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ARTICLE

Enantioselective oxidation of sulfides with H_2O_2 catalyzed by a pre-formed manganese complex

Wen Dai[ab], Guosong Li[a], Lianyue Wang[a], Bo Chen[ab], Sensen Shang[ab], Ying Lv[a], and Shuang Gao*[a]

A facile and environmentally friendlymethod is presented for the asymmetric oxidation of sulfideswith H_2O_2,utilizingan pre-formed manganese complex. Just in the presence of a low catalytic amount of carboxylic acid (CA), a variety of sulfides substrates, including aryl alkyl, aryl benzyl and cyclic sulfides, reacted to form chiral sulfoxides in high yields (up to 95%) andexcellent enantioselectivities (>99% ee) under mild conditons. Moreover, the practical utility of the method has been demonstrated by the synthesis of esomeprazole and albendazole sulfoxide (**ABZO**).
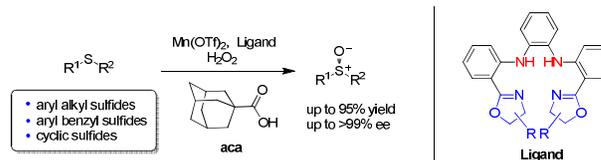
Introduction

Chiral sulfoxides are useful auxiliaries and ligands in modern organic synthesis and an important class of biologically active molecules (e.g., modafinil, sulindac and esomeprazole).[1-17] In view of the importance of optical pure sulfoxides, intensive effort has been devoted to the development of various methods towards sulfoxides with high enantiomeric purity.[6, 18-21] Among all methods developed so far, the asymmetric oxidation of corresponding sulfides is one of the most powerful and reliable route. Thus, the last few decades have witnessed the significant advances in the field of asymmetric sulfoxidation. Since Kagan and Modena reported the first enantioselective titanium-catalyzed asymmetric oxidation of sulfides in 1984,[22] several other elegant metal-based catalyst systems have also been developed.[23-30–31-51] However, there are disadvantages associated with these catalyst systems such as harsh reaction conditions, long reaction timeor toxic and expensive catalysts. In addition, although high enantioselectivity has been achieved for certain classes of sulfides, they often lack generality. For example, methods for cyclic, sterically hindered or long alkyl substituted sulfideshave been still rarely exploited. Consequently, finding a general catalytic system with high conversion and selectivity that utilizes a readily available and

non-toxic catalyst and environmentally benign oxidants remains an attractive goal.
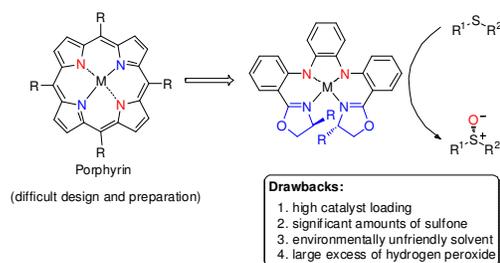
Scheme 1.Strategy for the development of asymmetric sulfoxidation.

Recently, we described a new approach to asymmetric oxidation of sulfides that involved the application of a porphyrin-inspired manganesecomplexes with H_2O_2, leading to excellent enantioselectivities (Scheme 1).[52] However, the excellent enantioselectivities were mainly attributed to the synergistic combination of initial asymmetric sulfoxidation with the following oxidative kinetic resolution process.So the formation of significant amounts of sulfone which made the separation and purification difficult wasinevitable and a large excess of hydrogen peroxide (2.0 equiv) was required.In addition, a high catalyst loading (1 mol%) was requiredand the dichloromethane was employed as the solvent which

isenvironmentallyunfriendly.With this background in mind, we wish to describe the expansion of this early investigation resulting in improved yields by furtherlowering the catalyst loading and suppressing the sulfones formation under relatively green processes, while retaining good enantioselectivities and further reducing the amount of hydrogen peroxide through variation of acidadditive, solvent and ligand. Herein, we report a rapid, efficient and environmentally benignasymmetric sulfoxidation method with H_2O_2 by an pre-formed manganese complex, providing a broad range of sulfoxides in high yields with absence or very limited amount of overoxidation to produce sulfone. The practical utility of the method has further been underscored by the synthesis of esomeprazole and **ABZO**.

Results and discussion

Early study has shown that CA played a key positive role inenhancing enantioselectivities in Mn or Fe-catalyzed asymmetric epoxidation.[53-55] Because of that, an extensive study was performed to investigate the role of CA in our catalyst system.Initially, thioanisole(**1a**) was employed as the model substrate. The reactions were conducted with **1a** (1.0 equiv), CA (1.0 equiv), H_2O_2 (1.2 equiv) and 1 mol% of catalyst which was generatedfrom $Mn(OTf)_2$ and **L2**,in isopropanol (IPA) at −10 °C. Poor activity was observed when inorganic acid H_3PO_4 or sodium acetate was used (Table 1, entries1 and 2). Then the reaction was carried out by replacing the H_3PO_4 or sodium acetate with a wide variety of aliphatic acids. Improved performance both in terms of yields and enantioselectivities could be gained (entries3–12). The results indicated that both the proton and carboxylic group were needed in the asymmetric sulfoxidation process.Among these aliphatic acids, the adamantane carboxylic acid (**aca**) provided the best result (90% yield, 80% ee; entry 5). Perhaps the sterically hindered **aca** acting as an auxiliary ligandincorporated into the activespecies which could impart highly rigid environment around the active species lead to a drasticincrease in enantioselectivity.[56] Unfortunately, when the heterocyclic aromatic carboxylic acid nicotinic acid was surveyed, the conversion was relatively low (entry13). In addition to the racemic CA, the chiral carboxylic acidsS-Ibuprofen and (*1S*)-(-)-camphanic acid were also investigated. Disappointedly, only moderate yields and enantioselectivities were obtained (entries14 and 15). After testing CA loading, the amount of CA was successfully lowered to 20 mol% with no decrease of yield and enantioselectivity (entries16 and 17). Further reducing the CA loading to 10% mol resulted in a lower enantioselectivity with the yield being maintained (entry 18). Finally, the influence of temperature was examined. The enantioselectivity had anobviousincrease when the temperature was decreased to −20 °C(entry 19). The enantioselectivity almost remained the same by further lowering the temperature to -30 °C(entry 20).

Table 1.Screening of the identity and amount of CA.

entry	additive	yield(%)[a]	ee(%)[b]
1	AcONa	< 5	-
2	H_3PO_4	<5	-
3	CH_3COOH	90	62
4		66	82
5		65	76
6	**aca**	90	80
7		72	70
8		70	80
9		71	80
10		62	50
11		80	58
12		76	48
13		14	60
14		70	70
15		70	48
16[c]	**aca**	91	80
17[d]	**aca**	89	81
18[e]	**aca**	89	77
19[f]	**aca**	88	87
20[g]	**aca**	86	84

[a] Isolated yields.[b] Determined by chiral HPLC analysis.[c] **aca** (0.5 equiv). [d] **aca** (20 mol%). [e] **aca** (10 mol% equiv).[f] **aca** (20 mol%), -20 °C. [g] **aca** (20 mol%), -30 °C.

Next, we extended our search to the influence of the solvent. Further assessment of solvent revealed that transformation was very sensitive to reaction medium. In the initial screening, various single solvents were applied. The reaction occurred smoothly in the protic polar EtOH with good yield and enantioselectivity (Table 2, entry 1). When the oxidation was carried out in aprotic solvent, only the low conversion was observed (entries 2–6). Then, we focused on

screening various mixed solvents of DCM and aprotic solvent, affording the desired sulfoxide in moderate yields and enantioselectivities (entries 7–11). Gratifyingly, replacement of the mixed solvents of DCM and aprotic solvent with DCM and protic solvent resulted in significant improvement in yields (entries 12–15). Perhaps the protic solvent can coordinate to the manganese catalyst, thereby displacing the sulfoxide, which significantly suppresses over-oxidation of sulfoxide.[43] Among the mixed solvents o of DCM and protic solvent, the solvent of DCM and IPA with a volumeratio of 1/2 gave the best result (entry 14). Pleasingly, replacing the mixed solvent of DCM and IPA with CH_3CN and IPA resulted in slight increase in yields with enantioselectivity being remained (88% yield, 90% ee; entry 16).

Table 2. Investigation of solvent.
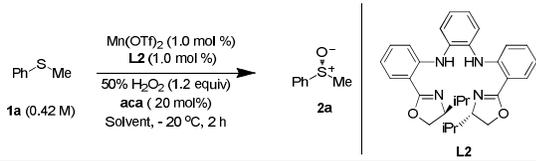
entry	solvent	yield(%)[a]	ee(%)[b]
1	EtOH	86	80
2	DCM	32	76
3	CHCl$_3$	8	70
4	CCl$_4$	< 5	-
5	dioxane	< 5	-
6	toluene	<5	-
7	DCM/Toluene (1:2)	69	78
8	DCM/THF (1:2)	76	80
9	DCM/AcOEt (1:2)	74	82
10	DCM/hexane (1:2)	72	76
11	DCM/cyclohexane(1:2)	64	79
12	DCM/EtOH (1:2)	91	82
13	DCM/n-BuOH (1:2)	92	80
14	DCM/IPA (1:2)	86	90
15	DCM/t-BuOH (1:2)	90	85
16	CH$_3$CN/i-PrOH(1:2)	88	90

[a] Isolated yields.[b] Determined by chiral HPLC analysis.

Various ligands were then screened under the mixed solvent CH_3CN and IPA with a ratio of 1/2 to find the optimum ligand for our catalyst system. Replacing of ligand **L2** with various ligands containing mono-substituted oxazolines also resulted in good yields and enantioselectivities (Table 3, entries 1–6). However, when the ligand **L8** bearing methyl-substituted oxazolines was used, both yield and enantioselectivity dropped drastically (entry 7). The result suggested that the

hydrophobicity of catalyst imposed by ligand is crucial to maintaining the good activity of catalyst. It is speculated that hydrophobic structure of ligands allows the substrate to approach the active center of catalysts more easily and reduces the decomposition of hydrogen peroxide.[56] Then ligand **L9**, with bis-substituted oxazolines, was also been examined. Unfortunately, only a low enantioselectivity was obtained, albeit with good yield (entry 8). Taking all of our findings into consideration, ligand **L2** was identified as the ligand providing the best yield and enantioselectivity.Remarkably, the catalyst loading was successfully lowered to 0.5 mol% withouterosion of yield and enantioselectivity, and even a catalyst loading of 0.25 mol% gave a good result (entries 9–10). Finally, the loading of H_2O_2 was investigated. We found that 1.2 equiv of H_2O_2 was necessary in order to achievethe best result (entry 11).

Table 3. Investigationof effect ofligand structure.
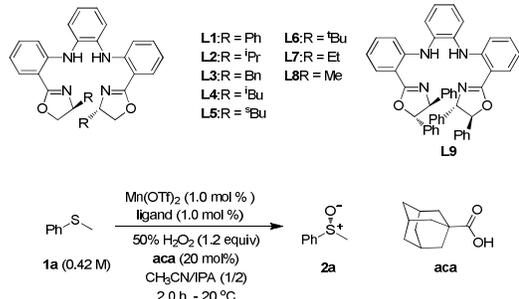
entry	ligand	% yield[a]	% ee[b]
1	**L1**	80	85
2	**L3**	92	80
3	**L4**	90	84
4	**L5**	89	86
5	**L6**	74	80
6	**L7**	92	81
7	**L8**	38	74
8	**L9**	85	8
9[c]	**L2**	87	91
10[d]	**L2**	84	89
11[e]	**L2**	82	89

[a] Isolated yields.[b] Determined by chiral HPLC analysis. [c] Mn(OTf)$_2$ (0.5mol%), **L2** (0.5 mol%). [d] Mn(OTf)$_2$ (0.25 mol%), **L2**(0.25 mol%).[e]50% H_2O_2(1.1 equiv).

With the optimized conditions in hand, the asymmetric oxidation of a series of representativesulfides was examined (Table 4). A broad range of aryl methyl sulfides were smoothly converted to the corresponding sulfoxides in high yields with excellent enantioselectivities within short times regardless of the electronic properties and position of the substituent on the aromatic ring (entries 1–10). Good yields and excellent were

preserved even when extending the alkyl chain linearly from C1 (methyl) to C5 (pentyl) (entries 13–20). It is noteworthy thatcondensed aromatic substrate 2-(methylthio)naphthalene and 2-(phenylthio)ethanol could also be oxidized in good yields with excellent enantioselectivities (entries 11 and 12). Encouraged by these results, we turned our attention to the sterically hindered aryl benzyl sulfides. Gratifyingly, high yields and excellent enantioselectivities could be achieved (entries 21–27). In order to extend the substrate scope further, we expected that the cyclic sulfides would be oxidized. Fortunately, the present oxidation could also be successfully applied to cyclic sulfides, giving the corresponding sulfoxides in high yields with excellent enantioselectivities (entries 28 and 29).

Table 4. Substrate scopeof asymmetric sulfoxidation.

entry	product	% yield[a]	% ee[b]
1	(2a)	88	90
2	(2b)	94	95
3	(2c)	90	90
4	(2d)	90	90
5	(2e)	93	94
6	(2f)	92	94
7	(2g)	91	90
8	(2h)	92	95
9	(2i)	90	90
10	(2j)	95	80
11	(2k)	88	87
12	(2l)	89	95
13	(2m)	92	97
14	R = Et (2n)	92	92
15	R = n-Bu (2o)	93	84
16[c]	R = n-Bu (2o)	87	95
17[c]	R = n-pentyl (2p)	88	95

18	R = Et (2q)	95	94
19[c]	R = n-Bu (2r)	92	91
20[c]	R = n-pentyl (2s)	90	91
21	(2t)	90	98
22	(2u)	90	99
23	(2v)	91	92
24	(2w)	90	98
25	(2x)	95	>99
26	(2y)	93	93
27	(2z)	94	>99
28	(3a)	76	92
29	(3b)	91	94
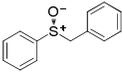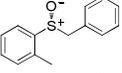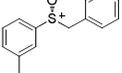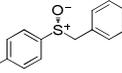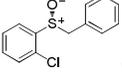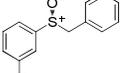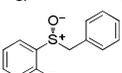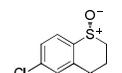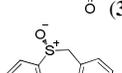
[a] Isolated yields. [b] Determined by chiral HPLC analysis. [c] 50% H_2O_2 (1.3 equiv)

On the basis of our previous work,[52] a possible mechanism is proposed (Scheme 2).Although the CA additive used in the current catalyst system differs from our previous work, the reaction mechanism should be the same. At the initial stage, the starting Mn(II) complex is converted to the Mn(III) intermediate **3**. Then the active species Mn(V)-oxo complex **4** is formed via synergistic cooperation of ligands and CA in promoting O-O cleavage in the intermediate **3**. The formed Mn(V)-oxo complex directly oxidizes the sulfides to the corresponding sulfoxides along with the formation of Mn(III) intermediate **3**.
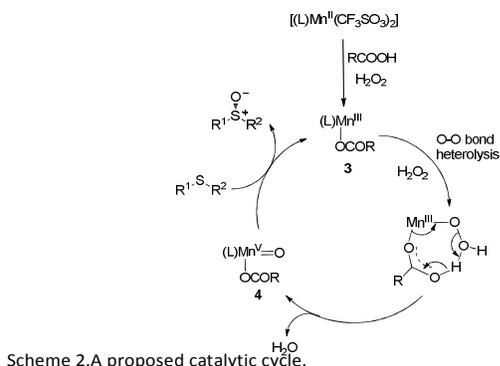

Scheme 2. A proposed catalytic cycle.

The successful results of asymmetric oxidation of sulfides prompted us to further explorethe oxidative kinetic resolution of racemic sulfoxides.As outlined in Scheme 3,we performed the experiments under the optimized conditions using racemic methyl phenyl sulfoxide **2a** and benzyl phenyl sulfoxide**2x** and found that the oxidation of (S)-enantiomer was obviously preferential to (R)-enantiomer with a relative ratio of 7.7 and 11.0, respectively.
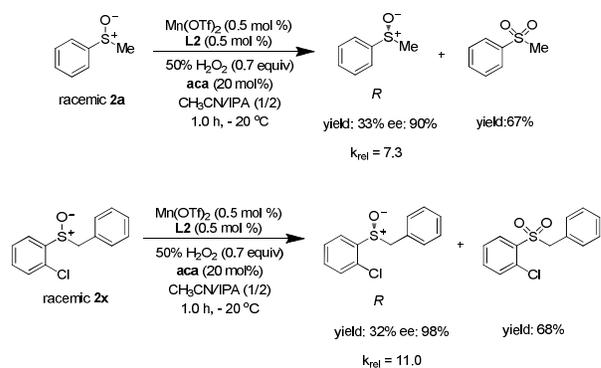
Scheme 3. Oxidative kinetic resolution of racemic **2a** and **2x**.

To further evaluate the practical utility, the asymmetric sulfoxidation was enlarged to a gram scale under the optimized conditions, and the desired product**2b**was furnished with 95% yield and 91% ee (Scheme 4).
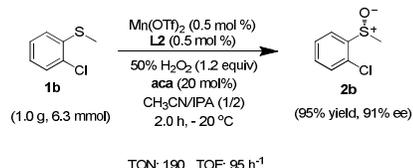
Scheme 4.Gram-scale synthesis of sulfoxide**2b**.

To broaden the application of our methodology, we first focused on the development of a facile route to esomeprazole, which is chiral proton pump inhibitor for the treatment of gastroesophageal reflux disease.[9, 57]Compound **3a**which is the key intermediate for the synthesis of the esomeprazole was treated under the current system, affording the desired product in in 76% yield with up to 87% ee. Furthermore, the synthesis

of **ABZO** was also been achieved. The **ABZO** is the pharmacologically active ingredient of albendazole (**ABZ**) which is a broad-spectrum benzimidazole anthelmintic drug widely used in human and veterinary medicine.[58, 59]The asymmetric oxidation of **ABZ** was carried out in mixed solvent of CH_3CN, IPA and acetic acid with a ratio 1/2/2 because of the solubility of substrate, providing the **ABZO** in 48% yield and 97% ee (Scheme 5).
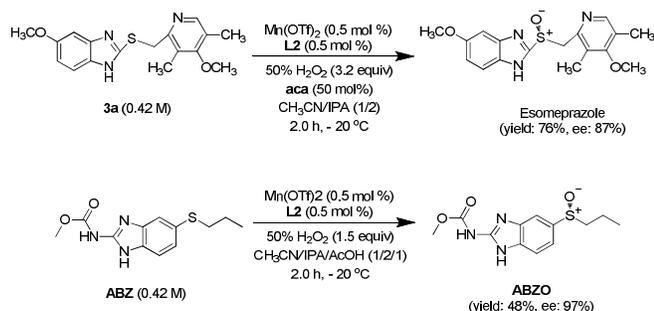
Scheme 5.Synthesis of esomeprazole and **ABZO**.

Conclusions

In summary, we have developed a highly enantioselective asymmetric oxidation of a variety of sulfides by a low loading (0.5 mol%) of inexpensive and readily availablepre-formed manganese complex with H_2O_2.The optically active sulfoxides were obtainedin high yields(up to 95%) with excellent enantioselectivities (>99% ee). The practical application utility of the current system has further been demonstrated by the synthesis ofesomeprazole and **ABZO**.Furthermore, the new methodology was successfully applied to the oxidative kinetic resolution of racemicsulfoxides, providing an alternative approach for the synthesis of optically active sulfoxides. Extension of the strategy to other reactions is ongoing in our laboratory.

Experimental section

General information.

Unless otherwise stated, all reactions and manipulations were carried out under argonatmosphere using standard Schlenk techniques or in an argon-filled glove-box. All chemicals were obtained from commercial sources and were used without further purification.Solvents were treated prior to use according to the 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 $CDCl_3$ or DMSOon 400MHz spectrometers.The chemical shifts for ^{1}H NMR were recorded in ppm downfield from tetramethylsilane (TMS) as the internal standard. The chemical shifts for ^{13}C NMR were recorded in ppm downfield using the central peak of $CDCl_3$ (77.16 ppm) or DMSO (40.58 ppm)as the internal standard. ^{13}CNMR was broad-band decoupled from hydrogen nuclei. Coupling constants (J) are reported in hertz and refer to apparent peak multiplications.

Representative procedures for the asymmetric sulfoxidation.[56]

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 6 h. To the solution of manganese complex was directly added substrate (0.42 mmol), adamantane carboxylic acid (15 mg, 0.084 mmol) and isopropanol (1 mL). Then decrease the temperature to -20 °C, 50 % H_2O_2(34.3 mg, 0.51 mmol) was rapidly added and the mixture was stirred at -20 °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 (10mL x3). Then, the organic layer was combined and 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 sulfoxide.

(R)-(methylsulfinyl)benzene(2a).[52] Colorless oil, purified by column chromatography on silica gel (20% EtOAc in petroleum ether) (52.0 mg, 88% yield, 90% ee). HPLC (DAICEL OD-H, hexane/isopropanol 70:30, flow rate: 0.5 mL/min,220 nm): t_r (major) = 11.1 min, t_r (minor) =13.5 min.

(R)-1-chloro-2-(methylsulfinyl)benzene (2b).[52]Colorless oil, purified by column chromatography on silica gel (20% EtOAc in petroleum ether) (68.9 mg, 94% yield, 95% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.7 Hz, 1H), 7.50 (m, 1H), 7.41 (m, 1H), 7.36 (d, J = 7.7 Hz, 1H), 2.79 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ144.4, 132.5, 130.3, 128.7, 125.9, 42.2; MS (EI) m/z 174.0 (M$^+$); HPLC (DAICEL OD-H, hexane/isopropanol 90:10, flow rate: 0.5 mL/min,220 nm): t_r (major) = 19.4 min, t_r (minor) =20.7 min.

(R)-1-chloro-3-(methylsulfinyl)benzene (2c).[52]Colorless oil, purified by column chromatography on silica gel (20% EtOAc in petroleum ether) (66.0 mg, 90% yield, 98% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ7.64 (s, 1H), 7.46 (m, 3H), 2.72 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 148.5, 136.3, 131.8, 131.2, 124.2, 122.2, 44.6; MS (EI) m/z 174.0 (M$^+$); HPLC (DAICEL OD-H, hexane/isopropanol 95:5, flow rate: 0.5 mL/min,220 nm): t_r (major) = 37.6 min, t_r (minor) = 40.6 min.

(R)-1-chloro-4-(methylsulfinyl)benzene (2d).[52]Colorless oil, purified by column chromatography on silica gel (20% EtOAc in petroleum ether) (66.0 mg, 90% yield, 90% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 8.5 Hz, 2H), 2.68 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ δ 144.9, 137.8, 130.2, 125.5, 44.6; MS (EI) m/z 174.0 (M$^+$); HPLC (DAICEL OB-H, hexane/isopropanol 70:30, flow rate: 0.5 mL/min,220 nm): t_r (minor) = 13.2 min, t_r (major) = 18.4 min.

(R)-1-bromo-2-(methylsulfinyl)benzene (2e).[52]Colorless oil, purified by column chromatography on silica gel (20% EtOAc in petroleum ether) (85.6 mg, 93% yield, 94% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ7.93 (dd, J = 7.8, 1.3 Hz, 1H), 7.63 – 7.51 (m, 2H), 7.35 (dd, J = 7.8, 1.3 Hz, 1H), 2.80 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$)δ133.5, 132.8, 129.3, 126.3, 119.0, 42.5; MS (EI) m/z 220.0 (M$^+$); HPLC (DAICEL OD-H,

hexane/isopropanol 90:10, flow rate: 0.5 mL/min,220 nm): t_r (major) = 20.8 min, t_r (minor) = 22.8 min.

(R)-1-bromo-3-(methylsulfinyl)benzene (2f).[52]Colorless oil, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (84.6 mg, 92% yield, 94% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ7.78 (s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.37 (m,1H), 2.71 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$)δ134.7, 131.4, 127.1, 124.2, 122.7, 44.6; MS (EI) m/z 220.0 (M$^+$); HPLC (DAICEL OD-H, hexane/isopropanol 90:10, flow rate: 0.5 mL/min,220 nm): t_r (major) = 25.0 min, t_r (minor) = 26.9 min.

(R)-1-bromo-4-(methylsulfinyl)benzene (2g).[52]Colorless oil, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (83.7 mg, 91% yield, 90% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.63 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 2.68 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$)δ145.5, 133.1, 126.0, 125.7, 44.6; MS (EI) m/z 220.0 (M$^+$); HPLC (DAICEL OB-H, hexane/isopropanol 70:30, flow rate: 0.5 mL/min,220 nm): t_r (minor) = 14.5 min, t_r (major) = 18.7 min.

(R)-1-fluoro-2-(methylsulfinyl)benzene (2h).[10] Yellow oil, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (61.1 mg, 92% yield, 95% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.87 (m, 1H), 7.50 (m, 1H), 7.40 (m,1H), 7.18 – 7.08 (m, 1H), 2.84 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 157.5 (d, *J* = 247.5 Hz), 132.7, 132.6, 125.4, 115.8, 115.6, 42.1; MS (EI) m/z 158.0 (M$^+$); HPLC (DAICEL OB-H, hexane/isopropanol 70:30, flow rate: 0.5 mL/min,220 nm): t_r (minor) = 11.7 min, t_r (major) = 19.2 min.

(R)-1-methoxy-2-(methylsulfinyl)benzene (2i).[60]Colorless oil, purified by column chromatography on silica gel (50% EtAc in petroleum ether) (64.3 mg, 90% yield, 90% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.82 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.55 – 7.37 (m, 1H), 7.19 (m, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 3.89 (s, 3H), 2.77 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 154.8, 133.2, 131.9, 124.6, 121.7, 110.6, 55.7, 41.2; MS (EI) m/z 170.1 (M$^+$); HPLC (DAICEL OD-H, hexane/isopropanol 90:10, flow rate: 0.5 mL/min,254 nm): t_r (minor) = 25.8 min, t_r (major) =29.0 min.

(R)-methyl 2-(methylsulfinyl)benzoate (2j).[60]Colorless oil, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (79.1 mg, 95% yield, 80% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.27 (d, *J* = 7.9 Hz, 1H), 8.05 (d, *J* = 7.7 Hz, 1H), 7.85 – 7.71 (m, 1H), 7.54 (m, 1H), 3.91 (s, 3H), 2.81 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$)δ 166.30, 151.0, 134.7, 131.3, 130.8, 127.0, 124.7, 53.2, 44.6; MS (EI) m/z 198.0 (M$^+$); HPLC (DAICEL OD-H, hexane/isopropanol 90:10, flow rate: 0.5 mL/min,254 nm): t_r (minor) = 25.8 min, t_r (major) =29.0 min.

(R)-2-(phenylsulfinyl)ethanol(2k).[61]Colorless oil, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (62.9 mg, 88% yield, 87% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.60 (m, 2H), 7.47 (m, 3H), 4.34 (s, 1H), 4.10 (m, 1H), 3.96 – 3.84 (m, 1H), 3.05 (m, 1H), 2.96 – 2.86 (m, 1H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$)δ143.6, 131.8, 130.0, 124.6, 60.1, 56.8; MS (EI) m/z 170.2 (M$^+$); HPLC (DAICEL OD-H,

hexane/isopropanol 70:30, flow rate: 0.5 mL/min,220 nm): t_r (major) = 10.0 min, t_r (minor) = 11.1 min.

(R)-2-(methylsulfinyl)naphthalene(2l).[6]White solid, purified by column chromatography on silica gel (50% EtAc in petroleum ether) (71.1 mg, 89% yield, 95% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.22 (s, 1H), 7.99 (d, *J* = 8.6 Hz, 1H), 7.93 (m, 2H), 7.60 (m, 3H), 2.79 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 142.9, 134.5, 133.0, 129.6, 128.5, 128.1, 127.8, 127.4, 124.1, 119.5, 43.8; MS (EI) m/z 190.0 (M$^+$); HPLC (DAICEL OD-H, hexane/isopropanol 70:30, flow rate: 0.5 mL/min,220 nm): t_r (major) = 15.1 min, t_r (minor) = 17.2 min.

(R)-1-chloro-3-(ethylsulfinyl)benzene (2m).[62]Colorless oil, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (73.0 mg, 92% yield, 97% ee). ^{1}H NMR (400 MHz, CDCl$_3$) 1H NMR (400 MHz, CDCl3) δ 7.62 (d, *J* = 0.9 Hz, 1H), 7.46 (m, 3H), 2.93 (m, 1H), 2.83 – 2.66 (m, 1H), 1.22 (t, *J* = 7.4 Hz, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 145.6, 135.6, 131.1, 130.3, 124.3, 122.3,50.3,5.8; MS (EI) m/z 188.0 (M$^+$); HPLC (DAICEL OB-H, hexane/isopropanol 70:30, flow rate: 0.5 mL/min,220 nm): t_r (minor) = 11.7 min, t_r (major) = 15.5 min.

(R)-1-chloro-2-(ethylsulfinyl)benzene (2n).[62]Colorless oil, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (73.0 mg, 92% yield, 92% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.88 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.51 (m, 1H), 7.42 (m, 2H), 3.13 (m, 1H), 2.86 (m, 1H), 1.25 (t, *J* = 7.4 Hz, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 141.0, 131.9, 130.1, 130.0, 127.7, 126.6, 47.1, 5.7; MS (EI) m/z 188.0 (M$^+$); HPLC (DAICEL OD-H, hexane/isopropanol 90:10, flow rate: 0.5 mL/min,220 nm): t_r (major) = 15.1 min, t_r (minor) = 16.0 min.

(R)-1-(butylsulfinyl)-2-chlorobenzene (2o).[62]Colorless oil, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (79.2 mg, 87% yield, 95% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.51 (m, 1H), 7.41 (m, 2H), 3.08 (m, 1H), 2.78 (m, 1H), 1.94 – 1.84 (m, 1H), 1.68 – 1.33 (m, 3H), 0.94 (t, *J* = 7.3 Hz, 3H).;^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 142.0, 131.8, 130.0, 129.7, 127.8, 126.2, 54.2, 24.1, 21.8, 13.6; HRMS (ESI-TOF) m/z calcd for C$_{10}$H$_{14}$ClOS [M+H]+217.0454, found 217.0455; HPLC (DAICEL OB-H, hexane/isopropanol 70:30, flow rate: 0.5 mL/min,220 nm): t_r (minor) = 9.2 min, t_r (major) = 15.0 min.

(R)-1-chloro-2-(pentylsulfinyl)benzene (2p).[62]Colorless oil, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (85.3 mg, 88% yield, 95% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.51 (m,1H), 7.41 (m, 2H), 3.07 (m, 1H), 2.77 (m, 1H), 1.93 – 1.82 (m, 1H), 1.71 – 1.58 (m, 1H), 1.54 – 1.29 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 142.0, 131.8, 130.0, 129.7, 127.8, 126.1, 54.5, 30.6, 22.2, 21.8, 13.8; HRMS (ESI-TOF) m/z calcd for C$_{11}$H$_{16}$ClOS [M+H]+231.0610, found 231.0626; HPLC (DAICEL OB-H, hexane/isopropanol 85:15, flow rate: 0.5 mL/min,220 nm): t_r (minor) = 9.7 min, t_r (major) =21.9 min.

(R)-1-bromo-2-(ethylsulfinyl)benzene (2q).[62]Colorless oil, purified by column chromatography on silica gel (20% EtAc

in petroleum ether) (93.0 mg, 95% yield, 94% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.86 (dd, J = 8.0, 1.6 Hz, 1H), 7.56 (m, 2H), 7.36 (m, 1H), 3.13 (m, 1H), 2.85 (m, 1H), 1.26 (t, J = 7.4 Hz, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 142.9, 133.0, 132.1, 128.2, 127.0, 118.8, 47.4, 5.8; MS (EI) m/z 233.9 (M[+]); HPLC (DAICEL OD-H, hexane/isopropanol 90:10, flow rate: 0.5 mL/min,220 nm): t$_r$ (major) = 15.2 min, t$_r$ (minor) = 17.3 min.

(R)-1-bromo-2-(butylsulfinyl)benzene (2r).[62]Colorless oil, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (104.0 mg, 90% yield, 91% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 (dd, J = 8.0, 1.6 Hz, 1H), 7.56 (m, 2H), 7.36 (m, 1H), 3.10 (m, 1H), 2.76 (m, 1H), 1.90 (m, 1H), 1.69 – 1.57 (m, 1H), 1.56 – 1.39 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 143.8, 132.9, 132.1, 128.4, 126.6, 118.7, 54.6, 24.2, 21.8, 13.7; HRMS (ESI-TOF) m/z calcd for C$_{10}$H$_{14}$BrOS [M+H]+ 260.9949, found 260.9941; HPLC (DAICEL OB-H, hexane/isopropanol 70:30, flow rate: 0.5 mL/min,220 nm): t$_r$ (minor) = 8.8 min, t$_r$ (major) = 15.7 min.

(R)-1-bromo-2-(pentylsulfinyl)benzene (2s).[62]Colorless oil, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (100.9 mg, 92% yield, 91% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 (dd, J = 8.0, 1.6 Hz, 1H), 7.66 – 7.47 (m, 2H), 7.36 (m, 1H), 3.09 (m, 1H), 2.84 – 2.65 (m, 1H), 1.91 (m, 1H), 1.74 – 1.60 (m, 1H), 1.54 – 1.30 (m, 4H), 0.90 (t, J = 7.1 Hz, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$)δ 143.8, 132.9, 132.1, 128.4, 126.6, 118.7, 54.8, 30.6, 22.3, 22.0, 13.8; HRMS (ESI-TOF) m/z calcd for C$_{11}$H$_{16}$BrOS [M+H]+ 277.0085, found 277.0080; HPLC (DAICEL OB-H, hexane/isopropanol 70:30, flow rate: 0.5 mL/min,220 nm): t$_r$ (minor) = 9.4 min, t$_r$ (major) = 15.4 min.

(R)-(benzylsulfinyl)benzene (2t).[43, 52]White solid, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (81.8 mg, 90% yield, 98% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ7.44 – 7.35 (m, 4H), 7.29 – 7.22 (m, 4H), 7.01 – 6.91 (m, 2H), 4.08 (d, J = 12.6 Hz, 1H), 3.98 (d, J = 12.6 Hz, 1H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 131.7, 130.9, 129.4, 129.0, 128.8, 125.0, 64.2; HRMS (ESI-TOF) m/z calcd for C$_{13}$H$_{13}$OS [M+H]+217.0687, found 217.0684; HPLC (DAICEL OD-H, hexane/isopropanol 90:10, flow rate: 1.0 mL/min,220 nm): t$_r$ (major) = 14.1 min, t$_r$ (minor) = 17.6 min.

(R)-1-(benzylsulfinyl)-2-methylbenzene (2u).[43, 52]White solid, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (87.1 mg, 90% yield, 99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.70 (m, 1H), 7.33 (m, 2H), 7.25(d, J = 7.8, 1H), 7.23 (d, J = 7.8, 1H), 7.20 (m, 1H), 7.15 – 7.05 (m, 1H), 6.96 (m, 2H), 4.07 (d, J = 12.5 Hz, 1H), 3.98 (d, J = 12.5 Hz, 1H), 2.05 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 136.1, 131.5, 130.9, 130.7, 129.0, 128.8, 127.7, 124.8, 62.9, 18.6; HRMS (ESI-TOF) m/z calcd for C$_{14}$H$_{15}$OS [M+H]+231.0844, found 231.0844; HPLC (DAICEL OD-H, hexane/isopropanol 90:10, flow rate: 1.0 mL/min,220 nm): t$_r$ (major) = 13.2 min, t$_r$ (minor) = 16.7 min.

(R)-1-(benzylsulfinyl)-3-methylbenzene (2v).[43, 52]White solid, purified by column chromatography on silica gel (20% EtAc

in petroleum ether) (88.0 mg, 91% yield, 92% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32 – 7.20 (m, 5H), 7.20 – 7.11 (m, 2H), 6.98 (dd, J = 7.7, 1.4 Hz, 2H), 4.06 (d, J = 12.6 Hz, 1H), 3.95 (d, J = 12.6 Hz, 1H), 2.32 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ139.6, 132.5, 131.0, 129.2, 129.0, 128.8, 125.3, 122.1, 64.3, 21.9; HRMS (ESI-TOF) m/z calcd for C$_{14}$H$_{15}$OS [M+H]+231.0847, found 231.0844; HPLC (DAICEL OD-H, hexane/isopropanol 90:10, flow rate: 1.0 mL/min,220 nm): t$_r$ (major) = 12.3 min, t$_r$ (minor) = 15.4 min.

(R)-1-(benzylsulfinyl)-4-methylbenzene (2w).[43, 52]White solid, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (87.1 mg, 90% yield, 98% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ7.24 (m, 5H),7.22(d, J = 7.6 Hz, 2H), 6.98 (d, J = 7.6 Hz, 2H), 4.08 (d, J = 12.5 Hz, 1H), 3.95 (d, J = 12.5 Hz, 1H), 2.38 (s, 3H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 130.9, 130.1, 129.2, 129.0, 128.8, 125.1, 64.3, 22.0; HRMS (ESI-TOF) m/z calcd for C$_{14}$H$_{15}$OS [M+H]+231.0847, found 231.0844; HPLC (DAICEL OD-H, hexane/isopropanol 90:10, flow rate: 1.0 mL/min,220 nm): t$_r$ (major) = 13.5 min, t$_r$(minor) = 16.4 min.

(R)-1-(benzylsulfinyl)-2-chlorobenzene (2x).[48]White solid, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (100.0 mg, 95% yield, >99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) 1H NMR (400 MHz, CDCl3) δ 7.48 – 7.43 (m, 1H), 7.38 (m, 2H), 7.32 (m, 1H), 7.28 – 7.22 (m, 3H), 7.05 (dd, J = 7.7, 1.2 Hz, 2H), 4.29 (d, J = 13.1 Hz, 1H), 4.03 (d, J = 13.1 Hz, 1H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 140.8, 131.9, 130.4, 130.1, 129.4, 129.3, 128.3, 127.6, 126.8,59.7; HRMS (ESI-TOF) m/z calcd for C$_{13}$H$_{12}$ClOS [M+H]+251.0297, found 251.0293; HPLC (DAICEL OB-H, hexane/isopropanol 90:10, flow rate: 1.0 mL/min,220 nm): t$_r$ (minor) = 10.4 min, t$_r$ (major) = 13.2 min.

(R)-1-(benzylsulfinyl)-3-chlorobenzene (2y).[48]White solid, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (98.0 mg, 93% yield, 93% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.45 – 7.40 (m, 1H), 7.37 – 7.25 (m, 5H), 7.20 (d, J = 7.7 Hz, 1H), 7.04 – 6.92 (m, 2H), 4.10 (d, J = 12.6 Hz, 1H), 4.00 (d, J = 12.6 Hz, 1H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 145.0, 135.3, 131.3, 130.4, 130.0,128.7, 128.6, 128.5,124.5, 122.5, 63.6; HRMS (ESI-TOF) m/z calcd for C$_{13}$H$_{12}$ClOS [M+H]+ 251.0297, found 251.0299; HPLC (DAICEL OD-H, hexane/isopropanol 95:5, flow rate: 0.7 mL/min,220 nm): t$_r$ (major) = 37.0 min, t$_r$ (minor) = 39.4 min.

(R)-1-(benzylsulfinyl)-2-bromobenzene (2z).[48]White solid, purified by column chromatography on silica gel (20% EtAc in petroleum ether) (116.5 mg, 94% yield, >99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.56 (dd, J = 7.7, 1.1 Hz, 1H), 7.43 (dd, J = 7.7, 1.9 Hz, 1H), 7.40 – 7.21 (m, 5H), 7.07 (m, 2H), 4.30 (d, J = 13.1 Hz, 1H), 4.04 (d, J = 13.1 Hz, 1H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$)δ 142.5, 132.6, 132.2, 130.4, 129.4, 128.9, 128.8, 128.1, 127.2, 118.8, 59.9; HRMS (ESI-TOF) m/z calcd for C$_{13}$H$_{12}$BrOS [M+H]+296.9772, found 296.9774; HPLC (DAICEL OB-H, hexane/isopropanol 90:10, flow rate: 1.0 mL/min,220 nm): t$_r$= 14.9 min.

(R)-6-chlorothiochroman-4-one 1-oxide (3a).[63] White solid, purified by column chromatography on silica gel (50% EtAc

in petroleum ether) (68.5 mg, 76% yield, 92% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.07 (d, J = 2.2 Hz, 1H), 7.77 (d, J = 8.3 Hz, 1H), 7.67 (dd, J = 8.3, 2.2 Hz, 1H), 3.46 – 3.39 (m, 3H), 2.92 – 2.81 (m, 1H); ^{13}C {^{1}H} NMR (101 MHz, CDCl$_3$) δ 190.9, 143.9, 139.1, 134.5, 130.5, 130.2, 129.0, 46.8, 30.3; HRMS (ESI-TOF) m/z calcd for C$_9$H$_8$ClO$_2$S [M+H]+ 214.9934, found 214.9935;HPLC (DAICEL AD-H, hexane/isopropanol 90:10, flow rate: 1.0 mL/min,220 nm): t$_r$ (major) = 30.2 min, t$_r$ (minor) = 31.3 min.

(R)-dibenzo[b,e]thiepin-11(6H)-one 5-oxide (3b).[63]White solid, purified by column chromatography on silica gel (20% EtOAc in petroleum ether) (92.6 mg, 91% yield, 94% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.27 – 8.11 (m, 2H), 8.03 (m, 1H), 7.78 (m, 1H), 7.62 (m, 2H), 7.49 (m, 1H), 7.40 (d, J = 7.5 Hz, 1H), 4.85 (d, J = 13.6 Hz, 1H), 4.29 (d, J = 13.6 Hz, 1H);^{13}C {^{1}H} NMR (100 MHz, CDCl$_3$) δ 190.3, 147.0, 138.1, 134.1, 133.4, 132.5, 132.0, 131.4, 130.8, 129.1, 128.0, 124.3, 61.1; HRMS (ESI-TOF) m/z calcd for C$_{14}$H$_{11}$O$_2$S [M+H]+ 243.0480, found 243.0483; HPLC (DAICEL OD-H, hexane/isopropanol 80:20, flow rate: 1.0 mL/min,220 nm): t$_r$ (minor) = 17.8 min, t$_r$ (major) =20.8 min.

Experimental procedure for thegram scale synthesis of 2b.

A mixture of Mn(OTf)$_2$ (11. 1mg, 0.032 mmol) and **L2** (15.2mg, 0.032 mmol) in CH$_3$CN (5 mL) was stirred at room temperature for 8 h. To the solution of manganese complex was added **1b** (1.0 g, 6.30 mmol), adamantane carboxylic acid (227mg, 1.26 mmol)and IPA (10 mL). Then decrease the temperature to -20 °C, 50 % H$_2$O$_2$(514mg, 7.56 mmol) was added dropwise to the stirring reaction over 1 min and the mixture was stirred at -20 °C for 2 h. The reaction was quenched by adding the sat. aq. NaHCO$_3$ (15 mL)and extracted with EtOAc (15 mL x 4). The organic layer was separated and washed with brine, dried over MgSO$_4$ and concentrated at reduced pressure. The residue was purified by silica gel column chromatographyto afford the **2b** (1.04 g, 95% yield, 91% ee).

Experimental procedure for thesynthesis of esomeprazole.[56]

A solution of Mn(OTf)$_2$ (0.0084 M solution in CH$_3$CN, 0.25 mL, 0.0021 mmol) was added to **L2** (0.0084 M solution in CH$_3$CN, 0.25 mL, 0.0021 mmol) at room temperature. The reaction mixture was stirred at room temperature for 6 h. To the solution of manganese complex was directly added **3a** (138 mg, 0.42 mmol), adamantane carboxylic acid (37.5 mg, 0.21 mmol) and isopropanol (1 mL). Then decrease the temperature to -20 °C, 50 % H$_2$O$_2$(91.1 mg, 1.34 mmol) was rapidly added and the mixture was stirred at -20 °C for 2.0 h. At this point, a saturated aqueous solution of NaHCO$_3$ (4 mL) was added and the resulting mixture was extracted with EtOAc (10mL x3). Then, the organic layer was combined and washed with brine, dried over MgSO$_4$ and concentrated at reduced pressure. The residue was purified by silica gel column chromatography to afford the esomeprazole (110 mg, 76% yield, 87% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ12.45 (s, 1H), 8.17 (s, 1H), 7.58 (s, 1H), 6.88 (dt, J = 23.3, 11.7 Hz, 2H), 4.83 – 4.65 (m, 2H), 3.80 (s, 3H), 3.56 (s, 3H), 2.18 (s, 3H), 2.08 (s, 3H);^{13}C {^{1}H} NMR (100

MHz, CDCl$_3$) δ164.9, 150.2, 149.3, 127.5, 126.9, 61.2, 60.4, 56.3, 13.9, 12.0;HRMS (ESI-TOF) m/z calcd for C$_{17}$H$_{20}$N$_3$O$_3$S [M+H]+ 346.1225, found 346.1231; HPLC (DAICEL OD-H, hexane/isopropanol 80:20, flow rate: 1.0 mL/min,220 nm): t$_r$ (minor) = 10.9 min, t$_r$ (major) = 13.4 min.

Experimental procedure for thesynthesis of ABZO.[56]

A solution of Mn(OTf)$_2$ (0.0084 M solution in CH$_3$CN, 0.25 mL, 0.0021 mmol) was added to **L2** (0.0084 M solution in CH$_3$CN, 0.25 mL, 0.0021 mmol) at room temperature. The reaction mixture was stirred at room temperature for 6 h. To the solution of manganese complex was directly added **ABZ** (111.4 mg, 0.42 mmol, dissolved with 1.0 mL CH$_3$COOH) and isopropanol (1 mL). Then decrease the temperature to -20 °C, 50 % H$_2$O$_2$(42.8 mg, 0.63 mmol) was rapidly added and the mixture was stirred at -20 °C for 2.0 h. At this point, a saturated aqueous solution of NaHCO$_3$ (10 mL) was added and the resulting mixture was extracted with EtOAc (5mL x 6). Then, the organic layer was combined and washed with brine, dried over MgSO$_4$ and concentrated at reduced pressure. The residue was purified by silica gel column chromatography to afford the esomeprazole(56.7 mg, 48% yield, 99% ee). ^{1}H NMR (400 MHz, DMSO) δ 11.81 (s, 2H), 7.68 (s, 1H), 7.53 (d, J = 8.3 Hz, 1H), 7.29 (dd, J = 8.3, 1.5 Hz, 1H), 3.75 (s, 3H), 2.86 – 2.66 (m, 2H), 1.64 – 1.52 (m, 1H), 1.45 (m, 1H), 0.91 (t, J = 7.8 Hz, 3H);^{13}C {^{1}H} NMR (100 MHz, DMSO)δ 155.5, 149.7, 137.2, 117.8, 59.3, 53.6, 16.5, 14.0; HRMS (ESI-TOF) m/z calcd for C$_{12}$H$_{15}$N$_3$O$_3$S [M+H]+ 282.0912, found 282.0918; HPLC (DAICEL OB-H, hexane/isopropanol 80:20, flow rate: 1.0 mL/min,220 nm): t$_r$ (minor) = 11.4 min, t$_r$ (major) = 16.4 min.

Acknowledgements

Notes and references

^{a}Dalian National Laboratory for Clean Energy, Dalian Institute of Chemical Physics, Chinese Academy of Sciences,Dalian, 116023, People's Republic of China. E-mail: sgao@dicp.ac.cn; Fax: +086-0411-84379248; Tel: +086-0411-84379248

^{b}University of Chinese Academy of Sciences, Beijing, 10049, People's Republic of China.

1. R. Bentley, *Chem. Soc. Rev.*, 2005, **34**, 609-624.
2. M. C. Carreño, G. Hernández-Torres, M. Ribagorda and A. Urbano, *Chem. Commun.*, 2009, 6129-6144.
3. I. Fernández and N. Khiar, *Chem. Rev.*, 2003, **103**, 3651-3706.
4. S. Kobayashi, C. Ogawa, H. Konishi and M. Sugiura, *J. Am. Chem. Soc.*, 2003, **125**, 6610-6611.
5. J. Legros, J. R. Dehli and C. Bolm, *Adv. Synth. Catal.*, 2005, **347**, 19-31.
6. S. Liao, I. Ćorić, Q. Wang and B. List, *J. Am. Chem. Soc.*, 2012, **134**, 10765-10768.
7. M. Mellah, A. Voituriez and E. Schulz, *Chem. Rev.*, 2007, **107**, 5133-5209.
8. H. Myrick, R. Malcolm, B. Taylor and S. LaROWE, *Ann. Clin. Psychiatry*, 2004, **16**, 101-109.

9. E. Wojaczynska and J. Wojaczynski, *Chem. Rev.*, 2010, **110**, 4303-4356.

10. R. DeepanáChakravarthy and D. KumaráChand, *Green Chem.*, 2014, **16**, 2190-2196.

11. C. O. Kinen, L. I. Rossi and R. H. de Rossi, *Green Chem.*, 2009, **11**, 223-228.

12. P. C. áBulman Page, *Green Chem.*, 2012, **14**, 2221-2225.

13. J. J. Boruah, S. P. Das, S. R. Ankireddy, S. R. Gogoi and N. S. Islam, *Green Chem.*, 2013, **15**, 2944-2959.

14. B. Li, A.-H. Liu, L.-N. He, Z.-Z. Yang, J. Gao and K.-H. Chen, *Green Chem.*, 2012, **14**, 130-135.

15. M. V. Gómez, R. Caballero, E. Vazquez, A. Moreno, A. de la Hoz and A. Diaz-Ortiz, *Green Chem.*, 2007, **9**, 331-336.

16. W. Al-Maksoud, S. Daniele and A. B. Sorokin, *Green Chem.*, 2008, **10**, 447-451.

17. A. Rezaeifard, M. Jafarpour, A. Naeimi and R. Haddad, *Green Chem.*, 2012, **14**, 3386-3394.

18. P. K. Dornan, K. G. Kou, K. Houk and V. M. Dong, *J. Am. Chem. Soc.*, 2013, **136**, 291-298.

19. M. Hibi, T. Kawashima, H. Yajima, S. V. Smirnov, T. Kodera, M. Sugiyama, S. Shimizu, K. Yokozeki and J. Ogawa, *Tetrahedron: Asymmetry*, 2013, **24**, 990-994.

20. Z.-Z. Li, S.-Y. Yao, J.-J. Wu and B.-H. Ye, *Chem. Commun.*, 2014, **50**, 5644-5647.

21. K. A. Stingl and S. B. Tsogoeva, *Tetrahedron: Asymmetry*, 2010, **21**, 1055-1074.

22. P. Pitchen, E. Dunach, M. Deshmukh and H. Kagan, *J. Am. Chem. Soc.*, 1984, **106**, 8188-8193.

23. C. Bolm and F. Bienewald, *Angew. Chem. Int. Ed. Engl.*, 1996, **34**, 2640-2642.

24. C. Drago, L. Caggiano and R. F. Jackson, *Angew. Chem.*, 2005, **117**, 7387-7389.

25. J. Skarżewski, E. Ostrycharz and R. Siedlecka, *Tetrahedron: Asymmetry*, 1999, **10**, 3457-3461.

26. J. Sun, C. Zhu, Z. Dai, M. Yang, Y. Pan and H. Hu, *J. Org. Chem.*, 2004, **69**, 8500-8503.

27. M. Hinch, O. Jacques, C. Drago, L. Caggiano, R. F. Jackson, C. Dexter, M. S. Anson and S. J. Macdonald, *J. Mol. Catal. A: Chem.*, 2006, **251**, 123-128.

28. I. Mohammadpoor-Baltork, M. Hill, L. Caggiano and R. F. Jackson, *Synlett*, 2006, **2006**, 3540-3544.

29. B. Pelotier, M. S. Anson, I. B. Campbell, S. J. Macdonald, G. Priem and R. F. Jackson, *Synlett*, 2002, **2002**, 1055-1060.

30. A. H. Vetter and A. Berkessel, *Tetrahedron Lett.*, 1998, **39**, 1741-1744.

31. M. Palucki, P. Hanson and E. N. Jacobsen, *Tetrahedron Lett.*, 1992, **33**, 7111-7114.

32. C. Kokubo and T. Katsuki, *Tetrahedron*, 1996, **52**, 13895-13900.

33. K. Noda, N. Hosoya, R. Irie, Y. Yamashita and T. Katsuki, *Tetrahedron*, 1994, **50**, 9609-9618.

34. S. Schoumacker, O. Hamelin, J. Pécaut and M. Fontecave, *Inorg. Chem.*, 2003, **42**, 8110-8116.

35. K. P. Bryliakov and E. P. Talsi, *Angew. Chem.*, 2004, **116**, 5340-5342.

36. K. P. Bryliakov and E. P. Talsi, *Chem. Eur. J.*, 2007, **13**, 8045-8050.

37. H. Egami and T. Katsuki, *J. Am. Chem. Soc.*, 2007, **129**, 8940-8941.

38. J. Legros and C. Bolm, *Angew. Chem. Int. Ed.*, 2003, **42**, 5487-5489.

39. J. Legros and C. Bolm, *Angew. Chem.*, 2004, **116**, 4321-4324.

40. J. Legros and C. Bolm, *Chem. Eur. J.*, 2005, **11**, 1086-1092.

41. J. Fujisaki, K. Matsumoto, K. Matsumoto and T. Katsuki, *J. Am. Chem. Soc.*, 2010, **133**, 56-61.

42. P. Kelly, S. E. Lawrence and A. R. Maguire, *Synlett*, 2007, **2007**, 1501-1506.

43. G. E. O'Mahony, A. Ford and A. R. Maguire, *J. Org. Chem.*, 2012, **77**, 3288-3296.

44. T. Yamaguchi, K. Matsumoto, B. Saito and T. Katsuki, *Angew. Chem. Int. Ed.*, 2007, **46**, 4729-4731.

45. F. Di Furia, G. Modena and R. Seraglia, *Synthesis*, 1984, **1984**, 325-326.

46. M. I. Donnoli, S. Superchi and C. Rosini, *J. Org. Chem.*, 1998, **63**, 9392-9395.

47. N. Komatsu, Y. Nishibayashi, T. Sugita and S. Uemura, *Tetrahedron Lett.*, 1992, **33**, 5391-5394.

48. F. Naso, M. A. M. Capozzi, A. Bottoni, M. Calvaresi, V. Bertolasi, F. Capitelli and C. Cardellicchio, *Chem. Eur. J.*, 2009, **15**, 13417-13426.

49. P. Saisaha, J. W. de Boer and W. R. Browne, *Chem. Soc. Rev.*, 2013, **42**, 2059-2074.

50. B. Saito and T. Katsuki, *Tetrahedron Lett.*, 2001, **42**, 3873-3876.

51. Y. Yamanoi and T. Imamoto, *J. Org. Chem.*, 1997, **62**, 8560-8564.

52. W. Dai, J. Li, B. Chen, G. Li, Y. Lv, L. Wang and S. Gao, *Org. Lett.*, 2013, **15**, 5658-5661.

53. O. Cussó, I. Garcia-Bosch, X. Ribas, J. Lloret-Fillol and M. Costas, *J. Am. Chem. Soc.*, 2013, **135**, 14871-14878.

54. O. Y. Lyakin, R. V. Ottenbacher, K. P. Bryliakov and E. P. Talsi, *ACS Catalysis*, 2012, **2**, 1196-1202.

55. R. V. Ottenbacher, D. G. Samsonenko, E. P. Talsi and K. P. Bryliakov, *ACS Catalysis*, 2014, **4**, 1599-1606.

56. W. Dai, S. Shang, B. Chen, G. Li, L. Wang, L. Ren and S. Gao, *J. Org. Chem.*, 2014, **79**, 6688-6694.

57. H. Cotton, T. Elebring, M. Larsson, L. Li, H. Sörensen and S. von Unge, *Tetrahedron: Asymmetry*, 2000, **11**, 3819-3825.

58. M. Del Nozal, L. Toribio, J. Bernal, E. Nieto and J. Jiménez, *J. Biochem. Bioph. Methods*, 2002, **54**, 339-345.

59. W. Thormann, F. Prost and A. Procházková, *J. Pharm. Biomed. Anal.*, 2002, **27**, 555-567.

60. A. Massa, V. Mazza and A. Scettri, *Tetrahedron: Asymmetry*, 2005, **16**, 2271-2275.

61. F. Secundo, G. Carrea, S. Dallavalle and G. Franzosi, *Tetrahedron: Asymmetry*, 1993, **4**, 1981-1982.

62. S. Liao and B. List, *Adv. Synth. Catal.*, 2012, **354**, 2363-2367.

63. K. Matsumoto, T. Yamaguchi and T. Katsuki, *Heterocycles*, 2008, **76**, 191-196.

Footnotes

Enantioselective oxidation of sulfides with H_2O_2 catalyzed by an *in situ*-formed manganese complex

Wen Dai [ab], Guosong Li [a], Lianyue Wang [a], Bo Chen [ab], Sensen Shang [ab], Ying Lv [a], and Shuang Gao*[a]

[a] Dalian National Laboratory for Clean Energy, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, 116023, People's Republic of China. E-mail: sgao@dicp.ac.cn; Fax: +086-0411-84379248; Tel: +086-0411-84379248

[b] University of Chinese Academy of Sciences, Beijing, 10049, People's Republic of China.
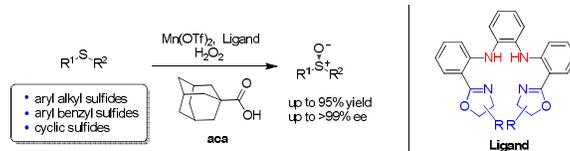
A facile and environmentally friendly method is presented for the asymmetric oxidation of sulfides with H_2O_2 by an *in situ*-formed manganese complex, affording the corresponding chiral sulfoxides in high yields and excellent enantioselectivities.