Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 4549–4556

TETRAHEDRON

Chiral ligand-controlled catalytic asymmetric epoxidation of α,β-unsaturated carbonyl compounds with peroxide

Yoshihito Tanaka, Katsumi Nishimura and Kiyoshi Tomioka*

Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan

Received 2 April 2003; accepted 24 April 2003

Abstract—Asymmetric epoxidation reaction of α,β-unsaturated carbonyl compounds with alkylperoxide was catalyzed by an external chiral tridentate aminodiether–lithium peroxide giving epoxides with good enantiomeric excess. Slow addition of alkylhydroperoxide was beneficial for a catalytic asymmetric reaction. Lone pair electron-differentiating coordination of a carbonyl oxygen to lithium is another critical factor for high enantioselectivity.

1. Introduction

Reflecting the importance of chiral epoxides in chemical synthesis of biologically active compounds, many asymmetric epoxidation reactions of olefins have been reported. These reactions are categorized into two types: one is an electrophilic addition of chirally modified oxygen reagents to olefins, and the other is a nucleophilic addition of chirally modified oxygen reagents to electron-deficient olefins such as α,β-unsaturated carbonyl compounds. The typical examples of the former type reaction are Sharpless–Katsuki asymmetric epoxidation of allylic alcohol[1] and asymmetric epoxidation using chiral salen complexes[2] as well as chiral ketones in situ convertible to dioxirane species.[3] Recently, the latter type asymmetric epoxidation of an electron-deficient olefin has attracted widespread attention,[4] and efficient methods using highly reactive oxygen-equivalent reagents have been reported. The characteristic of such oxygen-equivalent active reagents is a combined use of external chiral ligands and peroxides activated by zinc,[5] magnesium,[6] and lanthanides.[7,8]

We have been involved in development of methodologies for the catalytic asymmetric conjugate addition and 1,2-addition reactions of organolithiums and lithium ester enolates with α,β-unsaturated carbonyl compounds, ketones and imines under the catalysis of external chiral ligands.[9,10] We have also found that these methodologies are applicable to asymmetric conjugate addition reactions of heteroatom nucleophiles such as lithium thiolate[11] and lithium amide.[12] In this paper, we describe a catalytic asymmetric epoxidation reaction of α,β-unsaturated carbonyl compounds using an external chiral ligand and lithium alkylperoxide as an oxygen nucleophile (Scheme 1). Our strategy for the nucleophilic asymmetric epoxidation relies on the double activation of a peroxide by lithiation and subsequent chelate formation with a chiral ligand.[13]

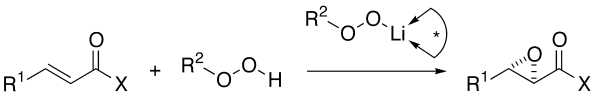
2. Results and discussion

2.1. Synthesis of chiral ligands

The tridentate ligands having a methoxyphenyl group, **1**[14] and **2**,[15] were prepared according to previously reported our procedure (Fig. 1). Chiral ligand **5** was prepared from proline-derived chloride **3**[16] and guaiacol **4**.[17] Chiral ligand **9** having a cyclohexane ring was prepared from amino alcohol **6**[18] and chromium complex **7**[19] through *O*-arylation and subsequent dechromination of **8** with iodine.

The bidentate ligands **10**–**13** were prepared according to previously reported our procedure (Fig. 2).[20]

A chiral ligand having a methoxyethyl side chain **17** was synthesized according to our previously reported procedure (Fig. 3).[21] The ligands having a chiral side chain, **18***r* and **18***s*, were synthesized by an alkylation of **14**[22] with the corresponding chiral styrene oxides **15**[23] and subsequent methylation of **16** with methyl tosylate.



Scheme 1. Asymmetric conjugate addition-type epoxidation with chiral ligand-lithium hydroperoxide catalysis.

Keywords: conjugate addition; lithium cumene hydroperoxide; enantioselectivity; slow addition; chiral ligand.

* Corresponding author. Tel.: +81-75-753-4553; fax: +81-75-753-4604; e-mail: tomioka@pharm.kyoto-u.ac.jp

0040–4020/03/$ - see front matter
doi:10.1016/S0040-4020(03)00658-6

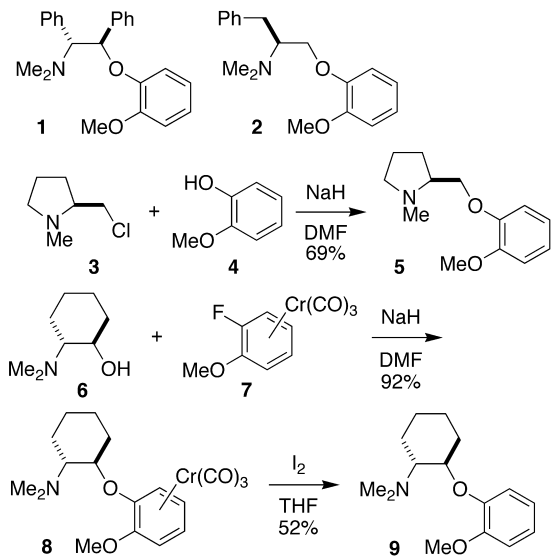


Figure 1. Synthesis of chiral ligands having a methoxyphenyl group.

Chiral ligands **19** and **20** having a methoxypropyl and a methoxybenzyl side chains were synthesized by direct alkylation of **14** with the corresponding tosylate[24] or chloride.[25] The methoxymethylphenyl ligand **24** was synthesized from **14** through arylation with fluorobenzenecarboxylate,[26] reduction of the ester **22**, and finally methylation of the hydroxy group of **23** (Fig. 4).

2.2. Asymmetric epoxidation of BHA cinnamate

We began our study by the examination of an asymmetric epoxidation reaction of an α,β-unsaturated BHA (3,5-di-*tert*-butyl-4-hydroxyanisole) ester **25**, which was a highly effective acceptor for the chiral ligand-controlled catalytic asymmetric conjugate addition of organolithiums.[10d,e] We also expected that the bulkiness of the BHA group prevents transesterification with lithium alkoxide which is generated as a side product from lithium peroxide during progress of the reaction. The reaction of **25** with 1.5 equiv. of lithium *tert*-butylperoxide **26**-**Li**, generated by treating *tert*-butylhydroperoxide with butyllithium, in the absence of a chiral ligand in toluene gave a desired epoxide **27** only in 10% yield after stirring at 0°C for 36 h (Fig. 5). On the other hand, the reaction of **25** with 1.5 equiv. of **26**-**Li** in the presence of 1.8 equiv. of a chiral ligand **1** in toluene at 0°C for 36 h gave **27** in 62% yield without contamination of transesterificated *tert*-butyl ester.[27] This enhancement effect on the reaction rate well indicates the applicability of our strategy in the catalytic asymmetric epoxidation reaction. The rate-enhancement with chiral ligand is probably due to deaggregation of lithium *tert*-butylperoxide as has been known for the reactivity of organolithiums.[28] The enantioselectivity was determined to be 72% by a chiral stationary phase HPLC analysis (Daicel Chiralpak AD). These results clearly indicate that the chiral ligand **1** not only activates the

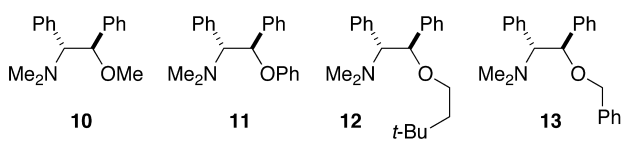


Figure 2. The bidentate ligands having a diphenylethane unit.

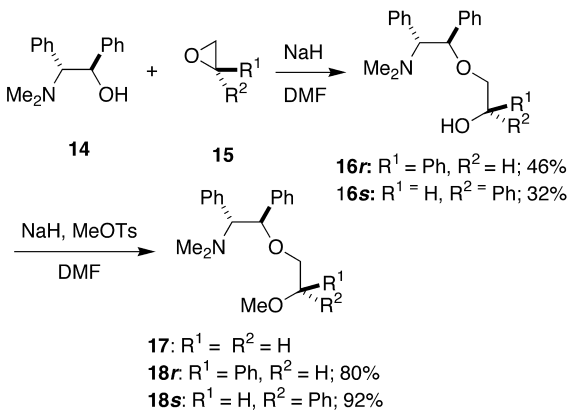


Figure 3. Synthesis of bidentate ligands having a methoxyethyl side chain.

lithium peroxide but also controls the stereochemistry of the nucleophilic epoxidation reaction. The absolute configuration of optically active **27** was determined to be (2*R*,3*S*) by reducing **27** with lithium aluminum hydride in THF to the corresponding diols of the established absolute stereochemistry (*R*)-3-phenylpropane-1,2-diol,[29] and (*R*)-1-phenylpropane-1,3-diol[30] in 65 and 24% yields, respectively. It is important to note that the chiral ligand **1** was quantitatively recovered without any loss of optical purity, and was reusable.

The reaction of **25** with more bulky lithium cumene peroxide **28**-**Li**[31] gave **27** in an improved 82% yield with the same 72% ee (Fig. 6). More bulky lithium tritylperoxide **29**-**Li**[32] gave **27** in 82% yield with a diminished 59% ee, perhaps due to the partial prevention of chelate formation with a chiral ligand by a bulky trityl group.

2.3. Catalytic asymmetric epoxidation of chalcone by a slow addition procedure

The reaction of chalcone **30**, which has higher reactivity than the enoate **25**, with 1.5 equiv. of lithium cumene

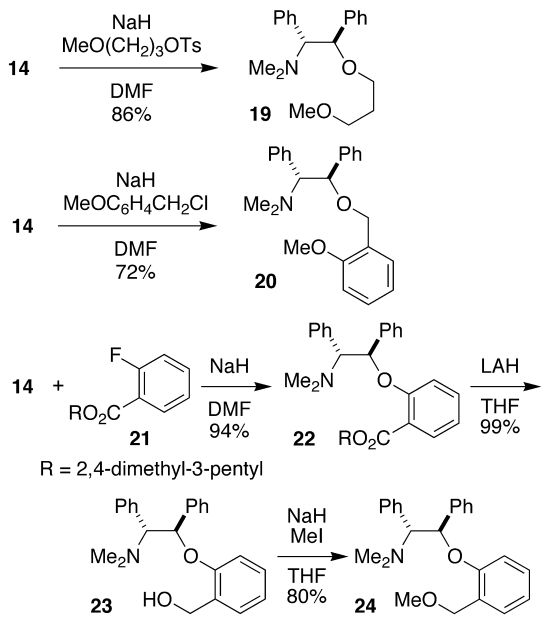


Figure 4. Synthesis of ligands having a methoxypropyl-type side chain.

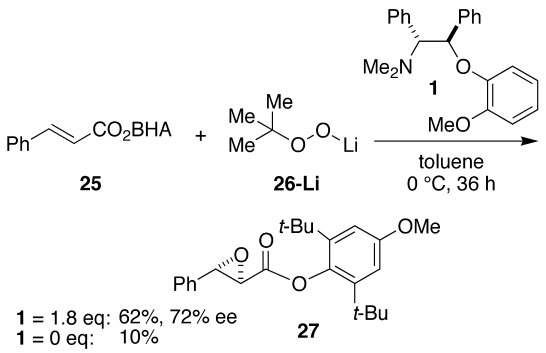


Figure 5. Epoxidation of an enoate **25** in the presence and absence of **1**.

peroxide **28**-**Li** in the presence of 1.8 equiv. of **1** in toluene at 0°C proceeded smoothly within 0.5 h to give an epoxide **31** in 75% yield with 47% ee (Fig. 7). Encouraged by the rapid reaction as well as relatively high enantioselectivity, a catalytic reaction was examined. However, the reaction of **30** with 0.15 equiv. of **28**-**Li** in the presence of 0.2 equiv. of **1** and 1.35 equiv. of cumene hydroperoxide resulted in **31** only in 15% ee.

The decreased enantioselectivity is ascribable to the coordination of an excess of hydroperoxide to lithium kicking out a chiral ligand from coordination. Suppression of the influence of an excess of the hydroperoxide is possible by a slow addition of cumene hydroperoxide. Thus, a solution of the hydroperoxide in toluene was slowly added over 3 h to a mixture of chalcone **30**, 0.15 equiv. of lithium cumene peroxide **28**-**Li**, and 0.2 equiv. of chiral ligand **1** in toluene at 0°C. The reaction completed within another 1 h to give **31** in 99% yield with an improved 40% ee, indicating the effectiveness of the slow addition procedure for the catalytic reaction.

2.4. Structural requirements of a chiral ligand

The chiral ligand **2**, which has no substituent on the carbon attached to a methoxyphenoxy group, gave an epoxide **31** in 74% yield and 15% ee (Table 1, entry 2). An analogous ligand **5** gave **31** in 69% yield, but in marginal ee (entry 3). The ligand **9** having two stereocenters on a cyclohexane ring, gave **31** in 72% yield and 18% ee of the opposite absolute configuration (entry 4). These results indicate that two adjacent *trans*-phenyl substituents on an ethylene bridge of the chiral ligand are important for reasonably high enantioselectivity. We then examined the bidentate chiral ligands **10**–**13** having a diphenylethane unit (entries 5–8). The enantioselectivity was ranged and increased from 7 to 42% as the increased bulkiness of the substituent on an ether oxygen. It is noteworthy that these bidentate chiral ligands gave an epoxide **31** of the opposite absolute configuration. The difference of the sense of enantiofacial selection between the tridentate and bidentate chiral ligands

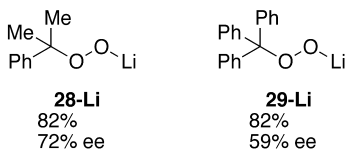


Figure 6. Asymmetric epoxidation of **25** to **27** with use of **28**- and **29**-**Li**.

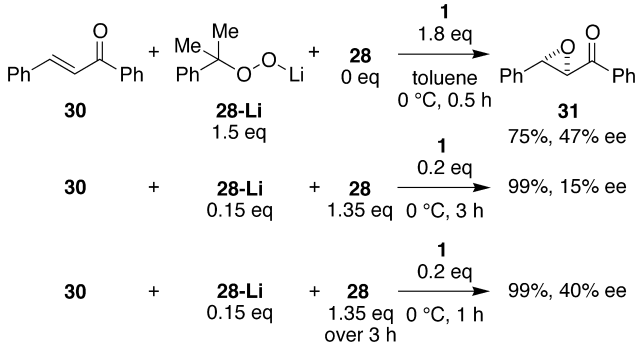


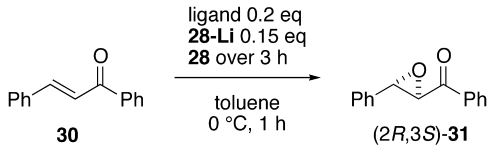
Figure 7. Asymmetric epoxidation of chalcone **30** under **28**-**Li**-**1** catalysis.

indicates that a methoxy group attached on a phenoxy group is not mere steric hindrance unit, but coordinates to lithium forming bicyclo[3.3.0] complex as shown in Figure 8.

The coordinating ability of the chiral ligand also affected the enantioselectivity. The tridentate ligands **17**, **18***r* and **18***s* bearing an alkyl ether side chain, which have stronger coordinating ability than a phenolic ether, were expected to form bicyclo[3.3.0] complexes more firmly (entries 9–11). However, the opposite enantiofacial selection was observed by the use of **17** and **18***s*. The ligand **18***r* gave **31** with decreased selectivity of 16% ee. The change of enantioselectivity was presumably caused by difficulty in the coordination of a carbonyl oxygen of chalcone to lithium because of strong coordination to satisfy tetravalency of lithium by the methoxy group of these chiral ligands **17** and **18***s*, though the highest 44% ee was realized by **18***s*.

The influence by the length of the side chain connecting two ether oxygens was examined. The tridentate ligands **19**, **20** and **24** bearing the methoxypropyl-type side chains were expected to form stable bicyclo[4.3.0] complexes (entries 12–14). The chiral ligands **19** and **20** gave **31** with 15 and 23% ee of the opposite absolute configuration. The enantioselectivity by **24** was nearly marginal.

Table 1. Catalytic asymmetric epoxidation of **30** in the presence of various chiral ligands



Entry	Chiral ligand	Yield (%)	ee (%)	Configuration
1	**1**	99	40	2*R*,3*S*
2	**2**	74	15	2*R*,3*S*
3	**5**	69	0	2*R*,3*S*
4	**9**	72	*ent*-18	2*S*,3*R*
5	**10**	97	*ent*-7	2*S*,3*R*
6	**11**	69	*ent*-7	2*S*,3*R*
7	**12**	88	*ent*-22	2*S*,3*R*
8	**13**	85	*ent*-42	2*S*,3*R*
9	**17**	97	*ent*-19	2*S*,3*R*
10	**18***r*	88	16	2*R*,3*S*
11	**18***s*	56	*ent*-44	2*S*,3*R*
12	**19**	86	*ent*-15	2*S*,3*R*
13	**20**	95	*ent*-23	2*S*,3*R*
14	**24**	70	2	2*R*,3*S*

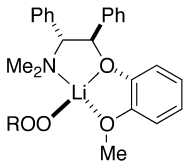


Figure 8. Anticipated bicyclo[3.3.0] complex of lithium peroxide and **1**.

These results indicate the following structural requirements of a chiral ligand in this epoxidation reaction: (1) *vicinal-trans*-diphenyl groups on the ethylene bridge connecting an amino group and an ether oxygen, (2) a tridentate ligand which forms bicyclo[3.3.0] complex by the coordination to lithium, and (3) a hemilabile[33] methoxyphenyl side chain which allows a coordinating atom exchange with a carbonyl oxygen of an enone.

2.5. The structural factor of substituent on ketone for high enantioselectivity

The lone pair electron-differentiating coordination of a carbonyl oxygen to lithium is responsible for the high enantioselectivity.[14] A bulky substituent on a ketone carbonyl group prevents the lone-pair electron coordination at this side and directs the coordination to lithium predominantly at the side of a C=C double bond, opposite to that bulky substituent. The results of asymmetric epoxidation of two ketones having *tert*-butyl and trityl groups are shown in Figure 9.

The reaction of a *tert*-butyl enone **32a** gave a desired epoxide **33a** in 76% yield with improved 71% ee as compared with 40% ee of chalcone. Trityl enone **32b** also improved the selectivity to give **33b** in 62% yield with 51% ee. These selectivity improvements indicate that the lone pair electron-differentiating coordination of a carbonyl oxygen is operative in this asymmetric epoxidation reaction. Good selectivity observed in the reaction of a bulky BHA enoate **25** would also based on this lone pair-differentiating coordination (Fig. 5).

2.6. Generality of the reaction

Some enones bearing an aromatic substituent at the β-position were oxidized in a selectivity ranging from 56 to 71% ee under the catalytic reaction conditions (Table 2, entries 1–5). An exception is an enone having sp^3 substituent at the β-position, giving an epoxide with a diminished ee of 37% (entry 6).

3. Conclusion

A conjugate addition-type catalytic asymmetric epoxidation reaction of α,β-unsaturated carbonyl compounds was investigated. Our findings in this work are (1) a chiral ligand not only activates the lithium peroxide, but also controls the absolute stereochemistry of the epoxidation reaction, (2) a tridentate aminodiether ligand having a hemilabile methoxyphenyl side chain is effective for high enantioselectivity, (3) the lone pair electron-differentiating coordination of a carbonyl oxygen to lithium is operative, and (4) a slow addition procedure is effective for the catalytic asymmetric reaction. These become a certain basis of the development of more sophisticated conjugate addition-type, ligand-controlled catalytic asymmetric epoxidation reaction of α,β-unsaturated carbonyl compounds.

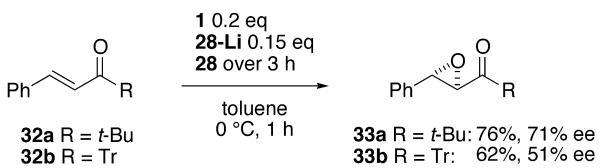
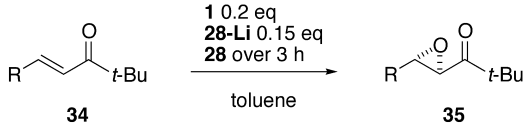


Figure 9. Catalytic asymmetric epoxidation of *tert*-butyl and trityl enones.

Table 2. Catalytic asymmetric epoxidation of *tert*-butyl enones



34 35

Entry	R	Temperature (°C)	Addition (h)	Time (h)	Yield (%)	ee (%)
1	Ph	0	3	1	76	71[a]
2	1-naphthyl	0	3	1	55	56
3	2-naphthyl	rt	24	12	74	58
4	4-ClC_6H_4	0	3	1	81	66
5	4-$MeOC_6H_4$	rt	24	12	68	64[a]
6	$Ph(CH_2)_2$	0	3	1	55	37[b]

[a] The absolute configuration was determined according to the Ref. 5.
[b] The absolute configuration was determined according to the Ref. 34. The absolute configuration of other products was tentatively assigned by analogy.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were taken in $CDC1_3$. Chemical shift values are expressed in ppm relative to internal tetramethylsilane. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; m, multiplet. Purification was carried out using silica gel column chromatography unless otherwise noted. All reactions were carried out under an argon atmosphere unless otherwise stated.

4.2. Synthesis of chiral ligands

4.2.1. (*S*)-2-(2-Methoxyphenoxymethyl)-1-methylpyrrolidine (5). A mixture of 2-methoxyphenol **4** (8.80 mL, 80 mmol), NaH (60%, 3.20 g, 80 mmol, washed with hexane) in DMF (15 mL) was stirred at rt for 40 min. A solution of *N*-methyl(2-chloromethyl)pyrrolidine hydrochloride **3** (3.40 g, 20 mmol) in DMF (130 mL) was added over 40 min at 0°C. The whole was stirred at rt for 4 h and then quenched with water, and then extracted with EtOAc. Organic layers were washed successively with 10% NaOH, and brine, and then dried over K_2CO_3. Concentration followed by chromatography ($CHCl_3$/MeOH=10:1) gave **5** (3.05 g, 69%) as a pale yellow oil of bp 160°C/4 mm Hg and $[\alpha]_D^{25}=-59.8$ (*c* 1.00, $CHCl_3$). IR (neat): 1590, 1500 cm^{-1}. ^1H NMR: 1.69–1.88 (3H, m), 2.07 (1H, m), 2.27 (1H, m), 2.50 (3H, s), 2.74 (1H, m), 3.09 (1H, m), 3.85 (3H, s), 3.90

(1H, dd, J=6.7, 9.5 Hz), 4.03 (1H, dd, J=5.5, 9.5 Hz), 6.87–6.94 (4H, m). ^{13}C NMR: 23.0, 29.0, 41.7, 56.0, 57.7, 64.2, 72.4, 112.0, 113.5, 120.8, 121.1, 148.7, 149.6. MS (EI) m/z: 221 [M^+]. Anal. calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.81: H, 8.86: N, 6.34.

4.2.2. (1*R*,2*R*)-[2-(2-Methoxyphenoxy)cyclohexyl]dimethylamine (9). A mixture of amino alcohol **6** (616 mg, 4.3 mmol) and NaH (60%, 206 mg, 5.16 mmol) in DMF (11 mL) was stirred for 1 h at 70°C. Fluoroanisole-chromiumtricarbonyl **7** (1.35 g, 5.16 mmol) in DMF (3 mL) was added at 0°C. The whole was stirred for 0.5 h at rt and quenched with water at 0°C, and then extracted with EtOAc. Organic layers were washed with brine and dried over K_2CO_3. Concentration followed by chromatography (EtOAc/Et_3N=50:1) gave a yellow oil (1.53 g, 92%). A solution of I_2 (4.04 g, 15.9 mmol) in THF (25 mL) was added to a solution of the above oil in THF (25 mL) at −78°C over 1 h, and the mixture was stirred for 0.5 h at −78°C. After stirring for 0.5 h at 0°C, 10% $Na_2S_2O_3$ was added, and the mixture was extracted with MTBE. To the aqueous layer was added 30% K_2CO_3 (pH>10) and extracted with MTBE. Combined organic layers were washed with 30% K_2CO_3 and brine, and then dried over K_2CO_3. Concentration, chromatography (EtOAc/MeOH=10:1–1:1), and then Kugelrohr distillation gave colorless oil (518 mg, 52%) of bp 185°C/1.5 mm Hg and $[\alpha]_D^{25}$=−59.5 (c 1.91, $CHCl_3$). IR (neat): 1590, 1500 cm^{-1}. ^{1}H NMR: 1.15–1.44 (4H, m), 1.63–1.72 (2H, m), 1.89 (1H, m), 2.10 (1H, m), 2.42 (6H, s), 2.73 (1H, ddd, J=3.7, 9.5, 11 Hz), 3.84 (3H, s), 4.22 (1H, ddd, J=4.3, 9.5, 9.5 Hz), 6.85–6.95 (4H, m). ^{13}C NMR: 24.1, 24.8, 26.0, 30.8, 41.3, 55.8, 66.2, 78.1, 112.3, 117.0, 120.7, 121.5, 147.0, 150.9. MS (EI) m/z: 249 [M^+], 126. Anal. calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.05; H, 9.06; N, 5.66.

4.2.3. (1*R*,2*R*)-[2-((*R*)-2-Hydroxy-2-phenylethoxy)-1,2-diphenylethyl]dimethylamine (16*r*). A solution of amino alcohol **14** (724 mg, 3 mmol) and NaH (60%, 144 mg, 3.6 mmol) in DMF (10 mL) was stirred for 1 h at 70°C. A solution of (*R*)-styrene oxide **15** (721 mg, 6 mmol) in DMF (5 mL) was added at 0°C, and the whole was stirred for 20 h at 70°C and then quenched with water at 0°C, and then extracted with EtOAc. Organic layers were washed with brine and then dried over K_2CO_3. Concentration and chromatography (EtOAc/MeOH=10:1–3:1) gave a colorless gum (491 mg, 46%) of bp 250°C/1 mm Hg and $[\alpha]_D^{25}$=−43.1 (c 1.63, $CHCl_3$). IR (neat): 3300, 1600, 1490 cm^{-1}. ^{1}H NMR: 2.33 (6H, s), 3.45 (1H, dd, J=9.2, 11 Hz), 3.53 (1H, dd, J=3.4, 11 Hz), 4.06 (1H, d, J=10 Hz), 4.95 (1H, d, J=10 Hz), 5.00 (1H, dd, J=3.4, 9.2 Hz), 6.98–7.40 (15H, m). ^{13}C NMR: 41.5, 71.3, 72.5, 73.3, 79.7, 126.1, 127.3, 127.62, 127.65, 128.0, 128.3, 130.0, 133.1, 138.7, 140.9. MS (CI) m/z: 362 [M+H^+], 224, 134. HRMS (CI) m/z: calcd for $C_{24}H_{28}NO_2$: 362.2120 [M+H]. Found: 362.2116.

4.2.4. (1*R*,2*R*)-[2-((*R*)-2-Methoxy-2-phenylethoxy)-1,2-diphenylethyl]dimethylamine (18*r*). A solution of **16***r* (1.45 g, 4.0 mmol) and NaH (60%, 192 mg, 4.8 mmol) in DMF (10 mL) was stirred for 0.5 h at rt. Methyl toluenesulfonate (0.72 mL, 4.8 mmol) was added at 0°C, and the whole was stirred for 0.5 h at 0°C and quenched with water, and then extracted with MTBE. Organic layers were washed with brine and then dried over K_2CO_3. Concentration and Kugelrohr distillation gave a colorless gum (1.20 g, 80%) of bp 250°C/1 mm Hg and $[\alpha]_D^{25}$=−60.7 (c 1.07, $CHCl_3$). IR (neat): 1600, 1490 cm^{-1}. ^{1}H NMR: 2.24 (6H, s), 3.24 (3H, s), 3.37 (1H, dd, J=4.6, 11 Hz), 3.60 (1H, dd, J=7.0, 11 Hz), 3.68 (1H, d, J=8.2 Hz), 4.42 (1H, dd, J=4.6, 7.0 Hz), 4.69 (1H, d, J=8.2 Hz), 6.92–6.94 (2H, m), 7.02–7.11 (8H, m), 7.27–7.35 (5H, m). ^{13}C NMR: 42.7, 56.8, 73.2, 74.9, 82.5, 83.2, 126.8, 127.1, 127.2, 127.4, 127.6, 127.8, 128.0, 128.3, 129.5, 137.0, 139.6, 139.8. MS (CI) m/z: 376 [M+H^+], 224, 134. Anal. calcd for $C_{25}H_{29}NO_2$: C, 79.96; H, 7.78; N, 3.73. Found: C, 80.17; H, 7.81; N, 3.63.

4.2.5. (1*R*,2*R*)-[2-((*S*)-2-Hydroxy-2-phenylethoxy)-1,2-diphenylethyl]dimethylamine (16*s*). By the same procedure for **16***r*, **16***s* was prepared with (*S*)-styrene oxide **15** in 32% yield as colorless rods of mp 117–117.5°C (hexane) and $[\alpha]_D^{25}$=−28.5 (c 1.00, $CHCl_3$). IR (nujol): 3200, 1600, 1490 cm^{-1}. ^{1}H NMR: 2.33 (6H, s), 3.36 (1H, dd, J=10, 10 Hz), 3.86 (1H, dd, J=2.7, 10 Hz), 4.02 (1H, d, J=10 Hz), 4.77 (1H, d, J=10 Hz), 4.96 (1H, dd, J=2.7, 10 Hz), 6.55 (1H, brs), 6.98–7.39 (15H, m). ^{13}C NMR: 41.7, 73.7, 74.5, 78.0, 84.1, 126.1, 127.3, 127.4, 127.6, 127.8, 128.1, 128.2, 130.0, 133.1, 139.8, 140.6. MS (CI) m/z: 362 [M+H^+], 224, 134. Anal. calcd for $C_{24}H_{27}NO_2$: C, 79.74; H, 7.53; N, 3.87. Found: C, 79.92; H, 7.53; N, 3.77.

4.2.6. (1*R*,2*R*)-[2-((*S*)-2-Methoxy-2-phenylethoxy)-1,2-diphenylethyl]dimethylamine (18*s*). By the same procedure for **18***r*, **18***s* was prepared from **16***s* in 92% yield as a colorless oil of bp 240°C/0.7 mm Hg and $[\alpha]_D^{25}$=+73.0 (c 1.06, $CHCl_3$). IR (neat): 1600, 1490 cm^{-1}. ^{1}H NMR: 2.36 (6H, s), 3.31 (3H, s), 3.37 (1H, dd, J=3.4, 11 Hz), 3.44 (1H, dd, J=8.6, 11 Hz), 3.77 (1H, d, J=9.2 Hz), 4.48 (1H, dd, J=3.4, 8.6 Hz), 4.97 (1H, d, J=9.2 Hz), 6.99–7.30 (15H, m). ^{13}C NMR: 41.9, 56.8, 73.2, 74.8, 83.1, 84.2, 126.77, 126.80, 127.1, 127.4, 127.6, 127.7, 128.0, 128.2, 129.5, 136.2, 138.9, 140.1. MS (CI) m/z: 376 [M+H^+], 224, 134. Anal. calcd for $C_{25}H_{29}NO_2$: C, 79.96; H, 7.78; N, 3.73. Found: C, 79.71; H, 7.96; N, 3.56.

4.2.7. (1*R*,2*R*)-[2-(3-Methoxypropoxy)-1,2-diphenylethyl]dimethylamine (19). A solution of **14** (2.41 g, 10 mmol) and NaH (480 mg, 12 mmol) in DMF (25 mL) was stirred at 60°C for 2 h. 3-Methoxypropyl tosylate (2.93 g, 12 mmol) in DMF (5 mL) was added over 10 min at 0°C. The mixture was stirred at 100°C for 2.5 h and quenched with ice water, and then extracted with toluene. Organic layers were washed with brine and then dried over K_2CO_3. Concentration and chromatography gave a colorless oil (2.70 g, 86%) of bp 210°C/0.7 mm Hg and $[\alpha]_D^{25}$=+17.5 (c 1.24, $CHCl_3$). IR (neat): 1600, 1490 cm^{-1}. ^{1}H NMR: 1.87 (2H, tt, J=6.4, 6.4 Hz), 2.33 (6H, s), 3.29 (3H, s), 3.35–3.43 (3H, m), 3.51 (1H, dt, J=6.4, 9.2 Hz), 3.72 (1H, d, J=8.9 Hz), 4.67 (1H, d, J=8.9 Hz), 6.97–7.14 (10H, m). ^{13}C NMR: 30.0, 42.4, 58.5, 65.8, 69.8, 74.8, 82.9, 126.8, 127.1, 127.5, 127.6, 127.9, 129.5, 137.0, 140.4. MS (CI) m/z: 314 [M+H^+], 224, 134. Anal. calcd for $C_{20}H_{27}NO_2$: C, 76.64; H, 8.68; N, 4.47. Found: C, 76.47; H, 8.62; N, 4.38.

4.2.8. (1*R*,2*R*)-[2-(2-Methoxybenzyloxy)-1,2-diphenylethyl]dimethylamine (20). A solution of **14** (121 mg,

0.5 mmol) and NaH (30 mg, 0.75 mmol) in DMF (1 mL) was stirred at 70°C for 1 h. A solution of 4-methoxybenzylchloride (118 mg, 0.75 mmol) in DMF (0.5 mL) was added at 0°C. The mixture was stirred at 80°C for 0.5 h and quenched with ice water, and then extracted with toluene. Organic layers were washed with brine and then dried over K_2CO_3. Concentration and Kugelrohr distillation (200–250°C/0.8 mm Hg) gave a colorless oil (130 mg, 72%) of $[\alpha]_D^{25}=-27.3$ (*c* 0.99, $CHCl_3$). IR (neat): 1600, 1590, 1490 cm^{-1}. ^1H NMR: 2.26 (6H, s), 3.77 (1H, d, *J*=8.5 Hz), 3.78 (3H, s), 4.36 (1H, d, *J*=12 Hz), 4.52 (1H, d, *J*=12 Hz), 4.78 (1H, d, *J*=8.5 Hz), 6.84–7.41 (14H, m). ^{13}C NMR: 42.4, 54.9, 65.3, 75.0, 81.3, 109.9, 120.1, 126.5, 126.7, 127.0, 127.3, 127.5, 128.1, 128.6, 129.4, 129.7, 136.9, 140.2, 157.3. MS (CI) *m/z*: 362 [M+H$^+$], 134. Anal. calcd for $C_{24}H_{27}NO_2$: C, 79.73; H, 7.53; N, 3.88. Found: C, 79.47; H, 7.49; N, 3.90.

4.2.9. 2,4-Dimethyl-3-pentyl 2-fluorobenzoate (21). A mixture of 2-fluorobenzoic acid (14 g, 100 mmol), 2,4-dimethyl-3-pentanol (42 mL, 300 mmol), and *p*-TsOH·H_2O (190 mg, 1 mmol) in toluene (15 mL) was heated under reflux with Dean–Stark trap for 48 h. Usual workup and distillation (125–126°C/7 mm Hg) afforded colorless oil (6.33 g, 27%). IR (neat): 1710 cm^{-1}. ^1H NMR: 0.96 (12H, d, *J*=6.7 Hz), 2.02 (2H, dq, *J*=6.1, 6.7 Hz), 4.88 (1H, t, *J*=6.1 Hz), 7.14 (1H, ddd, *J*=0.9, 8.2, 10.7 Hz), 7.21 (1H, ddd, *J*=0.9, 7.3, 8.2 Hz), 7.50 (1H, m), 7.95 (1H, dd, *J*=1.8, 7.3 Hz). ^{13}C NMR: 17.5, 19.8, 29.8, 84.1, 117.2 (d, *J*=22.6 Hz), 119.6 (d, *J*=10.3 Hz), 124.1 (d, *J*=4.1 Hz), 132.3, 134.3 (d, *J*=9.3 Hz), 162.1 (d, *J*=257 Hz), 164.8 (d, *J*=4.1 Hz). MS (EI) *m/z*: 238 [M$^+$], 195. Anal. calcd for $C_{14}H_{19}FO_2$: C, 70.56; H, 8.04. Found: C, 70.77; H, 8.03.

4.2.10. (1*R*,2*R*)-2,4-Dimethyl-3-pentyl 2-(2-dimethylamino-1,2-diphenylethoxy)benzoate (22). A solution of **14** (2.41 g, 10 mmol) and NaH (60%, 480 mg, 12 mmol) in DMF (10 mL) was stirred at 70°C for 1 h. The mixture was cooled to 0°C and **21** (3.57 g, 15 mmol) was added. After stirring at rt for 2 h, cold water was added, and the mixture was extracted with toluene. Organic layers were washed with water and brine, and then dried over K_2CO_3. Concentration and chromatography (benzene/acetone=1:0 to 4:1) afforded colorless gum (4.33 g, 94%) of bp 240°C/0.7 mm Hg and $[\alpha]_D^{25}=+114.6$ (*c* 1.22, $CHCl_3$). IR (neat): 1720, 1600 cm^{-1}. ^1H NMR: 1.04–1.06 (total 12H, four d, *J*=6.7 Hz), 2.08 (2H, m), 2.35 (6H, s), 3.89 (1H, d, *J*=7.0 Hz), 4.96 (1H, dd, *J*=6.1, 6.1 Hz), 5.67 (1H, d, *J*=7.0 Hz), 6.83–6.87 (2H, m), 7.00–7.10 (10H, m), 7.13 (1H, m), 7.71 (1H, dd, *J*=1.8, 7.6 Hz). ^{13}C NMR:17.5, 17.7, 19.68, 19.70, 29.6, 29.7, 43.9, 75.5, 81.4, 82.8, 114.2, 119.8, 122.1, 126.9, 127.2, 127.5, 127.6, 127.7, 129.5, 131.0, 132.4, 138.0, 138.7, 156.6, 166.2. MS (CI) *m/z*: 460 [M+H$^+$]. Anal. calcd for $C_{30}H_{37}NO_3$: C, 78.40; H, 8.11; N, 3.05. Found: C, 78.14; H, 8.15; N, 3.07.

4.2.11. (1*R*,2*R*)-[2-(2-Hydroxymethylphenoxy)-1,2-diphenylethyl]dimethylamine (23). A solution of **22** (2.15 g, 4.7 mmol) in THF (5 mL) was added to a suspension of lithium aluminum hydride (267 mg, 7 mmol) in THF (5 mL) at 0°C. The whole was heated under reflux for 0.5 h. Water (0.3 mL), 15% aq. NaOH (0.3 mL), and water (0.9 mL) were added successively. Filtration, concentration, and chromatography (benzene/acetone=1:0 to 4:1) gave a colorless gum (1.63 g, 99%) of bp 240°C/0.2 mm Hg. $[\alpha]_D^{25}=+88.6$ (*c* 1.00, $CHCl_3$). IR (neat): 3200 cm^{-1}. ^1H NMR: 2.18 (6H, s), 4.09 (1H, d, *J*=11 Hz), 4.26 (1H, d, *J*=12 Hz), 5.19 (1H, d, *J*=12 Hz), 5.43 (1H, d, *J*=11 Hz), 6.73–7.30 (14H, m). ^{13}C NMR: 40.5, 62.8, 75.3, 79.9, 112.8, 120.9, 127.2, 127.6, 127.7, 128.2, 128.8, 129.3, 130.0, 131.2, 131.7, 139.5, 158.1. MS (FAB) *m/z*: 348 [M+H$^+$], 134. HRMS (FAB) *m/z*: calcd for $C_{23}H_{26}NO_2$: 348.1964 [M+H]. Found: 348.1970.

4.2.12. (1*R*,2*R*)-[2-(2-Methoxymethylphenoxy)-1,2-diphenylethyl]dimethylamine (24). A solution of **23** (105 mg, 0.3 mmol) and NaH (60%, 18 mg, 0.45 mmol) in THF (0.7 mL) was stirred at rt for 1 h. The mixture was cooled to 0°C, methyl iodide (0.02 mL, 0.33 mmol) was added. After stirring at rt for 3 h, cold water was added, and the mixture was extracted with Et_2O. Organic layers were washed with brine and then dried over K_2CO_3. Concentration and chromatography (benzene/acetone=4:1) gave a colorless gum (87 mg, 80%) of bp 240°C/1 mm Hg and $[\alpha]_D^{25}=+56.8$ (*c* 0.80, $CHCl_3$). IR (neat): 1600, 1490 cm^{-1}. ^1H NMR: 2.37 (6H, s), 3.46 (3H, s), 3.83 (1H, d, *J*=6.4 Hz), 4.59 (1H, d, *J*=13 Hz), 4.67 (1H, d, *J*=13 Hz), 5.66 (1H, d, *J*=6.4 Hz), 6.71–7.35 (14H, m). ^{13}C NMR: 43.9, 58.3, 69.6, 75.8, 80.3, 113.1, 120.5, 127.1, 127.3, 127.4, 127.5, 127.7, 128.2, 128.6, 129.6, 137.4, 138.8, 155.0. MS (CI) *m/z*: 362 [M+H$^+$], 134. Anal. calcd for $C_{24}H_{27}NO_2$: C, 79.74; H, 7.53; N, 3.87. Found: C, 79.91; H, 7.25; N, 3.81.

4.3. Asymmetric epoxidation of BHA enoate

4.3.1. 2,6-Di-*tert*-butyl-4-methoxyphenyl 3-phenyloxirane-2-carboxylate (27). A hexane solution of BuLi (0.96 mL, 1.5 mmol) was added to cumene hydroperoxide **28** (228 mg, 1.5 mmol) in toluene (1 mL) at −78°C, and the mixture was stirred for 10 min. After an addition of a solution of **1** (625 mg, 1.8 mmol) in toluene (3 mL), the mixture was stirred for 10 min at 0°C. A solution of **25** (367 mg, 1.0 mmol) in toluene (3 mL) was added at −78°C. The whole was stirred for 36 h at 0°C, and quenched with satd NH_4Cl, and then extracted with Et_2O. Organic layers were successively washed with 10% Na_2SO_3, 10% HCl, satd $NaHCO_3$ and brine, and then dried over Na_2SO_4. Concentration and chromatography (hexane/Et_2O=10:1) gave **27** (372 mg, 82%) as a colorless gum of 72% ee (Daicel Chiralpak AD, hexane/2-PrOH=200:1, 0.5 mL/min, 254 nm, 30.5 min and 51.2 min for major and minor enantiomers). IR (nujol): 1760 cm^{-1}. ^1H NMR: 1.35 (9H, s), 1.38 (9H, s), 3.74 (1H, d, *J*=1.7 Hz), 3.81 (3H, s), 4.33 (1H, d, *J*=1.7 Hz), 6.87 (1H, d, *J*=3.0 Hz), 6.88 (1H, d, *J*=3.0 Hz), 7.33–7.43 (5H, m). ^{13}C NMR: 31.4, 31.5, 35.6, 35.7, 55.2, 57.4, 58.3, 111.8, 125.7, 128.8, 129.1, 134.8, 141.0, 143.3, 143.4, 156.6, 168.8. MS (EI) *m/z*: 382 [M$^+$]. Anal. calcd for $C_{24}H_{30}O_4$: C, 75.36; H, 7.91. Found: C, 75.47: H, 8.19. Aqueous layer was made alkaline with 40% NaOH (pH>11), and extracted with Et_2O, which was washed with brine, and dried over K_2CO_3. Concentration afforded **1** as colorless needles (613 mg, 98% recovery).

Determination of the absolute configuration of **27**. A solution of **27** (58% ee, 975 mg, 2.5 mmol) in THF (14 mL) was added to a suspension of lithium aluminum

hydride (296 mg, 7.8 mmol) in THF (60 mL) at 0°C, and the mixture was heated under reflux for 5 h. Water (0.3 mL), 15% NaOH (0.3 mL), and water (0.9 mL) were successively added, and then filtered. Concentration and chromatography (benzene/Et_2O=1:1) gave (*R*)-3-phenylpropane-1,2-diol (224 mg, 59%, 160–190°C/2 mm Hg) and (*R*)-1-phenylpropane-1,3-diol (85 mg, 22%, 160–190°C/2 mm Hg).

4.3.2. (*R*)-3-Phenylpropane-1,2-diol.[29] $[\alpha]_D^{20}$=+19.9 (*c* 1.03 EtOH). IR (neat): 3300 cm^{-1}. ^1H NMR: 1.95 (1H, brs), 2.06 (1H, brs), 2.78 (1H, dd, *J*=7.6, 14 Hz), 2.80 (1H, dd, *J*=5.6, 14 Hz), 3.53 (1H, dd, *J*=7.3, 11 Hz), 3.71 (1H, dd, *J*=3.0, 11 Hz), 3.95 (1H, m), 7.22–7.38 (5H, m). MS (EI) *m/z*: 152 [M^+], 121.

4.3.3. (*R*)-1-Phenylpropane-1,3-diol.[30] $[\alpha]_D^{25}$=+36.0 (*c* 0.84, $CHCl_3$). IR (neat): 3240 cm^{-1}. ^1H NMR: 2.00 (2H, m), 2.31 (1H, brs), 2.77 (1H, brs), 3.88 (2H, t, *J*=5.3 Hz), 4.97 (1H, dd, *J*=4.0, 8.6 Hz), 7.24–7.38 (5H, m). MS (EI) *m/z*: 152 [M^+], 107.

4.4. Catalytic asymmetric epoxidation of enones

4.4.1. Phenyl((2*R*,3*S*)-3-phenyloxiranyl)methanone (31). Under the same procedure for **33a**. **31** as a white solid of mp 74–76°C and $[\alpha]_D^{20}$=−79.4 (*c* 2.79, THF) was obtained in 99% yield and 40% ee (Shiseido chiral RU-1, MeOH, 0.3 mL/min, 254 nm, 24.3 min and 28.1 min for minor and major enantiomers). IR (nujol): 1680 cm^{-1}. ^1H NMR: 4.08 (1H, d, *J*=1.8 Hz), 4.31 (1H, d, *J*=1.8 Hz), 7.36–7.43 (5H, m), 7.49 (2H, m), 7.63 (1H, m), 8.01 (2H, m). MS (EI) *m/z*: 224 [M^+].

4.4.2. Typical procedure for the catalytic reaction. 2,2-Dimethyl-1-((2*R*,3*S*)-3-phenyloxiranyl)propan-1-one (33a). A hexane solution of BuLi (1.59 M, 0.28 mL, 0.45 mmol) was added to a solution of cumene hydroperoxide (68 mg, 0.45 mmol) in toluene (0.3 mL) at −78°C, and the mixture was stirred for 10 min at −78°C. A solution of **1** (208 mg, 0.6 mmol) in toluene (1.5 mL) was added, and the mixture was stirred for 10 min at 0°C. A solution of **32a** (565 mg, 3 mmol) in toluene (3.5 mL) was added over 6 min at −78°C. A solution of cumene hydroperoxide (617 mg, 4.05 mmol) in toluene (2.7 mL) was added dropwise over 3 h at 0°C. The whole was stirred for another 1 h at 0°C and quenched with satd NH_4Cl, and then extracted with toluene. Combined organic layers were successively washed with 10% Na_2SO_3 and brine, and then dried over Na_2SO_4. Concentration and chromatography (benzene/acetone=10:1) gave **33a** (466 mg, 76%) as a white solid of mp 57–58°C and $[\alpha]_D^{20}$=−182.5 (*c* 1.06, CH_2Cl_2) and **1** (183 mg, 88% recovery). The ee was determined to 71% (Daicel Chiralpak AD, hexane/2-PrOH=99:1, 1 mL/min, 230 nm, 14.0 min and 17.6 min for major and minor enantiomers). IR (nujol): 1700 cm^{-1}. ^1H NMR: 1.24 (9H, s), 3.86 (2H, s), 7.30–7.40 (5H, m). ^{13}C NMR: 25.7, 43.6, 59.1, 59.3, 125.6, 128.7, 128.9, 135.6, 208.1. MS (EI) *m/z*: 204 [M^+], 147.

4.4.3. 2,2,2-Triphenyl-1-((2*R*,3*S*)-3-phenyloxiranyl)ethanone (33b). By the same procedure for **33a**, **33b** was obtained in 62% as a white solid of mp 109–109.5°C and $[\alpha]_D^{25}$=−65.8 (*c* 1.03, $CHCl_3$). The ee was determined to 51% (Daicel Chiralpak AD, hexane/2-PrOH=95:5, 1.0 mL min, 254 nm, 19.6 min and 22.2 min for minor and major enantiomers). IR (nujol): 1730 cm^{-1}. ^1H NMR: 3.56 (1H, d, *J*=1.5 Hz), 3.75 (1H, d, *J*=1.5 Hz), 6.89 (2H, m), 7.17–7.35 (18H, m). ^{13}C NMR: 61.0, 61.9, 125.5, 127.2, 128.2, 128.4, 128.5, 130.2, 140.9, 201.5. MS (CI) *m/z*: 391 [M+H^+], 243. HRMS (CI) *m/z*: calcd for $C_{28}H_{23}O_2$: 391.1698 [M+H]. Found: 391.1700.

4.4.4. 2,2-Dimethyl-1-((2*R*,3*S*)-3-naphthalen-1-yloxiranyl)propan-1-one (35, R=1-naphthyl). By the same procedure for **33a**, **35** was obtained in 55% as a white solid of mp 53–54°C and $[\alpha]_D^{25}$=−25.2 (*c* 1.03, $CHCl_3$). The ee was determined to 56% (Daicel Chiralpak AD, hexane/2-PrOH=99:1, 1.0 mL/min, 230 nm, 13.6 min and 18.2 min for major and minor enantiomers). IR (nujol): 1710 cm^{-1}. ^1H NMR: 1.29 (9H, s), 3.86 (1H, d, *J*=1.8 Hz), 4.55 (1H, d, *J*=1.8 Hz), 7.46–7.57 (4H, m), 7.85 (1H, d, *J*=7.9 Hz), 7.91 (1H, m), 7.98 (1H, m). ^{13}C NMR: 25.8, 43.8, 57.8, 58.2, 122.3, 125.4, 126.1, 126.7, 128.8, 128.9, 131.2, 131.8, 133.3, 208.4. MS (EI) *m/z*: 254 [M^+], 169. Anal. calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.29; H, 7.13.

4.4.5. 2,2-Dimethyl-1-((2*R*,3*S*)-3-naphthalen-2-yloxiranyl)propan-1-one (35, R=2-naphthyl). By the same procedure for **33a**, **35** was obtained in 74% as a white solid of mp 94.5–96°C and $[\alpha]_D^{25}$=−149.2 (*c* 1.06, $CHCl_3$). The ee was determined to 58% (Daicel Chiralpak AD, hexane/2-PrOH=99:1, 1.0 mL/min, 230 nm, 17.4 min and 41.5 min for major and minor enantiomers). IR (nujol): 1700 cm^{-1}. ^1H NMR: 1.25 (9H, s), 3.95 (1H, d, *J*=1.8 Hz), 4.02 (1H, d, *J*=1.8 Hz), 7.35 (1H, dd, *J*=1.8, 8.5 Hz), 7.49–7.53 (2H, m), 7.82–7.87 (4H, m). ^{13}C NMR: 25.7, 43.6, 59.3, 59.6, 122.4, 125.5, 126.5, 126.6, 127.80, 127.83, 128.7, 133.00, 133.04, 133.6, 208.1. MS (EI) *m/z*: 254 [M^+], 141. Anal. calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.27; H, 6.86.

4.4.6. 1-((2*R*,3*S*)-4-Chlorophenyloxiranyl)-2,2-dimethylpropan-1-one (35, R=4-ClC_6H_4). By the same procedure for **33a**, **35** was obtained in 81% as a white solid of mp 46–49°C and $[\alpha]_D^{25}$=−170.5 (*c* 1.03, $CHCl_3$). The ee was determined to 66% ee (Daicel Chiralpak AD, hexane/2-PrOH=99:1, 1.0 mL/min, 230 nm, 12.8 min and 22.0 min for major and minor enantiomers). IR (nujol): 1700 cm^{-1}. ^1H NMR: 1.24 (9H, s), 3.80 (1H, d, *J*=1.8 Hz), 3.84 (1H, d, *J*=1.8 Hz), 7.24 (2H, d, *J*=8.5 Hz), 7.35 (2H, d, *J*=8.5 Hz). ^{13}C NMR: 26.1, 44.1, 59.1, 59.5, 127.4, 129.4, 134.6, 135.2, 208.2. MS (EI) *m/z*: 238 [M^+]. Anal. calcd for $C_{13}H_{15}ClO_2$: C, 65.41; H, 6.33. Found: C, 65.29; H, 6.29.

4.4.7. 1-((2*R*,3*S*)-4-Methoxyphenyloxiranyl)-2,2-dimethylpropan-1-one (35, R=4-$MeOC_6H_4$). By the same procedure for **33a**, **35** was obtained in 68% as a colorless oil and $[\alpha]_D^{20}$=−155.4 (*c* 2.32, $CHCl_3$). The ee was determined to 64% (Daicel Chiralpak AD, hexane/EtOH=98:2, 1.0 mL/min, 230 nm, 21.3 min and 25.8 min for major and minor enantiomers). IR (neat): 1720 cm^{-1}. ^1H NMR: 1.23 (9H, s), 3.80 (1H, d, *J*=1.8 Hz), 3.82 (3H, s), 3.85 (1H, d, *J*=1.8 Hz), 6.90 (2H, d, *J*=8.5 Hz), 7.23 (2H, d, *J*=8.5 Hz). ^{13}C NMR: 25.7, 43.5, 55.4, 59.2, 59.4, 114.2, 127.0, 127.5, 160.2, 208.3. MS (EI) *m/z*: 234 [M^+].

4.4.8. 2,2-Dimethyl-1-((2*R*,3*S*)-3-phenethyloxiranyl)propan-1-one (35, R=Ph(CH$_2$)$_2$). By the same procedure for **33a**, **35** was obtained in 55% as a colorless oil and $[\alpha]_D^{26}=-16.0$ (*c* 1.34, CH_2Cl_2). The ee was determined to 37% (Daicel Chiralpak AD, hexane/2-PrOH=99:1, 1.0 mL/min, 220 nm, 11.6 min and 22.7 min for major and minor enantiomers). IR (neat): 1710 cm^{-1}. ^{1}H NMR: 1.17 (9H, s), 1.93–2.04 (2H, m), 2.73–2.86 (2H, m), 2.99 (1H, dt, *J*=1.8, 6.1 Hz), 3.62 (1H, d, *J*=1.8 Hz), 7.19–7.31 (5H, m). ^{13}C NMR: 25.7, 31.9, 33.5, 43.6, 55.4, 59.3, 126.3, 128.30, 128.34, 140.6, 209.3. MS (EI) *m*/*z*: 175 [M$^+$−*t*-Bu], 147.

Acknowledgements

This research was supported by a Grant-in-Aid for Scientific Research on Priority Areas (A) 'Exploitation of Multi-Element Cyclic Molecules' from the Ministry of Education, Culture, Sports, Science and Technology, Japan. K. N. was supported by a fellowship from the JSPS.

References

1. (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974–5976. (b) Hanson, R. M.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 1922–1925. (c) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765–5780.
2. (a) Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Deng, L. *J. Am. Chem. Soc.* **1991**, *113*, 7063–7064. (b) Mukaiyama, T.; Yamada, T.; Nagata, T.; Imagawa, K. *Chem. Lett.* **1993**, 327–330. (c) Imanishi, H.; Katsuki, T. *Tetrahedron Lett.* **1997**, *38*, 251–254. (d) Review: Katsuki, T. *Adv. Synth. Catal.* **2002**, *344*, 131–147.
3. (a) Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Am. Chem. Soc.* **1996**, *118*, 9806–9807. (b) Matsumoto, K.; Tomioka, K. *Tetrahedron Lett.* **2002**, *43*, 631–633, and references cited therein. (c) Review: Shi, Y. *J. Synth. Org. Chem. Jpn* **2002**, *60*, 342–349.
4. Review on asymmetric epoxidation of electron-deficient olefins Porter, M. J.; Skidmore, *J. Chem. Commun.* **2000**, 1215–1225.
5. Enders, D.; Zhu, J.; Raabe, G. *Angew. Chem., Int. Ed.* **1996**, *35*, 1725–1728.
6. Elston, C. L.; Jackson, R. F. W.; MacDonald, S. J. F.; Murray, P. J. *Angew. Chem., Int. Ed.* **1997**, *36*, 410–412.
7. (a) Bougauchi, M.; Watanabe, S.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1997**, *119*, 2329–2330. (b) Review: Nemoto, T.; Ohshima, T.; Shibasaki, M. *J. Synth. Org. Chem. Jpn* **2002**, *60*, 94–105.
8. Asymmetric epoxidation using chiral hydroperoxide Adam, W.; Rao, P. B.; Degen, H.-G.; Saha-Möller, C. R. *J. Am. Chem. Soc.* **2000**, *122*, 5654–5655.
9. (a) Tomioka, K. *Synthesis* **1990**, 541–549. (b) Tomioka, K.; Nagaoka, Y. *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; Vol. III. Chapter 31. (c) Tomioka, K. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, 2000; Chapter 12.
10. (a) Tomioka, K.; Shindo, M.; Koga, K. *J. Am. Chem. Soc.* **1989**, *111*, 8266–8268. (b) Shindo, M.; Koga, K.; Tomioka, K. *J. Am. Chem. Soc.* **1992**, *114*, 8732–8733. (c) Fujieda, H.; Kanai, M.; Kambara, T.; Iida, A.; Tomioka, K. *J. Am. Chem. Soc.* **1997**, *119*, 2060–2061. (d) Asano, Y.; Iida, A.; Tomioka, K. *Tetrahedron Lett.* **1997**, *38*, 8973–8976. (e) Asano, Y.; Iida, A.; Tomioka, K. *Chem. Pharm. Bull.* **1998**, *46*, 184–186. (f) Mizuno, M.; Fujii, K.; Tomioka, K. *Angew. Chem., Int. Ed.* **1998**, *37*, 515–517. (g) Taniyama, D.; Hasegawa, M.; Tomioka, K. *Tetrahedron Lett.* **2000**, *41*, 5533–5536. (h) Iguchi, M.; Tomioka, K. *Org. Lett.* **2002**, *4*, 4329–4331.
11. Nishimura, K.; Ono, M.; Nagaoka, Y.; Tomioka, K. *J. Am. Chem. Soc.* **1997**, *119*, 12974–12975.
12. Doi, H.; Sakai, T.; Iguchi, M.; Yamada, K.; Tomioka, K. *J. Am. Chem. Soc.* **2003**, *125*, 2886–2887.
13. Preliminarily communication of this work Tanaka, Y.; Nishimura, K.; Tomioka, K. *Heterocycles* **2002**, *58*, 71–73.
14. Nishimura, K.; Tomioka, K. *J. Org. Chem.* **2002**, *67*, 431–434.
15. Tomioka, K.; Sudani, M.; Shinmi, Y.; Koga, K. *Chem. Lett.* **1985**, 329–332.
16. Chavdarian, C. G.; Sanders, E. B.; Bassfield, R. L. *J. Org. Chem.* **1982**, *47*, 1069–1073.
17. Jones, C. A.; Jones, I. G.; North, M.; Pool, C. R. *Tetrahedron Lett.* **1995**, *36*, 7885–7888.
18. Overman, L. E.; Sugai, S. *J. Org. Chem.* **1985**, *50*, 4154–4155.
19. Mahaffy, C. A. L. *J. Organomet. Chem.* **1984**, *262*, 33–37.
20. Tomioka, K.; Okuda, M.; Nishimura, K.; Manabe, S.; Kanai, M.; Nagaoka, Y.; Koga, K. *Tetrahedron Lett.* **1998**, *39*, 2141–2144.
21. Shindo, M.; Koga, K.; Tomioka, K. *J. Org. Chem.* **1998**, *63*, 9351–9357.
22. Weijlard, J.; Pfister, K.; Swanezy, E. F.; Robinson, C. A.; Tishler, M. *J. Am. Chem. Soc.* **1951**, *73*, 1216–1218.
23. Mizuno, M.; Kanai, M.; Iida, A.; Tomioka, K. *Tetrahedron* **1997**, *53*, 10699–10708.
24. Hussein, M. A.; Iida, A.; Tomioka, K. *Tetrahedron* **1999**, *55*, 11219–11228.
25. Grice, R.; Owen, L. N. *J. Am. Chem. Soc.* **1963**, *85*, 1947–1954.
26. Hattori, T.; Satoh, S.; Miyano, S. *Bull. Chem. Soc. Jpn* **1993**, *66*, 3840–3842.
27. The reaction of the corresponding ethyl ester gave an epoxide mixture of ethyl and *t*-butyl esters.
28. McGarrity, J. F.; Ogle, C. A.; Brich, Z.; Loosli, H.-R. *J. Am. Chem. Soc.* **1985**, *107*, 1810–1815.
29. Bergstein, W.; Kleemann, A.; Martens, J. *Synthesis* **1981**, 76–78.
30. Masamune, S.; Sato, T.; Kim, B. M.; Wollmann, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 8279–8281.
31. *Purification of Laboratory Chemicals*; 3rd ed. Perrin, D. D., Armarego, W. L., Eds.; Pergamon: New York, 1988.
32. Bissing, D. E.; Matuszak, C. A.; McEwen, W. E. *J. Am. Chem. Soc.* **1964**, *86*, 3824–3828.
33. Kuriyama, M.; Nagai, K.; Yamada, K.; Miwa, Y.; Taga, T.; Tomioka, K. *J. Am. Chem. Soc.* **2002**, *124*, 8932–8939.
34. Adger, B. M.; Barkley, J. V.; Bergeron, S.; Cappi, M. W.; Flowerdew, B. E.; Jackson, M. P.; McCague, R.; Nugent, T. C.; Roberts, S. M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3501–3508.