Enantioselective Epoxidation of Unfunctionalized Olefins Catalyzed by Threitol-Strapped Manganese Porphyrins

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Catalytic asymmetric epoxidation has received considerable attention over the past 15 years. Some catalysts routinely give greater than 90% enantiomeric excess (ee) in the asymmetric epoxidation of functionalized olefins.[2] Stereoselective epoxidation of unfunctionalized olefins, however, is a more challenging problem because these systems rely solely on nonbonding interactions to achieve asymmetric induction. A large number of chiral salen catalysts have been prepared[3] that give up to 92% ee in the epoxidation of unfunctionalized, cis-disubstituted olefins.[3f] Chiral metalloporphyrins also catalyze the asymmetric epoxidation of unfunctionalized olefins,[4] although they generally give lower ees than the best salen systems. Since chiral porphyrin catalyst structures are not easily varied, optimization of these catalysts has not yet been possible. Herein we report the preparation of the first members of a family of easily modified chiral porphyrins. The manganese derivative of one of these systems (**3b**) is the most effective asymmetric catalyst in the epoxidation of simple, monosubstituted olefins and gives optical yields up to 88% ee in the epoxidation of cis-disubstituted olefins when iodosylbenzene is the oxidant. The crystal structure of the chiral porphyrin **1** is also presented.

The chiral frameworks of these porphyrins are constructed from acetal derivatives of (*S,S*)-1,4-ditosylthreitol (**4**). When **4** is condensed with 1,2-bis(2-formylphenoxy)ethane (**5**), a diacetal (**6**) is obtained. Condensation of **6** with tetrakis(2-hydroxyphenyl)porphine[5] (**7**) gives three isomers (Scheme I): **1** (In/In), **2** (In/Out), and **3a** (Out/Out) that differ by the stereochemistry at the acetal carbon atom. Isomers **1** and **3a** have C_2 symmetry and are distinguishable from **2** (which has C_1 symmetry) by ^{1}H NMR spectroscopy. The assignment of the C_2 isomers is based upon an X-ray crystal structure of **1**·2CD_2Cl_2 (Figure 1).[6,7] From these crystallographic data and van der Waals radii, the cavity above this porphyrin is estimated to be ca. 7.5 Å wide. Since the manganese derivative of **1** is not an effective asymmetric epoxidation catalyst, this cavity is probably too large to interact effectively with substrates. The manganese derivative of the out/out isomer (**3b**) is a better catalyst, presumably because the bridge pulls the chiral threitol units closer to the center of the macrocycle where oxygen transfer occurs.

A key feature of **3b** is that only one face of the porphyrin is chiral. Thus, for optimum asymmetric induction, the open face

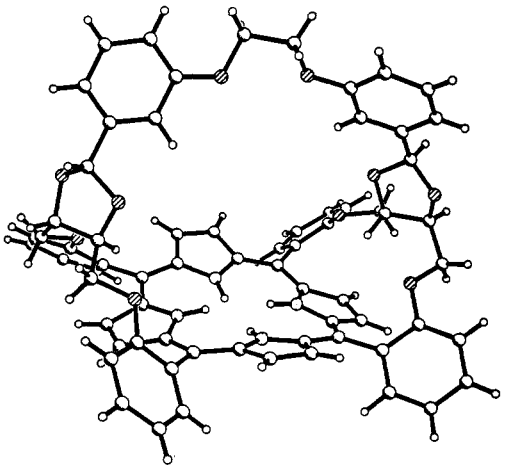
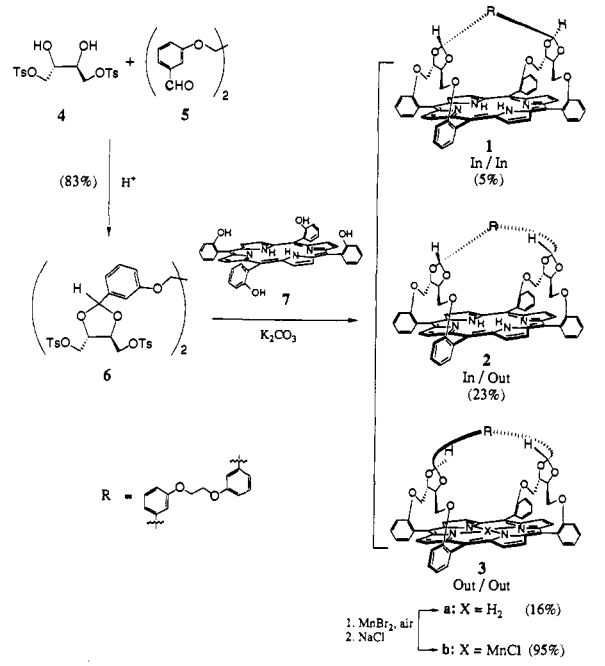


Figure 1. Drawing of the structure of **1**. Oxygen atoms are cross-hatched. The 50% thermal ellipsoids are shown, except for hydrogen atoms, which are drawn artificially small. The half hydrogen atoms in the center of the porphyrin are also shown. The molecule has a crystallographically imposed C_2 axis. Distances and angles are normal. Note the severe ruffling of the porphyrin core.

Scheme I. Synthesis of the Threitol-Strapped Porphyrins **1–3**



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(6) Analytical data for the porphyrins and their precursors as well as experimental data for the epoxidation reactions are given in the supplementary material.

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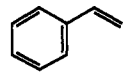
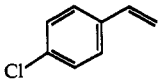
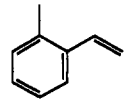
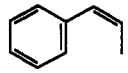
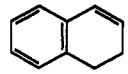
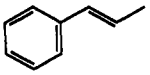
Table I. Asymmetric Epoxidation of Aromatic Olefins with **3b**[a]

substrate	reaction T, °C	yield, %[b]	ee, %[c]	configuration[d]	best reported ee, %[e]
	25	86	69	*R*(+)	57[f]
	25	82	70	*R*(+)	51[g]
	25	65[h]	79	(−)[i]	16[g]
	25	89	77	1*R*,2*S*(−)	92[j]
	0	76	80	1*R*,2*S*(−)	
	25	85	84	1*R*,2*S*(+)	
	0	67	87	1*R*,2*S*(+)	83[k]
	−10	26	88	1*R*,2*S*(+)	
	25	81	21	1*S*,2*S*(−)	56[k]

[a] Reactions were generally run for 1 h with 1.0 μmol of **3b**, 100 μmol of iodosylbenzene, 250 μmol of 1,5-dicyclohexylimidazole, 20 μL of nonane or dodecane, and 1.00 mmol of olefin in 2 mL of CH_2Cl_2. [b] Yields are based upon iodosylbenzene and were determined by GC analysis. [c] Determined by Cyclodex-B chiral capillary column or by ^1H NMR spectroscopy in the presence of Eu(hfc)$_3$. [d] Assigned by comparison of polarimetry measurements with literature. [e] These values correspond to the highest ee's previously reported for nonenzymatic catalysts. Metalloporphyrin catalysts are used for *p*-chlorostyrene and 2-methylstyrene with oxidant as the limiting reagent. Metallosalen catalysts are used for the remaining olefins with the olefin as the limiting reagent. [f] From ref 3a. [g] From ref 4a. [h] A 30% yield of aldehyde was also detected. [i] The absolute configuration was not determined. [j] From ref 3f. [k] From ref 3c.

of the porphyrin must be inactivated. This is accomplished by adding 1,5-dicyclohexylimidazole to the epoxidation reactions. This bulky ligand presumably binds to the unhindered face of the manganese porphyrin,[10] and the large size of this imidazole disfavors its binding within the chiral cavity. Similar approaches have been used successfully for enantioselective[4h] and shape-selective[11] porphyrin epoxidation catalysts.

Preliminary results for the epoxidation of various mono- and disubstituted aromatic olefins with **3b** are presented in Table I. Reactions with **3b** give optical yields up to 88% ee and give greater than 80% conversion to oxidized products.[12] These are the highest ees reported in the epoxidation of these olefins with chiral metalloporphyrin catalysts and are the highest obtained with any catalyst for styrene, *p*-chlorostyrene, 2-methylstyrene, and 1,2-dihydronaphthalene. While mono- and cis-disubstituted olefins are epoxidized with a high degree of stereoselectivity, trans-disubstituted olefins are poor substrates. In all cases, lower ee's are obtained in reactions run without 1,5-dicyclohexylimidazole. The enantiomer of **3b** based upon (*R*,*R*)-1,4-ditosylthreitol was also prepared and gives results similar to those presented in Table I, affording epoxides with the opposite stereochemistry.

A limitation of **3b** and most other asymmetric epoxidation catalysts derived from porphyrins or salens is their propensity toward oxidative degradation. This instability appears to be inherent in metallosalen catalysts, likely deriving from the oxidizibility of the salen ligand, and results in low catalyst turnovers. While meso-substituted porphyrin macrocycles are more oxidatively stable, the high reactivity of metalloporphyrin-based oxidants can lead to the alteration or destruction of the asymmetric environment by intra- or intermolecular oxidation of the chiral units. Thus, while high numbers of turnovers are achievable with metalloporphyrins, asymmetric derivatives often become less selective. This problem can be minimized with asymmetric porphyrin catalysts by employing an excess of olefin in the epoxidation reaction (e.g., Table I). However, enantioselectivities can be sensitive to the ratios of olefin to oxidant used.[13]

These threitol-strapped porphyrins are readily varied by employing other aldehydes or ketones in place of **5**. We can thus prepare a family of acetal- and ketal-containing systems that have different steric environments. This approach is not limited to mono-faced porphyrins; the corresponding bis-faced porphyrin catalysts have been prepared from tetrakis(2,6-dihydroxyphenyl)-porphine and will be the subject of subsequent papers. We believe a systematic study of these systems could lead to a better understanding of the mechanism of oxo-transfer from metalloporphyrins to olefins and to even more effective asymmetric catalysts for olefin epoxidation.

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Supplementary Material Available: Synthetic details for the preparation of **1–3**; final values of positional and thermal parameters from the X-ray structure of **1** (7 pages). Ordering information is given on any current masthead page.

(7) **1** crystallizes as **1**·2CD_2Cl_2 with four formula units in space group C_4^6–$I4_1$ of the tetragonal system in a cell of dimensions a = 18.925(5) and c = 16.974(10) Å (T = 115 K). Diffraction data were collected at 115 K on a CAD4 diffractometer out to θ = 33.5° (Mo Kα radiation). A total of 7181 reflections were measured, of which 6855 are unique. The fortuitous presence of CD_2Cl_2 molecules of crystallization permitted determination of the chirality of the porphyrin and established it as **1** rather than **3a**. The program SHELXL92[8] was used to refine the Flack x parameter[9]. A value of x = 0.14(10) was obtained; expected values are 0 for the correct and +1 for the inverted absolute structure. The final refinement on F_o of 393 variables converged to values of $R(F)$ = 0.061 and R_w = 0.061 for the 4341 reflections having $F_o^2 \geq 3\sigma(F_o^2)$. **1** has a crystallographically imposed C_2 axis, as expected. There are two solvent molecules, each lying on a twofold axis. One is well ordered, while the other has its C atom disordered about the twofold axis. The disorder in this solvent molecule has not been modeled completely satisfactorily, as judged by residual electron density in the area. Final values of positional and thermal parameters are given in the supplementary material.

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(12) With 2-methylstyrene, 30% of (2-methylphenyl)acetaldehyde is produced as a byproduct.

(13) When the olefin-to-oxidant ratio is changed from 10:1 to 1:1, the respective change in selectivity is 70% to 66% ee for p-chlorostyrene and 84% to 48% ee for 1,2-dihydronaphthalene.