An Efficient Catalyst for Asymmetric Epoxidation of Terminal Olefins

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Prodigious effort has been devoted to the development of catalytic enantioselective olefin epoxidation because chiral epoxides are appealing synthetic intermediates.[1] Highly selective asymmetric epoxidation of allylic alcohols has been accomplished with titanium tartrate complexes.[2] Mn(salen) complexes derived from chiral C_2 symmetrical 1, 2-diamines have generated good optical selectivities for 1, 2-cis alkenes and a number of tri- and tetrasubstituted olefins.[3] However, development of a highly selective epoxidation catalyst for terminal olefins has been far less successful, despite the fact that the target chiral epoxides have broad applications. Herein we present a highly efficient catalyst based on a novel chiral iron porphyrin. This system gives very high enantioselectivities and large turnover numbers for styrene derivatives and nonconjugated terminal alkenes.

Studies with metalloporphyrins as oxygenating catalysts were stimulated by the attempts to model the reactivity of the cytochrome P-450 family of heme enzymes.[4] The rigid macrocyclic core and alterable periphery of porphyrins make them attractive templates for building asymmetric catalysts. Chiral groups have been attached to porphyrins in many different geometries, aiming at systems which might give high enantioselectivities and large turnover numbers, but as yet no porphyrin-based catalyst has been sufficiently refined to find application in general synthesis.[5] The porphyrin catalyst we present, **1**, has a previously overlooked $\alpha\alpha\beta\beta$ geometry, with one pseudo-C_2 axis within the porphyrin plane.[6] An important feature of this geometry is that it provides open space for substrate access, but at the same time imposes substantial steric bulk in the proximity of the metal center. This feature contributes to high catalytic activity and selectivity.

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Scheme 1
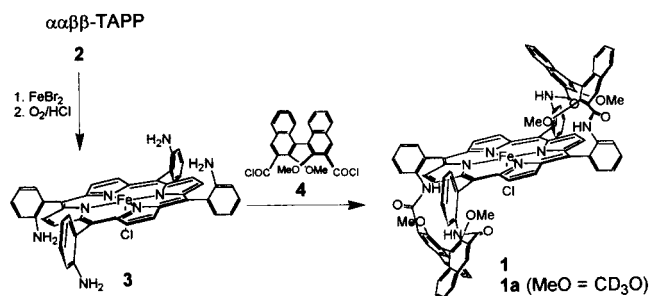
Table 1. Epoxidation of Unfunctionalized Olefins Catalyzed with **1**[a]

|		% Yield[b]	% ee[c]	Configuration[d]
1		95	83	S
2[e]		89[f]	75	S
3		75	88	S
4		90	82	S
5[e]		85[f]	74	S
6		74	55	S
7		78	72	S
8[e]		75[f]	68	S
9		80	55	1S,2R
10		78	49	1S,2R
11		85	>90[g]	n. d.[h]
12		73	82	n. d.[h]

[a] Reaction conditions: **1** (1.0 μmol), substrate (1.0 mmol), and PhIO (0.10 mmol) react at room temperature in CH_2Cl_2 (2 mL). [b] Yields are based on consumed PhIO. [c] Determined by GC with use of a Cyclodex-B chiral column. [d] Assigned by comparing the GC retention time with standard samples. [e] Reaction conditions: PhIO (ca. 1.2 mmol) is added in 10 portions at room tempetature to a mixture of **1** (1.0 μmol) and substrate (1.0 mmol) in CH_2Cl_2 (2 mL); each subsequent portion is added when the previous batch of oxidant has been consumed. [f] Isolated yield based on the substrate. [g] Determined by ^{1}H NMR with Eu(hfc)$_3$ as a chiral shift agent. [h] The absolute configuration was not determined.

Complex **1** is synthesized from $\alpha\alpha\beta\beta$ tetrakis(aminophenyl)-porphyrin (TAPP, **2**)[7] (Scheme 1), in 53% overall yield in two steps.[8]

Epoxidation reactions catalyzed with **1** were first examined with iodosylbenzene as the oxidant and excess olefin substrates (**1**: PhIO:substrate = 1:100:1000). These epoxidations show an unprecedented selectivity pattern for a number of unfunctionalized olefins. As shown in Table 1, this catalyst yields high enantioselectivities for epoxidation of styrene (83% ee), pentafluorostyrene (88% ee), and *m*-chlorostyrene (82% ee). It is significant that this system manifests unusual chiral induction for nonconjugated terminal olefins such as 3,3-dimethylbutene and vinyltrimethylsilane. The ee values obtained for these two olefins exceed the highest values from any previously reported catalytic systems, including the remarkable Mn(salen) derivatives.[3]

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(8) The identity of **1** was established by MS, UV−visible spectra, and conversion to its metal-free form.
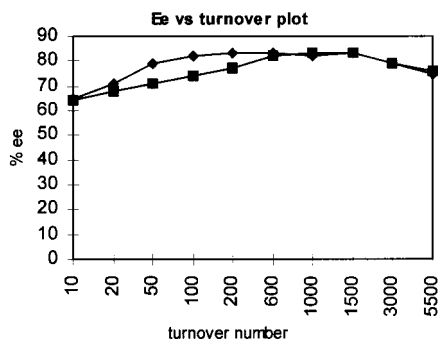
Figure 1. (◆) Epoxidation catalyzed with **1**. (■) Epoxidation catalyzed with **1a**.

Other useful features of **1** include its exceptional activity and stability. For example, **1** catalyzes the epoxidation of styrene at a rate of 40 turnovers/min and affords up to 5500 turnovers while maintaining a reasonable ee of 75%. Epoxidations of some substrates with olefin as the limiting reagent have also been tested and the results are given in Table 1. Although the catalyst degrades in the presence of excess oxidant, portionwise addition of iodosylbenzene allows complete conversion of the substrates with 0.1 mol % catalyst. Styrene, *m*-chlorostyrene, and *m*-nitrostyrene are epoxidized in good isolated yields and slightly lower but reasonable ee values (Table 1, entries 2, 5, and 8, cf. entries 1, 4, and 7). A typical problem with previously studied epoxidation systems is that selectivity is gained at the expense of activity and catalyst life, or *vice versa*; the high enantioselectivity *and* activity obtained with **1** clearly show the advantage of the (open access) + (critical directing bulk) strategy.[9] It is noteworthy that the same strategy has been successfully used in the development of chiral Mn(salen) catalysts.

A detailed investigation of the ee vs turnover plot reveals an unexpected trend in the ee−turnover relationship: there is a *rise* in ee values during the initial period of the reaction, from 65% at 10 turnovers to 83% at 200 turnovers (Figure 1). From 100 to 2000 turnovers, the reaction maintains a maximum ee of 82−83%.
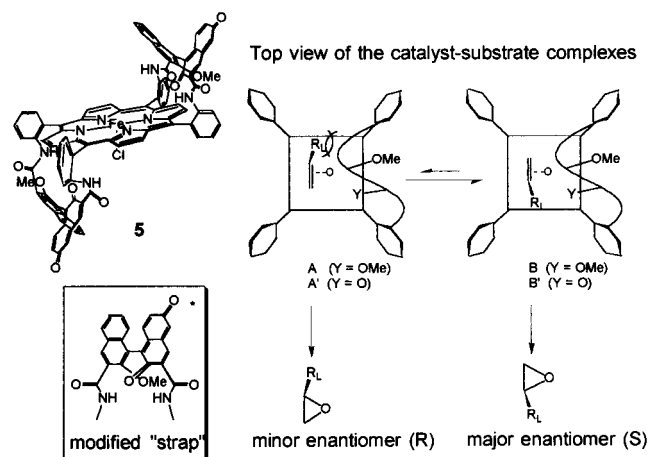
We believe that oxidative modification of the catalyst is responsible for these observations. Previous studies[10] and CPK models indicate a close contact between the methoxy group on one naphthyl lobe and the oxo−metal center in metalloporphyrins fitted with a binaphthyl strap. We propose that in the initial stage of the reaction, the catalyst is self-modified via oxidative demethylation and subsequent reaction to form **5**, which is a more selective catalyst (Scheme 2). The critical geometry that governs the enantiofacial selectivity is consistent with the observed direction of stereochemical induction and with our hypothesis that **5** should exhibit a better enantioselectivity.

As shown in Scheme 2, with the (*R*)-binaphthyl strapped porphyrin catalyst, complex A with the larger R_L group close to the inward leaning lobe of binaphthyl is less favored. In contrast, complex B, with R_L in the space next to the outward leaning lobe, is the favored low-energy path, which leads to the observed major enantiomer, (*S*)-epoxide. The increased enantioselectivity going from **1** to **5** can also be rationalized by the same scheme: decreasing the steric bulk of the inward pointing methoxy would make more room to accommodate R_L in complex B′, making it a more favored conformation, while not affecting the energy of

Scheme 2

* The modified binaphthyl may have 2,6- or 2,8-dione structure. Only 2,6-isomer is shown in the figure.

complex A′. The larger energy gap between the two diastereomeric complexes translates into increased selectivity for **5**.

This catalyst modification has been confirmed by comparing mass spectra of the recovered catalyst with that of the original complex. Because the mass of **5** coincides with its precursor, **1**, we failed in our first attempt to identify these structural changes. However, the CD_3O-analogue **1a** shows loss of 3 and 6 amu after one reaction run, corresponding to the transformation to a quinone-like structure on one or both sides, respectively. An epoxidation study with **1a** reveals a more subtle piece of information (Figure 1): the ee−turnover plot of catalyst **1a** also shows an initial rise, but a slower one, before it reaches the 82−83% ee plateau. This means the rate of the modification process is slower for the deuterated complex; a similar isotope effect is observed in our recent studies of iron porphyrin catalyzed oxidations of C_6H_5-CH_3 and $C_6D_5CD_3$.[11] We believe this, combined with the mass spectroscopic studies, is strong evidence that **5** is the actual catalyst giving high enantioselectivities.[12]

We have also studied the ligand effect on the stereoselectivity in epoxidation of styrene, and found that using DMSO as a ligand raises the ee to 88%, the highest reported for any catalytic system to date.[13]

In conclusion, we have shown that the C_2 symmetric iron porphyrin, **1**, is an efficient catalyst for asymmetric epoxidation of terminal olefins. The high ee values and turnover numbers obtained with some simple terminal olefins are exceptional compared to previously reported catalytic systems, while the ready availability of **1** makes it a potential catalyst for practical applications.

Supporting Information Available: Experimental procedures and characterizations of new compounds along with the GC and NMR data for the determination of the enantiomeric excesses of the formed epoxides (PDF). See any current masthead page for Web access instructions.

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(9) A comparison has been made between **1** and a closely related Fe porphyrin complex, amide-linked "twin-coronet" porphyrin derived from tetrakis(2,6-diamino-4-*tert*-butylphenyl)porphyrin. **1** gives both a higher % ee and a greater reaction rate. See also: Naruta, Y.; Tani, F.; Maruyama, K. *Tetrahedron Lett*. **1992**, *33*, 6323.

(10) Naruta, Y.; Maruyama, K. *Tetrahedron Lett*. **1987**, *28*, 4553.

(11) Collman, J. P.; Chien, A.; Eberspacher, T. Unpublished results.

(12) Epoxidation of styrene with a recovered catalyst or a catalyst premodified by stirring with cyclopentene and PhIO does give higher ee (83%) even at low turnover numbers.

(13) A slightly higher ee % value was obtained in the initial stages of epoxidation of styrene catalyzed by a chiral Fe porphyrin. Groves, J. T.; Crowley, S. J.; Shalyaev, K. V. *Chirality* **1998**, *10*, 106.