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Asymmetric Epoxidation of Olefins with Hydrogen Peroxide by an in Situ-Formed Manganese Complex

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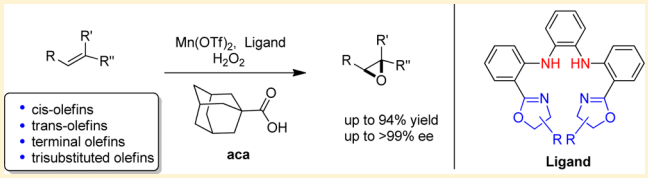
Supporting Information

ABSTRACT: Asymmetric epoxidation of a variety of cis, trans, terminal, and trisubstituted olefins in excellent yields (up to 94%) and enantioselectivities (>99% ee) by an in situ-formed manganese complex using H_2O_2 has been developed. A relationship between the hydrophobicity of the catalyst imposed by ligand and the catalytic activity has been observed. The influence of the amount and identity of the acid additive was examined, and improved enantioselectivities were achieved through the use of a catalytic amount of a carboxylic acid additive.

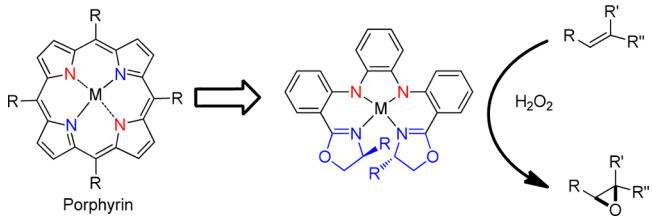


INTRODUCTION

Optically pure epoxides play a significant role in organic chemistry.[1] In addition, they have also been extensively applied in constituting pharmacophores in drug molecules, including several marketed pharmaceuticals such as L-carnitine, timolol, and propranolol.[2] Asymmetric epoxidation (AE) provides a powerful synthetic method toward optical pure epoxides.[3] In line with toughening environmental concerns, current challenges for AE lay in exploring more sustainable and efficient catalyst systems. To address these questions, extensive research has focused on the development of biomimetic methods by mimicking the reactivity of natural metalloenzymes, as metalloenzyme-catalyzed reactions often exhibit exquisite substrate specificity and operate under green processes.[4] Cytochromes P450 as a superfamily of heme enzymes can catalyze oxygenation reactions of a variety of substrates.[5] Inspired by the cytochrome P450 enzyme, substantial efforts have been focused on the development of biomimetic metalloporphyrin catalysts capable of catalyzing AE of olefins. Notably, as early as 1983, Groves and Meyers reported an iron porphyrin-catalyzed AE of styrenes.[6] Since then, Fe, Ru, and Mn complexes bearing chiral porphyrin ligands that can catalyze AE of olefins have been identified.[7] Despite these advances, however, metalloporphyrin-type catalysts for AE of olefins have not been sufficiently refined to find application in the preparation of natural products and pharmaceuticals. First, the synthesis of the chiral porphyrin ligands containing a variety of functional groups is a formidable challenge, rendering the optimization and screening of a desired catalyst notoriously difficult. In addition, the substrate scope is limited. Consequently, the development of catalytic systems with high conversion and selectivity that utilize readily available, cheap, and nontoxic catalysts and environmentally benign oxidants is strongly desired.

Inspired by the metalloporphyrins, we previously developed a new class of manganese complexes featuring chiral oxazoline moieties and proved that they were efficient catalysts for AE of olefins with H_2O_2 in the presence of acetic acid (Scheme 1).[4s] In

Scheme 1. Strategy for the Development of an Asymmetric Epoxidation Method



2012, Lyakin et al.[8] first disclosed that different carboxylic acid (CA) additives in organometallic catalysis had a significant influence on the enantioselectivity of AE of olefins. In this case, the best enantioselectivities (up to 93% ee) were obtained in the presence of 2-ethylhexanoic acid. Very recently, Costas and coworkers demonstrated that the ligand could synergistically cooperate with the CA in promoting efficient O−O cleavage in the epoxidation of olefins with hydrogen peroxide, and excellent yields and enantioselectivities were achieved for epoxidation of various olefins (up to 99% ee and 99% yield).[4i] With this background in mind, extensive ranges of ligands and CA additives were screened in attempt to further optimize our catalyst system. Herein we report a rapid, efficient, and highly enantioselective epoxidation method with H_2O_2 by an in situ-

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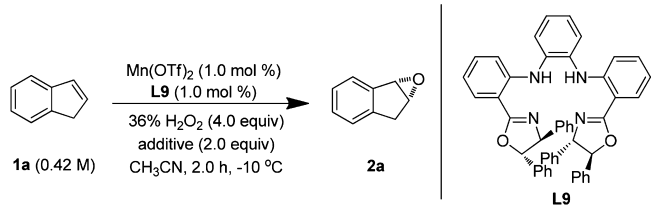
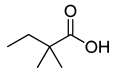
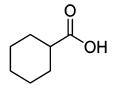
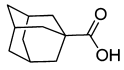
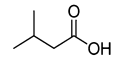
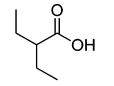
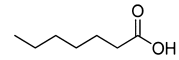
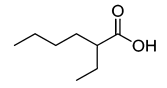
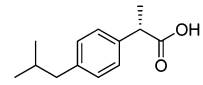
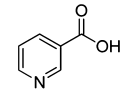
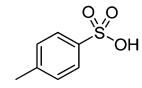
Table 1. Catalytic Activity with Regard to the Amount and Identity of the Additive



entry	additive	yield(%)	ee(%)[a]
1	HCO_2H	< 5	-
2	CH_3CO_2H	76	63
3	AcONa	< 5	-
4	CF_3CO_2H	< 5	-
5	H_3PO_4	<5	-
6		46	65
7		90	67
8		84	65
9		32	70
10		92	70
11		90	76
	aca		
12		72	70
13		92	64
14		88	61
15		79	70
16		10	73
17		93	46
18		< 5	-
19[b]	**aca**	89	72
20[c]	**aca**	92	75
21[d]	**aca**	86	76

[a]Determined by chiral HPLC analysis. [b]**aca** (1.0 equiv). [c]**aca** (0.5 equiv). [d]**aca** (0.3 equiv).

formed manganese complex that provides a broad range of epoxides in high yields. Improved enantioselectivities were attained through the use of a catalytic amount of a CA additive.

RESULTS AND DISCUSSION

First, the effect of the CA additive was investigated in an attempt to optimize the catalyst system and, in particular, to improve the epoxidation stereoselectivity. The epoxidation of indene (**1a**) was initially performed in acetonitrile at −10 °C with the manganese complex generated in situ from 1 mol % $Mn(OTf)_2$ and 1 mol % **L9** in the presence of H_2O_2/HCOOH. Only low conversion was observed (Table 1, entry 1). Then the reaction was carried out by replacing the HCOOH with acetic acid. The corresponding epoxide **2a** was obtained in 76% yield with 63% ee (entry 2). Poor activity was observed when the acetic acid was replaced by the strong acid CF_3SO_3H or *p*-toluenesulfonic acid, the inorganic acid H_3PO_4, or sodium acetate (entries 3−5 and 18). The results indicated that both the proton and the carboxylic group are needed to accelerate and favor the O−O cleavage in the epoxidation process. Replacing the acetic acid with a wide variety of aliphatic acids led to a notable improvement in terms of reactivity and enantioselectivity (entries 6−15). Among these aliphatic acids, adamantane carboxylic acid (**aca**) provided the best result (90% yield and 76% ee; entry 11). Perhaps the sterically hindered **aca**, which could impart a highly rigid environment around the metal center, resulted in significantly increased enantioselectivity. Interestingly, the heterocyclic aromatic carboxylic acid nicotinic acid was also compatible with our catalyst system, affording a high yield with modest enantioselectivity (entry 17). In addition to racemic CA additives, a chiral carboxylic acid was also tested. Unfortunately, only a low yield was obtained (entry 16). After the CA loading was tested, the amount of CA was successfully lowered to 50 mol % with no decrease in yield and enantioselectivity (entries 19 and 20). Further lowering the acid loading to 30 mol % showed a decrease in yield, albeit with an almost identical enantioselectivity (entry 21).

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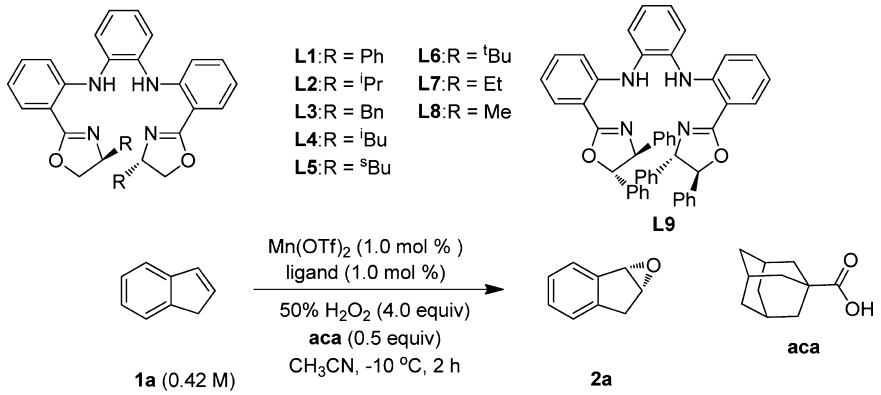
Table 2. Investigation of the Effect of Ligand Structure



entry	ligand	% yield	% ee[a]
1	**L1**	87	89
2	**L2**	94	92
3	**L3**	84	88
4	**L4**	42	84
5	**L5**	32	84
6	**L6**	86	88
7	**L7**	66	89
8	**L8**	<5	–
9[b]	**L2**	92	93
10[c]	**L2**	73	89
11[d]	**L2**	88	93
12[e]	**L2**	90	90
13[f]	**L2**	91	93

[a]Determined by chiral HPLC analysis. [b]$Mn(OTf)_2$ (0.5 mol %), **L2** (0.5 mol %). [c]$Mn(OTf)_2$ (0.25 mol %), **L2** (0.25 mol %). [d]$Mn(OTf)_2$ (0.5 mol %), **L2** (0.5 mol %), H_2O_2 (3.5 equiv). [e]$Mn(OTf)_2$ (0.5 mol %), **L2** (0.5 mol %), 0 °C. [f]$Mn(OTf)_2$ (0.5 mol %), **L2** (0.5 mol %), −30 °C.

An extensive ligand study was then performed to find the optimum ligand for our catalyst system. Replacing ligand **L9** containing bis-substituted oxazolines with ligands containing monosubstituted oxazolines resulted in a significant increase in enantioselectivity (Table 2, entries 1−7). However, ligand **L8** bearing methyl-substituted oxazolines performed poorly in terms of both yield and enantioselectivity (entry 8). The results implied that ligands with large hydrophobic groups have an obvious advantage over ligand **L8** with small hydrophobic groups. Presumably, this unfortunate situation arises largely because the hydrophobic structure of the ligand allows the substrate to approach the active center of the catalyst more easily. In addition, the decomposition of hydrogen peroxide could be greatly reduced. Following a broad screening of ligands, we identified **L2** as the ligand producing the best yield and enantioselectivity (entry 2). It is noteworthy that the catalyst loading was successfully lowered to 0.5 mol % with no decrease in yield and enantioselectivity (entry 9). Remarkably, further lowering the catalyst loading to 0.25 mol % showed a slight decrease in yield and enantioselectivity (entry 10). Then the loading of H_2O_2 was also investigated. We found that 4 equiv of H_2O_2 was necessary in order to obtain a good yield (entries 2 and 11). Finally, the influence of temperature was examined. The enantioselectivity had a slight decrease when the temperature was increased to 0 °C (entry 12). The enantioselectivity almost remained the same when the temperature was further lowered to −30 °C (entry 13).

After the optimized conditions were identified, the scope of the asymmetric epoxidation was investigated. As expected, a series of cyclic cis olefins, including chromene derivatives, indene, and 1,2-dihydronaphthalene could be efficiently epoxidized within short times, providing the corresponding chromene derivatives (Table 3, entries 2−9), indene (entry 1), and 1,2-dihydronaphthalene (entry 10) epoxides in high yields with excellent enantioselectivities. The substrates could bear a wide range of groups, such as nitrile, ester, acetylamino, and phenyl. It is noteworthy that a good yield and high enantioselectivity were also obtained for the reaction of the acyclic cis olefin *cis*-*β*-methylstyrene (entries 11 and 12). Encouraged by these results, we turned our attention to the challenging terminal olefins. Initial epoxidation of styrene using **aca** provided a moderate yield and low enantioselectivity (entry 13). The enantioselectivity and yield improved when 3 equiv of cyclohexanecarboxylic acid was employed (entries 14 and 15). When ligand **L2** was replaced with **L6**, the reaction of styrene proceeded with better enantioselectivity, albeit with a decreased yield (entry 16). The yield was significantly promoted when the catalyst loading was increased to 2.0 mol % (entries 17 and 18). The reaction of 4-methylphenylene gave the epoxide in good yield with remarkable enantioselectivity (entry 19). To further explore the generality of the current catalyst system, we investigated the epoxidation for trans olefins. The reaction of *trans*-stilbene gave the epoxide with excellent enantioselectivity in low yield (entry 20). Meanwhile, the epoxidation of *trans*-*β*-methylstyrene gave moderate yield and enantioselectivity (entry 21). Finally, good yield and moderate enantioselectivity were also obtained in the reaction of trisubstituted olefin 1-phenylcyclohexene when the reaction was carried out with 1 mol % $Mn(OTf)_2$ and ligand **L2** in the presence of 3 equiv of acetic acid (entries 22 and 23).

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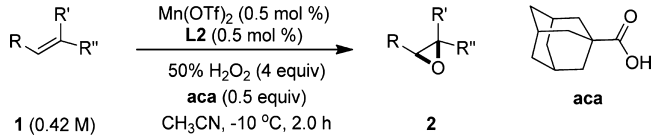
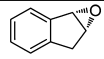
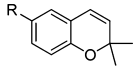
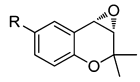
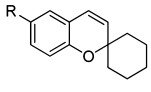
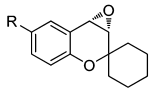
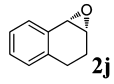
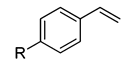
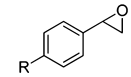
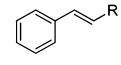
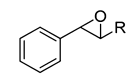
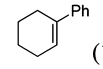
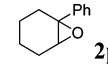
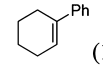
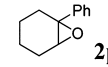
Table 3. Substrate Scope of Epoxidation



entry	alkene	product	% yield	% ee[a]
1	 (**1a**)	 **2a**	92	93
				
2[b]	R = CN (**1b**)	**2b**	90	98
3[b]	R = COOMe (**1c**)	**2c**	91	>99
4[b]	R = Ph (**1d**)	**2d**	92	97
5[b]	R = NHAc (**1e**)	**2e**	94	>99
				
6[b]	R = CN (**1f**)	**2f**	90	>99
7[b]	R = COOMe (**1g**)	**2g**	89	98
8[b]	R = Ph (**1h**)	**2h**	94	95
9[b]	R = NHAc (**1i**)	**2i**	93	>99
10[b]	 (**1j**)	 **2j**	92	95
11	 (**1k**)	 **2k**	67	83
12[c]	 (**1k**)	 **2k**	90	84

entry	alkene	product	% yield	% ee[a]
				
13	R = H (**1l**)	**2l**	78	39
14[d]	R = H (**1l**)	**2l**	70	49
15[e]	R = H (**1l**)	**2l**	92	50
16[f]	R = H (**1l**)	**2l**	16	66
17[g]	R = H (**1l**)	**2l**	38	66
18[h]	R = H (**1l**)	**2l**	74	69
19[h]	R = Me (**1m**)	**2m**	88	68
				
20	R = Ph (**1n**)	**2n**	17	97
21	R = Me (**1o**)	**2o**	32	67
22	 (**1p**)	 **2p**	42	51
23[i]	 (**1p**)	 **2p**	85	59

[a]Determined by chiral HPLC analysis. [b]$Mn(OTf)_2$ (0.25 mol %), **L2** (0.25 mol %). [c]$Mn(OTf)_2$ (1.0 mol %), **L2** (1.0 mol %). [d]Cyclohexanecarboxylic acid (0.5 equiv). [e]Cyclohexanecarboxylic acid (3.0 equiv). [f]$Mn(OTf)_2$ (0.5 mol %), **L6** (0.5 mol %), cyclohexanecarboxylic acid (3.0 equiv). [g]$Mn(OTf)_2$ (1.0 mol %), **L6** (1.0 mol %), cyclohexanecarboxylic acid (3.0 equiv). [h]$Mn(OTf)_2$ (2.0 mol %), **L6** (2.0 mol %), cyclohexanecarboxylic acid (3.0 equiv). [i]$Mn(OTf)_2$ (1.0 mol %), **L2** (1.0 mol %), 50% H_2O_2 (4.0 equiv), acetic acid (3.0 equiv).

On the basis of our previous study and the pertinent literature, we propose a possible catalytic cycle (Scheme 2).[4i,j,s,8,9] (L)Mn(II) is initially converted to intermediate **3**. Then the active species, Mn(V)−oxo complex **4**, is formed via CA-assisted heterolytic cleavage of the O−O bond in intermediate **3**. The active species **4** epoxidizes the olefins to the corresponding products along with the formation of intermediate **3**.

To investigate the tolerance of our catalyst system to water, the experiment was performed at 1% H_2O_2, and the desired product **2a** was obtained in 90% yield with 92% ee (Scheme 3). The result indicated that the reaction could proceed at a low concentration of H_2O_2, which makes the procedure safe.

To further evaluate the practical utility of the catalyst system, the AE of **1a** was enlarged to a gram scale under the optimized conditions, and the desired product was obtained in 93% yield with 92% ee (Scheme 4).

CONCLUSION

In summary, the catalytic AE of a variety of olefins with H_2O_2 based on an inexpensive and readily available in situ-formed manganese complex has been developed. Optically active epoxides with excellent enantioselectivities (>99% ee) were obtained in synthetically valuable yields (up to 94%). Improvement of the enantioselectivity was attained by the use of a

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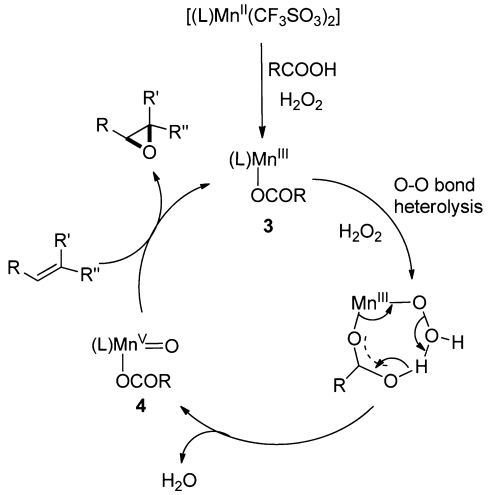
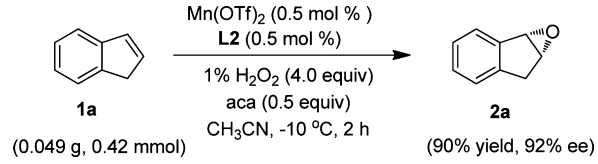
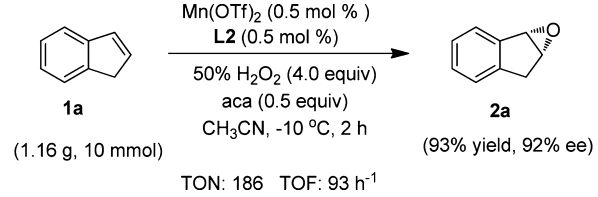
Scheme 2. Proposed Catalytic Cycle



Scheme 3. Water Tolerance of the Reaction



Scheme 4. Gram-Scale Synthesis of Epoxide 2a



catalytic amount of a carboxylic acid additive. Furthermore, suitable hydrophobicity of the catalyst imposed by the ligand is essential to the catalytic activity, providing a useful guiding principle for future rational design of catalysts. Extension of the strategy to other reactions is in progress.

EXPERIMENTAL SECTION

General Information. Unless otherwise stated, all reactions and manipulations were carried out under an argon atmosphere using standard Schlenk techniques or in an argon-filled glovebox. All chemicals were obtained from commercial sources and were used without further purification. Solvents were treated prior to use according to standard methods. Column chromatography was carried out on silica gel (300−400 mesh) using a forced flow of eluent at 0.3−0.5 bar pressure. NMR spectra were recorded at room temperature in $CDCl_3$ on 400 MHz spectrometers. The chemical shifts for ^1H NMR were recorded in parts per million downfield from tetramethylsilane (TMS) with $CDCl_3$ (7.26 ppm) as the internal standard. The chemical shifts for ^{13}C NMR were recorded in parts per million downfield using the central peak of $CDCl_3$ (77.16 ppm) as the internal standard. ^{13}C NMR was broadband decoupled from hydrogen nuclei. Coupling constants (J) are reported in hertz and refer to apparent peak multiplications.

Characterization of Starting Materials. Ligands **L6**−**L9** were prepared following the procedure described in the reported literature.[4s,10] **L1**−**L5** are known compounds.[4s]

L6. Yellow solid, 2.14 g, 42% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 10.38 (2H, s), 7.71 (2H, d, J = 7.8 Hz), 7.46 (2H, m), 7.17 (4H, d, J = 3.5 Hz), 7.10−6.98 (2H, m), 6.68 (2H, m), 4.17 (2H, m), 3.87−4.0 (4H, m), 0.66 (18H, s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.9, 146.6, 135.9, 132.2, 130.2, 124.1, 123.8, 117.2, 113.7, 111.3, 67.5, 56.3, 33.9, 26.3; HRMS (ESI-TOF) m/z calcd for $C_{32}H_{39}N_4O_2$ $[M + H]^+$ 511.3073, found 511.3073.

L7. Yellow solid, 2.08 g, 46% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 10.34 (2H, s), 7.72 (2H, dd, J = 8.0, 1.2 Hz), 7.47 (2H, m), 7.23−7.11 (4H, m), 7.09−7.03 (2H, m), 6.73−6.61 (2H, m), 4.29 (2H, m), 4.12−3.94 (2H, m), 3.82 (2H, t, J = 7.9 Hz), 1.39 (4H, m), 0.74 (6H, t, J = 7.4 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.8, 146.6, 135.6, 132.3, 130.2, 124.2, 124.0, 117.1, 113.7, 111.2, 71.1, 68.7, 29.4, 10.6; HRMS (ESI-TOF) m/z calcd for $C_{28}H_{31}N_4O_2$ $[M + H]^+$ 455.2447, found 455.2473.

L8. Yellow solid, 1.66 g, 39% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 10.29 (2H, s), 7.72 (2H, dd, J = 7.6, 1.6 Hz), 7.48 (2H, m), 7.22−7.15 (2H, t, J = 7.6 Hz), 7.09 (4H, m), 6.69 (2H, t, J = 7.6 Hz), 4.39−4.27 (2H, m), 4.25−4.10 (2H, m), 3.74 (2H, t, J = 7.8 Hz), 1.08 (6H, d, J = 6.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.7, 146.8, 135.7, 132.3, 130.2, 124.5, 117.1, 113.6, 111.1, 72.8, 62.6, 21.9; HRMS (ESI-TOF) m/z calcd for $C_{26}H_{27}N_4O_2$ $[M + H]^+$ 427.2134, found 427.2157.

L9. Yellow solid, 3.65 g, 52% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 10.36 (2H, s), 7.79 (2H, dd, J = 7.9, 1.3 Hz), 7.54−7.43 (2H, m), 7.40−7.30 (6H, m), 7.29−7.25 (4H, m), 7.18−7.02 (16H, m), 6.69−6.63 (2H, m), 5.03 (4H, m); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.6, 147.0, 140.8, 132.7, 130.6, 129.4, 129.0, 127.9, 126.9, 126.6, 124.6, 124.4, 117.3, 114.0, 87.6, 79.0; HRMS (ESI-TOF) m/z calcd for $C_{48}H_{39}N_4O_2$ $[M + H]^+$ 703.3073, found 703.3077.

Representative Procedure for the Asymmetric Epoxidation of Olefins. A solution of $Mn(OTf)_2$ (0.0084 M solution in CH_3CN, 0.25 mL, 0.0021 mmol) was added to **L2** (0.0084 M solution in CH_3CN, 0.25 mL, 0.0021 mmol) at room temperature. The reaction mixture was stirred at room temperature for 4 h. To the solution of the manganese complex were directly added the substrate (0.42 mmol), CA (0.21 mmol, diluted with 0.5 mL of CH_3CN), and CH_3CN (1 mL), and then the temperature was decreased to −10 °C. H_2O_2 (50%, 1.68 mmol, diluted with 0.5 mL of CH_3CN) was rapidly added, and the mixture was stirred at −10 °C for 2.0 h. At this point, a saturated aqueous solution of $NaHCO_3$ (8 mL) was added, and the resulting mixture was extracted with EtOAc (10 mL × 3). Then the organic layers were combined, washed with brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by silica gel column chromatography to afford the corresponding epoxide.

*(1aS,6aR)-6,6a-Dihydro-1aH-indeno[1,2-b]oxirene (**2a**).*[11] Colorless oil, purified by column chromatography on silica gel (5% EtOAc in petroleum ether) (51.0 mg, 92% yield, 93% ee). ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (1H, m), 7.27−6.67 (3H, m), 4.28 (1H, s), 4.14 (1H, s), 3.22 (1H, d, J = 18.0 Hz), 2.98 (1H, d, J = 18.1 Hz); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.1, 141.4, 129.1, 126.8, 126.7, 125.8, 59.71, 58.3, 35.2; MS (EI) m/z 132 (M^+); HPLC (DAICEL OJ-H, hexane/isopropanol 80:20, flow rate 0.5 mL/min, 220 nm) t_r (minor) = 16.6 min, t_r (major) = 18.9 min.

*(1aS,7bS)-2,2-Dimethyl-2,7b-dihydro-1aH-oxireno[2,3-c]-chromene-6-carbonitrile (**2b**).*[1c] White solid, purified by column chromatography on silica gel (20% EtOAc in petroleum ether) (76.1 mg, 90% yield, 98% ee). ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (1H, d, J = 2.0 Hz), 7.52 (1H, dd, J = 8.5 Hz, 2.1 Hz), 6.86 (1H, d, J = 8.5 Hz), 3.91 (1H, d, J = 4.4 Hz), 3.54 (1H, d, J = 4.4 Hz), 1.60 (3H, s), 1.30 (3H, s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 156.5, 134.4, 133.8, 121.1, 119.0, 118.7, 104.4, 74.7, 62.3, 49.9, 25.5, 23.0; MS (EI) m/z 201 (M^+); HPLC (DAICEL OJ-H, hexane/isopropanol 50:50, flow rate 0.5 mL/min, 254 nm) t_r (minor) = 17.2 min, t_r (major) = 28.0 min.

*(1aS,7bS)-Methyl 2,2-Dimethyl-2,7b-dihydro-1aH-oxireno[2,3-c]-chromene-6-carboxylate (**2c**).*[1c] White solid, purified by column chromatography on silica gel (10% EtOAc in petroleum ether) (89.5 mg, 91% yield, >99% ee). ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (1H, d, J = 2.2 Hz), 7.93 (1H, dd, J = 8.1, 2.2 Hz), 6.83 (1H, d, J = 8.5 Hz), 3.95 (1H, d, J = 4.4 Hz), 3.89 (3H, s), 3.52 (1H, d, J = 4.4 Hz), 1.60 (3H, s), 1.28 (3H, s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.4, 156.8, 132.1, 131.6, 123.0, 119.7, 118.0, 74.2, 62.4, 52.0, 51.6, 25.6, 23.0; MS (EI) m/z 234 (M^+); HPLC (DAICEL OJ-H, hexane/isopropanol 90:10, flow rate 0.5 mL/min, 254 nm) t_r = 37.3 min.

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*(1aS,7bS)-2,2-Dimethyl-6-phenyl-2,7b-dihydro-1aH-oxireno[2,3-c]chromene (**2d**).*[1c] White solid, purified by column chromatography on silica gel (10% EtOAc in petroleum ether) (97.4 mg, 92% yield, 97% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (3H, m), 7.47 (1H, dd, J = 8.4, 2.3 Hz), 7.42 (3H, m), 7.31 (1H, m), 6.88 (1H, d, J = 8.4 Hz), 3.96 (1H, d, J = 4.4 Hz), 3.52 (1H, d, J = 4.4 Hz), 1.60 (3H, s), 1.30 (3H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.1, 140.5, 134.3, 129.0, 128.8, 128.3, 126.9, 126.7, 118.4, 73.3, 62.8, 51.1, 25.7, 22.7; MS (EI) m/z 252 (M^+); HPLC (DAICEL OD-H, hexane/isopropanol 95:5, flow rate 0.5 mL/min, 220 nm) t_r (minor) = 14.3 min, t_r (major) = 17.7 min.

*N-((1aS,7bS)-2,2-Dimethyl-2,7b-dihydro-1aH-oxireno[2,3-c]-chromen-6-yl)acetamide (**2e**).*[1c] Yellow solid, purified by column chromatography on silica gel (50% EtOAc in petroleum ether) (92.0 mg, 94% yield, >99% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (1H, d, J = 2.2 Hz), 7.34 (1H, s), 7.15 (1H, dd, J = 8.6, 2.3 Hz), 6.73 (1H, d, J = 8.6 Hz), 3.86 (1H, d, J = 4.3 Hz), 3.47 (1H, d, J = 4.4 Hz), 2.14 (3H, s), 1.56 (3H, s), 1.23 (3H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.3, 149.3, 131.3, 122.4, 122.0, 120.3, 118.3, 77.3, 77.0, 76.7, 73.1, 62.8, 51.0, 25.6, 24.3, 22.5; MS (EI) m/z 233 (M^+); HPLC (DAICEL OJ-H, hexane/isopropanol 50:50, flow rate 0.5 mL/min, 254 nm) t_r = 10.1 min.

*(1a′S,7b′S)-1a′,7b′-Dihydrospiro[cyclohexane-1,2′-oxireno[2,3-c]chromene]-6′-carbonitrile (**2f**).*[1c] White solid, purified by column chromatography on silica gel (20% EtOAc in petroleum ether) (91.1 mg, 90% yield, >99% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35−7.37 (1H, m), 7.46 (1H, d, J = 8.5 Hz), 6.85 (1H, d, J = 8.5 Hz), 3.82 (1H, d, J = 4.3 Hz), 3.48 (1H, d, J = 4.3 Hz), 2.03−1.30 (10H, m); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 156.8, 134.9, 134.3, 122.6, 119.7, 119.4, 104.7, 75.9, 62.5, 50.0, 34.4, 31.3, 25.7, 21.7, 21.3; MS (EI) m/z 241 (M^+); HPLC (DAICEL OJ-H, hexane/isopropanol 50:50, flow rate 0.5 mL/min, 254 nm) t_r = 23.3 min.

*(1a′S,7b′S)-Methyl 1a′,7b′-Dihydrospiro[cyclohexane-1,2′-oxireno[2,3-c]chromene]-6′-carboxylate (**2g**).*[1c] White solid, purified by column chromatography on silica gel (10% EtOAc in petroleum ether) (102.4 mg, 89% yield, 98% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (1H, d, J = 1.7 Hz), 7.93 (1H, dd, J = 8.5, 1.8 Hz), 6.88 (1H, d, J = 8.5 Hz), 3.91 (1H, d, J = 4.4 Hz), 3.89 (3H, s), 3.51 (1H, d, J = 4.4 Hz), 2.10 (1H, m), 1.85 (1H, m), 1.76−1.33 (10H, m); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.5, 156.6, 132.1, 131.6, 123.0, 120.5, 118.0, 74.8, 62.0, 51.9, 50.1, 34.0, 30.7, 25.3, 21.2, 20.8; MS (EI) m/z 274 (M^+); HPLC (DAICEL OJ-H, hexane/isopropanol 50:50, flow rate 0.5 mL/min, 254 nm) t_r (minor) = 15.4 min, t_r (major) = 16.7 min.

*(1a′S,7b′S)-6′-Phenyl-1a′,7b′-dihydrospiro[cyclohexane-1,2′-oxireno[2,3-c]chromene] (**2h**).*[1c] White solid, purified by column chromatography on silica gel (10% EtOAc in petroleum ether) (115.3 mg, 94% yield, 95% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (3H, d, J = 7.7 Hz), 7.46 (1H, d, J = 8.3 Hz), 7.41 (2H, m), 7.30 (1H, m), 6.92 (1H, d, J = 8.4 Hz), 3.92 (1H, d, J = 4.3 Hz), 3.51 (1H, d, J = 4.3 Hz), 1.97 (2H, m), 1.68 (5H, m), 1.54−1.34 (3H, m); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.4, 141.1, 134.8, 129.5, 129.3, 128.8, 127.4, 127.3, 121.7, 119.0, 74.4, 63.0, 51.2, 34.7, 30.9, 26.0, 21.8, 21.5; MS (EI) m/z 292 (M^+); HPLC (DAICEL OD-H, hexane/isopropanol 90:10, flow rate 0.5 mL/min, 254 nm) t_r (minor) = 11.9 min, t_r (major) = 15.9 min.

*N-((1a′S,7b′S)-1a′,7b′-Dihydrospiro[cyclohexane-1,2′-oxireno-[2,3-c]chromen]-6′-yl)acetamide (**2i**).*[1c] Yellow solid, purified by column chromatography on silica gel (50% EtOAc in petroleum ether) (107.8 mg, 93% yield, >99% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 2.6 Hz, 1H), 7.26 (s, 1H), 7.17 (1H, dd, J = 8.6, 2.6 Hz), 6.79 (1H, d, J = 8.6 Hz), 3.83 (1H, d, J = 4.4 Hz), 3.46 (1H, d, J = 4.4 Hz), 2.14 (3H, s), 1.92−1.78 (1H, m), 1.72−1.48 (7H, m), 1.41−1.30 (2H, m); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.2, 149.0, 131.2, 122.3, 122.0, 121.2, 118.4, 73.7, 62.4, 50.5, 34.1, 30.1, 25.4, 24.3, 21.1, 20.9; MS (EI) m/z 273 (M^+); HPLC (DAICEL OJ-H, hexane/isopropanol 50:50, flow rate 0.5 mL/min, 254 nm) t_r = 22.9 min.

*(1aR,7bS)-1a,2,3,7b-Tetrahydronaphtho[1,2-b]oxirene (**2j**).*[11] Colorless oil, purified by column chromatography on silica gel (5% EtOAc in petroleum ether) (57.0 mg, 92% yield, 95% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (1H, d, J = 7.3 Hz), 7.28−7.18 (2H, m), 7.08 (1H, d, J = 7.3 Hz), 3.84 (1H, d, J = 4.2 Hz), 3.73 (1H, d, J = 4.2 Hz), 2.89−2.71 (1H, m), 2.54 (1H, m), 2.41 (1H, m), 1.76 (1H, m); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.3, 130.1, 129.0, 129.0, 55.7, 53.3, 25.0, 22.4; MS (EI) m/z 146 (M^+); HPLC (DAICEL OB-H, hexane/isopropanol 99:1, flow rate 0.5 mL/min, 220 nm) t_r (major) = 22.6 min, t_r (minor) = 29.2 min.

*cis-2-Methyl-3-phenyloxirane (**2k**)..*[4i,12] Colorless oil, purified by column chromatography on silica gel (1% EtOAc in petroleum ether) (51.0 mg, 90% yield, 84% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.26 (5H, m), 4.06 (1H, d, J = 4.2 Hz), 3.34 (1H, m), 1.09 (3H, d, J = 5.4 Hz); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 135.50, 128.0, 127.5, 126.6, 57.6, 55.2, 12.5; HPLC (DAICEL OD-H, hexane/isopropanol 99:1, flow rate 0.5 mL/min, 220 nm), t_r (major) = 10.1 min, t_r (minor) = 13.0 min.

*2-Phenyloxirane (**2l**).*[4s] Colorless oil, purified by column chromatography on silica gel (5% EtOAc in petroleum ether) (37.3 mg, 74% yield, 69% ee). HPLC (DAICEL OD-H, hexane/isopropanol 99:1, flow rate 0.5 mL/min, 220 nm) t_r (major) = 11.2 min, t_r (minor) = 14.1 min.

*2-(p-Tolyl)oxirane (**2m**).*[4s] Colorless oil, purified by column chromatography on silica gel (5% EtOAc in petroleum ether) (49.5 mg, 88% yield, 68% ee). HPLC (DAICEL OD-H, hexane/isopropanol 99:1, flow rate 0.5 mL/min, 220 nm) t_r (major) = 11.5 min, t_r (minor) = 12.7 min.

*(2S,3S)-2,3-Diphenyloxirane (**2n**).*[4s] White solid, purified by column chromatography on silica gel (1% EtOAc in petroleum ether) (14.0 mg, 17% yield, 97% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (10H, s), 3.87 (2H, s); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.7, 129.2, 128.9, 126.1, 63.4; MS (EI) m/z 196 (M^+); HPLC (DAICEL OD-H, hexane/isopropanol 99:1, flow rate 0.5 mL/min, 220 nm) t_r (major) = 16.7 min, t_r (minor) = 20.7 min.

*trans-2-Methyl-3-phenyloxirane (**2o**)..*[4i,12] Colorless oil, purified by column chromatography on silica gel (1% EtOAc in petroleum ether) (18.0 mg, 32% yield, 67% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.24 (5H, m), 3.57 (1H, d, J = 2.1 Hz), 3.03 (1H, dq, J = 5.1, 2.1 Hz), 1.45 (3H, d, J = 5.1 Hz); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.8, 128.4, 128.0, 125.6, 59.5, 59.0, 17.9; HPLC (DAICEL OD-H, hexane/isopropanol 99:1, flow rate 0.5 mL/min, 220 nm) t_r (minor) = 12.0 min, t_r (major) = 12.4 min.

*1-Phenyl-7-oxabicyclo[4.1.0]heptane (**2p**).*[12] Colorless oil, purified by column chromatography on silica gel (1% EtOAc in petroleum ether) (62.2 mg, 85% yield, 59% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.29 (4H, m), 7.28−7.21 (1H, m), 3.07 (1H, d, J = 3.1 Hz), 2.33−2.22 (1H, m), 2.12 (1H, m), 2.03−1.95 (2H, m), 1.66−1.46 (3H, m), 1.36−1.26 (1H, m); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.6, 128.3, 127.2, 125.3, 61.9, 60.2, 28.9, 24.7, 20.1, 19.8; HPLC (DAICEL OD-H, hexane/isopropanol 99:1, flow rate 0.5 mL/min, 220 nm) t_r (major) = 11.1 min, t_r (minor) = 12.7 min.

Experimental Procedure for the Gram-Scale Synthesis of 2a. A mixture of $Mn(OTf)_2$ (0.018 g, 0.05 mmol) and **L2** (0.024 g, 0.05 mmol) in CH_3CN (10 mL) was stirred at room temperature for 8 h. To the solution of the manganese complex were added indene (1.16 g, 10 mmol) and adamantane carboxylic acid (0.90 g, 5.0 mmol), and then the temperature was decreased to −10 °C. H_2O_2 (50%, 2.72 g, 40 mmol, diluted with 2.5 mL of CH_3CN) was added dropwise to the stirring reaction mixture over 2 min, and the mixture was stirred at −10 °C for 2 h. The reaction was quenched by the addition of sat. aq. $NaHCO_3$ (15 mL), and the mixture was extracted with EtOAc (15 mL × 4). The organic layer was separated, washed with brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by silica gel column chromatography to afford **2a** (1.21 g, 92% yield, 93% ee).

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for compounds **L6**−**L9**, **2a**−**k**, and **2n**−**p** and HPLC data for epoxides **2a**−**p**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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