries) to quantify enantiomeric excesses. Scheme 1 shows the synthetic route to the *p*-substituted benzaldehydes.

3.1. (*R*,*R*,*R*,*R*)-9-Formyl-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracene 6

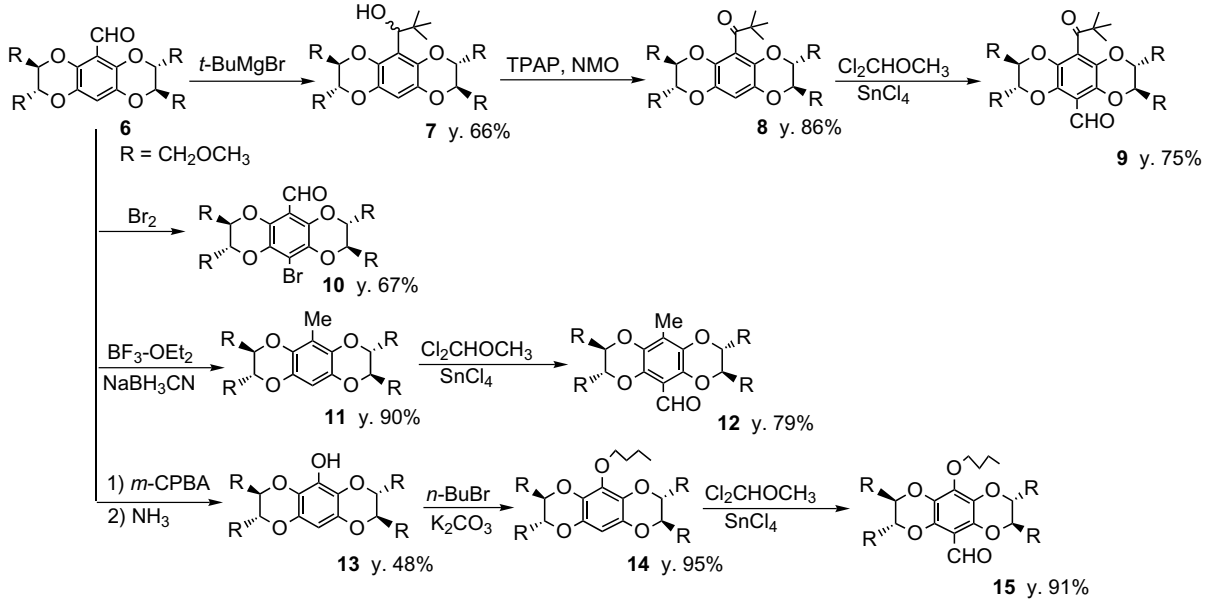
Prepared by the same method as Ref. 8.

3.2. (*R*,*R*,*R*,*R*)-9-(2,2-Dimethyl-1-(*R*,*S*)-hydroxypropyl)-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracene 7

To a solution of aldehyde **6** (266 mg, 0.67 mmol) in THF (6 mL) was added *tert*-butylmagnesium bromide 1.0 M THF solution (1.4 mL, 1.4 mmol) at 0 °C under an argon atmosphere, and the mixture stirred at room temperature for 15 h. Saturated NH_4Cl (aq) was added, followed by extraction with EtOAc. The organic layer was dried over Na_2SO_4 and evaporated. Purification by silica gel column chromatography (EtOAc/*n*-hexane) afforded **7** as a colorless solid (200 mg, 0.44 mmol, 66% yield); ^{1}H NMR ($CDCl_3$) δ 0.96 (9H, s), 3.38, 3.40 (12H, m), 3.6–3.7 (8H, m), 4.1–4.3 (4H, m), 4.83 (1H), 6.45 (1H).

3.3. (*R*,*R*,*R*,*R*)-9-Pivaloyl-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracene 8

To a mixture of substrate **7** (181 mg, 0.40 mmol), *N*-methylmorpholine *N*-oxide (139 mg, 1.2 mmol) and molecular sieves 4 Å (300 mg) in CH_3CN (3 mL) was added tetrapropylammonium perruthenate (14 mg, 0.10 mmol), and the mixture was stirred for 5 h at 40 °C. The mixture was passed through a short silica gel column (EtOAc) and purification of the product by silica gel column chromatography (EtOAc/*n*-hexane) afforded **8** as colorless solid (154 mg, 0.34 mmol, 86% yield); ^{1}H NMR ($CDCl_3$) δ 1.20 (9H, s), 3.36 (6H, s), 3.40 (6H, s), 3.67 (8H, m), 4.14 (4H, m), 6.50 (1H, s);



Scheme 1. Synthetic scheme for *p*-substituted benzaldehydes. Reagents and conditions: TPAP tetra-*n*-propylammonium perruthenate; NMO *N*-methylmorpholine *N*-oxide.

^{13}C NMR ($CDCl_3$) δ 26.7, 44.8, 59.5, 71.1, 71.2, 73.1, 73.3, 105.0, 119.3, 132.8, 136.7, 211.2.

3.4. (*R*,*R*,*R*,*R*)-9-Formyl-10-pivaloyl-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracene 9

A solution of **8** (147 mg, 0.32 mmol) in CH_2Cl_2 (7 mL) was cooled to 0 °C under an argon atmosphere. $SnCl_4$ (76 μL, 0.64 mmol) and dichloromethyl methyl ether (35 μL, 0.39 mmol) were sequentially added dropwise via a syringe and the reaction mixture refluxed for 2 h. The reaction mixture was poured into ice water and extracted with CH_2Cl_2. The organic layer was washed with saturated $NaHCO_3$ aqueous solution and brine, and dried over Na_2SO_4. The solvent was evaporated and purification of the residue by silica gel column chromatography (EtOAc/*n*-hexane) afforded **9** as a yellow solid (117 g, 0.24 mmol, 75% yield); ^{1}H NMR ($CDCl_3$) δ 1.24 (9H, s), 3.36 (6H, s), 3.42 (6H, s), 3.64 (4H, dd, J = 3.8 Hz, 11.1 Hz), 3.73 (4H, m), 4.21 (4H, m), 10.42 (1H, s); ^{13}C NMR ($CDCl_3$) δ 26.6, 44.8, 59.7, 70.9, 71.0, 73.9, 108.8, 120.7, 132.4, 139.1, 187.3, 211.0.

3.5. (*R*,*R*,*R*,*R*)-10-Bromo-9-formyl-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracene 10

To a solution of aldehyde **6** (398 mg, 1.0 mmol) in CCl_4 (5 mL) was added bromine (56 μL, 1.1 mmol) via a syringe under an argon atmosphere at 0 °C. The reaction mixture was stirred for 2 h and poured into water. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and evaporated. Purification by silica gel column chromatography (EtOAc/*n*-hexane) afforded **10** as a yellow solid (321 mg, 0.67 mmol, 67% yield); ^{1}H NMR ($CDCl_3$) δ 3.43 (6H, s), 3.45 (6H, s), 3.77 (8H, m), 4.28 (4H, m), 10.43 (1H, s); ^{13}C NMR ($CDCl_3$) δ 59.7, 59.8, 70.8, 70.9, 73.8, 73.9, 112.6, 121.3, 134.9, 139.0, 187.3.

3.6. (*R*,*R*,*R*,*R*)-9-Methyl-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracene 11

To a solution of aldehyde **6** (398 mg, 1.0 mmol) and boron trifluoride diethyl etherate (0.39 mL) in THF (5 mL) was added $NaBH_3CN$ (165 mg, 2.5 mmol). The mixture was refluxed for 15 h and then cooled to room temperature and poured into EtOAc. The organic layer was washed with saturated $NaHCO_3$ (aq) and brine. The organic layer was dried over Na_2SO_4 and evaporated. Purification of the residue by silica gel column chromatography (EtOAc/*n*-hexane) afforded **11** as a yellow solid (345 mg, 0.90 mmol, 90% yield); ^{1}H NMR ($CDCl_3$) δ 2.09 (3H, s), 3.41 (6H, s), 3.43 (6H, s), 3.69 (8H, m), 4.16 (4H, m), 6.38 (1H, s); ^{13}C NMR ($CDCl_3$) δ 8.2, 59.5, 59.6, 71.4, 71.5, 73.0, 73.1, 102.1, 114.2, 135.1, 136.4.

3.7. (*R*,*R*,*R*,*R*)-9-Formyl-10-methyl-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracene 12

Prepared by the same method as **9** (79% yield, yellow solid); ^{1}H NMR ($CDCl_3$) δ 2.15 (3H, s), 3.43 (6H, s), 3.44 (6H, s), 3.74 (8H, m), 4.22 (4H, m), 10.41 (1H, s); ^{13}C NMR ($CDCl_3$) δ 8.6, 59.6, 71.2, 71.3, 72.9, 73.4, 109.1, 117.7, 134.9, 136.6, 200.1.

3.8. (*R*,*R*,*R*,*R*)-9-Hydroxy-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracene 13

A solution of aldehyde **6** (800 mg, 2.0 mmol) and *m*-CPBA (693 mg, 4.0 mmol) in CH_2Cl_2 (20 mL) was

refluxed for 7 h. The reaction mixture was evaporated carefully and the residue dissolved in EtOAc. This solution was washed with saturated $NaHCO_3$ (aq) and brine, and dried over Na_2SO_4. The solvent was evaporated and the residue dissolved in EtOH (40 mL) and 23% NH_3 (aq 24 mL). The reaction mixture was stirred at room temperature under an argon atmosphere for 15 h and evaporated. 2 M HCl was added to the residue and the aqueous layer extracted with EtOAc. The organic layer was washed with saturated $NaHCO_3$ (aq) and brine, dried over Na_2SO_4 and evaporated. Purification of the residue by silica gel column chromatography (EtOAc/*n*-hexane) afforded **13** as a colorless solid (371 mg, 0.96 mmol, 48% yield); ^{1}H NMR ($CDCl_3$) δ 3.39 (12H, s), 3.6–3.7 (8H, m), 4.20 (4H, m), 5.51 (1H, br s), 6.12 (1H, s); ^{13}C NMR ($CDCl_3$) δ 59.4, 59.5, 71.1, 71.2, 73.2, 73.3, 95.6, 125.6, 133.7, 137.0.

3.9. (*R*,*R*,*R*,*R*)-9-*n*-Butoxy-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracene 14

A mixture of phenol **13** (231 mg, 0.60 mmol), *n*-butyl bromide (161 μL, 1.5 mmol), and K_2CO_3 (207 mg, 1.5 mmol) in DMF (5 mL) was stirred at 80 °C under an argon atmosphere. The reaction mixture was poured into water and extracted with EtOAc. The organic layer was dried over Na_2SO_4 and evaporated. Purification of the residue by silica gel column chromatography (EtOAc/*n*-hexane) afforded **14** as a colorless solid (251 mg, 0.57 mmol, 95% yield); ^{1}H NMR ($CDCl_3$) δ 0.95 (3H, 7.3 Hz), 1.51 (2H, m), 1.69 (2H, m), 3.41 (6H, s), 3.42 (6H, s), 3.68 (8H, m), 4.04 (2H, y, J = 6.6 Hz), 4.18 (4H, m), 6.29 (1H, s); ^{13}C NMR ($CDCl_3$) δ 13.8, 19.0, 32.1, 59.5, 71.2, 72.7, 73.1, 73.3, 99.4, 131.1, 136.4, 136.9.

3.10. (*R*,*R*,*R*,*R*)-10-*n*-Butoxy-9-formyl-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracene 15

Prepared by the same method as **9** (91% yield, yellow solid); ^{1}H NMR ($CDCl_3$) δ 0.95 (3H, s), 1.47 (2H, m), 1.73 (2H, m), 3.41 (6H, s), 3.43 (6H, s), 3.72 (8H, m), 4.17 (2H, t, J = 6.4 Hz), 4.25 (4H, m), 10.36 (1H, s); ^{13}C NMR ($CDCl_3$) δ 13.8, 18.9, 32.1, 59.5, 59.7, 70.9, 71.0, 72.7, 73.6, 109.0, 130.5, 139.8, 142.3, 187.0.

3.11. 5,10,15,20-Tetrakis[(*R*,*R*,*R*,*R*)-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracen-9-yl]porphyrin 1

A solution of aldehyde **6** (456 mg, 1.1 mmol) in $CHCl_3$ (114 mL) was purged with argon gas for 30 min. Under an argon atmosphere, boron trifluoride diethyl etherate (48 μL, 0.38 mmol) and then pyrrole (79 μL, 1.1 mmol) were added slowly via a syringe and the mixture stirred for 1 h. Chloranil (211 mg, 0.86 mmol) was added to the mixture and the reaction mixture was refluxed for another 1 h. The reaction mixture was then cooled to room temperature and triethylamine (53 μL) and a pad of silica gel added. The mixture was evaporated to dryness and passed through a short silica gel column (EtOAc). Purification was carried out by preparative TLC (EtOAc/*n*-hexane) with **1** being obtained as a brown solid (189 mg, 0.11 mmol, 37% yield); ^{1}H NMR ($CDCl_3$) δ −2.71 (2H, br s), 2.66 (24H, s), 3.04 (8H, dd, J = 4.6 Hz, 11.1 Hz), 3.16 (8H, dd, J = 3.7 Hz, 11.0 Hz), 3.41 (24H, s), 3.71 (16H, d, J = 4.4 Hz), 3.97 (8H, m), 4.31 (8H, m), 7.02 (4H, s), 8.78 (8H, s); ^{13}C NMR ($CDCl_3$) δ 59.0, 59.5, 70.5, 71.4, 73.1, 73.2, 105.6, 106.9, 108.7, 109.2, 120.2, 136.7, 137.7; MS (FAB, 3-nitrobenzyl alcohol) *m*/*z* (relative intensity) 1783 (100), 1784 (32); HRMS (FAB, 3-nitrobenzyl alcohol) Calcd for $C_{92}H_{110}N_4O_{32}$: 1782.7103. Found: 1782.6995; UV (CH_3CN) λ_{max} 415 nm (ε = 239,000 $cm^{-1}M^{-1}$), 510 (17,000), 584 (6200).

3.12. 5,10,15,20-Tetrakis[(*R*,*R*,*R*,*R*)-10-pivaloyl-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracen-9-yl]porphyrin 2

Prepared by the same method as **1** (39% yield, brown solid); ^{1}H NMR ($CDCl_3$) δ −2.74 (2H, br s), 1.49 (36H, s), 2.61 (24H, s), 3.01 (8H, m), 3.16 (8H, dd, J = 3.7 Hz, 11.0 Hz), 3.37 (24H, s), 3.67 (16H, m), 3.97 (8H, m), 4.29 (8H, m), 8.81 (8H, s); ^{13}C NMR ($CDCl_3$) δ 27.0, 33.4, 59.0, 59.5, 70.3, 71.1, 73.2, 73.3, 95.0, 102.2, 108.6, 115.3, 131.3, 137.6, 148.5, 191.1; MS (FAB, 3-nitrobenzyl alcohol) *m*/*z* (relative intensity) 2118 (100); HRMS (FAB, 3-nitrobenzyl alcohol) Calcd for $C_{112}H_{142}N_4O_{36}$: 2118.9404. Found: 2118.9390; UV (CH_3 CN) λ_{max} 416 nm (ε = 272,000 $cm^{-1}M^{-1}$), 510 (16,000), 584 (5000).

3.13. 5,10,15,20-Tetrakis[(*R*,*R*,*R*,*R*)-10-bromo-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracen-9-yl]porphyrin 3

Prepared by the same method as **1** (47% yield, brown solid); ^{1}H NMR ($CDCl_3$) δ −2.74 (2H, br s), 2.63 (24H, s), 3.13 (8H, dd, J = 4.5 Hz, 11.1 Hz), 3.20 (8H, dd, J = 3.5 Hz, 11.1 Hz), 3.44 (24H, s), 3.76 (16H, m), 3.99 (8H, m), 4.39 (8H, m), 8.77 (8H, s); ^{13}C NMR ($CDCl_3$) δ 59.0, 59.8, 70.2, 71.0, 73.1, 73.8, 99.8, 108.8, 105.0, 118.5, 130.1, 134.9, 137.9; MS (FAB, 3-nitrobenzyl alcohol) *m*/*z* (relative intensity) 2096 (100); HRMS (FAB, 3-nitrobenzyl alcohol) Calcd for $C_{92}H_{107}Br_4N_4O_{32}$: 2095.3602. Found: 2095.3796; UV (CH_3CN) λ_{max} 416 nm (ε = 254,000 $cm^{-1}M^{-1}$), 509 (16,400), 583 (5200).

3.14. 5,10,15,20-Tetrakis[(*R*,*R*,*R*,*R*)-10-methyl-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracen-9-yl]porphyrin 4

Prepared by the same method as **1** (32% yield, brown solid); ^{1}H NMR ($CDCl_3$) δ −2.69 (2H, br s), 2.46 (12H, s), 2.64 (24H, s), 3.07 (8H, dd, J = 4.8 Hz, 11.0 Hz), 3.17 (8H, dd, J = 3.9 Hz, 11.0 Hz), 3.42 (24H, s), 3.73 (16H, d, J = 4.4 Hz), 3.94 (8H, m), 4.31 (8H, m), 8.76 (8H, s); ^{13}C NMR ($CDCl_3$) δ 8.7, 59.1, 59.6, 70.5, 71.5, 72.8, 73.0, 109.4, 111.1, 114.6, 116.4, 134.8, 137.3, 142.2; MS (FAB, 3-nitrobenzyl alcohol) *m*/*z* (relative intensity) 1839 (100), 1840 (37); HRMS (FAB,

3-nitrobenzyl alcohol) Calcd for $C_{96}H_{118}N_4O_{32}$: 1838.7762. Found: 1838.7720; UV (CH_3CN) λ_{max} 417 nm ($\varepsilon = 275{,}000\,cm^{-1}M^{-1}$), 511 (18,500), 586 (5500).

3.15. 5,10,15,20-Tetrakis[(*R*,*R*,*R*,*R*)-10-*n*-butoxy-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracen-9-yl]porphyrin 5

Prepared by the same method as **1** (32% yield, brown solid); ^1H NMR ($CDCl_3$) δ 2.71 (2H, br s), 1.10 (12H, t, $J = 7.4$ Hz), 1.71 (8H, m), 1.94 (8H, m), 2.63 (24H, s), 3.08 (8H, dd, $J = 4.9$ Hz, 11.1 Hz), 3.17 (4H, dd, $J = 4.0$ Hz, 11.1 Hz), 3.41 (24H, s), 3.74 (16H, m), 3.95 (8H, m), 4.32 (8H, m), 4.39 (8H, t, $J = 6.6$ Hz), 8.76 (8H, s); ^{13}C NMR ($CDCl_3$) δ 14.0, 19.3, 32.4, 59.0, 59.5, 70.4, 71.3, 72.7, 73.0, 73.8, 109.0, 113.8, 130.9, 132.1, 133.4, 136.9, 137.7; MS (FAB, 3-nitrobenzyl alcohol) *m*/*z* (relative intensity) 2074 (100); HRMS (FAB, 3-nitrobenzyl alcohol) Calcd for $C_{108}H_{142}N_4O_{36}$: 2070.9404. Found: 2070.9316; UV (CH_3CN) λ_{max} 417 nm ($\varepsilon = 237{,}000\,cm^{-1}M^{-1}$), 511 (16,700), 586 (5100).

3.16. Bromo-[5,10,15,20-tetrakis[(*R*,*R*,*R*,*R*)-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracen-9-yl]porphyrinato]iron(III) 1–Fe(Br)

To a mixture of porphyrin **1** (150 mg, 84 μmol) and iodine (213 mg, 0.84 mmol) in toluene (15 mL) was added $Fe(CO)_5$ (1.9 mL, 15 mmol) via a syringe under an argon atmosphere. The mixture was refluxed for 5 h and then passed through an alumina short column (CH_2Cl_2). The porphyrin fraction was washed with 5% aqueous HBr solution and dried with KBr. The solvent was evaporated and recrystallization (CH_2Cl_2/*n*-hexane) afforded **1**–Fe(Br) as a brown solid (88 mg, 46 μmol, 55% yield); MS (FAB, 3-nitrobenzyl alcohol) *m*/*z* (relative intensity) 1838 (100), 1839 (31); HRMS (FAB, 3-nitrobenzyl alcohol) Calcd for $C_{92}H_{108}FeN_4O_{32}$: 1836.6296. Found: 1836.6250; UV (CH_3CN) λ_{max} 414 nm ($\varepsilon = 59{,}700\,cm^{-1}M^{-1}$), 511 (10,300).

3.17. Bromo-5,10,15,20-tetrakis((*R*,*R*,*R*,*R*)-10-pivaloyl-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracen-9-yl)porphyrinato]iron(III) 2–Fe(Br)

Prepared by the same method as **1**–Fe(Br) (58% yield, brown solid); MS (FAB, 3-nitrobenzyl alcohol) *m*/*z* (relative intensity) 2174 (100); HRMS (FAB, 3-nitrobenzyl alcohol) Calcd for $C_{112}H_{140}FeN_4O_{36}$: 2172.8597. Found: 2172.8603; UV (CH_3CN) λ_{max} 415 nm ($\varepsilon = 79{,}700\,cm^{-1}M^{-1}$), 511 (13,100).

3.18. Bromo-[5,10,15,20-tetrakis((*R*,*R*,*R*,*R*)-10-bromo-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracen-9-yl)porphyrinato]iron(III) 3–Fe(Br)

Prepared by the same method as **1**–Fe(Br) (55% yield, brown solid); MS (FAB, 3-nitrobenzyl alcohol) *m*/*z* (relative intensity) 2153 (100), 2155 (52); HRMS (FAB, 3-nitrobenzyl alcohol) Calcd for $C_{92}H_{104}Br_4FeN_4O_{36}$: 2148.2717. Found: 2148.2878; UV (CH_3CN) λ_{max} 415 nm ($\varepsilon = 71{,}500\,cm^{-1}M^{-1}$), 511 (11,900).

3.19. Bromo-[5,10,15,20-tetrakis[(*R*,*R*,*R*,*R*)-10-methyl-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracen-9-yl]porphyrinato]iron(III) 4–Fe(Br)

Prepared by the same method as **1**–Fe(Br) (61% yield, brown solid); MS (FAB, 3-nitrobenzyl alcohol) *m*/*z* (relative intensity) 1893 (100); HRMS (FAB, 3-nitrobenzyl alcohol) Calcd for $C_{96}H_{116}FeN_4O_{32}$: 1892.6922. Found: 1892.6775; UV (CH_3CN) λ_{max} 416 nm ($\varepsilon = 72{,}400\,cm^{-1}M^{-1}$), 511 (12,600).

3.20. Bromo-[5,10,15,20-tetrakis[(*R*,*R*,*R*,*R*)-10-*n*-butoxy-2,3,6,7-tetramethoxymethyl-1,4,5,8-tetraoxa-1,2,3,4,5,6,7,8-octahydroanthracen-9-yl]porphyrinato]iron(III) 5–Fe(Br)

Prepared by the same method as **1**–Fe(Br) (54% yield, brown solid); MS (FAB, 3-nitrobenzyl alcohol) *m*/*z* (relative intensity) 2124 (100); HRMS (FAB, 3-nitrobenzyl alcohol) Calcd for $C_{108}H_{140}N_4O_{36}$: 2124.8597. Found: 2124.8650; UV (CH_3CN) λ_{max} 416 nm ($\varepsilon = 74{,}700\,cm^{-1}M^{-1}$), 512 (12,900).

3.21. Typical procedure for asymmetric epoxidation of aromatic olefins

A mixture of styrene (28 μL, 0.25 mmol) and a catalyst (0.25 μmol) in dry toluene (500 μL) was cooled to −20 °C under an argon atmosphere. Iodosylbenzene (5.5 mg, 25 μmol) was added and the reaction stirred for 3 h. Triphenylphosphine (33 mg, 0.13 mmol) in toluene (100 μL) was then added to stop the reaction. The reaction mixture was analyzed by HPLC or the epoxide was purified by silica gel column chromatography and analyzed by ^1H NMR with (+)-Eu(hfc)$_3$. The absolute configuration was determined by a comparison with an authentic sample.

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References

1. Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5791.
2. For reviews, see: (a) Collman, J. P.; Zhang, X.; Lee, V. J.; Uffelman, E. S.; Brauman, J. I. *Science* **1993**, *261*, 1404; (b) Besse, P.; Veschambre, H. *Tetrahedron* **1994**, *50*, 8885; (c) Campbell, L. A.; Kodadek, T. *J. Mol. Catal. A–Chem.* **1996**, *113*, 293; (d) Marchon, J.-C.; Ramasseul, R. In *Handbook of Porphyrins and Phthalocyanines*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic: New York, 2003; Vol. 11, p 75; (e) Naruta, Y. In *Metalloporphyrins in Catalytic Oxidations*; Sheldon, R. A., Ed.; Marcel Dekker: New York, 1994; p 241.

3. Collman, J. P.; Lee, V. J.; Kellen-Yuen, C. J.; Zhang, X.; Ibers, J. A.; Brauman, J. I. *J. Am. Chem. Soc.* **1995**, *117*, 692.
4. Gross, Z.; Ini, S. *J. Org. Chem.* **1997**, *62*, 5514.
5. Lai, T.-S.; Ng, K.-H.; Liu, H.-Y.; Chang, C.-K.; Yeung, L.-L. *Synlett* **2002**, 1475.
6. Liu, S.-Q.; Pécaut, J.; Marchon, J. C. *Eur. J. Inorg. Chem.* **2002**, *7*, 1823.
7. (a) Naruta, Y.; Tani, F.; Ishihara, N.; Maruyama, K. *J. Am. Chem. Soc.* **1991**, *113*, 6865; (b) Naruta, Y.; Ishihara, N.; Tani, F.; Maruyama, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 158.
8. Nakagawa, H.; Sei, Y.; Yamaguchi, K.; Nagano, T.; Higuchi, T. *J. Mol. Catal. A–Chem.* **2004**, *219*, 221.
9. Only a small amount of by-product via H^--migration (phenylacetaldehyde derivatives) was detected in each reaction (<2%).
10. Traylor, T. G.; Xu, F. *J. Am. Chem. Soc.* **1988**, *110*, 1953.
11. In Fig. 2, the plot of 4-substituted styrenes deviates from the linear correlation rather than that of 3-substituted styrenes. The deviation would be caused by the steric or electronic interaction between the substituents at the 4-position of styrenes and methoxymethyl moieties of the porphyrin.
12. Palucki, M.; Finney, N. S.; Pospisil, P. J.; Güler, M. L.; Ishida, T.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 948.
13. The major enantiomer of the *cis*-oxide had a (1*S*,2*R*)-configuration, which was derived from minor benzyl cation intermediate. The *cis*/*trans* ratio at the ring closure step should be different between the major pathway and the minor one, because the major and minor intermediates are diastereomers and therefore the lifetime and the steric circumstances between these intermediates would differ. There would be a tendency that the favored intermediate selectively affords the major diastereomer of the product, while the minor intermediate preferentially gives the minor diastereomer: Zhang, W.; Lee, N. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1994**, *116*, 425.
14. In iron porphyrin-catalyzed oxidation with iodosylarenes, a Ph-IO-ligated complex of the catalyst is proposed to be a major active oxidant in the presence of olefins. For the mechanism of the oxidation by metalloporphyrin with PhIO, see: (a) Collman, J. P.; Chien, A. S.; Eberspacher, T. A.; Brauman, J. I. *J. Am. Chem. Soc.* **2000**, *122*, 11098; (b) Nam, W.; Lim, M. H.; Lee, H. J.; Kim, C. *J. Am. Chem. Soc.* **2000**, *122*, 6641; (c) Machii, K.; Watanabe, Y.; Morishima, I. *J. Am. Chem. Soc.* **1995**, *117*, 6691; (d) Nam, W.; Valentine, J. S. *J. Am. Chem. Soc.* **1990**, *112*, 4977.
15. Berkessel, A.; Kaiser, P.; Lex, J. *Chem. Eur. J.* **2003**, *9*, 4746.