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Enantioselective Manganese-Porphyrin-Catalyzed Epoxidation and C−H Hydroxylation with Hydrogen Peroxide in Water/Methanol Solutions

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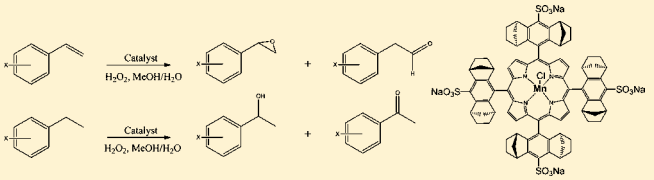
ABSTRACT: The asymmetric epoxidation of alkene and hydroxylation of arylalkane derivatives by H_2O_2 to give optically active epoxides (enantiomeric excess (ee) up to 68%) and alcohols (ee up to 57%), respectively, were carried out in water/methanol solutions using chiral water-soluble manganese porphyrins as catalysts.



INTRODUCTION

The use of water instead of organic solvents in transition-metal homogeneous catalysis has received remarkable attention,[1−3] because water is inexpensive, nontoxic, nonflammable, and environmentally sustainable and, sometimes it allows simple separation and reuse of the catalyst. Moreover, catalysis often permits the use of less-toxic reagents, as in the case of oxidation by hydrogen peroxide. Hydrogen peroxide (H_2O_2) is widely accepted as a green oxidant, because it is relatively nontoxic and breaks down in the environment into benign byproducts.[4,5] Over the last three decades, there have been large advances in the development of catalytic methodology for epoxidation reactions.[6] However, asymmetric epoxidations in aqueous solution with H_2O_2 are still rare,[7] although a nice possibility has been recently reported using iron and a chiral nonporphyrin ligand.[8] The main obstacle when using H_2O_2 is the high activity of transition-metal complexes in the catalase reaction and the homolytic cleavage of the peroxidic O−O bond with the formation of the hydroxyl radical.[9]

A few examples of the use of H_2O_2 can be found in the literature with manganese porphyrins as catalysts, giving low enantiomeric excess (ee) for epoxidation reaction in organic solvents or in a biphasic medium.[10−12] However, to our knowledge, there are no examples of asymmetric hydroxylation by H_2O_2 in water catalyzed by Mn porphyrins. Our group[11] reported the asymmetric oxidation of sulfides into sulfoxides using macroporous resins containing chiral metalloporphyrins, and, more recently, catalytic sulfoxidation reactions with H_2O_2 in water using a chiral iron porphyrin as a catalyst.[12] We now want to describe here chiral epoxidation of alkenes in water/methanol solutions using H_2O_2 as an oxidant catalyzed by new optically active water-soluble manganese porphyrins (Figure 1). Because high-valency manganese(IV or V)-oxo porphyrins are capable of activating C−H bonds of alkanes,[13,14] we also have considered the possibility of catalytic asymmetric hydroxylation with chiral water-soluble manganese porphyrins, using H_2O_2 as an oxidant.

RESULTS

Preparation of Water-Soluble Chiral Manganese Porphyrins. The starting point of the work described here was the introduction of four sulfonate groups into an optically active porphyrin with the objective of preparing chiral water-soluble porphyrins. We choose a C_2-symmetric group that contains two norbornane groups fused to the central benzene ring, which was previously reported by Halterman and Jan.[15] Initially, we planned to introduce first the sulfonic acid in the porphyrin ring and then manganese insertion. The sulfonation of the Halterman porphyrin was performed as we previously reported.[16] A 10-fold excess of $MnBr_2{\cdot}4H_2O$ was necessary to get the expected metalloporphyrin (Figure 1) in a reasonable yield (80%). The expected compound was characterized by UV−visible spectrum, and mass spectrum (see the Experimental Section). It is easily soluble in methanol and water.

Catalytic Asymmetric Epoxidation. Because of the high solubility of the catalyst in methanol, the epoxidation of styrene was first examined in this solvent at room temperature and with imidazole as a co-catalyst. The rate of the epoxidation reaction was very low to give 6% conversion after 1 h and 31% conversion after 4 h (Table 1, entry 1). However, in the presence of 25% phosphate buffer (pH 7), we noticed a large acceleration, since the conversion increases to 68% after 1 h and a quasi-completion after 4 h (93%) (Table 1, entry 2). In a typical oxidation, 1 equiv of the Mn porphyrin catalyst **1**, 24 equiv of imidazole, 120 equiv of H_2O_2, and 40 equiv of substrate were used under anaerobic conditions. The reaction is quasi-complete after 4 h at room temperature and the corresponding epoxide was obtained with good yield (93%) and 47% ee (Table 1, entry 2). This situation was amplified with a 50/50 ratio of methanol/water, giving 100% conversion after 1 h but with a small decrease of the ee (from 47% to 41%). Surprisingly, completion of the reaction in pure water (without methanol) requires 4 h under similar conditions (Table 1, entry 4). Probably, the weak solubility of styrene in water may explain this result. It should be noted that an increase of the epoxidation reaction was reported recently,[17] because of the presence of water in saturated CH_2Cl_2 solution for similar

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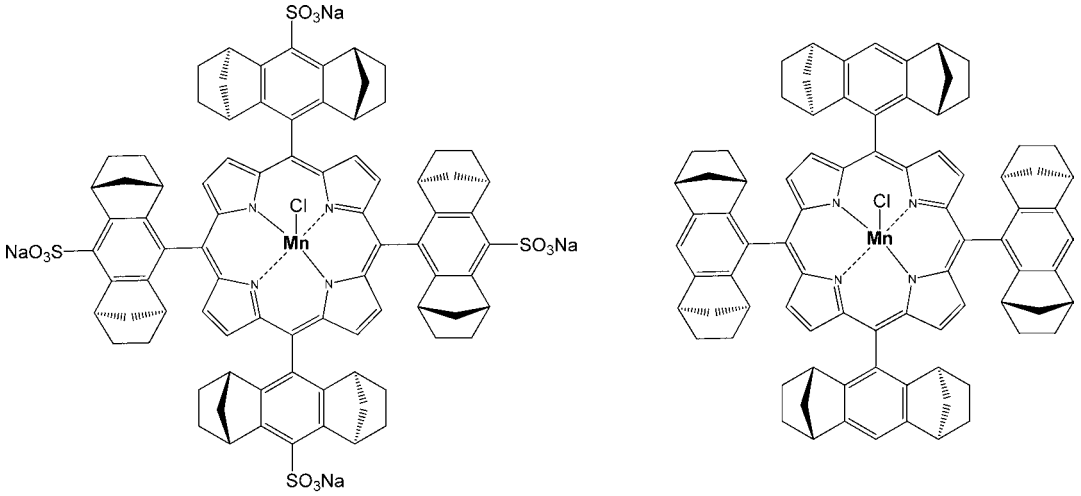

Figure 1. Structures of catalyst **1** and **2**.

Table 1. Effects of the Amount of H_2O, Relative to MeOH on Mn HaltS−H_2O_2−Imidazole System[a]

entry	MeOH/H_2O	conversion (%)	enantiomeric excess, ee (%)	time (h)
1	1/0	6	47	1
		31	47	4
2	3/1	68	47	1
		93	47	4
3	1/1	100	41	1
4[b]	0/1	7	37	1
		100	35	4
5[b,c]	0/1	46	36	1
		100	36	4

[a]The reaction was conducted with syringe-pump addition of 3 equiv (relative to alkene) of H_2O_2 (30% in H_2O, diluted 5 times in MeOH) and imidazole (20 equiv relative to Mn) at 25 °C to a solution of styrene/imidazole/Mn HaltS mixture (40:4:1) in 0.4 mL of MeOH/buffer solution (pH 7). [b]The reaction was conducted with syringe-pump addition of 3 equiv (relative to alkene) of H_2O_2 (30% in H_2O, diluted 5 times in H_2O and imidazole (20 equiv, relative to Mn) at 25 °C to a solution of styrene/imidazole/Mn HaltS mixture (40:4:1) in 0.4 mL of MeOH/buffer solution (pH 7). [c]The reaction was conducted in buffer solution (pH 10.5).

systems with achiral metalloporphyrins. The key role of imidazole in metalloporphyrin-catalyzed oxygenations with H_2O_2, evidenced by Mansuy et al.[18] in olefin epoxidation with iodosyl benzene, is confirmed herein, since only a weak conversion (4%) was detected in the absence of this ligand (see Table 2, entry 3).

We also investigated the epoxidation of various substituted styrenes with the same catalyst (**1**). Results for the catalytic epoxidation of several alkenes are summarized in Table 2. As shown in Table 2, epoxide yields in the range of 45%−100% were obtained with enantiomeric excess (ee) as high as 68% for 1,2-dihydronaphthalene. Small amounts of aldehydes (<3%) were also detected as byproduct, excepted for the reaction with 4-methylstyrene. As expected from the reactivity of electrophilic oxo-manganese porphyrins, the best yields were obtained with styrenes bearing electron-releasing substituents whereas no clear trend was evident for optical yields upon changing the substituent. Using the hydrophobic catalyst (**2**), without any sulfonate groups (Figure 1), instead of **1** in dichloromethane/methanol solvent gave a low conversion (38%) with 43% ee. A similar value (52%) was reported by Halterman and co-workers[19] in organic solvent (CH_2Cl_2) using NaOCl as an oxidant.

pH-Dependent H_2O_2 Oxidation. To explore whether the pH affects the yield and the ee at different pH values, we chose styrene as a substrate because it is commonly applied for the catalytic activity of manganese porphyrins. The experiments for pH-dependent styrene oxidation were carried out in the presence of H_2O_2 at 25 °C with the ratio H_2O_2/styrene being 3 and the yields and ee values were observed after 4 h. The results are summarized in Table 3. We found that the reaction rate increases with increasing pH showing 100% conversion at pH 10.5 after 1 h (Table 3, entry 4). In contrast, at acidic pH (pH 4), we observed only 12% conversion after 1 h. It is worth noting that the substitution of imidazole by N-methyl imidazole as Mn ligand has a large negative effect, since only 5% conversion is observed after 1 h (Table 3, entry 5).

Influence of an Excess of Oxidant. Since the oxide yields in the oxidation were high (95% after 4 h) with 5 equiv of H_2O_2, we have examined the effect of decreasing the ratio H_2O_2/styrene on chemical yield. As expected, Table 4 shows that a decrease of the oxidant/styrene ratio from 5 to 1.2 provides a decrease of the epoxidation yield, varying from 83% to 50% after 1 h. However, the yield (64%) is still acceptable after 4 h, according to the high reactivity of the system, in the presence of water.

Influence of the Nature of Oxidant. The nature of the active oxygen complex, which is able to transfer its O atom to alkenes and hydrocarbons, although not completely established, is generally considered to be a high-valency Mn-oxo complex, at least formally, a Mn^{V}=O species, although a Mn^{III}−OOH could be invoked.[20] In order to characterize the oxidizing species, in the chiral Mn system, we have compared the yield and enantiomeric excess using different oxidants (see Table 5). Using an identical concentration of oxidant and styrene (Mn/imidazole/oxidant/styrene =1/24/40/40), Table 5 shows that there is an increase of the yield when the oxidant is iodobenzene diacetate (from 49% to 75%). However, it is remarkable that, with three different oxidants—*meta*-chloroperoxybenzoic acid, H_2O_2, and $PhI(OAc)_2$—the ee values are similar, according to a probable common optically active intermediate. With *t*-buOOH, only traces of styrene epoxide are observed, as previously reported with oxidation of styrene catalyzed by Mn porphyrins.[21]

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Table 2. Asymmetric Oxidation of Alkenes Catalyzed by Mn HaltS−H_2O_2−Imidazole System[a]

entry	substrate	conversion (%)[b]	epoxide/aldehyde ratio (%)[b]	enantiomeric excess, ee (%)[c]	config[d]	time (h)
1	styrene	88	99/1	47	R	4
2	styrene[e]	2				4
3	styrene[f]	4		51	R	4
4	styrene[g]	76	98/2	46	R	1
4	4-methylstyrene	96	76/24	20[h]	R	1
5	4-(trifluoromethyl)styrene	62	100/0	38	R	5
6	4-chlorostyrene	90	99/1	48	R	5
7	3- methylstyrene	98	99/1	46	R	4
8	2- methylstyrene	93	99/1	46	R	4
9	3- (trifluoromethyl)styrene	70	100/0	52	R	4
10	2- (trifluoromethyl)styrene	56	100/0	46	R	1.5
11	1,2-dihydronaphthalene[g]	52	100/0	68	1R, 2S	2
12	1,2-dihydronaphthalene	27	100/0	65	1R, 2S	2
13	indene	100	100/0	40[h]	1R, 2S	0.5
14	2,2-dimethyl-2H-1-benzopyran-6-carbonitrile	45	100/0	57	+	4

[a]The reaction was conducted with syringe-pump addition of 3 equiv (relative to alkene) of H_2O_2 (30% in H_2O, diluted 5 times in MeOH) and imidazole (20 equiv relative to Mn) over 1 h at 25 °C to a solution of alkene/imidazole/Mn HaltS mixture (40:4:1) in MeOH/PBS (pH 7) (3/1). [b]Determined by gas chromatography (GC) on the crude reaction mixture. [c]Determined by GC on a chiral CP-Chirasil-Dex column. [d]Absolute configuration of the epoxide of styrene was determined by comparison with the authentic optically pure (R) (+) styrene oxide. Others were deduced from analogy of the GC behavior and of the optical rotatory of (R) (+) styrene oxide. [e]Without catalyst. [f]Without imidazole. [g]One equivalent (1 equiv) of $PhI(OAc)_2$ was used. [h]Determined by chiral high-performance liquid chromatography (HPLC) on a chiral OB-H column.

Table 3. Asymmetric Oxidation of Styrene Catalyzed by Mn HaltS−H_2O_2−Imidazole System at Different pH Values[a]

entry	pH	conversion (%)	enantiomeric excess, ee (%)	time (h)
1	4	12	43	1
		81	41	4
2	7	68	48	1
		93	47	4
3	9	79	44	1
		94	44	4
4	10.5	100	40	1
5[b]	10.5	5	49	1
		32	49	4

[a]The reaction was conducted with syringe-pump addition of 3 equiv (relative to alkene) of H_2O_2 (30% in H_2O, diluted 5 times in MeOH) and imidazole (20 equiv relative to Mn) at 25 °C, to a solution of an alkene/imidazole/Mn HaltS mixture (40:4:1) in 0.4 mL of MeOH/buffer solution (3/1). [b]*N*-methylimidazole was used as an axial ligand.

Table 4. Effects of the Amount of H_2O_2 (x), Relative to Styrene with the Mn HaltS−H_2O_2−Imidazole System[a]

entry	amount of H_2O_2, x (equiv)	conversion (%)	ee (%)	time (h)
1	5	83	46	1
		95	45	4
2	3	75	48	1
		93	47	4
3	2	68	44	1
		90	44	4
4	1.2	50	43	1
		64	43	4
5[b]	1.2	12	37	1
		92	36	4
6[c]	1.2	52	42	1
		64	43	4

[a]The reaction was conducted with syringe-pump addition of x equiv (relative to alkene) of H_2O_2 (30% in H_2O, diluted 5 times in MeOH) and imidazole (20 equiv relative to Mn) at 25 °C to a solution of styrene/imidazole/Mn HaltS mixture (40:4:1) in 0.4 mL of MeOH/buffer solution pH 7 (3/1). [b]The reaction was conducted in buffer solution (pH 10.5) as solvent. [c]The reaction was conducted in a mixture of MeOH/buffer solution (pH 10.5) (3/1).

Table 5. Asymmetric Epoxidation of Styrene with the Mn HaltS−Imidazole System in the Presence of Different Oxidants[a]

entry	oxidant	conversion (%)	ee (%)
1	*m*-CPBA	47	46
2	H_2O_2	49	47
3	$PhI(OAc)_2$	75	46
4	*t*-BuOOH	traces	

[a]A solution of MnHaltS/imidazole/styrene/oxidant (1:24:40:40) in 0.4 mL of MeOH/buffer solution (pH 7) mixture was stirred for 1 h at 25 °C.

Catalytic Asymmetric Hydroxylation. Treatment of ethylbenzene (1 equiv) with hydrogen peroxide (5 equiv) and a catalytic quantity of complex **1** in H_2O/MeOH (1/1) at room temperature for 7 h afforded (88% conversion) a mixture of 1-phenyl ethanol (57%) acetophenone (43%). The enantiopurity of the phenyl ethanol was determined to be 38% by chiral capillary GC analysis.

As shown in Table 6, 2-, 3-, and 4-ethyltoluenes, as well as 1-bromo-4-ethylbenzene, are also effective substrates for the 1-catalyzed asymmetric hydroxylation and the corresponding 1-arylethanols were produced in comparable yields and ee values of 49%−57% (entries 4−7). Cyclic alkanes such as Indane and tetrahydronaphtalene are more reactive substrates since a high conversion was obtained after 1 h but enantioselectivities decreased to 32% and 43%, respectively.

DISCUSSION

Epoxidation. Catalytic asymmetric epoxidation (Figure 2) in a safe and benign water solvent is still a challenge for chemists.[22] Since the asymmetric epoxidation with an iron-porphyrin complex bearing chiral groups at *meso*-carbon atoms was reported in 1983,[23] a wide variety of chiral metalloporphyrins with iron,

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Table 6. Asymmetric Hydroxylation Catalyzed by the Mn HaltS–H_2O_2–Imidazole System[a]

entry	substrate	conversion	alcohol/ketone ratio (%)	ee (%)	config[b]	time (h)
1[d]	ethyl benzene	88	57/43	38	S	7
2[c]	indane	88	77/23	32	S	1
3[c]	tetralin	90	62/38	43	S	1
4[c]	4-ethyltoluene	97	93/7	57	S	7
5[c]	3-ethyltoluene	98	84/16	50	S	7
6[c]	2-ethyltoluene	88	87/13	52	S	7
7[d]	1-bromo-4-ethylbenzene	100	80/20	49	S	7

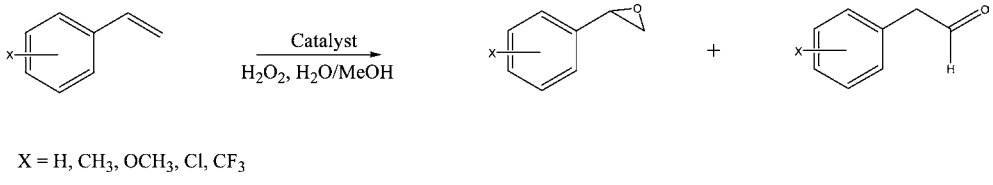
[a]The reaction was conducted with syringe-pump addition of 5 equiv (relative to arylalkane) of H_2O_2 (30% in H_2O, diluted 5 times in MeOH) and imidazole (20 equiv relative to Mn) over 1 h at 25 °C to a solution of arylalkane/imidazole/Mn HaltS mixture (40:4:1) in 0.4 mL of MeOH/PBS (pH 7) (1/1). [b]Absolute configuration of the alcohol of ethylbenzene was determined by comparison with the authentic optically pure (S)-(−)-1-phenylethanol. Others were deduced from analogy behavior and the sign of optical rotation. [c]Yield, ee, and alcohol/ketone ratio were determined by chiral HPLC. [d]Yield, ee, and alcohol/ketone ratio were determined by GC on a chiral CP-Chirasil-Dex column.

manganese, and ruthenium at the central metal have been introduced as epoxidation catalysts.[24] Iodosylbenzene is generally used as the stoichiometric oxidant for these enantioselective reactions. Prior to this work, aqueous hydrogen peroxide has been used once as the oxidant for enantioselective epoxidation using a manganese-glycoconjugated porphyrin as the catalyst in a biphasic medium, but the enantioselectivity was modest.[25] Herein, we will first focus on our catalytic results obtained with water-soluble manganese porphyrins for epoxidation reaction. Thus, factors affecting the catalytic epoxidation of olefins by chiral manganese porphyrins and hydrogen peroxide have been extensively investigated. First, it was recognized that the presence of water in methanol can be quite successful and that working in basic buffered solutions deeply increases the efficiency of the system. A deprotonation of imidazole may play a significant role in the presence of water, in particular at pH 10.5. The imidazolate form of the co-catalyst is a much stronger donor than the imidazole itself, providing electron density to Mn(III) and thus promoting oxygen transfer. This explanation was recently suggested by Mohajer, Kopenol, and co-workers.[17] The failure of *N*-methylimidazole to increase the reaction rate supports this hypothesis. To the best of our knowledge, efficient asymmetric oxidation of alkenes with an equimolar amount of H_2O_2, with respect of the substrate catalyzed by metalloporphyrins, has never been achieved.

Hydroxylation. Metalloporphyrin catalysts for selective C–H bond hydroxylation have attracted considerable attention since the discovery of the first examples reported by Groves et al. in 1979.[26] Most of the reactions have been realized in organic solvents. (See Figure 3.) In some cases, water was also used as a solvent in the metalloporphyrin-catalyzed hydroxylation of various substrates.[27,28] There are three important reviews dealing with these reactions.[29−31] However, to our knowledge, there is no asymmetric hydroxylation catalyzed by chiral manganese porphyrins in water using hydrogen peroxide as an oxidant. This is mainly due to three difficulties: (i) the preparation of optically active water-soluble chiral metalloporphyrins showing catalytic activity; (ii) the high activity of transition-metal complexes in the catalase reaction and the homolytic cleavage of the peroxidic O–O bond with formation of hydroxyl radical; and (iii) the functionalization of C–H bonds, which is one of the most difficult transformations, because of high thermal stability. To our benefit, we were able to achieve asymmetric hydroxylation of benzylic C–H bonds in aromatic hydrocarbons with our system. Although the enantiomeric excess of the products was moderate, the Mn-based hydroxylation gave good yields of the corresponding secondary alcohols, thanks to the manganese porphyrin catalytic efficiency.

Mechanism. Synthetic manganese(III) porphyrins have been extensively studied as CYP450 models in oxygen-atom-transfer reactions,[20,32] and high-valency manganese-oxo porphyrins have been frequently proposed as reactive intermediates in the oxidation reactions.[9,33,34] In particular, water-soluble cationic manganese porphyrins, such as Mn(V) N-substituted pyridylporphyrins, have been recognized for more than a decade as very efficient catalysts for O-atom transfer reactions in aqueous solution.[35,36] From the mechanistic viewpoint, the key oxomanganese(V) porphyrin intermediate has been isolated and characterized spectroscopically. In 1999, Jin and Groves[36] generated a Mn(V)O porphyrin complex in the reaction of Mn(III) tetrakis(*N*-methyl-2-pyridyl)porphyrin with oxidants such as *m*-chloroperoxybenzoic acid, HSO_5^- (oxone), and OCl^- in aqueous solution.[32] A possible conclusion from this work was that oxo-aqua- and oxo-hydroxo-manganese(V) are reactive oxidants while the stable species observed at high pH are trans-dioxo complexes. Definitive spectroscopic evidence for trans-dioxo-manganese porphyrins [O═Mn(V)═O] was reported by the same group.[37]

Using a tetrasulfonated porphyrin, it seems however that the Mn(V)oxo complex is not stable in basic solution. Thus, the water-soluble manganese(III) porphyrin complex **1** (λ = 470 nm, ε = 35.50 cm^{-1} mM^{-1}) after the addition of 2 equiv of H_2O_2 generates a new compound (λ = 425 nm, ε = 23.38 cm^{-1} mM^{-1}) in H_2O at pH 14 (20 °C) (see Figure 4). The absorption band corresponds to a Mn(IV) species. This compound reacts very slowly with a large excess of styrene after 4 h, giving back the starting compounds. The complex **2** in CH_3CN (λ = 480 nm, ε = 39.00 cm^{-1} mM^{-1}) was treated with tetramethylammonium hydroxide (TMAH) (λ = 444 nm, ε = 135.31 cm^{-1} mM^{-1}) and then with 2 equiv of H_2O_2 to generate a new compound (λ = 440 nm, ε = 140.50 cm^{-1} mM^{-1}) and showed a spectrum (Figure 5) that is very similar to the spectrum observed with the tetramesitylporphyrin Mn(V) complex, previously reported by



X = H, CH_3, OCH_3, Cl, CF_3

Figure 2. Asymmetric epoxidation of alkenes catalyzed by MnHaltS(Cl).

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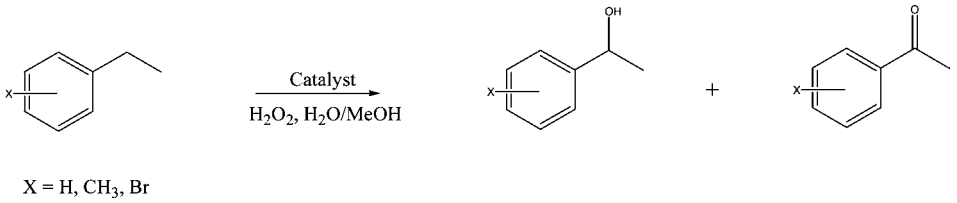

Figure 3. Asymmetric hydroxylation of arylalkanes catalyzed by MnHaltS(Cl).

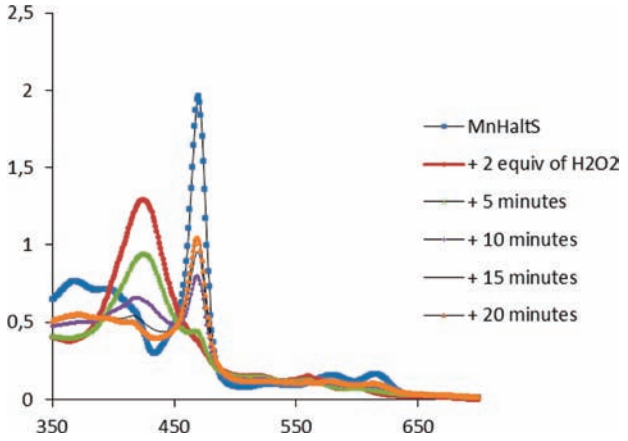

Figure 4. UV/vis of MnHaltS. Reaction conditions: 2 equiv of H_2O_2 was injected into a 1-cm UV cuvette containing a solution of MnHaltS (20 μM) in H_2O (pH 14) at room temperature.

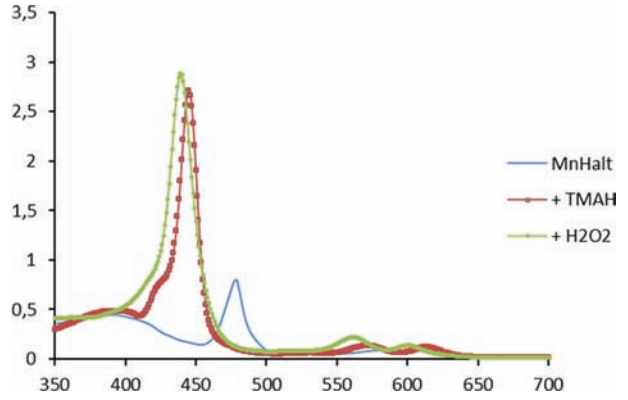

Figure 5. UV/vis of MnHalt. Reaction conditions: 2 equiv of H_2O_2 was injected into a 1-cm UV cuvette containing a solution of MnHalt (20 μM) in CH_3CN, in the presence of TMAH, at room temperature.

Nam and co-workers[38] and definitively characterized by Groves and co-workers as the dioxo complex O═Mn(V)═O.[37] It is worth noting that a Mn(V)dioxo complex bearing four negative charges from the sulfonate groups will present a supplemental negative charge, because of the Mn(V) oxidation state. This could be an explanation for the difficulty in detecting the Mn(V) dioxo band in water and also to explain the high reactivity of the system under basic conditions. A more-thorough investigation will be necessary to confirm this hypothesis.

Because the yield of epoxidation and hydroxylation depends on the efficiency of the oxygen atom transfer, and the degree of asymmetric induction depends on the chirality of the catalyst, we can infer the state of the catalyst from its catalytic activity under various conditions. The enantioselectivity of the reaction is induced by the chiral environment around the active site in the catalyst. If the contribution of H_2O_2 homolytic cleavage is important, the yield may be relatively high, but the enantioselectivity may be relatively low. Indeed, Tables 1 and 2 show that the yield of oxidation and the enantioselectivity in its formation are not necessarily correlated. Generally, the ee values vary over a small range (45%−65%), whereas the yield can increase to completion under the best conditions, as in high pH situations. Consequently, homolytic cleavage of H_2O_2, generating OH radicals, is not probable under our conditions.

■ CONCLUSION

In conclusion, we have developed an efficient and enantioselective epoxidation of terminal alkenes and hydroxylation of C−H bonds using a safe and easily accessible oxidant catalyzed by water-soluble chiral manganese porphyrins. Only a small excess of alkene versus oxidant was necessary. Ongoing work includes investigations of an extended range of substrates, particularly those of pharmaceutical importance, further optimization of the reaction medium, and more experiments to identify the precise role of chirality in the mechanism.

■ EXPERIMENTAL SECTION

General. All reactions were performed under argon. Solvents were distilled from an appropriate drying agent prior to use: CH_2Cl_2 from CaH_2, $CHCl_3$ from P_2O_5, and all other solvents were HPLC grade. Commercially available reagents were used without further purification unless otherwise stated. All reactions were monitored by TLC with Merck precoated aluminum foil sheets (Silica gel 60 with fluorescent indicator UV_{254}). Compounds were visualized with UV light at 254 nm. Column chromatographies were carried out using silica gel from Merck (0.063−0.200 mm). ^{1}H NMR and ^{13}C NMR in MeOD were recorded using Bruker (Advance 500dpx and 300dpx spectrometers) at 500 MHz (or 400 MHz) and 175 MHz, respectively. High-resolution mass spectra were recorded on a ZabSpec TOF Micromass spectrometer in ESI positif mode at the CRMPO. Liquid UV−visible spectra were recorded on a UVIKON XL from Biotech. Solid UV−visible spectra were recorded on a Cary 5000 NIR spectrophotometer. All catalytic reactions were controlled on a Varian CP-3380 GC system that was equipped with a CP-Chirasil-Dex Column. The enantiomeric excess of epoxides and alcohols were determined on a HPLC Varian Prostar 218 system equipped with Chiralcel OB-H, OD-H, and OJ-H columns. The absolute configuration of epoxides and alcohols was obtained from optical rotations.

Tetrasodium-5,10,15,20-tetrakis[(1S,4R,5R,8S)-10-sulfonato-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethano anthracene-9-yl]-porphyrin (H_2HaltSNa). Halterman porphyrin[15] (100 mg, 0.087 mmol) and sulfuric acid 95% (10 mL) were stirred for 4−5 h at room temperature. To the resulting solution was added slowly on ice to give a green mixture. After addition of the ice, some water (30 mL) was added and the pH was regulated at 7 by adding sodium carbonate. The solution was evaporated and the residue was treated by a mixture of acetone/methanol to precipitate the salt. The filtrate with Mn porphyrin was concentrated, solubilized in water, and purified by passage through a Sephadex column (G25). The solution was evaporated by vacuum evaporation. Yield = 82%.

^{1}H NMR (MeOD, 500 MHz): δ 8.78 (Br s, 8H, β pyrrole), 4.60 (s, 8H, CH), 2.72 (s, 8H, CH), 1.97 (m, 16H, CH_2), 1.58−0.90 (m, 32H, CH_2).

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^{13}C NMR (MeOD, 125 MHz): 170.42, 163.45−162.63 (br, weak signal), 150.25, 142.61, 133.31, 131.18, 129.02−128.25 (br, weak signal), 121.67, 119.30, 117.43, 117.01, 114.68, 45.02, 43.83, 27.65, 27.56. MALDI-TOF Linear: calcd m/z = 1483.849 $[M-3Na+2H]^-$ for $C_{84}H_{74}N_4NaO_{12}S_4$, found 1483.849 (425 ppm). UV−vis (MeOH) λ_{max} 416 nm (ε = 210 cm^{-1} mM^{-1}), 515 nm (ε = 6.56 cm^{-1} mM^{-1}), 551 nm (ε = 1.28 cm^{-1} mM^{-1}), 579 nm (ε = 1.48 cm^{-1} mM^{-1}), 631 nm (ε = 0.64 cm^{-1} mM^{-1}).

Chloro{tetrasodium-5,10,15,20-tetrakis[(1S,4R,5R,8S)-10-sulfonato-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethano anthracene-9-yl]-porphyrin} manganese(III). Under argon, the porphyrin (H_2)HaltSNa (120 mg, 0.077 mmol) and 2,6-lutidine (83 mg, 0.77 μmol) were dissolved in refluxing dimethylformamide (DMF) (25 mL). After waiting for several minutes to allow the porphyrin to dissolve, $MnBr_2{\cdot}4H_2O$ (222 mg, 0.77 mmol, 10 equiv) was added to the solution. The reaction was followed by UV−vis treatment. After refluxing for 1.5−2 h, the mixture was allowed to cool to room temperature and evaporated by vacuum evaporation. The crude product was dissolved in a mixture of hydrochloric acid (5%) and methanol (15 + 3 mL), and stirred for 20 min. The solvent was then evaporated and the product was treated with a cationic exchange resin (Dowex 50) to give a green solid: Yield = 80%. MALDI-TOF Linear: calcd m/z = 1514.364 $[M-4Na+3H]^-$ for $C_{84}H_{75}MnN_4O_{12}S_4$, found 1514.363. UV−vis (MeOH) λ_{max} 470 nm (ε = 35.50 cm^{-1} mM^{-1}), 567 nm (ε = 3.47 cm^{-1} mM^{-1}), 600 nm (ε = 2.43 cm^{-1} mM^{-1}).

Gas Chromatography Conditions for the Oxidation of Styrene Derivatives. CP-Chirasil-Dex column, temperature: 80 °C (hold 1 min) to 120 at 2.5 °C min^{-1} over 18 min and then to 180 at 2.5 °C min^{-1}, pressure = 15 psi, injector (pulsed split mode) at 200 °C, detector (FID) at 220 °C.

Typical Procedure for Asymmetric Oxidation of Alkenes with MnHaltS. *(+)-6-Cyano-3,4-epoxy-3,4-dihydro-2,2-dimethyl-2H-1-benzopyran.* Manganese porphyrin complex **1** (6.6 mg, 4 μmol) and imidazole (1 mg, 14.6 μmol) were placed in a Schlenk tube under argon. The solvent (3 mL MeOH + 1 mL PBS, pH 7) was then added via syringe, followed by the alkene 6-cyano-3,4-dihydro-2,2-dimethyl-2H-1-benzopyran (30 mg, 162 μmol). To this solution, a mixture of hydrogen peroxide (48.5 μL, 486 μmol) and imidazole (5.34 mg, 78.4 μmol) dissolved in 1 mL of methanol, were slowly added via a syringe pump over 4 h at 25 °C and the reaction mixture was stirred for 1 h. The reaction was quenched with $NaHCO_3$. The solution was extracted with dichloromethane (DCM) three times and then dried over $MgSO_4$. The product was purified with neutral silica gel (eluent: DCM) to give the corresponding epoxide (16 mg, 49% yield). ^{1}H NMR (MeOD, 400 MHz): δ 7.82 (d, 1H, J = 2 Hz), 7.6 (dd, 1H, J = 2 Hz), 6.88 (d, 1H, J = 8.5 Hz), 4.02 (d, 1H, J = 4.4 Hz), 3.66 (d, 1H, J = 4.4 Hz), 1.55 (s, 3H), 1.28 (s, 3H). HPLC (chiralcel OJ-H; flow rate = 0.5 mL min^{-1}; hexane/*i*-PrOH (70/30), 25 °C, detection at 220 nm): $t_R(+)$ = 24.7 min, $t_R(-)$ = 43 min. $[\alpha]^{22}$D + 62°, (MeOH).

(R)-(+)-Styrene Oxide. GC t_R(R) = 10.2 min, t_R(S) = 10.9 min.

(R)-(+)-4-Methylstyrene Epoxide. HPLC t_R(S) = 34.5 min, t_R(R) = 37.3 min (chiralcel OD-H; flow rate = 0.3 mL min^{-1}; hexane/*i*-PrOH (98/2), 25 °C, detection at 220 nm.

(R)-(+)-3-Methylstyrene Oxide. GC t_R(R) = 14.2 min, t_R(S) = 14.7 min.

(R)-(+)-2-Methylstyrene Oxide. GC t_R(R) = 14.3 min, t_R(S) = 14.9 min.

(R)-(+)-4-Trifluoromethylstyrene Oxide. GC t_R(R) = 11.9 min, t_R(S) = 12.8 min.

(R)-(+)-3-Trifluoromethylstyrene Oxide. GC t_R(S) = 10.9 min, t_R(S) = 11.1 min.

(R)-(+)-2-Trifluoromethylstyrene Oxide. GC t_R(R) = 13.4 min, t_R(S) = 13.9 min.

(R)-(+)-4-Chlorostyrene Oxide. GC t_R(R) = 8.1 min, t_R(S) = 8.4 min.

(1R, 2S)-(−)-Epoxyindane. HPLC t_R(1S,2R) = 30.1 min, t_R(1R,2S) = 43 min (chiralcel OB-H; flow rate = 0.5 mL min^{-1}; hexane/*i*-PrOH (95/5), 25 °C, detection at 220 nm).

(1R,2S)-(+)-1,2-Dihydronaphthalene Oxide. GC t_R(1S,2R) = 10.1 min, t_R(1R,2S) = 10.6 min.

Typical Procedure for Asymmetric Oxidation of Alkanes with MnHaltS (1). 1,2,3,4-tetrahydronaphtalen-1-ol: Manganese porphyrin complex **1** (9 mg, 5.4 μmol) and imidazole (1.5 mg, 22 μmol) were placed in a Schlenk tube under argon. The solvent (2 mL MeOH + 2 mL PBS, pH 7) was then added via syringe, followed by 1,2,3,4-tetrahydronaphtalene (29.19 mg, 220 μmol). To this solution, a mixture of hydrogen peroxide (110 μL, 1100 μmol) and imidazole (8 mg, 117.5 μmol) dissolved in 1 mL of methanol, were slowly added via a syringe pump over 1 h at 25 °C and the reaction mixture was stirred for 1 h. The reaction was quenched with $NaHCO_3$. The solution was extracted with DCM three times and dried over $MgSO_4$. The product was purified with neutral silica gel (eluent: DCM) to give 1,2,3,4-tetrahydronaphthalen-1-ol (15 mg, 45% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42−7.43 (m, 1H), 7.19−7.21 (m, 2H), 7.09−7.11 (m, 1H), 4.79 (t, 1H, J = 4.4 Hz), 2.69−2.87 (m, 2H), 1.88−2.02 (m, 3H), 1.74−1.84 (m, 1H), 1.69 (Br s, 1H). HPLC (chiralcel OB-H; flow rate: 0.5 mL min^{-1}; hexane/*i*-PrOH (95/5), 25 °C, detection at 220 nm): $t_R(+)$ = 16.4 min, $t_R(-)$ = 25 min, $[\alpha]^{22}_D$ + 11 ($CHCl_3$), and 1-tetralone (12.5 mg, 39% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.03 (dd, 1H, J = 0.8 Hz), 7.48 (m, 1H), 7.3 (t, 1H, J = 7.5 Hz), 7.25 (d, 1H, J = 7.5 Hz), 2.97 (t, 2H, J = 5.9 Hz), 2.66 (dt, 2H, J = 6.1 and 13.1 Hz) 1.74−1.84, 2.11−2.17 (m, 2H). HPLC: t_R = 25.9 min.

(S)-(−)-1-Phenylethanol. HPLC t_R(R) = 19.8 min, t_R(S) = 30.2 min (chiralcel OB-H; flow rate = 0.5 mL min^{-1}; hexane/*i*-PrOH (95/5), 25 °C, detection at 220 nm. GC t_R(R) = 17.1 min, t_R(S) = 17.9 min.

(S)-(+)-1-Indanol. HPLC $t_R(+)$ =14.5 min, $t_R(-)$ = 42.49 min (chiralcel OB-H; flow rate = 0.3 mL min^{-1}; hexane/*i*-PrOH (97/3), 25 °C, detection at 220 nm).

(S)-(−)-1-(4-Methylphenyl)ethanol. HPLC t_R(S) = 18.3 min, t_R(R) = 24.2 min (chiralcel OB-H; flow rate = 0.5 mL min^{-1}; hexane/*i*-PrOH (95/5), 25 °C, detection at 220 nm).

(S)-(−)-1-(3-Methylphenyl)ethanol. HPLC t_R(S) = 19.3 min, t_R(R) = 27.9 min (chiralcel OB-H; flow rate = 0.5 mL min^{-1}; hexane/*i*-PrOH (95/5), 25 °C, detection at 220 nm).

(S)-(−)-1-(2-Methylphenyl)ethanol. HPLC t_R(R) = 16.1 min, t_R(S) = 24.5 min (chiralcel OB-H; flow rate = 0.5 mL min^{-1}; hexane/*i*-PrOH (95/5), 25 °C, detection at 220 nm).

(S)-(−)-4-Bromo-α-methylbenzenemethanol. HPLC t_R(R) = 31.2 min, t_R(S) = 32 min (chiralcel OB-H; flow rate = 0.5 mL min^{-1}; hexane/*i*-PrOH (95/5), 25 °C, detection at 220 nm). GC: t_R(R) = 31.2 min, t_R(S) = 32 min.

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Notes

The authors declare no competing financial interest.

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